DECOMPOSITION OF DITHIOBIS(THIOFORMATES) WITH *p*-CHLOROBENZENETHIOL

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(Received March 6th, 1972, accepted with revisions April 13th, 1972)

ABSTRACT

A simple and fast procedure is described for the decomposition of dithiobis(thioformates) (ROCSSCOR] by reaction with two equivalents of *p*-chlorobenzenethiol in pyridine for 10 min at 25° The procedure is effective even with derivatized starch, which is insoluble under the reaction conditions Use of less than two equivalents of *p*-chlorobenzenethiol gives the intermediate, mixed disulfide Other functional groups that react with this reagent are ROCSSSSCOR, ROCSOMe, ROCSCOR, ROCSP(OMe)$_2$, and ROCSC$_6$H$_4$(NO$_2$)$_2$ However, the functional groups ROCOR, ROCSCH$_2$Ar, ROCSMe, ROCSR, RSCSR, ROCNEt$_2$, ROCOR, and ROSO$_2$C$_6$H$_4$Me do not react (R = carbohydrate moiety)

INTRODUCTION

Dithiobis(thioformate) groups, formed by the oxidative coupling of xanthates, are useful as intermediates to introduce various functional groups into carbohydrates Nucleophilic attack by amines, alcohols, and phenols at the thiocarbonyl carbon atom gives thiocarbamoyl[1,2], alkyloxythiocarbonyl[3], and aryloxythiocarbonyl [3]derivatives, respectively Treatment of certain sugar dithiobis(thioformates) with tertiary amines affords thionocarbonate[4,5] and dithiocarbonate[6] derivatives Frequently, the reaction mixtures contain unreacted sugar dithiobis(thioformate), which is difficult to separate from the desired product Attempts to decompose the dithiobis(thioformate) selectively with base in the presence of the various products have been only partially

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successful We now find that such selective decomposition is readily accomplished on treatment with *p*-chlorobenzenethiol (**21**) In a preliminary communication, S J Brois *et al* [7] described the decomposition of sulfenyl thiocarbonates with thiols to give mixed disulfides

$$RSS\overset{O}{\overset{\|}{C}}OR' + R'SH \longrightarrow RSSR' + COS + R'OH$$

RESULTS AND DISCUSSION

When pyridine solutions of the dithiobis(thioformate) derivatives of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose, 1,2-*O*-isopropylidene-α-D-glucofuranose, 1,2 - 3,4-di-*O*-isopropylidene-α-D-galactopyranose (**22**), methyl 2,3,4-tri-*O*-methyl-α-D-glucopyranoside, and methyl 4,6-*O*-benzylidene-α-D-glucopyranoside were treated with two equivalents of **21**, the dithiobis(thioformate) group immediately decomposed and released the parent sugar alcohol quantitatively Even starch dithiobis(thioformates), which are insoluble in pyridine, readily decomposed when treated with **21**

The decomposition probably occurs by the following mechanism

$$ROC\overset{S}{\overset{\|}{S}}SC\overset{S}{\overset{\|}{O}}R + HSC_6H_4Cl \longrightarrow ROC\overset{S}{\overset{\|}{S}}H + ROC\overset{S}{\overset{\|}{S}}SC_6H_4Cl \quad (1)$$

$$ROC\overset{S}{\overset{\|}{S}}SC_6H_4Cl + HSC_6H_4Cl \longrightarrow ROC\overset{S}{\overset{\|}{S}}H + ClC_6H_4SSC_6H_4Cl \quad (2)$$

$$ROC\overset{S}{\overset{\|}{S}}H \longrightarrow ROH + CS_2 \quad (3)$$

This mechanism is supported by the following observations made for the decomposition of bis(1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose) 6,6'-[dithiobis(thioformate)] (**1**)

(*1*) Carbon disulfide is produced, in amounts depending on the quantity of **21** used, up to a maximum of about 1 6 moles of carbon disulfide per mole of **1**

Moles of *p*-chlorobenzenethiol	0 5	1	2	3
Moles of carbon disulfide	0 48	0 96	1 6	1 6

When known amounts of carbon disulfide were added to a solution of pyridine and **21**, recoveries were 80–85%

(*2*) Upon addition of one equivalent of **21**, t l c of the mixture showed a new component that was isolated and identified as the intermediate $ROC\overset{S}{\overset{\|}{S}}SC_6H_4Cl$, namely, 1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose 6-[S,*S*-(*p*-chlorophenyl)trithioperoxycarbonate] (**2**) Addition of **21** in pyridine to **2** gave the expected sugar alcohol The structure of **2** was formulated on the basis of elemental analysis, i r., and n m r data Treatment of a dilute solution of **2** with alkali gave, according to the u v spectrum, a xanthate that decomposed upon acidification. The structure was

confirmed by the independent synthesis of **2** by a disulfide exchange-reaction[8] between **1** and bis(*p*-chlorophenyl) disulfide

$$ROCSSCOR + ClC_6H_4SSC_6H_4Cl \longrightarrow ROCSSC_6H_4Cl$$

Compounds having different functional groups were treated with **21** to test the selectivity of the reagent The results are summarized in Table I References are given in the table for the synthesis of all compounds mentioned, except for 6-*O*-[2,4-dinitro-

TABLE I

MAJOR COMPONENTS OF THE REACTION OF *p*-CHLOROBENZENETHIOL WITH VARIOUS SUGAR DERIVATIVES[a]

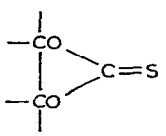
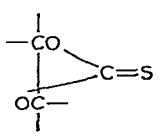
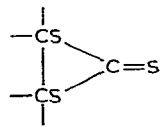
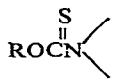
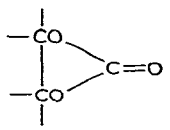
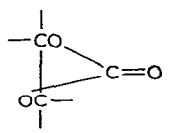
Starting compound	*Structure*	*Reaction component*	*Reference*
3	$ROCSSSSCOR$	ROH	9
4	$ROCSOMe$		10
5	$ROCSCOR$	$ROCSC_6H_4Cl + ROH$	11
6	$ROCSP(OMe)_2$		11
7	$ROCSC_6H_3(NO_2)_2$		
8		No change	4
9	$ROCOC_6H_5$	No change	3
10		No change	12
11	$ROCOR$	No change	13
12	$ROCSCH_2C_6H_5$	No change	
13	$ROCSMe$	No change	14
14	$ROCSR$	No change	9

TABLE I (*Continued*)

Starting compound	*Structure*	*Reaction component*	*Reference*
15		No change	15
16		No change	
17		No change	4
18		No change	12
19	$ROSO_2C_6H_4Me$	No change	

[a]Key to compounds in Table I **3**, Bis(1,2 3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-D-galactopyranose) tetrasulfide **4**, 1,2 3,4-Di-*O*-isopropylidene-6-*O*-[methoxythio(thiocarbonyl)]-α-D-galactopyranose, **5**, Bis(1,2 3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-D-galactopyranose) monosulfide, **6**, 1,2 3,4-Di-*O*-isopropylidene-α-D-galactopyranose-6-*O*-dithiocarbonate anhydrosulfide with *O,O'*-dimethyl phosphorothioate, **7**, 6-*O*-[2,4-Dinitrobenzenethio(thiocarbonyl)]-1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose, **8**, 1,2-*O*-Isopropylidene-α-D-glucofuranose 5,6-thionocarbonate, **9**, 1,2 5,6-Di-*O*-isopropylidene-3-*O*-phenoxythiocarbonyl-α-D-glucofuranose, **10**, Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-thionocarbonate, **11**, Bis(1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose) thionocarbonate, **12**, 3-O-[Benzylthio(thiocarbonyl)]-1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose, **13**, 1,2 5,6-Di-*O*-isopropylidene-3-*O*-[methylthio(thiocarbonyl)]-α-D-glucofuranose, **14**, Bis(6-deoxy-1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl) 6-*O*,6'-*S*-dithiocarbonate, **15**, 1,2-*O*-Isopropylidene-5,6-dithio-β-L-idofuranose 5,6-trithiocarbonate, **16**, 3-*O*-Diethylthiocarbamoyl-1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose, **17**, 1,2-*O*-Isopropylidene-α-D-glucofuranose 5,6-carbonate, **18**, Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-carbonate, **19**, Methyl 6-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside

benzenethio(thiocarbonyl)]-1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose (**7**) and 3-*O*-[benzylthio(thiocarbonyl)]-1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose (**12**), the syntheses of which are described in the Experimental

The structure of 1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose 6-[*S*-(*p*-chlorophenyl)dithiocarbonate] (**20**), which was obtained from the decomposition of **5**, **6**, and **7**, was formulated from elemental analysis, and I R, U V, and N M R-spectral data Treatment of **20** with alkali did not produce a xanthate (U V)

EXPERIMENTAL

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 from samples as Nujol mulls or films, u v spectra, with a Perkin–Elmer Model 202 spectrophotometer, and n m r spectra, with a Varian HA-100 spectrometer with tetramethylsilane as the internal reference standard ($\tau = 10.00$). For t.l c., Silica Gel G served 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 All other reagents were of good grade and were used without further purification The susceptibility of a sample toward *p*-chlorobenzenethiol (**21**) was tested by reaction of 0 1 mmole of sample with 0 2 mmole of **21** for 10 min at 25°

Determination of carbon disulfide — In a sidearm test-tube, bis(1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose) 6,6′-[dithiobis(thioformate]) (**1**) (67 mg) was dissolved in pyridine (1 ml) containing **21** (30 mg) The mixture was flushed with air, and the gases were washed with sulfuric acid (2 5M) to remove pyridine The carbon disulfide was collected in ethanol (1 liter) containing 0 4% of diethylamine The yield of carbon disulfide was 82 5%, based on the assumption that each mole of **1** produces two moles of carbon disulfide The calculation was based on λ_{max} 290 nm (ε 13,400 in ethanol containing 0 4% of diethylamine) When known amounts of carbon disulfide were added to solutions of **21** in pyridine that were then flushed with air, recoveries ranged between 80 and 85% In other experiments, the amount of **1** added was kept constant at 67 mg, but the amount of **21** was varied Addition of 45 mg gave 80% of the expected carbon disulfide, whereas addition of 15 mg and 7 5 mg gave 48% and 24% respectively

Decomposition of **1** *with* **21** — (*a*) Compound **1** (67 mg) was dissolved in pyridine (1 ml) that contained **21** (30 mg) T l c showed the presence of a single sugar component, corresponding (t l c and i r) to 1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose (**22**)

(*b*) Compound **1** (670 mg) was dissolved in a solution of **21** (70 mg) in pyridine (1 ml) T l c showed the presence of three sugar components, identified as **22**, **1**, and 1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose 6-[*S*,*S*-(*p*-chlorophenyl)trithio-peroxycarbonate (**2**) Compound **2** was purified by preparative t l c to yield 100 mg of syrup, λ_{max}^{EtOH} 250 nm (ε 17,700) together with a narrow shoulder centered about 290 nm (ε 5,470), $[\alpha]_D^{23}$ −140° (*c* 2, acetone), the i r spectrum showed characteristic absorption at 1010 and 1250 cm^{-1} for –OC(S)S–, 820 and 1500 cm^{-1} for a 1,4-substituted benzene ring, and 742 cm^{-1} for C–Cl The n m r spectrum showed a multiplet that resembled two doublets centered at τ 2 6 and corresponded to four protons of the disubstituted aromatic ring

Anal Calc for $C_{19}H_{23}ClO_6S_3$ C, 47 64, H, 4 88; Cl, 7 40, S, 20 08 Found: C, 47 58, H, 5 07, Cl, 7 44, S, 19 82

Compound **2** was independently synthesized by a disulfide exchange-reaction between **1** and bis(*p*-chlorophenyl) disulfide[16] Bis(*p*-chlorophenyl) disulfide (2 88 g)

was added to a solution of **1** (670 mg) in pyridine (10 ml) After being kept for 1 h at 25°, excess solvent was evaporated, and the mixture was extracted with hexane T l c of the extract showed mainly one component, which was purified by adsorption onto silicic acid and elution with *n*-hexane followed by *n*-hexane–chloroform (1:3 *v/v*) to yield 704 mg of **2**, characterized by elemental analysis, u v , and i r spectra

When a dilute solution of **2** (4-5 mg/100 ml ethanol) was treated with sodium hydroxide (5M, 0 1 ml), its u v spectrum showed a strong absorption maximum at 304 nm (ROC(S)S–) that immediately disappeared upon acidification with dilute hydrochloric acid

Addition of **21** (50 mg) to **2** (100 mg) in pyridine (1 ml) gave the starting sugar alcohol (t l c and i r.)

6-O-[2,4-Dinitrobenzenthio(thiocarbonyl)]-1,2 3,4-di-O-isopropylidene-α-D-galactopyranose (**7**) — A solution of **22** (5 g) in methyl sulfoxide (5 ml) was treated with carbon disulfide (5 ml) The mixture was cooled in an ice bath, treated with sodium hydroxide (5M, 5 ml), and kept for 10 min at 5° 1-Chloro-2,4-dinitrobenzene (3 5 g) was added with stirring The mixture immediately turned dark and product **7** crystallized out of the mixture during about 10 min The crystals were filtered, washed with water, and dissolved in ether Upon partial evaporation of the solvent, the product recrystallized from the solution to yield 3 0 g, m p 123–125°, $[\alpha]_D^{23}$ +0 02° (*c* 4, acetone), λ_{max}^{EtOH} 270 nm (ε 12,900)

Anal Calc for $C_{19}H_{22}N_2O_{10}S_2$ C, 45 23, H, 4 39, N, 5 57, S, 12 78 Found C, 45 00, H, 4 44; N, 5 48, S, 12 53

T l c of the mother liquor showed several spots, the major one having the same mobility as **7** The liquor was purified by desorption from silicic acid with hexane and hexane–chloroform (1 3 *v/v*) as eluents

A solution of **7** (500 mg) in pyridine (1 ml) was treated with **21** (150 mg) The mixture turned dark red immediately and t l c showed mainly two components, the one having the lower R_F value corresponding to **22** The other (150 mg) was isolated by preparative t l c and was shown to be 1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose 6-[*S*-(*p*-chlorophenyl)dithiocarbonate] (**20**), initially obtained as a colorless syrup but which crystallized on being kept, m p 83–85°, $[\alpha]^{23}$ −61 5° (*c* 1, acetone), λ_{max}^{EtOH} 288 nm (ε 11,200), n m r multiplet centered at τ 2 6 (four protons of the disubstituted aromatic ring)

Anal Calc for $C_{19}H_{23}ClO_6S_2$ C, 51 05, H, 5 18, Cl, 7 93; S, 14 34 Found C, 51.15, H, 5 46, Cl 8,10; S, 14 04,

Treating an alcoholic solution of the ester with alkali did not produce xanthate (u v.) under the conditions used for **2** Consequently, alkali treatment could be used to differentiate between **20** and **2** In another experiment, **7** was treated in pyridine with **21** Carbon disulfide was detected by the procedure already described

3-O-[Benzylthio(thiocarbonyl)]-1,2 5,6-di-O-isopropylidene-α-D-glucofuranose (**12**) — To a solution of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose (5 g) in methyl sulfoxide (5 ml), carbon disulfide (5 ml), and sodium hydroxide (5M, 5 ml) were added The xanthate solution thus formed was kept for 10 min at 5°, treated with

α-bromotoluene (2 ml), and kept for an additional 10 min When the mixture was poured into ice–water (500 ml), a thin syrup precipitated, which was collected and analyzed as **12** (3 7 g) Traces of α-bromotoluene were removed by preparative t l c , λ_{max}^{EtOH} 285 nm (ε 11,900), $[\alpha]_D^{23}$ −28° (*c* 1.0, acetone)

Anal Calc for $C_{20}H_{26}O_6S_2$ C, 56 33, H, 6 14, S, 15 03. Found C, 56 02, H, 6 23, S, 14 80

*Decomposition of 1,2 3,4-di-*O*-isopropylidene-α-*D*-galactopyranose 6-*O*-dithiocarbonate anhydrosulfide with* O,O'*-dimethyl phosphorothioate* (**6**) — To a solution of **21** (150 mg) in pyridine (5 ml), **6** (220 mg) was added T l c showed one major component, which was isolated by preparative t l c and identified as **20** by u v , i r , and sulfur analysis The yield was 165 mg A minor component (10 mg) was isolated and shown (t l c and i r) to be **22**

*Decomposition of bis(1,2 3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-*D*-galactopyranose) monosulfide* (**5**) — When **5** (250 mg) was treated in pyridine solution (4 ml) containing **21** (120 mg), **20** (140 mg) was obtained, together with **22** (90 mg)

ACKNOWLEDGMENTS

We are grateful to Mrs Clara McGrew and Mrs Bonita Heaton for the microanalysis and to Curtis Glass and Larry Tjarks for n m r spectral data K L Loening of Chemical Abstracts Service named compounds **2** and **20**

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