# REACTION OF TRIMETHYL PHOSPHITE WITH BIS(1,2:3,4-DI-*O*-ISOPROPYLIDENE-α-D-GALACTOPYRANOSE) 6,6′-[DITHIOBIS(THIOFORMATE)]

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## ABSTRACT

1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose 6-*O*-dithiocarbonate anhydrosulfide with *O*,*O*′-dimethyl phosphorothioate (**3**) was prepared by reaction of bis(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose) 6,6′-[dithiobis(thioformate)] (**2**) with trimethyl phosphite (**1**). Compound **3** decomposes on standing to give D-galactose. Upon treatment with alkali, **3** forms the corresponding xanthate salt; with acid **3** loses the phosphonate and the acetal groups; with chlorine followed by sodium iodide it forms the corresponding chlorothioformate derivative; with pyridine it gives bis(1,2:3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-D-galactopyranose) monosulfide (**6**); and with hydrogen peroxide it initiates the polymerization of acrylamide to from a high-molecular-weight product.

## INTRODUCTION

Trimethyl phosphite (**1**) has been used for the desulfurization of cyclic thionocarbonate to form olefins[1]. Recently the reactions of some xanthate esters, namely, *O*,*S*-dimethyl dithiocarbonate, *O*-ethyl,*S*-methyl dithiocarbonate, and *O*,*S*-diethyl dithiocarbonate with **1** or with triethyl phosphite were investigated[2]. The following took place concurrently: (a) A transesterification reaction to form mixed xanthates, (b) the Michaelis–Arbuzov reaction[3] to form alkyl phosphonates and dithiolcarbonates, and (c) a phosphite-catalyzed rearrangement–transesterification reaction to form dithiolcarbonates.

In this report the reaction of bis(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose) 6,6′-[dithiobis(thioformate)] (**2**) with **1** is described, together with some properties of the major product thereof.

## RESULTS AND DISCUSSION

Treatment of an acetone solution of **2** with **1** gave a crystalline product that was isolated in 46% yield and characterized as 1,2:3,4-di-*O*-isopropylidene-α-D-galacto-

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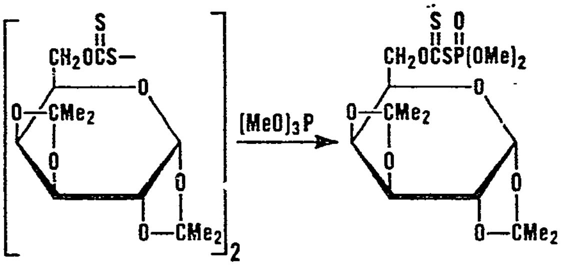
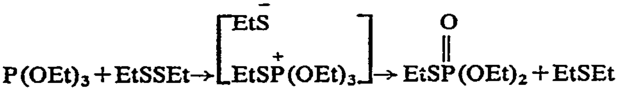


**2** **3**

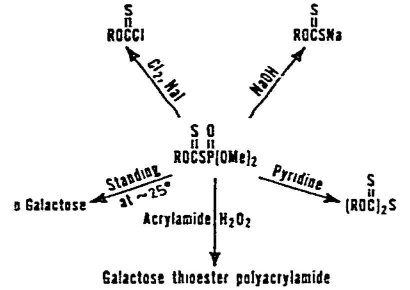
Scheme 1

pyranose 6-*O*-dithiocarbonate anhydrosulfide with *O*,*O*′-dimethyl phosphorothioate (**3**). The structure was formulated on the following basis: Elemental analysis gave the correct empirical formula of $C_{15}H_{25}O_9PS_2$; n.m.r. data which exhibited besides the expected pattern for the isopropylidene groups and H-1, two singlets at τ 6.10 and 6.25 each representing three protons (OMe); the i.r. spectrum showed characteristic absorptions at 1037 and 1250 $cm^{-1}$ for $\text{-O}\overset{S}{\overset{\|}{C}}\text{S-}$ and absorption at 1275 $cm^{-1}$ for $\text{-}\overset{O}{\overset{\|}{P}}\text{-}$. The spectrum of **2** exhibited the maxima at 1037 and 1250 $cm^{-1}$ but none at 1275 $cm^{-1}$. The reaction of **1** with **2** is analogous to the reported reaction of triethyl phosphite with diethyl disulfide and for which a common mechanism with an Arbuzov type of reaction has been suggested[4].



$$P(OEt)_3 + EtSSEt \rightarrow \left[\begin{matrix}\overset{-}{EtS} \\ Et\overset{+}{S}P(OEt)_3\end{matrix}\right] \rightarrow EtS\overset{O}{\overset{\|}{P}}(OEt)_2 + EtSEt$$

*Reactions of* **3**. — Several reactions of **3** are summarized in Scheme 2.



R = 6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose-6-yl

Scheme 2

*Shelf life.* — Whereas 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**4**) was stable on standing, extensive hydrolysis occurred when **3** was kept under the same conditions. Thus, at room temperature in an open flask, **3** lost 29% of its weight in 96 days. The residue after purification was characterized as D-galactose by i.r. spectroscopy and by its conversion into galactaric acid by oxidation with concentrated nitric acid.

*Alkali stability.* — Xanthates are fairly stable on treatment with alkali under mild conditions. Thus, no change in u.v. absorption was observed when 1,2:3,4-di-*O*-isopropylidene-6-*O*-[(methylthio)thiocarbonyl]-α-D-galactopyranose was treated with sodium hydroxide. When **3** was treated under the same conditions, however, there was an immediate shift in the absorption maximum from 270 to 304 nm, indicative of the decomposition of **3** to the sodium xanthate salt. Upon acidification, the peak at 304 nm disappeared with evolution of carbon disulfide, as expected for xanthates. T.l.c. of the acidified mixture showed one component, corresponding to **4**.

$$\mathrm{RO\overset{S}{\overset{\|}{C}}S\overset{O}{\overset{\|}{P}}(OMe)_2 \xrightarrow{NaOH} RO\overset{S}{\overset{\|}{C}}SNa \xrightarrow{H^+} ROH+CS_2}$$

Quantitative measurement of the carbon disulfide evolved gave 0.143 meq., which indicates that the decomposition of **3** in alkali is more complex than depicted above.

*Acid stability.* — Compound **3** was labile toward acid under mild conditions. Thus, when a methanol–hydrochloric acid (0.1M) solution of **3** was kept at room temperature for 3 days or refluxed for 2 h, the absorption maximum at 270 nm completely disappeared. The detection of acetone in the reaction flasks showed that hydrolysis of isopropylidene groups in **3** also took place.

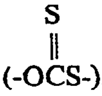
*With chlorine and sodium iodide.* — The reaction of chlorine with some thiocarbonyl sugar derivatives has been previously reported[5]. Bis(*O*-thiocarbonyl) disulfide $(\mathrm{RO\overset{S}{\overset{\|}{C}}S\text{-}})_2$ and (methylthio)thiocarbonyl $(\mathrm{RO\overset{S}{\overset{\|}{C}}SMe})$ derivatives were shown to add two chlorine atoms to each carbon–sulfur double bond to yield the corresponding chloromethylsulfenyl chlorides. Upon reaction of bis[6-*O*-chloromethylsulfenyl chloride)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose) disulfide with sodium iodide, the corresponding chlorothioformate (**5**) was obtained in high yield[6]. Reaction of **3** with chlorine followed by treatment with sodium iodide also gave **5**, but in low yield.

*With pyridine.* — In a preliminary study, **2** was treated with **1** in the presence of pyridine. T.l.c. showed two components present, which were isolated and identified as the correponding (methylthio)thiocarbonyl derivative and bis(1,2:3,4-di-*O*-isopropylidene 6-*O*-thiocarbonyl-D-galactopyranose) monosulfide (**6**). The (methylthio)thiocarbonyl product was previously prepared by reaction of the xanthate with iodomethane[7] and **6** had previously been prepared by reaction of **5** with pyridine[8]. Whereas **2** underwent no change on treatment with pyridine in the absence of **1**, compound **3** decomposed to give a single component (t.l.c.) identified as **6**. These results suggest that formation of **6** from **2** in the presence of **1** proceeds via **3**.

*With acrylamide–hydrogen peroxide.* — A high-molecular-weight polymer was obtained upon treatment of an acetone solution of **3** with acrylamide in the presence of hydrogen peroxide. The product was precipitated with ethanol to give a white, fibrous material having an absorption maximum at 280–285 nm, where compounds of the type  $\mathrm{RO\overset{\overset{S}{\|}}{C}SR}$ absorb. A similar product was obtained by treatment of the xanthate salt of **4** or the corresponding hydroxythio(thiocarbonyl) derivative ( $\mathrm{RO\overset{\overset{S}{\|}}{C}SOH}$) (**7**) with acrylamide–hydrogen peroxide mixture[9]. It has been suggested[9] that **7** is intermediate in the initiation process of the polymerization of acrylamide with the xanthate salt of **4**, since the salt is easily converted into **7** by hydrogen peroxide treatment. It is possible that **7** is also intermediate in the polymerization of acrylamide when **3** is the initiator, since treatment of **3** with peroxide gave a component with the same $R_F$ as **7**.

## 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 or 621 spectrophotometer having silver chloride optics as Nujol mulls or films, and the u.v. spectra were recorded with a Perkin–Elmer Model 202 spectrophotometer. N.m.r. spectra were recorded by a Varian HA-100 spectrometer with tetramethylsilane as internal reference standard ($\tau = 10.00$). 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. Trimethyl phosphite (**1**), obtained from Eastman Kodak, Rochester, N.Y., was distilled and the b.p. 110–112° fraction was used. All other reagents were good grade and used without further purification. Bis(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose) 6,6′-[dithiobis(thioformate)] **2** was prepared as described previously[10].

*1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose 6-*O*-dithiocarbonate anhydrosulfide with *O,O*-dimethyl phosphorothioate* (**3**). — A solution of **2** (4.3 g) in acetone (15 ml) was cooled to 5° and **1** (1 ml) was added dropwise with stirring. The mixture was kept for 5 min at 5° and for another 15 min at 25°, and then concentrated to a thin syrup, whereupon *n*-hexane (10 ml) was added. After evaporation of excess solvent, *n*-hexane (10 ml) was again added. Upon scratching the surface of the reaction flask, **3** crystallized out. The crystals were washed three times with 10-ml portions of *n*-hexane and dried to yield 2.6 g (46%). The product was recrystallized from *n*-hexane, m.p. 105-106°, $[\alpha]_D$ $-55°$ ($c$ 1, $CHCl_3$); $\lambda_{max}^{EtOH}$ 220 ($\varepsilon$ 7000) and 270 nm (10,000); i.r. data 1037 and 1250 $cm^{-1}$ ( $\mathrm{-O\overset{\overset{S}{\|}}{C}S-}$), and 1275 $cm^{-1}$ –P=O); n.m.r. data: two 3-proton singlets at $\tau$ 6.10 and 6.25.

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*The mention of firm names or trade products does not imply that they are endorsed or recommended by the Department of Agriculture over other firms or similar products not mentioned.

*Anal.* Calc. for $C_{15}H_{25}O_9PS_2$: C, 40.5; H, 5.6; P, 7.3; S, 14.5. Found: C, 40.6; H, 5.8; P, 7.3; S, 15.0.

*Shelf life.* — A tared beaker containing crystalline **3** (124 mg) was kept at 25° and weighed periodically. After 96 days, the weight of compound was 88 mg (loss of 29%). The solid, after washing with acetone was identified as D-galactose by i.r. and by oxidation to galactaric acid according to a standard procedure[11].

*Alkali stability.* — A solution of **3** (13.6 mg) in ethanol (100 ml) was treated with 5M sodium hydroxide (1 ml). An immediate shift in the u.v. spectra to $\lambda_{max}$ 303 nm was observed, indicating that **3** decomposed to the corresponding xanthate. On acidification, the peak at 303 nm disappeared. In another experiment, **3** (29.7 mg) was placed in a test tube equipped with a side-arm and dissolved in ethanol (1 ml). After addition of 5M sodium hydroxide (0.1 ml), the mixture was kept for 15 min and then acidified. Carbon disulfide was collected and quantitatively determined[12] to be 0.144 meq.

*Acid stability.* — A solution of **3** (7 mg) in methanol–hydrochloric acid (0.1M) was refluxed and samples were withdrawn periodically. The rate of hydrolysis was followed by u.v. spectroscopy (270 nm).

| Time (min): | 20 | 45 | 75 | 120 |
|---|---|---|---|---|
| Hydrolysis (%): | 45 | 70 | 86 | 100 |

Complete hydrolysis also occurred when a solution of **3** (7 mg) in methanol hydrochloric acid (0.1M) was kept for 3 days at 25°. Acetone was detected in both hydrolyzates by a standard procedure[13], indicating the hydrolysis of acetal groups.

*Reaction with chlorine and sodium iodide.* — A solution of **3** (265 mg) in diethyl ether (15 ml) was cooled to 5° and treated with chlorine until a faint yellow color persisted. After standing for 10 min, the mixture was evaporated in the hood to a thin syrup, which was dissolved in acetone (5 ml) and treated dropwise with a solution of sodium iodide (200 mg) in acetone (5 ml). The solution, which turned dark brown immediately owing to release of iodine, was kept for 10 min. Upon addition of *n*-hexane (20 ml) a dark-green solid precipitated that was removed by filtration. The solvent was evaporated, and the syrup was dissolved in a small volume of acetone to remove free sulfur. T.l.c. showed one major component ($R_F$ 0.6), which was isolated and identified by m.p. (82–84°) and by u.v. and i.r. spectra as 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 6-chlorothioformate (**5**), the yield 50 mg.

*Reaction with pyridine.* — To a solution of **2** (100 mg) in ether (3 ml), pyridine (0.2 ml) and **1** (0.2 ml) were added. After 15 min, the mixture showed two major spots by t.l.c. These were isolated and identified by their $R_F$, u.v., and i.r. spectra as the known corresponding methylthio(thiocarbonyl) and the known bis(1,2:3,4-di-*O*-isopropylidene 6-*O*-thiocarbonyl-D-galactopyranose) monosulfide (**6**). The ratio of methylthio(thiocarbonyl) product to monosulfide product formed was about 1:2. When **3** (100 mg) in ether (3 ml) was treated with pyridine (0.2 ml) and was kept as above, t.l.c. showed one major component identified as **6**.

*Polymerization of acrylamide.* — A solution of **3** (50 mg) in acetone (1 ml) was added to a preheated (55°) mixture containing acrylamide (10 g) and hydrogen peroxide (30%, 1 ml) in 50 ml of water. The mixture turned viscous after 10 min and the polymer was precipitated into ethanol in a Waring Blendor. The solid was collected and retreated in a Waring Blendor with ethanol, filtered, and dried to yield 7.5 g of product containing about 0.1% sulfur. The u.v. spectrum showed a maximum about 280 nm indicating the presence of an ester linkage of the type $\mathrm{RO}\overset{\overset{\mathrm{S}}{\|}}{\mathrm{C}}\mathrm{SR}$. The product has intrinsic viscosity $[\eta]$ of 2.87 in M sodium nitrate at 30° and molecular weight average $\bar{M}_w$ 758,000 calculated according to the viscometric relation[14]

$$[\eta] = 3.73 \times 10^{-4}\, \bar{M}_w 0.66.$$

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