cenetetrone-3-sulfonate (XIX). This oxidation can be considered, in conjunction with the oxidation of XIV to XV, to be a further instance of periodate oxidation without carbon–carbon bond cleavage.

Experimental

Substrates.—5,5-Dimethyl-1,3-cyclohexanedione, m.p. 147.5–149° (accepted 148–149°), and 2,4-pentanedione were obtained commercially. The sample of 1,3-cyclohexanedione, m.p. 105–105.5° (accepted 105–106°), was provided by Professor M. S. Newman of this University and a sample of 1,3-cyclopentanedione, m.p. 149–150° after sublimation (accepted 151.5–152.5°[23]), was kindly provided by Dr. R. G. Wilkinson of the Lederle Laboratories Division of the American Cyanamid Co.

The remaining diketones were prepared: 5-methyl-1,3-cyclohexanedione,[24] m.p. 128–129° (reported[24] 128–129°); 1,3-indandione,[25] m.p. 129–130° (reported[25] 130–132°); 2-methyl-1,3-cyclohexanedione, m.p. 208–209° (reported[26] 204°); 2-ethyl-1,3-cyclohexanedione,[26] m.p. 178–179° (reported[26] 178°); 2-benzyl-1,3-cyclohexanedione,[27] m.p. 188–189° (reported[27] 184–185°); 1-phenyl-1,3-butanedione,[28] m.p. 57–58° (reported 57–58°; 61°); 1,3-diphenyl-1,3-propanedione,[28] m.p. 77–78° (reported 77–78°); 2,3-dihydroxy-2-cyclohexenone,[20] m.p. 112–114° (reported[20] 114°); and 1,2,3-cyclohexanetrione,[20] m.p. 103–104° (reported[20] 104–105°).

Effect of Hydrogen Ion Concentration (Fig. 1).—A series of phosphate buffers was prepared which gave final reaction mixture pH values of 0.90, 3.30, 5.30, 6.02, 7.03, 8.00, 9.40, 10.88 and 12.88.[29] Potassium salts were used above pH 7 and sodium salts below. The relative rates of oxidation were obtained by measuring oxidant consumption (arsenite method[4,14]) in solutions 0.0310 M in oxidant (sodium metaperiodate), 0.0054 M in substrate (5,5-dimethyl-1,3-cyclohexanedione) and 0.50 M in buffer. Solutions were maintained at room temperature and reactions were performed simultaneously.

Relative Oxidation Rates.—Solutions of the diketones I–IV (unsubstituted on C-2) in water were prepared and combined with sodium metaperiodate solutions at 0° to yield reaction mixtures 0.0609 M in oxidant and 0.0075 M in substrate. The relative rates of oxidation were obtained (Fig. 2) by measurement of oxidant consumption (arsenite method[4,14]).

Weighed amounts of the diketones VII–IX (substituted on C-2) were added to a reaction mixture containing one part of lithium periodate solution (obtained by neutralizing a solution of periodic acid with lithium carbonate), one part of saturated lithium acetate and two parts of acetic acid at room temperature. Compound VII was not oxidized simultaneously with VIII and IX. The reaction mixtures were 0.0620 M in lithium periodate and 0.00566 M in substrate. Periodate consumption was measured by the arsenite method[4,14] (Fig. 3).

Kinetic Studies (Fig. 4).—A series of solutions of VII in water ranging from 4.70×10^{-3} M to 2.04×10^{-4} M were prepared by successive dilution of a solution 1.88×10^{-2} M in VII which had been titrated to pH 6.2 with sodium hydroxide. A solution of oxidant, 9.75×10^{-5} M, was prepared and buffered to pH 6.20 with phosphate (0.02 M). Equal volumes of these solutions were mixed and relative rates were obtained by measuring the oxidant consumption colorimetrically at 222.5 mμ.[17,19,30] All solutions had been allowed to equilibrate to a constant temperature (22.5°).

Relative Rate Studies.—Aqueous solutions of the three compounds I, XIV and XV, were prepared and combined with an equal volume of sodium metaperiodate solution giving reaction mixtures 5.875×10^{-4} M in substrate and 4.875×10^{-5} M in oxidant. The optical densities at 222.5 mμ[17,19,30] of these reactions were observed at the stated time intervals (Fig. 6).

Acknowledgment.—The authors wish to express their appreciation to Dr. G. J. Buist for advice on obtaining and interpreting the kinetic data and to Dr. R. A. Gibbons for many helpful suggestions.

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[23] J. H. Boothe, R. G. Wilkinson, S. Kushner and J. H. Williams, THIS JOURNAL, **75**, 1732 (1953).

[24] A. W. Crossley and Nora Renouf, *J. Chem. Soc.*, **107**, 602 (1915); Jean P. Blanchard and H. L. Goering, THIS JOURNAL, **73**, 5863 (1951).

[25] W. Wislicenus, *Ber.*, **20**, 593 (1887).

[26] H. Stetter and W. Dierichs, *Chem. Ber.*, **85**, 61 (1952).

[27] H. Stetter and W. Dierichs, *ibid.*, **85**, 1061 (1952).

[28] L. Claisen, *Ann.*, **291**, 52 (1896).

[29] Beckman Model G pH meter.

[30] Beckman ultraviolet spectrophotometer, model DU; 1-cm. quartz cell.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

An Anomalous Reaction of Methyl 3,4-*O*-Isopropylidene-β-D-arabinopyranoside 2-*O*-(*S*-Sodium Dithiocarbonate)

BY A. B. FOSTER[1] AND M. L. WOLFROM

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Reaction of methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside 2-*O*-(*S*-sodium dithiocarbonate) (III) in the presence of ethyl iodide, *n*-propyl bromide, isopropyl bromide or *t*-butyl chloride did not lead to the expected 2-*O*-(*S*-alkyl dithiocarbonate) esters. The product in each case was bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-thionocarbonate (V), the structure of which is proved.

In a previous paper[2] the preparation of *O*-(*S*-alkyl dithiocarbonate) ("xanthate") esters of certain carbohydrate derivatives by the general route I → II → III → IV was described. Thus the *S*-methyl and *S*-triphenylmethyl esters of methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside 2-*O*-(dithionate) (IV, R′ = CH_3– and $(C_6H_5)_3CH$–, respectively) were obtained by treatment of the intermediate *S*-sodium derivative III with methyl iodide and triphenylmethyl chloride, respectively. In seeking to extend this reaction, other alkyl halides such as ethyl iodide, *n*-propyl bromide, isopropyl bromide and *t*-butyl chloride were used. The expected products were not formed but in each case bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-thionocarbonate (V, m.p. 210–211°, $[\alpha]_D$ −254° in benzene) was isolated. The yield of V obtained with various alkyl halides was as follows: ethyl iodide, 58.4%, *n*-propyl bromide, 30.8%, isopropyl bromide, 69.1% and *t*-butyl chloride, 6%. This paper is concerned with the proof of structure of this unexpected product V.

Alkaline hydrolysis of V gave sirupy methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside (I) which was

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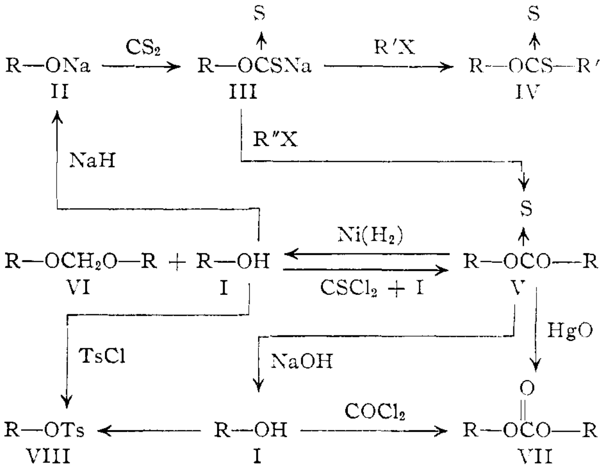
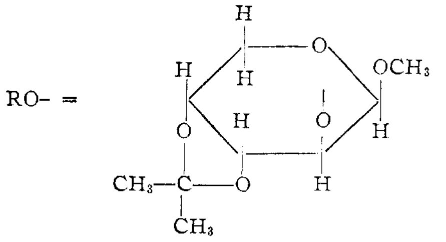
[1] Fellow of the Rockefeller Foundation, 1953–1954.

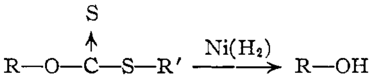
[2] M. L. Wolfrom and A. B. Foster, THIS JOURNAL, **78**, 1399 (1956).



R'X = $(C_6H_5)_3CCl$ or CH_3I
R''X = C_2H_5I, n-C_3H_7Br, $(CH_3)_2CHBr$ or t-C_4H_9Cl
Ts = p-CH_3—C_6H_4—SO_2—



characterized as the known crystalline 2-*p*-toluenesulfonate VIII. Reductive desulfurization of V with Raney nickel gave a mixture of products from which compound I was isolated and characterized as VIII. A second, crystalline product (m.p. 88–89°, $[\alpha]_D$ −159° in benzene) was also isolated and on the basis of analytical data it was identified as 2,2'-*O*-methylene bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) (VI). The reductive desulfurization of *O*-(*S*-methyl dithiocarbonate) esters of certain carbohydrate derivatives[2,3] appears to give predominantly the parent alcohol.



$$R{-}O{-}\overset{S\uparrow}{C}{-}S{-}R' \xrightarrow{Ni(H_2)} R{-}OH$$

The thionocarbonate likewise underwent scission to the parent alcohol but also gave some of the more normal product wherein the sulfur atom was cleaved and replaced directly with its equivalent of hydrogen.

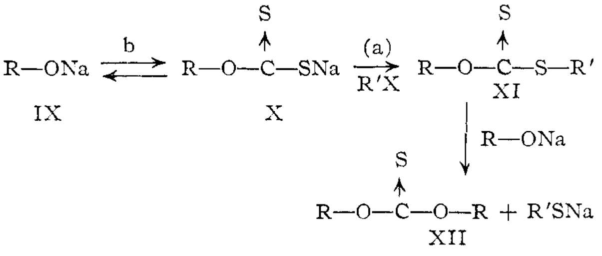
Reaction of methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside (I) with thiophosgene[4] in the presence of pyridine gave bis-(methyl-3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-thionocarbonate (V) which was identical with the product obtained in the anomalous dithiocarbonate reactions. Under similar conditions, the use of phosgene gave an analogous product, bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-carbonate (VII, m.p. 166–167°, $[\alpha]_D$ −267° in benzene). Treatment of the thionocarbonate V with mercuric oxide gave the carbonate VII.

Failure to isolate the *O*-(*S*-alkyl dithiocarbonate) esters of I with alkyl groups higher than methyl is surprising since similar derivatives have been described in the case of α- and β-cholestanol,[5] cholesterol[5,6] and 2,2,6,6-tetramethylcyclohexanol.[7]

The comparable specific optical rotations in benzene of V (−254°) and VII (−267°) are of interest since each is considerably higher than that of the parent alcohol, methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside (I, −195° in benzene). The product VI, isolated after the reductive desulfurization of V and which has no thiono or ketone group, has a specific optical rotation (−159° in benzene) less than in I, as might be expected. (The specific rotation of methyl 3,4-*O*-isopropylidene-2-*O*-methyl-β-L-arabinopyranoside[8] in chloroform is +199°). From the evidence available it is not possible to indicate which of the contributions of the individual carbon atoms of the parent alcohol I, to the total optical activity of the molecules is influenced by the presence of the thiono group in V and the keto group in VII.

Although the mechanism of the apparently anomalous reactions recorded in this paper cannot be precisely formulated at present, some pertinent observations and suggestions may be made. Freudenberg and Wolf[9] found that although 2,3,5,6-di-*O*-isopropylidene-D-mannose gave a crystalline 1-*O*-(*S*-methyl dithiocarbonate), long standing of the reaction mixture gave a second product, bis-(2,3,5,6-di-*O*-isopropylidene-D-mannose) 1-thionocarbonate. The same product could be obtained in better yield by the action of the sodio derivative of the parent alcohol on the *O*-(*S*-methyl dithiocarbonate) ester. No yields, conditions or specific rotations were given for the thionocarbonate and although the correct elemental analysis was found, no molecular weight or proof of structure was recorded. Furthermore, a dithiocarbonate group on carbon 1 represents an esterified hemiacetal hydroxyl whose reactivity is considerably different from that of a secondary hydroxyl function.

The reactions herein described may be explained on the assumption that certain equilibria are present. If the rate of reaction (a) in the preparation of the *O*-(*S*-methyl dithiocarbonate) ester (which follows the expected course) is more rapid than the rate of reaction of XI with RONa (IX) then IX will be removed before it can react to any extent with XI. With the higher alkyl halides



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(3) M. L. Wolfrom and M. A. El-Taraboulsi, *Abstracts Papers Am. Chem. Soc.*, **121**, 8P (1952).

(4) Compare A. Schönberg, L. v. Vargha and W. Paul, *Ann.*, **483**, 107 (1930).

(5) G. L. O'Connor and H. R. Nace, THIS JOURNAL, **74**, 5454 (1952).

(6) G. L. O'Connor and H. R. Nace, *ibid.*, **75**, 2118 (1953).

(7) P. V. Laakso, *Suomen Kemistilehti*, **13B**, 8 (1940); *C. A.*, **34**, 5059 (1940).

(8) J. Honeyman, *J. Chem. Soc.*, 990 (1946).

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

a much slower reaction (a) would permit the reaction of IX and XI. This is supported by the fact that a much longer reaction time was necessary, when the higher alkyl halides were used, in order to completely decompose the gelatinous dithiocarbonate salt intermediate X. The low yield of XII when *t*-butyl chloride was used also accords with this mechanism and may be explained by the tendency of the alkyl halide to undergo an elimination reaction rather than to form an ester capable of reacting with the sodio derivative. Produced, together with XII, on the above mechanism, would be the corresponding sodium mercaptide. It was noticeable that the insoluble material removed before the isolation of XII had a strong odor of mercaptan.

Experimental

Reaction of Methyl 3,4-*O*-Isopropylidene-β-D-arabinopyranoside 2-*O*-(*S*-Sodium Dithiocarbonate) (III) in the Presence of Certain Alkyl Halides.—A solution of 5.3 g. of methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside (I)[10] in 15 ml. of dry benzene was added to an excess of sodium hydride in 100 ml. of dry benzene and the solution was boiled under reflux for 5 hr. The cooled solution was decanted from the excess sodium hydride. Then 15 ml. of carbon disulfide was added and the mixture was boiled under reflux for 1 hr. Addition of the carbon disulfide generally caused the immediate precipitation of gelatinous methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside 2-*O*-(*S*-sodium dithiocarbonate) (III). After the addition of 5 ml. of ethyl iodide, refluxing was continued for 20 hr. The cooled mixture was filtered through carbon, concentrated to 5–10 ml. and diluted with 200 ml. of hexane. Rapid crystallization of bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-thionocarbonate (V) occurred. Recrystallization from the same solvent mixture afforded 3.43 g. (58.4%) of colorless needles, m.p.[11] 210–211°, $[\alpha]^{25}\mathrm{D}$ −254° (*c* 1.3, benzene).

Anal. Calcd. for $C_{18}H_{27}O_9S(OCH_3)$: C, 50.66; H, 6.67; S, 7.11; OCH_3, 13.78; mol. wt., 450. Found: C, 50.69; H, 6.66; S, 7.12; OCH_3, 13.74; mol. wt., 452, 458 (Rast in camphor).

The following yields of V were obtained when ethyl iodide in the preceding method was replaced by other alkyl halides: *n*-propyl bromide, 1.81 g. (30.8%), m.p. 198–205°; isopropyl bromide, 4.06 g. (69.1%), m.p. 207–209°; *t*-butyl chloride, 0.36 g. (6%), m.p. 207–209°. The melting point was raised in each case to 210–211° after one recrystallization from benzene–hexane.

Alkaline Hydrolysis of Bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-Thionocarbonate (V).—A solution of 1 g. of V in 20 ml. of benzene and 35 ml. of ethanol, to which had been added 2 ml. of 5 *N* sodium hydroxide, was boiled under reflux for 30 min. Thereafter the solution was diluted with 100 ml. of water and extracted several times with chloroform. The combined and dried (sodium sulfate) extracts were concentrated and the residue distilled. Methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside (I) was obtained as a colorless liquid, 0.37 g., b.p. 130–135° (bath temperature) (0.05 mm.), n^{28} 1.4600, $[\alpha]^{28}\mathrm{D}$ −194° (*c* 1.48, benzene). Overend and Stacey[10] quote b.p. 115° (bath temperature) (0.01 mm.), n^{17} 1.4617, $[\alpha]\mathrm{D}$ −197.6° in chloroform. Treatment of 0.2 g. of I with *p*-toluenesulfonyl chloride in pyridine afforded 0.23 g. of the known 2-(*p*-toluenesulfonate) which had m.p. 131–132° alone or in admixture with an authentic specimen, $[\alpha]^{25}\mathrm{D}$ −200° (*c* 2.5, benzene). Jones, Kent and Stacey[12] quote m.p. 134° for methyl 3,4-*O*-isopropylidene-2-*O*-*p*-toluenesulfonyl-β-D-arabinopyranoside but give no rotation. Honeyman[8] quotes m.p. 136° and $[\alpha]\mathrm{D}$ +181.3° in chloroform for methyl 3,4-*O*-isopropylidene 2-*O*-*p*-toluenesulfonyl-β-L-arabinopyranoside. The authors observed m.p. 131–132° and $[\alpha]^{25}\mathrm{D}$ +195° (*c* 1.13, benzene) for this derivative of L-arabinose.

Reductive Desulfurization of V.—Freshly prepared Raney nickel, from 50 g. of alloy, suspended in ethanol, was added to a solution of 3.2 g. of V in 50 ml. of benzene and 50 ml. of ethanol, and the mixture was boiled under reflux for 4 hr. The nickel was collected by filtration and was exhaustively extracted with methanol in a soxhlet apparatus. The extract was filtered, concentrated and the residue distilled. The first fraction distilled mainly at 130–135° (bath temperature) (0.05–0.1 mm.). Distillation was completed by elevation of the bath temperature to 165°. By this procedure, 0.76 g. of methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside (I) was obtained, n^{28} 1.4585, $[\alpha]^{25}\mathrm{D}$ −195° (*c* 1.25, benzene). *p*-Toluenesulfonylation of 0.15 g. of the above liquid gave 0.125 g. of the crystalline 2-*p*-toluenesulfonate, m.p. 131–132° alone and in admixture with authentic material. The second fraction comprised the residue which did not distil. It was dissolved in 5–8 ml. of benzene and the solution was diluted with 150 ml. of hexane, whereupon there separated 1.03 g. of colorless prisms of 2-*O*-methylene bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) (VI), m.p. 88–89°, $[\alpha]^{25}\mathrm{D}$ −159° (*c* 1.3, benzene).

Anal. Calcd. for $C_{19}H_{32}O_{10}$: C, 54.3; H, 7.6; mol. wt., 420. Found: C, 54.23; H, 7.80; mol. wt., 386 (Rast in camphor).

Reaction of Methyl 3,4-*O*-Isopropylidene-β-D-arabinopyranoside (I). (a) With Phosgene.—A solution of 0.8 g. of phosgene in 50 ml. of dry benzene was added to a solution of 2.0 g. of I in 15 ml. of dry pyridine. After 3 hr. the mixture was poured into ice and water and extracted several times with benzene. The combined extracts were washed once with water, dried (sodium sulfate) and concentrated to 20 ml. Addition of 200 ml. of hexane gave 1.6 g. of colorless fine needles of bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-carbonate (VII). After recrystallization from benzene–hexane the constants were m.p. 166–167°, $[\alpha]^{25}\mathrm{D}$ −267° (*c* 2.0, benzene).

Anal. Calcd. for $C_{18}H_{27}O_{10}(OCH_3)$: C, 52.52; H, 6.91; OCH_3, 14.31; mol. wt., 434. Found: C, 52.85; H, 7.15; OCH_3, 14.43; mol. wt., 448 (Rast in camphor).

(b) **With Thiophosgene.**[13]—By the same procedure as that described above for phosgene, 2 ml. of thiophosgene in 50 ml. of dry benzene was treated with 4 g. of I in 25 ml. of dry pyridine, and 0.7 g. of bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-thionocarbonate (V) was subsequently isolated. The product showed m.p. 210–211.5° and 210–211° in admixture with the substance obtained in the anomalous dithiocarbonate reaction described initially in the Experimental section.

Reaction of Bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-Thionocarbonate (V) with Mercuric Oxide.[4]—A solution of 0.61 g. of V in 30 ml. of benzene was boiled under reflux in the presence of 2 g. of yellow mercuric oxide, with continuous and vigorous stirring, over a period of 4 days with the mercuric oxide being frequently removed and replaced by a fresh amount until the orange color remained. Thereafter the mixture was filtered, the filtrate was concentrated to small volume and diluted with 200 ml. of hexane. Bis-(methyl 3,4-*O*-isopropylidene-β-D-arabinopyranoside) 2-carbonate (0.35 g., 59.5%) separated as colorless needles, m.p. 167–168° alone or in admixture with the product obtained from the reaction of I with phosgene.

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[10] W. G. Overend and M. Stacey, *J. Chem. Soc.*, 1235 (1949).

[11] All melting points are uncorrected.

[12] J. K. N. Jones, P. W. Kent and M. Stacey *J. Chem. Soc.*, 1341 (1947).

[13] This experiment was carried out by Mr. R. A. Plunkett of this Laboratory.