less needles, m.p. 181–184°, $[\alpha]^{25}\text{D}$ +115° (*c* 1.02, DMF), $\lambda_{\max}^{\text{MeOH}}$ 235 and 270 mμ (ε 7820 and 8510).

Anal. Calcd. for $C_9H_{12}N_6O_3$: C, 42.8; H, 4.80; N, 33.3. Found: C, 43.4; H, 4.98; N, 33.0.

2′-Deoxy-5′-*O*-tritylcytidine 3′-Methanesulfonate (5).—A solution of 0.100 g. (0.000213 mole) of **8** in 5 ml. of pyridine was cooled to 0° and 0.02 ml. (0.024 g., 0.000213 mole) of methanesulfonyl chloride was added; the mixture was stirred at 3° for 2 days. The solution was poured with vigorous stirring into 300 ml. of ice–water. The resulting solid was removed by filtration and air dried to give 0.086 g. of crude product, m.p. 137–154°. One recrystallization from ethyl acetate–petroleum ether (b.p. 30–60°) yielded 0.061 g. (54%) of **5** as colorless needles, m.p. 142.5–146°, $[\alpha]^{25}\text{D}$ +40.5° (*c* 0.37, EtOH), $\lambda_{\max}^{\text{EtOH}}$ 265 mμ (ε 7550), $\lambda_{\max}^{0.1\,N\ \text{NaOH}}$ 270 mμ (ε 8650), $\lambda_{\max}^{0.1\,N\ \text{HCl}}$ 270 mμ (ε 10,800).

Anal. Calcd. for $C_{29}H_{29}N_3O_6S\cdot0.5H_2O$: C, 62.6; H, 5.42; N, 7.56; S, 5.58. Found: C, 62.5; H, 5.47; N, 7.61; S, 5.11.

***N*-Benzoyl-2′-deoxycytidine 5′-Benzoate 3′-Methanesulfonate (2).**—A solution containing 1.00 g. (0.00302 mole) of **4** and 0.688 g. (0.47 ml., 0.006 mole) of methanesulfonyl chloride in 25 ml. of pyridine was stirred for 18 hr. at 3° and then 2.5 hr. at room temperature. The solution was cooled to 0°, about 1 ml. of water was added, and the solution was stirred an additional 0.5 hr. The mixture was then poured with vigorous stirring into 200 ml. of ice–water, and the precipitated solid was removed by filtration to yield 0.94 g. of crude product, m.p. 89–95°. One recrystallization from absolute ethanol gave 0.543 g. (35%) of **2** as colorless needles: m.p. 144–149° dec.; $[\alpha]^{25}\text{D}$ +30° (*c* 1.28, DMF); $\lambda_{\max}^{\text{MeOH}}$ 228, 259, and 302 mμ (ε 28,000, 25,100, and 10,300).

Anal. Calcd. for $C_{24}H_{23}N_3O_8S$: C, 56.1; H, 4.51; N, 8.18; S, 6.24. Found: C, 56.5; H, 4.69; N, 8.07; S, 6.05.

Attempted Preparation of *N*-Benzoyl-2′,5′-dideoxy-3′-iodocytidine 5′-Benzoate (1).—A mixture of 0.250 g. (0.00063 mole) of **2** and 0.0189 g. (0.00126 mole) of sodium iodide in 30 ml. of 2,4-pentanedione was heated under nitrogen at 100° for 2 hr. After cooling to room temperature the mixture of sodium *p*-toluenesulfonate and *N*-benzoylcytosine (**6**) was filtered off. The latter (0.088 g., 70%) was isolated by its water insolubility. The filtrate was evaporated *in vacuo* at 80° to yield a dark red oil whose thin layer chromatogram [using silica gel G impregnated with phosphor; solvent system butanol–water (86:14)] revealed three components, R_f 0.61, 0.68, and 0.77. This material was not examined further.

Acknowledgment.—We wish to thank Mr. L. M. Brancone and staff for elemental analyses and Mr. W. Fulmor and staff for the spectral determinations.

Lead Tetraacetate Oxidation of Some Thiocarbonyl Sugar Derivatives[1a]

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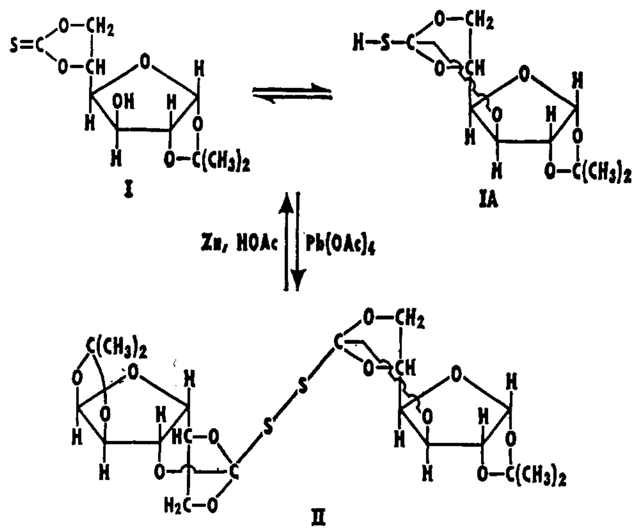
Consumption of lead tetraacetate by the sulfur atom in various sugar thiocarbonyl derivatives was traced, and the resulting oxidized products were isolated and identified. The nature of the oxidation varied with the structure of the sugar derivative used. A rapid consumption of 0.5 mole of lead tetraacetate per mole of 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-thionocarbonate (I) gave crystalline bis(1,2-*O*-isopropylidene-α-D-glucofuranose 3,5,6-orthocarbonyl) disulfide (II). The 3-*O*-acetyl (III) and 3-*O*-*p*-tolylsulfonyl (V) derivatives of I consumed one molar equivalent of the oxidant and formed elemental sulfur and the corresponding 5,6-carbonate derivatives IV and VI. Bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide and bis-(1,2:3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-D-galactopyranose) disulfide were virtually unaffected by the oxidant. One molecular equivalent of lead tetraacetate was consumed by 1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose 5,6-trithiocarbonate (IX) and its 3-*O*-acetyl (XI) and 3-*O*-*p*-tolylsulfonyl (XIII) derivatives resulting in the formation of the corresponding oxythiocarbonyl compounds X, XII, and XIV.

The sulfur atom of various thio sugars is readily oxidized by periodate[2] and lead tetraacetate.[3-5] Among effects observed are the formation of sulfoxides and sulfones by periodate[2] and the cleavage of dibenzyl mercaptal groups by lead tetraacetate. In the present work the action of lead tetraacetate on sugar derivatives containing a thiocarbonyl group is investigated. The rates of consumption of the oxidant by different thiocarbonyl sugar derivatives in glacial acetic acid at 25° are shown in Figure 1.

In previous work[6] it was proposed that I is in equilibrium with an ortho ester type structure (IA, Scheme I) containing a sulfhydryl group. This proposal was based on the formation of ortho ester type structures on methylation and benzylation of I and on the detection of a sulfhydryl group with 2,2-diphenyl-1-picrylhydrazyl. The presence of such an equilibrium is now confirmed by the isolation and identification of a crystalline dimer product containing a disulfide grouping on oxidation of I with lead tetraacetate. As expected

SCHEME I



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(1) (a) Presented before Division of Carbohydrate Chemistry, 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965. (b) This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article is not copyrighted.

(2) D. Horton and D. H. Hutson, *Advan. Carbohydrate Chem.*, **18**, 123 (1963).

(3) E. J. Bourne, W. M. Corbett, N. Stacey, and R. Stephens, *Chem. Ind.* (London), 107 (1954).

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(5) S. B. Baker, *ibid.*, **74**, 827 (1952).

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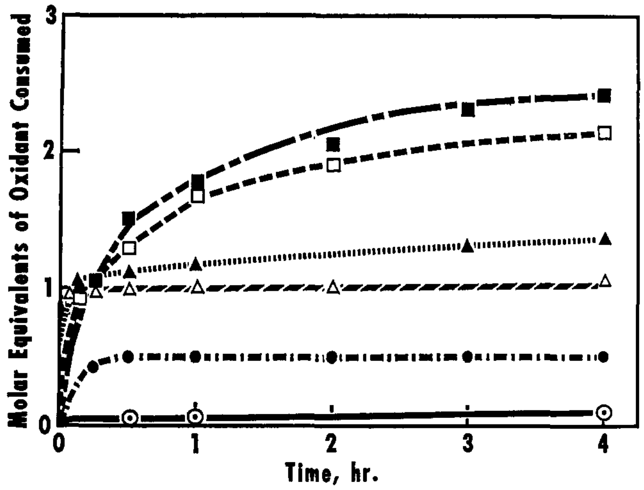
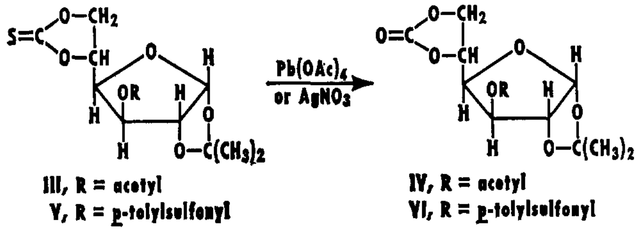


Figure 1.—Lead tetraacetate consumption of bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide (⊙), 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-thionocarbonate (I) (●), 3-*O*-acetyl-1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose 5,6-trithiocarbonate (XI) (△), 1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose 5,6-trithiocarbonate (IX) (▲), 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-thionocarbonate (III) (□), and bis(1,2-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide (■).

from the findings of Field and Lawson[7] on the oxidation of sulfhydryl compounds, 1 mole of I rapidly consumed 0.5 mole of lead tetraacetate (Figure 1). The oxidized product was isolated and shown to be bis(1,2-*O*-isopropylidene-α-D-glucofuranose 3,5,6-orthocarbonyl) disulfide (II). The structure of II was formulated on the basis of the following data: Elemental analysis and a molecular weight determination gave the formula, $C_{20}H_{26}O_{12}S_2$. The infrared spectrum of II showed no hydroxyl absorption. Absence of a thiocarbonyl group was shown by the fact that this compound, in contrast to I, did not react with silver nitrate to yield silver sulfide, did not give a positive test with iodine–sodium azide,[8] and showed no absorption at 234 mμ. Oxidation of II with bromine in acidic medium showed the presence of 1 mole of disulfide per mole of II. Reduction of II with zinc and acetic acid under mild conditions gave I presumably *via* IA. The n.m.r. spectrum of II was compared with that for 1,2-*O*-isopropylidene-α-D-glucofuranose 3,5,6-(*S*-methyl monothioorthocarbonate)[6] and was indistinguishable except for the signal at τ 7.78 assigned to the protons of the *S*-methyl group in the monomer derivative.

In the course of oxidation of the 3-*O*-acetyl (III) and 3-*O*-*p*-tolylsulfonyl (V) derivatives of I with lead tetraacetate (Scheme II), a rapid consumption of 1 mole of oxidant per mole of ester derivative was observed (Figure 1). The oxidized sugars were isolated as crystalline products and shown by their infrared spectra and mixture melting points with authentic samples to be the corresponding known carbonates IV and VI. Extraction of the mother liquor with carbon disulfide led to the isolation of elemental sulfur. Treating acetonic solutions of III and V with an aqueous solution of silver nitrate also gave IV and VI but with the formation of silver sulfide.[9]

SCHEME II

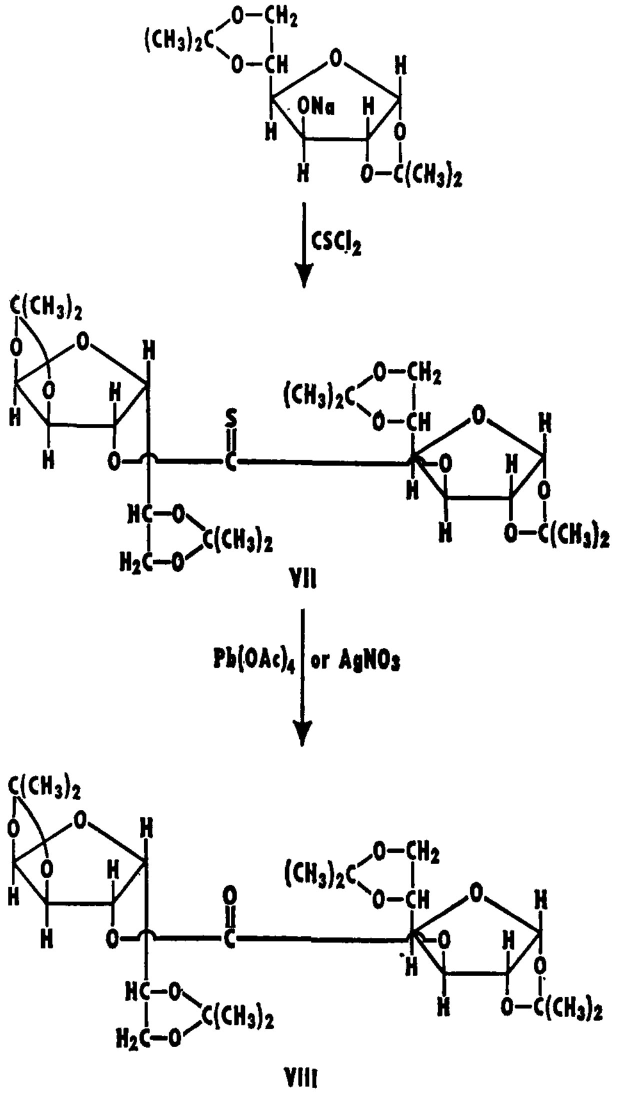


III, R = acetyl
V, R = *p*-tolylsulfonyl

IV, R = acetyl
VI, R = *p*-tolylsulfonyl

Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-thionocarbonate (VII) was prepared to examine the mode of lead tetraacetate oxidation of the thiocarbonyl group in a noncyclic thionocarbonate. This compound was prepared by the reaction of thiophosgene with the alcoholate of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (Scheme III). The consumption of lead tetraacetate by VII was more rapid than with III and V as 1.5 molecular equivalents were consumed in the first few minutes and up to 3.5 molecular equivalents during 4 hr. The corresponding bis-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-carbonate (VIII) was recovered from the oxidation

SCHEME III



VII

VIII

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(7) L. F. Field and J. E. Lawson, *J. Am. Chem. Soc.*, **80**, 838 (1958).

(8) F. Feigl, "Spot Tests," Vol. II, 4th Ed., Elsevier Publishing Company, New York, N. Y., 1954, p. 164.

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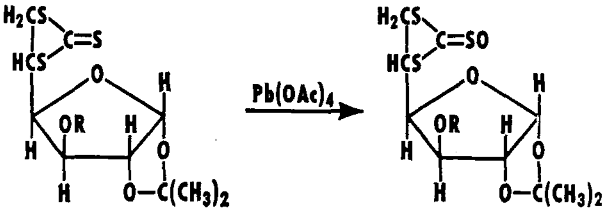
mixture but in poor yield, perhaps due to some overoxidation. The carbonate was recovered in nearly theoretical yield on treatment of VII with silver nitrate. The reason for the difference in behavior between VII and III or V toward lead tetraacetate is at present obscure.

Only a negligible amount of oxidant was consumed by bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide[9] or by bis(1,2:3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-D-galactopyranose) disulfide, most of each material being recovered after a 4-hr. reaction period. The relative stability of the  $(R{-}O{-}\overset{\overset{\displaystyle S}{\|}}{C}{-}S)_2$ grouping toward lead tetraacetate oxidation was demonstrated also by the fact that bis(1,2-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide[9] consumed only slightly more than the two molecular equivalents expected for the two diol groups present.

One molecular equivalent of lead tetraacetate was rapidly consumed by 1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose 5,6-trithiocarbonate (IX) (Figure 1) and by its 3-*O*-acetyl (XI) and 3-*O*-tosyl (XIII) derivatives, as well as by ethylene trithiocarbonate which was examined as a related model compound. In each instance, the oxidation product isolated had an empirical formula corresponding to that of the parent compound *plus* one atom of oxygen and showed absorption maxima at about 347 and 284 mμ. These data are consistent with oxidation of thiocarbonyl to oxythiocarbonyl groups (Scheme IV). The alternative possibility, that the other two sulfur atoms had been oxidized, is unlikely because this would have required the consumption of 2 moles of oxidant per mole and the formation of two sulfoxide groups. In accord with the suggested presence of only one sulfoxide-type structure, when X was reduced with two molar equivalents of L-cysteine, IX was obtained in 70% yield and L-cystine in 75% yield. By analogy it has been shown that the reduction of methionine sulfoxide[10] and of other sulfoxides[11] requires 2 moles of L-cysteine per mole.

SCHEME IV



IX, R = H **X, R = H**
XI, R = acetyl **XII, R = acetyl**
XIII, R = p-tolylsulfonyl **XIV, R = p-tolylsulfonyl**

It is noteworthy that compounds X, XII, and XIV are not stable under the experimental conditions used since the isolated crude oxidized products showed the presence of a carbonyl group in the infrared. This carbonyl group is presumably due to the decomposition of the oxythiocarbonyl group and not to the direct oxidation of the thiocarbonyl to the carbonyl group as in the oxidation of III to IV. This assumption is based on the facts that no free sulfur was found in the oxidation mixture of IX and that on repeated treatment of X under the same conditions as used for the oxidation, only about 30% of X could be recovered. The remaining product showed a lower sulfur content and had carbonyl absorption in the infrared. Apparently XII and XIV are somewhat more stable than X since they were recovered in higher yields.

Recently, Klingsberg[12] reported the formation of an oxythiocarbonyl derivative on peracetic acid oxidation of 4,5-dicyano-1,3-dithiole-2-thione. Other types of oxythiocarbonyl derivatives have also been reported.[13–15] These structures suggest the possibility of geometrical isomerism about the C═S bond, and at least once two such isomers were isolated and identified.[16]

The solvent used in lead tetraacetate oxidations has been shown to affect the nature of the reaction. The oxidation of di-*n*-butyl sulfide was reported to give the corresponding sulfoxide in varying yields dependent on the solvent used.[17] The lead tetraacetate oxidation of *p*-cresol gave 2,2′-dihydroxy-5,5′-dimethyldiphenyl when benzene was used as solvent[17] and reportedly gave 4-methyl-2,2-diacetoxy-3,5-cyclohexadien-1-one when the solvent was acetic acid.[18] Bourne, *et al.*,[3] have shown that 2,3,4,5,6-penta-*O*-acetyl-*aldehydo*-D-glucose dibenzyl mercaptal rapidly consumed lead tetraacetate in glacial acetic acid but that the reaction was barely detectable in 1:1 mixture of benzene–acetic acid. They postulated that the lead tetraacetate in acetic acid did not oxidize the sulfur atoms to form sulfoxides or sulfones but rather oxidatively coupled the mercaptans formed on cleavage of the molecule. They also postulated that in nonionizing solvents this reaction did not occur. In the present study we found that the solvent usually influenced the amount of lead tetraacetate consumed. For example, I consumed 0.5 mole of oxidant in glacial acetic acid, whereas the consumption was 0.8 mole in glacial acetic acid–benzene (3:1.5 v./v.) and more than 2 moles in anhydrous pyridine. Likewise, IX consumed 3 moles of lead tetraacetate in chloroform solution and only 1 mole in glacial acetic acid. The same amount of oxidant was consumed by XIII with either acetic acid or acetic anhydride as the solvent.

Experimental

Melting points were determined in capillary tubes in a Büchi[19] melting point apparatus and were corrected. Optical rotations were measured at 5893 Å. with a Rudolph polarimeter. Molecular weights were determined by the Rast method in camphor or in a vapor pressure osmometer (Mechrolab, Inc., Mountain View, Calif.) in acetone as specified. Ultraviolet spectra were determined with a Beckman DU spectrometer in methanol or

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[11] K. Balenovic and N. Bregant, *Chem. Ind.* (London), 1577 (1964).

[12] E. Klingsberg, *J. Am. Chem. Soc.*, **86**, 5290 (1964).

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[19] 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.

ethanol as specified. Infrared spectra were recorded by a Perkin–Elmer Infracord spectrophotometer with silver chloride optics as Nujol mulls or films. Samples for sulfur analysis were combusted by the Schöniger flask technique and determined by the method of White.[20] N.m.r. spectra were recorded by a Varian A-60 n.m.r. spectrometer with tetramethylsilane as a reference.

Lead Tetraacetate Uptake.—The lead tetraacetate used was prepared according to Vogel.[21] Measurement of lead tetraacetate uptake was performed as described by Perlin.[22] Each time 0.145 mmole of the sugar sulfur derivative was dissolved in 30 ml. of glacial acetic acid, and 20 ml. of lead tetraacetate stock solution (a saturated solution of lead tetraacetate in glacial acetic acid) was added. The solution was kept at 25°, and 5-ml. portions of the reaction mixture were withdrawn periodically and added to 30 ml. of "stopping" solution (20 g. of potassium iodide and 250 g. of sodium acetate trihydrate per liter of water). The liberated iodine was then titrated with a standard solution of sodium thiosulfate.

Bis(1,2-*O*-isopropylidene-α-D-glucofuranose 3,5,6-orthocarbonyl) Disulfide (II).—One gram of I was dissolved in 150 ml. of glacial acetic acid with gentle warming. After cooling the solution to 25°, 100 ml. of lead tetraacetate stock solution was added. The oxidation mixture was allowed to stand at 25° for 10 min., and then 1.5 l. of "stopping" solution was added and the excess of iodine was titrated with an aqueous solution of sodium thiosulfate. The suspension was centrifuged and most of the supernatant was decanted. The precipitate was recovered by filtration, washed with water, and crystallized from an ethanol–water mixture to afford 600 mg. (60%) of bis(1,2-*O*-isopropylidene-α-D-glucofuranose 3,5,6-orthocarbonyl) disulfide (II) as white needles, m.p. 268–270°, $[\alpha]^{20}\text{D}$ +68° (*c* 1.1, $CHCl_3$).

Anal. Calcd. for $C_{20}H_{26}O_{12}S_2$: C, 46.0; H, 5.0; S, 12.2; mol. wt., 522. Found: C, 45.9; H, 5.1; S, 12.2; mol. wt., 520 (Rast in camphor). When treated with bromine,[23] II consumed 4.75 moles of the oxidant per mole (requires 5.0 moles per mole).

A suspension of 150 mg. of II in 3 ml. of glacial acetic acid and 0.4 ml. of water was treated with 450 mg. of zinc dust. The mixture was heated to 60–65° for 2.5 hr., then cooled to 25°, and filtered. The filtrate was evaporated under reduced pressure and extracted with dioxane. The extract was evaporated to dryness, suspended in water, and centrifuged. The supernatant was decanted, and the crystalline residue was dried. Its infrared spectrum proved identical with I except for the presence of a cyclic carbonyl peak presumably due to some hydrolysis of the thiocarbonyl group. Treatment of II with acetic acid (without zinc dust) under similar conditions led to the recovery of II unchanged. An acetonic solution of I thus obtained when treated with an aqueous solution of silver nitrate, following the procedure reported elsewhere,[9] gave the corresponding carbonate in about 90% yield, m.p. 226° undepressed on admixture with an authentic sample.

Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-Thionocarbonate (VII).—1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (3.3 g.) was dissolved in 50 ml. of anhydrous ethyl ether, and an excess of sodium metal was added. The mixture was kept at 25° for 16 hr., then filtered, and concentrated to a thick sirup. Dioxane (15 ml.) was added and the solution was heated to 55°. A solution of 10 ml. of dry dioxane containing 1.5 ml. of thiophosgene was slowly added during 10 min. Heating was continued for an additional 10 min. after which the dark brown solution was allowed to evaporate in a hood. After most of the dioxane had evaporated, 100 ml. of water was added and the mixture was extracted with hexane. The extract was evaporated to yield 1.7 g. of crude VII, which was crystallized from ethanol–water mixture, m.p. 148°, $\lambda_{\max}^{\text{CH}_3\text{OH}}$ 305 mμ (ε 34) and 233 (9600).

Anal. Calcd. for $C_{25}O_{12}H_{38}S$: C, 53.3; H, 6.8; S, 5.7. Found: C, 53.2; H, 6.8; S, 5.8.

Bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-Carbonate (VIII).—To a solution of 100 mg. of VII in 3 ml. of acetone, barium carbonate (100 mg.) was added, followed by addition of a solution of 100 mg. of silver nitrate in 0.3 ml. of water (addition of barium carbonate to the reaction mixture was to avoid some hydrolysis of the 5,6-isopropylidene radical by the nitric acid produced). The mixture was allowed to stand at 25° for 30 min. and then filtered. The clear filtrate was evaporated to dryness to afford 70 mg. of VIII, which was recrystallized from ethanol–water mixture, m.p. 156° (Vargha[24] reported m.p. 149°). The infrared spectrum exhibited a strong carbonyl band at 5.7 μ.

Anal. Calcd. for $C_{25}H_{38}O_{13}$: C, 55.0; H, 6.9. Found: C, 54.6; H, 6.9.

Lead Tetraacetate Oxidation of III, V, and VII.—Compounds III and V were prepared by reaction of a pyridine solution of I with acetic anhydride and *p*-toluenesulfonyl chloride, respectively, according to a method reported previously.[9] A solution of 200 mg. of III in 20 ml. of lead tetraacetate stock solution was allowed to stand at 25° for 5 min. Then 200 ml. of "stopping" solution was added, and the excess of iodine was titrated with an aqueous solution of sodium thiosulfate. The reaction mixture was extracted thoroughly with several portions of ethyl ether. The combined ether extracts were washed with water, then dried over magnesium sulfate, filtered, and evaporated to dryness. The resulting sirup was crystallized from an ethanol–water mixture to yield 115 mg. (62%) of 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-carbonate (IV). A similar procedure was applied for V and VII to give 1,2-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-glucofuranose 5,6-carbonate (VI) in 62% yield and bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-carbonate (VIII) in 32% yield, respectively. Compounds IV, VI, and VIII were identified by comparison of their infrared spectra and melting points and mixture melting points with authentic samples.

Isolation of Elemental Sulfur from the Oxidation of III.—To isolate the elemental sulfur produced on oxidation of III, the procedure reported in the previous section was repeated by oxidizing 1.0 g. of III. The mixture, after titration of excess iodine, was extracted with two portions of carbon disulfide (250 ml. each). The extract was evaporated to dryness, and the precipitate was extracted again with carbon disulfide. Evaporation of the extract gave 55 mg. (52%) of crystals (S, 96%), m.p. 112–114°.

Bis(1,2:3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-D-galactopyranose) Disulfide.—To an efficiently stirred suspension of anhydrous α-D-galactose (100 g.) in anhydrous acetone (1250 ml.), pulverized anhydrous zinc chloride (250 g.) was added along with 12 ml. of concentrated sulfuric acid. The mixture was stirred at 25° for 4 hr., neutralized with sodium carbonate, and filtered. The residue remaining after evaporation of the acetone was extracted with ethyl ether, and the extract was washed with water and dried over anhydrous magnesium sulfate. The ether solution was filtered and evaporated to yield crude 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (62 g.), which without further purification was dissolved in anhydrous ethyl ether (150 ml.) and treated with metallic sodium (10 g.). After standing at 25° for 24 hr., the excess sodium was removed by filtration, and the ether solution was treated with carbon disulfide (50 ml.) at 25° for 10 min. After decantation of most of the ether and excess carbon disulfide, the remaining sirup was dissolved in water (50 ml.) and the pH of the solution was adjusted to 7 with 0.5 *N* acetic acid. The product was oxidatively coupled by addition of 0.3 *M* iodine solution, and excess iodine was titrated with aqueous sodium thiosulfate. On evaporation of the remaining ether, a yellow sirup precipitated. The sirup was washed with water and crystallized from an ethanol–water mixture to yield 42 g. of bis(1,2:3,4-di-*O*-isopropylidene-6-*O*-thiocarbonyl-α-D-galactopyranose) disulfide, m.p. 133–134°, $[\alpha]^{20}\text{D}$ −152° (*c* 1.0, acetone), $\lambda_{\max}^{\text{CH}_3\text{OH}}$ 288 mμ (ε 8900) and 240 (18,900) compared to $\lambda_{\max}^{\text{CH}_3\text{OH}}$ 280 mμ (ε 8100) and 230 (17,200) for bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide.

Anal. Calcd. for $C_{26}H_{38}O_{12}S_4$: C, 46.6; H, 5.7; S, 19.1; mol. wt., 670. Found: C, 46.8; H, 5.8; S, 19.0; mol. wt., 631 (vapor pressure osmometer in acetone).

3-*O*-Acetyl-1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose 5,6-Trithiocarbonate (XI).—A solution of 200 mg. of IX[6] in 2 ml. of anhydrous pyridine was treated with 1 ml. of acetic anhydride. The clear solution after standing at 25° for 2 days was poured into ice–water. The precipitate was collected by filtration, washed with water, and crystallized from ethanol–water mixture

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to afford XI, 193 mg. (85%), m.p. 138–139°, $[\alpha]^{20}\mathrm{D}$ −31° (*c* 1, $CHCl_3$), $\lambda_{\max}^{CH_3OH}$ 316 mμ (ε 11,000).

Anal. Calcd. for $C_{12}H_{16}O_5S_3$: C, 42.9; H, 4.8; S, 28.6. Found: C, 42.7, H, 4.9; S, 28.2.

1,2-*O*-Isopropylidene-5,6-dithio-3-*O*-(*p*-tolylsulfonyl)-β-L-idofuranose 5,6-Trithiocarbonate (XIII).—To a solution of 200 mg. of IX in 4 ml. of anhydrous pyridine, *p*-toluenesulfonyl chloride (1 g.) was added. The solution after standing at 25° for 3 days was poured into ice–water. The precipitate thus formed was collected by filtration, washed with water, and crystallized from ethanol–water mixture to afford XIII, 285 mg. (94%), m.p. 153–155°, $[\alpha]^{20}\mathrm{D}$ −15° (*c* 1, $CHCl_3$), $\lambda_{\max}^{CH_3OH}$ 316 mμ (ε 13,800).

Anal. Calcd. for $C_{17}H_{20}O_6S_4$: C, 45.6; H, 4.5; S, 28.6. Found: C, 45.7; H, 4.7; S, 28.0.

Lead Tetraacetate Oxidation of IX, XI, XIII, and Ethylene Trithiocarbonate and Isolation of the Corresponding Oxythiocarbonyl Products.—A solution of 1.0 g. of IX in 100 ml. of lead tetraacetate stock solution was allowed to stand at 25° for 10 min. before addition of 300 ml. of stopping solution. Aqueous sodium thiosulfate was then added to react with the free iodine, and the solution was extracted twice with 250-ml. portions of chloroform. The chloroform extract was washed with three 100-ml. portions of water and dried over anhydrous magnesium sulfate. After filtration, the chloroform was evaporated to yield 620 mg. of crude sirup, which partially crystallized from ethanol–water mixture to yield 350 mg. (33%) of 1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose oxythiocarbonyl-5,6-trithiocarbonate (X), m.p. 185–187°, $[\alpha]^{20}\mathrm{D}$ +262° (*c* 0.5, $CHCl_3$), $\lambda_{\max}^{CH_3OH}$ 348 mμ (ε 10,600) and 284 (4900).

Anal. Calcd. for $C_{10}H_{14}O_5S_3$: C, 38.7; H, 4.5; S, 31.0; mol. wt., 310. Found: C, 38.7; H, 4.7; S, 31.0; mol. wt., 292 (Rast in camphor).

Similarly, oxidation of 1.0 g. of XI gave 843 mg. of crude amorphous product, which crystallized from a benzene–hexane mixture to yield 500 mg. (48%) of 3-*O*-acetyl-1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose oxythiocarbonyl-5,6-trithiocarbonate (XIII), m.p. 160–161°, $[\alpha]^{20}\mathrm{D}$ +203° (*c* 0.32, $CHCl_3$), $\lambda_{\max}^{CH_3OH}$ 347 mμ (ε 10,250) and 285 (4400).

Anal. Calcd. for $C_{12}H_{16}O_6S_3$: C, 40.9; H, 4.5; S, 27.2. Found: C, 41.3; H, 4.7; S, 26.8.

The oxidation of 1.0 g. of XIII by a similar procedure gave 920 mg. (89%) of a crude amorphous product, m.p. 82–90°, $[\alpha]^{20}\mathrm{D}$ +16° (*c* 0.5, $CHCl_3$), $\lambda_{\max}^{CH_3OH}$ 347 mμ (ε 10,100) and 282 (5100).

Anal. Calcd. for $C_{17}H_{20}O_7S_4$: C, 44.0; H, 4.3; S, 27.6. Found: C, 44.6; H, 4.7; S, 27.0.

Ethylene trithiocarbonate prepared according to the procedure of Culvenor, Davies, and Pausacker[25] gave m.p. 34–35° (reported 36°), $\lambda_{\max}^{CH_3OH}$ 316 mμ (ε 13,900). The product obtained by oxidation of ethylene trithiocarbonate with lead tetraacetate was isolated. The procedure, similar to that used to isolate X, gave a sirup that crystallized from a benzene–hexane mixture as yellow needles in 30% yield, m.p. 61°, $\lambda_{\max}^{CH_3OH}$ 347 mμ (ε 10,000) and 284 (5100).

Anal. Calcd. for $C_3H_4OS_3$: C, 23.7; H, 2.6; S, 63.2. Found: C, 23.7; H, 2.8; S, 63.4.

Reduction of X by L-Cysteine.—To a solution of 50 mg. of X in 4 ml. of methanol, 200 mg. of L-cysteine hydrochloride monohydrate was added along with 1 ml. of water. Upon standing at 25° for 15 hr. a white precipitate formed which was filtered and dried to yield 29 mg. of L-cystine (identified by comparing its infrared spectrum with an authentic sample). The filtrate was evaporated to dryness and extracted with chloroform; the extract was washed with water and dried over anhydrous magnesium sulfate. The inorganic salt was discarded by filtration, and the clear chloroform solution was evaporated to yield 33 mg. of yellow crystals identified as IX by infrared, melting point, and mixture melting point with an authentic sample.

Reduction of Ethylene Oxythiocarbonyltrithiocarbonate.—The reduction was followed spectrometrically since the oxidized product showed absorption maxima at 347 and 285 mμ, but the absorption maximum of the parent compound was at 315 mμ. Hence, 30.4 mg. of the oxidized ethylene trithiocarbonate was dissolved in 8 ml. of methanol to which 105 mg. of cysteine hydrochloride in 2 ml. of water was added. A blank solution containing 105 mg. of cysteine hydrochloride was run simultaneously. Both solutions were kept at 25°. Measurements in the spectrometer were made periodically by taking 1-ml. aliquots and diluting to 250 ml. with methanol. After 45 hr. no absorption maxima were found at 347 or 285 mμ, and a new peak at 315 mμ appeared with a molar extinction coefficient that corresponded to 75% of the theoretical value of the reduced product. A white precipitate, identified as L-cystine, was isolated from the flask containing the oxythio compound, whereas the blank solution was still clear. The ultraviolet spectrum of a solution of the oxythio compound in methanol–water was unchanged on standing at 25° for 5 days.

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Reissert Compound Studies. VIII. The Preparation and Reactions of 2-Arylsulfonyl- and 2-Alkylsulfonyl-1,2-dihydroisoquinaldonitriles[1,2]

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The title compounds (II) are prepared from isoquinolines, potassium cyanide, and sulfonyl chlorides. Basic cleavage of these compounds yields isoquinaldonitrile and acid hydrolysis yields isoquinoline. Treatment of quinoline with potassium cyanide and benzenesulfonyl chloride yields only quinaldonitrile.

The preparation of Reissert compounds[3] (such as I) from a wide variety of quinolines[4] or isoquinolines,[5] potassium cyanide, and an acyl halide[6] or anhydride[6] is a well-known reaction.

We have now observed that a similar reaction occurs with isoquinoline, potassium cyanide, and an alkyl- or arylsulfonyl chloride to lead to the formation of 2-arylsulfonyl- and 2-alkylsulfonyl-1,2-dihydroisoquinaldonitriles (II, Chart I). The compounds of the type II which we have prepared are included in Table I. In general the methylene chloride–water method[4–7] of Reissert compound formation was used with no attempt to find ideal conditions. In the reaction of isoquinoline,

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