

# The Displacement Reactions of *p*-Toluenesulfonylsorbofuranoses with Thiolates in Liquid Ammonia and in Dimethylformamide<sup>1</sup>

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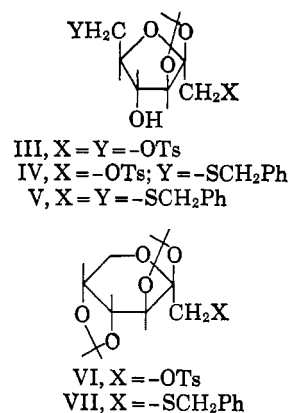
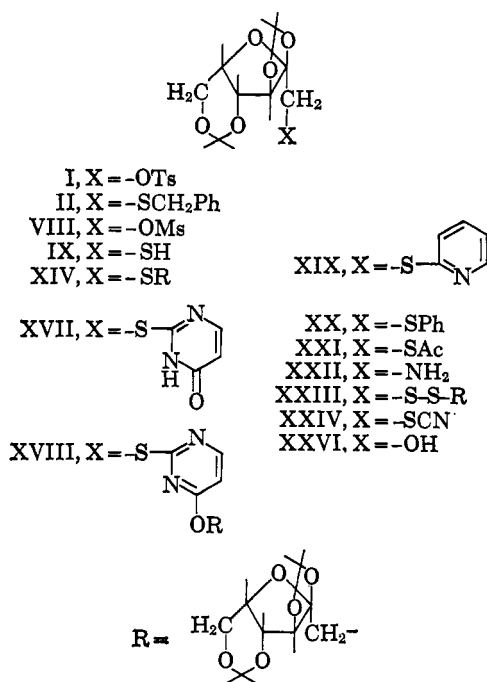
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Comparative studies of nucleophilic displacement reactions of the sterically hindered *p*-toluenesulfonyloxy groups of sorbofuranoses were carried out in liquid ammonia and in *N,N*-dimethylformamide. Various *S*-substituted thiosorbofuranoses were readily obtainable in both solvents.

In previous papers,<sup>2,3</sup> we have reported that various nucleophilic displacement reactions of the sterically hindered *p*-toluenesulfonyloxy groups of 2,3-*O*-isopropylidene- $\alpha$ -*L*-sorbofuranose proceeded smoothly in liquid ammonia, but not in another protic solvent such as an alcohol. When 1-*O*-*p*-toluenesulfonyl-2,3:4,6-di-*O*-isopropylidene- $\alpha$ -*L*-sorbofuranose (I) was treated with sodium benzylthiolate, 1-*S*-benzyl-2,3:4,6-di-*O*-isopropylidene-1-thio- $\alpha$ -*L*-sorbofuranose (II) was readily obtainable in liquid ammonia, but not in an alcohol.

but not in methanol (see Experimental Section). The remarkable difference on the reactions of these sterically hindered *p*-toluenesulfonyloxy groups appears to be due to solvation abilities of the two solvents for anions.



Feather and Whistler<sup>4</sup> reported that the reaction of 1,6-di-*O*-*p*-toluenesulfonyl-2,3-*O*-isopropylidene- $\beta$ -*D*-fructofuranose (III) with sodium benzylthiolate in methanol gave only the monosubstituted compound, 1-*O*-*p*-toluenesulfonyl-6-*S*-benzyl-2,3-*O*-isopropylidene-6-thio- $\beta$ -*D*-fructofuranose (IV). On the other hand, we observed that the use of liquid ammonia as a solvent led to the formation of the disubstituted product, 1,6-di-*S*-benzyl-2,3-*O*-isopropylidene-1,6-dithio- $\beta$ -*D*-fructofuranose (V). Similarly, 1-*O*-*p*-toluenesulfonyl-2,3:4,5-di-*O*-isopropylidene- $\beta$ -*D*-fructopyranose (VI)<sup>5</sup> was converted into 1-*S*-benzyl-2,3:4,5-di-*O*-isopropylidene-1-thio- $\beta$ -*D*-fructopyranose (VII) in liquid ammonia,

The significant increase in rate of nucleophilic or basic attack in aprotic solvents, such as tetrahydrofuran, dioxane, *N,N*-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO), has been the subject of considerable interests in recent years.<sup>6-11</sup> Solvation of attacking species in these solvents may be one factor responsible for the above finding. An anion poorly solvated in a polar aprotic solvent is more reactive than the highly solvated species in protic solvents,<sup>8,12</sup> so that one can expect a higher reactivity in aprotic solvents than that in hydroxylic solvents. In liquid ammonia solution, a cation solvates with liquid ammonia through the lone pair of the nitrogen atom, but because of the low acidity of liquid ammonia, an anion is expected to be in a poorly solvated form. Accordingly, the comparative study of a nucleophilic displacement reaction in liquid ammonia with that in an aprotic solvent was undertaken.

The reaction of I with sodium benzylthiolate in liquid ammonia proceeded at room temperature yielding II.<sup>2</sup> Expectedly, the same reaction in aprotic solvents such as tetrahydrofuran, dioxane, DMF, and DMSO was successful; however, it required a high reaction temperature. Similar observations were obtained in the reaction of 1-*O*-methanesulfonyl-2,3:4,6-di-*O*-isopropylidene- $\alpha$ -*L*-sorbofuranose (VIII). The conversion of I with sodium hydrosulfide into 1-thio-

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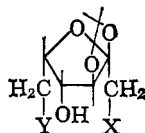
2,3:4,6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (IX) was achieved in DMF and in DMSO, but not in tetrahydrofuran and in dioxane. Highly polar solvents such as DMF and DMSO may be necessary for this kind of nucleophilic displacement and less polar solvents may not allow sufficient amounts of the anion to exist for the reaction to occur. Therefore, comparative studies of displacement reactions of I with various thiolates were carried out in liquid ammonia and in DMF. The results were summarized in Table I.

TABLE I  
REACTION PRODUCTS OF I WITH VARIOUS THIOLATES IN LIQUID AMMONIA AT 100°C AND IN DMF AT THE BOILING POINT

Thiolates	Products	
	Liq. NH <sub>3</sub>	DMF
NaSCH <sub>2</sub> Ph	II	II
NaSH	IX <sup>b</sup>	IX <sup>b</sup>
CH <sub>3</sub> CSNH <sub>2</sub> <sup>c</sup>	IX <sup>b</sup>	...
NH <sub>2</sub> CSNH <sub>2</sub> <sup>c</sup>	IX <sup>b</sup>	...
CH <sub>3</sub> NHCSNH <sub>2</sub> <sup>c</sup>	XIV <sup>b</sup>	...
CH <sub>3</sub> NHCSNHCH <sub>3</sub> <sup>c</sup>	XIV <sup>b</sup>	...
PhNHCSNHPh <sup>c</sup>	XIV <sup>b</sup>	XIV <sup>b</sup>
2-Thiouracil <sup>c</sup>	IX <sup>b</sup>	XVII
2-Thiouracil <sup>d</sup>	IX <sup>b</sup>	XVIII
2-Thiopyridone <sup>c</sup>	XIX	XIX
Thiophenol <sup>c</sup>	XX	XX
KSac	...	XXI
KSC(=S)OC <sub>2</sub> H <sub>5</sub>	...	IX
KSCN	XXII	XXIII <sup>b</sup> + XXIV

<sup>a</sup> An autoclave (stainless steel) was used.<sup>15</sup> <sup>b</sup> Further investigation seems to be required for the explanation on the formation of different types, IX, XIV, and XXIII. <sup>c</sup> As monosodium salt. <sup>d</sup> As the disodium salt.

When the reaction of I with sodium salt of thioacetamide was carried out in liquid ammonia, IX was obtained as a product, but from the reaction in DMF was recovered only the starting sugar. The same result was obtained by the reaction of I with the sodium salt of thiourea in both solvents. The formation of IX may be interpreted by one of the following two reaction schemes. One is a route of I  $\rightarrow$  S-(1-deoxy-2,3:4,6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose-1)thioacetamide (X) or S-(1-deoxy-2,3:4,6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose-1)thiourea (XI)  $\rightarrow$  IX, but these intermediates X and XI were not obtainable even under a mild reaction condition such as we employed. Another route includes the reaction of sodium hydrosulfide, which was possibly formed by the decomposition of thioacetamide or thiourea, with I to afford IX. To ascertain which route is more probable, the reaction of 1,6-di-O-*p*-toluenesulfonyl-2,3-O-isopropylidene- $\alpha$ -L-sorbofuranose (XII)<sup>13</sup> was studied. While treatment of XII with the above sodium salts in liquid ammonia affords 1,6-dithio-2,3-O-isopropylidene- $\alpha$ -L-sorbofuranose (XIII),<sup>2</sup> treatment of XII with sodium hydro-



XII, X = Y = -OTs  
XIII, X = Y = -SH  
XXV, X = Y = -SCN

sulfide yields only the monothio sugar.<sup>3</sup> This result indicates the former scheme is correct.

For the purpose of synthesis of a thiourea derivative of the related sugar, a derivative of thiourea stable in liquid ammonia or in DMF even at a high temperature was desired. The use of N-methyl and N-phenyl derivatives of thiourea gave none of the expected product as shown in Table I. Treatment of N-methyl or N,N'-dimethylthiourea with I in liquid ammonia gave 1-S-(1'-deoxy-2',3':4',6'-di-O-isopropylidene- $\alpha$ -L-sorbofuranose-1')-2,3:4,6-di-O-isopropylidene-1-thio- $\alpha$ -L-sorbofuranose (XIV), but in DMF gave only the starting material I. On the other hand, when I was treated with N,N'-diphenylthiourea in liquid ammonia, XIV was obtained accompanying N,N'-diphenylguanidine (XV) and this reaction in DMF gave XIV and N,N'-diphenylurea (XVI). This thiourea also reacted with XII to yield XIII. The results showed that the reaction route should be similar to that of thiourea.

Treatments of I with monopotassium salt of 2-thiouracil in liquid ammonia and in DMF afforded IX and S-(1'-deoxy-2',3':4',6'-di-O-isopropylidene- $\alpha$ -L-sorbofuranose-1')-2-thiouracil (XVII), respectively. The fact that heating of XVII in liquid ammonia solution yielded IX supported the view that the reaction route in liquid ammonia should be *via* XVII as a probable intermediate. Treatment of the dipotassium salt of 2-thiouracil in liquid ammonia and in DMF gave IX and S,O-di-(1'-deoxy-2',3':4',6'-di-O-isopropylidene- $\alpha$ -L-sorbofuranose-1')-2-thiouracil (XVIII), respectively. The structure of XVIII was confirmed by the infrared spectrum which exhibited the band of the pyrimidine ring and no carbonyl group absorption. Thus, it was indicated that in the two solvents the thiouracil anions are rather stable, and the substituted products XVII and XVIII were stable in DMF, but unstable in liquid ammonia solution, decomposing into IX. When I was treated with the sodium salt of 2-thiopyridone or thiophenol in the above two solvents, the product was S-(1'-deoxy-2',3':4',6'-di-O-isopropylidene- $\alpha$ -L-sorbofuranose-1')-2-thiopyridine (XIX) or 1-S-phenyl-2,3:4,6-di-O-isopropylidene-1-thio- $\alpha$ -L-sorbofuranose (XX). This means that both the anions and substituted products are stable in the two solvents. In the reaction of potassium thioacetate or potassium ethylxanthate with I, the use of liquid ammonia as a solvent gave no thio sugar, but the use of DMF gave 1-S-acetyl-2,3:4,6-di-O-isopropylidene-1-thio- $\alpha$ -L-sorbofuranose (XXI) or IX. When I was treated with potassium thiocyanate in liquid ammonia or in DMF, 1-deoxy-1-amino-2,3:4,6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (XXII) was obtained in the former solvent as previously reported,<sup>3</sup> and the disulfide of IX (XXIII) and 1-deoxy-1-thiocyanato-2,3:4,6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (XXIV) were obtained in the latter solvent. Treatment of XII with potassium thiocyanate in DMF did not give thiocyanato sugar, 1,6-dideoxy-1,6-dithiocyanato-2,3-O-isopropylidene- $\alpha$ -L-sorbofuranose (XXV), but XIII, which was considered to be formed by the decomposition of XXV. The results indicate that these thiolate anions are not stable in liquid ammonia, but are relatively stable in DMF.

In conclusion, it can be stated that, with few exceptions [e.g., -SAc and -SC(=S)OC<sub>2</sub>H<sub>5</sub>], nucleophilic displacements by sulfur anions appear to occur more readily in liquid ammonia than in DMF. When reaction does take place in DMF, however, its utilization can serve for the isolation of intermediates that are solvolyzed to other products in liquid ammonia.

### Experimental Section<sup>14</sup>

**1,6-Di-S-benzyl-2,3-O-isopropylidene-1,6-dithio- $\beta$ -D-fructofuranose (V).**—A solution of  $\alpha$ -toluenethiol (1.2 g.) and sodium (0.2 g.) in liquid ammonia (10 ml.) was added to a solution of III (0.8 g.) in liquid ammonia (10 ml.). After standing at room temperature for 2 weeks, ammonia was allowed to evaporate and the residue was washed with water, dried, and recrystallized from *n*-hexane. Colorless needles (0.4 g.) were obtained, m.p. 94°,  $[\alpha]^{24.5D} +34.1^\circ$  (*c* 0.987).

*Anal.* Calcd. for C<sub>28</sub>H<sub>28</sub>O<sub>4</sub>S<sub>2</sub>: C, 63.89; H, 6.46; S, 14.51. Found: C, 63.94; H, 6.60; S, 14.56.

**1-S-Benzyl-2,3:4,5-di-O-isopropylidene-1-thio- $\beta$ -D-fructopyranose (VII).**—A solution of  $\alpha$ -toluenethiol (1.5 g.) and sodium (0.28 g.) in liquid ammonia (10 ml.) was mixed with a solution of VI (1.5 g.) in liquid ammonia (10 ml.). After heating on a boiling-water bath for 20 hr., the ammonia was allowed to evaporate and the residue was washed with water and dried. The residue was purified by silica gel chromatography with benzene and ether (3:2, v./v.) to obtain 0.75 g. of VII as a sirup,  $[\alpha]^{26D} -81.1^\circ$  (*c* 1.504).

*Anal.* Calcd. for C<sub>19</sub>H<sub>26</sub>O<sub>6</sub>S: C, 62.29; H, 7.10; S, 8.74. Found: C, 62.56; H, 7.26; S, 8.87.

**The Reaction of I with  $\alpha$ -Toluenethiol in Aprotic Solvents.**—From a methanol solution of  $\alpha$ -toluenethiol (2 g.) and sodium (0.3 g.), the solvent was removed under nitrogen. The mixture of the residue and I (2 g.) was dissolved or suspended into 80 ml. of DMF, DMSO, tetrahydrofuran, or dioxane. The solution was refluxed (in the case of DMSO, heated at 150–160°) for 10 hr. The solution was diluted with water, extracted with chloroform, washed with water, and dried, and the solvent was removed. Recrystallization of the residue from *n*-hexane–chloroform gave II (1.5 g.) which was identified with an authentic sample.<sup>2</sup>

**1-O-Methanesulfonyl-2,3:4,6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (VIII).**—Into a solution of 2,3:4,6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (XXVI) (1 g.)<sup>16</sup> in dry pyridine (10 ml.), methanesulfonyl chloride (1 ml.) in portions was stirred while the mixture was kept cold in ice-water. After having been stirred at room temperature for 4 hr., the reaction mixture was poured into a saturated sodium carbonate solution and then extracted with chloroform which had been washed with water, dried, and evaporated under reduced pressure to dryness. The recrystallization of the residue from ethyl acetate and *n*-hexane gave cubes (1.1 g.), m.p. 115°,  $[\alpha]^{23.6D} -4.7^\circ$  (*c* 1.111).

*Anal.* Calcd. for C<sub>13</sub>H<sub>22</sub>O<sub>6</sub>S: C, 46.15; H, 6.51; S, 9.46. Found: C, 46.35; H, 6.55; S, 9.37.

Thus-obtained VIII was allowed to react with various thiolates and gave the same products in a procedure similar to I.<sup>2,3</sup>

**The Reaction of I with Sodium Hydrosulfide in Aprotic Solvents.**—A solution of I (1.5 g.) and sodium hydrosulfide (0.5 g.) in DMF (30 ml.) was refluxed for 8 hr. The solution was diluted with water, extracted with chloroform, washed with water, and dried, and the solvent was removed. Recrystallization from *n*-hexane and ethyl acetate gave IX (0.3 g.). The reaction also took place in DMSO as a solvent at 150–160°.

**The Reactions of I with Thioacetamide and Thioureas.**—To a solution of sodium (0.11 g.) in liquid ammonia (20 ml.) was added thioacetamide or thioureas until the blue color of sodium was discharged. After that, I (1.5 g.) was added to the solution

and the solution was heated on a boiling-water bath for 20 hr. After the liquid ammonia had been removed, the residue was diluted with water and then extracted with chloroform. The chloroform was washed with water, dried, and evaporated. Recrystallization of the residue from *n*-hexane and ethyl acetate gave the thio sugar in a pure state. (1) The reaction with thioacetamide yielded colorless needles (0.4 g.), m.p. 136°, which were identical with an authentic sample of IX.<sup>2,3</sup> (2) The reaction with thiourea also yielded IX (0.4 g.). (3) The reaction with *N*-methylthiourea gave XIV (0.46 g.), m.p. 134–135°,  $[\alpha]^{23.6D} -58.0^\circ$  (*c* 0.685) (*Anal.* Calcd. for C<sub>24</sub>H<sub>30</sub>O<sub>10</sub>S: C, 55.48; H, 7.87; S, 6.17. Found: C, 55.65; H, 7.89; S, 6.16.). (4) The reaction with *N,N'*-dimethylthiourea yielded XIV (0.4 g.), which was identical with the sample obtained above.

**The Reaction of XII with Thiourea.**—Thiourea (1 g.) in liquid ammonia (15 ml.) was neutralized with sodium. To the liquid ammonia solution was added XII (1 g.) and the solution was heated on a boiling-water bath for 20 hr. After the liquid ammonia had been allowed to evaporate, the residue was diluted with water and extracted with chloroform. The extract was washed with water, dried, and evaporated. Recrystallization of the residue gave XIII (0.26 g.), m.p. 89° (recrystallized from ethyl acetate and *n*-hexane),  $[\alpha]^{25D} +27.5^\circ$  (*c* 1.116).<sup>17</sup> Thus-obtained XIII is identical with an authentic sample.<sup>2</sup>

**The Reactions of I with *N,N'*-Diphenylthiourea. A. In DMF.**—*N,N'*-Diphenylthiourea (2.8 g.) was dissolved in methanol (10 ml.) containing sodium (0.29 g.) and the solvent was removed at room temperature under reduced pressure. To the residue was added I (3 g.) in DMF (50 ml.). The solution was refluxed for 20 hr. After cooling, the solution was filtered; the filtrate was evaporated under reduced pressure. The residue was extracted with chloroform and the solvent was removed. Recrystallization of the residue from *n*-hexane gave XIV (0.1 g.). From the *n*-hexane-insoluble part, XVI (0.1 g.) was obtained.

**B. In Liquid Ammonia.**—To liquid ammonia (20 ml.) containing sodamide (prepared from 0.23 g. of sodium in liquid ammonia) was added *N,N'*-diphenylthiourea (3.0 g.). After complete dissolution of sodamide, I (2.0 g.) was added to the ammonia solution. The solution was heated on a boiling-water bath for 20 hr. After the ammonia had been removed, the residue was diluted with a little water and extracted with chloroform, and the chloroform was evaporated. The residue was extracted with hot *n*-hexane. From the part soluble in *n*-hexane, XIV (0.1 g.) was obtained, and, from the insoluble part, XV (0.3 g.) was obtained.

**The Reactions of I with Thiouracil. A. The Reaction of I with the Monopotassium Salt of 2-Thiouracil. 1. In DMF.**—2-Thiouracil (0.85 g.) was dissolved in hot water (*ca.* 100 ml.) containing potassium carbonate (0.51 g.) and the water was removed under reduced pressure. The residue was well dried in a desiccator. Thus-obtained monopotassium salt of 2-thiouracil was added to DMF (30 ml.) containing I (2.8 g.). The solution was refluxed for 20 hr. After cooling, the solution was filtered, the filtrate was evaporated to dryness under reduced pressure, and the residue was extracted with chloroform. The solvent was removed and the residue was washed with hot *n*-hexane. Recrystallization of remaining crystals from alcohol gave colorless prisms of XVII (0.3 g.): m.p. 204°;  $[\alpha]^{26.5D} +8.7^\circ$  (*c* 0.999);  $\lambda_{\max}^{\text{N}^{\text{H}}\text{O}^{\text{H}}}$  1552–1568 (C=C, C=N), 1665 cm.<sup>-1</sup> (C=O).

*Anal.* Calcd. for C<sub>16</sub>H<sub>22</sub>N<sub>2</sub>O<sub>6</sub>S: C, 51.89; H, 5.95; N, 7.59; S, 8.65. Found: C, 52.17; H, 6.20; N, 7.64; S, 8.48.

**2. In Liquid Ammonia.**—When the above-described reaction was carried out in liquid ammonia solvent at 100° for 20 hr., IX (0.4 g.) was obtained.

**B. The Reaction of I with Dipotassium Salt of 2-Thiouracil. 1. In DMF.**—2-Thiouracil (1.28 g.) was dissolved in hot water (100 ml.) containing potassium carbonate (1.5 g.) and the water was removed under reduced pressure. The thus-obtained dipotassium salt of 2-thiouracil was well dried in a desiccator and added to DMF (50 ml.) containing I (4 g.), and the solution was refluxed for 15 hr. After cooling, the solution was filtered, the filtrate was evaporated to dryness under reduced pressure, and the residue was washed with water. The thus-obtained sirup was purified by alumina column chromatography with benzene–chloroform (1:1, v./v.). XVIII (0.24 g.) was obtained as a pale yellow sirup,  $[\alpha]^{24.5D} +4.3^\circ$  (*c* 1.112),  $\lambda_{\max}^{\text{N}^{\text{H}}\text{O}^{\text{H}}}$  1555 cm.<sup>-1</sup> (pyrimidino).

(14) Melting points were measured on a Kofler block. Optical rotations were determined in a 1-cm. microtube in chloroform containing 1% of ethanol, and concentrations were recorded in percentages. Liquid ammonia solution was prepared in a glass pressure vessel,<sup>15</sup> transferred into an autoclave (stainless steel), and then heated.

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(17) Previously reported values<sup>2</sup> of the melting point and specific rotation were misprinted.

*Anal.* Calcd. for  $C_{25}H_{46}N_2OS$ : C, 54.90; H, 6.54; N, 4.58; S, 5.23. Found: C, 54.75; H, 6.71; N, 4.68; S, 5.56.

2. In Liquid Ammonia.—When the above-described reaction was carried out in liquid ammonia (30 ml.) instead of DMF, at 100° for 15 hr., IX (0.45 g.) was obtained.

**The Reactions of I with 2-Thiopyridone.** A. In DMF.—2-Thiopyridone (0.75 g.) was dissolved in water (50 ml.) containing potassium carbonate (1.0 g.) and the water was removed under reduced pressure. The dried residue was added to a solution of I (2.5 g.) in DMF (40 ml.) and the solution was refluxed for 8 hr. After cooling, the solution was filtered and the filtrate was evaporated under reduced pressure. The residue was chromatographed on an alumina with benzene. The first elute yielded XIX. Recrystallization of crude crystals from *n*-hexane gave pure cubic crystals (0.2 g.), m.p. 69°,  $[\alpha]^{25}_D -0.7^\circ$  (*c* 1.1130),  $\lambda_{max}^{Nujol} 1576 \text{ cm.}^{-1}$  (pyridine).

*Anal.* Calcd. for  $C_{17}H_{23}NO_5S$ : C, 57.79; H, 6.52; N, 3.97; S, 9.07. Found: C, 57.74; H, 6.62; N, 3.80; S, 9.10.

B. In Liquid Ammonia.—When the above reaction was carried out in liquid ammonia (20 ml.) at 100° for 20 hr., the same result was obtained.

1-S-Phenyl-2,3,4,6-di-O-isopropylidene-1-thio- $\alpha$ -L-sorbofuranose (XX).—A mixture of sodium (1 g.) and thiophenol (5 g.) was dissolved by adding methanol (*ca.* 6 ml.). The solution was mixed with a liquid ammonia (30 ml.) solution of I (10 g.) and the mixture was heated on a boiling-water bath for 25 hr. Ammonia was allowed to evaporate, and the residue was diluted with water, extracted with chloroform, washed with water, dried, and evaporated. Recrystallization of the residue from *n*-hexane gave XX (4.2 g.), m.p. 64°,  $[\alpha]^{24.5}_D -17.5^\circ$  (*c* 1.058).

*Anal.* Calcd. for  $C_{18}H_{24}O_6S$ : C, 61.36; H, 6.82; S, 9.09. Found: C, 61.44; H, 6.86; S, 9.19.

The same result was obtained when DMF was used as a solvent.

**The Reaction of I with Potassium Thiolacetate.**—A solution of I (2 g.) and potassium thiolacetate (0.56 g.) in DMF (50 ml.) was refluxed for 2.5 hr. The solution was filtered, and the filtrate was evaporated. The residue was extracted with chloroform, the extract was washed with water and dried, and the solvent was removed. Distillation of the residue gave XXI

(0.6 g.), b.p. 162° (7.5 mm.),  $[\alpha]^{25}_D -6.6^\circ$  (*c* 0.992),  $\lambda_{max}^{film} 1672 \text{ cm.}^{-1}$  (SO<sub>2</sub>CH<sub>3</sub>).

*Anal.* Calcd. for  $C_{14}H_{22}O_6S$ : C, 52.80; H, 6.94; S, 10.04. Found: C, 52.76; H, 7.00; S, 9.69.

**The Reaction of I with Potassium Ethylxanthate.**—A solution of I (2 g.) and potassium ethylxanthate (0.8 g.) in DMF (40 ml.) was refluxed for 6 hr. After removal of solvent under reduced pressure, the residue was chromatographed on an alumina column with benzene. After the starting material was recovered from the benzene fraction, IX (0.5 g.) was obtained which was eluted with ether.

**The Reaction of I with Potassium Thiocyanate.**—A solution of I (8 g.) and potassium thiocyanate (8 g.) in DMF (50 ml.) was refluxed for 12 hr. The solution was filtered, and the filtrate was evaporated under reduced pressure. The residue was extracted with hot *n*-hexane. From the *n*-hexane-soluble part, XXIII (1.1 g.) was obtained. It had m.p. 148° (recrystallized from *n*-hexane),  $[\alpha]^{25}_D -23.4^\circ$  (*c* 1.1152).

*Anal.* Calcd. for  $C_{24}H_{38}O_{10}S_2$ : C, 52.36; H, 6.91; S, 11.62. Found: C, 52.47; H, 7.02; S, 11.53.

Distillation of the *n*-hexane-insoluble part gave XXIV (1.5 g.), b.p. 170° (7 mm.),  $[\alpha]^{25}_D -10.6^\circ$  (*c* 1.1028),  $\lambda_{max}^{film} 2245 \text{ cm.}^{-1}$  (SC≡N).

*Anal.* Calcd. for  $C_{18}H_{19}NO_5S$ : C, 51.83; H, 6.31; N, 4.65; S, 10.63. Found: C, 52.10; H, 6.43; N, 4.63; S, 10.62.

**The Reaction of XII with Potassium Thiocyanate.**—A mixture of potassium thiocyanate (8 g.), XII (8 g.), and DMF (40 ml.) was refluxed for 8 hr. The solution was filtered, and the filtrate was evaporated to dryness under reduced pressure. The residue was extracted with chloroform, the extract was washed with water and dried, and the solvent was removed. Recrystallization of the residue from *n*-hexane and chloroform gave colorless needles (2.8 g.), m.p. 89°,  $[\alpha]^{24.5}_D -27.5^\circ$  (*c* 0.9431). Thus-obtained XIII was identical with an authentic sample.<sup>2</sup>

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## Carbohydrates of the Coffee Bean. IV. An Arabinogalactan<sup>1</sup>

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Essentially all of the L-arabinose and D-galactose present in the green coffee bean (*Coffea arabica*) are shown to occur as a water-soluble arabinogalactan (2:5). The L-arabinose can be removed from this polysaccharide by dilute acid leaving a galactan. Methylation analysis of the arabinogalactan and of its component galactan can be interpreted tentatively as indicating I which has a backbone chain of  $\beta$ -D-(1 $\rightarrow$ 3)-linked galactopyranose units to some of which are attached at the C-6 position terminal L-arabinofuranose side chains containing an occasionally interposed (1 $\rightarrow$ 3)-linked D-galactopyranose entity.

The green coffee bean (*Coffea arabica*) has a high content (50–60%) of polysaccharides, the constituent sugars of which have been determined<sup>2,3</sup> to be D-mannose (preponderant), L-arabinose, D-galactose, and D-glucose. This communication is concerned with the nature of the L-arabinose and D-galactose content which is now established to be in the form of an arabinogalactan. Although the arabinogalactan is slightly water soluble, the polysaccharide is difficult to extract completely from the very hard green coffee bean, probably because of the cellular structure of this botanical

entity. The arabinogalactan appears to be associated, at least in part, with the protein fraction,<sup>4</sup> likewise mainly water soluble, and with the characteristic coffee acids, largely aromatic in nature. We report some preliminary evidence that some of these acids may be esterified with the arabinogalactan since an alkaline treatment was required to purify the polysaccharide and since some spectral evidence for the presence of aromatic esters could be adduced.

Two methods were employed in the isolation of the arabinogalactan from the green coffee bean. In both methods the ground beans were extracted successively<sup>3</sup> with ethanol-water, benzene-ethanol, water at 25°, and ammonium oxalate. In the one case (method A) the residue (fraction 1) from the above treatment was extracted with hot water, the extract was digested with proteolytic enzymes (chymotrypsin and trypsin to-

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