3. The following specific rotations were measured with precision in aqueous solution; β-thiophenol xyloside, m. p. 144°, $[\alpha]^{20}_{D}$ −70.8°; β-thiophenol cellobioside, m. p. 230°, $[\alpha]^{17}_{D}$ −59.2°; β-thiophenol lactoside, m. p. 220°, $[\alpha]^{19}_{D}$ −39.3° and β-thiophenol glucoside, m. p. 133°, $[\alpha]^{19}_{D}$ −70.5°.

4. The molecular rotations in water of the above four β-thiophenol glycosides displayed irregularities which could not be explained. In consequence, optical data cannot at present be safely used as an aid in determining the stereochemical configuration of the thioglycosides.

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[CONTRIBUTION FROM THE POLARIMETRY SECTION, BUREAU OF STANDARDS, U. S. DEPARTMENT OF COMMERCE]

RELATIONS BETWEEN ROTATORY POWER AND STRUCTURE IN THE SUGAR GROUP. XXII. EVIDENCE CONCERNING THE RINGED STRUCTURE OF BETA-THIOPHENOL CELLOBIOSIDE AND OF BETA-THIOPHENOL LACTOSIDE[1,2]

BY CLIFFORD B. PURVES

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A noteworthy property of the β-thioglycosides which serves to distinguish them from the isomeric α-forms, and also from the glycosides of the hydroxy alcohols, may be seen in their great stability toward acid hydrolysis.[3] The glycosidic unions in β-thiophenol lactoside and cellobioside are no exceptions to the general rule and the comparative indifference of the thio linking in such derivatives of the disaccharides makes possible a simple way of examining their constitution. For example, if thiophenol lactoside be submitted to the action of aqueous acid under conditions just sufficiently drastic for the complete hydrolysis of the disaccharide itself, the union of thiophenol with the potentially reducing carbon atom of the sugar residue is largely preserved and galactose and a thiophenol glucoside may be expected to form the main products of the reaction. The former component may readily be modified before its examination, either as regards the position of the oxygen ring or otherwise, and the isolation of galactose of the ordinary type therefore provides no evidence concerning its original state in the disaccharide molecule. It is otherwise

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[1] Published by permission of the Director of the Bureau of Standards, U. S. Department of Commerce.

[2] The author has arranged with Dr. C. S. Hudson, under whose direction the research was carried out, that it will be included as No. XXII in his series entitled "Relations between Rotatory Power and Structure in the Sugar Group." No. XXI was published in THIS JOURNAL, **51,** 3619 (1929).

[3] Schneider, Sepp and Stiehler, *Ber.*, **51,** 220 (1918).

with the thioglycosidic component, for here the reducing position is shielded by the stable thiophenol radical and a change in the structure of this unit of thiophenol lactoside during the experiment may be discounted with some confidence. Thiophenol lactoside and cellobioside have accordingly been submitted to the action of aqueous acid and the specimens of thiophenol glucoside so obtained have been examined in order to see whether they were of the normal or gamma type.

After making certain that thiophenol glucoside itself was very nearly stable under the experimental conditions to be employed in the hydrolyses, thiophenol lactoside was heated with normal sulfuric acid for one and three-fourths hours. The trace of thiophenol set free during this operation was readily removed by chloroform and it was possible to determine the final specific rotation of the solution to be $[\alpha]_D$ $-10.66°$. An equimolecular mixture of galactose and β-thiophenol glucoside possesses the closely similar rotation of $[\alpha]_D$ $-9.56°$ in distilled water. Ethyl acetate separated the non-reducing product from the crystalline galactose, which was also identified, and the extract was found to contain 75.4% of the theoretical amount of β-thiophenol glucoside in one experiment and 84% in a second. The physical constants of the product, m. p. 125–128°, $[\alpha]_D$ $-65.9°$ in water, although improved by subsequent recrystallization, could not be made to agree with those of pure β-thiophenol glucoside, m. p. 133°, and $[\alpha]_D$ $-70.5°$ and the impure specimen was acetylated. A tetra-acetyl-β-thiophenol glucoside was thus obtained in 90% yield which possessed the same crystalline form, melting point and specific rotation as a standard preparation from glucose itself. Fischer and Delbrück[4] also carried out this hydrolysis with a similar result but unfortunately the scale of their experiment was too small to permit of the rigorous characterization of the particular type of thioglucoside which had been formed. It was therefore necessary to repeat their work.

The partial hydrolysis of β-thiophenol cellobioside was carried out in precisely similar fashion and yielded glucose, identified as glucosazone, and slightly impure β-thiophenol glucoside of the ordinary variety, identified as such and also as the pure tetra-acetate, m. p. 117°, $[\alpha]_D$ $-17.84°$ in chloroform. Although the hydrolysis of the thiocellobioside was discontinued when the specific rotation of the solution had increased to $[\alpha]_D$ $-23.0°$, that is, in close agreement with that of an equimolecular mixture of glucose and β-thiophenol glucoside, $[\alpha]_D$ $-21.5°$ in water, the yield of thiophenol glucoside extracted by ethyl acetate was only 51% of the theoretical. The easy separation of amorphous galactose from thiophenol glucoside by the same solvent stands in contrast to this observation.

From the foregoing, thiophenol lactoside and thiophenol cellobioside may be regarded as thiophenol glucosides of the normal ringed type substi-

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[4] Fischer and Delbrück, *Ber.*, **42**, 1476 (1909).

tuted by galactose and by glucose residues, respectively. This conclusion is entirely in accord with the commonly accepted constitution of the corresponding methyl glycosides due to Haworth and his collaborators[5] whose publications include a comprehensive review of the literature. As these authors examined the structure of methyl lactoside and cellobioside by the methylation method, the present work provides a direct and independent confirmation of an important part of their findings.

Experimental

Stability of β-Thiophenol Glucoside toward Aqueous Acid.—A solution of the glucoside in 0.5 *N* sulfuric acid had an initial observed reading of −3.005° in a 2-dm. tube and, after heating for two hours at 80° and for one hour at 100°, the liquid remained perfectly clear and did not smell of thiophenol. On cooling, the observed rotation was −2.995° and thiophenol glucoside was therefore stable under these conditions.

When the thioglucoside was boiled under a reflux condenser with sulfuric acid of normality 0.8 *N*, an initial reading of −1.240° changed to one of −1.222° in the course of three hours, while the solution acquired a faint odor of thiophenol. As complete hydrolysis to glucose and thiophenol required a change in the observed reading from −1.240 to 0.611°, that which occurred was of the order of 1%.

Thiophenol Glucoside from Thiophenol Lactoside.—Five grams of the thiophenol lactoside was dissolved in normal sulfuric acid and the solution, volume exactly 50 cc., was heated for an hour on the water-bath. The specific rotation increased during this time from $[\alpha]_D$ −38.3° (observed in a 2-dm. tube, the rotation was 7.65° to the left) to $[\alpha]_D$ −19.1° (observed α −3.81°) but subsequent determinations were made uncertain by the presence of thiophenol. After continuing the heating for forty-five minutes, the cloudy solution was neutralized with aqueous alcoholic caustic soda and after a filtration was found to turn plane-polarized light 0.96° to the left when in a 2-dm. tube. As the total volume was now 116 cc., the observation corresponds to a specific rotation of $[\alpha]_D$ −10.66°, corrected on the assumption that the change to galactose and β-thiophenol glucoside had been quantitative. The theoretical rotation for such an equimolecular mixture is $[\alpha]_D$ −9.56°, measured in distilled water.

The solvents were removed by evaporation under diminished pressure, the dry residue was repeatedly extracted with ethyl acetate and 2.4137 g. of fine needles was recovered from the concentrated extracts by the cautious addition of ether. The crude product, melting at 125–128° and with a specific rotation in water of $[\alpha]_D^{20}$ −65.91° (0.2105 g. in 25 cc. had α −1.115° when observed in a 2-dm. tube) was therefore recovered in 75.4% of the theoretical yield. After two recrystallizations from ethyl acetate, the preparation had a melting point of 130–132°, of 132–133° when mixed with an authentic specimen of pure β-thiophenol glucoside and a specific rotation of $[\alpha]_D^{19}$ −69.2° in water. The constants for pure β-thiophenol glucoside are m. p. 133° and $[\alpha]_D^{20}$ −70.5° in water.

Acetic anhydride and anhydrous sodium acetate acetylated the material and tetra-acetyl-β-thiophenol glucoside was recovered in 90% yield after being recrystallized from alcohol. The physical constants, m. p. 117° and $[\alpha]_D^{17}$ −18.0° in chloroform (0.6701 g. in 25 cc. had an observed reading of 0.965° to the left in a 2-dm. tube), were in excellent agreement with those accepted as correct for tetra-acetyl β-thiophenol glucoside, m. p. 117° and $[\alpha]_D^{20}$ −17.5° in the same solvent. A mixture of the two specimens also melted at 117°.

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[5] Haworth and Long, *J. Chem. Soc.*, **131**, 544 (1927); Haworth, Long and Plant, *ibid.*, 2809 (1927).

The residue from the hydrolysis which was insoluble in ethyl acetate was extracted with methyl alcohol to recover the reducing sugar, which slowly crystallized from the extract after the alcohol had been replaced by a little glacial acetic acid; yield, 0.826 g., or 41% of the theoretical. The crystals were those of α-galactose and without further purification displayed a mutarotation in water of $[\alpha]_D$ 140° (extrapolated) to an equilibrium rotation of $[\alpha]_D$ 77.35°, in fair agreement with the constants accepted for the pure sugar, $[\alpha]_D$ 144° to $[\alpha]_D$ 80.5° (0.4929 g. in 25 cc. gave a final observed reading of 3.051° to the right in a 2-dm. tube).

Thiophenol Glucoside from Thiophenol Cellobioside.—4.7926 g. of pure β-thiophenol cellobioside was dissolved in normal sulfuric acid and the solution, volume exactly 100 cc. and having an observed rotation in a 2-dm. tube of −5.29°, was heated on a steam-bath for three hours. At the end of that time the liquid was cooled, made up to its original bulk with water and shaken with a few cc. of chloroform to dissolve a trace of thiophenol and a small orange precipitate. The optical rotation of the aqueous portion had then increased to −2.29°, corresponding to a specific rotation of $[\alpha]_D^{17}$ −23.0° when calculated on the basis that the hydrolysis to glucose and thiophenol glucoside had been quantitative. The theoretical specific rotation for this mixture is $[\alpha]_D^{20}$ −21.5°, measured in distilled water.

After removing the free acid as barium sulfate, the solution was evaporated to dryness under diminished pressure and the residue was extracted ten times in succession with boiling ethyl acetate. The thiophenol glucoside isolated from the extract and once recrystallized weighed 1.505 g. or 50% of the theoretical, melted at 125–127°, at 128–129° when mixed with authentic β-thiophenol glucoside and had a specific rotation in water of $[\alpha]_D^{26}$ −65.13° (0.4578 g. in 25 cc. had an observed reading in a 2-dm. tube of 2.386° to the left). It was thus impure and was acetylated in the usual way to give an almost quantitative yield of tetra-acetyl-β-thiophenol glucoside whose melting point of 117° was not depressed by admixture with the standard substance. The specific rotation of $[\alpha]_D^{18}$ −18.25° in chloroform (0.3051 g. in 25 cc. had α −0.445° in a 2-dm. tube) was reduced to $[\alpha]_D^{18}$ −17.84° by a recrystallization from alcohol (0.4737 g. in 25 cc. of chloroform had α −0.676° in a 2-dm. tube) and thus agreed well with the standard rotation of $[\alpha]_D^{20}$ −17.5° for tetra-acetyl-β-thiophenol glucoside.

The residue from the ethyl acetate extractions failed to crystallize but yielded an osazone, decomposing at 204° when heated on the water-bath with phenylhydrazine and acetic acid. After a purification from aqueous pyridine, 0.1 g. was made up to 5 cc. with ethyl alcohol containing 40% by volume of pyridine and the solution was examined polarimetrically after having stood for eighteen hours in a 0.5-dm. tube. The observed rotation, −0.40°, was identical with that possessed by an authentic sample of glucosazone in the same circumstances.[6]

The author wishes to thank Dr. C. S. Hudson for his interest in the research and for many valuable suggestions. He also expresses his great indebtedness to the Commonwealth Fund of New York for the Fellowship which made the research possible.

Summary

1. β-Thiophenol lactoside and β-thiophenol cellobioside, on partial hydrolysis with aqueous acid, yielded a β-thiophenol glucoside identical in all respects with a specimen prepared from glucose itself.

2. It was concluded from the above evidence that the glucose resi-

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[6] Levene and LaForge, *J. Biol. Chem.*, **20**, 429 (1915).

due common to the thioglycosides of both these disaccharides possessed an oxygen bridge linking in the normal position.

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[CONTRIBUTION FROM THE POLARIMETRY SECTION, BUREAU OF STANDARDS, U. S. DEPARTMENT OF COMMERCE]

RELATIONS BETWEEN ROTATORY POWER AND STRUCTURE IN THE SUGAR GROUP. XXIII. THE PREPARATION AND THE STRUCTURE OF BETA-THIOPHENOL MALTOSIDE AND OF ITS HEPTA-ACETATE[1,2]

BY CLIFFORD B. PURVES

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β-Thiophenol cellobioside and β-thiophenol lactoside, according to the evidence presented in the preceding paper,[2] may be regarded as derivatives of a β-thiophenol glucoside of the normal ring structure. The two compound thioglycosides were submitted to the action of aqueous acid in such a way that glucose, or galactose, and thiophenol glucoside formed the main products of the partial hydrolysis. On examination, the specimens of thiophenol glucoside so prepared were found to be identical in all respects with one derived from acetobromoglucose and potassium thiophenate. It was this fact which led to the above conclusion, although it will be noticed that the reasoning involved the assumption that the relatively great stability of the thioglycosides toward acid hydrolysis precluded any change in their ring structure during the course of the experiment.

The examination of maltose in similar fashion was beset with the difficulties found in obtaining an adequate supply of hepta-acetyl-β-thiophenol maltoside in a pure condition. These were largely due to the unsatisfactory nature of the reaction between hydrogen bromide in glacial acetic acid–chloroform solution and maltose β-octa-acetate, which fails to result in a crystalline acetobromo derivative. This compound formed the starting point in the preparation of the thiophenol glycoside acetate. When the action of the hydrogen bromide solution was limited to two and one-half hours at 0°, 60% of the octa-acetate was recovered unchanged after the remainder had been condensed with potassium thiophenate, in spite of the fact that a 500% excess of the gas had been used and that similar acetates, such as those of glucose or cellobiose, give almost quanti-

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[1] Publication approved by the Director of the Bureau of Standards, U. S. Department of Commerce.

[2] The author has arranged with Dr. C. S. Hudson, under whose direction the research was carried out, that it will be included as No. XXIII in his series entitled "Relations between Rotatory Power and Structure in the Sugar Group." No. XXII was published in THIS JOURNAL, **51,** 3627 (1929).