ml. with distilled water. All reactions were conducted at room temperature (23–25°).

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Addendum. During the preparation of this report an abstract by B. Kadis[17] appeared which proposed a similar Meerwein-Ponndorf-Verley reduction mechanism for DPN reduction.

LAWRENCE, KAN.

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

Ethyl 1-Thio-α-D-galactofuranoside

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Partial demercaptalation of D-galactose diethyl dithioacetal (mercaptal) (I) leads to the synthesis of ethyl 1-thio-α-D-galactofuranoside (II) characterized by periodate oxidation and by its crystalline tetraacetate IV.

Schneider and co-workers[2,3] synthesized alkyl 1-thio-α-D-glucosides by treating an aqueous solution of D-glucose dialkyl dithioacetal (mercaptal) at room temperature with one mole of mercuric chloride and neutralizing the acid formed with alkali. With more mercuric chloride, complete demercaptalation occurred to produce the free sugar in aqueous solution or the alkyl glycoside in alcohol solution. However, attempts to prepare an ethyl 1-thio-D-galactoside (II) by treatment of D-galactose diethyl dithioacetal (I) with one mole of mercuric chloride, under neutral conditions, failed.[3,4] There was obtained instead, in ethanolic solution, equimolar amounts of ethyl β-D-galactofuranoside and starting material (I), which Green and Pacsu[4] ascribed to the reactivity of the thioglycoside (II) to solvolysis promoted by mercuric chloride. Green and Pacsu[4] concluded, on the basis of rotation values and ease of acid hydrolysis, that the glycosides formed from the dithioacetals were furanosides. Utilizing periodate oxidation data, Wolfrom and co-workers[5] verified this ring assignment for ethyl 1-thio-α-D-glucofuranoside derived from the dithioacetal.

We report herein the synthesis of sirupy ethyl 1-thio-α-D-galactofuranoside (II) and its crystalline tetraacetate (IV), using essentially the method of Green and Pacsu[4] but supplemented with chromatographic techniques not at the time available to these workers. A reappraisal of the feasibility of partial demercaptalation of I to II stemmed from the need of the analogous 2-acetamido-2-deoxy-1-thio-α-D-galactofuranoside as an intermediate in the synthesis of 2-amino-2-deoxy-L-arabinose from 2-amino-2-deoxy-D-galactose.[6] D-Galactose diethyl dithioacetal (I) was treated with an aqueous solution of mercuric chloride in the presence of mercuric oxide, to produce nearly equimolar amounts of ethyl 1-thio-α-D-galactofuranoside (II) and D-galactose (III). The latter substance (III) was removed by its exhaustive fractional precipitation from alcoholic solution. The mother liquor was acetylated and further purified by silicate column elution chromatography to give crystalline IV, recrystallized from diethyl ether–petroleum ether, m.p. 50.5–51.5°, $[\alpha]_D$ +118° (chloroform) and +127° (ethanol). This substance showed weak infrared absorption at 648 and 682 cm.$^{-1}$ Sheppard[7] cites 600–700 cm.$^{-1}$ as the region for C—S bond absorption.

The ring structures of II and IV were assigned on the basis of sodium metaperiodate oxidation (Table I) of sirupy II, $[\alpha]_D$ +124° (water), obtained from pure IV by deacetylation. The oxidation conditions employed were essentially those of Wolfrom and Yosizawa.[6] It has been shown[5,6] that the rapid liberation of one mole of formaldehyde by periodate ion is characteristic of 1-thiohexofuranosides and it is further known that the presence of the thioethoxyl group results in some overoxidation of an obscure nature.[8] Although a number of 1-thio-β-D-glycopyranosides have been reported,[8,9] to our knowledge II is the first 1-thio-D-galactoside to be recorded.

(1) National Science Foundation Research Associate (Z. Y.) and Predoctoral Fellow (B. O. J.), 1957–1958, under Grant NSF-G4494 to The Ohio State University.

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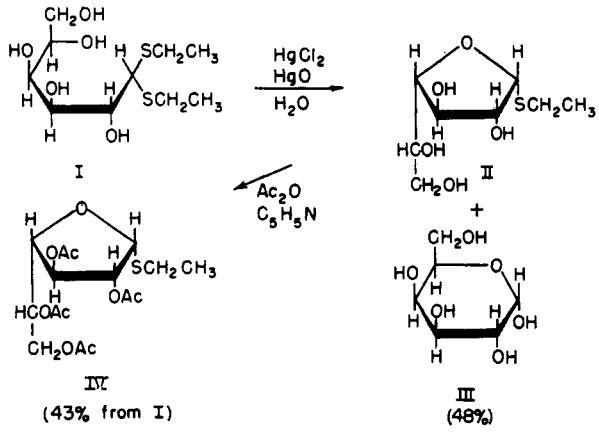
TABLE I

SODIUM METAPERIODATE OXIDATION OF ETHYL 1-THIO-α-D-GALACTOFURANOSIDE (II, 1%) AT 5°, *p*H 4.5 IN THE DARK

Time, Hr.	Oxidant[a] Added	Oxidant[a] Used[b]	Formaldehyde[a] Formed[c]	Formic Acid[a] Formed[d]
0.5	6	2.76	0.99	<0.10
1.0	6	3.12	—	<0.10
2.0	6	3.65	—	—
4.0	6	4.38	—	0.25
24.0	6	5.23	—	0.30
0.5	2	1.46	0.98	0.00
1.8	2	1.83	—	—

[a] Moles per mole of sample. [b] Determined iodometrically. [c] By dimedon assay. [d] Titrable acidity, phenolphthalein endpoint.



EXPERIMENTAL

Ethyl tetra-O-acetyl-1-thio-α-D-galactofuranoside (IV). The preparation of ethyl 1-thio-α-D-galactofuranoside (II) essentially followed the procedure of Green and Pacsu[4] for preparing ethyl 1-thio-α-D-glucofuranoside from D-glucose diethyl dithioacetal. D-Galactose diethyl dithioacetal[10] (I, 19 g., m.p. 140–142°) was dissolved in 800 ml. of water at 70°, and the solution cooled to 50°. In this solution was suspended washed yellow mercuric oxide,[11] prepared from 18.1 g. of mercuric chloride and 5.33 g. of sodium hydroxide, and then an aqueous solution of mercuric chloride (9.04 g. in 500 ml., 0.5 equiv.) was added dropwise, with vigorous stirring, over a period of 30 min. The stirring was continued for 40 min. more, after which 8 ml. of pyridine was added and the reaction mixture was filtered through an asbestos mat. The combined filtrate and washings were concentrated under reduced pressure and the resultant sirup was dried by repeated evaporation from ethanol solution under reduced pressure. Paper chromatography at this stage, using Whatman No. 1 filter paper with 1-butanol, ethanol, and water (40:11:19 by vol.) as developer and periodate-permanganate-benzidine indicator,[12] separated two compounds, one with the same R_F value, 0.22, as D-galactose (III), and a nonreducing substance, R_F 0.67, different from I, R_F 0.79. Separation was made by twice dissolving the sirup in methanol (300 ml.), filtering insoluble material which separated on standing and evaporating the solvent from the filtrate under reduced pressure. The resultant sirup was similarly subjected to two fractional precipitations from ethanol (300 ml.). The final sirup was dissolved in 100 ml. of ethanol and the solution was maintained at 5° for 10 hr. The insoluble material which separated was removed by filtration and, together with the previously collected precipitates, was found to be identical chromatographically with D-galactose (III); total yield 5.75 g. (48% from I). The mother liquor, after concentration to a thick sirup, was dried over phosphorus pentoxide under reduced pressure; yield 9.2 g. The dried sirup was acetylated with a mixture of 50 ml. each of acetic anhydride and pyridine at room temperature for 24 hr. The reaction mixture was then poured into 500 ml. of ice and water and extracted with chloroform. The extract was washed successively with water, sodium bicarbonate aqueous solution, and water and evaporated under reduced pressure to a sirup, which was dried by repeated evaporation from ethanol; yield 14.6 g. This material was dissolved in 50 ml. of benzene and was placed on a column (110 × 75 mm., diam.) of Magnesol[13]–Celite[14] (5:1 by wt.) and developed with 3000 ml. of a mixture of benzene and ethanol (100:1 by vol.). The eluate was concentrated to a sirup and further dried by repeated evaporation with ethanol. On drying over phosphorus pentoxide under reduced pressure, the residual sirup crystallized in long, fine white needles; yield 11.18 g. (43% from I) of ethyl tetra-*O*-acetyl-1-thio-α-D-galactofuranoside (IV), m.p. 50.5–51.5°. Two recrystallizations from diethyl ether–petroleum ether gave essentially the same crystals, m.p. 50.5–51.5°, $[\alpha]_D^{25}$ +118° (*c* 1.11, chloroform), +127° (*c* 2.20, ethanol), X-ray powder diffraction data[15]: 9.48 vs (1), 8.82 m, 5.12 s (2, 2), 4.63 s (2, 2), 4.23 vw, 4.09 vw, 3.95 m, 3.81 m, 3.60 w, 3.43 m, 3.04 m, 2.66 vw, 2.45 w, 2.22 vw, 1.81 vw. The substance showed weak infrared absorption bands (potassium bromide pellet) at 648 and 682 cm.$^{-1}$

Anal. Calcd. for $C_{16}H_{24}O_9S$: C, 48.97; H, 6.16; S, 8.17; $COCH_3$, 43.87. Found: C, 48.99 H, 6.27; S, 8.03; $COCH_3$ (Kunz[16] method), 43.66; Fehling test (−).

Ethyl 1-thio-α-D-galactofuranoside (II). An amount of 0.4 g. of IV was dissolved in 30 ml. of methanol nearly saturated with anhydrous ammonia at 0°. The solution was maintained at room temperature for 2 hr., filtered and concentrated under reduced pressure below 35° to a thick sirup. This was connected overnight to a vacuum system to sublime traces of acetamide. The sirupy residue was further dried by repeated evaporation of its methanol solution and by storing over phosphorus pentoxide under reduced pressure. It was characterized as ethyl 1-thio-α-D-galactofuranoside (II), $[\alpha]_D^{25}$ +124° (*c* 1.36, water). Attempts to crystallize II failed.

Anal. Calcd. for $C_8H_{16}O_5S$: C, 42.84; H, 7.19; S, 14.30. Found: C, 42.82; H, 7.16; S, 14.02; Fehling test (−).

Periodate oxidation (Table I) together with the above data indicate that II is ethyl 1-thio-α-D-galactofuranoside, and that IV is its tetra-*O*-acetyl derivative. Paper chromatography, using Whatman No. 1 filter paper, with 1-butanol, pyridine, and water (3:2:1.5 by vol.) as developer and periodate permanganate–benzidine indicator[12] showed that II was chromatographically pure, and had a $R_{Galactose}$ value of 3.0 (the R_F values of II and III were 0.67 and 0.22, respectively).

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(14) No. 535, a siliceous filter-aid produced by the Johns-Manville Co., New York, N. Y.

(15) Interplanar spacing, Å, CuK_α radiation. Relative intensity, estimated visually: s, strong; m, medium; w, weak; v, very. First three strongest lines are numbered (1, strongest); duplicate numbers indicate approximately equal intensities.

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