Anal. Calcd for $C_8H_8BrN_3$: C, 42.50; H, 3.57; N, 18.59. Found: C, 42.25; H, 3.50; N, 18.48.

Calculation of Chemical Shifts.—The ring-current calculations were done by the method of Pople.[17] The geometries of a regular hexagon and a regular pentagon were assumed for the six- and five-membered rings, respectively. The lengths of the sides were taken to be 1.08 A. Each ring was assumed to have six π electrons. Electron density field effects were calculated by the method of Schweizer and co-workers.[11] The electron densities used in these calculations are those obtained from a modified HMO calculation.[1]

(17) J. A. Pople, *J. Chem. Phys.*, **24**, 1111 (1956).

Synthesis of Purine and Pyrimidine Nucleosides of Thiopentoses[1]

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Condensation of 2,3,5-tri-*O*-acetyl-4-thio-α,β-D-ribofuranosyl chloride (I) with 2,4-diethoxy-5-methylpyrimidine followed by methanolysis produces the α and β anomers of 1-(4-thio-D-ribofuranosyl)thymine (IIIa and b). When condensation was made with compound I and 2,4-diethoxypyrimidine the corresponding uracil (VIa and b) or cytosine (VIIa and b) nucleosides were produced, after methanolysis or ammonolysis. In all instances α-D and β-D anomers were formed in ratio of 1:2. A similar sequence of reactions was used for the preparation of nucleosides of 5-thio-D-xylose. A purine nucleoside of 5-thio-D-xylose was prepared by condensing compound VIII with 6-benzamido-9-chloromercuripurine. In the D-xylose series only one anomeric nucleoside was isolated.

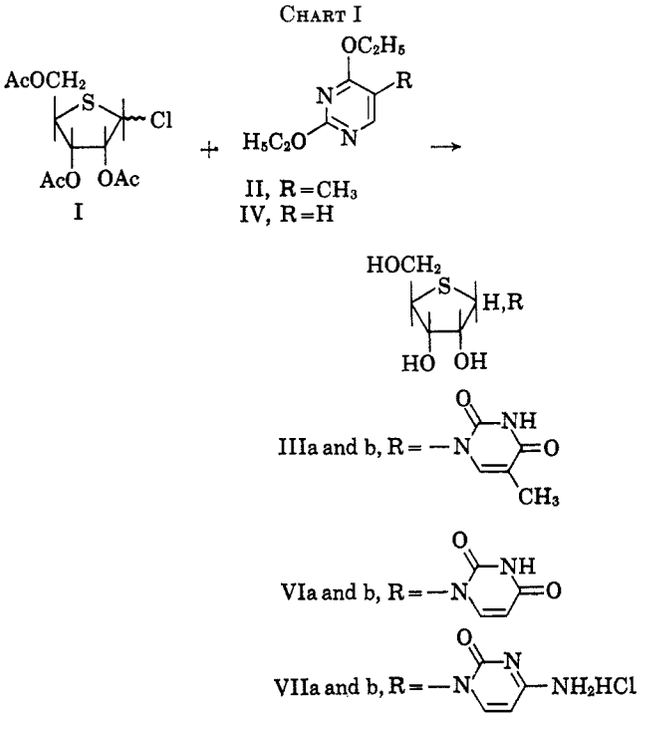
In recent years this laboratory has been active in the synthesis of aldoses in which the normal ring oxygen is replaced with a sulfur atom. Such so-called thio sugars or their derivatives represent a new class of compounds which may have unusual physiological properties.

The D and L isomers of 9-(4-thioribofuranosyl)-adenine nucleosides have been previously described.[2] We wish to report herein the synthesis of pyrimidine and purine nucleosides of 4-thio-D-ribofuranose[3] and 5-thio-D-xylopyranose.[4]

The most promising methods available for the synthesis of pyrimidine and purine nucleosides appeared to be the method of Hilbert–Johnson and the mercury salt procedure. These methods have been used here. Attempts to use the mercury procedure for the synthesis of pyrimidine nucleoside were repeatedly unsuccessful due presumably to the instability of the thio sugar.

The starting material for the synthesis of the 4-thio-D-ribofuranose nucleoside was methyl 4-deoxy-2,3-*O*-isopropylidene-4-thioacetyl-β-D-ribofuranoside. Treatment of this compound with aqueous acetic acid followed by acetolysis under the usual conditions[5] gave two anomeric 1,2,3,5-tetra-*O*-acetyl-4-thio-D-ribofuranoses. The anomeric mixture was converted to the syrupy 2,3,5-tri-*O*-acetyl-4-thio-D-ribofuranosyl chloride (I), which was further condensed with an excess of 2,4-diethoxy-5-methylpyrimidine[6] to yield the corresponding blocked pyrimidine nucleoside. In this condensation α-D and β-D anomers of 1-(2,3,5-tri-*O*-acetyl-4-thio-D-ribofuranosyl)-4-ethoxy-5-methyl-2(1H)-pyrimidinone were isolated as a syrup which was separated on a silica gel column. The first anomer had a rotation of $[\alpha]_D$ −14.9° and after methanolysis gave thymine nucleoside IIIa, $[\alpha]_D$ −44°, while the second blocked nucleoside with $[\alpha]_D$ +8° gave after methanolysis another anomer (IIIb) with a rotation of $[\alpha]_D$ +20°. (See Chart I.)

CHART I



When the sugar chloride I was condensed with 2,4-diethoxypyrimidine[7,8] under the same conditions, two anomeric forms of 1-(2,3,5-tri-*O*-acetyl-4-thio-D-ribofuranosyl)-4-ethoxy-2(1H)-pyrimidinone were isolated. The anomer Va, with a rotation of $[\alpha]_D$ +1.3°, after methanolysis gave uracil nucleoside VIa, $[\alpha]_D$ −22°, while the other anomer Vb, with a rotation of −7.4°, gave uracil nucleoside VIb, $[\alpha]_D$ +3.1°, after methanolysis. When either compound Va or Vb was treated with methanolic ammonia, the corresponding

(1) Journal Paper No. 2654 of Purdue Agricultural Experiment Station, Lafayette, Ind. Presented in part at the 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965.

(2) E. J. Reist, D. E. Gueffroy, and L. Goodman, *J. Am. Chem. Soc.*, **86**, 5658 (1964).

(3) R. L. Whistler, W. E. Dick, T. R. Ingle, R. M. Rowell, and B. Urbas, *J. Org. Chem.*, **29**, 3723 (1964).

(4) D. L. Ingles and R. L. Whistler, *ibid.*, **27**, 3896 (1962).

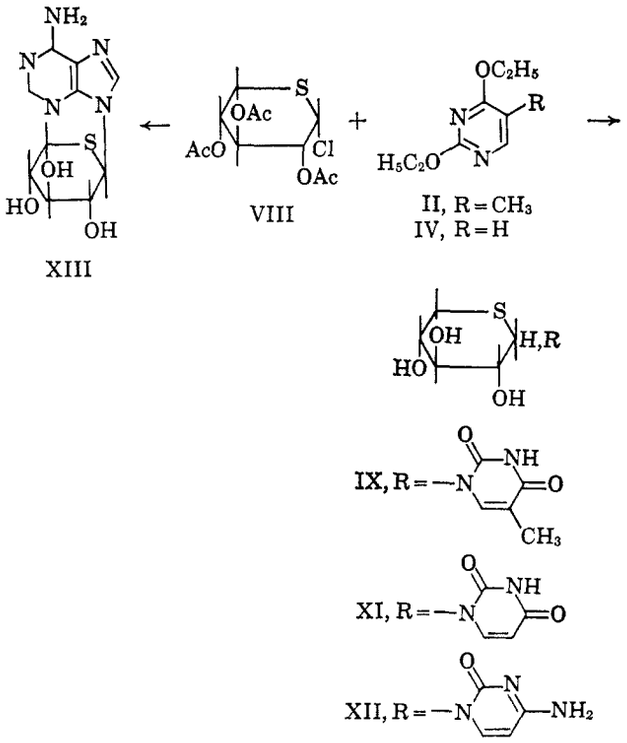
(5) M. S. Feather and R. L. Whistler, *Tetrahedron Letters*, **No. 15**, 667 (1962).

(6) W. Schmidt-Nickels and T. B. Johnson, *J. Am. Chem. Soc.*, **52**, 4511 (1930).

(7) G. E. Hilbert, *ibid.*, **59**, 330 (1937).

(8) G. E. Hilbert and E. F. Jansen, *ibid.*, **58**, 60 (1936).

CHART II



cytosine nucleosides of 4-thio-D-ribose (VIIa and b) were formed and characterized as the hydrochlorides.

Recently, Fox and co-workers[9] have compiled conclusive evidence that the synthesis of pyrimidine nucleoside by the Hilbert and Johnson's method can yield mixtures of α and β nucleoside of pentoses when there is a participating group in the 2-position. They found that the "*trans* rule" is not wholly operative. The same conclusion was drawn by Naito and Kawakami[10] from their work with poly-*O*-acyl-D-ribo- and D-xylopyranosyl halides. The results of our experiments, in which the α and β anomeric nucleosides are formed in the ratio of 1:2, respectively, support these findings. In this work α-D and β-D anomeric assignments are made on the basis of rotation; the most positive rotating anomer is designated as α-D.

A similar series of reactions was conducted with 5-thio-D-xylose. (See Chart II.) Thus, 1,2,3,4-tetra-*O*-acetyl-5-thio-D-xylopyranose, treated with ethereal hydrogen chloride, produced crystalline α-D and β-D anomers of the sugar chloride. Condensation of the sugar chloride VIII with 2,4-diethoxypyrimidine gave crystalline 1-(2,3,4-tri-*O*-acetyl-5-thio-D-xylopyranosyl)-4-ethoxy-2(1H)-pyrimidinone (X). If this compound was treated with methanolic hydrogen chloride, the crystalline uracil derivative of 5-thio-D-xylose (XI) was obtained, whereas, when it was treated with methanolic ammonia, the crystalline cytosine nucleoside of 5-thio-D-xylose was isolated. Condensation of compound VIII with 2,4-diethoxy-5-methylpyrimidinone gave a syrupy condensation product which after methanolysis gave crystalline 1-(5-thio-D-xylopyranosyl)thymine (IX). The purine nucleoside of 5-thio-D-xylose was prepared by condensation of the sugar chloride VIII with 6-benzamido-9-chlormercuripurine[11] to give 9-(2,3,4-tri-*O*-acetyl-5-thio-D-xylopyranosyl)-6-benzamidopurine. The product was treated with methanolic sodium methoxide and the resulting material was purified through the picrate to give crystalline 9-(5-thio-D-xylopyranosyl)adenine.

Two anomeric nucleosides might be expected in the synthesis of pyrimidine and purine nucleoside of 5-thio-D-xylose by both procedures but only one form was isolated.

Experimental Section

Analytical Methods.—Chromatographic determination of purity of nucleosides was made at 25° on Whatman No. 1 filter paper, using (A) 1-butanol–acetic acid–water (5:2:3 v/v), (B) water-saturated 1-butanol, or (C) 5% aqueous disodium hydrogen phosphate as developing solvents. The components were located by visual examination with an ultraviolet lamp. Thin layer chromatograms were made on silica gel[12] G coated plates and spots were located by spraying with 5% ethanolic sulfuric acid and charring. Melting points are corrected and were determined on a Fisher-Johns apparatus. Optical rotations are equilibrium values.

Methyl 4-Deoxy-2,3-*O*-isopropylidene-4-thioacetyl-β-D-ribopyranoside.—The method previously described for the synthesis of this compound[3] was improved through shortening the displacement reaction with thioacetate anion from 3 to 2 hr and by evaporating the combined heptane extracts to dryness and acetylating the residue with acetic anhydride in pyridine. The product was recrystallized from hexane to give a 70–80% yield.

1,2,3,5-Tetra-*O*-acetyl-4-thio-α,β-D-ribofuranose.—Methyl 2,3-*O*-isopropylidene-4-thioacetyl-β-D-ribopyranoside (10.5 g, 0.04 mole) was dissolved in 200 ml of 50% aqueous acetic and the mixture was heated at 70° for 4 hr. After hydrolysis the solution was evaporated under reduced pressure and dried by alcohol distillation. The product was a white solid which was dissolved in an ice-cold solution of 76 ml of glacial acidic acid, 76 ml of acetic anhydride, and 5 ml of sulfuric acid,[5] and was stored at 0° for 2 days. At the end of this time, sodium acetate (20 g) was added to the reaction mixture which was stirred for 30 min and poured into a mixture of ice and water. The solution was extracted three times with 100-ml portions of chloroform, and the combined extracts were washed several times with water, dried over sodium sulfate, and evaporated under reduced pressure to a syrup (12.9 g, 96%). Thin layer chromatography showed that the syrupy material obtained was composed of two acetates, which were separated by chromatography on a silica gel column[13] irrigated with hexane–ethylacetate (7:3 v/v). The β-D-acetate (10 g) which separated from the column first, crystallized immediately upon evaporation of the solvent. It had mp 60–65°, raised on recrystallization from methanol to mp 66°, $[\alpha]^{25}D$ −102° (*c* 2.04, chloroform).

Anal. Calcd for $C_{13}H_{18}O_8S$: C, 46.70; H, 5.43; S, 9.59. Found: C, 46.90; H, 5.61; S, 9.58.

The second acetate, the α-D anomer, was isolated as 1.8 g of syrup, which was further purified by distillation at 110–115° and 0.02 mm: $[\alpha]^{25}D$ +123.4° (*c* 2.44, chloroform).

Anal. Found: C, 46.84; H, 5.4; S, 9.34.

1,2,3,5-Tetra-*O*-benzoyl-4-thio-D-ribofuranose.—1,2,3,5-Tetra-*O*-acetyl-4-thio-α,β-D-ribofuranose (3.3 g, 0.01 mole) was dissolved in 50 ml of 2 *N* methanolic sodium methoxide and allowed to stand at 25° for 2 hr. The solution was then passed through a column of Amberlite IR-120 (H^+). Evaporation of the effluent under reduced pressure gave 1.5 g of slightly yellow syrupy 4-thio-D-ribofuranose. This was dissolved in 80 ml of pyridine and cooled to 0°, and 7.0 g of benzoyl chloride was added dropwise, with stirring.[14] After the addition was completed, the reaction mixture was stored overnight at 25° and then poured into a mixture of ice and water. The water solution was extracted three times with 100-ml portions of chloroform, and the combined extracts were washed sequentially with water,

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(12) Brickman Instruments Inc., Great Neck, N. Y.

(13) J. T. Baker Chemical Co., Phillipsburg, N. J.

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10% copper sulfate, and again with water. The chloroform solution was dried over sodium sulfate, and then concentrated to a syrup which crystallized from hot ethanol to give 3.5 g (60%) of a tetrabenzoate, mp 124–125°, $[\alpha]^{27}D$ −41.7° (*c* 1.77, chloroform).

Anal. Calcd for $C_{33}H_{26}O_8S$: C, 68.03; H, 4.50; S, 5.50. Found: C, 67.85; H, 4.57; S, 5.57.

1-(4-Thio-α,β-D-ribofuranosyl)thymine (IIIa and b).—1,2,3,5-tetra-*O*-acetyl-4-thio-α,β-D-ribofuranose (1.7 g, 0.005 mole) and 2 ml of acetyl chloride in 100 ml of anhydrous ether were saturated with dry hydrogen chloride at 0°. After 4 days at 5° the solution was concentrated under reduced pressure to a syrup. Traces of hydrogen chloride were removed by repeated distillation with anhydrous benzene under reduced pressure. The yield was 1.7 g of 2,3,5-tri-*O*-acetyl-4-thio-D-ribofuranosyl chloride (I). 2,4-Diethoxy-5-methylpyrimidine[6] (II, 1.7 g) was added to the chloro sugar and the mixture was kept at 90–95° (oil bath) for 5 days. The dark solution was diluted with 5 ml of ether. Upon the addition of hexane a gummy material separated which was chromatographed on a silica gel column (30 × 2 cm) using chloroform–acetone (15:1 v/v) as a solvent to give two anomeric blocked nucleosides. The faster moving compound on evaporation gave 0.52 g (23.8%) of syrup, $[\alpha]^{25}D$ −14.9° (*c* 2.8, chloroform), which was dissolved in 5 ml of 2% methanolic hydrogen chloride and left for 3 days at 25° in a flask protected by a drying tube. After removal of solvent, the product, 1-(4-thio-β-D-ribofuranosyl)thymine (IIIa), was crystallized from acetone–ether to give a product which had mp 175–176°; $[\alpha]^{25}D$ −44.7° (*c* 1.05, water); $\lambda_{max}^{pH\ 2}$ 271 mμ (ε 10,336), $\lambda_{min}^{pH\ 2}$ 237 mμ (ε 2553); $\lambda_{max}^{pH\ 12}$ 271 mμ (ε 8500), $\lambda_{min}^{pH\ 12}$ 247 mμ (ε 4680).

Anal. Calcd for $C_{10}H_{14}N_2O_5S$: C, 43.79; H, 5.14; N, 10.21; S, 11.69. Found: C, 43.63; H, 5.18; N, 10.05; S, 11.53.

The slower moving blocked nucleoside was isolated as a syrup, 0.240 g (11%), $[\alpha]^{25}D$ +8.6° (*c* 2.33, chloroform), which was worked up as described above. Recrystallization of this anomeric nucleoside (IIIb) was accomplished by dissolving in a minimum amount of methanol and adding ether: mp 217–218° dec; $[\alpha]^{25}D$ +20.9° (*c* 1.34, water); $\lambda_{max}^{pH\ 2}$ 270.5 mμ (ε 12,982), $\lambda_{min}^{pH\ 2}$ 236 mμ (ε 3403); $\lambda_{max}^{pH\ 12}$ 270.5 mμ (ε 11,261), $\lambda_{min}^{pH\ 12}$ 243 mμ (ε 5657).

Anal. Found: C, 43.84; H, 5.43; N, 10.03; S, 11.42.

The products (IIIa and b) were homogeneous on paper chromatography and had $R_{thymine}$ 0.82 and 0.93, respectively, in solvent A, 1.06 and 1.04 in solvent B, and 1.09 and 1.06 in solvent C.

1-(4-Thio-α,β-D-ribofuranosyl)uracil (VIa and b).—An excess of 2,4-diethoxypyrimidine[15,16] (IV, 2.1 g) and 2.1 g of chloro sugar I were heated at 90–95° in an oil bath for 5 days. After cooling to 25° the reaction mixture was diluted with 10 ml of ether and a syrup was precipitated by addition of hexane. The crude syrup was chromatographed on a column of silica gel, using chloroform–acetone (20:1 v/v) as a solvent. Two anomers of 1-(2,3,5-tri-*O*-acetyl-4-thio-D-ribofuranosyl)-4-ethoxy-2(1H)-pyrimidinone (Va and b) were separated.

The first compound (Va) was a yellow gum, 0.66 g, $[\alpha]^{25}D$ +1.3° (*c* 3.05, chloroform), which was homogenous as shown by thin layer chromatograms. It was dissolved in 10 ml of ether and left at 25° for 10 days during which time crystals were deposited which were collected by filtration and recrystallized three times from ethanol to yield 80 mg of pure material, mp 189–190°, $[\alpha]^{25}D$ −88° (*c* 1.6, chloroform).

Anal. Calcd for $C_{17}H_{22}N_2O_8S$: C, 49.27; H, 5.35; N, 6.76; S, 7.74. Found: C, 49.38; H, 5.34; N, 6.51; S, 7.80.

The crude compound Va (0.3 g) was treated with 2% methanolic hydrogen chloride for 3 days at 25° to give crystalline 1-(4-thio-β-D-ribofuranosyl)uracil (VIa), which was recrystallized from ethanol yielding 0.12 g, mp 191–192°, $[\alpha]^{25}D$ −22.9° *c* 2.1, water), $\lambda_{max}^{pH\ 2}$ 266 mμ (ε 10,291), $\lambda_{min}^{pH\ 2}$ 233 mμ (ε 2427), $\lambda_{max}^{pH\ 12}$ 266 mμ (ε 8283), $\lambda_{min}^{pH\ 12}$ 244 mμ (ε 5313). The same compound VIa was obtained when crystalline compound Va was treated with methanolic hydrogen chloride.

Anal. Calcd for $C_9H_{12}N_2O_5S$: C, 41.54; H, 4.64; N, 10.76; S, 12.32. Found: C, 41.32; H, 4.67; N, 10.51; S, 12.40.

The second compound (Vb) separated from the column gave, on evaporation, 0.32 g of a yellow gum, $[\alpha]^{21}D$ −7.4 (*c* 2.6, chloroform), which was further treated with 2% methanolic hydrogen chloride at 25° for 3 days to give a crystalline α-D anomer of compound VIb, which when recrystallized from ethanol–ether gave 70 mg: mp 246–248° dec, $[\alpha]^{25}D$ +3.1° (*c* 1.28, water), $\lambda_{max}^{pH\ 2}$ 266 mμ (ε 12,228), $\lambda_{min}^{pH\ 2}$ 232 mμ (ε 3015), $\lambda_{max}^{pH\ 12}$ 266 mμ (ε 8489), $\lambda_{min}^{pH\ 12}$ 242 mμ (ε 4827).

Anal. Found: C, 41.41; H, 4.91; N, 10.53; S, 12.18.

On paper chromatography the compounds VIa and VIb had R_{uracil} 0.85 and 0.93, respectively, in solvent A, 1.08 and 1.07 in solvent B, and 1.06 and 1.03 in solvent C.

1-(4-Thio-α,β-D-ribofuranosyl)cytosine (VIIa and b) Hydrochloride.—1-(2,3,4-Tri-*O*-acetyl-4-thio-D-ribofuranosyl)-4-ethoxy-2(1H)-pyrimidinone (Va, 0.3 g), $[\alpha]D$ +1.3°, was dissolved in 5 ml of methanol, and the mixture was saturated at 0° with anhydrous ammonia and then heated in a sealed tube at 90° for 3 days. The reaction solution was concentrated under reduced pressure to a yellow gum, which was dissolved in 4 ml of ethanol, and 2 drops of concentrated hydrochloride acid were added. After cooling, the crystalline product was collected by filtration and recrystallized from 90% ethanol. The yield of the analytically pure β-D anomer of compound VIIa was 90 mg: mp 226–228° dec; $[\alpha]^{25}D$ −3.4° (*c* 3.2, water); $\lambda_{max}^{pH\ 2}$ 214, 282 mμ (ε 10,468, 14,392); $\lambda_{min}^{pH\ 2}$ 241 mμ (ε 1626).

Anal. Calcd for $C_9H_{14}ClN_3O_4S$: C, 36.54; H, 4.77; N, 14.21; S, 10.84. Found: C, 36.29; H, 4.76; N, 14.32; S, 10.67.

The other anomer of 1-(4-thio-D-ribofuranosyl)cytosine (VIIb) hydrochloride was obtained when compound Vb, $[\alpha]^{25}D$ −7.4°, was treated with methanolic ammonia on the same way as above. The product was recrystallized from 90% ethanol: mp 208–210 dec.; $\lambda_{max}^{pH\ 2}$ 215, 283 mμ (ε 11,002, 13,486); $\lambda_{min}^{pH\ 2}$ 242 mμ (ε 1981); $[\alpha]^{25}D$ +0.7° (*c* 8.5, water).

Anal. Found: C, 36.59; H, 4.71; N, 14.15; S, 10.82.

The compounds VIIa and VIIb on paper chromatography had $R_{cytosine}$ 0.88 and 0.94, respectively, in solvent A, 1.08 and 1.02 in solvet B, and 1.05 and 1.03 in solvent C.

5-Thio-D-xylopyranose.—A solution of 20.6 g (0.1 mole) of 1,2-*O*-isopropylidene-5-deoxy-5-mercapto-α-D-xylofuranose and 500 ml of 20% acetic acid were heated at 70° for 8 hr. After hydrolysis the solution was evaporated under reduced pressure to give a syrup which crystallized when dried by repeated distillation of ethanol. The sugar was recrystallized from an ethanol–water mixture to give 13.3 g (80%), mp 128° (lit. mp 122–123°,[17] 127°[18]; 52.2% yield[4]).

2,3,4-Tri-*O*-acetyl-5-thio-α,β-D-xylopyranosyl Chloride.—A solution of 1,2,3,4-tetra-*O*-acetyl-5-thio-D-xylopyranose[17] (16.7 g, 0.05 mole) in 400 ml of dry ether was saturated with dry hydrogen chloride at 0°. The solution was stored for 3 days at 0–5°, resaturated with hydrogen chloride, and stored for an additional 7 days. The crystalline product was separated by filtration and recrystallized from hot ether to afford 3 g (18.3%) of the sugar chloride, mp 144–146°, $[\alpha]^{22}D$ −47° (*c* 1.0, carbon tetrachloride).

Anal. Calcd for $C_{11}H_{15}ClO_6S$: C, 42.52; H, 4.86; Cl, 11.41; S, 10.32. Found: C, 42.83; H, 4.83; Cl, 11.70; S, 10.19.

The mother liquor after isolation of the above anomer was concentrated under reduced pressure to a syrup. Traces of hydrogen chloride were removed by repeated distillation of benzene under reduced pressure. The syrup then crystallized from ether to yield 10 g (61%) of 2,3,4-tri-*O*-acetyl-5-thio-D-xylopyranosyl chloride (VIII), mp 128–130°, $[\alpha]^{22}D$ +158° (*c* 1.02, carbon tetrachloride).

Anal. Found: C, 42.60; H, 4.96; Cl, 11.76; S, 10.30.

1-(5-Thio-D-xylopyranosyl)thymine (IX).—A mixture of 3.1 g (0.01 mole) of the chloro sugar VIII and 3.3 g of 2,4-diethoxy-5-methylpyrimidine was heated at 120–125° in an oil bath for 3 days. To the cooled reaction mixture an equal amount of ether was added and the mixture was filtered. Upon the addition of hexane an oily product separated which was dissolved in ether and reprecipitated by the addition of more hexane. The dry product was dissolved in 5 ml of hot methanol, 10 ml of 2% methanolic hydrogen chloride was added, and the solution kept at 25° for 3 days. The crystalline product was collected by filtration, washed with ethanol, and recrystallized from 90% ethanol to give 0.4 g of nucleoside, mp 296–298° dec (uncor), $[\alpha]^{25}D$ +12.2° (*c* 1.3, 50% aqueous pyridine), $\lambda_{max}^{pH\ 2}$ 269 mμ (ε 11,272), $\lambda_{min}^{pH\ 2}$ 236 mμ (ε 2409), $\lambda_{max}^{pH\ 12}$ 269 mμ (ε 8868), $\lambda_{min}^{pH\ 12}$ 246 mμ (ε 5393).

(15) G. E. Hilbert and T. B. Johnson, *J. Am. Chem. Soc.*, **52**, 1152 (1930).
(16) G. E. Hilbert and T. B. Johnson, *ibid.*, **52**, 2001 (1930).
(17) T. J. Adley and L. N. Owen, *Proc. Chem. Soc.*, 418 (1961).
(18) J. C. P. Schwarz and K. C. Yule, *ibid.*, 417 (1961).

The product was chromatographically pure and had on paper chromatography $R_{thymine}$ values of 0.79, 1.08, and 1.09 in solvents A, B, and C, respectively.

Anal. Calcd for $C_{10}H_{14}N_2O_5S$: C, 43.79; H, 5.14; N, 10.21; S, 11.69. Found: C, 43.54; H, 5.02; N, 10.44; S, 11.62.

1-(2,3,4-Tri-*O*-acetyl-5-thio-D-xylopyranosyl)-4-ethoxy-2(1H)-pyrimidinone (X).—A mixture of 3.1 g (0.01 mole) of the chloro sugar VIII and 3.1 g of 2,4-diethoxypyrimidine was heated at 100° for 24 hr and then at 120–125° for 24 hr. The cooled reaction mixture was diluted with an equal amount of ether, filtered, and stored overnight at 0°. Compound X crystallized from the solution and was removed by filtraion to yield 0.6 g of material, mp 188°. Additional product was obtained from the concentrated mother liquor to give a total yield of 0.91 g (22%). Three recrystallizations from ethanol gave an analytically pure product, mp 201°, $[\alpha]^{22}D$ +27.9° (*c* 1.04, chloroform).

Anal. Calcd for $C_{17}H_{22}N_2O_8S$: C, 49.27; H, 5.35; N, 6.76; S, 7.74. Found: C, 49.07; H, 5.48; N, 6.40; S, 7.99.

1-(5-Thio-D-xylopyranosyl)uracil (XI).—To a solution of 0.41 g (0.001 mole) of compound X in 5 ml of methanol was added 1 ml of methanol previously saturated at 0° with hydrogen chloride. The solution was kept at 25° for 3 days during which time compound XI crystallized from the solution and was removed by filtration to give 0.24 g, mp 275–278°. Two recrystallization from 90% ethanol gave a pure product: mp 284–285° dec (uncor); $[\alpha]^{25}D$ +40.1° (*c* 1.52, water); $\lambda_{max}^{pH\ 2}$ 265 mμ (ε 11,692), $\lambda_{min}^{pH\ 2}$ 231 mμ (ε 2311); $\lambda_{max}^{pH\ 12}$ 265 mμ (ε 9051), $\lambda_{min}^{pH\ 12}$ 243 mμ (ε 6153). On chromatographic examination this nucleoside had R_{uracil} values of 0.87, 1.06, and 1.05 in solvents A, B, and C, respectively.

Anal. Calcd for $C_9H_{12}N_2O_5S$: C, 41.54; H, 4.64; N, 10.76; S, 12.32. Found: C, 41.33; H, 4.64; N, 10.63; S, 12.12.

1-(5-Thio-D-xylopyranosyl)cytosine (XII).—Compound X (0.3 g) was partially dissolved in 6 ml of methanol; the mixture was saturated at 0° with anhydrous ammonia and heated in a sealed tube at 90° for 3 days. The resultant solution was concentrated under reduced pressure to dryness. Crystallization of the residue from 90% ethanol gave compound XII (0.20 g): mp 287–288° dec (uncor); $[\alpha]^{25}D$ +26.3° (*c* 1.48, water); $\lambda_{max}^{pH\ 2}$ 281, 215 mμ (ε 14,313, 10,490), $\lambda_{min}^{pH\ 2}$ 242 mμ (ε 1981); $\lambda_{max}^{pH\ 12}$ 273, 231 mμ (ε 10,488, 8699), $\lambda_{min}^{pH\ 12}$ 251 mμ (ε 7398). The paper chromatography $R_{cytosine}$ values were 0.89, 1.05, and 1.03 in solvents A, B, and C, respectively.

Anal. Calcd for $C_9H_{13}N_3O_4S$: C, 41.69; H, 5.05; N, 16.21; S, 12.36. Found: C, 41.84; H, 5.23; N, 15.84; S, 12.50.

9-(5-Thio-D-xylopyranosyl)adenine (XIII).—A solution of 6.2 g (0.02 mole) of the sugar chloride VIII in 20 ml of azeotropically dried toluene was added to a mixture of 9.5 g of 6-benzamido-9-chloromercuripurine[19] in 500 ml of toluene previously dried by azeotropic distillation. The mixture was refluxed with stirring for 6 hr. The hot solution was filtered, and the filter cake was washed with toluene. The combined filtrate was concentrated under reduced pressure to a volume of 100 ml and precipitated with 400 ml of hexane. The precipitated blocked nucleoside was filtered and dissolved in 200 ml of chloroform. The chloroform solution was washed with two 100-ml portions of 30% potassium iodide, then with two 100-ml portions of water and dried over sodium sulfate. The solution was evaporated under reduced pressure to give a yellow gum, which was dissolved in 10 ml of ethyl acetate and stored overnight at 0°. The crystalline product (6-benzamidopurine) was removed by filtration and washed with ethyl acetate. The combined mother liquors were evaporated to dryness and the residue was dissolved in 20 ml of methanol, a catalytic amount of metallic sodium was added, and the solution was held at 25° for 10 hr and then refluxed for 15 min and evaporated to dryness. The residue was dissolved in 10 ml of water and neutralized with dilute acetic acid. To the neutralized solution was added 15 ml of a 10% ethanolic picric acid solution, and the mixture was left at 0° for 10 hr. The yellow picrate which formed was removed by filtration: yield 1.1 g, mp 230–231° dec (from water).

Anal. Calcd for $C_{16}H_{16}N_8O_{10}S$: C, 37.50; H, 3.15; N, 21.87; S, 6.26. Found: C, 37.68; H, 3.45; N, 22.09; S, 6.25.

The above picrate was dissolved, with stirring in hot water, and IR-400 (CO_3^{2-}) resin was added until the solution was colorless. The resin was then removed by filtration, and the filtrate was concentrated under reduced pressure to a white solid, which was recrystallized three times from absolute ethanol, giving 0.55 g (10%) of pure material which had mp 266–267° (uncor), $[\alpha]^{27}D$ +63.1° (*c* 1.52, 50% aqueous pyridine), $\lambda_{max}^{pH\ 2}$ 258 mμ (ε 14,752), $\lambda_{max}^{pH\ 7,12}$ 260 mμ (ε 15,104). The product was chromatographically pure and had on paper chromatography $R_{adenine}$ 0.95, 1.12, and 1.16 in solvents A, B, and C, respectively.

Anal. Calcd for $C_{10}H_{13}N_5O_3S \cdot 0.5C_2H_5OH$: C, 43.11; H, 5.26; N, 22.87; S, 10.47. Found: C, 42.95; H, 5.25; N, 23.24; S, 10.28.

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Synthesis of Septanose Derivatives of 6-Deoxy-6-mercapto-D-galactose[1]

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6-*O*-Tosyl-2,3,4,5-tetra-*O*-acetyl-D-galactose diethyl mercaptal was treated with thiolacetate to give the 6-deoxy-6-thioacetyl derivative. This on treatment with mercuric chloride and then hydrogen sulfide produced 6-deoxy-6-mercapto-2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-galactose, which on acetylation gave the crystalline α and β anomers of the pentaacetylthioseptanose. These, with hydrogen chloride, produced the α and β anomeric chlorides of which the α-D crystallized. These were converted to anomers of the methyl D-galactothioseptanoside tetraacetate of which the β-D anomer crystallized and on deacetylation gave crystalline methyl β-D-galactothioseptanoside, which hydrolyzed in 0.5 *N* acid at 25° with $k = 9.6 \times 10^2$ min^{-1}. The appropriate structure is shown by periodate oxidation.

This laboratory has been interested for some time in the preparation of metabolically important sugars and sugar derivatives wherein the normal ring oxygen is replaced by sulfur. Sulfur as a thiol in the appropriate location of a sugar molecule is found to react readily with the potentially aldehydic carbon to form, depending on the location of the mercapto group, either a thiofuranose or thiopyranose ring. Such thio sugars behave chemically in much the same way as the normal oxygen sugars. In the course of characterization of thio sugar ring systems, it is of interest to determine if a 6-deoxy-6-mercaptohexose can form a seven-membered septanose ring. A thiepane ring has been made by the interaction of sodium sulfide with 1,6-dibromohexane.[2] Thiolevoglucosan[3,4] has been pre-

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