hr. with 48% hydrobromic acid. At the end of this period the acid was removed and the residue digested with ethanol. Filtration of the suspension removed some unchanged starting material, but concentration of the filtrate afforded a small amount of a new compound, m.p. 300° dec. Recrystallization of this substance from ethanol–ethyl acetate afforded a colorless microcrystalline powder, m.p. 301.5° dec.

Anal. Calcd. for $C_{11}H_8BrNO_4 \cdot 0.5\ H_2O$: C, 43.01; H, 2.95; N, 4.59. Found: C, 42.73; H, 3.09; N, 4.62.

2,3-Dicarboxyquinolizinium Bisulfate.—A solution of the betaine (XV, 0.1 g.) in concentrated sulfuric acid (6 ml.) was heated for 1 hr. at 170°. The solution was cooled and slowly added to 30 ml. of cold ether. Collection of the colorless precipitate gave 0.1 g. (71%) of a very hygroscopic material, m.p. 234–235° dec.

Anal. Calcd. for $C_{11}H_9NSO_8$: neut. equiv., 105. Found: neut. equiv., 104.

When the bisulfate was washed with water or barium chloride solution (colorless precipitate), the betaine (XV) was recovered.

7,10-Dimethoxy-11-phenylacridizinium (XIV) Perchlorate.—A solution of 2,5-dimethoxybenzyl bromide[14] (15 g.) and 2-benzoylpyridine (12.8 g.) in dimethylformamide (15 ml.) was allowed to stand for 5 days at room temperature. When ether was added an oil separated. The ether was decanted and the oil transferred to a round bottom flask by use of methanol. After evaporation of the methanol, 90 g. of polyphosphoric acid was added, and the mixture stirred and heated at 90–100° for an hour. The acid was cooled and hydrolyzed by addition of ice. To the filtered phosphoric acid solution, an excess of 35% perchloric acid was added. The precipitate was collected and recrystallized from ethanol as orange needles, 9.6 g. (36%), m.p. 254–255° dec.; λ_{max} 250 mμ (log ε 5.08), 323* (3.31), 409 (4.02), and 455* (3.84).

Anal. Calcd. for $C_{21}H_{18}ClNO_6$: C, 60.65; H, 4.36; N, 3.37 Found: C, 60.64; H, 4.45; N, 3.51.

The **picrate** crystallized from ethanol as orange needles, m.p. 197–198° dec.

Anal. Calcd. for $C_{27}H_{20}N_4O_9$: C, 59.55; H, 3.73; N, 10.29. Found: C, 59.60; H, 3.64; N, 10.29.

Betaine (XVI) of 1-Phenyl-2,3-dicarboxyquinolizinium Hydroxide.—Five grams of 7,10-dimethoxy-11-phenylquinolizinium (XIV) perchlorate was oxidized in the usual way with 8 *M* nitric acid. The residue left by removal of most of the nitric acid was taken up in 50 ml. of water and the water evaporated *in vacuo*. After repetition of the process several times the product was allowed to crystallize from about 20 ml. of water, 1.78 g. (51%), 203° dec. (with gas evolution). Recrystallization of the product from methanol gave colorless needles, 210.5° dec. (gas evolution); λ_{max} 227 mμ (log ε 4.26), 255 (4.22), 332* (3.96), and 342 (4.12).

Anal. Calcd. for $C_{17}H_{11}NO_4$: C, 69.61; H, 3.78; N, 4.78. Found: C, 69.72; H, 3.86; N, 5.10.

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Hexofuranosyl Nucleosides from Sugar Dithioacetals[1]

M. L. WOLFROM, P. MCWAIN,[2] R. PAGNUCCO,[3] AND A. THOMPSON

Department of Chemistry, The Ohio State University, Columbus 10, Ohio

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Improved procedures were found for the partial hydrolysis of the diethyl dithioacetals of D-glucose and D-galactose (I) to their tetra-*O*-acetyl-1-thio-α-D-glycofuranosides (IIa and II). The acetylated thioglycoside of D-glucofuranose (IIa) was converted with bromine to tetra-*O*-acetyl-D-glucofuranosyl bromide (sirup) which was condensed with the chloromercuri derivative of 2,6-diacetamidopurine (IV) to give the acetylated nucleoside and this on partial deacetylation yielded 2-acetamido-9-β-D-glucofuranosyladenine (VIa). Tetra-*O*-acetyl-β-D-galactofuranosyl chloride (III), similarly prepared from the dithioacetal (I), was transformed to 9-β-D-galactofuranosyladenine (VIII, dimorphous), 2-acetamido-9-β-D-galactofuranosyladenine (VI), and 2,6-diamino-9-β-D-galactofuranosylpurine (VII).

In the pentose series, a sugar may be forced into its furanose form by suitable blocking of the terminal position. This procedure is not applicable in the hexose series and special methods are required to obtain furanoside derivatives. Haworth[4] and associates utilized carbonate esters in several successful syntheses of hexofuranosides. In the galactose structure, a furanose pentaacetate is obtainable by direct acetylation of the sugar and is separable from the pyranose pentaacetate by laborious fractional crystallization methods.[5] Todd and co-workers[6] have reported a crude picrate of 9-β-D-galactofuranosyl-2-methylthioadenine, prepared by using tetra-*O*-acetyl-β-D-galactofuranose derived from such an acetylation of D-galactose.

In the glucose series, the isopropylidene cyclic acetals (1,2 and 1,2:5,6)[7] possess a furanose ring and have been utilized in the synthesis of 9-β-D-glucofuranosyladenine[8] as well as 6-deoxy-D-glucofuranosyl[9] and 6-deoxy-6-iodo-L-iodofuranosyl[10] nucleosides. The nucleosides of L-rhamnofuranose,[11] 6-deoxy-D-allofuranose,[12] and 6-deoxy-L-talofuranose[13] were likewise synthesized utilizing 2,3-*O*-isopropylidene-L-rhamnofuranose[14] as the initial source of the hexofuranose.

Most aldose dithioacetals undergo partial demercaptalation under suitable conditions to form thioglycofuranosides.[15] Ethyl 1-thio-α-D-glucofuranoside has been obtained in 63% yield[16] from D-glucose diethyl dithioacetal by partial demercaptalation with aqueous mercuric chloride and mercuric oxide and it undergoes

(1) Preliminary communication, Abstracts, 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962, p. 7D.

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(3) Fellow under support of the National Science Foundation Grant NSF-G14629 (Ohio State University Research Foundation Project 1178).

(4) W. N. Haworth, "The Constitution of Sugars," Longmans Green and Co., New York, N. Y., 1929, p. 52.

(5) C. S. Hudson and J. M. Johnson, *J. Am. Chem. Soc.*, **38**, 1223 (1916); H. H. Schlubach and V. Prochownick, *Ber.*, **63**, 2298 (1930); R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *J. Am. Chem. Soc.*, **73**, 3742 (1951).

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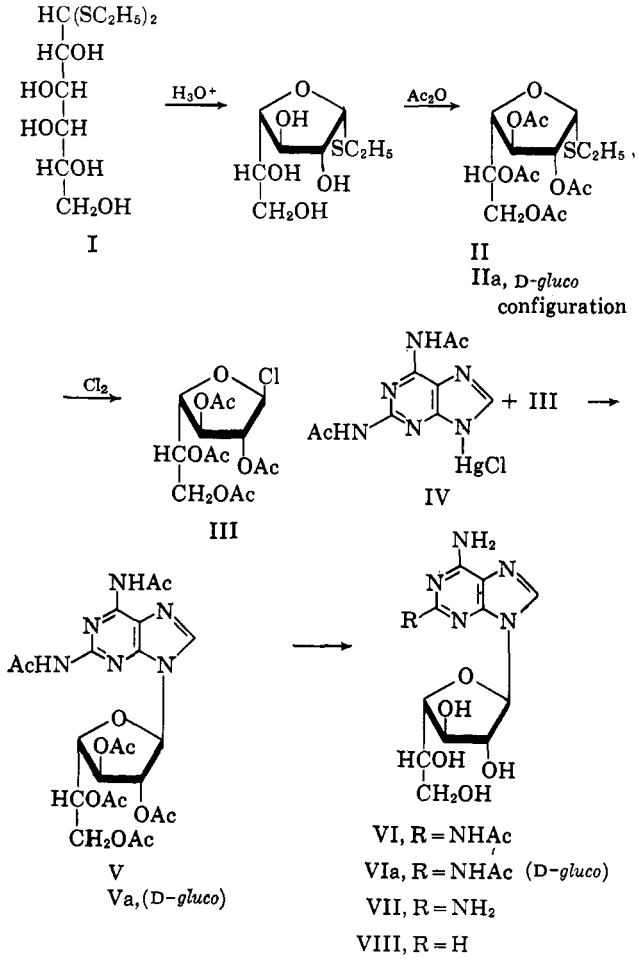
conversion to ethyl 1-thio-β-D-glucofuranoside and ethyl 1-thio-α- and β-D-glucopyranoside under mild acidic conditions. Acetylation of ethyl 1-thio-α-D-glucofuranoside gives the crystalline tetraacetate.[15] Partial demercaptalation of D-galactose diethyl dithioacetal similarly[17] yields ethyl 1-thio-α-D-galactofuranoside, isolated in 43% yield as the 2,3,5,6-tetraacetate by chromatographic techniques.

The present work describes the conversion of D-glucose diethyl dithioacetal and D-galactose diethyl dithioacetal into the corresponding ethyl tetra-*O*-acetyl-1-thio-α-D-furanosides (II and IIa) by partial demercaptalation with dilute hydrochloric acid and mercuric oxide followed by acetylation. These furanose intermediates were then utilized in the synthesis of hexofuranosyl nucleosides.

An acetylated thioglycoside is convertible with bromine to the acetylated glycosyl bromide in a reaction established by Bonner[18] and extended by Weygand and associates.[19] This reaction was utilized in the present work for the conversion of ethyl tetra-*O*-acetyl-1-thio-α-D-glucofuranoside (IIa) to the sirupy tetra-*O*-acetyl-D-glucofuranosyl bromide.[20] Extension of this reaction to the synthesis of the crystalline tetra-*O*-acetyl-β-D-galactofuranosyl chloride (III) of Hudson and Johnson[5] has been made by Wolfrom and Groebke.[21]



The chloride III was converted to a nucleoside by coupling with 2,6-diacetamido-9-chloromercuripurine (IV), by the general method of Davoll and Lowy,[22a] to give, after deacetylation, the crystalline 2,6-diamino-9-β-D-galactofuranosylpurine (VII). Partial deacetylation led to the crystalline 2-acetamido-9-β-D-galactofuranosyladenine (VI). Coupling of tetra-*O*-acetyl-β-D-galactofuranosyl chloride with 6-benzamido-9-chloromercuripurine, followed by deacylation, gave the crystalline 9-β-D-galactofuranosyladenine (VIII).

In our experience, the employment of the tetra-*O*-acetylglycosyl chloride is perferable to the use of the corresponding bromide in this relatively high temperature reaction. Judged by its rotation, the tetra-*O*-acetyl-D-galactofuranosyl chloride possessed the β-D anomeric structure which in turn gave rise to a β-D nucleoside. An anomerization of the β-D chloride may have occurred prior to reaction as the β-D-halo derivatives of the *gluco* and *galacto* series are known to be unstable and readily anomerize in solution. An alternative explanation has been given by Baker and associates[22b] who postulated the formation, from either anomeric halide, of a transient 1,2-ortho ester carbonium ion which would then form the 1,2-*trans* glycoside on attack by the nitrogen heterocycle.

The sirupy tetra-*O*-acetyl-D-glucofuranosyl bromide was likewise condensed with 2,6-diacetamido-9-chloromercuripurine (IV) to give an amorphous 2,6-diacetamido-9-(tetra-*O*-acetyl-β-D-glucofuranosyl)purine (Va) which on partial deacetylation yielded the crystalline 2-acetamido-9-β-D-glucofuranosyladenine (VIa).

Experimental[23]

Improved Preparation of Ethyl Tetra-*O*-acetyl-1-thio-α-D-galactofuranoside (II).—D-Galactose diethyl dithioacetal (I), 28.6 g. (0.13 mole), 600 ml. of water, and 8.5 ml. (0.1 mole) of concentrated hydrochloric acid were stirred vigorously 20 hr. at 20°. Yellow mercuric oxide, 32.9 g. (1.5 moles), was added and stirring was continued for 5 hr. After cooling in iced water, the suspension was filtered and the colorless filtrate was concentrated under reduced pressure to a thin sirup. A white precipitate, 0.1 g., formed during the concentration and was discarded. The aqueous sirup was dissolved in absolute methanol and thrice evaporated. Crystalline D-galactose was recovered by successive treatments of the residue with absolute methanol and absolute ethanol and standing at 0°, 8.07 g. (44.5%), m.p. 167–170°. The alcoholic mother liquor was concentrated under reduced pressure and dried to a nonreducing glass, 11.8 g. (56%). The glass was suspended in 40 ml. of pyridine, treated with 75 ml. of acetic anhydride, the mixture allowed to stand 21 hr. at room temperature, and then poured with stirring into iced water. The product was extracted with chloroform, the extract washed with several portions of water, dried (anhydrous sodium sulfate), and evaporated under reduced pressure. Anhydrous ether was added and evaporated to give a colorless sirup which crystallized on storage in an evacuated desiccator over phosphorus pentaoxide

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(22)(a) J. Davoll and B. A. Lowy, *J. Am. Chem. Soc.*, **73**, 1650 (1951); (b) see J. J. Fox and I. Wempen, *Advan. Carbohydrate Chem.*, **14**, 377 (1959).

(23) The ultraviolet absorption analyses were made on a Cary recording spectrophotometer, Model 10, Applied Physics Corp., Pasadena, Calif. The infrared spectral data were obtained with an infrared recording spectrophotometer, Model B, Baird Associates, Inc., Cambridge, Mass. Structural assignments were made essentially according to W. B. Neely [*Advan. Carbohydrate Chem.*, **12**, 13 (1957)] and B. R. Baker and K. Hewson [*J. Org. Chem.*, **22**, 959 (1957)]. Chromatographic data refer to descending chromatograms on Whatman No. 1 paper with 1-butanol–ethanol–water (40:11:19 v./v.) with indication by ultraviolet light and by sodium metaperiodate and ammoniacal silver nitrate sprays according to L. Hough and J. K. N. Jones ["Methods in Carbohydrate Chemistry," Vol. I., R. L. Whistler and M. L. Wolfrom, Ed., Academic Press, New York, N. Y., 1963, p. 28].

and sodium hydroxide, 19.0 g. (48.5%), m.p. 43.5–47°, $[\alpha]^{29}D$ +104° (*c* 1.14, chloroform). The ethyl tetra-*O*-acetyl-1-thio-α-galactofuranoside[17] so obtained was of sufficient purity for use in the next step.

2,6-Diacetamido-9-(tetra-*O*-acetyl-β-D-galactofuranosyl)purine (V).—Tetra-*O*-acetyl-β-D-galactofuranosyl chloride[21] (III, 2.0 g.) was added to an azeotropically dried mixture of 2,6-diacetamido-9-chloromercuripurine[22] (IV, 2.8 g.), Celite[24] (1 g.), cadmium carbonate (1.8 g.), and toluene (100 ml.). The suspension was stirred 4 hr. under reflux, the hot mixture filtered, the filter cake extracted with warm chloroform, and the combined filtrate and chloroform solution evaporated under reduced pressure to a sirup. The sirup was extracted with chloroform. The chloroform solution was washed with 30% aqueous potassium iodide, then with water, and dried (magnesium sulfate). Evaporation of the chloroform solution under reduced pressure yielded a white amorphous solid, 1.24 g. (40.4%), m.p. 100–112°, $[\alpha]^{20}D$ −28.5 ± 3° (*c* 0.3, chloroform); absorption spectra data[23]: $\lambda_{max}^{95\%\ EtOH}$ 236.2, 273 5, 279.5 mμ; λ_{max}^{KBr} 3.15, 3.25 (NH), 5.75 (ester carbonyl), 5.95 (amide carbonyl), 6.15, 6.25, 6.75 (NH and purine ring), 7.30 (methyl hydrogen), 9.04, 9.25, 9.60, 9.82 μ (C–O–C).

Anal. Calcd. for $C_{23}H_{28}O_{11}N_6$: C, 48.92; H, 5.06; N, 14.89. Found: C, 49.12; H, 5.01; N, 15.80.

Attempts to crystallize V were unsuccessful.

2-Acetamido-9-β-D-galactofuranosyladenine (VI).—The partial deacetylation of V was effected with boiling methanolic *n*-butylamine.[25] Amorphous V (700 mg.) was dissolved in methanol (25 ml.) containing *n*-butylamine (1.0 ml.) and heated 6 hr. under reflux, during which time precipitation of a colorless crystalline solid resulted. After partial evaporation and cooling, the crystalline material was removed by filtration, 340 mg. (88%), m.p. 212–213°. The crude crystalline material was decolorized (activated carbon) in water and recrystallized from aqueous ethanol to give analytically pure material, m.p. 240–241°, $[\alpha]^{23}D$ −53 ± 5° (*c* 0.18, water); absorption spectra data[23]: $\lambda_{max}^{H_2O}$ 226.0, 268.0 mμ; λ_{max}^{KBr} 2.95, 3.15 (OH, NH), 5.88 (amide), 6.10, 6.24, 6.44, 6.80 (NH_2, NH, and purine ring), 8.90, 9.08, 9.30, 9.55 μ (C–O–C, C–OH); X-ray powder diffraction data[26]: 10.40 s, 8.27 vs (1), 5.95 vw, 5.34 m, 4.58 m, 4.24 m, 3.97 vs (2), 3.65 vs (3), 3.43 vw, 3.19 vw, 2.96 w.

Anal. Calcd. for $C_{13}H_{18}N_6O_6$: C, 44.05; H, 5.12; N, 23.73. Found: C, 43.85; H, 5.17; N, 23.90.

Compound VI moved on paper chromatography[23] as a single zone, R_{ad} 0.49.

2,6-Diamino-9-β-D-galactofuranosylpurine (VII).—Crystalline VI, 170 mg., was suspended in 10 ml. of absolute methanol, treated with a solution of sodium methoxide made by dissolving two freshly cut pea size pellets of sodium metal in 20 ml. of absolute methanol and the mixture refluxed 5.5 hr. The solution was cooled, neutralized with glacial acetic acid, and treated with 5 ml. of 10% methanolic picric acid. Precipitation resulted immediately. The yellow picrate was cooled, separated by filtration, and washed with absolute methanol, 180 mg., m.p. 220–228° dec. The picrate was dissolved in boiling water and regenerated with Dowex-1 (CO_3^{-2}) anion-exchange resin. The colorless solution was concentrated under reduced pressure to give a sirup which crystallized on evaporation from absolute ethanol, 65 mg. (43.5%), m.p. 224–225°, $[\alpha]^{20}D$ −64° (*c* 0.23, water); absorption spectra data[23]: λ_{max}^{water} 258, 281 mμ; λ_{max}^{KBr} 3.04 (OH, NH), 6.04, 6.30, 6.88 (NH and purine ring), 9.14, 9.70 μ (C–OH); X-ray powder diffraction data[26]: 7.53 m, 6.07 w, 5.74 m, 5.22 m, 4.82 m, 4.46 m, 4.26 s (3), 3.81 s (1), 3.48 s (2), 3.25 w, 3.07 vw, 2.95 vw, 2.76 vw. The material moved as a single spot, R_{Ad} 0.31, on paper chromatography.[23]

Anal. Calcd. for $C_{11}H_{16}N_6O_5$: C, 42.30; H, 5.17; N, 26.91. Found: C, 42.13; H, 5.74; N, 26.22.

The complete deacetylation of V with boiling methanolic sodium methoxide in 6 hr. gave 33.4% VII while deacetylation with boiling methanolic *n*-butylamine produced 68% VI and 14% VII.

9-β-D-Galactofuranosyladenine (Dimorphous) (VIII).—Crystalline tetra-*O*-acetyl-β-D-galactofuranosyl chloride[21] (III, 1.6 g.) was added to an azeotropically dried mixture of 6-benzamido-9-chloromercuripurine[27] (2.07 g.), Celite[24] (1 g.), cadmium carbonate (1.8 g.), and toluene (150 ml.). The suspension was stirred 4.25 hr. under reflux, the hot mixture filtered, the filtrate extracted with warm chloroform, and the combined extracts evaporated under reduced pressure to a sirup. The sirup was extracted with chloroform, washed with 30% aqueous potassium iodide, then with water, and dried (magnesium sulfate). Evaporation of the chloroform under reduced pressure gave a white amorphous solid, 1.71 g. (69.0%), m.p. (range) 67–87°, $[\alpha]^{20}D$ −15° (*c* 1.25, chloroform); absorption spectra data[23]: λ_{max}^{KBr} 2.8–3.0 (broad, NH), 3.33 (C–H), 5.65 (ester carbonyl), 5.82 (amide carbonyl), 6.05, 6.18, 6.28, 6.6, 6.7, 6.86 (NH, purine ring, benzene ring), 7.29 (methyl hydrogen), 8.15 (C–O–C, acetate), 9.4–9.7 μ (broad, C–O–C).

Deacetylation and debenzoylation of 6-benzamido-9-(tetra-*O*-acetyl-β-D-galactofuranosyl)purine was effected with boiling methanolic *n*-butylamine.[25] The acylated nucleoside (0.26 g.) was dissolved in methanol (20 ml.) containing *n*-butylamine (0.5 ml.) and the solution was refluxed 6 hr. The sirup obtained on solvent removal, under reduced pressure, was dissolved in methanol, and ether added to incipient turbidity. Crystals formed on standing in the refrigerator. Filtration of the fine white crystals was effected in a drybox because of their extremely hygroscopic nature, 0.05 g. (37%), m.p. 209–212° dec., $[\alpha]^{24}D$ −52 ± 3° (*c* 0.3, water); absorption spectra data[23]: $\lambda_{max}^{H_2O}$ 262.5 mμ; λ_{max}^{KBr} 3.05, 3.15 (OH, NH), 6.15, 6.25, 6.40, 6.85 (NH_2, NH, and purine ring), 9.15, 9.45, 9.70, 9.95 μ (C–O–C, C–OH); X-ray powder diffraction data[26]: 9.35 m, 6.63 m, 5.77 m, 5.47 s (3), 5.13 s (2), 4.60 m, 4.20 w, 3.88 m, 3.63 s (1), 3.39 s, 3.27 m, 3.12 w, 2.98 vw, 2.81 w, 2.74 w, 2.41 m, 2.29 w, 2.19 w.

Anal. Calcd. for $C_{11}H_{15}N_5O_5$: C, 44.43; H, 5.09; N, 23.54. Found: C, 44.13; H, 5.42; N, 22.50.

Crude 6-benzamido-9-(tetra-*O*-acetyl-β-D-galactofuranosyl)-purine (0.5 g.) was dissolved in 10 ml. of absolute ethanol, and 2 ml. of a 10% ethanolic picric acid solution added. The mixture was boiled 4 min. during which time yellow crystals separated from the solution and were removed by filtration of the hot solution, 0.33 g. This product was recrystallized three times from ethanol, m.p. 208–209°; X-ray powder diffraction data[26]: 8.89 vw, 8.01 w, 7.41 m, 6.44 vw, 6.09 m, 5.70 vw, 5.28 w, 5.01 w, 4.60 vw, 4.44 m (3), 4.05 w, 3.87 w, 3.34 m (1), 3.21 m (2). Removal of the picrate anion[27] by stirring, in an aqueous acetone solution, the *O*-acetylated picrate (0.134 g.) with Dowex-1 (CO_3^{-2}) anion-exchange resin[28] gave a white gummy material which failed to crystallize from common solvents. The gummy 9-(tetra-*O*-acetyl-β-D-galactofuranosyl)adenine was deacetylated with boiling methanolic *n*-butylamine as described above. A white crystalline solid precipitated from the hot solution. Upon cooling and filtering, pure 9-β-D-galactofuranosyladenine (VIII) was obtained, 0.043 g. (75%), m.p. 224–225°, $[\alpha]^{24}D$ −52 ± 2° (*c* 0.3, water), spectral and X-ray powder diffraction data identical with those cited before. A recrystallization of the previously prepared hygroscopic VIII (m.p. 209–212° dec.), utilizing the higher melting VIII (m.p. 224–225°) as nucleating agent, yielded white crystals, m.p. 224–225°.

Ethyl Tetra-*O*-acetyl-1-thio-α-D-glucofuranoside (IIa).—D-Glucose diethyl dithioacetal was partially demercaptalated to ethyl 1-thio-α-D-glucofuranoside by a modification of the procedure of Pacsu and co-workers[15,16] and Wolfrom and co-workers.[17] D-Glucose diethyl dithioacetal, 28.0 g. (0.10 mole), was stirred 1 hr. at room temperature with 600 ml. of water containing 8.0 ml. of concentrated hydrochloric acid. The suspension was neutralized with 32.9 g. (0.05 mole excess) of yellow mercuric oxide. The heavy suspension was stirred 1 hr., then cooled in iced water, and filtered. The colorless filtrate was evaporated under reduced pressure to 75 ml. and maintained at 0°. Crystallization of a nonreducing solid resulted, 18.8 g. (84%), m.p. 143–146°. Recrystallization from hot methanol gave ethyl 1-thio-α-D-glucofuranoside,[16,29] m.p. 151–153°, $[\alpha]^{24}D$ +121° (*c* 1.23, water). Acetylation of 5.0 g. of the thiofuranoside with 18 ml. of pyridine and 25 ml. of acetic anhydride at room temperature for 24 hr. gave a neutral sirup which crystallized from 50% aqueous ethanol on evaporation under reduced pressure, 9.5 g., m.p. 62–64°.[29]

(24) A silicous filter aid, Johns-Manville Co., New York, N. Y.

(25) L. Goldman, J. W. Marsico, and R. B. Angier, *J. Am. Chem. Soc.*, **78**, 4173 (1956); E. J. Reist and B. R. Baker, *J. Org. Chem.*, **23**, 1083 (1958); B. R. Baker and K. Hewson, *ibid.*, **22**, 959 (1957).

(26) Interplanar spacing, Å., Cu K_α radiation. Relative intensity, estimated visually: s, strong; m, medium; w, weak; v, very; three strongest lines numbered (1, strongest).

(27) J. R. Parikh, M. E. Wolff, and A. Burger, *J. Am. Chem. Soc.*, **79**, 2778 (1957).

(28) A product of the Dow Chemical Co., Midland, Mich.

(29) M. L. Wolfrom, D. I. Weisblat, and A. R. Hanze, *J. Am. Chem. Soc.*, **66**, 2065 (1944).

2,6-Diacetamido-9-(tetra-*O*-acetyl-β-D-glucofuranosyl)purine.—Ethyl tetra-*O*-acetyl-1-thio-α-D-glucofuranoside (IIa) was converted to a sirupy tetra-*O*-acetyl-D-glucofuranosyl bromide by the method of Weygand and co-workers[19] and this derivative was converted to a nucleoside by the general method of Davoll and Lowy.[22] Crystalline ethyl tetra-*O*-acetyl-1-thio-α-D-glucofuranoside (IIa, 8.5 g.) was dissolved in absolute ether (90 ml.) and treated under magnetic stirring at room temperature with bromine (1.25 ml.). After 7 min. stirring, the amber solution was evaporated under reduced pressure; petroleum ether (b.p. 30–60°) was added and the mixture was twice evaporated to a dry sirup, 9.9 g. This product, dissolved in dry toluene, was added to an azeotropically dried mixture of 2,6-diacetamido-9-chloromercuripurine (10.1 g.),[22] cadmium carbonate (10 g.), Celite (5 g.),[24] and toluene (275 ml.), and the suspension was heated 2.5 hr. at reflux. Filtration of the hot suspension and collection of the material soluble in hot chloroform, followed by washing of the chloroform extract with 30% aqueous potassium iodide, then with water, and drying (sodium sulfate), gave a sirup, 13.63 g. (quantitative). Solid material was obtained by the addition of absolute ether to a concentrated ethanolic solution, m.p. 107–116°, $[\alpha]^{29}D$ +30 ± 3° (*c* 0.37, chloroform); absorption spectra data[23]: λ_{max}^{EtOH} 237, 264, 288 mμ; λ_{max}^{KBr} 3.15, 3.25, 3.35 (NH), 5.70–5.95 (ester carbonyl, amide carbonyl), 6.10–6.25, 6.60–6.90 (NH and purine ring), 7.25–7.35 (methyl hydrogen), 9.24–9.80 μ (C–O–C). This amorphous substance could not be obtained in analytical purity

Anal. Calcd. for $C_{23}H_{28}O_{11}N_6$: C, 48.92; H, 5.00; N, 14.89. Found: C, 48.26; H, 5.10; N, 12.74.

2-Acetamido-9-β-D-glucofuranosyladenine (VIa).—Partial deacetylation of 2,6-diacetamido-9-(tetra-*O*-acetyl-β-D-glucofuranosyl)purine (Va, 850 mg.) in absolute methanol (50 ml.) and *n*-butylamine (1.5 ml.)[25] by refluxing 5 hr. resulted in crystallization from the hot mixture. Pink needles separated at 0°, 380 mg. (81%). Recrystallization (carbon) from water gave colorless needles, m.p. 241–242° dec., $[\alpha]^{28}D$ −77 ± 8° (*c* 0.13, water); absorption spectra data[23]: $\lambda_{max}^{H_2O}$ 226, 269 mμ; λ_{max}^{KBr} 2.98, 3.18 (OH, NH), 5.90 (amide), 6.10, 6.25, 6.38, 6.85 (NH_2, NH, and purine ring), 9.00, 9.15, 9.40, 9.60 μ (C–O–C, C–OH); X-ray powder diffraction data[26]: 8.85 s (3), 7.90 s (2), 4.93 m, 4.51 m, 3.97 s (1), 3.88 vw, 3.60 w, 3.48 vw, 3.38 w, 3.03 m, 2.92 vw, 2.85 vw, 2.69 vw, 2.61 vw, 2.45 vw, 2.36 vw, 2.32 vw, 2.18 vw, 1.95 w. This material moved as a single zone on paper chromatography,[23] R_{Ad} 0.61.

Anal. Calcd. for $C_{13}H_{18}N_6O_6$: C, 44.05; H, 5.12; N, 23.73. Found: C, 43.83; H, 5.19; N, 23.85.

Structural Investigations of Acetylated Sugar Phenylhydrazine Derivatives

M. L. WOLFROM, G. FRAENKEL, D. R. LINEBACK,[1] AND F. KOMITSKY, JR.[2]

Department of Chemistry, The Ohio State University, Columbus 10, Ohio

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The n.m.r. spectra of the following compounds were investigated to ascertain the utility of this technique in assigning cyclic or acyclic structures to such derivatives: D-*arabino*-3,4,5,6-tetraacetoxy-1-phenylazo-*trans*-1-hexene (I), D-*arabino*-3,4,5,6-tetraacetoxy-1-(*p*-bromophenyl)azo-*trans*-1-hexene (II), D-*lyxo*-3,4,5,6-tetraacetoxy-1-phenylazo-*trans*-1-hexene (III), penta-*O*-acetyl-*aldehydo*-D-galactose phenylhydrazone (IV), penta-*O*-acetyl-*aldehydo*-D-galactose *p*-nitrophenylhydrazone (V), penta-*O*-acetyl-D-mannose *p*-nitrophenylhydrazone (VI), D-glucose "α"-phenylhydrazone pentaacetate (VII), tetra-*O*-acetyl-D-*arabino*-hexose phenylosazone (VIII), and tetra-*O*-acetyl-D-*lyxo*-hexose phenylosazone (IX). It was found that the presence of a low field signal, due to a formyl proton on C-1, is indicative of an acyclic structure in sugar derivatives. Fischer's D-glucose "α"-phenylhydrazone pentaacetate has been so found to be 1-acetyl-1-phenyl-2-(tetra-*O*-acetyl-β-D-glucopyranosyl)-hydrazine. Definitive evidence for the chelate structure of phenylosazones has been obtained. Three striking examples of magnetic nonequivalence of two apparently equivalent protons due to asymmetry at an adjacent center have been found, all occurring in acyclic galactose derivatives. Optical rotatory dispersions of III, IV, V, VI, and VIII have been determined and analyzed.

The structure of the crystalline tetra-*O*-acetyl derivative isolated by Wolfrom and Blair[3] from the acetylation of D-mannose phenylhydrazone has been shown to be D-*arabino*-3,4,5,6-tetraacetoxy-1-phenylazo-*trans*-1-hexene (I) by means of n.m.r. spectroscopy[4] as applied to the *p*-bromophenyl analog, D-*arabino*-3,4,5,6-tetraacetoxy-1-(*p*-bromophenyl)azo-*trans*-1-hexene (II). The analysis of the n.m.r. spectrum of I (Fig. 1) itself is now reported (Table I), along with that of II for comparative purposes. In the spectrum of I, the quartet at τ 2.68, half buried in the phenyl multiplet, shows a coupling constant in common with the quartet at τ 3.25. The low field quartet is assigned to the C-1 proton, which is coupled with the C-2 and C-3 protons. The quartet at higher field is due to the C-2 proton, coupled with its adjacent protons. The allylic C-3 proton, coupled with the protons on C-1, C-2, and C-4, gives an octet at τ 4.08. The quartet at τ 4.37 is assigned to the C-4 proton and the multiplet centered at τ 4.78 to the C-5 proton. The C-6 protons give the multiplet centered at τ 5.80. The complexity of this multiplet is probably due to slight nonequivalence of the C-6 protons due to asymmetry at C-5.

It has been shown that D-*lyxo*-3,4,5,6-tetraacetoxy-1-phenylazo-*trans*-1-hexene (III), an analog of I and II, may be prepared[4] through elimination of 1 mole of acetic acid from penta-*O*-acetyl-*aldehydo*-D-galactose phenylhydrazone[5] (IV) by heating in aqueous ethanol solution. The analysis of the n.m.r. spectrum of III is tabulated in Table I. A doublet at τ 2.70 and a quartet at τ 3.29 were assigned to the C-1 and C-2 protons, respectively. Two masses of lines centered at τ 4.50 and 5.86 of relative areas 2:3 are due to the protons on C-3 and C-4 and those on C-5 and C-6, respectively. This spectrum differs from those of the previously discussed *arabino* analogs in that the C-3 and C-5 proton signals are shifted upfield and there is no observable coupling between the C-1 and C-3 protons. In general, however, this spectrum substantiates the previous assignments, as one may expect such differences as noted due to the difference in configuration.

The analysis of the n.m.r. spectrum (Fig. 2) of penta-*O*-acetyl-*aldehydo*-D-galactose phenylhydrazone (IV), of proven acyclic structure,[5,6] is given in Table II.

(1) Fellow of the Corn Industries Research Foundation.

(2) National Science Foundation Cooperative Graduate Fellow.

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