from isopropyl alcohol–ether. The ultraviolet spectrum showed λ_{max}^{MeOH} 208 mμ (ε 6900). 1,4,5,6-Tetrahydropyrimidine hydrochloride (Aldrich Chemical Co.) had λ_{max}^{MeOH} 207 mμ (ε 7200).

Anal. Calcd for $C_4H_9ClN_2O$: C, 35.17; H, 6.64; O, 11.71. Found: C, 35.08; H, 6.36; O, 11.83.

A picrate, mp 149–150°, was prepared in and recrystallized from isopropyl alcohol.

Anal. Calcd for $C_{10}H_{11}N_5O_8$: C, 36.48; H, 3.37; N, 21.28; O, 38.88. Found: C, 36.37; H, 3.33; N, 20.97; O, 38.65.

1,4,5,6-Tetrahydro-2-methyl-5-hydroxypyrimidine (II).—Redistilled 1,3-diaminopropan-2-ol (10.0 g, 0.11 mole) and ethyl acetate (10.0 g, 0.11 mole) were dissolved in 85 ml of xylene in a 250-ml flask equipped with a Dean–Stark trap and a magnetic stirrer. After 14 hr of reflux, the reaction mixture was cooled, and the xylene was decanted. The residual yellow oil was transferred to a smaller flask by dissolving in ethanol, which was removed under reduced pressure to give 10.0 g of a viscous yellow oil which solidified on standing overnight. The crude product was slowly dissolved by refluxing in 1400 ml of acetone (2 hr), and the solution was concentrated on the steam bath. Cyclohexane (200 ml) was added, and the acetone was boiled off until a cloud point was reached (total volume, 900 ml). On standing overnight at room temperature, the product II was obtained as white needles: 4.3 g (35%), mp 143.5–145.5°. An additional crop of 0.8 g was obtained from the filtrate. Recrystallization from acetone–cyclohexane gave product, mp 145.5–146.5°. The compound was soluble enough in carbon tetrachloride to obtain a dilute solution infrared spectrum using 20-mm quartz cells: ν_{max} 3625 (free OH), 3595 (OH bonded to π), 3465 (ν_{N-H}), 3280 cm^{-1} (OH bonded to N). Its infrared spectrum (KBr) showed strong bands at 1645 ($\nu_{C=N}$)[3] and 1538 cm^{-1} (δ_{NH})[3]; the ultraviolet spectrum showed λ_{max}^{MeOH} 207 mμ (ε 7000).

Anal. Calcd for $C_5H_{10}N_2O$: C, 52.59; H, 8.83; O, 14.01; mol wt, 114.2. Found: C, 53.10; H, 8.72; O, 14.17; mol wt, 114 (mass spectrum); neut equiv, 117.

2-Hydroxy-3-acetamidopropylamine.—About 0.5 g of II was dissolved in 50 ml of water. After 42 hr at 40°, the solution was stripped to dryness under reduced pressure to give a white, crystalline residue. Three recrystallizations from acetonitrile gave needles: mp 89–90°, ν_{max}^{KBr} 1560 and 1640 cm^{-1}. This product gave an identical nmr spectrum and titration curve as was previously obtained from solutions of II, after complete hydrolysis.

Anal. Calcd for $C_5H_{12}N_2O_2$: C, 45.44; H, 9.15; N, 21.20; neut equiv, 132.17. Found: C, 45.49; H, 9.31; N, 20.94; neut equiv, 132.5 (pK_a = 8.95 at 0.0050 ionic strength).

Reactions of 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl Isothiocyanate with Partially Protected Sugar Derivatives

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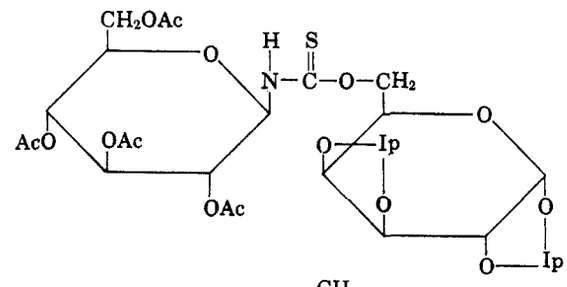
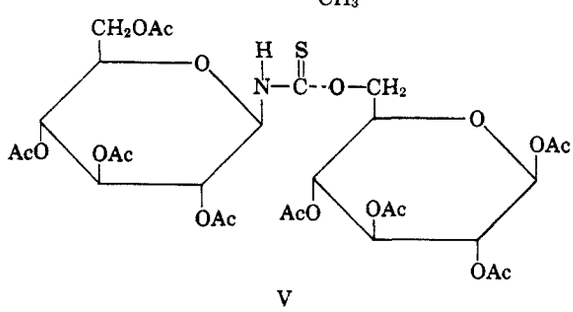
Sugar isothiocyanates have been used previously in a reaction with simple amino acids to form *N*-glycosides of the thiourea and hydantoin series.[1] The present note describes the reaction with the hydroxyl and amino groups of partially substituted sugars.

Condensation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate (I)[2] with 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (II)[3] produced 6-*O*-[*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thiocarbamyl]-1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (IV). After removal of a by-product, 1,3-bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thiourea (VI), by fractional recrystallization, IV was isolated as an amorphous powder in a 42% yield. Data from elementary analyses, infrared spectrophotometry, and molecular weight determination supported the presumed structure IV (see Chart I) and thin layer chromatography revealed its purity.

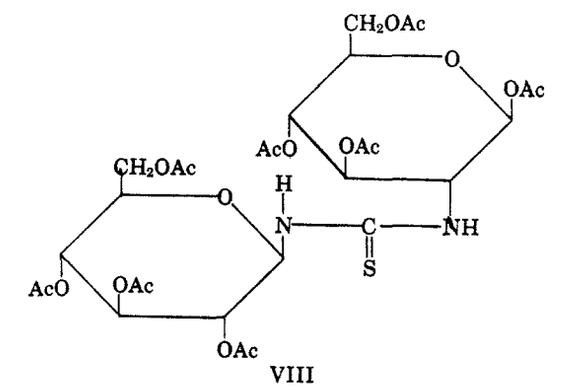
CHART I



IV, Ip = CH_3 / CH_3 >C



V



VIII

Condensation of I with 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (III)[4] gave crystalline 1,2,3,4-tetra-*O*-acetyl-6-*O*-[*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thiocarbamyl]-β-D-glucopyranose (V) in a 27% yield after removal of by-product VI and unreacted III.

Under the same conditions, I underwent condensation with 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (VII)[5] to give 1,3,4,6-tetra-*O*-acetyl-2-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylthioureido]-2-deoxy-β-D-glucopyranose (VIII) in a 58% yield.

An attempted condensation of I with 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose[6] failed and most of the starting material could be recovered. Under more severe conditions, a mixture of several unidentified

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(2) E. Fisher, *Ber.*, **47**, 1377 (1914).
(3) K. P. Link and H. M. Sell, *Biochem. Prepn.*, **3**, 75 (1953).
(4) D. D. Reynolds and W. L. Evans, *Org. Syn.*, **22**, 56 (1942).
(5) M. Bergmann and L. Zervas, *Ber.*, **64b**, 975 (1931).
(6) W. L. Glen, G. S. Myers, and G. A. Grant, *J. Chem. Soc.*, 2568 (1951).

products was obtained as indicated by a chromatographic examination.

The results so far suggest that primary hydroxyl groups and amino groups of partially protected sugars react with sugar isothiocyanates in the anticipated way without difficulty. With secondary hydroxyl groups, however, no such reaction occurs to any appreciable extent. The work on this type of reaction and on an application of the method to polysaccharides is being continued.

Experimental Section

Specific rotations were determined in semimicropolarimeter tubes with lengths of 2 or 1 dm, with a Zeiss polarimeter having a scale reading to 0.01°. Infrared spectra were determined on a Nihon-Bunko spectrophotometer, Model IR-S, using a KBr pellet. The silicic acid used for chromatography was "Silicagel Kanto" from Kanto Kagaku Co., Tokyo (100–200 mesh), without pretreatment. The eluents were used in the following sequence individually or in binary mixtures: benzene, ether, ethyl acetate, acetone, and methyl alcohol. The silica gel used for thin layer chromatography was Wakogel B-O from Wako Chemical Co., Tokyo, activated at 110°. Evaporations were done *in vacuo* at 35–40° (bath temperature). The microanalyses were carried out by the member of the Central Analysis Room, Faculty of Pharmaceutical Sciences, University of Tokyo.

6-*O*-[*N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)thiocarbamyl]-1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (IV).—To a solution of 0.70 g of 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (II) in 10 ml of dry pyridine was added 1.0 g of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate (I), and the solution was kept at 55° for 48 hr. The reaction mixture was concentrated to a syrup; the syrup was freed from pyridine by codistillation with toluene, diluted with a small amount of ethyl alcohol, and left at room temperature. The white needles deposited were recrystallized from ethyl alcohol to give 0.13 g of 1,3-bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thiourea (VI): mp 209–210°; $[\alpha]^{20}D$ −2.3° (*c* 1.30, chloroform); λ_{max}^{KBr} 2.98 (NH), 5.71 (OAc), 6.13, and 6.54 μ (NHCS).

Anal. Calcd for $C_{29}H_{40}N_2O_{18}S$: C, 47.28; H, 5.47; N, 3.80. Found: C, 47.44; H, 5.36; N, 3.62.

The filtrate was concentrated and the residue was dissolved in benzene and chromatographed on silica gel. After elution with a mixture of benzene–ether (4:1) and reprecipitation from chloroform and hexane, 0.70 g (42%) of IV was obtained as an amorphous powder. The purity of the product was examined by thin layer chromatography using pyridine–*n*-butyl alcohol–water (15:70:15, v/v) and 5% methyl alcohol in benzene as developing solvents and anisaldehyde–sulfuric acid[7] to detect the spots. In each case, one spot developed with R_f 0.91 and 1.58, respectively (with f being 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose); $[\alpha]^{20}D$ −34.2° (*c* 0.79, chloroform); λ_{max}^{KBr} 3.06 (NH), 5.71 (OAc), 6.13, 6.58 (NHCS), and 8.50 μ (isopropylidene).

Anal. Calcd for $C_{27}H_{39}NO_{15}S$: C, 49.92; H, 6.05; N, 2.15; mol wt, 650. Found: C, 50.57; H, 6.12; N, 2.17; mol wt (Rast), 650.

1,2,3,4-Tetra-*O*-acetyl-6-*O*-[*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thiocarbamyl]-β-D-glucopyranose (V).—An amount of 0.90 g of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (III) in 15 ml of dry pyridine was condensed with 1.0 g of I; the reaction products were separated as described above. Elution of the silica gel column with benzene–ether (4:1, v/v) produced, after evaporation of the solvent and recrystallization from a mixture of chloroform and ether, 0.23 g of the starting material III. Benzene–ether (3:2, v/v) eluted a fraction which, after recrystallization from ethyl alcohol, gave 0.50 g (27%) of V as white needles: mp 167–169°; $[\alpha]^{25}D$ +24.4° (*c* 0.78, chloroform); λ_{max}^{KBr} 3.00 (NH), 5.71 (OAc), 6.13, and 6.54 μ (NHCS).

Anal. Calcd for $C_{29}H_{39}NO_{19}S$: C, 47.21; H, 5.33; N, 1.90. Found: C, 47.27; H, 5.44; N, 2.13.

Further elution of the column with the same solvent gave 0.20 g of crystalline material, mp 207–209°, identical with VI by mixture melting point.

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1,2,4,6-Tetra-*O*-acetyl-2-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylthioureido]-2-deoxy-β-D-glucopyranose (VIII).—A portion of 1.0 g of I was added to a solution of 0.90 g of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (VII) in 15 ml of dry pyridine; the mixture was kept at 55° for 48 hr, then concentrated to dryness, and the remaining pyridine was removed by codistillation with toluene. The residue was recrystallized twice from ethyl alcohol to give 1.10 g (58%) of VIII in the form of white needles: mp 178°; $[\alpha]^{20}D$ +4.9° (*c* 1.72, chloroform); λ_{max}^{KBr} 2.96 (NH), 5.71 (OAc), 6.13, and 6.50 μ (NHCS).

Anal. Calcd for $C_{29}H_{40}N_2O_{18}S$: C, 47.28; H, 5.47; N, 3.80. Found: C, 46.91; H, 5.65; N, 3.82.

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The Formation of 1,1′-(2-Deoxy-D-ribofuranosyl-2′-deoxy-D-ribofuranoside) Tetra-O-*p*-toluate in the Synthesis of 2-Deoxy-D-ribofuranosyl Nucleosides[1]

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In the course of preparing moderately large-scale quantities of the α and β anomers of 2′-deoxythioguanosine[2] by the coupling of the mercury complex of 2-acetamido-6-chloropurine[2] and 2-deoxy-α-D-ribofuranosyl chloride,[3] we have had occasion to examine the coupling mixture after removal of the nucleosides and unreacted purine starting materials. The resulting residue after evaporation of solvents was a partially crystalline syrup whose infrared spectrum indicated the absence of hydroxyl absorption and was quite similar to that of the methyl glycoside of 2-deoxy-D-ribofuranose 3,5-di-O-*p*-toluate. Crystallization of the crude syrup from methanol gave a well-defined chromatographically pure solid in poor yield, mp 149–150°, $[\alpha]^{23.8}D$ −15° ($CHCl_3$), whose elementary analysis was in accord with the empirical formula $C_{42}H_{42}O_{11}$ indicating a composition for the product as one composed of two di-*p*-toluoyl-2-deoxyribosyl segments plus an atom of oxygen. An osmometric molecular weight determination also favored a "dimeric" formula of this type. The crystalline material on solution in glacial acetic acid and treatment with anhydrous hydrogen chloride gave a good yield of 2-deoxy-α-D-ribofuranosyl chloride 3,5-di-O-*p*-toluate with melting point, optical rotation, and infrared spectrum identical with that of a sample prepared in the same manner from 1-O-methyl-2-deoxy-D-ribofuranose 3,5-di-O-*p*-toluate.[3] For recovery of the rather expensive halo sugar, it has

(1) (a) 1,1′-(2-Deoxy-D-*erythro*-pentofuranosyl-2′-deoxy-D-*erythro*-pentafuranoside) tetra-O-*p*-toluate. (b) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. SA-43-ph-3764. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

(2) R. H. Iwamoto, E. M. Acton, and L. Goodman, *J. Med. Chem.*, **6**, 684 (1963).

(3) M. Hoffer, *Chem. Ber.*, **93**, 2777 (1960); M. Hoffer, R. Duschinsky, J. J. Fox, and N. Yung, *J. Am. Chem. Soc.*, **81**, 4112 (1959); A. K. Bhattacharya, R. K. Ness, and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 428 (1963).