attempted distillation or addition of water to the mixture, the product showed a tendency to polymerize as noted by several other workers.[19]

Reaction of 1,3,5-Trichloro-2,4,6-trioxohexahydro-*s*-triazine with 2,5-Dihydrofuran Using Wet Acetone as the Solvent.—To 11.62 g (0.05 mole) of trichloroisocyanuric acid completely dissolved in 250 ml of acetone containing 3 ml of water and stirred at 0° was added 7.0 g (0.10 mole) of 2,5-dihydrofuran. The reaction mixture was clear and colorless for about 90 min. Then a yellow color appeared for a short period of time and the solution immediately turned white as cyanuric acid precipitated. After allowing the reaction mixture to stir overnight, the cyanuric acid was separated by filtration. The filtrate (150 ml) was distilled through a 16-cm Vigreux column giving 2.26 g (18.5%) of clear *trans*-3-chloro-4-hydroxytetrahydrofuran product, bp 108–110° (19 mm). The physical constants of the product were identical with those reported in the literature for *trans*-3-chloro-4-hydroxytetrahydropyran.[11]

Anal. Calcd for $C_4H_6ClO_2$: C, 39.20; H, 5.76; Cl, 28.93. Found: C, 39.40; H, 5.87; Cl, 29.14.

Reaction of 1,3,5-Trichloro-2,4,6-trioxohexahydro-*s*-triazine with 5,6-Dihydro-4H-pyran Using Wet Acetone as the Solvent.—To 10 ml (9.27 g, 0.11 mole) of 5,6-dihydro-4H-pyran, wet with 3 ml of water and stirred at 25° in 100 ml of acetone, 11.62 g (0.05 mole) of trichloroisocyanuric acid was slowly added over a period of 8 hr. Upon contact of the trichloroisocyanuric acid with the liquid surface of the reaction mixture, a vigorous reaction was observed. After allowing the reaction mixture to stir overnight, the cyanuric acid was removed and nitrogen was then allowed to pass through the filtrate for 3–4 hr. The filtrate was distilled through a 16-cm Vigreux column under reduced pressure. 2-Hydroxy-3-chlorotetrahydropyran, 5.09 g, 34%, bp 95–97° (3 mm), $n^{20}D$ 1.4840, was isolated as the first fraction. It consisted of a light brown viscous liquid which solidified to a white, crystalline mass on setting for about 24 hr, mp 60–62°. These physical constants agree with those reported in the literature.[12]

Anal. Calcd for $C_5H_8ClO_2$: C, 43.97; H, 6.64; Cl, 25.96. Found: C, 44.08; H, 6.68; Cl, 25.98.

(3-Chlorotetrahydropyranyl-2) ether (6.39 g, 45%), bp 100–103° (12 mm), was isolated as the second fraction. On setting at room temperature, the entire liquid turned to a crystalline mass, mp 105–106°. A sample was prepared for analysis by sublimation of a portion of these crystals resulting in colorless crystals, mp 107–108°. This compound was shown to be identical with that prepared above by hydrolysis of *trans*-2,3-dichlorotetrahydropyran as verified by mixture melting point and infrared spectra.

Anal. Calcd for $C_{10}H_{16}Cl_2O_3$: C, 47.07; H, 6.18. Found: C, 46.94; H, 6.07.

(19) (a) B. Funk, *Ber.*, **26**, 2575 (1893); (b) F. Fichter and A. Beisswenger, *ibid.*, **36**, 1200 (1903); (c) W. H. Carothers, *J. Am. Chem. Soc.*, **51**, 2548 (1929).

5-Hydroxytetrahydropyrimidine and Its 2-Methyl Homolog

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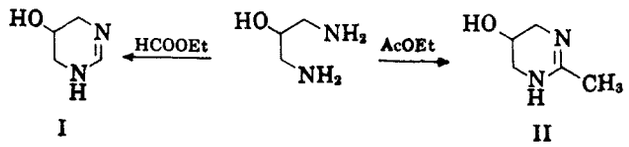
The recent report[1] of unsuccessful attempts to prepare 1,4,5,6-tetrahydro-5-hydroxypyrimidine (I) prompts us to report the synthesis of this compound and of its 2-methyl homolog, as prepared in connection with other studies in these laboratories.

Thus, I was obtained in yields of 10 to 27% by the condensation of 1,3-diaminopropan-2-ol with ethyl formate in ethanol solution. The 2-methyl homolog



I II

(II) was prepared in xylene solution, *i.e.*, using conditions similar to those reported for the synthesis of the 2-benzyl analog.[2] Attempts to prepare I in xylene generally resulted in the formation of a brown tar.

As in the case of the parent 1,4,5,6-tetrahydropyrimidine,[3] both I and II are very strong bases that hydrolyze in water, with a half-life of about 10 min and 2 hr, respectively, at 25°. The hydrolyses were conveniently followed titrimetrically. Here, two inflection points were obtained, the first corresponding to the end point of the strongly basic starting material, the second to that of its less basic amido hydrolysis product. Because of this rapid reaction with water, the pK_a (10.9 at 0.0050 ionic strength) of I was obtained as the pH, measured immediately upon the addition of a calculated 0.5 equiv of hydrochloric acid. The less rapidly hydrolyzed II, however, was dissolved and immediately titrated with little or no detectable hydrolysis, as judged from the plot of its titration curve. Its pK_a value (11.4 at 0.0050 ionic strength) was taken from the half-neutralization point of the initial titration curve.

From the hydrolysis of II, 2-hydroxy-3-acetamidopropylamine was isolated as a crystalline product. The hydrolysis product of I was obtained as an oil, which could not be induced to crystallize.

Because of their hydrolytic instability, both I and II gave rapidly changing nmr spectra in heavy water. At an ambient probe temperature of 42°, for example, I was completely hydrolyzed in 5 min, a rate too fast to be measured by this method. No attempt was made to follow the reaction by nmr at a lower temperature. The slower hydrolysis of II, however, was conveniently followed by nmr at ambient (37°) conditions.

Experimental Section[4]

1,4,5,6-Tetrahydro-5-hydroxypyrimidine (I).—Into a flask equipped with a magnetic stirrer, reflux condenser, and addition funnel was placed 10.0 g (0.11 mole) of redistilled 1,3-diaminopropan-2-ol (Eastman, P 3424), mp 42–45°, dissolved in 40 ml of absolute ethanol. Ethyl formate (8.2 g, 0.11 mole) was added rapidly with stirring, and the temperature rose from 27 to 45° during 5 min. The mixture was refluxed for 15 min, and the ethanol was removed at 110 mm and a pot temperature of 53°. The clear, viscous oil solidified on attempted distillation at 0.4 mm, when the pot reached 100°. A crude yield of 10.8 g was obtained. Two recrystallizations of 6.9 g from acetonitrile gave 2.4 g of I as white flakes: mp 154–155°, ν_{max}^{KBr} 1635 ($\nu_{C=N}$)[5] and 1530 (δ_{NH})[5] cm^{-1}, λ_{max}^{MeOH} 208 mμ (ε 6800).

Anal. Calcd for $C_4H_8N_2O$: C, 47.97; H, 8.07; O, 16.00; mol wt, 100.096. Found: C, 47.87; H, 8.22; O, 16.22; mol wt, 100.099 (mass spectrum); neut equiv, 100.[5]

A hydrochloride, mp 168–170°, was prepared using anhydrous hydrogen chloride in isopropyl alcohol and was recrystallized

(1) R. F. Evans and J. S. Shannon, *J. Chem. Soc.*, 1406 (1965).

(2) C. A. Dornfield, U. S. Patent 2,704,757 (1955); *Chem. Abstr.*, **50**, 5040g (1956).

(3) D. J. Brown and R. F. Evans, *J. Chem. Soc.*, 527 (1962).

(4) Melting points are uncorrected. Infrared spectra were run on a Perkin-Elmer 237B grating spectrophotometer. Ultraviolet spectra were obtained by Mr. I. Master with a Cary 14 spectrophotometer, mass spectral data by Mr. L. Daasch with a Consolidated Electrodynamics 21-110 spectrometer, and some of the titration data by Mr. C. Andreasen with a Beckman Zeromatic pH meter.

(5) The hydrolysis reaction does not affect the calculated neutral equivalent, which was obtained from the second inflection point.

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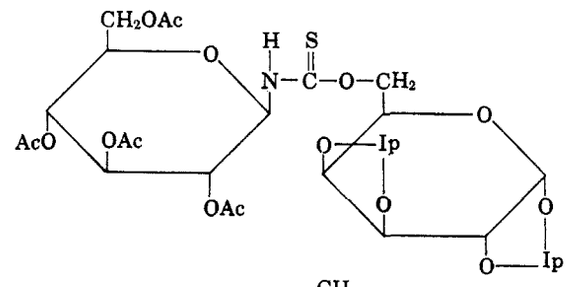
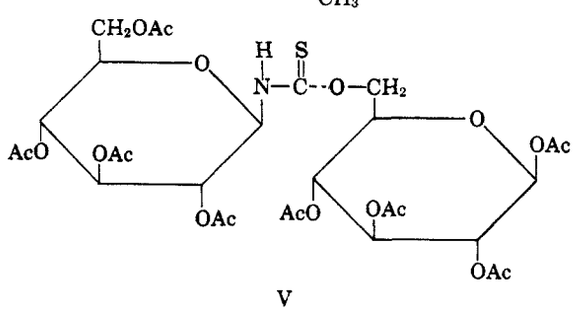
Sugar isothiocyanates have been used previously in a reaction with simple amino acids to form *N*-glycosides of the thiourea and hydantoin series.[1] The present note describes the reaction with the hydroxyl and amino groups of partially substituted sugars.

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.

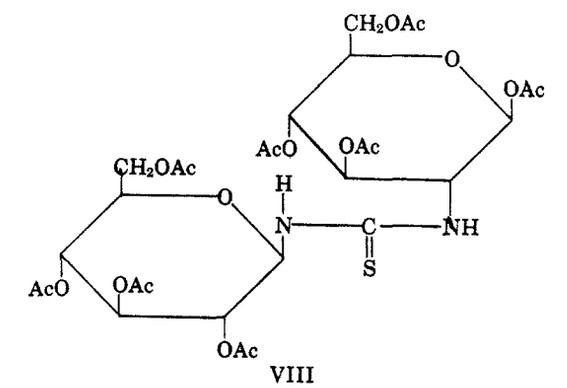
CHART I



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

(1) K. Haring and T. B. Johnson, *J. Am. Chem. Soc.*, **55**, 395 (1933).
(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).