crystallized from *n*-hexane to a constant melting point of 58°; $\bar{\nu}$ in cm.$^{-1}$ (film) 1795 (C=O) and 1660 (C=O); λ_{max}^{EtOH} ($\epsilon \times 10^{-4}$) 255 (1.11).

Anal. Calcd. for $C_{11}H_{14}O_3 \cdot 1/4H_2O$: C, 66.48; H, 7.35. Found: C, 66.65; H, 7.15.

2-(2-Oxopropyl)-5,5-dimethylcyclohexane-1,3-dione (IX).—A mixture of 11.3 g. (0.210 mole) of sodium methoxide, 30 g. (0.214 mole) of 5,5-dimethylcyclohexane-1,3-dione, and 20.3 g. (17.5 ml., 0.221 mole) of chloroacetone in 145 ml. of ethanol was heated under reflux for 15 min. and then cooled. The sodium chloride which formed was removed by filtration, and the filtrate was concentrated *in vacuo*. The residual sirup was dissolved in a mixture of chloroform (50 ml.) and 10% sodium hydroxide (50 ml.). The aqueous phase was separated and reextracted with chloroform (50 ml.). The aqueous phase was cooled in an ice bath, made acidic with concentrated hydrochloric acid, and extracted with chloroform (3 × 50 ml.). The combined organic extracts were dried with anhydrous magnesium sulfate, filtered, and the filtrate was evaporated *in vacuo* to dryness. Recrystallization of the crude product from a mixture of chloroform and hexane gave 17.3 g. of the desired product (IX), m.p. 134–136°. Concentration of the mother liquor gave an additional 12.7 g. of IX, m.p. 132–133°. The total yield was 30.0 g. (71.5%). Recrystallization from a mixture of chloroform and hexane gave the analytical sample, m.p. 134–136°; $\bar{\nu}$ in cm.$^{-1}$ (KBr) 1725 (C=O), 1650 and 1570 (enolic β-diketone); λ_{max}^{EtOH} ($\epsilon \times 10^{-4}$) 262 (1.44); λ_{max}^{NaOH} ($\epsilon \times 10^{-4}$) 289 (2.46).

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.33; H, 8.22. Found: C, 67.47; H, 8.22.

2,6,6-Trimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran (X).—2-(2-Oxopropyl)-5,5-dimethylcyclohexane-1,3-dione (2.00 g., 10.2 mmoles) was added to a mixture of 22 ml. of water and 3.5 ml. of concentrated hydrochloric acid, and the mixture was heated under reflux for 75 min. The cooled reaction mixture was extracted with chloroform (2 × 20 ml.); the combined chloroform extracts were dried with anhydrous magnesium sulfate, filtered, and the filtrate was evaporated *in vacuo* to dryness; yield, 1.73 g. (95.1%), m.p. 72°. Sublimation from an oil bath at 60°/0.2 mm. gave the analytical material, m.p. 72°; $\bar{\nu}$ in cm.$^{-1}$ (KBr) 1690 (C=O), 1585 (furan); $\lambda_{max}^{CHCl_3}$ ($\epsilon \times 10^{-3}$) 271 (5.17).

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.07; H, 7.91. Found: C, 73.92; H, 7.94.

3-Acetoxy-2-(2-oxopropyl)-5,5-dimethylcyclo-2-hexenone (VIII).—A mixture of 5.00 g. (25.5 mmoles) of 2-(2-oxopropyl)-5,5-dimethylcyclohexane-1,3-dione and 36.0 ml. of acetic anhydride was heated under reflux for 10 min., and the reaction mixture was concentrated *in vacuo*. Distillation of the residual oil gave 4.35 g. (71.6%) of pure product, b.p. 89°/0.03 mm.; $\bar{\nu}$ in cm.$^{-1}$ (film) 1775 (C=O, enol ester), 1720 (C=O), 1675 (α,β-unsaturated ketone); λ_{max}^{EtOH} in mμ ($\epsilon \times 10^{-3}$) 239 (8.80).

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.50; H, 7.61. Found: C, 65.56; H, 8.05.

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Synthesis of Amino Sugars by Reduction of Hydrazine Derivatives. 5-Amino-3,6-anhydro-5-deoxy-L-idose Derivatives[1-3]

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A comparison was made of the relative efficiencies of the nucleophilic reagents hydrazine and azide ion, for displacement of secondary *p*-tolylsulfonyloxy groups in certain sugar rings, as a preparative route to amino sugars. Both reagents appeared equally effective in displacing the 5-substituent of 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (I, Ia) to give derivatives with the L-idose configuration. In another derivative (V, VII), where approach of the attacking group was more sterically hindered, hydrazine was the more effective reagent.

The displacement of sulfonate esters of secondary hydroxyl groups in sugar rings, under conditions where neighboring group participation cannot assist the reaction, requires use of powerful nucleophilic reagents under forcing conditions, and proceeds with Walden inversion. The displacement of "isolated" secondary *p*-tolylsulfonyloxy groups by hydrazine is a typical reaction of this type, and has been useful as a synthetic route to new and rare amino sugars,[3,4] since the hydrazino derivatives are readily reduced to amino derivatives. Under suitable conditions the hydrazinolysis reaction gives hydrazino derivatives in high yield, but side reactions leading to unsaturated derivatives[5] may occur and the possibility exists that polysubstituted hydrazines might form. An alternative synthetic route, displacement of an isolated secondary *p*-tolylsulfonyloxy group by azide ion, a powerful nucleophile, would be expected to give an azido derivative with inversion, and formation of polysubstituted derivatives would be excluded. Azido groups are readily reduced to amino groups. Displacement of a *primary* *p*-tolylsulfonyloxy group by azide ion occurs readily[6] and is the procedure of choice for synthesis of ω-aminodeoxy sugars, such as 6-amino-6-deoxy-D-glucose[7] since the disubstituted derivatives formed as side products[8] in syntheses by the hydrazine method, cannot form.

(1) Supported by Grant No. CY-3232 (C4) from the Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Bethesda 14, Md. (R. F. Project 759D).

(2) Reported in part in *Abstr. Papers Am. Chem. Soc.*, **141**, 7D (1962).

(3) Previous publication on this subject: D. Horton, M. L. Wolfrom, and A. Thompson, *J. Org. Chem.*, **26**, 5069 (1961).

(4) M. L. Wolfrom, F. Shafizadeh, and R. K. Armstrong, *J. Am. Chem. Soc.*, **80**, 4885 (1958); M. L. Wolfrom, F. Shafizadeh, R. K. Armstrong, and T. M. Shen Han, *ibid.*, **81**, 3716 (1959); R. Kuhn and G. Baschang, *Ann.*, **628**, 193 (1959); W. Roth and W. Pigman, *J. Org. Chem.*, **26**, 2455 (1961).

(5) K. Freudenberg and F. Brauns, *Ber.*, **55**, 3233 (1922).

Azide ion also has been used for displacement of *secondary* sulfonate ester or halogen groups *trans* to an adjacent sulfur atom in a sugar ring, and this displacement proceeds, by neighboring group participation, through an episulfonium ion intermediate with net retention of configuration.[9] The present investigation is concerned with displacement of *isolated* *p*-tolylsulfonyloxy groups in sugar rings by azide ion, a reaction expected to occur with inversion by a direct bimolecular displacement, and comparison of this reaction with the hydrazinolysis procedure as a synthetic route for amino sugars.[9a]

Two derivatives were selected for study, one in which there was little possibility of steric hindrance in the displacement reaction, and a second derivative in which the approaching reagent was likely to encounter steric hindrance. The first derivative, 3,6 - anhydro - 1,2 - *O* - isopropylidene - 5 - *O* - *p*-tolylsulfonyl-α-D-glucofuranose (I)[10] has (see Ia) three fused five-membered rings which hold the molecule in a rigid arrangement with the acetal ring at 120° to the plane of the furanose ring and below it, with the 3,6-anhydro ring oriented similarly *above* the plane of the furanose ring. The *p*-tolylsulfonyloxy group is *endo*, that is, it projects *into* the V formed by the furanose and 3,6-anhydro rings. The second derivative, 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (V) has two fused five-membered rings, with the 1,2-acetal ring at approximately 120° to the furanose ring, and below it. The *p*-tolylsulfonyloxy group is *exo* (see VII) to the fused bicyclic system. It is known[11] that *endo* *p*-tolylsulfonyloxy groups are more readily displaced, by nucleophilic reagents, from such bicyclic fused five-membered ring systems, than are *exo* groups. This is due to the less hindered, rear side approach of the displacing group in the former case.

The first derivative (I = Ia) reacted with hydrazine to give, in 80% yield, the crystalline 5,6-anhydro-5-deoxy-5-hydrazino-1,2-*O*-isopropylidene-β-L-idofuranose (II), further characterized as a Schiff base with 2-hydroxy-1-naphthaldehyde. The hydrazino derivative could be quantitatively reduced to the crystalline 5-amino analog (IV) by merely stirring with an excess of active Raney nickel. This procedure is a considerable simplification of previously described methods[3,4] involving hydrogenation under pressure. Substance IV was further characterized as the *N*-acetyl derivative, and as the Schiff bases with salicylaldehyde and 2-hydroxy-1-naphthaldehyde. The reaction of I with excess sodium azide was studied under a variety of conditions. The isolated product was examined by infrared spectroscopy for the appearance of the highly characteristic azide group absorption at 4.8 μ and the disappearance of the aromatic ring and sulfonate group absorptions. Reaction was apparently complete in *N*,*N*-dimethylformamide containing some urea and 5% of water after thirty-six hours at 115°. A high yield of 3,6 - anhydro - 5 - azido - 5 - deoxy - 1,2 - *O* - isopropylidene-β-L-idofuranose (III) was obtained. This derivative was readily reduced with Raney nickel at room temperature to give 5-amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene - β - L - idofuranose (IV) in excellent yield. Since this derivative is the same as that formed in the hydrazinolysis reaction it is evident that both reactions followed an identical steric course and both gave the desired product in over-all yields of about 80%.

The hydrazinolysis of 1,2:5,6-di-*O*-isopropylidene 3-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (V) has been studied by a number of workers[4,5,12] and 50–80% yields of 3-deoxy-3-hydrazino-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose have been recorded. This reaction was found to proceed in 75–80% yield under the hydrazinolysis conditions used in this study with I. Attempted displacement of the 3-*p*-tolylsulfonyloxy group of V with azide ion, however, under the optimum conditions established with I, gave a 90% return of crystalline starting material. Even when the temperature was raised to the boiling point of the solvent mixture, the displacement occurred only slowly and with extensive decomposition.

The remarkable difference in reactivity of the two reagents toward V and the similarity of their behavior toward I may be rationalized by considering the factors governing the approach of the reagent to each species. In the case of I there is no hindrance of access to either hydrazine or azide ion on the side of C-5 opposite from the *p*-tolylsulfonyloxy group as is seen in the perspective representation Ia, and the two reagents may effect displacement with equal facility. However, in the case of compound V, an approaching azide ion, a negatively charged group, must enter the V, formed by the fused rings, to attack C-3 from the side opposite from the *p*-tolylsulfonyloxy group. To do so it must overcome electrostatic repulsions from the ring oxygen, the C-1 oxygen, and the C-2 oxygen, factors which would be expected to limit its reac-

(6) F. D. Cramer, H. Otterbach, and H. Springmann, *Chem. Ber.*, **92**, 384 (1959).

(7) F. D. Cramer, in "Methods in Carbohydrate Chemistry," Vol. I, R. L. Whistler and M. L. Wolfrom, eds., Academic Press, New York, N. Y., 1962, p. 242.

(8) K. Freudenberg and R. M. Hixon, *Ber.*, **56**, 2119 (1923); W. M. Corbett and D. Winters, *J. Chem. Soc.*, 4823 (1961).

(9) C. D. Anderson, W. W. Lee, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **83**, 1900 (1961); J. E. Christensen and L. Goodman, *ibid.*, **83**, 3827 (1961).

(9a) NOTE ADDED IN PROOF. Since this manuscript was submitted a communication has been submitted and published [E. J. Reist, R. R. Spencer, B. R. Baker, and L. Goodman, *Chem. Ind.* (London), 1794 (1962).] which describes the conversion of methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(methylsulfonyl)-α-D-galactopyranoside into sirupy methyl 4-azido-2,3,6-tri-*O*-benzoyl-4-deoxy-α-D-glucopyranoside in 79% yield by the action of sodium azide in boiling *N*,*N*-dimethylformamide.

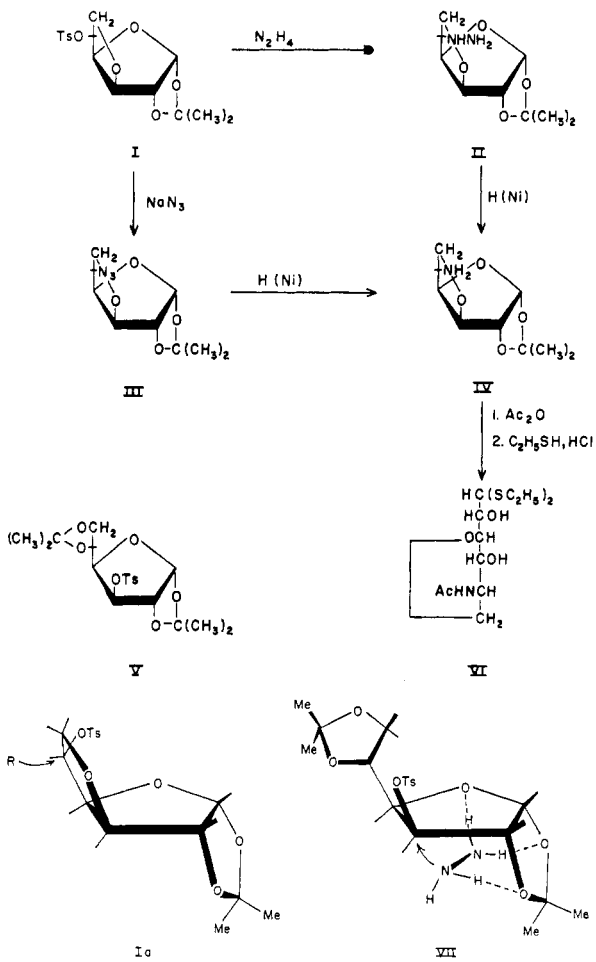
(10) H. Ohle, L. von Vargha, and H. Erlbach, *Ber.*, **61**, 1211 (1928).

(11) A. C. Cope and T. Y. Shen, *J. Am. Chem. Soc.*, **78**, 3177 (1956).

(12) R. U. Lemieux and P. Chu, *ibid.*, **80**, 4745 (1958); B. Coxon and L. Hough, *J. Chem. Soc.*, 1643 (1961).

tivity. On the other hand, a hydrazine molecule does not carry a charge, and furthermore, an intermediate tridentate hydrogen-bonded complex VII is sterically feasible. Such a structure would stabilize the hydrazine molecule in the most favorable orientation to effect nucleophilic attack on C-3.

5-Amino-3,6-anhydro-1,2-*O*-isopropylidene-β-L-idofuranose (IV) is of interest as an example of a 5-amino-5-deoxyhexose derivative; derivatives of 5-amino-5-deoxyhexuloses have been prepared[13] by the microbiological oxidation of 2-acetamido-2-deoxy-D-glucitol. The furanose ring of IV could be readily opened, after *N*-acetylation, by treatment with ethanethiol and hydrochloric acid, and the resultant crystalline diethyl dithioacetal (VI) was further characterized as the 2,4-diacetate. Direct acid hydrolysis of IV gave 5-amino-3,6-anhydro-5-deoxy-L-idose as the sirupy hydrochloride. This product showed no carbonyl absorption in the infrared, and thus presumably was a furanose or aldehydrol form. A six-membered ring involv-



ing the nitrogen atom is impossible from steric considerations, since the 3,6-anhydro ring does not permit C-1 to approach the amino group. Acetylation of the anhydro amino sugar failed to give a crystalline product.

Attempts were made to open the anhydro ring of IV with boron trichloride or boron tribromide, reagents which are used for cleavage of ether and acetal groups in carbohydrate derivatives.[14] Paper chromatography of the products, however, indicated that the reaction probably had only cleaved the isopropylidene acetal group.

Experimental[15]

3,6-Anhydro-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (I).—This compound was prepared in essentially quantitative yield from 1,2-*O*-isopropylidene-5,6-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranose[16] by the method of Ohle, von Vargha, and Erlbach.[10] The physical constants were in close agreement with those cited.

3,6-Anhydro-5-deoxy-5-hydrazino-1,2-*O*-isopropylidene-β-L-idofuranose (II).—3,6-Anhydro-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (17.5 g.) in anhydrous hydrazine (100 g.) was boiled for 36 hr. under reflux with a slow stream of nitrogen. The cooled solution was extracted with five 250-ml. portions of peroxide-free ether, and the extract was evaporated to low volume to give the crystalline product; yield 8.7 g. (80%). Pure material was obtained as long needles on crystallization from ether; m.p. 99–101°, $[\alpha]^{20}D$ +30° (*c* 0.5, methanol).

Anal. Calcd. for $C_9H_{16}N_2O_4$: N, 12.96. Found: N, 12.90.

The crystalline product became sirupy after storage for 3 days in a vacuum desiccator over phosphorus pentaoxide.

3,6-Anhydro-5-deoxy-5-[(2-hydroxy-1-naphthylmethylene)-hydrazino]-1,2-*O*-isopropylidene-β-L-idofuranose.—A solution of 3,6-anhydro-5-deoxy-5-hydrazino-1,2-*O*-isopropylidene-β-L-idofuranose (2.1 g.) in methanol (5 ml.) was treated with a solution of 2-hydroxy-1-naphthaldehyde (4 g.) in methanol (70 ml.). The product separated after 3 hr.; yield 1.6 g. (42%). Recrystallization from methanol gave pure material as small yellow prisms; m.p. 185–187°, $[\alpha]^{20}D$ +22° (*c* 0.5, chloroform), $\lambda_{max(\mu)}^{KBr}$ 6.20, 6.27 (C = N, aryl C = C), 6.65, 13.20, 14.30 (aryl C = C); X-ray powder diffraction data[17]: 9.07 w, 7.73 m, 6.71 s (3), 5.93 s (2), 5.45 w, 5.17 m, 4.86 m, 4.65 w, 4.48 s (1), 4.25 m, 3.99 m.

Anal. Calcd. for $C_{20}H_{22}N_2O_5$: C, 64.86; H, 5.90; N, 7.56. Found: C, 64.88; H, 5.61; N, 7.65.

3,6-Anhydro-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (III).—To a solution of 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (17.5 g.) in purified *N*,*N*-dimethylformamide (150 ml.) was added water (8 ml.), sodium azide (4 g.), and urea (0.5 g.). The mixture was heated for 36 hr. at 115° under a stream of nitrogen, the solvent was then evaporated under reduced pressure, and the residue was dissolved in 1,2-dichloroethane. The solution was washed with water, dried (magnesium sulfate), and the solvent evaporated to give a colorless sirup; yield 9.5 g. (83%). This sirup was crystallized from hexane

(13) J. K. N. Jones, M. B. Perry, and J. C. Turner, *Can. J. Chem.*, **39**, 965, 2400 (1961).

(14) T. G. Bonner, E. J. Bourne, and S. McNally, *J. Chem. Soc.*, 2929 (1960); T. G. Bonner and N. M. Saville, *ibid.*, 2851 (1960).

(15) Melting points were taken on a Fisher–Johns apparatus. The infrared spectra were determined with a Baird-Atomic Model B infrared spectrophotometer. Specific rotations were measured with a 4-dm. polarimeter tube. Paper chromatographic data refer to descending chromatograms on Whatman no. 1 paper, with 5:5:3:1 ethyl acetate–pyridine–water–acetic acid, according to the procedure of F. G. Fischer and H. J. Nebel, *Z. physiol. Chem.*, **302**, 10 (1955).

(16) L. D. Hall, L. Hough, and R. A. Pritchard, *J. Chem. Soc.*, 1537 (1961).

(17) Interplanar spacing, Å, Cu$K\alpha$ radiation. Relative intensity, estimated visually: s, strong; m, medium; w, weak; v, very. First few strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities.

as large prisms; yield 4.7 g., m.p. 48–49°, $[\alpha]^{20}D$ +42° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 4.82 (−N_3), aromatic and sulfonate absorptions absent; X-ray powder diffraction data[17]: 12.54 w, 9.41 m, 7.90 s (4), 6.46 w, 5.81 m, 5.11 vs (1), 4.80 s, 4.25 vs (2), 3.89 s (3), 3.78 vw, 3.58 w, 3.40 vw, 3.26 s, 3.15 vw, 3.06 vw, 2.97 vw.

Anal. Calcd. for $C_9H_{13}N_3O_4$: C, 47.57; H, 5.73; N, 18.50. Found: C, 47.84; H, 5.69; N, 18.70.

Further crystalline material was obtained from the sirup, but traces of *N,N*-dimethylformamide appeared to inhibit complete crystallization. The sirupy and crystalline material had identical infrared spectra, and gave the same reduction product (see below).

5-Amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (IV). (a).—A solution of 3,6-anhydro-5-deoxy-5-hydrazino-1,2-*O*-isopropylidene-β-L-idofuranose (5 g.) in methanol (120 ml.) was treated with Raney nickel[18] (10 g.). The mixture was stirred occasionally, fresh catalyst (10 g.) was added after 24 hr., and after 48 hr. the solution was filtered and concentrated, to give a crystalline product as fine needles; yield 4.6 g. (100%). Pure material was obtained on recrystallization from ether; m.p. 113–114°, $[\alpha]^{20}D$ +18.5° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 3.00 (NH), 7.21 (CCH_3).

Anal. Calcd. for $C_9H_{15}NO_4$: C, 53.73; H, 7.46; N, 6.46. Found: C, 53.46; H, 7.19; N, 6.40.

The substance is hygroscopic, but is stable on storage in a desiccator.

(b). A solution of crude sirupy 3,6-anhydro-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (5.7 g.) in methanol (150 ml.) was treated with Raney nickel[18] (40 g.) for 48 hr., filtered, and concentrated, to give crystalline 5-amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose; yield 4.8 g. (92%), physical constants in full agreement with those cited under (a). The pure crystalline azido derivative reacted analogously.

3,6-Anhydro-5-deoxy-1,2-*O*-isopropylidene-5-salicylideneamino-β-L-idofuranose.—5-Amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (1 g.) in methanol (25 ml.) was treated with salicylaldehyde (2 ml.) for 12 hr. at room temperature, and yellow needles of the Schiff base were filtered; yield 700 mg. (47%), m.p. 174–175°, $[\alpha]^{20}D$ +123° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 6.10, 6.20, 6.25 (C = N, aryl C = C), 6.66 (aryl C = C), 7.23 (CCH_3), 13.07, 14.3 (aryl C = C); X-ray powder diffraction data[17]: 8.12 s (2, 2), 7.50 w, 6.63 w, 5.85 vw, 5.57 vw, 5.37 s (1), 5.04 s (2, 2), 4.66 m, 4.53 s, 4.31 m, 4.11 w, 4.04 m, 3.90 vw, 3.35 s (3), 3.11 vw, 2.98 vw.

Anal. Calcd. for $C_{16}H_{19}NO_5$: C, 62.95; H, 6.23; N, 4.59. Found: C, 62.74; H, 5.98; N, 4.90.

3,6-Anhydro-5-deoxy-5-[(2-hydroxy-1-naphthylmethylene)-amino]-1,2-*O*-isopropylidene-β-L-idofuranose. Solutions of 5-amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (1 g.) in methanol (5 ml.) and 2-hydroxy-1-naphthaldehyde (2 g.) in methanol (40 ml.) were mixed, left 1 day at room temperature, and the yellow crystalline product filtered; yield 1.2 g. (68%), m.p. 196°, $[\alpha]^{20}D$ +82° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 6.19, 6.27 (C = N, aryl C = C), 6.63 (aryl C = C), 7.22 (CCH_3), 13.2, 14.3 (aryl C = C); X-ray powder diffraction data[17]: 8.55 s (1, 1), 8.27 w, 7.03 m, 6.22 vw, 5.99 w, 5.75 m, 5.52 s (3), 5.25 s (1, 1), 4.90 s (2, 2), 4.68 s (2, 2), 4.43 s, 4.01 m, 3.48 s (1, 1).

Anal. Calcd. for $C_{20}H_{21}NO_5$: C, 67.60; H, 5.91; N, 3.94. Found: C, 67.58; H, 5.68; N, 4.04.

5-Acetamido-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose.—A solution of 5-amino-3,6-anhydro-1,2-*O*-isopropylidene-β-L-idofuranose (1 g.) in methanol (10 ml.) was treated with acetic anhydride (1 ml.). After 1 hr. at room temperature, water (50 ml.) was added, and after a further 2 hr. excess acetic acid was removed by stirring with Dowex-1 ion exchange resin (carbonate form). The filtered solution was evaporated to give a glass which gave a negative ninhydrin reaction; yield practically quantitative. The product crystallized very slowly and incompletely during 3 months as large prisms; yield 270 mg. (22%), m.p. 84°, $[\alpha]^{20}D$ −6° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 6.10, 6.42 (NHAc), OH or NH_2 absent; X-ray powder diffraction data[17]: 13.19 m, 7.69 vs (1, 1), 6.73 vw, 5.95 s (2, 2), 5.40 s (2, 2), 5.01 m, 4.45 vs (1, 1), 3.99 w, 3.79 m, 3.60 w, 3.41 m, 3.15 m, 2.95 w.

Anal. Calcd. for $C_{11}H_{17}NO_5$: N, 5.76. Found: N, 6.06.

5-Acetamido-3,6-anhydro-5-deoxy-L-idose diethyl dithioacetal (VI).—A solution of 5-acetamido-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (10 g. as sirup from the preceding preparation) in concentrated hydrochloric acid (70 ml.) at 0° was shaken with ethanethiol (50 ml.) for 24 hr. at 0°. The mixture was diluted with cold methanol and neutralized (lead carbonate). The solution was filtered, evaporated, and the residue was crystallized as needles from ethyl acetate (100 ml.); yield 9.5 g. (70%), m.p. 108°, $[\alpha]^{20}D$ +2° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 6.03, 6.54 (NHAc); X-ray powder diffraction data[17]: 13.29 s (3), 11.26 m, 9.61 vs (1), 8.19 vw, 6.07 m, 5.64 w, 5.47 w, 5.08 m, 4.70 s (2) 4.33 s, 3.87 vvw, 3.74 s, 3.55 vw, 3.29 m, 3.16 w, 2.92 w.

Anal. Calcd. for $C_{12}H_{23}NO_4S_2$: C, 46.60; H, 7.44; N, 4.53; S, 20.71. Found: C, 46.74; H, 7.97; N, 4.73; S, 21.15.

5-Acetamido-2,4-di-*O*-acetyl-3,6-anhydro-5-deoxy-L-idose diethyl dithioacetal.—The preceding product (1 g.) was treated with pyridine (10 ml.) and acetic anhydride (3 ml.) for 24 hr. at 5°, poured on ice, and the product extracted with 1,2-dichloroethane. The extract was washed with water, then shaken with an aqueous solution of cadmium chloride (to remove traces of pyridine). The pyridine–cadmium chloride complex was filtered and the dried (magnesium sulfate) organic phase was evaporated. The resultant sirup crystallized as large prisms from ether–hexane; yield 800 mg. (69%), m.p. 70°, $[\alpha]^{20}D$ +17° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 5.71 (OAc), 6.00, 6.39 (NHAc).

Anal. Calcd. for $C_{16}H_{27}NO_6S_2$: C, 48.60; H, 6.90; N, 3.50; S, 16.30. Found: C, 48.40; H, 6.60; N, 3.60; S, 16.60.

Hydrolysis of 5-Amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose.—A solution of this derivative (1 g.) in *N* hydrochloric acid (50 ml.) was heated for 2 hr. at 98°, then evaporated below 40° to give a sirup, which gave a positive ninhydrin reaction; R_f 0.43. This product, presumably 5-amino-3,6-anhydro-5-deoxy-L-idose hydrochloride, could not be obtained crystalline. A product with identical chromatographic behavior was obtained by hydrolysis of 5-acetamido-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose.

Acetylation of the sirupy product with pyridine (10 ml.) and acetic anhydride (3 ml.) for 24 hr. at room temperature, and processing as described above gave an amorphous product; yield 750 mg. (53%), $[\alpha]^{20}D$ +90° (*c* 0.5, chloroform); $\lambda^{KBr}_{max(\mu)}$ 5.75 (OAc), 6.02 (Amide I), 6.40 (Amide II).

Treatment of 5-Amino-3,6-anhydro-5-deoxy-L-idose Derivatives with Boron Trichloride and Boron Tribromide.—Samples (10 mg.) of 5-amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose and the *N*-acetyl analog were treated with boron trichloride (5 ml.) for 12 hr. at −70°, then allowed to evaporate slowly at room temperature. The residues were treated with methanol and repeatedly evaporated with small quantities of methanol. Paper chromatography of the product showed in each case a zone with R_f 0.43 as the principal ninhydrin positive component, which was indistinguishable on paper chromatograms from an acid hydrolyzate of 5-amino-3,6-anhydro-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose. The experiments were repeated using boron tribromide in place of boron trichloride. The reaction mixture became black after a few hours. The paper

(18) Raney Nickel Catalyst No. 28, The Raney Catalyst Co., Inc., Chattanooga, Tenn.

chromatographic behavior of the products was essentially the same as in the reaction with boron trichloride.

Reaction of 1,2:5,6-Di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranose with Sodium Azide.—A mixture of the sulfonate ester derivative (5 g.), *N*,*N*-dimethylformamide (100 ml.), sodium azide (2 g.), water (5 ml.), and urea (1 g.) was heated for 36 hr. at 115° under a stream of nitrogen, and the reaction mixture was processed by the procedure used for 3,6-anhydro-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose. Crystalline starting material was obtained; yield 4.5 g. (90%). When the experiment was repeated at reflux temperature, decomposition occurred during the heating period, and the recovery of starting material fell to 1.3 g. (27%). The remaining dark sirup failed to crystallize, but exhibited a weak infrared absorption at 4.8 μ, characteristic of the azido group.

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Thiono- and Thiolcarbonates

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The esterification of allyl alcohol and substituted allyl alcohols with aryl chlorothionoformates yields pure S-allyl aryl thiolcarbonates, which arise from rearrangement of the intermediate thionocarbonates accompanied by an allylic shift. The reaction between 3,4-dichlorophenyl chlorothionoformate and ethylenechlorohydrin gave S-(2-chloroethyl) 3,4-dichlorophenyl thiolcarbonate, although similar reactions with ethanol, 2,2-dichloroethanol, and, 2,2,2-trichloroethanol gave the unrearranged thionocarbonates.

The preparation of several aryl ethyl thionocarbonates has been reported,[1,2] but apparently no investigation of the biological activity of aryl alkyl thionocarbonates has been made. More interest has been shown in diaryl thionocarbonates, which may be prepared by treating phenols with thiophosgene or by treating aryl chlorothionoformates with phenols in the presence of pyridine.[3]

It was found that aryl thionocarbonates are best prepared by adding aryl chlorothionoformates to alcohols in pyridine solution at low temperatures. The procedure described by Rivier,[1,2] in which the chlorothionoformate is refluxed in ethanol, gives moderate yields with lower molecular weight alcohols. However, some of the products prepared in this way are contaminated with small amounts of the isomeric thiolcarbonates, as indicated by the presence of a weak carbonyl band at 1720–1727 cm.$^{-1}$ No rearrangement occurred in the base-promoted esterification of unsubstituted alkanols. Further, the esterification of long-chain alcohols could be achieved only in the presence of pyridine.

The new aryl chlorothionoformates are described in Table I. The aryl alkyl thionocarbonates as well as some new diaryl thionocarbonates (some of which were obtained as by-products in the preparation of the chlorothionoformates) are listed in Table II.

TABLE I

CHLOROTHIONOFORMATES ROC(S)Cl

				C		H		Cl		S	
R	Yield, %	B.p., °C./mm.	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
3-Chlorophenyl	78	72/2.2[a]	$C_7H_4Cl_2OS$	40.60	40.25	1.95	2.26	34.24	34.22	15.48	15.23
4-Chlorophenyl	81	82/0.8[b]	$C_7H_4Cl_2OS$	40.60	41.00	1.95	1.93	34.24	34.21	15.48	15.66
3,4-Dichlorophenyl	83	98–100/1.3[c]	$C_7H_3Cl_3OS$	34.81	34.92	1.25	1.54	44.04	43.82	13.37	13.31
4-*t*-Butylphenyl	81	84/0.1[d]	$C_{11}H_{13}ClSO$	57.76	58.15	5.73	5.99	15.50	15.58	14.02	13.68
2-Chloro-4-nitrophenyl	50	116–118/0.25[e]	$C_7H_3C_2NO_3S$[f]	33.35	33.17	1.20	1.22	28.13	28.54	12.72	12.78

[a] $n^{25}D$ 1.59025, D^{20}_4 1.4076; [b] $n^{25}D$ 1.51273, D^{20}_4 1.4180; [c] m.p. 58–60°; [d] $n^{25}D$ 1.54901, D^{20}_4 1.4360; [e] m.p. 58–60°; [f] Calcd. N, 5.56. Found: N, 5.57.

The reaction of aryl chlorothionoformates with allyl alcohol and with substituted allyl alcohols yielded S-allyl O-aryl thiolcarbonates exclusively, as shown by the very strong C=O absorption at 1720–1727 cm.$^{-1}$. The attachment of the allyl group to the sulfur atom was established by the isolation of 2-chloro-4-nitrophenol from the hydrolysis of S-(1-methylallyl) O-(2-chloro-4-nitrophenyl) thiolcarbonate. The S-allyl derivatives were obtained by both preparative procedures. In an attempt to isolate the intermediate thionocarbonate, *p*-tolyl chlorothionoformate was treated with 2-buten-1-ol in pyridine solution at room temperature. The product, which was isolated in an analytically pure state by extraction with ether and drying at room temperature, exhibited the strong C=O absorption at 1723 cm.$^{-1}$ characteristic of thiolcarbonates.

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