treated with 30 ml. of 0.5 *N* perchloric acid in anhydrous acetic acid[37] followed by 16 ml. of acetic anhydride. The solution was left at room temperature for 5 hr., diluted with 30 ml. of water, and stored at 5° overnight. The pale yellow solution was passed over a column containing 50 ml. of Amberlite IRA-410 (acetate form) and the column was washed with water. The effluent and washings were combined, treated with 4 ml. of 2 *N* hydrochloric acid, and lyophilyzed to give 2.74 g. of XXI as a very hygroscopic solid. The infrared spectrum showed no amide bands but exhibited large bands at 1750 and 1605 cm.$^{-1}$ due to acetate and amine hydrochloride groups. The product became discolored and decomposed after 48 hr. at room temperature. For microanalysis a sample was dried at room temperature overnight in a vacuum desiccator. In subsequent preparations the product was used in the next step within 24 hr.

Anal. Calcd. for $C_{20}H_{34}N_2O_{12}\cdot 2HCl\cdot 4H_2O$: N, 4.41; Cl, 11.17. Found: N, 4.42; Cl, 11.17.

Deamination of XXI. Isolation and Characterization of L-Galactose (XXII).—To a cooled (0°) solution containing 1.72 g. of XXI in 10 ml. of water and 5 ml. of 2 *N* acetic acid was added a cold solution of 0.46 g. of sodium nitrite in 5 ml. of water with stirring in an atmosphere of nitrogen. The solution was allowed to stand at 5° overnight, and then extracted with three 30-ml. portions of ethyl acetate. The extracts were dried over sodium sulfate and evaporated to a sirup (0.96 g.). The sirup showed an elongated spot (5 cm.) $R_{galactose}$ 2.42 in isopropyl alcohol–water (4:1 by volume, solvent D). The sirup (0.9 g.) was dissolved in 50 ml. of 1 *N* sulfuric acid and heated on a steam bath for 1.5 hr. The cooled solution was extracted with two 15-ml. portions of ethyl acetate and the extracts were discarded. The aqueous phase was evaporated to a small volume and neutralized with barium hydroxide. The precipitate was filtered through a thin bed of Celite and the filtrate was passed over a column containing 15 ml. of Dowex 50X4 (H^+). The effluent was stirred with Amberlite IR45 (OH^-) until neutral, and evaporated to a colorless sirup (0.32 g.). Examination on paper chromatograms in solvent D showed essentially three distinct spots with R_f 0.3, 0.38, and 0.45 in increasing order of intensity. The medium and fast spots were subsequently identified as galactose and ribose, respectively. The sirup was separated on two Whatman no. 3 sheets (19 × 40 cm) in solvent D. The respective zones were cut and eluted to give three fractions: (1) R_f 0.45, 0.2 g. (ribose); (2) R_f 0.38, 37 mg. (galactose) and (3) R_f 0.30, 21.9 mg. (not further investigated).

A solution containing 22 mg. of material from fraction 2 was dissolved in 0.5 ml. of water and treated with 0.16 ml. of a solution containing 12 ml. of methylphenylhydrazine in 50 ml. of ethanol and 1.5 ml. of acetic acid. The solution was warmed briefly, then cooled, and the crystalline product was filtered to give 12 mg. of L-galactose methylphenylhydrazone. Recrystallization from aqueous ethanol gave pure material, m.p. 191–192°. An authentic sample of D-galactose methylphenylhydrazone prepared in the same way had m.p. 191–192°, m.m.p. 190–191°.

A portion (8 mg.) was acetylated in pyridine and acetic anhydride to give L-galactose methylphenylhydrazone pentaacetate (XXIII), m.p. 141–142°; $[\alpha]^{23}D$ −28° ± 0.7° (*c* 0.142, in 95% ethanol).[38] An authentic sample of D-galactose methylphenylhydrazone pentaacetate had m.p. 142–143°; mixed with XXIII, m.p. 129–131°; $[\alpha]^{23}D$ 38.9° ± 0.7° (*c* 0.142, in 95% ethanol).[38]

In another experiment the deamination product was hydrolyzed with 1 *N* sulfuric acid and processed as before. A portion of the neutralized hydrolyzate (0.15 g.) was dissolved in solvent C and added to a column containing 20 g. of cellulose powder[32]; the column was developed with the same solvent mixture and 3-ml. fractions were collected. The fractions consisting mainly of galactose were combined and evaporated to give 8 mg. of a sirup. Purification by preparative paper chromatography gave 6 mg. of a sirup having a strong negative rotation. On paper chromatograms the sirup gave one spot corresponding to galactose.

Deamination of III and XXIII.—To a solution containing 65 mg. of III in 3 ml. of water was added 0.12 g. of sodium nitrite followed by 4 ml. of 10% acetic acid at 0°. After standing at 5° overnight, the solution was passed over a cold column containing 3 ml. of Dowex 50X 4 (H^+), and the effluent and washings were evaporated to a small volume. Paper chromatography at this stage showed the presence of ribose and a faster elongated zone. The product was hydrolyzed with dilute hydrochloric acid and processed as before to give a dark sirup (20 mg.). Chromatography on paper showed the presence of ribose (strong), galactose (weak), and considerable tailing.

Deamination of XX in the same way showed the presence of ribose and galactose as before. When deamination was arrested after 2 hr. at 0° and processed as before, paper chromatography showed the presence of ribose (strong), galactose (weak), and at least two faster moving spots which gave a pink color with aniline hydrogen phthalate.[30]

NOTE ADDED IN PROOF.—2,6-Diamino-2,6-dideoxy-L-idose has been synthesized recently and found to be identical with paromose.[39]

Acknowledgment.—The authors wish to thank Dr. J. M. Vandenbelt and his associates of Parke, Davis & Company for spectral, X-ray diffraction, and optical rotation data, and C. E. Childs and associates for microanalyses.

(37) Prepared by mixing 1.43 g. of 70% perchloric acid with 2.3 ml. of acetic anhydride and diluting to 100 ml. with acetic acid.

(38) Measured with the Bendix-Ericsson polarimeter. We wish to thank Miss E. M. Tanner of Parke, Davis & Co., Hounslow, England, for this measurement.

(39) W. M. zu Reckendorf, *Angew. Chem.*, **75**, 573 (1963).

Synthesis of 5-Acetamido-5-deoxypentoses. Sugar Derivatives Containing Nitrogen in the Ring[1]

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The synthesis of 5-acetamido-5-deoxypentopyranoses and the isomeric 5-acetamido-5-deoxypentofuranoses having the D-xylo, D-ribo, and L-arabino configurations is described. In the D-ribo series, 5-acetamido-5-deoxy-D-ribofuranose was the predominant product of two independent syntheses. The stability, chromatographic properties, and n.m.r. spectra of these compounds are reported. The pentopyranose derivatives represent a new class of carbohydrate derivatives in which the ring oxygen is replaced by nitrogen.

In a preceding publication[2] the successful adaptation of the alkaline degradation of 1,1-bis(alkylsulfonyl)aminohexitol derivatives[3] to a 1,1-bis(alkylsulfonyl)-2,6-diacetamido-2,6-dideoxyhexitol was demonstrated. The expected degradation product was a 5-acetamido-5-deoxypentose. Since the 5-acetamido-5-deoxypentoses were not known at that time, their synthesis for use as model compounds was undertaken in this laboratory. Such derivatives are shown to be formed as an equilibrium mixture of 5-acetamido-5-

(1) Preliminary communication, Abstracts of Papers of the 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April, 1963, p. 19C.

(2) T. H. Haskell and S. Hanessian, *J. Org. Chem.*, **28**, 2598 (1963).

(3) L. Hough and M. Taha, *J. Chem. Soc.*, 3564 (1961).

deoxypentofuranose and 5-acetamido-5-deoxypentopyranose forms.

There is at present considerable interest in the synthesis of sugar derivatives containing a hetero atom in the ring. Replacement of the ring oxygen by sulfur was already demonstrated with the successful synthesis of 5-thio-D-xylopyranose,[4-6,8] 5-thio-D-ribopyranose,[7] methyl 5-thio-D-ribopyranoside,[8] and methyl 2-deoxy-5-thio-D-ribopyranoside.[8] The synthesis of 5-acetamido-5-deoxy-D-xylofuranose and the isomeric form containing nitrogen in the ring by the partial hydrolysis of suitably blocked 5-acetamido-5-deoxy-D-xylose derivatives was very recently reported by Paulsen[9] and by Jones and Szarek.[10] The synthesis of 5-acetamido-5-deoxy-L-arabinofuranose and its isomeric heterocyclic form also was disclosed recently by Jones and Turner.[11] These products were obtained by acid hydrolysis of 5-acetamido-5-deoxy-1,2-*O*-isopropylidene-L-arabinofuranose.

We wish to report our results on the synthesis of 5-acetamido-5-deoxy-D-xylopyranose (I), 5-acetamido-5-deoxy-L-arabinopyranose (XIII),[12] and the corresponding isomeric 5-acetamido-5-deoxypentofuranose derivatives. The new 5-acetamido-5-deoxy-D-ribopyranose (XXII) and 5-acetamido-5-deoxy-D-ribofuranose (XXIII) also are reported.

Selective N-acetylation[13] of 5-amino-5-deoxy-1,2-*O*-isopropylidene-D-xylose *p*-toluenesulfonate[14] (III) afforded 5-acetamido-5-deoxy-1,2-*O*-isopropylidene-D-xylofuranose (IV) as a homogenous sirup. Hydrolysis in dilute sulfuric acid (pH 1.3–1.6) for three to four days at room temperature gave a mixture of I and 5-acetamido 5-deoxy-D-xylofuranose (V). Separation by cellulose column chromatography gave I as a crystalline solid, m.p. 163–164°, $[\alpha]^{23}D$ −21.8° (water) and V as a colorless sirup, $[\alpha]^{23}D$ 30° (water).[15] Both compounds were homogeneous on paper chromatograms with V having a higher mobility than I. The six-membered ring structure of I was indicated by the absence of the amide II band in its infrared spectrum in contrast to that of V. The presence of four acetylatable hydroxyl groups in I was demonstrated by titration data. The two forms I and V gave the same 5-acetamido-5-deoxy-D-xylose benzylphenylhydrazone (VI) and 5-acetamido-5-deoxy-D-xylitol (VII), indicating a difference only in ring size between I and V. Solutions of I or V were

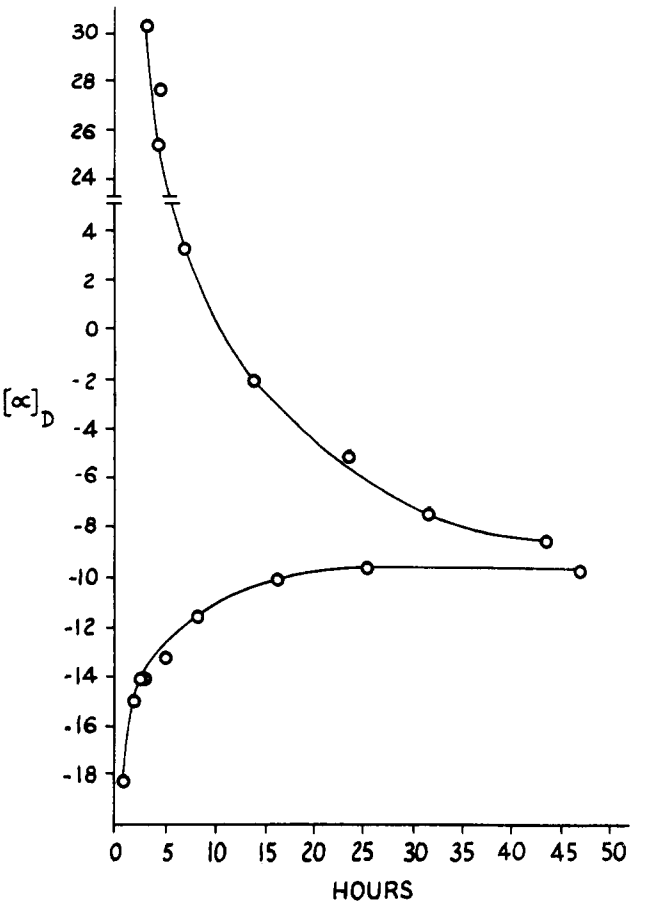
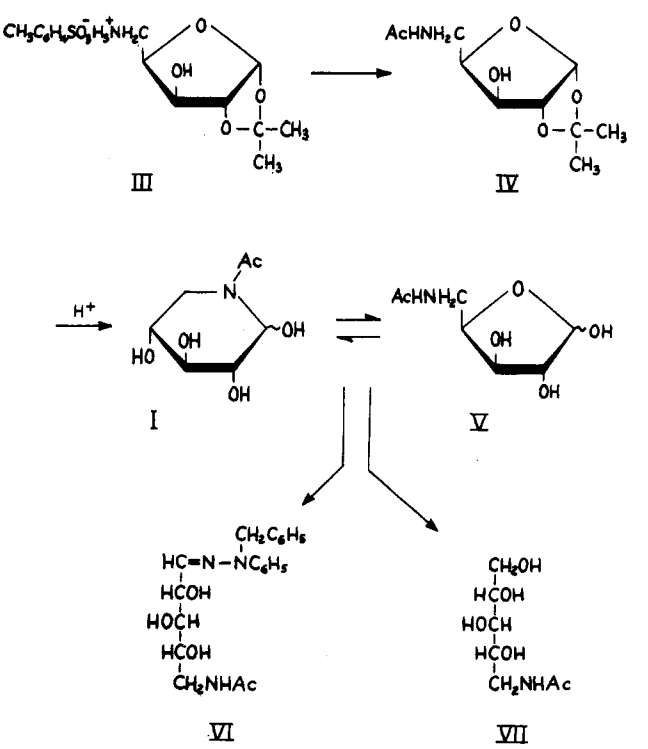


Fig. 1.—Change of optical rotation in 0.1*N* hydrochloric acid with time of I and V.

equilibrated in the presence of acids and bases with the formation of a mixture of the two isomers. Equilibration could also be induced by heating solutions of I or V. The optical rotational properties of I and V were of interest. Aqueous solutions of both did not muta-



(4) J. C. P. Schwarz and K. C. Yule, *Proc. Chem. Soc.*, 417 (1961).
(5) T. J. Adley and L. N. Owen, *ibid.*, 418 (1961).
(6) R. L. Whistler, M. S. Feather, and D. L. Ingles, *J. Am. Chem. Soc.*, **84**, 122 (1962).
(7) C. J. Clayton and N. A. Hughes, *Chem. Ind.* (London), 1796 (1962).
(8) D. L. Ingles and R. L. Whistler, *J. Org. Chem.*, **27**, 3896 (1962).
(9) H. Paulsen, *Angew. Chem.*, **74**, 901 (1962).
(10) J. K. N. Jones and W. A. Szarek, *Can. J. Chem.*, **41**, 636 (1963).
(11) J. K. N. Jones and J. C. Turner, *J. Chem. Soc.*, 4699 (1962).
(12) The names 5-acetamido-5-deoxy-D-xylopiperidinose and 1-acetyl-L-gluco(manno)-2,3,4,5-tetrahydroxypiperidine were given to the D-xylo and L-arabino derivatives, respectively, by Paulsen[9] and Jones and Turner.[11] Throughout this manuscript the term 5-acetamido-5-deoxypentopyranose will be used to designate compounds such as I and XIII, in an effort to render them more readily recognizable as a class of carbohydrate derivatives. Initially,[1] these compounds were tentatively termed as N-acetylpentoazopyranoses in analogy with the pentothiapyranoses.[4-8] We thank Dr. D. Horton of Ohio State University and Dr. L. Capell of the Chemical Abstracts service for suggesting the presently adopted nomenclature.
(13) S. Roseman and J. Ludowieg, *J. Am. Chem. Soc.*, **76**, 301 (1954).
(14) S. Akiya and T. Osawa, *Yakugaku Zasshi*, **76**, 1276 (1956); *Chem. Abstr.*, **51**, 4284 (1957).
(15) Paulsen[9] reports m.p. 154°, $[\alpha]D$ −19.5° and $[\alpha]D$ 32.5° for I and V, respectively. Jones and Szarek[10] report m.p. 153–154°, $[\alpha]D$ −11.3° and $[\alpha]D$ 13.2°, for I and V, respectively (in methanol).

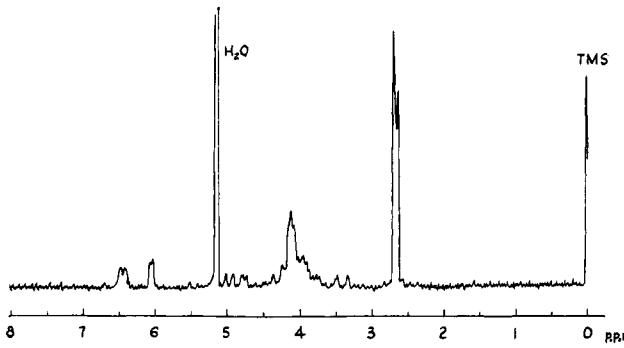
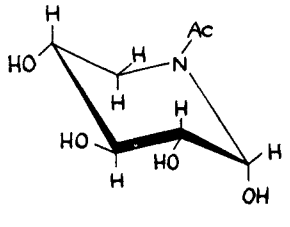


Fig. 2.—N.m.r. spectrum of I in deuterium oxide at 60 Mc. using tetramethylsilane as external standard.

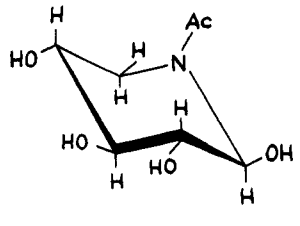
rotate at room temperature in the course of seventy-two hours. A change in optical rotation was observed only when the solutions were acidified by adding one drop of 5 *N* hydrochloric acid and an equilibrium rotation of $-8 \pm 1°$ was attained in twenty-four hours with I and in thirty-two hours with V. These results are shown in Fig. 1. Examination of these equilibrated solutions on paper chromatograms revealed the presence of I and V with the former predominating. A slow moving ninhydrin-positive spot was also present indicating the possible cleavage of the amide bond.

Equilibration in basic media was much faster. Thus, after two hours in aqueous ammonia (pH 11), a solution containing initially I or V was found to consist of a mixture of both.

Structures I and V could be readily differentiated by examination of their n.m.r. spectra in deuterium oxide (tetramethylsilane used as external standard). The spectrum of I (Fig. 2) showed two distinct peaks at δ 2.63 and 2.67 due to the N-acetyl methyl groups of two possible structures, 5-acetamido-5-deoxy-α-D-xylopyranose (VIII) and 5-acetamido-5-deoxy-β-D-xylopyranose (IX). Although evidence indicating the formation of VIII and IX in aqueous solution was not secured from mutarotation studies, their presence was suggested by the appearance of a doublet at δ 6.05 and another at 6.45. These could be attributed to the C-1 axial hydrogen in IX and the C-1 equatorial hydrogen[16,17] in VIII, respectively. The spectrum of V showed a singlet at δ 2.44 due to the N-acetyl methyl hydrogens. Evidence in favor of anomerization was obtained by the appearance of a weak doublet at δ 5.87 and another at 5.63. When the spectra were determined in acidified deuterium oxide the spectra of I and V consisted of peaks corresponding to a mixture of both, indicating equilibration. These data indicate that, under the influence of acids, bases, or heat, compounds of structure I and V are equilibrated by a mechanism involving a change in the type of ring closure.

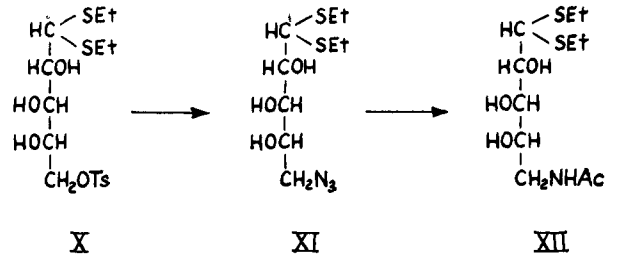


VIII

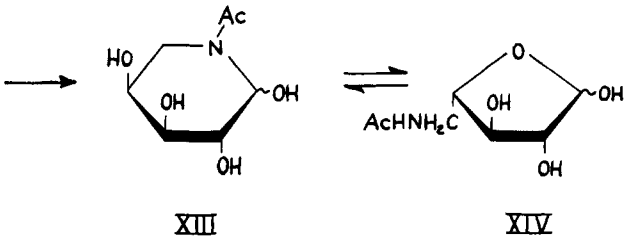


IX

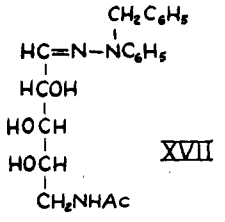
Reaction of 5-*O*-*p*-tolylsulfonyl-L-arabinose diethyl dithioacetal[18] (X) with an excess of sodium azide[19] in dimethyl sulfoxide at 80–85° overnight afforded crystalline 5-azido-5-deoxy-L-arabinose diethyl dithioacetal (XI) in 80% yield. Reduction of XI with lithium aluminum hydride in ether followed by N-acetylation of the product in methanol and acetic anhydride afforded crystalline 5-acetamido-5-deoxy-L-arabinose diethyl dithioacetal (XII). Demercaptalation of XII with cadmium carbonate and mercuric chloride in aqueous solution[18] gave a colorless sirup containing 5-acetamido-5-deoxy-L-arabinopyranose (XIII) and 5-acetamido-5-deoxy-L-arabinofuranose (XIV) as shown by paper chromatography. Separation by cellulose column chromatography gave XIII as colorless crystals, m.p. 144–145°, $[\alpha]^{23}D$ 18.5° (water), and XIV as a colorless sirup, $[\alpha]^{23}D$ 0° (water).[20]



X XI XII



XIII XIV



XVII

The virtual absence of mutarotation in XIII and XIV was indicated by the negligible change in optical rotation in twenty-four hours. Dilute hydrochloric acid, however, caused the rotation to reach an equilibrium value of $[\alpha]D$ 8.5° in the case of XIII within twenty-four hours while the rotation of XIV remained

(16) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958). These authors give examples showing that the equatorial proton absorbs at a larger δ value than its axial counterpart.

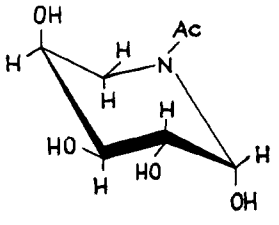
(17) For examples in the carbohydrate field see, P. W. K. Woo, H. W. Dion, Lois Durham, and H. S. Mosher, *Tetrahedron Letters*, 735 (1962); P. W. K. Woo, H. W. Dion, and L. F. Johnson, *J. Am. Chem. Soc.*, **84**, 1066 (1962).

(18) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 189 (1936).

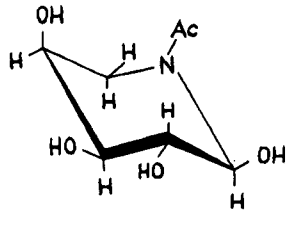
(19) The replacement of ω-*p*-tolylsulfonyl groups by azide ion in sugar derivatives has been described [F. Cramer, H. Otterbach, and H. Springmann, *Chem. Ber.*, **92**, 384 (1959)]. When using the conditions described by these authors, poor yields (10–15%) of the expected product resulted.

(20) Jones and Turner[11] report $[\alpha]D$ 19.4° and $[\alpha]D$ 0° for amorphous XIII and sirupy XIV, respectively.

unchanged. Examination of these equilibrated solutions by paper chromatography indicated the presence of a mixture of both compounds, in addition to a slower moving ninhydrin-positive and reducing component. The n.m.r. spectra of XIII and XIV showed peaks characteristic of the respective structures as in I and V. The spectrum of XIII showed two peaks at δ 2.59 and 2.63 due to the N-acetyl methyl groups of the two possible structures, 5-acetamido-5-deoxy-β-L-arabinopyranose (XV) and 5-acetamido-5-deoxy-α-L-arabinopyranose (XVI). Further evidence suggesting the formation of XV and XVI in solution was indicated by the appearance of a doublet at δ 6.05 due to the C-1 axial hydrogen in XVI and another at δ 6.48 due to the C-1 equatorial hydrogen[16,17] in XV. The spectrum of XIV showed the characteristic singlet at δ 2.47. The behavior of XIII and XIV in acids and bases was similar to that of I and V. The same 5-acetamido-5-deoxy-L-arabinose benzylphenylhydrazone (XVII) was obtained from both XIII and XIV, indicating a difference only in ring size.

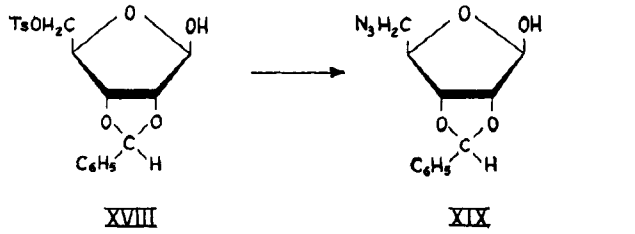


XV

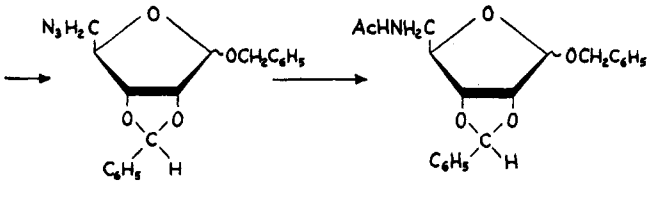


XVI

Reaction of 2,3-*O*-benzylidene-5-*O*-*p*-tolylsulfonyl-β-D-ribofuranose[21] (XVIII) with sodium azide in dimethyl sulfoxide afforded crystalline 5-azido-2,3-*O*-benzylidene-5-deoxy-β-D-ribofuranose (XIX) in 93% yield. Sirupy benzyl 5-azido-2,3-*O*-benzylidene-5-deoxy-D-ribofuranoside (XX) was obtained by treating XIX with benzyl alcohol containing 1% hydrogen chloride. Reduction of XX with lithium aluminum hydride in ether followed by N-acetylation gave benzyl 5-acetamido-2,3-*O*-benzylidene-5-deoxy-D-ribofuranoside (XXI) as a sirup. Hydrogenolysis of XXI with palladium catalyst[22] in ethanol afforded a mixture of 5-acetamido-5-deoxy-D-ribopyranose (XXII) and 5-acetamido-5-deoxy-D-ribofuranose (XXIII). In contrast to the corresponding derivatives in the xylose and arabinose series, the six-membered form in the ribose series was formed in very small amount.

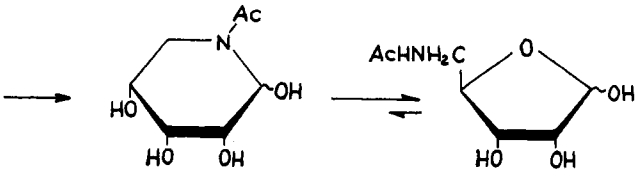


XVIII XIX

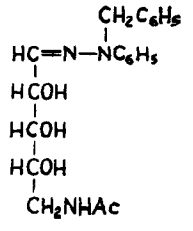


XX XXI

Another distinction was that the five-membered form XXIII had only a slightly faster mobility on paper chromatograms in several solvent systems than its six-membered isomer, XXII. The furanose ring structure of XXIII was ascertained by the detection of an amide II band in the infrared spectrum and the appearance of a signal at δ 2.45 in the n.m.r. spectrum due to the N-acetyl methyl hydrogens. A crystalline 5-acetamido-5-deoxy-D-ribose benzylphenylhydrazone (XXIV) was obtained from XXIII. The six-membered ring structure of XXII was indicated by the appearance of a signal due to the N-acetyl methyl hydrogens at δ 2.66 and from equilibration studies. The addition of acids or bases to a solution containing XXII gave a mixture consisting predominantly of XXIII. Equilibration of a solution containing XXIII gave only small amounts of XXII and consisted in major portion of XXIII, indicating that in the ribose series, the equilibrium is largely in favor of the five-membered furanose form.



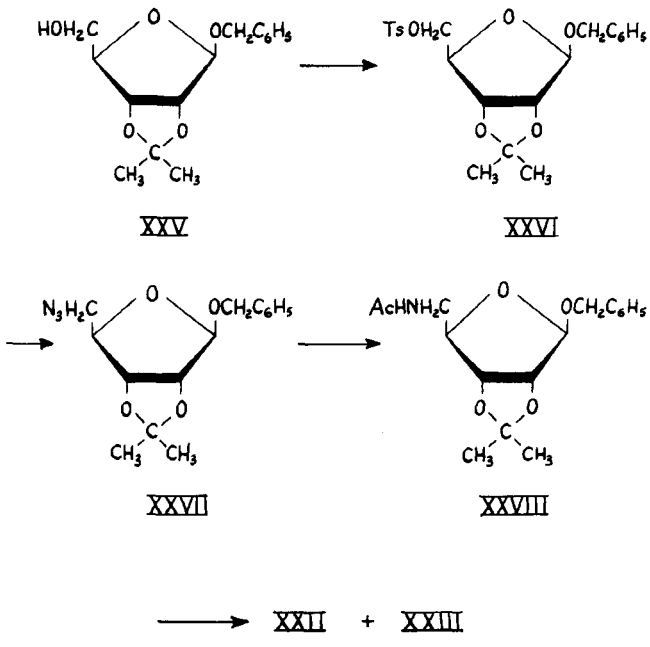
XXII XXIII



XXIV

The synthesis of XXII and XXIII was accomplished by a different approach. Reaction of benzyl 2,3-*O*-isopropylidene-β-D-ribofuranoside[23] (XXV) with *p*-toluenesulfonyl chloride in pyridine afforded crystalline benzyl 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-β-D-ribofuranoside (XXVI). The latter reacted with sodium azide in dimethyl sulfoxide to give benzyl 5-azido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (XXVII) as a colorless mobile liquid. Reduction of XXVII with lithium aluminum hydride in ether followed by N-acetylation gave benzyl 5-acetamido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (XXVIII). Acid hydrolysis of the latter was attempted in a mixture of dioxane and dilute sulfuric acid[23] and also in 60% acetic acid. The latter method

(21) E. Vis and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **79**, 1182 (1957).
(22) R. Mozingo, *Org. Syn.*, **26**, 77 (1947).
(23) E. B. Rauch and D. Lipkin, *J. Org. Chem.*, **27**, 403 (1962).



XXV XXVI XXVII XXVIII

⟶ XXII + XXIII

was preferred since it gave the least amounts of side products.

Investigation of the products from both hydrolyzates by paper chromatography revealed the presence of XXII and XXIII in essentially the same proportions as in the previous synthesis. Thus, the formation of the five-membered furanose form XXII was favored under neutral or acidic conditions as shown by the preceding two syntheses, respectively.

The infrared spectra of the benzylphenylhydrazone derivatives VI, XVII, and XXIV revealed some interesting features with respect to the position of the amide absorption band. The ribose derivative XXIV showed a band at 1627 cm.$^{-1}$ in contrast to VI and XVII with bands at 1645 and 1640 cm.$^{-1}$, respectively. Furthermore, the amide II band in XXIV could not be clearly detected as in VI and XXIV. The OH absorption region in XXIV was also different and showed evidence of hydrogen bonding. The acyclic structure of VI, XVII, and XXIV was ascertained by studying their n.m.r. spectra in deuteriochloroform. All three showed a characteristic signal in the range δ 1.98–2.01 due to the methyl hydrogens of the N-acetyl group. The benzylic hydrogens appeared at δ 5.06 and the aromatic hydrogens at δ 7.23 and 7.25.

Experimental

Solvent systems for paper chromatography and column chromatography were solvent A, 1-butanol–ethanol–water (4:1:5 by volume); solvent B, pyridine–butanol–water (6:4:3 by volume); and solvent C, ethyl acetate–pyridine–water (120:50:40 by volume). Spray reagents were alkaline silver nitrate[24] and aniline hydrogen phthalate.[25]

5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-D-xylofuranose (IV).—To a solution containing 7.2 g. of III[14] in 100 ml. of water and 15 ml. of methanol was added 110 ml. of Dowex-2 (CO_3)[26] followed by 2.5 ml. of acetic anhydride. The mixture was stirred 90 min. at 5° and filtered. The filtrate passed through a column containing cold Dowex 50 (H^+); the effluent was stirred briefly with Amberlite IR-45 (OH^-)[27] and evaporated to a colorless sirup (3.3 g.). The infrared spectrum showed the characteristic amide bands.

5-Acetamido-5-deoxy-D-xylofuranose (V).—A solution of IV (3.1 g.) in 75 ml. of dilute sulfuric acid (pH 1.4) was allowed to stand at room temperature for 4 days. Neutralization with barium carbonate, followed by filtration and evaporation, gave 3.0 g. of a colorless sirup. Paper chromatography revealed the presence of two spots, R_f 0.25 and 0.39 in solvent A. The product was dissolved in 30 ml. of solvent C and added to a column containing 100 g. of cellulose powder.[28] Fractions containing the component with R_f 0.39 were combined, and evaporated to a sirup which was repeatedly evaporated from ethanol to give V (700 mg.) as a colorless mobile liquid. This compound was homogenous on rechromatography and had R_f 0.39 in solvent A and R_f 0.66 in solvent B; it produced an orange-pink coloration with the aniline hydrogen phthalate spray. Solutions of V were stable when stored at 5° for prolonged periods. Under the influence of acids, bases, or heat, solutions of V equilibrated to form a mixture of V and I in major part. Optical rotation data gave $[\alpha]^{23}D$ 30° (constant 24 hr.) (*c* 0.6, in water); $[\alpha]^{23}D$ 26.6° → 20° (1 hr.) → 16.7° (2 hr.) → 11.7° (4 hr.) → 3.3° (7 hr.) → 5° (24 hr.) → −7.5° (32 hr.) (*c* 0.6, in 0.1 *N* hydrochloric acid). Examination of such equilibrated solutions by paper chromatography showed the presence of I, V, and a slow moving ninhydrin-positive and reducing component.

5-Acetamido-5-deoxy-D-xylopyranose (I).—Fractions containing the component with R_f 0.25 from the previous experiment were combined and evaporated to a sirup. The latter was repeatedly evaporated from ethanol to give a colorless sirup which crystallized within 1 hr. Trituration with a mixture of ethanol and acetone followed by filtration gave I (830 mg.) as colorless crystals. Recrystallization from a mixture of ethanol and acetone containing a few drops of water gave pure material, m.p. 163–164°. Optical rotation data gave −21.8° (constant 72 hr.) (*c* 2.69, in water); −18.3° → −15.1° (1 hr.) → −14.2° (1.5 hr.) → −13.4° (4 hr.) → −11.6° (7 hr.) → −9.7° (24 hr.) (*c* 2.69, in 0.1 *N* hydrochloric acid). The infrared spectrum of I showed an amide band at 1610 cm.$^{-1}$. No amide II band was detected. On paper chromatograms in solvents A and B, I migrated as a homogeneous spot, R_f 0.25 and 0.56, respectively. The same behavior toward acids, bases, and heat was observed with I as with V. X-Ray powder diffraction data[29] gave 8.22 wm, 7.34 m, 6.17 s, 5.80 m, 5.16 m, 4.23 m, 4.08 s, 3.75 m, 3.64 w, 3.48 w, 3.39 w, 3.23 w, 3.08 w, and 2.88 m.

Anal. Calcd. for $C_7H_{13}NO_5$: C, 43.97; H, 6.85; N, 7.32; OH (acetyl titration), 35.5. Found: C, 43.76; H, 6.85; N, 7.32; OH, 36.93.

5-Acetamido-5-deoxy-D-xylose Benzylphenylhydrazone (VI).—A solution of I or V (120 mg.) in aqueous ethanol containing 384 mg. of sodium acetate and 154 mg. of benzylphenylhydrazine hydrochloride was refluxed for 2.5 hr. The resulting yellow solution was evaporated to dryness; the residue was dissolved in 2 ml. of water and was extracted with chloroform. The extracts were dried and decolorized with carbon. The solution was evaporated to dryness; the residue was dissolved in methanol and ether was added to the point of incipient turbidity. The crystalline product was filtered and washed with ether to give 80 mg. of VI; recrystallized from the same mixture, m.p. 132–133°; $[\alpha]^{23}D$ 0° ± 1.7° (*c* 3.56, in methanol); infrared absorption data gave λ_{max}^{KBr} 3310 (OH), 1645 (amide I), and 1562 cm.$^{-1}$ (amide II); X-ray powder diffraction data[29] were 17.5 vw, 9.02 s, 6.42 ms, 5.31 s, 4.72 s, 4.53 mb, 4.23 s, 4.03 m, 3.85 mb, 3.53 s, 3.37 mb, 3.22 vw.

The product was identical with the same derivative in the L series.[2]

5-Acetamido-5-deoxy-D-xylitol (VII).—To a cold solution of V (80 mg.) in 2 ml. of water was added 20 mg. of sodium borohydride. After standing at 5° for 90 min. and 30 min. at room temperature, the solution was neutralized with acetic acid and passed over a column containing 10 ml. of Dowex 50 (H^+). The effluent was stirred briefly with Amberlite IR-45 (OH^-) and then evaporated to dryness. The residue was evaporated from ethanol several times to give a colorless nonreducing sirup (78 mg.), $[\alpha]^{23}D$ 73.2° (*c* 0.43, in 5% ammonium molybdate); $[\alpha]^{23}D$

(24) W. E. Trevelyan, D. P. Proctor and, J. S. Harrison, *Nature*, **166**, 444 (1950).

(25) S. M. Partridge, *ibid.*, **164**, 443 (1949).

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

(27) A product of Rohm and Haas Co., Philadelphia, Pa.

(28) Genuine Whatman, standard grade, W. and R. Balston, Ltd., England.

(29) Interplanar spacing, Cu Kα radiation. Relative intensity estimated visually: s, strong; m, medium; w, weak; v, very; b, broad.

31.2° (*c* 0.48, in acidified ammonium molybdate.[30] The product was homogenous on paper chromatograms and showed R_f 0.26 in solvent A. The same product was obtained from I but the reduction was slower. A portion of VII (50 mg.) was acetylated in the usual way to give a colorless sirup, R_f 0.88 in solvent A; $[\alpha]^{23}D$ −10.58° (*c* 3.98 in chloroform). The n.m.r. spectrum of this peracetylated product, 5-acetamido-5-deoxy-D-xylitol tetraacetate, in deuteriochloroform gave peaks consistent with the structure.

5-Azido-5-deoxy-L-arabinose Diethyl Dithioacetal (XI).—To a solution containing 54 g. of sodium azide in 400 ml. of dimethyl sulfoxide was added 43 g. of X in 50 ml. of dimethyl sulfoxide in small portions. The solution was heated overnight at 75–80° and filtered while hot. The filtrate was diluted with 2 l. of acetone and the resulting salts were filtered and washed with acetone. The reddish-colored filtrate was evaporated to a small volume at 40° or below, then at 40–50° (0.1 mm.). The solution was diluted with 1.5 l. of cold water with stirring to give the crystalline product (17.2 g.), m.p. 97–98°. Extraction of the aqueous solution with ether afforded additional product (5.1 g.). Recrystallization was effected from a mixture of acetone, ether, and 2,2,4-trimethylpentane, m.p. 100–101°; $[\alpha]^{23}D$ 83.3° (*c* 0.6, in chloroform).

Anal. Calcd. for $C_9H_{19}N_3O_3S_2$: C, 38.37; H, 6.81; N, 14.93; S, 22.80. Found: C, 38.60; H, 6.72; N, 14.58; S, 22.88.

5-Acetamido-5-deoxy-L-arabinose Diethyl Dithioacetal (XII).—A solution containing 10 g. of XI in 400 ml. of ether was added dropwise over a period of 1 hr. to a stirred suspension of lithium aluminum hydride (10 g.) in 200 ml. of ether. The mixture was refluxed for 3 hr. and cooled. The excess reagent was decomposed by adding ethanol and was filtered. The insoluble precipitate was washed thoroughly with ethanol and the combined filtrates were evaporated to a solid mass. The latter was dissolved in an excess of methanol, cooled, and treated with 10 ml. of acetic anhydride. After standing overnight at room temperature, the clear solution was evaporated to a sirup, the latter was triturated with cold water to cause crystallization. The product was obtained in two crops (total yield, 5. g), m.p. 130–131°. Extraction of the aqueous solution with ether afforded a further 1 g. of product. Recrystallization from a mixture of ethanol, ether, and 2,2,4-trimethylpentane afforded pure material, m.p. 133–134°; $[\alpha]^{23}D$ 90° (*c* 1, in chloroform).

Anal. Calcd. for $C_{11}H_{23}NO_4S_2$: C, 44.42; H, 7.79; N, 4.79; S, 21.56. Found: C, 44.54; H, 7.75; N, 5.07; S, 21.82.

5-Acetamido-5-deoxy-L-arabinofuranose (XIV).—A solution containing 4.7 g. of XII, 17.3 g. of mercuric chloride, and 17.3 g. of cadmium carbonate in 260 ml. of water was stirred for 30 min. at room temperature, then for 1 hr. at 75°. The mixture was filtered and the filtrate treated with hydrogen sulfide. The resulting salts were filtered and the filtrate neutralized by stirring with Amberlite IR-45 (OH^-). Evaporation afforded a sirup which was dissolved in aqueous ethanol. It was filtered from some insoluble material and the filtrate evaporated to a pale yellow sirup (3.5 g.). This product showed two spots, R_f 0.165, 0.32 when chromatographed in solvent A.

A portion (1.0 g.) was fractionated on a column containing 70 g. of cellulose powder[28] using solvent C. Fractions containing the component with R_f 0.32 were combined and concentrated to a sirup which was evaporated from ethanol twice to give XIV (0.53 g.) as a colorless sirup. Optical rotation data were (*c* 2.09, in water or 0.1 *N* hydrochloric acid): $[\alpha]^{23}D$ 0° (constant 24 hr.). Paper chromatographic examination of this solution showed spots corresponding to XIII and XIV. The infrared spectrum of XIV showed characteristic amide bands at 1640 and 1560 cm.$^{-1}$. In solvent B, XIV had R_f 0.76 and produced a pink color with the aniline hydrogen phthalate reagent. The stability of XIV in acids, bases, and toward heat paralleled that of I and V.

5-Acetamido-5-deoxy-L-arabinopyranose (XIII).—Fractions containing the component with R_f 0.16 from the preceding cellulose column chromatography experiment were combined and evaporated to dryness. The residue was evaporated from ethanol several times to give XIII as a colorless sirup (260 mg.) which crystallized. The crystals were triturated with a mixture of acetone and ethanol containing a few drops of water and filtered to give 200 mg. of XIII, m.p. 145–146°. Optical rotational data gave $[\alpha]^{24}D$ 18.5° (constant, 24 hr.) (*c* 2.02, in water); $[\alpha]^{24}D$ 17° → 11° (7 hr.) → 8.6° (24 hr.) (in 0–1 *N* hydrochloric acid). Examination of this solution by paper chromatography indicated the presence of XIII, XIV, and a new spot R_f 0.11 in solvent A. The infrared spectrum of XIII showed an amide band at 1635 cm.$^{-1}$, but lacked the amide II band. In solvent B, XIII gave a single spot, R_f 0.75.

Anal. Calcd. for $C_7H_{13}NO_5$: C, 43.97; H, 6.85; N, 7.32. Found: C, 43.69; H, 6.93; N, 7.30.

5-Acetamido-5-deoxy-L-arabinose Benzylphenylhydrazone (XVII).—A solution of XIII or XIV (100 mg.) in aqueous ethanol containing 300 mg. of sodium acetate and 125 mg. of benzylphenylhydrazine hydrochloride was refluxed for 2.5 hr. The solution was processed as usual to give a yellow sirup which crystallized from a mixture of acetone, ether, and pentane to give XVII (85 mg.). Recrystallization from the same mixture gave pure material, m.p. 155–156°, $[\alpha]^{23}D$ −12.2° (*c* 2.05, in methanol); infrared absorption data gave λ_{max}^{KBr} 3310 (OH), 1640 (amide I), and 1555 cm.$^{-1}$ (amide II). X-Ray powder diffraction pattern data[29] gave 16.07 m, 10.11 vw, 8.55 m, 7.28 w, 6.56 w, 5.66 mb, 5.20 vw, 5.0 vs, 4.71 vw, 4.47 s, 4.32 m, and 4.12 w.

Anal. Calcd. for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.89; H, 6.74; N, 11.14.

5-Azido-2,3-*O*-benzylidene-5-deoxy-β-D-ribofuranose (XIX).—A solution containing 1.5 g. of XVIII[21] and 1 g. of sodium azide in 25 ml. of dimethyl sulfoxide was stirred at 70° overnight. The cooled solution was diluted with 500 ml. of acetone. The salts were filtered and the filtrate was evaporated to a small volume. The solution was diluted with 300 ml. of cold water and the deposited crystals were filtered to give 500 mg. of product. Extraction of the filtrate with ether gave another 365 mg. of product (total 865 mg.), m.p. 80–81°. Recrystallization from aqueous isopropyl alcohol afforded colorless needles, m.p. 81–82°; $[\alpha]^{23}D$ −13.2° (*c* 0.70, in chloroform); infrared absorption data, λ_{max}^{KBr} 3500 (OH) and 2100 cm.$^{-1}$ (N_3).

Anal. Calcd. for $C_{12}H_{13}N_3O_4$: C, 54.75; H, 4.97; N, 15.96. Found: C, 55.05; H, 5.02; N, 15.80.

Benzyl 5-Acetamido-2,3-*O*-benzlidene-5-deoxy-D-ribofuranoside (XXI).—A suspension of XIX (0.9 g.) in 18 ml. of benzyl alcohol containing 1% hydrogen chloride was stirred at room temperature for 45 min. The colorless solution was neutralized with lead carbonate and the solvent evaporated at 55° (0.7 mm.). The residue was evaporated from toluene several times and finally from ethanol and ether to give benzyl 5-azido-2,3-*O*-benzylidene-5-deoxy-D-ribofuranoside (XX) (1.2 g.) as a colorless sirup. The infrared absorption spectrum showed characteristic bands due to azide and aromatic groups. This product, in 10 ml. of ether, was added dropwise to a stirred suspension of lithium aluminum hydride (4 g.) in 30 ml. of ether over a period of 30 min. The mixture was refluxed 2.5 hr., the excess reagent decomposed upon addition of ethanol and the salts filtered. The clear filtrate was evaporated to a sirup and the latter acetylated in methanol and acetic anhydride to give XXI as a colorless sirup (550 mg.); infrared absorption data, λ_{max}^{film} 1660 (amide I) and 1555 cm.$^{-1}$ (amide II).

Benzyl 2,3-*O*-Isopropylidene-5-*O*-*p*-tolylsulfonyl-β-D-ribofuranoside (XXVI).—A stirred solution containing 3.5 g. of XXV[23] in 10 ml. of pyridine was treated at −10° with 3.6 g. of *p*-toluenesulfonyl chloride in 10 ml. of pyridine over a period of 1 hr. After stirring overnight, the solution was poured into ice–water. The crystalline product was filtered and recrystallized twice from ethanol to give 5.3 g. of product, m.p. 92–93°; $[\alpha]^{23}D$ −56° (*c* 1.07, in chloroform); infrared absorption data, λ_{max}^{KBr} 1196 and 1184° cm.$^{-1}$ (sulfonate).

Anal. Calcd. for $C_{22}H_{27}O_7S$: C, 60.68; H, 6.25; S, 7.36. Found: C, 60.40; H, 6.06; S, 7.14.

Benzyl 5-Azido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (XXVII).—A solution containing XXVI (3 g.) and 2.3 g. of sodium azide in 25 ml. of dimethyl sulfoxide was stirred at 85° overnight. The yellow solution was diluted with 50 ml. of water and extracted with three 50-ml. portions of ether. The extracts were dried and evaporated to a small volume. Evaporation at 40° (0.5 mm.) afforded a pale yellow sirup. The latter was purified by distillation at 140–150° (0.5 mm.) to give a colorless viscous liquid $[\alpha]^{23}D$ −82° (*c* 0.67 in methanol); infrared absorption data, λ_{max}^{film} 2100 cm.$^{-1}$ (N_3).

Anal. Calcd. for $C_{15}H_{19}N_3O_4$: C, 58.8; H, 6.25; N, 13.71. Found: C, 59.03; H, 6.23; N, 13.6.

Benzyl 5-Acetamido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (XXVIII).—To a stirred suspension of lithium aluminum hydride (2.4 g.) in 100 ml. of ether was added dropwise a solution of XXVII (1.9 g.) in 30 ml. of ether. The mixture was

(30) N. K. Richtmyer and C. S. Hudson, *J. Am. Chem. Soc.*, **73**, 2249 (1951).

refluxed for 3 hr., excess reagent was decomposed by adding ethanol and the salts were filtered. The filtrate was evaporated to dryness. The residue was N-acetylated in methanol with acetic anhydride and processed as usual to give the crystalline product (1.5 g.). Recrystallization from ether–pentane gave 1.3 g. of a solvated product, m.p. 65–66°. Vapor phase chromatography indicated the presence of solvated ether and/or pentane molecules. The product melted when dried *in vacuo* at 50° or at room temperature; infrared absorption data, λ_{max}^{KBr} 1670, 1658 (amide I), and 1568 cm.$^{-1}$ (amide II).

Anal. Calcd. for $C_{17}H_{23}NO_5$: C, 63.51; H, 7.21; N, 4.31. Found: C, 62.67; H, 7.29; N, 4.48.

5-Acetamido-5-deoxy-D-ribofuranose (XXIII). A. From XXI.—A solution containing 330 mg. of XXI in 75 ml. of ethanol was hydrogenated 2.5 hr. over 20% palladium catalyst[22] (0.5 g.) at room temperature. Filtration and evaporation of the solution gave a colorless sirup (120 mg.) which showed two spots, R_f 0.34 and 0.27 in solvent A. These components were separated by preparative paper chromatography to give XXIII (80 mg.) (R_f 0.34 component) as a colorless sirup; $[\alpha]^{24}D$ 19° (constant, 24 hr.) (*c* 1.16, in water). Solutions of XXIII equilibrated in the presence of acids and bases (much faster) to a mixture consisting mainly of XXIII and XXII in minor amounts. The infrared spectrum of XXIII showed an amide I band at 1640 cm.$^{-1}$ and an amide II band at 1560 cm.$^{-1}$.

B. From XXVIII.—A solution containing 400 mg. of XXVIII in 10 ml. of 60% acetic acid was heated 1 hr. on the steam bath. Evaporation of the solution gave a residue which contained essentially the same two components as before. These were separated by chromatography over cellulose to give XXIII (200 mg.) (R_f 0.34 component) as a colorless sirup.

5-Acetamido-5-deoxy-D-ribopyranose (XXII). A. From XXI.—The component with R_f 0.27 from the hydrogenolysis of XXI was isolated by elution of the appropriate zone as described before to give XXII (20 mg.) as a colorless sirup. This product was homogeneous on paper chromatograms in several solvent systems. Solutions of XXII in the presence of acids or bases were equilibrated to give a mixture consisting predominantly of XXIII with only small amounts of XXII, as evidenced by paper chromatography experiments.

B. From XXVIII.—Fractions containing the component with R_f 0.27 from the cellulose column chromatography experiment described before, were combined and processed as usual to give XXII (13 mg.) as a colorless sirup. Its properties were identical with the product obtained from XXI.

5-Acetamido-5-deoxy-D-ribose Benzylphenylhydrazone (XXIV).—A solution of XXIII (35 mg.) in aqueous ethanol containing 50 mg. of sodium acetate and 22 mg. of benzylphenylhydrazine hydrochloride was refluxed for 2.5 hr. The resulting yellow solution was processed as usual to give a yellow sirup which was covered with 10 ml. of ether and stored at 5°. The crystals that formed were collected and washed with petroleum ether (b.p. 50–60°) to give 35 mg. of product. Recrystallization from a mixture of methanol, ether, and petroleum ether gave pure material, m.p. 143–144°; $[\alpha]^{23}D$ −36.4° (*c* 1.725, in methanol); λ_{max}^{KBr} 3450, 3290 (OH), 1627 (amide I), and 1556 cm.$^{-1}$ (amide II, shoulder). X-Ray powder diffraction data[29] gave 11.95 w, 10.59 s, 7.34 w, 6.86 m, 5.83 w, 5.44 m, 5.10 s, 4.93 w, 4.73 m, 4.51 m, 4.35s, 4.04 wb, and 3.79 w.

Anal. Calcd. for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.49; H, 6.66; N, 11.11.

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Use of a Complex Neighboring Group to Prepare Aminomercaptofuranose Sugars[1]

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The conversion of methyl 3-amino-3-deoxy-α-D-arabinofuranoside (I) to methyl 3-amino-3-deoxy-2-thio-α-D-ribofuranoside hydrochloride (VI) using a dithiocarbamoyl neighboring group is described. The use of an alternative procedure resulted in a C-3 to C-5 neighboring group participation and ultimately yielded methyl 3-amino-3-deoxy-2-*O*-methylsulfonyl-5-thio-α-D-arabinofuranoside hydrochloride (XIII).

The preparation of methyl 3-amino-3-deoxy-2-thio-α-D-allopyranoside hydrochloride, described previously,[2] utilized the *S*-methyldithiocarbamoyl neighboring group in going from a *trans*-amino alcohol to a *cis*-amino mercaptan; the over-all result of the synthetic work was the conversion of a D-altrose derivative to a D-allose derivative. In the course of that work it was noted that when sodium methoxide was used to effect the neighboring group participation the nitrogen atom of the group was the displacing agent, but when refluxing pyridine was employed the sulfur atom was the displacing agent. In a later article zu Reckendorf and Bonner[3] reported that the *S*-methyldithiocarbamoyl group in a suitably blocked D-glucosamine derivative gave sulfur participation when methanolic sodium methoxide was used to effect participation; these authors suggested that the conformational differences in the participating and leaving groups in the blocked 3-amino-3-deoxy-D-altrose glycoside and in the blocked 2-amino-2-deoxy-D-glucose glycoside, both pyranosides, might explain the different reaction courses in these two series. It was of interest to extend the study of the dithiocarbamoyl group to the furanose sugar system where the geometrical situation of the participating and leaving groups would be quite different from the pyranose sugars; this manuscript describes the conversion of methyl 3-amino-3-deoxy-α-D-arabinofuranoside (I) to methyl 3-amino-3-deoxy-2-thio-α-D-ribofuranoside (VI) using the complex neighboring group approach.

Methyl 3-amino-3-deoxy-α-D-arabinofuranoside (I) was prepared from methyl 2,3-anhydro-α-D-lyxofuranoside by the literature procedure.[4] The conventional reaction of I with carbon disulfide and methyl iodide furnished the dithiocarbamate II as a crystalline solid, further characterized as the dibenzoate III. The reaction of II with nearly the stoichiometric amount of methyl chloroformate yielded the 5-*O*-methoxycarbonyl derivative (IV) as an oil; use of the trityl blocking group for

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