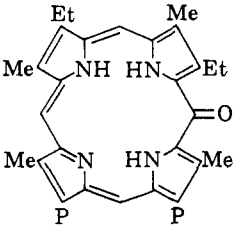
404, 585, and 635 mμ (log ϵ_{max} *ca.* 5.08, 4.30, and 4.48)) was formed. If the cyclization was carried out with methyl orthoformate–trichloroacetic acid, and followed by aeration without added base, a green compound (λ_{max} 404 and 700 mμ (log ϵ_{max} *ca.* 5.00 and 4.48)) was formed, which readily changed into VII or its salts (λ_{max} 416, 560, and 615 mμ (log ϵ_{max} *ca.* 5.40, 4.30, and 4.30)). This green compound is probably a tautomeric form of VII.



VII

Acetylation of VII gave β-acetoxymesoporphyrin IX dimethyl ester, m.p. 233.5–234.5° (λ_{max} 400, 498, 530, 568, and 620 mμ (log ϵ_{max} 5.30, 4.21, 3.80, 3.81, and 3.26[11])). Reduction of VII by sodium amalgam in methanol–acetic acid[12] gave *directly* mesoporphyrin IX dimethyl ester, which crystallized from the reaction mixture (24% yield from VI). *This work also opens a synthetic route to α-oxyporphyrins which have been postulated as intermediates in the catabolism of porphyrins leading to bile pigments.*[13]

Acknowledgment. We thank Dr. J. A. Ballantine for his pioneer studies of pyrroketones.

209 (1938), has very similar visible absorption. We favor the keto structure VII, which would gain aromaticity from dipolar character, but the tautomeric hydroxy structure is not excluded.

(11) *meso*-Monomethylaetioporphyrins likewise have, *e.g.*, λ_{max} 408, 505, 539, 579, and 630 mμ (log ε 5.14, 4.04, 3.63, 3.62, and 3.06): R. J. Abraham, A. H. Jackson, G. W. Kenner, and D. Warburton, *J. Chem. Soc.*, 861 (1963).

(12) H. Fischer and A. Treibs, *Ann.* **457**, 209 (1927).

(13) R. Lemberg and J. W. Legge, "Haematin Compounds and Bile Pigments," Interscience Publishers, Inc., New York, N. Y., 1949, p. 458.

(14) C.S.I.R. South Africa overseas bursar.

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Received, November 30, 1964

Synthesis of 4-Acetamido-1,2,3,5-tetra-O-acetyl-4-deoxy-D-ribofuranose. A Pyrrolidine Sugar[1-3]

Sir:

In some work reported recently from these laboratories,[4] the synthesis of 4-thioribofuranose derivatives in which the ring hetero atom was sulfur rather than oxygen was described. The recent discoveries of the widespread occurrence in nature of various amino sugars such as the N-acetylnonulosaminic acids[5] which have an amine function δ to the reducing carbon made it of interest to attempt the preparation of 4-amino-4-deoxy-D-ribose derivatives with the idea of preparing a furanose sugar with nitrogen as the ring heterocycle.[6]

The synthesis of 4-acetamido-4-deoxy-D-ribofuranose derivatives was accomplished by two independent routes and is the subject of this communication.

Tosylation of methyl 2-O-benzoyl-β-L-arabinopyranoside (I)[7] yielded 46% of methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (II), m.p. 163–165° (from benzene, Skellysolve B).[8] Treatment of II with sodium azide in N,N-dimethylformamide (DMF) at 120° for 6 hr. gave a 74% yield of methyl 4-azido-2-O-benzoyl-4-deoxy-3-O-(*p*-tolylsulfonyl)-α-D-xylopyranoside (III), m.p. 100–101° (from 2-propanol). That the 4-tosylate of II had been displaced by the azide rather than the 3-tosylate was shown by the reaction of III with methanolic sodium methoxide. The resulting epoxide (VI) was obtained in 78% yield, m.p. 44.5–45.5°. Catalytic reduction of the azide III gave a 97% yield of crystalline amine (IV), m.p. 111–112°, which could be acetylated in 67% yield to the N-acetate (V), m.p. 150–151°.

The reaction of the N-acetate (V) with sodium acetate in aqueous DMF effected the displacement with inversion of the 3-tosylate by the neighboring 4-N-acetate[9] to give, after debenzoylation, a 63% yield of crystalline methyl 4-acetamido-4-deoxy-α-D-ribopyranoside (VII), m.p. 157.0–158.0° (from 2-propanol). The vicinal-*cis* relationship of the hydroxyl groups of VII was demonstrated by the preparation of the isopropylidene derivative (VIII), m.p. 114–115° (from benzene–cyclohexane).

Acetylation of VII gave the triacetate (IX) as an analytically pure oil. Acetolysis of either the N-acetate (VII) or triacetate (IX) gave an analytically pure sirup which was free of NH absorption at 6.5 μ in the infrared and which showed the presence of five acetyl groups between τ 7.88 and 8.02 by n.m.r. From these data, the pentaacetate was assigned the furanose structure (X). The isomeric pyranose N,N-diacetate (XI) would be expected to have N-acetate absorption at *ca.* τ 7.6 by n.m.r.[10]

Treatment of the acetolysis product X with 0.5% methanolic hydrogen chloride followed by reacetylation gave a 57% yield of a sirup which was essentially homogeneous on thin layer chromatography[8] and which showed the necessary four acetyl bands at τ 7.87–7.98 for the furanoside structure (XII). Deacetylation of XII with methanolic sodium methoxide gave the glycoside (XIII) as a sirup which was characterized as the tri-*p*-nitrobenzoate (XIV), m.p. 175.5–177.0° (from absolute ethanol).

Acetolysis of XIV gave the analytically pure anomers

(1) 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. PH-43-64-500. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

(2) Portions of this work were described at the 148th National Meeting of the American Chemical Society, August 31,1964. See Abstracts, p. 3D.

(3) Nomenclature used by *Chemical Abstracts*.

(4) E. J. Reist, D. E. Gueffroy, and L. Goodman, *J. Am. Chem. Soc.*, **85**, 3715 (1963); **86**, 5658 (1964).

(5) F. Zilliken and M. W. Whitehouse, *Advan. Carbohydrate Chem.*, **13**, 237 (1958).

(6) In a recent paper by W. A. Szarek and J. K. N. Jones, *Can. J. Chem.*, **42**, 20 (1964), the synthesis of a 4-acetamidotetrose, namely, methyl 4-acetamido-4-deoxy-L-erythrofuranoside, was described. It should be noted that this C_4 sugar cannot form a pyranoside, hence is forced into the furanoside configuration.

(7) M. A. Oldham and J. Honeyman, *J. Chem. Soc.*, 986 (1946).

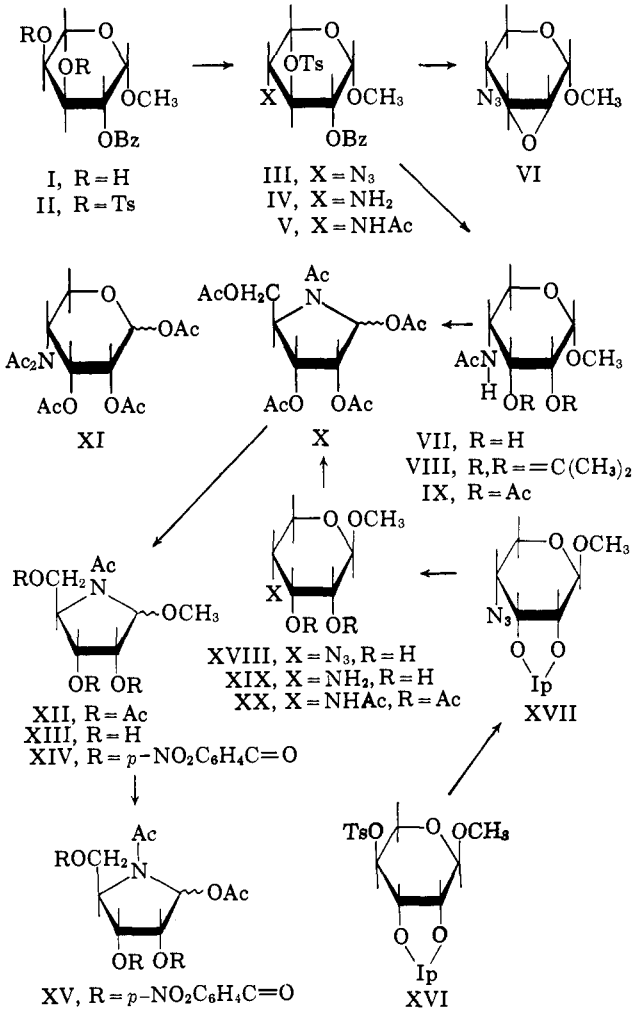
(8) Melting points are corrected. All compounds analyzed satisfactorily and had infrared spectra which were compatible with the assigned structures. Thin layer chromatograms were run on silica gel G using ethyl acetate as the developing solvent.

(9) B. R. Baker and R. E. Schaub, *J. Org. Chem.*, **19**, 646 (1954).

(10) F. A. L. Anet, R. A. B. Bannard, and L. D. Hall, *Can. J. Chem.*, **41**, 2331 (1963).

of the 1-O-acetate (XV) from which one anomer could be removed by crystallization from 2-propanol–ethyl acetate, m.p. 164.5–165.5°.

The second synthetic sequence to 4-acetamido-4-deoxy-D-ribofuranose derivatives started with the displacement of methyl 2,3-O-isopropylidene-4-O-(*p*-tolylsulfonyl)-α-L-lyxopyranoside[4] (XVI) by sodium azide in DMF to give methyl 4-azido-4-deoxy-2,3-O-isopropylidene-β-D-ribopyranoside (XVII) as an analytically pure oil, b.p. 76–78° (0.3 mm.), in 30% yield. Deacetonation of XVII with acetic acid gave a quantitative yield of the azide XVIII which was hydrogenated directly over 5% palladium-on-carbon to afford the crystalline methyl 4-amino-4-deoxy-β-D-ribopyranoside (XIX), m.p. 109.5–111.0° (from ethyl acetate) in 30% yield. Acetylation of XIX gave the sirupy triacetate (XX). Acetolysis of XX gave the pentaacetate (X) which was identical in all respects with the pentaacetate (X) obtained by route I starting with the ditosylate (II). Identity was further confirmed by conversion of the pentaacetate (X) from route II to the same crystalline trinitrobenzoate (XIV) obtained from route I.



The contraction of the 4-acetamido-4-deoxyribopyranosides to the furanose ring under acid conditions is noteworthy. This is in direct contrast to the behavior of methyl 4-acetamido-2,3,6-tri-O-acetyl-4-deoxy-α-D-glucopyranoside which maintained the pyranose ring under these same conditions.[11] It is interesting to note that 5-acetamido-5-deoxy-D-ribose showed a greater tendency toward furanose formation than did the analogous xylose and arabinose derivatives.[12]

(11) E. J. Reist, D. F. Calkins, R. R. Spencer, and L. Goodman, unpublished results.

(12) S. Hanessian and T. H. Haskell, *J. Org. Chem.*, **28**, 2604 (1963).

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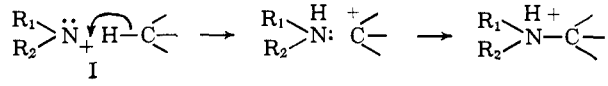
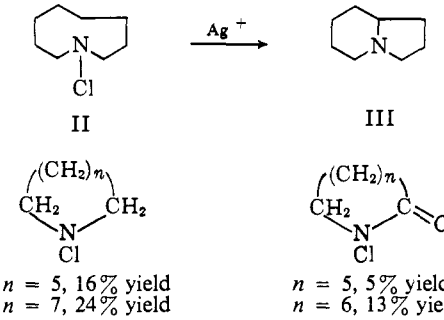
Transannular Reactions of Nitrenium Ions[1]

Sir:

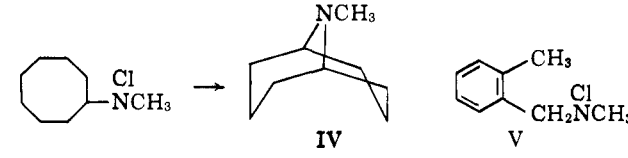
Interest in substitution of nitrogen at saturated unactivated carbon[2] led us to examine the reactions of nitrenium ions (I). The anticipated process was



Initially, medium-ring secondary amines and amides were chosen for study in view of the well-known transannular hydride abstraction by carbonium ions in the carbocyclic analogs.[3] The corresponding N-chloro derivatives were prepared using dichloramine T in pentane or pentane–ether mixture or N-chlorosuccinimide in methylene chloride. These were freed from solvent and dissolved in aqueous dioxane, and the nitrenium ion was generated by the action of silver ions. The reaction proceeded fairly rapidly at room temperature in the case of the chloramines but slowly at 80° with the chloramides. The maximum yield of transannular insertion product was obtained with N-chloroazacyclononane (II). Indolizidine (III) was formed in 68% yield and identified by comparison of he picrate with an authentic sample.[4]



The use of the reaction in a geometrically less ideal case is illustrated in a synthesis of N-methylgranatanine (IV) in 5% yield from N-chloro-N-methylcyclooctylamine. Chloramine V under the above conditions



gave *o*-tolualdehyde (35%) and the parent secondary

(1) Presented in part at the Symposium on Reactive Intermediates in Organic Chemistry, Laval University, Aug. 27–29, 1964.
(2) R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964).
(3) V. Prelog and G. J. Traynham in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., pp. 593–615.
(4) M. G. Reinecke and L. R. Kray, *J. Org. Chem.*, **29**, 1736 (1964). We thank Dr. Reinecke for reference samples.