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Synthesis of Pyrrole Nucleosides by the Photo-dehydrogenation of Δ^3-Pyrroline Derivatives

Masajiro KAWANA and Sakae EMOTO

The Institute of Physical and Chemical Research, Yamato-machi, Kita-Adachi-gun, Saitama

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1-(β-D-Glucopyranosyl)pyrrole (VI) was prepared by the photo-dehydrogenation of 1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-Δ^3-pyrroline (IV) in the presence of oxygen and benzophenone, followed by deacetylation. The nucleoside (VI) was also derived directly from 1-(D-glucosyl)-Δ^3-pyrroline (III) by photochemical means. The synthesis of 1-(α-D-ribofuranosyl)-pyrrole (XI), its β-anomer (XII), and 1-(β-D-ribopyranosyl)pyrrole (XIII) was accomplished by photodehydrogenation of 1-(2′,3′-*O*-isopropylidene-D-ribosyl)-Δ^3-pyrroline, followed by the removal of the protecting group. The treatment of 1-(2′,3′-*O*-isopropylidene-α-D-ribofuranosyl)pyrrole (VIII) with 80% aqueous acetic acid afforded a novel α-cyclonucleoside, 1-(2-*C*,2′-*O*-isopropylidene-α-D-ribofuranosyl)pyrrole (XIV), besides XI—XIII. The formation of pyrrole by the photo-dehydrogenation of Δ^3-pyrroline (II) itself was confirmed by gas chromatography.

The photo-dehydrogenation of partially-hydrogenated nitrogen-heterocycles, such as tetraphenyl chlorin[1] and 2,3-dihydro-β-carbolines,[2] has been reported. Preobrazhenskaya,[3] Walton,[4] and their co-workers demonstrated that 1-(D-glycosyl)indoles were synthesized from the corresponding indolines using a reagent useful for dehydrogenation, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).

In the course of the step-by-step synthesis of pyrrole nucleosides, we found that 1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-Δ^3-pyrroline (IV) could be photochemically dehydrogenated to yield 1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)pyrrole (V).[5] We wish now to present these results in detail, and to describe the photochemical formation of anomeric D-ribosylpyrroles and the formation of a novel α-cyclonucleoside by the migration of an isopropylidene group.

Results and Discussion

The synthesis of 1-(D-glucosyl)-Δ^3-pyrroline (III) was performed by heating a mixture of α-D-glucose (I) and crude Δ^3-pyrroline (II)[6] under conditions similar to those used for the synthesis of 1-(D-glucosyl) piperidine[7] (Fig. 1); the purification[8] of crude II was not necessary for the present purposes because only III was crystallized by the addition of acetone to the reaction mixture.

The structure of III was tentatively identified. The observed values for the elemental analysis of III were in good agreement with the theoretical values. The NMR spectrum in deuterium oxide (D_2O) exhibited two singlets, at τ 6.24 and 4.23, due to the methylene and olefinic protons of the Δ^3-pyrroline ring respectively.[8] The signals of the anomeric proton appeared in the τ 6.0—5.6 region,[9] but they were not sufficiently resolved for interpretation.

The treatment of III with acetic anhydride in pyridine gave IV in a 73% yield. Its IR spectrum was devoid of N–H, O–H, and *N*-acetyl carbonyl absorption bands. The NMR spectrum in deuterio-chloroform($CDCl_3$) revealed four singlets, at τ 7.99—7.93, for the acetyl protons, and two singlets, at τ 6.22 and 4.32, for the methylene and olefinic protons of the Δ^3-pyrroline ring respectively. The signal of the anomeric proton appeared as a doublet centered at τ *ca.* 5.7 with the coupling constant of *ca.* 8 cps; the values could not be accurately measured, however, because the high-field part of the doublet was overlapped by other signals.

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2) R. A. Uphaus, L. I. Grossweiner, J. J. Katz and K. D. Kopple, *Science*, **129**, 641 (1959); Y. Kanaoka, E. Sato and O. Yonemitsu, *Chem. & Ind.*, **1968**, 1250.

3) M. N. Preobrazhenskaya, M. M. Vigdorchik and N. N. Suvorov, *Tetrahedron*, **23**, 4653 (1967).

4) E. Walton, F. W. Holly and S. R. Jenkins, *J. Org. Chem.*, **33**, 192 (1968).

5) M. Kawana and S. Emoto, This Bulletin, **41**, 2552 (1968).

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7) J. E. Hodge and C. E. Rist, *ibid.*, **74**, 1497 (1952).

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9) S. Inouye, T. Tsuruoka, T. Ito and T. Niida, *Tetrahedron*, **24**, 2125 (1968).

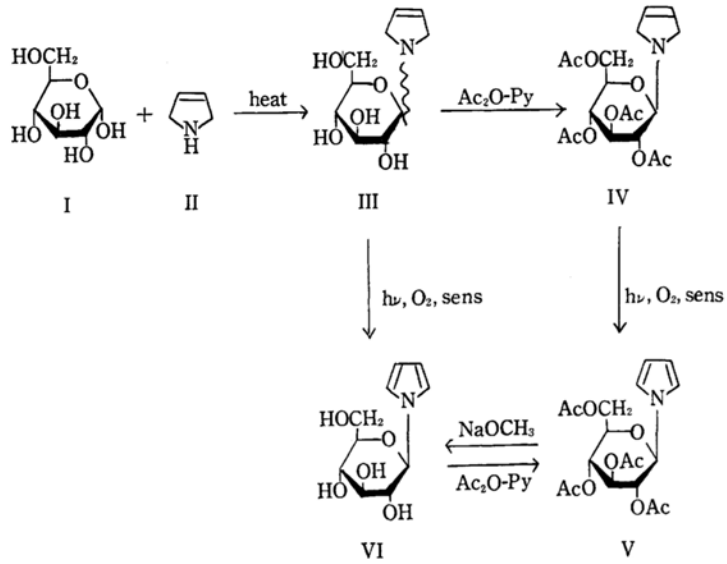

Fig. 1

This large coupling constant is indicative of a *trans*-diaxial relationship between H-1′ and H-2′, and it corresponds to the β-configuration.[10]

Further proof of the glucopsranosylamine structure of IV was obtained by the ready degradation[11] of IV with 0.7% aqueous formic acid to the known 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose.[12]

When a benzene solution of IV was allowed to evaporate repeatedly in an open vessel, the thin-layer chromatographic analysis showed that IV was gradually converted into V. This conversion was markedly accelerated by the irradiation of UV light with a Pyrex filter, under bubbling oxygen, and in the presence of benzophenone as a sensitizer.[13] Under such conditions V was obtained as the main product: it was isolated by crystallization in a 85% yield. The dehydrogenation of IV with DDQ in the dark was also effective, producing V in a good yield.

The IR and UV spectra of V showed the presence of a pyrrole ring[14,15] (*cf.* Table 1 and the Experimental section). The NMR spectrum in $CDCl_3$ exhibited two pseudo-triplets of equal intensity, centered at τ 3.83 and 3.21 for the protons at C-3, 4 and C-2, 5 of the pyrrole ring respectively (Table 2).[16] The signal of the anomeric proton was not separated from the others.

The anomeric configuration of V was deduced by comparing the chemical shifts of the acetyl signals of IV and V in the NMR spectroscopy. Cushley *et al.*[17] have found that when the C-2′ acetyl group and the pyrimidine in acetylated pyranosyl pyrimidine nucleosides are in a *trans*-diequatorial relationship, there is a small but significant down-field shift (*ca.* 0.05 ppm) of the C-2′ acetyl signal upon the saturation of the 5, 6-double bond of the pyrimidine. In the case of acetylated β-ribo- and β-gluco-pyranosylindoline-indole systems, a large down-field shift (at least 0.29 ppm) of the C-2′ acetyl signal occurs upon the removal of the anisotropy due to the 2,3-double bond of the indole.[18] A similar down-field shift was observed in the present pyrrole nucleoside. The acetyl signals of V appeared at τ 7.99—7.93 as three singlets and at τ 8.15 as one singlet assignable to the C-2′ acetyl group; all would be in an area of positive shielding due to the anisotropy of the pyrrole ring.[19] Therefore, the

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14) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Fracisco, and Nankodo Co., Tokyo (1964), p. 26.

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16) N. S. Bhacca, L. F. Johnson and J. N. Shoolery, "High Resolution ¡NMR Spectra Catalog," Varian Associates, Palo Alto, Calif. (1962), Spectrum No. 55.

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19) A. P. Martinez and W. W. Lee, *J. Org. Chem.*, **34**, 416 (1969).

Table 1. The physical properties of the pyrrole nucleosides

Compound	Mp °C	$[\alpha]_D$ deg.	(c, solvent)	Temp., °C	UV λ_{max}, mμ (ε)	solvent
V	178.0—178.5	−10.9	(0.67, $CHCl_3$)	22	211 (8150)	EtOH
VI	Hygroscopic glass	+10.3	(0.74, H_2O)	25	210 (6950)	H_2O
VIII	Hygroscopic syrup	−45.9	(0.27, $CHCl_3$)	20	214 (6400)	EtOH
IX	65—66	−57.6	(0.46, $CHCl_3$)	20	215 (6800)	EtOH
X	94.0—94.5	−62.9	(0.14, $CHCl_3$)	23	215 (7000)	EtOH
XI	Hygroscopic syrup	+19.0	(0.20, H_2O)	22	210 (6500)	H_2O
XII	Hygroscopic syrup	−69.4	(0.17, H_2O)	20	212 (6800)	H_2O
XIII	Hygroscopic glass	−34.0	(0.05, H_2O)	22	209 (8200)	H_2O
XIV	107—109	+68.8	(0.17, H_2O)	20	217 (7200)	H_2O

Table 2. The NMR spectra[a] of the pyrrole nucleosides

Compound	H-1′ [1][d] ($J_{1',2'}$)	C-5′ OH [1][g] ($J_{5'OH,5'}$)	Isopropylidene methyls [3]×2		H-3,4 [2]	H-2,5 [2]	Solvent
V[b]	5.0—4.4	—	—	—	3.83 (pt)	3.21 (pt)	$CDCl_3$
VI	4.86 (d, 8.4)[e]	—	—	—	3.74 (pt)	3.01 (pt)	D_2O
VIII	4.08 (d, 3.3)	4.91 (t, 4.8)	8.71 (s)	8.56 (s)	3.99 (pt)	3.12 (pt)	DMSO-d_6
IX	4.32 (d, 2.6)	5.01 (t, 5.4)	8.69 (s)	8.49 (s)	3.93 (pt)	3.02 (pt)	DMSO-d_6
X	4.81 (d, 8.4)[f]	[4.46 (d, 5.7)][h]	8.64 (s)	8.42 (s)	3.91 (pt)	3.05 (pt)	DMSO-d_6
XI	4.28 (d, 3.8)	5.20 (t, 5.4)	—	—	4.02 (pt)	3.06 (pt)	DMSO-d_6
XII	4.59 (d, 5.0)	5.07 (t, 5.1)	—	—	3.96 (pt)	3.06 (pt)	DMSO-d_6
XIII	4.90 (d, 9.0)	[5.23—4.98 (m)][i]	—	—	3.98 (pt)	3.12 (pt)	DMSO-d_6
XIV[c]	4.42 (d, 2.6)	5.23 (t, 5.4) [4.89 (d, 6.0)][j]	8.57 (s)	8.44 (s)	4.15 (q)[k] 3.94 (pt)[l]	3.30(q)[m]	DMSO-d_6

a) τ-Value (peak multiplicity, and coupling constant (cps)); see Experimental section.
b) The acetyl signals appeared at τ 8.15 (3H), 7.99, 7.95, and 7.93 as singlets.
c) The signal of H-2′ appeared as a quartet ($J_{1',2'}$=2.6 cps, $J_{2',3'}$=3.6 cps) centered at τ 5.58. Irradiation of H-1′ caused the quartet to collapse to a doublet ($J_{2',3'}$=3.6 cps), and irradiation of H-2′ caused a doublet due to H-1′ to collapse to a singlet.
d) Numbers in brackets refer to number of the protons obtained integration.
e) Letters in parentheses refer to singlet (s), doublet (d), triplet (t), pseudo-triplet (pt), quartet (q), and multiplet (m).
f) A poorly resolved doublet.
g) The signals disappeared by the addition of D_2O.
h) C-4′ OH.
i) C-2′, 3′, and 4′ OHs.
j) C-3′ OH.
k) H-3 (1H, $J_{3,4}$=3.0 cps, $J_{3,5}$=1.5 cps).
l) H-4 (1H, $J_{3,4}$=3.0 cps).
m) H-5 (1H, $J_{3,5}$=1.5 cps, $J_{4,5}$=2.4 cps).

C-2′ acetyl signal is shifted by at least 0.16 ppm down-field in changing from V to IV. This suggests that V has the β-configuration.

The deacetylation of V in the usual manner gave, after chromatography, analytically pure 1-(β-D-glucopyranosyl)pyrrole (VI) as a hygroscopic glass in a 76% yield. The paper and gas chromatographic analyses showed that the product was anomerically pure. The NMR spectrum of VI in D_2O revealed a doublet due to the anomeric proton with the large coupling constant of 8.4 cps, thus establishing the β-configuration.[10] Therefore, it was confirmed that the proposed sutrcture for V was correct and that the β-configuration of IV was retained in the course of the dehydrogenation with photochemical means as well as with DDQ.

Plisov[20] reported that when a mixture of glucose and pyrrole was heated the product, which consisted of two components, was obtained as a crystal (mp 190°C) after crystallization from pyridine. However, its structure was unsubstantiated by experimental details or physical data. Moreover, Plisov's product was not identical with VI, at least not in respect to their solubility in pyridine, in which the latter was readily soluble.

An alternative route to obtain VI is the direct photo-dehydrogenation of III. When a suspension of III in ethanol was irradiated under the conditions described above, analytically pure VI

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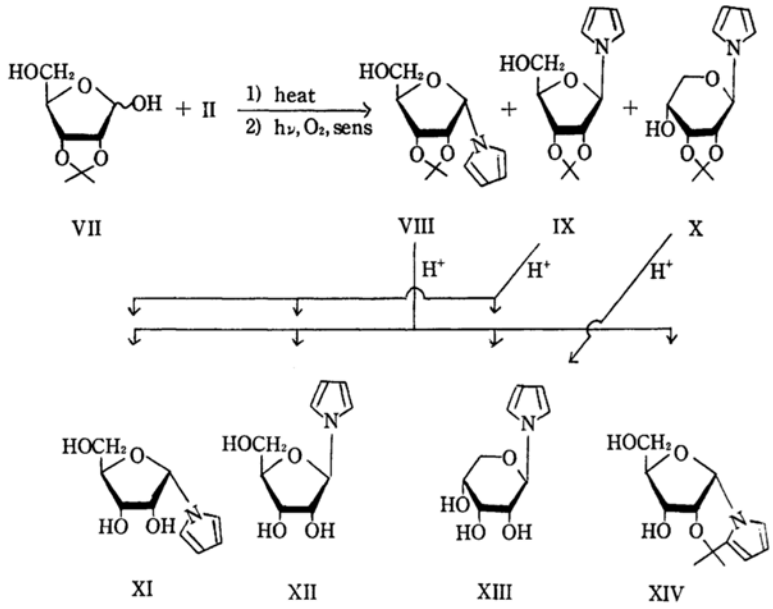

Fig. 2

was produced in a 62% yield after chromatography. The product was identical in every respect with a specimen prepared from V. Further, the acetylation of the product gave V in a 92% yield.

The preparation of the D-ribosylpyrrole nucleosides was undertaken starting with pure II[8] and 2′,3′-*O*-isopropylidene-D-ribose (VII)[21] (Fig. 2). Thus, a mixture of II and VII was heated to give syrupy products which could contain 1-(2′,3′-*O*-isopropylidene-D-ribosyl)-Δ^3-pyrroline. The irradiation of the syrup in ethanol under the conditions described above provided the isomeric nucleosides (40%), namely, 1-(2′,3′-*O*-isopropylidene-α-D-ribofuranosyl)pyrrole (VIII), 1-(2′,3′-*O*-isopropylidene-β-D-ribofuranosyl)pyrrole (IX), and 1-(2′,3′-*O*-isopropylidene-β-D-ribopyranosyl)pyrrole (X), in a ratio of approximately 1 : 8 : 1 (Table 1). Interestingly, the treatment of the syrup with DDQ produced these nucleosides (54%) in a ratio of approximately 7 : 2 : 1, the α-furanosyl anomer (VIII) being predominant.

The removal of the isopropylidene group of IX with 80% aqueous acetic acid, followed by column chromatography on Dowex 1 (OH^-),[22] gave 1-(α-D-ribofurayosyl)pyrrole (XI), 1-(β-D-ribofuranosyl)pyrrole (XII), and 1-(β-D-ribopyranosyl)-pyrrole (XIII) in 3.5, 87, and 2.5% yields respectively. This suggests that pyrrole nucleosides as well as indole nucleosides[3] isomerize under mild acidic conditions. The removal of the isopropylidene group of VIII also gave XI, XII, and XIII in 21, 22, and 3% yields respectively. In addition, 1-(2-*C*, 2′-*O*-isopropylidene-α-D-ribofuranosyl)pyrrole (XIV) was obtained in a 29% yield from VIII. It can be considered that XIV is formed by an acid-catalyzed intramolecular reaction similar to that of the substituted indole with the dimethyl ketal group.[23] To our knowledge, XIV is a new type of α-cyclonucleoside.[24] The removal of the protecting group of X provided only XIII in a 90% yield.

The analytical and spectroscopic data for VIII—XIV supported the assigned structres (Tables 1 and 2). The NMR spectra of VIII, IX, XI, and XII in deuterated dimethyl sulfoxide (DMSO-d_6)[25] showed a C-5′ hydroxyl proton as each triplet; these protons disappeared upon the addition of D_2O. This indicates that these nucleosides have the furanosyl structure. Therefore, VIII and IX as well as XI and XII are a pair of anomers; they can be assigned to the α- and β-configurations respectively on the basis of the following NMR data:

(1) The signals of the anomeric protons of the β-anomers, IX and XII, were found in a higher field than those of the α-anomers, VIII and XI respectively; Nishimura and Shimizu[26] have found that the anomeric protons of nucleosides occur in

21) P. A. Levene and E. T. Stiller, *J. Biol. Chem.*, **102**, 187 (1933).

22) C. A. Dekker, *J. Am. Chem. Soc.*, **87**, 4027 (1965).

23) G. Büchi, P. Kulsa and R. L. Rosati, *ibid.*, **90**, 2448 (1968).

24) M. Ikehara, M. Kaneko and Y. Nakahara, *Tetrahedron Letters*, **1968**, 4707.

25) O. L. Chapman and R. W. King, *J. Am. Chem. Soc.*, **86**, 1256 (1964).

26) T. Nishimura and B. Shimizu, *Chem. Pharm. Bull.*, **13**, 803 (1965).

a higher field when the C-1′ and 2′ substituents are *trans* than when they are *cis*.[27]

(2) The difference in the coupling constants of the anomeric protons between the β-anomers, IX and XII, was much greater than the difference in those between the α-anomers, VIII and XI; Jardetzky[28] has reported that when the ribofuranose ring is constrained by fusion with a second ring, the coupling constant of the anomeric proton of β-nucleoside is reudced.[29]

(3) The signals of the protons of the isopropylidene group for the α-anomer, VIII, appeared in a higher field than those for the β-anomer, IX, presumably because of the anisotropic effect of the pyrrole ring.[17-19,30]

(4) The signals of the C-5′ hydroxyl proton of the β-anomer, XII, appeared in a lower field than those of the α-anomer, XI, as has been observed in the case of the anomeric 7-D-ribofuranosyladenines.[27b]

Further, the order of elution from the anion-exchange column[22] supported these assignments; the α-anomer, XI, was eluted faster than the β-anomer, XII (see the Experimental section).[31]

The pyranosyl structure of X was proved by the appearance of a doublet due to the C-4′ hydroxyl proton in the NMR spectrum (in DMSO-d_6).[25] The signals of the anomeric protons of X and XIII appeared as doublets with large coupling constants, thus establishing the β-configurations.[10]

The NMR spectrum of XIV in DMSO-d_6 showed the presence of an isopropylidene group and a 1,2-disubstituted pyrrole ring. The signals of the C-3′ and 5′ hydroxyl protons appeared as a doublet (J= 6.0 cps) and a triplet respectively. In spin-decoupling experiments, the irradiation of the anomeric proton caused a quartet centered at τ 5.58 to collapse to a doublet (J=3.6 cps). This indicated that the quartet arises from H-2′ and that the C-2′ hydroxyl group is substituted.

The value for the coupling constant of the anomeric proton of XIV was 2.6 cps, a value which corresponded to a dihedral angle of H-C_1'-C_2'-H, 54° or 123°, according to the Karplus equation.[32] An examination of the Dreiding models showed that the former was suitable for the dihedral angle of the α-configuration, but that neither of them was suitable for that of the β-configuration. Additional support of the α-configuration of XIV was obtained by a comparison of the optical rotations of XI, XII, and XIV (Table 1); XI and XII obey the Hudson's isorotation rules,[33] and XI and XIV have the same sign of rotation.

An attempt was made to examine whether II itself was converted into pyrrole by photochemical means. A solution of crude II[6] in ethanol was irradiated under the conditions described above, and aliquots were examined by gas chromatography. A peak due to II disappeared after 2 hr, the formation of pyrrole being identified. The photo-dehydrogenation reaction in the presence of oxygen and benzophenone provides an alternative to a number of known pyrrole syntheses using II or its derivatives.[34,35]

Experimental

Some of the physical data for the pyrrole nucleosides are listed in Tables 1 and 2. All the melting points are uncorrected.

The irradiation of UV light was performed with a super-high-pressure mercury lamp (100 W, Matsuda SHL-100UV-1). The optical rotations were measured with a Perkin-Elmer 141 photoelectric polarimeter in a 1-dm tube. The IR spectra were obtained using a Perkin-Elmer 521 grating infrared spectrophotometer. The UV spectra were taken on a Cary 14 recording spectrophotometer.

The NMR spectra were determined on a Nippon Denshi C-60 spectrometer using sodium 2, 2-dimethyl-2-silapentane-5-sulfonate (tetramethylsilane for the $CDCl_3$ solutions) as the internal standard. The chemical shifts were recorded as ppm on the τ scale, with the coupling constants (the directly-measured line-spacings) as cps.

The gas chromatography (GC) was performed at 180°C with a Shimadzu GC-4A gas chromatograph equipped with a flame ionization detector using a glass column (1.8 m×4 mm) packed with 3% OV-17 on Shimalite W (80−100 mesh); nitrogen was used as the carrier gas (flow rate, 64 ml/min). The individual nucleoside was treated with a pyridine solution of hexamethyldisilazane and trimethylchlorosilane at room temperature, and the resulting solution was injected into the gas chromatograph.[36]

The thin-layer and paper chromatographies (TLC and PC) were run by the ascending technique on a silica gel G (E. Merck) plate and a filter paper No. 51

27) See, for example: a) T. Nishimura, B. Shimizu and I. Iwai, *Chem. Pharm. Bull.*, **12**, 1471 (1964). b) J. A. Montgomery and H. J. Thomas, *J. Am. Chem. Soc.*, **87**, 5442 (1964). c) K. Imai, A. Nohara and M. Honjo, *Chem. Pharm. Bull.*, **14**, 1377 (1966). d) J. A. Montgomery and H. J. Thomas, *J. Heterocycl. Chem.*, **5**, 303 (1968).

28) C. D. Jardetzky, *J. Am. Chem. Soc.*, **84**, 62 (1962).

29) See, for example: N. J. Leonard and R. A. Laursen, *ibid.*, **85**, 2026 (1963); Ref. 27c.

30) J. F. Codington, R. J. Cushley and J. J. Fox, *J. Org. Chem.*, **33**, 466 (1968).

31) See, for example: G. Schramm, G. Lüzmann and F. Bechmann, *Biochim. Biophys. Acta*, **145**, 221 (1967); E. J. Reist, D. F. Calkins and L. Goodman, *J. Am. Chem. Soc.*, **90**, 3852 (1968).

32) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

33) C. S. Hudson, *J. Am. Chem. Soc.*, **31**, 66 (1909); E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., New York (1962), p. 110.

34) J. P. Wibaut and W. Proost, *Rec. Trav. Chim.*, **52**, 333 (1933).

35) R. Kreher and H. Pawelczyk, *Angew. Chem.*, **76**, 536 (1964).

36) Y. Sasaki and T. Hashizume, *Anal. Biochem.*, **16**, 1 (1966).

(Toyo Roshi) respectively. The following solvent systems were used as developers: (A) *n*-hexane - ethyl acetate (1 : 1); (B) ethyl acetate - isopropanol - water (65 : 30 : 5); (C) ethyl acetate - *n* - hexane - methanol (7 : 2: 1); (D) *n* - butanol - water (87 : 13). The spots were detected by iodine vapor or a 1% solution of *p*-dimethylaminobenzaldehyde[37] in methanol - concentrated hydrochloric acid (3 : 1).

1-(D-Glucosyl)-Δ^3-pyrroline (III). A mixture of I (1.8 g, 0.01 mol) and crude II[6] (1.4 g, 0.02 mol) was heated at 80—85°C (bath-temperature) for 15 min in a flask equipped with a tight stopper. To the cooled reaction mixture there was added acetone (50 m*l*). The syrupy product rapidly solidified on scratching. After being cooled overnight at 0°C, the product was filtered, washed with cold acetone, and dried. Recrystallization from acetone-methanol gave III (1.7 g, 73.9%): mp 130—135°C (decomp.); $[\alpha]_D^{20}$ −28.8° (4 min) → +13.0° (46 hr, constant, *c* 0.40, H_2O); IR, ν_{max}^{KBr} 3408, 3290, 2886, 2850, 1085, 1025 cm^{-1}; NMR (in D_2O), τ 6.24 (singlet, methylene protons of the Δ^3-pyrroline ring), 5.98, 5.88, and 5,75 (*ca.* 1.5H, broad peaks), 4.23 (2H, singlet, olefinic protons).

Found: C, 51.78; H, 7.14; N, 6.09%. Calcd for $C_{10}H_{17}O_5N$: C, 51.94; H, 7.41; N, 6.06%.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl)-Δ^3-pyrroline(IV). To a mixture of acetic anhydride (2.7 g, 26 mmol) and dry pyridine (4.1 g, 52 mmol), there was added III (1.16 g, 5 mmol) at −10—−5°C, and then the mixture was stirred for 1.5 hr. After the reaction mixture had been allowed to stand at −5°C for 24 hr, ethanol (1 m*l*) was added to decompose an excess of acetic anhydride, and then the pyridine was removed at room temperature *in vacuo*. The residue was dissolved in ether, and the solution was washed with water, aqueous sodium bicarbonate, and water successively and then dried over anhydrous magnesium sulfate. The evaporation of the ether gave a crystalline mass (1.67 g) which, after recrystallization from degassed *n*-hexane - isopropanol with charcoal treatment in the dark, afforded a crude material (1.51 g, mp 118—122°C). Further recrystallization from degassed *n*-hexane - ethanol in the dark gave IV (1.45 g, 72.5%): mp 121—122°C; $[\alpha]_D^{25}$ −23.7° (*c* 0.49, degassed $CHCl_3$); R_f (TLC, solvent A), 0.27; IR, ν_{max}^{KBr} 2892, 2850, 1753, 1738, 1380, 1240, 1038 cm^{-1}; NMR (in $CDCl_3$), τ 7.99, 7.97, 7.95, and 7.93 (12H, each singlet, acetyl protons), 6.22 (singlet, methylene protons of Δ^3-pyrroline ring), *ca.* 5.7 (doublet, $J_{1',2'}$ = *ca.* 8 cps, anomeric proton), 4.32 (2H, singlet, olefinic proton).

Found: C, 54.10; H, 6.05; N, 3.51%. Calcd for $C_{18}H_{25}O_9N$: C, 54.13; H, 6.31; N, 3.51%.

Degradation of 1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-Δ^3-pyrroline (IV). To a solution of IV (200 mg, 0.5 mmol) in degassed acetone (2 m*l*) there was added 0.7% aqueous formic acid (10 m*l*) at room temperature in the dark. After 15 min, the acetone was removed at 25°C *in vacuo*. The residue was extracted with chloroform, and the extract was washed with water, aqueous sodium bicarbonate, and water successively and dried over anhydrous magnesium sulfate. The evaporation of the chloroform at room temperature *in vacuo* gave 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose as a syrup (145 mg, 83.3%) : $[\alpha]_D^{20}$ +76.6° (constant, *c* 1.44, 95% EtOH) (lit,[12a] $[\alpha]_D^{24}$ +80.2° (constant, *c* 3.37, 95% EtOH)). This product was identical with an equilibrated authentic sample[12b] in all respects (IR, NMR, and TLC).

1-(2′,3′,4′,6′,-Tetra-*O*-acetyl-β-D-glucopyranosyl)-pyrrole (V). *(A) Photo-dehydrogenation.* A mixture of IV (200 mg, 0.5 mmol) and benzophenone (13.7 mg, 0.075 mmol) in bezene (10 m*l*) was irradiated externally in a water-cooled Pyrex vessel under bubbling oxygen at 20°C for 1 hr. The evaporation of the benzene at 50°C *in vacuo* gave a crystalline mass which, after recrystallization from ethanol, afforded V (169 mg, 84.9%): R_f (TLC, solvent A), 0.50; IR, ν_{max}^{KBr} 3145, 3134, 3120, 3102, 1740, 1493, 740 cm^{-1}.

Found: C, 54.53; H, 5.73; N, 3.52%. Calcd for $C_{18}H_{23}O_9N$: C, 54.40; H, 5.83; N, 3.53%.

(B) Chemical dehydrogenation. All the experiments were carried out in the dark. To a suspension of DDQ (119 mg, 0.52 mmol) in dry benzene (5 m*l*), there was added a solution of IV (200 mg, 0.5 mmol) in dry benzene (4 m*l*). The reaction mixture was then allowed to stand at room temperature for 1 hr under occasional shaking. The resultant precipitates were filtered and washed with benzene. The removal of the benzene at 60°C *in vacuo* gave crystals which, after recrystallization from ethanol, afforded V (178 mg, 89.4%). The IR spectral comparison and a mixed-melting-point determination showed this material to be identical with the sample prepared by the method A.

(C) Acetylation of VI. A mixture of acetic anhydride (570 mg, 5.6 mmol) and dry pyridine (790 mg, 10 mmol) was stirred into a solution of VI (130 mg, 0.57 mmol) in dry pyridine (500 mg). After the stirring had been continued at this temperature for 1 hr, the reaction mixture was allowed to stand overnight at 0°C. Ethanol (0.5 m*l*) was added to decompose an excess of acetic anhydride, and the pyridine was removed at room temperature *in vacuo*. The resultant crystals were washed with water, filtered, and dried. Recrystallization from ethanol gave V (207 mg, 92.0%). The IR spectral comparison, a mixed-melting-point determination, and the TLC analysis showed this product to be identical with the sample prepared by the method A.

1-(β-D-Glucopyranosyl)pyrrole (VI). *(A) Deacetylation of V.* To a solution of absolute methanol (12 m*l*) containing sodium methoxide (54 mg, 1.0 mmol), there was added V (397 mg, 1.0 mmol), after which the mixture was stirred at room temperature for 50 min. After the removal of the methanol at 25°C *in vacuo*, the residue was dissolved in water (5 m*l*). The solution was treated with ion-excange resin (Dowex 50W, H^+ form) (1 g) for 1 min, the resin was then immediately filtered and washed with water. After the filtrate had been treated with charcoal, the evaporation of the water at 60°C *in vacuo* gave a glassy mass (193 mg). The product was chromatographed on a silica-gel (Merck) (24 g) column with ethyl acetate - ethanol (8 : 2), yielding VI (173 mg, 75.5%) : R_f, 0.66 (TLC, solvent B), 0.38 (PC, solvent D); retention time (GC), 24.1 min; IR, ν_{max}^{KBr} 3400, 1491, 738 cm^{-1}.

Found: C, 52.15; H, 6.38; N, 6.09%. Calcd for $C_{10}H_{15}O_5N$: C, 52.39; H, 6.60; N, 6.11%.

(B) Photo-dehydrogenation of III. A suspension of III (462 mg, 2.0 mmol) in 99.5% ethanol (15 m*l*) containing

37) F. Feigl, "Spot Test in Organic Analysis," translated by R. E. Oesper, Elsevier Publishing Co., Amsterdam and Maruzen Co., Tokyo (1960), p. 289.

benzophenone (55 mg, 0.3 mmol) was irradiated externally in a water-cooled Pyrex vessel under bubbling oxygen at 19°C for 1 hr. After the ethanol had been removed at 30°C *in vacuo*, the residue was chromatographed on a Dowex 1-X2 (OH^- form) (10 g) column (2× 8.5 cm). The elution with water - methanol (7 : 3) gave a slightly contaminated product (313 mg). Further purification by silica-gel (Merck) (24 g) column chromatography with ethyl acetate - ethanol (8 : 2) afforded analytically-pure VI (284 mg, 62.0%). This product was identical with a specimen prepared by the method A in all respects (optical rotation, TLC, PC, GC, IR, UV, and NMR).

1-(2′,3′-*O*-Isopropylidene-α-D-ribofuranosyl)-pyrrole (VIII), 1-(2′,3′-*O*-isopropylidene-β-D-ribofuranosyl)pyrrole (IX), and 1-(2′,3′-*O*-isopropylidene-β-D-ribopyranosyl)pyrrole (X). *(A) Photo-dehydrogenation.* A mixture of VII[21] (571 mg, 3.0 mmol) and pure II[8] (249 mg, 3.6 mmol) was placed in a flask equipped with a tight stopper and heated at 95—100°C (bath-temperature) for 3 hr. After being cooled immediately, the reaction mixture was diluted with absolute ethanol (15 m*l*), after which benzophenone (55 mg, 0.3 mmol) was added. The mixture was irradiated externally in a water-cooled Pyrex vessel under bubbling dry oxygen at 18°C for 2 hr. The evaporation of the ethanol at 30°C *in vacuo* gave a syrup, which was then dissolved in ether (80 m*l*). The ethereal solution was washed with water (4×10 m*l*), dried over anhydrous sodium sulfate, and concentrated at below 30°C *in vacuo*. The resultant syrup was chromatographed on a silica-gel (Merck) (100 g) column using *n*-hexane - ethyl acetate (6 : 4). Three products were obtained in the following sequence: IX (230 mg, 32.0%); X (22 mg, 3.1%); a mixture (7 mg, 1.0%, *ca.* 6 : 4) of VIII and X, and VIII (25 mg, 3.5%).

The α-anomer (VIII) was analyzed without further purification: R_f (TLC, solvent A), 0.30; IR, $\nu_{max}^{CHCl_3}$ 3640, 3158, 3100, 1488 cm^{-1}.

Found: C, 60.26; H, 7.12; N, 5.81%. Calcd for $C_{12}H_{17}O_4N$: C, 60.24; H, 7.16; N, 5.85%.

Recrystallization of IX from *n*-hexane - benzene gave the analytical samples as colorless crystals: R_f (TLC, solvent A), 0.59; IR, ν_{max}^{KBr} 3454, 3128, 3112, 1490, 742 cm^{-1}.

Found: C, 60.02; H, 7.22; N, 5.88%. Calcd for $C_{12}H_{17}O_4N$: C, 60.24; H, 7.16; N, 5.85%.

The recrystallization of X from *n*-hexane - benzene gave the analytical sample as colorless crystals: R_f (TLC, solvent A), 0.38; IR, ν_{max}^{KBr} 3478, 3134, 3118, 3102, 1489, 726 cm^{-1}.

Found: C, 60.37; H, 6.99; N, 5.93%. Calcd for $C_{12}H_{17}O_4N$: C, 60.24; H, 7.16; N, 5.85%.

(B) Chemical dehydrogenation. A mixture of VII[21] (761 mg, 4.0 mmol) and pure II[8] (332 mg, 4.8 mmol) was heated under the conditions described above. The cooled reaction mixture was then suspended in dry benzene (5 m*l*). This suspension was stirred, drop by drop, into a mixture of DDQ (908 mg, 4.0 mmol) and dry benzene (20 m*l*) at room temperature. After the addition had been completed, the stirring was continued for 5 min. The resultant precipitates were filtered and washed with benzene, and the filtrate was diluted with ether (50 m*l*). The solution was wased with dilute aqueous sodium carbonate and water successively, dried over anhydrous sodium sulfate, and concentrated at below 30°C *in vacuo*. The residue gave, after chromatography on a silica-gel (Merck) (150 g) column using *n*-hexane - ethyl acetate (6 : 4), IX (115 mg, 12.0%), X (29 mg, 3.0%), crude VIII (114 mg, 11.9%) slightly contaminated with X, and VIII (263 mg, 27.5%) in sequence. The IR and NMR spectral comparison, a mixed-melting-point determination, and the TLC analysis showed these products to be identical with the specimens prepared by the method A.

1-(β-D-Ribofuranosyl)pyrrole (XII). A solution of IX (239 mg, 1.0 mmol) in 80% aqueous acetic acid (2 m*l*) was heated at 100°C (bath-temperature) for 40 min. After the acetic acid and the water had been removed by repeated evaporation with ethanol (50 m*l*, total) at 60°C *in vacuo*, the residue was chromatographed on a column (2×14 cm) of Dowex 1-X2 (OH^- form) (20 g). Elution was effected with water - methanol (7 : 3), 10-m*l* fractions being collected.

Fractions 4—6 contained the starting material (2 mg).

Fractions 7—9 contained an unknown substance (1 mg).

Fractions 12—15 and 18—25 contained XIII (5 mg, 2.5%) and XI (7 mg, 3.5%) respectively; these products were identified by a color reaction[37] with *p*-dimethylaminobenzaldehyde on developed TLC plates.

Fractions 25—47 were combined; the evaporation of the solvents gave XII (174 mg, 87.4%): R_f, 0.50 (TLC, solvent C) (color reaction,[37] purple), 0.67 (PC, solvent, D); retention time (GC), 8.9 min.

Found: C, 54.01; H, 6.31; N, 7.08%. Calcd for $C_9H_{13}O_4N$: C, 54.26; H, 6.58; N, 7.03%.

1-(α-D-Ribofuranosyl)pyrrole (XI) and 1-(2-*C*, 2′-*O*-Isopropylidene-α-D-ribofuranysyl)pyrrole (XIV). A solution of VIII (200 mg, 0.84 mmol) in 80% aqueous acetic acid (1.8 m*l*) was heated at 100°C bath-temperature) for 1 hr. The solvents were then removed in a manner similar to that described above. The residue was chromatographed on a column (2× 14 cm) of Dowex 1-X2 (OH^- form) (20 g) using water - ethanol (7 : 3), 10-m*l* fractions being collected.

Fractions 4—5 contained an unknown substance (2 mg).

Fractions 6—11 were combined and the solvents were removed to afford syrupy products, which contained a small amount of the starting material. Further purification by column chromatography on a silica-gel (Merck) (15 g) column with *n*-hexane - ethyl acetate (2 : 8) gave XIV (58 mg, 29.0%) as a glass which crystallized when scratched: R_f, 0.57 (TLC, solvent C) (color reaction,[37] reddish purple); IR, ν_{max}^{KBr} 3568, 3390, 3130, 3100, 1483, 717 cm^{-1}.

Found: C, 60.28; H, 7.29; N, 5.74%. Calcd for $C_{12}H_{17}O_4N$: C, 60.24; H, 7.16; N, 5.85%.

Fractions 15—21 contained XIII (*ca.* 5 mg, 3%) and an unknown substance (*ca.* 5 mg); the former was identified by color reaction[37] with *p*-dimethylaminobenzaldehyde on a developed TLC plate.

Fractions 24—32 were combined and the solvents removed to yield XI (35 mg, 21.0%): R_f, 0.43 (TLC, solvent C) (color reaction,[37] orange), 0.61 (PC, solvent D); retention time (GC), 9.6 min.

Found: C, 54.22; H, 6.36; N, 7.11%. Calcd for $C_9H_{13}O_4N$: C, 54.26; H, 6.58; N, 7.03%.

Fractions 40—68 contained XII (36 mg, 21.6%), the NMR spectrum of which was identical with that of a specimen prepared from IX.

1-(β-D-Ribopyranosyl)pyrrole (XIII). A solution of X (24 mg, 0.1 mmol) in 80% aqueous acetic acid (0.5 m*l*) was heated at 100°C (bath-temperature) for 15 min. The solvents were removed in a manner similar to that described above. The residue was chromatographed on a column (2×8.5 cm) of Dowex 1-X2 (OH^- form)(10 g) with water - methanol (7 : 3), 10-m*l* fractions being collected. Fractions 7—11 were combined and the solvents removed to yield XIII (18 mg, 90.0%): R_f, 0.40 (TLC, solvent C) (color reaction,[37] brownish purple), 0.56 (PC, solvent D); retention time (GC), 9.0 min.

Found: N, 6.82%. Calcd for $C_9H_{13}O_4N$: N, 7.03%.

Photo-dehydrogenation of Δ^3-Pyrroline (II). A solution of crude II[6] (69 mg, 1.0 mmol) in dry benzene (10 m*l*) containing benzophenone (14 mg, 0.077 mmol) was irradiated under conditions similar to those used for the preparation of V. Aliquots were examined by the GC (stainless steel column (3 m×3 mm) packed with 3% OV-17 on Shimalite W (80—100 mesh), flow rate 18 m*l*/min, column temperature 60°C). After 2 hr, a broad peak (retention time, 13 min) due to II disappeared and a new peak (retention time, 8.1 min) was observed. Under the same conditions, the pyrrolidine remained unchanged.

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