Synthesis of Pyrrole Nucleosides by Photodehydrogenation of a Δ^3-Pyrroline Derivative

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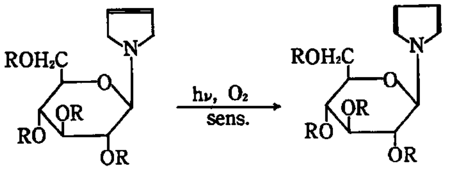
Although extensive studies of the synthesis of the nucleosides of heterocycles have been carried out by many workers, simple pyrrole nucleosides have been neglected. Plisov1) reported that when a mixture of glucose and pyrrole was heated, a probable product (mp 190°C) formed by the condensation of the two was obtained after crystallization from pyridine. However, its structure was unsubstantiated by experimental details or physical data.

We wish to report the synthesis of pyrrole nucleosides by means of a novel photochemical dehydrogenation of a Δ^3-pyrroline derivative. D-Glucose was heated with Δ^3-pyrroline2) (2 mol eq.) without solvents at 80—85°C to produce 1-(D-glucosy)-Δ^3-pyrroline (I) in a 74% yield, the structure being tentatively identified; mp 130—135°C (decomp.), $[\alpha]_D^{20}$ −28.8°(4 min) → +13.0° (46 hr, constant, *c* 0.40, H_2O). 60-Mc NMR (in D_2O); τ 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%.

On acetylation with acetic anhydride in pyridine, I gave 1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-Δ^3-pyrroline (II) in a 73% yield; mp 121—122°C, $[\alpha]_D^{25}$ −23.7° (*c* 0.49, degassed $CHCl_3$). 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%. The site of the glycosidic linkage of the pyrroline ring and the pyranose structure were confirmed by, respectively, the IR spectrum of II and the degradation of II with aqueous formic acid to the known 2,3,4,6-tetra-*O*-acetyl-D-glucose. The NMR spectrum (in $CDCl_3$) was consistent with the structure of II. The methylene and olefinic protons of the pyrroline ring appeared as a singlet at τ 6.22 and 4.32 respectively. The anomeric proton was observed as a doublet centered at τ *ca.* 5.7 (*J*=*ca.* 8 cps), thus indicating the β configuration.

After a solution of II in benzene containing benzophenone as a sensitizer3) had been irradiated4) externally in a Pyrex vessel under bubbling O_2 at 20°C for 1 hr, the TLC analysis of the reaction mixture showed the presence of one main product as well as of several minor by-products. The evaporation of the benzene gave, after recrystallization from ethanol, 1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)pyrrole (III) in a 85% yield; mp 178—178.5°C, $[\alpha]_D^{22}$ −10.9° (*c* 0.67, $CHCl_3$). UV; λ_{max}^{EtOH} 211 mμ (ε 8150). 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%. A reagent useful for dehydrogenation, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, was also effective in obtaining III from II in the dark.



I: R=H
II; R=$COCH_3$

III: R=$COCH_3$
IV: R=H

The NMR spectrum (in $CDCl_3$) of III showed two characteristic triplets, centered at τ 3.83 and 3.21, indicative of the presence of the pyrrole ring. The position of the 2′-acetyl signal (τ 8.15) was at a higher field than the other acetyl signals (τ 7.99—7.93), as has been observed in the case of acetylated nucleosides.5)

The deacetylation of III with sodium methoxide in methanol afforded 1-(β-D-glucopyranosyl)pyrrole (IV) (76% yield) as a hygroscopic glassy mass after chromatography on a silica-gel column (ethyl acetate-ethanol, 4 : 1); mp *ca.* 80°C, $[\alpha]_D^{25}$ +10.3° (*c* 0.74, H_2O). UV; $\lambda_{max}^{H_2O}$ 210 mμ (ε 6950). 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%. Its purity was ascertained by GLC and TLC analyses. The NMR spectrum (in D_2O) exhibited two characteristic triplets centered at τ 3.74 and 3.01 for the protons of the pyrrole ring, and a doublet centered at τ 4.86 (*J*=8.4 cps) for the anomeric proton. Therefore, the β configurations of III and IV were assigned. Further investigations are in progress.

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2) L. H. Andrews and S. M. McElvain, *J. Am. Chem. Soc.*, **51**, 887 (1929).

3) D. C. Neckers, "Mechanistic Organic Photochemistry," Reinhold Publishing Co., New York (1967), p. 163.

4) Super-high-pressure mercury lamp (100 W), Matsuda SHL-100UV-1.

5) R. J. Cushley, K. A. Watanabe and J. J. Fox, *J. Am. Chem. Soc.*, **89**, 394 (1967).