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SYNTHESIS OF PSICOFURANINE

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IN connexion with the preparation of antimetabolites possessing potential cancerostatic activity, we focused our interest on nucleosides containing D-psicose or its derivatives as an anomalous sugar moiety. We chose psicofuranine (6-amino-9-D-psicofuranosyl purine) as model substance for these syntheses.

Psicofuranine has been discovered by a group of American authors who described its isolation, elucidated its structure and, in a preliminary communication, reported, without experimental details, its synthesis.[1,2]

The starting material for our synthesis was D-psicose,[3] which on treatment with methanolic 0.2 N hydrogen chloride solution at 20° for 20 min afforded a mixture of anomeric methylpsicofuranosides (I, II). The mixture was separated by means of preparative paper chromatography (Whatman No. 3 paper; 1-butanol-ethanol-water, 40:11:19). Anomer I: $R_{fructose}$ 1.66, (Whatman No. 1 paper; the above solvents) $[\alpha]_D^{20}$ -40.2° (methanol), periodic acid oxidation: 1.05 moles (Found: C, 42.95; H, 7.36; CH_3O, 15.84. Calc. for $C_7H_{14}O_6$: C, 43.29; H, 7.27; CH_3O, 15.98). Anomer II: $R_{fructose}$ 1.86, $[\alpha]_D^{20}$ +42.8° (methanol), periodic acid oxidation: 0.94 moles (Found: C,

1 T.E. Eble, H. Hoeksema, G.A. Boyack and G.M. Savige, Antibiotics and Chemotherapy 9, 419 (1959).

2 W. Schroeder and H. Hoeksema, J. Amer. Chem. Soc. 81, 1767 (1959).

3 M.L. Wolfrom, A. Thompson and E.F. Evans, J. Amer. Chem. Soc. 67, 1793 (1945).

43.05; H, 7.24. Calc. for $C_7H_{14}O_6$: C, 43.29; H, 7.27). The mixture of methyl glycosides was benzoylated and chromatographed on neutral alumina to yield amorphous mixture of 2-O-methyl-1,3,4,6-tetrabenzoyl-psicofuranoses (III). (Found: C, 68.54; H, 4.98. Calc. for $C_{35}H_{30}O_{10}$: C, 68.84; H, 4.95). A methylenchloride solution of substance III was treated with 20 per cent hydrogen bromide in acetic acid at 0° for 20 min and the crude bromide was used for further procedure. Synthesis of the blocked nucleoside was carried out by a reaction of the above bromide with chloromecuri salt of 6-benzamidopurine in diethylacetamide at room temperature for 5 days. The crude nucleoside was treated with 0.05 N barium methylate solution, chromatographed on Dowex-50 (NH_4^+) column and eluted with 0.01 N ammonia solution. The eluate was paper chromatographed in the above mentioned solvents in order to remove adenine. The eluted nucleoside was purified on IRC-50 column. The eluate after crystallization from hot water afforded a product of m.p. 211-212° in 4.6 per cent yield (calc. for substance III); $[\alpha]_D^{20}$ -65.7° (dimethylformamide; periodic acid oxidation: 1.06 moles (Found: C, 44.79; H, 5.09; N, 23.78. Calc. for $C_{11}H_{15}O_5N_5$: C, 44.44; H, 5.09; N, 23.56). λ_{max} 261 mμ (log ε 4.126) in buffered solution (pH 8.22).

The physical constants and biological activity were in good accordance with properties of psicofuranine given in the literature.[4]

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[4] W.E. Magee and F.S. Eberts, Cancer Res. 21, 611 (1961).