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Synthesis of 1-β-D-Ribofuranosyl-5-ethoxycarbonyl-4-hydroxy-1,2-dihydropyrid-2-one*

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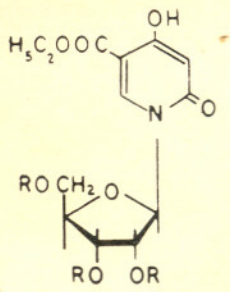
1-β-D-Ribofuranosyl-5-ethoxycarbonyl-4-hydroxy-1,2-dihydropyrid-2-one has been synthesized starting from 2,4-dihydroxy-5-ethoxycarbonylpyridine. The monomercury derivative of the starting compound on condensation with 2,3,5-tri-O-benzoylribofuranosyl chloride affords benzoylated nucleoside which on debenzoylation in the presence of catalytic amount of sodium methoxide in the methanol furnishes the desired nucleoside.

PYRIDINE nucleotide coenzymes act as redox systems in biophase in which the positions 1 and 4 of the pyridine nucleus are involved in hydrogen transfer processes[1-4]. 1-β-D-Ribofuranosyl-5-ethoxycarbonyl-4-hydroxy-1,2-dihydropyrid-2-one (Ia), although structurally related to DPN, would not readily undergo hydrogen transfer process and thus appeared a good possible antagonist of these coenzymes. This compound would also be an analogue of orotidine.



I a, R = H
b, R = -COC$_6$H$_5$

Only recentlysome N-glucosides of 5- and 3,5-disubstituted pyrid-2-ones[5,6] have been synthesized from the corresponding 2-O-glucosides by N-migration of the sugar residue. With the exception of the work of Pfleiderer *et al.*[7], who have prepared 1-β-ribofuranosyl-3-carbamoyl-1,4-dihydropyrid-4-one, such compounds have not been reported so far.

(Ia) was prepared starting from 2,4-dihydroxy-5-ethoxycarbonylpyridine[8], which was converted to its monomercury compound and condensed with 2,3,5-tri-O-benzoylribofuranosyl chloride followed by debenzoylation according to the method of Davoll and Lowy[9].

A solution of 2,4-dihydroxy-5-carbethoxypyridine (0·915 g.) in hot water (50 ml.)was added under stirring to a solution of mercuric acetate (1·98 g.) in methanol (50 ml.). The reaction mixture was refluxed for 2 hr, cooled, filtered and washed successively with water, ethanol and ether. The white amorphous compound so obtained was dried *in vacuo* at 80°; yield 1·67 g. (Found: C, 25·11; H, 2·39; N, 2·96. $C_8H_8HgNO_4$ requires C, 25·09; H, 2·09; N, 3·6%).

The mercury compound (2·0 g.) was condensed[10] with 2,3,5-tri-O-benzoylribofuranosyl chloride[11] (prepared from 2·5 g. of 1-aceto-2,3,5-tri-O-benzoylribose) in refluxing xylene. The crude benzoylated nucleoside (3·03 g.) in chloroform was chromatographed over silica gel and eluted with chloroform containing increasing quantity of methanol. The $CHCl_3$ eluate (250 ml.) gave a non-nitrogenous compound (0·139 g.), which was discarded. The chloroform-methanol eluate (8:2, vol./vol.) gave the protected nucleoside (Ib, 2·36 g.) as a glass. Thin layer chromatography in benzene-methanol (9:1, vol./vol.) showed a single spot, R_f 0·83 (Found: C, 64·41; H, 4·60; N, 1·78. $C_{34}H_{29}NO_{11}$ requires C, 65·06; H, 4·62; N, 2·23%).

(Ib) (1·0 g.) was dissolved in methanol and debenzoylated with catalytic amount of sodium methoxide[12]. The removal of methanol gave a gum, which became amorphous on trituration with ether. The amorphous compound was purified by dissolving in methanol (charcoal) and precipitation with water to give (Ia); yield 0·15 g.; R_f† 0·94 (butanol saturated with water) (Found: C, 50·01; H, 5·73; N, 4·10. $C_{13}H_{17}NO_8$ requires C, 49·5; H, 5·4; N, 4·44%).

The structures of the mercury compound and the riboside (Ia) were supported by the presence in IR spectrum (KBr, Perkin-Elmer infracord) of strong bands at 1730 (α,β-unsaturated ester) and 1670 cm.$^{-1}$ (α,β-unsaturated six-membered lactam).

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†Paper chromatography was carried out on Whatman No. 1 paper by descending technique.