The Synthesis of 2-Ethyl-6-(β-D-ribofuranosyl)oxazolo[5,4-*d*]pyrimidin-7-one

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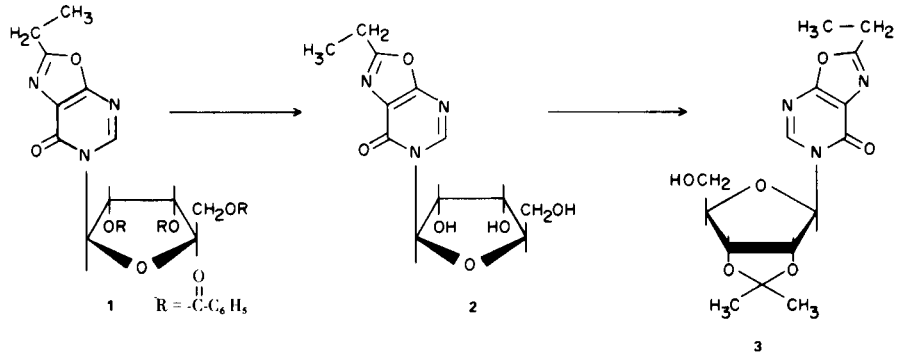
Sir:

The isolation (1) and characterization (2) of uric acid riboside from ox blood as 3-(D-ribofuranosyl)uric acid has generated interest in the chemical synthesis (3) of bicyclic heterocyclic (five-membered ring fused to a six-membered ring) nucleosides with the glycoside residing on a nitrogen in the six-membered (pyrimidine) ring. This interest has been further stimulated by the recent isolation (4) of 7-(D-ribosyl)pyrazolo[3,4-*d*]pyrimidine-4,6-dione (oxoallopurinol riboside) from the urine of patients treated with allopurinol and the report (5) that oxoallopurinol riboside, presumably as the corresponding 5′-phosphate derivative, exerts an inhibition of pyrimidine biosynthesis *de novo*. We now wish to report the synthesis of the first oxazolopyrimidine nucleoside [2-ethyl-6-(β-D-ribofuranosyl)oxazolo[5,4-*d*]pyrimidin-7-one] which can be viewed as a hypoxanthine type riboside with the ribosyl moiety residing in the pyrimidine ring.

The conversion of 2-ethyloxazolo[5,4-*d*]pyrimidin-7-one (6) into a trimethylsilyl derivative was accomplished with hexamethyldisilazane at reflux temperature. This silyl derivative was condensed (7) with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in benzene at reflux temperature in the presence of mercuric oxide/mercuric bromide to furnish a good yield (76%) of nucleoside material. This nucleoside was assigned the tentative structure **1** on the basis of the following data: elemental analysis and pmr spectra revealed at 1:1 composition of carbohydrate and heterocycle, and the uv spectra was very similar to the uv spectra of the starting material which indicated that ribosylation had occurred at N6 where the proton normally resides. The blocking groups were removed from the carbohydrate moiety with methanolic ammonia to afford a nucleoside (55% yield) which was subsequently assigned the structure 2-ethyl-6-(β-D-ribofuranosyl)oxazolo[5,4-*d*]-pyrimidin-7-one (**2**), m.p. 172°. That complete deblocking had occurred, with the oxazole ring still intact was established by uv and pmr spectroscopy. The site of ribosylation was established as N6 by a comparison of the uv spectral data obtained for 2 (uv λ max (methanol), 235 sh, 240, 246 sh, 275 nm) and that reported (8) for 2,6-dimethyloxazolo[5,4-*d*]pyrimidin-7-one.

This left only the anomeric configuration in question and an examination of the peaks assigned to the anomeric proton (H1′) of **1** and **2** in the pmr revealed a coupling constant ($J_{1',2'}$) of a magnitude which precluded an unequivocal anomeric assignment (9). The isopropylidene derivative **3** was prepared from **2** using a standard procedure (10) (2,2-dimethoxypropane in the presence of perchloric acid and acetone). The pmr spectrum of **3** revealed a singlet at δ 6.30 for the anomeric proton which now allowed an unequivocal assignment of β for the anomeric configuration. Therefore, all nucleosides reported in this communication must possess the β anomeric configuration with the ribofuranosyl moiety residing at N6 of the oxazolo[5,4-*d*]pyrimidine ring.



We have also established that the oxazole moiety of the bicyclic nucleoside **2** is susceptible to ring opening, through the frequent monitoring by pmr spectroscopy of a reaction solution of **2** dissolved in aqueous sodium deuteroxide.

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