SYNTHESIS OF SOME β-D-RIBOFURANOSYL-4,7-METHANOINDAZOLES AND PYRAZOLO[1,5-*a*]AZEPINES

Shin-ichi NAGAI and Jinsaku SAKAKIBARA

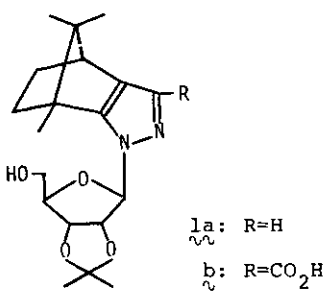
Faculty of Pharmaceutical Sciences, Nagoya City University,

3-1 Tanabe-dori, Mizuho-ku, Nagoya, 467, Japan

We have prepared a series of optically active (4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazoles and elucidated their appreciable pharmacological activities. Since it is considered that the introduction of β-D-ribofuranosyl group into the pyrazole ring of 4,7-methano-1*H*-indazole might bring about interesting biological activity change, we report the convenient synthesis of a new class of pyrazole N- and C-β-D-ribofuranosides.

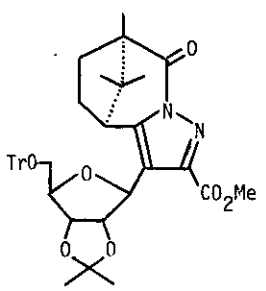
Condensation of 2,3-*O*-isopropylidene-D-ribosylhydrazine with (1*R*,4*S*)-3-hydroxymethylenebornan-2-ones led to selective N-1 ribosylation of pyrazole ring to provide (4*S*,7*R*)-1-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-4,7-methano-1*H*-indazoles (1a-b), and corresponding deprotected 4,7-methano-1*H*-indazole after treatment with acid. Structure determination including anomeric configuration assignment was discussed based on ^{1}H-NMR spectroscopy.

1,3-Dipolar cycloaddition of (1*R*,4*S*)-3-diazobornan-2-one with methyl 3-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)propiolate followed by [1,5]sigmatropic rearrangement was used as a key reaction step in a novel synthesis of pyrazole C-ribofuranoside; (4*S*,7*R*)-3-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-8-oxo-4,7-methano-8*H*-pyrazolo[1,5-*a*]azepine (2). The chemical structure and the binding position of β-D-ribofuranosyl group were confirmed. The isopropylidene and trityl groups were easily removed to give (4*S*,7*R*)-8-oxo-3-(β-D-ribofuranosyl)-4,7-methano-8*H*-pyrazolo[1,5-*a*]azepine.



1a: R=H

b: R=CO_2H



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