PP6. NEW BENZIMIDAZOLE 3'-DEOXYNUCLEOSIDES

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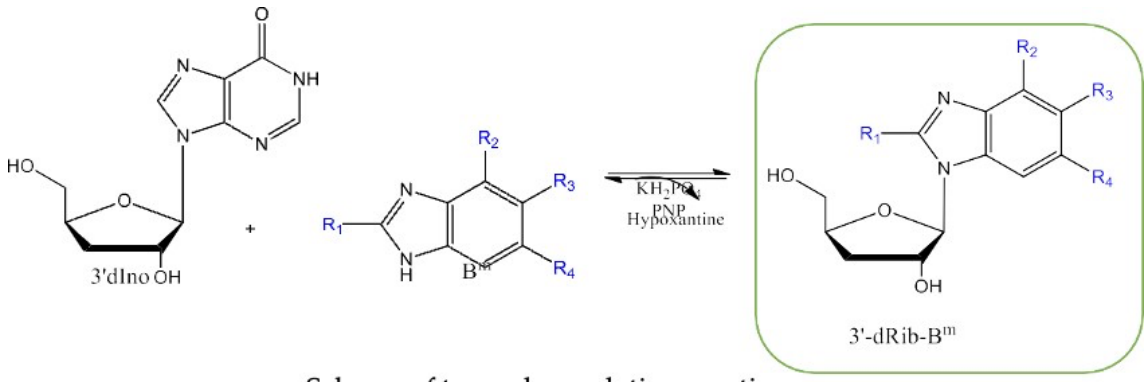
Compounds containing benzimidazole fragment exhibit pronounced antiviral, antispasmodic, neuroleptic, and antihistamine activity. The biological activity profileof benzimidazole nucleosides can be changed by introducing a substituent into the benzimidazole ring and/or carbohydrate residue.

A series of new modified substituted benzimidazole nucleosides (3'd-Rib-B^m) has been prepared by enzymatic method with yields from 8 to 72% and with purity morethan 95%.



Scheme of transglycosylation reaction.

R1 = H, NH2; R2 = H, F; R3 = H, F, OMe; R4 = H, F, OMe.

3'-Deoxyinosine (3'd-Ino) and substituted benzimidazoles (B^m) have been used as substrates in the transglycosylation reaction in the presence of recombinant purine nucleoside phosphorylase (PNP).

At the first step, each reaction was optimized for substrate ratio and amount of PNP. Conditions: 50 °C, 2 mM potassium-phosphate buffer, pH 7.0. The next step was preparative synthesis followed by isolation of enzymatic reaction products. Thestructures of 3'd-Rib-B^m were confirmed by NMR and mass-spectrometry. In the case of asymmetrically substituted benzimidazoles N1 and N3 regio-isomers were formed.