Abstract

The key intermediate 6-amino-7-iodo-7-deazapurine 3′-deoxy-3′-fluororibonucleoside was synthesized using multistep sequence of several reactions, which started from the commercially available D-xylose and 6-chloro-7-deazapurine. The synthetic strategy was based on fluorination of sugar and glycosylation with corresponding nucleobase afterwards. The fluorination of 5-protected-1,2-isopropylidine xylose with different protecting groups at position 5 always led to elimination. It was later discovered that isopropylidine forces the conformation, which is unfavorable for substitution. During the extensive optimization it was also found out that DAST appears to be an optimal fluorinating agent. Fluorination was performed on 2,3-unprotected xylose, which was subsequently used for glycosylation. After several unsuccessful attempts on "protection group free" glycosylation, Vorbrüggen glycosylation was successful and gave desired 3′-fluoro nucleoside in good yield. However, benzoyl group had to be introduced into position 2′. The protected nucleoside was then aminated and simultaneously deproctected with solution of aqueous NH_3 and 1,4-dioxane. The obtained key intermediate was used for synthesis of a small series of desired 6-amino-7-hetaryl nucleoside using Pd-catalyzed Suzuki reaction under aqueous conditions. The series of 6-amino-7-hetaryl-7-deazapurine-3-fluororibonucleosides were synthesized and tested for their biological activities.

Keywords

Nucleosides, 7-deazapurines, fluorinated nucleosides.