Abstract

This thesis describes the synthesis, photophysical properties and biological profiling of several series of polycyclic hetero-fused 7-deazapurine nucleosides.

Modified 7-deazapurine ribonucleosides display a variety of biological effects. Previously, small (hetero)aromatic rings-fused 7-deazapurine nucleosides show submicromolar cytostatic effects or antiviral activities. Thus, the two isomeric series of new benzothieno-fused deazapurine nucleosides were designed as the extended analogues to the cytotoxic thieno-fused nucleosides and hetero-analogues of antiviral naphtho-fused nucleosides. The goal of the first part of my work was to synthesize these target compounds. Key steps include Negishi coupling of zincated pyrimidine with iodobenzothiophene, thermal or photochemical cyclization, glycosylation and final diversification. The furyl and benzofuryl derivatives exerted moderate anticancer and anti-HCV activities. Most of the free nucleosides showed moderate to strong fluorescence, and the corresponding 2′-deoxyribonucleoside triphosphate was incorporated into modified DNA and their fluorescence properties were studied

The tri- and tetracyclic fused nucleobases can be synthesized either by multistep heterocyclization approach or through cross-coupling of zincated pyrimidine with hetaryl halides, but for some heterocycles, the corresponding halides are inaccessible, expensive or unreactive. The second part of my work aimed to overcome this synthetic problem. A new approach for synthesizing polycyclic hetero-fused 7-deazapurine heterocycles and the corresponding nucleosides was developed based on C-H functionalization of diverse (hetero)aromatics with dibenzothiophene-*S*-oxide followed by the Negishi cross-cooupling with bis(4,6-dichloropyrimidin-5-yl)zinc. This cross-coupling afforded a series of (het)aryl-pyrimidines that were used to obtain the corresponding 2'-deoxy- and ribonucleosides through the classic approach as in the first project . Most of the deoxyribonucleosides showed good cytotoxic activity, especially for CCRF-CEM cell line. Phenyl- and thienyl-thieno-fused 7-deazapurine nucleosides were fluorescent and the former one was converted to 2'-deoxyribo-nucleoside triphosphate for enzymatic synthesis of labeled oligonucleotides.