Summary of PhD Thesis: Synthesis of novel types of *C*-nucleosides

General and modular approach for the preparation of disubstituted pyrimidine and pyridine *C*-2'-deoxyribonucleosides and benzyl homo *C*-ribonucleosides was developed. The key intermediate 2,4-dichloropyrimidine *C*-2'-deoxyribonucleoside was efficiently prepared from easily available TBS-protected deoxyribose glycal in three steps. Its mild nucleophilic substitutions or cross-coupling reactions proceeded regioselectively at position 4, while at elevated temperatures or with excess of reagent, a double substitution occurred. The 2-chloro-4-substituted intermediates underwent another substitution or coupling to afford a two-dimensional library of diverse 2,4-disubstituted pyrimidin-5-yl *C*-2'-deoxyribonucleotides. Modular methodology for the synthesis of 2,6-disubstituted pyridine *C*-2'-deoxyribonucleosides was based on the Heck coupling of bromo-chloro-iodopyridines with TBS-protected deoxyribose glycal. Obtained 2-bromo-6-chloro- and 6-bromo-2-chloropyridin-3-yl deoxyribonucleosides were used for further transformations. Some of their Pd-catalyzed cross-coupling reactions proceeded chemoselectively at the position of the bromine, whereas nucleophilic substitutions were unselective and gave mixtures of products. The mono-substituted intermediates were used for another coupling or nucleophilic substitution giving rise to a small library of 2,6-disubstituted pyridine *C*-2'-deoxyribonucleosides. Some of the disubstituted pyridine *C*-2'-deoxyribonucleosides were converted to triphosphates and will be tested for polymerase incorporation in the quest for the extension of the genetic alphabet. New 2-substituted benzyl *C*-ribonucleosides and -nucleotides were designed as carba analogues of phosphoribosylanthranilate, a key intermediate in tryptophan biosynthesis. The synthesis was based on the preparation of TBS-protected 2-bromobenzyl *C*-ribonucleoside by addition of (2-bromobenzyl)magnesium bromide to ribonolactone followed by reduction and subsequent functional group transformations. Pd-catalyzed hydrogenation, cross-couplings, amination or hydroxylation, as well as lithiation followed by reaction with CO_2 and amidations, gave a large series of 2-substituted derivatives that were deprotected to afford free homo-*C*-ribonucleosides. Some of the title nucleosides were converted to 5'-monophosphates. All final compounds did not exert any antiviral or cytostatic effects.