Abstract

This PhD thesis reports the development of novel C-H activation strategies and aqueous-phase Suzuki-Miyaura cross-coupling reactions for the synthesis of modified deazapurine nucleobases.

The methodologies of chemo- and regioselective synthesis of highly functionalized deazapurines have been developed by using modern C-H activation chemistry. Various functional groups such as amino-, imido-, silyl- and phosphonyl- were introduced by C-H activation reactions.

Amino deazapurine derivatives were synthesized by developed Pd/Cu-catalyzed direct C-H amination and C-H chloroamination of 6-substituted 7-deazapurines with *N*-chloro-*N*-alkyl-arylsulfonamides. C-H imidation reactions of pyrrolopirimidines were performed under ferrocene catalysis with *N*-succinimido- or *N*-phtalimidoperesters. In order to obtain silylated derivatives, Ir-catalyzed C-H silylations of phenyldeazapurines with alkyl silanes were designed. Highly interesting deazapurine phosphonates were prepared by using Mn-promoted C-H phosphonation method and were further transformed into the corresponding phosphonic acids. All of the developed direct C-H functionalization reactions proceeded regioselectively at position 8 in deazapurine core, except for C-H silylation where reaction undergoes mainly as directed *ortho* C-H silylation on phenyl ring, leading to new interesting nucleobase derivatives.

The second part of this thesis focused on the modification of position 6 and 7 of 7-deazapurine bases by the aqueous Suzuki-Miyaura cross-coupling reactions with diverse (het)aryl boronic acids. A series of 6-(het)aryl-7-deazapurine bases bearing F at position 7 and H, F, Cl, Me or NH_2 at position 2 was prepared. 7-(Het)aryl-7-deazapurine nucleobases were synthesized from SEM-protected-7-iodo-7-deazapurines by using a protecting group strategy. After cleavage of the SEM group, the 6-methoxy derivatives were transformed into 7-deazahypoxanthines and 7-deazaguanines by *O*-demethylation reactions.

C-H functionalization strategies in combination with aqueous Suzuki-Miyaura cross-coupling reactions were shown to be a powerful tool for the modification of the deazapurine scaffold. Diverse functional groups were introduced directly by C-H activation reactions, whereas for (het)aryl substituents aqueous Suzuki-Miyaura cross-couplings were used. This approach allowed multifunctionalization of deazapurine all around the heterocycle system.