# Abstract

Within presented dissertation thesis Pd-catalyzed direct C-H arylation of 1,3-dimethyluracil to position 5 or 6 was developed. An interesting dichotomy in the regioselectivity and mechanism of reactions were observed. A reaction of 1,3-dimethyluracil with diverse aryl halides performed in the absence of CuI led preferentially to 5-aryl-1,3-dimethyluracils, while with the addition of CuI 6-aryl-1,3-dimethyluracils were formed as the major products. Reactions mediated only in the presence of copper(I) iodide (in the absence of a Pd-catalyst) proceeded with lower yields but led exclusively to 6-arylated derivatives. In order to prepare free 5- and 6 arylated uracils for biological activity screening, the developed methodologies for the direct C-H arylations were applied to various 1,3-protected uracils. Benzyl-protected uracil was selected as the best candidate both in terms of stability during the arylations, as well as facile cleavage of the benzyl groups during deprotection of arylated uracils. Synthesis of various substituted 5- and 6-aryl-1,3-dibenzyluracils proceeded with the same regioselectivity as with the model compound 1,3-dimethyluracil. For deprotection of synthesized derivatives either transfer hydrogenolysis over Pd/C or treatment with $BBr_3$ in case of uracils bearing bulky aromatic substituents was used. Furthermore, novel and efficient synthesis of 2,4-diarylpyrimidines was developed based on the use of phosphonium-mediated Suzuki coupling of 2-(methylsulfanyl)uracil at position 4 followed by the Liebeskind–Srogl cross-coupling at position 2 under microwave irradiation. The synthesized 2,4-diarylpyrimidines were tested *in vitro* for their cytostatic activity against human cancer cell lines. The possibility of subsequent direct arylation of 2,4-diarylpyrimidines was also investigated. Finally, diverse electrophilic, nucleophilic and radical direct trifluoromethylations of 1,3-dimethyluracil were systematically studied in order to prepare either 5- or 6-(trifluoromethyl)uracil derivatives and consequently explore possibilities of direct arylation to free 5 or 6 position. The radical trifluoromethylation by $CF_3SO_2Na$ in presence of *t*-BuOOH gave 1,3-dimethyl-5-(trifluoromethyl)uracil in good yield. The 6-(trifluoromethyl)uracil derivative was only prepared in a mixture with 1,3-dimethyl-5-(trifluoromethyl)uracil by Ir-catalyzed borylation followed by treatment with the Togni's reagent. This isomer was isolated from the mixture only in a very low yield, therefore, the attempts of subsequent C-H arylation were performed only on 1,3-dimethyl-5-(trifluoromethyl)uracil. Its Pd-catalyzed arylation with various aryl halides proceeded successfully only with 4-iodotoluene, wherein in the presence of CsF as a base and copper iodide the desired 6-tolyl-5-trifluoromethyluracil derivative was successfully prepared.