

**UNIVERSITY GRADUATE SCHOOL BULLETIN  
ANNOUNCEMENT**

**Florida International University**  
*University Graduate School*

Doctoral Dissertation Defense

**Abstract**

Novel Approaches for the Synthesis of C-5 Modified Pyrimidine Nucleosides

by

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The antiviral or anticancer activities of C-5 modified pyrimidine nucleoside analogues validate the need for the development of their syntheses. In the first half of this dissertation, I have explored the Pd-catalyzed cross-coupling reaction of allylphenylgermanes with aryl halides in the presence of  $\text{SbF}_5/\text{TBAF}$  to give various biaryls by transferring multiple phenyl groups, which has also been applied to the 5-halo pyrimidine nucleosides for the synthesis of 5-aryl derivatives. In order to avoid the usage of organometallic reagents, I developed Pd-catalyzed direct arylation of 5-halo pyrimidine nucleosides. It was discovered that 5-aryl pyrimidine nucleosides could be synthesized by Pd-catalyzed direct arylation of  $N^3$ -free 5-halo uracil and uracil nucleosides with simple arenes or heteroaromatics in the presence of TBAF within 1 h. Both  $N^3$ -protected and  $N^3$ -free uracil and uracil nucleosides could undergo base-promoted Pd-catalyzed direct arylation, but only with electron rich heteroaromatics.

In the second half of this dissertation, 5-acetylenic uracil and uracil nucleosides have been employed to investigate the hydrogermylation, hydrosulfonylation as well as hydroazidation for the synthesis of various functionalized 5-vinyl pyrimidine nucleosides. Hydrogermylation of 5-alkynyl uracil analogues with trialkylgermane or tris(trimethylsilyl)germane hydride gave the corresponding vinyl trialkylgermane, or tris(trimethylsilyl)germane uracil derivatives. During the hydrogermylation with triphenylgermane, besides the vinyl triphenylgermane uracil derivatives, 5-[2-(triphenylgermyl)acetyl]uracil was also isolated and characterized and the origin of the acetyl oxygen was clarified. Tris(trimethylsilyl)germane uracil derivatives have been coupled to aryl halides *via* the Pd-catalyzed cross-coupling reactions but with decent yield. Iron-mediated regio- and stereoselective hydrosulfonylation of the 5-ethynyl pyrimidine analogues with sulfonyl chloride or sulfonyl hydrazine to give 5-(1-halo-2-tosyl)vinyluracil nucleoside derivatives has been developed. Nucleophilic substitution of the 5-( $\beta$ -halovinyl)sulfonyl nucleosides with various nucleophiles have been performed to provide highly functionalized 5-vinyl pyrimidine nucleosides *via* the addition-elimination mechanism. The 5-( $\beta$ -keto)sulfonyluracil derivative has also been synthesized *via* the aerobic difunctionalization of 5-ethynyluracil analogue with sulfinic acid in the presence of catalytic amount of pyridine. Silver catalyzed hydroazidation of protected 2'-deoxy-5-ethynyluridine with  $\text{TMSN}_3$  in the presence of catalytic amount of water to give 5-( $\alpha$ -azidovinyl)uracil nucleoside derivatives was developed. Strain promoted Click reaction of the 5-( $\alpha$ -azidovinyl)uracil with cyclooctyne provide the corresponding fully conjugated triazole product.

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