Part I. Tandem Aldol-Allylation Reactions Promoted by Strained Silacycles

Part II. Design and Synthesis of Modified Fluorescent Nucleotides for DNA Sequencing by Synthesis

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ABSTRACT

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Part II. Design and Synthesis of Modified Fluorescent Nucleotides for DNA Sequencing by Synthesis

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The first part of this thesis presents the tandem aldol-allylation reactions promoted by strained 1,3-dioxa-2-silacyclopentane rings. Our studies have proven that both the aldehyde- and ketone-derived allylenolsilanes could react with aldehydes smoothly in the absence of catalysts to afford homoallylic 1,3-diols with high diastereoselectivity. Pinacol was employed to constitute the strained 1,3-dioxa-2-silacyclopentane ring as an effective platform to activate the reactivity of silane reagents due to the effect of *strain-release Lewis acidity*. The tandem aldol-allylation reactions proceed via a cyclic transition state with a six-membered chair-like conformation (*type I* allylation). Homoallylic 1,3-diols with up to four stereocenters can be generated using tandem aldol-allylation reactions in one step conveniently and rapidly, which has become an important method to construct 1,3-diol fragments for the total synthesis of natural products.

The second part of this thesis describes the design and synthesis of both photocleavable

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and chemically cleavable 3' modified fluorescent nucleotides. Four 3' allyl modified nucleoside triphosphates (3'-*O*-allyl-dNTP-NH_2) were synthesized from readily available chemicals in reasonable yields after which modified fluorescent nucleotides were prepared via coupling reactions of these nucleoside triphosphates with corresponding fluorescent dyes. These fluorescent nucleotides have been applied for DNA sequencing by synthesis both in solution phase and on a glass chip and have proven to be good reversible terminators for DNA SBS. They could be accurately incorporated into a growing DNA strand in the DNA polymerase reaction and the 3' capping group could be cleaved conveniently in aqueous palladium (II)-phosphine solution after fluorophore detection. This valuable approach has offered an alternative DNA analysis method to overcome the disadvantages and limitations of conventional electrophoresis-based sequencing methods.

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