

# Samarium(II)-mediated Reactions in Organic Synthesis

Method Development and Mechanistic Investigation



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AKADEMISK AVHANDLING

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## Abstract

This thesis describes the development of methods using divalent samarium reagents in organic synthesis. The main focus is placed on functional group reductions, but reductive formation of carbon-carbon bonds has also been investigated.

The reduction of aliphatic nitro compounds was successfully performed using  $\text{SmI}_2$ , amine and water giving the resulting amine in high yield (90%). The reaction was found to tolerate a wide range of other functional groups.

The reductive cleavage of benzyl heteroatom bonds using  $\text{SmI}_2$ , amine and water was mechanistically studied and it was found that the reaction order was unity in all components. Furthermore, water displayed a complex relationship and was found to inhibit the reaction at high concentration. The results obtained were used to develop a novel method for the defunctionalization of benzylic alcohols, amines and thiols.

A protocol for efficient removal of the toluenesulfonyl protecting group has been developed. The method was tolerant to highly sensitive functional groups and structures. The deprotection was very fast and high yielding (generally over 90%) at rt for all the evaluated substrates.

An important addition to a new carbon-carbon bond forming reaction was found during the efforts to synthesize 3-cyanochromones. The combination of two counter ions, iodide and HMDS, results in a  $\text{Sm}(\text{II})$ -reagent that displays a unique reactivity in a Reformatsky inspired method.

The  $\text{SmI}_2$ /amine/ $\text{H}_2\text{O}$  system could also be used for the reductive defluorination of polyfluorinated esters and amides. Pentafluoropropionyl esters and amides were efficiently modified to yield the  $\beta$ ,  $\beta$ ,  $\beta$ -trifluoropropionyl derivative in high yield. It was interesting to find that the incorporation of a chiral auxiliary induced some selectivity (2:1) in this reduction.

**Keywords:** Samarium(II) iodide, reduction, single electron transfer, nitro group reduction, mechanistic study, bond cleavage, deoxygenation, additives, toluenesulfonyl deprotection, defluorination.

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