CHAPTER IV

Bismuth (III) Chloride
Catalyzed Organic Transformations
INTRODUCTION

Each step of a synthesis involves a chemical reaction, reagents and conditions for these reactions need to be designed to give a good yield and a pure product, with as little work as possible. A method may already exist in the literature for making one of the early synthetic intermediates and this method will usually be used, rather than "trying to reinvent the wheel". However most intermediates are compounds that have never been made before, and these will normally be made using general methods developed by researchers. To be useful, these methods need to give high yields and to be reliable for a broad range of substrates.

Methodology research usually involves three main stages—discovery, optimization and studies of scope and limitations. The discovery may be due to serendipity or may be from a flash of insight. Optimization is where one or two starting compounds are tested in the reaction under a wide variety of conditions of temperature, solvent and reaction time, etc., until the optimum conditions for product yield and purity found. Then the researcher tries to extend the method to a broad range of different starting materials in order to find the scope and limitations. Some larger research groups may then perform a total synthesis to showcase the new methodology and demonstrate its value in a real application.

When a chemical reaction is to be carried out selectively at one reactive site in a multifunctional compound, other reactive sites must be temporarily blocked. Thus protecting groups are most frequently used reagents in organic synthesis. The selection of a protecting group is an important step in synthesis of various biologically important compounds. As the chemists proceeded to synthesize more complicated structures, they developed more satisfactory protective groups and more effective methods for the formation and cleavage of protected compounds.

Methoxymethyl ether (MOM), 2-methoxyethoxymethyl ether (MEM), tetrahydropyranyl ether (THP), trimethylsilyl ether (TMS), trityl ether, etc., are few protecting groups that are commonly employed while protecting hydroxyl group in organic synthesis. Various reagents like ZnBr₂, AlCl₃Et₂, Yb(OTf)₃, Ce(OTf)₃, CeCl₃/Nal, I₂/MeOH, BiCl₃ are few common Lewis acids employed for the deprotection of protecting groups.
The triphenylmethyl (trityl) group is a commonly used protecting group for primary alcohols in carbohydrate and nucleoside chemistry due to its ease of installation, removal and stability towards a variety of reagents. In general, detritylation is accomplished under strong acidic conditions such as HCO₂H, 80% CH₃CO₂H, mineral acids, or using Lewis acids such as ZnBr₂, AlCl₃, Yb(OTf)₃ and Ce(OTf)₃. Other reagents including CeCl₃/NaI, I₂/MeOH and triethylsilane have also been employed for the removal of trityl group. However, under protic acid conditions, sensitive substrates frequently undergo acid catalyzed deglycosylations and Lewis acid detritylation procedures require either anhydrous conditions, use of reagents in stoichiometric quantities and extended reaction times and heating. Thus there is still a need to develop a mild and more effective method to overcome the above drawbacks for trityl deprotection.

Most bismuth compounds are relatively non-toxic, easy to handle and can tolerate small amounts of moisture. With increasing environmental concerns and the need for green reagents, the interest in bismuth and its compounds has increased tremendously in the last decade. Several review articles and a monograph has focused on the applications of Bismuth(III) chloride compounds in organic synthesis.

Bismuth(III) chloride has been used for chemo selective deprotection of O, O-acetals using catalytic activity of BiCl₃ in CH₃OH as the solvent by Sabitha et. al. (Scheme 1).

![Scheme 1]
Chapter IV, Section A. Introduction

Sabitha et al.\textsuperscript{16} have developed BiCl\textsubscript{3} in CH\textsubscript{3}CN for the selective cleavage of alkyl TBDMS groups in the presence of aryl TBDMS groups (Scheme 2).

![Scheme 2]

The regeneration of carbonyl compounds from oximes is an important synthetic transformation, especially in light of the fact that oximes can be synthesized from non-carbonyl compounds. Baruah et al.\textsuperscript{17} have developed an efficient method that utilizes BiCl\textsubscript{3} under microwave irradiation condition for oxime deprotection (Scheme 3).

![Scheme 3]

1,1-Diacetates (acylals) have attracted recent attention since they are easily synthesized and can serve as selective protecting groups for aldehydes. Mohamadpoor and Aliyan et al.\textsuperscript{18} have developed Bismuth(III) chloride in CHCl\textsubscript{3} as a mild reagent for deprotection of 1,1-diacetates (Scheme 4).

![Scheme 4]

Bismuth(III) chloride was found to be good catalyst by Oussaid et al.\textsuperscript{19} for the cleavage of 2-tert-butoxy derivatives of thiophenes and furans (Scheme 5).

![Scheme 5]
**Chapter IV, Section A, Introduction**

Bismuth(III) chloride has been shown to be an efficient catalyst for the synthesis of 2,3-unsaturated glycopyranosides from alcohols and thiols (Scheme 6).

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\text{Scheme 6}
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Herein, we wish to report a mild and efficient procedure for the selective cleavage of trityl ethers using Bismuth(III) chloride in acetonitrile at room temperature.

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\text{Scheme 7}
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