PREFACE

Sulfoximines have emerged as new and valuable pharmacophore in drug discovery. At present, some sulfoximine compounds are in different phases of clinical trials for various diseases. Moreover, sulfoximines were also explored in organic synthesis as building blocks, organocatalysts, ligands, chiral auxiliaries and directing groups, etc,

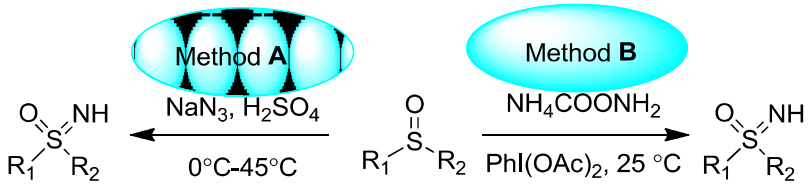
In this context, the thesis entitled, **"Development of new synthetic routes for the preparation of *N*-aryl, acyl and phosphoryl sulfoximines"** will demonstrate various methods for *N*-functionalization of the sulfoximines. **The chapter 1** will provide a general introduction to sulfoximines, its biological and chemical applications. **The chapter 2** will disclose copper catalyzed *N*-arylation of sulfoximines using aryldiazonium salts under mild conditions. **The chapter 3** will highlight the development of catalyst-free and straightforward iminocarbonylation approach for the synthesis of *N*-acyl sulfoximines. The c**hapter 4** will describe the SeO_2-mediated α-keto *N*-acylation of *NH*-sulfoximines using acetophenones in the absence of any additives under mild reaction conditions. The **chapter 5** will demonstrate the copper(II) acetate mediated an efficient *N*-phosphorylation of sulfoximines with different dialkyl phosphites under mild reaction conditions. Finally, the c**hapter 6** will summarize and conclude the total thesis work.

GENERAL EXPERIMENTAL CONSIDERATIONS

All the reactions were carried out in oven dried glasswares. Starting materials were prepared using modified literature procedures and modified procedures as described in the experimental sections. Solvents and chemicals were purchased from commercial sources (Aldrich, Alfa Aesar, SD fine and Avra) and used without further purifications, unless otherwise stated. **Melting points** of products were measured Staurt SMP10 melting point apparatus using in open capillary tubes. **FT-IR** for the products were recorded on ALPHA BRUKER Eco-ATR fitted out on ZnSe ATR crystal in the range of 500-3000 cm^{-1}. **^{1}HNMR and ^{13}C NMR** spectra were recorded on Bruker Avance 500 MHz NMR spectrometer using deuterated solvents. Chemical shifts are given in ppm, using tetramethylsilane (TMS) as an internal standard. **Mass spectra (HRMS)** were measured on water's Quattro Micro V 4.1. Electronic absorption spectra were recorded on Shimadzu UV-2450 spectrophotometer. **Thin layer chromatography (TLC)** was performed using pre-coated plates obtained from E. Merck (TLC silica gel 60 F254). The TLC's were visualized in UV Chamber with 254 nm wavelength lamp, sometimes stained by in iodine chamber. **Column chromatography** was performed on silica gel (60-120 or 100-200 mesh) using different eluents. The other details of the experiments are given in respective chapters.

Synthesis of *HN*-Sulfoximines

Synthesis of NH-sulfoximines for thesis work was achieved from sulfoxides using the literature procedures [1-5]. In particular, following two methods, method **A** and method **B** has been used (scheme **1**). Detailed synthetic procedures are given below,



Scheme 1: Synthesis of sulfoximines.

Method A: Sulfoxide (4.0 mmol) and sodium azide (1.2 eq. 4.8 mmol) were stirred in $CHCl_3$ (15-20 mL) in an oven-dried round bottom flask at 0°C for 10 minutes. After that conc. H_2SO_4 (approx. 2.0 mL for 1 g of sulfoxide) was added dropwise to the reaction mixture over 10-15 minutes at 0 °C. The resulting reaction mixture was warmed up to 45 °C in oil bath and stirred for overnight. After that the reaction mixture was cooled and the pasty-mass was dissolved with ice-water. The organic layer was decanted and the aqueous layer was washed with minimum amount of $CHCl_3$. The aqueous layer was made slightly alkaline using 20% NaOH solution and extracted with $CHCl_3$ (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude residue was purified using column chromatography on silica gel (60-120 mesh) using ethyl acetate and hexane as eluent to afford the desired sulfoximines in good to excellent yields.

Method B: Sulfoxide (4.0 mmol), $PhI(OAc)_2$ (3.0 eq.) and ammonium carbamate (4.0 eq.) were added into a 250 mL round bottom flask containing MeOH (10.0 mL). The reaction mixture was stirred for 30 min at 25 °C in an open. The progress of reaction was analyzed by TLC. After completion, methanol was removed under vacuo and the crude residue was purified by silica-gel column chromatography using ethyl acetate/ hexane as eluent to obtain the desired sulfoximines.

References

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