CHAPTER-6

SUMMARY AND CONCLUSIONS

6.1 Summary and Conclusions

The thesis entitled "**Synthesis and Applications of *N*-Nitrosamines in Organic Syntheses"** described the synthesis of *N*-nitrosamines and their different reactions related to it such as denitrosation, nitration and reduction. The contents of the thesis have been divided into six chapters including summary and conclusions.

Chapter 1 gave a general introduction to nitroso compounds such as *C*-nitroso compounds, *S*-nitroso compounds, *O*-nitroso compounds and *N*-nitroso compounds. Among them, the physical, chemical and biological properties as well as structural and stereochemical features of *N*-nitroso compounds have been discussed broadly. In addition, various synthetic applications of *N*-nitrosamines, *i.e.* reduction to dialkylhydrazines, oxidation to nitramines, and cyclization to sydnones and sydnoneimines, etc. have been elaborated (Figure 6.1). A recent application of *N*-nitrosamines as a traceless directing group for the C-H activation reaction has been discussed. The objectives of the thesis work have been incorporated in this chapter.

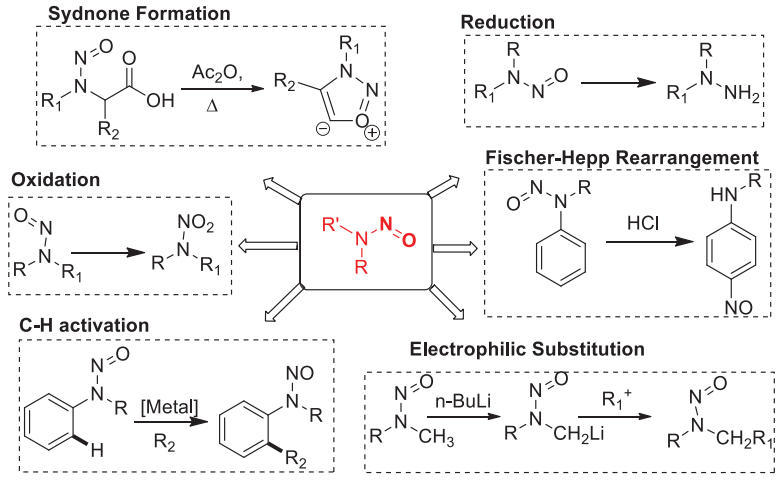
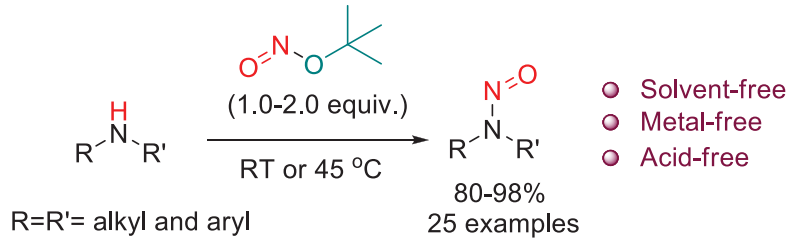


Figure 6.1 Applications of *N*-nitroamines in organic synthesis.

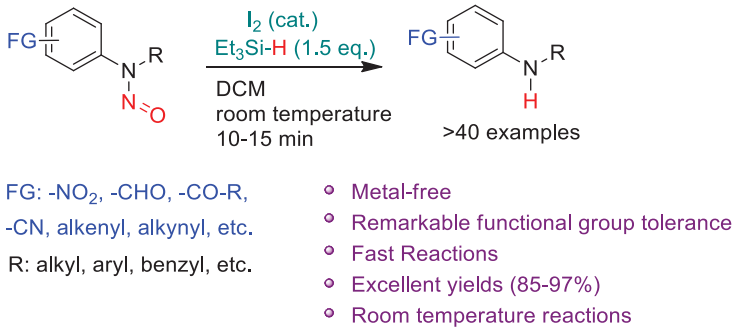
Chapter 2 described an efficient synthesis of *N*-nitrosamines under solvent, metal and acid free conditions using *tert*-butyl nitrite, etc. (Scheme 6.2). A number of aryl, benzyl and alkyl secondary amines underwent *N*-nitrosation with good to excellent yields along with *tert*-butanol as the only by-product. Acid labile protecting groups such as *tert*-butyldimethylsilyl (TBDMS) and *tert*-butyloxycarbonyl (Boc) as well as sensitive functional groups such as phenols, olefin and alkyne were found remained intact. Apart from this, TBN is also found to be an efficient reagent for the transformation of aryl hydrazines to aryl azides and benzamides into substituted benzoic acids under mild conditions.



Scheme 6.2 Synthesis of *N*-nitrosamines using *tert*-butyl nitrite.

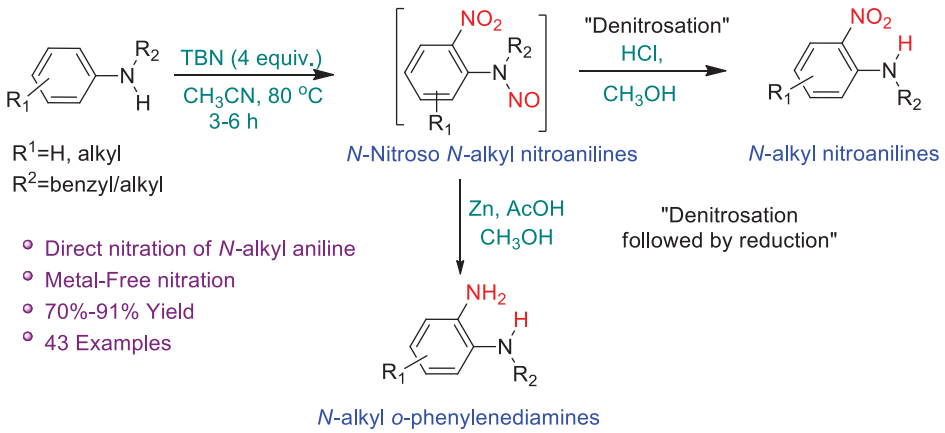
Chapter 3 presented an efficient and practical method for the denitrosation of *N*-nitrosamines using iodine and triethylsilane (Scheme 6.3). The reactions proceeded at room temperature in a short span of time and gave typical yields of 85-97%. Reduction susceptible functionalities such as alkene, alkyne, nitrile, nitro, aldehyde, ketone and ester were found to be stable under the standard reaction conditions. Applications of this denitrosation protocol were demonstrated in different multistep organic synthesis. In

addition, the nitroso moiety was explored also as a protecting group for secondary amines, which can be easily denitrosated using this protocol.



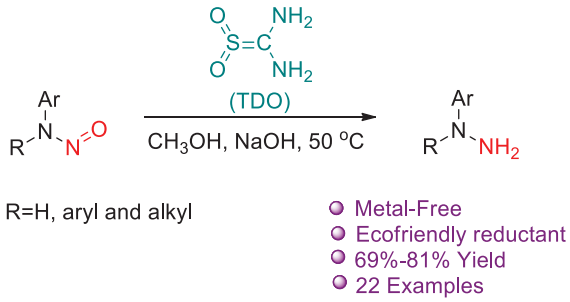
Scheme 6.3 Denitrosation of *N*-nitrosamines.

Chapter 4 disclosed a direct method for the regioselective ring nitration of *N*-alkyl anilines using *tert*-butyl nitrite (TBN) under metal and catalyst-free conditions. These reactions proceeded efficiently with wide range of substrates providing synthetically useful *N*-nitroso *N*-alkyl nitroanilines in excellent yields which can be easily converted into *N*-alkyl nitroanilines and *N*-alkyl phenylenediamines using 25% aqueous HCl in methanol and Zn/AcOH respectively, respectively (Scheme 6.4**)**. Different control experiments have been performed to understand the ring nitration mechanism of the reaction.



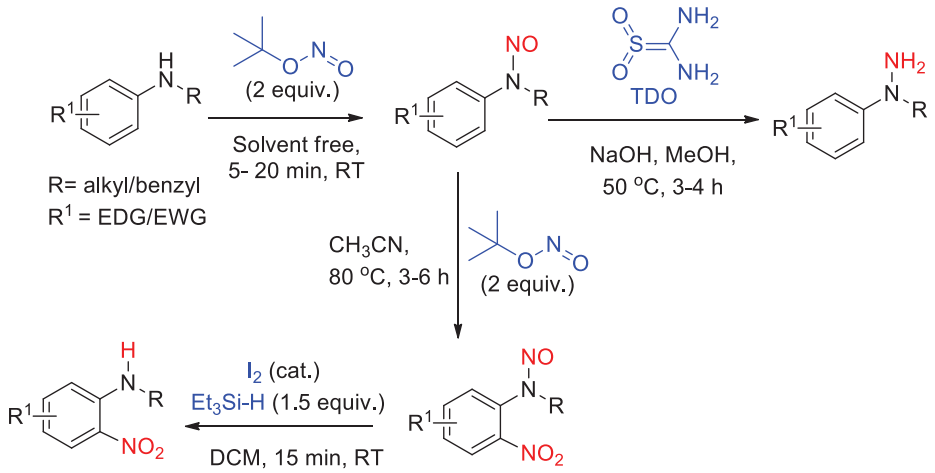
Scheme 6.4 Synthesis of nitro compounds.

Chapter 5 illustrated the first green approach for the preparation of α-substituted aryl hydrazines from corresponding *N*-nitroso compounds using eco-friendly reductant thiourea dioxide (Scheme 6.5**)**. Thiourea dioxide is found to be superior among the sulphur containing reducing agents such as sodium dithionite, sodium bisulfite, sodium sulfite and provides a high yield of desired hydrazines. Moreover, sensitive functional groups such as olefin and alkyne are found to be stable during the reduction. The innocuous reagent, simple and convenient procedure and excellent yield make the protocol attractive for the preparation of aryl hydrazines from *N*-nitrosamines.



Scheme 6.5 Synthesis of arylhydrazines.

In conclusion, *N*-nitroamines are versatile class of organic molecules explored in different organic reactions. The synthesis of *N*-nitrosamines has been successfully accomplished using *tert*-butyl nitrite under solvent free conditions. The reaction of *N*-alkyl anilines with excess amount of *tert*-butyl nitrite provides synthetically useful *N*-nitroso *N*-alkyl nitroanilines. Denitrosation of *N*-nitrosamine in *N*-nitroso *N*-alkyl nitroanilines was achieved using I_2/Et_3SiH under mild conditions. Selective reduction of aryl *N*-nitrosamine to aryl *N*-hydrazines has been achieved using green reductant thiourea dioxide (Scheme 6.6).



Scheme 6.6 Synthesis and applications of *N*-nitrosamines.

All the demonstrated protocols in the thesis are superior to most of the existing protocols in terms of reaction condition and yield. Innocuous reagent, convenient procedure and high yield make these methods more attractive in organic synthesis. Hence, the developed methodologies will find wide applications in organic synthesis.