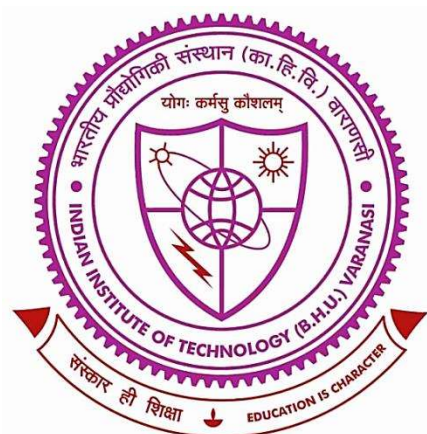


Synthesis and Applications of *N*-Nitroso Compounds in the Preparation of Benzotriazoles, Benzimidazoles, Azides and Amides



**Thesis submitted in partial fulfilment for the
Award of Degree**

Doctor of Philosophy

by

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CHAPTER-6

Summary and Conclusions

The thesis entitled “**Synthesis and Applications of *N*-Nitroso Compounds in the preparation of Benzotriazoles, Benzimidazoles, Azides and Amides**” described the synthesis and some applications of *N*-nitrosamines and *N*-nitrosamides. The contents of the thesis have been divided into six chapters including summary and conclusion.

Chapter 1 gave a general introduction of nitroso compounds such as *N*-nitrosamines, *N*-nitrosamides and their biological and synthetic application in organic chemistry (Figure 6.1). *N*-Nitroso compounds are present in a wide range of foods, cosmetics and natural products. *N*-Nitroso compounds have been used in various treatments including cancer, cardiovascular diseases, central nervous disorders and diseases related to immunity and physiological disorders. On the other hand, *N*-nitrosamines are the versatile class of organic compounds explored in organic synthesis as starting material, reagents, masking groups, directing groups, etc. In addition, various synthetic applications of *N*-nitrosamines, *i.e.* hydrazine synthesis, *ortho*-nitration of amine, denitrosation of nitrosamine and cyclization to sydnone and fisher-hepp rearrangement, etc. have been elaborated. *N*-Nitrosamide undergoes variety of reactions including reduction, oxidation transamidation, esterification, etc. 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.

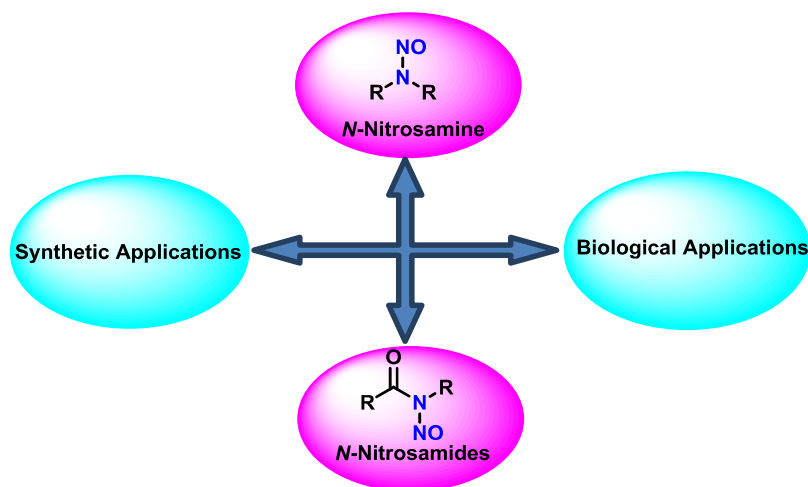
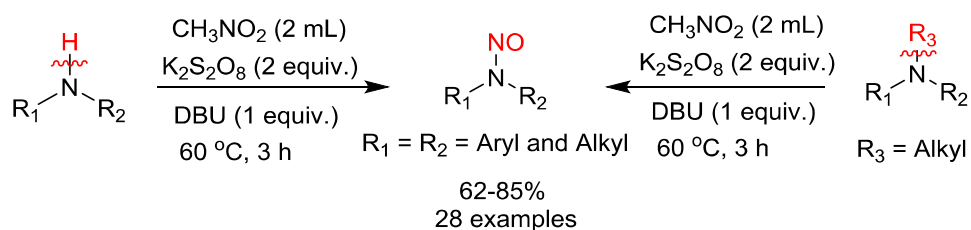


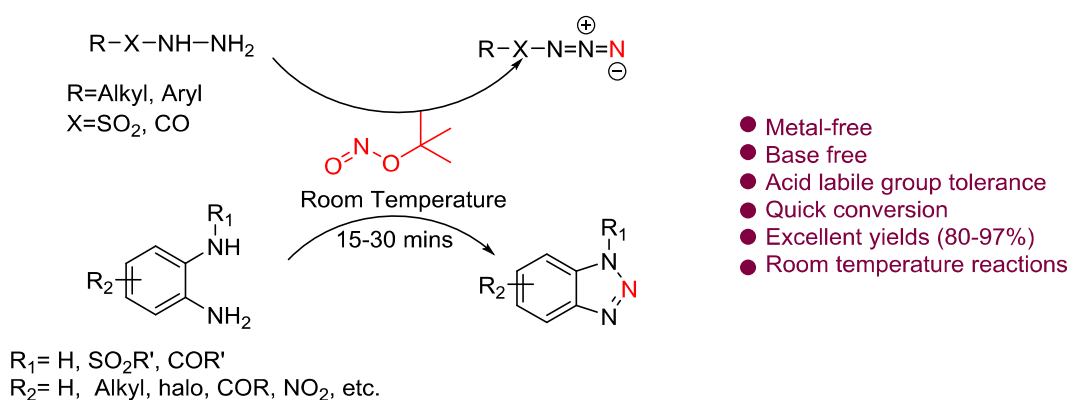
Figure 6.1 *N*-nitrosamine and amides

Chapter 2 described a potassium persulfate-promoted *N*-nitrosation of secondary and tertiary amines with nitromethane under mild conditions, etc. (Scheme 6.1). A variety of alkyl, benzyl and aryl secondary amines underwent *N*-nitrosation with nitromethane in the presence of potassium persulfate and DBU in good to excellent yields. Also diallylamine underwent *N*-nitrosation smoothly, while the double bond was remaining intact. In the case of tertiary amines dealkylative *N*-nitrosation was successfully demonstrated under optimized condition. *N*-nitrosation of aliphatic as well as aromatic secondary and tertiary amine was successfully achieved. Inexpensive reagents, broad substrate scope and efficient conversion make the current protocol more attractive in organic synthesis.



Scheme 6.1 Synthesis of *N*-nitrosamines from secondary as well as *tert*-amines

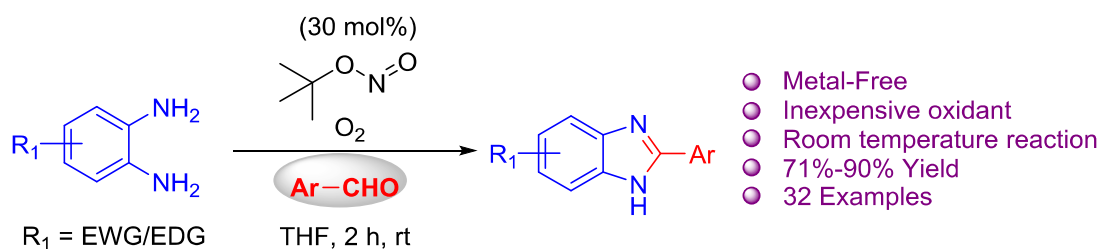
Chapter 3 presented the mild and practical methods for the (i) transformation of *o*-phenylenediamines into benzotriazoles and (ii) conversion of sulfonyl and acyl hydrazines into corresponding sulfonyl and acyl azides using *tert* butyl nitrite (TBN) (Scheme 6.2). All the reactions were carried out at room temperature to obtain the desired products in excellent yields. Moreover, this protocol does not require any catalyst, acidic medium or high temperature. Acid labile (i.e. *tert*-butoxycarbonyl (Boc), trimethylsilyl (TMS) and *tert*-butyldimethylsilyl (TBS)) groups were found to be very stable during triazole formation with TBN. The developed methodology has been used for the conversion of hydrazides into azides as a key one-pot click reaction with alkynes and coupling reaction with boronic acid for the synthesis of benzene sulfonyl triazoles and benzene sulfonamides.



Scheme 6.2 *tert*-Butyl nitrite mediated triazole and azide formation

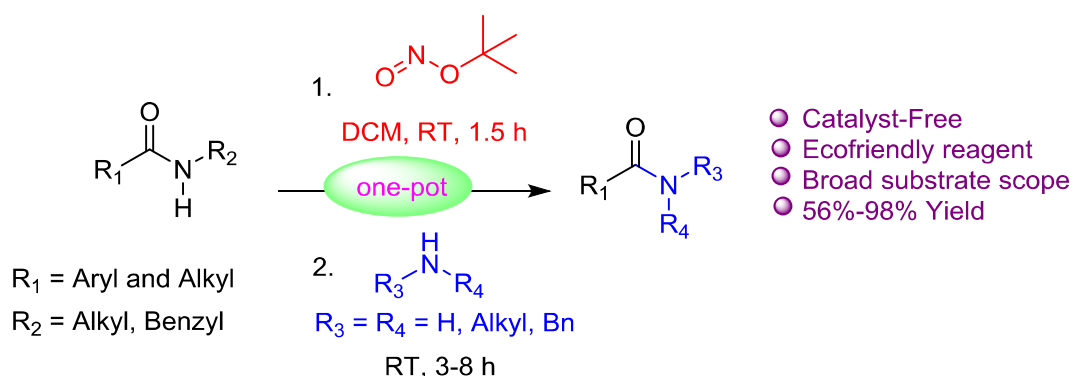
Chapter 4 disclosed an efficient catalytic method for the preparation of benzimidazoles from *o*-phenylenediamine and aldehydes in the presence of *tert*-butyl nitrite (Scheme 6.3). All the reactions were carried out at room temperature in the presence of oxygen as an oxidant. The reactions proceeded well with aromatic, aliphatic

and heteroaromatic aldehydes. This current methodology showed a broad substrate scope while the desired products were obtained in good to excellent yields.



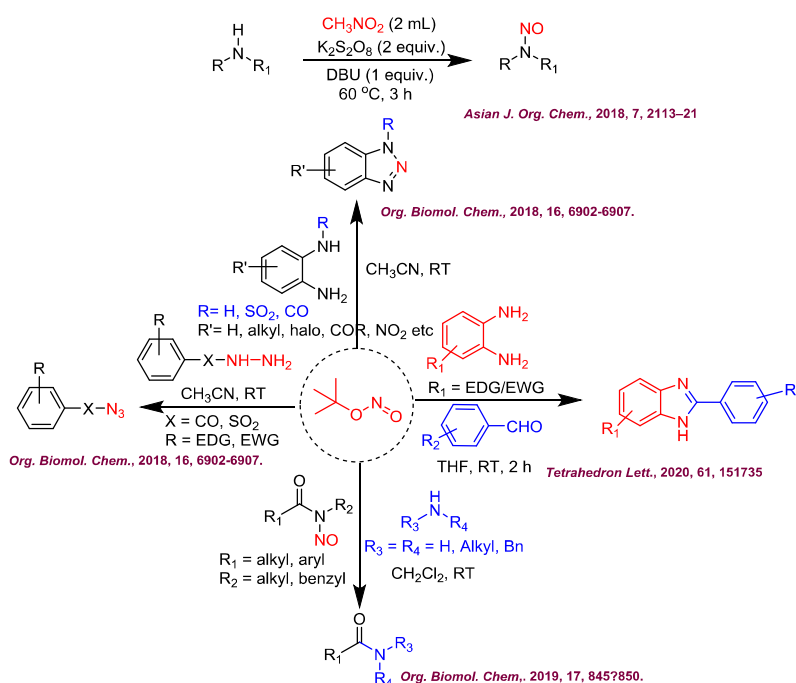
Scheme 6.3 Synthesis of benzimidazoles

Chapter 5 illustrated an efficient one-pot procedure for the transamidation of secondary amides under metal and catalyst free conditions using *tert*-Butyl nitrite (Scheme 6.4). Transamidation of various secondary amides was demonstrated with different amines including primary, secondary, cyclic and acyclic amines in the presence of *tert*-butyl nitrite. The reaction proceeds through the *N*-nitrosamide intermediate. All the reactions were carried out at room temperature to obtain the desired products in good to excellent yields. Moreover, the developed methodology does not require any catalyst, acidic medium or high temperature which demonstrates the broad scope of the methodology.



Scheme 6.4 Transamidation of secondary amides in the presence of TBN

Chapter 6 provides the summary and conclusion. The synthesis of *N*-nitrosamines from various secondary and tertiary amines with nitromethane is described in the presence of potassium persulfate and DBU. We have reported the *tert*-butyl nitrite mediated nitrogen transfer reactions for the synthesis of benzotriazoles and azides at room temperature. We have also developed an efficient one-pot procedure for the transamidation of secondary amides under metal and catalyst free conditions (Scheme 6.5).



The demonstrated synthetic protocols in the thesis are simple and easy to operate. Most these reactions were carried out at room temperature or little elevated temperature which is easy to attain. Use of innocuous reagent and high yields make these methods more attractive in organic synthesis. Hence, the developed methodologies are expected find wide applications in organic synthesis.