AZIRIDINE CYCLOADDITION TO HETEROCUMULENES AS A ROUTE TO FIVE MEMBERED HETEROCYCLES

BY

SUSAN JOSHI

Thesis submitted in fulfilment

of

the requirements of the degree of

DOCTOR OF PHILOSOPHY

to the

Department of Chemistry

INDIAN INSTITUTE OF TECHNOLOGY, DELHI

MARCH, 1999

Dedicated

to

My husband

&

parents

CERTIFICATE

This is to certify that the thesis entitled, "**Aziridine Cycloaddition to Heterocumulenes as a route to Five Membered Heterocycles**" being submitted by Ms. Susan Joshi to the Indian Institute of Technology, Delhi, for the award of degree of Doctor of Philosophy in chemistry is a record of bonafide research work carried out by her. Ms.Susan Joshi has worked under my guidance and supervision and has fulfilled the requirements for the submission of this thesis, which to my knowledge, has reached the requisite standard.

The results contained in this dissertation have not been submitted, in part or in full, to any other University or Institute for the award of any degree or diploma.

PROF. U. K. NADIR
Department of Chemistry
Indian Institute of Technology
New Delhi – 110 016
INDIA

ACKNOWLEDGEMENT

I wish to express my deep sense of gratitude and respect to **Prof. Upender Krishan Nadir** for his patience, understanding, and guidance throughout the course of this work.

I wish to express sincere thanks to Prof. G. N. Rao, Prof. N. K. Jha, Prof. A. S. Brar, and Prof. M. N. Gupta for providing necessary facilities

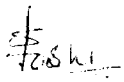
I would like to thank Prof. T. P. Singh, Dr. Punit Kaur, and Mr. Parveen Kumar (Bio Physics Department, AIIMS) for carrying out x-ray studies.

My sincere thanks are due to Ms. Anju Bhalotra, Dr. Jyotsna Sharma, Mr. I. Charles, Mr. Nabin K. Meher, Dr. Arif Ali Khan, Mr.Achintya Das , Mr. J. Patrik and other colleagues for their help and support.

I wish to express my deep sense of gratitude to my husband Mr. Damodar Bhakta Shrestha for his help, patience understanding and immense support without which this work would never have been possible. My humble regards are due to my parents, -in laws, and family members for their encouragement. Special thanks go to my son Krishodar Dev Bhakta Shrestha and sister Sunita Joshi.

I would also like to thank the technical staffs of Glass Blowing, Instrument, and NMR Laboratories for their kind cooperation.

Finally, I am thankful to Asian Development Bank for the financial support to carry out this research work.



(Susan Joshi)

ABSTRACT

This dissertation describes investigations which were undertaken as part of a programme to develop synthetic methods based on elaboration of three membered heterocycles. The present study concerns itself with improving and defining the scope and limitations of the reaction of N-arylsulphonylaziridines with isocyanates and isothiocyanates in the presence of iodide ion as a route to 2-imidazolidinones and 2-iminothiazolidines respectively. Feasibility of such reactions had been established by us before. It has now been found that reaction of N-arylsulphonylaziridines with isocyanates proceeds better and improved yields of the product are obtained when lithium iodide rather than sodium iodide is used as the source of iodide ions. The investigations also revealed that the solvent has relatively little effect on the product yield. The scope of the method has been extended by successfully carrying out the reaction also with benzyl isocyanate, p-toluenesulphonyl isocyanate and benzoyl isocyanate. However, with trimethylsilyl isocyanate no imidazolidinone was obtained.

An attempt to use reaction of aziridines with a chiral isocyanate for synthesis of enantiopure diamines was unsuccessful.

N-Arylsulphonylaziridines reacted smoothly with R(+)phenylethyl isocyanate to give a mixture of diastereomeric imidazolidinones. However, their separation (and therefore subsequent transformation to enantiopure diamines) could not be effected.

Reaction of N-arylsulphonylaziridines with isothiocyanates was also investigated. With lithium iodide as a catalyst iminothiazolidines were the product. Besides the spectral and analytical data, the structure was also confirmed by x-ray crystallographic data. Some improvement in product yields was achieved by using DMF and DMSO instead of acetone and THF. The reaction worked as well with benzoyl isothiocyanate as with alkyl and aryl isothiocyanates.

Elaboration of N-arylsulphonylaziridines with sodium thiocyanate was also studied. In the presence of a phase transfer catalyst iminothiazolidines were obtained in good yields. Among the phase transfer catalysts tried, tetrabutylammonium hydrogen sulphate gave the best yields. It was also shown that this method works well for the preparation of variously substituted alkyl and aryl 2-iminothiazolidines. However, in the reaction of 2,3- diaryl-N-arylsulphonylaziridines only the trans isomers were transformed into the

corresponding cis–thiazolidine; the cis isomer did not react and could be recovered back unchanged. These results have been rationalized. Although the thiazolidines were assigned structure on the basis of spectral and analytical data, structure of **77a** was also confirmed by x-ray crystallography.

CONTENTS