

STUDIES ON SYNTHESIS OF MOLECULAR RECEPTORS BASED ON CHOLIC ACID

BY

**RHIDDI BIR SINGH
DEPARTMENT OF CHEMISTRY**

**THESIS SUBMITTED
IN FULFILMENT OF THE REQUIREMENTS OF
DEGREE OF
DOCTOR OF PHILOSOPHY**

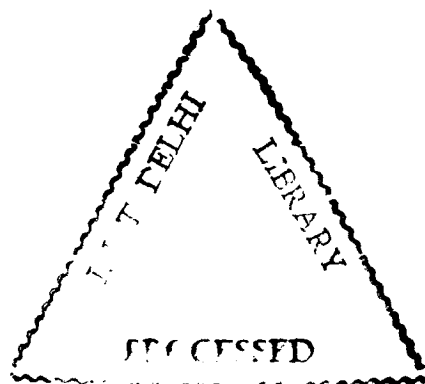
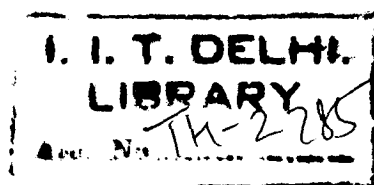
To the



**INDIAN INSTITUTE OF TECHNOLOGY, DELHI
HAUZ KHAS, NEW DELHI-110016**

JULY, 1997

TH
577.354
SIN-S



CERTIFICATE

This is to certify that the thesis entitled "**STUDIES ON SYNTHESIS OF MOLECULAR RECEPTORS BASED ON CHOLIC ACID**", being submitted by **Rhiddi Bir Singh**, to the Indian Institute of Technology, Delhi for the award of the degree of Doctor of Philosophy in Chemistry is a record of bonafide research work carried out by him. Mr. Rhiddi Bir Singh 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.



(P.S. PANDEY)

Assistant Professor

Thesis Supervisor

Department of Chemistry

Indian Institute of Technology

New Delhi-110 016

INDIA.

ACKNOWLEDGEMENT

I wish to express my deep sense of gratitude to Dr.P.S.Pandey, Assistant Professor, Department of Chemistry, Indian Institute of Technology, Delhi for his proper guidance, invaluable suggestions and encouragement throughout the research work.

I would like to thank Prof.A.S.N.Murthy, Prof. G.N.Rao, Prof.N.K.Jha and Prof.A.S.Brar for providing necessary facilities to carry out the research work.

I am grateful to my colleagues Mrs.Susan Joshi and lab.mate Mrs.H.Zeba for their support.

It gives me pleasure to acknowledge the Memorandum of Understanding between the Research Centre for Applied Science and Technology, Tribhuvan University, Kathmandu, Nepal and Indian Institute of Technology, Delhi for providing me the opportunity to pursue this academic program. In this regard I would like to highlight the kind courtesy offered by Prof.M.Sharma, the Executive Director, RECAST, and Prof.D.D.Shakya officiating Executive Director, RECAST, T.U., Kathmandu.

I am deeply indebted to my parents Dr.Shankar Bir Singh and Mrs.Tirtha Devi Singh and my brothers and relatives for their support provided to me.

At the end I would like to heartfully thank my wife Mrs.Belai Meeta Singh and daughters Ms.Rhiju Singh and Rubena Singh for their support, patience, love and affection.

The help provided by all the technical and other staff of IIT Delhi is duly appreciated.



Rhiddi Bir Singh

ABSTRACT

This dissertation deals with the studies on synthesis of molecular receptors based on cholic acid. The first part of the work involves the development of a general synthetic strategy for the construction of a new type of steroidal macrocycles, head to head cholaphanes. We have found that for the macrocyclization, the Cs-salt method developed by Kellogg works remarkably well and gives very high yields of cholaphanes. A number of cholaphanes derived from cholic, deoxycholic and lithocholic acids with ethylene diamine and m-xylene diamine as spacers have been synthesized.

In the second part of the work, the above macrocyclization methodology has been extended to the synthesis of steroid based NADH-analogues. Various pyridinocholaphanes involving cholic, deoxycholic and lithocholic acids have been synthesized. These pyridinocholaphanes can easily be converted into dihydropyridine systems following the standard procedure of methylation and then reduction by sodium dithionite. We expect that these steroid based dihydropyridine systems may act as enzyme models for dehydrogenases. In addition, pyridinocholaphanes based on monosteroid, methyl cholate, have also been made. Interestingly, it has been found that the Cs-salt macrocyclization results in a highly regioselective formation of the cholaphanes involving 3α and 12α -positions of methyl cholate.

CONTENTS

	Page Nos.
Certificate	i
Acknowledgements	ii
Abstract	iii
CHPATER-I : INTRODUCTION	1
CHAPTER-II : STEROID BASED RECEPTORS	32
CHAPTER-III: STEROID BASED NADH ANALOGUES	62
CHAPTER-IV: EXPERIMENTAL	87
CONCLUSION	113
REFERENCES	114