Mrs P. Nanda

SYNTHESIS, TAUTOMERISM AND EVALUATION OF CHROMOGENIC CALIX[N]ARENES FOR IONIC AND MOLECULAR RECOGNITION

by

MEENAKSHI NANDA

Department of Chemistry

Submitted
in fulfilment of the requirement of the degree of

Doctor of Philosophy

to the

Indian Institute of Technology, Delhi

August , 2001

CERTIFICATE

This is to certify that the thesis entitled *"Synthesis, Tautomerism and Evaluation of Chromogenic Calix[n]arenes for Ionic and Molecular Recognition"* being submitted by **Ms. Meenakshi Nanda** to the Department of Chemistry, Indian Institute of Technology, Delhi, for the award of the degree of **Doctor of Philosophy** is a record of bonafide research work carried out by her.

Meenakshi Nanda 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 thesis have not been submitted in part or in full to any other University or Institute for the award of any degree or diploma.

(H.M. Chawla)
Thesis Supervisor

Professor,
Department of Chemistry
Indian Institute of Technology,
New Delhi – 110016, India.

ACKNOWLEDGEMENTS

It gives me an immense pleasure and great opportunity to express my profound sense of gratitude and indebtedness to Professor H.M. Chawla, for his painstaking guidance, invaluable suggestions and constant encouragement throughout the execution of research work embodied in this thesis.

I wish to express my sincere thanks to the Head of the Department, Department of Chemistry, Indian Institute of Technology, New Delhi for providing facilities available in the Department.

I also express my sense of thankfulness to Dr. N. Pant and Dr. R. Varadarajan for fruitful discussions and encouragement.

I am extremely thankful to my research colleagues Anuradha, Vandna, Lukesh and Satish for their help and cooperation. I am also thankful to my friends and seniors, Dr. Ipsita, Dr. Shailja, Dr. P. Wadhwani, Dr. Abhishek Upadhyay, Dr. N. Venkatesan, Dr.(Mrs.) Meena and Dr. K. Srinivas for freely sharing their experiences in research.

I am extremely thankful to my dear friend Himanshu who has not only been a sincere advisor but has kept my spirits high during ups and downs of circumstances during the tenure of my research.

My humble regards to my parents and my brother who have had the rough end of bargain but never complained. Their constant encouragement and help in every possible way has made it possible to pursue and complete my research work.

I wish to record my appreciation and warm feelings of gratitude to my loving husband and father-in-law to enable me to conclude my research work embodied in this thesis.

I thankfully acknowledge the award of a research fellowship from Council of Scientific and Industrial Research, New Delhi during the tenure of my research work. Last but not the least I express my sense of gratitude to the supporting staff of the Department for timely help and to Mrs. Seema Arora and Ms. Biji for typing and word-processing of this manuscript.

Meenakshi Nanda

MEENAKSHI NANDA

ABSTRACT

The thesis titled ***Synthesis, Tautomerism and Evaluation of Chromogenic Calix[n]arenes for Ionic and Molecular Recognition*** concerns with some aspects of chemistry of recently rediscovered calix[n]arenes. These molecules possess a cavity in their molecular architecture due to the presence of distinct hydrophobic and hydrophilic sites to constitute what are popularly known as their upper and the lower rims respectively. Calixarenes are amenable to chemical modifications to provide a variety of molecular receptors with tunable selectivity and specificity. The research work embodied in the thesis has been divided into five chapters.

Chapter I gives an overview of research work reported in the literature on chemistry of calix[n]arenes during the last ten years with special emphasis on their applications in diverse fields. **Chapter II** describes the experiments conducted to synthesize and characterize novel chromogenic calix[n]arenes while **Chapter III** describes a study on their tautomerism. The synthesis of azo calix[n]arenes has been achieved by the azo coupling of hydroxy calix[n]arenes with diazotized aromatic amines, amino acids and esters. The synthesized compounds have been characterized and their conformations established by spectroscopic (IR, NMR, UV, FAB mass) analysis and chemical derivatization as well as by visualization and analysis through CPK models.

It has been observed that while some azo calixarenes exist in their azo form, others exist as their quinone-hydrazone tautomeric analogues. The calix-quinone hydrazone form seems to be stabilized by non covalent interactions and hydrogen bonds. Tautomerization of one form of azo calix[n]arenes to the other has been determined to be dependant upon pH, solvent, substitution pattern, conformation and size of calix[n]arenes under study. Details of

experiments conducted to determine tautomerization constants have been provided in **Chapter III** along with plausible explanation for the observations on synthesized new azo calix[n]arenes.

Chapter IV of the thesis explores the evaluation of synthesized calix[n]arenes as plausible ionophores through UV-visible spectral investigations. Mole ratio plots and application of Hildebrand Benesi equation have been used for determining the stoichiometry of the complexes formed. It has been determined that 5-(2′ - carboxyphenylazo)-25,26,27,28-tetrahydroxycalix[4]arene in its cone conformation interacts strongly with copper (II) and 1, 3-alternate conformation of azo pyridylcalix[4]arene is highly selective towards caesium ion.

Since calix[4]arenes possess a cavity in their molecular architecture encompassed by hydrophobic and hydrophilic upper and lower rims, they can recongnize ionic and molecular species either through the complementarityof size and shape of the cavity or through can self organization to provide voids to accommodate suitable guest molecules. In order to obtain suitably functionalized calix[n]arenes for self organization, several calix[n]arenes containing long hydrocarbon chains at the lower and the upper rim were envisaged as they can entwine to produce aggregates of varying shapes and sizes. Efforts were made to arrive at long hydrocarbon chain containing calix[n]arenes through Friedel-Crafts alkylation and acylation. Results of our preliminary investigations reported in **Chapter V** reveal that Friedel-Crafts acylation of calix[n]arenes is successful only when the reaction is carried out in the presence of nitrobenzene as the solvent. While acylation of calix[n]arenes at the lower rim has been observed to be generally useful with short chain alkyl halides complications are encountered while using long chain alkyl halides. Plausible explanation for the observations has been provided in the thesis.

TABLE OF CONTENTS

LIST OF FIGURES AND SCHEMES

NOTES

1. All melting points reported in this thesis are uncorrected and were taken on an electric melting point apparatus (Toshniwal, India).
2. UV spectra were taken on Hitachi 330 and Perkin Elmer's (Lambda-3B) spectrophotometers.
3. IR spectra were recorded in KBr discs on a [5-DX] Nicolet FT-IR and Nicolet protégé 460 ESP spectrophotometers.
4. ^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on Jeol [JNM-FX-100] (IIT Delhi) and Bruker Spectrospin-300MHz FT-NMR spectrometers using TMS as internal standard and values reported are on δ scale. The abbreviation such as s, bs, d, t, q and m indicate singlet, broad singlet, doublet, triplet, quartet and multiplet respectively.
5. FAB-mass spectra of some of the synthesized compounds were recorded on a JEOL SX 103/DA-6000 Mass Spectrometer available at Central Drug Research Institute, Lucknow. *m*-Nitrobenzyl alcohol was used as the matrix.
6. Elemental Analysis was carried on Perkin Elmer's 240C-CHN Analyzer.
7. The completion of the reaction and the purity of the synthesized compounds were checked by TLC performed on silica gel coated glass plates using iodine for visualizing the spots.
8. Purification of several of the synthesized compounds was carried out by column chromatography over silica gel (60-120 mesh) obtained from Qualigens Fine Chemicals Limited, Mumbai.

The solvents used were purified and dried before use by procedures described in "Purification of Laboratory Chemicals" by W.L.F. Armarego and D.D. Perrin. Bath Press and Bath, Britain.

For the sake of convenience, the names of calixarenes used in this thesis have been shortened. For example, 5, 11, 17, 23-tetra-*tert*-butylcalix[4]arene or even parent calix[4]arene while 5, 11, 17, 23, 29, 35-hexa-*tert*-butyl-49, 50, 51, 52, 53, 54-hexahydroxycalix[6]arene and 5, 11, 17, 23, 29, 35, 41, 47-octa-*tert*-butyl-49, 50, 51, 52, 53, 54, 55, 56-octahydroxycalix[8]arene are referred as *p-tert*-butylcalix[6]arene and *p-tert*-butylcalix[8]arene respectively. Similarly names of 25, 26, 27, 28-tetrahydroxycalix[4]arene, 37, 38, 39, 40, 41, 42-hexahydroxycalix[6]arene and 49,50,51,52,53,5,55,56-octahydroxycalix[8]arene have been shortened to tetrahydroxycalix[4]arene, hexahydroxycalix[6]arene and octahydroxycalix[8]arene respectively and even further shortened to calix[4]arene, calix[6]arene and calix[8]arene respectively.

Abbreviations used in this thesis are:

DMSO for Dimethylsulphoxide;

THF for Tetrahydrofuran;

DMF for N, N-Dimethylformamide

DMSO-d_6 for Hexadeuterated Dimethylsulphoxide;

$CDCl_3$ for Deuterated chloroform;

D_2O for Deuterated water;