DESIGN, SYNTHESIS AND EVALUATION OF SOME METALLO-SUPRAMOLECULAR RECEPTORS FOR IONIC AND MOLECULAR RECOGNITION

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by

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Submitted

in fulfilment of the requirements of the degree of Doctor of Philosophy

to the

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DEDICATED
TO
My Mother and Father

CERTIFICATE

This is to certify that the thesis titled **"Design, synthesis and evaluation of some metallo supramolecular receptors for ionic and molecular recognition"** being submitted by **Mr. Lakhbeer Singh Arora** to the Indian Institute of Technology Delhi, for the award of degree of **Doctor of Philosophy** is a record of bonafide research work carried out by him. **Mr. Lakhbeer Singh Arora** 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 are original and have not been submitted, in part or full, to any other University or Institute for the award of any other degree or diploma.

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ABSTRACT

The thesis entitled, "**Design, synthesis and evaluation of some metallo supramolecular receptors for ionic and molecular recognition**" presents the research work carried out for metallo-supramolecular complexes includes synthesis, characterization and applications of some novel calix[4]arene derivatives. This has been achieved by modification, optimization and novelty of procedures available in the literature. Synthesized new chemical entities have been characterized by employing various spectroscopic techniques, *i.e.* ^{1}H NMR, ^{13}C NMR, FT-IR and high resolution mass spectral analysis *etc.* Their ionic and molecular recognition potential has been examined by using UV-Visible, NMR, fluorescence and colorimetric methods of analysis. The accomplished research work has been divided into six chapters.

Chapter I of the thesis highlights some of the general aspects of supramolecular chemistry and metallo-supramolecular chemistry. A review on metallo-supramolecular chemistry including calix[4]arene receptors published in the scientific literature during the last ten years has been presented for sensing cations, anions, amino acids, nucleic acids, peptides *etc.*

Chapter II of the thesis primarily focuses on the synthesis and characterization of some new macrocyclic calix[4]arenes derivatives by incorporation of Schiff base unit as a binding site and benzothiazolyl groups as signaling unit both at the upper and lower rims of the calix[4]arene molecular architecture.

Chapter III describes the research work carried out to synthesize the triazolyl calix[4]arene based molecular receptors and their characterization by various spectroscopic methods including ^{1}H NMR, ^{13}C NMR, IR spectroscopy and mass spectrometry.

Chapter IV describes the experiments done to investigate the ionic and molecular recognition properties of molecular receptors synthesized in chapter III by using UV-visible, fluorescence spectroscopic and colorimetric methods. The synthesized receptor exhibits selective recognition and high binding affinity for copper and ferric ions.

Chapter V describes the experiments done to evaluate the *in situ* generated metallo-supramolecular complexes for the recognition of anions and amino acids by utilizing UV-visible, fluorescence, spectroscopic and colorimetric methods. It has been found that one

of the Cu-complex shows high recognition potential for glycine among various other amino acids.

Chapter VI describes the experiments carried out to synthesize lower rim-ether derivatives of calix[4]arenes. Literature protocols have been modified to generate alkyl iodide in *in situ* by using potassium iodide which facilitates the reaction to accomplish in less time and gave higher product yield.

सार

थीसिस, "आयनिक और आण्विक मान्यता के लिए कुछ धातु के सुपरमोल्यूलर रिसेप्टर्स के डिजाइन, संश्लेषण और मूल्यांकन" प्रस्तुत करता है " धातु-सुपरमोल्यूलर परिसरों के लिए किए गए शोध कार्य में कुछ उपन्यास कैलिक्स[4]अरेन (calix[4]arene) डेरिवेटिव्स के संश्लेषण, विशेषता और अनुप्रयोग शामिल हैं। यह साहित्य में उपलब्ध प्रक्रियाओं के संशोधन, अनुकूलन और नवीनता द्वारा हासिल किया गया है। संश्लेषित नई रासायनिक इकाइयों को विभिन्न स्पेक्ट्रोस्कोपिक (spectroscopic) तकनीकों यानी 1 एच एनएमआर, 13 सी एनएमआर, एफटी-आईआर और उच्च रिज़ॉल्यूशन द्रव्यमान वर्णक्रमीय विश्लेषण इत्यादि द्वारा नियोजित किया गया है। विश्लेषण के तरीके यूवी-विज़िबल, एनएमआर, फ्लोरोसेंस और कलरिमेट्रिक का उपयोग करके उनकी आयनिक और आणविक पहचान क्षमता की जांच की गई है। पूरा शोध कार्य छह अध्यायों में बांटा गया है।

थीसिस के अध्याय-I में सुपरमोल्यूलर रसायन शास्त्र और धातु-सुपरमोल्यूलर रसायन शास्त्र के कुछ सामान्य पहलुओं पर प्रकाश डाला गया है। पिछले दस वर्षों के दौरान वैज्ञानिक साहित्य में प्रकाशित कैलिक्स[4]अरेन (calix[4]arene) रिसेप्टर्स समेत धातु-सुपरमोल्यूलर रसायन शास्त्र पर एक रिव्यू संवेदनाशन, आयनों, एमिनो एसिड, न्यूक्लिक एसिड, पेप्टाइड्स इत्यादि के लिए प्रस्तुत किया गया है।

थीसिस का अध्याय-II मुख्य रूप से कैलिक्स के ऊपरी और निचले रिम्स पर दोनों सिग्नलिंग इकाई के रूप में बाध्यकारी साइट और बेंजोथियाज़ोलिल समूहों के रूप में शिफ बेस यूनिट को शामिल करके कुछ नए मैक्रोसाइक्लिक कैलिक्स[4]अरेन (calix[4]arene) डेरिवेटिव्स के संश्लेषण और विशेषता पर केंद्रित है।

अध्याय-III में त्रैजोलिल कैलिक्स[4]अरेन (calix[4]arene) आधारित आणविक रिसेप्टर्स को सिन्सेंटिज़ करने के लिए किए गए शोध कार्य का वर्णन किया गया है और विभिन्न स्पेक्ट्रोस्कोपिक तरीकों से उनकी विशेषता 1 एच एनएमआर, 13 सी एनएमआर, आईआर स्पेक्ट्रोस्कोपी और मास स्पेक्ट्रोमेट्री शामिल है।

अध्याय-IV यूवी-दृश्य, फ्लोरोसेंस स्पेक्ट्रोस्कोपिक और कलरिमेट्रिक तरीकों का उपयोग करके अध्याय III में संश्लेषित आणविक रिसेप्टर्स के आयनिक और आणविक मान्यता गुणों की जांच के लिए किए गए प्रयोगों का वर्णन करता है। संश्लेषित रिसेप्टर तांबे और फेरिक आयनों के लिए चुनिंदा मान्यता और उच्च बाध्यकारी संबंध प्रदर्शित करता है।

अध्याय-V यूवी-दृश्य, फ्लोरोसेंस, स्पेक्ट्रोस्कोपिक और कलरिमेट्रिक तरीकों का उपयोग करके आयनों और एमिनो एसिड की पहचान के लिए इन्सुयू जेनरेट मेटालो-सुपरमोल्यूलर कॉम्प्लेक्स का मूल्यांकन करने के लिए किए गए प्रयोगों का वर्णन करता है। यह पाया गया है कि क्यू-कॉम्प्लेक्स में से एक विभिन्न अन्य एमिनो एसिड के बीच ग्लाइसीन के लिए उच्च मान्यता क्षमता दिखाता है।

अध्याय-VI कैलिक्स[4]अरेन (calix[4]arene) के निचले रिम-ईथर डेरिवेटिव को संश्लेषित करने के लिए किए गए प्रयोगों का वर्णन करता है। पोटेशियम आयोडाइड का उपयोग करके इन्सुटी में एल्काइल आयोडाइड उत्पन्न करने के लिए साहित्य प्रोटोकॉल को संशोधित किया गया है। यह कम समय में प्रतिक्रिया को पूरा करने में मदद करता है और उच्च उत्पाद उपज देता है।

CONTENTS

List of Figures

List of Tables

List of Schemes

List of Abbreviations

Abbreviation	Full form
NMR	Nuclear magnetic resonance
EDTA	Ethelene diamine tetra acetate ion
GC-MS	Gas chromatography-Mass spectrometry
XRD	X-ray Diffraction
CuAAC	Copper-catalyzed Alkyne Azide Cycloaddition
TBAF	Tetrabutylammonium fluoride
ICT	Internal charge transfer
ORTEP	Oak Ridge Thermal Ellipsoid Plot
UV	Ultraviolet
Vis.	Visible
PP_i	Pyrophosphate($P_2O_7^{4-}$)
DMSO	Dimethyl Sulfoxide
DMSO-d_6	Deuterated Dimethyl sulfoxide
TBA	Thiobarbituric acid
IR	Infrared
HRMS-ESI	High resolution mass spectrometry-Electron spray ionization
THF	Tetrahydrofuran
µM	Micro molar
MeCN-d_3	Deuterated acetonitrile
Asu	2-amino octanoic acid
Abu	3-aminobutyric acid
GABA	4-aminobutyric acid
L-Pro	L-proline

Aib	2-methylalanine
L-Met	L-methionine
D,L-Val	D,L- valine
L-Ile	L-isoleucine
L-Leu	L-leucine
L-Cys	L-cystine
D,L-Ser	D,L-serine
D,L-Ala	D,L-alanine
Asp	Aspartic acid
Gly	Glycine
L-Glu	L-glutamic acid
DMF	Dimethylformamide
DCM	Dichloromethane
Cu^{+2}	Cupric ion
Ag^{+}	Argentum ion
F^{-}	Fluoride ion
CH_2Cl_2	Dichloromethane
CH_3CN	Acetonitrile
Zn^{2+}	Zinc ion
Ni^{2+}	Nickel ion
Cd^{2+}	Cadmium ion
Cu^{+}	Cuprous ion
S^{2-}	Sulfide ion
HPO_4^{2-}	Monohydrogen phosphate ion
H_2O	Water
CH_3COO^{-}	Acetate ion

$PhCOO^-$	Benzoate ion
$H_2PO_4^-$	Dihydrogen phosphate ion
Ca^{2+}	Calcium ion
MeOH	Methanol
Co^{2+}	Cobalt ion
Na^+	Sodium ion
NH_4^+	Ammonium ion
K^+	Potassium ion
Mg^{2+}	Magnesium ion
Mn^{2+}	Manganese ion
Pb^{2+}	Lead ion
Hg^{2+}	Mercuric ion
Fe^{2+}	Ferrous ion
Fe^{3+}	Ferric ion
Cl^-	Chloride ion
Br^-	Bromide ion
HSO_4^-	Hydrogen sulphate ion
CN^-	Cyanide ion
Bi^{2+}	Bismuth ion
KBr	Potassium bromide
KCl	Potassium chloride
KI	Potassium iodide
I^-	Iodide ion
Au^{3+}	Auric ion
$H_2AsO_4^-$	Dihydrogen Arsenate ion
$HCr_2O_7^-$	Hydrogen Chromate ion

Ca	Calcium
Hg	Mercury
NaOH	Sodium hydroxide