SELF-ASSEMBLY AND ANION RECOGNITION PROPERTIES OF DESIGNER PSEUDOPEPTIDIC MOLECULES

BIJESH M B

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY DELHI

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by

BIJESH M B

Department of Chemistry

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to the

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Dedicated to my beloved parents and Teachers

CERTIFICATE

This is to certify that the thesis entitled, "***Self-assembly and anion recognition properties of designer pseudopeptidic molecules***", being submitted by Mr. Bijesh M. B., 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. Bijesh M.B. has worked under my guidance and supervision and has fulfilled all the requirements for the submission of this thesis, which to my knowledge has reached the requisite standard. The results embodied in this thesis have not been submitted in part or in full, to any other University or Institute for award of any degree or diploma.

Dr. V. Haridas
Supervisor
Associate Professor
Department of Chemistry
Indian Institute of Technology Delhi
Hauz Khas, New Delhi-110016, India.

IIT Delhi

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ABSTRACT

The thesis entitled, "**Self-assembly and anion recognition properties of designer pseudopeptidic molecules**" outlines the design, synthesis and characterization of novel pseudopeptidic macrocycles and acyclic molecules and their potential applications for the construction of structural and stimuli responsive materials. The thesis has been divided into five chapters.

Chapter I

Chapter I is a retrospective view of the advancements in the chemistry of pseudopeptides in the context of supramolecular chemistry. The milestones and major challenges in the design and synthesis of the pseudopeptidic molecules have been reviewed. The focus has been majorly on the applications of pseudopeptidic molecules as self-assembled materials and molecular recognition motifs. A special attention was devoted to explaining their self-assembling and molecular recognition properties emphasizing molecular structure.

Chapter II

Chapter II describes the design, synthesis and self-assembling properties of a series of pseudopeptidic cyclophanes, in a view to unravel the forces leading to the formation of spherical vesicles and fibres.

Chapter III

Chapter III comprises of the new design of acyclic pseudopeptides, with a minimalist approach, to craft chiral materials. The molecular engineering is demonstrated to alter the dimensions and to control the self-assembled architectures. The effect of molecular parameters and environmental factors, which are responsible for the formation of chiral assembly, has been studied.

Chapter IV

Chapter IV attempts to justify the subtle role of molecular structure in promoting the anion recognition and self-assembling properties of the norbornene based cyclic and acyclic peptides. Besides anion recognition, self-assembling properties of the norbornene based peptides were studied.

Chapter V

Chapter V shows a facile route for the synthesis of peptide based polymers by ring opening metathesis polymerization (ROMP) of norbornene monomers. The design, synthesis and self-assembling properties of ROMP polymers were studied.

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LIST OF ABBREVIATIONS

%	Percent
δ	Chemical shift
^{o}C	Degree centigrade
AFM	Atomic force microscopy
aq.	Aqueous
Ar	Aryl
ArH	Aromatic proton
Ac	Acyl
Boc	t-butyloxycarbonyl
br	Broad
CD	Circular dichroism
Conc.	Concentrated
CuCl	Copper (I) chloride
CuAAC	Copper catalyzed azide alkyne cycloaddition
d	Doublet
Da	Dalton
DCM	Dichloromethane
dd	Double doublet
DCC	N,N'-dicyclohexylcarbodiimide
DFT	Density functional theory
DIPEA	N,N'-Diisopropylethylamine
DMF	N,N-dimethylformamide

DMSO	Dimethylsulfoxide
DOSY	Diffusion-ordered spectroscopy
ESI	Electronspray ionization
FIB	Focused ion beam
Fmoc	Fluorenylmethyloxycarbonyl
g	Gram
G2	Grubbs second generation catalyst
GPC	Gel permeation chromatography
h	Hour
Hz	Hertz
HRMS	High resolution mass spectrum
HRTEM	High resolution transmission electron microscope
IR	Infrared
J	Coupling constant
m	Multiplet
MD	Molecular dynamics
MeOH	Methanol
μM	Micro molar
μm	Micro meter
mg	Milli gram
mL	Milli liter
min	Minutes
mmol	Milli moles

mol	Mole
Mp	Melting point
m/z	Mass/charge
NMR	Nuclear magnetic resonance
PD	Poly dispersity
ppm	Parts per million
PXRD	Powder x-ray diffraction
q	Quartet
RT	Room temperature
s	Singlet
t	triplet
TBABr	Tetrabutylammonium bromide
TBACl	Tetrabutylammonium chloride
TBAF	Tetrabutylammonium fluoride
$TBAH_2PO_4$	Tetrabutylammonium dihydrogen phosphate
TBAI	Tetrabutylammonium iodide
TFA	Trifluoroacetic acid
TLC	Thin layer chromatography
TMEDA	tetramethylethylenediamine
TMV	Tobacco mosaic virus
UV	Ultra violet

NOTES

1. All amino acids used in the reactions were of L-configuration. Standard single/triple letter codes are used to represent the amino acids.

2. All solvents employed in the reaction were distilled or dried from appropriate drying agent prior to use. Unless otherwise stated, all reagents were used without further purification.

3. Melting points were recorded in a Fisher-Johns melting point apparatus.

4. IR spectra were recorded on a Nicolet, Protégé 460 spectrometer as KBr pellets.

5. ^{1}H NMR spectra were recorded on Bruker-DPX-300 (^{1}H, 300 MHz; ^{13}C, 75 MHz) spectrometer using tetramethylsilane (1H) as an internal standard. Coupling constants are in Hz and the ^{1}H NMR data are reported as s (singlet), d (doublet), br (broad), br d (broad doublet), t (triplet), q (quartet), m (multiplet).

6. Reactions were monitored wherever possible by thin layer chromatography (TLC). Silica gel G (Merck) was used for TLC and column chromatography was done on silica gel (100-200 mesh) columns, which were generally made from slurry in hexane, hexane/ethyl acetate or chloroform.

7. CD measurements were made using AVIV-420/ Jasco spectropolarimeter. Quartz cell of 0.1 cm was used for the measurements.

8. UV-Vis spectroscopy - The absorption spectra were recorded on a Shimadzu UV-2450 spectrometer.

9. SEM images were recorded using ZEISS EVO Series Scanning Electron Microscope EVO 50 operating at an accelerating voltage of 0.2 − 30 kV. For SEM, a 10 μL aliquot of the sample solution was drop-casted on a glass cover slip, dried and coated with ~10 nm of gold.

10. FIB-SEM A 10µl aliquot of the sample solution was put on a fresh piece of glass, which is attached to a stub via carbon tape. The sample was dried at room temperature and coated with ~10nm of gold. Samples were analyzed using FEI Quanta 3D FEG High resolution scanning electron microscope (FESEM) combined with High-current ion column with Ga liquid-metal ion source.

11. HRTEM images were recorded on a TECHNAI G2 (20S-TWIN) electron microscope operated at an accelerating voltage of 200 kV. Samples were prepared by drop-casting the sample on 200 square mesh carbon-coated copper grids.

12. AFM images were recorded using Bruker Dimension Icon atomic force microscope. Tapping mode is used for the analysis. About 10µl aliquot of the sample solution was transferred onto freshly cleaved mica and allowed to dry and imaged using AFM.

13. X-ray diffraction study was carried out on a BRUKER AXS SMART-APEX diffractometer with a CCD area detector (Mo Kα = 0.71073Å, monochromator: graphite). Frames were collected at T = 298 by ω, ϕ and 2θ-rotation at 10 s per frame with SMART. The measured intensities were reduced to F2 and corrected for absorption with SADABS. Structure solution, refinement, and data output were carried out with the SHELXTL program. Non-hydrogen atoms were refined anisotropically. C-H hydrogen atoms were placed in geometrically calculated positions by using a riding model. Image was created with the Diamond program.

14. GPC- Molecular weight distribution was analyzed by Agilent 1260 Multi Detector System, with triple detector equipped with a chloroform column (PL gel mixed B, 75 mmx 300 mm, 1 mL /min flow) using refractive index detector.

15. Optical microscopy: Samples for optical microscope were prepared by dissolving compound in methanol. A 5 μL aliquot of the sample solution was placed on a glass slide and allowed to dry in air at room temperature. The glass slide was then covered using a cover slip and analysed using a Nikon T*i* Eclipse inverted optical microscope.

16. Powder X-ray diffractogram was recorded using Rigaku Ultima IV type II automatic high resolution modulator type X-ray diffractometer system with scintillation detector or on a Bruker D8 Advance diffractometer using radiation αNi-filtered CuK.