RECOGNITION BEHAVIOR AND ELECTROCHEMICAL PROPERTIES OF GATED MOLECULAR BASKETS

Thesis

Presented in Partial Fulfillment of the Requirements for the Degree Master of Science
in the Graduate School of The Ohio State University

By
Meng Wu, M.S.
Graduate Program in Chemistry

The Ohio State University
2010

Thesis Committee:
Jovica D. Badjić, Advisor
James P. Stambuli
Christopher M. Hadad
ABSTRACT

The design of dynamic molecular hosts has been of considerable interest in recent years. Molecular hosts such as capsules and metal-mediated assemblies have been synthesized to selectively encapsulate guests. They are now widely used to mimic enzymes, catalyze chemical reactions, stabilize unstable intermediates. Efforts in our group have been focused on design, synthesis and study of a family of novel molecular hosts called “molecular baskets”. Using metal-mediated coordination or hydrogen bonding to fold the baskets, a range of guests varying in size, shape and electronic characteristics can be enclosed inside the cavity. Via the dynamic gating, the molecular baskets are examined for regulating the in/out exchange of guests.

This thesis prescribes electrochemical behavior and regulation of molecular encapsulation upon reduction/oxidation of baskets. The phthalimide groups in baskets are capable of accepting electrons and becoming reduced. We chose to examine phenyl-based basket as a host and 1,1,1-tribromoethane as a guest. Accordingly, we found that basket responds to reduction by passing electrons to the enclosed guests, and then releasing the reduced guest. Furthermore, the basket can reduce more than one guest, thereby behaving as an electrochemical catalyst. The mechanism of guest encapsulation and release upon reduction/oxidation stimulus was proposed. Understanding how the molecular basket regulate encapsulation of guest upon redox stimulus provides an opportunity for investigating electro-catalytic use of capsules in promoting chemical reactions.
ACKNOWLEDGEMENTS

First of all, I would like to express my gratitude to my advisor, Dr. Jovica Badjić, for his guidance and help for my research and for his counsel regarding matters of scientific as well as non-scientific nature, which has made this research a real pleasure and helped me to envisage my future career.

Also I sincerely thank Dr. Amar Flood and Parimal Kumar in Indiana University Bloomington for their collaboration in electrochemical characterization and original thoughts.

I also want to thank Dr. Baoyu Wang for teaching me numerous lab techniques, sharing experience and collaboration. Other group members (past and present) Matt Gardlik, Steven Reith, Chris Baddley, Yuning Chang, Sandra Stajanović, Yi’an Ruan, Teodora Zujović, Muhhamet Setin and Lauren Sefton make the graduate school days easier. I am grateful for their friendship, help and support.

My parents, for always support anything I do.

My husband, who is also an excellent chemist, for giving me lots of advice and support.
VITA

May 16, 1983 ......................................................... Born – Zhengzhou, Henan, China

2001-2005 ................................................................. B. S. Chemistry, 
Wuhan Institute of Technology, China

2005-2007 ............................................................. M. S. Polymer Chemistry & Physics, 
Wuhan University, China

2007-2010 ............................................................ towards M. S. Chemistry, 
The Ohio State University, USA

FIELDS OF STUDY

Major Field: Chemistry
# TABLE OF CONTENTS

Abstract .......................................................................................................................... ii

Acknowledgements ......................................................................................................... iii

Vita .................................................................................................................................... iv

List of Figures .................................................................................................................. vii

List of Abbreviations ....................................................................................................... ix

Chapter One: Introduction

1.1 Basic Concepts in Supramolecular chemistry ......................................................... 1

1.1.1 Molecular Recognition and Supramolecular Interactions ................................. 1

1.1.2 Self-Assembly ........................................................................................................ 2

1.1.3 Host-Guest Chemistry .......................................................................................... 5

1.2 Electrochemistry of Supramolecular Systems .......................................................... 9

1.2.1 Basic Concepts in Electrochemistry ................................................................. 9

1.2.2 Supramolecular Electrochemistry ....................................................................... 11

1.3 Gated Molecular Baskets ....................................................................................... 13

1.4 Objectives ................................................................................................................. 15
Chapter Two: Recognition Behavior and Electrochemical Properties of Gated Molecular Baskets

2.1 Introduction and Hypothesis ................................................................. 24

2.2 Synthesis of the Baskets 2.1 ................................................................. 28

2.3 NMR Spectroscopic Studies of Basket 2.1* and Basket 2.1 ...................... 30

2.3.1 Basket Selection ............................................................................... 30

2.3.2 Guest Selection ............................................................................... 30

2.3.3 NMR Spectroscopic Measurements .................................................. 31

2.4 UV Spectroscopic Studies ..................................................................... 38

2.5 Electrochemical Properties Studies ....................................................... 40

2.5.1 Cyclic voltammetry of trifluoro-basket 2.1* and a model compound .... 40

2.5.2 Cyclic voltammetry of basket 2.1 and 1,1,1-tribromoethane ............... 42

2.5.3 CV titration of 1,1,1-tribromoethane into basket 2.1 ......................... 42

2.6 Conclusions .......................................................................................... 46

2.7 Experimental ......................................................................................... 47
LIST OF FIGURES

1.1: Selected molecular hosts.................................................................6

1.2: Naphthalene Diels-Alder in a self-assembled molecular flask......................7

1.3: Stabilization of reactive organometallic intermediates inside a self-assembled nanoscale host (a) [G⊂M₄L₆] supramolecular tetrahedral assembly; (b) G-BF₄ complexe; (c) [G⊂Ga₄L₆]¹¹⁻ .................................................................8

1.4: Selected supramolecular enzyme mimics................................................9

1.5: Cyclic voltammetry waveform................................................................10

1.6: Typical cyclic voltammogram...............................................................11

1.7: Cyclic voltammograms of C₆₀/γ-CD in water solution studied for different applied negative potential reversals...............................................................12

1.8: Selected dynamic molecular baskets synthesized by our group.................13

1.9: Side view of energy-minimized structure of a folded basket....................13

1.10: Previous synthesized molecular baskets...............................................14

1.11: Trifluoro-based (left) and phenyl-based (right) molecular basket folded via hydrogen bonding.................................................................15

1.12: Gated molecular baskets being reduced...............................................16

2.1: Selected dynamic molecular baskets synthesized by our group................24

2.2: Interconversion of two C₃ symmetric enantiomers.................................25

2.3: Trifluoro-based molecular basket folded via hydrogen bonding..............26

2.4: Gated molecular baskets being reduced...............................................27

2.5: Synthetic route for tris-anhydride.........................................................28

2.6: Synthetic route for acetylated(aminomethyl)pyridine.............................28
2.7: Synthetic route for target molecular basket……………………………………………………………………………………………………29

2.8: Variable temperature $^1$H NMR spectra (400 MHz) of basket 2.1 in CD$_2$Cl$_2$ (1.4 mM), containing 1.5 molar equivalents of CH$_3$CBr$_2$CH$_3$ (2.1mM, δ=2.47)…………………………………32

2.9: Variable temperature $^1$H NMR spectra (400 MHz) of basket 2.1 in CD$_2$Cl$_2$ (1.1 mM), containing 0.8 molar equivalents of CH$_3$CBr$_3$ (0.9mM, δ=3.35)…………………………………32

2.10: Van’t Hoff plot (Left: 2,2-dichloropropane; Right: 1,1,1-tribromoethane)………………33

2.11: $^1$H NMR spectra (400 MHz) of basket 2.1 in CD$_2$Cl$_2$. (1.4 mM, 298K), obtained after incremental additions of CH$_3$CBr$_2$CH$_3$………………………………………………………………………………………………………………34

2.12: $^1$H NMR spectra (400 MHz) of basket 2.1 in CD$_2$Cl$_2$, (1.1 mM, 298K), obtained after incremental additions of CH$_3$CBr$_3$………………………………………………………………………………………………………………34

2.13: Nonlinear fitting Curve (Left: 2,2-dichloropropane; Right: 1,1,1-tribromoethane)………………35

2.14: Selected $^1$H DOSY NMR (500 MHz, 298K) spectrum of CD$_2$Cl$_2$ solution of (a) phenyl-based basket; (b) model compound……………………………………………………………………………………………………………………37

2.15: UV-Vis calibration curve of basket 2.1 in CH$_2$Cl$_2$ with a concentration range from 1.9μM to 9.5μM (1cm pathlength cell)………………………………………………………………………………………………………………………………………………38

2.16: (a) UV-vis spectra of titrating of CH$_3$CBr$_3$ (from 0 to 5 equivalents) to a CH$_2$Cl$_2$ solution of basket 2.1 (50μM, 1mm pathlength cell); (b) plot of UV absorption versus number of equivalent of guest titrated……………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………
2.21: Cyclic voltammetry of the encapsulation, retention and release Process. (0.5mM of basket 2.1 in a CH₂Cl₂ solution, 0.1 M TBAPF₆, room temperature)  (a) Empty basket; (b) basket with 2.5 equivalents of guest; (c) after evaporating solvent for 1 day; (d) after evaporating solvent for 5 days. Scan rate = 0.2 V/s………………………………………………45

2.22: Illustration of encapsulation, retention and release process in Figure 2.21………45

2.23: Proposed mechanism of guest encapsulation and release upon reduction/oxidation stimulus of basket 2.1…………………………………………………………………………………46
LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ac</td>
<td>acetyl</td>
</tr>
<tr>
<td>br</td>
<td>broad (IR or NMR)</td>
</tr>
<tr>
<td>n-</td>
<td>normal-</td>
</tr>
<tr>
<td>t-</td>
<td>tert-</td>
</tr>
<tr>
<td>°C</td>
<td>degree Celsius</td>
</tr>
<tr>
<td>calcd</td>
<td>calculated</td>
</tr>
<tr>
<td>δ</td>
<td>chemical shift in parts per million downfield from tetramethylsilan</td>
</tr>
<tr>
<td>d</td>
<td>doublet (spectra); day(s)</td>
</tr>
<tr>
<td>DCM</td>
<td>dichloromethane</td>
</tr>
<tr>
<td>DDQ</td>
<td>2,3-dichloro-5,6-dicyano-(p)-benzoquinone</td>
</tr>
<tr>
<td>DMF</td>
<td>N,N-dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
</tr>
<tr>
<td>DMAD</td>
<td>dimethyl acetylenedicarboxylate</td>
</tr>
<tr>
<td>equiv.</td>
<td>equivalence</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
<tr>
<td>g</td>
<td>gram</td>
</tr>
<tr>
<td>h</td>
<td>hour (s)</td>
</tr>
<tr>
<td>HRMS</td>
<td>high resolution mass spectrometry</td>
</tr>
<tr>
<td>(J)</td>
<td>coupling constant in Hz (NMR)</td>
</tr>
<tr>
<td>LDA</td>
<td>lithium diisopropylamide</td>
</tr>
<tr>
<td>m</td>
<td>milli; mutilplet (NMR)</td>
</tr>
<tr>
<td>(\mu)</td>
<td>micro</td>
</tr>
<tr>
<td>M</td>
<td>mole per liter (concentration)</td>
</tr>
<tr>
<td>Me</td>
<td>methyl</td>
</tr>
<tr>
<td>MHz</td>
<td>megahertz</td>
</tr>
</tbody>
</table>

x
min  minute (s)
mol  mole (s)
mp   melting point
MS   mass spectrometry; molecular seives
m/z  mass to charge ratio (MS)
NMR  nuclear magnetic resonance
Ph   phenyl
ppm  parts per million
q    quartes (NMR)
r.t.  room temperature
s    singlet (NMR)
t    tertiary (tert)
t    triplet (NMR)
TEA  triethylamine
TFAA trifluoroacetic anhyride
THF  tetrahydrofuran
TLC  thin layer chromatography
V    volt
CHAPTER ONE
INTRODUCTION

1.1 Basic Concepts in Supramolecular chemistry

1.1.1 Molecular Recognition and Supramolecular Interactions

Molecular recognition is an essential feature of many biological systems. Examples include the highly specific substrate recognition by enzyme; molecular recognition system of DNA base pairs that can be used in nanotechnology to direct the assembly of well-defined structured materials; expression of genetic information based on specific interactions between nucleic acids and protein; antigen and antibody; biotin and avidin.

Molecular Recognition became a very popular phrase in the early 1980s and has drawn tremendous attention during the past four decades. The term “molecular recognition” refers to both inter- and intramolecular interactions through non-covalent bonding. Non-covalent bondings can be divided into several classes. Ion-ion interactions are the strongest among non-covalent bonds, followed by the interactions between ions and dipoles. Interactions between two dipoles are somewhat weaker. Hydrogen bonds have the energy range from 5 to 30 kJ/mol, weaker than ionic bonds but stronger than van der Waals forces, which arise from the interaction of an electron cloud polarized by nuclei and with the energy less than 5 kJ/mol. Hydrophobic effect is another universally acknowledged class. Traditionally, enthalpy was relied upon as the
way to engender a favorable free energy of assembly. Components gather together is not favored by entropy. However, hydrophobic effect is a strategy for the free energy of assembly to be primarily driven by entropy when the assembly releases solvent molecules. Non-covalent forces also include cation-\(\pi\) interaction and \(\pi-\pi\) interaction involving electron-rich and electron-poor components. Compared to other interactions, cation-\(\pi\) interaction had been relatively underappreciated until evidence suggested that protein might use cation--\(\pi\) interactions to bind cationic substrates. \(\pi-\pi\) interaction also plays an important role in stabilizing macromolecular structures involving nucleic acids, protein and liquid crystal copolymers. A typical characteristic of non-covalent interactions is that they are reversible with a short lifetime. The final supramolecular system is in thermodynamic equilibrium with its components so that there is a capacity for self-correction.

1.1.2 Self-Assembly

Supramolecular chemistry describes two phenomena: self-assembly and host-guest chemistry. Self-assembly, defined as the process by which an organized system forms spontaneously and reversibly from its components, refers to, in specific, intermolecular process. Under certain conditions, small molecules with matching electrostatics may interact with one another to form large supramolecular complexes through non-covalent forces. As supramolecular systems become more investigated, subclasses of self-assembly have been proposed. Static self-assembly refers to processes that leads to structures in local or global equilibrium, reducing free energy. While dynamic self-assembly refers to processes that leads to stable non-equilibrium structures.
Numerous examples of self-assembly can be found in the natural world that include both organic and inorganic systems.\textsuperscript{23, 24} As a matter of fact, biological processes could not exist without them. Therefore, self-assembly is used as a strategy to mimic natural process. In the meanwhile, self-assembled devices and mechanically-interlocked molecular architectures, such as rotaxanes based “molecular shuttles”, \textsuperscript{25-33} catenanes and multi-ring systems,\textsuperscript{34-39} knots\textsuperscript{40} and the Molecular Borromean Rings, are designed to perform specific tasks. Each component of the supramolecular device can only perform a simple action. But the entire assembly may achieve a more intricate function.\textsuperscript{41, 42}

In the past two decades, a large number of self-assembling capsules have been synthesized to study their functions. Usually, self-assembling capsules have well-defined inner cavities capable of encapsulating one large molecular guest or several small guests, or working as molecular catalysts.\textsuperscript{43, 44} As well, self-assembling capsules are not as challenging as other synthetic supramolecular capsules to obtain. Among different subsets of self-assembling capsules, the following systems are intensively investigated: hydrogen-bonded systems, metal-ligand systems and hydrophobic assemblies\textsuperscript{45}.

Hydrogen bond-mediated self-assembly systems are the central attraction to many chemists because of their directional characteristics and specificity.\textsuperscript{46} Besides self-assembling dendrimers,\textsuperscript{47-50} peptide-based hydrogen bonding lattice,\textsuperscript{51, 52} and base pairing based receptors,\textsuperscript{53} chemists developed a large number of capsules which consist of several subunits carrying hydrogen bond donors and acceptors.\textsuperscript{54} Another model is the dimeric molecules reversibly formed by two identical or different concave molecules via hydrogen bonding in non-polar solvents. The final supramolecular capsules carry larger inner cavity than either components which allow encapsulation of larger compounds.
Examples include Rebek and Boehmer’s egg-shaped capsules based on two reversibly dimerized calix[n]arene units\textsuperscript{55-57} and Rebek’s expanded version introducing spacers containing glycoluril structures;\textsuperscript{58} Atwood’s carerand-like calix[4]resorcinarene dimer utilizing a rim-to-rim fashion;\textsuperscript{59} capsules based on dimerized calixpyrrole;\textsuperscript{60} and self-assembly based on the association of porphyrin and cyclodextrin.\textsuperscript{61}

Hydrogen bond are somewhat weaker compared to metal-ligand interactions. So in a self-assembling process, a metal-ligand bond can replace several hydrogen bonds,\textsuperscript{62} which makes the assembling process more efficient. Moreover, metal-ligand bonds are quite directional since $d$ orbitals are engaged in the coordination. Additionally, the syntheses are often simpler compared with the all-organic compounds. And the suprastructure of macrocycle can be studied via X-ray crystallography by virtue of their great ionic character.\textsuperscript{45}

In the 1960s and 1970s, Lehn, Cram and Pederson studied the selective and spontaneous binding of cation to crown ethers. The recent examples in metal-ligand assemblies include Stang’s nanoscale dodecahedra held by Pt-pyridine bonds and cuboctahedron assembled by triangle-tectons and connectors;\textsuperscript{63-65} Raymond’s group also designed and synthesized a series of high-symmetry pseudo-octahedral clusters with bidentate chelators coordinated to tri- or tetravalent metal ions;\textsuperscript{66-68} and Fujita’s group reported a number of molecular cages, capsules, prisms and bowls, based on palladium or platinum coordination-directed self-assemble.\textsuperscript{69-71}

Hydrophobic assemblies are often referred to cyclodextrins, cyclophanes and glycophanes. Besides the hydrophobic cavity, the latter two involve aromatic walls for recognition improvements.\textsuperscript{72-75}
1.1.3 Host-Guest Chemistry

Intermolecular noncovalent interactions between host and guest molecules play a central role in the biomimetic and biological chemistry. Usually the system involves two or more molecules: a host and one or more guests to form a supramolecular complex via non-covalent contacts. According to Cram, the host component is a molecule or ion whose binding sites converge in the complex and the guest component is any molecule or ion whose binding sites diverge in the complex.73,76

The origination of host-guest chemistry dated back to 1891 when the discovery of cyclodextrin was firstly published using the name of “cellulosine” by Villiers77. In the 1950s, Cramer et al began to work on the complex forming properties of cyclodextrin. Research concerning calixarenes began in the late 1970s. Then in the 1980s, calixarene ion sensors and cyclodextrin-drug complexes were started to be investigated. In 1987, Cram, Lehn and Pedersen won the Nobel Prize for their research and work in Supramolecular Chemistry. Nowadays, cyclodextrin complexed pharmaceuticals are widely used and produced.78

During the past decades, a large number of synthetic hosts emerged and showed excellent selectivity in guest encapsulation. However, having novel structures, they are often challenging synthetic targets. Besides the concave structure, design of hosts should meet the requirements of showing specific selectivity such as regio- or stereo-selectivity to the target guests. Sometimes, hosts are designed to achieve maximum binding to guests for best resemble of biological process. And some of the hosts are designed to accommodate guest molecules reversibly for delivery or reactor purpose. Common host molecules are crown ethers87, polyammonium macrocycles, cyclodextrins79-80,
calixarenes\textsuperscript{81-83}, resorcinarenes\textsuperscript{84-87} and porphyrins\textsuperscript{88-90} (Figure 1.1). Cucurbiturils\textsuperscript{91, 92}, cryptophanes\textsuperscript{93, 94} carcerands\textsuperscript{95-97} and carceplexes\textsuperscript{1} are also intensively studied as host molecules.

Figure 1.1: Selected molecular hosts

Capsules which are built covalently were utilized to catalyze a variety of reactions. However, preparation and design of these capsules are limited as the scale and complexity of guest increases. Usually, complicated syntheses were involved to make the investigation quite challenging.\textsuperscript{98, 99} The non-covalent interaction based capsules show their advantages upon comparison. Having the confined inner space and the capacity for guest encapsulation, synthetic hosts can be utilized as molecular reactors, catalysts, scavenger receptors and sensors. Moreover, the inner cavity can be expanded via non-covalent bonding linkers to give more flexible space. Therefore, they are proven to be more versatile to different types of reactions.
Reactions with harsh conditions can be performed with a milder condition in supramolecular hosts. Fujita’s group successfully achieved regio- and stereo-selectivity on Diels-Alder reactions of naphthalenes using a coordination-driven self-assembled molecular flask. Naphthalens are originally not reactive to perform Diels-Alder reactions due to the thermodynamic stability of aromatic rings. However, the molecular flask brings reactants into close apoximity and enforces a preorganization of the reactants (Figure 1.2).

![Figure 1.2: Naphthalene Diels-Alder in a self-assembled molecular flask](image)

Guests can be stabilized in supramolecular hosts with contribution of both thermodynamic and kinetic factors. Reactive intermediates can be stabilized within hosts without escaping from them. Raymond’s group reported the stabilization of reactive organometallic intermediates such as ruthenium and iridium complexes in their chiral metal-ligand assembly. Shown in Figure 1.3, the BF$_4$ complex of selective compound G decompose within minutes in water, the corresponding host-guest complexe are stable for weeks. The assembly has been used to mediate catalytic organometallic reactions. Enantio-selectivity can also be gained within the confined cavities.
Figure 1.3: Stabilization of reactive organometallic intermediates inside a self-assembled nanoscale host\textsuperscript{103} (a) [G\(\subset\)M\(_4\)L\(_6\)] supramolecular tetrahedral assembly; (b) G-BF\(_4\) complex; (c) [G\(\subset\)Ga\(_4\)L\(_6\)]\textsuperscript{11-}.

Besides, water-soluble capsules can extract hydrophobic species into their rigid cavity for transport process.\textsuperscript{106-108} In addition, supramolecular hosts showed their value for chirality sensing\textsuperscript{109} and metal ions sensing.\textsuperscript{110}

Among numerous applications, the one which draws considerable attention is the utilization of supramolecular hosts as synthetic supramolecular enzymes. In 1980s, Cram proposed the formulation of carcerands as a potential enzyme mimic.\textsuperscript{111, 112} However, supramolecular hosts are less complex and smaller than enzyme, which greatly limits the application. But, using the smaller and less complex mimics, scientist can examine the importance of each factor contributes to the enzyme catalytic processes.\textsuperscript{113} Another emphasis of investigation is to achieve rate acceleration and high turnover.\textsuperscript{113} The ideal supramolecular enzyme should not only carry a binding site,\textsuperscript{114} but also have the ability to kinetically trap the reactants and release products easily. Figure 1.4 shows two supramolecular enzyme mimics, on the left is a transaminase mimic based on cyclophane\textsuperscript{115} and the right one is a calixarene based ribonuclease mimic.\textsuperscript{116}
1.2 Electrochemistry of Supramolecular Systems

1.2.1 Basic Concepts in Electrochemistry

Electrochemistry is a branch of chemistry that focuses on understanding chemical process involving electron transfer between electrode and electrolyte or other species in solution. Electroanalytical methods are a class of analytical techniques which measure current and potential of the analyte in solution. Generally speaking, oxidation and reduction (redox) reactions are studied in electrochemistry by applying external voltage. Potentiometry, Coulometry, Voltammetry are three major techniques in electroanalytical methods. Potentiometry measures the potential difference between two electrodes under the conditions of no current flow. Coulometry determines the amount of matter transformed during electrolysis by measuring the amount of electricity (in coulombs) required to perform the electrolysis. Voltammetry measures the current when the potential is changed. In cyclic voltammetry (CV), the current response of a stationary electrode is excited by a triangular potential wave form. The potential of the working electrode is scanned back after reaching the switching potential. Figure 1.5 shows a
typical excitation signal. In this example, the potential is varied linearly from +0.8 V to
0.0 V, the scan direction is reversed and the potential is returned to its original value of
+0.8 V. The scan rate in either direction is 40 mV/s and the excitation cycle is repeated
twice. +0.8 and 0.0 V are the switching potentials in this case. The range of switching
potentials chosen is one in which a diffusion-controlled oxidation or reduction of one or
more analytes occurs.\textsuperscript{120}

Figure 1.5: Cyclic voltammetry waveform

The current response of K$_3$Fe(CN)$_6$ solution is shown in Figure 1.6 as an example.
Scan starts from a potential of +0.8 V, from +0.7 to +0.4 V, there is no current observed
because of no reducible or oxidizable species present. A cathodic current appears from
+0.4 V when Fe(CN)$_6^{3-}$ is reduced to Fe(CN)$_6^{4-}$. The current keeps increasing as the
surface concentration of Fe(CN)$_6^{3-}$ becomes smaller and smaller. The current at the peak
contains the initial current surge and the normal diffusion-controlled current. At -0.15 V,
scan direction is switched. Reduction of Fe(CN)$_6^{3-}$ continues because the potential is
negative enough. When the potential is positive enough, the reduction of Fe(CN)$_6^{3-}$ stops.
Fe(CN)$_6^{4-}$ accumulated near the electrode is oxidized by the anodic current, resulting the
anodic current peak. Again, anodic current peak decreases as the surface concentration of
Fe(CN)$_6^{4-}$ become smaller. For a reversible electrode reaction, cathodic and anodic peak
current are equal in absolute value. The difference in peak potentials \(|E_{pc} - E_{pa}| = 0.0592/n\), where \(n\) is the number of electrons involved in the half-reaction.\(^{120}\)

**Figure 1.6:** Typical cyclic voltammogram\(^{120}\)

### 1.2.2 Supramolecular Electrochemistry

Electrochemical methods are important analytical tools for supramolecular events. For instance, redox potentials can be determined and correlated with molecular properties.\(^ {121}\) Electrochemical methods such as CV have been used to control the change of binding state and monitor redox-driven movements in interlock supramolecular systems especially the molecular shuttles and molecular switches.\(^ {122, 123}\) CV can also be used to test the stability of supramolecular capsules.\(^ {124}\) For example, Fujita’s palladium-based cage, shown in **Figure 1.2**, proved to be unstable below -0.8 V, showing irreversible redox waves.\(^ {125}\) According to Echegoyen, electrochemistry acts as “effector”
to direct and control supramolecular interactions, and “detector” to monitor the changes.\textsuperscript{121}

**Figure 1.7:** Cyclic voltammograms of C\textsubscript{60}/γ-CD in water solution studied for different applied negative potential reversals\textsuperscript{126}

Cyclic voltammetry of C\textsubscript{60}/γ-CD in water containing 0.15m LiClO\textsubscript{4} at different scan rates were obtained. As is shown in **Figure 1.7**, only the first electroreduction, the (C\textsubscript{60}\textsuperscript{0}/γ-CD)/(C\textsubscript{60}\textsuperscript{−}/γ-CD) couple, is a reversible, diffusion-controlled one-electron-transfer process in the 20-500 mVs\textsuperscript{-1} potential scan rate range used with a E\textsubscript{1/2} = -0.57. The second electronreduction, (C\textsubscript{60}\textsuperscript{−}/γ-CD)/(C\textsubscript{60}\textsuperscript{2−}/γ-CD), located at -1.03 V, is reversible at scan rates over 200 mVs\textsuperscript{-1} (**Figure 1.7**, second curve from top). This process is not reversible at lower scan rate. The third electroreduction at Epc= -1.34 V is irreversible at all scan rate (**Figure 1.7**, third curve from top). The authors speculated that C\textsubscript{60}\textsuperscript{−} is still embedded in γ-CD whereas C\textsubscript{60}\textsuperscript{2−} is released and undergoes a chemical reaction with water. So the third irreversible electroreduction may correspond to the product and to the (C\textsubscript{60}\textsuperscript{−2}/γ-CD)/(C\textsubscript{60}\textsuperscript{−3}/γ-CD) couple.\textsuperscript{126}
1.3 Gated Molecular Baskets

A family of molecular hosts called “molecular baskets” (Figure 1.8 and 1.9) were synthesized and reported by Badjic’s group.\textsuperscript{127} Those baskets are composed of a flat aromatic base, three bicyclo[2.2.1]heptane ring, three phthalimide groups connected with functional gates, each of which involves a methylene rotor. The three bicycle[2.2.1] rings...
adopt a syn conformation that allows all three arms point to the same direction to form a rigid bowl-shaped cavitand.\textsuperscript{127}

Compared to the previously synthesized molecular baskets (Figure 1.10), our cavitand can fold into a gated basket by intramolecular hydrogen bonding or metal-to-ligand coordination of the heterocyclic “flaps” appended to the basket’s rim. Those gates can control the baskets’ folding and the formation of a “dynamic” interior. When folded with the transition metal, the baskets tends to encapsulate linear guests by coordinating the guest with metal cation. The in/out transport of guest can also be controlled by the rapid opening and closing of the hydrogen bonding ‘flaps’. In this way, the guest exchange is restricted by the baskets’ conformational behavior, providing much information about the relationship between molecular exchange kinetics and the host’s dynamics.

![Previous Synthesized Molecular Baskets](image1)

**Figure 1.10: Previous Synthesized Molecular Baskets\textsuperscript{130-132}**

In my particular case, the host I’m using contain either a trifluoro or a phenyl group of the gate, and that closes the basket via hydrogen bonding (Figure 1.11). This molecular basket is able to encapsulate numerous guests and regulate the encapsulation by the opening and closing of their trifluoro- or phenyl- gates.\textsuperscript{127-129}
1.4 Objectives

There has been considerable interest in the design and study of supramolecular molecules that can regulate kinetics and thermodynamics of molecular recognition. Based on the previous study, gated molecular baskets have been shown to encapsulate a range of guest molecules varying in size, shape and electronic characteristics. The molecular baskets can regulate the trafficking of guests using a set of functionalized gates, which assemble via intramolecular hydrogen bonding to enfold space. The rotary motion of gates forms a dynamic space to impose on guests to exchange to and from the interior. The in and out rate of guest’s encapsulation as a function of the dynamics of gates were examined, allowing us to predict and control the time that guest molecules spend inside the baskets.

However, the regulation of kinetics of molecular recognition and guest translocation by applying an external stimulus is still a challenging task. Manipulation of redox-active host-guest systems through molecular recognition is central to study catalytic
behavior. Specifically, the focus of the study is to investigate electrochemical behavior and molecular encapsulation regulation upon reduction/oxidation of the basket (Figure 1.8). As we know, the phthalimide moieties on the platform of basket have the tendency of accepting electrons. If the basket is reduced by accepting electrons, the platform becomes electron rich and perhaps changes the affinity for guests. So what will happen with the guest’s encapsulation? Will the basket pass the electrons to the guest, push out the reduced guest and exchange for another guest? Understanding the electrochemical behavior will aid in the future development of catalytic properties of our baskets.

Figure 1.12: Gated Molecular Baskets Being Reduced
References

(23) Ball, P. Nature 2001, 409, 413.


(49) Felber, B.; Diederich, F. *PNAS* **2002**, 99, 4778.


(73) Cram, D. J.; Cram, J. M. Science **1974**, 183, 803


CHAPTER TWO
RECOGNITION BEHAVIOR AND ELECTROCHEMICAL PROPERTIES OF GATED MOLECULAR BASKETS

2.1 Introduction and Hypothesis

The design of dynamic molecular hosts has been of great interest in recent years. Numerous molecular hosts\(^1\text{-}^4\) have been made to selectively encapsulate guests. These molecular hosts have been widely used for enzymes mimic,\(^5\) reactions catalysis,\(^6\text{-}^7\), unstable intermediate stabilization\(^8\).

![Figure 2.1: Selected dynamic molecular baskets synthesized by our group\(^9\text{-}^{15}\)](image)

\[ R = \]

\[ \text{Figure 2.1: Selected dynamic molecular baskets synthesized by our group}^{9\text{-}15} \]
Efforts in our group have been focused on design, synthesis and study of molecular recognition behavior of a series of molecular baskets (Figure 2.1). The baskets contain a semi-rigid and curved C$_3$ symmetrical tris-norbornadiene framework, three aromatic rings installed as gates at the rim. The interconversion of two C$_3$ symmetric enantiomers, 1A and 1B, each containing hydrogen bondings displayed in a clockwise or counterclockwise orientation, has been verified from the NMR exchange of the “hinge” Ha/b resonances appearing as a singlet at high and an AB quartet at low temperatures (Figure 2.2).

Transition metals such as Cu(I) and Ag(I) can be used to fold the container via metal-ligand coordination, thus enforcing encapsulation by guest’s binding to the transition metals. Using hydrogen bonding to fold the baskets, a range of guests varying in size, shape and electronic characteristics can be enclosed inside the capsule. This property can be related to the considerable volume of the “dynamic” inner space.
created by the flaplike motion of gates. Via the dynamic gating, the molecular baskets are capable of regulate the in/out exchange of guests. The dynamic regulation of molecular encapsulation creates a unique opportunity to explore the interdependence of kinetic stability and chemical reactivity, as well as the controlled translocation of molecules in artificial environments. By switching the gates on top of the baskets, their conformational dynamics would be affected, allowing the regulation of the guest’s kinetic stability. Upon studying the kinetic discrimination of guests quantitatively, conclusion was drawn that encapsulation kinetics is governed by guest’s profile and the host/guest interaction potential.

![Figure 2.3: Trifluoro-based molecular basket folded via hydrogen bonding](image)

In my particular case, the basket I’m using contain a trifluoro or a phenyl group at the gate, and fold via hydrogen bonding. These molecular baskets are able to encapsulate certain guests and regulate the encapsulation by opening and closing their trifluoro- or phenyl- gates (Figure 2.3).
Specifically, the focus of this study is to investigate electrochemical behavior and molecular encapsulation upon reduction/oxidation of the basket (Figure 2.4). The phthalimide groups in the basket are capable of accepting electrons and being reduced. Upon reducing the basket, the thermodynamic affinity of basket for the encapsulated guests could change. To investigate how the redox-stimulus affect the regulation of guests encapsulation is of our interest. In overall, understanding the electrochemical behavior will aid future developments of using dynamic hosts as catalysts for promoting useful reactions.

Figure 2.4: Gated molecular baskets being reduced
2.2 Synthesis of the Baskets 2.1

Figure 2.5: Synthetic route for tris-anhydride$^9$-$^{11}$

Figure 2.6: Synthetic route for 3-amino-5-(aminomethyl) pyridine$^25$
The original synthetic route of tris-anhydride 2.4 (Figure 2.5) was reported by our group. Since the original route required high pressure, another method was developed with a higher overall yield. Using acetone as template, the reaction of cyclotrimerization’s yield was significantly improved. I started my research with synthesizing 2.4 following the optimized synthetic route and then I prepared 3-amino-5-(aminomethyl) pyridine 2.3 (Figure 2.6). Coupling of 2.4 with 2.3 gives the amino-based basket 2.2. Basket 2.1* (Figure 2.7) was obtained by coupling 2.2 with trifluoroacetic anhydride. Reacting 2.2 with benzoyl chloride affords Basket 2.1 (Figure 2.7).
2.3 NMR Spectroscopic Studies of Basket 2.1* and Basket 2.1

2.3.1 Basket Selection

$^1$H NMR signals of 2.1* and 2.1 (Figure 2.7) were previously assigned.\textsuperscript{14} $^1$H NMR spectrum (400 MHz, 298 K) of 2.1* and 2.1 in CD$_2$Cl$_2$ has been assigned to a C$_3$ symmetrical molecule. The signal for the N-H proton in 2.1 appeared downfield ($\delta$=11.20 ppm). Respectively, the $^1$H NMR resonance for the N-H proton in 2.1* was found at an even lower field ($\delta$=12.21 ppm). $^1$H NMR chemical shifts of the N-H signals are indicators for the strength and the proportion of the intramolecular hydrogen bonding. The lower field the chemical shift is at, the higher electrostatic potential energy at the N-H and Pyr-N sites is. Therefore, the lifetime of encapsulated guest can be controlled and predicted by choosing a proper R substituent. The trifluoro-based basket and the phenyl-based basket were selected because their gates connect via strong hydrogen bonding that retards the flaplike motion of the gates. According to the previous publications, the lifetime of encapsulated guest $t$-BuBr is 14 s with the trifluoro-based basket and 2.5 s with the phenyl-based basket, much longer than baskets with other R substituted gates.\textsuperscript{14}

2.3.2 Guest Selection

An ideal guest should bind strongly to the selected baskets. In addition, it must have different cathodic and anodic potentials from those of baskets on cyclic voltammogram. It is essential not to have overlap peaks on the cyclic voltammogram. Quaternary ammonium cation was taken into consideration. According to Rebek and co-workers, for encapsulations guided by nonspecific host/guest intermolecular contacts, a guest would occupy 55% of the host cavity.\textsuperscript{19,20} Since our basket has a calculated cavity size of 221±9 Å$^3$, quaternary ammonium cations with size less than or equal to 120 Å$^3$, such as...
ethyltrimethylammonium cation and tetramethylammonium cation, were tested,. However, based on variable temperature $^1$H NMR spectrum, none of those quaternary ammonium cations could be encapsulated inside. The reason might be the poor solubility of those cations in CD$_2$Cl$_2$ or CDCl$_3$ solutions.

Subsequently, 2,2-Dibromopropane (CH$_3$CBr$_2$CH$_3$) and 1,1,1-tribromoethane (CH$_3$CBr$_3$) were selected. They were shown to reside inside baskets with a relatively high affinity.$^{12}$

2.3.3 NMR Spectroscopic Measurements

Binding constants of guests, 2,2-Dibromopropane and 1,1,1-tribromoethane, with phenyl-based basket 2.1 were respectively measured utilizing variable temperature $^1$H NMR and titration methods. The guest compound was added to 2.1 in CD$_2$Cl$_2$, and the solution was subjected to variable temperature $^1$H NMR study (Figure 2.8 and 2.9). At lower temperatures, singlet from CH$_2$ moieties on the gate ($\delta = 4.58$ ppm) changes from the singlet into a quartet, proving that hydrogen bonding on 2.1 is dynamic and displays either a clockwise or counterclockwise direction. When a guest occupied the inner space of 2.1, upfield peaks of encapsulated guest were noticed, and two sets of N-H (original $\delta = 11.20$ ppm) resonances appeared: the downfield one corresponded to the “empty” and the upfield one to the filled basket. Integration of the resonances afforded the binding constant, and from a Van’t Hoff plot (Figure 2.10), thermodynamic parameters ($\Delta H^\circ$, $\Delta S^\circ$) for the encapsulation were obtained. For 2,2-Dibromopropane, $\Delta H^\circ = -5.9$ kcal/mol, $\Delta S^\circ = -10.3$ e.u., $K_{300} = 119 \pm 5$ M$^{-1}$ and for 1,1,1-tribromoethane, $\Delta H^\circ = -6.8$ kcal/mol, $\Delta S^\circ = -9.9$ e.u., $K_{300} = 630 \pm 5$ M$^{-1}$. Unfavorable entropy is compensated with a lower enthalpy to contribute to the stabilities of the complexes ($\Delta G^\circ$, 300 K).
Figure 2.8: Variable temperature $^1$H NMR spectra (400 MHz) of phenyl-based basket in CD$_2$Cl$_2$ (1.4 mM), containing 1.5 molar equivalents of CH$_3$CBr$_2$CH$_3$ (2.1 mM, $\delta = 2.47$).

Figure 2.9: Variable temperature $^1$H NMR spectra (400 MHz) of phenyl-based basket in CD$_2$Cl$_2$ (1.1 mM), containing 0.8 molar equivalents of CH$_3$CBr$_3$ (0.9 mM, $\delta = 3.35$).
The binding constants obtained by variable temperature $^1$H NMR spectroscopy was confirmed by $^1$H NMR titration experiments. At 298 K, a gradual addition of guests to a solution of phenyl-based basket in CD$_2$Cl$_2$ caused considerable changes in its $^1$H NMR spectrum. The N-H resonance shifted to a lower field, as the concentration of guests was gradually increased (Figure 2.11 and 2.12). The non-linear curve fitting of the binding isotherm, to a 1:1 stoichiometric model, yielded the association constants (Figure 2.13).$^{21-24}$
Figure 2.11: $^1$H NMR spectra (400 MHz) of phenyl-based basket in CD$_2$Cl$_2$, (1.4 mM, 298K), obtained after incremental additions of CH$_3$CBr$_2$CH$_3$.

Figure 2.12: $^1$H NMR spectra (400 MHz) of phenyl-based basket in CD$_2$Cl$_2$, (1.1 mM, 298K), obtained after incremental additions of CH$_3$CBr$_3$. 
The bonding constants obtained from titration experiments (Figure 2.13) match well with those obtained from variable temperature measurements. The binding of 2,2-dichloropropane to 2.1 is somewhat weaker compared with 1,1,1-tribromoethane, which is used for electrochemical measurements. The binding constant of 1,1,1-tribromoethane is $630 \pm 5 \text{ M}^{-1}$ and $692 \pm 140 \text{ M}^{-1}$ from two different sets of experiments.

Molecular basket 2.1 was shown to stay predominantly monomeric and incapable of
intermolecular aggregation in solution. $^1$H NMR DOSY measurements (500 MHz, 298 K, CD$_2$Cl$_2$) of 2.1 (Figure 2.14 (a)) revealed that the apparent diffusion coefficients $D$ are practically invariant at three different concentrations. The resulting mean average diffusion coefficient ($D$) was read, directly from the spectra, to be $8.62 \pm 0.6 \times 10^{-10}$ m$^2$s$^{-1}$. And the hydrodynamic radius were calculated (from three independent measurements) to be $7.32 \pm 0.4$ Å by $r = \frac{K_B T}{6 \pi \eta D}$, where $r$ is the hydrodynamic radius, $\eta$ is the solution viscosity, $K_B$ is the Boltzmann’s constant and $T$ is absolute temperature.

$^1$H NMR DOSY measurements (500 MHz, 298 K, CD$_2$Cl$_2$) of model compound (Figure 2.14 (b)) was also done for comparison. The mean average diffusion coefficient ($D$) and the hydrodynamic radius (from three independent measurements) are $17.78 \times 10^{-10}$ m$^2$s$^{-1}$ and 3.55 Å, further proving 2.1 stays monomeric in solution.
Figure 2.14: Selected $^1$H DOSY NMR (500 MHz, 298K) spectrum of CD$_2$Cl$_2$ solution of (a) phenyl-based basket; (b) model compound.
2.4 UV Spectroscopic Studies

UV-Vis Spectrum revealed the formation of host-guest complexes. A calibration curve of 2.1 in CH$_2$Cl$_2$ was obtained with the concentration range from 1.9 μM to 9.5 μM (Figure 2.15). The concentration was confirmed by $^1$H NMR spectroscopy by adding certain amount of benzene as an internal standard. This calibration curve was used to calibrate the concentration of 2.1 in CH$_2$Cl$_2$ solution in the next titration experiment.

![UV-Vis calibration curve of 2.1 in CH$_2$Cl$_2$ with a concentration range from 1.9 μM to 9.5 μM (1 cm pathlength cell).](image)

Figure 2.15: UV-Vis calibration curve of 2.1 in CH$_2$Cl$_2$ with a concentration range from 1.9 μM to 9.5 μM (1 cm pathlength cell).
Figure 2.16: (a) UV-vis spectra of titrating of CH₃CBr₃ (from 0 to 5 equivalents) to a CH₂Cl₂ solution of 2.1 (50 μM, 1mm pathlength cell); (b) plot of UV absorption versus number of equivalent of guest titrated.

Upon titrating 1,1,1-tribromoethane to a solution of phenyl-basket 2.1, an increase of intensity at 258nm and 282 nm was observed (Figure 2.16a). Since 1,1,1-tribromoethane doesn’t have UV absorption, baskets with guests encapsulated should have the absorbance at the same or very close wavelength as the empty baskets. As the concentration of host-guest complex increases, the intensity of absorbance increases. Red line on Figure 2.16a represents empty basket, blue line represents basket with 1.0 equivalent of guest titrated. After 2.0 equivalents of guest were titrated (green line), the intensity of absorption started to increase very slowly. The basket got fully saturated after 3.0 equivalents of guest were titrated into the solution (Figure 2.16b).
2.5 Electrochemical Properties Studies

2.5.1 Cyclic voltammetry of trifluoro-based basket 2.1* and a model compound

![Cyclic voltammetry of a CH$_2$Cl$_2$ solution containing (a) 0.5 mM trifluoro-based model compound and 0.1 M TBAPF$_6$; (b) 0.5 mM of basket 2.1* and 0.1 M TBAPF$_6$. Measurements performed at room temperature. Scan rate = 0.2 V/s.](image)

**Figure 2.17**: Cyclic voltammetry of a CH$_2$Cl$_2$ solution containing (a) 0.5 mM trifluoro-based model compound and 0.1 M TBAPF$_6$; (b) 0.5 mM of basket 2.1* and 0.1 M TBAPF$_6$. Measurements performed at room temperature. Scan rate = 0.2 V/s.

Cyclic voltammetry (CV) of 0.5mM trifluoro-based basket 2.1* and 0.5mM trifluoro-based model compound (Figure 2.17 (a)) revealed a single wave at a half-wave potential of -1.40 V and -1.45 V, respectively (Figure 2.17). The half-wave potential corresponds to the reduction of the phthalimide group. In comparison with model compound, the single wave of basket 2.1* reveals that there is no detectable electronic communication among its three arms. Furthermore, no apparent oxidation was detected. This might be caused by the strong electronegativity of trifluoromethyl groups. A proposed reasoning is shown in Figure 2.18. The phthalimide moiety on the basket’s platform (Figure 2.18 (a)) was first reduced by accepting one electron. When scanning
back, if the reduced forms of the basket (Figure 2.18 (b)) are oxidized by anodic current, an anodic current same as cathodic current should be observed. However, only a small anodic current was observed, indicating that most of (b) underwent a reaction to form a product which cannot be oxidized by this low potential. And only a small amount of (b) were oxidized back to (a) to give the small anodic peak. It is proposed that the radical anion of phthalimide deprotonated the amide and the anion was stabilized by -COCF₃ group which is strong electro-withdrawing (Figure 2.18 (c)).

![Reaction Diagram]

**Figure 2.18:** Proposed reasoning for unapparent anodic peak in cyclic voltammetry of trifluoro-based basket

Back to the Figure 2.17, peak intensity of model compound and basket 2.1* are 4 μA and 10 μA, respectively. Peak intensity of 2.1* is around 2.5 fold to the peak intensity of model compound, which suggests the reduction of basket to be multi-electron process. Cyclic voltammetry of different scan rates at both room temperature and -15°C shows no change in redox properties of model compound and basket 2.1*.
2.5.2 Cyclic voltammetry of basket 2.1 and 1,1,1-tribromoethane

Cyclic voltammetry of 0.5mM phenyl-based basket 2.1 showed a single wave at a half-wave potential of -1.60V (Figure 2.19a). Lower half-wave potential than basket 2.1* suggests its reluctance to be reduced. The shape of the voltammetric wave observed suggests a reversible electrochemical redox process. In another word, the radical anion of phthalimide in 2.1 does not deprotonate the amide, compared with trifluoro-based basket. Cyclic voltammetry of 0.5 mM 1,1,1-tribromoethane shows an irreversible reduction process at -1.86V (Figure 2.19b). Coulometry will be performed later on to determine the amount of electrons transferred.

![Cyclic voltammetry of a CH$_2$Cl$_2$ solution containing (a) 0.5 mM basket 2.1 and 0.1 M TBAPF$_6$; (b) 0.5 mM 1,1,1-tribromoethane and 0.1 M TBAPF$_6$. Measurements performed at room temperature. Scan rate = 0.2 V/s.](image)

Figure 2.19: Cyclic voltammetry of a CH$_2$Cl$_2$ solution containing (a) 0.5 mM basket 2.1 and 0.1 M TBAPF$_6$; (b) 0.5 mM 1,1,1-tribromoethane and 0.1 M TBAPF$_6$. Measurements performed at room temperature. Scan rate = 0.2 V/s.

2.5.3 Cyclic voltammetry titration of 1,1,1-tribromoethane into basket 2.1

Having basket 2.1 and guest’s cyclic voltammetry at hand, cyclic voltammetry titration of guest to a CH$_2$Cl$_2$ solution of 2.1 was performed to gain a better understanding of how the electronically reduced basket regulate the encapsulation of guest (Figure 2.20). This measurement was performed at room temperature, using 0.5mM solution of
basket 2.1. The volume of solution was kept nearly constant by adding small volume of guest solution or neat guest. As shown in Figure 2.20b, anodic peak was getting smaller upon titrating 0.0 to 1.1 equivalents of guest molecules. Encapsulation of guest was shown since guest’s peak at -1.7 V was not observed. Figure 2.20c shows the titration of guest from 1.1 to 2.5 equivalents. Basket got fully saturated and a more negative, irreversible reduction wave at E= -1.7 V was observed which was assigned to reduction of free guests (Figure 2.19 (b)). In addition, there was no obvious shift of the anodic peaks during the titration (Figure 2.20). It is hypothesized that the basket was reduced first, and then passed the electrons to the guest inside. This contributes to the gradually invisible oxidation peak for the basket.

**Figure 2.20:** Cyclic voltammetry titration of 1,1,1-tribromoethane to a CH₂Cl₂ solution of basket 2.1 (0.5mM, 0.1 M TBAPF₆, room temperature) (a) 0 – 2.5 equivalent of guest; (b) 0 – 1.1 equivalent of guest; (c) 1.1 – 2.5 equivalent of guest. Scan rate = 0.2 V/s.
Furthermore, cathodic current of the saturation peak suggests one basket and not only one guest (two or more). Giving this significant information, it is reasonable to hypothesize that during the scan, more than one guest was encapsulated and accepted the electron from one basket. So during this process, basket works like a catalyst, encapsulating one guest, passing the electron to this guest, freeing the reduced guest and then repeating this to another guest. Further support for this hypothesis can be performed by changing the scan rate of CV. If the scan can be completed in a shorter period of time, say, 0.3 V/s, the cathodic current at the saturation peak might be smaller.

Further measurements were done by evaporating the solvents of the CH$_2$Cl$_2$ solution containing 0.5 mM basket 2.1 and 2.5 equivalents of guest (Figure 2.21). 1,1,1-tribromoethane is a liquid which is very easy to evaporate. After one day, all the CH$_2$Cl$_2$ solvents was evaporated, electrochemical test was performed again to show a CV resembling basket with 0.8 equivalents of guest. This indicates basket is able to retain guest in its cavity. Subsequently, this solution was kept evaporating for another five days, giving a CV resembling basket with trace amount of guest. Since the basket’s CV after this process showed no changes, the CV response of basket with excess CH$_3$CBr$_3$ is not due to chemical breakdown of the basket. This process of encapsulation, retention and release was illustrated in Figure 2.22.
Figure 2.21: Cyclic voltammetry of the encapsulation, retention and release Process. (0.5mM of basket 2.1 in a CH₂Cl₂ solution, 0.1 M TBAPF₆, room temperature) (a) Empty basket; (b) basket with 2.5 equivalents of guest; (c) after evaporating solvent for 1 day; (d) after evaporating solvent for 5 days. Scan rate = 0.2 V/s.

Figure 2.22: Illustration of encapsulation, retention and release process in Figure 2.21.
2.6 Conclusions

The fluoro-based and phenyl-based molecular baskets are capable of encapsulating a range of guests inside their cavities. Their flaplike motion of gates creates the “dynamic” inner space. Via the dynamic gating, the molecular baskets are capable of regulate the in/out exchange of guests.

Binding constants of 1,1,1-tribromoethane guest encapsulated inside the baskets were obtained from different NMR techniques. UV titration further proved the encapsulation. It was shown in this study that the molecular basket responds to reduction/oxidation stimulus by passing electrons to the enclosed guests, and then release the reduced guest. One basket can repeat the process on more than one guests, acting like a catalyst. The mechanism of guest encapsulation and release upon reduction/oxidation stimulus is shown below (Figure 2.23). More proof of this proposed mechanism will be explored in the future.

![Proposed mechanism of guest encapsulation and release upon reduction/oxidation stimulus of basket 2.1.](image_url)

**Figure 2.23:** Proposed mechanism of guest encapsulation and release upon reduction/oxidation stimulus of basket 2.1.
2.7 Experimental

**General.** All chemicals were purchased from commercial sources, and used as received unless stated otherwise. All solvents were dried prior to use according to standard literature protocols. Chromatography purifications were performed using silica gel 60 (Sorbent Technologies 40-75μm, 200 x 400 mesh). Thin-layer chromatography (TLC) and preparatory TLC were performed on silica-gel plate w/UV254 (200μm). Chromatograms were visualized by UV-light and stained using 20% phosphomolybdic acid in ethanol, if required. \(^1\)H and \(^{13}\)C NMR spectra were recorded, at 400 MHz and 100 MHz respectively, on a Bruker DPX-400 spectrometer. DOSY spectra were recorded, at 500 MHz, on a Bruker DRX-500 spectrometer. They were referenced using the solvent residual signal as an internal standard (CDCl\(_3\) and CD\(_2\)Cl\(_2\) from Cambridge Isotope Laboratories). The chemical shift values are expressed as δ values and the couple constants values (\(J\)) are in Hertz (Hz). The following abbreviations have been used for signal multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad. Reported temperatures were corrected with neat methanol. FT-IR spectra were recorded on a Perkin Elmer Spectrum GX FT-IR spectrophotometer. HR MALDI-TOF mass spectra were measured on a Bruker Reflex III MALDI-TOF spectrometer and samples were made using 2,5-Dihydroxybenzoic acid as matrix. Electrochemistry experiments were executed using a Princeton Applied Research Potentiostat/Galvanostat model 263A, a glassy-carbon solid electrode as the working electrode, Ag/AgCl as the reference electrode and a platinum wire as the counter electrode.
Preparation of the Compounds.

**Compound 2.8.** A mixture of freshly distilled cyclopentadiene (2.65 g, 0.04 mol) and cis-1,4-dichloro-2-butene (4.16 g, 0.033 mol) in benzene (3 mL) was heated at 200 °C overnight in a sealed tube. The reaction mixture was then cooled to room temperature, and benzene was evaporated under reduced pressure. The remaining residue was distilled in vacuo to afford 5 as a colorless oil (4.5 g, 71 %). B.p. = 85.0 °C at 0.5 mmHg; \(^1\)H NMR (400 MHz, CDCl\(_3\), 25 °C): \(\delta = 6.25\) (dd, 2H, \(J_1 = J_2 = 1.8\) Hz), 3.31 (dd, 2H, \(J_1 = 5.7\) Hz, \(J_2 = 10.7\) Hz), 3.14-3.09 (m, 4H), 2.63-2.60 (m, 2H), 1.55 (m, 1H), and 1.37 ppm (d, 1H, \(J = 8.6\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), 25 °C): \(\delta = 135.6\) (CH), 48.4 (CH\(_2\)), 46.6 (CH), 45.6 (CH), and 45.0 ppm (CH\(_2\)). MS(ESI): \(m/z\) calcd for C\(_9\)H\(_{12}\)Cl\(_2\)Na: 213.0 [\(M+Na\)]\(^+\); found: 213.0.

**Compound 2.9.** To a nonane (30 mL) solution of 2.8 (1.67 g, 8.7 mmol) at 150 °C, neat bromine (1.54 g, 8.7 mmol) was added slowly over five minutes. The mixture was stirred at the same temperature for 15 minutes, upon which the solvent was removed. The residue was purified by column chromatography (SiO\(_2\), hexanes/CH\(_2\)Cl\(_2\), 8:2) to afford 6 as a white solid (1.84 g, 61 %). M. p. 96 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\), 25 °C): \(\delta = 4.46\) (d, 2H, \(J = 2.0\) Hz), 3.66 (dd, 2H, \(J_1 = 6.6\) Hz, \(J_2 = 11.4\) Hz), 3.41 (dd, 2H, \(J_1 = 9.8\) Hz, \(J_2 = 11.3\) Hz), 2.89 (t, 2H, \(J = 1.8\) Hz), 2.54-2.51 (m, 2H), 2.40 (d, 1H, \(J = 11.0\) Hz), and 1.56 ppm (dt, 1H, \(J_1 = 1.6\) Hz, \(J_2 = 11.0\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), 25 °C): \(\delta = 52.7\) (CH), 50.9 (CH), 43.5 (CH), 40.9 (CH\(_2\)), and 34.4 ppm (CH\(_2\)). HRMS(ESI): \(m/z\) calcd for C\(_9\)H\(_{12}\)Br\(_2\)Cl\(_2\)Na: 372.8558 [\(M+Na\)]\(^+\); found: 372.8571.
**Compound 2.10.** To a solution of **2.9** (2.4 g, 6.8 mmol) in THF (68 mL) at 0 °C, potassium tert-butoxide (14.5 g, 0.14 mol) was added under an argon atmosphere. The reaction mixture was left to stir for 2 h, before being washed with water (6 mL), and extracted with hexane (3 x 50 mL). The organic phase was dried (MgSO₄), and evaporated under reduced pressure. The solid residue was purified by column chromatography (SiO₂, hexanes) to afford **7a** as a colorless oil (1.1 g, 82 %). ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 6.20 (d, 1H, J = 3.1 Hz), 5.31 (s, 1H), 5.25 (s, 1H), 5.13 (s, 1H), 5.00 (s, 1H), 3.36 (s, 1H), and 3.30 ppm (s, 1H); ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ = 135.4 (CH), 103.4 (CH₂), 102.4 (CH₂), 58.7 (CH), 52.2 (CH) and 50.9 ppm (CH₂); HRMS(ESI): m/z calcd for C₉H₁₀Br: 196.9960 [M+H]+; found: 197.0033.

**Compound 2.12.** A toluene (150 mL) solution of **2.10** (5.37 g, 27.2 mmol) and freshly distilled dimethyl acetylenedicarboxylate (5.32 g, 37.4 mmol) was allowed to stir at reflux for 12 h. The solvent was removed at a reduced pressure to yield an amber oil (9.24 g). The oil was dissolved in dichloromethane (200 mL) and solid 2,3-dichloro-5,6-dicyano-p-benzoquinone (7.10 g, 31.3 mmol) was added. The mixture was mechanically stirred under argon (12 h, rt), before it was “washed” with a saturated aqueous NaHCO₃ solution (3 x 200 mL) and dried (MgSO₄), and the organic layer was concentrated in vacuo. The solid residue was purified by column chromatography (SiO₂, CH₂Cl₂) to yield **6** (6.54 g, 71%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃, 298 K): δ 2.35 (1H, d, J = 7.6 Hz), 2.63 (1H, d, J = 8.0 Hz), 3.85 (1H, s), 3.88 (6H, s), 4.00 (1H, s), 6.73 (1H, d, J = 3.2 Hz), 7.51 (1H, s), and 7.65 ppm (1H, s); ¹³C NMR (100 MHz, CDCl₃, 298 K): δ 51.7,
52.6, 52.7, 58.2, 68.8, 121.5, 122.1, 128.9, 130.1, 135.8, 153.3, 153.9, 168.1, and 168.4 ppm; HRMS (EI): \( m/z \) calcd for C\textsubscript{15}H\textsubscript{14}BrO\textsubscript{4} 337.0075 [M + H]\(^+\); found 337.0061.

**Compound 2.13.** To a solution of dry diisopropylamine (830 \( \mu \)L, 5.90 mmol) in THF (20 mL) at -78 °C was added \( n \)-butyl lithium (1.6 M in hexanes, 3.60 mL, 5.76 mmol), and the mixture was stirred for 40 min under an atmosphere of argon. A solution of 2.12 (1.50 g, 4.45 mmol) in THF (10 mL) was then added dropwise over a period of 10 min, and the resulting mixture was stirred for an additional 30 min. Following, a solution of trimethyltin chloride (937 mg, 4.76 mmol) in THF (10 mL) was added dropwise over a period of 10 min, and the resulting mixture was gradually warmed to room temperature over a period of 3 h. Aqueous NH\textsubscript{4}Cl (4 mL) was used to quench the base, followed with the removal of the organic layer in vacuo. The solid residue was washed with water (60 mL) and extracted with diethyl ether (2 \( \times \) 70 mL). The combined organic phase was dried (MgSO\textsubscript{4}) and concentrated in vacuo. The solid residue was purified by column chromatography (SiO\textsubscript{2}, hexanes/ethyl acetate, 2:1) to yield 7 as a white solid (1.59 g, 72\%). Mp 139-140 °C; \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}, 27 °C): \( \delta \) 0.24 (9H, t, \( J = 40 \) Hz), 2.27 (1H, d, \( J = 7.6 \) Hz), 2.57 (1H, d, \( J = 7.6 \) Hz), 3.91 (7H, s), 4.09 (1H, s), 7.47 (1H, s), and 7.65 ppm (1H, s); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}, 27 °C): \( \delta \) -9.3, 52.5, 52.6, 57.0, 60.2, 68.4, 121.1, 122.0, 129.0, 129.8, 147.0, 152.2, 153.6, 154.0, 168.4, and 168.5 ppm; HRMS (EI): \( m/z \) calcd for C\textsubscript{16}H\textsubscript{16}BrO\textsubscript{4}Sn 500.9723 [M + H]\(^+\); found 500.9687.

**Compound 2.14\textsubscript{syn}.** A mixture of 2.13 (1.09 g, 2.18 mmol) and Cu(NO\textsubscript{3})\textsubscript{2} \cdot 2H\textsubscript{2}O (2.53 g, 10.9 mmol) in acetone (53 mL) was stirred at 50 °C overnight. The solvent was
removed in vacuo and the remaining residue was washed with a 10% aqueous NH₃ solution (60 mL) and extracted with diethyl ether (3 × 100 mL). The combined phase was dried (MgSO₄) and concentrated in vacuo. The solid residue was purified by column chromatography (SiO₂, dichloromethane/acetone, 9:1) to yield 2.14syn (75.8 mg, 13.6%) as a white solid. Mp 215 °C; ¹H NMR (400 MHz, CDCl₃, 27 °C): δ 2.54 (6H, s), 3.80 (18H, S), 4.43 (6H, s), and 7.45 ppm (6H, s); ¹³C NMR (100 MHz, CDCl₃, 27 °C): δ 48.8, 52.3, 65.4, 121.6, 129.8, 137.8, 152.8, and 168.1 ppm. HRMS (ESI): m/z calcd for C₄₅H₃₆O₁₂Na 791.2099 [M + Na]⁺; found 791.2098.

Compound 2.15. An aqueous solution of LiOH · xH₂O (60 mg, 1.43 mmol; 2 mL) was added to a solution of 2.14syn (30 mg, 0.04 mmol) in THF (2 ml), and subsequently heated at 80 °C for 2 h. The aqueous phase was acidified with a 10% aqueous HCl solution (1 mL), and the resulting precipitate filtered, washed with water (2 mL), and dried at 90 °C under high vacuum. 2.15 was obtained as a white solid (25.4 mg, 95 %). M.p. >300 °C; ¹H NMR (400 MHz, CD₃SOCD₃, 25 °C): δ = 12.67 (br, 6H), 7.46 (s, 6H), 4.62 (s, 6H), and 2.42 ppm (s, 6H); ¹³C NMR (100 MHz, CD₃SOCD₃, 25 °C): δ =168.8 (C), 153.3 (C), 138.3 (C), 130.6 (C), 121.5 (CH), 65.3 (CH₂), and 48.3 ppm (CH); HRMS(ESI): m/z calcd for C₃₉H₂₄O₁₂Na 707.1150 [M+Na]⁺; found: 707.1165.

Compound 2.14. A solution of 2.15 (15 mg, 0.03 mmol) and Ac₂O (2 mL) was heated at 130 °C for 2 h. The solvent was removed in high vacuo to afford 2.4 as a white solid (13.0 mg, 90 %). M.p. >300 °C; ¹H NMR (400 MHz, CD₃SOCD₃, 25 °C): δ =7.99 (s, 6H), 4.77 (s, 6H), and 2.56 ppm (s, 6H); ¹³C NMR (100 MHz, CD₃SOCD₃, 25 °C): δ =163.0
(C), 159.8 (C), 138.0 (C), 129.4 (C), 117.9 (CH), 65.0 (CH2), 48.3 (CH); HRMS(ESI): m/z calcd for C39H18O92Na 653.0843 [M+Na]+; found: 653.0826.

**Compound 2.2.** Tris-anhydride (compound 2.4) (6.3 mg, 10.0 mol) was added portionwise to a stirred solution of dry DMSO (1.0 mL) containing 5-(aminomethyl) pyridin-3-amine24 (4.9 mg, 40.0 mol) at room temperature. After 2 h, neat pyridine (0.1 mL) was added dropwise and the temperature was raised to 115 ºC. The reaction was allowed to complete over ~12 h (overnight), after which the solvent was evaporated in vacuum and the residue was purified by column chromatography (SiO2, CH2Cl2/CH3OH = 6:1) to yield a white solid product (6.6 mg, 70 %). 1H NMR (500 MHz, DMSO-d6, 300 K): δ = 7.81 (s, 6H), 7.79 (s, 3H), 7.63 (s, 3H), 6.64 (s, 3H), 5.24 (s, 6-NH), 4.73 (s, 6H), 4.48 (s, 6H), 2.52 (s, 6H); 13C NMR (126 MHz, DMSO-d6, 300 K): δ = 167.5, 157.8, 144.7, 137.9, 135.9, 135.5, 132.2, 129.7, 118.0, 116.2, 65.2, 48.2, 38.3 ppm; HR MALDI-TOF m/z calcd for C57H39N9O6K: 984.266 [M+K]+, found: 984.229.

**Basket 2.1*:** A solution of trifluoroacetic anhydride (8.4 mg, 40.0 mol) in THF (100 L) was added dropwise to a stirred solution (THF, 0.8 mL) of compound 2.2 (4.7 mg, 5.0 mol) containing triethylamine (5.1 mg, 50.0 mol) at 0 ºC. The stirring was continued for 1.0 h, after which the solvent was evaporated in vacuum and the residue was purified by preparatory TLC (SiO2, CH2Cl2/CH3OH = 20:1) to yield a white solid product (4.3 mg, 70 %). 1H NMR (400 MHz, CDCl3, 300 K): δ = 12.22 (s, 3-NH), 8.32 (s, 3H), 8.31 (s, 6H), 7.42 (s, 6H), 4.78 (s, 6H), 4.44 (s, 6H), 2.55 (dd, J = 11.6 Hz, 8.4 Hz, 6H); 13C NMR (126 MHz, CDCl3, 300 K): δ = 166.8, 156.9, 157 (q, CF3C=O), 147.0, 142.5, 137.6,
135.7, 133.9, 132.7, 130.1, 117 (q, CF₃), 116.1, 66.0, 49.0, 38.1 ppm; HR MALDI-TOF m/z calcd for C₆₃H₃₆F₉N₉O₉K: 1272.213 [M+K]⁺, found: 1272.207.

**Basket 2.1.** A solution of benzoyl chloride (2.3 mg, 16.4 mol) in THF (100 L) was added dropwise to a stirred solution (THF, 0.5 mL) of compound 2.2 (3.0 mg, 3.2 mol) containing triethylamine (3.2 mg, 32.0 mol) at 0 °C. The stirring was continued for 1.5 h, after which the solvent was evaporated in vacuum and the residue was purified by preparatory TLC (SiO₂, CH₂Cl₂/CH₃OH = 15:1) to yield a white solid product (3.2 mg, 80 %). ¹H NMR (400 MHz, CDCl₃, 300 K): δ = 11.38 (s, 3- NH), 8.53 (s, 6H), 8.06 (s, 3H), 8.04 (s, 3H), 7.98 (s, 3H), 7.40-7.55 (m, 15H), 4.66 (s, 6H), 4.41 (s, 6H), 2.53 (s, 6H); ¹³C NMR (63 MHz, CDCl₃, 27 °C): δ = 167.2, 166.9, 156.7, 145.6, 143.1, 137.5, 135.4, 135.3, 133.9, 133.1, 132.0, 130.1, 128.5, 127.8, 116.0, 65.8, 49.0, 38.3 ppm; HR MALDI-TOF m/z calcd for C₇₈H₅₁N₉O₉Na: 1280.371 [M+Na]⁺, found: 1280.404.

**1,1,1-Tribromoethane 5:** To a solution of diisopropylamine (3.0 mL, 2.2 g, 21.4 mmol) in dry THF (30 mL) at −30°C was added dropwise n-butyllithium (1.6 M in hexanes, 13.0 mL, 20.8 mmol). The resulting solution was warmed to 0°C, stirred for 10 min, and then cooled to −95°C. Bromoform (1.75 mL, 5.06 g, 20.0 mmol) was added dropwise and the mixture was stirred for 10 min before a solution of methyl iodide (1.4 mL, 3.2 g, 22.5 mmol) in THF (10 mL) was added dropwise. The resulting mixture was stirred at −95° for 1.5 hr, slowly warmed to −70°C, quenched with 1.0 mL of aqueous NH₃/NH₄Cl buffer (pH 9.0), and warmed to room temperature. The mixture was partitioned with 1:1 H₂O:Et₂O (80 mL), separated, and the aqueous layer was washed once with Et₂O (40 mL).
The organic fractions were combined, dried with Na$_2$SO$_4$, concentrated in vacuum, and the resulting crude mixture was purified by Kügelrohr distillation (50°C, 80 mm Hg) to yield 1,1,1-tribromoethane (3.17 g, 59%) as a colorless liquid. $^1$H NMR (400 MHz, CDCl$_3$, 300 K): $\delta = 3.38$ (s) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$, 300 K): $\delta = 51.9$, 31.4 ppm.
References:


REFERENCES

    Taylor & Francis Group, LLC. 2007
(49) Felber, B.; Diederich, F. PNAS 2002, 99, 4778.
(60) Ballester, P.; Gil-Ramirez, G. PNAS, 2009, 106, 10455.


Soc. 2009, 131, 7250. (c) Rieth, S.; Bao, X.; Wang, B. Y.; Hadad, M. C.; Badjic, J. D.

(131) Borsato, G.; De Lucchim O.; Fabris, F.; Groppo, L.; Lucchini, V.; Zambon, A. J.
(132) Borsato, G.; De Lucchim O.; Fabris, F.; Lucchini, V.; Pasqualotti, M.; Zambon, A.
Ed. 2004, 43, 5503.
Science 1991, 253, 872.
1997, 119, 9513.
(141) Raymond, K. N. 2009, 460, 585.
(142) Pluth, M. D.; Bergman, R. G.; Raymond, K. N. Angew. Chem. Int. Ed. 2007, 46,
8587.
(144) Leung, D. H.; Bergman, R. G.; Raymond, K. N. J. Am. Chem. Soc. 2006, 128,
9781.
(145) Ziegler, M.; Brumaghim, J. L.; Raymond, K. N. Angew. Chem. Int. Ed. 2000, 39,
4119.
Soc. 2006, 128, 5887.
(147) Yan, Z.; Xia, S.; Gardlik, M.; Seo, W.; Maslak, V.; Gallucci, J.; Hadad, C. M.;


