TOWARDS AUTONOMOUS MOLECULAR MACHINES: SWITCHING COUPLED TO AN OSCILLATING REACTION

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TOWARDS AUTONOMOUS MOLECULAR MACHINES: SWITCHING COUPLED TO AN OSCILLATING REACTION

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ABSTRACT

TOWARDS AUTONOMOUS MOLECULAR MACHINES: SWITCHING COUPLED TO AN OSCILLATING REACTION

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September 2007, 49 pages

We have designed and synthesized a bistable pseudo-rotaxane carrying a fluorescent boradiazaindacene (BODIPY) unit. The intensity of the emission signal is dependent on the position of the cucurbituril (CB7) unit over the axle component. Thus, pH modulated switching of the CB7 wheel is accompanied by significant changes in the emission spectrum. Additionally, a thiosulfate-sulfite-iodate oscillating reaction which generates large amplitude pH oscillations can be carried out in the same solution. In such a solution, in response to changing pH, the position of the wheel component seems to change without outside intervention.

Keywords: Supramolecular chemistry, rotaxane, pseudorotaxane, shuttling, oscillatory reactions, luminescence

ÖZ

OTONOM MOLEKÜLER MAKİNELERE DOĞRU: OSİLASYONLU REAKSİYON ORTAMINDA GERÇEKLEŞEN YER DEĞİŞTİRME

İçli, Burçak

Yüksek Lisans, Kimya Bölümü

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Floresan boradiazaindasen (BODIPY) içeren iki durumlu psödo-rotaksan tasarlanıp sentezlenmiştir. Emisyon sinyal şiddetinin molekülün aks bileşeni üzerinde kükürbituril (CB7) yapısının pozisyonuna bağlı olarak değiştiği gözlemlenmiştir. Bunun sonucunda, pH ile modüle edilen CB7'nin yer değistirme hareketinin eşliğinde emisyon spektrumunda önemli değişiklikler mevcuttur. İlaveten, geniş aralıklarda pH salınımına yol açan tiosülfat-sülfit-iyodat salınım reaksiyonu bu sistem içerisinde gerçekleştirilebilmiştir. Böyle bir çözelti içerisinde pH'ın değişmesiyle yapıdaki halka bileşeni dışarıdan müdahale olmadan konum değişikliğini gerçekleştirmiştir.

Anahtar Kelimeler: Supramoleküler kimya, rotaksan, psödorotaksan, salınım hareketi, salınım reaksiyonları, lüminesans

Dedicated to my family ...

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LIST OF ABBREVIATIONS

ATPase	Adenosintriphospatase
NMR	Nuclear Magnetic Resonans
UV-VIS	Ultraviole Visible
PET	Photoinduced Electron Transfer
PCT	Photoinduced Charge Transfer
CB[6]	Cucurbit[6]uril
BODIPY	Boradiazaindacene
CB7	Cucurbit[7]uril
CSTR	Continuous-flow stirred tank reactor

CHAPTER 1

INTRODUCTION

1.1 What Is Supramolecular Chemistry?

Molecular chemistry, the chemistry of the covalent bond, is concerned with uncovering and mastering the rules that govern the structures, properties and transformations of molecular species

Supramolecular chemistry, originated from Paul Ehrlich's receptor idea, Alfred Werner's coordination chemistry and Emil Ficher's lock-and-key image, may be defined as "chemistry beyond the molecule," bearing on the organized entities of higher complexity that result from the association of two or more chemical species held together by intermolecular forces. Its development requires the use of all resources of molecular chemistry combined with the desired manipulation of noncovalent interactions. [1]

Supramolecular chemistry aims to develop highly complex chemical systems from components interacting by non-covalent intermolecular forces [2]. It is

concerned with next step in increasing complexity beyond the molecule toward the supramolecule and organized polymolecular systems, held together by non-covalent interactions(Fig.1.1).

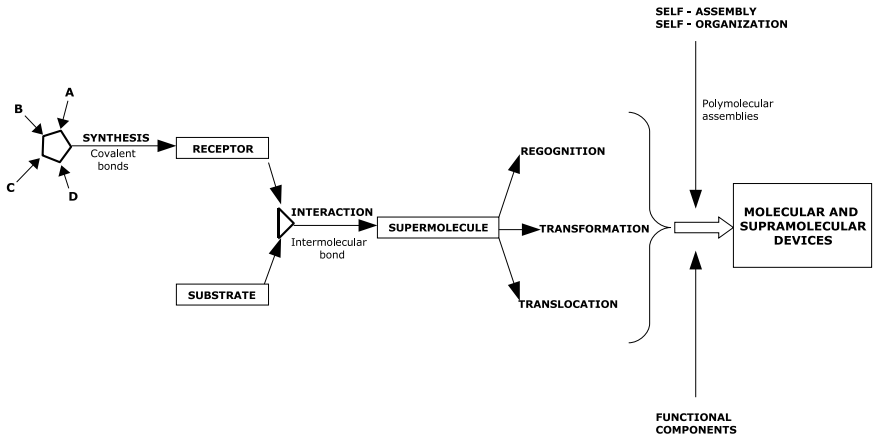

Figure 1.1: From molecular to supramolecular chemistry: Molecules, supramolecules, molecular and supramolecular devices.

The breadth and especially the unifying power of the concept became progressively more and more apparent, so that recent years have seen an explosive growth as measured by the increasing number of laboratories that join the field and whose work has been reported in a vast range of publications, books, journals, meetings and symposia. Supramolecular chemistry has thus developed into a coherent and extremely lively body of concepts and objects, progressively generating and incorporating novel areas of investigation [3].

1.2 The Concept of Molecular Level Machines and Devices

The progress of human civilization has always been related to the construction of novel devices and machines. How can we define a device or a machine? A

device is a contrivance or an invention serving a particular purpose, especially a machine used to perform one or more relatively simple tasks. A machine is any combination of mechanism for utilizing, modifying, applying or transmitting energy, whether simple or complex [4].

In chemistry, a molecular level device can be defined as an assembly of a discrete number of molecular components designed to perform a specific function. Each molecular component performs a more complex function, which results from the cooperation of the various components. A molecular level machine is a particular type of molecular level device in which the relative positions of the component parts can change as a result of some external stimulus [5]. Molecular level devices and machines operate via electronic and/or nuclear rearrangements and, like macroscopic devices and machines, need energy to operate and signals to communicate with the operator.

In the last fifty years, a great variety of new devices and machines has come into use for collecting, processing, displaying, and storing information. The outstanding development of information technology has been closely related to the progressive miniaturization of the components employed for the construction of such devices and machines. One might wonder whether we really do need to keep making things smaller. The answer is that further miniaturization will not only reduce the size and increase the power of computers, but is also expected to open the way to new technologies capable of revolutionizing medicine, producing a wealth of new materials providing renewable energy sources and solving the problem of environmental pollution [6].

It is becoming increasingly apparent, however, that modern computer technology, which relies on silicon based chips, is rapidly approaching the limits of its physical capabilities. To proceed toward further miniaturization, science and technology will have to find new ways [6].

An alternative and promising strategy toward technology on the nanometer scale is offered by the bottom-up approach, which starts from atom or molecules and builds up to nanostructures [6].

The idea that atoms could be used to construct nanoscale machines was first raised by Feynman [7] and depicted in a visionary way in the mid-1980s by K.Eric Drexler [8].

In the late 1970s, in the frame of research on supramolecular chemistry, studies on molecular electronic devices began to flourish and the idea arose in a few laboratories that molecules could be much more convenient building blocks than atoms to construct nanoscale devices and machines. This idea based on the following points: (i) Molecules are stable species, whereas atoms are difficult to handle; (ii)Nature uses molecules, not atoms to construct the great number and variety of nanodevices and nanomachines that sustain life; (iii)Most laboratory chemical processes deal with molecules, not atoms; (iv)Molecules are objects that already exhibit distinct shapes and carry device-related properties (e.g. properties that can be manipulated by photochemical and electrochemical inputs); and (v)Molecules can self-assemble or can be connected to make larger structures [9].

In the following years, supramolecular chemistry grew very rapidly and it became clear that the supramolecular bottom-up approach opens virtually un-

limited possibilities.

1.3 Molecular Switches

The expression "molecular level switch" usually has two distinct meanings. The first definition is a molecular level device, incorporated in a molecular level wire, that can reversibly interrupt the movement of electrons or electronic energy across it, in response to some external stimulus. The second definition, which covers a much larger field and can also be thought to include the first definition, relates to the binary logic of computing, and describes any molecular logic system that can be reversibly interconverted between two(or more) different states by some external stimulus [6]. Those external stimulus could be light energy(photons), electrical energy (electrons or holes) and chemical energy (protons, metal ions, specific molecules etc.).

When switching involves large nuclear movements, particularly in supramolecular systems, the mechanical aspect might became more interesting than the switching process itself [5, 10]. In this perspective we can move to the molecular machines idea.

1.4 Basic Principles of Molecular Machines

The concept of a machine at the molecular level is not a new one. The mother nature has already its perfectly working molecular level machines, biological molecular machines. A fascinating example of it is F_1-ATPase, a rotary motor. Its rotary motion controlled by the pH gradient between inside and outside of the

membrane in our body (fig.1.2).

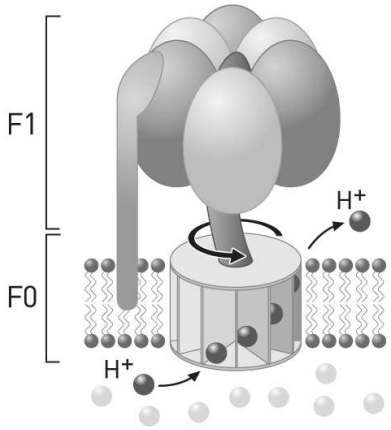

Figure 1.2: F_1-ATPase

Recently, inspired from numbers of examples, the concept of the artificial molecular machine builds up in the minds.

A molecular level machine can be defined as an assembly of a discrete number of molecular components designed to perform mechanical like movements (output) as a consequence of appropriate external stimuli (input) [5].

Molecular level machines must contain a motor, which in principle consists of a mobile and a stationary part. An external operator should be able, by means of a given input, to induce the displacement of the movable component from the stationary one [6].

Like macroscopic machines, molecular level machines are characterized by [6]:

- The kind of energy supplied to make them work

  To make a molecular machine work, energy must be supplied to its motor. There are three types of energy input for the molecular machines: Light energy, electrochemical energy and chemical energy (fig.1.3).

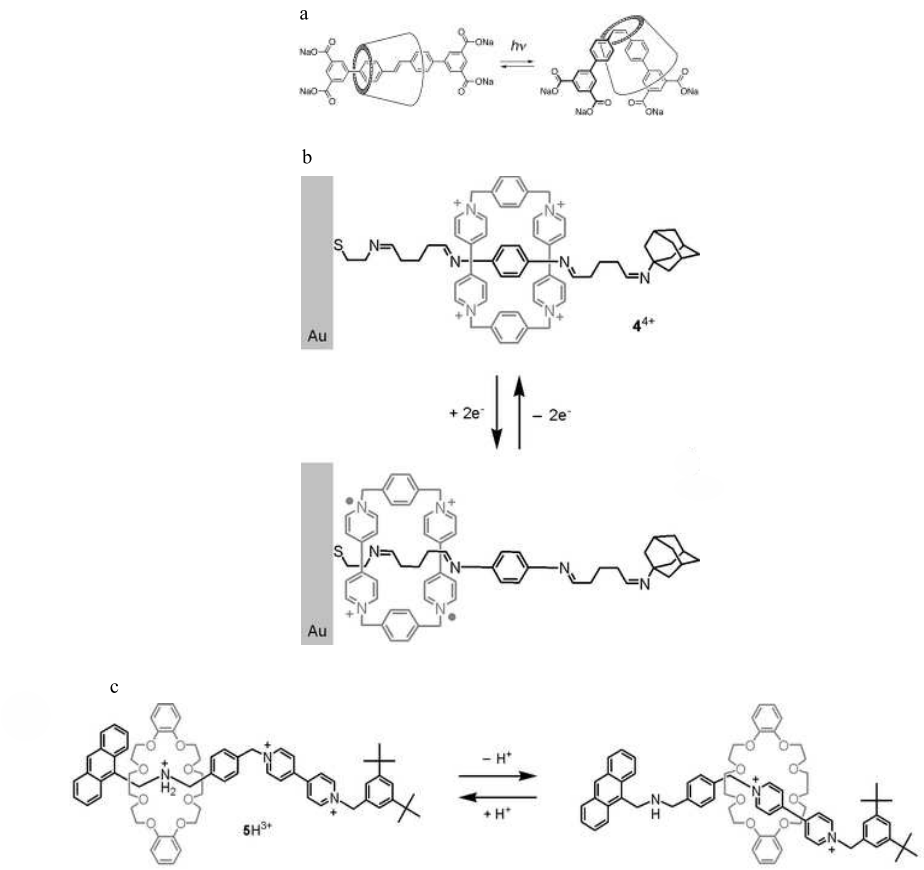

Figure 1.3: Molecular machines characterized according to their energy input. a)Photoinduced shuttling in a stilbene-based CD rotaxane [11]. b)Electrochemically driven shuttling of the cyclophane upon reduction or oxidation [12]. c)Chemically, acid-base, switchable rotaxane [13].

- The kind of movement performed by their components

  The movements performed by the component parts of artificial molecular level machines can be of variety of types (fig.1.4).

  - Translocation (allosteric, tweezer like, assembly-disassembly)
  - Rotary
  - Dethreading-Rethreading
  - Linear

– Opening-Closing

– Contraction etc.

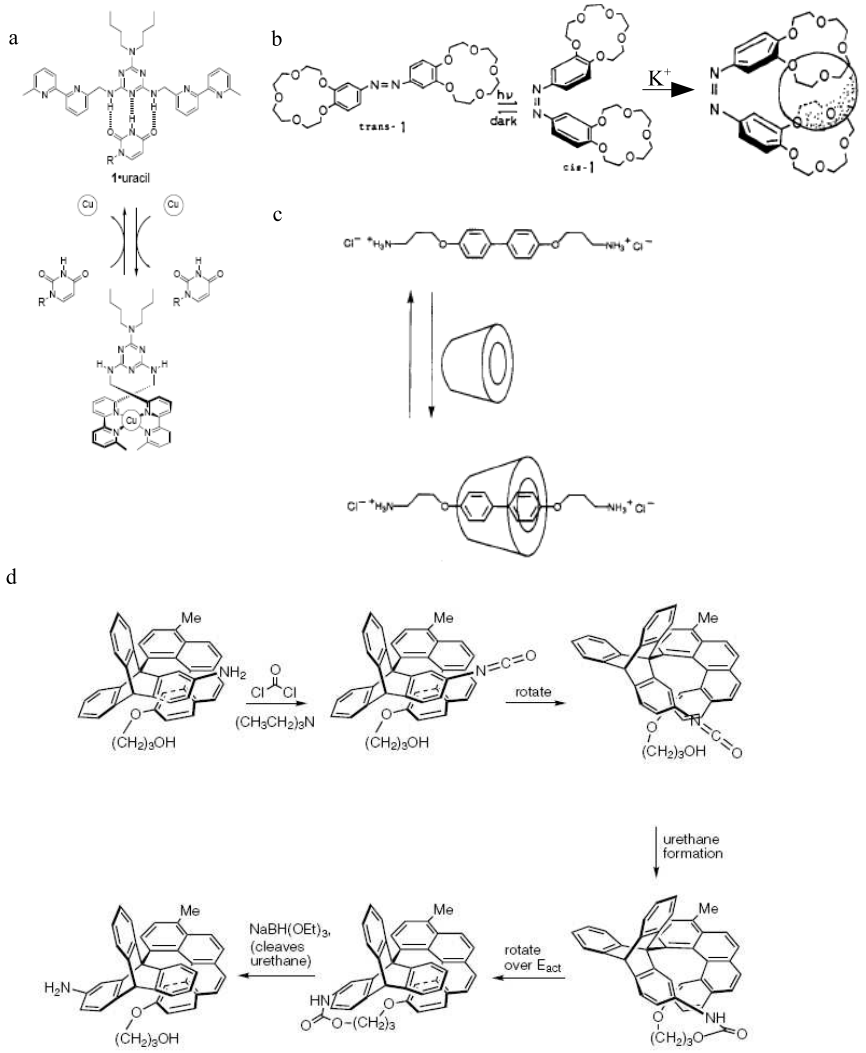

Figure 1.4: Examples to the movements performed by molecular machines. Conformational changes in artificial systems: Movements related to opening, closing and translocation (allosteric (a) [14], tweezer like (b) [15]); Amine-acid controlled dethreading-rethreading cycle of the pseudorotaxane (c) [16]; Sequence of events causing unidirectional rotation powered by phosgene as a chemical fuel (d) [17])

- The manner in which their operation can be controlled and monitored

  In order to control and monitor the machine operation, the motions of the component parts should cause readable changes in some properties of

the the system; any kind of chemical or physical technique can be useful, particularly the various types of spectroscopic methods (Nuclear Magnetic Resonance (NMR), UV-VIS Absorption, Luminescence)

- The ability to make it repeat its operation in a cyclic fashion

  A machine must work by repeating cycles. Any chemical reaction related to the movements performed by the component parts must be reversible. This requirement is reasonably well met by many proton-transfer (acid-base) and electron-transfer (redox) reactions, by photoinduced isomerization reactions.

- The function performed

  The functions that can be performed by using the movements of the component in artificial molecular level machines are various and still unpredictable.

1.5 Rotaxanes and Pseudorotaxanes

Rotaxanes are made from an axle threaded in to a wheel via the intermolecular forces. The axle is restrained to remain inside the wheel by switchable stopper groups that prevent deslipping. In contrast, a pseudorotaxane is formed when noncovalent forces bind an axle inside a macrocyle without help of stoppers (fig.1.5). The name, rotaxane, is derived from the Latin for wheel (*rota*) and axle (*axis*).

There are many pathways to build up a rotaxane or a pseudorotaxane. All of these pathways only give high yields of them if attractive forces between wheel

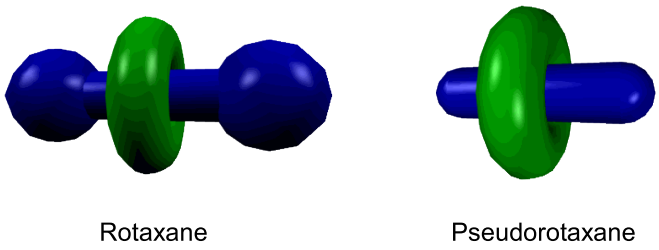

Figure 1.5: Schematic representation of a rotaxane and a pseudorotaxane

and axle are operative. This idea led to the development of several different template effects based on noncovalent bonding between axle and wheel.

- Metal ion template (Metal coordination)

  This type of templates are introduced to the literature by J.P Sauvage and his coworkers [18]. First example is the copper(I) ion bound to the phenanthroline ligand inside a macrocycle. (fig.1.6)

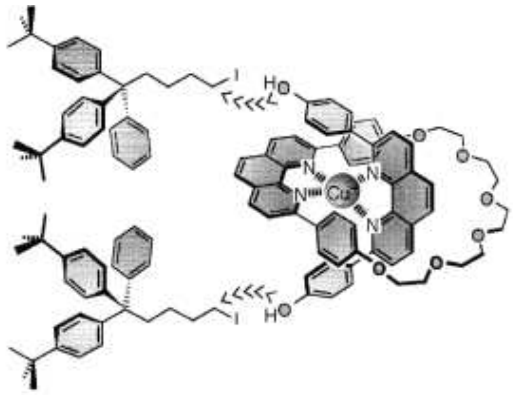

Figure 1.6: Metal ion templated rotaxane

- $\pi - \pi$ interaction

  Stoddart and his group utilized π-donor, π-acceptor interaction between electron poor paraquat and electron rich hydroquinone moieties in order to

preorganize a rotaxane (fig.1.7) [19].

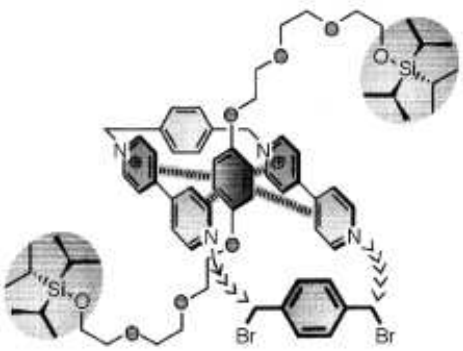

Figure 1.7: Rotaxane based on $\pi - \pi$ interaction

- Hydrogen bonding

  Hydrogen bonding is an excellent candidate for noncovalent templating, in particular because hydrogen bonds are directional in nature and thus may help to appropriately position two building blocks for a rotaxane relative to each other. Hydrogen bonding could be used a nonionic template in rotaxane synthesis. The first examples of this idea is actualized by Vogtle and his group (fig.1.8) [20].

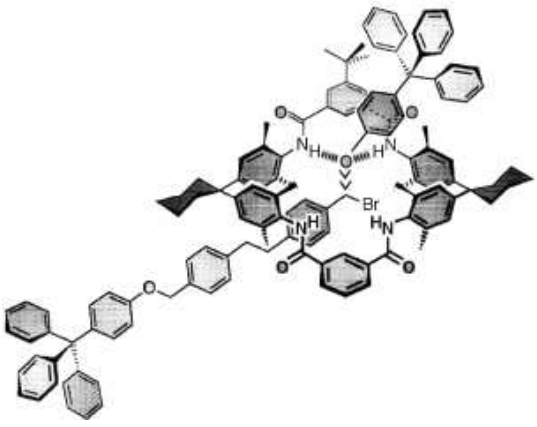

Figure 1.8: Hydrogen bond assisted nonionic template synthesis of rotaxanes

- Electrostatic interactions (ion-ion, ion-dipole, and dipole-dipole)

  There are several examples of rotaxanes and pseudorotaxanes assisted by electrostatic interactions. The most employed one is the anion template (fig.1.9).

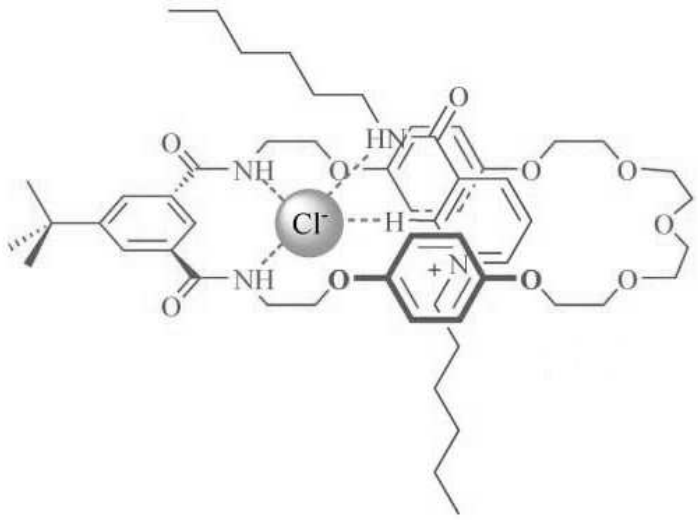

Figure 1.9: Anion templated pseudorotaxane [21]

- hydrophilic and hydrophobic interactions

  The hydrophobic environment created by the molecules such as cyclodextrins and cucurbiturils attract the hydrophobic moieties to it selfs creating hydrophobic interaction templated rotaxanes or pseudorotaxanes (fig.1.10).

1.6 Molecular Machines Based On Rotaxanes and Pseudorotaxanes: Linear movements of Molecular Shuttles

Linear like movements are essential both in Nature and in technology. In the artificial macroscopic world, most machines are powered by engines working on the principle of linear alternating motion of a piston in a cylinder.

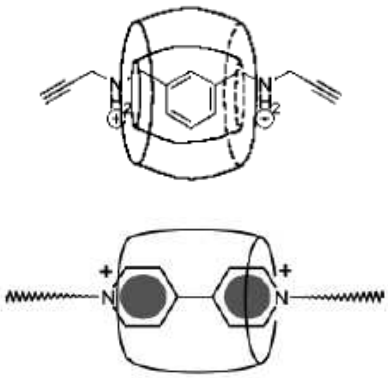

Figure 1.10: Pseudorotaxane designed and synthesized on the basis of Cucurbituril hydrophobic binding interactions

Simple artificial molecular level systems capable of performing linear movements are not difficult to construct since the development of rotaxane chemistry. Such artificial systems are completely different from natural linear motors not only structuraly and functionally, but also because most of them can be powered by chemical, photochemical or electrochemical inputs [6].

In this section, I will briefly discuss artificial molecular level machines based on rotaxanes and pseudorotaxanes.

If, during the template directed synthesis of a rotaxane, location of two identical recognition sites within its dumbbell component can be arranged, the results is a degenerate, conformational equilibrium state in which the macrocyclic component spontaneously shuttles back and forth along the linear portion of the dumbbell [22, 23]. When the two recognition sites, stations, in the dumbbell component differ in their constitution, a rotaxane can exist as two different equilibrating conformations the population which reflect their relative free energies determined primarily by the strengths of the two different sets of noncovalent bonding interactions [6].

A molecular shuttle resides preferentially in "state 0" until a stimulus is applied that switches off the stronger of the two recognition sites, thus inducing the macrocycle to move to the second weaker recognition site, "state 1". In appropriately designed rotaxanes this nondegenerate process can be controlled reversibly by use of chemical, electrochemical or photochemical stimuli. By switching off and on again the recognition properties of one of the two recognition sites, the relative proportions of the two species can be controlled reversibly. (fig.1.11)

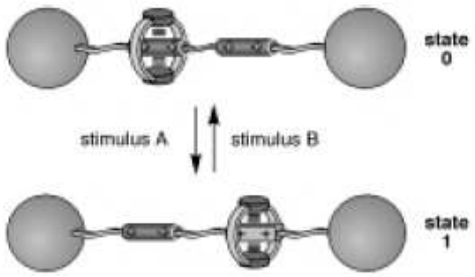

Figure 1.11: Controllable switching of a rotaxane by appropriate stimuli

Here is a chemically controlled molecular machine. An exiting development in the field of linear artificial molecular machines: Molecular scale muscle (fig.1.12) [24]. Under the action of an external stimulus both strings (mimicking the muscle filaments (fig.1.12a)) can move along one another, but the assembly stay together thanks to the pseudorotaxane nature of the system. Switch from the non contracted situation to contracted situation is obtained by replacing the four coordinate metal of the compound represented on the left of the fig.1.12b (Cu(I)) by a five coordinate center (white disc; Zn(II)).

There also exist chemically shuttling molecular machines which are animated by pH change. An enhanced example of it, is demonstrated by the group of

J. F. Stoddart in the research area (fig.1.13) [25]. On addition of excess i-

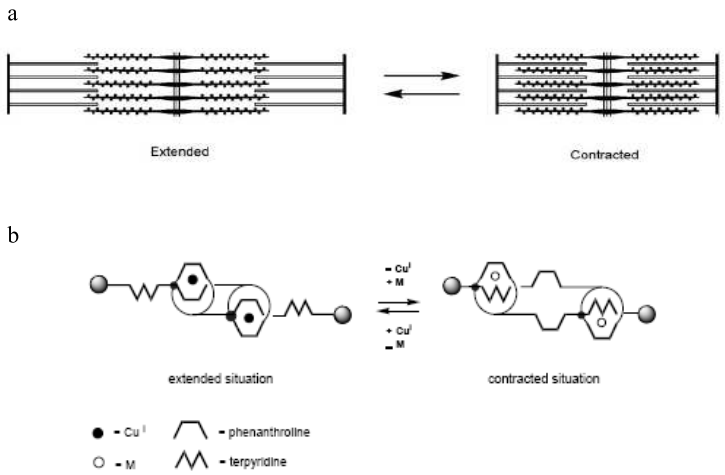

Figure 1.12: Functioning principle of a unimolecular synthetic muscle

Pr_2NEt to a solution of rotaxane, deprotonation of the ammonium recognition site occurs. As a result, the intercomponent hydrogen bonds are destroyed

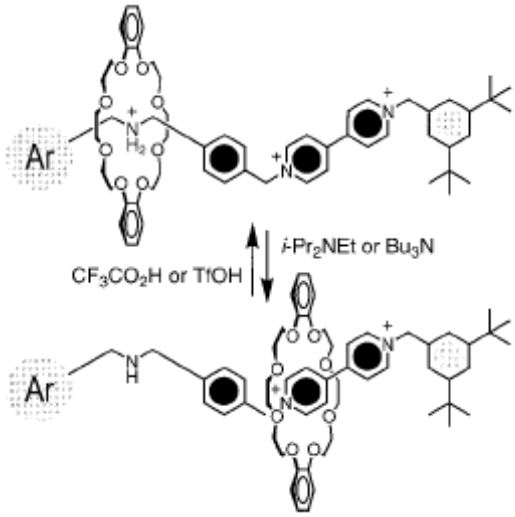

Figure 1.13: The acid base controllable molecular shuttle

and the macrocycle shuttles to the bipyridinium recognition site. The original conformation is restored by addition of CF_3CO_2H, because protonation of the ammonium recognition site is followed by the shuttling of the macrocycle back

to encircle the NH_2^+ center.

A work done by Stoddart and his group has made a new contribution to the field. Their system can be switched by two different mechanism. Theirs is a chemically and electrochemically switching molecular shuttle (fig.1.14) [26].

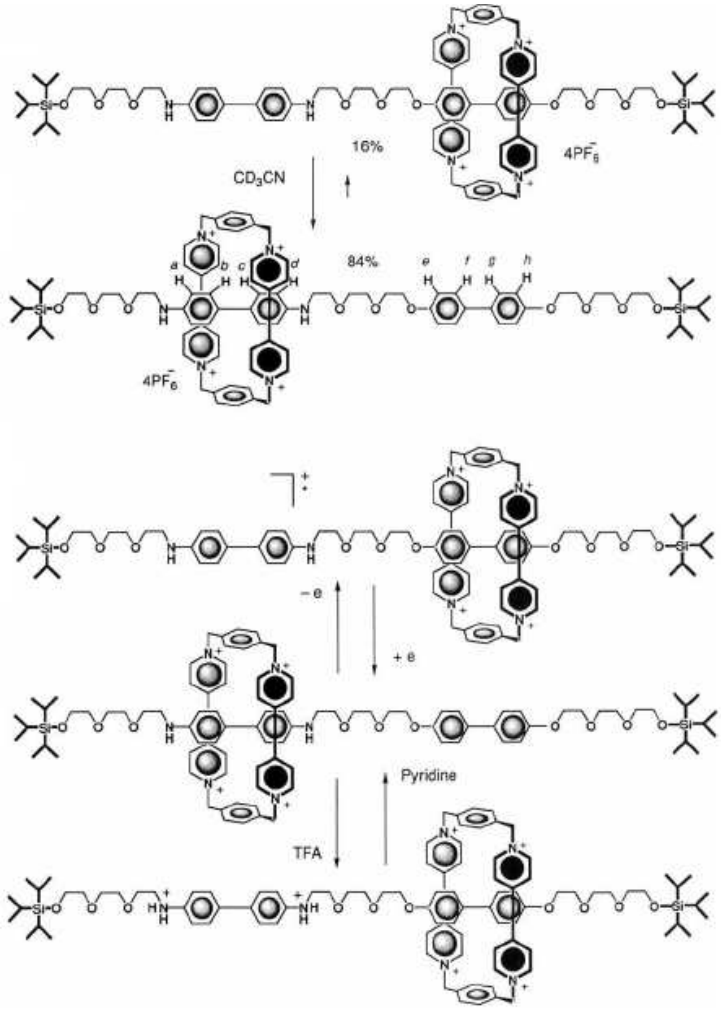

Figure 1.14: The shuttling of the macrocyclic component of the rotaxane along its dumbell shaped component can be controlled chemically or electrochemically by protonating-deprotonating or oxidizing-reducing the benzidine unit.

Several examples of rotaxanes or pseudorotaxanes that behave as light driven molecular shuttles are known. An advanced example is actualized by He Tian (fig.1.15). Since the absorption and spectral changes related to the interconversion

between the four states of the system could be interpreted in terms of AND and XOR binary logic functions, rotaxane was shown to perform as a reversible half-adder device with all optical input and output signals [27].

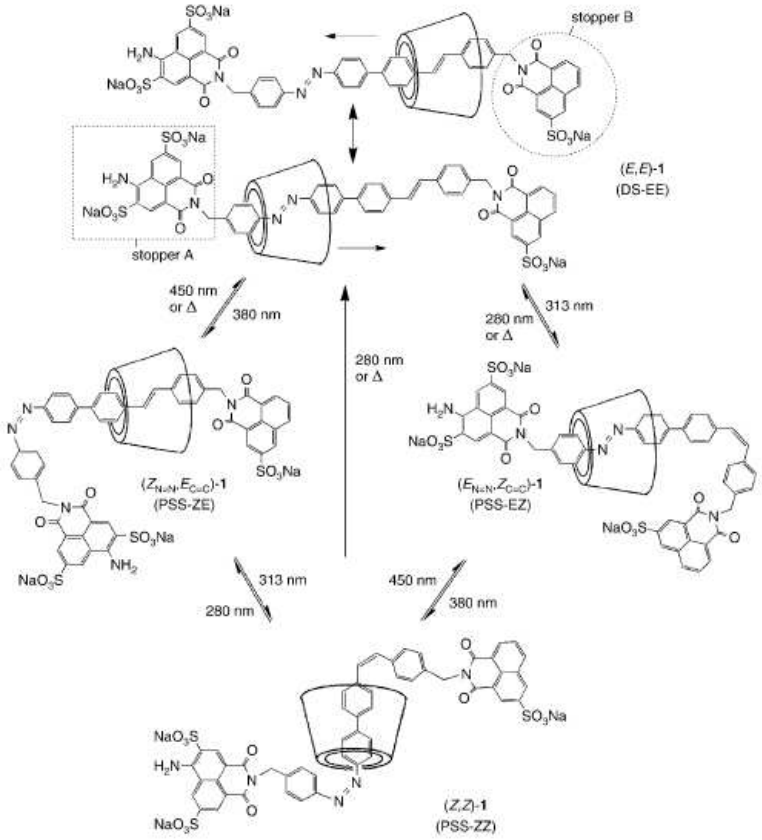

Figure 1.15: A half adder based on a photochemically driven rotaxane

The Cucurbit[n]uril family is ideally suited for molecular switches that can toggle between two different states by appropriate stimuli. Kim and coworkers have reported many molecular shuttles based on Cucurbituril family. From latest examples, a bistable rotaxane which behaves as a kinetically controlled machine can be examined (fig.1.16). Switching from one state to the other is driven by pH change but the reverse process requires pH change plus thermal activation. De-

protonation of the protonated diaminobutane unit in the rotaxane promotes the movement of CB[6] from station A to station B. Diisopropylethylamine was found to be an ideal base to drive the switching process because it is strong enough to deprotonate the NH_2^+ while behaving concurrently as an unreactive nucleophile towards the viologen units. Reprotonation can be performed by addition of a suitable acid such as DCl [28].

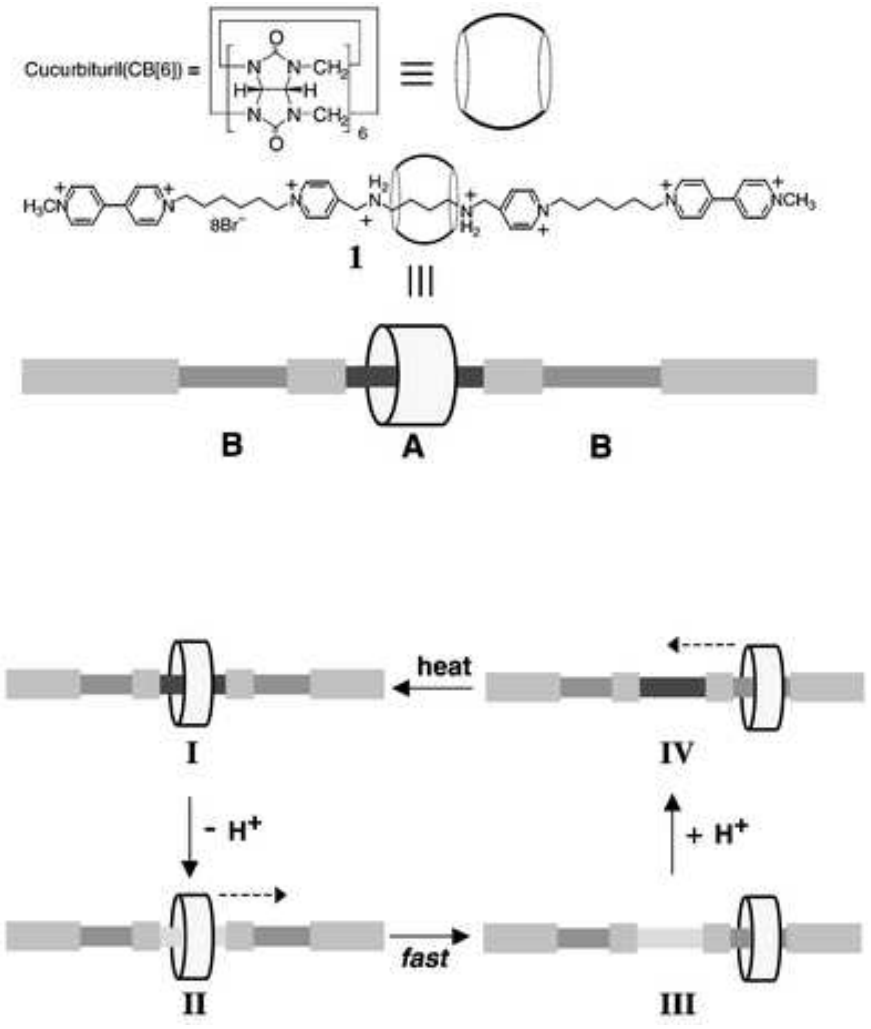

Figure 1.16: The cucurbituril based rotaxane and its switching scheme

Cucurbit[n]urils

Cucurbiturils are macrocyclic compounds made by an acid-catalyzed condensation reaction of glycoluril and formaldehyde. Characteristic structural features of cucurbiturils are the hydrophobic cavity and the polar carbonyl groups surrounding the portals. Cucurbit[5]uril and cucurbit[7]uril are quite soluble in water. The solubility of cucurbiturils in common organic solvents is less than 10^{-5} M, and therefore the host-guest chemistry of cucurbiturils has mainly been studied in aqueous media. Several intermolecular interactions promote the binding of guests by cucurbiturils. First, similar to cyclodextrins, a hydrophobic effect applies: This composite effect is derived from the interplay between the release of high-entropy water upon inclusion of nonpolar organic residues and concomitant differential dispersion interactions inside the cavity and in the bulk water. Second, ion-dipole interactions of metal cations or organic ammonium ions with any of the two ureido carbonyl rims may come into play, while hydrogen-bonding interactions prevail less frequently [29].

Variation of the sizes of the cavity and the portal leads to a variety of cucurbiturils with different molecular recognition properties. The larger cavity of cucurbit[7]uril means that it forms 1:1 complexes with ammonium-functionalized adamantane or ferrocene, as well as viologen dications and 2,6-bis(4,5-dihydro-1H-imidazol-2-yl)naphthalene. Cucurbit[7]uril can form complexes with viologen dications in two different ways: Methyl and ethyl viologen dications form inclusion complexes in which the viologen is located within the cavity, while butyl (and other viologens with longer aliphatic substituents on the nitrogen atom) form ex-

ternal complexes in which the viologen nucleus is not engulfed by the host. Salts strongly influence the apparent association constant of cucurbit[7]uril with the methylviologen dication, with a more pronounced effect for solutions containing divalent Ca^{+2} ions than for solutions containing monovalent Na^{+} ions [29].

1.7 Photophysical Methods

During the last two decades, there has been an enormous increase in the use of photophysical methods in supramolecular chemistry. Photophysical methods generally offer numerous advantages of crucial importance for supramolecular chemists, particularly high sensitivity, i.e., reliable output at low concentration. Also important is the possibility of selectively probing individual chromophoric parts of molecules and supramolecules. The accessibility of the information from dilute samples is important to a supramolecular chemist, as the typical features studied in supramolecular chemistry, such as receptor substrate association and formation and dissociation of supramolecular associates and complexes, typically suffer from side effects such as receptor-receptor self-association and component homoassociation at higher concentrations. Additional advantages of photophysical methods are the usually nondestructive nature of the measurements and the small sample volume required for the experiments [30].

1.7.1 Fluorescence Phenomena

The most widely used mode of fluorescence modulation is the decrease or increase of fluorescence intensity at a single emission wavelength upon analyte binding. It is mostly used in recognition processes. Light signals emitted by purpose-

built molecular devices gives us the information about binding of the analyte. Mostly used phenomena in supramolecular recognition by chemosensors are PET (Photoinduced Electron Transfer) and PCT (Photoinduced Charge Transfer), which are discussed in the following subsection. Most recently the fluorescence signaling phenomena found its place in molecular switches (molecular logic gates) [31] and rotaxane based molecular switches [32, 33].

1.7.1.1 Photoinduced Electron Transfer (PET) [31]

Due to its central role in photosynthesis there is a lot to find out in this subject. Nevertheless, there is not much work done in the area, but some pioneering efforts being scattered across the last two decade.

Fluorescent signaling via the PET strategy is distinguished by its intrinsically supramolecular nature since distinct components perform each one (or more) of the necessary functions. A fluorophore module is the site of both photonic transactions of excitation and emission. A receptor module is responsible for guest complexation and decomplexation. A spacer module holds the fluorophore and receptor close to, but separate from, each other. This also means that true molecular engineering applies. Further, PET signaling systems have natural "all or none" switchability: Guest-induced "off-on" and "on-off" fluorescence are both designable.

The work done by Weller on 1970 uncover the thermodynamic basis of PET. Figure 1.17 provides a summary in terms of frontier orbital energies. It also shows how PET systems employ thermal back electron transfer as a self repair

mechanism.

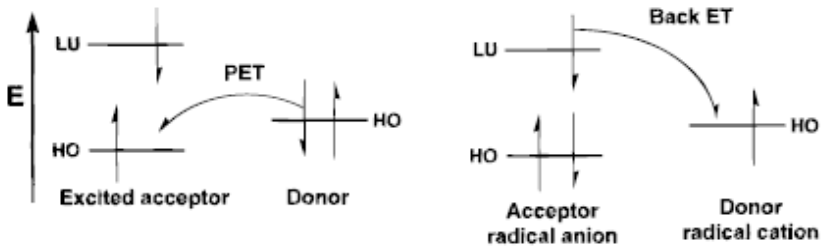

Figure 1.17: Frontier orbital energy diagrams illustrating thermodynamics of PET and back electron transfer.

Stoichiometric host-guest recognition is more popular avenue for fluorescence PET signaling. This strategy is schematized in Figure 1.18. A somewhat more

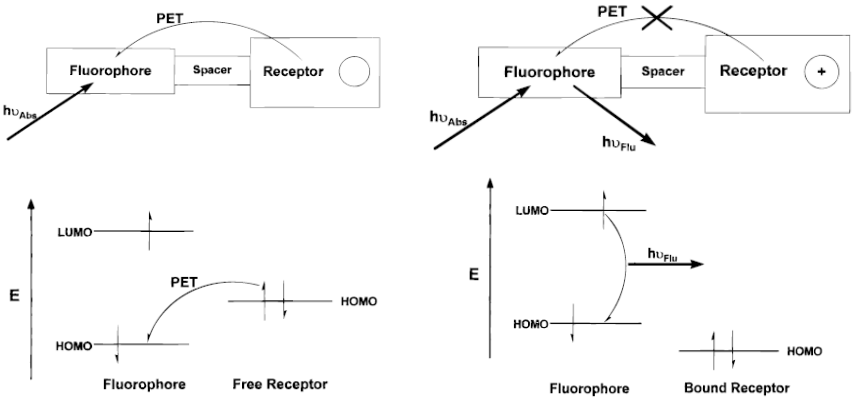

Figure 1.18: Spaced fluorophore-receptor system in the "off" state (top left). The thermodynamic condition for PET is that the excited-state energy of the fluorophore must be sufficient to oxidize the receptor and reduce the fluorophore. Spaced fluorophore-receptor system in the "on" state (top right). PET is thermodynamically disfavored since the oxidation potential of the receptor is raised by cation entry. Frontier orbital energy diagrams for both (bottom).

quantitative view is in terms of the frontier molecular orbital energies given in the bottom part of Figure 1.18. The fact that cationic guests are chosen in these figures simply reflects their dominance in the literature thus far. One reason for this dominance is that receptor design for metal ions is relatively rational.

Examples based on the boradiazaindacene derivatives to the Fluorescence PET signaling systems are given in the subsection "Boradiazaindacene Fluorophore".

1.7.1.2 Photoinduced Charge Transfer (PCT) [34]

When a fluorophore contains an electron-donating group (often an amino group) conjugated to an electron-withdrawing group, it undergoes intramolecular charge transfer from the donor to the acceptor upon excitation by light. The consequent change in dipole moment results in a Stokes shift that depends on the microenvironment of the fluorophore; polarity probes have been designed on this basis. It can thus be anticipated that cations in close interaction with the donor or the acceptor moiety will change the photophysical properties of the fluorophore because the complexed cation affects the efficiency of intramolecular charge transfer.

When a group (like an amino group) playing the role of an electron donor within the fluorophore interacts with a cation, the latter reduces the electron-donating character of this group; owing to the resulting reduction of conjugation, a blue shift of the absorption spectrum is expected together with a decrease of the extinction coefficient. Conversely, a cation interacting with the acceptor group enhances the electron-withdrawing character of this group; the absorption spectrum is thus red-shifted and the molar absorption coefficient is increased. The fluorescence spectra are in principle shifted in the same direction as those of the absorption spectra. In addition to these shifts, changes in quantum yields and lifetimes are often observed. All these photophysical effects are obviously dependent on the charge and the size of the cation, and selectivity of these effects

are expected.

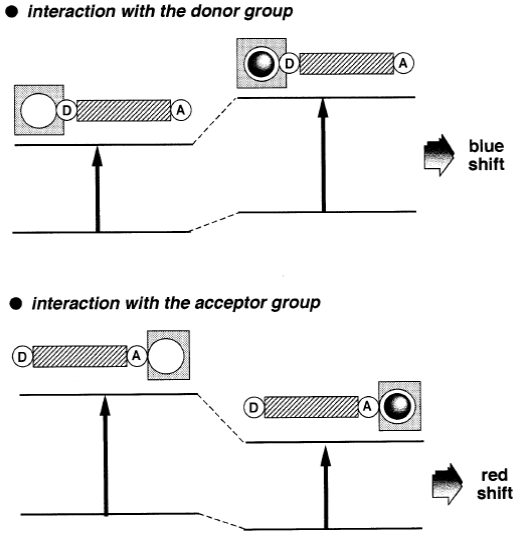

Figure 1.19: Spectral displacements of PCT sensors resulting from interaction of a bound cation with an electron-donating or electron-withdrawing group.

The photophysical changes upon cation binding can also be described in terms of charge dipole interaction. Let us consider only the case where the dipole moment in the excited state is larger than that in the ground state. Then, when the cation interacts with the donor group, the excited state is more strongly destabilized by the cation than the ground state, and a blue shift of the absorption and emission spectra is expected (however the fluorescence spectrum undergoes only a slight blue shift in most cases, fluorescence emission spectra are less affected due to cation ejection during the excited state). Conversely, when the cation interacts with the acceptor group, the excited state is more stabilized by the cation than the ground state, and this leads to a red shift of the absorption and emission spectra (Fig.1.19).

Examples based on the boradiazaindacene derivatives to the fluorescence PCT signaling systems are given in the subsection "Boradiazaindacene Fluorophore".

Boradiazaindacene Fluorophore

The BODIPY (Boradiazaindacene) dyes were first prepared by Treibs and Kreuzer in 1968 [35]. Treibs and Kreuzer described two synthetic routes to monomeric, stable boron-dipyrromethene (BODIPY) complexes. First, the BF_3-catalyzed condensation of 2.5-dimethylpyrrole with acetic anhydride affords the corresponding pentamethyl, mono- or bis-acylated BDPY dyes in around 10 % yield. Alternatively, treatment of a dipyrromethene with triethylamine and BF_3-etherate affords the BODIPY dye in 55-80 % yield.

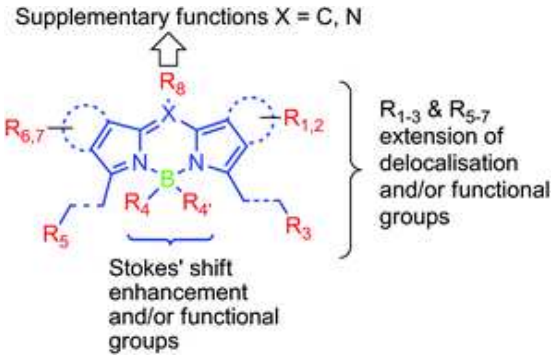

Figure 1.20: Possible modification sites for BODIPY fluorophores

BODIPY derivatives are highly fluorescent dyes with large solubility possibilities and being amenable to structural modification (fig.1.20) that have applications in many different areas. In 8-phenylboradiazaindacene derivatives, the phenyl π-system is virtually decoupled from the rest of the molecule especially when the 1 and 7 positions are substituted. Strong PET activity is possible from this orthogonal substituent, creating yet to be explored opportunities for molecular sensing/signaling. 4-hydroxyphenyl- [36] (fig.1.21a), -Calix[4]arene- [37] (fig.1.21b), 4-Dialkylaminophenyl- [38] (fig.1.21c) and 4-Azathiacrownphenyl-

[39] (fig.1.21d) substituted boradiazaindacenes showed interesting PET-mediated

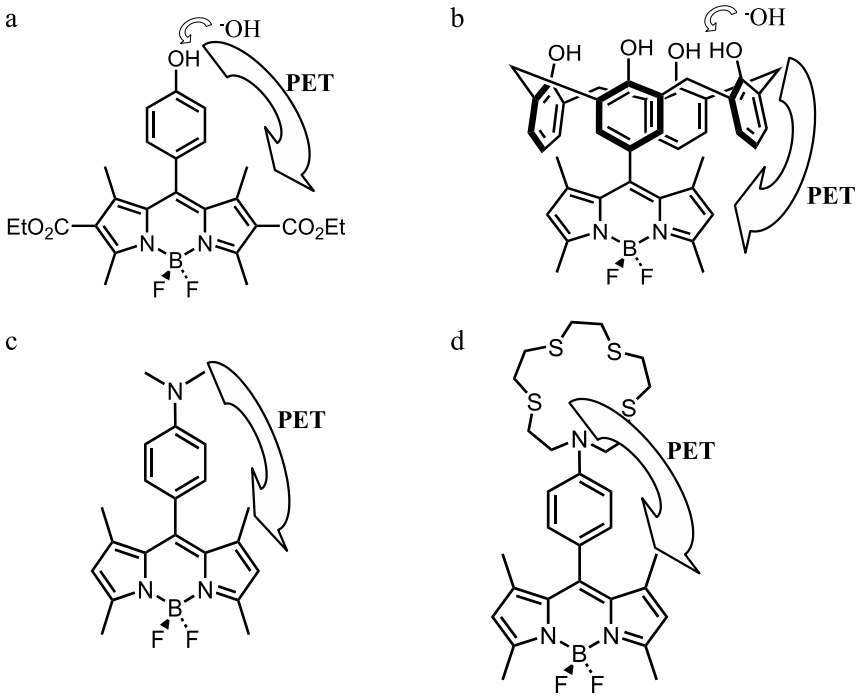

Figure 1.21: Fluorescence PET signaling systems

fluorescence signals. Remarkable photophysical properties of these dyes, like high quantum yield, high extinction coefficient, and narrow emission peak leading to higher peak emission intensity, would be exploited in many areas [37].

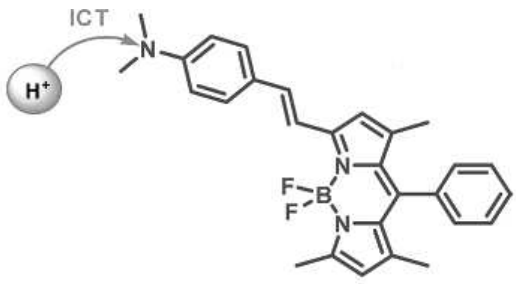

Figure 1.22: Blue shifted PCT signaling system

Substitution at the 3rd or the 5th position of BODIPY result in extended conjugated derivatives. 4-Dialkylaminophenyl- substituted one result in bora-

diazaindacene type PCT fluorophore [40]. Addition of strong acid result in a considerable blue shift in both absorbance and the emission spectra (fig.1.22).

1.8 Oscillatory Reactions

Most reactions proceed smoothly, at varying rates, to a final state of equilibrium. Some, however, do not. They oscillate in time: Reactant, product, or intermediate species concentrations fluctuate wildly, often leading to easily observable oscillations in time of these concentrations.

These reaction systems are of great interest. The most famous oscillating chemical reaction is the Belousov-Zhabotinsky (BZ) reaction. This is also the first chemical reaction to be found that exhibits spatial and temporal oscillations.

In a greatly simplified way the process can be interpreted as follows. In a first phase (I), Ce^{4+}ions are reduced to $Ce^{3+}$and, at the same time, malonic acid is brominated. In a second phase (II), Ce^{3+} is oxidized back to Ce^{4+} by the bromate ions present. The net oscillating process is arrived at by combining these two steps. This rhythmically changing potential can be visualized by the introduction of ferroin, a redox indicator which change color between its oxidized and reduced form (blue-red).

1.8.1 pH Oscillation Reactions

In the abundant literature of oscillatory reactions there are very few results concerning the periodic change of pH. This is because most of the reactions exhibiting oscillatory kinetics occur in fairly acidic medium. There are only three reported pH oscillation in closed systems; sodium dithionate decomposition system [41],

iodate-iodine-hydrogen peroxide system [42], Belousov-Zhabotinskii oscillating system without strong acid [43]. Each case the pH changes hardly exceed the experimental error [44].

But recently G. Rabai and M. T. Beck observed pH oscillations between pH 4-7 in an iodate-Thiosulfate-Hydrogen sulfite system with sharp minima in pH [44].

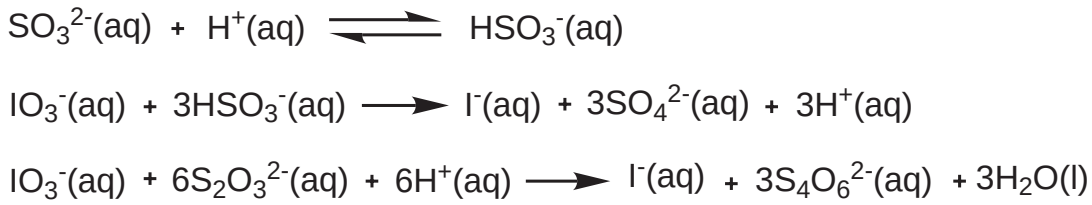

Figure 1.23: The key reactions of iodate-sulfite-thiosulfate pH oscillation system

There exist also high-amplitude pH oscillation systems in a continuously fed stirred tank reactor (CSTR) in which one can observe clear pH oscillations. The system which is found by G. Rabai and M. T. Beck is the most similar system to CSTR systems as showing high-amplitude pH oscillations with sharp changes in pH.

CHAPTER 2

EXPERIMENTAL

2.1 Instrumentation

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Instruments Avance Series-Spectrospin DPX-400 Ultra shield (400 MHz) High Performance digital FT-NMR spectrometer (METU, NMR Laboratory). All chemical shifts are referenced to residual signals previously refenced to TMS and splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), p (pentet), dt (doublet of triplet) and br (broad).

Electronic absorption spectra were recorded on a Shimadzu UV-1601 spectrophotometer. A Perkin-Elmer LS 50 B luminescence spectrometer was used for recording the fluorescence emission spectra. All instrumental parameters were controlled by Fluorescence Data Manager Software (FLDM). Measurements were conducted at 25°C using a 1x0.5 cm rectangular quartz cuvette.

ESI-MS analysis were recorded on a Micromass LCT and Micromass Q-Tof

II spectrometers (Ohio State Univ., Campus Chemical Instrument Center-Mass Spectrometry and Proteomics Facility).

Chemicals and solvents were purchased from Aldrich and used without further purification. Column chromatography of all the products were performed using Merck Silica Gel 60 (particle size: 0.040-0.063 mm, 230-400 mesh ASTM) and Aldrich Octadecyl-functionalized Silica Gel (particle size: 200-400 mesh) pretreated with eluent. Reactions were monitored by thin layer chromatography using Merck Silica Gel 60 Kiesegel F254 TLC Aluminum Sheets 20x20 cm.

2.2 Switching - Oscillating reaction assay

IST (Iodate, Sulfite, and Thiosulfate) system [44] is used as the oscillation reaction system. The total volume of the solution after mixing was 3 mL. The following stock solutions were prepared in advance 0.04 M KIO_3 (2140 mg/25 mL), 0.0975 M Na_2SO_3 (1228 mg/20 mL), and 0.07 M $Na_2S_2O_3$ (1737 mg/15 mL). A 0.0115 M H_2SO_4 stock solution was made by diluting 15.97 mL of %96 sulfuric acid in a 500.0 mL volumetric flask and than further diluting 10.0 mL of this solution into a second 500.0 mL volumetric flask. Deionized, distilled water was used for all of the dilutions.

The pH switching pseudorotaxane system is the the complex formed from Cucurbit[7]uril (CB7) wheel component and bipyridine-boradiazaindacene axle component. To obtain the better solubility for the CB7 0.1 M of NaCl concentration is adjusted in the solution.

To perform the measurement, first 3.486 mg of CB7 and 17.53mg NaCl placed

in to the quartz cuvette than 750 μL from the sulfite stock solution, 1200 μL from the sulfuric acid stock solution, and 450 μL from thiosulfate stock solution were added. After mixing for a short time, axle component is added to the solution than continued mixing for a better dissolvation. Mixing is done by a magnetic stirrer. To initiate the oscillatory reaction, 600 μL from the iodate stock solution was added last. The emission spectrum of the switching pseudorotaxane system is followed at 560 nm during the oscillatory reaction.

2.3 NMR binding assay

Only axle component (compound **3**) and 1: 1, axle: CB7 assay sets are prepared for the ^{1}H-NMR measurements. 1 mg of axle component is dissolved as possible in 1.2 mL of D_2O which contain 23.378 mg (0.1 M) of NaCl for better CB7 dissolvation. For the second set 1 mg of CB7 is added to the 0.6 mL of prepared solution to obtain 1.42 mM concentration of it. ^{1}H-NMR spectra of prepared samples are taken in situ.

Set 1: axle component

fig.3.7a

Set 2: 1: 1, axle: CB7

fig.3.7b

PS: Cucurbi[7]turil molecule used in the Switching - Oscillating reaction and NMR binding assays was purchased from Aldrich.

2.4 Synthesis of 8-(Chloromethyl) boradiazaindacene (1)

Chloroacetyl chloride (1.76 g, 15.6 mmol) and 2,4-dimethyl-3-ethylpyrrol (2.74 g, 22.24 mmol) were dissolved in 125 mL of CH_2Cl_2 under Ar atmosphere, CH_2Cl_2 was sparged with Ar for 0.5 hour prior to use. Then the mixture was stirred overnight at room temperature. To the blackish solution was added 4-6 mL of triethylamine, followed by 10 mL of $BF_3.OEt_2$. The mixture was stirred under an Ar atmosphere for another night at room temperature. Finally the reaction mixture was washed with water, dried over Na_2SO_4, filtered and evaporated to dryness. The crude compound was purified by column chromatography on silica gel (first chloroform than 16 : 1 hexanes-EtOAc). Red pure final product was obtained, (2 g , 36%) [45].

^{1}H-NMR (400MHz; $CDCl_3$): δ (ppm) 0.98 (6H, t, J= 7.5 Hz, CH_3), 2.33 (4H, q, J= 7.5 Hz, CH_2), 2.37 (6H, s, CH_3), 2.43 (6H, s, CH_3), 4.73 (2H, s, CH_2)(Fig.A.1);

^{13}C-NMR (100MHz; $CDCl_3$): δ (ppm) 12.0, 12.2, 14.2, 16.6, 37.4, 130.5, 133.0, 133.8, 135.8, 154.5 (Fig.A.1);

ESI-HRMS calcd for [M + Na] 375.1587 found 375.1584 Δ=0.8 ppm. (Fig.B.1)

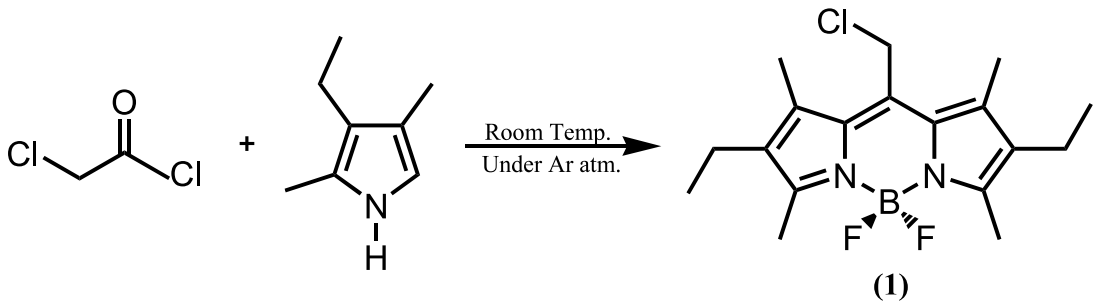

Figure 2.1: Reaction scheme for the formation of **1**

2.5 Synthesis of carboxyl ended alkyl chain functionalized viologen mono cation (2)

4,4'-Bipyridine (1.2 g, 7.695 mmol), 6-Bromohexanoic acid (500 mg, 2.565 mmol) and potassium iodide (426 mg, 2.565 mmol) were dissolved in 20 mL of acetonitrile under Ar atmosphere, acetonitrile was sparged with Ar for 0.5 hour prior to use. Then the mixture was stirred overnight at 30°C. Cloudy solution was reduced to 5 mL and to the resulting solution was added 200 mL of diethylether. Light yellow solids were collected by filtration and washed with 50 mL of diethylether, (637.1 mg, 91%) [46].

^{1}H-NMR (400MHz; DMSO): δ (ppm) 1.3-1.38 (2H, m, CH_2), 1.53-1.6 (2H, m, CH_2), 1.94-2.02 (2H, m, CH_2), 2.22-2.26 (2H, m, CH_2), 4.64-4.72 (2H, m, CH_2), 8.06 (2H, d, J = 5.8 Hz , CH), 8.65 (2H, d, J= 6.6 Hz , CH), 8.88 (2H, d, J= 5.8 Hz, CH), 9.26 (2H, d, J= 6.6 Hz , CH)(Fig.A.2);

^{13}C-NMR (100MHz; DMSO): δ (ppm) 23.8, 24.9, 30.3, 33.3, 60.2, 121.9, 125.4, 140.9, 145.3, 150.9, 152.3, 174.3 (Fig.A.2);

ESI-HRMS calcd for [M] 271.1447 found 271.1447 Δ=0.0 ppm. (Fig.B.2)

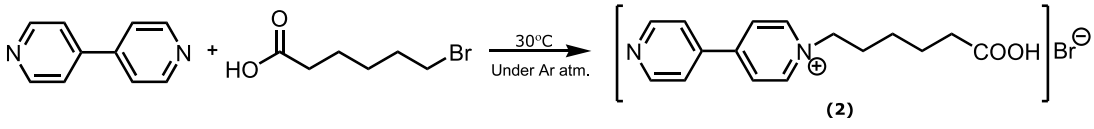

Figure 2.2: Reaction scheme of compound **2**

2.6 Synthesis of water soluble functionalized Bozadiazaindacene (3)

Monoquarternary salt **2** (205.2 mg, 0.756 mmol), borodiazaindacene derivative **1** (400 mg, 352.66 mmol) were dissolved in 20 mL of acetonitrile under Ar atmosphere, acetonitrile was sparged with Ar for 0.5 hour prior to use. Then the mixture was stirred overnight at 25°C. Red solution was reduced to 5 mL and to the resulting solution was added 200 mL of diethylether. Dark red solids were collected by filtration and washed with 100 mL of diethylether than 100 mL of cold water. The crude compound was purified by column chromatography on octadecyl functionalized silica gel (2 : 1 methanol-acetonitrile). Red pure final product was obtained (165 mg, 41%) [46].

^{1}H-NMR (400MHz; DMSO): δ (ppm) 1.06 (6H, br t, CH_3), 1.39-1.41 (2H, m, CH_2), 1.60-1.64 (2H, m, CH_2), 2.03-2.06 (2H, m, CH_2), 2.15 (2H, br t, CH_2), 2.28-2.32 (4H, m, CH_2), 2.48 (6H, s, CH_3), 2.57 (6H, s, CH_3), 4.68-4.77 (2H, m, CH_2), 6.33 (2H, s, CH_2), 8.13 (H, d, J= 5.8 Hz, CH), 8.70 (1H, d, J= 6.5 Hz, CH), 8.80 (2H, d, J= 6.5 Hz, CH), 8.95 (1H, d, J= 5.8 Hz, CH), 9.31 (1H, d, J= 6.5 Hz, CH), 9.40 (1H, d, J= 6.5 Hz, CH), 9.45 (1H, d, J= 6.5 Hz, CH)(Fig.A.3);

^{13}C-NMR (100MHz; DMSO): δ (ppm) 12.6, 12.9, 13.1, 14.9, 15.1, 16.9, 24.1, 24.2, 25.3, 30.7, 30.8, 33.3, 33.8, 55.4, 115.9, 122.7, 125.3, 125.9, 127.3, 128.2, 131.9, 132.4, 133.1, 133.7, 134.7, 137.5, 137.6, 145.1, 145.8, 150.8, 154.7, 156.8, 174.8 (Fig.A.3);

ESI-HRMS calcd for [M] 588.3436 found 588.3448. (Fig.B.3)

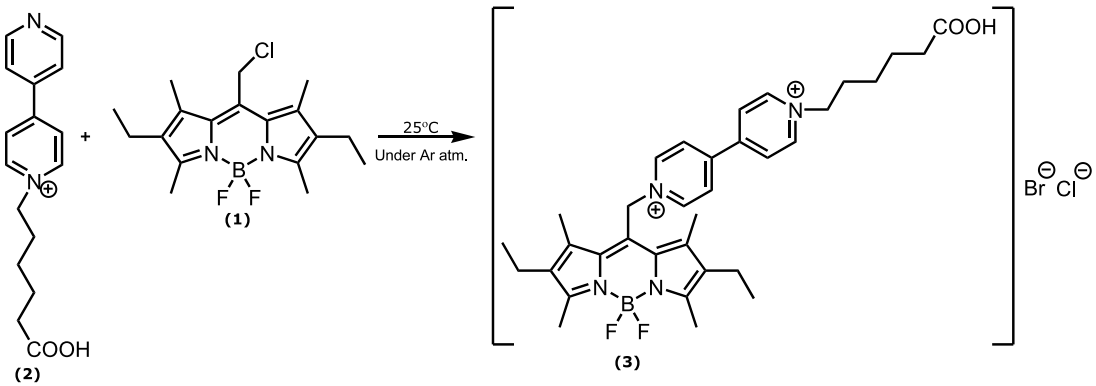

Figure 2.3: Reaction scheme of compound **3**

CHAPTER 3

RESULTS AND DISCUSSIONS

3.1 Novel pH switchable pseudorotaxane

Interlocked molecules such as rotaxanes and catenanes, once considered nothing more than chemical curiosities, found their way into the pages of *The New York Times* [47]. The reason for this popular and scientific interest lies in the fact that at present the interlocked molecules seem to be omnipresent in all molecular device design and they are most likely candidates as components for many others to come. Especially, those with more than one switchable "state" corresponding to different energy minima are considered early examples of molecular machines. For example, the "wheel" component of a rotaxane can switched between two "stations" by external stimuli such as, pH changes, irradiation or applied potential. The switching process can be followed by the changes in the NMR or electronic absorption spectra, and rarely by the emission changes. Kim and co-workers published [32] the first example of probable emission changing "shuttling" between

the two states.

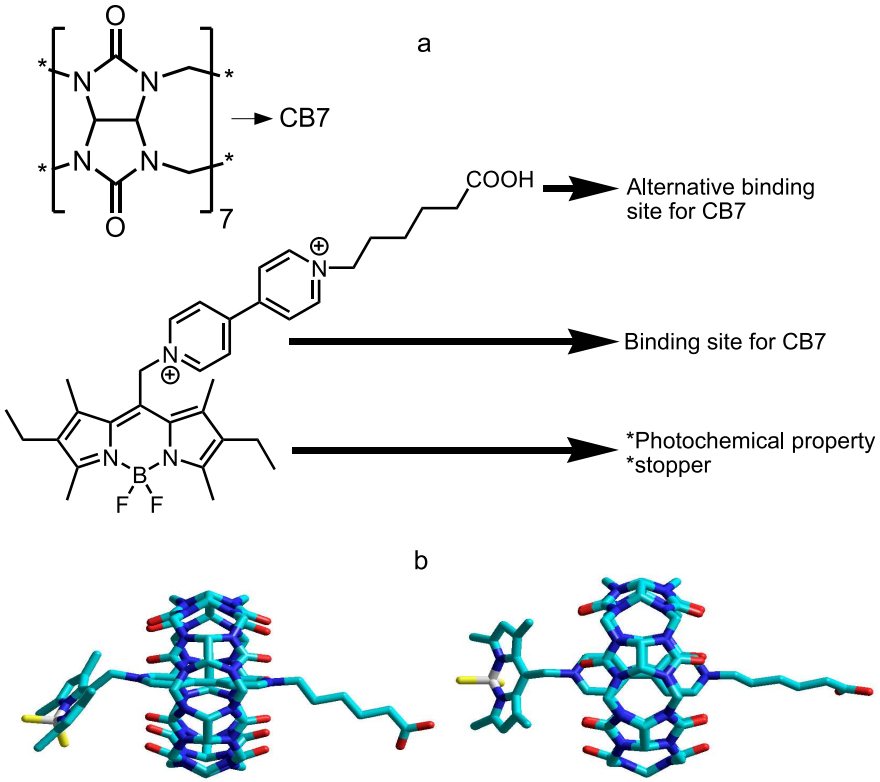

Figure 3.1: a)axle and the wheel components of the pseudorotaxane b) Hyperchem drawings of the novel pH switchable pseudorotaxane

In our laboratory, we have amassed considerable experience in the photophysics of the boradiazaindacene fluorophore [48, 49, 50]. We know that this particular fluorophore is subject to both reductive and oxidative photoinduced electron transfer. The recent literature [51] on the cucurbit[7]uril (CB7) complexation with certain bipyridyl dication derivatives persuade us to design a bipyridyl-boradiazaindacene conjugate with two distinct stations for shuttling (fig.3.1). In this system changing pH from neutral to acidic results in shuttling of the cucurbituril from one station to the other. In addition, this shuttling is accompanied by a change in the emissive properties of the BODIPY dye, which is only observed in the presence of cucurbituril. This system yields a clear demonstration of shuttling

in aqueous solution as a result of the protonation/deprotonation equilibrium of the carboxylic acid group incorporated into the pseudorotaxane structure.

3.2 Mechanism of the motion

The cucurbit[7]uril component moves in response to pH: around neutrality, ion-dipole interactions between the carbonyls on the portals of the CB7 and the bipyridinium dications; the hydrophobic interactions between the axle and the CB7 enhance the binding of the wheel CB7 to the bipyridinium moiety of the axle. In addition the minus charge on the deprotonated carboxly terminal push CB7

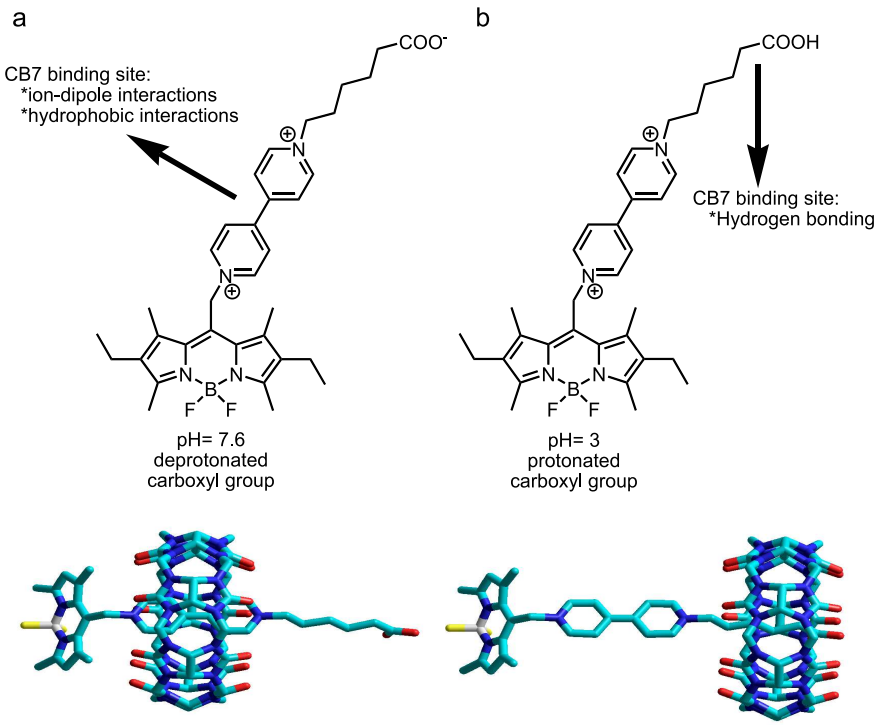

Figure 3.2: Mechanism of the motion: a)station under neutral conditions, b) station under acidic conditions

thorough the bipyridinium dication (fig.3.2a). However under acidic conditions, a different station is favored, the carboxylic acid terminal of the axle. H-bonding

interactions between the protonated carboxyl terminal and the carbonyls on the portals of the CB7 is stronger than the interactions between the CB7 and the bipyridinium dication. (fig.3.2b)

3.3 Proof of the motion

The switching process can be followed by the changes in the NMR or electronic absorption spectra, and rarely by the emission changes. Emissive properties of the BODIPY dye enable us to follow the switching by emission changes. But, unlike the earlier work, we first firmly established that the pH changes alone, do not change the emission spectrum of the boradiazaindacene "axle" component. Around neutral conditions CB7 wheel component bound to the bipyridinium di-

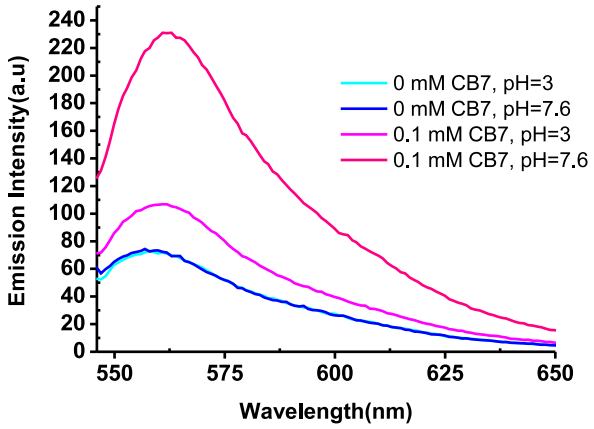

Figure 3.3: Switching fallowed by changes in emission spectrum: 0 mM concentration signals prove that the pH changes alone do not change the emission spectrum of the boradiazaindacene. In the presence of the CB7 unit under acidic conditions emission intensity is low as expected due to the oxidative PET process, however around neutrality binding of the CB7 wheel to the bipyridinium moiety increased the emission intensity.

cation and reduce the quenching of the emission, however under acidic conditions,

a different station is favored, with decreased emission intensity due to oxidative PET process. (fig.3.3)

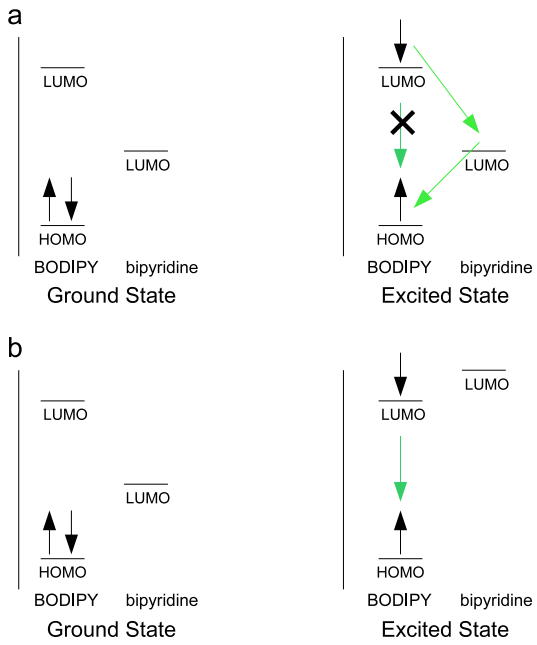

Figure 3.4: a)Energy diagrams explaining oxidative PET process, b)Energy diagrams explaining increase of the emission by stopping oxidative PET process

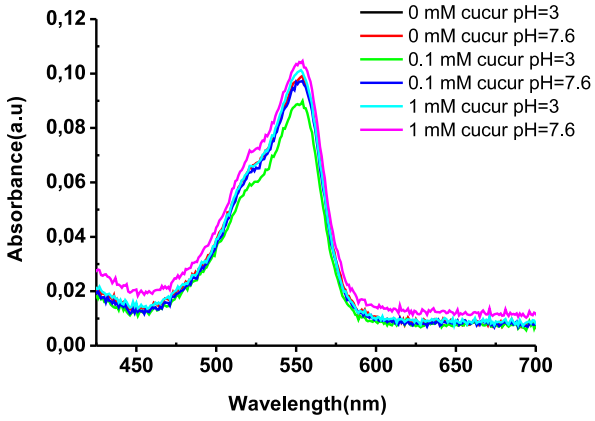

Figure 3.5: Absorption spectrum of the switching assay

During the oxidative PET process at the excited state, excited electrons of BODIPY prefers the way through the LUMO level of bipyridinium component

instead of direct relaxation. (fig.3.4a) But when we have the binding of CB7 to the bipyridinium, bipyridinium's LUMO level is destabilized (its energy level increased up to the LUMO level of BODIPY dye). In this case relaxation through the LUMO level of bipyridinium is not possible anymore. Direct relaxation take place by giving increased emission. (fig.3.4b)

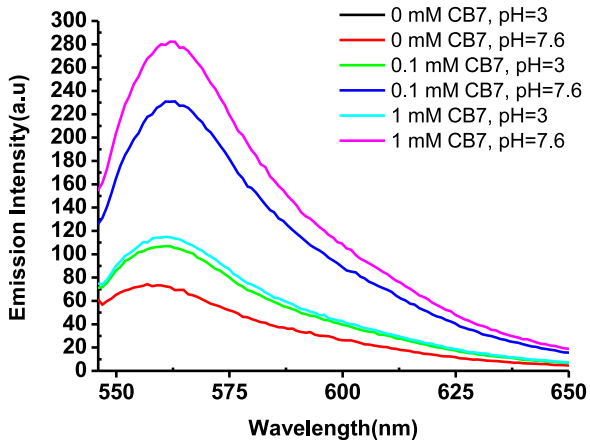

Figure 3.6: Switching with increased concentration of CB7

The absorption spectrum of the system is not affected by this process because the ground state energy level is not changed. (fig.3.4) It is demonstrated unequivocally at the absorption spectrum (fig.3.5).

The same effects are also observed with increasing concentrations of CB7 wheel component. (fig.3.6)

Pseudorotaxane formation is also supported by the ^{1}H-NMR spectrum of the complex (fig.3.7). For the ^{1}H-NMR spectrum of the axle alone in aqueous media we observe 8 different signals for the protons belonging the bipyridine component due to the 3D structure (fig.3.7a). However, with the CB7 in the media we only

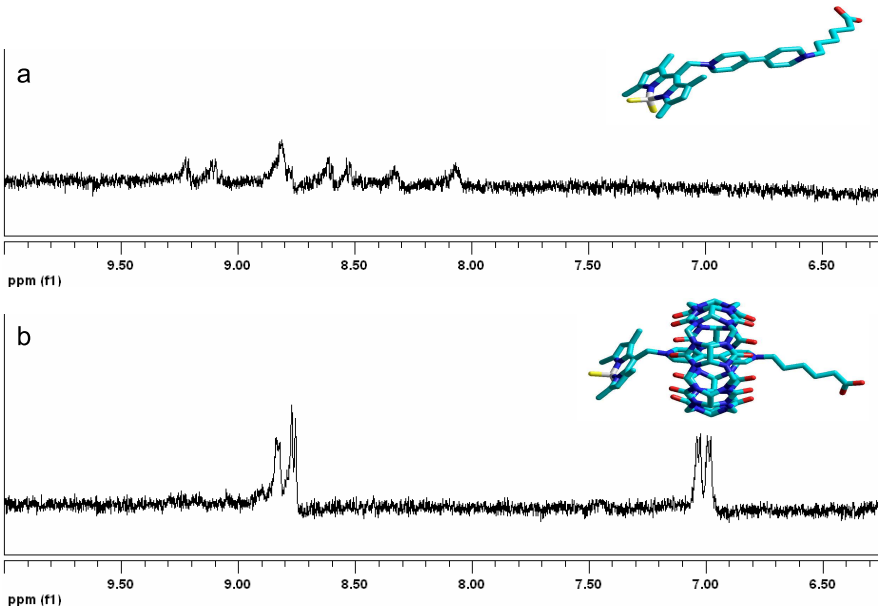

Figure 3.7: ^{1}H-NMR of the bipyridine-boradiazaindacene axle component alone (a), ^{1}H-NMR of the pseudorotaxane (b)

observe 2 signals. The forming complex create an homogeneous environment for the bipyridine moiety resulting in 2 different proton, the insider and the outsider protons. Insider protons are also effected by the shielding effect of the CB7 and shift to the higher field of the spectrum. (fig.3.7b) The Maldi-tof Mass spectrum of the complex is also a proof for the formation of the pseudorotaxane (fig.B.4). ESI-HRMS found for [M - F] is 1731.7770 which is compatible with the theoretical value.

3.4 Switching coupled to the oscillation reaction

While this is an important demonstration of fluorescence signaled shuttling, we wanted to couple this to another chemical process, eliminating the need for external manipulation of the pH for the switching. Unfortunately, unlike the well-known Belousov-Zhabotinsky reaction, pH oscillating reactions are not partic-

ularly impressive in closed systems, and large amplitude oscillations are only observed in the continuous-flow stirred tank reactors (CSTR). Nevertheless, as a proof of principle, we carried out the switching experiment in a solution geared for pH oscillations, containing thiosulfate, sulfite, and iodate ions. Once the oscillation was started by the addition of the final reagent, pH rises 0.2 units and drops sharply to near 5.0 and then slowly rises to near neutral values. These pH changes are accompanied by fluorescence changes indicating that the shuttling between the two stations is also taking place in the solution. (fig.3.8)

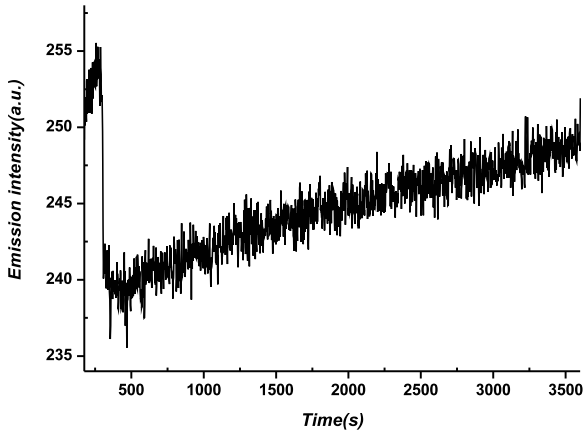

Figure 3.8: Emission intensity vs time graph during the pH oscillation reaction

CHAPTER 4

CONCLUSIONS

In summary, we have synthesised a novel water soluble, pH controlled pseudorotaxane and prove its motion by different methods. Additionally, we shoved that in a novel pseudo-rotaxane system, the switching can be carried out autonomously if the process can be coupled to an oscillating reaction. Other designs based on our findings, incorporating separated compartments and/or CSTR systems are very likely to result in sustained autonomous switching and autonomously functioning molecular machines. Further work along these lines is in progress.

Such electronic devices at a molecular level are one of the chemists potential answers to the vision of Feynmans "bottom-up" approach: "There is plenty of room at the bottom". Because the ongoing reduction of the size of conventional electronic devices has limitations that cannot be overcome with current technology, it seems promising to start with molecules and construct electronic devices at a nanometer level.

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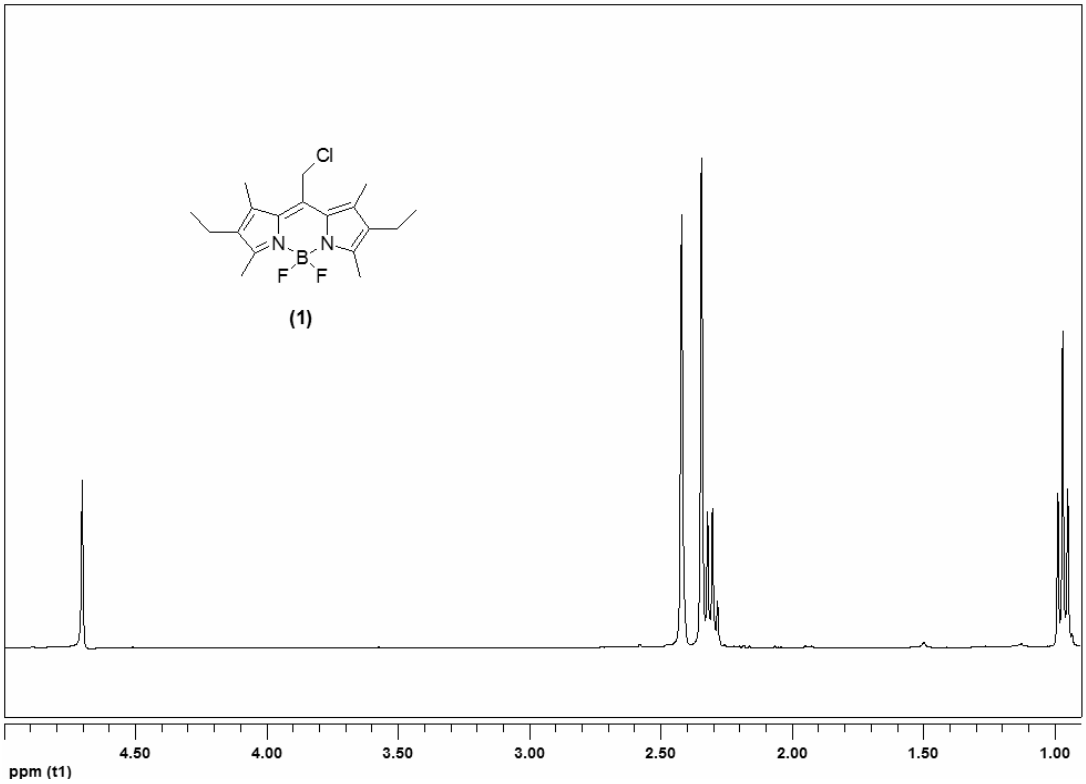
APPENDIX A

^{1}H and ^{13} C NMR SPECTRA OF SYNTHESIZED COMPOUNDS

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Instruments Avance Series-Spectrospin DPX-400 Ultra shield (400 MHz) High Performance digital FT-NMR spectrometer (METU, NMR Laboratory). All chemical shifts are referenced to residual signals previously refenced to TMS and splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), p (pentet), dt (doublet of triplet) and br (broad).



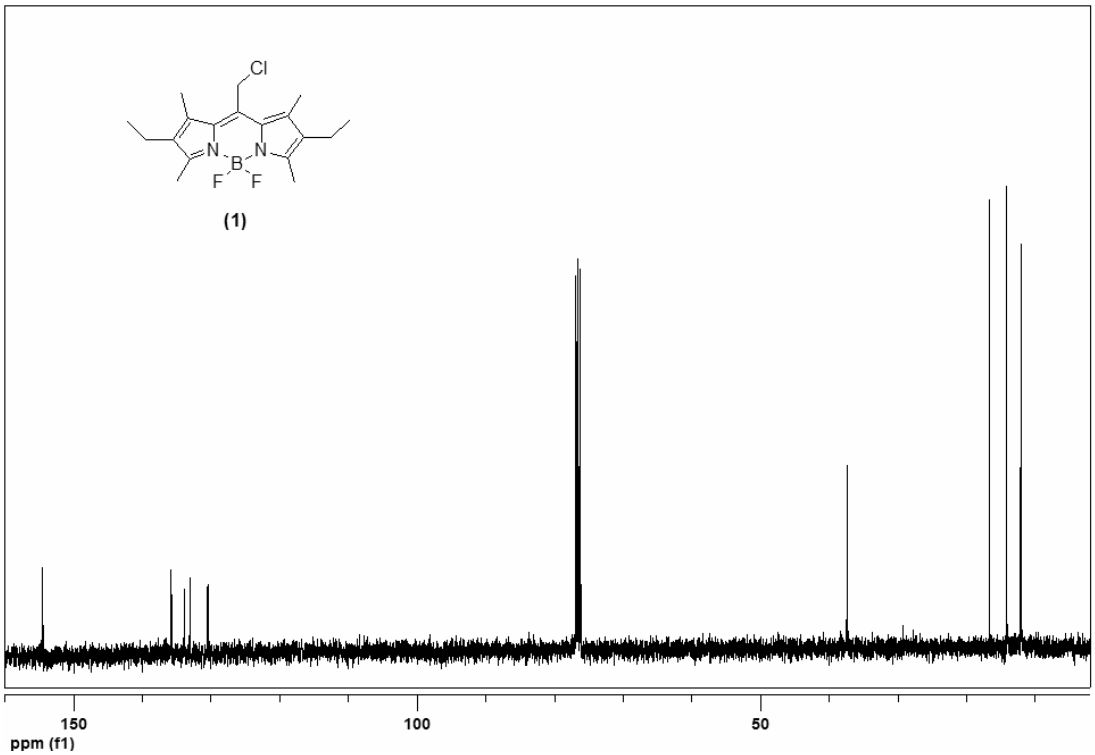


Figure A.1: ^{1}H and ^{13}C NMR spectra of compound **1**

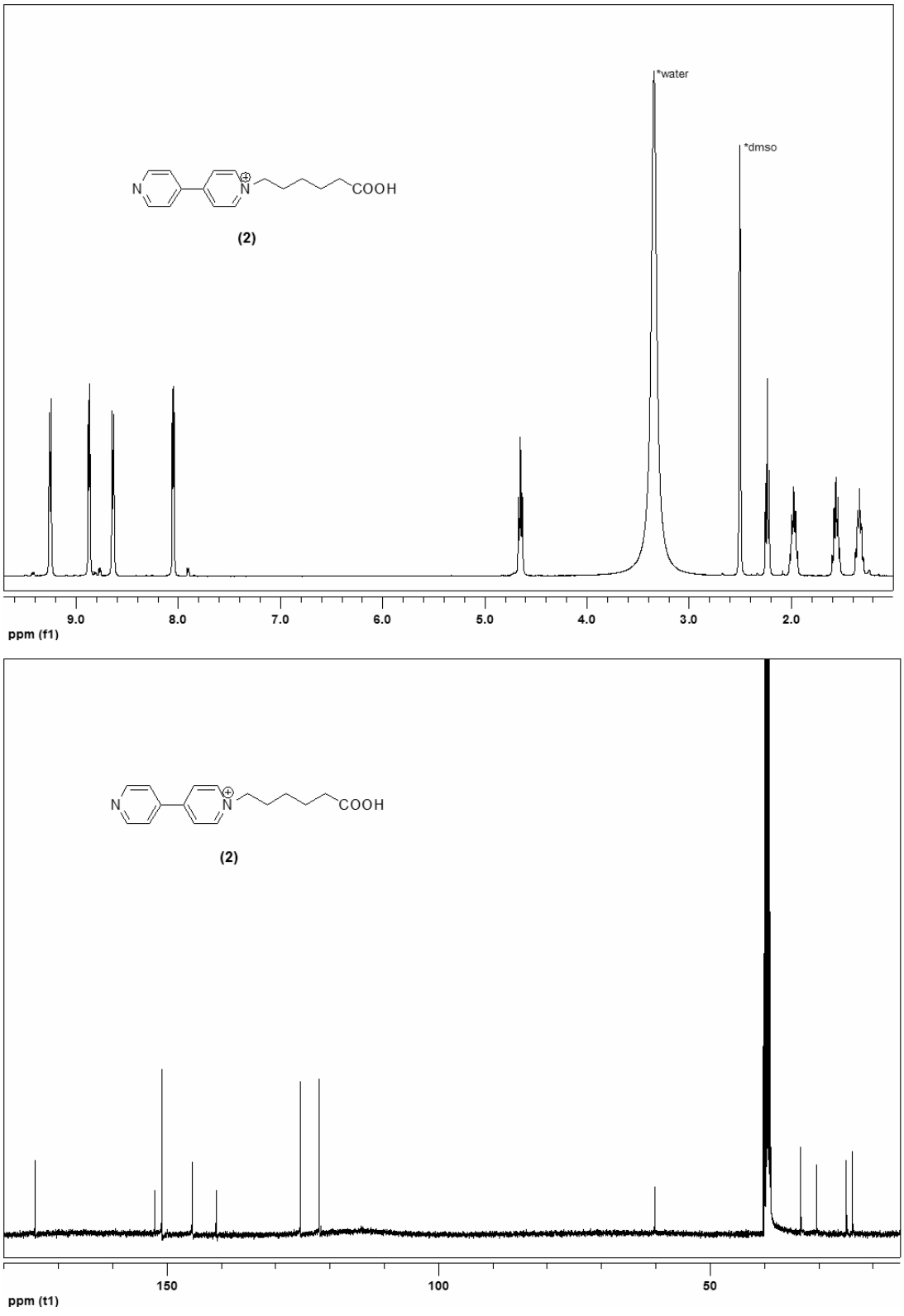


Figure A.2: ^{1}H and ^{13}C NMR spectra of compound **2**

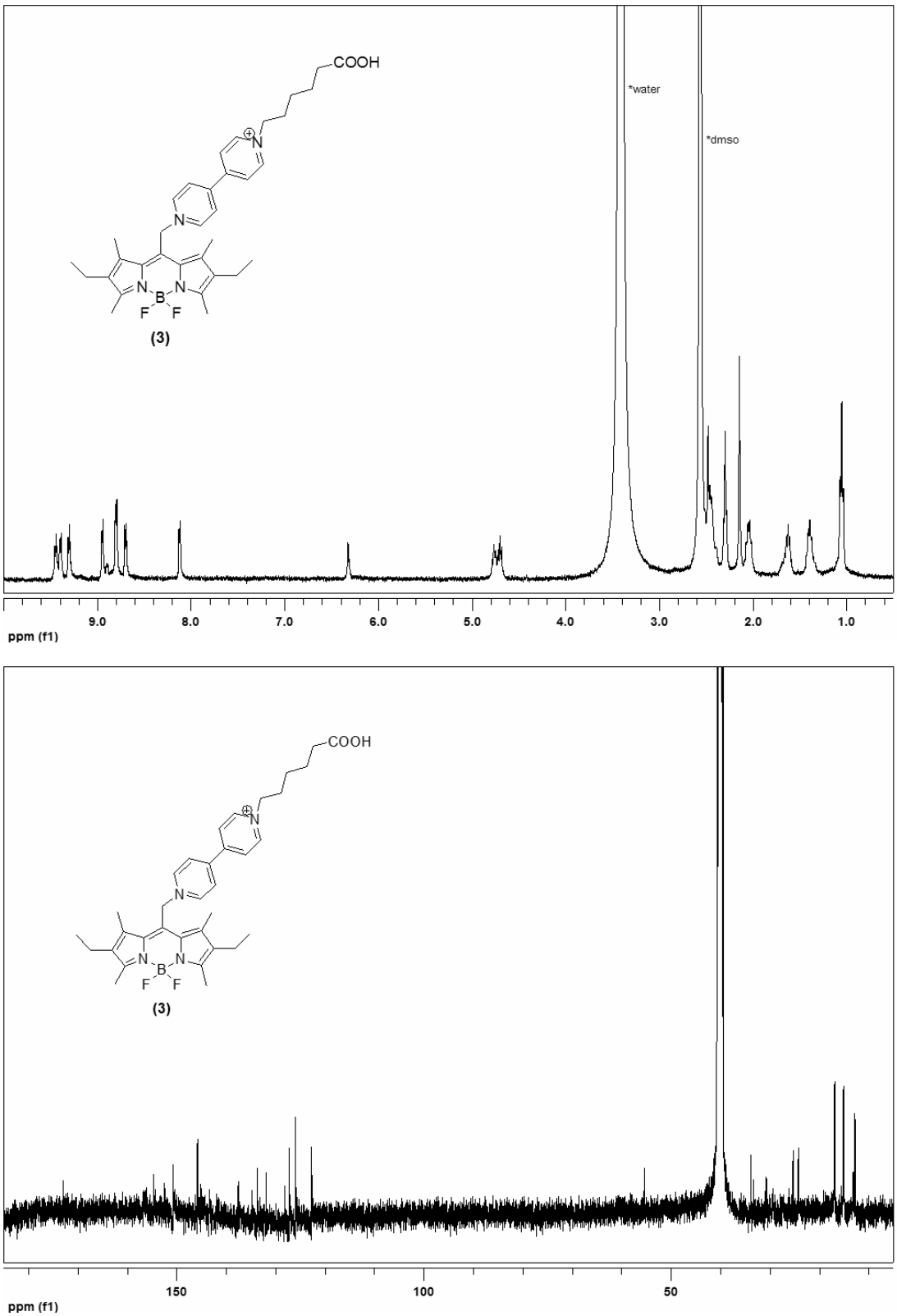


Figure A.3: ^{1}H and ^{13}C NMR spectra of compound **3**

APPENDIX B

MASS SPECTRA OF SYNTHESIZED COMPOUNDS

ESI-MS analysis were recorded on a Micromass LCT and Micromass Q-Tof II spectrometers (Ohio State Univ., Campus Chemical Instrument Center-Mass Spectrometry and Proteomics Facility).

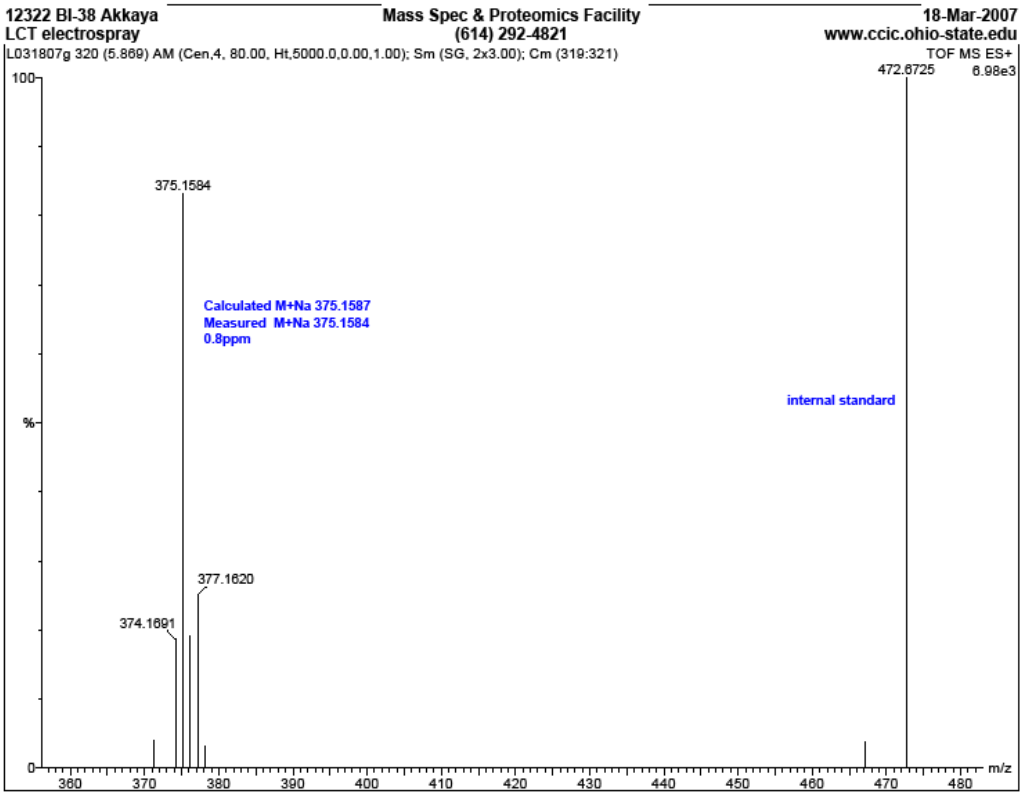


Figure B.1: Mass spectrum of compound **1**

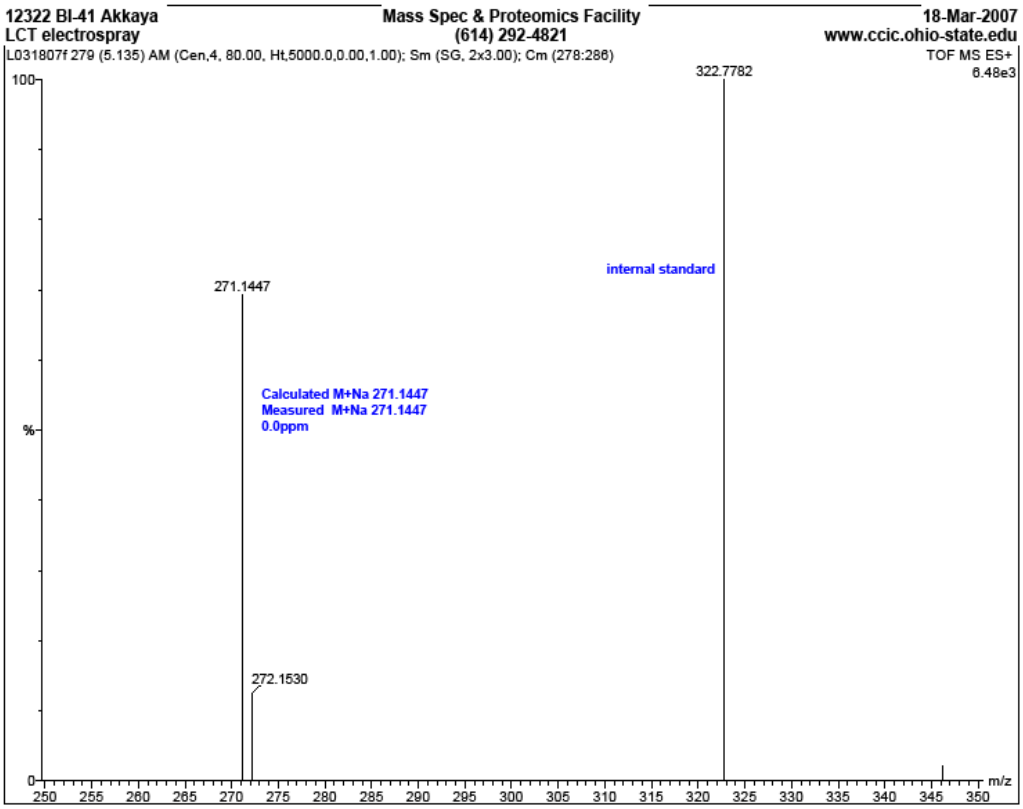


Figure B.2: Mass spectrum of compound **2**

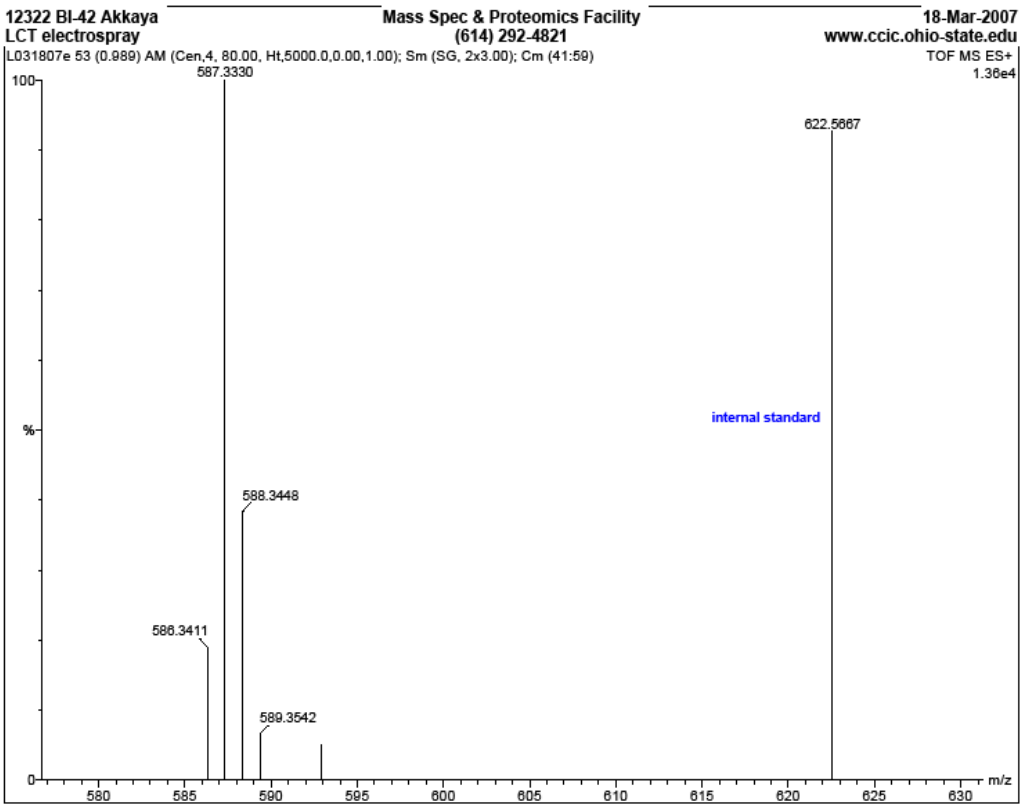


Figure B.3: Mass spectrum of compound **3**

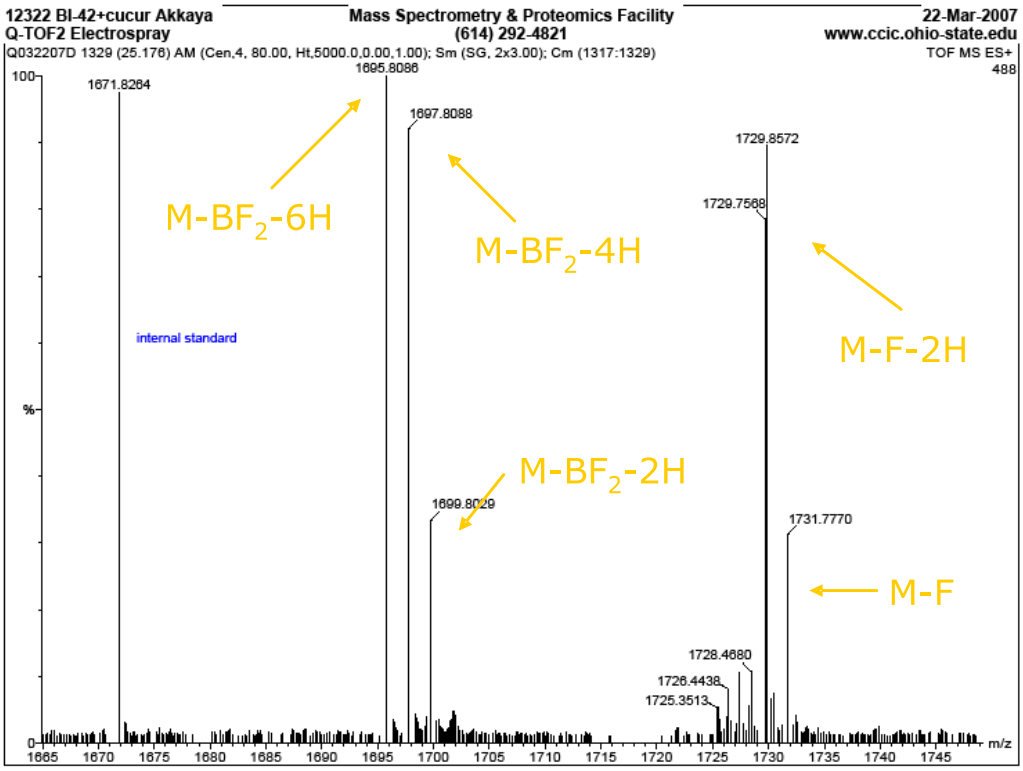


Figure B.4: Mass spectrum of the pseudorotaxane