

Imidazolium- and Triazolium-Based Interlocked Structures for Anion Recognition and Sensing

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This thesis describes the synthesis and investigation of novel anion templated interlocked structures which incorporate the positively charged imidazolium and triazolium binding motifs for applications in anion recognition and sensing.

Chapter One introduces the fields of anion supramolecular chemistry and mechanically interlocked structures, focusing on topics of particular relevance to this thesis, including anion recognition, anion sensing and the templated synthesis of interlocked architectures.

Chapter Two details the incorporation of the imidazolium motif into the axle components of anion templated rotaxane hosts to achieve selective anion recognition by virtue of their interlocked binding cavities. The effects of exploiting imidazolium motifs with contrasting hydrogen bond donor arrangements and reducing the macrocycle size on the anion recognition properties of such systems were investigated using ^1H NMR spectroscopy.

Chapter Three reports the work undertaken to utilise fluorescent reporter groups as stoppers in the synthesis of anion sensing rotaxanes. Imidazolium- and triazolium-based systems containing either luminescent ruthenium(II) bipyridyl complexes or the organic fluorophore anthracene were prepared and their anion sensing behaviours explored using fluorescence spectroscopy. Synthetic efforts to construct suitable photo-active rotaxanes are detailed.

Chapter Four describes investigations of the novel naphthalimide triazolium motif both for use in interlocked molecular motion systems, and for fluorescence sensing applications. The preparation of a naphthalimide triazolium rotaxane, capable of selective, anion-induced, uni-directional shuttling which was investigated extensively using ^1H NMR spectroscopy and optically signalled by perturbations in the UV/Vis spectrum, is detailed. Preliminary research studies into the potential to exploit this motif for surface-based fluorescence sensing devices are also included.

Chapter Five presents research into the utilisation of acyclic receptors displaying considerable binding-induced conformational changes for fluorescence anion sensing. The recognition properties of a series of imidazolium-based receptors were studied, whilst the ability of a pyrene-appended analogue to signal anion complexation *via* changes in excimer emission is reported. The control of interpenetrated assembly formation using anion-induced conformational changes within the threading component of a pseudorotaxane is also discussed.

Chapter Six provides the experimental procedures and characterisation details for the compounds synthesised in this thesis.

Chapter Seven is a summary of conclusions from Chapters Two, Three, Four and Five.

Supplementary information relating to titration protocols, crystallographic data and surface studies is provided in the Appendices.

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Abbreviations

δ	chemical shift
Δ	change, heat
λ	wavelength
μ	micro
ν	frequency
$\text{\AA}$	Ångström
A^-	anion
AIBN	azobisisobutyronitrile
<i>anti</i>	anticlinal
app	apparent
aq	aqueous
Ar	aromatic
ATP	adenosine triphosphate
a.u.	arbitrary unit
bipy	2,2'-bipyridine, 2,2'-bipyridyl
Boc	<i>tert</i> -butoxycarbonyl
br	broad
^t Bu	<i>tert</i> -butyl
°C	degree centigrade
calc.	calculated
cat.	catalytic
Celite [®]	diatomaceous silica
conc.	concentrated
COSY	correlation spectroscopy
CuAAC	copper(I)-catalysed alkyne-azide cycloaddition
<i>d</i>	deuterated
d	doublet
D	dimensional
DEAD	diethyl azodicarboxylate
dec.	decomposed
DFT	density functional theory
DIPEA	<i>N,N'</i> -diisopropylethylamine

Abbreviations

DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethylsulfoxide
DNA	deoxyribose nucleic acid
EDC·HCl	<i>N</i> -(3-dimethylaminopropyl)- <i>N</i> '-ethylcarbodiimide hydrochloride
ESI	electrospray ionisation
equiv.	equivalent
Et	ethyl
excit	excitation
FI	field ionisation
g	gas, gram
Grubbs' I	Grubbs' first-generation catalyst
Grubbs' II	Grubbs' second-generation catalyst
h	hour, Planck constant
HOBt	hydroxybenzotriazole
HOMO	highest occupied molecular orbital
Hz	Hertz
ⁱ Pr	isopropyl
I	intensity
ICT	internal charge transfer
IL	ionic liquid
<i>J</i>	coupling constant
K	Kelvin
<i>K</i>	association constant
kcal	kilocalorie
L	litre
LUMO	lowest occupied molecular orbital
m	metre, milli, multiplet
M	mega, metal, molar (mol.dm ⁻³), molecular ion
<i>m/z</i>	mass/charge ratio
MALDI	matrix assisted laser desorption/ionisation
max	maximum
MD	molecular dynamics
Me	methyl
min	minute
MLC	metal-ligand complex
MLCT	metal-to-ligand charge transfer

Abbreviations

mol	mole
Mp	melting point
MS	mass spectrometry
Ms	mesityl
n	nano
NBS	<i>N</i> -bromosuccinimide
NMR	nuclear magnetic resonance
OAc	acetate
Oxone [®]	potassium peroxymonosulfate
<i>p</i>	para
PET	photo-induced electron transfer
pH	$-\log_{10}[\text{H}^+]$
pK _a	$-\log_{10}[\text{K}_a]$
ppm	parts per million
R	alkyl or aryl group
RCM	ring closing metathesis
ROESY	rotating-frame nuclear Overhauser effect spectroscopy
q	quartet
quin	quintet
s	second, singlet
SAM	self-assembled monolayer
sat.	saturated
S _N 2	bimolecular nucleophilic substitution
<i>syn</i>	synclinal
t	triplet
TBA	tetrabutylammonium
TBTA	tris[(1-benzyl-1 <i>H</i> -1,2,3-triazol-4-yl)methyl]amine
<i>tert</i>	tertiary
THF	tetrahydrofuran
TFA	trifluoroacetic acid
Ts	tosyl
UV/Vis	ultraviolet-visible
V	volt
wt	weight

Publications and Copyrights

Chapter Two

Work detailed in Sections 2.2 and 2.3 has been included in the following publication and permission to reproduce has been granted by John Wiley and Sons (licence number 296081053184):

‘Investigating the Imidazolium-Anion Interaction through the Anion Templated Construction of Interpenetrated and Interlocked Assemblies’, G. T. Spence, Dr. C. J. Serpell, Dr. J. Sardinha, Dr. P. J. Costa, Prof. V. Felix, Prof. P. D. Beer, *Chemistry – A European Journal*, 2011, **17**, 12955–12966.

DOI: 10.1002/chem.201102005.

<http://onlinelibrary.wiley.com/doi/10.1002/chem.201102005/abstract>

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‘Investigating the Effect of Macrocycle Size on Anion Templated Imidazolium Interpenetrated and Interlocked Assemblies’, G. T. Spence, Nicholas G. White, Prof. P. D. Beer, *Organic and Biomolecular Chemistry*, 2012, **10**, 7282-7291.

DOI: 10.1039/C2OB26237A.

<http://pubs.rsc.org/en/content/articlelanding/2012/OB/C2OB26237A>

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‘Anion-Induced Shuttling of a Naphthalimide Triazolium Rotaxane’, G. T. Spence, Dr. M. B. Pitak, Prof P. D. Beer, *Chemistry - A European Journal*, 2012, **18**, 7100–7108.

DOI: 10.1002/chem.201200317

<http://onlinelibrary.wiley.com/doi/10.1002/chem.201200317/abstract>

Chapter Five

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‘Anion Binding Induced Conformational Changes Exploited for Recognition, Sensing and Pseudorotaxane Disassembly’, G. T. Spence, Carmen Chan, Dr. Fridrich Szemes, Prof. P. D. Beer, *Dalton Transactions*, 2012, **41**, 13474–13485.

DOI: 10.1039/C2DT31640D.

<http://pubs.rsc.org/en/content/articlelanding/2012/dt/c2dt31640d>

Conference Posters

Work detailed in this thesis has also been included in the following conference posters:

‘Investigating the Imidazolium Motif for Anion Recognition Using Templated Interlocked Structures’, G. T. Spence, Dr. C. J. Serpell, Prof. P. D. Beer, 6th International Symposium on Macrocyclic and Supramolecular Chemistry (6-ISMSC) Brighton (3rd-7th July 2011).

‘Anion-Induced Shuttling of a Naphthalimide Triazolium Rotaxane’, G. T. Spence, Prof. P. D. Beer, RSC Macrocyclic and Supramolecular Chemistry Meeting, Bath (19th-20th December 2011).

Chapter One: Introduction

1.1 Anion Supramolecular Chemistry

Supramolecular chemistry is a wide-reaching, often interdisciplinary, field which encompasses the fundamental understanding of non-covalent interactions and their use in the construction of intricate architectures and functional systems.¹ Many areas of supramolecular chemistry are directly inspired by specific examples in Nature, and one of the most elegant natural ‘supramolecular’ systems is DNA (Figure 1.1). Specific hydrogen bonding interactions between complementary strands of nucleotide bases, as well as stabilising aromatic stacking interactions between the hydrophobic residues, are responsible for the iconic double helical structure.² The vitally important function of DNA – coding the genetic material necessary for life – relies on the fidelity of base-pairing, and the use of numerous other supramolecular interactions in translation, transcription and replication processes. As well as taking inspiration from the complexity and near-perfection of this and countless other examples from Nature, some chemists have even utilised DNA itself in the construction of synthetic supramolecular systems.^{3, 4}

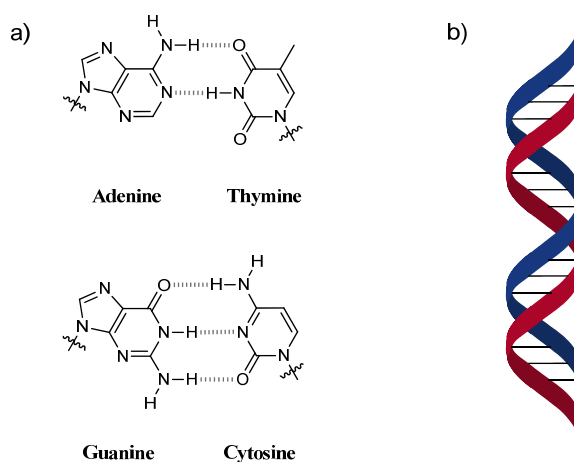


Figure 1.1 a) Hydrogen bonded nucleotide base-pairs, and b) the resulting double helical structure of DNA.

The beginnings of synthetic supramolecular chemistry can arguably be traced back to 1967 when Pedersen discovered the cation binding ability of crown ethers, such as dibenzo-18-crown-6 (**1.1**) (Figure 1.2a),⁵ introducing the area of host-guest chemistry. From there the scope of supramolecular chemistry expanded, for example through Lehn's three-dimensional cryptand hosts,⁶ and Cram's more rigid spherands,⁷ all capable of effective cation recognition. This, along with many other advances, led to the Nobel Prize in Chemistry in 1987 being awarded to Pedersen, Lehn and Cram *"for their development and use of molecules with structure-specific interactions of high selectivity"*.⁸⁻¹⁰

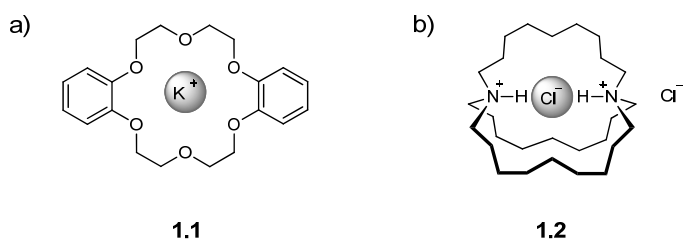


Figure 1.2 a) Pedersen's crown ether receptor **1.1** and b) Park and Simmon's [9.9.9]-'katapinate' **1.2**.

The first anion receptors were reported less than a year after Pedersen's crown ethers, with Park and Simmons' protonated macrobicyclic amine derivatives, such as **1.2** (Figure 1.2b), being shown to encapsulate halide anions in aqueous media.¹¹ Surprisingly, despite this early contribution, anion supramolecular chemistry remained largely neglected in comparison with the cation coordination chemistry field until the late 1970s and early 1980s. Indeed it is the explosion of interest during the past two decades that has established anion supramolecular chemistry as a rapidly growing research field and a significant area of supramolecular chemistry.

This introductory chapter will focus initially on the fundamentals of anion supramolecular chemistry, followed by an introduction to the construction and applications of mechanically interlocked systems, topics of relevance to the research theme of this thesis. At the end of this chapter, the aims of the project and a contents outline of this thesis will be detailed.

1.1.1 Importance of Anions

In Nature, anions are extremely prevalent and important to a large number of key biological processes. The above discussion of DNA is particularly relevant, as its nucleotide sugar-phosphate backbone is negatively charged – a fact used by many DNA binders, for example cisplatin¹² which becomes positively charged upon hydrolysis *in vivo*. Another phosphate-containing polyanion is ATP, crucial in the biological storage of energy. The binding, transport and utilization of ATP, and other related high-energy phosphate derivatives, are vital for cellular activity.

In addition to phosphates, numerous other anions have crucial biological roles. The recognition and transport of many anions are responsible for maintaining cellular flux, osmotic pressure and activating signal transduction pathways.¹³ The scope of such systems is demonstrated by the number of different mitochondrial anion transport proteins known, which includes transporters for the halides, sulfate and carboxylates.¹⁴

Chloride is especially important to human health, as it is known to help regulate blood pressure, metabolism and the acid-base balance within the body.¹³ The mis-regulation of cellular chloride transport can have dramatic and life-threatening effects, resulting in several diseases such as cystic fibrosis,¹⁵ which causes extreme degeneration of the lungs and other organs, and Dent's disease,¹⁶ a condition responsible for renal malfunction.

Environmentally, several anions are of particular concern in both natural and anthropogenic settings. While sulfate and nitrate are present in acid rain,¹⁷ the nuclear and agricultural industries can create major anionic pollution hazards in the form of pertechnetate from nuclear fuel reprocessing,¹⁸ and nitrate- and phosphate-containing fertilizers which are responsible for eutrophication.¹⁹

1.1.2 Fundamentals of Anion Supramolecular Chemistry

It is clear from the prevalence of negatively charged species in the natural world, that there is a need to recognise and sense anions. However, as a consequence of the inherent properties of anions,²⁰ there are many challenges to overcome in achieving the required level of recognition and

selectivity for the construction of effective anion receptors and sensors. These properties and the possible non-covalent interactions of anions need to be considered, as well as more general supramolecular chemistry principles for the design of host-guest systems.

1.1.2.1 Properties of Anions

Anions are larger than the equivalent, isoelectronic cations, and as a consequence have lower charge-to-radius ratios. Hence, the electrostatic interactions employed in many anion receptors (*vide infra*) are less effective due to the more diffuse nature of the target guests.

Common anionic species of interest, including those discussed in Section 1.1.1, have a range of geometries (Figure 1.3), which although requires a greater degree of design to synthesise complementary anion receptors, can allow for inter-anion discrimination on the basis of differing geometries.

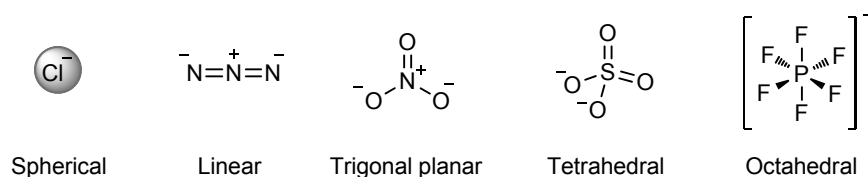


Figure 1.3 Differing geometries of anionic species.

The charge of many anions is pH dependent, due to their ability to become protonated under acidic conditions. The pH dependence of the host is also important, with the opposing ability of many positively charged receptors such as polyammonium-based systems to be deprotonated at high pH. For binding based on electrostatic interactions, it is necessary for both the anion and the receptor to maintain their charges, leading to a functional “pH-window” for many receptor-anion systems.

Finally, anions are typically more heavily solvated than cations of the same charge and of comparable size.²¹ Solvation greatly influences non-covalent binding interactions and will be discussed further in Section 1.1.2.3.

1.1.2.2 Non-Covalent Interactions for Anion Recognition

Electrostatic interactions cover all types of Coulombic attraction between opposite charges and are usually divided into three classes (Figure 1.4). *Ion-ion interactions* are the strongest electrostatic interactions and hence are often employed in anion receptors to facilitate binding in competitive media, such as polar, protic solvents. However, these are generally non-directional and are mainly used in conjunction with other, more directional interactions. Specifically, *ion-dipole interactions* are considerably weaker, but readily exploited in supramolecular chemistry since the orientation of the dipole is important to maximise the strength of these interactions. *Dipole-dipole interactions* are the final class of electrostatic interactions, but evidently cannot be employed directly for anion complexation.

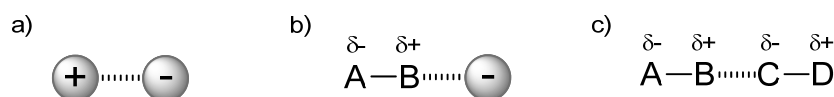


Figure 1.4 a) Ion-ion, b) anion-dipole and c) dipole-dipole electrostatic interactions.

A specific case of dipole interaction is hydrogen bonding, in which a hydrogen atom is covalently attached to an electronegative atom, or electron-withdrawing group, and interacts with a neighbouring dipole or anion *via* its partial positive charge (Figure 1.5a). Hydrogen bonds are extremely prevalent both in Nature and synthetic supramolecular systems, most commonly exploiting N-H and O-H donors. However, C-H hydrogen bonding interactions can also be employed for effective anion binding (*vide infra*). Hydrogen bonds are usually thought of as directional, particularly in comparison to other electrostatic interactions, but are known to come in a variety of strengths, lengths and geometries.¹

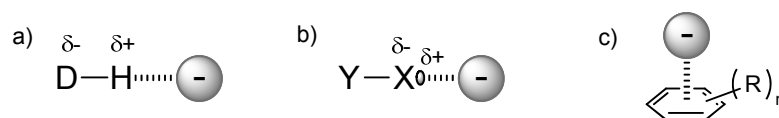


Figure 1.5 Anion complexation by a) hydrogen bonding, b) halogen bonding and c) anion- π interactions. D = electronegative atom or electron-withdrawing group; Y = carbon, nitrogen or halogen; X = halogen; R = electron-withdrawing group.

Halogen bonding is a similar, but more directional interaction which has previously been underexploited in solution-phase supramolecular chemistry. With countless examples in the solid state,²² halogen bonding was only used for anion binding in solution for the first time by Taylor *et al.* in 2010.²³ This counter-intuitive interaction arises from the highly localised region of positive charge that exists on the opposite side of a covalently bound halogen into which electron density can be donated (Figure 1.5b). The size and polarization of the “ σ -hole” is maximised by the electron-withdrawing nature of Y, and by employing the larger, more polarisable halogens (X = Br, I).

Anion- π interactions are another example of a solid state phenomenon which is less commonly present in solution-phase supramolecular host systems.²⁴ The interaction between an electron deficient aromatic surface and an anion (Figure 1.5c) is dominated by electrostatic contributions and anion-induced polarisation of the π -system.

Often considered to be molecular, rather than supramolecular, interactions due to the extent of orbital overlap involved, metal-ligand bonds and Lewis acid-base coordination are frequently employed in supramolecular chemistry to achieve anion binding.¹³

Finally, although not an interaction or force, the hydrophobic effect can play a significant role in anion recognition.²⁵ The entropic and enthalpic gains achieved through the exclusion of non-polar particles from polar solvents, particularly water, can aid binding of an anionic guest within a previously solvated hydrophobic host cavity.

1.1.2.3 Principles of Host-Guest Chemistry

Supramolecular host-guest chemistry relies on the ability to maximise the binding strength and selectivity of receptors by the application of several fundamental principles. Complementarity and preorganisation facilitate effective receptor design, the concept of effective molarity allows the cooperativity of multi-site binding systems to be quantified, whilst an understanding of solvation effects is necessary in almost every aspect of solution-phase chemistry.

When the binding cavity of a host species is complementary in size and shape to the target guest, the favourable non-covalent interactions responsible for complexation are enhanced. This also leads to the potential for greater selectivity over non-complementary guests. In biology, the

“lock-and-key” hypothesis for enzyme-substrate interactions exemplifies complementarity,²⁶ although the term “induced-fit” is now preferentially applied to emphasise the subtle conformational adjustments that occur upon binding.²⁷ The concept of complementarity in the design of synthetic receptors is illustrated by Lehn’s polyammonium macrocycles **1.3** and **1.4** (Figure 1.6), which display selective binding in aqueous solution for dicarboxylate guests of complementary size to their cavities.²⁸ Namely, the strongest complexes of the smaller host macrocycle (**1.3**) are with shorter dicarboxylates ($x = 2, 3$), whereas the larger host (**1.4**) binds longer guests ($x = 5, 6$) more strongly.

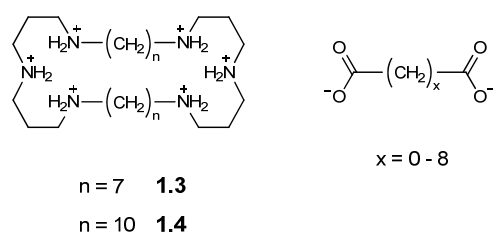


Figure 1.6 Lehn’s polyammonium macrocyclic hosts and dicarboxylate guests.

The principle of preorganisation was developed by fellow Nobel laureate Cram in the 1980s,⁹ and states that binding strength is maximised when a receptor is designed with a well-defined shape, such that it is locked in the correct conformation for binding. This simple, but important, principle is illustrated by the anion binding abilities of isophthalamide derivatives **1.5** and **1.6** (Figure 1.7).²⁹ The intramolecular hydrogen bonding interactions between the hydroxyl and carbonyl groups of **1.6** orientate the amide N-H bonds in a convergent manner prior to complexation. This results in enhanced chloride binding in CD_3CN when compared to non-preorganised receptor **1.5**.

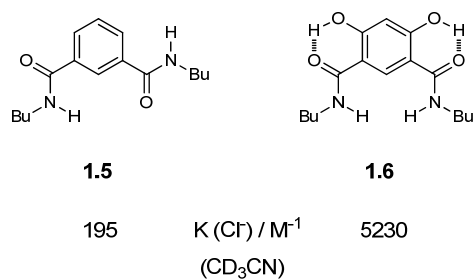


Figure 1.7 The preorganisation of an isophthalamide receptor and associated enhancement of anion binding.

A consequence of preorganisation is that macrocyclic derivatives display greater affinity for guests than their open-chain analogues. This is termed the *macrocyclic effect* and has both enthalpic and entropic contributions. This effect has been illustrated recently by Flood *et al.*,³⁰ with tetra-triazole macrocycle **1.7** binding chloride *via* C-H hydrogen bonding interactions in CH₂Cl₂, six orders of magnitude more strongly than acyclic oligomer **1.8** (Figure 1.8). Macrocycle **1.7** also demonstrates the concept of size complementarity, with significant selectivity exhibited for chloride and bromide over fluoride and iodide, due to an optimal geometrical arrangement of C-H hydrogen bond donors for spherical halide guests of these intermediate sizes.

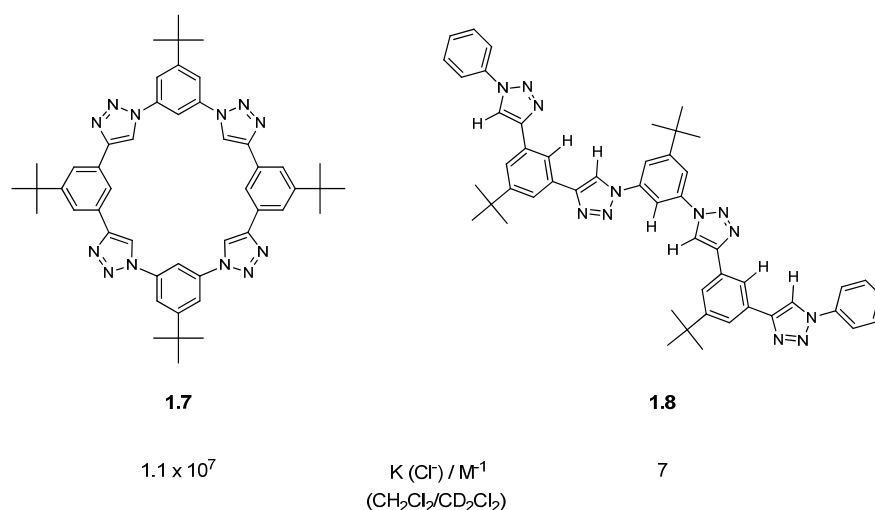


Figure 1.8 Flood's tetra-triazole macrocycle **1.7** and oligomer **1.8**.

Receptors containing more than one recognition site can display cooperative binding to target guest species, with the combined association either stronger than the product of the individual interactions in systems which exhibit *positive cooperativity*, or weaker in the case of *negative cooperativity*.³¹ The calculation of the 'effective molarity' of such systems – defined as shown in Figure 1.9 – quantifies the extent of cooperativity by relating the equilibria constants for the individual and combined processes.

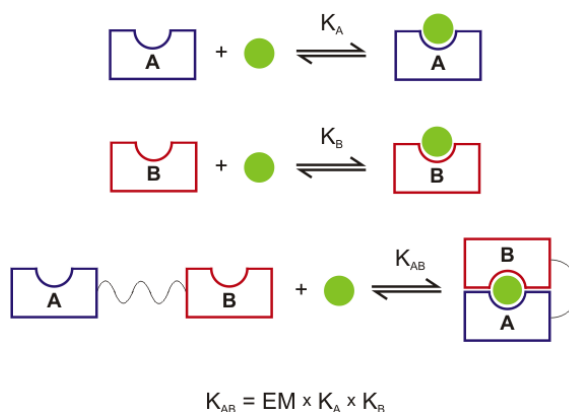


Figure 1.9 The extent of cooperativity exhibited by host systems containing more than one recognition site can be quantified using the concept of effective molarity (EM, units of concentration); K_A , K_B and K_{AB} = equilibrium constants (units of concentration⁻¹).

Every binding event requires the desolvation of both host and guest species, followed by resolution of the resulting host-guest complex. This process involves both enthalpic and entropic contributions which overall dictate whether or not the complexation process is favourable.

In anion recognition, appropriate choice of solvent for a specific receptor is vital. Protic, polar solvents heavily solvate charged species and are able to participate in hydrogen bonding with both the anion and the receptor, whilst this is not the case in aprotic, organic solvent media. Furthermore, anions are solvated to different extents, related to the Hofmeister series of anion hydrophobicity.²⁰ Thus, it is a considerable challenge for a neutral receptor to compete with a protic solvent in recognising heavily solvated anions, for example sulfate or fluoride in aqueous solution.

1.1.3 Anion Receptors

1.1.3.1 Anion Recognition in Nature

Natural anion receptors, most commonly proteins, display extremely strong and selective binding by employing many of the supramolecular chemistry principles discussed above. The preorganised cavities of such proteins typically contain specific combinations of amino acid side-chains possessing numerous hydrogen bond donor groups, arranged with a high level of complementarity.

Sulfate binding protein (SBP) is found in *Salmonella typhimurium* and is involved in sulfate transport, binding the anion in a cleft between its two globular domains *via* seven hydrogen bonds with the surrounding neutral residues (Figure 1.10a).³² Phosphate binding protein (PBP) is responsible for bacterial cell transport of phosphate, with the binding site again found between two globular domains, inaccessible to the surrounding aqueous media.³³ In this case, the hydrogen phosphate anion is bound by twelve hydrogen bonds including the presence of a hydrogen bond accepting aspartate residue (Asp56), with additional electrostatic stabilisation from the guanidinium group of Arg135 (Figure 1.9b).

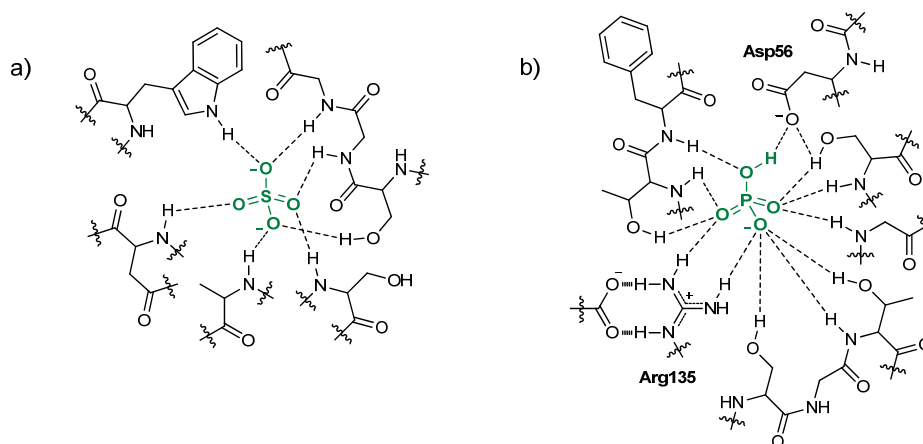
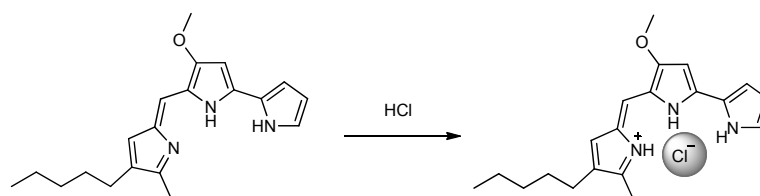


Figure 1.10 Highly selective anion binding exhibited by a) sulfate binding protein (SBP) and b) phosphate binding protein (PBP).

In addition to proteins, small molecule anionophores play important roles in Nature, for example the pyrrole-based prodiginine family of anion transporters. Prodigiosin 1 is able to transport chloride across membranes either through H⁺/Cl⁻ symport (Scheme 1.1) or Cl⁻/A⁻ antiport mechanisms,^{34, 35} and forms the basis of many synthetic analogues.³⁶



Scheme 1.1 Prodigiosin 1 H⁺/Cl⁻ symport.

1.1.3.2 Synthetic Anion Receptors

In this section, common anion binding motifs will be introduced, several of which have been seen in earlier examples in this chapter. For motifs of particular relevance to this thesis – amide, imidazolium and triazolium – their application in specific receptor examples will be discussed in detail, along with several recent systems exploiting less common interactions.

Due to the very nature of anions, positively charged groups possess inherent anion binding abilities. The electrostatic interaction is often complemented by additional interactions, most commonly hydrogen bonding. Ammonium,^{11, 28} pyridinium,³⁷ imidazolium,^{38, 39} triazolium⁴⁰ and guanidinium⁴¹ are examples of positively charged motifs exploited for anion recognition (Figure 1.11).

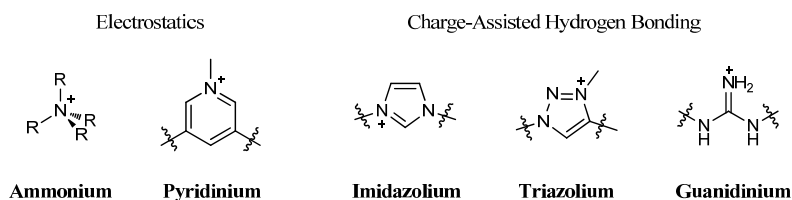


Figure 1.11 Positively charged anion binding motifs.

Neutral hydrogen bonding motifs are also commonly incorporated into anion receptor structural frameworks, including amide,^{42, 43} pyrrole,⁴⁴ indolocarbazole,⁴⁵ urea/thiourea^{46, 47} and triazole⁴⁸ groups (Figure 1.12). In addition, halogenated aromatics are capable of halogen bonding in carefully designed solution-phase receptors,²³ and boron complexes display anion binding *via* Lewis acid-base interactions.⁴⁹

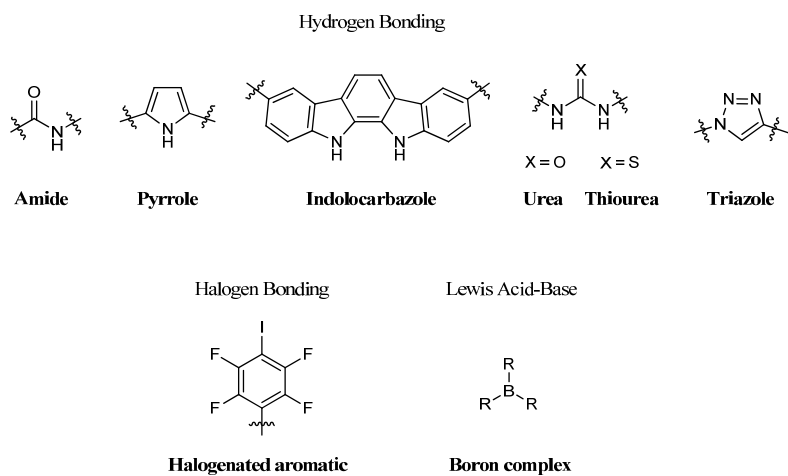


Figure 1.12 Neutral anion binding motifs.

Amide hydrogen bonding interactions are found in countless anion receptors in Nature – not least due to the central presence of amide groups in peptide frameworks. Consequently, many synthetic anion host systems contain integrated amide functionalities, a task aided by the multitude of amide coupling reactions available to the organic chemist.

The first amide-based anion receptor was reported in 1986 by Pascal *et al.* (Figure 1.13a).⁴² Cyclophane host **1.9** bound fluoride anions within its host cavity in DMSO, due to three convergent hydrogen bonds. Over a decade later, Crabtree discovered the anion complexation ability of the bis-amide containing isophthalamide motif through studying the relatively simple acyclic receptor **1.10** (Figure 1.13b).⁴³ Since then, this motif has been used extensively in a large number of more complicated macrocyclic¹³ and interlocked host structures (*vide infra*).

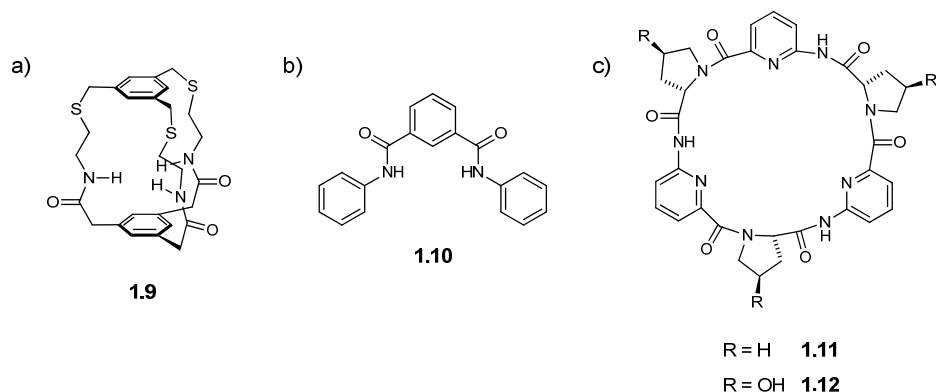


Figure 1.13 a) Pascal's cyclophane **1.9**, b) Crabtree's isophthalamide receptor **1.10**, and c) Kubik's cyclopeptide receptors **1.11** and **1.12**.

The scope of neutral amide-containing anion receptors has been demonstrated by the investigation of cyclopeptide derivatives by Kubik, achieving impressive anion binding in aqueous media.^{50, 51} For example, macrocycle **1.11** (Figure 1.13c) binds sulfate and the halides in a 2:1 host:guest stoichiometry in 8:2 D₂O/CD₃OD. The anionic guests were each held between two receptors *via* six hydrogen bonds and completely desolvated. The hydrophobic effect is thought to play a significant role in this complexation event, with the more hydrophilic cyclopeptide **1.12** exhibiting 1:1 binding stoichiometry and reduced affinity.

Since the first imidazolium anion receptors were reported by Sato⁵² and Alcalde⁵³ in 1999 (Figure 1.14a and b), this motif has been used increasingly for anion recognition.^{38, 39} Such systems typically contain multiple imidazolium groups for convergent charge-assisted C-H hydrogen bond donation. Sato's tripodal receptor **1.13** was found to bind halide anions strongly in CD₃CN, whilst Alcalde's family of 'imidazoliophane' macrocycles, including **1.14**, bound a variety of anions, for example fluoride, dihydrogen phosphate and acetate, in *d*₆-DMSO.

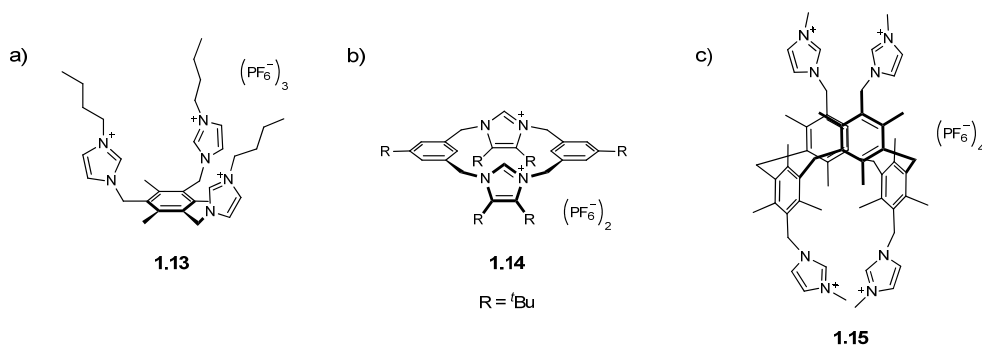


Figure 1.14 a) Sato's, b) Alcalde's and c) Steed's imidazolium-based anion receptors.

More recently, Steed *et al.* synthesised tetrapodal imidazolium-based receptor **1.15** (Figure 1.14c),⁵⁴ which exhibited a 1:2 host:guest stoichiometry due to the 1,3-alternate conformation of the calix[4]arene scaffold. Interestingly, upon addition of chloride in CD_3CN , conformational effects induced by the first binding event resulted in allosteric enhancement of the affinity for the second anion, an affect not observed with other anions such as bromide and acetate. This communication between different binding sites is reminiscent of the allosteric regulation displayed by proteins, for example in the binding of multiple oxygen molecules to hemoglobin.⁵⁵

Similar to imidazolium, the triazolium motif is able to bind anions *via* charge-assisted C-H hydrogen bonding. Triazole groups themselves can also participate in anion binding, with macrocyclic triazole receptors such as **1.7** (Figure 1.8) being investigated intensely by Flood.⁵⁶ Alkylation of the triazole N^3 further polarises the $\text{C}^5\text{-H}$ bond and introduces a formal positive charge, thus increasing anion binding affinity. Pandey *et al.* were the first to report triazolium-based anion recognition, synthesising the steroid-based bis-triazolium receptor **1.16** (Figure 1.15).⁴⁰ This receptor exhibits high affinity for dihydrogen phosphate in CDCl_3 , with selectivity over the halides and acetate. Interestingly, cyclic analogues displayed lower affinity for dihydrogen phosphate and reduced selectivity, suggesting that in this case the flexibility possessed by **1.16** is favourable in allowing the receptor to adopt a suitable binding geometry for the tetrahedral phosphate anionic guest.

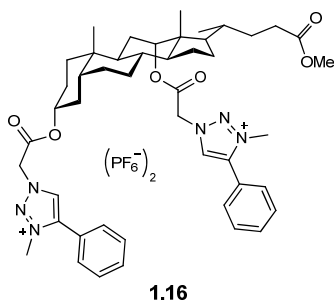


Figure 1.15 Pandey's bis-triazolium phosphate receptor.

Whilst charge-assisted hydrogen bonding is well known and exemplified by the above imidazolium and triazolium receptors, only recently has anion binding *via* analogous charge-assisted halogen bonding been reported. Beer *et al.* synthesised bromoimidazolium macrocycle **1.17** (Figure 1.16),⁵⁷ which was based on Alcade's imidazoliophanes discussed above. The bidentate receptor binds bromide selectively over the other halides in 9:1 CD₃OD/D₂O, exhibiting higher bromide affinity and greater selectivity than its protic, hydrogen bonding analogue.

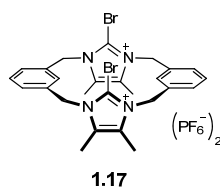
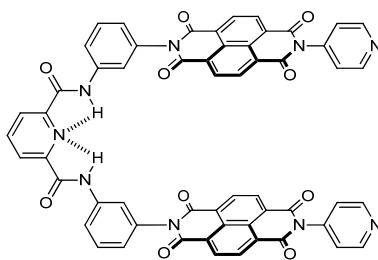


Figure 1.16 Bromide selective bromoimidazoliophane **1.17**.

The potential of anion- π receptors was recently demonstrated by Saha. The ability of bis-naphthalene diimide (NDI) derivatives, for example **1.18** (Figure 1.17), to bind fluoride anions selectively in 85:15 DMSO/H₂O *via* anion- π and charge/electron transfer (CT/ET) interactions was shown.⁵⁸ The electron-deficient NDI groups are preorganised by pyridine-amide hydrogen bonding in **1.18**, with novel CT/ET events promoting fluoride binding, resulting in a striking colorimetric response. This is an example of an optical sensor, and the area of anion sensing will be discussed in detail in the next section.

**1.18****Figure 1.17** Saha's anion- π fluoride receptor **1.18**.

1.1.4 Anion Sensors

For practical applications, it is important not only to selectively bind biologically or environmentally relevant negatively charged species, but to produce systems that are capable of sensing target anions. The IUPAC definition of a chemical sensor is “*a device that transforms chemical information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal*”.⁵⁹ Consequently, a sensor must be capable of producing a detectable, macroscopic signal, and contain a communication pathway between the recognition event and the production of that signal. Typically, optical or electrochemical methods of signalling and detection are employed.

The most common approach to anion sensing is the attachment of a reporter group to an anion receptor (Figure 1.18a). A slight variation of this modular arrangement is when the anion binding motif is able to be integrated within the reporter group. Alternative strategies, particularly for optical anion sensing, include using displacement assays (Figure 1.18b) and chemodosimeters (Figure 1.18c). In displacement assays, a complex is pre-formed between a signalling molecule, often an organic dye, and a receptor. The system is designed such that the target analyte binds preferentially to the receptor, displacing the dye and bringing about an associated signalling response.⁶⁰ A chemodosimeter is a sensor which undergoes a specific chemical reaction with the target analyte, often anionic nucleophilic attack, inducing a measurable change in the sensor signal.⁶¹ A different approach for electrochemical anion detection involves ion-selective electrodes (ISEs), in which an anion is extracted into a

membrane by a non-electroactive host, with the resulting membrane potential detected by the device.¹³ Recently Flood *et al.* have investigated the halide selectivity of ISEs using a tetratriazole macrocycle similar in structure to receptor **1.7** (Figure 1.8).⁶²

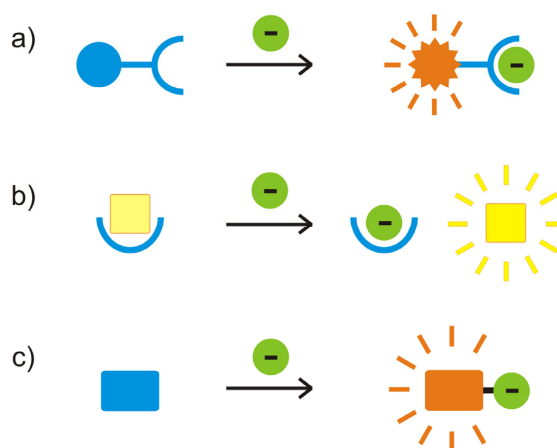


Figure 1.18 Generalised methods of anion sensing: a) attachment of a reporter group to an anion receptor, b) displacement assay, and c) chemodosimeter approach.

This section will focus on the use of discrete molecular sensors incorporating a recognition site and a reporter group (Figure 1.18a), for both optical and electrochemical anion sensing, as well as discussing the potential of surface-attached sensors.

1.1.4.1 Fluorescent Anion Sensors

Optical sensing is often divided into two classes depending on the mode of signalling: *fluorescent* sensors signal binding through changes in their excited-state emission, while *colorimetric* sensors display ground-state absorbance changes within the visible spectrum.

Luminescence is the spontaneous emission of radiation from an excited state, with the term *fluorescence* applying to such emission that arises from a singlet excited state.⁶³ Fluorescent sensing, often using organic fluorophores, can be achieved by changes in emission wavelength and/or intensity, and is advantageous due to its inherent high sensitivity.

Many metal-ligand complexes (MLCs) emit from a triplet metal-to-ligand charge transfer (³MLCT) excited state, in theory falling into the category of *phosphorescence* – formally forbidden

emission from triplet excited states. However, these transitions are partially allowed due to spin-orbit coupling, and MLCs do not share many of the qualities of phosphorescence species, such as long emission lifetimes. Hence the exact boundaries of terminology can be unclear, with emissive MLCs often more generally referred to as luminescent. Throughout this thesis, the common literature convention of including MLC systems in references to *fluorescent* sensing methods, whilst maintaining the distinction in specific *luminescent* MLC examples, will be followed.

There are many methods of communication employed by fluorescent sensors to signal anion binding. This section will focus on those of particular relevance to this thesis – photo-induced electron transfer (PET), excimer formation and the rigidity effect – whilst others, including electronic energy transfer (EET) and internal charge transfer (ICT), have also been exploited for effective anion sensing.^{64, 65}

Photo-induced electron transfer (PET) is a mechanism for fluorescence quenching, in which a proximal orbital, filled or empty, can facilitate through-space, non-radiative electron transfer to an excited fluorophore (Figure 1.19a). This excited-state process returns the fluorophore to the ground state without the emission of radiation. Any perturbations in the potential of the proximal orbital alters the extent of quenching and hence the fluorescence emission.

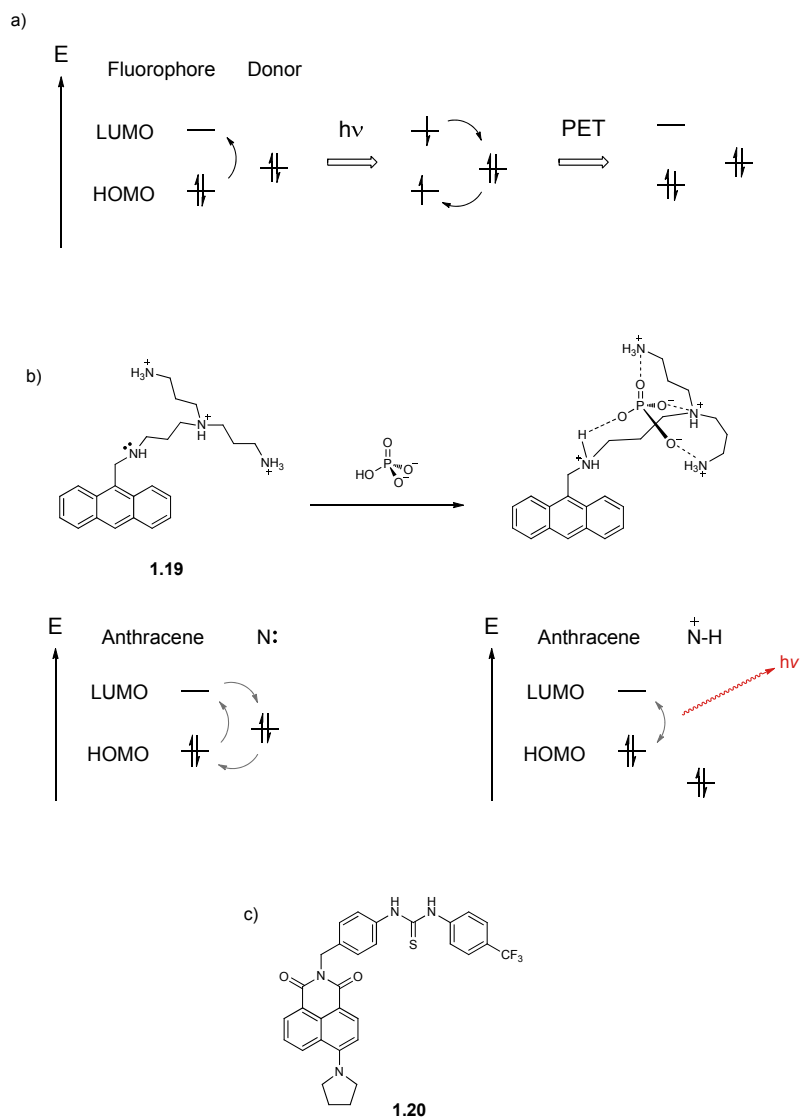


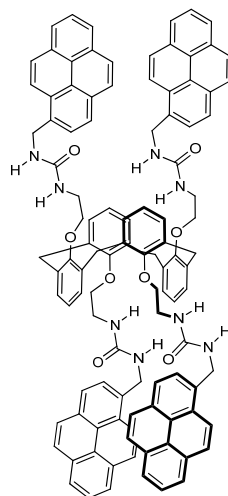
Figure 1.19 a) Mechanism for PET quenching of a fluorophore by a proximal donor group,⁶⁶ b) Czarnik's anthracene-based sensor **1.19**, and c) Gunnlaugsson's naphthalimide-based sensor **1.20**.

The use of PET in anion sensing systems can be illustrated by Czarnik's phosphate sensor **1.19** (Figure 1.19b),⁶⁷ in which the benzylic nitrogen lone pair quenches the anthracene fluorescence in the unbound polyammonium receptor. Phosphate binding in aqueous solution results in protonation of the quenching nitrogen atom, removing the PET process and hence switching 'on' the anthracene emission.

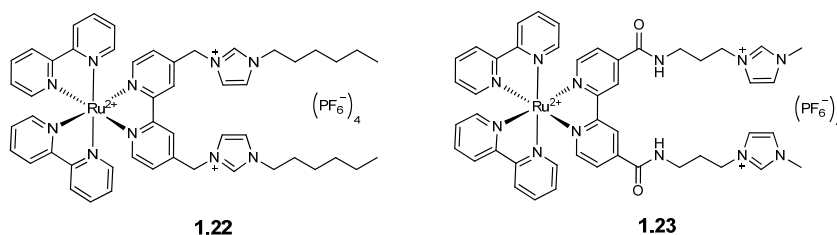
More recently, PET anion sensors have been synthesised incorporating a range of fluorophores and binding motifs.⁶⁵ For example, with Gunnlaugsson's naphthalimide thiourea receptor **1.20** (Figure 1.19c) fluorescence quenching was observed upon dihydrogen phosphate addition in DMSO,⁶⁸ accompanied by no changes in the ground state absorbance of the receptor, which is indicative of ideal PET sensing behaviour.

In addition to PET, anion sensing using organic fluorophores is also possible *via* excimer formation. An excimer complex is formed between a fluorophore in its excited state and an identical fluorophore in the ground state, with the resulting emission red shifted compared to the monomer and without vibronic bands.⁶³ Planar, π -delocalised groups, such as anthracene and pyrene, have the propensity to form excimers, and the extent of formation is dependent on the ability of the groups to overlap. Receptors that contain two or more such fluorophores and exhibit binding-induced conformational changes which alter the proximity of the fluorophores to each other, are capable of excimer sensing behaviour.^{65, 66} In these systems, dual emission from both the monomer and the excimer is frequently observed, resulting in ratiometric sensing methods.

Pyrene-functionalised 1,3-alternate calix[4]arene receptor **1.21** (Figure 1.20) illustrates the potential of intramolecular excimer anion sensors.⁶⁹ In the unbound receptor, emission is dominated by the pyrene excimer band, as the receptor conformation enables efficient stacking of the fluorophores. Upon selective chloride binding to the urea motifs in 95:5 MeCN/CHCl₃, an increase in monomer emission is accompanied by a decrease in the excimer band, as the pyrene groups are 'held apart' by the bound anion. A number of other effective anion sensors have also been reported exploiting similar pyrene excimer signalling methods.⁷⁰

**1.21****Figure 1.20** Chloride selective pyrene-functionalised receptor **1.21**.

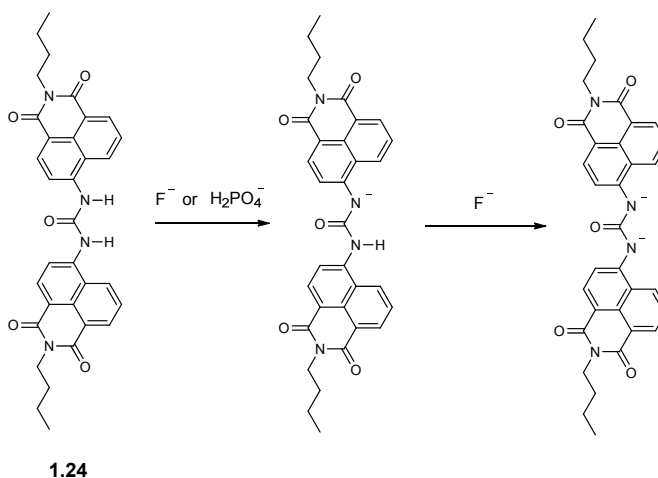
The rigidity effect has been used to explain the ability of certain transition metal containing receptors to signal anion binding by enhancements in emission.⁷¹ It has been suggested that anion coordination increases the rigidity of the receptors, reducing non-radiative decay through vibrational and rotational pathways, hence resulting in increased emission intensities. For example, Beer's ruthenium(II) bipyridyl receptors **1.22** and **1.23** (Figure 1.21) have been shown to display luminescent enhancements upon addition of chloride, bromide and dihydrogen phosphate in 9:1 MeCN/H₂O.⁷² In both receptors, this was accompanied by small hypsochromic shifts in emission wavelength, as the ³MLCT state responsible for the luminescence is raised in energy upon anion complexation.

**1.22****1.23****Figure 1.21** Beer's ruthenium(II) bipyridyl luminescent anion receptors **1.22** and **1.23**.

1.1.4.2 Colorimetric Anion Sensors

Ideally, the absorbance changes exhibited by colorimetric sensors are to such an extent that they are clearly visible to the naked eye, with this mode of detection having obvious advantages. Commonly, the chromophores employed are organic molecules which absorb in the visible range due to adequate conjugation, and if anion addition perturbs the chromophore sufficiently, a colour change is observed.

Whilst the chemodosimeter and displacement approaches are widely used,^{60, 61} many examples of colorimetric anion sensing involve sensor deprotonation by basic anions. For example, Fabbri's symmetric bis-naphthalimide urea-based receptor **1.24** undergoes two sequential deprotonation events upon the addition of fluoride in DMSO (Scheme 1.2),⁷³ which are accompanied by yellow-to-red and red-to-blue colour changes. The less basic dihydrogen phosphate only causes mono-deprotonation, whereas weakly basic anions, for example nitrate and chloride, do not induce any such changes.



Scheme 1.2 Sequential deprotonation of bis-naphthalimide receptor **1.24**.

For colorimetric sensors which signal *via* deprotonation events, the solvent in which they operate is especially important. In the presence of protic solvents, such as water, anions become less basic due to increased solvation, whilst the large excess of alternative proton sources hinders sensor deprotonation. Furthermore, this approach is evidently not applicable to the detection of weakly basic anions.

1.1.4.3 Electrochemical Anion Sensors

To achieve electrochemical anion sensing, redox-active groups, for example ferrocene and cobaltocenium, are incorporated within anion receptors in such a way that binding perturbs the redox centre.¹³ This is usually in the form of perturbations in either the reduction (in the case of cobaltocenium to cobaltocene) or the oxidation (ferrocene to ferrocenium) potential, with the presence of the bound anion often stabilising one species of the redox couple to a greater extent than the other. For example, the stabilisation of oxidised ferrocenium results in a cathodic shift in the ferrocene/ferrocenium redox couple. This is illustrated by polyaza-ferrocene macrocycle **1.25** (Figure 1.22a),⁷⁴ which exhibited a cathodic shift of 50 mV upon phosphate addition in a pH neutral aqueous environment. Similarly, fluoride, acetate and dihydrogen phosphate anions induced cathodic shifts of 50–100 mV in Molina's bisferrocenyl thiourea receptor **1.26** in DMF (Figure 1.22b).⁷⁵

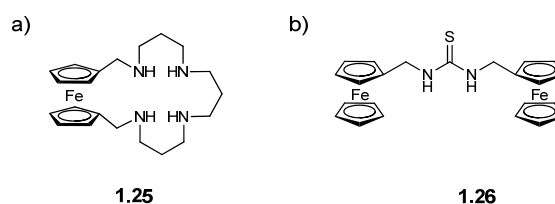


Figure 1.22 a) Polyaza-ferrocene macrocycle **1.25**, and b) bisferrocenyl thiourea-based sensor **1.26**.

1.1.4.4 Surface-Attached Anion Sensors

The surface attachment of sensors for use as molecular devices is an area of intense research, particularly the attachment of functional self-assembled monolayers (SAMs) onto gold and glass surfaces.^{76, 77} Importantly, these systems have a number of significant advantages when compared with solution-phase analogues. Sensor reusability is essential for practical situations, and that aspect of surface-attached devices, along with their durability, makes them highly desirable for commercial applications. Additionally, solubility problems are avoided, and the preorganisation of many receptor molecules on the surface can have beneficial amplification effects. As well as gold and glass SAM systems, the use of nanoparticles for a multitude of sensing applications is also an area of great potential.^{78, 79}

Gold surfaces have been readily exploited for electrochemical devices including anion sensors,⁸⁰ with the first ferrocene-containing SAM, **1.27**, reported by Alonso *et al.* (Figure 1.23a).⁸¹ Dihydrogen phosphate addition to a CH_2Cl_2 solution brought about a 290 mV cathodic shift of the ferrocene/ferrocenium redox couple of **1.27**, consistent with anionic stabilisation of the oxidised state. In addition to the surface attachment of redox-active groups such as ferrocene, non-electrochemically active receptors can also be utilised for surface-attached sensing *via* electrochemical impedance spectroscopy, by using appropriate electrodes and a suitable redox-active species in solution.⁷⁷

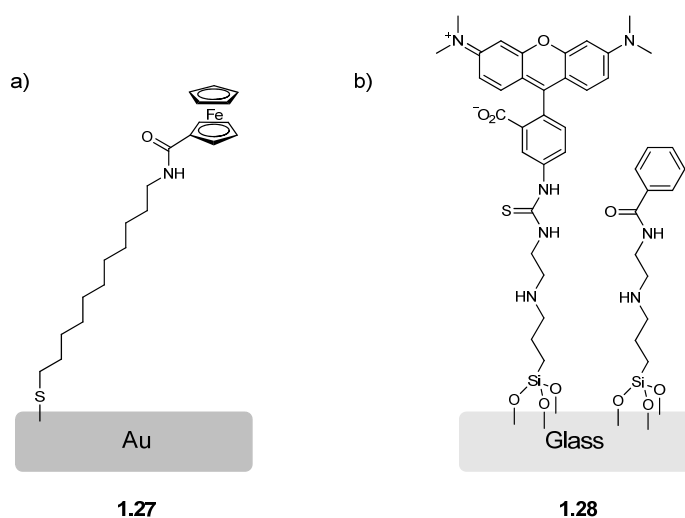


Figure 1.23 a) Alonso's ferrocene-containing SAM **1.27**, and b) Crego-Calama's fluorescent SAM **1.28** capable of anion discrimination.

In contrast, optical anion sensing using SAMs has been hindered by the inherent ability of gold surfaces to efficiently quench fluorophore emission.⁸² Whilst glass-attached fluorescent SAMs have been extensively employed to sense other types of analyte,⁷⁶ there are still few surface-immobilised anion sensors operating by fluorescence. One such system was reported in 2004 by Crego-Calama *et al.*,⁸³ in which a relatively simple approach was shown to produce effective cation and anion sensing behaviour. Of the systems investigated, SAM **1.28** was composed of amide and thiourea anion binding motifs and the tetramethylrhodamineisothiocyanate (TRITC) fluorophore (Figure 1.23b). Upon exposure to a MeCN solution containing acetate, the SAM fluorescence was enhanced by 87%, whilst quenching of 56% was observed with dihydrogen phosphate.

1.2 Mechanically Interlocked Structures

Within supramolecular chemistry, the area of mechanically interlocked structures is based on the concept of *mechanical*, rather than *chemical*, bonds.⁸⁴ Two or more interpenetrated components that cannot be separated without the cleavage of a chemical bond are mechanically interlocked, and such systems can possess complicated molecular topologies.⁸⁵

The most common classes of interlocked structures are catenanes and rotaxanes, derived from the respective latin words for chain, wheel and axle – ‘catena’, ‘rota’ and ‘axis’. A catenane is composed of mechanically interlocked rings (Figure 1.24a), whilst a rotaxane contains a macrocyclic component threaded over an axle and held in place by two bulky stoppers (Figure 1.24b). A related supramolecular structure is the pseudorotaxane, in which an axle without stoppers resides within a macrocycle (Figure 1.24c). This interpenetrative, but not interlocked, assembly is often the precursor to catenanes and rotaxanes. In addition to interlocked structures, other complex molecular topologies are possible, including knotted architectures such as the trefoil knot (Figure 1.24d).

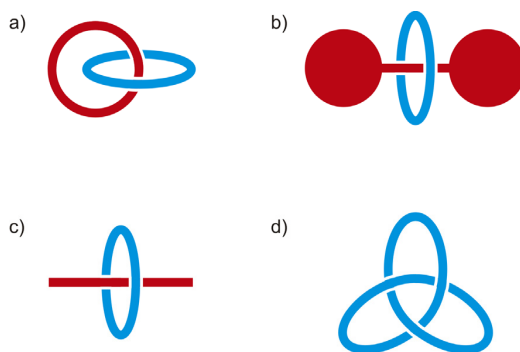


Figure 1.24 Schematic representations of a) a catenane, b) a rotaxane, c) a pseudorotaxane and d) a trefoil knot.

These topological concepts have been translated into numerous synthetic systems, such as Sauvage’s seminal copper(I) templated catenane **1.29** (Figure 1.25a),⁸⁶ which was the first example of the effective templated synthesis of an interlocked structure (see Section 1.2.2.1).

In addition to interlocked structures consisting of two components, higher order catenanes and rotaxanes can also be constructed. An [n]catenane is composed of n interlocked rings, with Stoddart’s

“olympiadane”, shown in Figure 1.25b, an impressive example of a [5]catenane.⁸⁷ Similarly, an [n]rotaxane can contain either multiple macrocycles around a single axle,⁸⁸ or multiple axles threaded through a single macrocycle.⁸⁹ By extension, poly-catenanes and -rotaxanes contain many interlocked components.^{90, 91}

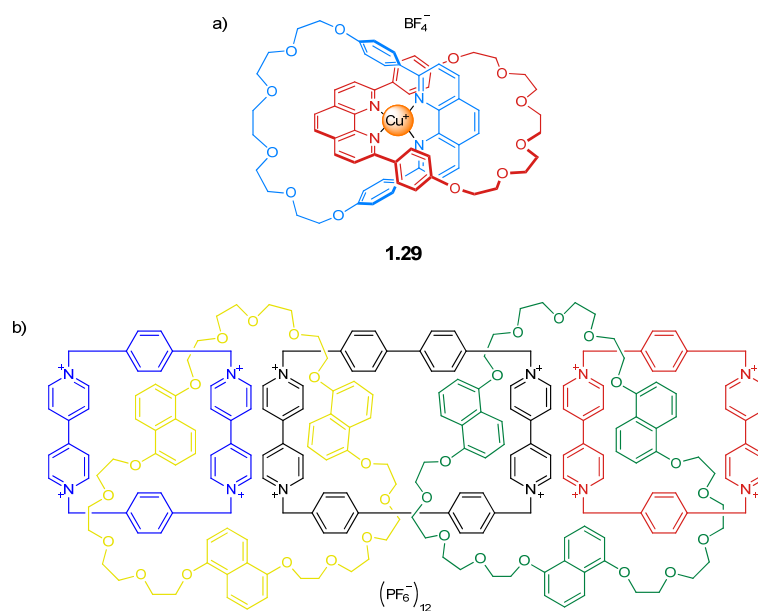


Figure 1.25 a) Sauvage's [2]catenane **1.29** and b) Stoddart's [5]catenane "Olympiadane".

Whilst the concept of the mechanical bond can be quite familiar to us – the links in chains, wheels around axles – there are relatively few examples of such systems in Nature. Catenanes of mitochondrial DNA were first reported in 1967 using electron microscopy and arise from errors in the replication of circular DNA.^{92, 93} More recently, a new class of 'knotted' proteins has been found,⁹⁴ with investigations into these structures enabling further insight into protein folding mechanisms.

Interest in synthetic interlocked structures was driven initially by academic curiosity and the considerable challenge of preparing catenanes and rotaxanes in reasonable yields. However, recent developments have highlighted the potential of interlocked structures for many nanotechnological applications, for example as switchable molecular devices, sensors and unique materials. In this section, the general synthetic strategies for constructing interlocked molecules will be discussed,

followed by the specific methods of templated synthesis, and the potential applications of such architectures.

1.2.1 Synthetic Strategies

There are a number of ways of approaching interlocked structure formation. The most common strategies employed for the synthesis of catenanes are *cyclisation* (Figure 1.26a) and *double cyclisation* (Figure 1.26b), in which one or both of the rings are formed in the fabrication of the interlocked product. Rotaxane formation is usually achieved by either ‘*clipping*’ (Figure 1.26c), the cyclisation of a macrocycle around an axle, ‘*stoppering*’ (Figure 1.26d), the addition of stopper groups to a pseudorotaxane, or ‘*snapping*’ (Figure 1.26e), the combining of two half-axes within a macrocycle.

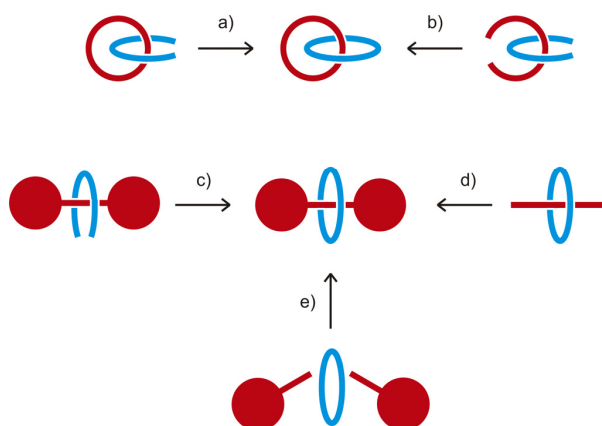


Figure 1.26 Common methods of interlocked structure formation: a) cyclisation and b) double cyclisation of catenanes, and c) clipping, d) stoppering and e) snapping approaches for rotaxane synthesis.

Less common methods include ‘*magic ring*’ catenation,^{95, 96} in which closed macrocycles re-open and subsequently close in an interlocked arrangement, and similar ‘*magic ring/rod*’ approaches to rotaxane formation.^{97, 98} In addition, there have been several rotaxane systems synthesised by ‘*slippage*’,^{99, 100} in which the macrocycle ‘slips’ over the stopper groups of the axle, ‘*swelling*’,^{101, 102} when the stopper groups are ‘swollen’ after the macrocycle has freely threaded onto the axle, and ‘*shrinking*’,^{103, 104} a reduction in the size of the macrocycle after threading.

A variety of chemical reactions have been employed in the application of these general strategies, including Grubbs'-catalysed ring closing metathesis (RCM), for example in the formation of catenane **1.30** by cyclisation (Figure 1.27a),¹⁰⁵ and amide condensation.^{106, 107} Recently, the copper(I)-catalysed alkyne-azide cycloaddition (CuAAC), a 'click' reaction,¹⁰⁸ has been readily utilised in the formation of countless interlocked structures,¹⁰⁹ such as the stoppering of rotaxane **1.31** (Figure 1.27b).¹¹⁰ The key attributes of 'click' reactions – quantitative, tolerant of other functional groups and mild reaction conditions – make them ideal for this application.

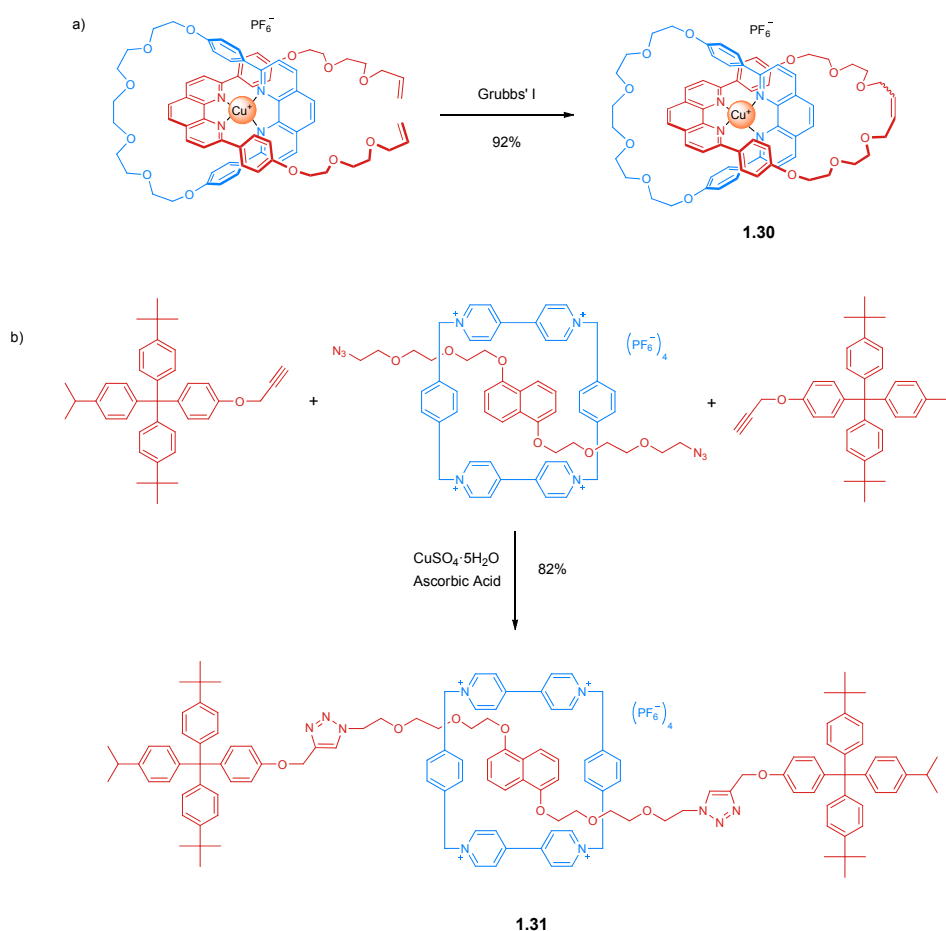


Figure 1.27 Examples of using a) ring closing metathesis (RCM) and b) the CuAAC 'click' reaction in the formation of interlocked structures.

The effective synthesis of both **1.30** and **1.31** was made possible by templating the association of the components prior to the reaction forming the interlocked structure, using copper(I) chelation

and charge-transfer donor-acceptor interactions respectively. The templated synthesis of interlocked structures will be discussed in detail in the next section.

Finally, it is important to note that the two systems shown in Figure 1.27 are examples of kinetic ‘trapping’, in which an irreversible reaction captures the interlocked product. The formation of interlocked structures under thermodynamic control is also possible using reversible covalent reactions.¹¹¹ If the system is designed such that the interlocked product is thermodynamically favoured, efficient ‘recycling’ of unwanted, non-interlocked by-products is possible, leading to dynamic ‘magic ring/rod’ systems. Amongst other reactions, reversible RCM (thermodynamic under certain reaction conditions),⁹⁷ and the formation of imines¹¹² and hydrazones¹¹³ have all been used in the effective formation of interlocked structures under thermodynamic control.

1.2.2 Templated Synthesis

Initial approaches to the challenge of synthesising interlocked structures were statistical, relying on the low probabilities of macrocyclisation reactions occurring in interlocked co-conformations. This method was first investigated in the 1960s by Wasserman^{114, 115} and Harrison and Harrison¹¹⁶, but is severely limited by its inherent low yields. An alternative covalent-directed approach was carried out by Schill,¹¹⁷ involving the lengthy and challenging synthesis of covalently attached components arranged in such a way that cleaving the linkage yields the desired interlocked product. Whilst several examples of successful covalent-directed systems have been recently reported,^{118, 119} the effective synthesis of interlocked structures requires an alternative approach, namely templation.

Templates are widely used in the construction of numerous supramolecular systems and can be classified several different ways. Thermodynamic templates bind to the product, shifting equilibria towards that species, whilst kinetic templates stabilise transition states that result in irreversible product formation.¹²⁰ In addition, the topology of the template can lead to linear, cyclisation or interweaving templation.¹²¹

For interlocked structures, it is possible for a template to be integrated within the resulting interlocked framework, or discrete and removable (Figure 1.28a and b), and to classify whether the templation is ‘passive’ or ‘active’. A passive template is responsible for the association of the components prior to the reaction that forms the interlocked structure (Figure 1.28b). However, an active template mediates both the association and catalyses the reaction (Figure 1.28c).

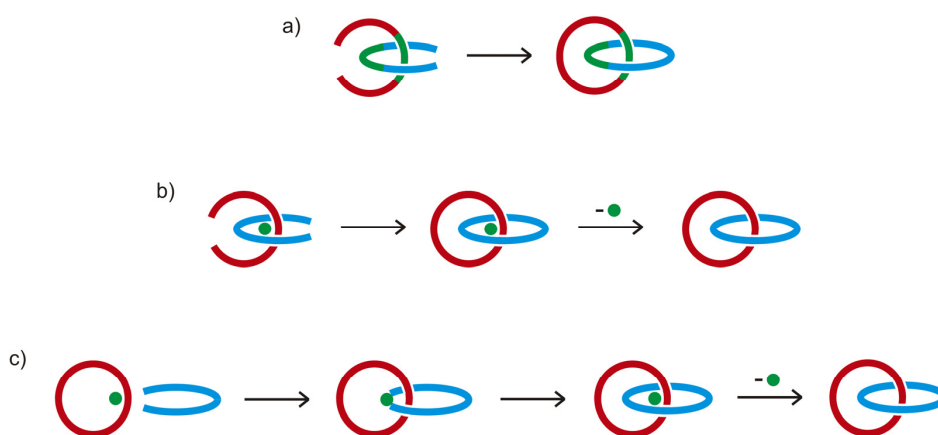


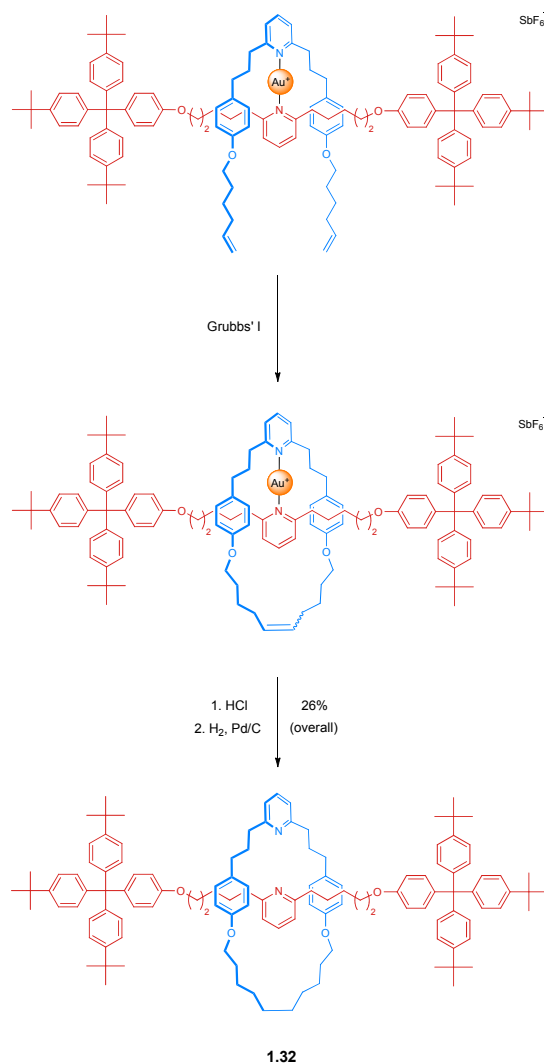
Figure 1.28 Classification of interlocked templation: a) template integrated within the resulting interlocked framework, b) discrete passive templation, and c) active templation.

The following sections will discuss the different methods of templation used for the synthesis of interlocked structures – namely metal, organic cation, neutral and anion templation.

1.2.2.1 Metal Templation

The templated synthesis of interlocked structures was pioneered by Sauvage in the 1980s, who exploited the tetrahedral arrangement of two bidentate phenanthroline ligands around a passive copper(I) template to construct catenanes such as **1.29** and **1.30** (Figures 1.25a and 1.27a),^{86, 105} before applying these principles to a range of systems with increasing complexity.¹²² Metal templation benefits from the strength of metal-ligand bonds, as well as the well-defined geometries of the resulting complexes. In addition to copper(I), many other metals and geometries have been employed in the synthesis of metal templated interlocked structures.¹²³ The use of linear two-coordinate gold(I)

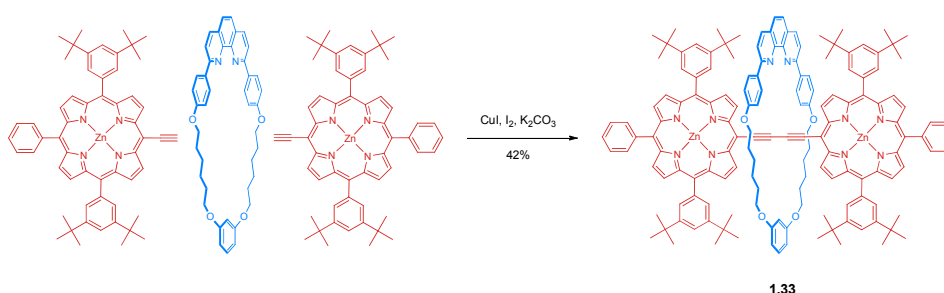
by Leigh *et al.* to template the formation of rotaxane **1.32** demonstrates the scope of this approach (Scheme 1.3).¹²⁴



Scheme 1.3 Synthesis of Leigh's gold(I) templated rotaxane **1.32**.

The ability of metals to catalyse numerous organic reactions has enabled their use as active templates for interlocked structure formation.¹²⁵ The first example of active metal templation for mechanical bond formation was reported by Leigh in 2006,¹²⁶ in which a rotaxane was synthesised using the CuAAC 'click' reaction. Other copper-catalysed processes have also been exploited, such as the Cadiot-Chodkiewicz reaction¹²⁷ and Glaser coupling,¹²⁸ for example, porphyrin-stoppered rotaxane

1.33 synthesised by Anderson *et al.* (Scheme 1.4).¹²⁹ Rotaxanes constructed this way are examples of the general ‘snapping’ method previously discussed (Figure 1.26e). This active metal templation approach to interlocked molecular construction has been expanded to reactions involving other metals, such as the palladium(II)-catalysed Heck reaction¹³⁰ and nickel(II)-catalysed reductive homocoupling,¹³¹ and has great potential due its scope and efficiency.



Scheme 1.4 Synthesis of Anderson’s porphyrin-stoppered rotaxane **1.33** *via* active metal Glaser coupling.

1.2.2.2 Organic Cation Templatation

Beyond metal templation, organic cations are also able to template the formation of interlocked structures, with Stoddart providing the major contributions to this area. “Olympiadane” and rotaxane **1.31** (Figures 1.25b and 1.27b) both contain electron-accepting positively charged bis(4,4’-bipyridinium) macrocycles which form favourable charge-transfer donor-acceptor interactions with electron-donating dioxynaphthalene derivatives. The donor-acceptor interaction between 4,4’-bipyridinium dications and dioxynaphthalene was first exploited for catenane formation in 1989,¹³² and has since been utilised in the templation of many other systems.¹³³

The association between crown ethers and secondary dialkylammonium salts is another recognition process that was first exploited in the formation of an interlocked structure by Stoddart (Figure 1.29a).⁸⁸ This interaction is driven by hydrogen bonding and is responsible for the templated synthesis of rotaxane **1.34**. Subsequently, Loeb *et al.* found that the additional ability of crown ethers to form pseudorotaxanes with 1,2-bis(pyridinium)ethane dications¹³⁴ was able to template the formation of rotaxane systems including **1.35** (Figure 1.29b).¹³⁵

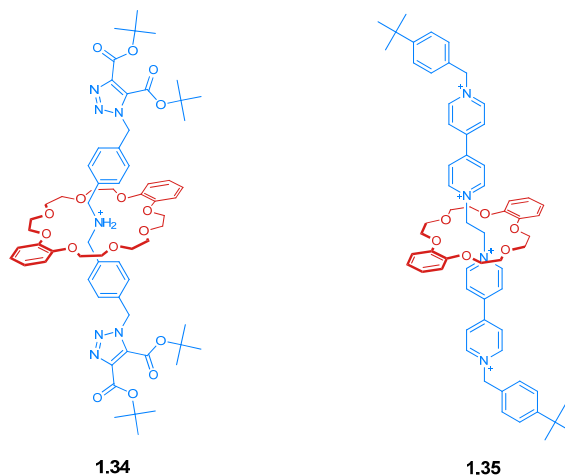
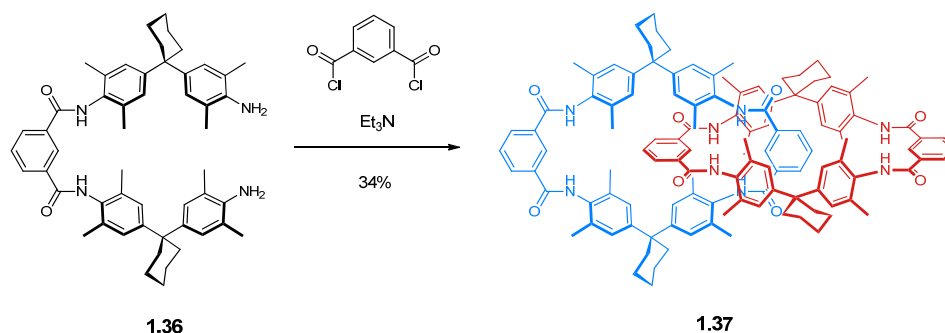


Figure 1.29 Rotaxanes synthesised using templating interactions between crown ethers and a) dialkylammonium and b) 1,2-bis(4,4'-dipyridinium)ethane derivatives.

These systems are examples of ‘integrated’ templation (Figure 1.28a), as the templating groups, and more importantly templating interactions, are present in the resulting interlocked structures. This is also the case for the following section on neutral templation.

1.2.2.3 Neutral Templation

The presence of charged groups, such as metal or organic cations, is not always necessary for the templation of interlocked structures, as neutral recognition motifs can be effectively employed. An early example of this was the serendipitous discovery of amide-based catenanes by both Hunter¹⁰⁶ and Vögtle¹⁰⁷ in 1992, templated by hydrogen bonding interactions. Hunter’s catenane, **1.37** (Scheme 1.5), was isolated from the condensation reaction between isophthalic dichloride and bis-amine **1.36** in 34% yield. A similar approach was exploited by Leigh,¹³⁶ with a variety of motifs able to be encapsulated by amide macrocycles *via* hydrogen bond templation.^{137, 138}



Scheme 1.5 Synthesis of catenane **1.37** via hydrogen-bond templation.

As well as charged donor-acceptor interactions (Section 1.2.2.2), it is possible to use neutral electron-deficient groups, such as aromatic diimides, to template the formation of interlocked structures *via* donor-acceptor interactions. This is demonstrated by the synthesis of neutral catenane **1.38** by Sanders *et al.* (Figure 30a),¹³⁹ in which the stacking of a naphthalene diimide (NDI) derivative both inside and outside a bis-oxynaphthalene macrocycle was responsible for the donor-acceptor-donor-acceptor (DADA) catenane arrangement. More recently, Sanders has exploited reversible covalent chemistry, specifically disulfide exchange, to construct aqueous dynamic combinatorial libraries capable of producing a variety of catenanes based on similar donor and acceptor motifs.^{140, 141} In these libraries, unusual catenanes including **1.39** (Figure 1.30b) were formed which did not follow the previous DADA component arrangement, suggesting that the hydrophobic effect contributes to the catenation process as well as donor-acceptor interactions.

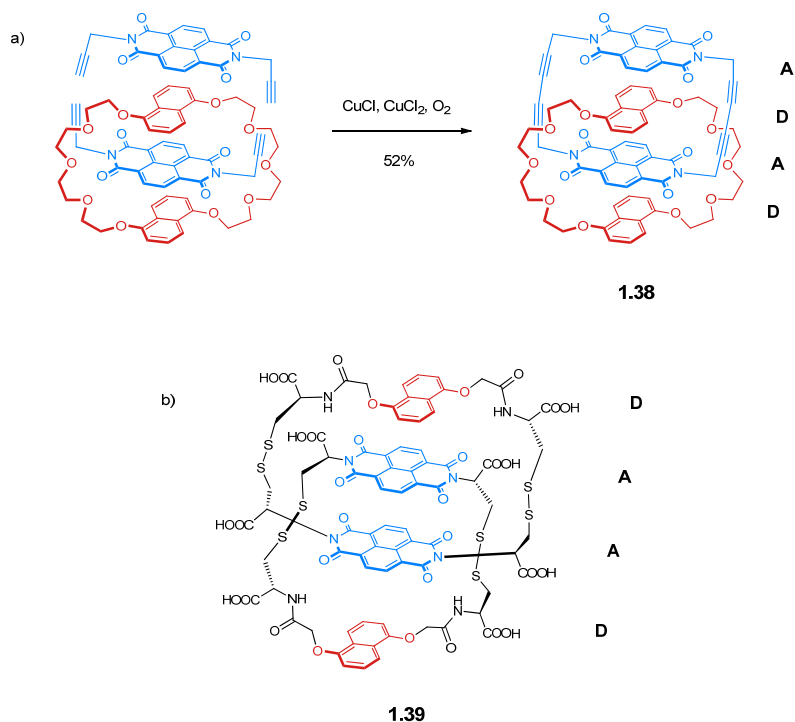
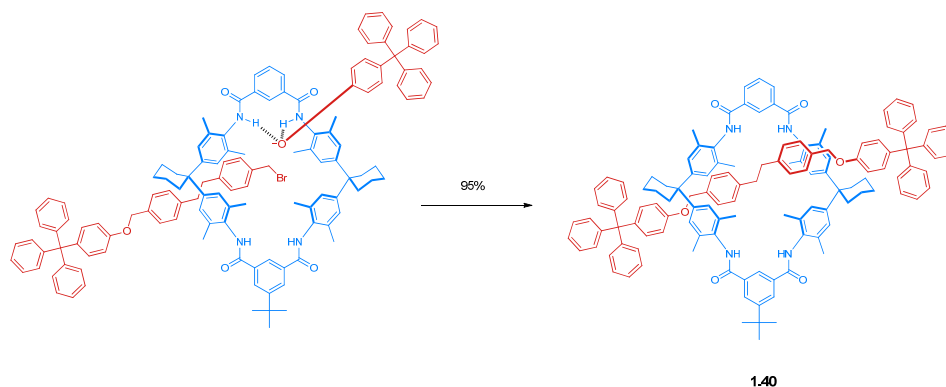


Figure 1.30 a) Synthesis of neutral donor-acceptor catenane **1.38** and b) the structure of DAAD disulfide catenane **1.39**. D = donor (red); A = acceptor (blue).

The templation of interlocked structures purely by the hydrophobic effect has also been reported, most commonly using cyclodextrin inclusion complexes in aqueous environments.¹⁴²⁻¹⁴⁴

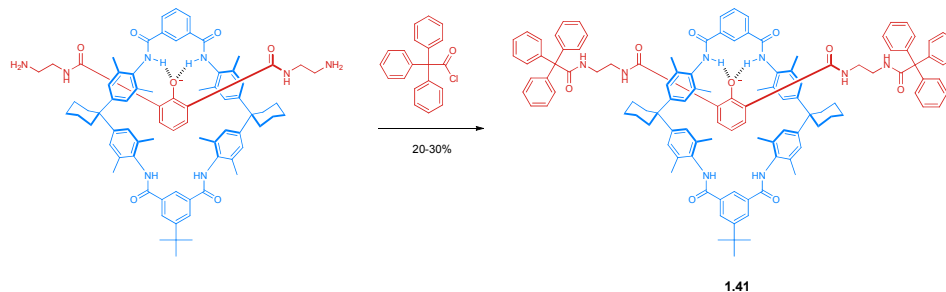
1.2.2.4 Anion Templation

The use of anions to template the formation of interlocked structures has been less widespread than the other methods previously discussed, presumably due to the specific challenges associated with anion complexation (Section 1.1.2.1). The first anion templated interlocked structure was reported by Vögtle in 1999,¹⁴⁵ in which the anion binding ability of a lactam macrocycle was exploited to synthesise rotaxane **1.40** (Scheme 1.6). The complexation of the phenolate half-axle within the macrocycle cavity ensured the subsequent S_N2 reaction yielded the target rotaxane, which is formed with the consumption of the anionic template.



Scheme 1.6 Synthesis of Vögtle's anion templated rotaxane **1.40**.

Similarly, Schalley *et al.* employed the isophthalamide-phenolate interaction to template the synthesis of rotaxane **1.41** (Scheme 1.7).¹⁴⁶ In this system, the anion templates pseudorotaxane formation before stoppering by amide condensation captures the interlocked structure. This is an example of 'integrated' templation as the anion, and the associated hydrogen bonding interactions, remain part of the rotaxane.



Scheme 1.7 Synthesis of Schalley's anion templated rotaxane **1.41**.

Inspired by Sauvage's copper(I) templated interlocked structures (Figures 1.25a and 1.27a), Beer investigated the ability of isophthalamide derivatives to form orthogonal complexes with pyridinium bis-amide ion pairs (Figure 1.31a),¹⁴⁷ with the objective of achieving discrete anion templation. The orthogonal arrangement of components around the chloride anion in **1.42** has successfully been exploited to form a number of anion templated interlocked structures,^{148, 149} as demonstrated by the synthesis of catenane **1.43** by RCM cyclisation (Figure 1.31b).¹⁵⁰

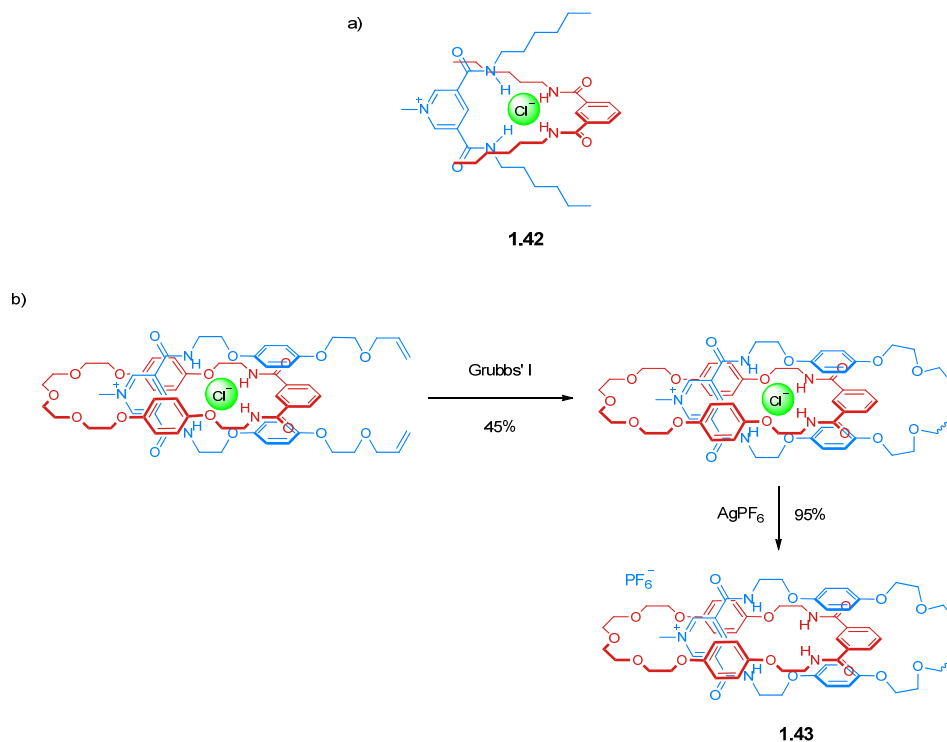


Figure 1.31 a) Orthogonal arrangement of components around a chloride template, and b) synthesis of a chloride templated catenane **1.43**.

The scope of this approach has also been extended to synthesise interlocked structures incorporating different anion recognition groups and templated by anions other than chloride. For example sulfate templated pyridinium nicotinamide catenane **1.44** (Figure 1.32a),¹⁵¹ and bromide templated triazolium rotaxane **1.45** (Figure 1.32b).¹⁵²

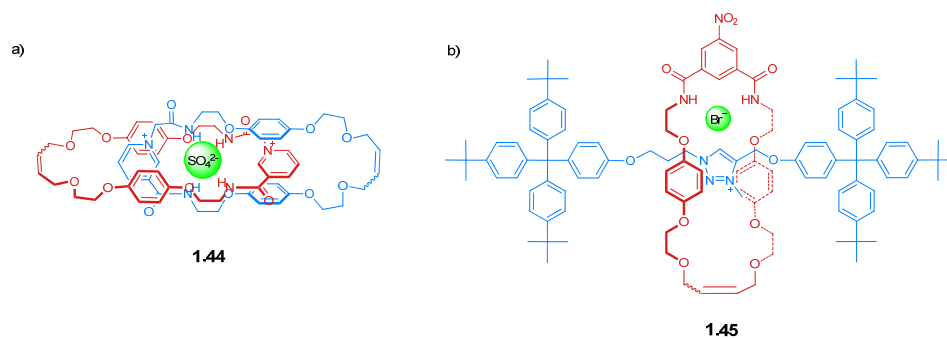


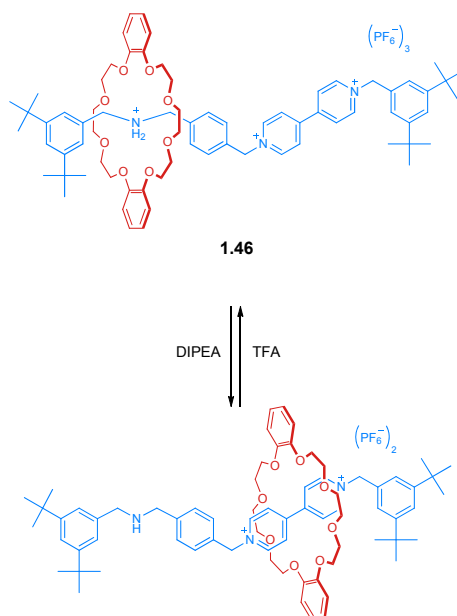
Figure 1.32 a) Sulfate templated pyridinium nicotinamide catenane **1.44**, and b) bromide templated triazolium rotaxane **1.45**.

1.2.3 Applications of Interlocked Structures

With their effective synthesis possible through a range of different templation methods, the potential applications of interlocked structures are currently being extensively investigated.

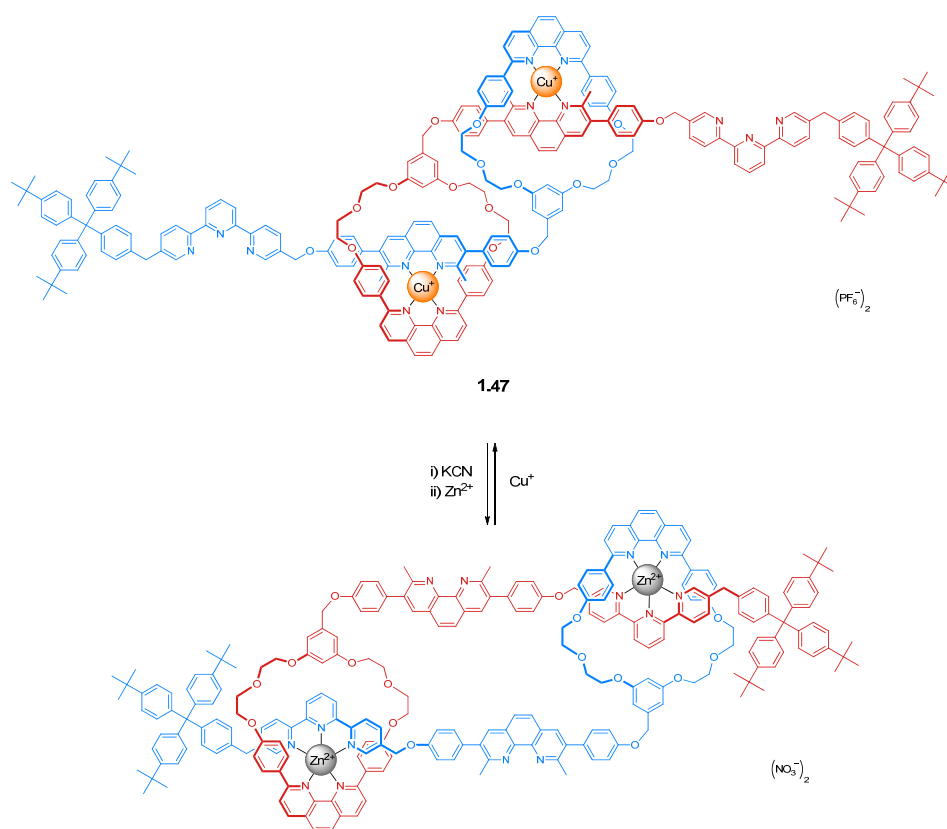
1.2.3.1 Switchable Molecular Devices

A major area of interest is the use of interlocked structures as switchable molecular devices, even ‘machines’, with molecular motion possible by changes in the relative positions of their constituent parts.¹⁵³⁻¹⁵⁵ The most common types of molecular motion are ring pirouetting in catenanes,¹⁵⁶ and rotaxane shuttling such as that exhibited by **1.46** (Scheme 1.8).¹⁵⁷ Asymmetric rotaxane **1.46** was constructed using the templating interaction between ammonium cations and crown ethers (Section 1.2.2.2) and designed to contain an additional bipyridinium station within its axle component. Upon deprotonation of the ammonium group, the macrocycle shuttles to the bipyridinium station due to favourable donor-acceptor interactions. This motion is completely reversible by subsequent addition of acid.



Scheme 1.8 pH-induced shuttling rotaxane **1.46**.

More complex interlocked structures are capable of other types of molecular motion, for example ‘Janus’ [2]rotaxane **1.47** displays muscle-like expansion and contraction (Scheme 1.9).¹⁵⁸ A Janus [2]rotaxane consists of two interlocked components, each of which contains a half-axle attached to a macrocycle. The threading of each component through the macrocycle of the other enables any shuttling motion to result in expansion and contraction of the entire system. In rotaxane **1.47**, this action is mediated by metal exchange, due to the different coordination requirements of copper(I) and zinc(II). Recently, the same stimulus has been employed to induce macrocycle ‘flapping’ within a [3]rotaxane.¹⁵⁹

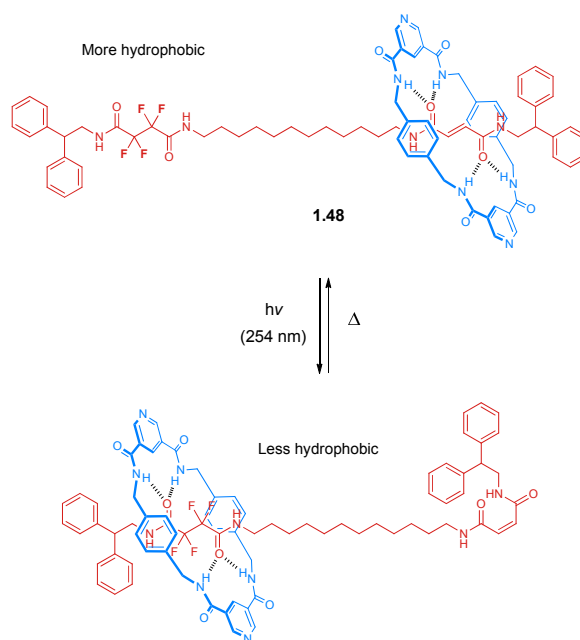


Scheme 1.9 Muscle-like motion of Janus [2]rotaxane **1.47** mediated by metal exchange.

In addition to pH and metal exchange, other types of stimuli have been exploited to induce controlled, reversible changes in the co-conformations of interlocked structures, such as

electrochemical,¹⁵⁶ photochemical,¹⁶⁰ anion¹⁶¹ or cation¹⁶² addition, and changes in the solvent environment.¹⁶³

However, the challenge of constructing functional molecular machines – capable of “doing work” – is a considerable one, extending beyond systems which act as simple switches.¹⁵⁵ An important development towards achieving this goal is the ability to organise the spatial arrangements of the molecules to enable synchronised action, such as on a surface. An early example of a macroscopic function arising from the surface-attachment of a switchable molecular device is Leigh’s rotaxane **1.48** (Scheme 1.10), which was physisorbed onto a gold SAM surface.¹⁶⁴ The shuttling, initiated by photo-isomerisation, resulted in a reduction in the hydrophobic nature of the surface, with the associated changes in contact angle being able to be exploited for droplet transport.



Scheme 1.10 Photo-isomerisation of rotaxane **1.48**.

1.2.3.2 Recognition and Sensing

Interlocked structures can be designed to contain unique three dimensional cavities, somewhat reminiscent of those possessed by selective binding enzymes (Section 1.1.3.1). These interlocked host

cavities have been exploited in the construction of effective receptors and sensors for a number of different target guest species.

Systems synthesised using discrete templates often display strong binding to the templating species. For example, the formation of catenane **1.49** (Figure 1.33) was amplified by the presence of acetylcholine in a dynamic combinatorial library based on hydrazone formation.¹¹³ Upon isolation, this major product was shown to bind the template more strongly in 95:5 CHCl₃/DMSO than other, non-interlocked components of the library.

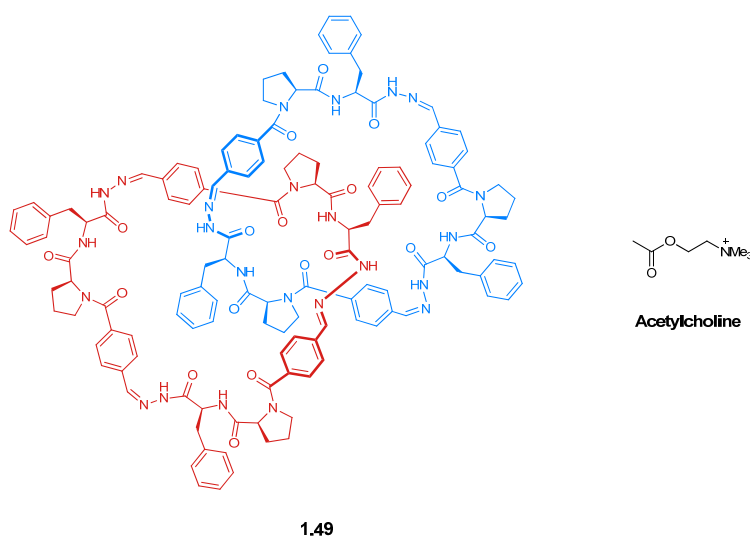


Figure 1.33 Catenane **1.49**, capable of strong binding to its acetylcholine template.

In an effort to amplify selective anion recognition, Beer has exploited anion templated interlocked structures, including **1.43–1.45** (Figures 1.31 and 1.32), to achieve a high degree of selectivity for the templating species over other, more basic anions.^{148–152} For example, this approach to anion recognition and sensing has also been investigated more recently by Jeong, with indolocarbazole-based catenane **1.50** (Figure 1.34) synthesised by chloride templation.¹⁶⁵ Upon removal of the template, the interlocked host cavity binds chloride selectively over a variety of other, non-complementary anions, such as the more basic acetate and dihydrogen phosphate guest species. In addition, anion binding was signalled by an increase in fluorescence emission from the indolocarbazole fluorophore.

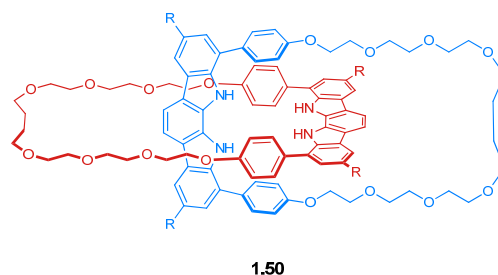
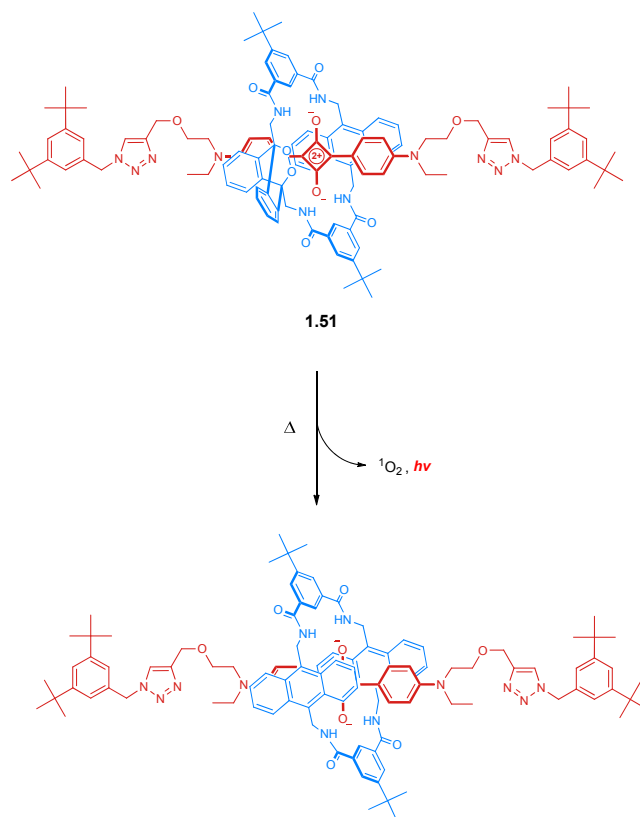


Figure 1.34 Jeong's indolocarbazole catenane **1.50**. R = CO₂(CH₂)₇CH₃.

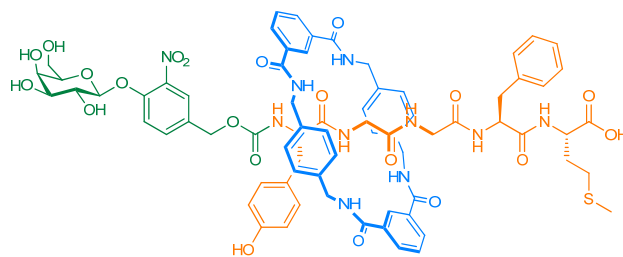
1.2.3.3 Medical Applications

The mechanical bond in rotaxanes and catenanes can also significantly modify the properties of the individual, interlocked components. For example, the encapsulation of near-infrared squaraine dyes within rotaxanes such as **1.51** results in both enhanced stability against nucleophilic attack and novel chemiluminescence (Scheme 1.11).¹⁶⁶ Upon warming, the endoperoxide macrocycle of **1.51** undergoes a cycloreversion reaction, releasing singlet oxygen which excites the squaraine fluorophore. This chemiluminescent behaviour is highly desirable for *in vivo* imaging applications.



Scheme 1.11 Chemiluminescence exhibited by squaraine rotaxane endoperoxide **1.51**.

The concept of achieving enhanced stability by encapsulation within an interlocked architecture has also been employed in several studies investigating the potential of rotaxanes to act as prodrugs.¹⁶⁷⁻¹⁶⁹ In one of Leigh's model systems, rotaxane **1.52** (Figure 1.35) contained bioactive peptide met-enkephalin (depicted in orange) and exhibited greater stability compared to both the axle component and the parent peptide.¹⁶⁸ Enzyme-mediated hydrolysis removes the monosaccharide-based stopper (depicted in green), releasing the peptide. Another area of interest for potential drug delivery applications is the use of switchable molecular devices for the controlled release of molecules from 'nanovalve'-containing nanoparticles.¹⁷⁰

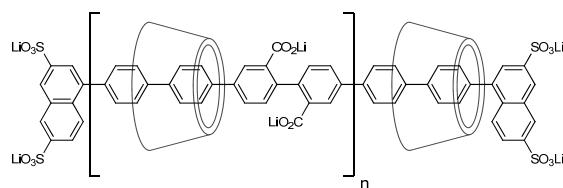
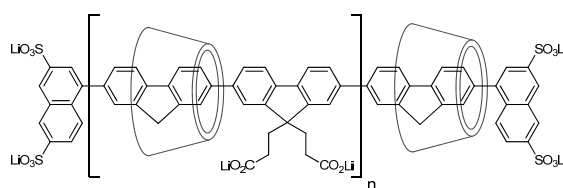
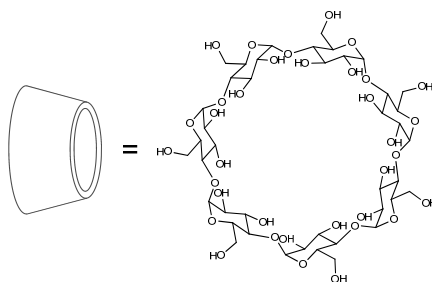


1.52

Figure 1.35 Leigh's rotaxane propeptide **1.52**.

1.2.3.4 Electronic and Material Properties

Interlocked structures can also be specifically designed to possess unique electronic and material properties. For example, porphyrin-containing interlocked structures provide model systems for artificial photosynthetic reaction centre (PRC) mimics,^{171, 172} whilst cyclodextrin-based rotaxane polymers can act as insulated molecular wires (IMWs).¹⁷³ As discussed previously, encapsulation of reactive species within rotaxane structures can greatly increase stability, and this can be achieved by threading cyclodextrin units along the reactive conjugated polymers used in IMWs. Additionally, reduced intermolecular interactions and solid-state packing effects can enhance the efficiency of electronic processes, including electroluminescence, which is important in the application of such polymers within organic light-emitting diodes. This is demonstrated by the increased electroluminescence efficiencies exhibited by β -cyclodextrin polyrotaxanes **1.53** and **1.54** (Figure 1.36) compared to the corresponding free poly(*para*-phenylene) and polyfluorene polymers respectively.¹⁷⁴

**1.53****1.54****Figure 1.36** Polyrotaxanes **1.53** and **1.54** which act as insulated molecular wires.

Certain cyclodextrin-containing rotaxane polymers also exhibit interesting properties due to the ability of the cyclodextrin macrocycles to slide along the polymer chains. Incredibly, hydrogels composed of such structures have recently been exploited as “self-healing” coatings for cars and mobile phones.¹⁷⁵

1.3 Project Aims and Thesis Contents

The aim of this project is to synthesise novel interlocked structures *via* anion templation. Such host structures contain three dimensional, hydrogen bond donor cavities, which are designed to recognise and sense anionic guest species. Specifically, the positively charged imidazolium and triazolium anion binding motifs will be exploited.

Whilst triazolium rotaxane **1.45** has previously been synthesised (Figure 1.32b), to the best of our knowledge no mono-imidazolium interlocked structures have been reported. **Chapter Two** details the anion templated synthesis of imidazolium-based rotaxane structures for anion recognition (Figure 1.36), investigating the effects of incorporating imidazolium motifs with contrasting hydrogen bond donor arrangements into the axle component and reducing the macrocycle size on binding strength and selectivity.

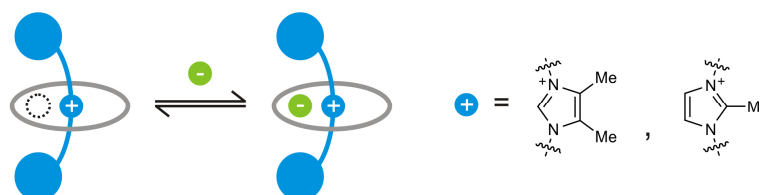


Figure 1.36 Imidazolium-based anion templated interlocked structures for anion recognition.

Attempts to construct imidazolium- and triazolium-based anion sensing rotaxanes by incorporation of fluorescent reporter groups as stoppers (Figure 1.37) are described in **Chapter Three**. Specifically, luminescent ruthenium(II) bipyridyl complexes and the fluorescent anthracene motif are employed.

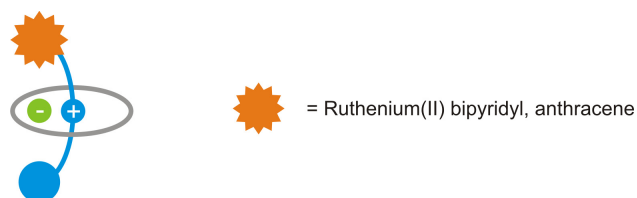


Figure 1.37 Incorporation of fluorescent reporter groups into rotaxane systems as axle stoppers.

The novel naphthalimide triazolium motif (Figure 1.38) is investigated in **Chapter Four**, both for selective anion-induced molecular motion, and surface-attached fluorescent sensing.

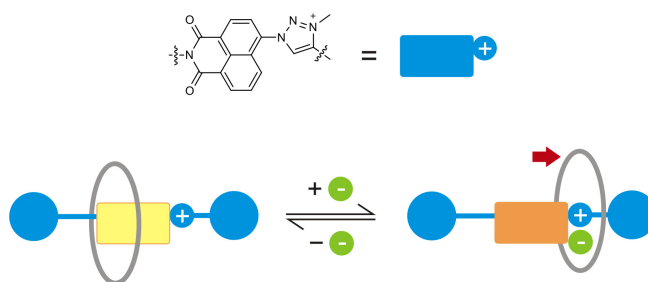


Figure 1.38 Anion-induced molecular motion of a naphthalimide triazolium rotaxane.

Chapter Five discusses preliminary investigations to exploit anion binding induced conformational changes in acyclic systems for sensing applications (Figure 1.39), as well as the control of interpenetrated assembly formation. The use of pyrene fluorophores within such a system gives the opportunity of ratiometric sensing *via* monitoring the monomer and excimer emissions upon anion addition.

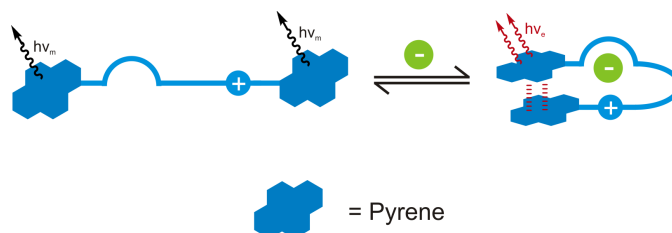


Figure 1.39 Exploiting binding-induced conformational changes for anion sensing. $h\nu_m$ = monomer emission, $h\nu_e$ = excimer emission.

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Chapter Two: Anion Templated Imidazolium Interlocked Structures for Anion Recognition[†]

2.1 Introduction

2.1.1 The Imidazolium Motif

The imidazolium motif is widely employed in many diverse areas of chemistry. Ionic liquids (ILs), highly desirable due to their physico-chemical properties, are often 1,3-dialkylimidazolium salts.^{1, 2} In addition to the rapidly increasing applications of such salts in sustainable chemistry as potentially ‘green’ solvents,^{3, 4} imidazolium ILs have also facilitated developments in materials science including ionic liquid crystals,⁵ and in nanotechnology they can act as highly effective stabilisers for transition metal nanoparticles.^{6, 7} In organometallic chemistry, imidazolium salts are utilised as precursors for *N*-heterocyclic carbene (NHC) ligands.⁸ Finally, as discussed in the introductory chapter (Section 1.1.3.2), this positively charged heterocycle has been employed in many anion recognition and sensing systems.^{9, 10}

In anion coordination chemistry, the desire to maximise imidazolium charge-assisted C-H hydrogen bonding directs the design of such anion receptors,¹¹ which often incorporate several imidazolium groups for convergent hydrogen bond donation. However, to the best of our knowledge, no investigation into the nature of the imidazolium-anion binding interaction has been undertaken in the field of anion recognition. In contrast, this interaction in ILs has been extensively studied and is still a matter of lively debate.¹²⁻²¹ Evidence from solid state structures, a variety of experimental techniques, and theoretical calculations has been used to discuss the relative contributions of

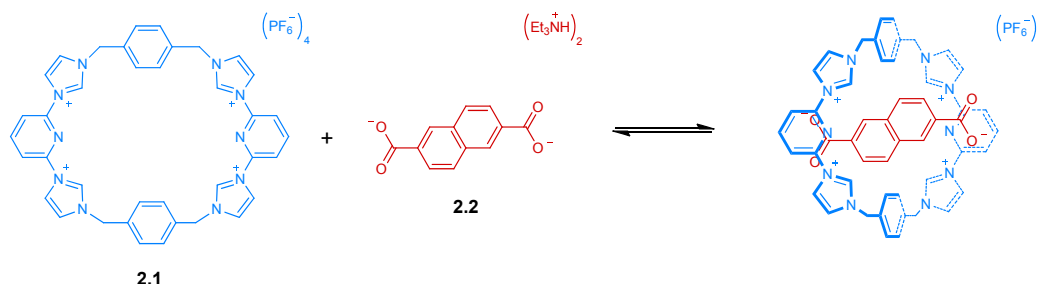
[†] Parts of this chapter have been published in the following publications and are reproduced with permission from John Wiley and Sons and The Royal Society of Chemistry:

G. T. Spence, C. J. Serpell, J. Sardinha, P. J. Costa, V. Félix and P. D. Beer, *Chem. Eur. J.*, 2011, **17**, 12955-12966.

G. T. Spence, N. G. White and P. D. Beer, *Org. Biomol. Chem.*, 2012, **10**, 7282-7291.

electrostatics and hydrogen bonding, and the orientational dependence of the hydrogen bonding interactions. The corresponding interaction in anion coordination chemistry is fundamentally different due to the fact that anion binding studies are carried out in dilute solution, and due to the geometrically constrained arrangement of hydrogen bond donors that exist in anion host systems.

Recently, the imidazolium group has been exploited in a number of pseudorotaxanes,²²⁻²⁶ and bis- and tetra-imidazolium rotaxanes.^{27, 28} For example, Sessler and co-workers investigated the ability of tetra-imidazolium macrocycle **2.1** to form pseudorotaxane assemblies with dicarboxylate anionic guests, such as **2.2**, in *d*₆-DMSO (Scheme 2.1).²⁵ This approach was subsequently applied to the construction of an analogous three dimensional metal-organic rotaxane framework based on carboxylate-zinc(II) coordination.²⁷ It is noteworthy that to date no mono-imidazolium interlocked structures have been synthesised, either for anion recognition or in others area of supramolecular chemistry.

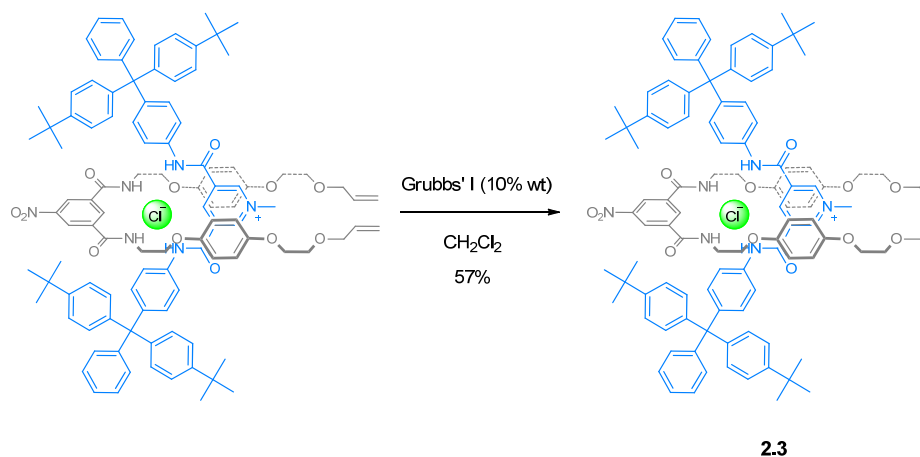


Scheme 2.1 Pseudorotaxane assembly formed between tetra-imidazolium macrocycle **2.1** and dicarboxylate guest **2.2**.

2.1.2 Anion Templated Interlocked Structures for Selective Anion Recognition

With the objective of preparing selective and potent anion receptors, Beer and co-workers have established an anion templation strategy for the construction of interlocked host systems. For example, rotaxane **2.3**, composed of 3,5-bis-amide-pyridinium axle and isophthalamide macrocycle components, was synthesised *via* a Grubbs'-catalysed ring closing metathesis (RCM) 'clipping' method (Scheme 2.2).²⁹ Association of the axle and bis-vinyl macrocycle precursor is mediated by orthogonal binding to the templating chloride anion, with donor-acceptor interactions between the

electron-deficient pyridinium and electron-rich hydroquinone groups providing secondary stabilisation. The target interlocked structure was formed following RCM of the macrocycle precursor around the axle.



Scheme 2.2 Chloride templated synthesis of rotaxane **2.3** *via* Grubbs'-catalysed RCM.

Upon removal of the halide template from the interlocked host cavity, the rotaxane exhibited strong binding affinity for chloride in 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$, with larger oxoanions, dihydrogen phosphate and acetate, bound significantly more weakly as they are unable to penetrate the binding pocket. This trend is opposite to that of anion basicity, and is due to the creation of a three dimensional binding cavity within the interlocked structure.

2.1.3 Chapter Objectives

The aim of this chapter is to construct anion templated rotaxane systems in which the axle components contain substituted mono-imidazolium groups with contrasting hydrogen bond donor arrangements. The orientation of the imidazolium motif with respect to potential hydrogen bonds will be controlled by methyl group substitution dictating that anion binding occurs *via* favourable hydrogen bonding to $\text{C}^2\text{-H}$ in 4,5-dimethylimidazolium derivatives (Figure 2.1a), and to $\text{C}^{4/5}\text{-H}$ in 2-methylimidazolium derivatives (Figure 2.1b).

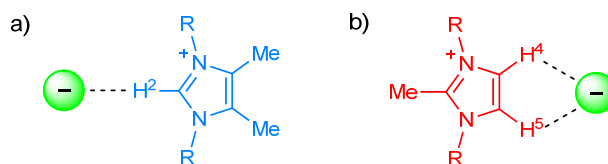
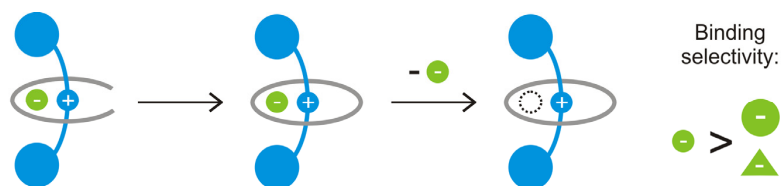


Figure 2.1 Using methyl group substitution to control the orientation of anion binding in a) 4,5-dimethyl- and b) 2-methylimidazolium derivatives.

It is anticipated that the anion templation strategy employed will produce host structures capable of selective anion binding (Scheme 2.3), as discussed in Section 2.1.2. Furthermore, the manipulation of the imidazolium hydrogen bond donor arrangement will enable insights to be obtained about the nature of the interaction between imidazolium cations and coordinating anions, and the impact this has on the anion recognition properties of imidazolium acyclic and rotaxane host systems. Finally, the effect of reducing the macrocycle size in imidazolium interpenetrated and interlocked assemblies will also be explored.



Scheme 2.3 Anion templated synthesis of rotaxane host structure capable of selective cavity binding.

2.1.4 Previous Imidazolium Pseudorotaxane Investigations

The ability of unsubstituted imidazolium threading component **2.4** to form anion templated pseudorotaxanes with isophthalamide macrocycles, such as **1** (Figure 2.2), has been reported previously,²² with the most stable assemblies observed when chloride was the templating anion. Macrocycle **1** was designed to incorporate an anion binding cleft to mediate the association, and electron-rich hydroquinone groups to participate in stabilising donor-acceptor interactions with the electron-deficient imidazolium thread.

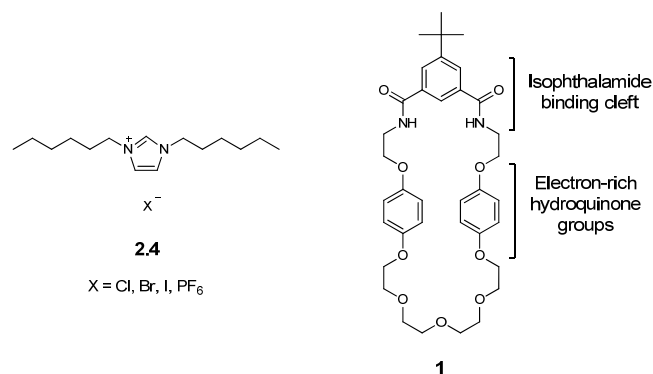


Figure 2.2 Imidazolium thread **2.4** and isophthalamide macrocycle **1**.

Additionally, as control systems for a recent investigation into halogen bonding interpenetrative assembly, the pseudorotaxanes formed between substituted imidazolium threads **2**·Cl and **3**·Cl and macrocycle **1** were studied (Figure 2.3).²³ 2-Methylimidazolium thread **3**·Cl was found to form a significantly more stable interpenetrated assembly than 4,5-dimethylimidazolium thread **2**·Cl, with apparent association constants of 245(5) and 97(3) M^{-1} respectively in $CDCl_3$. It was postulated that this result was due to a beneficial cooperative chelating hydrogen bonding mode with the halide anion, along with potential $C-H\cdots O$ hydrogen bonding from the imidazolium 2-methyl group of **3**·Cl to the polyether chain of **1**.

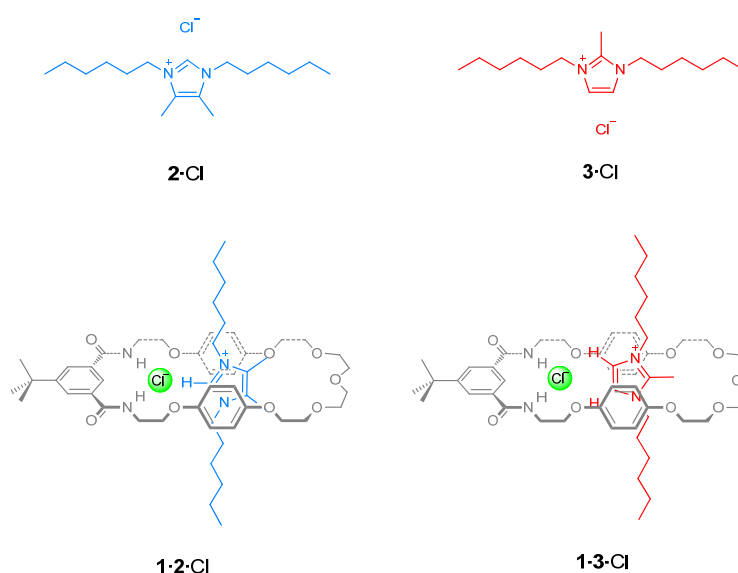


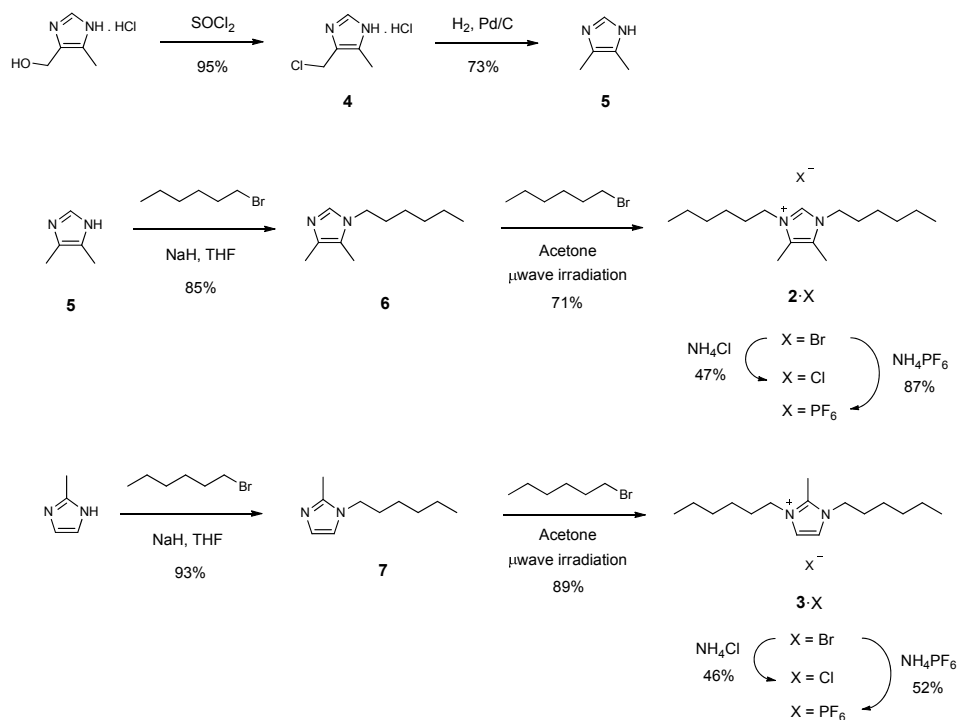
Figure 2.3 Imidazolium threads **2**·Cl and **3**·Cl, and pseudorotaxane assemblies **1**·**2**·Cl and **1**·**3**·Cl.

2.2 Simple Acyclic Imidazolium Derivatives

In light of the previous pseudorotaxane findings, it was decided to study initially the anion recognition properties of simple acyclic imidazolium derivatives containing the 4,5-dimethyl- and 2-methyl-imidazolium motifs.

2.2.1 Synthesis

4,5-Dimethyl- and 2-methyl-imidazolium threading components **2**·PF₆ and **3**·PF₆ were synthesised as their non-coordinating hexafluorophosphate salts (Scheme 2.4). Whilst 2-methylimidazole is commercially available, 4,5-dimethylimidazole was prepared in two steps using literature procedures.³⁰ (4-Methyl-1*H*-imidazol-5-yl)methanol hydrochloride was first chlorinated, and the resulting 5-(chloromethyl)-4-methyl-1*H*-imidazole hydrochloride (**4**) reduced using Pd/C and H₂ in a high pressure reactor. Imidazole **5** and 2-methylimidazole were each reacted with NaH and 1-bromohexane in dry THF to give **6** and **7** in yields of 85% and 93% respectively.²³ Microwave irradiation at 150 °C for 30 min with 1-bromohexane afforded the target threads **2**·Br and **3**·Br as their bromide salts.²³ Anion exchange to the hexafluorophosphate salts was achieved by repeated washing of CH₂Cl₂ solutions of **2**·Br and **3**·Br with aqueous NH₄PF₆. The chloride salts **2**·Cl and **3**·Cl, used later in pseudorotaxane investigations (Section 2.4.2), were similarly prepared using aqueous NH₄Cl.



2.2.2 ¹H NMR Anion Binding Titrations

The anion binding properties of **2**·PF₆ and **3**·PF₆ were studied by ¹H NMR titration experiments in CDCl₃. Upon addition of tetrabutylammonium (TBA) halide and dihydrogen phosphate salts,³¹ significant downfield shifts were observed for C²-H in **2**·PF₆ and C^{4/5}-H in **3**·PF₆, Δδ = + 2.11 and + 0.33 ppm respectively after 10.0 equivalents of TBA chloride (Figures 2.4 and 2.5). These shifts indicate that anion binding was occurring in the expected modes for the different substituted imidazolium motifs.

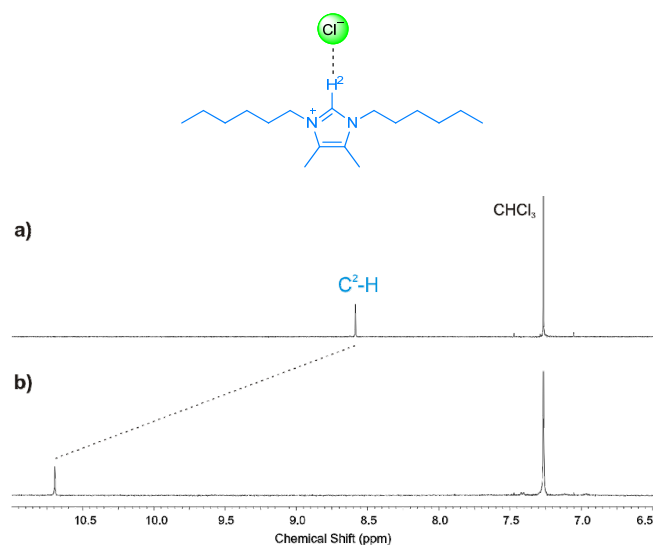


Figure 2.4 Partial ^1H NMR spectra (500 MHz, 2.0×10^{-3} M) in CDCl_3 at 293 K of a) 4,5-dimethylimidazolium derivative $2 \cdot \text{PF}_6$, and b) $2 \cdot \text{PF}_6$ plus 10.0 equivalents of TBACl.

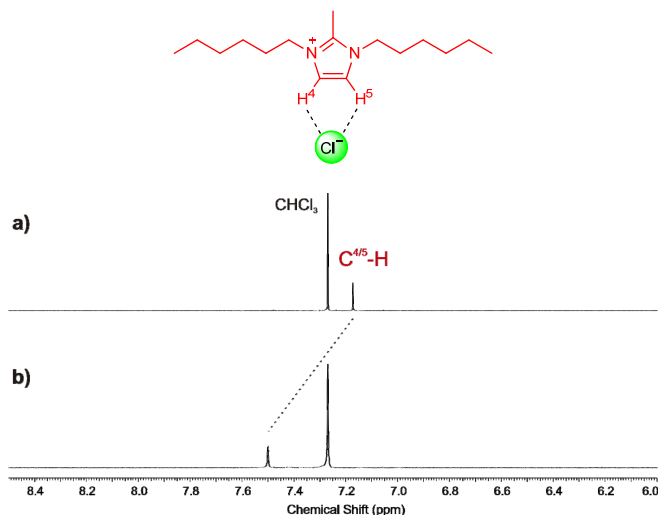


Figure 2.5 Partial ^1H NMR spectra (500 MHz, 2.0×10^{-3} M) in CDCl_3 at 293 K of a) 2-methylimidazolium derivative $3 \cdot \text{PF}_6$, and b) $3 \cdot \text{PF}_6$ plus 10.0 equivalents of TBACl.

By monitoring these protons throughout the titration experiments (Figure 2.6), WinEQNMR2³² analysis of the data determined 1:1 stoichiometric association constants shown in Table 2.1. The strength of anion binding for both systems follows the trend in anion basicity, with dihydrogen phosphate bound stronger than chloride, followed by bromide and iodide. Furthermore, acyclic receptor $2 \cdot \text{PF}_6$ exhibits much stronger anion binding affinity compared to $3 \cdot \text{PF}_6$. This could be

rationalised by the differing acidities of the respective imidazolium protons involved in hydrogen bonding,¹² with estimated pKa values of 24.9 for C²-H and 33.0 for C^{4/5}-H.³³ Also, the electrostatic contribution to binding is greater in **2**·PF₆ compared with **3**·PF₆, due to the smaller distance between the bound anion and the centre of imidazolium positive charge, calculated to be midpoint between the two nitrogens by Tsuzuki.¹³ This difference in electrostatic distances is illustrated in the solid state crystal structures discussed in the next section.

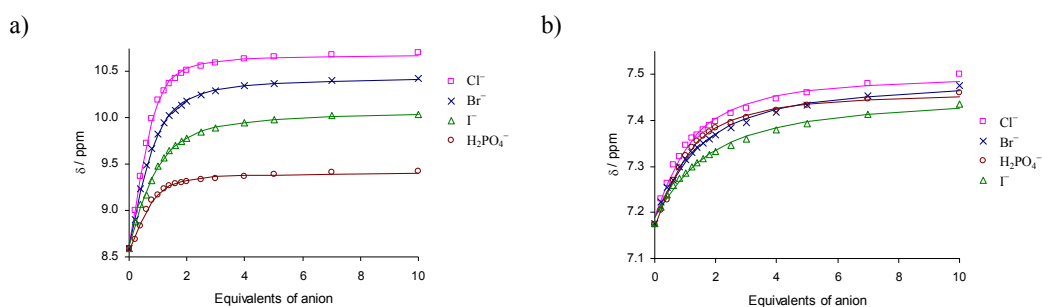


Figure 2.6 Changes in the chemical shift of a) imidazolium proton (C²-H) in **2**·PF₆ and b) imidazolium protons (C^{4/5}-H) in **3**·PF₆ upon addition of anions in CDCl₃ at 293 K. Symbols represent experimental data points; lines represent calculated titration curves.

Table 2.1 Association constants, K (M⁻¹), of **2**·PF₆ and **3**·PF₆ with anions in CDCl₃ at 293 K. Obtained by monitoring the imidazolium proton(s). Errors are given in parentheses.

Anion	2 ·PF ₆ K (M ⁻¹)	3 ·PF ₆ K (M ⁻¹)
Cl ⁻	3044 (108)	782 (42)
Br ⁻	2736 (186)	523 (60)
I ⁻	1609 (115)	402 (44)
H ₂ PO ₄ ⁻	4301 (572)	1000 (83)

2.2.3 Solid-State Crystal Structures

Crystals of **2**·Cl and **3**·Cl suitable for single crystal X-ray diffraction structural analysis were obtained by leaving the viscous oils to stand for 2–3 months (Figure 2.7). The crystals were grown and

the structures solved by Dr. Christopher Serpell, with the following analysis carried out in collaboration.

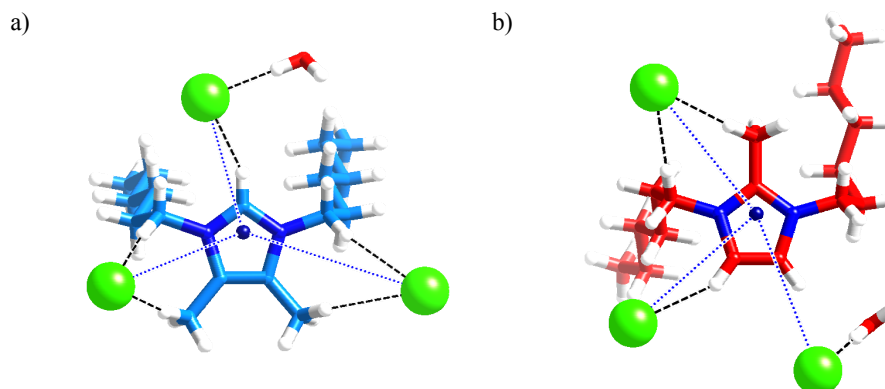


Figure 2.7 Crystal structures of a) $2 \cdot \text{Cl}^{34}$ and b) $3 \cdot \text{Cl}$. The centre of positive charge¹³ is marked by a dark blue sphere, with corresponding distances to anions shown in dotted blue lines. $\text{H} \cdots \text{Cl}$ close contacts are displayed using dashed black lines.

To consider the imidazolium-anion interactions, the hydrogen bonding parameters and electrostatic distances present in the crystal structures were compared. In $2 \cdot \text{Cl}$ the closest chloride to the centre of positive charge is positioned at 4.188(2) Å *via* a $\text{C}^2\text{-H}$ hydrogen bond with a $\text{C-H} \cdots \text{Cl}$ angle of 149.0° and $\text{C} \cdots \text{Cl}$ distance of 3.461(1) Å (Figure 2.7a). The two next-nearest chloride anions are at distances of 5.119(2) and 5.637(1) Å from the centre of positive charge. As expected, in the $3 \cdot \text{Cl}$ structure the chloride closest to the centre of positive charge is further away, at a distance of 4.847(6) Å, and is coordinated by an imidazolium $\text{C}^{4/5}\text{-H}$ hydrogen bond with a $\text{C} \cdots \text{Cl}$ distance of 3.528(4) Å and a $\text{C-H} \cdots \text{Cl}$ angle of 150.2° (Figure 2.7b). In this case, the next two closest anions are at 5.090(2) and 5.195(11) Å.

The observable parameters pertaining to imidazolium ring hydrogen bonding strength – atomic distances and angles – imply that there is little difference in the anion-proton interactions between the two structures. However, in $3 \cdot \text{Cl}$ the closest halide anion is at a relatively longer distance from the centre of positive charge than in $2 \cdot \text{Cl}$. This indicates that the greater anion binding strength of $2 \cdot \text{PF}_6$ observed in the solution studies discussed above, may be a consequence of the actual geometry of the complex permitting a closer approach of opposite charges rather than a function of classical hydrogen bonding.

2.2.4 Pseudorotaxane Solid-State and Modelling Studies

It was decided to study interpenetrated assemblies **1·2·Cl** and **1·3·Cl** (Section 2.1.4) further in the context of this investigation. Additional evidence for the solution phase co-conformations of these pseudorotaxanes was provided by 2D ^1H - ^1H NMR ROESY spectroscopy carried out by Dr. Christopher Serpell,^{34, 35} and both **2·Cl** and **3·Cl** threads were found to be in the expected orientations within macrocycle **1**, with the imidazolium protons pointing towards the anion binding cleft (Figure 2.3).

In addition, crystals suitable for single-crystal X-ray diffraction structural determination were prepared for **1·2·Cl** and **1·3·Cl** by slow evaporation of dilute CHCl_3 solutions of the pseudorotaxane assemblies (Figure 2.8). The crystals were grown and the structures solved by Dr. Christopher Serpell using synchrotron radiation at Diamond Light Source beamline I19, with the following analysis carried out in collaboration.

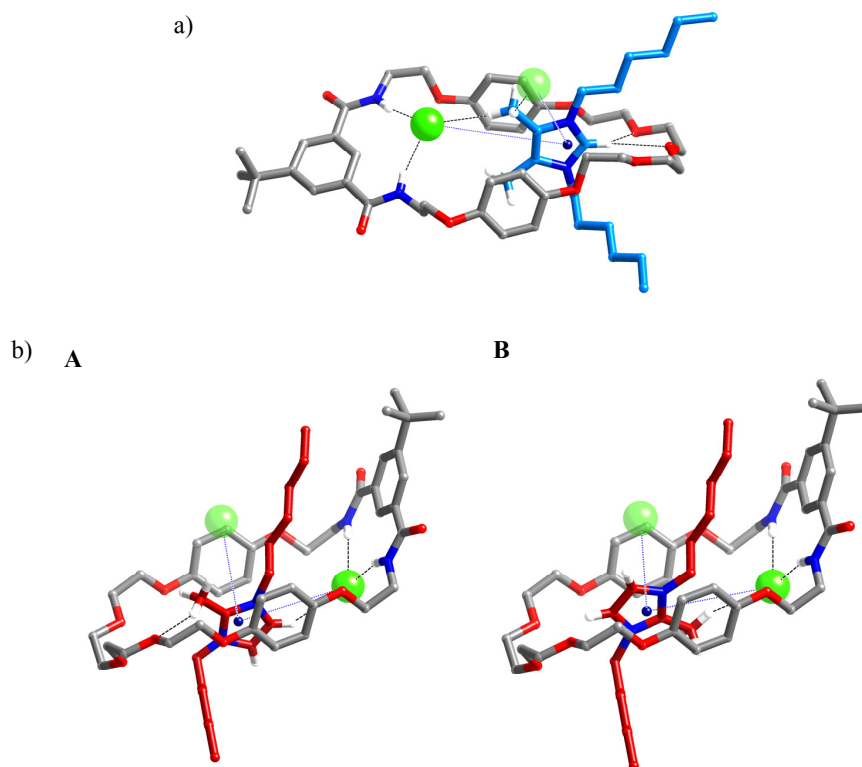


Figure 2.8 Crystal structures of interpenetrated assemblies a) **1·2·Cl**, and b) **1·3·Cl**. For **1·3·Cl** both geometries of the disordered thread are shown (A and B – occupancies 0.514(8) and 0.486(8) respectively). The centres of the imidazolium positive charges are marked by dark blue spheres, with corresponding distances to anions shown in dotted blue lines. $\text{H}\cdots\text{Cl}$ and $\text{H}\cdots\text{O}$ close contacts are displayed using dashed black lines. Protons omitted for clarity where appropriate. In each case the chloride anion from an adjacent assembly is depicted as a transparent sphere.

In contrast to the solution-phase evidence, the solid-state structure of the 4,5-dimethylimidazolium system **1·2·Cl** revealed the opposite of the expected co-conformation, with the imidazolium C² proton pointing towards the polyether chain of the macrocycle, and the methyl groups directed towards the chloride anion (Figure 2.8a). This results in a large distance between the centre of the imidazolium positive charge and the anion, which is apparently templating the pseudorotaxane, at 5.885(2) Å. However, examination of the entire structure reveals that the chloride anion occupying the cavity of the adjacent pseudorotaxane is in fact closer at 5.272(3) Å. This provides increased electrostatic stabilisation and, along with several close contacts between imidazolium methyl protons and the two nearest anions, aids the construction of an extended network which is necessary for crystal formation.

Conversely, disorder was present in the **1·3·Cl** structure, owing to the thread existing in two contrasting co-conformations of approximately equal occupancy – with either the C^{4/5} protons (**1·3·Cl-A**) or the 2-methyl group (**1·3·Cl-B**) pointing towards the anion (Figure 2.8b). In co-conformation A, the closest chloride anion to the imidazolium positive charge is located in the pseudorotaxane cavity at 4.994(1) Å, the next nearest being at 5.853(3) Å. However, when the methyl group points towards the anion in the cavity (B), the anion in an adjacent pseudorotaxane is slightly closer than the anion in the same assembly, at 5.182(3) and 5.367(1) Å respectively. Additional inter-assembly hydrogen bonds are also observed in both co-conformations, although just longer than the sum of the corresponding van der Waals radii, further strengthening the network of intermolecular forces.

Hence, whilst pseudorotaxane formation in solution is dominated by electrostatic and hydrogen bonding interactions within each individual assembly, their solid-state orientations are much less dependent on this interaction due to the proximity of adjacent units and the requirements for crystal formation.

To attempt to account for the disparity in the solution-phase and solid-state pseudorotaxane co-conformations, molecular dynamics (MD) simulations and density functional theory (DFT) calculations were carried out on **1·2·Cl** and **1·3·Cl** by Dr. João Sardinha, Dr. Paulo Costa and Prof. Vítor Félix at the University of Aveiro.³⁵

Initially, the pseudorotaxanes assemblies were studied by means of MD simulations, with the starting structures chosen as the observed solid-state co-conformations (Figure 2.8). The selected structures were immersed in periodic cubic boxes of CHCl₃ molecules and their dynamic behaviour was investigated by MD simulations for 20 ns. In all simulations the chloride anion was kept firmly bonded to the isophthalamide macrocyclic cleft *via* two N-H...Cl hydrogen bonds.

For **1·2·Cl**, rotation of the imidazolium thread was observed in one simulation (Figure 2.9), resulting in conversion from the starting structure (termed **1·2·Cl-A**) to the solution-phase co-conformation (**1·2·Cl-B**) *via* an extremely short-lived intermediate co-conformation, **1·2·Cl-C** (1.2 ps). It should be noted that this thread rotation event was only observed in one out of three MD

simulation runs, however this is thought to be unsurprising given the extreme nature of the co-conformational change.

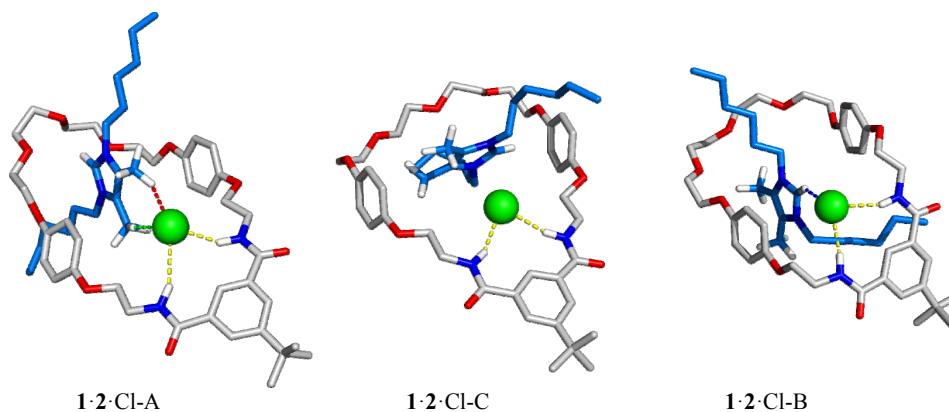


Figure 2.9 Representative snapshots of **1·2·Cl-A** MD run taken at different simulation times and illustrating the rotational conversion **1·2·Cl-A** → **1·2·Cl-C** → **1·2·Cl-B**. The N-H...Cl hydrogen bonds are drawn as yellow dashed lines, while the C-H...Cl hydrogen bonds are drawn as blue (C²-H...Cl), red (C⁴-CH₃...Cl) and green (C⁵-CH₃...Cl).

In contrast, the analogous 2-methylimidazolium thread rotation from **1·3·Cl-B** to the co-conformation observed in solution (**1·3·Cl-A**) did not occur within the MD simulation time. It is postulated that this is either due to insufficient sampling of the conformational space or because the starting structure is trapped in a potential energy surface well. Similarly, pseudorotaxane co-conformations **1·2·Cl-B** and **1·3·Cl-A**, consistent with the solution-phase NMR evidence, were stable over the entire time of their respective simulation runs.

Subsequently, the structural and energetic preferences of **1·2·Cl** and **1·3·Cl** co-conformations were investigated by DFT calculations. For 4,5-dimethylimidazolium assembly **1·2·Cl**, solution-phase co-conformation B was calculated to be 7.86 kcal.mol⁻¹ lower in energy than solid-state A using representative structures obtained from the MD simulations. However the differences were much smaller for the two solid-state co-conformations of 2-methylimidazolium assembly **1·3·Cl**, with co-conformation A found to be lower in energy than B by only 0.23 kcal.mol⁻¹ using the MD structures, and 1.55 kcal.mol⁻¹ using the X-ray crystal structures. This demonstrates that whilst the solution-phase co-conformation (**1·3·Cl-A**) is energetically preferred, the energy difference is small enough to be overcome in the solid-state (**1·3·Cl-B**) by the need to form crystalline networks.

2.2.5 Summary

The anion recognition properties of the simple acyclic imidazolium derivatives were found to follow the trend in anion basicity, with considerably stronger binding observed for 4,5-dimethylimidazolium **2**·PF₆ over 2-methylimidazolium **3**·PF₆. Following analysis of the solid-state structures of **2**·Cl and **3**·Cl, it is postulated that this difference is due more to the electrostatic distances arising from the geometries of the complexes than conventional hydrogen bonding parameters.

Due to the level of complexity and multitude of interactions present, little can be inferred about the direct balance between electrostatics and imidazolium hydrogen bonding from the solid-state pseudorotaxane structures. However, it is possible to rationalise their co-conformations by considering both the intra- and inter-assembly electrostatic interactions, which are not always accompanied by corresponding imidazolium-anion hydrogen bonds. Theoretical modelling studies were also used to confirm and quantify the relatively higher stabilities of the observed solution-phase interpenetrated structures.

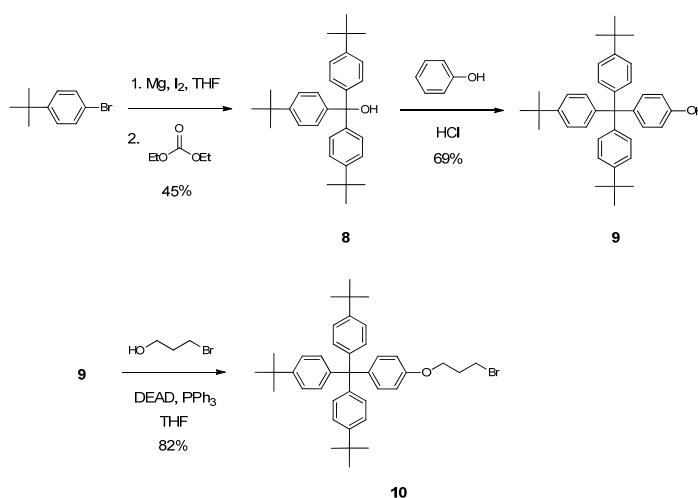
2.3 Synthesis, Characterisation and Anion Recognition Properties of 4,5-Dimethyl- and 2-Methyl-imidazolium Rotaxanes

With the anion recognition properties of simple acyclic derivatives and the analysis of previously reported pseudorotaxane assemblies providing insights into the imidazolium-anion interaction, it was of interest to prepare anion templated rotaxane host systems containing 4,5-dimethyl- and 2-methyl-imidazolium axle components.

2.3.1 Rotaxane Synthesis and Characterisation

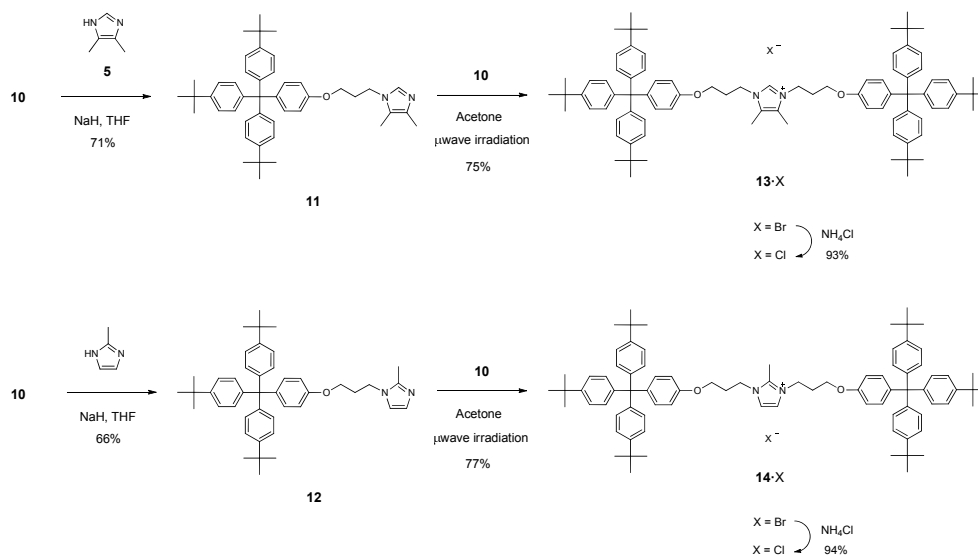
For rotaxane formation, the same ‘clipping’ approach using Grubbs’-catalysed RCM described in Section 2.1.2 (Scheme 2.2) was employed, which requires the synthesis of axle components containing bulky stopper groups. To this end, terphenyl-stoppered bromo-functionalised

derivative **10** was synthesised using literature procedures (Scheme 2.5).^{36, 37} Firstly, a Grignard reaction involving 1-bromo-4-*tert*-butyl benzene and diethyl carbonate yielded tris(4-(*tert*-butyl)phenyl)methanol (**8**), which was then heated overnight in molten phenol under acidic conditions to afford terphenyl **9** in 69% yield. Finally, target compound **10** was prepared *via* a Mitsunobu reaction between **9** and 3-bromo-propan-1-ol.



Scheme 2.5 Synthesis of terphenyl-stoppered bromo-functionalised derivative **10**.

Substituted imidazolium axle components **13**·Cl and **14**·Cl were synthesised from **10**, and 4,5-dimethyl- and 2-methyl-imidazole respectively (Scheme 2.6). Similar to Scheme 2.4, initial substitution was achieved using NaH in dry THF to yield mono-stoppered imidazole derivatives **11** and **12**. For the subsequent alkylation, microwave irradiation at 150 °C for 3 h in acetone was required, affording **13**·Br and **14**·Br in 75% and 77% yields respectively. Anion exchange to the desired chloride salts, **13**·Cl and **14**·Cl, was achieved in near quantitative yields.



Scheme 2.6 Synthesis of 4,5-dimethyl- and 2-methylimidazolium axle components **13·Cl** and **14·Cl**.

Based on macrocycle **1**, macrocycle precursor **15** contains an isophthalamide group for anion binding, hydroquinone groups for donor-acceptor interactions, and terminal vinyl groups for RCM (Figure 2.10).²⁹ Whilst the isophthalamide unit in **1** was functionalised with a *tert*-butyl group to aid solubility for pseudorotaxane studies, **15** contains an electron-withdrawing nitro isophthalamide substituent to increase the acidity of the amide protons for enhanced rotaxane anion binding strength.

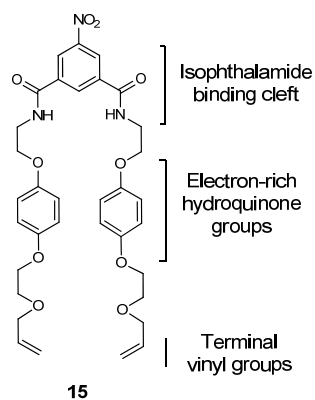
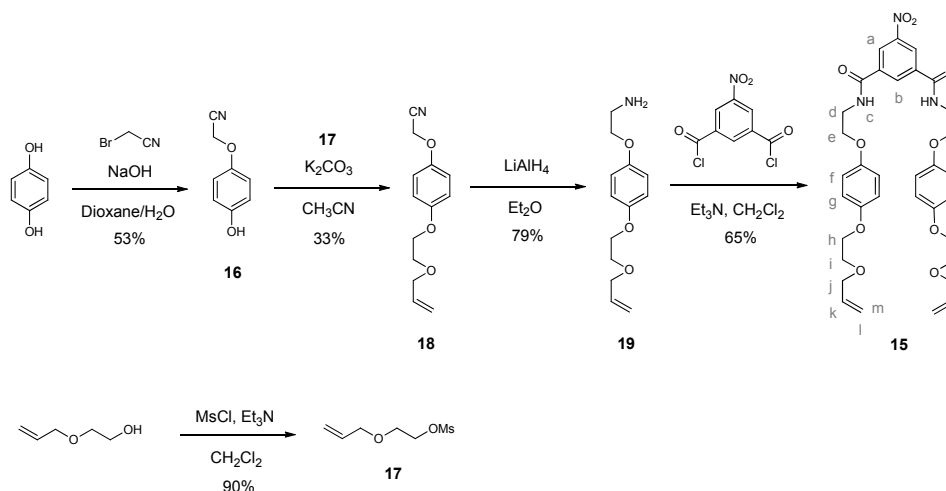


Figure 2.10 Bis-vinyl macrocycle precursor **15**.

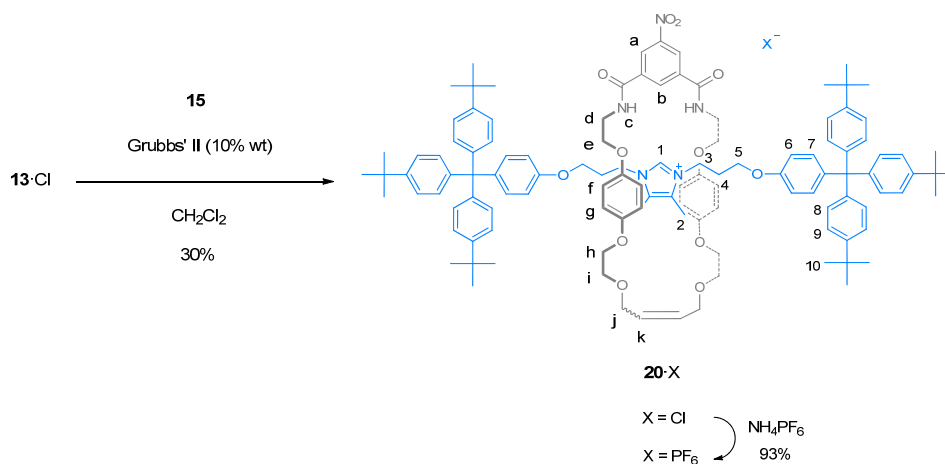
The synthesis of macrocycle precursor **15** is shown in Scheme 2.7. Hydroquinone was first mono-functionalised using bromoacetonitrile to give 2-(4-hydroxyphenoxy)acetonitrile (**16**) in 53%

yield.³⁸ Reaction of **16** with 2-(allyloxy)ethyl methanesulfonate (**17**), prepared from 2-allyloxyethanol in 90% yield,³⁹ afforded vinyl-functionalised nitrile derivative **18**.⁴⁰ Reduction using LiAlH_4 ,⁴⁰ followed by condensation with 5-nitroisophthaloyl dichloride gave the target compound **15**.²⁹



Scheme 2.7 Synthesis of macrocycle precursor **15**.

Following the successful synthesis of the required components, 4,5-dimethylimidazolium rotaxane **20**·Cl was synthesised by reaction of an equimolar solution of axle **13**·Cl and macrocycle precursor **15** in dry CH_2Cl_2 with Grubbs' second-generation RCM catalyst (Scheme 2.8). The product was isolated in 30% yield following purification by preparative silica gel thin layer chromatography using 94:6 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to remove free axle, followed by 4:6 $\text{CH}_2\text{Cl}_2/\text{MeCN}$ to separate the rotaxane from macrocyclic by-products. The ^1H NMR spectrum of **20**·Cl, along with those of axle **13**·Cl and macrocycle precursor **15**, is shown in Figure 2.11.



Scheme 2.8 Synthesis of 4,5-dimethylimidazolium rotaxanes **20-Cl** and **20-PF₆**.

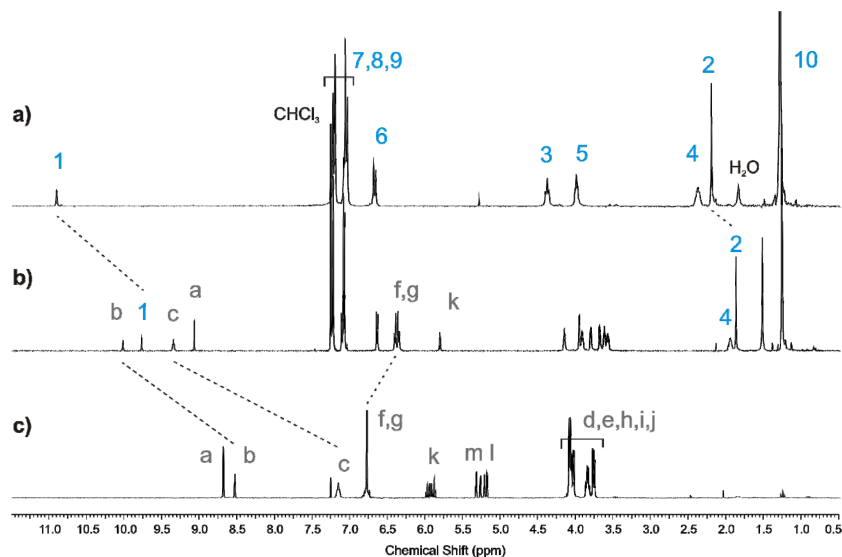


Figure 2.11 ^1H NMR spectra (300 MHz) in CDCl_3 at 293 K of a) axle **13-Cl**, b) rotaxane **20-Cl**, and c) macrocycle precursor **15**.

Upon rotaxane formation, an upfield shift of imidazolium proton 1 and downfield shifts of isophthalamide protons b and c were observed. These correspond to polarisation of the templating chloride anion away from the imidazolium group of the axle and towards the hydrogen bond donors of the macrocycle. Additionally, the signals associated with the hydroquinone environments f and g have split slightly and moved significantly upfield in the rotaxane. These diagnostic shifts are due to the favourable donor-acceptor interactions between the electron-deficient imidazolium axle and the

macrocycle electron-rich aromatic groups. It is notable that an upfield shift of the axle methyl protons **2** was also observed, presumably due to the hydroquinone ring currents.

Subsequent exchange of the chloride template for the non-coordinating hexafluorophosphate anion afforded rotaxane **20**·PF₆ in 93% yield (Scheme 2.8). Upfield shifts in the ¹H NMR signals corresponding to the interlocked cavity protons involved in anion binding (b, c and 1) were observed upon removal of the coordinating halide, along with considerable broadening (Figure 2.12). A greater splitting in the hydroquinone proton signals (f and g) was also observed, possibly due to different extents of donor-acceptor interactions in **20**·PF₆ compared with **20**·Cl.

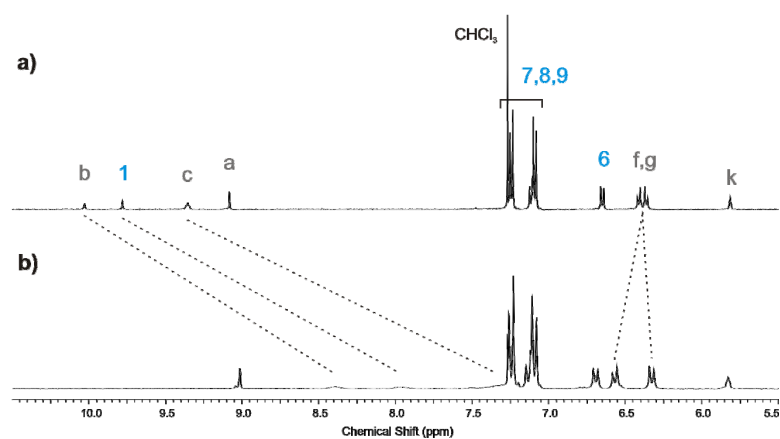
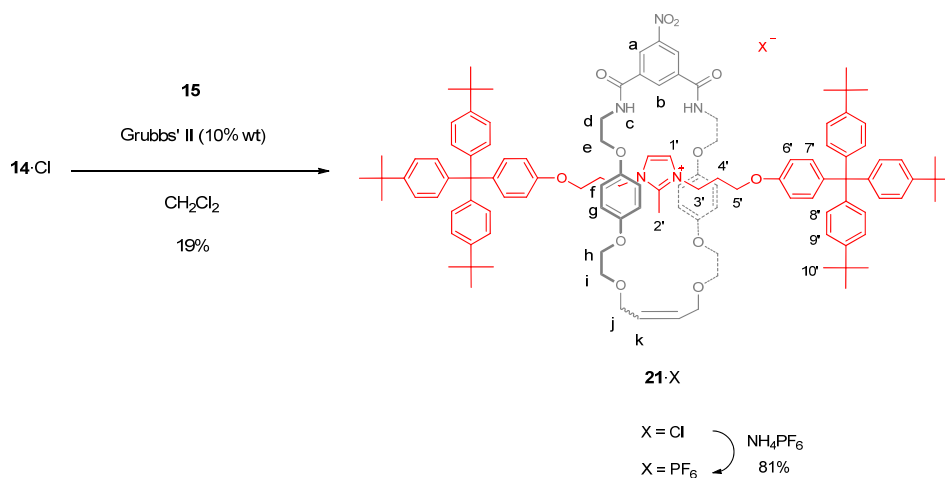


Figure 2.12 Partial ¹H NMR spectra (500 MHz) in CDCl₃ at 293 K of a) rotaxane **20**·Cl, and b) rotaxane **20**·PF₆.

The analogous 2-methylimidazolium rotaxanes **21**·Cl and **21**·PF₆ were synthesised using the same method (Scheme 2.9), however for this system, a reduced yield of 19% was obtained for the rotaxanation step. It is notable that this trend in rotaxane yields between the two substituted imidazolium motifs is opposite to the previously reported trend observed for pseudorotaxane formation, where the 2-methylimidazolium thread **3**·Cl formed a significantly more stable assembly with macrocycle **1** than the 4,5-dimethyl analogue **2**·Cl.²³



Scheme 2.9 Synthesis of 2-methylimidazolium rotaxanes **21·Cl** and **21·PF₆**.

Similar shifts in the ^1H NMR spectra of **21·Cl** and **21·PF₆** were observed as discussed above for the formation of **20·Cl** and **20·PF₆** (Figures 2.13 and 2.14), due to the same anion binding and donor-acceptor factors. However, a greater hydroquinone splitting was observed for **21·Cl** compared with **20·Cl**, with little change upon anion exchange to **21·PF₆**.

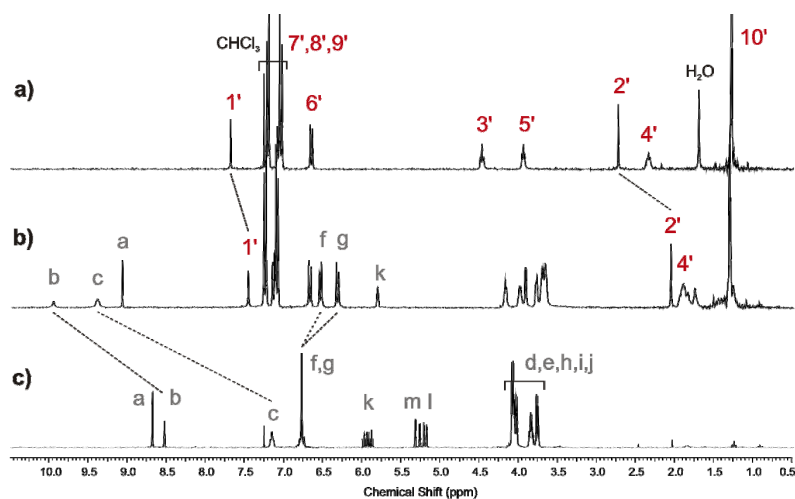


Figure 2.13 ^1H NMR spectra (300 MHz) in CDCl_3 at 293 K of a) axle **14·Cl**, b) rotaxane **21·Cl**, and c) macrocycle precursor **15**.

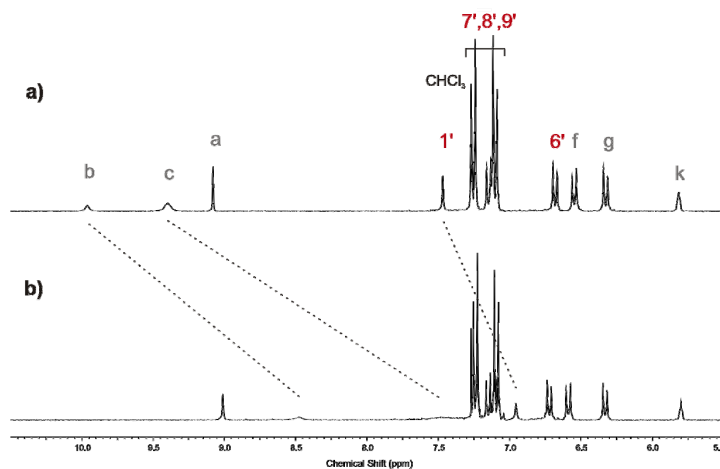


Figure 2.14 Partial ^1H NMR spectra (300 MHz) in CDCl_3 at 293 K of a) rotaxane $\mathbf{21}\cdot\text{Cl}$, and b) rotaxane $\mathbf{21}\cdot\text{PF}_6$.

Further characterisation of these interlocked structures was obtained by high resolution electrospray mass spectrometry and 2D ^1H - ^1H NMR ROESY spectroscopy. A number of through-space axle-macrocycle intercomponent ROESY correlations were observed for each structure and are shown in Figures 2.15–2.18. Although difficulties in identifying some correlations were experienced due to the broadening of several proton peaks and crowded aromatic regions, the spectra indicate that the orientations of the axles within the macrocycles is as expected – with the imidazolium ring protons pointing towards the macrocycle isophthalamide anion binding cleft. Importantly, this is the case for both the chloride and hexafluorophosphate salts of the 4,5-dimethyl- and 2-methyl-imidazolium rotaxanes, suggesting no major co-conformational changes occur upon anion exchange.

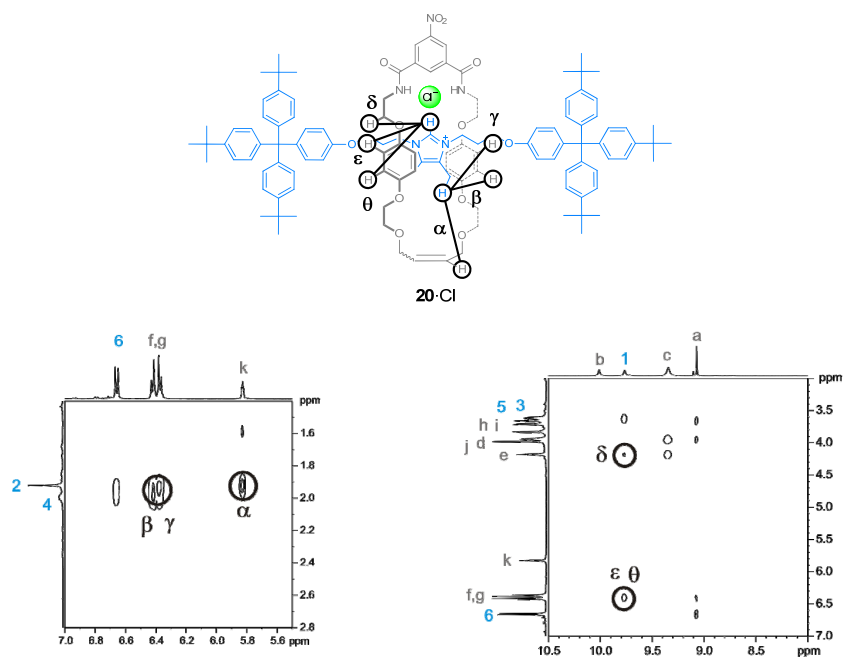


Figure 2.15 Portions of the ^1H - ^1H NMR ROESY spectrum of **20**·Cl (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures.

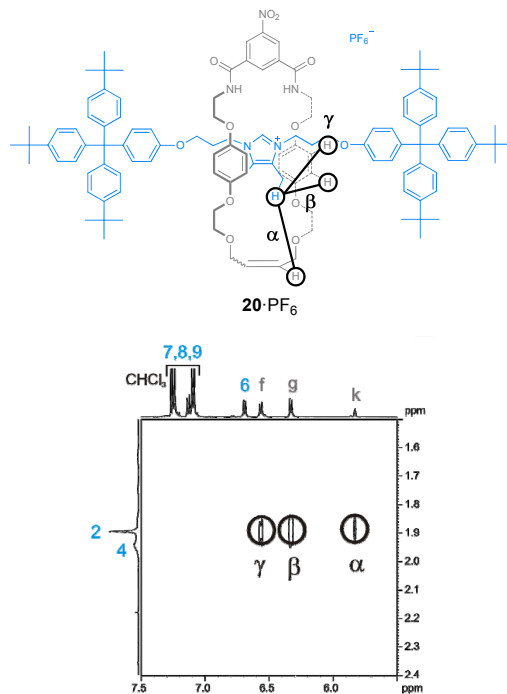


Figure 2.16 Portion of the ^1H - ^1H NMR ROESY spectrum of **20**·PF₆ (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures.

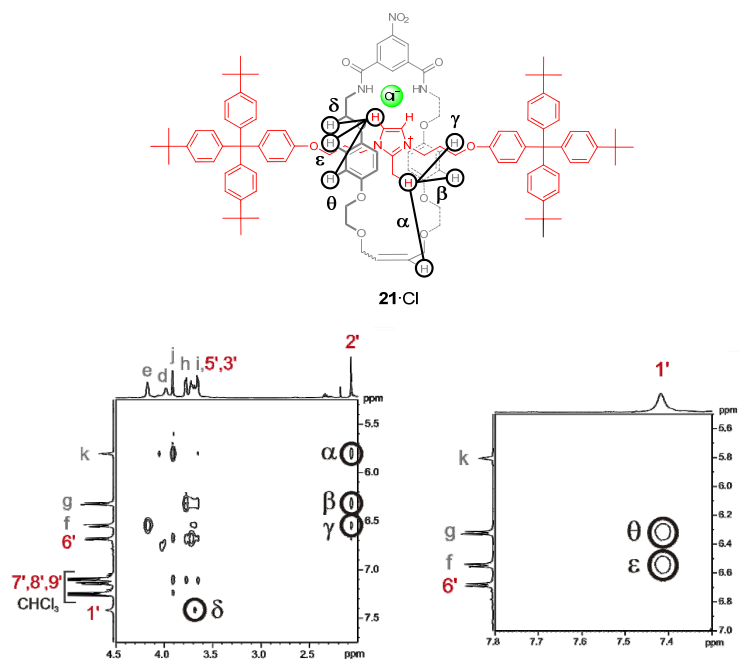


Figure 2.17 Portion of the ^1H - ^1H NMR ROESY spectrum of **21**·Cl (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures.

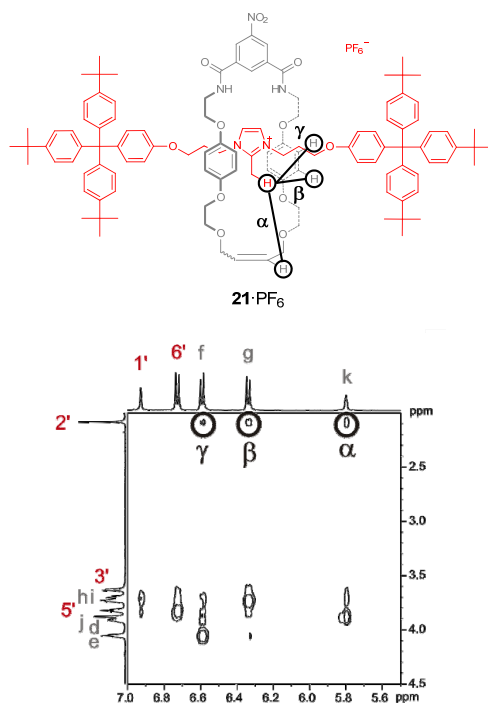


Figure 2.18 Portion of the ^1H - ^1H NMR ROESY spectrum of **21**·PF₆ (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures.

2.3.2 ^1H NMR Anion Binding Titrations

The anion binding properties of rotaxanes **20**·PF₆ and **21**·PF₆ were investigated by ^1H NMR titration experiments using TBA salts in 1:1 CDCl₃/CD₃OD. This more competitive solvent mixture, compared with the titrations for the acyclic imidazolium derivatives, was used due to the stronger anion complexation exhibited by the rotaxane systems *via* convergent, cooperative hydrogen bonding. In addition, the insolubility of TBA acetate in CDCl₃ prevented its use in the acyclic binding studies, however titrations with this anion were possible under these solvent conditions. Downfield shifts for the C-H peaks involved in anion binding (b, 1 and 1') were observed throughout these titrations, however it was not possible to follow the amide protons (c) due to deuterium exchange. The spectral changes observed for **20**·PF₆ and **21**·PF₆ upon addition of one equivalent of TBA chloride are shown in Figures 2.19 and 2.20.

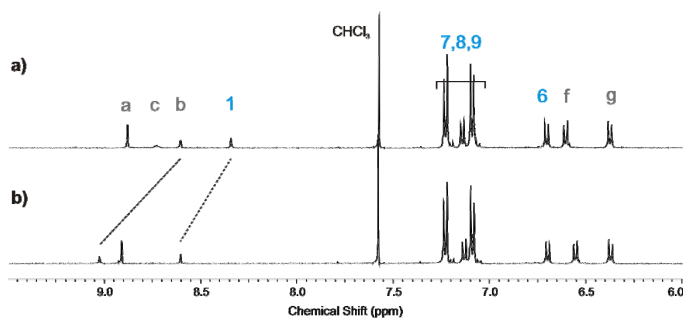


Figure 2.19 Partial ^1H NMR spectra (500 MHz, 2.0 $\times 10^{-3}$ M) in 1:1 CDCl₃/CD₃OD at 293 K of a) rotaxane **20**·PF₆, and b) rotaxane **20**·PF₆ plus 1.0 equivalent of TBACl.

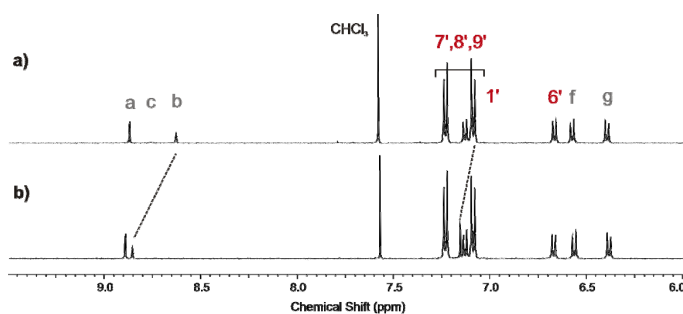


Figure 2.20 Partial ^1H NMR spectra (500 MHz, 2.0 $\times 10^{-3}$ M) in 1:1 CDCl₃/CD₃OD at 293 K of a) rotaxane **21**·PF₆, and b) rotaxane **21**·PF₆ plus 1.0 equivalent of TBACl.

Association constants were determined from the titration data by monitoring cavity proton b and WinEQNMR2 analysis (Table 2.2). These protons are directly involved in anion binding, and their signals could be accurately monitored throughout all titration experiments (Figure 2.21).

Table 2.2 Association constants, K (M^{-1}), of rotaxanes **20**·PF₆ and **21**·PF₆ with anions in 1:1 CDCl₃/CD₃OD at 293 K. Obtained by monitoring proton b. Errors are given in parentheses.

Anion	20 ·PF ₆ K (M^{-1})	21 ·PF ₆ K (M^{-1})
Cl [−]	652 (52)	360 (24)
Br [−]	674 (21)	446 (30)
I [−]	578 (38)	360 (27)
H ₂ PO ₄ [−]	173 (7)	153 (15)
OAc [−]	99 (9)	108 (6)

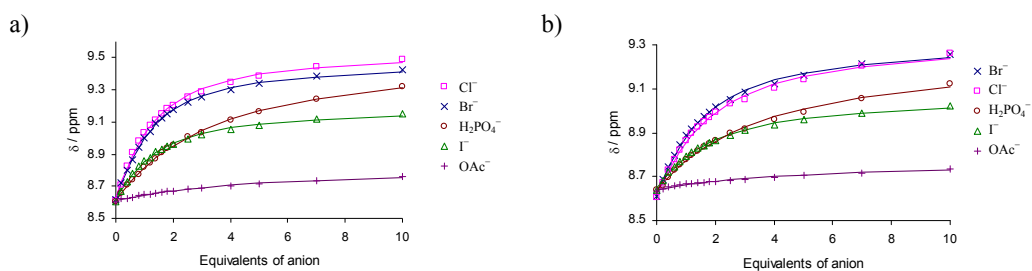


Figure 2.21 Changes in the chemical shift of proton b upon addition of anions to a) rotaxane **20**·PF₆ and b) rotaxane **21**·PF₆ in 1:1 CD₃Cl/CD₃OD at 293 K. Symbols represent experimental data points; lines represent calculated titration curves.

Table 2.2 shows that for both rotaxane hosts, **20**·PF₆ and **21**·PF₆, the halides are bound considerably more strongly than the more basic oxoanions dihydrogen phosphate and acetate. Importantly, this is a reversal in selectivity compared with the acyclic imidazolium derivatives **2**·PF₆ and **3**·PF₆. This has been achieved by the creation of a three dimensional interlocked cavity of complementary size and shape for the spherical halide guest species, with the oxoanions too large to penetrate the respective rotaxane binding pockets.

The suggestion of a different binding mode, external to the rotaxane cavity, for dihydrogen phosphate and acetate is supported by differential behaviour of methyl signal 2 in **20**·PF₆ during the titrations (Figure 2.22a). Slight downfield shifts of 0.05–0.07 ppm are observed upon addition of the

halide anions, whereas these protons shift upfield by 0.02 ppm with dihydrogen phosphate and do not shift with acetate (<0.01 ppm). Hence, the contrasting binding modes displayed by **20**·PF₆ appear to alter the position of the imidazolium methyl protons with respect to the hydroquinone ring currents in different ways. The methyl protons (2') of rotaxane **21**·PF₆ shift upfield to varying extents during the titrations, however without the same distinction between the halides and oxoanions (Figure 2.22b). It is thought that the different binding modes still occur in this system, but that they do not affect the shielding of the imidazolium methyl group in the same way as in **20**·PF₆.

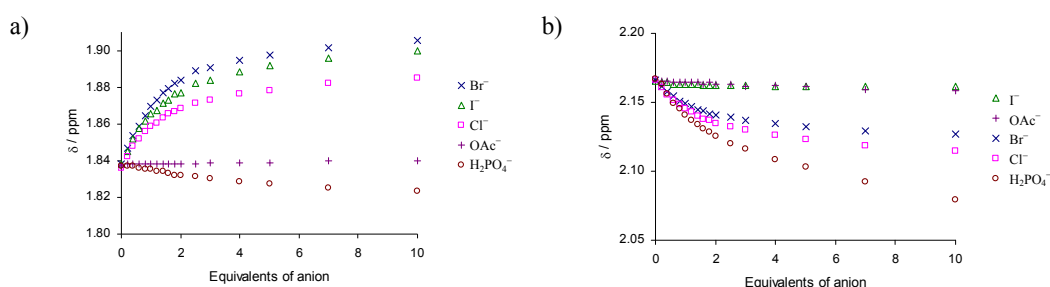


Figure 2.22 Changes in the chemical shift of imidazolium methyl protons upon addition of anions to a) rotaxane **20**·PF₆ (protons 2) and b) rotaxane **21**·PF₆ (protons 2') in 1:1 CD₃Cl/CD₃OD at 293 K.

It is noteworthy that no selectivity is exhibited between the halides by either rotaxane. This suggests that there is a certain amount of flexibility within the interlocked structures, allowing for the cavity to expand and encapsulate the spherical halide anions of increasing size.

Despite the contrasting hydrogen bonding arrangements of the imidazolium groups in **20**·PF₆ and **21**·PF₆, there is no significant difference in the anion binding selectivity of the rotaxanes. Hence, it can be concluded that the distinct imidazolium hydrogen bond donor arrangement within the interlocked binding cavity is of little importance in determining the selectivity properties of the rotaxane. This is contrary to what might be expected by incorporating geometrically contrasting imidazolium hydrogen bonding motifs into the topologically well-defined cavities of interlocked host structures.

Importantly the halide binding affinity exhibited by 4,5-dimethylimidazolium **20**·PF₆ is stronger than 2-methylimidazolium **21**·PF₆ (674 and 446 M⁻¹ respectively for bromide), but the difference is much less pronounced than that observed for the analogous acyclic imidazolium

derivatives. The incorporation of substituted imidazolium groups into the rotaxane host systems appears to have reduced the impact of the different motifs on anion binding strength, presumably due to the additional effect of the identical macrocycle components in **20**·PF₆ and **21**·PF₆. However, as discussed in Section 2.2 for the analogous acyclic imidazolium derivatives, the observed halide anion binding affinities of both rotaxanes may still be considered to be electrostatically dominated, and less dependent on the exact hydrogen bonding orientations, with the corresponding axle imidazolium cation to halide anion distances explaining the difference in binding strengths between the two rotaxane host systems.

2.3.3 Summary

The first mono-imidazolium interlocked structures were synthesised and their anion recognition properties investigated. Due to their three dimensional interlocked binding cavities, the rotaxane hosts displayed significant selectivity for the spherical halide anions over larger, more basic oxoanions, however with limited preference between the halides. The only difference in the anion binding properties between the rotaxanes, which incorporate imidazolium groups of contrasting hydrogen bond donor geometries in their axle components, was stronger binding exhibited by the 4,5-dimethylimidazolium system.

These findings, along with the acyclic and pseudorotaxane studies, suggest that viewing the interaction between the imidazolium cation and counter anion as charge-assisted hydrogen bonding is inadequate when considering the construction, co-conformations and properties of interpenetrated and interlocked assemblies. In the field of anion coordination chemistry, such electrostatically dominated interactions might be better described as charge-driven hydrogen bonding, especially when designing future imidazolium-based anion host systems.

2.4 Pseudorotaxane Investigations using a Smaller Macrocycle

Whilst the imidazolium-containing rotaxanes synthesised above displayed significant selectivity for the halides over the larger oxoanions, it would be desirable to find ways through rotaxane host design modification to increase both the binding affinity and halide selectivity. As the macrocycle used previously appears to allow for significant flexibility between the components of the imidazolium interlocked structures when considering the relatively small size of the imidazolium motif, it was decided to investigate the effect of reducing the size of the macrocycle on the formation of imidazolium pseudorotaxane assemblies and, ultimately, the anion recognition properties of imidazolium rotaxane systems.

2.4.1 Synthesis of a Smaller Macrocycle

Compared to the previously investigated macrocycle **1**, isophthalamide macrocycle **22** contains a shorter linker between the isophthalamide motif and the electron-rich aromatic groups, in this case phenolic rather than hydroquinone (Figure 2.23). These changes reduce the distance between the anion binding cleft of the macrocycle, responsible for pseudorotaxane association, and those groups capable of participating in secondary stabilisation of the resulting assembly, namely the electron-rich aromatics for donor-acceptor interactions and the polyether chain for potential hydrogen bonding with imidazolium methyl groups. The isophthalamide motif is functionalised with a *tert*-butyl group for direct comparison with the previous pseudorotaxane findings using **1**, and while similar macrocycle derivatives have been reported,⁴¹⁻⁴³ **22** is novel due to this functionalisation.

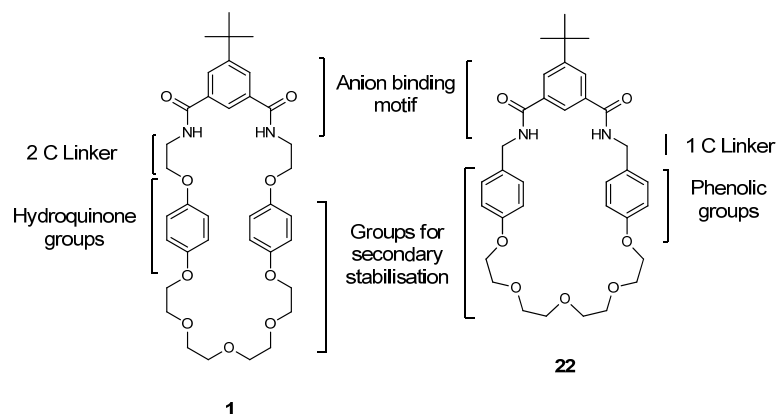
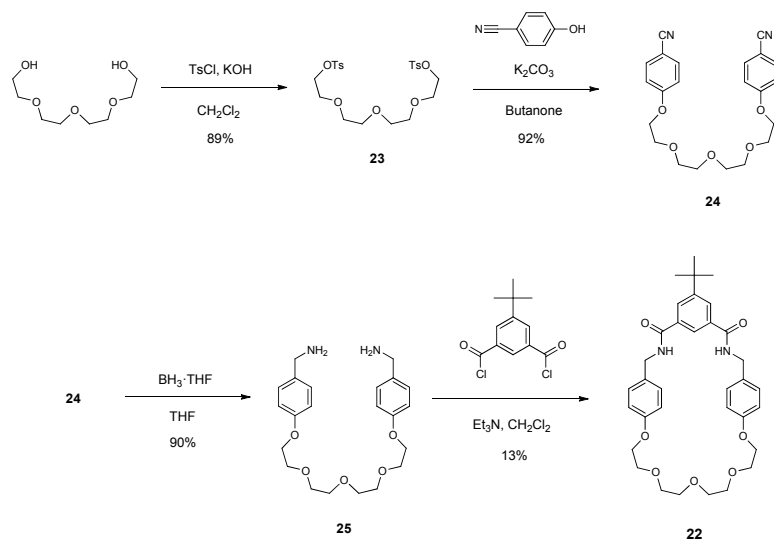


Figure 2.23 a) Macrocycle **1**, and b) target smaller macrocycle **22**.

The synthesis of target macrocycle **22** is detailed in Scheme 2.10, beginning with the tosylation of tetraethylene glycol to afford **23** in 89% yield.⁴⁴ Nitrile **24** was prepared by subsequent reaction of **23** with 4-hydroxybenzonitrile and K_2CO_3 ,⁴² and then reduced using BH_3 to yield bis-amine **25**. Upon initial isolation, **25** was a pale yellow oil, however after drying *in vacuo* and storage at $-20\text{ }^\circ\text{C}$, a white solid was formed as reported in the literature.⁴² Condensation of bis-amine **25** with 5-(*tert*-butyl)isophthaloyl dichloride in the presence of 2.5 equivalents of Et_3N gave macrocycle **22** in 13% yield. It should be noted that significantly higher macrocyclisation yields for similar systems have been achieved using high dilution methods,^{42, 43} however these conditions were not used to allow for direct comparison with the yield from the templated reaction discussed later (Section 2.5.1).



Scheme 2.10 Synthesis of macrocycle **22**.

Crystals of macrocycle **22** suitable for single-crystal X-ray diffraction structural analysis were obtained by recrystallisation from hot MeCN, with the structure solved by Nicholas White using synchrotron radiation at Diamond Light Source beamline I19 (Figure 2.24). In the solid-state, the amide groups of **22** are approximately *syn-anti* and form an extended hydrogen bonding network with the amide and polyether groups of adjacent macrocycles.

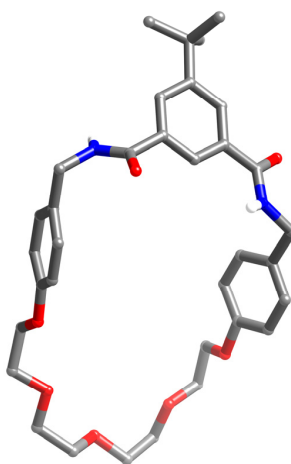


Figure 2.24 Crystal structure of macrocycle **22**. Protons and lower occupancy positions of disorder are omitted for clarity.

2.4.2 Pseudorotaxane Studies

Pseudorotaxane ^1H NMR studies were carried out in CDCl_3 using macrocycle **22** and imidazolium threads **2**·Cl and **3**·Cl. The spectra for macrocycle **22**, 4,5-dimethylimidazolium thread **2**·Cl and an equimolar solution of both components are shown in Figure 2.25, with the observed chemical shift changes indicative of the formation of anion templated pseudorotaxane **2**·**22**·Cl. Specifically, polarisation of the templating chloride anion away from the thread and towards the macrocycle hydrogen bond donors is responsible for downfield shifts in the signals corresponding to macrocycle protons c and d, and an upfield shift in imidazolium thread proton 1. Additionally, macrocycle phenolic protons g are shifted significantly upfield upon pseudorotaxane formation, due to favourable donor-acceptor interactions with the electron-deficient imidazolium thread. Similar shifts were also observed for the formation of the analogous 2-methylimidazolium pseudorotaxane **3**·**22**·Cl (Figure 2.26).

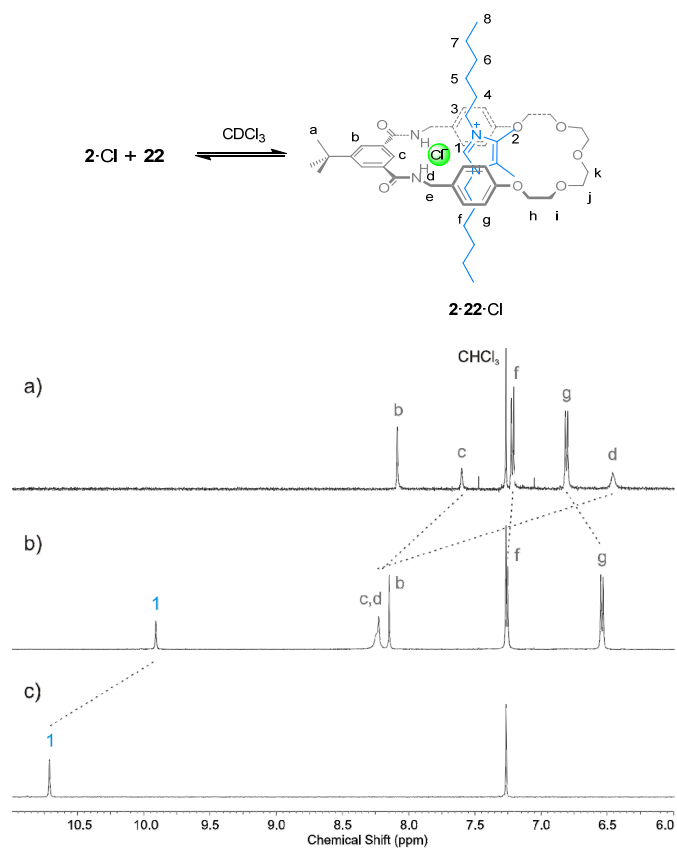


Figure 2.25 Partial ^1H NMR spectra (500 MHz) in CDCl_3 at 293 K of a) macrocycle **22**, b) macrocycle **22** plus 1.0 equivalent of thread **2·Cl**, and c) thread **2·Cl**.

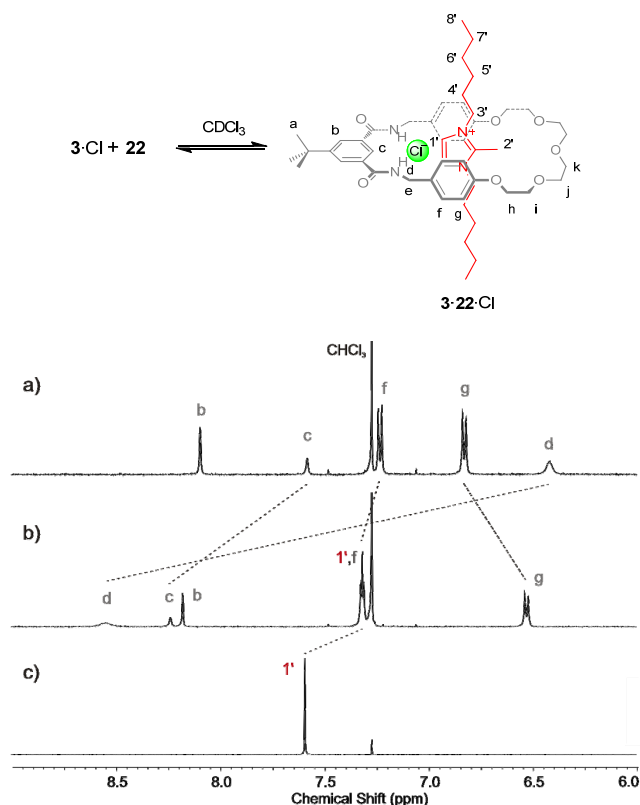


Figure 2.26 Partial ^1H NMR spectra (500 MHz) in CDCl_3 at 293 K of a) macrocycle **22**, b) macrocycle **22** plus 1.0 equivalent of thread **3·Cl**, and c) thread **3·Cl**.

Quantitative ^1H NMR titration experiments were undertaken, with aliquots of threading components **2·Cl** and **3·Cl** added to CDCl_3 solutions of macrocycle **22**. In addition, control titrations were carried out using hexafluorophosphate threads **2·PF₆** and **3·PF₆**, and TBA chloride. The macrocycle phenolic protons f and g were monitored throughout all of the titration experiments and the shifts observed are shown in Figure 2.27. The minor shifts in the signal corresponding to protons g during the control titrations (Figures 2.27c, d and e, $|\Delta\delta| \leq 0.07$ ppm) indicate that the significant upfield shifts observed upon addition of **2·Cl** and **3·Cl** (Figures 2.27a and b, $\Delta\delta = -0.44$ and -0.43 ppm respectively) are not simply due to the macrocycle sequestering the anion, and that pseudorotaxane formation requires the presence of the halide template.

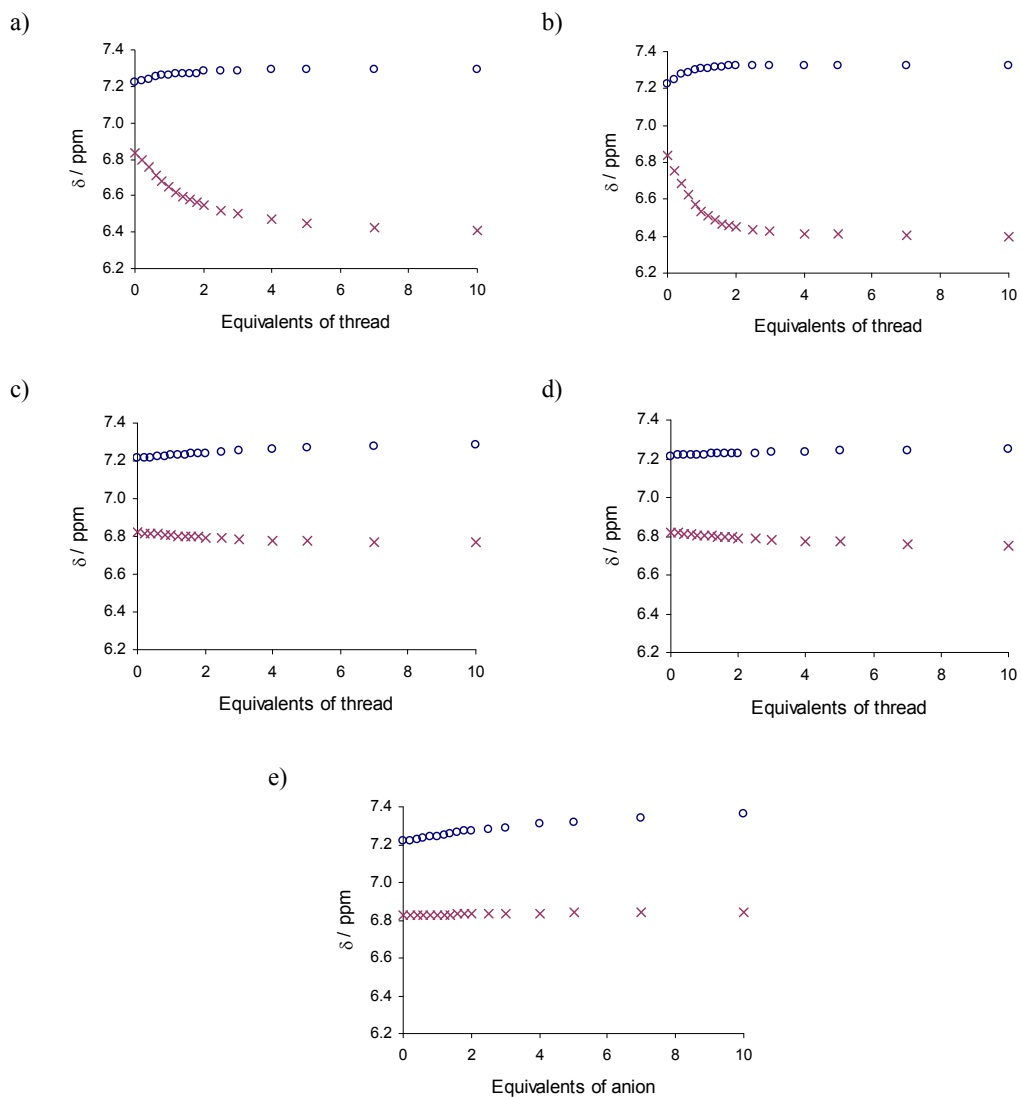


Figure 2.27 Changes in the chemical shift of phenolic protons f (○) and g (×) upon addition of a) thread 2·Cl, b) thread 3·Cl, c) thread 2·PF₆, d) thread 3·PF₆, and e) TBACl to macrocycle **22** in CDCl₃ at 293 K (500 MHz, 2.0 × 10⁻³ M)

Further evidence for pseudorotaxane formation was obtained from 2D ¹H-¹H NMR ROESY spectroscopy, with several intercomponent correlations observed for both systems (Figures 2.28 and 2.29).

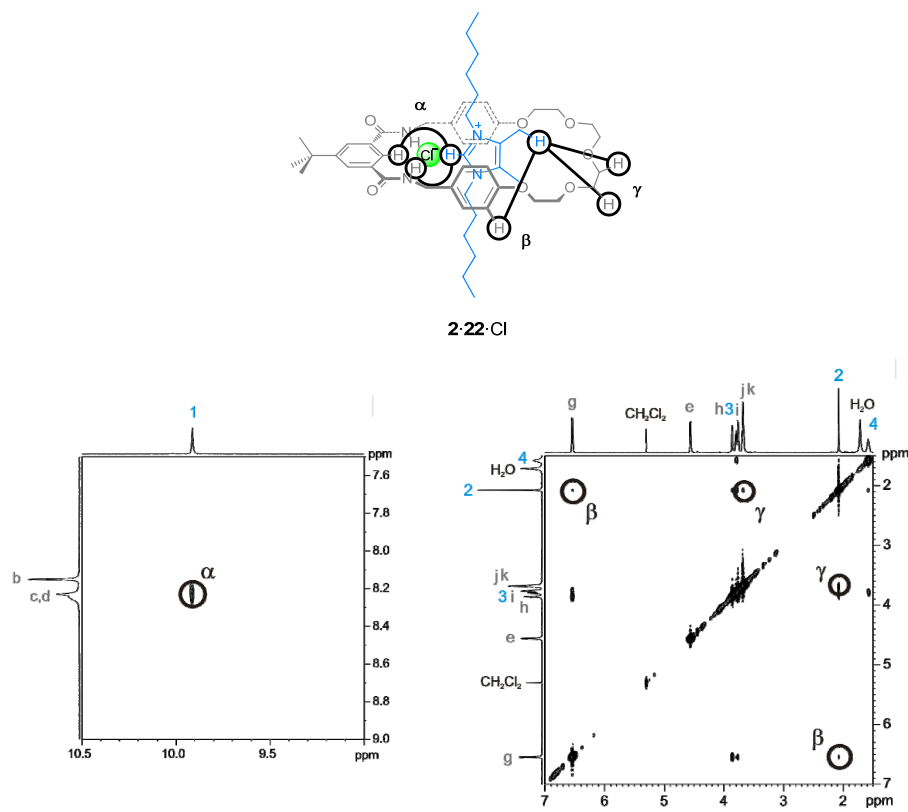


Figure 2.28 Portion of the ^1H - ^1H NMR ROESY spectrum of **2·22·Cl** (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structure.

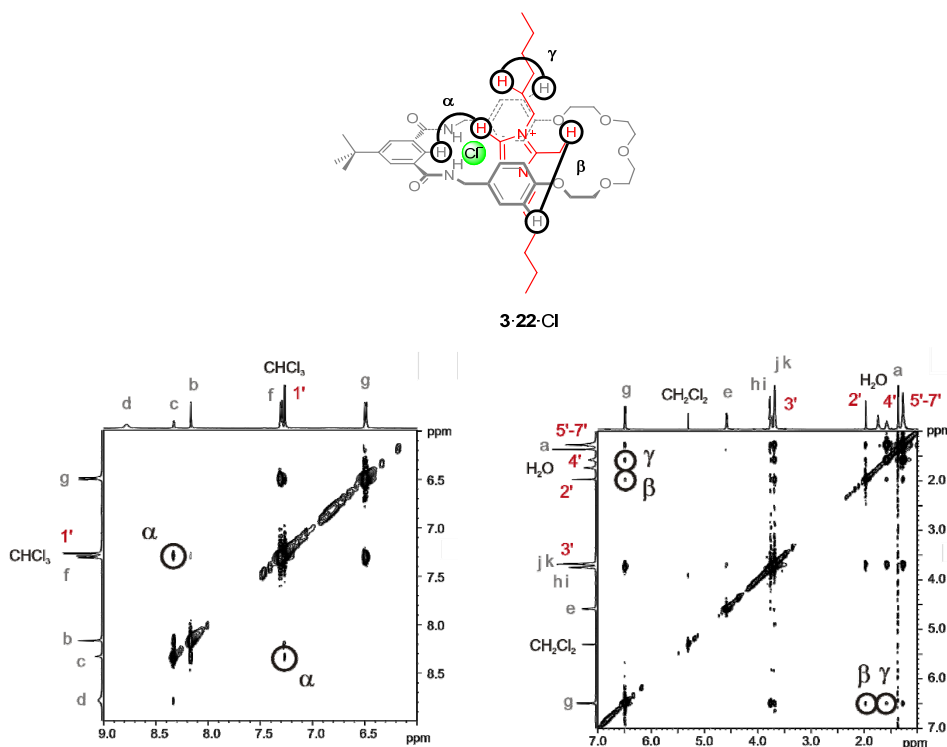


Figure 2.29 Portion of the ^1H - ^1H NMR ROESY spectrum of **3·22·Cl** (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structure.

Furthermore, crystals of **3·22·Cl** suitable for single-crystal X-ray diffraction structural analysis were obtained by slow diffusion of $i\text{Pr}_2\text{O}$ into an equimolar CDCl_3 solution of thread **3·Cl** and macrocycle **22**, and the structure was solved by Nicholas White. It was found to contain two independent pseudorotaxane assemblies in the asymmetric unit, however each have very similar geometries (with only slight differences in atomic distances) and only one is shown in Figure 2.30. In contrast to the analogous pseudorotaxane constructed using the larger macrocycle (Section 2.2.4), only one co-conformation is observed for **3·22·Cl**, which is in agreement with the solution phase orientation of the 2-methylimidazolium thread (Figure 2.29). Moreover, the inter-assembly electrostatic interactions that contributed to the unexpected co-conformations in the solid-state structures of **1·2·Cl** and **1·3·Cl** appear to be less important in the structure of **3·22·Cl**. The halide anion in the same assembly is much closer to the positive charge of the imidazolium thread than the next nearest anion, with corresponding distances of 4.928(2) or 4.978(3) Å (for the two assemblies in

the asymmetric unit) compared to 6.820(2) or 7.032(3) Å. Hydrogen bonds between the imidazolium methyl groups and several polyether oxygen atoms are observed, with one such close contact shown in Figure 2.30 (C...O distance of 3.228(14) or 3.175(15) Å). While the smaller macrocyclic host **22** may appear to exhibit a greater extent of complementarity with 2-methylimidazolium thread **3**·Cl than macrocycle **1**, it is difficult to draw any substantial conclusions from the solid-state co-conformational differences due to the multitude of contributing factors, not least the different crystal growth conditions used for **1**·**3**·Cl and **3**·**22**·Cl.

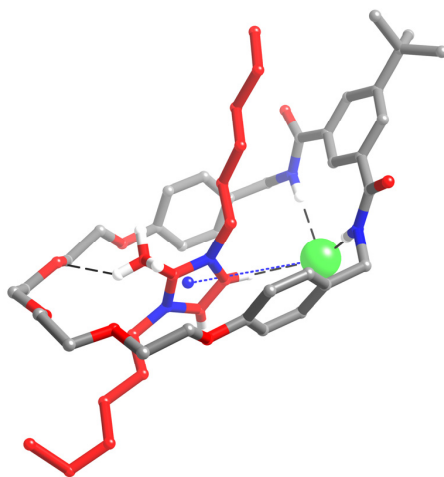


Figure 2.30 Crystal structure of pseudorotaxane **3**·**22**·Cl. One of the two independent pseudorotaxane assemblies in the asymmetric unit is shown. The centre of the imidazolium positive charge is marked by a dark blue sphere, with the corresponding distance to the halide anion shown in a dotted blue line. H...Cl and H...O close contacts are displayed using dashed black lines. Protons omitted for clarity where appropriate.

To calculate the relative stabilities of assemblies **2**·**22**·Cl and **3**·**22**·Cl, macrocycle amide protons **d** were monitored throughout the titration experiments (Figures 2.31a and b) and WinEQNMR2 analysis gave the apparent pseudorotaxane association constants shown in Table 2.3. The amide protons were chosen for consistency with the previously reported analogous imidazolium pseudorotaxane studies, the results of which are also shown in Table 2.3.²³ In addition, the association constant for the binding of chloride to macrocycle **22** was obtained (Figure 2.31c).

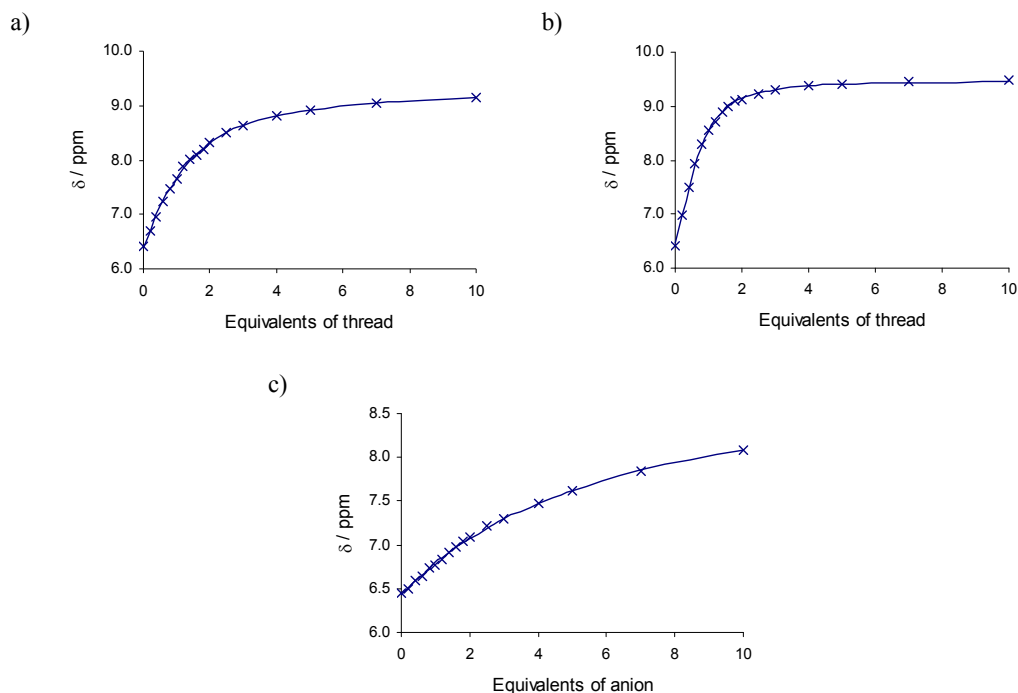


Figure 2.31 Changes in the chemical shift of amide protons d upon addition of a) thread **2**·Cl, b) thread **3**·Cl, and c) TBACl to macrocycle **22** in CDCl₃ at 293 K (500 MHz, 2.0×10^{-3} M). Crosses represent experimental data points; lines represent calculated titration curves.

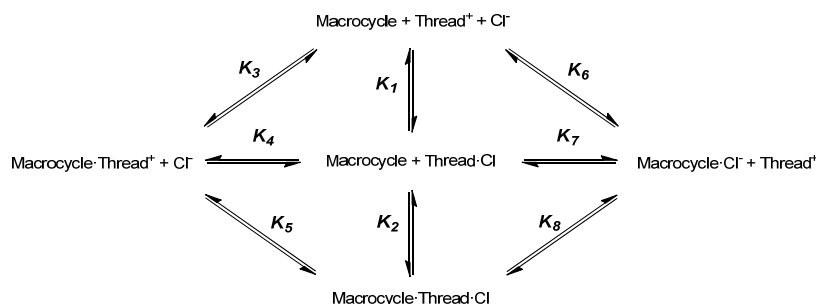
Table 2.3 Association constants, K (M⁻¹), for pseudorotaxane formation using macrocycles **22** and **1** and threads **2**·Cl and **3**·Cl, and association constants for macrocycle chloride binding, in CDCl₃ at 293 K. Obtained by monitoring macrocycle amide protons. Errors are given in parentheses.

Guest	Macrocycle 22 K (M ⁻¹)	Macrocycle 1 K (M ⁻¹) ²³
2 ·Cl	644 (24)	97 (3)
3 ·Cl	3287 (177)	245 (5)
TBACl	82 (5)	36 (1)

2.4.2.1 Pseudorotaxane Equilibria

Before the pseudorotaxane data given in Table 2.3 can be discussed, it is important to consider the multitude of equilibria occurring during the titrations (Scheme 2.11). The titration protocol involved the addition of a thread ion pair (**2**·Cl or **3**·Cl) to a macrocycle (**1** or **22**), which is represented at the centre of Scheme 2.11 with the equilibrium of interest, anion templated pseudorotaxane

formation, given by K_2 . Whilst WinEQNMR2 analysis of the titration data determined apparent 1:1 association constants for this process, these assemblies are strictly ternary complexes. Hence, it is necessary to assess the assumption that the values reflect the relative stabilities of the anion templated pseudorotaxane assemblies.



Scheme 2.11 Anion templated pseudorotaxane formation equilibria.

Due to strong ion-pairing in non-competitive solvents such as CDCl_3 , the dissociation of the thread ion pair, K_1 , is usually considered to have a minor effect in solution and this is likely to be a valid assumption for the two imidazolium systems. However, any ion pair dissociation would be more significant for the considerably weaker binding 2-methylimidazolium motif compared with the 4,5-dimethyl analogue (Section 2.2.2). If so, this would result in an underestimation of K_2 for the pseudorotaxane titrations involving $\mathbf{3} \cdot \text{Cl}$ ($\mathbf{1} \cdot \mathbf{3} \cdot \text{Cl}$ and $\mathbf{3} \cdot \mathbf{22} \cdot \text{Cl}$) compared with those involving $\mathbf{2} \cdot \text{Cl}$. Hence, while the apparent association constants for $\mathbf{1} \cdot \mathbf{3} \cdot \text{Cl}$ and $\mathbf{3} \cdot \mathbf{22} \cdot \text{Cl}$ were observed to be greater than those for $\mathbf{1} \cdot \mathbf{2} \cdot \text{Cl}$ and $\mathbf{2} \cdot \mathbf{22} \cdot \text{Cl}$ (Table 2.3), these considerations mean that the differences in the ‘true’ association constants may actually be slightly larger.

As well as the thread ion pair equilibrium K_1 , there are a number of other equilibria to consider, including K_3 , K_4 and K_5 which represent non-anion-templated pseudorotaxane formation. The possibility of this mechanism occurring was investigated by the control titrations with $\mathbf{2} \cdot \text{PF}_6$ and $\mathbf{3} \cdot \text{PF}_6$ (Figures 2.27c and d) and found to be minor compared with the anion templated process.⁴⁵ Equilibria K_6 , K_7 and K_8 concern chloride binding to the macrocycle *via* abstraction from the imidazolium thread. The association constants for chloride binding to macrocycles **1** and **22** were calculated from the titrations using TBA chloride (36 and 82 M^{-1} respectively, Table 2.3). As these

values are considerably less than the analogous binding strengths of the 4,5-dimethyl- and 2-methyl-imidazolium motifs (3044 and 782 M^{-1} respectively, Table 2.1), it can be assumed that K_6 , K_7 and K_8 also have only a small effect on pseudorotaxane formation.

Hence, the apparent association constants calculated from the titration data can be thought to reflect the relative stabilities of the anion templated pseudorotaxane assemblies.

2.4.2.2 Discussion of Titration Data

Smaller macrocycle **22** displays enhanced chloride binding affinity compared to **1** (Table 2.3), presumably due to less flexibility in the macrocyclic system leading to reduced entropic losses upon complexation. Importantly, both 4,5-dimethyl- and 2-methyl-imidazolium assemblies **2**·**22**·Cl and **3**·**22**·Cl exhibit much greater stability when compared with the analogous pseudorotaxane assemblies containing macrocycle **1**, which suggests a higher degree of complementarity exists with the smaller macrocycle interpenetrated structures. Additionally, the difference between the systems containing contrasting imidazolium motifs is more pronounced with macrocycle **22** than **1**. To explain these findings, the shifts observed for imidazolium methyl protons (2 and 2') during the pseudorotaxane titrations were studied (Figure 2.32).

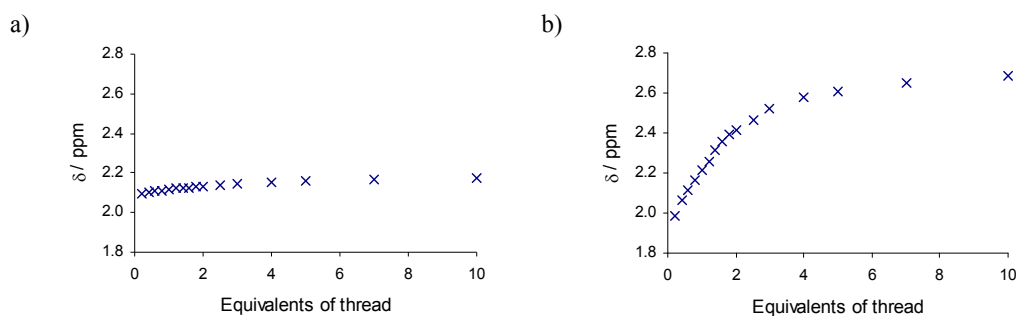


Figure 2.32 Changes in the chemical shift of imidazolium methyl protons upon addition of a) thread **2**·Cl (protons 2) and b) thread **3**·Cl (protons 2') to macrocycle **22** in CDCl_3 at 293 K. Crosses represent experimental data points.

Whilst the 4,5-dimethylimidazolium protons 2 of **2**·Cl shifted only slightly upon addition to macrocycle **22** (Figure 2.32a, $\Delta\delta = +0.08$ ppm after 10.0 equivalents), the 2-methylimidazolium protons 2' of **3**·Cl shifted significantly downfield during the corresponding titration (Figure 2.32b,

$\Delta\delta = +0.70$ ppm). These shifts are due to hydrogen bonding between the thread methyl groups and the polyether chain of macrocycle **22**, with the 2-methylimidazolium group of thread **3**·Cl much more favourably aligned for these interactions than the 4,5-dimethylimidazolium groups of **2**·Cl (Figures 2.25 and 2.26). This results in considerable secondary stabilisation of **3**·**22**·Cl, explaining its increased stability compared to **2**·**22**·Cl.

Smaller downfield shifts were observed for these protons in the larger macrocycle pseudorotaxane systems **1**·**2**·Cl and **1**·**3**·Cl ($\Delta\delta = +0.03$ and $+0.15$ ppm respectively).²³ These shifts suggest that the observed trend in the pseudorotaxane stabilities of **1**·**2**·Cl and **1**·**3**·Cl is also due to the presence of these hydrogen bonding interactions in the 2-methylimidazolium system. However, the much larger shifts observed for assemblies **2**·**22**·Cl and **3**·**22**·Cl reflect the higher degree of complementarity in the smaller macrocycle systems. The hydrogen bonding interactions between the imidazolium methyl groups and macrocycle polyether chain do not contribute as much in the 4,5-dimethylimidazolium systems, but the stabilisation from the donor-acceptor interactions is also increased due to the reduced size of the linker between the anion binding cleft and the electron-rich aromatic groups.

It is noteworthy that bis-vinyl macrocycle precursor **15** (Section 2.3.1) lacks the preorganised polyether chain required for the secondary hydrogen bonds to occur. Presumably this is the reason why the trend in the rotaxane yields reflects the different anion binding affinities (4,5-dimethyl- greater than 2-methyl-imidazolium), rather than the trend in pseudorotaxane formation.

2.4.3 Summary

Smaller macrocycle **22** was synthesised and found to form anion templated pseudorotaxanes with substituted imidazolium threads **2**·Cl and **3**·Cl. 2-Methylimidazolium assembly **3**·**22**·Cl exhibited significantly greater stability than 4,5-dimethylimidazolium **2**·**22**·Cl, due to secondary stabilising hydrogen bonding interactions between the 2-methyl group of **3**·Cl and the macrocycle polyether chain. Crucially, both of these interpenetrated assemblies were more stable than the analogous pseudorotaxanes with larger macrocycle **1**, indicating a greater degree of complementarity for both

secondary hydrogen bonding and donor-acceptor interactions between thread and macrocycle components.

2.5 Synthesis of Smaller Macrocycle Rotaxane Systems

Having demonstrated that reducing the macrocycle size favours chloride anion templated imidazolium pseudorotaxane formation, attempts to synthesise analogous rotaxane structures were undertaken.

2.5.1 Rotaxane Synthesis by Condensation

The synthesis of anion templated interlocked structures *via* a novel amide condensation route has recently been established by Beer *et al.*⁴⁶ Initially, 3,5-bis-amide-pyridinium thread **2.5** was found to template the formation of macrocycle **2.7** in 42% yield (Figure 2.33a), with a reduced macrocyclisation yield of 21% observed in the absence of **2.5**. This approach was then successfully applied to the formation of rotaxane **2.9** by using stoppered axle **2.8** as the template (Figures 2.33b and c). Templatation occurs due to the formation of an intermediate assembly produced *via* anion binding to the halide template by the axle and half-formed macrocycle (represented in Figure 2.33c), which is further stabilised by secondary hydrogen bonding and donor-acceptor interactions. Since this discovery, a number of other anion templated interlocked structures based on the 3,5-bis-amide-pyridinium motif have been synthesised.^{38, 47, 48}

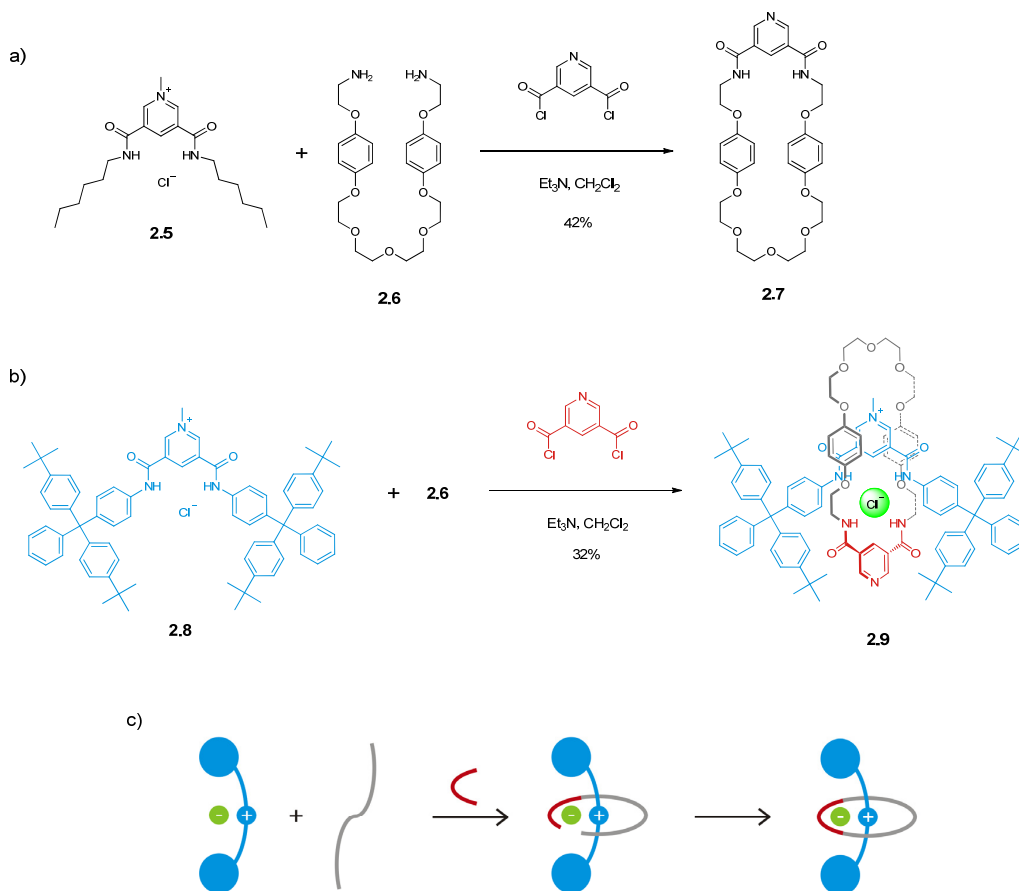
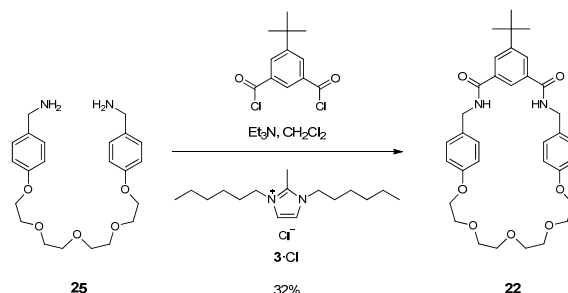


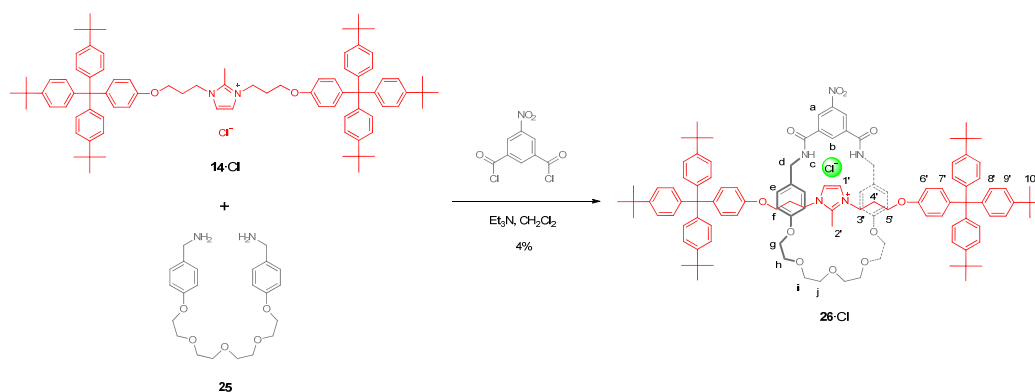
Figure 2.33 Previously reported templated synthesis of a) macrocycle **2.7** and b) rotaxane **2.9**, and c) schematic representation of rotaxane formation.

Encouraged by the strong stability of pseudorotaxane assembly **3·22·Cl**, the macrocyclisation reaction to form **22** was carried out in the presence of one equivalent of 2-methylimidazolium thread **3·Cl** (Scheme 2.12). Pleasingly, a significant enhancement of the yield from 13% to 32% was observed. The presence of **3·Cl** in the reaction mixture appears to favour [1+1]-macrocyclisation over higher order macrocyclic and oligomeric by-products.



Scheme 2.12 Templated synthesis of macrocycle **22**.

In light of this result, the analogous rotaxane synthesis was attempted using axle **14·Cl**, bis-amine **25** and 5-nitroisophthaloyl dichloride (Scheme 2.13). Rotaxane **26·Cl** was isolated from the reaction mixture by preparative silica gel thin layer chromatography using 1:1 $\text{CH}_2\text{Cl}_2/\text{MeCN}$ followed by 96:4 $\text{CH}_2\text{Cl}_2/\text{MeOH}$, but in a very low yield of 4%. The ^1H NMR spectrum for 2-methylimidazolium rotaxane **26·Cl** is shown in Figure 2.34, with the signal corresponding to macrocycle phenolic protons **f** appearing further downfield than those in macrocycle **22** (at 6.36 ppm compared with 6.69 ppm). Importantly, this is in agreement with the analogous shifts observed in the pseudorotaxane investigations (Figure 2.26), indicating interlocked structure formation. Additionally, imidazolium methyl protons **2'** are considerably shifted upfield compared to axle **14·Cl** ($\Delta\delta = -1.08$ ppm), presumably due to the macrocycle phenolic ring currents.



Scheme 2.13 Synthesis of 2-methylimidazolium rotaxane **26·Cl**.

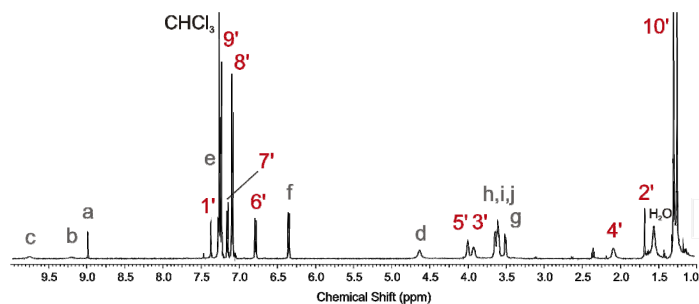


Figure 2.34 ^1H NMR spectrum (500 MHz) of rotaxane **26**·Cl in CDCl_3 at 293 K.

Further characterisation of the rotaxane was provided by high resolution electrospray mass spectrometry and 2D ^1H - ^1H NMR ROESY spectroscopy, with the interlocked nature of **26**·Cl confirmed by a number of intercomponent ROESY correlations (Figure 2.35).

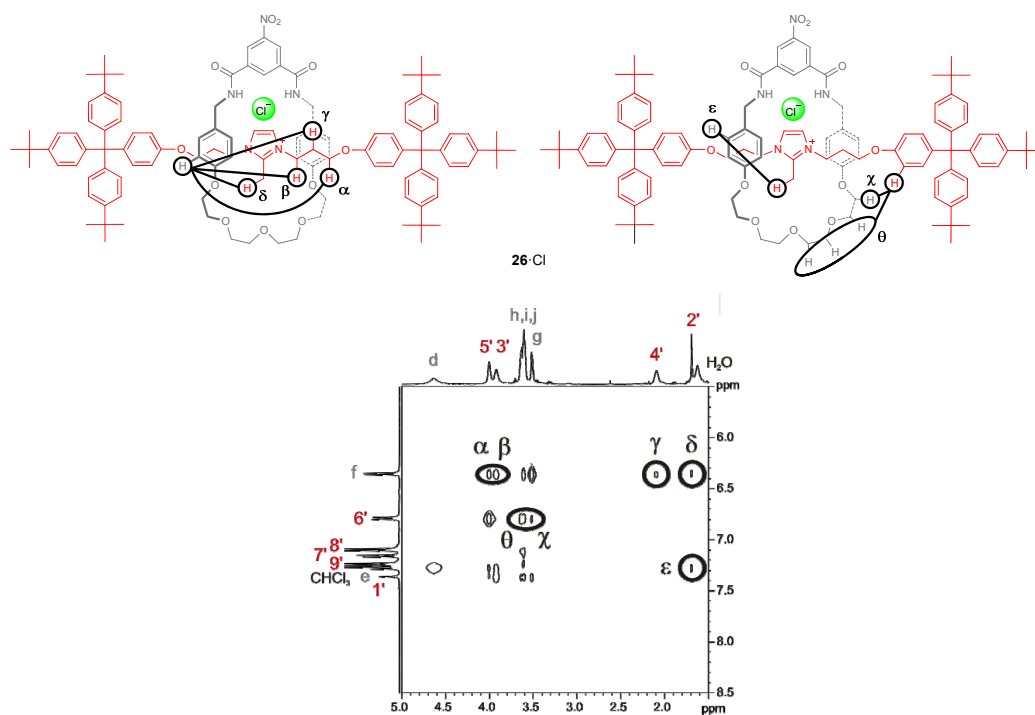


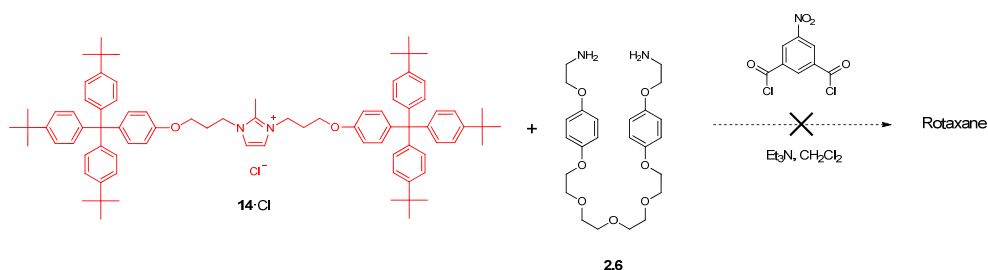
Figure 2.35 Portion of the ^1H - ^1H NMR ROESY spectrum of **26**·Cl (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures.

The synthesis of **26**·Cl was repeated with a large excess of bis-amine **25** and 5-nitroisophthaloyl dichloride (ten equivalents) in an attempt to favour interlocked structure formation,

however after removal of the increased oligomeric by-products, ^1H NMR integration of the crude mixture revealed no significant enhancement in the rotaxane yield.

Although 2-methylimidazolium rotaxane **26**·Cl is the first non-pyridinium interlocked structure prepared *via* this anion templated condensation strategy, this is not a viable route for the effective synthesis of anion host systems due to the very low yield. It is unclear why this is the case, given that the macrocyclisation yield was considerably enhanced in the presence of thread **3**·Cl.

For comparison, an analogous synthetic method was attempted using 2-methylimidazolium axle **14**·Cl and bis-amine **2.6** (donated by Nicholas White) as shown in Scheme 2.14. However rotaxane formation was unsuccessful, with no interlocked product detected in the reaction mixture. This is potentially due to the lower degree of complementarity for the secondary stabilising interactions between imidazolium derivatives and these larger macrocycle systems. Compared with 3,5-bis-amide-pyridinium axle **2.8** (Figure 2.33b), the weaker anion complexation ability of the imidazolium motif and the reduced area of electron-deficient π -surface for the donor-acceptor interactions may explain the lack of success in effective imidazolium rotaxane synthesis *via* this condensation approach.

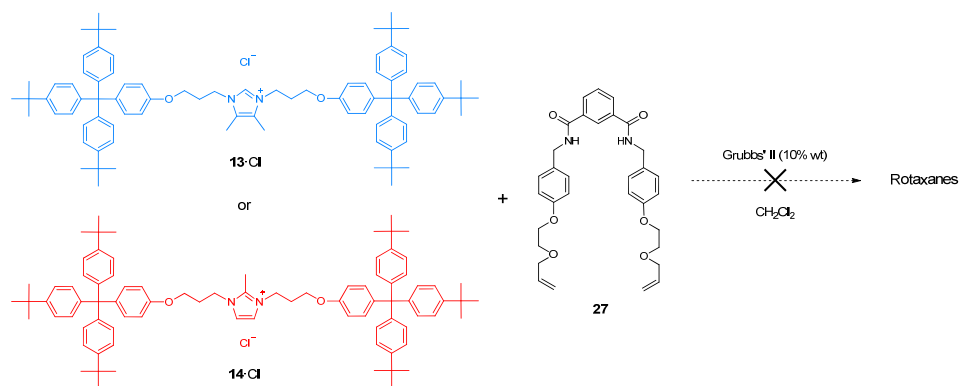


Scheme 2.14 Attempted rotaxane synthesis by condensation with macrocycle precursor **2.6**.

2.5.2 Attempted Rotaxane Synthesis by RCM

Following the success in employing Grubbs'-catalysed RCM to synthesise imidazolium rotaxanes **20**·Cl and **21**·Cl (Section 2.3.1), it was decided to use a similar approach in the formation of systems incorporating smaller macrocyclic components. Using vinyl-appended macrocycle precursor

27, which is based on macrocycle **22** and donated by Laura Hancock, rotaxane synthesis was attempted using both 4,5-dimethyl- and 2-methyl-imidazolium axles **13**·Cl and **14**·Cl (Scheme 2.15). However in both cases, no interlocked products were formed, with only the axles and the closed macrocycle identifiable in the reaction mixtures.

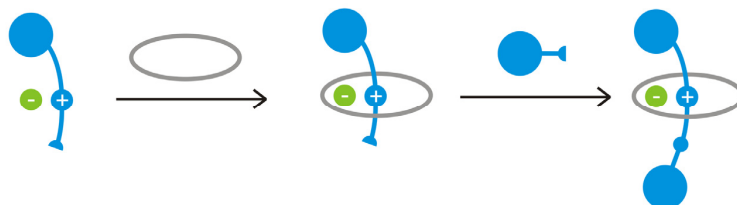


Scheme 2.15 Attempted synthesis of rotaxanes *via* RCM using smaller macrocycle precursor **27**.

It is not clear why these rotaxation reactions were unsuccessful in the formation of the target rotaxanes, in contrast to the systems successfully prepared using larger macrocycle precursor **15**. Potentially, the steric considerations for Grubbs'-catalysed RCM, the reduced anion complexation ability of the isophthalamide motif in **27** compared with 5-nitroisophthalamide **15**, and the less electron-rich phenolic groups of **27** compared with the hydroquinone groups of **15**, may be responsible for no interlocked species being isolated.

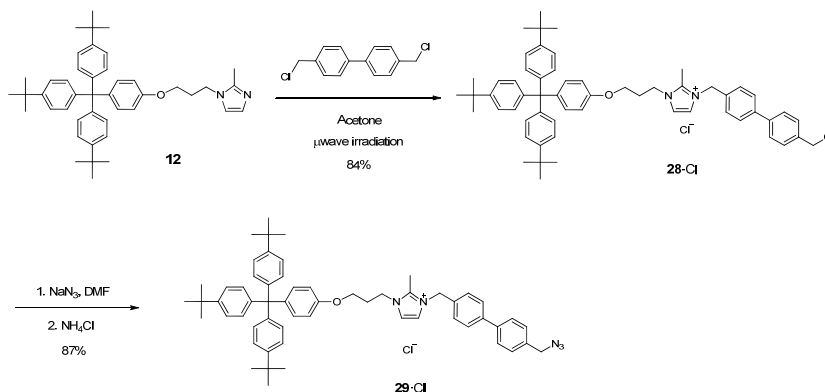
2.5.3 Rotaxane Synthesis by 'Stoppering'

Having attempted amide condensation and RCM 'clipping' methods for rotaxane formation, an alternative 'stoppering' approach was employed, illustrated in Scheme 2.16. It was hoped that the ability of the 2-methylimidazolium motif to form strong anion templated pseudorotaxanes with smaller macrocycle **22** could be exploited for effective rotaxane synthesis.



Scheme 2.16 Schematic representation of the asymmetric stoppering approach for anion templated rotaxane formation.

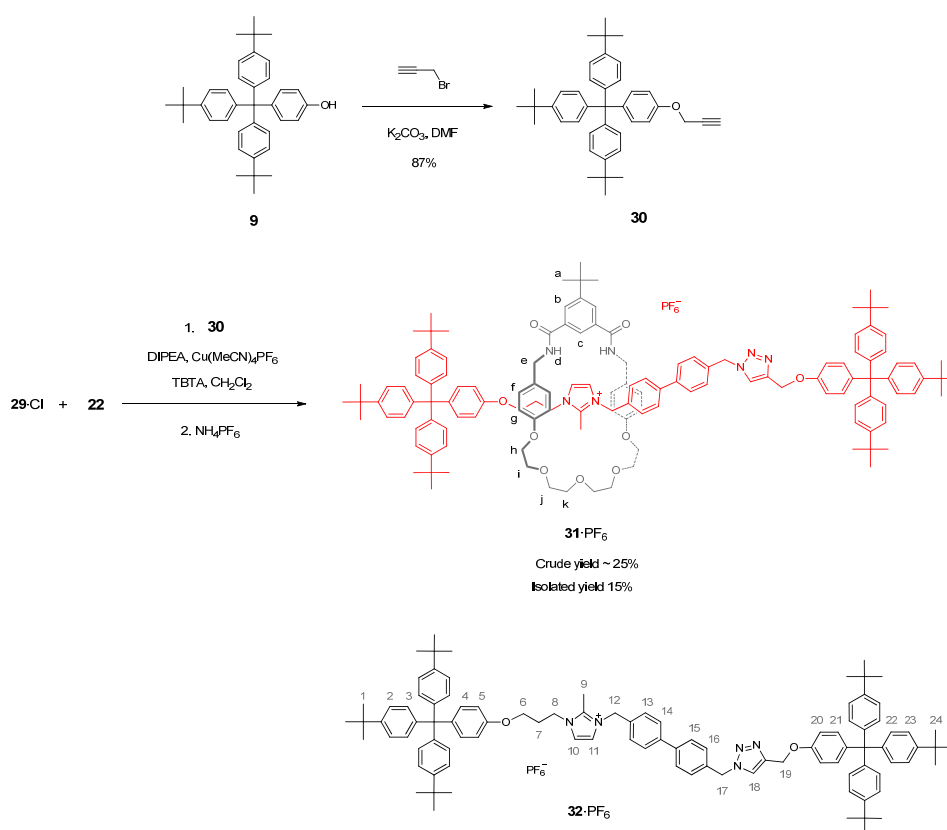
As discussed in the introductory chapter (Section 1.2.1), the copper(I)-catalysed alkyne-azide cycloaddition (CuAAC) ‘click’ reaction⁴⁹ has been extensively used in the synthesis of interlocked structures, especially in systems prepared *via* ‘stoppering’. Hence, mono-stoppered 2-methylimidazolium thread **29**·Cl, incorporating a terminal azide group, was synthesised as shown in Scheme 2.17. Imidazole derivative **12** was reacted with an excess of 4,4’-bis(chloromethyl)-1,1’-biphenyl under microwave irradiation to give the desired alkylated product **28**·Cl in 84% yield. Conversion of the terminal chloro-functionality to the key azide group was achieved using NaN_3 , and repeated washing with aqueous NH_4Cl , afforded target thread **29**·Cl.



Scheme 2.17 Synthesis of mono-stoppered 2-methylimidazolium thread **29**·Cl.

For ‘click’ coupling with azide **29**·Cl, stopper alkyne **30** was synthesised from terphenyl derivative **9** and propargyl bromide in 87% yield using a literature procedure (Scheme 2.18).⁵⁰ The subsequent ‘click’ reaction between these two components was carried out in the presence of macrocycle **22** (one equivalent compared to azide **29**·Cl), using DIPEA as the base, $\text{Cu}(\text{MeCN})_4\text{PF}_6$ as

the catalyst and TBTA as a stabilising ligand. Although ^1H NMR integration of the reaction mixture indicated a crude yield of approximately 25% for interlocked structure formation, difficulties in purification resulted in rotaxane **31**·PF₆ being isolated in 15% yield following preparative silica gel chromatography, anion exchange to the hexafluorophosphate salt and trituration with methanol (Scheme 2.18). ‘Clicked’ axle **32**·PF₆ was also isolated from the reaction mixture.



Scheme 2.18 Synthesis of 2-methylimidazolium rotaxane **31**·PF₆.

To aid purification, rotaxane synthesis was attempted in the absence of the TBTA stabilising ligand. However, in addition to the expected reduction in reaction rate (completion after three days compared to 15 h with TBTA), a considerable loss in the yield of rotaxane was observed (10% by NMR integration). It is not evident why the presence of TBTA would favour interlocked structure formation to such an extent, however recent studies have shown that triazole-based stabilising ligands,

including TBTA, are able to similarly favour ‘click’ macrocyclisation over oligomerisation in certain systems.^{51, 52}

The ^1H NMR spectrum of $\mathbf{31} \cdot \text{PF}_6$, along with those of its component macrocycle $\mathbf{22}$ and axle $\mathbf{32} \cdot \text{PF}_6$, is shown in Figure 2.36. Importantly, the signal corresponding to macrocycle phenolic protons **g** is shifted upfield in rotaxane $\mathbf{31} \cdot \text{PF}_6$ due to the donor-acceptor interactions characteristic of interlocked structures of this type ($\Delta\delta = -0.47$ ppm). Shielding from the macrocycle electron-rich aromatic groups are responsible for upfield shifts in axle protons **8**, **9** and **12**, all of which are α - to the imidazolium ring, whilst macrocycle protons **e** are split in the rotaxane, reflecting the asymmetry of the axle component. Finally, amide protons **d** appear at a significantly higher chemical shift in interlocked host $\mathbf{31} \cdot \text{PF}_6$ than in macrocycle $\mathbf{22}$.

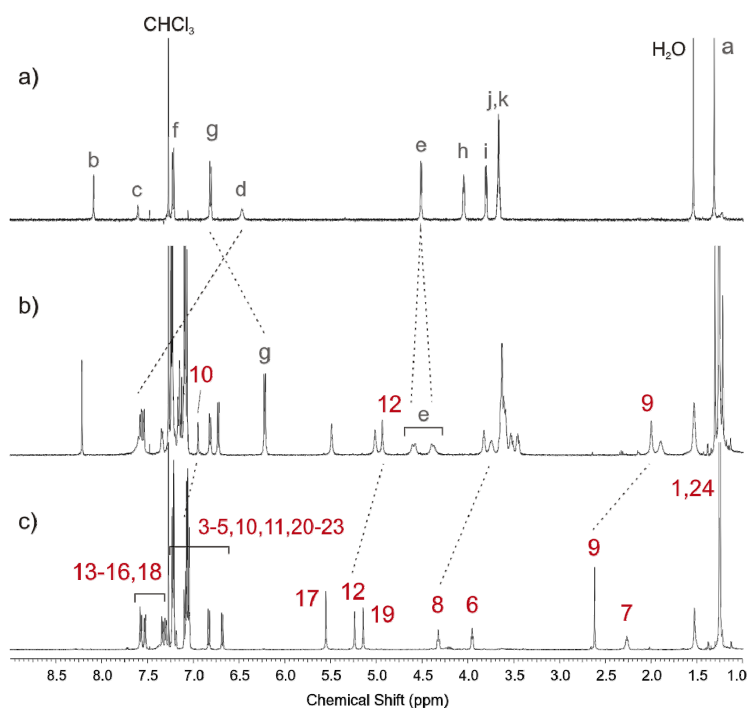


Figure 2.36 ^1H NMR spectra (500 MHz) in CDCl_3 at 293 K of a) macrocycle $\mathbf{22}$, b) rotaxane $\mathbf{31} \cdot \text{PF}_6$, and c) axle $\mathbf{32} \cdot \text{PF}_6$.

The interlocked nature of rotaxane $\mathbf{31} \cdot \text{PF}_6$ was confirmed by high resolution electrospray mass spectrometry and 2D ^1H - ^1H NMR ROESY spectroscopy, and the observed intercomponent ROESY correlations are shown in Figure 2.37. There is the potential for a number of possible interactions

between the macrocycle and axle components of rotaxane **31**·PF₆, especially between the macrocycle amide groups and axle triazole unit formed in the ‘stopping’ reaction.⁵³ It was expected that even in the absence of a coordinating anion, the macrocycle would reside primarily over the axle imidazolium group due to the favourable donor-acceptor interactions, and the observed correlations indicate that this is indeed the case.

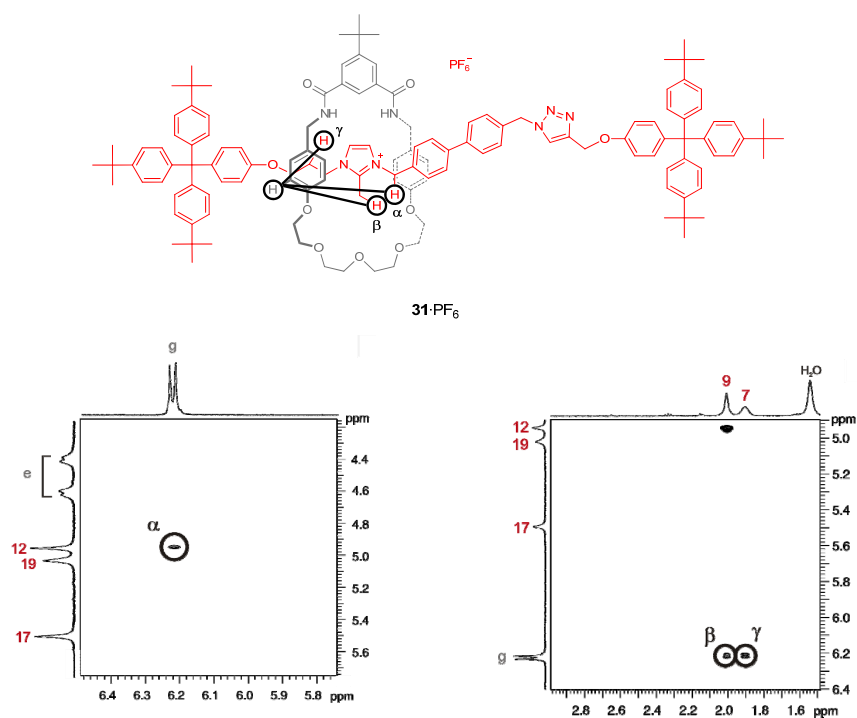


Figure 2.37 Portions of the ¹H-¹H NMR ROESY spectrum of **31**·PF₆ (CDCl₃, 500 MHz, 293 K). Intercomponent correlations are marked on the structure.

2.5.4 Anion Binding Properties of a Smaller Macrocycle Imidazolium Rotaxane

In order to investigate the anion recognition properties of 2-methylimidazolium rotaxane **31**·PF₆, ¹H NMR titration experiments were carried out in 1:1 CDCl₃/CD₃OD, with spectra from the titration of **31**·PF₆ with TBA chloride shown in Figure 2.38. Throughout the titrations, downfield shifts were observed for the rotaxane cavity protons involved in anion binding, namely isophthalamide proton c and amide protons d of the macrocycle and axle imidazolium protons 10 and 11. However,

the amide protons (d) were not able to be followed due to deuterium exchange. Interestingly, only moderate shifts in imidazolium protons 10 and 11 were observed, possibly due to opposing contributions from anion binding and donor-acceptor interactions. Importantly, no significant shifts occurred in the signals corresponding to macrocycle phenolic protons g, axle CH₂ protons 9 and 12, and triazole proton 18, indicating no major co-conformational changes occur upon anion binding, and that the axle triazole group does not participate in any interactions with the anion.

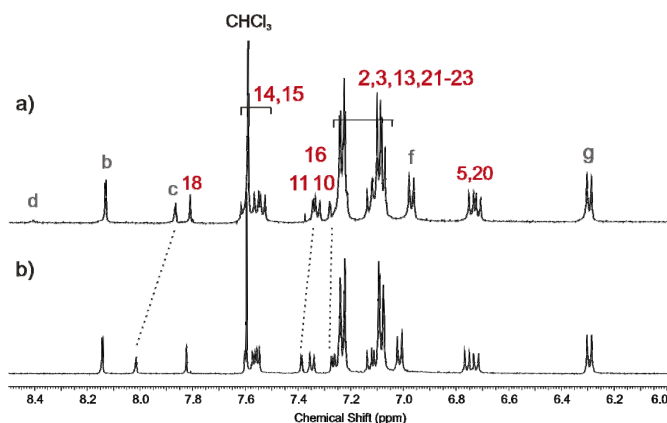


Figure 2.38 Partial ¹H NMR spectra (500 MHz, 1.5×10^{-3} M) in 1:1 CDCl₃/CD₃OD at 293 K of a) rotaxane **31**·PF₆ and b) rotaxane **31**·PF₆ plus 5.0 equivalents of TBACl.

Para-isophthalamide proton c was followed during the titration experiments (Figure 2.39) and 1:1 association constants were obtained using WinEQNMR2 analysis of the data (Table 2.4).

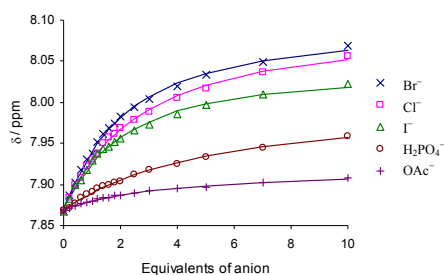
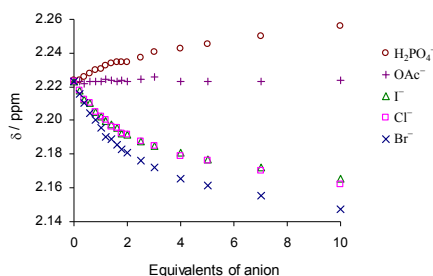


Figure 2.39 Changes in the chemical shift of proton c upon addition of anions to rotaxane **31**·PF₆ in 1:1 CD₃Cl/CD₃OD at 293 K. Symbols represent experimental data points; lines represent calculated titration curves.

Table 2.4 Association constants, K (M^{-1}), of rotaxane **31**·PF₆ with anions in 1:1 CDCl₃/CD₃OD at 293 K. Obtained by monitoring proton c. Errors are given in parentheses.

Anion	K (M^{-1})
Cl [−]	307 (21)
Br [−]	397 (24)
I [−]	424 (37)
H ₂ PO ₄ [−]	128 (12)
OAc [−]	171 (21)

Rotaxane host **31**·PF₆ exhibits significantly stronger binding for the spherical halide guests over the larger, more basic oxoanions dihydrogen phosphate and acetate. This selectivity has again been achieved by the creation of a three dimensional binding cavity within the interlocked structure, and the behaviour of imidazolium methyl protons 9 during the titrations is evidence for different binding modes for the halides and oxoanions, internal and external to the rotaxane host cavity (Figure 2.40). These protons shift upfield upon addition of the halides ($\Delta\delta = -0.06$ – 0.08 ppm after 10.0 equivalents), slightly downfield with dihydrogen phosphate ($+0.03$ ppm), and do not shift with acetate (< 0.01 ppm).

**Figure 2.40** Changes in the chemical shift of imidazolium methyl protons 9 upon addition of anions to rotaxane **31**·PF₆ in 1:1 CD₃Cl/CD₃OD at 293 K.

However, as with rotaxanes **20**·PF₆ and **21**·PF₆ (Section 2.3.2), there is little discrimination between the halides, although it does appear that bromide and iodide are bound slightly more strongly than chloride. Furthermore, the selectivity for the halides over the oxoanions is similar to that

exhibited by the analogous 2-methylimidazolium rotaxane **31**·PF₆, which contains a larger macrocycle component (Section 2.3.2).

It is difficult to make a direct comparison between the anion binding properties of 2-methylimidazolium rotaxanes **21**·PF₆ and **31**·PF₆, due to a number of structural differences, besides the intended reduction in the size of the macrocycle. Firstly, host **31**·PF₆ contains the 5-*tert*-butyl-isophthalamide motif, compared to the 5-nitro-isophthalamide group of rotaxane **21**·PF₆. As mentioned in Section 2.3.1, the nitro functionalisation increases the acidity of the isophthalamide amide protons, and this has been shown to have a large effect on the strength of rotaxane anion binding.⁵⁴ Secondly, although the ¹H NMR studies indicate that the macrocycle component of **31**·PF₆ lies predominately over the imidazolium group of the axle, there are many possible co-conformational equilibria arising from the extended asymmetrical axle component. Both of these factors would significantly weaken the anion binding ability of rotaxane **31**·PF₆ compared to **21**·PF₆ and, given that the halide binding strengths of these two systems are approximately equal (~ 400 M⁻¹), it is postulated that reducing the size of the macrocycle component is responsible for enhancing anion complexation if these considerations are taken into account.

Unfortunately, no significant changes in the binding selectivity, either between the halides and oxoanions or within the halides themselves, were observed for **31**·PF₆ in comparison with **21**·PF₆.

2.5.5 Summary

The smaller macrocycle investigated for anion templated pseudorotaxane assembly in Section 2.4 was integrated into 2-methylimidazolium rotaxane systems. Initially ‘clipping’ approaches were employed, with an amide condensation strategy yielding the target rotaxane (**26**·Cl) in a very low yield, whilst a Grubbs’-catalysed RCM method, similar to that described in Section 2.3, was unsuccessful. An alternative ‘stoppering’ approach was exploited using the ‘click’ reaction to successfully synthesise interlocked host **31**·PF₆ in a reasonable yield.

Rotaxane **31**·PF₆ was shown to exhibit selective halide binding over more basic oxoanions due to its three dimensional interlocked host cavity. Compared to the analogous rotaxane containing a

larger macrocycle (**21**·PF₆), host **31**·PF₆ displayed similar anion recognition properties, although a number of factors besides macrocycle size are also thought to affect anion binding.

2.6 Conclusions

Imidazolium motifs with contrasting hydrogen bonding arrangements were incorporated into simple acyclic receptors and interlocked rotaxane systems *via* chloride anion templation. In addition, the effect of reducing the size of the macrocyclic component in imidazolium pseudorotaxane and rotaxane assemblies was studied. Several different methods of rotaxane synthesis were employed in this chapter – RCM, amide condensation and the ‘click’ reaction, in both ‘clipping’ and ‘stoppering’ strategies – which demonstrates the scope of the anion templation strategy.

Whilst the imidazolium-anion interaction appears to be dominated by electrostatics rather than the exact hydrogen bonding arrangement, the rotaxane structures synthesised were capable of selective anion recognition by virtue of their unique interlocked host cavities. Stronger binding affinities were observed for the complementary spherical halide guests over more basic, but larger, oxoanions. The incorporation of 4,5-dimethyl- and 2-methyl-imidazolium motifs within the axle component and a reduction in the macrocycle size did influence rotaxane anion binding strength, however no significant changes in selectivity were observed. This indicates that further modifications to the design of anion templated imidazolium rotaxanes are necessary to influence their binding selectivities.

It is difficult to discriminate between the halides on the basis of size due to small differences in ionic radii – bromide is only 8% larger than chloride, with a further 12% increase for iodide.⁵⁵ Thus, the lack of halide discrimination exhibited by the imidazolium rotaxanes can be rationalised given that there is a certain degree of flexibility within the interlocked structures and the potentially weak directionality of imidazolium-anion hydrogen bonding.

Having prepared the first mono-imidazolium interlocked structures and investigated their anion recognition properties, the construction of fluorescence anion sensing rotaxanes will be explored in the following chapter.

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Chapter Three: Using Fluorescent Reporter Groups as Stoppers in the Synthesis of Anion Sensing Rotaxanes

3.1 Introduction

3.1.1 Incorporating Fluorescent Reporter Groups into Interlocked Structures

Having successfully synthesised imidazolium-based anion templated rotaxane host structures capable of selective binding (Chapter Two), an extension of this work would be to prepare selective anion sensors *via* the same method. This may be achieved by the incorporation of a fluorophore into the interlocked structural framework, provided that the selective binding event is effectively communicated to the reporter group.

There are different ways of incorporating fluorescent reporter groups into interlocked structures, dependent on the exact system and functional requirements. In the introductory chapter, two such structures were discussed in which a fluorophore is embedded within the interlocked framework, either in the macrocycle components of indolocarbazole catenane **1.50** (Figure 1.34) or in the axle of squaraine rotaxane **1.51** (Scheme 1.11). Similarly, rotaxane **3.1** contains a rhenium(I) bipyridyl reporter group within its macrocycle (Figure 3.1a) and displayed luminescent enhancements upon anion binding in the host cavity.¹

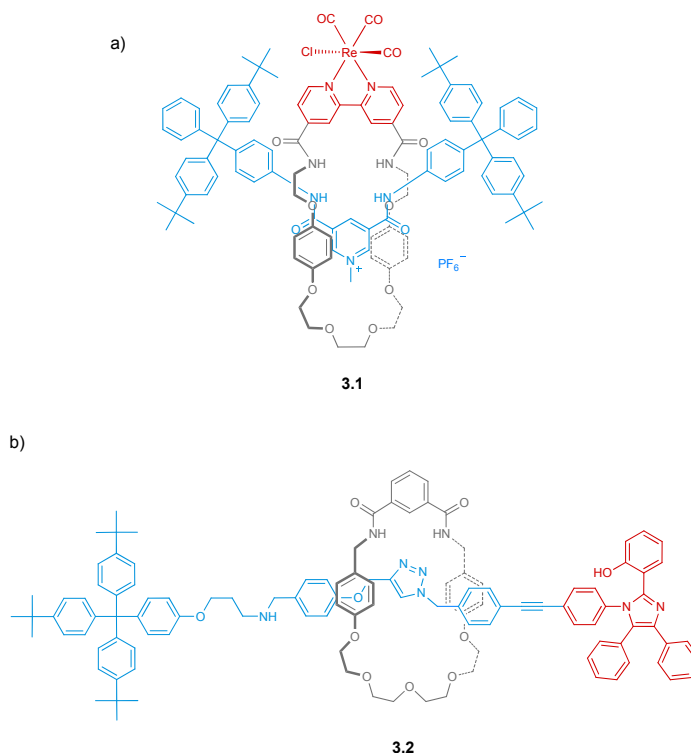


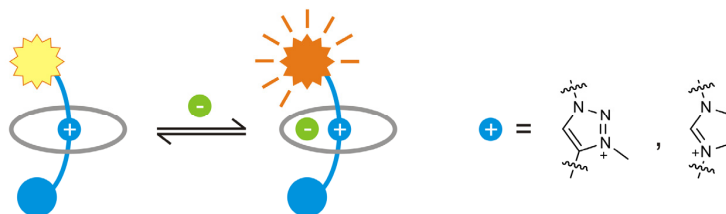
Figure 3.1 Rotaxanes incorporating fluorescent reporter groups (depicted in red) a) within the macrocycle component in **3.1**, and b) as one of the stopper groups in **3.2**.

An alternative approach is to utilise the fluorophore as a stopper in the construction of rotaxane systems, which relies on the size of the reporter group being sufficient to prevent de-threading of the particular macrocycle component employed. For example, the fluorescent hydroxy-substituted tetraphenylimidazole group of rotaxane **3.2** (Figure 3.1b) produces different signalling responses dependent on the position of the macrocycle along the axle, which is controlled by acid/base stimuli resulting in either protonation of the axle amine group, deprotonation of the stopper hydroxyl motif or the intermediate co-conformation shown in Figure 3.1b.²

3.1.2 Chapter Objectives

This chapter aims to exploit the host binding cavities of rotaxanes to construct systems capable of selective fluorescence anion sensing (Scheme 3.1). The synthesis of rotaxane structures

containing a positively charged triazolium or imidazolium anion binding motif in their axle components and incorporating a fluorophore as one of the stopper groups will be investigated.



Scheme 3.1 Anion sensing *via* incorporation of a fluorophore as a stopper group in a triazolium- or imidazolium-based rotaxane host structure.

The fluorescent reporter groups utilised in this chapter are the luminescent ruthenium(II) bipyridyl and the organic fluorophore anthracene. The use of both of these motifs in anion sensing systems – employing the rigidity effect and photo-induced electron transfer (PET) as their signalling mechanisms – was discussed in the introductory chapter (Section 1.1.4.1). Furthermore, both have been exploited previously as stoppers in the construction of rotaxane systems. Examples include the ruthenium(II) bipyridyl functionalised rotaxane **3.3** (Figure 3.2a),³ which underwent molecular shuttling upon photochemical stimulus in the presence of a suitable electron donor, and Leigh's anthracene-stoppered rotaxane **3.4** (Figure 3.2b),⁴ in which the position of the macrocycle relative to the axle was signalled through PET quenching of the fluorophore by the macrocycle pyridinium groups.

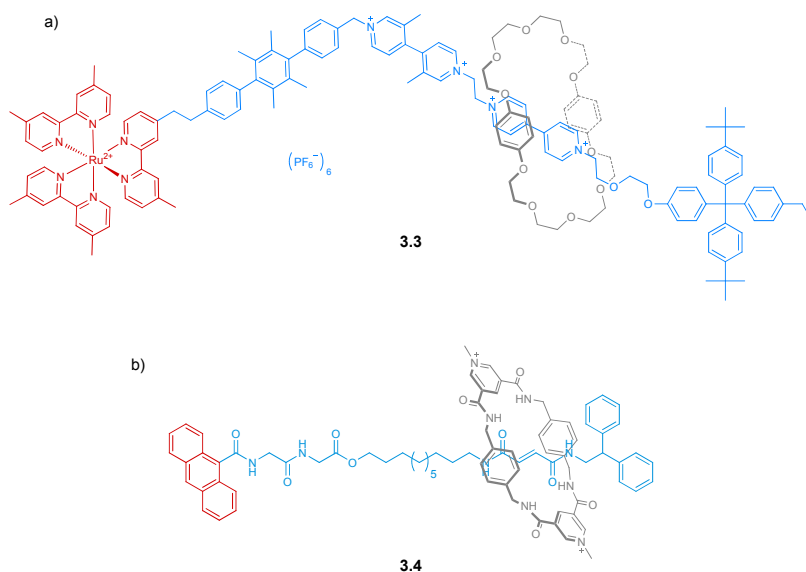


Figure 3.2 Rotaxanes utilising a) ruthenium(II) bipyridyl in **3.3**, and b) anthracene in **3.4**, to act as stopper groups.

3.2 Synthesis of a Ruthenium(II)-Appended Triazolium Rotaxane

In this section, the design and synthesis of a triazolium-based rotaxane incorporating a luminescent ruthenium(II) bipyridyl stopper group is described.

Upon the absorption of light by ruthenium(II) polypyridyl complexes, metal-to-ligand charge transfer (MLCT) species are formed, resulting in characteristic luminescence.⁵ This transition occurs because the ligand π^* orbitals lie directly between the t_{2g} and e_g^* metal d orbitals, and the energy level diagram for this transition in $[\text{Ru}(\text{bipy})_3]^{2+}$ is shown in Figure 3.3a. For ruthenium(II) complexes this absorption is near 450 nm and, following excitation ($+h\nu_a$), the complex then undergoes intersystem crossing (ISC) to the $^3\text{MLCT}$ state (Figure 3.3b). This process occurs with high efficiency despite being formally forbidden, due to the heavy atom nature of the metal. Once in the $^3\text{MLCT}$ state, radiative ($-h\nu_e$) and non-radiative (k_{nr}) decay processes return the system to the ground state (S_0) with emission at approximately 650 nm. Importantly, any diminution in the non-radiative pathways results in an increase in luminescent emission, and this is the basis for the *rigidity effect*, in which the

rigidification of a ruthenium(II)-appended receptor resulting from guest binding disfavours vibrational and rotational decay processes.⁶

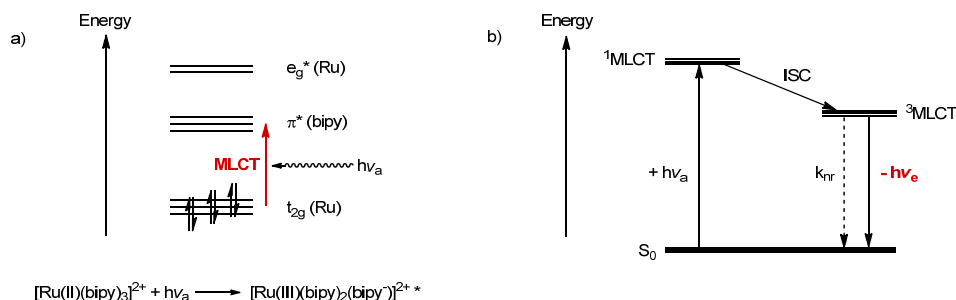


Figure 3.3 a) Metal-to-ligand charge transfer (MLCT) transition and b) Jablonski diagram for $[\text{Ru}(\text{bipy})_3]^{2+}$.

The initial target system is shown in Figure 3.4 and comprises a triazolium anion binding motif, a pyridyl-triazole ligand for metal complexation and ruthenium(II) bipyridyl as a reporter group. The ability of the pyridyl-triazole ligand, prepared by ‘click’ chemistry, to chelate to ruthenium(II) bipyridyl complexes has been reported recently,⁶⁻⁸ whilst the metal complex is anticipated to be of sufficient size to act as a rotaxane stopper group. A terphenyl and ruthenium(II) bipyridyl stoppered axle was prepared, and its anion binding and sensing behaviour studied.

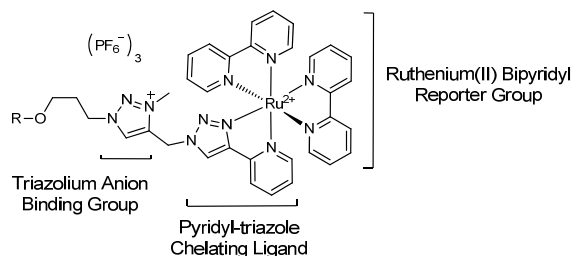
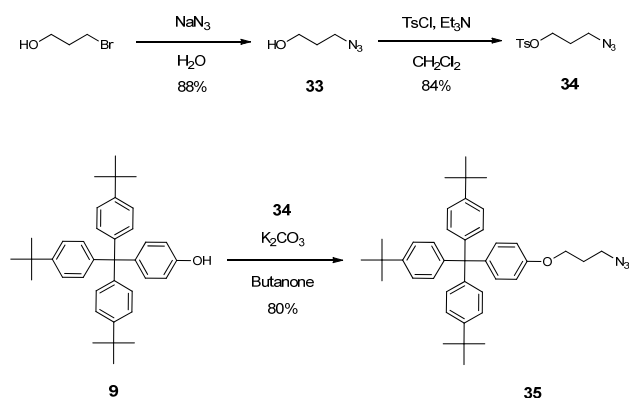


Figure 3.4 Target axle system containing triazolium anion binding group, pyridyl-triazole chelating ligand and ruthenium(II) bipyridyl reporter group. (R= terphenyl).

3.2.1 Synthesis of Ruthenium(II)-Stoppered Triazolium Axle

The preparation of the target triazolium axle began with the conversion of 3-bromo-1-propanol to 3-azido-1-propanol (**33**) and the subsequent reaction with tosyl chloride to

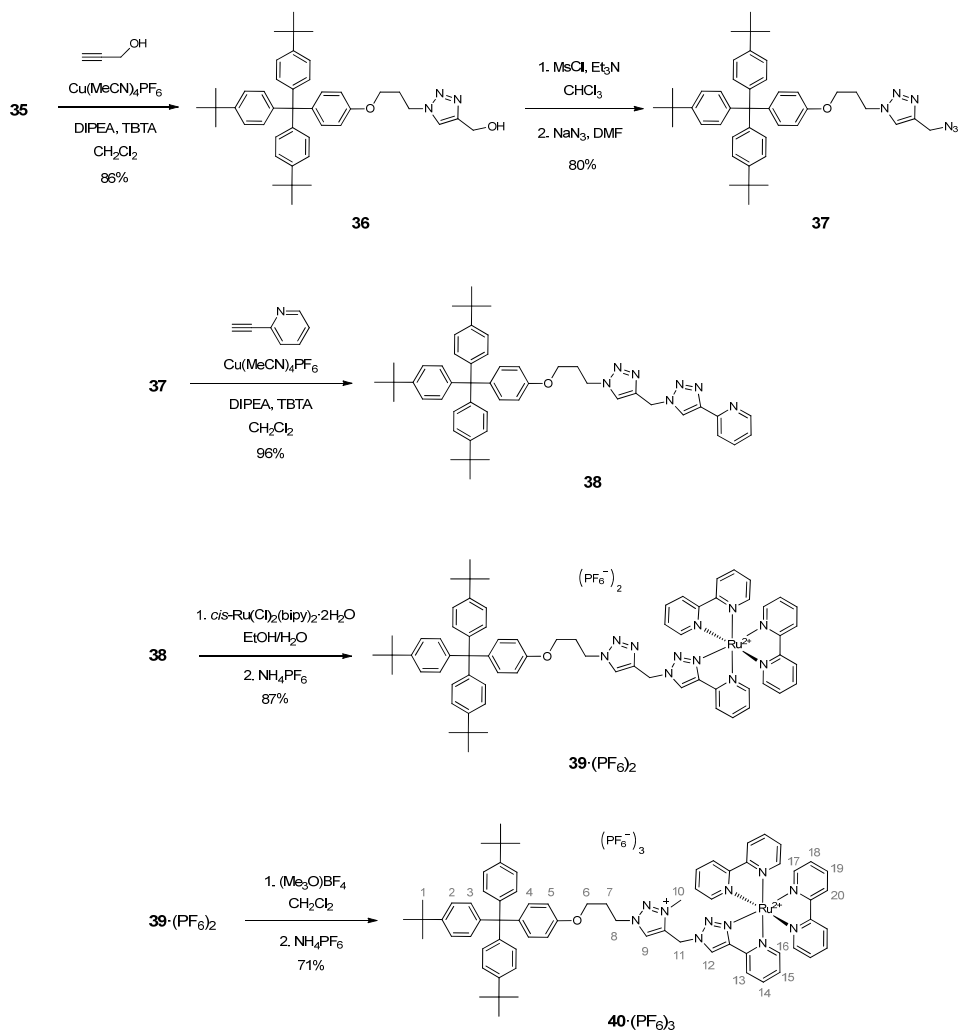
form tosylate **34**, with both products isolated in high yields (Scheme 3.2). 4-(Tris(4-(*tert*-butyl)phenyl)methyl)phenol (**9**), synthesised as detailed in Scheme 2.5, was reacted with tosylate **34** and K_2CO_3 to give **35** in 80% yield.⁷



Scheme 3.2 Synthesis of stopped azide **35**.

Stopped azide **35** was then reacted with propargyl alcohol under ‘click’ reaction conditions using a copper(I) catalyst to afford the relatively insoluble hydroxyl triazole **36** (Scheme 3.3). This was converted to azide **37** *via* the mesylate in 80% yield over the two steps, and a further ‘click’ reaction with 2-ethynyl pyridine gave bis-triazole pyridyl derivative **38**. The triazole and pyridyl proton signals in the 1H NMR spectrum of **38** were considerably broadened in a range of solvents which is thought to be due to aggregation effects. Whilst this prevented characterisation by ^{13}C NMR, high resolution electrospray MS confirmed the formation of the product.

Ruthenium(II) complexation was achieved by heating ligand **38** at reflux with $Ru(Cl)_2(bipy)_2$ in an $EtOH/H_2O$ solvent mixture. Purification by silica gel gradient column chromatography using the highly polar $MeCN/H_2O/sat. KNO_3(aq)$ eluent mixture and anion exchange to the hexafluorophosphate salt afforded ruthenium(II)-triazole derivative $39 \cdot (PF_6)_2$ in 87% yield. Finally, reaction of $39 \cdot (PF_6)_2$ with methylating reagent $(Me_3O)BF_4$ and anion exchange gave the target ruthenium(II)-stopped triazolium axle $40 \cdot (PF_6)_3$ in a yield of 71%.



Scheme 3.3 Synthesis of ruthenium(II)-stoppered triazolium axle **40**·(PF₆)₃.⁸

3.2.2 Anion Binding and Sensing Behaviour of Ruthenium(II)-Stoppered Triazolium Axle

To investigate the anion complexation ability of axle **40**·(PF₆)₃ and establish the mode of binding, a qualitative ¹H NMR study was carried out in the competitive solvent mixture of 1:1 CDCl₃/CD₃OD. Upon addition of 10 equivalents of TBA chloride, the peaks corresponding to triazolium and triazole protons 9 and 12 were shifted significantly downfield (Figure 3.5), indicative

of C-H hydrogen bonding to the halide anion by both the triazole and triazolium groups. Slight downfield shifts were also observed for proximal protons 11 and 13.

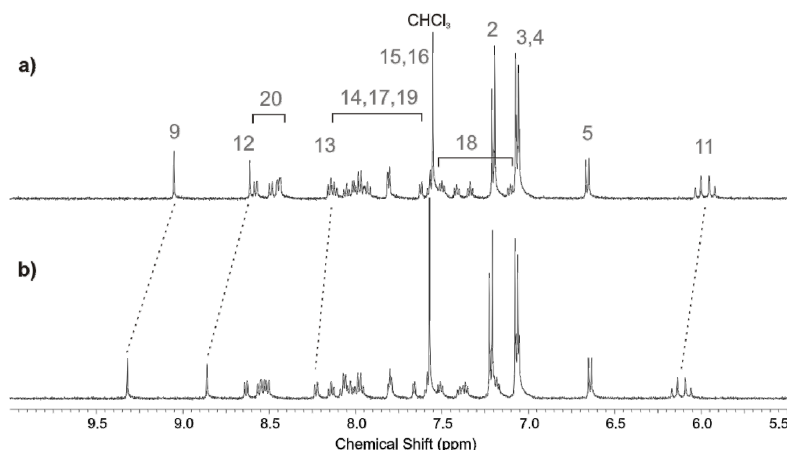


Figure 3.5 Partial ^1H NMR spectra (500 MHz) in 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$ at 293 K of a) axle $\mathbf{40} \cdot (\text{PF}_6)_3$, and b) axle $\mathbf{40} \cdot (\text{PF}_6)_3$ plus 10 equivalents of TBACl.

In the ^1H NMR spectra of axle $\mathbf{40} \cdot (\text{PF}_6)_3$, both in the absence and presence of coordinating anions, the signal corresponding to the bridging methylene protons 11 appears as an AB quartet. This is also the case in the spectrum of triazole derivative $\mathbf{39} \cdot (\text{PF}_6)_2$, with the inequivalence arising from the chirality of the adjacent metal centre.⁹ This inequivalence was not observed for methylene protons 6–8 which are further away from the ruthenium(II) bipyridyl group.

The ability of axle $\mathbf{40} \cdot (\text{PF}_6)_3$ to sense anions was then investigated using luminescence spectroscopy. The luminescent properties of $\mathbf{40} \cdot (\text{PF}_6)_3$ in acetone are summarised in Table 3.1,¹⁰ with the observed excitation and emission wavelengths typical for the MLCT transition of ruthenium(II) polypyridyl complexes. It should be noted that the relative emission intensity (given in Table 3.1 and for other systems later in this chapter) is influenced by a number of factors, importantly the absorption at the excitation wavelength as well as the fluorescence quantum yield.

Table 3.1 Luminescent properties of ruthenium(II)-appended axle $\mathbf{40} \cdot (\text{PF}_6)_3$ in acetone ($c = 2.2 \times 10^{-4} \text{ M}$, 293 K) – maximum excitation wavelength ($\lambda_{\text{excit,max}}$), maximum emission wavelength ($\lambda_{\text{emission,max}}$) and emission intensity.

Axle $\mathbf{40} \cdot (\text{PF}_6)_3$		
$\lambda_{\text{excit,max}}$ (nm)	$\lambda_{\text{emission,max}}$ (nm)	Intensity (a.u.)
471	614	12

Preliminary titration experiments were then undertaken by adding increasing amounts of the TBA salts of chloride, bromide and dihydrogen phosphate to separate acetone solutions of $\mathbf{40} \cdot (\text{PF}_6)_3$ until the emission intensity remained constant. All three anions produced increases in emission intensity along with slight bathochromic shifts (Figure 3.6 and Table 3.2).

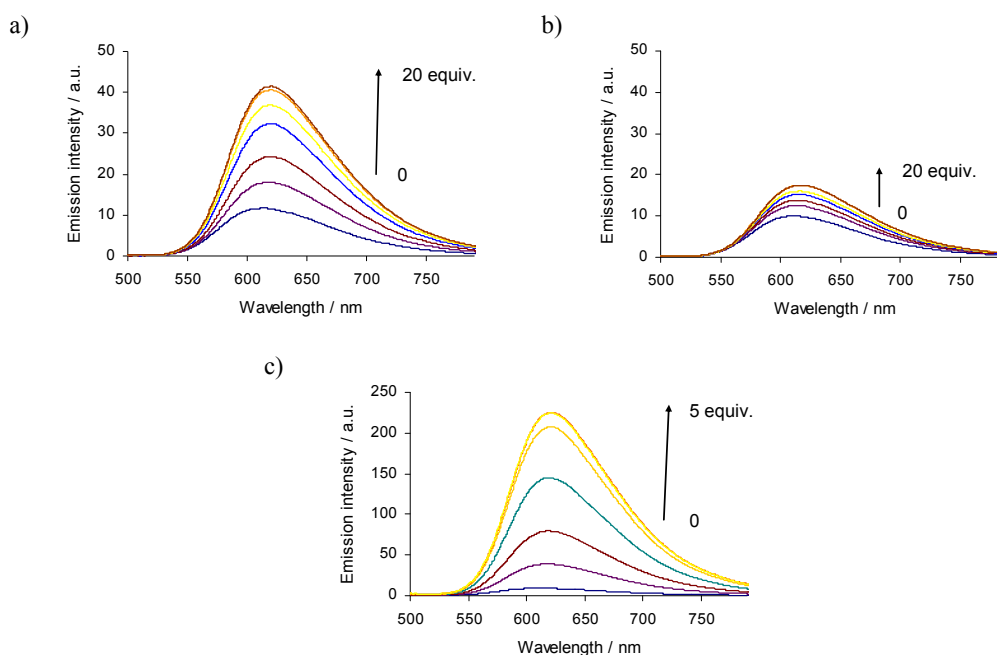


Figure 3.6 Changes in the emission spectrum of axle $\mathbf{40} \cdot (\text{PF}_6)_3$ in acetone ($c = 2.2 \times 10^{-4} \text{ M}$, $\lambda_{\text{excit}} = 471 \text{ nm}$, 293 K) upon addition of a) TBACl, b) TBABr, and c) TBAH_2PO_4 . Note: different scale on the y-axis (emission intensity) and different number of anion equivalents added for TBAH_2PO_4 .

Table 3.2 Percentage changes in emission intensity and changes in emission wavelength of axle **40**·(PF₆)₃ in acetone ($c = 2.2 \times 10^{-4}$ M, $\lambda_{\text{excit}} = 471$ nm, 293 K) upon addition of * 20 equivalents of TBACl and TBABr and † 5 equivalents of TBAH₂PO₄.

Anion	ΔI (%)	$\Delta\lambda_{\text{emission,max}}$ (nm)
Cl [−]	+ 255 *	+ 6 *
Br [−]	+ 75 *	+ 4 *
H ₂ PO ₄ [−]	+ 2370 †	+ 7 †

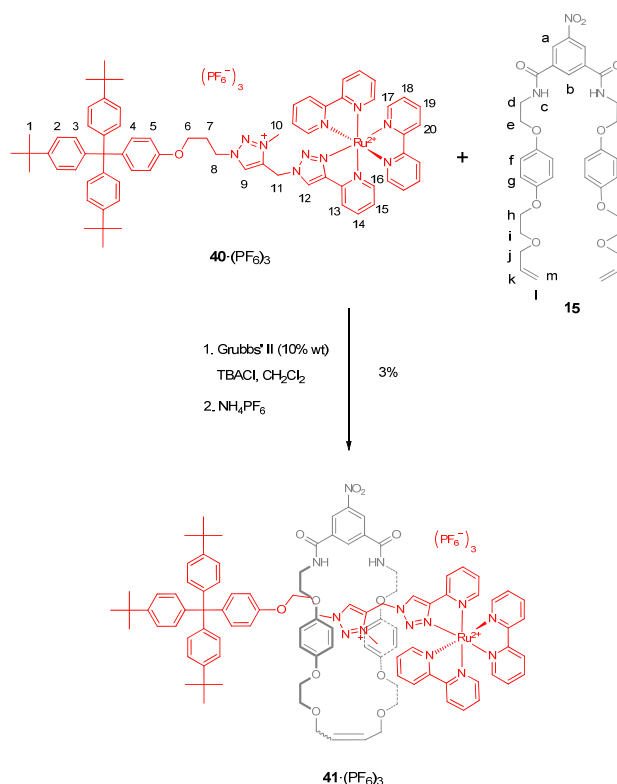
As expected for an acyclic receptor, sensing saturation was reached after the addition of fewer equivalents of anion for the more basic dihydrogen phosphate (5 equivalents), than for the halides (20 equivalents). The cause of the luminescent enhancements is postulated to be the rigidity effect, namely that increased rigidity upon anion binding leads to a diminution of vibrational and rotational non-radiative decay processes. However there was a large difference in the magnitude of these enhancements, with chloride addition causing an increase of 255%, significantly greater than for bromide (75%), but an order of magnitude less than with dihydrogen phosphate (2370%). Similar differential changes in emission intensity have also been reported for other ruthenium(II)-based anion receptors, for example **1.22** and **1.23** in Figure 1.21.¹¹ Unfortunately, SPECFIT¹² analysis failed to determine accurate association constant values as the titration data did not appear to fit simple stoichiometric binding models. Further titration experiments would be necessary to fully understand the nature of the signalling processes involved.

Interestingly, the bathochromic shifts exhibited by axle **40**·(PF₆)₃ upon anion addition indicate decreases in the energy of the MLCT band. This is in contrast to that observed in the majority of ruthenium(II) bipyridyl anion sensing systems, including **1.22** and **1.23**, where anion complexation destabilises the excited state, which involves the transfer of an electron to the functionalised bipyridyl ligand (Figure 3.3a). However, the MLCT transition and the changes upon anion binding will be significantly different in axle **40**·(PF₆)₃ as the π^* orbitals of pyridyl-triazole ligands are known to be at a higher energy to those of bipyridyl ligands.¹³

3.2.3 Synthesis of Ruthenium(II)-Appended Triazolium Rotaxane

Having prepared the ruthenium(II)-stoppered axle **40**·(PF₆)₃, the aim was to integrate this component into a photo-active rotaxane, capable of sensing anions selectively within its three dimensional interlocked host cavity.

The same anion templation strategy for rotaxane formation was employed as in Chapter Two, namely ‘clipping’ using vinyl-appended macrocycle precursor **15** and Grubbs’-catalysed RCM (Scheme 3.4). In this case, because axle **40**·(PF₆)₃ was isolated as the non-coordinating hexafluorophosphate salt, one equivalent of TBA chloride was added to the reaction mixture to act as the anion template. Following purification by silica gel column chromatography and subsequent anion exchange, the interlocked product **41**·(PF₆)₃ was isolated in a very low yield of 3%. The diagnostic regions of the ¹H NMR spectra of axle **40**·(PF₆)₃, rotaxane **41**·(PF₆)₃ and macrocycle precursor **15** in 1:1 CDCl₃/CD₃OD are shown in Figure 3.7.



Scheme 3.4 Synthesis of ruthenium(II)-appended triazolium rotaxane **41**·(PF₆)₃.

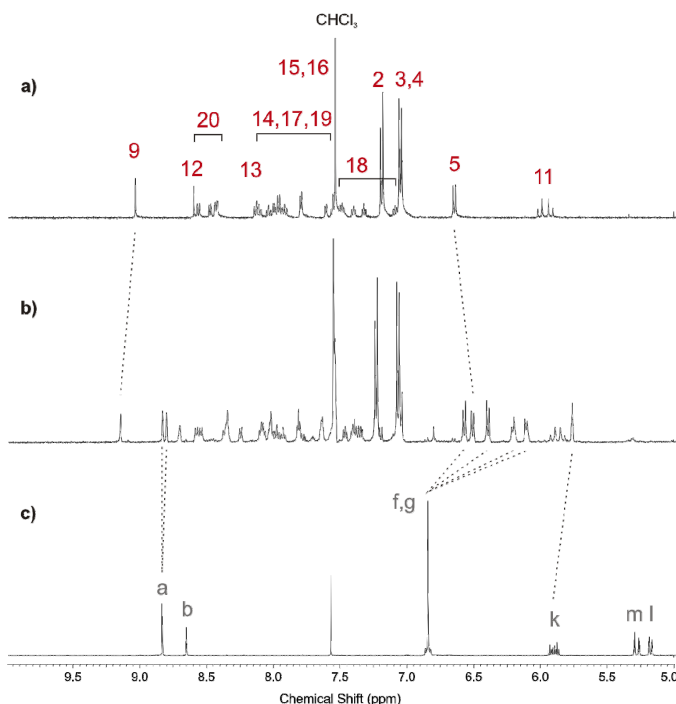


Figure 3.7 Partial ^1H NMR spectra (300 MHz) in 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$ at 293 K of a) axle **40**· $(\text{PF}_6)_3$, b) rotaxane **41**· $(\text{PF}_6)_3$, and c) macrocycle precursor **15**.

Importantly, the signal corresponding to the macrocycle hydroquinone protons f and g are shifted upfield in the interlocked product, due to favourable donor-acceptor interactions with the axle triazolium group. In contrast to the spectra of previous anion templated interlocked structures where this signal appears as two doublets (Chapter Two), in the spectrum of rotaxane **41**· $(\text{PF}_6)_3$ these protons are actually split into two sets of doublets, with the source of the second splitting thought to be the chirality of the adjacent metal centre. In addition to the hydroquinone protons, this effect also results in an observable split in the signal corresponding to macrocycle isophthalamide protons a in the interlocked product.

Further evidence for interlocked structure formation was obtained from MALDI-MS, where the observed peak is in agreement with that calculated for the rotaxane after the loss of one hexafluorophosphate counter anion (Figure 3.8).

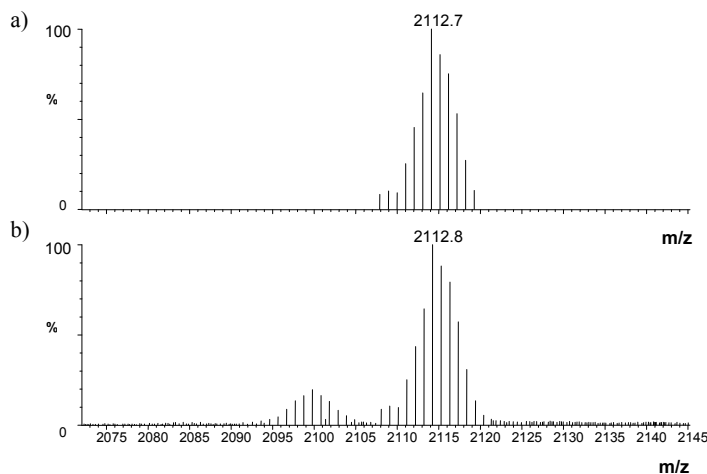


Figure 3.8 a) Theoretical isotope model and b) measured MALDI-MS spectrum of **41**·(PF₆)₃ [M – PF₆]⁺, C₁₀₃H₁₁₁N₁₄O₁₁RuP₂F₁₂.

In order to fully characterise rotaxane **41**·(PF₆)₃, and undertake quantitative anion binding and sensing studies, larger quantities of the interlocked product were required. Optimisation of the rotaxane reaction was attempted, with the number of equivalents of the macrocycle precursor and the chloride anion template systematically varied as well as the concentration of the reaction mixture. However, low yields of between 1-5% were obtained for each set of conditions used.

The conformation of the axle component after coordination to the halide template may be responsible for these low rotaxane yields. As discussed in the previous section, ¹H NMR studies indicated that both the triazolium and triazole groups of axle **40**·(PF₆)₃ are involved in anion binding, with the proposed binding conformation shown in Figure 3.9. In the synthesis of rotaxane **41**·(PF₆)₃, steric interactions between the large ruthenium(II) bipyridyl group and the macrocycle precursor would destabilise the orthogonal chloride templated assembled complex required for interlocked structure formation. Additionally, it is likely that optimisation of the donor-acceptor interactions between the hydroquinone groups of **15** and the triazolium group of **40**·(PF₆)₃ would not be possible.

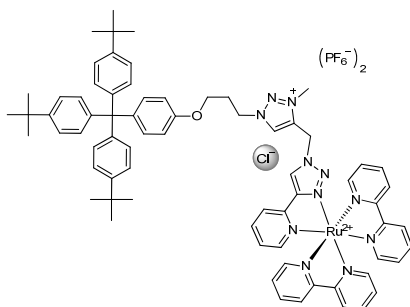


Figure 3.9 Proposed conformation of chloride binding by axle **40**·(PF₆)₃.

It is noteworthy that one equivalent of TBA chloride was added to the reaction mixture to template rotaxane formation, rather than using the halide salt of the axle (Chapter Two). This is necessary due to the 3+ charge of axle **40** and the insolubility of the chloride salts of ruthenium(II) derivatives, but may have a detrimental impact on rotaxane formation because of additional anion complexation equilibria. However, this strategy was employed in the preparation of triazolium rotaxane **1.45** (Figure 1.32b),¹⁴ which was synthesised in a satisfactory yield of 31%.

3.2.4 Summary

Ruthenium(II)-stoppered triazolium axle **40**·(PF₆)₃ was synthesised and shown to sense anions *via* the rigidity effect as chloride, bromide and dihydrogen phosphate complexation was accompanied by significant increases in luminescence emission intensity.

This axle component was integrated into a rotaxane system (**41**·(PF₆)₃), confirming that the ruthenium(II) bipyridyl group is of sufficient size to act as a stopper group for the isophthalamide macrocycle component. However, the low yield of rotaxane formation prevented both full characterisation of the interlocked structure and any binding or sensing studies.

Modified triazolium axle designs, attempting to avoid similar unfavourable anion binding conformations, were considered. However, due to the linear syntheses involved in the preparation of axle **40**·(PF₆)₃ and other potential triazolium systems, it was decided to explore alternative anion binding groups that could be incorporated into ruthenium(II)-stoppered axles, specifically the previously investigated imidazolium motif.

3.3 Ruthenium(II)-Based 2-Methylimidazolium Systems

Encouraged by the successful synthesis of the mono-imidazolium anion templated rotaxane host systems detailed in Chapter Two, the synthesis of a ruthenium(II)-appended 2-methylimidazolium system was planned (Figure 3.9). It was hoped that the anion binding arrangement would prevent the problems encountered in the triazolium system discussed in the previous section, with bound anions interacting predominantly with the two imidazolium protons and therefore located further away from the sterically bulky ruthenium(II) bipyridyl moiety.

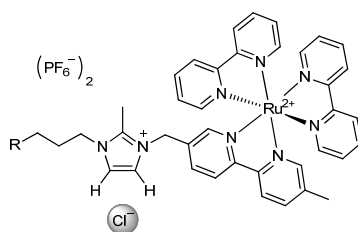
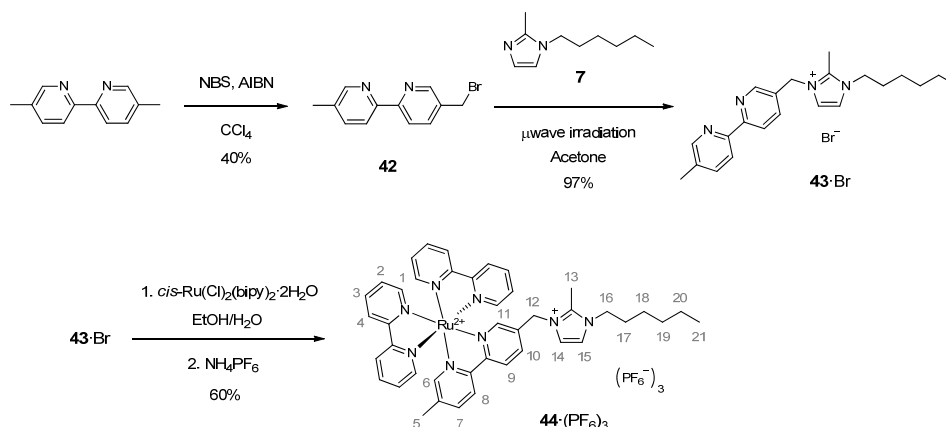


Figure 3.9 Target ruthenium(II)-appended 2-methylimidazolium system.

3.3.1 Synthesis of Ruthenium(II)-Appended 2-Methylimidazolium Thread

Initially, an unstoppered thread was synthesised following the procedures shown in Scheme 3.5. Mono-bromination of 5,5'-dimethyl-2,2'-bipyridine was achieved by a radical reaction using NBS and AIBN,¹⁵ with silica gel column chromatography facilitating the separation of product **42** from the unreacted starting material and dibromo by-products. Alkylation of *N*-hexyl 2-methylimidazole (**7**), synthesised as described in Scheme 2.4, with **42** using microwave irradiation gave imidazolium **43**·Br in quantitative yield. Ruthenium(II) complexation afforded target thread **44**·(PF₆)₃ in 60% yield after purification by column chromatography and anion exchange to the hexafluorophosphate salt.



Scheme 3.5 Synthesis of ruthenium(II)-appended 2-methylimidazolium thread **44**·(PF₆)₃.¹⁶

3.3.2 Anion Binding, Sensing and Pseudorotaxane Studies using Ruthenium(II)-Appended 2-Methylimidazolium Thread

A ¹H NMR titration experiment with thread **44**·(PF₆)₃ and TBA chloride was undertaken in 9:1 *d*₆-acetone/D₂O, with these solvent conditions necessary for the solubility of **44**·(PF₆)₃. Upon halide anion addition, a number of shifts in the aromatic proton signals were observed (Figure 3.10), although interestingly only one imidazolium peak (H₁₄) moves downfield, the other (H₁₅) remaining stationary. The shift in the peak corresponding to H₁₄ was monitored throughout the titration (Figure 3.11), and WinEQNMR2¹⁷ analysis determined a 1:1 stoichiometric association constant for the binding of chloride to thread **44**·(PF₆)₃ of 582(31) M⁻¹.

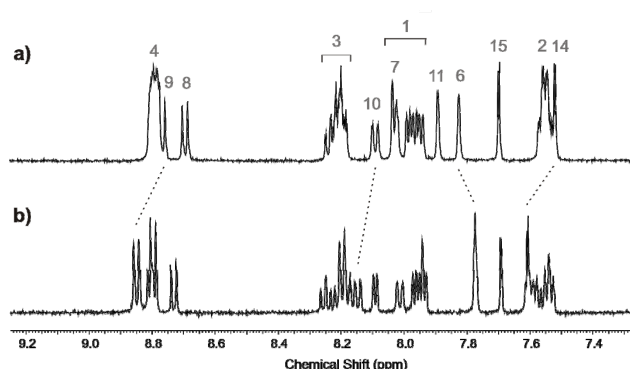


Figure 3.10 Partial ¹H NMR spectra (500 MHz, 2.0 × 10⁻³ M) in 9:1 *d*₆-acetone/D₂O at 293 K of a) thread **44**·(PF₆)₃, and b) thread **44**·(PF₆)₃ plus 10.0 equivalents of TBACl.

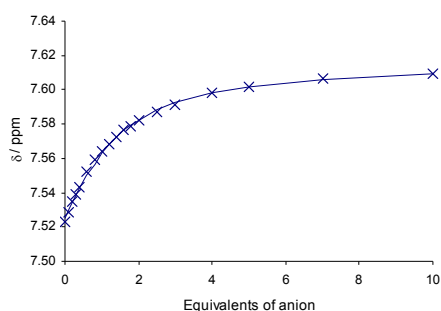


Figure 3.11 Changes in the chemical shift of imidazolium proton H_{14} upon addition of TBACl to thread **44**·(PF₆)₃ in 9:1 *d*₆-acetone/D₂O at 293 K. Symbols represent experimental data points; line represents calculated titration curve.

Luminescence studies in 9:1 acetone/H₂O (Table 3.3) revealed that significant quenching of the MLCT emission band occurred upon the addition of both chloride and dihydrogen phosphate to thread **44**·(PF₆)₃ (Figure 3.12). This is in contrast to the anion-induced enhancements displayed by axle **40**·(PF₆)₃ (Section 3.2.2). Emission intensity was reduced by 15% and 26% with chloride and dihydrogen phosphate respectively, and these changes were also accompanied by slight bathochromic shifts in the wavelength of emission (Table 3.4).

Table 3.3 Luminescent properties of ruthenium(II)-appended thread **44**·(PF₆)₃ in 9:1 acetone/H₂O ($c = 2.2 \times 10^{-4}$ M, 293 K) – maximum excitation wavelength ($\lambda_{\text{excit,max}}$), maximum emission wavelength ($\lambda_{\text{emission,max}}$) and emission intensity.

Thread 44 ·(PF ₆) ₃		
$\lambda_{\text{excit,max}}$ (nm)	$\lambda_{\text{emission,max}}$ (nm)	Intensity (a.u.)
492	630	499

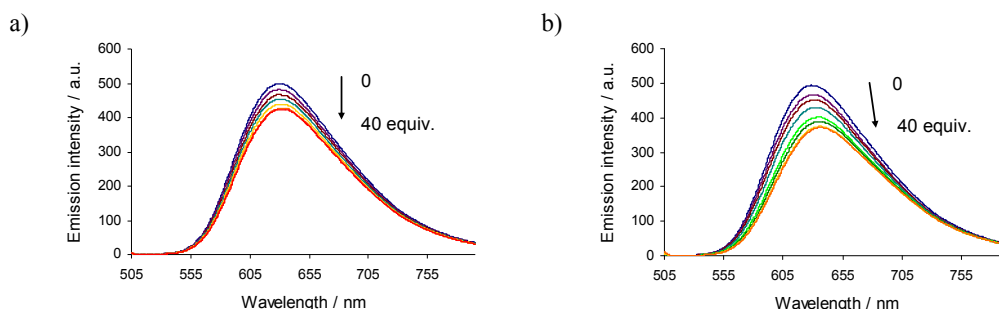


Figure 3.12 Changes in the emission spectrum of thread **44**·(PF₆)₃ in 9:1 acetone/H₂O (*c* = 2.2 × 10^{−4} M, λ_{excit} = 492 nm, 293 K) upon addition of a) TBACl, and b) TBAH₂PO₄.

Table 3.4 Percentage changes in emission intensity and changes in emission wavelength of thread **44**·(PF₆)₃ in 9:1 acetone/H₂O (*c* = 2.2 × 10^{−4} M, λ_{excit} = 492 nm, 293 K) upon addition of 40 equivalents of TBACl and TBAH₂PO₄.

Anion	ΔI (%)	$\Delta\lambda_{\text{emission,max}}$ (nm)
Cl [−]	− 15	+ 2
H ₂ PO ₄ [−]	− 25	+ 6

To investigate this luminescent response further, Ru(bipy)₃(PF₆)₂ (**45**·(PF₆)₂) was prepared as a control system. Both the luminescent properties of **45**·(PF₆)₂ (Table 3.5) and its response to chloride addition (Figure 3.13 and Table 3.6) were similar to those displayed by thread **44**·(PF₆)₃. Importantly, the same quenching of emission intensity was observed with chloride – a 14% reduction compared to 15% for **44**·(PF₆)₃, and 2 nm bathochromic shifts for both systems.

Table 3.5 Luminescent properties of Ru(bipy)₃(PF₆)₂ (**45**·(PF₆)₂) in 9:1 acetone/H₂O (*c* = 2.2 × 10^{−4} M, 293 K) – maximum excitation wavelength ($\lambda_{\text{excit,max}}$), maximum emission wavelength ($\lambda_{\text{emission,max}}$) and emission intensity.

Ru(bipy) ₃ (PF ₆) ₂ (45 ·(PF ₆) ₂)		
$\lambda_{\text{excit,max}}$ (nm)	$\lambda_{\text{emission,max}}$ (nm)	Intensity (a.u.)
492	624	454

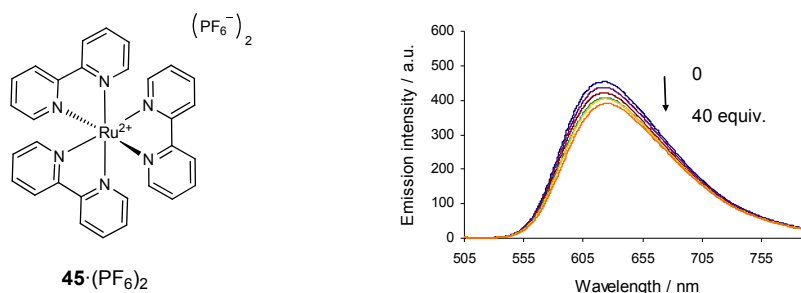


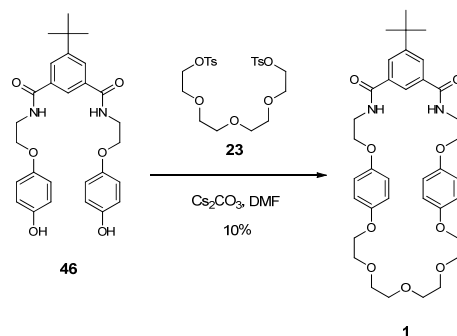
Figure 3.13 Changes in the emission spectrum of $\text{Ru}(\text{bipy})_3(\text{PF}_6)_2$ ($\mathbf{45} \cdot (\text{PF}_6)_2$) in 9:1 acetone/ H_2O ($c = 2.2 \times 10^{-4} \text{ M}$, $\lambda_{\text{excit}} = 492 \text{ nm}$, 293 K) upon addition of TBACl.

Table 3.6 Percentage changes in emission intensity and changes in emission wavelength of $\text{Ru}(\text{bipy})_3(\text{PF}_6)_2$ ($\mathbf{45} \cdot (\text{PF}_6)_2$) in 9:1 acetone/ H_2O ($c = 2.2 \times 10^{-4} \text{ M}$, $\lambda_{\text{excit}} = 492 \text{ nm}$, 293 K) upon addition of 40 equivalents of TBACl and TBAH_2PO_4 . Note: precipitation occurred with TBAH_2PO_4 .

Anion	ΔI (%)	$\Delta \lambda_{\text{emission, max}}$ (nm)
Cl^-	- 14	+ 2
H_2PO_4^-	-	-

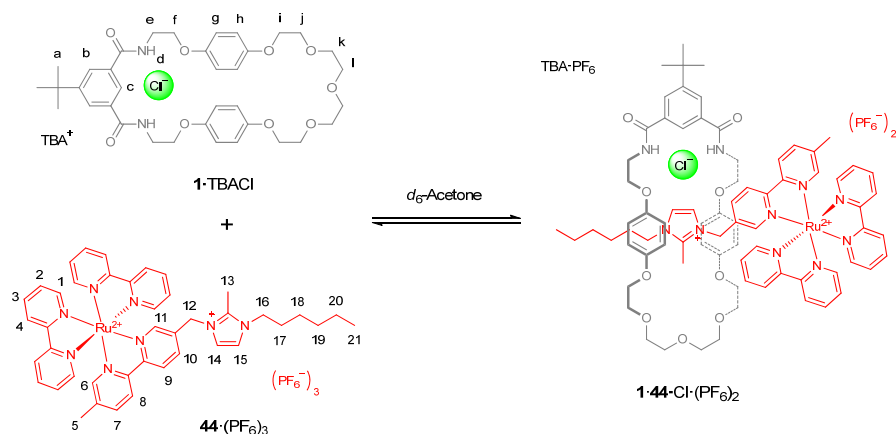
These findings imply that the specific anion binding event to the imidazolium motif of $\mathbf{44} \cdot (\text{PF}_6)_3$ is not effectively communicated to the luminescent reporter group, and that the relatively minor quenching response is due to direct interactions between the anion and the ruthenium(II) metal centre. It appears that the lack of flexibility of thread $\mathbf{44} \cdot (\text{PF}_6)_3$, designed to avoid similar anion binding conformational effects as triazolium axle $\mathbf{40} \cdot (\text{PF}_6)_3$ (Section 3.2), has disfavoured sensing *via* the rigidity effect. However, it was hoped that a rotaxane containing such an axle component would still exhibit selective sensing behaviour.

The ability of thread $\mathbf{44} \cdot (\text{PF}_6)_3$ to form an anion templated interpenetrated assembly was investigated by a ^1H NMR pseudorotaxane titration experiment with isophthalamide macrocycle **1**. The synthesis of **1** has been reported previously,¹⁸ and the availability of precursor **46**, donated by Dr. Kathleen Mullen, enabled the macrocycle to be synthesised under high dilution reaction conditions (Scheme 3.6).



Scheme 3.6 Synthesis of isophthalamide macrocycle **1** from precursor **46**.

A different protocol was necessary for the pseudorotaxane titration with thread **44**·(PF₆)₃ compared with those carried out in Chapter Two. This was due to the insolubility of ruthenium(II)-appended receptors at the required concentrations in appropriate solvents, and prevents the calculation of an accurate value for the apparent association constant. Increasing amounts of thread **44**·(PF₆)₃ were added to an equimolar solution of macrocycle **1** and TBA chloride in *d*₆-acetone (Scheme 3.7), and perturbations indicative of interpenetrated assembly formation were observed (Figure 3.14). Whilst the signals corresponding to the macrocycle hydroquinone protons g and h were already split in **1**·TBACl due to chloride anion binding to the isophthalamide motif, these peaks shifted significantly upfield, diagnostic of the favourable donor-acceptor interactions present in pseudorotaxane assembly **1**·**44**·Cl·(PF₆)₂. Furthermore, upfield shifts were observed for macrocycle hydrogen bond donor protons c and d due to polarisation of the halide template towards the imidazolium group of the thread. By monitoring hydroquinone protons g and h throughout the titration (Figure 3.15), the apparent pseudorotaxane association constant of **1**·**44**·Cl·(PF₆)₂ was estimated by WinEQNMR2 as greater than 10⁴ M⁻¹.



Scheme 3.7 Anion templated pseudorotaxane formation using ruthenium(II)-appended 2-methylimidazolium thread **44**·(PF₆)₃ and isophthalamide macrocycle **1**.

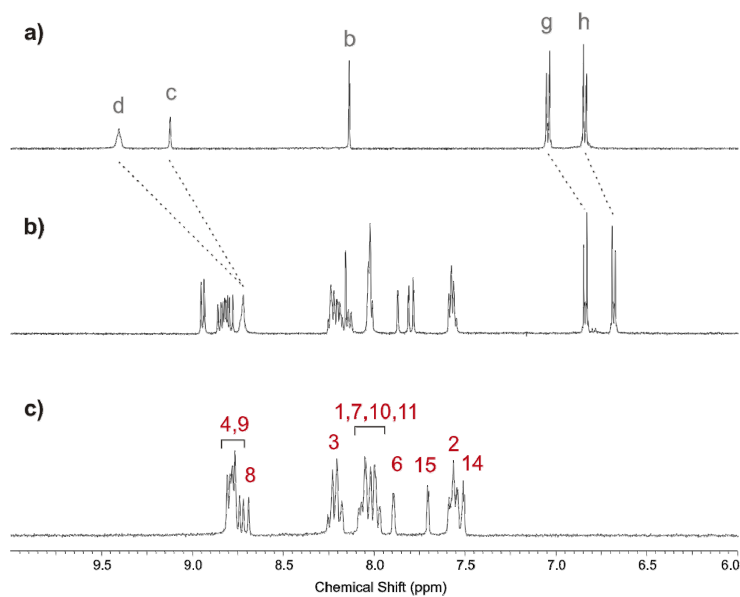


Figure 3.14 Partial ¹H NMR spectra (500 MHz, 2.0 × 10^{−3} M) in *d*₆-acetone at 293 K of a) macrocycle **1** plus 1.0 equivalent of TBACl, b) macrocycle **1** plus 1.0 equivalent of TBACl and 1.0 equivalent of thread **44**·(PF₆)₃, and c) thread **44**·(PF₆)₃.

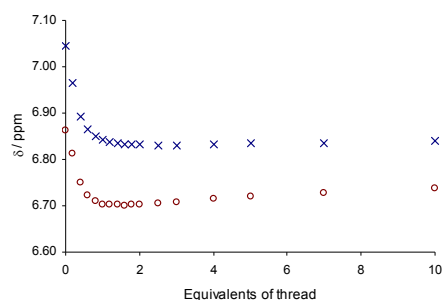
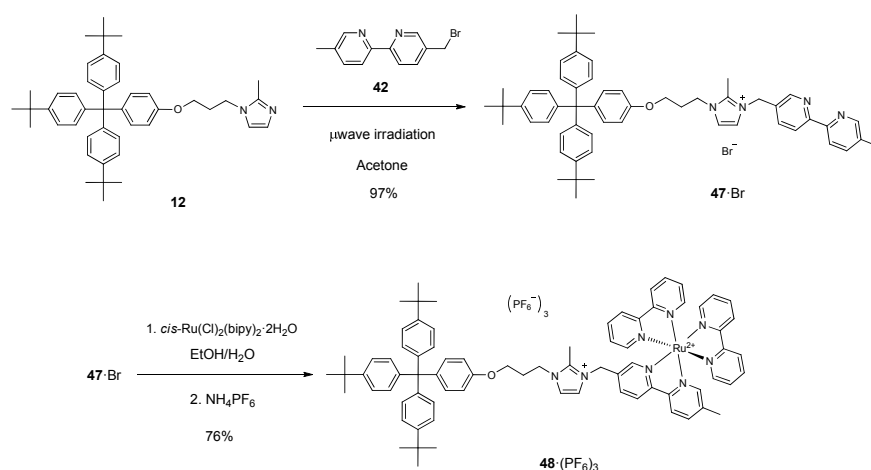


Figure 3.15 Changes in the chemical shift of hydroquinone protons g (×) and h (o) upon addition of thread **44**·(PF₆)₃ to an equimolar solution of macrocycle **1** and TBACl in *d*₆-acetone at 293 K.

3.3.3 Synthesis of Ruthenium(II)-Stopped 2-Methylimidazolium Axle and Attempted Rotaxane Synthesis

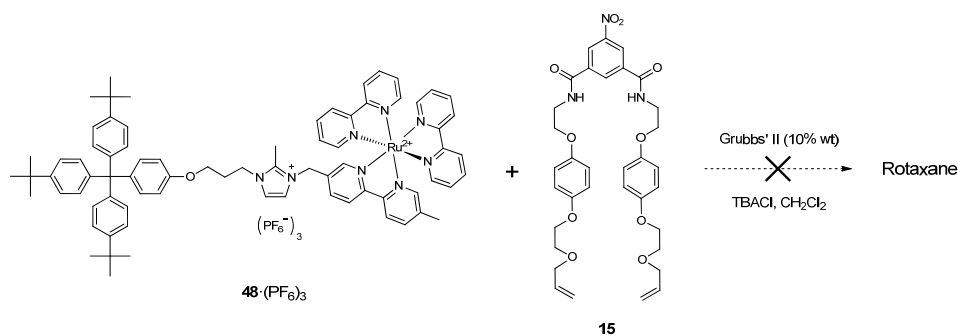
Having established that the ruthenium(II)-appended 2-methylimidazolium thread **44**·(PF₆)₃ was capable of forming a stable chloride templated pseudorotaxane assembly with isophthalamide macrocycle **1**, the synthesis of an analogous rotaxane system was attempted.

Ruthenium(II)-stopped 2-methylimidazolium axle **48**·(PF₆)₃ was synthesised by alkylation of the mono-stoppered 2-methylimidazole **12** (synthesised as described in Scheme 2.6) with bromo-functionalised bipyridyl derivative **42**, followed by ruthenium(II) complexation and anion exchange (Scheme 3.8).



Scheme 3.8 Synthesis of ruthenium(II)-stopped 2-methylimidazolium axle **48**·(PF₆)₃.

The reaction of axle **48**·(PF₆)₃ and macrocycle precursor **15** with Grubbs' second-generation RCM catalyst in the presence of one equivalent of TBA chloride was attempted (Scheme 3.9). However, no evidence of interlocked product was detected in the reaction mixture.



Scheme 3.9 Attempted rotaxane synthesis using ruthenium(II)-stoppered 2-methylimidazolium axle **48**·(PF₆)₃ and vinyl-appended macrocycle precursor **15**.

As the bis-terphenyl stoppered 2-methylimidazolium rotaxane was formed *via* a similar method in a reasonable yield (Section 2.3.1), it is disappointing that no interlocked product was detected. With the problems encountered in the synthesis of ruthenium(II)-triazolium rotaxane **41**·(PF₆)₃ tentatively rationalised by the conformation of the axle upon chloride binding (Section 3.2.2), the binding properties of the ruthenium(II)-appended 2-methylimidazolium motif were revisited (Section 3.3.2).

The changes in the ¹H NMR spectrum of 2-methylimidazolium thread **44**·(PF₆)₃ upon chloride addition were shown in Figure 3.10, and it was noted that only one imidazolium proton signal shifted downfield (H₁₄). Furthermore, signals corresponding to bipyridyl protons 9 and 10 also moved significantly downfield during the titration. This implies that asymmetrical anion binding to the imidazolium motif is occurring (Figure 3.16), presumably due to increased acidity of the bipyridyl protons brought about by metal chelation. If the same chloride binding mode was exhibited by axle **48**·(PF₆)₃, the steric considerations arising from the proximity of the halide template to the large ruthenium(II) bipyridyl group would considerably disfavour anion templated rotaxane formation with macrocycle precursor **15**.

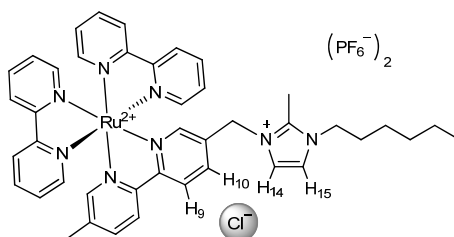


Figure 3.16 Proposed conformation of chloride binding for ruthenium(II)-appended thread **44**·(PF₆)₃.

3.3.4 Summary

The anion binding and sensing abilities of ruthenium(II)-appended 2-methylimidazolium thread **44**·(PF₆)₃ were investigated using ¹H NMR and luminescence titration experiments. However, **44**·(PF₆)₃ exhibited significant luminescence quenching upon addition of anions, rather than the desired emission enhancements. Moreover, whilst thread **44**·(PF₆)₃ displayed strong chloride templated pseudorotaxane formation with isophthalamide macrocycle **1**, rotaxane formation with the analogous ruthenium(II)-stoppered axle **48**·(PF₆)₃ was unsuccessful.

3.4 Conclusions from Sections 3.2 and 3.3

The aim of preparing a selective anion sensing rotaxane utilising a luminescent ruthenium(II) bipyridyl reporter group as a stopper was not achieved due to a number of synthetic and sensing difficulties.

In both the ruthenium(II)-appended triazolium and imidazolium systems, the key demands of positioning the reporter group close to the anion binding site and attempting to construct a flexible axle to encourage communication by the rigidity effect, have had the undesired consequences of preventing rotaxane formation due to steric effects arising from the modes of anion binding. In addition, ineffective sensing behaviour was also exhibited by the 2-methylimidazolium system, discouraging further synthetic investigations, for example using the ‘stoppering’ approach employed in Chapter Two.

Following the synthetic and sensing difficulties experienced with ruthenium(II) bipyridyl complexes, a different fluorescent reporter group was investigated for use as a potential stopper in anion templated rotaxanes, namely anthracene, with the objective of achieving selective anion sensing *via* photo-induced electron transfer (PET).

3.5 Anthracene Photo-Induced Electron Transfer Systems

Photo-induced electron transfer (PET) was introduced as a method of fluorescence anion sensing in Chapter One (Section 1.1.4.1) and although there are a number of notable exceptions, for example Czarnik's phosphate sensor **1.19** (Figure 1.19b), the majority of such systems operate *via* anion-induced fluorescence quenching, including Gunnlaugsson's receptor **1.20** (Figure 1.19c).

Research was recently carried out by Richard Ferguson to prepare anthracene-based 'OFF-ON' anion sensors such as **3.5** (Figure 3.17a).¹⁹ The theory behind the design of this receptor was based on de Silva's alkali metal sensor **3.6** (Figure 3.17b),²⁰ in which the electron-withdrawing nitrile group is necessary to facilitate PET quenching of the anthracene fluorophore by the adjacent crown ether functionalised aromatic. Upon cation binding to the crown ether, this PET process is reduced and the fluorescence emission enhanced. It was thought that, instead of influencing the electron-donating ability of the electron-rich aromatic, the PET process could be controlled by adjusting the electron-withdrawing nature of the group attached on the opposite side of the anthracene motif. This could be achieved by using a positively charged anion binding group, for example 3,5-bis-imidazolium-pyridine in **3.5**, which would still act to facilitate PET quenching of the fluorophore in the unbound receptor (Figure 3.17c). However, upon anion complexation, this group would become less electron-withdrawing, reducing the extent of the PET process and hence turning 'on' the fluorescence. As hoped, this OFF-ON sensing behaviour was observed for receptor **3.5** upon the addition of a variety of anions, including chloride, bromide and acetate, in CHCl₃.¹⁹

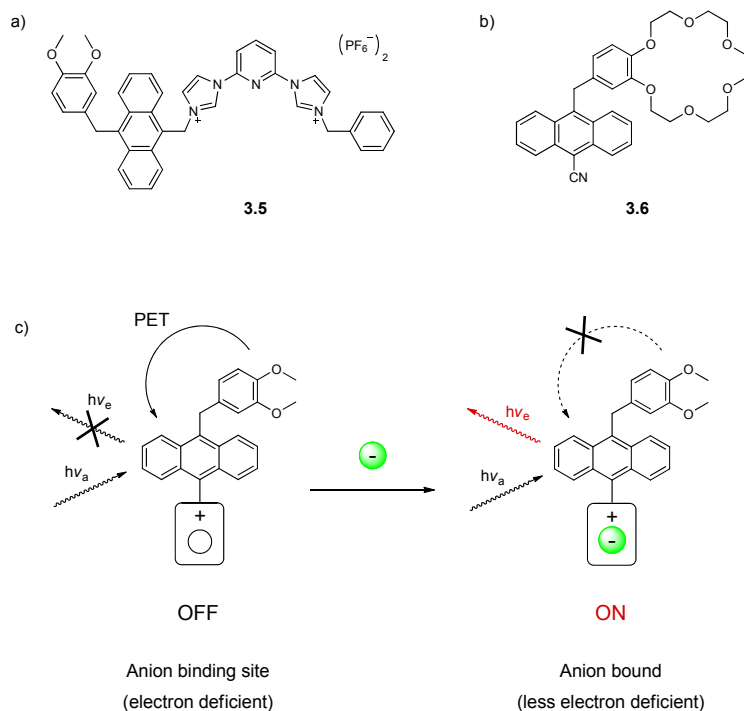


Figure 3.17 a) Richard Ferguson's anion sensor **3.5**, b) de Silva's alkali metal sensor **3.6**, and c) the mechanism for 'OFF-ON' PET anion sensing behaviour exhibited by **3.5**.

To exploit the desirable anion sensing behaviour demonstrated by receptor **3.5**, and to build on the mono-imidazolium rotaxane work detailed in Chapter Two, a target anthracene-based mono-imidazolium system was designed (Figure 3.18). Initially, the synthesis of a simple receptor was planned ($\text{R} = \text{alkyl}$), to establish whether this would display the same sensing behaviour as reported for **3.5**. If successful, this system could then be incorporated into a rotaxane structure as the axle component ($\text{R} = \text{terphenyl stopper}$), which relies on the use of the anthracene group as a stopper.

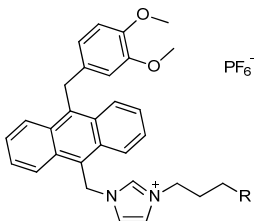
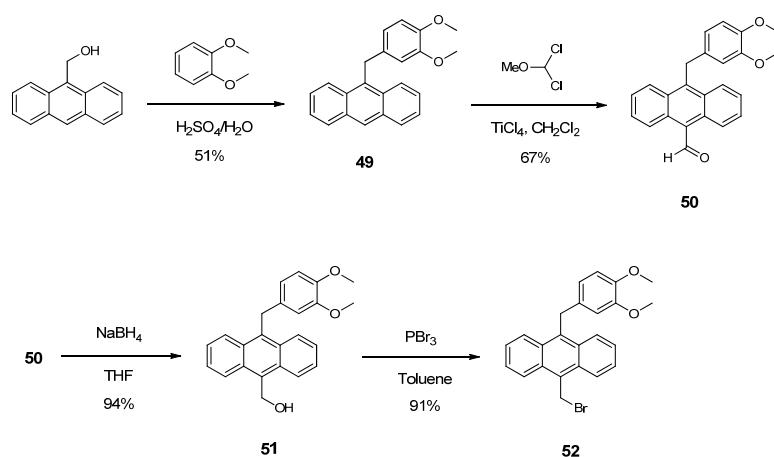


Figure 3.18 Target anthracene-based imidazolium system.

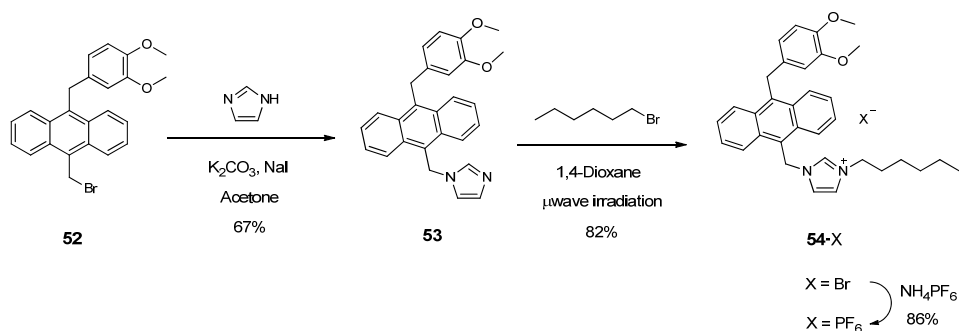
3.5.1 Synthesis of Anthracene-Appended Imidazolium Receptors

Initially, the bromo-functionalised anthracene derivative **52** was synthesised according to previously reported procedures (Scheme 3.10).¹⁹ The reaction of 9-anthracenemethanol with 1,2-dimethoxybenzene in an acidic aqueous solvent mixture gave **49** in a yield of 51%, which was converted to aldehyde **50** via a formylation reaction using α,α -dichloromethyl methyl ether and TiCl_4 . Reduction of **50** using NaBH_4 afforded **51**, and bromination using PBr_3 gave bromo-derivative **52** in 91% yield.



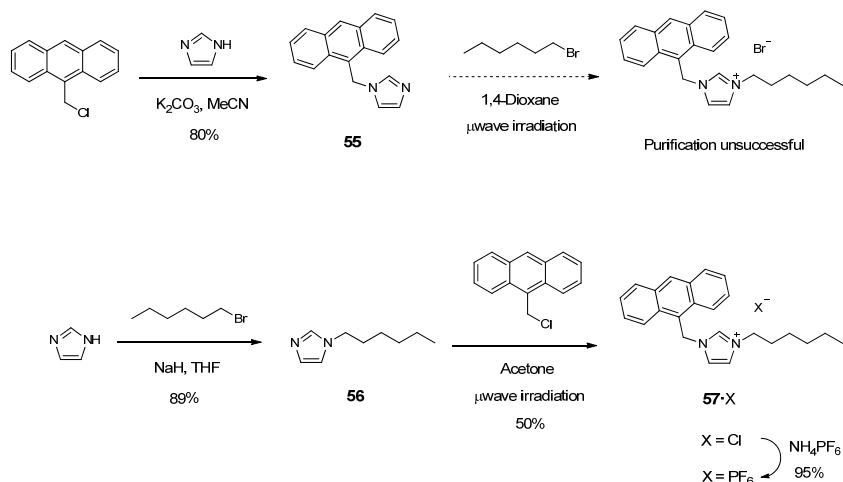
Scheme 3.10 Synthesis of anthracene bromo-derivative **52**.

Alkylation of imidazole with compound **52** was then achieved using K_2CO_3 and NaI in acetone, yielding imidazole derivative **53** in 67% (Scheme 3.11). Microwave irradiation was necessary for the alkylation of **53** with 1-bromohexane in 1,4-dioxane, which was followed by anion exchange to afford the target receptor as the non-coordinating hexafluorophosphate salt **54**· PF_6 .



Scheme 3.11 Synthesis of anthracene-appended imidazolium receptor **54**·PF₆.

An analogous control system which does not contain the electron-rich dimethyloxybenzene substituent of **54**·PF₆ was also prepared (Scheme 3.12) in order to study the effect this additional group has on the fluorescence sensing behaviour of the receptor. Initially, a similar synthetic procedure to that described Scheme 3.11 was employed, with anthracene-appended imidazole **55** prepared from 9-(chloromethyl)anthracene in 80% yield. Alkylation of **55** with 1-bromohexane occurred under microwave irradiation in 1,4-dioxane, however purification of the resulting imidazolium was unsuccessful due to a highly fluorescent impurity formed during the microwave reaction which could not be removed. Instead, an alternative synthesis was carried out by first functionalising imidazole with 1-bromohexane using NaH in dry THF to give *N*-hexylimidazole (**56**) in 89% yield.²¹ Subsequent alkylation of **56** with 9-(chloromethyl)anthracene under microwave irradiation in acetone resulted in pure **57**·Cl precipitating out of the reaction mixture upon cooling, and anion exchange afforded hexafluorophosphate salt **57**·PF₆ in quantitative yield.



Scheme 3.12 Synthesis of model anthracene imidazolium **57·PF₆**.

3.5.2 Anion Binding and Sensing Behaviour of Anthracene-Appended Imidazolium Receptors

To confirm the anion binding modes of **54·PF₆** and **57·PF₆**, the ¹H NMR spectra of these receptors were compared with those of their halide salt precursors, **54·Br** and **57·Cl**. For example, the spectra of **57·Cl** and **57·PF₆** in CDCl₃ are shown in Figure 3.19. A significant upfield shift in the signal corresponding to imidazolium proton 7 was observed upon exchange of the coordinating halide for a non-coordinating hexafluorophosphate counter anion ($\Delta\delta = -2.58$ ppm), indicating the loss of the expected C-H hydrogen bonding to the chloride anion in **57·Cl**. The adjacent CH₂ group 6 also shifted upfield, whilst slight downfield shifts were observed for imidazolium protons 8 and 9. Similar shifts confirmed the same anion binding mode for receptor **54·PF₆** upon comparison with the spectrum for **54·Br**.

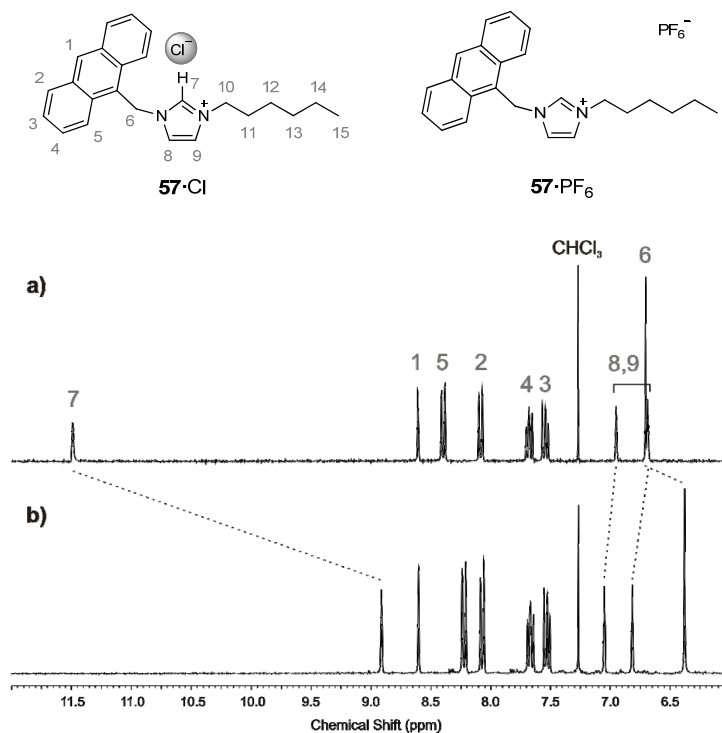


Figure 3.19 Partial ^1H NMR spectra (300 MHz) in CDCl_3 at 293 K of a) thread **57**·Cl, and b) thread **57**· PF_6 .

Having established the mode of anion binding, the fluorescent properties and anion sensing behaviour of receptors **54**· PF_6 and **57**· PF_6 were investigated. First, model system **57**· PF_6 was studied and its fluorescent properties in CHCl_3 and acetone are summarised in Table 3.7.

Table 3.7 Fluorescent properties of model receptor **57**· PF_6 in CHCl_3 and acetone at the given concentrations at 293 K – maximum excitation wavelength ($\lambda_{\text{excit,max}}$), maximum emission wavelength ($\lambda_{\text{emission,max}}$) and emission intensity.

Model receptor 57 · PF_6		
	CHCl_3	Acetone
Concentration (M)	1×10^{-6}	1×10^{-6}
$\lambda_{\text{excit,max}}$ (nm)	350	350
$\lambda_{\text{emission,max}}$ (nm)	398	394
Intensity (a.u.)	831	998

The addition of increasing amounts of TBA chloride to CHCl_3 and acetone solutions of $57\cdot\text{PF}_6$ resulted in only slight changes in the emission spectra (Figure 3.20), with fluctuations of the emission intensities of less than 7% in CHCl_3 and 4% in acetone. Hence, the lack of a significant fluorescence response makes compound $57\cdot\text{PF}_6$ an effective control system for comparison with receptor $54\cdot\text{PF}_6$, which contains the modified anthracene motif designed to exhibit favourable OFF-ON anion sensing behaviour.

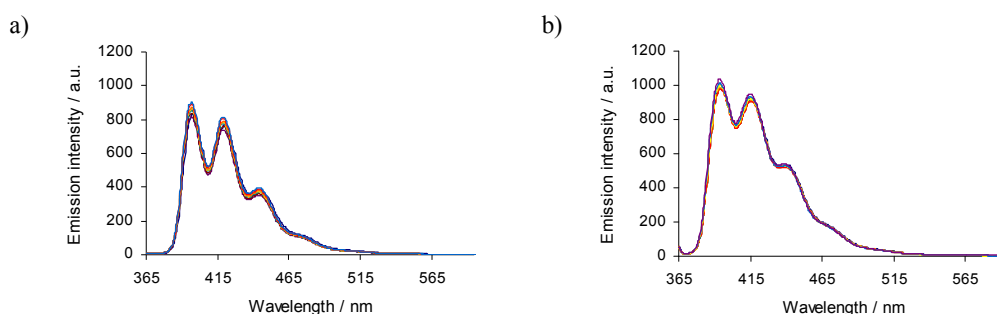


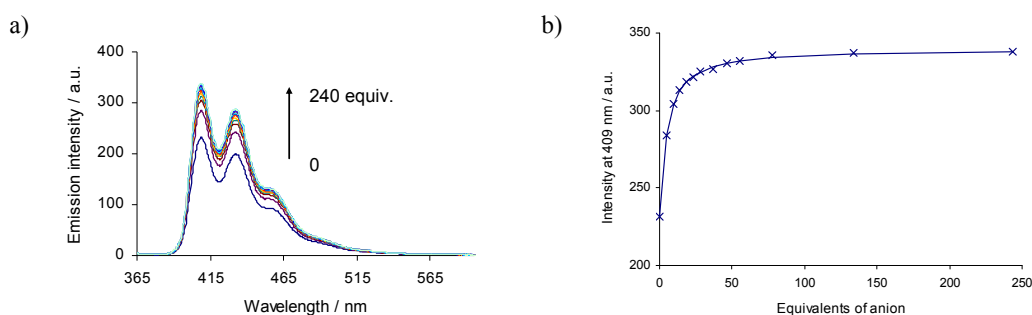
Figure 3.20 Changes in the emission spectrum of model receptor $57\cdot\text{PF}_6$ ($c = 1 \times 10^{-6}$ M, $\lambda_{\text{excit}} = 350$ nm, 293 K) upon addition of TBACl in a) CHCl_3 (0 to 400 equivalents), and b) acetone (0 to 600 equivalents).

Again, the fluorescent properties of $54\cdot\text{PF}_6$ were investigated in CHCl_3 and acetone (Table 3.8). However, in contrast to that observed for $57\cdot\text{PF}_6$, the concentration required for similar emission intensities was an order of a magnitude greater in acetone than in CHCl_3 . Solvent-dependent fluorescent effects are well known for PET systems,²² as polar solvents stabilise the excited state intermediate, a radical ion pair, to a greater extent than less polar solvents. Hence the concentration difference for $57\cdot\text{PF}_6$ is in agreement with the proposed PET mechanism in Figure 3.17c, as increased quenching of the anthracene fluorescence would be expected in acetone compared with CHCl_3 .

Table 3.8 Fluorescent properties of receptor **54**·PF₆ in CHCl₃ and acetone at the given concentrations at 293 K – maximum excitation wavelength ($\lambda_{\text{excit,max}}$), maximum emission wavelength ($\lambda_{\text{emission,max}}$) and emission intensity.

Receptor 54 ·PF ₆		
	CHCl ₃	Acetone
Concentration (M)	5×10^{-7}	5×10^{-6}
$\lambda_{\text{excit,max}}$ (nm)	350	350
$\lambda_{\text{emission,max}}$ (nm)	409	407
Intensity (a.u.)	232	115

Upon addition of TBA chloride to **54**·PF₆ in both CHCl₃ and acetone solutions, significant emission intensity enhancements were observed with no changes in the emission wavelengths (Figures 3.21a and 3.22a), in agreement with the proposed ‘OFF-ON’ PET anion sensing mechanism. By monitoring the intensity at the maximum emission wavelength throughout the titration experiments (Figures 3.21b and 3.22b), log *K* values were determined using SPECFIT analysis and are given in Table 3.9 along with the percentage change in emission intensity upon sensing saturation.

**Figure 3.21** a) Changes in the emission spectrum of receptor **54**·PF₆ in CHCl₃ ($c = 5.0 \times 10^{-7}$ M, $\lambda_{\text{excit}} = 350$ nm, 293 K) upon addition of TBACl, and b) corresponding changes in emission intensity at 409 nm (crosses represent experimental data points, line represents calculated titration curve).

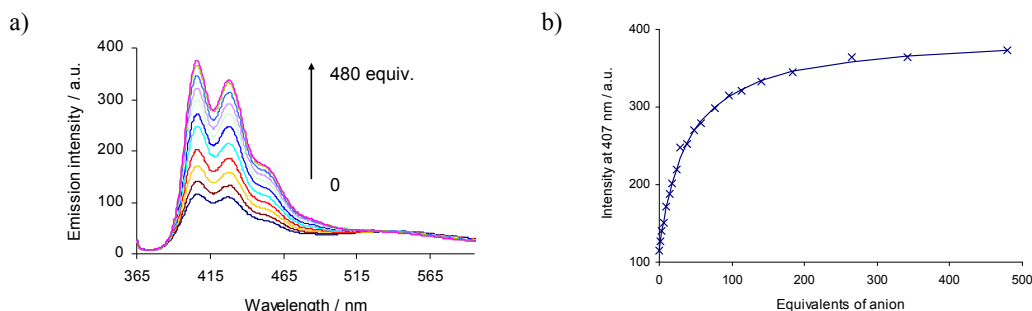


Figure 3.22 a) Changes in the emission spectrum of receptor **54**·PF₆ in acetone ($c = 5.0 \times 10^{-6}$ M, $\lambda_{\text{excit}} = 350$ nm, 293 K) upon addition of TBACl, and b) corresponding changes in emission intensity at 407 nm (crosses represent experimental data points, line represents calculated titration curve).

Table 3.9 Percentage changes in emission intensity upon sensing saturation and the log K values for the addition of TBACl to thread **54**·PF₆ in CHCl₃ and acetone ($c = 5.0 \times 10^{-7}$ and 5.0×10^{-6} M respectively, $\lambda_{\text{excit}} = 350$ nm, 293 K). Sensing saturation was reached after the addition of * 100 and † 300 equivalents of anion. log K values calculated using SPECFIT, errors given in parentheses.

Solvent	ΔI (%)	log K
CHCl ₃ ($c = 5.0 \times 10^{-7}$ M)	45 *	5.65 (0.02)
Acetone ($c = 5.0 \times 10^{-6}$ M)	216 †	3.71 (0.04)

Due to the less competitive nature of the solvent compared with acetone, fewer equivalents of chloride were required for sensing saturation to be reached in CHCl₃, indicating much stronger halide binding, especially given the lower concentration at which this titration was carried out. The considerable difference in chloride binding strengths for receptor **54**·PF₆ in the two solvents is reflected in the calculated log K values. However, the change in emission intensity upon sensing saturation is much greater in acetone than CHCl₃ – 216% and 45% respectively. This is thought to be due to the different extents of PET quenching in the unbound receptor between the two solvent environments and the degree to which this process is reduced upon anion binding.

To assess the sensing response of receptor **54**·PF₆ to other anions, a simple investigation was carried out in acetone, the solvent in which greater changes in emission intensity were observed with chloride. The addition of 300 equivalents of bromide, nitrate, azide and hydrogen sulfate anions,²³ and

the observed effect on the emission intensity of **54**·PF₆ are given in Table 3.10, along with the original response with chloride.

Table 3.10 Percentage changes in emission intensity of receptor **54**·PF₆ in acetone (c = 5.0 × 10⁻⁶ M, λ_{excit} = 350 nm, 293 K) upon addition of 300 equivalents of a variety of anions as their TBA salts.

Anion	ΔI (%)
Cl ⁻	+ 216
Br ⁻	+ 27
NO ₃ ⁻	+ 40
N ₃ ⁻	- 20
HSO ₄ ⁻	+ 242

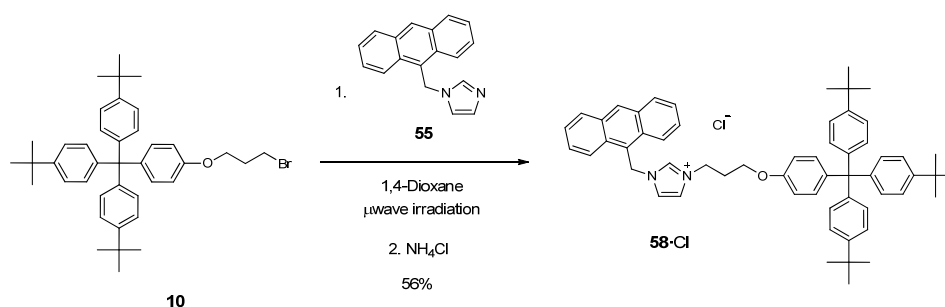
The percentage changes in emission intensity upon bromide, nitrate and azide addition were much less than that observed for chloride, with bromide and nitrate resulting in slight enhancements and azide quenching the fluorescence of **54**·PF₆. Interestingly, a greater increase in emission was brought about by the more basic hydrogen sulfate, 242% compared with 216% for chloride. It is not clear why **54**·PF₆ displayed a reduction in emission upon azide addition, the opposite of the enhancements observed with the other anions which could be explained by the mechanism in Figure 3.17c.

The fluorescence studies reveal that the modified anthracene group in imidazolium receptor **54**·PF₆ results in desirable ‘OFF-ON’ fluorescence anion sensing behaviour, in contrast to the unsubstituted anthracene control system **57**·PF₆. This can be explained by considering the effect of complexation on an existing PET process. Encouraged by these findings, the potential for the anthracene-based component to act as a stopper group in rotaxane synthesis was investigated.

3.5.3 Synthesis of Anthracene-Stoppered Imidazolium Axle and Investigation into the Potential for Interlocked Structure Formation

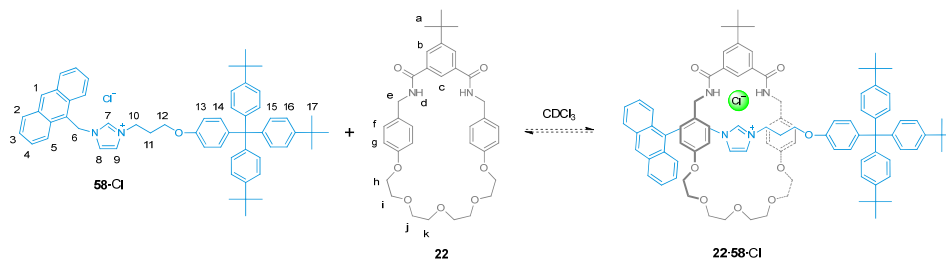
Whilst anthracene has been used previously as a stopper group in rotaxane systems (for example **3.4** in Figure 3.2), it was anticipated that the isophthalamide macrocycle components based on **1** (Scheme 3.6) would be considerably too large to be ‘stoppered’ by this motif. However, it was decided to investigate whether smaller macrocycle **22** (Section 2.4) was sufficiently reduced in size for this purpose.

Imidazolium **58**·Cl was synthesised to act as a model axle (Scheme 3.13), as it was thought that the size of the anthracene group itself would be the limiting factor for systems stoppered by the PET sensing component of receptor **54**·PF₆. Imidazole **55** was alkylated with compound **10** (synthesised as described in Scheme 2.5) using microwave irradiation in 1,4-dioxane, and anion exchange afforded the desired chloride salt **58**·Cl in 56% yield.



Scheme 3.13 Synthesis of model axle **58**·Cl.

A simple ¹H NMR titration experiment was carried out using imidazolium **58**·Cl to determine whether the anthracene motif was large enough to prevent the anion templated threading of macrocycle **22** (Scheme 3.14). One equivalent of **22** was added to a CDCl₃ solution of **58**·Cl, and the aromatic region of the resulting spectrum, along with the spectra of the two individual components, is shown in Figure 3.23.



Scheme 3.14 ^1H NMR experiment using model axle **58-Cl** and macrocycle **22**.

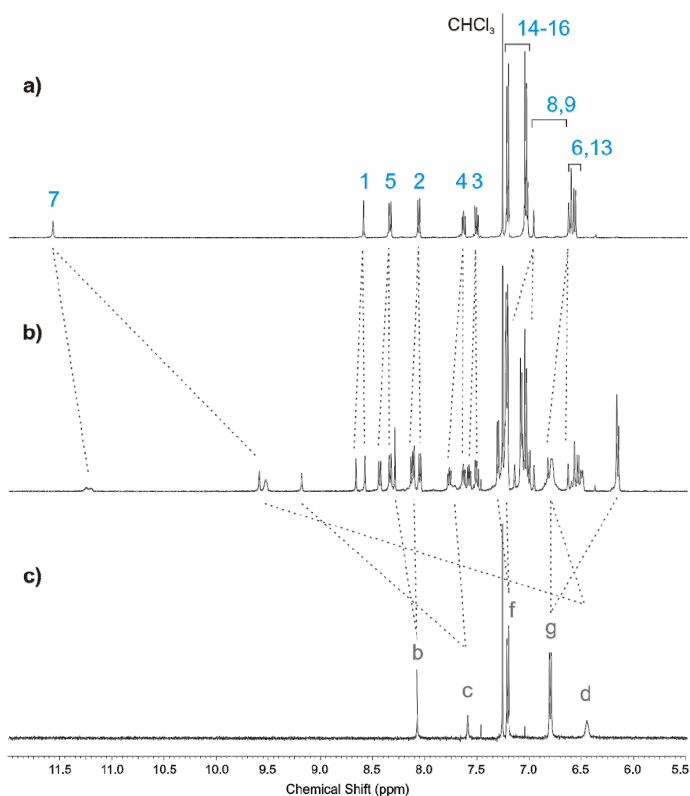


Figure 3.23 Partial ^1H NMR spectra (500 MHz) in CDCl_3 at 293 K of a) axle **58-Cl**, b) axle **58-Cl** plus 1.0 equivalent of macrocycle **22**, and c) macrocycle **22**.

The resulting spectrum contains twice as many axle and macrocycle peaks as expected, with one set of peaks remaining at approximately the same chemical shifts as the individual components. The other peaks displayed significant shifts and are assigned to the chloride templated interpenetrated assembly **22·58-Cl**. Importantly, macrocycle protons **g** were shifted upfield due to the donor-acceptor interactions between the electron-rich phenolic and electron-deficient imidazolium groups in **22·58-Cl**. Furthermore, polarisation of the halide template away from the imidazolium group of **58-Cl** and

towards the macrocycle hydrogen bond donors resulted in downfield shifts of c and d, and an upfield shift in axle proton 7. The relative integrations of these two sets of peaks was 0.7 : 1.0 (assembly : individual components), which increased to 0.9 : 1.0 after heating the solution at 50 °C for 15 h.

An analogous control experiment was carried out with bis-terphenyl stoppered, 4,5-dimethylimidazolium axle **13**·Cl (Section 2.3.1) and macrocycle **22**. In this case, the spectrum of the equimolar solution was purely a superposition of the component spectra, with no additional peaks, as any threading of the macrocycle is prevented by the large stopper groups of the axle.

These findings indicate that the threading process shown in Scheme 3.14 occurs at room temperature, in slow exchange on the NMR timescale. Hence, the anthracene motif is not large enough to act as a stopper for macrocycle **22**. However, anthracene does create sufficient kinetic barrier to prevent pseudorotaxane assembly from occurring in fast exchange, as observed for analogous unstoppered, alkyl-imidazolium threads (for example in Sections 2.4.2 and 3.3.2). Similar anion templated ‘slippage’ behaviour has been investigated previously,²⁴ including quantitative kinetic studies, but is undesirable in the construction of anion sensing rotaxanes.

3.5.4 Anthracene Triazolium System

In an effort to solve the problem regarding the size requirement for the stopper groups, the target system shown in Figure 3.24 was designed. This receptor exploits the triazolium anion binding motif, incorporates the required anthracene unit *via* alkylation, and includes scope for stopper group functionalisation at R¹ and R². In addition, it retains the positive charge of the receptor adjacent to the anthracene component, which was found to be necessary for the desirable PET sensing behaviour of similar systems.¹⁹ Steric effects arising from the functionalised triazolium group would need to be taken into account if such an axle component was to be utilised for rotaxane formation, however the potential of this synthetic approach was first investigated.

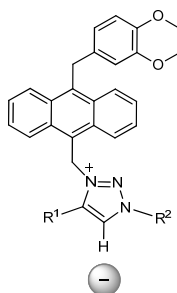
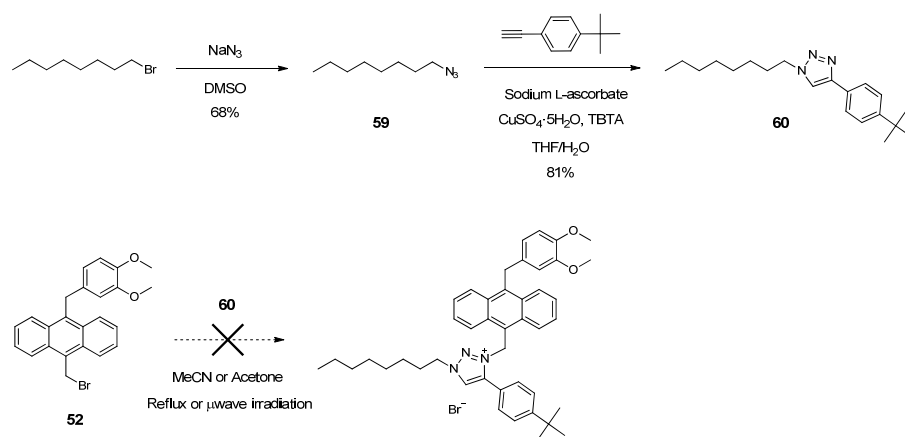


Figure 3.24 Target anthracene triazolium system.

Initially, simple triazole compound **60** was synthesised as a model system for investigating the alkylation reaction (Scheme 3.15).²⁵ Azide **59** was prepared from 1-bromooctane and reacted under ‘click’ conditions with 4-*tert*-butylphenylacetylene using a copper(II) catalyst and sodium L-ascorbate as an *in situ* reducing agent in a THF/H₂O solvent mixture. Following purification by column chromatography, triazole **60** was isolated in 81% yield. Alkylation of **60** with **52** was then attempted using a number of different reaction conditions. Unfortunately, **52** was found to be unstable upon heating in MeCN under both reflux and microwave irradiation, whilst no alkylated products were detected when the reaction was carried out in acetone, even after prolonged microwave irradiation at 150 °C.



Scheme 3.15 Synthesis of model triazole **60** and attempted alkylation using anthracene bromide derivative **52**.

Alkylation reactions can often be synthetically difficult and the functionalisation of triazole derivatives at N⁵ is not widely reported.²⁶ The failure to find successful alkylation conditions prevented the further investigation of this approach.

3.5.5 Summary

Anthracene-appended imidazolium receptors **54**·PF₆ and **57**·PF₆ were synthesised, and their fluorescent properties and anion sensing abilities studied. Control receptor **57**·PF₆ displayed no significant sensing response, whereas **54**·PF₆ exhibited emission intensity enhancements upon chloride addition in CHCl₃ and acetone, and with a variety of other anions in acetone. This desirable ‘OFF-ON’ fluorescence could be explained by a previously exploited sensing strategy involving the modulation of a PET quenching process.

Unfortunately, a ¹H NMR experiment using model axle **58**·Cl demonstrated that the anthracene motif is too small to act as a stopper group in rotaxane synthesis with macrocycle **22**. In addition, an unsuccessful alkylation reaction prevented the investigation of an alternative approach using the triazolium anion binding motif.

3.6 Conclusions for Section 3.5

An anthracene-based imidazolium receptor was found to exhibit desirable fluorescence anion sensing behaviour. However, this could not be exploited in the construction of an analogous anion sensing rotaxane due to the stopper group size requirements. Selectivity in binding arising from the imidazolium interlocked host cavity, along with the differential sensing responses of the component itself, may have resulted in a potent and effective sensing system.

To overcome this issue, either the anthracene component must be functionalised to increase its size or a smaller macrocycle employed. The synthetic difficulties encountered in previous attempts to adapt the modified anthracene component,¹⁹ suggest that the best approach would be to explore alternative macrocyclic systems. As **22** was found to be too large for rotaxane formation but small

enough to allow ‘slippage’ behaviour, it is thought that only a slightly smaller macrocyclic system would be required. A reduction in the length of the polyether chain, reducing the overall size by three atoms, might be sufficient (Figure 3.25). Alternatively, the symmetrical macrocycle utilised in Leigh’s anthracene-stoppered rotaxane **3.4** (Figure 3.2b) could be investigated as this has been shown to be of the correct size, although it does contain two isophthalamide anion binding clefts. It is anticipated that reducing the macrocycle size in these ways would be viable given the small size of the imidazolium motif.

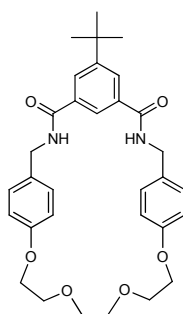


Figure 3.25 Possible macrocycle component for use in an anthracene-stoppered rotaxane.

Furthermore, there is potential to employ other strategies to exploit the desirable fluorescence sensing behaviour of this system, rather than incorporation into rotaxane host structures. For example, the surface attachment of acyclic anion receptors for the fabrication of sensing devices is discussed in the next chapter.

3.7 References

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8. Due to asymmetry, all of the bipyridyl ligand protons in the ruthenium(II)-stoppered triazolium axle are inequivalent. However for clarity, they are grouped with analogous protons and labelled 17, 18, 19 and 20.
9. Whilst the ruthenium(II) centre is chiral due to the asymmetry of the substituted ligand, the axle is synthesised as the racemate. However in both enantiomers, the two methylene protons reside in different environments.
10. These studies were carried out in acetone, as this relatively non-competitive solvent allowed for initial assessment of the sensing behaviour of the axle without the addition of a great excess of anion.
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Chapter Four: Naphthalimide Triazolium Systems for Anion Sensing and Interlocked Molecular Motion[†]

4.1 Introduction

4.1.1 The Naphthalimide Motif

The naphthalimide motif has been exploited in numerous fluorescence sensing systems.¹ Most commonly this is in the form of 4-amino-1,8-naphthalimide derivatives (Figure 4.1a), for example Gunnlaugsson's thiourea-based anion receptor **1.20** (Figure 1.19c). These derivatives typically have high quantum yields and long wavelength emissions (450–550 nm), arising from internal charge transfer (ICT) excited states caused by the electron-donating amine and electron-withdrawing imide groups.

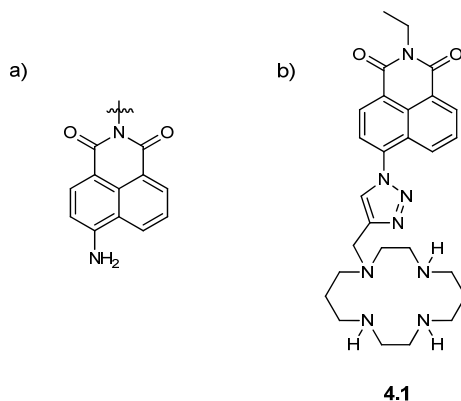


Figure 4.1 a) 4-Amino-1,8-naphthalimide, and b) Watkinson's cyclam-based Zn(II) sensor **4.1**.

In general, the naphthalimide motif can be readily functionalised at the imide and at several different positions on the naphthalene group. The thiourea group of receptor **1.20** was attached *via* the

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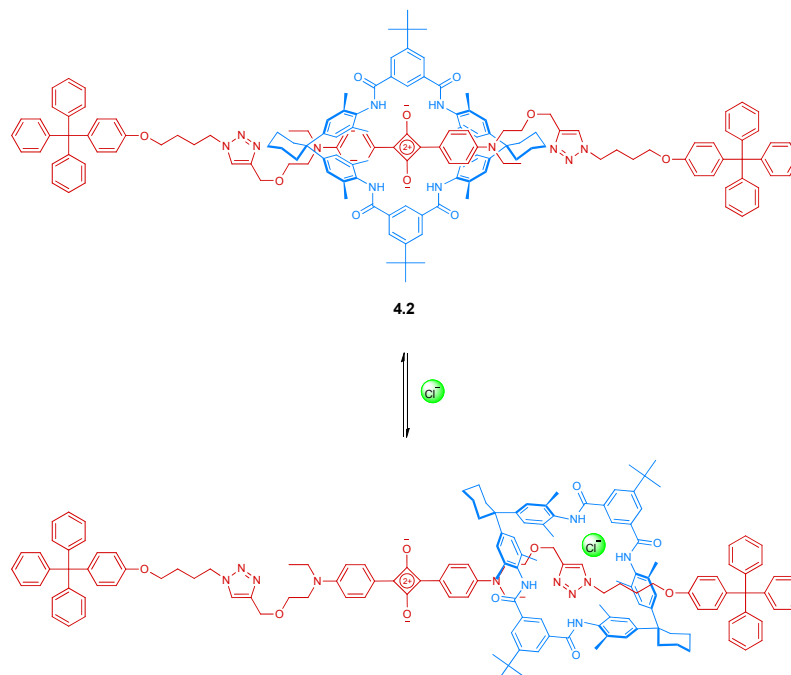
G. T. Spence, M. B. Pitak and P. D. Beer, *Chem. Eur. J.*, 2012, **18**, 7100–7108.

imide, and functionalisation of naphthalene C⁴ with a triazole is demonstrated by Watkinson's cyclam-based Zn(II) sensor **4.1** (Figure 4.1b).²

4.1.2 Anion-Induced Molecular Motion

As discussed in the introductory chapter (Section 1.2.3.1), the ability of mechanically interlocked molecules to undergo controlled, reversible molecular motion *via* changes in the relative positions of their constituent parts is receiving an ever increasing amount of interest due to the promise of potential nanotechnological applications as molecular switches and machines.³⁻⁵ However, in contrast to the large number of examples controlled by cationic, photochemical or electrochemical inputs, there are still relatively few interlocked structures capable of molecular motion mediated by anions as an external stimulus.⁶⁻¹⁵ Of these, only a small number have been shown to display selectivity between different coordinating anions.^{11, 12}

A key development in molecular motion devices is the ability to detect co-conformational changes through optical or electrochemical signalling. Of those systems in which motion is induced by the addition of coordinating anions, only Smith's chloride-selective squaraine rotaxane **4.2** (Scheme 4.1) displayed an associated signalling response.¹² Upon anion addition, macrocycle translocation occurs from the central squaraine station of rotaxane **4.2** to one of two triazole groups of the axle. The rotaxane fluorescence is partially quenched when the macrocycle resides over the squaraine unit, hence an increase in fluorescence emission is observed upon shuttling, with the greatest enhancement observed for the chloride-induced co-conformational change. This system also demonstrates a common feature of interlocked systems exhibiting molecular motion behaviour, namely the potential for two orthogonal sets of intercomponent interactions. In this case, the initial hydrogen bonding interactions between the axle squaraine group and the macrocycle amides are replaced by cooperative hydrogen bond donation from the triazole and amide groups to the bound anion.



Scheme 4.1 Anion-induced shuttling exhibited by Smith's squaraine rotaxane **4.2** which is accompanied by an increase in the fluorescence emission intensity.

In alternative types of anion-induced molecular motion other than the addition of coordinating anions, UV/Vis spectroscopy has also been effectively employed as a signalling method.^{6, 16} In these systems, co-conformational changes were driven either by a change in the non-coordinating counter anion,⁶ or by the photo-induced creation of a radical naphthalimide anion within the rotaxane structure.¹⁶

4.1.3 Chapter Objectives

The aims of this chapter are to investigate the novel naphthalimide triazolium motif (Figure 4.2a) for use in fluorescence anion sensing systems and in the construction of interpenetrated and interlocked assemblies capable of molecular motion.

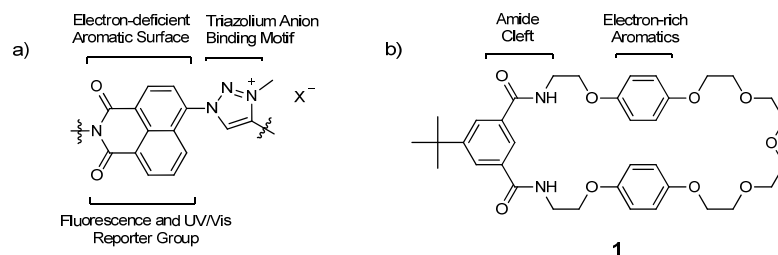
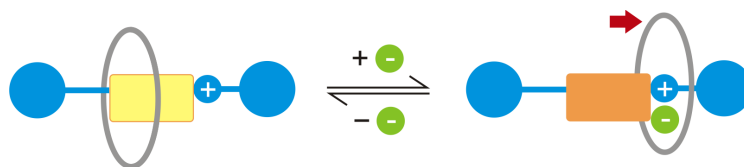


Figure 4.2 a) Target naphthalimide triazolium motif, and b) macrocycle **1**.

Similar to the related naphthalene diimide (NDI) motif, naphthalimide is intrinsically electron-deficient, and would be further polarized by the direct attachment of the positively charged triazolium heterocycle. The electron-deficient aromatic surface and imide carbonyl groups of this target system are expected to interact strongly with a macrocycle containing electron-rich aromatics and an amide cleft (for example macrocycle **1**, Figure 4.2b). Furthermore, the thread triazolium and macrocycle amide groups would allow for cooperative hydrogen bonding to a coordinating anion. Hence, incorporation of the naphthalimide triazolium motif into the stoppered axle component of an anion templated rotaxane system may produce an interlocked structure capable of anion-induced molecular motion (Scheme 4.2). It is hoped that this motion would be signalled by perturbations in the axle naphthalimide absorbance band and/or by changes in its fluorescence emission.



Scheme 4.2 Desired anion-induced shuttling behaviour of a naphthalimide triazolium rotaxane.

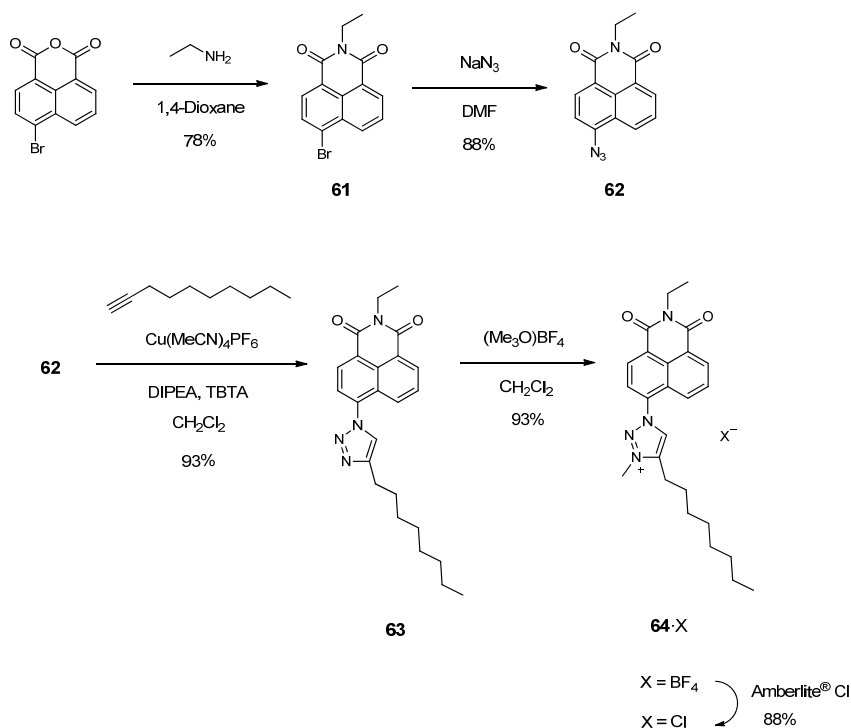
4.2 Simple Acyclic Naphthalimide Triazolium Receptor

To establish the anion binding and sensing properties of this novel motif, a simple acyclic naphthalimide triazolium receptor was synthesised and studied using ^1H NMR, fluorescence and

UV/Vis spectroscopies. In addition, investigations were carried out into the ability of the receptor to act as a threading component in the formation of pseudorotaxane assemblies.

4.2.1 Synthesis of Naphthalimide Triazolium Receptor

The synthesis of alkyl-substituted naphthalimide triazolium receptor **64**·BF₄ is shown in Scheme 4.3. *N*-Ethyl-4-bromo-1,8-naphthalimide (**61**) was synthesised by heating commercially available 4-bromo-1,8-naphthalic anhydride and EtNH₂ at reflux in 1,4-dioxane.¹⁷ Reaction of **61** with NaN₃ afforded *N*-ethyl-4-azido-1,8-naphthalimide (**62**),¹⁸ isolated in a yield of 88%. A copper(I)-catalysed 'click' reaction with 1-decyne gave triazole **63** which was subsequently methylated using (Me₃O)BF₄ to afford target naphthalimide triazolium receptor **64**·BF₄ in a yield of 93%. For use in the pseudorotaxane investigations, the chloride salt **64**·Cl was prepared from **64**·BF₄ using an Amberlite[®] anion exchange resin.



Scheme 4.3 Synthesis of naphthalimide triazolium derivatives **64**·BF₄ and **64**·Cl.

4.2.2 Anion Binding and Sensing Behaviour of Naphthalimide Triazolium Receptor

To confirm the anion binding mode of the naphthalimide triazolium motif, the ^1H NMR spectra of **64**· BF_4 and **64**·Cl in CDCl_3 were compared (Figure 4.3). Upon the change in the counter anion from the non-coordinating tetrafluoroborate to the coordinating chloride, the peak corresponding to triazolium proton 8 shifted downfield ($\Delta\delta = +0.9$ ppm), indicative of C-H hydrogen bonding to the halide. Adjacent naphthalimide proton 7 was also shifted significantly further downfield in the spectrum of **64**·Cl compared with that of **64**· BF_4 ($\Delta\delta = +0.5$ ppm). This proton is considerably acidic due to the electron-withdrawing nature of the imide group and was demonstrated recently to be capable of participating in anion binding by Flood and coworkers.¹⁹ However, geometric constraints arising from the exact position of the triazolium group with respect to the naphthalimide motif in **64**·Cl disfavors any such cooperative anion binding, with the two groups expected to be non-coplanar.

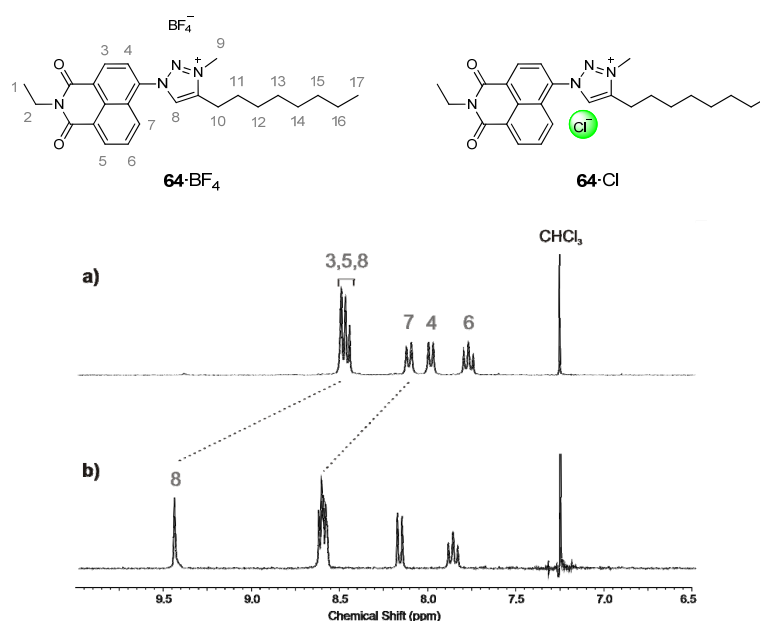


Figure 4.3 Partial ^1H NMR spectra (300 MHz) in CDCl_3 of a) receptor **64**· PF_6 , and b) **64**·Cl.

Having established its anion binding mode, the fluorescent properties of triazolium receptor **64**· BF_4 were investigated, along with those of the triazole precursor **63**, in CH_2Cl_2 (Table 4.1).²⁰

Table 4.1 Fluorescent properties of triazole **63** and triazolium **64**·BF₄ in CH₂Cl₂ at the given concentrations at 293 K – maximum excitation wavelength ($\lambda_{\text{excit,max}}$), maximum emission wavelength ($\lambda_{\text{emission,max}}$) and emission intensity.

	63	64 ·BF ₄
Concentration (M)	1 x 10 ⁻⁷	1 x 10 ⁻⁵
$\lambda_{\text{excit,max}}$ (nm)	345	340
$\lambda_{\text{emission,max}}$ (nm)	411	401
Intensity (a.u.)	327	433

Whilst the maximum excitation and emission wavelengths are only slightly different between triazole **63** and triazolium **64**·BF₄, the concentration required for similar emission intensities is two orders of magnitude greater for **64**·BF₄ than **63**. Evidently the addition of the positive charge results in a considerable reduction in fluorescence intensity, but does not perturb the excitation or emission wavelengths to the same degree. In comparison with 4-amino-1,8-naphthalimide derivatives, it is thought that the analogous triazole and triazolium nitrogen lone pairs in **63** and **64**·BF₄ would participate in any ICT processes to a much lesser extent due to their reduced electron-donating nature, as well as the expected non-coplanar arrangement with the naphthalimide motif. This is evidenced by the fact that the emission wavelengths of **63** and **64**·BF₄ are closer to that of unsubstituted 1,8-naphthalimide than of 4-amino-1,8-naphthalimide systems (~380 and 490 nm respectively in CH₂Cl₂).^{1, 21}

In addition, the absorbance properties of **63** and **64**·BF₄ were studied using UV/Vis spectroscopy (Table 4.2). Upon conversion from triazole **63** to triazolium **64**·BF₄, slight changes in the absorbance occurred, but no major wavelength shift or change in extinction coefficient were observed.

Table 4.2 UV/Vis spectroscopic properties of triazole **63** and triazolium **64**·BF₄ in CH₂Cl₂ (c = 1 x 10⁻⁵ M, 293 K) – maximum absorbance wavelength ($\lambda_{\text{abs,max}}$) and extinction coefficient (ϵ).

	63	64 ·BF ₄
$\lambda_{\text{abs,max}}$ (nm)	344	331, 344
ϵ (M ⁻¹ cm ⁻¹)	1.8 x 10 ⁴	1.6 x 10 ⁴

To assess the sensing ability of naphthalimide triazolium receptor **64**·BF₄, preliminary fluorescence titration experiments were carried out in CHCl₃.²² The changes in the emission spectrum of **64**·BF₄ were monitored upon addition of 2.5, 10.0 and 60.0 equivalents of a variety of anions as their TBA salts – chloride, bromide, nitrate, azide, dihydrogen phosphate and hydrogen sulfate. The spectra corresponding to the chloride and hydrogen sulfate titrations are shown in Figure 4.4, with the observed percentage changes in emission intensity after addition of 60.0 equivalents of each of the anions and corresponding changes in emission wavelength given in Table 4.3.

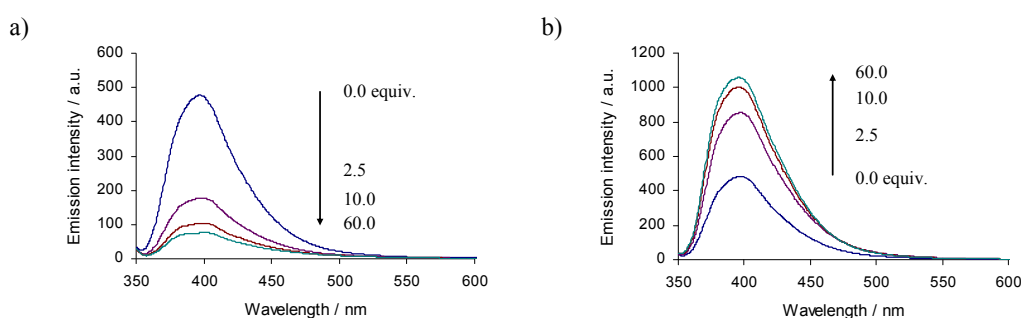


Figure 4.4 Changes in the emission spectrum of triazolium **64**·BF₄ in CHCl₃ ($c = 1 \times 10^{-5}$ M, $\lambda_{\text{excit}} = 340$ nm, 293 K) upon addition of a) TBACl and b) TBAHSO₄. Note: different y-axis scales.

Table 4.3 Percentage changes in emission intensity of triazolium **64**·BF₄ in CHCl₃ ($c = 1.0 \times 10^{-5}$ M, $\lambda_{\text{excit}} = 340$ nm, 293 K) upon addition of 60.0 equivalents of a variety of anions as their TBA salts.

Anion	ΔI (%)	$\Delta \lambda_{\text{emission,max}}$ (nm)
Cl [−]	− 84	+ 4
Br [−]	− 96	+ 7
NO ₃ [−]	− 73	+ 2
N ₃ [−]	− 94	+ 13
H ₂ PO ₄ [−]	− 24	− 2
HSO ₄ [−]	+ 120	− 1

Upon chloride addition to **64**·BF₄, a considerable quenching of the fluorescence was observed, along with a broadening of the emission peak and a slight bathochromic shift in the maximum

emission wavelength (Figure 4.4a). Similar behaviour also occurred with bromide, nitrate and azide, while dihydrogen phosphate resulted in a reduced quenching response and a small hypsochromic shift (Table 4.3). In contrast, addition of hydrogen sulfate resulted in a large emission enhancement with only a minor change in wavelength (Figure 4.4b).

The effective sensing behaviour exhibited by naphthalimide triazolium receptor **64**·BF₄ confirms the potential of this motif for use in anion sensing systems. The exact mechanism responsible for these anion-induced fluorescence changes is unclear, especially relating to the contrasting response upon hydrogen sulfate addition.²³ However, no significant perturbations were observed in the UV/Vis spectrum of **64**·BF₄ during the titration experiments, indicating that it is an excited state process.

4.2.3 Pseudorotaxane Investigations

To probe the potential of the naphthalimide triazolium motif to form interpenetrated and interlocked assemblies capable of anion-induced co-conformational changes, pseudorotaxane studies were carried out initially using receptor **64**·BF₄ as a threading component with isophthalamide macrocycle **1** (Figure 4.5). As mentioned in Section 4.1.2, it was anticipated that these components would undergo interpenetrative assembly due to strong donor-acceptor interactions between the electron-deficient naphthalimide thread and electron-rich hydroquinone groups of the macrocycle. In addition, anion binding is possible through both the triazolium thread and macrocycle isophthalamide motifs. Thus the co-conformation of the pseudorotaxane between thread **64**·BF₄ and macrocycle **1** might be controlled by the presence, or absence, of a coordinating anion.

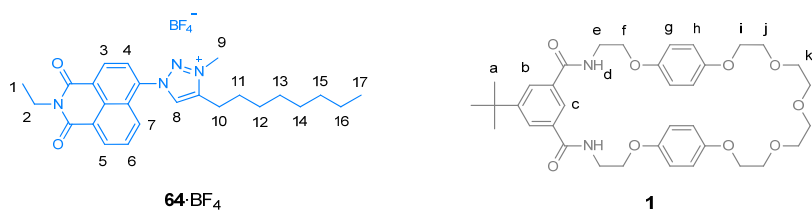
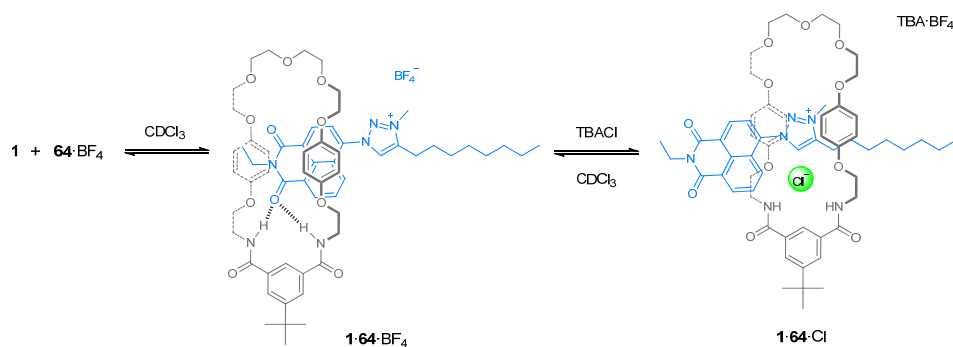


Figure 4.5 Naphthalimide triazolium thread **64**·BF₄ and isophthalamide macrocycle **1**.

The addition of one equivalent of **64**·BF₄ to macrocycle **1** in CDCl₃ was monitored by ¹H NMR spectroscopy (Scheme 4.4 and Figure 4.6a and b). Pseudorotaxane formation was indicated by a significant upfield shift of macrocycle hydroquinone protons g and h ($\Delta\delta = -0.5$ ppm), due to the highly favourable donor-acceptor interactions with the electron-deficient naphthalimide thread. Furthermore, hydrogen bonding interactions between the imide carbonyl groups of **64**·BF₄ and the macrocycle amide groups resulted in downfield shifts in macrocycle isophthalamide protons c and d. These complementary donor-acceptor and hydrogen bonding interactions imply that the macrocycle resides directly over the naphthalimide group of the thread in pseudorotaxane assembly **1**·**64**·BF₄, as shown in Scheme 4.4.



Scheme 4.4 Formation of pseudorotaxane **1**·**64**·BF₄ and anion-induced change in co-conformation.

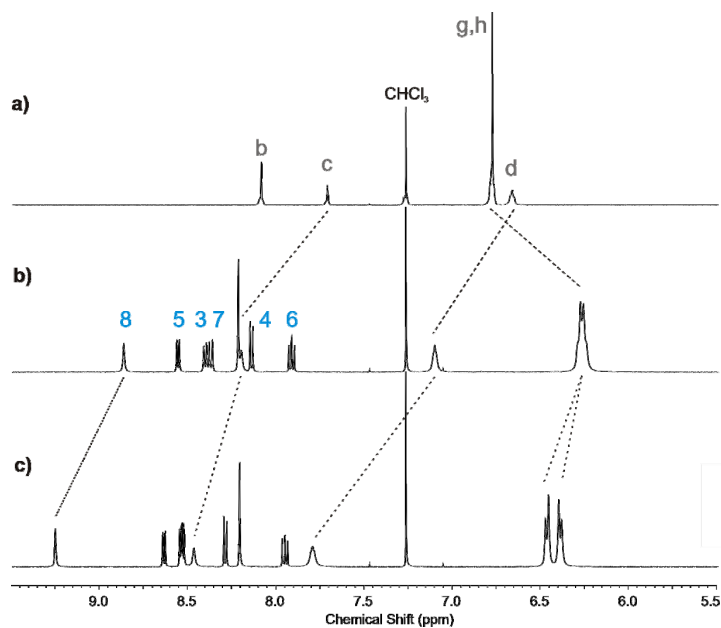


Figure 4.6 Partial ^1H NMR spectra (500 MHz) in CDCl_3 at 293 K of a) macrocycle **1**, b) **1** + 1.0 equivalent of thread **64**· BF_4 , and c) **1**·**64**· BF_4 + 1.0 equivalent of TBACl.

Upon subsequent addition of one equivalent of TBA chloride to **1**·**64**· BF_4 , the observed spectral changes were consistent with a significant change in pseudorotaxane co-conformation, with the macrocycle moving over to the triazolium component of the thread (Scheme 4.4). Cooperative hydrogen bonding to the halide anion by the macrocycle isophthalamide cleft and thread triazolium group is indicated by downfield shifts in triazolium proton 8 and macrocycle protons c and d (Figure 4.6c). The hydroquinone protons shift downfield from their position in **1**·**64**· BF_4 ($\Delta\delta = +0.2$ ppm), due to the reduced shielding effect of the triazolium group, compared with the larger naphthalimide group, and are split in the presence of the halide anion.

Further evidence for the respective interpenetrated natures of assemblies **1**·**64**· BF_4 and **1**·**64**·Cl was provided by 2D ^1H - ^1H NMR ROESY spectroscopy, with a large number of couplings between protons of the macrocycle and the thread observed for both pseudorotaxane co-conformations (Figures 4.7 and 4.8).

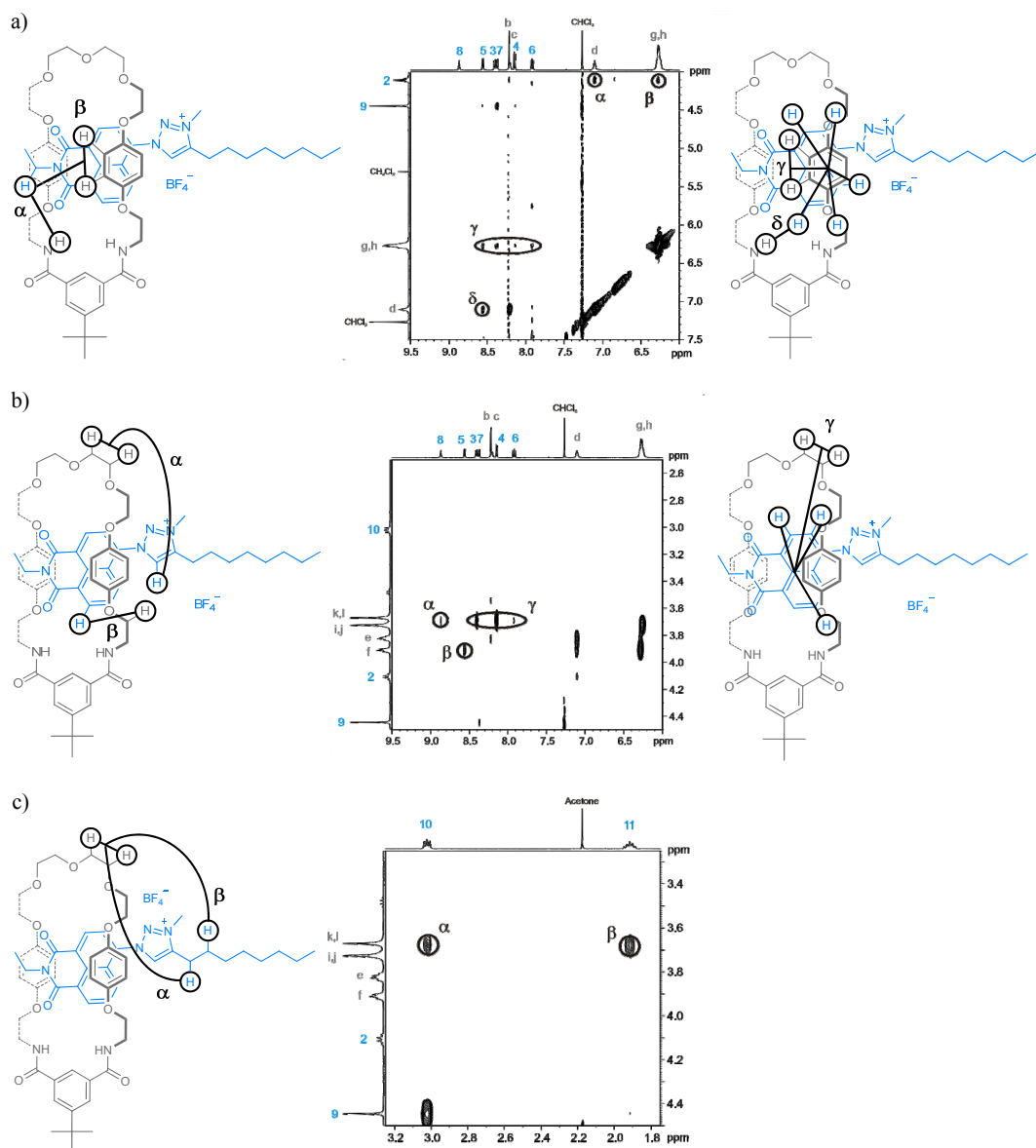


Figure 4.7 Portions of the ^1H - ^1H NMR ROESY spectrum of $1\cdot 64\cdot \text{BF}_4$ (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures.

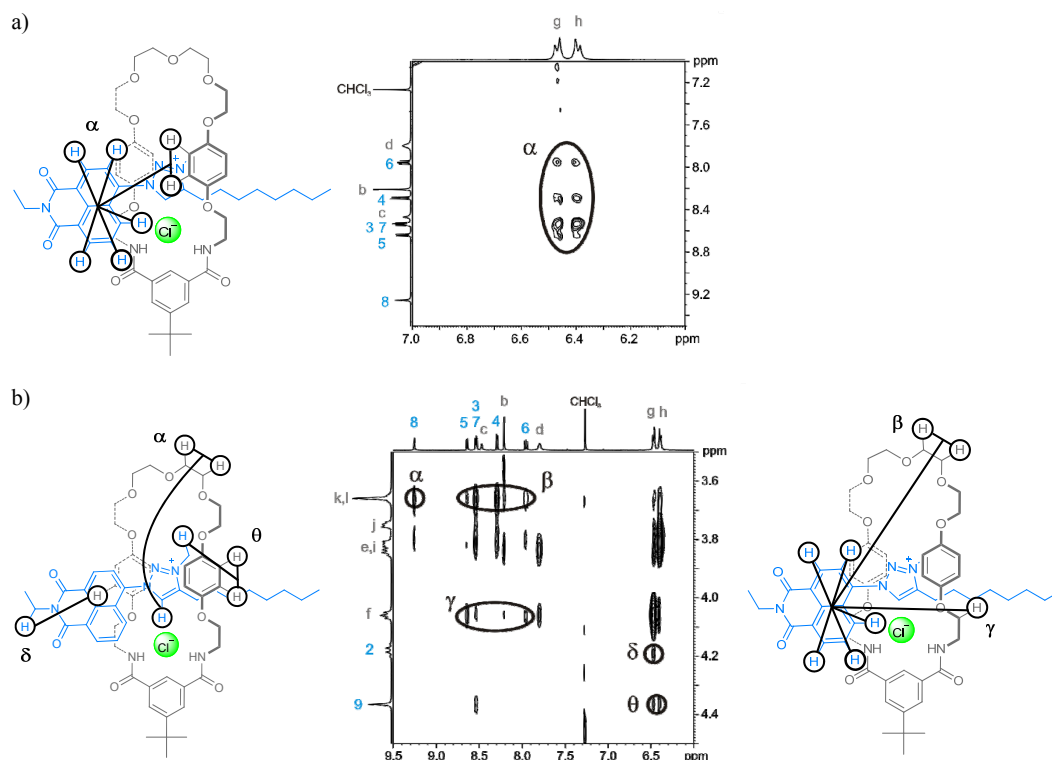


Figure 4.8 Portions of the ^1H - ^1H NMR ROESY spectrum of $1 \cdot 64 \cdot \text{Cl}$ (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures.

To quantify the stabilities of the two assemblies, ^1H NMR pseudorotaxane titrations were carried out in CDCl_3 . Both $64 \cdot \text{BF}_4$ and $64 \cdot \text{Cl}$, were titrated into solutions of macrocycle 1 and the signals corresponding to the hydroquinone protons g and h monitored throughout each titration (Figure 4.9). Association constants were obtained by WinEQNMR2²⁴ analysis, which determined values of $830(30) \text{ M}^{-1}$ for $1 \cdot 64 \cdot \text{BF}_4$ and $800(20) \text{ M}^{-1}$ for $1 \cdot 64 \cdot \text{Cl}$. Thus, the two pseudorotaxane assemblies exhibit similar thermodynamic stabilities compared to the respective threading components, $64 \cdot \text{BF}_4$ and $64 \cdot \text{Cl}$. However, it should be noted that the latter value is an apparent 1:1 association constant for a ternary complex (as discussed in Section 2.4.2), whilst the former, with the non-coordinating tetrafluoroborate anion, is a true 1:1 association constant.

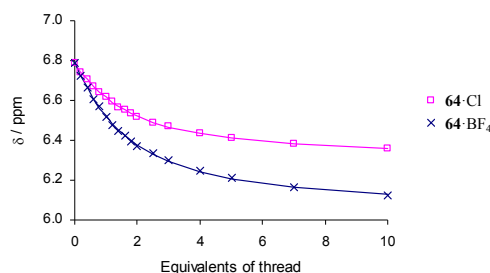


Figure 4.9 Changes in the chemical shift of hydroquinone protons (g and h) in **1** upon addition of thread (**64**·BF₄ or **64**·Cl) in CDCl₃ at 293K (500 MHz, 1.0 × 10⁻³ M). Symbols represent experimental data points; lines represent calculated titration curves.

The pseudorotaxane association constant for **1**·**64**·BF₄ reflects the strength of intercomponent naphthalimide-hydroquinone donor-acceptor and imide-amide hydrogen bonding interactions present in this assembly. In contrast, the value for **1**·**64**·Cl represents only the intercomponent triazolium-hydroquinone donor-acceptor and macrocycle-halide hydrogen bonding contributions, and does not take into account the electrostatic and hydrogen bonding interactions between the triazolium thread and the chloride anion, as these are already present in **64**·Cl. However, the triazolium-halide ion-pair interaction is highly favourable in this non-competitive solvent mixture, both in **64**·Cl and **1**·**64**·Cl, and thus can be said to drive the anion-induced co-conformational change exhibited by **1**·**64**·BF₄ upon the addition of TBACl in CDCl₃ (Scheme 4.4 and Figure 4.6).

Attempts were made to study both the formation and co-conformations of the pseudorotaxane assemblies using UV/Vis spectroscopy in CHCl₃. These titrations were undertaken at the same concentration as the ¹H NMR experiments (1 × 10⁻³ M) to avoid the need for large excesses of either component, both of which are UV active. Upon addition of macrocycle **1** to thread **64**·BF₄ (Figure 4.10a), the appearance and increase in macrocycle absorbance (Figure 4.10b) was accompanied by a decrease in absorption and a slight bathochromic shift in the naphthalimide triazolium band. Hence, the donor-acceptor interactions between the macrocycle hydroquinone groups and the naphthalimide triazolium thread responsible for pseudorotaxane assembly result in significant perturbations in the UV/Vis spectra.

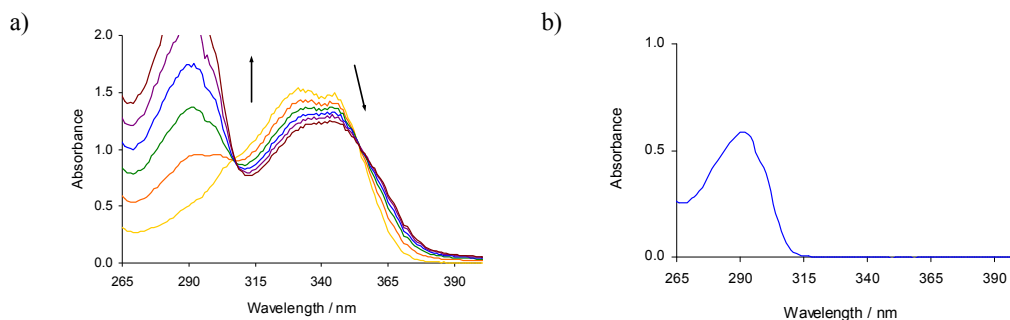


Figure 4.10 UV/Vis spectra in CHCl_3 at 293 K of a) thread $\mathbf{64} \cdot \text{BF}_4$ ($1.0 \times 10^{-3} \text{ M}$) upon addition of 0.0, 1.0, 2.0, 3.0, 4.0 and 5.0 equivalents of macrocycle **1**, and b) macrocycle **1** ($1.0 \times 10^{-5} \text{ M}$). Note: a different pathlength cuvette was used in the spectrum in b).

To investigate whether changes in the pseudorotaxane co-conformation could also be observed by UV/Vis spectroscopy, the effect of chloride addition to solutions of $\mathbf{64} \cdot \text{BF}_4$ and **1** was studied, however no changes in absorbance were observed.

Similar pseudorotaxane fluorescence investigations were not possible at this concentration, hence it was decided to proceed to the synthesis of an analogous naphthalimide triazolium rotaxane and study its fluorescent properties in detail.

4.2.4 Summary

The anion binding and fluorescence sensing properties of receptor $\mathbf{64} \cdot \text{BF}_4$, containing the novel naphthalimide triazolium motif, were investigated, with anion complexation found to result in considerable changes in emission intensity.

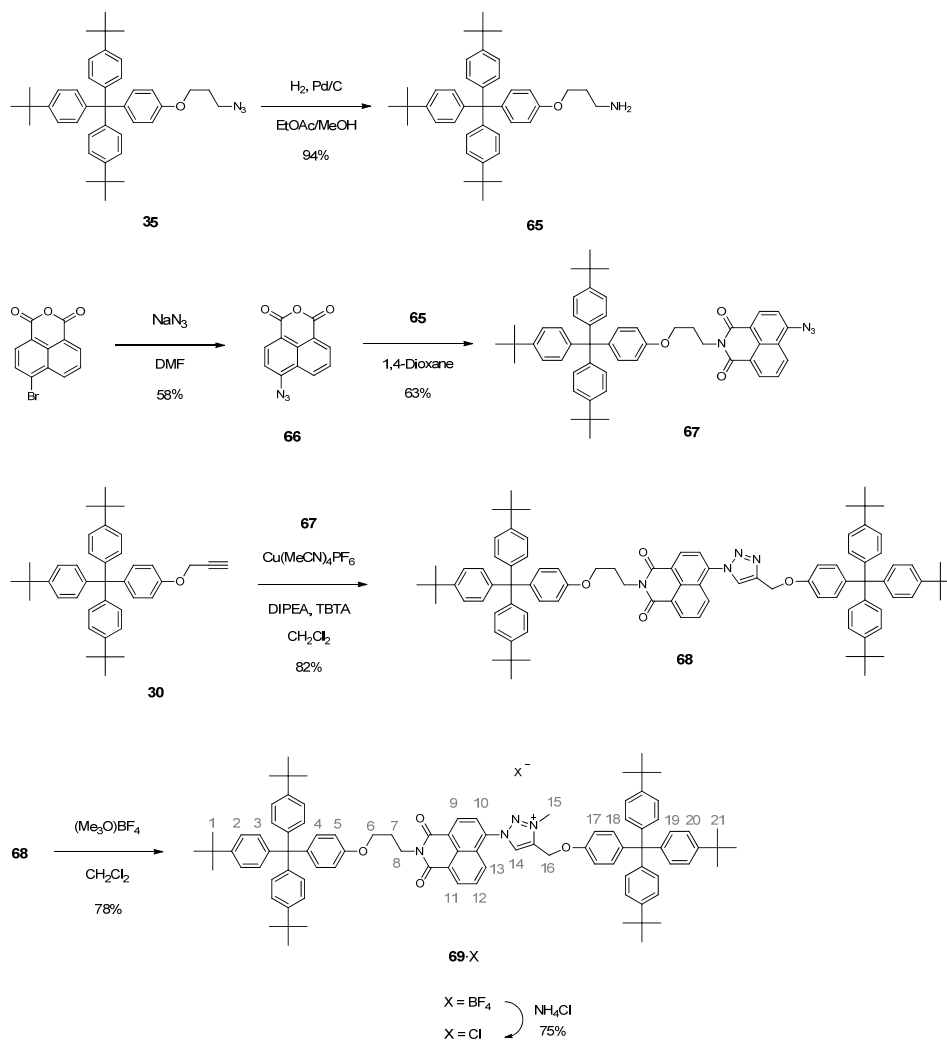
The ability of receptor $\mathbf{64} \cdot \text{BF}_4$ to act as a threading component with macrocycle **1** in the formation of pseudorotaxane assemblies of different co-conformations in the presence and absence of a coordinating halide anion were confirmed using ^1H NMR studies. In addition, pseudorotaxane formation was signalled by significant changes in the absorbance band of the naphthalimide triazolium thread, although changes in the co-conformation of the interpenetrated assembly were not detectable by UV/Vis spectroscopy.

4.3 Naphthalimide Triazolium Rotaxane

Encouraged by the pseudorotaxane findings, the construction of an interlocked rotaxane structure incorporating the naphthalimide triazolium motif was undertaken with the expectation that this system would be capable of undergoing anion-induced, controlled molecular motion. It was hoped that the interlocked nature of the host structure would enable the effective signalling of co-conformational changes by UV/Vis absorbance perturbations. Furthermore, the fluorescent properties of the rotaxane would be investigated.

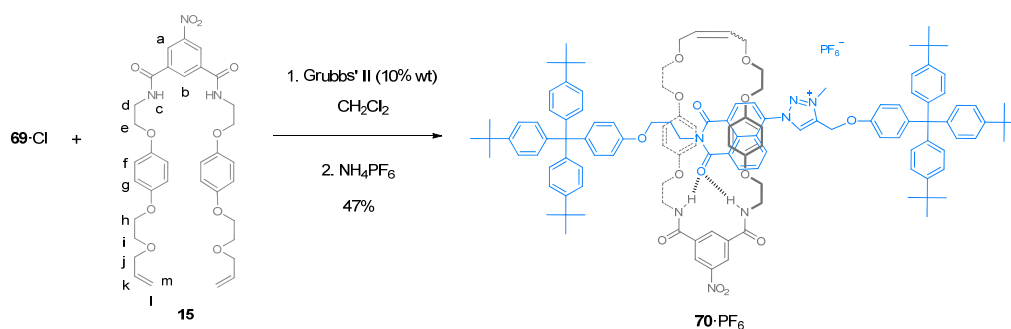
4.3.1 Rotaxane Synthesis and Characterisation

Initially, the synthesis of a stoppered naphthalimide triazolium axle (**69**·Cl) was carried out as detailed in Scheme 4.5. Stoppered azide **35** (synthesised as described in Scheme 3.2) was reduced using Pd/C and H₂,¹¹ with amine **65** isolated in a yield of 94%. A condensation reaction between **65** and 4-azido-1,8-naphthalic anhydride (**66**), synthesised from 4-bromo-1,8-naphthalic anhydride,²⁵ afforded stoppered naphthalimide azide **67** in 63% yield. Alkyne **30** (Scheme 2.18) and **67** then underwent a copper(I)-catalysed “click” reaction, which was followed by methylation using (Me₃O)BF₄ to give triazolium axle **69**·BF₄. Finally, anion exchange to the target chloride salt **69**·Cl was achieved in a yield of 75%.



Scheme 4.5 Synthesis of naphthalimide triazolium axle **69·Cl**.

This asymmetric axle component was then utilised for rotaxane formation with bis-vinyl macrocycle precursor **15**, employing the previously described anion templated RCM ‘clipping’ method (Chapters Two and Three). Reaction of **69·Cl** with 1.5 equivalents of **15** in dry CH_2Cl_2 with Grubbs’ second-generation RCM catalyst afforded the target rotaxane **70·PF₆** (Scheme 4.6), which was isolated in 47% yield. Purification required exchange of the chloride template to the non-coordinating hexafluorophosphate counter anion between the application of two different preparative silica gel thin layer chromatographic conditions.



Scheme 4.6 Synthesis of naphthalimide triazolium rotaxane **70**·PF₆.

The ¹H NMR spectrum of rotaxane **70**·PF₆, along with the spectra of axle **69**·BF₄ and macrocycle precursor **15**, is shown in Figure 4.11. Upon rotaxane formation, the signals associated with the hydroquinone environments f and g move significantly upfield ($\Delta\delta = -0.9$ ppm) due to the expected donor-acceptor interactions. This shift is consistent with the proposed co-conformation of **70**·PF₆, based on that observed for pseudorotaxane **1**·**64**·BF₄ (Figure 4.6). In addition, macrocycle protons b and c shifted downfield, presumably due to hydrogen-bonding interactions with the axle imide group, along with axle triazolium proton 14.

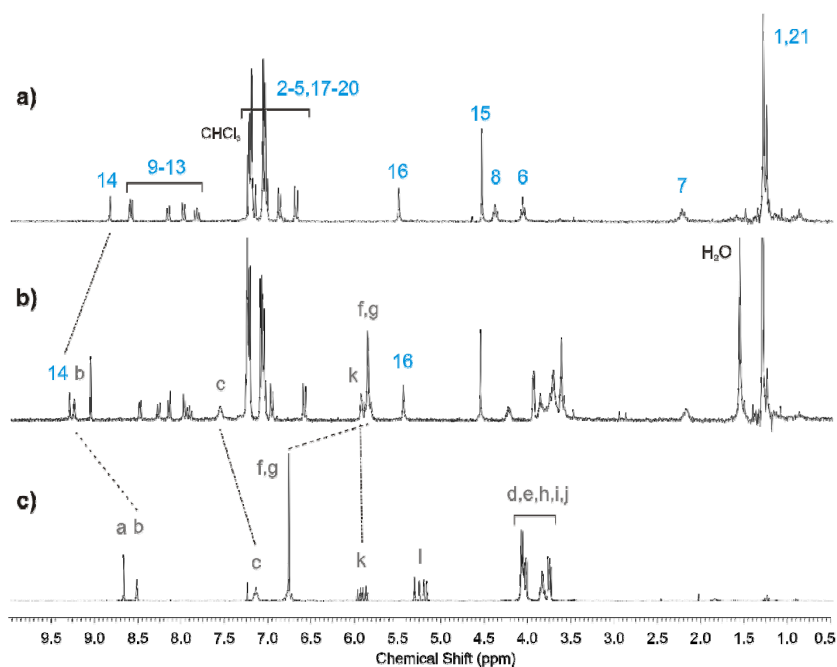


Figure 4.11 ¹H NMR spectra (300 MHz) in CDCl₃ at 293 K of a) axle **69**·BF₄, b) rotaxane **70**·PF₆, and c) macrocycle precursor **15**.

Further characterisation of the interlocked product was provided by high resolution electrospray MS and 2D ^1H - ^1H NMR ROESY spectroscopy. The observed intercomponent couplings are shown in Figure 4.12 and support the proposed co-conformation. For example, through-space interactions were observed between axle alkyl protons 7 and 8, and macrocycle hydroquinone protons f and g (α and β in Figure 4.12a).

Importantly, rotaxane formation was also attempted in the absence of the coordinating halide counter anion by using axle **69**·BF₄, however no rotaxane product was observed in the reaction mixture. This may be rationalised when taking into account that the formation of the analogous pseudorotaxane assembly constructed in the absence of chloride, **1**·**64**·BF₄, is driven by the donor-acceptor interactions between the macrocycle hydroquinone and axle naphthalimide groups. The preorganisation of the hydroquinone groups of **1** is necessary for this association to occur, but does not exist in macrocycle precursor **15** and is only created in the RCM reaction. Therefore, the synthesis of rotaxane **70**·PF₆ requires the presence of a chloride anion, which successfully templates the association of the two components prior to macrocycle formation by virtue of binding interactions with the axle triazolium and macrocycle precursor isophthalamide groups.

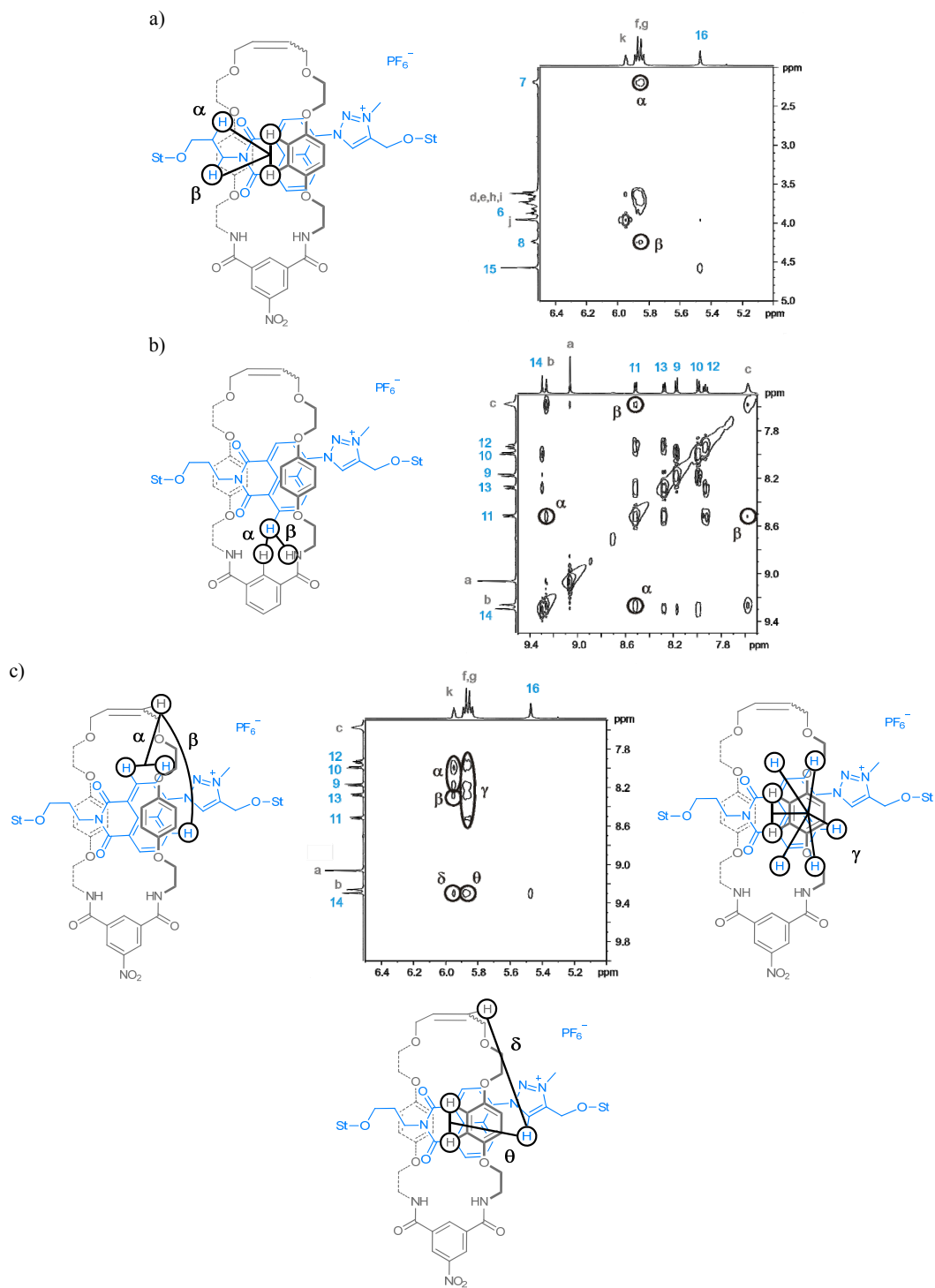
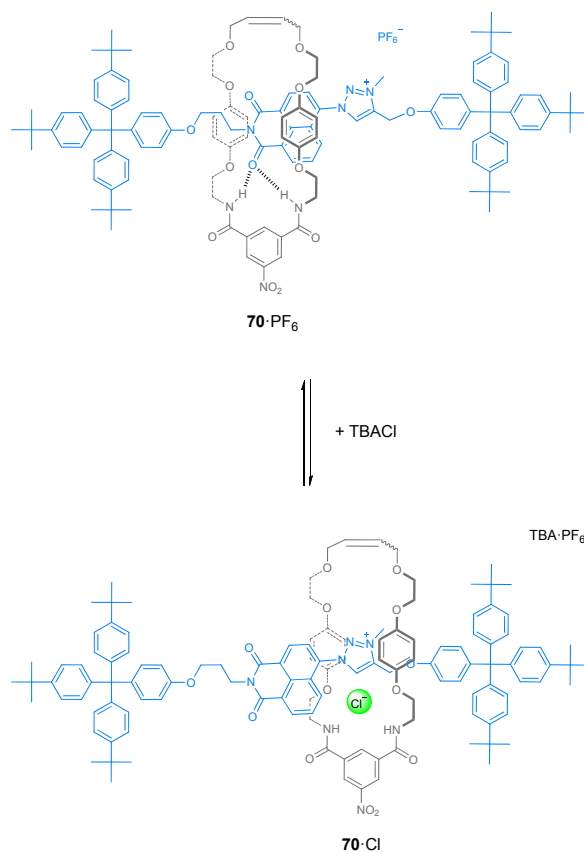


Figure 4.12 Portions of the ^1H - ^1H NMR ROESY spectrum of $70 \cdot \text{PF}_6$ (CDCl_3 , 500 MHz, 293K). Intercomponent correlations are marked on the structures (St = terphenyl).

4.3.2 Anion-Induced Shuttling NMR Studies

Having synthesised naphthalimide triazolium rotaxane **70**·PF₆, ¹H NMR spectroscopy was used to investigate its chloride anion induced co-conformational behaviour (Scheme 4.7).



Scheme 4.7 Anion-induced molecular shuttling exhibited by rotaxane **70**·PF₆.

The ¹H NMR spectrum of rotaxane **70**·PF₆ in CDCl₃ is shown in Figure 4.13, along with the spectrum observed after addition of one equivalent of TBACl. Downfield shifts in protons 14, b, c, f and g were observed, as well as a significant upfield shift in the signal corresponding to axle protons 16. The downfield shifts in protons 14, b and c are indicative of cooperative hydrogen bonding to the chloride anion by the macrocycle isophthalamide and axle triazolium binding motifs. The creation of a unique anion binding cavity within the rotaxane requires macrocycle translocation (Scheme 4.7), and the different extents of shielding associated with the two rotaxane co-conformations are reflected in

the shifts observed for protons f, g and 16. The macrocycle hydroquinone protons experience a greater shielding effect when they reside over the naphthalimide group of the axle in the starting co-conformation (**70**·PF₆), compared with over the triazolium group in **70**·Cl. This reduction in shielding results in a downfield shift of macrocycle hydroquinone protons f and g after the addition of TBACl (Figure 4.13b), and is similar to that observed between pseudorotaxane co-conformations **1**·**64**·BF₄ and **1**·**64**·Cl (Figure 4.6). Moreover, when the macrocycle resides over the triazolium group, axle CH₂ protons 16 become partially shielded by the hydroquinone groups. This shielding effect is not present in **70**·PF₆, thus an upfield shift in the signal corresponding to protons 16 is observed upon halide anion addition. It is notable that only minimal shifts in the axle naphthalimide protons were observed upon chloride addition to the rotaxane, indicating no significant interactions between these protons and the halide anion.

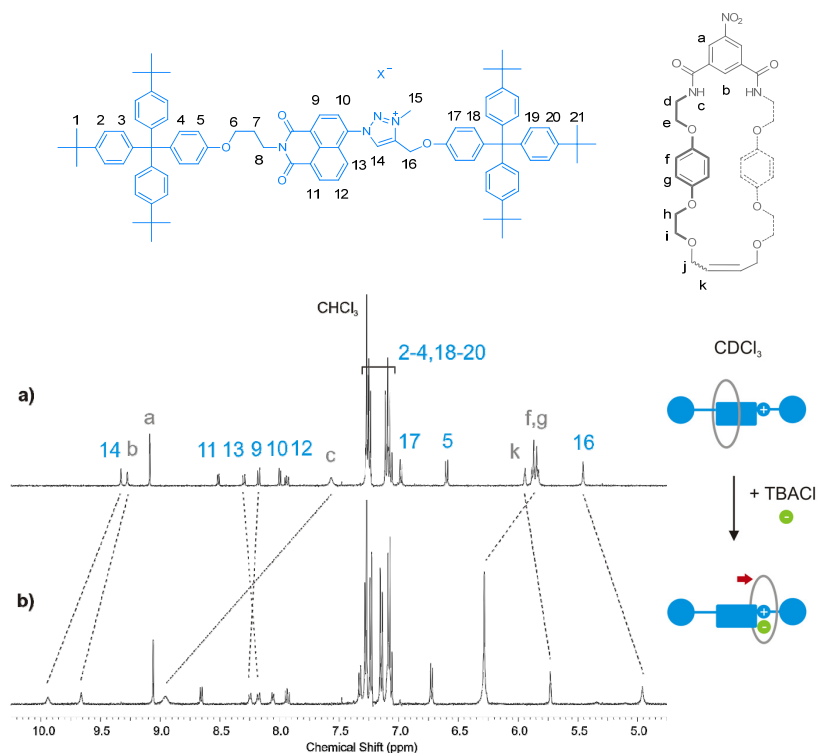


Figure 4.13 Partial ¹H NMR spectra (500 MHz, 2.0 × 10⁻³ M) in CDCl₃ at 293 K of a) rotaxane **70**·PF₆, and b) rotaxane **70**·PF₆ + 1.0 equivalent of TBACl.

Crystals suitable for single-crystal X-ray diffraction structural determination of rotaxane **70**·Cl were analysed by Dr. Matseusz Pitak (National Crystallography Service, University of Southampton) using synchrotron radiation at Diamond Light Source beamline I19. The co-conformation of the interlocked structure in the solid state is in agreement with that proposed for the solution phase, namely with the macrocycle hydroquinone groups residing over the axle triazolium group (Figure 4.14). Importantly, the chloride anion is bound within the rotaxane host cavity by hydrogen bonding interactions to protons b, c, 14 and 16, with distances of C-H^b...Cl⁻ 3.348(9) Å, N-H^c...Cl⁻ 3.218(8) Å, N-H^{c'}...Cl⁻ 3.297(8) Å, C-H¹⁴...Cl⁻ 3.309(6) Å and C-H¹⁶...Cl⁻ 3.391(6) Å.

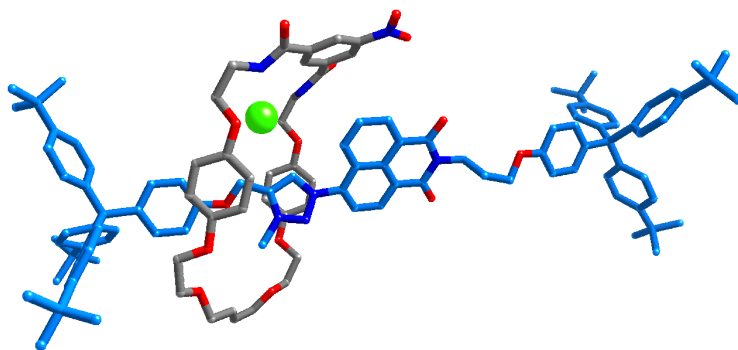


Figure 4.14 Crystal structure of rotaxane **70**·Cl. Protons and lower occupancy positions of disorder are omitted for clarity.

Further examination of the crystalline network reveals that the naphthalimide group of the axle component is involved in donor-acceptor interactions with a hydroquinone group of an adjacent rotaxane molecule (centroid-to-centroid distance 3.471(4) Å, ring dihedral angle 8.3(3)°), as shown in Figure 4.15. This illustrates the potential for this interaction, with the analogous intercomponent donor-acceptor interactions responsible for the proposed solution phase co-conformation of **70**·PF₆.

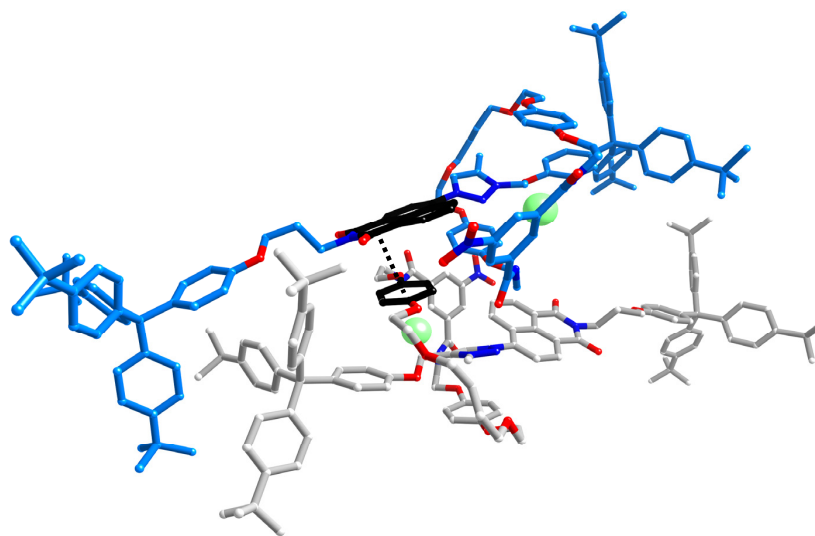


Figure 4.15 Inter-rotaxane donor-acceptor interactions present in the crystalline network of **70·Cl**.

The anion-induced co-conformational change exhibited by naphthalimide triazolium rotaxane was further supported by 2D ^1H - ^1H NMR ROESY spectroscopy, as the observed intercomponent couplings were in agreement with the proposed solution phase co-conformation of **70·Cl** (Figure 4.16). Specifically, through-space interactions between terphenyl stopper axle protons 17 and macrocycle hydroquinone protons f and g were observed (α in Figure 4.16a), whilst in contrast with the ROESY spectrum of **70·PF₆** (Figure 4.12), there were no couplings between the hydroquinone protons and axle alkyl protons 7 and 8.

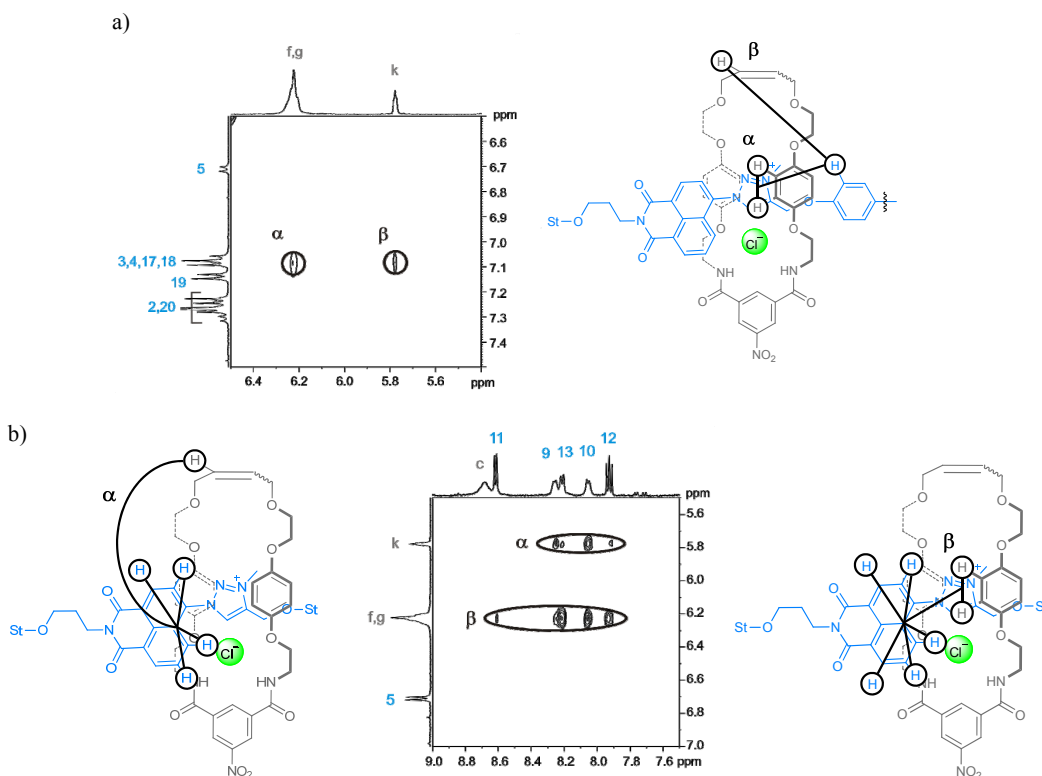


Figure 4.16 Portions of the ^1H - ^1H NMR ROESY spectrum of **70**·Cl (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structures (St = terphenyl).

On account of the change in rotaxane co-conformation being driven by the hydrogen bonding interactions between the isophthalamide and triazolium groups of **70**· PF_6 and the coordinated chloride anion, increasing the competitive nature of the solvent *via* protic solvent addition should weaken these interactions and eventually reverse the molecular motion shuttling process. Upon addition of increasing amounts of CD_3OD to a CDCl_3 solution of **70**·Cl (Figure 4.17), the observed ^1H NMR shifts indicated that macrocycle translocation back to the initial co-conformation was indeed occurring – the spectrum for 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$ is shown in Figure 4.17b. The loss of the halide anion from the rotaxane binding cavity is reflected in an upfield shift in isophthalamide proton b (the signals corresponding to triazolium proton 14 and amide protons c were not observed after CD_3OD addition due to deuterium exchange). The return to the starting co-conformation, and the associated changes in the shielding effects, is evidenced by an upfield shift in hydroquinone protons f and g and a downfield

shift in axle protons 16 – the reverse of the shifts observed upon chloride anion addition to **70**·PF₆ in CDCl₃ (Figure 4.13).

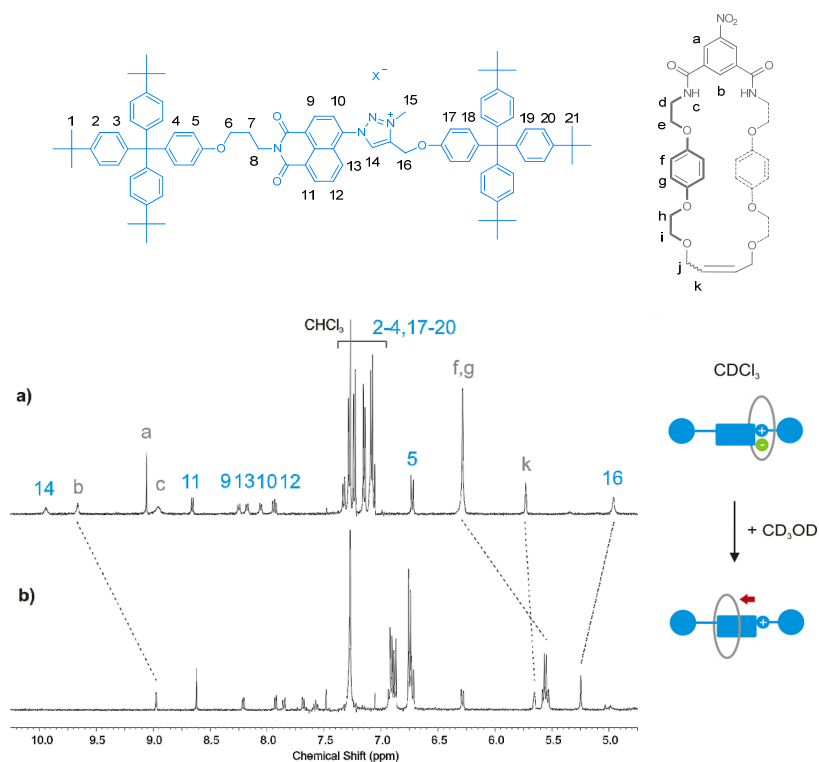


Figure 4.17 Partial ¹H NMR spectra (500 MHz, 2.0 × 10^{−3} M) at 293 K of a) rotaxane **70**·PF₆ + 1.0 equivalent of TBACl in CDCl₃, and b) rotaxane **70**·PF₆ + 1.0 equivalent of TBACl in 1:1 CDCl₃/CD₃OD.

The change in rotaxane co-conformation can be monitored by following the relative positions of the macrocycle hydroquinone and alkene proton signals throughout the halide and CD₃OD ¹H NMR titration experiments (Figure 4.18). These protons are not involved in anion binding and their shifts reflect the different extents of donor-acceptor interactions and associated shielding effects present in the two co-conformations. The gradual changes in the relative positions of these peaks indicate that the molecular motion exhibited by rotaxane **70**·PF₆ is a dynamic process which is fast on the NMR timescale. Importantly, the shuttling behaviour is reversible and can be controlled by dual stimulus – namely halide anion addition followed by an increase in the competitive nature of the solvent.

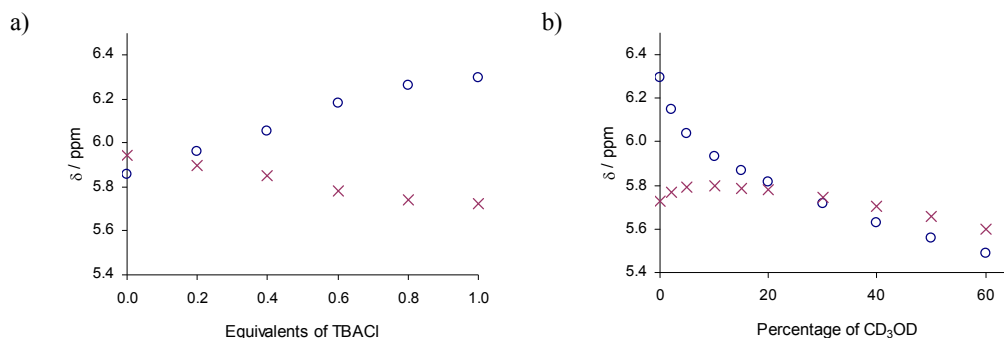


Figure 4.18 Changes in the chemical shift of alkene protons k (×) and hydroquinone protons f and g (o) in rotaxane **70**·PF₆ in CDCl₃ at 293 K upon a) addition of TBACl, and b) subsequent addition of CD₃OD.

4.3.3 Anion Binding NMR Studies

The anion binding properties of rotaxane **70**·PF₆ with a range of TBA anion salts – chloride, bromide, iodide, dihydrogen phosphate and acetate – were investigated by ¹H NMR titration experiments. Whilst complexation was too strong for accurate association constant values to be determined in CDCl₃, anion binding did not occur in the more competitive 1:1 CDCl₃/CD₃OD solvent mixture which was used both for the imidazolium rotaxanes in Chapter Two and for triazolium rotaxane **1.45** (Figure 1.32b).²⁶ This is presumably due to the extra energetic cost of macrocycle translocation required for the formation of the interlocked host cavity in **70**·PF₆. Hence, the intermediate 4:1 CDCl₃/CD₃OD solvent mixture was used.

Upon addition of TBACl to **70**·PF₆ in these solvent conditions, a downfield shift for macrocycle isophthalamide C-H proton b was observed (Figure 4.19). Initial downfield shifts for the axle triazolium proton 14 and macrocycle amide N-H protons c were also observed, however it was not possible to follow these protons throughout the titration due to deuterium exchange. Additional shifts occurred for the signals corresponding to protons 16, f, g and k, due to the shielding effects discussed previously and seen in Figure 4.13.

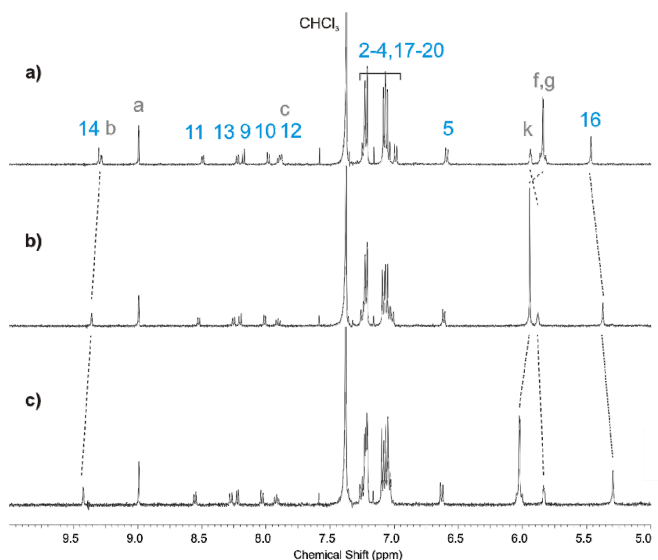


Figure 4.19 Partial ^1H NMR spectra (500 MHz, 2.0×10^{-3} M) in 4:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$ at 293 K of a) rotaxane $70\cdot\text{PF}_6$, b) rotaxane $70\cdot\text{PF}_6$ plus 1.0 equivalent of TBACl, and c) rotaxane $70\cdot\text{PF}_6$ plus 5.0 equivalents of TBACl.

During the titration experiments with bromide, iodide, acetate and dihydrogen phosphate, downfield shifts in macrocycle isophthalamide and amide anion binding protons b and c were observed as expected, however axle triazolium proton 14 exhibited anion dependent differential behaviour. Before deuterium exchange, this proton signal shifted downfield upon addition of chloride and dihydrogen phosphate, did not shift significantly upon bromide and acetate addition, and shifted slightly upfield with iodide (Figure 4.20). These contrasting observations are thought to be the consequence of the combination of downfield and upfield perturbations resulting from hydrogen bonding interactions with the anion and increased shielding from the hydroquinone groups upon macrocycle translocation. The relative magnitudes of these effects are likely to be dependent on the nature of the anion, relating to anion basicity and any differences in the exact co-conformation of the rotaxane host structure.

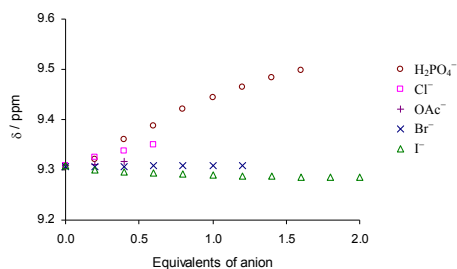


Figure 4.20 Changes in the chemical shift of triazolium proton 14 in **70**·PF₆ upon addition of anions in 4:1 CDCl₃/CD₃OD at 293 K before broadening due to deuterium exchange.

Using WinEQNMR2, 1:1 stoichiometric association constants were determined from the titration data by monitoring macrocycle isophthalamide proton b of the rotaxane host (Figure 4.21 and Table 4.4). This proton is directly involved in anion binding and could be accurately monitored throughout all titration experiments.

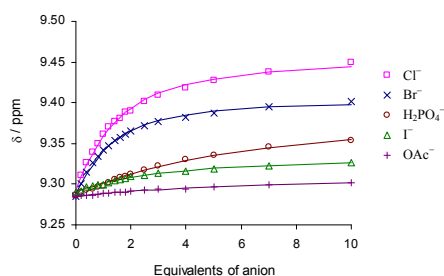


Figure 4.21 Changes in the chemical shift of isophthalamide proton b in **70**·PF₆ upon addition of anions in 4:1 CDCl₃/CD₃OD at 293 K. Symbols represent experimental data points; lines represent calculated titration curves.

Table 4.4 Association constants, K (M⁻¹), of rotaxane **70**·PF₆ with anions in 4:1 CDCl₃/CD₃OD at 293 K. Obtained by monitoring proton b. Errors are given in parentheses.

Anion	K (M ⁻¹)
Cl ⁻	527 (47)
Br ⁻	673 (7)
I ⁻	173 (17)
H ₂ PO ₄ ⁻	83 (6)
OAc ⁻	59 (1)

Table 4.4 shows that the smaller halide anions – chloride and bromide – are bound with considerable higher affinity than the larger iodide and more basic oxoanions dihydrogen phosphate and acetate. This is due to the three dimensional anion binding cavity created within the interlocked structure upon co-conformational change, which is of complementary size and shape for the smaller halide guest species, with bromide bound slightly more strongly than chloride.

The possibility of a different binding mode, external to the rotaxane cavity, for the larger anions (iodide, dihydrogen phosphate and acetate) is supported by differential shifts observed for axle CH₂ protons 16 during the titration experiments (Figure 4.22). These protons shifted significantly upfield upon addition of chloride and bromide ($\Delta\delta = -0.19$ and -0.16 ppm respectively after 10.0 equivalents), assigned to increased shielding from hydroquinone groups upon macrocycle translocation. In contrast, very slight downfield shifts of 0.02–0.05 ppm occurred with the larger anions indicating that any alteration in the relative position of the macrocycle upon addition of iodide and the oxoanions is not sufficient to perturb these protons.

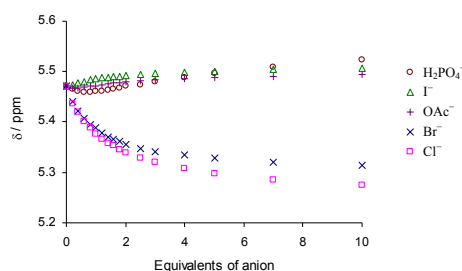


Figure 4.22 Changes in the chemical shift of CH₂ protons 16 in **70**·PF₆ upon addition of anions in 4:1 CDCl₃/CD₃OD at 293 K.

Some change in the co-conformation of the rotaxane host **70**·PF₆ is necessary for all of the anions to interact with both axle and macrocycle C-H and amide N-H hydrogen bond donor anion binding motifs, however these ¹H NMR shifts indicate that complete macrocycle translocation from the naphthalimide group of the axle to the triazolium group (as seen in the solid state, Figure 4.14) only occurs with the strongly bound chloride and bromide anions. The larger anions are not able to bind effectively within the rotaxane host cavity, resulting in weaker complexation and a reduction in the extent of macrocycle translocation, presumably to retain some of the favourable naphthalimide-

hydroquinone donor-acceptor interactions. This potential selectivity is also supported by the behaviour of hydroquinone and alkene protons (f, g and k) during the titrations (Figure 4.23 and Table 4.5). Considerably smaller perturbations were observed with iodide, dihydrogen phosphate and acetate than with chloride and bromide, again indicating that the extent of co-conformational change is much less with the weaker bound anions.

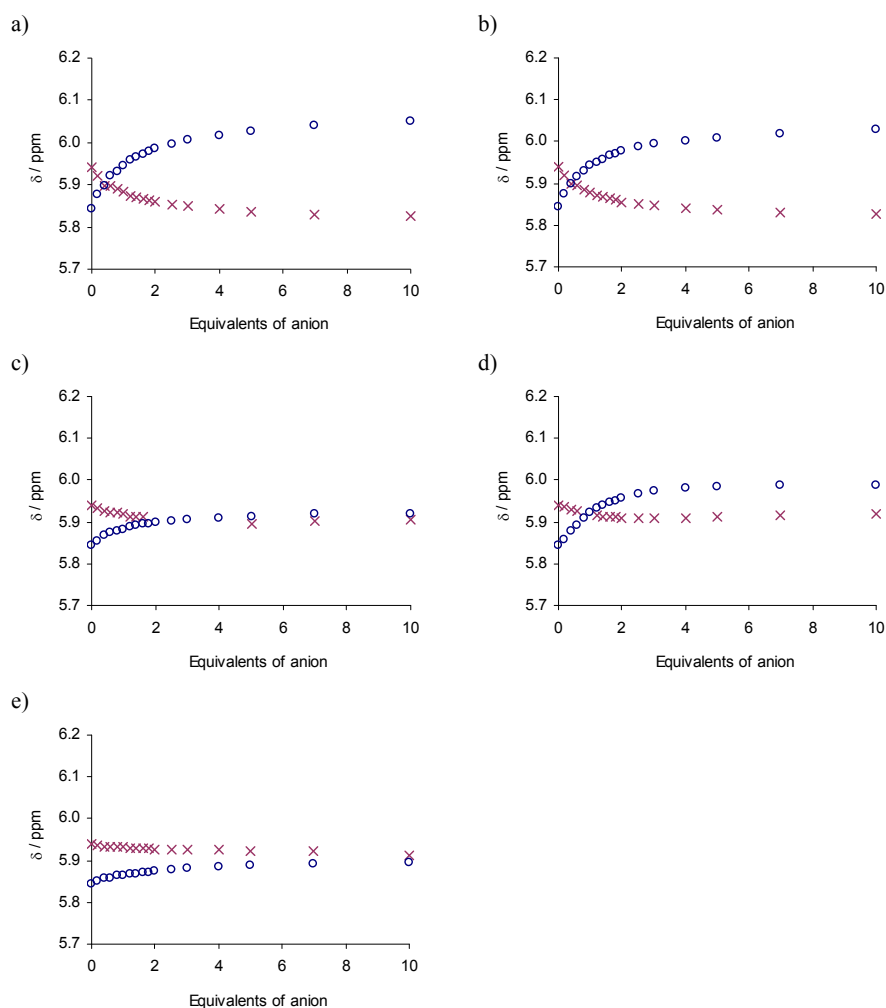


Figure 4.23 Changes in the chemical shift of alkene protons k (x) and hydroquinone protons f and g (o) for **70**·PF₆ in 4:1 CDCl₃/CD₃OD at 293 K upon addition of a) TBACl, b) TBABr, c) TBAI, d) TBAH₂PO₄, and e) TBAOAc.

Table 4.5 Final differences in the chemical shifts of hydroquinone protons (f and g) and alkene protons (k) in **70**·PF₆ upon addition of 10.0 equivalents of anion in 4:1 CDCl₃/CD₃OD at 293 K.

Anion	$\Delta\delta$ (ppm)
Cl ⁻	+ 0.23
Br ⁻	+ 0.20
I ⁻	+ 0.01
H ₂ PO ₄ ⁻	+ 0.07
OAc ⁻	- 0.02

It is noteworthy that some selectivity within the halides is displayed by triazolium rotaxane **70**·PF₆, in contrast to the lack of halide discrimination exhibited by the imidazolium rotaxane hosts in Chapter Two. Similar selectivity has also been observed for a number of other anion templated rotaxane systems based on the triazolium motif investigated in the Beer Group,²⁷ with chloride and bromide bound significantly more strongly than iodide, and is evidently due to the unique properties of triazolium-isophthalamide interlocked binding cavities.

4.3.4 UV/Vis Studies

Having quantified the selectivity in the anion-induced shuttling of rotaxane **70**·PF₆ using ¹H NMR titration experiments, investigations were then carried out into whether the change in the interlocked co-conformation could be detected by UV/Vis spectroscopy. The magnitude of any such response to different anions and the reversibility of the molecular motion were studied in the less competitive CHCl₃ solvent conditions, to ensure saturation in binding, and the associated co-conformational changes, after the addition of only several equivalents of anion.

As previously observed for naphthalimide triazolium thread **64**·BF₄ (Section 4.2.2), axle **69**·BF₄ did not display any perturbations in its UV/Vis spectrum upon addition of anions in CHCl₃ (Figure 4.24a). However, the addition of TBACl to rotaxane **70**·PF₆ yielded a slight hypsochromic shift of the naphthalimide absorbance band, along with an enhancement in absorption (Figure 4.24b). These gradual changes were observed upon addition of up to two equivalents of chloride, after which the UV/Vis spectra remained unchanged. Hence, the relative position of the macrocycle within the

rotaxane host structure does indeed affect the naphthalimide absorbance band, presumably due to changes in the donor-acceptor interactions present in the two co-conformations. It is thought that macrocycle translocation is signalled effectively, in contrast to the pseudorotaxane assemblies, due to the interlocked nature of rotaxane **70**·PF₆.

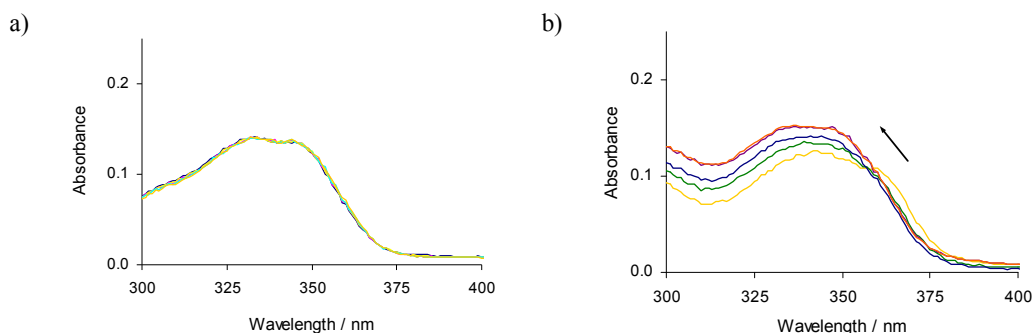


Figure 4.24 Changes in the UV/Vis spectra of a) axle **69**·BF₄, and b) rotaxane **70**·PF₆, in CHCl₃ (1.0×10^{-5} M) at 293 K upon addition of 0.0, 0.5, 1.0, 2.0 and 5.0 equivalents of TBACl.

Similar perturbations were also observed upon addition of bromide, iodide and dihydrogen phosphate to rotaxane **70**·PF₆ and are shown in Figure 4.25.²⁸ With chloride and bromide, increases in absorbance at 340 nm of 15% and 16% were observed after saturation, whilst dihydrogen phosphate addition resulted in a considerably smaller change of 6% (Table 4.6). This indicates that the reduced extent of macrocycle translocation with the larger oxoanion is reflected directly in the UV/Vis response to dihydrogen phosphate. However, although complete macrocycle translocation was also not observed for iodide in the ¹H NMR studies, this was not evident in the UV/Vis investigations, in which a 14% increase in absorbance occurred upon iodide addition.

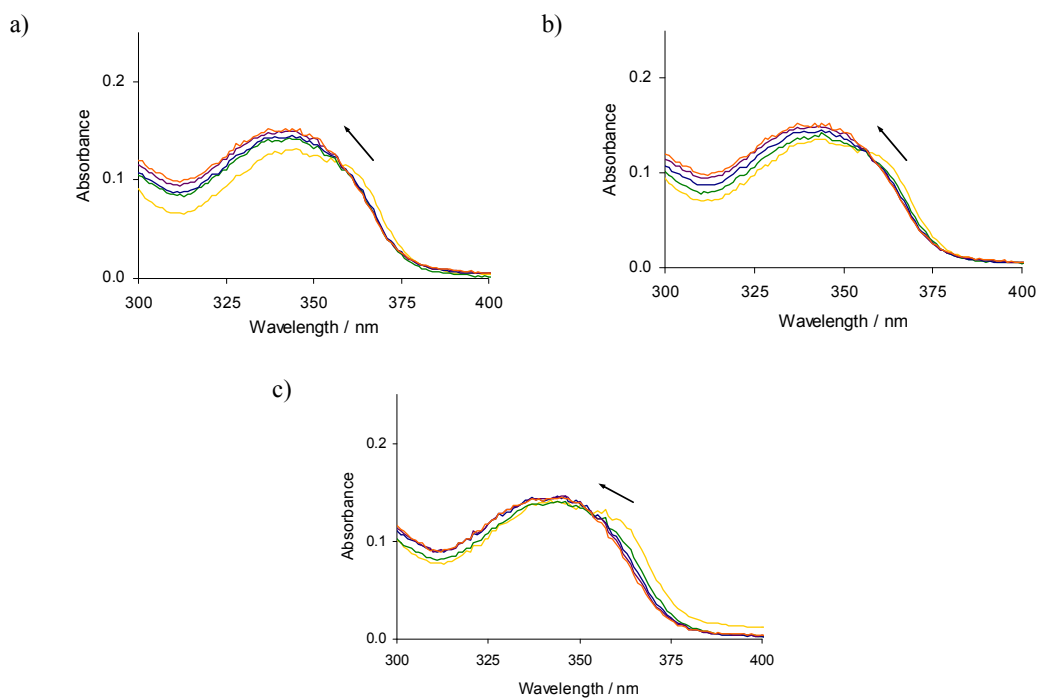


Figure 4.25 UV/Vis spectra of rotaxane **70**·PF₆ in CHCl₃ (1.0 × 10⁻⁵ M) at 293 K upon addition of 0.0, 0.5, 1.0, 2.0 and 5.0 equivalents of a) TBABr, b) TBAI, and c) TBAH₂PO₄.

Table 4.6 Percentage increases of absorbance at 340 nm after saturation for the addition of anions to rotaxane **70**·PF₆ in CHCl₃ (1.0 × 10⁻⁵ M) at 293 K.

Anion	Absorbance increase (%)
Cl ⁻	15
Br ⁻	16
I ⁻	14
H ₂ PO ₄ ⁻	6

To investigate whether the reversibility of this shuttling behaviour could be demonstrated, an excess of AgPF₆ was added to a solution of the rotaxane **70**·PF₆ in the presence of five equivalents of TBACl. The solution was sonicated to aid complete anion exchange by virtue of silver salt precipitation and filtered through Celite[®].²⁹ Importantly, the naphthalimide absorbance band was then shifted back to its initial position (Figure 4.26), indicating a return to the original co-conformation.

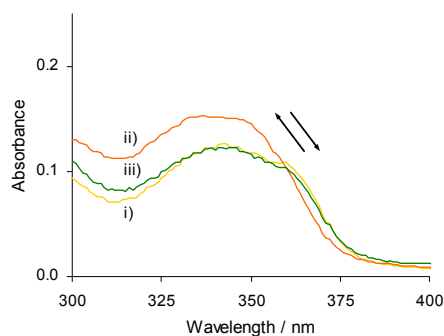


Figure 4.26 UV/Vis spectra in CHCl_3 at 293 K of i) rotaxane **70**· PF_6 (1.0×10^{-5} M), ii) after addition of 5.0 equivalents of TBACl, and iii) after subsequent addition of AgPF_6 and filtration.

4.3.5 Fluorescence Investigations

The fluorescent properties of this system was also investigated, however both axle **69**· BF_4 and rotaxane **70**· PF_6 displayed negligible excitation dependent emission in a number of different solvents, and produced minor, irreproducible responses to anions. It was thought that the rotaxane system might exhibit reduced fluorescence due to quenching effects arising from the proximity of the macrocycle component to the fluorophore, but these results indicate that this is not the reason for the ineffective fluorescence behaviour observed for both the axle and the rotaxane.

Whilst the naphthalimide triazolium motif has the potential for complicating twisted internal charge transfer (TICT) behaviour,³⁰ this was not evident in the fluorescent properties and sensing abilities of thread **64**· BF_4 (Section 4.2.2). It is unclear why the presence of the two stopper groups in axle **69**· BF_4 would have such a drastic effect on the fluorescence.

4.3.6 Summary

Naphthalimide triazolium rotaxane host system **70**· PF_6 was synthesised using chloride anion templation and studied by ^1H NMR, UV/Vis and fluorescence spectroscopies.

The ^1H NMR investigations demonstrated that the rotaxane exhibited selective, uni-directional, anion-induced shuttling which was driven by anion complexation and controlled by

the dual stimulus of anion addition and increasing the competitive nature of the solvent. The three dimensional anion binding cavity of rotaxane **70**·PF₆, created upon co-conformational change, is responsible for selectivity in both the anion recognition properties and the extent of macrocycle translocation. The solid state crystal structure of the rotaxane in the presence of chloride supports the proposed solution phase co-conformational behaviour.

Changes in the co-conformation of **70**·PF₆ upon anion addition were detected by UV/Vis spectroscopy due to the sensitivity of the axle naphthalimide absorbance band to the position of the macrocycle component within the interlocked structure. Furthermore, the chloride-induced shuttling behaviour was demonstrated to be reversible upon addition of silver hexafluorophosphate. However, ineffective fluorescence emission from both the rotaxane and its separate axle component were observed.

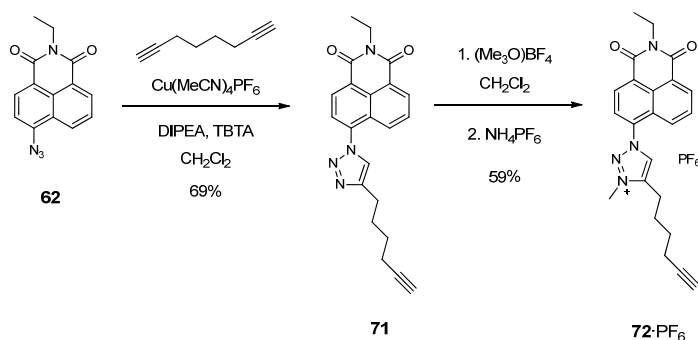
4.4 Towards Surface-Attached Anion Sensors

The use of surface-based devices for sensing applications was introduced in Chapter One (Section 1.1.4.4) and has much potential due to the avoidance of solubility issues, the preorganisation of multiple receptor units onto the surface, and the major advantage of sensor reusability. There are an increasing number of examples of the use of ‘click’ chemistry to attach functional groups onto surfaces and nanoparticles,^{31, 32} and this approach is attractive due to the versatility and efficiency of the vital ‘click’ surface attachment reaction.

With the objective of exploiting the fluorescence behaviour of naphthalimide triazolium thread **64**·BF₄ in the fabrication of effective anion sensing devices, preliminary investigations into the surface-attachment of this system were carried out. It was hoped that ‘click’ chemistry could aid the creation of the target functionalised self-assembled monolayers (SAMs). Furthermore, it was noted that the anthracene-based sensing system studied in Chapter Three (Section 3.5) could easily be utilised in a similar way.

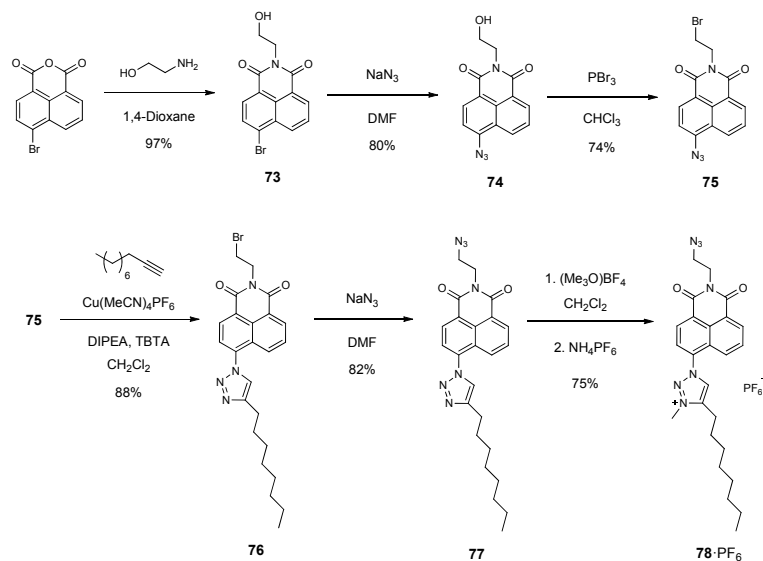
4.4.1 Synthesis of Naphthalimide Triazolium Receptors for ‘Click’ Surface Attachment

Initially, the synthesis of a naphthalimide triazolium receptor incorporating a terminal alkyne functionality was carried out (Scheme 4.8). A ‘click’ reaction between naphthalimide azide **62** and an excess of 1,7-octadiyne afforded triazole **71** in a yield of 69%. Alkylation of **71** using $(\text{Me}_3\text{O})\text{BF}_4$ was then followed by anion exchange to the triazolium hexafluorophosphate salt **72**· PF_6^- . This anion exchange was carried out to avoid the possibility of mixed-salt products upon the ‘click’ surface attachment, which would also use $\text{Cu}(\text{MeCN})_4\text{PF}_6$ as the catalyst.



Scheme 4.8 Synthesis of naphthalimide triazolium alkyne **72**· PF_6 .

In addition, a similar azide-appended system was synthesised (Scheme 4.9). In this case, the ‘click’ functionality is attached through the imide group of the naphthalimide triazolium motif, compared with the triazolium-attached terminal alkyne of **72**· PF_6 , which would allow for versatility in the method of ‘click’ surface attachment, along with alteration of the orientation of the receptor with respect to the surface. Firstly, a condensation reaction between 4-bromo-1,8-naphthalic anhydride and 2-aminoethanol afforded *N*-hydroxyethyl-4-bromo-1,8-naphthalimide (**73**) in quantitative yield.³³ Subsequent high yielding reactions with NaN_3 followed by PBr_3 bromination gave *N*-(2-bromoethyl)-4-azido-1,8-naphthalimide (**75**), which underwent a ‘click’ reaction with 1-decyne to form triazole **76**. Displacement of the bromo-functionality of **76** was achieved using NaN_3 , giving **77** in a yield of 82%. Lastly, alkylation was followed by anion exchange to afford the target azide-appended triazolium receptor **78**· PF_6 .



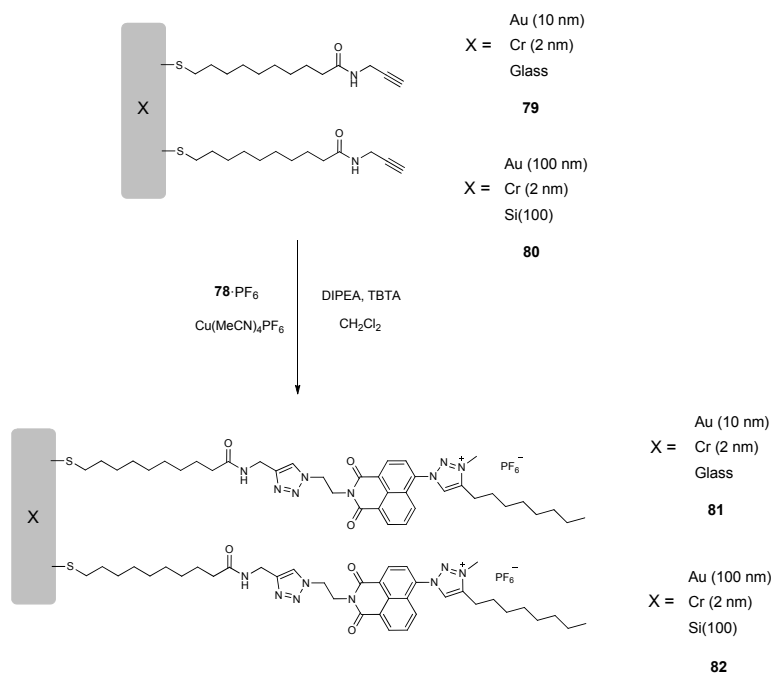
Scheme 4.9 Synthesis of naphthalimide triazolium azide **78**·PF₆.

4.4.2 Initial Gold Surface Attachment and Sensing Investigations

Although gold surfaces are known to efficiently quench fluorescence,³⁴ increasing the distance between the surface and the fluorophore has been shown to reduce the quenching effect sufficiently, for example allowing gold nanoparticles to be exploited for fluorescence sensing applications.³⁵⁻³⁷ Hence, it was decided to investigate the potential of functionalised gold surfaces for use in this project.

These preliminary studies were carried out by Habibur Rahman (Dr Jason Davis' Group, University of Oxford) and further experimental details are given in Appendix A.5. Two different gold-coated surfaces were used to allow for complementary characterisation techniques, both to confirm the desired 'click' attachment and carry out fluorescence sensing studies. An optically transparent gold surface – a glass cover-slip coated with 2 nm Cr and 10 nm Au – is compatible with UV/Vis and fluorescence spectroscopy, whilst a thicker, non-transparent surface – Si(100) coated with 2 nm Cr and 100 nm Au – was also used to study the surface functionalisation through accurate ellipsometry measurements.

Alkyne functionalised SAMs on the two different surfaces (**79** and **80**) were each exposed to ‘click’ reaction conditions with naphthalimide triazolium azide **78**·PF₆ (Scheme 4.10). In addition, control experiments were carried out using identical reaction conditions in the absence of the ‘click’ catalyst, and all surfaces were repeatedly washed to aid the removal of any unattached reagents. The resulting SAMs **81** and **82** would be compared with their respective control samples to ascertain whether covalent functionalisation, rather than simple surface adsorption, had occurred.



Scheme 4.10 ‘Click’ functionalisation of gold-coated surfaces with naphthalimide triazolium azide **78**·PF₆.

Solvent-free UV/Vis spectroscopy was carried out on the transparent gold SAM **81**, with the observation of an absorbance band at around 340 nm confirming the presence of the naphthalimide triazolium motif on **81** (Figure 4.27a). In contrast, this band was not observed for the corresponding control sample (Figure 4.27b).

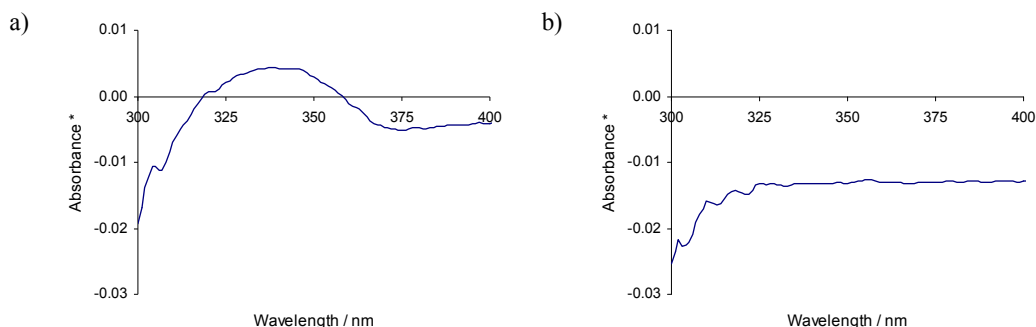


Figure 4.27 Solvent-free UV/Vis spectra for a) transparent gold SAM **81**, and b) the corresponding control system. * Negative absorbance values observed due to difficulties in setting an accurate background spectrum.

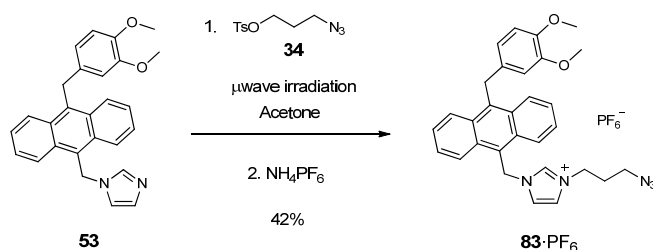
Further evidence that the ‘click’ functionalisation had been successful was obtained from ellipsometry measurements using the thicker gold surfaces. Values for SAM layer thickness of 4.4 nm for **82** and 1.3 nm for the control sample are in agreement with the expected increase from the ‘click’ attachment of azide **78**·PF₆.

Having established that the ‘click’ functionalisation had occurred, fluorescence spectroscopy was used to investigate whether an effective signal could be detected from transparent gold SAM **81**, and whether the solution-phase sensing behaviour of the naphthalimide triazolium receptor **64**·BF₄ would also be displayed by the surface-attached system **81**. Unfortunately, no significant fluorescence emission was observed, either solvent-free or in a number of organic solvents, with no change after the addition of TBA chloride or TBA hydrogen sulfate. Hence, it is postulated that the quenching ability of the gold has not been overcome by the relatively long linker between the surface and the naphthalimide triazolium group in **81**.

Alternative surfaces, which would not readily induce similar fluorescence quenching, could be utilised, and the intended future work relating to this collaborative project is outlined in Section 4.5.

To complement the naphthalimide triazolium derivatives **72**·PF₆ and **78**·PF₆ in future surface investigations, azide-appended, anthracene-based imidazolium **83**·PF₆ was also synthesised (Scheme 4.11). The analogous alkyl receptor displayed ‘OFF-ON’ PET anion sensing behaviour which was unable to be exploited in an interlocked system due to the size requirements for rotaxane stopper groups. Imidazole derivative **53** (synthesised as detailed in Scheme 3.11) was alkylated with

tosylate **34** (Scheme 3.2) using microwave irradiation in acetone. The target hexafluorophosphate salt **83**·PF₆ was then isolated after anion exchange in an overall yield of 42%.



Scheme 4.11 Synthesis of azide-appended, anthracene-based imidazolium receptor **83**·PF₆.

4.4.3 Summary

Azide- and alkyne-appended naphthalimide triazolium derivatives were synthesised, along with an azide-appended anthracene imidazolium system, for use in the fabrication of anion sensing surface devices *via* ‘click’ attachment. Preliminary studies were carried out with UV/Vis spectroscopy and ellipsometry measurements indicating successful functionalisation of alkyne-terminated gold-based SAMs with the naphthalimide azide. However no effective fluorescence signal was detected, making this system unsuitable for use as a surface-based anion sensing device.

4.5 Conclusions

The novel naphthalimide triazolium motif was found to exhibit favourable anion binding and fluorescence sensing properties. In addition, pseudorotaxane investigations using the tetrafluoroborate and chloride salts of a naphthalimide triazolium threading component and an isophthalamide-containing macrocycle revealed the ability of this motif to form interpenetrated assemblies with counter anion dependent co-conformations. This behaviour was reflected in the selective, uni-directional, anion-induced shuttling displayed by the analogous rotaxane which was studied extensively using ¹H NMR spectroscopy. Moreover, perturbations of the naphthalimide axle

absorbance band – due to co-conformational dependent donor-acceptor interactions with the macrocycle hydroquinone groups – enabled the reversible, anion-induced rotaxane shuttling to be signalled and monitored by UV/Vis spectroscopy. However, the magnitudes of the absorbance changes were relatively small, reflecting the amplitude of the shuttling motion.

This system provides a rare example of anion-induced molecular motion which is optically signalled and exhibits selectivity between different coordinating anions, and hence establishes the potential of the anion templation strategy for the effective preparation of such devices.

In this chapter, the naphthalimide triazolium motif was incorporated into electron-deficient threading and axle components for use with electron-rich macrocycles. In future work, attempts could also be made to prepare a number of bis-naphthalimide triazolium macrocycles as shown in Figure 4.28. In addition to their anion recognition properties, the ability of these electron-deficient macrocycles to form pseudorotaxane assemblies with a range of possible electron-rich threading components could be studied using ^1H NMR and UV/Vis spectroscopies.

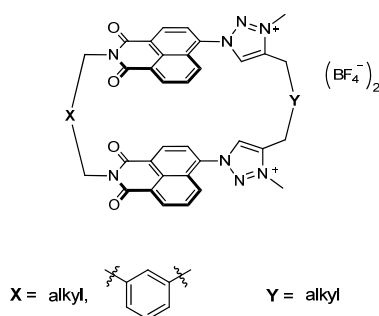
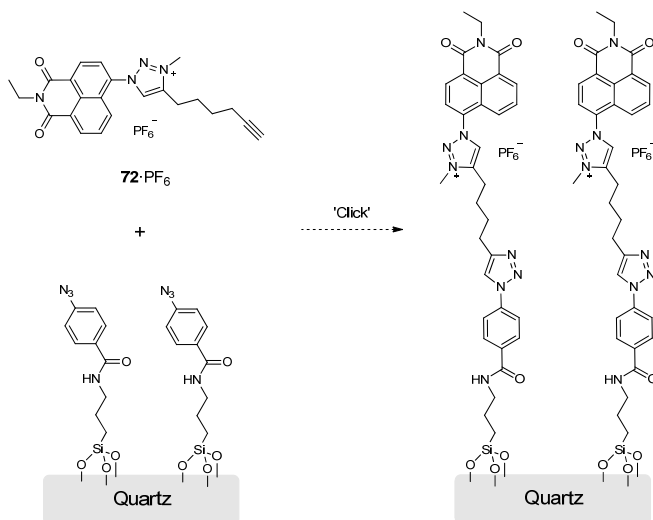


Figure 4.28 Potential bis-naphthalimide triazolium macrocyclic systems.

Unfortunately, the fluorescence sensing behaviour of the acyclic naphthalimide triazolium receptor was not reflected in that of the analogous axle or rotaxane systems. It would be of interest to investigate whether any bis-naphthalimide triazolium macrocycles synthesised exhibit more effective fluorescence.

Preliminary work was also carried out in an attempt to exploit the desirable fluorescence anion sensing abilities of both the naphthalimide triazolium group and the ‘OFF-ON’ anthracene imidazolium system from Chapter Three in the construction of surface-attached devices. Initial

gold-based SAM studies confirmed successful ‘click’ functionalisation, however no fluorescence signal was observed, thought to be due to the quenching effect of the gold. Efforts are currently underway to fabricate the quartz-based SAM shown in Scheme 4.12, which should avoid similar quenching of the fluorescence. In addition, the possibility of using the naphthalimide triazolium motif in electrochemical sensing could be explored by investigating the redox behaviour of the group itself, or *via* electrochemical impedance spectroscopy with an additional redox-active species in solution.³⁸



Scheme 4.12 Target naphthalimide triazolium quartz-based SAM system.

4.6 References

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Chapter Five: Exploiting Binding-Induced Conformational Changes for Anion Recognition, Sensing and Pseudorotaxane Disassembly[†]

5.1 Introduction

5.1.1 Anion-Induced Conformational Changes

To maximise favourable interactions, most anion receptors incorporating more than one binding motif exhibit slight geometrical adjustments upon complexation, however some systems can be designed to undergo larger anion-induced conformational changes. Whilst the previous chapter illustrated the potential of binding-induced co-conformational changes in anion templated interlocked hosts, this chapter will focus on flexible, acyclic systems.

For example, anion-controlled foldamers are oligomeric receptors which fold to encapsulate anionic guest species, forming stable secondary structures.¹ In their folded forms, they often contain helical cavities which can shield complementary anions from the surrounding media. This is demonstrated by the ability of neutral, indolocarbazole-based oligomer **5.1** (Figure 5.1a) to bind halide anions in water *via* N-H hydrogen bonding interactions aided by the hydrophobic effect.²

Anion-induced conformational changes can also be exploited in the use of acyclic receptors for effective anion sensing. In Steed's dialkyne urea-based receptor **5.2** (Figure 5.1b), only chloride binding induces complete planarisation of the extensive chromophore, bringing about a maximum fluorescence response.³ Whilst fluoride, acetate and dihydrogen phosphate are all bound considerably

[†] Parts of this chapter have been published in the following publications and are reproduced with permission from The Royal Society of Chemistry:

G. T. Spence, C. Chan, F. Szemes and P. D. Beer, *Dalton Trans.*, 2012, **41**, 13474–13485.

more strongly than chloride in the 7:3 $\text{CHCl}_3/\text{DMSO}$ solvent conditions, the sensing selectivity of **5.2** arises from key geometrical differences in the receptor-anion complexes.

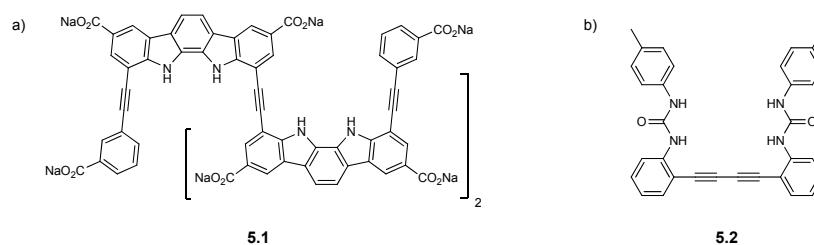
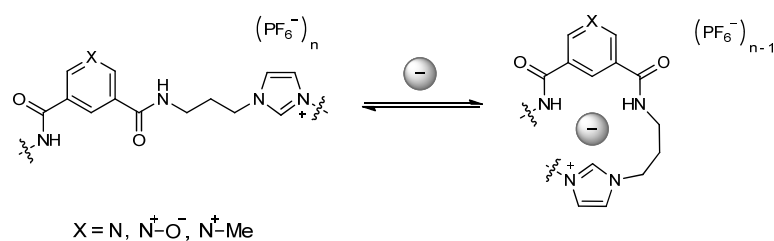


Figure 5.1 a) Indolocarbazole-based oligomer **5.1**, and b) chloride-selective dialkyne urea-based receptor **5.2**.

5.1.2 Chapter Objectives

The initial aim of this chapter is to synthesise and study the recognition properties of an acyclic receptor incorporating the 3,5-bis-amide-pyridine motif, a flexible propyl linker and an imidazolium group, as shown in Scheme 5.1 ($X = \text{N}$). It is thought that in solution this receptor would preferentially adopt an ‘open’ *syn-anti* amide conformation to minimise its overall dipole moment.^{4, 5} However upon anion addition, cooperative hydrogen bonding and electrostatic interactions with the amide and imidazolium motifs would require a substantial conformational change to a more ‘closed’ receptor geometry, which is facilitated by the flexible linker.

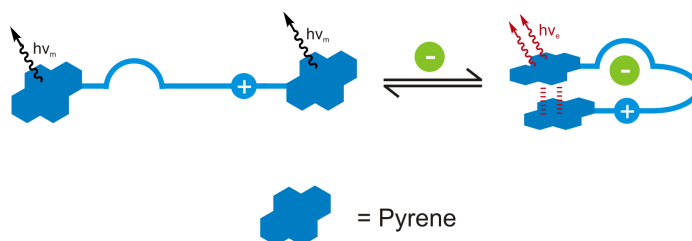


Scheme 5.1 Anion binding motif designed to undergo a substantial conformation change upon anion complexation.

In addition, the effect of changing the pyridine group ($X = \text{N}$) to the pyridine *N*-oxide ($X = \text{N}^+-\text{O}^-$) and pyridinium ($X = \text{N}^+-\text{Me}$) motifs will be investigated. These changes increase the

acidity of the amide protons, and in the case of the pyridinium receptor, introduce a second overall positive charge.

The potential for exploiting this type of binding-induced conformational change for fluorescence anion sensing will also be explored. As discussed in the introductory chapter (Section 1.1.4.1), excimer signalling mechanisms have been employed in numerous anion sensors using pyrene as a reporter group.^{6, 7} It is hoped that similar behaviour would be observed by appending two pyrene groups onto the flexible receptor motif discussed above and monitoring the monomer and excimer emission bands (Scheme 5.2).



Scheme 5.2 Exploiting binding-induced conformational changes for fluorescence anion sensing ($h\nu_m$ = monomer emission, $h\nu_e$ = excimer emission).

Furthermore, investigations will be undertaken into whether interpenetrative assembly can be controlled by anion-induced conformational changes in the threading component.

5.2 Acyclic Receptors[‡]

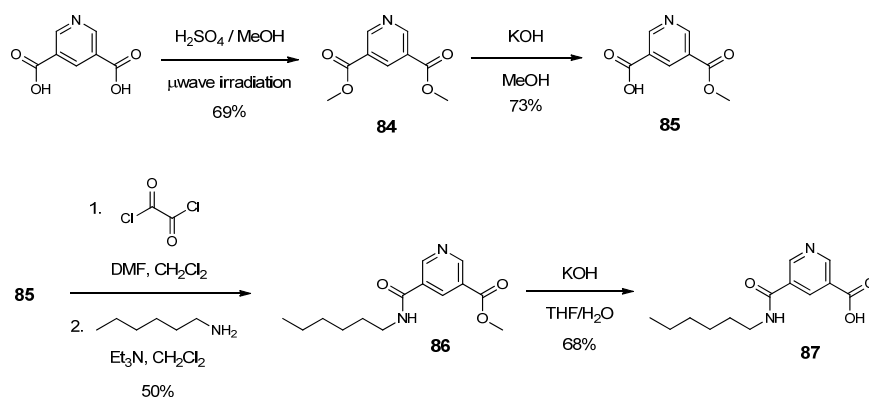
5.2.1 Synthesis and Characterisation

Initially, the preparation of the target acyclic receptors required the parallel synthesis of asymmetric pyridine and imidazolium components.

Dimethyl pyridine-3,5-dicarboxylate (**84**) was synthesised from pyridine-3,5-dicarboxylic acid using microwave irradiation in a $\text{H}_2\text{SO}_4/\text{MeOH}$ mixture (Scheme 5.3).⁸ Selective mono-hydrolysis of

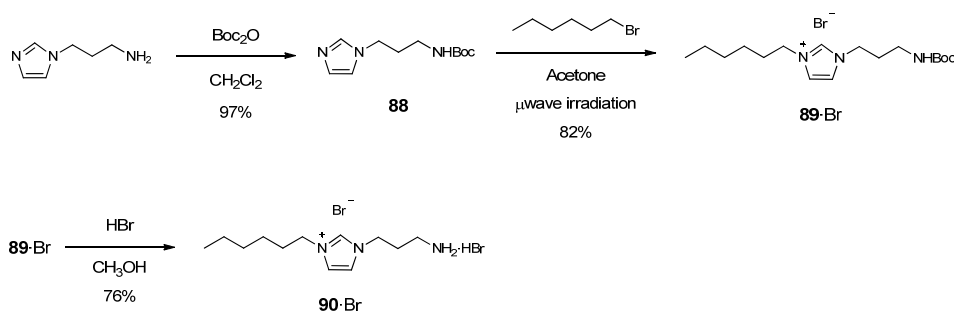
[‡] Section 5.2 and parts of sections 5.3 and 5.4 were carried out in collaboration with Carmen Chan.

84 was achieved by stirring overnight with 1.1 equivalents of KOH to afford 5-(methoxycarbonyl)nicotinic acid (**85**) in a yield of 73%.⁹ A condensation reaction with 1-aminohexane *via* the acid chloride of **85** gave methyl 5-(hexylcarbamoyl)nicotinate (**86**), and subsequent hydrolysis of the methyl ester group of **86** afforded 5-(hexylcarbamoyl)nicotinic acid (**87**) in 68% yield.



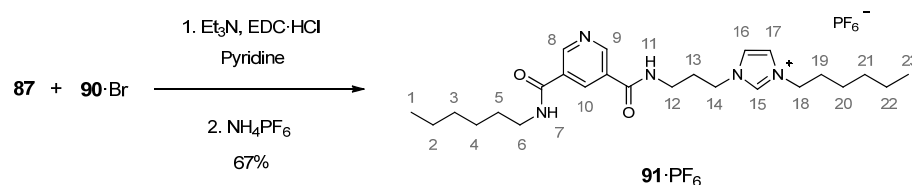
Scheme 5.3 Synthesis of 5-(hexylcarbamoyl)nicotinic acid (**87**).

Commercially available 1-(3-aminopropyl)-imidazole was reacted with Boc_2O to form Boc-protected imidazole **88** (Scheme 5.4).¹⁰ This protection was undertaken to avoid any complications in the following alkylation step, which was achieved using 1-bromohexane and microwave irradiation in a yield of 82%. Deprotection of imidazolium **89**·Br with HBr was followed by precipitation to give the desired product **90**·Br in 76% yield.



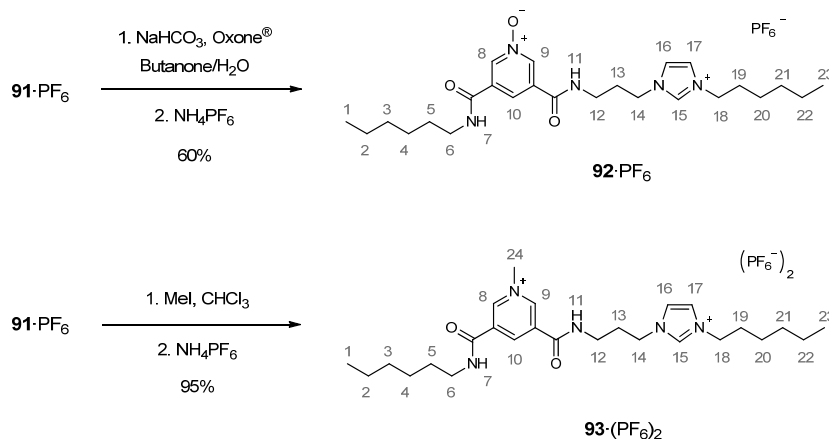
Scheme 5.4 Synthesis of imidazolium amine derivative **90**·Br.

An EDC amide-coupling procedure was then utilised for the successful covalent linking of components **87** and **90**·Br (Scheme 5.5). The target pyridine receptor **91**·PF₆ was isolated after anion exchange to the non-coordinating hexafluorophosphate salt in a yield of 67%.



Scheme 5.5 Synthesis of pyridine receptor **91**·PF₆.

The analogous pyridine *N*-oxide and pyridinium receptors **92**·PF₆ and **93**·(PF₆)₂ were synthesised according to the procedures detailed in Scheme 5.6. Firstly, **91**·PF₆ was stirred in a biphasic mixture of butanone/H₂O with NaHCO₃ and the oxidising agent Oxone[®], with subsequent washing with aqueous NH₄PF₆ affording pyridine *N*-oxide **92**·PF₆. Receptor **91**·PF₆ was also alkylated using MeI in a quantitative yield and anion exchange gave pyridinium **93**·(PF₆)₂.



Scheme 5.6 Synthesis of pyridine *N*-oxide and pyridinium receptors **92**·PF₆ and **93**·(PF₆)₂.

The ¹H NMR spectra of receptors **91**·PF₆, **92**·PF₆ and **93**·(PF₆)₂ in CD₃CN are shown in Figure 5.2. As expected, significant shifts in the aromatic signals corresponding to protons 8, 9 and 10 were observed upon conversion of pyridine **91**·PF₆ to its pyridine *N*-oxide and pyridinium analogues. Furthermore, the appearance of methyl proton signal 24 in the spectra of **93**·(PF₆)₂ confirms pyridine alkylation.

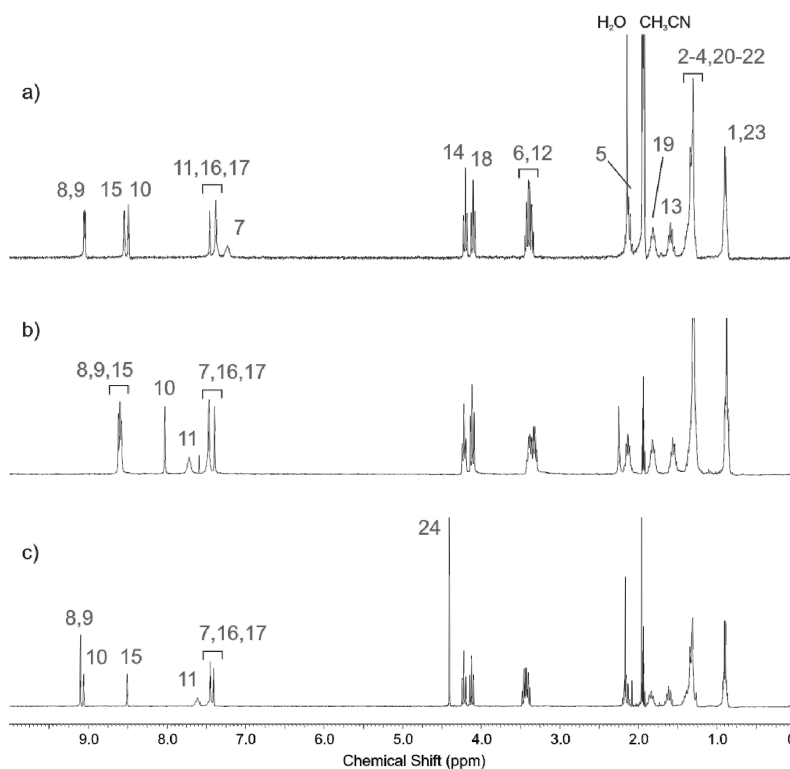


Figure 5.2 ^1H NMR spectra (300 MHz) in CD_3CN at 293 K of a) pyridine receptor $\mathbf{91} \cdot \text{PF}_6$, b) pyridine *N*-oxide receptor $\mathbf{92} \cdot \text{PF}_6$, and c) pyridinium receptor $\mathbf{93} \cdot (\text{PF}_6)_2$.

5.2.2 Anion Binding Studies

To investigate the anion recognition properties of receptors $\mathbf{91} \cdot \text{PF}_6$, $\mathbf{92} \cdot \text{PF}_6$ and $\mathbf{93} \cdot (\text{PF}_6)_2$, ^1H NMR titration experiments were undertaken. Firstly, confirmation of the proposed binding interactions was achieved by the addition of TBA chloride to pyridine receptor $\mathbf{91} \cdot \text{PF}_6$ in CD_3CN (Figure 5.3). Downfield shifts were observed for the signals corresponding to protons 7, 10, 11 and 15, indicative of the expected N-H and C-H hydrogen bonding interactions to the bound halide anion.

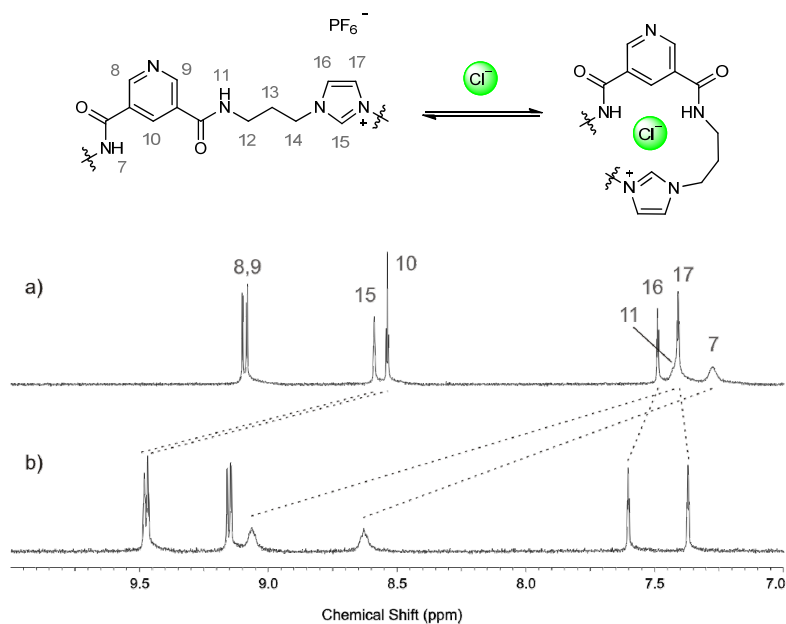


Figure 5.3 Partial ^1H NMR spectra (500 MHz, 2.0×10^{-3} M) in CD_3CN at 293 K of a) pyridine receptor **91**· PF_6 , and b) pyridine receptor **91**· PF_6 plus 1.0 equivalent of TBACl.

Quantitative binding studies were not able to be undertaken in this solvent, as chloride binding was too strong for an accurate association constant to be obtained using WinEQNMR2¹¹ ($K > 10^4 \text{ M}^{-1}$). Introducing 1% D_2O into the solvent media increased its competitive nature sufficiently, and titration experiments in 99:1 $\text{CD}_3\text{CN}/\text{D}_2\text{O}$ were carried out with a variety of anions as their TBA salts – the halides, fluoride,¹² chloride, bromide and iodide, and oxoanions dihydrogen phosphate and nitrate. The downfield shifts observed for the signal corresponding to para-pyridyl proton 10 were monitored throughout the titrations (Figure 5.4), and WinEQNMR2 analysis of the titration data determined the 1:1 stoichiometric association constants given in Table 5.1.

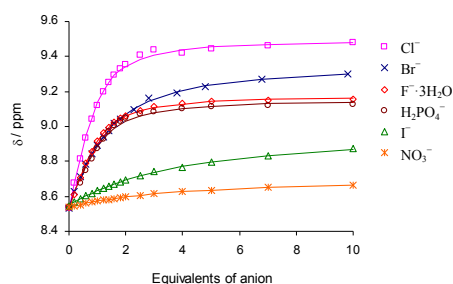


Figure 5.4 Changes in the chemical shifts of proton 10 in pyridine receptor **91**·PF₆ upon addition of anions in 99:1 CD₃CN/D₂O at 293 K. Symbols represent experimental data points; lines represent calculated titration curves.

Table 5.1 Association constants, K (M⁻¹), of pyridine receptor **91**·PF₆ with anions in 99:1 CD₃CN/D₂O at 293 K. Obtained by monitoring proton 10. Errors are given in parentheses.

Anion	91 ·PF ₆ K (M ⁻¹)
F ⁻ ·3H ₂ O	1877 (98)
Cl ⁻	1484 (41)
Br ⁻	666 (22)
I ⁻	136 (5)
H ₂ PO ₄ ⁻	1622 (208)
NO ₃ ⁻	137 (3)

The strongest binding to receptor **91**·PF₆ was displayed by fluoride, dihydrogen phosphate and chloride, with bromide bound significantly more weakly, and the lowest association constants obtained for iodide and nitrate. To interpret these findings, it is important to consider that the strength of complexation between an anion receptor and appropriate guest species is a balance between anion basicity, size complementarity, and the extent of anion solvation. Fluoride and dihydrogen phosphate are the most basic of the anions studied, but also the most solvated.¹³ However in this solvent mixture, with only 1% D₂O, the increased solvation does not prevent these species displaying the highest binding affinities with receptor **91**·PF₆. As strong binding was also observed for the less basic chloride, it appears that this spherical anion is of complementary size and shape for hydrogen bonding and electrostatic interactions with **91**·PF₆ in its ‘closed’ conformation. The other anions – the larger

bromide and iodide, and the trigonal planar nitrate – are not sufficiently basic and do not possess the same degree of complementarity to display effective binding to the host receptor.

The anion recognition properties of pyridine *N*-oxide receptor **92**·PF₆ were similarly investigated using ¹H NMR titration experiments in 99:1 CD₃CN/D₂O with the same anionic guest species. Downfield shifts in the signals corresponding to C-H hydrogen bond donors 10 and 15 were observed upon chloride addition (Figure 5.5), whilst amide protons 7 and 11 were not observed in the ¹H NMR spectrum due to deuterium exchange. The shifts observed for proton signal 10 during the titration experiments were monitored to obtain accurate association constants using WinEQNMR2 (Figure 5.6 and Table 5.2).

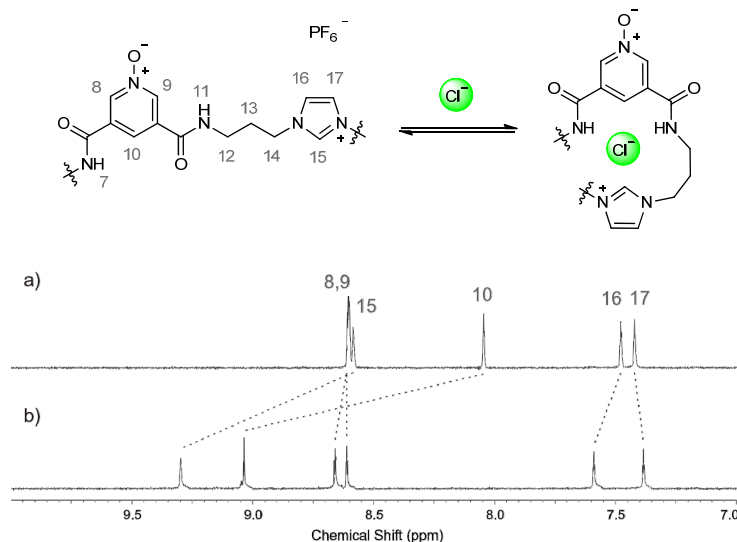


Figure 5.5 Partial ¹H NMR spectra (500 MHz, 2.0 x 10⁻³ M) in 99:1 CD₃CN/D₂O at 293 K of a) pyridine *N*-oxide receptor **92**·PF₆, and b) pyridine *N*-oxide receptor **92**·PF₆ plus 1.0 equivalent of TBACl.

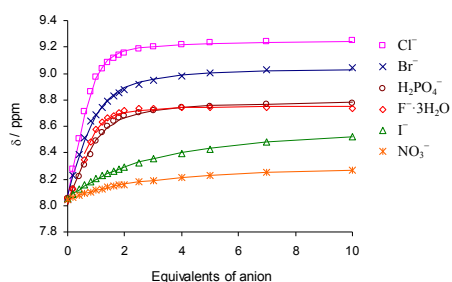


Figure 5.6 Changes in the chemical shifts of proton 10 in receptor **92**·PF₆ upon addition of anions in 99:1 CD₃CN/D₂O at 293K. Symbols represent experimental data points; lines represent calculated titration curves.

Table 5.2 Association constants, K (M⁻¹), of receptor **92**·PF₆ with anions in 99:1 CD₃CN/D₂O at 293 K. Obtained by monitoring proton 10. Errors are given in parentheses.

Anion	92 ·PF ₆ K (M ⁻¹)
F ⁻ ·3H ₂ O	5731 (957)
Cl ⁻	6506 (664)
Br ⁻	1858 (155)
I ⁻	209 (8)
H ₂ PO ₄ ⁻	2012 (270)
NO ₃ ⁻	217 (5)

For every anion, an increase in the association constant was observed for **92**·PF₆ in comparison with pyridine receptor **91**·PF₆, due to increased acidity of the hydrogen bond donors associated with the pyridine *N*-oxide motif (7, 10 and 11). In this system, chloride and fluoride are bound most strongly, with considerably weaker binding observed for both bromide and dihydrogen phosphate. Iodide and nitrate are again the most weakly bound anions.

The increased hydrogen bond donor acidity appears to have magnified the importance of complementarity in determining the anion recognition properties of receptor **92**·PF₆, with the smaller halides favoured over larger, less complementary anions. This is illustrated by the considerable enhancements in the association constants for fluoride, chloride and bromide when comparing receptor **92**·PF₆ with the pyridine analogue **91**·PF₆ (factors of 3.1, 4.4 and 2.8 respectively), whilst only minor enhancements were observed for the larger iodide and the non-spherical dihydrogen phosphate and

nitrate (factors of between 1.2–1.6). Significantly, dihydrogen phosphate – amongst the most strongly bound guests for **91**·PF₆ – is bound only as strongly as bromide by receptor **92**·PF₆.

Due to the increase in overall charge, pyridinium receptor **93**·(PF₆)₂ required the more competitive 95:5 CD₃CN/D₂O solvent mixture for quantitative binding studies. In these solvent conditions, imidazolium proton 15 as well as amide protons 7 and 11 were not able to be seen due to deuterium exchange (Figure 5.7). However, the para-pyridinium proton signal 10 was observed to shift downfield upon anion addition.

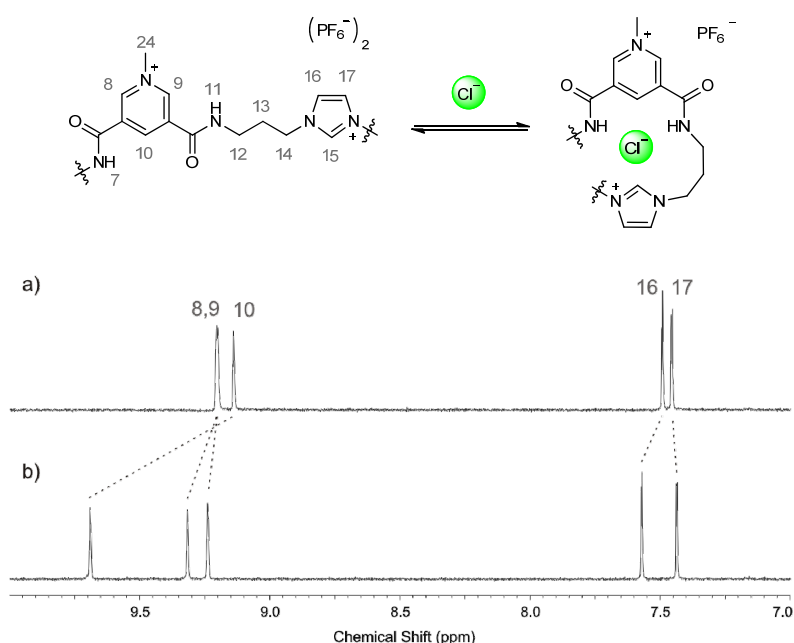


Figure 5.7 Partial ¹H NMR spectra (500 MHz, 2.0 x 10⁻³ M) in 95:5 CD₃CN/D₂O at 293 K of a) pyridinium receptor **93**·(PF₆)₂, and b) pyridinium receptor **93**·(PF₆)₂ plus 1.0 equivalent of TBACl.

The titration data were analysed using WinEQNMR2 (Figure 5.8) and the association constants obtained are given in Table 5.3. The insolubility of TBA acetate in CD₃CN prevented investigations into the acetate binding affinities of receptors **91**·PF₆ and **92**·PF₆, however the increased percentage of D₂O in these solvent conditions enabled its use with **93**·(PF₆)₂.

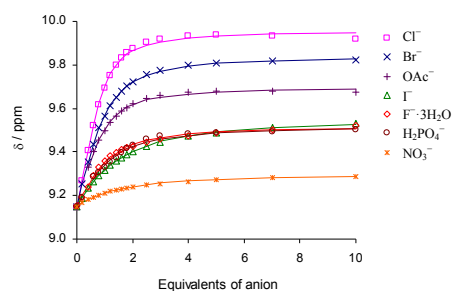


Figure 5.8 Changes in the chemical shifts of proton 10 in receptor **93**·(PF₆)₂ upon addition of anions in 95:5 CD₃CN/D₂O at 293K. Symbols represent experimental data points; lines represent calculated titration curves.

Table 5.3 Association constants, K (M⁻¹), of receptor **93**·(PF₆)₂ with anions in 95:5 CD₃CN/D₂O at 293 K. Obtained by monitoring proton 10. Errors are given in parentheses.

Anion	93 ·(PF ₆) ₂ K (M ⁻¹)
F ⁻ ·3H ₂ O	1267 (111)
Cl ⁻	3558 (282)
Br ⁻	1966 (18)
I ⁻	543 (15)
H ₂ PO ₄ ⁻	1022 (100)
NO ₃ ⁻	470 (29)
OAc ⁻	2415 (168)

Chloride displayed the highest binding affinity with pyridinium receptor **93**·(PF₆)₂, significantly greater than acetate and bromide. Fluoride and dihydrogen phosphate were bound considerably more weakly, followed by iodide and nitrate.

By increasing the aqueous content of the solvent mixture compared with the previous studies using **91**·PF₆ and **92**·PF₆, the effect of anion solvation on the strength of complexation is increased. Hence, the heavily solvated fluoride and dihydrogen phosphate display much weaker binding to receptor **93**·(PF₆)₂ in comparison with chloride, and are also bound significantly more weakly than the much less basic bromide. As acetate binding was not able to be studied with the other receptors, it is more difficult to assess the factors contributing to this event with **93**·(PF₆)₂. The strong association constant observed can be rationalised by considering that acetate is highly basic and significantly less heavily solvated than fluoride and dihydrogen phosphate.¹³ However, the binding of acetate is weaker

than chloride due to its reduced size and shape complementarity with the ‘closed’ conformation of receptor **93**·(PF₆)₂.

It should be noted that during the fluoride titration experiments with receptors **91**·PF₆, **92**·PF₆ and **93**·(PF₆)₂, no ¹H NMR signals corresponding to HF₂[−] were observed (~ 16 ppm),^{14, 15} indicating that receptor deprotonation did not occur with this highly basic halide anion.

5.2.3 Summary

Flexible, acyclic receptors **91**·PF₆, **92**·PF₆ and **93**·(PF₆)₂ were synthesised and their anion recognition properties investigated using ¹H NMR spectroscopy. The binding strengths and selectivities of these receptors were dependent on a number of key factors influenced by changes in the hydrogen bond donor acidities, the overall charge of the receptor and, importantly, the solvent conditions in which the studies were undertaken.

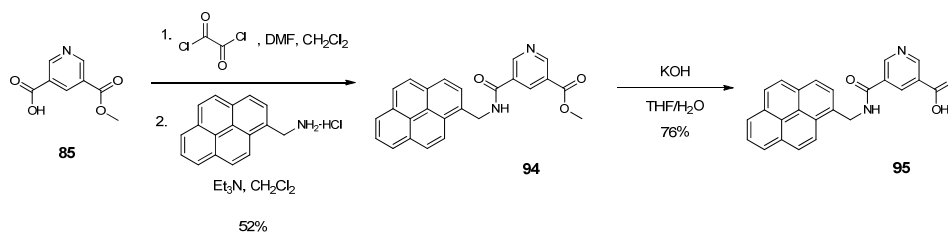
5.3 Pyrene-Appended Fluorescent Anion Sensor

With the objective of exploiting the conformational changes exhibited by the acyclic receptors for effective fluorescence anion sensing, an analogous system incorporating pyrene reporter groups was synthesised. It was hoped that the anion-induced conformational changes would be signalled by changes in the pyrene monomer and excimer emission bands.

5.3.1 Synthesis and Characterisation

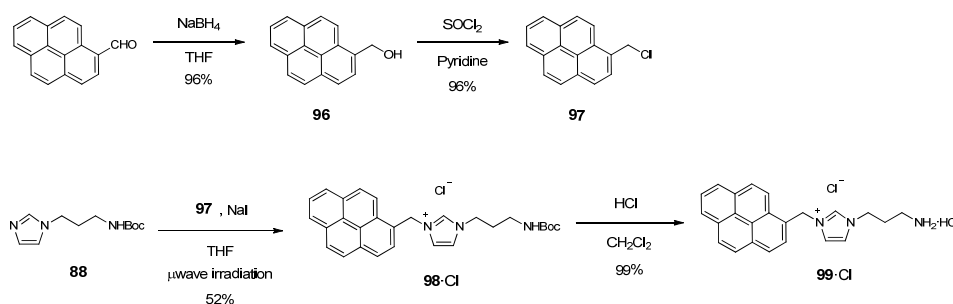
A similar synthetic route to the target pyrene-appended receptor was employed as used for pyridine receptor **91**·PF₆ (Section 5.2.1).

Initially, acid **85** was converted to the corresponding acid chloride and reacted *in situ* with 1-pyrenemethylamine hydrochloride to afford **94** in a yield of 52% (Scheme 5.7). Subsequent removal of the methyl ester group using KOH gave pyrene-appended acid **95**.



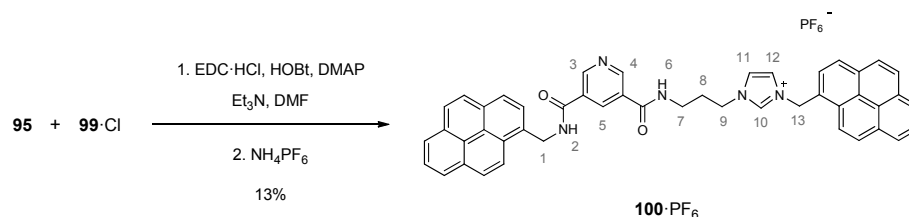
Scheme 5.7 Synthesis of 5-((pyren-1-ylmethyl)carbamoyl)nicotinic acid (**95**).

Preparation of the desired imidazolium component required the synthesis of 1-(chloromethyl)pyrene (**97**) based on literature procedures (Scheme 5.8),¹⁶ beginning with the reduction of 1-pyrenecarboxyaldehyde using NaBH_4 , followed by chlorination using SOCl_2 . Successful alkylation of imidazole derivative **88** using **97** was achieved by heating the reagents with NaI in THF under microwave irradiation at 110 °C for 2 h. The product **98·Cl** was isolated in a yield of 52% after recrystallisation, and acidic reaction conditions resulted in quantitative Boc-deprotection to give the desired pyrene-appended imidazolium amine derivative **99·Cl**.



Scheme 5.8 Synthesis of pyrene-appended imidazolium amine derivative **99·Cl**.

Solubility issues hindered the key EDC coupling reaction between acid **95** and amine **99·Cl**, and a number of different reaction conditions were employed to attempt to synthesise target receptor **100·PF₆** in a reasonable yield. Reaction of the components in DMF with HOBT and DMAP as well as the EDC reagent and Et_3N successfully afforded **100·PF₆** in a low yield of 13% following purification using preparative silica gel thin layer chromatography and subsequent anion exchange (Scheme 5.9).



Scheme 5.9 Synthesis of pyrene-appended receptor **100·PF₆**.

Further solubility difficulties were encountered, as pyrene-appended receptor **100·PF₆** was only partially soluble in a range of solvents at appropriate concentrations for ¹H NMR studies (10⁻³ M). However at more dilute concentrations, for example those required for UV/Vis and fluorescence spectroscopy (10⁻⁵ to 10⁻⁷ M), solubility was sufficient in 1:1 CH₂Cl₂/acetone. Hence, this solvent mixture was used for the anion binding and sensing investigations detailed in the next section, although quantitative ¹H NMR studies were not possible. The ¹H NMR spectrum of **100·PF₆** in 1:1 CD₂Cl₂/*d*₆-acetone is shown in Figure 5.9.¹⁷

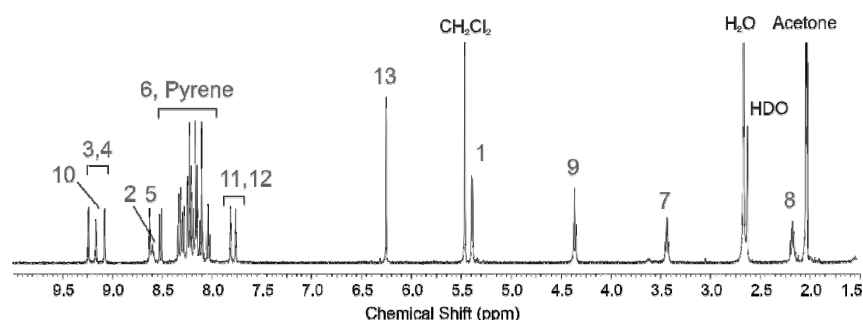


Figure 5.9 ¹H NMR spectrum (500 MHz) in 1:1 CD₂Cl₂/*d*₆-acetone at 293 K of pyrene-appended receptor **100·PF₆**.

5.3.2 Anion Binding and Sensing Studies

To confirm the anion binding mode of pyrene-appended receptor **100·PF₆**, a qualitative ¹H NMR study was undertaken in 1:1 CD₂Cl₂/*d*₆-acetone. As expected, the signals corresponding to the N-H and C-H hydrogen bond donors 2, 5, 6 and 10 shifted significantly downfield upon addition of TBA chloride (Figure 5.10).

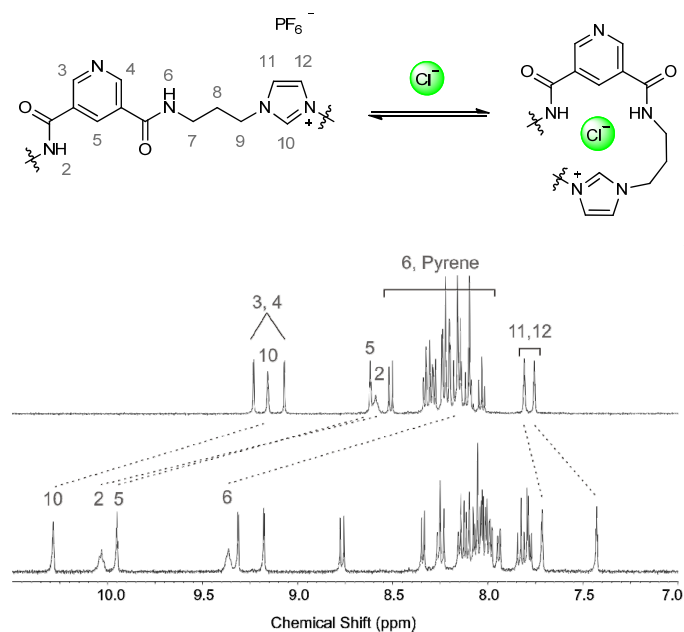


Figure 5.10 Partial ^1H NMR spectra (500 MHz) in 1:1 $\text{CD}_2\text{Cl}_2/d_6\text{-acetone}$ at 293 K of a) pyrene-appended receptor **100**· PF_6^- , and b) pyrene-appended receptor **100**· PF_6^- + ~ 2 equivalents of TBACl.

The fluorescent properties of receptor **100**· PF_6^- were studied in 1:1 $\text{CH}_2\text{Cl}_2/\text{acetone}$, with dual emission from both pyrene monomer and excimer species observed (Figure 5.11). Monomer emission results in peaks at 381 and 398 nm, whilst the excimer band is broader and red-shifted, appearing at 484 nm.

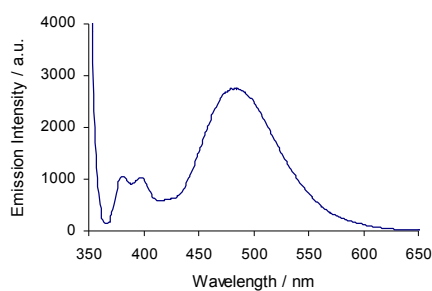


Figure 5.11 Emission spectrum of pyrene-appended receptor **100**· PF_6^- in 1:1 $\text{CH}_2\text{Cl}_2/\text{acetone}$ ($c = 5 \times 10^{-7}$ M, $\lambda_{\text{excit}} = 345$ nm, 293 K).

The presence of a considerable excimer band in the fluorescence spectrum of **100**· PF_6^- is unsurprising given the flexibility of the receptor and the propensity of pyrene moieties to form excited

state dimers. Importantly, the ratio of excimer and monomer emissions did not change significantly at a number of concentrations between 1×10^{-6} and 1×10^{-7} M (excimer:monomer ~ 3). This indicates that, as expected at these dilute concentrations, the excimer emission arises from intramolecular excimer formation rather than equivalent intermolecular interactions.

To investigate the anion sensing behaviour of **100**-PF₆, fluorescence titration experiments were then undertaken with a variety of anions as their TBA salts – halides fluoride, chloride and bromide, oxoanions dihydrogen phosphate, acetate and nitrate, and the linear azide. Upon addition of up to 100 equivalents of chloride and bromide, a decrease in monomer emission was accompanied by an increase in the excimer band (Figure 5.12). In both cases, no changes in the emission wavelengths were observed and sensing saturation was reached prior to the end of the titration. The enhancements in the excimer band of **100**-PF₆ upon chloride and bromide addition were calculated to be 66% and 22% respectively, whilst the excimer to monomer emission intensity ratio similarly increased from 2.8 in the unbound receptor to 7.6 upon addition of chloride, and 5.7 with bromide.

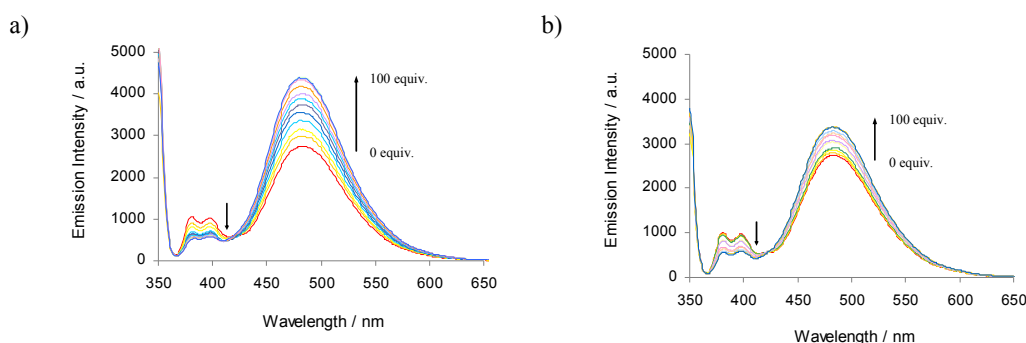
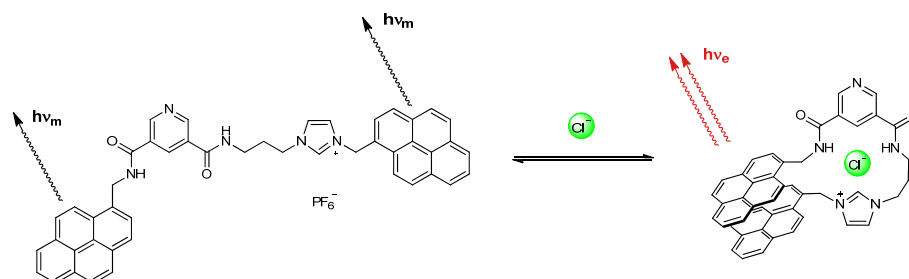


Figure 5.12 Changes in the emission spectrum of pyrene-appended receptor **100**-PF₆ in 1:1 CH₂Cl₂/acetone ($c = 5 \times 10^{-7}$ M, $\lambda_{\text{excit}} = 345$ nm, 293 K) upon addition of a) TBACl and b) TBABr.

These fluorescence responses can be attributed to the halide binding induced conformational change exhibited by receptor **100**-PF₆ upon chloride and bromide addition bringing the two pyrene groups closer together and hence increasing the extent of excimer emission (Scheme 5.10). The different excimer enhancements observed for these two halide anions reflect the geometries of their receptor-anion complexes with respect to optimum excimer formation. Furthermore, the clear

isoemissive points in the titration spectra are indicative of only one complexation mechanism occurring, which is then effectively signalled by the fluorescent reporter groups.



Scheme 5.10 Chloride-induced conformational change of pyrene-appended receptor **100**·PF₆ which results in enhancement of excimer fluorescence emission ($h\nu_m$ = monomer emission, $h\nu_e$ = excimer emission).

The fluorescence changes during these binding titrations were analysed using SPECFIT¹⁸ (Figure 5.11), and log K values of 5.75(0.15) and 5.29(0.08) were obtained for chloride and bromide binding respectively. These findings indicate that chloride is bound more strongly than bromide, however in these non-competitive solvent conditions, only slight discrimination in terms of binding affinities is possible between the two anions.

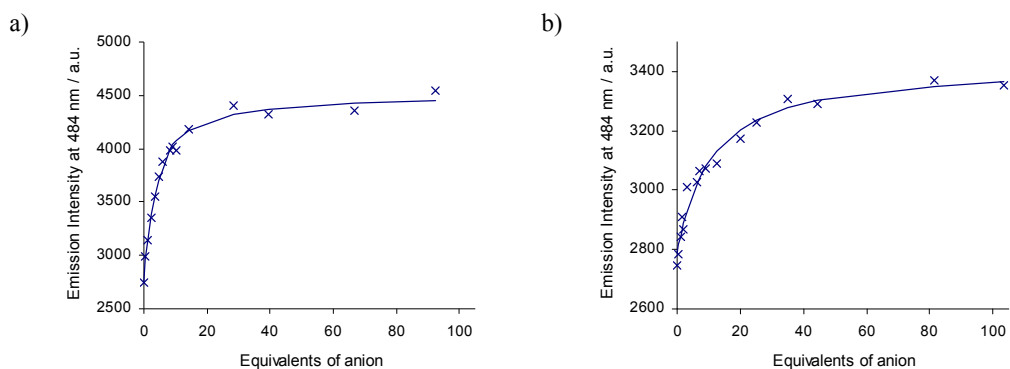


Figure 5.11 a) Changes in the emission intensity of pyrene-appended receptor **100**·PF₆ in 1:1 CH₂Cl₂/acetone ($c = 5 \times 10^{-7}$ M, $\lambda_{\text{excit}} = 345$ nm, 293 K) at 484 nm upon addition of a) TBACl, and b) TBABr. Symbols represent experimental data points, lines represent calculated titration curves. Note: different y-axis scales.

Whilst the chloride- and bromide-induced sensing behaviour of receptor **100**·PF₆ could easily be assigned to the conformational changes exhibited upon anion binding, contrasting fluorescence responses were observed for the other anions. For example, fluoride addition initially resulted in considerable quenching of both the monomer and excimer emission bands (Figure 5.12), with the

excimer emission quenched by 78%. However after approximately nine equivalents, both bands increased in intensity, although only partial restoration of emission occurred (excimer emission returned to 45% of that in **100**·PF₆). These changes are accompanied by a slight hypsochromic shift (3 nm) in the excimer emission peak.

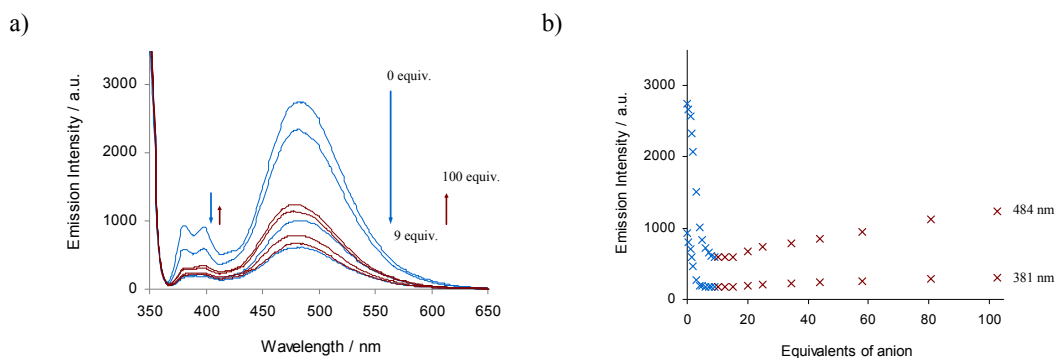


Figure 5.12 a) Changes in the emission spectrum of pyrene-appended receptor **100**·PF₆ in 1:1 CH₂Cl₂/acetone ($c = 5 \times 10^{-7}$ M, $\lambda_{\text{excit}} = 345$ nm, 293 K) upon addition of TBAF·3H₂O, and b) corresponding changes in emission intensity at 381 and 484 nm. Blue represents 0 to 9 equivalents, red 9 to 100 equivalents.

Similar two-stage fluorescence responses – initial quenching of both bands followed by subsequent restoration/enhancement – were also observed with dihydrogen phosphate and acetate (Figures 5.13a and b). Differences in the exact number of equivalents of anion added at the response ‘turning point’ were observed (7 and 6 equivalents for dihydrogen phosphate and acetate respectively), as well as in the final extent of excimer emission restoration or enhancement (97% restoration for H₂PO₄ and an enhancement of +21% with acetate). Moreover, whilst dihydrogen phosphate addition resulted in a hypsochromic shift in the excimer emission wavelength of 7 nm, no such shift occurred during the acetate titration.

A further type of fluorescence behaviour was induced by nitrate and azide addition (Figures 5.13c and d). In these titrations, the same initial dual quenching of emission bands was observed, although to a much lesser extent. This was followed by enhancement in only the excimer emission band to beyond its original intensity (+7% and +18% for nitrate and azide respectively), with the monomer emission remaining approximately at its quenched level. Unfortunately, all of these

responses were unable to be fitted accurately by SPECFIT analysis using a range of potential host:guest stoichiometries.

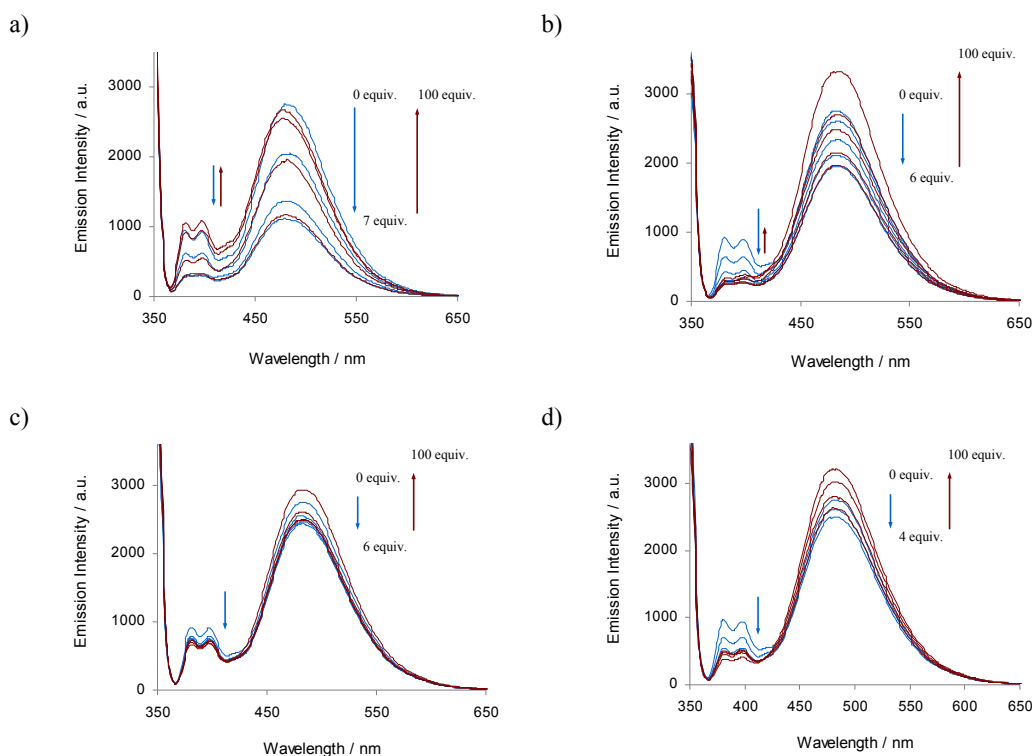
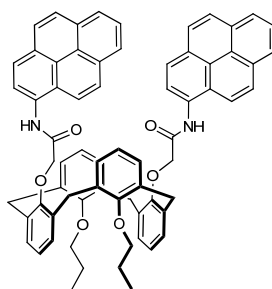


Figure 5.13 Changes in the emission spectrum of pyrene-appended receptor **100**-PF₆ in 1:1 CH₂Cl₂/acetone ($c = 5 \times 10^{-7}$ M, $\lambda_{\text{excit}} = 345$ nm, 293 K) upon addition of a) TBAH₂PO₄, b) TBAOAc, c) TBANO₃, and d) TBAN₃. Blue and red spectra represent different stages of fluorescence behaviour.

It is unclear why such contrasting fluorescence sensing responses were observed for these anions compared with that observed for chloride and bromide. The initial simultaneous quenching of both monomer and excimer emissions is similar to that observed in several other pyrene-appended receptors,^{19, 20} for which the behaviour was attributed to photo-induced electron transfer (PET) processes. Furthermore, similar two-stage behaviour was exhibited by pyrene-appended, calixarene-based receptor **5.3** (Figure 5.14).²¹ Upon addition of fluoride to **5.3** in MeCN, initial quenching of both the monomer and excimer emission bands was followed by subsequent enhancements at higher fluoride concentrations, accompanied by a hypsochromic shift in the excimer emission.



5.3

Figure 5.14 Kim and Lee's pyrene-appended, calixarene-based fluoride sensor **5.3**.

This behaviour was ascribed to a fluoride-selective charge transfer process, which in turn resulted in a change in the nature of the excimer. The charge transfer process induced a large shift in the UV/Vis absorption wavelength of **5.3**, whilst changes in the nature of any excimer species – from ‘dynamic’ excited state dimers to ‘static’ ground state interactions – are signalled by differences in the excitation spectra when monitoring either the monomer or excimer emissions.²² However for receptor **100**·PF₆, no such changes in either the UV/Vis absorption wavelength or the normalised excitation spectra were observed upon addition of the anions. Hence, whilst the fluoride responses exhibited by receptors **5.3** and **100**·PF₆ appear similar, they must be the result of different processes.

In addition to the desired hydrogen bonding interactions, deprotonation of the receptor amide protons might be significant in this non-aqueous solvent mixture with the basic fluoride, dihydrogen phosphate and acetate anions. A qualitative ¹H NMR experiment was undertaken to investigate the potential for deprotonation of receptor **100**·PF₆ by fluoride in these solvent conditions, however no HF₂[−] was observed, even after the addition of a large excess of fluoride.

5.3.3 Summary

Pyrene-appended receptor **100**·PF₆ was synthesised and shown to signal anion binding through changes in its monomer and excimer emission bands. Whilst the fluorescence behaviour upon chloride and bromide addition could be explained by considering the effect of binding-induced conformational changes on the proximity of the pyrene groups, different responses were observed for

the other anions which could not be rationalised. However, the ability of receptor **100**·PF₆ to provide a certain degree of inter-anion discrimination is illustrated by comparing the fluorescence spectra after sensing saturation had been reached (Figure 5.15).

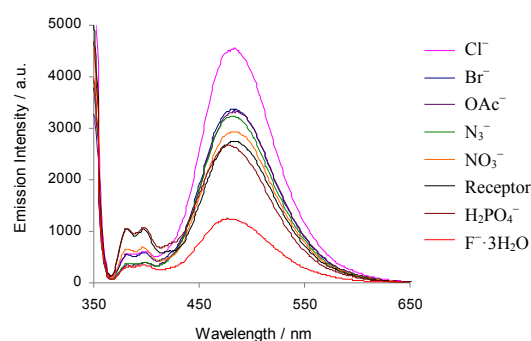


Figure 5.15 Emission spectra corresponding to pyrene-appended receptor **100**·PF₆ in 1:1 CH₂Cl₂/acetone ($c = 5 \times 10^{-7}$ M, $\lambda_{\text{excit}} = 345$ nm, 293 K) before and after addition of 100 equivalents of a variety of anions.

5.4 Pyridine *N*-Oxide Pseudorotaxane Investigations

Recently, the ability of the pyridine *N*-oxide motif to form interpenetrated pseudorotaxane assemblies with isophthalamide macrocycles by virtue of hydrogen bonding and secondary donor-acceptor interactions has been discovered by Jiang and co-workers (Figure 5.16a).²³ In addition, they illustrated that the formation of pseudorotaxane assembly **5.4** was able to be controlled by acid and base stimuli. Furthermore, Laura Hancock studied the formation of a similar assembly using thread **5.5** and the larger macrocycle **1** (Figure 5.16b),⁸ and calculated an association constant of 5950 M⁻¹ for this interaction in CDCl₃.

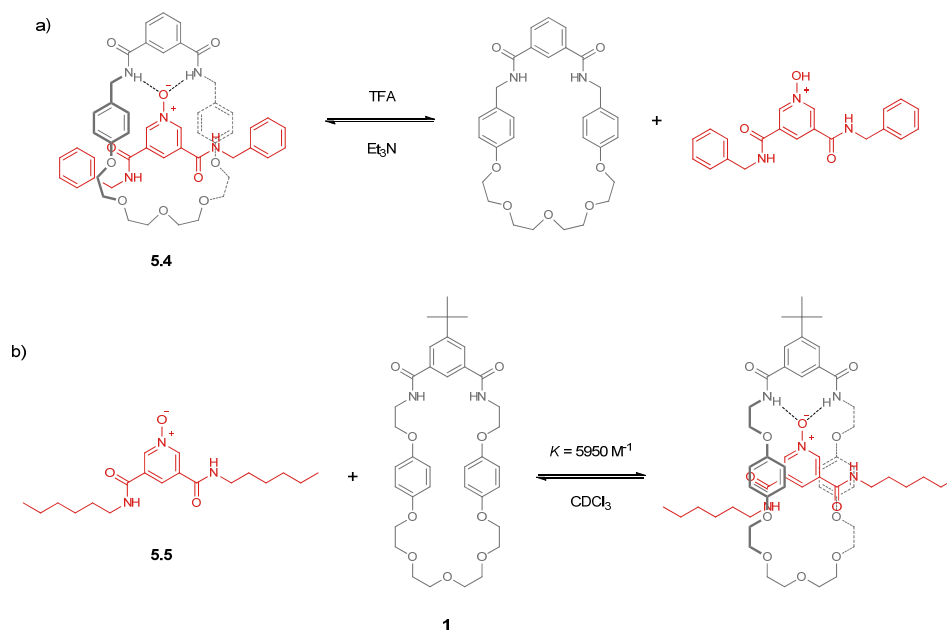


Figure 5.16 a) Jiang's acid-base switchable pyridine *N*-oxide pseudorotaxane **5.4**, and b) Laura Hancock's similar system exploiting macrocycle **1**.

5.4.1 Pseudorotaxane Assembly

The potential for pyridine *N*-oxide receptor **92**·PF₆ to act as a threading component in the construction of pseudorotaxane assemblies with macrocycles **1** and **22** (Figure 5.17) was investigated using ¹H NMR spectroscopy.

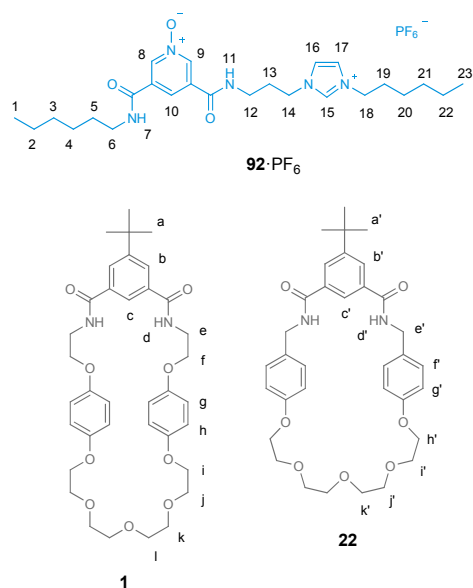
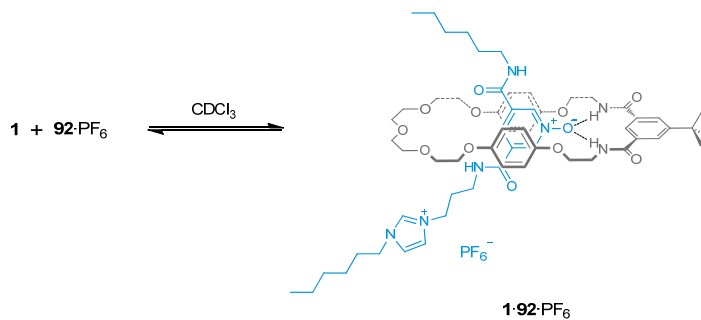


Figure 5.17 Pyridine *N*-oxide thread **92**·PF₆ and macrocycles **1** and **22** used in pseudorotaxane investigations.

Initially, one equivalent of thread **92**·PF₆ was added to a CDCl₃ solution of macrocycle **1** (Scheme 5.11). The resulting ¹H NMR spectrum, along with those of the individual components, is shown in Figure 5.18.



Scheme 5.11 Formation of pseudorotaxane assembly **1**·**92**·PF₆.

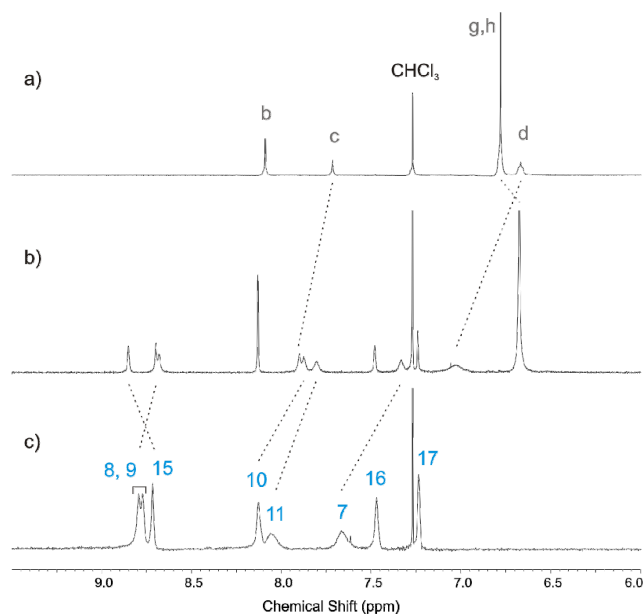


Figure 5.18 Partial ^1H NMR spectra (500 MHz) in CDCl_3 at 293 K of a) macrocycle **1**, b) macrocycle **1** plus 1.0 equivalent of thread **92**· PF_6 , and c) thread **92**· PF_6 .

Upon addition of pyridine *N*-oxide thread **92**· PF_6 , the signals corresponding to the isophthalamide proton **c** and amide protons **d** of macrocycle **1** both shifted downfield, indicative of C-H and N-H hydrogen bonding interactions with the *N*-oxide motif. Importantly, as seen in previous pyridine *N*-oxide pseudorotaxane systems, upfield shifts in the macrocycle hydroquinone signal (protons **g** and **h**) due to the secondary donor-acceptor interactions confirm the formation of assembly **1**·**92**· PF_6 . Upfield shifts were also observed for a number of thread protons (7–11), resulting from the interpenetrated nature of **1**·**92**· PF_6 and the macrocycle hydroquinone ring currents.

To quantify the stability of assembly **1**·**92**· PF_6 , a ^1H NMR titration experiment was undertaken, with the signal corresponding to hydroquinone protons **g** and **h** of macrocycle **1** monitored upon addition of thread **92**· PF_6 (Figure 5.19). WinEQNMR2 analysis of the titration data determined an association constant of $315(35) \text{ M}^{-1}$.

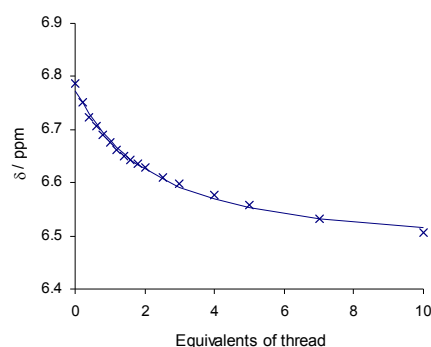


Figure 5.19 Changes in the chemical shift of hydroquinone protons (g and h) in **1** upon addition of thread **92**·PF₆ in CDCl₃ at 293K (500 MHz, 2.0 × 10⁻³ M). Symbols represent experimental data points; line represents calculated titration curve.

Pseudorotaxane **1**·**92**·PF₆ exhibits considerably lower stability compared with the analogous assembly studied by Laura Hancock between thread **5.5** and macrocycle **1** (Figure 5.16b), with association constants of 315 and 5950 M⁻¹ respectively. Evidently, the incorporation of an imidazolium group into the threading component has greatly disfavoured pseudorotaxane formation. The possibility of a hydrogen bonding interaction between the imidazolium and *N*-oxide motifs of **92**·PF₆ (Figure 5.20), which may account for the reduced stability of assembly **1**·**92**·PF₆, was supported by a significant downfield shift in imidazolium proton 15 in the CDCl₃ ¹H NMR spectrum of **92**·PF₆ compared with its pyridine precursor receptor **91**·PF₆ (Δδ = + 0.35 ppm). It is noteworthy that this proton shifts further downfield in the formation of **1**·**92**·PF₆ (Figure 5.18), possibly due to alternative hydrogen bonding interactions with macrocycle **1**.

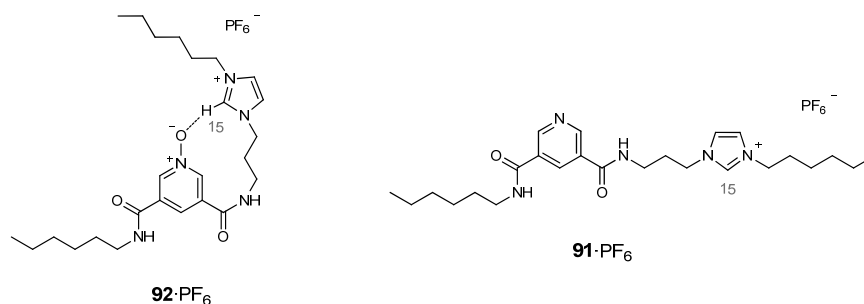
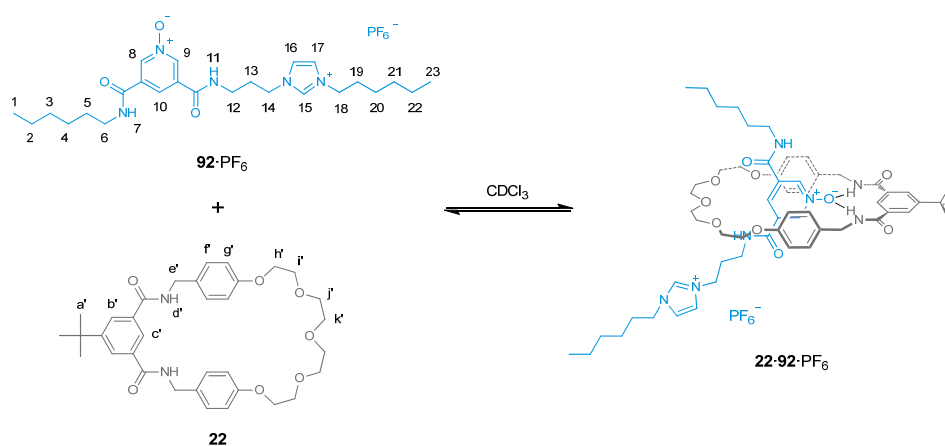


Figure 5.20 Proposed intramolecular hydrogen bonding interaction in **92**·PF₆, and pyridine receptor **91**·PF₆.

In an attempt to gain further confirmation of the interpenetrated nature of assembly **1**·**92**·PF₆, a 2D ¹H-¹H ROESY spectrum was obtained using an equimolar solution of **1** and **92**·PF₆. However, no intercomponent correlations were observed, which may be due to the relatively weak interaction between the two components.

To study the effect of reducing the size of the macrocycle component on pseudorotaxane formation, similar investigations were undertaken using smaller macrocycle **22** (Scheme 5.12 and Figure 5.21).



Scheme 5.12 Formation of pseudorotaxane assembly **22**·**92**·PF₆.

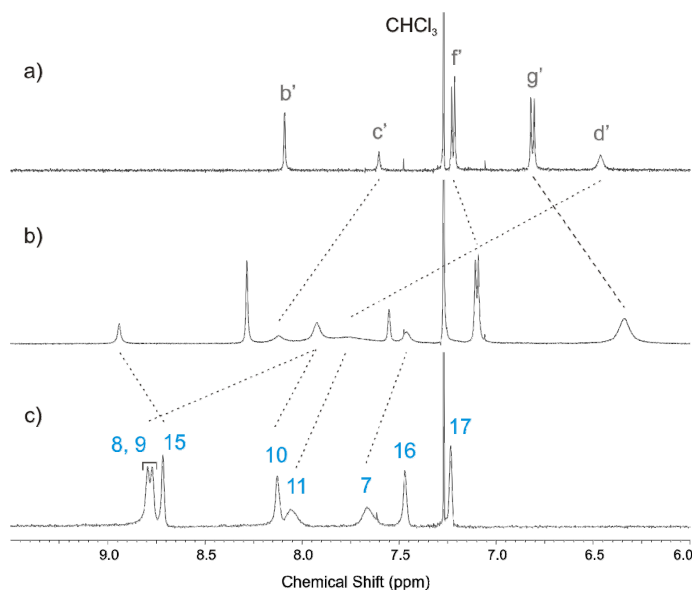


Figure 5.21 Partial ^1H NMR spectra (500 MHz) in CDCl_3 at 293 K of a) macrocycle **22**, b) macrocycle **22** plus 1.0 equivalent of thread **92**· PF_6 , and c) thread **92**· PF_6 .

Formation of pseudorotaxane **22**·**92**· PF_6 was indicated by characteristic shifts analogous to those observed for assembly **1**·**92**· PF_6 (Figure 5.18), namely downfield perturbations in the signals corresponding to macrocycle protons c' and d' , and upfield shifts for macrocycle phenolic protons f' and g' and thread protons 7–11. Interestingly, the spectrum of **22**·**92**· PF_6 is considerably broadened, compared with that of **1**·**92**· PF_6 .²⁴

In contrast with assembly **1**·**92**· PF_6 , the interpenetrated nature of **22**·**92**· PF_6 was able to be confirmed by 2D ^1H - ^1H NMR ROESY spectroscopy, with several intercomponent interactions observed and shown in Figure 5.22.

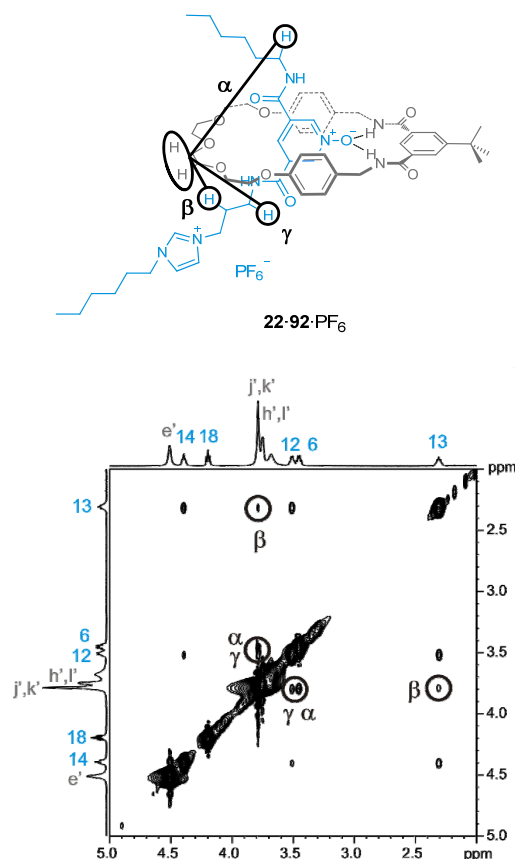


Figure 5.22 Portion of the ^1H - ^1H NMR ROESY spectrum of **22·92·PF₆** (CDCl_3 , 500 MHz, 293 K). Intercomponent correlations are marked on the structure.

A quantitative ^1H NMR titration was undertaken using macrocycle **22** and thread **92·PF₆** (Figure 5.23), however the association was too strong for an accurate value to be obtained using WinEQNMR2 ($K > 10^4 \text{ M}^{-1}$). This indicates that macrocycle **22** exhibits a much greater degree of complementarity with pyridine *N*-oxide thread **92·PF₆** compared with the larger macrocycle system **1·92·PF₆** ($K = 315 \text{ M}^{-1}$). Specifically, reducing the distance between the isophthalamide binding motif and electron-rich aromatics in **22** appears to have increased the strength of the stabilising donor-acceptor interactions between these aromatic groups and the electron-deficient pyridine *N*-oxide motif of the thread.

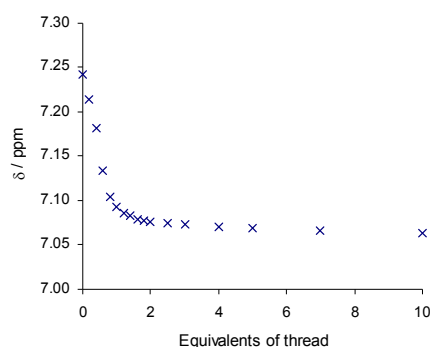
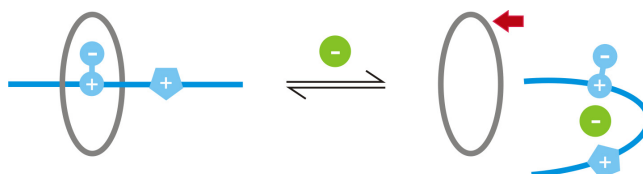


Figure 5.23 Changes in the chemical shift of phenolic protons f' in **22** upon addition of thread **92**·PF₆ in CDCl₃ at 293K (500 MHz, 2.0 x 10⁻³ M).

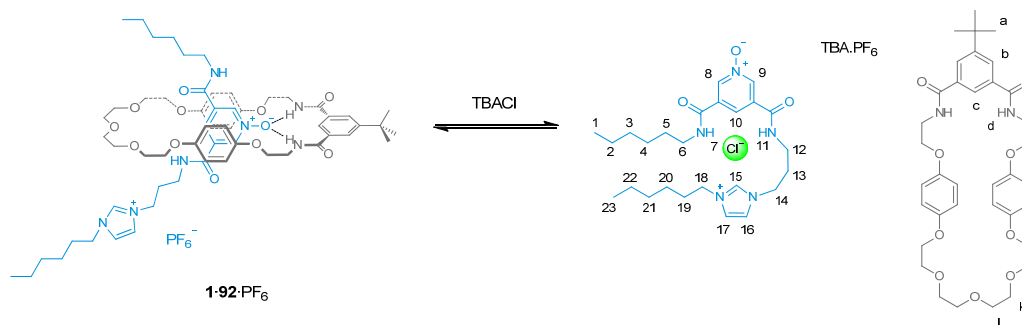
5.4.2 Anion-Induced Pseudorotaxane Disassembly

Having established the ability of pyridine *N*-oxide derivative **92**·PF₆ to form pseudorotaxanes with isophthalamide macrocycles **1** and **22**, the behaviour of these interpenetrated assemblies upon chloride addition was investigated. It was expected that the halide binding induced conformational change exhibited by **92**·PF₆ (Section 5.2.2) would result in pseudorotaxane disassembly (Scheme 5.13).



Scheme 5.13 Schematic representation of anion-induced pseudorotaxane disassembly.

Increasing amounts of TBA chloride were added to an equimolar solution of macrocycle **1** and thread **92**·PF₆ in CDCl₃ (Scheme 5.14), with the corresponding ¹H NMR spectra shown in Figure 5.24.



Scheme 5.14 Anion-induced disassembly of pseudorotaxane **1·92·PF₆**.

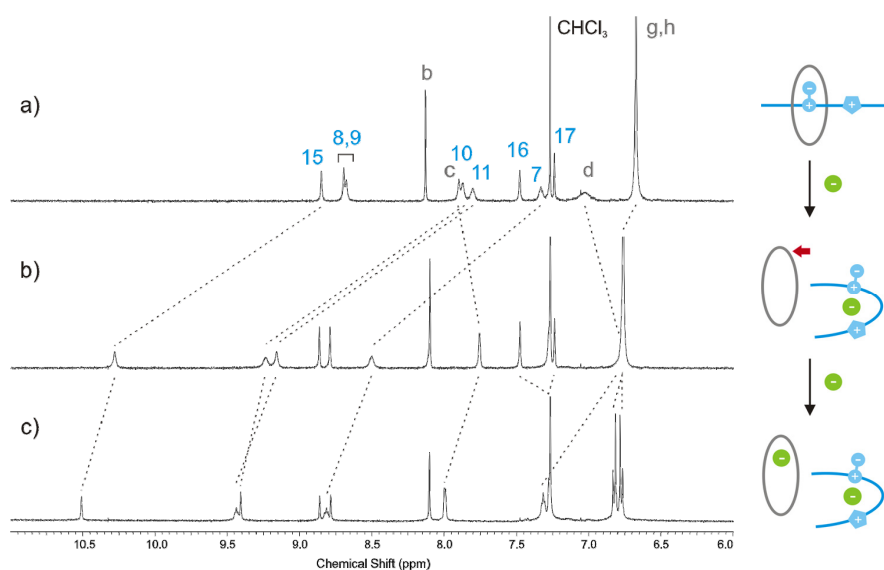


Figure 5.24 Partial ^1H NMR spectra (500 MHz, 2.0×10^{-3} M) in CDCl_3 at 293 K of a) 1:1 macrocycle **1** and thread **92·PF₆**, b) plus 1.0 equivalent of TBACl, and c) plus 5.0 equivalents of TBACl.

Up to one equivalent of chloride, shifts indicative of halide binding to thread **92·PF₆** and simultaneous pseudorotaxane disassembly were observed (Figure 5.24b). Importantly, in addition to downfield shifts in thread protons 7, 10, 11 and 15, the macrocycle proton perturbations observed upon pseudorotaxane formation were reversed – the signals corresponding to protons c and d shifted back upfield and a downfield shift was observed for protons g and h. Beyond one equivalent, anion binding to the free macrocycle also occurs, resulting in additional downfield shifts for the macrocycle hydrogen bond donor atoms (c and d) and a splitting in the signal corresponding to hydroquinone protons g and h (Figure 5.24c).

An identical ^1H NMR study was undertaken with the assembly containing the smaller macrocycle component, $\mathbf{22}\cdot\mathbf{92}\cdot\text{PF}_6$, however upon anion addition the spectrum became even more broadened. This indicates that anion-induced disassembly did not occur for this pseudorotaxane due to the increased strength of interpenetrative association.

5.4.3 Summary

Pyridine *N*-oxide receptor $\mathbf{92}\cdot\text{PF}_6$ was shown to form interpenetrated assemblies with isophthalamide macrocycles $\mathbf{1}$ and $\mathbf{22}$. The pseudorotaxanes exhibited considerably different stabilities relating to the degree of complementarity within the systems, with the weaker pseudorotaxane displaying chloride-induced disassembly due to the conformational change undergone by the thread upon anion binding.

5.5 Conclusions

Preliminary investigations to exploit the anion binding induced conformational changes exhibited by acyclic systems for anion recognition and sensing were carried out. A series of imidazolium-containing acyclic receptors were synthesised and their anion selectivities found to be influenced by a number of factors. The anion sensing ability of an analogous bis-pyrene-appended receptor was studied using fluorescence spectroscopy, with a variety of responses observed upon anion addition *via* excimer signalling mechanisms. In addition, the conformational behaviour exhibited by a pyridine *N*-oxide receptor was utilised in the anion-induced disassembly of a pseudorotaxane assembly.

To extend the sensing investigations, the naphthalimide motif (Chapter Four) is also known to form excimers,²⁵ but less readily than pyrene. This may be advantageous, as a similar naphthalimide-appended receptor (Figure 5.25), would be expected to display reduced excimer emission in its unbound state compared with the large excimer band observed in the pyrene-appended

system (Section 5.3.2). Hence, an amplified ‘OFF-ON’ excimer sensing response might be observed upon anion addition and the associated conformational change.

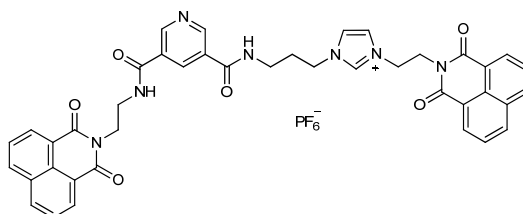


Figure 5.25 Possible naphthalimide-appended receptor system.

Furthermore, there is potential to construct an interlocked rotaxane system based on the pseudorotaxane assembly studies, which may be capable of anion-mediated shuttling molecular motion. The synthesis would require incorporating the pyridine *N*-oxide and imidazolium groups into a mono-stoppered axle component (Figure 5.26), with subsequent ‘click’ stoppering using alkyne **30** in the presence of excess macrocycle **1** relying on the interaction between the axle *N*-oxide and macrocycle isophthalamide motifs to template rotaxane formation. Similar to the pseudorotaxane disassembly behaviour detailed in Section 5.4.2, it is thought that the conformational change exhibited by the axle upon anion binding would result in translocation of the macrocycle component away from the pyridine *N*-oxide group.

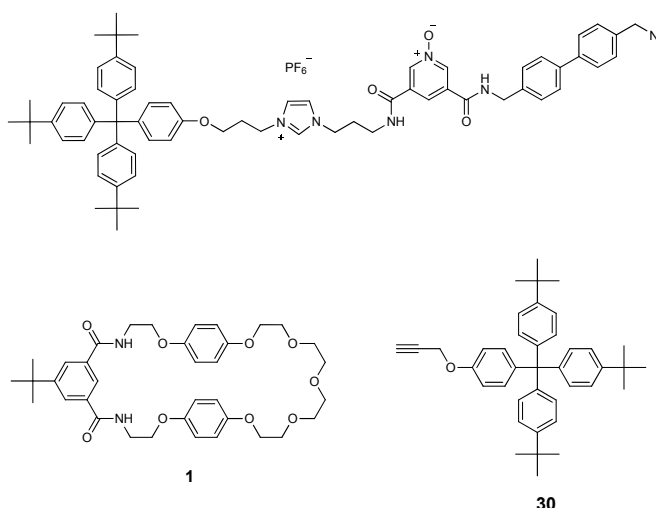


Figure 5.26 Potential mono-stoppered pyridine *N*-oxide axle for use in the synthesis of a rotaxane system with macrocycle **1** and alkyne **30**.

5.6 References

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17. Due to the solubility difficulties associated with this pyrene-appended receptor, the syntheses of analogous pyridine N-oxide and pyridinium receptors were not attempted.
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22. F. M. Winnik, *Chem. Rev.*, 1993, **93**, 587-614.
23. M. Chen, S. Han, L. Jiang, S. Zhou, F. Jiang, Z. Xu, J. Liang and S. Zhang, *Chem. Commun.*, 2010, **46**, 3932-3934.
24. Similar broadening was observed by Jiang for pseudorotaxanes containing analogous macrocycle components, such as the system shown in Figure 5.16a.
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Chapter Six: Experimental

6.1 General Considerations

6.1.1 Instrumental Methods

NMR spectra were recorded on Varian Mercury 300, Varian Unity Plus 500 and Bruker AVII 500 (with ^{13}C Cryoprobe) spectrometers at 293 K. Low resolution electrospray ionisation (ESI) mass spectrometry (MS) was performed using a Waters LCT Premier spectrometer, high resolution ESI MS using Bruker μTOF and 9.4 T FT-ICR-MS spectrometers, field ionisation (FI) MS using a Water GCT Classic spectrometer, and MALDI MS using a Waters MALDI Micro MX spectrometer. Melting points were recorded on a Gallenkamp capillary melting point apparatus and are uncorrected. Microwave reactions were undertaken using a Biotage Initiator 2.0 microwave.

6.1.2 Solvents and Reagents

Commercially available solvents and chemicals were used without further purification unless otherwise stated. Dry solvents were obtained by purging with $\text{N}_{2(\text{g})}$ and then passing through an MBraun MPSP-800 column. Water was de-ionised and microfiltered using a Milli-Q Millipore machine. Et_3N was distilled and stored over KOH. All tetrabutylammonium salts (except $\text{TBAF} \cdot 3\text{H}_2\text{O}$), Grubbs' second-generation catalyst, AgPF_6 , TBTA and $\text{Cu}(\text{MeCN})_4\text{PF}_6$ were stored in a vacuum desiccator prior to use.

Compound **27** was prepared and donated by Dr. Laura Hancock, compound **46**¹ by Dr. Kathleen Mullen, **2.6**² by Nicholas White, and TBTA³ by Lydia Gilday.

6.1.2 Compound Characterisation

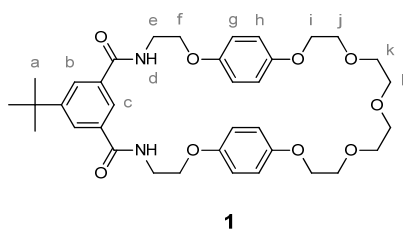
In general, the preparation of previously reported compounds was confirmed by ^1H and ^{13}C NMR spectroscopy and low resolution mass spectrometry (MS). Novel compounds were characterised by ^1H and ^{13}C NMR, low and high resolution MS. Further characterisation was obtained from, where appropriate, ^{19}F NMR and melting points. Where necessary, ^1H NMR assignments were aided by 2D ^1H - ^1H NMR COSY and ROESY spectroscopies.

6.2 Synthetic Procedures

The synthetic procedures undertaken to prepare the compounds described in this thesis are detailed herein, in the order of compound numbering.⁴ SAMs **79**, **80**, **81** and **82** were prepared by Habibur Rahman and more details are given in Appendix A.5. Care was taken not to heat compounds **33** and **34** when dry, as it has been shown that low molecular weight azides can be explosive.

6.2.1 Synthetic Procedures for Chapter Two

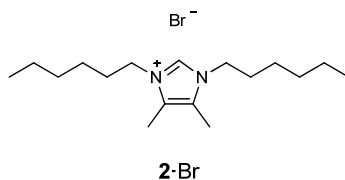
Isophthalamide macrocycle (**1**)¹



Tetra-(ethyleneglycol)di-*p*-toluene sulfonate (**23**) (1.29 g, 2.56 mmol) and precursor **46** (1.26 g, 2.56 mmol) were dissolved in DMF (500 mL). This solution was added dropwise over 12 h to a suspension of Cs_2CO_3 (1.67 g, 5.12 mmol) in DMF (200 mL) at 80 °C. The reaction mixture was then heated at 80 °C for a further 48 h. After this time, the solvent was removed *in vacuo* and the resulting residue stirred in toluene (300 mL) at 90 °C for 2 h. The solution was filtered, reduced to a volume of

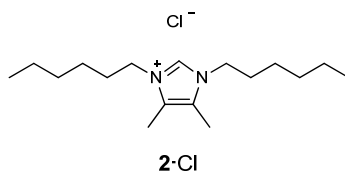
100 mL and cooled to 4 °C. The resulting precipitate was collected by filtration and dried *in vacuo* to yield the product as a white solid (159 mg, 0.244 mmol, 10%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.09 (2H, d, ³*J* = 1.3 Hz, H_b), 7.73 (1H, app s, H_c), 6.78 (8H, s, H_g & H_h), 6.70 (2H, br s, H_d), 4.07–4.13 (4H, m, H_e or H_f), 4.01–4.05 (4H, m, H_e or H_f), 3.82–3.90 (8H, m, H_i & H_j), 3.68–3.74 (8H, m, H_k & H_l), 1.37 (9H, s, H_a). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 167.3, 153.3, 152.9, 152.5, 134.4, 128.2, 120.8, 115.6, 115.4, 70.8, 70.7, 69.7, 68.1, 67.2, 39.6, 35.1, 31.1. **MS-ESI** *m/z* 673.3 (100%, [M + Na]⁺, C₃₆H₄₆N₂NaO₉, calc. 673.3), 668.3 (90%, [M + NH₄]⁺); 685.3 ([M + Cl]⁺).

1,3-Dihexyl-4,5-dimethyl-1*H*-imidazol-3-ium bromide (2·Br)⁵



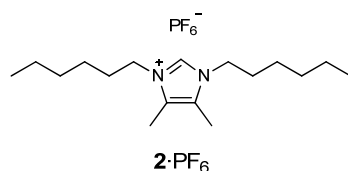
1-Hexyl-4,5-dimethyl-1*H*-imidazole (**5**) (584 mg, 3.01 mmol) and 1-bromohexane (588 mg, 3.31 mmol) were dissolved in acetone (15 mL) and heated under microwave irradiation at 150 °C for 30 min. After this time, the solvent was removed *in vacuo* and the resulting residue triturated with hexane (3 x 5 mL) to yield the product as an orange oil (692 mg, 2.30 mmol, 71%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 10.32 (1H, s, NC-*H*), 4.19 (4H, t, ³*J* = 7.6 Hz, 2 x N-CH₂-), 2.23 (6H, s, 2 x NC-CH₃), 1.77–1.87 (4H, m, 2 x NCH₂-CH₂-), 1.24–1.37 (12H, m, 6 x -CH₂-), 0.82–0.88 (6H, m, 2 x CH₂-CH₃). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 136.0, 126.0, 47.2, 31.0, 30.0, 25.9, 22.3, 13.8, 8.5. **MS-ESI** *m/z* 265.3 (100%, [M – Br]⁺, C₁₇H₃₃N₂, calc. 265.3), 611.5 (95%, [2M – Br]⁺).

1,3-Dihexyl-4,5-dimethyl-1*H*-imidazol-3-ium chloride (2·Cl)⁵

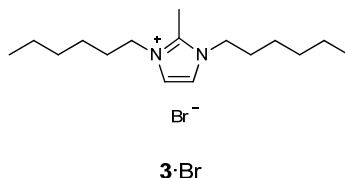


1,3-Dihexyl-4,5-dimethyl-1*H*-imidazol-3-ium bromide (**2**·Br) (350 mg, 1.16 mmol) was dissolved in CH₂Cl₂ (10 mL) and washed with 1.0 M NH₄Cl_(aq) (10 x 10 mL), H₂O (3 x 10 mL) and brine (1 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a yellow waxy solid (164 mg, 0.55 mmol, 47%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 10.72 (1H, s, NC-*H*), 4.22 (4H, t, ³*J* = 7.6 Hz, 2 x N-CH₂-), 2.23 (6H, s, 2 x NC-CH₃), 1.77–1.90 (4H, m, 2 x NCH₂-CH₂-), 1.27–1.40 (12H, m, 6 x -CH₂-), 0.84–0.91 (6H, m, 2 x CH₂-CH₃). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 136.7, 125.8, 47.2, 31.0, 30.0, 25.9, 22.3, 13.8, 8.4. **MS-ESI** *m/z* 265.3 (100%, [M – Cl]⁺, C₁₇H₃₃N₂, calc. 265.3), 565.5 (45%, [2M – Cl]⁺).

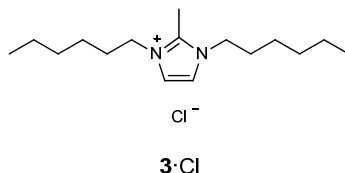
1,3-Dihexyl-4,5-dimethyl-1*H*-imidazol-3-ium hexafluorophosphate (2·PF₆)



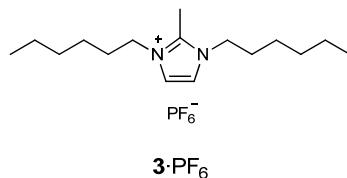
1,3-Dihexyl-4,5-dimethyl-1*H*-imidazol-3-ium bromide (**2**·Br) (300 mg, 0.87 mmol) was dissolved in CH₂Cl₂ (10 mL) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (4 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as an orange oil (312 mg, 0.76 mmol, 87%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.48 (1H, s, NC-*H*), 4.03 (4H, t, ³*J* = 7.6 Hz, 2 x N-CH₂-), 2.25 (6H, s, 2 x NC-CH₃), 1.79 (4H, quin, ³*J* = 7.5 Hz, 2 x NCH₂-CH₂-), 1.27–1.36 (12H, m, 6 x -CH₂-), 0.86–0.90 (6H, m, 2 x CH₂-CH₃). **¹⁹F NMR** (282.5 MHz, CDCl₃) δ (ppm) –72.9 (d, ¹*J* = 712 Hz, PF₆). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 133.7, 126.8, 47.3, 31.0, 29.6, 25.9, 22.4, 13.9, 8.3. **MS-ESI** *m/z* 265.2632 ([M – PF₆]⁺, C₁₇H₃₃N₂, calc. 265.2638), 265.3 (100%, [M – PF₆]⁺), 675.5 (25%, [2M – PF₆]⁺).

1,3-Dihexyl-2-methyl-1*H*-imidazol-3-ium bromide (3·Br)⁵

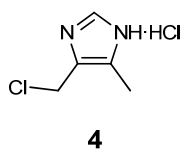
1-Hexyl-2-methyl-1*H*-imidazole (**7**) (500 mg, 3.01 mmol) and 1-bromohexane (546 mg, 3.31 mmol) were dissolved in acetone (15 mL) and heated under microwave irradiation at 150 °C for 30 min. After this time, the solvent was removed *in vacuo* and the resulting residue triturated with Et₂O (3 x 5 mL) to yield the product as a yellow oil (886 mg, 2.67 mmol, 89%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.53 (2H, s, NC-*H*), 4.26 (4H, t, ³*J* = 7.6 Hz, 2 x N-CH₂-), 2.82 (3H, s, NC-CH₃), 1.78–1.91 (4H, m, 2 x NCH₂-CH₂-), 1.26–1.41 (12H, m, 6 x -CH₂-), 0.84–0.93 (6H, m, 2 x CH₂-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 142.8, 121.6, 48.9, 31.0, 29.7, 25.8, 22.2, 13.7, 10.8. MS-ESI *m/z* 251.3 (100%, [M – Br]⁺, C₁₆H₃₁N₂, calc. 251.2), 583.5 (35%, [2M – Br]⁺).

1,3-Dihexyl-2-methyl-1*H*-imidazol-3-ium chloride (3·Cl)⁵

1,3-Dihexyl-2-methyl-1*H*-imidazol-3-ium bromide (**3·Br**) (342 mg, 1.03 mmol) was dissolved in CH₂Cl₂ (10 mL) and washed with 1.0 M NH₄Cl_(aq) (10 x 10 mL), H₂O (3 x 10 mL) and brine (1 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as an off white waxy solid (135 mg, 0.47 mmol, 46%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.59 (2H, s, NC-*H*), 4.25 (4H, t, ³*J* = 7.3 Hz, 2 x N-CH₂-), 2.79 (3H, s, NC-CH₃), 1.81 (4H, quin, ³*J* = 7.3 Hz, 2 x NCH₂-CH₂-), 1.24–1.37 (12H, m, 6 x -CH₂-), 0.81–0.91 (6H, m, 2 x CH₂-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 142.9, 121.7, 48.9, 31.1, 29.8, 26.0, 22.3, 13.8, 10.6. MS-ESI *m/z* 251.3 (100%, [M – Cl]⁺, C₁₆H₃₁N₂, calc. 251.2), 537.5 (15%, [2M – Cl]⁺).

1,3-Dihexyl-2-methyl-1*H*-imidazol-3-ium hexafluorophosphate (3·PF₆)

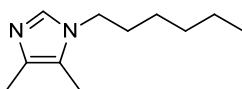
1,3-Dihexyl-2-methyl-1*H*-imidazol-3-ium bromide (**3·Br**) (200 mg, 0.60 mmol) was dissolved in CH₂Cl₂ (10 mL) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (4 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a pale yellow waxy solid (123 mg, 0.31 mmol, 52%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.22 (2H, s, NC-*H*), 4.05 (4H, t, ³*J* = 7.5 Hz, 2 x N-CH₂), 2.60 (3H, s, NC-CH₃), 1.79 (4H, quin, ³*J* = 7.5 Hz, 2 x NCH₂-CH₂-), 1.27–1.36 (12H, m, 6 x -CH₂-), 0.85–0.90 (6H, m, 2 x -CH₃). ¹⁹F NMR (282.5 MHz, CDCl₃) δ (ppm) –73.6 (d, ¹*J* = 714 Hz, PF₆). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 143.0, 121.1, 48.6, 31.0, 29.5, 25.9, 22.3, 13.9, 9.3. MS-ESI *m/z* 251.2475 ([M – PF₆]⁺, C₁₆H₃₁N₂, calc. 251.2482), 251.2 (100%, [M – PF₆]⁺), 647.5 (35%, [2M – PF₆]⁺).

5-(Chloromethyl)-4-methyl-1*H*-imidazole hydrochloride (4**)⁶**

(4-Methyl-1*H*-imidazol-5-yl)methanol hydrochloride (5.00 g, 34.0 mmol) was stirred in SOCl₂ (12 mL) at room temperature under N_{2(g)} for 1 h. After this time, CHCl₃ (50 mL) was added and the resulting precipitate collected by filtration, washed with CHCl₃ (2 x 25 mL) and dried *in vacuo* to yield the product as a white solid (5.38 g, 32.2 mmol, 95%). ¹H NMR (300 MHz, *d*₆-DMSO) δ (ppm) 9.04 (1H, s, NC-*H*), 4.90 (2H, s, -CH₂-), 2.32 (3H, s, -CH₃). ¹³C NMR (75.5 MHz, *d*₆-DMSO) δ (ppm) 133.5, 128.0, 124.7, 33.8, 8.5. MS not observed.

4,5-Dimethyl-1*H*-imidazole (5)⁶**5**

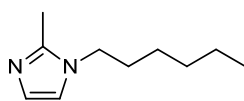
5-(Chloromethyl)-4-methyl-1*H*-imidazole hydrochloride (**4**) (3.00 g, 18.0 mmol) was dissolved in EtOH (20 mL) in a high pressure reactor and Pd/C (10% loading, 0.30 g, 10% by weight) added. H_{2(g)} was bubbled through the reaction mixture, which was subsequently stirred at room temperature under 5 atm H_{2(g)} for 24 h, with the gas replenished batchwise as it was consumed. After removal of the catalyst by filtration through Celite[®], the solvent was removed *in vacuo* and the resulting residue dissolved in sat. Na₂CO_{3(aq)} (50 mL). Extraction with Et₂O (5 x 50 mL) and removal of the solvent under a stream of N_{2(g)} yielded the product as white solid (1.26 g, 13.1 mmol, 73%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.43 (1H, s, NC-*H*), 2.17 (6H, s, -CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 132.3, 126.5, 10.6. MS not observed.

1-Hexyl-4,5-dimethyl-1*H*-imidazole (6)⁵**6**

NaH (60% dispersion in mineral oil, 250 mg, 6.24 mmol) was suspended in dry THF (10 mL) at 0 °C under N_{2(g)}. 4,5-Dimethyl-1*H*-imidazole (**5**) (500 mg, 5.20 mmol) in dry THF (10 mL) was added dropwise to this solution, followed by 1-bromohexane (0.73 mL, 5.20 mmol) in dry THF (10 mL). The reaction mixture was allowed to warm to room temperature and stirred for 15 h. After this time, H₂O (10 mL) was added carefully and the organic solvent removed *in vacuo*. The product was extracted with Et₂O (3 x 10 mL), the combined organic fractions washed with H₂O (1 x 20 mL) and brine (1 x 20 mL) and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as a yellow oil (793 mg, 4.39 mmol, 85%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.23 (1H, s, NC-*H*), 3.72

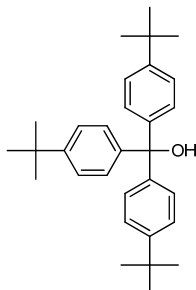
(2H, t, $^3J = 7.3$ Hz, N-CH₂-), 2.11 (3H, s, NC-CH₃), 2.07 (3H, s, NC-CH₃), 1.60–1.69 (2H, m, NCH₂-CH₂-), 1.22–1.31 (6H, m, 3 x -CH₂-), 0.82–0.88 (3H, m, CH₂-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 134.5, 133.0, 122.0, 45.1, 31.2, 30.6, 26.2, 22.4, 13.9, 12.4, 8.3. MS-ESI *m/z* 181.2 ([M + H]⁺, C₁₁H₂₁N₂, calc. 181.2).

1-Hexyl-2-methyl-1*H*-imidazole (7)⁵

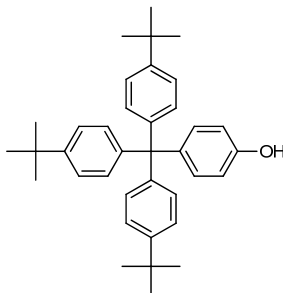


7

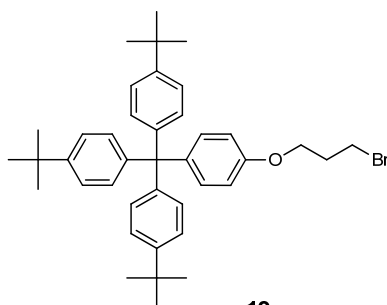
NaH (60% dispersion in mineral oil, 1.75 g, 43.8 mmol) was suspended in dry THF (75 mL) at 0 °C under N_{2(g)}. 2-Methyl-1*H*-imidazole (3.00 g, 36.5 mmol) in dry THF (25 mL) was added dropwise to this solution, followed by 1-bromohexane (5.13 mL, 36.5 mmol) in dry THF (25 mL). The reaction mixture was allowed to warm to room temperature and stirred for 15 h. After this time, H₂O (100 mL) was added carefully and the organic solvent removed *in vacuo*. The product was extracted with Et₂O (3 x 50 mL), the combined organic fractions washed with H₂O (1 x 75 mL) and brine (1 x 75 mL), dried over MgSO₄ and the solvent removed *in vacuo*. The residue was triturated with hexane (3 x 30 mL) to yield the product as a yellow oil (5.63 g, 33.9 mmol, 93%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 6.90 (1H, s, NC-*H*), 6.81 (1H, s, NC-*H*), 3.81 (2H, t, $^3J = 7.0$ Hz, N-CH₂-Alkyl), 2.37 (3H, s, NC-CH₃), 1.67–1.75 (2H, m, NCH₂-CH₂-), 1.24–1.35 (6H, m, 3 x -CH₂-), 0.84–0.93 (3H, m, CH₂-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) 144.3, 126.9, 118.9, 46.0, 31.3, 30.7, 26.2, 22.4, 13.9, 13.0. MS-ESI *m/z* 167.1 ([M + H]⁺, C₁₀H₁₉N₂, calc. 167.1).

Tris(4-(*tert*-butyl)phenyl)methanol (8)⁷**8**

Mg turnings (9.72 g, 400 mmol) were washed with petroleum ether and dried using a heat gun *in vacuo*. Dry THF (40 mL) was added to cover the turnings, followed by a few I₂ crystals. To this solution was added a 10 mL aliquot of a solution of 1-bromo-4-*tert*-butyl benzene (61.4 mL, 360 mmol) in dry THF (200 mL) and the reaction mixture stirred under gentle heating for 30 min to initiate the reaction. The remaining solution was then added dropwise at such a rate to maintain a gentle reflux. After complete addition, the reaction was heated at reflux for 1 h. Diethyl carbonate (14.2 g, 120 mmol) in dry THF (60 mL) was then added dropwise and the mixture heated at reflux for a further 1 h. The reaction mixture was allowed to cool to room temperature and then poured carefully onto a mixture of ice (300 g) and conc. H₂SO₄ (30 mL). The organic solvent was removed *in vacuo* and the aqueous phase extracted with CH₂Cl₂ (4 x 300 mL). The combined organic fractions were concentrated *in vacuo*, washed with 5% NaHCO_{3(aq)} (300 mL) and H₂O (300 mL), and dried over MgSO₄. The solvent was removed *in vacuo* and the crude yellow solid recrystallised from cyclohexane to yield the product as a white solid (23.0 g, 53.7 mmol, 45%). **¹H NMR** (300 MHz, CDCl₃) 7.31–7.35 (6H, m, Ar-*H*), 7.17–7.22 (6H, m, Ar-*H*), 2.74 (1H, s, -OH), 1.32 (27H, s, -*t*Bu). **¹³C NMR** (75.5 MHz, CDCl₃) 149.8, 144.2, 127.5, 124.7, 81.5, 34.4, 31.4. **MS-ESI** *m/z* 427.3 (60%, [M – H][–], C₃₁H₃₉O, calc. 427.3), 855.6 (100%, [2M – H][–]).

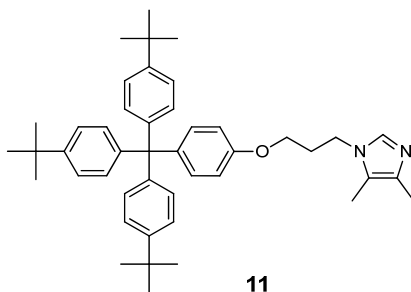
4-(Tris(4-(*tert*-butyl)phenyl)methyl)phenol (9)⁷**9**

To a solution of tris(4-(*tert*-butyl)phenyl)methanol (**8**) (13.0 g, 33.0 mmol) in molten phenol (100 g) was added conc. HCl (1 mL) and the reaction mixture heated at 120 °C under N_{2(g)} for 15 h. After this time, the reaction mixture was cooled to room temperature, KOH_(aq) (120 g in 300 mL H₂O) added and the solution filtered. The pale yellow precipitate was washed with H₂O (500 mL), 20% acetic acid_(aq) (500 mL) and H₂O (500 mL), and dissolved in CHCl₃ (1 L). The solution was dried over MgSO₄, decolourised over activated charcoal and the solvent removed *in vacuo*. The resulting white solid was suspended in hexane (250 mL) and heated at reflux for 30 min. The suspension was filtered to yield the product as a white solid (11.5 g, 22.7 mmol, 69%). ¹H NMR (300 MHz, CDCl₃) 7.22–7.26 (6H, m, Ar-*H*), 7.04–7.11 (8H, m, Ar-*H*), 6.68–6.73 (2H, m, OAr-*H*), 4.60 (1H, s, -OH), 1.31 (27H, s, -*t*Bu). ¹³C NMR (75.5 MHz, CDCl₃) 148.3, 144.1, 139.8, 132.4, 130.7, 124.0, 113.9, 70.0, 34.3, 31.4. MS-ESI *m/z* 503.4 ([M – H][–], C₃₇H₄₃O, calc. 503.3).

1-(3-bromo-propoxy)-4-(tris(4-*tert*-butyl-phenyl)-methyl)-benzene (10)⁸**10**

4-(Tris-(4-*tert*-butyl-phenyl)-methyl)-phenol (**9**) (3.00 g, 5.94 mmol), 3-bromo-propan-1-ol (1.07 mL, 11.9 mmol) and PPh₃ (3.12 g, 11.9 mmol) were dissolved in dry THF (150 mL) at 0 °C. DEAD (1.87 mL, 11.9 mmol) was added dropwise and the reaction mixture was allowed to warm to room temperature and stirred for 48 h. After this time, the solvent was removed *in vacuo*, the residue dissolved in CH₂Cl₂ (50 mL) and precipitated with MeOH (150 mL). The precipitate was filtered, washed with further MeOH (3 x 50 mL) and redissolved in CH₂Cl₂ (50 mL). The solution was passed through a plug of silica using CH₂Cl₂ as the eluent and the solvent removed *in vacuo* to yield the product as a white solid (3.05 g, 4.88 mmol, 82%). ¹H NMR (300 MHz, CDCl₃) 7.24 (6H, d, ³J = 8.2 Hz, Ar-*H*), 7.08–7.12 (8H, m, Ar-*H*), 6.76–6.79 (2H, m, OAr-*H*), 4.09 (2H, t, ³J = 5.9 Hz, O-CH₂-), 3.61 (2H, t, ³J = 6.5 Hz, -CH₂-Br), 2.28–2.35 (2H, m, CH₂-CH₂-CH₂), 1.32 (27H, s, -*t*Bu). ¹³C NMR (75.5 MHz, CDCl₃) 156.4, 148.3, 144.1, 139.8, 132.3, 130.7, 124.0, 113.0, 65.1, 63.0, 34.3, 32.5, 31.4, 30.2. MS-FI *m/z* 624.3 ([M]⁺, C₄₀H₄₉BrO, calc. 624.3).

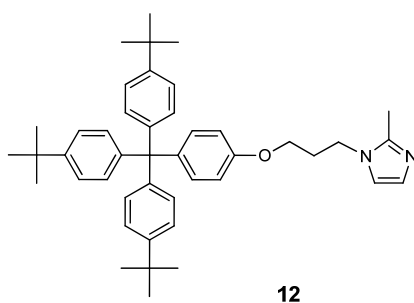
4,5-Dimethyl-1-(3-(4-(tris(4-(*tert*-butyl)phenyl)methyl)phenoxy)propyl)-1*H*-imidazole (11**)**



NaH (60% dispersion in mineral oil, 250 mg, 6.24 mmol) was suspended in dry THF (20 mL) at 0 °C under N_{2(g)}. To this solution was added 4,5-dimethyl-1*H*-imidazole (**5**) (500 mg, 5.21 mmol) in dry THF (15 mL) dropwise and the mixture stirred at room temperature for 1 h. After this time, bromo-functionalised stopper **10** (651 mg, 1.04 mmol) in dry THF (15 mL) was added dropwise and the solution stirred for 15 h. After careful addition of H₂O (50 mL) and removal of THF *in vacuo*, the product was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic fractions were washed with H₂O (1 x 100 mL) and brine (1 x 100 mL), dried over MgSO₄ and the solvent removed *in vacuo*.

Purification was undertaken by silica gel column chromatography using 97:3 CH₂Cl₂/MeOH to elute the product as a white solid (471 mg, 0.73 mmol, 71%). **Mp** 225–230 °C (dec.). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 7.36 (1H, s, NC-*H*), 7.22–7.26 (6H, m, Ar-*H*), 7.06–7.11 (8H, m, Ar-*H*), 6.73–6.77 (2H, m, OAr-*H*), 4.03 (2H, t, ³*J* = 7.0 Hz, O-CH₂-), 3.90 (2H, t, ³*J* = 5.6 Hz, N-CH₂-), 2.13–2.16 (8H, m, 2 x NC-CH₃ & CH₂-CH₂-CH₂), 1.31 (27H, s, ⁻Bu). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 156.2, 148.3, 144.0, 140.0, 135.0, 133.8, 132.3, 130.7, 124.0, 122.0, 112.9, 63.5, 63.0, 41.4, 34.3, 31.4, 30.4, 12.7, 8.3. **MS-ESI** *m/z* 641.4471 ([M + H]⁺, C₄₅H₅₇N₂O, calc. 641.4465), 641.5 ([M + H]⁺) – only observed peak in low resolution mass spectrum.

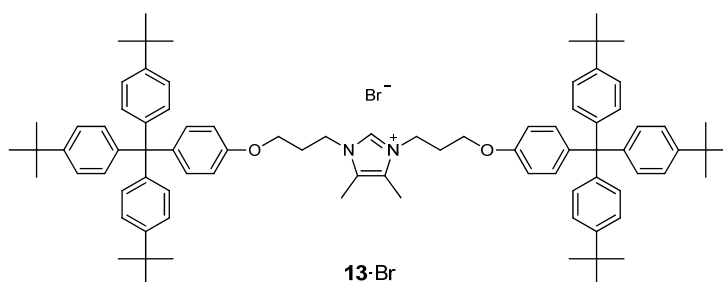
2-Methyl-1-(3-(4-(tris(4-*tert*-butyl)phenyl)methyl)phenoxy)propyl)-1*H*-imidazole (12)



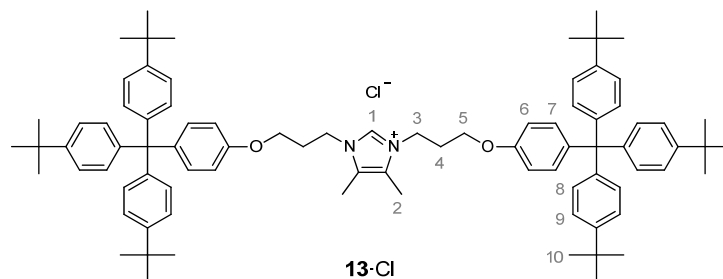
NaH (60% dispersion in mineral oil, 479 mg, 12.0 mmol) was suspended in dry THF (10 mL) at 0 °C under N_{2(g)}. To this solution was added 2-methylimidazole (1.90 g, 24.0 mmol) in dry THF (30 mL) dropwise, and the mixture stirred at room temperature for 1 h. After this time, bromo-functionalised stopper **10** (1.50 g, 2.40 mmol) in dry THF (10 mL) was added dropwise and the solution stirred for 15 h. After careful addition of H₂O (50 mL) and removal of THF *in vacuo*, the product was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic fractions were washed with H₂O (1 x 100 mL) and brine (1 x 100 mL), dried over MgSO₄ and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 98:2 CH₂Cl₂/MeOH to elute the product as a white solid (987 mg, 1.57 mmol, 66%). **Mp** > 250 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 7.22–7.26 (6H, m, Ar-*H*), 7.06–7.11 (8H, m, Ar-*H*), 6.92 (1H, s, NC-*H*), 6.84 (1H, s, NC-*H*), 6.73–6.76 (2H, m, OAr-*H*), 4.08 (2H, t, ³*J* = 6.7 Hz, O-CH₂-), 3.89 (2H, t, ³*J* = 5.6 Hz, N-CH₂-), 2.37 (3H, s, NC-CH₃), 2.14–2.21

(2H, m, CH₂-CH₂-CH₂), 1.31 (27H, s, -^tBu). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 156.1, 148.3, 144.0, 140.1, 132.3, 130.7, 127.3, 124.0, 119.0, 112.9, 63.4, 63.0, 42.4, 34.3, 31.4, 30.3, 12.9 (one peak missing – coincidental). MS-ESI *m/z* 627.4309 ([M + H]⁺, C₄₄H₅₅N₂O, calc. 627.4309), 627.4 ([M + H]⁺) – only observed peak in low resolution mass spectrum.

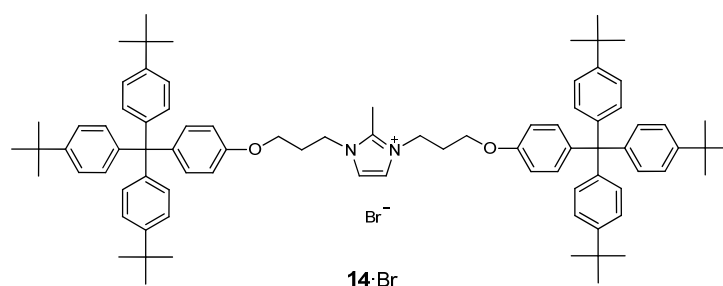
4,5-Dimethylimidazolium bromide axle (13·Br)



Imidazole derivative **11** (200 mg, 0.31 mmol) and bromo-functionalised stopper **10** (254 mg, 0.42 mmol) were suspended in acetone (20 mL) and heated under microwave irradiation at 150 °C for 3 h. The solvent was removed *in vacuo* and the residue purified by silica gel column chromatography using 97.5:2.5 CH₂Cl₂/MeOH to elute the product as a white solid (294 mg, 0.23 mmol, 75%). **13** mp 230–235 °C (dec.). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 10.61 (1H, s, NC-*H*), 7.20–7.25 (12H, m, Ar-*H*), 7.04–7.10 (16H, m, Ar-*H*), 6.66–6.71 (4H, m, OAr-*H*), 4.40 (4H, t, ³*J* = 7.0 Hz, 2 x N-CH₂-), 4.00 (4H, t, ³*J* = 5.3 Hz, 2 x O-CH₂-), 2.34–2.42 (4H, m, 2 x CH₂-CH₂-CH₂), 2.21 (6H, s, 2 x NC-CH₃), 1.30 (54H, s, -^tBu). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 155.8, 148.3, 144.0, 140.2, 136.5, 132.3, 130.6, 126.2, 124.0, 112.8, 63.8, 63.0, 44.2, 34.3, 31.3, 29.6, 8.3. MS-ESI *m/z* 1185.8171 ([M – Br]⁺, C₈₅H₁₀₅N₂O₂, calc 1185.8171), 1186.0 ([M – Br]⁺) – only observed peak in low resolution mass spectrum.

4,5-Dimethylimidazolium chloride axle (13·Cl)

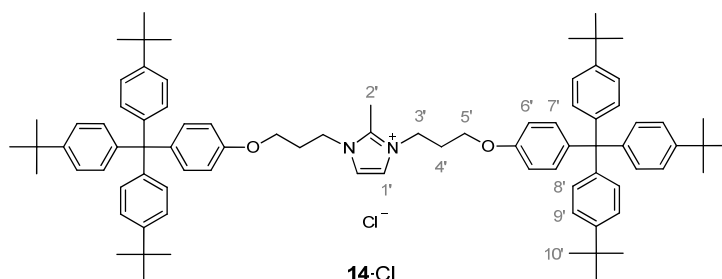
4,5-Dimethylimidazolium bromide axle (**13·Br**) (300 mg, 0.24 mmol) was dissolved in CH_2Cl_2 (30 mL) and washed with 1.0 M $\text{NH}_4\text{Cl}_{(\text{aq})}$ (10 x 25 mL), H_2O (4 x 25 mL) and brine (1 x 25 mL). The organic fraction was dried over MgSO_4 and the solvent removed *in vacuo* to yield the product as a white solid (269 mg, 0.22 mmol, 93%). **Mp** 240–245 °C (dec.). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 10.87 (1H, s, H_1), 7.20–7.25 (12H, m, H_9), 7.04–7.10 (16H, m, H_7 & H_8), 6.66–6.71 (4H, m, H_6), 4.39 (4H, t, $^3J = 7.0$ Hz, H_3), 4.00 (4H, t, $^3J = 5.3$ Hz, H_5), 2.35–2.42 (4H, m, H_4), 2.21 (6H, s, H_2), 1.30 (54H, s, H_{10}). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 155.8, 148.3, 144.0, 140.2, 137.2, 132.3, 130.6, 126.1, 124.0, 112.8, 63.8, 63.0, 44.2, 34.3, 31.4, 29.6, 8.3. **MS-ESI** m/z 1185.8172 ($[\text{M} - \text{Cl}]^+$, $\text{C}_{85}\text{H}_{105}\text{N}_2\text{O}_2$, calc. 1185.8171), 1185.8 ($[\text{M} - \text{Cl}]^+$) – only observed peak in low resolution mass spectrum.

2-Methylimidazolium bromide axle (14·Br)

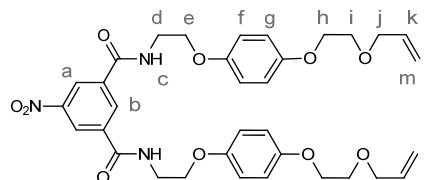
Imidazole derivative **12** (200 mg, 0.32 mmol) and bromo-functionalised stopper **10** (260 mg, 0.42 mmol) were suspended in acetone (15 mL) and heated under microwave irradiation at 150 °C for

3 h. The solvent was removed *in vacuo* and the residue purified by silica gel column chromatography using 97.5:2.5 CH₂Cl₂/MeOH to elute the product as a white solid (308 mg, 0.25 mmol, 77%). **Mp** > 250 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 7.54 (2H, s, NC-*H*), 7.21–7.24 (12H, m, Ar-*H*), 7.04–7.11 (16H, m, Ar-*H*), 6.66–6.69 (4H, m, OAr-*H*), 4.46 (4H, t, ³*J* = 6.5 Hz, 2 x N-CH₂-), 3.98 (4H, t, ³*J* = 5.3 Hz, 2 x O-CH₂-), 2.77 (3H, s, NC-CH₃), 2.34–2.37 (4H, m, 2 x CH₂-CH₂-CH₂), 1.30 (54H, s, -*t*Bu). **¹³C NMR** (125.8 MHz, CDCl₃) δ (ppm) 155.6, 148.4, 144.1, 143.9, 140.5, 132.5, 130.7, 124.1, 121.8, 112.8, 63.4, 63.0, 46.0, 34.3, 31.4, 29.7, 10.8. **MS-ESI** *m/z* 1171.8024 ([M – Br]⁺, C₈₄H₁₀₃N₂O₂, calc. 1171.8014), 1171.8 ([M – Br]⁺) – only observed peak in low resolution mass spectrum.

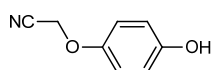
2-Methylimidazolium chloride axle (14·Cl)



2-Methylimidazolium bromide axle (**14**) (350 mg, 0.28 mmol) was dissolved in CH₂Cl₂ (40 mL) and washed with 1.0 M NH₄Cl_(aq) (10 x 25 mL), H₂O (4 x 25 mL) and brine (1 x 25 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a white solid (317 mg, 0.26 mmol, 94%). **Mp** > 250 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 7.69 (2H, s, H_{1'}), 7.20–7.23 (12H, m, H_{9'}), 7.04–7.10 (16H, m, H_{7'} & H_{8'}), 6.65–6.68 (4H, m, H_{6'}), 4.48 (4H, t, ³*J* = 6.8 Hz, H_{3'}), 3.95 (4H, t, ³*J* = 5.3 Hz, H_{5'}), 2.74 (3H, s, H_{2'}), 2.31–2.39 (4H, m, H_{4'}), 1.29 (54H, s, H_{10'}). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 155.6, 148.4, 143.9, 143.8, 140.5, 132.5, 130.6, 124.1, 122.1, 112.8, 63.4, 63.0, 45.8, 34.3, 31.4, 29.1, 10.3. **MS-ESI** *m/z* 1171.8006 ([M – Cl]⁺, C₈₄H₁₀₃N₂O₂, calc. 1171.8014), 1171.9 ([M – Cl]⁺) – only observed peak in low resolution mass spectrum.

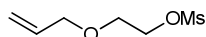
Bis-vinyl macrocycle precursor (15)⁹**15**

5-Nitroisophthalic acid (680 mg, 3.20 mmol) was added to SOCl_2 (10 mL) and the mixture was heated at reflux under $\text{N}_{2(g)}$ for 3 days. The excess SOCl_2 was then removed by distillation and the resulting residue further dried *in vacuo* after additions of dry CH_2Cl_2 (3 x 1 mL). The crude dichloride (assumed quantitative conversion) was immediately dissolved in dry CH_2Cl_2 (100 mL) and added dropwise to a solution of 2-(4-(2-(allyloxy)ethoxy)phenoxy)ethanamine (**19**) (1.60 g, 6.74 mmol) and Et_3N (13.5 mL) in dry CH_2Cl_2 (100 mL) which has been stirred at 0 °C for 10 min. The reaction mixture was stirred at 0 °C for 2 h, after which time the solution was washed with 10% $\text{HCl}_{(aq)}$ (3 x 100 mL) and H_2O (3 x 100 mL), dried over MgSO_4 and the solvent removed *in vacuo*. The resulting residue was purified by silica gel column chromatography using 7:3 $\text{EtOAc}/\text{CH}_2\text{Cl}_2$ to elute the product as a pale yellow solid (1.35 g, 2.08 mmol, 65%). **¹H NMR** (300 MHz, CDCl_3) δ (ppm) 8.70 (2H, d, $^3J = 1.5$ Hz, H_a), 8.54 (1H, t, $^3J = 1.5$ Hz, H_b), 7.17 (2H, br s, H_c), 6.76–6.82 (8H, m, H_f & H_g), 5.94 (2H, ddt, $^3J = 17.3$ Hz, $^3J = 10.3$ Hz, $^3J = 5.7$ Hz, H_k), 5.31 (2H, ddt, $^3J = 17.3$ Hz, $^2J = 1.5$ Hz, $^4J = 1.5$ Hz, H_m), 5.21 (2H, ddt, $^3J = 10.3$ Hz, $^2J = 1.5$ Hz, $^4J = 1.5$ Hz, H_l), 4.03–4.10 (12H, m, H_e & H_h & H_j), 3.83–3.88 (4H, m, H_d), 3.76–3.79 (4H, m, H_i). **¹³C NMR** (75.5 MHz, CDCl_3) δ (ppm) 164.6, 153.3, 152.5, 148.2, 136.3, 134.4, 131.2, 124.6, 117.5, 115.6, 115.3, 72.4, 68.6, 67.9, 66.8, 40.1. **MS-ESI** m/z 672.3 ($[\text{M} + \text{Na}]^+$, $\text{C}_{34}\text{H}_{39}\text{NaN}_3\text{O}_{10}$, calc. 672.3).

2-(4-Hydroxyphenoxy)acetonitrile (16)¹⁰**16**

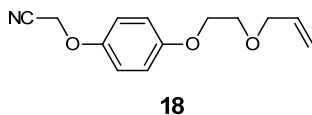
A solution of NaOH (6.66 g, 167 mmol) and hydroquinone (9.14 g, 83.0 mmol) in a previously degassed 1,4-dioxane/H₂O mixture (175 mL/200 mL) was stirred under N_{2(g)}. Bromoacetonitrile (5.80 mL, 83.0 mmol) in 1,4-dioxane (25 mL) was then added dropwise and the reaction mixture left to stir at room temperature for 2 h. After acidification of the solution with 3 M HCl_(aq) (75 mL), the product was extracted with CH₂Cl₂ (3 x 200 mL) and the combined organic fractions washed with brine (2 x 150 mL), dried over MgSO₄ and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 98:2 CH₂Cl₂/MeOH to elute the product as a yellow oil (6.60 g, 44.3 mmol, 53%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 6.91 (2H, d, ³J = 9.1 Hz, Ar-*H*), 6.80 (2H, d, ³J = 9.1 Hz, Ar-*H*), 5.12 (1H, br s, -OH), 4.71 (2H, s, -CH₂-). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 151.8, 150.4, 116.9, 116.3, 67.0, 55.0. MS-ESI *m/z* 148.0 ([M - H]⁻, C₈H₆NO₂, calc. 148.0).

2-(Allyloxy)ethyl methanesulfonate (17)¹¹

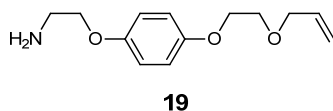


17

2-Allyloxyethanol (7.50 mL, 70.1 mmol) and Et₃N (20.5 mL, 147 mmol) were dissolved in dry CH₂Cl₂ (100 mL) and stirred at 0 °C under N_{2(g)}. MsCl (6.40 mL, 82.7 mmol) in dry CH₂Cl₂ (50 mL) was then added dropwise and the resultant mixture was left to warm to room temperature for 1 h. After this time, the mixture was washed with H₂O (2 x 75 mL), 1 M HCl_(aq) (3 x 75 mL) and brine (3 x 75 mL), and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as an orange oil (10.5 g, 63.2 mmol, 90%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 5.90 (1H, ddt, ³J = 17.1 Hz, ³J = 10.6 Hz, ³J = 5.9 Hz, -CH=CH₂), 5.30 (1H, ddt, ³J = 17.1 Hz, ²J = 1.5 Hz, ⁴J = 1.5 Hz, -CH=CH₂), 5.22 (1H, ddt, ³J = 10.6 Hz, ²J = 1.5 Hz, ⁴J = 1.5 Hz, -CH=CH₂), 4.37–4.40 (2H, m, O-CH₂-CH), 4.03–4.06 (2H, m, -CH₂-OMs), 3.70–3.73 (2H, m, O-CH₂-CH₂OMs), 3.07 (3H, s, -CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 133.9, 117.7, 72.1, 69.1, 67.7, 37.6. MS-ESI *m/z* 203.0 ([M + Na]⁺, C₆H₁₂NaO₄S, calc. 203.0).

2-(4-(2-(Allyloxy)ethoxy)phenoxy)acetonitrile (18)¹²

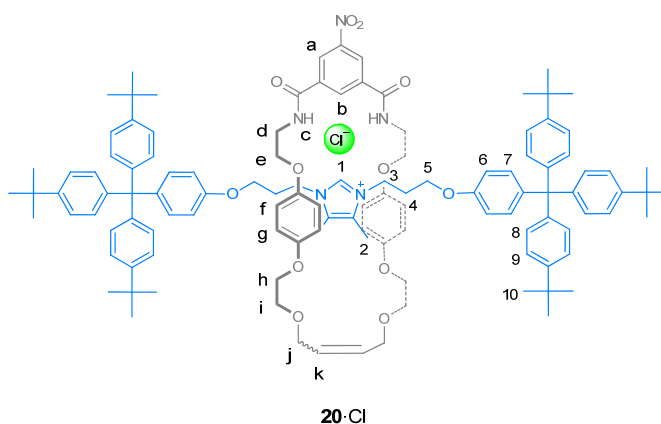
2-(4-Hydroxyphenoxy)acetonitrile (**16**) (3.30 g, 22.0 mmol), 2-(allyloxy)ethyl methanesulfonate (**17**) (3.98 g, 22.0 mmol) and K_2CO_3 (3.35 g, 24.0 mmol) were dissolved in dry MeCN (150 mL) and the solution heated at reflux under $\text{N}_{2(\text{g})}$ for 15 h. The reaction mixture was then cooled to room temperature, filtered and the solvent removed *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (75 mL) and washed with 1 M $\text{HCl}_{(\text{aq})}$ (2 x 50 mL), H_2O (2 x 50 mL) and brine (2 x 50 mL). The solution was dried over MgSO_4 and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 7:3 hexane/EtOAc to elute the product as a white solid (1.68 g, 7.20 mmol, 33%). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm) 6.89–6.97 (4H, m, Ar-H), 5.95 (1H, ddt, $^3J = 17.2$ Hz, 10.2 Hz, 5.9 Hz, -CH=CH₂), 5.32 (1H, ddt, $^3J = 17.2$ Hz, $^2J = 1.3$ Hz, $^4J = 1.3$ Hz, -CH=CH₂), 5.22 (1H, ddt, $^3J = 10.2$ Hz, $^2J = 1.3$ Hz, $^4J = 1.3$ Hz, -CH=CH₂), 4.72 (2H, s, -CH₂-CN), 4.09–4.14 (4H, m, O-CH₂-CH & OAr-CH₂-CH₂), 3.78–3.81 (2H, m, O-CH₂-CH₂OAr). $^{13}\text{C NMR}$ (75.5 MHz, CDCl_3) δ (ppm) 154.8, 150.8, 134.5, 117.4, 116.6, 115.8, 72.3, 68.4, 68.0, 54.8 (one peak missing – coincidental). **MS-ESI** m/z 256.1 ($[\text{M} + \text{Na}]^+$, $\text{C}_{13}\text{H}_{15}\text{NaNO}_3$, calc. 256.1).

2-(4-(2-(Allyloxy)ethoxy)phenoxy)ethanamine (19)¹²

2-(4-(2-(Allyloxy)ethoxy)phenoxy)acetonitrile (**18**) (2.50 g, 10.7 mmol) in dry Et_2O (50 mL) was added dropwise to a suspension of LiAlH_4 (691 mg, 18.2 mmol) in dry Et_2O (50 mL) under $\text{N}_{2(\text{g})}$. The reaction mixture was heated at reflux for 3 h and then allowed to cool to room temperature. H_2O (5 mL) was added dropwise to the solution, followed by 10% $\text{NaOH}_{(\text{aq})}$ (5 mL) and finally H_2O (10 mL). Al salts were removed by filtration and stirred in Et_2O (3 x 100 mL). The combined organic

fractions were then dried over MgSO_4 and the solvent removed *in vacuo* to yield the product as an orange oil (2.02 g, 8.50 mmol, 79%). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 6.81–6.88 (4H, m, Ar-*H*), 5.93 (1H, ddt, $^3J = 17.0$ Hz, $^3J = 10.6$ Hz, $^3J = 5.6$ Hz, -CH=CH₂), 5.30 (1H, app d, $^3J = 17.0$ Hz, -CH=CH₂), 5.20 (1H, app d, $^3J = 10.6$ Hz, -CH=CH₂), 4.07–4.10 (4H, m, O-CH₂-CH & CH₂-CH₂-OAr), 3.93 (2H, t, $^3J = 5.1$ Hz, -CH₂-CH₂NH₂), 3.78 (2H, t, $^3J = 4.8$ Hz, O-CH₂-CH₂OAr), 3.05 (2H, t, $^3J = 5.1$ Hz, -CH₂-NH₂), 1.59 (2H, br s, -NH₂). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 153.1, 153.0, 134.5, 117.3, 115.6, 115.3, 72.3, 70.7, 68.6, 68.0, 41.6. **MS-ESI** m/z 238.1 ($[\text{M} + \text{H}]^+$, $\text{C}_{13}\text{H}_{20}\text{NO}_3$, calc. 238.1).

4,5-Dimethylimidazolium chloride rotaxane (20·Cl)

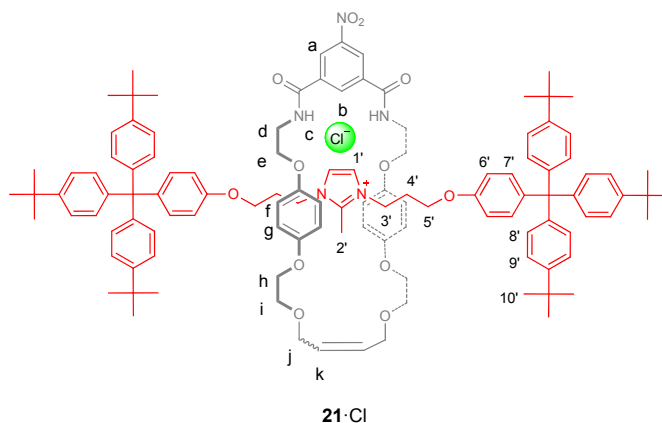


Axle **13·Cl** (200 mg, 0.164 mmol) and macrocycle precursor **15** (106 mg, 0.164 mmol) were dissolved in dry CH_2Cl_2 (50 mL) and stirred for 1 h. Grubbs' second-generation catalyst (10.6 mg, 10% by weight) was then added and the reaction mixture stirred at room temperature under $\text{N}_2(\text{g})$ for 2 days. The solvent was removed *in vacuo* and the crude product purified by preparative silica gel thin layer chromatography (94:6 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ followed by 4:6 $\text{CH}_2\text{Cl}_2/\text{MeCN}$) to yield the product as an off-white solid (90 mg, 0.049 mmol, 30%). **Mp** 167–169 °C (dec.). **^1H NMR** (500 MHz, CDCl_3) δ (ppm) 10.03 (1H, s, H_b), 9.79 (1H, s, H_i), 9.36 (2H, br s, H_c), 9.09 (2H, s, H_a), 7.23–7.26 (12H, m, H₉), 7.08–7.13 (16H, m, H₇ & H₈), 6.64–6.66 (4H, m, H₆), 6.36–6.42 (8H, m, H_f & H_g), 5.82 (2H, br s, H_k), 4.15–4.17 (4H, m, H_e), 3.97 (4H, br s, H_j), 3.92–3.94 (4H, m, H_d), 3.81–3.82 (4H, m, H_h), 3.69–3.70

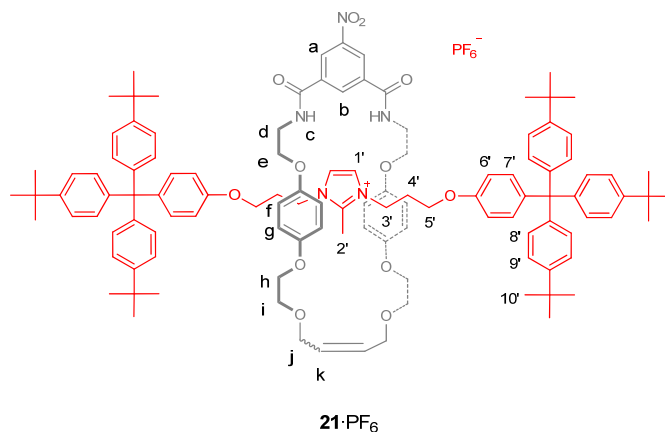
248

$([M - PF_6]^+, C_{117}H_{140}N_5O_{12}, \text{ calc. } 1808.0526), 1808.1 ([M - PF_6]^+)$ – only observed peak in low resolution mass spectrum.

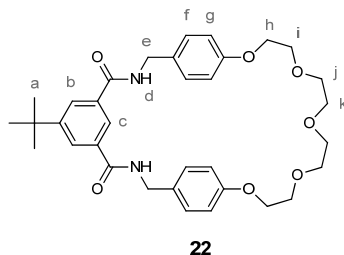
2-Methylimidazolium chloride rotaxane (21·Cl)



Axle **14·Cl** (200 mg, 0.166 mmol) and macrocycle precursor **15** (108 mg, 0.166 mmol) were dissolved in dry CH_2Cl_2 (50 mL) and stirred for 1 h. Grubbs' second-generation catalyst (10.8 mg, 10% by weight) was then added and the reaction mixture stirred at room temperature under $N_{2(g)}$ for 2 days. The solvent was removed *in vacuo* and the crude product purified by preparative silica gel thin layer chromatography (95:5 $CH_2Cl_2/MeOH$ followed by EtOAc) to yield the product as an off-white solid (58 mg, 0.031 mmol, 19%). **Mp** 162–164 °C (dec.). **1H NMR** (500 MHz, $CDCl_3$) δ (ppm) 9.96 (1H, s, H_b), 9.40 (2H, br s, H_c), 9.08 (2H, s, H_a), 7.47 (2H, s, $H_{1'}$), 7.24–7.27 (12H, m, $H_{9'}$), 7.09–7.16 (16H, m, $H_{7'}$ & $H_{8'}$), 6.67–6.70 (4H, m, $H_{6'}$), 6.55 (4H, d, $^3J = 8.8$ Hz, H_f), 6.33 (4H, d, $^3J = 8.8$ Hz, H_g), 5.82 (2H, br s, H_k), 4.17–4.20 (4H, m, H_e), 3.97–4.02 (4H, m, H_d), 3.92 (4H, br s, H_j), 3.78–3.79 (4H, m, H_h), 3.65–3.73 (12H, m, H_i & $H_{3'}$ & $H_{5'}$), 2.07 (3H, s, $H_{2'}$), 1.86–1.94 (4H, m, $H_{4'}$), 1.31 (54H, s, $H_{10'}$). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ (ppm) 164.3, 155.7, 153.2, 152.0, 148.9, 148.4, 143.9, 142.5, 140.6, 135.7, 132.4, 130.6, 129.2, 126.3, 124.1, 121.2, 115.1, 113.7, 112.8, 70.8, 69.4, 67.4, 67.0, 63.5, 63.0, 45.1, 39.9, 34.3, 31.4, 28.8, 8.7 (one peak missing – coincidental). **MS-ESI** m/z 1794.0417 ($[M - Cl]^+$, $C_{116}H_{138}N_5O_{12}$, calc. 1794.0388), 1793.9 ($[M - Cl]^+$) – only observed peak in low resolution mass spectrum.

2-Methylimidazolium hexafluorophosphate rotaxane (21·PF₆)

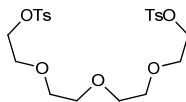
Rotaxane **21**·Cl (29 mg, 0.016 mmol) was dissolved in CH₂Cl₂ (10 mL) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (4 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as an off-white solid (25 mg, 0.13 mmol, 81%). **Mp** 156–160 °C (dec.). **¹H NMR** (500 MHz, CDCl₃) δ (ppm) 9.01 (2H, s, H_a), 8.48 (1H, s, H_b), 7.22–7.26 (12H, m, H_{9'}), 7.07–7.17 (16H, m, H_{7'} & H_{8'}), 6.96 (2H, s, H_{1'}), 6.71–6.74 (4H, m, H_{6'}), 6.59 (4H, d, ³*J* = 8.8 Hz, H_f), 6.33 (4H, d, ³*J* = 8.8 Hz, H_g), 5.80 (2H, br s, H_k), 4.17–4.20 (4H, m, H_e), 3.90–3.94 (4H, m, H_d), 3.89 (4H, br s, H_j), 3.81–3.84 (4H, m, H_{5'}), 3.62–3.75 (12H, m, H_h & H_i & H_{3'}), 2.07 (3H, s, H_{2'}), 1.89–1.96 (4H, m, H_{4'}), 1.31 (54H, s, H_{10'}). **¹⁹F NMR** (282.5 MHz, CDCl₃) δ (ppm) –70.4 (d, ¹*J* = 759 Hz, PF₆). **¹³C NMR** (125.8 MHz, CDCl₃) δ (ppm) 164.5, 155.8, 153.2, 152.2, 148.9, 148.4, 144.0, 142.8, 140.6, 136.4, 132.4, 130.6, 129.6, 126.4, 124.1, 120.7, 115.3, 113.9, 112.8, 70.8, 69.4, 67.4, 66.8, 63.6, 63.1, 45.2, 39.9, 34.3, 31.4, 28.5, 8.7 (one peak missing – coincidental). **MS-ESI** *m/z* 1793.9404 ([M – PF₆]⁺, C₁₁₆H₁₃₈N₅O₁₂, calc. 1794.0388), 1794.1 ([M – PF₆]⁺) – only observed peak in low resolution mass spectrum.

Smaller isophthalamide macrocycle (22)

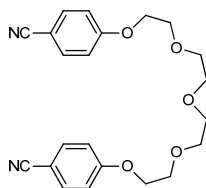
Procedure A: 5-*tert*-Butylisophthalic acid (329 mg, 1.48 mmol) was suspended in SOCl_2 (5 mL) and heated at reflux under $\text{N}_{2(\text{g})}$ for 15 h. The excess SOCl_2 was then removed by distillation, and the residue dried *in vacuo*. The crude dichloride (assumed quantitative conversion) was immediately dissolved in dry CH_2Cl_2 (30 mL) and added dropwise to a solution of bis-amine **25** (600 mg, 1.48 mmol) and Et_3N (0.52 mL, 3.71 mmol) in dry CH_2Cl_2 (75 mL) which had been stirred for 30 min. The reaction mixture was then stirred at room temperature under $\text{N}_{2(\text{g})}$ for 2 h, after which time the solution was washed with 10% $\text{HCl}_{(\text{aq})}$ (2 x 50 mL) and H_2O (2 x 50 mL) and dried over MgSO_4 . The solvent was removed *in vacuo* and purified by silica gel column chromatography using 97:3 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ followed by 7:3 $\text{CHCl}_3/\text{acetone}$ to elute the product as a white solid (117 mg, 0.20 mmol, 13%).

Procedure B: Same as *A*, but with 2-methylimidazolium thread **3**·Cl (425 mg, 1.48 mmol) added at the same time as bis-amine **25**, yielding the product as described above (280 mg, 0.47 mmol, 32%).

Mp > 250 °C. **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.04 (2H, s, H_b), 7.82 (1H, s, H_c), 7.15 (4H, d, $^3J = 8.2$ Hz, H_f), 6.69 (4H, d, $^3J = 8.2$ Hz, H_g), 6.47 (2H, br s, H_d), 4.51 (4H, d, $^3J = 5.3$ Hz, H_e), 3.97–4.02 (4H, m, H_h), 3.77–3.80 (4H, m, H_i), 3.67–3.69 (8H, m, H_j & H_k), 1.30 (9H, s, H_a). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 166.8, 157.9, 152.6, 133.8, 130.3, 129.5, 128.4, 120.7, 114.5, 70.7, 69.6, 67.2, 43.8, 35.0, 31.1 (one peak missing – coincidental). **MS-ESI** m/z 613.2896 ($[\text{M} + \text{Na}]^+$, $\text{C}_{34}\text{H}_{42}\text{N}_2\text{NaO}_7$, calc. 613.2884), 613.3 (100%, $[\text{M} + \text{Na}]^+$), 1203.7 (15%, $[2\text{M} + \text{Na}]^+$), 625.3 (50%, $[\text{M} + \text{Cl}]^-$), 703.3 (100%, $[\text{M} + \text{CF}_3\text{COO}]^-$), 625.3 (30%, $[2\text{M} + \text{Cl}]^-$).

Tetra-(ethyleneglycol)di-*p*-toluene sulfonate (23)¹³**23**

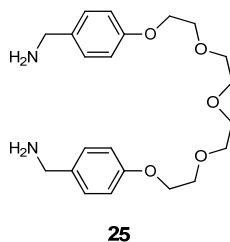
TsCl (5.53 g, 29.0 mmol) and tetraethylene glycol (2.50 mL, 14.5 mmol) were dissolved in CH₂Cl₂ (25 mL). Powdered KOH (6.49 g, 116 mmol) was added portionwise to the solution at 0 °C and the reaction mixture stirred at this temperature for 3 h. After this time, CH₂Cl₂ (25 mL) was added, the mixture poured onto ice (75 g) and the organic layer separated. The aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL), the combined organic fractions washed with H₂O (50 mL) and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as a colourless oil (6.46 g, 12.9 mmol, 89%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.78 (4H, d, ³J = 8.4 Hz, Ar-*H*), 7.33 (4H, d, ³J = 8.4 Hz, Ar-*H*), 4.13–4.17 (4H, m, 2 x -CH₂-), 3.66–3.69 (4H, m, 2 x -CH₂-), 3.54–3.57 (8H, m, 4 x -CH₂-), 2.44 (6H, s, 2 x -CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 144.8, 132.9, 129.8, 127.9, 70.6, 70.5, 69.2, 68.6, 21.6. MS-ESI *m/z* 525.1 ([M + Na]⁺, C₂₂H₃₀NaO₉S₂, calc. 525.1)

Bis(benzonitrile)tetraethylene glycol (24)¹⁴**24**

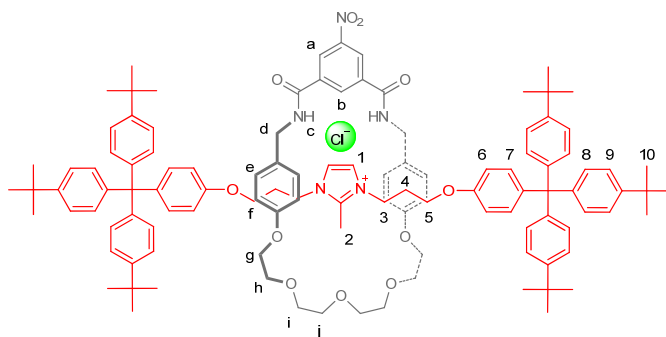
To a solution of tetra-(ethyleneglycol)di-*p*-toluene sulfonate (**23**) (4.30 g, 8.56 mmol) and 4-hydroxybenzonitrile (2.07 g, 17.4 mmol) in 2-butanone (200 mL) was added K₂CO₃ (6.51 g, 47.1 mmol) and the reaction mixture heated at reflux for 5 days. After cooling to room temperature, the solution was filtered and the solvent removed *in vacuo*. The resulting residue was purified by silica gel column chromatography using 9:1 CH₂Cl₂/EtOAc to elute the product as a white solid (3.11 g,

7.84 mmol, 92%). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm) 7.58 (4H, d, $^3J = 8.8$ Hz, Ar-*H*), 6.96 (4H, d, $^3J = 8.8$ Hz, Ar-*H*), 4.15–4.19 (4H, m, 2 x $-\text{CH}_2-$), 3.85–3.89 (4H, m, 2 x $-\text{CH}_2-$), 3.66–3.74 (8H, m, 4 x $-\text{CH}_2-$). $^{13}\text{C NMR}$ (75.5 MHz, CDCl_3) δ (ppm) 162.0, 133.9, 119.1, 115.3, 104.1, 70.9, 70.6, 69.4, 67.7. **MS-ESI** m/z 419.2 ($[\text{M} + \text{Na}]^+$, $\text{C}_{22}\text{H}_{24}\text{NaN}_2\text{O}_5$, calc. 419.2); 431.2 ($[\text{M} + \text{Cl}]^-$).

Bis(methanamine)tetraethylene glycol (25)¹⁴



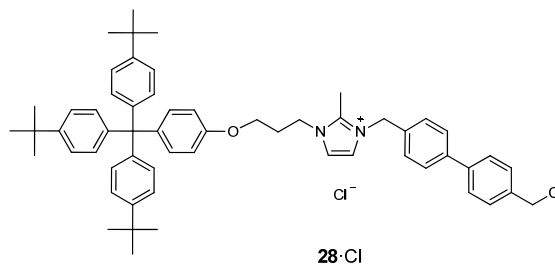
Bis(benzonitrile)tetraethylene glycol **24** (1.00 g, 2.52 mmol) was dissolved in dry THF (25 mL) and added dropwise to 1 M $\text{BH}_3 \cdot \text{THF}$ (7.37 mL, 7.37 mmol) which had been preheated to 70 °C. The reaction mixture was heated at reflux under $\text{N}_{2(g)}$ for 4 h. After this time, the solution was cooled to 0 °C, MeOH added carefully until the resulting effervescence ceased, followed by conc. HCl (25 mL). The organic solvents were removed *in vacuo* and 10% $\text{NaOH}_{(aq)}$ was added to basify the aqueous solution. The product was extracted with CH_2Cl_2 (3 x 100 mL), and the combined organic fractions washed with brine (1 x 100 mL) and dried over MgSO_4 . The solvent was removed *in vacuo* to yield the product as a white solid after storage at –20 °C (914 mg, 2.26 mmol, 90%). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm) 7.21 (4H, d, $^3J = 8.8$ Hz, Ar-*H*), 6.88 (4H, d, $^3J = 8.8$ Hz, Ar-*H*), 4.09–4.13 (4H, m, 2 x $-\text{CH}_2-\text{NH}_2$), 3.83–3.87 (4H, m, 2 x $-\text{CH}_2-$), 3.80 (4H, s, 2 x $-\text{CH}_2-$), 3.69–3.74 (8H, m, 4 x $-\text{CH}_2-$), 1.56 (4H, br s, 2 x $-\text{NH}_2$). $^{13}\text{C NMR}$ (75.5 MHz, CDCl_3) δ (ppm) 157.7, 135.7, 128.2, 114.6, 70.8, 70.6, 69.7, 67.4, 45.9. **MS-FI** m/z 404.3 ($[\text{M}]^+$, $\text{C}_{22}\text{H}_{32}\text{N}_2\text{O}_5$, calc. 404.2).

Smaller macrocycle 2-methylimidazolium chloride ‘condensation’ rotaxane (**26**·Cl)**26**·Cl

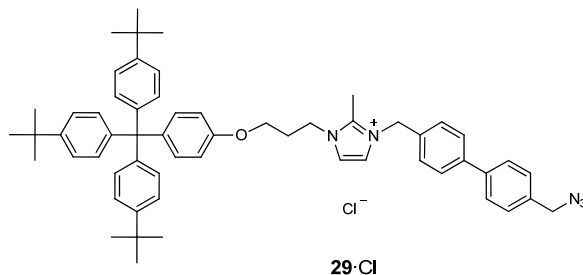
5-Nitroisophthalic acid (14 mg, 0.066 mmol) was suspended in SOCl_2 (1 mL) and heated at reflux under $\text{N}_{2(g)}$ for 15 h. The excess SOCl_2 was then removed by distillation, and the residue dried *in vacuo*. The crude dichloride (assumed quantitative conversion) was immediately dissolved in dry CH_2Cl_2 (5 mL) and added dropwise to a solution of bis-amine **25** (27 mg, 0.066 mmol), axle **14**·Cl (80 mg, 0.066 mmol) and Et_3N (23 μL , 0.166 mmol) in dry CH_2Cl_2 (13 mL) which had been stirred for 30 min. The reaction mixture was then stirred at room temperature under $\text{N}_{2(g)}$ for 2 h, after which time the solution was washed with 10% $\text{HCl}_{(aq)}$ (2 x 10 mL) and H_2O (2 x 10 mL) and dried over MgSO_4 . The solvent was removed *in vacuo* and the residue purified by preparative silica gel thin layer chromatography (1:1 $\text{CH}_2\text{Cl}_2/\text{MeCN}$ followed by 96:4 $\text{CH}_2\text{Cl}_2/\text{MeOH}$) to yield the product as an off-white solid (5 mg, 0.003 mmol, 4%). **Mp** 183–185 °C (dec.). **^1H NMR** (500 MHz, CDCl_3) δ (ppm) 9.78 (2H, br s, H_c), 9.23 (1H, br s, H_b), 9.01 (2H, s, H_a), 7.38 (2H, s, H_1), 7.27–7.30 (4H, m, H_e), 7.23–7.26 (12H, m, H_9), 7.17 (4H, d, $^3J = 8.8$ Hz, H_7), 7.09–7.12 (12H, m, H_8), 6.79 (4H, d, $^3J = 8.8$ Hz, H_6), 6.36 (4H, d, $^3J = 8.8$ Hz, H_f), 4.61–4.65 (4H, m, H_d), 3.98–4.00 (4H, m, H_5), 3.90–3.93 (4H, m, H_3), 3.57–3.65 (12H, m, H_h & H_i & H_j), 3.48–3.51 (4H, m, H_g), 2.04–2.09 (4H, m, H_4), 1.66 (3H, s, H_2), 1.27 (54H, s, H_{10}). **^{13}C NMR** (125.8 MHz, CDCl_3) δ (ppm) 164.9, 157.1, 156.0, 149.0, 148.4, 144.0, 143.4, 140.1, 136.4, 133.6, 132.4, 130.6, 130.4, 126.2, 124.1, 121.5, 113.1, 112.9, 71.1, 70.5, 67.8, 66.7, 64.3, 63.1, 53.4, 45.8, 42.3, 34.3, 31.4, 8.0 (one peak missing – coincidental). **MS-ESI** m/z

1752.0318 ($[M - Cl]^+$, $C_{114}H_{136}N_5O_{11}$, calc. 1752.0264), 1751.9 ($[M - Cl]^+$) – only observed peak in low resolution mass spectrum.

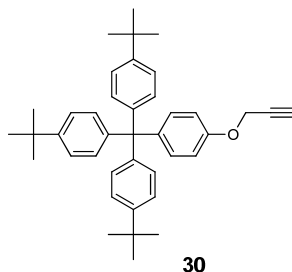
Mono-stoppered chloro-functionalised 2-methylimidazolium chloride (28·Cl)



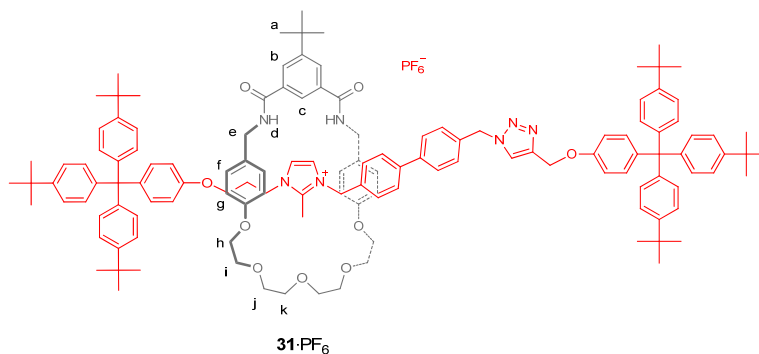
Imidazole derivative **12** (300 mg, 0.48 mmol) and 4,4'-bis(chloromethyl)-1,1'-biphenyl (600 mg, 0.68 mmol) were dissolved in acetone (30 mL) and heated under microwave irradiation at 150 °C for 2 h. The solvent was then removed *in vacuo* and the residue purified by silica gel gradient column chromatography using 95:5 to 85:15 $CH_2Cl_2/MeOH$ to elute the product as a white solid (353 mg, 0.40 mmol, 84%). **Mp** > 250 °C. **1H NMR** (300 MHz, $CDCl_3$) δ (ppm) 7.62 (1H, d, $^3J = 2.4$ Hz, NC-*H*), 7.57 (2H, d, $^3J = 8.0$ Hz, Ar-*H*), 7.54 (1H, d, $^3J = 2.4$ Hz, NC-*H*), 7.51 (2H, d, $^3J = 8.0$ Hz, Ar-*H*), 7.44 (2H, d, $^3J = 8.0$ Hz, Ar-*H*), 7.40 (2H, d, $^3J = 8.0$ Hz, Ar-*H*), 7.20–7.26 (6H, m, Ar-*H*), 7.03–7.11 (8H, m, Ar-*H*), 6.67 (2H, d, $^3J = 8.8$ Hz, OAr-*H*), 5.57 (2H, s, N- CH_2 -Ar), 4.63 (2H, s, - CH_2 -Cl), 4.51 (2H, t, $^3J = 6.5$ Hz, N- CH_2 - CH_2), 4.02 (2H, t, $^3J = 5.6$ Hz, O- CH_2 - CH_2), 2.84 (3H, s, NC- CH_3), 2.37–2.41 (2H, m, CH_2 - CH_2 - CH_2), 1.30 (27H, s, -*t*Bu). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ (ppm) 155.7, 148.3, 144.1, 143.9, 141.2, 140.4, 139.9, 137.0, 132.4, 132.1, 130.6, 129.1, 128.8, 128.0, 127.3, 124.0, 122.3, 121.8, 112.8, 63.6, 63.0, 52.0, 50.6, 45.8, 34.2, 31.3, 29.2, 10.8 (one peak missing – coincidental). **MS-ESI** m/z 841.4869 ($[M - Cl]^+$, $C_{58}H_{66}ClN_2O$, calc. 841.4858), 841.4 ($[M - Cl]^+$) – only observed peak in low resolution mass spectrum.

Mono-stoppered azido-functionalised 2-methylimidazolium chloride (29·Cl)

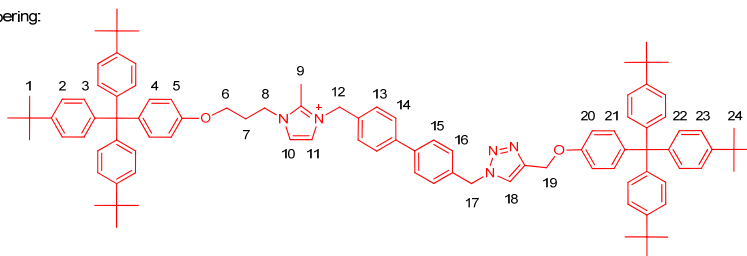
Imidazolium **28**·Cl (350 mg, 0.40 mmol) and NaN₃ (78 mg, 1.20 mmol) were dissolved in DMF (15 mL) and heated at 80 °C under N_{2(g)} for 15 h. After this time, H₂O (40 mL) was added and the crude product extracted with CH₂Cl₂ (3 x 50 mL). The combined organic fractions were washed with H₂O (1 x 20 mL), dried over MgSO₄ and the solvent removed *in vacuo*. The resulting residue was dissolved in CH₂Cl₂ (15 mL), washed with 1.0 M NH₄Cl_(aq) (5 x 10 mL), H₂O (2 x 10 mL) and brine (1 x 10 mL), and dried over MgSO₄. The solvent was then removed *in vacuo* to yield the product as a white solid (306 mg, 0.35 mmol, 87%). **Mp** > 250 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 7.64 (1H, d, ³J = 2.3 Hz, NC-*H*), 7.51–7.60 (5H, m, 2 x Ar-*H* & NC-*H*), 7.35–7.42 (4H, m, 2 x Ar-*H*), 7.20–7.26 (6H, m, Ar-*H*), 7.03–7.11 (8H, m, Ar-*H*), 6.68 (2H, d, ³J = 8.8 Hz, OAr-*H*), 5.58 (2H, s, N-CH₂-Ar), 4.51 (2H, t, ³J = 6.8 Hz, N-CH₂-CH₂), 4.39 (2H, s, -CH₂-N₃), 4.02 (2H, t, ³J = 5.6 Hz, O-CH₂-CH₂), 2.84 (3H, s, NC-CH₃), 2.37–2.42 (2H, m, CH₂-CH₂-CH₂), 1.30 (27H, s, -^tBu). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 155.7, 148.4, 144.1, 144.0, 141.3, 140.4, 139.8, 134.9, 132.4, 132.0, 130.6, 128.8, 128.7, 128.0, 127.5, 124.1, 122.3, 121.8, 112.8, 63.5, 63.0, 54.4, 52.1, 45.9, 34.3, 31.3, 29.2, 10.8 (one peak missing – coincidental). **MS-ESI** *m/z* 848.5257 ([M – Cl]⁺, C₅₈H₆₆N₅O, calc. 848.5262), 848.5 ([M – Cl]⁺) – only observed peak in low resolution mass spectrum.

Stopper alkyne (30)¹⁵

4-(Tris(4-(*tert*-butyl)phenyl)methyl)phenol (**9**) (2.50 g, 4.95 mmol), propargyl bromide (80% in toluene, 0.80 mL, 7.43 mmol) and K₂CO₃ (3.42 g, 24.8 mmol) were suspended in dry DMF (40 mL) and heated at 80 °C under N_{2(g)} for 15 h. After this time, the resulting brown suspension was concentrated *in vacuo*, H₂O (100 mL) added and the product extracted with EtOAc (3 x 100 mL). The combined organic fractions were then dried over MgSO₄ and the solvent removed *in vacuo*. The pale brown residue was suspended in boiling MeCN (150 mL) and hot CHCl₃ (15 mL) added to dissolve the solid. The solution was then concentrated *in vacuo* to a volume of 100 mL and cooled. The precipitate was filtered and washed with ice-cold MeCN (3 x 10 mL) to yield the product as an off-white solid (2.12 g, 3.91 mmol, 79%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.22–7.28 (6H, m, Ar-*H*), 7.06–7.15 (8H, m Ar-*H*), 6.83–6.88 (2H, m, OAr-*H*), 4.67 (2H, d, ⁴*J* = 2.4 Hz, -CH₂-), 2.52 (1H, t, ⁴*J* = 2.4 Hz, ≡CH), 1.31 (27H, s, -*t*Bu). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 155.4, 148.3, 144.0, 140.5, 132.3, 130.7, 124.0, 113.3, 78.8, 75.3, 63.0, 55.7, 34.3, 31.4. MS-ESI *m/z* 565.4 (100%, [M + H]⁺, C₄₀H₄₆NaO, calc. 565.3), 581.4 (90%, [M + K]⁺).

Smaller macrocycle 2-methylimidazolium hexafluorophosphate ‘stoppered’ rotaxane (**31**·PF₆)

Axle numbering:

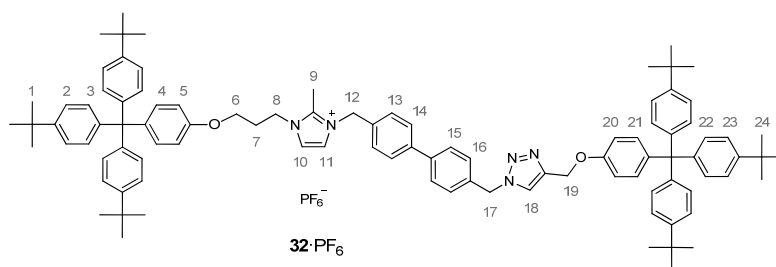


To a solution of macrocycle **22** (67 mg, 0.113 mmol), azide **29**·Cl (100 mg, 0.113 mmol) and alkyne **30** (74 mg, 0.136 mmol) in dry CH₂Cl₂ (25 mL) was added TBTA (6 mg, 0.011 mmol) and DIPEA (39 μ L, 0.226 mmol) followed by Cu(MeCN)₄PF₆ (8 mg, 0.023 mmol). The reaction mixture was stirred under N_{2(g)} for 72 h and then the solvent removed *in vacuo*. Purification was undertaken by preparative silica gel thin layer chromatography using 94:6 CH₂Cl₂/MeOH. The crude product was dissolved in CH₂Cl₂ (10 mL), washed with 0.1 M NH₄PF_{6(aq)} (10 x 5 mL) and H₂O (4 x 5 mL), and dried over MgSO₄. The solvent was removed was then removed *in vacuo* and the residue triturated with methanol (3 x 3 mL) to yield the product as an off-white solid (36 mg, 0.017 mmol, 15%).

¹H NMR (500 MHz, CDCl₃) δ (ppm) 8.22 (2H, d, ³J = 1.5 Hz, H_b), 7.53–7.63 (7H, m, H_c & H_d & H₁₄ & H₁₅), 7.34 (2H, d, ³J = 7.8 Hz, H₁₆), 7.20–7.26 (15H, m, H₂ & H₁₃ & H₁₈ & H₂₃), 7.13–7.18 (6H, m, H_f & H₄), 7.06–7.11 (15H, m, H₃ & H₁₁ & H₂₁ & H₂₂), 6.95 (1H, d, ³J = 2.0 Hz, H₁₀), 6.82 (2H, d, ³J = 8.8 Hz, H₂₀), 6.73 (2H, d, ³J = 8.8 Hz, H₅), 6.22 (4H, d, ³J = 8.3 Hz, H_g), 5.49 (2H, s, H₁₇), 5.02 (2H, s, H₁₉), 4.94 (2H, s, H₁₂), 4.60 (2H, d, ²J = 13.2 Hz, H_e), 4.38 (2H, d, ²J = 13.2 Hz, H_{e'}), 3.81–3.85 (2H, m, H₆), 3.72–3.77 (2H, m, H₈), 3.57–3.67 (12H, m, H_i & H_j & H_k), 3.50–3.55 (2H, m, H_h),

3.44–3.48 (2H, m, H_{16}), 1.99–2.02 (3H, m, H_9), 1.87–1.92 (2H, m, H_7), 1.31 (9H, s, H_a), 1.26 (27H, s, H_1 or H_{24}), 1.26 (27H, s, H_1 or H_{24}). ^{19}F NMR (282.5 MHz, CDCl_3) δ (ppm) – 71.8 (d, $^1J = 714$ Hz, PF_6). ^{13}C NMR (125.8 MHz, CDCl_3) δ (ppm) 167.6, 156.8, 156.1, 156.0, 152.2, 148.4, 148.3, 144.0, 142.9, 141.4, 140.5, 140.4, 140.2, 134.2, 134.1, 133.9, 132.4, 132.3, 131.7, 130.7, 130.6, 130.3, 129.9, 128.8, 128.5, 128.0, 127.9, 124.1, 124.0, 122.7, 122.1, 120.5, 113.2, 113.1, 112.9, 71.2, 70.7, 70.0, 66.8, 64.1, 63.1, 62.0, 53.9, 51.4, 45.4, 42.0, 35.0, 34.3, 31.4, 31.2, 29.7, 29.1, 8.9 (five peaks missing – coincidental). MS-ESI m/z 1002.5831 ($[\text{M} - \text{PF}_6 + \text{Na}]^{2+}$, $\text{C}_{132}\text{H}_{154}\text{N}_7\text{NaO}_9$, calc. 1002.5864), 1002.6 (85%, $[\text{M} - \text{PF}_6 + \text{Na}]^{2+}$), 1981.9 (100%, $[\text{M} - \text{PF}_6]^+$).

2-Methylimidazolium hexafluorophosphate ‘clicked’ axle ($32 \cdot \text{PF}_6$)

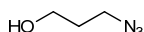


Isolated from the reaction mixture for the preparation of rotaxane $31 \cdot \text{PF}_6$ as a white solid. ^1H NMR (500 MHz, CDCl_3) δ (ppm) 7.56–7.59 (3H, m, H_{14} & H_{18}), 7.53 (2H, d, $^3J = 8.1$ Hz, H_{15}), 7.34 (2H, d, $^3J = 8.1$ Hz, H_{16}), 7.30 (2H, d, $^3J = 8.1$ Hz, H_{13}), 7.21–7.24 (13H, m, H_2 & H_{11} & H_{23}), 7.19 (1H, s, H_{10}), 7.03–7.11 (16H, m, H_3 & H_4 & H_{21} & H_{22}), 6.83 (2H, d, $^3J = 8.8$ Hz, H_{20}), 6.68 (2H, d, $^3J = 9.3$ Hz, H_5), 5.56 (2H, s, H_{17}), 5.24 (2H, s, H_{12}), 5.15 (2H, s, H_{19}), 4.33 (2H, t, $^3J = 6.6$ Hz, H_8), 3.96 (2H, t, $^3J = 5.4$ Hz, H_6), 2.62 (3H, s, H_9), 2.24–2.29 (2H, m, H_7), 1.26 (27H, s, H_1 or H_{24}), 1.25 (27H, s, H_1 or H_{24}). ^{19}F NMR (282.5 MHz, CDCl_3) δ (ppm) – 73.3 (d, $^1J = 713$ Hz, PF_6). ^{13}C NMR (75.5 MHz, CDCl_3) δ (ppm) 156.1, 155.7, 148.4, 148.3, 144.8, 144.2, 144.0, 143.9, 141.1, 140.4, 140.4, 140.2, 134.0, 132.4, 132.3, 132.0, 130.7, 130.6, 128.8, 128.7, 128.1, 127.8, 124.1, 124.0, 122.6, 122.1, 121.7, 113.1, 112.8, 63.5, 63.0, 62.0, 53.8, 52.1, 45.9, 34.3, 31.4, 29.2, 10.9 (three peaks

missing – coincidental). **MS-ESI** m/z 1391.8887 ($[M - PF_6]^+$, $C_{98}H_{112}N_5O_2$, calc. 1391.8843), 1391.8 (100%, $[M - PF_6]^+$) – only observed peak in low resolution mass spectrum.

6.2.2 Synthetic Procedures for Chapter Three

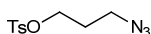
3-Azido-1-propanol (33)¹⁵



33

3-Bromo-1-propanol (1.30 mL, 14.4 mmol) and NaN_3 (1.87 g, 28.8 mmol) were dissolved in H_2O (40 mL) and the solution heated at 80 °C for 15 h. After this time, the reaction mixture was extracted with EtOAc (5 x 40 mL) and the combined organic fractions washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* to yield the product as a pale yellow oil (1.28 g, 12.6 mmol, 88%). **1H NMR** (300 MHz, $CDCl_3$) δ (ppm) 3.75 (2H, t, $^3J = 6.0$ Hz, $-CH_2-OH$), 3.45 (2H, t, $^3J = 6.6$ Hz, $-CH_2-N_3$), 1.79–1.87 (2H, m, $CH_2-CH_2-CH_2$). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ (ppm) 59.8, 48.4, 31.4. **MS** not observed.

3-azidopropyl tosylate (34)¹⁵

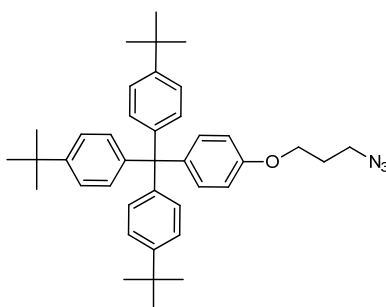


34

3-Azido-1-propanol (1.20 g, 11.9 mmol) and Et_3N (3.33 mL, 23.7 mmol) were dissolved in dry CH_2Cl_2 (100 mL) and cooled to 0 °C. $TsCl$ (2.50 g, 13.1 mmol) was added portionwise over 30 min and the reaction mixture stirred at room temperature under $N_{2(g)}$ for 15 h. After this time, the solution was washed with H_2O (75 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. Purification was undertaken by silica gel gradient column chromatography using 7:3 to 1:1 hexane/ CH_2Cl_2 to elute the product as a colourless oil (2.54 g, 9.95 mmol, 84%). **1H NMR** (300 MHz, $CDCl_3$) δ (ppm) 7.81 (2H, d, $^3J = 9.0$ Hz, Ar-*H*), 7.37 (2H, d, $^3J = 9.0$ Hz, Ar-*H*), 4.11 (2H, t, $^3J = 6.0$ Hz, $-CH_2-O$), 3.38 (2H, t,

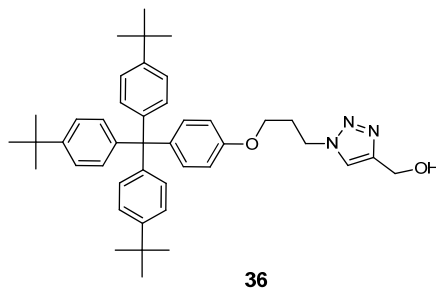
$^3J = 6.6$ Hz, $-\text{CH}_2\text{-N}_3$), 2.46 (3H, s, $-\text{CH}_3$), 1.85–1.94 (2H, m, $\text{CH}_2\text{-CH}_2\text{-CH}_2$). ^{13}C NMR (75.5 MHz, CDCl_3) δ (ppm) 145.0, 132.7, 129.9, 127.9, 67.0, 47.2, 28.4, 21.6. **MS-ESI** m/z 278.0 ($[\text{M} + \text{Na}]^+$, $\text{C}_{10}\text{H}_{13}\text{N}_3\text{NaO}_3\text{S}$, calc. 278.1).

1-(3-azido-propoxy)-4-(tris-(4-*tert*-butyl-phenyl)-methyl)-benzene (35)¹⁵

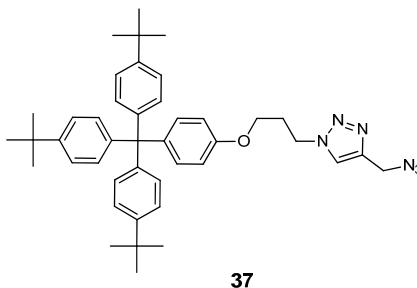


35

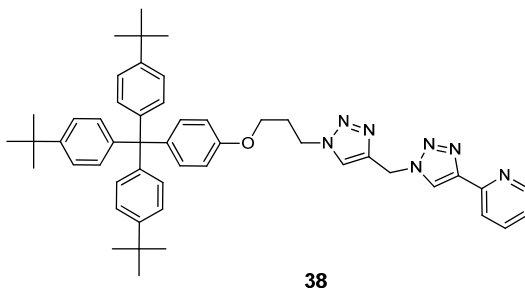
To a solution of 4-(tris(4-(*tert*-butyl)phenyl)methyl)phenol (**9**) (3.00 g, 5.94 mmol) and 3-azidopropyl tosylate (**34**) (1.67 g, 6.54 mmol) in 2-butanone (75 mL) was added K_2CO_3 (4.11 g, 29.7 mmol), and the reaction mixture was heated at reflux under $\text{N}_{2(g)}$ for 15 h. After this time, the solution was allowed to cool to room temperature, filtered and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 7:3 hexane/ CH_2Cl_2 to elute the product as a white solid (2.77 g, 4.71 mmol, 80%). ^1H NMR (300 MHz, CDCl_3) δ (ppm) 7.22–7.27 (6H, m, Ar-*H*), 7.06–7.13 (8H, m, Ar-*H*), 6.77 (2H, d, $^3J = 9.1$ Hz, OAr-*H*), 4.04 (2H, t, $^3J = 5.9$ Hz, $-\text{CH}_2\text{-O}$), 3.53 (2H, t, $^3J = 6.7$ Hz, $-\text{CH}_2\text{-N}_3$), 2.00–2.09 (2H, m, $\text{CH}_2\text{-CH}_2\text{-CH}_2$), 1.32 (27H, s, $-\text{tBu}$). ^{13}C NMR (75.5 MHz, CDCl_3) δ (ppm) 156.4, 148.3, 144.1, 139.8, 132.3, 130.7, 124.0, 112.9, 64.3, 63.0, 48.3, 34.3, 31.4, 28.8. **MS-ESI** m/z 605.4 ($[\text{M} + \text{NH}_4]^+$, $\text{C}_{40}\text{H}_{53}\text{N}_4\text{O}$, calc. 605.4).

Mono-stoppered hydroxy-triazole derivative (36)

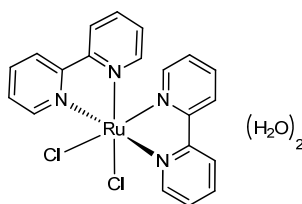
To a solution of azide (**35**) (500 mg, 0.85 mmol) and propargyl alcohol (0.06 mL, 1.02 mmol) in dry CH_2Cl_2 (60 mL) was added TBTA (10 mg, cat.) and DIPEA (0.30 mL, 1.70 mmol), followed by $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (159 mg, 0.43 mmol). The reaction mixture was stirred under $\text{N}_{2(\text{g})}$ for 15 h. After this time, the solvent was removed *in vacuo* and purification undertaken by silica gel column chromatography using 97:3 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as an off-white solid (469 mg, 0.73 mmol, 86%). **Mp** 235–240 °C (dec.). **^1H NMR** (300 MHz, d_6 -DMSO) δ (ppm) 8.01 (1H, s, NC-*H*), 7.27–7.33 (6H, m, Ar-*H*), 7.03–7.10 (8H, m, Ar-*H*), 6.83 (2H, d, $^3J = 8.5$ Hz, OAr-*H*), 5.15 (1H, t, $^3J = 5.4$ Hz, -OH), 4.45–4.52 (4H, m, - CH_2 -N & - CH_2 -OH), 3.89–3.95 (2H, m, - CH_2 -OAr), 2.16–2.31 (2H, m, CH_2 - CH_2 - CH_2), 1.25 (27H, s, -*t*Bu). **^{13}C NMR** (75.5 MHz, d_6 -DMSO) δ (ppm) 156.1, 147.7, 143.9, 139.1, 131.4, 130.0, 124.4, 113.4, 109.5, 64.2, 62.6, 55.1, 46.4, 34.0, 31.3, 29.6 (one peak missing – coincidental or due to weakness of sample). **MS-ESI** m/z 666.4040 ($[\text{M} + \text{Na}]^+$, $\text{C}_{43}\text{H}_{53}\text{N}_3\text{NaO}_2$, calc. 666.4030), 644.4 (50%, $[\text{M} + \text{H}]^+$), 666.4 (60%, $[\text{M} + \text{Na}]^+$), 702.5 (100%, $[\text{M} + \text{MeCN} + \text{NH}_4]^+$).

Mono-stoppered azido-triazole derivative (37)

Triazole **36** (700 mg, 1.09 mmol) was suspended in CHCl_3 (100 mL) and Et_3N (0.30 mL, 2.17 mmol) added dropwise, followed by MsCl (0.10 mL, 1.30 mmol). The reaction mixture was stirred under $\text{N}_{2(\text{g})}$ for 5 h, the solvent removed *in vacuo* and the residue dissolved in dry DMF (15 mL). NaN_3 (1.41 g, 21.7 mmol) was added and the solution stirred under $\text{N}_{2(\text{g})}$ for 3 days. After this time, H_2O (100 mL) was added and the reaction mixture extracted with CHCl_3 (3 x 100 mL). The combined organic fractions were washed with brine (100 mL), dried over MgSO_4 and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 1:1 EtOAc/hexane to elute the product as a white solid (585 mg, 0.87 mmol, 80%). **Mp** 214–216 °C (dec.). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 7.57 (1H, s, NC-*H*), 7.22–7.27 (6H, m, Ar-*H*), 7.06–7.13 (8H, m, Ar-*H*), 6.75 (2H, d, $^3J = 8.8$ Hz, OAr-*H*), 4.62 (2H, t, $^3J = 6.9$ Hz, $\text{CH}_2\text{-CH}_2\text{-N}$), 4.49 (2H, s, $\text{-CH}_2\text{-N}_3$), 3.95 (2H, t, $^3J = 5.6$ Hz, $\text{-CH}_2\text{-OAr}$), 2.36–2.44 (2H, m, $\text{CH}_2\text{-CH}_2\text{-CH}_2$), 1.31 (27H, s, -tBu). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 156.1, 148.3, 144.0, 140.2, 132.3, 130.7, 124.0, 122.8, 112.9, 63.7, 63.0, 47.3, 45.6, 34.3, 31.4, 29.9 (one peak missing – coincidental). **MS-ESI** m/z 691.4095 ($[\text{M} + \text{Na}]^+$, $\text{C}_{43}\text{H}_{52}\text{N}_6\text{NaO}$, calc. 691.4095), 669.5 (35%, $[\text{M} + \text{H}]^+$), 691.5 (100%, $[\text{M} + \text{Na}]^+$), 728.6 (75%, $[\text{M} + \text{MeCN} + \text{NH}_4]^+$).

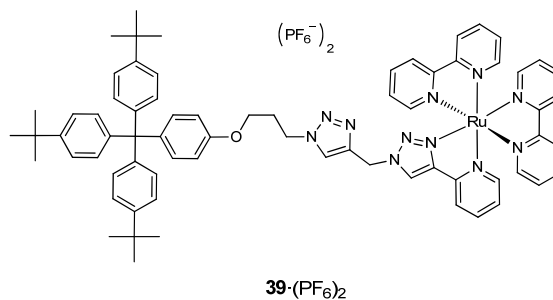
Mono-stoppered bis-triazole pyridyl derivative (38)

To a solution of azide **37** (800 mg, 1.20 mmol) and 2-ethynyl pyridine (0.15 mL, 1.44 mmol) in dry CH_2Cl_2 (60 mL) was added TBTA (20 mg, cat.) and DIPEA (0.42 mL, 2.40 mmol), followed by $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (89 mg, 0.24 mmol). The reaction mixture was stirred under $\text{N}_{2(g)}$ for 15 h. After this time, 0.1 M $\text{NH}_4\text{Cl}_{(aq)}$ (50 mL) was added and the solution stirred for a further 30 min. The aqueous fraction was separated and extracted with CH_2Cl_2 (2 x 50 mL), and the combined organic fractions were washed with brine (100 mL), dried over MgSO_4 and the solvent removed *in vacuo*. Purification was undertaken by silica gel gradient column chromatography using CH_2Cl_2 to remove any unreacted starting material and 98:2 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a yellow solid (894 mg, 1.16 mmol, 96%). **Mp** > 250 °C (dec.). **^1H NMR** (300 MHz, d_6 -DMSO) δ (ppm) 8.38–8.72 (2H, m, Pyridine-*H* & NC-*H*), 8.28 (1H, s, NC-*H*), 7.78–8.10 (2H, m, Pyridine-*H*), 7.25–7.30 (6H, m, Ar-*H*), 6.95–7.11 (8H, m, Ar-*H*), 6.77 (2H, d, $^3J = 8.8$ Hz, OAr-*H*), 5.77 (2H, s, NC- CH_2 -N), 4.52 (2H, t, $^3J = 6.8$ Hz, CH_2 - CH_2 -N), 3.92 (2H, t, $^3J = 5.3$ Hz, - CH_2 -OAr), 2.19–2.32 (2H, m, CH_2 - CH_2 - CH_2), 1.24 (27H, s, ^tBu). **MS-ESI** m/z 794.4526 ($[\text{M} + \text{Na}]^+$, $\text{C}_{50}\text{H}_{57}\text{N}_7\text{NaO}$, calc. 794.4517), 772.5 (60%, $[\text{M} + \text{H}]^+$), 794.5 (100%, $[\text{M} + \text{Na}]^+$).

***cis*-Bis(2,2'-bipyridine) ruthenium(II) dichloride dihydrate^{16, 17}**

$\text{RuCl}_3 \cdot 3\text{H}_2\text{O}$ (3.00 g, 11.5 mmol) and LiCl (3.31 g, 78.0 mmol) were dissolved in DMF (50 mL) and heated to 50 °C. 2,2'-Bipyridine (3.67 g, 23.5 mmol) was added and the reaction mixture heated at reflux under $\text{N}_{2(\text{g})}$ for 8 h. After this time, the solution was allowed to cool to room temperature, poured into rapidly stirring acetone (100 mL) and cooled to -20 °C. The resulting precipitate was filtered, washed with H_2O (3 x 15 mL) and Et_2O (3 x 15 mL). The residue was then suspended in boiling EtOH for 3 min, filtered and dried *in vacuo* to yield the product as a black solid (3.56 g, 6.84 mmol, 59%). $^1\text{H NMR}$ (300 MHz, d_6 -DMSO) δ (ppm) 9.97 (1H, d, $^3J = 5.3$ Hz, Bipy-*H*), 8.64 (1H, d, $^3J = 8.2$ Hz, Bipy-*H*), 8.48 (1H, d, $^3J = 7.6$ Hz, Bipy-*H*), 8.03–8.11 (1H, m, Bipy-*H*), 7.74–7.80 (1H, m, Bipy-*H*), 7.64–7.72 (1H, m, Bipy-*H*), 7.51 (1H, d, $^3J = 5.3$ Hz, Bipy-*H*) 7.06–7.14 (1H, m, Bipy-*H*). **MS-ESI** m/z 449.0 ($[\text{M} - \text{Cl} - (\text{H}_2\text{O})_2]^+$, $\text{C}_{20}\text{H}_{16}\text{ClN}_4\text{Ru}$, calc. 449.0).

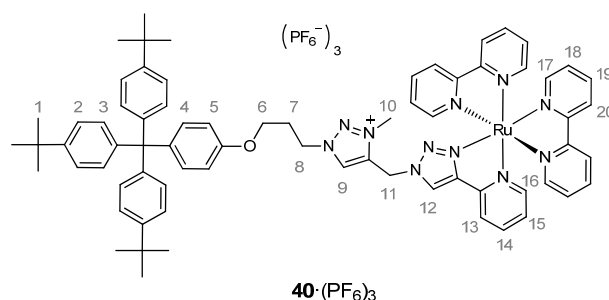
Ruthenium(II)-stoppered triazole axle ($39 \cdot (\text{PF}_6)_2$)



Ligand **38** (450 mg, 0.58 mmol) and *cis*- $\text{Ru}(\text{bipy})_2\text{Cl}_2 \cdot 2\text{H}_2\text{O}$ (317 mg, 0.61 mmol) were dissolved in EtOH/ H_2O (62 mL/8 mL) and heated at reflux for 15 h. After this time, the solvent was removed *in vacuo* and purification undertaken by silica gel gradient column chromatography using 92:6 MeCN/ H_2O to 92:6:2 MeCN/ $\text{H}_2\text{O}/\text{KNO}_3$ as the eluent. The crude product was dissolved in CH_2Cl_2 (100 mL), washed with 0.1 M $\text{NH}_4\text{PF}_6(\text{aq})$ (4 x 50 mL) and water (2 x 50 mL), and dried over MgSO_4 . The solvent was removed *in vacuo* to yield the product as an orange solid (746 mg, 0.51 mmol, 87%). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ (ppm) 8.62 (1H, s, NC-*H*), 8.28–8.43 (4H, m, Bipy-*H*), 8.15 (1H, s, NC-*H*), 7.79–8.00 (8H, m, Bipy-*H*, 2 x Pyridine-*H*), 7.74 (1H, t, $^3J = 7.8$ Hz, Bipy-*H*), 7.68 (1H, d, $^3J = 5.4$ Hz, Bipy-*H*), 7.57 (1H, app d, $^3J = 4.9$ Hz, Pyridine-*H*), 7.53 (1H, app t,

$^3J = 6.6$ Hz, Pyridine-*H*), 7.40–7.50 (2H, m, Bipy-*H*), 7.24–7.32 (2H, m, Bipy-*H*), 7.19–7.23 (6H, m, Ar-*H*), 7.05–7.10 (8H, m, Ar-*H*), 6.71 (2H, d, $^3J = 8.8$ Hz, OAr-*H*), 5.73 (1H, d, $^2J = 15.5$ Hz, NC-CH₂-N), 5.60 (1H, d, $^2J = 15.5$ Hz, NC-CH₂-N), 4.58 (2H, t, $^3J = 7.1$ Hz, CH₂-CH₂-N), 3.96 (2H, t, $^3J = 5.6$ Hz, -CH₂-OAr), 2.30–2.41 (2H, m, CH₂-CH₂-CH₂), 1.25 (27H, s, -^{*t*}Bu). **¹⁹F NMR** (282.5 MHz, *d*₆-acetone) δ (ppm) –73.9 (d, $^1J = 710$ Hz, PF₆). **¹³C NMR** (75.5 MHz, *d*₆-acetone) δ (ppm) 153.2, 153.0, 152.9, 152.7, 149.2, 149.1, 145.3, 139.4, 139.0, 138.9, 138.7, 132.8, 132.7, 131.4, 131.2, 128.8, 128.8, 127.2, 127.1, 125.5, 125.4, 125.2, 125.0, 124.6, 123.8, 114.1, 65.4, 64.0, 48.2, 48.1, 34.9, 31.7, 30.9 (multiple peaks missing – coincidental). **MS-ESI** *m/z* 592.7520 ([M – (PF₆)₂]²⁺, C₇₀H₇₃N₁₁ORu, calc. 592.7526), 592.8 ([M – PF₆]²⁺) – only observed peak in low resolution mass spectrum.

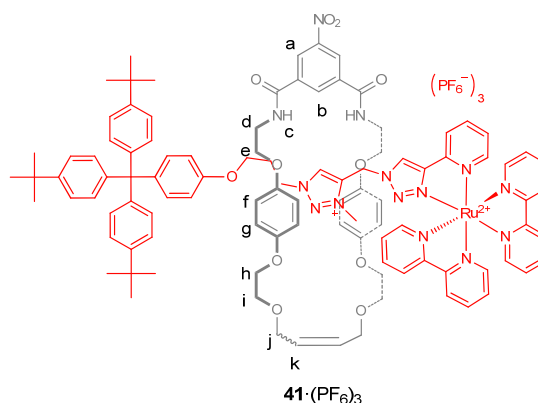
Ruthenium(II)-stoppered triazolium axle (40·(PF₆)₃)¹⁸



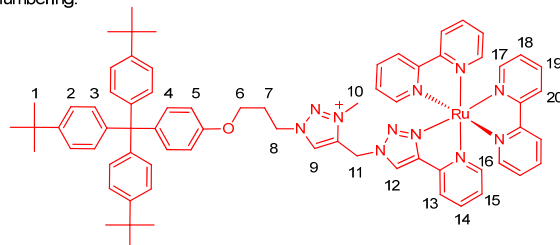
Triazole **39**·(PF₆)₂ (300 mg, 0.20 mmol) and (Me₃O)BF₄ (75 mg, 0.50 mmol) were dissolved in dry CH₂Cl₂ (40 mL) and the reaction mixture stirred under N_{2(g)} for 3 days. After this time, MeOH (0.1 mL) was added to the solution, the solvent removed *in vacuo* and purification undertaken by silica gel column chromatography using 92:6:2 MeCN/H₂O/KNO₃ as the eluent. The crude product was dissolved in CH₂Cl₂ (50 mL), washed with 0.1 M NH₄PF_{6(aq)} (4 x 25 mL) and water (2 x 25 mL), and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as an orange solid (235 mg, 0.14 mmol, 71%). **¹H NMR** (500 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 9.05 (1H, s, H₉), 8.61 (1H, s, H₁₂), 8.58 (1H, d, $^3J = 8.8$ Hz, 1 x H₂₀), 8.49 (1H, d, $^3J = 8.3$ Hz, 1 x H₂₀), 8.43–8.46 (2H, m, 2 x H₂₀), 7.91–8.17 (7H, m, H₁₃ & H₁₄ & 1 x H₁₇ & 4 x H₁₉), 7.79–7.82 (2H, m, 2 x H₁₇), 7.61–7.64 (1H, m,

1 x H₁₇), 7.55–7.60 (2H, m, H₁₅ & H₁₆), 7.48–7.52 (1H, m, 1 x H₁₈), 7.38–7.44 (1H, m, 1 x H₁₈), 7.31–7.37 (1H, m, 1 x H₁₈), 7.18–7.22 (6H, m, H₂), 7.03–7.13 (9H, m, H₃ & H₄ & 1 x H₁₈), 6.66 (2H, d, ³J = 9.3 Hz, H₅), 6.02 (1H, d, ²J = 16.4 Hz, H_{11'}), 5.94 (1H, d, ²J = 16.4 Hz, H_{11''}), 4.76 (2H, t, ³J = 6.8 Hz, H₈), 4.10 (3H, s, H₁₀), 3.95–4.03 (2H, m, H₆), 2.38–2.46 (2H, m, H₇), 1.23 (27H, s, -^tBu). ¹⁹F NMR (282.5 MHz, d₆-acetone) δ (ppm) –73.4 (d, ¹J = 715 Hz, PF₆⁻). ¹³C NMR (75.5 MHz, d₆-acetone) δ (ppm) 158.2, 153.4, 153.4, 153.0, 153.0, 152.7, 149.2, 145.4, 139.4, 139.1, 138.9, 138.8, 132.8, 131.3, 129.0, 128.8, 128.7, 128.2, 127.9, 127.5, 125.4, 125.3, 125.1, 124.9, 124.5, 124.0, 114.0, 65.4, 53.0, 44.1, 39.3, 34.9, 31.7, 29.8 (multiple peaks missing – coincidental and obscured by solvent signal). MS-ESI *m/z* 1270.4673 ([M – (PF₆)₃ + 2.Cl]⁺, C₇₁H₇₆Cl₂N₁₁ORu, calc. 1270.4662), not observed in low resolution mass spectrum.

Ruthenium(II)-appended triazolium rotaxane (41·(PF₆)₃)¹⁹



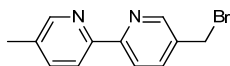
Axle numbering:



Axle **40**·(PF₆)₃ (50 mg, 0.031 mmol), TBACl (9 mg, 0.031 mmol) and macrocycle precursor **15** (20 mg, 0.031 mmol) were dissolved in dry CH₂Cl₂ (25 mL) and stirred for 1 h. Grubbs'

second-generation catalyst (2.0 mg, 10% by weight) was then added and the reaction mixture stirred under $N_{2(g)}$ for 2 days. The solvent was removed *in vacuo* and purification undertaken by silica gel column chromatography using 92:6:2 MeCN/H₂O/KNO₃ as the eluent. The crude product was dissolved in CH₂Cl₂ (5 mL), washed with 0.1 M NH₄PF_{6(aq)} (4 x 5 mL) and water (2 x 5 mL), and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as an orange solid (2.0 mg, 0.001 mmol, 3%). **¹H NMR** (500 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 9.16 (1H, s, H₉), 8.85 (1H, br s, H_a), 8.82 (1H, br s, H_{a'}), 8.72 (1H, br s, H_b or H₁₂), 8.54–8.61 (2H, m, Ar-*H*), 8.34–8.40 (3H, m, Ar-*H* & H_b or H₁₂), 8.26 (1H, d, ³*J* = 8.3 Hz, Ar-*H*), 7.92–8.12 (6H, m, Ar-*H*), 7.81–7.85 (2H, m, Ar-*H*), 7.63–7.67 (2H, m, Ar-*H*), 7.46–7.50 (1H, m, Ar-*H*), 7.34–7.44 (4H, m, Ar-*H*), 7.20–7.26 (8H, m, Ar-*H*), 7.05–7.10 (8H, m, H₃ & H₄), 6.59 (2H, d, ³*J* = 8.8 Hz, H_f or H_{g'}), 6.52 (2H, d, ³*J* = 8.8 Hz, H₅), 6.41 (2H, d, ³*J* = 8.8 Hz, H_f or H_{g''}), 6.20–6.24 (2H, m, H_f or H_{g'}), 6.10–6.14 (2H, m, H_f or H_{g''}), 5.92 (1H, d, ²*J* = 16.9 Hz, H_{11'}), 5.85 (1H, d, ²*J* = 16.9 Hz, H_{11''}), 5.78 (2H, br s, H_k), 4.02 (3H, s, H₁₀), 3.46–4.04 (14H, m, H_d & H_e & H_h & H_{i-j} & H₆ & H₈), 1.73–1.79 (2H, m, H₇), 1.26 (27H, s, H₁). **¹⁹F NMR** (282.5 MHz, *d*₆-acetone) δ (ppm) – 72.6 (d, ¹*J* = 707 Hz, PF₆). **MS-MALDI** *m/z* 2112.7 ([M – (PF₆)₂]⁺, C₁₀₃H₁₁₁N₁₄O₁₁RuP₂F₁₂, calc. 2112.8).

5-(Bromomethyl)-5'-methyl-2,2'-bipyridine (42)²⁰

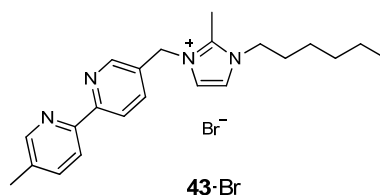


42

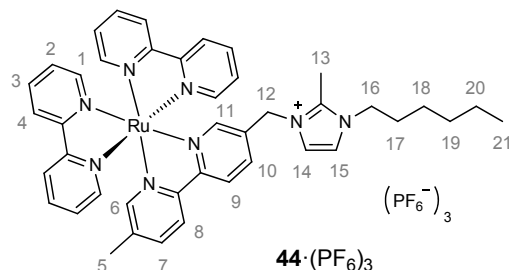
5,5'-Dimethyl-2,2'-bipyridine (1.00 g, 5.43 mmol), NBS (0.97 g, 5.43 mmol) and AIBN (10 mg, cat.) were dissolved in CCl₄ (50 mL) and the reaction mixture heated at reflux under $N_{2(g)}$ for 16 h. After this time, the solution was filtered while hot, cooled to room temperature and left for 2 days. The resulting precipitate was removed by filtration and the filtrate solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 98:2 CH₂Cl₂/MeOH to elute the product as an off-white solid (573 mg, 2.17 mmol, 40%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.67 (1H, d, ⁴*J* = 2.4 Hz, Bipy-*H*), 8.51 (1H, d, ⁴*J* = 1.8 Hz, Bipy-*H*), 8.36 (1H, d, ³*J* = 8.2 Hz, Bipy-*H*), 8.29 (1H,

d, $^3J = 7.6$ Hz, Bipy-*H*), 7.84 (1H, dd, $^3J = 8.2$ Hz, $^4J = 2.4$ Hz, Bipy-*H*), 7.60–7.66 (1H, m, Bipy-*H*), 4.54 (2H, s, -CH₂-), 2.40 (3H, s, -CH₃). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 156.2, 153.0, 149.7, 149.2, 137.5, 137.5, 133.7, 133.2, 120.7, 120.7, 29.8, 18.4. **MS-ESI** m/z 263.0 (70%, [M + H]⁺, C₁₂H₁₂BrN₂, calc. 263.02), 287.0 (100%, [M + Na]⁺).

Bipyridyl-appended 1-hexyl-2-methylimidazolium bromide (43·Br)

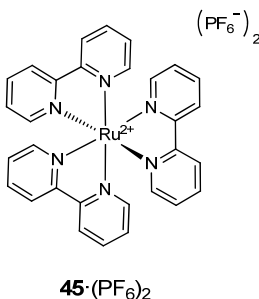


Imidazole derivative **7** (172 mg, 1.04 mmol) and 5-(bromomethyl)-5'-methyl-2,2'-bipyridine (**42**) (300 mg, 1.14 mmol) were dissolved in acetone (10 mL) and heated under microwave irradiation at 150 °C for 30 min. The solvent was removed *in vacuo* and the residue washed with Et₂O (3 x 10 mL) to yield the product as a pale yellow solid (433 mg, 1.01 mmol, 97%). **Mp** 118–121 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.67 (1H, d, $^4J = 2.1$ Hz, Bipy-*H*), 8.54 (1H, app s, Bipy-*H*), 8.40 (1H, d, $^3J = 8.4$ Hz, Bipy-*H*), 8.27 (1H, d, $^3J = 7.9$ Hz, Bipy-*H*), 8.03 (1H, dd, $^3J = 8.4$ Hz, $^4J = 2.1$ Hz, Bipy-*H*), 7.78 Hz (1H, d, $^3J = 2.1$ Hz, NC-*H*), 7.67 (1H, dd, $^3J = 7.9$ Hz, $^4J = 2.1$ Hz, Bipy-*H*), 7.35 (1H, d, $^3J = 2.1$ Hz, NC-*H*), 5.86 (2H, s, N-CH₂-Bipy), 4.14 (2H, t, $^3J = 7.6$ Hz, N-CH₂-CH₂), 2.87 (3H, s, NC-CH₃), 2.42 (3H, s, Bipy-CH₃), 1.76–1.89 (2H, m, NCH₂-CH₂-), 1.26–1.38 (6H, m, 3 x -CH₂-), 0.84–0.93 (3H, m, CH₂-CH₃). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 156.7, 152.2, 149.5, 148.7, 143.9, 137.9, 137.1, 134.3, 128.3, 121.4, 121.3, 120.9, 49.4, 48.8, 31.0, 29.4, 25.9, 22.3, 18.4, 13.9, 9.8 (one peak missing – coincidental). **MS-ESI** m/z 349.2391 ([M - Br]⁺, C₂₂H₂₉N₄, calc. 349.2387), 349.2 ([M - Br]⁺) – only observed peak in low resolution mass spectrum.

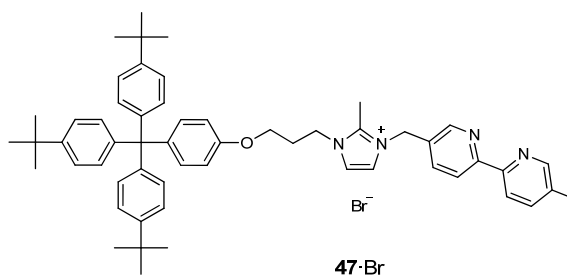
Ruthenium(II)-appended 2-methylimidazolium thread (44·(PF₆)₃)²¹

Imidazolium **43**·Br (100 mg, 0.23 mmol) and *cis*-Ru(bipy)₂Cl₂·2H₂O (125 mg, 0.24 mmol) were dissolved in EtOH/H₂O (18 mL/2 mL) and heated at reflux for 15 h. After this time, the solvent was removed *in vacuo* and purification was undertaken by silica gel column chromatography using 92:6:2 MeCN/H₂O/KNO₃ as the eluent. The crude product was dissolved in the minimum amount of H₂O and NH₄PF₆ (200 mg) added. The resulting precipitate was filtered, washed with water (2 x 50 mL), and dried *in vacuo* to yield the product as a red solid (164 mg, 0.14 mmol, 60%).

¹H NMR (300 MHz, *d*₆-acetone) δ (ppm) 8.74–8.84 (5H, m, H₄ & H₉), 8.71 (1H, d, ³*J* = 8.2 Hz, H₈), 8.17–8.27 (4H, m, H₃), 7.96–8.11 (7H, m, H₁ & H₇ & H₁₀ & H₁₁), 7.90 (1H, s, H₆), 7.71 (1H, d, ³*J* = 2.4 Hz, H₁₅), 7.53–7.61 (4H, m, H₂), 7.52 (2H, d, ³*J* = 2.4 Hz, H₁₄), 5.53 (2H, s, H₁₂), 4.28 (2H, t, ³*J* = 7.6 Hz, H₁₆), 2.66 (3H, s, H₁₃), 2.22 (3H, s, H₅), 1.78–1.89 (2H, m, H₁₇), 1.25–1.39 (6H, m, H_{18–20}), 0.81–0.91 (3H, m, H₂₁). **¹⁹F NMR** (282.5 MHz, *d*₆-acetone) δ (ppm) –72.4 (d, ¹*J* = 708 Hz, PF₆). **¹³C NMR** (75.5 MHz, *d*₆-acetone) δ (ppm) 158.1, 152.9, 152.8, 152.8, 152.7, 152.7, 151.0, 140.2, 139.7, 139.1, 139.0, 138.0, 135.2, 128.9, 128.9, 128.9, 128.8, 125.4, 125.3, 125.2, 125.0, 123.1, 122.7, 49.5, 49.0, 32.0, 26.6, 23.2, 18.6, 14.3, 10.0 (multiple peaks missing – coincidental and obscured by solvent signal). **MS-ESI** *m/z* 1053.2095 ([M – PF₆]⁺, C₄₂H₄₅F₁₂N₈P₂Ru, calc. 1053.2100), not observed in low resolution mass spectrum.

Ruthenium(II) tris-(2,2'-bipyridine) bis-hexafluorophosphate ($45 \cdot (\text{PF}_6)_2$)²²

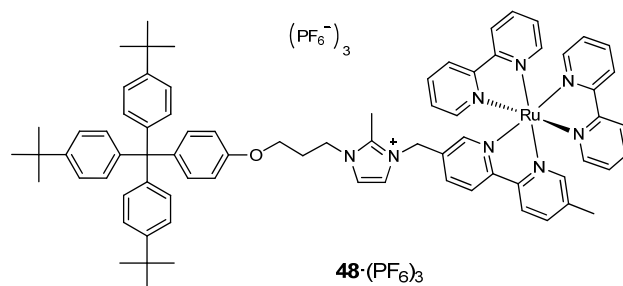
cis-Ru(bipy)₂Cl₂ · 2H₂O (57 mg, 0.11 mmol) and 2,2'-bipyridine (16 mg, 0.10 mmol) were dissolved in EtOH/H₂O (18 mL/2 mL) and heated at reflux for 15 h. After this time, the solvent was removed *in vacuo* and purification was undertaken by silica gel gradient column chromatography using MeCN to 92:6:2 MeCN/H₂O/KNO₃ as the eluent. The crude product was dissolved in the minimum amount of H₂O and NH₄PF₆ (100 mg) added. The resulting precipitate was filtered, washed with water (2 x 25 mL), and dried *in vacuo* to yield the product as a bright orange solid (63 mg, 0.07 mmol, 73%). ¹H NMR (300 MHz, *d*₆-acetone) δ (ppm) 8.83 (6H, app d, ³*J* = 8.2 Hz, Bipy-*H*), 8.17–8.27 (6H, m, Bipy-*H*), 8.07 (6H, app d, ³*J* = 5.9 Hz, Bipy-*H*), 7.53–7.64 (6H, m, Bipy-*H*). ¹⁹F NMR (282.5 MHz, *d*₆-acetone) δ (ppm) –72.6 (d, ¹*J* = 707 Hz, PF₆). ¹³C NMR (75.5 MHz, *d*₆-acetone) δ (ppm) 158.2, 152.8, 139.0, 128.8, 125.4. MS not observed.

Mono-stoppered bipyridine-appended imidazolium bromide (47 · Br)

Imidazole derivative **12** (100 mg, 0.16 mmol) and 5-(bromomethyl)-5'-methyl-2,2'-bipyridine (**42**) (63 mg, 0.24 mmol) were dissolved in acetone (5 mL) and heated under microwave irradiation at

150 °C for 30 min. The solvent was removed *in vacuo* and the residue washed with Et₂O (3 x 10 mL) to yield the product as an off-white solid (138 mg, 0.16 mmol, 97%). **Mp** 235–240 °C (dec.). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.55 (1H, d, ⁴*J* = 2.4 Hz, Bipy-*H*), 8.39–8.44 (1H, m, Bipy-*H*), 8.32 (1H, d, ³*J* = 8.2 Hz, Bipy-*H*), 8.16 (1H, d, ³*J* = 7.6 Hz, Bipy-*H*), 7.87 (1H, dd, ³*J* = 8.2 Hz, ⁴*J* = 2.4 Hz, Bipy-*H*), 7.50–7.56 (1H, m, Bipy-*H*), 7.45 (1H, d, ³*J* = 2.1 Hz, NC-*H*), 7.37 (1H, d, ³*J* = 2.1 Hz, NC-*H*), 7.11–7.19 (6H, m, Ar-*H*), 6.94–7.06 (8H, m, Ar-*H*), 6.64 (2H, d, ³*J* = 8.8 Hz, OAr-*H*), 5.61 (2H, s, NC-CH₂-Ar), 4.37 (2H, t, ³*J* = 6.8 Hz, N-CH₂-CH₂), 3.96 (2H, t, ³*J* = 5.3 Hz, -CH₂-OAr), 2.79 (3H, s, NC-CH₃), 2.24–2.37 (5H, m, Ar-CH₃ & CH₂-CH₂-CH₂), 1.22 (27H, s, ⁻Bu). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 157.1, 155.7, 152.5, 149.7, 148.8, 148.3, 144.4, 143.9, 140.4, 137.5, 137.4, 134.0, 132.4, 130.6, 128.2, 127.3, 124.0, 120.8, 112.8, 63.4, 50.0, 45.9, 34.2, 31.3, 18.4, 11.4 (four peaks missing – coincidental and due to weakness of sample). **MS-ESI** *m/z* 809.5152 ([M – Br]⁺, C₅₆H₆₅N₄O, calc. 809.5153), 809.49 ([M – Br]⁺) – only observed peak in low resolution mass spectrum.

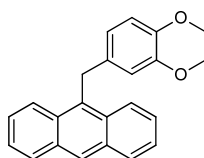
Ruthenium-stoppered 2-methylimidazolium axle (48·(PF₆)₃)



Imidazolium **47**·Br (70 mg, 0.08 mmol) and *cis*-Ru(bipy)₂Cl₂·2H₂O (42 mg, 0.08 mmol) were dissolved in EtOH/H₂O (18 mL/2 mL) and heated at reflux for 15 h. After this time, the solvent was removed *in vacuo* and purification was undertaken by silica gel column chromatography using 92:6:2 MeCN/H₂O/KNO₃ as the eluent. The crude product was dissolved in CH₂Cl₂ (50 mL), washed with 0.1 M NH₄PF_{6(aq)} (4 x 25 mL) and water (2 x 25 mL), and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as a red solid (101 mg, 0.06 mmol, 76%). **¹H NMR** (300 MHz,

d_6 -acetone) δ (ppm) 8.65–8.82 (5H, m, Bipy-*H*), 8.53 (1H, d, $^3J = 8.2$ Hz, Bipy-*H*), 7.88–8.24 (12H, m, Bipy-*H*), 7.74 (1H, d, $^3J = 2.4$ Hz, NC-*H*), 7.49–7.57 (4H, m, 1 x NC-*H* & Bipy-*H*), 7.28–7.33 (6H, m, Bipy-*H*), 7.22–7.27 (1H, m, Bipy-*H*), 7.08–7.16 (6H, m, Ar-*H*), 7.04 (2H, d, $^3J = 8.8$ Hz, Ar-*H*), 6.58 (2H, d, $^3J = 8.8$ Hz, Ar-*H*), 5.53 (2H, s, N-CH₂-Ar), 4.50 (2H, t, $^3J = 6.8$ Hz, CN-CH₂-CH₂), 4.06 (2H, t, $^3J = 5.6$ Hz, O-CH₂-), 2.65 (3H, s, NC-CH₃), 2.24 (3H, s, Ar-CH₃), 2.01–2.05 (2H, m, CH₂-CH₂-CH₂), 1.29 (27H, s, ⁻Bu). ¹⁹F NMR (282.5 MHz, d_6 -acetone) δ (ppm) –72.4 (d, $^1J = 706$ Hz, PF₆). ¹³C NMR (75.5 MHz, d_6 -acetone) δ (ppm) 155.7, 153.0, 152.9, 152.7, 152.7, 151.2, 149.3, 145.3, 140.3, 139.7, 139.1, 139.0, 139.0, 138.3, 132.8, 131.4, 129.0, 128.9, 128.8, 125.4, 125.3, 125.2, 125.1, 125.0, 123.3, 122.8, 114.0, 68.7, 65.3, 49.0, 47.0, 35.0, 31.7, 30.0, 18.6, 10.1 (multiple peaks missing – coincidental). MS-ESI m/z 1513.4837 ([M – PF₆]⁺, C₇₆H₈₁F₁₂N₈OP₂Ru, calc. 1513.4876), not observed in low resolution mass spectrum.

9-(3,4-Dimethoxybenzyl)anthracene (49)²³

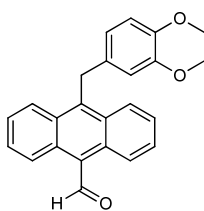


49

9-Anthracenemethanol (200 mg, 0.96 mmol) was added to a solution of conc. H₂SO₄ (6 mL) and H₂O (4 mL) at 0 °C and stirred for 10 min. 1,2-Dimethoxybenzene (0.12 mL, 0.96 mmol) was added and the reaction mixture stirred at 0 °C for a further 30 min. The solution was then heated at 30 °C for 3 h, after which time it was allowed to cool to room temperature and poured into ice water (~ 30 mL). The resulting precipitate was filtered and dissolved in the minimum amount of boiling 1:1 CHCl₃/EtOH. The solution was cooled, CHCl₃ removed *in vacuo* and the resulting precipitate filtered, washed with EtOH and dried *in vacuo* to yield the product as a yellow solid (162 mg, 0.49 mmol, 51%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.45 (1H, s, Ar-*H*), 8.20–8.27 (2H, m, Ar-*H*), 8.02–8.08 (2H, m, Ar-*H*), 7.44–7.51 (4H, m, Ar-*H*), 6.80 (1H, d, $^4J = 2.1$ Hz, Ar-*H*), 6.67 (1H, $^3J = 8.2$ Hz, Ar-*H*), 6.48–6.55

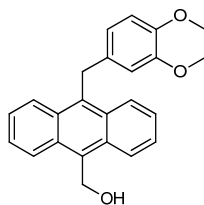
(1H, m, Ar-*H*), 4.97 (2H, s, Ar-CH₂-Ar), 3.79 (3H, s, O-CH₃), 3.74 (3H, s, O-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 148.9, 147.3, 133.4, 132.0, 131.7, 130.5, 129.1, 126.5, 125.9, 124.9, 124.8, 120.0, 111.5, 111.2, 55.8, 55.8, 33.1. **MS-ESI** *m/z* 329.1 ([M + H]⁺, C₂₃H₂₁O₂, calc. 329.2).

10-(3,4-Dimethoxybenzyl)anthracene-9-carbaldehyde (50)²³

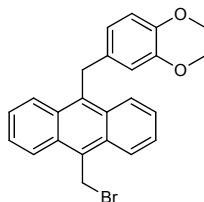


50

To a solution of 9-(3,4-dimethoxybenzyl)anthracene (**49**) (600 mg, 1.83 mmol) in dry CH₂Cl₂ (25 mL) at 0 °C was added dropwise TiCl₄ (1.0 M in CH₂Cl₂, 3.65 mL, 3.65 mmol), followed by α,α-dichloromethylmethylether (0.31 mL, 3.47 mmol). The reaction mixture was stirred at 0 °C for 1 h, allowed to warm to room temperature and stirred for a further 15 h. After this time, conc. HCl (10 mL) at 0 °C was added, followed by CH₂Cl₂ (50 mL). The organic fraction was separated, washed with water (3 x 50 mL), dried over MgSO₄ and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 7:3 CH₂Cl₂/hexane to elute the product as a dark yellow solid (438 mg, 1.23 mmol, 67%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 11.56 (1H, s, -CHO), 8.99 (2H, app d, ³*J* = 9.1 Hz, Ar-*H*), 8.34 (2H, app d, ³*J* = 9.1 Hz, Ar-*H*), 7.68 (2H, ddd, ³*J* = 9.1 Hz, ³*J* = 6.6 Hz, ⁴*J* = 1.5 Hz, Ar-*H*), 7.51–7.59 (2H, m, Ar-*H*), 6.78 (1H, d, ⁴*J* = 2.1 Hz, Ar-*H*), 6.68 (1H, d, ³*J* = 8.5 Hz, Ar-*H*), 6.45–6.52 (1H, m, Ar-*H*), 5.03 (2H, s, Ar-CH₂-Ar), 3.80 (3H, s, O-CH₃), 3.75 (3H, s, O-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 193.6, 149.0, 147.5, 140.1, 132.3, 131.7, 130.0, 128.4, 126.1, 125.6, 125.1, 124.1, 120.0, 111.3, 111.2, 55.8, 34.0 (one peak missing – coincidental). **MS-ESI** *m/z* 357.0 ([M + H]⁺, C₂₄H₂₁O₃, calc. 357.1).

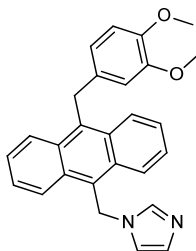
(10-(3,4-Dimethoxybenzyl)anthracen-9-yl)methanol (51)²³**51**

A solution of 10-(3,4-dimethoxybenzyl)anthracene-9-carbaldehyde (**50**) (290 mg, 0.81 mmol) in dry THF (25 mL) was heated at reflux and NaBH₄ (123 mg, 3.26 mmol) added carefully over 10 min. The reaction mixture was heated at reflux for a further 45 min. After this time, the solution was allowed to cool to room temperature and poured into water (75 mL). The resulting precipitate was extracted with CHCl₃ (3 x 50 mL) and the combined organic fractions washed with brine (100 mL) and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as a yellow solid (273 mg, 0.76 mmol, 94%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.51 (2H, app d, ³J = 8.5 Hz, Ar-*H*), 8.29 (2H, app d, ³J = 8.5 Hz, Ar-*H*), 7.54–7.62 (2H, m, Ar-*H*), 7.46–7.53 (2H, m, Ar-*H*), 6.81 (1H, d, ⁴J = 2.0 Hz, Ar-*H*), 6.66 (1H, d, ³J = 8.2 Hz, Ar-*H*), 6.47–6.52 (1H, m, Ar-*H*), 5.73 (2H, s, -CH₂-OH), 4.99 (2H, s, Ar-CH₂-Ar), 3.79 (3H, s, O-CH₃), 3.75 (3H, s, O-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 148.9, 147.3, 133.7, 133.1, 130.6, 130.4, 130.2, 126.0, 125.6, 124.6, 120.0, 111.5, 111.2, 57.6, 55.8, 33.5 (two peaks missing – coincidental). MS-ESI *m/z* 417.2 ([M + NH₄ + MeCN]⁺, C₂₆H₂₉N₂O₃, calc. 417.2).

9-(Bromomethyl)-10-(3,4-dimethoxybenzyl)anthracene (52)²³**52**

(10-(3,4-Dimethoxybenzyl)anthracen-9-yl)methanol (**51**) (100 mg, 0.28 mmol) was suspended in dry toluene (10 mL) at 0 °C. PBr_3 (0.03 mL, 0.36 mmol) was added and the reaction mixture was stirred at room temperature for 2 h. After this time, toluene (20 mL) was added and the solution washed with sat. $\text{NaHCO}_{3(\text{aq})}$ (30 mL), water (2 x 30 mL) and brine (30 mL), and dried over MgSO_4 . The solvent was removed *in vacuo* to yield the product as a dark orange solid (107 mg, 0.25 mmol, 91%). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.38 (2H, app d, $^3J = 8.8$ Hz, Ar-*H*), 8.30 (2H, app d, $^3J = 8.8$ Hz, Ar-*H*), 7.65 (2H, ddd, $^3J = 8.8$ Hz, $^3J = 6.5$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 7.51 (2H, ddd, $^3J = 8.8$ Hz, $^3J = 6.5$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 6.81 (1H, d, $^4J = 1.8$ Hz, Ar-*H*), 6.66 (1H, d, $^3J = 8.5$ Hz, Ar-*H*), 6.38–6.55 (1H, m, Ar-*H*), 5.60 (2H, s, $-\text{CH}_2-\text{Br}$), 4.96 (2H, s, Ar- CH_2 -Ar), 3.79 (3H, s, O- CH_3), 3.77 (3H, s, O- CH_3). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 148.9, 147.3, 134.7, 132.9, 130.5, 129.6, 127.4, 126.3, 125.8, 125.7, 124.1, 120.0, 111.4, 111.2, 55.8, 33.6, 27.6 (one peak missing – coincidental). **MS** not observed.

1-((10-(3,4-Dimethoxybenzyl)anthracen-9-yl)methyl)-1*H*-imidazole (53)

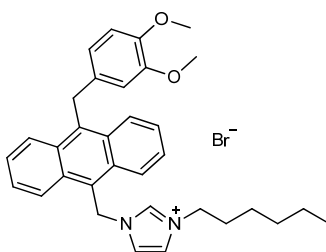


53

Imidazole (41 mg, 0.60 mmol) was stirred with K_2CO_3 (91 mg, 0.66 mmol) in acetone (5 mL) for 15 min. To this solution was added 9-(bromomethyl)-10-(3,4-dimethoxybenzyl)anthracene (**52**) (50 mg, 0.12 mmol) in acetone (5 mL), and NaI (5 mg, cat.). The reaction mixture was then stirred for 15 h, after which the solution was filtered and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 97.5:2.5 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a dark orange solid (33 mg, 0.08 mmol, 67%). **Mp** 167–169 °C. **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.31–8.36 (2H, m, Ar-*H*), 8.23–8.28 (2H, m, Ar-*H*), 7.48–7.60 (5H, m, 1 x NC-*H* & Ar-*H*), 7.02 (1H,

s, NC-*H*), 6.91 (1H, s, NC-*H*), 6.82 (1H, d, $^4J = 2.4$ Hz, Ar-*H*), 6.68 (1H, d, $^3J = 8.5$ Hz, Ar-*H*), 6.48 (1H, dd, $^3J = 8.5$ Hz, $^4J = 2.4$ Hz, Ar-*H*), 6.12 (2H, s, N-CH₂-Ar), 5.02 (2H, s, Ar-CH₂-Ar), 3.79 (3H, s, O-CH₃), 3.77 (3H, s, O-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 149.0, 147.4, 136.8, 135.0, 132.9, 130.7, 130.4, 129.2, 126.9, 125.9, 125.8, 124.2, 123.7, 120.0, 118.9, 111.4, 111.3, 55.8, 43.3, 33.5 (one peak missing – coincidental). MS-ESI *m/z* 409.1906 ([M + H]⁺, C₂₇H₂₅N₂O₂, calc. 409.1911), 409.2 (100%, [M + H]⁺), 431.2 (45%, [M + Na]⁺).

1-((10-(3,4-Dimethoxybenzyl)anthracen-9-yl)methyl)-3-hexyl-imidazolium bromide (54·Br)

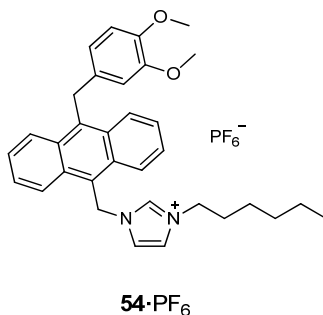


54·Br

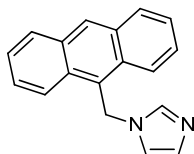
1-((10-(3,4-Dimethoxybenzyl)anthracen-9-yl)methyl)-1*H*-imidazole (**53**) (80 mg, 0.20 mmol) and 1-bromohexane (0.14 mL, 0.97 mmol) were dissolved in 1,4-dioxane (2 mL) and heated under microwave irradiation at 120 °C for 3 h. Purification was undertaken by silica gel gradient column chromatography using 97:3 CH₂Cl₂/MeOH to 95:5 CH₂Cl₂/MeOH to elute the product as a pale yellow solid (100 mg, 0.16 mmol, 82%). ¹H NMR (500 MHz, CDCl₃) δ (ppm) 11.06 (1H, s, NC-*H*), 8.44 (2H, app d, $^3J = 8.8$ Hz, Ar-*H*), 8.32 (2H, app d, $^3J = 8.8$ Hz, Ar-*H*), 7.62–7.68 (2H, m, Ar-*H*), 7.49–7.54 (2H, m, Ar-*H*), 7.13 (1H, br s, NC-*H*), 6.80 (1H, t, $^4J = 1.7$ Hz, NC-*H*), 6.79 (1H, d, $^4J = 2.0$ Hz, Ar-*H*), 6.70 (2H, s, N-CH₂-Ar), 6.64 (1H, d, $^3J = 8.3$ Hz, Ar-*H*), 6.41–6.46 (1H, m, Ar-*H*), 4.96 (2H, s, Ar-CH₂-Ar), 4.26 (2H, t, $^3J = 7.6$ Hz, N-CH₂-CH₂), 3.75 (3H, s, O-CH₃), 3.73 (3H, s, O-CH₃), 1.84–1.90 (2H, m, NCH₂-CH₂-), 1.19–1.30 (6H, m, 3 x -CH₂-), 0.76–0.82 (3H, m, CH₂-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 149.0, 147.5, 137.2, 136.4, 132.6, 130.9, 130.3, 127.9, 126.1, 126.0, 123.5, 121.5, 121.2, 121.1, 119.9, 111.5, 111.3, 55.9, 55.8, 50.3, 46.0, 33.6, 31.0,

30.0, 25.8, 22.3, 13.8. **MS-ESI** m/z 493.2852 ($[M - Br]^+$, $C_{33}H_{37}N_2O_2$, calc. 493.2850), 493.3 ($[M - Br]^+$) – only observed peak in low resolution mass spectrum.

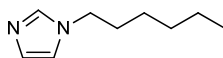
1-((10-(3,4-Dimethoxybenzyl)anthracen-9-yl)methyl)-3-hexyl-imidazolium receptor (54·PF₆)



1-((10-(3,4-Dimethoxybenzyl)anthracen-9-yl)methyl)-3-hexyl-1*H*-imidazol-3-ium bromide (**54·Br**) (50 mg, 0.09 mmol) was dissolved in CH_2Cl_2 (20 ml) and washed with 0.1 M $NH_4PF_6(aq)$ (10 x 10 mL) and H_2O (4 x 10 mL). The organic fraction was dried over $MgSO_4$ and the solvent removed *in vacuo* to yield the product as a pale yellow solid (48 mg, 0.07 mmol, 86%). **¹H NMR** (500 MHz, $CDCl_3$) δ (ppm) 8.99 (1H, s, NC-*H*), 8.36 (2H, app d, $^3J = 8.8$ Hz, Ar-*H*), 8.29 (2H, app d, $^3J = 8.8$ Hz, Ar-*H*), 7.65–7.70 (2H, m, Ar-*H*), 7.52–7.56 (2H, m, Ar-*H*), 7.07 (1H, t, $^4J = 1.7$ Hz, NC-*H*), 6.87 (1H, t, $^4J = 2.0$ Hz, NC-*H*), 6.81 (1H, d, $^4J = 2.0$ Hz, Ar-*H*), 6.66 (1H, d, $^3J = 8.3$ Hz, Ar-*H*), 6.42–6.48 (3H, m, Ar-*H* & N- CH_2 -Ar), 4.99 (2H, s, Ar- CH_2 -Ar), 4.17 (2H, t, $^3J = 7.6$ Hz, N- CH_2 - CH_2), 3.77 (3H, s, O- CH_3), 3.74 (3H, s, O- CH_3), 1.81–1.88 (2H, m, N CH_2 - CH_2 -), 1.18–1.29 (6H, m, 3 x - CH_2 -), 0.76–0.80 (3H, m, CH_2 - CH_3). **¹⁹F NMR** (282.5 MHz, $CDCl_3$) δ (ppm) –72.2 (d, $^1J = 693$ Hz, PF_6). **¹³C NMR** (75.5 MHz, $CDCl_3$) δ (ppm) 149.0, 147.5, 136.7, 135.6, 132.6, 130.9, 130.3, 128.1, 126.1, 126.0, 123.1, 121.6, 121.6, 120.8, 119.9, 111.5, 111.2, 55.9, 55.8, 50.4, 45.8, 33.6, 30.9, 29.7, 25.8, 22.3, 13.8. **MS-ESI** m/z 493.2840 ($[M - PF_6]^+$, $C_{33}H_{37}N_2O_2$, calc. 493.2850), 493.3 ($[M - PF_6]^+$) – only observed peak in low resolution mass spectrum.

1-(Anthracen-9-ylmethyl)-1*H*-imidazole (55)²⁴**55**

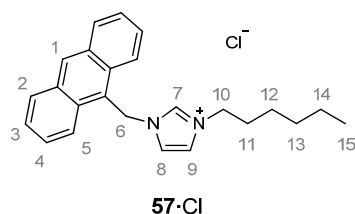
Imidazole (2.10 g, 30.9 mmol) was stirred with K₂CO₃ (4.70 g, 34.0 mmol) in dry MeCN (150 mL) for 15 min. To this solution was added 9-(chloromethyl)anthracene (700 mg, 3.09 mmol) and NaI (20 mg, cat.). The reaction mixture was then stirred for 15 h, after which time the solution was filtered and the solvent removed *in vacuo*. The residue was dissolved in CH₂Cl₂ (100 mL), washed with water (3 x 50 mL), brine (50 mL) and dried over MgSO₄. Purification was undertaken by column chromatography using 4:4:1 CHCl₃/Et₂O/EtOH to elute the product as an off-white solid (638 mg, 2.47 mmol, 80%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.58 (1H, s, NC-*H*), 8.18–8.23 (2H, m, Ar-*H*), 8.06–8.11 (2H, m, Ar-*H*), 7.47–7.62 (4H, m, Ar-*H*), 7.00 (1H, s, NC-*H*), 6.87 (1H, s, NC-*H*), 6.09 (2H, s, -CH₂-). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 136.8, 131.4, 130.7, 129.4, 129.3, 127.3, 125.3, 124.6, 122.9, 118.9, 43.0 (one peak missing – coincidental). MS-ESI *m/z* 259.1235 ([M + H]⁺, C₁₈H₁₅N₂, calc. 259.1230), 259.1 ([M + H]⁺) – only observed peak in low resolution mass spectrum.

1-Hexyl-1*H*-imidazole (56)⁵**56**

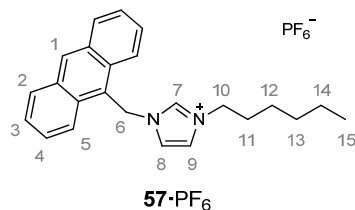
NaH (60% dispersion in mineral oil, 736 mg, 18.4 mmol) was suspended in dry THF (15 mL) at 0 °C under N_{2(g)}. Imidazole (1.00 g, 14.7 mmol) in dry THF (10 mL) was added dropwise to this solution, followed by 1-bromohexane (1.03 mL, 7.35 mmol) in dry THF (15 mL). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. After this time, H₂O (50 mL) was added carefully and the organic solvent removed *in vacuo*. The product was extracted with Et₂O (3 x 25 mL),

the combined organic fractions washed with H₂O (1 x 20 mL) and brine (1 x 20 mL), and dried over MgSO₄. The solvent was removed *in vacuo* to yield the product as a colourless oil (1.00 g, 6.57 mmol, 89%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 7.54 (1H, s, NC-*H*), 7.06 (1H, s, NC-*H*), 6.90–6.92 (1H, s, NC-*H*), 3.93 (2H, t, ³*J* = 7.0 Hz, N-CH₂-), 1.71–1.82 (2H, m, NCH₂-CH₂-), 1.24–1.32 (6H, m, 3 x -CH₂-), 0.84–0.91 (3H, m, -CH₃). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 136.9, 128.8, 118.8, 47.1, 31.2, 30.9, 26.1, 22.4, 13.9. **MS-ESI** *m/z* 153.2 ([M + H]⁺, C₉H₁₇N₂, calc. 153.1).

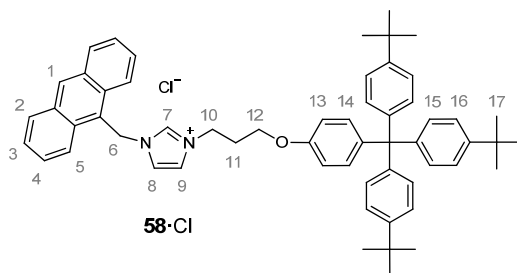
1-(Anthracen-9-ylmethyl)-3-hexyl-1*H*-imidazol-3-ium chloride (57·Cl)



1-Hexyl-1*H*-imidazole (**56**) (112 mg, 0.74 mmol) and 9-(chloromethyl)anthracene (200 mg, 0.88 mmol) were dissolved in acetone (5 mL) and heated under microwave irradiation at 150 °C for 2 h. The solution was cooled to −4 °C and the resulting precipitate collected, washed with Et₂O (2 x 10 mL) and dried *in vacuo* to yield the product as a pale yellow solid (139 mg, 0.37 mmol, 50%). **Mp** 163–166 °C (dec.). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 11.49 (1H, s, H₇), 8.61 (1H, s, H₁), 8.40 (2H, app d, ³*J* = 8.8 Hz, H₅), 8.08 (2H, app d, ³*J* = 8.2 Hz, H₂), 7.65–7.71 (2H, m, H₄), 7.50–7.58 (2H, m, H₃), 6.94–6.96 (1H, m, H₈ or H₉), 6.71 (2H, s, H₆), 6.68–6.70 (1H, m, H₈ or H₉), 4.29 (2H, t, ³*J* = 7.6 Hz, H₁₀), 1.86–1.96 (2H, m, H₁₁), 1.25–1.37 (6H, m, H₁₂ & H₁₃ & H₁₄), 0.82–0.90 (3H, m, H₁₅). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 137.7, 131.2, 130.9, 130.5, 129.5, 128.2, 125.5, 122.8, 122.0, 121.2, 121.0, 50.2, 45.5, 30.9, 30.0, 25.8, 22.3, 13.8. **MS-ESI** *m/z* 343.2169 ([M – Cl]⁺, C₂₄H₂₇N₂, calc. 343.2169), 343.2 (100%, [M – Cl]⁺), 721.5 (10%, [2M – Cl]⁺).

1-(Anthracen-9-ylmethyl)-3-hexyl-1*H*-imidazol-3-ium hexafluorophosphate (57·PF₆)

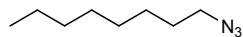
1-(Anthracen-9-ylmethyl)-3-hexyl-1*H*-imidazol-3-ium chloride (**57·Cl**) (60 mg, 0.16 mmol) was dissolved in CH₂Cl₂ (20 ml) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (4 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a pale yellow solid (73 mg, 0.15 mmol, 95%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.91 (1H, s, H₇), 8.60 (1H, s, H₁), 8.22 (2H, app d, ³J = 8.8 Hz, H₅), 8.07 (2H, app d, ³J = 8.2 Hz, H₂), 7.63–7.71 (2H, m, H₄), 7.49–7.57 (2H, m, H₃), 7.05 (1H, s, H₈ or H₉), 6.82 (1H, s, H₈ or H₉), 6.38 (2H, s, H₆), 4.16 (2H, t, ³J = 7.6 Hz, H₁₀), 1.80–1.90 (2H, m, H₁₁), 1.17–1.32 (6H, m, H₁₂ & H₁₃ & H₁₄), 0.76–0.85 (3H, m, H₁₅). ¹⁹F NMR (282.5 MHz, CDCl₃) δ (ppm) –72.3 (d, ¹J = 712 Hz, PF₆). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 135.7, 131.3, 131.0, 130.8, 129.5, 128.6, 125.7, 122.3, 121.6, 121.5, 121.1, 50.4, 45.6, 30.9, 29.7, 25.8, 22.3, 13.8. **MS-ESI** *m/z* 343.2173 ([M – PF₆]⁺, C₂₄H₂₇N₂, calc. 343.2169), 343.3 ([M – PF₆]⁺) – only observed peak in low resolution mass spectrum.

Mono-stoppered anthracene-appended imidazolium chloride (58·Cl)

1-(Anthracen-9-ylmethyl)-1*H*-imidazole (**55**) (48 mg, 0.18 mmol) and bromo-functionalised stopper **10** (150 mg, 0.24 mmol) were dissolved in 1,4-dioxane (2 mL) and heated under microwave

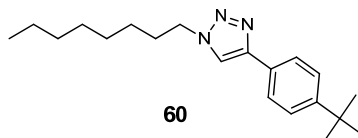
irradiation at 120 °C for 2 h. Purification was undertaken by silica gel gradient column chromatography using 98:2 to 9:1 CH₂Cl₂/MeOH as the eluent. The crude product was dissolved in CH₂Cl₂ (10 mL) and washed with 1.0 M NH₄Cl_(aq) (10 x 5 mL), H₂O (3 x 10 mL) and brine (10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a pale orange solid (84 mg, 0.10 mmol, 56%). **Mp** > 170 °C (dec.). **¹H NMR** (500 MHz, CDCl₃) δ (ppm) 11.58 (1H, s, H₇), 8.60 (1H, s, H₁), 8.35 (2H, app d, ³J = 8.8 Hz, H₅), 8.07 (2H, app d, ³J = 7.8 Hz, H₂), 7.61–7.67 (2H, m, H₄), 7.50–7.54 (2H, m, H₃), 7.20–7.24 (6H, m, H₁₆), 7.02–7.07 (8H, m, H₁₄ & H₁₅), 6.97 (1H, s, H₈ or H₉), 6.64 (1H, s, H₈ or H₉), 6.61 (2H, s, H₆), 6.58 (2H, d, ³J = 8.8 Hz, H₁₃), 4.55 (2H, t, ³J = 6.8 Hz, H₁₀), 3.99 (2H, t, ³J = 5.6 Hz, H₁₂), 2.42–2.48 (2H, m, H₁₁), 1.26 (27H, s, H₁₇). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 155.7, 148.3, 143.9, 140.3, 133.8, 132.3, 131.3, 130.9, 130.6, 129.5, 128.4, 125.6, 124.1, 122.7, 121.8, 120.8, 112.8, 112.7, 63.8, 47.6, 45.7, 34.2, 31.3, 29.7 (two peaks missing – coincidental). **MS-ESI** *m/z* 803.4929 ([M – Cl]⁺, C₅₈H₆₃N₂O, calc. 803.4935), 803.6 ([M – Cl]⁺) – only observed peak in low resolution mass spectrum.

1-azido-octane (59)^{25, 26}

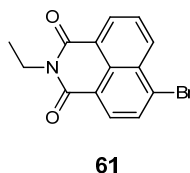


59

1-Bromooctane (500 mg, 2.59 mmol) and NaN₃ (252 mg, 3.88 mmol) were dissolved in DMSO (4 mL) and the reaction mixture stirred for 4 h. After this time, H₂O (25 mL) was added and the solution extracted with Et₂O (3 x 10 mL). The combined organic fractions were washed with brine (10 mL) and the solvent removed *in vacuo* to yield the product as a colourless oil (274 mg, 1.77 mmol, 68%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 3.26 (2H, t, ³J = 7.0 Hz, -CH₂-N₃), 1.53–1.68 (2H, m, -CH₂-CH₂N₃), 1.21–1.44 (10H, m, 5 x -CH₂-), 0.84–0.94 (3H, m, -CH₃). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 51.5, 31.8, 29.2, 29.1, 28.8, 26.7, 22.6, 14.1. **MS** not observed.

4-(4-(*tert*-Butyl)phenyl)-1-octyl-1*H*-1,2,3-triazole (60)²⁷

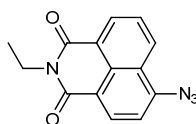
1-Azido-octane (**59**) (200 mg, 1.29 mmol), 4-*tert*-butylphenylacetylene (0.28 mL, 1.55 mmol) and TBTA (2 mg, cat.) were dissolved in 1:1 H₂O/THF (6 mL) and the solution was degassed with N_{2(g)}. CuSO₄·5H₂O (7 mg, 0.03 mmol) and sodium L-ascorbate (26 mg, 0.13 mmol) were added and the reaction mixture stirred under N_{2(g)} for 15 h. After this time, the solvent was removed *in vacuo* and the residue dissolved in EtOAc (20 mL). The solution was washed with 1 M NaOH_(aq) (10 mL), water (2 x 10 mL) and brine (10 mL), and dried over MgSO₄. Purification was undertaken by silica gel gradient column chromatography using CH₂Cl₂ to 9:1 CH₂Cl₂/MeOH to elute the product as a white solid (325 mg, 1.04 mmol, 80%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.77 (2H, d, ³*J* = 8.5 Hz, Ar-*H*), 7.72 (1H, s, NC-*H*), 7.46 (2H, d, ³*J* = 8.5 Hz, Ar-*H*), 4.40 (2H, t, ³*J* = 7.3 Hz, N-CH₂-), 1.90–2.00 (2H, m, NCH₂-CH₂-), 1.25–1.38 (19H, m, 5 x -CH₂- & -*t*Bu), 0.84–0.92 (3H, m, CH₂-CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 151.1, 147.6, 127.9, 125.7, 125.4, 119.1, 50.3, 34.6, 31.7, 31.3, 30.3, 29.0, 28.9, 26.5, 22.6, 14.0. **MS-ESI** *m/z* 372.3 ([M + NH₄ + MeCN]⁺, C₂₂H₃₈N₅, calc. 372.3). **MS-FI** *m/z* 313.2518 ([M]⁺, C₂₂H₃₁N₃, calc. 313.2514).

6.2.3 Synthetic Procedures for Chapter Four***N*-Ethyl-4-bromo-1,8-naphthalimide (61)**²⁸

To a stirred solution of 4-bromo-1,8-naphthalic anhydride (1.00 g, 3.61 mmol) in 1,4-dioxane (50 mL) was added EtNH₂ (70% in H₂O, 0.34 mL, 4.28 mmol) and the reaction mixture heated at reflux under

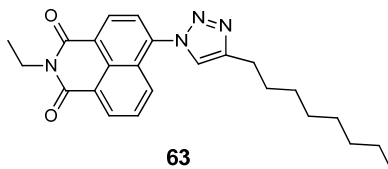
$\text{N}_{2(\text{g})}$ for 15 h. The reaction mixture was allowed to cool and H_2O (50 mL) added. The resulting precipitate was filtered, washed with H_2O (3 x 30 mL) and dried *in vacuo* to yield the product as a yellow solid (856 mg, 2.82 mmol, 78%). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.68 (1H, dd, $^3J = 7.5$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.59 (1H, dd, $^3J = 8.4$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.44 (1H, d, $^3J = 7.9$ Hz, Ar-*H*), 8.06 (1H, d, $^3J = 7.9$ Hz, Ar-*H*), 7.86 (1H, dd, $^3J = 8.4$ Hz, $^3J = 7.5$ Hz, Ar-*H*), 4.25 (2H, q, $^3J = 7.0$ Hz, N- $\text{CH}_2\text{-CH}_3$), 1.35 (3H, t, $^3J = 7.0$ Hz, $\text{CH}_2\text{-CH}_3$). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 163.4, 163.4, 133.2, 131.9, 131.1, 131.0, 130.6, 130.2, 128.9, 128.0, 123.1, 122.3, 35.6, 13.3. **MS-FI** m/z 303.0 ($[\text{M}]^+$, $\text{C}_{14}\text{H}_{10}\text{BrNO}_2$, calc. 303.0).

***N*-Ethyl-4-azido-1,8-naphthalimide (62)²⁹**

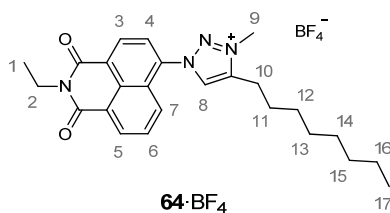


62

N-Ethyl-4-bromo-1,8-naphthalimide (**61**) (800 mg, 2.63 mmol) and NaN_3 (838 mg, 12.9 mmol) were dissolved in DMF (10 mL) and the solution heated at 110 °C for 1.5 h. The reaction mixture was allowed to cool, poured into H_2O (20 mL) and the product extracted with EtOAc (3 x 20 mL). The combined organic fractions were washed with brine (1 x 50 mL), dried over MgSO_4 and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 4:1 hexane/EtOAc to elute the product as a dark orange solid (613 mg, 2.30 mmol, 88%). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.62 (1H, dd, $^3J = 7.5$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.56 (1H, d, $^3J = 7.9$ Hz, Ar-*H*), 8.42 (1H, dd, $^3J = 8.5$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 7.73 (1H, dd, $^3J = 8.5$ Hz, $^3J = 7.5$ Hz, Ar-*H*), 7.45 (1H, d, $^3J = 7.9$ Hz, Ar-*H*), 4.23 (2H, q, $^3J = 7.0$ Hz, N- $\text{CH}_2\text{-CH}_3$), 1.33 (3H, t, $^3J = 7.0$ Hz, $\text{CH}_2\text{-CH}_3$). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 163.8, 163.3, 143.3, 132.1, 131.6, 129.1, 128.7, 126.8, 124.3, 122.6, 118.9, 114.6, 35.5, 13.3. **MS-FI** m/z 266.1 ($[\text{M}]^+$, $\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_2$, calc. 266.1).

Naphthalimide triazole thread (63)

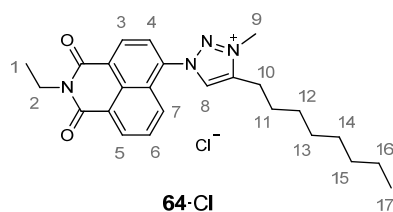
To a solution of *N*-ethyl-4-azido-1,8-naphthalimide (**62**) (300 mg, 1.13 mmol) and 1-decyne (0.24 mL, 1.35 mmol) in dry CH_2Cl_2 (25 mL) was added TBTA (5 mg, cat.) and DIPEA (0.40 mL, 2.25 mmol), followed by $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (86 mg, 0.23 mmol). The reaction mixture was stirred under $\text{N}_{2(g)}$ for 15 h. After this time, the solvent removed *in vacuo* and purification was undertaken by silica gel column chromatography using 98.5:1.5 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a pale yellow solid (424 mg, 1.05 mmol, 93%). **Mp** 107–109 °C. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ (ppm) 8.68–8.72 (2H, m, Ar-*H*), 8.28 (1H, d, $^3J = 8.2$ Hz, Ar-*H*), 7.78–7.88 (3H, m, NC-*H* & Ar-*H*), 4.28 (2H, q, $^3J = 7.4$ Hz, N- $\text{CH}_2\text{-CH}_3$), 2.90 (2H, t, $^3J = 7.0$ Hz, NC- $\text{CH}_2\text{-}$), 1.77–1.89 (2H, m, NC- $\text{CH}_2\text{-CH}_2\text{-}$), 1.27–1.49 (13H, m, 5 x $\text{-CH}_2\text{-}$ & N- $\text{CH}_2\text{-CH}_3$), 0.86–0.92 (3H, m, Alkyl- CH_3). $^{13}\text{C NMR}$ (75.5 MHz, CDCl_3) δ (ppm) 163.5, 162.9, 138.5, 132.1, 130.6, 129.6, 129.0, 128.4, 126.5, 123.7, 123.3, 123.0, 35.7, 31.8, 29.3, 29.2, 25.6, 22.6, 14.1, 13.3 (four peaks missing – coincidental). **MS-ESI** m/z 427.2103 ($[\text{M} + \text{Na}]^+$, $\text{C}_{24}\text{H}_{28}\text{N}_4\text{NaO}_2$, calc. 427.2104), 405.3 (40%, $[\text{M} + \text{H}]^+$), 427.2 (100%, $[\text{M} + \text{Na}]^+$).

Naphthalimide triazolium tetrafluoroborate thread (64·BF₄)

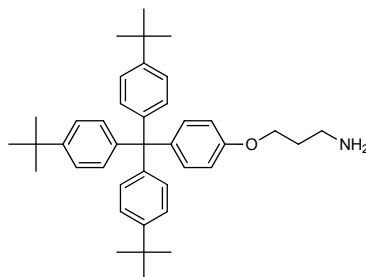
Triazole **63** (390 mg, 0.96 mmol) and $(\text{Me}_3\text{O})\text{BF}_4$ (192 mg, 1.30 mmol) were dissolved in dry CH_2Cl_2 (20 mL) and stirred under $\text{N}_{2(g)}$ for 15 h. After this time, MeOH (0.1 mL) was added to the reaction mixture and the solvent removed *in vacuo*. Purification was undertaken by silica gel column

chromatography using 97.5:2.5 CH₂Cl₂/MeOH to elute the product as a pale yellow solid (450 mg, 0.89 mmol, 93%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.54–8.61 (2H, m, H₃ & H₅), 8.50 (1H, s, H₈), 8.17 (1H, d, ³*J* = 8.8 Hz, H₇), 8.02 (1H, d, ³*J* = 7.6 Hz, H₄), 7.86 (1H, t, ³*J* = 8.8 Hz, H₆), 4.41 (3H, s, H₉), 4.23 (2H, q, ³*J* = 7.0 Hz, H₂), 3.01 (2H, t, ³*J* = 7.9 Hz, H₁₀), 1.80–1.91 (2H, m, H₁₁), 1.42–1.52 (2H, m, H₁₂), 1.23–1.39 (11H, m, H₁ & H_{13–16}), 0.85–0.90 (3H, m, H₁₇). **¹⁹F NMR** (282.5 MHz, CDCl₃) δ (ppm) –153.5 (s, BF₄), –153.5 (s, BF₄). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 162.7, 146.6, 135.0, 132.4, 129.9, 129.8, 129.5, 128.3, 128.1, 125.7, 125.4, 125.3, 122.6, 38.2, 35.9, 31.7, 29.2, 29.1, 26.7, 23.5, 22.6, 14.1, 13.2 (two peaks missing – coincidental). **MS-ESI** *m/z* 419.2442 ([M – BF₄]⁺, C₂₅H₃₁N₄O₂, calc. 419.2442), 419.2 (100%, [M – BF₄]⁺), 925.6 (30%, [2M – BF₄]⁺).

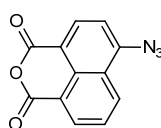
Naphthalimide triazolium chloride thread (64·Cl)



Triazolium **64**·BF₄ (96 mg, 0.19 mmol) was dissolved in 7:3 acetone/H₂O (10 mL) and passed through an anion exchange resin, Amberlite[®] IRA402 (chloride). The solvent was removed *in vacuo* to yield the product as a pale yellow solid (76 mg, 0.17 mmol, 88%). **Mp** 167–169 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 9.46 (1H, s, H₈), 8.59–8.65 (3H, m, H₃, H₅ & H₇), 8.18 (1H, d, ³*J* = 7.6 Hz, H₄), 7.88 (1H, t, ³*J* = 7.9 Hz, H₆), 4.53 (3H, s, H₉), 4.26 (2H, q, ³*J* = 7.0 Hz, H₂), 3.16 (2H, t, ³*J* = 7.9 Hz, H₁₀), 1.86–1.93 (2H, m, H₁₁), 1.42–1.55 (2H, m, H₁₂), 1.22–1.42 (11H, m, H₁ & H_{13–16}), 0.87–0.91 (3H, m, H₁₇). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 162.8, 162.2, 146.6, 135.0, 132.4, 130.5, 129.9, 129.9, 128.8, 128.4, 125.8, 125.4, 125.2, 122.7, 38.8, 35.9, 31.7, 29.3, 29.1, 27.1, 24.0, 22.6, 14.1, 13.2 (one peak missing – coincidental). **MS-ESI** *m/z* 419.2439 ([M – Cl]⁺, C₂₅H₃₁N₄O₂, calc. 419.2442), 419.3 ([M – Cl]⁺) – only observed peak in low resolution mass spectrum.

1-(3-Amino-propoxy)-4-(tris-(4-*tert*-butyl-phenyl)-methyl)-benzene (65)³⁰**65**

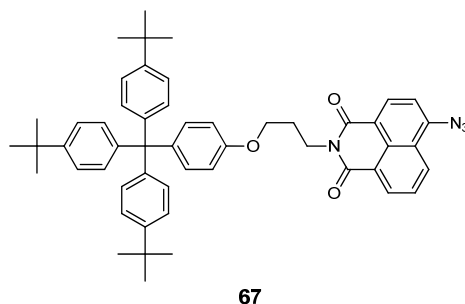
A solution of azide **35** (300 mg, 0.510 mmol) in 1:1 EtOAc/MeOH (25 mL) was heated at reflux in the presence of Pd/C (10% loading, 30 mg, 10% weight) under H_{2(g)} for 3 h. The reaction mixture was then filtered through Celite[®] and the solvent removed *in vacuo*. The residue was purified by silica gel gradient column chromatography using CH₂Cl₂ to elute any unreacted starting material and 85:15 CH₂Cl₂/MeOH to elute the product as a white solid (269 mg, 0.48 mmol, 94%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.22–7.26 (6H, m, Ar-*H*), 7.07–7.11 (8H, m, Ar-*H*), 6.75–6.80 (2H, m, OAr-*H*), 4.03 (2H, t, ³*J* = 6.2 Hz, -CH₂-OAr), 2.91 (2H, t, ³*J* = 6.8 Hz, -CH₂-NH₂), 1.88–1.96 (2H, m, CH₂-CH₂-CH₂), 1.31 (27H, s, -*t*-Bu). MS-ESI *m/z* 562.4 ([M + H]⁺, C₄₀H₅₂NO, calc. 562.4).

4-Azido-1,8-naphthalic anhydride (66)³¹**66**

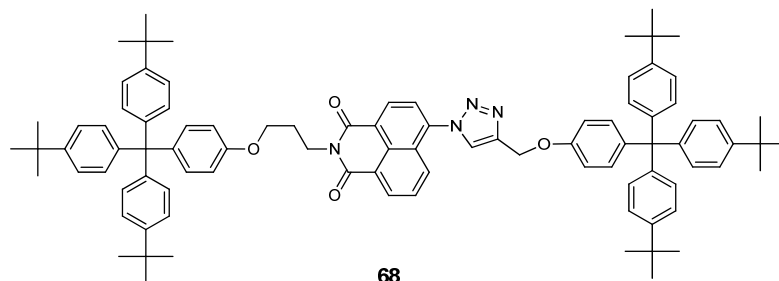
4-Bromo-1,8-naphthalic anhydride (800 mg, 2.89 mmol) and NaN₃ (244 mg, 3.75 mmol) were dissolved in DMF (25 mL) and the solution heated at 110 °C for 1.5 h. The reaction mixture was then allowed to cool, poured into H₂O (50 mL) the product extracted with EtOAc (3 x 50 mL). The combined organic fractions were washed with brine (1 x 100 mL), dried over MgSO₄ and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using CH₂Cl₂ to

elute the product as a dark orange solid (403 mg, 1.68 mmol, 58%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.53–8.70 (3H, m, Ar-*H*), 7.82 (1H, dd, $^3J = 8.2$ Hz, $^3J = 7.0$ Hz, Ar-*H*), 7.54 (1H, d, $^3J = 8.2$ Hz, Ar-*H*). **¹³C NMR** (75.5 MHz, *d*₆-DMSO) δ (ppm) 160.7, 160.1, 144.1, 133.3, 133.3, 130.7, 129.5, 127.6, 123.6, 119.2, 116.3, 114.7. **MS-FI** *m/z* 239.0 ([M]⁺, C₁₂H₅N₃O₃, calc. 239.0).

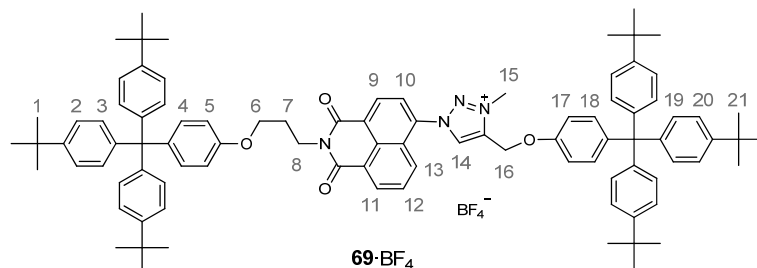
Mono-stoppered naphthalimide azide (67)



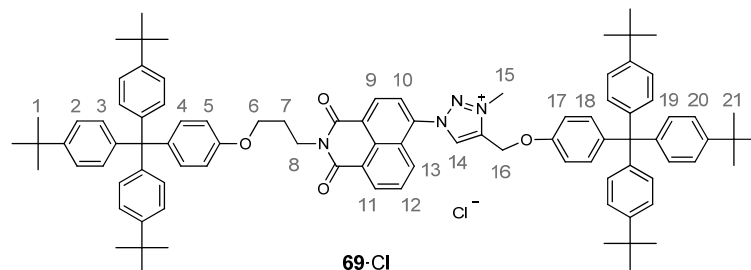
To a stirred solution of 4-azido-1,8-naphthalic anhydride (**66**) (148 mg, 0.62 mmol) in 1,4-dioxane (16 mL) was added amine **65** (400 mg, 0.72 mmol) and the reaction mixture heated at reflux under N_{2(g)} for 15 h. After this time, the reaction mixture was allowed to cool and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using CH₂Cl₂ to elute the product as a yellow solid (308 mg, 0.39 mmol, 63%). **Mp** > 180 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.62 (1H, dd, $^3J = 7.2$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.57 (1H, d, $^3J = 7.8$ Hz, Ar-*H*), 8.44 (1H, dd, $^3J = 8.7$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 7.73 (1H, dd, $^3J = 8.7$ Hz, $^3J = 7.2$ Hz, Ar-*H*), 7.45 (1H, d, $^3J = 7.8$ Hz, Ar-*H*), 7.21–7.26 (6H, m, Ar-*H*), 7.00–7.10, (8H, m, Ar-*H*), 6.66–6.71 (2H, m, OAr-*H*), 4.40 (2H, t, $^3J = 7.0$ Hz, N-CH₂-), 4.09 (2H, t, $^3J = 6.2$ Hz, O-CH₂-), 2.20–2.29 (2H, m, CH₂-CH₂-CH₂), 1.31 (27H, s, ^{*t*}Bu). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 164.0, 163.6, 156.6, 148.2, 144.1, 143.4, 139.4, 132.3, 132.1, 131.8, 130.7, 129.2, 128.8, 126.8, 124.3, 124.0, 122.6, 118.9, 114.7, 112.9, 66.0, 63.0, 38.0, 34.4, 31.4, 28.0. **MS-ESI** *m/z* 805.4094 ([M + Na]⁺, C₅₂H₅₄N₄NaO₃, calc. 805.4094), 805.5 (100%, [M + Na]⁺), 821.5 (65%, [M + K]⁺).

Naphthalimide triazole axle (68)

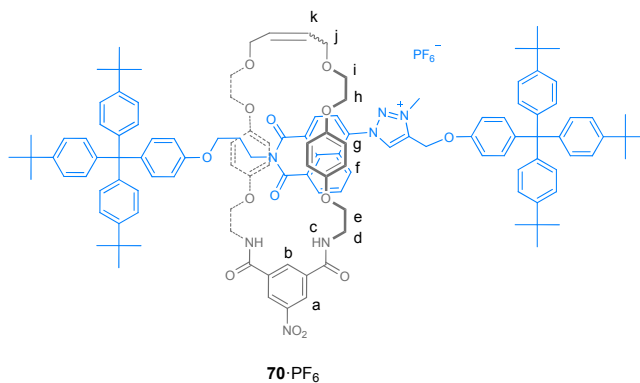
To a solution of azide **67** (192 mg, 0.25 mmol) and alkyne **30** (160 mg, 0.29 mmol) in dry CH_2Cl_2 (10 mL) was added TBTA (3 mg, cat.) and DIPEA (0.09 mL, 0.49 mmol), followed by $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (18 mg, 0.05 mmol). The reaction mixture was stirred under $\text{N}_{2(g)}$ for 15 h. After this time, the solvent was removed *in vacuo* and purification undertaken by silica gel column chromatography using 99.5:0.5 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a yellow solid (267 mg, 0.20 mmol, 82%). **Mp** 192–195 °C. **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.68–8.72 (2H, m, Ar-*H*), 8.26 (1H, dd, $^3J = 8.8$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.09 (1H, s, NC-*H*), 7.79–7.85 (2H, m, Ar-*H*), 7.21–7.27 (10H, m, Ar-*H*), 7.15–7.18 (2H, m, Ar-*H*), 7.03–7.12, (16H, m, Ar-*H*), 6.91–6.95 (2H, m, OAr-*H*), 6.68–6.71 (2H, m, OAr-*H*), 5.38 (2H, s, NC- CH_2 -O), 4.44 (2H, t, $^3J = 6.8$ Hz, N- CH_2 -), 4.12 (2H, t, $^3J = 5.9$ Hz, O- CH_2 -), 2.23–2.32 (2H, m, CH_2 - CH_2 - CH_2), 1.31 (27H, s, -*t*Bu), 1.31 (27H, s, -*t*Bu). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 163.6, 163.1, 156.6, 155.9, 148.4, 148.2, 144.1, 144.0, 140.6, 139.5, 138.1, 132.4, 132.3, 132.1, 130.7, 129.4, 129.1, 128.7, 126.4, 125.0, 124.1, 124.0, 123.6, 123.0, 113.2, 113.0, 66.0, 63.1, 61.9, 38.3, 34.3, 31.4, 28.0 (multiple peaks missing – coincidental). **MS-ESI** m/z 1348.7681 ($[\text{M} + \text{Na}]^+$, $\text{C}_{92}\text{H}_{100}\text{N}_4\text{NaO}_4$, calc. 1348.7670), 1348.9 ($[\text{M} + \text{Na}]^+$) – only observed peak in low resolution mass spectrum.

Naphthalimide triazolium tetrafluoroborate axle (69·BF₄)

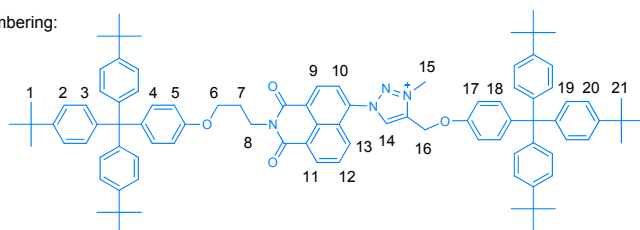
Triazole **68** (300 mg, 0.23 mmol) and (Me₃O)BF₄ (45 mg, 0.31 mmol) were dissolved in dry CH₂Cl₂ (15 mL) and stirred under N_{2(g)} for 15 h. After this time, MeOH (0.1 mL) was added to the reaction mixture and the solvent removed *in vacuo*. The residue was purified by recrystallisation from CH₂Cl₂/MeOH to yield the product as a pale yellow solid (250 mg, 0.18 mmol, 78%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.85 (1H, s, H₁₄), 8.60–8.63 (2H, m, H₉ & H₁₁), 8.18 (1H, d, ³J = 8.5 Hz, H₁₃), 8.01 (1H, d, ³J = 7.6 Hz, H₁₀), 7.85 (1H, t, ³J = 8.5 Hz, H₁₂), 7.17–7.26 (12H, m, H₂ & H₂₀), 7.04–7.09 (16H, m, H₃ & H₄ & H₁₈ & H₁₉), 6.89 (2H, d, ³J = 8.8 Hz, H₁₇), 6.70 (2H, d, ³J = 9.4 Hz, H₅), 5.52 (2H, s, H₁₆), 4.55 (3H, s, H₁₅), 4.40 (2H, t, ³J = 7.0 Hz, H₈), 4.08 (2H, t, ³J = 6.2 Hz, H₆), 2.22–2.26 (2H, m, H₇), 1.30 (54H, s, H₁ & H₂₁). **¹⁹F NMR** (282.5 MHz, CDCl₃) δ (ppm) – 153.3 (s, BF₄), –153.4 (s, BF₄). **¹³C NMR** (125.8 MHz, CDCl₃) δ (ppm) 163.0, 162.4, 156.6, 154.5, 148.6, 148.3, 144.1, 143.7, 142.5, 141.5, 139.6, 134.6, 133.1, 132.9, 132.2, 131.3, 130.7, 130.6, 130.6, 130.0, 126.7, 125.7, 125.2, 124.2, 124.0, 123.2, 113.2, 113.0, 65.9, 63.1, 63.0, 58.0, 39.6, 38.6, 34.3, 34.3, 31.4, 29.7, 28.0 (three peaks missing – coincidental). **MS-ESI** *m/z* 1340.8005 ([M – BF₄]⁺, C₉₃H₁₀₃N₄O₄, calc. 1340.8007), 1340.9 ([M – BF₄]⁺) – only observed peak in low resolution mass spectrum.

Naphthalimide triazolium chloride axle (69·Cl)

Axle **69**·BF₄ (125 mg, 0.09 mmol) was dissolved in CH₂Cl₂ (35 mL) and washed with 1.0 M NH₄Cl_(aq) (20 x 15 mL), H₂O (3 x 15 mL) and brine (1 x 15 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a white solid (91 mg, 0.07 mmol, 75%). **Mp** 214–217 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 9.50 (1H, s, H₁₄), 8.63–8.70 (2H, m, H₉ & H₁₁), 8.49 (1H, d, ³*J* = 7.6 Hz, H₁₃), 8.09 (1H, d, ³*J* = 7.6 Hz, H₁₀), 7.90 (1H, dd, ³*J* = 8.8 Hz, ³*J* = 7.6 Hz, H₁₂), 7.17–7.26 (12H, m, H₂ & H₂₀), 7.02–7.11 (16H, m, H₃ & H₄ & H₁₈ & H₁₉), 6.96 (2H, d, ³*J* = 8.8 Hz, H₁₇), 6.67–6.74 (2H, m, H₅), 5.74 (2H, s, H₁₆), 4.65 (3H, s, H₁₅), 4.42 (2H, t, ³*J* = 7.0 Hz, H₈), 4.09 (2H, t, ³*J* = 6.2 Hz, H₆), 2.21–2.31 (2H, m, H₇), 1.31 (27H, s, H₁ or H₂₁), 1.30 (27H, s, H₁ or H₂₁). **¹³C NMR** (125.8 MHz, CDCl₃) δ (ppm) 163.0, 162.4, 156.6, 154.6, 148.5, 148.3, 144.1, 143.8, 142.0, 141.9, 139.6, 134.8, 132.8, 132.6, 132.2, 130.7, 130.7, 130.2, 130.0, 128.6, 128.3, 126.2, 125.6, 125.3, 124.2, 124.0, 122.8, 113.3, 113.0, 65.9, 63.1, 63.0, 58.3, 40.0, 38.5, 34.3, 34.3, 31.4, 29.7, 28.0 (two peaks missing – coincidental). **MS-ESI** *m/z* 1340.7984 ([M – Cl]⁺, C₉₃H₁₀₃N₄O₄, calc. 1340.8007), 1340.9 ([M – Cl]⁺) – only observed peak in low resolution mass spectrum.

Naphthalimide triazolium hexafluorophosphate rotaxane (70·PF₆)

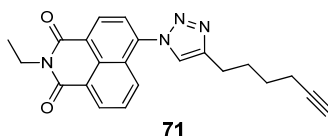
Axle numbering:



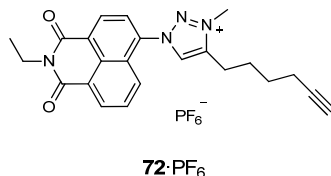
Axle **69**·Cl (40 mg, 0.029 mmol) and bis-vinyl macrocycle precursor **15** (28 mg, 0.044 mmol) were dissolved in dry CH₂Cl₂ (10 mL) and stirred for 30 min. Grubbs' second-generation catalyst (2.8 mg, 10% by weight) was then added and the reaction mixture stirred at room temperature under N_{2(g)} for 15 h. The solvent was removed *in vacuo* and macrocyclic by-products removed by preparative silica gel thin layer chromatography (6:4 CH₂Cl₂/MeCN). The crude product and unreacted axle **69**·Cl were dissolved in CH₂Cl₂ (20 mL) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (4 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo*. Purification was undertaken by preparative silica thin layer chromatography (96:4 CH₂Cl₂/MeOH) to yield the product as a yellow solid (29 mg, 0.014 mmol, 47%). **Mp** 179–181 °C. **¹H NMR** (500 MHz, CDCl₃) δ (ppm) 9.30 (1H, s, H₁₄), 9.26 (1H, app s, H_b), 9.06 (1H, d, ⁴J = 1.3 Hz, H_a), 8.52 (1H, d, ³J = 7.3 Hz, H₁₁), 8.28 (1H, d, ³J = 8.5 Hz, H₁₃), 8.18 (1H, d, ³J = 7.9 Hz, H₉), 7.99 (1H, d, ³J = 7.9 Hz, H₁₀), 7.93 (1H, dd, ³J = 8.5 Hz, ³J = 7.3 Hz, H₁₂), 7.58 (2H, br s, H_c), 7.22–7.27 (12H, m, H₂ & H₂₀), 7.05–7.12 (16H, m, H₃ & H₄ & H₁₈ & H₁₉), 6.98 (2H, d, ³J = 8.8 Hz, H₁₇), 6.61 (2H, d, ³J = 8.8 Hz, H₅), 5.92–5.98 (2H, m, H_k), 5.80–5.91 (8H, m, H_f & H_g), 5.47 (2H, s, H₁₆), 4.58 (3H, s, H₁₅), 4.21–4.27 (2H, m,

$^3J = 7.0$ Hz, H_8), 3.95 (4H, br s, H_j), 3.86–3.89 (2H, m, H_6), 3.59–3.85 (16H, m, H_d & H_e & H_h & H_i), 2.16–2.23 (2H, m, H_7), 1.32 (27H, s, H_1 or H_{21}), 1.31 (27H, s, H_1 or H_{21}). **^{19}F NMR** (282.5 MHz, CDCl_3) δ (ppm) – 73.4 (d, $^1J = 712$ Hz, PF_6). **^{13}C NMR** (125.8 MHz, CDCl_3) δ (ppm) 165.8, 164.9, 162.6, 156.3, 154.7, 152.0, 151.6, 149.2, 148.6, 148.3, 144.1, 143.7, 142.4, 140.4, 140.2, 136.0, 133.9, 132.9, 132.8, 132.3, 131.3, 130.8, 130.7, 130.6, 129.6, 129.5, 129.4, 128.8, 127.5, 126.7, 125.6, 125.2, 124.2, 124.1, 122.2, 114.2, 113.9, 113.1, 112.9, 70.7, 69.5, 67.1, 66.9, 65.4, 63.1, 63.0, 58.3, 40.9, 39.2, 38.8, 34.3, 34.3, 31.4, 31.4, 28.0 (two peaks missing – coincidental). **MS-ESI** m/z 1962.0347 ($[\text{M} - \text{PF}_6]^+$, $\text{C}_{125}\text{H}_{138}\text{N}_7\text{O}_{14}$, calc. 1962.0329), 1961.9 ($[\text{M} - \text{PF}_6]^+$) – only observed peak in low resolution mass spectrum.

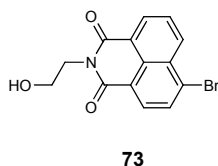
***N*-Ethyl-naphthalimide triazole alkyne (71)**



To a solution of *N*-ethyl-4-azido-1,8-naphthalimide (**62**) (50 mg, 0.19 mmol) and 1,7-octadiyne (0.12 mL, 0.94 mmol) in dry CH_2Cl_2 (5 mL) was added TBTA (2 mg, cat.) and DIPEA (67 μL , 0.38 mmol), followed by $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (14 mg, 0.04 mmol). The reaction mixture was stirred under $\text{N}_{2(g)}$ for 15 h. After this time the solvent was removed *in vacuo* and purification undertaken by silica gel column chromatography using 99:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a pale yellow solid (48 mg, 0.13 mmol, 69%). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.68–8.71 (2H, m, 2 x Ar-*H*), 8.27 (1H, dd, $^3J = 8.8$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 7.80–7.85 (3H, m, NC-*H* & Ar-*H*), 4.27 (2H, q, $^3J = 7.0$ Hz, N- CH_2 -), 2.93 (2H, t, $^3J = 7.6$ Hz, NC- CH_2 -), 2.30 (2H, td, $^3J = 6.9$ Hz, $^4J = 2.6$ Hz, CH_2 -CCH), 1.90–2.01 (3H, m, $\text{C}\equiv\text{CH}$ & NCCH_2 - CH_2 -), 1.66–1.76 (2H, m, CH_2 - CH_2 - CH_2), 1.33–1.39 (3H, m, - CH_3). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 163.5, 163.0, 148.7, 138.4, 132.1, 130.6, 129.6, 129.1, 128.5, 126.5, 123.8, 123.3, 123.1, 123.0, 84.1, 68.6, 35.8, 28.3, 28.0, 25.1, 18.2, 13.3. **MS-FI** m/z 372.1576 ($[\text{M}]^+$, $\text{C}_{22}\text{H}_{20}\text{N}_4\text{O}_2$, calc. 372.1586). **MS-ESI** m/z 395.2 (100%, $[\text{M} + \text{Na}]^+$), 767.4 (30%, $[2\text{M} + \text{Na}]^+$).

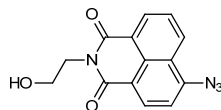
N-Ethyl-naphthalimide triazolium hexafluorophosphate alkyne (72·PF₆)

Triazole **71** (44 mg, 0.12 mmol) and (Me₃O)BF₄ (23 mg, 0.16 mmol) were dissolved in dry CH₂Cl₂ (5 mL) and stirred under N_{2(g)} for 15 h. After this time, MeOH (0.1 mL) was added to the reaction mixture and the solvent removed *in vacuo*. Purification was undertaken using preparative silica gel thin layer chromatography (96:4 CH₂Cl₂/MeOH), with the crude product dissolved in CH₂Cl₂ (20 mL) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (4 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a white solid (38 mg, 0.07 mmol, 59%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 9.30 (1H, s, NC-*H*), 8.73 (1H, d, ³*J* = 7.9 Hz, Ar-*H*), 8.66 (1H, dd, ³*J* = 7.4 Hz, ⁴*J* = 1.1 Hz, Ar-*H*), 8.28–8.34 (2H, m, 2 x Ar-*H*), 7.99 (1H, dd, ³*J* = 8.8 Hz, ³*J* = 7.4 Hz, Ar-*H*), 4.60 (3H, s, N-CH₃), 4.16 (2H, q, ³*J* = 7.0 Hz, N-CH₂-), 3.23 (2H, t, ³*J* = 7.9 Hz, NC-CH₂-), 2.37 (1H, t, ⁴*J* = 2.6 Hz, C≡CH), 2.28 (2H, td, ³*J* = 7.0 Hz, ⁴*J* = 2.6 Hz, -CH₂-CCH), 1.99–2.10 (2H, m, NCCH₂-CH₂-), 1.69–1.79 (2H, m, CH₂-CH₂-CH₂), 1.26 (3H, t, ³*J* = 7.0 Hz, -CH₃). **¹⁹F NMR** (282.5 MHz, CDCl₃) δ (ppm) -73.8 (d, ¹*J* = 712 Hz, PF₆). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 164.0, 163.5, 136.8, 133.2, 132.1, 131.1, 130.9, 130.0, 129.1, 127.6, 127.2, 127.1, 124.7, 84.7, 70.9, 39.2, 36.6, 28.8, 26.9, 23.9, 18.7, 13.8 (one peak missing – coincidental). **MS-ESI** *m/z* 387.1811 ([M - PF₆]⁺, C₂₃H₂₃N₄O₂, calc. 387.1816), 387.2 ([M - PF₆]⁺) – only peak observed in low res spectrum.

N-Hydroxyethyl-4-bromo-1,8-naphthalimide (73)³²

To a stirred solution of 4-bromo-1,8-naphthalic anhydride (2.00 g, 7.22 mmol) in 1,4-dioxane (75 mL) was added 2-aminoethanol (0.53 mL, 8.78 mmol) and the reaction mixture heated at reflux under $N_{2(g)}$ for 15 h. After this time, the solution was allowed to cool and H_2O (75 mL) added. The resulting precipitate was filtered, washed with H_2O (3 x 50 mL), dissolved in 1,4-dioxane (75 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* to yield the product as a yellow solid (2.25 g, 7.03 mmol, 97%). **Mp** 188–190 °C. 1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.70 (1H, dd, $^3J = 7.2$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.60 (1H, dd, $^3J = 8.4$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.44 (1H, d, $^3J = 7.9$ Hz, Ar-*H*), 8.07 (1H, d, $^3J = 7.9$ Hz, Ar-*H*), 7.87 (1H, dd, $^3J = 8.4$ Hz, $^3J = 7.2$ Hz, Ar-*H*), 4.46 (2H, t, $^3J = 5.6$ Hz, N- CH_2 -), 3.98 (2H, app q, $^3J = 5.6$ Hz, $-CH_2-OH$), 2.27 (1H, t, $^3J = 5.6$ Hz, $-OH$). ^{13}C NMR (75.5 MHz, d_6 -DMSO) δ (ppm) 163.0, 162.9, 132.5, 131.5, 131.3, 130.9, 129.7, 129.0, 128.7, 128.2, 122.8, 122.0, 57.7, 42.0. **MS-ESI** m/z 341.9738 ($[M + Na]^+$, $C_{14}H_{10}BrNNaO_3$, calc. 341.9736), 342.0 (100%, $[M + Na]^+$), 663.0 (90%, $[2M + Na]^+$).

***N*-Hydroxyethyl-4-azido-1,8-naphthalimide (74)**

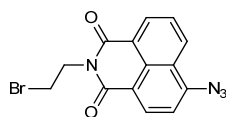


74

N-Hydroxyethyl-4-bromo-1,8-naphthalimide (**73**) (300 mg, 0.94 mmol) and NaN_3 (359 mg, 5.52 mmol) were dissolved in DMF (5 mL) and the solution heated at 110 °C for 1.5 h. After this time, the reaction mixture was allowed to cool, poured into H_2O (20 mL) and the product extracted with EtOAc (3 x 20 mL). The combined organic fractions were washed with brine (1 x 50 mL), dried over $MgSO_4$ and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 98:2 $CH_2Cl_2/MeOH$ to elute the product as a dark orange solid (213 mg, 0.75 mmol, 80%). **Mp** 163–167 °C. 1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.67 (1H, d, $^3J = 7.5$ Hz, Ar-*H*), 8.61 (1H, d, $^3J = 7.5$ Hz, Ar-*H*), 8.48 (1H, d, $^3J = 8.5$ Hz, Ar-*H*), 7.77 (1H, t, $^3J = 7.5$ Hz, Ar-*H*), 7.50 (1H, d, $^3J = 8.5$ Hz, Ar-*H*), 4.47 (2H, t, $^3J = 5.3$ Hz, N- CH_2 -), 3.98–4.01 (2H,

m, $-CH_2-OH$), 2.33 (1H, br s, $-OH$). ^{13}C NMR (75.5 MHz, d_6 -DMSO) δ (ppm) 163.2, 162.8, 142.6, 131.4, 131.3, 128.1, 127.2, 123.3, 122.1, 118.1, 115.8, 57.8, 41.8 (one peak missing – coincidental). **MS-ESI** m/z 305.0645 ($[M + Na]^+$, $C_{14}H_{10}N_4NaO_3$, calc. 305.0651), 305.1 (100%, $[M + Na]^+$), 587.2 (40%, $[2M + Na]^+$).

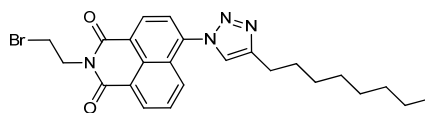
***N*-(2-Bromoethyl)-4-azido-1,8-naphthalimide (75)**



75

N-Hydroxyethyl-4-azido-1,8-naphthalimide (**74**) (600 mg, 2.13 mmol) was dissolved in $CHCl_3$ (50 mL) and stirred at 0 °C as PBr_3 (0.94 mL, 9.99 mmol) was added dropwise. The reaction mixture was then heated at reflux for 15 h. After this time, the solution was diluted with CH_2Cl_2 (100 mL), washed with H_2O (2 x 75 mL) and brine (1 x 75 mL), and dried over $MgSO_4$. The solvent was removed *in vacuo* and purification was undertaken by silica gel column chromatography using CH_2Cl_2 to elute the product as an orange solid (543 mg, 1.57 mmol, 74%). **Mp** 161–164 °C. 1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.65 (1H, dd, $^3J = 7.5$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 8.59 (1H, d, $^3J = 7.6$ Hz, Ar-*H*), 8.46 (1H, dd, $^3J = 8.4$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 7.76 (1H, dd, $^3J = 8.4$ Hz, $^3J = 7.5$ Hz, Ar-*H*), 7.48 (1H, d, $^3J = 7.6$ Hz, Ar-*H*), 4.60 (2H, t, $^3J = 7.0$ Hz, $-CH_2-Br$), 3.67 (2H, t, $^3J = 7.0$ Hz, N- CH_2 -). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 163.8, 163.3, 143.8, 132.5, 132.0, 129.2, 129.1, 126.9, 124.4, 122.2, 118.4, 114.7, 41.2, 27.8. **MS-FI** m/z 343.9905 ($[M]^+$, $C_{14}H_9BrN_4O_2$, calc. 343.9909).

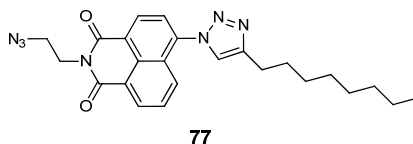
***N*-(2-Bromoethyl) naphthalimide triazole (76)**



76

To a solution of *N*-(2-bromoethyl)-4-azido-1,8-naphthalimide (**75**) (100 mg, 0.29 mmol) and 1-decyne (63 μ L, 0.35 mmol) in dry CH_2Cl_2 (10 mL) was added TBTA (2 mg, cat.) and DIPEA (0.10 mL, 0.58 mmol), followed by $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (22 mg, 0.06 mmol). The reaction mixture was stirred under $\text{N}_{2(g)}$ for 15 h. After this time, the solvent removed *in vacuo* and purification was undertaken by silica gel column chromatography using 98:2 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a yellow solid (123 mg, 0.25 mmol, 88%). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.69–8.73 (2H, m, 2 x Ar-*H*), 8.33 (1H, dd, $^3J = 8.8$ Hz, $^4J = 1.2$ Hz, Ar-*H*), 7.78–7.88 (3H, m, NC-*H* & Ar-*H*), 4.64 (2H, t, $^3J = 7.0$ Hz, $-\text{CH}_2\text{-Br}$), 3.70 (2H, t, $^3J = 7.0$ Hz, N- CH_2 -), 2.89 (2H, t, $^3J = 8.2$ Hz, NC- CH_2 -), 1.75–1.86 (2H, m, $\text{NCCH}_2\text{-CH}_2$ -), 1.27–1.51 (10H, m, 5 x $-\text{CH}_2$ -), 0.86–0.92 (3H, m, $-\text{CH}_3$). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 163.5, 163.0, 149.3, 138.8, 132.5, 131.1, 130.1, 129.1, 128.5, 126.5, 123.3, 123.2, 123.0, 122.5, 41.3, 31.8, 29.3, 29.3, 29.2, 27.6, 25.6, 22.6, 14.1 (one peak missing – coincidental). **MS-ESI** m/z 505.1202 ($[\text{M} + \text{Na}]^+$, $\text{C}_{24}\text{H}_{27}\text{BrNaN}_4\text{O}_2$, calc. 505.1210), 485.1 (100%, $[\text{M} + \text{H}]^+$), 507.1 (55%, $[\text{M} + \text{Na}]^+$), 967.3 (50%, $[2\text{M} + \text{H}]^+$), 989.3 (85%, $[2\text{M} + \text{Na}]^+$).

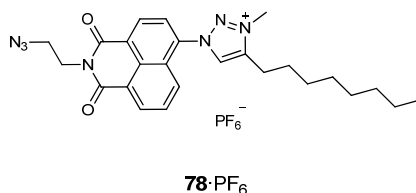
N-(2-Azidoethyl)-naphthalimide triazole (**77**)



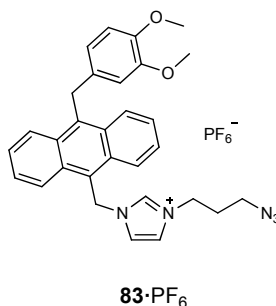
Triazole **76** (100 mg, 0.21 mmol), NaN_3 (40 mg, 0.62 mmol) were dissolved in dry DMF (10 mL) and the solution heated at 110 $^{\circ}\text{C}$ for 1.5 h. After this time, the reaction mixture was allowed to cool, poured into H_2O (30 mL) and the product extracted with EtOAc (3 x 25 mL). The combined organic fractions were then washed with brine (1 x 50 mL), dried over MgSO_4 and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 98:2 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a yellow solid (77 mg, 0.17 mmol, 82%). **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 8.70–8.74 (2H, m, 2 x Ar-*H*), 8.31–8.35 (1H, m, Ar-*H*), 7.78–7.88 (3H, m, 2 x Ar-*H* & NC-*H*), 4.47 (2H, t, $^3J = 6.2$ Hz, $-\text{CH}_2\text{-N}_3$), 3.70 (2H, t, $^3J = 6.2$ Hz, N- CH_2 -), 2.89 (2H, t, $^3J = 7.9$ Hz, NC- CH_2 -), 1.76–1.87 (2H, m, $\text{NCCH}_2\text{-CH}_2$ -), 1.27–1.51 (10H, m, 5 x $-\text{CH}_2$ -), 0.86–0.92 (3H, m, $-\text{CH}_3$). **^{13}C NMR**

(75.5 MHz, CDCl₃) δ (ppm) 163.7, 163.2, 149.3, 138.8, 132.5, 131.1, 130.1, 129.2, 128.5, 126.5, 123.3, 123.2, 123.0, 122.5, 48.8, 39.0, 31.8, 29.3, 29.3, 29.2, 25.6, 22.6, 14.1 (one peak missing – coincidental). **MS-ESI** m/z 468.2114 ([M + Na]⁺, C₂₄H₂₇NaN₇O₂, calc. 468.2118), 446.2 (55%, [M + H]⁺), 468.2 (65%, [M + Na]⁺), 913.5 (100%, [2M + Na]⁺).

***N*-(2-Azidoethyl)-naphthalimide triazolium hexafluorophosphate (78·PF₆)**

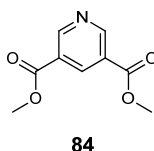


Triazole **77** (77 mg, 0.17 mmol) and (Me₃O)BF₄ (35 mg, 0.23 mmol) were dissolved in dry CH₂Cl₂ (5 mL) and stirred under N_{2(g)} for 15 h. After this time, MeOH (0.1 mL) was added to the reaction mixture and the solvent removed *in vacuo*. Purification was undertaken using preparative silica gel thin layer chromatography (96:4 CH₂Cl₂/MeOH), with the crude product dissolved in CH₂Cl₂ (20 mL) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (4 x 10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a pale yellow solid (77 mg, 0.13 mmol, 75%). **¹H NMR** (300 MHz, *d*₆-acetone) δ (ppm) 9.27 (1H, s, NC-*H*), 8.77 (1H, d, ³*J* = 7.9 Hz, Ar-*H*), 8.68–8.72 (1H, m, Ar-*H*), 8.34 (1H, dd, ³*J* = 8.5 Hz, ⁴*J* = 1.2 Hz, Ar-*H*), 8.31 (1H, d, ³*J* = 7.9 Hz, Ar-*H*), 8.01 (1H, dd, ³*J* = 8.5 Hz, ³*J* = 7.3 Hz, Ar-*H*), 4.59 (3H, s, N-CH₃), 4.40 (2H, t, ³*J* = 6.3 Hz, -CH₂-N₃), 3.68 (2H, t, ³*J* = 6.3 Hz, N-CH₂-), 3.18 (2H, t, ³*J* = 7.9 Hz, NC-CH₂-), 1.88–1.99 (2H, m, NCCH₂-CH₂-), 1.49–1.59 (2H, m, NCCH₂CH₂-CH₂-), 1.23–1.43 (8H, m, 4 x -CH₂-), 0.81–0.86 (3H, m, -CH₃). **¹⁹F NMR** (282.5 MHz, *d*₆-acetone) δ (ppm) –73.5 (d, ¹*J* = 712 Hz, PF₆). **¹³C NMR** (75.5 MHz, *d*₆-acetone) δ (ppm) 164.5, 164.0, 147.6, 137.1, 133.7, 132.1, 131.6, 131.1, 130.2, 130.0, 127.4, 127.2, 124.5, 49.8, 40.4, 39.3, 33.0, 30.2, 28.0, 24.5, 23.8, 14.8 (three peaks missing – coincidental). **MS-ESI** m/z 460.2447 ([M – PF₆]⁺, C₂₅H₃₀N₇O₂, calc. 460.2455), 460.2 ([M – PF₆]⁺) – only peak observed in low res spectrum.

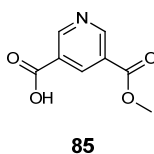
Azide-appended anthracene-based imidazolium receptor (83·PF₆)

Imidazole derivative **53** (50 mg, 0.12 mmol) and tosylate **34** (124 mg, 0.48 mmol) were dissolved in 1,4-dioxane (3 mL) and the reaction mixture heated under microwave irradiation at 120 °C for 4 h. After this time, the solvent was removed *in vacuo* and purification was undertaken using preparative silica gel thin layer chromatography (94:6 CH₂Cl₂/MeOH). The crude product was dissolved in CH₂Cl₂ (20 mL) and washed with 0.1 M NH₄PF_{6(aq)} (10 x 10 mL) and H₂O (10 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a pale yellow solid (32 mg, 0.05 mmol, 42%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.96 (1H, s, NC-*H*), 8.46–8.55 (4H, m, Ar-*H*), 7.78–7.85 (2H, m, 2 x NC-*H*), 7.57–7.69 (4H, m, Ar-*H*), 7.01 (1H, d, ⁴*J* = 2.0 Hz, Ar-*H*), 6.71 (1H, d, ³*J* = 8.4 Hz, Ar-*H*), 6.67 (2H, s, N-CH₂-Ar), 6.44 (1H, dd, ³*J* = 8.4 Hz, ⁴*J* = 2.2 Hz, Ar-*H*), 5.10 (2H, s, Ar-CH₂-Ar), 4.38 (2H, t, ³*J* = 7.0 Hz, N-CH₂-CH₂), 3.43 (2H, t, ³*J* = 6.4 Hz, -CH₂-N₃), 2.10–2.19 (2H, m, CH₂-CH₂-CH₂). **¹⁹F NMR** (282.5 MHz, CDCl₃) δ (ppm) –72.5 (d, ¹*J* = 708 Hz, PF₆). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 150.5, 149.0, 138.1, 137.0, 134.1, 132.2, 131.4, 128.5, 127.3, 127.0, 124.6, 124.0, 123.9, 123.0, 121.0, 113.6, 113.0, 56.2, 48.8, 48.3, 46.9, 33.8, 30.0 (one peak missing – coincidental). **MS-ESI** *m/z* 492.2401 ([M – PF₆]⁺, C₃₀H₃₀N₅O₂, calc. 492.2394), 492.2 ([M – PF₆]⁺) – only observed peak in low resolution mass spectrum.

6.2.4 Synthetic Procedures for Chapter Five

Dimethyl pyridine-3,5-dicarboxylate (**84**)^{33, 34}

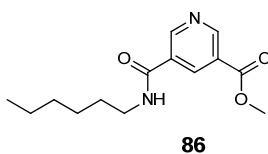
Conc. H_2SO_4 (5.00 mL) was added dropwise to a solution of 3,5-pyridinedicarboxylic acid (2.50 g, 15.0 mmol) in MeOH (9 mL). The reaction mixture was heated under microwave irradiation at 120 °C for 20 min, left to cool to room temperature, and slowly poured onto ice (50 g). 25% $\text{NH}_4\text{OH}_{(\text{aq})}$ was added until the solution turned strongly alkaline and the solution extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried over MgSO_4 and the solvent removed *in vacuo* to yield the product as a white solid (2.03 g, 10.4 mmol, 69%). ^1H NMR (300 MHz, CDCl_3) δ (ppm) 9.36–9.39 (2H, m, Pyridine-*H*), 8.86–8.90 (1H, m, Pyridine-*H*), 4.00 (6H, s, $-\text{CH}_3$). ^{13}C NMR (75.5 MHz, CDCl_3) δ (ppm) 164.9, 154.2, 138.0, 126.0, 52.7. MS-ESI m/z 196.1 ($[\text{M} + \text{H}]^+$, $\text{C}_9\text{H}_{10}\text{NO}_4$, calc. 196.1).

5-(Methoxycarbonyl)nicotinic acid (**85**)³⁵

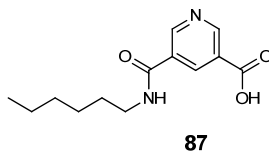
Dimethyl pyridine-3,5-dicarboxylate (**84**) (2.00 g, 10.2 mmol) was dissolved in a 0.1 M solution of KOH in MeOH (113 mL, 11.3 mmol) and the reaction mixture stirred at room temperature for 16 h. The solvent was removed *in vacuo* and the residue dissolved in H_2O (75 mL). The aqueous solution was then washed with Et_2O (3 x 50 mL) and acidified with 10% citric acid_(aq). The resulting precipitate was collected by filtration and dried *in vacuo* to yield the product as a white solid (1.35 g, 7.45 mmol,

73%). **¹H NMR** (300 MHz, *d*₆-DMSO) δ (ppm) 9.22–9.26 (2H, m, 2 x Pyridine-*H*), 8.61–8.63 (1H, m, Pyridine-*H*), 3.92 (3H, s, -CH₃). **¹³C NMR** (75.5 MHz, *d*₆-DMSO) δ (ppm) 165.7, 164.8, 154.1, 153.5, 137.5, 127.1, 125.9, 53.0. **MS-ESI** *m/z* 180.0 ([M – H][–], C₈H₆NO₄, calc. 180.0).

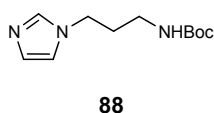
Methyl 5-(hexylcarbamoyl)nicotinate (86)



To a suspension of 5-(methoxycarbonyl)nicotinic acid (**85**) (800 mg, 4.42 mmol) in dry CH₂Cl₂ (35 mL) at 0 °C was added dropwise oxalyl chloride (0.75 mL, 8.86 mmol), followed by dry DMF (0.40 mL, cat.). The reaction mixture was stirred at room temperature under N_{2(g)} until the solution became homogenous (~ 1 h). After this time, the solvent and excess oxalyl chloride were removed *in vacuo*. The crude acid chloride (assumed quantitative conversion) was immediately dissolved in dry CH₂Cl₂ (40 mL) and added dropwise to a solution of hexylamine (0.64 mL, 4.84 mmol) and Et₃N (9.20 mL, 66.0 mmol) in dry CH₂Cl₂ (30 mL) at 0 °C. The reaction mixture was stirred at room temperature under N_{2(g)} for 2 h, washed with 10% HCl_(aq) (2 x 50 mL), 10% NaOH_(aq) (50 mL) and brine (50 mL). The organic fraction was dried over MgSO₄ and the solvent removed *in vacuo*. Purification was undertaken by silica gel column chromatography using 9:1 CH₂Cl₂/acetone to elute the product as a pale yellow solid (588 mg, 2.22 mmol, 50%). **Mp** 73–74 °C. **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 9.30–9.35 (1H, m, Pyridine-*H*), 9.16–9.21 (1H, m, Pyridine-*H*), 8.63 (1H, t, ⁴*J* = 2.0 Hz, Pyridine-*H*), 6.20 (1H, br s, NH), 4.00 (3H, s, O-CH₃), 3.46–3.54 (2H, m, NH-CH₂-), 1.62–1.71 (2H, m, NHCH₂-CH₂-), 1.29–1.46 (6H, m, 3 x -CH₂-), 0.91 (3H, t, ³*J* = 7.0 Hz, CH₂-CH₃). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 165.1, 164.5, 152.7, 151.9, 135.5, 130.2, 125.7, 52.7, 40.3, 31.4, 29.5, 26.6, 22.5, 14.0. **MS-FI** *m/z* 264.1479 ([M]⁺, C₁₄H₂₀N₂O₃, calc. 264.1474). **MS-ESI** *m/z* 263.2 ([M – H][–]).

5-(Hexylcarbamoyl)nicotinic acid (87)

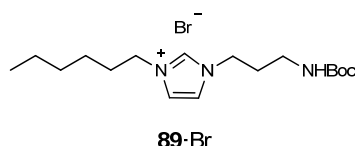
Methyl 5-(hexylcarbamoyl)nicotinate (**86**) (400 mg, 1.51 mmol) was dissolved in THF (16 mL) and a solution of KOH (92.0 mg, 1.67 mmol) in H₂O (20 mL) was added. The reaction mixture was stirred at room temperature for 16 h. After this time, 10% citric acid_(aq) (3 mL) was added and the resulting precipitate collected by filtration, washed with H₂O (2 x 30 mL) and CHCl₃ (2 x 30 mL), and dried *in vacuo* to yield the product as a white solid (256 mg, 1.02 mmol, 68%). **Mp** > 250 °C. **¹H NMR** (300 MHz, *d*₆-DMSO) δ (ppm) 9.17 (1H, d, ⁴*J* = 2.1 Hz, Pyridine-*H*), 9.15 (1H, d, ⁴*J* = 2.1 Hz, Pyridine-*H*), 8.84 (1H, br t, ³*J* = 5.6 Hz, NH), 8.65 (1H, t, ⁴*J* = 2.1 Hz, Pyridine-*H*), 3.22–3.31 (2H, m, NH-CH₂-), 1.47–1.58 (2H, m, NHCH₂-CH₂-), 1.23–1.36 (6H, m, 3 x -CH₂-), 0.85 (3H, t, ³*J* = 6.6 Hz, -CH₃). **¹³C NMR** (75.5 MHz, *d*₆-DMSO) δ (ppm) 163.7, 152.1, 152.0, 135.5, 39.4, 31.0, 28.9, 26.2, 22.1, 13.9 (three peaks missing – coincidental). **MS-FI** *m/z* 250.1322 ([M]⁺, C₁₃H₁₈N₂O₃, calc. 250.1317).

***tert*-Butyl (3-(1*H*-imidazol-1-yl)propyl)carbamate (**88**)³⁶**

To a solution of 1-(3-aminopropyl)-imidazole (2.00 mL, 16.8 mmol) in dry CH₂Cl₂ (30 mL) was added dropwise a solution of Boc₂O (3.66 g, 16.8 mmol) in dry CH₂Cl₂ (15 mL) over 15 min. The reaction mixture was stirred at room temperature for 16 h. The solvent was then removed *in vacuo* and the residue dissolved in CHCl₃ and triturated with hexane to yield the product as a yellow oil (3.66 g, 16.2 mmol, 97%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 7.49 (1H, s, NC-*H*), 7.07 (1H, s, NC-*H*), 6.94 (1H, s, NC-*H*), 4.59 (1H, br s, NH), 4.00 (2H, t, ³*J* = 7.0 Hz, N-CH₂-), 3.10–3.20 (2H, m, NH-CH₂-),

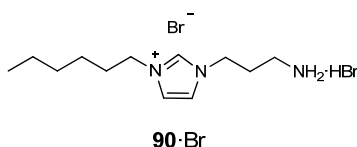
1.92–2.03 (2H, m, CH₂-CH₂-CH₂), 1.46 (9H, s, -^tBu). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 156.0, 137.0, 129.5, 118.8, 79.5, 44.3, 37.6, 31.6, 28.3. **MS-FI** *m/z* 225.1 ([M]⁺, C₁₁H₁₉N₃O₂, calc. 225.1).

1-(3-((*tert*-Butoxycarbonyl)amino)propyl)-3-hexyl-1*H*-imidazol-3-ium bromide (89·Br)



1-Bromohexane (0.34 mL, 2.42 mmol) was added to a solution of imidazole derivative **88** (500 mg, 2.22 mmol) in acetone (15 mL) and the reaction mixture heated under microwave irradiation at 150 °C for 30 min. The solvent was removed *in vacuo* and the residue dissolved in CH₂Cl₂ and triturated with hexane to yield the product as an orange oil (713 mg, 2.30 mmol, 82%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 10.46 (1H, s, NC-*H*), 7.62 (1H, s, NC-*H*), 7.26 (1H, s, NC-*H*), 5.66 (1H, br s, NH), 4.45 (2H, t, ³*J* = 6.5 Hz, N-CH₂-), 4.30 (2H, t, ³*J* = 7.3 Hz, N-CH₂-Alkyl), 3.15–3.23 (2H, m, NH-CH₂-), 2.12–2.22 (2H, m, N-CH₂-CH₂-Alkyl), 1.87–2.01 (2H, m, NHCH₂-CH₂-), 1.43 (9H, s, -^tBu), 1.27–1.39 (6H, m, 3 x -CH₂-Alkyl), 0.88 (3H, t, ³*J* = 7.6 Hz, -CH₃). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 163.7, 156.7, 137.2, 122.8, 121.5, 79.4, 50.2, 47.4, 36.7, 31.0, 30.1, 28.4, 25.9, 22.3, 13.9. **MS-ESI** *m/z* 310.3 ([M – Br]⁺, C₁₇H₃₂N₃O₂, calc. 310.3) – not observed in high resolution mass spectrum.

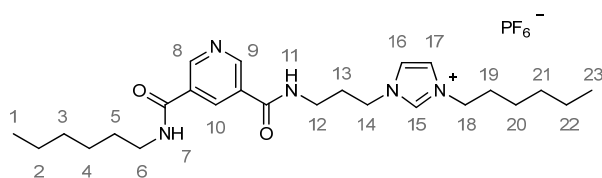
1-(3-Aminopropyl)-3-hexyl-1*H*-imidazol-3-ium bromide hydrobromide (90·Br)



To a solution of imidazolium **89·Br** (400 mg, 1.02 mmol) in MeOH (5 mL) was added 48% HBr_(aq) (0.56 mL, 10.2 mmol) and the reaction mixture stirred at room temperature for 16 h. After this time, the solvent was removed *in vacuo* and the residue dissolved in the minimum amount of 1:1 CH₂Cl₂/MeOH. The product was precipitated by addition of Et₂O (20 mL), collected by filtration

and washed with further Et₂O (3 x 20 mL) to yield the product as a light brown solid (289 mg, 0.779 mmol, 76%). **¹H NMR** (300 MHz, *d*₆-DMSO) δ (ppm) 9.26 (1H, s, NC-*H*), 7.78–7.89 (4H, m, 2 x NC-*H* & -NH₂), 4.27 (2H, t, ³*J* = 6.8 Hz, N-CH₂-), 4.17 (2H, t, ³*J* = 7.4 Hz, N-CH₂-Alkyl), 2.76–2.85 (2H, m, -CH₂-NH₂), 2.03–2.14 (2H, m, -CH₂-CH₂NH₂), 1.74–1.85 (2H, m, N-CH₂-CH₂-Alkyl), 1.21–1.32 (6H, m, 3 x -CH₂-), 0.87 (3H, t, ³*J* = 7.1 Hz, -CH₃). **¹³C NMR** (75.5 MHz, *d*₆-DMSO) δ (ppm) 136.2, 122.6, 122.4, 48.9, 46.0, 35.7, 30.6, 29.3, 27.5, 25.2, 21.9, 13.9. **MS** not observed.

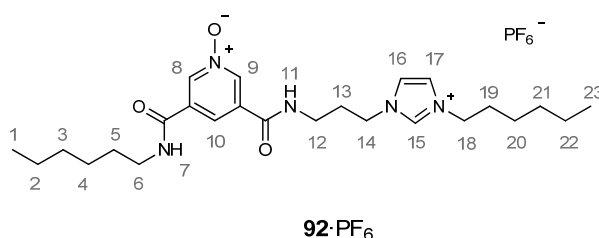
Pyridine imidazolium hexafluorophosphate receptor (91·PF₆)



91·PF₆

Imidazolium **90**·Br (269 mg, 0.725 mmol) and Et₃N (0.13 mL, 0.930 mmol) were dissolved in pyridine (10 mL). To this solution, 5-(hexylcarbamoyl)nicotinic acid **87** (210 mg, 0.839 mmol) and EDC·HCl (190 mg, 0.991 mmol) were added. The reaction mixture was stirred at 35 °C under N_{2(g)} for 16 h. After this time, pyridine and Et₃N were removed *in vacuo* and the residue vigorously stirred in CH₂Cl₂ (15 mL) and H₂O (8 mL) for 30 min. The organic fraction was separated, washed with H₂O (25 mL) and brine (25 mL), dried over MgSO₄, and the solvent removed *in vacuo*. The residue was recrystallised from acetone/ⁱPr₂O, dissolved in CH₂Cl₂ (10 mL) and stirred vigorously with a 0.1 M NH₄PF_{6(aq)} (10 mL) for 30 min. The organic fraction was separated, washed with H₂O (10 mL), dried over MgSO₄, and the solvent removed *in vacuo* to yield the product as a pale yellow solid (284 mg, 0.483 mmol, 67%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 9.00–9.14 (2H, m, H₈ & H₉), 8.77 (1H, s, H₁₀), 8.37 (1H, s, H₁₅), 7.62–7.70 (1H, m, H₁₁), 7.49–7.51 (1H, m, H₁₆), 7.28–7.33 (1H, m, H₇), 7.24–7.26 (1H, m, H₁₇), 4.26 (2H, t, ³*J* = 6.6 Hz, H₁₄), 4.13 (2H, t, ³*J* = 7.3 Hz, H₁₈), 3.35–3.49 (4H, m, H₆ & H₁₂), 2.13–2.23 (2H, m, H₁₃), 1.80–1.92 (2H, m, H₁₉), 1.55–1.67 (2H, m, H₅), 1.22–1.40 (12H, m, H_{2,4} & H₂₀₋₂₂), 0.83–0.90 (6H, m, H₁ & H₂₃). **¹³C NMR** (125.8 MHz, CDCl₃) δ (ppm) 165.9, 165.1, 135.7,

132.9, 122.7, 121.9, 50.2, 47.5, 40.4, 36.3, 31.5, 30.9, 29.7, 29.2, 26.6, 25.8, 22.5, 22.3, 14.0, 13.6 (five peaks missing – coincidental). **¹⁹F NMR** (282.5 MHz, CDCl₃) δ (ppm) – 71.2 (d, ¹J = 713 Hz, PF₆). **MS-ESI** *m/z* 422.3168 ([M – PF₆]⁺, C₂₅H₄₀N₅O₂, calc. 422.3177), 422.3 ([M – PF₆]⁺) – only observed peak in low resolution mass spectrum.

Pyridine *N*-oxide imidazolium hexafluorophosphate receptor (92·PF₆)

Receptor **91**·PF₆ (280 mg, 0.536 mmol) and NaHCO₃ (1.35 g, 16.1 mmol) were stirred in a biphasic mixture of 1:1 2-butanone/H₂O (100 mL). To this mixture was added dropwise a saturated solution of Oxone[®] (988 mg, 1.61 mmol) in H₂O (7 mL) and the reaction stirred vigorously for 2 h. After this time, NaCl (3.76 g, 64.3 mmol) was added and the product extracted with CHCl₃ (3 x 20 mL). The combined organic fractions were dried over MgSO₄, and the solvent removed *in vacuo*. The resulting residue was stirred vigorously in a biphasic mixture of CH₂Cl₂ (10 mL) and 0.1 M NH₄PF_{6(aq)} (10 mL) for 30 min. The organic fraction was separated, washed with H₂O (10 mL), dried over MgSO₄, and the solvent removed *in vacuo* to yield the product as a pale yellow solid (193 mg, 0.320 mmol, 60%).

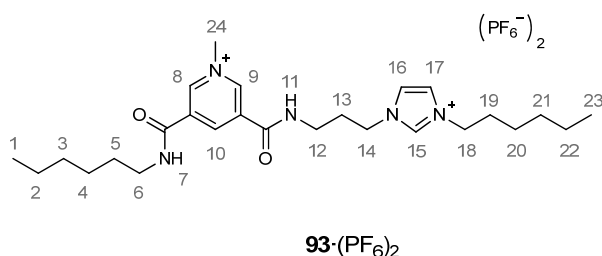
¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.79 (1H, s, H₈ or H₉), 8.77 (1H, s, H₈ or H₉), 8.72 (1H, s, H₁₅), 8.13 (1H, s, H₁₀), 8.06 (1H, br s, H₁₁), 7.67 (1H, br s, H₇), 7.47 (1H, s, H₁₆), 7.23 (1H, s, H₁₇), 4.30 (2H, t, ³J = 7.1 Hz, H₁₄), 4.14 (2H, t, ³J = 7.3 Hz, H₁₈), 3.35–3.49 (4H, m, H₆ & H₁₂), 2.15–2.26 (2H, m, H₁₃), 1.81–1.93 (2H, m, H₁₉), 1.56–1.66 (2H, m, H₅), 1.24–1.41 (12H, m, H₂₋₄ & H₂₀₋₂₂), 0.84–0.91 (6H, m, H₁ & H₂₃).

¹³C NMR (125.8 MHz, CDCl₃) δ (ppm) 163.3, 162.4, 140.3, 135.9, 134.3, 133.7, 122.6, 121.9, 50.1, 47.3, 40.6, 36.5, 31.5, 30.9, 29.7, 29.1, 26.7, 25.8, 22.5, 22.3, 14.0, 13.8 (three peaks missing – coincidental).

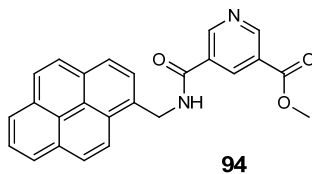
¹⁹F NMR (282.5 MHz, CDCl₃) δ (ppm) –71.5 (d, ¹J = 707 Hz, PF₆).

MS-ESI m/z 458.3107 ($[M - PF_6]^+$, $C_{25}H_{40}N_5O_3$, calc. 458.3126), 458.3 ($[M - PF_6]^+$) – only observed peak in low resolution mass spectrum.

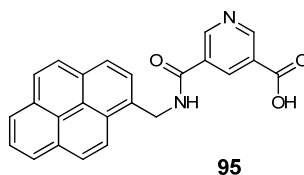
***N*-Methyl pyridinium imidazolium hexafluorophosphate receptor ($93 \cdot (PF_6)_2$)**



Receptor **91**·PF₆ (120 mg, 0.204 mmol) was dissolved in MeI (10 mL) and CHCl₃ (2 mL), and the reaction mixture heated at reflux for 16 h. The solvent was removed *in vacuo* and the resulting residue stirred vigorously in a biphasic mixture of CHCl₃ (10 mL) and 0.1 M NH₄PF_{6(aq)} (10 mL) for 30 min. The organic layer was separated, washed with H₂O (10 mL), dried over MgSO₄, and the solvent removed *in vacuo* to yield the product as a pale yellow solid (145 mg, 0.194 mmol, 95%). **¹H NMR** (300 MHz, CD₃CN) δ (ppm) 9.10–9.11 (2H, m, H₈ & H₉), 9.05–9.07 (1H, m, H₁₀), 8.51 (1H, s, H₁₅), 7.61 (1H, br s, H₁₁), 7.42–7.49 (2H, m, H₇ & H₁₆), 7.40–7.42 (1H, m, H₁₇), 4.41 (3H, s, H₂₄), 4.22 (2H, t, $^3J = 7.0$ Hz, H₁₄), 4.13 (2H, t, $^3J = 7.3$ Hz, H₁₈), 3.38–3.49 (4H, m, H₆ & H₁₂), 2.11–2.21 (2H, m, H₁₃), 1.80–1.89 (2H, m, H₁₉), 1.57–1.67 (2H, m, H₅), 1.27–1.45 (12H, m, H₂₋₄ & H₂₀₋₂₂), 0.86–0.94 (6H, m, H₁ & H₂₃). **¹³C NMR** (125.8 MHz, CD₃CN) δ (ppm) 162.3, 161.6, 147.6, 147.5, 142.1, 136.6, 135.7, 135.4, 123.6, 123.6, 50.7, 50.1, 48.1, 41.3, 37.6, 32.3, 31.8, 30.5, 29.9, 27.3, 26.5, 23.4, 23.2, 14.4, 14.4 (one peak missing – coincidental). **¹⁹F NMR** (282.5 MHz, CD₃CN) δ (ppm) – 72.7 (d, $^1J = 685$ Hz, PF₆). **MS-ESI** m/z 602.3049 ($[M - PF_6]^+$, $C_{26}H_{43}F_6N_5O_2P$, calc. 602.3053), 602.3 ($[M - PF_6]^+$) – only observed peak in low resolution mass spectrum.

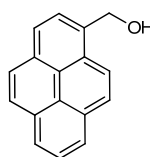
Methyl-5-((pyren-1-ylmethyl)carbamoyl)nicotinate (94)

To a suspension of 5-(methoxycarbonyl)nicotinic acid (**85**) (500 mg, 2.76 mmol) in dry CH_2Cl_2 (85 mL), oxalyl chloride (0.46 mL, 5.52 mmol) was added dropwise at 0 °C, followed by dry DMF (0.16 mL, cat.). The reaction mixture was stirred at room temperature under $\text{N}_{2(g)}$ until the solution became homogenous (~ 1 h). After this time, the solvent and excess oxalyl chloride were removed *in vacuo*. The crude acid chloride (assumed quantitative conversion) was immediately dissolved in dry CH_2Cl_2 (30 mL) and added dropwise to a solution of 1-pyrenemethylamine hydrochloride (813 mg, 3.04 mmol) and Et_3N (5.80 mL, 41.6 mmol) in dry CH_2Cl_2 (30 mL) at 0 °C. The reaction mixture was stirred at room temperature under $\text{N}_{2(g)}$ for 2 h, then washed with 10% $\text{HCl}_{(aq)}$ (2 x 75 mL), 10% $\text{NaOH}_{(aq)}$ (75 mL) and brine (75 mL). The organic layer was dried over MgSO_4 and the solvent removed *in vacuo*. Purification was undertaken by gradient column chromatography using 99:1 to 97:3 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to elute the product as a pale yellow solid (570 mg, 1.45 mmol, 52%). **Mp** 181–183 °C. **^1H NMR** (300 MHz, CDCl_3) δ (ppm) 9.25 (1H, s, Pyridine-*H*), 9.18 (1H, s, Pyridine-*H*), 8.60 (1H, s, Pyridine-*H*), 8.03–8.42 (9H, m, Ar-*H*), 6.60 (1H, br s, NH), 5.40 (2H, s, $-\text{CH}_2-$), 3.92 (3H, s, $-\text{CH}_3$). **^{13}C NMR** (75.5 MHz, CDCl_3) δ (ppm) 164.8, 164.2, 152.7, 151.9, 135.4, 131.4, 131.1, 130.6, 130.0, 129.4, 129.1, 128.5, 127.7, 127.4, 127.2, 126.2, 125.6, 125.5, 125.0, 124.8, 124.5, 122.5, 52.6, 42.7 (one peak missing – coincidental). **MS** not observed.

5-((Pyren-1-ylmethyl)carbamoyl)nicotinic acid (95)

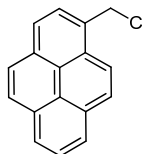
Methyl-5-((pyren-1-ylmethyl)carbamoyl)nicotinate (**94**) (355 mg, 0.900 mmol) was dissolved in THF (9 mL) and KOH (64 mg, 1.14 mmol) in H₂O (9 mL) was added. The reaction mixture was stirred at room temperature for 16 h. After this time, 10% citric acid_(aq) (20 mL) was added and the resulting precipitate collected by filtration, washed with H₂O (2 x 20 mL) and CHCl₃ (2 x 20 mL), and dried *in vacuo* to yield the product as a yellow solid (259 mg, 0.682 mmol, 76%). **Mp** > 250 °C. **¹H NMR** (300 MHz, *d*₆-DMSO) δ (ppm) 9.64 (1H, br t, $^3J = 5.4$ Hz, NH), 9.29 (1H, d, $^4J = 2.1$ Hz, Pyridine-*H*), 9.18 (1H, d, $^4J = 2.1$ Hz, Pyridine-*H*), 8.76 (1H, t, $^4J = 2.1$ Hz, Pyridine-*H*), 8.06–8.52 (9H, m, Ar-*H*), 5.27 (2H, d, $^3J = 5.4$ Hz, -CH₂-). **¹³C NMR** (75.5 MHz, *d*₆-DMSO) δ (ppm) 165.8, 164.0, 152.3, 152.2, 132.4, 130.8, 130.3, 130.2, 129.6, 128.2, 127.2, 127.7, 127.4, 127.1, 127.0, 126.4, 126.3, 125.3, 125.2, 124.8, 124.1, 123.9, 123.2, 41.2. **MS-FI** *m/z* 380.1173 ([M]⁺, C₂₄H₁₆N₂O₃, calc. 380.1161). **MS-ESI** *m/z* 379.1 ([M - H]⁻).

Pyren-1-ylmethanol (**96**)³⁷

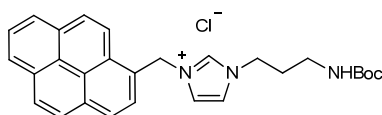


96

NaBH₄ (164 mg, 4.33 mmol) was added portionwise over 2 min to a solution of 1-pyrenecarboxyaldehyde (2.00 g, 8.68 mmol) in THF (20 mL). The reaction mixture was stirred at room temperature for 16 h. After this time, the solution was poured into H₂O (100 mL) and the resulting precipitate was collected by filtration, washed with H₂O (3 x 100 mL) and dried *in vacuo* to yield the product as a yellow solid (1.93 g, 8.31 mmol, 96%). **¹H NMR** (300 MHz, CDCl₃) δ (ppm) 8.01–8.42 (9H, m, Ar-*H*), 5.43 (2H, d, $^3J = 5.9$ Hz, -CH₂-), 1.90 (1H, br t, $^3J = 5.9$ Hz, -OH). **¹³C NMR** (75.5 MHz, CDCl₃) δ (ppm) 133.7, 131.2, 130.7, 128.7, 127.8, 127.4, 127.3, 125.9, 125.2, 124.9, 124.7, 122.9, 63.8. **MS-ESI** *m/z* 225.1 ([M + Na]⁺, C₁₇H₁₂NaO, calc. 225.1).

1-(Chloromethyl)pyrene (97)³⁷**97**

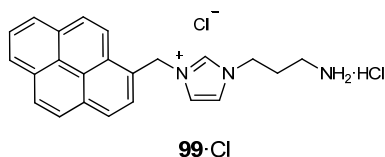
Pyren-1-ylmethanol (**96**) (1.60 g, 6.89 mmol) and pyridine (0.95 mL, 11.7 mmol) were dissolved in dry CH₂Cl₂ (40 mL) and cooled to 0 °C. SOCl₂ (0.95 mL, 13.0 mmol) was then added dropwise and the reaction mixture was stirred at room temperature for 16 h. After this time, the solution was poured into H₂O (100 mL) and further CH₂Cl₂ added (50 mL). The organic fraction was separated, washed with 5% NaHCO_{3(aq)} (40 mL) and brine (40 mL), dried over MgSO₄ and the solvent removed *in vacuo* to yield the product as a yellow solid (1.65 g, 6.58 mmol, 96%). ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.02–8.42 (9H, m, Ar-*H*), 5.35 (2H, s, -CH₂-). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 131.9, 130.6, 130.2, 129.1, 128.3, 128.0, 127.6, 127.3, 126.6, 126.2, 125.6, 125.0, 124.7, 124.6, 122.7, 44.8 (one peak missing – coincidental). MS-FI *m/z* 250.1 ([M]⁺, C₁₇H₁₁Cl, calc. 250.1).

1-(3-((*tert*-Butoxycarbonyl)amino)propyl)-3-(pyren-1-ylmethyl)-imidazolium chloride (98·Cl)**98·Cl**

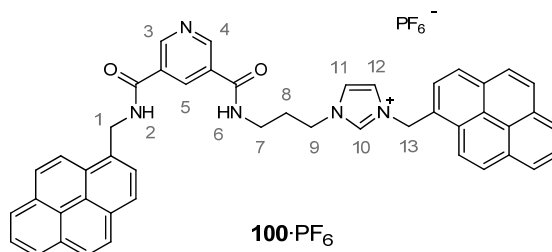
1-(Chloromethyl)pyrene (**97**) (500 mg, 1.99 mmol) and imidazole derivative **88** (408 mg, 1.81 mmol) were dissolved in dry THF (12 mL). To this solution was added NaI (5 mg, cat.), and the reaction mixture heated under microwave irradiation at 110 °C for 2 h. After this time, the solvent was removed *in vacuo* and the residue dissolved in CH₂Cl₂ (50 mL). The solution was washed with H₂O (3 x 30 mL) and brine (30 mL), dried over MgSO₄ and the solvent removed *in vacuo*. The resulting residue was recrystallized from CH₂Cl₂/Et₂O and dried *in vacuo* to yield the product as a dark orange solid (453 mg, 0.948 mmol, 52%). **Mp** 152–154 °C. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 11.05 (1H,

s, NC-*H*), 7.99–8.35 (9H, m, Ar-*H*), 7.33 (1H, s, NC-*H*), 7.00 (1H, s, NC-*H*), 6.25 (2H, s, N-CH₂-Ar), 5.90 (1H, br s, NH), 4.38 (2H, t, ³*J* = 5.8 Hz, N-CH₂-CH₂), 3.14–3.22 (2H, m, NH-CH₂-), 2.10–2.20 (2H, m, CH₂-CH₂-CH₂), 1.38 (9H, s, ^{*t*}Bu). ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) 156.6, 137.7, 132.3, 130.9, 130.3, 129.5, 129.2, 128.4, 128.2, 127.0, 126.4, 126.0, 125.9, 125.0, 124.8, 124.8, 124.1, 122.2, 121.5, 121.4, 79.2, 51.3, 47.4, 36.6, 30.4, 28.3. **MS-ESI** *m/z* 440.2326 ([M – Cl]⁺, C₂₈H₃₀N₃O₂, calc. 440.2333), 440.3 ([M – Cl]⁺) – only observed peak in low resolution mass spectrum.

1-(3-Aminopropyl)-3-(pyren-1-ylmethyl)-imidazolium chloride hydrochloride (**99**·Cl)



To a solution of imidazolium **98**·Cl (300 mg, 0.630 mmol) in CH₂Cl₂ (15 mL) was added conc. HCl_(aq) (1.08 mL) in CH₂Cl₂ (6 mL). The reaction mixture was stirred at room temperature for 16 h. After this time, the solvent was removed *in vacuo* and the residue dissolved in the minimum amount of 1:1 CH₂Cl₂/MeOH. The product was precipitated by addition of Et₂O (20 mL), collected by filtration and washed with further Et₂O (3 x 20 mL) to yield the product as a dark orange solid (257 mg, 0.623 mmol, 99%). **Mp** > 190 °C (dec.). ¹H NMR (300 MHz, *d*₆-DMSO) δ (ppm) 9.44 (1H, s, NC-*H*), 8.11–8.52 (9H, m, Ar-*H*), 7.89 (2H, s, 2 x NC-*H*), 6.24 (2H, s, N-CH₂-Ar), 4.31 (2H, t, ³*J* = 6.7 Hz, N-CH₂-CH₂), 2.70–2.80 (2H, m, NH₂-CH₂-), 2.05–2.17 (2H, m, CH₂-CH₂-CH₂). ¹³C NMR (75.5 MHz, *d*₆-DMSO) δ (ppm) 136.6, 131.5, 130.7, 130.2, 128.9, 128.6, 128.2, 128.1, 127.3, 127.3, 126.7, 126.0, 125.8, 125.3, 124.1, 123.7, 122.9, 122.7, 122.4, 50.1, 46.1, 35.4, 27.5. **MS-FI** *m/z* 339.1736 ([M – HCl – H – Cl]⁺, C₂₃H₂₁N₃, calc. 339.1736). **MS-ESI** *m/z* 412.2 ([M + H]⁺).

Bis-pyrene receptor (100·PF₆)

5-((Pyren-1-ylmethyl)carbamoyl)nicotinic acid (**95**) (92 mg, 0.242 mmol), DMAP (7 mg, cat.) and HOBT (33 mg, 0.244 mmol) were dissolved in dry DMF (10 mL) and cooled to 0 °C. EDC·HCl (51 mg, 0.266 mmol) was then added and the reaction mixture stirred at 0 °C under N_{2(g)} for 1 h. After this time, a solution of imidazolium **99**·Cl (100 mg, 0.243 mmol) and Et₃N (0.07 mL, 0.502 mmol) in dry DMF (10 mL) was added dropwise at 0 °C, and the reaction mixture stirred at room temperature under N_{2(g)} for 16 h. To the reaction mixture was added 3.3% citric acid_(aq) (20 mL) and the product extracted with CHCl₃ (3 x 10 mL). The combined organic fractions were then washed with 10% NaOH_(aq) (10 mL), dried over MgSO₄ and the solvent removed *in vacuo*. Purification was undertaken by preparative silica gel thin layer chromatography (92:6:2 MeCN/H₂O/sat. KNO_{3(aq)}) followed by 86:12:2 MeCN/H₂O/sat. KNO_{3(aq)}). The crude product was stirred vigorously in a biphasic mixture of CH₂Cl₂ (5 mL) and 0.1 M NH₄PF_{6(aq)} (5 mL) for 30 min. The organic layer was then washed with H₂O (5 mL), dried over MgSO₄, and the solvent removed *in vacuo* to yield the product as a pale yellow solid (27 mg, 0.031 mmol, 13%). ¹H NMR (500 MHz, 1:1 CD₂Cl₂/d₆-acetone) δ (ppm) 9.23 (1H, d, ³J = 2.2 Hz, H₃ or H₄), 9.16 (1H, s, H₁₀), 9.07 (1H, d, ³J = 2.2 Hz, H₃ or H₄), 8.62 (1H, t, ³J = 2.2 Hz, H₅), 8.59 (1H, br s, H₂), 8.51 (1H, d, ³J = 9.3 Hz, Pyrene-H), 8.02–8.33 (18H, m, 17 x Pyrene-H & H₆), 7.80–7.82 (1H, m, H₁₁ or H₁₂), 7.75–7.76 (1H, m, H₁₁ or H₁₂), 6.25 (2H, s, H₁₃), 5.39 (2H, d, ³J = 5.9 Hz, H₁), 4.36 (2H, t, ³J = 6.6 Hz, H₉), 3.42–3.46 (2H, m, H₇), 2.15–2.21 (2H, m, H₈). ¹³C NMR (125.8 MHz, CD₃CN) δ (ppm) 165.9, 165.5, 151.4, 151.3, 136.9, 134.5, 133.2, 132.8, 132.1, 131.9, 131.7, 131.6, 131.3, 130.5, 130.3, 130.1, 129.9, 129.6, 129.3, 128.6, 128.2, 128.1, 128.1, 128.1, 127.6, 127.1, 127.0, 126.8, 126.3, 126.2, 126.1, 126.0, 125.7, 125.6, 125.4, 125.2, 124.9, 124.0, 123.5, 123.5, 123.5, 51.8, 48.1, 42.5, 36.7, 30.4. ¹⁹F NMR (282.5 MHz, CD₃CN) δ (ppm) – 72.9 (d,

$^1J = 705 \text{ Hz}$, PF_6). **MS-ESI** m/z 702.2857 ($[\text{M} - \text{PF}_6]^+$, $\text{C}_{47}\text{H}_{36}\text{N}_5\text{O}_2$, calc. 702.2864), 702.3 ($[\text{M} - \text{PF}_6]^+$) – only observed peak in low resolution mass spectrum.

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19. All of the bipyridyl ligand protons in this ruthenium(II)-appended triazolium system are inequivalent. For clarity, they are grouped with analogous protons and labelled 17, 18, 19 and 20.
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Chapter Six: Experimental

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Chapter Seven: Summary of Conclusions

Chapter Two

Rotaxane host structures incorporating imidazolium-based axle components were synthesised using an anion templation strategy and shown to exhibit selective recognition for halide guest species over more basic, but larger, oxoanions. This reversal in selectivity compared with acyclic imidazolium derivatives has been achieved by virtue of the three dimensional, interlocked binding cavities of the rotaxanes. The effect of altering the imidazolium hydrogen bond donor arrangement, with associated changes in the imidazolium-anion electrostatic distances, on the recognition properties displayed by such host structures was investigated, as well as increasing the degree of complementarity between the interlocked components by reducing the macrocycle size. Both factors influenced the strength of anion complexation, but did not significantly alter binding selectivity.

Chapter Three

With the objective of exploiting the selective recognition properties of anion templated interlocked structures for use in anion sensing rotaxanes, appropriate axle components were prepared utilising fluorescent reporter groups as stoppers. However, difficulties in their incorporation into rotaxane structures were encountered. For the ruthenium(II) bipyridyl reporter group, this was postulated to be due to steric effects associated with the conformation of the axle in the presence of the halide template, highlighting the challenge in employing anion complexation to template the association of components in such a way to favour interlocked structure formation. In contrast, the fluorophore anthracene was found to be too small to act as an effective stopper group for the macrocycles utilised in this thesis, although other potential macrocycles could be investigated in future studies.

Chapter Four

The novel naphthalimide triazolium motif was investigated for use in interlocked molecular motion and fluorescence anion sensing systems. Orthogonal anion binding and donor-acceptor interactions between this motif and a macrocycle containing isophthalamide and hydroquinone groups facilitated the synthesis of a rotaxane capable of anion-induced, uni-directional shuttling. This reversible motion could be controlled by anion addition and the nature of the solvent conditions, and was signalled by perturbations in its UV/Vis spectrum. Selectivity for the smaller halides was exhibited both in the anion binding properties of the rotaxane and the extent of macrocycle translocation. Preliminary collaborative work was also carried out to exploit the fluorescence of the naphthalimide triazolium motif in the construction of surface-based anion sensing devices. Whilst 'click' functionalisation of gold surfaces was successful, the effective fluorescence was diminished, postulated to be due to quenching from the gold. Research is currently being undertaken to functionalise alternative surfaces and study their fluorescent properties.

Chapter Five

The utilisation of anion-induced conformational changes exhibited by flexible acyclic receptors, based on the 3,5-bis-amide-pyridine and imidazolium binding motifs, in fluorescence sensing applications was explored. A series of such receptors were synthesised and the factors influencing their anion recognition properties investigated. An analogous bis-pyrene-appended receptor was designed to sense anions *via* excimer signalling methods and displayed differential fluorescence responses to a range of anions. Whilst only some of the responses could be explained by the effect of the binding-induced conformational changes on excimer formation, this does confirm the potential of this approach for future investigations. Furthermore, the halide-induced conformation changes exhibited by a pyridine *N*-oxide threading component allowed for the control of interpenetrated pseudorotaxane assembly formation. This study could be extended by synthesising an interlocked rotaxane system designed to undergo anion-induced shuttling.

Appendices

A.1 ^1H NMR Titration Protocols

A.1.1 General Notes

All ^1H NMR titrations were conducted at 293 K with the spectra recorded on a Varian Unity Plus 500 spectrometer.

The titration data were analysed initially using approximations of Job plots to confirm the binding stoichiometries.¹ The molar fraction (χ_{H} = number of moles of host / total number of moles in the system) and the difference in the chemical shift of the monitored proton ($\Delta\delta$ compared with the free host) was calculated for each data point within a titration, and a graph of $\Delta\delta \cdot \chi_{\text{H}}$ against χ_{H} was plotted. In a Job plot, 1:1 binding stoichiometry is indicated by a maxima centred on $\chi_{\text{H}} = 0.5$.

Association constants were obtained using WinEQNMR2² computer programme as the associations were found to be fast on the NMR timescale for all systems. The values of the observed chemical shift in the monitored proton and species concentrations were entered for every titration point and estimates for the binding constant and limiting chemical shifts were made. The parameters were refined using non-linear least-squares analysis to obtain the best fit between observed and calculated chemical shifts for a 1:1 binding stoichiometry. The program reveals the accuracy of the calculated binding isotherm, and the input parameters were varied until the best-fit values of the stability constants, and their errors, converged.

In this thesis, for ease of comparison and to provide the best indication of the accuracy of the fit, the calculated association constants and their errors are given as absolute values without any rounding, e.g. 3044(108) M^{-1} . As a consequence, the association constants are often quoted to significant figures beyond that of their error values and this is taken into consideration when discussing binding trends.

A.1.2 Anion Binding Titrations

General procedure: to a 0.60 mL, 2.0×10^{-3} M solution of the host were added aliquots of the guest such that spectra were recorded at 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 2.5, 3.0, 4.0, 5.0, 7.0 and 10.0 equivalents, with a total of 100 μ L added.

For comparison with previous studies, the titrations with macrocycle **22** (Section 2.4.2) were undertaken with a 0.5 mL solution. Due to limited material, titrations with smaller macrocycle imidazolium rotaxane **31**·PF₆ (Section 2.5.4) were undertaken with a 0.5 mL, 1.5×10^{-3} M solution.

A.1.3 Pseudorotaxane Titrations

General procedure: to a 0.50 mL, 2.0×10^{-3} M solution of the host macrocycle were added aliquots of the guest thread such that spectra were recorded at 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 2.5, 3.0, 4.0, 5.0, 7.0 and 10.0 equivalents, with a total of 100 μ L added.

To avoid to solubility difficulties, the following variations on the general procedure were necessary: for ruthenium-appended 2-methylimidazolium pseudorotaxane **1**·**44**·Cl·(PF₆)₂ (Section 3.3.2), a 0.50 mL, 2.0×10^{-3} M host solution of 1:1 macrocycle **1** and TBACl was used, and a total of 200 μ L of thread **44**·(PF₆)₃ was added; for naphthalimide triazolium pseudorotaxanes **1**·**64**·BF₄ and **1**·**64**·Cl (Section 4.2.3), a 0.5 mL, 1.0×10^{-3} M host solution was used, and a total of 200 μ L of the guest solution was added; and for pyridine *N*-oxide pseudorotaxanes **1**·**92**·PF₆ and **22**·**92**·PF₆ (Section 5.4.1), the titrations were undertaken with a 0.6 mL host solution.

A.1.4 Additional Titrations

For the shuttling experiment with naphthalimide triazolium rotaxane **70**·PF₆ (Section 4.3.2), to a 0.50 mL, 2.0×10^{-3} M CDCl₃ solution of the host were added aliquots of TBACl such that spectra were recorded at 0.2, 0.4, 0.6, 0.8 and 1.0 equivalents, with a total of 10 μ L added. Subsequently,

aliquots of CD₃OD were added corresponding to overall solution percentages of 2, 5, 10, 15, 20, 30, 40, 50 and 60%.

For the chloride-induced disassembly of pseudorotaxanes **1**·**92**·PF₆ and **22**·**92**·PF₆ (Section 5.4.2), to a 0.60 mL, 2.0 × 10⁻³ M solution of 1:1 macrocycle (**1** or **22**) and pyridine *N*-oxide receptor **92**·PF₆ were added aliquots of TBACl as in the anion binding titrations (Section A.1.2).

A.2 Fluorescence Titration Protocols

A.2.1 General Notes

Unless otherwise stated, the fluorescence emission spectra were recorded on a Perkin Elmer LS-55 spectrophotometer using a Hellma Quartz cuvette of pathlength 10 mm at 293 K.

A starting volume of 2.5 mL was used in each titration and the concentration of the emissive species was chosen to give a fluorescence signal within the sensitivity of the spectrometer. The host concentrations and the excitation wavelengths are given in the main text. During the detailed titrations, increasing amounts of guest were added to obtain a satisfactory titration curves with 15–20 data points. When the concentration of the host was maintained throughout the titration experiments, this was achieved by making the guest stock solutions using the host stock solution.

Where possible, the titration data were analysed using SPECFIT³ computer programme to determine log *K* values. The parameters were refined using a non-linear least-squares method.

A.2.2 Specific Titrations

Ruthenium(II)-stoppered triazolium axle **40**·(PF₆)₃ (Section 3.2.2): for TBACl and TBABr, up to 20 equivalents were added corresponding to approximately 1.0 mL. For TBAH₂PO₄, up to 5 equivalents were added corresponding to approximately 0.25 mL.

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Ruthenium(II)-appended 2-methylimidazolium thread **44**·(PF₆)₃ and Ru(bipy)₃(PF₆)₂ (**45**·(PF₆)₂) (Section 3.3.2): a total of 40 equivalents of the guests, corresponding to approximately 1.0 mL, were added and the concentration of the host remained constant.

Anthracene-appended receptors **54**·PF₆ and **57**·PF₆ (Section 3.5.2): aliquots of the guests were added corresponding to the number of equivalents detailed in the text, such that a total of 0.5–1.0 mL was added and the concentration of the host remained constant.

Naphthalimide triazolium receptor **64**·PF₆ (Section 4.2.2): aliquots of the guests were added such that spectra were recorded at 2.5, 10.0 and 60.0 equivalents, with a total of 120 µL added.

Pyrene-appended receptor **100**·PF₆ (Section 5.3.2): spectra were recorded on a Hitachi F-4500 spectrophotometer. A total of 100 equivalents of the guests, corresponding to approximately 0.20 mL, were added and the concentration of the host remained constant. Excitation spectra were recorded during these titrations by monitoring both the monomer and excimer emission bands (381 and 484 nm).

A.3 UV/Vis Titration Protocols

A.3.1 General Notes

Unless otherwise stated, the electronic absorption spectra were recorded on a PGT60 U spectrophotometer using a Hellma Quartz cuvette of pathlength 10 mm at 293 K.

A.3.2 Naphthalimide Triazolium Receptor (Section 4.2.2)

UV/Vis spectra were obtained during the fluorescence titration experiments detailed in Section A.2.2.

A.3.3 Naphthalimide Triazolium Pseudorotaxane (Section 4.2.3)

To a 0.40 mL, 1.0×10^{-3} M CHCl_3 solution of $\mathbf{64} \cdot \text{BF}_4$ in Hellma Quartz cuvette of pathlength 1 mm, was added aliquots of macrocycle **1** such that spectra were recorded at 1.0, 2.0, 3.0, 4.0 and 5.0 equivalents, with a total of 50 μL added.

Separate experiments to investigate the effect of anion addition on $\mathbf{1} \cdot \mathbf{64} \cdot \text{BF}_4$ were carried out such that aliquots of TBACl corresponding to 1.0 and 5.0 equivalents (10 μL and 50 μL) were added to solutions containing the thread, thread plus 1.0 equivalent of macrocycle, and thread plus 5.0 equivalents of macrocycle.

A.3.4 Naphthalimide Triazolium Axle and Rotaxane (Section 4.3.4)

To a 2.5 mL, 1.0×10^{-5} M CHCl_3 solution of the host were added aliquots of the guests such that spectra were recorded at 0.5, 1.0, 2.0 and 5.0 equivalents, with a total of 100 μL added. The concentration of the host was kept constant. For the TBACl titration with $\mathbf{70} \cdot \text{PF}_6$, subsequent addition of 10 mg of AgPF_6 was followed by sonication for 1 min, filtration through Celite[®], before the UV-Vis spectrum was repeated.

A.3.5 Pyrene-Appended Receptor (Section 5.3.2)

To a 2.5 mL, 1.0×10^{-5} M solution of the host in 1:1 CH_2Cl_2 /acetone were added aliquots of the guests corresponding to approximately 5.0 equivalents, such that 100 μL was added and the concentration of the host remained constant. The spectrum of $\mathbf{100} \cdot \text{PF}_6$ is shown in Figure A.1.

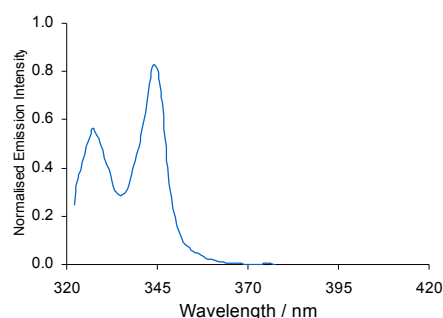


Figure A.1 UV/Vis spectrum of pyrene-appended receptor **100**·PF₆ in 1:1 CH₂Cl₂/acetone ($c = 1 \times 10^{-5}$ M). Note: wavelengths lower than 322 nm were not possible due to the presence of acetone in the solvent mixture. Extinction coefficient of **100**·PF₆, $\epsilon_s = 8.3 \times 10^4 \text{ M}^{-1}\text{cm}^{-1}$.

A.4 Crystal Structure Data

As mentioned in the main text, crystals of **2**·Cl, **3**·Cl, **1**·**2**·Cl and **1**·**3**·Cl were solved by Dr. Christopher Serpell, **22** and **3**·**22**·Cl by Nicholas White, and **70**·Cl by Dr. Mateusz Pitak (National Crystallography Service, University of Southampton).

A.4.1 Acyclic Imidazolium Derivatives (Section 2.2.3)

Single crystal X-ray diffraction data were collected using graphite monochromated Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$) on an Nonius KappaCCD diffractometer. The diffractometer was equipped with a Cryostream N₂ open-flow cooling device,⁴ and the data were collected at 150(2) K. Series of ω -scans were performed in such a way as to cover a half-sphere of data to a maximum resolution of 0.77 $\text{\AA}$. Cell parameters and intensity data (including inter-frame scaling) were processed using the DENZO-SMN package.⁵ The structure was solved by direct methods using the SIR92 software⁶ and refined using full-matrix least-squares on F^2 within the CRYSTALS suite.⁷ All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were visible in the Fourier difference map, but were placed geometrically before being refined against the data using restraints to

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ensure reasonable bond lengths, after which they were constrained using rides.⁸ A hydrate was formed in both cases.

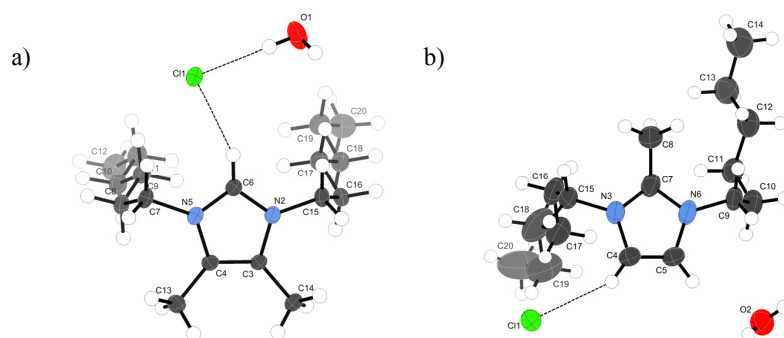


Figure A.2 X-ray crystal structures of a) 2·Cl⁻ and b) 3·Cl⁻. Thermal ellipsoids displayed at 50% probability.

Table A.1 Selected crystallographic data for **2·Cl** and **3·Cl**.

Compound	2·Cl	3·Cl
Chemical formula	C ₁₇ H ₃₃ N ₂ ·H ₂ O·Cl	C ₁₆ H ₃₁ N ₂ ·H ₂ O·Cl
Formula Mass	318.93	304.90
Crystal system	Triclinic	Monoclinic
<i>a</i> /Å	8.59220(10)	15.255(2)
<i>b</i> /Å	9.22060(10)	10.2625(17)
<i>c</i> /Å	13.5538(2)	12.6316(19)
<i>α</i> /°	71.2430(8)	90
<i>β</i> /°	75.9650(7)	104.481(7)
<i>γ</i> /°	74.6033(8)	90
Unit cell volume/Å ³	965.65(2)	1914.7(5)
Temperature/K	150	150
Space group	<i>P</i> $\bar{1}$	<i>P</i> 2 ₁ / <i>c</i>
No. of formula units per unit cell, <i>Z</i>	2	4
No. of reflections measured	17053	10028
No. of independent reflections	4400	3410
<i>R</i> _{int}	0.022	0.035
Final <i>R</i> _I values (<i>I</i> > 2σ(<i>I</i>))	0.0390	0.0905
Final <i>wR</i> (<i>F</i> ²) values (<i>I</i> > 2σ(<i>I</i>))	0.0898	0.2492
Final <i>R</i> _I values (all data)	0.0471	0.1018
Final <i>wR</i> (<i>F</i> ²) values (all data)	0.1021	0.2608
CCDC	770530	827242

A.4.2 Initial Imidazolium Pseudorotaxanes (Section 2.2.4)

Single crystal X-ray diffraction data were collected using silicon double crystal monochromated synchrotron radiation ($\lambda = 0.68890$ Å) at Diamond Light Source beamline I19 using a custom-built Rigaku diffractometer equipped with a Cryostream N₂ open-flow cooling device.⁴ The data were collected at 150(2) K via a series of ω -scans were performed in such a way as to cover a half-sphere of data to a maximum resolution of 0.77 Å. Cell parameters and intensity data (including inter-frame scaling) were processed using the CrystalClear package.¹⁰ The structures were solved by

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direct methods using SIR92 and refined against F (1·2·Cl and 1·3·Cl) with a 2σ cutoff using all data within the CRYSTALS suite.⁷

Disordered portions of 1·3·Cl were modelled using disorder over two sites with refined occupancies. Thermal and geometric restraints were applied where appropriate. Hydrogen atoms were placed geometrically and subsequently constrained using rides.⁸ Absent high angle data were omitted from the refinement using the Wilson plot.

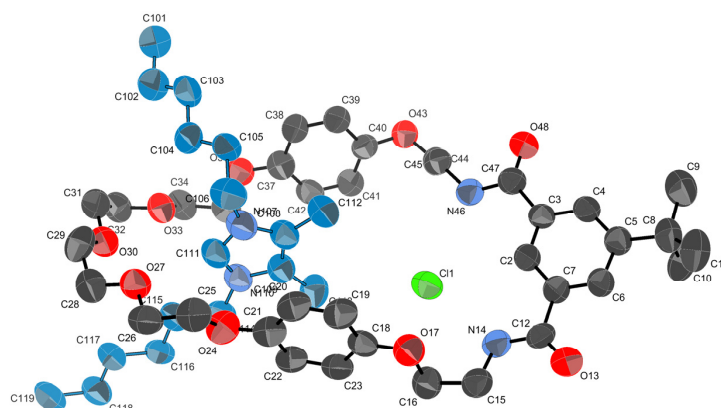


Figure A.3 X-ray crystal structure of pseudorotaxane 1·2·Cl. Thermal ellipsoids displayed at 50% probability. Hydrogen atoms omitted for clarity.

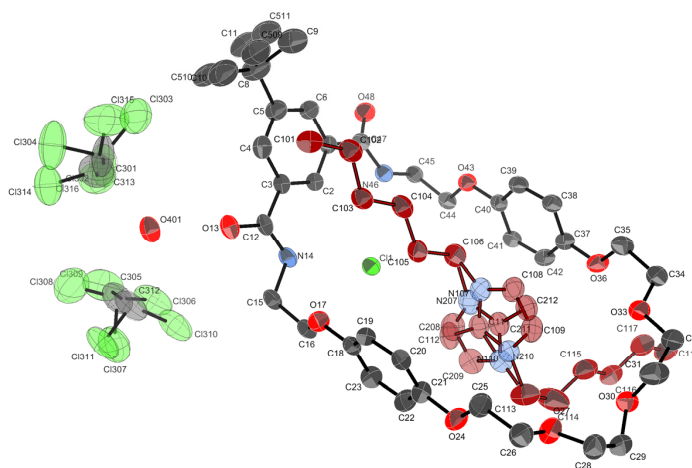


Figure A.4 X-ray crystal structure of pseudorotaxane 1·3·Cl. Thermal ellipsoids displayed at 50% probability. Hydrogen atoms omitted for clarity.

Table A.2 Selected crystallographic data for **1·2·Cl** and **1·3·Cl**.

Compound reference	1·2·Cl	1·3·Cl
Chemical formula	C ₃₆ H ₄₆ N ₂ O ₉ ·C ₁₇ H ₃₃ N ₂ ·Cl	C ₃₆ H ₄₆ N ₂ O ₉ ·C ₁₆ H ₃₁ N ₂ ·2(CHCl ₃)·H ₂ O·Cl
Formula Mass	951.68	1194.43
Crystal system	Monoclinic	Monoclinic
<i>a</i> /Å	20.11(6)	19.916(4)
<i>b</i> /Å	11.07(3)	14.499(3)
<i>c</i> /Å	23.83(7)	22.327(5)
<i>α</i> /°	90	90
<i>β</i> /°	106.09(4)	104.771(2)
<i>γ</i> /°	90	90
Unit cell volume/Å ³	5097(25)	6234(2)
Temperature/K	150	150
Space group	<i>P</i> 121/ <i>c</i> 1	<i>P</i> 21/ <i>c</i>
No. of formula units per unit cell, <i>Z</i>	4	4
No. of reflections measured	43342	79706
No. of independent reflections	12040	20693
<i>R</i> _{int}	0.207	0.087
Final <i>R</i> _{<i>I</i>} values (<i>I</i> > 2σ(<i>I</i>))	0.1477	0.0910
Final <i>wR</i> (<i>F</i> ²) values (<i>I</i> > 2σ(<i>I</i>))	0.1715	0.0995
Final <i>R</i> _{<i>I</i>} values (all data)	0.1749	0.1160
Final <i>wR</i> (<i>F</i> ²) values (all data)	0.1928	0.0995
CCDC	827243	827244

A.4.3 Smaller Macrocycle (Section 2.4.1)

Single crystal X-ray diffraction data were collected using silicon double crystal monochromated synchrotron radiation ($\lambda = 0.68890$ Å) at Diamond Light Source beamline I19 using a custom-built Rigaku diffractometer equipped with a Cryostream N₂ open-flow cooling device.⁴ The data were collected at 100(2) K via a series of ω -scans that were performed in such a way as to cover a half-sphere of data to a maximum resolution of 0.77 Å. Cell parameters and intensity data (including inter-frame scaling) were processed using CrysAlis Pro.¹¹

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The structures were solved by charge-flipping methods using SUPERFLIP¹² and refined using full-matrix least-squares on F^2 within the CRYSTALS suite.⁷ All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were generally visible in the difference map and their positions and displacement parameters were refined using restraints prior to inclusion into the model using riding constraints.⁸

Both hydroquinone rings, as well as part of the polyether chain of the macrocycle are disordered. This was modelled by having two positions for all these atoms; the occupancies of the positions were refined and then fixed. Some residual electron density is present around one of the disordered hydroquinone groups – attempts to model this as a third position of the disorder were unsuccessful.

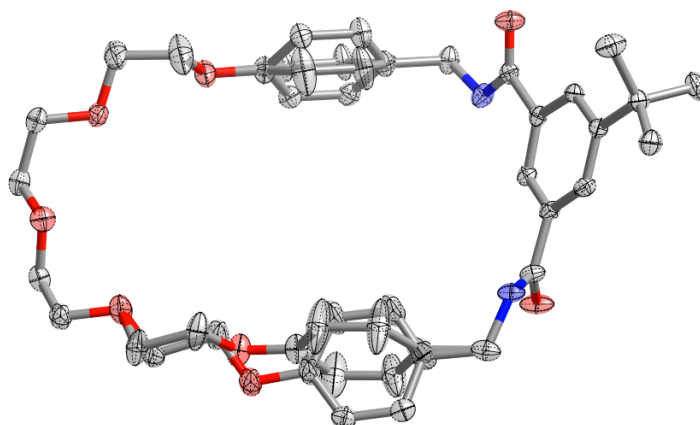


Figure A.5 X-ray crystal structure of **22**. Thermal ellipsoids displayed at 50% probability. Hydrogen atoms omitted for clarity.

Table A.3 Selected crystallographic data for **22**

Compound reference	22
Chemical formula	C ₃₄ H ₄₂ N ₂ O ₇
Formula Mass	590.72
Crystal system	Monoclinic
<i>a</i> /Å	18.3395(6)
<i>b</i> /Å	19.6643(5)
<i>c</i> /Å	8.8486(2)
α /°	90
β /°	100.766(3)
γ /°	90
Unit cell volume/Å ³	3134.93(15)
Temperature/K	100
Space group	<i>P</i> 21/ <i>c</i>
No. of formula units per unit cell, <i>Z</i>	4
No. of reflections measured	42173
No. of independent reflections	11113
<i>R</i> _{int}	0.0466
Final <i>R</i> _I values (<i>I</i> > 2σ(<i>I</i>))	0.0738
Final <i>wR</i> (<i>F</i> ²) values (<i>I</i> > 2σ(<i>I</i>))	0.1580
Final <i>R</i> _I values (all data)	0.0860
Final <i>wR</i> (<i>F</i> ²) values (all data)	0.1692
CCDC	888917

A.4.4 Smaller Macrocycle 2-Methylimidazolium Pseudorotaxane (Section 2.4.2)

Single crystal X-ray diffraction data for **3**·**22**·Cl were collected using graphite monochromated Cu Kα radiation (λ = 1.54184 Å) on an Oxford Diffraction SuperNova diffractometer. The diffractometer was equipped with a Cryostream N₂ open-flow cooling device,⁴ and the data were collected at 150(2) K. Series of ω -scans were performed in such a way as to collect all unique reflections to a maximum of 0.80 Å. Cell parameters and intensity data (including inter-frame scaling) were processed using CrysAlis Pro.

The structures were solved by charge-flipping methods using SUPERFLIP¹² and refined using full-matrix least-squares on *F*² within the CRYSTALS suite.⁷ All non-hydrogen atoms were refined

with anisotropic displacement parameters. Hydrogen atoms were generally visible in the difference map and their positions and displacement parameters were refined using restraints prior to inclusion into the model using riding constraints.⁸

The molecule could only be successfully solved in the non-centrosymmetric spacegroup, P1, with a Z' of 2. This suggests that a centre of inversion may be present, giving the centrosymmetric space group, with $Z' = 1$. Attempts to find such a smaller cell using the ADDSYM feature of PLATON were unsuccessful.¹³ Inspection of the atom positions reveals that the two independent pseudorotaxanes are not in fact related by a centre of inversion, and so this structure was refined and finalised in the P1 spacegroup.

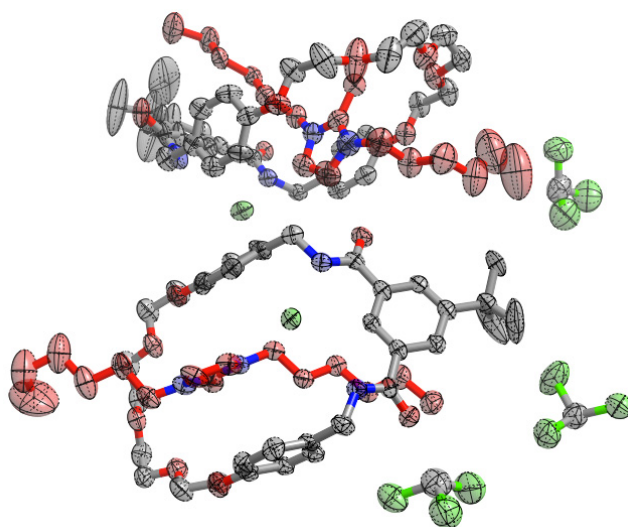


Figure A.6 X-ray crystal structure of **3·22·Cl**. Thermal ellipsoids displayed at 50% probability. Hydrogen atoms omitted for clarity.

Table A.4 Selected crystallographic data for **3·22·Cl**

Compound reference	3·22·Cl
Chemical formula	C ₃₄ H ₄₂ N ₂ O ₇ ·C ₁₆ H ₃₁ N ₂ ·Cl·1.5(CHCl ₃)
Formula Mass	1056.67
Crystal system	Triclinic
<i>a</i> /Å	9.0382(4)
<i>b</i> /Å	16.6844(6)
<i>c</i> /Å	19.2103(12)
<i>α</i> /°	79.817(4)
<i>β</i> /°	77.978(4)
<i>γ</i> /°	89.217(3)
Unit cell volume/Å ³	2787.9(2)
Temperature/K	150
Space group	<i>P</i> 1
No. of formula units per unit cell, <i>Z</i>	2
No. of reflections measured	28075
No. of independent reflections	13586
<i>R</i> _{int}	0.0504
Final <i>R</i> _{<i>I</i>} values (<i>I</i> > 2σ(<i>I</i>))	0.1155
Final <i>wR</i> (<i>F</i> ²) values (<i>I</i> > 2σ(<i>I</i>))	0.3081
Final <i>R</i> _{<i>I</i>} values (all data)	0.1210
Final <i>wR</i> (<i>F</i> ²) values (all data)	0.3195
CCDC	888918

A.4.5 Naphthalimide Triazolium Rotaxane (Section 4.3.2)

Single-crystal analysis of **70·Cl** was performed with the use of monochromated synchrotron radiation ($\lambda=0.68890$ Å) at Diamond Light Source beamline I19 using a Crystal Logic diffractometer and Rigaku Saturn 724+ detector equipped with a Cryostream N₂ open-flow cooling device,⁴ at 100 K. Data were processed using the CrystalClear-SM Expert 2.0 r7 package.¹⁴ The crystal structure was solved by direct methods, and full-matrix least-squares refinement on *F*_o² was carried out using SHELX-97¹⁵ software package. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were added at calculated positions and refined using a riding model with isotropic displacement parameters based on the equivalent isotropic displacement parameter

(Ueq) of the parent atom. The collected X-ray data were very weak and intensity decayed rapidly for higher resolution shells. The resulting data completeness up to 24.21° θ -angle is only 88.7%. Approximately 15% of the unit cell volume comprises a large region of diffused disordered solvent which could not be modelled as discrete atomic sites. SQUEEZE¹⁶ routine of PLATON¹³ was applied to remove the contributions to the structure factors from the solvent molecules.

In the crystal structure both isophthalamide macrocycle and naphthalimide triazolium axle exhibit positional disorder. In the isophthalamide macrocycle, two components of the disordered phenyl group were constrained to adopt hexagonal geometry with fixed and equal C-C distances using the AFIX 66 instruction. Furthermore, for disordered components vibrational restraints (SIMU/DELU), similar displacement restraints (EADP) and same distance restraints (DFIX/DANG) were used to maintain sensible geometries and atomic displacement ellipsoids.

ISOR restraint was necessary to restrain C10B, C17A, C17B, C18 and O5A to have approximate isotropic behaviour. Using these restraints/constraints good convergence was obtained at the end of the structure refinement.

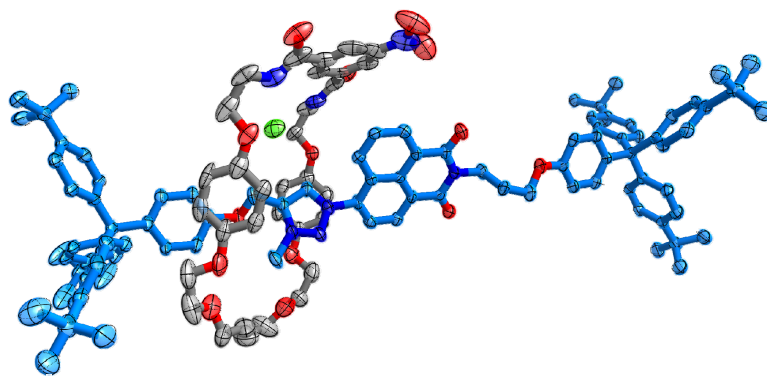


Figure A.7 X-ray crystal structure of **70·Cl**. Displacement ellipsoids – 50% probability. Hydrogen atoms are omitted for clarity.

Table A.5 Selected crystallographic data for **70**·Cl.

Chemical formula	C ₉₃ H ₁₀₃ N ₄ O ₄ ·C ₃₂ H ₃₅ N ₃ O ₁₀ ·Cl
Formula Mass	1997.87
Crystal system	Monoclinic
<i>a</i> /Å	11.519(6)
<i>b</i> /Å	14.600(7)
<i>c</i> /Å	73.86(4)
α /°	90°
β /°	90.161(7)°
γ /°	90°
Unit cell volume/Å ³	12422(11)
Temperature/K	100(2)
Space group	<i>P</i> 2 ₁ / <i>c</i>
No. of formula units per unit cell, <i>Z</i>	4
No. of reflections measured	66330
No. of independent reflections	19476
<i>R</i> _{int}	0.1266
Final <i>R</i> ₁ values (<i>I</i> > 2σ(<i>I</i>))	0.1006
Final w <i>R</i> (<i>F</i> ²) values (<i>I</i> > 2σ(<i>I</i>))	0.2514
Final <i>R</i> ₁ values (all data)	0.2029
Final w <i>R</i> (<i>F</i> ²) values (all data)	0.3173
CCDC	862707

A.5 Surface Assembled Monolayers (SAMs) (Section 4.4.2)

A.5.1 Surface Specifications

Two types of surface were employed – firstly, cleaned Si(100) wafers (Si-Mat) with a 2 nm Cr (RD Mathis) adhesion layer followed by a 100 nm layer of Au (Alfa Aesar, 99.99%), and secondly, glass cover-slips were deposited with a 2 nm Cr adhesion layer followed by a 10 nm layer of Au. Both substrates were cleaned in diluted piranha solution (3:1 H₂SO₄/H₂O₂) for 2 min immediately before use. Note: piranha solution is extremely caustic and potentially explosive, so should be handled with extreme care and under adequate supervision.

A.5.2 Synthesis of SAMs

The following procedure was carried out on both types of surface.¹⁷ Each surface was immersed in a 1 mM solution of 11-mercaptoundecanoic acid in EtOH for 24 h, washed with EtOH and dried under N₂. Subsequently, the surface was treated with a solution of EDC·HCl (0.4 M) and *N*-hydroxysuccinimide (0.1 M) in H₂O for 30 min, followed by immersion in an aqueous solution of propargylamine (1mM) for 24 h. Any unreacted esters were blocked by immersion in an aqueous solution of ethanolamine (1 M) for 20 min. The resulting surfaces were washed with H₂O to give SAMs **79** and **80**.

SAMs **79** and **80** were each immersed in a CH₂Cl₂ solution containing azide **78**·PF₆ (1 mM), TBTA (1 mM), Cu(MeCN)₄PF₆ (1 mM) and DIPEA (10 mM) for 24 h. After this time, the surfaces were sonicated, washed with CH₂Cl₂ and dried under N₂ to give SAMs **81** and **82**. Identical control reactions were undertaken in the absence of the copper(I) catalyst.

A.5.3 Ellipsometry Measurements

Ellipsometry measurements were performed using a Picometer Ellipsometer (Beaglehole Instruments, Wellington, New Zealand) with a refractive index of 1.45 for the monolayer over the gold layer (with pseudo optical constants of $n + ik = 0.7699 + i \times 3.7439$ determined from a fit to a bare gold substrate). The measurements were repeated to determine accurate values to ± 0.3 nm.

A.6 References

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