

Interlocked and transition metal based halogen bonding host systems for anion recognition and sensing

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This thesis describes the integration of the halogen bonding iodotriazole motif into a range of interlocked and transition metal based architectures for anion recognition and sensing.

Chapter One introduces the field of anion supramolecular chemistry, describing the non-covalent interactions exploited by host structures. In particular, this chapter reviews hydrogen bonding and halogen bonding acyclic, macrocyclic and mechanically interlocked molecules for anion recognition.

Chapter Two describes the synthesis of acyclic and interlocked tetra-iodotriazole based receptors. In particular, the preparation of a family of [2]catenanes and [2]rotaxanes via a chloride anion template approach is discussed, followed by an investigation of their anion binding properties determined through ^1H NMR titration experiments.

Chapter Three presents a new methylene-spaced bis-iodotriazole motif and investigates its ability to complex a range of transition metals for anion recognition and sensing. With the aim of forming a [2]rotaxane via an active metal template method, a range of macrocycles containing the motif are prepared. Towards the construction of a fullerene containing rotaxane, bimetallic C_{60} fullerene containing halogen bonding and hydrogen bonding anion receptors are prepared and their sensing capabilities investigated via luminescence spectroscopy.

Chapter Four incorporates a novel benzimidazole-iodotriazole motif into a naphthalimide based axle containing dynamic [2]rotaxane. The requirement for both benzimidazole axle protonation and the presence of a chloride coordinating anion is demonstrated to be crucial for facilitating macrocycle shuttling translocation along the axle component of the [2]rotaxane. The ability of the motif to coordinate photoactive transition metals is also reported.

Chapter Five presents a summary of the major conclusions from the research described throughout the thesis.

Chapter Six details the synthetic protocols and characterisation data for each novel compound discussed in the previous chapters. Spectroscopic titration experiment protocols are also outlined.

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Harry Klein

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Abbreviations

δ	chemical shift
Δ	change in (a measurement)
λ	wavelength
μ	micro
ν	frequency
$^{\circ}$	degree
$^{\circ}\text{C}$	degrees Celsius
*	excited state
$\text{\AA}$	Ångstrom
A^{-}	anion
abs	absorption
aq.	aqueous
Asp	aspartate
ADP	adenosine diphosphate
AMP	adenosine monophosphate
AMT	active metal template
asc	ascorbate
ATP	adenosine triphosphate
a.u.	arbitrary units
bpy	2,2'-bipyridine
BOC	di- <i>tert</i> -butyl dicarbonate
br	broad
Bu	butyl
cat.	catalytic
conc.	concentrated
COSY	homonuclear correlation spectroscopy
CuAAC	copper(I)-catalysed azide–alkyne cycloaddition
<i>d</i>	deuterated
d	doublet
DBU	1,8-diazabicycloundec-7-ene
dd	doublet of doublets
DEAD	diethyl azidocarboxylate
DIPEA	<i>N,N</i> -di- <i>iso</i> -propylethylamine
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
e	electron
EDTA	ethylenediaminetetraacetic acid
eq.	equivalent
ESI	electrospray ionisation

Et	ethyl
ext.	external
Fc	ferrocene
g	gram
G	Gibbs Free Energy
h	Planck's constant, hour
HB	hydrogen bond
HOMO	highest occupied molecular orbital
Hz	hertz
I	intensity
int.	internal
IUPAC	International Union of Pure and Applied Chemistry
J	Joule
J	coupling constant
k	kilo
K	Kelvin
K_a	association constant
L	litre
LUMO	lowest occupied molecular orbital
M	mega, molar, molecular ion
m	metre, milli, multiplet
m/z	mass-to-charge ratio
macro	macrocycle
MALDI	matrix assisted laser desorption/ionisation
max.	maximum
Me	methyl
MIM	mechanically interlocked molecule
min(s)	minute(s)
MLCT	metal-to-ligand charge transfer
mol	mole
MOM	methoxymethyl ether
MS	mass spectrometry
Ms, mesyl	methanesulfonyl chloride
n	nano
NDI	naphthalenediimide
naph	naphthalimide
NMP	<i>N</i> -methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
<i>o</i>	<i>ortho</i>
OAc	acetate
<i>p</i>	<i>para</i>
PET	photoinduced electron transfer
pH	$-\log_{10}[\text{H}^+]$

Ph	phenyl
ppm	parts per million
Pyr	pyridine/pyridinium
q	quartet
quin.	quintet
R	chemical substituent
RCM	ring closing metathesis
ROESY	rotating-frame nuclear Overhauser effect correlation spectroscopy
s	second, singlet
sat.	saturated
t	triplet
<i>t, tert.</i>	tertiary
TBA	tetrabutyl ammonium
TBTA	tris[(1-benzyl-1 <i>H</i> -1,2,3-triazol-4-yl)methyl]amine
TEA	tetraethyl ammonium
THF	tetrahydrofuran
TLC	thin layer chromatography
TOF	time of flight
TPA	tetrapropyl ammonium
Ts, tosyl	<i>para</i> -toluenesulfonyl chloride
TTF	tetrathiafulvalene
UV	ultra-violet
V	volt
vis.	visible
wt.	weight
X	halogen atom
XB	halogen bond

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Chapter One

Introduction

1 Introduction

1.1 Anion Supramolecular Chemistry

In his 1988 Nobel Lecture, Jean-Marie Lehn defined supramolecular chemistry as “*chemistry beyond the molecule*”.^{1,2} It is the field encompassing non-covalent interactions between molecular entities and their reversible association through intermolecular bonds.³ The concept of a supramolecular synthon was outlined by Desiraju and explained how supramolecules can be built from intermolecular bonding networks, analogous to well understood covalent interactions.⁴⁻⁶ The field is highly inter-disciplinary and vast, extending from organic and coordination chemistry through to physical and biochemistry. Indeed, it is from Nature that supramolecular chemistry takes its inspiration; non-covalent interactions are highly prevalent in biological processes including enzymatic substrate recognition and DNA replication.

The pioneering work into the coordination of alkali metal cations earned Pedersen, Lehn and Cram the 1987 Chemistry Nobel Prize “*for their development and use of molecules with structure-specific interactions of high selectivity*”. Pedersen described the synthesis of crown ethers that bound a range of alkali metal cations in their central cavity. In particular, the principle of host-guest size match complementarity was demonstrated; dibenzo-18-crown-6 was found to be highly selective for potassium (Figure 1.1a).⁷ Building on this fundamental work, Lehn developed macrobicyclic compounds known as cryptands whose three-dimensional cavities further enhanced binding strength and selectivity (Figure 1.1b).⁸ The concept of preorganisation was introduced by Cram, who stated “*the more highly hosts and guests are organised for binding and low solvation prior to their complexation, the most stable will be their complexes*”.⁹ This was illustrated through the synthesis of highly rigid macrocycles named spherands which exhibited remarkable alkali metal recognition properties (Figure 1.1c).¹⁰

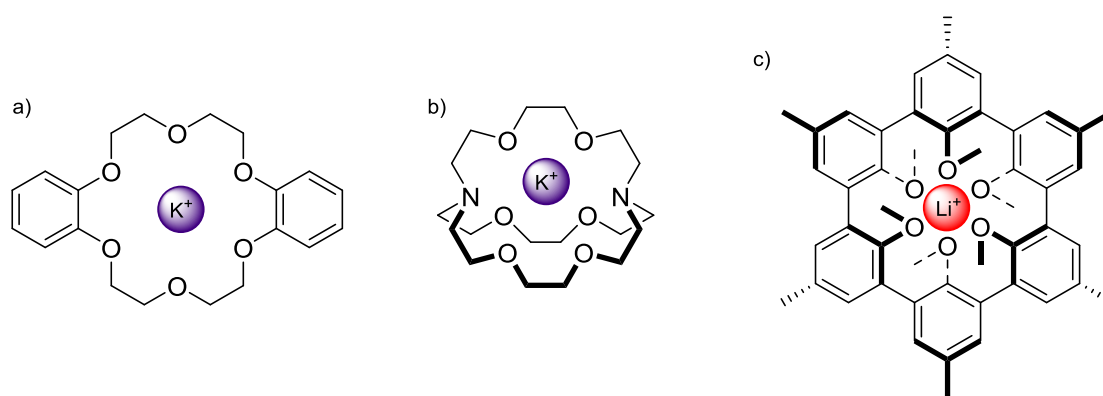


Figure 1.1 – Alkali metal cation receptors reported by 1987 Chemistry Nobel Prize winners, displaying selectivity due to host-guest size match: a) Pedersen's dibenzo-18-crown-6,⁷ b) Lehn's [2.2.2]cryptand,⁸ c) Cram's spherand.¹⁰

The field of anion host-guest supramolecular chemistry traces its origins to seminal work reported by Park and Simmons in 1968, in which they utilised macrobicyclic ammonium cages to encapsulate halide anions in acidic aqueous solution via a combination of electrostatics and hydrogen bonding (Figure 1.2).¹¹ In spite of this work appearing only a year after the crown ethers, the field of anion supramolecular chemistry has been slow to develop; it is only in the past two decades or so that significant advancements have been made in this area. This is somewhat surprising in view of the importance of anions, which is discussed in the following section.

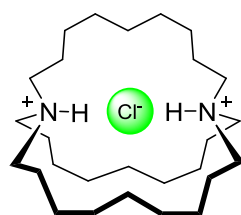


Figure 1.2 - Park and Simmons' ammonium cage structure selective for chloride.¹¹

1.1.1 Importance of anions

Anions are ubiquitous in Nature; as Sessler and co-authors have written: *“the recognition, transport, or transformation of anions is involved at some level in almost every conceivable biochemical operation”*.¹² Perhaps the most well-known example is the carrier of genetic information, DNA, which is comprised of a polyanionic phosphate backbone.¹³ This arrangement is also exploited by adenosine triphosphate (ATP), often labelled as the energy currency of the body (Figure 1.3). As alluded to previously, enzymes are uniquely adapted to bind particular substrates selectively and around 70% of these carry a negative charge.¹²

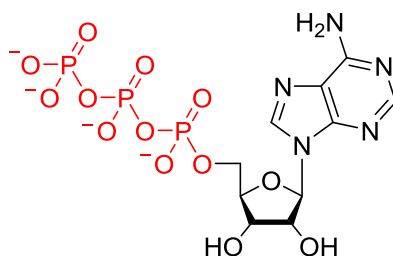


Figure 1.3 – Polyanionic ATP, “the energy currency of the body”.

A class of anions particularly pertinent to this thesis are the halides. These play a vital role *in vivo*, for example iodide is essential for the biosynthesis of hormones in the thyroid gland.¹⁴ The most abundant extra-cellular anion is chloride, constituting around 0.15% of a human’s total body weight.¹⁵ It plays a role in many crucial processes including metabolism and maintaining the pH of the body.^{16,17} Meanwhile, misregulation of intercellular transportation within anion channels can have life altering consequences; the hereditary disease cystic fibrosis¹⁸ and neurological diseases such as Alzheimer’s¹⁹ have both been linked to this.

Environmentally, industrial anthropological activity leads to various anions entering waste streams. Oxoanions phosphate and nitrate are components of fertilisers, leading to their leaching into rivers and lakes causing eutrophication - the dense growth of algae on the

surface depletes the water of oxygen and releases harmful toxins (Figure 1.4).²⁰ Meanwhile, fossil fuel combustion results in the release of SO_2 , this combines with water to produce the sulfate present in acid rain.²¹ Another notable example is pertechnetate, a radioactive by-product from the nuclear industry.²²



Figure 1.4 - Left) Eutrophication causing algal bloom²³; right) The effect of acid rain on trees.²⁴

The design of host systems capable of anion recognition is of intense current interest and importance, with tangible real-world applications. Relevant to the theme of this thesis, the remainder of this introduction will focus on the fundamental principles of anion recognition, highlighting examples in which host design dictates anion affinity and selectivity trends in organic and aqueous solvent media.

1.1.2 Inherent challenges of anion coordination

The design of selective anion hosts, often referred to as receptors, is particularly challenging due to the intrinsic properties associated with anions. The key challenges that a receptor must overcome are outlined below.

Size: Anions are larger than their isoelectronic cations, reducing their comparative charge to radius ratio.²⁵ For example, isoelectronic iodide (I⁻) and caesium (Cs⁺) ions have an ionic radii of 2.06 Å and 1.81 Å respectively (Table 1.1).²⁶ Consequently, electrostatic interactions are significantly weaker between an anion host and guest species.

Table 1.1 - Comparison of ionic radii of isoelectronic cations and anions in octahedral environments.

Cation ionic radius (Å)		Anion ionic radius (Å)	
Na⁺	1.16	F ⁻	1.19
K⁺	1.52	Cl ⁻	1.67
Rb⁺	1.66	Br ⁻	1.82
Cs⁺	1.81	I ⁻	2.06

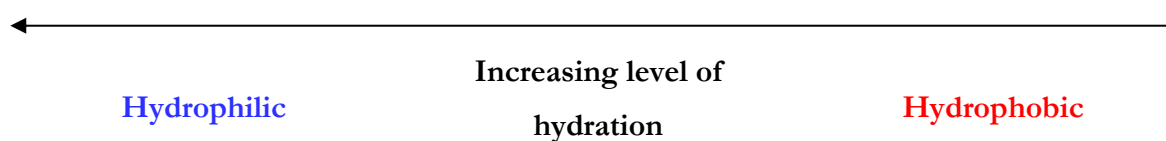
Geometry: Whilst cations tend to be spherical, anions exist in a wide range of geometries beyond the spherical halides. Polyatomic species exist in a variety of geometries: linear (azide, hydroxide), trigonal planar (nitrate), tetrahedral (sulfate, phosphate) and octahedral (hexafluorophosphate). Despite the inherent difficulty in synthesising receptors to match these geometries, careful design can lead to enhanced recognition due to size/shape complementarity.

Solvation: Solvent effects play a fundamental role in controlling binding strength and selectivity of a receptor. This is especially the case with anions, which display large free energies of solvation, typically greater than for cations of comparable charge and size (Table 1.2). The most pronounced effect occurs with polar, protic solvents such as water and methanol since the hydroxylic solvent can form strong hydrogen bonds with both the anion and the receptor. A host structure must compete with the solvation of the anion in order for recognition to occur.

Table 1.2 - Comparison of hydration energies for isoelectronic cations and anions.²⁷

$\Delta G_{hyd} \text{ (kJmol}^{-1}\text{)}$		$\Delta G_{hyd} \text{ (kJmol}^{-1}\text{)}$	
Na⁺	-365	F ⁻	-465
K⁺	-295	Cl ⁻	-340
Rb⁺	-	Br ⁻	-315
Cs⁺	-250	I ⁻	-275

The level of solvation of anions in aqueous media is governed by the Hofmeister series, which orders anions according to their hydrophobicity and, therefore, the degree of hydration (Figure 1.5).^{25,28,29} One of the major challenges in anion receptor design is the recognition of hydrophilic anions in aqueous media.

Figure 1.5 - The Hofmeister Series.²⁹

Non-polar (especially chlorinated) solvents are prone to ion-pair effects in which the interaction between the anion and counter-cation is strong enough to compete with the anion association to the receptor. Sessler and co-workers have demonstrated how the impact of ion-pair binding upon anion recognition is not only solvent dependent, but also depends upon the nature of the counter-cation.³⁰⁻³² The association constant between calix[4]pyrrole and tetrabutylammonium (TBA) chloride was an anomalously low value in dichloromethane in comparison with more polar solvents, which was attributed to strong ion-pairing between chloride and the TBA cation (Figure 1.6a). Moreover, the size of counter-cation had a

dramatic impact on chloride affinity arising from unfavourable steric considerations; the calix[4]pyrrole cavity was able to complex tetraalkylammonium cations of suitable size and shape concomitantly with chloride. This resulted in an enhancement in chloride association strength in dichloromethane as the carbon chain length of the quaternary ammonium counter-cation was reduced (Figure 1.6b).

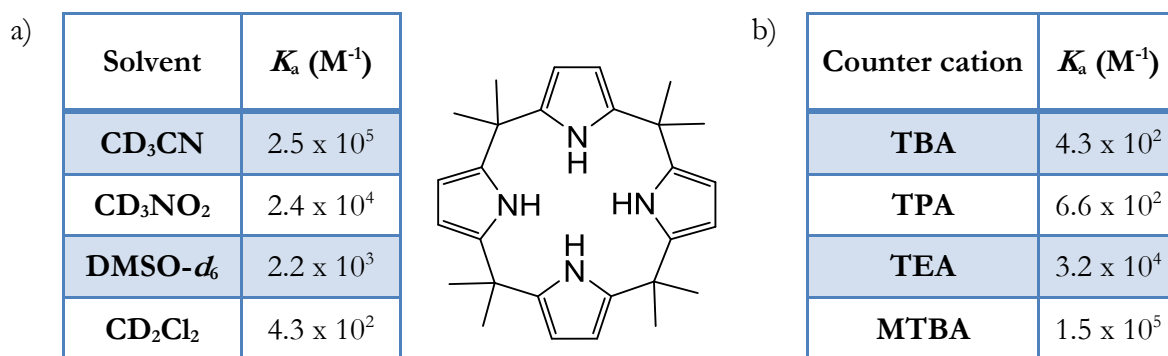


Figure 1.6 - Chloride association constants of calix[4]pyrrole in: a) a range of solvents,³⁰ b) with varied counter cation.³¹

pH-dependence: A challenge in aqueous media is the pH dependence of both the anion and the receptor. At a low pH the negatively charged anion is susceptible to protonation, with many anions existing under multiple protonation equilibria. For example, carboxylate anions typically remain unprotonated at pH values greater than 5 or 6, whilst on the other hand high pH can lead to deprotonation of protonated polyammonium receptors. Hence, only a narrow pH window exists in which anion binding can occur (Figure 1.7). Furthermore, in polar organic solvents such as DMSO strongly basic anions may deprotonate acidic sites on the receptor. For example, Gale described deprotonation of a sulfonamide host on addition of fluoride, acetate, dihydrogen phosphate and benzoate in DMSO.³³⁻³⁵

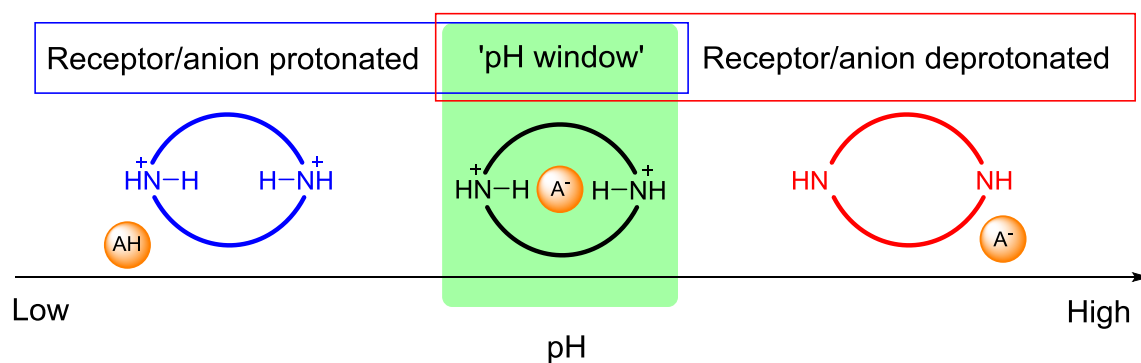


Figure 1.7 - Schematic illustration of the 'pH window' at which anion recognition by a pH-dependant receptor may occur.

1.1.3 Classical non-covalent interactions for anion recognition

Fundamental to effective anion recognition is the combination of multiple non-covalent interactions. These are almost universally weaker than a covalent bond; whilst the C-H covalent bond enthalpy is greater than 400 kJmol^{-1} , individual non-covalent bond strengths typically tend to be less than 50 kJmol^{-1} . However, in concert, the cumulative effect of multiple non-covalent interactions can facilitate the formation of highly stable assemblies.^{36,37} The key classical non-covalent interactions that can be employed in the creation of synthetic host structures for anion recognition are discussed in the following section.

Electrostatics: There are a variety of interactions encompassed within the term electrostatics, referring to an attractive interaction between opposite charges. The strongest of these is between two oppositely charged ions, an *ion-ion* interaction, and the association strengths of these are similar to those exhibited by covalent bonds.²⁷ However, the absence of directionality dictates a lack of selectivity by a highly positively charged host system, which will usually form the strongest association with the most highly charged anion guest species. For example, a range of polyammonium macrocycles reported by Lehn bound nucleotide phosphate species in the order $\text{AMP}^{2-} < \text{ADP}^{3-} < \text{ATP}^{4-}$.³⁸ A special case of an electrostatic

ion-dipole interaction which is of the utmost importance in anion host-guest chemistry is the hydrogen bond.

Hydrogen bonding: This interaction is of paramount importance in Nature, for stabilisation of the secondary and tertiary structures of proteins, DNA base-pair recognition (Figure 1.8) and is commonly exploited by enzymes for binding guest species.^{39,40} Hydrogen bond strengths vary considerably – from 4-170 kJmol⁻¹ – depending on both the nature of the species and the directionality of the hydrogen bond (the strongest interactions occur when the bond angle is 180°).⁴¹ This directional fidelity has resulted in hydrogen bonding being very widely utilised in anion host design as illustrated in the review of abiotic host structures in section 1.2. A complementary non-covalent interaction, highly relevant to this thesis, is the halogen bond, which is discussed in detail in section 1.3.

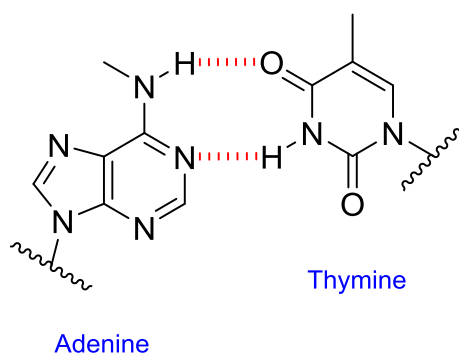


Figure 1.8 - Example of hydrogen bonding in Nature: the **AT** DNA base pair.

Anion- π interactions: This interaction is between a negatively charged species that is attracted to the centre of an electron-deficient aromatic surface. Theoretical calculations estimate the strength to be in the range 20-70 kJmol⁻¹.^{42,43} First discovered through examination of solid state X-ray structures,^{44,45} more recently this interaction has been exploited in the solution phase for binding anionic guests.^{46,47} A recent example by Matile and Schalley reported an electron-deficient naphthalenediimide (NDI) derivative that

facilitated the transport of chloride across phospholipid membranes via anion- π interactions (Figure 1.9).^{48,49} Due to their weak nature, these interactions are often combined with other non-covalent interactions for anion association in aprotic, weakly competitive organic solvents.

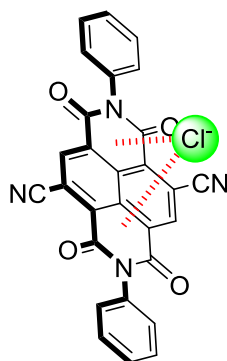


Figure 1.9 - An example of an anion- π interaction reported by Matile.⁴⁹

Coordinate bonds: Although strictly a dative covalent bond, arising from the high degree of orbital overlap between donor and acceptor species, coordinate bonds are frequently utilised in anion recognition due to the strong interaction between a Lewis acidic host and an anionic Lewis base. Organoboron compounds have been exploited for anion recognition resulting from this interaction; for example Gabbai reported a cationic borane receptor that bound fluoride strongly ($K_a = 10500 \text{ M}^{-1}$) in 9:1 $\text{H}_2\text{O}/\text{CH}_3\text{OH}$ via a coordinate bond to the boron centre (Figure 1.10).^{50,51}

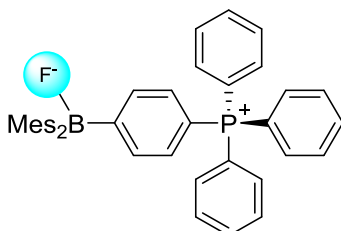


Figure 1.10 - Gabbai's cationic borane receptor that bound fluoride via a coordinate bond.⁵¹

Receptors capable of anion recognition in highly competitive solvent media typically employ a combination of the aforementioned non-covalent interactions. In the following sections the use of such interactions by biological and abiotic cationic and neutral anion receptors is discussed.

1.1.4 Biological anion receptors

Biological receptors commonly utilise a combination of electrostatic and hydrogen bonding interactions to facilitate highly selective and strong anion association in aqueous media. Recent advances in X-ray crystallography have enabled the elucidation of structures of many anion binding proteins, importantly revealing the modes of recognition. For example, the phosphate binding protein (PBP) is responsible for transporting phosphate into bacterial cells.⁵² It is a single polypeptide chain, with a molecular mass of around 34400, and is composed of two separate globular domains separated by a deep cavity that selectively binds the hydrogen phosphate anion via twelve hydrogen bonds (Figure 1.11a).⁵³ The key protein residue is Asp-56 which forms a hydrogen bond with the proton on the anion and carries a negative charge that repels oxodiansions. This allows for phosphate discrimination over similar shaped tetrahedral sulfate by over five orders of magnitude.

Bacteria GFAJ-1 reside in Mono Lake, California, that contains very low levels of phosphate in the presence of one of the highest concentrations of arsenate, a toxic species with an almost identical chemical structure to phosphate. The bacteria thrive in this environment, leading to a report claiming the organism was able to metabolise arsenate and NASA declaring that the discovery “*will impact the search for evidence of extra-terrestrial life*”.⁵⁴ However, it was later proven that GFAJ-1 exhibits an almost 4500-fold discrimination for phosphate

over arsenate and is able to sequester the trace amounts of phosphate present in the lake in order to survive.⁵⁵

Another example is the most abundant autotroph in aquatic environments, cyanobacteria, which is dependent on nitrate for photosynthesis and growth.⁵⁶ This algae contains a nitrate binding protein that resides at the membrane surface and transports nitrate to the membrane core. A complementary cavity, capable of five hydrogen bonding interactions with nitrate ensures this anion is exclusively bound by the protein (Figure 1.11b).⁵⁷

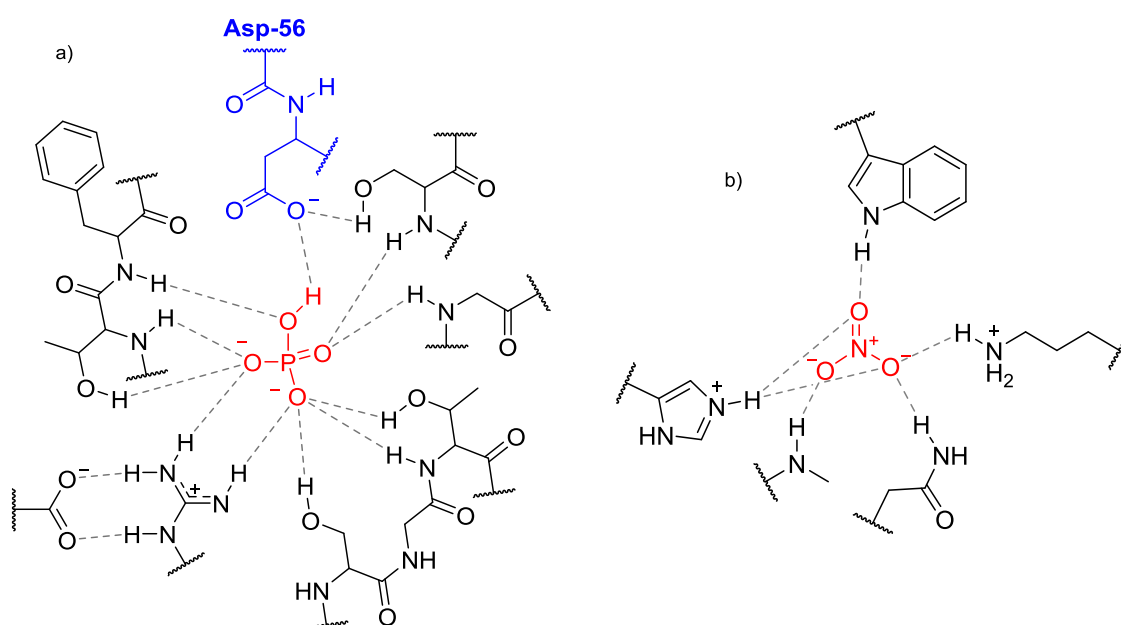


Figure 1.11 – Schematic representation of hydrogen bonding array of: a) phosphate binding protein,⁵² b) nitrate binding protein in cyanobacteria.⁵⁷

1.2 Synthetic anion receptors

Influenced by how anion binding proteins achieve their remarkable levels of selectivity, via their complementary and highly preorganised three-dimensional cavities, an enormous range of acyclic, macrocyclic and interlocked abiotic receptors have been constructed. These synthetic receptors can be divided into two major categories: *cationic* and *neutral*. Cationic receptors commonly exploit charge assisted ion-dipole electrostatic interactions to enable the

host to function in competitive protic media, such as methanol and water. Neutral anion receptors are largely designed to operate in relatively non-polar aprotic solvents and rely on a wide variety of non-covalent interactions, in particular hydrogen bonds. Originating from the cation host-guest supramolecular chemistry field, there are several key design principles that effective anion host systems often exploit, which are discussed in the following section.

1.2.1 Principles of anion receptor design

The concepts of the macrocyclic effect and preorganisation commonly exploited in cation recognition have been applied in anion receptor design.⁵⁸⁻⁶¹ For example, Flood reported a preorganised macrocycle containing convergent triazole C-H donors that bound chloride over four orders of magnitude greater than a flexible acyclic analogue in CD_2Cl_2 (Figure 1.12).⁶²

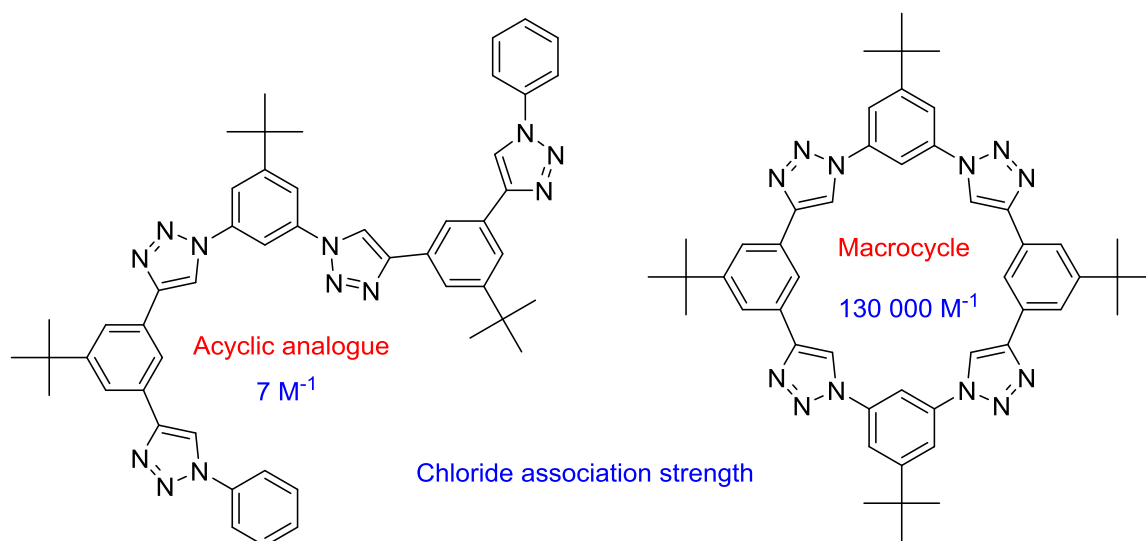


Figure 1.12 - Structures by Flood highlighting the macrocyclic effect.⁶²

Macrocycle ring size and shape is important for selective anion recognition as a consequence of complementarity. An example of macrocycle geometry governing anion selectivity has been reported by Jurczak and co-workers, who synthesised a series of macrocyclic

tetraamides of varying size (Figure 1.13). Whilst the smallest macrocycle ($n=1$) was selective for acetate in $\text{DMSO}-d_6$, the larger macrocycles ($n=2$, $n=3$) preferentially bound dihydrogen phosphate.⁶³

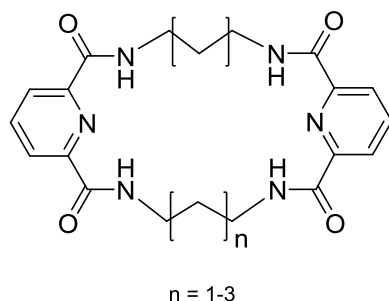


Figure 1.13 - Jurczak's anion binding macrocyclic receptor.⁶³

An example illustrating the effect preorganisation can have upon synthetic receptor binding strength was reported by Smith *et al.*, who compared the acetate binding affinity of two isophthalamide receptors.⁶⁴ By incorporating a boronic ester into the structure, the amide groups were held in a favourable syn-syn conformation for anion association, a consequence of intramolecular hydrogen bonding (Figure 1.14). This resulted in a twenty-fold increase in acetate binding strength in $\text{DMSO}-d_6$.

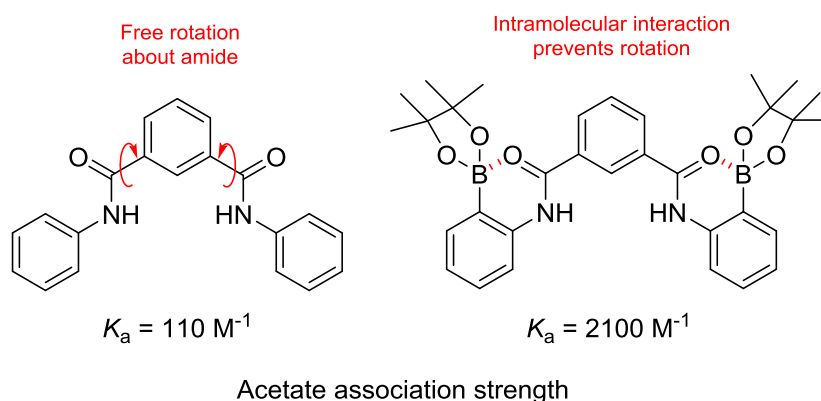


Figure 1.14 – Smith's isophthalamide receptors highlighting the effect of preorganisation.⁶⁴

1.2.2 Cationic receptors

Synthetic cationic receptors exploit electrostatics in order to bind anions. The strength of such Coulombic interactions often facilitates cationic host structures to operate in competitive polar, protic media. The lack of directionality, however, may be detrimental to anion selectivity. One way to overcome this is to combine positive charge with directional hydrogen bonding and during the past few decades a wide variety of potent cationic receptors containing ammonium, pyridinium, guanidinium, imidazolium and triazolium motifs have been constructed.

Park and Simmons reported the first example of a cationic host structure for anion recognition.¹¹ Their work investigated a number of bicyclic lipophilic cryptand-like structures, referred to as katapinands, based upon two ammonium bridgeheads separated by methylene spacer groups. These structures were capable of encapsulating chloride in 50% trifluoroacetic acid solution.⁶⁵ Seminal contributions by Lehn and co-workers inspired the rapid growth of this field; they demonstrated that polyammonium azacryptand receptors, based upon tren units, could be selectivity tuned for target anions by varying the geometry of the host.⁶⁶ Specifically, the cryptand containing ethylene spacers (Figure 1.15a) exhibited remarkable fluoride selectivity in acidic water ($\log K_a = 8.8$), whilst a larger ellipsoid shaped analogue was selective for azide ($\log K_a = 4.6$) (Figure 1.15b).⁶⁷⁻⁶⁹ Polyammomium receptors have also been used to bind biologically relevant anions; Valtancoli and Perra have reported receptors capable of enveloping the phosphate site of ATP based upon cyclic and bicyclic structures (Figure 1.15c).^{70,71}

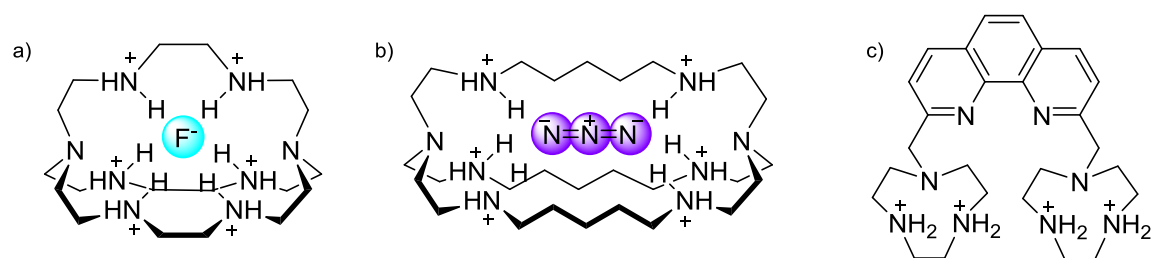


Figure 1.15 - Examples of polyammonium based anion receptors: a) Lehn's fluoride selective⁶⁶ and b) azide selective azacryptands,⁶⁸ c) Perra's bicyclic ATP receptor.⁷⁰

The guanidinium motif has been incorporated into a wide variety of anion receptor host frameworks. The parallel arrangement of the hydrogen bond donor sites facilitates selectivity for polyatomic anions, whilst the highly basic nature of the group ($pK_a = 11-13$) ensures the protonated state exists over a wide pH range. An early report by Hamilton described the selective binding of glutarate in 3:1 DMSO/D₂O by an acyclic bis-guanidinium receptor (Figure 1.16a).⁷² Strong anion recognition by guanidinium-based hosts has been achieved through supplementing the interaction with additional hydrogen bond donor groups; for example Schmuck's tridentate guanidinium-carbonylpyrrole based receptor bound citrate in water with high affinity,⁷³ whilst Kataev reported a bis-guanidinium structure selective for orthophosphate in 1:1 CD₃OD/D₂O solution (Figure 1.16b).^{74,75}

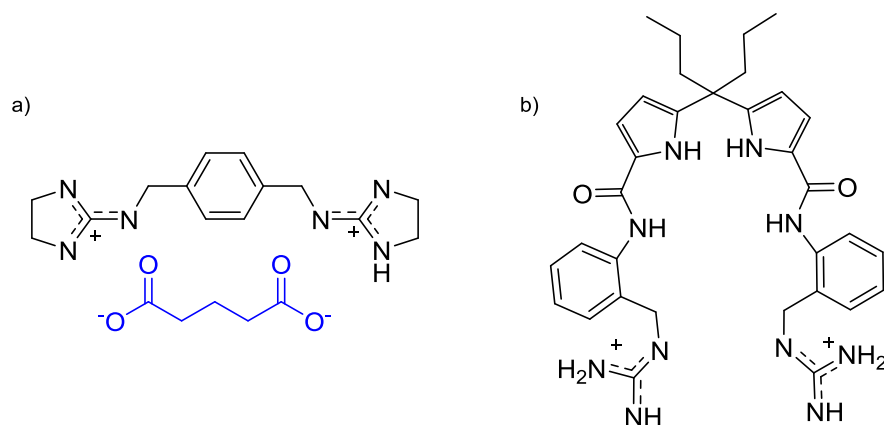


Figure 1.16 - Guanidinium-based anion receptors: a) Hamilton's acyclic glutarate receptor,⁷² b) Kataev's bis-guanidinium orthophosphate receptor.⁷⁴

Unlike protonated ammonium hosts, quaternary ammonium receptors are pH independent. A series of tetracationic quaternary ammonium cage compounds reported by Schmidtchen were capable of binding halides in water, with the selectivity trend reflecting the size of the cage (Figure 1.17a).^{76,77}

Hosts containing charge-assisted acidic C-H donor groups also have the advantage of being pH independent. Pyridinium examples include Arakawa's quaternary tetrapyridinium macrocycle, a receptor for a range of tricarboxylate anions (Figure 1.17b),⁷⁸ and Steed's tripodal pyridinium-based system that in addition to electrostatics exploited π -donor-acceptor interactions to recognise ATP in 1:1 water/acetonitrile (Figure 1.17c).⁷⁹

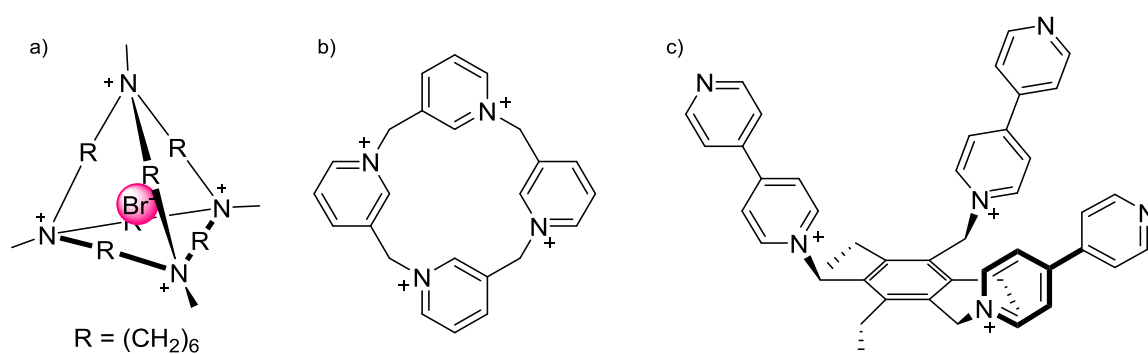


Figure 1.17 - Cationic anion receptors: a) Schmidtchen's bromide selective cage,⁷⁶ b) Arakawa's pyridinium tricarboxylate receptor,⁷⁸ c) Steed's tripodal ATP receptor.⁷⁹

In more recent years imidazolium and triazolium based receptors have gained substantial interest resulting from their synthetic accessibility and versatility for incorporation into preorganised acyclic and macrocyclic structures. Fabbriizzi reported a tris-imidazolium tripodal bipyridine Fe(II) receptor (Figure 1.18a) where the complexed metal helped to preorganise the C-H donors of the imidazolium moieties, resulting in the host being selective for azide in 4:1 CD₃CN/D₂O.⁸⁰ In another example, Kim and co-workers synthesised a tetra-

cationic calix[4]imidazolium receptor, which selectively bound fluoride in D_2O (Figure 1.18b).⁸¹

The 1,2,3-triazole motif has gained extensive interest in anion supramolecular chemistry as a result of recent advances in copper(I)-catalysed alkyne-azide cycloaddition (CuAAC) ‘click’ chemistry allowing for its facile integration into host structural frameworks.^{82,83} Methylation of the heterocycle to produce the triazolium species further polarises the C-H bond, increasing potential anion association strength. For example, Kumar and Pandey described several deoxycholic acid-based cyclic systems containing this motif which were highly selective for $H_2PO_4^-$ in $CDCl_3$.⁸⁴ Flood reported a tris-triazole macrocyclic trimer, synthesised via self-association in one step from an acyclic azide/alkyne,⁸⁵ which was alkylated by Nakamura to form the tris-triazolium species (Figure 1.18c).⁸⁶ Interestingly, this large macrocycle bound the halides in CD_2Cl_2 in order of size, rather than anion basicity strength, following the trend $I^- > Br^- > Cl^-$.

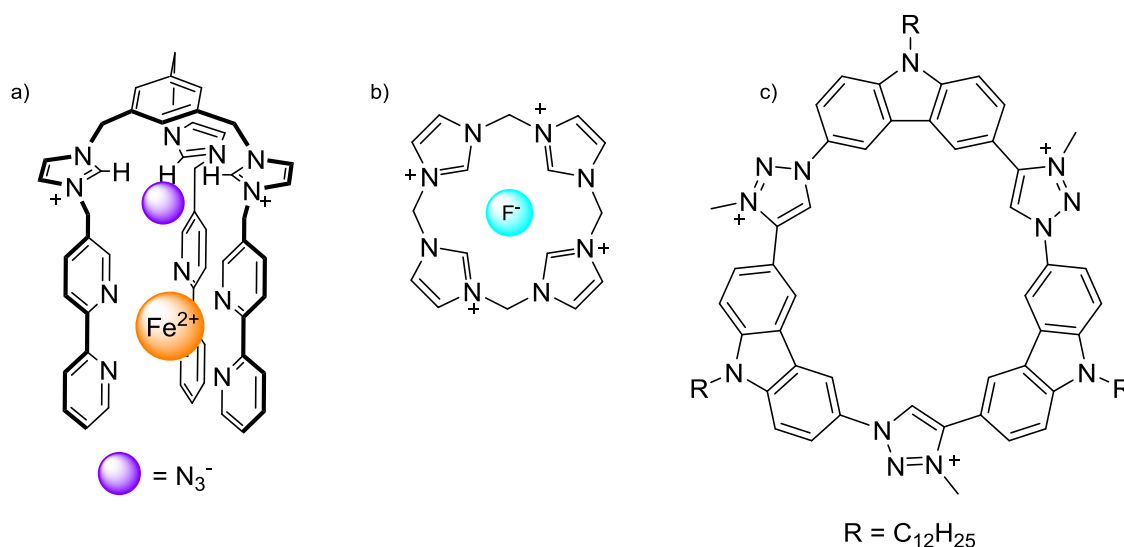


Figure 1.18 - Examples of cationic anion receptors: a) Fabbrizzi's azide selective imidazolium receptor,⁸⁰ b) Kim's fluoride selective calix[4]imidazolium,⁸¹ c) Nakamura's tris-triazolium iodide receptor.⁸⁶

1.2.3 Neutral receptors

Neutral anion receptors predominantly bind anions via hydrogen bonds and are primarily designed to operate in organic solvent media. A variety of hydrogen bond donor motifs have been used in neutral synthetic anion host design, including amides,⁸⁷ ureas,⁸⁸ thioureas,⁸⁹ pyrroles⁹⁰ and triazoles.⁹¹

Research in this area began with utilisation of amide N-H hydrogen bond donors for anion binding. In 1986, Pascal reported a macrobicyclic host containing three convergent amide groups that bound fluoride in DMSO-*d*₆ (Figure 1.19a).⁹² In a notable publication, Crabtree reported a series of simple isophthalamide based receptors that selectively bound chloride in CD₂Cl₂ (Figure 1.19b).⁹³ Pyrroles have frequently been incorporated into synthetic anion receptors over the last two decades.⁹⁰ Work on this motif has been pioneered by Sessler, with a particularly effective example being a strapped calix[4]pyrrole that bound dihydrogenphosphate and hydrogenpyrophosphate strongly in a 4% water/acetonitrile solution.^{94,95} Pulpoka and co-workers have also exploited this framework, recently reporting an azocalix[4]arene strapped calix[4]pyrrole that exhibited a colour change in the presence of a variety of anions in CH₃CN (Figure 1.19c).⁹⁶ On addition of fluoride, acetate, benzoate, and hydrogenpyrophosphate the solution changed colour from orange to sky blue, blue, pink, and yellow respectively.

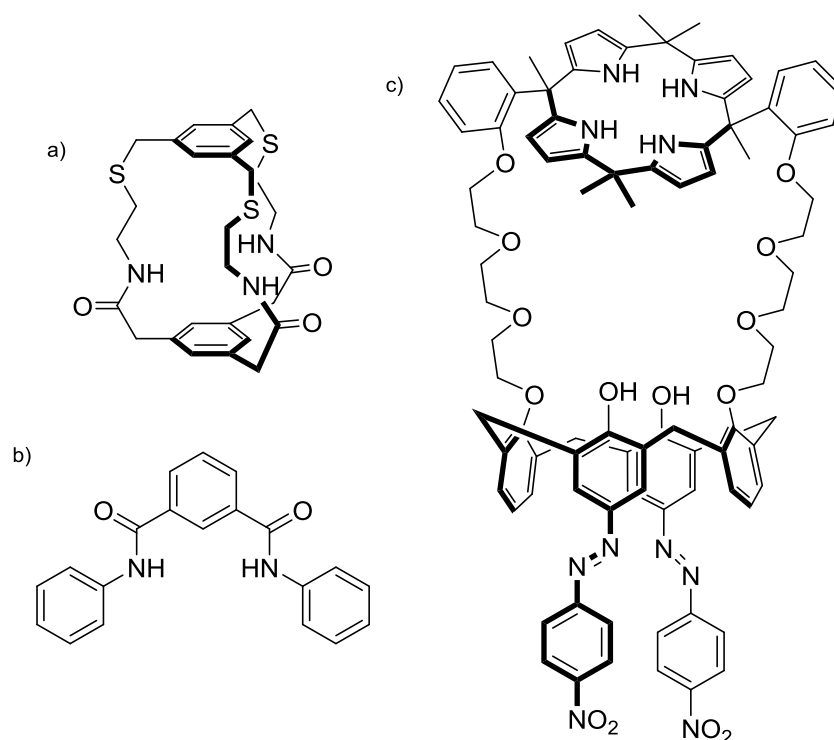


Figure 1.19 - Examples of neutral N-H bond donors for anion recognition: a) Pascal's cage,⁹² b) Crabtree's isophthalamide-based chloride receptor,⁹³ c) Pulpoka's strapped calix[4]pyrrole.⁹⁶

Described as a non-classical hydrogen bonding interaction, the heterocyclic 1,2,3-triazole motif utilises its polarised C-H bond to bind anions.⁹⁷ An example of anion recognition in aqueous media has been reported by Flood using a preorganised foldamer triazole receptor design (Figure 1.20).^{98,99} In 1:1 water/acetonitrile solution, chloride addition induced the formation of a 2:1 stoichiometric host:guest double helix assembly, with 80% of the receptor's π -surfaces buried. This conformational change, termed hydrophobic collapse, shielded the bound halide anion from the solvent, creating a microenvironment favourable for Cl^- binding via multiple triazole C-H bonds.

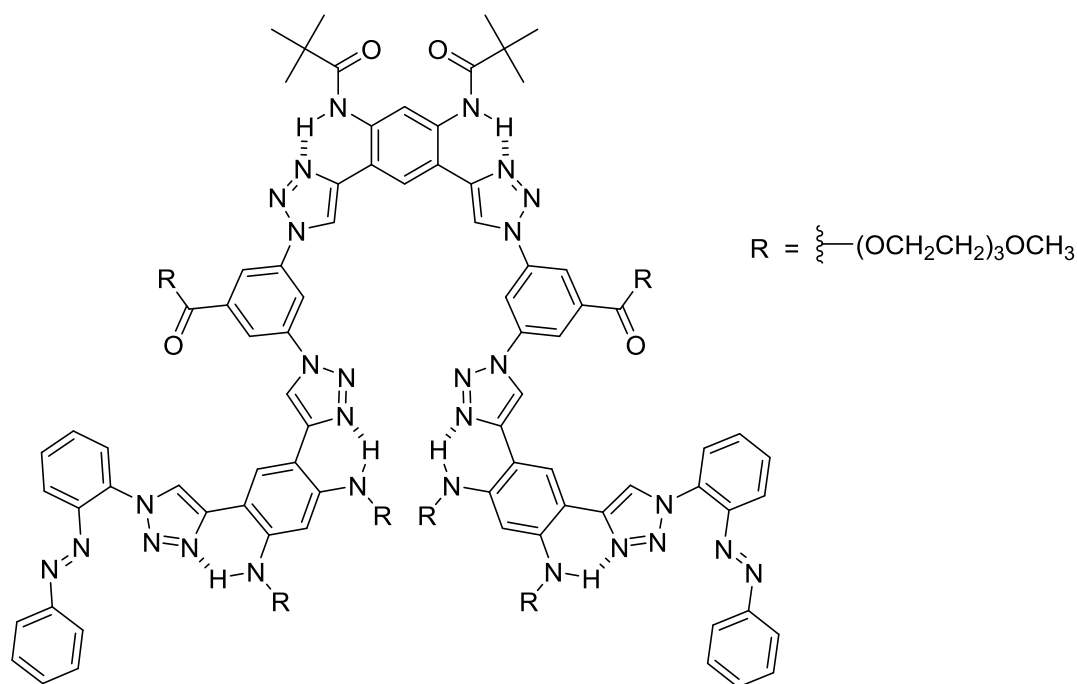


Figure 1.20 - Flood's chloride binding preorganised foldamer.^{98,99}

Progress towards anion recognition in pure water by neutral host structures has been pioneered by Kubik using macrocyclic pseudo-peptide receptors.¹⁰⁰⁻¹⁰² Remarkable iodide and sulfate binding in 4:1 D₂O/CD₃OD was demonstrated by a neutral hexapeptide macrocycle that formed 2:1 stoichiometric host-guest complexes with these anions through a combination of both amide N-H hydrogen bonds and the hydrophobic effect. Furthermore, linking two of these macrocycles together to form a 'molecular oyster' (Figure 1.21a) created a structure capable of binding iodide and sulfate in 95:5 D₂O/CD₃OD.¹⁰³ Sindelar has recently reported a bambusuril macrocyclic structure capable of binding anions extremely strongly in water (Figure 1.21b).¹⁰⁴ The peripheral carboxylate groups ensured water solubility of the host, whilst the hydrophobic core cavity bound anions via convergent glycoluril C-H hydrogen bond donors. The anion selectivity trend mirrored anion hydration energies, with the association constants for iodide ($K_a=1 \times 10^7 \text{ M}^{-1}$) and perchlorate ($K_a=5.5 \times 10^7 \text{ M}^{-1}$) being remarkably high for a neutral cavity-containing receptor operating in D₂O.

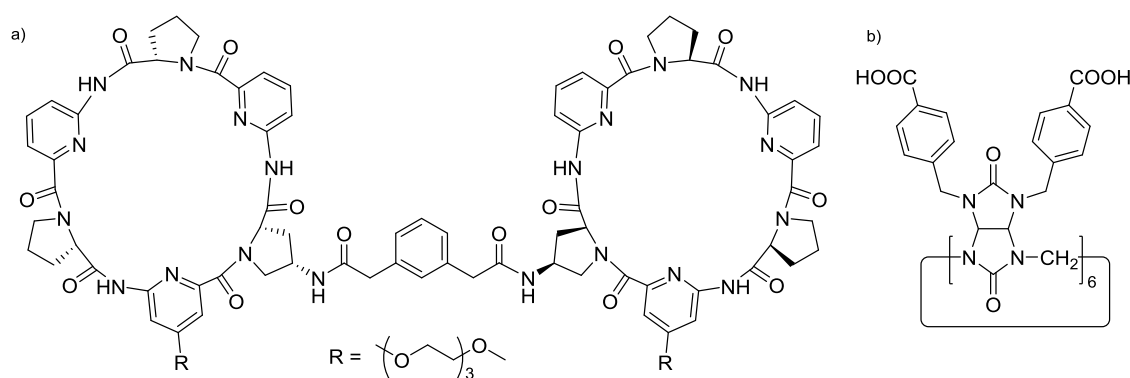


Figure 1.21 – Neutral hosts for binding anions in aqueous media: a) Kubik's 'molecular oyster',¹⁰⁰ b) Sindelar's water soluble bambusuril macrocycle.¹⁰⁴

1.3 Halogen bonding

First observed by Guthrie in the late 19th century, it took over 100 years for Dumas to coin the name 'halogen bond'. As defined by IUPAC:¹⁰⁵

"a halogen bond occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity".

The interaction is analogous to a hydrogen bond (HB) and is modelled as a polarised halogen atom X, bound to an electron withdrawing group R.¹⁰⁶ This results in the halogen having a region of positive electrostatic potential, referred to as the σ -hole, positioned at the pole of the halogen atom at the terminus of the R—X axis (Figure 1.22).¹⁰⁷ This acts as a halogen bond (XB) donor, accepting electron density from a Lewis base, such as an anion. Typically the halogen atom X is iodine as its increased size and greater degree of polarisation compared to other halogens results in the strongest XB interaction.

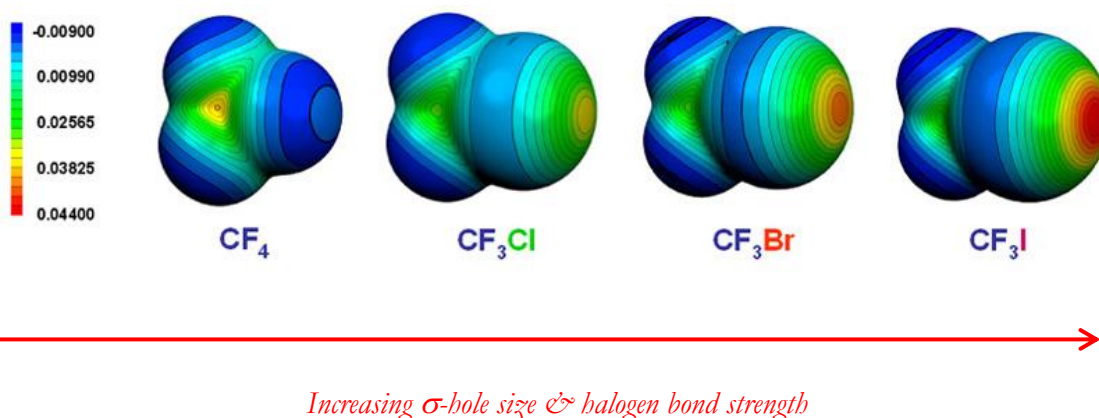


Figure 1.22 - Molecular electrostatic surface potentials, in Hartrees, of CF_3X .¹⁰⁷ Region of positive potential (red) represents σ -hole. Region of negative potential shown in blue. Reprinted with permission from ref 107. Copyright 2007 Springer.

For many years, halogen bonding has been exploited predominantly in solid state crystal engineering (Figure 1.23a) and materials design applications.¹⁰⁸⁻¹¹⁰ Surprisingly, it is only during the past decade or so that solution phase XB studies have begun to emerge. The interaction is gaining prominence in anion recognition as a result of its high directionality and bond strengths comparable to that of the HB ($10\text{-}180\text{ kJmol}^{-1}$).¹¹¹ Furthermore, the tunability of the electron withdrawing group allows for enhancement of the interaction, for example, when X is bound to carbon the XB strength increases with decreasing sp-hybridisation such that $\text{C}(\text{sp}^3)\text{-X} < \text{C}(\text{sp}^2)\text{-X} < \text{C}(\text{sp})\text{-X}$.¹¹² As a result of this, solution phase halogen bonding has recently found applications in solution phase catalysis (Figure 1.23b),¹¹³⁻¹¹⁵ medicinal chemistry¹¹⁶⁻¹¹⁸ (Figure 1.23c) and anion transport.¹¹⁹⁻¹²¹

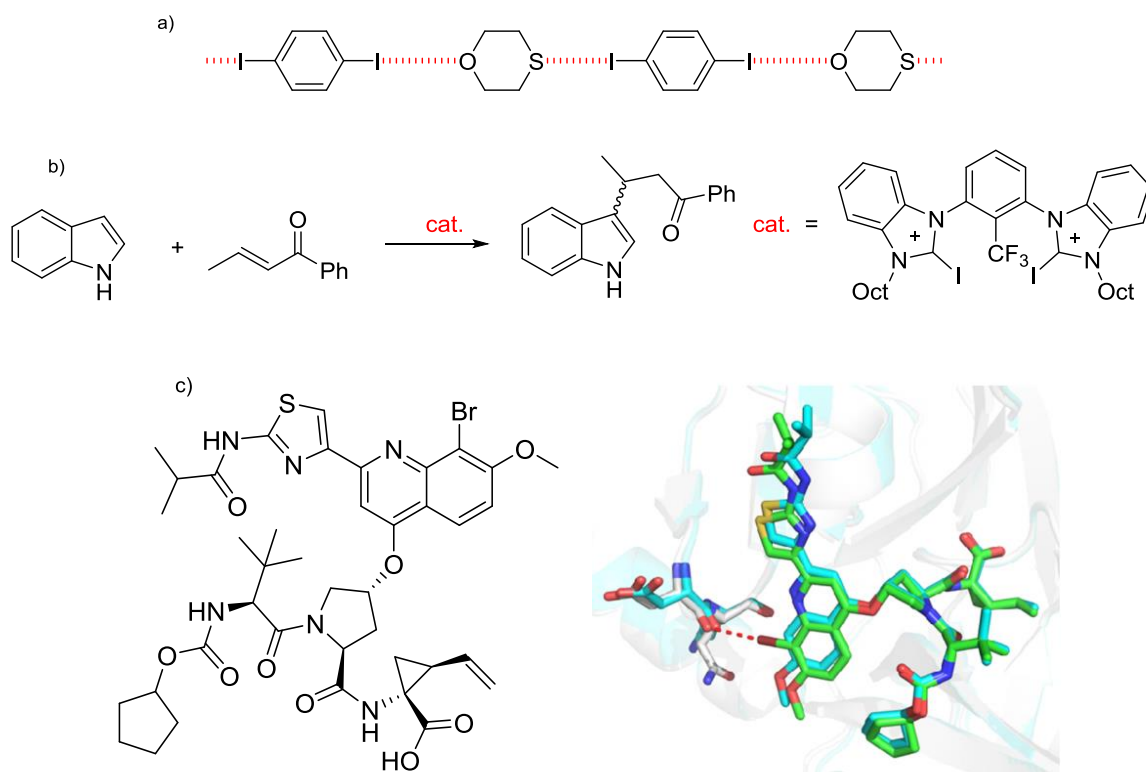


Figure 1.23 - Uses of halogen bonding: a) XB in the solid state,¹¹⁰ b) reaction utilising XB catalyst,¹¹⁵ c) halogen bonding inhibitor of hepatitis C virus.^{118,122}

1.3.1 Halogen bonding anion receptors

Compared to the extensive array of hydrogen bonding hosts for anion recognition, there are far fewer examples of XB receptors for this purpose.¹²² Early work in this field focused upon haloperfluoroarene systems. One of the first reported examples was Resnati's heteroditopic tripodal receptor designed for the recognition of sodium halide salts. The polyether chains were preorganised by a bound sodium cation, with preferential binding exhibited for iodide over the other halides in CDCl_3 (Figure 1.24a).¹²³ Proof that this was a result of halogen bonding was provided by an X-ray crystal structure determination of the sodium iodide complex. The tripodal framework was later exploited by Taylor, who reported a host structure with three convergent halogen bonding iodoperfluoroarene arms that was selective for chloride over a range of other anions in acetone- d_6 (Figure 1.24b).¹²⁴ The XB

iodoperfluoroarene motif has recently been utilised in anion transport across lipid bilayer membranes; Matile has observed transport of chloride and hydroxide by a range of ditopic calix[4]arene structures (Figure 1.24c).^{119,121}

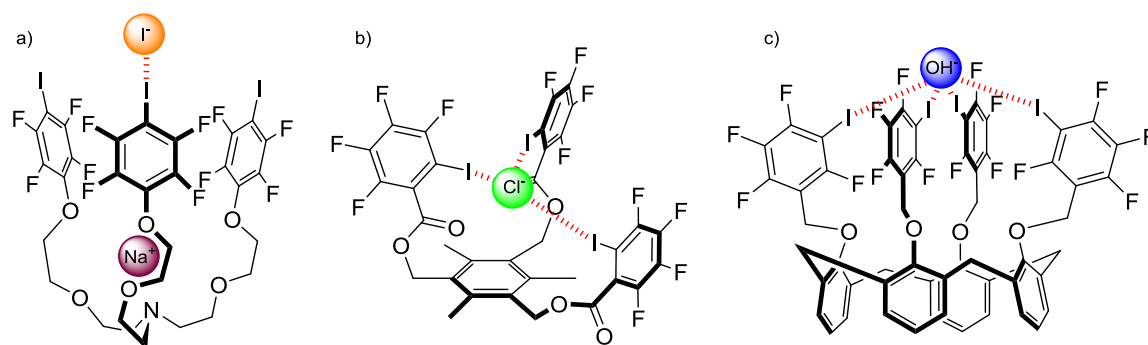


Figure 1.24 - Halogen bonding anion receptors based upon halogenated aromatic hosts: a) Resnati's heteroditopic receptor,¹²³ b) Taylor's tripodal receptor,¹²⁴ c) Matile's calix[4]arene receptor.¹²⁵

Progress in halogen bonding anion recognition has proceeded to halo-functionalised heterocycles; straightforward syntheses allow halogen atoms to be appended to imidazole and triazole heterocyclic rings which can be protonated or alkylated in order to form potent haloimidazolium and halotriazolium charge assisted XB donors. Ghosh and co-workers recently incorporated the XB iodoimidazolium motif into preorganised bipodal and tripodal hosts capable of recognising halide anions in CD_3CN (Figure 1.25a). The bipodal (Cl^-) and tripodal (Br^-) structures displayed a different anion selectivity trend, dictated by complementarity and geometry.^{126,127} Schubert and co-workers investigated how a variety of factors such as charge, functional groups and non-covalent bond donors affect anion recognition through preparation of a series of bidentate receptors (Figure 1.25b).¹²⁸ The 5-iodo-1,2,3-triazolium motif exhibited a strong affinity for sulfate in $\text{DMSO}-d_6$, whilst in each case the XB receptor outperformed its HB analogue.

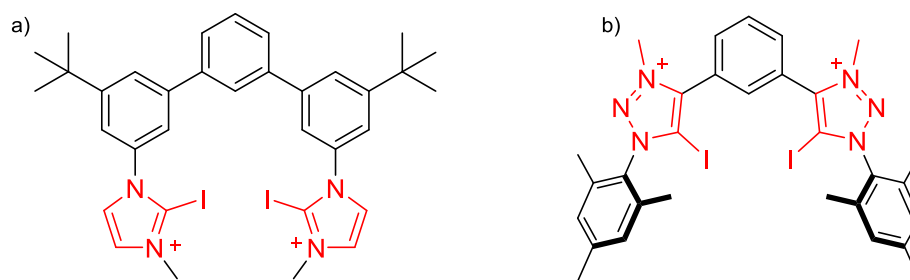


Figure 1.25 - Halo-heterocyclic XB donors: a) Ghosh's bipodal iodoimidazolium receptor,¹²⁶ b) Schubert's iodotriazolium sulfate selective host.¹²⁸

1.4 Anion sensing

Anion host molecules with the additional capability of eliciting a detectable macroscopic response upon anion binding are referred to as anion sensors. Examples of these are becoming increasingly prevalent; an easily observed output response is desirable for anion detection in environmental or industrial settings. There are three main methods by which synthetic anion sensors operate.

The most common example is the appendage of a photo-active optical or electrochemical reporter group in close proximity to the host's anion recognition site where binding modifies the output of the optical or redox-active probe. These hosts are known as chemosensors (Figure 1.26a). Typically the target anion analyte is bound through non-covalent interactions in a reversible process and the real-time response is proportional to analyte concentration.¹²⁹

Another signalling mechanism is a displacement assay; the host is designed to associate a dye guest which is expelled from the cavity by preferential binding of an anion, an event that causes a change in the optical properties of the dye (Figure 1.26b).¹³⁰ Finally, chemodosimeters are receptors that undergo a specific irreversible chemical reaction with the target anion to induce a change in the sensory properties of the host.¹³¹ The following section focuses upon the design of synthetic chemosensors for anion recognition via a detectable optical or electrochemical output from the reporter group.

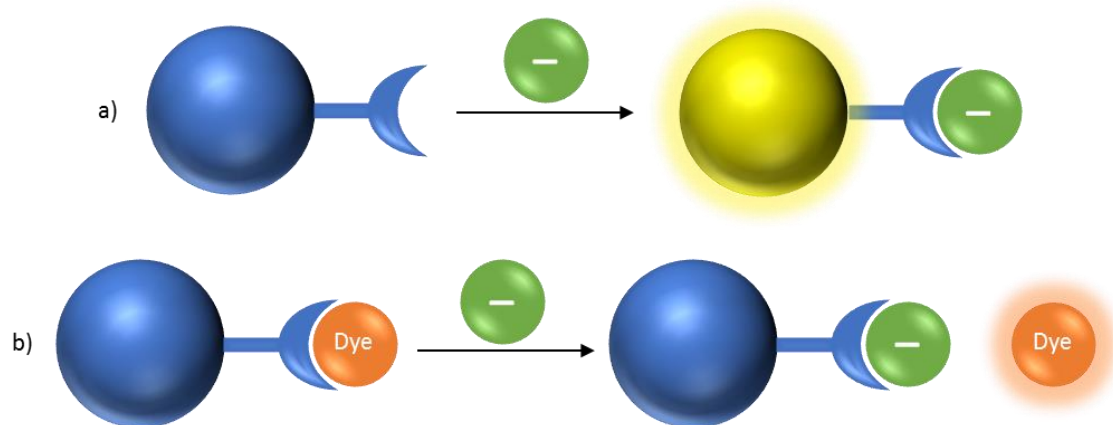


Figure 1.26 - Schematic representation of anion sensing methods: a) reporter attached to receptor (chemosensor),¹³¹ b) displacement assay.¹³⁰

1.4.1 Optical anion sensors

Optical anion sensors typically display a highly sensitive fluorescent or luminescent response to anion addition; recognition causes changes to the excited-state fluorescence or phosphorescence emission. This may proceed through a variety of signal transduction pathways such as: photo-induced electron transfer (PET), electronic energy transfer, monomer-excimer formation or the rigidity effect.¹³² This section will discuss organic and transition metal based optical anion sensors.

1.4.1.1 Organic sensors

Organic fluorophores exhibit highly guest sensitive responses and, advantageously, are often straightforward to integrate in close proximity to a receptor's anion recognition site. Gunnlaugsson described a sensor based upon the fluorescent 1,8-naphthalimide group tethered to an anion-binding thiourea.¹³³ Upon addition of fluoride in DMSO the fluorescence is switched off via the PET process. Continued addition of fluoride caused the colour of the solution to change from a light yellow to deep purple, a result of deprotonation

of the 4-amino moiety on the naphthalimide group, in an example of dual sensing action. Conversely, Czarnik reported a phosphate sensor with an anthracene backbone; in the unbound state the benzylic nitrogen lone pair quenched the fluorescence through a PET mechanism. In water at pH 6, hydrogen phosphate anion complexation resulted in protonation of the nitrogen atom, inhibiting the quenching process and switching on the anthracene fluorescence (Figure 1.27a).¹³⁴

The incorporation of XB donors into anion sensors is a relatively new area of research. A recent example by Molina and co-workers reported an open chain bis-iodotriazolium receptor capped with pyrene units (Figure 1.27b).^{135,136} Upon addition of a range of anions it was found that only hydrogenpyrophosphate caused a dramatic enhancement of the emission intensity, a consequence of excimer formation. Binding of this anion (in 9:1 CD₃CN/CD₃OD) was almost an order of magnitude greater than the HB host analogue in a rare example of oxoanion selectivity by an XB receptor.

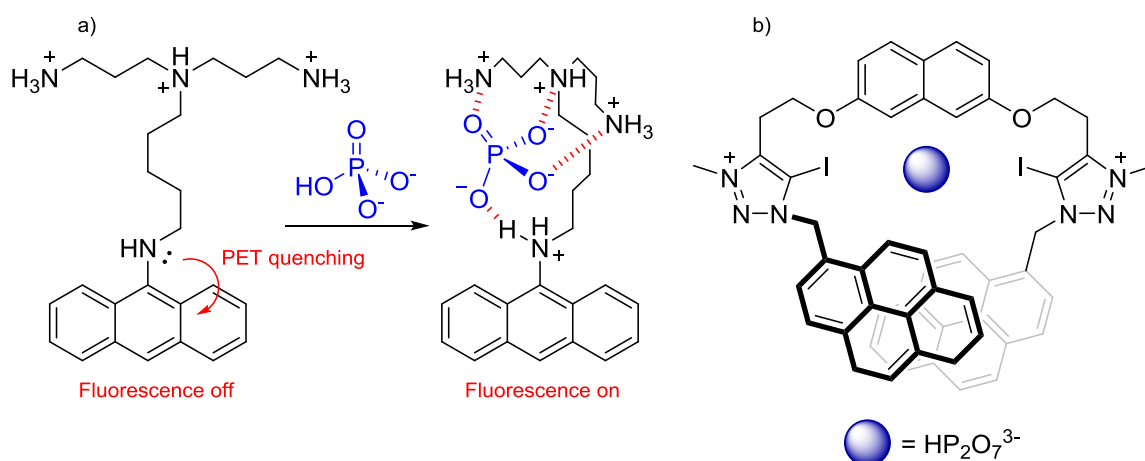


Figure 1.27 - Luminescent organic anion sensors: a) Czarnik's anthracene sensor, PET quenching mechanism removed upon hydrogen phosphate addition,¹³⁴ b) Molina's pyrene XB hydrogenpyrophosphate sensor.¹³⁵

1.4.1.2 *Transition metal based sensors*

The incorporation of a photo-active transition metal based reporter group into an anion host framework offers several advantages.¹³⁷ Firstly, the metal's positive charge and Lewis acidic electron deficient nature leads to strong electrostatic interactions, whilst metal complexation further polarises the potential HB or XB donors of the anion binding site, often enhancing anion association through charge assisted bonding interactions. Furthermore, their rigid structures enforce geometric constraints upon the molecule; this is particularly useful for enhancing selectivity.

Popular transition metal based optical probes include the kinetically inert second and third row metals Ru(II), Ir(III) and Re(I) whose photophysical properties are well established.¹³⁸⁻¹⁴¹ Examples incorporating the ruthenium(II) bipyridyl motif include Gunnlaugsson's urea-functionalised complex¹⁴² that displayed a metal-to-ligand charge transfer (MLCT) emission enhancement upon binding H_2PO_4^- in CH_3CN , in contrast to a quenching response in the presence of $\text{HP}_2\text{O}_7^{3-}$ (Figure 1.28a), and Ye's bimetallic imidazole complex that selectively detected micromolecular quantities of cyanide in water under physiological conditions through a decrease in MLCT emission intensity.¹⁴³ Huang and co-workers reported a series of hosts incorporating an iridium(III) polypyridyl moiety as a chromophore. Significant changes were observed in both the absorption and emission spectra upon addition of F^- , OAc^- , and H_2PO_4^- in CH_3CN , with the colour change from yellow-green to brown detectable by the naked eye (Figure 1.28b).¹⁴⁴ Beer reported the bimetallic Re(I) pyrimidine based XB host which bound a range of anions in 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$, in particular iodide, with the binding event inducing a notable increase in the metal's MLCT absorption band (Figure 1.28c).¹⁴⁵

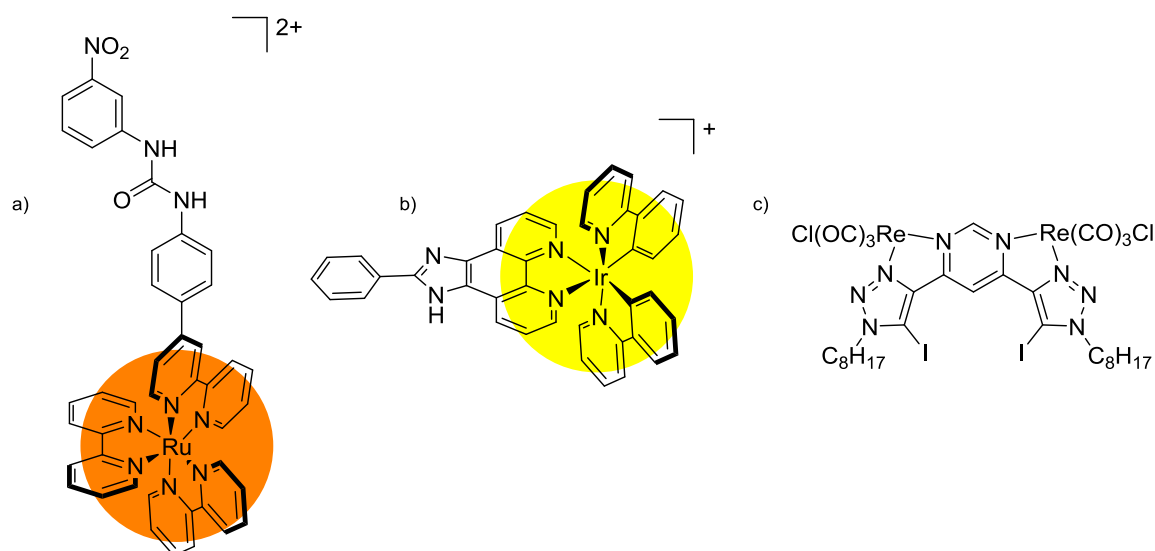


Figure 1.28 - Transition metal based anion sensors: a) Gunnlaugsson's Ru(II) dihydrogen phosphate sensor,¹⁴² b) Huang's Ir(III) fluoride sensor,¹⁴⁴ c) Beer's bimetallic Re(I) iodide sensor.¹⁴⁵

1.4.2 Electrochemical anion sensors

Electrochemical sensors typically incorporate a redox active centre into the structural framework of an anion host system. The bound anion stabilises one of the oxidised or reduced species of the redox couple, perturbing the voltammetric potential of either the oxidation or reduction process.

Since seminal work by Beer and co-workers was reported nearly three decades ago, metallocene based electrochemical anion receptors have been prominent in the literature.¹⁴⁶⁻

¹⁴⁸ A recent example by Molina described a bis-ferrocene anion receptor linked by a triazole motif that sensed AcO^- , H_2PO_4^- and $\text{HP}_2\text{O}_7^{3-}$ through large cathodic shifts in the receptor's ferrocene/ferrocenium redox couple in acetonitrile (Figure 1.29a).¹⁴⁹ Another prevalent redox reporter group studied is the tetrathiafulvalene (TTF) moiety. Schöllhorn has recently described a halogen bonding, redox responsive iodo-TTF derivative which upon chloride addition in DMF displayed cathodic shifts of 37 mV and 50 mV for the first and second oxidation redox couples respectively (Figure 1.29b).¹⁵⁰

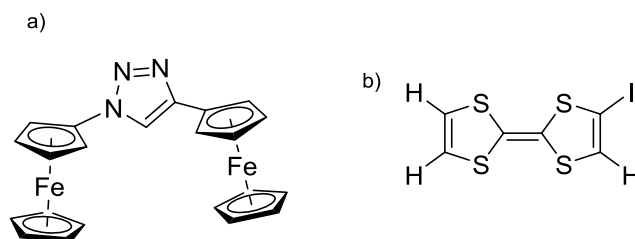


Figure 1.29 - Electrochemical anion sensors: a) Molina's bis-ferrocene receptor,¹⁴⁹ b) Schöllhorn's TTF-based chloride sensor.¹⁵⁰

1.5 Mechanically interlocked molecules

Mechanically interlocked molecules (MIMs) consist of two or more component parts, connected through a *mechanical bond*, such that they cannot be separated without breaking or distorting a chemical bond.¹⁵¹ First explored purely for synthetic curiosity, they are now finding numerous applications in nanotechnology as molecular machines,^{152,153} functional materials,¹⁵⁴ sensors,¹⁵⁵ and in catalysis¹⁵⁶⁻¹⁵⁸ and drug delivery.¹⁵⁹

The most well established MIMs are [n]catenanes and [n]rotaxanes where [n] dictates the number of individual molecular components (Figure 1.30). Catenanes consist of linked macrocycles, analogous to a chain, whilst rotaxanes consist of macrocyclic components threaded around a central axle capped with large termini – commonly referred to as *stopper groups* – which prevent macrocycle disconnection. A rotaxane without these bulky end groups is termed a pseudorotaxane; whilst formally not an interlocked molecule these act as useful precursors to interlocked assemblies. More recently, a number of more complex interlocked topologies have been constructed such as knots,¹⁶⁰⁻¹⁶² Borromean rings¹⁶³ and the Solomon link.¹⁶⁴ The following section will outline synthetic strategies towards catenanes and rotaxanes and describe examples of these structures for anion recognition and sensing.

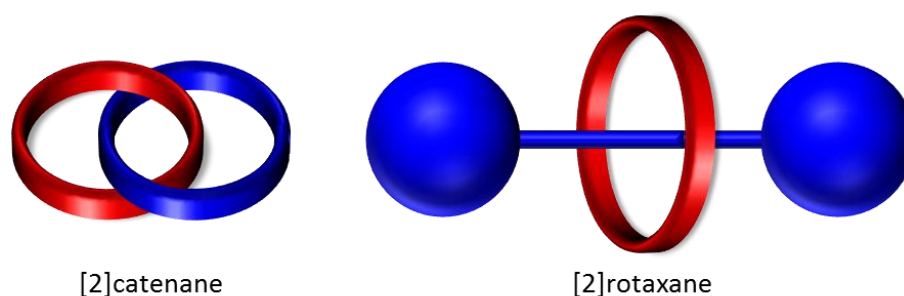


Figure 1.30 - Schematic representations of two interlocked structures.

1.5.1 Synthetic approaches to rotaxanes and catenanes

Rotaxanes are most commonly constructed via one of two methods, termed 'clipping' and 'stoppering' (Figure 1.31a). The former proceeds via the closing of the macrocyclic component(s) around a pre-formed axle and the latter involves the attachment of the stopper groups to a pseudorotaxane. Less common methods include: 'slippage',¹⁶⁵ which involves the slipping of a macrocycle over the top of a stopper group onto the axle at elevated temperatures; 'shrinkage',¹⁶⁶ the shrinking of a large macrocycle after it has been threaded onto an axle such that it becomes too small to fall off; and 'swelling',¹⁶⁷ increasing the size of the stopper groups of a pseudorotaxane assembly. Catenanes are commonly produced through the closure of an acyclic molecule around a macrocycle or a double cyclisation of two acyclic precursors (Figure 1.31b).

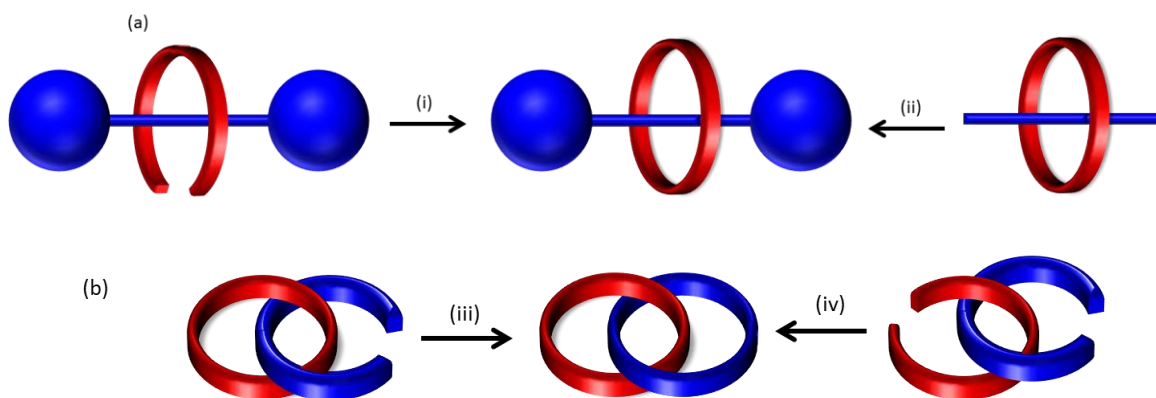
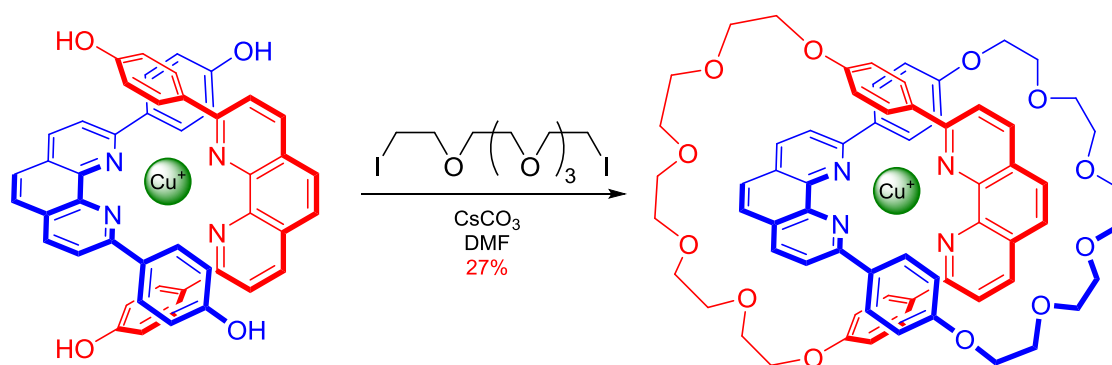


Figure 1.31 - Strategies towards MIM formation: a) rotaxane synthesis by (i) clipping and ii) stoppering, b) catenane synthesis by iii) single and iv) double macrocycle cyclisation.

1.5.2 Templated synthesis of MIMs

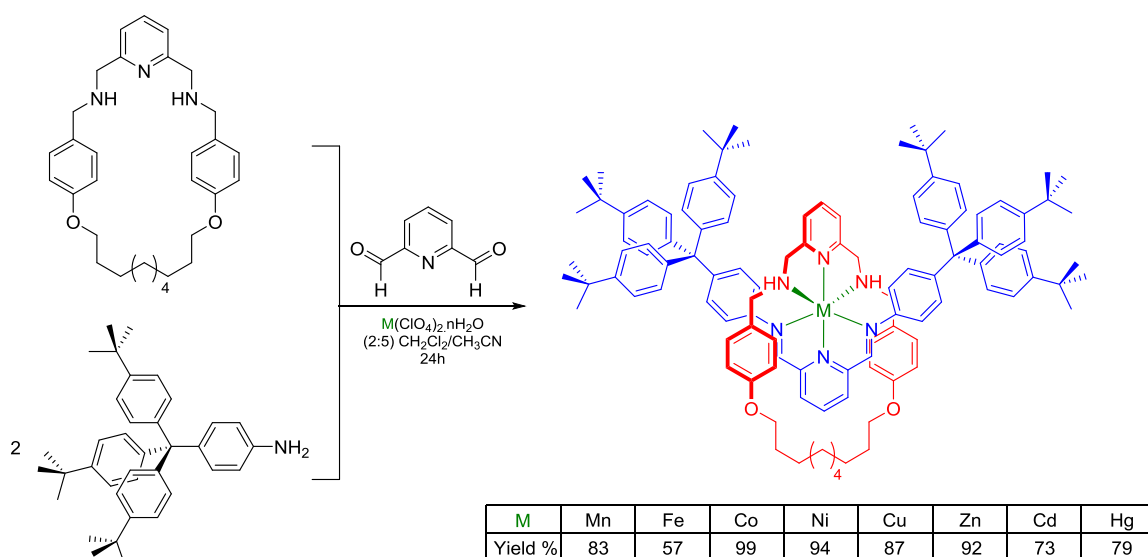
The original examples of interlocked structures relied upon purely statistical methods; the first reported [2]catenane by Wasserman¹⁶⁸ in 1960 and [2]rotaxane by Harrison¹⁶⁹ in 1967 were both prepared in very poor yields. Whilst Schill¹⁷⁰ reported catenane formation through interpenetration of connected component parts and cleavage of a covalent bond as the final step, it was the seminal work by Sauvage that transformed the field.^{171,172} A Cu(I) template was utilised to bring together two phenanthroline ligands in an orthogonal, tetrahedral coordinating arrangement, where upon a Williamson ether double cyclisation reaction resulted in the isolation of a [2]catenane in far higher yields than any previous method (Scheme 1.1). This inspired and initiated the study of the templated synthesis of MIMs. The following section will outline cationic, neutral and anionic template strategies that exploit a range of non-covalent π -donor- π -acceptor, HB and XB interactions in order to produce interlocked structures.



Scheme 1.1 - Sauvage's seminal Cu(I) templated [2]catenane.¹⁷¹

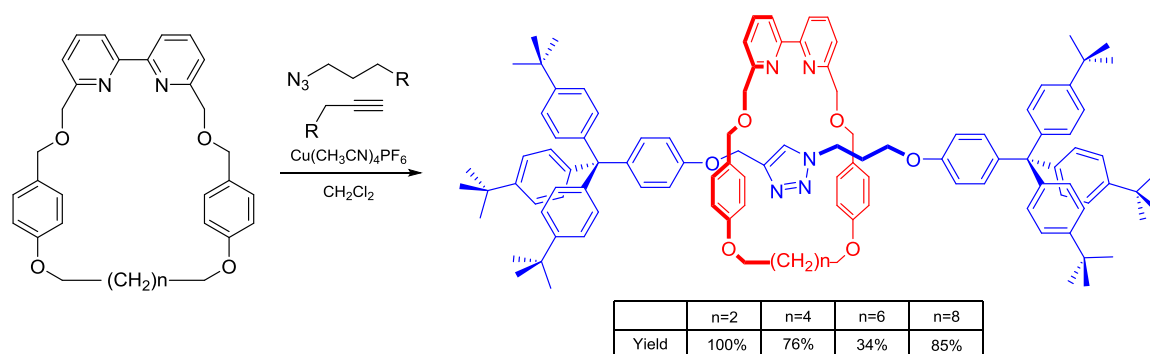
1.5.2.1 Cation templated interlocked structures

Sauvage exploited the versatility of his copper(I) template method in order to synthesise a variety of higher order MIM compounds, including a [3]catenane,¹⁷³ a [3]rotaxane¹⁷⁴ and a trefoil knot.¹⁷⁵ Numerous other transition metal cations with a range of stereochemical preferences have since been exploited for interlocked structure formation, including Pd(II)¹⁷⁶ and Pt(II)¹⁷⁷ (square planar) Au(I)¹⁷⁸ (linear), and Ru(II)¹⁷⁹ and Co(III)¹⁸⁰ (octahedral). Leigh reported the use of several transition metals (including those in the first row from Mn(II) to Zn(II)) to facilitate the production of [2]rotaxanes; the metal templated a pseudorotaxane assembly which was stoppered via a Schiff-base reaction (Scheme 1.2).¹⁸¹ Impressive yields of isolated rotaxane were achieved in each case, in particular with Co(II) (99%). More recently, MIM synthesis by a cationic template has been extended to alkali metals, with an ion-dipole interaction between Na⁺ and a polyether chain proven to be a viable template strategy.^{182,183}



Scheme 1.2 - Leigh's series of transition metal templated [2]rotaxanes.¹⁸¹

A significant development in the field of cation templated MIM construction was reported by Leigh in 2006 in an approach termed active metal template (AMT) synthesis.¹⁸⁴ In this method the metal plays a dual role in both templating the assembly of the component parts whilst acting as a catalyst for formation of a covalent bond to produce the interlocked structure.¹⁸⁵ First performed via a CuAAC reaction, Goldup and co-workers have since exploited this AMT method to prepare a series of [2]rotaxanes in near quantitative yield (Scheme 1.3).¹⁸⁶ Since its inception, a variety of active metal templates have been employed, with interlocked structures being formed through Cu(I) Glaser coupling,¹⁸⁷ Pd(II) alkyne homo-coupling^{188,189} and Ni(II) alkyl homo-coupling reactions.¹⁹⁰



Scheme 1.3 - Goldup's example of AMT synthesis for construction of a [2]rotaxane.¹⁸⁶

Organic cations have also been employed as templates for MIM construction.¹⁹¹⁻¹⁹⁴ Stoddart has exploited the aromatic donor-acceptor charge-transfer interaction between an electron rich group (alkoxynaphthalene, hydroquinone etc.) and an electron poor cationic 4,4'-bipyridinium motif to form a variety of impressive interlocked structures, including a [5]catenane termed Olympiadane.¹⁹⁵⁻¹⁹⁷ The hydrogen bonding interaction between a protonated axle component and a crown ether is often exploited in MIM design. For example, Schalley reported a hetero[3]rotaxane containing two secondary ammonium sites upon the axle and two crown ether macrocyclic components (Figure 1.32a).¹⁹⁸ The sequence specificity of the rotaxane was ascribed to the ability of the larger dibenzo-24-crown-8 ring to pass over the central phenyl group, which could not be achieved by the smaller benzo-21-crown-7 macrocycle. Additionally, Loeb has utilised hydrogen bonding interactions to produce a series of interlocked structures containing the benzimidazolium motif, deprotonation of which yields a neutral interlocked assembly (Figure 1.32b).¹⁹⁹⁻²⁰¹

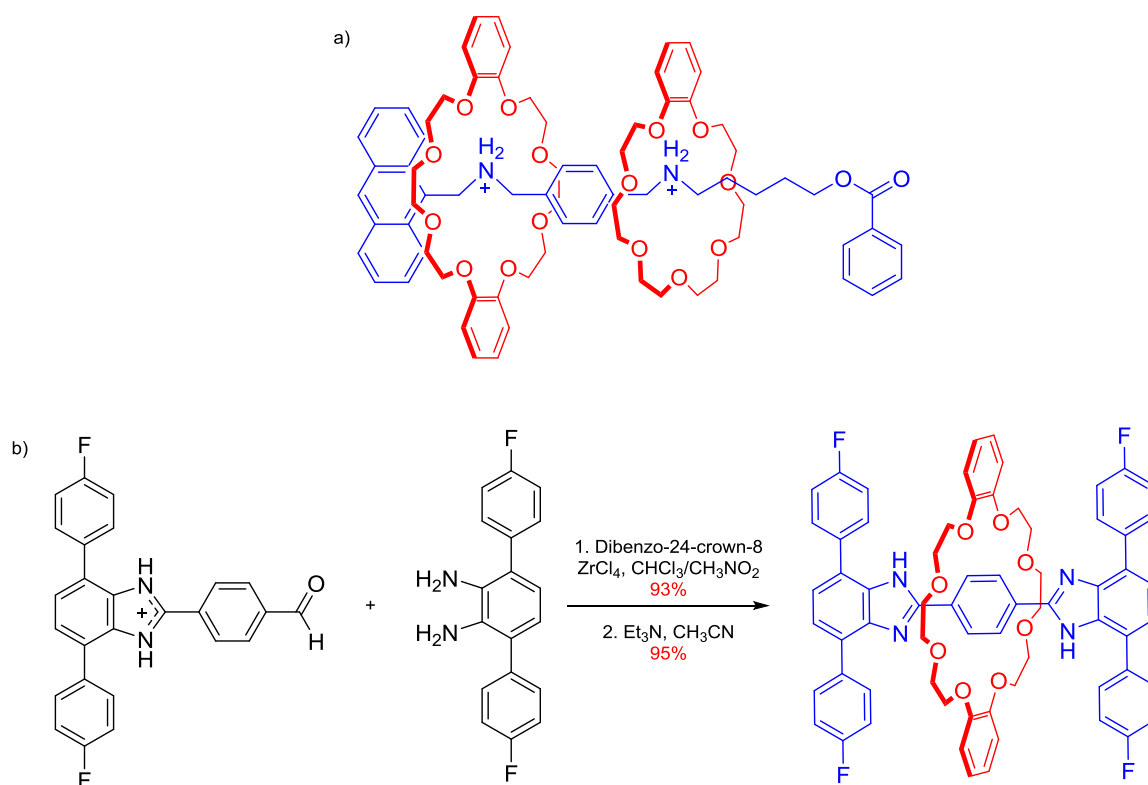
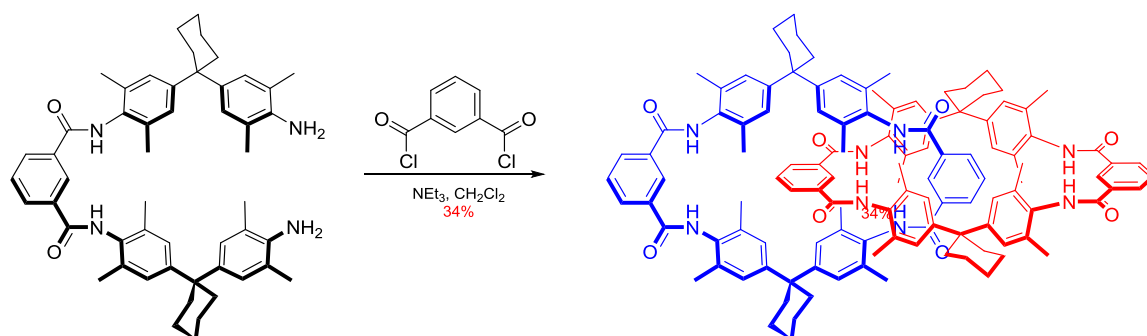


Figure 1.32 - Crown ether based rotaxanes formed via organic cation hydrogen bonding templates: a) Schalley's self-sorting [3]rotaxane,¹⁹⁸ b) Loeb's H-shaped [2]rotaxane.²⁰⁰

1.5.2.2 Neutral templated interlocked structures

The first examples of interlocked structures constructed via a neutral template were independently reported by Vögtle and Hunter in 1992.^{202,203} In both cases, MIM construction was achieved through an acid condensation double cyclisation reaction between a bis-acid chloride and a bis-amine (Scheme 1.4). Formation of the [2]catenanes was attributed to the ability of the initially produced tetralactam macrocycle to form intermolecular carbonyl-isophthalamide hydrogen bonds. Subsequently, a range of neutral templated interlocked structures have been reported that exploit hydrogen bonding interactions between the axle and macrocyclic components.²⁰⁴ Zwitterionic axles are often employed; examples include Leigh's nitron-based rotaxane (Figure 1.33a)²⁰⁵ and Smith's squaraine dye-based rotaxanes and catenanes (Figure 1.33b).²⁰⁶⁻²¹⁰



Scheme 1.4 - Hunter's homo-[2]catenane formed via a hydrogen bond template.²⁰³

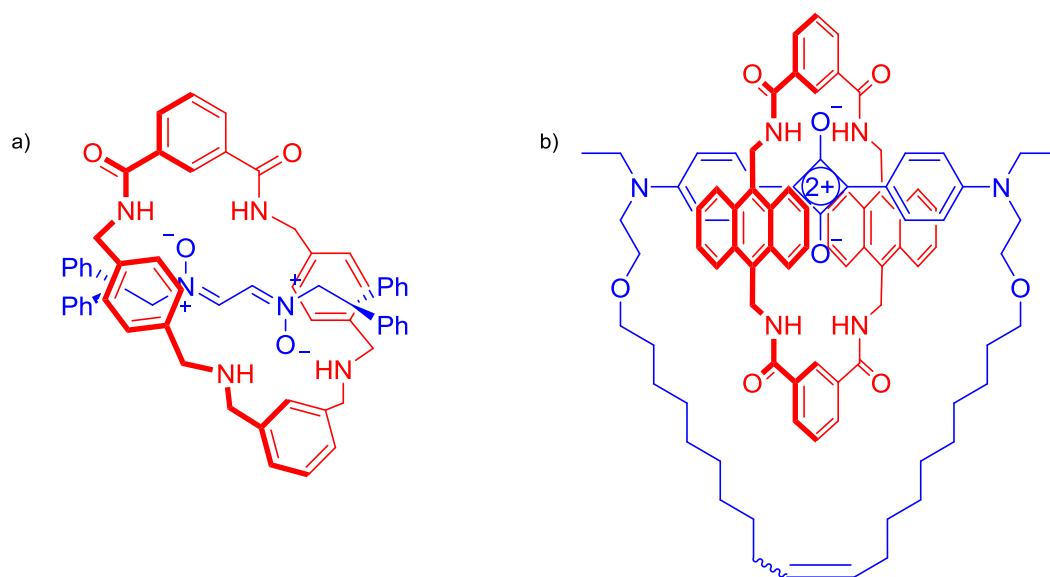


Figure 1.33 - Interlocked structures prepared using neutral template interactions: a) Leigh's nitron-based system,²⁰⁵ b) Smith's squaraine dye-based catenane.²¹⁰

Sanders has utilised the π -donor- π -acceptor interactions between electron-rich dioxynaphthalene donor units and electron-poor diimide motifs to prepare neutral [2]catenanes.^{211,212} A particular example exploiting this interaction utilised water soluble dioxynaphthalene and naphthalenediimide derivatives to afford a [2]catenane via a dynamic combinatorial library approach (Figure 1.34).²¹³ Importantly, donor-acceptor interactions often play an additional role in interlocked structure formation even when utilising a discrete template.

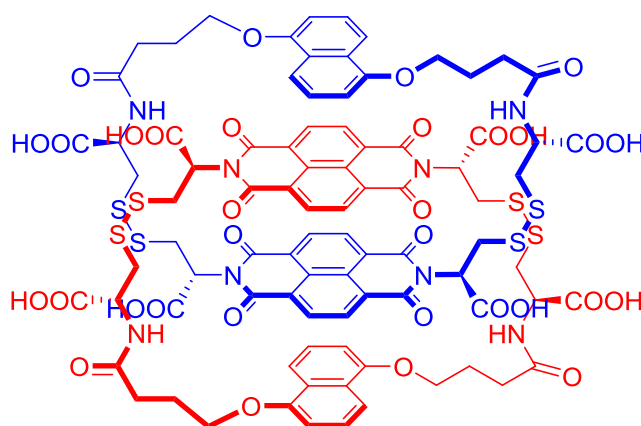


Figure 1.34 - Sanders' donor-acceptor templated [2]catenane.²¹³

1.5.2.3 Anion templated interlocked structures

The first use of an anionic template for MIM synthesis was published by Vögtle in 1999 who exploited the hydrogen bonding interaction between a tetralactam macrocycle and a phenoxide anion. On addition of an electrophilic stopper derivative, the nucleophilic substitution reaction produced the corresponding [2]rotaxane in an impressive 95% yield (Figure 1.35).²¹⁴ More recently, Flood reported the dipropargylphosphate anion templated formation of an interpenetrated assembly containing two “cyanostar” macrocycles held in place through hydrogen bonds. The [3]rotaxane was subsequently prepared by a CuAAC click reaction with two equivalents of an azide-functionalised stopper component (Scheme 1.5).²¹⁵

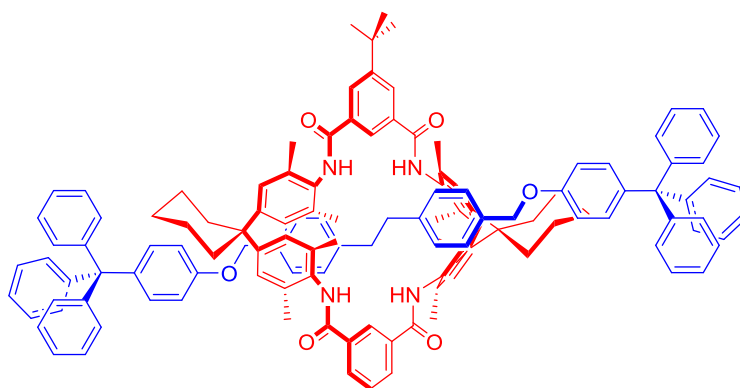
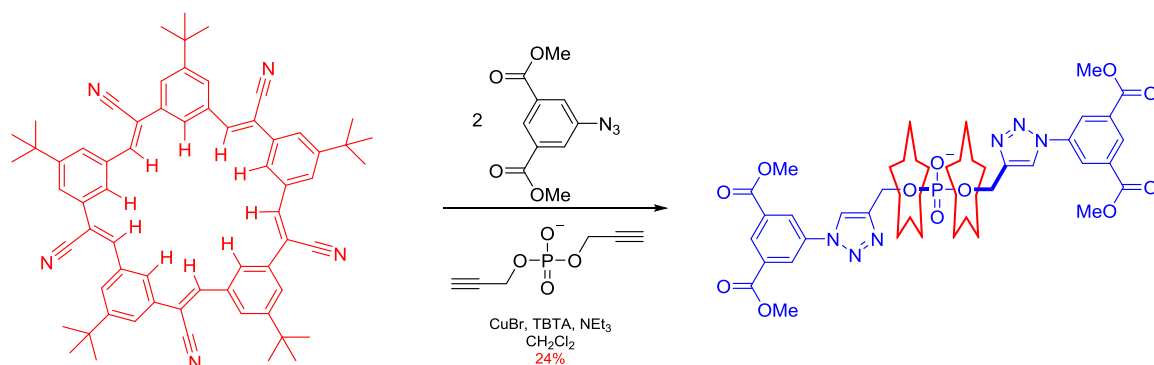


Figure 1.35 - Vogtle's seminal phenoxide templated rotaxane.²¹⁴



Scheme 1.5 - Flood's phosphate templated cyanostar [3]rotaxane.²¹⁵

Taking inspiration from the Sauvage Cu(I) template model, Beer reported the first example of a discrete inorganic anion used as a template for interlocked structure formation. After observing that the chloride anion could be used to assemble an orthogonal complex between a bis-amide pyridinium moiety and a neutral isophthalamide species, a pseudorotaxane was formed by incorporating the latter into a macrocycle (Figure 1.36).²¹⁶ Stabilisation of this interpenetrative complex assembly was achieved through four amide N-H $\cdots$ Cl⁻ hydrogen bonds and aromatic donor-acceptor interactions between the electron-poor pyridinium moiety and the electron-rich macrocyclic hydroquinone groups.

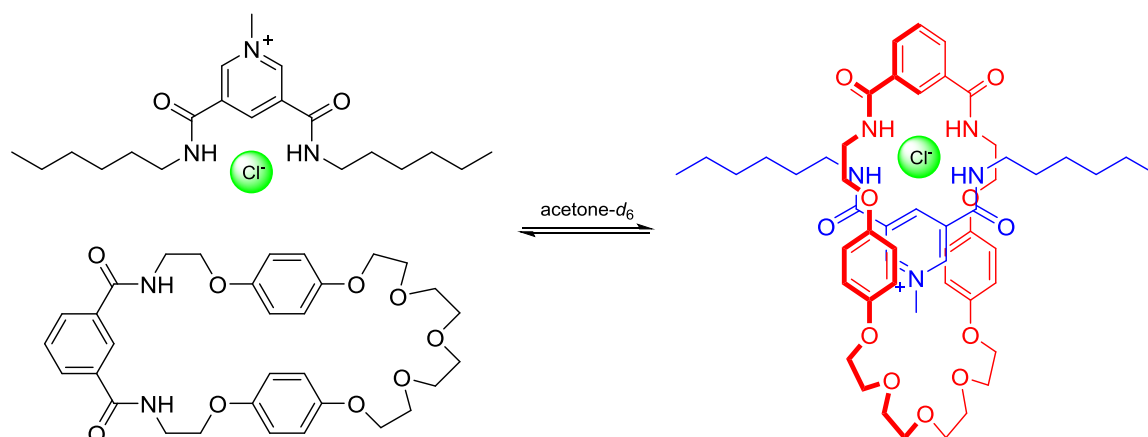
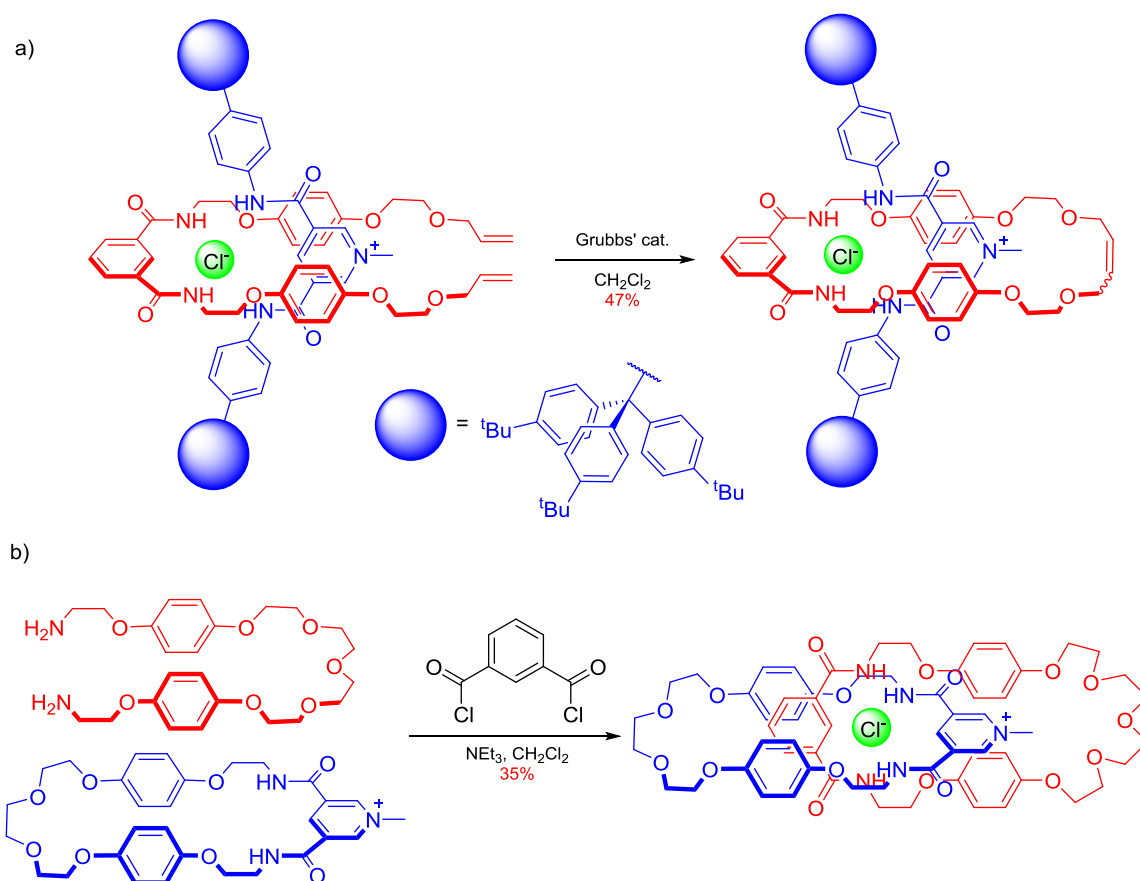


Figure 1.36 - Beer's chloride anion templated pseudorotaxane assembly.²¹⁶

This work led to the formation of a chloride anion templated [2]rotaxane by clipping a bis-vinyl macrocycle precursor around a pre-formed axle via a ring closing metathesis (RCM) reaction (Scheme 1.6a).²¹⁷ Two years later, the first discrete anion templated [2]catenane was prepared via the same chloride template method.²¹⁸ More recently, the condensation reaction between a bis-amine macrocycle precursor, a 3,5-bis-amide pyridinium containing axle or macrocycle and a bis-acid chloride has been employed as another route to anion-templated MIMs (Scheme 1.6b).^{219,220}



Scheme 1.6 - Chloride templated strategies towards interlocked structure formation: a) RCM reaction for [2]rotaxane synthesis,²¹⁷ b) Bis-amide condensation reaction for [2]catenane synthesis.²²⁰

A range of anion templates have since been used, including bromide,²²¹ sulfate,²⁰⁴ nitrate,²²² and nitrite.²²³ Furthermore, this method has been extended to access a range of higher order structures, for example a ‘handcuff’ catenane²²⁴ and a Janus rotaxane.²²⁵ Halogen bonding interlocked structures have also been prepared via anion templation. The first example was reported by Beer in 2010; a bromide templated XB [2]rotaxane formed via RCM (Figure 1.37).²²¹

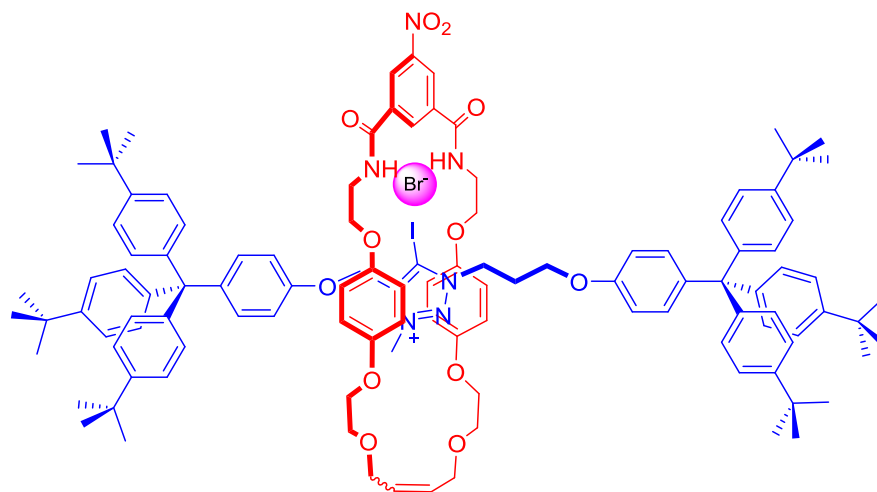


Figure 1.37 - The first anion (bromide) templated XB [2]rotaxane, reported by Beer.²²¹

1.5.3 Applications of MIMs

The synthesis of MIMs in appreciable yields has become possible through a range of different template methods, allowing for their use in a plethora of applications, including in nanotechnology as machines and switches,^{152,153} as sensors¹⁵⁵ and in catalysis.¹⁵⁶ Resulting from their unique property of having multiple component parts linked through mechanical bonds, interlocked structures may exhibit motion of one component about the other(s). In the case of a [2]rotaxane the macrocycle can exhibit translational shuttling or rotary motion about the axle, whilst [2]catenanes may also exhibit intra-ring rotary motion as either macrocycle circulates the other. This concept has recently been extended by Loeb, who reported the first example of ring through ring shuttling by a [3]rotaxane (Figure 1.38).²⁰¹

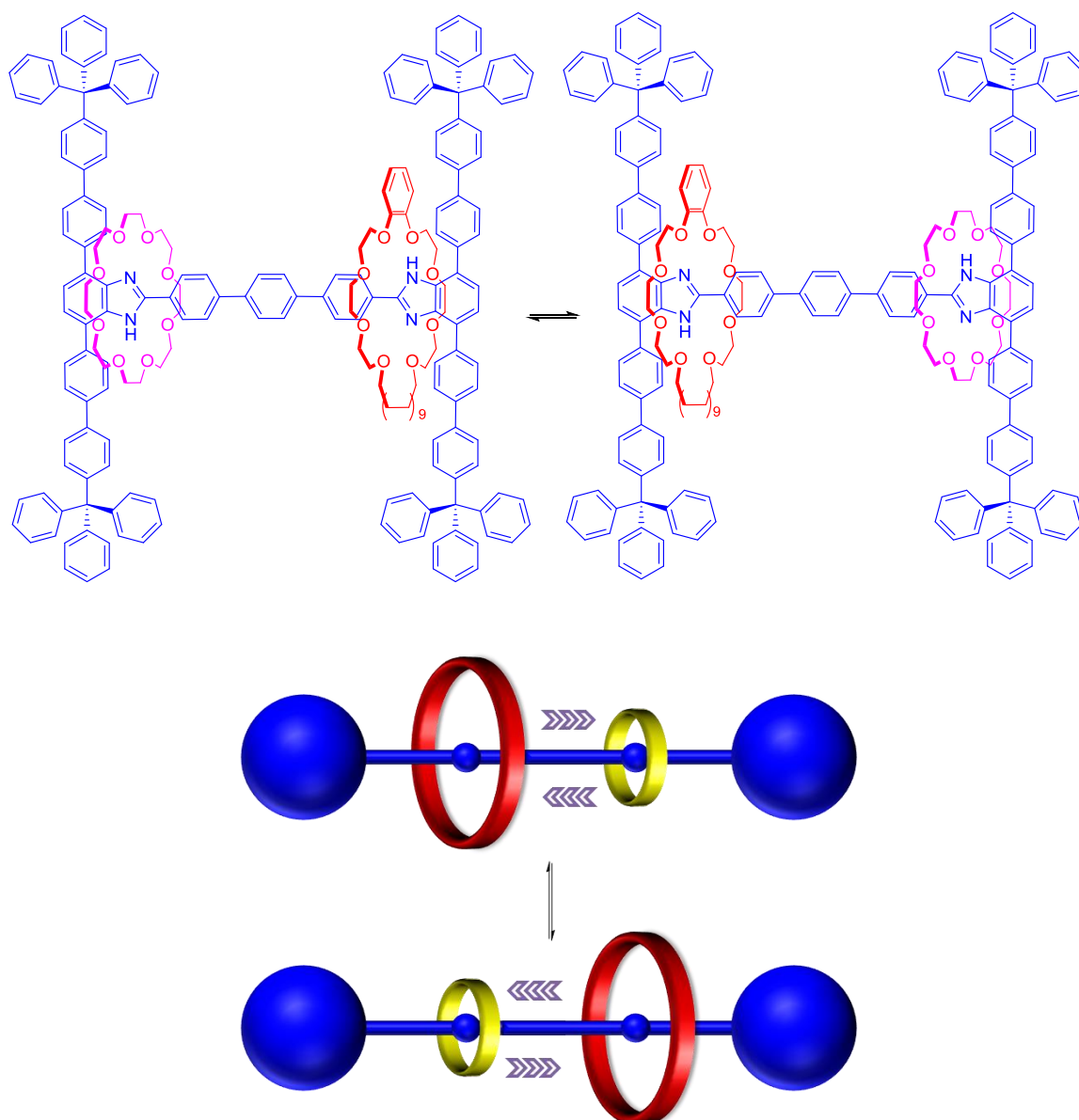


Figure 1.38 – Loeb's [3]rotaxane capable of ring-through-ring molecular shuttling.²⁰¹

The pioneers of molecular machines were Sauvage, for his seminal work in discovering an efficient route towards interlocked structures (Scheme 1.1),¹⁷¹ Stoddart, who created the first molecular shuttle (Figure 1.39)¹⁹¹ and Feringa, who developed the first synthetic molecular motor.^{226,227} This work culminated in the three being awarded the 2016 Chemistry Nobel Prize.²²⁸

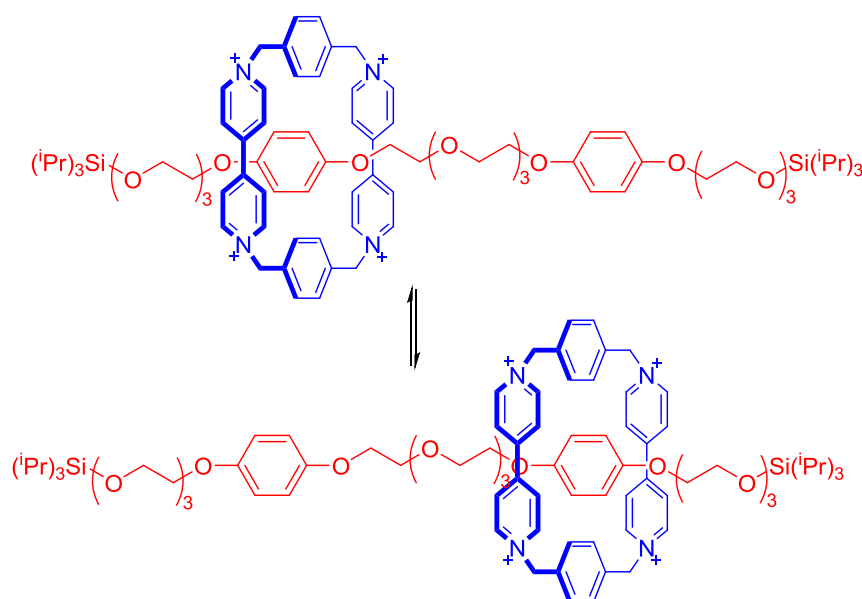
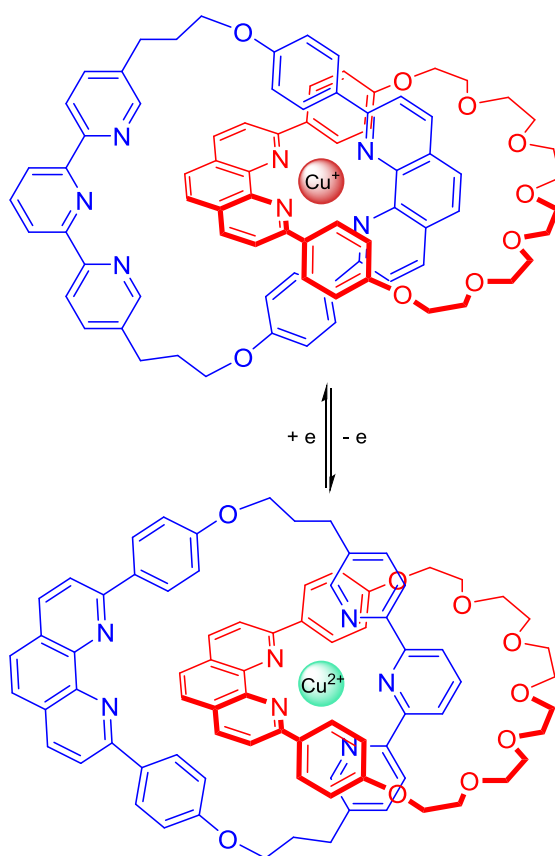


Figure 1.39 – Stoddart's dynamic rotaxane.¹⁹¹

Such dynamic conformational behaviour can be used for molecular switch/machine applications and a variety of external stimuli have been reported to facilitate molecular motion, including light,²²⁹⁻²³¹ redox,^{232,233} pH change²³⁴ and cation addition.²³⁵ Soon after their initial discoveries, both Sauvage and Stoddart reported examples of molecular motion as a result of an external stimulus. Sauvage described a hetero-[2]catenane in which one macrocycle contained a phenanthroline bidentate ligand and the other contained two metal binding sites; phenanthroline and tridentate terpyridine. Redox controlled motion was demonstrated by chemical or electrochemical oxidation of Cu(I) to Cu(II) which induced pirouetting of the macrocycle from the tetrahedral four-coordinating Cu(I) state to the five-coordinating Cu(II) state in a reversible process (Scheme 1.7).²³⁶ Meanwhile, Stoddart reported a [2]rotaxane in which it was possible to control the motion of an electron-deficient bis-4,4'-bipyridinium containing macrocycle across an axle containing two electron-rich stations in response to a chemical or electrochemical stimulus.²³⁷ MIM based molecular motion has since been expanded in the construction of a range of elaborate functional

molecular machines and switches including logic gates,²³⁸ artificial molecular muscles,^{239,240} a molecular elevator²⁴¹ and Leigh's sequence specific peptide synthesiser.^{242,243}



Scheme 1.7 - Stimulus controlled motion reported by Sauvage; altering the redox state of the bound copper leads to pirouetting of the blue macrocycle.²³⁶

The three-dimensional cavities inherent in interlocked structures have also been exploited for charged guest recognition and sensing. Cation recognition has been reported by Swager, who demonstrated the strong coordination of Zn(II) by a phenanthroline rotaxane in CH_2Cl_2 .^{244,245} Addition of the metal caused a conformational change in the molecule and consequentially quenched the emission arising from the excimer formed by the free MIM. Hiratani reported a fluorescent [1]rotaxane that selectively bound Li^+ in 9:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ (Figure 1.40).²⁴⁶ The cation binding event caused a conformational change, resulting in the appended anthracene fluorophore moving into the close proximity of the naphthalene ring within the

macrocycle. Consequently, excitation of the naphthalene led to an enhanced energy transfer to the anthracene, allowing Li^+ binding to be sensed through a significant enhancement in the fluorescence intensity.

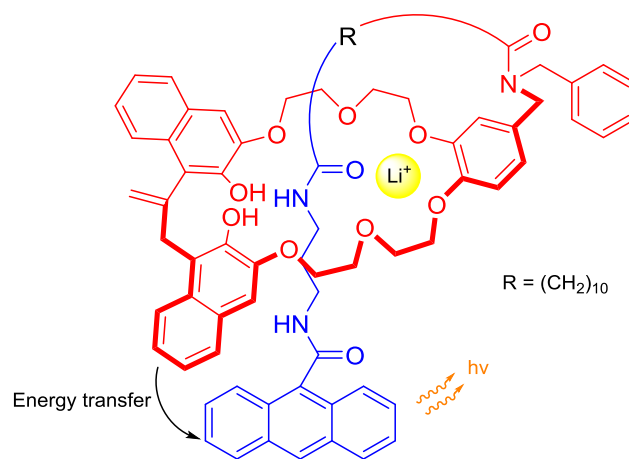


Figure 1.40 - Hiratani's Li^+ cation selective [1]rotaxane.²⁴⁶

Of relevance to the theme of this thesis, anion recognition by interlocked structures has become a prevalent area of research in recent years. Removal of an anion template that has been used to facilitate MIM formation reveals a binding cavity often complementary for the templating species. Several organic fluorophores have been integrated into interlocked architectures, such as Jeong's indolocarbazole catenane that produced a fluorescence enhancement upon the addition of several anions, in particular chloride and acetate, in 99:1 acetone/water (Figure 1.41).²⁴⁷

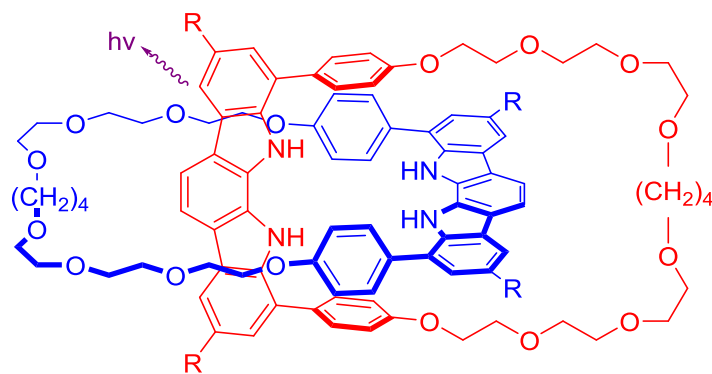


Figure 1.41 - Jeong's catenane which exhibited significant rise in emission intensity in 99:1 acetone/water on addition of several anions, $R = \text{CO}_2(\text{CH}_2)_7\text{CH}_3$.²⁴⁷

Incorporation of redox active reporter groups within interlocked structures has facilitated the preparation of electrochemical anion sensors. Beer reported a redox active ferrocene-appended rotaxane that selectively recognised chloride in CH_3CN (Figure 1.42a).²⁴⁸ This was confirmed by the maximum cathodic shift of the ferrocene/ferrocenium redox couple occurring after addition of one equivalent of Cl^- , compared to an excess quantity required for the H_2PO_4^- , BzO^- and HSO_4^- anions.

Several examples of XB anion sensors have been recently reported by Beer. A Ru(II) -bipyridyl system exhibited a significant enhancement in MLCT emission intensity upon the addition of iodide in water (Figure 1.42b),²⁴⁹ whilst a four XB donor Re(I) -complexed [2]rotaxane selectively sensed halides over oxoanions through quenching of MLCT emission in 1:1 $\text{H}_2\text{O}/\text{CH}_3\text{CN}$ (Figure 1.42c).²⁵⁰

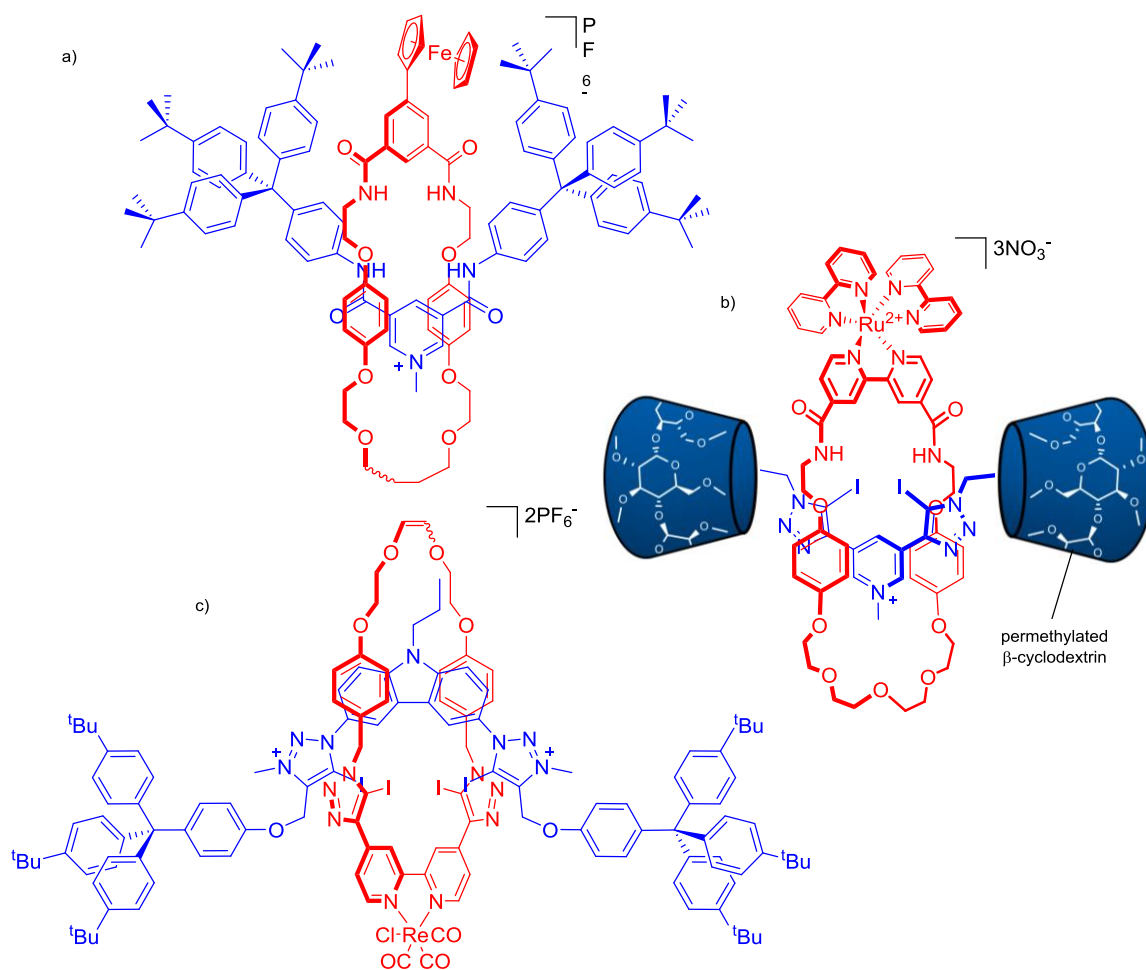


Figure 1.42 - Interlocked anion receptors reported by Beer: a) ferrocene appended redox-active chloride sensor,²⁴⁸ b) Ru(II)-based water soluble iodide receptor,²⁴⁹ c) halide binding Re(I)-based [2]rotaxane.²⁵⁰

Anion sensing via a dynamic molecular motion approach is an emerging area of host-guest chemistry. One of the first examples was reported by Lin in 2013, who described a diketopyrrolopyrrole (DPP)-based [2]rotaxane that sensed fluoride through a quenching of luminescence in DMSO, concomitant with a colour change from pink to pale green (Figure 1.43).²⁵¹ With no fluoride present the macrocycle formed a hydrogen bonding network with the pyridine motif of the axle component and pink emission from the DPP stopper group was observed. Addition of excess fluoride led to deprotonation of the amide groups and thus the macrocycle was free to shuttle along the axle, leading to a quenching of the DPP emission in the process.

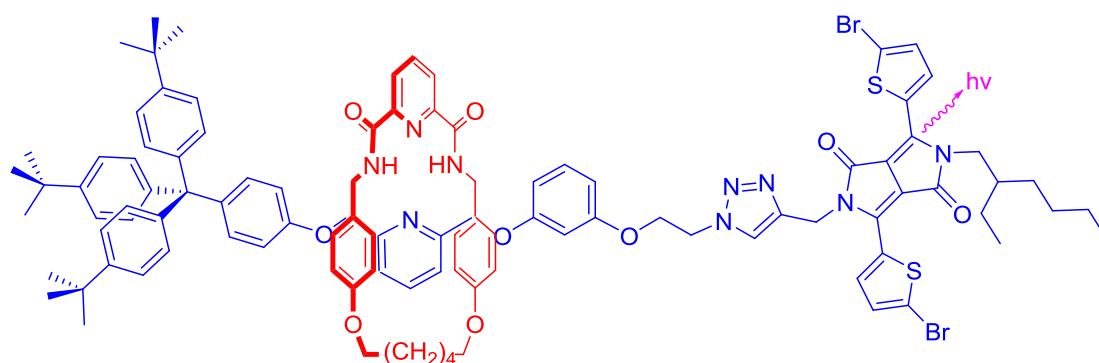
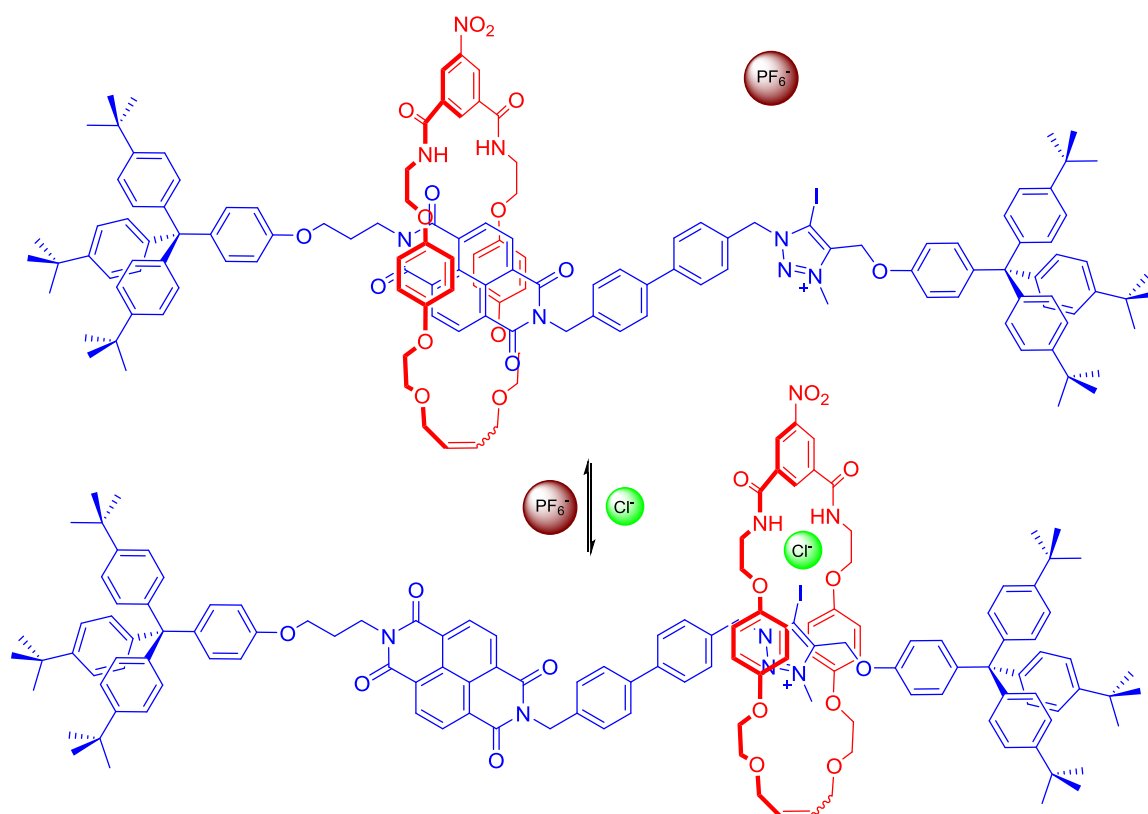


Figure 1.43 - Lin's dynamic rotaxane; colour changed from pink to pale green in the presence of fluoride in DMSO due to break up of hydrogen bonding network between macrocycle and axle.²⁵¹

A notable recent example of a molecular shuttle for anion recognition was reported by Beer which employed an XB recognition site.²⁵² As the PF_6^- salt the macrocycle resided at the electron deficient NDI station. However, on exchange to Cl^- a favourable XB interaction between the halide anion and the axle caused the macrocycle to move to the triazolium station, where it bound the anion in combination with the axle through amide-based hydrogen bonding (Scheme 1.8). A distinct naked-eye colour change from yellow to colourless was observed resulting from the loss of donor-acceptor interactions between the electron-rich macrocycle hydroquinone motifs and the extended π surface of the NDI axle station.



Scheme 1.8 - Anion induced motion of a [2]rotaxane, reported by Beer.²⁵²

1.6 Project Objectives

The broad theme of the research in this thesis is the integration of the halogen bonding 5-iodo-1,2,3-triazole motif into acyclic and interlocked receptors for anion recognition and sensing applications in competitive organic-aqueous media. Photophysical probes are incorporated into target structures in order to provide a sensory response to anion association. Novel approaches towards the synthesis of a dynamic molecular switch capable of anion induced molecular motion are also investigated.

Chapter Two discusses the preparation of a series of tetra-iodotriazole containing interlocked structures; comprising of monocationic and dicationic pairs of [2]catenanes and [2]rotaxanes. Extensive ^1H NMR titration experiments determine anion selectivity trends, with comparisons made to a previously reported bis-iodotriazole [2]catenane.

Chapter Three investigates a novel methylene-spaced bis-triazole ligand motif and its ability to co-ordinate a range of photophysically active transition metal complexes. Hydrogen and halogen bonding analogues of several bis-triazole transition metal complexes are reported and their chloride association strengths determined by ^1H NMR titration experiments. Attempts to integrate this motif into a range of macrocyclic structures are outlined with the aim of rotaxane formation via AMT. Bimetallic Ir(III) receptors based upon two bis-triazole motifs appended to a C_{60} fullerene are prepared and their anion recognition and sensing properties investigated through fluorescence spectroscopy.

Chapter Four focuses upon the synthesis of a novel benzimidazole-iodotriazole motif and its incorporation into a two station [2]rotaxane for preparation of a dynamic interlocked structure exhibiting anion induced molecular motion. Transition metal co-ordination properties of the motif are also investigated.

1.7 References

1. J. M. Lehn, *Science*, 1993, **260**, 1762-1763.
2. J. M. Lehn, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 89-112.
3. J. M. Lehn, *Science*, 1985, **227**, 849-856.
4. E. J. Corey, *Pure Appl. Chem.*, 1967, **14**, 19.
5. G. R. Desiraju, *Angew. Chem. Int. Ed. Engl.*, 1995, **34**, 2311-2327.
6. G. R. Desiraju, *Nature*, 2001, **412**, 397.
7. C. J. Pedersen, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1021-1027.
8. J. M. Lehn, *Acc. Chem. Res.*, 1978, **11**, 49-57.
9. D. J. Cram, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1009-1020.
10. D. J. Cram, T. Kaneda, R. C. Helgeson and G. M. Lein, *J. Am. Chem. Soc.*, 1979, **101**, 6752-6754.
11. C. H. Park and H. E. Simmons, *J. Am. Chem. Soc.*, 1968, **90**, 2431-2432.
12. J. L. Sessler, P. Gale, W.-S. Cho, J. F. Stoddart, S. J. Rowan, T. Aida and A. E. Rowan, *Anion Receptor Chemistry*, The Royal Society of Chemistry, 2006.
13. S. A. Benner, *ACS Cent. Sci.*, 2016, **2**, 882-884.
14. F. Delange, *Thyroid*, 1994, **4**, 107-128.
15. L. G. Wesson, *Physiology of the Human Kidney*, Grune and Stratton, 1969.
16. N. Goel, *Chloride and its Clinical Implications in Today's Clinical Practice: Not an Orphan Electrolyte*, 2015.
17. S. Ebihara, K. Shirato, N. Harata and N. Akaike, *J. Physiol.*, 1995, **484**, 77-86.
18. A. L. Berger, C. O. Randak, L. S. Ostedgaard, P. H. Karp, D. W. Vermeer and M. J. Welsh, *J. Biol. Chem.*, 2005, **280**, 5221-5226.
19. G. J. Bosman, K. Renkawek, F. P. Van Workum, I. G. Bartholomeus and W. J. De Grip, *Gerontology*, 1997, **43**, 67-78.
20. B. Moss, *Philos. Trans. Royal Soc. B*, 2008, **363**, 659-666.
21. B. Kravitz, A. Robock, L. Oman, G. Stenchikov and A. B. Marquardt, *J. Geophys. Res.: Atmospheres*, 2009, **114**, D14109.
22. E. A. Katayev, G. V. Kolesnikov and J. L. Sessler, *Chem. Soc. Rev.*, 2009, **38**, 1572-1586.
23. M. F. Chislock, E. Doster, R. A. Zitomer and A. E. Wilson, *Eutrophication: Causes, Consequences, and Controls in Aquatic Ecosystems*, *Nature Education Knowledge*, 2013, 4-10.
24. S. Morgan, *Acid Rain*, *Franklin Watts Ltd.*, 2007, 4.
25. P. D. Beer and P. A. Gale, *Angew. Chem. Int. Ed.*, 2001, **40**, 486-516.
26. R. Shannon, *Acta Crystallogr. A*, 1976, **32**, 751-767.
27. J. W. A. Steed, J. L. Atwoods, *Supramolecular Chemistry, Second Edition*, Wiley, 2009.
28. F. Hofmeister, *Arch. Für Exp. Pathol. Pharmacol.*, 1888, **24**, 247-260.
29. Y. Zhang and P. S. Cremer, *Current Opinion in Chemical Biology*, 2006, **10**, 658-663.
30. D. E. Gross, F. P. Schmidtchen, W. Antonius, P. A. Gale, V. M. Lynch and J. L. Sessler, *Chem. Eur. J.*, 2008, **14**, 7822-7827.
31. J. L. Sessler, D. E. Gross, W.-S. Cho, V. M. Lynch, F. P. Schmidtchen, G. W. Bates, M. E. Light and P. A. Gale, *J. Am. Chem. Soc.*, 2006, **128**, 12281-12288.
32. A. H. Flood, *Beilstein J. Org. Chem*, 2016, **12**, 611-627.
33. S. Camiolo, P. A. Gale, M. B. Hursthouse, M. E. Light and A. J. Shi, *Chem. Commun.*, 2002, 758-759.
34. T. Gunnlaugsson, P. E. Kruger, P. Jensen, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett.*, 2003, **44**, 8909-8913.
35. C. Caltagirone, G. W. Bates, P. A. Gale and M. E. Light, *Chem. Commun.*, 2008, 61-63.
36. W. M. Haynes, *CRC Handbook of Chemistry and Physics, 96th Edition*, CRC Press, 2015.

37. J. Emsley, *Chem. Soc. Rev.*, 1980, **9**, 91-124.
38. M. W. Hosseini and J. M. Lehn, *Helv. Chim. Acta.*, 1987, **70**, 1312-1319.
39. J. D. Watson and F. H. C. Crick, *Nature*, 1953, **171**, 737.
40. E. Arunan, R. G. R. Desiraju, R. A. Klein, J. Sadlej, S. Scheiner, I. Alkorta, D. C. Clary, R. H. Crabtree, J. J. Dannenberg, P. Hobza, H. G. Kjaergaard, A. C. Legon, B. Mennucci and D. J. Nesbitt, *Pure Appl. Chem.*, 2011, **83**, 1619.
41. T. Steiner, *Angew. Chem. Int. Ed.*, 2002, **41**, 48-76.
42. O. B. Berryman, V. S. Bryantsev, D. P. Stay, D. W. Johnson and B. P. Hay, *J. Am. Chem. Soc.*, 2007, **129**, 48-58.
43. H. T. Chifotides and K. R. Dunbar, *Acc. Chem. Res.*, 2013, **46**, 894-906.
44. Y. S. Rosokha, S. V. Lindeman, S. V. Rosokha and J. K. Kochi, *Angew. Chem. Int. Ed.*, 2004, **43**, 4650-4652.
45. S. Demeshko, S. Dechert and F. Meyer, *J. Am. Chem. Soc.*, 2004, **126**, 4508-4509.
46. D.-X. Wang and M.-X. Wang, *J. Am. Chem. Soc.*, 2013, **135**, 892-897.
47. B. L. Schottel, H. T. Chifotides and K. R. Dunbar, *Chem. Soc. Rev.*, 2008, **37**, 68-83.
48. R. E. Dawson, A. Hennig, D. P. Weimann, D. Emery, V. Ravikumar, J. Montenegro, T. Takeuchi, S. Gabutti, M. Mayor, J. Mareda, C. A. Schalley and S. Matile, *Nat. Chem.*, 2010, **2**, 533.
49. J. T. Davis, *Nat. Chem.*, 2010, **2**, 516.
50. C. R. Wade, A. E. J. Broomsgrove, S. Aldridge and F. P. Gabbaï, *Chem. Rev.*, 2010, **110**, 3958-3984.
51. Y. Kim and F. P. Gabbaï, *J. Am. Chem. Soc.*, 2009, **131**, 3363-3369.
52. H. Luecke and F. A. Quiocho, *Nature*, 1990, **347**, 402.
53. D. Gonzalez, M. Richez, C. Bergonzi, E. Chabriere and M. Elias, *Sci. Rep.*, 2014, **4**, 6636.
54. F. Wolfe-Simon, J. S. Blum, T. R. Kulp, G. W. Gordon, S. E. Hoefft, J. Pett-Ridge, J. F. Stolz, S. M. Webb, P. K. Weber, P. C. W. Davies, A. D. Anbar and R. S. Oremland, *Science*, 2011, **332**, 1163-1166.
55. M. Elias, A. Wellner, K. Goldin-Azulay, E. Chabriere, J. A. Vorholt, T. J. Erb and D. S. Tawfik, *Nature*, 2012, **491**, 134.
56. M. G. Guerrero, J. M. Vega and M. Losada, *Ann. Rev. Plant Biol.*, 1981, **32**, 169-204.
57. N. M. Koropatkin, H. B. Pakrasi and T. J. Smith, *Proc. Natl. Acad. Sci. U.S.A.*, 2006, **103**, 9820-9825.
58. B. Zhang and R. Breslow, *J. Am. Chem. Soc.*, 1993, **115**, 9353-9354.
59. C. A. Hunter and H. L. Anderson, *Angew. Chem. Int. Ed.*, 2009, **48**, 7488-7499.
60. G. Schwarzenbach, *Helv. Chim. Acta.*, 1952, **35**, 2344-2359.
61. A. E. Martell, R. D. Hancock and R. J. Motekaitis, *Coord. Chem. Rev.*, 1994, **133**, 39-65.
62. Y. Li and A. H. Flood, *Angew. Chem. Int. Ed.*, 2008, **47**, 2649-2652.
63. M. Chmielewski and J. Jurczak, *Tetrahedron Lett.*, 2004, **45**, 6007-6010.
64. M. P. Hughes and B. D. Smith, *J. Org. Chem.*, 1997, **62**, 4492-4499.
65. J. Llinares, D. Powell and K. Bowman-James, *Coord. Chem. Rev.*, 2003, **240**, 57-75.
66. B. Dietrich, B. Dilworth, J. M. Lehn, J. P. Souchez, M. Cesario, J. Guilhem and C. Pascard, *Helv. Chim. Acta.*, 1996, **79**, 569-587.
67. B. Dietrich, J. Guilhem, J. M. Lehn, C. Pascard and E. Sonveaux, *Helv. Chim. Acta.*, 1984, **67**, 91-104.
68. R. J. Motekaitis, A. E. Martell, I. Murase, J. M. Lehn and M. W. Hosseini, *Inorg. Chem.*, 1988, **27**, 3630-3636.
69. J. M. Lehn, E. Sonveaux and A. K. Willard, *J. Am. Chem. Soc.*, 1978, **100**, 4914-4916.
70. C. Bazzicalupi, A. Bencini, C. Giorgi, B. Valtancoli, V. Lippolis and A. Perra, *Inorg. Chem.*, 2011, **50**, 7202-7216.

71. J. Pouessel, C. Bazzicalupi, A. Bencini, H. Bernard, C. Giorgi, H. Handel, I. Matera, N. L. Bris, R. Tripier and B. Valtancoli, *Chem. Asian J.*, 2011, **6**, 1582-1594.
72. E. Fan, S. A. Van Arman, S. Kincaid and A. D. Hamilton, *J. Am. Chem. Soc.*, 1993, **115**, 369-370.
73. C. Schmuck and M. Schwegmann, *J. Am. Chem. Soc.*, 2005, **127**, 3373-3379.
74. E. A. Kataev, C. Müller, G. V. Kolesnikov and V. N. Khrustalev, *Eur. J. Org. Chem.*, 2014, **2014**, 2747-2753.
75. M. J. Langton, C. J. Serpell and P. D. Beer, *Angew. Chem. Int. Ed.*, 2016, **55**, 1974-1987.
76. F. P. Schmidtchen, *Angew. Chem. Int. Ed. Engl.*, 1977, **16**, 720-721.
77. F. P. Schmidtchen, *Chemische Berichte*, 1981, **114**, 597-607.
78. S. Shinoda, M. Tadokoro, H. Tsukube, S. Shinoda and R. Arakawa, *Chem. Commun.*, 1998, **0**, 181-182.
79. W. J. Belcher, M. Fabre, T. Farhan and J. W. Steed, *Org. Biomol Chem.*, 2006, **4**, 781-786.
80. V. Amendola, M. Boiocchi, B. Colasson, L. Fabbrizzi, M.-J. R. Douton and F. Ugozzoli, *Angew. Chem. Int. Ed.*, 2006, **45**, 6920-6924.
81. Y. Chun, N. Jiten Singh, I.-C. Hwang, J. Woo Lee, S. U. Yu and K. S. Kim, *Nat. Commun.*, 2013, **4**, 1797.
82. V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2002, **41**, 2596-2599.
83. J. Cai and J. L. Sessler, *Chem. Soc. Rev.*, 2014, **43**, 6198-6213.
84. A. Kumar and P. S. Pandey, *Org. Lett.*, 2008, **10**, 165-168.
85. S. Lee, B. E. Hirsch, Y. Liu, J. R. Dobscha, D. W. Burke, S. L. Tait and A. H. Flood, *Chem. Eur. J.*, 2016, **22**, 560-569.
86. S. Jin, S.-i. Kato and Y. Nakamura, *Chem. Lett.*, 2016, **45**, 869-871.
87. C. R. Bondy and S. J. Loeb, *Coord. Chem. Rev.*, 2003, **240**, 77-99.
88. C. Jia, B. Wu, S. Li, X. Huang, Q. Zhao, Q.-S. Li, and X.-J. Yang, *Angew. Chem. Int. Ed.*, 2011, **50**, 486-490.
89. V. Blažek Bregović, N. Basarić and K. Mlinarić-Majerski, *Coord. Chem. Rev.*, 2015, **295**, 80-124.
90. J. L. Sessler, S. Camiolo and P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 17-55.
91. Y. Hua and A. H. Flood, *Chem. Soc. Rev.*, 2010, **39**, 1262-1271.
92. R. A. Pascal, J. Spergel and D. Van Engen, *Tetrahedron Lett.*, 1986, **27**, 4099-4102.
93. K. Kavallieratos, S. R. de Gala, D. J. Austin and R. H. Crabtree, *J. Am. Chem. Soc.*, 1997, **119**, 2325-2326.
94. P. Anzenbacher, K. Jursíková and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 9350-9351.
95. S. Indrajit, L. J. Tae and L. Chang-Hee, *Eur. J. Org. Chem.*, 2015, **2015**, 3859-3885.
96. P. Thiampanya, N. Muangsins and B. Pulpoka, *Org. Lett.*, 2012, **14**, 4050-4053.
97. V. Haridas, S. Sahu, P. P. Praveen Kumar and A. R. Sapala, *RSC Adv.*, 2012, **2**, 12594-12605.
98. Philip A. Gale, Ethan N. W. Howe and X. Wu, *Chem*, 2016, **1**, 351-422.
99. Y. Hua, Y. Liu, C.-H. Chen and A. H. Flood, *J. Am. Chem. Soc.*, 2013, **135**, 14401-14412.
100. S. Kubik, R. Kirchner, D. Nolting and J. Seidel, *J. Am. Chem. Soc.*, 2002, **124**, 12752-12760.
101. S. Kubik, R. Goddard, R. Kirchner, D. Nolting and J. Seidel, *Angew. Chem. Int. Ed.*, 2001, **40**, 2648-2651.
102. S. Kubik and R. Goddard, *Proc. Natl. Acad. Sci. U.S.A.*, 2002, **99**, 5127-5132.
103. F. Sommer and S. Kubik, *Org. Biomol Chem.*, 2014, **12**, 8851-8860.

104. M. A. Yawer, V. Havel, and V. Sindelar, *Angew. Chem. Int. Ed.*, 2015, **54**, 276-279.
105. G. R. Desiraju, P. S. Ho, L. Kloo, A. C. Legon, R. Marquardt, P. Metrangolo, P. Politzer, G. Resnati and K. Rissanen, *Pure Appl. Chem.*, 2013, **85**, 1711.
106. A. J. Parker, J. Stewart, K. J. Donald and C. A. Parish, *J. Am. Chem. Soc.*, 2012, **134**, 5165-5172.
107. T. Clark, M. Hennemann, J. S. Murray and P. Politzer, *J. Mol. Model.*, 2007, **13**, 291-296.
108. R. Bertani, P. Sgarbossa, A. Venzo, F. Lelj, M. Amati, G. Resnati, T. Pilati, P. Metrangolo and G. Terraneo, *Coord. Chem. Rev.*, 2010, **254**, 677-695.
109. K. Rissanen, *CrystEngComm*, 2008, **10**, 1107-1113.
110. D. Cinčić, T. Frišić, W. Jones, *Chem. Eur. J.*, 2008, **14**, 747-753.
111. G. Cavallo, P. Metrangolo, R. Milani, T. Pilati, A. Priimagi, G. Resnati and G. Terraneo, *Chem. Rev.*, 2016, **116**, 2478-2601.
112. P. Metrangolo, H. Neukirch, T. Pilati and G. Resnati, *Acc. Chem. Res.*, 2005, **38**, 386-395.
113. F. Kniep, S. H. Jungbauer, Q. Zhang, S. M. Walter, S. Schindler, I. Schnapperelle, E. Herdtweck and S. M. Huber, *Angew. Chem. Int. Ed.*, 2013, **52**, 7028-7032.
114. O. Coulembier, F. Meyer and P. Dubois, *Polym. Chem.*, 2010, **1**, 434-437.
115. J.-P. Gliese, S. H. Jungbauer and S. M. Huber, *Chem. Commun.*, 2017, **53**, 12052-12055.
116. R. Wilcken, M. O. Zimmermann, A. Lange, A. C. Joerger and F. M. Boeckler, *J. Med. Chem.*, 2013, **56**, 1363-1388.
117. R. Wilcken, X. Liu, M. O. Zimmermann, T. J. Rutherford, A. R. Fersht, A. C. Joerger and F. M. Boeckler, *J. Am. Chem. Soc.*, 2012, **134**, 6810-6818.
118. M. Llinàs-Brunet, M. D. Bailey, N. Goudreau, P. K. Bhardwaj, J. Bordeleau, M. Bös, Y. Bousquet, M. G. Cordingley, J. Duan, P. Forgione, M. Garneau, E. Ghio, V. Gorys, S. Goulet, T. Halmos, S. H. Kawai, J. Naud, M.-A. Poupart and P. W. White, *J. Med. Chem.*, 2010, **53**, 6466-6476.
119. A. V. Jentzsch, D. Emery, J. Mareda, S. K. Nayak, P. Metrangolo, G. Resnati, N. Sakai and S. Matile, *Nat. Commun.*, 2012, **3**, 905.
120. A. Vargas Jentzsch, A. Hennig, J. Mareda and S. Matile, *Acc. Chem. Res.*, 2013, **46**, 2791-2800.
121. A. Vargas Jentzsch and S. Matile, *J. Am. Chem. Soc.*, 2013, **135**, 5302-5303.
122. L. C. Gilday, S. W. Robinson, T. A. Barendt, M. J. Langton, B. R. Mullaney and P. D. Beer, *Chem. Rev.*, 2015, **115**, 7118-7195.
123. A. Mele, P. Metrangolo, H. Neukirch, T. Pilati and G. Resnati, *J. Am. Chem. Soc.*, 2005, **127**, 14972-14973.
124. M. G. Sarwar, B. Dragisic, S. Sagoo and M. S. Taylor, *Angew. Chem. Int. Ed.*, 2010, **49**, 1674-1677.
125. A. Vargas Jentzsch, D. Emery, J. Mareda, P. Metrangolo, G. Resnati and S. Matile, *Angew. Chem. Int. Ed.*, 2011, **50**, 11675-11678.
126. S. Chakraborty, R. Dutta and P. Ghosh, *Chem. Commun.*, 2015, **51**, 14793-14796.
127. A. Brown and P. D. Beer, *Chem. Commun.*, 2016, **52**, 8645-8658.
128. R. Tepper, B. Schulze, M. Jäger, C. Friebe, D. H. Scharf, H. Görls and U. S. Schubert, *J. Org. Chem.*, 2015, **80**, 3139-3150.
129. K. Kaur, R. Saini, A. Kumar, V. Luxami, N. Kaur, P. Singh and S. Kumar, *Coord. Chem. Rev.*, 2012, **256**, 1992-2028.
130. S. L. Wiskur, H. Ait-Haddou, J. J. Lavigne and E. V. Anslyn, *Acc. Chem. Res.*, 2001, **34**, 963-972.
131. P. A. Gale and C. Caltagirone, *Chem. Soc. Rev.*, 2015, **44**, 4212-4227.
132. R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419-4476.

133. T. Gunnlaugsson, P. E. Kruger, T. C. Lee, R. Parkesh, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett.*, 2003, **44**, 6575-6578.
134. M. E. Huston, E. U. Akkaya and A. W. Czarnik, *J. Am. Chem. Soc.*, 1989, **111**, 8735-8737.
135. F. Zapata, A. Caballero, P. Molina, I. Alkorta and J. Elguero, *J. Org. Chem.*, 2014, **79**, 6959-6969.
136. P. A. Gale and C. Caltagirone, *Coord. Chem. Rev.*, 2018, **354**, 2-27.
137. K.-C. Chang, S.-S. Sun, M. O. Odago and A. J. Lees, *Coord. Chem. Rev.*, 2015, **284**, 111-123.
138. P. D. Beer, S. W. Dent and T. J. Wear, *J. Chem. Soc., Dalton Trans.*, 1996, **0**, 2341-2346.
139. L. H. Uppadine, F. R. Keene and P. D. Beer, *J. Chem. Soc., Dalton Trans.*, 2001, **0**, 2188-2198.
140. P. Plitt, D. E. Gross, V. M. Lynch and J. L. Sessler, *Chem. Eur. J.*, 2007, **13**, 1374-1381.
141. J. W. Steed, *Chem. Soc. Rev.*, 2009, **38**, 506-519.
142. J. A. Kitchen, E. M. Boyle and T. Gunnlaugsson, *Inorg. Chim. Acta*, 2012, **381**, 236-242.
143. H.-J. Mo, Y. Shen and B.-H. Ye, *Inorg. Chem.*, 2012, **51**, 7174-7184.
144. Q. Zhao, S. Liu, M. Shi, F. Li, H. Jing, T. Yi and C. Huang, *Organometallics*, 2007, **26**, 5922-5930.
145. T. K. Mole, W. E. Arter, I. Marques, V. Félix and P. D. Beer, *J. Organomet. Chem.*, 2015, **792**, 206-210.
146. P. D. Beer and J. Cadman, *Coord. Chem. Rev.*, 2000, **205**, 131-155.
147. Y. Willener, K. M. Joly, C. J. Moody and J. H. R. Tucker, *J. Org. Chem.*, 2008, **73**, 1225-1233.
148. P. D. Beer and A. D. Keefe, *J. Organomet. Chem.*, 1989, **375**, C40-C42.
149. T. Romero, R. A. Orenes, A. Tárraga and P. Molina, *Organometallics*, 2013, **32**, 5740-5753.
150. R. Oliveira, S. Groni, C. Fave, M. Branca, F. Mavré, D. Lorcy, M. Fourmigué and B. Schöllhorn, *Phys. Chem. Chem. Phys.*, 2016, **18**, 15867-15873.
151. J. F. Stoddart, *Angew. Chem. Int. Ed.*, 2017, **56**, 11094-11125.
152. R. Klajn, J. F. Stoddart and B. A. Grzybowski, *Chem. Soc. Rev.*, 2010, **39**, 2203-2237.
153. S. Erbas-Cakmak, D. A. Leigh, C. T. McTernan and A. L. Nussbaumer, *Chem. Rev.*, 2015, **115**, 10081-10206.
154. S. F. M. van Dongen, S. Cantekin, J. A. A. W. Elemans, A. E. Rowan and R. J. M. Nolte, *Chem. Soc. Rev.*, 2014, **43**, 99-122.
155. N. H. Evans, C. J. Serpell and P. D. Beer, *Chem. Commun.*, 2011, **47**, 8775-8777.
156. Y. Takashima, M. Osaki, Y. Ishimaru, H. Yamaguchi and A. Harada, *Angew. Chem. Int. Ed.*, 2011, **50**, 7524-7528.
157. V. Blanco, A. Carlone, K. D. Hänni, D. A. Leigh and B. Lewandowski, *Angew. Chem. Int. Ed.*, 2012, **51**, 5166-5169.
158. K. Eichstaedt, J. Jaramillo-Garcia, D. A. Leigh, V. Marcos, S. Pisano and T. A. Singleton, *J. Am. Chem. Soc.*, 2017, **139**, 9376-9381.
159. R. Barat, T. Legigan, I. Tranoy-Opalinski, B. Renoux, E. Péraudeau, J. Clarhaut, P. Poinot, A. E. Fernandes, V. Aucagne, D. A. Leigh and S. Papot, *Chem. Sci.*, 2015, **6**, 2608-2613.
160. J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, K. Rissanen and D. Schultz, *J. Am. Chem. Soc.*, 2012, **134**, 9488-9497.
161. J.-F. Ayme, G. Gil-Ramírez, D. A. Leigh, J.-F. Lemonnier, A. Markevicius, C. A. Muryn and G. Zhang, *J. Am. Chem. Soc.*, 2014, **136**, 13142-13145.

162. J.-F. Ayme, J. E. Beves, C. J. Campbell and D. A. Leigh, *Chem. Soc. Rev.*, 2013, **42**, 1700-1712.
163. K. S. Chichak, S. J. Cantrill, A. R. Pease, S.-H. Chiu, G. W. V. Cave, J. L. Atwood and J. F. Stoddart, *Science*, 2004, **304**, 1308-1312.
164. T. Prakasam, M. Lusi, M. Elhabiri, C. Platas-Iglesias, J.-C. Olsen, Z. Asfari, S. Cianfèrani-Sanglier, F. Debaene, L. J. Charbonnière and A. Trabolsi, *Angew. Chem. Int. Ed.*, 2013, **52**, 9956-9960.
165. P. R. Ashton, M. Belohradsky, D. Philp and J. F. Stoddart, *J. Chem. Soc., Chem. Commun.*, 1993, **0**, 1269-1274.
166. I. Yoon, M. Narita, T. Shimizu and M. Asakawa, *J. Am. Chem. Soc.*, 2004, **126**, 16740-16741.
167. J.-L. Ko, S.-H. Ueng, C.-W. Chiu, C.-C. Lai, Y.-H. Liu, S.-M. Peng and S.-H. Chiu, *Chem. Eur. J.*, 2010, **16**, 6950-6960.
168. E. Wasserman, *J. Am. Chem. Soc.*, 1960, **82**, 4433-4434.
169. I. T. Harrison and S. Harrison, *J. Am. Chem. Soc.*, 1967, **89**, 5723-5724.
170. G. Schill and A. Lüttringhaus, *Angew. Chem. Int. Ed. Engl.*, 1964, **3**, 546-547.
171. C. O. Dietrich-Buchecker, J.-P. Sauvage and J. P. Kintzinger, *Tetrahedron Lett.*, 1983, **24**, 5095-5098.
172. C. O. Dietrich-Buchecker, J.-P. Sauvage and J. M. Kern, *J. Am. Chem. Soc.*, 1984, **106**, 3043-3045.
173. J.-P. Sauvage and J. Weiss, *J. Am. Chem. Soc.*, 1985, **107**, 6108-6110.
174. A. Joosten, Y. Trolez, J.-P. Collin, V. Heitz and J.-P. Sauvage, *J. Am. Chem. Soc.*, 2012, **134**, 1802-1809.
175. C. O. Dietrich-Buchecker and J.-P. Sauvage, *Angew. Chem. Int. Ed. Engl.*, 1989, **28**, 189-192.
176. A.-M. L. Fuller, D. A. Leigh, P. J. Lusby, A. M. Z. Slawin and D. B. Walker, *J. Am. Chem. Soc.*, 2005, **127**, 12612-12619.
177. S. Li, J. Huang, F. Zhou, T. R. Cook, X. Yan, Y. Ye, B. Zhu, B. Zheng and P. J. Stang, *J. Am. Chem. Soc.*, 2014, **136**, 5908-5911.
178. S. M. Goldup, D. A. Leigh, P. J. Lusby, R. T. McBurney and A. M. Slawin, *Angew. Chem. Int. Ed.*, 2008, **47**, 6999-7003.
179. J.-P. Sauvage and M. Ward, *Inorg. Chem.*, 1991, **30**, 3869-3874.
180. D. A. Leigh, P. J. Lusby, R. T. McBurney, A. Morelli, A. M. Z. Slawin, A. R. Thomson and D. B. Walker, *J. Am. Chem. Soc.*, 2009, **131**, 3762-3771.
181. L. Hogg, D. A. Leigh, P. J. Lusby, A. Morelli, S. Parsons and J. K. Y. Wong, *Angew. Chem. Int. Ed.*, 2004, **43**, 1218-1221.
182. S.-T. Tung, C.-C. Lai, Y.-H. Liu, S.-M. Peng and S.-H. Chiu, *Angew. Chem. Int. Ed.*, 2013, **52**, 13269-13272.
183. S.-T. Tung, C.-C. Lai, Y.-H. Liu, S.-M. Peng and S.-H. Chiu, *Chem. Eur. J.*, 2014, **20**, 4563-4567.
184. V. Aucagne, K. D. Hänni, D. A. Leigh, P. J. Lusby and D. B. Walker, *J. Am. Chem. Soc.*, 2006, **128**, 2186-2187.
185. J. D. Crowley, S. M. Goldup, A.-L. Lee, D. A. Leigh and R. T. McBurney, *Chem. Soc. Rev.*, 2009, **38**, 1530-1541.
186. H. Lahlali, K. Jobe, M. Watkinson and S. M. Goldup, *Angew. Chem. Int. Ed.*, 2011, **50**, 4151-4155.
187. S. Saito, E. Takahashi and K. Nakazono, *Org. Lett.*, 2006, **8**, 5133-5136.
188. J. Berná, J. D. Crowley, S. M. Goldup, K. D. Hänni, A.-L. Lee and D. A. Leigh, *Angew. Chem. Int. Ed.*, 2007, **46**, 5709-5713.
189. M. J. Langton, J. D. Matichak, A. L. Thompson and H. L. Anderson, *Chem. Sci.*, 2011, **2**, 1897-1901.

190. S. M. Goldup, D. A. Leigh, R. T. McBurney, P. R. McGonigal and A. Plant, *Chem. Sci.*, 2010, **1**, 383-386.
191. P. L. Anelli, N. Spencer and J. F. Stoddart, *J. Am. Chem. Soc.*, 1991, **113**, 5131-5133.
192. P. R. Ashton, O. A. Matthews, S. Menzer, F. M. Raymo, N. Spencer, J. F. Stoddart, D. J. Williams, *Liebigs Annalen*, 1997, **1997**, 2485-2494.
193. W. R. Dichtel, O. Š. Miljanić, J. M. Spruell, J. R. Heath and J. F. Stoddart, *J. Am. Chem. Soc.*, 2006, **128**, 10388-10390.
194. M. E. Belowich, C. Valente, R. A. Smaldone, D. C. Friedman, J. Thiel, L. Cronin and J. F. Stoddart, *J. Am. Chem. Soc.*, 2012, **134**, 5243-5261.
195. D. B. Amabilino, P. R. Ashton, A. S. Reder, N. Spencer and J. F. Stoddart, *Angew. Chem. Int. Ed. Engl.*, 1994, **33**, 1286-1290.
196. C. M. Gothard, C. J. Bruns, N. A. Gothard, B. A. Grzybowski and J. F. Stoddart, *Org. Lett.*, 2012, **14**, 5066-5069.
197. J. Sun, Y. Wu, Z. Liu, D. Cao, Y. Wang, C. Cheng, D. Chen, M. R. Wasielewski and J. F. Stoddart, *J. Phys. Chem. A*, 2015, **119**, 6317-6325.
198. W. Jiang, H. D. F. Winkler and C. A. Schalley, *J. Am. Chem. Soc.*, 2008, **130**, 13852-13853.
199. N. Noujeim, K. Zhu, V. N. Vukotic and S. J. Loeb, *Org. Lett.*, 2012, **14**, 2484-2487.
200. K. Zhu, N. Vukotic and S. J. Loeb, *Angew. Chem. Int. Ed.*, 2012, **51**, 2168-2172.
201. K. Zhu, G. Baggi and S. J. Loeb, *Nat. Chem.*, 2018, **10**, 625-630.
202. F. Vögtle, S. Meier and R. Hoss, *Angew. Chem. Int. Ed. Engl.*, 1992, **31**, 1619-1622.
203. C. A. Hunter, *J. Am. Chem. Soc.*, 1992, **114**, 5303-5311.
204. K. M. Mullen and P. D. Beer, *Chem. Soc. Rev.*, 2009, **38**, 1701-1713.
205. D. M. D'Souza, D. A. Leigh, L. Mottier, K. M. Mullen, F. Paolucci, S. J. Teat and S. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 9465-9470.
206. J. J. Gassensmith, J. M. Baumes and B. D. Smith, *Chem. Commun.*, 2009, 6329-6338.
207. E. Arunkumar, C. C. Forbes, B. C. Noll and B. D. Smith, *J. Am. Chem. Soc.*, 2005, **127**, 3288-3289.
208. M. S. Vickers and P. D. Beer, *Chem. Soc. Rev.*, 2007, **36**, 211-225.
209. J. J. Gassensmith, S. Matthys, J.-J. Lee, A. Wojcik, P. V. Kamat and B. D. Smith, *Chem. Eur. J.*, 2010, **16**, 2916-2921.
210. J.-J. Lee, J. M. Baumes, R. D. Connell, A. G. Oliver and B. D. Smith, *Chem. Commun.*, 2011, **47**, 7188-7190.
211. D. G. Hamilton, J. K. M. Sanders, J. E. Davies, W. Clegg and S. J. Teat, *Chem. Commun.*, 1997, 897-898.
212. F. B. L. Cougnon, H. Y. Au-Yeung, G. D. Pantoş and J. K. M. Sanders, *J. Am. Chem. Soc.*, 2011, **133**, 3198-3207.
213. H. Y. Au-Yeung, G. D. Pantoş and J. K. M. Sanders, *Proc. Natl. Acad. Sci. U.S.A.*, 2009, **106**, 10466-10470.
214. G. Hübner, J. Gläser, C. Seel and F. Vögtle, *Angew. Chem. Int. Ed.*, 1999, **38**, 383-386.
215. S. Lee, C.-H. Chen and A. H. Flood, *Nat. Chem.*, 2013, **5**, 704.
216. J. A. Wisner, P. D. Beer, N. G. Berry and B. Tomapatanaget, *Proc. Natl. Acad. Sci. U.S.A.*, 2002, **99**, 4983-4986.
217. J. A. Wisner, P. D. Beer, M. G. B. Drew and M. R. Sambrook, *J. Am. Chem. Soc.*, 2002, **124**, 12469-12476.
218. M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul and A. R. Cowley, *J. Am. Chem. Soc.*, 2004, **126**, 15364-15365.
219. L. M. Hancock and P. D. Beer, *Chem. Eur. J.*, 2009, **15**, 42-44.
220. L. M. Hancock, L. C. Gilday, N. L. Kilah, C. J. Serpell and P. D. Beer, *Chem. Commun.*, 2011, **47**, 1725-1727.

221. N. L. Kilah, M. D. Wise, C. J. Serpell, A. L. Thompson, N. G. White, K. E. Christensen and P. D. Beer, *J. Am. Chem. Soc.*, 2010, **132**, 11893-11895.
222. M. J. Langton and P. D. Beer, *Chem. Commun.*, 2014, **50**, 8124-8127.
223. M. J. Langton, O. A. Blackburn, T. Lang, S. Faulkner and P. D. Beer, *Angew. Chem. Int. Ed.* 2014, **53**, 11463 –11466.
224. N. H. Evans, C. J. Serpell and P. D. Beer, *Angew. Chem. Int. Ed.*, 2011, **50**, 2507-2510.
225. N. H. Evans and P. D. Beer, *Chem. Eur. J.*, 2011, **17**, 10542-10546.
226. N. Koumura, R. W. J. Zijlstra, R. A. van Delden, N. Harada and B. L. Feringa, *Nature*, 1999, **401**, 152.
227. D. A. Leigh, *Angew. Chem. Int. Ed.*, 2016, **55**, 14506-14508.
228. Nobel Prizes 2016, *Angew. Chem. Int. Ed.*, 2016, **55**, 13925-13925.
229. V. Balzani, M. Clemente-León, A. Credi, B. Ferrer, M. Venturi, A. H. Flood and J. F. Stoddart, *Proc. Natl. Acad. Sci. U.S.A.*, 2006, **103**, 1178-1183.
230. V. Fritz, M. W. Manfred, M. Ute, B. Martin and R. Kari, *Angew. Chem. Int. Ed. Engl.*, 1993, **32**, 1295-1297.
231. A. M. Brouwer, C. Frochot, F. G. Gatti, D. A. Leigh, L. c. Mottier, F. Paolucci, S. Roffia and G. W. H. Wurpel, *Science*, 2001, **291**, 2124-2128.
232. P. Raiteri, G. Bussi, C. S. Cucinotta, A. Credi, J. F. Stoddart, and M. Parrinello, *Angew. Chem. Int. Ed.*, 2008, **47**, 3536-3539.
233. P. R. Ashton, R. Ballardini, V. Balzani, A. Credi, K. R. Dress, E. Ishow, C. J. Kleverlaan, O. Kocian, J. A. Preece, N. Spencer, J. F. Stoddart, M. Venturi and S. Wenger, *Chem. Eur. J.*, 2000, **6**, 3558-3574.
234. F. Coutrot, C. Romuald and E. Busseron, *Org. Lett.*, 2008, **10**, 3741-3744.
235. A. V. Leontiev, C. J. Serpell, N. G. White and P. D. Beer, *Chem. Sci.*, 2011, **2**, 922-927.
236. A. Livoreil, C. O. Dietrich-Buchecker and J.-P. Sauvage, *J. Am. Chem. Soc.*, 1994, **116**, 9399-9400.
237. R. A. Bissell, E. Córdova, A. E. Kaifer and J. F. Stoddart, *Nature*, 1994, **369**, 133.
238. C. P. Collier, E. W. Wong, M. Belohradský, F. M. Raymo, J. F. Stoddart, P. J. Kuekes, R. S. Williams and J. R. Heath, *Science*, 1999, **285**, 391-394.
239. C. Romuald, E. Busseron and F. Coutrot, *J. Org. Chem.*, 2010, **75**, 6516-6531.
240. C. Romuald, A. Arda, C. Clavel, J. Jimenez-Barbero and F. Coutrot, *Chem. Sci.*, 2012, **3**, 1851-1857.
241. J. D. Badjić, V. Balzani, A. Credi, S. Silvi and J. F. Stoddart, *Science*, 2004, **303**, 1845-1849.
242. E. R. Kay and D. A. Leigh, *Angew. Chem. Int. Ed.*, 2015, **54**, 10080-10088.
243. B. Lewandowski, G. De Bo, J. W. Ward, M. Papmeyer, S. Kuschel, M. J. Aldegunde, P. M. E. Gramlich, D. Heckmann, S. M. Goldup, D. M. D'Souza, A. E. Fernandes and D. A. Leigh, *Science*, 2013, **339**, 189-193.
244. M. J. MacLachlan, A. Rose and T. M. Swager, *J. Am. Chem. Soc.*, 2001, **123**, 9180-9181.
245. J. E. M. Lewis, M. Galli and S. M. Goldup, *Chem. Commun.*, 2017, **53**, 298-312.
246. K. Hiratani, M. Kaneyama, Y. Nagawa, E. Koyama and M. Kanasato, *J. Am. Chem. Soc.*, 2004, **126**, 13568-13569.
247. M. K. Chae, J.-m. Suk and K.-S. Jeong, *Tetrahedron Lett.*, 2010, **51**, 4240-4242.
248. N. H. Evans and P. D. Beer, *Org. Biomol Chem.*, 2011, **9**, 92-100.
249. M. J. Langton, I. Marques, S. W. Robinson, V. Félix and P. D. Beer, *Chem. Eur. J.*, 2016, **22**, 185-192.
250. B. R. Mullaney, A. L. Thompson and P. D. Beer, *Angew. Chem. Int. Ed.*, 2014, **53**, 11458-11462.
251. M. V. R. Raju and H.-C. Lin, *Org. Lett.*, 2013, **15**, 1274-1277.

252. T. A. Barendt, S. W. Robinson and P. D. Beer, *Chem. Sci.*, 2016, **7**, 5171-5180.

Chapter Two

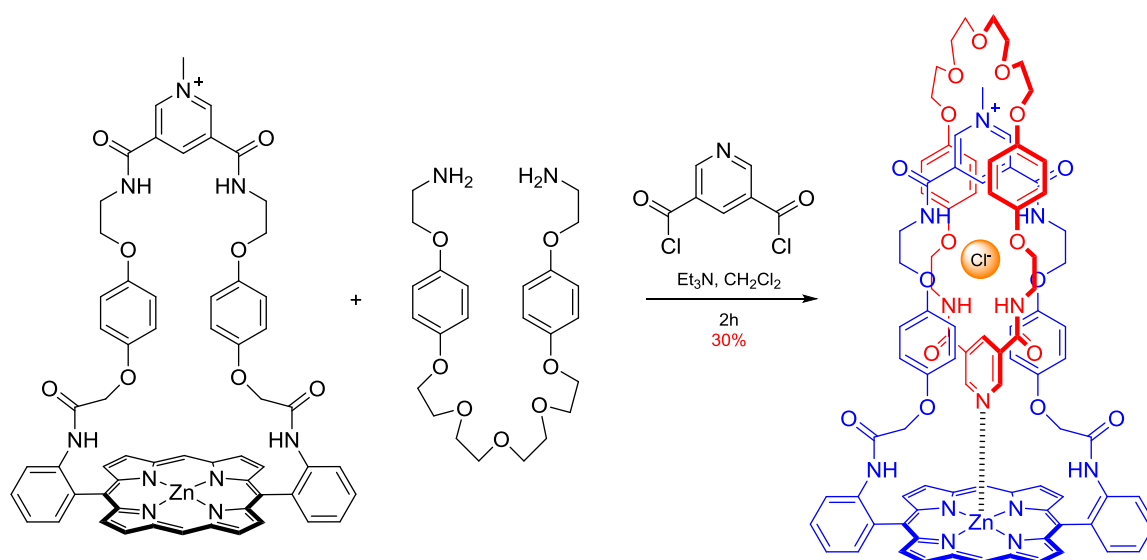
Halogen bonding tetra-iodotriazole containing
host structures for anion recognition

2 Halogen bonding tetra-iodotriazole containing host structures for anion recognition

2.1 Introduction

The first example of interlocked structure formation via a chloride template approach was reported by Beer in 2002, which utilised a ring closing metathesis (RCM) reaction on a pseudorotaxane assembly to synthesise a [2]rotaxane.¹ Subsequently, in 2004, the first [2]catenane was described employing the same halide template method,² since which time many examples have been reported utilising a range of discrete anions including Br^- , NO_3^- , NO_2^- and SO_4^{2-} to template the preparation of interlocked structures.³⁻⁶ Another reaction exploited for anion template rotaxane and catenane formation is the bis-amide condensation of a bis-amine macrocycle precursor and a bis-acid chloride around a preformed axle or macrocycle.^{7,8}

Removal of the discrete anion template after MIM formation reveals a three-dimensional anion binding cavity in the proximity of the mechanical bond, which is often selective for the templating anion guest species. For example, Beer's chloride-templated strapped-porphyrin containing catenane (formed via the bis-amide condensation method) exhibited an association constant of 2144 M^{-1} for chloride in $\text{DMSO}-d_6$, with no evidence of binding other halides observed (Scheme 2.1).⁹



Scheme 2.1 - Beer's chloride selective strapped-porphyrin catenane, formed via a chloride templated bis-amide condensation method.⁹

The 1,2,3-triazole moiety has been integrated into a range of interlocked structures for anion recognition owing to its synthetic accessibility and potential for further functionalisation. Li and co-workers reported a homo-indolocarbazole based [2]catenane formed by the copper(I)-catalysed alkyne-azide cycloaddition (CuAAC) 'click' reaction; in the presence of chloride two indolocarbazole bis-alkyne molecules formed an orthogonal assembly and upon bis-azide addition the [2]catenane was produced in a double cyclisation reaction in 18% yield (Figure 2.1a).¹⁰ Removal of the template revealed a cavity selective for chloride in CH₂Cl₂. A particularly potent motif for initiating interlocked structure formation via anion templation is 3,5-bis(triazole)-pyridinium; the convergent hydrogen bond (HB) donor sites and cationic charge allows for strong non-covalent interactions with the anion guest species. The motif was first reported by Beer, who's [2]rotaxane exhibited a preference for bromide in 1:1 CDCl₃/CD₃OD (Figure 2.1b).¹¹ The analogous [2]catenane displayed selectivity for halides over dihydrogen phosphate in 1:1 CDCl₃/CD₃OD.¹²

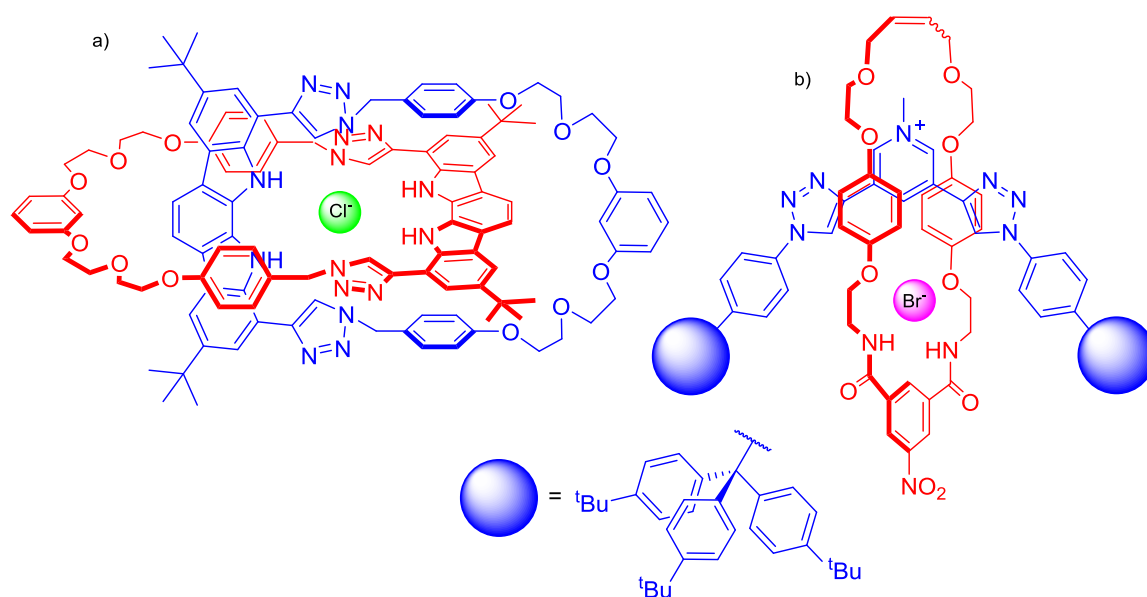


Figure 2.1 - a) Li's triazole based chloride selective homo-[2]catenane,¹⁰ b) Beer's bromide selective [2]rotaxane based upon 3,5-bis(triazole)-pyridinium motif.¹¹

Replacement of the triazole motif with a 5-iodo-1,2,3-triazole analogue has recently been achieved, resulting in a remarkable enhancement in anion guest association as a consequence of the potent halogen bond (XB).¹³ In a highly competitive solvent mixture of 45:45:10 CDCl₃/CD₃OD/D₂O, catenane **2.1**·PF₆ bound bromide and iodide with an association constant $>10^4$ M⁻¹ (Figure 2.2), compared to the HB analogue which exhibited the strongest association with chloride ($K_a = 680$ M⁻¹) in 1:1 CDCl₃/CD₃OD. The increase in strength of halide anion association resulting from the incorporation of halogen bonding interactions, as illustrated in this example, provides the underlying motivation for the project described in this chapter.

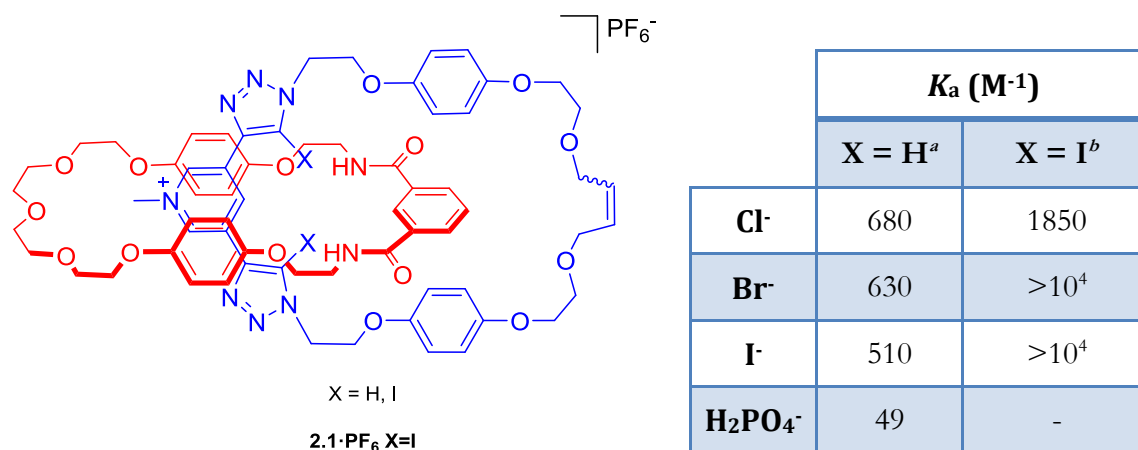


Figure 2.2 - HB and XB catenanes reported by Beer, with association constants calculated using WinEQNMR2.^{13, 14} Solvent: ^a=CDCl₃/CD₃OD (1:1), ^b=CDCl₃/CD₃OD/D₂O (45:45:10).

2.1.1 Chapter aims

This chapter investigates how increasing the number of XB donors in a host structure impacts on its anion recognition properties through the preparation of a series of novel acyclic and interlocked tetra-iodotriazole containing receptors based upon the 3,5-bis-iodotriazole pyridinium motif. In particular XB catenanes and rotaxanes are rare; the work presented in Figure 2.2 is extended through the preparation of novel monocationic and dicationic analogues of tetra-iodotriazole [2]catenanes and [2]rotaxanes. Their anion recognition properties, determined by ¹H NMR titration studies, are discussed, with comparisons made to the previously reported bis-iodotriazole [2]catenane **2.1·PF₆**.¹³

2.2 Tetra-iodotriazole acyclic receptor

The synthesis of an acyclic receptor offers a convenient method to probe a target motif before embarking on the extensive synthesis of an interlocked structure. The target acyclic

system was designed to contain four iodotriazole moieties, with the aim of generating an anion binding site in which all four are convergent (Figure 2.3).

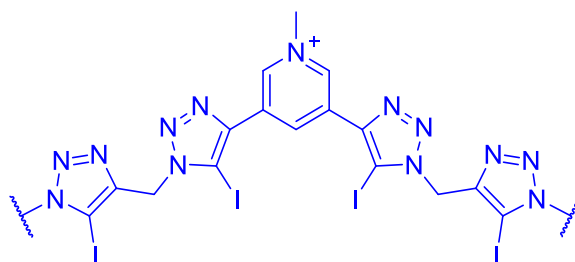


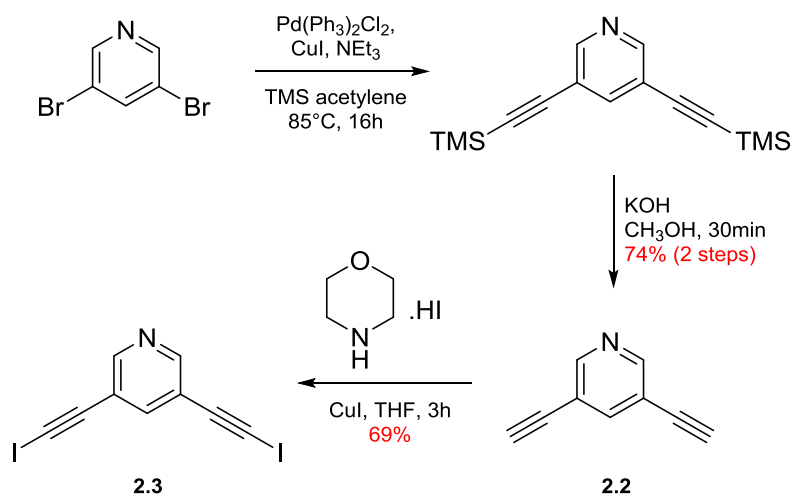
Figure 2.3 - Tetra-iodotriazole pyridinium motif investigated in this chapter.

2.2.1 Synthesis

The regioisomer synthesis of 1,2,3-triazoles was first reported by Sharpless in 2002 through the [3+2] cycloaddition of an azide with a terminal alkyne using a Cu(I) catalyst, a process known as the copper-catalysed azide-alkyne cycloaddition (CuAAC) ‘click’ reaction.¹⁵ This proceeds regioselectively to yield the 1,4-substituted triazole and was later developed to give the 5-iodo analogue via the corresponding iodoalkyne.¹⁶ More recently, Brotherton reported a “one-pot” method; the active Cu(I) catalyst and the electrophilic source of iodine, triiodide, are both formed *in situ* on addition of Cu(II) and NaI.¹⁷ This offers a convenient and efficient route to the iodotriazole motif which has been demonstrated to act as a powerful halogen bond (XB) donor to Lewis base species such as anions.

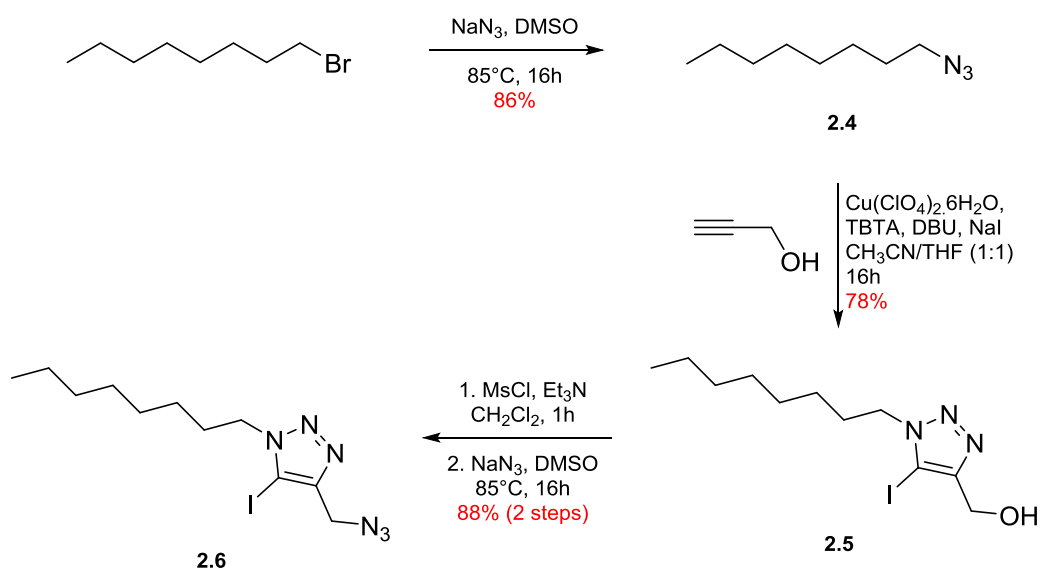
The first step of the synthesis towards the target acyclic receptor was to form the central pyridine-bis-iodoalkyne synthon. 3,5-Bis(ethynyl)pyridine **2.2** was synthesised through literature procedures (Scheme 2.2).^{12,18} Initially, a Sonogashira coupling was carried out between the commercially available 3,5-dibromopyridine and trimethylsilyl-acetylene to afford the off-white TMS-protected diethynylpyridine intermediate. Subsequently, the TMS group was cleaved with potassium hydroxide in methanol to afford 3,5-diethynylpyridine **2.2**.

The bis-iodoalkyne derivative **2.3** was obtained through the reaction of **2.2** with *N*-iodomorpholine in the presence of CuI, isolated in 69% yield after purification via column chromatography.

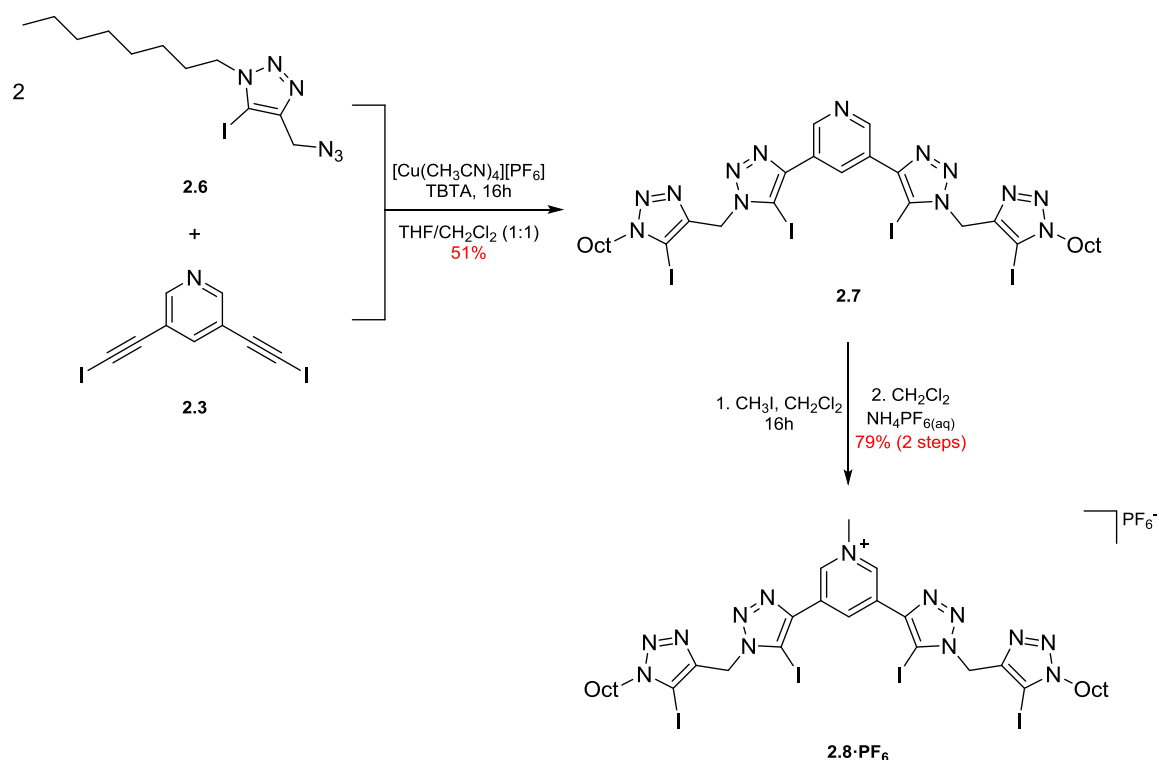


*Scheme 2.2 - Preparation of pyridine-bis-iodoalkyne **2.3**.*

Synthesis of a target azide functionalised iodotriazole derivative **2.6** began with the preparation of octyl azide **2.4** via the substitution reaction between octyl bromide and NaN_3 in DMSO (Scheme 2.3). Utilising the one-pot iodo-click reaction, azide **2.4** and propargyl alcohol were reacted with an excess of Cu(I) and NaI, a stoichiometric amount of DBU and a catalytic amount of TBTA to yield iodotriazole alcohol **2.5** in 78% yield after purification. Conversion of the terminal hydroxyl group of alcohol **2.5** to a mesylate, through the use of mesyl chloride in the presence of an excess of NEt_3 , was achieved, before subsequent substitution to the corresponding azide by refluxing with NaN_3 in DMSO afforded target azide **2.6** in 88% yield.

Scheme 2.3 - Synthesis of azide **2.5**.

Bis-iodoalkyne **2.3** and two equivalents of azide **2.6** were reacted under standard two-pot iodo-click conditions (a catalytic amount of both Cu(I) and TBTA) to obtain tetra-iodotriazole **2.7** in 51% yield (Scheme 2.4). Subsequently, this was methylated at the pyridine nitrogen position using excess CH_3I in dry CH_2Cl_2 to yield pyridinium tetra-iodotriazole **2.8·I**. The iodide salt was converted to the non-coordinating hexafluorophosphate salt **2.8·PF₆**, necessary for anion binding studies, through repeated washing with $\text{NH}_4\text{PF}_6(\text{aq})$.

Scheme 2.4 - Preparation of acyclic receptor **2.8·PF₆**.

The ^1H NMR spectrum of **2.8·PF₆** in 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$ exhibited characteristic peaks confirming its successful synthesis (Figure 2.4). The appearance of environment *d* was a result of the methylene spacer group between the two triazole moieties and was diagnostic of the success of the click reaction. Proton *c* displayed a significant downfield shift compared to the unmethylated **2.7**, consistent with previously reported examples,¹³ whilst the 3H singlet at a chemical shift of ~ 3 ppm corresponded to protons *a*, indicative of successful pyridine methylation. The ^1H - ^1H COSY NMR spectrum revealed coupling of protons *b* and *c* in the pyridinium ring, as well as expected interactions arising from the proximity of proton environments in the octyl chains (Figure 2.4).

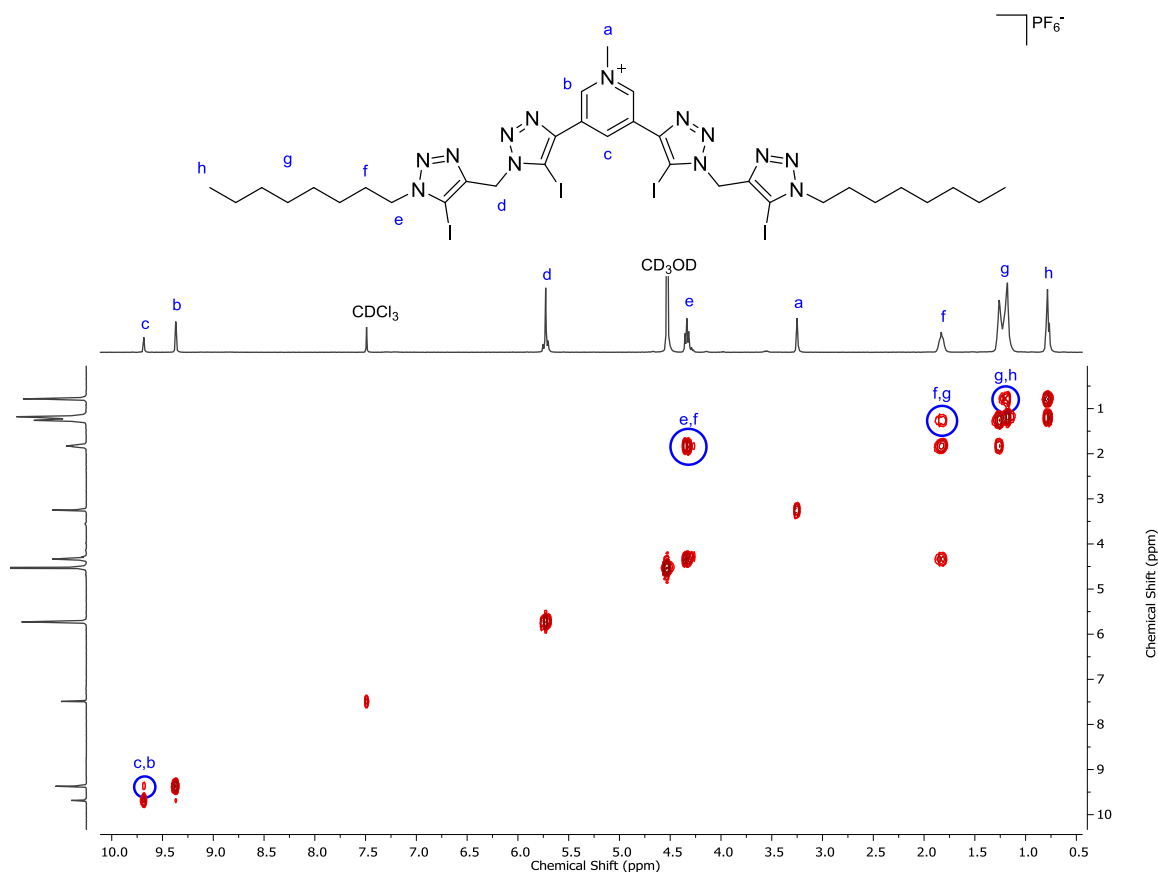


Figure 2.4 - ^1H - ^1H COSY NMR spectrum of **2.8**· PF_6 (1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$, 400 MHz, 298K).

2.2.2 ^1H NMR anion recognition studies

The anion binding properties of acyclic receptor **2.8**· PF_6 were investigated through ^1H NMR titration experiments in $\text{DMSO}-d_6$. The chemical shift of the receptor's proton resonances were monitored upon addition of aliquots of a variety of anions added as their tetrabutylammonium (TBA) salts.

Initially, pyridinium protons *c* and *b* were very closely resonant; however, upon anion addition these signals diverged significantly. Large downfield perturbations were observed for proton *c*, with only small shifts exhibited for other environments, suggesting binding in the central vicinity of the receptor. An example of ^1H NMR titration data recorded for the addition of TBACl to **2.8**· PF_6 is depicted in Figure 2.5.

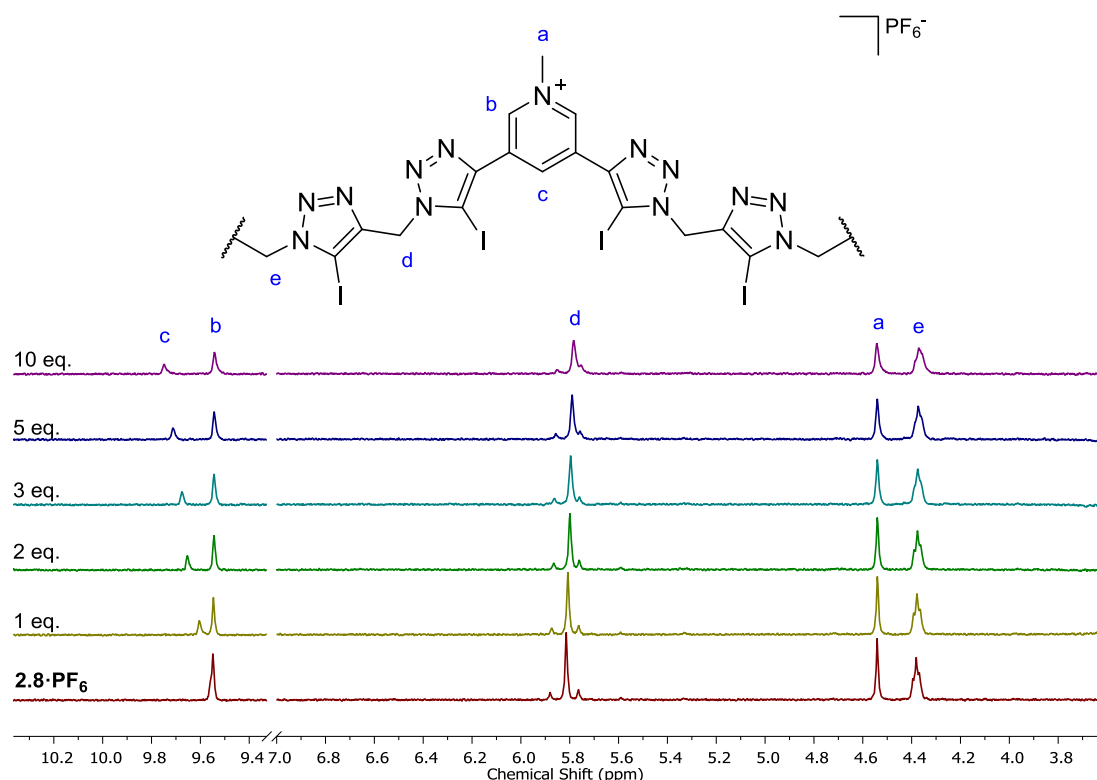


Figure 2.5 - Truncated ^1H NMR spectra of **2.8**· PF_6 on addition of equivalents of TBACl (DMSO-d_6 , 500 MHz, 298K).

Through monitoring the chemical shift of internal pyridinium proton *c*, binding isotherms were plotted (Figure 2.6). The titration data collected was analysed using the WinEQNMR2 software package.¹⁴ In the case of chloride, bromide, iodide and acetate, 1:1 stoichiometric association constants were determined (Table 2.1). With respect to halide recognition, the receptor follows anion basicity trends, as expected in an aprotic solvent, with chloride complexed stronger than the larger and less basic anions. Meanwhile, sulfate was bound in a 2:1 stoichiometric host:guest complex, likely a result of the dianionic nature of the oxoanion tolerating binding to two monocationic charged receptor molecules via electrostatic interactions. This is consistent with a significant increase in binding strength; the association constant K_1 is over an order of magnitude higher than that of chloride.

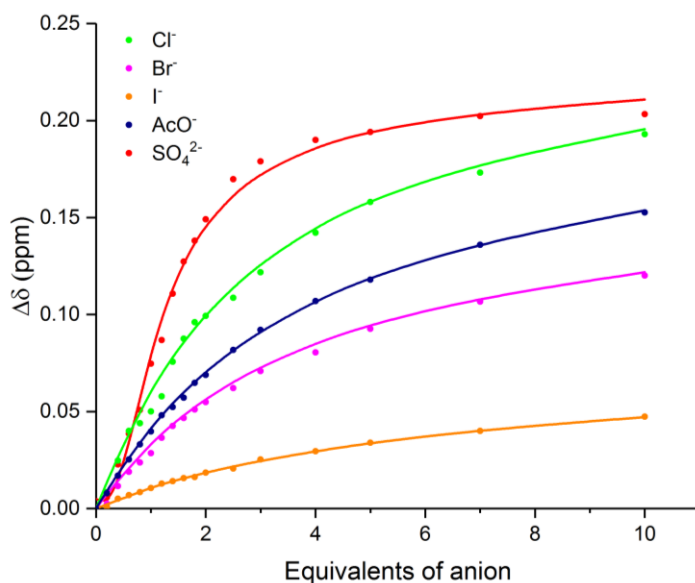
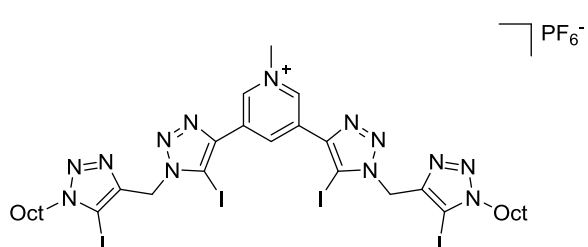


Figure 2.6 - Anion binding titrations of **2.8·PF₆** in DMSO-*d*₆ following proton c; experimental titration data displayed as circles, WinEQNMR2¹⁴ fitted binding isotherms displayed as lines (500 MHz, 298 K). Receptor concentration 2 mM.

Table 2.1 - Association constants (*K_a*) determined for **2.8·PF₆** upon addition of various anions (added as their TBA salts). Solvent: DMSO-*d*₆, 298 K.

	Anion	<i>K_a</i> (M ⁻¹) ^a
	Cl ⁻	199
	Br ⁻	142
	I ⁻	74
	OAc ⁻	139
	SO ₄ ²⁻	<i>K</i> ₁ = 2663 <i>K</i> ₂ = 313

^[a] Calculated from chemical shift of proton c. Association constants calculated using WinEQNMR2.¹⁴ Estimated standard errors < 10%.

2.2.3 Pseudorotaxane assembly study

In order to ascertain the potential of receptor **2.8·PF₆** to act as a thread and form an interpenetrated assembly with an appropriate macrocycle using a templating anion, a ¹H

NMR pseudorotaxane titration study was undertaken (Figure 2.7). The macrocycle used in this investigation was an isophthalamide based system **2.9**, provided by a former member of the group Dr. Stuart Cornes, which had been prepared following a literature procedure.⁷

¹H NMR spectroscopy was used to perform qualitative pseudorotaxane studies and monitor formation of the interpenetrated assembly. The ¹H NMR spectrum of an equimolar solution of thread **2.8**·PF₆, macrocycle **2.9** and TBACl in acetone-d₆ revealed evidence of pseudorotaxane formation when compared with the spectra of the individual components (Figure 2.7).

The macrocyclic hydroquinone protons *5* and *6* were split and moved significantly upfield, a consequence of the π - π aromatic donor-acceptor interactions between this electron-rich group and the electron deficient pyridinium motif of the thread. The external aromatic protons *1* and *2* of the macrocycle and *b* of the thread exhibited only very small shifts, indicating their lack of association to the halide anion. Conversely, substantial shifts were observed for internal aromatic protons *3* and *c* and amide protons *4* ($\Delta\delta$ = 0.57 ppm, 0.76 ppm and 0.87 ppm respectively), suggesting their proximity to the anion binding site and successful formation of an interpenetrated assembly.

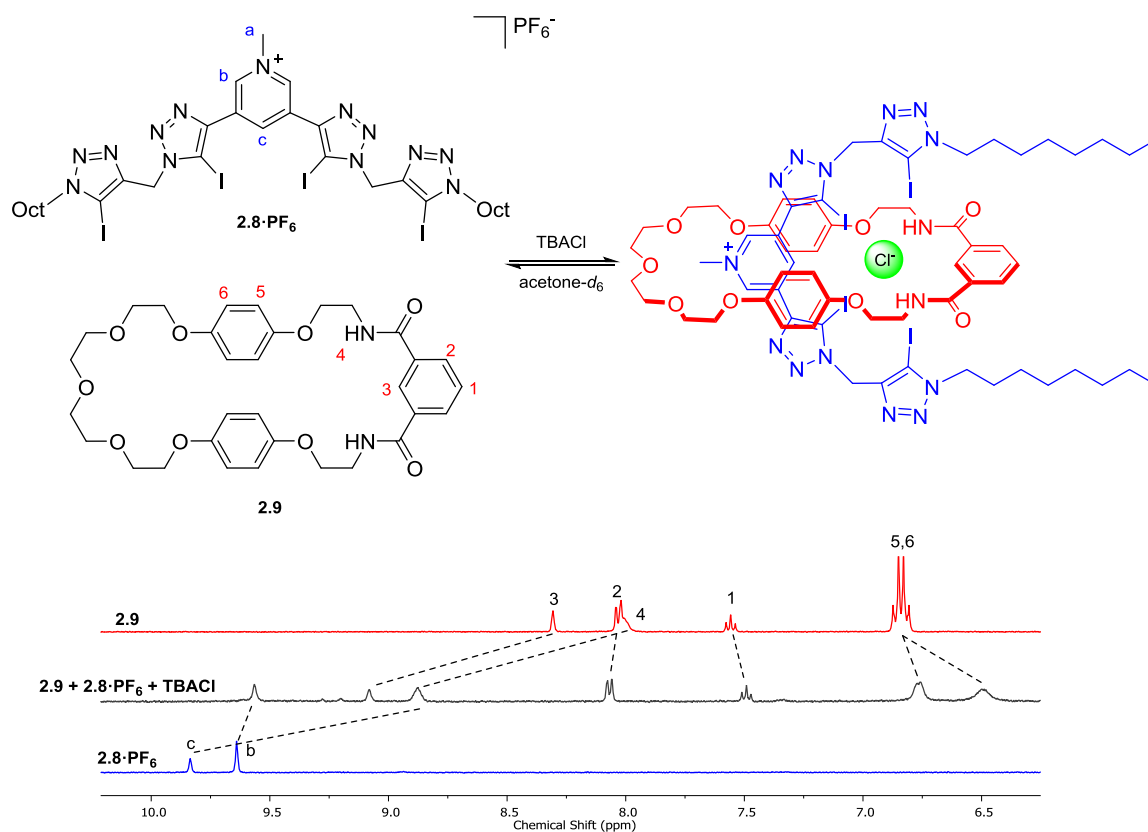


Figure 2.7 - ^1H NMR spectra of macrocycle **2.9**, thread **2.8-PF₆** and an equimolar solution of the two in the presence of TBACl, suggesting pseudorotaxane formation (acetone- d_6 , 400 MHz, 298 K).

These observations indicated that the new tetra-iodotriazole pyridinium motif was an ideal candidate for incorporation into interlocked structures for anion recognition. This led to its integration into a pair of [2]catenanes (section 2.3) and [2]rotaxanes (section 2.4) with the expectation that the respective three-dimensional XB/HB cavity inherent in such a MIM host structure will exhibit enhanced anion association strength and selectivity in comparison to the acyclic XB receptor analogue **2.8-PF₆**.

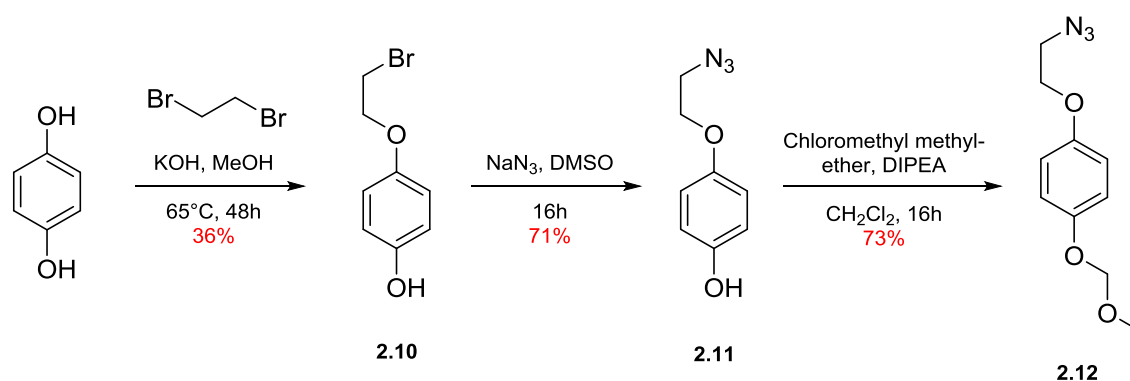
2.3 Tetra-iodotriazole [2]catenanes

Two tetra-iodotriazole [2]catenanes containing the tetra-iodotriazole pyridinium motif studied in section 2.2 were prepared via a multi-step synthetic pathway. Catenane formation

was achieved through a chloride anion template bis-amide condensation ‘clipping’ reaction around a pre-formed tetra-iodotriazole pyridinium macrocycle.

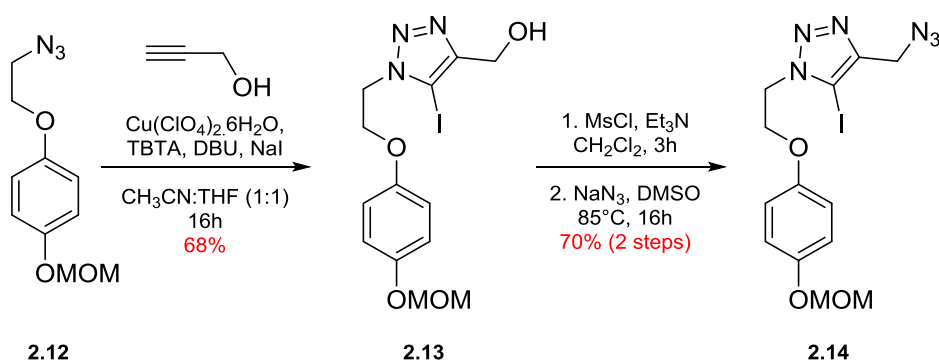
2.3.1 Macrocycle synthesis

The initial steps towards macrocycle formation followed previously reported literature routes (Scheme 2.5).¹⁹ Hydroquinone was refluxed with 1,2-dibromoethane for two days in the presence of KOH in a statistical reaction to give bromoalcohol **2.10**, followed by conversion to azide **2.11** through reaction with NaN₃ in DMSO. The terminal hydroxyl functionality was protected with the methoxymethyl ether (MOM) group through stirring with chloromethyl methyl ether and N,N-diisopropylethylamine (DIPEA), which after purification by column chromatography afforded protected azide **2.12** in 73% yield.



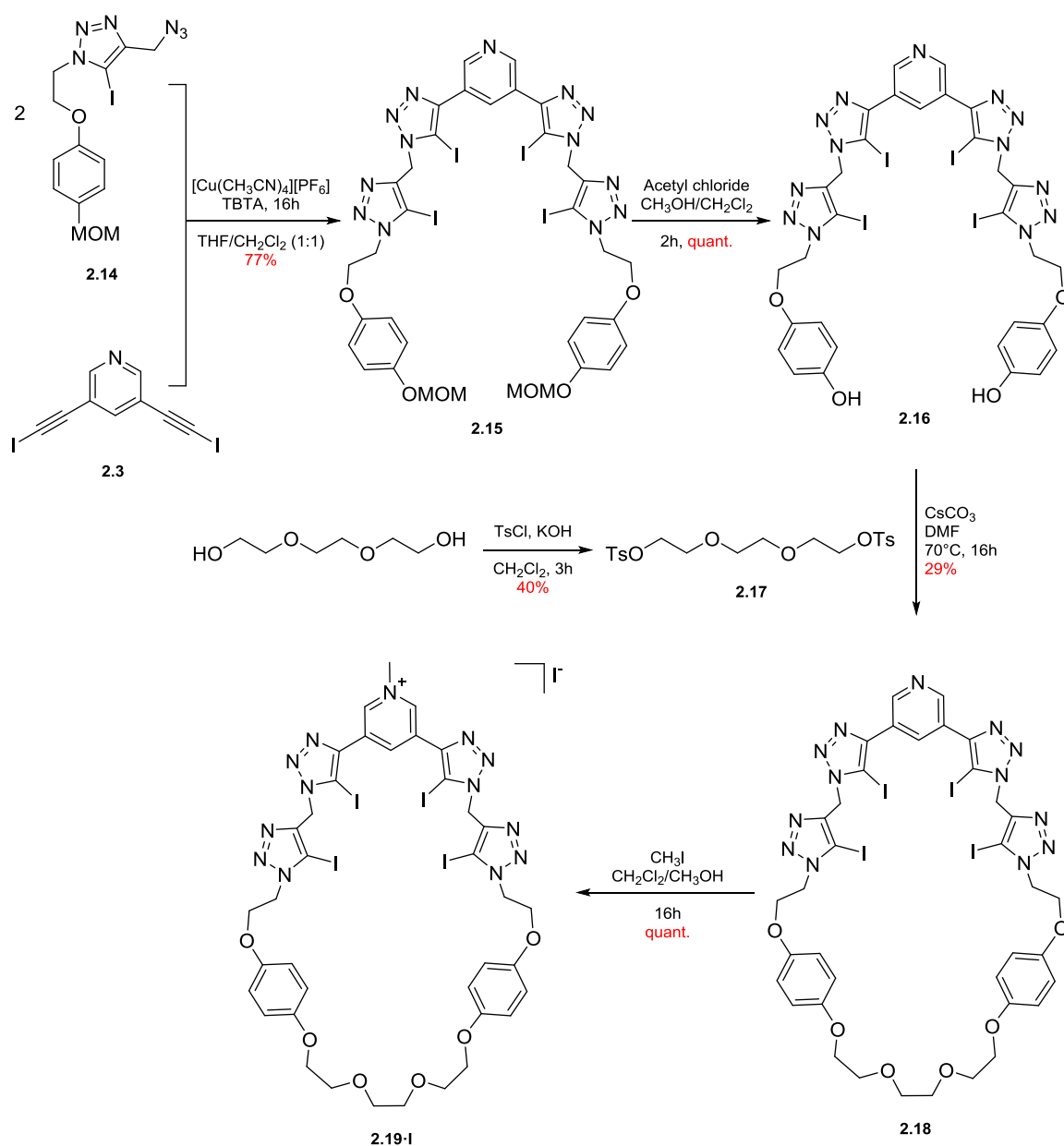
Scheme 2.5 - Synthesis of MOM-protected azide **2.12**.

Next, a one-pot iodo-click reaction was performed between azide **2.12** and propargyl alcohol, following the same conditions outlined in the synthesis of alcohol **2.4** (Scheme 2.6), affording iodotriazole alcohol **2.13** in 68% yield after purification. Subsequent conversion of the terminal hydroxyl group to an azide was performed, the route proceeding via a mesylate intermediate to give protected iodotriazole azide **2.14**.



Scheme 2.6 - Synthesis of iodotriazole azide **2.14**.

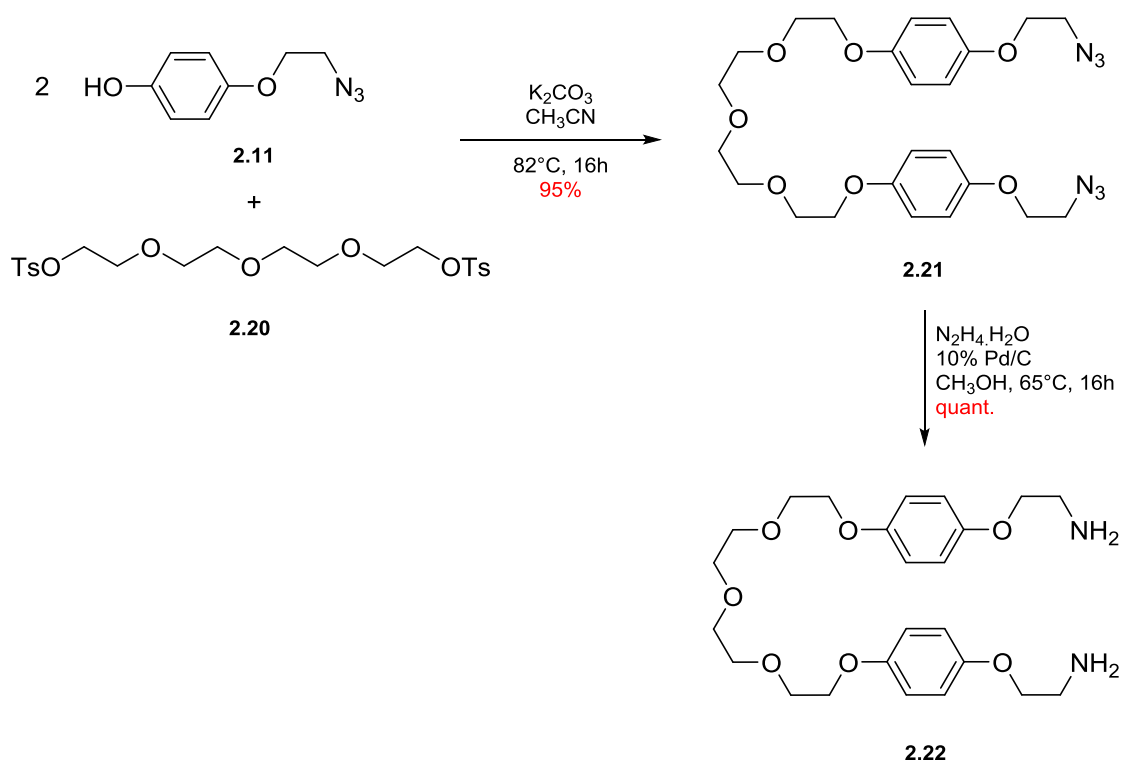
Following the iodo-click CuAAC conditions employed in the synthesis of **2.7**, the reaction between bis-iodoalkyne **2.3** and two equivalents of azide **2.14** afforded tetra-iodotriazole **2.15** in 77% yield (Scheme 2.7). Subsequently, the protecting group was cleaved on addition of acetyl chloride in CH₃OH/CH₂Cl₂ to give macrocycle precursor **2.16**. Meanwhile, bis-tosylate precursor **2.17** was synthesised by addition of tosyl chloride to triethylene glycol according to a literature procedure.²⁰ Under high dilution, macrocycle formation was achieved through reaction of **2.16** with an equimolar amount of **2.17** under basic conditions of Cs₂CO₃ in DMF to afford tetra-iodotriazole macrocycle **2.18** in a moderate yield of 29% after purification by preparative thin layer chromatography (TLC). Finally, methylation using CH₃I in CH₂Cl₂/CH₃OH produced macrocycle **2.19·I** as a white powder in quantitative yield (Scheme 2.8).

Scheme 2.7 - Synthesis of macrocyclic catenane precursor **2.19-I**.

2.3.2 Synthesis of monocationic catenane

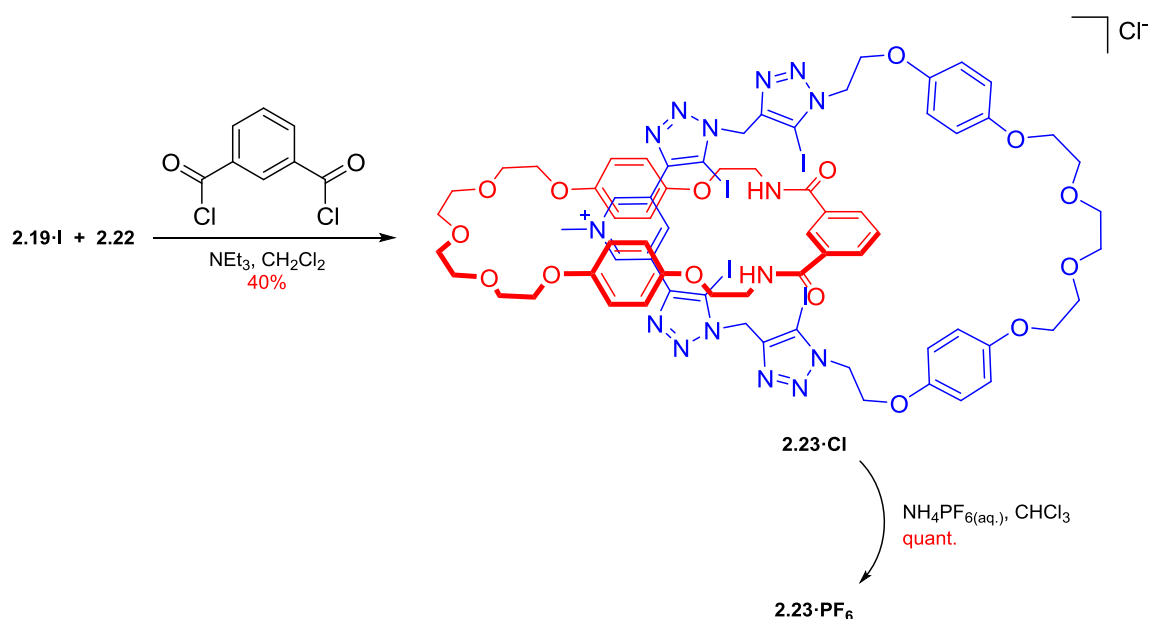
Synthesis of the bis-amine macrocycle precursor **2.22** for catenane formation began with reaction between two equivalents of azide **2.11** and bis-tosylate **2.20** in the presence of K_2CO_3 in dry CH_3CN to produce bis-azide **2.21** in near quantitative yield (Scheme 2.8).

Reduction of the azide functionalities with hydrazine hydrate and 10% Pd/C afforded bis-amine **2.22** as a brown oil.



Scheme 2.8 - Preparation of bis-amine macrocycle precursor **2.22**.

Monocationic catenane **2.23·Cl** was synthesised through a chloride template bis-amide condensation reaction of the addition of isophthaloyl dichloride to a mixture of bis-amine **2.22** and macrocycle **2.19·I** in CH_2Cl_2 containing an excess of NEt_3 (Scheme 2.9). After stirring overnight, catenane **2.23·Cl** was isolated in 40% yield after purification by preparative TLC. Catenane **2.23·Cl** was characterised via ^1H , ^{13}C and two-dimensional ^1H - ^1H COSY and ROESY NMR spectroscopy and high resolution ESI mass spectrometry. Through anion exchange with excess $NH_4PF_6(aq)$ the product was converted to the corresponding non-coordinating PF_6^- salt, **2.23·PF₆**, for anion recognition studies.



Scheme 2.9 - Synthesis of tetra-iodotriazole catenane **2.23·PF₆**.

Evidence for the successful synthesis of **2.23·Cl** was observed through comparison of its ^1H NMR spectrum with the NMR spectra of the two constituent macrocycles **2.9** and **2.19·I** (Figure 2.8). Upon catenane formation notable shifts of internal aromatic protons ϵ and β were seen, whilst the isophthalamide macrocycle **2.9** hydroquinone peaks **5** and **6** moved significantly upfield and split into two environments. This is indicative of π - π donor-acceptor aromatic interactions between the electron-rich hydroquinone groups and the electron-deficient pyridinium motif resulting in desymmetrisation of the proton environments.

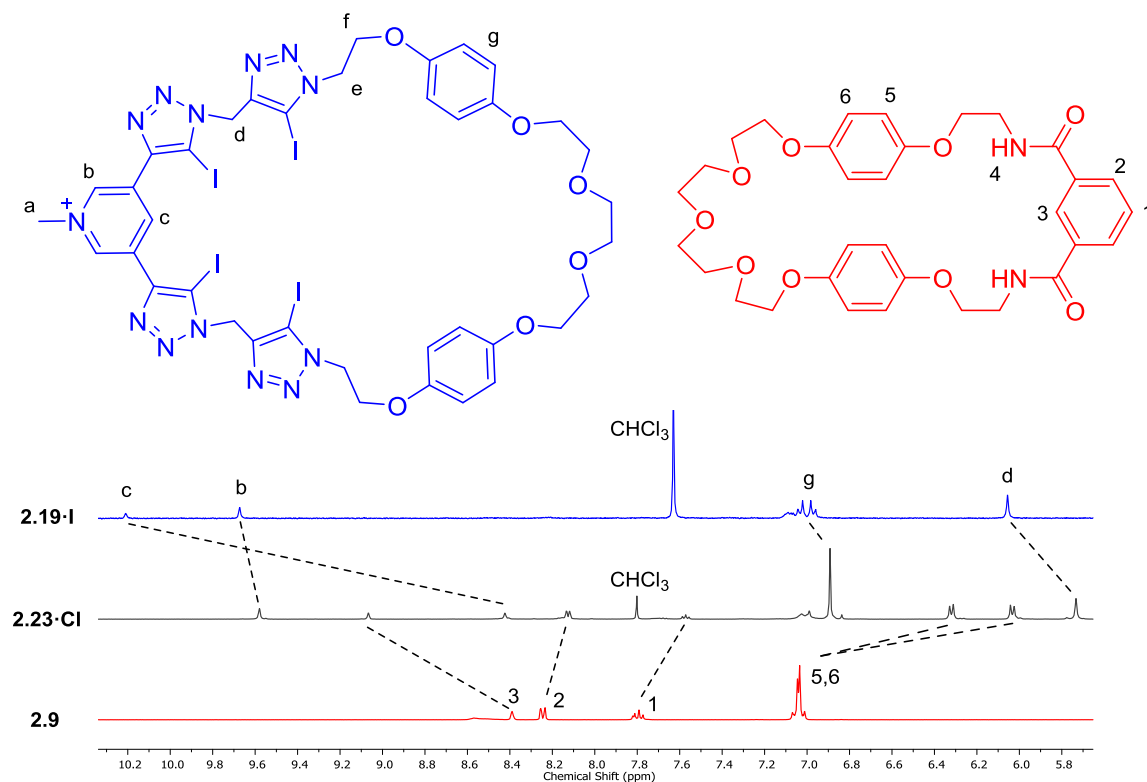


Figure 2.8 - Truncated ^1H NMR spectra of catenane **2.23-Cl** and comparison with constituent macrocycles **2.19-I** and **2.9**. Shifts due to catenane formation indicated (1:1 $\text{CDCl}_3/\text{CH}_3\text{OD}$, 400 MHz, 298 K).

Further confirmation of catenane formation was obtained from two-dimensional ^1H - ^1H ROESY NMR spectroscopy (Figure 2.9). Cross peaks were observed between the resonances of the isophthalamide macrocycle hydroquinone protons **5** and **6** and the tetra-iodotriazole macrocycle pyridinium protons **b** and **c**, implying their close proximity to one another. Moreover, a cross peak between methylene spacer proton **d** of the XB macrocycle component and benzyl proton **3** of the isophthalamide macrocycle was seen.

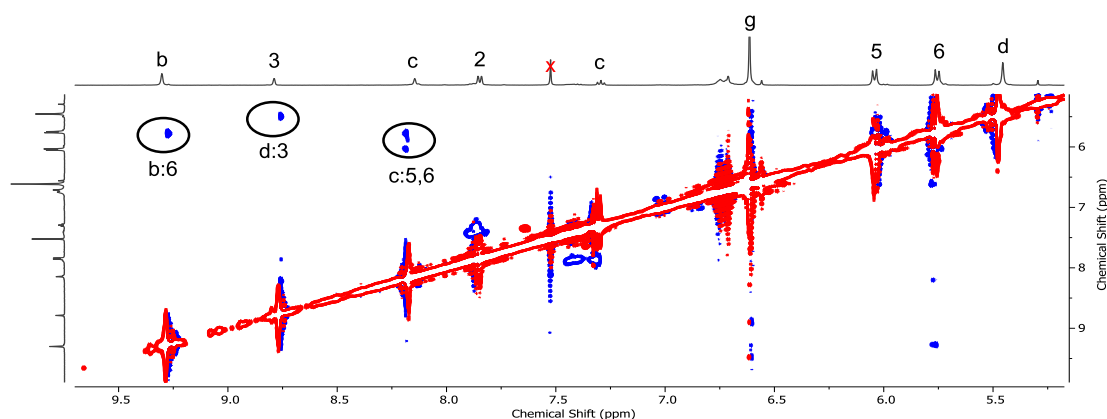
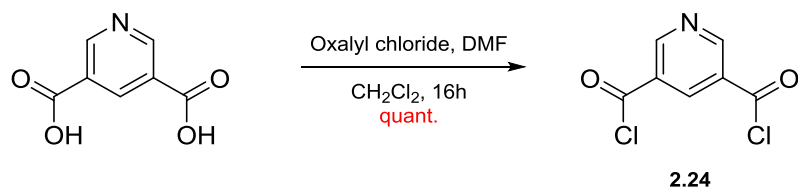


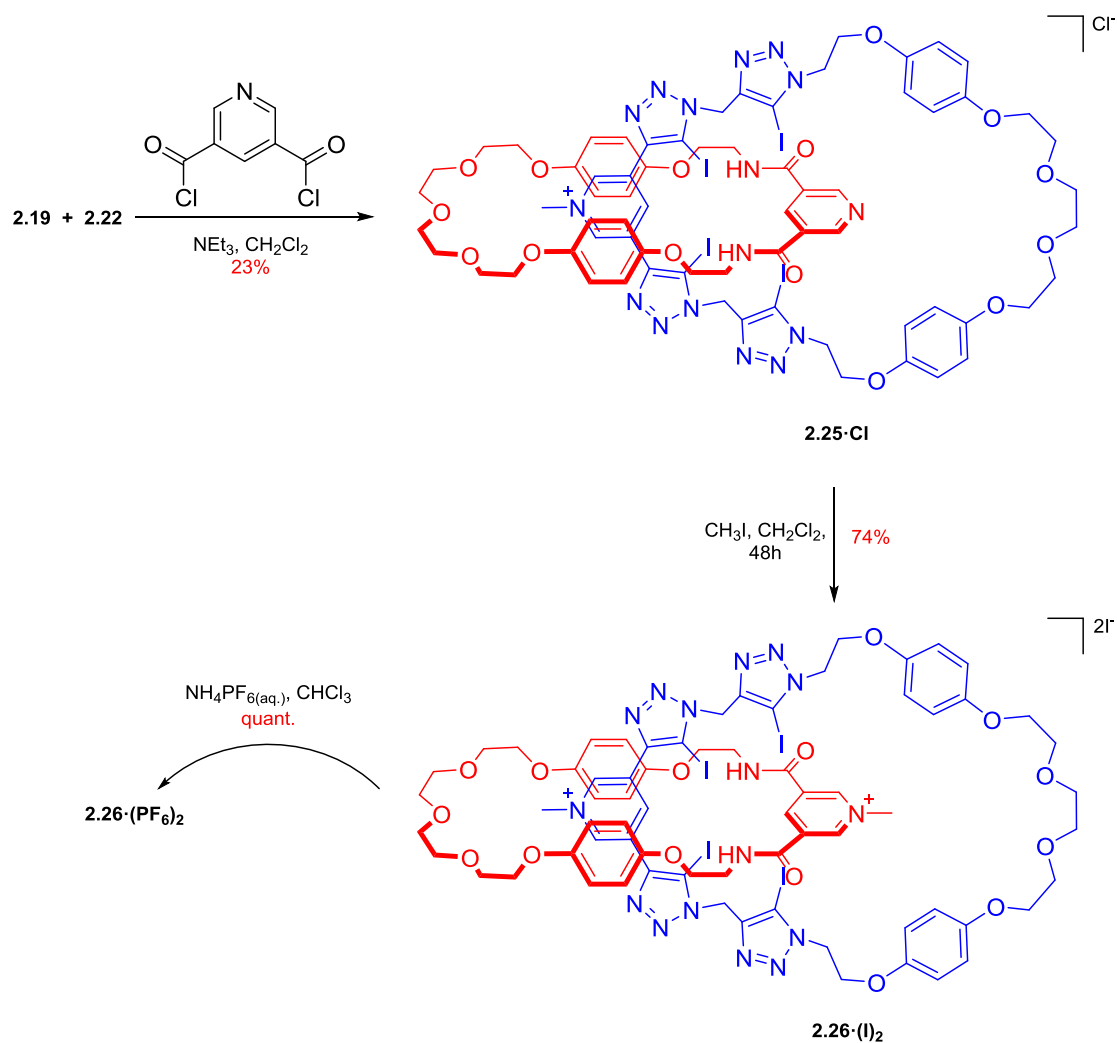
Figure 2.9 - Truncated ^1H - ^1H ROESY NMR spectrum of monocationic catenane **2.23·Cl** (1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$, 500 MHz, 298 K).

2.3.3 Synthesis of dicationic [2]catenane

Attention turned to the synthesis of a dicationic XB catenane. An analogous route to the synthesis of monocationic catenane **2.23·Cl** was employed, utilising the chloride template bis-amide condensation reaction. The bis-acid chloride employed was pyridine derivative **2.24** in order to incorporate a nitrogen site for subsequent methylation to produce the dicationic interlocked receptor (Scheme 2.10). Synthesis of **2.24** was achieved via the heating of 3,5-pyridinedicarboxylic acid with oxalyl chloride overnight in DMF. After removal of the solvent, pyridine bis-acid chloride **2.24** was immediately added to a solution containing tetra-iodotriazole macrocycle **2.19·I**, bis-amine **2.22** and an excess of NEt_3 (Scheme 2.11). Purification of the crude product via preparative TLC afforded monocationic catenane **2.25·Cl** in 23% yield. Finally, methylation using CH_3I gave dicationic catenane **2.26·(I)**₂ which was converted to the corresponding PF_6^- salt **2.26·(PF₆)**₂ via anion exchange. The dicationic interlocked product was characterised by ^1H , ^{13}C , ^{19}F and two-dimensional ROESY NMR spectroscopy and high resolution ESI mass spectrometry.



*Scheme 2.10 - Synthesis of pyridine bis-acid chloride **2.24**.*



*Scheme 2.11 - Synthesis of tetra-iodotriazole catenane **2.26·(PF₆)₂**.*

The ^1H - ^1H ROESY NMR spectrum of monocationic catenane **2.25·Cl**, the product of the interlocked assembly step, confirmed the success of its formation (Figure 2.10). Cross peaks were observed between isophthalamide macrocycle hydroquinone protons 5 and 6 with internal pyridinium proton ϵ of the tetra-iodotriazole macrocycle. Interestingly, there is a

cross peak between the aforementioned hydroquinone protons with the hydroquinone protons, *g*, of the opposite macrocycle. This is likely indicative of rotational movement of one macrocycle about the other, which further causes a desymmetrisation of proton environment *g*.

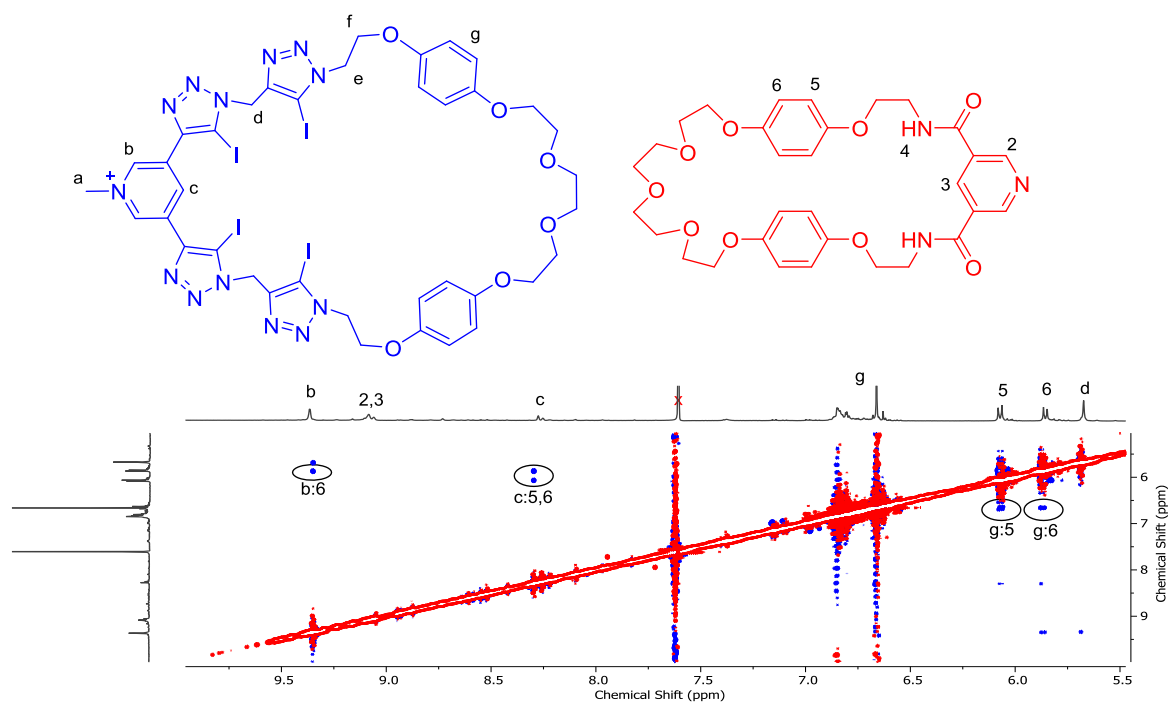


Figure 2.10 - Truncated ^1H - ^1H ROESY NMR spectrum of catenane **2.25·Cl** (1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$, 500 MHz, 298 K).

Diagnostic peaks in the ^1H NMR spectrum of dicationic catenane **2.26·(PF₆)₂** confirmed its successful synthesis, with protons *b*, *c*, *d*, 5 and 6 exhibiting similar resonances to the monocationic analogue **2.23·PF₆** (Figure 2.11). Tetra-iodotriazole macrocycle hydroquinone protons *g* move upfield as expected. Compared to **2.23·PF₆**, there is a marked downfield shift exhibited by pyridinium bis-amide macrocycle protons 2 and 3, a consequence of the more electron withdrawing nature of the charged ring substituent.

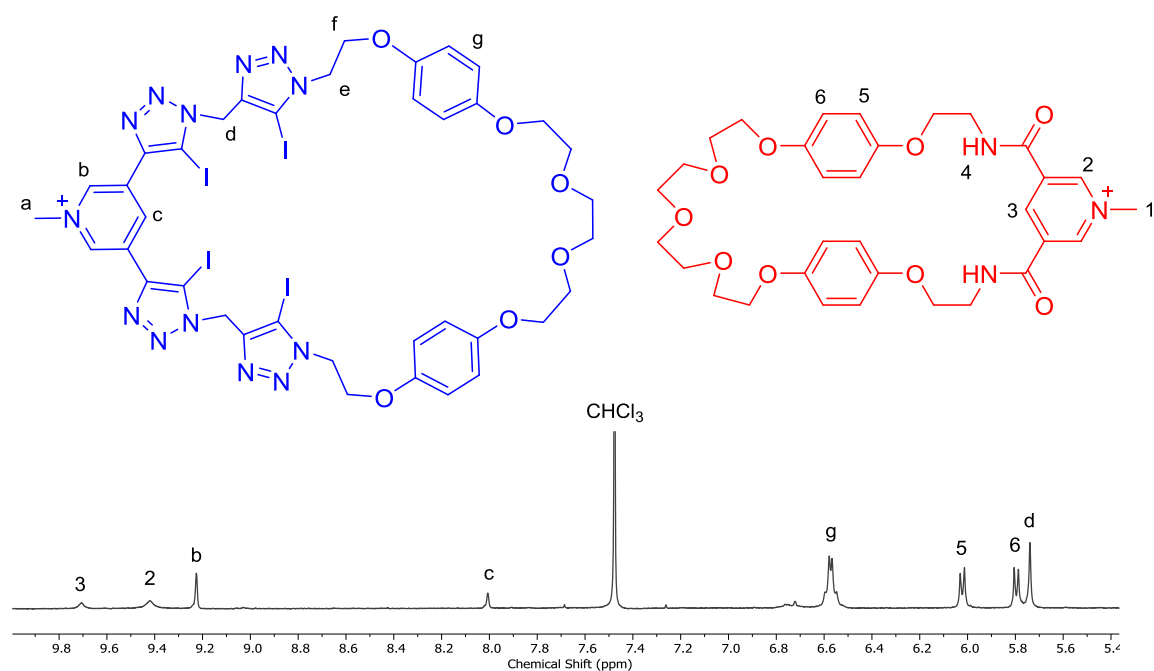


Figure 2.11 - Truncated ^1H NMR spectrum of catenane **2.26**·(PF_6) $_2$ (1:1 $\text{CDCl}_3/\text{CH}_3\text{OD}$, 400 MHz, 298 K).

2.3.4 ^1H NMR anion recognition studies

After the successful synthesis of monocationic catenane **2.23**· PF_6 and dicationic catenane **2.26**·(PF_6) $_2$, their anion binding properties were investigated through ^1H NMR titration experiments in the competitive solvent mixture 45:45:10 $\text{CDCl}_3/\text{CD}_3\text{OD}/\text{D}_2\text{O}$. Shifts in the ^1H NMR spectrum were monitored upon addition of up to ten equivalents of chloride, bromide, iodide, sulfate, perrhenate and nitrate added as their TBA salts.

Upon anion addition to monocationic catenane **2.23**· PF_6 substantial upfield perturbations were exhibited by internal pyridinium macrocycle proton ϵ , with downfield shifts seen for internal isophthalamide proton δ . The significant shift of protons in these environments suggested anion binding was occurring in the three-dimensional cavity formed by the mechanical bond. An example of titration data obtained upon TBAI addition is depicted in Figure 2.12, with spectra shown at several stages of the experiment. The resulting binding isotherms obtained from monitoring the downfield shift of internal isophthalamide

macrocycle proton **3** are plotted in Figure 2.13. Unfortunately, during the titration experiments upon dicationic catenane **2.26**·(**PF**₆)₂ precipitation negated quantitative anion binding data being determined.

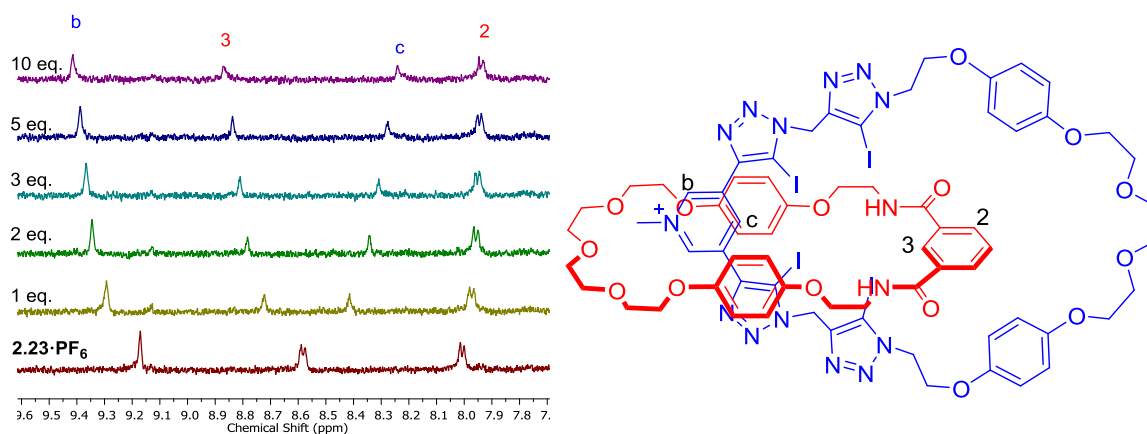


Figure 2.12 - Truncated ¹H NMR spectra of **2.23**·**PF**₆ on addition of equivalents of TBAI in 45:45:10 CDCl₃/CD₃OD/D₂O (500 MHz, 298 K).

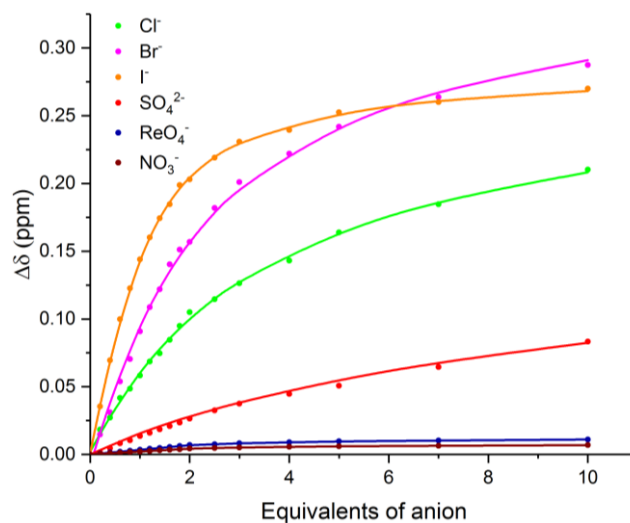


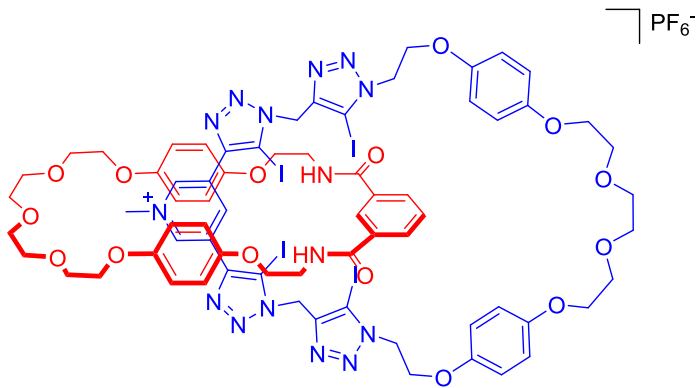
Figure 2.13 - Anion binding titrations of **2.23**·**PF**₆ following internal isophthalamide proton **3**. Performed in solvent mixture 45:45:10 CDCl₃/CD₃OD/D₂O; experimental titration data displayed as circles, WinEQNMR2¹⁴ fitted binding isotherms displayed as lines (500 MHz, 298 K). Receptor concentration 1 mM.

WinEQNMR2 analysis¹⁴ of the titration data of **2.23**·**PF**₆ determined association constants for the formation of 1:1 stoichiometric host-guest complexes (Table 2.2). A strong

preference was exhibited for the spherical halide anions over the oxoanions. More specifically, no observable binding was seen for perrhenate or nitrate, whilst only very weak binding was displayed for sulfate. This may be attributed to the large size of the oxoanions and unfavourable geometry rendering them unable to penetrate the interlocked catenane binding pocket. The observed halide selectivity was in line with the hydration of each anion according to the Hofmeister series, with iodide bound most strongly followed by bromide and chloride.

Although the previously reported bis-iodotriazole catenane **2.1**·PF₆ exhibited significantly stronger halide binding capability (Table 2.2), the tetra-iodotriazole catenane **2.23**·PF₆ displayed a notable preference for I⁻ over Br⁻ not observed with **2.1**·PF₆. Steric considerations may account for the diminished halide binding strength of **2.23**·PF₆.

Table 2.2 - Association constants (K_a) determined for **2.23**·PF₆ and **2.1**·PF₆ with various anions (added as their TBA salts). Solvent: 45:45:10 CDCl₃/CD₃OD/D₂O, 298 K.

 2.23·PF₆	PF ₆ ⁻		
	Anion	K_a (M ⁻¹) ^a	
		2.23 ·PF ₆	2.1 ·PF ₆ ¹³
	Cl ⁻	210	1850
	Br ⁻	351	>10 ⁴
	I ⁻	1176	>10 ⁴
	SO ₄ ²⁻	55	-
	ReO ₄ ⁻	NB ^b	-
	NO ₃ ⁻	NB ^b	-

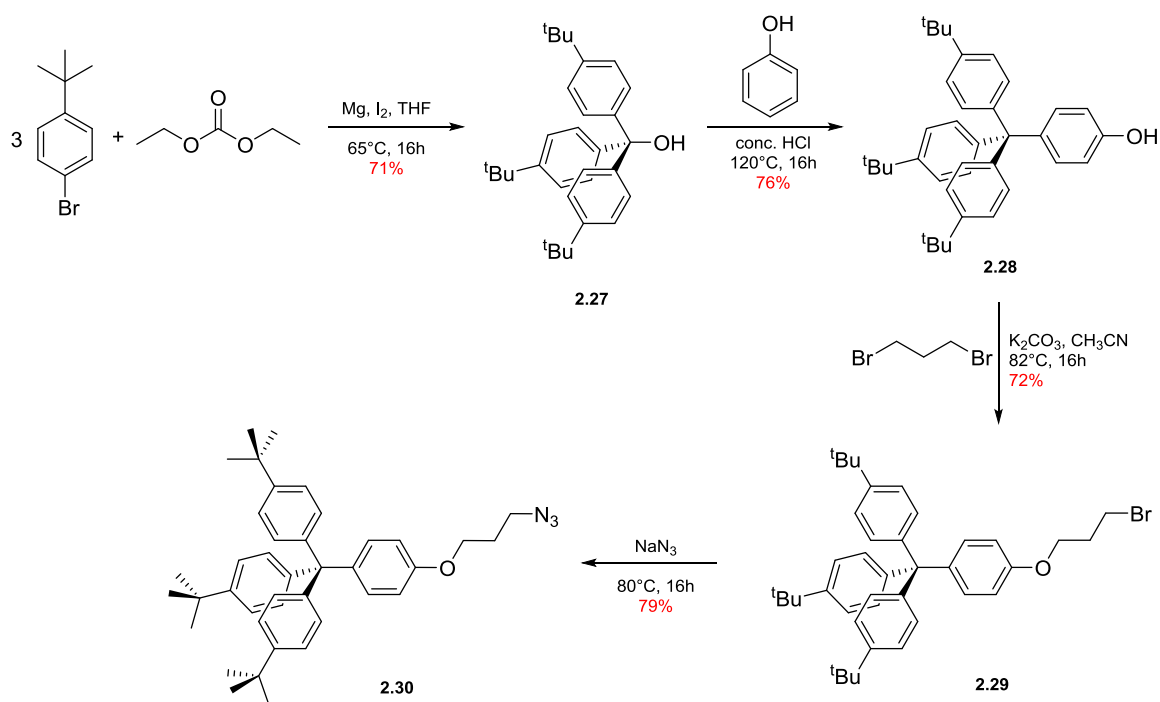
^[a]Calculated from chemical shift of internal isophthalamide proton. Association constants calculated using WinEQNMR2.¹⁴ ^[b]Negligible change in chemical shift observed. Estimated standard errors < 10%.

2.4 Tetra-iodotriazole [2]rotaxanes

Following the preparation of XB [2]catenane **2.23**·**PF**₆ and its success in binding a range of anions, attempts were made to incorporate the tetra-iodotriazole motif into the axle component of a [2]rotaxane. The utilisation of stopper groups may aid XB rotaxane solubility and allow for the preparation of a dicationic rotaxane host structure for enhancement in anion binding strength resulting from additional electrostatic interactions.

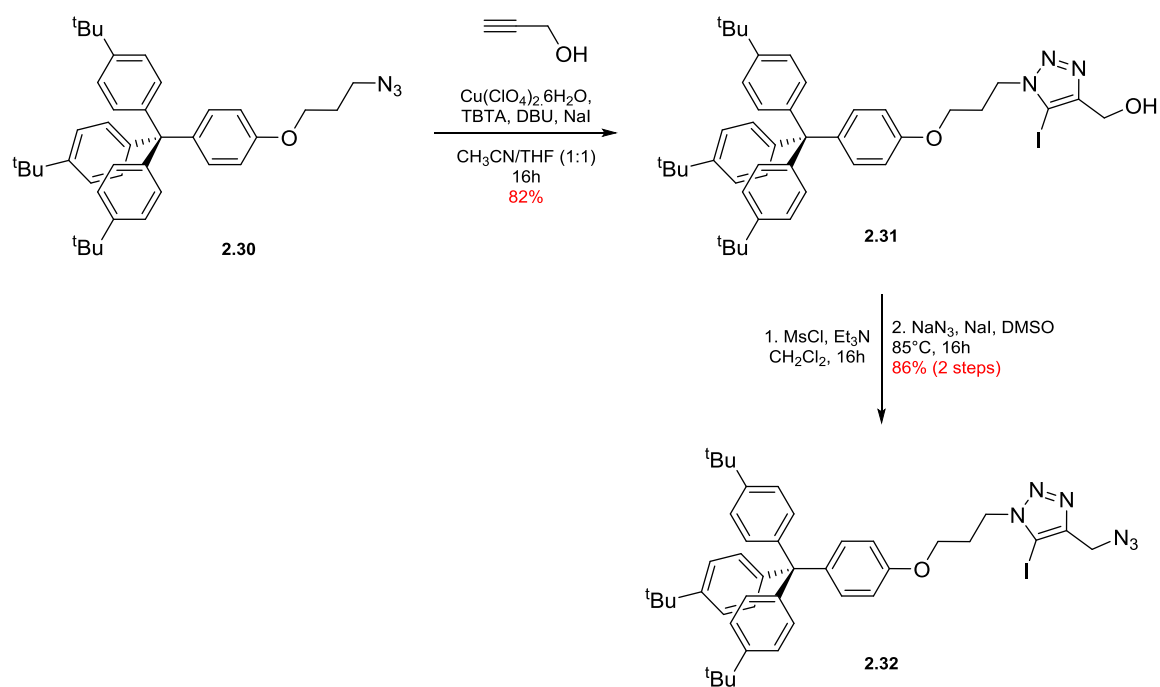
2.4.1 Axle synthesis

The synthesis of the axle component first required the preparation of suitably sized stoppered synthons capable of ensuring the macrocycle would not de-thread. A trityl-stoppered azide derivative was prepared following a reported literature procedure (Scheme 2.12).²¹ Firstly, trityl alcohol **2.27** was formed through the Grignard reaction between 1-bromo-4-*tert*-butyl benzene and diethyl carbonate in the presence of magnesium turnings and catalytic iodine. This was dissolved in molten phenol containing a small amount of concentrated HCl to afford trityl phenol **2.28**. Reaction of **2.28** with an excess of 1,3-dibromopropane and K₂CO₃ in CH₃CN gave trityl bromide **2.29**. Substitution with NaN₃ afforded the target trityl stopper propyl-azide **2.30** in 79% yield.



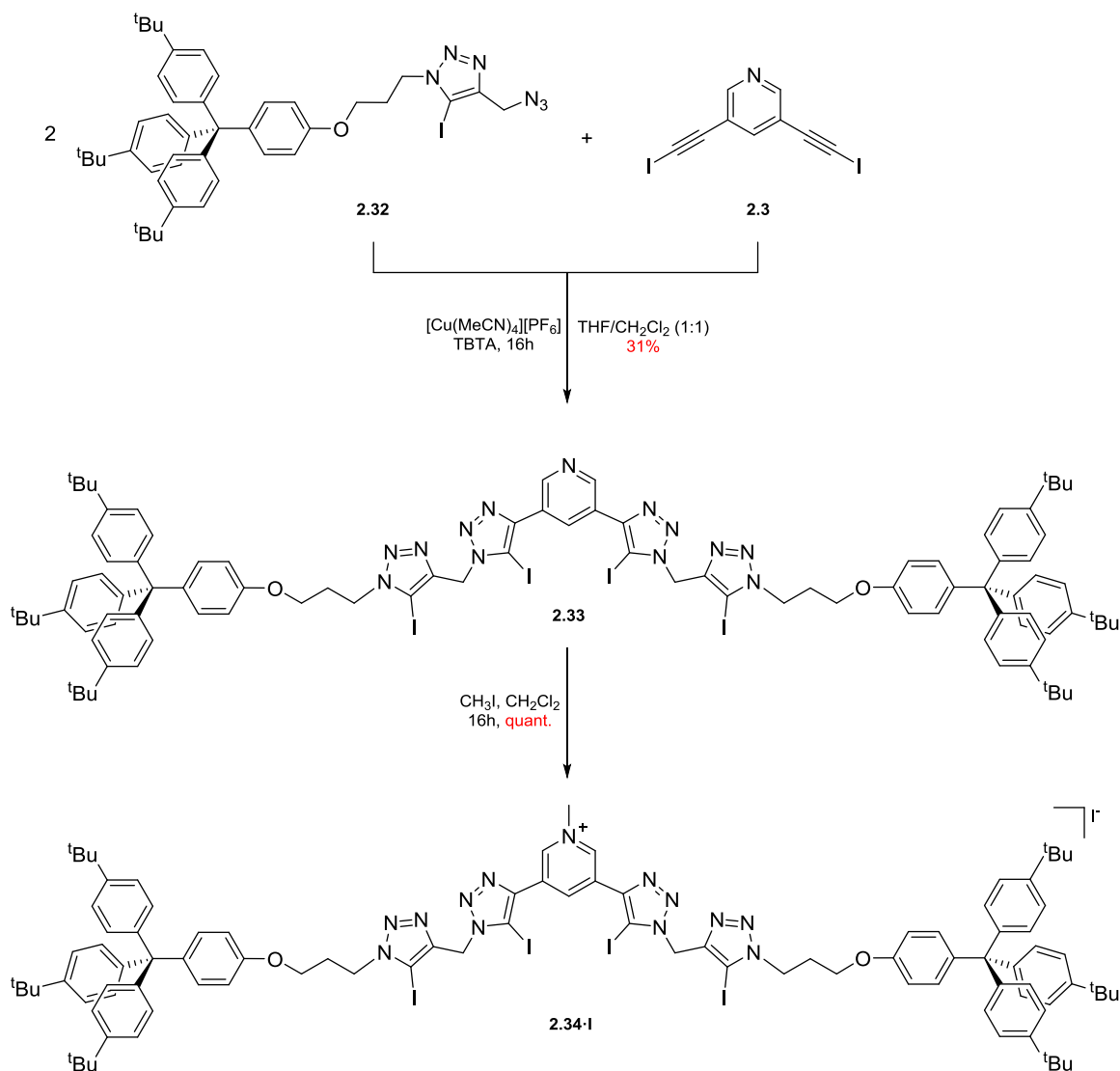
Scheme 2.12 - Synthesis of trityl propyl-azide stopper **2.30**.

The next step in the synthesis was the one-pot iodo-click reaction between trityl azide **2.30** and propargyl alcohol to afford trityl iodotriazole alcohol **2.31** in 82% yield (Scheme 2.13). The terminal hydroxyl group was converted to mesylate by addition of mesyl chloride in the presence of excess NEt_3 and this intermediate was immediately reacted further with NaN_3 in DMSO to produce trityl iodotriazole-azide **2.32** in 86% yield after purification by column chromatography.



Scheme 2.13 - Preparation of trityl iodotriazole azide **2.32**.

The CuAAC reaction of bis-iodoalkyne **2.3** with two equivalents of trityl azide **2.32** gave tetra-iodotriazole **2.33** in 31% yield (Scheme 2.14). The moderate yield may be attributed to the poor solubility of the mono-clicked intermediate which precipitated during the reaction. Methylation with CH_3I afforded the stoppered tetra-iodotriazole pyridinium axle **2.34·I**.

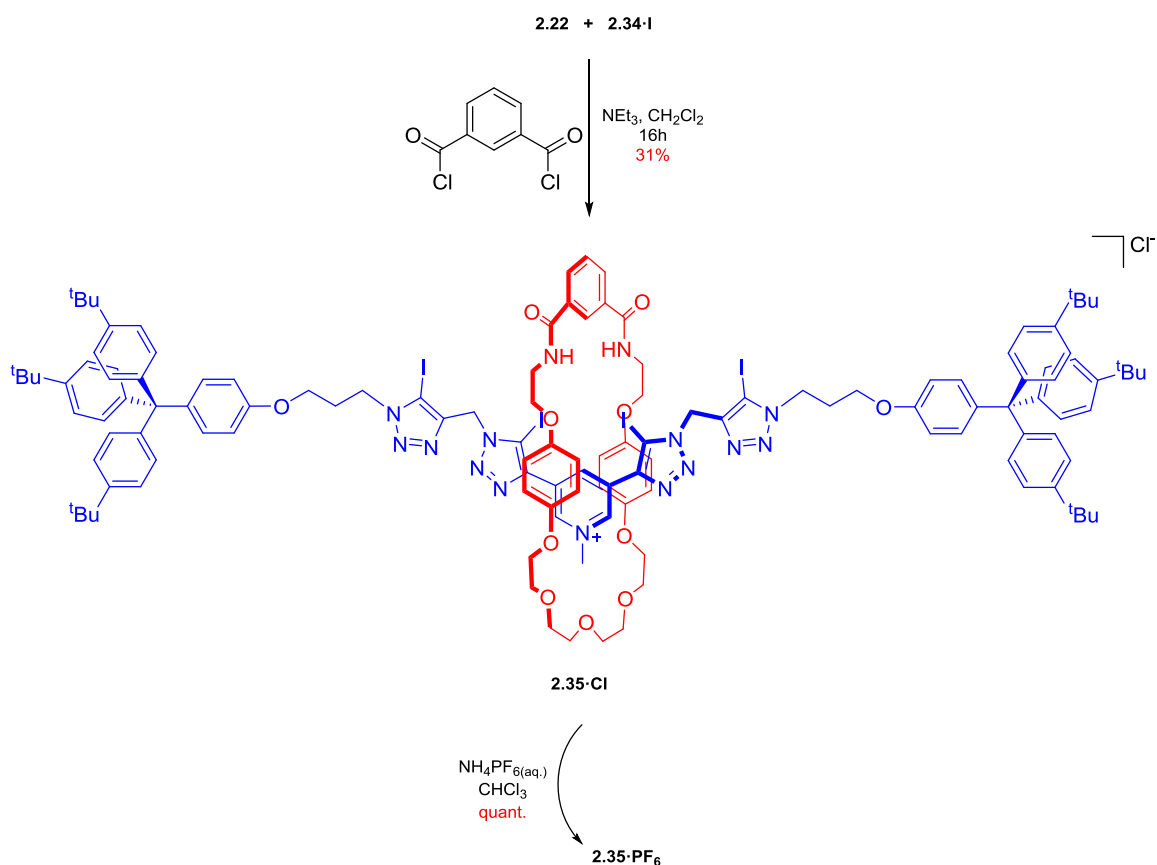


Scheme 2.14 - Synthesis of tetra-iodotriazole pyridinium axle **2.34-I**.

2.4.2 Synthesis of monocationic rotaxane

Rotaxane formation was achieved via a chloride anion template clipping procedure by performing a bis-amide condensation reaction around the pyridinium moiety of the axle, following an identical procedure utilised in the catenane formation reactions discussed in section 2.3. Isophthaloyl dichloride was added to a CH_2Cl_2 solution of axle **2.34-I** and bis-amine **2.22** containing an excess of NEt_3 (Scheme 2.15). After stirring for 16 hours,

purification was achieved via preparative TLC to afford rotaxane **2.35·Cl** in 31% yield and converted to the hexafluorophosphate salt **2.35·PF₆** for ¹H NMR titration studies.



Scheme 2.15 - Formation of tetra-iodotriazole [2]rotaxane **2.35·PF₆**.

Rotaxane characterisation was determined through ¹H, ¹³C, ¹⁹F and two-dimensional ¹H-¹H ROESY NMR spectroscopy and high resolution ESI mass spectrometry. Key shifts exhibited in the CDCl₃ ¹H NMR spectrum of **2.35·Cl** were diagnostic of rotaxane formation when compared to that of free axle **2.34·I** and macrocycle **2.9** (Figure 2.14). Firstly, perturbations in the resonances of pyridinium axle protons *b* and *c* and isophthalamide macrocycle protons 1, 2 and 3 were directly comparable to that seen for catenane **2.23·Cl**, including a significant upfield shift of *c* and a large downfield shift exhibited by 3. In the non-protic solvent utilised, amide protons 4 are visible and these moved ~1.5 ppm downfield.

Typical of interlocked assembly formation, isophthalamide protons **5** and **6** moved upfield due to π - π donor-acceptor interactions with the pyridinium motif, whilst their splitting into two environments was a consequence of a loss of symmetry. Finally, a significant shift of note was the upfield movement of methylene spacer protons **d**.

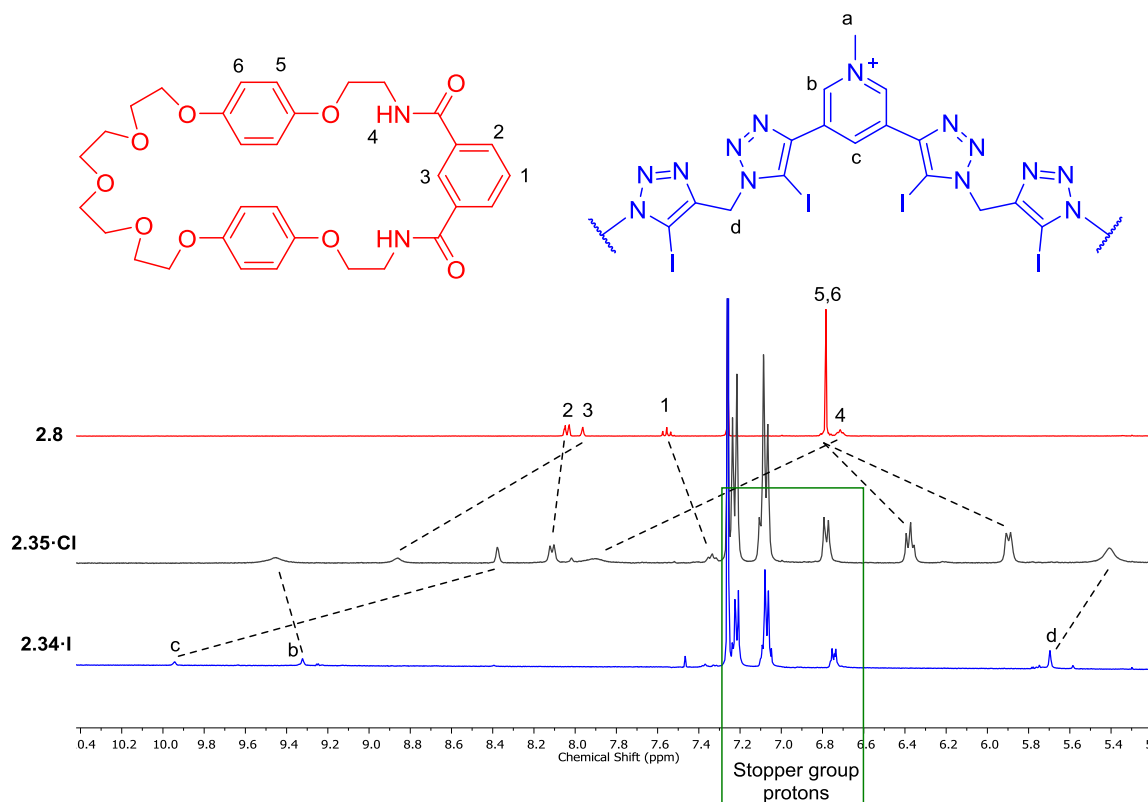


Figure 2.14 - Truncated ^1H NMR spectra of rotaxane **2.35·Cl** and comparison with constituent parts: axle **2.34·I** and macrocycle **2.9**. Shifts due to rotaxane formation indicated (CDCl_3 , 400 MHz, 298 K).

Cross peaks in the two-dimensional ^1H - ^1H ROESY NMR spectrum of **2.35·Cl** further confirmed the success of rotaxane formation (Figure 2.15). Peaks were observed between macrocycle hydroquinone protons **5** and **6** with internal pyridinium proton **c**, whilst a further through-space interaction between **6** and methyl protons **a** was exhibited.

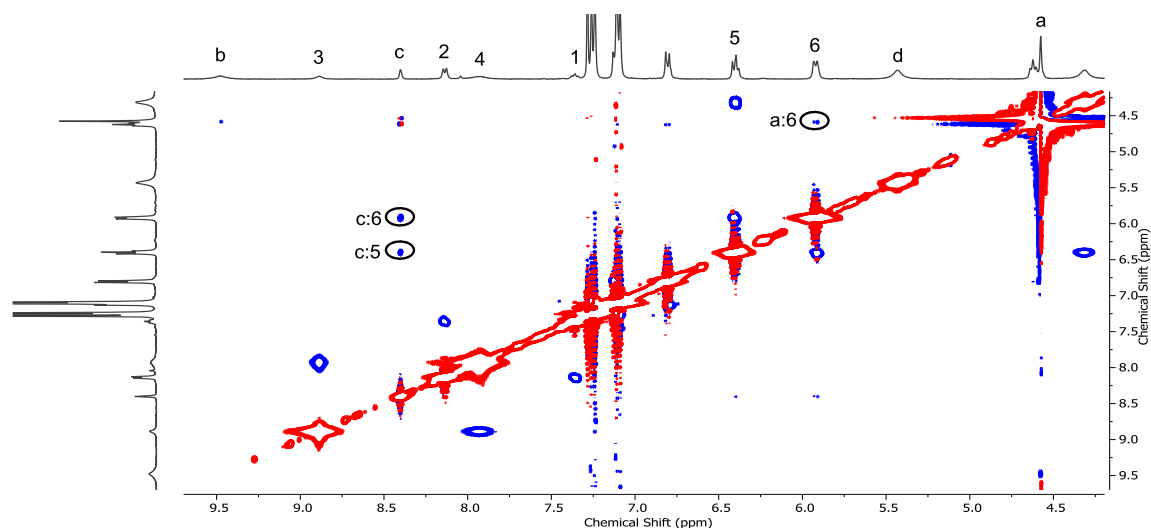
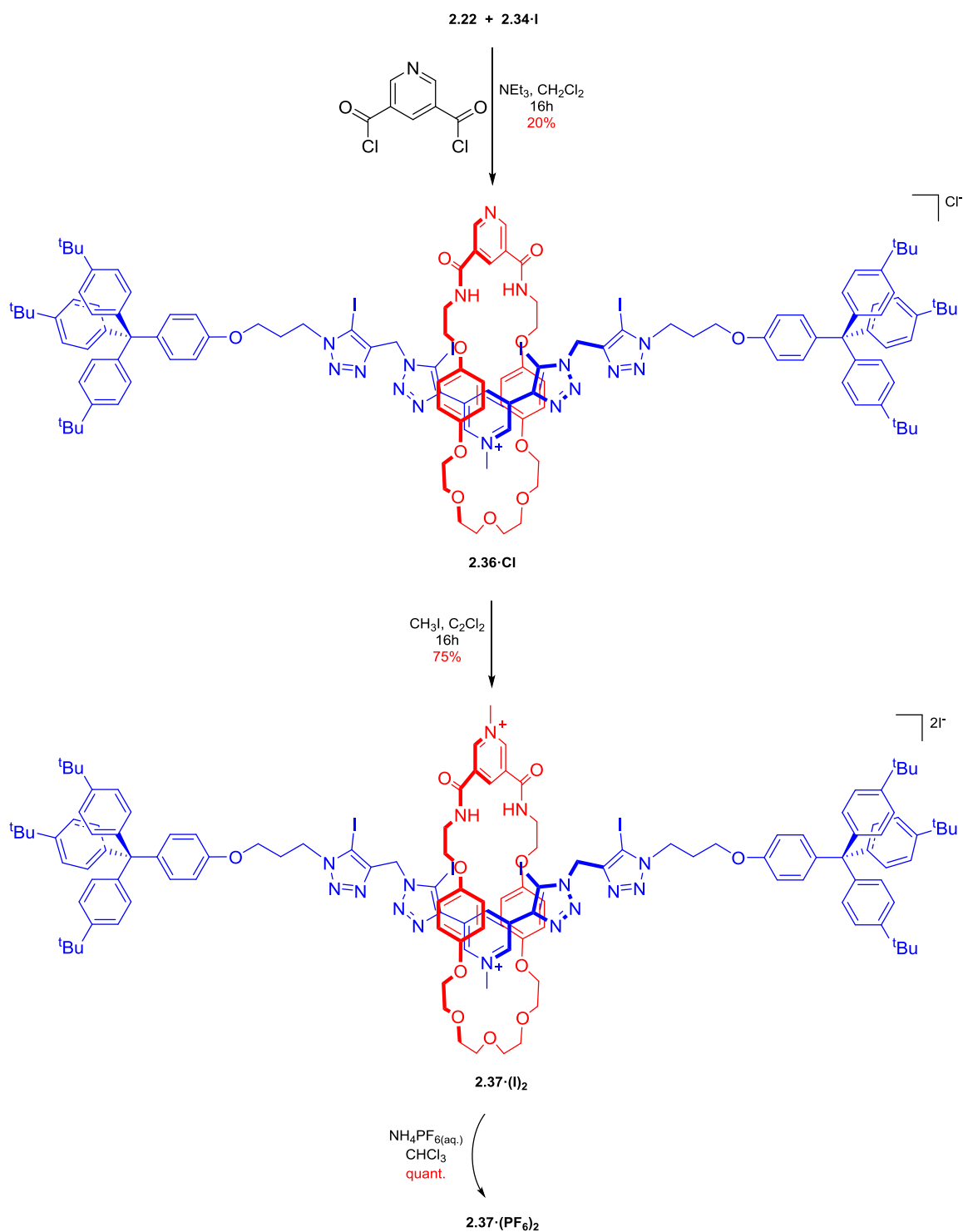


Figure 2.15 - Truncated ^1H - ^1H ROESY NMR spectrum of monocationic rotaxane **2.35·Cl** (CDCl_3 , 500 MHz, 298 K).

2.4.3 Synthesis of dicationic rotaxane

Following the previously described chloride anion template bis-amide condensation procedure, rotaxane **2.36·Cl** was prepared from addition of pyridine bis-acid chloride **2.24** to bis-amine **2.22** and axle **2.34·I** (Scheme 2.16). After 16 hours, purification via preparative TLC gave monocationic rotaxane **2.36·Cl** in 20% yield, which was subsequently methylated at the pyridine position through reaction with CH_3I in CH_2Cl_2 to afford dicationic [2]rotaxane **2.37·(I)**₂. This was converted to its PF_6^- salt **2.37·(PF₆)**₂ for anion binding studies.



Scheme 2.16 - Preparation of dicationic tetra-iodotriazole [2]rotaxane **2.37·(PF₆)₂**.

Notable peaks in the 1:1 CDCl₃/CD₃OD ¹H NMR spectrum of rotaxane **2.37·(PF₆)₂** included significantly downfield shifted resonances of internal macrocycle proton 3 and

amide protons **4** and an upfield shift of axle proton **c** (Figure 2.16). Meanwhile, cross peaks in the two-dimensional ^1H - ^1H ROESY NMR spectrum further confirmed successful rotaxane formation, with peaks observed between macrocycle hydroquinone protons **5** and **6** with internal axle proton **c**; whilst a through-space interaction between **5** and external axle proton **b** was also observed (Figure 2.17).

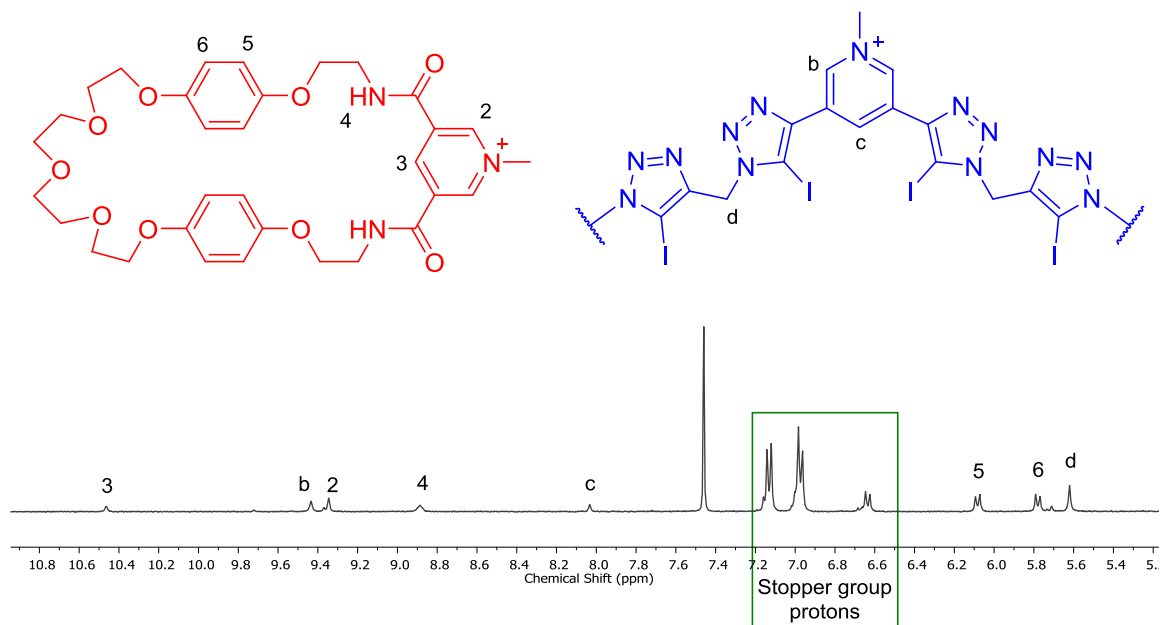


Figure 2.16 - Truncated ^1H NMR spectra of rotaxane **2.37**·(PF_6)₂ (CDCl_3 , 400 MHz, 298 K).

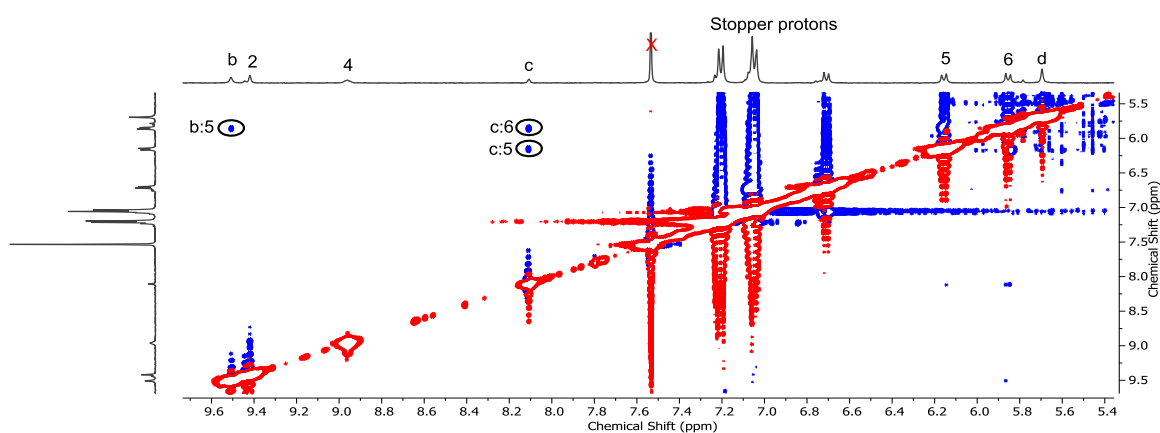


Figure 2.17 - Truncated ^1H - ^1H ROESY NMR spectrum of dicationic rotaxane **2.37**·(**I**)₂ (1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$, 500 MHz, 298 K).

2.4.4 ^1H NMR anion recognition studies

The anion binding properties of monocationic rotaxane **2.35**· PF_6 and dicationic rotaxane **2.37**·(PF_6)₂ were investigated via ^1H NMR titration studies in the competitive solvent mixture 45:45:10 $\text{CDCl}_3/\text{CD}_3\text{OD}/\text{D}_2\text{O}$. Addition of ten equivalents of chloride, bromide and iodide as their TBA salts led to significant perturbations in the spectra of both, whilst **2.35**· PF_6 was also titrated with sulfate.

In the case of monocationic rotaxane **2.35**· PF_6 substantial downfield shifts were exhibited by the internal macrocycle proton β upon anion addition, whilst a noticeable upfield shift was seen for internal axle proton ϵ , suggesting anion binding in the three-dimensional cavity formed by the mechanical bond. To allow for comparison with catenane **2.23**· PF_6 , proton β was monitored upon anion addition with the resulting binding isotherms plotted in Figure 2.18a. Bromide caused the largest perturbation (0.36 ppm), followed by iodide (0.34 ppm) and then chloride (0.27 ppm). Small perturbations were also caused by sulfate (0.11 ppm).

For the dicationic rotaxane **2.37**·(PF_6)₂ significant perturbations in the ^1H NMR spectrum were exhibited by protons β and ϵ , analogous to **2.35**· PF_6 . Additionally, pyridinium protons a and b external to the binding cavity were perturbed, suggesting that association was not occurring in the centre of the interlocked cavity, perhaps due to increased electrostatics in the system. Further evidence for this is suggested by the smaller $\Delta\delta$ shifts exhibited in the case of each anion. Halide anion binding isotherms were obtained through monitoring the upfield shifts of axle pyridinium proton ϵ (Figure 2.18b).

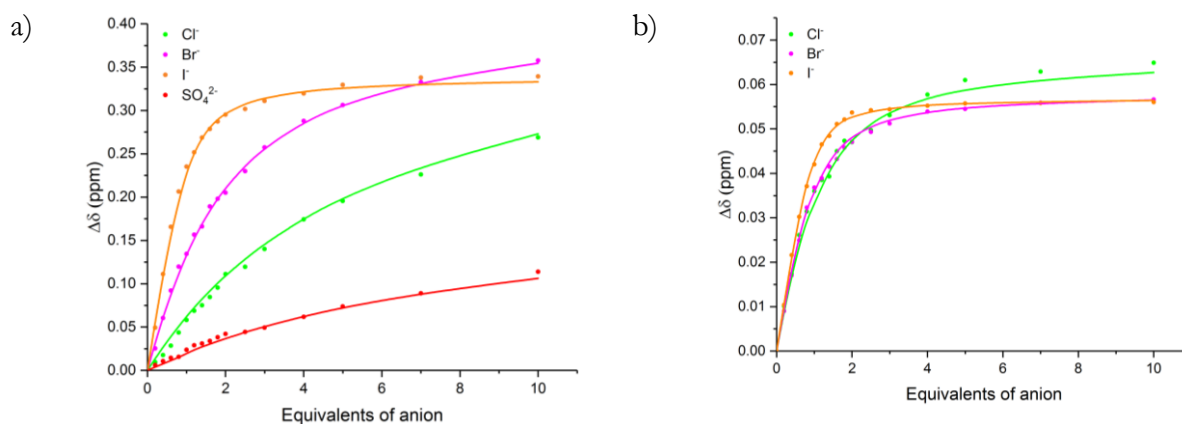


Figure 2.18 - Anion binding titrations of (a) **2.35·PF₆** and (b) **2.37·(PF₆)₂**. Performed in solvent mixture 45:45:10 CDCl₃/CD₃OD/D₂O; experimental titration data displayed as circles, WinEQNMR2¹⁴ fitted binding isotherms displayed as lines (298 K).

WinEQNMR2 analysis¹⁴ of the titration data for both rotaxanes gave 1:1 stoichiometric halide association constants (Table 2.3). Compared to catenane **2.23·PF₆**, the monocationic rotaxane **2.35·PF₆** displayed the same binding trend, iodide >> bromide > chloride.

Importantly however, the strength of iodide association by rotaxane **2.35·PF₆** was notably larger (ca. threefold) than observed for catenane **2.23·PF₆**, concomitant with a diminished chloride association. It is postulated that this was a result of sterics; the interlocked binding cavity was less hindered in the rotaxane in comparison to the catenane, thus reducing steric repulsion upon binding of larger anions. Furthermore, rotaxane **2.35·PF₆** exhibited far superior anion selectivity than the analogous catenane **2.23·PF₆**, with an impressive *circa* 40-fold increase in association constant observed for iodide over chloride, compared to a five-fold increase in the case of the catenane.

WinEQNMR2 analysis¹⁴ of the sulfate titration data gave a 1:2 host:guest stoichiometric association constant, a consequence of the anion's dicationic charge. Despite the increased electrostatic interactions with sulfate, rotaxane **2.35·PF₆** exhibited remarkable iodide selectivity, with the first association constant for sulfate binding, K_1 , an order of magnitude lower than the K_a for iodide.

In the case of dicationic rotaxane **2.37**·(**PF**₆)₂, the same halide preference iodide >> bromide > chloride was observed, whilst in each case there was a large increase in association strength, resulting from increased electrostatic interactions. Compared to **2.35**·**PF**₆, iodide binding affinity by **2.37**·(**PF**₆)₂ was three-times greater, whilst bromide and chloride were bound with an increased association constant of around an order of magnitude. Overall, a clear preference for iodide was exhibited by dicationic rotaxane **2.37**·(**PF**₆)₂, with the degree of discrimination for each halide similar to that of monocationic catenane **2.23**·**PF**₆. Of the three tetra-iodotriazole interlocked host structures investigated in this chapter, as well as the previously reported bis-iodotriazole catenane **2.1**·**PF**₆, monocationic rotaxane **2.35**·**PF**₆ exhibited the highest degree of selectivity for iodide over the other halides by an impressive margin.

Table 2.3 - Association constants (K_a) determined for **2.23**·**PF**₆, **2.35**·**PF**₆ and **2.37**·(**PF**₆)₂ with various anions (added as their TBA salts). Solvent: 45:45:10 CDCl₃/CD₃OD/D₂O, 298 K.

Anion	K_a (M ⁻¹) ^a		
	2.23 · PF ₆	2.35 · PF ₆	2.37 ·(PF ₆) ₂
Cl ⁻	210	89	1012
Br ⁻	351	342	2141
I ⁻	1176	3127	6145
SO ₄ ²⁻	55	$K_1 = 394$ $K_2 = 45$	- ^b

^[a]Association constants calculated using WinEQNMR2.¹⁴ Estimated standard errors < 10%. ^[b]Negligible change in chemical shift observed.

2.5 Conclusions

The research undertaken in this chapter has demonstrated the power of XB donor systems to achieve selective anion recognition in competitive aqueous solvent media. In particular,

the tetra-iodotriazole framework based upon the 3,5-bis-iodotriazole pyridinium motif has been proven to be a potent XB structure for anion binding.

Initially, an acyclic tetra-iodotriazole receptor **2.8**·PF₆ was prepared and its anion recognition properties determined in DMSO-*d*₆. Moderate binding was observed for the halides and acetate, whilst stronger association with sulfate was attributed to increased electrostatic interactions. A successful investigation into the feasibility of this motif to form a chloride anion template interpenetrated assembly was also performed, with evidence for pseudorotaxane formation elucidated from ¹H NMR spectroscopy.

Two novel tetra-iodotriazole [2]catenanes, monocationic **2.23**·PF₆ and dicationic **2.26**·(PF₆)₂, were prepared via a bis-amide condensation chloride anion template ‘clipping’ procedure. The monocationic catenane **2.23**·PF₆ bound the halides in the competitive solvent mixture 45:45:10 CDCl₃/CD₃OD/D₂O with the selectivity trend: iodide > bromide > chloride, as well as exhibiting weak binding of sulfate. In particular, when compared to the previously reported bis-iodotriazole catenane **2.1**·PF₆ depicted in Figure 2.2,¹³ which did not discriminate between Br⁻ and I⁻, **2.23**·PF₆ exhibited a clear selectivity for iodide over the other halides and several oxoanions.

An enhancement in anion association strength compared to catenane **2.23**·PF₆ was exhibited by analogous tetra-iodotriazole [2]rotaxanes, monocationic **2.35**·PF₆ and dicationic **2.37**·(PF₆)₂, which were prepared via the same chloride anion template method. Monocationic rotaxane **2.35**·PF₆ displayed a remarkable selectivity for iodide; with the association constant an order of magnitude greater than bromide and sulfate and almost a 40-fold increase compared to chloride. Dicationic rotaxane **2.37**·(PF₆)₂ demonstrated larger association constant magnitudes for each halide, attributed to an increased electrostatic contribution to anion binding, with the degree of halide anion selectivity comparable to that of monocationic catenane **2.23**·PF₆.

2.6 Future Work

Future work could focus on investigating the synthesis of all halogen bonding interlocked structures by modification of the isophthalamide macrocycle to an iodotriazole based XB analogue (Figure 2.19a). This may impact on anion selectivity trends through increased steric constraints upon the binding site, biasing the systems towards smaller anions such as chloride or bromide. Finally, in order to favour convergence of the four iodotriazole motifs the methylene spacer could be extended, either to an ethylene or propylene chain; this increased distance may allow more flexibility of the XB donor units and allow for convergent encapsulation of the anion (Figure 2.19b).

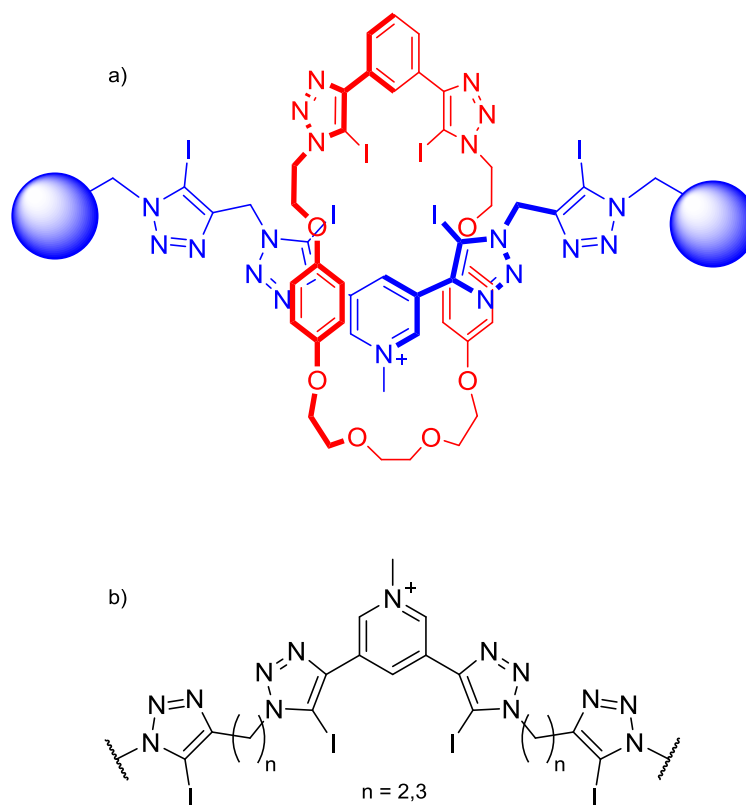


Figure 2.19 - Future work: a) all XB [2]rotaxane, b) tetra-iodotriazole with extended linkers between XB donor sites.

2.7 References

1. J. A. Wisner, P. D. Beer, M. G. B. Drew and M. R. Sambrook, *J. Am. Chem. Soc.*, 2002, **124**, 12469-12476.
2. M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul and A. R. Cowley, *J. Am. Chem. Soc.*, 2004, **126**, 15364-15365.
3. K. M. Mullen and P. D. Beer, *Chem. Soc. Rev.*, 2009, **38**, 1701-1713.
4. M. J. Langton and P. D. Beer, *Chem. Commun.*, 2014, **50**, 8124-8127.
5. N. H. Evans, C. J. Serpell and P. D. Beer, *Angew. Chem. Int. Ed.*, 2011, **50**, 2507-2510.
6. N. H. Evans and P. D. Beer, *Chem. Eur. J.*, 2011, **17**, 10542-10546.
7. L. M. Hancock and P. D. Beer, *Chem. Eur. J.*, 2009, **15**, 42-44.
8. L. M. Hancock, L. C. Gilday, N. L. Kilah, C. J. Serpell and P. D. Beer, *Chem. Commun.*, 2011, **47**, 1725-1727.
9. A. Brown, M. J. Langton, N. L. Kilah, A. L. Thompson and P. D. Beer, *Chem. Eur. J.*, 2015, **21**, 17664-17675.
10. Y. Zhao, Y. Li, Y. Li, H. Zheng, X. Yin and H. Liu, *Chem. Commun.*, 2010, **46**, 5698-5700.
11. N. G. White and P. D. Beer, *Org. Biomol. Chem.*, 2013, **11**, 1326-1333.
12. N. G. White and P. D. Beer, *Chem. Commun.*, 2012, **48**, 8499-8501.
13. S. W. Robinson, C. L. Mustoe, N. G. White, A. Brown, A. L. Thompson, P. Kennepohl and P. D. Beer, *J. Am. Chem. Soc.*, 2015, **137**, 499-507.
14. M. J. Hynes, *J. Chem. Soc., Dalton Trans.*, 1993, **0**, 311-312.
15. V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2002, **41**, 2596-2599.
16. J. E. Hein, J. C. Tripp, L. B. Krasnova, K. B. Sharpless and V. V. Fokin, *Angew. Chem. Int. Ed.*, 2009, **48**, 8018-8021.
17. W. S. Brotherton, R. J. Clark and L. Zhu, *J. Org. Chem.*, 2012, **77**, 6443-6455.
18. H. Goto, J. M. Heemstra, D. J. Hill and J. S. Moore, *Org. Lett.*, 2004, **6**, 889-892.
19. J. Y. C. Lim, T. Bunchuay and P. D. Beer, *Chem. Eur. J.*, 2017, **23**, 4700-4707.
20. R.-P. Moldovan, R. Teodoro, Y. Gao, W. Deuther-Conrad, M. Kranz, Y. Wang, H. Kuwabara, M. Nakano, H. Valentine, S. Fischer, M. G. Pomper, D. F. Wong, R. F. Dannals, P. Brust and A. G. Horti, *J. Med. Chem.*, 2016, **59**, 7840-7855.
21. H. Zheng, W. Zhou, X. Yin, Y. Li, H. Liu, Y. Li, *Chem. Eur. J.*, 2009, **15**, 13253-13262.

Chapter Three

Transition metal-based halogen and hydrogen
bonding hosts for anion sensing

3 Transition metal-based halogen and hydrogen bonding hosts for anion sensing

3.1 Introduction

The integration of transition metal complexes into anion binding host structures can enhance both anion binding strength and selectivity, as described in section 1.4. A positively charged metal centre enables electrostatic interactions between the host and the anionic guest, whilst a metal chelated in close proximity to a binding site may facilitate charge assisted bonding interactions.¹ For example, in the case of XB-based iodotriazole systems, polarisation of the C-I bond increases the size and potency of the σ -hole leading to an enhanced interaction with a Lewis basic guest.² Furthermore, a preorganised metal complex may impart geometric constraints upon the binding site, which can impact anion selectivity. Additionally, certain transition metal complexes are photo-active and the incorporation of such species into receptor design produces a chemosensor, with the capability of eliciting a detectable optical response to an anion binding event.

Whilst many examples exist of transition metal-based HB hosts for anion sensing, there are far fewer metal complexed XB receptors designed for this purpose. In particular, reports of anion binding via charged-assisted metal-bound XB moieties are rare. Recently, Ghosh has described an XB iodotriazole containing heteroleptic Ru(II) complex selective for H_2PO_4^- in CH_3CN containing up to 20% H_2O (Figure 3.1).³ Anion addition caused a significant intensity enhancement in the MLCT luminescence emission spectrum of the host, whilst the association constant for H_2PO_4^- binding was almost four-times larger in magnitude for the XB chemosensor compared to the HB analogue.

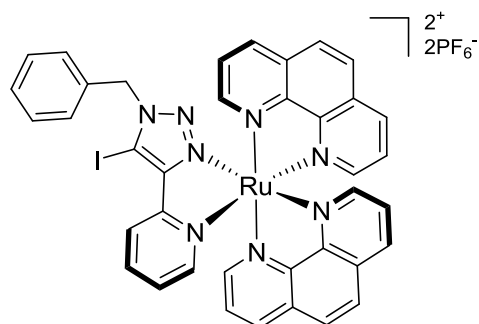


Figure 3.1 - Ghosh's Ru(II) dihydrogenphosphate sensor.³

The integration of a transition metal complex into an interlocked XB structure has been recently achieved by Beer. A [2]rotaxane containing a bidentate bis-iodotriazole macrocycle component was initially prepared via an active metal template (AMT) strategy and complexed to a Re(I) metal centre (Figure 3.2).⁴ The rotaxane was selective for chloride in CHCl_3 , as determined by UV/vis absorption anion titration experiments. Furthermore, methylation of the axle's iodotriazole motif afforded a rotaxane selective for bromide in 9:1 acetone- d_6 /D $_2$ O.⁵ Disappointingly, neither of these Re(I) rotaxanes exhibited MLCT luminescence, and attempts to chelate other photoactive metal centres such as Ru(II) and Os(II) were unsuccessful. This provides the motivation for the work investigated in this chapter.

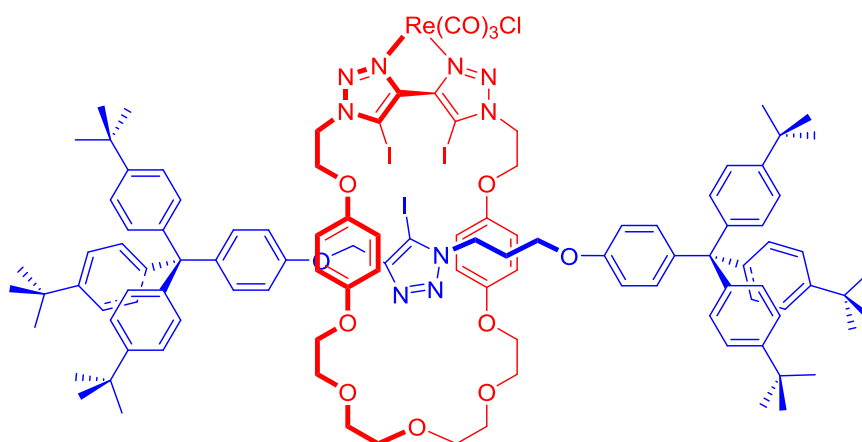


Figure 3.2 - Beer's chloride selective Re(I) [2]rotaxane.⁴

3.1.1 Chapter aims

The unsymmetrical methylene-spaced bis-iodotriazole motif was shown in Chapter Two to be able to form effective XB host structures for anion recognition. It is also a potential candidate to act as a new bidentate ligand for transition metals owing to the neighbouring *N*-triazole donors. The work in this chapter describes the synthesis of acyclic ligands, based upon this motif, and their coordination properties to kinetically inert Re(I), Ru(II), Os(II) and Ir(III) transition metals. In particular, metallo XB and HB acyclic receptors are prepared for anion recognition and sensing investigations (Figure 3.3). Following this, attempts to prepare interlocked structures containing the bis-triazole motif are outlined; with the ultimate aim of forming XB transition metal based MIMs for anion sensing.

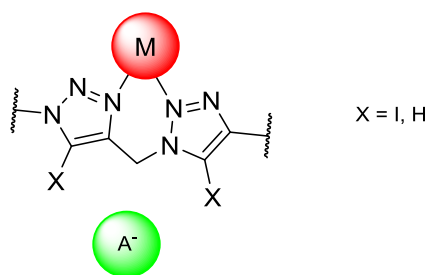


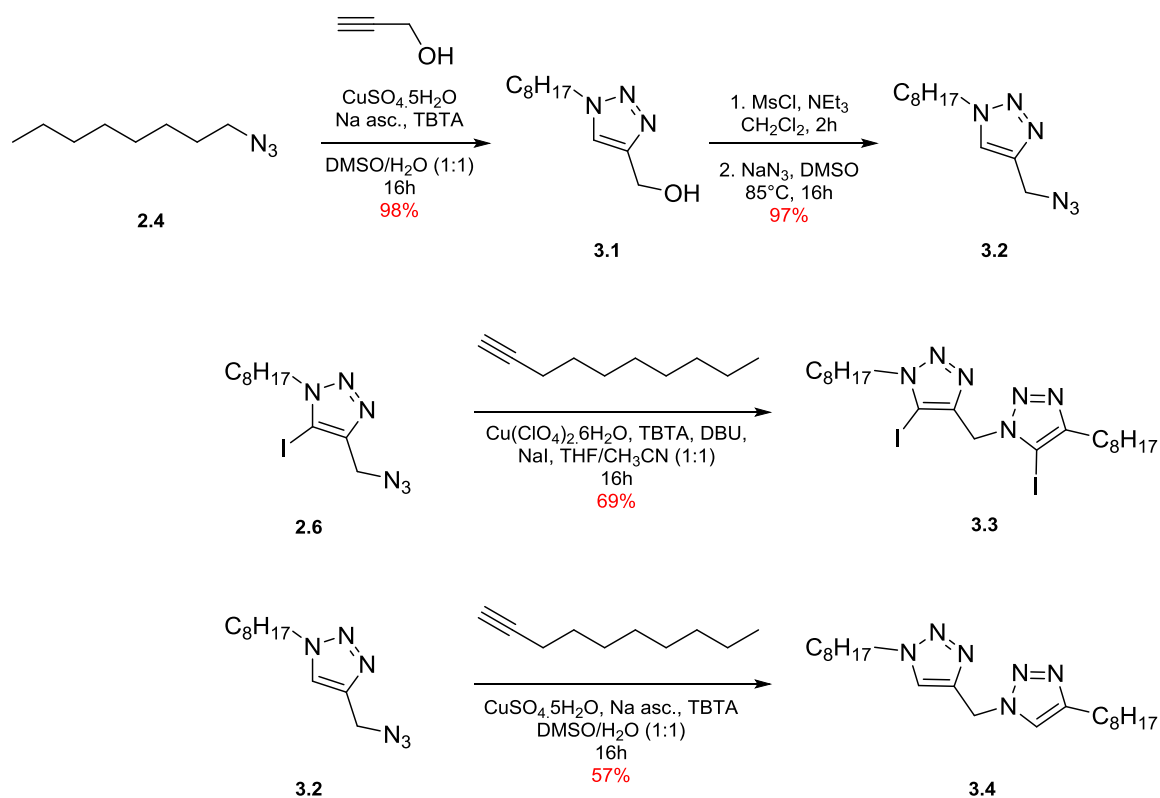
Figure 3.3 - Methylene-spaced bis-triazole ligand investigated in this chapter. *M* = transition metal complex, *A⁻* = anion.

3.2 Acyclic receptors

Acyclic XB and HB ligands were synthesised based upon the unsymmetrical methylene-spaced bis-triazole motif. Subsequently, these were coordinated to Re(I), Ru(II), Os(II) and Ir(III) transition metals and their anion binding and sensing properties investigated using ¹H NMR and luminescence spectroscopy.

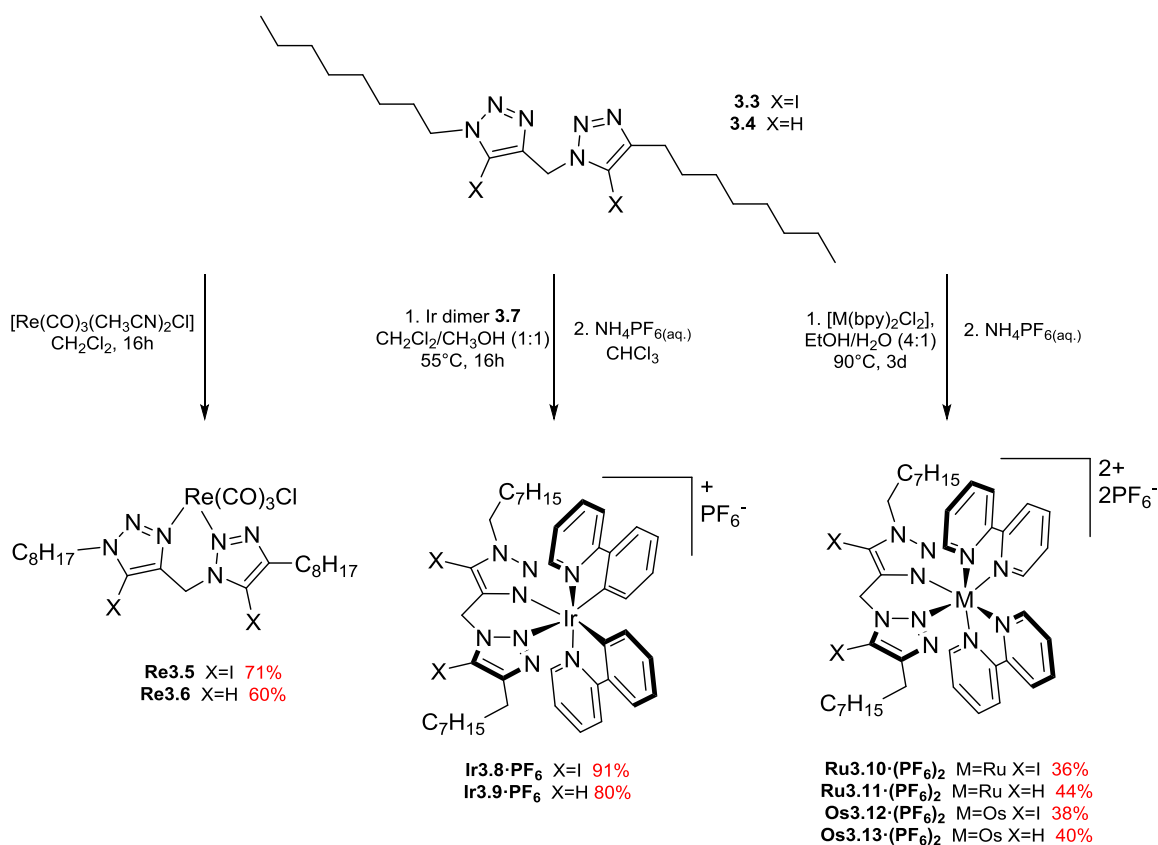
3.2.1 Synthesis

Iodotriazole azide **2.6** was required for the synthesis of the target XB containing acyclic ligand; meanwhile the initial step towards the HB analogue proceeded via the CuAAC protocol click reaction between octyl azide **2.4** and propargyl alcohol. The addition of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ and sodium ascorbate and a catalytic amount of TBTA to an equimolar DMSO/ H_2O solution of **2.4** and propargyl alcohol afforded triazole alcohol **3.1** in a 98% yield (Scheme 3.1). Conversion of the terminal hydroxyl group to the corresponding mesylate was achieved through use of MsCl in the presence of excess NEt_3 , before azide substitution by heating with NaN_3 in DMSO gave triazole azide **3.2** in excellent yield. Iodotriazole azide **2.6** and triazole azide **3.2** were each reacted with 1-decyne under CuAAC conditions to afford the target bis-iodotriazole and bis-triazole ligands **3.3** and **3.4** in good yields (Scheme 3.1).



Scheme 3.1 - Synthesis of methylene-spaced bis-triazole ligands **3.3** and **3.4**.

A series of metal complexation reactions were performed with ligands **3.3** and **3.4** (Scheme 3.2). Coordination with Re(I) was achieved by first generating the $[\text{Re}(\text{CO})_3(\text{CH}_3\text{CN})_2\text{Cl}]$ intermediate, following a literature procedure,⁶ before addition of XB **3.3** and HB **3.4** ligands gave complexes **Re3.5** (XB) and **Re3.6** (HB). Complexation of the ligands with Ir(III) was performed through reaction with the $[\text{Ir}_2(\text{ppy})_4\text{Cl}_2]$ dimer **3.7**, which had been previously prepared from $\text{IrCl}_3 \cdot x\text{H}_2\text{O}$ and 2-phenyl pyridine.⁷ Heating the bis-triazole species **3.3** and **3.4** overnight with **3.7** in 1:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ afforded complexes **Ir3.8·Cl** (XB) and **Ir3.9·Cl** (HB) after purification via preparative TLC. A non-coordinating counter anion was necessary for anion binding studies, therefore **Ir3.8·Cl** and **Ir3.9·Cl** were washed repeatedly with aqueous NH_4PF_6 to give complexes **Ir3.8·PF₆** and **Ir3.9·PF₆**. The Ru(II) complexes **Ru3.10·(Cl)₂** (XB) and **Ru3.11·(Cl)₂** (HB) and Os(II) complexes **Os3.12·(Cl)₂** (XB) and **Os3.13·(Cl)₂** (HB) were prepared through reaction with $[\text{M}(\text{bpy})_2\text{Cl}_2]$ in hot 4:1 ethanol/water for several days. The PF_6^- salts were isolated through precipitation with aqueous NH_4PF_6 (Scheme 3.2).



Scheme 3.2 - Synthesis of XB and HB transition metal-based receptors.

Each metal complex was characterised by ¹H, ¹³C, and ¹⁹F NMR spectroscopy and high resolution ESI mass spectrometry. Metal complexation was ascertained through a diagnostic splitting of the methylene spacer protons (*e* and *e'*) of the respective ligand in the ¹H NMR spectrum (Figure 3.4). These protons appeared as a single resonance, a 2H singlet, in the spectra of free ligands **3.3** and **3.4**. Upon complexation of the ligands to the chiral metal centre these methylene protons became non-equivalent and exhibited geminal coupling to one another, appearing as two 1H doublets in the ¹H NMR spectrum (Figure 3.4).

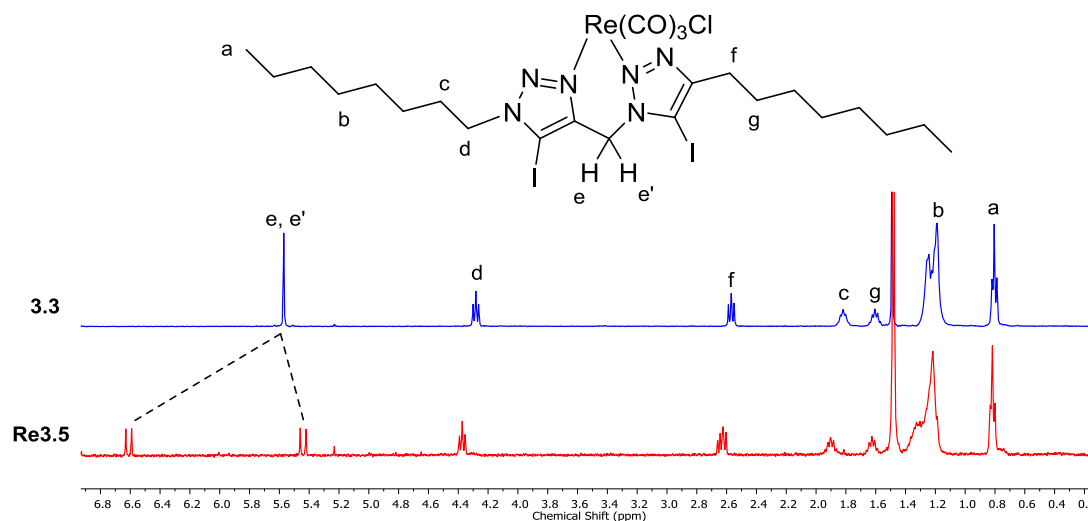


Figure 3.4 - ^1H NMR spectrum of **3.3** and **Re3.5** in CDCl_3 , indicating diagnostic methylene proton splitting upon Re(I) complexation (400 MHz, 298 K).

3.2.2 Preliminary structure elucidation via X-ray crystallography

In order to gain an insight into the geometry of the metal complexes and the nature of any possible charge assisted anion interactions, attempts were made to grow crystals suitable for structural determination by X-ray diffraction from a solution of the transition metal PF_6^- salts in the presence and absence of a large excess of TBACl. Only in one case were crystals of suitable quality obtained for X-ray diffraction structural analysis.

A chloroform solution of HB complex **Ru3.11**·(PF_6)₂, layered with hexane and left for one week, afforded crystals that could be investigated via X-ray diffraction. The highly disordered alkyl chains prevented a complete structural determination of the metallo receptor, however, a preliminary structure, solved by Dr. Asha Brown, revealed bidentate binding at the *N*-triazole positions, forming a six-membered ring upon metal coordination (Figure 3.5). This further confirmed the loss of symmetry of the methylene protons.

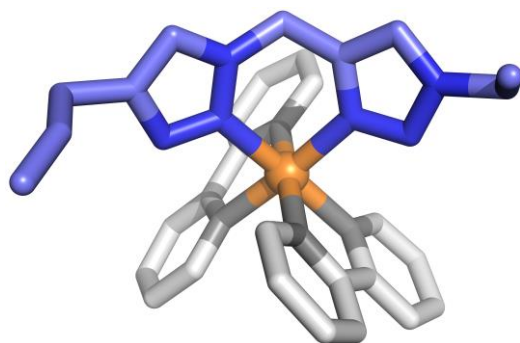


Figure 3.5 - Preliminary crystal structure of **Ru3.11**·(**PF₆**)₂. Data obtained at Diamond Light Source, structure determined by Dr. Asha Brown.

3.2.3 ¹H NMR anion binding studies

The anion binding properties of the XB and HB metal complexes were studied through ¹H NMR titration experiments. Initially, receptors **Re3.5** and **Re3.6** were investigated to give a direct comparison between XB and HB analogues. The chemical shifts of the receptors' proton resonances were monitored upon addition of aliquots of a variety of anions added as their tetrabutylammonium (TBA) salts in acetone-*d*₆. The XB receptor **Re3.5** exhibited significant perturbations of the methylene spacer protons upon addition of I⁻ and Br⁻, with $\Delta\delta$ shifts of up to 0.12 ppm, whilst very small $\Delta\delta$ ppm perturbations were observed upon addition of Cl⁻ and NO₃⁻ (Figure 3.6). By contrast, for HB receptor **Re3.6** these shifts were considerably larger, with $\Delta\delta$ perturbations ranging from 0.15 – 0.72 ppm upon halide and nitrate addition. The resonances of triazole protons, *b* and *i*, were also notably modified, with $\Delta\delta$ shifts ranging from 0.09 – 0.45 ppm.

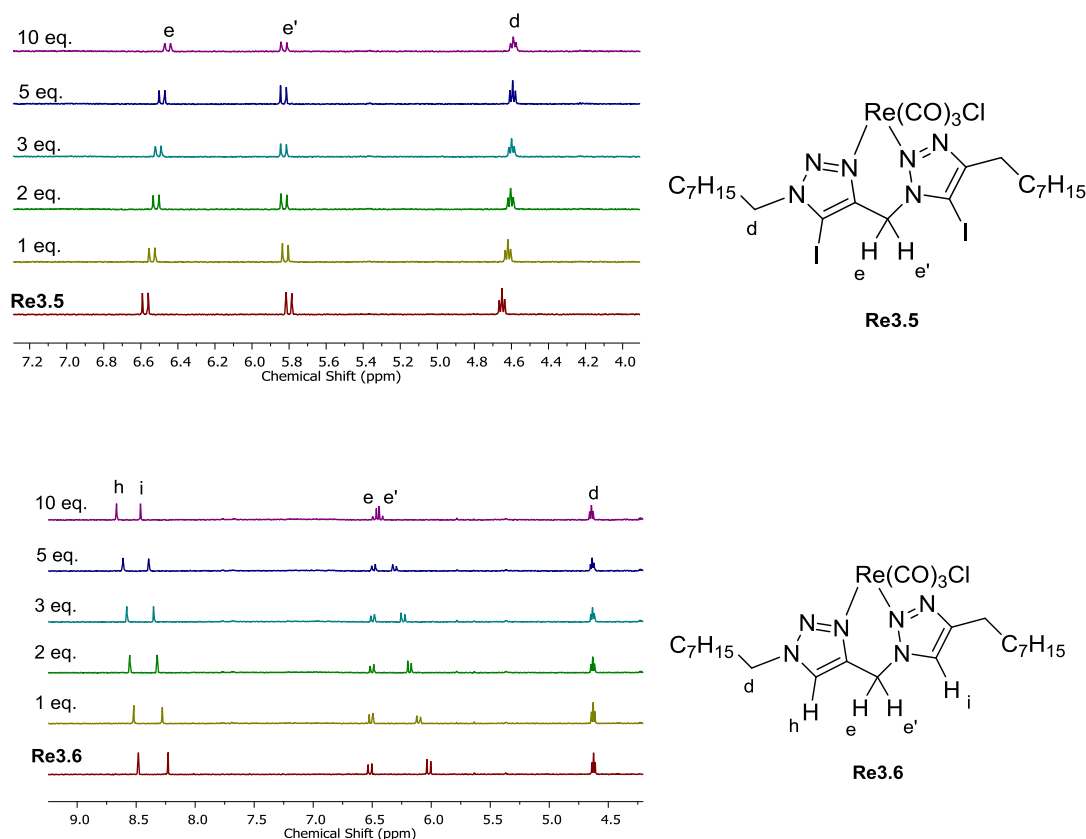


Figure 3.6 - Truncated ^1H NMR spectra of **Re3.5** and **Re3.6** on addition of equivalents of TBABr in acetone- d_6 (500 MHz, 298 K).

WinEQNMR2 analysis⁸ of the titration data, monitoring the shift of the methylene protons *e* and *e'* (Figure 3.7) determined 1:2 stoichiometric host:guest association constants given in Table 3.1. Amongst the halides the XB receptor exhibited notably stronger binding of I^- and Br^- compared to the HB analogue, displaying the selectivity trend $\text{I}^- > \text{Br}^- \gg \text{Cl}^-$, NO_3^- . In stark contrast, for HB receptor **Re3.6**, NO_3^- was bound the strongest, followed by Cl^- , I^- and finally Br^- .

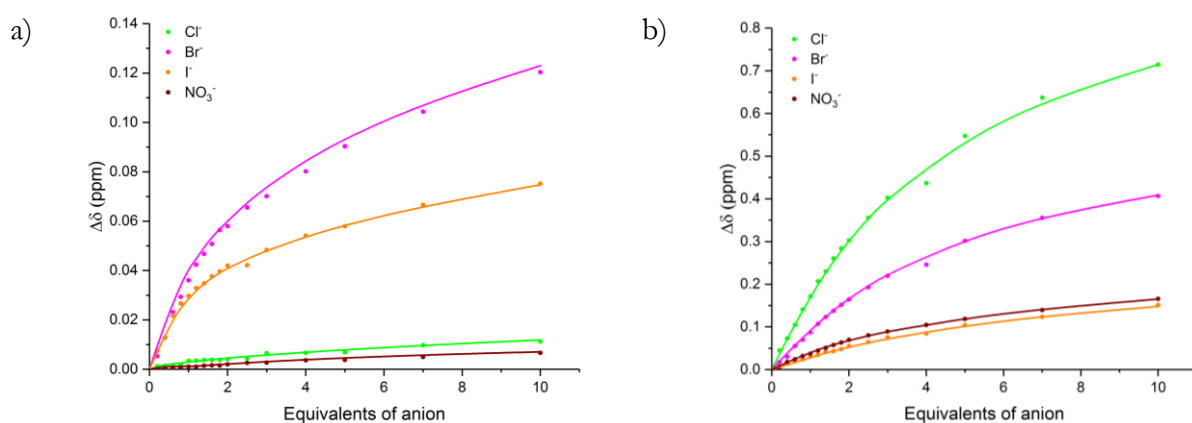


Figure 3.7 - Anion binding isotherms of a) **Re3.5** and b) **Re3.6** following chemical shifts of asymmetric methylene spacer protons in acetone- d_6 ; experimental titration data displayed as circles, WinEQNMR2 fitted binding isotherms displayed as lines (500 MHz, 298 K).⁸ Receptor concentration = 1.5 mM.

Table 3.1 - Association constants determined using WinEQNMR2 (298 K),⁸ units M^{-1} , errors <10%. Performed in acetone- d_6 ; Anions added as TBA salts. ^aVery small $\Delta\delta$ ppm perturbations observed. Receptor concentration = 1.5 mM.

Anion	Re3.5		Re3.6	
	K_1	K_2	K_1	K_2
Cl^-	- ^a	- ^a	1635	118
Br^-	4106	49	902	114
I^-	4893	37	1398	44
NO_3^-	- ^a	- ^a	2943	57

The nitrate selectivity displayed by HB receptor **Re3.6** was postulated to be due to shape complementarity between the receptor and the anion. The trigonal planar anion is well suited to bind at both triazole HB donor sites (Figure 3.8). Conversely, this may not be possible for **Re3.5** due to the enforced directionality of the XB and hence very weak binding was observed for this receptor with nitrate.

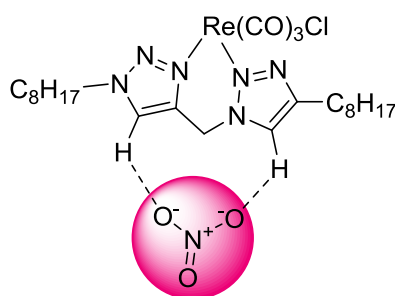


Figure 3.8 - Speculated nature of association between **Re3.6** and nitrate.

For the cationic transition metal receptors, preliminary ^1H NMR titration experiments were undertaken with chloride in acetone- d_6 (Table 3.2). The XB derivatives all exhibited stronger binding than their HB analogues. Furthermore, these cationic complexes displayed considerably greater Cl^- binding strength than the overall neutral Re(I) receptors; a consequence of charge assisted halogen bonding in which the C-X bond is further polarised by the charged metal centre, as well as favourable electrostatic interactions. Chloride binding by **Ru3.10**·(PF_6) $_2$ and **Os3.12**·(PF_6) $_2$ was too strong to allow the accurate determination of their association constants ($K_1 > 10^4 \text{ M}^{-1}$). Unfortunately, the methylene proton signals of **Ir3.9**· PF_6 could not be monitored during the Cl^- titration experiment due to overlapping peaks, resulting in the association constant not being obtained.

Table 3.2 - Association constants determined using WinEQNMR2 (298 K),⁸ units M^{-1} , errors <10%. Performed in acetone- d_6 ; Anions added as TBA salts. ^aCould not be plotted due to overlap of peaks. ^bNot calculated since $K_1 > 10^4 \text{ M}^{-1}$. Receptor concentration = 1.5 mM.

Complex	Ir(III)		Ru(II)		Os(II)	
	3.8· PF_6	3.9· PF_6	3.10·(PF_6) $_2$	3.11·(PF_6) $_2$	3.12·(PF_6) $_2$	3.13·(PF_6) $_2$
K_1	6338	^a	$>10^4$	6884	$>10^4$	5742
K_2	336	^a	^b	28	^b	327

3.2.4 Preliminary photophysical investigations

Preliminary photophysical studies were performed with each transition metal receptor in acetonitrile. Whilst the Re(I) complexes were not photo-active, the Ir(III), Ru(II) and Os(II) receptors all exhibited metal to ligand charge transfer (MLCT) absorption bands in their UV-vis spectra, as well as being notably emissive (Table 3.3). The respective absorbance and emission photophysical data are similar to Ir(III) 2-phenylpyridine and Ru(II) and Os(II) 2,2'-bipyridine based metal complexes reported in the literature.⁹⁻¹²

Table 3.3 - Photophysical data calculated at 1×10^{-5} M in CH_3CN at 298 K. MLCT absorbance wavelength ($\lambda_{\text{abs,MLCT}}$), excitation wavelength (λ_{ex}), maximum emission wavelength ($\lambda_{\text{em,max}}$).

Complex	$\lambda_{\text{abs,MLCT}}$ (nm)	λ_{ex} (nm)	$\lambda_{\text{em,max}}$ (nm)
Ir3.8 ·PF ₆ , Ir3.9 ·PF ₆	380	370	476, 505
Ru3.10 ·(PF ₆) ₂ , Ru3.11 ·(PF ₆) ₂	425	426	546, 601
Os3.12 ·(PF ₆) ₂ , Os3.13 ·(PF ₆) ₂	440	450	748

Preliminary qualitative luminescence titrations with Cl[−] were performed with the XB receptors **Ir3.8**·PF₆, **Ru3.10**·(PF₆)₂ and **Os3.12**·(PF₆)₂. The response in the emission spectrum of each was monitored upon addition of 100 equivalents of Cl[−] (added as TBACl) to each complex in acetonitrile (Figure 3.9). Modest spectral changes were observed with **Ru3.10**·(PF₆)₂ and **Os3.12**·(PF₆)₂, with a 15% enhancement and a 7% quenching in emission intensity observed respectively. The iridium XB receptor **Ir3.8**·PF₆ displayed a more impressive response, with a 42% switch-on in luminescence.

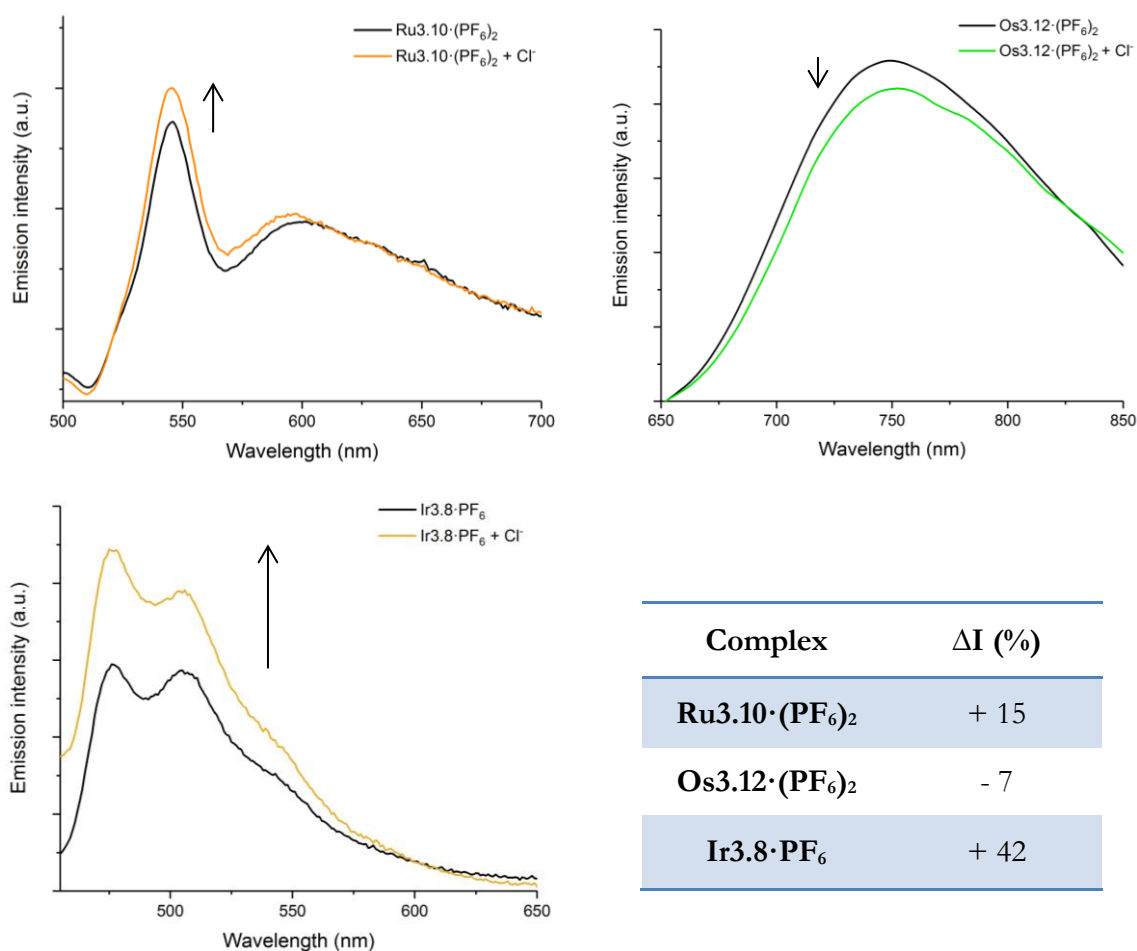


Figure 3.9 - Emission spectra of transition metal complexes **Ru3.10·(PF₆)₂**, **Os3.12·(PF₆)₂** and **Ir3.8·PF₆** their response to addition of 100 equivalents of chloride. Photophysical data calculated at 1×10^{-5} M in CH₃CN at 298 K.

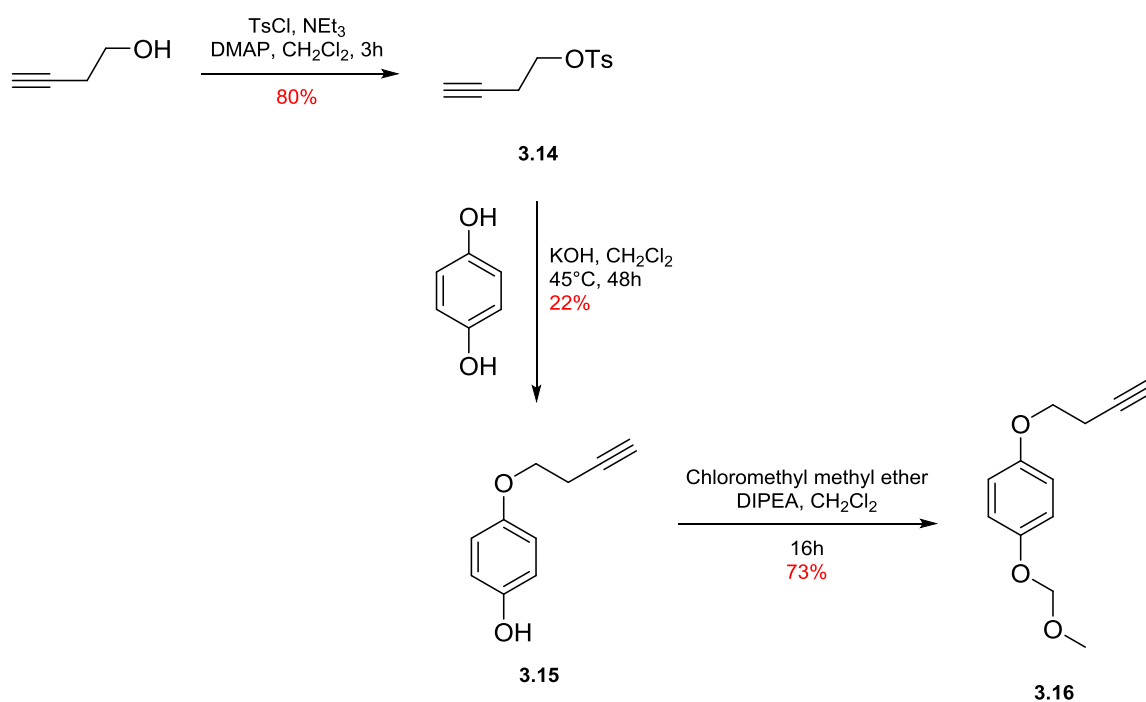
3.3 Attempts to prepare transition metal-based interlocked structures

AMT synthesis utilising the triazole moiety to bind a Cu(I) template has recently been an active area of research within the Beer group.^{4,5,13} By employing a macrocycle that enforces endotopic binding of the Cu(I) catalyst, a CuAAC reaction between stopper azide and stopper alkyne axle precursors can occur within the macrocycle facilitating rotaxane formation. Taking into account the successful transition metal binding by the methylene-

spaced bis-iodotriazole motif, the bidentate ligand's incorporation into a macrocycle for AMT rotaxane preparation was undertaken.

3.3.1 Macrocycle Synthesis

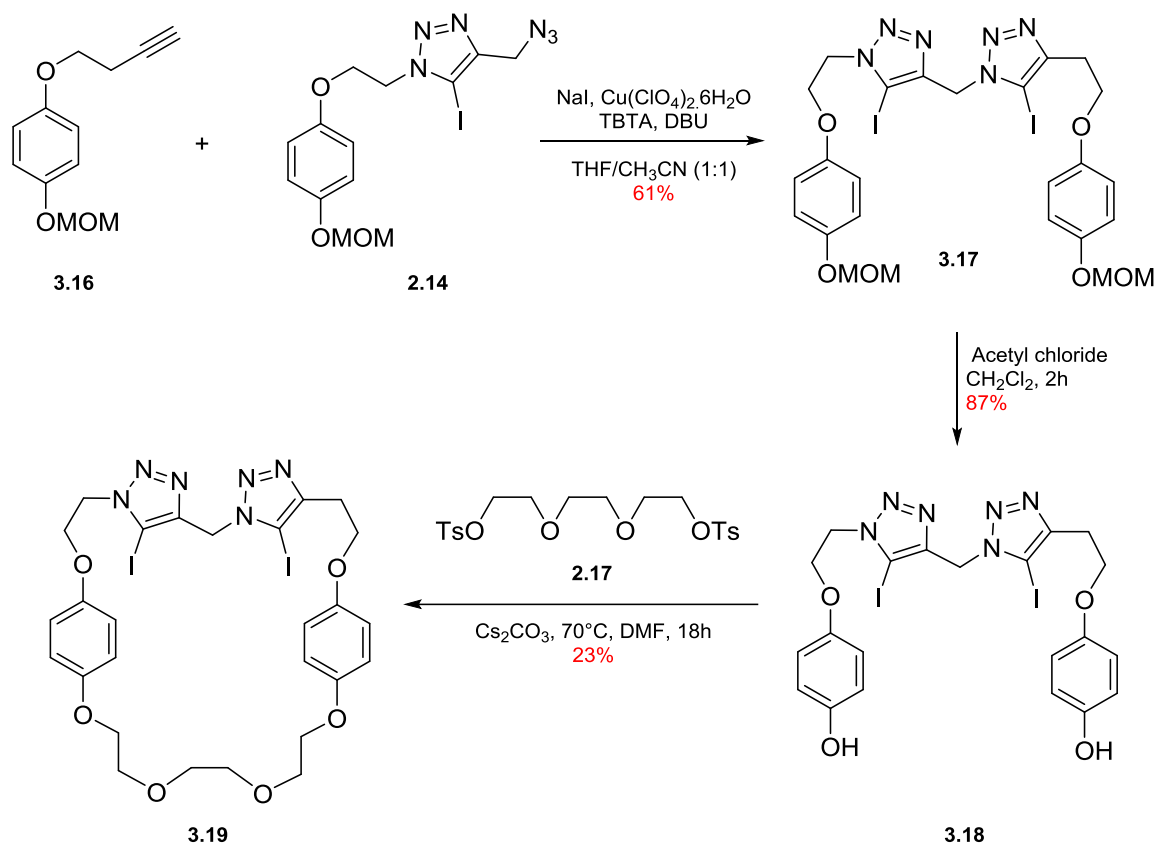
A macrocycle was targeted based upon previously synthesised MOM-protected azide **2.14** (Chapter Two). A corresponding alkyne was prepared, beginning with the reaction between 3-butyne-1-ol and tosyl chloride to form tosyl alkyne **3.14** (Scheme 3.3). This was reacted for two days with hydroquinone in the presence of KOH in a statistical reaction to afford the mono-substituted product **3.15**. Protection of the phenol group with chloromethyl methyl ether led to the isolation of target MOM-protected alkyne **3.16** in 73% yield.



Scheme 3.3 - Synthesis of MOM-protected alkyne **3.16**.

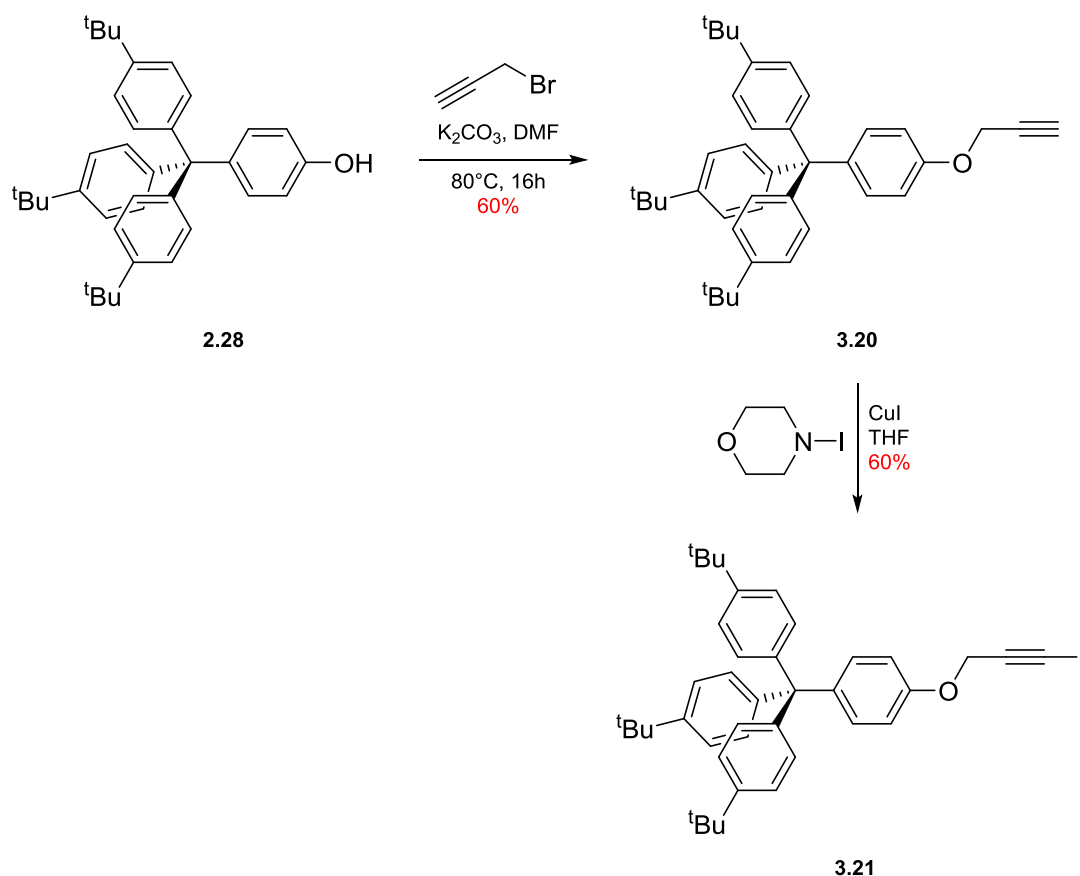
Alkyne **3.16** was reacted with azide **2.14** under one-pot iodo-click conditions to give bis-iodotriazole **3.17** as a precipitate in good yield (Scheme 3.4). The MOM-protecting groups were cleaved using acetyl chloride in 1:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$, giving bis-phenol **3.18**. Under

basic, high dilution conditions in DMF, reaction between **3.16** and bis-tosylate **2.17** afforded macrocycle **3.19** in 23% yield after purification by preparative TLC.



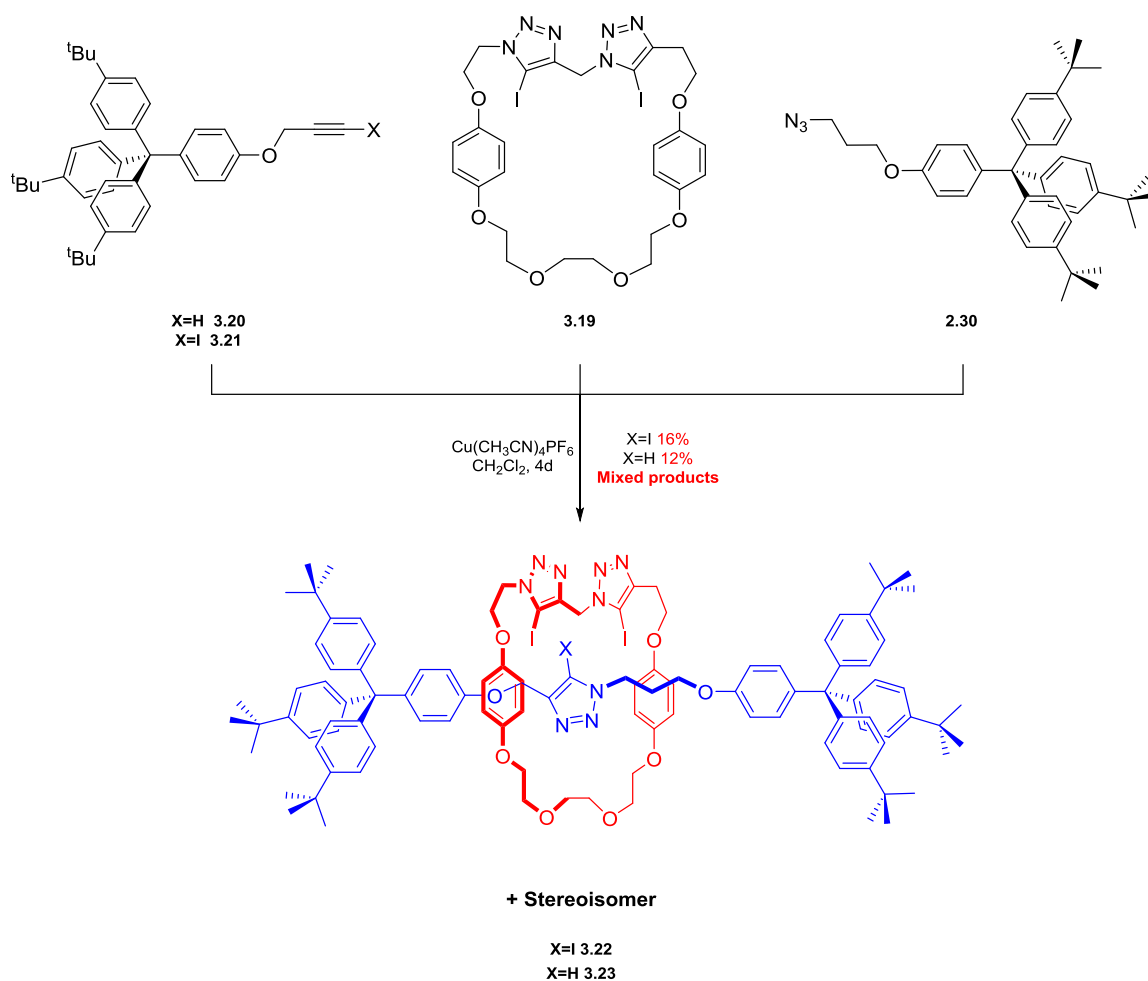
Scheme 3.4 - Synthesis of macrocycle **3.19**.

Stopper propyl azide **2.30**, prepared in Chapter Two, was identified as a suitable axle precursor stopper derivative for the AMT reaction. The synthesis of trityl stopper alkyne axle precursor **3.21** was undertaken according to Scheme 3.5.¹⁴ Phenol **2.28** was reacted with propargyl bromide in the presence of K₂CO₃ to afford stopper alkyne **3.20** in 60% yield. The iodoalkyne derivative **3.21** was prepared by stirring **3.20** overnight in the presence of N-iodomorpholine and a catalytic amount of CuI.



Scheme 3.5 - Preparation of stopper alkyne **3.20** and iodoalkyne derivative **3.21**.

Attempted AMT rotaxane reactions were performed following literature conditions.¹⁵ Macrocycle **3.19** was dissolved in a solution of CH_2Cl_2 containing an equimolar amount of Cu(I) catalyst $[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ before addition of five equivalents of both stopper azide **2.30** and either alkyne **3.20** or iodoalkyne derivative **3.21** (Scheme 3.6). Monitoring the reactions by TLC and ESI-MS showed evidence of rotaxane formation and the interlocked products were isolated in modest yields of 12% and 16% respectively after purification by preparative TLC.



Scheme 3.6 - Synthesis of rotaxanes **3.22** and **3.23** via AMT reaction.

Since both the macrocycle and axle components of both rotaxanes were unsymmetrical, the resulting ^1H NMR spectra were challenging to interpret. The ^1H NMR spectrum of rotaxane **3.23** is shown in Figure 3.10. There are key features that indicated successful rotaxane formation. The upfield and split nature of the macrocycle hydroquinone environments was diagnostic of interlocked structure formation and suggested a π - π interaction with the axle, whilst there was significant broadening of the crown ether resonances. The doubling of the peaks in the vicinity of the mechanical bond was indicative of the two isomeric rotaxane products formed in the AMT reaction. These include the axle triazole proton and the peak at ~ 5.6 ppm corresponding to the methylene protons between the iodotriazole groups. Similar

shifts were exhibited in the ^1H NMR spectrum of XB rotaxane **3.22**. On account of the low yields and complex ^1H NMR spectra, alternative symmetric macrocycles were targeted for AMT investigation.

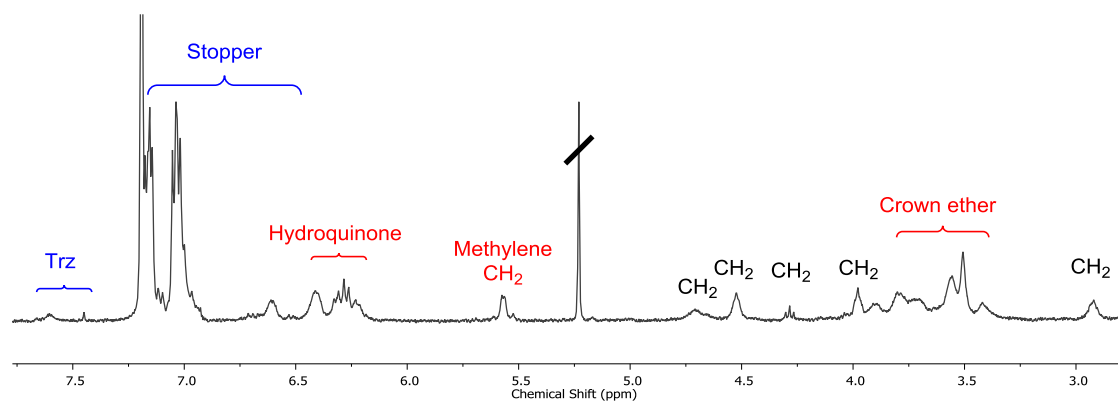


Figure 3.10 - Truncated ^1H NMR of rotaxane **3.23**. Key proton resonances labelled (CDCl_3 , 500 MHz, 298 K).

3.3.2 Symmetric macrocycles for AMT rotaxane synthesis

As a proof of concept, the methylene-spaced bis-iodotriazole motif was shown to be amenable to MIM formation via AMT. In order to overcome the issues arising from the unsymmetrical macrocycle, novel symmetric macrocycles were targeted based upon work performed in Chapter Two (Figure 3.11).

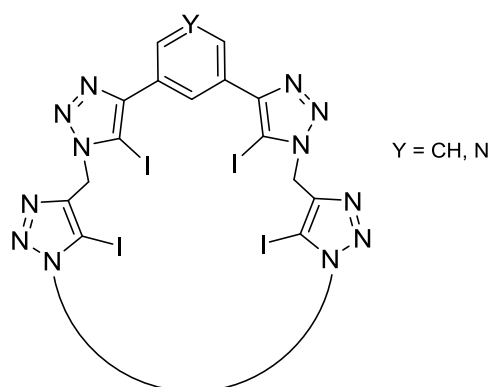
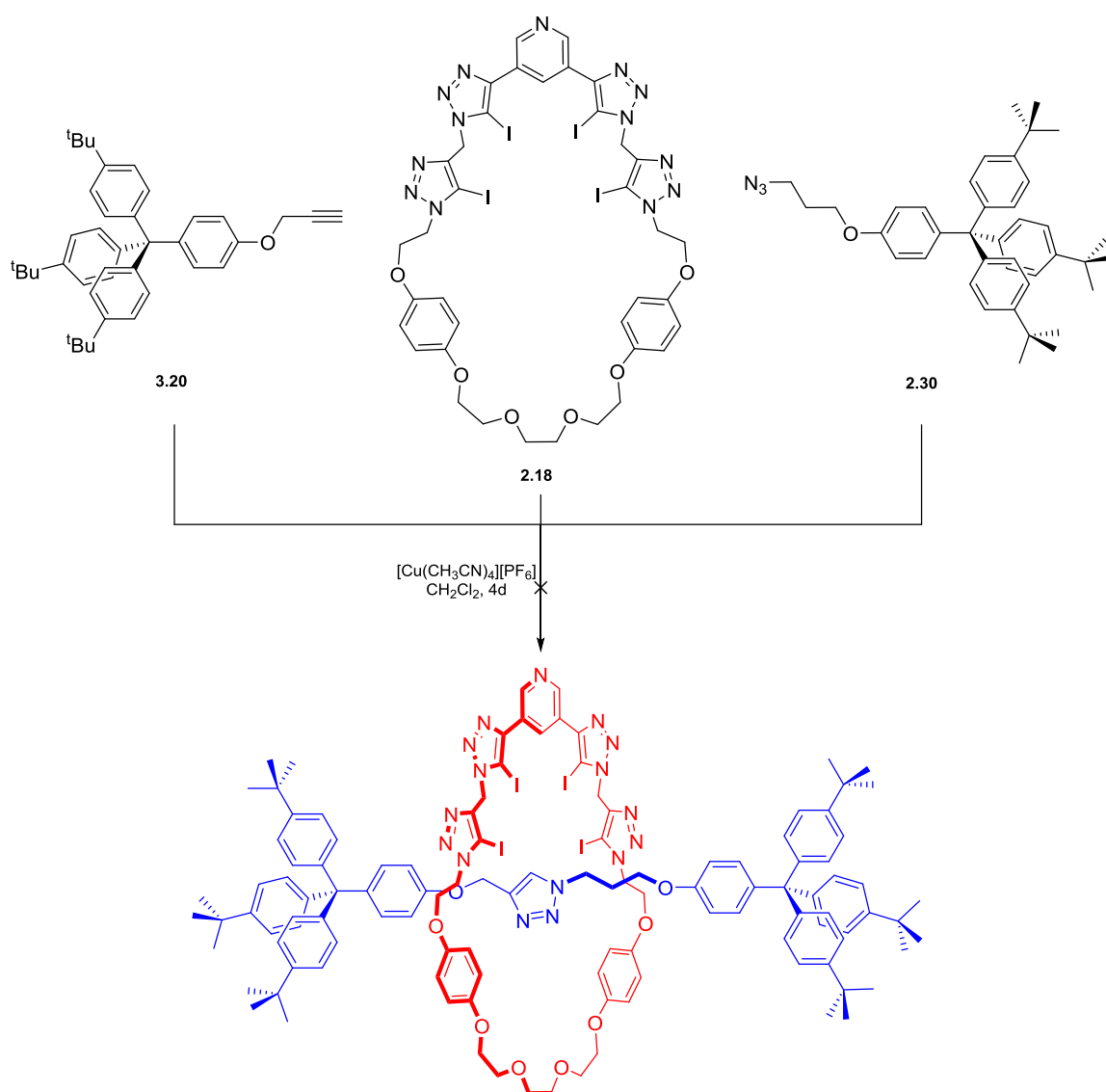
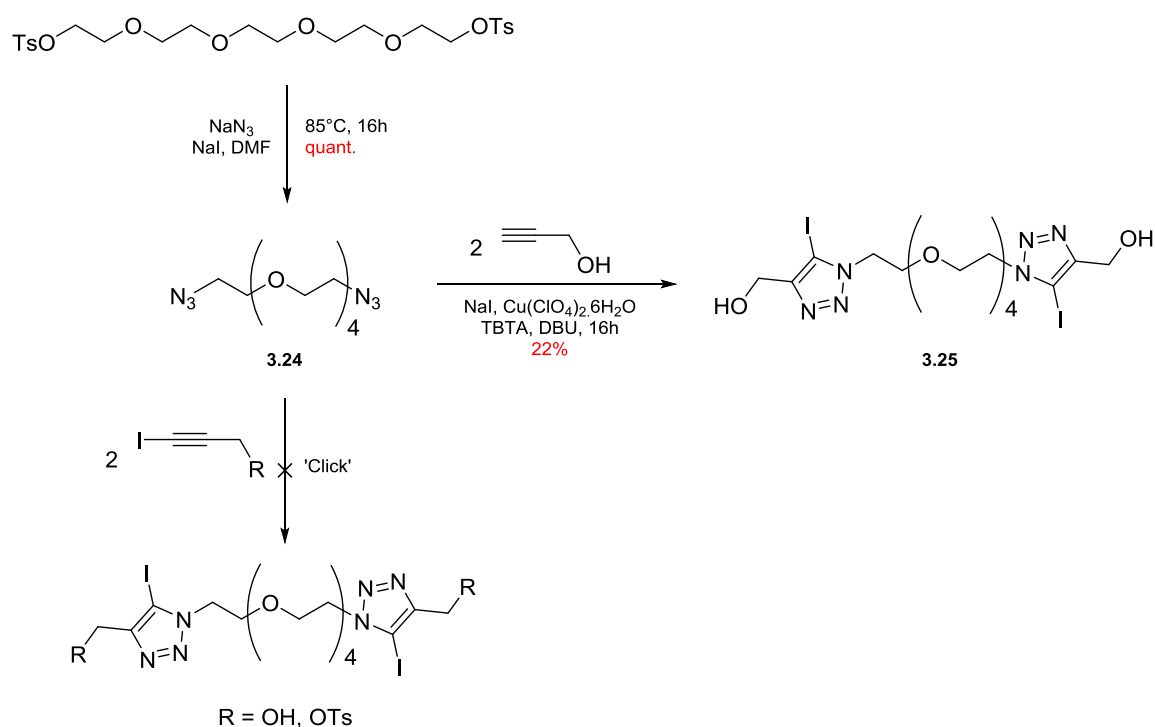


Figure 3.11 - Schematic representation of target symmetric macrocycles.

An initial attempted AMT reaction was performed using tetra-iodotriazole macrocycle **2.18** and stoppers **3.20** and **3.21** (Scheme 3.7). However, monitoring this reaction by TLC and ESI-MS spectroscopy only resulted in detection of the macrocycle and the triazole axle product, with no evidence of rotaxane. The failure of this reaction was ascribed to a combination of large macrocycle size and the pyridine site offering a competing position for Cu(I) coordination exotopically. Therefore, two smaller symmetric tetra-iodotriazole macrocycles were targeted.



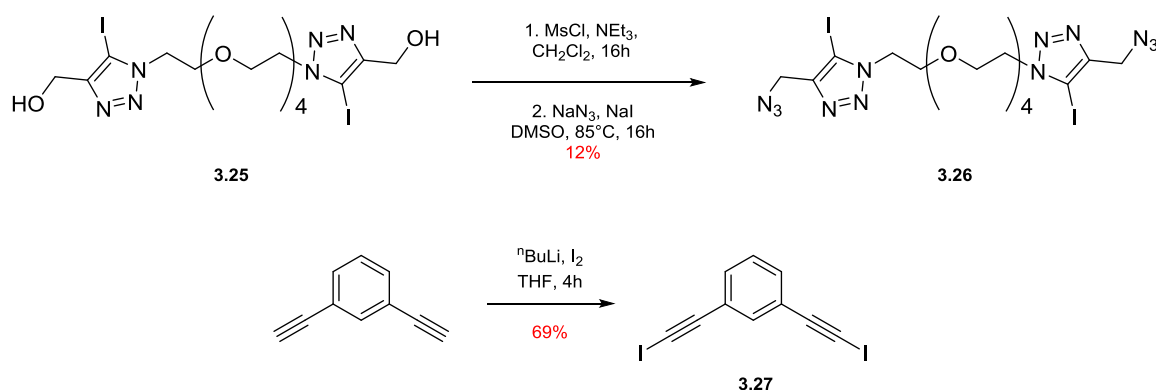
Scheme 3.7 - Attempted rotaxane formation via AMT reaction utilising macrocycle **2.18**.



Scheme 3.8 - Preparation of bis-iodotriazole alcohol 3.25.

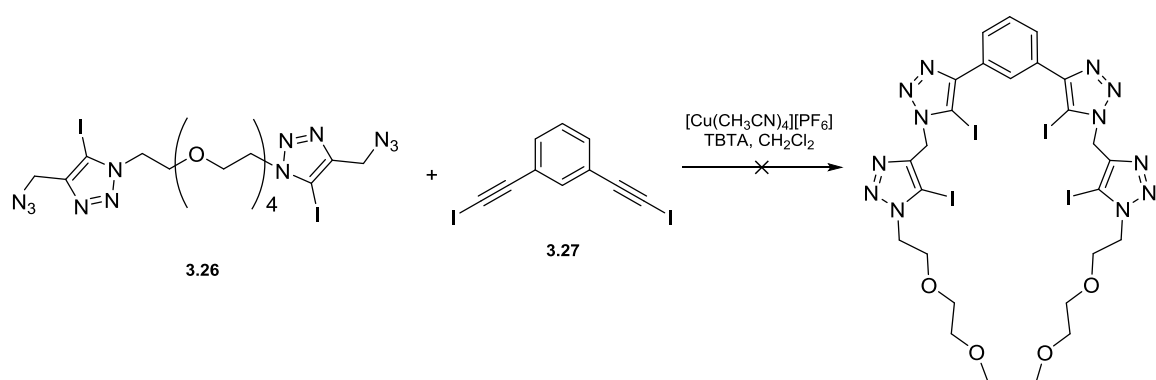
The terminal hydroxyl groups of bis-iodotriazole alcohol **3.25** were converted to azide groups by first reacting with excess MsCl in the presence of NEt₃, before heating overnight with NaN₃ in DMSO to give bis-iodotriazole azide **3.26** (Scheme 3.9). This was isolated in low yield, ascribed to the solubility of azide **3.26** in aqueous solvents causing loss of product in the work-up process. Meanwhile, 3,5-bis-iodoalkyne benzene **3.27** was prepared by

addition of $n\text{BuLi}$ and I_2 to 1,3-diethynyl benzene in dry THF at -78°C following a literature procedure.¹⁶



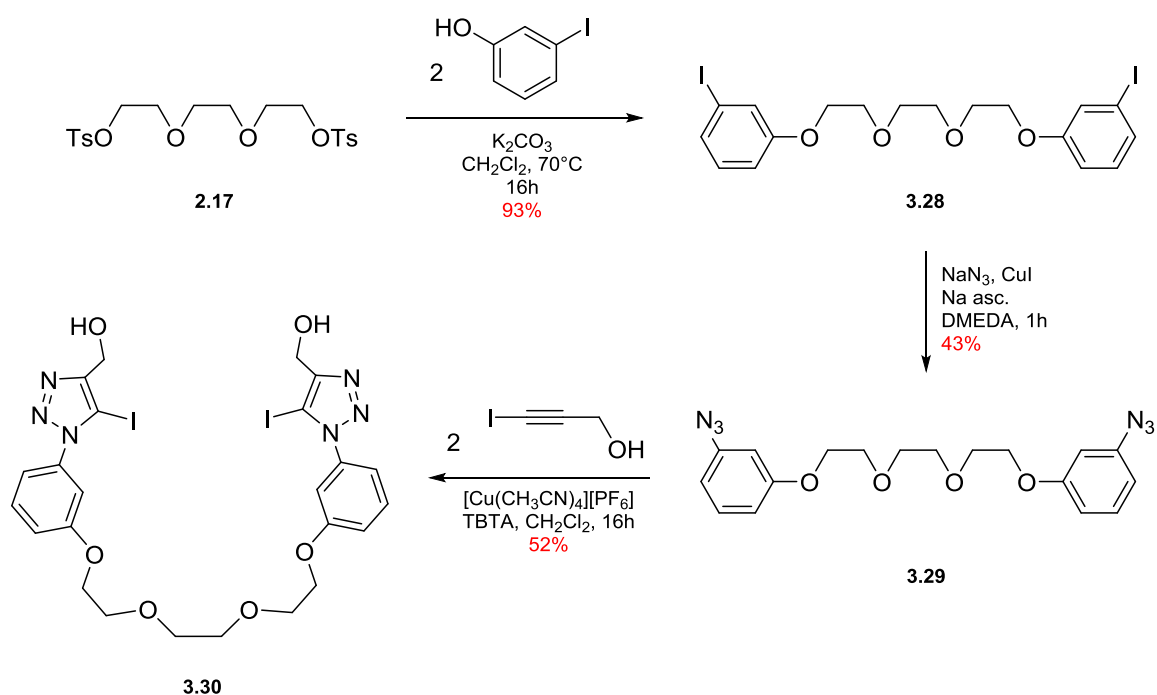
*Scheme 3.9 - Synthesis of macrocyclic precursor synthons **3.26** and **3.27**.*

Despite several attempts, the CuAAC macrocyclisation reaction between **3.26** and **3.27** was unsuccessful (Scheme 3.10). This was postulated to be a consequence of the flexibility of the bis-azide disfavoured the second CuAAC reaction to close the macrocyclic ring in the absence of a template. Therefore, another macrocycle was targeted incorporating structurally rigid phenyl moieties into the polyether framework.



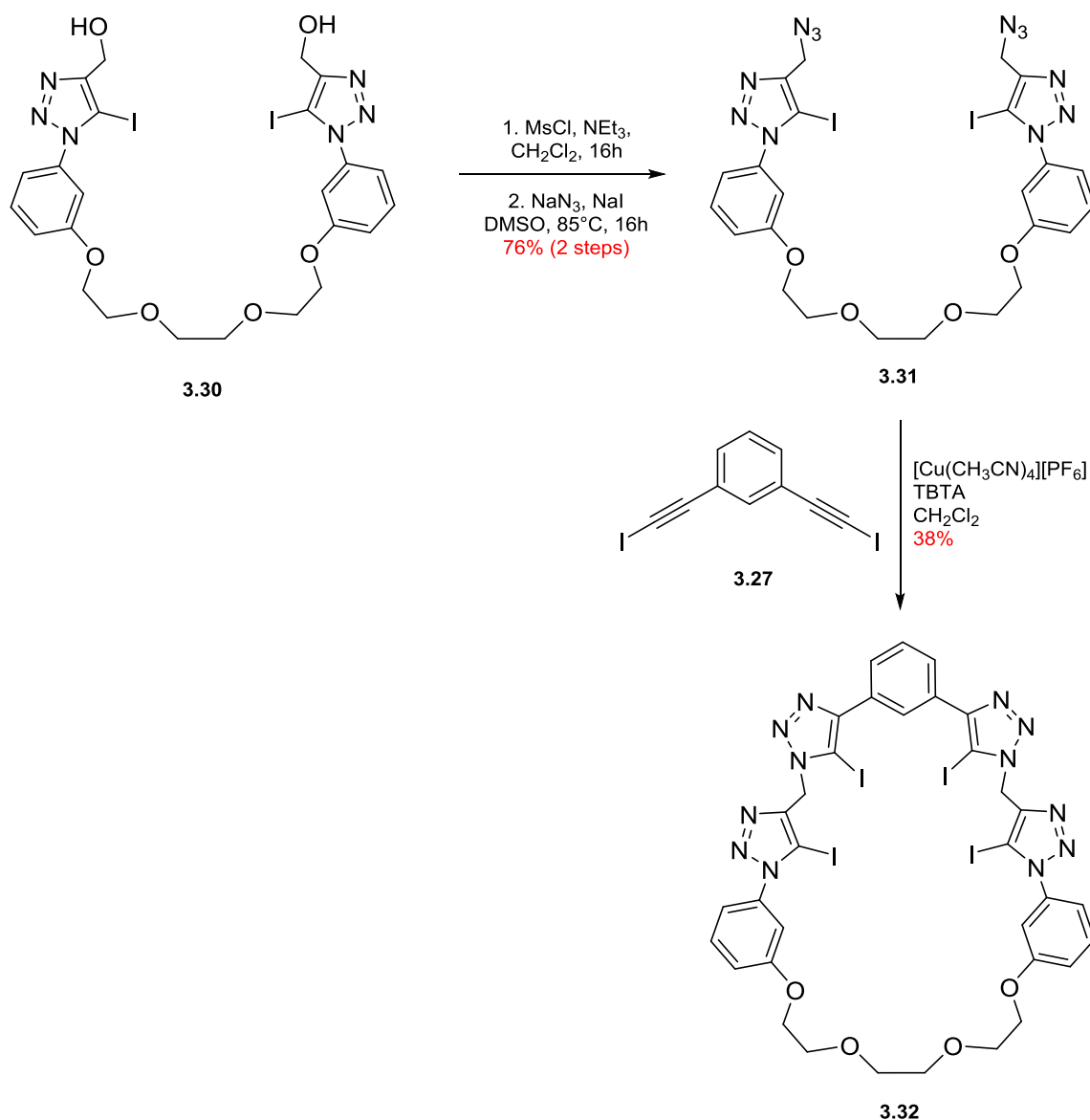
*Scheme 3.10 - Attempted macrocycle formation reaction via bis-CuAAC reaction between **3.26** and **3.27**.*

The synthesis began with the reaction between bis-tosylate **2.17** and 3-iodophenol to give bis-iodophenyl complex **3.28** in 93% yield (Scheme 3.11).¹⁷ The terminal iodine atoms were converted to azide groups through reaction with NaN₃ in the presence of CuI, sodium ascorbate and DMEDA, affording bis-azide **3.29**. Although the CuAAC reaction between **3.29** and iodopropargyl tosylate was unsuccessful, it was possible to click **3.29** with iodopropargyl alcohol in the presence of a catalytic amount of [Cu(CH₃CN)₄][PF₆] and TBTA to afford bis-iodotriazole alcohol **3.30**.



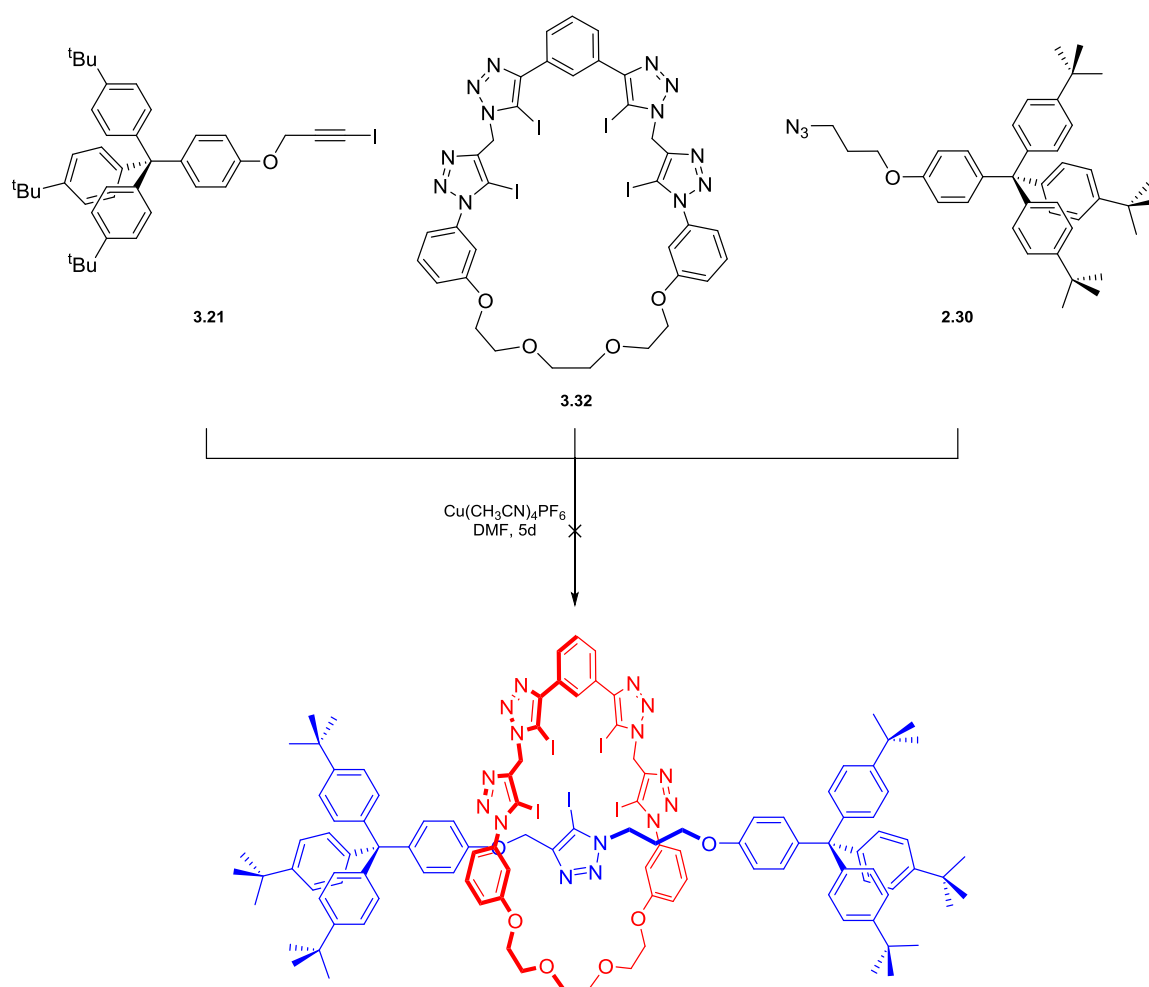
Scheme 3.11 - Synthesis of bis-iodotriazole alcohol **3.30**.

The terminal hydroxyl groups of **3.30** were converted to azides via the mesylate intermediate to give bis-iodotriazole azide **3.31** in 76% yield over the two steps (Scheme 3.12). Finally, tetra-iodotriazole macrocycle **3.32** was successfully synthesised through a bis-CuAAC reaction of **3.31** with bis-iodoalkyne **3.27**. The product was isolated in 38% yield after purification via preparative TLC.



Scheme 3.12 - Synthesis of tetra-iodotriazole macrocycle **3.32**.

Although soluble in DMSO, allowing for its characterisation, macrocycle **3.32** was poorly soluble in most organic solvents. Unfortunately, this was not conducive to rotaxane formation via an AMT approach, with the CuAAC reaction typically performed in chlorinated solvents or THF. An attempt was made to perform the AMT reaction in DMF with stoppers **3.21** and **2.30**, however this did not produce any evidence of either [2]rotaxane or free axle being formed (Scheme 3.13).



Scheme 3.13 - Attempted synthesis of [2]rotaxane via AMT with macrocycle **3.32**.

The poor solubility of macrocycle **3.32** did not allow for further investigations to be carried out with regards to forming an interlocked structure. Future work will focus on increasing the solubility of the macrocycle through functionalisation of the bis-iodoalkyne benzene precursor, for example by affixing a polyethylene glycol solubilising group onto the phenyl ring (Figure 3.12). The macrocycle's improved solubility should then allow for AMT attempts in suitable solvents for a CuAAC reaction to occur.

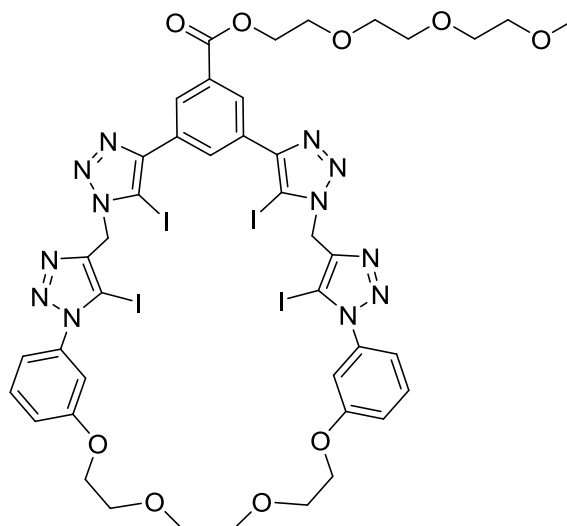


Figure 3.12 - Potential tetra-iodotriazole macrocyclic target for [2]rotaxane formation via AMT.

3.4 Fullerene functionalised hosts for anion sensing

An alternative route towards formation of a transition metal-based halogen bonding interlocked structure is to include the metal into the axle component of the molecule. The C_{60} fullerene moiety provides an interesting functionality to incorporate into these systems. With a diameter of approximately 1 nm¹⁸ it has sufficient steric bulk to act as an effective stopper group for MIMs, whilst it is both photo- and redox-active.¹⁹ This section will briefly introduce the chemistry of C_{60} and investigate attempts to integrate the fullerene into transition metal-based anion receptors and ultimately, in the longer term, into XB rotaxane host frameworks.

3.4.1 Introduction to fullerene C_{60}

Fullerenes are a class of reporter group that have rarely been incorporated into anion binding host structures. This is somewhat surprising since they have the potential to provide an electrochemical or photophysical response to an anion binding event. Of particular interest

here is C_{60} . Not only does it exhibit a strong UV-Vis absorption,²⁰ its rigid geometry and electron-deficient nature causes it to be electrochemically active and readily reduced, with the ability to accept up to six electrons per molecule to form C_{60}^{6-} .²¹ Importantly, as a consequence of this electron deficiency, C_{60} has been proven to effectively quench photoluminescence emission from transition metal complexes.²² Therefore, appendage of C_{60} in close proximity to a photo-active transition metal-based anion binding site has the potential to provide a ratiometric probe for anion sensing through monitoring the emission of the coordinated metal.

The exohedral functionalisation of C_{60} is commonly achieved via the Prato²³ or Bingel²⁴ reactions. Of these, the Bingel reaction is often preferred due to the milder reaction conditions required, higher reaction yields and accessibility to a wider range of chemical functionalities. The route commonly proceeds via the cyclopropanation reaction of a malonate species onto the surface of a fullerene and is carried out in the presence of a halogenating agent and a base, with addition occurring regioselectively at the joining of two hexagonal rings on the surface of the fullerene (Figure 3.13).²⁵ An α -halo-malonate is formed *in situ* which, via a base-promoted nucleophilic mechanism, affixes to the fullerene surface. Intramolecular displacement of the halide by the C_{60} anion results in formation of the cyclopropane ring.

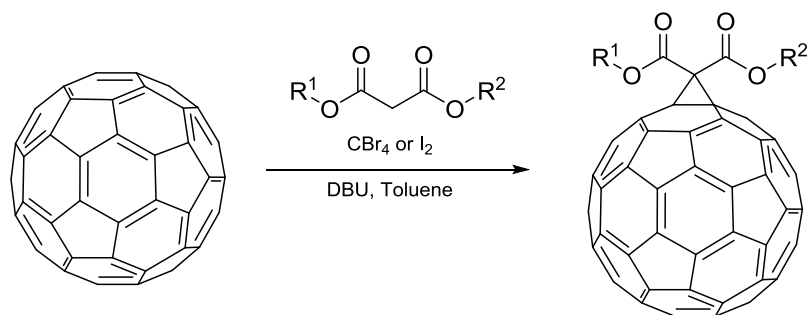


Figure 3.13 - The Bingel reaction for exohedral functionalisation of C_{60} .²⁴

An emerging area of fullerene research concerns their ability to trap a range of metal ions within the carbon cage. Of particular interest are endohedral lanthanide fullerenes where lanthanides such as gadolinium and erbium are encapsulated within the fullerene cage. Such materials are currently being investigated as potentially effective MRI (Gd) and optical (Er) contrast agents.²⁶ More generally, extensive research has been focused on harnessing the unique properties of C_{60} for biomedical purposes; recent examples include drug delivery²⁷ and radiotherapy.²⁸

There exists only one reported example of anion recognition by a fullerene containing molecule. In 2018, Beer and co-workers described a [3]rotaxane containing a four-station bis-NDI and central C_{60} bis-triazolium axle component and two ferrocene appended macrocycles (Figure 3.14).¹⁹ The molecule acted as an anion responsive molecular shuttle, with the ferrocenyl-isophthalamide macrocycle residing at the NDI stations when the counter anion was PF_6^- . Exchange to the Cl^- salt caused the macrocycles to move to the central triazolium stations, concomitant with a switch-on of the molecule's NDI fluorescence and photoinduced electron transfer from ferrocene to the proximal C_{60} .

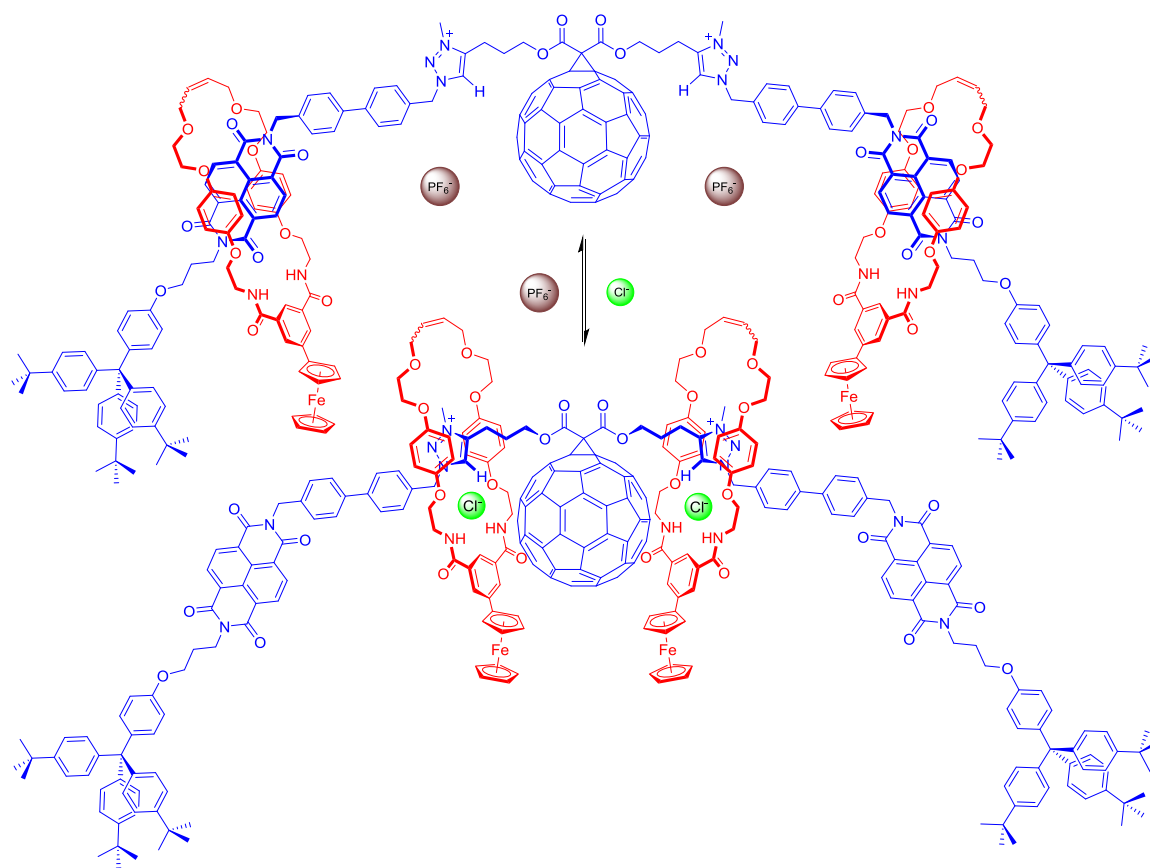


Figure 3.14 - Beer's fullerene appended [3]rotaxane molecular shuttle, exhibiting anion induced motion.¹⁹

Utilising the C_{60} motif to modulate photophysical behaviour, such as in this example, provides an elaborate means for sensing anions. Combining the photo-active transition metal based XB/HB bis-triazole acyclic receptor motifs described in section 3.2 with a C_{60} fullerene centre to produce a new class of anion sensor is the focus of the remainder of this chapter.

3.4.2 Project Aims

The aim of this project was to prepare novel halogen and hydrogen bonding C_{60} fullerene based luminescent transition metal receptors, designed to sense anions. A C_{60} appended molecular scaffold incorporating the methylene-spaced bis-iodo and bis-proto-triazole anion binding motif into the 'arms' of the molecule was the initial synthetic target, which upon

metal coordination would produce the potential anion sensor (Figure 3.15). This project was undertaken in collaboration with Peter Greenman, a Part II final year MChem undergraduate.

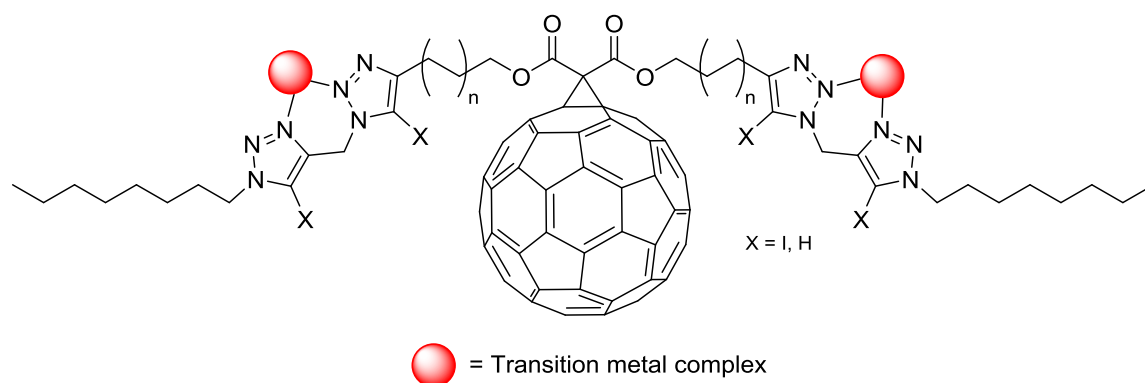
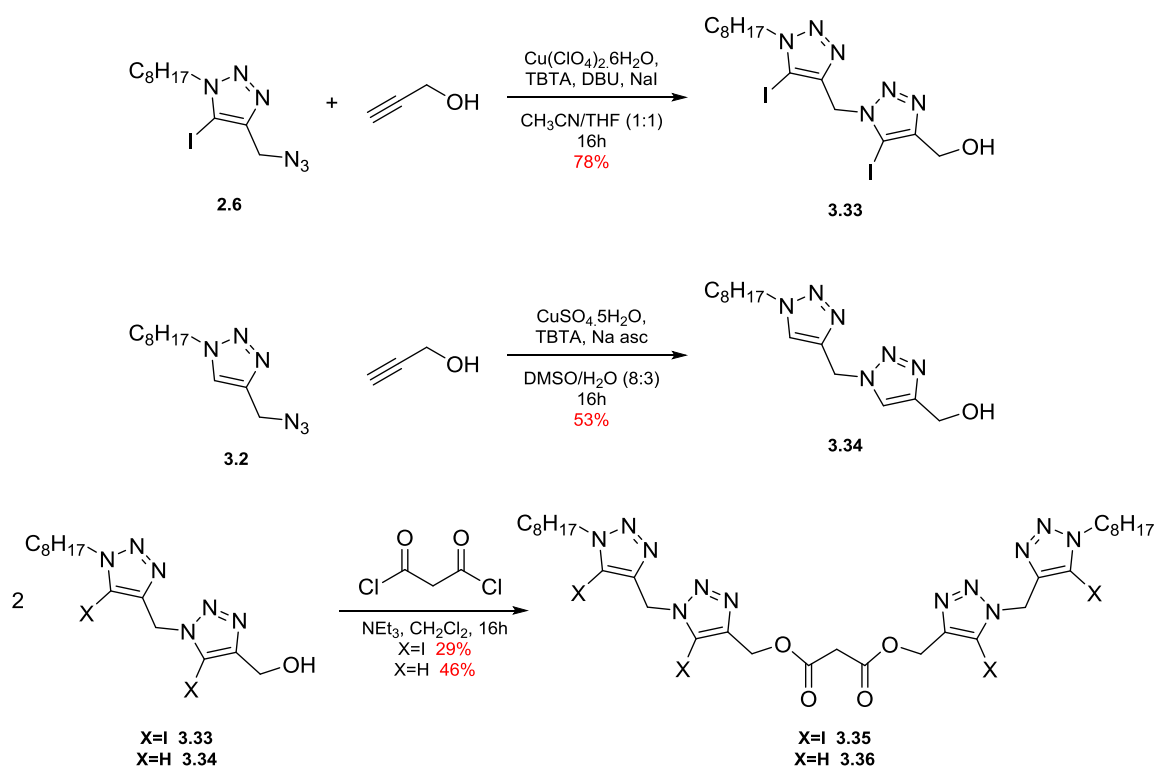


Figure 3.15 - Initial target bimetallic fullerene-based anion receptor.

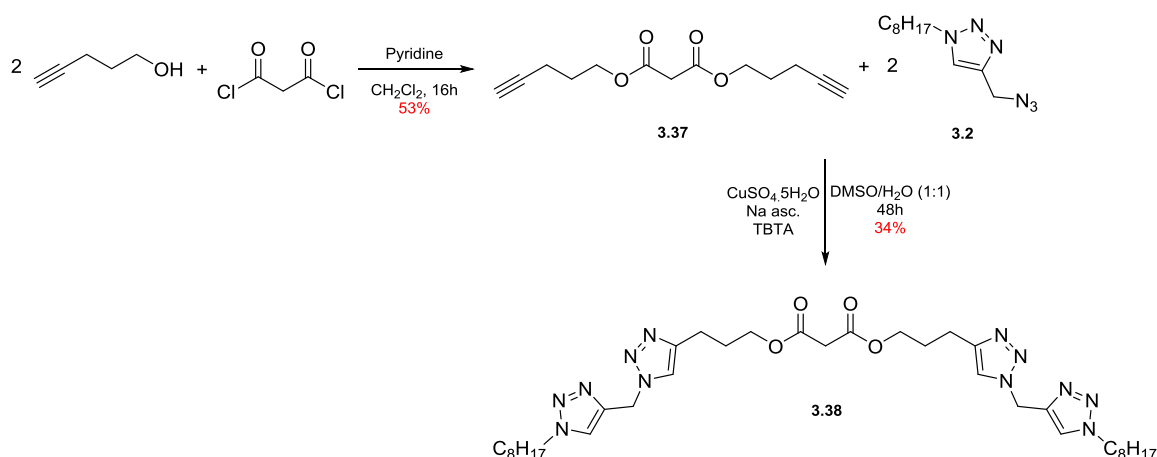
3.4.3 Triazole functionalisation of C₆₀

The first synthetic route undertaken towards the target molecule proceeded through the initial preparation of a tetra-triazole malonate precursor for subsequent Bingel reaction with the fullerene. The iodotriazole azide **2.6** and triazole azide **3.2** were reacted with propargyl alcohol, under iodo-click and proto-click CuAAC conditions respectively, to afford triazole alcohols **3.33** and **3.34** (Scheme 3.14). Both reactions gave the desired product in good yield after purification by column chromatography. Subsequently, bis-ester condensation reactions in the presence of NEt₃ were undertaken between the triazole alcohols and malonyl chloride. This afforded the tetra-triazole malonyl species **3.35** and **3.36** in 29% and 46% yield respectively (Scheme 3.14).



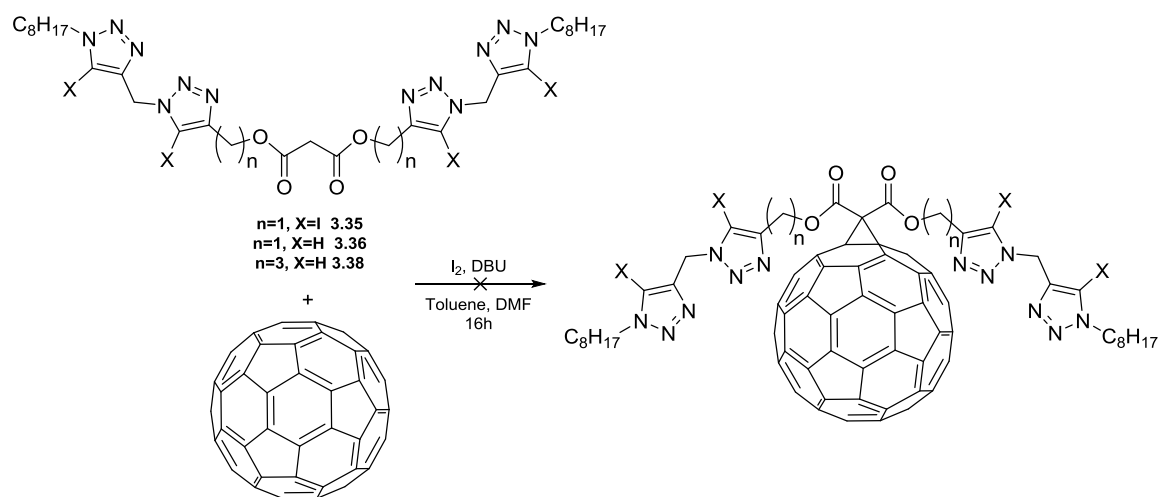
*Scheme 3.14 - CuAAC reaction of triazole azides **2.6** and **3.2** with propargyl alcohol to form triazole alcohols **3.33** and **3.34**, with conversion to tetra-triazole malonyl species **3.35** and **3.36**.*

A tetra-triazole malonate analogue containing propyl chains between the triazole and malonyl functionalities was also prepared. Malonyl chloride was reacted overnight with two equivalents of 4-pentyn-1-ol and an excess of pyridine to give malonyl bis-alkyne **3.37** (Scheme 3.15). A CuAAC reaction was subsequently performed with two equivalents of triazole azide **3.2** to afford malonyl tetra-triazole **3.38** in a moderate yield of 34%.



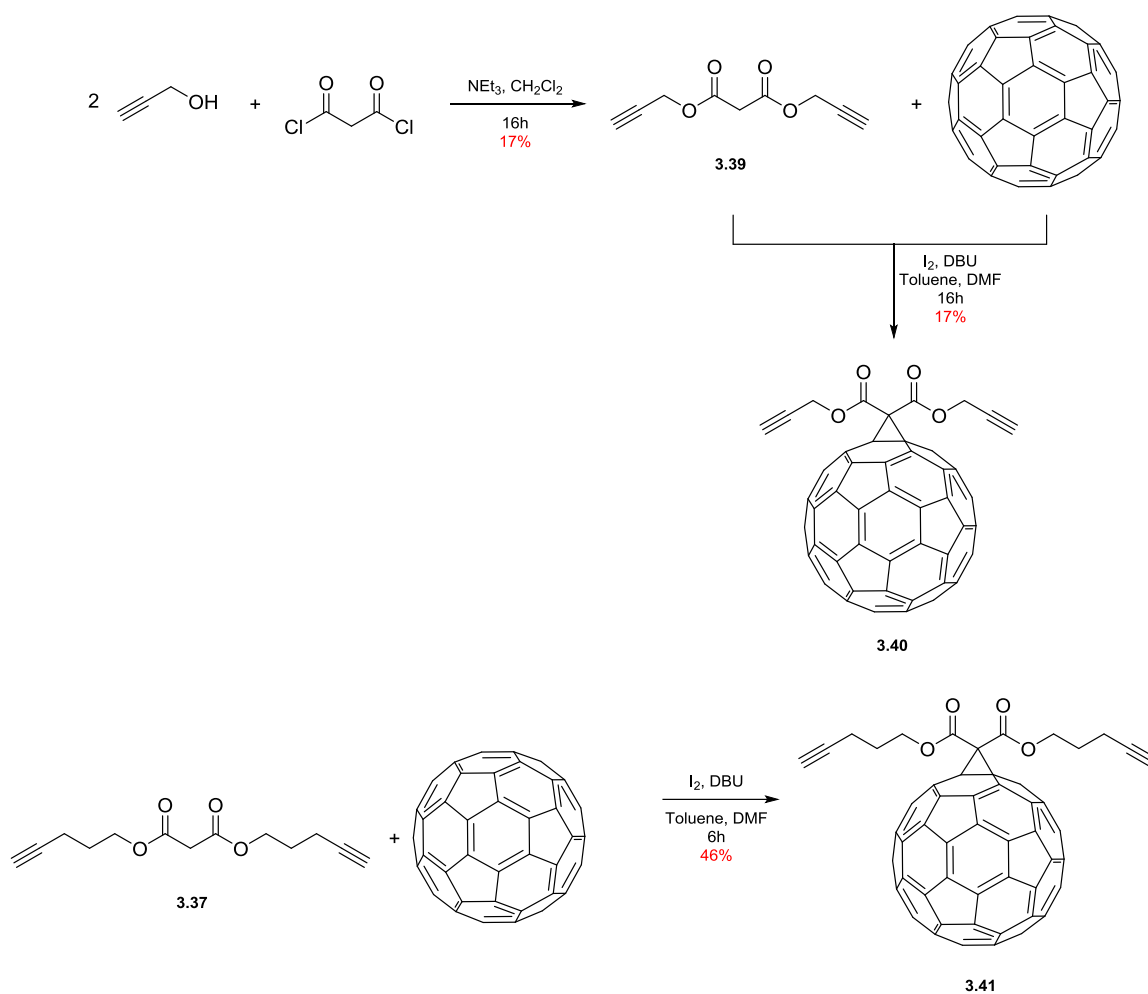
Scheme 3.15 - Synthesis of malonyl bis-alkyne **3.37** and CuAAC reaction to afford tetra-triazole **3.38**.

A literature procedure was followed for the Bingel reaction between tetra-triazole malonates **3.35**, **3.36** and **3.37** with C_{60} fullerene (Scheme 3.16).²⁹ Equimolar amounts of the reagents were dissolved in toluene, an excess amount of I_2 and DBU were added and the mixture stirred overnight. However, in each case the reaction was unsuccessful with no evidence of product observed by MALDI-TOF spectrometry, ^1H NMR spectroscopy or UV-vis analysis. This was likely a result of the methylene-spacer protons between the triazole moieties being highly acidic and able to react with C_{60} under Bingel reaction conditions. A test reaction confirmed this; equimolar amounts bis-triazole **3.4** and C_{60} were stirred in toluene in the presence of an excess of I_2 and DBU. Monitoring the reaction by TLC confirmed that both starting materials were fully consumed after six hours, although a pure product was not isolated.



Scheme 3.16 – Attempted Bingel reaction of tetra-triazole malonates with C_{60} .

An alternative synthetic approach was undertaken with the aim of furnishing C_{60} with bis-alkyne functionality prior to forming the tetra-triazole component. Bis-alkyne **3.39** was formed through an addition-elimination reaction between two equivalents of propargyl alcohol and malonyl chloride in the presence of NEt_3 (Scheme 3.17). Bingel reaction conditions following a literature procedure³⁰ afforded fullerene bis-alkyne C_{60} derivative **3.40** in only 17% yield. The yield was significantly improved upon reaction of the longer malonate bis-alkyne **3.37** with C_{60} , following a procedure outlined by Nierengarten,²⁹ affording C_{60} bis-alkyne **3.41** in 46% yield (Scheme 3.17). As a consequence, work was continued using this fullerene bis-alkyne derivative.



Scheme 3.17 - Formation of fullerene bis-alkyne species **3.40** and **3.41** via the Bingel reaction.

Successful formation of the fullerene compound **3.41** was confirmed through MALDI-TOF spectrometry and ^1H NMR spectroscopy, as well as by UV-vis spectroscopy. The appearance of an absorption peak at 426 nm in the UV-vis absorption spectrum is diagnostic of C₆₀-cyclopropane functionalisation (Figure 3.16).

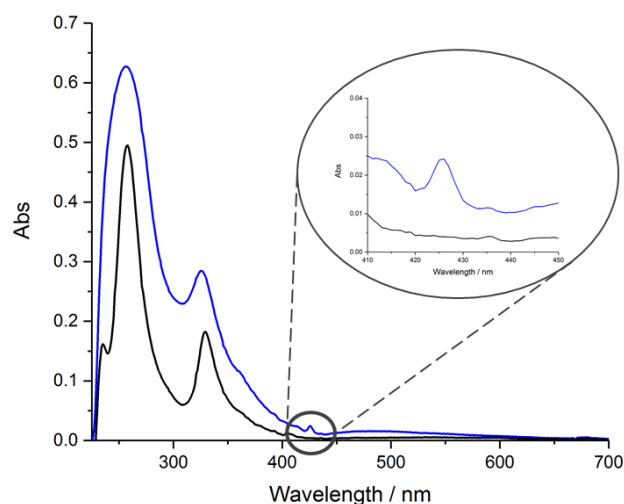
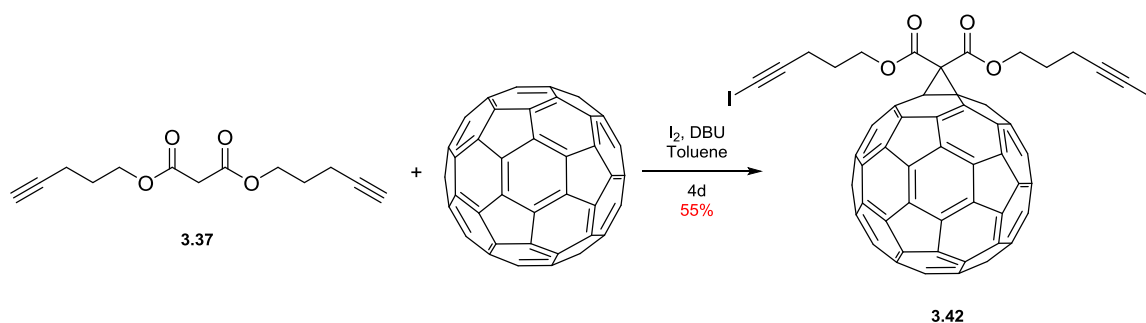


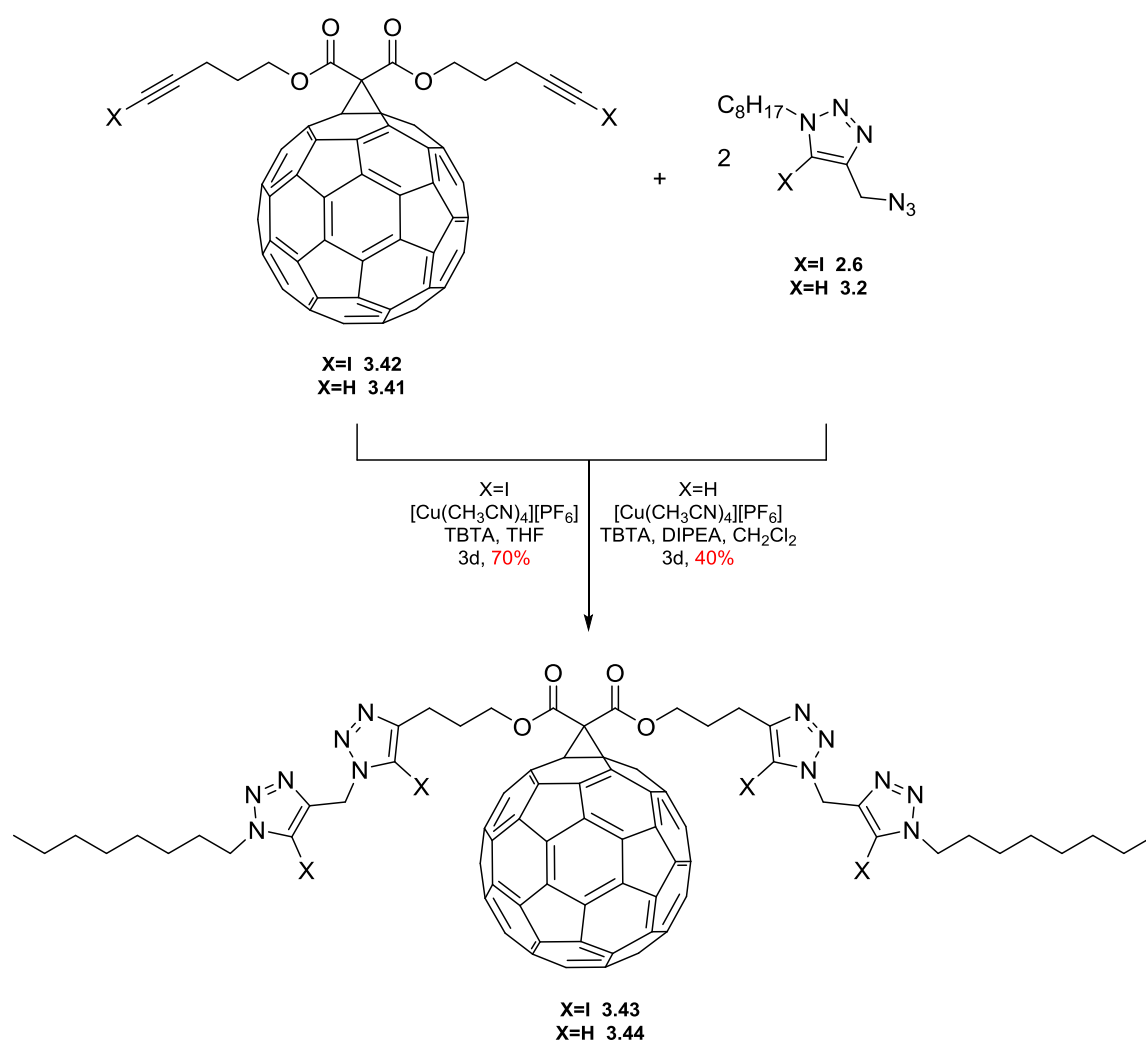
Figure 3.16 - UV-Vis spectrum of C_{60} (black) and fullerene bis-alkyne **3.41** (blue) recorded in CH_2Cl_2 at 1×10^{-5} M (298K). Peak at 426 nm diagnostic of cyclopropane formed in C_{60} attachment.

In the process of synthesising **3.41** it was observed by MALDI-TOF spectrometry that base-promoted iodine substitution of the terminal alkyne protons could occur, which was useful for the synthesis of the XB target molecule. By modifying the conditions during the attachment of bis-alkyne **3.37** to C_{60} it was possible to achieve the preparation of the desired bis-iodoalkyne product. Through reaction of **3.37** and C_{60} in toluene containing a large excess of I_2 and DBU (5.5 and 6.5 equivalents respectively) for four days, bis-iodoalkyne fullerene **3.42** was isolated in 55% yield after purification by column chromatography (Scheme 3.18).



Scheme 3.18 - Preparation of fullerene bis-iodoalkyne **3.42** via *in situ* base-promoted substitution of terminal alkynes to iodoalkynes during C_{60} addition.

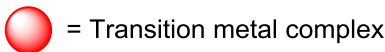
A CuAAC reaction was performed between two equivalents of iodotriazole azide **2.6** and fullerene bis-iodoalkyne **3.42**, affording the C₆₀ appended tetra-iodotriazole XB compound **3.43** in 70% yield. An analogous synthesis between triazole azide **3.2** and fullerene bis-alkyne **3.41** gave HB derivative **3.44** in 40% yield. In both cases the reactions were left for several days in order to ensure complete conversion at both alkyne sites and proceeded with catalytic addition of [Cu(CH₃CN)₄][PF₆] and TBTA, with DIPEA added in the synthesis of **3.44** (Scheme 3.19).



Scheme 3.19 - CuAAC reactions to afford tetra-triazole fullerene products **3.43** and **3.44**.

Following the analogous procedures outlined in section 3.2.1, attempts were made to prepare target bimetallic Re(I), Ru(II) and Ir(III) XB and HB tetra-triazole C₆₀ receptors (Scheme 3.20). Firstly, fullerene tetra-triazole **3.44** was reacted with two equivalents of [Re(CO)₃(CH₃CN)₂Cl] in CH₂Cl₂,⁶ however, despite adding a large excess of the Re(I) source only the mono-complexed product was observed by MALDI-TOF spectrometry, with a peak at m/z 1698.74 corresponding to [M-Cl]⁺. An alternative route was attempted, heating **3.44** with Re(CO)₅Cl in toluene for four days; again this resulted in isolation of the same mono-substituted product (determined by MALDI-TOF and ¹H NMR spectroscopy). The same issues were encountered for both Re(I) complexation reactions with fullerene tetra-iodotriazole **3.43** (with MALDI-TOF spectrometry revealing only one peak at m/z 2236.93, corresponding to [M+H]⁺).

Two methods were undertaken to complex Ru(II) to **3.43**. Firstly, four equivalents of [Ru(bpy)₂Cl₂] were added to a solution of **3.43** in ethanol/water and heated at reflux overnight, however no evidence of product formation was observed. Next, the reagents were suspended in ethanol and heated at 125°C under microwave irradiation for one hour but this resulted in the same outcome. A final attempt towards formation of a bimetallic tetra-triazole fullerene derivative was made through the reaction between **3.43** and Ir(III) dimer **3.7**. The reagents were refluxed in 1:1 dichloromethane/ethanol, but, once again, there was no evidence of the desired product being formed. It was postulated tentatively that the difficulties encountered in all these metal complexation reactions may have been a consequence of an interaction between the lone electron pairs of the triazole nitrogen atoms and the electron deficient C₆₀.



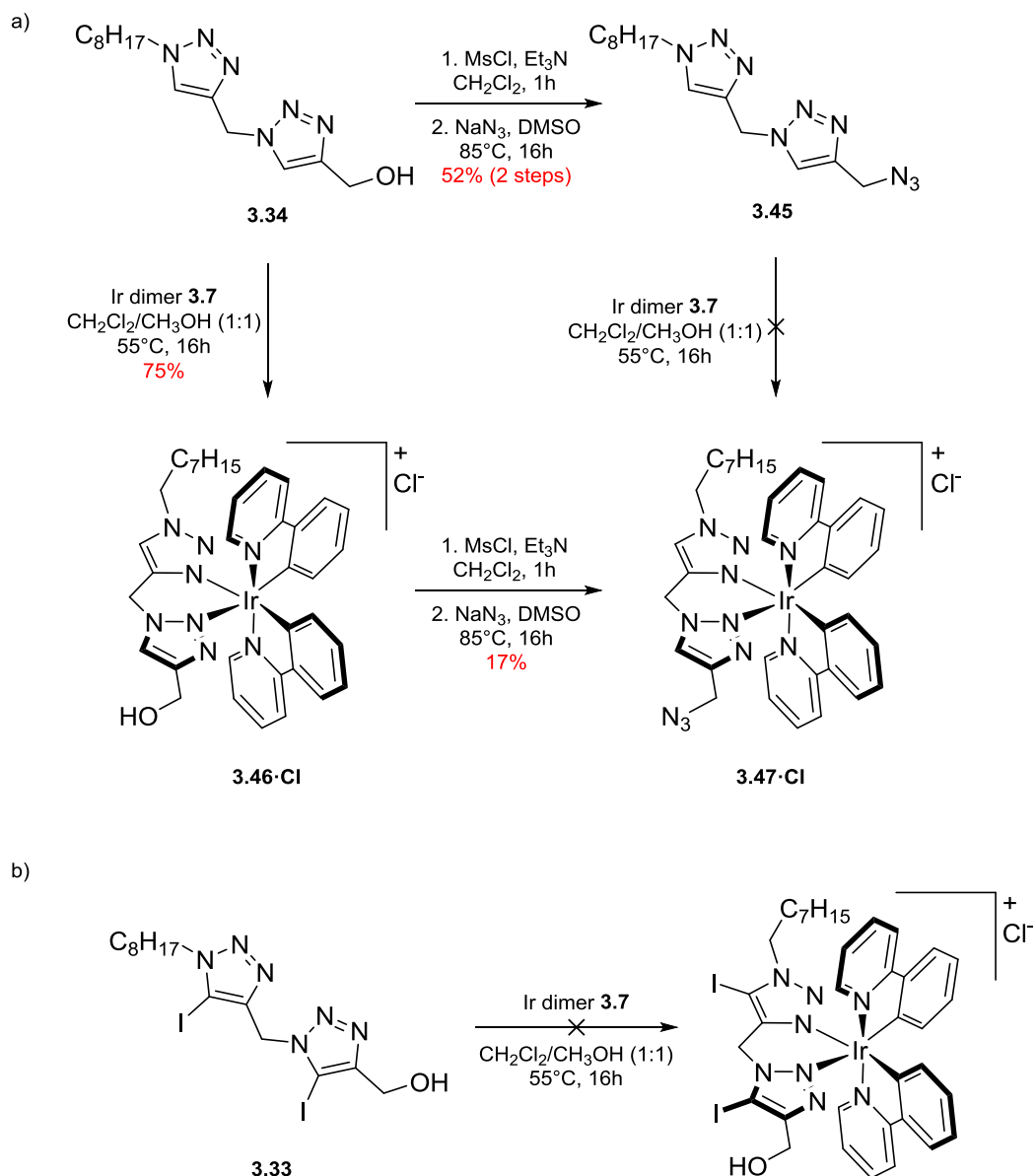
Re(I)	3.43, 3.44	[Re(CO) ₃ (CH ₃ CN) ₂ Cl], CH ₂ Cl ₂ , 5 days [Re(CO) ₅ Cl], toluene, 100°C, 4 days
Ru(II)	3.43	[Ru(bpy) ₂ Cl ₂], EtOH/H ₂ O (4:1), 90°C, 16h [Ru(bpy) ₂ Cl ₂], EtOH, 125°C (μwave), 1h
Ir(III)	3.43	Ir dimer 3.7 , CH ₂ Cl ₂ /CH ₃ OH (1:1), 55°C, 3 days

Scheme 3.20 - Attempted transition metal complexation reactions with 3.43 and 3.44.

3.4.4 C₆₀ functionalisation by transition metal complexes

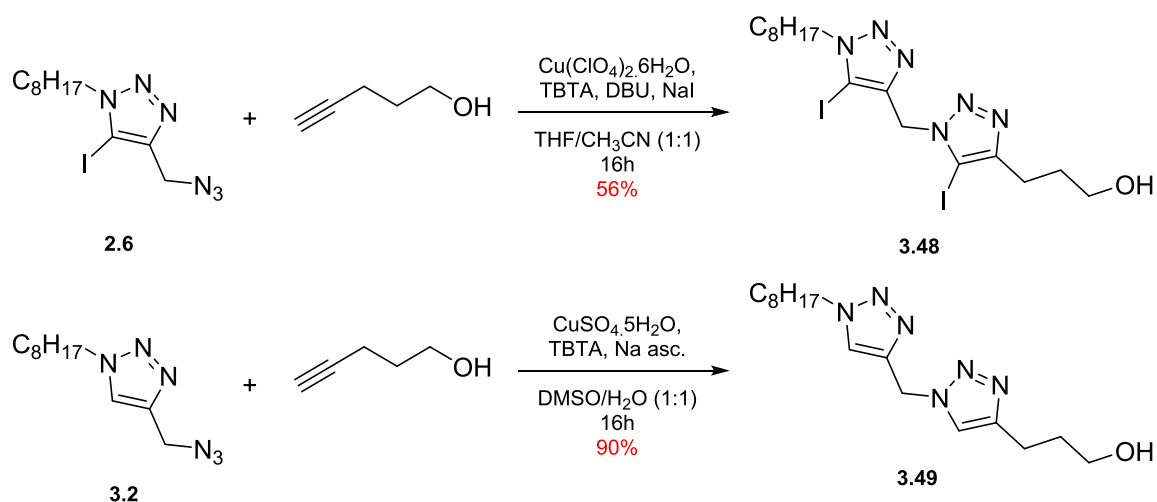
The final strategy employed was to initially synthesise the bis-triazole metal complexed azide before performing a CuAAC reaction with fullerene bis-alkyne **3.41** to append the C₆₀ moiety. Bis-triazole alcohol **3.34** was converted to its mesylate and subsequent azide derivative **3.45** by first reacting with MsCl, before overnight reflux with NaN₃ in DMSO to afford **3.45** in 52% yield (Scheme 3.21a). Ir(III)(ppy)₂ was selected as a suitable transition metal complex due to its photophysical activity and because the overall dicationic charge of the bimetallic product would be reasonably soluble in polar organic media as compared to a tetracationic bimetallic species with Ru(II). Bis-triazole azide **3.45** was refluxed overnight with Ir(III) dimer **3.7** in 1:1 CHCl₃/CH₃OH before purification via precipitation with NH₄PF_{6(aq)}. Despite isolation of a pure product, the ¹H NMR spectrum exhibited an unexpected upfield shift of the protons neighbouring the azide and a 1H doublet appeared at 10.2 ppm. Furthermore, ESI-MS analysis revealed a signal at m/z 790.3 which indicated the loss of N₂.

Modification of the route to proceed via the initial addition of Ir(III) dimer **3.7** to bis-triazole alcohol **3.34** before conversion of the hydroxyl group to an azide, via the mesylate intermediate, was also attempted. After successful preparation of Ir(III) alcohol **3.46·Cl** in good yield the azide conversion was achieved to afford Ir(III) bis-triazole azide **3.47·Cl** in a modest yield of 17%. The same route was followed in an attempt to prepare the XB analogue; bis-iodotriazole alcohol **3.33** was heated with Ir(III) dimer **3.7** in 1:1 CHCl₃/CH₃OH for 16 hours (Scheme 3.21b). However, despite several attempts, the desired product could not be obtained.



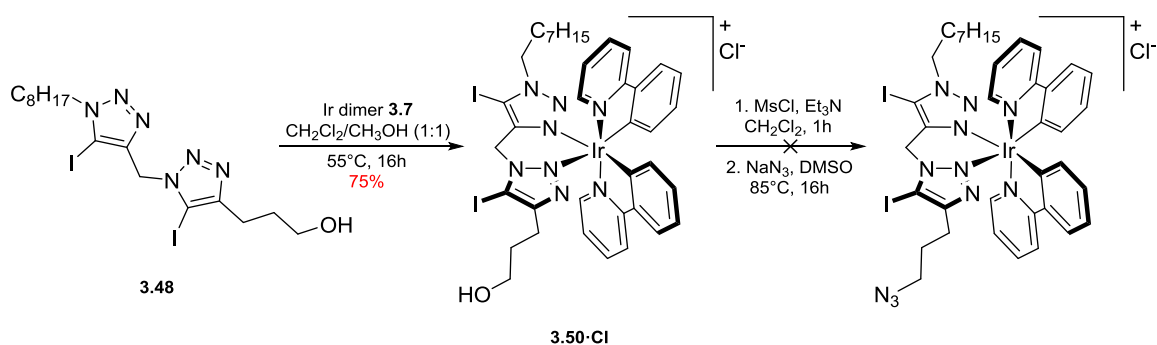
Scheme 3.21 – a) Synthesis of bis-triazole azide **3.45**, Ir(III) alcohol **3.46-Cl** and Ir(III) azide **3.47-Cl**; b) attempted Ir(III) complexation of bis-iodotriazole alcohol **3.33**.

In order to circumvent the failed reactions encountered in the above syntheses, the distance between the terminal hydroxyl group and the methylene-spaced bis-triazole motif was extended through lengthening the methylene carbon chain to propyl. CuAAC reactions were performed between 4-pentyn-1-ol and **2.6** and **3.2** to obtain bis-iodotriazole alcohol **3.48** and bis-triazole alcohol **3.49** respectively (Scheme 3.22).



Scheme 3.22 - Preparation of bis-triazole alcohols **3.48** and **3.49**.

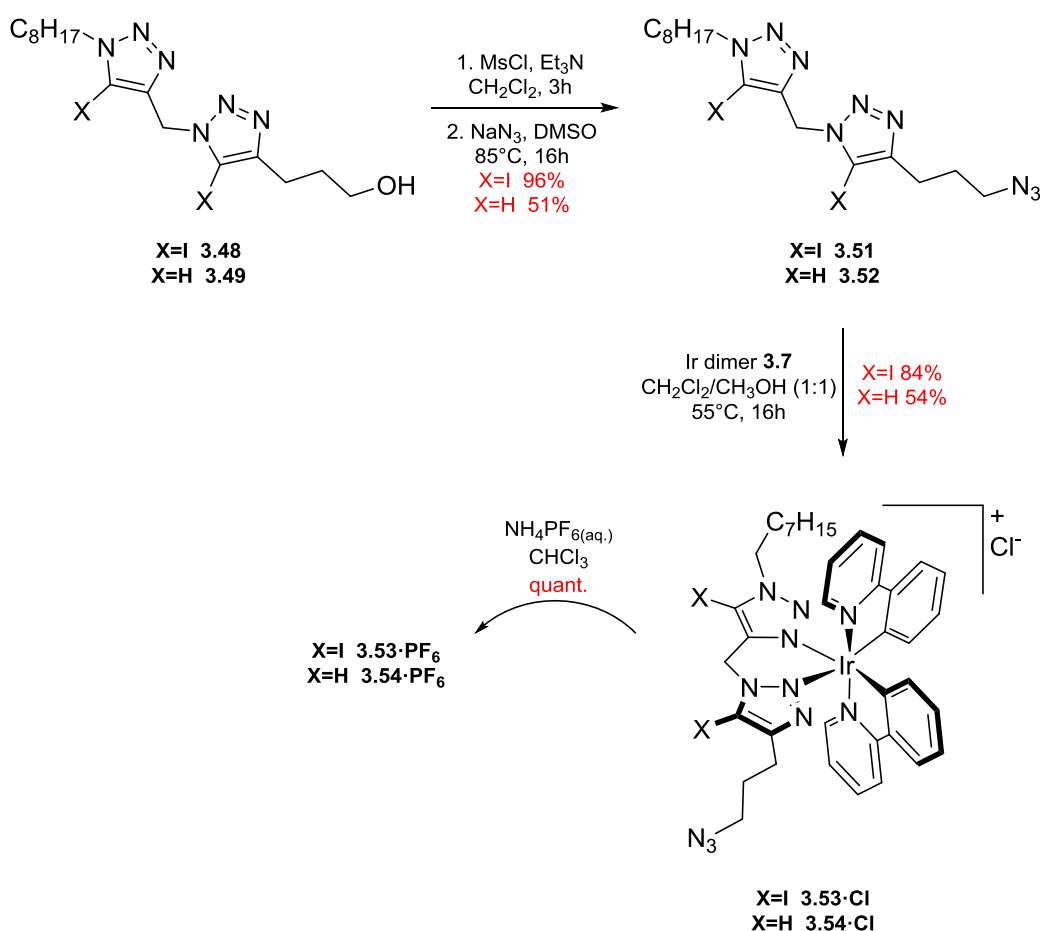
Bis-iodotriazole alcohol **3.48** was complexed with Ir(III) dimer **3.7** through refluxing the two reagents overnight in 1:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$, giving Ir(III) alcohol **3.50·Cl** (Scheme 3.23). Despite performing the previously established synthetic route towards conversion of the terminal hydroxyl group to an azide, via the mesylate intermediate, it was not possible to isolate the desired azide derivative.



Scheme 3.23 - Synthesis of Ir(III) alcohol **3.50·Cl** and unsuccessful conversion to Ir(III) azide.

The final attempted route was the conversion of the terminal hydroxyl group of alcohol **3.48** to an azide prior to Ir(III) complexation, with the hope that the extended carbon chain between the bis-triazole motif and the azide group would ensure no possible interaction

between the azide and the metal centre. Bis-triazole alcohols **3.48** and **3.49** were reacted with MsCl in CH₂Cl₂, before heating overnight with NaN₃ gave bis-triazole azides **3.51** and **3.52** respectively (Scheme 3.24). Compound **3.51** was dissolved in 1:1 CH₂Cl₂/CH₃OH and heated overnight with Ir(III) dimer **3.7**. After removing the solvent the crude solid was purified by preparative TLC to afford Ir(III) azide **3.53·Cl** which was washed with aqueous NH₄PF₆ (the chloride counter anion was not conducive to a subsequent CuAAC reaction) to give **3.53·PF₆** in good overall yield. The same synthetic route was carried out with bis-triazole azide **3.52** to afford Ir(III) azide **3.54·Cl** which was converted to PF₆⁻ salt **3.54·PF₆** (Scheme 3.24).



Scheme 3.24 - Preparation of bis-triazole Ir(III) azides **3.53·PF₆** (XB) and **3.54·PF₆** (HB).

The anion exchange caused significant perturbations in the ^1H NMR spectrum of **3.54**· PF_6 , indicative of non-covalent HB interactions with Cl^- not present with PF_6^- (Figure 3.17). Upfield perturbations of 0.7 ppm and 0.41 ppm were exhibited by the methylene spacer protons, which existed in two distinct environments after complexation of Ir(III). Furthermore, the triazole peaks both moved upfield with a $\Delta\delta$ of 0.65 ppm. Since no other peaks were perturbed in the presence of chloride, this indicated anion binding at the anticipated binding site.

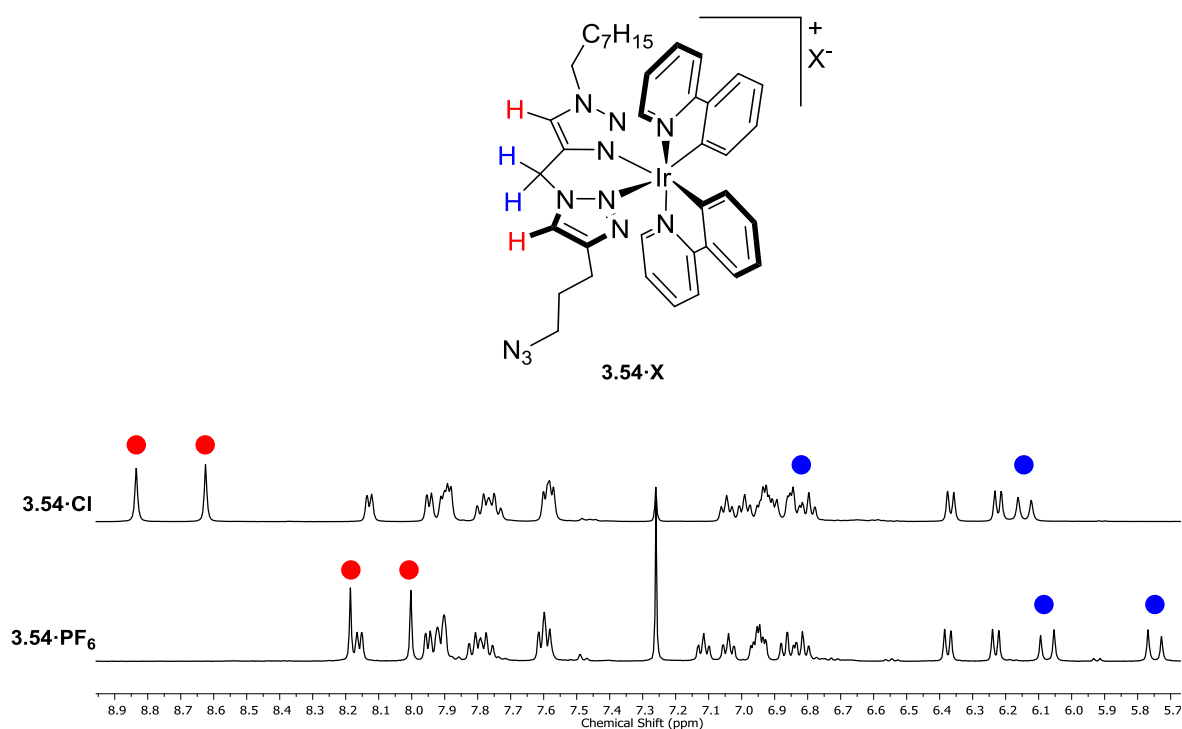
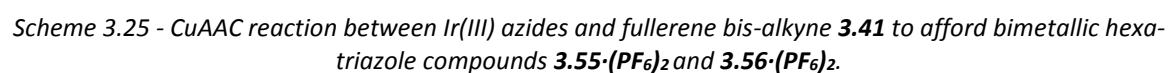


Figure 3.17 – Truncated ^1H NMR spectrum showing shifts in proton environments on anion exchange from **3.54**· Cl to **3.54**· PF_6 indicating loss of anion association (CDCl_3 , 400 MHz, 298K).

The final step required a CuAAC reaction between two equivalents of Ir(III) azides **3.53**· PF_6 and **3.54**· PF_6 and fullerene bis-alkyne **3.41**. The azide was dissolved in CH_2Cl_2 and **3.41** was added, followed by a catalytic amount of TBTA and $[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ and the reaction stirred for three days. Purification was achieved by size-exclusion chromatography, using



Evidence for the formation of the target bimetallic fullerenes was obtained through ^1H and ^{19}F NMR spectroscopy, high resolution ESI mass spectrometry and UV-vis and luminescence spectroscopy. The ^1H NMR spectrum of HB bimetallic receptor **3.56**·(PF_6)₂ indicated its successful formation when compared to the corresponding spectra of the starting materials (Figure 3.18). Proton signal *d* was assigned to the proto-triazole formed in the CuAAC reaction and a significant downfield shift of methylene proton *e* adjacent to the new triazole group was observed. Whilst the ppy-based resonances were similar for the bimetallic product compared to that of the azide starting material, there were perturbations exhibited by methylene spacer protons *i* and *i'* and proto-triazole protons *j* and *h*. Modest changes were also exhibited by protons *a*, *b* and *c* that originated from the fullerene bis-alkyne starting material. Similar shifts were seen in the ^1H NMR spectrum of XB bimetallic receptor **3.55**·(PF_6)₂.

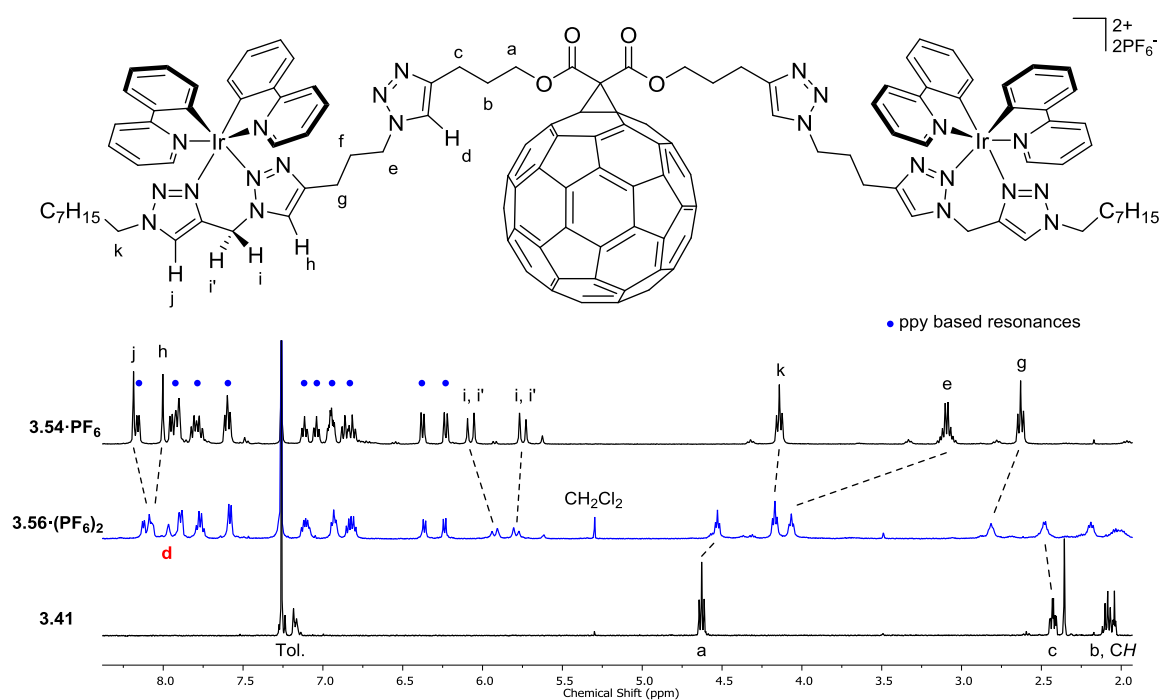


Figure 3.18 – Truncated ^1H NMR spectrum of bimetallic HB receptor **3.56**·(PF_6)₂ compared to starting materials **3.54**· PF_6 and **3.41**. Changes in key resonances indicated, peaks arising from ppy ligands indicated by blue dots (CDCl_3 , 400 MHz, 298 K).

Further evidence for product formation was obtained from a comparison of photophysical data (Table 3.4). The overlaid emission spectra shown in Figure 3.19 reveals the Ir(III) azide **3.53**·**PF₆** exhibited an intense emission with a maximum at 482 nm, whilst fullerene bis-alkyne **3.41** showed emission close to the near IR region (Figure 3.19a). The product **3.55**·(**PF₆**)₂ exhibited maxima corresponding to both constituent parts of the molecule. Importantly, there was a significant reduction of the Ir(ppy)₂ based emission; a consequence of the electron-deficient nature of the C₆₀ causing quenching via the PET effect. Similarly, in the case of HB analogue **3.56**·(**PF₆**)₂ an even more pronounced quenching of the Ir(III) based emission was observed (Figure 3.19b).

Table 3.4 - Excitation wavelength and emission maxima of bimetallic fullerene complexes **3.55**·(**PF₆**)₂ and **3.56**·(**PF₆**)₂ and their constituent starting reagents. Photophysical data calculated at 1×10^{-5} M in CHCl₃ at 298 K. Excitation wavelength (λ_{ex}), maximum emission ($\lambda_{\text{em,max}}$).

Compound	λ_{ex} (nm)	Ir(III) $\lambda_{\text{em,max}}$ (nm)	Fullerene $\lambda_{\text{em,max}}$ (nm)
3.41	390	-	700
3.53 · PF₆	400	496, 513	-
3.55 ·(PF₆) ₂	400	494, 523	>700
3.54 · PF₆	400	483, 513	-
3.56 ·(PF₆) ₂	400	482, 513	699

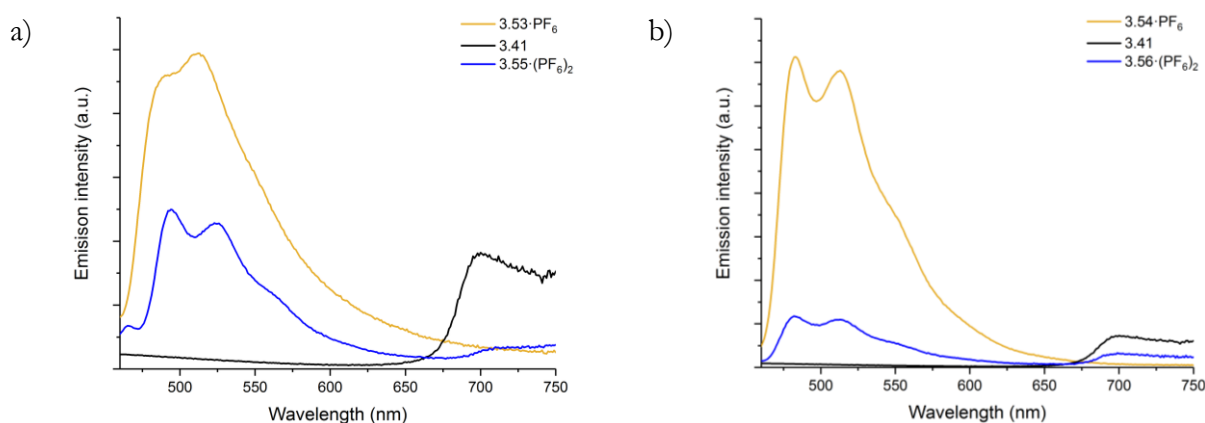


Figure 3.19 - Emission spectra of Ir(III) fullerene complexes a) **3.55**·(**PF₆**)₂ and b) **3.56**·(**PF₆**)₂ and their respective starting materials. Photophysical data calculated at 1×10^{-5} M in CHCl₃ at 298 K.

3.4.5 Anion binding and sensing studies

The highly emissive photophysical properties of the bimetallic Ir(III) fullerene compounds **3.55**·(PF₆)₂ and **3.56**·(PF₆)₂ led to their anion sensing capabilities being investigated using luminescence spectroscopy. Titration experiments were undertaken by adding up to 300 equivalents of TBA salts of a variety of anions to separate chloroform solutions of each receptor. The response of XB receptor **3.55**·(PF₆)₂ to each anion is shown in Figure 3.20. In each graph the black line indicates the spectrum of **3.55**·(PF₆)₂ with no anion present and the blue line signifies the spectrum after addition of 300 equivalents of the respective anion.

All anions induced significant changes in the emission intensity of the XB receptor (Table 3.5) and in all cases other than iodide an overall emission enhancement was observed. Upon addition of chloride and dihydrogen phosphate an initial quenching was observed until around five equivalents, beyond which a significant emission enhancement was seen. There was a noticeable trend amongst the halide anions, with chloride inducing a far larger emission enhancement than bromide whilst a significant quenching was caused by iodide, attributed to the heavy atom effect.³¹ The oxoanions all induced a 'switch-on' in receptor emission, with a larger emission increase with the tetrahedral dihydrogen phosphate anion compared to the trigonal planar nitrate anion. Surprisingly, dihydrogen phosphate also caused a greater emission increase than D-tartrate despite the latter carrying a dianionic charge. Finally, the most significant emission enhancement was observed on sulfate addition; the combination of tetrahedral shape and dianionic charge had the largest impact on receptor luminescence emission with an increase of 252%.

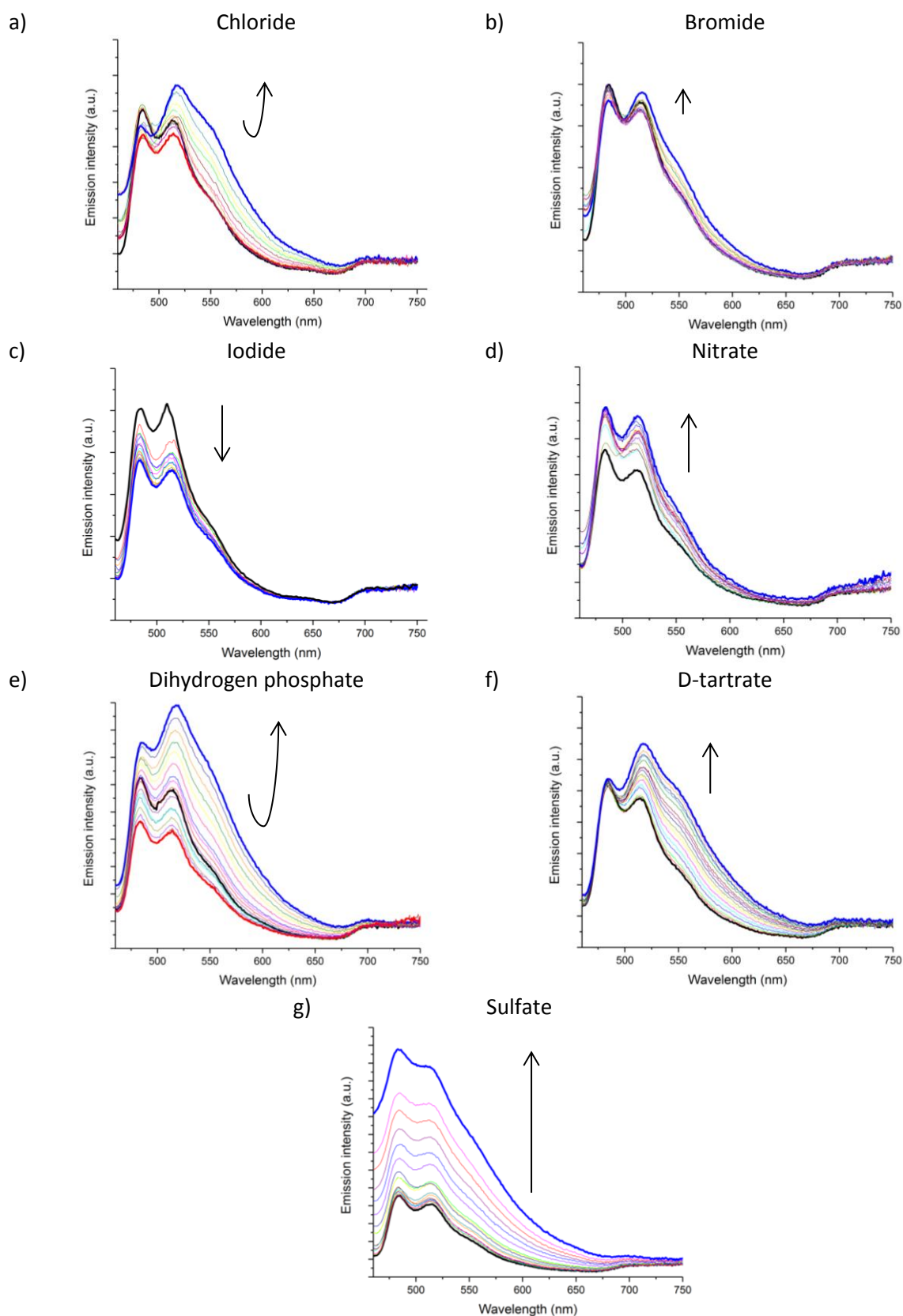


Figure 3.20 - Changes in emission spectra of XB bimetallic fullerene $3.55 \cdot (\text{PF}_6)_2$ in CHCl_3 upon addition of up to 300 equivalents of TBA salts of: a) chloride, b) bromide, c) iodide, d) nitrate, e) dihydrogen phosphate, f) D-tartrate, g) sulfate (conc. = $1 \times 10^{-5} \text{ M}$, $\lambda_{\text{ex}} = 400 \text{ nm}$, 298 K). Black line represents 0 eq. (of anion), blue line 300 eq., red line emission minima in cases of a quenching event prior to luminescence enhancement.

Table 3.5 - Percentage changes in emission intensity of XB bimetallic fullerene **3.55**·(**PF**₆)₂ in CHCl₃ upon addition of 300 equivalents of anions as their TBA salts (concentration = 1x10⁻⁵ M, λ_{ex} = 400 nm, 298 K).

Anion	ΔI (%)
Cl ⁻	+ 42
Br ⁻	+ 9
I ⁻	- 21
NO ₃ ⁻	+ 33
H ₂ PO ₄ ⁻	+ 73
C ₄ H ₄ O ₆ ²⁻	+ 57
SO ₄ ²⁻	+ 252

Analogous luminescence emission titration experiments were performed with HB Ir(III) fullerene receptor **3.56**·(**PF**₆)₂ with up to 300 equivalents of a variety of anions added as their TBA salts (Figure 3.21). Again, each anion induced detectable changes in the emission intensity of the receptor (Table 3.6). The trends in the emission data were remarkably similar to that of the XB analogue. Amongst the halides, chloride induced a significant switch-on in receptor emission, whilst iodide had a quenching effect. Interestingly, bromide also caused a minor emission quenching rather than the slight enhancement that was seen with the XB receptor. As was the case with **3.55**·(**PF**₆)₂, the luminescence of **3.56**·(**PF**₆)₂ was significantly increased on addition of the D-tartrate dianion. The anion with the largest impact upon the emission of the receptor was once again the tetrahedral sulfate dianion, with a switch-on effect of 258%. Unfortunately, in both cases Bindfit^{32,33} data analysis of the emission anion titration data failed to determine accurate quantitative association constant values.

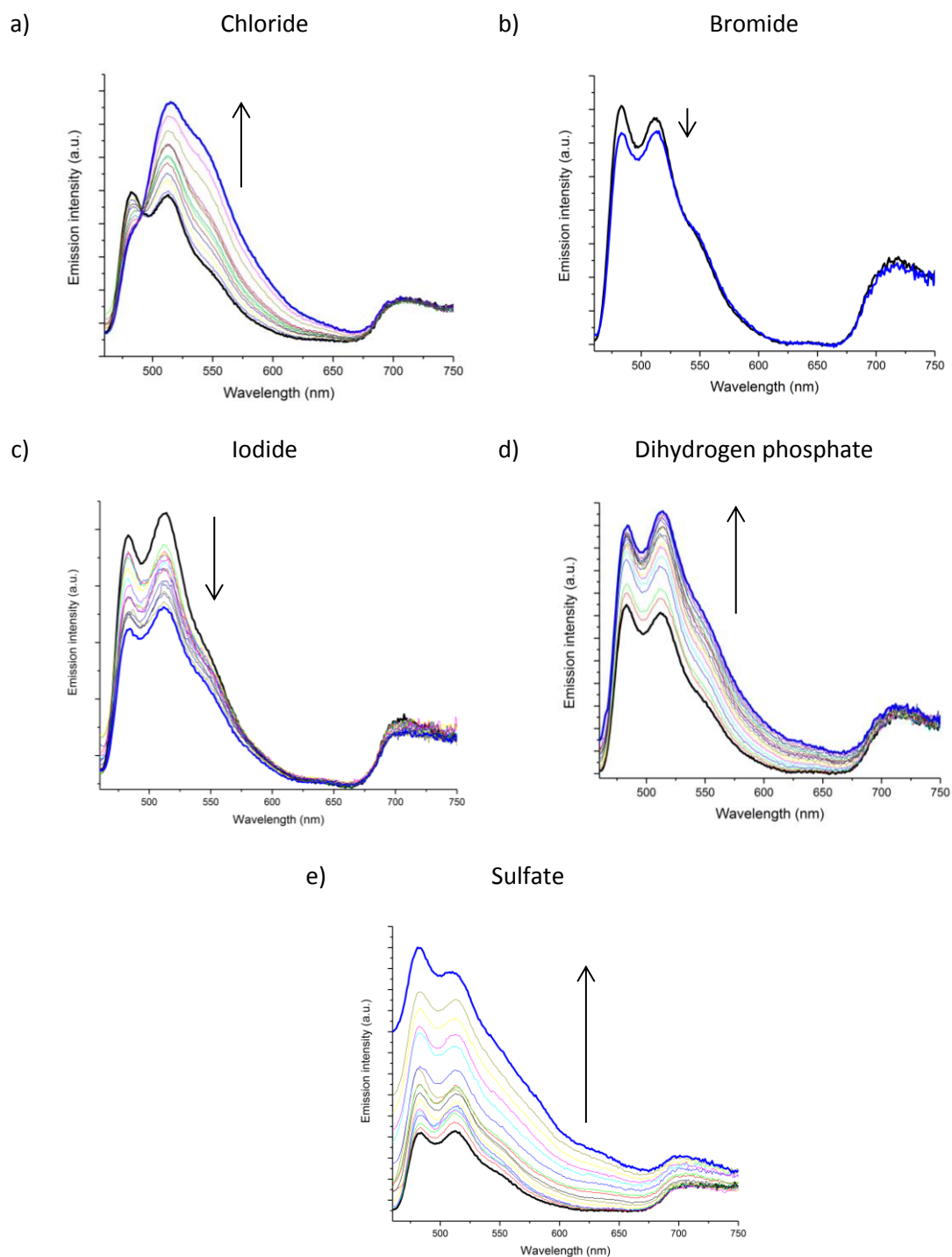


Figure 3.21 - Changes in the emission spectrum of HB bimetallic fullerene $3.56 \cdot (\text{PF}_6)_2$ in CHCl_3 upon addition of up to 300 equivalents of TBA salts of: a) chloride, b) bromide, c) iodide, d) dihydrogen phosphate, e) sulfate (concentration = 1×10^{-5} M, $\lambda_{\text{ex}} = 400$ nm, 298 K). Black line represents 0 eq. (of anion), blue line 300 eq.

*Table 3.6 - Percentage changes in emission intensity of HB bimetallic fullerene **3.56**·(PF₆)₂ in CHCl₃ upon addition of 300 equivalents of anions as their TBA salts (concentration = 1x10⁻⁵ M, λ_{ex} = 400 nm, 298 K).*

Anion	ΔI (%)
Cl ⁻	+ 53
Br ⁻	- 3
I ⁻	- 22
C ₄ H ₄ O ₆ ²⁻	+ 61
SO ₄ ²⁻	+ 258

The similarities between the qualitative luminescence anion sensing data for the XB and HB bimetallic fullerene derivatives **3.55**·(PF₆)₂ and **3.56**·(PF₆)₂ suggest that anion binding was dominated by electrostatic interactions. This correlates with the largest enhancement caused by sulfate, the most charge dense of the anions studied. The emission enhancements can partly be ascribed to the rigidity effect; increased rigidity upon anion binding leads to a reduction of vibrational and rotational non-radiative decay processes. It is tentatively postulated that the anions causing the largest emission enhancement, in particular sulfate, may be a consequence of both arms of the receptor binding the anion in a cooperative pincer-like 1:1 stoichiometric fashion. Hence, the relative distance of the C₆₀ moiety to the metal centres is increased, resulting in the PET quenching to be less efficient (Figure 3.22).

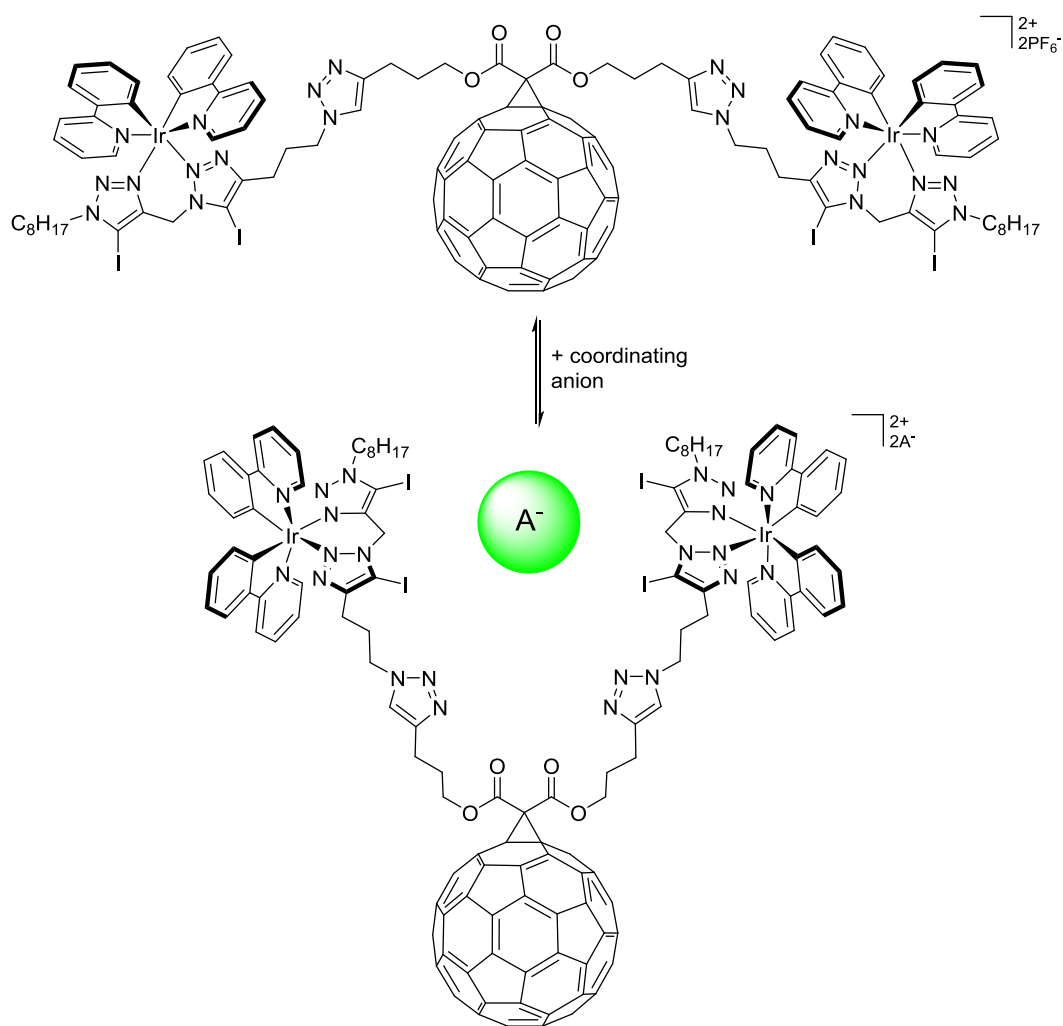


Figure 3.22 - Postulated binding mode of bimetallic fullerene receptor **3.55**·(PF_6)₂ with sufficiently shaped/charged anions.

3.5 Conclusions

The methylene-spaced bis-triazole motif was found to be a suitable bidentate ligand for a variety of transition metal complexes. Both XB and HB analogues of an acyclic ligand were prepared and successfully coordinated to a range of metals, with the Ir(III), Ru(II) and Os(II) complexes found to be photoactive. Chloride anion association was monitored by ^1H NMR titration studies; in each case the XB ligand was found to exhibit superior binding strength in comparison to the HB analogue.

Work towards a transition metal based interlocked structure was undertaken by exploiting two separate methods. Firstly, a macrocycle was prepared containing the methylene-spaced bis-iodotriazole motif and rotaxane assembly was attempted via AMT. Whilst rotaxane formation was successful, the interlocked product could only be isolated in low yield. Larger symmetric tetra-iodotriazole macrocycles were prepared, however low cyclisation yields and poor solubility curtailed AMT rotaxane synthesis being undertaken.

Novel bimetallic Ir(III) fullerene C₆₀ anion receptors were prepared following a challenging synthesis involving functionalisation of C₆₀ with a bis-alkyne and subsequent CuAAC reaction with an Ir(III)-based azide reagent. Qualitative luminescence emission anion titration experiments were performed with each receptor in CHCl₃. Notable spectroscopic changes were exhibited upon addition of the halide anions and D-tartrate to both **3.55**·(PF₆)₂ and **3.56**·(PF₆)₂. Impressively, the sulfate dianion induced significant enhancements in the emission spectra, with a luminescence switch-on of over 250% exhibited on addition of 300 equivalents of sulfate to each bimetallic fullerene anion receptor.

3.6 Future work

Following the successful isolation of the Ir(III) azide compounds and their attachment to a C₆₀ fullerene bis-alkyne, this work may now be extended towards the formation of interlocked structures for anion sensing. Employing a macrocycle capable of AMT rotaxane synthesis, it may be possible to form a [3]rotaxane during the CuAAC reaction between the Ir(III) azide and the fullerene bis-alkyne (Figure 3.23). Owing to the three-dimensional nature of the metal complex the Ir(III) azides prepared in this chapter may be sufficiently

bulky to act as stopper groups. If not, larger stopper groups could be integrated into the structure of the Ir(III) azide in order to prevent macrocycle de-threading.

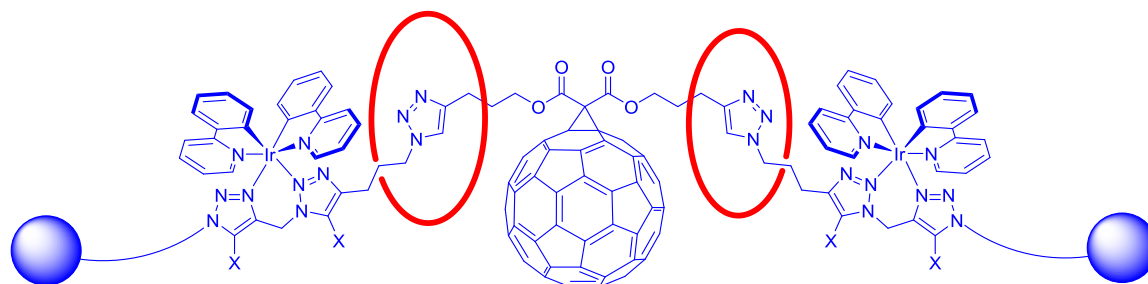


Figure 3.23 - Target Ir(III) based [3]rotaxane.

3.7 References

1. K.-C. Chang, S.-S. Sun, M. O. Odago and A. J. Lees, *Coord. Chem. Rev.*, 2015, **284**, 111-123.
2. F. Zapata, A. Caballero, N. G. White, T. D. W. Claridge, P. J. Costa, V. t. Félix and P. D. Beer, *J. Am. Chem. Soc.*, 2012, **134**, 11533-11541.
3. B. Chowdhury, S. Sinha and P. Ghosh, *Chem. Eur. J.*, 2016, **22**, 18051-18059.
4. M. J. Langton, Y. Xiong and P. D. Beer, *Chem. Eur. J.*, 2015, **21**, 18910-18914.
5. X. Li, J. Y. C. Lim and P. D. Beer, *Faraday Discuss.*, 2017, **203**, 245-255.
6. T. K. Mole, W. E. Arter, I. Marques, V. Félix and P. D. Beer, *J. Organomet. Chem.*, 2015, **792**, 206-210.
7. K. Hasan, A. K. Bansal, I. D. W. Samuel, C. Roldán-Carmona, H. J. Bolink and E. Zysman-Colman, *Sci. Rep.*, 2015, **5**, 12325.
8. M. J. Hynes, *J. Chem. Soc., Dalton Trans.*, 1993, 311-312.
9. T. Duan, T.-K. Chang, Y. Chi, J.-Y. Wang, Z.-N. Chen, W.-Y. Hung, C.-H. Chen and G.-H. Lee, *Dalton Trans.*, 2015, **44**, 14613-14624.
10. Y. Chi, T.-K. Chang, P. Ganesan and P. Rajakannu, *Coord. Chem. Rev.*, 2017, **346**, 91-100.
11. E. J. O'Reilly, L. Dennany, D. Griffith, F. Moser, T. E. Keyes and R. J. Forster, *Phys. Chem. Chem. Phys.*, 2011, **13**, 7095-7101.
12. S. Welter, N. Salluce, A. Benetti, N. Rot, P. Belser, P. Sonar, A. C. Grimsdale, K. Müllen, M. Lutz, A. L. Spek and L. De Cola, *Inorg. Chem.*, 2005, **44**, 4706-4718.
13. J. Y. C. Lim, T. Bunchuay and P. D. Beer, *Chem. Eur. J.*, 2017, **23**, 4700-4707.
14. N. L. Kilah, M. D. Wise, C. J. Serpell, A. L. Thompson, N. G. White, K. E. Christensen and P. D. Beer, *J. Am. Chem. Soc.*, 2010, **132**, 11893-11895.
15. V. Aucagne, K. D. Hänni, D. A. Leigh, P. J. Lusby and D. B. Walker, *J. Am. Chem. Soc.*, 2006, **128**, 2186-2187.
16. A. Borissov, J. Y. C. Lim, A. Brown, K. E. Christensen, A. L. Thompson, M. D. Smith and P. D. Beer, *Chem. Commun.*, 2017, **53**, 2483-2486.
17. B. Qiao, A. Sengupta, Y. Liu, K. P. McDonald, M. Pink, J. R. Anderson, K. Raghavachari and A. H. Flood, *J. Am. Chem. Soc.*, 2015, **137**, 9746-9757.

18. H. J. Johnston, G. R. Hutchison, F. M. Christensen, K. Aschberger and V. Stone, *Toxicol. Sci.*, 2010, **114**, 162-182.
19. T. A. Barendt, I. Rašović, M. A. Lebedeva, G. A. Farrow, A. Auty, D. Chekulaev, I. V. Sazanovich, J. A. Weinstein, K. Porfyrakis and P. D. Beer, *J. Am. Chem. Soc.*, 2018, **140**, 1924-1936.
20. V. S. Pavlovich and E. M. Shpilevsky, *Appl. Spectrosc.*, 2010, **77**, 335-342.
21. Q. Xie, E. Perez-Cordero and L. Echegoyen, *J. Am. Chem. Soc.*, 1992, **114**, 3978-3980.
22. J. K. Kim, S. Bae, W. Kim, M. J. Jeong, S. H. Lee, C.-L. Lee, W. K. Choi, J. Y. Hwang, J. H. Park and D. I. Son, *Nano Energy*, 2015, **13**, 258-266.
23. M. Maggini, G. Scorrano and M. Prato, *J. Am. Chem. Soc.*, 1993, **115**, 9798-9799.
24. C. Bingel, *Ber. Dtsch. Chem. Ges.*, 1993, **126**, 1957-1959.
25. X. Gao, K. Ishimura, S. Nagase and Z. Chen, *J. Phys. Chem. A*, 2009, **113**, 3673-3676.
26. A. A. Popov, S. Yang and L. Dunsch, *Chem. Rev.*, 2013, **113**, 5989-6113.
27. A. Montellano, T. Da Ros, A. Bianco and M. Prato, *Nanoscale*, 2011, **3**, 4035-4041.
28. K. Stankov, I. Borisev, V. Kojic, L. Rutonjski, G. Bogdanovic and A. Djordjevic, *J. Nanosci. Nanotechnol.*, 2013, **13**, 105-113.
29. R. Pereira de Freitas, J. Iehl, B. Delavaux-Nicot and J.-F. Nierengarten, *Tetrahedron*, 2008, **64**, 11409-11419.
30. V. P. Gubskaya, S. K. Latypov, F. G. Sibgatullina, A. A. Balandina, T. A. Zhelonkina, G. M. Fazleeva, L. N. Islamova, D. R. Sharafutdinova, I. A. Nuretdinov and O. G. Sinyashin, *Russ. Chem. Bull.*, 2012, **61**, 1169-1175.
31. A. Chmyrov, T. Sandén and J. Widengren, *J. Phys. Chem. B*, 2010, **114**, 11282-11291.
32. P. Thordarson, *Chem. Soc. Rev.*, 2011, **40**, 1305-1323.
33. D. Brynn Hibbert and P. Thordarson, *Chem. Commun.*, 2016, **52**, 12792-12805.

Chapter Four

Halogen bonding benzimidazole-iodotriazole
motif for dynamic MIM construction and
transition metal complexation

4 Halogen bonding benzimidazole-iodotriazole motif for dynamic MIM construction and transition metal complexation

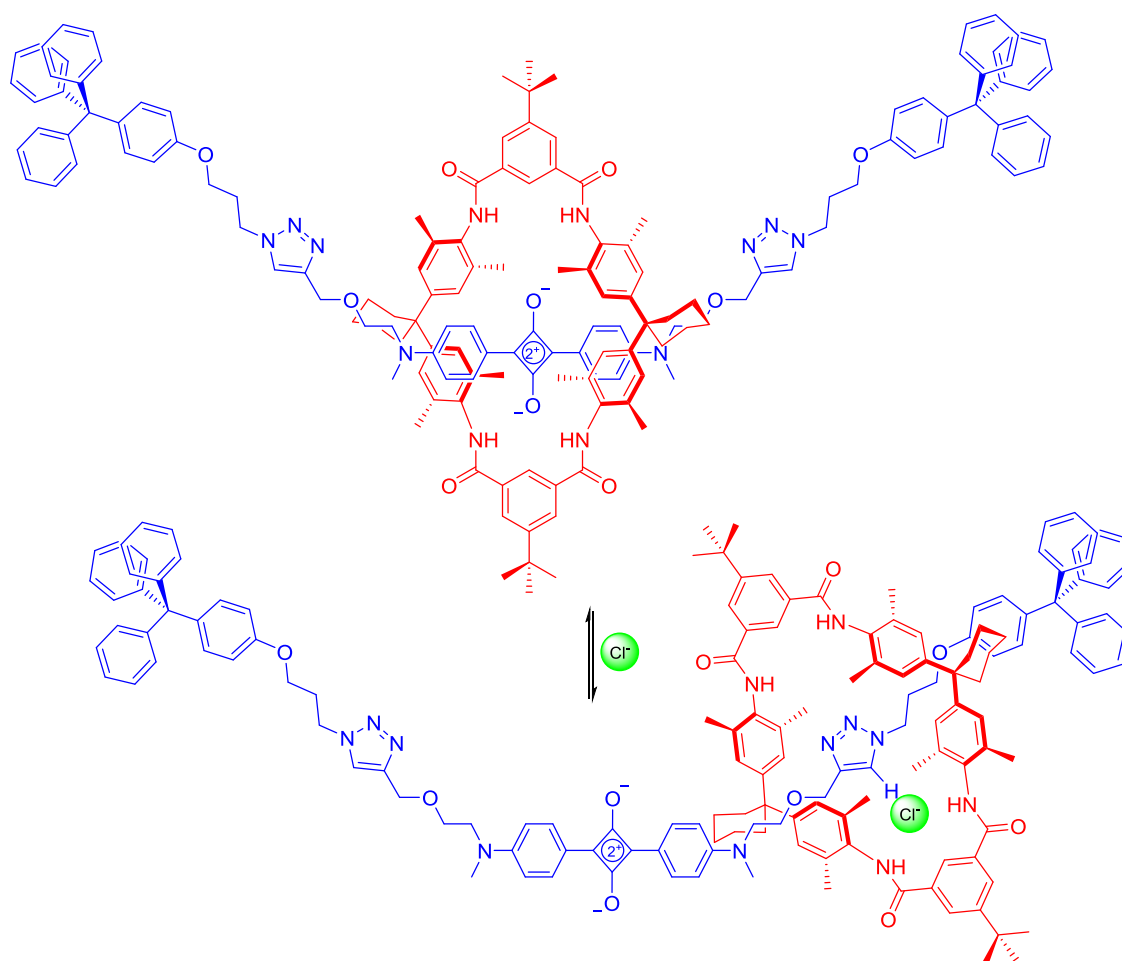
4.1 Introduction

4.1.1 Dynamic interlocked structures for anion recognition

As described in section 1.5.3 of Chapter One, a variety of external stimuli have been exploited to control molecular motion and sensing within interlocked structures, with examples including light,¹⁻³ redox,^{4,5} pH⁶ and cation binding.⁷ Molecular machines displaying anion induced motion typically employ the interchange between non-coordinating and coordinating anions (such as PF_6^- and Cl^-) to trigger the translocation of one component of the MIM relative to the other.

Anion responsive dynamic MIMs may incorporate photoactive reporter groups into the framework to provide a macroscopic detectable output to molecular motion. The co-conformational change can modify the optical properties of the structure, for example as a consequence of the photo-induced electron transfer (PET) effect.^{8,9} Anion binding by the interlocked host that leads to a co-conformational change, for example in a dynamic rotaxane, may perturb energy levels of the fluorophore through modification of the proximity of the electron donor and fluorophore electron acceptor. This alters the luminescence emission of the MIM, detection of which is indicative of molecular motion. An example of an anion responsive [3]rotaxane molecular shuttle exploiting this effect is depicted in Chapter Three (Figure 3.14).¹⁰

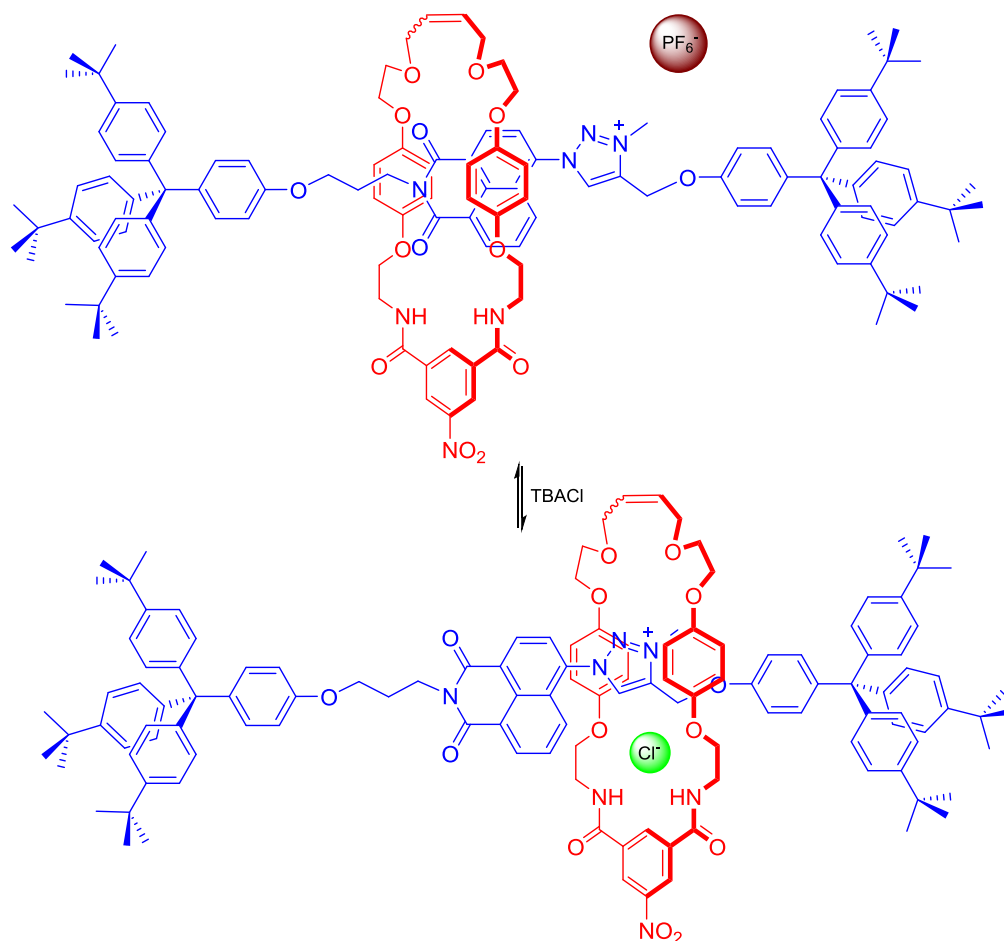
Smith's [2]rotaxane is another example of a molecular shuttle exploiting anion binding induced motion of the macrocyclic component in order to produce a detectable optical response (Scheme 4.1). In the absence of an anion the macrocycle resided at the squaraine unit, partially quenching the dye's fluorescence emission by PET.¹¹ In chloroform, chloride addition facilitated the translocation of the macrocycle to one of the triazole sites resulting in a switch-on of the rotaxane fluorescence.



Scheme 4.1 - Smith's chloride sensing squaraine-based [2]rotaxane molecular shuttle. Anion addition induced increase in rotaxane fluorescence.¹¹

Another anion responsive [2]rotaxane was reported by Beer, integrating a naphthalimide motif adjacent to an anion binding triazolium moiety of an axle component (Scheme 4.2).¹² As the PF_6^- salt in CDCl_3 , the isophthalamide macrocycle resided at the naphthalimide

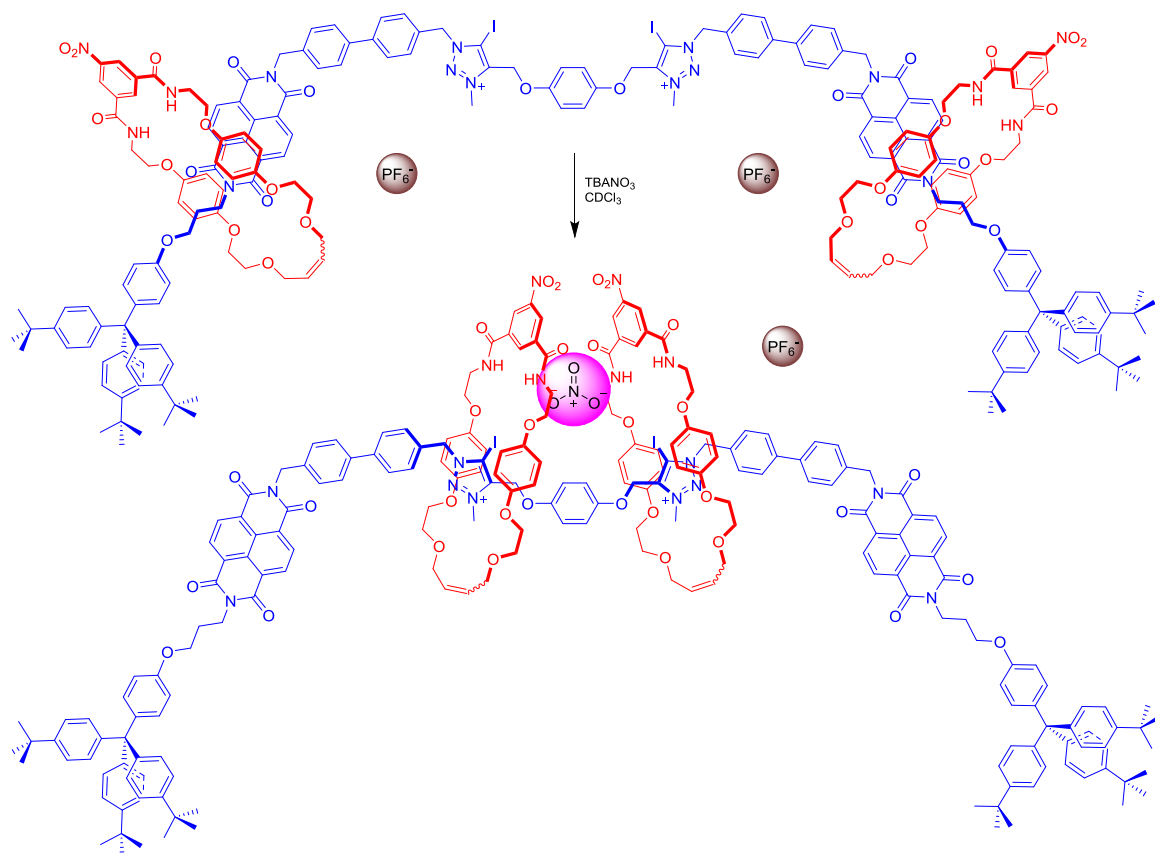
station facilitated by aromatic stacking donor-acceptor interactions. Addition of chloride induced a translocation of the macrocycle to the triazolium station where the halide was bound via macrocycle amide and axle triazolium hydrogen bonding interactions. This conformational change was observed by ^1H NMR and UV-vis spectroscopy.



Scheme 4.2 - Beer's [2]rotaxane exhibiting anion induced motion.¹²

Recently, Beer has incorporated halogen bonding into a dynamic [3]rotaxane, that produced a naked-eye colourimetric response upon anion addition (Scheme 4.3).¹³ As the non-coordinating PF_6^- salt the two isophthalamide macrocycles occupied the naphthalenediimide (NDI) stations. Upon addition of a coordinating anion both macrocycles moved to the iodotriazolium stations and bound the anion in a convergent fashion, forming a 1:1

stoichiometric host-guest complex. This was accompanied by a colour change, from yellow to colourless, as the hydroquinone–NDI aromatic stacking donor-acceptor interactions were disrupted. In 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$ the strongest association was exhibited with nitrate, whilst it is worth noting that the XB version exhibited stronger anion recognition than the HB derivative.



Scheme 4.3 - Beer's nitrate selective [3]rotaxane that exhibited a colourimetric response to coordinating anion addition.¹³

4.1.2 Benzimidazole-based structures for anion recognition

The reaction between an *o*-phenylenediamine and an aldehyde to afford a 2-substituted benzimidazole moiety has been reported extensively in the literature, dating back to the 1920s.¹⁴ Derivatives of the benzimidazole motif have gained recent interest as biologically

active molecules, with instances reported of their use in anticancer, antiviral and anti-anxiety treatments.^{15,16}

Benzimidazole containing molecules have been utilised extensively as anion receptors. For example, Jang reported a tripodal fluorescent receptor bearing benzimidazole motifs as recognition sites (Figure 4.1a).¹⁷ In 9:1 CH₃CN/H₂O there were modest optical changes upon addition of a range of anions, other than iodide which caused almost complete quenching of the receptor fluorescence emission. Another example has been reported by Lin; reaction between an *o*-phenylenediamine and an aldehyde afforded a benzimidazole-based receptor that exhibited very little interaction with any anion in DMSO other than fluoride, which bound with an association constant $K_a = 3.9 \times 10^4 \text{ M}^{-1}$ and induced a colour change from light yellow to red, likely as a result of host deprotonation (Figure 4.1b).¹⁸

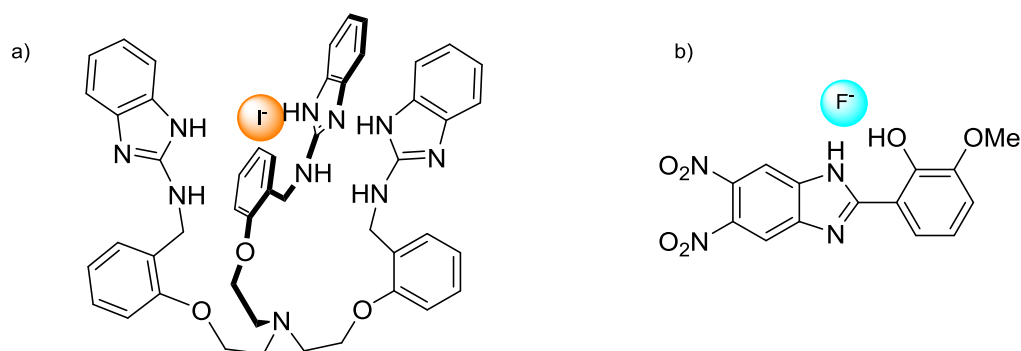


Figure 4.1 - Benzimidazole-based anion receptors: a) Jang's iodide selective tripod,¹⁷ b) Lin's fluoride binding receptor.¹⁸

The potential of the benzimidazole motif to participate in transition metal complexation provides further motivation for its integration into anion receptors. An example reported by Baitalik utilised a tridentate benzimidazole ligand capable of binding to Ru(II)terpyridine derivatives. The resulting complexes exhibited selectivity for fluoride and acetate in acetonitrile (Figure 4.2a).¹⁹ Pandiyan and Singh exploited a tripodal benzimidazole ligand to facilitate construction of a novel anion sensor; in 9:1 CH₃CN/H₂O their Ru(III)-based host

exhibited a significant fluorescence switch-on in the presence of chloride as a result of a switching off of the PET effect in the excited state (Figure 4.2b).²⁰

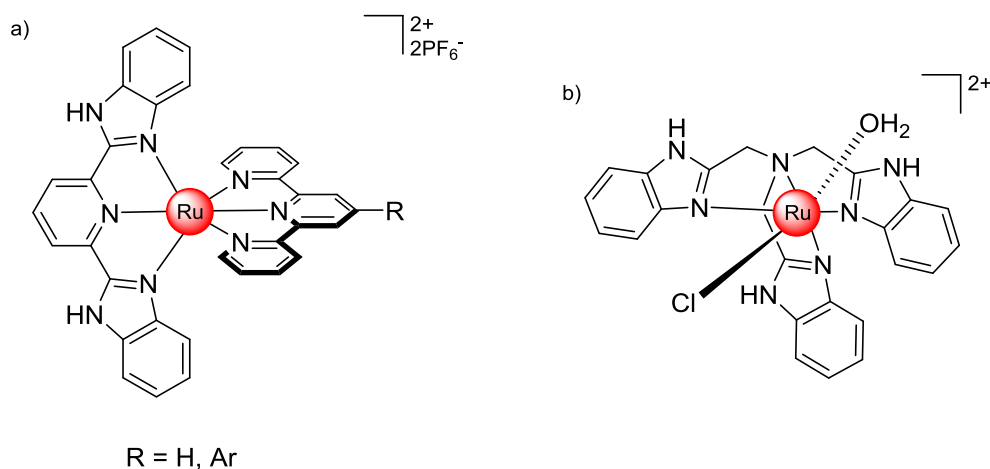


Figure 4.2 – Benzimidazole coordinated transition metal-based anion receptors: a) Baitalik's fluoride and acetate sensor,¹⁹ b) Pandiyan and Singh's chloride sensor - exhibited fluorescence enhancement via termination of PET upon chloride addition.²⁰

The integration of 2-substituted benzimidazole derivatives into dynamic interlocked structures has been studied extensively by Loeb and co-workers.²¹⁻²³ Facile protonation of the unsaturated nitrogen atom creates a site capable of hydrogen bonding to a crown ether macrocycle, forming a pseudorotaxane that can be converted to a rotaxane via a range of reactions. A recent example explored how the rate of shuttling of a crown ether macrocycle along the axle of a [2]rotaxane could be controlled via protonation of an axle benzimidazole site (in CH_2Cl_2 or CH_3CN). When protonated the macrocycle was fixed in place through a hydrogen bonding network, whilst deprotonation led to an increased shuttling rate concomitant with a change in the colour of the solution from yellow to colourless as the aromatic stacking interactions were disrupted (Figure 4.3).²⁴

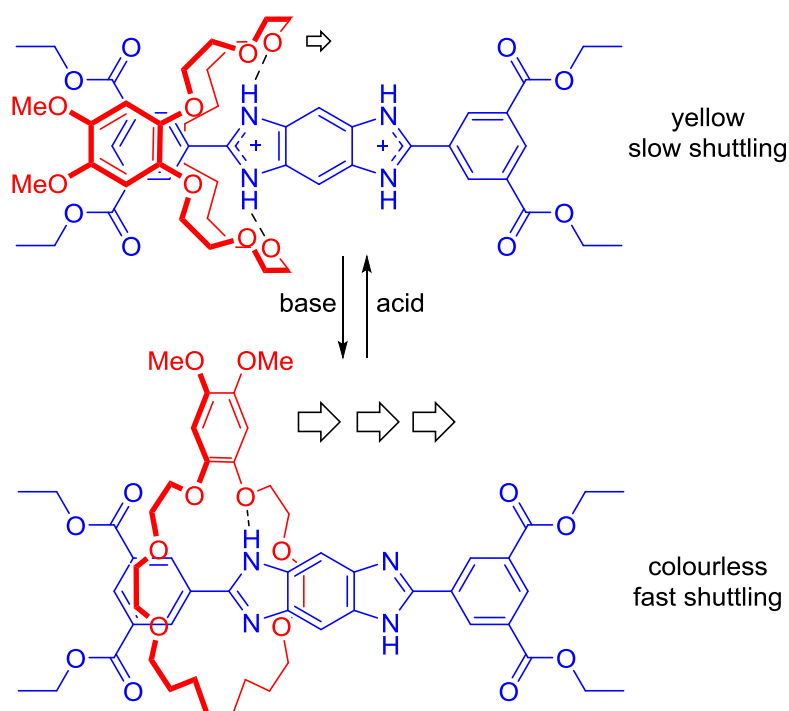


Figure 4.3 - Loeb's molecular shuttle; rate of shuttling controlled by protonation of benzimidazole nitrogen site.²⁴

In summary, the 2-substituted benzimidazole motif has been proven to be a versatile structure throughout supramolecular chemistry. Furthermore, its facile protonation has been shown to be a straightforward method in the design of interlocked structures and molecular machines. The potential to conjugate a benzimidazole moiety with an iodotriazole motif in order to prepare novel XB dynamic interlocked receptors capable of anion sensing via macrocycle translocation is the major focus of the work in this chapter.

4.1.3 Chapter aims

This chapter investigates the reaction between an *o*-phenylenediamine and an aldehyde to prepare a novel 2-substituted benzimidazole-iodotriazole motif. The potential to form interlocked structures based upon this structure is explored via a pseudorotaxane study and subsequently its integration into a naphthalimide-based axle containing [2]rotaxane capable

of anion induced molecular motion is outlined. Finally, the transition metal complexation properties of the benzimidazole-iodotriazole motif are investigated.

4.2 Acyclic receptor synthesis

4.2.1 Initial investigation into benzimidazole-iodotriazole motif

In the literature, a wide variety of different reaction conditions are described for the condensation reaction between an *o*-phenylenediamine and an aldehyde to form a benzimidazole. There are two possible products of this reaction, the 2-substituted derivative and the 1,2-disubstituted product (Figure 4.4), with the former targeted in this work since this maintains the imidazole N-H hydrogen bond donor desired for anion recognition.²⁵

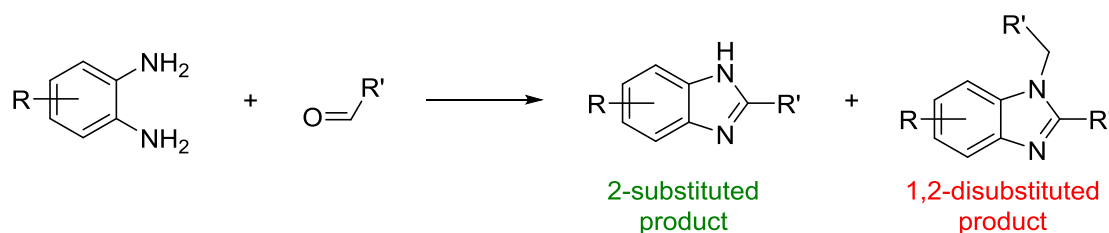
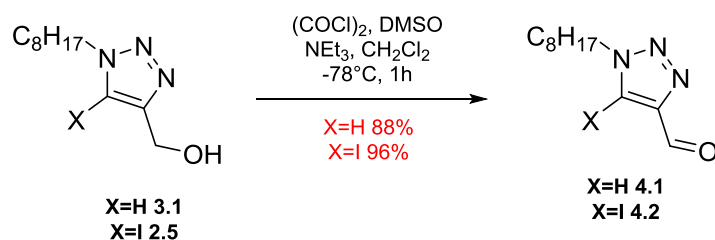


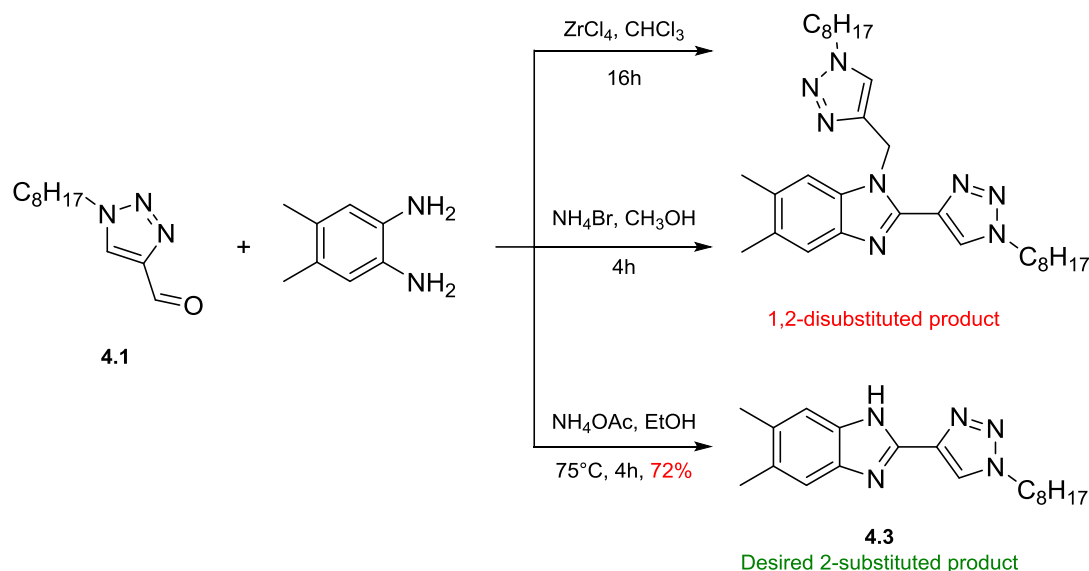
Figure 4.4 – Possible products arising from condensation reaction between *o*-phenylenediamine and aldehyde to form benzimidazole.

The initial objective was to prepare an XB benzimidazole-iodotriazole acyclic receptor to investigate the suitability of the motif for forming an interlocked assembly. To optimise the conditions of the 2-substituted benzimidazole formation reaction, the commercially available 4,5-dimethyl-1,2-phenylenediamine was used. Triazole and iodotriazole aldehydes **4.1** and **4.2** were formed through the ‘Swern’ oxidation of the corresponding alcohols **3.1** and **2.5**; an excess of oxalyl chloride and DMSO were dissolved in CH₂Cl₂ at -78°C before addition of the alcohol and NEt₃ resulted in isolation of both aldehydes in high yield (Scheme 4.4).



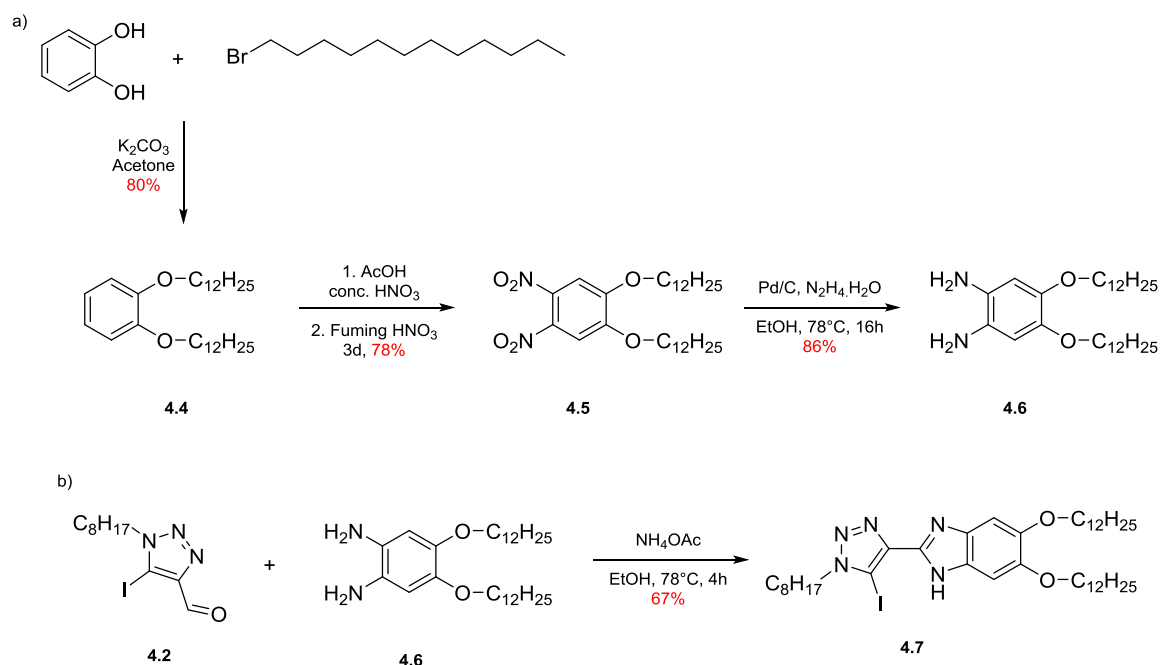
Scheme 4.4 - Synthesis of triazole aldehyde **4.1**.

Several methods were attempted towards formation of the desired 2-substituted HB and XB benzimidazole products (Scheme 4.5). Using powerful Lewis acid catalyst ZrCl_4 and stirring overnight in CHCl_3 resulted in formation of the 1,2-disubstituted product, whilst performing the reaction in the presence of NH_4Br in CH_3OH solution produced the same outcome. Finally, a route outlined by Sharghi selective for the 2-substituted product was found.²⁶ Aldehyde **4.1** was added to a small excess of the diamine in the presence of one equivalent of NH_4OAc . After heating in ethanol at reflux for four hours, cooling to room temperature allowed benzimidazole-triazole **4.3** to be isolated in good yield.



Scheme 4.5 – Attempts to form benzimidazole-triazole **4.3**.

An analogous reaction was performed using XB aldehyde **4.2** and *o*-phenylenediamine **4.6**, which was prepared according to literature procedures. Catechol and 1-dodecyl bromide were added to acetone and heated at reflux for two days in the presence of K_2CO_3 to afford ether **4.4** (Scheme 4.6a).²⁷ Nitro groups were substituted in the 3- and 4- positions through stirring for three days in the presence of fuming nitric acid to give di-nitro structure **4.5**, before reduction utilising Pd/C and hydrazine hydrate afforded *o*-phenylenediamine **4.6** in good yield.²⁸ Iodotriazole aldehyde **4.2** and diamine **4.6** were heated at reflux in the presence of NH_4OAc to give target benzimidazole-iodotriazole **4.7** in 67% yield (Scheme 4.6b).



Scheme 4.6 - a) Synthesis of *o*-phenylenediamine **4.6**, b) preparation of benzimidazole-iodotriazole **4.7**.

4.2.2 Pseudorotaxane assembly study

Following the successful synthesis of benzimidazole-iodotriazole **4.7**, an investigation was undertaken to assess the ability of this motif to form an interpenetrated pseudorotaxane assembly with an isophthalamide hydroquinone polyether macrocycle in the presence of a

templating anion. This required protonation of **4.7** in order to increase the strength of anion binding to template the pseudorotaxane formation.

Initially, the benzimidazole was protonated at the unsaturated nitrogen site following a literature procedure, with the reaction monitored by ^1H NMR spectroscopy.²⁹ Benzimidazole-iodotriazole **4.7** was dissolved in $\text{DMSO-}d_6$ and addition of one equivalent of HBF_4 afforded benzimidazolium-iodotriazole **4.7·HBF₄** (Figure 4.5). Protonation led to the disappearance of the N-H proton resonance in the ^1H NMR spectrum and caused the two distinct benzene proton environments to exhibit a single 2H peak.

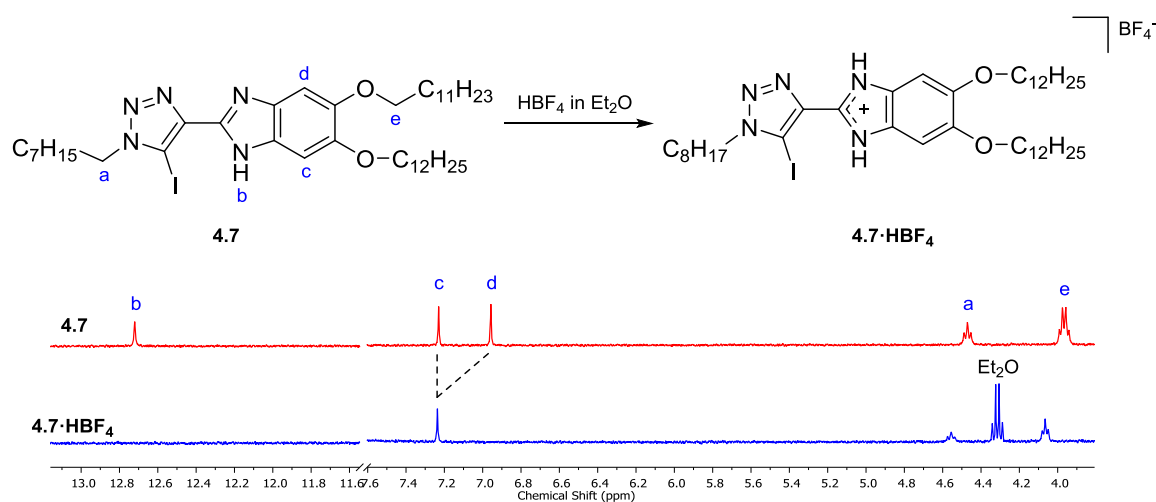
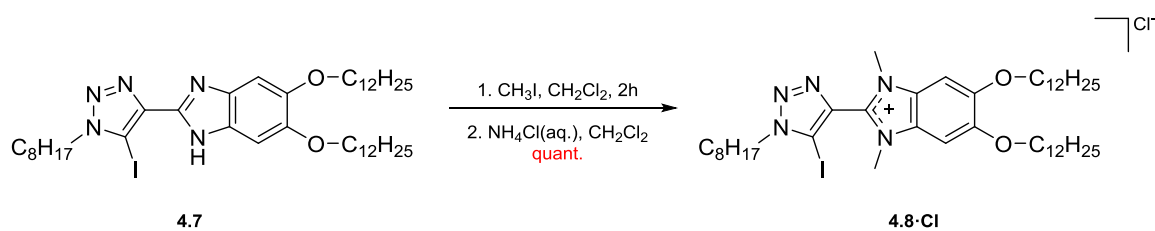


Figure 4.5 - Protonation of **4.7** to afford benzimidazolium-iodotriazole **4.7·HBF₄**. Truncated ^1H NMR spectrum in $\text{DMSO-}d_6$ shows convergence of benzene protons c and d (400 MHz, 298 K).

In spite of the lipophilic alkyl substituents, **4.7·HBF₄** exhibited poor solubility in solvents suitable for pseudorotaxane studies. As a consequence, methylation of **4.7** was performed to give a cationic derivative for interpenetrative assembly investigation. Benzimidazole-iodotriazole **4.7** was reacted with a large excess of CH_3I in CH_2Cl_2 to afford the benzimidazolium-iodotriazole chloride salt **4.8·Cl** after anion exchange by repeated washing with aqueous ammonium chloride solution (Scheme 4.7).



*Scheme 4.7 - Synthesis of methylated benzimidazolium-iodotriazole **4.8·Cl**.*

^1H NMR spectroscopy was used to undertake a qualitative pseudorotaxane assembly study. An equimolar mixture of **4.8·Cl** and isophthalamide macrocycle **2.9** in CDCl_3 was prepared and the ^1H NMR spectrum compared with spectra of the individual components (Figure 4.6). Spectral changes were observed that were diagnostic of the formation of an interpenetrated assembly. Significant upfield shifts of macrocycle hydroquinone protons *5* were attributed to aromatic stacking donor-acceptor interactions with the electron deficient benzimidazolium group. Interestingly, the thread-based phenyl protons *d* split into two environments as a result of the loss of symmetry. There was also a slight upfield perturbation of methyl protons *f* (not shown in Figure 4.6 due to overlap with the crown ether region). Finally, downfield shifts of macrocycle amide protons *4* were observed due to their interaction with the chloride anion.

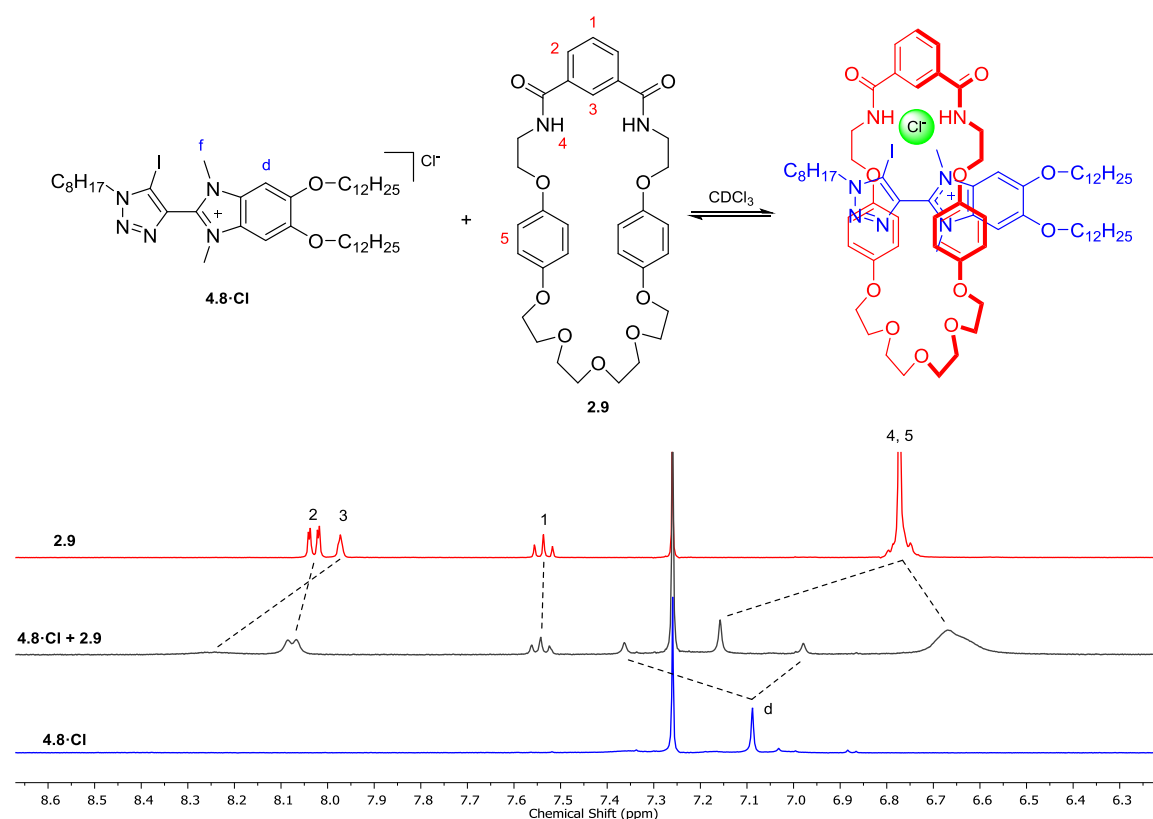


Figure 4.6 - ^1H NMR spectra of macrocycle **2.9**, benzimidazolium-iodotriazole **4.8-Cl** and an equimolar solution of the two, suggesting pseudorotaxane formation (CDCl_3 , 400 MHz, 298 K).

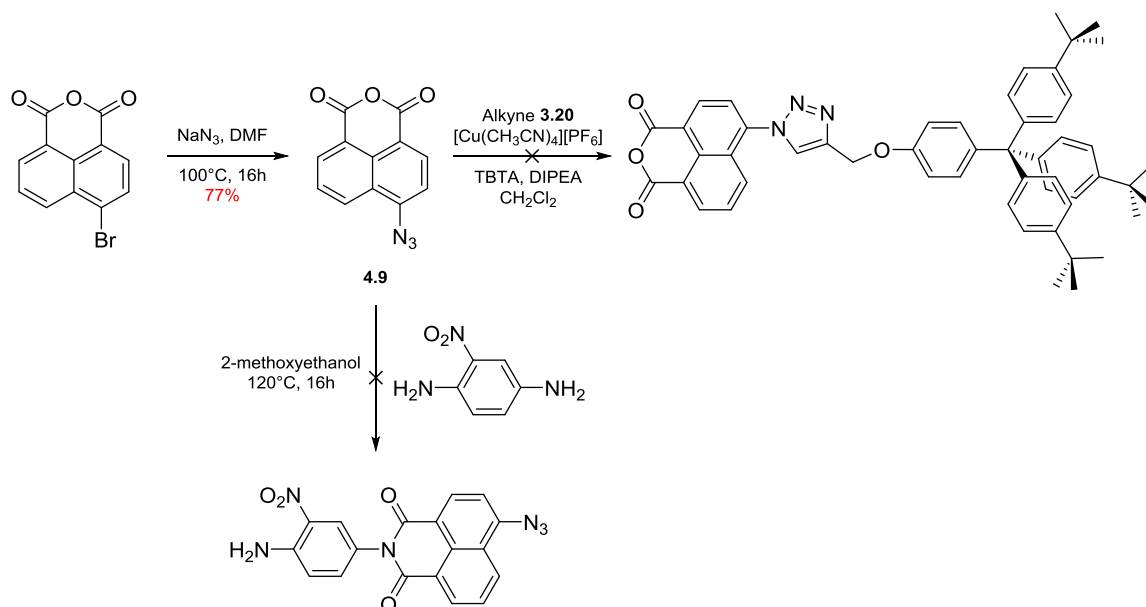
4.3 Preparation of a dynamic [2]rotaxane

Encouraged by the success of the pseudorotaxane studies, the preparation of a dynamic interlocked [2]rotaxane incorporating the benzimidazolium-iodotriazole motif into the axle component was undertaken. It was envisaged that by also including an electron deficient aromatic station in the axle which was capable of donor-acceptor aromatic stacking interactions with the hydroquinone groups of macrocycle **2.9**, the target rotaxane may be capable of anion induced switchable motion. Naphthalimide was selected as an ideal candidate for this purpose; not only is it electron deficient but it is photoactive so may provide an optical response to molecular motion.

4.3.1 Synthesis of axle precursors

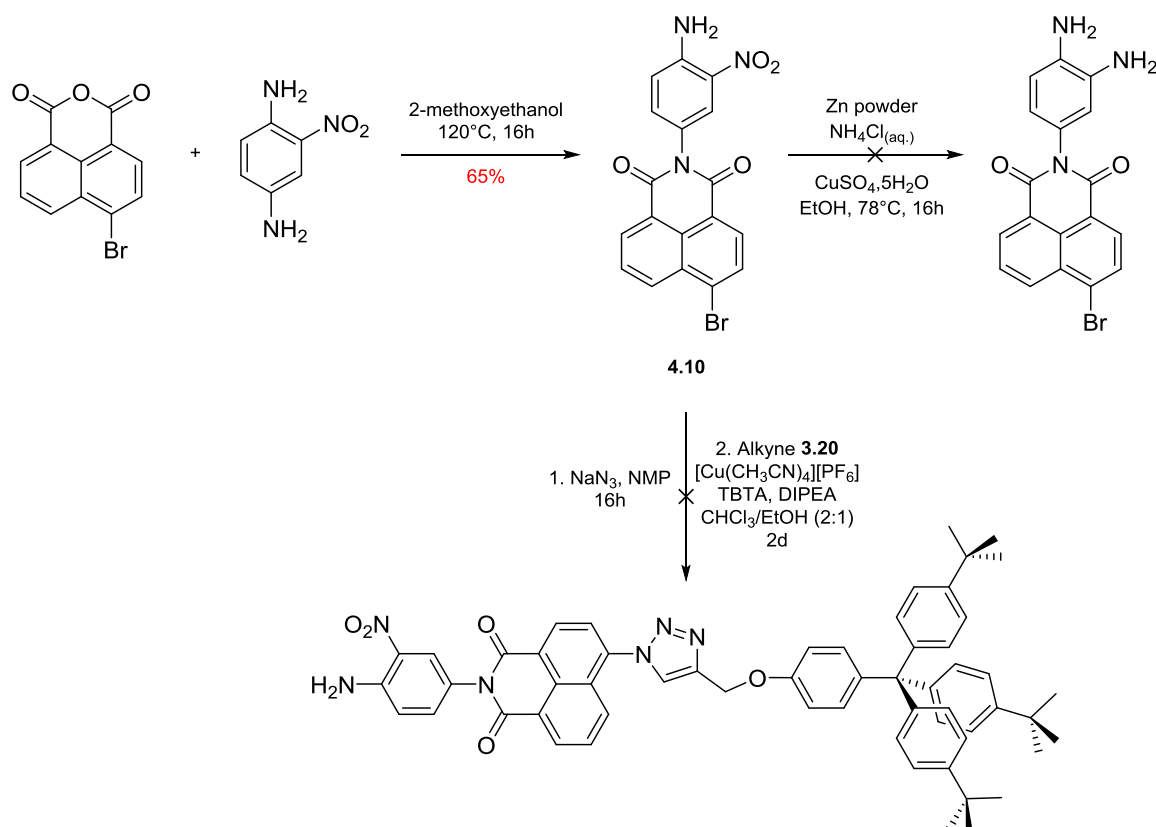
The protocol for rotaxane preparation was to first synthesise separate stopper azide and alkyne functionalised axle precursors, with one component containing a benzimidazole-iodotriazole site. Through protonation of this motif with HCl and subsequent addition of isophthalamide macrocycle **2.9**, it was envisaged that the target [2]rotaxane would be formed via a chloride anion template CuAAC stoppering reaction.

Initially, 4-bromo-1,8-naphthalic anhydride and NaN₃ were heated in DMF for 16 hours and the azide substituted product **4.9** was isolated in good yield (Scheme 4.8). Subsequently, a CuAAC reaction with stopper alkyne **3.20** was attempted; however there was no evidence of the reaction occurring. Separately, azide **4.9** and 2-nitro-1,4-phenylenediamine were stirred overnight in 2-methoxyethanol at 120°C in an attempt to protect the reactive anhydride position before the click reaction, however, this was also unsuccessful.



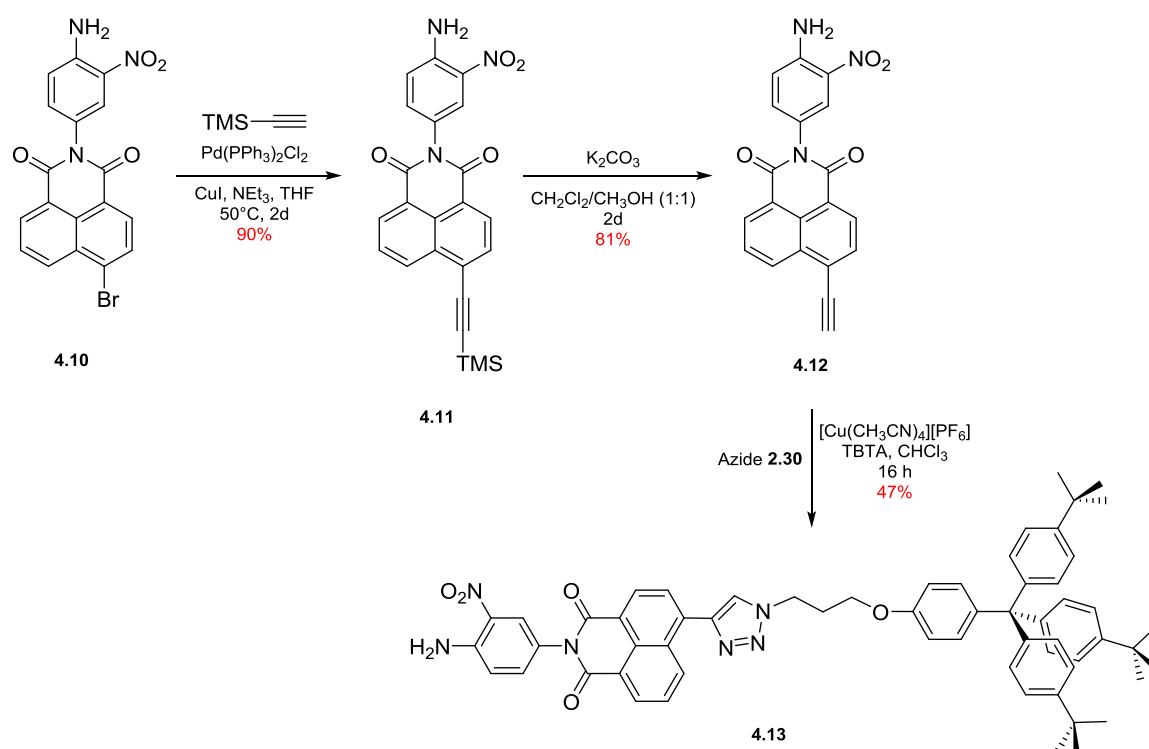
Scheme 4.8 - Synthesis of azide **4.9** and attempts towards further synthons.

Following a literature procedure,³⁰ 4-bromo-1,8-naphthalic anhydride and 2-nitro-1,4-phenylenediamine were stirred in 2-methoxyethanol overnight at 120°C to afford the nitro-amine product **4.10** in 65% yield (Scheme 4.9). An attempt was made to convert this to the azide derivative and perform the CuAAC reaction with stopper alkyne **3.20** *in situ*. Nitro-amine **4.10** and NaN₃ were dissolved in *N*-methyl-2-pyrrolidone (NMP) and stirred overnight in the dark, after which a 2:1 chloroform/ethanol solution of alkyne **3.20**, TBTA, DIPEA and [Cu(CH₃CN)₄][PF₆] was added. This mixture was stirred for two days, after which, unfortunately, there was no evidence of the desired product. With the aim to functionalise the nitro-group of the molecule, a reduction of **4.10** was attempted using Zn powder, NH₄Cl and a source of Cu(II) following a literature procedure.³¹ The reagents were stirred in ethanol at reflux overnight; however, this reaction was also unsuccessful.



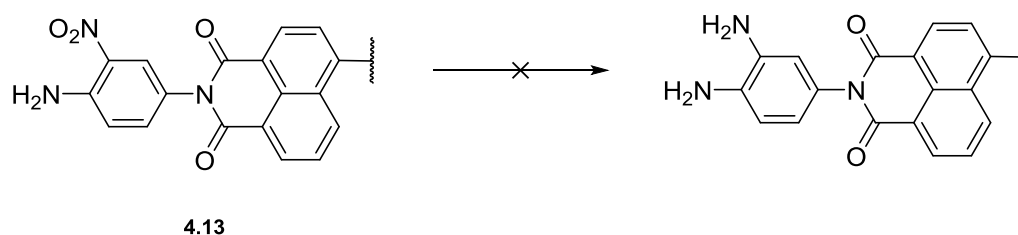
Scheme 4.9 - Synthesis of nitro-amine **4.10** and subsequent attempted further functionalisation.

To circumvent the issues encountered in the previous routes, the synthesis was modified to incorporate an alkyne functionality into the naphthalimide system, with the intention to attach a stopper group via a CuAAC reaction with stopper azide **2.30**. A Sonogashira coupling reaction was performed between nitro-amine **4.10** and TMS-acetylene, following literature conditions used to prepare a similar compound (Scheme 4.10).³² The reagents were stirred at 50°C for two days in the presence of NEt₃, CuI and Pd(PPh₃)₂Cl₂ to afford TMS-protected naphthalimide alkyne **4.11** in high yield. The TMS-protecting group was cleaved through stirring overnight in CH₂Cl₂/CH₃OH (1:1) containing an excess of K₂CO₃ to give naphthalimide alkyne **4.12**. A CuAAC reaction was performed between alkyne **4.12** and stopper azide **2.30**; the reagents were dissolved in CHCl₃ along with TBTA and [Cu(CH₃CN)₄][PF₆] and the solution stirred overnight, with stopper naphthalimide **4.13** isolated in 43% yield after purification by column chromatography.



Scheme 4.10 - Preparation of stopper naphthalimide **4.13** via Sonogashira coupling of **4.10** with TMS acetylene and subsequent deprotection and CuAAC reaction with azide **2.30**.

The reduction of the nitro group of naphthalimide **4.13** to afford the *o*-phenylenediamine synthon required for the benzimidazole formation reaction was attempted via several methods. Firstly, **4.13** was dissolved in THF containing 10% Pd/C and the solution was flushed with H₂ and stirred under an atmosphere of H₂ for two days (Figure 4.7). Despite several attempts there was no evidence of formation of the desired product. Next, **4.13**, an excess of hydrazine hydrate and a catalytic amount of 10% Pd/C were heated at reflux in THF, however this resulted in the same outcome. Finally, Zn powder, CuSO₄·5H₂O and saturated NH₄Cl solution were added to an ethanol solution of **4.13** and heated at reflux for five hours; once again the target product was not isolated.

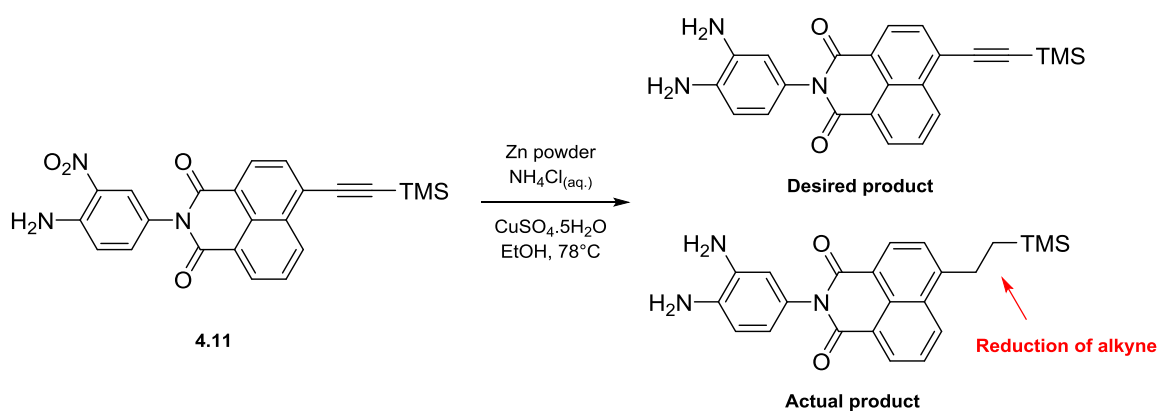


Entry	Reagents and conditions
1	10% Pd/C, THF, H ₂ atm., two days
2	Hydrazine hydrate, 10% Pd/C, THF (66°C), one hour
3	Zn powder, saturated NH ₄ Cl solution, CuSO ₄ ·5H ₂ O, EtOH (78°C), five hours

Figure 4.7 - Attempts at reduction of nitro-amine **4.13** to diamine. Stopper triazole group omitted for clarity.

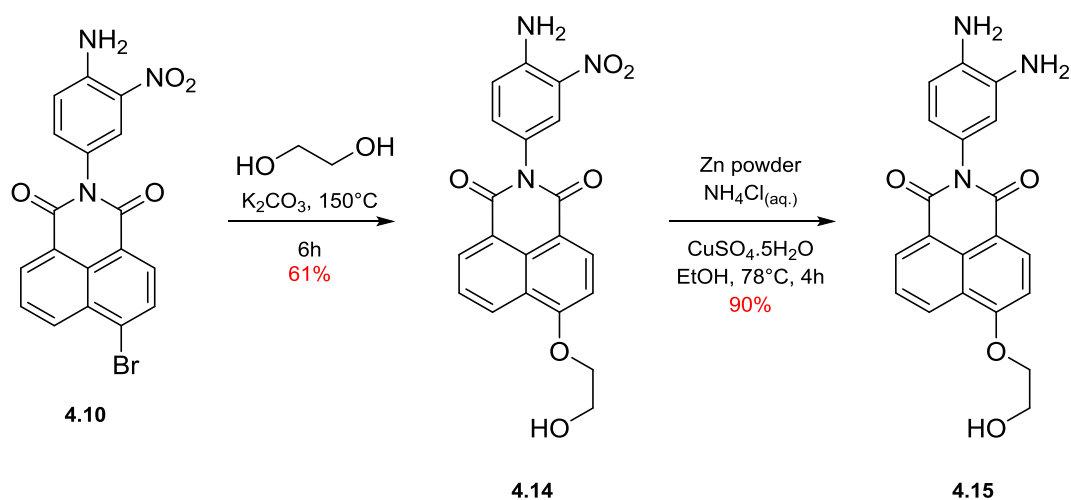
It was postulated that additional functional groups in the molecule were impacting on the reduction reaction. Therefore, a reduction was attempted with TMS-protected alkyne **4.11**; this was dissolved in ethanol containing Zn powder, two crystals of CuSO₄·5H₂O and saturated aqueous NH₄Cl solution (Scheme 4.11). After stirring for five hours at reflux,

products were collected *in vacuo* after filtration through Celite®. Although reduction at the nitro position was successful, reduction of the alkyne to an alkane had also occurred.



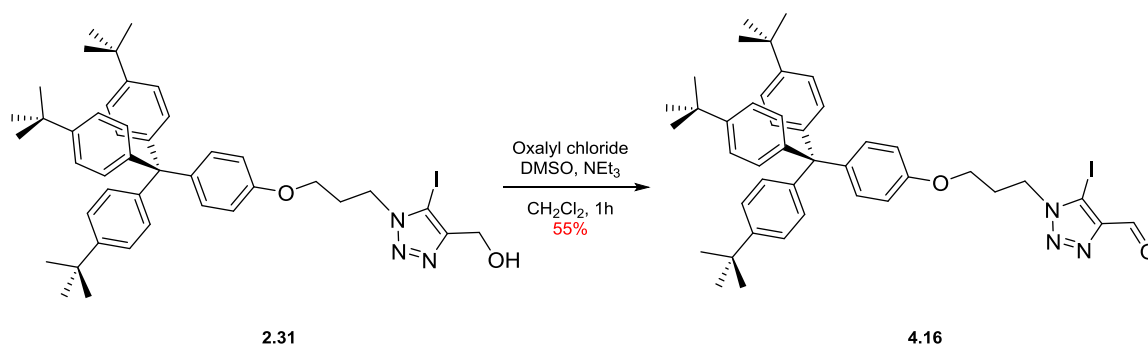
Scheme 4.11 - Reduction of TMS-protected alkyne **4.11** forming unexpected alkane product.

With the direct conjugated connection of a triazole group to the naphthalimide structure proving to be a significant challenge, an alternative synthetic route was sought. A short carbon chain between the naphthalimide and the triazole was targeted in order to avoid their conjugation whilst also allowing the reduction of the nitro group to be performed earlier in the synthesis, leading to initial stoppering of the diamine part of the molecule. Nitro-amine derivative **4.10** and K_2CO_3 were stirred in ethylene glycol at 150°C for six hours, to produce alcohol **4.14** in good yield (Scheme 4.12). Reduction of the nitro group was achieved through reaction with Zn powder, $\text{NH}_4\text{Cl}_{(\text{aq.})}$ and a catalytic amount of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ in hot ethanol to afford diamine **4.15** in high yield.



Scheme 4.12 - Synthesis of nitro-alcohol **4.14** and subsequent reduction to diamine **4.15**.

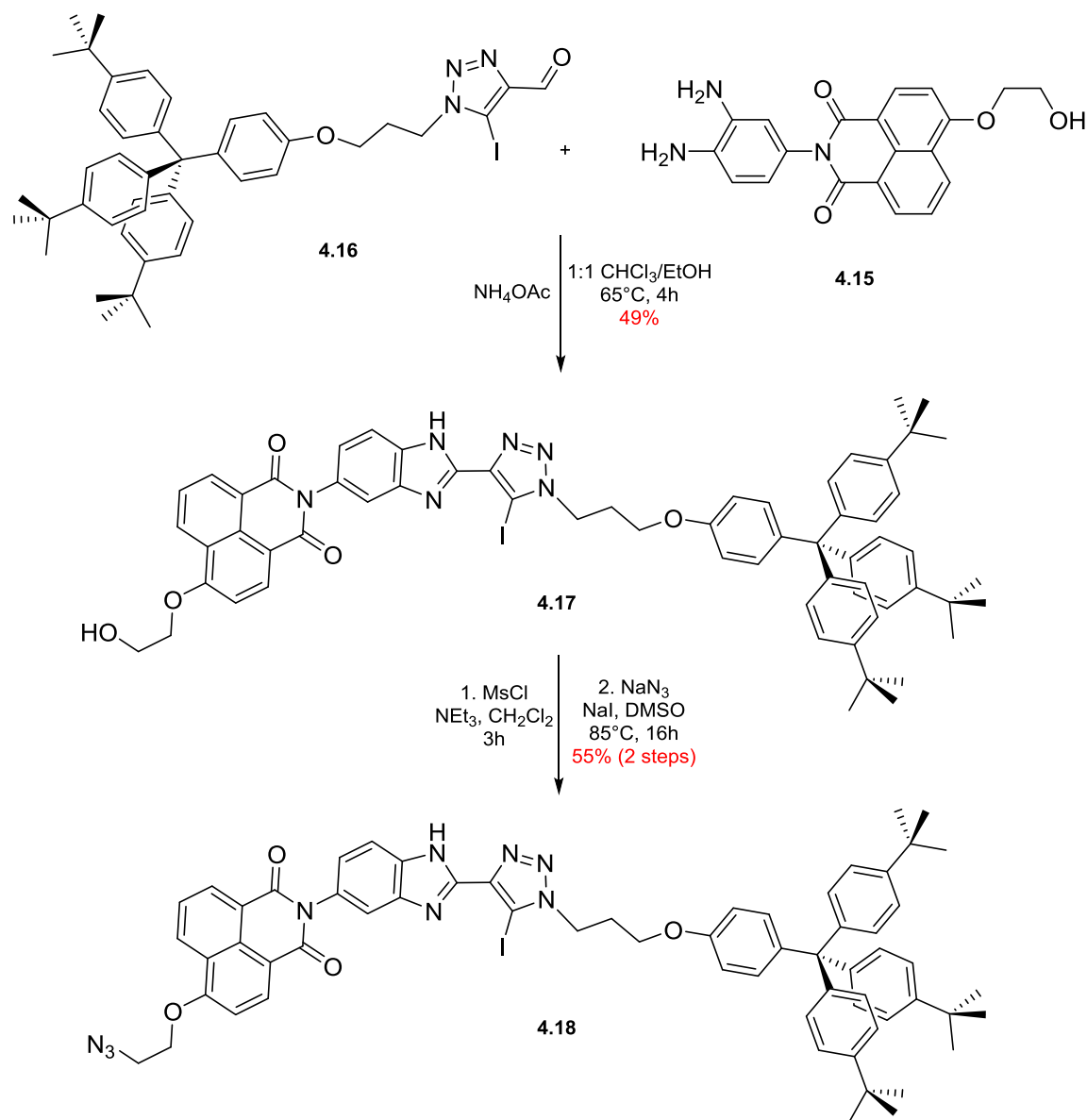
With diamine **4.15** in hand, a suitable stopper iodotriazole aldehyde was prepared. A Swern oxidation reaction was performed upon stopper iodotriazole alcohol **2.31** (Scheme 4.13). Oxalyl chloride and DMSO were dissolved in CH_2Cl_2 and cooled to -78°C , whereupon addition of **2.31** and NEt_3 led to the formation of stopper iodotriazole aldehyde **4.16** in good yield after purification via column chromatography.



Scheme 4.13 - Preparation of stopper iodotriazole aldehyde **4.16**.

Aldehyde **4.16** and diamine **4.15** were reacted under the benzimidazole formation reactions optimised in section 4.1.2. Together with NH_4OAc , the reagents were stirred in 1:1 chloroform/ethanol at 65°C for four hours (chloroform was necessary to dissolve aldehyde

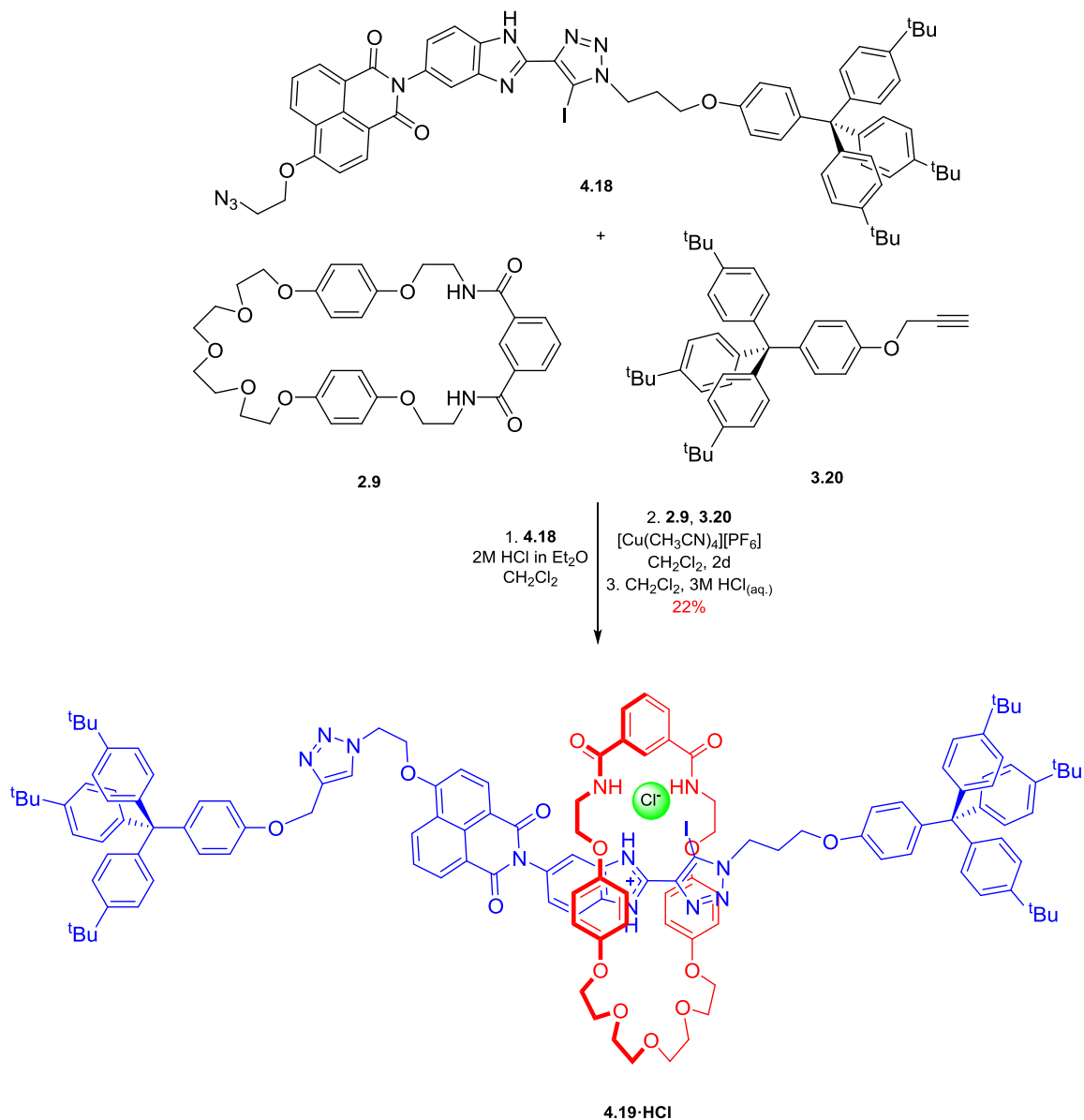
4.16), affording benzimidazole-iodotriazole alcohol **4.17** in 49% yield after purification. The terminal alcohol group of **4.17** was converted to the mesylate through stirring with MsCl and NEt₃, before benzimidazole-iodotriazole azide **4.18** was successfully isolated after heating overnight with NaN₃ in DMSO (Scheme 4.14).



*Scheme 4.14 - Benzimidazole formation reaction between aldehyde **4.16** and diamine **4.15** to afford alcohol **4.17** and conversion to azide **4.18** via the mesylate intermediate.*

4.3.2 Synthesis of [2]rotaxane

Successful isolation of azide **4.18** allowed for attempts at rotaxane formation via a chloride anion template stoppering method. Upon protonation of the benzimidazole-iodotriazole motif using HCl and forming a pseudorotaxane similar to that studied in section 4.2.2, it was postulated that a CuAAC reaction with stopper alkyne **3.20** would form the desired [2]rotaxane. Azide **4.18** was dissolved in CH₂Cl₂ and an excess of 2M HCl in Et₂O was added to protonate the benzimidazole moiety. After removal of the solvent *in vacuo*, the cationic thread was again dissolved in CH₂Cl₂ and isophthalamide macrocycle **2.9** was added to the solution followed by [Cu(CH₃CN)₄][PF₆] and stopper alkyne **3.20**. After stirring for two days, target [2]rotaxane **4.19·HCl** was isolated in 22% yield after purification by preparative TLC and washing the resultant solid with 3M HCl (Scheme 4.15).



Scheme 4.15 – Protonation of azide **4.18** and subsequent addition of macrocycle **2.9** and alkyne **3.20** to afford [2]rotaxane **4.19·HCl** via a stoppering method.

Rotaxane characterisation was determined through ¹H, ¹³C, and two-dimensional ¹H-¹H COSY and ROESY NMR spectroscopy and high resolution ESI mass spectrometry. Key features were exhibited in the CDCl₃ ¹H NMR spectrum of **4.19·HCl** that were diagnostic of successful [2]rotaxane formation (Figure 4.8). The appearance of a new proton resonance *b* was a consequence of proto-triazole formation and a downfield shift of neighbouring methylene axle protons *a* relative to the alkyne starting material was also observed.

Compared to free isophthalamide macrocycle **2.9**, the hydroquinone resonances (protons **5** and **6**) were split and shifted upfield, associated with desymmetrisation of the macrocycle and aromatic donor-acceptor interactions with the electron deficient axle. Furthermore, a downfield perturbation was exhibited by macrocyclic proton **3** arising from an HB interaction with the chloride anion. Interestingly, the ^1H - ^1H COSY NMR spectrum revealed a split of the macrocyclic alkyl protons labelled with circles (Figure 4.9). This was postulated to be a consequence of a strong association between the axle and macrocycle components.

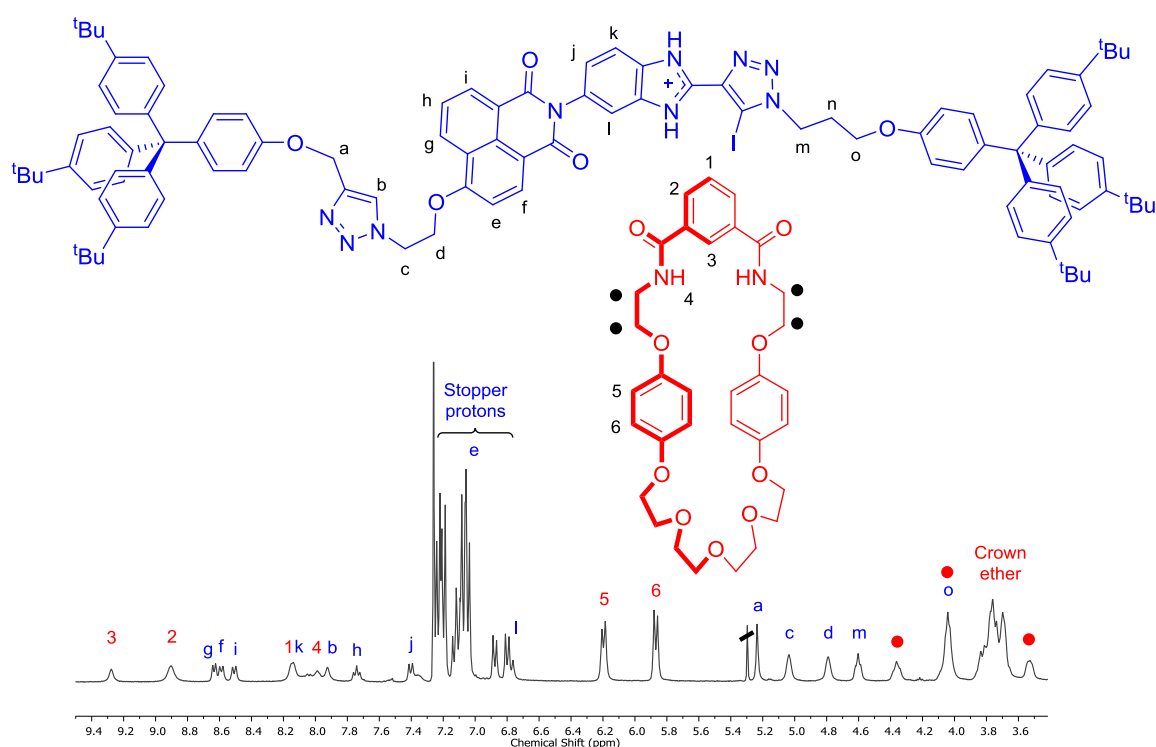


Figure 4.8 - Truncated ^1H NMR of rotaxane **4.19·HCl** (CDCl_3 , 298 K, 400 MHz). Split macrocycle alkyl peaks shown as circles.

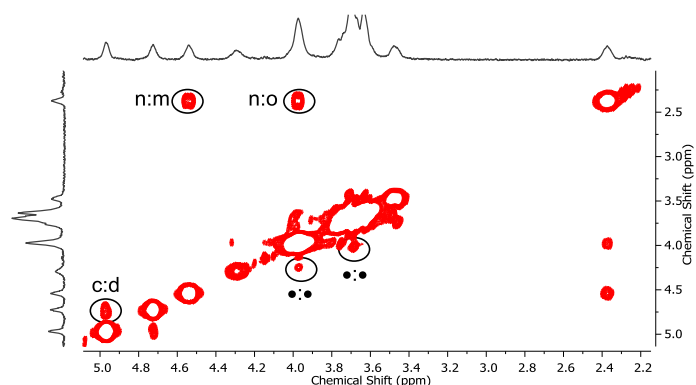


Figure 4.9 - ^1H - ^1H COSY NMR spectrum of **4.19·HCl** suggesting desymmetrisation of macrocycle (CDCl_3 , 298 K, 400 MHz).

Cross peaks between the separate axle and macrocycle components were observed in the two-dimensional ^1H - ^1H ROESY NMR spectrum of **4.19·HCl** that further confirmed the success of formation of an interlocked molecule (Figure 4.10). A through space interaction was observed between hydroquinone resonance *g* and axle based phenyl proton *j* whilst a further cross-peak was seen between a macrocycle methylene environment (labelled with a circle) and axle proton *l*. Crucially, no through space couplings were observed between the macrocycle and the stopper-based protons of the axle, indicating that the macrocycle was residing at the benzimidazolium-iodotriazole station.

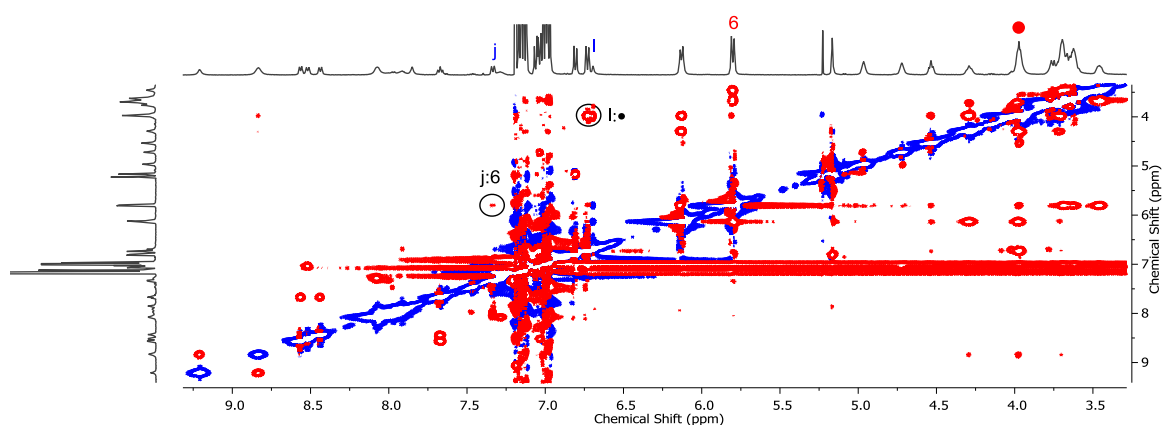
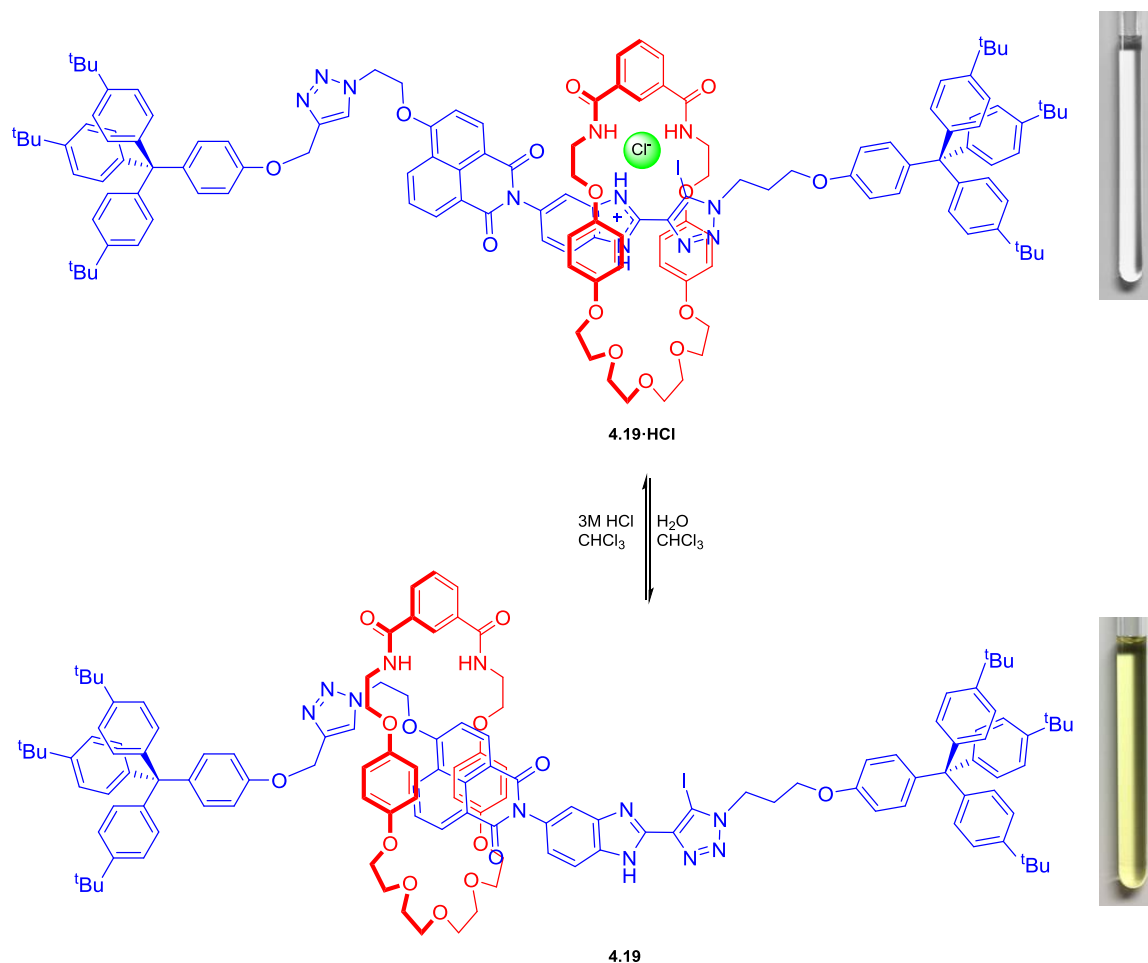


Figure 4.10 - Truncated ^1H - ^1H ROESY spectrum of cationic rotaxane **4.19·HCl** (CDCl_3 , 500 MHz, 298 K). Split macrocycle alkyl peaks shown as circles.

4.3.3 Studies of dynamic behaviour of rotaxane

After successful isolation and characterisation of benzimidazolium-iodotriazole rotaxane **4.19·HCl**, the anion responsive shuttling of the macrocycle along the axle was investigated. Firstly, the rotaxane was deprotonated to form **4.19** by repeated washing with water (Scheme 4.16).^{*} This induced an immediate naked-eye colour change; whilst **4.19·HCl** was colourless in chlorinated solvents the aqueous basic wash resulted in a yellow solution. This was ascribed to the movement of the macrocycle to the electron deficient naphthalimide station and the formation of charge transfer interactions with the electron rich hydroquinone groups. The process was found to be reversible; washing the yellow solution with 3M HCl resulted in an immediate loss of colour. Characterisation of this new co-conformation of [2]rotaxane **4.19** was performed via ^1H , ^{13}C , and two-dimensional ^1H - ^1H ROESY NMR spectroscopy.

^{*} This was possible due to the low pKa (≈ 6) of benzimidazolium;³³ the same colour change was exhibited upon washing with triethylamine.



*Scheme 4.16 - Deprotonation of rotaxane **4.19·HCl** and induced co-conformational change. Solution phase colour change indicative of dynamic motion of macrocycle.*

The ^1H - ^1H ROESY NMR spectrum of neutral rotaxane **4.19** revealed several characteristic cross-peaks that confirmed a change in position of the macrocycle on the axle relative to monocationic rotaxane **4.19·HCl** (Figure 4.11). Firstly, new through space interactions were seen between internal isophthalamide proton **3** and alkyl protons *a*, *c* and *d* of the axle. There were further interactions between hydroquinone proton **5** and a naphthalimide environment, triazole proton *b* and the stopper proton region. Importantly, neither of the through space interactions between the axle benzimidazolium-iodotriazole motif and the macrocycle that had been exhibited by **4.19·HCl** were observed.

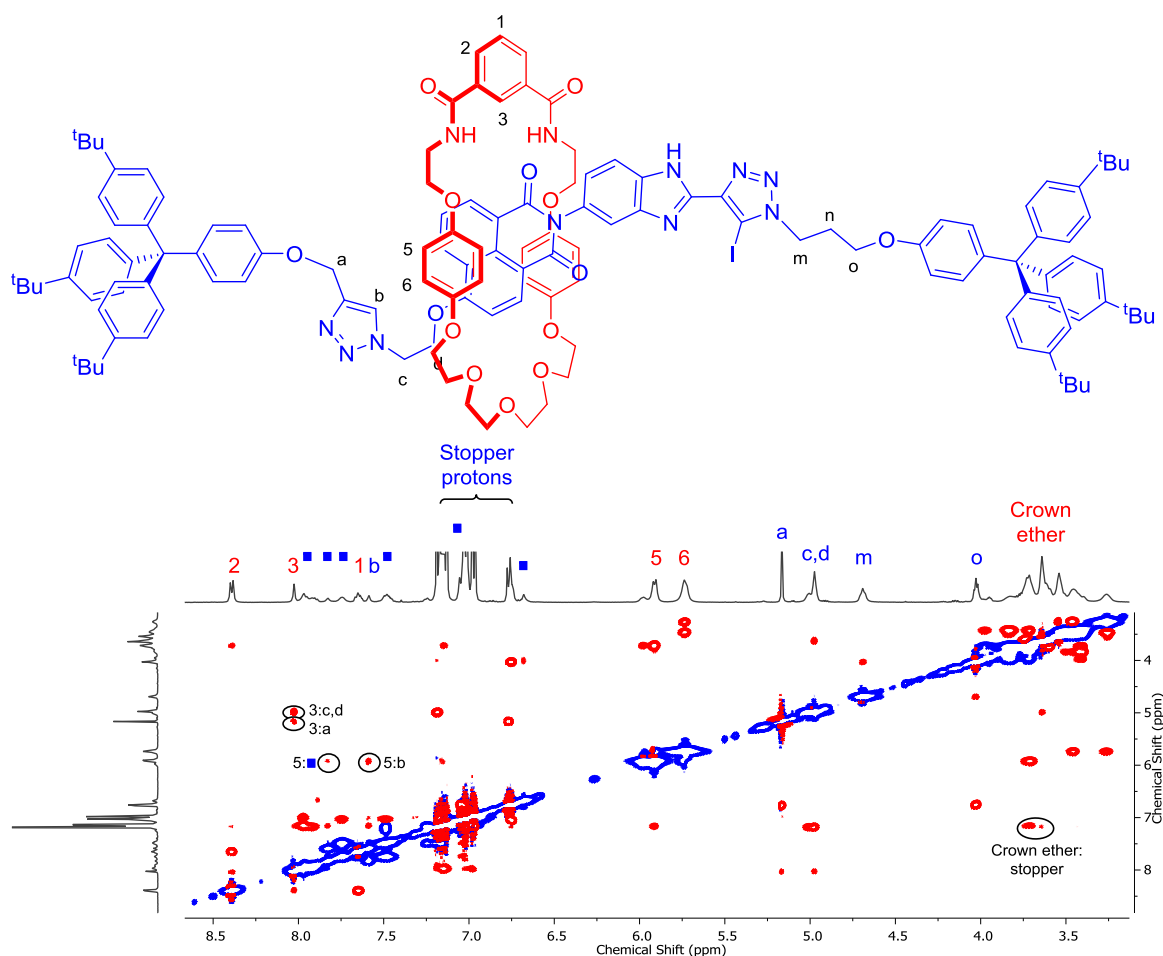


Figure 4.11 - Truncated ^1H - ^1H ROESY spectrum of neutral rotaxane **4.19** (CDCl_3 , 500 MHz, 298 K). Axle-based naphthalimide and benzyl protons shown as squares.

The two-dimensional ^1H - ^1H ROESY NMR spectrum indicated that in the neutral state, the co-conformation of rotaxane **4.19** exhibited dynamic behaviour with the macrocycle residing predominantly at the naphthalimide station of the axle. Upon deprotonation, the macrocycle was unlocked to shuttle along the axle and this facilitated new interactions between the components, such as the aromatic stacking donor-acceptor interactions between the hydroquinone and the naphthalimide motifs. The naked-eye change in colour of the solution as a result of macrocycle translocation is consistent with previously reported examples (outlined in Scheme 4.2 and Scheme 4.3) and is indicative of this type of π - π interaction.^{12,13}

The UV-vis electronic absorption spectra of both co-conformations of the [2]rotaxane were obtained at 1×10^{-4} M in CHCl_3 (Figure 4.12) with both displaying absorbance in the region expected for a 1,8-naphthalimide derivative.³⁴ Notable spectral differences were observed between the two. In the region >350 nm the λ_{max} was shifted to a longer wavelength upon rotaxane deprotonation ($\lambda_{\text{max}} = 361$ nm to 380 nm) and this was concomitant with the appearance of a new absorbance band at $\lambda > 400$ nm, postulated to be a consequence of charge transfer interactions arising between the macrocycle and the naphthalimide station of the axle. The shift in rotaxane absorbance from the UV to the visible region explains the naked-eye colour difference between the two co-conformations.

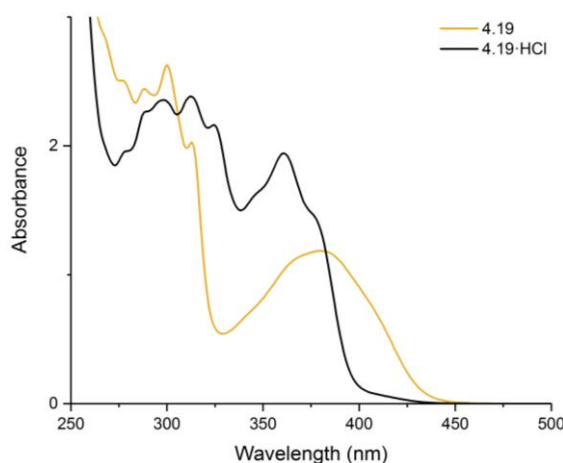


Figure 4.12 - UV-vis absorption spectra of **4.19·HCl** (black) and **4.19** (yellow) in CHCl_3 (concentration 1×10^{-4} M, 298 K).

The fluorescence emission spectra of rotaxane **4.19** and **4.19·HCl** were obtained in CHCl_3 at a concentration of 1×10^{-5} M (Figure 4.13). The position of these maxima and shape of the emission bands in CHCl_3 was comparable to literature data of another 1,8-naphthalimide based compound.³⁴ There was a large difference in the fluorescence emission intensity arising from each co-conformation. Whilst the neutral rotaxane **4.19** exhibited a weak emission maximum at 422 nm, there was a remarkable enhancement in rotaxane fluorescence after washing with 3M HCl to generate **4.19·HCl** (Figure 4.13).

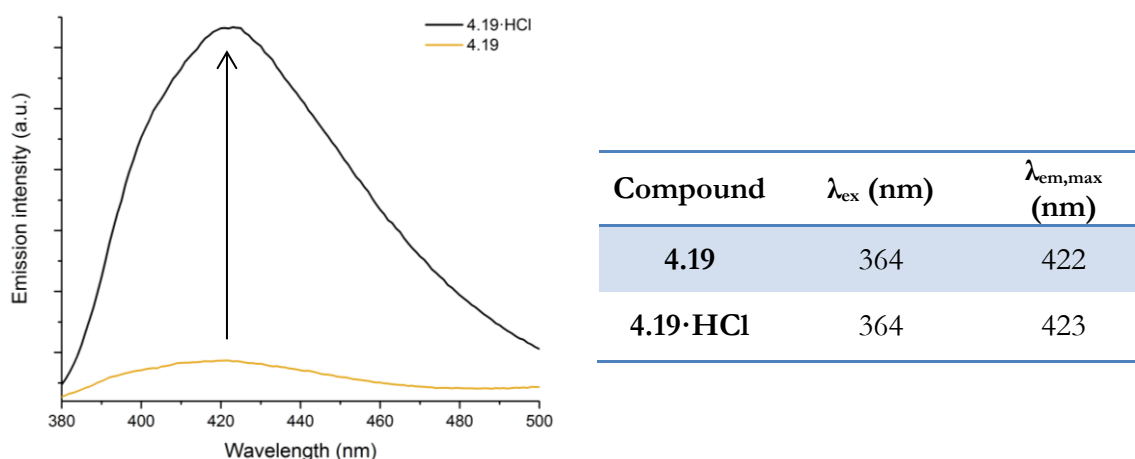
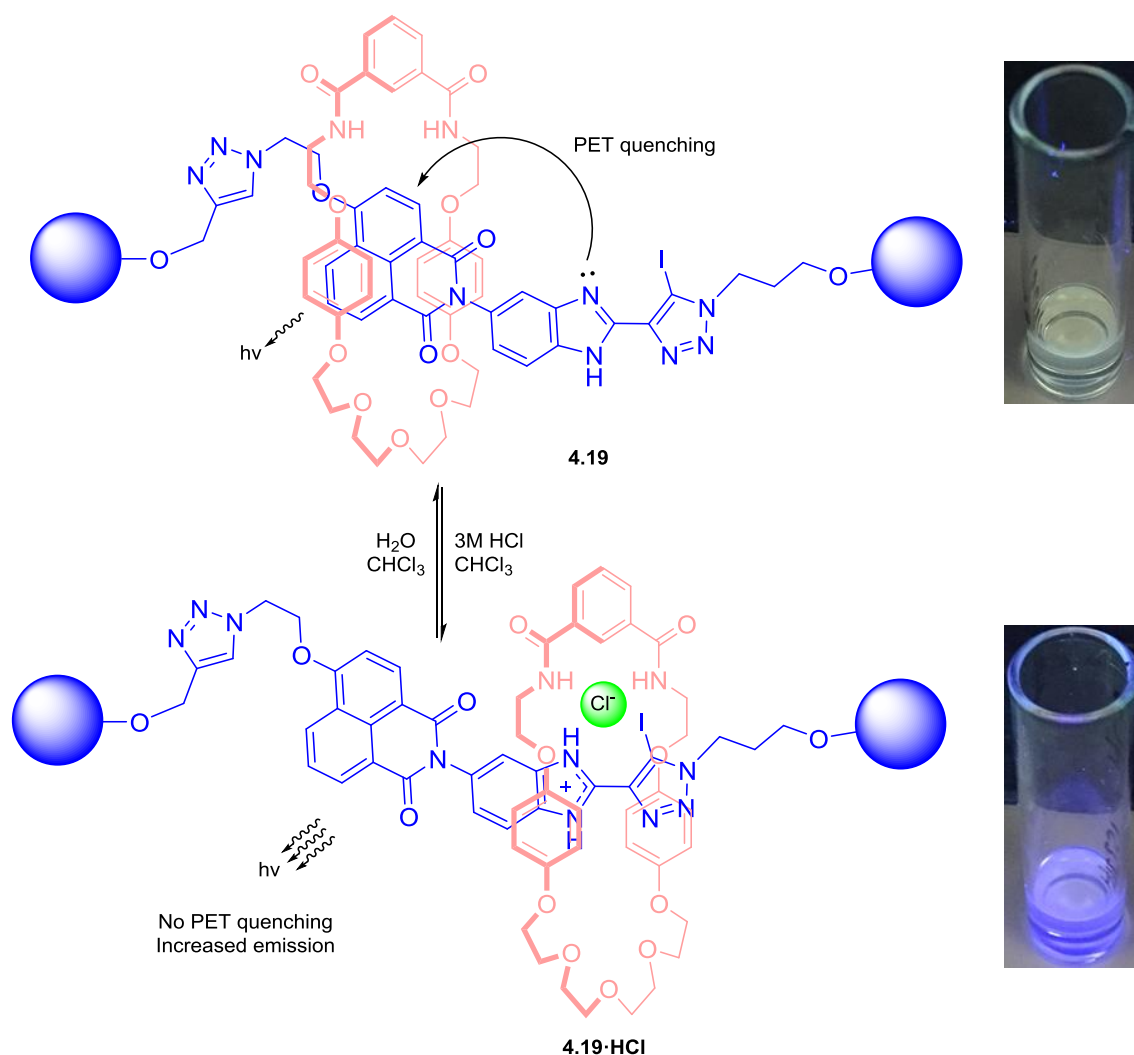


Figure 4.13 – Fluorescence emission spectra of **4.19** (yellow) and **4.19·HCl** (black) in CHCl_3 (concentration 1×10^{-5} M, 298 K). Excitation wavelength (λ_{ex}), maximum emission ($\lambda_{\text{em,max}}$).

The large increase in rotaxane fluorescence intensity was ascribed to a termination of the PET effect. For neutral rotaxane **4.19** the lone pair of electrons of the benzimidazole motif quench the naphthalimide fluorophore via the PET effect. After protonation to cationic rotaxane **4.19·HCl** the lone pair is no longer available, thus a significant enhancement in fluorescence was observed. This is analogous to Czarnik's anthracene-based phosphate sensor, outlined in section 1.4.1.1 (Figure 1.27).³⁵ The switch-on effect could be observed by naked-eye; excitation via long-wave UV radiation at 365 nm resulted in a stark change in receptor emission (Scheme 4.17).[†]

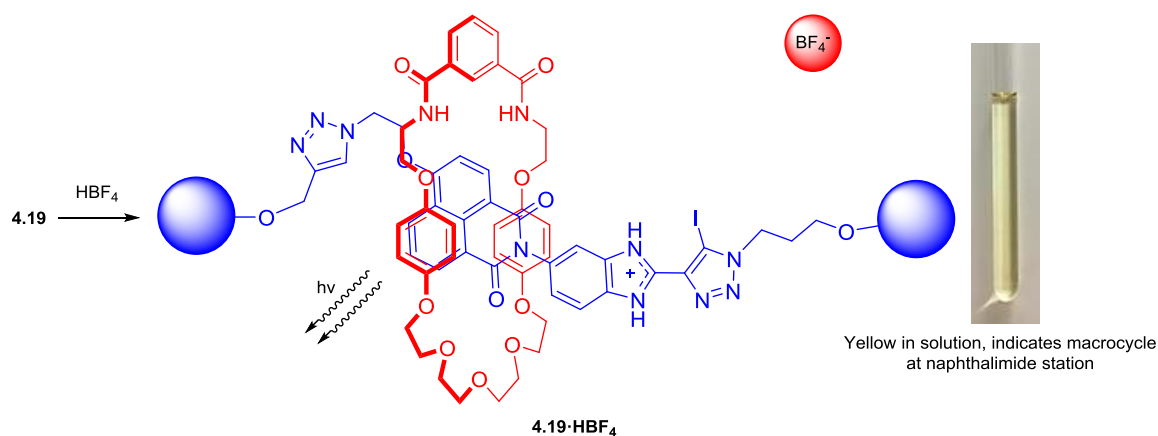
[†] It is worth noting that this switch-on in excited state emission upon protonation would also be observed in the case of the free axle.



Scheme 4.17 – Termination of PET effect as a result of benzimidazole protonation; visible by naked-eye. Stopper groups removed for clarity.

In order to ascertain the effect of the counter anion upon the system, a protonated derivative of **4.19** was prepared employing a non-coordinating counter anion. Neutral rotaxane **4.19** was taken up in CH_2Cl_2 and tetrafluoroboric acid diethyl ether complex was added to form rotaxane **4.19·HBF₄** (Scheme 4.18). Notably, the solution remained yellow, attributed to aromatic stacking donor-acceptor interactions between the electron rich macrocyclic hydroquinone groups and the electron deficient axle based naphthalimide. This suggested the

requirement of a coordinating anion, such as chloride, to facilitate the shuttling of the macrocycle to the axle benzimidazolium-iodotriazole station.[‡]



*Scheme 4.18 - Protonation of neutral rotaxane **4.19** with HBF₄ to afford cationic rotaxane **4.19·HBF₄**. Colour of solution indicative of macrocycle position.*

Further evidence for the position of the macrocycle about the axle in rotaxane **4.19·HBF₄** was ascertained from UV-vis data obtained in CHCl₃ at a concentration of 1x10⁻⁴ M (Figure 4.14). The absorbance spectrum was similar to that of neutral rotaxane **4.19**, exhibiting the broad peak ascribed to the charge transfer interactions arising from the macrocycle interacting with the naphthalimide station.

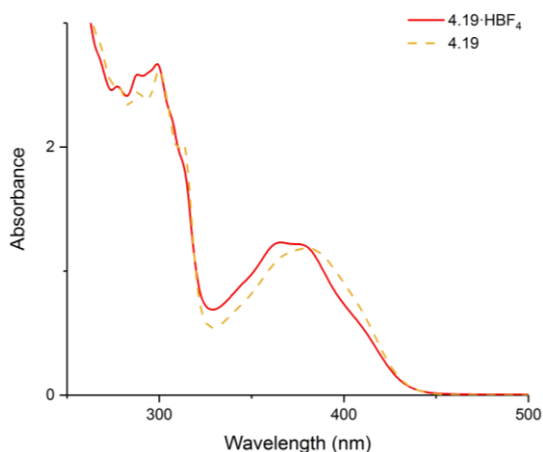


*Figure 4.14 - UV-vis absorption spectra of **4.19·HBF₄** (red) and **4.19** (yellow, dashed) in CHCl₃ (concentration 1x10⁻⁴ M, 298 K).*

[‡] Unfortunately, poor solubility of rotaxane **4.19·HBF₄** at suitable concentrations in CDCl₃ did not allow for comparable ¹H or ¹H-¹H ROESY NMR spectra to be obtained.

Indeed, a qualitative UV-vis spectroscopic anion titration experiment with **4.19**·**HBF₄** upon addition of 50 equivalents of TBACl revealed the absorbance spectrum resembled that of **4.19**·**HCl**, indicative of translocation of the macrocycle to the benzimidazolium-iodotriazole station (Figure 4.15a). This was accompanied by an observable naked-eye colour change of the UV-vis sample from yellow to colourless. Furthermore, there was a noticeable increase in the fluorescence emission maxima of the rotaxane upon chloride addition (Figure 4.15b), postulated to be a consequence of the removal of macrocycle-based PET quenching of the naphthalimide station after its translocation. This is analogous to the example reported by Smith, outlined in Figure 4.1, in which the movement of the macrocycle away from the squaraine fluorophore led to an enhancement in rotaxane excited state emission.¹¹ Interestingly, no change in fluorescence emission was observed upon chloride addition to a sample of neutral rotaxane **4.19**, suggesting the necessity of protonation, as well as the presence of a coordinating anion, to facilitate macrocycle translocation.

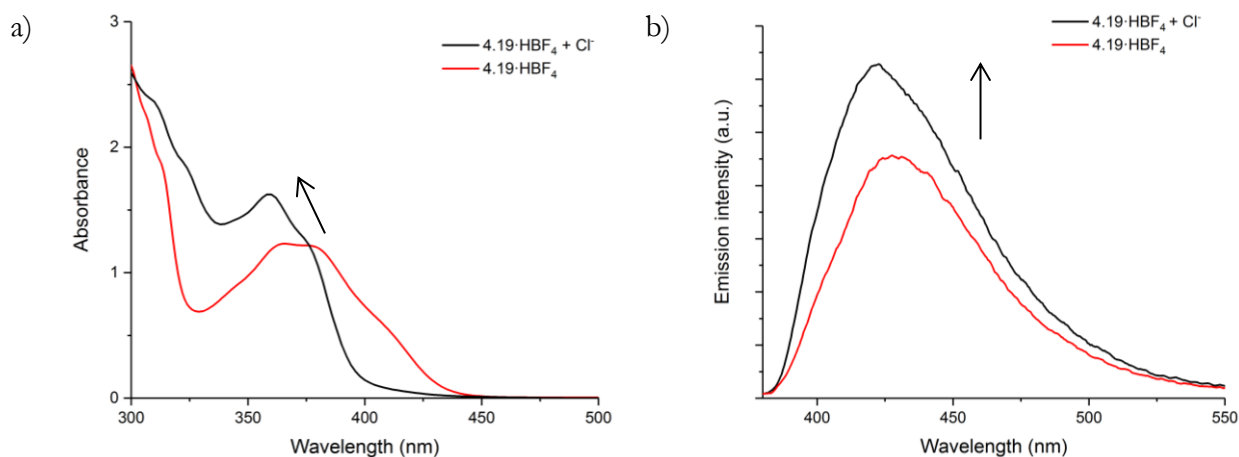


Figure 4.15 – a) UV-vis absorbance and b) fluorescence emission spectra of **4.19**·**HBF₄** and its response upon addition of 50 equivalents of Cl⁻ (concentration 1×10^{-4} M, CHCl₃, 298 K).

The spectroscopic data suggested that macrocycle translocation to the axle benzimidazolium-iodotriazole station was dependent upon both the pH and the coordinating nature of the

counter anion; only upon protonation of rotaxane **4.19** with a coordinating halide acid was a naked-eye detectable absorbance change, from yellow to colourless, observed.

4.4 Towards transition metal based dynamic [2]rotaxanes

Covalently linking the benzimidazole moiety to another donor motif, such as pyridine^{19,36,37} and pyrazole,³⁸ has been shown to produce ligands for transition metal coordination. With this in mind, the benzimidazole-iodotriazole motif was identified as a potential bidentate ligand for this purpose, with the complexed transition metal facilitating anion binding via hydrogen bonding and charge assisted halogen bonding (Figure 4.16). As discussed in Chapter Three, the incorporation of photoactive transition metals into anion receptor design produces potential optical sensors for anions. Hence, the motif offers the opportunity for the incorporation of transition metals into rotaxane structural frameworks for anion sensing applications.

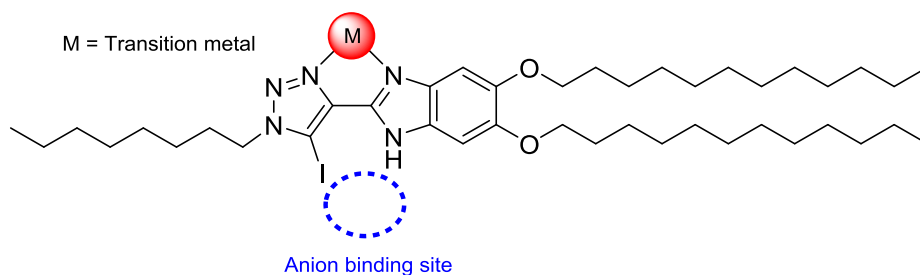
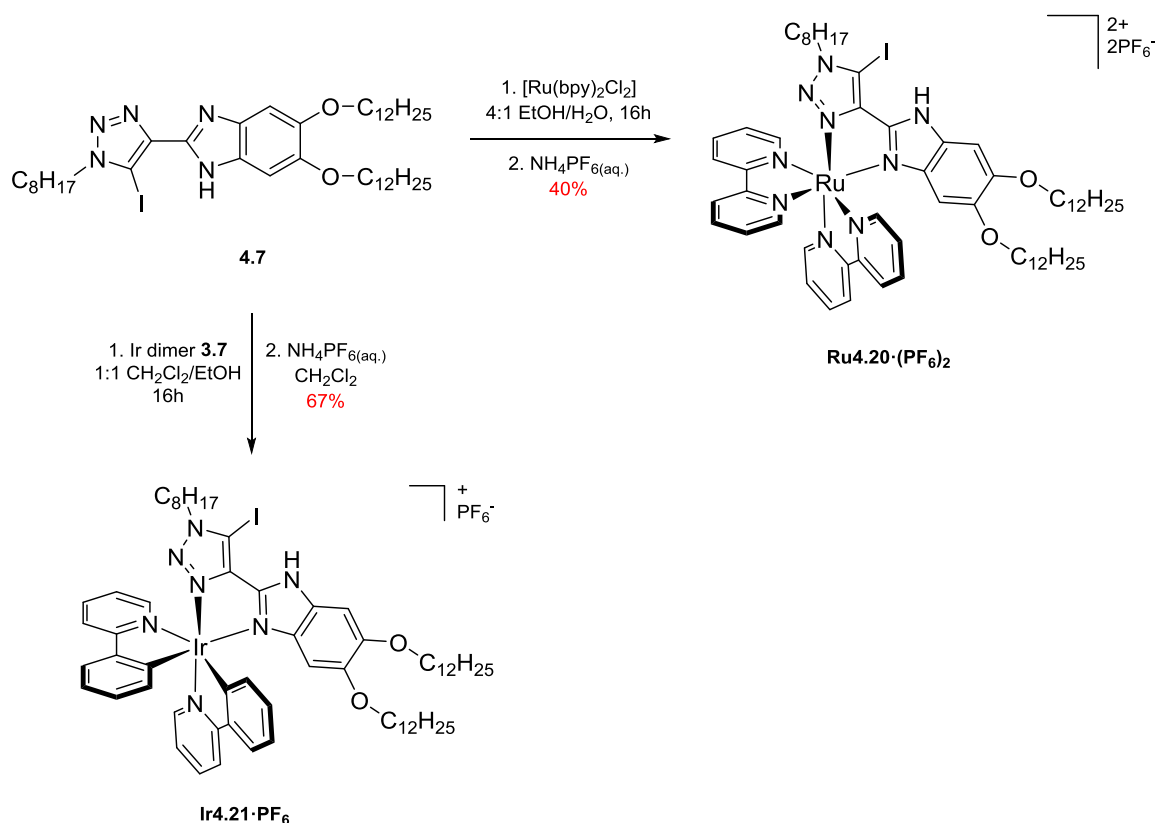


Figure 4.16 - Schematic representation of anion binding via hydrogen bonding and charge assisted halogen bonding by a transition metal complexed benzimidazole-iodotriazole compound.

4.4.1 Transition metal based acyclic receptor synthesis

Benzimidazole-iodotriazole **4.7** was complexed with ruthenium(II) through heating at 90°C for three days with [Ru(bpy)₂Cl₂] in 4:1 EtOH/H₂O (Scheme 4.19). After cooling to room temperature, dropwise addition of a saturated aqueous solution of NH₄PF₆ allowed

Ru4.20·(PF₆)₂ to be isolated in 40% yield. Complexation of Ir(III) was achieved through overnight heating of **4.7** and [Ir₂(ppy)₄Cl₂] dimer **3.7** in 1:1 CH₂Cl₂/EtOH at 55°C. After purification by preparative TLC and anion exchange, **Ir4.21·PF₆** was isolated in 67% yield (Scheme 4.19)



*Scheme 4.19 - Synthesis of transition metal benzimidazole complexes: Ru(II) based **Ru4.20·(PF₆)₂** and Ir(III) based **Ir4.21·PF₆**.*

Both metal complexes were characterised by ¹H and ¹⁹F NMR spectroscopy and high-resolution ESI mass spectrometry. Notable shifts were observed in the ¹H NMR spectrum of **Ir4.21·PF₆**, relative to that of the acyclic ligand, indicative of successful formation of the complex (Figure 4.17). The resonances for benzyl protons *b* and *b'* were split significantly, with the separation between the two peaks over 1.75 ppm, whilst two environments were also seen for protons *c* and *c'*. Similar shifts were observed in the ¹H NMR spectrum of **Ru4.20·(PF₆)₂**.

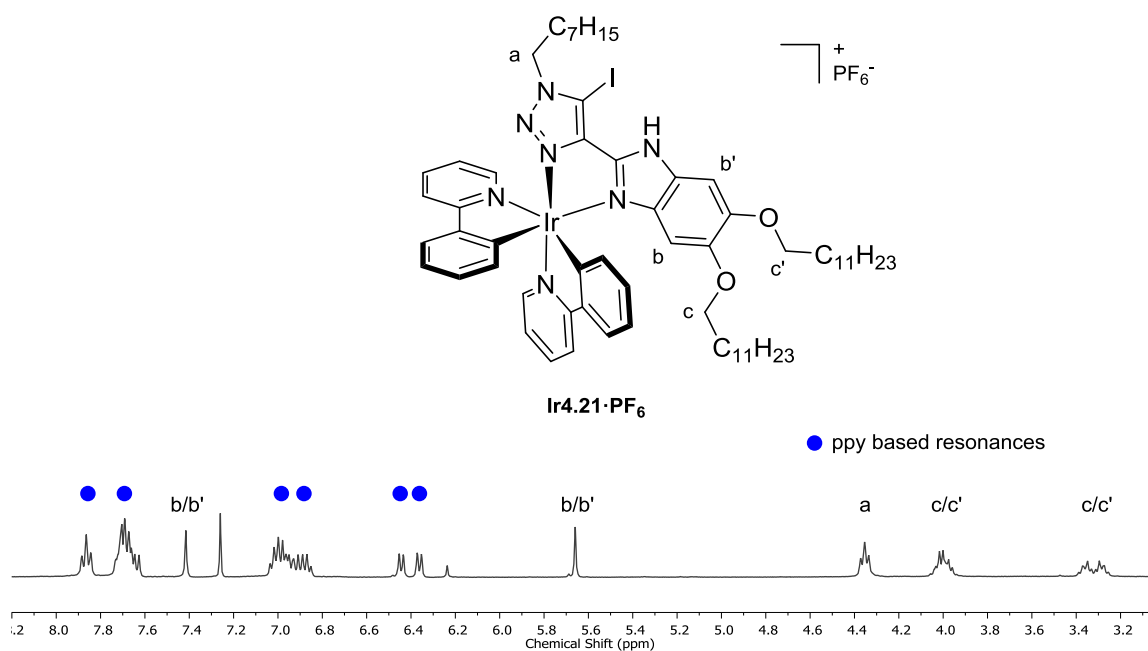


Figure 4.17 - Truncated ^1H NMR spectrum of **Ir4.21**· PF_6 (400 MHz, 298 K). Key proton resonances labelled.

4.4.2 Preliminary luminescence titration studies

Preliminary photophysical studies were performed with **Ru4.20**·(PF_6)₂ and **Ir4.21**· PF_6 in acetonitrile at 1×10^{-5} M. UV-vis experiments revealed MLCT absorbance bands in agreement with similar literature compounds.^{39,40} Furthermore, the luminescence emission spectra revealed that both receptors were notably emissive and these emission maxima were comparable to previously reported Ru(II) 2-2'-bipyridine and Ir(III) 2-phenylpyridine benzimidazole based metal complexes in acetonitrile (Table 4.1).^{37,41}

Table 4.1 – Photophysical data of transition metal complexes **Ru4.20·(PF₆)₂** and **Ir4.21·PF₆** (concentration = 1×10^{-5} M in CH₃CN at 298 K).

Complex	$\lambda_{\text{abs,MLCT}}$ (nm)	λ_{ex} (nm)	$\lambda_{\text{em,max}}$ (nm)
Ru4.20·(PF₆)₂	425	420	651
Ir4.21·PF₆	380	400	500

Preliminary chloride anion luminescence sensing experiments were performed through qualitative titration studies. The effect upon luminescence output following the addition of 100 equivalents of TBACl was monitored. A pronounced emission enhancement (76%) was observed in the case of **Ru4.20·(PF₆)₂**, together with a 10 nm bathochromic shift of the $\lambda_{\text{em,max}}$ (Figure 4.18a). A luminescence change upon chloride addition was also observed for **Ir4.21·PF₆**, with a modest increase of 6% (Figure 4.18b). These emission enhancements were ascribed to chloride binding increasing the rigidity of the host, thereby disfavours non-radiative decay processes.

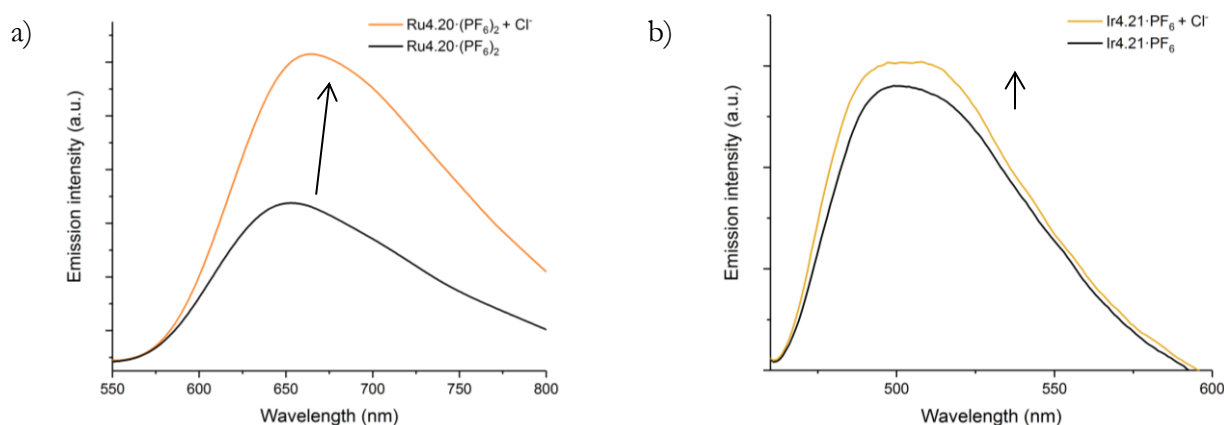


Figure 4.18 - Emission spectra of transition metal complexes a) **Ru4.20·(PF₆)₂** and b) **Ir4.21·PF₆** and their response to addition of 100 equivalents of chloride. Photophysical data calculated at 1×10^{-5} M in CH₃CN at 298 K.

In summary, the acyclic benzimidazole-iodotriazole motif **4.7** was found to be a suitable ligand for Ru(II) 2,2'-bipyridine and Ir(III) 2-phenylpyridine based transition metal complexes. Both **Ru4.20·(PF₆)₂** and **Ir4.21·PF₆** exhibited a notable enhancement in their emission maxima on addition of 100 equivalents of chloride. In future, neutral rotaxane **4.19** could undergo complexation with Ru(II) and Ir(III) to form an interlocked structure with anion sensing capabilities.

4.5 Conclusions and future work

The novel conjugated benzimidazole-iodotriazole motif has been exploited for XB anion recognition. Acyclic derivative **4.7** was found to be amenable to protonation or methylation to form benzimidazolium-iodotriazole compounds **4.7·HBF₄** and **4.8·Cl** with the latter demonstrated to form an interpenetrated assembly with an isophthalamide macrocycle in the presence of a chloride anion template.

Next, the benzimidazole-iodotriazole motif was incorporated into a naphthalimide containing axle component of a [2]rotaxane via a chloride anion template stoppering method. The rotaxane displayed a rare example of molecular motion dependent upon both the pH and the nature of the counter anion. Movement of the macrocycle along the axle could be monitored via a naked-eye colourimetric response. Whilst the non-protonated rotaxane **4.19** was yellow in solution, upon protonation with HCl there was an immediate loss of colour, attributed to translocation of the macrocycle from the naphthalimide axle station to the benzimidazolium-iodotriazole station. This dynamic shuttling process removed the charge transfer interactions between the macrocyclic hydroquinone functionalities and the naphthalimide group in the axle. This translocation was confirmed via differences in the two-dimensional ¹H-¹H ROESY NMR spectroscopy spectra of **4.19** and **4.19·HCl**. The change in

macrocycle position and protonation state was also characterised by UV-vis and fluorescence spectroscopy, with a clear change in rotaxane absorbance and emission when switching from the neutral rotaxane to the protonated analogue.

Protonation of **4.19** with HBF_4 suggested no co-conformational change via UV-vis spectroscopy. Importantly, chloride addition to $\mathbf{4.19} \cdot \text{HBF}_4$ induced noticeable changes in both the absorbance and emission spectrum of the rotaxane, suggesting macrocycle translocation to the benzimidazolium-iodotriazole station. Crucially, only when protonated with a coordinating halide acid did co-conformational change occur; i.e. the [2]rotaxane co-conformation was found to be dependent on both the pH and the nature of the counter anion (Figure 4.19). The requirement for both stimuli to be present to facilitate macrocycle translocation is akin to the behaviour of an AND molecular logic gate.^{42,43}

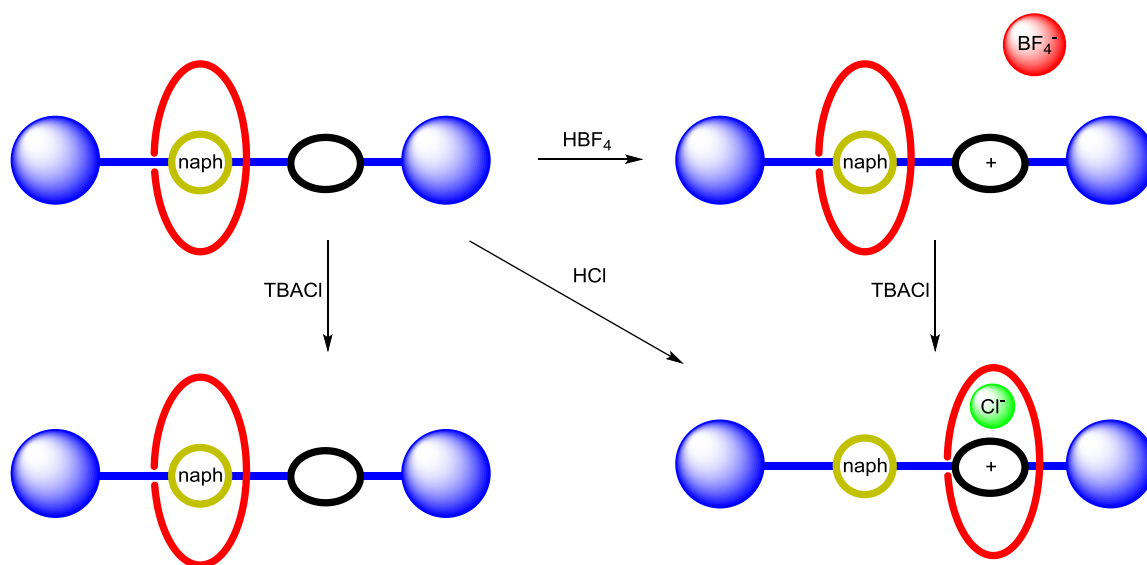


Figure 4.19 - Schematic outline of molecular switching exhibited by rotaxane **4.19**. Both protonation and chloride addition is required to induce macrocycle translocation.

The benzimidazole-iodotriazole motif has also been shown to act as a bidentate ligand for photoactive transition metal complexes. Future work will exploit this motif in order to coordinate such complexes to the axle or macrocycle component of dynamic rotaxanes

(Figure 4.20). The resulting metallo-rotaxanes will contain multiple spectroscopic probes for ratiometric anion sensing.

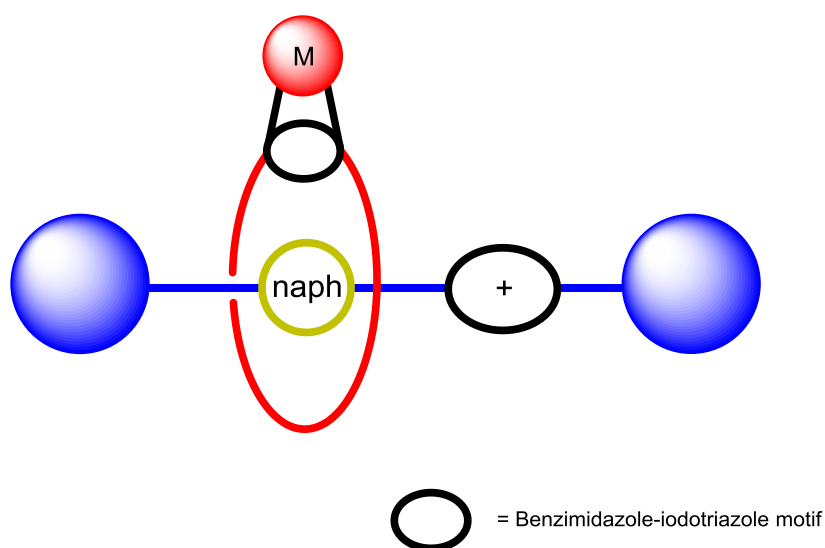


Figure 4.20 - Future target [2]rotaxane with transition metal complexed macrocycle component. *M* = transition metal complex.

4.6 References

1. V. Balzani, M. Clemente-León, A. Credi, B. Ferrer, M. Venturi, A. H. Flood and J. F. Stoddart, *Proc. Natl. Acad. Sci. U.S.A.*, 2006, **103**, 1178-1183.
2. F. Vögtle, W. M. Müller, U. Müller, M. Bauer and K. Rissanen, *Angew. Chem. Int. Ed.*, 1993, **32**, 1295-1297.
3. A. M. Brouwer, C. Frochot, F. G. Gatti, D. A. Leigh, L. C. Mottier, F. Paolucci, S. Roffia and G. W. H. Worpel, *Science*, 2001, **291**, 2124-2128.
4. P. Raiteri, G. Bussi, C. S. Cucinotta, A. Credi, J. F. Stoddart and M. Parrinello, *Angew. Chem. Int. Ed.*, 2008, **47**, 3536-3539.
5. P. Ashton, R. Ballardini, V. Balzani, A. Credi, K. R. Dress, E. Ishow, C. J. Kleverlaan, O. Kocian, J. A. Preece, N. Spencer, J. F. Stoddart, M. Venturi and S. Wenger, *Chem. Eur. J.*, 2000, **6**, 3558-3574.
6. F. Coutrot, C. Romuald and E. Busseron, *Org. Lett.*, 2008, **10**, 3741-3744.
7. A. V. Leontiev, C. J. Serpell, N. G. White and P. D. Beer, *Chem. Sci.*, 2011, **2**, 922-927.
8. R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419-4476.
9. H. Zhang, J. Hu and D.-H. Qu, *Org. Lett.*, 2012, **14**, 2334-2337.
10. T. A. Barendt, I. Rašović, M. A. Lebedeva, G. A. Farrow, A. Auty, D. Chekulaev, I. V. Sazanovich, J. A. Weinstein, K. Porfyrakis and P. D. Beer, *J. Am. Chem. Soc.*, 2018, **140**, 1924-1936.
11. J. J. Gassensmith, S. Matthys, J.-J. Lee, A. Wojcik, P. V. Kamat and B. D. Smith, *Chem. Eur. J.*, 2010, **16**, 2916-2921.

12. G. T. Spence, M. B. Pitak and P. D. Beer, *Chem. Eur. J.*, 2012, **18**, 7100-7108.
13. T. A. Barendt, A. Docker, I. Marques, V. Félix and P. D. Beer, *Angew. Chem. Int. Ed.*, 2016, **55**, 11069-11076.
14. M. A. Phillips, *J. Chem. Soc.*, 1928, 2393-2399
15. Salahuddin, M. Shaharyar and A. Mazumder, *Arab. J. Chem.*, 2017, **10**, 157-173.
16. D. T. Nannapaneni, A. V. Gupta, M. I. Reddy and R. C. Sarva, *J. Young Pharm.*, 2010, **2**, 273-279.
17. N. Singh and D. O. Jang, *Org. Lett.*, 2007, **9**, 1991-1994.
18. M. Yu, H. Lin, G. Zhao and H. Lin, *J. Mol. Recognit.*, 2007, **20**, 69-73.
19. C. Bhaumik, S. Das, D. Saha, S. Dutta and S. Baitalik, *Inorg. Chem.*, 2010, **49**, 5049-5062.
20. H. Sharma, H. J. Guadalupe, J. Narayanan, H. Hofeld, T. Pandiyan and N. Singh, *Anal. Methods*, 2013, **5**, 3880-3887.
21. S. Erbas-Cakmak, D. A. Leigh, C. T. McTernan and A. L. Nussbaumer, *Chem. Rev.*, 2015, **115**, 10081-10206.
22. K. Zhu, G. Baggi and S. J. Loeb, *Nat. Chem.*, 2018, **10**, 625-630.
23. G. Gholami, K. Zhu, G. Baggi, E. Schott, X. Zarate and S. J. Loeb, *Chem. Sci.*, 2017, **8**, 7718-7723.
24. V. N. Vukotic, K. Zhu, G. Baggi and S. J. Loeb, *Angew. Chem. Int. Ed.*, 2017, **56**, 6136-6141.
25. K. Bahrami, M. M. Khodaei and A. Nejati, *Green Chem.*, 2010, **12**, 1237-1241.
26. H. Sharghi, O. Asemani and R. Khalifeh, *Synth. Commun.*, 2008, **38**, 1128-1136.
27. K. A. Hope-Ross, P. A. Heiney and J. F. Kadla, *Can. J. Chem.*, 2010, **88**, 639-645.
28. M. M. G. Antonisse, B. H. M. Snellink-Ruël, I. Yigit, J. F. J. Engbersen and D. N. Reinhoudt, *J. Org. Chem.*, 1997, **62**, 9034-9038.
29. N. Noujeim, K. Zhu, V. N. Vukotic and S. J. Loeb, *Org. Lett.*, 2012, **14**, 2484-2487.
30. T. Tang, Y. Zhou, Y. Chen, M. Li, Y. Feng, C. Wang, S. Wang and X. Zhou, *Anal. Methods*, 2015, **7**, 2386-2390.
31. A. M. Agafontsev, T. A. Shumilova, P. A. Panchenko, S. Janz, O. A. Fedorova and E. A. Kataev, *Chem. Eur. J.*, 2016, **22**, 15069-15074.
32. M. Liu, J. Deng, C. Lai, Q. Chen, Q. Zhao, Y. Zhang, H. Li and S. Yao, *Talanta*, 2012, **100**, 229-238.
33. J. Catalan and J. Elguero, *Adv. Heterocycl. Chem.*, 1987, **41**, 187-274.
34. H. Xiao, M. Chen, G. Shi, L. Wang, H. Yin and C. Mei, *Res. Chem. Intermediat.*, 2010, **36**, 1021-1026.
35. M. E. Huston, E. U. Akkaya and A. W. Czarnik, *J. Am. Chem. Soc.*, 1989, **111**, 8735-8737.
36. G. S. Yellol, J. G. Yellol, V. B. Kenche, X. M. Liu, K. J. Barnham, A. Donaire, C. Janiak and J. Ruiz, *Inorg. Chem.*, 2015, **54**, 470-475.
37. J. Yeonah, C. D. Sunesh, R. K. Chitumalla, J. Jang and Y. Choe, *Org. Electronics*, 2018, **54**, 167-176.
38. S. Bhattacharyya, K. Purkait and A. Mukherjee, *Dalton Trans.*, 2017, **46**, 8539-8554.
39. Y. Kotani, A. Matsuda, M. Tatsumisago, T. Minami and M.-a. Haga, *J. Mater. Chem.*, 1999, **9**, 3041-3044.
40. K. Hasan, A. K. Bansal, I. D. W. Samuel, C. Roldán-Carmona, H. J. Bolink and E. Zysman-Colman, *Sci. Rep.*, 2015, **5**, 12325.
41. E. J. O'Reilly, L. Dennany, D. Griffith, F. Moser, T. E. Keyes and R. J. Forster, *Phys. Chem. Chem. Phys.*, 2011, **13**, 7095-7101.
42. S. Erbas-Cakmak, S. Kolemen, A. C. Sedgwick, T. Gunnlaugsson, T. D. James, J. Yoon and E. U. Akkaya, *Chem. Soc. Rev.*, 2018, **47**, 2228-2248.

43. M. A. Romero, R. J. Fernandes, A. J. Moro, N. Basílio and U. Pischel, *Chem. Commun.*, 2018, **54**, 13335-13338.

Chapter Five

Summary of conclusions

5 Summary of Conclusions

The aim of the work described in this thesis was to integrate halogen bond donor groups, specifically the iodotriazole motif, into a range of interlocked and transition metal based architectures for anion recognition and sensing. Each chapter has investigated a different strategy towards the construction of XB anion receptors.

Chapter Two focused on the incorporation of multiple XB donor groups into preorganised, interlocked host systems via a novel tetra-iodotriazole pyridinium motif. A monocationic tetra-iodotriazole [2]catenane was found to bind a range of anions, with selectivity for iodide, in a competitive aqueous-organic solvent, exhibiting significant $\text{I}^- > \text{SO}_4^{2-} \approx \text{Br}^- > \text{Cl}^-$ anion discrimination. Analogous monocationic and dicationic XB [2]rotaxanes were demonstrated to be superior anion hosts in comparison to the XB catenane. The monocationic rotaxane displayed a remarkable *circa* 40-fold selectivity for iodide over chloride (Figure 5.1), whilst the dicationic rotaxane bound each anion significantly more strongly as a result of increased electrostatic interactions.

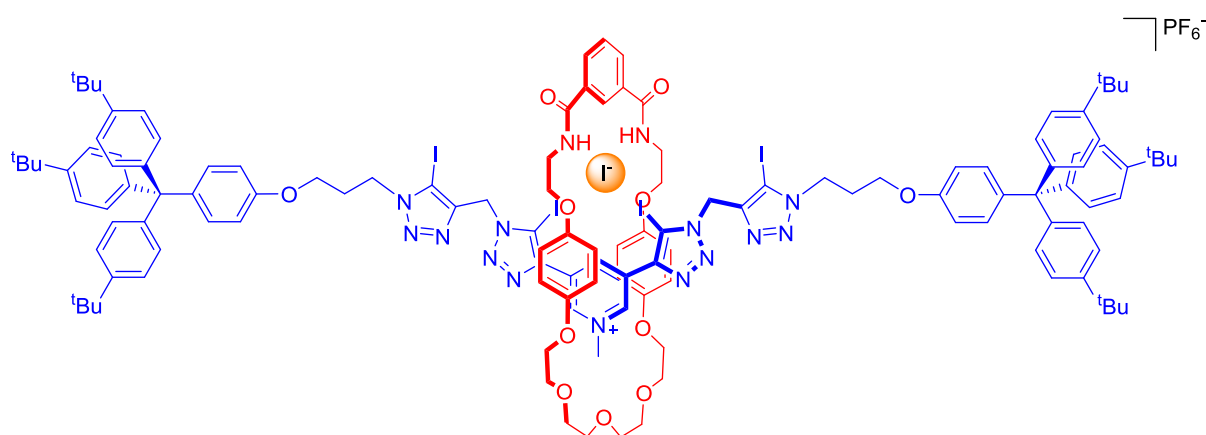


Figure 5.1 – Iodide selective monocationic tetra-iodotriazole [2]rotaxane reported in Chapter Two.

Chapter Three investigated the coordination of photoactive transition metal complexes by a bidentate methylene-spaced bis-iodotriazole motif. Acyclic ligands were prepared and chelated to Re(I), Ir(III), Ru(II) and Os(II) and the resulting transition metal based XB receptors were shown to bind chloride significantly more strongly than the HB counterpart. Luminescence spectroscopy demonstrated the Ir(III), Ru(II) and Os(II) XB receptors to be capable of sensing chloride in acetonitrile.

Bimetallic Ir(III) C₆₀ fullerene based XB and HB anion receptors were prepared and shown to sense anions via luminescence spectroscopy. Impressively, sulfate induced an enhancement in fluorescence intensity of >250% for both bimetallic hosts, postulated to be a consequence of a pincer-like motion of the arms of the receptors resulting in reduced PET quenching of the Ir(III) emission by the electron deficient fullerene (Figure 5.2).

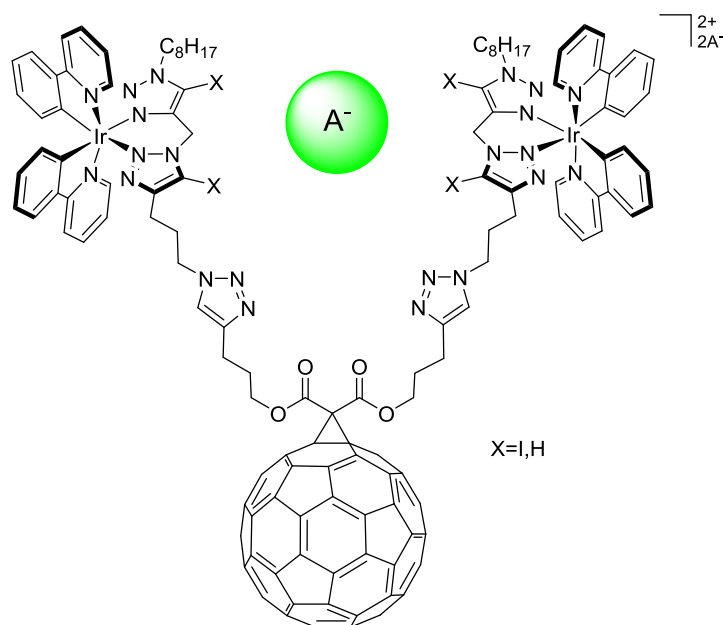


Figure 5.2 – Postulated anion binding mode of synthesised bimetallic fullerene hosts investigated in Chapter Three.

Chapter Four described a novel benzimidazole-iodotriazole motif that was exploited in the formation of a dynamic interlocked structure, as well as acting as a bidentate ligand for

photoactive transition metal complexes. Utilising a chloride anion template stopping approach, a [2]rotaxane was prepared via a CuAAC reaction between stopper alkyne and a protonated naphthalimide based benzimidazolium-iodotriazole chloride stopper azide in the presence of an isophthalamide macrocycle. The rotaxane displayed molecular motion dependent upon both the pH and the nature of the counter anion. Only upon protonation of the neutral rotaxane with HCl, or addition of chloride to the rotaxane protonated with the non-coordinating counter anion BF_4^- , was macrocycle translocation observed. This indicated the need for both stimuli to induce the motion and, therefore, the rotaxane acted as an AND molecular logic gate (Figure 5.3). The benzimidazole-iodotriazole motif was also found to chelate to photoactive Ru(II) and Ir(III) metal complexes to produce acyclic receptors that displayed a luminescence response upon anion addition.

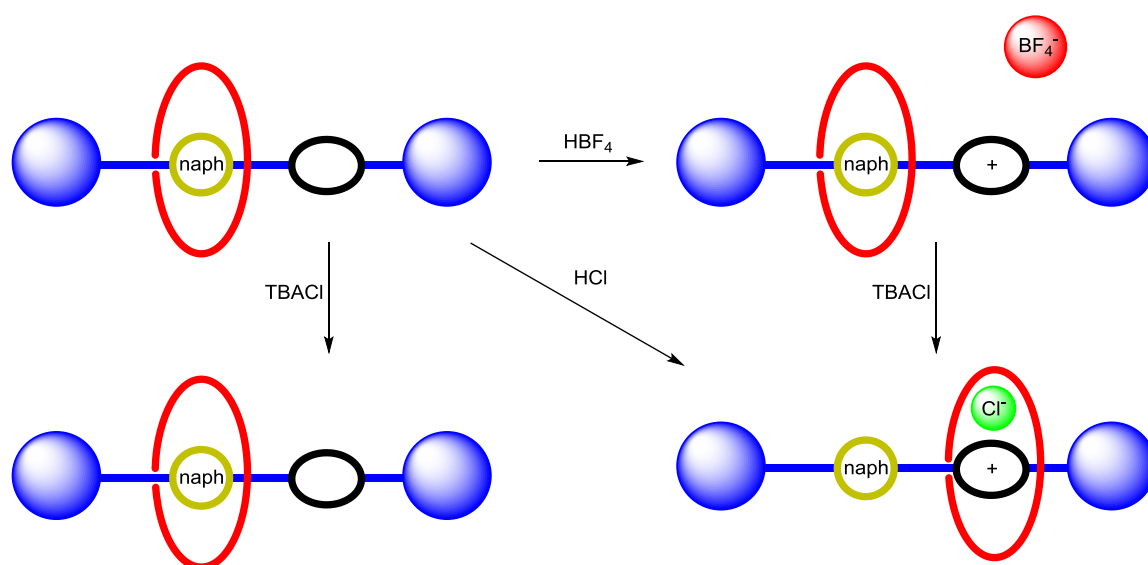


Figure 5.3 - Schematic outline of molecular switching exhibited by rotaxane presented in Chapter Four. Both protonation and chloride addition is required to induce macrocycle translocation.

In summary, this work has investigated different methods for building anion host structures based upon the halogen bond. The versatility of the iodotriazole motif has been exploited throughout this research: for formation of highly preorganised interlocked hosts, as a

transition metal ligand for charge-assisted halogen bonding, and for building a dynamic anion and pH responsive shuttle. In the future, the concepts outlined here could be further developed by using the halogen bond in tandem with other non-covalent interactions, such as chalcogen bonding, to create dynamic transition metal based interlocked host structures with unique anion recognition and sensing properties.

Chapter Six

Experimental

6 Experimental

6.1 General Remarks

6.1.1 Solvent and reagents

All commercial solvents and reagents were used as purchased, unless otherwise stated. Anhydrous solvents were degassed with N₂ and dried by passing them through an MBraun-800 column. Water was distilled and microfiltered using a Milli-Q Millipore machine. NEt₃ was distilled and stored over KOH pellets. Tetrabutylammonium (TBA) salts and [Cu(CH₃CN)₄][PF₆] were stored in a desiccator prior to use. Chromatography was performed using silica gel (particle size: 40-63 µm) or preparative TLC plates (20 x 20 cm, 1 cm silica thickness). Size exclusion chromatography was undertaken using Biobeads SX-1. Compound **2.9** was prepared and donated by Dr. Stuart Cornes.

6.1.2 Instrumental Methods

NMR spectra were recorded on Bruker AVIII HD Nanobay 400 MHz, Bruker AVIII 500 MHz and Bruker AVIII 500 MHz (with ¹³C cryoprobe) spectrometers. Spectra are all referenced to the residual solvent peak.¹ In the case of mixed solvent systems being used the spectra are referenced to the solvent component containing the most deuterium atoms. Electrospray mass spectrometry (ESI-MS) was performed using a Waters Micromass LCT spectrometer (low resolution) and Bruker microTOF spectrometer (high resolution). MALDI MS was recorded using a Waters MALDI Micro MX spectrometer. UV-vis absorption spectra were recorded on a PTG60 U spectrophotometer using a Hellma Quartz

cuvette of pathlength 10 mm at 298 K. Fluorescence emission spectra were recorded on a Horiba Fluorolog 3 spectrophotometer using the same cuvette at 298 K.

6.1.3 ^1H NMR anion binding titration protocol

^1H NMR titration experiments were performed on a Bruker AVIII 500 MHz spectrometer. In each experiment, a solution of the tetrabutylammonium (TBA) salt of the anion was added to a solution of the receptor molecule in the same solvent at 298 K (TBA was selected as the counter-cation due to its non-coordinating nature). A solution of the salt was added to 0.50 mL of solution of receptor at stated concentration, where 10.0 μL of salt solution corresponded to 1.0 equivalent. Aliquots of the salt were added in 0, 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. In all cases the bound and unbound species were found to be in fast exchange on the NMR timescale.

The values of the observed chemical shift and concentration of anion were entered into the WinEQNMR2² computer programme for each titration point. An estimation of the association constant and the limiting chemical shifts were required as input parameters for WINEQNMR2. These parameters were refined using nonlinear least-squares analysis to obtain the best fit between empirical and calculated chemical shifts based on a 1:1 or 1:2 binding stoichiometry (where appropriate). The input parameters were varied until convergence of the best fit values of the binding constants and their errors were obtained. WINEQNMR2 provides an estimate of the standard error of measurement, in each case this was found to be <10% of the absolute value of the association constant quoted. These errors were taken into account when comparing K_a values.

6.1.4 Fluorescence anion binding titration protocol

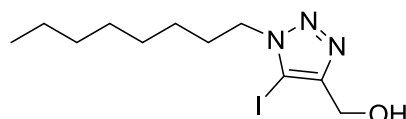
Fluorescence emission spectra were recorded on a Horiba Fluorolog 3 spectrophotometer using a Hellma Quartz cuvette of pathlength 10 mm at 298 K. In each case, samples were diluted to a concentration of 1×10^{-5} M. For titration experiments, a starting volume of 0.8 mL was used at 1×10^{-5} M and up to the stated number of equivalents of each anion was added as the TBA salt. Importantly, the concentration of the host was maintained throughout the experiments by preparing the anion stock solution from the host stock solution.

The percentage change in fluorescence emission ($\Delta\%$) in Chapters Three and Four were calculated from the sum of each point of the titration curves at 0 equivalents and at the end of the experiment and calculating the increase or decrease as a percentage of the starting value. The measurement of the global change over the spectrum was used as it was considered more accurate than choosing a single wavelength since it accounted for chromatic shifting.

6.2 Synthesis and characterisation of novel compounds

6.2.1 Chapter Two

Iodotriazole alcohol 2.5

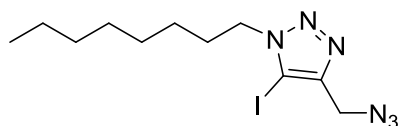


To a solution of azide **2.3** (1 g, 6.45 mmol) in dry THF (10 mL) was added NaI (3.56 g, 24.6 mmol) and $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (4.54 g, 12.3 mmol). The reaction mixture was stirred for 5 minutes in the dark. TBTA (cat.) was added before addition of DBU (0.93 g, 6.08 mmol) in

CH₃CN (10 mL) dropwise. Finally, propargyl alcohol (0.344 g, 6.14 mmol) was added and the reaction stirred for 16 hours. The solvent was removed *in vacuo* and the crude product taken up in CH₂Cl₂ (50 mL) and washed with EDTA/NH₄OH solution (2x30 mL) and brine (2x30 mL). The combined organics were dried over MgSO₄ and concentrated *in vacuo*. Purification was achieved by column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) to afford **2.5** as an off-white powder (1.437 g, 69%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 4.72 (d, J = 4.9 Hz, 2H, OH-CH₂), 4.36 (t, J = 7.4 Hz, 2H, N-CH₂), 2.37 (d, J = 6.8 Hz, 1H, -OH), 1.85 – 1.93 (m, 2H, N-CH₂-CH₂), 1.23 – 1.39 (m, 10H, 5xCH₂), 0.83 – 0.92 (m, 3H, -CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 150.71, 78.48, 56.77, 50.94, 31.85, 30.06, 29.17, 29.08, 26.52, 22.75, 14.22; **HRMS (ESI):** m/z 338.07201 [M+H]⁺ ([C₁₁H₂₀IN₃O·H]⁺ calc. 338.07238).

Iodotriazole azide **2.6**

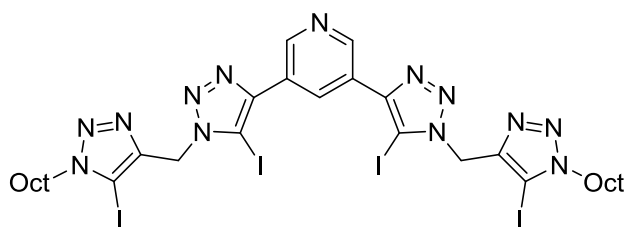


Alcohol **2.5** (1.2 g, 3.56 mmol) and NEt₃ (1.04 mL, 7.48 mmol) were dissolved in dry CH₂Cl₂ (10 mL) and stirred for 5 minutes at 0°C. MsCl (0.33 mL, 4.27 mmol) in dry CH₂Cl₂ (5 mL) was added dropwise and the reaction stirred for 1 hour at RT. The reaction mixture was washed with water (2x10 mL), 1M HCl_(aq) (3x10 mL) and brine (3x10 mL) and dried over MgSO₄. The solvent was removed *in vacuo* to afford a yellow oil which was used without further purification. The crude oil (1.48 g, 3.56 mmol) and NaN₃ (0.75 g, 14.2 mmol) were dissolved in dry, degassed DMSO (20 mL). The mixture was heated at 85°C for 16 hours under N₂. The mixture was cooled to RT and partitioned between water (15 mL) and EtOAc (15 mL). The aqueous layer was washed with EtOAc (2x15 mL). The combined organics

were washed with brine (3x15 mL), dried over MgSO_4 and concentrated *in vacuo* to afford a colourless oil (0.935 g, 89%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 4.43 (s, 2H, $\text{N}_3\text{-CH}_2$), 4.38 (t, $J = 7.3$ Hz, 2H, NH-CH_2), 1.87 - 1.96 (m, 2H, $\text{NH-CH}_2\text{-CH}_2$), 1.24 - 1.38 (m, 10H, $5\times\text{CH}_2$), 0.84 - 0.92 (m, 3H, $-\text{CH}_3$); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 146.72, 79.77, 51.18, 45.75, 31.84, 30.01, 29.17, 29.07, 26.50, 22.75, 14.22; **HRMS (ESI)**: m/z 363.0784 $[\text{M}+\text{H}]^+$ ($[\text{C}_{11}\text{H}_{19}\text{N}_6\text{I}\cdot\text{H}]^+$ calc. 363.0794).

Tetra-iodotriazole pyridine **2.7**

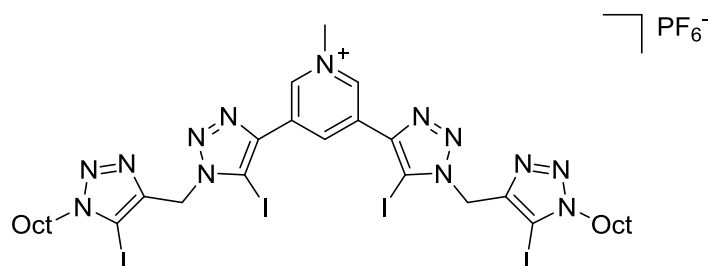


$[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ (4.68 mg, 0.0125 mmol) and TBTA (6.65 mg, 0.0125 mmol) were added to a dry, degassed mixture of THF (1.5 mL) and CH_2Cl_2 (1.5 mL). Azide **2.5** (100 mg, 0.276 mmol) and pyridine bis-iodoalkyne **2.3** (47.6 mg, 0.125 mmol) were added and the reaction stirred for 16 hours at RT. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with EDTA/ NH_4OH solution (2x15 mL) and water (2x15 mL). The combined organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved by preparative TLC (silica, 97.5:2.5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ x2) to afford **2.7** as a white powder (70.0 mg, 51%).

^1H NMR (400 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) 9.12 (d, $J = 2.3$ Hz, 2H, PyrH), 8.84 (d, $J = 2.3$ Hz, 1H, PyrH), 5.75 (s, 4H, methylene CH_2), 4.38 (t, $J = 7.6$ Hz, 4H, N-CH_2), 1.84 - 1.93 (m, 4H, $\text{NH-CH}_2\text{-CH}_2$), 1.17 - 1.36 (m, 20H, CH_2), 0.80 - 0.86 (m, 6H, $-\text{CH}_3$). **^{13}C NMR** (101 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) 147.91, 147.49, 145.17, 133.89, 127.34,

51.60, 47.31, 32.16, 30.29, 29.49, 29.36, 26.78, 23.03, 14.25. **HRMS (ESI):** m/z 1103.98576 $[M+H]^+$ ($[C_{31}H_{41}I_4N_{13}\cdot H]^+$ calc. 1103.98594).

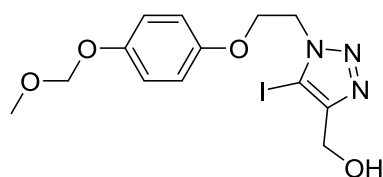
Tetra-iodotriazole acyclic receptor **2.8**·PF₆



CH₃I (0.3 mL) was added to a stirred solution of **2.6** (70 mg, 0.0635 mmol) in 9:1 CH₂Cl₂/CH₃OH (3 mL). The reaction was stirred for 16 hours. The solvent was removed *in vacuo* and purification was achieved by preparative TLC (silica, 95:5 CH₂Cl₂/CH₃OH x2) to afford **2.7** as a white powder (61.9 mg, 79%).

¹H NMR (400 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 9.69 (d, J = 1.7 Hz, 1H, int. PyrH), 9.37 (d, J = 1.7 Hz, 2H, ext. PyrH), 5.71 (s, 4H, methylene CH₂), 4.34 (t, J = 7.3 Hz, 4H, N-CH₂), 1.78 – 1.87 (m, 4H, NH-CH₂-CH₂), 1.15 – 1.31 (m, 20H, CH₂), 0.74 – 0.83 (m, 6H, -CH₃). **¹³C NMR** (101 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 144.42, 143.02, 141.63, 136.41, 131.96, 82.58, 51.02, 46.81, 31.57, 29.68, 28.89, 28.76, 26.16, 22.42, 13.61. **¹⁹F NMR** (377 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) -74.07 (d, J = 708.8 Hz, PF₆). **HRMS (ESI):** m/z 1118.00067 $[M+H]^+$ ($[C_{11}H_{19}N_6I\cdot H]^+$ calc. 1118.00159).

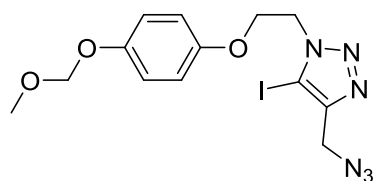
MOM-protected iodotriazole alcohol **2.13**



To a solution of NaI (1.05 g, 7.24 mmol) and $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (1.34 g, 2.62 mmol) in dry THF (5 mL) was added azide **2.12** (0.422 g, 1.89 mmol). The mixture was stirred for 5 minutes in the dark. TBTA (cat.), DBU (0.26 mL, 1.79 mmol) in dry CH_3CN (5 mL) and finally propargyl alcohol (0.104 mL, 1.81 mmol) were added and the reaction was stirred for 16 hours in the dark. The solvent was removed *in vacuo* and the residue was taken up in CH_2Cl_2 (40 mL). The organics were washed with EDTA/ NH_4OH solution (3x15 mL), H_2O (15 mL) and brine (15 mL), dried over MgSO_4 and the solvent removed *in vacuo*. The crude product was purified via column chromatography (silica, 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **2.13** as a white solid (0.642 g, 88%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 6.92 – 6.83 (m, 2H, hydroquinone *ArH*), 6.78 – 6.66 (m, 2H, hydroquinone *ArH*), 5.02 (s, 2H, O- CH_2 -O), 4.63 – 4.71 (m, 4H, O- CH_2 - CH_2 & C- CH_2 -OH), 4.30 (t, J = 5.6 Hz, 2H, N- CH_2), 3.46 (s, 3H, - CH_3), 2.54 (t, J = 6.2 Hz, 1H, -OH); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 153.02, 152.02, 150.86, 117.74, 115.65, 95.29, 80.08, 66.78, 56.71, 56.01, 49.88; **MS (ESI)**: m/z 428.0 $[\text{M}+\text{Na}]^+$ ($[\text{C}_{13}\text{H}_{16}\text{IN}_3\text{O}_4 \cdot \text{Na}]^+$ calc. 428.0).

MOM-protected iodotriazole azide **2.14**

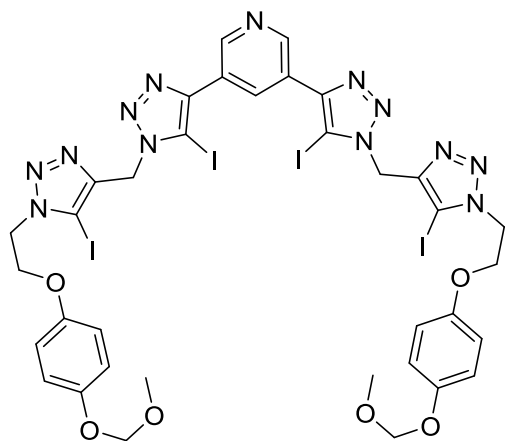


Alcohol **2.13** (0.496 g, 1.22 mmol) and NEt_3 (0.358 mL, 2.57 mmol) were added to dry CH_2Cl_2 (5 mL) and stirred for 5 minutes at 0°C . MsCl (0.142 mL, 1.84 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and added dropwise and the reaction stirred for 3 hours at RT. The reaction mixture was washed with water (2x10 mL), 1M $\text{HCl}_{(\text{aq})}$ (3x10 mL) and brine (3x10 mL) and dried over MgSO_4 . The solvent was removed *in vacuo* to afford a yellow oil which was used without further purification. The crude product was dissolved in dry, degassed

DMSO (15 mL) and NaN_3 (0.317 g, 4.88 mmol) was added. The reaction was stirred at 85°C for 16 hours. After cooling to RT, the reaction was quenched with H_2O (120 mL) and extracted into EtOAc (50 mL). The organics were washed with brine (2x20 mL), dried over MgSO_4 and concentrated *in vacuo*. The crude product was purified via column chromatography (silica, 98:2 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **2.14** as a white powder (0.371 g, 70%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 6.95 (d, $J = 9.1$ Hz, 2H, hydroquinone ArH), 6.78 (d, $J = 9.1$ Hz, 2H, hydroquinone ArH), 5.09 (s, 2H, O- CH_2 -O), 4.76 (t, $J = 5.6$ Hz, 2H, O- CH_2 - CH_2), 4.45 (s, 2H, N_3 - CH_2), 4.39 (t, $J = 5.6$ Hz, 2H, N- CH_2), 3.46 (s, 3H, - CH_3); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 153.01, 152.11, 117.75, 115.69, 95.31, 81.42, 66.85, 56.04, 50.14, 45.77, 41.18; **MS (ESI)**: m/z 453.0 $[\text{M}+\text{Na}]^+$ ($[\text{C}_{13}\text{H}_{15}\text{IN}_6\text{O}_3\cdot\text{Na}]^+$ calc. 453.0).

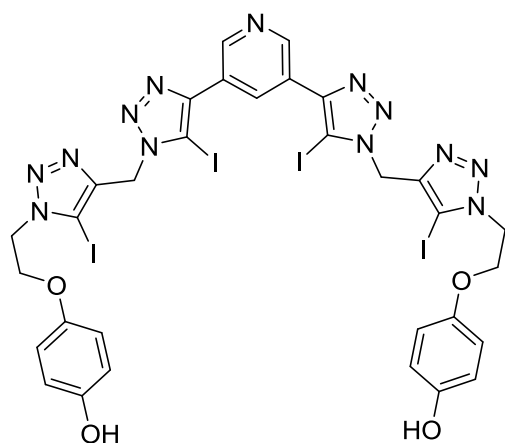
MOM-protected tetra-iodotriazole pyridine **2.15**



$[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ (7.91 mg, 0.021 mmol) and TBTA (11 mg, 0.021 mmol) were added to a dry, degassed mixture of THF (1.5 mL) and CH_2Cl_2 (1.5 mL). Azide **2.14** (0.200 g, 0.465 mmol) and pyridine bis-iodoalkyne **2.2** (80 mg, 0.211 mmol) were added and the reaction stirred for 16 hours at RT. The white precipitate that had formed was collected by filtration and washed with H_2O (5 mL), CH_3OH (5 mL) and Et_2O (5 mL) to afford a pure white powder (0.248 g, 77%).

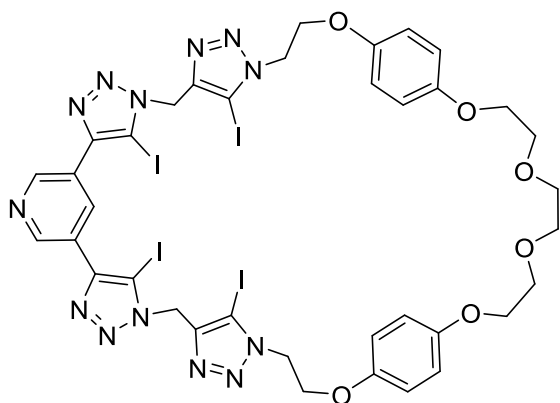
¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm) 9.14 (d, J = 2.2 Hz, 2H, PyrH), 8.82 (s, 1H, PyrH), 6.88 - 6.95 (m, 4H, hydroquinone ArH), 6.78 - 6.85 (m, 4H, hydroquinone ArH), 5.77 (s, 4H, methylene CH₂), 5.07 (s, 4H, O-CH₂-O), 4.75 (t, J = 5.1 Hz, 4H, O-CH₂-CH₂), 4.37 (t, J = 5.2 Hz, 4H, N-CH₂), 3.32 (s, 6H, -CH₃); solubility too low to obtain ¹³C NMR; not seen via ESI MS.

Tetra-iodotriazole phenol **2.16**



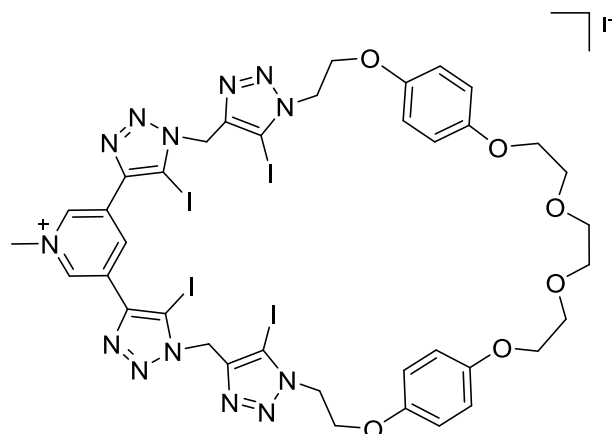
Acetyl chloride (0.172 mL, 2.42 mmol) was stirred at 0°C in CH₃OH (5 mL) for 5 minutes. The solution was allowed to warm to RT and stirred for a further 15 minutes before addition of a solution of tetra-iodotriazole **2.15** (100 mg, 0.081 mmol) in CH₂Cl₂ (5 mL). The solution was stirred for 6 hours before removal of the solvent *in vacuo* to afford **2.16** as a white powder (127 mg, quant.).

¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm) 9.15 (d, J = 2.1 Hz, 2H, ArH), 8.85 (t, J = 2.2 Hz, 1H, ArH), 6.68 - 6.73 (m, 4H, hydroquinone ArH), 6.61 - 6.66 (m, 4H, hydroquinone ArH), 5.77 (s, 4H, methylene CH₂), 4.72 (t, J = 5.2 Hz, 4H, O-CH₂-CH₂), 4.31 (t, J = 5.1 Hz, 4H, N-CH₂); **¹³C NMR** (126 MHz, DMSO-*d*₆) δ (ppm) 151.63, 150.57, 146.97, 145.93, 144.82, 115.74, 115.70, 85.86, 83.36, 66.68, 49.74, 46.57, 31.98, 31.98; **HRMS (ESI):** m/z 1151.83899 [M+H]⁺ for [(C₃₁H₂₅I₄N₁₃O₄·H)]⁺ calc. 1151.84039.

Tetra-iodotriazole pyridine macrocycle 2.18

Bis-alcohol **2.16** (93.2 mg, 0.0809 mmol), triethylene glycol di(*p*-toluenesulfonate) (37.1 mg, 0.0809 mmol) and Cs₂CO₃ (0.106 g, 0.324 mmol) were dissolved in dry, degassed DMF (20 mL) and the reaction was stirred at 70°C for 16 hours. The solvent was removed *in vacuo* and the residue taken up in CHCl₃ (30 mL) whereupon it was washed with H₂O (20 mL), dried and concentrated. Purification was achieved via preparative TLC (silica, 95:5 CH₂Cl₂/CH₃OH x2) to afford **2.18** as an off-white powder (29.7 mg, 29%).

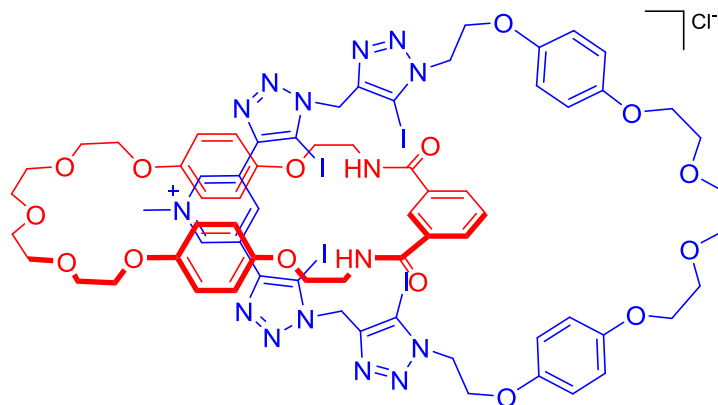
¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.15 (s, 2H, PyrH), 8.74 (s, 1H, PyrH), 6.67 – 6.74 (m, 4H, hydroquinone ArH), 6.58 – 6.66 (m, 4H, hydroquinone ArH), 5.72 (s, 4H, methylene CH₂), 4.69 (t, *J* = 5.4 Hz, 4H, O-CH₂-CH₂), 4.30 (t, *J* = 5.3 Hz, 4H, N-CH₂), 3.96 (t, *J* = 4.8 Hz, 4H, CH₂), 3.72 (t, *J* = 4.8 Hz, 4H, CH₂), 3.62 (s, 4H, CH₂). **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 152.57, 150.94, 147.03, 143.62, 132.02, 114.69, 114.61, 80.58, 69.86, 68.79, 67.08, 65.86, 52.40, 49.02, 45.81; **HRMS (ESI):** *m/z* 1265.90955 [M+H]⁺ ([C₃₇H₃₅I₄N₁₃O₆·H]⁺ calc. 1265.90847).

Tetra-iodotriazole pyridinium macrocycle **2.19·I**

CH₃I (0.6 mL) was added to a solution of macrocycle **2.18** (70 mg, 0.0553 mmol) in 9:1 CH₂Cl₂/CH₃OH (3 mL). The reaction was stirred for 16 hours. The solvent was removed *in vacuo* to afford **2.19** as a white powder (70.8 mg, quant.).

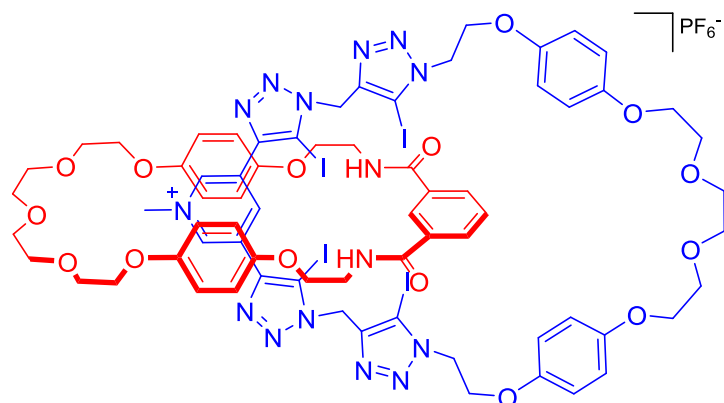
¹H NMR (400 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 9.84 (s, 1H, PyrH), 9.30 (s, 2H, PyrH), 6.56 – 6.69 (m, 8H, hydroquinone, ArH), 5.69 (s, 4H, methylene CH₂), 4.66 (d, *J* = 5.6 Hz, 4H, O-CH₂-CH₂-N), 4.53 (s, 3H, N⁺-CH₃), 4.28 (t, *J* = 5.6 Hz, 4H, O-CH₂-CH₂-N), 3.93 (t, *J* = 4.7 Hz, 4H, CH₂), 3.69 (t, *J* = 4.8 Hz, 4H, CH₂), 3.60 (s, 4H, CH₂); **¹³C NMR** (126 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 163.05, 153.06, 141.06, 132.05, 115.52, 115.37, 71.09, 70.42, 69.54, 67.81, 66.51, 36.31, 31.06, 29.35, 0.58; **HRMS (ESI):** *m/z* 1279.91999 [M+H]⁺ ([C₃₈H₃₈I₄N₁₃O₆·H]⁺ calc. 1279.92412).

Monocationic tetra-iodotriazole catenane **2.23·Cl**



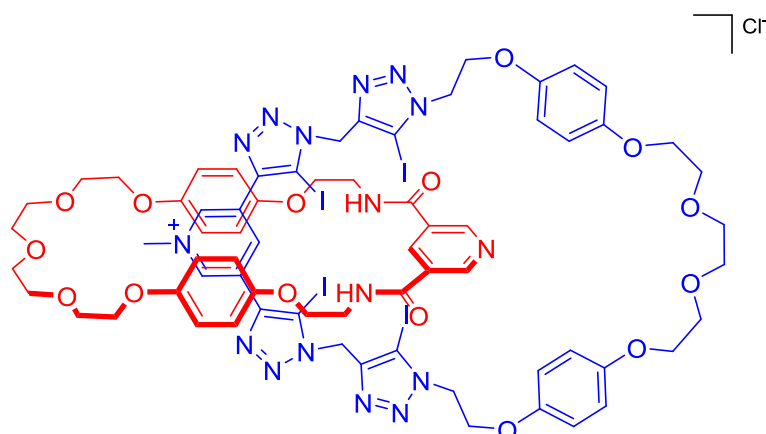
Macrocycle **2.19** (70.8 mg, 0.0553 mmol) and bis-amine **2.22** (77.1 mg, 0.166 mmol) were dissolved in dry CH_2Cl_2 (11 mL) and stirred for 5 minutes under N_2 . NEt_3 (50.1 μL , 0.0360 mmol) was added, followed immediately by isophthaloyl dichloride (33.6 mg, 0.166 mmol) in dry CH_2Cl_2 (1 mL) and the resulting solution stirred under N_2 for 16 hours at RT. The solution was washed with 10% $\text{HCl}_{(\text{aq})}$ (2x20 mL) and H_2O (2x20 mL). The organic phase was dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via preparative TLC (97:3 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ & 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to give **2.23·Cl** as a white solid (41.1 mg, 40%).

^1H NMR (500 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) 9.37 (s, 2H, ext. PyrH), 8.85 (s, 1H, int. ArH), 8.20 (s, 1H, int. PyrH), 7.91 (d, $J = 7.8$ Hz, 2H, ext. ArH), 7.49 (br. s, 2H, NH), 7.36 (t, $J = 7.8$ Hz, 1H, ext. ArH), 6.64 – 6.70 (m, 8H, pyr. macro. hydroquinone ArH), 6.11 (d, $J = 8.7$ Hz, 4H, isophthal. macro. hydroquinone ArH), 5.82 (d, $J = 8.7$ Hz, 4H, isophthal. macro. hydroquinone ArH), 5.52 (s, 4H, methylene CH_2), 4.78 (t, $J = 5.2$ Hz, 4H, O- CH_2 - CH_2 -N), 4.57 (s, 3H, N^+ - CH_3), 4.36 (t, $J = 5.1$ Hz, 4H, N- CH_2 - CH_2 -O), 3.54 – 4.01 (m, 36H, CH_2); **^{13}C NMR** (101 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) 167.29, 153.54, 152.83, 151.86, 144.70, 142.58, 131.69, 128.97, 115.72, 115.63, 115.44, 115.15, 114.32, 70.81, 70.05, 69.75, 68.10, 67.97, 67.68, 66.88, 66.77, 65.86, 50.08, 46.39, 40.06. **HRMS (ESI):** m/z 1874.17984 $[\text{M}]^+$ ($[\text{C}_{70}\text{H}_{76}\text{I}_4\text{N}_{15}\text{O}_{15}]^+$ calc. 1874.18185).

Monocationic tetra-iodotriazole catenane 2.23·PF₆

2.23·Cl (40.0 mg, 0.0209 mmol) was taken up in CHCl₃ (30 mL) and washed with 0.1 M NH₄PF_{6(aq)} (8x15 mL) and H₂O (2x15 mL). The organics were dried and the solvent removed *in vacuo* to afford **2.23·PF₆** as a white powder (38.1 mg, 90%).

¹H NMR (500 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 9.19 (s, 2H, ext. PyrH), 8.78 (s, 1H, int. ArH), 8.51 (s, 1H, int. PyrH), 8.11 (d, *J* = 7.9 Hz, 2H, ext. ArH), 7.49 (t, *J* = 7.9 Hz, 1H, ext. ArH), 6.63 – 6.74 (m, 8H, pyr. macro. hydroquinone ArH), 6.12 (d, *J* = 8.3 Hz, 4H, isophthal. macro. hydroquinone ArH), 5.93 (d, *J* = 8.3 Hz, 4H, isophthal. macro. hydroquinone ArH), 5.64 (s, 4H, methylene CH₂), 4.74 (t, *J* = 5.4 Hz, 4H, O-CH₂-CH₂-N), 4.59 (s, 3H, N⁺-CH₃), 4.35 (t, *J* = 5.5 Hz, 4H, N-CH₂-CH₂-O), 3.48 – 4.08 (m, 36H, CH₂); **¹³C NMR** (126 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 154.10, 153.48, 152.88, 145.64, 143.26, 135.27, 131.77, 130.96, 116.53, 116.20, 116.10, 115.43, 114.93, 71.53, 71.41, 71.23, 70.61, 70.31, 68.57, 68.30, 67.63, 50.86, 46.78, 40.62; **¹⁹F NMR** (377 MHz, 500 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) -71.35 (d, *J* = 716.3 Hz, PF₆).

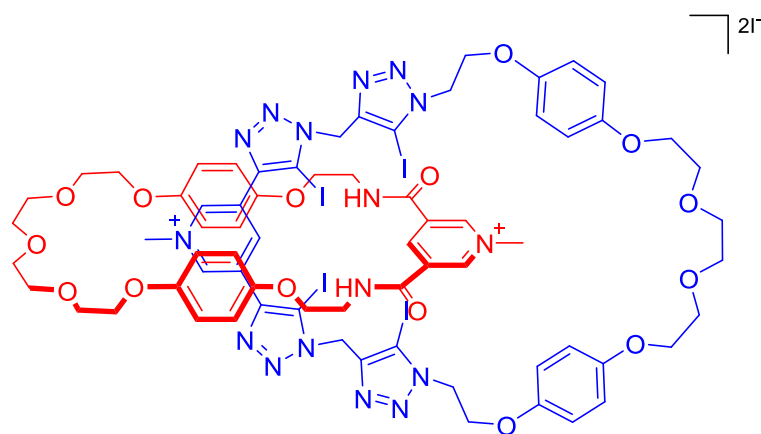
Tetra-iodotriazole catenane 2.25·Cl

Macrocycle **2.19** (25 mg, 0.0178 mmol) and bis-amine **2.22** (27.2 mg, 0.0533 mmol) were dissolved in dry CH_2Cl_2 (4 mL) and stirred for 5 minutes under N_2 . NEt_3 (20.4 μL , 0.1066 mmol) was added, followed immediately by bis-acid chloride **2.24** (12.0 mg, 0.0533 mmol) in dry CH_2Cl_2 (1 mL) and the resulting solution stirred under N_2 for 16 hours at RT. The solution was washed with 10% $\text{HCl}_{(\text{aq})}$ (2x20 mL) and H_2O (2x20 mL). The organic phase was dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via preparative TLC (97:3 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ & 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **2.25·Cl** as a white solid (7.83 mg, 22%).

^1H NMR (500 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) 9.36 (s, 2H, triazole macro. ext. PyrH), 9.08 (s, 2H, amide macro. ext. PyrH), 9.06 (s, 1H, amide. macro. int. PyrH), 8.27 (s, 1H, triazole macro. int. PyrH), 6.65 – 6.85 (m, 8H, triazole macro. hydroquinone ArH), 6.05 – 6.09 (m, 4H, amide macro. hydroquinone ArH), 5.84 – 5.87 (m, 4H, amide macro. hydroquinone ArH), 5.67 (s, 4H, methylene CH_2), 4.80 (t, $J = 5.1$ Hz, 4H, O- $\text{CH}_2\text{-CH}_2\text{-N}$), 4.60 (s, 3H, $\text{N}^+\text{-CH}_3$), 4.37 (t, $J = 5.1$ Hz, 4H, N- $\text{CH}_2\text{-CH}_2\text{-O}$), 3.57 – 4.14 (m, 36H, CH_2); **^{13}C NMR** (126 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) 167.01, 154.06, 153.87, 152.84, 152.48, 145.58, 143.29, 135.06, 134.76, 130.96, 116.43, 116.25, 116.21, 116.11, 115.36, 114.98, 71.52,

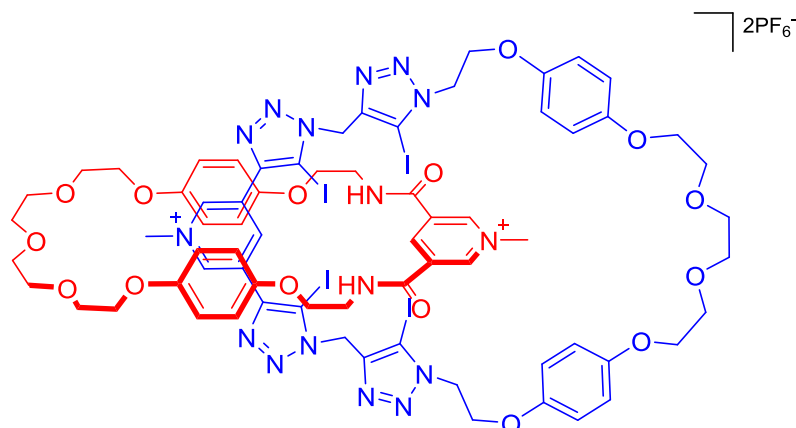
71.39, 71.27, 71.12, 70.61, 70.33, 68.66, 68.56, 67.56, 50.87, 46.79, 40.73, 40.51; **HRMS** (**ESI**): m/z 1875.17128 $[M]^+$ ($[C_{69}H_{75}I_4N_{16}O_{15}]^+$ calc. 1875.17710).

Dicationic tetra-iodotriazole catenane 2.26•(I)₂



CH₃I (0.1 mL) was added to a stirred solution of **2.25•Cl** (5 mg, 0.0267 mmol) in 9:1 CH₂Cl₂/CH₃OH (1 mL). The reaction was stirred for 2 days. The solvent was removed *in vacuo* and purification was achieved by preparative TLC (silica, 94:6 CH₂Cl₂/CH₃OH x3) to afford **2.26•(I)₂** as a white powder (3.3 mg, 63%).

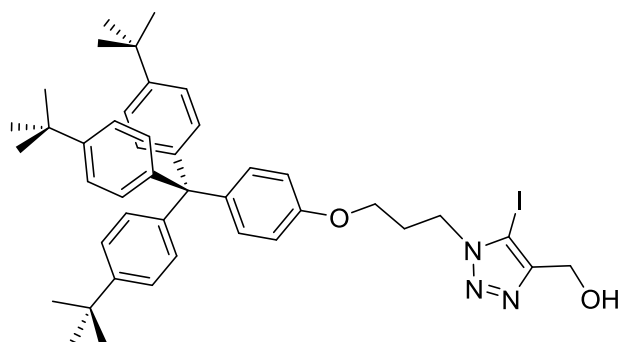
¹H NMR (500 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 9.71 (s, 1H, amide macro. int. PyrH), 9.42 (s, 2H, amide macro. ext. PyrH), 9.23 (s, 2H, triazole macro. ext. PyrH), 8.01 (s, 1H, triazole macro. int. PyrH), 6.53 – 6.61 (m, 8H, triazole macro. hydroquinone ArH), 6.02 (d, J = 8.6 Hz, 4H, amide macro. hydroquinone ArH), 5.79 (d, J = 8.6 Hz, 4H, amide macro. hydroquinone ArH), 5.74 (s, 4H, methylene CH₂), 4.70 (t, J = 5.3 Hz, 4H, O-CH₂-CH₂-N), 4.45 (s, 3H, N⁺-CH₃), 4.34 (t, J = 5.2 Hz, 4H, N-CH₂-CH₂-O), 3.63 (s, 3H, N⁺-CH₃), 3.16 – 4.11 (m, 36H, CH₂); **¹³C NMR** (126 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 161.66, 153.12, 152.45, 152.13, 151.85, 147.08, 144.93, 143.06, 134.52, 130.15, 115.99, 115.45, 114.74, 114.28, 70.94, 70.63, 69.92, 69.79, 68.02, 67.56, 66.65, 65.78, 40.45, 39.77, 29.52, 16.55, 16.39, 16.24; **HRMS (ESI)**: m/z 945.09827 $[M]^{2+}$ ($[C_{70}H_{78}I_4N_{16}O_{15}]^{2+}$ calc. 945.10002).

Dicationic tetra-iodotriazole catenane 2.26•(PF₆)₂

2.26•(I)₂ (3.3 mg, 0.0164 mmol) was taken up in CHCl₃ (30 mL) and washed with 0.1 M NH₄PF_{6(aq)} (8x10 mL) and H₂O (2x10 mL). The organics were dried and the solvent removed *in vacuo* to afford **2.26•(PF₆)₂** as a white powder (3.56 mg, quant.).

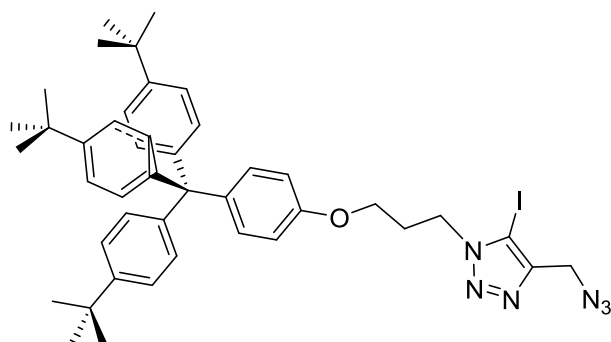
¹H NMR (400 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 9.79 (s, 1H, amide macro. int. PyrH), 9.35 – 9.24 (m, 4H, amide macro. ext. PyrH & triazole macro. ext. PyrH), 8.15 (s, 1H, triazole macro. int. PyrH), 6.47 – 6.62 (m, 8H, triazole macro. hydroquinone ArH), 5.96 – 6.07 (s, 4H, amide macro. hydroquinone ArH), 5.80 – 5.90 (s, 4H, amide macro. hydroquinone ArH), 5.72 (s, 4H, methylene CH₂), 4.62 – 4.67 (m, 4H, O-CH₂-CH₂-N), 4.47 (partially obscured by solvent, s, 3H, N⁺-CH₃), 4.28 – 4.36 (m, 4H, N-CH₂-CH₂-O), 3.05 – 4.07 (m, 39H, N⁺-CH₃ & CH₂); **¹⁹F NMR** (376 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) -74.16 (d, *J* = 710.6 Hz, PF₆).

Stopper iodotriazole alcohol 2.31



Stopper azide **2.30** (0.200 g, 0.340 mmol), NaI (0.188 g, 1.34 mmol) and $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (0.240 g, 0.642 mmol) were dissolved in dry THF (5 mL) and stirred for 5 minutes in the dark. TBTA (cat.), DBU (47.8 μL , 0.335 mmol) in dry CH_3CN (5 mL) and finally propargyl alcohol (18.2 mL, 0.324 mmol) were added and the reaction was stirred for 16 hours in the dark. The solvent was removed *in vacuo* and the residue was taken up in CH_2Cl_2 (30 mL). The organics were washed with EDTA/ NH_4OH solution (3x15 mL), H_2O (15 mL) and brine (15 mL), dried over MgSO_4 and the solvent removed *in vacuo*. Purification was achieved via column chromatography (silica, 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **2.31** as a white solid (0.146 g, 56%).

^1H NMR (500 MHz, CDCl_3) δ (ppm) 7.20 – 7.26 (m, 6H, ArH), 7.05 – 7.12 (m, 8H, ArH), 6.71 – 6.78 (m, 2H, ArH), 4.72 (d, J = 6.2 Hz, 2H, OH- CH_2 -C), 4.59 (t, J = 7.0 Hz, 2H, O- CH_2 - CH_2), 3.99 (t, J = 5.8 Hz, 2H, N- CH_2 - CH_2), 2.40 (tt, J = 7.0 Hz, J = 5.8 Hz, 2H, CH_2 - CH_2), 2.03 (t, J = 6.3 Hz, 1H, -OH), 1.30 (s, 27H, ^tBu); **^{13}C NMR** (126 MHz, CDCl_3) δ (ppm) 156.29, 148.49, 144.21, 132.45, 130.84, 124.21, 113.20, 63.98, 63.20, 56.88, 47.91, 34.45, 31.53, 29.81; **HRMS (ESI):** m/z 770.31766 $[\text{M}+\text{H}]^+$ ($[\text{C}_{43}\text{H}_{52}\text{IN}_3\text{O}_2 \cdot \text{H}]$ calc. 770.31770).

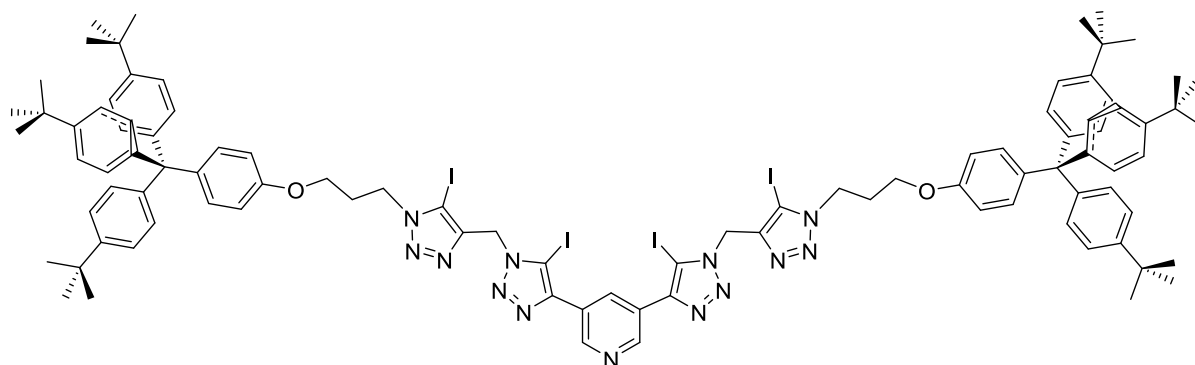
Stopper iodotriazole azide **2.32**

Alcohol **2.31** (0.149 g, 0.193 mmol) and NEt_3 (56.5 μL , 0.405 mmol) were added to dry CH_2Cl_2 (5 mL) and stirred for 5 minutes under N_2 at 0°C . MsCl (22.4 μL , 0.289 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and added dropwise and the reaction was stirred for 3 hours at RT. The organics were diluted with CH_2Cl_2 (20 mL) and washed with H_2O (2x15 mL), 1M $\text{HCl}_{(\text{aq})}$ (2x15 mL) and brine (2x15 mL). The aqueous layer was extracted with CH_2Cl_2 (15 mL) and the organics combined and dried over MgSO_4 . The solvent was removed *in vacuo* to afford a yellow oil which was used without further purification. The crude product was dissolved in dry, degassed DMSO (10 mL) before NaN_3 (0.050 g, 0.772 mmol) and NaI (cat.) were added. The reaction was stirred at 85°C for 16 hours. After cooling to RT, the reaction was quenched with H_2O (120 mL) and extracted into EtOAc (50 mL). The organics were washed with brine (2x20 mL), dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via column chromatography (silica, CH_2Cl_2) to afford **2.32** as a white powder (0.104 g, 86%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.19 – 7.27 (m, 6H, ArH), 7.04 – 7.13 (m, 8H, ArH), 6.72 – 6.77 (m, 2H, ArH), 4.60 (t, $J = 7.0$ Hz, 2H, $\text{O-CH}_2\text{-CH}_2$), 4.42 (s, 2H, $\text{N}_3\text{-CH}_2\text{-C}$), 4.00 (t, $J = 5.8$ Hz, 2H, $\text{N-CH}_2\text{-CH}_2$), 2.41 (tt, $J = 7.0$ Hz, $J = 5.8$ Hz, 2H, $\text{CH}_2\text{-CH}_2\text{-CH}_2$), 1.30 (s, 27H, ^tBu). **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 148.50, 144.22, 132.46, 130.85, 124.21,

113.21, 63.94, 63.21, 62.98, 48.16, 34.45, 31.53, 29.77; **HRMS (ESI):** m/z 795.32418 $[M+H]^+$ ($[C_{43}H_{51}IN_6O \cdot H]^+$ calc. 795.32418).

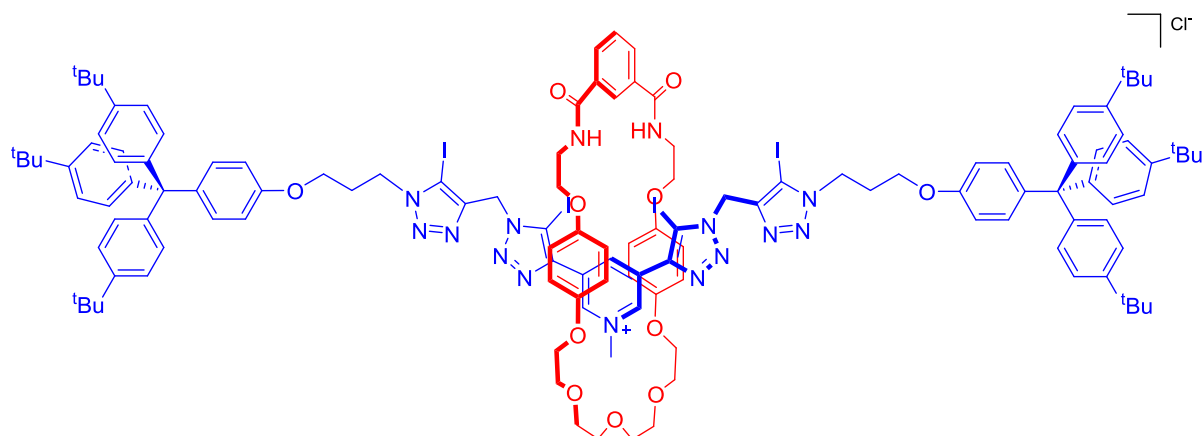
Tetra-iodotriazole pyridine **2.33**



$[Cu(CH_3CN)_4][PF_6]$ (2.13 mg, 0.0057 mmol) and TBTA (3.03 mg, 0.0057 mmol) were added to a dry, degassed mixture of THF (1.5 mL) and CH_2Cl_2 (1.5 mL). Azide **2.32** (100 mg, 0.126 mmol) and pyridine bis-iodoalkyne **2.2** (21.7 mg, 0.0571 mmol) were added and the reaction stirred for 16 hours at RT, after which a white precipitate had formed. This was collected by filtration and washed with CH_3OH (30 mL) and Et_2O (30 mL). Purification was achieved via column chromatography (silica, 95:5 CH_2Cl_2/CH_3OH) to give **2.33** as a white solid (76.0 mg, 67%).

^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.25 (s, 2H, PyrH), 8.90 (s, 1H, PyrH), 7.18 – 7.26 (m, 12H, ArH), 7.04 – 7.13 (m, 16H, ArH), 6.70 – 6.79 (m, 4H, ArH), 5.75 (s, 4H, methylene CH_2), 4.58 (t, $J = 7.0$ Hz, 4H, O- CH_2-CH_2), 4.00 (t, $J = 5.7$ Hz, 4H, N- CH_2-CH_2), 2.40 (tt, $J = 7.0$ Hz, $J = 5.7$ Hz, 4H, $CH_2-CH_2-CH_2$), 1.29 (s, 54H, tBu); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm) 156.25, 148.50, 144.20, 140.30, 132.47, 130.84, 124.22, 113.20, 63.91, 63.20, 48.23, 46.86, 34.45, 31.54, 29.75; **HRMS (ESI):** m/z 1969.48009 $[M+H]^+$ ($[C_{95}H_{105}I_4N_{13}O_2 \cdot H]^+$ calc. 1969.47992).

Monocationic tetra-iodotriazole rotaxane **2.35**·Cl



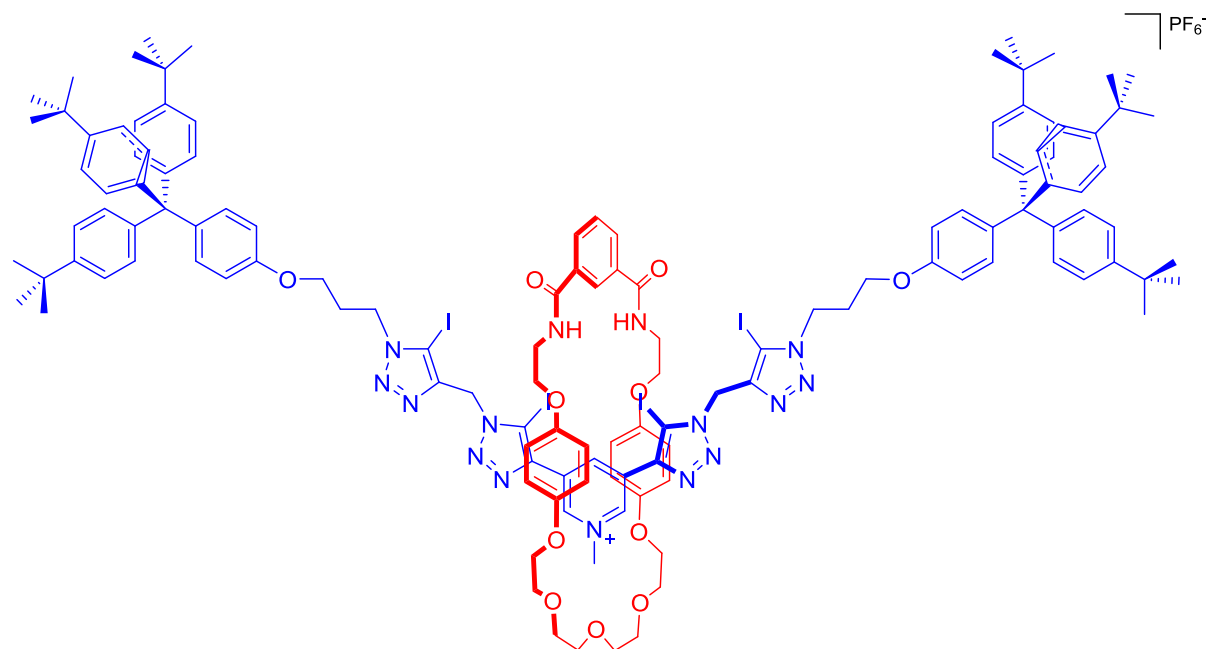
Axle **2.34**·**I** (30 mg, 0.0151 mmol) and bis-amine **2.22** (21 mg, 0.0454 mmol) were dissolved in dry CH₂Cl₂ (3 mL) and stirred for 5 minutes under N₂. NEt₃ (13.7 uL, 0.0983 mmol) was added, followed immediately by isophthaloyl dichloride (9.2 mg, 0.0454 mmol) in dry CH₂Cl₂ (1 mL) and the resulting solution stirred under N₂ for 16 hours at RT. The solution was washed with 10% HCl_(aq) (2x20 mL) and H₂O (2x20 mL). The organic phase was dried over MgSO₄ and concentrated *in vacuo*. Purification was achieved via preparative TLC (97:3 CH₂Cl₂/CH₃OH & 94:6 CH₂Cl₂/CH₃OH) to afford **2.35**·**Cl** as a white solid (12.7 mg, 33%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.48 (s, 2H, ext. PyrH), 8.89 (s, 1H, int. macro. ArH), 8.40 (s, 1H, int. PyrH), 8.14 (d, *J* = 7.8 Hz, 2H, ext. macro. ArH), 7.93 (s, 2H, NH), 7.36 (t, *J* = 7.8 Hz, 1H, ext. macro. ArH), 7.22 – 7.27 (m, 12H, stopper ArH), 7.07 – 7.14 (m, 16H, stopper ArH), 6.78 – 6.83 (m, 4H, stopper ArH), 6.36 – 6.44 (m, 4H, hydroquinone ArH), 5.89 – 5.95 (m, 4H, hydroquinone ArH), 5.43 (s, 4H, methylene CH₂), 4.62 (t, *J* = 7.2 Hz, 4H, O-CH₂-CH₂), 4.58 (s, 3H, N⁺-CH₃), 3.46 – 4.40 (m, 28H, CH₂), 2.44 (m, 4H, CH₂-CH₂-CH₂), 1.32 (s, 54H, ^tBu). **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 166.81, 156.35, 153.46, 151.50, 151.47, 148.45, 144.84, 144.23, 140.19, 134.16, 132.46, 130.85, 124.20, 115.23, 114.43, 113.21, 79.97, 71.26, 71.06, 70.41, 67.71, 66.50, 64.16, 64.11, 63.20, 48.25, 46.49,

40.22, 34.44, 32.08, 31.54, 29.91, 29.85, 22.85, 15.43, 14.28; **HRMS (ESI):** m/z 2577.75488

$[M]^+$ ($[C_{128}H_{146}I_4N_{15}O_{11}]^+$ calc. 2577.7533).

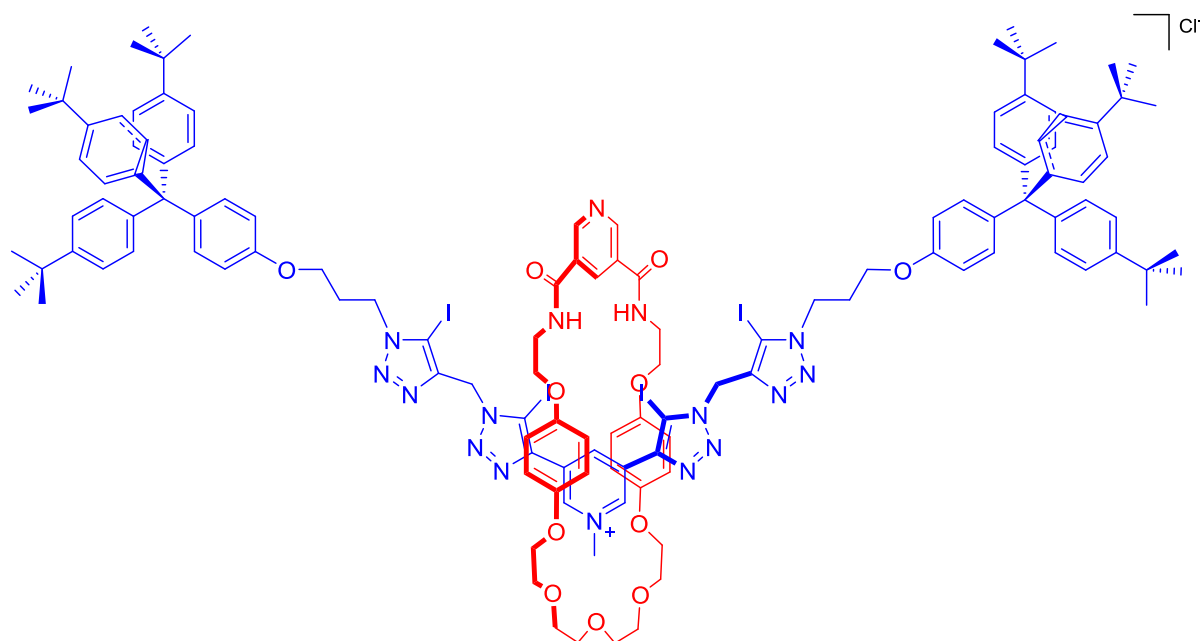
Monocationic tetra-iodotriazole rotaxane 2.35·PF₆



2.35·Cl (12.7 mg, 0.0047 mmol) was taken up in CHCl₃ (30 mL) and washed with 0.1 M NH₄PF_{6(aq)} (8x15 mL) and H₂O (2x15 mL). The organics were dried and the solvent removed *in vacuo* to afford **2.35·PF₆** as a white powder (12.8 mg, quant.).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.21 (s, 2H, ext. PyrH), 8.52 (s, 1H, int. macro. ArH), 8.01 – 8.14 (m, 3H, ext. macro. ArH & int. PyrH), 7.33 – 7.43 (m, 1H, ext. macro. ArH), 7.07 – 7.17 (m, 12H stopper ArH), 6.86 – 7.05 (m, 16H, stopper ArH) 6.61 – 6.74 (m, 4H, stopper ArH), 6.12 – 6.28 (m, 4H, hydroquinone ArH), 5.83 – 6.01 (m, 4H, hydroquinone ArH), 5.50 (s, 4H, methylene CH₂), 2.24 – 4.65 (m, 39H, N⁺-CH₃ & CH₂), 1.21 (s, 54H, 'Bu);

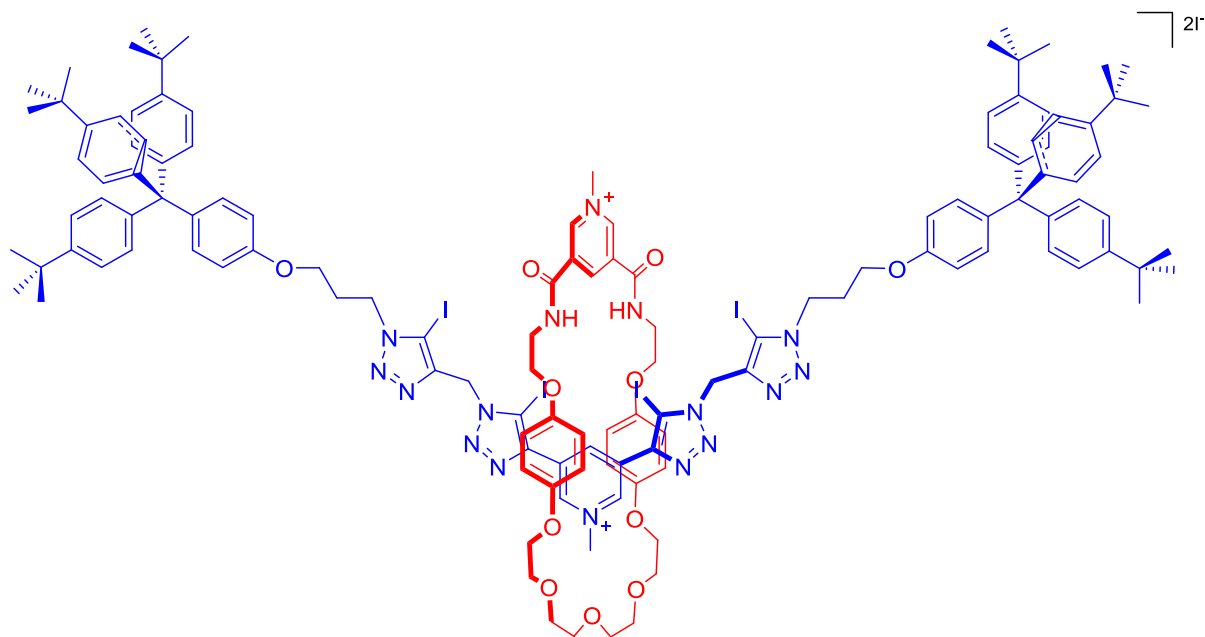
¹⁹F NMR (376 MHz, CDCl₃) δ (ppm) -71.33 (d, J = 714.4 Hz, PF₆).



¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.64 (s, 1H, macro. int. Pyr*H*), 9.23 (s, 2H, axle ext. Pyr*H*), 9.18 (s, 1H, axle int. Pyr*H*), 9.16 (s, 2H, macro. ext. Pyr*H*), 8.49 (br. s, 2H, NH), 7.13 – 7.17 (m, 12H, stopper Ar*H*), 6.97 – 7.03 (m, 16H, stopper Ar*H*), 6.68 (d, *J* = 8.4 Hz, 4H, stopper Ar*H*), 6.12 – 6.19 (m, 4H, hydroquinone Ar*H*), 5.94 – 6.06 (m, 4H, hydroquinone Ar*H*), 5.58 (s, 4H, methylene CH₂), 4.48 – 4.59 (m, 7H, N⁺-CH₃ & O-CH₂-CH₂), 3.33 – 3.96 (m, 28H, CH₂), 2.27 – 2.37 (m, 4H, CH₂-CH₂-CH₂), 1.22 (s, 54H, ^tBu); **¹³C NMR** (126 MHz,

CDCl_3) δ (ppm) 165.70, 156.13, 152.82, 151.98, 148.36, 148.34, 144.50, 144.19, 144.06, 140.11, 132.32, 130.70, 124.07, 115.19, 114.50, 113.02, 70.92, 70.82, 70.06, 67.74, 63.76, 63.06, 48.30, 46.49, 40.16, 34.31, 31.40, 30.96, 29.72, 29.66; **HRMS (ESI):** m/z 2578.74331 $[\text{M}]^+$ ($[\text{C}_{127}\text{H}_{145}\text{I}_4\text{N}_{16}\text{O}_{11}]^+$ calc. 2578.74856).

Dicationic tetra-iodotriazole rotaxane 2.37•(I)₂

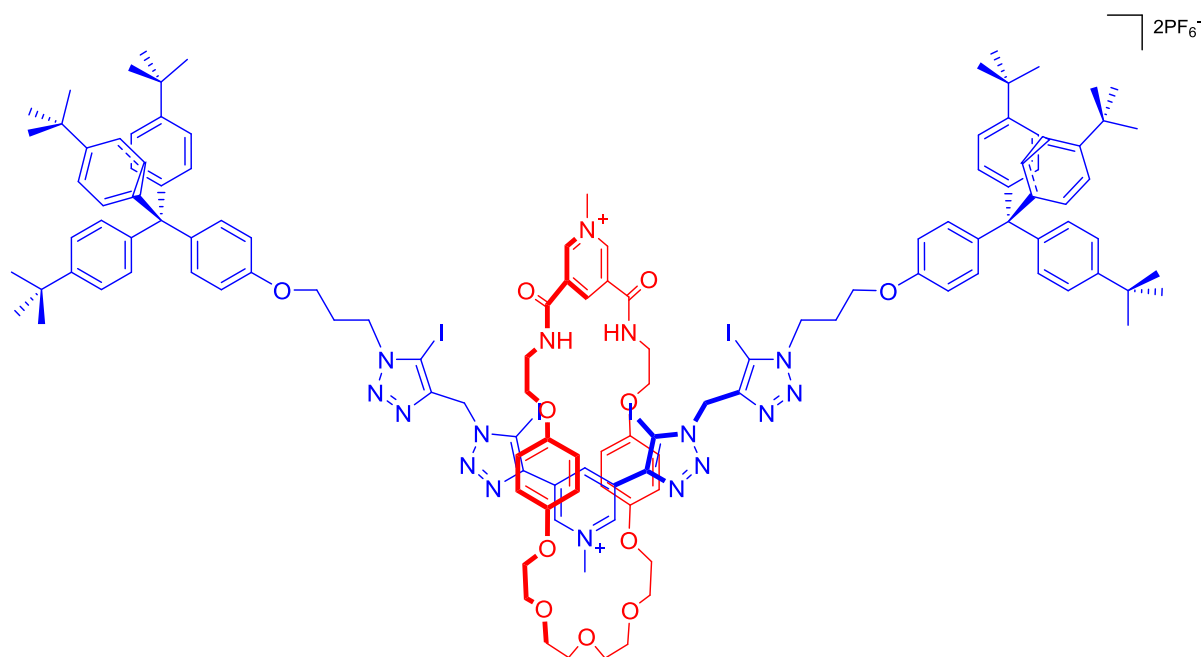


CH_3I (0.15 mL) was added to a stirred solution of **2.36•Cl** (8 mg, 0.0031 mmol) in 9:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (1.5 mL). The reaction was stirred for 16 hours. The solvent was removed *in vacuo* and purification was achieved by preparative TLC (silica, 94:6 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **2.37•(I)₂** as a white powder (8.19 mg, 94%).

¹H NMR (500 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) 10.53 (s, 1H, macro. int. PyrH), 9.51 (s, 2H, axle ext. PyrH), 9.43 (s, 2H, macro ext. PyrH), 8.96 (s, 2H, NH), 8.11 (s, 1H, axle int. PyrH), 7.18 – 7.24 (m, 12H, stopper ArH), 7.02 – 7.10 (m, 16H, stopper ArH), 6.68 – 6.73 (m, 4H, stopper ArH), 6.12 – 6.18 (m, 4H, hydroquinone ArH), 5.84 – 5.88 (m, 4H, hydroquinone ArH), 5.70 (s, 4H, methylene CH_2), 4.61 – 4.66 (O- $\text{CH}_2\text{-CH}_2$ & $\text{N}^+\text{-CH}_3$ obscured by CH_3OH peak), 4.43 (s, 3H, $\text{N}^+\text{-CH}_3$), 3.55 – 4.30 (m, 28H, CH_2), 2.34 – 2.43 (m,

4H, CH₂-CH₂-CH₂), 1.28 (s, 54H, ¹Bu); ¹³C NMR (126 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 161.02, 156.12, 152.41, 151.76, 148.29, 148.26, 147.63, 144.11, 143.14, 140.02, 133.87, 130.60, 130.56, 130.20, 123.99, 123.97, 114.77, 114.10, 112.98, 70.96, 70.73, 69.94, 67.53, 65.37, 63.78, 62.97, 46.70, 40.43, 34.09, 31.04, 31.03, 29.53, 29.46; HRMS (ESI): *m/z* 1296.88394 [M]²⁺ ([C₁₂₈H₁₄₈I₄N₁₆O₁₁]²⁺ calc. 1296.88574).

Dicationic tetra-iodotriazole rotaxane **2.37**·(PF₆)₂



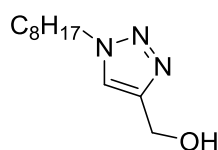
2.37·(I)₂ (8.19 mg, 0.0029 mmol) was taken up in CHCl₃ (20 mL) and washed with 0.1 M NH₄PF_{6(aq)} (8x10 mL) and H₂O (2x10 mL). The organics were dried and the solvent removed *in vacuo* to afford **2.37**·(PF₆)₂ as a white powder (8.30 mg, quant.).

¹H NMR (400 MHz, 1:1 CDCl₃/CD₃OD) δ (ppm) 10.46 (s, 1H, macro. int. PyrH), 9.43 (s, 2H, axle ext. PyrH), 9.36 (s, 2H, macro. ext. PyrH), 8.89 (s, 2H, NH), 8.03 (s, 1H, axle int. PyrH), 7.10 – 7.18 (m, 12H, stopper ArH), 6.94 – 7.02 (m, 16H, stopper ArH), 6.60 – 6.67 (m, 4H, stopper ArH), 6.08 (d, *J* = 8.6 Hz, 4H, hydroquinone ArH), 5.78 (d, *J* = 8.5 Hz, 4H, hydroquinone ArH), 5.62 (s, 4H, methylene CH₂), 4.55 (m, 7H, O-CH₂-CH₂ & N⁺-CH₃),

4.35 (s, 3H, $\text{N}^+\text{-CH}_3$), 3.48 – 3.96 (m, 28H, CH_2), 2.26 – 2.34 (m, 4H, $\text{CH}_2\text{-CH}_2\text{-CH}_2$), 1.20 (s, 54H, tBu); ^{19}F NMR (377 MHz, 1:1 $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ (ppm) -74.23 (d, $J = 712.5$ Hz, PF_6).

6.2.2 Chapter Three

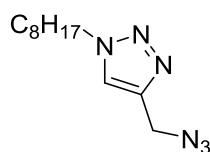
Triazole alcohol 3.1



Octyl azide (1 g, 6.45 mmol) and propargyl alcohol (0.344 g, 6.14 mmol) were added to $\text{DMSO}:\text{H}_2\text{O}$ (1:1, 30 mL). The flask was sealed and the mixture degassed with N_2 for 15 minutes. $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.323 g, 1.29 mmol), Na ascorbate (0.51 g, 2.58 mmol) and TBTA (cat.) were added and the reaction vigorously stirred under N_2 for 16 hours. The solution was diluted with water (100 mL) and extracted with EtOAc (30 mL). The organics were washed with EDTA/ NH_4OH (20 mL) solution, dried over MgSO_4 and concentrated *in vacuo* to afford white, crystalline product **3.1** (0.821 g, 63%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.51 (s, 1H, *trz-H*), 4.79 (d, $J = 5.3$ Hz, 2H, O-CH_2), 4.33 (t, $J = 7.3$ Hz, 2H, N-CH_2), 1.89 (m, 2H, $\text{N-CH}_2\text{-CH}_2$), 1.20 – 1.32 (m, 10H, CH_2), 0.87 (t, $J = 6.7$ Hz, 3H, $\text{CH}_2\text{-CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ (ppm) 171.29, 147.71, 121.54, 60.54, 56.76, 56.74, 50.54, 31.83, 30.44, 29.17, 29.09, 26.62, 22.73, 14.19.; HRMS (ESI): m/z 212.17585 $[\text{M}+\text{H}]^+$ ($[\text{C}_{11}\text{H}_{21}\text{N}_3\text{O} \cdot \text{H}]^+$ calc. 212.17574).

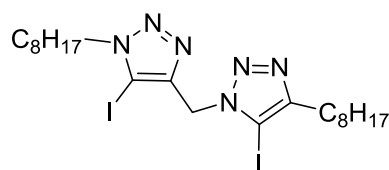
Triazole azide 3.2



Alcohol **3.1** (1 g, 4.73 mmol) and NEt₃ (1.01 mL, 7.27 mmol) were dissolved in dry CH₂Cl₂ (10 mL) and stirred under N₂ at 0°C for 5 minutes. MsCl (0.32 mL, 4.15 mmol) in dry CH₂Cl₂ (5 mL) was added dropwise and the reaction stirred for 1 hour. The mixture was washed with water (2x10 mL), 1M HCl_(aq) (3x10 mL) and brine (3x10 mL) and dried over MgSO₄. The solvent was removed *in vacuo* to afford a yellow oil. The oil (1.0288 g, 3.56 mmol) and NaN₃ (0.92 g, 14.2 mmol) were dissolved in dry, degassed DMSO (20 mL). The mixture was heated at 85°C for 16 hours under N₂. The mixture was cooled to RT and partitioned between water (15 mL) and Et₂O (15 mL). The aqueous layer was washed with Et₂O (2x15 mL). The combined organics were washed with brine (3x15 mL), dried over MgSO₄ and concentrated *in vacuo* to afford **3.2** as a colourless oil (0.209 g, 25%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.53 (s, 1H, trz-H), 4.47 (s, 2H, N₃-CH₂), 4.34 (t, *J* = 7.2 Hz, 2H, N-CH₂), 1.88 (m, 2H, N-CH₂-CH₂), 1.22 – 1.34 (m, 10H, CH₂), 0.81 – 0.90 (m, 3H, -CH₃); ¹³C NMR (101 MHz, CDCl₃) δ (ppm) 142.57, 122.10, 50.63, 45.84, 41.10, 31.78, 30.42, 29.11, 26.59, 22.68, 14.15; HRMS (ESI): *m/z* 237.18222 [M+H]⁺ ([C₁₁H₂₀N₆·H] calc. 237.18227).

Bis-iodotriazole ligand 3.3

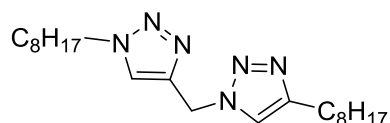


Iodotriazole azide **2.6** (400 mg, 1.10 mmol) and NaI (608 g, 4.40 mmol) were dissolved in dry THF (10 mL) and Cu(ClO₄)₂·6H₂O (777 mg, 2.20 mmol) was added. The reaction mixture was stirred for 5 minutes in the dark. TBTA (cat.) was added followed by dropwise addition of DBU (109 mg, 0.72 mmol) in CH₃CN (10 mL). Finally, 1-decyne (101 mg, 0.73 mmol) was added and the reaction stirred for 16 hours. The solvent was removed *in vacuo*

and the crude product taken up in CH_2Cl_2 (50 mL) and washed with EDTA/ NH_4OH solution (2x30 mL) and brine (2x30 mL). The combined organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved by column chromatography (silica, 98:2 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **3.3** as an off-white powder (493 mg, 69%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 5.64 (s, 2H, methylene CH_2), 4.35 (t, $J = 7.4$ Hz, 2H, N- CH_2), 2.64 (t, $J = 7.7$ Hz, 2H, C- CH_2 - CH_2), 1.89 (m, 2H, N- CH_2 - CH_2), 1.67 (m, 2H, C- CH_2 - CH_2), 1.23 – 1.35 (m, 20H, CH_2), 0.80 – 0.91 (m, 6H, $-\text{CH}_3$); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 152.71, 145.01, 136.06, 53.66, 51.12, 46.53, 32.02, 31.85, 29.98, 29.44, 29.35, 29.18, 29.07, 26.49, 26.26, 22.82, 22.75, 14.27, 14.23; **HRMS (ESI):** m/z 627.11588 $[\text{M}+\text{H}]^+$ ($[\text{C}_{21}\text{H}_{36}\text{N}_6\text{I}_2\text{H}]^+$ calc. 627.11636).

Bis-triazole ligand 3.4

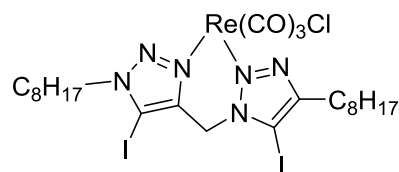


Triazole azide **3.2** (100 mg, 0.42 mmol) and 1-decyne (55.7 mg, 0.40 mmol) were added to $\text{DMSO}:\text{H}_2\text{O}$ (1:1, 30 mL). The flask was sealed and degassed with N_2 for 15 minutes. $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (20 mg, 0.08 mmol), Na ascorbate (31.7 mg, 0.16 mmol) and TBTA were dissolved in water and added and the reaction vigorously stirred for 16 hours. EDTA/ NH_4OH solution (20 mL) was added and the solution was diluted with water (100 mL). The product was extracted by washing in EtOAc (4x50 mL). The combined organics were dried over MgSO_4 and the solvent removed *in vacuo*. Purification was achieved through recrystallisation in CH_3OH with the pure product isolated as a white solid (90 mg, 57%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.55 (s, 1H, *trzH*), 7.43 (s, 1H, *trzH*), 5.62 (s, 2H, methylene CH_2), 4.32 (t, $J = 7.3$ Hz, 2H, N- CH_2 - CH_2), 2.67 (t, $J = 7.3$ Hz, 2H, C- CH_2 - CH_2), 1.83 – 1.91 (m, 2H, N- CH_2 - CH_2), 1.59 – 1.65 (m, 2H, C- CH_2 - CH_2), 1.20 – 1.32 (m, 20H,

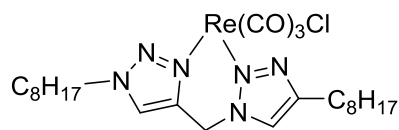
CH_2), 0.83 – 0.91 (m, 6H, $-\text{CH}_3$); ^{13}C NMR (126 MHz, CDCl_3) δ (ppm) 142.20, 122.84, 120.95, 50.74, 45.43, 31.98, 31.80, 30.31, 29.51, 29.45, 29.41, 29.33, 29.13, 29.02, 26.59, 25.84, 22.78, 22.71, 14.22, 14.17. **HRMS (ESI):** m/z 375.32305 $[\text{M}+\text{H}]^+$ ($[\text{C}_{21}\text{H}_{38}\text{N}_6\cdot\text{H}]^+$ calc. 375.32307).

XB receptor Re3.5



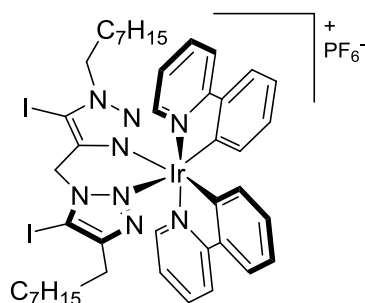
$\text{Re}(\text{CO})_5\text{Cl}$ (69.2 mg, 0.191 mmol) was dissolved in CH_3CN (20 mL) and stirred at reflux for 1 hour. The solution was allowed to cool to RT and the solvent was removed *in vacuo*. The remaining white powder was dissolved in CH_2Cl_2 (15 mL) and bis-iodotriazole **3.3** (100 mg, 0.160 mmol) was added. The mixture was stirred for 16 hours before the solvent was removed *in vacuo*. Purification was achieved by column chromatography (silica, 9:1 CH_2Cl_2 :hexane) to afford an off-white product (106.4 mg, 71%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 6.68 (d, $J = 15.4$ Hz, 1H, methylene CH_2), 5.51 (d, $J = 15.5$ Hz, 1H, methylene CH_2), 4.44 (t, $J = 7.6$ Hz, 2H, $\text{N}-\text{CH}_2-\text{CH}_2$), 2.69 (t, $J = 8.1$ Hz, 2H, $\text{C}-\text{CH}_2-\text{CH}_2$), 1.93 – 2.01 (m, 2H, $\text{N}-\text{CH}_2-\text{CH}_2$), 1.65 – 1.70 (m, 2H, $\text{C}-\text{CH}_2-\text{CH}_2$), 1.23 – 1.44 (m, 20H, CH_2), 0.85 – 0.92 (m, 6H, $-\text{CH}_3$); ^{13}C NMR (126 MHz, CDCl_3) δ (ppm) 194.90, 190.44, 154.45, 144.05, 83.55, 81.71, 52.88, 46.63, 31.93, 31.77, 29.80, 29.33, 29.30, 29.27, 29.07, 28.93, 28.77, 26.51, 26.43, 22.76, 22.69, 14.22, 14.17. **HRMS (ESI):** m/z 955.00678 $[\text{M}+\text{Na}]^+$ ($[\text{C}_{24}\text{H}_{36}\text{ClN}_6\text{I}_2\text{O}_3\text{ReNa}]^+$ calc. 955.00765).

HB receptor Re3.6

Re(CO)₅Cl (46 mg, 0.127 mmol) was dissolved in CH₃CN (15 mL) and stirred at reflux for 1 hour. The solution was allowed to cool to RT and the solvent was removed *in vacuo*. The remaining white powder was dissolved in CH₂Cl₂ (10 mL) and bis-triazole **3.4** (40 mg, 0.107 mmol) was added. The mixture was stirred for 16 hours before the solvent was removed *in vacuo*. Purification was achieved by column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) to afford the product as an off-white powder (45.2 mg, 60%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.73 (s, 1H, *trzH*), 7.51 (s, 1H, *trzH*), 6.63 (d, *J* = 15.2 Hz, 1H, methylene CH₂), 5.37 (d, *J* = 15.3 Hz, 1H, methylene CH₂), 4.42 (t, *J* = 7.5 Hz, 2H N-CH₂-CH₂), 2.74 (t, *J* = 8.2 Hz, 2H, C-CH₂-CH₂), 1.91 – 1.99 (m, 2H, N-CH₂-CH₂), 1.62 – 1.70 (m, 2H, C-CH₂-CH₂), 1.22 – 1.43 (m, 20H, CH₂), 0.84 – 0.92 (m, 6H, -CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 150.28, 139.08, 124.76, 123.53, 53.57, 52.28, 45.86, 31.97, 31.80, 30.03, 29.39, 29.33, 29.16, 29.12, 28.99, 26.55, 25.61, 22.79, 22.72, 14.24, 14.19; **HRMS (ESI)**: *m/z* 645.25612 [M-Cl]⁺ ([C₂₄H₃₈N₆O₃Re]⁺ calc. 645.25574).

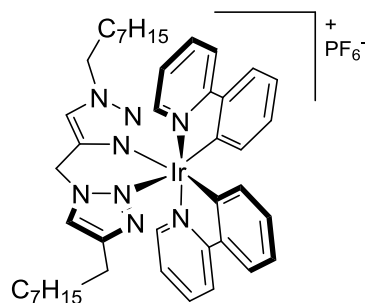
XB receptor Ir3.8·PF₆

Bis-iodotriazole **3.3** (10 mg, 0.0160 mmol) and [Ir₂(ppy)₄Cl₂] **3.7** (21.4 mg, 0.020 mmol) were suspended in CH₂Cl₂/CH₃OH (1:1, 5 mL) and stirred at 55°C for 16 hours. The solvent was

removed *in vacuo* and purification was achieved by preparative TLC (silica, 95:5 CH₂Cl₂/CH₃OH). The product was taken up in CH₂Cl₂ (20 mL) and washed with 0.1 M NH₄PF_{6(aq)} solution (8x10 mL) and H₂O (2x10 mL). The organics were dried over MgSO₄ and concentrated to afford **Ir3.8·PF₆** as a yellow crystalline solid (16.5 mg, 88%).

¹H NMR (500 MHz, acetone-*d*₆) δ (ppm) 8.41 (d, *J* = 5.8 Hz, 1H, *ArH*), 8.34 (d, *J* = 6.0 Hz, 1H, *ArH*), 8.20 (t, *J* = 8.3 Hz, 2H, *ArH*), 7.97 – 8.02 (m, 2H, *ArH*), 7.73 – 7.78 (m, 2H, *ArH*), 7.16 – 7.20 (m, 2H, *ArH*), 6.88 – 6.95 (m, 2H, *ArH*), 6.75 – 6.81 (m, 2H, *ArH*), 6.33 (d, *J* = 7.5 Hz, 1H, *ArH*), 6.22 (d, *J* = 7.7 Hz, 1H, *ArH*), 6.07 (d, *J* = 16.7 Hz, 1H, methylene CH₂), 6.01 (d, *J* = 16.7 Hz, 1H, methylene CH₂), 4.38 (t, *J* = 6.8 Hz, 2H, N-CH₂-CH₂), 2.47 – 2.59 (m, 2H, C-CH₂-CH₂), 1.66 – 1.74 (m, 2H, N-CH₂-CH₂), 1.40 – 1.47 (m, 2H, C-CH₂-CH₂), 1.25 – 1.34 (m, 10H, CH₂), 0.88 (t, *J* = 7.1 Hz, 6H, -CH₃); **¹³C NMR** (126 MHz, acetone-*d*₆) δ (ppm) 169.81, 169.12, 154.51, 152.41, 151.39, 151.21, 148.66, 145.45, 145.40, 145.24, 139.47, 139.38, 133.16, 132.55, 130.05, 130.03, 124.88, 124.78, 123.72, 123.62, 122.99, 122.95, 120.54, 120.40, 87.63, 86.13, 79.17, 78.99, 78.73, 53.07, 51.24, 47.13, 47.09, 32.58, 32.47, 26.93, 26.63, 26.35, 23.30, 23.26, 14.38, 14.36; **¹⁹F NMR** (377 MHz, CDCl₃) δ (ppm) -71.59 (d, *J* = 714.4 Hz, PF₆); **HRMS (ESI)**: *m/z* 1127.20238 [M]⁺ ([C₄₃H₅₂I₂IrN₈]⁺ calc. 1127.20281).

HB receptor **Ir3.9·PF₆**

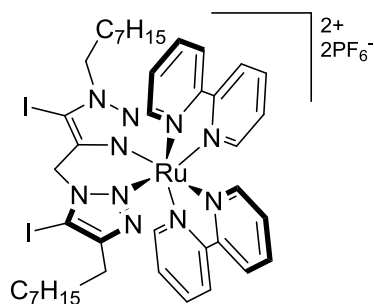


Bis-triazole **3.4** (2.6 mg, 0.0069 mmol) and [Ir₂(ppy)₄Cl₂] **3.7** (10 mg, 0.0087 mmol) were suspended in CH₂Cl₂/CH₃OH (1:1, 5 mL) and stirred at 55°C for 16 hours. The solvent was

removed *in vacuo* and purification was achieved by preparative TLC (silica, 95:5 CH₂Cl₂/CH₃OH). The product was taken up in CH₂Cl₂ (20 mL) and washed with 0.1 M NH₄PF_{6(aq)} solution (8x10 mL) and H₂O (2x10 mL). The organics were dried over MgSO₄ and concentrated to afford the product as a yellow crystalline solid (6.60 mg, 96%).

¹H NMR (500 MHz, acetone-*d*₆) δ (ppm) 8.51 (s, 1H, *trzH*), 8.40 (d, *J* = 5.5 Hz, 1H, *ArH*), 8.25 (s, 1H, *trzH*), 8.18 – 8.23 (m, 2H, *ArH*), 8.00 (t, *J* = 7.8 Hz, 2H, *ArH*), 7.72 – 7.79 (m, 2H, *ArH*), 7.17 – 7.25 (m, 2H, *ArH*), 6.88 – 6.94 (m, 2H, *ArH*), 6.74 – 6.81 (m, 2H, *ArH*), 6.36 (d, *J* = 7.6 Hz, 1H, *ArH*), 6.19 – 6.26 (m, 2H, *ArH*, methylene CH₂), 6.08 (d, *J* = 16.5 Hz, 1H, methylene CH₂), 4.29 – 4.40 (m, 2H, N-CH₂-CH₂), 2.54 (m, 2H, C-CH₂-CH₂), 1.65 – 1.73 (m, 2H, N-CH₂-CH₂), 1.42 – 1.50 (m, 2H, C-CH₂-CH₂), 1.15 – 1.24 (m, 10H, CH₂), 0.87 (t, *J* = 7.1 Hz, 6H, -CH₃); **¹³C NMR** (126 MHz, acetone-*d*₆) δ (ppm) 170.02, 169.35, 151.05, 150.95, 150.46, 149.34, 146.50, 145.48, 145.40, 140.07, 139.39, 139.26, 133.27, 132.51, 130.05, 130.01, 127.62, 127.04, 124.89, 124.80, 123.69, 123.55, 122.80, 122.78, 120.56, 120.40, 79.26, 79.19, 79.00, 78.74, 52.29, 45.70, 32.58, 32.46, 26.56, 25.75, 23.30, 23.26, 14.36; **¹⁹F NMR** (377 MHz, CDCl₃) δ (ppm) -71.34 (d, *J* = 713.6 Hz, PF₆); **HRMS (ESI):** *m/z* 875.40939 [M]⁺ ([C₄₃H₅₄IrN₈]⁺ calc. 875.40952).

XB receptor Ru3.10•(PF₆)₂

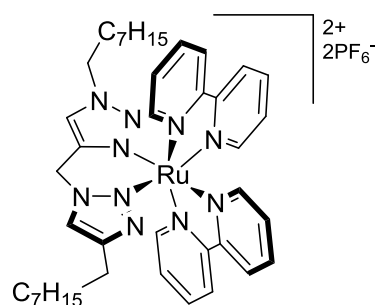


Bis-iodotriazole **3.3** (20 mg, 0.0319 mmol) and [Ru(bpy)₂Cl₂] (30.9 mg, 0.0637 mmol) were dissolved in EtOH/H₂O (4:1, 15 mL) and heated at 90°C for 16 hours. The EtOH was removed and the product extracted into CH₂Cl₂. Purification was achieved by preparative

TLC (silica, 9:1 CH₂Cl₂/CH₃OH). The resulting powder was dissolved in the minimum EtOH, precipitated with KPF₆⁻(aq) and washed with H₂O (3x10 mL) to afford **Ru3.10**·(PF₆)₂ as an orange crystalline solid (6.0 mg, 18%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.66 (d, *J* = 5.5 Hz, 1H, ArH), 8.45 (d, *J* = 8.2 Hz, 1H, ArH), 8.27 – 8.35 (m, 2H, ArH), 8.25 (d, *J* = 8.2 Hz, 1H, ArH), 8.02 – 8.10 (m, 3H, ArH), 7.90 – 7.95 (m, 2H, ArH), 7.76 – 7.81 (m, 2H, ArH), 7.61 (d, *J* = 5.9 Hz, 1H, ArH), 7.52 – 7.56 (m, 1H, ArH), 7.34 – 7.38 (m, 1H, ArH), 7.27 – 7.31 (m, 1H, ArH), 5.73 (d, *J* = 16.8 Hz, 1H, methylene CH₂), 5.47 (d, *J* = 16.8 Hz, 1H, methylene CH₂), 4.15 (t, *J* = 7.2 Hz, 2H, N-CH₂-CH₂), 2.38 – 2.51 (m, 2H, C-CH₂-CH₂), 1.50 – 1.57 (m, 2H, N-CH₂-CH₂), 1.31 – 1.38 (m, 2H, C-CH₂-CH₂), 1.12 – 1.25 (m, 10H, CH₂), 0.81 – 0.87 (m, 6H, -CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 155.42, 151.71, 138.35, 137.75, 137.63, 128.39, 127.46, 126.79, 126.64, 123.85, 123.34, 122.89, 31.78, 31.64, 29.11, 29.05, 28.90, 28.69, 28.58, 27.82, 26.13, 25.78, 22.60, 22.54, 13.98; **¹⁹F NMR** (376 MHz, CDCl₃) δ (ppm) -72.71 (d, *J* = 714.4 Hz, PF₆); **HRMS (ESI)**: *m/z* 520.07460 [M]²⁺ ([C₄₁H₅₂I₂N₁₀Ru]²⁺ calc. 520.07492).

HB receptor **Ru3.11**·(PF₆)₂

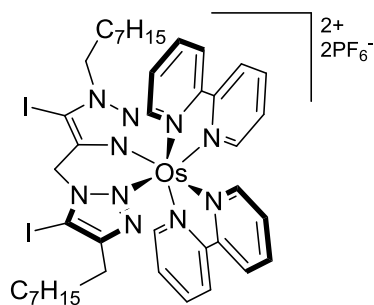


Bis-triazole **3.4** (30 mg, 0.0801 mmol) and [Ru(bpy)₂Cl₂] (77.6 mg, 0.160 mmol) were dissolved in EtOH/H₂O (4:1, 15 mL) and heated at 90°C for 16 hours. The EtOH was removed and the product extracted into CH₂Cl₂. Purification was achieved by preparative TLC (silica, 9:1 CH₂Cl₂/CH₃OH). The resulting powder was dissolved in the minimum

EtOH, precipitated with $\text{KPF}_6(\text{aq})$ and washed with H_2O (3x10 mL) to afford **Ru3.11**·(PF_6)₂ as an orange solid (36.4 mg, 42%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.54 (d, $J = 5.5$ Hz, 1H, ArH), 8.42 (d, $J = 8.2$ Hz, 1H, ArH), 8.35 (d, $J = 8.1$ Hz, 2H, ArH), 8.25 (d, $J = 8.1$ Hz, 1H, ArH), 8.04 – 8.10 (m, 3H, trzH, ArH), 7.90 – 7.97 (m, 3H, ArH), 7.84 – 7.86 (m, 2H, trzH, ArH), 7.66 – 7.69 (m, 2H, ArH), 7.48 (t, $J = 6.7$ Hz, 1H, ArH), 7.30 – 7.37 (m, 2H, ArH), 5.94 (d, $J = 16.7$ Hz, 1H, methylene CH_2), 5.53 (d, $J = 16.7$ Hz, 1H, methylene CH_2), 4.11 (t, $J = 7.2$ Hz, 2H, N- CH_2 - CH_2), 2.48 (t, $J = 7.6$ Hz, 2H, C- CH_2 - CH_2), 1.58 – 1.66 (m, 2H, N- CH_2 - CH_2), 1.38 – 1.45 (m, 2H, C- CH_2 - CH_2), 1.10 – 1.24 (m, 20H, CH_2), 0.78 – 0.86 (m, 6H, $-\text{CH}_3$); **^{13}C NMR** (126 MHz, CDCl_3) δ (ppm) 158.24, 158.01, 157.83, 157.72, 157.68, 152.90, 152.64, 152.13, 151.90, 150.98, 140.04, 138.20, 137.89, 137.56, 137.45, 128.32, 128.08, 127.29, 126.89, 126.75, 126.65, 123.92, 123.78, 123.39, 123.03, 52.16, 44.71, 31.97, 31.82, 29.33, 29.31, 29.08, 28.83, 28.61, 26.15, 26.09, 25.47, 22.79, 22.73, 14.26, 14.23; **^{19}F NMR** (376 MHz, CDCl_3) δ (ppm) -72.76 (d, $J = 713.8$ Hz, PF_6); **HRMS (ESI):** m/z 394.17828 $[\text{M}]^{2+}$ ($[\text{C}_{41}\text{H}_{54}\text{N}_{10}\text{Ru}]^{2+}$ calc. 394.17827).

XB receptor Os3.12·(PF_6)₂

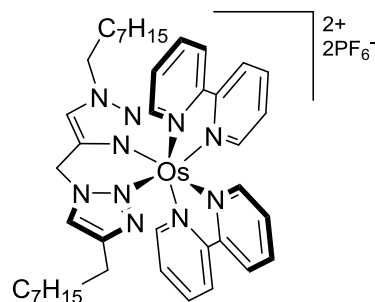


Bis-iodotriazole **3.3** (20 mg, 0.0319 mmol) and $[\text{Os}(\text{bpy})_2\text{Cl}_2]$ (39.6 mg, 0.0639 mmol) were dissolved in EtOH/ H_2O (4:1, 15 mL) and heated at 90°C for 3 days. The EtOH was removed and the product extracted into CH_2Cl_2 . Purification was achieved by preparative TLC (silica, 9:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$). The resulting powder was dissolved in the minimum

EtOH, precipitated with $\text{KPF}_6(\text{aq})$ and washed with H_2O (3x10 mL) to afford the product as a black solid (12.5 mg, 28%).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm) 8.56 – 8.58 (m, 1H, ArH), 8.37 – 8.41 (m, 1H, ArH), 8.26 – 8.32 (m, 2H, ArH), 8.13 – 8.21 (m, 2H, ArH), 7.95 – 8.00 (m, 2H, ArH), 7.71 – 7.78 (m, 2H, ArH), 7.55 – 7.62 (m, 2H, ArH), 7.38 – 7.44 (m, 2H, ArH), 5.91 (d, $J = 16.4$ Hz, 2H, methylene CH_2), 5.60 (d, $J = 16.7$ Hz, 2H, methylene CH_2), 4.11 (t, 2H, N- CH_2 - CH_2), 2.49 (t, $J = 7.2$ Hz, 2H, C- CH_2 - CH_2), 1.60 – 1.69 (m, 2H, N- CH_2 - CH_2), 1.40 – 1.44 (m, 2H, C- CH_2 - CH_2), 1.10 – 1.23 (m, 20H, CH_2), 0.83 – 0.91 (m, 6H, $-\text{CH}_3$); $^{19}\text{F NMR}$ (377 MHz, CDCl_3) δ (ppm) 72.97 (d, $J = 716.3$ Hz, PF_6^-); **MS (ESI)**: m/z 565.10 $[\text{M}]^{2+}$ ($[\text{C}_{41}\text{H}_{52}\text{I}_2\text{N}_{10}\text{Os}]^{2+}$ calc. 565.10).

HB receptor **Os3.13**·(PF_6)₂

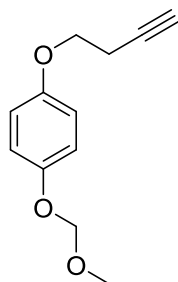


Bis-triazole **3.4** (20 mg, 0.0534 mmol) and $[\text{Os}(\text{bpy})_2\text{Cl}_2]$ (61.2 mg, 0.107 mmol) were dissolved in EtOH/ H_2O (4:1, 15 mL) and heated at 90°C for 3 days. The EtOH was removed and the product extracted into CH_2Cl_2 . Purification was achieved by preparative TLC (silica, 9:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$). The resulting solid was dissolved in the minimum EtOH, precipitated with $\text{KPF}_6(\text{aq})$ and washed with H_2O (3x10 mL) to afford black powder **Os3.13**·(PF_6)₂ (12.6 mg, 20%).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm) 8.59 (d, $J = 5.5$ Hz, 1H, ArH), 8.41 (d, $J = 8.1$ Hz, 1H, ArH), 8.29 – 8.34 (m, 2H, ArH), 8.21 (d, $J = 8.0$ Hz, 1H, ArH), 7.97 – 8.01 (m, 2H, trzH,

ArH), 7.81 – 7.87 (m, 3H, ArH), 7.70 – 7.78 (m, 3H, trzH, ArH), 7.63 (d, $J = 5.8$ Hz, 1H, ArH), 7.55 – 7.61 (m, 1H, ArH), 7.40 (t, $J = 6.7$ Hz, 1H, ArH), 7.18 – 7.24 (m, 2H, ArH), 5.92 (d, $J = 16.5$ Hz, 1H, methylene CH_2), 5.61 (d, $J = 16.3$ Hz, 1H, methylene CH_2), 4.12 (t, $J = 7.28$ Hz, 2H, N- $\text{CH}_2\text{-CH}_2$), 2.43 (t, $J = 7.6$ Hz, 2H, C- $\text{CH}_2\text{-CH}_2$), 1.52 – 1.60 (m, 2H, N- $\text{CH}_2\text{-CH}_2$), 1.33 – 1.40 (m, 2H, C- $\text{CH}_2\text{-CH}_2$), 1.02 – 1.23 (m, 20H, CH_2), 0.75 – 0.84 (m, 6H, - CH_3); **^{13}C NMR** (126 MHz, CDCl_3) δ (ppm) 160.80, 160.17, 160.10, 159.89, 152.29, 152.18, 151.30, 151.19, 150.70, 139.34, 137.26, 136.99, 136.84, 136.69, 128.51, 127.91, 127.73, 127.29, 127.08, 127.00, 124.01, 123.91, 123.48, 123.12, 52.26, 45.09, 31.98, 31.83, 29.33, 29.32, 29.11, 29.08, 28.85, 28.57, 26.17, 25.46, 22.80, 22.74, 14.27, 14.24; **^{19}F NMR** (377 MHz, CDCl_3) δ (ppm) -72.84 (d, $J = 716.3$ Hz, PF_6); **HRMS (ESI):** m/z 439.20666 $[\text{M}]^{2+}$ ($[\text{C}_{41}\text{H}_{54}\text{N}_{10}\text{Os}]^{2+}$ calc. 439.20684).

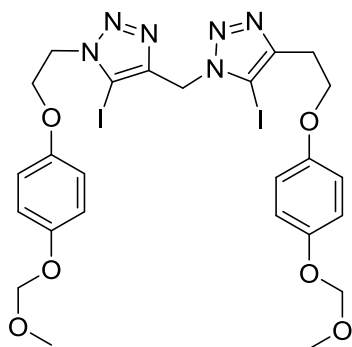
MOM-protected alkyne **3.16**



Alkyne **3.15** (0.325 mg, 2.0 mmol) was dissolved in dry CH_2Cl_2 (4 mL) and cooled to 0°C . DIPEA (0.42 mL, 2.40 mmol) was added dropwise over 5 minutes and the reaction stirred for a further 5 minutes. Chloromethyl methyl ether (0.182 mL, 2.40 mmol) was added dropwise over 5 minutes and the reaction stirred for 16 hours at RT. The solution was quenched with H_2O (10 mL) and the organics were washed with H_2O (10 mL), $\text{NaHCO}_{3(\text{aq})}$ (10 mL) and brine (10 mL). The organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via column chromatography (silica, CH_2Cl_2) to afford **3.16** as a colourless oil (0.301 g, 73%).

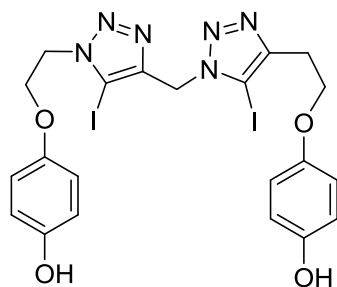
¹H NMR (400 MHz, CDCl₃) δ (ppm) 6.95 – 7.00 (m, 2H, ArH), 6.82 – 6.87 (m, 2H, ArH), 5.11 (s, 2H, O-CH₂-O), 4.06 (t, J = 7.0 Hz, 2H, O-CH₂-CH₂), 3.48 (s, 3H, -CH₃), 2.66 (td, J = 7.0 Hz, 2.7 Hz, 2H, -CH₂-CH), 2.03 (t, J = 2.7 Hz, 1H, -CH); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 153.50, 151.64, 117.59, 115.69, 95.25, 80.51, 69.81, 66.66, 55.87, 19.59. **MS (ESI)**: Not observed.

MOM-protected bis-iodotriazole 3.17



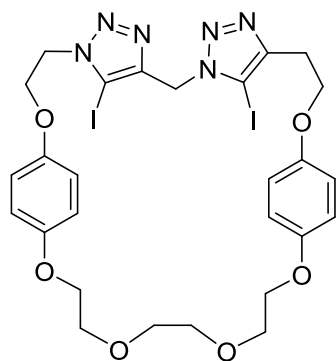
Azide **2.14** (0.219 g, 0.509 mmol), NaI (0.281 g, 1.94 mmol) and Cu(ClO₄)₂·6H₂O (0.359 g, 0.971 mmol) were dissolved in dry THF (3 mL) and stirred for 5 minutes in the dark. TBTA (cat.), DBU (0.072 mL, 0.476 mmol) in dry CH₃CN (3 mL) and finally alkyne **3.16** (0.100 mL, 0.485 mmol) were added and the reaction was stirred for 16 hours in the dark. The solvent was removed *in vacuo* and the residue was taken up in CH₂Cl₂ (20 mL) causing a white precipitate to form. This was collected to afford the pure product as a white powder (0.225 g, 61%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 6.91 – 6.98 (m, 4H, ArH), 6.73 – 6.86 (m, 4H, ArH), 5.67 (s, 2H, methylene CH₂), 5.09 (s, 4H, O-CH₂-O), 4.74 (t, J = 5.6 Hz, 2H, N-CH₂-CH₂), 4.37 (t, J = 5.6 Hz, 2H, O-CH₂-CH₂-N), 4.22 (t, J = 7.1 Hz, 2H, O-CH₂-CH₂-C), 3.47 (s, 3H, -O-CH₃), 3.46 (s, 3H, -O-CH₃), 3.13 (t, J = 7.1 Hz, 2H, C-CH₂-CH₂); Solubility too low to obtain ¹³C NMR; **MS (ESI)**: m/z 763.0 [M+H]⁺ ([C₂₅H₂₈I₂N₆O₆H]⁺ calc. 763.0).

Phenol bis-iodotriazole 3.18

Acetyl chloride (0.53 mL, 7.5 mmol) was added to CH₃OH (5 mL) at 0°C and the solution stirred for 5 minutes. The reaction stirred for a further 15 minutes at RT. Bis-triazole **3.17** (0.190 g, 0.25 mmol) was dissolved in CH₂Cl₂ (5 mL) and added portion-wise and the reaction was stirred for 2 hours. The solvent was removed *in vacuo* to leave an off white solid. This was purified through trituration in CH₂Cl₂/CH₃OH (1:1, 2 mL) to afford white powder **3.18** (0.146 g, 87%).

¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm) 6.60 – 6.77 (m, 8H, ArH), 5.60 (s, 2H, methylene CH₂), 4.70 (t, *J* = 5.2 Hz, 2H, N-CH₂-CH₂), 4.29 (t, *J* = 5.2 Hz, 2H, O-CH₂-CH₂-N), 4.09 (t, *J* = 7.0 Hz, 2H, O-CH₂-CH₂-C), 2.97 (t, *J* = 7.0 Hz, 2H, C-CH₂-CH₂). Solubility too low to obtain ¹³C NMR; **MS (ESI)**: *m/z* 674.9 [M+H]⁺ ([C₂₁H₂₀I₂N₆O₄H] calc.675.0).

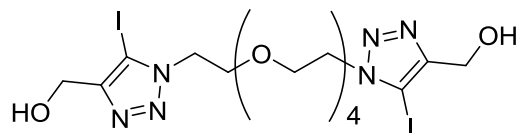
Bis-iodotriazole macrocycle 3.19

Bis-alcohol **3.18** (0.169 g, 0.25 mmol), triethylene glycol di(*p*-toluenesulfonate) (0.115 g, 0.25 mmol) and Cs₂CO₃ (0.326 g, 1.00 mmol) were dissolved in dry, degassed DMF (35 mL) and

stirred at 70°C for 18 hours. The solvent was removed *in vacuo* and the residue taken up in CHCl₃ (30 mL) whereupon it was washed with H₂O (20 mL), dried and concentrated. Purification was achieved via preparative TLC (silica, 97.5:2.5 CH₂Cl₂/CH₃OH - 2 runs) to afford **3.19** as an off-white powder (45.2 mg, 23%).

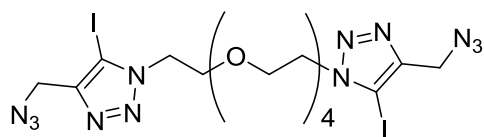
¹H NMR (400 MHz, CDCl₃) δ (ppm) 6.62 – 6.81 (m, 8H, ArH), 5.76 (s, 2H, methylene CH₂), 4.73 (t, J = 5.3 Hz, 2H, N-CH₂-CH₂), 4.31 (t, J = 5.3 Hz, 2H, O-CH₂-CH₂-N), 4.17 (t, J = 6.8 Hz, 2H, O-CH₂-CH₂-C), 4.05 (t, J = 4.7 Hz, 2H, CH₂), 3.98 (t, J = 4.7 Hz, 2H, CH₂), 3.77 – 3.85 (m, 4H, CH₂), 3.71 (s, 4H, CH₂), 3.11 (t, J = 6.8 Hz, 2H, C-CH₂-CH₂); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 153.71, 153.13, 152.68, 151.92, 149.64, 149.57, 144.64, 115.97, 115.74, 115.62, 115.54, 71.05, 70.93, 69.80, 69.77, 68.37, 68.17, 67.10, 67.05, 53.43, 49.72, 46.99, 26.38; **HRMS (ESI)**: m/z 789.03832 [M+H]⁺ ([C₂₇H₃₀I₂N₆O₆H]⁺ calc. 789.03890).

Bis-iodotriazole polyether alcohol **3.25**



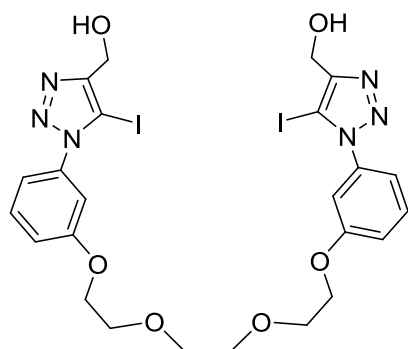
Cu(ClO₄)₂·6H₂O (1.64 g, 4.44 mmol) was added to a dry, degassed THF (5 mL) solution containing azide **3.24** (320 mg, 1.11 mmol) and NaI (1.33 g, 8.88 mmol). TBTA (11.8 mg, 0.022 mmol), DBU (0.334 mL, 2.22 mmol) in dry CH₃CN (5 mL) and propargyl alcohol (129 mg, 2.22 mmol) were added and the solution stirred for 16 hours. The solvent was removed *in vacuo* and the product purified via column chromatography (silica, 93:7 CH₂Cl₂/CH₃OH) to afford a white solid (163 mg, 22%).

¹H NMR (500 MHz, CDCl₃) δ (ppm) 4.72 (s, 4H, O-CH₂-CH₂-O), 4.56 (t, J = 5.6 Hz, 4H, CH₂), 3.94 (t, J = 5.6 Hz, 4H, CH₂), 3.53 – 3.60 (m, 12H); **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 71.05, 70.74, 70.57, 69.38, 56.71, 50.41; **HRMS (ESI)**: m/z 674.98372 [M+Na]⁺ ([C₁₆H₂₆I₂N₆O₆·Na]⁺ calc. 674.98954).

Bis-iodotriazole azide 3.26

Bis-alcohol **3.25** (450 mg, 0.69 mmol) and NEt_3 (0.394 mL, 2.82 mmol) were dissolved in dry CH_2Cl_2 (10 mL) and stirred under N_2 at 0°C for 5 minutes. MsCl (0.214 mL, 2.76 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise and the reaction stirred for 16 hours. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with water (2x10 mL), 1M $\text{HCl}_{(\text{aq})}$ (3x10 mL) and brine (3x10 mL) and dried over MgSO_4 . The solvent was removed *in vacuo* to afford a yellow oil. This was dissolved in dry, degassed DMSO (10 mL) containing NaN_3 (309 mg, 5.52 mmol) and heated at 85°C for 16 hours under N_2 . The mixture was cooled to RT and partitioned between water (50 mL) and EtOAc (20 mL). The aqueous layer was washed with EtOAc (3x30 mL). The combined organics were washed with brine (2x15 mL), dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved by column chromatography (silica, 96:4 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **3.26** as a colourless oil (57.6 mg, 12%).

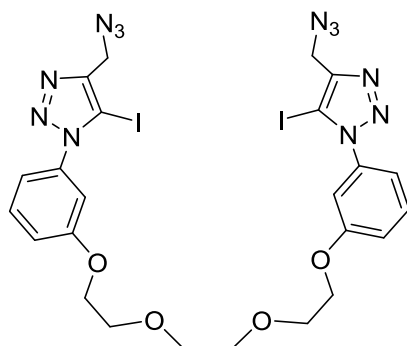
^1H NMR (400 MHz, CDCl_3) δ (ppm) 4.56 (t, $J = 5.6$ Hz, 4H, CH_2), 4.42 (s, 4H, $-\text{CH}_2\text{N}_3$), 3.94 (t, $J = 5.6$ Hz, 4H, CH_2), 3.54 – 3.60 (m, 12H, CH_2); **HRMS (ESI)**: m/z 725.00249 $[\text{M}+\text{Na}]^+$ ($[\text{C}_{16}\text{H}_{24}\text{I}_2\text{N}_{12}\text{O}_4\cdot\text{Na}]^+$ calc. 725.00250).

Bis-iodotriazole phenyl polyether alcohol 3.30

[Cu(CH₃CN)₄][PF₆] (63 mg, 0.25 mmol), TBTA (72 mg, 0.20 mmol) and iodopropargyl alcohol (270 mg, 1.48 mmol) were added to a solution of azide **3.29** (260 mg, 0.67 mmol) in dry CH₂Cl₂ (5 mL) and the mixture was stirred for 16 hours in the dark. A white precipitate was collected and purified via column chromatography (silica, 95:5 CHCl₃/CH₃OH) to afford the product as a white powder (261 mg, 52%).

¹H NMR (500 MHz, DMSO-*d*₆) δ (ppm) 7.49 (t, *J* = 8.1 Hz, 2H, *ArH*), 7.16 (dd, *J* = 8.5, 2.5, 2H, *ArH*), 7.10 (t, *J* = 2.5 Hz, 2H, *ArH*), 7.07 – 7.09 (m, 2H, *ArH*), 5.27 (t, *J* = 5.5 Hz, 2H, -OH), 4.50 (d, *J* = 5.5 Hz, 4H, -CH₂-OH), 4.12 – 4.18 (m, 4H, CH₂), 3.72 – 3.78 (m, 4H, CH₂), 3.60 (s, 4H, CH₂); **¹³C NMR** (126 MHz, DMSO) δ (ppm) 158.89, 151.22, 137.79, 130.39, 118.31, 116.43, 112.27, 84.94, 69.95, 68.80, 67.74, 54.98; **HRMS (ESI):** *m/z* 749.00679 [M+H]⁺ ([C₂₄H₂₆I₂N₆O₆.H]⁺ calc. 749.00760).

Bis-iodotriazole azide **3.31**

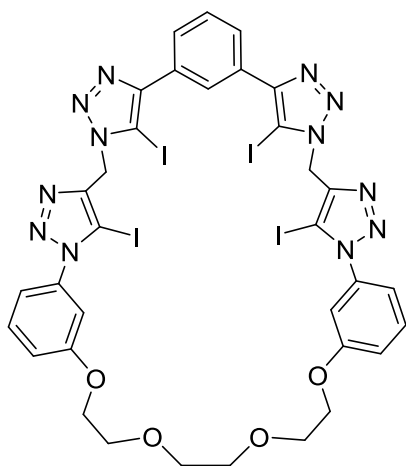


Bis-alcohol **3.30** (0.120 g, 0.16 mmol) and NEt₃ (91 uL, 0.657 mmol) were added to dry CH₂Cl₂ (5 mL), cooled to 0°C and stirred for 5 minutes under N₂. MsCl (50 uL, 0.644 mmol) was dissolved in dry CH₂Cl₂ (5 mL) and added dropwise and the mixture stirred at RT for 16 hours. The organics were diluted with CH₂Cl₂ (20 mL) and washed with H₂O (2x15 mL), 1M HCl_(aq) (2x15 mL) and brine (2x15 mL). The aqueous layer was extracted with CH₂Cl₂ (15 mL), the organics combined, dried over MgSO₄ and concentrated *in vacuo* to give a yellow oil. This was dissolved in dry, degassed DMSO (10 mL) before NaN₃ (0.083 g, 1.28 mmol) and

NaI (cat.) were added. The reaction was stirred at 85°C for 16 hours. After cooling to RT, the reaction was quenched with H₂O (120 mL) and extracted into EtOAc (50 mL). The organics were washed with brine (2x20 mL), dried over MgSO₄ and concentrated *in vacuo*. Purification was achieved via column chromatography (silica, 95:5 CH₂Cl₂/CH₃OH) to afford **3.31** as a white powder (0.097 g, 76%).

¹H NMR (500 MHz, CDCl₃) δ (ppm) 7.42 (t, *J* = 8.0 Hz, 2H, ArH), 7.07 – 7.12 (m, 4H, ArH), 7.04 – 7.06 (m, 2H, ArH), 4.50 (s, 4H, -CH₂-N₃), 4.17 (t, *J* = 4.7 Hz, 4H, CH₂), 3.88 (t, *J* = 4.7 Hz, 4H, CH₂), 3.74 (s, 4H, CH₂); **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 159.47, 147.41, 137.54, 130.24, 118.35, 117.04, 112.34, 81.31, 71.01, 69.68, 68.05, 45.85; **HRMS (ESI)**: *m/z* 799.02032 [M+H]⁺ ([C₂₄H₂₄I₂N₁₂O₄.H]⁺ calc. 799.02056).

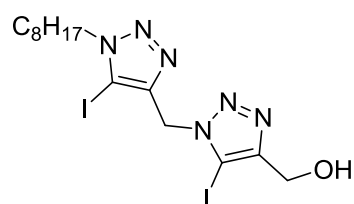
Tetra-iodotriazole macrocycle **3.32**



[Cu(CH₃CN)₄][PF₆] (9.06 mg, 0.024 mmol) and TBTA (12.9 mg, 0.024 mmol) were dissolved in CH₂Cl₂ (24 mL). Bis-azide **3.31** (97 mg, 0.12 mmol) and bis-iodoalkyne **3.27** (46 mg, 0.12 mmol) were added and the solution stirred for 2 days. A white precipitate formed that was collected by filtration. Purification was achieved via preparative TLC (silica, 96:4 CH₂Cl₂/CH₃OH, 2 runs) to afford macrocycle **3.32** a white solid (54 mg, 38%).

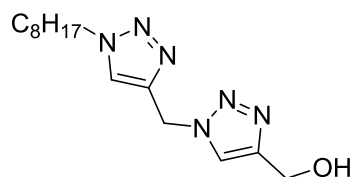
^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ (ppm) 8.53 – 8.57 (m, ArH), 7.94 – 8.01 (m, 2H, ArH), 7.65 (t, J = 8.1 Hz, 1H, ArH), 7.50 (t, J = 7.8 Hz, 2H, ArH), 7.08 – 7.21 (m, 6H, ArH), 5.83 (s, 4H, methylene CH_2), 4.12 – 4.19 (m, 4H, CH_2), 3.72 – 3.78 (m, 4H, CH_2), 3.60 (s, 4H, CH_2); **^{13}C NMR** (126 MHz, $\text{DMSO}-d_6$) δ (ppm) 158.91, 148.37, 145.63, 137.49, 130.90, 130.46, 129.25, 126.7, 118.36, 116.73, 112.34, 86.53, 79.18, 69.95, 69.92, 68.77, 67.75, 46.54, 40.02; **HRMS (ESI)**: m/z 1176.85941 $[\text{M}+\text{H}]^+$ ($[\text{C}_{34}\text{H}_{28}\text{I}_4\text{N}_{12}\text{O}_4\cdot\text{H}]^+$ calc. 1176.86080).

Bis-iodotriazole alcohol **3.33**



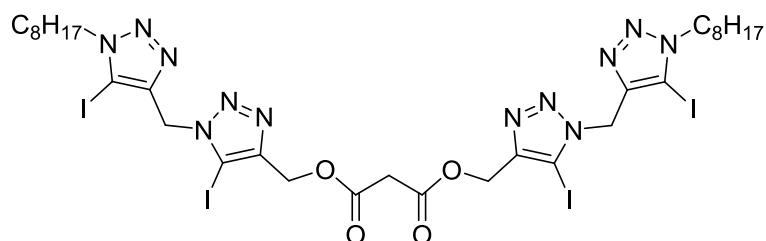
Azide **2.6** (0.54 g, 1.49 mmol), NaI (0.82 g, 5.68 mmol) and $\text{Cu}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}$ (1.05 g, 2.84 mmol) were sequentially added to dry THF (10 mL) and the reaction was stirred for 5 minutes in the dark. TBTA (cat.), DBU (0.21 mL, 1.41 mmol) in dry CH_3CN (10 mL) and propargyl alcohol (0.08 mL, 1.42 mmol) were added and the solution left to stir overnight under N_2 . The solvent was removed *in vacuo* and the crude solid taken up in CH_2Cl_2 (50 mL) and washed with EDTA/ NH_4OH solution (2x30 mL) and brine (2x50 mL). The combined organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved by column chromatography (silica, 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **3.33** as an off-white solid (0.62 g, 80%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 5.67 (s, 2H, methylene CH_2), 4.73 (s, 2H, $\text{CH}_2\text{-OH}$), 4.36 (t, J = 7.4 Hz, 2H, N- CH_2), 1.86 - 1.93 (m, 2H, $\text{CH}_2\text{-CH}_2\text{-N}$), 1.26 - 1.33 (m, 10H, CH_2), 0.88 (t, J = 6.8 Hz, 3H, $-\text{CH}_3$); **MS (ESI)**: m/z 544.97 $[\text{M}+\text{H}]^+$ ($[\text{C}_{14}\text{H}_{23}\text{ON}_6\text{I}_2\cdot\text{H}]^+$ calc. 545.00).

Bis-triazole alcohol 3.34

Azide **3.2** (1.09 g, 4.61 mmol), propargyl alcohol (0.26 g, 4.39 mmol), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.22g, 0.88 mmol), sodium ascorbate (0.35g, 1.76 mmol) and TBTA (cat.) were sequentially added to a degassed solution of DMSO/ H_2O (8:3, 55 mL) and the solution was stirred overnight under N_2 . The reaction was diluted with H_2O (200 mL) and extracted with CH_2Cl_2 (3x50 mL). The organics were washed with EDTA/ NH_4OH solution (3x30 mL) and brine (2x20 mL) and concentrated *in vacuo*. The product was recrystallised from CH_3OH , collected by filtration and washed with cold CH_3OH (20 mL) and cold Et_2O (20 mL) to afford **3.34** as an off-white solid (0.63 g, 53%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.70 (s, 1H, *trzH*), 7.57 (s, 1H, *trzH*), 5.66 (s, 2H, methylene CH_2), 4.77 (d, $J = 5.7$ Hz, 2H, $\text{CH}_2\text{-OH}$), 4.33 (t, $J = 7.4$ Hz, 2H, $\text{N-CH}_2\text{-CH}_2$), 2.27 (t, $J = 5.8$ Hz, OH), 1.85 - 1.92 (m, 2H, $\text{N-CH}_2\text{-CH}_2$), 1.25 - 1.31 (m, 10H, CH_2), 0.87 (t, $J = 6.6$ Hz, 3H, $-\text{CH}_3$); **HRMS (ESI)**: m/z 293.20798 $[\text{M}+\text{H}]^+$ ($[\text{C}_{14}\text{H}_{25}\text{ON}_6\cdot\text{H}]^+$ calc. 293.20844).

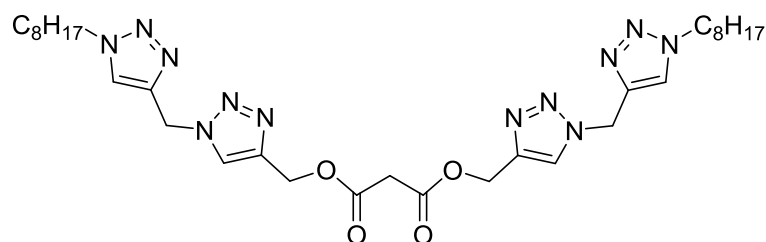
Propyl spaced malonyl tetra-iodotriazole 3.35

Alcohol **3.33** (0.62 g, 1.13 mmol) and NEt_3 (0.15 mL, 1.13 mmol) were added to dry CH_2Cl_2 (15 mL). Malonyl chloride (51 μL , 0.51 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and

added dropwise to the reaction mixture which was left to stir overnight under N₂. The solvent was removed *in vacuo* and the product purified by column chromatography (silica, 3:1 EtOAc/hexane) to afford the product as a white solid (0.17 g, 29%).

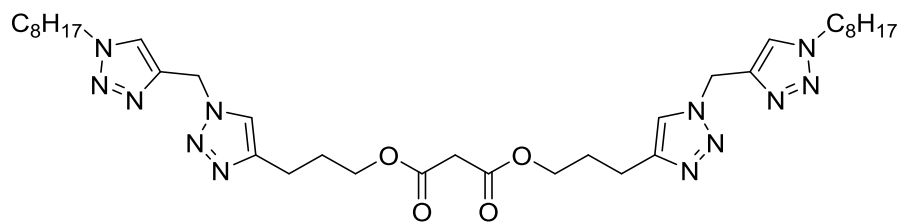
¹H NMR (400 MHz, CDCl₃) δ (ppm) 5.67 (s, 4H, methylene CH₂), 5.22 (s, 4H, C-CH₂-O), 4.36 (t, *J* = 7.3 Hz, 4H, N-CH₂-CH₂), 3.45 (s, 2H, *malonyl*), 1.86 - 1.92 (m, 4H, N-CH₂-CH₂), 1.23 - 1.36 ppm (m, 20H, CH₂), 0.86 - 0.90 (m, *J* = 6.8 Hz, 6H, -CH₃); **MS-ESI** *m/z* 1156.95 [M+H]⁺ ([C₃₁H₄₅O₄N₁₂L₄·H]⁺ calc. 1156.99).

Methyl spaced malonyl bis-triazole **3.36**

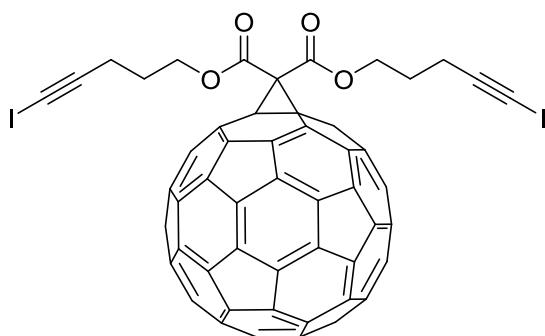


Alcohol **3.34** (0.50 g, 1.71 mmol) and NEt₃ (0.24 mL, 1.71 mmol) were added to dry CH₂Cl₂ (15 mL). Malonyl chloride (76 μL, 0.78 mmol) was dissolved in dry CH₂Cl₂ (10 mL) and added dropwise to the reaction mixture which was left to stir overnight under N₂. The solvent was removed *in vacuo* and the product purified by column chromatography (silica, 95:5 CH₂Cl₂/CH₃OH) to afford **3.36** as a white solid (0.23 g, 46%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.76 (s, 2H, *trzH*), 7.63 (s, 2H, *trzH*), 5.69 (s, 4H, methylene CH₂), 5.24 (s, 4H, C-CH₂-O), 4.34 (t, *J* = 7.3 Hz, 4H, N-CH₂-CH₂), 3.40 (s, 2H, *malonyl*), 1.86 - 1.93 (m, 4H, N-CH₂-CH₂), 1.25 - 1.33 (m, 20H, CH₂), 0.87 (t, *J* = 6.8 Hz, 6H, -CH₃); **MS-ESI**: *m/z* 653.40 [M+H]⁺ ([C₃₁H₄₉O₄N₁₂]⁺ calc. 653.35).

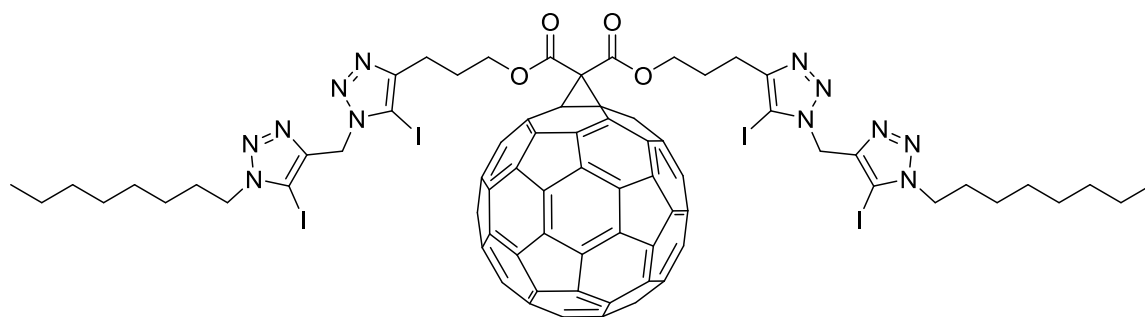
Propyl spaced malonyl bis-triazole 3.38

Bis-alkyne **3.37** (50 mg, 0.21 mmol) and azide **3.2** (105 mg, 0.44mmol) were added to a degassed mixture of DMSO/H₂O (1:1, 10 mL). CuSO₄·5H₂O (26 mg, 0.11 mmol), sodium ascorbate (42 mg, 0.21 mmol) and TBTA (cat.) were added and the solution was stirred for 2 days under N₂. The reaction was diluted with H₂O (150 mL), extracted with EtOAc (4x30 mL) and the organics were washed with EDTA/NH₄OH (20x20 mL) and brine (2x20mL). The combined organics were dried over MgSO₄ and concentrated *in vacuo* to afford the products as a white solid (51 mg, 34%). **¹H NMR** (400 MHz, CDCl₃) δ (ppm) 7.58 (s, 2H, *trzH*), 7.51 (s, 2H, *trzH*), 5.63 (s, 4H, methylene CH₂), 4.32 (t, *J* = 7.4 Hz, 4H, N-CH₂-CH₂), 4.18 (t, *J* = 6.4 Hz, 4H, O-CH₂), 3.36 (s, 2H, malonyl CH₂), 2.76 (t, *J* = 7.6 Hz, 4H, C-CH₂-CH₂), 2.03 (quin, *J* = 6.6 Hz, 4H, CH₂); 1.84 - 1.91 (m, 4H, N-CH₂-CH₂), 1.23 - 1.32 ppm (m, 20H, CH₂), 0.86 (t, *J* = 6.7 Hz, 6H, -CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 166.66, 147.26, 142.03, 122.91, 121.47, 77.48, 64.72, 50.75, 45.49, 41.67, 31.81, 30.32, 29.14, 29.04, 28.19, 26.60, 22.71, 22.11, 14.19; **MS (ESI)** *m/z* 709.40 [M+H]⁺ ([C₃₅H₅₆O₄N₁₂·H]⁺ calc. 708.91).

Fullerene bis-iodoalkyne 3.42

C₆₀ (200 mg, 0.28 mmol) dissolved in dry toluene (200 mL) was added to a solution of malonyl bis-alkyne **3.37** (66 mg, 0.28 mmol) in dry toluene (10 mL). I₂ (292 mg, 1.54 mmol) and DBU (338 μ L, 1.82 mmol) were added and the solution stirred for 16 hours under N₂. The solvent was removed *in vacuo* and purification was achieved via column chromatography (silica, CH₂Cl₂ & toluene) to afford **3.42** as a dark red solid (92 mg, 55%). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 4.60 (t, J = 6.2 Hz, 4H, O-CH₂), 2.60 (t, J = 6.9 Hz, 4H, C-CH₂), 2.07 (quin, J = 6.5 Hz, 4H, CH₂-CH₂-CH₂); MS-MALDI-TOF m/z 1205.825 [M] (C₇₃H₁₂O₄I₂ calc. 1205.883).

Tetra-iodotriazole fullerene **3.43**

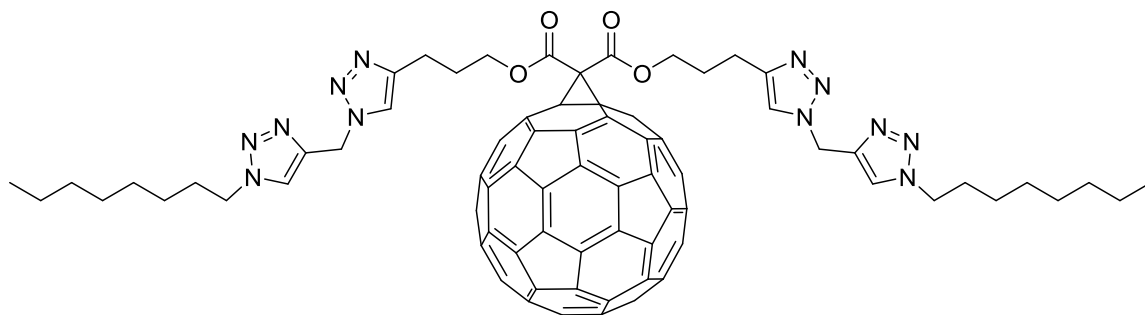


Azide **2.6** (36.9 mg, 0.10 mmol), fullerene bis-iodoalkyne **3.42** (56.8 mg, 0.048 mmol), [Cu(CH₃CN)₄][PF₆] (3.4 mg, 9.7 μ mol) and TBTA (2.6 mg, 4.8 μ mol) were added to dry THF (20 mL) and the solution was stirred for 3 days under N₂. The solvent was removed *in vacuo* and the residue was taken up in CH₂Cl₂ (20 mL), whereupon it was washed with EDTA/NH₄OH solution (2x20 mL), H₂O (2x20 mL) and brine (2x20 mL). The combined organics were dried over MgSO₄ and concentrated *in vacuo*. Purification by column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) afforded a dark red solid product (64 mg, 70%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 5.65 (s, 4H, methylene CH₂), 4.58 (t, J = 6.3 Hz, 4H, O-CH₂), 4.34 (t, J = 7.4 Hz, 4H, N-CH₂-CH₂), 2.85 (t, J = 7.5 Hz, 4H, C-CH₂), 2.29 (quin, J

= 6.9 Hz, 4H, CH_2), 1.84 - 1.92 (m, 4H, $\text{N-CH}_2\text{-CH}_2$), 1.24 - 1.34 (m, 20H, CH_2), 0.87 (t, J = 6.4 Hz, 6H, $-\text{CH}_3$); ^{13}C NMR (126 MHz, CDCl_3) δ (ppm) 163.66, 150.94, 145.40, 145.32, 144.87, 144.82, 144.77, 144.02, 143.15, 143.12, 142.34, 142.06, 141.12, 139.21, 80.15, 79.26, 71.72, 66.77, 51.15, 46.64, 31.85, 29.99, 29.18, 29.06, 27.74, 26.51, 22.88, 22.75, 14.24; **MS-MALDI-TOF** m/z 1930.653 [M] ($\text{C}_{95}\text{H}_{50}\text{O}_4\text{N}_{12}\text{I}_4$ calc. 1930.026).

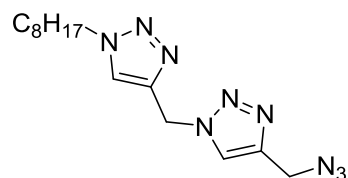
Tetra-triazole fullerene **3.44**



Azide **3.2** (31.0 mg, 0.131 mmol), fullerene bis-alkyne **3.41** (59.6 mg, 62 μmol), TBTA (0.33 mg, 0.62 μmol), $[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ (0.23 mg, 0.62 μmol) and DIPEA (43.5 μL , 0.25 mmol) were sequentially added to dry CH_2Cl_2 (10 mL) and left to stir at room temperature for 3 days. The mixture was diluted with CH_2Cl_2 (20 mL), washed with EDTA/ NH_4OH solution (2x20 mL) and brine (2x20 mL). The combined organic layers were dried over MgSO_4 , and concentrated *in vacuo*. Purification was achieved by column chromatography (silica, 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **3.44** as a dark brown solid (36 mg, 40%). ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.62 (s, 2H, *trzH*), 7.58 (s, 2H, *trzH*), 5.65 (s, 4H, methylene CH_2), 4.56 (t, J = 6.4 Hz, 4H, O-CH_2), 4.32 (t, J = 7.4 Hz, 4H, $\text{N-CH}_2\text{-CH}_2$), 2.95 (t, J = 7.6 Hz, 4H, $\text{C-CH}_2\text{-CH}_2$), 2.51 (t, J = 7.5 Hz, 4H, CH_2), 1.58 - 1.65 (m, 2H, $\text{N-CH}_2\text{-CH}_2$), 1.39 - 1.47 (m, 2H, $\text{C-CH}_2\text{-CH}_2$), 1.24 - 1.33 ppm (m, 20H, CH_2), 0.87 (t, J = 6.6 Hz, 6H, $-\text{CH}_3$); ^{13}C NMR (126 MHz, CDCl_3) δ (ppm) 163.71, 147.00, 145.41, 145.33, 145.26, 144.83, 144.78, 144.03, 143.13, 142.34, 142.00, 141.12, 139.13, 122.99, 121.60, 66.69, 50.77, 45.53, 31.83, 30.34,

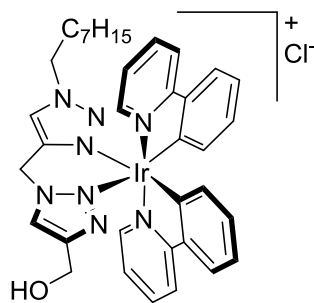
29.16, 29.06, 28.27, 26.63, 22.73, 22.26, 14.22. **MS-MALDI-TOF** m/z 1427.163 [M] ($C_{95}H_{54}O_4N_{12}$ calc. 1427.443).

Bis-triazole azide **3.45**



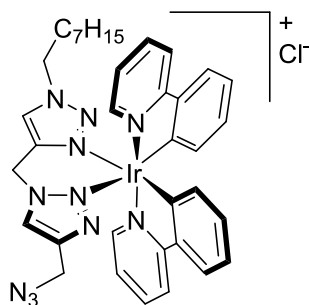
Alcohol **3.34** (717 mg, 2.45 mmol) and NEt_3 (0.85 mL, 6.13 mmol) were added to dry CH_2Cl_2 (30 mL) and stirred under N_2 at $0^\circ C$. $MsCl$ (0.285 mL, 3.68 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and added dropwise and the solution was stirred under N_2 for 1 hour at RT. The reaction was washed with H_2O (2x10 mL) and brine (3x10 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to leave a white solid. This was dissolved in degassed DMSO (10 mL) containing NaN_3 (89 mg, 1.37 mmol) and the resulting solution stirred at $85^\circ C$ overnight. The solution was cooled to room temperature, diluted with H_2O (150 mL) and extracted with $EtOAc$ (2x30 mL). The combined organic layers were washed with brine (2x20 mL), dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (silica, 97:3 CH_2Cl_2/CH_3OH) to afford **3.45** as a white solid (401 mg, 52%).

^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (s, 1H, *trzH*), 7.58 (s, 1H, *trzH*), 5.68 (m, 2H, methylene CH_2), 4.46 (s, 2H, CH_2-N_3), 4.33 (t, $J = 7.3$ Hz, 2H, N- CH_2-CH_2), 1.83 – 1.94 (m, 2H, N- CH_2-CH_2), 1.25-1.30 (m, 10H, CH_2), 0.87 (t, $J = 6.7$ Hz, 3H, $-CH_3$); **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 143.19, 141.52, 122.92, 122.67, 77.48, 77.36, 77.16, 76.84, 50.82, 45.76, 45.69, 31.82, 30.32, 29.14, 29.03, 26.59, 22.72, 14.20; **MS (ESI)**: m/z 318.2 $[M+H]^+$ ($[C_{14}H_{23}N_9 \cdot H]^+$ calc. 318.2).

Ir(III) bis-triazole alcohol 3.46·Cl

Bis-triazole alcohol **3.34** (16.4 mg, 0.059 mmol) and $[\text{Ir}_2(\text{ppy})_4\text{Cl}_2]$ **3.7** (30 mg, 0.028 mmol) were suspended in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (1:1, 5 mL) and stirred at 55°C for 16 hours. The solvent was removed *in vacuo* and the solid taken up in CH_2Cl_2 (10 mL). This was washed with H_2O (10 mL) and the organics were dried over MgSO_4 and concentrated to afford **3.46·Cl** as a yellow crystalline solid (33.4 mg, 75%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.21 (d, $J = 5.8$ Hz, 1H, ArH), 8.07 (s, 2H, trzH), 7.92 (d, $J = 5.6$ Hz, 1H, ArH), 7.87 (t, $J = 9.0$ Hz, 2H, ArH), 7.72 – 7.81 (m, 2H, ArH), 7.58 (d, $J = 7.8$ Hz, 1H, ArH), 7.52 (d, $J = 7.6$ Hz, 1H, ArH), 7.14 (td, $J = 5.8, 2.9$ Hz, 1H, ArH), 7.06 (td, $J = 5.8, 2.8$ Hz, 1H, ArH), 6.92 (t, $J = 7.5$ Hz, 1H, ArH), 6.85 (d, $J = 7.5$ Hz, 1H, ArH), 6.79 (td, $J = 7.4, 3.7$ Hz, 2H, ArH), 6.36 (d, $J = 7.6$ Hz, 1H, ArH), 6.18 (d, $J = 7.6$ Hz, 1H, ArH), 5.94 (d, $J = 16.5$ Hz, 1H, methylene CH_2), 5.69 (d, $J = 16.4$ Hz, 1H, methylene CH_2), 4.48 (s, 2H, $\text{CH}_2\text{-OH}$), 4.12 (t, $J = 7.1$ Hz, 2H, N- $\text{CH}_2\text{-CH}_2$), 1.58 – 1.67 (m, 3H, N- $\text{CH}_2\text{-CH}_2$ & OH), 1.08 – 1.30 (m, 10H, CH_2), 0.87 (t, $J = 7.2$ Hz, 3H, $-\text{CH}_3$); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 169.12, 168.28, 150.01, 149.94, 149.75, 148.19, 144.91, 144.24, 144.08, 138.74, 138.32, 137.91, 132.58, 131.60, 129.90, 129.73, 127.70, 126.38, 124.09, 123.96, 122.99, 122.90, 122.34, 122.30, 119.76, 119.22, 56.37, 51.89, 44.76, 31.84, 29.44, 29.06, 28.82, 26.06, 22.74, 14.23; **HRMS (ESI)**: m/z 793.29389 $[\text{M}]^+$ ($[\text{C}_{36}\text{H}_{40}\text{IrN}_8\text{O}]^+$ calc. 793.29488).

Ir(III) bis-triazole azide 3.47·Cl

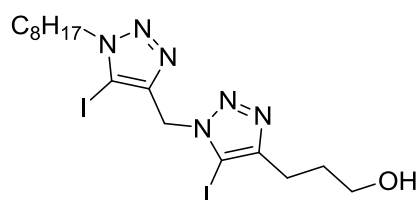
Ir(III) alcohol **3.46·Cl** (64.6 mg, 0.078 mmol) and NEt₃ (22.7 μ L, 0.16 mmol) were added to dry CH₂Cl₂ (5 mL) and stirred under N₂ at 0°C. MsCl (9.0 μ L, 0.12 mmol) was dissolved in dry CH₂Cl₂ (5 mL) and added dropwise and the solution was stirred under N₂ for 1 hour at RT. The reaction was washed with H₂O (2x10 mL), 1M HCl_(aq.) (2x10 mL) and brine (3x10 mL) and the combined organic layers were dried over MgSO₄ and concentrated *in vacuo* to leave a yellow solid. This was dissolved in degassed DMSO (6 mL) containing NaN₃ (20.3 mg, 0.31 mmol) and NaI (cat.) and the resulting solution stirred at 85°C overnight. The solution was cooled to room temperature, diluted with H₂O (100 mL) and extracted with EtOAc (2x30 mL). The combined organic layers were washed with brine (2x20 mL), dried over MgSO₄, concentrated *in vacuo* and purified by column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) to afford yellow solid **3.47·Cl** (11 mg, 17%).

¹H NMR (400 MHz, Chloroform-*d*) δ (ppm) 8.20 – 8.26 (m, 1H, ArH), 8.17 (s, 1H, trzH), 8.14 (s, 1H, ArH), 7.86 – 7.93 (m, 3H, ArH), 7.73 – 7.85 (m, 2H, ArH), 7.55 – 7.64 (m, 2H, ArH), 7.11 – 7.18 (m, 1H, ArH), 7.00 – 7.07 (m, 1H, ArH), 6.91 – 6.98 (m, 2H, ArH), 6.76 – 6.90 (m, 2H, ArH), 6.38 (d, *J* = 7.7 Hz, 1H, ArH), 6.18 (d, *J* = 7.7 Hz, 1H, ArH), 6.07 (d, *J* = 16.4 Hz, 1H, methylene CH₂), 5.73 (d, *J* = 16.2 Hz, 1H, methylene CH₂), 4.20 – 4.35 (m, 2H, methylene CH₂), 4.13 (t, *J* = 7.2, 2H, N-CH₂-CH₂), 1.60 – 1.68 (m, 2H, N-CH₂-CH₂), 1.09 – 1.18 (m, 10H, CH₂), 0.87 (t, *J* = 7.2 Hz, 3H, -CH₃); **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 169.41, 168.42, 149.86, 149.61, 147.66, 144.76, 144.52, 144.16, 143.92, 138.62, 138.40,

137.98, 132.67, 131.54, 130.09, 129.87, 128.13, 126.57, 124.17, 124.08, 122.94, 122.74, 122.57, 122.46, 119.91, 119.35, 52.01, 44.87, 31.84, 29.49, 29.06, 28.82, 26.08, 22.74, 14.23;

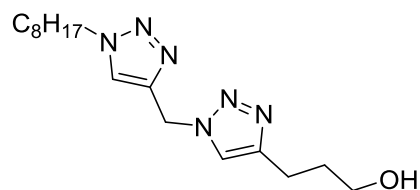
HRMS (ESI): m/z 818.30068 $[M]^+$ ($[C_{36}H_{39}IrN_{11}]^+$ calc. 818.30137).

Bis-iodotriazole alcohol **3.48**



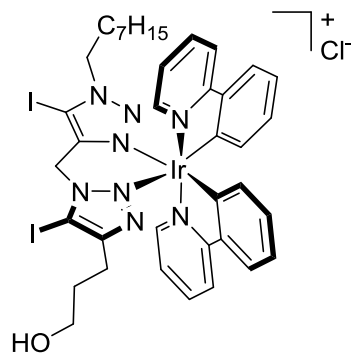
Azide **2.6** (150 mg, 0.41 mmol) was dissolved in dry THF (5 mL) and NaI (181 mg, 1.60 mmol) and $Cu(ClO_4)_2 \cdot 6H_2O$ (292 mg, 0.79 mmol) were added. The reaction mixture was stirred for 5 minutes in the dark. TBTA (cat.) was added followed by DBU (57 μ L, 0.39 mmol) in CH_3CN (5 mL) dropwise. Finally, 4-pentyn-1-ol (54.5 mg, 0.39 mmol) was added and the reaction stirred for 16 hours. The solvent was removed *in vacuo* and the crude product taken up in CH_2Cl_2 (30 mL) and washed with EDTA/ NH_4OH solution (2x30 mL) and brine (2x30 mL). The combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. Purification was achieved by column chromatography (silica, 95:5 CH_2Cl_2/CH_3OH) to afford **3.48** as an off-white powder (126.3 mg, 56%).

^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 5.63 (s, 2H, methylene CH_2), 4.34 (t, $J = 7.4$ Hz, 2H, $N-CH_2-CH_2$), 3.68 (t, $J = 6.3$ Hz, 2H, CH_2-OH), 2.77 (t, $J = 7.2$ Hz, 2H, $C-CH_2-CH_2$), 2.40 (br. s, 1H, $-OH$), 1.83 – 1.97 (m, 4H, CH_2), 1.20 – 1.35 (m, 10H, CH_2), 0.86 (t, $J = 6.8$ Hz, 3H, $-CH_3$); **^{13}C NMR** (126 MHz, $CDCl_3$) δ (ppm) 151.90, 144.85, 80.03, 78.61, 61.96, 51.11, 46.59, 31.81, 31.35, 29.94, 29.13, 29.02, 26.45, 22.82, 22.71, 14.19; **HRMS (ESI):** m/z 573.03302 $[M+H]^+$ ($[C_{16}H_{26}I_2N_6O \cdot H]^+$ calc. 573.03244).

Bis-triazole alcohol 3.49

Azide **3.2** (1.2 g, 5.08 mmol) and 4-pentanol-1-ol (407 mg, 4.84 mmol) were dissolved in degassed DMSO/H₂O (1:1, 20 mL). CuSO₄·5H₂O (242 mg, 0.97 mmol), Na ascorbate (383 mg, 1.93 mmol) and TBTA (cat.) were added and the solution was stirred overnight under N₂. The mixture was diluted with H₂O (200 mL) and extracted with CH₂Cl₂ (3x50 mL). The organics were washed with EDTA/NH₄OH solution (2x30 mL) and brine (2x30 mL), dried over MgSO₄ and concentrated *in vacuo* to afford the product as an off-white powder (1.40 g, 90%).

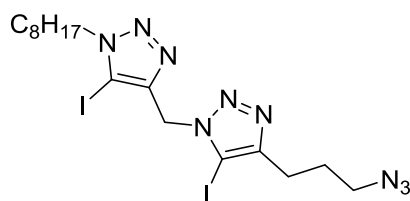
¹H NMR (500 MHz, CDCl₃) δ (ppm) 7.57 (s, 1H, *trzH*), 7.48 (s, 1H, *trzH*), 5.59 (s, 2H, methylene CH₂), 4.29 (t, *J* = 7.3 Hz, 2H, N-CH₂-CH₂), 3.65 (t, *J* = 6.1 Hz, 1H, CH₂-OH), 2.76 (t, *J* = 7.4 Hz, 2H, C-CH₂-CH₂), 1.82 – 1.91 (m, 4H, CH₂), 1.17 – 1.31 (m, 10H, CH₂), 0.83 (t, *J* = 6.9 Hz, 3H, -CH₃); **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 171.22, 122.67, 61.82, 60.46, 50.69, 45.37, 31.97, 31.74, 30.25, 29.07, 28.96, 26.52, 22.64, 22.19, 21.11, 14.26, 14.11; Not observed by MS.

Ir(III) bis-iodotriazole alcohol 3.50·Cl

Bis-triazole alcohol **3.48** (50 mg, 0.084 mmol) and $[\text{Ir}_2(\text{ppy})_4\text{Cl}_2]$ **3.7** (44.9 mg, 0.042 mmol) were suspended in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (1:1, 6 mL) and stirred at 55°C for 16 hours. The solvent was removed *in vacuo* and the solid taken up in CH_2Cl_2 (10 mL). This was washed with H_2O (10 mL) and the organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via preparative TLC (silica, 92:8 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **3.50•Cl** as a yellow/brown solid (69.7 mg, 75%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.24 (d, $J = 5.1$ Hz, 1H, ArH) 8.19 (d, $J = 5.7$ Hz, 1H, ArH), 8.05 – 8.12 (m, 1H, ArH), 7.70 – 7.92 (m, 4H, ArH), 7.55 (d, $J = 7.8$ Hz, 1H, ArH), 7.13 – 7.22 (m, 2H, ArH), 6.85 – 6.94 (m, 2H, ArH), 6.70 – 6.83 (m, 2H, ArH), 6.31 (d, $J = 7.6$ Hz, 1H, ArH), 6.17 (d, $J = 7.7$ Hz, 1H, ArH), 5.88 (d, $J = 16.4$ Hz, 1H, methylene CH_2), 5.66 (d, $J = 16.4$ Hz, 1H, methylene CH_2), 4.08 – 4.23 (t, $J = 7.5$ Hz, 2H, N- CH_2 - CH_2), 3.69 (s, 2H, CH_2 -OH), 2.77 (t, $J = 7.2$ Hz, 2H, C- CH_2 - CH_2), 1.84 – 1.99 (m, 4H, CH_2), 1.01 – 1.36 (m, 10H, CH_2), 0.76 – 0.85 (m, 3H, $-\text{CH}_3$); **HRMS (ESI):** m/z 1073.11033 $[\text{M}]^+$ ($[\text{C}_{38}\text{H}_{42}\text{I}_2\text{IrN}_8\text{O}]^+$ calc. 1073.11947).

Bis-iodotriazole azide **3.51**

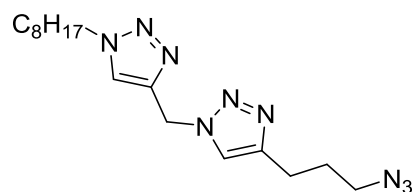


Bis-iodotriazole alcohol **3.48** (100 mg, 0.175 mmol) and NEt_3 (51.2 μL , 0.367 mmol) were added to dry CH_2Cl_2 (5 mL), cooled to 0°C and stirred for 5 minutes under N_2 . MsCl (27.0 μL , 0.350 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and added dropwise before being stirred at RT for 3 hours. The organics were diluted with CH_2Cl_2 (20 mL) and washed with H_2O (2x15 mL), 1M $\text{HCl}_{(\text{aq})}$ (3x15 mL) and brine (2x15 mL). The aqueous layer was extracted with CH_2Cl_2 (15 mL), the organics combined, dried over MgSO_4 and concentrated

in vacuo to give a yellow oil. This was dissolved in dry, degassed DMSO (15 mL) and NaN₃ (39.1 mg, 0.699 mmol) was added. The reaction was stirred at 85°C for 16 hours. After cooling to RT, the reaction was quenched with H₂O (120 mL) and extracted into EtOAc (3x50 mL). The organics were washed with brine (2x20 mL), dried over MgSO₄ and concentrated *in vacuo* to afford an off-white powder (0.108 g, 96%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 5.64 (s, 2H, methylene CH₂), 4.36 (t, *J* = 7.4 Hz, 2H, N-CH₂-CH₂), 3.36 (t, *J* = 6.8 Hz, 2H, CH₂-N₃), 2.75 (t, *J* = 7.4 Hz, 2H, C-CH₂-CH₂), 1.96 – 2.04 (m, 2H, CH₂), 1.84 – 1.93 (m, 2H, N-CH₂-CH₂), 1.22 – 1.35 (m, 10H, CH₂), 0.84 – 0.91 (m, 3H, -CH₃); **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 151.11, 144.86, 79.97, 78.73, 51.12, 50.67, 46.54, 41.11, 31.81, 29.94, 29.13, 29.01, 27.97, 26.45, 23.29, 22.71, 14.19; **HRMS (ESI):** *m/z* 598.03914 [M+H]⁺ ([C₁₆H₂₅I₂N₉H]⁺ calc. 598.03950).

Bis-triazole azide 3.52

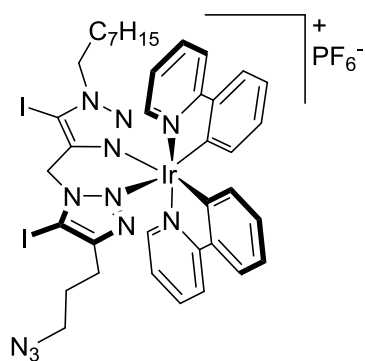


Bis-triazole alcohol **3.49** (1.2 g, 3.90 mmol) and NEt₃ (1.14 mL, 8.20 mmol) were added to dry CH₂Cl₂ (20 mL), cooled to 0°C and stirred for 5 minutes under N₂. MsCl (0.76 μL, 7.80 mmol) was dissolved in dry CH₂Cl₂ (10 mL) and added dropwise before being stirred at RT for 3 hours. The organics were diluted with CH₂Cl₂ (20 mL) and washed with H₂O (2x25 mL), 1M HCl_(aq) (3x25 mL) and brine (2x25 mL). The aqueous layer was extracted with CH₂Cl₂ (15 mL), the organics combined, dried over MgSO₄ and concentrated *in vacuo* to give a yellow oil. This was dissolved in dry, degassed DMSO (30 mL) and NaN₃ (0.875 g, 15.6 mmol) was added. The reaction was stirred at 85°C for 16 hours. After cooling to RT, the reaction was quenched with H₂O (200 mL) and extracted into EtOAc (4x50 mL). The

organics were washed with brine (2x50 mL), dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via column chromatography (silica, 98:2 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford off-white powder **3.52** (0.66 g, 51%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.57 (s, 1H, trzH), 7.48 (s, 1H, trzH), 5.62 (s, 2H, methylene CH_2), 4.31 (t, $J = 7.3$ Hz, 2H, N- CH_2 - CH_2), 3.32 (t, $J = 6.8$ Hz, 2H, CH_2 - N_3), 2.77 (t, $J = 7.5$ Hz, 2H, C- CH_2 - CH_2), 1.82 – 2.01 (m, 4H, CH_2), 1.17 – 1.35 (m, 10H, CH_2), 0.86 (t, $J = 6.7$ Hz, 3H, - CH_3); ^{13}C NMR (101 MHz, CDCl_3) δ (ppm) 147.20, 141.89, 122.85, 121.33, 50.75, 45.43, 31.78, 30.29, 29.11, 29.00, 28.56, 26.56, 22.78, 22.69, 14.16; Not seen by ESI MS.

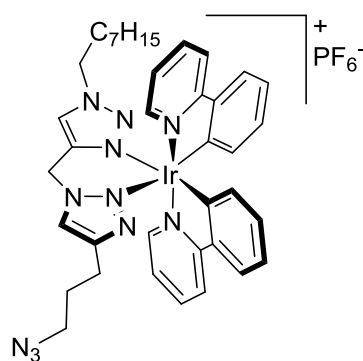
Ir(III) bis-iodotriazole azide **3.53**· PF_6



Bis-iodotriazole azide **3.51** (20 mg, 0.033 mmol) and $[\text{Ir}_2(\text{ppy})_4\text{Cl}_2]$ **3.7** (18 mg, 0.017 mmol) were suspended in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (1:1, 5 mL) and stirred at 55°C for 16 hours. The solvent was removed *in vacuo* and the solid taken up in CH_2Cl_2 (10 mL). This was washed with H_2O (10 mL) and the organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via preparative TLC (silica, 94:6 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$). The pure product was washed with 0.1 M $\text{NH}_4\text{PF}_6(\text{aq})$ (8x10 mL) and H_2O (2x10 mL), the organics combined, dried over MgSO_4 and the solvent removed *in vacuo* to afford **3.53**· PF_6 as a yellow solid (30.9 mg, 84%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.23 – 8.29 (m, 1H, ArH), 8.01 – 8.07 (m, 1H, ArH), 7.83 – 7.93 (m, 2H, ArH), 7.74 – 7.82 (m, 3H, ArH), 7.52 – 7.60 (m, 2H, ArH), 7.10 – 7.16 (m, 1H, ArH), 6.87 – 6.94 (m, 2H, ArH), 6.75 – 6.85 (m, 2H, ArH), 6.32 (d, $J = 7.6$ Hz, 1H, ArH), 6.20 (d, $J = 7.7$ Hz, 1H, ArH), 5.80 (d, $J = 16.8$ Hz, 1H, methylene CH_2), 5.67 (d, $J = 16.7$ Hz, 1H, methylene CH_2), 4.12 – 4.20 (m, 2H, N- CH_2 - CH_2), 2.96 – 3.10 (m, 2H, CH_2 - N_3), 2.50 – 2.67 (m, 2H, C- CH_2 - CH_2), 1.54 – 1.77 (m, 4H, CH_2), 1.05 – 1.35 (m, 10H, CH_2), 0.79 – 0.99 (m, 3H, $-\text{CH}_3$); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 168.61, 168.22, 153.16, 150.46, 149.94, 146.97, 144.17, 144.04, 143.81, 143.68, 138.48, 138.16, 132.53, 131.90, 129.82, 129.78, 123.97, 123.91, 123.70, 123.08, 122.57, 122.50, 119.62, 119.37, 85.42, 52.63, 49.93, 46.09, 31.84, 29.03, 28.82, 28.75, 27.05, 25.86, 23.26, 22.74, 14.24; **^{19}F NMR** (377 MHz, CDCl_3) δ (ppm) -72.33 (d, $J = 714.8$ Hz, PF_6); **HRMS (ESI):** m/z 1098.12584 $[\text{M}]^+$ ($[\text{C}_{38}\text{H}_{41}\text{I}_2\text{IrN}_{11}]^+$ calc. 1098.12595).

Ir(III) bis-triazole azide **3.54**· PF_6

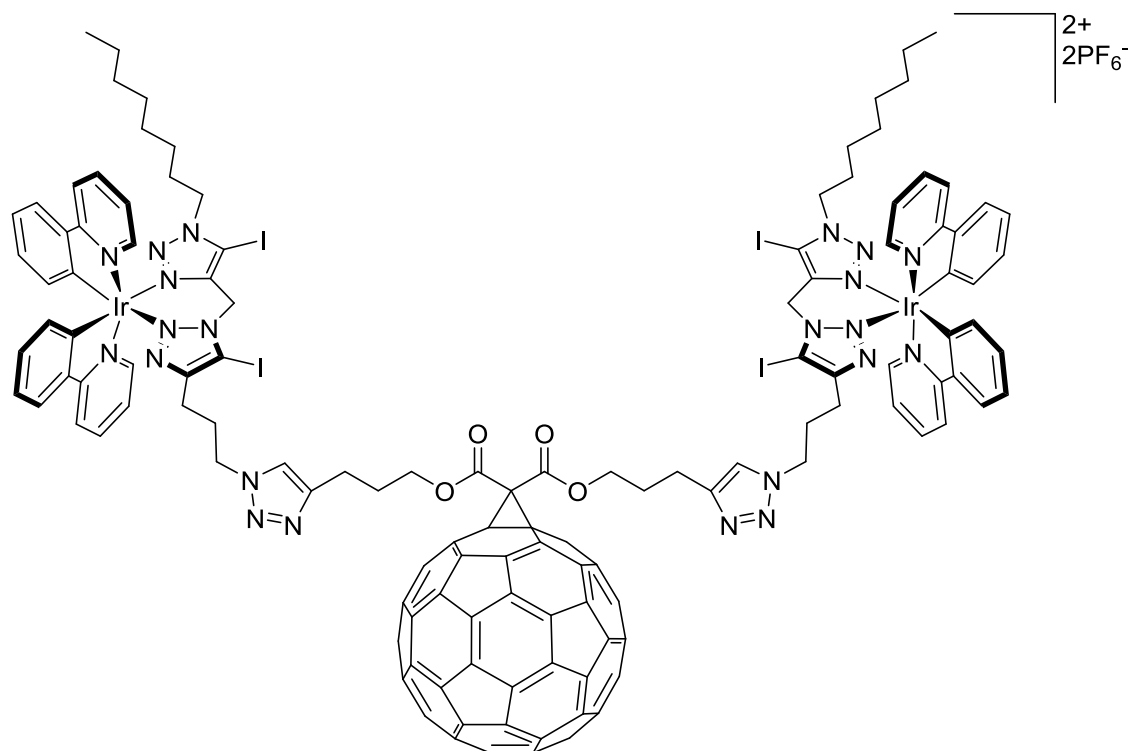


Bis-triazole azide **3.52** (25 mg, 0.072 mmol) and $[\text{Ir}_2(\text{ppy})_4\text{Cl}_2]$ **3.7** (38.8 mg, 0.036 mmol) were suspended in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (1:1, 5 mL) and stirred at 55°C for 16 hours. The solvent was removed *in vacuo* and the solid taken up in CH_2Cl_2 (10 mL). This was washed with H_2O (10 mL) and the organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved via preparative TLC (silica, 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$). The pure product was washed

with 0.1 M $\text{NH}_4\text{PF}_6(\text{aq})$ (8x10 mL) and H_2O (2x10 mL), the organics combined, dried over MgSO_4 and the solvent removed *in vacuo* to afford **3.54**• PF_6 as a yellow solid (38.7 mg, 54%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.19 (s, 1H, *trzH*), 8.16 (d, $J = 5.6$ Hz, 1H, *ArH*), 8.00 (s, 1H, *trzH*), 7.88 – 7.97 (m, 3H, *ArH*), 7.75 – 7.84 (m, 2H, *ArH*), 7.60 (ddd, $J = 7.5, 5.8, 1.4$ Hz, 2H, *ArH*), 7.12 (t, $J = 6.1$ Hz, 1H, *ArH*), 7.04 (t, $J = 6.1$ Hz, 1H, *ArH*), 6.90 – 6.98 (m, 2H, *ArH*), 6.79 – 6.89 (m, 2H, *ArH*), 6.38 (d, $J = 7.6$, 1H, *ArH*), 6.23 (d, $J = 7.4$ Hz, 1H, *ArH*), 6.07 (d, $J = 16.3$ Hz, 1H, methylene CH_2), 5.75 (d, $J = 16.3$ Hz, 1H, methylene CH_2), 4.14 (t, $J = 7.1$ Hz, 2H, $\text{N-CH}_2\text{-CH}_2$), 3.03 – 3.16 (d, $J = 7.0$ Hz, 2H, $\text{CH}_2\text{-N}_3$), 2.63 (t, $J = 7.2$ Hz, 2H, $\text{C-CH}_2\text{-CH}_2$), 1.59 – 1.78 (m, 4H, CH_2), 1.09 – 1.33 (m, 10H, CH_2), 0.88 (t, $J = 7.1$ Hz, 3H, $-\text{CH}_3$); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 169.49, 168.63, 149.64, 149.57, 148.30, 145.40, 144.15, 143.91, 139.55, 138.14, 137.82, 132.55, 131.72, 129.95, 129.76, 127.50, 127.25, 124.06, 122.38, 122.25, 119.72, 119.30, 51.83, 50.67, 50.29, 44.50, 31.80, 29.54, 29.04, 28.81, 27.80, 26.10, 22.70, 22.44, 14.19; **^{19}F NMR** (377 MHz, CDCl_3) δ (ppm) -72.11 (d, $J = 712.5$ Hz, PF_6); **HRMS (ESI)**: m/z 846.33236 $[\text{M}]^+$ ($[\text{C}_{38}\text{H}_{43}\text{IrN}_{11}]^+$ calc. 846.33267).

Di-Ir(III) fullerene hexa-triazole XB receptor $3.55 \cdot (\text{PF}_6)_2$

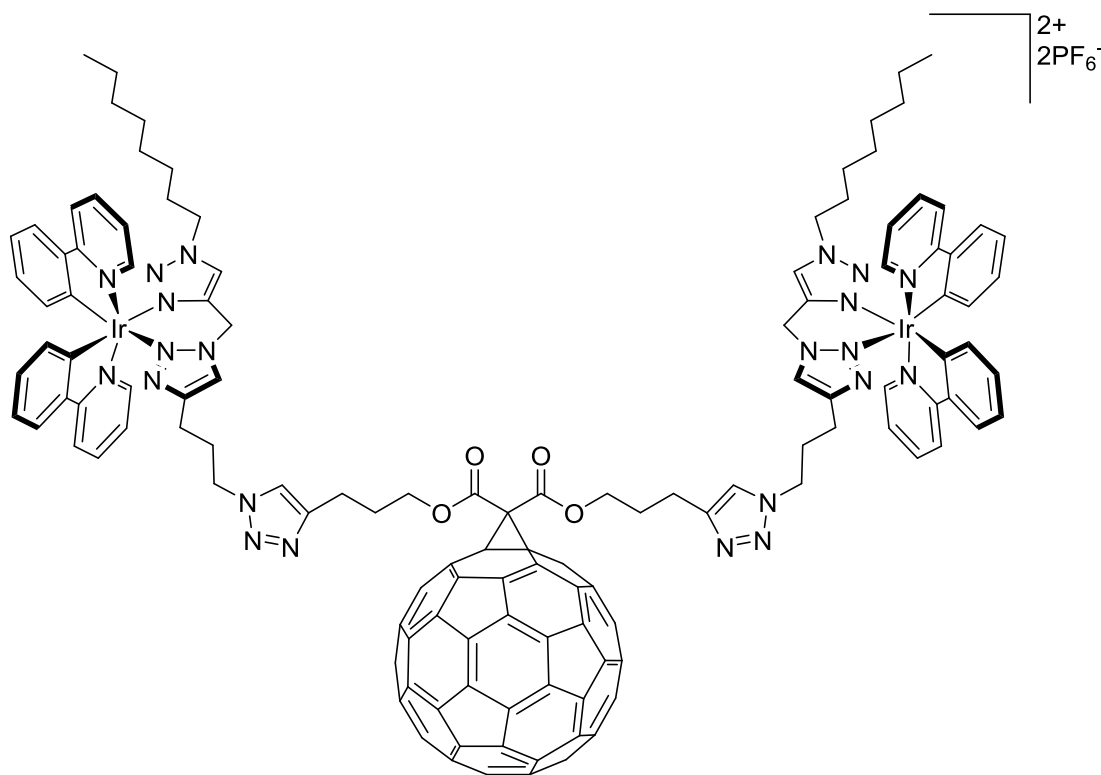


Ir(III) azide **3.53**· PF_6 (20 mg, 0.016 mmol) and fullerene bis-alkyne **3.41** (7.68 mg, 0.0080 mmol) were dissolved in dry CH_2Cl_2 (2 mL). TBTA (3.42 mg, 0.0064 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ (2.40 mg, 0.0064 mmol) were added and the solution stirred for 3 days. The reaction was diluted with CH_2Cl_2 (20 mL) and washed with EDTA/ NH_4OH solution (2x20 mL). The organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved through size-exclusion chromatography (CHCl_3) to afford **3.55**· $(\text{PF}_6)_2$ as a brown solid (11.9 mg, 43%).

^1H NMR (500 MHz, CDCl_3) δ (ppm) 8.28 – 8.37 (m, 2H, ArH), 8.09 – 8.15 (m, 2H, ArH), 8.01 – 8.09 (m, 2H, ArH), 7.83 – 7.92 (m, 4H, trzH, ArH), 7.76 – 7.83 (m, 2H, ArH), 7.68 – 7.76 (m, 4H, ArH), 7.48 – 7.66 (m, 6H, ArH), 6.92 (t, $J = 7.8$ Hz, 4H, ArH), 6.80 (t, $J = 7.7$ Hz, 4H, ArH), 6.26 – 6.33 (m, 2H, ArH), 6.19 – 6.25 (m, 2H, ArH), 5.67 – 5.83 (m, 4H, methylene CH_2), 3.84 – 4.62 (m, 16H, CH_2), 2.60 – 2.99 (m, 8H, CH_2), 1.84 – 1.92 (m, 4H, CH_2), 1.10 – 1.35 (m, 24H, CH_2), 0.80 – 0.91 (m, 6H, $-\text{CH}_3$); ^{13}C NMR (126 MHz, CDCl_3) δ

(ppm) 145.41, 145.39, 145.33, 144.83, 144.78, 144.75, 144.02, 143.99, 143.16, 143.16, 142.34, 141.12, 132.22, 122.56, 66.79, 51.18, 46.66, 31.87, 31.85, 30.00, 29.85, 29.19, 29.10, 29.07, 28.80, 26.51, 26.02, 22.78, 22.76, 14.28, 14.25; ^{19}F NMR (377 MHz, CDCl_3) δ (ppm) -72.09 (d, $J = 716.3$ Hz, PF_6); **HRMS (ESI):** m/z 1575.67057 $[\text{M}]^{2+}$ ($[\text{C}_{149}\text{H}_{96}\text{I}_4\text{Ir}_2\text{N}_{22}\text{O}_4]^{2+}$ calc. 1575.67222).

Di-Ir(III) fullerene hexa-triazole HB receptor 3.56·(PF₆)₂

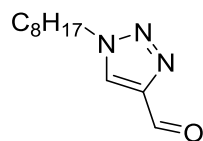


Ir(III) azide **3.54**· PF_6 (38.7 mg, 0.039 mmol) and fullerene bis-alkyne **3.41** (18.6 mg, 0.020 mmol) were dissolved in dry CH_2Cl_2 (3 mL). TBTA (8.28 mg, 0.016 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ (5.82 mg, 0.016 mmol) were added and the solution stirred for 3 days. The reaction was diluted with CH_2Cl_2 (20 mL) and washed with EDTA/ NH_4OH solution (2x20 mL). The organics were dried over MgSO_4 and concentrated *in vacuo*. Purification was achieved through size-exclusion chromatography (CHCl_3) and preparative TLC (silica, 98:2 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$) to afford **3.56**·(PF₆)₂ as a brown solid (30 mg, 52%).

¹H NMR (500 MHz, CDCl₃) δ (ppm) 8.13 (s, J = 5.9 Hz, 2H, ArH), 8.09 (s, 2H, trzH), 8.07 (s, 4H, trzH, ArH), 7.97 (s, 2H, trzH), 7.86 – 7.92 (m, 4H, ArH), 7.77 (q, J = 8.2 Hz, 4H, ArH), 7.58 (d, J = 7.7 Hz, 4H, ArH), 7.06 – 7.15 (m, 4H, ArH), 6.90 – 6.96 (m, 4H, ArH), 6.78 – 6.88 (m, 4H, ArH), 6.36 (d, J = 7.5 Hz, 2H, ArH), 6.24 (d, J = 7.7 Hz, 2H, ArH), 5.92 (d, J = 16.9 Hz, 2H, methylene CH₂), 5.79 (d, J = 16.4 Hz, 2H, methylene CH₂), 4.53 (t, J = 6.5 Hz, 4H, O-CH₂), 4.17 (t, J = 7.1 Hz, 4H, N-CH₂-CH₂), 4.07 (t, J = 6.9 Hz, 4H, N-CH₂-CH₂), 2.77 – 2.86 (m, 4H, CH₂), 2.43 – 2.53 (m, 4H, CH₂), 2.16 – 2.22 (m, 4H, O-CH₂-CH₂), 1.96 – 2.08 (m, 4H, CH₂), 1.62 – 1.73 (m, 4H, N-CH₂-CH₂), 1.10 – 1.35 (m, 20H, CH₂), 0.96 – 1.06 (m, 4H, CH₂), 0.81 – 0.91 (m, 6H, -CH₃); **¹³C NMR** (126 MHz, CDCl₃) δ (ppm) 163.75, 145.42, 145.33, 144.84, 144.78, 144.19, 144.04, 143.17, 143.14, 142.35, 142.05, 141.11, 139.22, 131.94, 124.10, 119.65, 119.35, 71.74, 66.86, 51.94, 31.85, 29.51, 29.10, 28.84, 26.15, 22.75, 21.85, 14.25; **¹⁹F NMR** (377 MHz, CDCl₃) δ (ppm) -71.85 (d, J = 716.3 Hz, PF₆); **HRMS (ESI):** m/z 1323.87862 [M]²⁺ ([C₁₄₉H₁₀₀Ir₂N₂₂O₄]²⁺ calc. 1323.87893).

6.2.3 Chapter Four

Triazole aldehyde 4.1

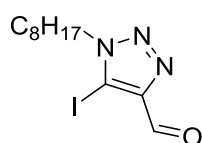


Oxalyl chloride (2 mL, 23.7 mmol) and dry DMSO (3.36 mL, 47.3 mmol) were dissolved in CH₂Cl₂ (30 mL) at -78°C and the mixture stirred for 15 minutes. Alcohol **3.1** (1 g, 4.72 mmol) in CH₂Cl₂ (20 mL) was added, and after 15 minutes this was followed by NEt₃ (9.89 mL, 71.0 mmol). After stirring for 1 hour, the solution was quenched with 1M HCl_(aq) (20 mL) and extracted with CH₂Cl₂ (2x20 mL). The organics were dried over MgSO₄ and the

solvent removed *in vacuo*. Purification was achieved via column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) to afford **4.1** as an off-white solid (0.87 g, 88%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 10.04 (s, 1H, CHO), 8.10 (s, 1H, *trzH*), 4.36 (t, *J* = 7.3 Hz, 2H, N-CH₂), 1.81 – 1.92 (m, 2H, N-CH₂-CH₂), 1.14 – 1.28 (m, 10H, CH₂), 0.74 – 0.83 (m, 3H, -CH₃); **MS (ESI)**: *m/z* 232.2 [M+Na]⁺ ([C₁₁H₁₉N₃O·Na]⁺ calc. 232.1).

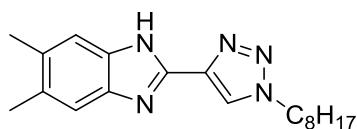
Iodotriazole aldehyde **4.2**



Oxalyl chloride (0.5 mL, 5.95 mmol) and dry DMSO (0.84 mL, 11.9 mmol) was dissolved in CH₂Cl₂ (20 mL) at -78°C and the mixture stirred for 15 minutes. Alcohol **2.5** (400 mg, 1.19 mmol) in CH₂Cl₂ (20 mL) was added, and after 15 minutes this was followed by NEt₃ (2.49 mL, 17.85 mmol). After stirring for 1 hour, the solution was quenched with 1M HCl_(aq) (20 mL) and extracted with CH₂Cl₂ (2x20 mL). The organics were dried over MgSO₄ and the solvent removed *in vacuo*. Purification was achieved via column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) to afford **4.2** as an off-white solid (199.7 mg, 50%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 10.14 (s, 1H, CHO), 4.45 (t, *J* = 7.3 Hz, 2H, N-CH₂), 1.94 (m, 2H, N-CH₂-CH₂), 1.31 (d, 10H, CH₂), 0.88 (t, *J* = 6.7 Hz, 3H, -CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 184.45, 111.48, 50.67, 22.75, 14.21, 31.83, 29.86, 29.16, 26.49; **MS (ESI)**: *m/z* 357.9 [M+Na]⁺ ([C₁₁H₁₈IN₃O·Na]⁺ calc. 350.0).

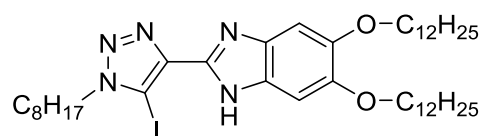
Benzimidazole-triazole **4.3**



Triazole aldehyde **4.1** (50 mg, 0.24 mmol), 4,5-dimethyl-1,2-phenylenediamine (34.3 mg, 0.25 mmol), and NH_4OAc (18.5 mg, 0.24) were dissolved in ethanol (5 mL) and stirred at reflux for 4 hours. After cooling to RT a precipitate formed which was collected by vacuum filtration to afford **4.3** as an off-white solid (56.0 mg, 72%).

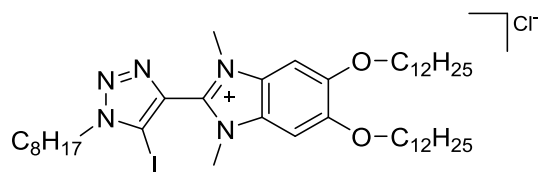
^1H NMR (400 MHz, CDCl_3) δ 8.38 (s, 1H, NH), 7.48 (s, 2H, ArH), 4.47 (t, $J = 7.1$ Hz, 2H, N- CH_2), 1.99 (t, $J = 7.2$ Hz, 2H, N- $\text{CH}_2\text{-CH}_2$), 1.16 – 1.42 (m, 10H, CH_2), 0.86 (t, $J = 6.4$ Hz, 3H, - CH_3); **^{13}C NMR** (101 MHz, CDCl_3) δ (ppm) 143.47, 140.36, 132.11, 122.94, 51.04, 31.83, 30.27, 29.84, 29.16, 29.09, 26.60, 22.71, 20.61, 14.18; **MS (ESI):** m/z 326.2 $[\text{M}+\text{H}]^+$ ($[\text{C}_{19}\text{H}_{28}\text{N}_5\cdot\text{H}]^+$ calc. 326.2).

Acyclic benzimidazole-iodotriazole **4.7**



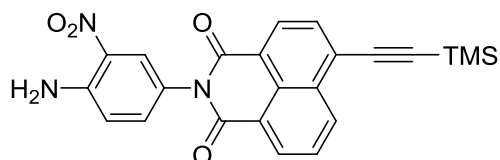
Diamine **4.6** (50 mg, 0.105 mmol), iodotriazole aldehyde **4.2** (33.5 mg, 0.10 mmol) and NH_4OAc (7.8 mg, 0.10) were dissolved in ethanol (5 mL) and stirred at 75°C for 4 hours. After cooling to RT the pure product was isolated by vacuum filtration to afford **4.7** as a brown solid (55.5 mg, 67%).

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ (ppm) 12.73 (s, 1H, NH), 7.24 (s, 1H, ArH), 6.97 (s, 1H, ArH), 4.48 (t, $J = 7.2$ Hz, 2H, N- CH_2), 3.98 (q, $J = 6.6$ Hz, 4H, O- CH_2), 1.89 (m, 2H, N- $\text{CH}_2\text{-CH}_2$), 1.74 (q, $J = 6.8$ Hz, 4H, O- $\text{CH}_2\text{-CH}_2$), 1.31 (m, 46H), 0.86 (t, $J = 6.5$ Hz, 9H); **HRMS (ESI):** m/z 792.46401 $[\text{M}+\text{H}]^+$ ($[\text{C}_{41}\text{H}_{70}\text{IN}_5\text{O}_2\cdot\text{H}]^+$ calc. 792.46470).

Methylated benzimidazolium-iodotriazole 4.8·Cl

CH₃I (1 mL) was added to a solution of benzimidazole-iodotriazole **4.7** (10 mg, 0.0126 mmol) in CH₂Cl₂ (1 mL). The reaction was stirred overnight in the dark. The solvent and excess CH₃I were removed *in vacuo* and the remaining solid taken up in CH₂Cl₂ (10 mL). This was washed with an aqueous solution of 1M NH₄Cl (3x10 mL) and the combined organics were dried over MgSO₄ and concentrated to afford the product as an off-white solid (10.8 mg, quant.)

¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.09 (s, 2H, ArH), 4.44 – 4.57 (m, N-CH₂, 2H), 4.02 – 4.16 (m, 4H, CH₂), 3.99 (s, 6H, N-CH₃), 1.81 – 2.06 (m, 6H, CH₂), 1.21 – 1.44 (m, 46H, CH₂), 0.88 (t, *J* = 6.1 Hz, 9H, -CH₃); **MS (ESI):** *m/z* 820.5 [M]⁺ ([C₄₃H₇₅IN₅O₂]⁺ calc. 820.5).

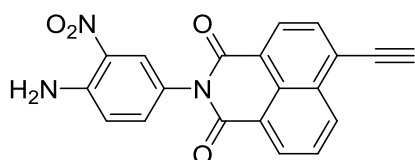
TMS-protected naphthalimide alkyne 4.11

A flask was charged with nitro-amine **4.10** (1.1 g, 2.67 mmol), Pd(PPh₃)₂Cl₂ (93.5 mg, 0.13 mmol) and CuI (24.5 mg, 0.13 mmol), sealed and evacuated with N₂. NEt₃ (1.87 mL, 13.35 mmol), THF (30 mL) and TMS acetylene (0.414 mL, 2.94 mmol) were added and the solution stirred for 2 days at 50°C. The mixture was poured into an aqueous solution of 1M NH₄Cl (100 mL) and extracted with EtOAc (4x30 mL). The organics were washed with brine (2x30 mL), dried over MgSO₄ and concentrated *in vacuo*. Purification was achieved via

column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH to afford yellow solid **4.11** (1.03 g, 90%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.66 – 8.74 (m, 2H, ArH), 8.56 (d, J = 7.6 Hz, 1H, ArH), 8.14 (d, J = 2.4 Hz, 1H, ArH), 7.94 (d, J = 7.6 Hz, 1H, ArH), 7.87 (t, J = 8.2, 1H, ArH), 7.29 – 7.33 (m, 1H, ArH), 6.96 (d, J = 8.8 Hz, 1H, ArH), 6.26 (s, 2H, -NH₂), 0.38 (s, 9H, -CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 164.32, 164.03, 144.90, 136.11, 133.24, 132.35, 132.08, 132.05, 131.42, 131.01, 128.36, 128.13, 127.79, 126.73, 124.01, 122.82, 122.17, 119.68, 106.17, 101.24, -0.02; Not seen by ESI MS.

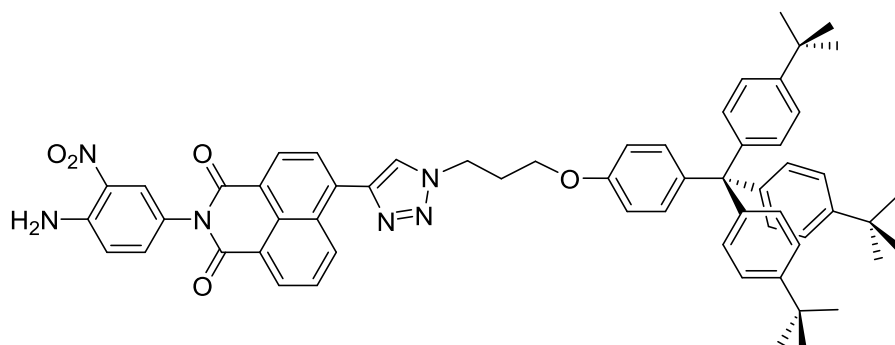
Naphthalimide alkyne **4.12**



K₂CO₃ (83.3 mg, 0.60 mmol) was dissolved in H₂O (0.5 mL) and added to a solution of TMS-protected alkyne **4.11** (500 mg, 1.16 mmol) in 1:1 CH₂Cl₂/CH₃OH (10 mL). The mixture was stirred for 2 days in the dark before the solvent was removed *in vacuo* and the solid taken up in EtOAc (20 mL), whereupon it was washed with H₂O (20 mL) and brine (20 mL). The aqueous layer was extracted with EtOAc (8x100 mL) and the organics dried over MgSO₄ and concentrated to afford **4.12** as a yellow solid (337 mg, 81%).

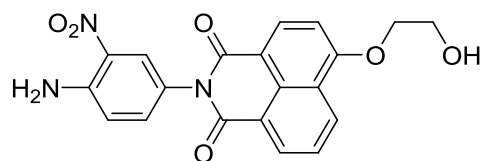
¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm) 8.70 (d, J = 8.4 Hz, 1H, ArH), 8.58 (d, J = 7.4 Hz, 1H, ArH), 8.47 (d, J = 7.5 Hz, 1H, ArH), 7.99 – 8.13 (m, 3H, ArH), 7.64 (s, 2H, -NH₂), 7.43 (d, J = 9.1 Hz, 1H, ArH), 7.14 (d, J = 9.2 Hz, 1H, ArH), 5.14 (s, 1H, -CH); **¹³C NMR** (101 MHz, DMSO) δ (ppm) 163.60, 163.31, 146.01, 136.65, 131.65, 131.32, 131.25, 129.86, 129.71, 128.39, 127.71, 125.85, 125.51, 123.34, 123.12, 119.33, 80.13, 79.29, 78.96, 78.63; **HRMS (ESI):** m/z 380.06421 [M+Na]⁺ ([C₂₀H₁₁N₃O₄·Na]⁺ calc. 380.06418).

Stopper triazole 4.13



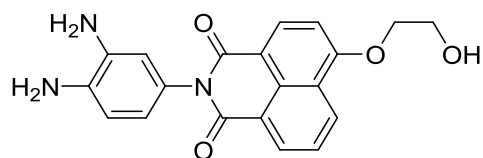
[Cu(CH₃CN)₄][PF₆] (20.78 mg, 0.056 mmol) and TBTA (29.5 mg, 0.056 mmol) were added to a dry, degassed mixture of CHCl₃ (20 mL). Azide **2.30** (350.8 mg, 0.588 mmol) and alkyne **4.12** (203 mg, 0.56 mmol) were added and the reaction stirred for 16 hours at RT. The reaction mixture was diluted with CH₂Cl₂ (20 mL) and washed with EDTA/NH₄OH solution (2x15 mL). The organics were dried over MgSO₄ and concentrated *in vacuo*. Purification was achieved by column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) to afford **4.13** as a yellow powder (251.1 mg, 47%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.04 – 9.09 (m, 1H, ArH), 8.63 – 8.69 (m, 2H, ArH), 8.14 – 8.17 (m, 1H, ArH), 8.03 (s, 1H, trzH), 7.96 (d, *J* = 7.6 Hz, 1H, ArH), 7.77 (t, *J* = 8.2 Hz, 1H, ArH), 7.30 – 7.35 (m, 1H, ArH), 7.19 – 7.24 (m, 6H, stopper-ArH), 7.03 – 7.14 (m, 8H, stopper-ArH), 6.95 – 6.99 (m, 2H, ArH), 6.76 – 6.81 (m, 2H, stopper-ArH), 6.30 (s, 2H, -NH₂), 4.77 (t, *J* = 6.9 Hz, 2H, N-CH₂), 4.05 (t, *J* = 5.6 Hz, 2H, O-CH₂), 2.49 – 2.57 (m, 2H, CH₂), 1.29 (s, 27H, -CH₃); ¹³C NMR (101 MHz, CDCl₃) δ (ppm) 148.58, 144.10, 136.20, 135.04, 133.50, 132.59, 132.20, 131.50, 130.81, 127.68, 127.53, 126.79, 124.32, 124.22, 119.62, 113.05, 63.20, 47.73, 34.44, 31.50, 31.06, 30.09, 29.85; HRMS (ESI): *m/z* 967.45148 [M+Na]⁺ ([C₆₀H₆₀N₆O₅·Na]⁺ calc. 967.45174).

Naphthalimide nitro-amine 4.14

K_2CO_3 (1.70 g, 12.2 mmol) and nitro-amine **4.10** (500 mg, 1.22) were mixed in ethylene glycol (20 mL) and stirred at 150°C for 6 hours. The reaction was cooled to RT, added to ice-cold H_2O (100 mL) and the precipitate collected by filtration whereupon it was washed with H_2O (3x50 mL) and Et_2O (5x50 mL) to afford **4.14** as a yellow solid (289.1 mg, 61%).

^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ (ppm) 8.72 (dd, $J = 8.4, 1.2$ Hz, 1H, ArH), 8.51 (dd, $J = 7.2, 1.2$ Hz, 1H, ArH), 8.45 (d, $J = 8.3$ Hz, 1H, ArH), 8.02 (d, $J = 2.4$ Hz, 1H, ArH), 7.86 (dd, $J = 8.4, 7.3$ Hz, 1H, ArH), 7.62 (s, 2H, $-\text{NH}_2$), 7.33 – 7.43 (m, 2H, ArH), 7.12 (d, $J = 8.9$ Hz, 1H, ArH), 5.13 (t, $J = 5.8$ Hz, 1H, $-\text{OH}$), 4.37 (t, $J = 4.7$ Hz, 2H, $\text{O}-\text{CH}_2$), 3.96 – 3.89 (m, 2H, $\text{OH}-\text{CH}_2$); **^{13}C NMR** (126 MHz, $\text{DMSO}-d_6$) δ (ppm) 164.07, 163.40, 159.98, 145.92, 136.88, 133.36, 131.16, 129.72, 129.13, 128.87, 126.24, 125.86, 123.50, 123.08, 122.47, 119.27, 114.62, 106.87, 71.07, 59.40; **HRMS (ESI):** m/z 394.10333 $[\text{M}+\text{H}]^+$ ($[\text{C}_{20}\text{H}_{15}\text{N}_3\text{O}_6\cdot\text{H}]^+$ calc. 394.10336).

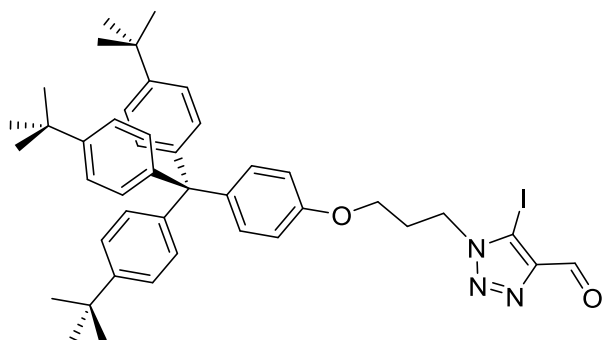
Naphthalimide diamine 4.15

Alcohol **4.14** (630 mg, 1.60 mmol), Zn powder (2.09 g, 32.0 mmol), 1M $\text{NH}_4\text{Cl}_{(\text{aq})}$ solution (15 mL) and $\text{CuSO}_4\cdot 5\text{H}_2\text{O}$ (10 crystals) were heated in ethanol (15 mL) at reflux for 5 hours. The mixture was filtered through Celite® whilst hot and the filtrate concentrated *in vacuo*.

The resulting solid was washed with H₂O (5x30 mL) to afford **4.15** as a yellow powder (524 mg, 90%).

¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm) 8.66 (dd, *J* = 8.4, 1.2 Hz, 1H, Ar*H*), 8.36 – 8.49 (m, 2H, Ar*H*), 7.81 (dd, *J* = 8.4, 7.3 Hz, 1H, Ar*H*), 7.30 (d, *J* = 8.4 Hz, 1H, Ar*H*), 6.54 (d, *J* = 8.1 Hz, 1H, Ar*H*), 6.36 (d, *J* = 2.3 Hz, 1H, Ar*H*), 6.26 (dd, *J* = 8.1, 2.3 Hz, 1H, Ar*H*), 5.09 (t, *J* = 5.8 Hz, 1H, -OH), 4.46 – 4.64 (s, 4H, -NH₂), 4.32 (t, *J* = 4.7 Hz, 2H, OH-CH₂), 3.89 (t, *J* = 5.0 Hz, 2H, O-CH₂); **¹³C NMR** (126 MHz, DMSO) δ (ppm) 164.07, 163.44, 159.79, 135.13, 134.82, 133.23, 131.08, 128.99, 128.64, 126.24, 125.31, 123.06, 122.55, 117.26, 114.75, 114.68, 113.93, 106.88, 71.02, 59.41, 54.92; **HRMS (ESI):** *m/z* 364.12910 [M+H]⁺ ([C₂₀H₁₇N₃O₄·H]⁺ calc. 364.12918).

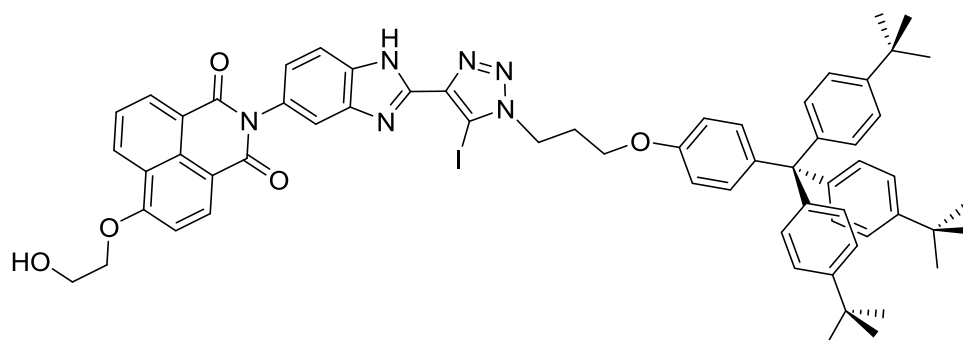
Stopper iodotriazole aldehyde **4.16**



Oxalyl chloride (0.137 mL, 1.6 mmol) and dry DMSO (0.23 mL, 3.25 mmol) were dissolved in CH₂Cl₂ (20 mL) at -78°C and the mixture stirred for 15 minutes. Stopper alcohol **2.31** (250 mg, 0.325 mmol) in CH₂Cl₂ (20 mL) was added, and after 15 minutes this was followed by NEt₃ (0.680 mL, 4.85 mmol). After stirring for 1 hour the solution was quenched with 1M HCl_(aq) (20 mL) and extracted with CH₂Cl₂ (3x20 mL). The organics were dried over MgSO₄ and the solvent removed *in vacuo*. Purification was achieved via column chromatography (silica, 98:2 CH₂Cl₂/CH₃OH) to afford **4.16** as an off-white solid (138 mg, 55%).

¹H NMR (400 MHz, CDCl₃) δ (ppm) 10.13 (s, 1H, CHO), 7.29 – 7.19 – 7.25 (m, 6H, ArH), 7.04 – 7.13 (m, 8H, ArH), 6.71 – 6.78 (m, 2H, ArH), 4.68 (t, *J* = 7.0 Hz, 2H, N-CH₂), 4.01 (t, *J* = 5.6 Hz, 2H, O-CH₂), 2.40 – 2.48 (m, 2H, CH₂), 1.30 (s, 27H, -CH₃); **¹³C NMR** (101 MHz, CDCl₃) δ (ppm) 184.34, 156.15, 148.51, 147.45, 144.18, 140.39, 132.48, 130.83, 124.21, 113.16, 82.18, 63.82, 63.21, 47.71, 34.45, 31.53, 29.61; **HRMS (ESI):** *m/z* 790.28418 [M+Na]⁺ ([C₄₃H₅₀IN₃O₂·Na]⁺ calc. 790.28399).

Benzimidazole-iodotriazole naphthalimide alcohol 4.17

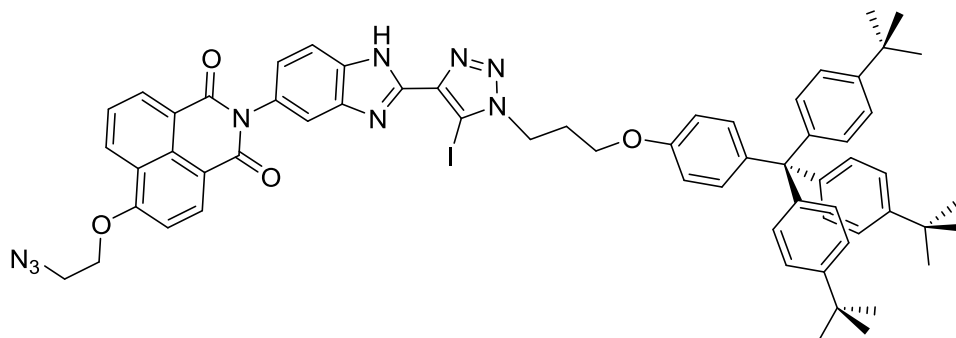


Diamine **4.15** (68 mg, 0.19 mmol), stopper iodotriazole aldehyde **4.16** (130 mg, 0.17 mmol) and NH₄OAc (13 mg, 0.17 mmol) were dissolved in 1:1 CHCl₃/EtOH (10 mL) and stirred at 65°C for 4 hours. After cooling to RT and removing the solvent *in vacuo* the product was purified by preparative TLC (silica, 95:5 CH₂Cl₂/CH₃OH) to afford **4.17** as a yellow solid (92.2 mg, 49%).

¹H NMR (400 MHz, 1:1 CDCl₃/CH₃OD) δ (ppm) 8.74 (d, *J* = 8.4 Hz, 1H, ArH), 8.49 – 8.59 (m, 2H, ArH), 7.67 – 7.77 (m, 2H, ArH), 7.58 (s, 1H, ArH), 7.09 – 7.19 (m, 8H, ArH & stopper-ArH), 6.96 – 7.05 (m, 8H, stopper-ArH), 6.68 – 6.75 (m, 2H, stopper-ArH), 4.68 (t, *J* = 7.0 Hz, 2H, N-CH₂), 4.35 (t, *J* = 4.6 Hz, 2H, OH-CH₂), 4.05 (t, *J* = 4.4 Hz, O-CH₂), 4.00 (t, *J* = 5.6 Hz, O-CH₂), 2.41 (t, *J* = 6.3 Hz, 2H, CH₂), 1.22 (s, 27H, -CH₃); **¹³C NMR** (126 MHz, 1:1 CDCl₃/CH₃OD) δ (ppm) 165.46, 164.88, 160.95, 156.25, 148.25, 144.14, 140.01, 134.17, 132.16, 132.03, 130.61, 129.86, 129.72, 126.00, 123.95, 123.82, 122.23, 114.77,

113.03, 106.27, 70.55, 63.96, 63.00, 60.14, 34.07, 31.00, 29.49; **HRMS (ESI):** m/z 1111.39605 $[M+H]^+$ ($[C_{63}H_{63}IN_6O_5 \cdot H]^+$ calc. 1111.39774).

Benzimidazole-iodotriazole naphthalimide azide **4.18**

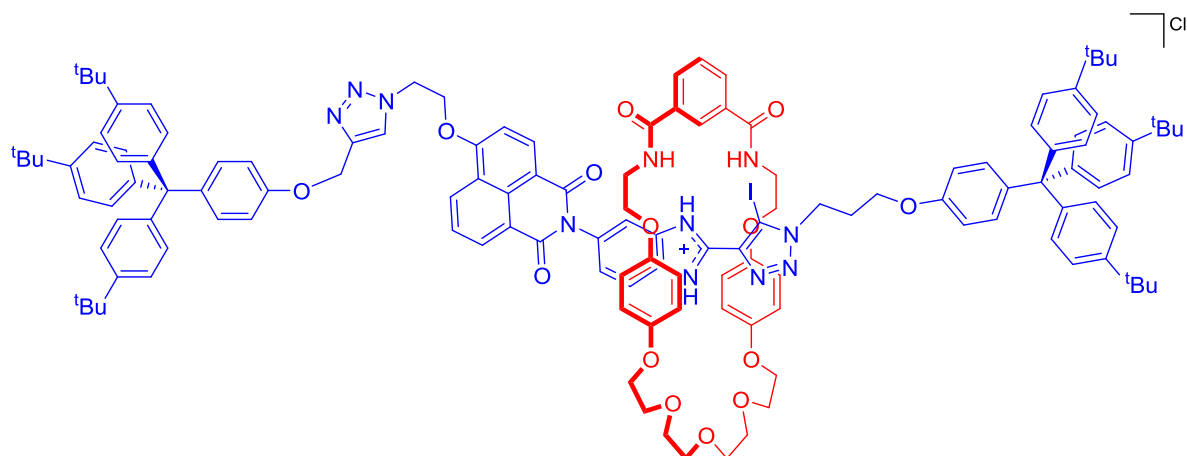


Alcohol **4.17** (50 mg, 0.089 mmol) and NEt_3 (40 μ L, 0.19 mmol) were dissolved in dry CH_2Cl_2 (5 mL) and stirred for 5 minutes at $0^\circ C$. $MsCl$ (20 mL, 0.18 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise and the reaction stirred for 3 hours at RT. The reaction mixture was washed with water (2x10 mL), 1M $HCl_{(aq)}$ (3x10 mL) and brine (3x10 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* to afford a yellow oil. This was dissolved in dry, degassed DMSO (10 mL) containing NaN_3 (19.9 mg, 0.356 mmol) and the mixture was heated at $85^\circ C$ for 16 hours under N_2 . The solution was cooled to RT and partitioned between water (50 mL) and EtOAc (50 mL). The aqueous layer was washed with EtOAc (2x15 mL). The combined organics were washed with brine (3x15 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification was achieved via preparative TLC (silica, 98:2 CH_2Cl_2/CH_3OH) to afford **4.18** as a yellow solid (28.1 mg, 55%).

^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.55 – 8.74 (m, 3H, ArH), 7.79 (t, $J = 7.8$ Hz, 1H, ArH), 7.18 – 7.25 (m, 8H, ArH & stopper-ArH), 7.02 – 7.13 (m, 10H, ArH & stopper-ArH), 6.73 – 6.81 (m, 2H, stopper-ArH), 4.73 (t, $J = 7.0$ Hz, 2H, N- CH_2), 4.49 (t, $J = 4.8$ Hz, 2H, O- CH_2), 4.00 – 4.08 (m, 2H, O- CH_2), 3.83 (t, $J = 4.8$ Hz, 2H, N_3 - CH_2), 2.43 – 2.42 (m, 2H, CH_2), 1.30 (s, 27H, $-CH_3$); **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 171.24, 148.39, 144.14,

132.38, 130.75, 124.15, 123.58, 63.12, 62.66, 60.48, 50.28, 41.00, 34.96, 34.37, 32.00, 31.46, 29.77, 29.43, 22.76, 21.13, 18.99; **HRMS (ESI):** m/z 1136.40198 $[M+H]^+$ ($[C_{63}H_{62}IN_9O_4 \cdot H]^+$ calc. 1136.40422).

Benzimidazolium-iodotriazole chloride [2]rotaxane 4.19·HCl

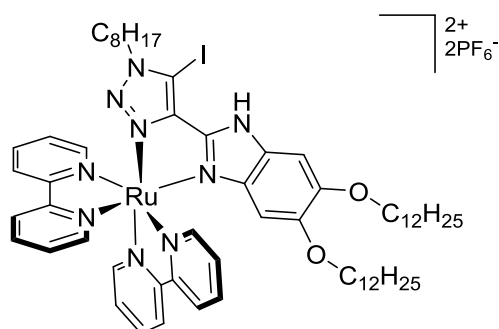


Naphthalimide azide **4.18** (50 mg, 0.044 mmol) was dissolved in dry CH_2Cl_2 (2 mL) and 2M HCl in Et_2O (2 drops) was added and the mixture stirred for 5 minutes. The solvent was removed *in vacuo* and the resulting solid dissolved in dry CH_2Cl_2 (2 mL). Isophthalamide macrocycle **2.9** (39.3 mg, 0.067 mmol) was added and the solution stirred for 5 minutes. $[Cu(CH_3CN)_4][PF_6]$ (16.4 mg, 0.044 mmol), and trityl alkyne **3.20** (36.0 mg, 0.067 mmol) were added and the reaction stirred for 2 days. The solution was diluted with CH_2Cl_2 (20 mL), washed with EDTA/ NH_4OH solution (2x20 mL), brine (2x20 mL) and H_2O (20 mL), the combined organics dried over $MgSO_4$ and the solvent removed *in vacuo*. Purification was achieved via preparative TLC (silica, 95:5 CH_2Cl_2/CH_3OH , 92.5:7.5 CH_2Cl_2/CH_3OH) and the resulting solid washed with 3M $HCl_{(aq)}$ (5x10 mL) to afford light-yellow solid **4.19·HCl** (22 mg, 22%).

^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.28 (s, 1H, int. mac. ArH), 8.85 – 8.96 (m, 2H, ext. mac. ArH), 8.63 (d, $J = 7.1$ Hz, 1H, ArH), 8.59 (d, $J = 7.8$ Hz, 1H, ArH), 8.51 (d, $J = 8.4$ Hz,

(s, 1H, *ArH*), 7.81 (s, 1H, *ArH*), 6.68 – 7.75 (m, 2H, *ArH*), 7.66 (s, 1H, *ArH*), 7.50 – 7.60 (m, 2H, *ArH*), 7.18 – 7.25 (m, 15H, *ArH* & stopper-*ArH*), 7.02 – 7.14 (m, 19H, *ArH* & stopper-*ArH*), 6.80 – 6.86 (m, 4H, stopper-*ArH* & mac. NH), 6.75 (s, 1H, *ArH*), 5.95 – 6.08 (m, 4H, hydroquinone CH_2), 5.76 – 5.85 (m, 4H, hydroquinone CH_2), 5.23 (s, 2H, O- CH_2 -C), 5.02 – 5.11 (m, 4H, N- CH_2 & O- CH_2), 4.73 – 4.80 (m, 2H, N- CH_2), 4.07 – 4.12 (s, 2H, O- CH_2), 3.43 – 3.94 (m, 20H, crown ether CH_2 & mac. CH_2), 3.28 – 3.38 (m, 2H, mac. CH_2), 2.47 – 2.55 (m, 2H, CH_2), 1.27 – 1.32 (m, 27H, $-\text{CH}_3$); ^{13}C NMR (126 MHz, CDCl_3) δ (ppm) 156.38, 156.28, 151.92, 148.58, 148.46, 144.24, 144.11, 132.51, 130.87, 130.81, 124.21, 113.96, 113.25, 71.30, 71.00, 70.18, 63.19, 34.45, 31.54, 31.52, 29.85.

Ru(II) complexed benzimidazole-iodotriazole **Ru4.20**·(PF_6)₂

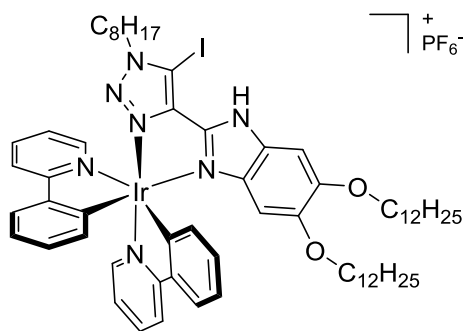


Benzimidazole-iodotriazole **4.7** (10 mg, 0.0126 mmol) and $[\text{Ru}(\text{bpy})_2\text{Cl}_2]$ (7.3 mg, 0.0152 mmol) were dissolved in EtOH/ H_2O (4:1, 5 mL) and heated at 90°C for 16 hours. The EtOH was removed and the resulting solution was precipitated with $\text{KPF}_6(\text{aq})$ and collected by vacuum filtration to afford **Ru4.20**·(PF_6)₂ as an orange crystalline solid (7.51 mg, 40%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.29 – 8.44 (m, 4H, *ArH*), 7.92 – 8.07 (m, 6H, *ArH*), 7.82 – 7.87 (m, 2H, *ArH*), 7.73 – 7.77 (m, 1H, *ArH*), 7.49 – 7.55 (m, 2H, *ArH*), 7.35 – 7.47 (m, 4H, *ArH*), 6.99 (s, 1H, *ArH*), 4.32 – 4.39 (m, 2H, N- CH_2), 3.97 – 4.06 (m, 2H, CH_2), 3.29 – 3.37 (m, 2H, CH_2), 3.15 – 3.23 (m, 2H, CH_2), 1.74 – 1.85 (m, 2H, N- CH_2 - CH_2), 1.24 (s,

46H, CH_2), 0.84 – 0.91 (m, 9H, $-\text{CH}_3$); ^{19}F NMR (376 MHz, CDCl_3) δ (ppm) -72.09 (d, J = 710.6 Hz, PF_6); **HRMS (ESI)**: m/z 602.74923 $[\text{M}]^{2+}$ ($[\text{C}_{61}\text{H}_{86}\text{IN}_9\text{O}_2\text{Ru}]^{2+}$ calc. 602.74908).

Ir(III) complexed benzimidazole-iodotriazole **Ir4.21**· PF_6



Benzimidazole-iodotriazole **4.7** (22.5 mg, 0.028 mmol) and $[\text{Ir}_2(\text{ppy})_4\text{Cl}_2]$ **3.7** (15.2 mg, 0.014 mmol) were suspended in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (1:1, 5 mL) and stirred at 55°C for 16 hours. The solvent was removed *in vacuo* and purification was achieved by preparative TLC (silica, 97:3 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$). The product was taken up in CH_2Cl_2 (20 mL) and washed with 0.1 M $\text{NH}_4\text{PF}_6(\text{aq})$ solution (8x10 mL) and H_2O (2x10 mL). The organics were dried over MgSO_4 and concentrated to afford **Ir4.21**· PF_6 as a yellow crystalline solid (27.2 mg, 67%).

^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.86 (t, J = 8.1 Hz, 2H, ArH), 7.60 – 7.76 (m, 6H, ArH), 7.42 (s, 1H, ArH), 6.83 – 7.05 (m, 6H, ArH), 6.44 (d, J = 7.6 Hz, 1H, ArH), 6.36 (d, J = 7.5 Hz, 1H, ArH), 5.66 (s, 1H, ArH), 4.35 (t, J = 7.4 Hz, 2H, N- CH_2), 3.95 – 4.05 (m, 2H, O- CH_2), 3.24 – 3.40 (m, 2H, O- CH_2), 1.73 – 1.87 (m, 4H, CH_2), 1.61 – 1.70 (m, 2H, N- CH_2 - CH_2), 1.28 (m, 46H), 0.85 – 0.91 (m, 9H, $-\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ (ppm) 168.61, 167.93, 149.65, 149.34, 149.07, 148.27, 147.36, 145.51, 144.57, 144.22, 137.61, 134.34, 132.57, 132.09, 130.06, 129.98, 124.36, 124.24, 123.19, 122.96, 122.51, 122.09, 119.24, 119.07, 98.62, 97.88, 97.36, 69.55, 68.85, 52.26, 32.08, 31.76, 29.83, 29.78, 29.74, 29.65, 29.20, 29.12, 28.80, 26.18, 26.11, 22.84, 22.74, 14.27, 14.22. ^{19}F NMR (377 MHz,

CDCl₃) δ (ppm) -71.08 (d, $J = 716.3$ Hz, PF₆); **HRMS (ESI):** m/z 1292.54732 [M]⁺ ([C₆₃H₈₆IN₇O₂Ir]⁺ calc. 1292.55114).

6.3 References

1. G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw and K. I. Goldberg, *Organometallics*, 2010, **29**, 2176-2179.
2. M. J. Hynes, *J. Chem. Soc., Dalton Trans.*, 1993, **0**, 311-312.