

Macrocyclic, interpenetrated and interlocked triazole and triazolium containing anion receptors

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This thesis describes the synthesis of macrocyclic, interpenetrated, and in particular, interlocked anion receptors containing the triazole and triazolium motifs.

Chapter One introduces the field of supramolecular chemistry with a focus on the areas of particular relevance to this thesis, namely anion coordination, anion templation and the synthesis of interlocked structures.

Chapter Two describes the preparation of acyclic and macrocyclic neutral bis-triazole receptors, and a study of their anion and transition metal cation recognition properties. The synthesis of an acyclic anion receptor incorporating the novel pyridinium-3,5-bis(triazole) motif is also reported.

Chapter Three details the incorporation of the pyridinium bis-triazole motif into pseudorotaxanes, catenanes and rotaxanes. A thorough study of the use of a variety of anions, including oxoanions, to template interpenetrated assemblies is described, and the anion binding affinities of the catenane and rotaxane hosts discussed in comparison to analogous amide based systems.

Chapter Four presents research into a series of triazolium containing rotaxanes. A number of structural modifications are made to the interlocked host molecules, and the effect of these changes on the anion recognition properties of the receptors is discussed.

Chapter Five investigates the incorporation of two or more cationic triazolium groups into cyclic and interlocked host systems in order to create highly charged receptors capable of anion recognition in aqueous media.

Chapter Six describes experimental procedures used in this work, and details the characterization of novel compounds.

Chapter Seven summarizes the major conclusions of this thesis.

Chapter Eight contains the references cited within Chapters One to Six.

Full crystallographic information and details of molecular modeling experiments are provided in Digital Appendices on an enclosed DVD.

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Patricia June White (1922–2011)

and

George Robert White (1920–2012)

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Previously published work

Some of the work described in this thesis has already been published.

Peer-reviewed journal articles

N. G. White and P. D. Beer, *A Catenane Host System Containing Integrated Triazole C–H Hydrogen Bond Donors for Anion Recognition*, Chem. Commun., 2012, **48**, 8499–8501.

N. G. White, S. Carvalho, V. Félix and P. D. Beer, *Anion Binding in Aqueous Media by a Tetra-triazolium Macrocyclic*, Org. Biomol. Chem., 2012, **10**, 6951–6959.

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Oral presentations

Towards Selective Anion Binding inside Interlocked Molecules.
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Towards Selective Anion Binding inside Interlocked Molecules.
Red Kite Crystallographers Meeting, Oxford, January 2012.

Poster presentations

N. G. White, N. L. Kilah, J. Mercurio, K. M. Mullen and P. D. Beer, *Towards Controlling Halide Selectivity in Triazolium-Based [2]Rotaxane Host Systems.* International Symposium on Macrocyclic and Supramolecular Chemistry VII, Dunedin, New Zealand, February 2012.

N. G. White and P. D. Beer, *Jack of All Trades and Master of None: Anion Binding, Metal Coordination and Pseudorotaxane Formation by 1,2,3-Triazoles.* International Symposium on Macrocyclic and Supramolecular Chemistry VI, Brighton, U.K., July 2011.

Further work conducted during the course of this thesis has also been published.

N.G. White and P.D. Beer, *A Ferrocene Redox-Active Triazolium Macrocyclic that Binds and Senses Chloride*, Beilstein J. Org. Chem., 2012, **8**, 246–252.
Invited contribution to special edition, “Supramolecular Chemistry II,” refereed as usual.

Abbreviations

χ_H	mole fraction of host
$\Delta\delta$	change in chemical shift relative to free host
λ	wavelength
μ	micro
Å	Angstrom
A	hydrogen bond acceptor
<i>anti</i>	anticlinal
app.	apparent
aq.	aqueous
ATP	adenosine triphosphate
$\text{BAr}^{\text{F}}_4^-$	tetrakis[3,5-bis(trifluoromethyl)phenyl]borate anion
Bn	benzyl
br.	broad
Bu	butyl
BzO^-	benzoate anion
calc.	calculated
<i>cf.</i>	<i>confer</i>
c	centi
° C	degrees Celsius
conc.	concentrated
COSY	homonuclear correlation spectroscopy
CuAAC	copper(I)-catalyzed azide alkyne cycloaddition
d	doublet
dd	double doublet
D	hydrogen bond donor
DIPEA	<i>N,N'</i> -diisopropylethylamine
DMF	<i>N,N'</i> -dimethylformamide
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
DVD	digital versatile disc
<i>e.g.</i>	<i>exempli gratia</i>
EI	electron ionization
en	ethylenediamine
equiv.	equivalent
ESI	electrospray ionization
Et	ethyl
F^2	square of the structure factor
g	gram
G	Gibbs free energy
Grubbs' II	Grubbs' second generation catalyst
H	enthalpy
HRESI-MS	high resolution electrospray ionization mass spectrometry
Hz	Hertz
<i>i.e.</i>	<i>id est</i>
IUPAC	International Union of Pure and Applied Chemistry
J	joule
J	coupling constant
^3J	three bond coupling constant
^4J	four bond coupling constant
K	Kelvin
K_a	association constant
L	litre

LRESI-MS	low resolution electrospray ionization mass spectrometry
<i>m</i>	<i>meta</i>
m	meter, milli, multiplet
M	mega, moles per litre
MD	molecular dynamics
Me	methyl
MIM	mechanically interlocked molecule
MM	molecular mechanics
mol	mole
n	nano
ⁿ Bu	normal butyl
neg.	negative
NMR	nuclear magnetic resonance
OAc ⁻	acetate anion
<i>p</i>	<i>para</i>
Pd ₂ (dba) ₃	tris(dibenzylideneacetone)dipalladium(0)
Ph	phenyl
pH	$-\log_{10}[\text{H}^+]$
p <i>K</i> _a	$-\log_{10} K_a$
pos.	positive
Pr	propyl
q	quartet
QM	quantum mechanics
quin	quintet
R	chemical substituent
RCM	ring closing metathesis
ROESY	rotating-frame nuclear Overhauser effect correlation spectroscopy
s	singlet
S	entropy
<i>syn</i>	synperiplanar
t	triplet
TBA	tetrabutylammonium cation
TBTA	tris[(1-benzyl-1,2,3-triazol-4-yl)methyl]amine
^t Bu	tertiary butyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TIPS	triisopropylsilyl
TMS	trimethylsilyl
tosyl	4-toluenesulfonyl
TRISPHAT ⁻	tris(tetrachlorobenzenediolato)phosphate anion
Ts	4-toluenesulfonyl
%VdW _{x,y}	% of the sum of the van der Waals radii of two atoms x and y
UV	ultraviolet

Chapter 1

Introduction

1.1 Supramolecular chemistry

The rapidly growing field of supramolecular chemistry is concerned with non-covalent interactions *between* molecules, in contrast to traditional organic chemistry's use of covalent bonds to construct discrete compounds. The inspiration for this comes from biology, which uses such interactions in numerous vital processes including enzyme-substrate binding, DNA transcription and replication, and cellular recognition.¹ The field can be divided into two complementary areas: host-guest chemistry, and self assembly.

Host-guest chemistry involves the design and synthesis of a host molecule that uses intermolecular forces to selectively bind a particular guest substrate. Self assembly is the generation of complex architectures from a number of smaller, simpler constituent parts, which have been designed to code this synthesis. This chapter will give an introduction to the field of supramolecular chemistry, with particular emphasis on areas relevant to this thesis: specifically anion recognition, and the assembly of interpenetrated and interlocked structures.

1.2 Non-covalent interactions

Supramolecular chemistry is concerned with interactions *between* molecules, as both host-guest and self assembly processes are governed by these intermolecular interactions. Such non-covalent forces are significantly weaker than covalent bonds (typically $< 50 \text{ kJ mol}^{-1}$ *cf.* covalent bonds, which are usually $300\text{--}500 \text{ kJ mol}^{-1}$ for bonds involving carbon atoms), and hence are often reversible, thus proceeding under thermodynamic control. This allows for error correction, as occurs, for example, in the self assembly of the DNA double helix.²

1.2.1 Coulombic forces

Three major groups of electrostatic forces feature strongly in supramolecular chemistry. The strength of ion-ion, ion-dipole and dipole-dipole interactions depends on the

magnitude of the charges involved, and their separation. Ion–ion attractions are entirely isotropic, while interactions involving dipoles have some directionality.²

Ubiquitous dispersion forces, involving attraction between random, spontaneous dipoles depend solely on the number of electrons in a system, and so are of little use in the strategic design of host–guest or self assembling systems.

1.2.2 Hydrogen bonding

A specific type of dipole–dipole interaction is the hydrogen bond, which was recently defined by IUPAC, “[a] hydrogen bond is an attractive interaction between a hydrogen atom from a molecule or a molecular fragment XH in which X is more electronegative than H , and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.”³ The origin of the interaction is primarily electrostatic, but importantly is anisotropic, with linear donor–H $\cdots$ acceptor arrangements giving the strongest bonds.³ The power of hydrogen bonds (particularly when working in concert) is demonstrated in Nature by the sulfate binding protein, which uses seven hydrogen bonds to selectively complex this anion in biological media (Figure 1.1).⁴

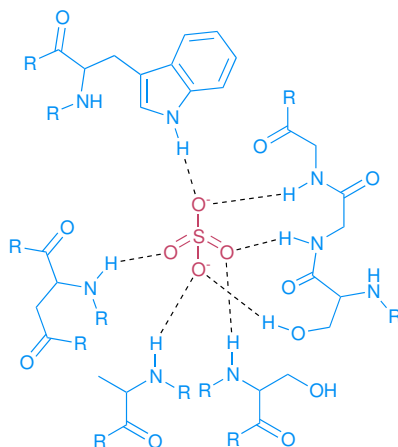


Figure 1.1: The hydrogen bonding arrangement in the crystal structure of sulfate binding protein.⁴

1.2.3 π – π , Donor–acceptor and solvophobic interactions

For a long time, the parallel offset arrangement of aromatic rings, so-called π – π interactions, have been considered a significant part of supramolecular,⁵ and indeed,

biological chemistry.⁶ However, recent theoretical studies have shown that with the exception of large polyaromatic systems,⁷ such π - π effects are simply a combination of solvation effects, dispersion forces and electrostatic attractions — factors that influence the interactions of all molecules.⁸ Indeed, Bloom and Wheeler have calculated that *non-aromatic* cyclic polyenes engage in stronger stacking interactions (and anion- π interactions, see Section 1.2.4) than analogous aromatic systems.⁹

Significant non-covalent forces between aromatic rings *are* present though, with two classes of interactions, solvophobic and donor-acceptor being frequently used in supramolecular chemistry. Donor-acceptor aromatic stacking refers to the favourable arrangement of electron-deficient and electron-rich rings (which can be amplified if one or both systems are charged). It should be noted that recent studies have demonstrated that these donor-acceptor arrangements are often highly influenced by interactions between substituents attached to the aromatic rings, as well as, or instead of, between the rings themselves,^{10,11} and solvophobic effects also play a part, particularly in polar solvent systems.^{12,13}

Solvophobic, or in the case of aqueous media, hydrophobic, effects refer to the favourable aggregation of apolar molecules in polar solvents.¹⁴ While not strictly a force, these occur because despite the favourable dispersion forces between polar solvents and non-polar molecules, such interactions require a large loss of entropy, which can be minimized by aggregation of apolar entities.^{15,16} Solvophobic effects and donor-acceptor forces can be used in concert to powerful effect, as demonstrated by Cubberley and Iverson (Figure 1.2).¹² Electron-deficient naphthalenediimide and electron-rich dihydroxynaphthalene associate in aprotic solvents due to favourable donor-acceptor interactions. This pairing is dramatically enhanced in polar protic solvents (methanol and water), due to solvophobic effects.

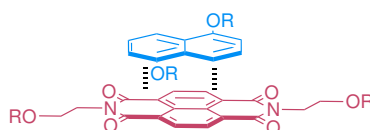


Figure 1.2: Dimeric system studied by Cubberley and Iverson.¹²

1.2.4 Cation– and anion– π interactions

The interaction of cations with aromatic rings (Figure 1.3a) that have a negative quadrupole moment is well-documented, and has been observed in the solid state, solution, and gas phases, as well as in biological systems.^{17–20} The discovery of interactions between anions and electron-deficient arenes (Figure 1.3b) has occurred more recently.²¹ Such anion– π associations are well-established in the gas phase²² and solid state,²³ although appear to be weak in solution, typically occurring in conjunction with other anion– π host interactions, such as hydrogen bonding.^{24–28} As with π – π stacking, it has been suggested that the term anion– π is misleading, as there is no special role of the π -electrons, and these should more correctly be considered in terms of electrostatic, donor–acceptor and solvophobic effects.⁹

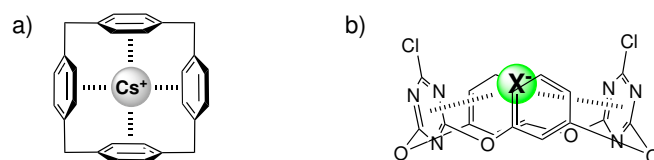


Figure 1.3: Interactions of anions with aromatic rings: a) cation– π interaction,²⁹ and b) anion– π contact.^{26,30}

1.2.5 Halogen bonding

An attractive interaction occurs between electron-deficient halogen atoms and neutral or anionic Lewis bases.³¹ This is because the formation of a σ -bond, R–X, causes an anisotropic distribution of electron density along this bond such that an electropositive region (known as the σ -hole) is present at the terminus of the large, polarisable halogen atom, X.³² The interaction between the σ -hole and electron-rich species is known as halogen bonding, and its strength can be greatly increased by the use of electron-withdrawing species to further polarize the R–X bond. Importantly, the three lone pairs of electrons present on the halogen form a “belt” of electron-density around the central region of this atom, repelling Lewis bases, and giving halogen bonds a more rigidly linear geometry than hydrogen bonds.³²

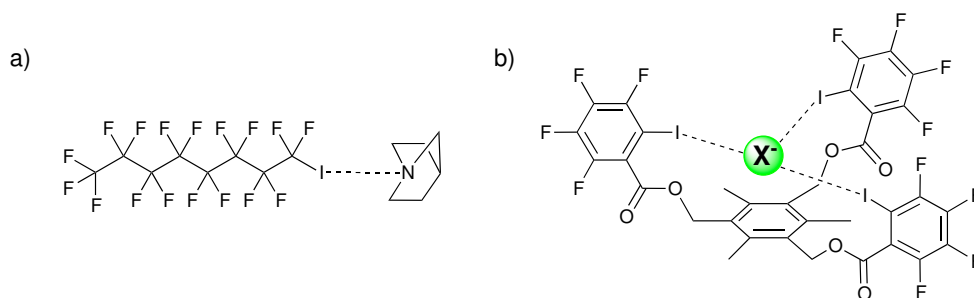


Figure 1.4: Halogen bonding between the σ -hole of halogen containing molecules and a) a neutral Lewis base,³³ b) an anion.³⁴

While such interactions (Figure 1.4) have been recognized in the solid state for some time,³⁵ their utility in solution phase chemistry has only recently become apparent.^{33,36,37} The strength of the interaction is considered to be similar to,³⁸ or even stronger than,^{39,40} hydrogen bonding. An effect similar to halogen bonding, but involving polarized group 15 and 16 centres is also possible,^{41,42} although, as yet, this has not been widely exploited in supramolecular systems.⁴³

1.2.6 Coordination bonds

While not strictly non-covalent, the coordinate bond formed between Lewis acids and Lewis bases exhibits many of the characteristics of such interactions, notably in that the formation of these sometimes labile bonds is often reversible. Coordination bonds have been used to powerful effect in both host-guest chemistry and self assembly.

1.3 Molecular recognition

Due to the wide-ranging roles played in Nature by charged species, interest in complexing cations and anions using synthetic hosts has been one of the driving forces behind the growth of supramolecular chemistry.⁴⁴ This section will give an overview of the design of synthetic receptors that utilize the non-covalent interactions introduced in Section 1.2. As the focus of this thesis is the recognition of anionic species, only a brief overview of receptors for cationic and neutral species is included.

1.3.1 Complementarity, preorganisation, the chelate effect and the macrocyclic effect

Because the field of supramolecular chemistry relies on the use of multiple weak non-covalent interactions acting in concert, it is vital that the two or more interacting components are *complementary* to one another in order to maximize the cumulative effect of these forces. In host-guest systems, this is typically achieved by matching the *size* and *shape* of a synthetic receptor's cavity with those of the target guest to allow selective binding over other mismatched size/shape substrates. This principle is illustrated by Flood's macrocyclic triazolophane host: chloride anion associates 40 times more strongly with the macrocycle than fluoride and 80 times more strongly than iodide in dichloromethane. This is a consequence of chloride being an appropriate size to fit in the centre of the macrocycle, while iodide is too large and fluoride binds asymmetrically (Figure 1.5).⁴⁵

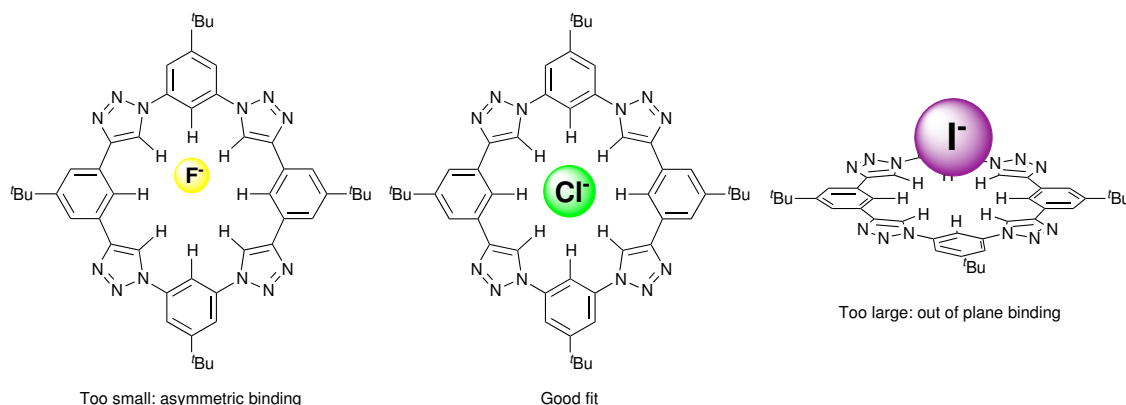
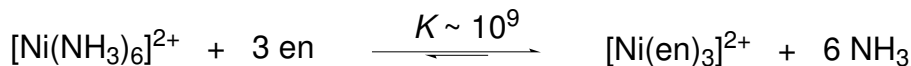


Figure 1.5: Halide anion recognition by Flood's triazolophane host.⁴⁵

This approach mimics that employed in biology by enzymes, which have been described using Fischer's "lock and key" model, which states that only a correctly-fitting and oriented substrate (key) will react with an enzyme active site (lock).⁴⁶ This has subsequently been refined as the "induced fit" model, which allows for subtle conformational changes in the enzyme's active site as a guest approaches.⁴⁷ The analogy is particularly relevant to synthetic receptors, as even very rigid host molecules, such as the triazolophane shown in Figure 1.5 exhibit deformation upon guest association.⁴⁸

Cram’s principle of preorganization states that “the more highly hosts and guests are organized for binding and low solvation prior to their complexation, the more stable will be their complexes.”⁴⁹ In a dynamic system, it may be more appropriate to consider that the more a host exists in a favourable conformation for association with a guest species, the stronger binding will be. Two effects that can contribute to this are the *chelate* and *macrocyclic* effects.

Originally defined in the context of transition metal coordination, but applicable to anion coordination, the chelate effect refers to the increased stability of complexes containing chelate rings over analogous non-chelated donors. This is due to both entropic and enthalpic factors: binding two monodentate ligands releases two solvent molecules, which is entropically neutral, whereas the release of two solvent molecules results from binding *one* bidentate ligand — an increase in disorder. Enthalpically, complex formation is favoured because the energy cost to bring two donor groups close together (*e.g.* two electron-rich amine groups in a metal complex) has already been paid for in the synthesis of the bidentate ligand (Figure 1.6).^{50,51}



Complex	ΔG^0 (kJ mol ⁻¹)	ΔH^0 (kJ mol ⁻¹)	ΔS^0 (kJ K ⁻¹ mol ⁻¹)
$[\text{Ni}(\text{NH}_3)_6]^{2+}$	-52	-100	-0.16
$[\text{Ni}(\text{en})_3]^{2+}$	-105	-117	-0.042

Figure 1.6: The chelate effect: coordination of three bidentate chelating ligands to nickel(II) cation is both entropically and enthalpically more favourable than coordination of six unidentate ligands.⁵¹

An extension of the chelate effect is the macrocyclic effect, which states that a complex containing a given ligand donor set in a cyclic structural framework will be more stable than the acyclic analogue. As an example, Hamilton’s macrocyclic host (Figure 1.7a) selectively complexes iodide and nitrate anions three orders of magnitude more strongly in 2% d₆-DMSO/CDCl₃ than the acyclic analogue (Figure 1.7b).⁵²

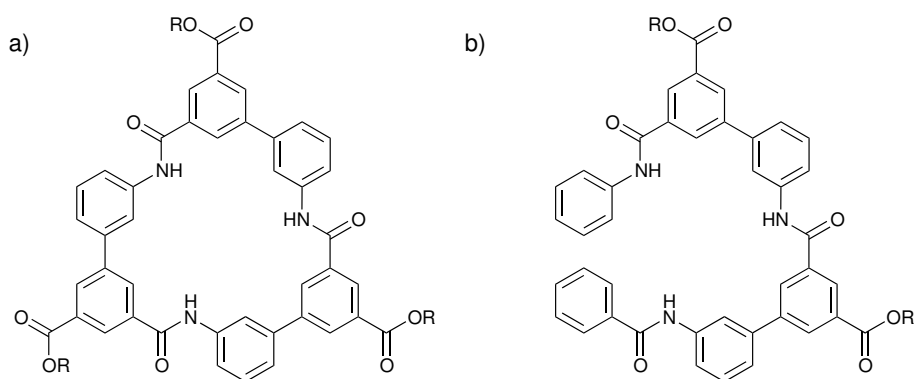


Figure 1.7: Hamilton's hosts for iodide and nitrate: a) macrocyclic receptor, b) acyclic receptor.⁵²

There are also other methods of organising receptors to enhance binding affinity: with Anslyn's citrate hosts (Figure 1.8),⁵³ the triethylbenzene receptor (Figure 1.8a) is preorganized to have the three guanidinium binding motifs co-facial as this minimizes steric strain around the hexasubstituted-benzene ring. This molecule exhibits stronger citrate association in D₂O than the unsubstituted analogue (Figure 1.8b), where the guanidinium groups are free to rotate around the methyl-amine bonds.

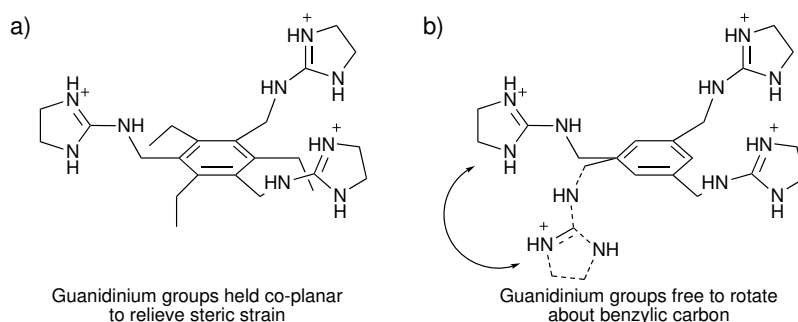


Figure 1.8: a) Anslyn's preorganized, and b) non-preorganized citrate hosts.⁵³

1.3.2 Hosts for cationic and neutral species

Cations are involved in some of the most important natural processes on the planet. For example, Mg²⁺ in chlorophyll (Figure 1.9g) is responsible for harvesting light energy in plant photosynthesis, and Fe²⁺ in haemoglobin facilitates respiration in mammals, while Na⁺ and K⁺ are important biological electrolytes, as well as mediating signals in the nervous system.² Many metal ions are highly toxic and are major contaminants in drinking

water,⁵⁴ and so development of receptors for these ions is an area of intense research activity.

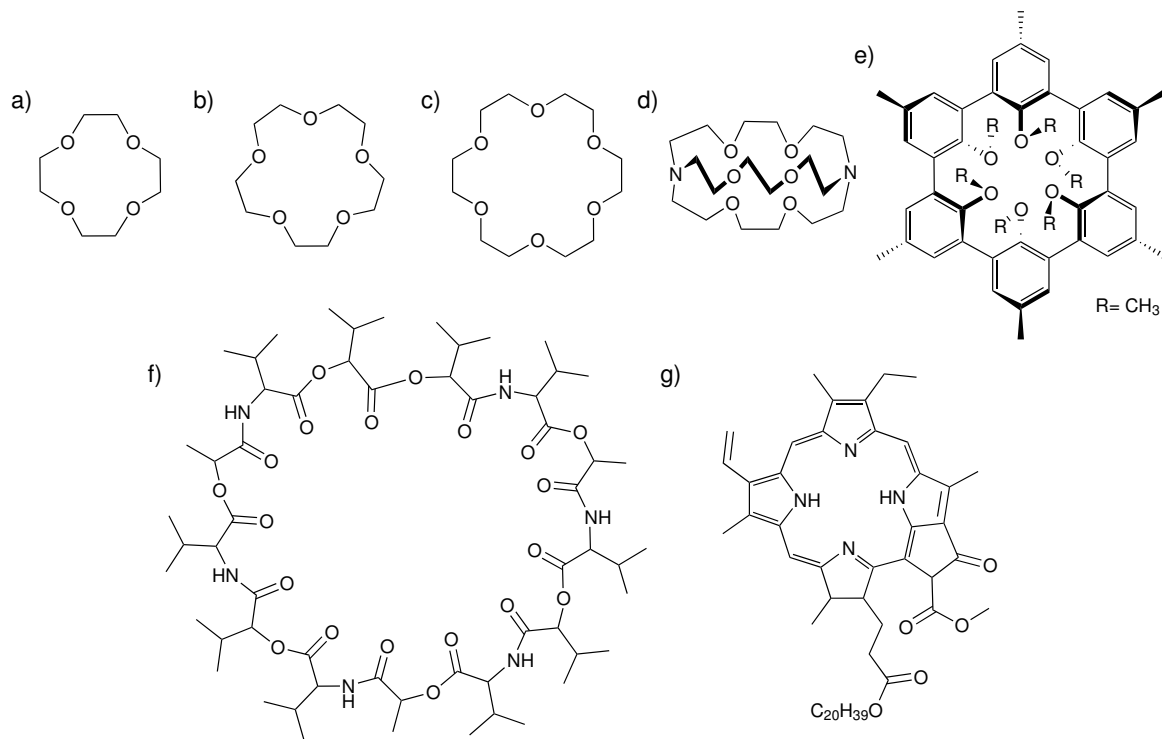


Figure 1.9: Notable cation receptors: a) 12-crown-4,^{55,56} b) 15-crown-5,^{55,56} c) 18-crown-6,^{55,56} d) cryptand,⁵⁷ e) spherand,⁵⁸ f) natural potassium host, valinomycin, g) the chlorin host of chlorophyll a.

Pedersen's synthesis of the crown ethers (Figure 1.9a–c) and discovery of their association with alkali metal cations is generally considered to have been the beginning of supramolecular chemistry.^{55,56} Binding occurs through multiple strong charge–dipole interactions between the alkali metal cation and oxygen dipoles, and in a demonstration of size complementarity, smaller crowns associate most strongly with the smaller ion Na^+ while large crowns display selective binding of K^+ and Cs^+ .⁵⁹ The structure of these hosts is reminiscent of the biological potassium receptor and transporter, valinomycin (Figure 1.9f).⁶⁰ Subsequent research has developed more preorganized receptors that display even higher binding affinities such as cryptands⁵⁷ and spherands⁵⁸ (Figure 1.9d,e).

Synthetic hosts for a wide variety of neutral molecules have also been reported, ranging from simple alkanes⁶¹ and aromatics⁶² to DNA nucleobases^{63,64} and saccharides⁶⁵. Recent work by Nitschke's group has demonstrated potential applications of such hosts, using them to selectively complex larger fullerenes (C₇₀ to C₈₄) from fullerene soot,⁶⁶ and to render pyrophoric white phosphorous water-stable (Figure 1.10a).⁶⁷ Crowley's palladium based host binds cisplatin, and releases it in response to a chemical stimulus, offering hope of targeted drug delivery (Figure 1.10b,c).⁶⁸

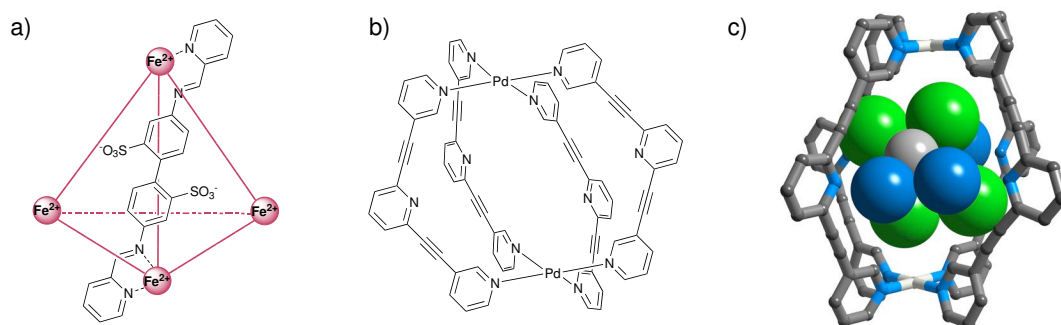


Figure 1.10: Hosts for neutral molecules: a) Nitschke's receptor for P₄,⁶⁷ b) Crowley's receptor for cisplatin,⁶⁸ c) single crystal X-ray structure of Crowley's host showing two encapsulated cisplatin molecules.⁶⁸

1.3.3 Hosts for anionic species

1.3.3.1 The importance of anions

Like cations, anions are extremely important in biology and the environment. For example, the phosphate scaffold that holds together the DNA double helix is polyanionic, and the majority of enzyme substrates and co-factors are negatively charged.⁶⁹ Furthermore, chloride channel malfunction causes cystic fibrosis⁷⁰ and problems in anion exchange channels are linked with Alzheimer's disease.⁷¹ Just as certain cations are major pollutants, so are specific anions, with nitrate and phosphate from soilwater fertilizer run-off causing eutrophication of lakes and rivers,⁶⁹ and increased nitrate levels in drinking water, arising from human activity, associated with a range of diseases.⁷²

The development of anion hosts is therefore of great importance, to further understand the behaviour of negatively charged species, particularly in aqueous and biological solutions, and to hopefully address the issues mentioned above. The field of anion receptor

chemistry is not nearly as developed as that of cation receptors, which can frequently achieve strong and selective binding of a wide range of cations in aqueous media. There are a number of reasons for this, which will be discussed in the following sections.

1.3.3.2 Challenges of anion coordination — properties of anions

As shown in Table 1.1, anions are larger than their isoelectronic cations. This increases the host ··· anion distance, significantly weakening any electrostatic interactions. As well as being larger, anions also have higher free energies of solvation than isoelectronic cations (Table 1.2). Coupled with the weakened electrostatic interactions caused by their increased size, this makes binding anions in water a challenge.

Table 1.1: Effective ionic radii of isoelectronic cations and anions.

Cation	Effective ionic radius (Å)	Anion	Effective ionic radius (Å)
Na ⁺	1.02	F ⁻	1.31
K ⁺	1.37	Cl ⁻	1.81
Rb ⁺	1.52	Br ⁻	1.96
Cs ⁺	1.67	I ⁻	2.20

Effective ionic radii, with a coordination number of six for all ions, as reported by Shannon.⁷³

Table 1.2: Hydration energies of isoelectronic cations and anions

Cation	$\Delta G_{\text{hydration}}$ (kJ mol⁻¹)^a	Anion	$\Delta G_{\text{hydration}}$ (kJ mol⁻¹)^a
Na ⁺	-365	F ⁻	-465
K ⁺	-295	Cl ⁻	-340
Rb ⁺	—	Br ⁻	-315
Cs ⁺	-250	I ⁻	-275

^aValues taken from Steed and Atwood.²

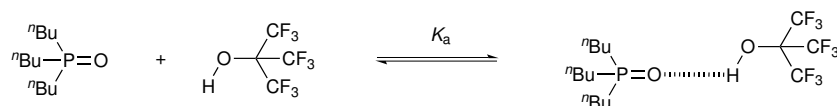
All anions display some level of pH dependence, meaning they remain negatively charged over a limited pH range. Protonated receptors (for example those based on ammonium groups) also have limited pH ranges, and care must be taken to ensure the anion and host system’s pH windows are compatible. While this is less of an issue for receptors designed to operate at neutral pH, very basic anions, such as fluoride and acetate, may still deprotonate acidic sites on receptors.⁷⁴

While cations are generally spherical, anions can have a range of geometries including spherical (halides), linear (CN^- , N_3^-), trigonal (NO_3^-), tetrahedral (BF_4^- , SO_4^{2-} , PO_4^{3-}), octahedral (PF_6^-) or even larger, more complex geometries (pyrophosphate, ATP). This has advantages and disadvantages: while it offers more opportunities for selectivity based on complementary shape matching, such receptors are typically far more difficult to design and synthesize.

1.3.3.3 Challenges of anion coordination — solvent effects

The strength of receptor–anion association is greatly affected by the nature of the solvent. Two effects must be considered: solvent association with the host molecule, and solvent association with the anion. Solvents that are hydrogen bond donors will compete with the host to complex an anion, while media with Lewis basic character will compete with an anion for the host’s hydrogen or halogen bond donors. Alcohols and water are especially competitive as they contain both Lewis base character and hydrogen bond donating ability. Seminal work by Hunter has shown that mixtures of solvents can be far more competitive than either of the individual solvents, particularly when one solvent is a good hydrogen bond donor, and the other a good hydrogen bond acceptor (Table 1.3).⁷⁵

Table 1.3: Association of tributylphosphine oxide and *perfluoro-t*butanol in d_8 -THF: CDCl_3 mixtures.



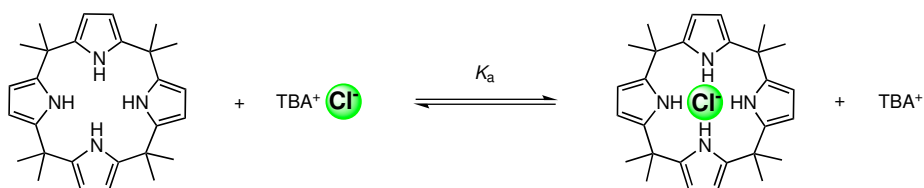
$\text{d}_8\text{-THF}:\text{CDCl}_3$ Ratio	K_a (M^{-1})
100:0	250
97:3	150
9:1	58
1:1	22
1:9	20
3:97	47
0:100	2500

In aprotic solvents, even very polar ones, such as DMSO, anion association trends with acyclic hydrogen bond based receptors are usually strongly correlated with anion basicity.

When protic solvents are used, this trend is partially reversed as the most basic anions tend to have high hydration energies and so are strongly solvated. This is particularly true with the halides, which typically show strong binding selectivities $F^- > Cl^- > Br^- > I^-$ in aprotic media, but which often show little selectivity in solvent media containing significant amounts of alcohol or water.⁷⁶ In aqueous solution, this is described by the Hofmeister series, which orders anions by their hydrophobicity: larger, more charge diffuse anions such as iodide will be more easily bound in water due to hydrophobic effects and reduced enthalpies of solvation.⁷⁷

While anion binding is generally stronger in less polar solvents, due to reduced competition from the media (Table 1.4), problems can also arise if apolar solvents are used. When determining anion association constant data, anions are typically added as tetrabutylammonium (TBA) salts, as this is considered to be a non-coordinating cation that does not contribute to binding equilibria. However, in chlorinated solvents, this is not the case, with the association constant of TBA cation and chloride anion having been calculated as $\sim 70,000 \text{ M}^{-1}$ in dichloromethane.⁷⁸ This $TBA \cdots anion$ ion-pairing leads to apparently anomalously low association in these solvents,^{79,80} with derivation of the true association requiring consideration of more complicated equilibria that allow for $TBA \cdots anion$ pairing.^{81,82}

Table 1.4: Association of calix[4]pyrrole and $TBA \cdot Cl$ in a range of solvents.⁸³



Solvent	$K_a \text{ (M}^{-1}\text{)}$
CD_3CN	250000
CD_3NO_2	24000
$d_6\text{-DMSO}$	2200
CD_2Cl_2	430 ^a

^aThe authors attributed this anomalously low value to ion-pairing.

1.3.4 Motifs for anion recognition

A wide range of functional groups have been incorporated into synthetic host systems to effect anion recognition, and these may be either cationic or neutral. Positively charged receptor groups provide strong electrostatic attraction for an anion, but may lack selectivity, due to the non-directionality of ion–ion interactions. Neutral hosts typically complex anions through polarized hydrogen bond donors, which although generally weaker, are more directional. The inherently weaker anion association of neutral systems, which are often insoluble in water, often necessitates the use of organic solvents for investigations of anion binding. This section will present different cationic and neutral functional groups that have been exploited for anion complexation, highlighting key examples. While these will be discussed separately, in practice, neutral and cationic functional groups are often both included in a receptor.

1.3.4.1 Protonated amine receptors

Shortly after Pedersen’s report of the cation binding abilities of crown ethers, Park and Simmons described a diaza-cryptand (Figure 1.11) that complexed chloride anion in acidic aqueous media.⁸⁴ Subsequent research has demonstrated that protonated amine systems ranging from simple alkyl amines such as ethylene diamine⁸⁵ and spermine^{86,87} to more complex macrocyclic,⁸⁸ bicyclic (Figure 1.11a)⁸⁹ and tricyclic (Figure 1.11b)⁹⁰ hosts strongly associate with a range of anions in acidic water. More recently, several expanded porphyrins in their protonated forms have also been used as anion hosts,⁷⁷ with this field being opened up by Sessler and Ibers’ serendipitous discovery of sapphyrin’s fluoride binding properties (Figure 1.11c,d).⁹¹

1.3.4.2 Quaternary ammonium receptors

To overcome the pH-dependence of polyammonium receptors, which typically require pH values below those found in biological and environmental systems,⁹⁵ the use of host systems incorporating alkylated quaternary amines has been developed. While not possessing hydrogen bond donating ability, such receptors still have strong electrostatic attraction for anions. Schmidtchen has pioneered the development of these receptors, synthesizing

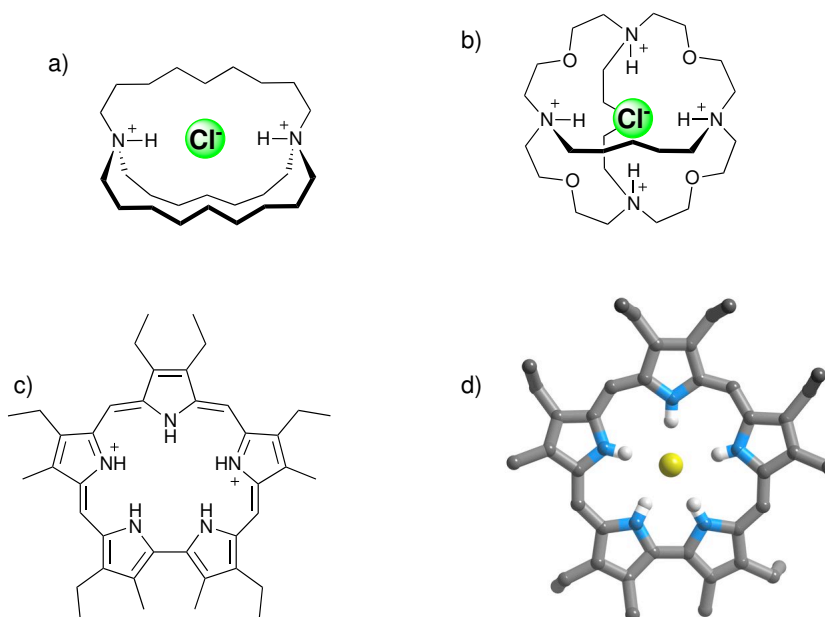


Figure 1.11: Examples of polyammonium and protonated pyrrole anion receptors: a) Park and Simmon's cryptand,⁸⁴ b) Lehn's chloride-selective macrotricyclic host,⁹⁰ c) diprotonated sapphyrin d) single crystal X-ray structure of diprotonated sapphyrin as its fluoride salt.⁹¹

tetrahedral cage compounds containing a central cavity surrounded by four quaternary ammonium groups, which strongly bind halide anions in water (Figure 1.12).⁹² A large increase in binding strength was observed when negatively charged substituents were attached to the ammonium groups, giving zwitterionic hosts.^{93,94} This was attributed to reduced competition for the binding site from counteranions present in the first generation receptors. A more recent study has shown that these cages complex a wide range of anions (halides, nitrate, borohydride, dicarboxylates).⁹⁴

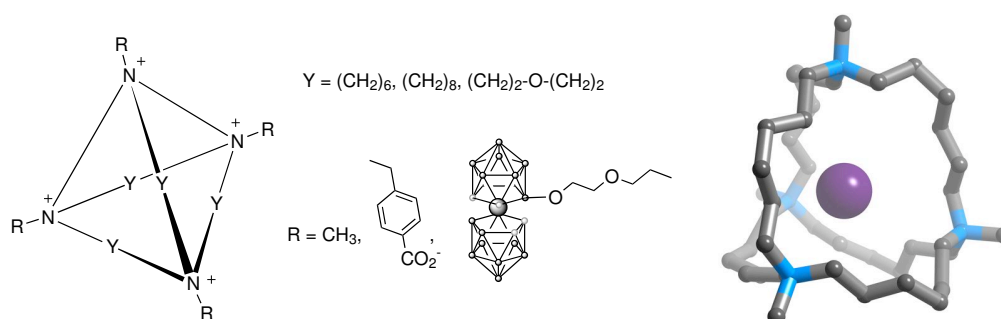


Figure 1.12: Diagrammatic (left) representation of Schmidtchen's tetracationic or zwitterionic cages and X-ray single crystal structure of the iodide salt of one of these (right).⁹²⁻⁹⁴

1.3.4.3 Guanidinium based receptors

While Schmidtchen's quaternary ammonium cages strongly complex anions in water, the ability to discriminate between anions is intrinsically limited, as the electrostatic attraction is non-directional, and the flexibility of the alkyl linkers prevents effective size discrimination. An alternative approach is to use guanidinium cations, as these remain protonated over a large pH range ($pK_a = 13.5$),⁹⁶ and incorporate both a positive charge and two hydrogen bond donors, which impart directionality to anion binding (Figure 1.13). Specifically, the Y-shape of the guanidinium group provides an ideal arrangement for binding of complementary carboxylates.^{97,98}

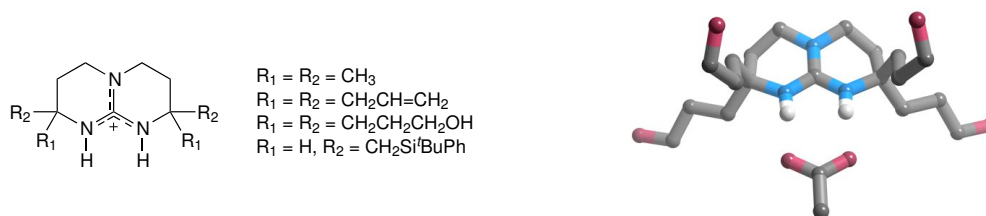


Figure 1.13: Diagrammatic (left) and X-ray single crystal structure (right) of guanidinium based host for carboxylate anions.⁹⁷

1.3.4.4 Receptors containing imidazolium and other C–H donors

Imidazolium groups can also act as potent anion binding motifs, as these groups offer both a positive charge and a polarized C–H hydrogen bond donor. In 1994, it was shown that imidazolium groups can form hydrogen bonds to anions in solution,⁹⁹ and this heterocycle has subsequently been incorporated into a range of synthetic host systems. Bis-imidazolium¹⁰⁰ and tetra-imidazolium¹⁰¹ macrocyclic hosts have been reported, as well as tris-imidazolium tripodal receptor systems.^{102,103} The synthesis of Alcade's bis-imidazolium macrocycle (Figure 1.14a), which complexes a range of anions in d₆-DMSO solution, provides an early demonstration of anion templation (see Section 1.4.1.2).¹⁰⁰ Other positively charged C–H donors have also been reported, for example Steed's pyridinium based hosts, which bind anions in CD₃CN¹⁰⁴ and d₆-DMSO¹⁰⁵ through electrostatic interactions and charge-assisted C–H hydrogen bonding (Figure 1.14b).

In the last few years, the use of the 1,2,3-triazole^{106–108} and 1,2,3-triazolium¹⁰⁹ heterocycles as anion complexing motifs has been reported. As the use of these groups

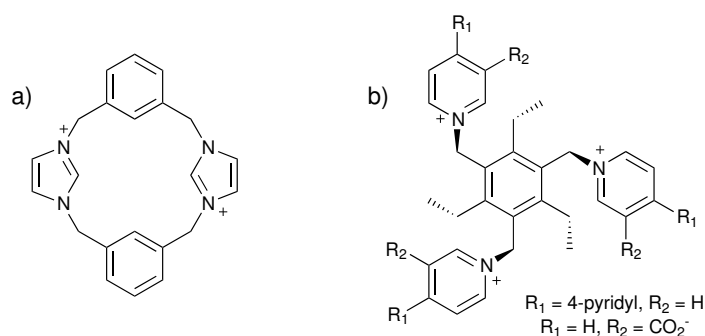


Figure 1.14: Charge-assisted C-H anion hosts: a) Alcalde's bis-imidazolium macrocycle,¹⁰⁰ b) Steed's pyridinium based receptors.^{104,105}

to bind anions (and template interlocked structure formation) is the key theme of this thesis, systems incorporating these motifs will be discussed separately in more detail in Section 1.5.

1.3.4.5 Amide and urea based receptors

The first amide based anion receptor was reported by Pascal and co-workers in 1986,¹¹⁰ however, it can be argued that it was Crabtree's introduction of the isophthalamide motif over a decade later that caused the expansion of this area of research.^{111,112} The simple acyclic receptor (Figure 1.15a) binds halides in CD_2Cl_2 solution. Subsequently, this, and similar, motifs have been incorporated into macrocycles and cryptands (Figure 1.15b),¹¹³ as well as more complex interpenetrated and interlocked structures (see later). Particularly noteworthy among neutral amide based hosts are Kubik's pseudo-peptide macrocycles, which bind sulfate and iodide strongly in 4:1 $\text{D}_2\text{O}:\text{CD}_3\text{OD}$ through a combination of favourable hydrogen bonding and solvophobic interactions (Figure 1.15c).¹¹⁴

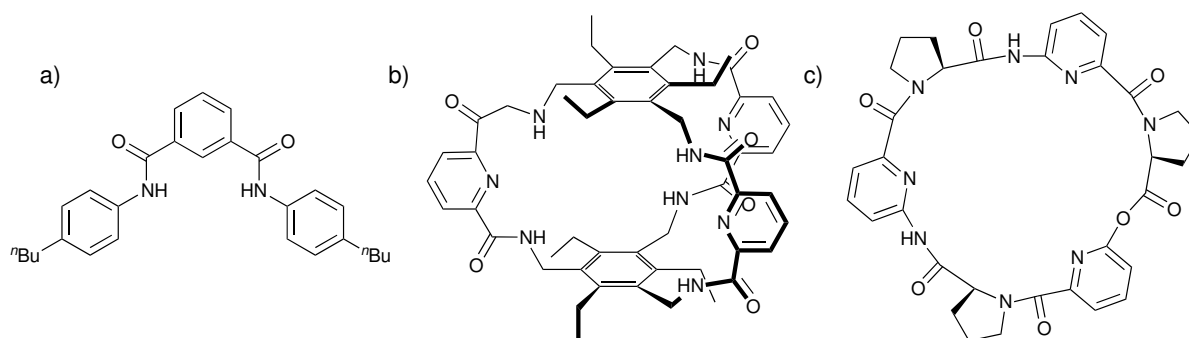


Figure 1.15: Amide based receptors: a) Crabtree's acyclic host,¹¹¹ b) Anslyn's cryptand,¹¹⁵ c) Kubik's pseudo-peptidic receptor.^{116,117}

Ureas, as well as thioureas, are potent hydrogen bond donors and have been used in numerous anion receptor systems.^{118,119} For example, Gale’s acyclic bis-urea host binds oxoanions up to three orders of magnitude more strongly than halides in d_6 -DMSO containing 0.5% D_2O (Figure 1.16).¹²⁰ A possible drawback of these type of receptors is that the high acidity of (thio)urea protons leaves these groups particularly liable to deprotonation by highly basic anions, for example fluoride, dihydrogen phosphate and acetate.¹²¹

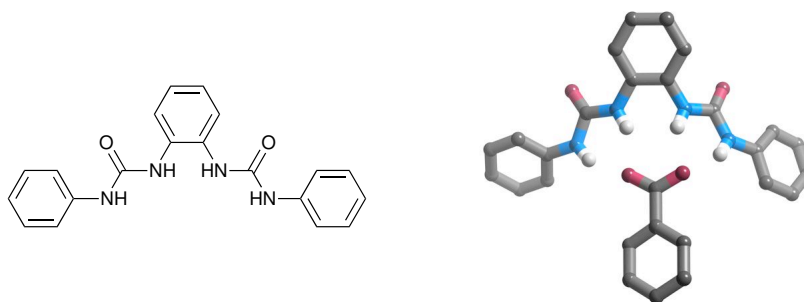


Figure 1.16: Diagram (left), and single crystal X-ray structure of the benzoate complex (right) of Gale’s bis-urea receptor.¹²⁰

1.3.4.6 Pyrrole, indole, carbazole and indolocarbazole based receptors

Since Sessler and co-workers’ seminal 1996 report of the anion binding properties of calix[4]pyrroles (Figure 1.17a),¹²² the use of neutral pyrrole based systems, and related conjugated congeners as anion hosts has received widespread attention.¹²³ Calix[4]pyrrole adopts a cone conformation upon anion complexation, such that all four pyrrole rings can form linear hydrogen bonds to an anion, with fluoride and chloride being bound most strongly in a range of polar organic solvents (Figure 1.17b, Table 1.4). Subsequently, more complex “strapped” systems have been synthesized,^{124,125} as well as larger calix[n]pyrroles and calix[n]bipyrroles.^{126–131}

Indole and carbazole are conjugated heterocycles incorporating pyrrole motifs, and as such have more acidic N–H bonds than simple pyrrole, making them potentially very powerful anion complexants.¹²³ Sessler reported the bis-indole host (Figure 1.17c), which selectively complexes dihydrogen phosphate in CD_2Cl_2 , and also shows a colorometric response to anions in this solvent. Since its introduction in 2005,¹³⁵ the indolocarbazole

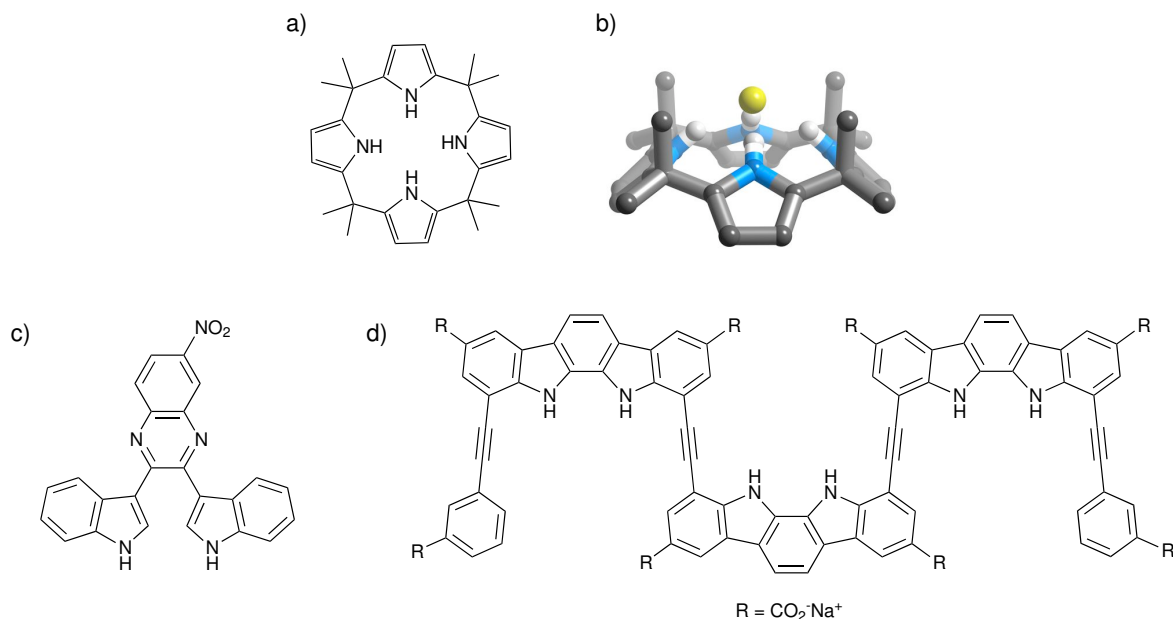


Figure 1.17: Anion receptors based on pyrrole functionality: a) calix[4]pyrrole,¹²² b) single crystal X-ray structure of calix[4]pyrrole with bound fluoride anion,¹³² c) Sessler's bis-indole dihydrogen phosphate host,¹³³ d) Jeong's indolocarbazole foldamer.¹³⁴

functionality has been incorporated into a range of receptors, which display a strong affinity for anions. Notably, Jeong has demonstrated that a neutral indolocarbazole foldamer can bind chloride anion in pure water through six hydrogen bonds from three indolocarbazole groups (Figure 1.17d).¹³⁴

In practice, neutral hosts often incorporate a range of the previously-mentioned functionalities, with several different hydrogen bond donors working in tandem to give hosts with strong anion affinities.^{118,136} The power of this approach is demonstrated by Gale's pyrrole-amide host (Figure 1.18), which can complex fluoride and dihydrogen phosphate anions in 3:1 d_6 -DMSO: D_2O .¹³⁷ As previously mentioned, the addition of cationic recognition elements can further enhance binding affinity.

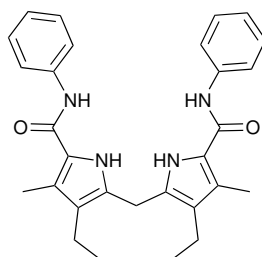


Figure 1.18: Gale's amido-pyrrole host.¹³⁷

1.3.4.7 Lewis acid and transition metal based receptors

An alternative method of guest complexation is to incorporate Lewis acidic elements into a host structural framework, facilitating anion binding by formation of a dative anion $\cdots$ Lewis acid bond. A wide range of electron deficient hosts have been used including three-coordinate boron,¹³⁸ tin,¹³⁹ and transition metals (Figure 1.19).^{140–142} Transition metals have also been used to preorganize neutral hydrogen bond donors, and add electrostatic attraction for anions.¹⁴³

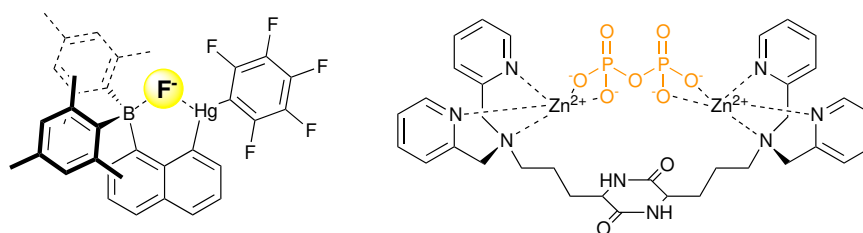


Figure 1.19: Hosts incorporating Lewis acids: Gabbaï's boron and mercury containing fluoride host (left),¹⁴⁴ and Joliffe's bis-zinc host for polyphosphate anions (right).¹⁴⁵

1.3.4.8 Halogen bonding receptors

Since the start of the work described in this thesis, the first solution phase receptors based on halogen bonding interactions have been reported. While neutral receptors so far function in only non-polar solvents,³⁴ cationic hosts display impressive anion affinities in polar organic,^{146,147} and aqueous media.^{40,148} Significant discrimination between anions, and even in some cases, between halides, has been reported in these systems. The strength of halogen bonding is demonstrated by Resnati's simple acyclic iodoimidazolium host, which despite containing only one charge-assisted halogen bond associates strongly with anions in d_6 -DMSO (Figure 1.20a,b) showing an unusual preference for dihydrogen phosphate. The combination of hydrogen and halogen bonding can also be used to powerful effect, with Taylor reporting such a neutral receptor that can complex anions strongly in CD_3CN (Figure 1.20c).¹⁴⁹

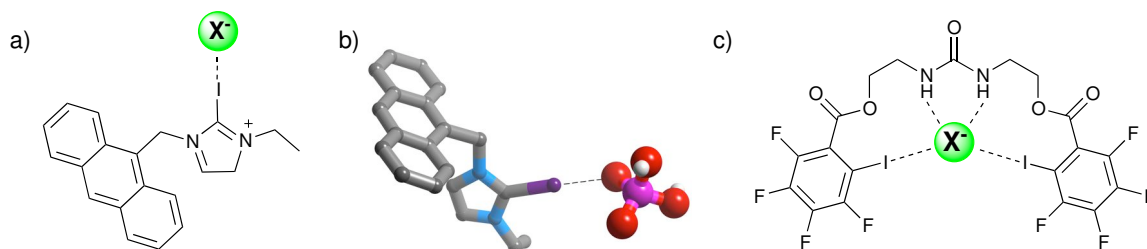


Figure 1.20: Halogen bond based receptors: a) Resnati's iodoimidazolium receptor,¹⁴⁶ b) solid state structure of Resnati's host as its dihydrogen phosphate salt,¹⁴⁶ c) Taylor's hydrogen and halogen bond containing host.¹⁴⁹

1.3.5 Anion sensing

Moving beyond the recognition of anions, a further important challenge is the *sensing* of negatively charged species. This requires the design of host molecules that display a change in a measurable macroscopic response (*e.g.* photochemical^{150,151} or electrochemical¹⁵²) upon anion complexation. Perhaps the most widely-used method is to incorporate a reporter group in proximity to the anion binding site, such that the anion binding event causes a change in the chemical environment of the reporter group, triggering a response. Other approaches have been developed for anion sensing including displacement assays,^{153,154} ion selective electrodes^{155,156} and the chemidosimeter approach.^{157,158}

Ferrocene is an ideal electrochemical reporter, as it can be readily incorporated into a covalent framework. Guest complexation typically results in a shift of the ferrocene/ferrocenium redox couple, due to stabilization of the ferrocenium oxidation state by a proximal anion. A range of ferrocene containing anion sensors have been reported, including acyclic,¹⁵⁹ macrocyclic¹⁶⁰ and interlocked^{161–163} systems. For example, Moody and Tucker's acyclic host (Figure 1.21) senses chiral carboxylates in acetonitrile — complexation of the anion at the urea group facilitates oxidation of the ferrocene moiety to ferrocenium, causing a cathodic shift of up to 90 mV upon addition of one equivalent of carboxylate.¹⁵⁹

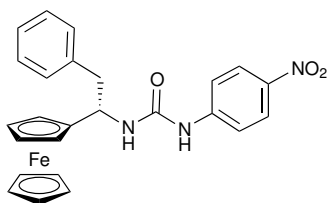


Figure 1.21: Tucker's sensor for chiral carboxylates.¹⁵⁹

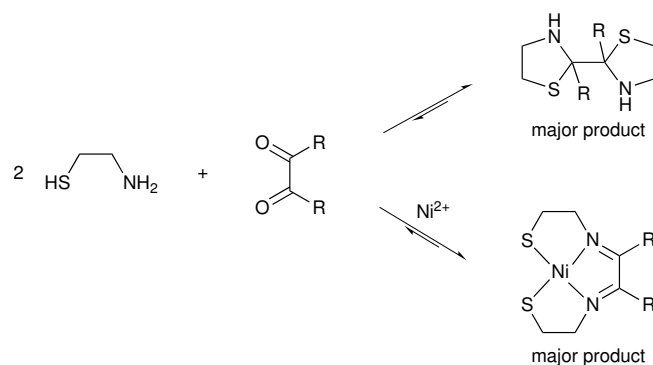
1.4 Self assembly

Self assembly is the association of suitably designed molecules to form a larger, non-covalently bonded entity, utilising in concert the forces and effects discussed in Section 1.2. Inspiration for the design of synthetic self assembled systems comes from Nature, which uses this approach to build up key biological structures, including the DNA double helix and cell walls.² The control of product formation can be directed by a template, and this approach to self assembly is discussed in the following section.

1.4.1 Templated self assembly

The use of templates in synthetic chemistry was pioneered by Busch, who demonstrated that nickel(II) ion could dramatically alter the product ratio of the reaction between mercapto-amines and diketones.^{164–167} Busch classified two types of templation that could occur — kinetic or thermodynamic. Both of these effects are involved in the reaction shown in Scheme 1.1 where coordination of two molecules of mercaptoethylamine to a nickel(II) ion preorganizes the amine groups such that they are ideally situated to react with a diketone (a kinetic effect). The tetradentate product is also thermodynamically preferred, as this provides a more favourable donor set for the metal ion than the alternate product, thiazoline.

A further classification has been suggested by Sanders, which describes the topology of the species arranged around the template: linear, cyclization or interweaving.¹⁶⁸ Interweaving templates are of particular interest to this work, as they facilitate the formation of interlocked structures (Section 1.4.2).



Scheme 1.1: Reaction products of mercaptoethylamine and α -diketones, with and without the presence of a nickel(II) template.^{164–167}

1.4.1.1 Templatation by cations

Imaginatively designed polydentate ligands in combination with cation templates have enabled the formation of extremely large and intricate systems to be achieved. For example, $[2 \times 2]$,¹⁶⁹ $[3 \times 3]$,¹⁷⁰ (Figure 1.22a) and larger¹⁷¹ grid complexes have been synthesized, as well as the near-quantitative formation of Borromean rings,¹⁷² (Figure 1.22b) and Fujita's range of large spheres and other polyhedra (Figure 1.22c).^{173–175} Selected examples are shown in Figure 1.22. In all these impressive systems, very large complex entities are made from comparatively simple starting materials, due to the directing influence of the metal ions' preferred coordination geometries.

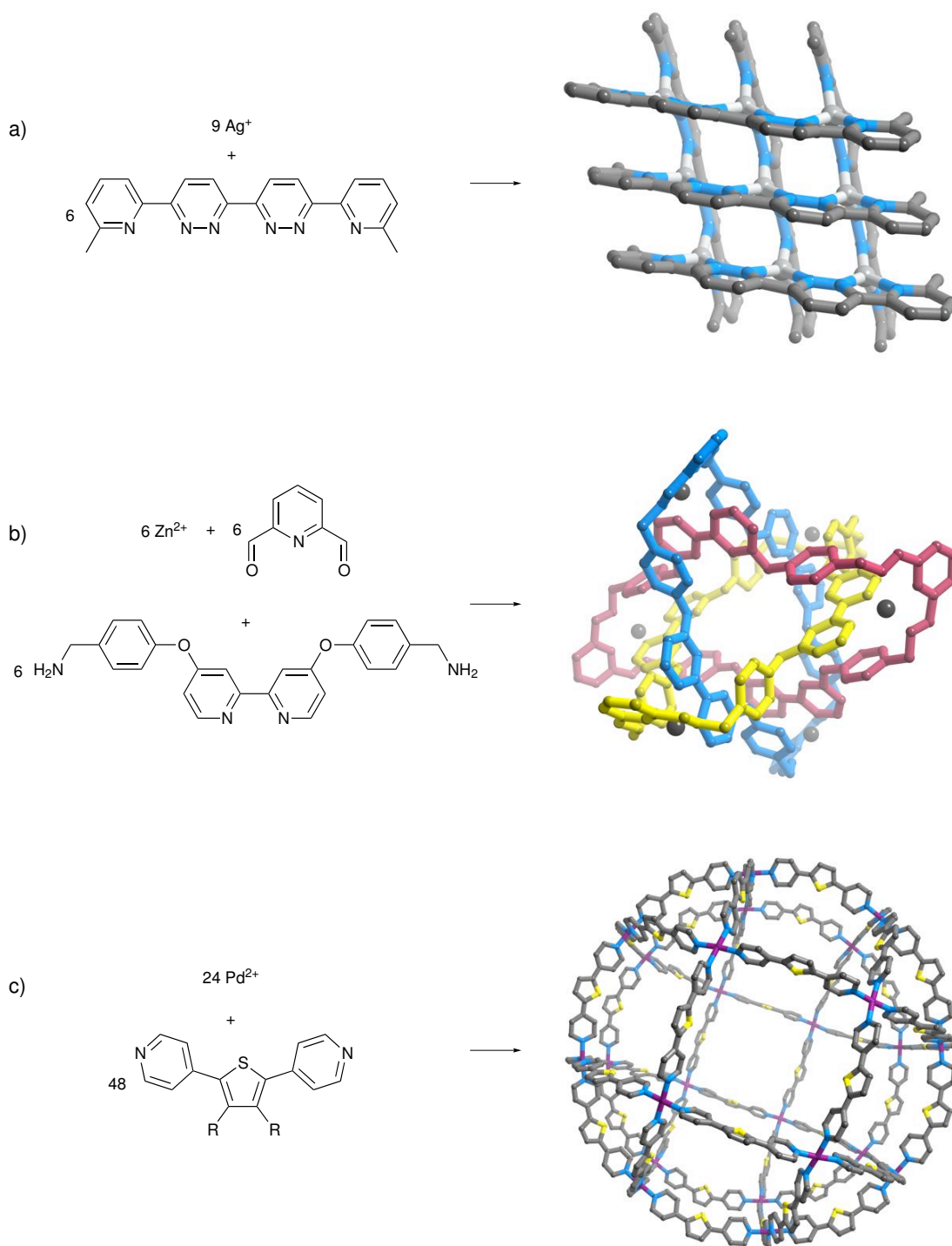


Figure 1.22: Examples of cation templation: X-ray crystal structures of a) Lehn's 3×3 grid complex,¹⁷⁰ b) Stoddart's Borromean rings,¹⁷² c) Fujita's Pd_{24} sphere.¹⁷³

1.4.1.2 Templation by anions

As mentioned previously, the development of anion coordination chemistry has lagged behind that of cation coordination, and as a consequence the strategic use of negatively

charged templates has not been extensively exploited. Many examples of anion templation have been serendipitous discoveries: Lehn demonstrated that the reaction of a tris-bipyridyl ligand with iron(II) chloride gave a pentanuclear helicate, while the use of iron(II) sulfate produced the analogous hexanuclear helix.^{176,177} More recently, Dunbar has shown that the nature of the product formed from the reaction of nickel(II) salts and dipyridyl tetrazine is strongly dependent on the counteranion present. Nickel tetrafluoroborate or perchlorate gives a tetranuclear square, while with hexafluoroantimonate a pentanuclear pentagon is produced (Figure 1.23).¹⁷⁸ Interestingly, addition of tetrafluoroborate, perchlorate or iodide anion to the hexafluoroantimonate pentagon causes quantitative conversion to the tetranuclear square species, while more forcing conditions are needed to see any conversion of the square to the pentagon.

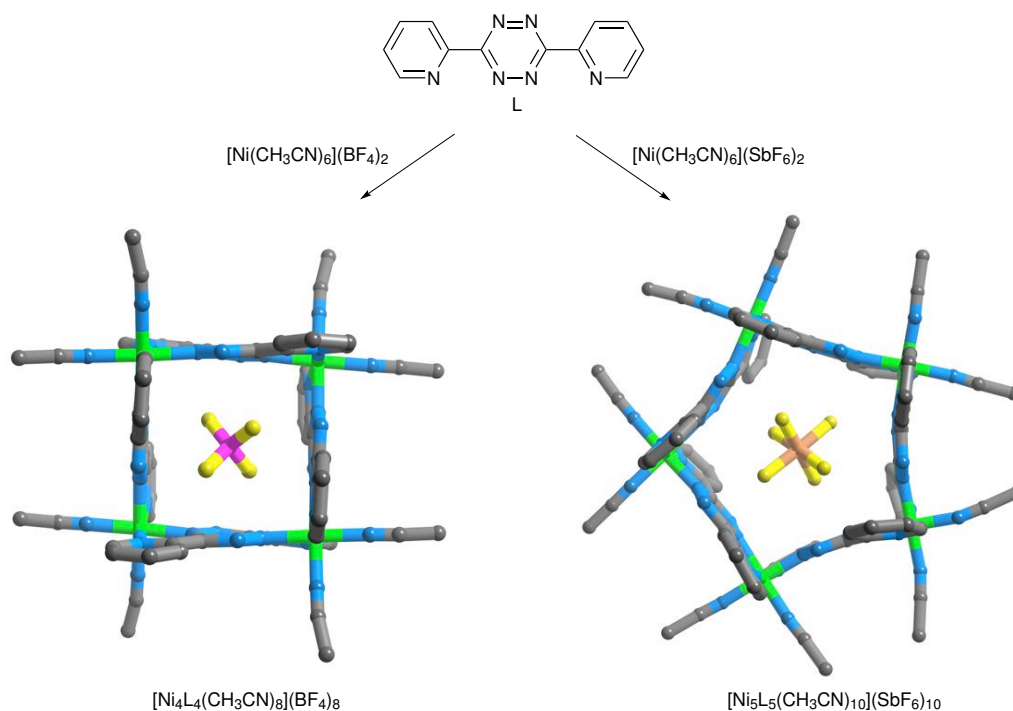
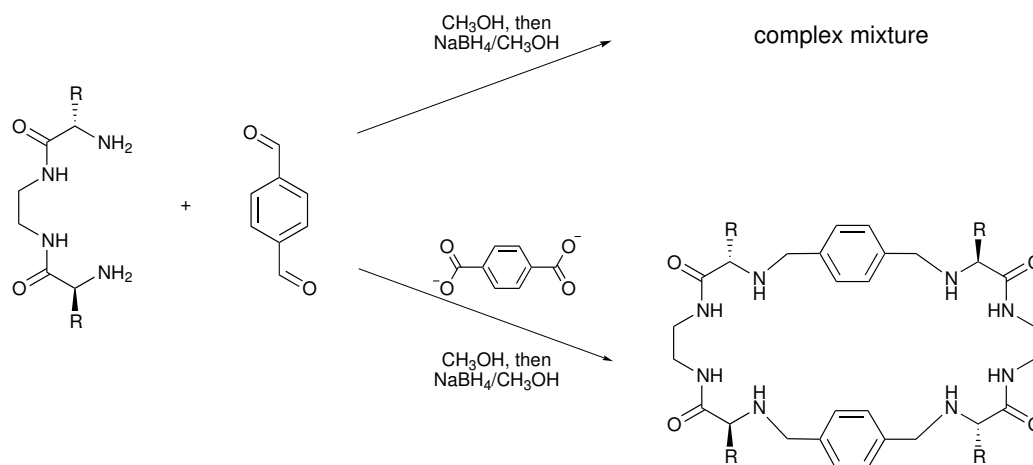


Figure 1.23: Dunbar's anion templated assembly of tetranuclear and pentanuclear metallomacrocycles.¹⁷⁸

The group of Alfonso and Luis have demonstrated that anionic templates can be used to direct macrocycle formation in research reminiscent of Busch's seminal work.¹⁶⁷ The reaction of a diamine and dialdehyde, followed by reduction, gives a complex mixture of oligomers; however when the reaction is conducted in the presence of the terephthalate

anion, the major product (> 90%) is the [2+2] macrocycle (Scheme 1.2).¹⁷⁹ Subsequent work from these authors has extended this approach to the synthesis of larger cages,¹⁸⁰ and to formation of different sized macrocycles by varying the nature of the anionic template.¹⁸¹



Scheme 1.2: Alfonso and Luis' anion templated synthesis of pseudopeptidic macrocycles.¹⁷⁹

1.4.2 Interpenetrated and interlocked molecules

Mechanically interlocked molecules (MIMs) have long been a target for synthetic chemists, both for their aesthetic appeal, and also for a range of postulated potential nanotechnological applications, which will be discussed in Section 1.4.3. The simplest, and by far the most common, interlocked species are $[n]$ catenanes and $[n]$ rotaxanes (Figure 1.24); a catenane consists of two or more interlocked rings, while a rotaxane is comprised of one or more rings threaded around one or more 'axle' components, which have bulky groups that prevent the ring dethreading. The numeric prefix, n , refers to the number of components that make up the interlocked species. Pseudorotaxanes are *interpenetrated* rather than *interlocked* species, but are often important precursor assemblies that can be converted into catenanes or rotaxanes by covalent bond formation.

1.4.2.1 Synthesis of interlocked molecules

A number of approaches to rotaxane synthesis have been described: the two most common being *clipping* and *stoppering* (Scheme 1.3a,b). Clipping involves the ring-closing

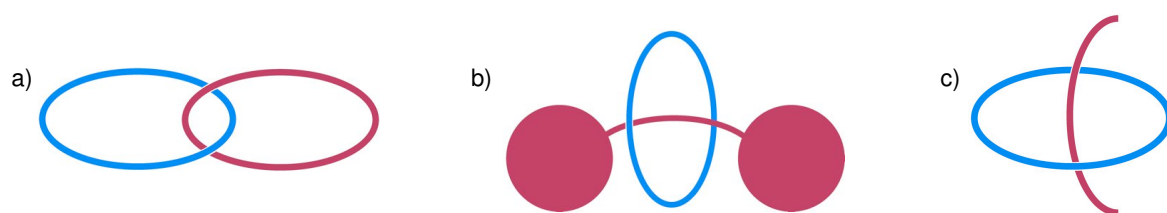
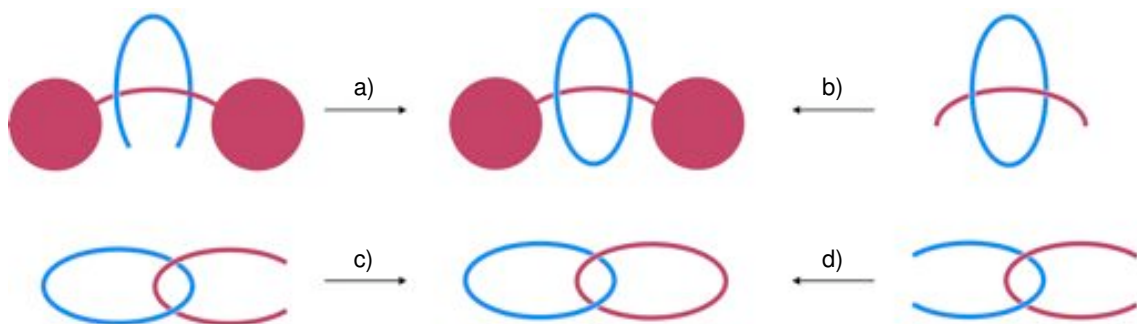


Figure 1.24: Schematic representation of the simplest types of interpenetrated and interlocked species: a) [2]catenane, b) [2]rotaxane, c) [2]pseudorotaxane.

of a macrocycle around an axle component to give a rotaxane, while stoppering involves appending bulky stopper groups to a pseudorotaxane assembly. More esoteric synthetic methods have also been described including slippage,^{182,183} shrinkage^{184,185} and swelling.¹⁸⁶ The snapping approach, where two parts of an axle component are bonded together through a macrocycle has recently received attention due to Leigh and colleagues' development of the 'active metal' route to interlocked molecules (see Section 1.4.2.2). In contrast, there are fewer synthetic routes to catenanes, with these usually being prepared either by clipping of one acyclic compound through a macrocycle, or by the tandem cyclization of two interweaved acyclic precursors (Scheme 1.3c,d).



Scheme 1.3: Synthetic routes to interlocked structures: a) clipping and b) stoppering syntheses of [2]rotaxanes; c) clipping, and d) double-cyclization of interweaved assembly to synthesize [2]catenanes.

1.4.2.2 Cation templated assembly of interlocked molecules

Early attempts to synthesize interlocked molecules relied on statistical approaches,^{187–190} or intricate syntheses using reversible reactions to allow covalent attachment of a directing template and its subsequent removal.¹⁹¹ Both of these routes were extremely low-yielding and laborious, and it was not until Sauvage's seminal report of the copper(I) templated synthesis of a [2]catenane^{192,193} that a viable method for producing interlocked molecules

was achieved.¹⁹⁴ It should be noted that this approach to interlocked structure formation is not strict self assembly, which would involve the MIM spontaneously assembling from the constituent parts. Rather, it is template directed self assembly of an interweaved species followed by covalent modification to afford the interlocked architecture.

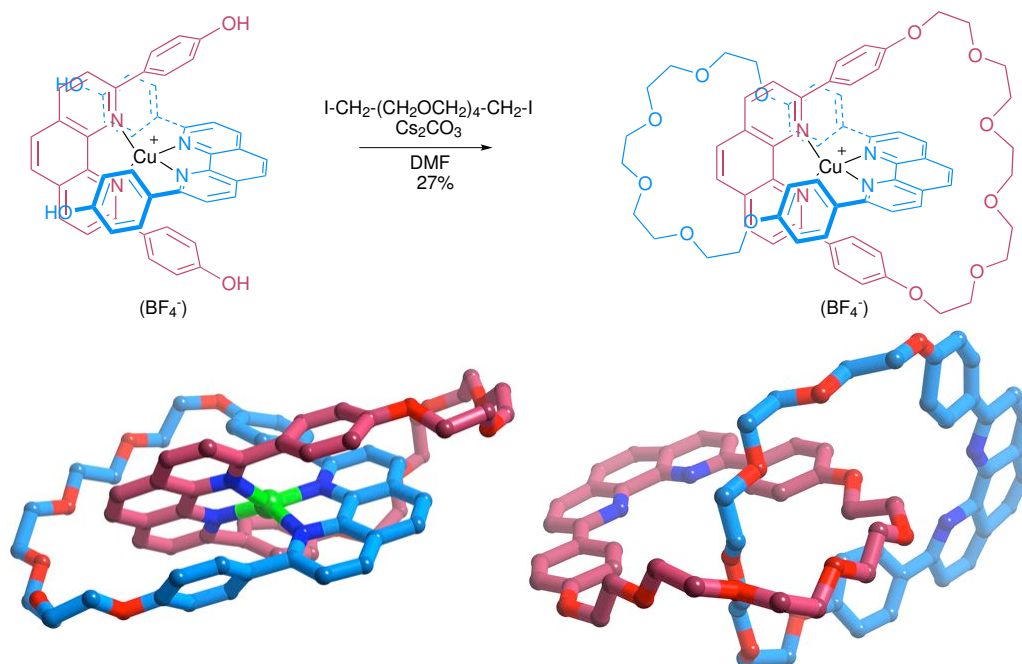


Figure 1.25: Sauvage's copper(I) templated catenane synthesis, which uses a clipping mechanism (top),¹⁹³ and single crystal X-ray structures of copper-coordinated catenane, and demetallated catenane.¹⁹⁵

Sauvage's synthesis relied on the orthogonal arrangement of two functionalized phenanthroline heterocycles around a tetrahedrally-coordinated copper(I) ion (Figure 1.25), whereupon cyclization of this interweaved precursor gave the copper complex of the [2]catenane,¹⁹² from which the transition metal ion could be removed.¹⁹³ Shortly afterwards, the same authors demonstrated the versatility of this approach by synthesizing a [3]catenane^{196,197} and a trefoil knot,¹⁹⁸ using a similar methodology.

Since the 1983 report of a copper(I) templated catenane, a range of transition metals with various coordination geometries have been used to template interlocked systems using both clipping¹⁹⁹ and stoppering strategies.^{200,201} As well as [2]rotaxanes and catenanes, a range of more complicated supramolecular architectures^{202–205} have been prepared using this method, for example, Borromean rings (Figure 1.22).¹⁷²

More recently, Leigh's group has developed the *active metal* route to interlocked molecules. Using this method, a catalytically-active metal is bound transiently within the macrocycle's cavity, and this templates covalent bond formation through the annulus of the macrocycle to give an interlocked species, with the metal acting as both template and catalyst.²⁰⁶

Another prolific area of research is the use of secondary ammonium cations in conjunction with polyether macrocycles to template the formation of interlocked species. The association between these two components was first reported in 1974,²⁰⁷ and it has subsequently been used to synthesize a range of pseudorotaxanes,²⁰⁸ rotaxanes^{209,210} and catenanes (Figure 1.26a).²¹¹ The power of this recognition element is demonstrated by Cronin and Stoddart's assembly of a [20]rotaxane in 90% isolated yield.²¹² The ammonium motif also has the advantage that once the interlocked molecule has been synthesized, the moiety can be reversibly deprotonated, allowing the potential for machine-like behaviour (Section 1.4.3).

An alternative approach is to use charge-assisted donor-acceptor interactions to assemble interlocked systems. This has been pioneered by Stoddart, who has used the attraction between electron-rich aromatics such as tetrathiafulvalene and dihydroxynaphthalene derivatives, and substituted 4,4'-bipyridinium groups to template the assembly of a range of pseudorotaxanes,^{213–215} rotaxanes²¹⁶ and catenanes²¹⁷ (Figure 1.26b).

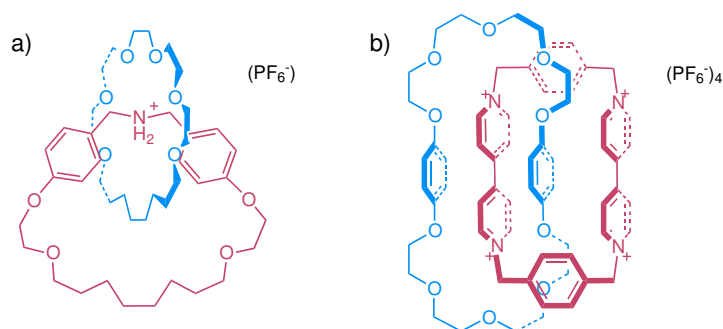


Figure 1.26: Catenanes synthesized using cationic templation: a) ammonium polyether [2]catenane,²¹¹ b) viologen based [2]catenane.²¹⁷

1.4.2.3 Assembly of interlocked molecules templated by neutral species

In 1992, Hunter showed that the condensation of isophthaloyl dichloride and a bis-amine gave the neutral octa-amide [2]catenane in 34% yield (Figure 1.27).²¹⁸ This product was formed through favourable inter-component hydrogen bonding of amide moieties. Leigh subsequently demonstrated the versatility of this approach by synthesizing a wide range of isophthalamide catenanes from isophthaloyl dichloride and a range of simple diamines,^{219,220} and more recently a range of neutral rotaxanes have been synthesized using inter-component hydrogen bonding.^{208,221,222}

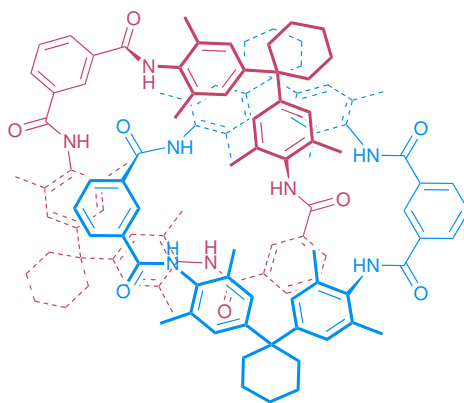


Figure 1.27: Hunter's octa-amide catenane.²¹⁸

Sanders has used a combination of electrostatic donor-acceptor attraction and solvophobic effects to form [2] and [3]catenanes from a dynamic combinatorial library (Figure 1.28). Modest amounts of catenane are detected in pure water, but the formation of interlocked products is dramatically enhanced by increasing ionic strength (*i.e.* by addition of inorganic salts), due to greater solvophobic effects.^{223–225} In a similar approach, Anderson has synthesized [3]rotaxanes by the stoppering reaction of pseudorotaxanes formed between apolar dyes and γ -cyclodextrin in water.²²⁶

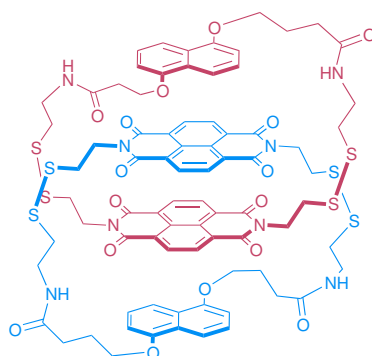


Figure 1.28: Sander's [2]catenane, the formation of which is templated by hydrophobic effects and donor-acceptor interactions.²²³

1.4.2.4 Anion templated assembly of interlocked molecules

In 1999, Vögtle exploited the association of a phenoxide anion and a tetra-amide macrocycle to form the first anion templated rotaxane. The phenoxide functionality is held inside the macrocycle, and subsequently reacts with a substituted benzyl bromide to form the MIM (Figure 1.29a).²²⁷ In Vögtle's system the phenoxide anion is consumed during the course of the synthesis. Schalley has also used phenoxide in the anion templated synthesis of rotaxanes, but in this case the phenol group remains after rotaxane formation (Figure 1.29b).²²⁸ More recently, Smith's group have condensed isophthalolyl dichloride and bis-amines around zwitterionic squaraine based functionalities, to give rotaxanes (Figure 1.29c)^{229,230} and catenanes,²³¹ with the templating zwitterion again present in the resulting interlocked architecture.

Shortly after Vögtle's report of an anion templated rotaxane, Beer demonstrated that a *discrete* anion template could be used to assemble interpenetrated and interlocked architectures.^{232–235} This approach relies on “sharing” of a halide anion between two components, with assistance from donor-acceptor stacking interactions and *N*-methyl-pyridinium⁺ · polyether hydrogen bonding (Figure 1.30a). The advantage of this method is that once the target MIM has been formed (Figure 1.30b), the anion template can be removed leaving a three-dimensional cavity, which allows selective binding of halides over larger, more basic oxoanions (Figure 1.30c,d).^{233,234,236} This anion templation approach has since been developed to give more intricate architectures such as a triply-interlocked capsule,²³⁷ and a “handcuff” catenane.²³⁸ Anion sensors^{148,161–163,239–241}

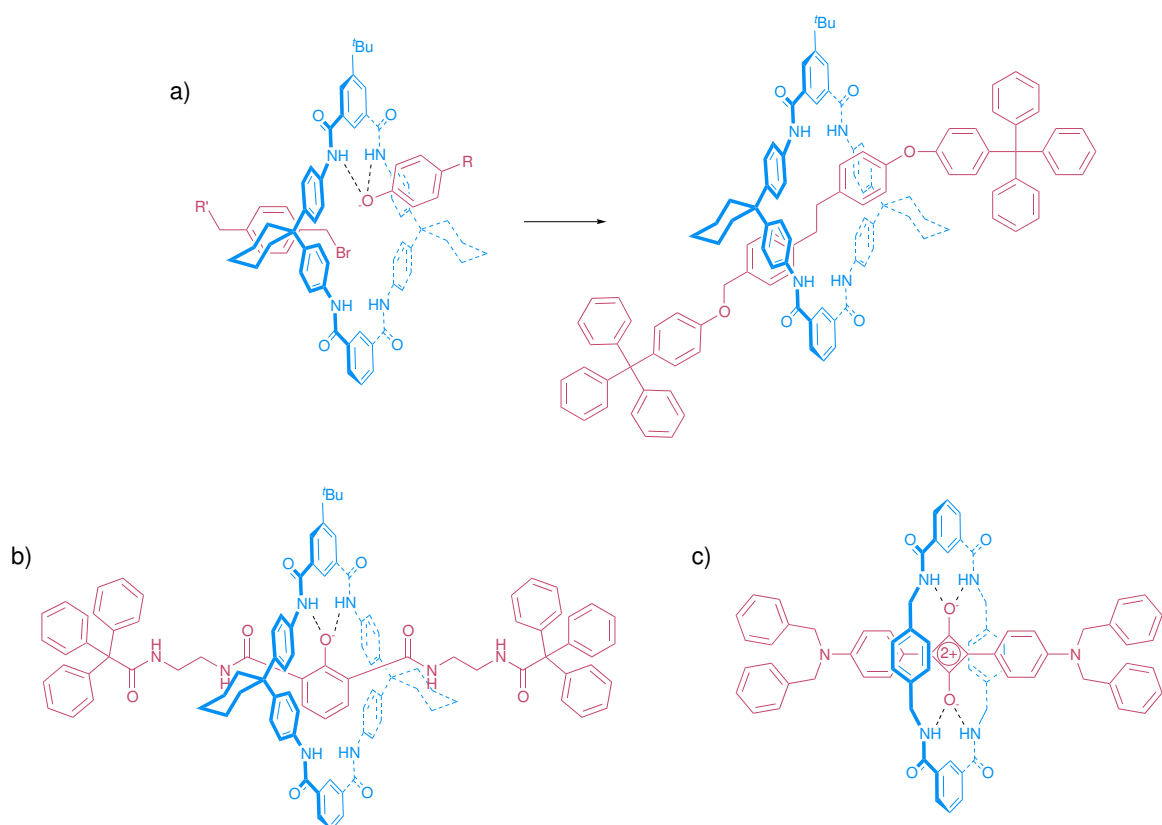


Figure 1.29: Rotaxanes synthesized using anion templation: a) synthesis of Vögtle's phenoxide templated rotaxane,²²⁷ b) Schalley's phenoxide rotaxane,²²⁸ c) Smith's squaramide rotaxane.²²⁹

have also been prepared, as well as interlocked host systems incorporating a range of anion complexing motifs including indolocarbazole,^{242,243} imidazolium²⁴⁴ and triazolium²⁴⁵ (Section 1.5).

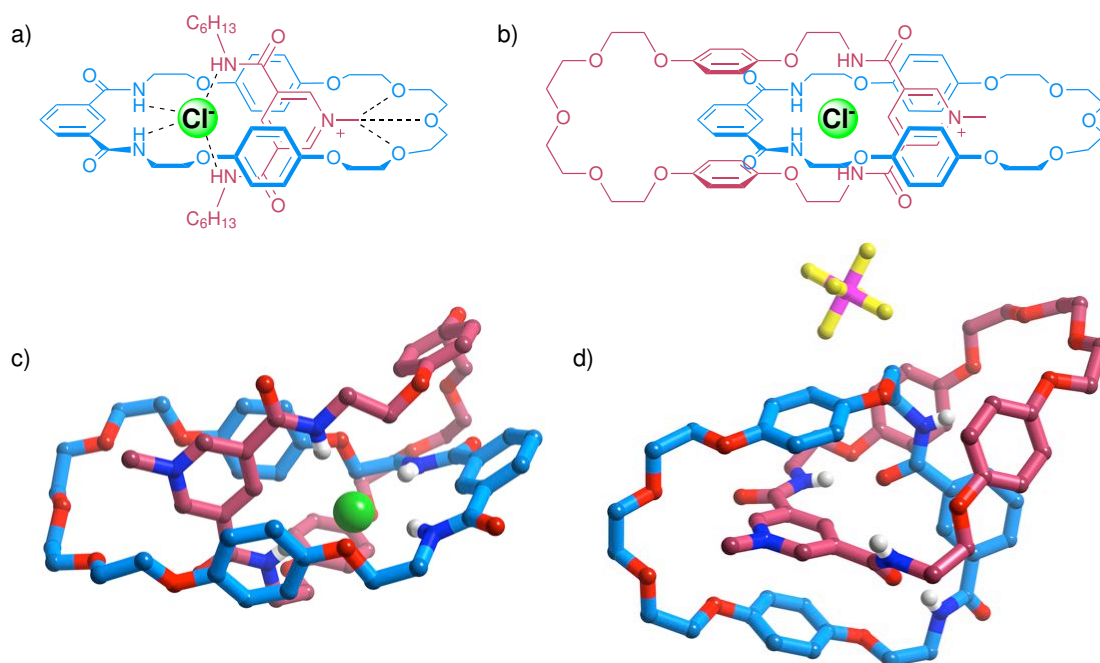


Figure 1.30: Discrete anion templation: a) chloride templated pseudorotaxane,²³² b) [2]catenane,²⁴⁶ c) solid state structure of Cl^- salt of this catenane,²⁴⁶ d) solid state structure of PF_6^- salt of this catenane showing “free” cavity ready for an anionic guest.²⁴⁶

1.4.3 Applications of interlocked molecules

Inspired by Nature’s use of “motors”²⁴⁷ and “walkers”²⁴⁸ to perform important biological tasks, chemists have sought to design systems that act as prototypical molecular machines. Interlocked systems are ideal for this, as their multiple components allow for molecular motion of one part of the molecule relative to the others. In a rotaxane, the macrocycle component may move along the axle component, or may rotate relative to it (Figure 1.31a), while a catenane offers the potential of rotation of one macrocycle around the other (Figure 1.31b).

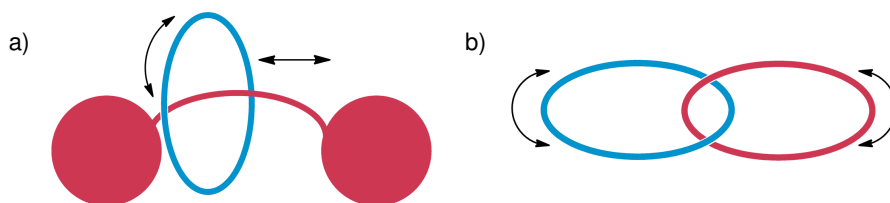


Figure 1.31: Molecular motion in interlocked structures: a) rotation or translation of a macrocycle in a rotaxane, b) rotation of either macrocycle in a catenane.

Initially, molecular motion was exploited in the preparation of rotaxane shuttles, such as that shown in Figure 1.32. When the secondary amine group is protonated, the polyether macrocycle resides over this group to take advantage of charge-assisted hydrogen bonding interactions; deprotonation causes translation of the macrocycle to the viologen group.^{209,249} More sophisticated molecular machines have since been reported, such as a [3]catenane, in which two smaller rings move unidirectionally around a larger ring in response to light stimuli,²⁵⁰ a rotaxane-functionalized surface that can “push” macroscopic liquids up an incline,²⁵¹ and “molecular muscles,” which can expand and contract in response to a stimulus.²⁵²

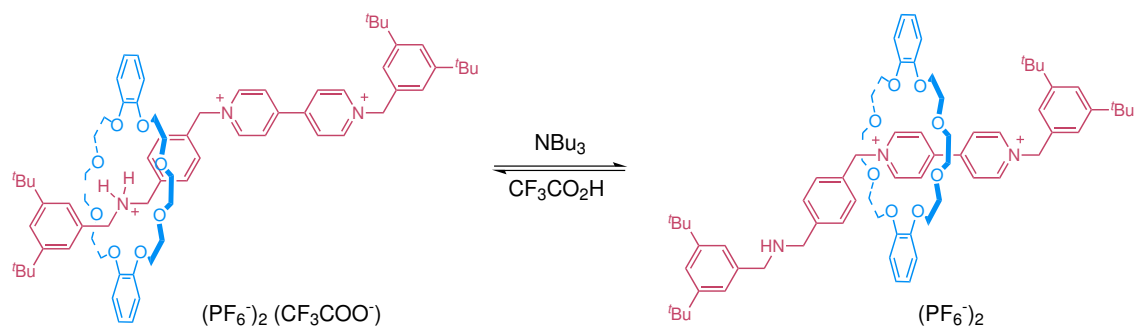


Figure 1.32: Stoddart's acid/base controlled molecular shuttle.^{209,249}

Another interesting use of interlocked hosts is to modulate the chemical properties of an encapsulated component of the MIM. For example, Anderson demonstrated that when an azo dye is protected inside a cyclodextrin rotaxane, the chromophoric properties of the rotaxane are essentially unchanged, but unwanted reductive bleaching of the dye is greatly slowed (Figure 1.33).²⁵³ A similar approach has also been used to protect a polypeptide from enzyme digestion — in this case, a removable stopper was used on the rotaxane axle component, which could be selectively detached to release the polypeptide from the protective macrocyclic component.²⁵⁴

Of particular interest to this work, MIMs can be potent hosts for a variety of guests, due to the three-dimensional binding pocket provided by the interlocked cavity. Sanders used acetylcholine to template formation of a catenane from a dynamic combinatorial library; isolation of this host from the library gave a receptor that strongly complexed the templating species.²⁵⁵ As previously intimated, interlocked hosts can provide strong

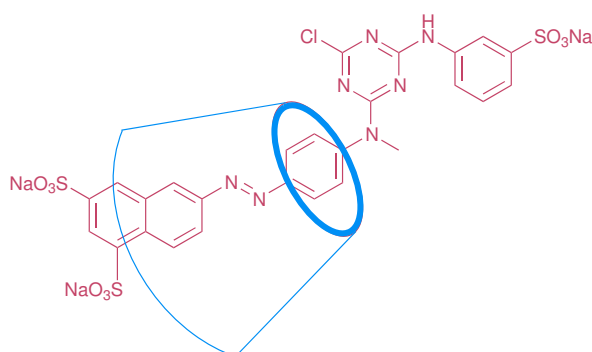


Figure 1.33: Anderson's cyclodextrin-encapsulated dye rotaxane.²⁵³

and selective anion recognition: for example, neutral indolocarbazole catenanes^{256,257} preferentially complex chloride in 99:1 d_6 -acetone: D_2O (Figure 1.34).²⁵⁶

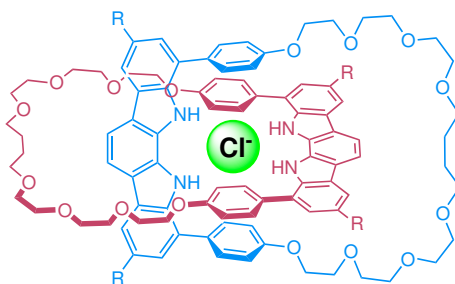


Figure 1.34: Jeong's indolocarbazole catenane.²⁵⁶

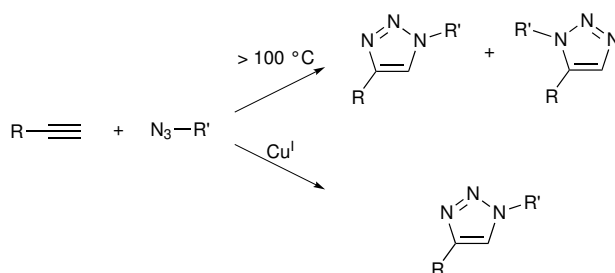
1.5 C–H hydrogen bond donors for anion binding and anion templated self assembly

In the year prior to the commencement of the work described in this thesis, several reports detailing favourable interactions between neutral C–H groups and anionic guests appeared in the literature.^{106–108,258,259} A large part of this interest surrounded the discovery that readily synthesized 1,2,3-triazole heterocycles can complex anions. This section will discuss anion complexation by neutral and charged C–H hydrogen bonds, with a particular focus on the 1,2,3-triazole and -triazolium motifs.

1.5.1 Click chemistry and the 1,2,3-triazole group

In 2001, Sharpless published a set of criteria for idealized chemical reactions, which would allow a “fast, modular, process-driven approach to molecular chemistry.”²⁶⁰ These reactions, which he termed *click* reactions would be (amongst other things) high-yielding, have wide scope, generate inoffensive by-products and allow simple product isolation.

The following year, Fokin and Sharpless,²⁶¹ and Meldal,²⁶² reported that the [3+2] cycloaddition of azides and terminal alkynes regioselectively gives 1,4-disubstituted-1,2,3-triazole compounds when conducted in the presence of a copper(I) catalyst. Sharpless termed this a click reaction on the basis of the criteria described above. Prior to the development of this copper(I)-catalyzed reaction, the cycloaddition of azides and alkynes required elevated temperatures and gave a mixture of 1,4- and 1,5-disubstituted-triazole groups (Scheme 1.4).²⁶³



Scheme 1.4: Thermal, and copper(I)-catalyzed synthesis of 1,2,3-triazole groups.^{261–263}

Since this important development, the reaction has been widely exploited in a range of uses across the chemical sciences.^{263,264} Of particular relevance to this thesis, the wide functional group tolerance and mild reaction conditions have proven ideal for use in the construction of MIMs.^{265,266} It should be noted that while the term “click” reaction is often used to describe the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC), many of the reactions to which this term is applied fail to meet several of Sharpless’ click criteria.²⁶⁰

1.5.1.1 Triazole anion hosts

In 1990, it was reported that a fluorinated macrocyclic ether associates with fluoride in d₈-THF solution and the solid state (Figure 1.35), with the complexation attributed to hydrogen bonding from polarized CH₂ groups.²⁶⁷ With the exception of this receptor, the

possibility of using only neutral C–H hydrogen bonds to complex anions was overlooked until very recently.²⁶⁸ While the existence of favourable interactions between anions and polarized C–H donors has been known for some time,^{258,269} it was not until 2008 that hosts specifically designed for binding anions *solely* through these interactions were reported.



Figure 1.35: Structure of Farnham and Dixon's fluoride host (left) and single crystal X-ray structure of the fluoride adduct (right). The macrocycle undergoes a conformational change upon fluoride binding to allow the polarized C–H donors to point into the host cavity.²⁶⁷

In this year, three groups independently demonstrated the ability of poly-triazole receptors to interact with halide anions in organic solvents.^{45,106–108} Hecht demonstrated that a poly-triazole foldamer undergoes a helix inversion in response to an achiral halide anion.¹⁰⁸ Craig reported a similar oligomer, which exhibits an open conformation in solution, but which folds into a helix on addition of chloride (Figure 1.36).¹⁰⁷ Flood prepared a rigid tetra-triazole macrocycle, which exhibits a very high affinity for chloride and bromide in dichloromethane, and displays a sensing response *via* a change in the host's UV absorption spectrum (Figure 1.5).^{45,106}

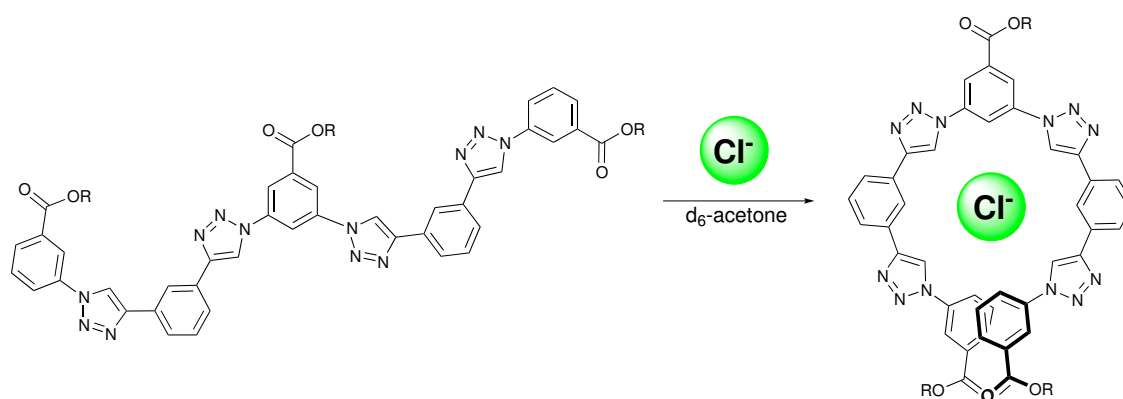


Figure 1.36: Craig's tetra-triazole foldamer.¹⁰⁷

Since the commencement of this project, investigation of the anion complexation properties of neutral triazole donors has flourished. The effect of solvent,⁷⁹ and

preorganization^{81,82,270} on binding affinities have been investigated, and a variety of sensing groups incorporated into triazole based hosts including ferrocene,²⁷¹ zinc-porphyrin,^{241,272} and naphthalimide.²⁷³

Prototypical devices involving triazole···anion interactions have also begun to emerge: Bachas has reported ion selective electrodes based on Flood’s triazolophanes,^{274,275} while Flood has demonstrated that levels of free chloride anion in solution can be manipulated using a triazole-azobenzene based switchable foldamer (Figure 1.37).²⁷⁶ Switching from the *cis* to *trans* conformation of the diazobenzene group by irradiating with visible light ($\lambda = 436$ nm) favours folding into a helical arrangement, due to solvophobic effects. This folded arrangement has an order of magnitude greater affinity for chloride than the unfolded conformation causing a measurable decrease in the conductance of the solution due to encapsulation of charged anion; the “switch” is fully reversible using UV light ($\lambda = 365$ nm).

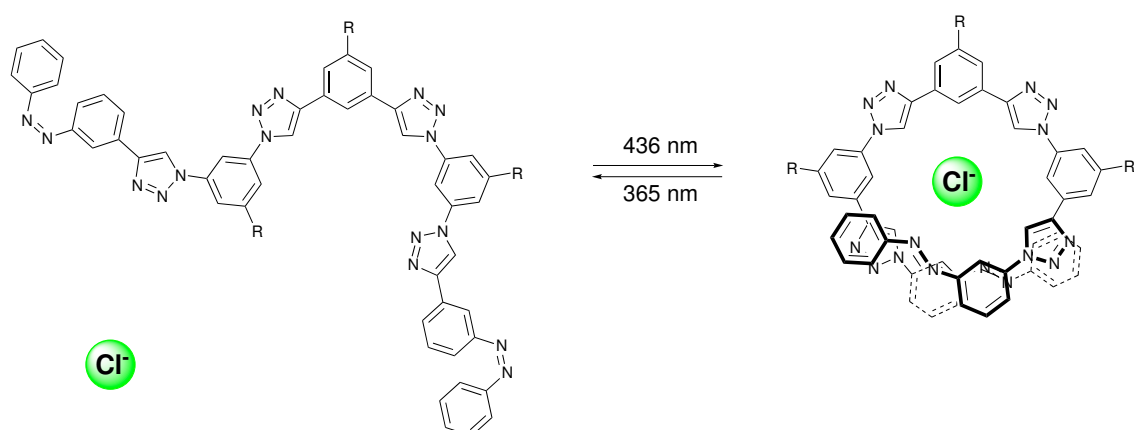


Figure 1.37: Flood’s oligomeric anion switch.²⁷⁶

1.5.1.2 Triazolium anion hosts

In 2008, Pandey reported acyclic and macrocyclic anion host systems based on a steroid scaffold containing two alkylated triazole, *i.e.* *triazolium* functionalities (Figure 1.38a). These were shown to selectively bind dihydrogen phosphate in CDCl_3 — interestingly, the acyclic receptor complexed this anion more strongly than the macrocycles, which was attributed to the greater flexibility of the former receptor allowing it to adapt a suitable geometry to bind the large tetrahedral species.¹⁰⁹ Surprisingly, since this work little use

has been made of the enhanced anion complexing properties of the triazolium group (unlike the neutral triazole heterocycle), with only a handful of anion receptors reported.^{241,277–279} Notably, Schubert has demonstrated the orthogonal arrangement of two triazole-triazolium hosts around a sulfate anion (Figure 1.38b).²⁷⁷

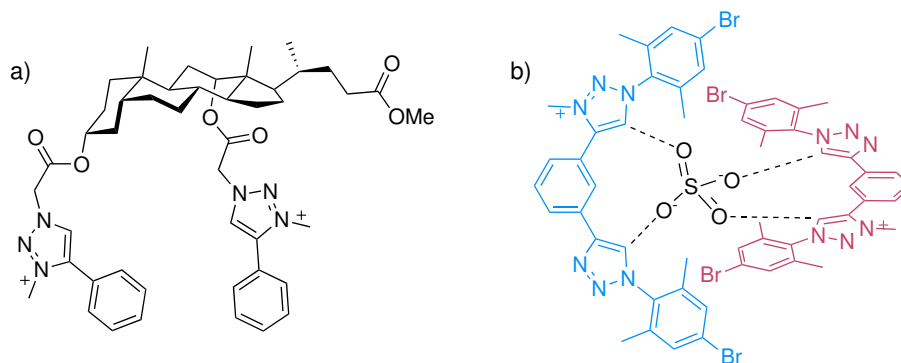


Figure 1.38: Anion receptors based on triazolium heterocycles: a) Pandey's steroidal host,¹⁰⁹ b) Schubert's orthogonal array of two triazole-triazolium receptors around a sulfate anion.²⁷⁷

1.5.2 C–H hydrogen bonding groups for anion templated synthesis of interlocked molecules

The synthetic versatility of the CuAAC reaction (Section 1.5.1) has led to the incorporation of the triazole functionality into a range of interlocked molecules, as the wide scope of this reaction is ideal for mechanical bond formation.^{265,266} Typically, however, these triazole groups serve only as a covalent linker and do not have a functional role in the resulting MIM. Only a few systems have been reported where triazole or triazolium heterocycles have an active role in an interlocked architecture — in these cases, the heterocycles act either as anion recognition elements, or as a station in a molecular machine.

Coutrot's group reported the first triazolium containing rotaxane,²⁸⁰ in which the rotaxane axle component has an aniline and triazolium station. When the aniline group is protonated, the dibenzo[24]crown-8 macrocycle resides at this location, deprotonation causes molecular motion with the cycle moving to the triazolium station (Figure 1.39). The triazole and triazolium groups have subsequently been incorporated into several two- and three-station molecular shuttles,^{281–284} and molecular muscles,^{285,286} in conjunction with substituted ammonium centres and polyether macrocycles.

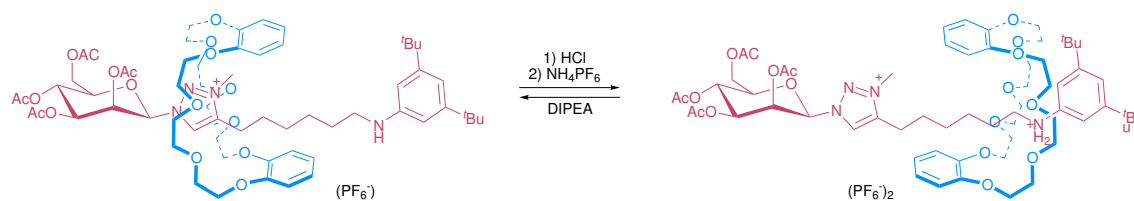


Figure 1.39: Coutrot's triazolium containing rotaxane.²⁸⁰

A year after Coutrot's triazolium containing rotaxane, Beer and co-workers demonstrated that triazolium based threading components could form stable chloride templated pseudorotaxanes with an isophthalamide macrocycle, and furthermore that the triazolium motif could be incorporated into a anion templated [2]rotaxane framework (Figure 1.40).²⁴⁵ Since the start of this project, Beer's group has also reported a closely-related imidazolium based rotaxane,²⁴⁴ as well as anion responsive molecular machines based on the imidazolium,²⁸⁷ and triazolium²⁸⁸ functional groups.

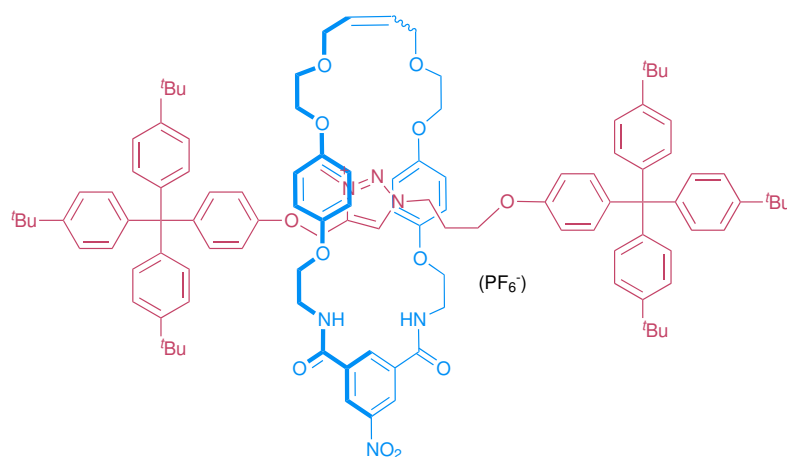


Figure 1.40: Beer's triazolium containing rotaxane.²⁴⁵

1.5.3 Project aims

The broad aims of the project are to incorporate triazole and triazolium motifs into macrocyclic, interpenetrated and, in particular, interlocked structural frameworks for use as potent, selective anion receptor systems.

Chapter Two focuses on systems involving *triazole* donors: a series of acyclic and macrocyclic bis-triazole receptors are reported, and their anion and transition metal recognition properties investigated. The new pyridinium-3,5-bis(triazole) motif (Figure 1.41) is introduced and its ability to complex anions is examined.

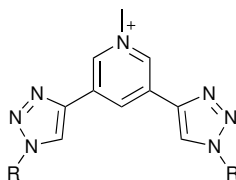


Figure 1.41: The pyridinium-3,5-bis(triazole) motif.

Chapter Three contains further research related to the pyridinium-3,5-bis(triazole) motif, with the ability of this group to form stable anion templated pseudorotaxane assemblies with isophthalamide macrocycles investigated, leading to its incorporation into [2]catenane and [2]rotaxane structural frameworks. The anion recognition properties of these interlocked host systems are thoroughly explored.

Chapter Four details the synthesis of a series of mono-triazolium rotaxane hosts with the aim of using design modifications to influence the strength and selectivity of anion binding: specifically, the size of the axle and macrocycle components are varied, as well as the nature of the substitution of the triazolium group. The affinities of these receptors for a range of anions is investigated and factors influencing complexation strength discussed in relation to the structure of the interlocked molecule.

Chapter Five investigates the integration of two or more triazolium moieties into host structural frameworks to create highly charged receptors capable of anion complexation in aqueous media. A tetra-triazolium macrocycle and bis-triazolium rotaxane are described, and the anion templated synthesis of highly charged tetra-triazolium interlocked receptors is explored.

Chapter 2

Acyclic and macrocyclic triazole receptors

2.1 Introduction

2.1.1 Anion recognition using triazole C–H donors

Since three independent reports in 2008 that synthetic hosts incorporating 1,2,3-triazole groups can interact with anions solely through polarized C–H hydrogen bonds,^{106–108} numerous anion receptors incorporating these heterocycles have been described.^{45,79,81,82,270–273,276,289–295} However, prior to the start of this work, only receptors that function in non-polar organic solvents (dichloromethane, chloroform, acetone) had been detailed.

The analogy between 1,2,3-triazole groups and amides has been demonstrated in the biological chemistry community, with triazoles used as amide surrogates in peptidic oligomers,^{296,297} nanotubes,²⁹⁸ and folded peptide structures.²⁹⁹ Less attention has been paid to this similarity by anion coordination chemists, however, despite the vast array of biological and synthetic anion host systems that incorporate amide donors.^{4,77,300}

Given the wide range of macrocyclic,³⁰¹ interpenetrated^{232,302} and interlocked^{233–236} receptors reported by the Beer group that bind anions using amide functionality, it was of interest to prepare triazole containing host analogues and investigate their anion recognition properties. The possibility of subsequent alkylation of such host systems to give the cationic triazolium receptor analogues, where anion binding affinities may be enhanced by virtue of the additional positive charge, could also be explored.

One of the first triazole anion hosts was synthesized by Craig, who reported bis-triazole and tetra-triazole oligomers that strongly bind halides and oxoanions in d_6 -acetone. Notably, the simple bis-triazole receptor shown in Figure 2.1a complexes chloride anion with an association constant of 1260 M^{-1} ,⁷⁹ comparable to the anion association of a previously reported bis-amide macrocycle (Figure 2.1b, $K_a = 2560\text{ M}^{-1}$).³⁰¹ Clearly, there are a number of differences between the two host systems (acyclic *vs* macrocyclic, nature of substitution of donor groups), however, this does suggest that the amide and triazole groups are at least comparable in terms of their anion recognition abilities.

While the work described in this thesis was being undertaken, Kubik and co-workers reported a similar study where amide units in cyclic peptides were replaced with

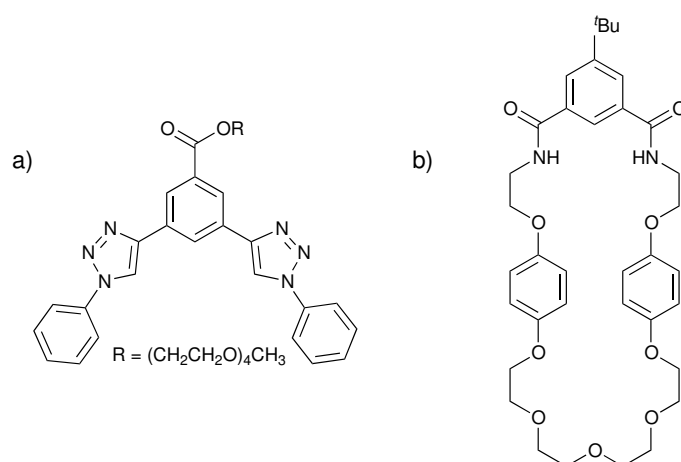


Figure 2.1: a) Craig's bis-triazole receptor;⁷⁹ b) Beer's bis-amide receptor.³⁰¹

1,2,3-triazole units (Figure 2.2).^{293,303} Interestingly, the authors reported that while the solution and solid state conformations of the triazole containing macrocycles were very similar to the peptides, their anion recognition properties were *intrinsically higher*. It should be noted, however, that this study involved the replacement of tertiary aprotic amides with protic triazole groups, and so the increased anion affinity is perhaps not surprising.

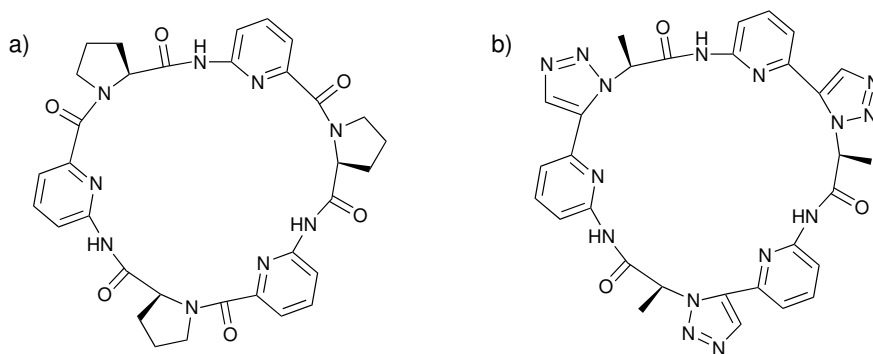


Figure 2.2: Amide and triazole containing macrocycles compared by Kubik: a) hexapeptide receptor; b) hexapseudopeptide receptor.²⁹³

2.1.2 Transition metal recognition using triazole nitrogen donors

The transition metal coordination chemistry of 1,2,4-triazole groups has been well-studied,^{304,305} driven, in part, by the interesting magnetic properties of the resulting paramagnetic complexes, with the heterocycle often bridging two metal cations.³⁰⁶

Conversely, the transition metal chemistry of 1,2,3-triazoles has been the subject of far less research,³⁰⁷ despite the ease of synthesis of these groups using the CuAAC reaction.

In the majority of cases where the 1,2,3-triazole group is used to coordinate to a metal ion, the triazole cycle is part of a polydentate ligand in conjunction with a more traditional donor such as a pyridine or amine group. For example, in 2007, the groups of Flood, and Hecht and Limberg independently reported the synthesis of the pyridine bis-triazole motif and its use as a ligand for transition metals (Figure 2.3).^{308,309} The motif is similar to the extensively studied terpyridine unit, and acts as an efficient tridentate donor to a range of transition metal ions, including Fe^{2+} , Ru^{2+} and Eu^{3+} .^{308–310}

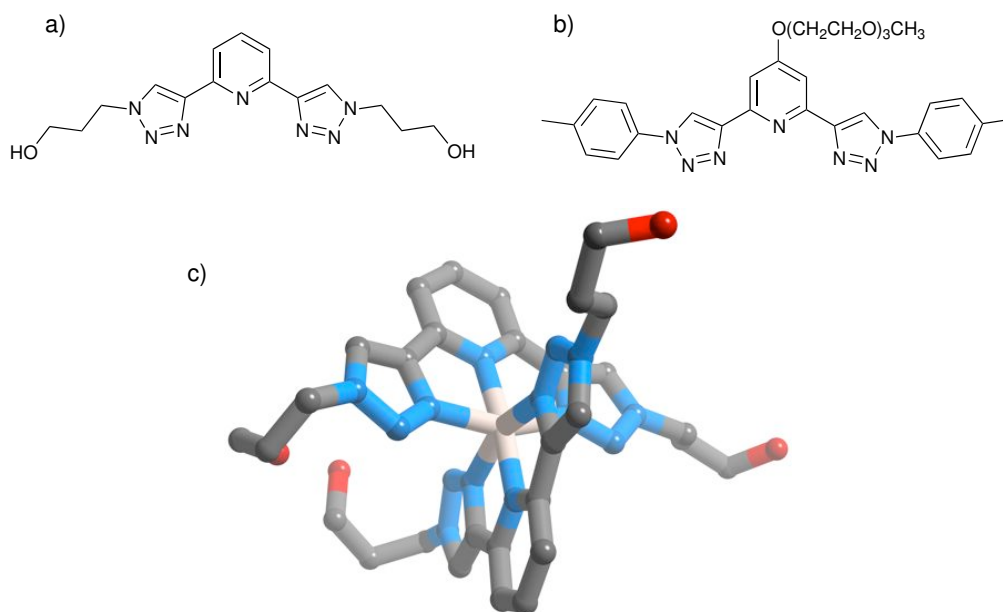


Figure 2.3: Pyridine bis-triazole ligands: a) example of ligands studied by Flood;³⁰⁸ b) example of ligands studied by Hecht;^{309,310} c) solid state structure of Ru^{2+} complex of Flood's ligand.³⁰⁸

In the last few years, “unsupported” triazole ligands, in which metal coordination occurs exclusively *via* triazole groups have begun to appear in the literature.^{311–318} Notably, Crowley and co-workers have demonstrated that silver(I) and palladium(II) complexes of such ligands can form interesting metallocsupramolecular architectures, such as cages and metallomacrocycles (Figure 2.4).^{314,319}

The ability of triazoles to act as ligands for transition metals offers the possibility of using metal coordination to template the formation of an interlocked architecture, which upon removal of the cation would be a potent anion host. Given the high yields that

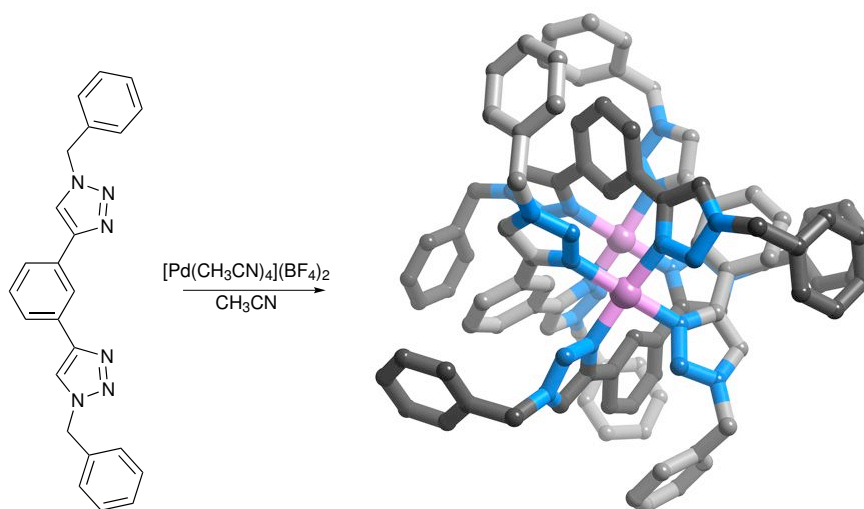


Figure 2.4: Crowley's dinuclear palladium coordination cage, formed using unsupported triazole ligands.³¹⁹

such metal templated reactions can have,²⁰² this may be an efficient method for preparing interlocked anion receptors.

2.1.3 Chapter objectives

In light of the facile synthesis and promising anion recognition properties of 1,2,3-triazole groups, this chapter will investigate a range of acyclic and macrocyclic hosts incorporating these heterocycles. Specifically, analogues of a series of previously reported amide containing hosts will be prepared, allowing a detailed comparison of the amide and triazole functionality in terms of their anion recognition properties.

The ability of triazole groups to complex transition metal cations will also be examined, with the ultimate aim of using metal cations to template the formation of triazole containing interlocked structures that can bind anions upon removal of the templating metal cation.

2.2 Acyclic bis-triazole receptors

Initially, it was decided to prepare simple acyclic bis-triazole-phenylene receptors to investigate the effects of structural modifications on anion recognition properties. Four new receptors were prepared, having the triazole groups linked to the central phenylene ring through either the *C* or *N*-terminus, and having alkyl or aryl substitution of the triazole functionality.

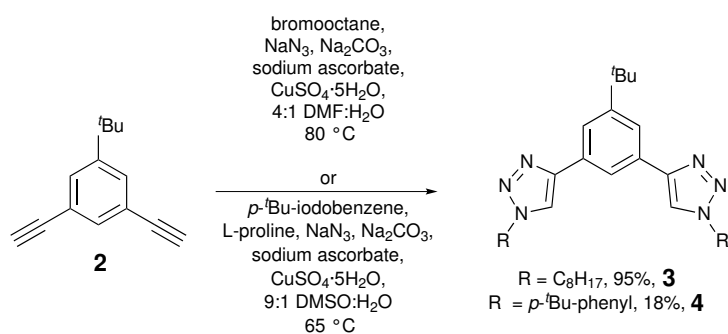
2.2.1 Synthesis of acyclic bis-triazole receptors

The acyclic receptors were synthesized in one-pot procedures from alkyl bromides or aryl iodides, and alkynes (Schemes 2.1 and 2.2).^{320,321} In such procedures, the reagents used to convert the halide into an azide, and to catalyze the CuAAC reaction were all present in the reaction vessel. For alkyl halides, this simply requires an azide source (typically sodium azide), and a suitable solvent system to at least partially dissolve all components. In the case of an aryl halide, a copper(I) catalyst, ligand and base are required to effect the conversion from aryl halide to aryl azide. Conveniently, these catalyst systems also catalyze the CuAAC reaction, allowing for efficient one-pot reactions.^{320,322} As well as being a more elegant route to the desired products, such one-pot syntheses eliminate the need to isolate and handle potentially unstable or explosive organo-azide compounds.

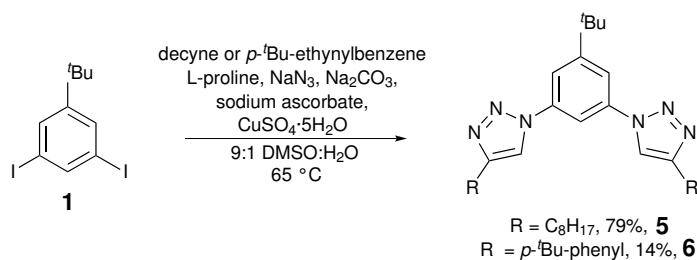
A modified literature procedure was used to prepare 5-*t*-butyl-1,3-diiodobenzene **1** in two steps and 52% yield from 4-*t*-butyl-aniline.³²³ Subsequent Sonogashira reaction³²⁴ with TMS-acetylene followed by removal of the TMS groups gave **2**^{325,326} in 37% overall yield from 4-*t*-butyl-aniline.

One-pot reactions of bis-alkyne **2** with either bromooctane or *p*-*t*-butyl-iodobenzene using copper(II) sulfate and sodium ascorbate as a copper(I) source, sodium azide, sodium carbonate as base and either a mixed dimethylformamide/water or dimethylsulfoxide/water solvent system gave the bis-triazole receptors **3** and **4** (Scheme 2.1). The reaction of bis-iodide **1** with decyne or *p*-*t*-butylphenylacetylene under the same conditions gave the new bis-triazole compounds **5** and **6** (Scheme 2.2).

Using this methodology, receptors **3** and **5**, containing alkyl substituents, could be prepared in very good yields (95 and 79%, respectively), but the aryl-substituted receptors

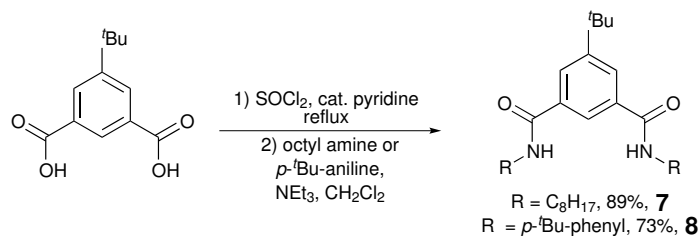


Scheme 2.1: Synthesis of *C*-linked acyclic receptors **3** and **4**.



Scheme 2.2: Synthesis of *N*-linked bis-triazole receptors **5** and **6**.

4 and **6** were formed in much lower yields (18 and 14%, respectively) and the reaction mixtures gave several side-products, which were difficult to separate from the desired product using chromatographic techniques. The reactions were repeated several times, with efforts being made to thoroughly de-oxygenate the reaction vessels, but no increase in yield was observed. The analogous amide containing receptors **7** and **8** were prepared from 5-^tbutylisophthalic acid by converting to the acid chloride with refluxing thionyl chloride and then condensing with the appropriate amine in dichloromethane, as shown in Scheme 2.3.



Scheme 2.3: Synthesis of bis-amide receptors **7** and **8**.

The new bis-triazole and bis-amide receptors were characterized by ^1H and ^{13}C NMR as well as by high resolution ESI mass spectrometry. Recrystallization from methanol

gave single crystals of **4**, **6** and **8** suitable for characterization by X-ray crystallography (Figure 2.5). All three structures feature significant intermolecular receptor...receptor and receptor...methanol solvate hydrogen bonding. Notably, hydrogen bond distances where the amide host acts as a donor are significantly shorter than when the triazole C–H bond acts as donor [$\text{N-H}_{\text{amide}} \cdots \text{acceptor} = 2.814(3)–3.016(3) \text{ \AA}$, $\angle \text{N-H} \cdots \text{acceptor} = 159–173^\circ$; $\text{C-H}_{\text{triazole}} \cdots \text{acceptor} = 3.146(4)–3.537(4) \text{ \AA}$, $\angle \text{C-H} \cdots \text{acceptor} = 154–171^\circ$].

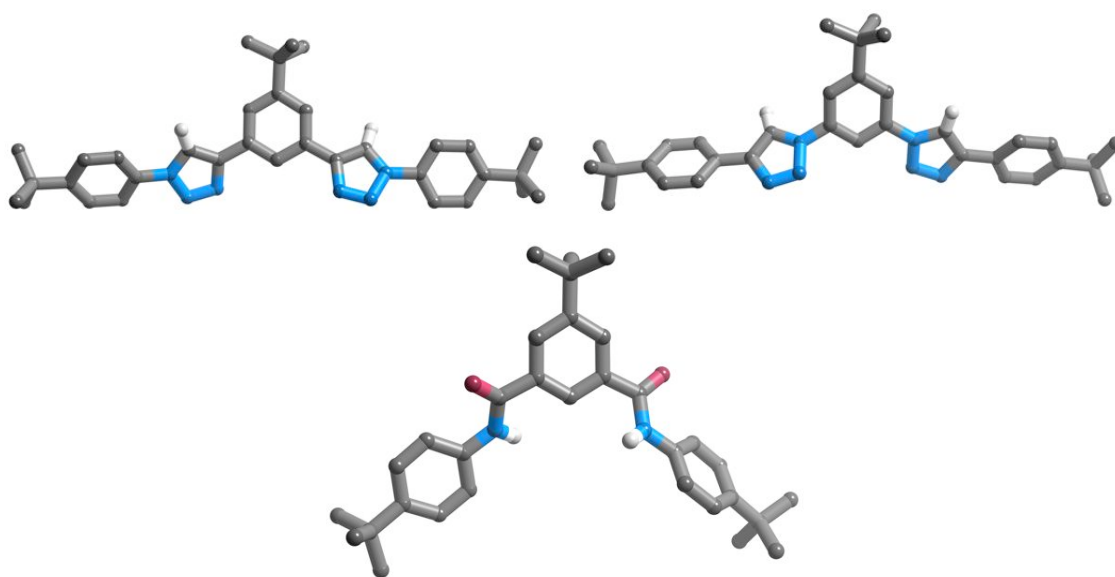


Figure 2.5: Solid state structures of **4**, **6** and **8**. Methanol solvates and most hydrogen atoms omitted for clarity.

2.2.2 Anion recognition properties of acyclic bis-triazole receptors

The chloride anion binding properties of these acyclic systems were investigated by ^1H NMR titration experiments in d_6 -acetone.³²⁷ Aliquots of a solution of $\text{TBA}\cdot\text{Cl}$ were added to a solution of the host and the changes in the ^1H NMR spectrum analysed. As shown in Figure 2.6 for the aryl-substituted receptors **4** and **6**, addition of chloride causes significant downfield shifts of signals *c* and *d* due to hydrogen bonding interactions with these protons. Resonances *a* and *b* diverge, due to increased inequivalence of these environments when chloride is complexed by the receptor. The shifts in resonances *c* and *d* are slightly greater for the *N*-linked receptor **6** (0.62 and 0.38 ppm for *c* and *d* respectively after 1.0 equivalents of chloride) than for the *C*-linked receptor (0.51 and 0.28 ppm for *c*

and *d* respectively after 1.0 equivalents of chloride). In comparison, addition of chloride anion to both alkyl-substituted receptors **3** and **5** results in much smaller shifts of protons *c* and *d* (Figure 2.7).

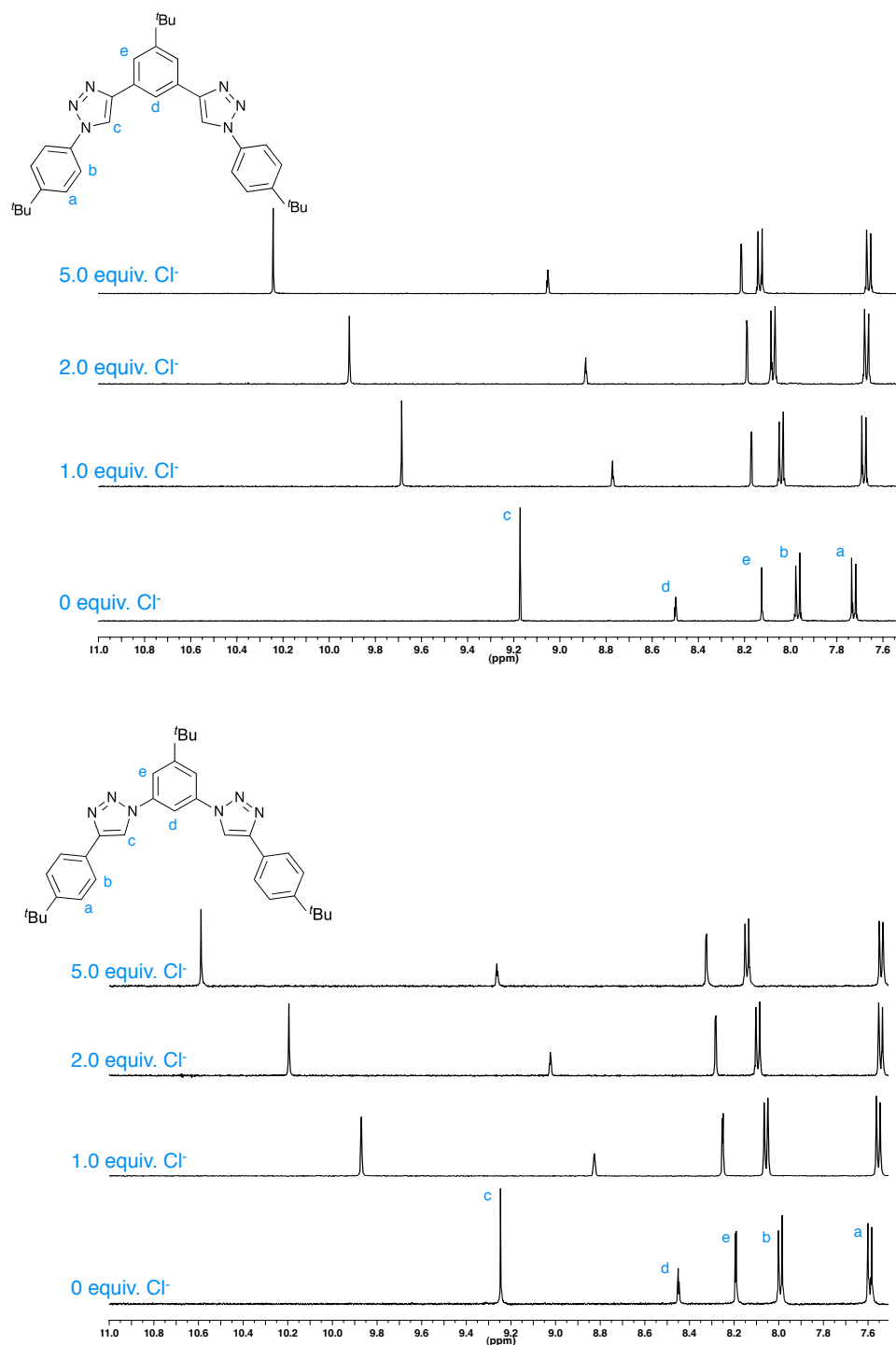


Figure 2.6: Truncated ¹H NMR spectra of **4** (top) and **6** (bottom) upon addition of TBA·Cl (d₆-acetone, 293 K, 500 MHz).

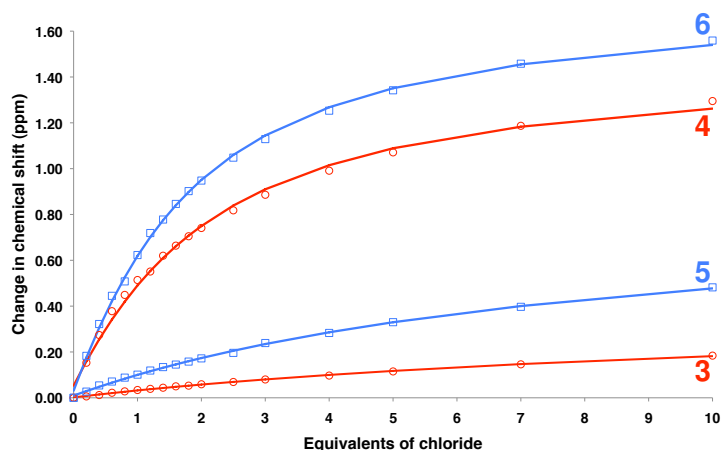


Figure 2.7: Experimental titration data (points) and fitted binding isotherms (lines) for addition of chloride anion to acyclic receptors, following triazole resonance, *c* (d₆-acetone, 293 K, 500 MHz).

WINEQNM2³²⁸ analysis of the titration data monitoring the triazole proton gave 1:1 stoichiometric association constants. Details of the use of this program to determine association constants, as well as the limitations and errors associated with these values are given in Section 6.1. As shown in Table 2.1, both aryl-substituted receptors **4** and **6** bind chloride much more strongly than alkyl-substituted hosts **3** and **5**, presumably due to the increased acidity of the triazole protons resulting from the aromatic phenyl substituents.

Table 2.1: Association of acyclic bis-triazole receptors with chloride anion; estimated standard errors are given in parentheses.

Substitution	Compound Number	K_a (M ⁻¹) ^a
<i>C</i> -linked, alkyl-substituted	3	32(3)
<i>C</i> -linked, aryl-substituted	4	309(29)
<i>N</i> -linked, alkyl-substituted	5	55(5)
<i>N</i> -linked, aryl-substituted	6	380(18)

^aChloride anion added as TBA salt, estimated standard errors are given in parentheses. Association constants calculated using WINEQNM2³²⁸ (d₆-acetone, 293 K).

Interestingly, both alkyl- and aryl-substituted *N*-linked systems show stronger anion association than the *C*-linked analogues. This is in agreement with a recent computational study by Flood and co-workers, which suggested that anion complexation would be marginally more energetically favourable for an *N*-linked bis-triazole-phenylene host than for a *C*-linked,⁴⁸ an effect which was attributed to the more electron-deficient character of the central phenylene proton in the *N*-linked system. The same authors have also

implied this to be the case experimentally, based on the asymmetrical binding of fluoride in tetratriazole macrocycles,⁴⁵ but we are unaware of any experimental studies that have investigated this phenomenon directly.

The chloride anion recognition properties of the strongest-binding receptor **6** still fall some way short of those reported by Craig for his acyclic bis-triazole system [380(18) *vs.* 1260 M⁻¹, respectively]. Although the core structure of the hosts is the same, Craig’s host contains an electron-withdrawing ester substituent *meta* to the two triazole donors, while **6** contains an electron-donating *t*butyl group, which presumably explains the observed differences (Hammett parameter, σ for *m*-CO₂Et = +0.37, σ for *m*-*t*butyl = -0.10).³²⁹

Analogous titration experiments were undertaken with the amide based receptors **7** and **8** to allow comparisons to be made between this functionality and the triazole motif. As shown in Figure 2.8, the two amide hosts complex chloride very strongly in d₆-acetone, with both alkyl and aryl-substituted receptors exhibiting far greater binding affinities than any of the bis-triazole systems [K_a = 2385(152) and >10⁴ M⁻¹, respectively].

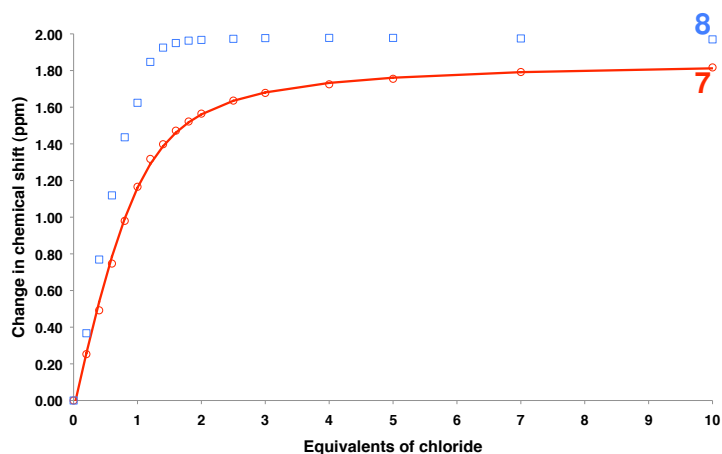


Figure 2.8: Experimental titration data (points) and fitted binding isotherms (lines) for addition of chloride anion to **7** and **8**, following amide resonance. Association of **8** and chloride was too strong for WINEQNMR2³²⁸ to quantify ($K_a > 10^4$ M⁻¹) (d₆-acetone, 293 K, 500 MHz).

Having investigated *acyclic* triazole and amide receptors, the incorporation of the bis-triazole motif into cyclic receptors was therefore attempted, to see if anion recognition strengths could be increased by taking advantage of the macrocyclic effect.

2.3 Bis-triazole macrocycles

2.3.1 Synthesis of bis-triazole macrocycles

It has recently been shown that macrocycles can be prepared in moderate to very good yields by the *intramolecular* CuAAC reaction of an acyclic precursor containing both azide and alkyne functionality.^{330–332} We were interested to see if a similar protocol could be used to give a general route to a range of bis-triazole macrocycles using an *intermolecular* CuAAC reaction between a bis-azide and a bis-alkyne. The systems shown in Figure 2.9 were targeted, as these are direct analogues of previously studied amide containing anion receptors, which have been incorporated into a range of interpenetrated and interlocked host molecules.*

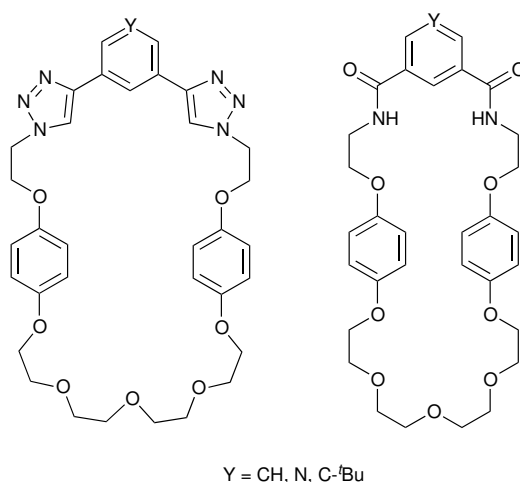
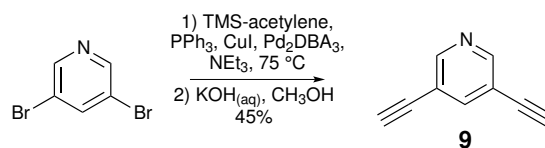


Figure 2.9: Targeted bis-triazole macrocycles, and previously reported isophthalamide analogues.^{232,302,333}

A range of bis-alkynes are commercially available, or readily prepared, allowing access to macrocycles with a range of substituents attached to the central phenylene ring. The bis-alkyne 3,5-diethynylpyridine **9** was prepared by a modification of literature procedures, as shown in Scheme 2.4.^{334,335} Sonogashira reaction³²⁴ of TMS-acetylene and 3,5-dibromopyridine gave the TMS-protected alkyne, which was deprotected with potassium hydroxide in methanol to give **9** as a volatile crystalline solid in 45% yield following purification by sublimation. Tertiary butyl substituted

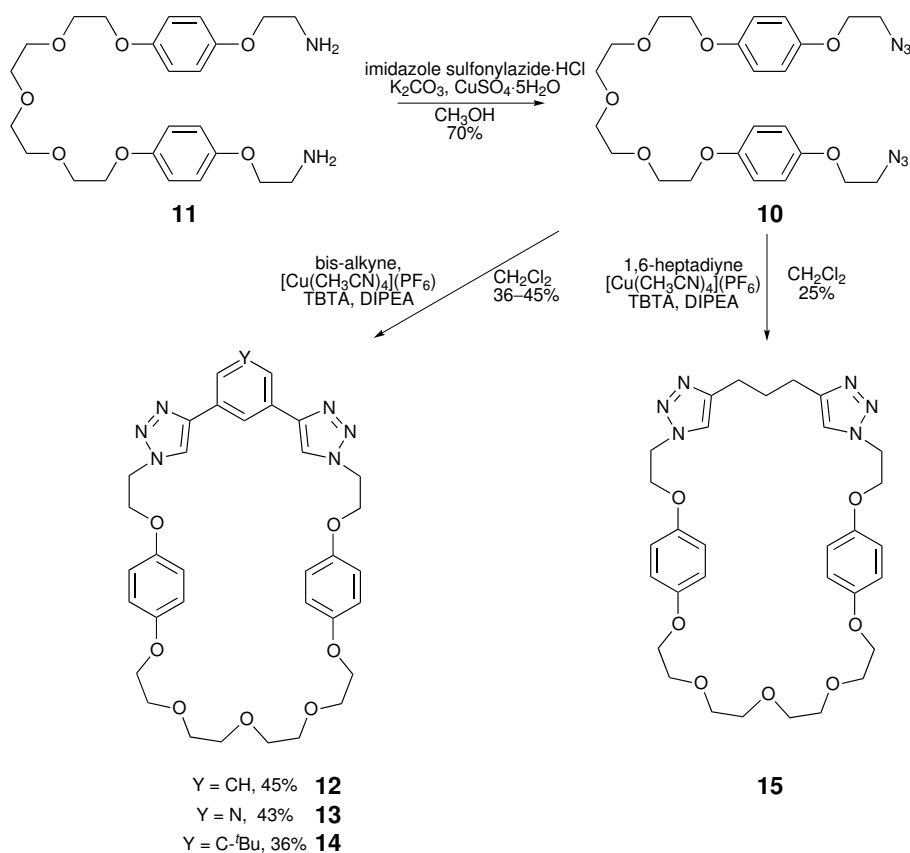
*Numerous attempts were made to prepare *N*-linked bis-triazole macrocycles but none of these were successful.



Scheme 2.4: Synthesis of **9**.

bis-alkyne 5-*t*-butyl-1,3-diethynylbenzene was prepared as described in Section 2.2.1, while 1,6-heptadiyne and 1,3-diethynylbenzene are commercially available.

Synthesis of the target macrocycle requires a bis-azide containing polyether and hydroquinone functionalities, and bis-azide **10** containing these groups was prepared as shown in Scheme 2.5. Initially, bis-amine **11** was prepared in 47% overall yield in four steps from commercially available reagents, as previously described.²⁴² Reaction of this amine with the hydrochloride salt of imidazole sulfonylazide³³⁶ in the presence of excess K₂CO₃ and catalytic copper(II) sulfate pentahydrate in methanol gave bis-azide **10** in 70% yield following purification by column chromatography and trituration with diethyl ether.



Scheme 2.5: Synthesis of bis-triazole macrocycles **12–15**.

Reaction of bis-azide **10** and bis-alkynes in dichloromethane at high dilution (2.0 mM), using $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ as catalyst, TBTA as ligand and DIPEA as base gave the four bis-triazole macrocycles **12–15** in 25–45% yield. The catalyst/ligand/base combination was chosen as James and co-workers have demonstrated that these conditions gave higher yields of macrocyclic products than a range of other reagent systems studied for intramolecular CuAAC reactions.³³² Yields were higher for bis-triazole macrocycles containing an aryl group between the triazole heterocycles (**12**, **13** and **14**), than for propyl containing compound **15**, presumably as the rigid aryl bis-alkynes are more preorganized for macrocyclization than flexible 1,6-heptadiyne.

The new macrocycles were characterized by ^1H and ^{13}C NMR spectroscopy, as well as by high resolution ESI mass spectrometry. Single crystals of **12**, **13** and **15** were obtained, allowing determination of the solid state structures by X-ray crystallography. As shown in Figure 2.10, in all three structures, the triazole groups adopt a *syn-syn* configuration, with the triazole protons pointing into the macrocycle cavity. Serpell and co-workers recently reported eight different forms of the crystal structure of the bis-amide analogue of **14** ($\text{Y} = \text{C}^t\text{Bu}$ in Figure 2.9), of which six polymorphs have a *syn-syn* arrangement of the amide groups.³³⁷ In these structures, there is little variation in the distances between the amide nitrogen atoms, and between the CH_2 groups attached to these ($\text{N}\cdots\text{N} = 5.10\text{--}5.24\text{ \AA}$, $\text{C}\cdots\text{C} = 7.56\text{--}7.70\text{ \AA}$). For **12** and **13**, the distance between the protic carbon atoms of the triazole groups are slightly larger ($5.39\text{--}5.59\text{ \AA}$), while the CH_2 groups are much further apart ($9.57\text{--}9.97\text{ \AA}$), due to the additional atom present in the triazole group, giving the triazole containing macrocycles a squatter, less elongated shape. This additional width is demonstrated by the distance between the centroids of the hydroquinone rings, which averages $7.75\text{ \AA}$ in the amide containing macrocycles and $8.19\text{ \AA}$ in the triazole analogues. The squatter nature of the triazole cycles is manifested in the reduced longitudinal distances between the interior isophthalamide proton and central polyether oxygen atom (mean value of $13.1\text{ \AA}$ *vs.* $13.7\text{ \AA}$ for the isophthalamide macrocycles).³³⁸

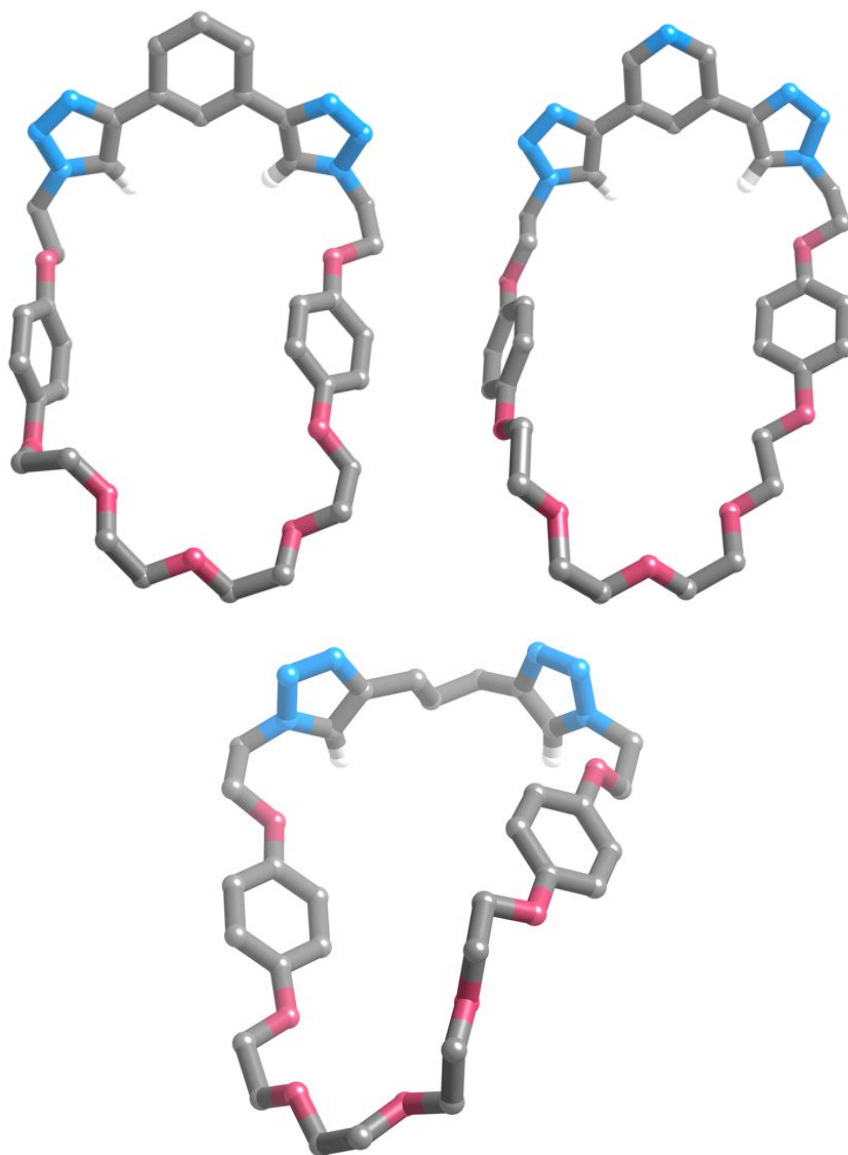


Figure 2.10: Solid state structures of **12**, **13** and **15**. Solvent molecules and most hydrogen atoms are omitted for clarity. Only one of the two independent macrocycles in the asymmetric unit of **12** is shown.

2.3.2 Anion recognition properties of bis-triazole macrocycles

The chloride recognition properties of the cyclic receptors were investigated by ^1H NMR titration experiments. Addition of this halide anion causes downfield shifts in triazole proton *c* and phenylene proton *d* due to hydrogen bonding between these hydrogen atoms and chloride, as shown in Figure 2.11 for macrocycle **12**. Hydroquinone resonances *a* and *b* diverge, due to increased inequivalence arising from anion association.

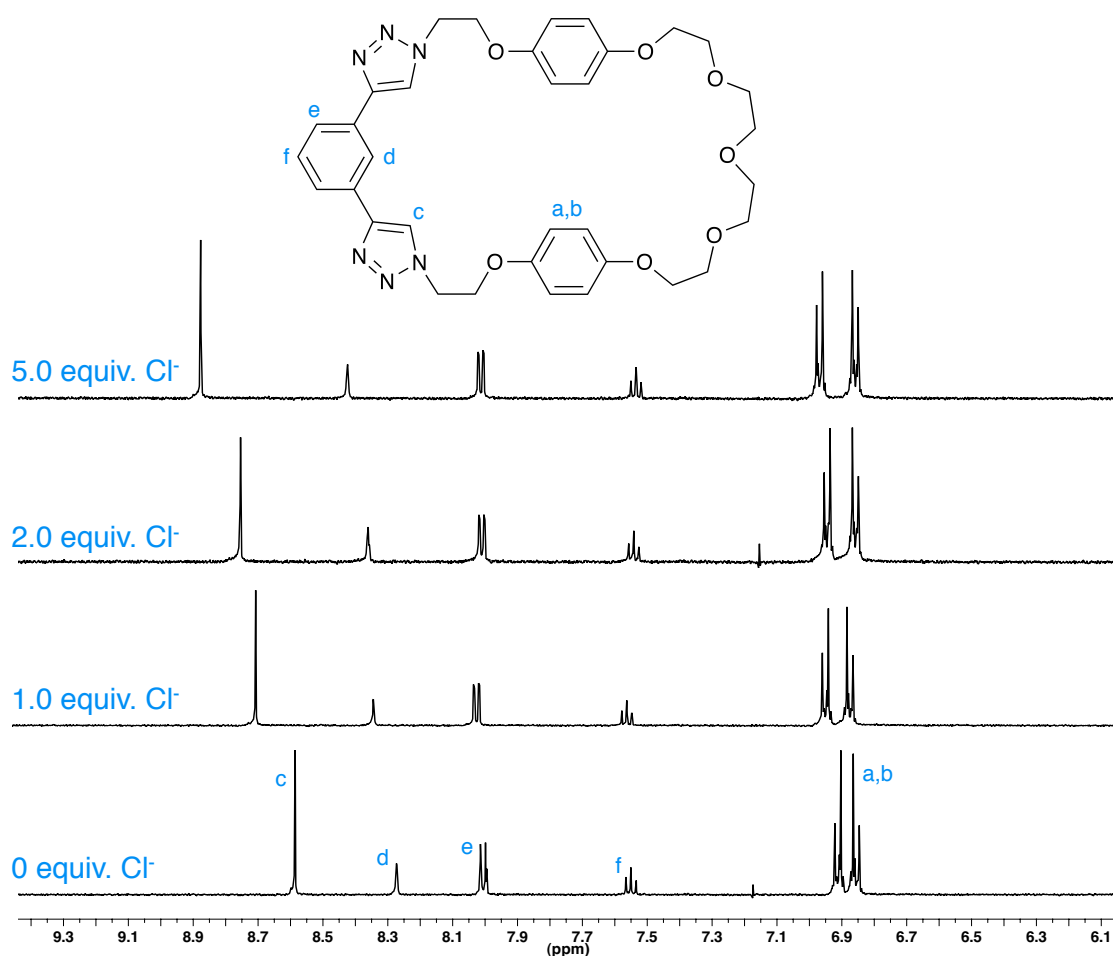


Figure 2.11: ^1H NMR spectra of **12** upon addition of TBA·Cl (d_6 -acetone, 293 K, 500 MHz).

Quantitative 1:1 stoichiometric anion association constants were calculated using WINEQNMR2,³²⁸ monitoring the triazole resonance. Chloride association with all four macrocycles was found to be relatively weak ($K_{\text{a}} < 100 \text{ M}^{-1}$, Figure 2.12 and Table 2.2). Association constants are also given for two analogous bis-amide containing macrocycles, which again complex chloride far more strongly.

Interestingly, the chloride association of macrocycle **14** [$49(4) \text{ M}^{-1}$] is only very slightly higher than the analogous acyclic receptor **3** [$32(3) \text{ M}^{-1}$, Table 2.1], suggesting the absence of a substantial macrocyclic effect. Furthermore, no macrocyclic effect is observed for the amide based systems, with acyclic receptor **7** and cyclic analogue **16** displaying indistinguishable chloride affinities [$2385(152)$ and 2560 ,³⁰² M^{-1} respectively].

Given that the two hydrogen bond donor groups in these acyclic and macrocyclic systems are already held close together by a central phenylene group, incorporation into

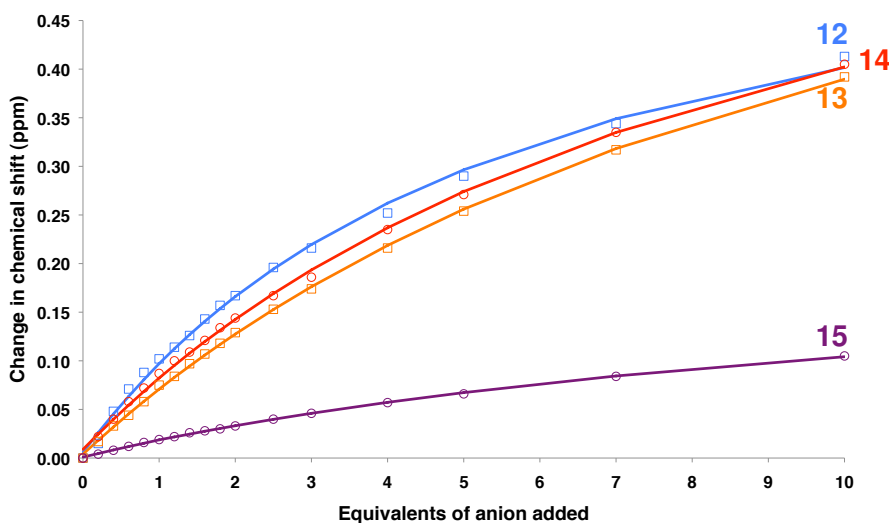


Figure 2.12: Experimental titration data (points) and fitted binding isotherms (lines) for addition of chloride anion to bis-triazole macrocycles, following triazole resonance, c (d_6 -acetone, 293 K, 500 MHz).

Table 2.2: Chloride anion association constants, K_a (M^{-1})^a for bis-triazole and bis-amide macrocycles.

Linker	Compound Number	Bis-triazole macrocycle	Bis-amide analogue
phenyl	12	93(8)	—
5-pyridyl	13	76(4)	4275(170) ^{b,c}
5- <i>t</i> -butylphenyl	14	49(4)	2560 ³⁰²
propyl	15	32(2)	—

^aChloride anion added as TBA salt, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (d_6 -acetone, 293 K). ^bTitration carried out with 1.0 mM starting concentration of host, due to its low solubility in d_6 -acetone. ^cPrepared in 13% overall yield in five steps from commercially available reagents according to literature procedures.³³⁹

a macrocyclic framework appears to have little effect on guest recognition properties. It could be considered that cyclic systems would enhance binding by favouring *syn-syn* arrangements of the triazole or amide groups in order to avoid ring strain caused by *anti* conformations, but this appears not to be the case.

2.4 Transition metal coordination properties of neutral bis-triazole acyclic receptors

Initial investigations of the abilities of **3–6** to complex metal cations were undertaken with the transition metal ions silver(I) and copper(I). In solution studies, the cations were added as their hexafluorophosphate salts to eliminate any significant competition from anion binding by the triazole groups. The solution behaviour was investigated using ^1H NMR titration experiments, and four complexes were also characterized in the solid state by single crystal X-ray crystallography. Attempts were made to investigate the complexes in solution using mass spectrometry; however, ambiguous data were obtained, which gave little information about the nature or nuclearity of the complexes in solution.

2.4.1 Complexation in solution

Addition of AgPF_6 or $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ to d_6 -acetone solutions of alkyl-substituted ligands **3** or **5** resulted in substantial movement of the signals corresponding to the phenylene and triazole protons. Unfortunately, neither the silver or copper salts used had sufficient solubility to allow quantitative titrations to be performed. Qualitatively, the data suggest very strong binding ($K_{\text{a}} > 10^4 \text{ M}^{-1}$).

2.4.1.1 Complexation in solution — copper(I)

Both *N*-linked and *C*-linked receptors display 1:1 binding stoichiometries with copper(I) cation (Figures 2.13 and 2.14), which is somewhat surprising given this metal’s known preference for a tetrahedral binding geometry. The X-ray crystal structures of the two uncomplexed receptors (Figure 2.5) however indicate neither would facilitate a conventional ML_2 binding arrangement. In the case of the *N*-linked receptors, the N_3 nitrogen atoms, which are the most electron-rich,³⁴⁰ are divergent and so do not allow for bidentate coordination. In the case of the *C*-linked receptors, these nitrogen atoms are convergent, but the distance between them is 5.4 Å, presumably too far apart for a small first-row transition metal cation such as copper(I).

When copper(I) is added to the *N*-linked receptor (Figure 2.13), downfield shifts are observed in the signals of the interior and exterior phenyl protons, *b* and *c*, as well as the triazole protons, *a* and the alkyl protons on the CH₂ groups adjacent to the triazole rings. In the case of the *C*-linked receptor (Figure 2.14), the situation is more complex: addition of a small amount of copper results in the appearance of five new peaks in the aromatic region, as well as two new triplet signals at 4.62 and 4.75 ppm. Continued addition of copper results in the new peaks growing at the expense of the signals from uncomplexed ligand. When one equivalent of copper has been added, only the five aromatic signals and two signals at 4.62 and 4.75 ppm remain.

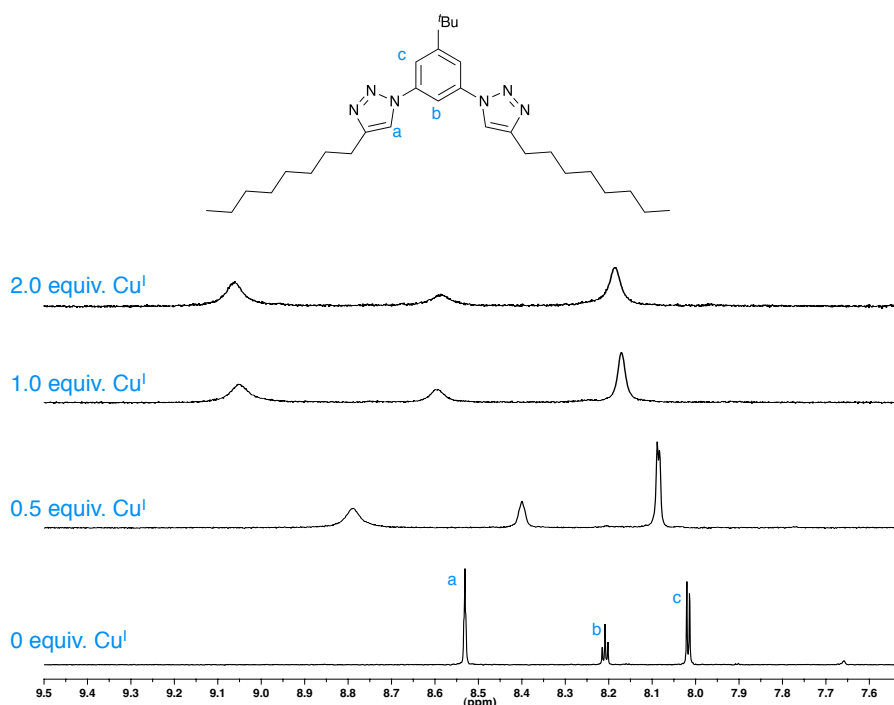


Figure 2.13: Truncated ¹H NMR spectra of **5** upon addition of [Cu(CH₃CN)₄](PF₆) (d₆-acetone, 293 K, 300 MHz).

These results suggest that copper(I) binding to ligand **3** is slow on the ¹H NMR timescale, and imply a desymmetrization of the ligand, such that the two alkyl groups adjacent to the triazole motifs are inequivalent, as are all five aromatic protons. Interestingly, proton *c* splits into two new resonances, both of which are shifted upfield relative to the free ligand. This is in contrast to the *N*-linked ligand, where all peaks move downfield upon complexation to copper and binding is fast on the NMR timescale.

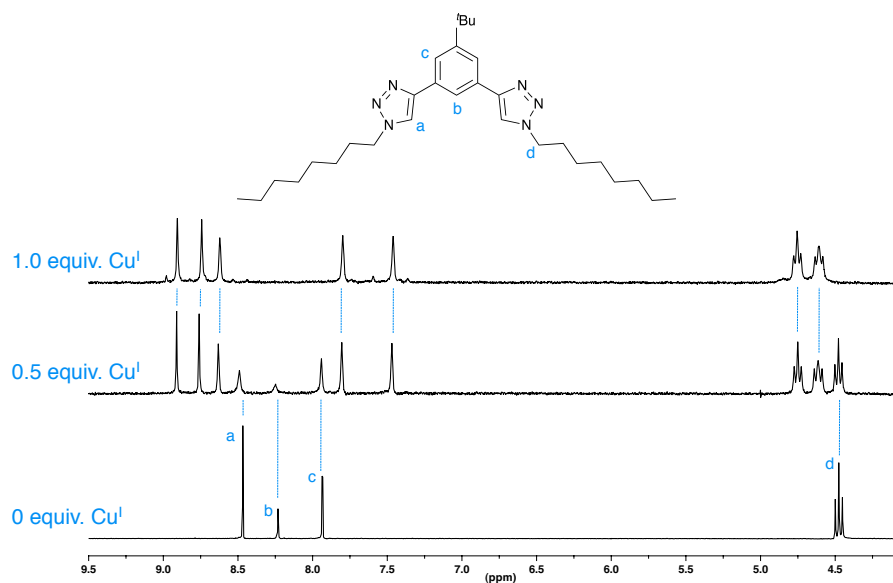


Figure 2.14: Truncated ^1H NMR spectra of **3** upon addition of $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (d_6 -acetone, 293 K, 300 MHz).

2.4.1.2 Complexation in solution — silver(I)

Addition of AgPF_6 to either the *C*-linked or *N*-linked receptors causes downfield shifts in the signals arising from the aromatic protons (Figures 2.15 and 2.16), as well as the CH_2 protons adjacent to the triazole groups. Only one set of peaks is visible in both cases, indicative of fast exchange on the NMR timescale. In the case of the *N*-linked ligand **5**, no further movement of the ligand peaks is observed after addition of 1.0 equivalent of metal, implying a 1:1 binding stoichiometry. When the *C*-linked ligand **3** is used, no movement is observed after 0.5 equivalents of $\text{Ag}(\text{I})$, implying a ML_2 stoichiometric complex. As observed in the copper(I) complex of this ligand, proton *c* shifts upfield, with all other protons moving downfield.

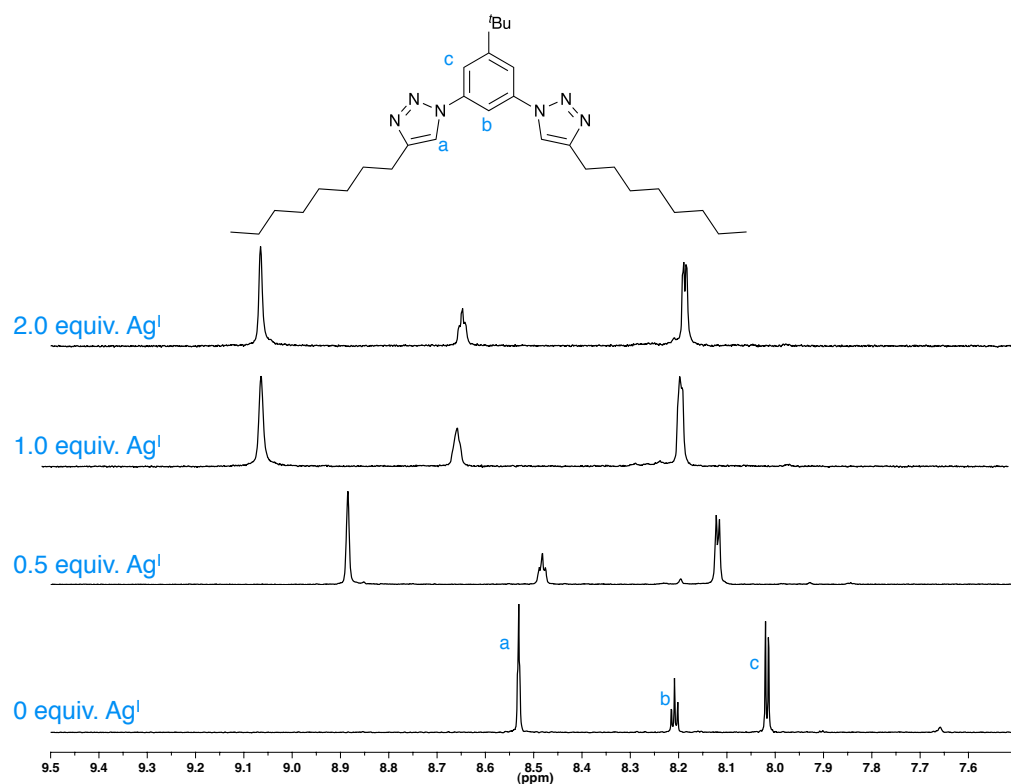


Figure 2.15: Truncated ^1H NMR spectra of **5** upon addition of AgPF_6 (d_6 -acetone, 293 K, 300 MHz).

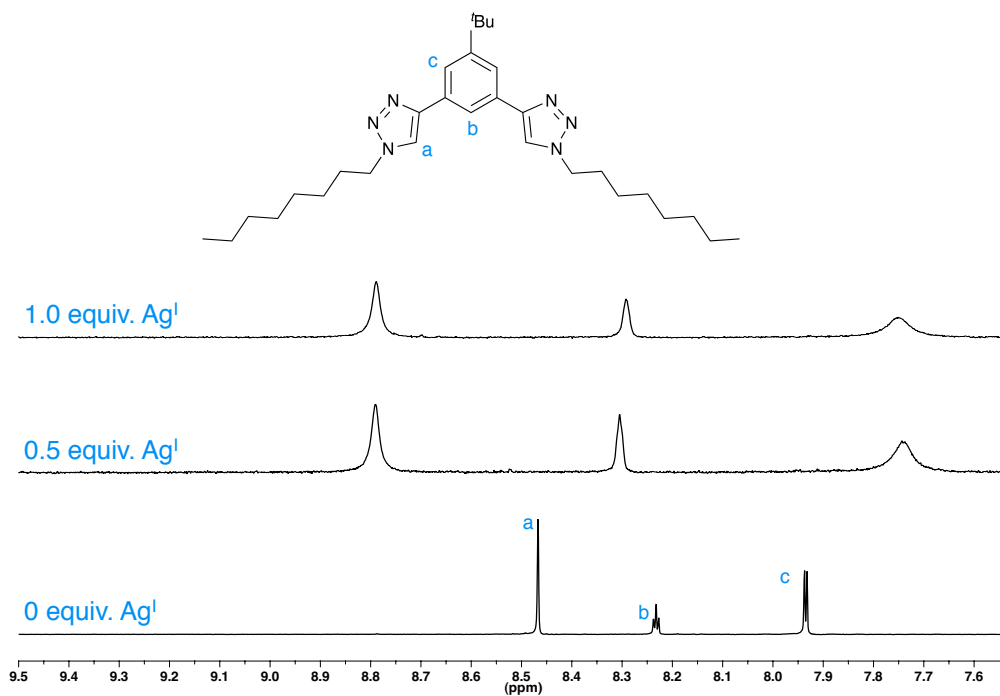


Figure 2.16: Truncated ^1H NMR spectra of **3** upon addition of AgPF_6 (d_6 -acetone, 293 K, 300 MHz).

2.4.2 Solid state structures of complexes

Single crystals suitable for X-ray diffraction analysis were obtained of four complexes of the aryl-substituted ligands **4** and **6**; no crystals were obtained of metal complexes of the alkyl-substituted ligands **3** and **5**. For three of these four metal complexes (Cu_3 and Ag_4 clusters) crystals were small and poorly diffracting. Attempts to use synchrotron radiation were unsuccessful, with the crystals appearing to suffer significant radiation damage. Instead, $\text{Cu } K\alpha$ radiation and very long collection times (three days to collect all unique reflections with a redundancy of one) were used. Despite these difficulties, the data allow unambiguous determination of the gross structure of the metal complexes and the coordination environments of the metal ions.

2.4.2.1 Solid state structures of copper(I) complexes

Single crystals were obtained by diethyl ether vapour diffusion into a d_6 -acetone solution of a 1:1 mixture of the *C*-linked aryl-substituted ligand **4** and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$. In the solid state, the structure forms the complex $[\text{Cu}_3\text{4}_4](\text{PF}_6)_3$ (Figure 2.17), with two complete complexes in the asymmetric unit. Each copper ion has a distorted tetrahedral geometry and coordinates to four triazole nitrogen atoms.

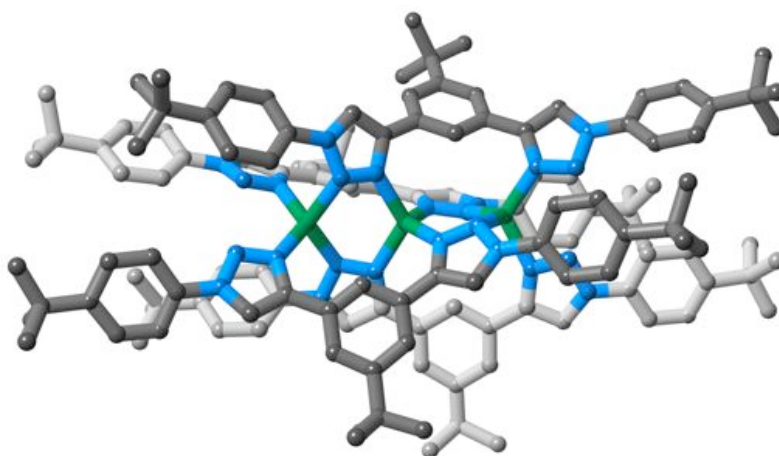


Figure 2.17: Solid state structure of $[\text{Cu}_3\text{4}_4](\text{PF}_6)_3$. Only one of the two independent Cu_3 complexes in the asymmetric unit is shown. Counteranions and hydrogen atoms omitted for clarity.

In this structure, copper–copper distances range between 3.3 and 3.4 Å. In each of the four ligands, one triazole ring binds to one copper ion, while the other acts as a

bridge between two coppers, such that the central metal binds to four bridging triazole groups, while the two outer copper ions each bind two monodentate and two bridging rings (Figure 2.18). Surprisingly, there are only slight differences in coordination bond lengths between the bridging and monodentate triazole donors, or between the different donors on the bridging atoms (monodentate, $\text{mean}_{\text{Cu-N}} = 2.03 \text{ \AA}$, bridging N_3 : $\text{mean}_{\text{Cu-N}} = 2.05 \text{ \AA}$; bridging N_2 : $\text{mean}_{\text{Cu-N}} = 2.08 \text{ \AA}$). A similar bridging/monodentate arrangement may explain the asymmetry of **3** observed in solution in the presence of Cu^{I} (Figure 2.14), as one side of each ligand is coordinated to two copper ions, making it more electron poor than the other side of the ligand, which binds only one metal ion, although it should be noted that different binding stoichiometries are observed in solution and the solid state.³⁴¹

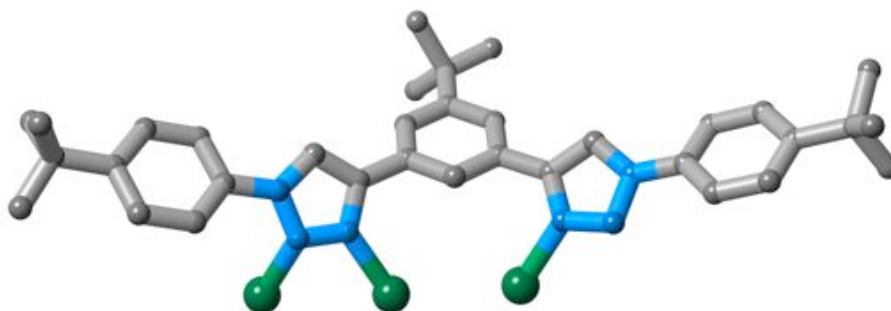


Figure 2.18: Truncated crystal structure of $[\text{Cu}_3\mathbf{4}](\text{PF}_6)_3$ showing only one ligand strand and the bridging and monodentate coordination modes present. This binding arrangement also occurs in silver complexes of **4** (see later).

2.4.2.2 Solid state structures of silver(I) complexes

Diffusion of diethyl ether vapour into a d_6 -acetone solution of a 1:1 mixture of *N*-linked ligand **6** and $\text{Ag}(\text{CF}_3\text{SO}_3)$ gave colourless crystals of $[\text{Ag}_2\mathbf{6}_2(\text{CF}_3\text{SO}_3)_2]$,³⁴² and in the solid state the complex forms a $[2+2]$ metallomacrocycle (Figure 2.19). The Ag^{I} ions in the metallomacrocycle each form two short Ag–N bonds [$2.1581(18)$ – $2.1729(19) \text{ \AA}$] to N_3 atoms on the triazole ligands, such that there is a close to linear N–Ag–N arrangement [$\angle\text{N–Ag–N} = 158.32(7), 160.43(7)^\circ$]. The coordination sphere on each silver ion is completed by a much weaker bond to an oxygen donor from a trifluoromethylsulfonate anion [$\text{Ag–O} = 2.4675(19), 2.603(2) \text{ \AA}$], which is approximately perpendicular to the Ag–N bonds. The structure is very similar to that obtained by Gower and Crowley, who reacted AgSbF_6 with the bis-triazole

ligand, 4,4'-benzene-1,3-diylbis[1-(pentafluorobenzyl)-1,2,3-triazole], although in this case, a solvent molecule provided the third donor for each silver ion.³²¹

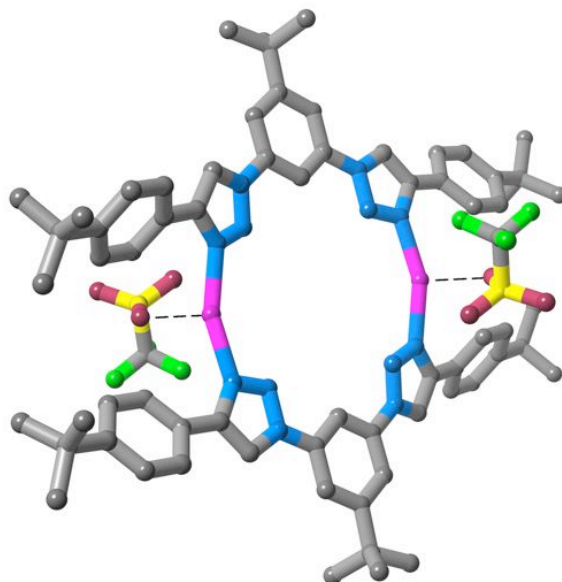


Figure 2.19: Solid state structure of $[\text{Ag}_2\mathbf{6}_2(\text{CF}_3\text{SO}_3)_2]$. Hydrogen atoms and diethyl ether solvate omitted for clarity. Only one of the two crystallographically independent metal complexes in the asymmetric unit cell is shown.

Diffusion of diethyl ether vapour into an acetone solution of a 1:1 mixture of AgPF_6 and *C*-linked ligand **4** gave crystals of a tetranuclear cluster, having the formula $[\text{Ag}_4\mathbf{4}_4(\text{OH}_2)_3(\text{C}_3\text{H}_6\text{O})](\text{PF}_6)_4$ (Figure 2.20). Each of the four ligand strands binds to three of the four silver ions, with one triazole ring binding in a monodentate fashion, and the other triazole bridging two further silver ions, as was observed in the copper complex of **4**. In this structure, however, each silver centre forms only three bonds to triazole donors, with an additional, weaker bond being formed to a solvent molecule (either water or acetone). The change in bond lengths between the three types of donor in the ligand is more pronounced than in the copper complex of this ligand (monodentate, $\text{mean}_{\text{Ag-N}} = 2.23 \text{ \AA}$, bridging N_3 : $\text{mean}_{\text{Ag-N}} = 2.28 \text{ \AA}$; bridging N_2 : $\text{mean}_{\text{Ag-N}} = 2.34 \text{ \AA}$).

Additionally, as a 1:2 binding stoichiometry was indicated by solution ^1H NMR studies with the closely related ligand **3** (Figure 2.16), diethyl ether vapour was diffused into a 1:2 mixture of AgPF_6 and **4**. Over a period of several months, small crystals formed, which were analysed by X-ray crystallography (Figure 2.21). These have the formula $[\text{Ag}_4\mathbf{4}_4(\text{PO}_2\text{F}_2)_2](\text{PO}_2\text{F}_2)(\text{PF}_6)$, and the overall structure is almost identical to that of

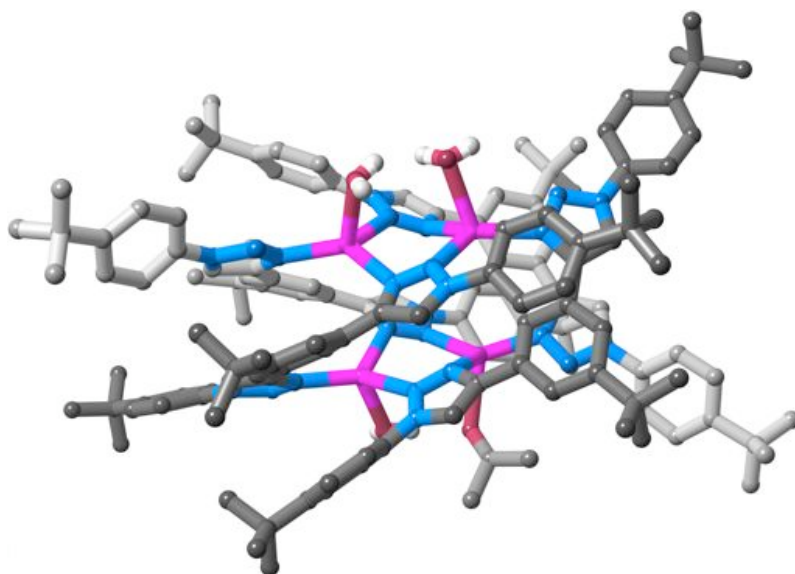


Figure 2.20: Solid state structure of $[\text{Ag}_{44}(\text{OH}_2)_3(\text{C}_3\text{H}_6\text{O})](\text{PF}_6)_4$. Hydrogen atoms and counteranions omitted for clarity.

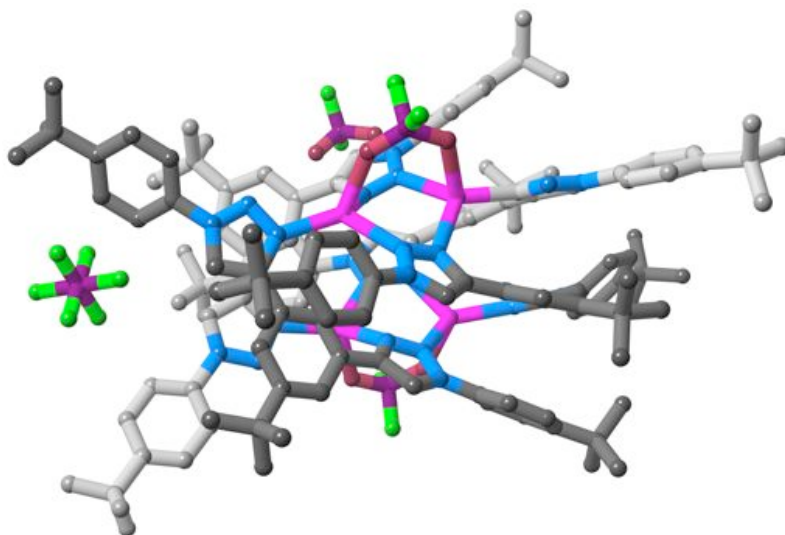


Figure 2.21: Solid state structure of $[\text{Ag}_{44}(\text{PO}_2\text{F}_2)_2](\text{PO}_2\text{F}_2)(\text{PF}_6)$. Hydrogen atoms omitted for clarity.

$[\text{Ag}_{44}(\text{OH}_2)_3(\text{C}_3\text{H}_6\text{O})](\text{PF}_6)_4$, but with the four coordinated solvent molecules replaced by bridging PO_2F_2^- anions.

The hydrolysis of PF_6^- anions to PO_2F_2^- is well known, and has been thoroughly investigated by Monzano, Otero and co-workers who have shown that Ag^{I} catalyzes this reaction in organic solvents containing trace amounts of water.³⁴³ To the best of our knowledge, however, there is only one other structure³⁴⁴ in the Cambridge Structure

Database where PO_2F_2^- coordinates to a metal centre — in the other thirty structures containing this anion, it is non-coordinating. Interestingly, even when two equivalents of ligand are used for each metal centre, a ML_2 complex is not formed, despite ^1H NMR studies showing that this is the stoichiometry present in solution.

2.4.3 Investigating the use of transition metal ions to template the assembly of triazole based pseudorotaxanes

The previous section demonstrated that copper(I) and silver(I) can complex bis-triazole ligands, and in one case [silver(I) and **4**] a ML_2 stoichiometry was preferred, at least in solution. It was therefore decided to investigate whether these metal coordination bonds could be used to template pseudorotaxane formation, with the ultimate aim of preparing interlocked structures.

2.4.3.1 Metal complexing properties of bis-triazole macrocycle **14**

Prior to investigation of metal templated pseudorotaxanes, the copper(I) and silver(I) complexing properties of a bis-triazole macrocycle were first studied. Tertiary butyl substituted **14** was used to ensure any metal complexes remained soluble in d_6 -acetone.

Addition of Ag(I) to this macrocycle results in small upfield shifts in protons *a* and *b* as well as the hydroquinone resonances *e* and *f*, while the triazole resonances *c* move downfield (Figure 2.22). Interestingly, the macrocycle peak shifts are much smaller than with acyclic ligand **3** (Figure 2.16). Peak movement stops after 1.0 equivalent of silver ion, suggesting a 1:1 ML stoichiometry in solution, in contrast to **3** which formed a ML_2 complex.

The copper(I)-complexing properties of **14** were also investigated. As shown in Figure 2.23, addition of copper(I) causes the macrocycle to become non-symmetrical, as was the case with **3** (Figure 2.14). Unlike with the acyclic ligand, however, the macrocycle has a ML_2 binding stoichiometry in solution, with no movement in the proton signals after half an equivalent of copper(I). While the reasons for this are not evident, it is promising for potential pseudorotaxane formation, which requires binding of both a threading component and macrocycle to a metal ion.

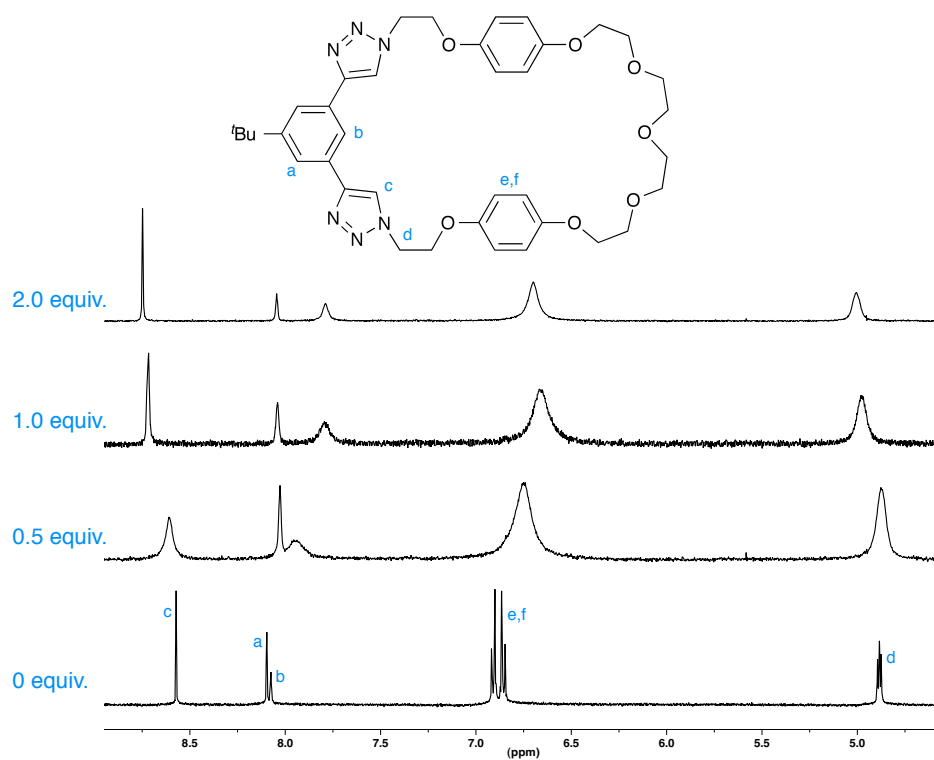


Figure 2.22: Truncated ^1H NMR spectra of **14** upon addition of AgPF_6 (d_6 -acetone, 293 K, 300 MHz).

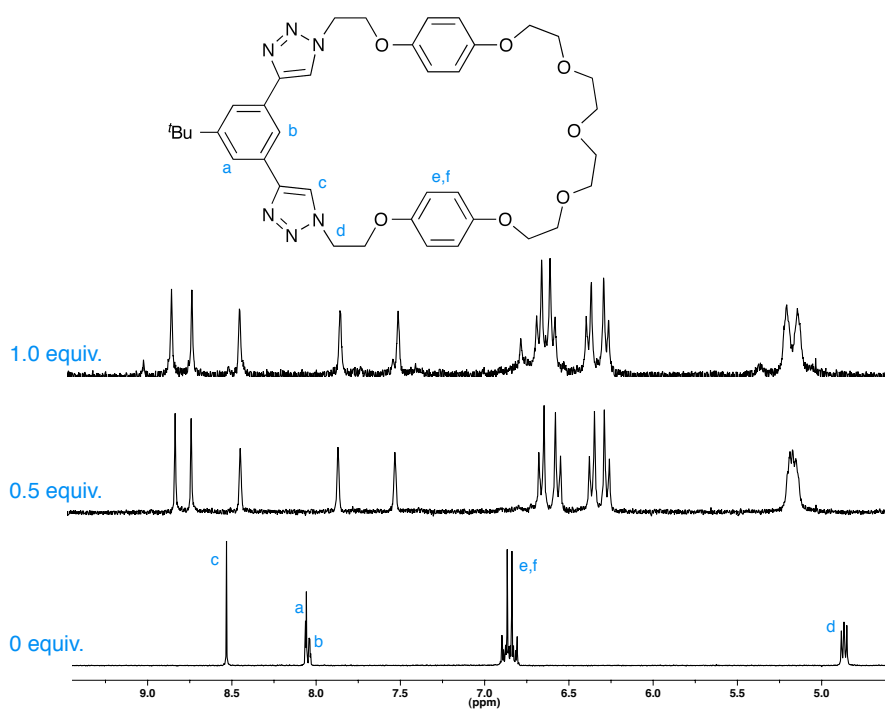


Figure 2.23: Truncated ^1H NMR spectra of **14** upon addition of $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (d_6 -acetone, 293 K, 300 MHz).

2.4.3.2 Investigation of metal templation of triazole containing interweaved assemblies

As copper(I) binds to macrocycle **14** with a ML_2 stoichiometry in solution, this cation was chosen for metal templated pseudorotaxane studies. One equivalent of $[Cu(CH_3CN)_4](PF_6)$ was added to a 1:1 mixture of **14** and thread **6**. The ^1H NMR spectra of these mixtures are shown in Figure 2.24; for comparison, the ^1H NMR spectrum of **14** in the presence of copper(I) is also included. The peaks corresponding to the copper complex of **14** do not move when threading component **6** is present, suggesting no pseudorotaxane formation.

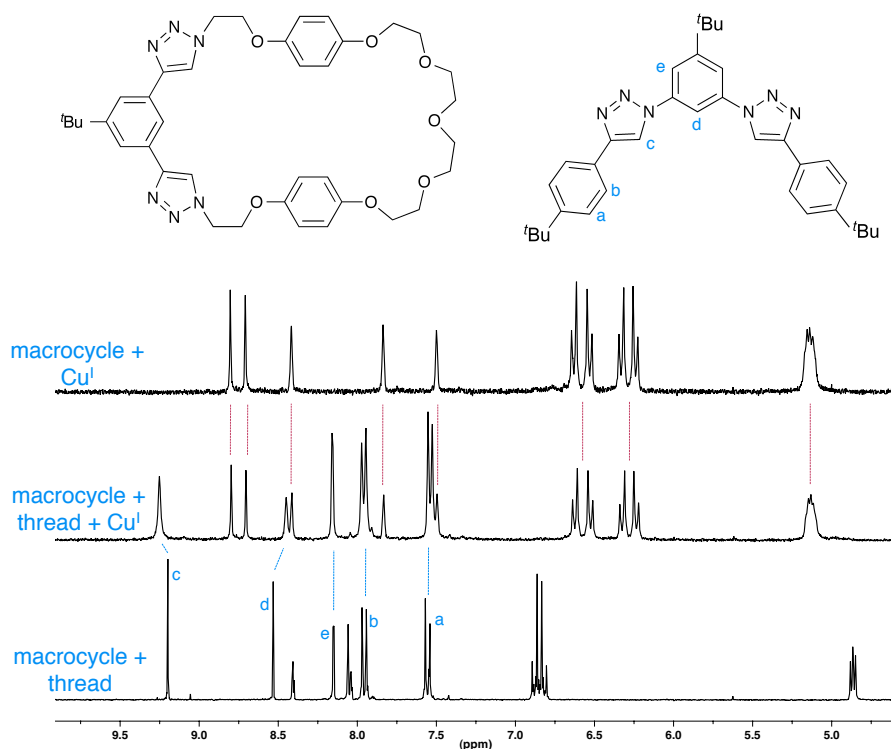


Figure 2.24: Truncated ^1H NMR spectra of **6** and **14** upon addition of copper(I) (d_6 -acetone, 293 K, 300 MHz).

A similar experiment was also attempted using the *C*-linked threading component **4** (Figure 2.25). The 1:1:1 mixture of **4**, **14** and $[Cu(CH_3CN)_4](PF_6)$ gave an unassignable ^1H NMR spectrum, possibly due to a range of different species existing in slow exchange.

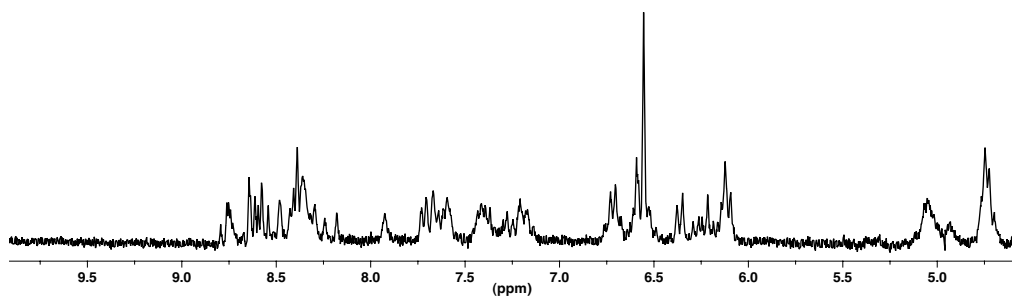
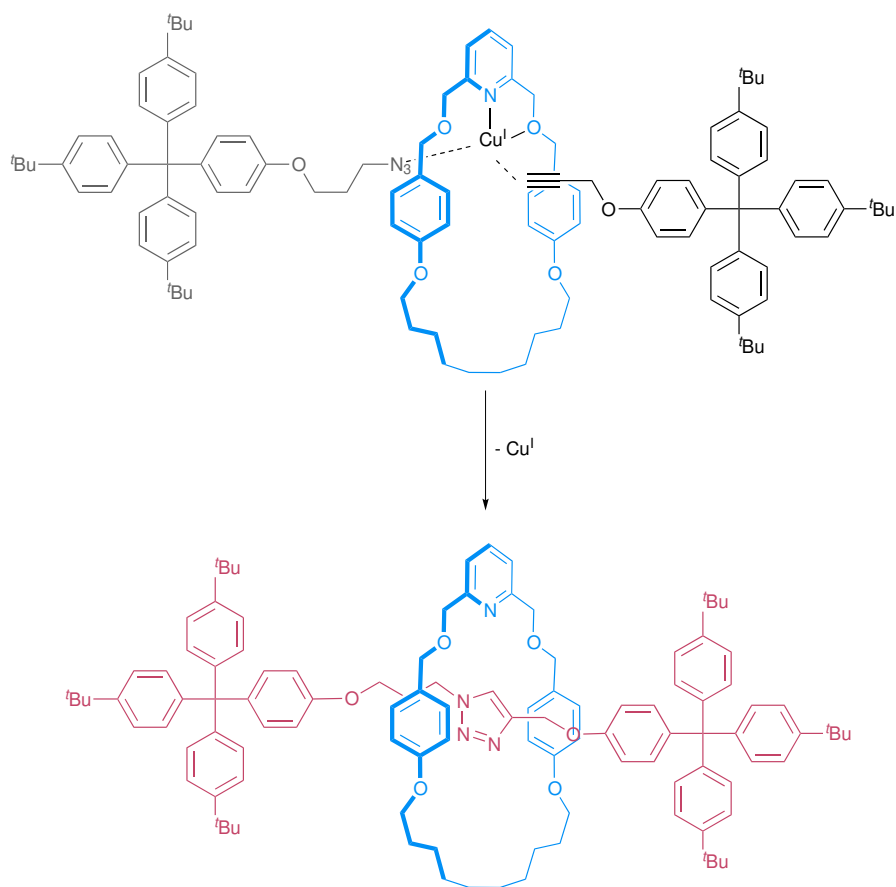


Figure 2.25: Truncated ^1H NMR spectra of a 1:1:1 mixture of thread **6**, macrocycle **14** and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (d_6 -acetone, 293 K, 300 MHz).

2.4.3.3 Investigation of active metal template route to triazole containing rotaxanes

Leigh and co-workers have reported that rotaxanes can be formed in good yield *via* a CuAAC active metal route (Scheme 2.6).³⁴⁵ The pyridine containing macrocycle acts as a ligand for the copper(I) ion, which then templates the CuAAC reaction of bulky azides and alkynes through the annulus of the macrocycle to give the interlocked product. As a final attempt at synthesizing triazole containing interlocked hosts using metal templation, the same reaction was attempted but using bis-triazole macrocycle **12** instead of Leigh's pyridine macrocycle. While the copper(I)–macrocycle complex did catalyze the CuAAC reaction, negligible ($< 1\%$) interlocked product was formed, suggesting that catalysis occurs outside the macrocycle cavity.

Due to the lack of success of these metal templation routes to triazole containing interlocked structures, it was instead decided to focus on using anion templated methodologies. For this reason, a cationic triazole containing motif was targeted, and its use for anion recognition and formation of interpenetrated and interlocked structures will be the topic of Section 2.5 and Chapter Three.



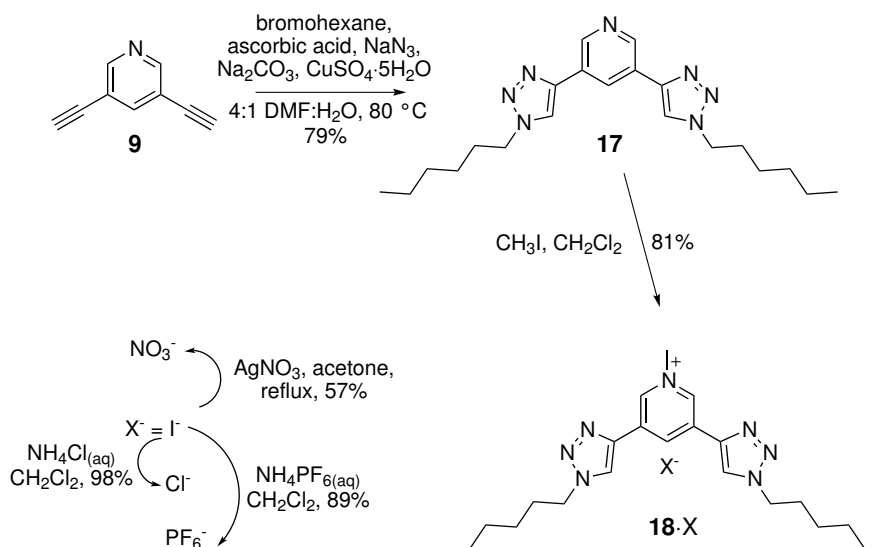
Scheme 2.6: Leigh's active metal synthesis of triazole containing rotaxanes.³⁴⁵

2.5 A cationic acyclic triazole containing receptor

2.5.1 Synthesis of pyridinium bis-triazole receptor

To further investigate the binding properties of the triazole group, a cationic receptor incorporating an *N*-methyl pyridinium motif was targeted, as this would allow analysis of both anion recognition properties and an investigation of the ability of such a molecule to form a pseudorotaxane with an appropriate macrocycle. One-pot conditions (see Section 2.2.1) were again used to synthesize the required pyridine bis-triazole moiety, starting from 3,5-diethynylpyridine (Scheme 2.7).

Reaction of **9** with sodium azide and bromohexane with copper(I) catalysis gave the neutral pyridine bis-triazole compound **17** in 79% yield after chromatographic purification. Pyridine groups are commonly methylated by heating to reflux in chloroform with excess methyl iodide or by heating in neat methyl iodide, however, these conditions have



Scheme 2.7: Synthesis of pyridinium bis-triazole host **18**.

been shown to effect the alkylation of triazole rings.²⁷⁷ Instead, stirring **17** in dry dichloromethane at room temperature with an excess of methyl iodide (25 equivalents) allowed for selective alkylation at the pyridine site, giving **18-I** in good yield (81%) following purification by column chromatography.

A range of salts of **18**⁺ were sought for investigations of pseudorotaxane formation (Chapter Three). Anion exchange by repeated washing of a dichloromethane solution of the iodide salt of **18**⁺ with NH₄Cl(aq) or NH₄PF₆(aq) gave **18-Cl** and **18-PF₆** in good yields (98 and 89%, respectively), while the nitrate salt **18-NO₃** was synthesized in 57% yield by heating **18-Cl** and silver nitrate to reflux in acetone followed by chromatographic purification. Attempts to prepare **18-BzO** in the same manner were unsuccessful, with apparent decomposition of **18**⁺ under these conditions.

The amide analogue of **18**⁺, pyridinium bis-amide thread **19**⁺ (Figure 2.26) was also synthesized, as previously described,²³² to allow comparisons of the amide and triazole functional groups.

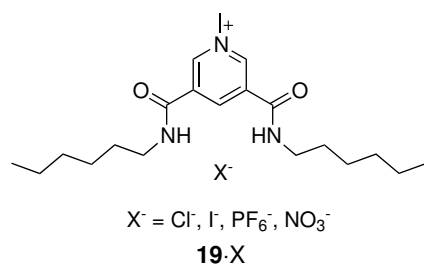


Figure 2.26: Previously reported pyridinium bis-amide threading component **19**⁺.²³²

2.5.2 Anion binding properties of pyridinium bis-triazole receptor

The anion complexation properties of **18**·PF₆ were investigated *via* ¹H NMR titration experiments in CD₃CN following the protocol outlined in Section 2.2.2 (an initial titration having determined that chloride association was too strong to be quantified in the less polar solvent, d₆-acetone). As shown in Figure 2.27, addition of chloride anion to **18**·PF₆ causes downfield shifts in the triazole and pyridinium ring protons, *b*, *c* and *d*. Addition of other anions (bromide, iodide, benzoate) caused similar shifts, with the magnitude of the shifts being larger for the oxoanion than for the halides, and the largest halide iodide causing the smallest perturbations, while dihydrogen phosphate caused immediate precipitation.

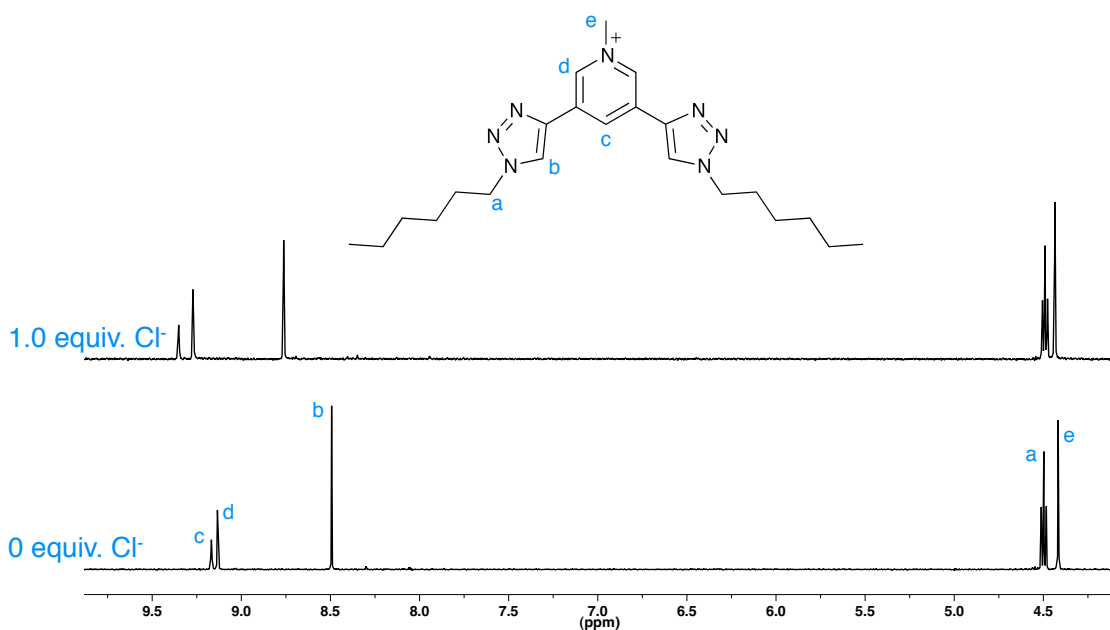


Figure 2.27: Truncated ¹H NMR spectra of **18**·PF₆ upon addition of TBA·Cl (CD₃CN, 293 K, 500 MHz).

Association constants were calculated using WINEQNMR2,³²⁸ monitoring the triazole resonance d (Table 2.3 and Figure 2.28). The anion binding selectivity of **18**·PF₆ follows anion basicity trends, as would be expected for an acyclic receptor in an aprotic solvent, with benzoate associating approximately twice as strongly as chloride, and the larger halides complexed even more weakly. Analogous titrations were also undertaken with the hexafluorophosphate salt of the pyridinium bis-amide thread **19**⁺ following the amide resonance. As shown in Table 2.3 and Figure 2.28, **19**·PF₆ binds anions far more strongly than **18**·PF₆, with very large shifts observed in the amide resonances upon addition of anions.

Table 2.3: Association constants, K_a (M⁻¹) for pyridinium based acyclic receptors **18**·PF₆ and **19**·PF₆ with various anions.^a

Anion	Triazole receptor 18 ·PF ₆	Amide receptor 19 ·PF ₆
Cl ⁻	206(11)	>10 ⁴
Br ⁻	106(3)	3432(143)
I ⁻	59(2)	664(52)
BzO ⁻	402(12)	>10 ⁴
H ₂ PO ₄ ⁻	precipitation	—

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (CD₃CN, 293 K).

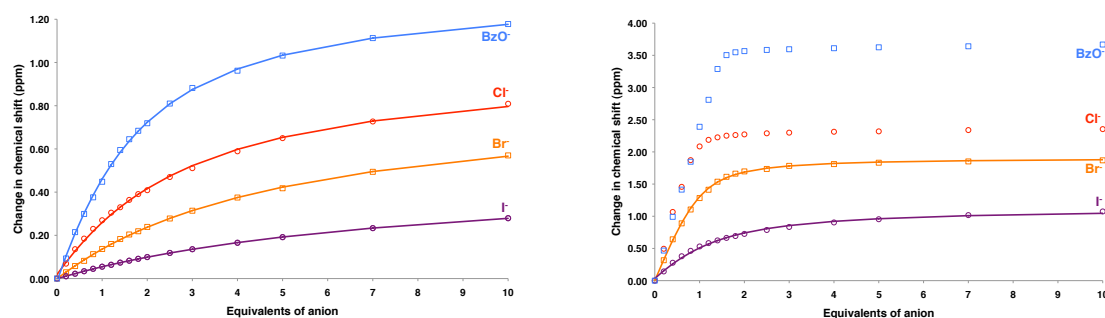


Figure 2.28: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to pyridinium bis-triazole receptor **18**·PF₆ (left) and **19**·PF₆ (right). Note the differing scales of the y -axes. Association of **19**·PF₆ with chloride and benzoate was too strong for WINEQNMR2³²⁸ to quantify ($K_a > 10^4$ M⁻¹) (CD₃CN, 293 K, 500 MHz).

Single crystals of **18**⁺ were obtained as the benzoate and hexafluorophosphate salts, and the solid state structures of these complexes were elucidated by X-ray crystallography (Figure 2.29). In the benzoate complex, the anion is not located between the two triazole groups, but instead forms a moderate hydrogen bond to one triazole group [C–H_{triazole}⋯O

= 3.031(3) Å; $\angle \text{C-H} \cdots \text{O} = 159^\circ$), and a weak hydrogen bond to a pyridinium methyl proton ($\text{C-H}_{\text{methyl}} \cdots \text{O} = 3.340(3)$ Å; $\angle \text{C-H} \cdots \text{O} = 173^\circ$). This arrangement presumably occurs as it allows further hydrogen bonding interactions with the water solvate to create a crystal lattice, which may not be possible with an alternative configuration. It does not appear to be a preferred arrangement in solution, as little movement of the methyl signal was observed during the benzoate association NMR titration experiment (0.05 ppm after one equivalent of anion *cf.* 0.53 ppm for the triazole resonance).

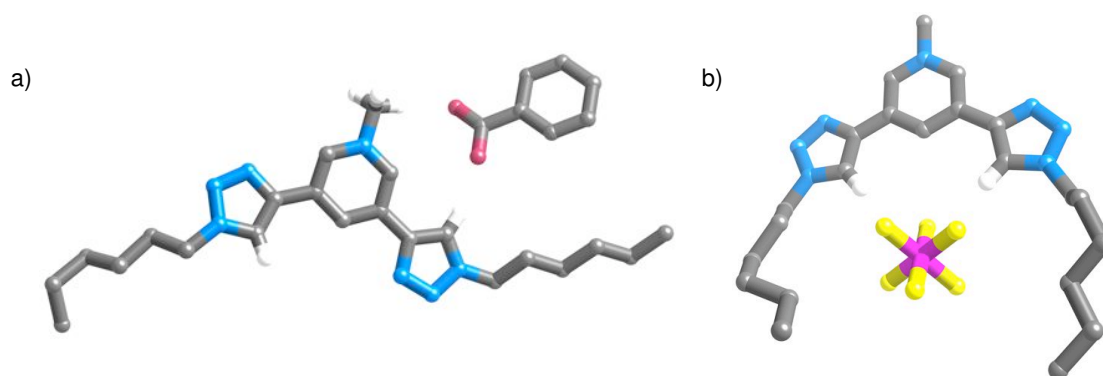


Figure 2.29: Solid state structures of $\mathbf{18}^+$ as a) benzoate, and b) hexafluorophosphate salts. Water solvate in $\mathbf{18}\cdot\text{BzO}$ and most hydrogen atoms omitted for clarity.

The hexafluorophosphate anion *does* adopt a bidentate binding arrangement between the two triazole donors, with reasonably short close contacts in the solid state from each of the triazole donors to fluorine atoms on the anion [$\text{C-H} \cdots \text{F} = 3.321(8)\text{--}3.393(8)$ Å; $\angle \text{C-H} \cdots \text{F} = 151\text{--}155^\circ$]. Distances between the triazole hydrogen atoms and fluorine atoms, as well as between the interior phenyl proton and fluorine atoms, range from 2.47–2.53 Å, slightly less than the sum of the van der Waals radii of hydrogen and fluorine (2.56 Å)^{346,347} suggesting the presence of weak hydrogen bonds.³

While acknowledging the dramatic differences in behaviour in the solution and the crystalline states, which favours intercomponent interactions as these allow crystal growth, the close contacts between $\mathbf{18}^+$ and hexafluorophosphate anions are of interest. Any interaction between the so-called “non-coordinating” anion and the receptor would cause an underestimation of the true association constants of other anions. This is particularly relevant given a recent report³⁴⁸ of an investigation of the binding of substituted tetrathiafulvalenes by a cationic paraquat based macrocycle. The authors found that

association could be more than doubled by using the large and even more weakly coordinating anion TRISPHAT⁻ instead of hexafluorophosphate (Figure 2.30).

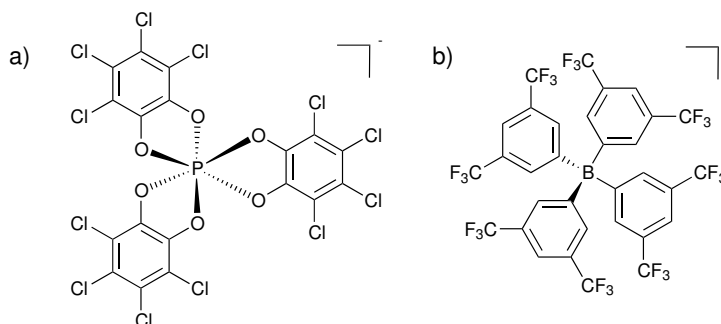


Figure 2.30: Extremely weakly coordinating anions: a) TRISPHAT⁻ ; b) BArF₄⁻.

To investigate this further, it was decided to prepare a salt of **18**⁺ with an extremely weakly coordinating anion to see if any perturbation of such a system could be detected on the addition of hexafluorophosphate. The tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate anion (BArF₄⁻) anion (Figure 2.30b) was chosen, as a sample of the sodium salt was available^{349,350} and this anion has shown to be among the least coordinating species known.³⁵¹ Sodium BArF₄⁻ and **18**-I were stirred in 1:1 dichloromethane:toluene at reflux temperature. Filtering and purification by preparative TLC gave pure **18**·BArF₄ in 89% yield.

Small single crystals of **18**·BArF₄ were obtained, and the structure determined by synchrotron X-ray crystallography (Figure 2.31). No contacts shorter than the sum of van der Waals radii are observed between the cation and anion in the solid state, consistent with the extremely non-coordinating nature of BArF₄⁻.

The possible association of hexafluorophosphate anion with **18**⁺ was investigated in two ways: firstly TBA·PF₆ was added to a d₆-acetone solution of **18**·BArF₄. No change in the ¹H NMR spectrum of the complex (Figure 2.32) was observed upon addition of hexafluorophosphate anion, suggesting minimal interaction in solution. Furthermore, repeating an anion binding titration experiment in d₆-acetone using **18**·BArF₄ instead of **18**·PF₆ did not alter the association constant obtained. Taken together, these two results suggest that hexafluorophosphate salts are an appropriate starting point for solution anion recognition experiments.

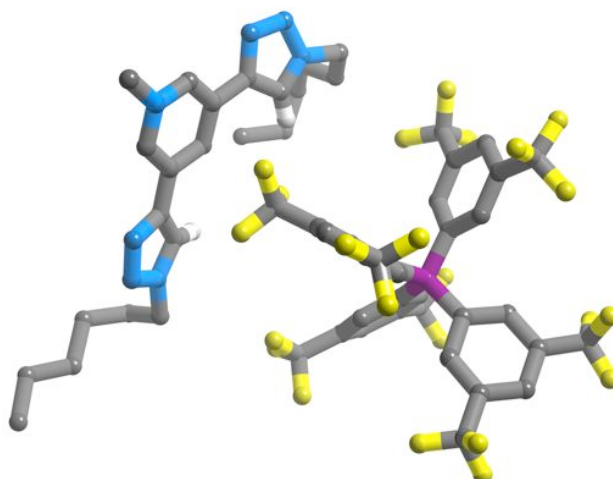


Figure 2.31: Structure of **18**·BARF₄ in the crystal. Most hydrogen atoms are omitted for clarity. Only one of the two independent ion pairs in the asymmetric unit cell is shown.

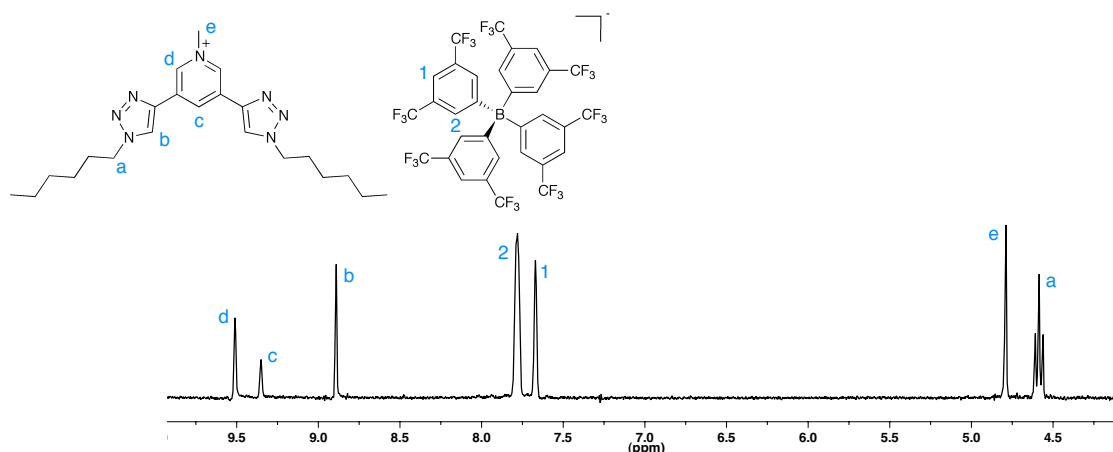


Figure 2.32: Truncated ¹H NMR spectrum of **18**·BARF₄ (d₆-acetone, 293 K, 300 MHz).

2.6 Conclusions and future work

2.6.1 Summary

Four acyclic bis-triazole receptors were prepared, with the nature of substitution and orientation of the triazole groups varied (alkyl or aryl-substituted, linked to the central phenylene ring through the heterocycle's *C* or *N*-terminus). The aryl-substituted hosts displayed anion affinities an order of magnitude greater than the alkyl-substituted compounds, while both *N*-linked systems bind chloride anion more strongly than their *C*-linked analogues. Four novel bis-triazole macrocycles were prepared in moderate yields *via* the intermolecular CuAAC reaction of a bis-azide and bis-alkynes. These cyclic hosts

displayed disappointing chloride anion recognition properties, particularly when compared with a previously-reported bis-triazole host,⁷⁹ or with bis-amide analogues.³⁰¹

Silver(I) and copper(I) cations were also demonstrated to bind to the acyclic and macrocyclic receptors in solution and the solid state. Four complexes were structurally characterized by X-ray crystallography: the *N*-linked receptor **6** forms a dinuclear metallomacrocyclic with silver cations, while the *C*-linked receptor **4** forms interesting trinuclear and tetranuclear complexes with copper and silver cations. Attempts to use either transition metal ion to template a pseudorotaxane assembly between a bis-triazole macrocycle and an acyclic bis-triazole molecule were unsuccessful.

The novel pyridinium-3,5-bis(triazole) motif was incorporated into an acyclic receptor, and its anion recognition properties studied. The new host was demonstrated to bind halide anions and benzoate in polar CD₃CN solution, although this association was considerably weaker than that of the bis-amide analogue.

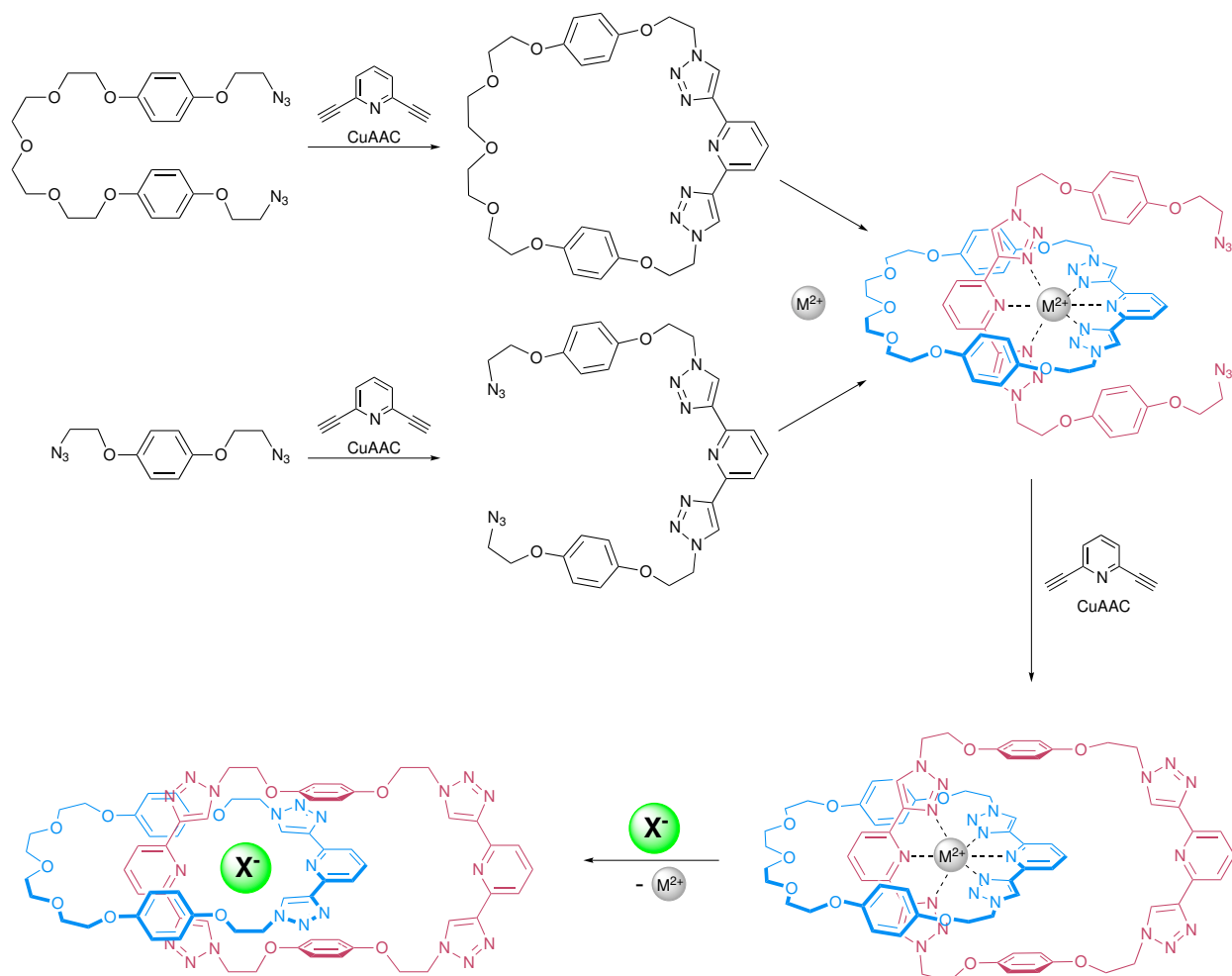
2.6.2 Future work

There are a number of possible avenues for future work arising from these results: most obviously, the triazole motif could be incorporated into interpenetrated and interlocked structures, and indeed this is the basis for Chapter 3. The relatively weak anion recognition properties of bis-triazole receptors could be dramatically enhanced by alkylation to yield bis-triazolium host systems, and this will be discussed in Chapter 5.

With regards to using metal templation to synthesize triazole containing anion receptors, a redesign of the system is required. This work attempted to use diamagnetic transition metals and bidentate ligands incorporating bis-triazole functionality, but the donor set did not have the correct size or geometry of donor atoms to facilitate an orthogonal arrangement around a tetrahedral metal centre.

Instead, it is suggested that octahedral metal ions along with the pyridine-2,6-bis(triazole) motif could be used to template interlocked structure formation (Scheme 2.8). A macrocycle and macrocycle precursor containing this motif could be readily prepared from 2,6-diethynylpyridine and known compounds: coordination of an octahedral metal ion would template pseudorotaxane formation, and the CuAAC

reaction utilized to give the catenane product. Removal of the templating metal ion would then give an interlocked host system incorporating multiple triazole donors for anion recognition.



Scheme 2.8: Possible synthesis of a triazole anion receptor using metal templation.

Chapter 3

Interpenetrated and interlocked structures incorporating the pyridinium bis-triazole motif

3.1 Introduction

3.1.1 Pseudorotaxanes incorporating triazole C–H donors

In 2001, Beer and co-workers reported the use of a discrete anion template to form the pseudorotaxane shown in Figure 3.1.²³² The interpenetrated assembly is held together by favourable anion···amide hydrogen bonding, and further stabilized by pyridinium···hydroquinone donor–acceptor interactions and pyridinium-methyl···polyether hydrogen bonding. In the ensuing decade, Beer’s group has reported a range of other pseudorotaxanes formed utilising bis-amide macrocycles, discrete anion templates, and a variety of threading components.^{39,80,239,242,244,245,288,302,352–356}

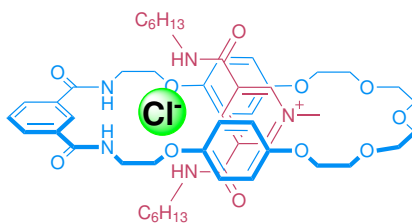


Figure 3.1: The first pseudorotaxane assembled using a discrete halide anion template.²³²

These pseudorotaxane investigations have used aprotic solvents, typically d_6 -acetone, and the strength of association has been observed to be strongly dependent on the choice of templating anion. Generally, chloride gives the strongest interweaved assemblies, followed by bromide, while pseudorotaxanes templated by iodide are generally weak, and negligible interpenetration is observed when hexafluorophosphate is used.

By contrast, only one system has used an oxoanion to template pseudorotaxane formation.²⁴² This assembly (Figure 3.2), which is also the only known pseudorotaxane formed by discrete anion templation of *neutral* components, takes advantage of an indolocarbazole thread and cannot be formed using chloride anion templation.³⁵⁷

It is also noteworthy that crystal structures of pseudorotaxanes formed by discrete anion templation are rare, and to the best of our knowledge, only chloride or bromide anion templated interpenetrated assemblies have been structurally characterized.^{232,239,244,302,356}

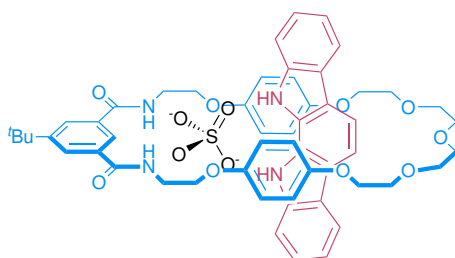


Figure 3.2: A pseudorotaxane assembled using an oxoanion template.²⁴²

While these are the only examples incorporating *discrete* anion templates,* other elegant uses of anionic species to form pseudorotaxanes have been reported. For example, Wisner has used “secondary coordination” of palladium dichloride complexes to amide based macrocycles (Figure 3.3a),^{359,360} and Sessler has threaded large aromatic dicarboxylate anions through cationic macrocycles to give pseudorotaxanes and poly-pseudorotaxanes (Figure 3.3b).^{361–363}

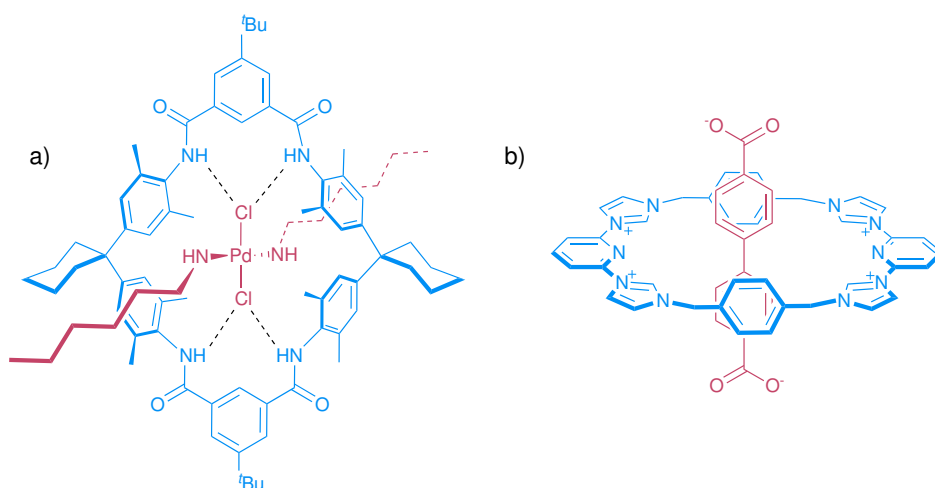


Figure 3.3: Other anion mediated pseudorotaxanes: a) Wisner's interweaved assembly templated using secondary coordination;³⁵⁹ b) Sessler's use of a large anion as a threading component.³⁶²

*Stoddart, Williams and co-workers have reported [4] and [5]pseudorotaxanes formed between benzyl ammonium threading components and expanded crown ether macrocycles, which encapsulate a PF_6^- anion in the solid state.³⁵⁸ While the authors postulate that the assembly has been “programmed” by the hexafluorophosphate anion, no other counteranions were studied and so the existence of any anion templation effect is debatable.

3.1.2 Incorporation of triazole C–H donors into interlocked anion host systems

The CuAAC reaction has proved ideal for the construction of a range of mechanically bonded architectures due to its efficacy, mild reaction conditions and functional group tolerance.^{201,202,265,266,364–366} Surprisingly, however, to the best of our knowledge, only one interlocked host has utilized the triazole group to complex anionic guests.²⁸² Li's rotaxane (Figure 3.4) acts as a dual-response molecular switch, with translocation of the macrocyclic component occurring in response to acid/base stimulus, and chloride anion addition causing subsequent rotation of this macrocycle.²⁸² Specifically, the authors report that the non-protonated form of the rotaxane displays modest association with halide anions in CD₃CN.

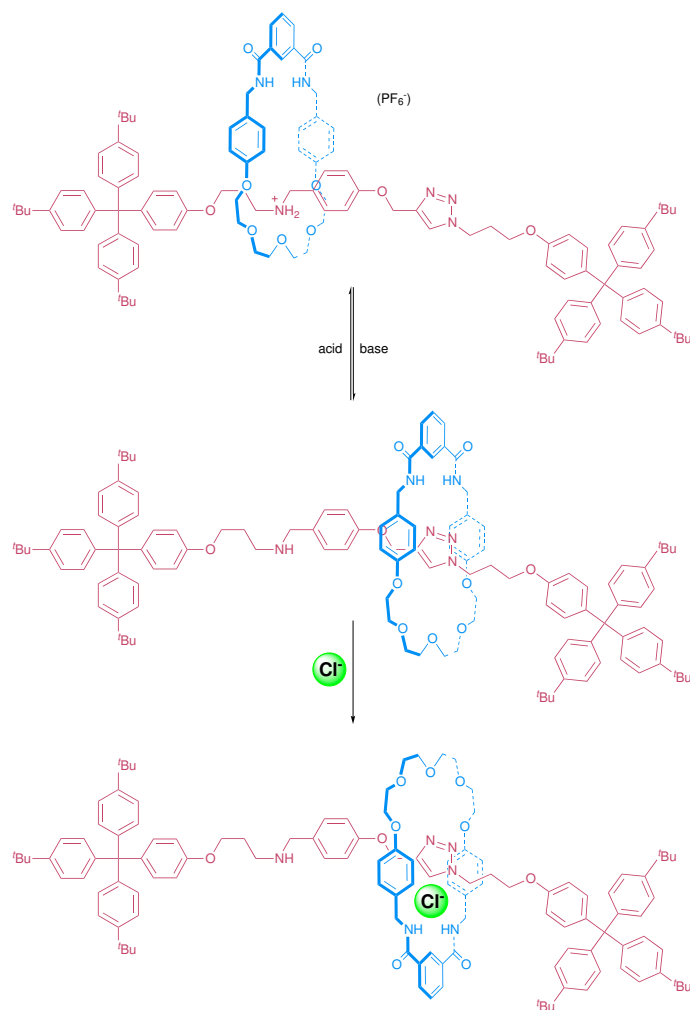


Figure 3.4: Li's dual-response triazole containing rotaxane.²⁸²

3.1.3 Chapter objectives

In an effort to further explore the similarities and differences between the amide and triazole functionalities in the recognition of anions, the incorporation of triazole heterocycles into anion templated pseudorotaxanes will be attempted. The synthesis of interpenetrated assemblies templated purely by C–H...anion hydrogen bonding will also be investigated using pyridinium bis-triazole compound **18**⁺ (Section 2.5.2).

The synthesis of interlocked catenane and rotaxane host systems incorporating the pyridinium-3,5-bis(triazole) motif will be attempted, with the aim of preparing receptors that exhibit strong and selective anion recognition in competitive solvent media. The anion recognition properties of the resulting triazole containing architectures will be investigated and discussed in comparison to previously published amide analogues.

3.2 Solution pseudorotaxane studies

3.2.1 Pseudorotaxane formation by triazole containing receptors

Initial qualitative ¹H NMR titration experiments investigating the ability of pyridinium bis-triazole threading component **18**⁺ to form anion templated pseudorotaxanes were undertaken in d₆-acetone, using isophthalamide macrocycle **16** and chloride as the templating anion. Addition of thread **18**·Cl to **16** caused diagnostic upfield shifts in the macrocycle’s hydroquinone resonances *6* and *7* (Figure 3.5), due to donor–acceptor interactions with the electron-deficient pyridinium ring, indicative of formation of interpenetrated assembly **16**·Cl·**18**. Also of note are protons *b*, *c* and *d*, which shift upfield as hydrogen bonding interactions between the threading component and chloride anion are weakened by “sharing” of the anion with the macrocycle. This also causes downfield movement of macrocycle resonances *2* and *3*, as these protons are now involved in hydrogen bonding with the halide anion.

The assembly was investigated further by ¹H-¹H 2D ROESY NMR (Figure 5.27), with a range of intercomponent through-space couplings observed, including between the thread’s triazole protons and macrocycle hydroquinone resonances. Additional couplings involving

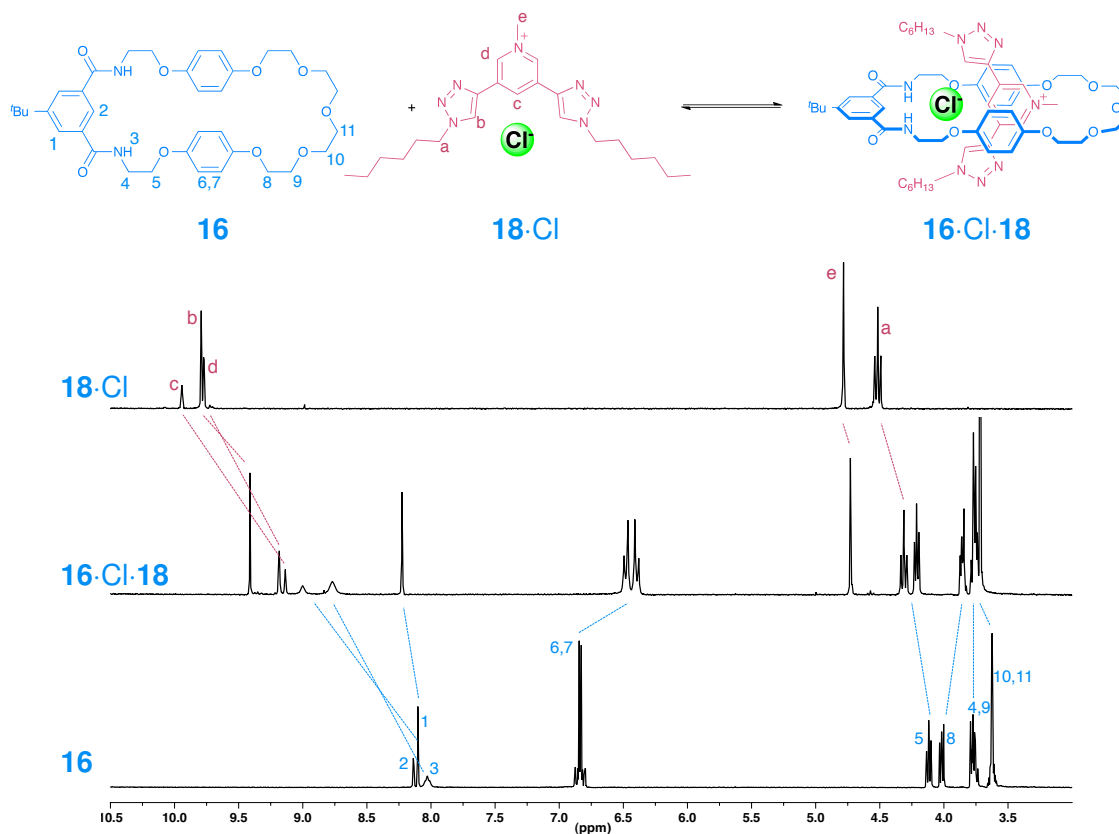


Figure 3.5: Pseudorotaxane formation between **16** and **18-Cl** (d_6 -acetone, 293 K, 300 MHz).

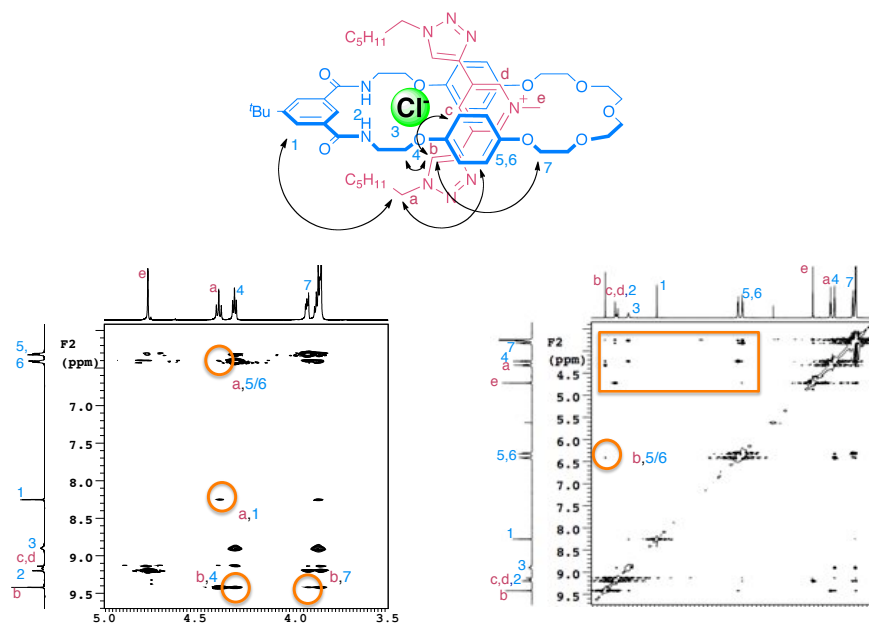


Figure 3.6: Truncated ROESY NMR of **16-Cl-18** showing selected intercomponent couplings. Spectrum on left is an expansion of area inside orange rectangle on right-hand spectrum (d_6 -acetone, 293 K, 500 MHz).

the macrocycle's interior phenylene proton and threading component's pyridinium signals could not be resolved due to the overlap of these signals.

The ability of anions other than chloride to template pseudorotaxane formation between **18**⁺ and **16** was also assessed: solutions containing a 1:1:1 stoichiometric ratio of **16**, **18**·PF₆ and TBA·X were analysed by ¹H NMR spectroscopy (X = Cl⁻, Br⁻, I⁻, NO₃⁻, OAc⁻, BzO⁻, HSO₄⁻). The spectra of the 1:1:1 mixtures are shown in Figure 3.7. Importantly, addition of **18**⁺ as its non-coordinating PF₆⁻ salt has a negligible effect on the macrocycle's proton resonances, indicating almost no pseudorotaxane formation in the absence of a suitable templating anion. The use of any of the other anions causes significant upfield shifts in the hydroquinone resonances, due to donor–acceptor interactions between the pyridinium and hydroquinone rings, consistent with pseudorotaxane formation in the presence of all studied anions. Downfield shifts are observed in protons *2*, *3*, *a* and *b* indicating hydrogen bond formation between both the macrocycle and the threading component and the anion, again a result of pseudorotaxane formation.

Single crystals of the pseudorotaxanes **16**·Cl·**18**, **16**·Br·**18**, **16**·I·**18** and **16**·NO₃·**18** suitable for X-ray diffraction studies were obtained. These structures are discussed in Section 3.3.1.

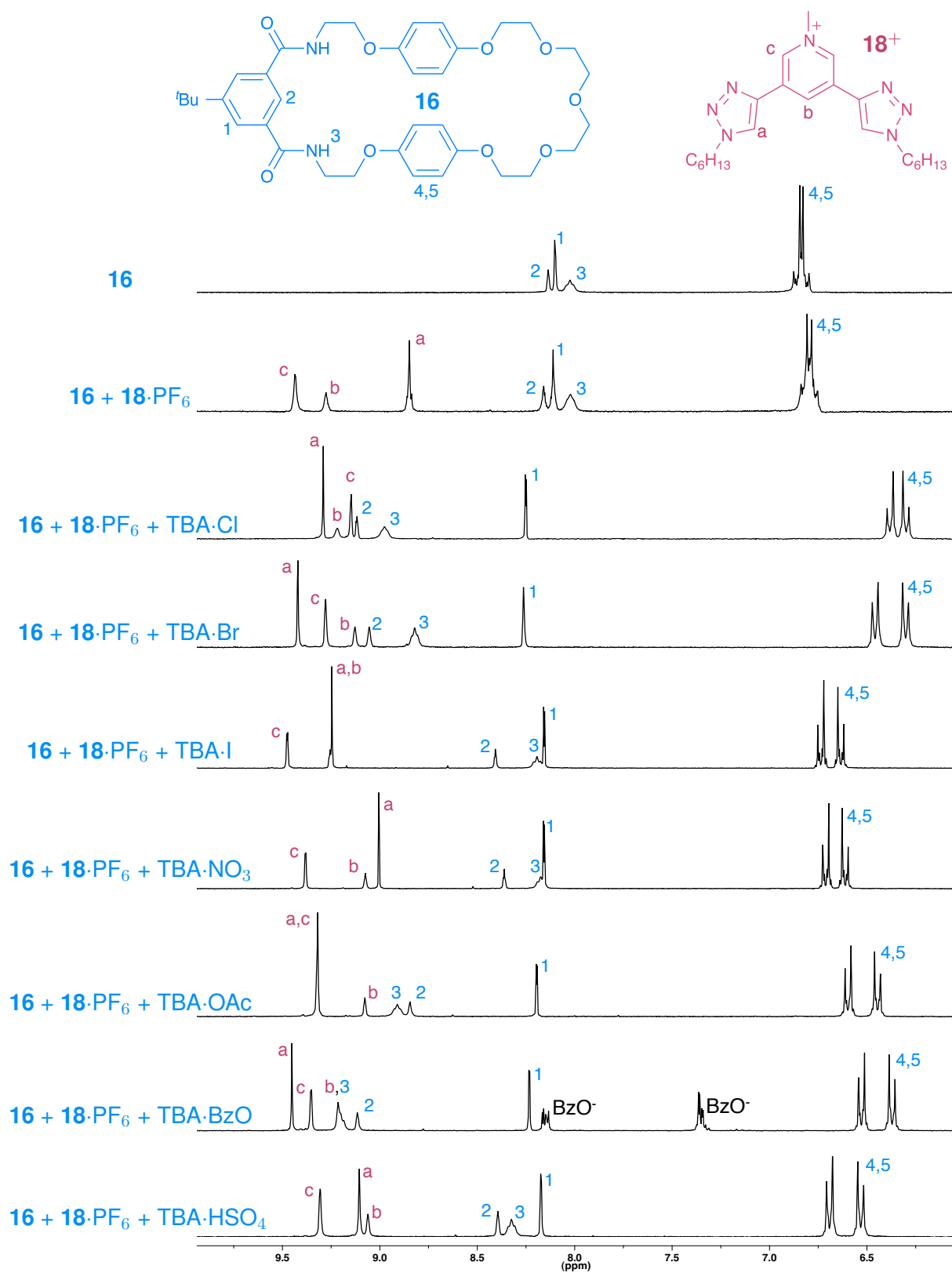


Figure 3.7: Truncated ¹H NMR spectra of **16**, **18**·PF₆ and TBA·X (d₆-acetone, 293 K, 300 MHz).

Table 3.1: Movement in hydroquinone signals of **16** upon addition of **18**·PF₆ and TBA·X.^a

Anion, X	Upfield resonance	Downfield resonance	Average resonance ^b
none ^c	−0.04	−0.04	−0.04
Cl [−]	−0.48	−0.51	−0.50
Br [−]	−0.40	−0.51	−0.46
I [−]	−0.12	−0.18	−0.15
NO ₃ [−]	−0.15	−0.20	−0.17
OAc [−]	−0.26	−0.37	−0.31
BzO [−]	−0.33	−0.44	−0.39
HSO ₄ [−]	−0.17	−0.28	−0.22

^ad₆-acetone, 293 K. ^bMovement of the midpoint of the hydroquinone signal. ^cThese small shifts occur due to **18**·PF₆ with no additional added anion.

As detailed in Table 3.1, the greatest upfield movement in the hydroquinone signals is observed when chloride and bromide anions are added, with large shifts also seen in the presence of benzoate and acetate. To investigate further, quantitative ¹H NMR titration experiments were undertaken in 1:1 CDCl₃:d₆-acetone, with aliquots of a solution of **18**·X added to a solution of macrocycle **20**;† this solvent mixture was used as **18**⁺ does not have sufficient solubility in d₆-acetone to allow quantitative titration experiments to be conducted. Unfortunately, it was not possible to prepare the acetate, benzoate or hydrogen sulfate salts of **18**⁺, and 1:1 mixtures of **18**·PF₆ and the TBA salts of these anions had insufficient solubility in the solvents used. Therefore, pseudorotaxane formation was studied using the hexafluorophosphate, chloride, iodide and nitrate salts of **18**⁺.

Apparent association constants were determined monitoring the hydroquinone signal using WINEQNM2³²⁸ (Table 3.2 and Figure 3.8). Only very weak pseudorotaxane formation is observed when **18**·PF₆ is used, while, as expected, an appropriate templating anion (Cl[−], NO₃[−], I[−]) leads to a far more stable interpenetrated assembly. The pseudorotaxane stabilities broadly follow anion basicity trends, as was previously observed for interpenetrated assemblies incorporating the analogous pyridinium bis-amide threading component **19**·X (X = Cl[−], Br[−], I[−]) in d₆-acetone.²³²

†The unsubstituted macrocycle was used to allow comparison with the analogous all-amide pseudorotaxane, Ref. 232.

Table 3.2: Apparent association constants, K_{app} for pseudorotaxane formation between **20** and **18**·X.

Anion, X	K_{app} (M^{-1})
Cl^-	799(69)
I^-	242(13)
NO_3^-	$\sim 600^{\text{b}}$
PF_6^-	38(3)

^aCalculated using WINEQNMR2,³²⁸ monitoring hydroquinone resonance. Estimated standard errors are given in parentheses (1:1 CDCl_3 : d_6 -acetone, 293 K). ^bMinor precipitation of **18**· NO_3 from the titrant solution was observed during the titration experiment: the amount of threading component added was corrected based on integration of the titration ^1H NMR spectra, but this value is an approximation only.

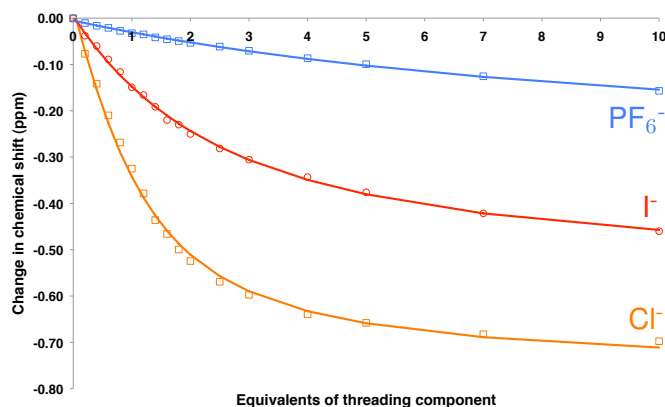


Figure 3.8: Experimental titration data (points) and fitted binding isotherms (lines) for addition of threading component with various counteranions to **20** (1:1 CDCl_3 : d_6 -acetone, 293 K, 500 MHz).

3.2.2 All-amide pseudorotaxanes

The ability of a pyridinium bis-*triazole* threading component to form anion templated pseudorotaxanes with isophthalamide macrocycles using oxoanion templates was demonstrated in the previous Section. It was decided to investigate whether pseudorotaxane assemblies incorporating the same macrocycle **16** and pyridinium bis-*amide* threading component **19**⁺ (Figure 2.26) could also form oxoanion templated pseudorotaxanes, or whether this was unique to triazole containing interweaved architectures. Qualitative 1:1:1 stoichiometric studies of mixtures of macrocycle **16**, thread **19**⁺ and TBA·X were undertaken in an analogous manner to those involving triazole thread **18**⁺.

As shown in Figure 3.9, all added anions cause upfield shifts in the hydroquinone resonances *4* and *5* consistent with donor–acceptor interactions between hydroquinone and pyridinium rings. Downfield movement of peaks on both macrocycle and threading component are also observed upon anion addition, indicating that both components are involved in hydrogen bonding to this species. Both of these events are entirely consistent with an interweaved assembly, demonstrating that oxoanions *can* be used to template the formation of amide based pseudorotaxanes, as well as those incorporating triazole donors.

Single crystals of the pseudorotaxanes **16·Cl·19**, **16·I·19**, **16·NO₃·19**, **16·OAc·19**, and **16·BzO·19** suitable for X-ray diffraction studies were obtained. These structures are discussed in Section 3.3.2.

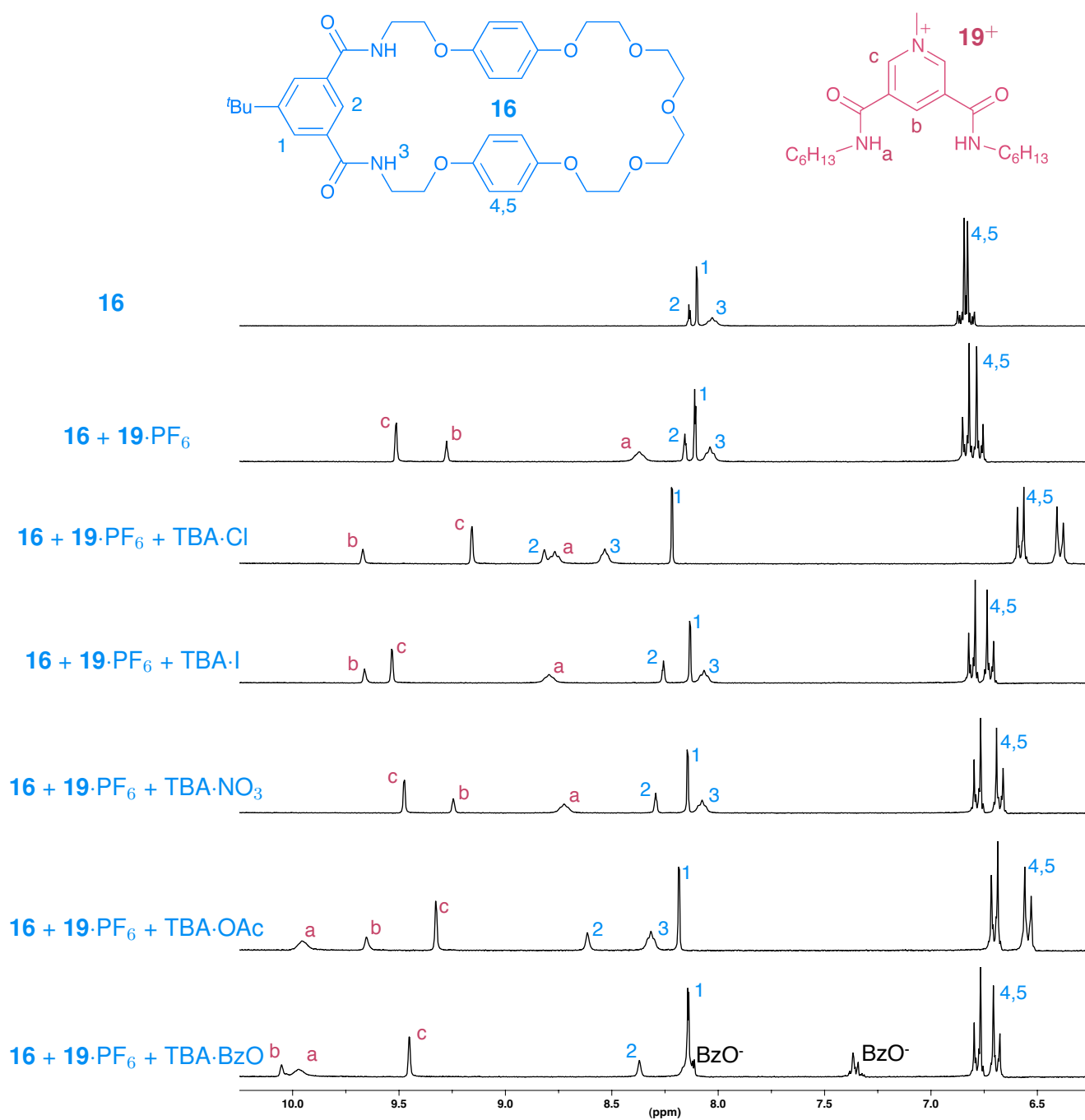


Figure 3.9: Truncated ^1H NMR spectra of **16**, **19**·PF₆ and TBA·X (d_6 -acetone, 293 K, 300 MHz).

The respective magnitudes of upfield shifts of the hydroquinone resonances are shown in Table 3.3, as well as those observed when bis-triazole threading component **18**⁺ was used (Section 3.2.1). In all cases, the average shift is significantly smaller for the amide containing thread than for the triazole. Generally, **18**·X induces an average hydroquinone movement of approximately 50% greater magnitude than the corresponding salt of **19**⁺, although in the case of the benzoate anion, the shift is four times larger. For this anion, very large changes are seen in the environments of hydrogen bond donor protons *a* and *b*, with smaller movements in macrocycle resonances, suggesting that pseudorotaxane formation is in competition with sequestering of the anion by the threading component.

Table 3.3: Movement in hydroquinone signals (ppm) of **16** upon addition of **19**·PF₆ and TBA·X.^a

Anion, X	Upfield resonance	Downfield resonance	Average	18 ⁺ <i>Average</i> ^b
none ^c	−0.02	−0.04	−0.03	−0.04
Cl [−]	−0.28	−0.42	−0.35	−0.50
I [−]	−0.05	−0.09	−0.07	−0.15
NO ₃ [−]	−0.08	−0.14	−0.11	−0.17
OAc [−]	−0.16	−0.27	−0.21	−0.31
BzO [−]	−0.08	−0.12	−0.10	−0.39

^ad₆-acetone, 293 K. ^bShift in hydroquinone resonance for this anion when **18**⁺ used (Table 3.1).

^cThese small shifts occur due to **19**·PF₆ with no additional added anion.

To investigate further, quantitative ¹H NMR titration experiments were undertaken with macrocycle **20**, and **19**·PF₆, **19**·Cl, **19**·I and **19**·NO₃ in 1:1 CDCl₃:d₆-acetone. As was the case with the triazole containing threading component, such NMR experiments could not be conducted using acetate or benzoate as the templating anion, as it was not possible to prepare the necessary salts of **19**⁺, and 1:1 mixtures of **19**·PF₆ and the TBA salts of these anions had insufficient solubility in the solvents used. Apparent association constants were determined using WINEQNMR2,³²⁸ monitoring the hydroquinone resonance, and are presented in Table 3.4, with the apparent association constants for the analogous triazole containing pseudorotaxanes also provided for comparison.

Perhaps surprisingly, the stability trend of pseudorotaxane assemblies **19**·X·**20** does not follow anion basicity trends, as has been reported for the same interpenetrated assemblies in d₆-acetone.²³² The most basic anion, chloride, gives a less stable pseudorotaxane than

Table 3.4: Apparent association constants, K_{app} (M^{-1}) for pseudorotaxane formation between **20** and **19**·X or **18**·X.

Anion, X	19 ·X· 20	18 ·X· 20
Cl ⁻	412(15)	799(69)
I ⁻	612(68)	242(13)
NO ₃ ⁻	703(109)	~ 600
PF ₆ ⁻	177(19)	38(3)

^aCalculated using WINEQNMR2,³²⁸ monitoring hydroquinone resonance. Estimated standard errors are given in parentheses (1:1 CDCl₃:d₆-acetone, 293 K).

iodide or nitrate. It is also noteworthy that hexafluorophosphate, iodide and nitrate anions all give far more stable pseudorotaxanes for amide threading component **19**⁺ than for triazole thread **18**⁺, whereas the chloride anion templated assembly is in fact considerably weaker. When hexafluorophosphate anion is used, significant pseudorotaxane formation is observed for **19**·PF₆·**20** in 1:1 CDCl₃:d₆-acetone [$K_{\text{app}} = 177(19) \text{ M}^{-1}$], but not for the same pseudorotaxane in d₆-acetone ($K_{\text{app}} = 35 \text{ M}^{-1}$)²³² or **18**·PF₆·**20** in 1:1 CDCl₃:d₆-acetone [$K_{\text{app}} = 38(3) \text{ M}^{-1}$].

The apparent association of **19**·Cl·**20** is anomalously low, as this is the only K_{app} for pseudorotaxanes involving either threading component that does not follow anion basicity trends, and in which the assembly containing **19**⁺ is weaker than the analogous system incorporating **18**⁺. Integration of the ¹H NMR signals corresponding to the threading component and macrocycle were carefully checked to rule out an incorrect stoichiometry giving an erroneous result, but no error was detected. The titration experiment was therefore repeated, and a concordant result of 405(25) M^{-1} was obtained, suggesting that experimental error is not the cause of the anomaly.

While the nature of the mixed solvent system makes understanding the trends of pseudorotaxane formation more difficult, it is speculated that part of the reason for the unexpectedly low association of **19**·Cl·**20** may be to do with a competing process to form a complex containing two threading components around one anion, *i.e.* **19**·Cl·**19**. This will be discussed further in Section 3.4.4.

3.2.2.1 Pseudorotaxanes incorporating hexafluorophosphate thread salts

To further investigate the formation of pseudorotaxanes in the absence of a coordinating anion template, the stability of the interpenetrated assemblies containing hexafluorophosphate anions were investigated in CDCl_3 , and compared with those in CDCl_3 : d_6 -acetone mixture, and in the case of **19**· PF_6 ·**20** in d_6 -acetone.²³²

As shown in Table 3.5, pseudorotaxane stability is strongly dependent on solvent, and in non-polar CDCl_3 significant pseudorotaxane formation *is* observed for these systems in the absence of an appropriate anion template. Presumably, this association arises due to donor–acceptor interactions and thread· · · macrocycle hydrogen bonding. The importance of the donor–acceptor interactions is illustrated by the fact that association of **19**· PF_6 and **20** is greater in 1:1 CDCl_3 : d_6 -acetone than in d_6 -acetone. This mixture is more *competitive* (in terms of hydrogen bonding) than pure d_6 -acetone,⁷⁵ but less *polar* and so presumably favours the donor–acceptor interaction, while weakening hydrogen bonding.

Table 3.5: Apparent association constants, K_{app} (M^{-1}) for pseudorotaxane formation between **20** and **19**· PF_6 or **18**· PF_6 in a range of solvent systems.

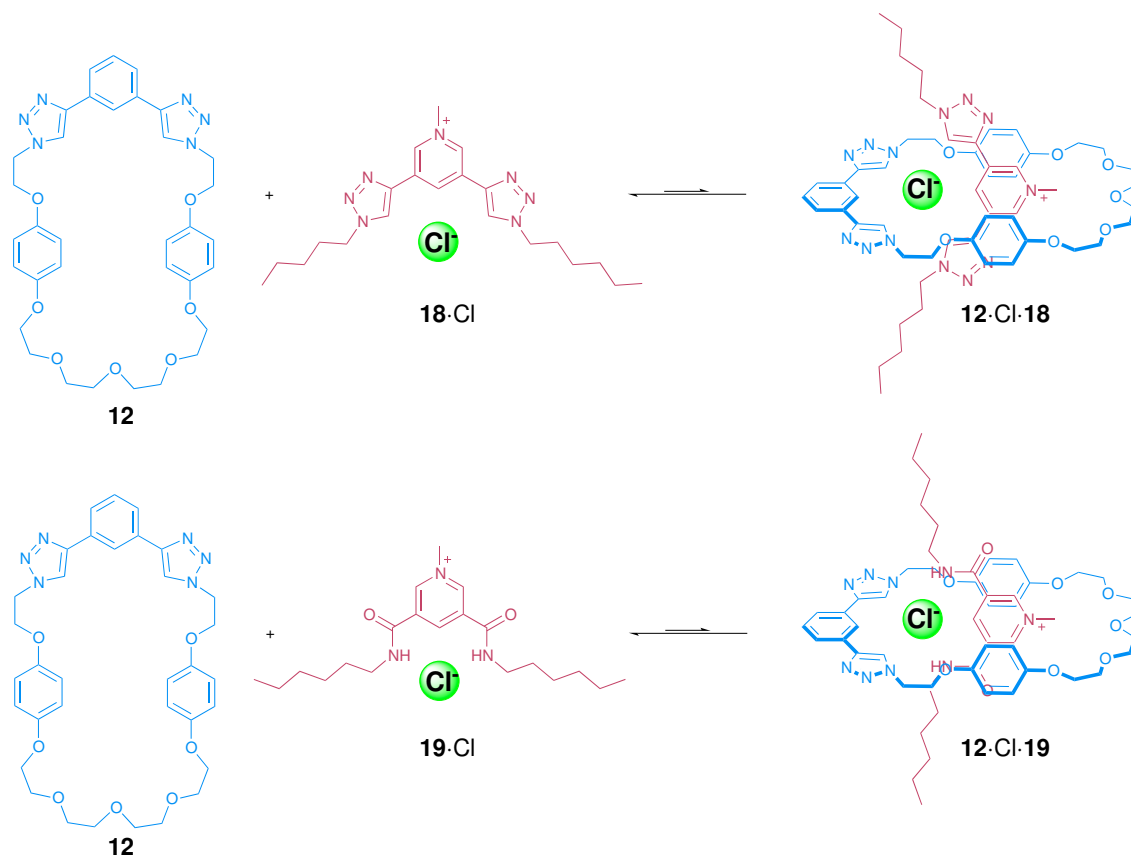
Solvent	19 · PF_6 · 20	18 · PF_6 · 20
CDCl_3	4330(401)	732(51)
1:1 CDCl_3 : d_6 -acetone	177(19)	38(3)
d_6 -acetone	35 ²³²	— ^b

^aCalculated using WINEQNMR2,³²⁸ monitoring hydroquinone resonance. Estimated standard errors are given in parentheses (293 K). ^bInsufficient solubility for titration to be performed.

In both CDCl_3 and 1:1 CDCl_3 : d_6 -acetone, amide containing threading component **19**· PF_6 forms a pseudorotaxane that is approximately five times more stable than with the triazole analogue **18**· PF_6 . This is probably due to the amide groups withdrawing more electron density from the central pyridinium ring than do the triazoles, giving stronger donor–acceptor and pyridinium-methyl· · · polyether hydrogen bonding interactions, both of which mediate pseudorotaxane formation in the absence of a coordinating anion.

3.2.3 Investigating the possibility of forming pseudorotaxanes using only C–H···anion hydrogen bonds

The assembly of an anion templated pseudorotaxane using only C–H···anion hydrogen bonds is unprecedented, and would be an important demonstration of the utility of such interactions in anion coordination chemistry. Therefore, the association between **18**·Cl and bis-triazole macrocycle **12** was investigated in 1:1 CDCl₃:d₆-acetone, however, association was very weak [$K_{\text{app}} = 22(2) \text{ M}^{-1}$], presumably due to the poor anion recognition ability of **12** (Section 2.3.2). The association between pyridinium bis-amide thread **19**·Cl and **12** was also very weak [$K_{\text{app}} = 64(4) \text{ M}^{-1}$], again due to the weak anion binding properties of the macrocycle (Scheme 3.1).



Scheme 3.1: Attempts to form pseudorotaxanes incorporating bis-triazole macrocycle **12**.

To allow formation of pseudorotaxanes based on C–H···anion hydrogen bonding, the integration of the the pyridinium-3,5-bis(triazole) motif into the *macrocyclic* receptor as

well as the threading component was attempted, in order to give a more potent anion receptor (Figure 3.10).

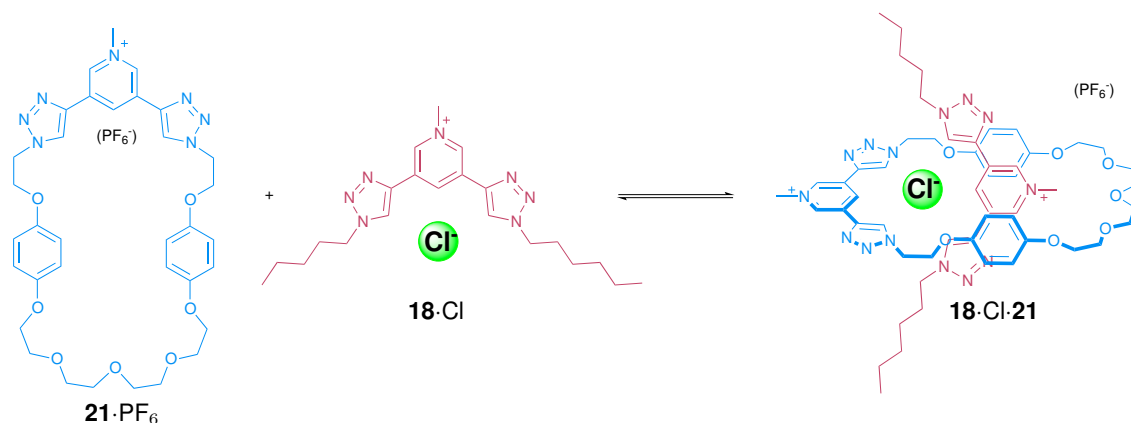
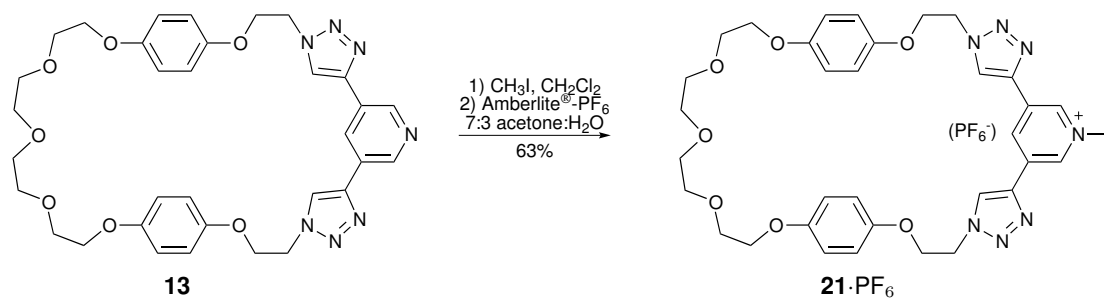


Figure 3.10: Targeted pseudorotaxane assembled using C–H···anion hydrogen bonding interactions.

The pyridinium-3,5-bis(triazole) macrocycle necessary for this pseudorotaxane was prepared from the pyridine containing macrocycle **13**, as shown in Scheme 3.2. Alkylation using methyl iodide in dry dichloromethane gave **21**·I as a sparingly soluble pale yellow powder. This was anion-exchanged using hexafluorophosphate-loaded Amberlite[®] resin to give **21**·PF₆ in 63% yield.

Attempts to determine the anion recognition properties of this macrocycle were stymied as addition of TBA·Cl in d₆-acetone caused immediate precipitation. Indeed, it was found that any source of chloride anion (including the threading component **18**·Cl) resulted in precipitation. The only solvent in which the macrocycle remained soluble in the presence of chloride anion was d₆-DMSO, but a quantitative ¹H NMR titration experiment showed anion association was very weak in this competitive solvent [$K_a = 67(1) \text{ M}^{-1}$], negating the possibility of anion templated pseudorotaxane assembly.



Scheme 3.2: Synthesis of **21**·PF₆.

3.3 Solid state structures of anion templated pseudorotaxanes

3.3.1 X-ray crystal structures of triazole containing pseudorotaxanes

Single crystals of the pseudorotaxane assembly of **16** and **18**⁺ were obtained with four different templating anions (Cl⁻, Br⁻, I⁻ and NO₃⁻) by diffusion of diethyl ether vapour into 1:1:1 stoichiometric mixtures of **16**, **18**·PF₆ and TBA·X. The X-ray single crystal structure of pseudorotaxane assembly **16**·Cl⁻·**18** is shown in Figure 3.11. The solid state structure of the pseudorotaxane assembly contains hydrogen bonds between the thread's triazole and *para*-pyridinium protons and the chloride anion, and the macrocycle's amide and interior phenylene donors and the anion. Additional stabilization is provided by hydroquinone...pyridinium donor-acceptor interactions utilizing both hydroquinone rings, and one significant hydrogen bond between an oxygen atom of the macrocycle's polyether group and the thread's pyridinium-methyl motif. Full details of these non-covalent interactions are provided in Table 3.6.

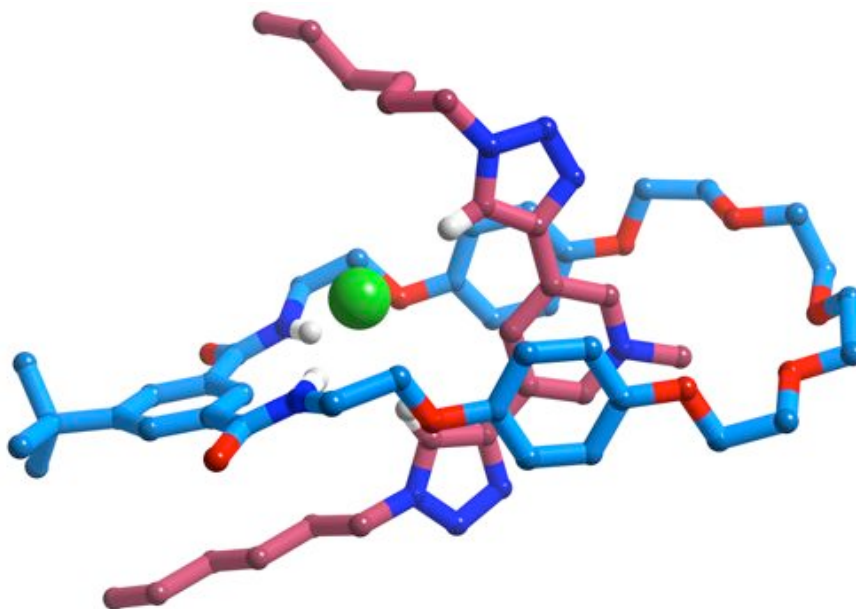


Figure 3.11: Solid state structure of **16**·Cl⁻·**18**. Most hydrogen atoms are omitted for clarity.

The structures of the bromide and iodide anion templated pseudorotaxane assemblies (Figure 3.12) initially appear to be very similar to that of **16**·Cl⁻·**18**. However, closer

inspection reveals that there are subtle, but important differences between the solid state assemblies (Table 3.6).

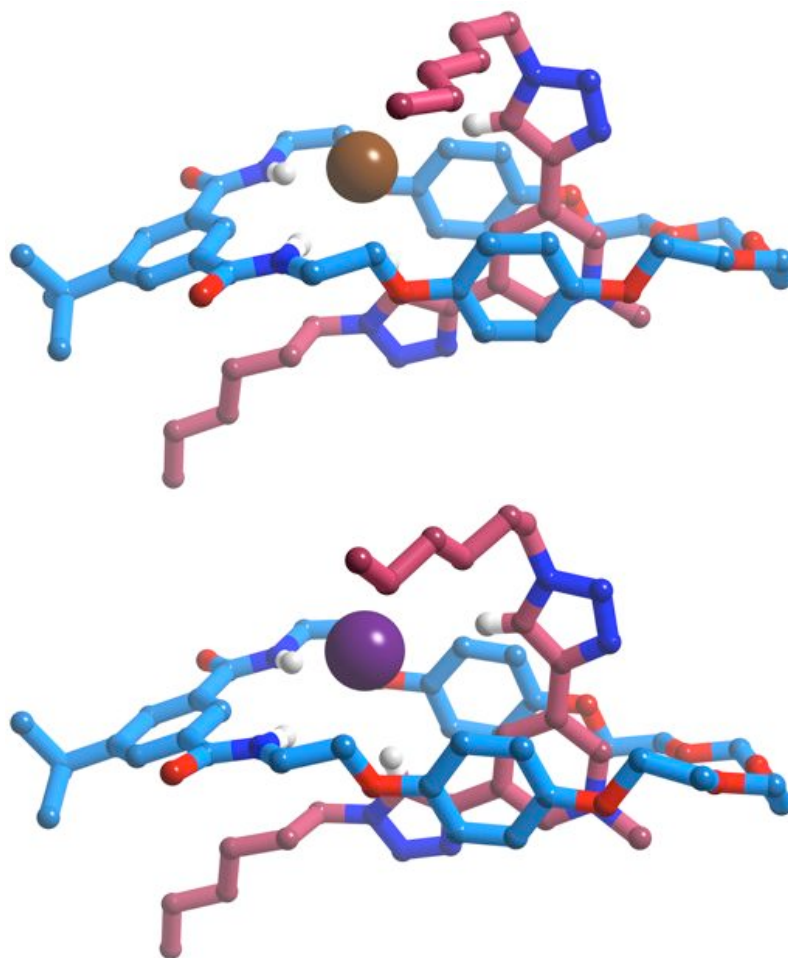


Figure 3.12: Solid state structures of **16·Br·18** and **16·I·18**. Solvent molecules, most hydrogen atoms, and minor position of iodide disorder are omitted for clarity.

In order to usefully compare hydrogen bonding interactions involving atoms of different sizes, the hydrogen bond distance has traditionally been considered in terms of the *donor*···acceptor distance as a percentage of the sum of the van der Waals radii of the donor atom and acceptor atom (%VdW_{D,A}). Recently, it has been suggested that a more useful measure is the percentage of the *hydrogen*···acceptor distance as a percentage of the sum of the van der Waals radii of the hydrogen atom and acceptor atom (%VdW_{H,A}).³ There are advantages and disadvantages to both methods: considering %VdW_{D,A} has the disadvantage that it ignores orientation, so hydrogen bonds that are poorly oriented and would traditionally be considered weak (*e.g.* $\angle\text{D-H}\cdots\text{A} < 150^\circ$)² are overstated. The

alternative description $\%VdW_{H,A}$ is a more complete measure of hydrogen bond strength, seeing as it is affected by both distance and directionality, but the $H \cdots$ acceptor distance is inevitably less accurate, due to the uncertainties associated with the positions of weakly diffracting hydrogen atoms (see Section 6.2.5.1). Thus while this value is perhaps the most informative, it should be taken as a guide only.

Both $\%VdW_{D,A}$ and $\%VdW_{H,A}$ are given in Table 3.6, as well as full details of $D \cdots A$ and $H \cdots A$ distances and $\angle D-H \cdots A$ angles to demonstrate the effect that these parameters have upon one another. In the interests of brevity, subsequent tables will not provide this level of detail, but these data can be obtained from the CIF files in the Appendix.

Table 3.6: Non-covalent interactions in solid state structures of pseudorotaxanes **16**·X·**18**.^a

	Cl ⁻	Br ⁻	I ^{-b}	NO ₃ ^{-c}
<i>Receptor···anion hydrogen bonding</i>				
<i>Macrocyclic</i>				
N–H···X ⁻	3.300(4)	3.596(4)	3.803(2)	3.121(2)
%VdW _{N,X}	100	106	108	102
∠N–H···X ⁻	159	164	161	169
H···X ⁻	2.43	2.75	2.97	2.27
%VdW _{H,X}	86	94	97	87
N–H···X ⁻	3.348(4)	3.639(4)	3.846(2)	3.161(2)
%VdW _{N,X}	101	107	109	103
∠N–H···X ⁻	152	159	147	170
H···X ⁻	2.51	2.82	3.09	2.28
%VdW _{H,X}	88	96	101	87
C–H _{phenylene} ···X ⁻	3.445(4)	3.801(5)	4.036(2)	3.114(2)
%VdW _{C,X}	100	107	110	97
∠C–H _{phenylene} ···X ⁻	142	175	173	177
H···X ⁻	2.66	2.87	3.09	2.15
%VdW _{H,X}	94	98	101	82
<i>Threading component</i>				
C–H _{triazole} ···X ⁻	3.431(4)	3.694(5)	3.885(3)	3.189(5), 3.210(4)
%VdW _{C,X}	99	104	109	99, 100
∠C–H _{triazole} ···X ⁻	166	168	166	140, 168
H···X ⁻	2.54	2.77	2.98	2.43, 2.30
%VdW _{H,X}	89	94	97	93, 88
C–H _{triazole} ···X ⁻	3.679(5)	3.882(5)	3.985(3)	3.597(5), 3.665(4)
%VdW _{C,X}	107	109	112	112, 114
∠C–H _{triazole} ···X ⁻	163	160	156	157, 155
H···X ⁻	2.78	2.99	3.11	2.76, 2.89
%VdW _{H,X}	98	102	101	106, 111
C–H _{pyridinium} ···X ⁻	3.641(5)	4.013(5)	4.187(3)	3.268(3), 3.431(4)
%VdW _{C,X}	106	113	118	101, 107
∠C–H _{pyridinium} ···X ⁻	178	169	167	150, 175
H···X ⁻	2.69	3.08	3.25	2.389, 2.462
%VdW _{H,X}	95	105	106	92, 94
<i>Pyridinium···hydroquinone donor–acceptor interactions</i>				
centroid···centroid	3.499(2)	3.546(3)	3.6123(14)	3.5863(11)
mean plane angle	7.1(2)	9.5(2)	11.25(12)	9.60(9)
centroid···centroid	3.623(3)	3.889(3)	—	—
mean plane angle	5.64(19)	10.4(2)	—	—
<i>Pyridinium-methyl···polyether hydrogen bonding</i>				
C–H _{methyl} ···O	3.379(5)	3.395(7)	3.369(3)	3.354(3)
%VdW _{C,O}	105	105	115	104
∠C–H _{methyl} ···O	172	164	158	143
H···O	2.41	2.47	2.47	2.54
%VdW _{H,O}	92	94	94	97
C–H _{methyl} ···O	—	3.391(7)	3.413(3)	—
%VdW _{C,O}	—	105	106	—
∠C–H _{methyl} ···O	—	148	147	—
H···O	—	2.55	2.57	—
%VdW _{H,O}	—	98	98	—

^aDistances in Å, angles in degrees, estimated standard uncertainties in parentheses. ^bThe minor component of the disordered iodide anion is excluded. ^cValues are given for both positions of the disordered nitrate anion.

In all three halide anion containing pseudorotaxanes, the strongest hydrogen bonds in terms of %VdW_{H,A} are provided by the macrocycle’s two amide groups, with the macrocycle also providing a weak donor from the phenylene proton. The threading component, however, is arranged asymmetrically such that only one of the triazole groups is a significant hydrogen bond donor. In the chloride complex, the *para*-pyridinium proton also acts as a donor, but this is not the case in the bromide or iodide pseudorotaxanes. As would be expected from their relative basicities, hydrogen bonds involving chloride anion are significantly stronger than those with bromide anion, with interactions involving iodide weaker still (%VdW_{H,Cl} = 86–98; %VdW_{H,Br} ≥ 94; %VdW_{H,I} ≥ 97).

The chloride anion templated pseudorotaxane features close contacts between both macrocycle hydroquinone rings and the thread’s pyridinium group [centroid ··· centroid: 3.499(2), 3.623(3) Å]. Increasing the size of the halide anion is correlated with a reduction in the strength of these interactions, with **16**·Br·**18** having one moderately close hydroquinone ··· pyridinium contact, and another much weaker one [centroid ··· centroid: 3.546(3), 3.889(3) Å]. When the largest halide anion iodide is used, there is only one weak hydroquinone ··· pyridinium contact [centroid ··· centroid: 3.6123(14) Å], with the other hydroquinone group further away (centroid ··· centroid > 4 Å). These reduced donor–acceptor interactions appear to be due to the larger halide anions forcing the two components further apart. Additional evidence is provided by the distances between the macrocycle’s interior phenylene carbon atom and thread’s *para*-pyridinium carbon atom, which increase from 6.26 to 7.03 to 7.25 Å for the structures containing Cl[−], Br[−] and I[−], respectively. This causes the thread to sit too “low” in the macrocycle (*i.e.* too close to the polyether chain) to allow optimal donor–acceptor interactions.

The different positions of the threading components in the macrocycle, caused by anion size, also appear to affect the pyridinium ··· polyether hydrogen bonding interactions. The chloride structure contains one such hydrogen bond (%VdW_{H,O} = 92), while the bromide and iodide structures contain two, although in each case one of these is very weak (%VdW_{H,O} = 94 and 98 in both structures). Hence, it appears that not only do the larger, less basic halides form weaker hydrogen bonds with the macrocycle and thread,

the interpenetrated components also undergo less favourable “secondary” interactions, explaining the observed weaker solution pseudorotaxane formation.

In the structure of **16**·NO₃·**18** (Figure 3.13), the nitrate anion is disordered over two positions *via* a rotation about one N–O bond, with each position having an occupancy of one half. Moderately strong hydrogen bonds are formed between the macrocycle’s amide groups and anion ($\%VdW_{H,O} = 87$), while the analogous interaction with the central phenylene proton is particularly strong ($\%VdW_{H,O} = 82$). Hydrogen bonds involving the threading component are weaker ($\%VdW_{H,O} > 88$), and, as was the case for the halide templated structures, only one triazole proton is involved in a significant interaction with the anion.

As expected based on the structures of the halide anion templated pseudorotaxanes, the large nitrate anion results in relatively weak donor–acceptor interactions, and these only involve one hydroquinone ring [centroid··centroid: 3.5863(11) Å]. Additionally, only one very weak pyridinium-methyl··ether hydrogen bond is present ($\%VdW_{H,O} = 97$).

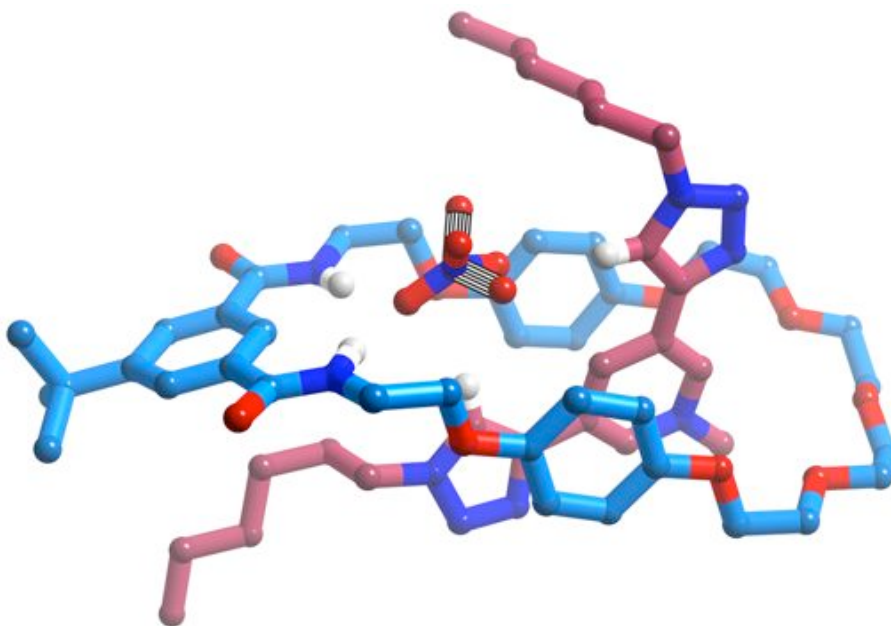


Figure 3.13: Structure of **16**·NO₃·**18** in the crystal. Both positions of the disordered nitrate anion are shown. Most hydrogen atoms are omitted for clarity.

3.3.1.1 Structure of 18·Cl·20

To allow direct comparison with the structure of previously reported pseudorotaxane **19·Cl·20**,²³² crystals of **18·Cl·20** were grown. Both structures contain no solvent of crystallization, and crystallize in the triclinic spacegroup $P\bar{1}$. The structures of this interpenetrated assembly (containing no *t*butyl group) and **16·Cl·18** (containing a *t*butyl group) are compared in Figure 3.14.

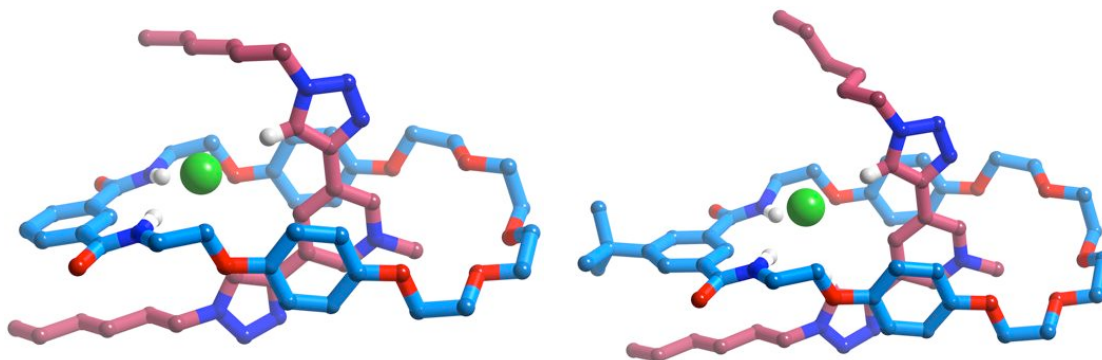


Figure 3.14: Structures of **18·Cl·20** (left) and **16·Cl·18** (right). Most hydrogen atoms are omitted for clarity.

The solid state structures are almost identical, hence in this case, the electron donating *t*butyl group has no significant effect on solid state pseudorotaxane structure. In fact, essentially all non-covalent interactions are indistinguishable with %VdW_{D,X} and %VdW_{H,X} within 1% for all hydrogen bonds, and donor–acceptor distances differing by less than 1% (these data are tabulated along with the analogous amide pseudorotaxanes in Table 3.7 in the following Section). The only slight difference is the hydrogen bond involving the macrocycle’s phenylene proton, which is significantly more linear in **18·Cl·20** than in *t*butyl containing **16·Cl·18** (158 *vs.* 142°, respectively), making the %VdW_{H,Cl} shorter (91 and 94, respectively).

3.3.2 X-ray crystal structures of amide pseudorotaxanes

3.3.2.1 Structures of 16·Cl·19 and 19·Cl·20

Single crystals of the all-amide pseudorotaxane **16·Cl·19** incorporating *t*butyl-substituted macrocycle **16** were obtained and the resulting structure compared with the previously reported structure of **19·Cl·20**²³² (containing no *t*butyl functionality, Figure 3.15).

The literature structure²³² crystallizes in the triclinic spacegroup, $P\bar{1}$ and contains no co-crystallized solvent molecules, while the structure of **16**·Cl·**19** crystallizes in the monoclinic spacegroup $P2_1/c$, and contains a half-occupancy diethyl ether solvate.

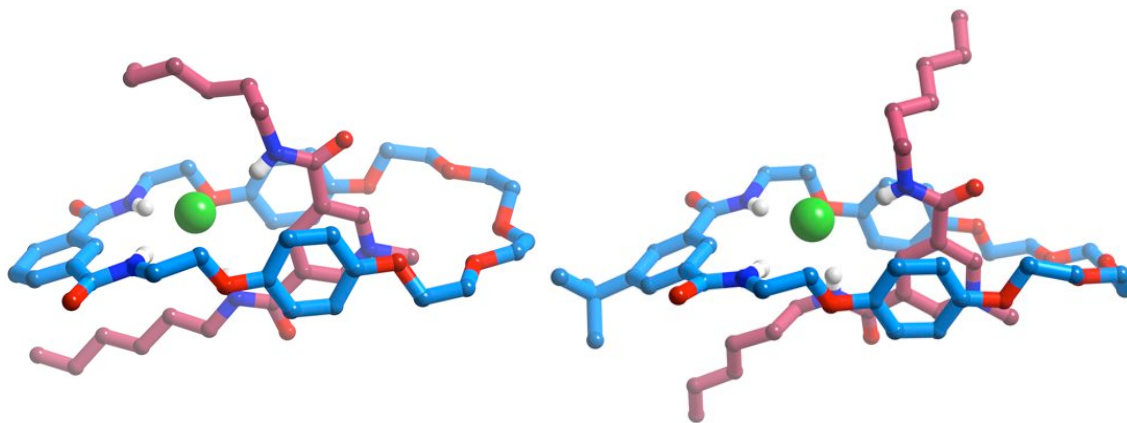


Figure 3.15: Solid state structures of **20**·Cl·**19**²³² (left) and **16**·Cl·**19** (right). Diethyl ether solvate and most hydrogen atoms are omitted for clarity.

In contrast to the triazole containing analogues of these structures (Section 3.3.1), there *are* significant differences between the solid state hydrogen bonding interactions in these two pseudorotaxanes. Interestingly, all hydrogen bonding interactions involving the *t*butyl-substituted macrocycle are slightly weaker than those involving the unsubstituted cycle (Table 3.7). Conversely, the threading component in **16**·Cl·**19** forms shorter hydrogen bonds than the thread in **19**·Cl·**20**. Pyridinium···hydroquinone donor–acceptor interactions and pyridinium-methyl···polyether hydrogen bonds are of similar magnitudes in each pseudorotaxane. Longer solid state hydrogen bonds involving **16** are perhaps unsurprising given its more electron rich nature, although it is noteworthy that a similar effect was not observed in the structures of the triazole containing analogues of these pseudorotaxanes.

3.3.2.2 Structures of **16**·I·**19** and **16**·NO₃·**19**

The single crystal structures of **16**·I·**19** and **16**·NO₃·**19** are shown in Figure 3.16. Hydrogen bonding distances in the iodide pseudorotaxane are relatively long, particularly between the macrocycle and anion ($\%VdW_{H,X} \geq 97$). Donor–acceptor interactions and

Table 3.7: Non-covalent interactions in solid state structures of chloride templated pseudorotaxanes.^a

	19·Cl·20 ²³²	16·Cl·19	18·Cl·20	16·Cl·18
<i>Receptor ··· anion hydrogen bonding</i>				
<i>Macrocycle</i>				
%VdW _{H_{amide},X}	90	91	86	86
%VdW _{H_{amide},X}	91	94	89	88
%VdW _{H_{phenylene},X}	92	95	91	94
<i>Threading component</i>				
%VdW _{H_{triazole/amide},X}	88	86	90	89
%VdW _{H_{triazole/amide},X}	92	89	97	98
%VdW _{H_{pyridinium},X}	88	90	94	95
<i>Pyridinium ··· hydroquinone donor–acceptor interactions</i>				
centroid ··· centroid	3.540	3.6072(11)	3.4881(11)	3.499(2)
centroid ··· centroid	3.695	3.6282(11)	3.6349(11)	3.623(3)
<i>Pyridinium-methyl ··· polyether hydrogen bonding</i>				
%VdW _{H_{methyl},O}	96	97	92	92
%VdW _{H_{methyl},O}	98	—	—	—

^aDistances in Å, estimated standard uncertainties in parentheses.

pyridinium-methyl···polyether chain hydrogen bonds are also weak. Details of non-covalent interactions for all pseudorotaxanes incorporating **16** and **19** are displayed in Table 3.8.

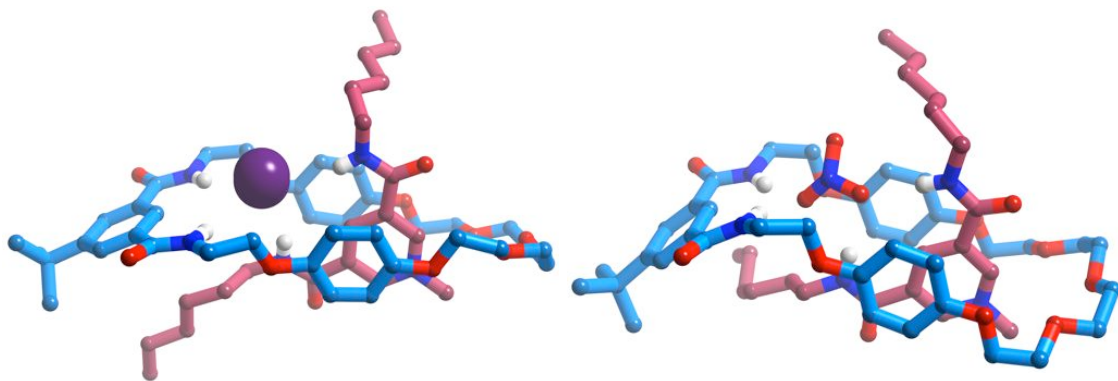


Figure 3.16: Solid state structures of **16·I·19** and **16·NO₃·19**. Diethyl ether solvates and most hydrogen atoms are omitted for clarity. Only one of the two independent complexes in the asymmetric unit cell of **16·NO₃·19** is shown.

There are two independent complexes present in the asymmetric unit of the structure of **16·NO₃·19**, and these have markedly different hydrogen bonding interactions with the anion. Notably, one complex has four very strong hydrogen bonds between amide and triazole groups and the nitrate anion (%VdW_{H₂O} = 79–83) with negligible

hydrogen bonding involving the phenylene and *para*-pyridinium protons. The other has generally weaker hydrogen bonds except for a strong $H_{\text{pyridinium}} \cdots \text{NO}_3$ interaction. No donor–acceptor close contacts are present in either complex, with one pyridinium-methyl $\cdots$ polyether hydrogen bond in each case.

Table 3.8: Non-covalent interactions in solid state structures of pseudorotaxanes **16·X·19**.^a

	16·Cl·19	16·I·19	16·NO₃·19^b	16·NO₃·19^b	16·OAc·19^b	16·OAc·19^b	16·BzO·19
<i>Receptor $\cdots$ anion hydrogen bonding</i>							
<i>Macrocycle</i>							
%VdW _{H_{amide},X}	91	97	87	83	79	81	80
%VdW _{H_{amide},X}	94	101	92	82	97	93	90
%VdW _{H_{phenylene},X}	95	101	100	98	89	87	92
<i>Threading component</i>							
%VdW _{H_{amide},X}	86	92	82	79	82	82	83
%VdW _{H_{amide},X}	89	95	94	79	92	83	85
%VdW _{H_{pyridinium},X}	90	99	83	102	81	79	77
<i>Pyridinium $\cdots$ hydroquinone donor–acceptor interactions</i>							
centroid $\cdots$ centroid	3.6072(11)	3.701(6)	—	—	—	—	—
centroid $\cdots$ centroid	3.6282(11)	3.915(6)	—	—	—	—	—
<i>Pyridinium-methyl $\cdots$ polyether hydrogen bonding</i>							
%VdW _{H_{methyl},O}	97	98	93	90	—	—	95
%VdW _{H_{methyl},O}	—	99	—	—	—	—	—

^aDistances in Å, estimated standard uncertainties in parentheses. ^bThese structures have a Z' of 2.

3.3.2.3 Structures of **16·OAc·19** and **16·BzO·19**

The structures of the oxoanion templated pseudorotaxanes **16·OAc·19** and **16·BzO·19** are shown in Figure 3.17. It is notable that the large anion benzoate causes a buckling of the macrocycle with the isophthalamide ring twisting substantially out of the plane of the rest of the cycle. As shown in Table 3.8, strong hydrogen bonds are present in both these complexes, as would be expected with these basic oxoanions. As with the nitrate templated pseudorotaxane, no donor–acceptor interactions are present, as the large carboxylate motif pushes the threading component too “low” in the macrocycle for these to occur. Because of this the methyl-pyridinium group has to twist out of the plane of the polyether chain, meaning pyridinium-methyl $\cdots$ polyether hydrogen bonds are either weak (BzO[−]) or absent completely (OAc[−]).

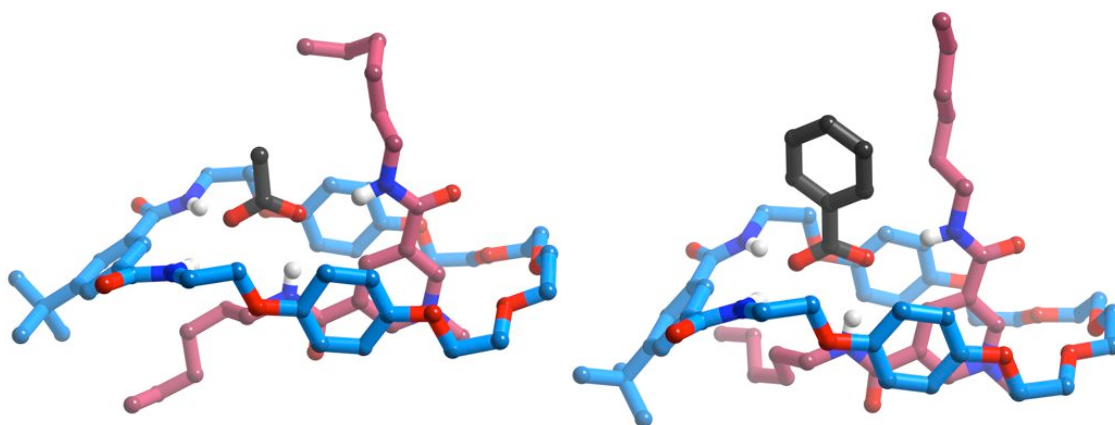


Figure 3.17: Solid state structures of **16·OAc·19** and **16·BzO·19**. Most hydrogen atoms are omitted for clarity. Only one of the two independent complexes in the asymmetric unit cell of **16·OAc·19** is shown.

3.3.3 Combined analysis of the non-covalent interactions in solid state structures of pseudorotaxanes

3.3.3.1 Receptor ··· anion hydrogen bonding

To obtain a very crude approximation of the relative contributions of the thread and macrocycle's hydrogen bonding to the pseudorotaxane assembly, the three %VdW_{H,X} values for the threading component and the three values for the macrocycle in each structure were averaged to give parameters %VdW_{mean,macrocycle} and %VdW_{mean,thread} (when %VdW_{H,X} was greater than 100%, a value of 100 was used, so as not to skew the data). These values are displayed in Table 3.9 for structures containing triazole and amide containing threading components.

While these numbers offer only an approximate description of the hydrogen bonding interactions, two clear trends are apparent. Firstly, acetate and benzoate have the lowest %VdW_{mean} values followed by nitrate, then chloride and bromide, with iodide anion forming the longest hydrogen bonds. This follows anion basicity trends, and also correlates well with solution binding data (with the exception of **19·Cl·20**, see Section 3.2.2).

Importantly, there is a very clear distinction between the triazole containing and amide containing pseudorotaxanes: in all structures containing amide thread **19**⁺, hydrogen bonding is much stronger between the thread and the anion, than between the macrocycle and the anion (mean %VdW_{thread} = 87, mean %VdW_{macrocycle} = 92). This is perhaps

Table 3.9: Summary of hydrogen bonding interactions in solid state pseudorotaxane structures.^a

Anion	18 ⁺ %VdW	18 ⁺ %VdW	19 ⁺ %VdW	19 ⁺ %VdW
	mean,macrocycle	mean,thread	mean,macrocycle	mean,thread
Cl ^{-b}	89 ^b	94 ^b	94 ^b	89 ^b
Cl ⁻	89	94	93	88
Br ⁻	96	98	—	—
I ⁻	99	99	99	95
NO ₃ ⁻	85 ^c	95 ^c	93 ^d	86 ^d
NO ₃ ⁻	85 ^c	94 ^c	88 ^d	86 ^d
OAc ⁻	—	—	88 ^d	85 ^d
OAc ⁻	—	—	87 ^d	81 ^d
BzO ⁻	—	—	87	82

^aObtained by averaging the %VdW_{H,X} values for the three donors in the macrocycle (phenylene and two amide groups), or the three donors in the threading component (*para*-pyridinium and two triazole or amide groups). ^bThese structures incorporate macrocycle **20**; all other structures contain **16**. ^cThe two sets of values correspond to the two positions of the disordered nitrate anion. ^dThe two sets of values correspond to the two independent complexes in the asymmetric unit cell.

not surprising when considering the far greater anion affinity of **19**⁺ compared with **16** (chloride anion association in d₆-acetone: $K_{a(19)} > 10^5 \text{ M}^{-1}$,³⁵² $K_{a(16)} = 2560 \text{ M}^{-1}$).³⁰² However, in pseudorotaxanes incorporating triazole thread **18**⁺ this is not the case, with shorter hydrogen bonds between anion and macrocycle than between anion and thread (Mean %VdW_{thread} = 96, mean %VdW_{macrocycle} = 91). This is surprising as cationic thread **18**⁺ similarly appears to be a superior anion complexant to neutral macrocycle **16** (chloride anion association in d₆-acetone: $K_{a(18)} > 10^4 \text{ M}^{-1}$; $K_{a(16)} = 2560 \text{ M}^{-1}$).³⁰² The same trends are also apparent when %VdW_{D,A} is considered instead of %VdW_{H,A}.

3.3.3.2 Donor–acceptor interactions

Increasing anion size greatly affects hydroquinone ··· pyridinium distances in both amide and triazole containing pseudorotaxane structures. The interweaved assemblies involving the larger halide anions, bromide and iodide, have much longer pyridinium ··· hydroquinone distances than those involving chloride anion, while significant donor–acceptor interactions are generally not observed in oxoanion templated pseudorotaxanes, due to the poor fit of these large anions.

Presumably a combination of weaker hydrogen bonding and reduced donor–acceptor interactions are responsible for the lower pseudorotaxane stabilities observed in solution

using bromide and iodide anion templation than when chloride is used. Interestingly, the nitrate anion templated pseudorotaxanes have approximately the same solution stability as those templated by chloride. While solid state %VdW hydrogen bonding values are much shorter for the nitrate templated pseudorotaxanes, the donor–acceptor interactions in these complexes are much weaker, with the combination of these factors perhaps offering some explanation of the strength of association in solution.

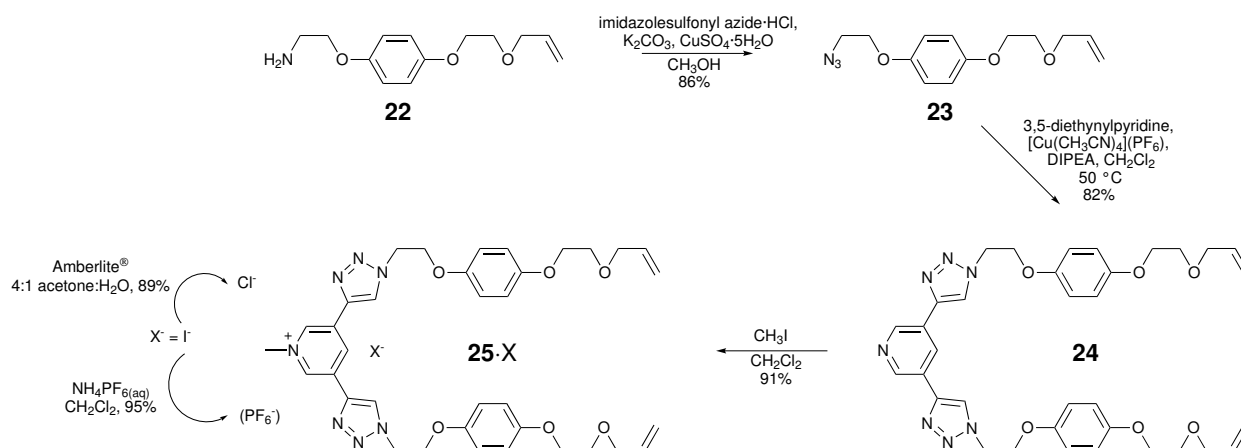
3.3.3.3 Pyridinium-methyl···polyether hydrogen bonding

There appears to be no obvious link between anion size and pyridinium-methyl···polyether hydrogen bonding. For example, the strongest of these interactions occur in the structure of **16**·NO₃·**19**, but the triazole analogue contains only very weak interactions.

3.4 A catenane host system incorporating triazole donors

3.4.1 Catenane synthesis

The strong pseudorotaxane formation between **18**·Cl and isophthalamide macrocycles **16** and **20** (Section 3.2.1) suggests that the pyridinium bis-triazole motif is a promising candidate for the synthesis of interlocked anion hosts. To investigate this, a vinyl-appended macrocycle precursor incorporating this motif was targeted for subsequent clipping catenane synthesis (Scheme 3.3).

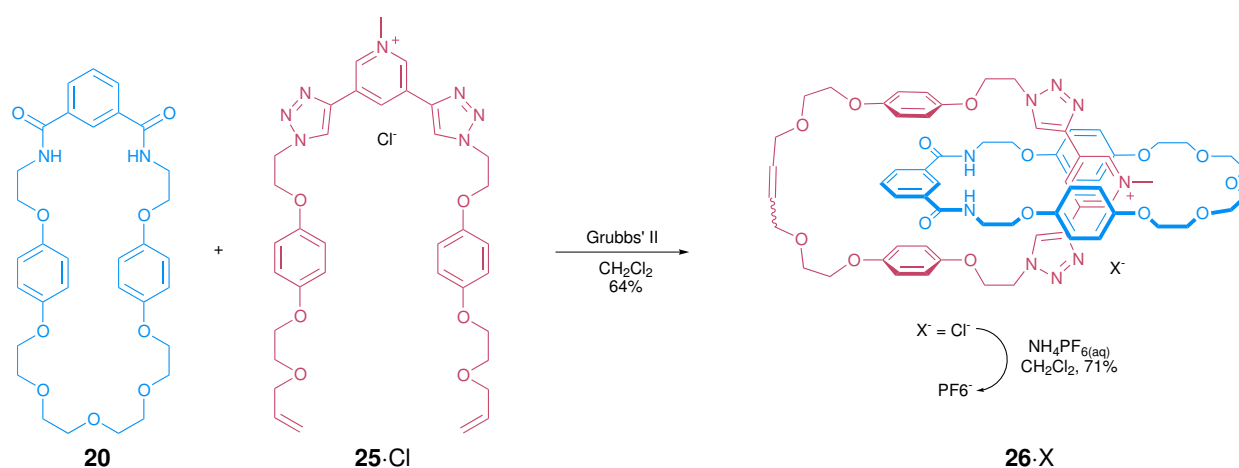


Scheme 3.3: Synthesis of macrocycle precursor **25**·X.

Known vinyl-appended amine **22** was prepared in 36% yield over four steps, as previously described,²³⁴ and converted to the azide **23** using imidazolesulfonyl azide·HCl, potassium carbonate and catalytic copper(II) sulfate in methanol. The CuAAC reaction of 2.2 equivalents of **23** with one equivalent of 3,5-diethynylpyridine was initially attempted in dichloromethane using [Cu(CH₃CN)₄](PF₆) TBTA and DIPEA. The TBTA ligand proved impossible to separate from the product, and so the reaction was instead conducted without this ligand at 50 °C. This gave pyridine precursor **24** in good yield (82%) after purification by column chromatography. Alkylation using excess methyl iodide in dry dichloromethane at room temperature gave pyridinium bis-triazole precursor **25·I** as a yellow powder in excellent yield (91%). Anion exchange to the hexafluorophosphate salt was achieved by repeatedly washing a dichloromethane solution of the iodide salt with aqueous ammonium hexafluorophosphate. Attempting to prepare the chloride salt in this manner was unsuccessful, due to the low solubility of **25·Cl** in dichloromethane; instead, the iodide salt of **25**⁺ was passed down a chloride-loaded Amberlite® resin column in 4:1 acetone:water to give **25·Cl** in 89% yield.

Chloride anion templated Grubbs' II-catalyzed ring closing metathesis of 1.2 equivalents of **25·Cl** and one equivalent of **20** in dry dichloromethane gave novel catenane **26·Cl** in 64% yield after purification by preparative TLC (Scheme 3.4). This yield is notably higher than that reported for the analogous all-amide catenane (45%),²³⁴ as would be predicted based on the more stable chloride anion templated pseudorotaxane assemblies formed between isophthalamide macrocycles and pyridinium bis-triazole than those with the corresponding pyridinium bis-amide threads. Anion exchange to the hexafluorophosphate salt was again achieved by repeatedly washing a dichloromethane solution of **26·Cl** with aqueous ammonium hexafluorophosphate.

The effect of varying the number of equivalents of vinyl-appended precursor, as well as the identity of the templating anion on the yield of catenane formation was investigated. Small-scale reactions were conducted, and the reaction mixture analysed by ¹H NMR spectroscopy, with approximate yields of [2]catenane being determined by integration of the crude spectra. As shown in Table 3.10, the presence of a halide anion plays a critical role in catenane formation, with negligible catenane formation when **25·PF₆** is



Scheme 3.4: Synthesis of catenane **26·Cl**.

used. Significant amounts of catenane are formed when iodide is used as the templating anion, although the yield is substantially lower than when chloride is used. Interestingly, the number of equivalents of vinyl precursor has almost no effect on the yield of catenane, possibly due to competing formation of oligomeric products when a large excess of **25·Cl** is present.

Table 3.10: Yields of catenane formation for different templating anions and number of equivalents of **25⁺**.

Macrocycle Precursor	Equivalents	Approximate conversion of 20 to catenane ^a	Isolated yield
25·PF₆	1.0	< 5%	—
25·I	1.0	35%	—
25·Cl	1.0	73%	—
25·Cl	1.2	72%	64%
25·Cl	1.5	72%	—
25·Cl	3.0	65%	61%

^aEstimated based on integration of ¹H NMR spectra of crude reaction mixture.

Catenane **26⁺** was characterized by ¹H, ¹³C, ¹⁹F and ³¹P NMR spectroscopy as well as by high resolution ESI mass spectrometry and single crystal X-ray crystallography (Section 3.4.3). As shown in Figure 3.18, dramatic changes in the proton NMR spectrum are observed upon anion exchange, with replacement of the hexafluorophosphate anion with chloride causing large downfield shifts in the catenane's cavity protons *c*, *d*, *g* and

4 as well as in the exterior pyridinium protons 2. An upfield movement of the neutral macrocycle's hydroquinone protons 5 and 6, and a downfield shift of pyridinium-methyl resonance *a* suggest that chloride association strengthens donor-acceptor interactions between hydroquinone and pyridinium rings, and hydrogen bonding interactions between the pyridinium methyl group and macrocycle polyether chain, possibly by “locking” the catenane in a co-conformation that facilitates these interactions.

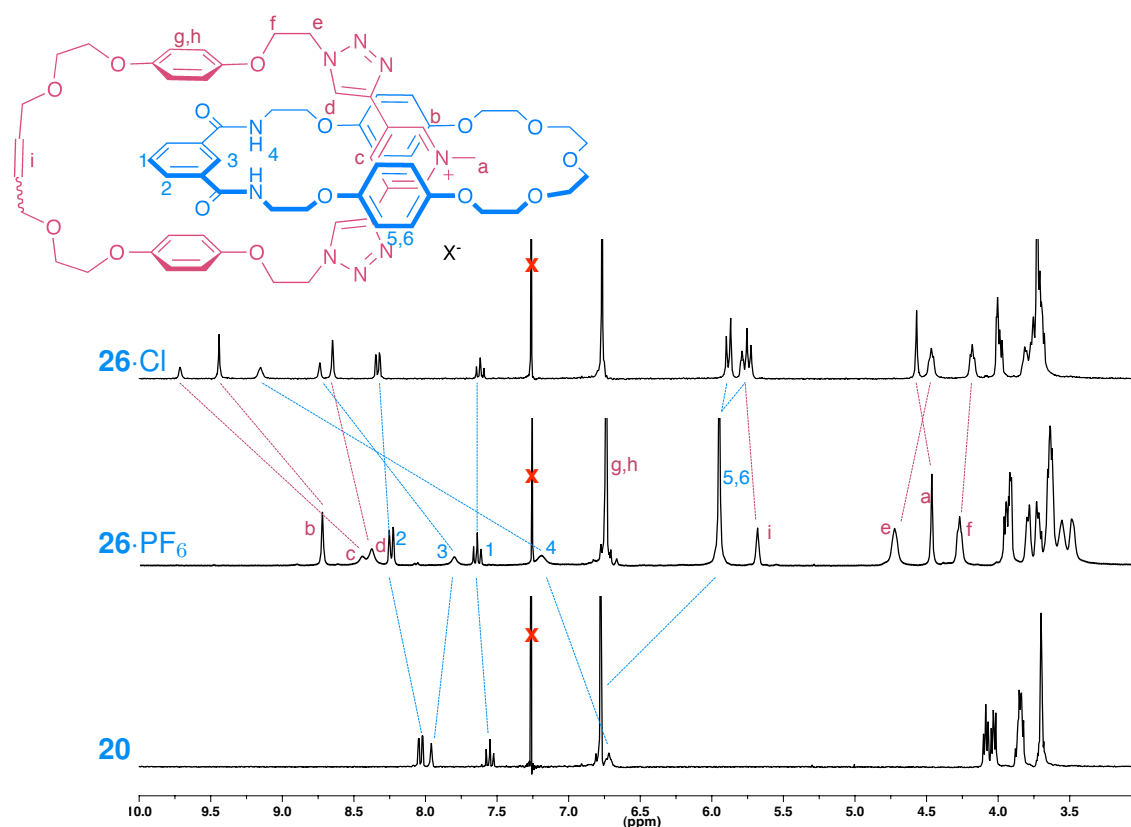


Figure 3.18: Truncated ¹H NMR spectra of **20**, **26**·PF₆ and **26**·Cl (CDCl₃, 293 K, 300 MHz).

Further proof of the interlocked nature of **26**·Cl was provided by 2D ROESY NMR spectroscopy (Figure 3.19), with several inter-component couplings observed between cavity protons and hydroquinone rings.

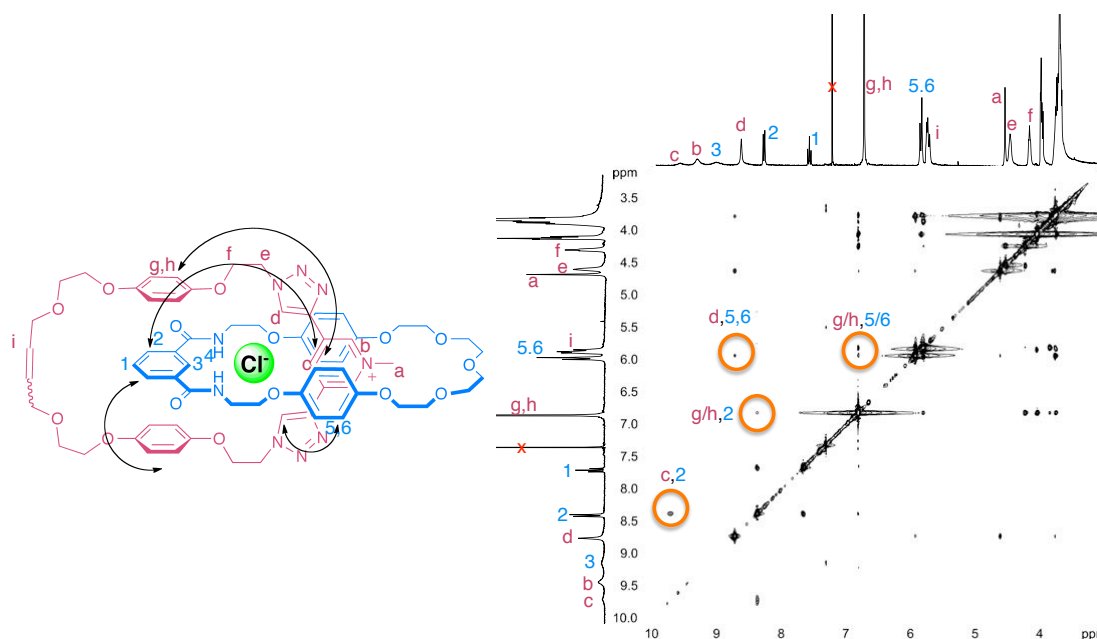


Figure 3.19: Truncated 2D ROESY NMR spectrum of **26**·Cl showing selected inter-component couplings (293 K, CDCl₃, 500 MHz).

3.4.2 Anion recognition properties of **26**·PF₆

Anion binding studies of **26**·PF₆ were conducted in the competitive solvent mixture 1:1 CDCl₃:CD₃OD, and stoichiometric 1:1 association constants were calculated using WINEQNMR2,³²⁸ monitoring the triazole proton resonance (Table 3.11, Figure 3.21). The strength of chloride anion recognition by new catenane **26**·PF₆ is approximately the same as the previously reported amide analogue **27**·PF₆ (Figure 3.20).²³⁴ This is perhaps surprising given the much greater anion affinity of pyridinium bis-amide threading component **19**⁺ than pyridinium bis-triazole **18**⁺, and demonstrates the crucial role of the three-dimensional cavity in the interlocked molecule, with host recognition properties dependent on more than simply the individual components.

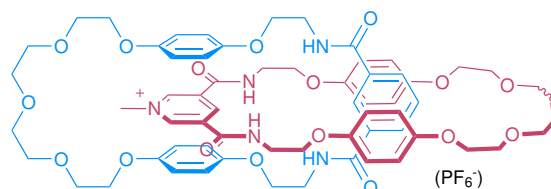


Figure 3.20: **27**·PF₆, the previously reported all-amide analogue of **26**⁺.²³⁴

Table 3.11: Association constants, K_a (M^{-1})^a for anions with all-amide and triazole containing catenanes

Anion	Triazole catenane 26 ·PF ₆	Amide catenane 27 ·PF ₆ ²³⁴
Cl ⁻	679(20)	730
Br ⁻	632(45)	—
I ⁻	509(10)	—
H ₂ PO ₄ ⁻	49(4)	$K_1 = 480, K_2 = 530$

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K).

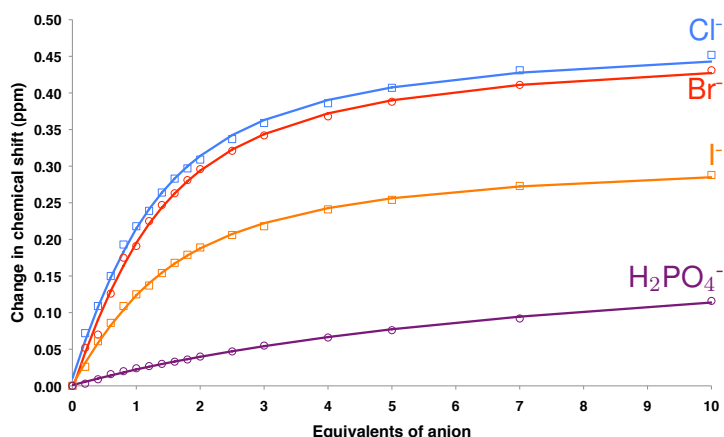


Figure 3.21: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **26**·PF₆ monitoring the triazole resonance (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

As previously discussed, macrocycles incorporating triazole groups have a wider, squatter shape than their amide analogues (Chapter Two), and this will affect the volume of the interlocked cavity. Rebek has demonstrated the crucial role that host cavity/guest size-matching has on a receptor's affinity for a guest,³⁶⁷ as would be expected when considering preorganization effects. Obtaining a reliable estimate of the cavity volume of the hosts in solution would require modelling experiments beyond the scope of this project, but it is important to note that cavity volume, as well as the nature of the anion binding motifs within this cavity will have a large effect on recognition properties.

All halides are bound strongly in this competitive solvent mixture, with the decreased basicity of the larger halides presumably compensated by their relatively smaller energies of solvation. Impressively, significant discrimination between the halides and basic dihydrogen phosphate is observed for **26**·PF₆, with chloride being complexed more than an order of magnitude more strongly than the oxoanion, whereas amide catenane **27**·PF₆

shows only a modest preference between chloride and dihydrogen phosphate. This demonstrates that incorporating triazole donors into the structural framework has a significant and beneficial effect on the anion discrimination properties of the interlocked host. Addition of other oxoanions (acetate, benzoate, nitrate) to the rotaxane caused very minor shifts in the triazole proton resonance (0.02–0.04 ppm after one equivalent of anion), and so quantitative association constants could not be determined for these anions.

3.4.3 X-ray crystal structures of **26**·X

Single crystals of **26**·Cl, **26**·Br and **26**·I suitable for X-ray diffraction studies were obtained by slow vapour diffusion methods. The structure of **26**·Cl in the crystal is shown in Figure 3.22: hydrogen bonds are observed between the chloride anion and amide, triazole and phenylene donors. In addition, aromatic donor–acceptor interactions are seen between electron-rich hydroquinone rings and the electron-deficient pyridinium group, as well as hydrogen bonding between the pyridinium-methyl group and polyether chain of the macrocycle. Details of non-covalent interactions for **26**·Cl, **26**·Br and **26**·I are given in Table 3.12.

The bromide salt of **26**⁺ crystallizes with two catenanes in the asymmetric unit of the crystal; only one of these is shown in Figure 3.23. In both of the two independent catenanes, one hydroquinone ring is involved in donor ··· acceptor interactions with the pyridinium motif, with the other electron-rich group further away (centroid ··· centroid distance > 4.0 Å).

Crystals of **26**·I were obtained from the NMR titration experiment sample containing one equivalent of **26**·PF₆ and a large excess of TBA·I. Crystals were extremely small and weakly-diffracting and required the use of synchrotron radiation to obtain diffraction data. The asymmetric unit of the crystal contains one catenane encapsulating one iodide anion, as well as a chloroform solvate, a TBA cation, and another anion located over two positions. For clarity, only the catenane and the encapsulated full-occupancy iodide anion are shown in Figure 3.24.

Hydrogen bond lengths generally increase for the larger, less basic halide anions (Table 3.12), and hydrogen bonds are generally longer for the pyridinium bis-triazole

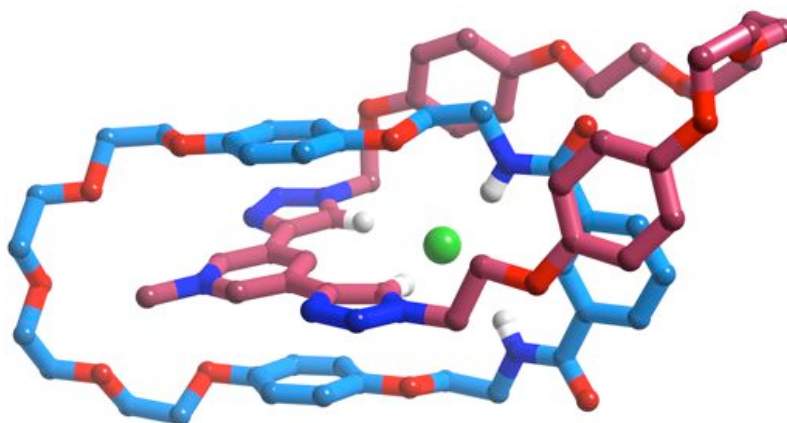


Figure 3.22: Structure of **26**·Cl in the crystal. Diethyl ether solvate, minor position of polyether disorder and most hydrogen atoms are omitted for clarity.

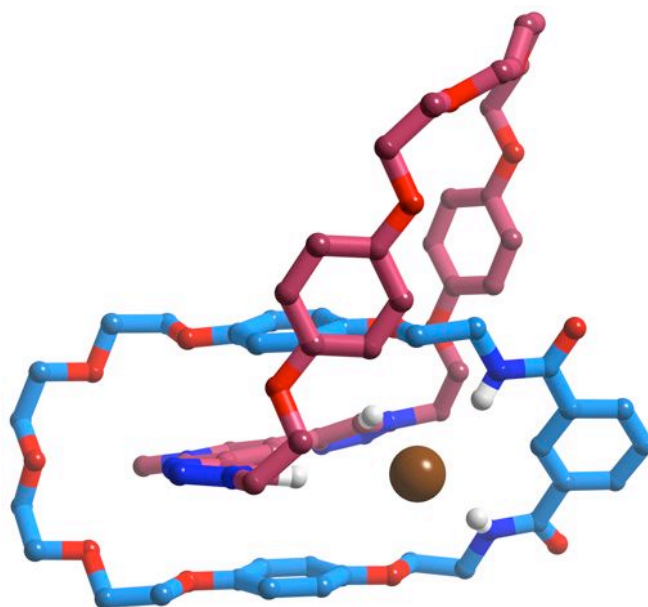


Figure 3.23: Structure of **26**·Br in the crystal. Methanol solvate, minor position of polyether disorder and most hydrogen atoms are omitted for clarity.

macrocycle than for the isophthalamide macrocycle, despite the positive charge of the former component. This is similar to the hydrogen bonding interactions seen in the pseudorotaxane analogues of these structures (Section 3.3.1). In the solid state structure of the amide analogue of this catenane **27**·Cl, the reverse is true with hydrogen bonds involving the cationic pyridinium containing macrocycle significantly shorter than those involving the isophthalamide macrocycle.²³⁴

Increasing anion size causes a change in the solid state co-conformation of **26**⁺ (Figure 3.25), with larger halides forcing the pyridinium group away from the

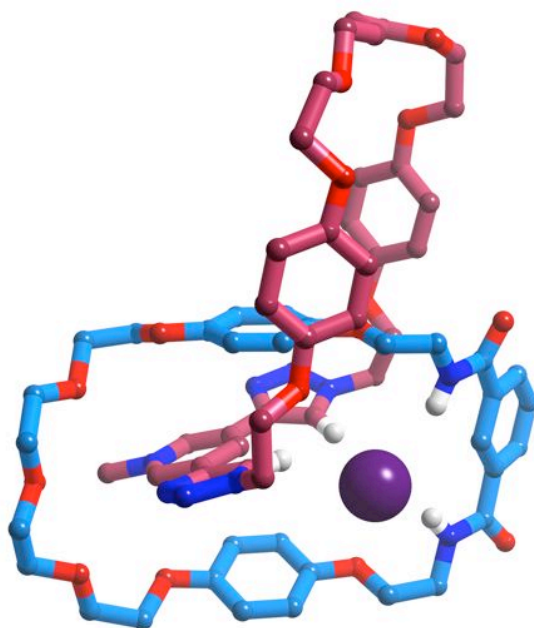


Figure 3.24: Structure of **26**·I in the crystal. Most hydrogen atoms, chloroform solvate, TBA cation and disordered I^-/I_3^- anion omitted for clarity.

isophthalamide motif and causing it to rotate out of the plane of the polyether chain. This also affects the pyridinium $\cdots$ hydroquinone interactions (Table 3.12): in the chloride salt, two short contacts are present, while in both crystallized co-conformers of the bromide salt, only one hydroquinone ring is involved in such an interaction, and in the iodide salt there are no pyridinium $\cdots$ hydroquinone close contacts. This trend is similar to that observed in the solid state structures of the related pseudorotaxane assemblies **18**·X·**20** (Section 3.3.1), and illustrates the significant effect that small changes in anion volume have on host co-conformation.

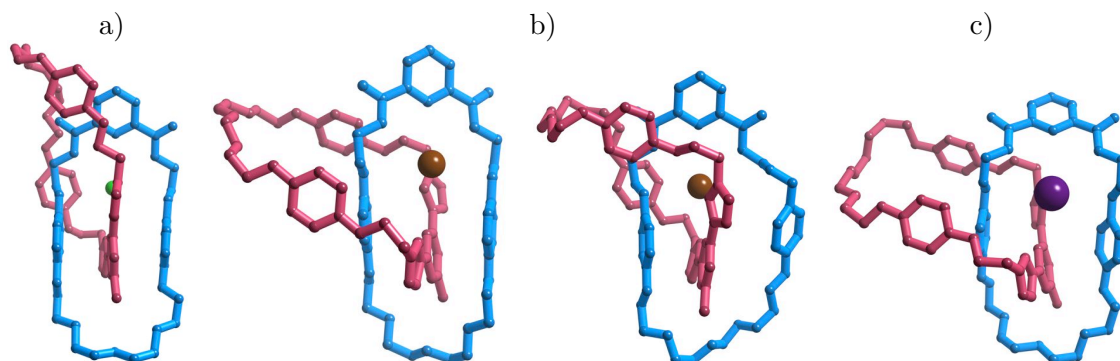


Figure 3.25: Comparison of the solid state co-conformations of **26**⁺, as a) the chloride salt; b) the two independent bromide salts in the asymmetric unit, and c) the iodide salt.

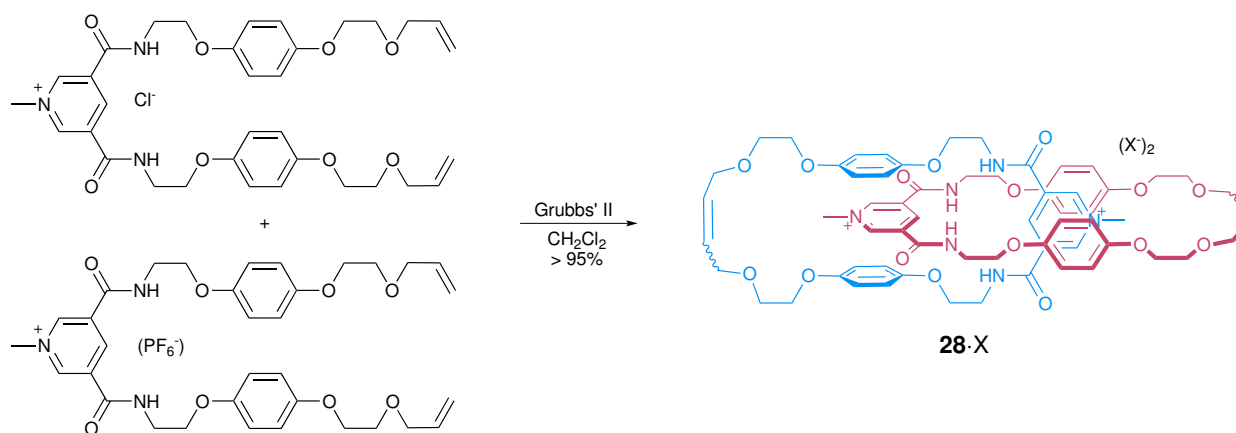
Table 3.12: Non-covalent interactions in solid state structures of **26**-halides.^a

	Cl ⁻	Br ⁻ ^b	Br ⁻ ^{b,c}	I ⁻
<i>Receptor ··· anion hydrogen bonding</i>				
<i>Isophthalamide macrocycle</i>				
%VdW _{H_{amide},X}	90	88	85	94
%VdW _{H_{amide},X}	94	94	100	99
%VdW _{H_{phenylene},X}	93	95	95	102
<i>Pyridinium bis-triazole macrocycle</i>				
%VdW _{H_{triazole},X}	92	96	93	101
%VdW _{H_{triazole},X}	95	121	99	102
%VdW _{H_{pyridinium},X}	95	110	96	106
<i>Pyridinium ··· hydroquinone donor-acceptor interactions</i>				
centroid ··· centroid	3.526(2)	3.645(2)	3.641(3)	—
centroid ··· centroid	3.574(2)	—	—	—
<i>Pyridinium-methyl ··· polyether hydrogen bonding</i>				
%VdW _{H_{methyl},O}	89	92	96	96
%VdW _{H_{methyl},O}	96	—	—	—

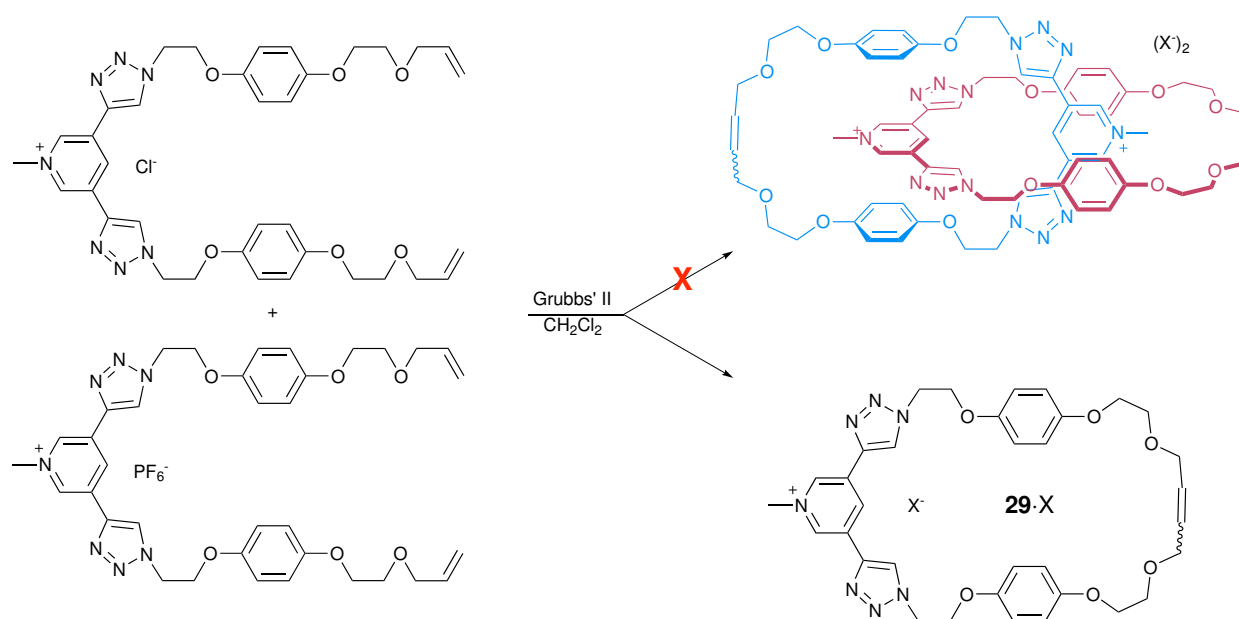
^aDistances in Å, estimated standard uncertainties in parentheses. ^bThis structure has a Z' of 2.^cMinor component of disordered polyether chain has not been included in this analysis.

3.4.4 Attempts to synthesize a catenane that binds anions solely through C–H ··· anion hydrogen bonds

The synthesis of dicationic pyridinium bis-amide *homo*-[2]catenanes in very high yields from bis-vinyl appended precursors has previously been reported (Scheme 3.5).^{368,369} The resulting doubly-charged catenanes are potent anion hosts, with receptor **28**·PF₆ binding chloride and sulfate in competitive 7:3 CD₃CN:D₂O solvent media.

Scheme 3.5: Synthesis of all-amide *homo*-catenane.³⁶⁹

Given the high yields of this catenation reaction, and the impressive anion recognition properties of the interlocked system, it was decided to attempt the synthesis of the analogous triazole containing catenane (Scheme 3.6), potentially the first example of an interlocked host system binding anions purely through C–H···anion interactions. The RCM reaction of one equivalent each of **25**·Cl and **25**·PF₆ in dichloromethane with Grubbs' II catalyst did not yield any evidence of catenane formation, however, with mass spectrometry and ¹H NMR of the crude reaction mixture showing macrocycle **29**⁺ as the only identifiable ring-closed product.



Scheme 3.6: Attempted synthesis of tetra-triazole *homo*-catenane.

The failure of this reaction may provide an explanation for the increased stability of pseudorotaxane **18**·Cl·**20** compared with **19**·Cl·**20**, and the higher yields of triazole containing catenane **26**⁺ than of the amide analogue **28**⁺. The very favourable association of two pyridinium bis-amide components around a chloride anion³⁶⁹ may lower yields of *hetero*-catenane formation, due to competing formation of the dicationic *homo*-catenane. It would also reduce observed pseudorotaxane stability, as **19**·Cl·**19** complexes form as well as interpenetrated assemblies (Figure 3.26). These competing processes are not observed for the pyridinium bis-triazole motif, possibly because its inherently lower anion binding affinity (Section 2.5.2) is not sufficient to overcome the mutual repulsion of the two cationic species, and thus catenane yield and pseudorotaxane stability are enhanced.

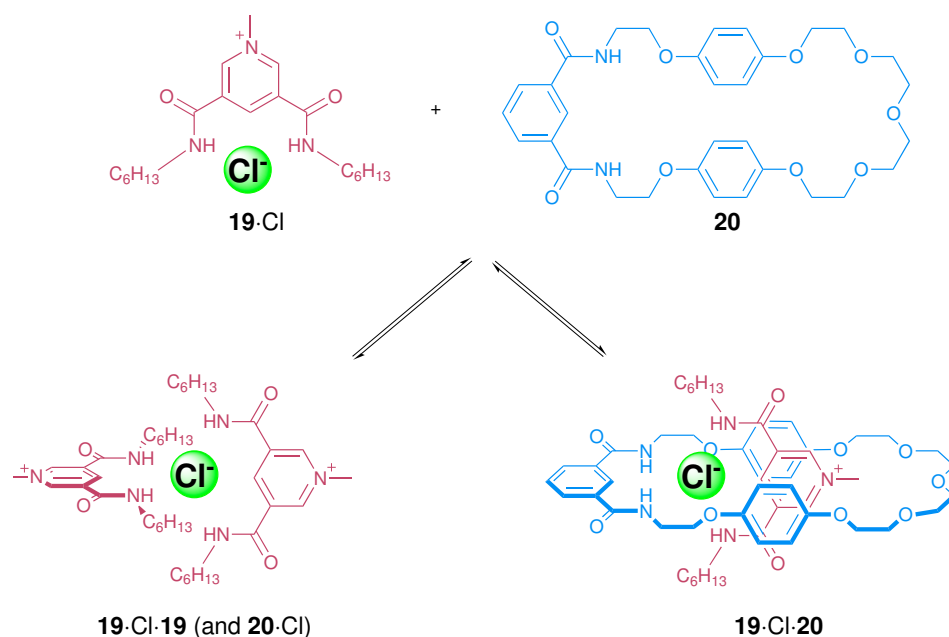


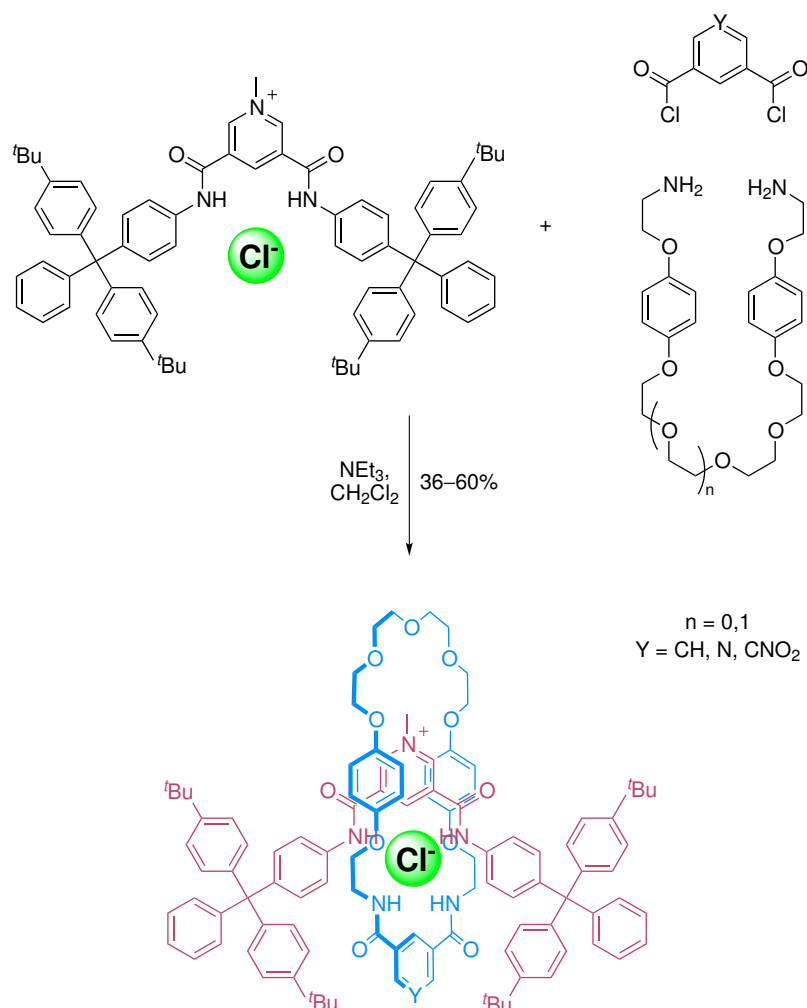
Figure 3.26: Postulated equilibria present in solutions of **19·Cl** and **20**.

3.5 A rotaxane host system incorporating triazole donors

3.5.1 Rotaxane synthesis *via* amide condensation

Catenane **26**· PF_6 displays an impressive ability to differentiate between halide and oxoanions, however, previously reported rotaxane anion receptors have shown stronger and more selective binding than catenane analogues.²³⁵ Therefore, it was decided to incorporate the same hydrogen bond donor set into a rotaxane structural framework, to see if the strength and selectivity of binding could be further improved by virtue of the enhanced rigidity of a rotaxane axle component containing aryl-substituted triazole donors.

It has been recently demonstrated that condensation of bis-amine **11** ($n = 1$ in Scheme 3.7) and an isophthaloyl chloride in the presence of a pyridinium containing axle component can lead to rotaxanes in high yields (Scheme 3.7).^{236,339} This synthetic route has been proven to be very versatile, as simply varying the bis-acid chloride component allows access to a range of rotaxanes, as was recently demonstrated by the preparation of eight closely-related rotaxane hosts using this method.²³⁶ This approach was therefore targeted as a convenient way to prepare pyridinium bis-triazole rotaxanes.

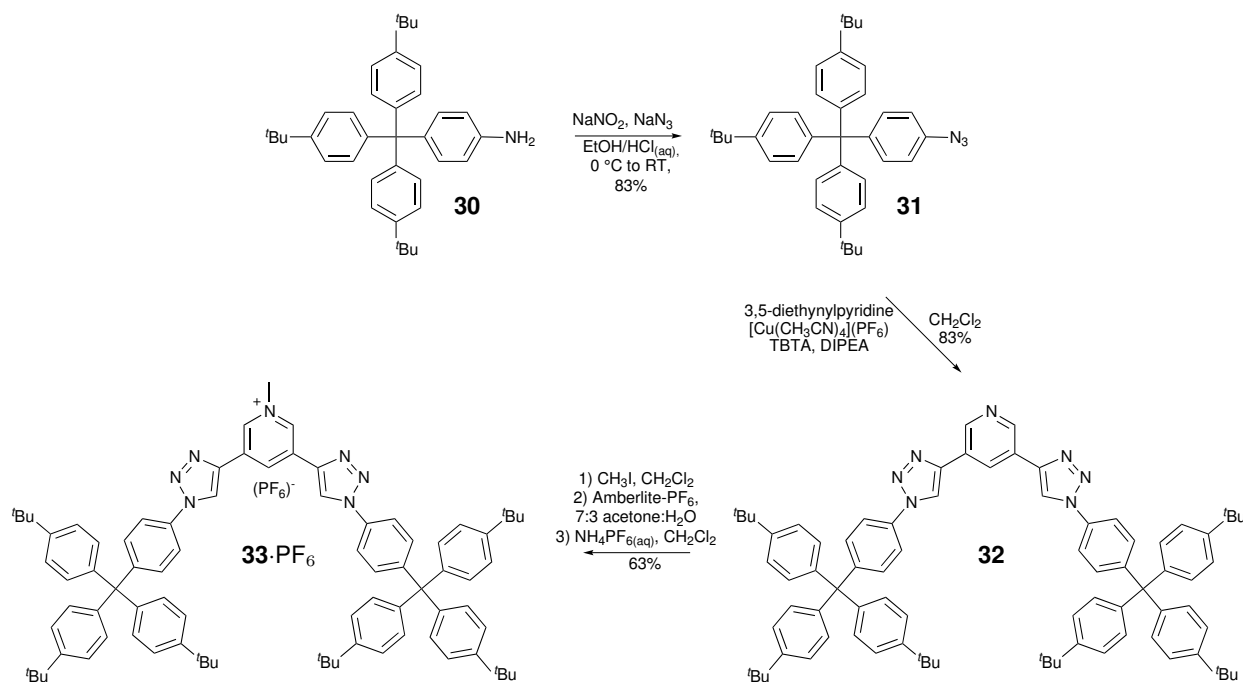


Scheme 3.7: Recently reported anion templated synthesis of rotaxanes by condensation of substituted isophthaloyl chloride and bis-amine.^{236,339}

3.5.1.1 Synthesis of axle component

The synthesis of an aryl-substituted pyridine bis-triazole axle component first required the preparation of an aryl azide-appended stopper. This was complicated by the low solvent compatibility of the large organic stopper and the sodium salts used to effect the amine to azide transformation. It was found however, that the aniline stopper **30** was very sparingly soluble in 9:1 ethanol:conc. $\text{HCl}_{(\text{aq})}$, and that this also dissolved the inorganic salts, so the reaction was conducted at low concentrations (4 mM) in this solvent mixture giving aryl azide **31** in good yield (83%). CuAAC reaction of **31** with 3,5-diethynyl pyridine in CH_2Cl_2 using $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$, TBTA and DIPEA as base gave the neutral axle component **32**, also in 83% yield. Alkylation of **32** was conducted using excess methyl

iodide in dry dichloromethane at room temperature to give sparingly soluble **33**·I. The low solubility of this compound necessitated anion exchange by suspending the iodide salt in acetone:water (7:3) and stirring with hexafluorophosphate-loaded Amberlite® beads — the partially anion-exchanged compound then had enough solubility in dichloromethane to be washed with $\text{NH}_4\text{PF}_6(\text{aq})$ solution, giving **33**· PF_6 in 63% yield from **32** (Scheme 3.8).

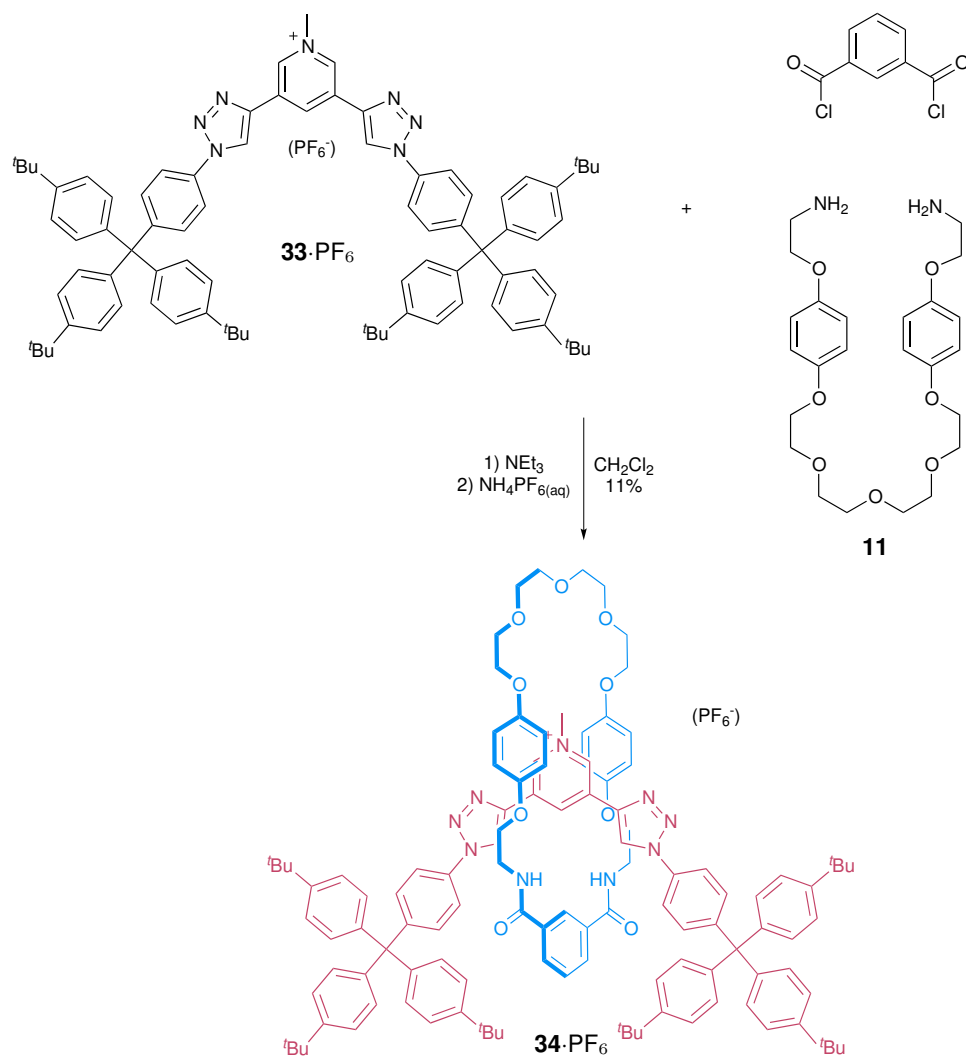


Scheme 3.8: Synthesis of **33**· PF_6 .

3.5.1.2 Rotaxane synthesis

Rotaxane formation was attempted by the condensation of bis-amine **11** and isophthaloyl chloride in the presence of **33**· PF_6 in dichloromethane (Scheme 3.9). The hexafluorophosphate salt of **33**⁺ was used because of the very low solubility of **33**·Cl in this solvent, but this is expected to have only a minor effect on rotaxane formation, as chloride anion is produced during amide condensation. Integration of the ^1H NMR spectrum of the crude reaction mixture indicated that the rotaxane was formed in approximately 20% yield, however purification by preparative TLC, followed by anion exchange by washing a dichloromethane solution of the rotaxane with aqueous $\text{NH}_4\text{PF}_6(\text{aq})$ gave almost pure **34**· PF_6 in modest yield (11%). A few milligrams of a pure sample was obtained by recrystallization from methanol containing a small amount of chloroform. Despite the

small quantity prepared, it was possible to characterize the rotaxane by ^1H (Figure 3.27) and ^{19}F NMR spectroscopy, and by high resolution ESI mass spectrometry.



Scheme 3.9: Synthesis of **34·PF₆**.

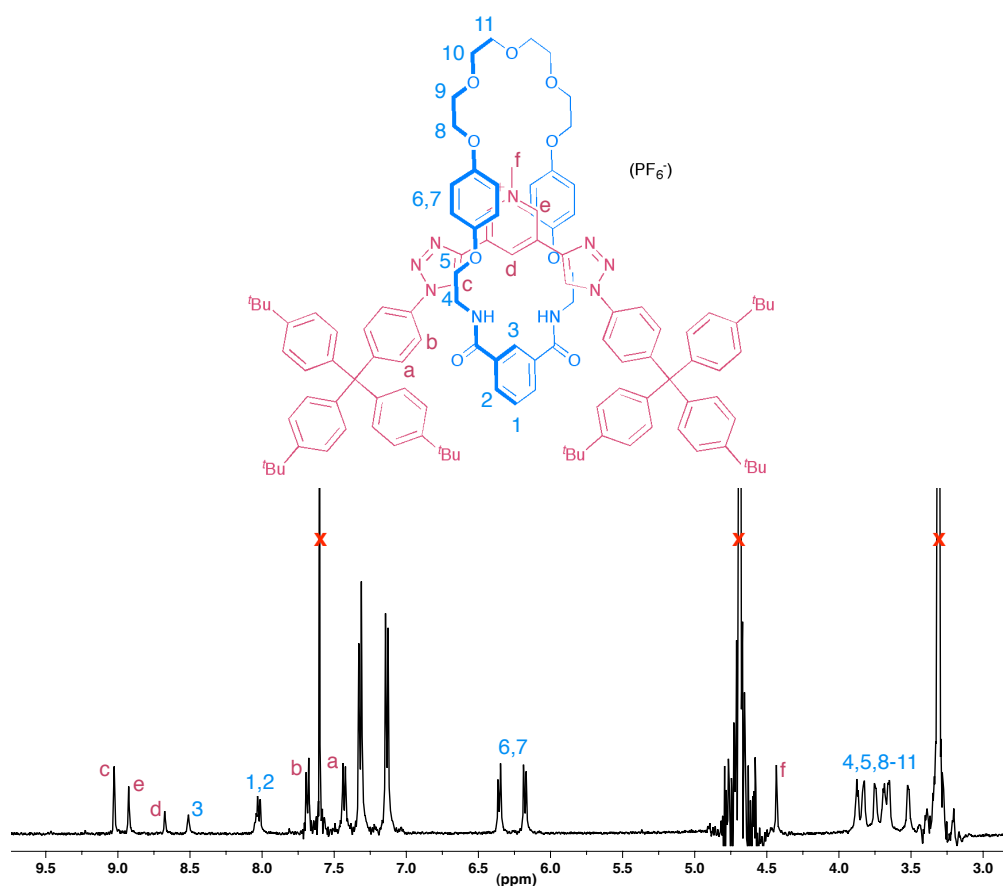


Figure 3.27: Truncated ^1H NMR spectrum of **34**-PF₆, red crosses correspond to residual solvent signals, unlabelled peaks are from bulky stopper groups (293 K, 1:1 CDCl₃:CD₃OD, 500 MHz).

Twinned crystals of **34**-PF₆ suitable for X-ray diffraction analysis were obtained, allowing unambiguous confirmation of the interlocked nature of the product (Figure 3.28), with the structure crystallising in the polar spacegroup *Cc* as the mixed dichloromethane/water solvate. Perhaps surprisingly, no significant donor–acceptor interactions are observed between the pyridinium and hydroquinone rings in the solid state (shortest centroid···centroid distance = 3.99 Å). Three weak rotaxane···PF₆[−] hydrogen bonds are present in the solid state (%VdW_{H,F} = 91–94), as well as one hydrogen bond between the pyridinium-methyl group and polyether chain (%VdW = 93). The two amide groups and two triazole groups all adopt a *syn* conformation, allowing the structure to pack through a series of strong intermolecular carbonyl···water···carbonyl hydrogen bonds [O–H···O = 2.59(3), 2.84(3) Å].

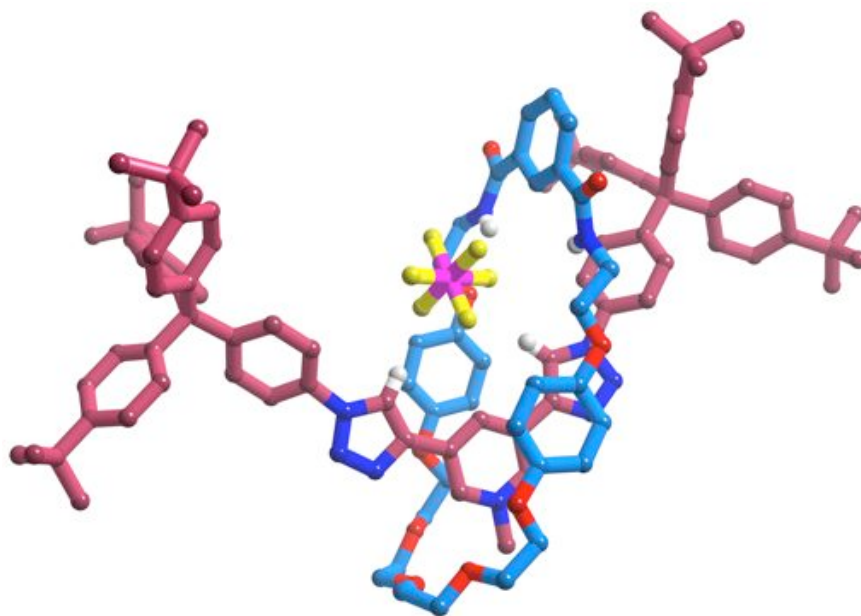


Figure 3.28: Structure of **34**·PF₆ in the crystal (crystallized from dichloromethane/diethyl ether). Solvent molecules, and most hydrogen atoms omitted for clarity.

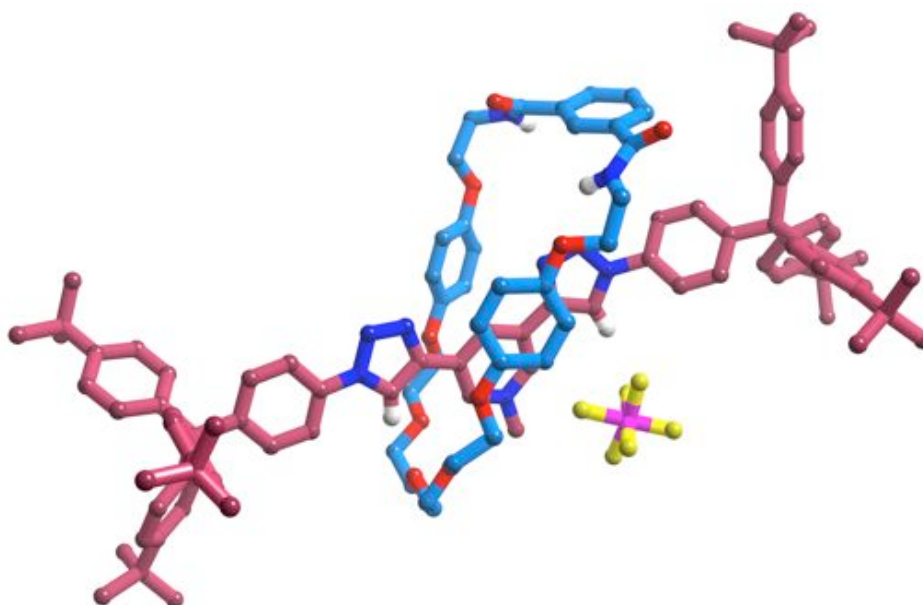


Figure 3.29: Structure of **34**·PF₆ in the crystal (crystallized from chloroform/methanol). Solvent molecules and most hydrogen atoms omitted for clarity.

Very poor quality data could also be obtained of a different solvate of the structure (crystallized from chloroform/methanol rather than dichloromethane/diethyl ether, Figure 3.29). While the data are too poor to allow detailed analysis of supramolecular close contacts, it is clear that this structure also does not feature any donor···acceptor

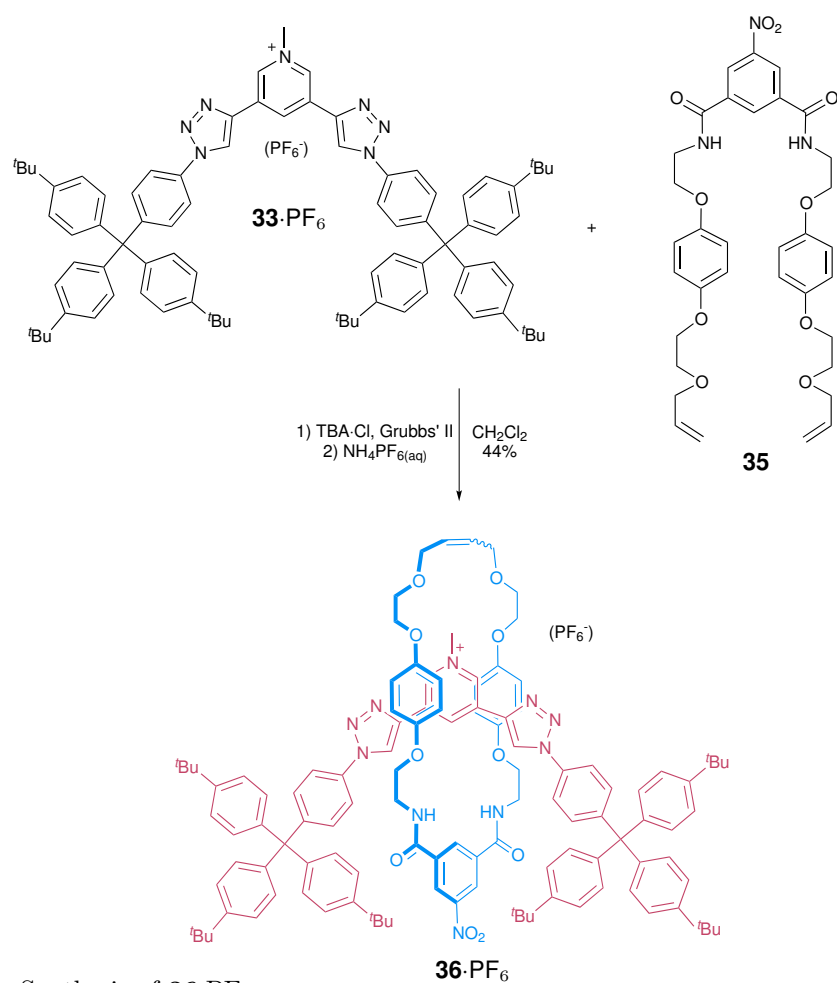
interactions or significant pyridinium-methyl...polyether hydrogen bonding in the solid state. Interestingly, the amide groups have an approximately *syn-anti* arrangement, while both triazole C–H donors have an *anti* orientation, presumably to facilitate intermolecular amide...carbonyl and carbonyl...methanol hydrogen bonds, which dictate the solid state packing of the rotaxane.

3.5.2 Rotaxane synthesis *via* clipping

Given the small amounts of rotaxane isolated using an amide condensation route, the synthesis of a rotaxane from axle component **33**⁺ *via* a clipping strategy was attempted. Bis(vinyl)-appended macrocycle precursor **35** was prepared in 28% overall yield in five steps from commercially available starting materials, as previously reported.³⁰¹ Due to the very low solubility of halide salts of **33**⁺ in dichloromethane, the PF₆[−] salt of the axle component was used, with TBA·Cl added as a source of templating chloride anion.

Grubbs' II-catalyzed RCM of a 1:1:1.5 stoichiometric ration of **33**:TBA·Cl:**35** in dichloromethane gave the desired rotaxane **36**⁺ (Scheme 3.10), with integration of the crude ¹H NMR spectrum indicating a yield of formation of approximately 65%. It is noteworthy that this yield is not dissimilar to the estimated 72% yield of formation of catenane **26**⁺. Purification by preparative TLC, followed by anion exchange to the hexafluorophosphate salt, and recrystallization from methanol containing a small amount of chloroform afforded pure **36**·PF₆ in 44% yield. The rotaxane was characterized by ¹H, ¹³C, ¹⁹F and ³¹P NMR spectroscopy, and by high resolution ESI mass spectrometry.

The interlocked nature of the rotaxane was confirmed by 2D NMR spectroscopy, with a number of inter-component couplings observed (Figure 3.30), including between the amide protons of the macrocycle and the internal pyridinium resonance of the axle component, and between the pyridinium and hydroquinone rings.



Scheme 3.10: Synthesis of **36·PF₆**.

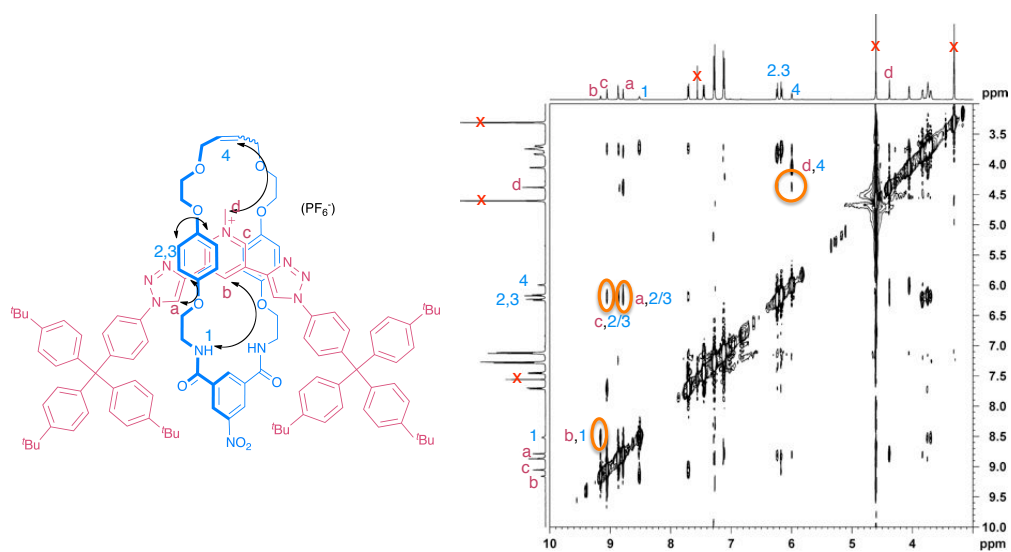


Figure 3.30: 2D ROESY NMR spectrum of **36·PF₆** showing selected inter-component couplings (1:1 $\text{CDCl}_3:\text{CD}_3\text{OD}$, 293 K, 500 MHz).

The synthesis of analogous rotaxanes containing a pyridinium bis-amide axle component has been reported to proceed in similar yields *via* clipping or amide condensation strategies. For example, the chloride salt of the nitro-substituted rotaxane ($Y = \text{C-NO}_2$ in Scheme 3.7) was prepared in 55% yield by the condensation strategy and 57% by clipping, whereas yields of 60% and 47% were obtained for the isophthalamide rotaxane ($Y = \text{H}$ in Scheme 3.7).^{233,301} Conversely, when a pyridinium bis-triazole axle component is used, the isolated yields and crude yields of rotaxane are significantly higher for clipping than condensation (65 and 20% crude yields, and 44 and 11% isolated yields, respectively).

The condensation method requires strong donor–acceptor and pyridinium-methyl $\cdots$ polyether hydrogen bonding between components to template the interweaved assembly, with this method giving modest yields of rotaxane containing the pyridinium bis-amide axle even when no source of templating chloride anion is present in the reaction mixture.²³⁶ For a clipping reaction, it would appear that the anion template is much more important as there is little opportunity for pyridinium-methyl $\cdots$ polyether hydrogen bonding in the rotaxane precursor assembly. Presumably in the case of the pyridinium bis-triazole rotaxanes, the anion templation effect is strong enough (in dichloromethane) to give good yields of rotaxane *via* clipping, but the weakened donor–acceptor interactions (see Section 3.2.2.1) are responsible for the reduced rotaxane yields when a condensation approach is used.

3.5.3 Anion recognition properties of pyridinium bis-triazole rotaxane

The anion recognition properties of **36**·PF₆ were investigated in competitive 1:1 CDCl₃:CD₃OD mixture. Addition of chloride anion to **36**·PF₆ (Figure 3.31) causes downfield shifts in the rotaxane’s cavity protons *a*, *b*, *c*, *2* and *3*, consistent with hydrogen bonding interactions with the anion, although interestingly, these perturbations are substantially smaller in magnitude than those observed upon addition of chloride anion to catenane **26**·PF₆.

In fact, while addition of chloride and bromide anions caused much smaller shifts in **36**·PF₆’s cavity protons than was observed with **26**·PF₆, iodide causes perturbations of a

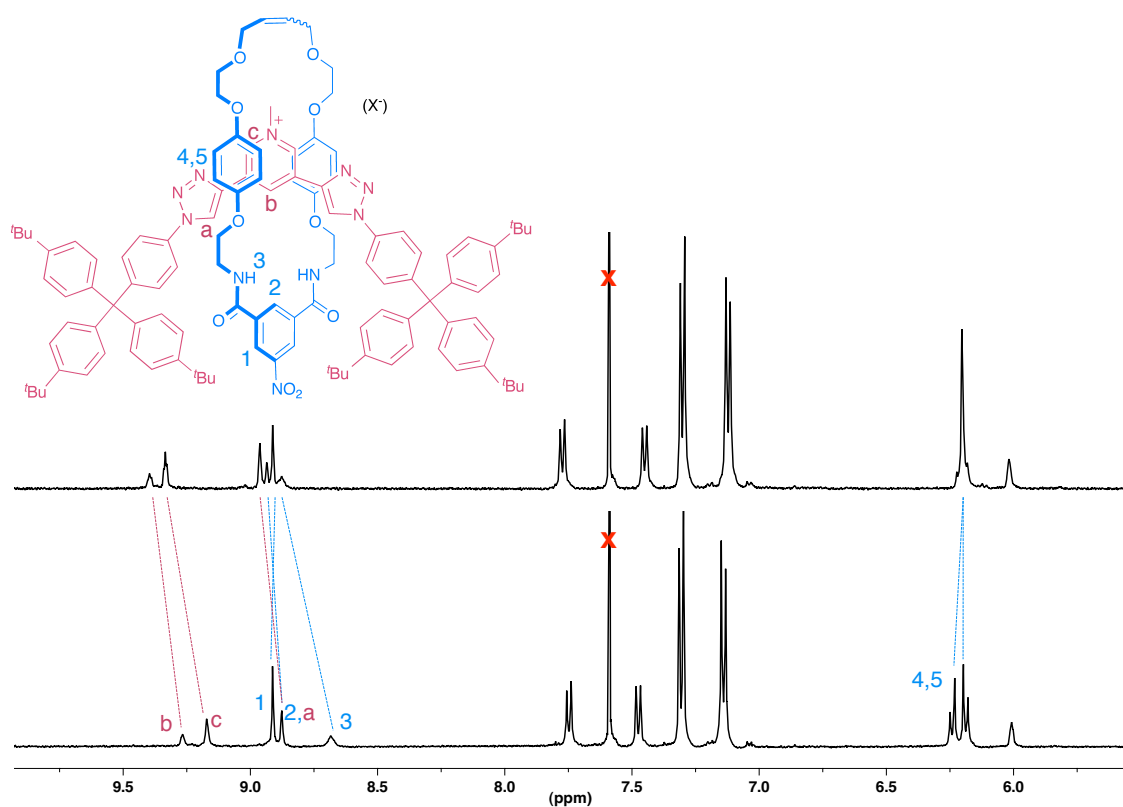


Figure 3.31: Truncated ^1H NMR spectrum of **36**·PF₆ (bottom), and **36**·PF₆ and one equivalent of TBA·Cl (top) (293 K, 1:1 CDCl₃:CD₃OD, 500 MHz)

similar magnitude in each receptor (Figure 3.32). Conversely, dihydrogen phosphate and acetate cause slightly larger shifts in the rotaxane host than in the catenane.

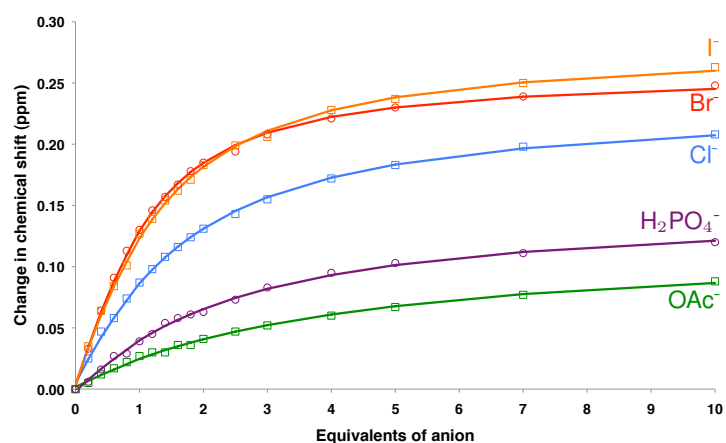


Figure 3.32: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **36**·PF₆ monitoring triazole resonance (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

Quantitative 1:1 anion association constants were obtained using WINEQNMR2,³²⁸ monitoring the triazole proton resonance. The association constants obtained are displayed in Table 3.13, along with those obtained for catenane **26**·PF₆, and those reported for the analogous all-amide rotaxane.²³³

Interestingly, rotaxane **36**·PF₆ displays a significant degree of selectivity between the halide anions, with an unusual preference for bromide. While **36**·PF₆ again exhibits a pronounced preference for halides over the oxoanions OAc[−] and H₂PO₄[−], the relative degree of selectivity is lower than that observed with catenane **26**·PF₆.

Table 3.13: Association constants, K_a (M^{−1}) for anions with interlocked host systems^a

Anion	All amide rotaxane·PF ₆ ³⁰¹	36 ·PF ₆	26 ·PF ₆
Cl [−]	4500	411(18)	679(20)
Br [−]	—	936(40)	632(45)
I [−]	—	640(29)	509(10)
H ₂ PO ₄ [−]	1500	186(9)	49(4)
OAc [−]	725	137(3)	— ^b

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K). ^bMovement of peaks too small to infer binding event.

This is perhaps unexpected, as amide based rotaxane host systems have typically exhibited a much larger degree of selectivity for halides over oxoanions than analogous catenanes, attributed to their more rigid nature.²³⁵ Enhanced selectivity *is* observed for the triazole containing rotaxane host over the catenane, but only *between* the halide anions. A possible explanation for this can be postulated by considering the differing binding modes of the various anions: the halides are believed to bind inside the interlocked hosts' three-dimensional cavities, allowing the more rigid rotaxane to exhibit a degree of selectivity that is absent in the catenane. Conversely, the oxoanions associate on the exterior of the host, and so are affected more by the strongest donor groups in the host, in this case the charged pyridinium bis-triazole motif, and less by the three-dimensional cavity. The aryl-substituted pyridinium bis-triazole group in the rotaxane is a more potent anion complexant than the alkyl-substituted motif present in the catenane, and so stronger recognition of the oxoanions, and concomitant reduced selectivity results.

Diffusion of diisopropyl ether vapour into a chloroform/methanol solution of **36**·PF₆ and excess TBA·Cl gave small single crystals of **36**·Cl suitable for synchrotron X-ray structural analysis (Figure 3.33). The chloride anion is bound within the rotaxane cavity, although interestingly neither donor–acceptor interactions between pyridinium and hydroquinone groups, nor pyridinium-methyl···polyether hydrogen bonds are present. Host···anion hydrogen bonds are shorter in the solid state structure of **36**·Cl than in **26**·Cl (Table 3.14), which is perhaps surprising, given the weaker recognition of chloride anion observed in solution. These results hint that “secondary” non-covalent interactions (*i.e.* those other than donor···anion hydrogen bonding) may have a greater effect on anion recognition strength than initially assumed — a subject that will be examined in more detail in Chapter Four.

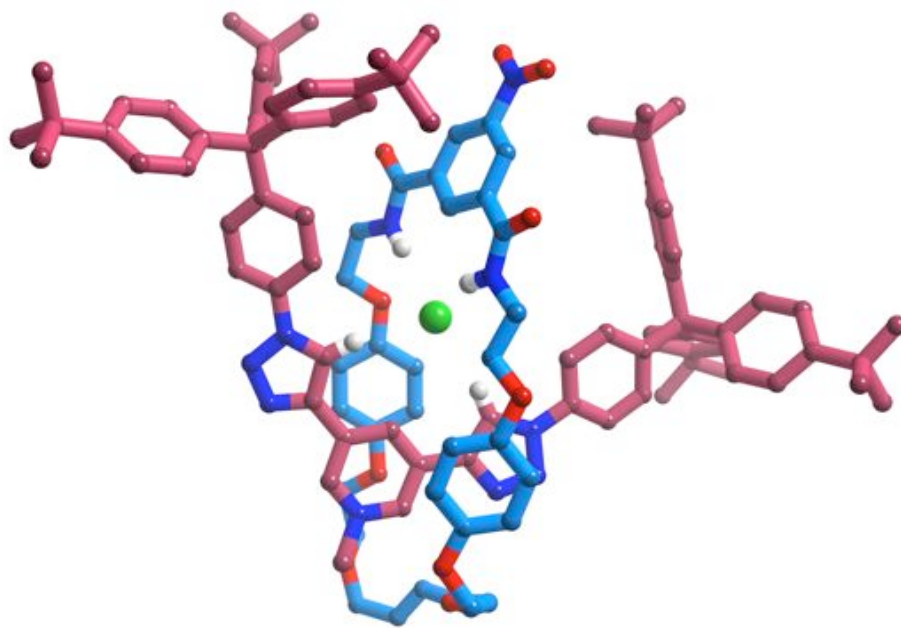


Figure 3.33: Structure of **36**·Cl in the crystal. Minor position of ^tbutyl disorder, and most hydrogen atoms omitted.

Table 3.14: Non-covalent interactions in solid state structures of **36**·Cl and **26**·Cl.^a

	Rotaxane 36 ·Cl	Catenane 26 ·Cl
<i>Receptor ··· anion hydrogen bonding</i>		
<i>Isophthalamide macrocycle</i>		
%VdW _{H_{amide},X}	90	84
%VdW _{H_{amide},X}	94	90
%VdW _{H_{phenylene},X}	93	90
<i>Pyridinium bis-triazole macrocycle</i>		
%VdW _{H_{triazole},X}	92	91
%VdW _{H_{triazole},X}	95	92
%VdW _{H_{pyridinium},X}	95	98
<i>Pyridinium ··· hydroquinone donor–acceptor interactions</i>		
centroid ··· centroid	3.526(2)	—
centroid ··· centroid	3.574(2)	—
<i>Pyridinium-methyl ··· polyether hydrogen bonding</i>		
%VdW _{H_{methyl},O}	89	97
%VdW _{H_{methyl},O}	96	—

^aDistances in Å, estimated standard uncertainties in parentheses.

3.5.4 Investigation of the synthesis of a “reversed” rotaxane

To investigate the effect of these secondary interactions on both the formation of interlocked hosts and the resulting receptor’s anion recognition properties, the synthesis of the “reversed” rotaxane **37**⁺ shown in Figure 3.34 was targeted, containing a pyridinium bis-triazole macrocycle and an isophthalamide axle component. This rotaxane contains a similar hydrogen bond donor set to **36**⁺, but is precluded from forming stabilising intramolecular donor–acceptor or pyridinium-methyl ··· polyether hydrogen bonds.

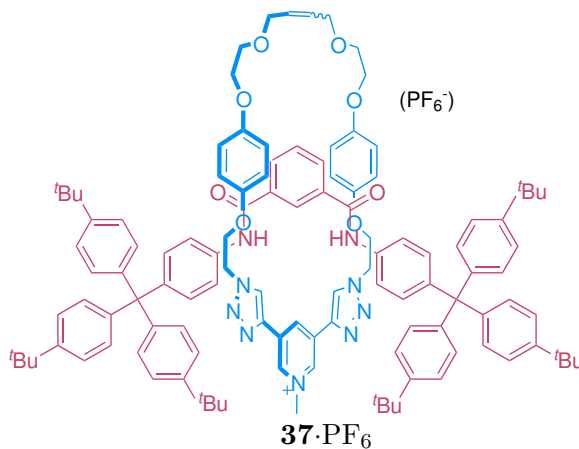
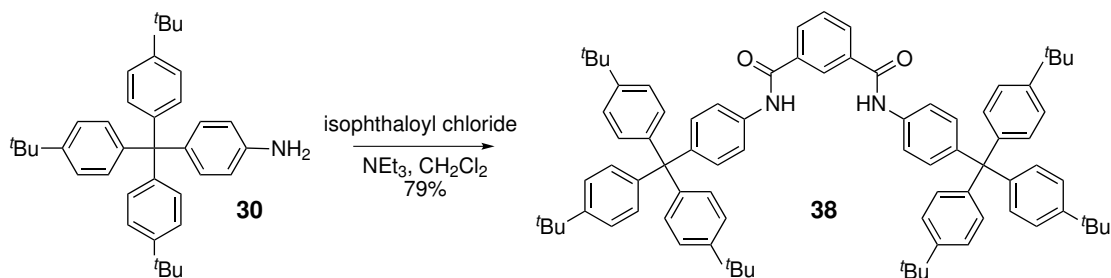


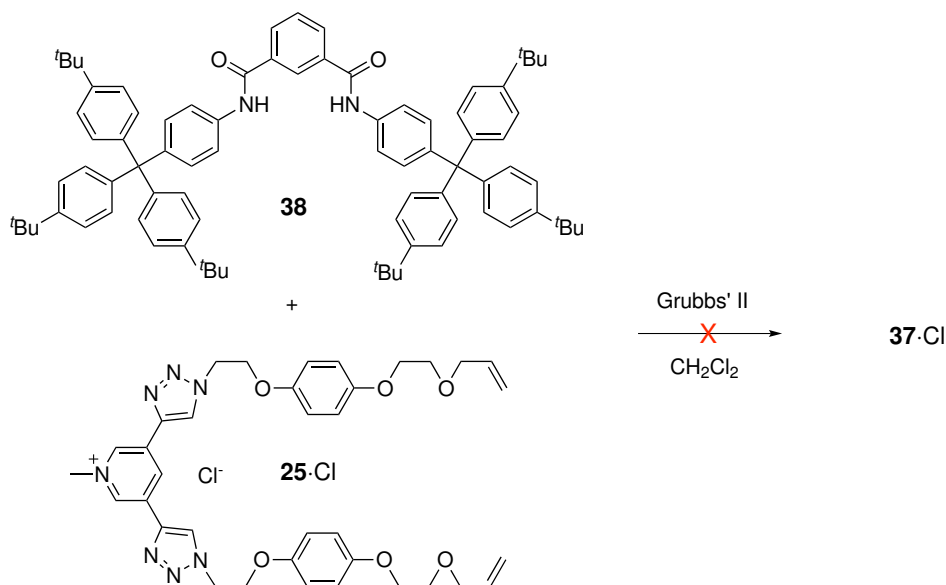
Figure 3.34: Targeted “reversed” rotaxane.

The axle component necessary for synthesis of this rotaxane was prepared by the condensation of aniline-stopper **30** and commercially available isophthaloyl chloride. Purification by column chromatography gave isophthalamide axle **38** in good yield (79%, Scheme 3.11).



Scheme 3.11: Synthesis of **38**.

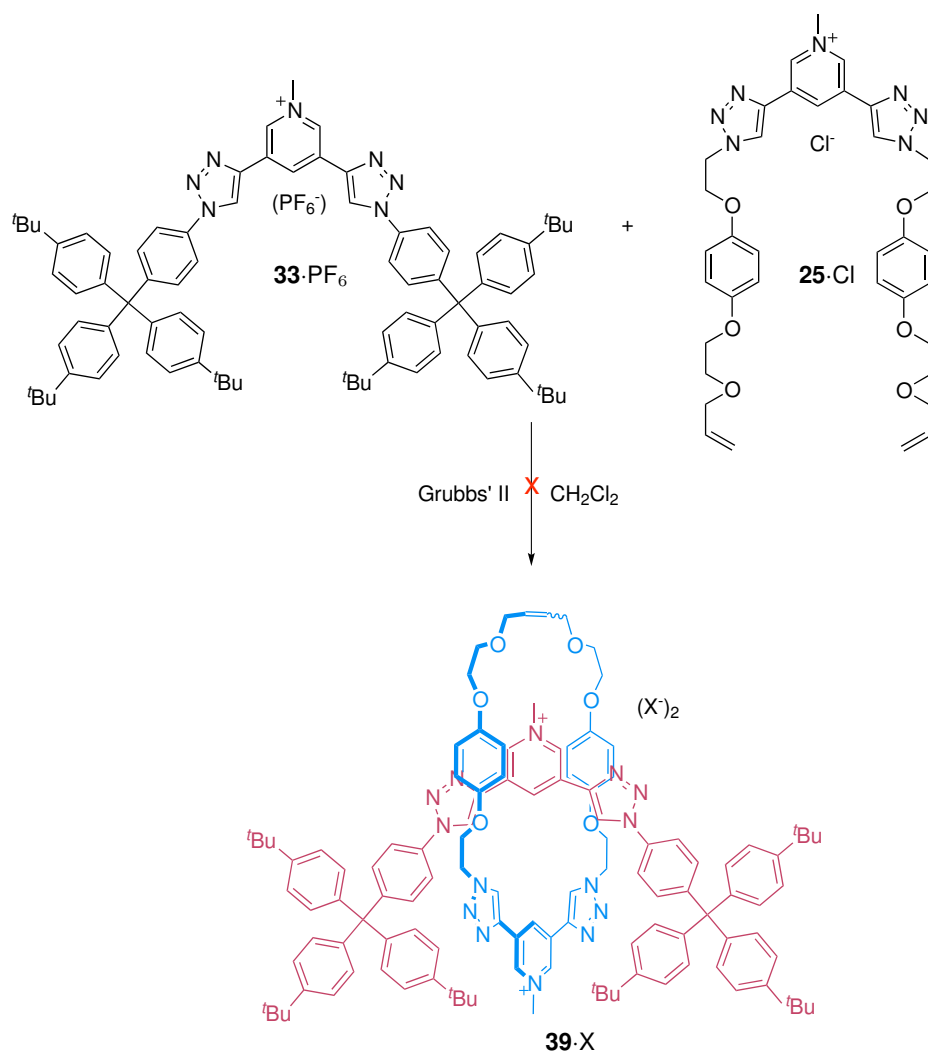
The synthesis of novel rotaxane **37**⁺ was attempted by chloride anion templated Grubbs' II-catalyzed RCM of pyridinium bis-triazole precursor **25**·Cl in the presence of axle component **38**⁺ (Scheme 3.12). Analysis of the crude reaction mixture using TLC, mass spectrometry and ¹H NMR revealed no evidence of rotaxane formation, demonstrating the vital role that the donor–acceptor and pyridinium-methyl···polyether interactions have in assembling the interweaved rotaxane precursor, and subsequent formation of the interlocked molecule.



Scheme 3.12: Attempted synthesis of **37**·Cl.

3.5.5 Attempts to synthesize a rotaxane that binds anions solely through C–H···anion hydrogen bonds

It has previously been reported that a dicationic rotaxane in which both axle and macrocyclic components contain a pyridinium bis-amide motif displays strong and selective anion recognition in competitive 65:35 d₆-acetone:D₂O.²³⁶ The synthesis of a pyridinium bis-triazole analogue of this, **39**²⁺, was targeted, again potentially an unprecedented example of an interlocked host molecule binding anions solely through C–H···anion hydrogen bonds.



Scheme 3.13: Attempted synthesis of **39-X**.

Anion templated rotaxane formation was attempted as shown in Scheme 3.13, using the chloride salt of macrocycle precursor **25**⁺ and the hexafluorophosphate salt of axle

33⁺. Analysis of the crude reaction mixture by TLC, ¹H NMR spectroscopy and mass spectrometry revealed no evidence of interlocked product formation, suggesting that the favourability of anion recognition is not enough to overcome the electrostatic repulsion between the two cationic components, as was observed for the attempted formation of an analogous catenane in Section 3.4.4.

3.6 Conclusions and future work

3.6.1 Summary

It was demonstrated that the new pyridinium bis-triazole threading component **18**⁺ can form stable anion templated interpenetrated assemblies with isophthalamide macrocycles. Interestingly, the chloride anion templated pseudorotaxane is more stable than that incorporating the analogous pyridinium bis-amide threading component **19**·Cl. Solution ¹H NMR data showed that a range of anions, *including oxoanions* can template pseudorotaxane formation and further experiments revealed that amide threading component **19**⁺ could also form oxoanion templated interweaved assemblies. A total of ten pseudorotaxane assemblies incorporating amide or triazole threading components, isophthalamide containing macrocycles, and a range of anions were structurally characterized by X-ray crystallography, and the structural differences and similarities between them were analysed. Notably, the first crystal structures of pseudorotaxanes incorporating a discrete nitrate and carboxylate template were presented.

A novel catenane incorporating the pyridinium bis-triazole motif was synthesized in 64% yield — significantly higher than the yield achieved for the amide catenane analogue. The catenane binds halide anions in competitive 1:1 CDCl₃:CD₃OD, and displays an impressive greater than ten-fold selectivity for these anions over dihydrogen phosphate, a dramatic improvement on the analogous amide containing catenane.²³⁴

Two rotaxane hosts incorporating the pyridinium bis-triazole motif were also prepared: a clipping approach gave a high yield of rotaxane (44% after anion exchange to the hexafluorophosphate salt), while an amide condensation route was less successful (11% yield after anion exchange). The interlocked host exhibits impressive selectivity for the

halide anions over more basic anions, although this is not quite as pronounced as for the corresponding catenane. Interestingly, the rigid rotaxane displays some preference *between* the halide anions, with bromide preferred to iodide or chloride, demonstrating again the potentially interesting recognition properties of triazole containing interlocked architectures.

3.6.2 Future work

The oxoanion templated assembly of interweaved assemblies may be exploited in the formation of interlocked architectures. Such systems would need to have large enough cavities to accommodate the increased size of the oxoanion, but the increased basicity of these anions would be expected to give high yields of products, and afford potent host systems with differing selectivity properties to those synthesized by halide templation. The larger cavities in these systems may also accommodate a range of larger guests, besides anions.

Iodination of 3,5-diethynyl pyridine would allow the synthesis of pyridinium bis-*iodotriazole* based receptors, possessing two iodotriazole halogen bond donors, as well as a positive charge provided by the pyridinium heterocycle. An example of a simple acyclic receptor incorporating this motif is presented in Figure 3.35. This was not attempted during this work, because of concerns that the distance between the halogen atoms would be too small to bind an anion in a bidentate manner, however Huber has very recently reported acyclic hosts incorporating the similarly-shaped phenyl-1,3-haloimidazolium motif, and shown that these halogen bond donors can convergently bind halide anions.¹⁴⁷ Hence, the pyridinium-3,5-bis(iodotriazole) motif offers a possible route to interlocked architectures containing convergent halogen bond donors.

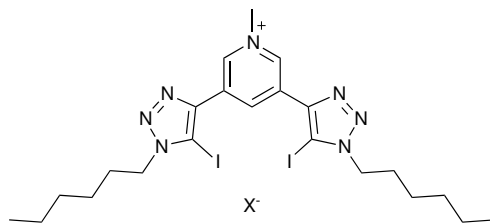


Figure 3.35: Simple halogen bonding analogue of **18**⁺.

Chapter 4

Triazolium rotaxanes

4.1 Introduction

The previously reported triazolium rotaxane **40**·PF₆ (Figure 4.1) displays an unusual selectivity preference for bromide anion, with this guest being complexed ten times more strongly than chloride ($K_a = 970$ and 90 M^{-1} for bromide and chloride anions, respectively).²⁴⁵ The ease of synthesis of triazole and triazolium groups *via* the CuAAC reaction offers the opportunity to prepare a series of closely related interlocked hosts and explore the effects that subtle structural changes have on the receptor's anion recognition properties.

4.1.1 Chapter objectives

Using **40**·PF₆ as the starting point, this chapter will detail the effects of three different structural modifications on rotaxane anion recognition: 1) varying the size and nature of substitution of the axle component, 2) varying the size of the macrocyclic component, and 3) incorporating additional hydrogen bond donors into the axle component.*

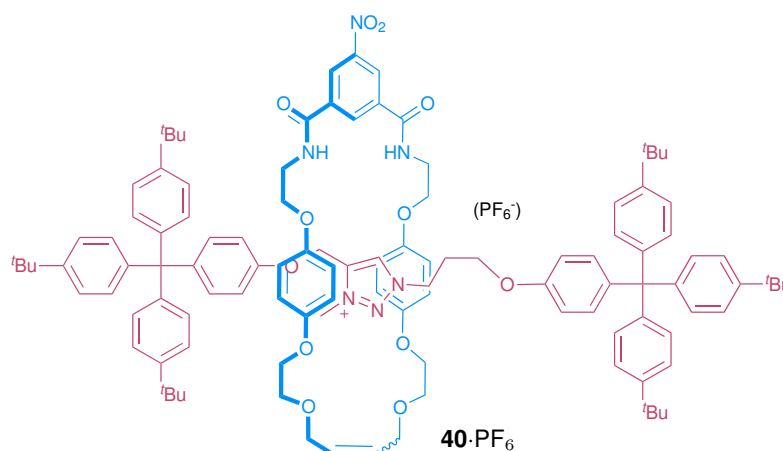


Figure 4.1: Previously reported triazolium rotaxane **40**·PF₆.²⁴⁵

*Numerous attempts were also made to synthesize a rotaxane incorporating a ferrocene group in the axle component. While several ferrocene-triazolium axle components were prepared, no rotaxanes could be isolated.

4.2 Varying the axle component

4.2.1 Introduction

In Chapter Two, it was shown that aryl-substituted bis-triazole receptors and bis-amide receptors exhibit far stronger chloride recognition than their alkyl-substituted analogues, due to the greater acidity of the hydrogen bond donors. Aryl-substituted *triazolium* containing axle components **41**·BF₄ and **42**·BF₄ were therefore targeted (Figure 4.2) in an effort to increase anion binding affinity. Importantly, these new axles have the bulky stopper groups attached directly to the anion recognition motif. It was hoped that this would affect the size and degree of preorganization of the interlocked cavity of the rotaxane host system, and could therefore modulate the anion selectivity preference, as well as recognition strength, of the resulting rotaxane hosts.

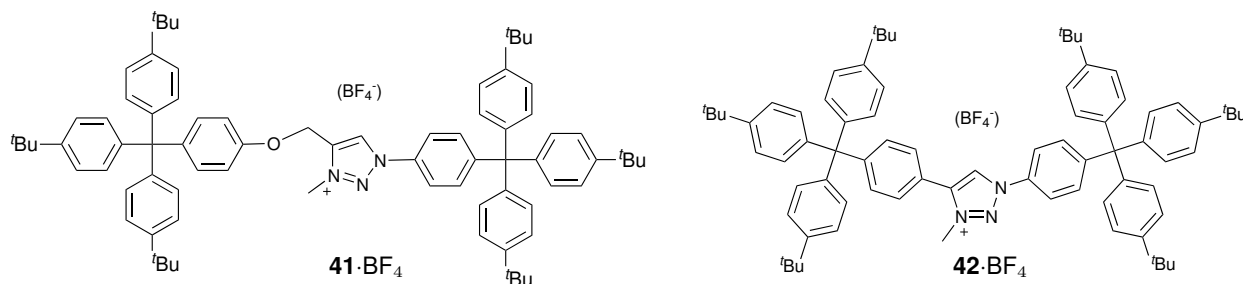
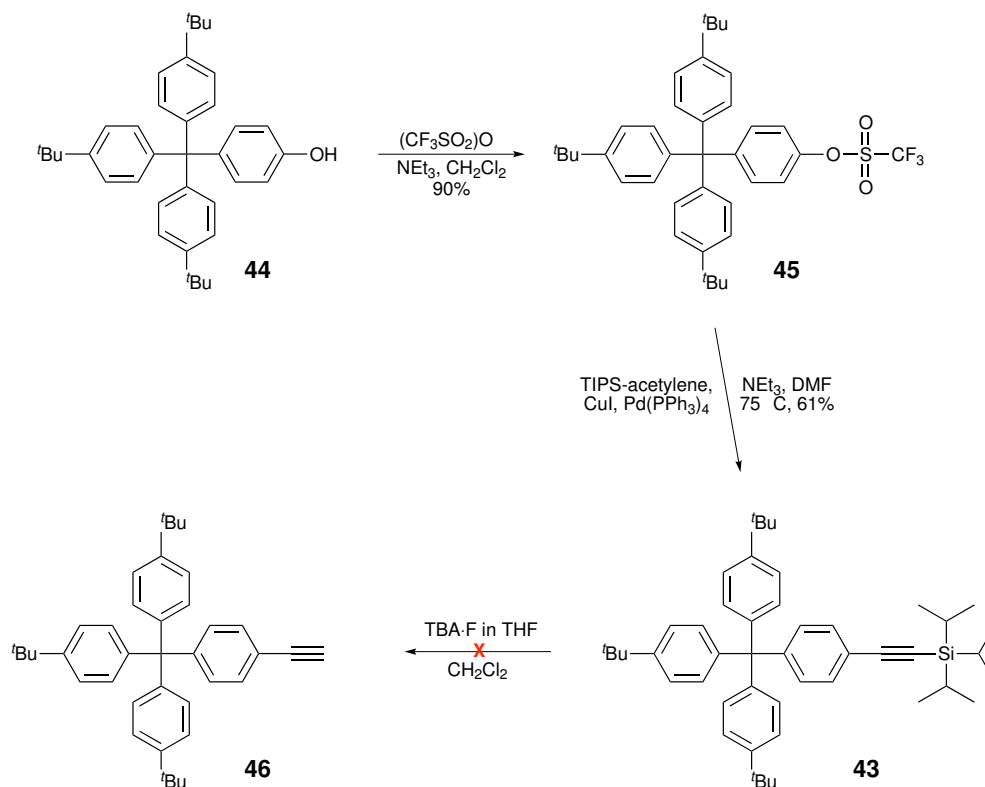


Figure 4.2: Targeted new axle components **41**·BF₄ and **42**·BF₄ containing aryl-substituted triazolium groups.

4.2.2 Synthesis of axle components

The synthesis of aryl-substituted triazolium axle components required the preparation of bulky stopper groups containing aryl azide and aryl alkyne functionality. Aryl azide stopper **31** was prepared as described in Chapter Three; the new aryl alkyne stopper **43** was prepared according to Scheme 4.1. Phenolic stopper **44** was prepared on a multi-gram scale in 50% yield over two steps from commercially available materials, as previously reported.³⁷⁰ Initially, several attempts were made to synthesize a bulky stopper with an aryl-bromide or iodide group suitable for subsequent Sonogashira reaction³²⁴ with an alkyne. The conversion of **44** to an aryl-bromide using phosphorous pentabromide, or of

aniline stopper **30** to a bromide or iodide with sodium nitrite in acid and a halide source (potassium iodide or copper(II) bromide) were unsuccessful.

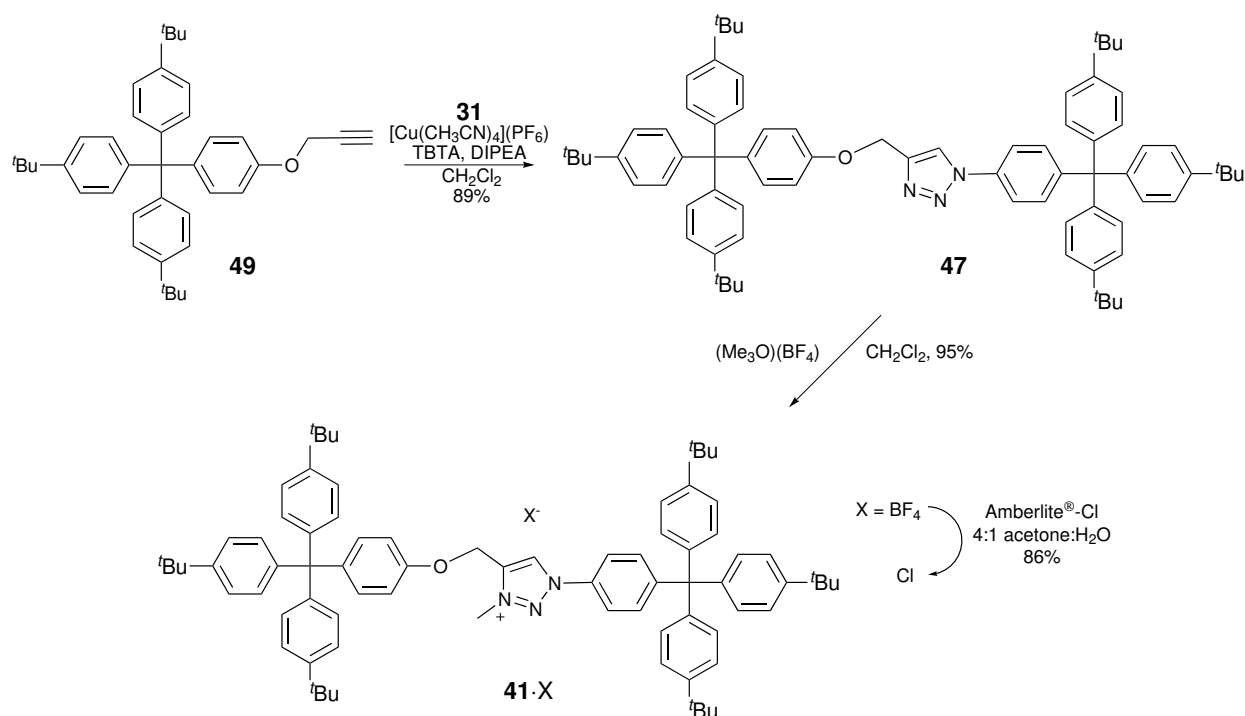


Scheme 4.1: Synthesis of **43**.

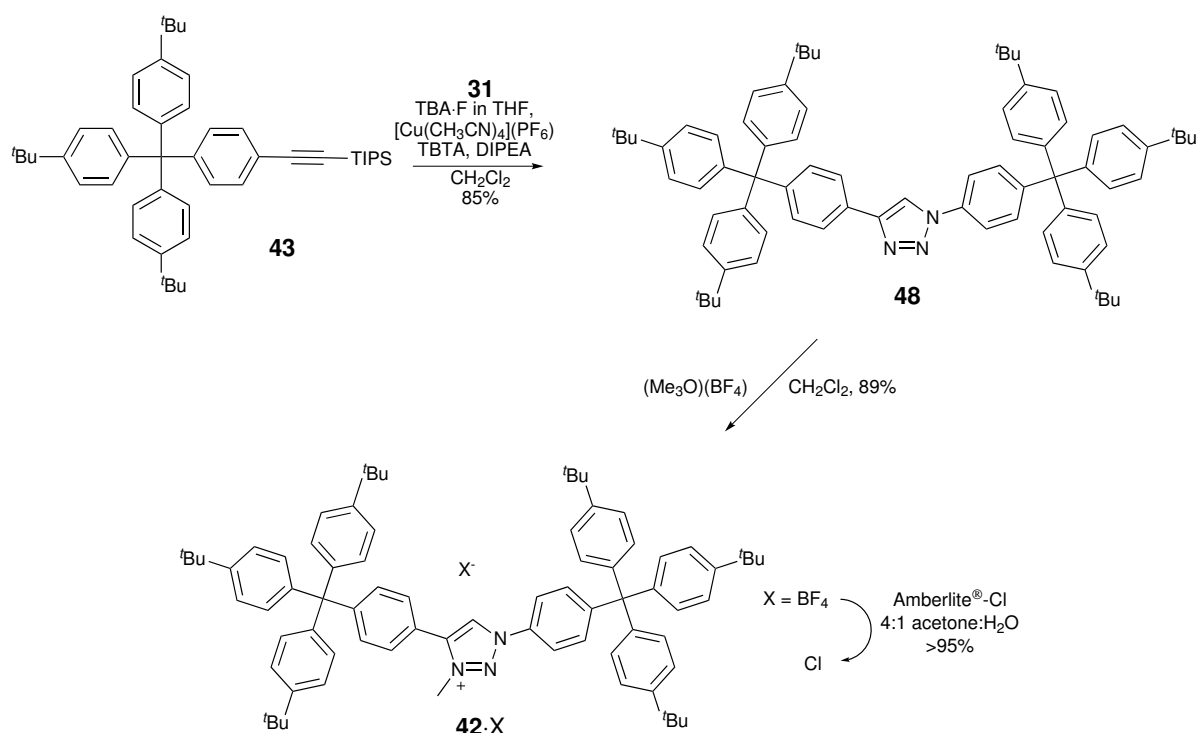
Instead, aryl triflate **45** was prepared in good yield (90%) using trifluoromethanesulfonic anhydride, and subsequent Sonogashira reaction³²⁴ with TIPS-acetylene gave TIPS-protected aryl alkyne **43** in 61% yield. Attempts to deprotect the silyl group and isolate **46** using TBA·F solution proved problematic with decomposition of the alkyne being observed. Therefore, the alkyne was prepared and isolated as the TIPS derivative, and in subsequent reactions deprotected *in situ*.

The CuAAC reaction was used to synthesize mono- and bis-aryl substituted neutral triazole axle components **47** and **48** (Schemes 4.2 and 4.3). Reaction of aryl azide **31** and alkyl-substituted alkyne **49** (prepared in 42% yield over three steps from commercially available materials, as previously described)³⁴⁵ in dichloromethane with catalytic $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$, TBTA and DIPEA gave **47** in good yield (89%). Reaction of **31** and **43** proceeded under similar conditions, but with the addition of TBA·F to remove the TIPS group: it was found that far greater yields (85%) were obtained when

stoichiometric rather than catalytic copper(I) was used (< 20% yield using 10% catalyst loading), presumably due to competing decomposition of the unprotected alkyne in the slower catalytic reaction. Alkylation using trimethyloxonoium tetrafluoroborate in dry dichloromethane gave the triazolium containing axle components **41**·BF₄ and **42**·BF₄ as their tetrafluoroborate salts in high yields (95 and 89%, respectively). Anion exchange using chloride-loaded Amberlite[®] resin gave **41**·Cl and **42**·Cl in 86% and quantitative yield, respectively.



Scheme 4.2: Synthesis of mono-aryl substituted axle component **41**·X.

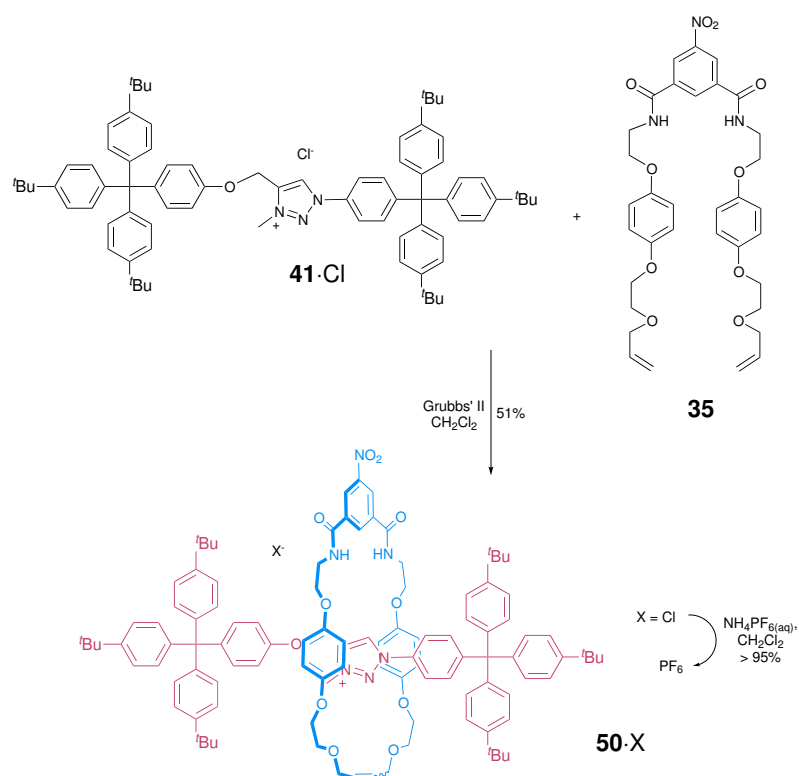


Scheme 4.3: Synthesis of bis-aryl substituted axle component **42·X**.

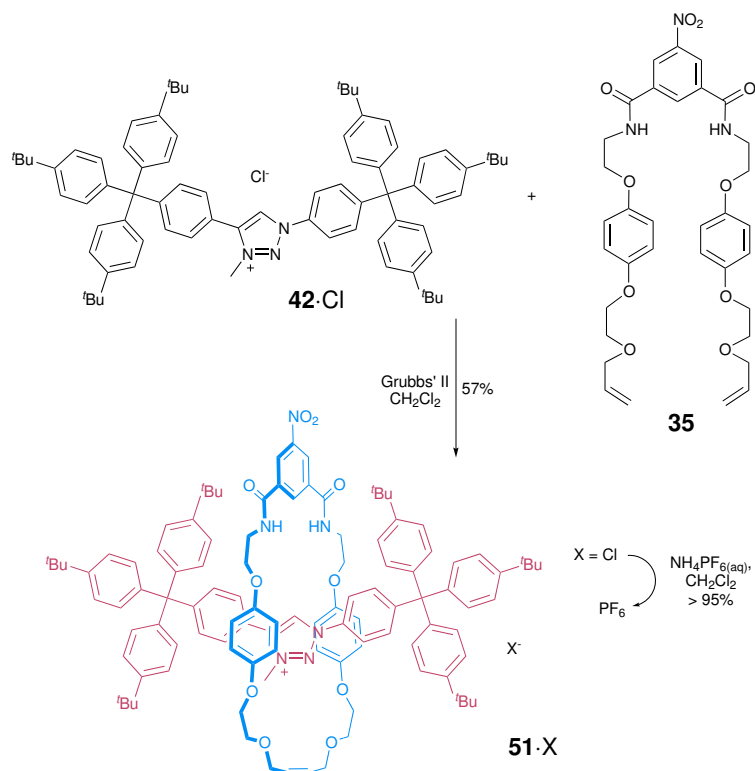
4.2.3 Rotaxane synthesis

The new rotaxanes were synthesized by chloride anion templated Grubb's-catalyzed RCM of vinyl-appended macrocycle precursor **35** and triazolium axle components **41·Cl** and **42·Cl**. Purification by preparative TLC, followed by recrystallization, gave the [2]rotaxanes **50·Cl** and **51·Cl** in 51 and 57% yields, respectively (Schemes 4.4 and 4.5). Removal of the templating chloride anion was achieved *via* repeated washing with $\text{NH}_4\text{PF}_6(\text{aq})$ to give **50·PF₆** and **51·PF₆** suitable for use in anion recognition studies.

The new rotaxanes were characterized by ^1H , ^{13}C , ^{19}F and ^{31}P NMR spectroscopy, and by high resolution ESI mass spectrometry. The interlocked nature of the hosts was confirmed using 2D NMR ROESY spectroscopy and X-ray crystallography. The ROESY NMR spectra of **50·PF₆** and **51·PF₆** are shown in Figures 4.3 and 4.4, respectively, with several inter-component couplings observed between macrocycle and axle in both cases, consistent with the formation of an interlocked structure.



Scheme 4.4: Synthesis of rotaxane **50·X**.



Scheme 4.5: Synthesis of rotaxane **51·X**.

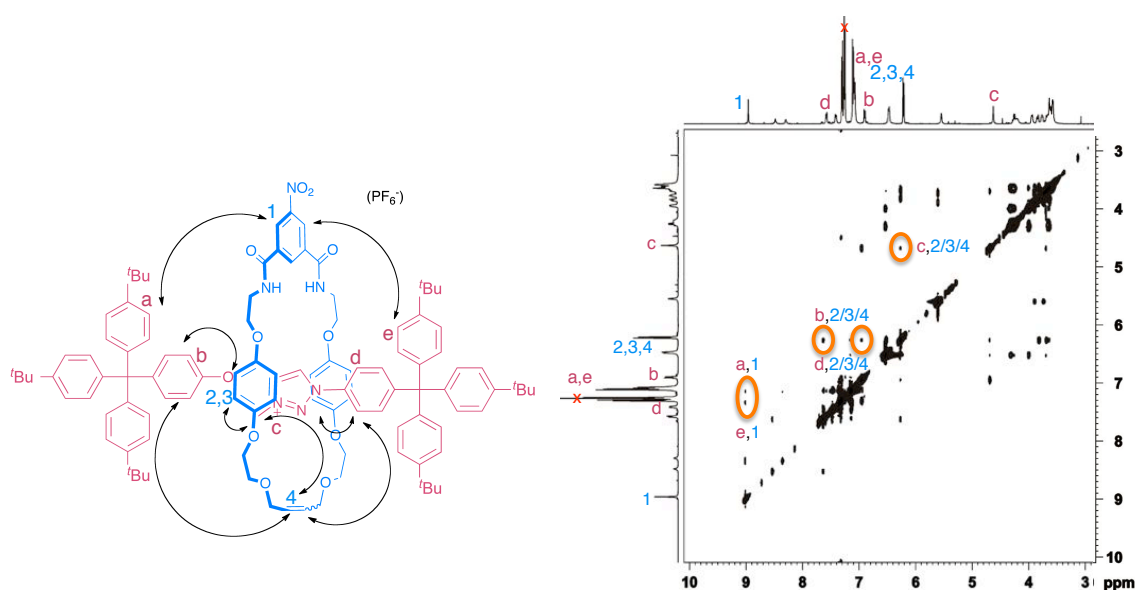


Figure 4.3: Truncated 2D ROESY NMR spectrum of **50**·PF₆ showing selected inter-component couplings. Further couplings involving the macrocycle alkyl protons are not depicted due to the overlap of these signals in the ¹H NMR spectrum (CDCl₃, 293 K, 500 MHz).

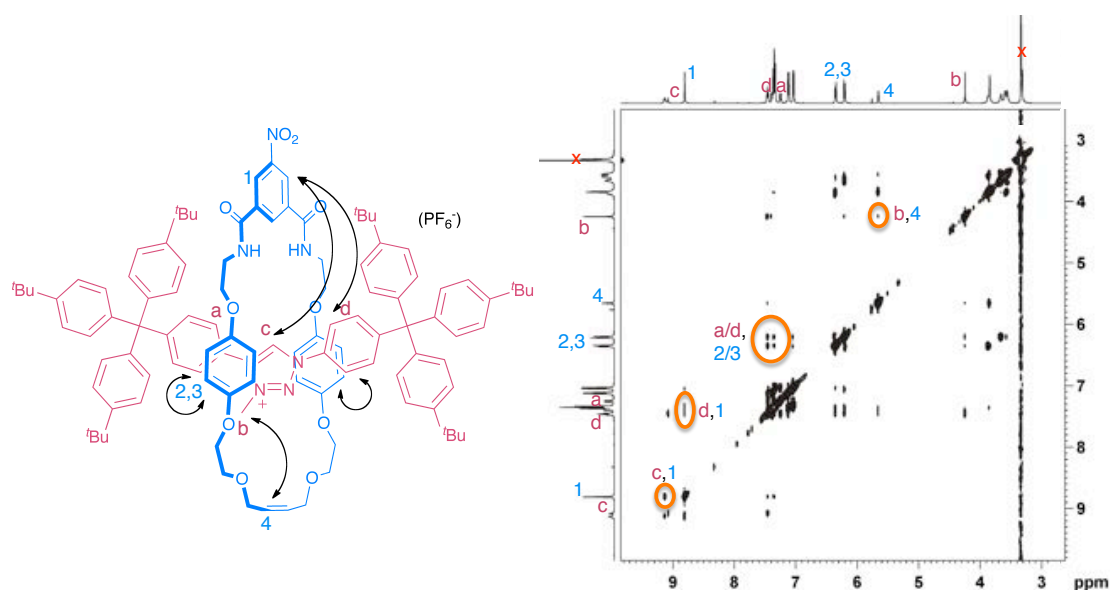


Figure 4.4: Truncated 2D ROESY NMR spectrum of **51**·PF₆ showing selected inter-component couplings. Further couplings involving the macrocycle alkyl protons are not depicted due to the overlap of these signals in the ¹H NMR spectrum (d₆-DMSO, 293 K, 500 MHz).

Definitive evidence of the interlocked nature of **50**⁺ was provided by single crystal X-ray structural analysis of the hexafluorophosphate salt. Crystals were obtained as either the pentane or dichloromethane solvate (grown by vapour diffusion of pentane into a chloroform/methanol solution, and diethyl ether into a dichloromethane/methanol

solution of the rotaxane, respectively). The two structures have very similar unit cells (axis lengths differ by no more than 0.05 Å, angles differ by no more than 0.3°), and contain very similar non-covalent interactions. Only the structure that crystallized as the dichloromethane solvate is shown in Figure 4.5. In each structure, one surprisingly strong hydrogen bond is observed between an amide group and a fluorine atom of the hexafluorophosphate anion, with the amide group twisting substantially out of the plane of the isophthalamide motif to facilitate this interaction [$N \cdots F = 3.010(7)$ Å, $\angle N-H \cdots F = 165^\circ$, $\%VdW_{H,F} = 84$; $N \cdots F = 3.001(5)$ Å, $\angle N-H \cdots F = 159^\circ$, $\%VdW_{H,F} = 85$ for dichloromethane and pentane solvates, respectively]. In both solvates, there is one strong [3.495(4) and 3.514(3) Å, for dichloromethane and pentane solvates, respectively] and one weak [3.949(4) and 3.936(3) Å, for dichloromethane and pentane solvates, respectively] donor–acceptor interaction between hydroquinone and pyridinium rings. Neither structure features triazolium-methyl $\cdots$ polyether hydrogen bonding.

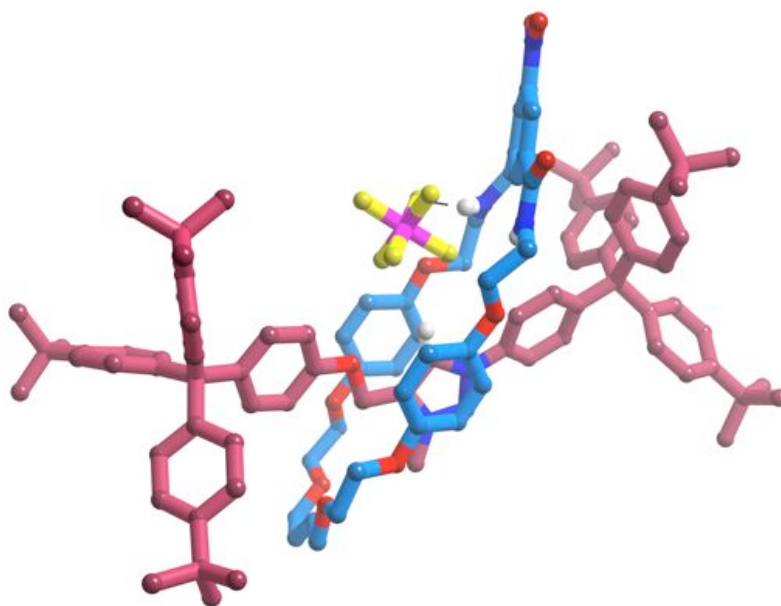


Figure 4.5: Solid state structure of **50**·PF₆. Dichloromethane solvate, most hydrogen atoms and *t*butyl disorder omitted for clarity. The strong H $\cdots$ F hydrogen bond is indicated with a dashed line.

The synthesis of **50**⁺ was initially carried out using the tetrafluoroborate salt of **41**⁺ and one equivalent of TBA·Cl or TBA·Br, as was reported for the synthesis of **40**⁺.²⁴⁵ While attempting to purify this rotaxane by recrystallization, single crystals suitable for X-ray diffraction studies were obtained: interestingly, the crystal is of the

tetrafluoroborate salt of the interlocked molecule, that is, **50**·BF₄ (Figure 4.6). While only a small quantity of material is necessary to provide crystals suitable for X-ray diffraction analysis, this result suggested the added TBA·anion was not being completely incorporated into the interweaved rotaxane precursor, and so the axle component was anion exchanged to the chloride salt using Amberlite[®] resin before rotaxane synthesis, as described in Section 4.2.3. This resulted in modest improvements in rotaxane yield ($\sim$ 40% using **41**·BF₄ and TBA·Cl or TBA·Br, 51% using **41**·Cl).

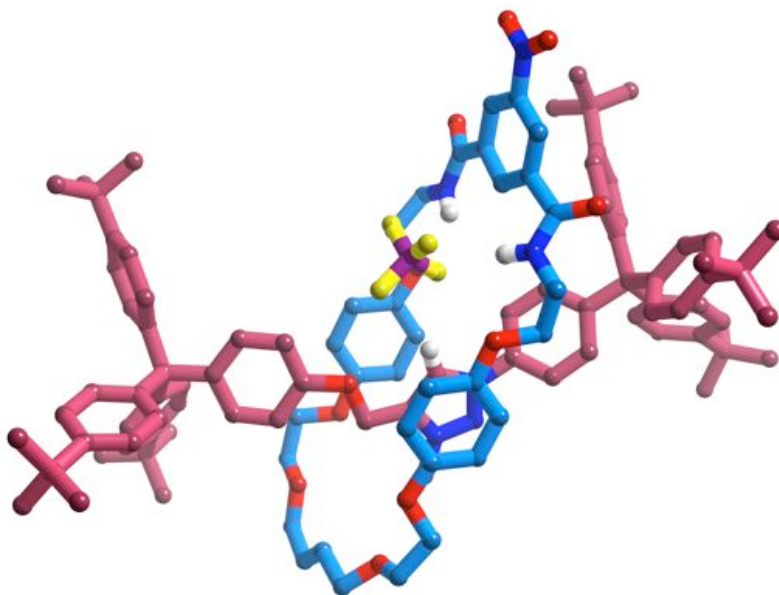


Figure 4.6: Solid state structure of **50**·BF₄. Most hydrogen atoms and chloroform solvate omitted for clarity.

The single crystal structure of the tetrafluoroborate salt of the rotaxane shows one fluorine atom of the anion pointing into the rotaxane cavity. It forms one moderate hydrogen bond to an amide proton [$N \cdots F = 3.112(13)$ Å, $\angle N-H \cdots F = 146^\circ$, $\%VdW_{H,F} = 91$], with very weak hydrogen bonds also observed to the other amide proton and triazolium proton ($\%VdW_{H,F} = 99$ and 97 , respectively). Pyridinium $\cdots$ hydroquinone donor–acceptor interactions are observed [centroid $\cdots$ centroid: $3.493(8)$, $3.801(9)$ Å], but there are no significant triazolium-methyl $\cdots$ polyether hydrogen bonds.

4.2.4 Anion recognition properties

4.2.4.1 Mono-aryl substituted rotaxane

The anion recognition properties of **50**·PF₆ were investigated using ¹H NMR titration experiments in polar 1:1 CDCl₃:CD₃OD solvent mixture. Addition of anions to the interlocked host causes downfield shifts in protons inside the rotaxane cavity (*2* and *a*) consistent with hydrogen bonding between these groups and anions (Figure 4.7). Proton *b* on the stopper group adjacent to the triazolium group also moves downfield upon addition of chloride anion, suggesting its involvement in anion recognition, although, interestingly proton *c* moves upfield when chloride is added. Hydroquinone resonances *3* and *4* shift upfield, suggesting enhanced donor–acceptor interactions upon anion complexation. Addition of bromide, iodide or acetate anions cause similar shifts to those observed upon addition of chloride, although the magnitude of the movement is smaller for iodide, and particularly, acetate (Figure 4.8).

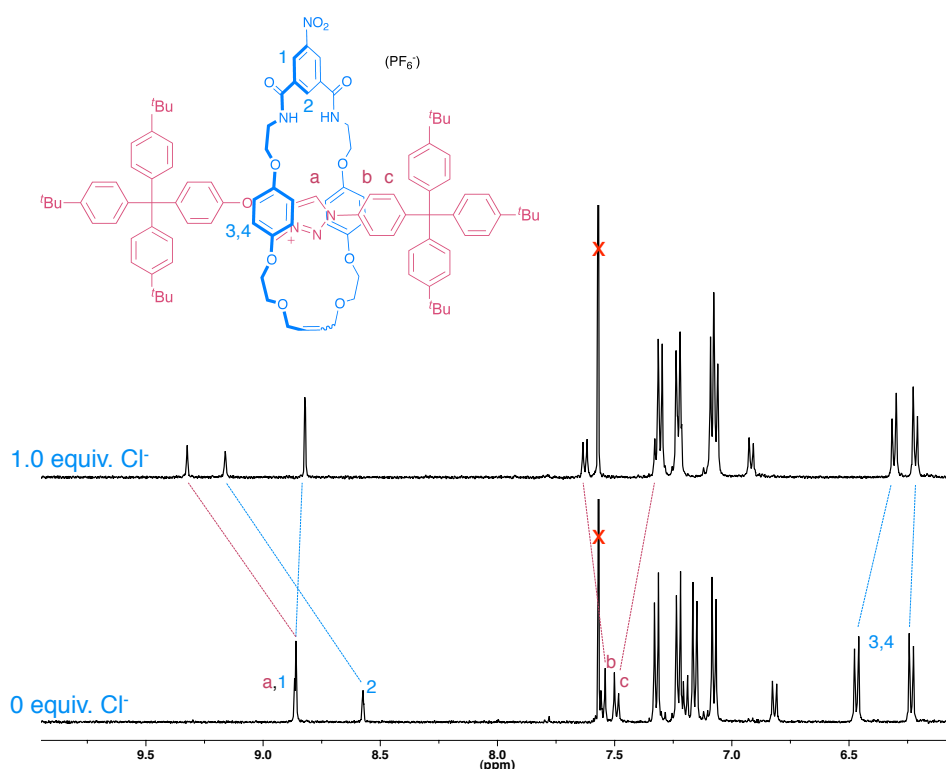


Figure 4.7: Truncated ¹H NMR spectra of **50**·PF₆ upon addition of TBA·Cl. Peak labelled x corresponds to residual CHCl₃ solvent signal, unlabelled peaks belong to bulky stopper groups (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

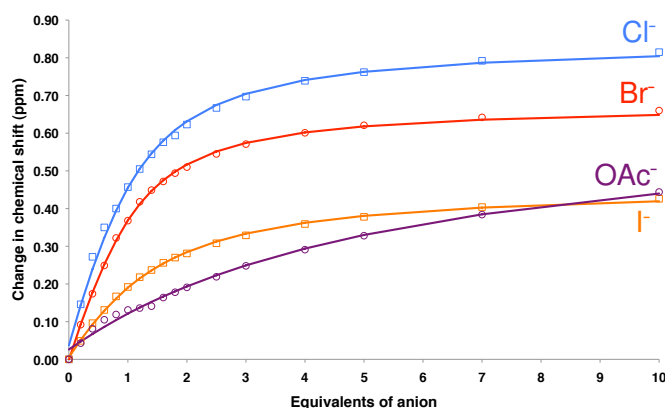


Figure 4.8: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **50**·PF₆, following interior phenylene resonance (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

WINEQNMR2³²⁸ was used to determine 1:1 stoichiometric association constants, monitoring the interior phenylene proton **2**. As shown in Table 4.1, rotaxane **50**·PF₆ displays impressive discrimination between halide anions and the basic oxoanion acetate. Both chloride and bromide are bound strongly, and there is a significant preference for these anions over larger iodide. The pronounced bromide selectivity reported for **40**⁺²⁴⁵ is not observed.

Table 4.1: Association of anions with **50**·PF₆.

Anion	K_a (M ⁻¹) ^a
Cl ⁻	1114(109)
Br ⁻	1322(21)
I ⁻	566(23)
OAc ⁻	92(15)

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K).

Very small single crystals of **50**·Cl were obtained, suitable for synchrotron X-ray structural analysis; the data are of poor quality, but allow unambiguous determination of the structure. The axle component is disordered end-to-end: this was modelled by having two positions for all atoms between the two bulky stopper groups (the occupancies of each position refined to 0.5). The chloride anion is bound inside the rotaxane cavity (Figure 4.9), forming hydrogen bonds to amide and phenylene donors from the macrocycle and the axle component's triazolium group. One of the hydrogen bonds to an amide

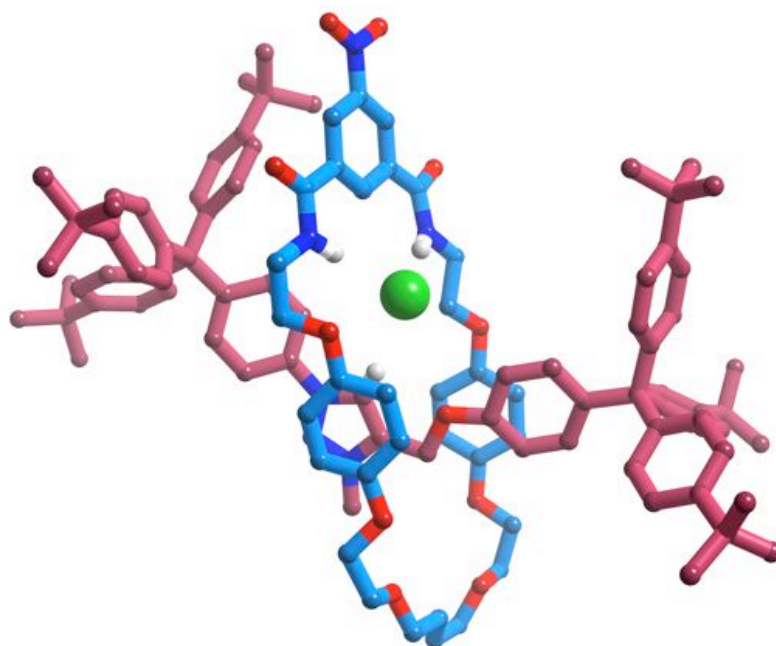


Figure 4.9: Solid state structure of **50**·Cl. Most hydrogen atoms and end-to-end disorder of axle component omitted for clarity.

proton is very strong [$N \cdots Cl = 3.245(9) \text{ \AA}$, $\angle N-H \cdots Cl = 180^\circ$, $\%VdW_{H,Cl} = 83$], while the others are weaker ($\%VdW_{H,Cl} = 91\text{--}95$). No hydrogen bond is observed between the stopper phenylene proton adjacent to the triazolium group and the chloride anion in the solid state. Only very weak pyridinium $\cdots$ hydroquinone contacts are observed [closest centroid $\cdots$ centroid = $3.846(8) \text{ \AA}$], and only one weak pyridinium-methyl $\cdots$ polyether hydrogen bond is present ($\%VdW_{H,O} = 96\%$).

4.2.4.2 Bis-aryl substituted rotaxane

The anion recognition properties of **51**·PF₆ were also investigated using ¹H NMR titration experiments in polar 1:1 CDCl₃:CD₃OD solvent mixture. Addition of anions to the interlocked host causes downfield shifts in protons inside the interlocked cavity (*2*, *3* and *a*) consistent with hydrogen bonding between these groups and anions (Figure 4.10); stopper phenylene proton *b* also moves downfield. Hydroquinone resonances *4* and *5* again shift upfield, suggesting enhanced donor–acceptor interactions upon anion complexation. Addition of bromide, iodide or acetate anions cause similar shifts to those observed upon

addition of chloride, although the magnitude of the movement is smaller for iodide and acetate (Figure 4.11).

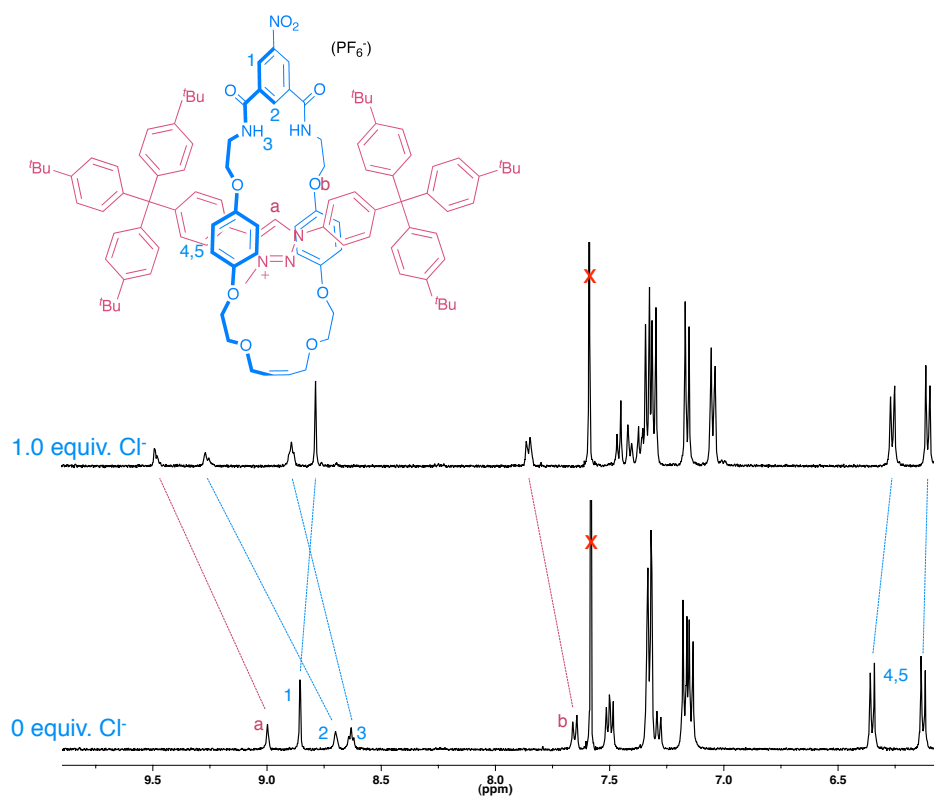


Figure 4.10: Truncated ^1H NMR spectra of **51**· PF_6 upon addition of TBA·Cl. Peak labelled x corresponds to residual CHCl_3 solvent signal, unlabelled peaks belong to bulky stopper groups (1:1 CDCl_3 : CD_3OD , 293 K, 500 MHz).

WINEQNMR2 was used to calculate 1:1 stoichiometric anion association constants, monitoring the triazolium phenylene proton *a*. As shown in Table 4.2, rotaxane **51**· PF_6 again displays impressive discrimination between halide anions and the basic oxoanion acetate. As with **50**· PF_6 , both chloride and bromide are bound strongly, and there is a significant preference for these anions over larger iodide; recognition of all anions is slightly stronger than was the case with **50**· PF_6 .

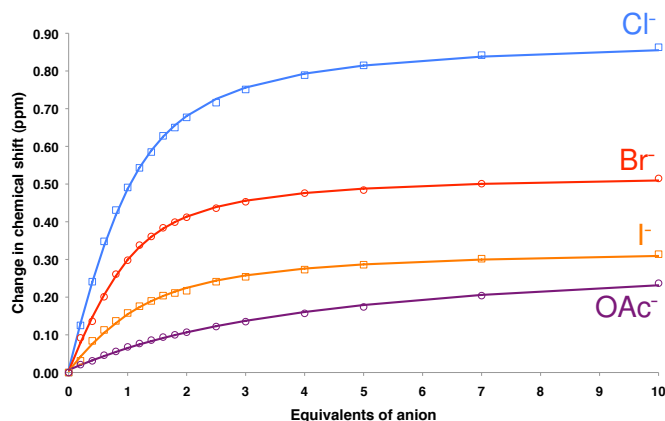


Figure 4.11: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **51**·PF₆, following triazolium resonance (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

Table 4.2: Association of anions with **51**·PF₆.

Anion	K_a (M ⁻¹) ^a
Cl ⁻	1287(50)
Br ⁻	1455(76)
I ⁻	772(62)
OAc ⁻	126(10)

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K).

Small single crystals of **51**·Cl were obtained, suitable for synchrotron X-ray structural analysis. The halide anion is bound inside the rotaxane cavity (Figure 4.12), forming hydrogen bonds to amide and phenylene donors from the macrocycle and the axle component's triazolium group. No significant hydrogen bonding is observed with the phenylene protons of either stopper group. There are two strong hydrogen bonds: from the triazolium group [C···Cl = 3.410(5) Å, ∠C–H···Cl = 168°, %VdW_{H,Cl} = 86] and from one of the amide groups [N···Cl = 3.256(7) Å, ∠N–H···Cl = 155°, %VdW_{H,Cl} = 85]. Hydrogen bonds from the other amide and phenylene proton are weaker (%VdW_{H,Cl} = 97 and 94, respectively). Moderately strong pyridinium···hydroquinone contacts are observed in the solid state [centroid···centroid = 3.657(4) and 3.657(4) Å], as well as one pyridinium-methyl···polyether hydrogen bond (%VdW_{H,O} = 90%).

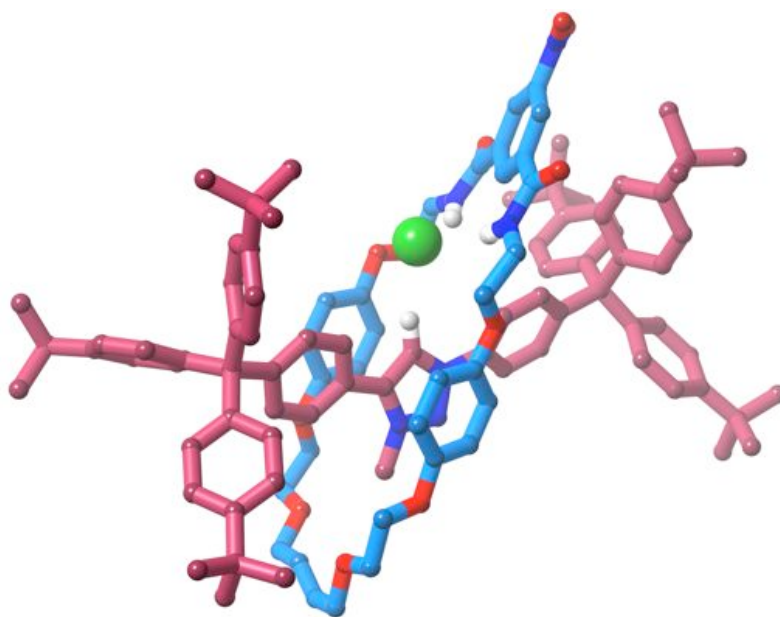


Figure 4.12: Solid state structure of **51**·Cl. Methanol solvate and most hydrogen atoms omitted for clarity.

4.2.5 Discussion of recognition strengths of rotaxanes

The three rotaxanes **40**·PF₆,²⁴⁵ **50**·PF₆ and **51**·PF₆ all have the same macrocyclic component and a triazolium containing axle component. The only difference between them is the nature of the substitution of this triazolium group, and these similarities allow a detailed comparison of their anion affinities to be made (Table 4.3). Both the new systems reported herein display very similar anion affinity trends (Cl⁻ ~ Br⁻ > I⁻ ≫ OAc⁻), which are markedly different than that of the previously reported triazolium rotaxane **40**·PF₆.²⁴⁵

Table 4.3: Association constants, K_a (M⁻¹) of triazolium containing rotaxanes with anions.^a

Anion	40 ·PF ₆	50 ·PF ₆	51 ·PF ₆
Cl ⁻	90 ^b	1114(109)	1287(50)
Br ⁻	970 ^b	1322(21)	1455(76)
I ⁻	420 ^c	566(23)	772(62)
OAc ⁻	40 ^c	92(15)	126(10)

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K). ^bValues taken from Ref. 245. ^cValues taken from Ref. 371.

Given that the level of halide selectivity displayed by **40**⁺ is unprecedented for an interlocked anion receptor in solvent containing significant amounts of methanol or water (see Section 1.3.3.3), the anion recognition properties of this host were revisited. The ¹H NMR titration experiments were conducted again using a sample of the rotaxane provided by James Mercurio. The resulting association constants (determined using WINEQNMR2,³²⁸ following the interior phenylene proton) are displayed in Table 4.4, along with the values determined for **50**·PF₆ and **51**·PF₆. The re-calculated values for **40**⁺ follow a similar trend to the other two triazolium containing rotaxanes, although binding is significantly weaker for this host system, and indeed, the re-calculated anion recognition properties of **40**·PF₆ are similar to those reported for closely-related rotaxanes containing alkyl-substituted 2-methylimidazolium and 4,5-dimethylimidazolium axle components.²⁴⁴

Table 4.4: Association constants, K_a (M⁻¹) of triazolium containing rotaxanes with anions.^a

Anion	40 ·PF ₆	50 ·PF ₆	51 ·PF ₆
Cl ⁻	424(20)	1114(109)	1287(50)
Br ⁻	423(14)	1322(21)	1455(76)
I ⁻	350(16)	566(23)	772(62)
OAc ⁻	42(3) ^b	92(15)	126(10)

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K). ^bValue taken from Ref.³⁷¹.

Table 4.4 shows that replacing the triazolium’s alkyl substituents with aryl significantly increases the binding strength of the rotaxane host architecture. The aryl-substituted rotaxanes also display some degree of preference for the smaller halide anions chloride and bromide over larger iodide. Chloride and bromide are bound with association constants approximately twice as large as iodide by **50**·PF₆ and **51**·PF₆, while **40**·PF₆ displays negligible discrimination between the halides.

Two possible effects could explain the increased halide anion binding affinities of **50**·PF₆ and **51**·PF₆ compared to **40**·PF₆: the greater acidity of the aryl-substituted triazolium group, and/or increased preorganization provided by the shorter, more rigid axle component. To try and separate these two possible effects, the anion recognition

strengths of the three axle components (**41**⁺, **42**⁺ and bis alkyl-substituted axle **52**⁺) were investigated using ¹H NMR titration experiments.

Anion binding by the axle components in 1:1 CDCl₃:CD₃OD was too weak to give useful data, and so experiments were conducted in 9:1 CDCl₃:CD₃OD. Addition of anions to the axle components as their tetrafluoroborate salts results in significant downfield shifts of triazolium resonance *c*, as well as a very small change in the environment of the alkyl or aryl proton adjacent to this group (resonance *d* in Figure 4.13). Quantitative 1:1 stoichiometric association constants were calculated for all three axle components using WINEQNMR2,³²⁸ monitoring the axle's triazolium proton.

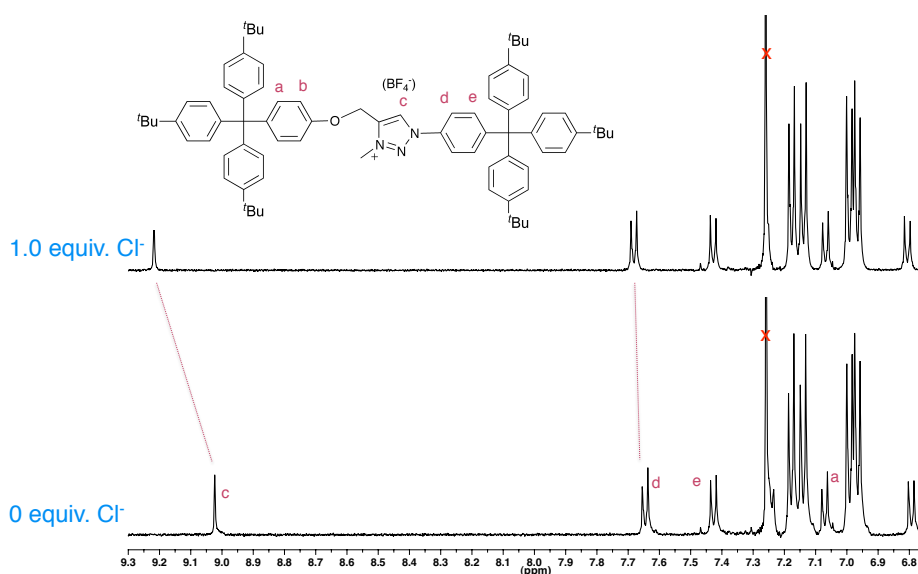


Figure 4.13: Truncated ¹H NMR spectra of **41**·BF₄ upon addition of TBA·Cl. Peak labelled x corresponds to residual CHCl₃ solvent signal, unlabelled peaks belong to bulky stopper groups (9:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

As shown in Table 4.5 and Figure 4.14, there is essentially no difference between the anion recognition strengths of the three axle components, and no axle shows any significant selectivity between the halides.[†]

These results are surprising, as the introduction of aryl substituents would be expected to increase the acidity of the triazolium proton, and hence guest binding strength, as was observed with *triazole* receptors (Chapter Two). We tentatively suggest that with the cationic *triazolium* motif, an electrostatic effect is also important. Aryl-substituted

[†]Titration experiments with acetate anion showed that this guest was also complexed approximately as strongly as the halides.

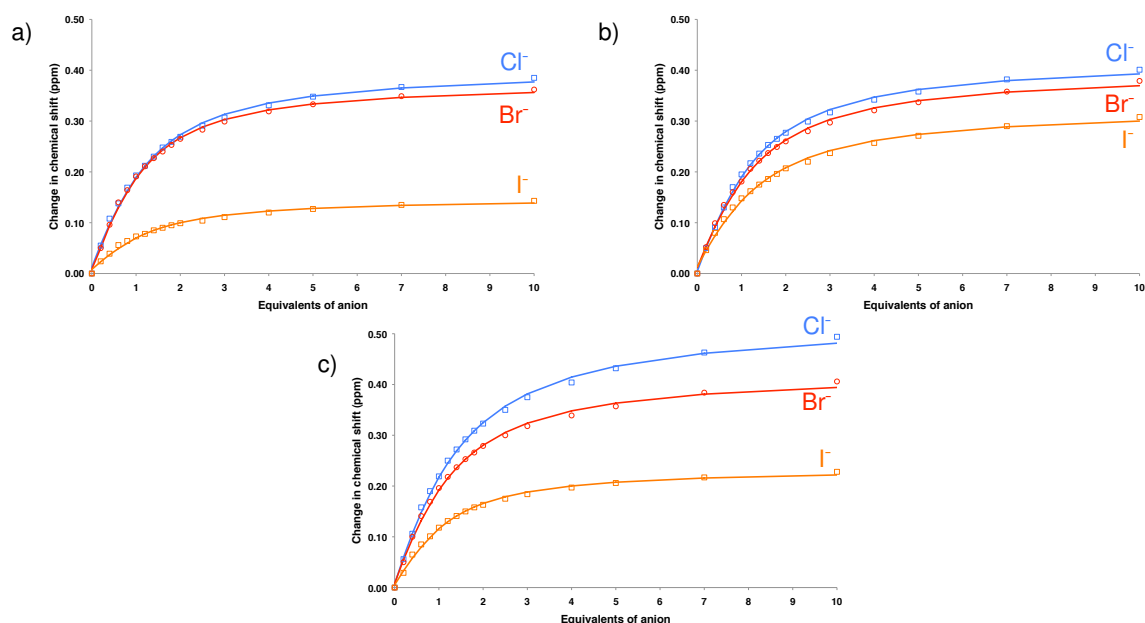


Figure 4.14: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to a) **52**·BF₄, b) **41**·BF₄, and c) **42**·BF₄ following triazolium resonance (9:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

Table 4.5: Association constants, K_a (M⁻¹) of triazolium containing axle components with anions.^a

Anion	52 ·BF ₄	41 ·BF ₄	42 ·BF ₄
Cl ⁻	735(55)	701(38)	552(33)
Br ⁻	891(60)	672(50)	688(20)
I ⁻	681(84)	584(54)	869(14)

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNM218³²⁸ (9:1 CDCl₃:CD₃OD, 293 K).

triazolium groups delocalize the positive charge, thus while alkyl-substituted axle component **52**⁺ is the weakest hydrogen bond donor, it has the most localized positive charge, and thus the greatest electrostatic attraction for an anion.

Whatever the causes, all axle components of each of the three triazolium containing rotaxanes have very similar anion binding strengths and selectivities, and the macrocyclic component is the same in all cases. This suggests that the observed differences in the anion recognition properties of the rotaxane host systems are not a result of the inherent binding characteristics of the rotaxane components, but rather the interaction between the components, where the level of *inter-component* preorganization plays an important role.

While the macrocycle resides over the triazolium group of the axle component in the solid state structures, in solution the rotaxane is dynamic with the wheel moving about the axle. The smaller and more compact the axle component, the fewer degrees of freedom are available to the macrocycle in the interlocked structure, hence the respective rotaxane is more preorganized for anion binding. In **50**·PF₆ and **51**·PF₆, the macrocycle is constrained to remain reasonably close to the triazolium group by the proximal bulky stopper groups, dramatically increasing halide anion binding affinity in comparison to the less preorganized and more flexible bis-alkyl triazolium axle containing rotaxane **40**·PF₆.

An interesting comparison of the anion binding affinities of the interlocked hosts reported in this Chapter with two pyridinium bis-amide rotaxanes (Figure 4.15) can be made. Pyridinium bis-amide rotaxane **53**·PF₆, which contains the same macrocyclic component as triazolium rotaxanes **50**·PF₆ and **51**·PF₆ displays comparable chloride association in 1:1 CDCl₃:CD₃OD to these triazolium hosts ($K_a = 4500 \text{ M}^{-1}$)³⁰¹ despite containing an axle component with three potentially strong hydrogen bond donors (*para*-pyridinium and two amides) compared with one triazolium donor in the axles of **50**⁺ and **51**⁺. This may be a result of the smaller axle component in the triazolium containing rotaxanes being more preorganized for anion recognition, or of the axle's positive charge being closer to the anion binding cavity and therefore increasing electrostatic interactions.

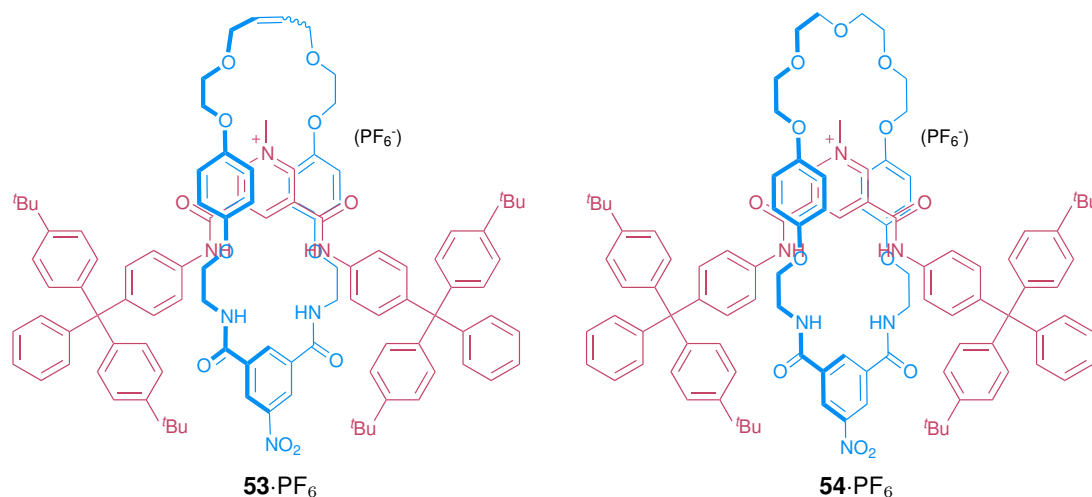


Figure 4.15: Previously reported pyridinium bis-amide rotaxanes.^{233,236}

On the other hand, rotaxane **54**·PF₆ exhibits very strong chloride binding in 1:1 CDCl₃:CD₃OD ($K_a > 10^4 \text{ M}^{-1}$).²³⁶ It would appear that the enhanced

pyridinium-methyl...polyether hydrogen bonding interactions available in **54**⁺ through the penta-oxy polyether chain help to constrain the macrocycle in place, which facilitates the preorganization of the interlocked cavity for anion recognition.[‡] It is noteworthy that in both the pyridinium bis-amide and triazolium containing rotaxanes, very small structural changes have a dramatic influence on the anion binding properties of the interlocked system. This is consistent with results described in Chapter Three, which showed that the anion binding properties of catenanes and rotaxanes depended on more than the respective anion recognition strengths of the individual components.

4.3 Varying the macrocyclic component

4.3.1 Introduction

To investigate whether the observed increased anion binding strength of triazolium containing rotaxanes with smaller axle components could be amplified still further, and to study the possibility of increasing the selectivity for the smaller halide anions, a new rotaxane consisting of the bis-aryl substituted axle component **42**⁺ and a smaller sized macrocycle was targeted. It was hoped that a smaller macrocycle may further minimize motion of this component, effectively “trapping” it in an ideal co-conformation for anion complexation. The synthesis of a rotaxane incorporating the longer, flexible bis-alkyl substituted axle component **52**⁺ and a smaller macrocycle was also attempted, in the hope that the relative contributions of axle and macrocycle size to rotaxane binding strength and selectivity could be assessed.

Very recently, it was reported that a small isophthalamide macrocycle formed stronger chloride anion templated pseudorotaxanes with a methylimidazolium threading component, and it was implied that the corresponding rotaxane host displayed greater chloride recognition than those containing a larger macrocycle.³⁵⁶ Increased yields of rotaxanes prepared by an active metal route have also been reported when using smaller macrocycles.³⁶⁶

[‡]Several attempts to prepare triazolium rotaxanes containing a similar penta-oxy macrocycle *via* amide condensation were unsuccessful, giving extremely low yields (< 2%) of interlocked molecule.

In order to allow direct comparisons with the rotaxanes prepared in the previous Section, a smaller analogue of macrocycle precursor **35** was targeted (Figure 4.16). This new macrocycle precursor **55** is four atoms smaller than **35** and retains the key features of this compound: namely, a nitro-substituted isophthalamide motif for anion recognition, electron-rich aromatic rings suitable for donor–acceptor interactions with the electron-deficient triazolium motif, and vinyl groups to allow rotaxane synthesis *via* RCM.

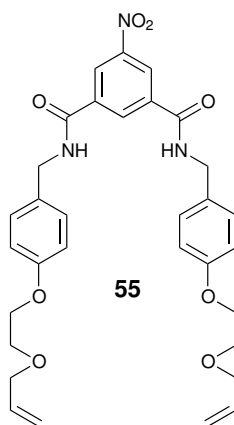
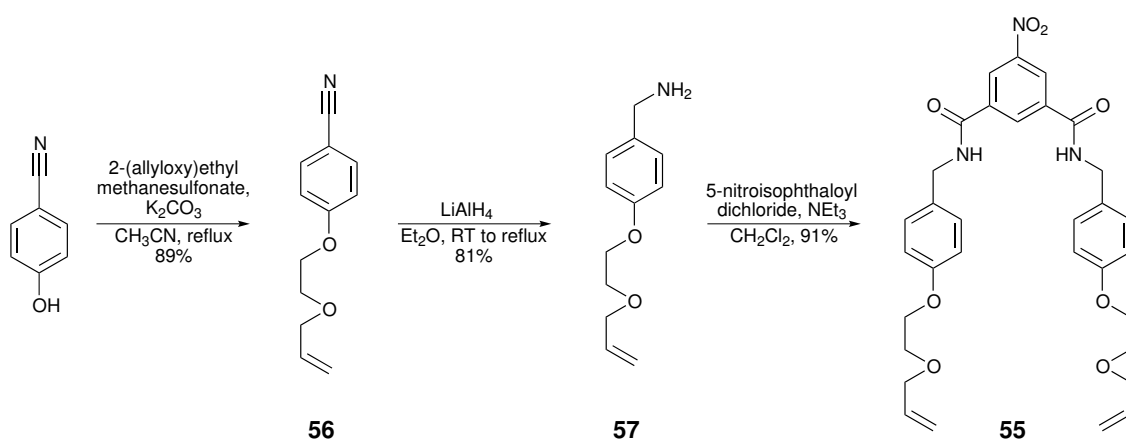


Figure 4.16: Targeted small macrocycle precursor **55**.

4.3.2 Synthesis of smaller macrocycle precursor

The smaller macrocycle precursor **55** was prepared as shown in Scheme 4.6. Commercially available 2-(allyloxy)ethanol was converted to the corresponding mesylate derivative, and then reacted with 4-cyanophenol in refluxing acetonitrile to give vinyl-appended nitrile **56** in 89% yield. This was reduced to the corresponding amine **57** using lithium aluminium hydride in 81% yield. 5-Nitroisophthalic acid was converted to the corresponding acid chloride using refluxing thionyl chloride, and then condensed with 2.2 equivalents of **57** to give the macrocycle precursor in good yield (89%).

Small quantities of the closed macrocycle **58** were isolated as by-products of rotaxane formation reactions (see later). This allowed the macrocycle to be characterized by ^1H and ^{13}C NMR spectroscopy, as well as by high resolution ESI mass spectrometry. Single crystals were also obtained, allowing characterization by X-ray diffraction structural analysis. In the solid state (Figure 4.17), the amide groups adopt an approximately *syn-syn*



Scheme 4.6: Synthesis of macrocycle precursor **55**.

conformation, but are twisted out of the plane of the isophthalamide ring, allowing packing through N–H···O and N–H··· π close contacts.

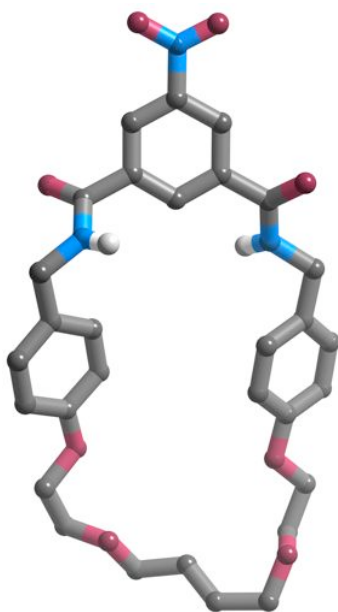
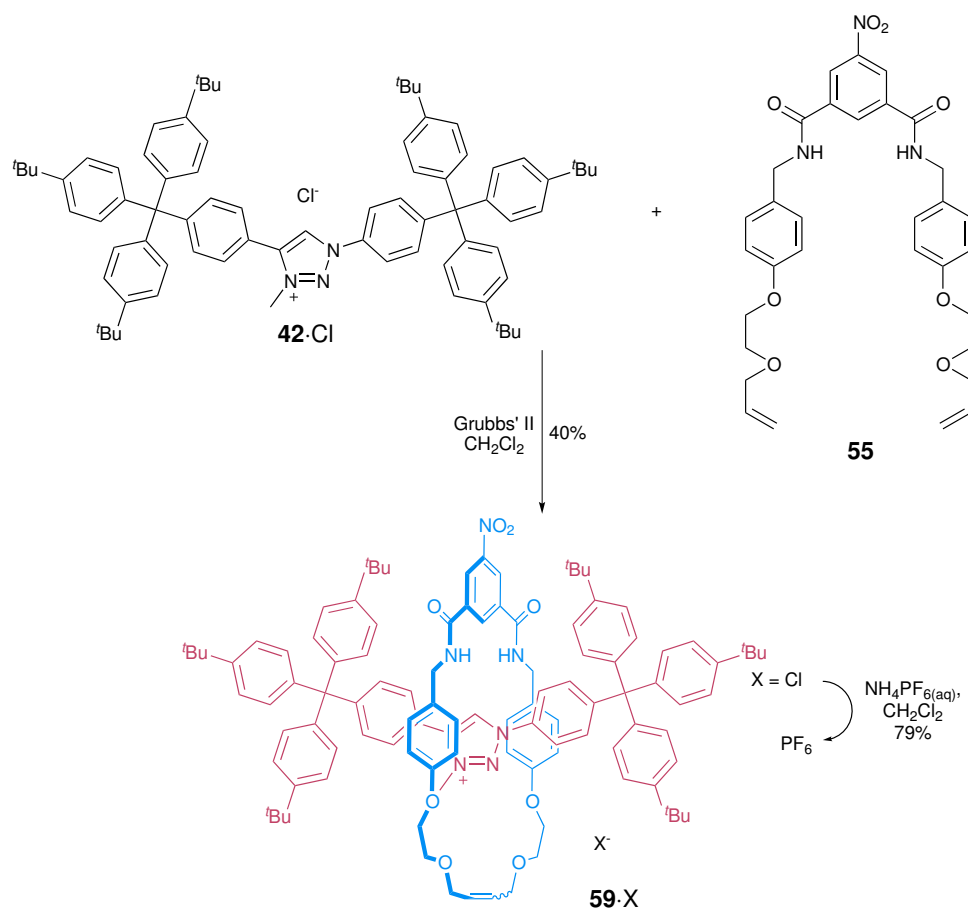


Figure 4.17: Solid state structure of **58**. Alkene disorder, and most hydrogen atoms are omitted for clarity.

4.3.3 Rotaxane synthesis

Chloride anion templated Grubbs' II-catalyzed RCM reaction of new macrocycle precursor **55** and triazolium axle component **42**·Cl gave the novel rotaxane **59**·Cl in 40% yield after purification by preparative TLC and recrystallization (Scheme 4.7). The templating anion was removed by repeated washing with $\text{NH}_4\text{PF}_6(\text{aq})$ to give **59**· PF_6 suitable for use in anion

recognition experiments. The interlocked host molecule was characterized by ^1H , ^{13}C , ^{19}F and ^{31}P NMR spectroscopy, as well as by high resolution ESI mass spectrometry.



Scheme 4.7: Synthesis of rotaxane **59**· PF_6 .

The interlocked nature of **59** $^+$ was confirmed by 2D ROESY NMR spectroscopy. Inter-component couplings are observed between the macrocycle's phenol resonance *2*, and alkene group *3*, and triazolium-methyl motif *a*, as well as between interior phenylene proton *1* and triazolium resonance *b*.

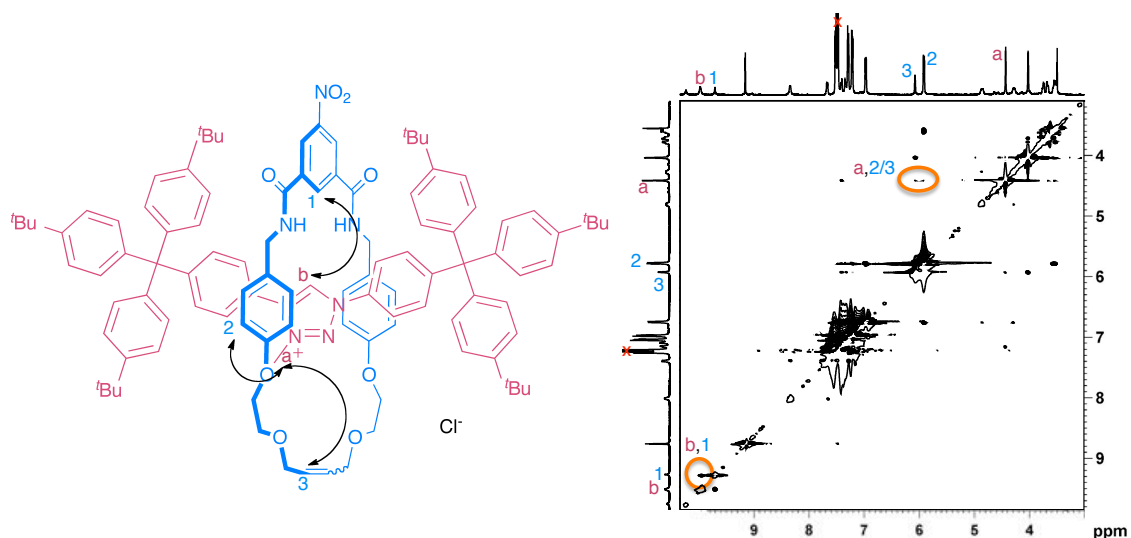
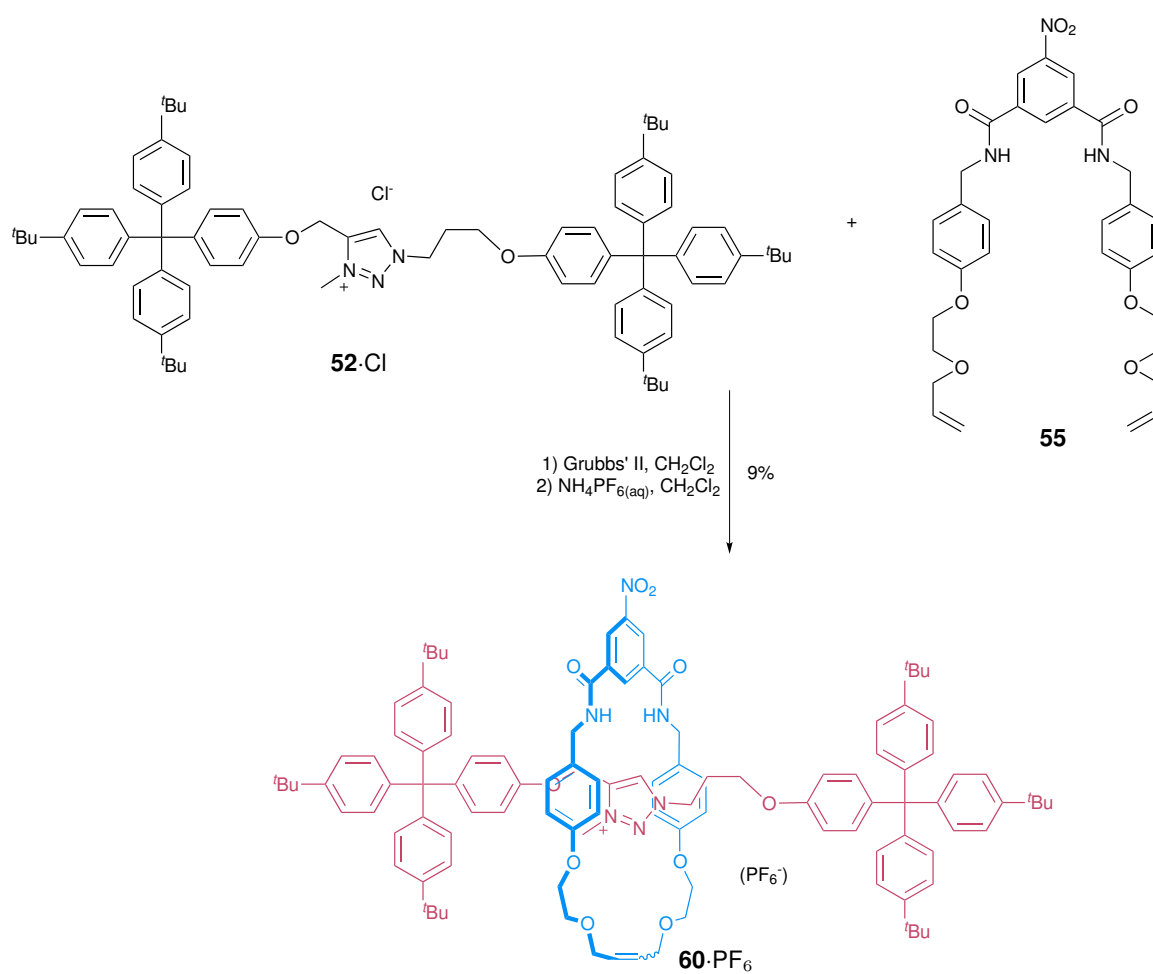


Figure 4.18: Truncated 2D ROESY NMR spectrum of **59**·Cl showing selected inter-component couplings (CDCl₃, 293 K, 500 MHz).

Chloride anion templated Grubbs' II-catalyzed RCM reaction of new macrocycle precursor **55** and bis-alkyl substituted triazolium axle component **52**·Cl gave the new rotaxane **60**·Cl in 9% yield after purification by preparative TLC and recrystallization, and anion exchange to the hexafluorophosphate salt (Scheme 4.8). While only a small amount of material could be isolated due to the low yield, this was sufficient to allow characterization by ¹H (Figure 4.19), ¹³C, ¹⁹F NMR spectroscopy, and by high resolution ESI mass spectrometry, as well as an initial investigation of the rotaxane's anion recognition properties.



Scheme 4.8: Synthesis of rotaxane **60**·PF₆.

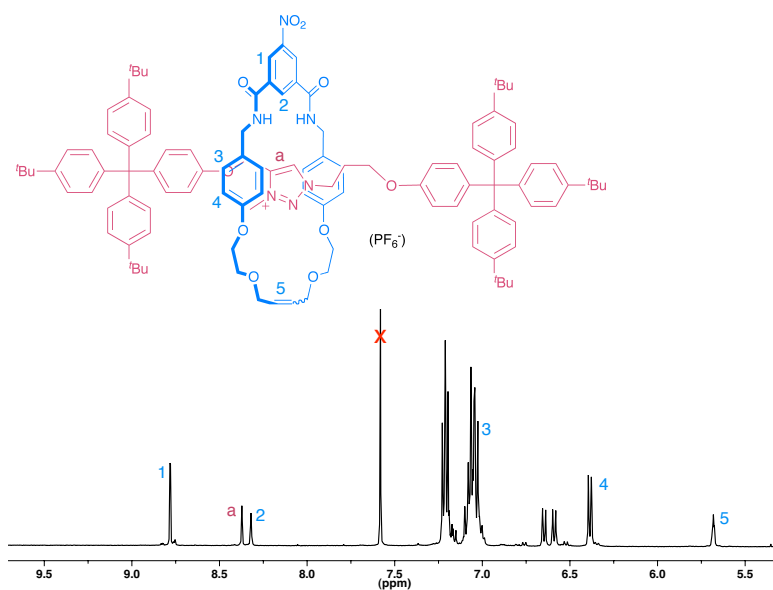


Figure 4.19: Truncated ¹H NMR spectrum of **60**·PF₆. Peak labelled x corresponds to residual CHCl₃ solvent signal, unlabelled peaks belong to bulky stopper groups (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

4.3.4 Anion recognition properties

The anion recognition properties of **59**·PF₆ were investigated using ¹H NMR titration experiments. Addition of halide anions caused downfield shifts in resonances *a* and *2* corresponding to the triazolium signal and interior C–H macrocycle proton, respectively (Figure 4.20). Notably, these shifts are smaller in magnitude than in rotaxanes **50**⁺ and **51**⁺ containing the larger macrocycle (Figures 4.7 and 4.10).

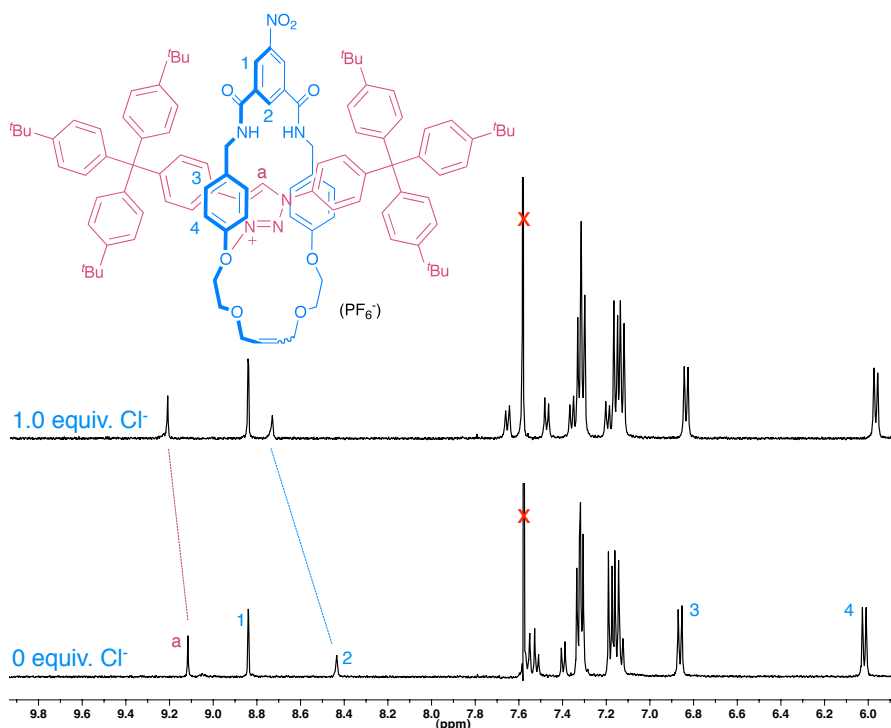


Figure 4.20: Truncated ¹H NMR spectra of **59**·PF₆ upon addition of TBA·Cl. Peak labelled x corresponds to residual CHCl₃ solvent signal, unlabelled peaks belong to bulky stopper groups (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

As shown in Table 4.6 and Figure 4.21, **59**·PF₆ retains the impressive selectivity for halide anions over acetate displayed by other triazolium based rotaxanes, with addition of the oxoanion causing almost no movement of the cavity proton resonances. The halide anion affinity of **59**·PF₆, however, is significantly lower than that of **50**·PF₆ and **51**·PF₆.

Table 4.6: Association of **59**·PF₆ with anions.

Anion	K_a (M ⁻¹) ^a
Cl ⁻	500(47)
Br ⁻	612(49)
I ⁻	402(12)
OAc ⁻	— ^b

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K). ^bShifts too small to calculate association constant (< 0.05 ppm after 10 equivalents of TBA·OAc).

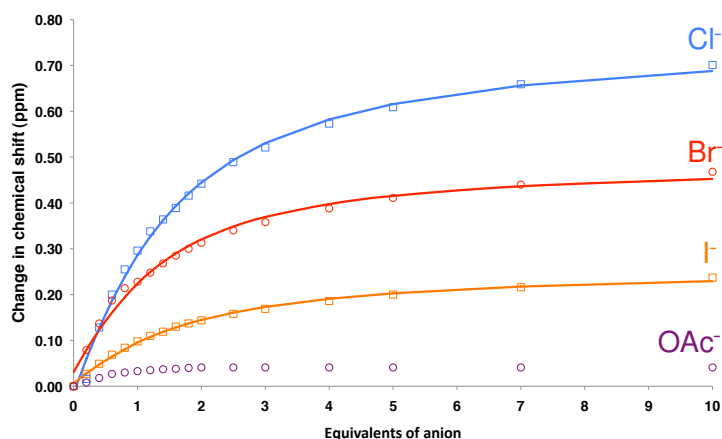


Figure 4.21: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **59**·PF₆ following triazolium resonance (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

The X-ray single crystal structure of **59**·Cl (Figure 4.22) provides some clues to this observed weaker binding. The macrocycle buckles substantially to accommodate the halide anion, and it would appear that this component is too small for the chloride anion to be encapsulated within the interlocked host cavity and at the same time facilitate favourable donor–acceptor interactions between the phenolic rings of the macrocycle and the axle component’s triazolium motif (closest centroid···centroid contact = 4.3 Å). This buckling is not observed in either **50**·Cl or **51**·Cl, which contain a larger macrocycle. It is suggested that the observed decreased halide binding affinity of **59**·PF₆ occurs because complexation of the anion necessitates a weakening of these favourable “secondary” interactions between the axle and macrocycle. A titration experiment was conducted to see if the smaller fluoride anion could be bound effectively by the host, but only very weak binding was observed.

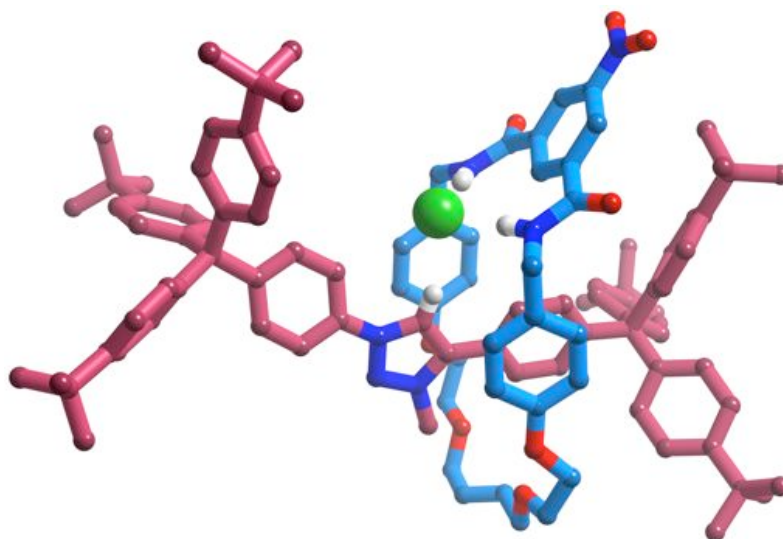


Figure 4.22: Solid state structure of **59**·Cl. Most hydrogen atoms omitted for clarity.

The chloride and iodide anion recognition properties of **60**·PF₆ were also investigated using quantitative ¹H NMR titration experiments (insufficient material was isolated to allow titration experiments with other anions). In both cases, anion binding was weak [257(10) and 275(15) M⁻¹ for chloride and iodide, respectively], presumably as a result of the macrocycle component being free to move along and about the axle component, *and* anion recognition requiring weakening of donor–acceptor interactions due to the small macrocyclic component.

4.4 Incorporating additional donors into axle components

4.4.1 Introduction

Given the significantly improved anion binding strengths and selectivities that were achieved simply by varying the nature of substitution of a triazolium group in triazolium containing rotaxanes, it was decided to investigate the effect of integrating an additional recognition motif into the axle component. James Mercurio reported a preliminary investigation into this in his Part II thesis,³⁷¹ preparing the triazolium-triazole rotaxane **61**·PF₆ shown in Figure 4.23. Anion recognition studies in 1:1 CDCl₃:CD₃OD (Table 4.7) showed that this additional donor group caused a significant increase in the bromide anion

affinity of the rotaxane, with the chloride and iodide anion recognition properties largely unchanged.

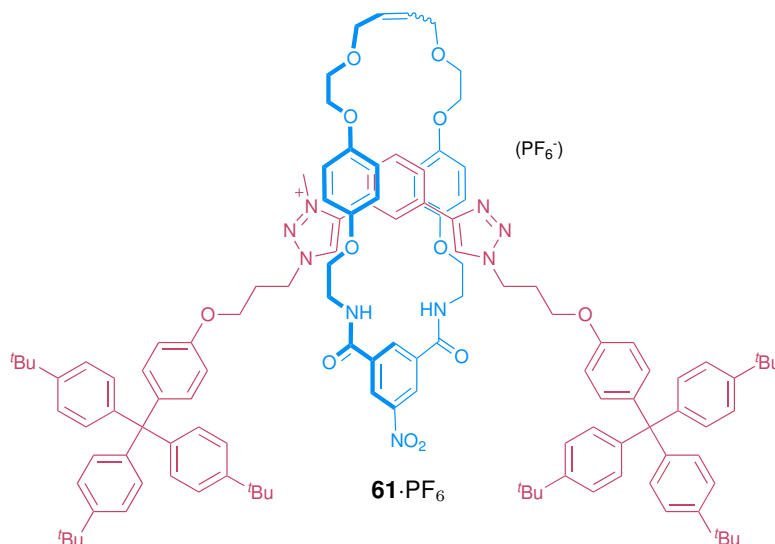


Figure 4.23: Previously reported triazolium rotaxane **61**·PF₆ containing additional anion recognition element in the axle component.³⁷¹

Table 4.7: Association constants, K_a (M⁻¹)^a for anions with **61**·PF₆.³⁷¹

Anion	40 ·PF ₆	61 ·PF ₆
Cl ⁻	424(20) ^b	405
Br ⁻	413(14) ^b	725
I ⁻	350(16) ^b	425

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2.³²⁸ (1:1 CDCl₃:CD₃OD, 293 K). ^bThese values obtained as described in Section 4.2.5.

Based on the results described in Section 4.2, it was decided to attempt the synthesis of rotaxanes with an additional hydrogen bond donor incorporated in the axle component, and with the bulky stopper groups attached directly to the hydrogen bond donor groups: specifically the two new axle components shown in Figure 4.24 were targeted. Axle component **62**⁺ will allow the synthesis of a more preorganized analogue of **61**⁺, which also incorporates an aryl-substituted rather than alkyl-substituted triazole donor. These two modifications will hopefully lead to greatly increased anion recognition strength. Axle component **63**⁺ incorporates both triazolium and amide motifs, and as such represents an interesting comparison with rotaxanes incorporating the pyridinium-3,5-bis(amide) motif

(Figure 4.15), with the axle's positive charge now located much closer to the anion binding cavity.

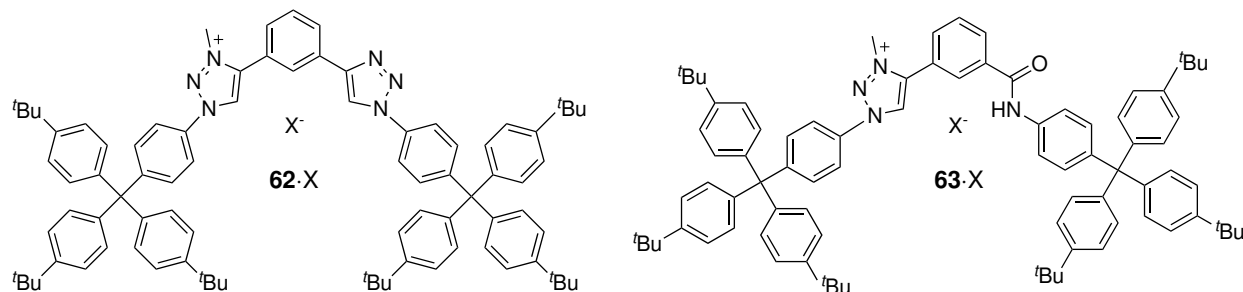
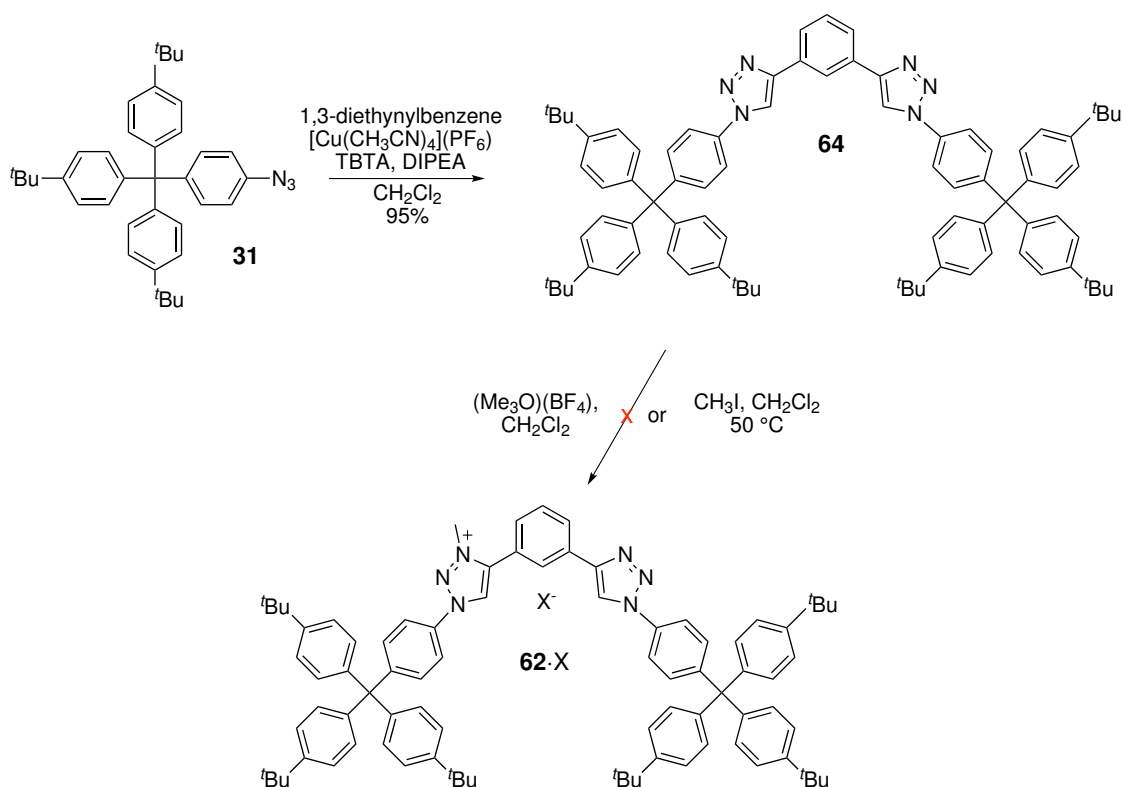


Figure 4.24: Targeted new axle components **62**⁺ and **63**⁺.

4.4.2 Attempted synthesis of aryl-substituted triazole-triazolium axle component **62**·X

The synthesis of **62**⁺ was attempted as outlined in Scheme 4.9. The CuAAC reaction between **31** and 1,3-diethynylbenzene in dichloromethane using [Cu(CH₃CN)₄](PF₆), TBTA and DIPEA gave bis-triazole axle component **64** in 95% yield after purification by column chromatography. Attempts to alkylate **64** proved problematic: the use of 1.1 equivalents of trimethyloxonium tetrafluoroborate as alkylating agent gave almost none of the desired mono-alkylated product, with large amounts of starting material, as well as very poorly soluble doubly-alkylated by-product being isolated after chromatographic purification.



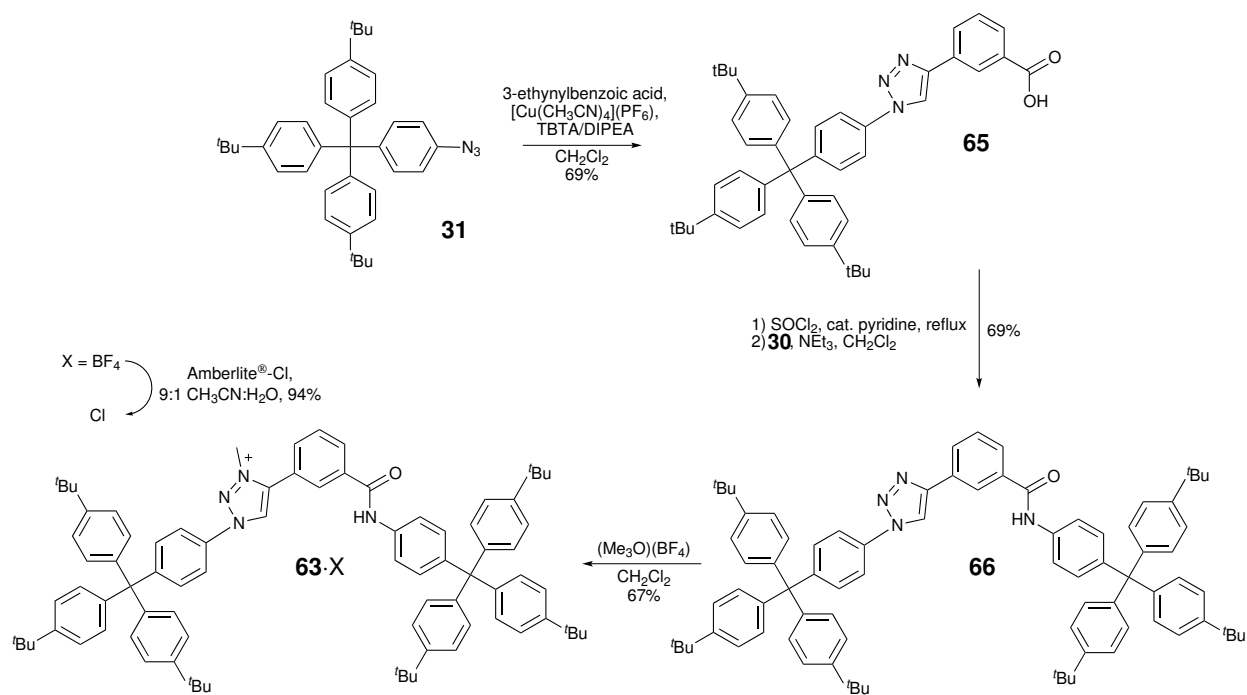
Scheme 4.9: Attempted synthesis of **62·X**.

Schubert and co-workers have reported using methyl iodide in dichloromethane at 50 °C to mono-alkylate compounds similar to **64** [aryl-substituted 1,3-phenylene-bis(triazoles)],²⁷⁷ and so this method was also attempted. Despite the use of a large excess (20 equivalents) of methyl iodide and long reaction time (7 days), only 7% of the desired mono-alkylated axle component was isolated. Given the difficulties in preparing this compound, and its apparent low solubility in organic solvents, attempts to synthesize **62·X** were abandoned, and efforts instead focused on the amide-triazolium axle **63⁺**.

4.4.3 Synthesis of amide-triazolium axle component **63·BF₄**

The synthesis of amide-triazolium axle component **63⁺** was achieved as shown in Scheme 4.10. The CuAAC reaction between azide stopper **31** and commercially available 3-ethynylbenzoic acid in dichloromethane gave acid-appended **65** in 69% yield. This was converted to the acid chloride using refluxing thionyl chloride, and then reacted with aniline-stopper **30** to give the neutral axle component **66**, also in 69% yield. Alkylation

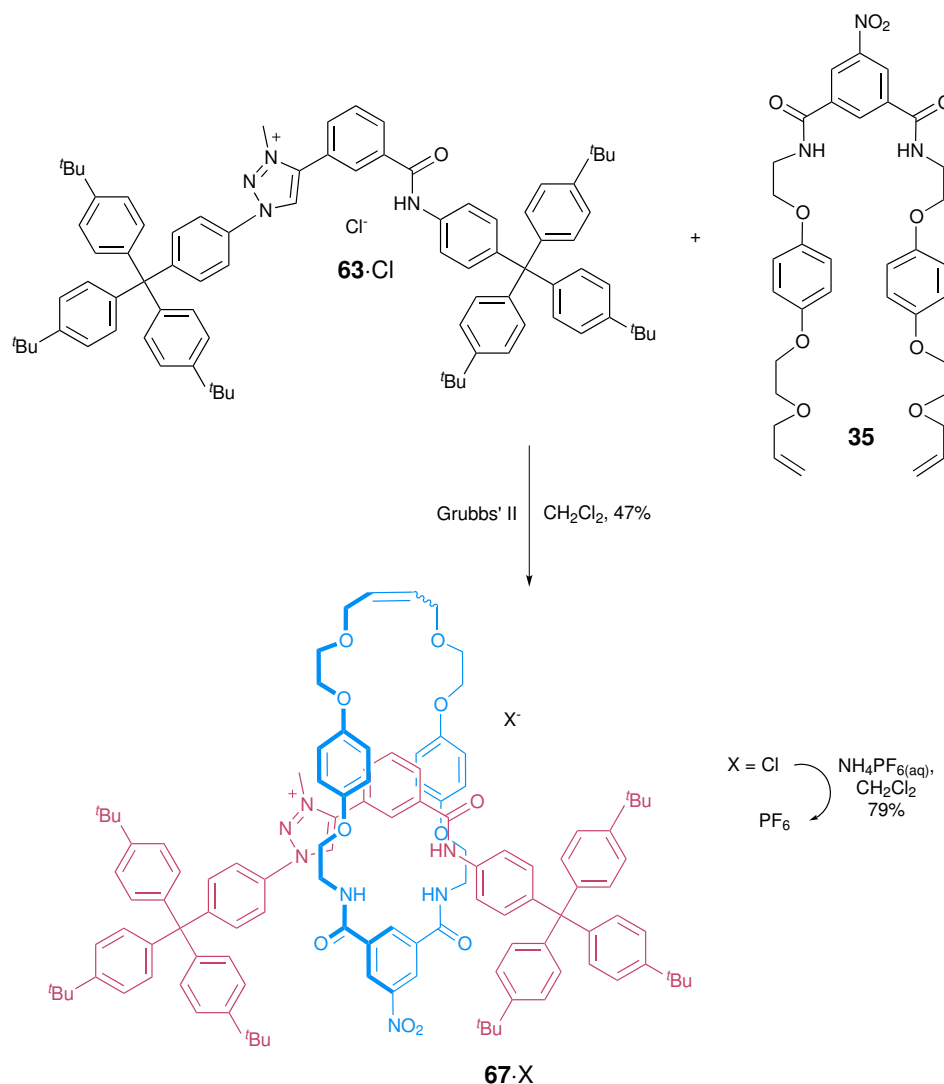
using trimethyloxonium tetrafluoroborate in dry dichloromethane gave **63**·BF₄ in 67% yield, which was converted to the chloride salt, suitable for use in anion templated rotaxane formation using chloride-loaded Amberlite[®] resin in 94% yield.



Scheme 4.10: Synthesis of **63**·Cl.

4.4.4 Synthesis of amide-triazolium rotaxane

Rotaxane **67**⁺ was prepared by the anion templated RCM of **63**·Cl and macrocycle precursor **35** in dichloromethane (Scheme 4.11). Purification *via* preparative TLC and recrystallization gave pure **67**·Cl in 47% yield. Anion exchange to **67**·PF₆ suitable for anion recognition studies was achieved by repeated washing with aqueous NH₄PF₆.



Scheme 4.11: Synthesis of **67**·PF₆.

The new rotaxane was characterized by ¹H, ¹³C, ¹⁹F and ³¹P NMR spectroscopy as well as by high resolution ESI mass spectrometry. The ¹H NMR spectra of the chloride and hexafluorophosphate salts are shown in Figure 4.25: in **67**·Cl, the host's cavity resonances *b*, *c* and *2* are observed significantly downfield compared to **67**·PF₆, consistent

with hydrogen bonding interactions between these protons and the halide anion. The hydroquinone signals in the chloride salt of the rotaxane are shifted upfield relative to the hexafluorophosphate salt, suggesting enhanced donor–acceptor interactions upon anion coordination.

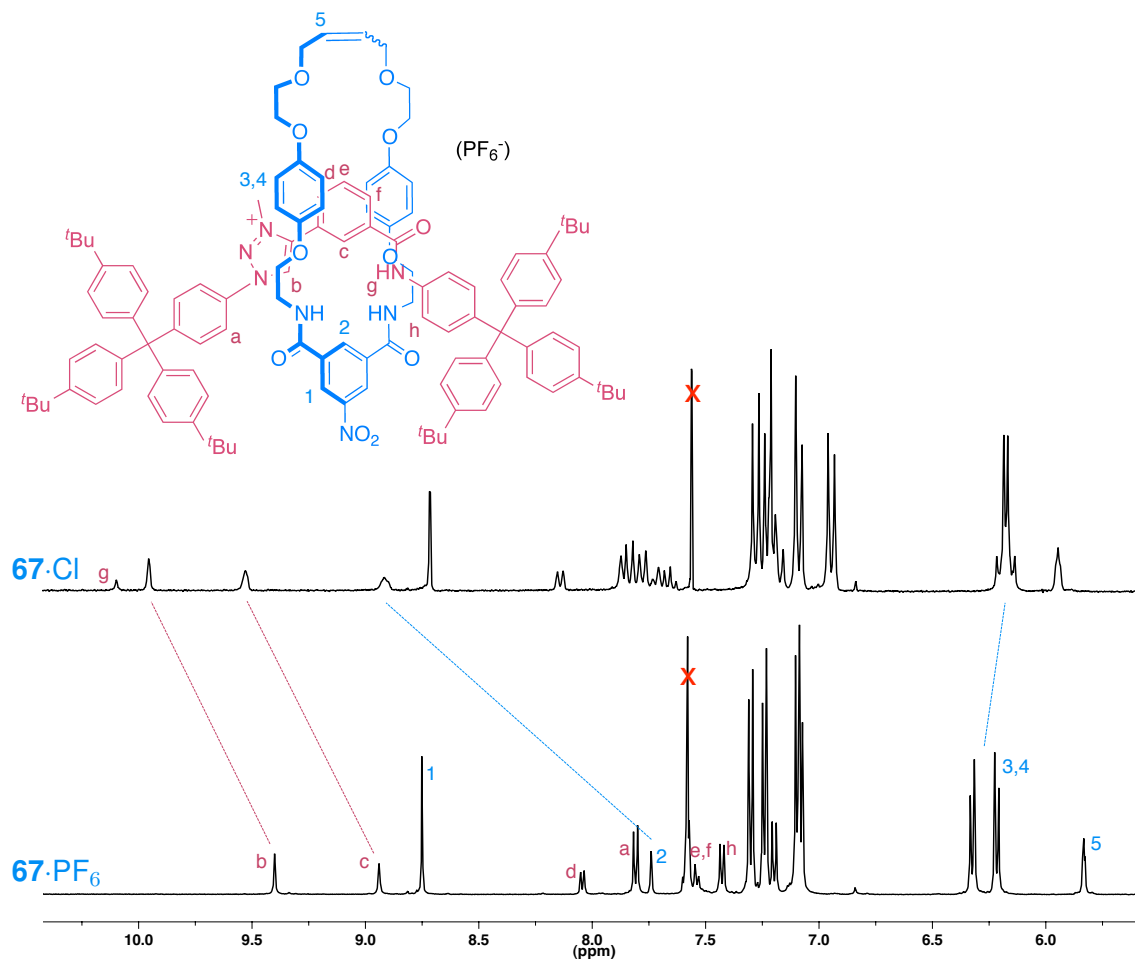


Figure 4.25: Truncated ^1H NMR spectra of **67**·Cl and **67**·PF₆. Peak labelled x corresponds to residual CHCl₃ solvent signal, unlabelled peaks belong to bulky stopper groups (1:1 CDCl₃CD₃OD, 293 K).

The interlocked nature of **67**·PF₆ was confirmed using 2D ROESY NMR spectroscopy (Figure 4.26). A range of inter-component couplings are observed including between macrocycle resonance **1** and the bulky stopper groups, as well as between the hydroquinone rings and triazolium-methyl group and stopper protons.

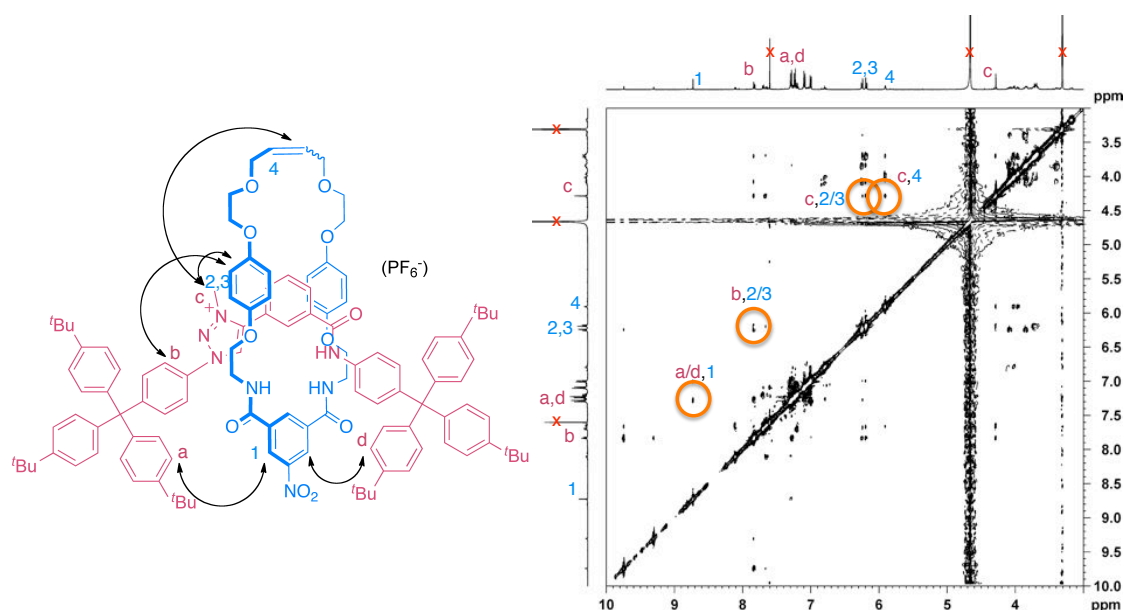


Figure 4.26: Truncated 2D ROESY NMR spectrum of **67**·PF₆ showing selected inter-component couplings. Further couplings involving the macrocycle alkyl protons are not depicted due to the overlap of these signals in the ¹H NMR spectrum (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

4.4.5 Anion recognition properties of **67**·PF₆.

The anion recognition properties of **67**·PF₆ were investigated *via* ¹H NMR titration experiments in the competitive solvent mixture 1:1 CDCl₃:CD₃OD. WINEQNMR2³²⁸ was used to determine 1:1 stoichiometric association constants monitoring the rotaxane's triazolium resonance (Figure 4.27 and Table 4.8).

Both chloride and bromide anions are bound strongly by the rotaxane, with addition of chloride causing significantly larger shifts than bromide. When iodide, acetate or dihydrogen phosphate anions are added to the interlocked receptor, only very small movements of the ¹H NMR signals are observed (less than 0.05 ppm over the course of the titration experiments). The triazolium signal (as well as the axle and macrocycle's interior phenylene protons) moves downfield, and then after 2–3 equivalents of anion begins

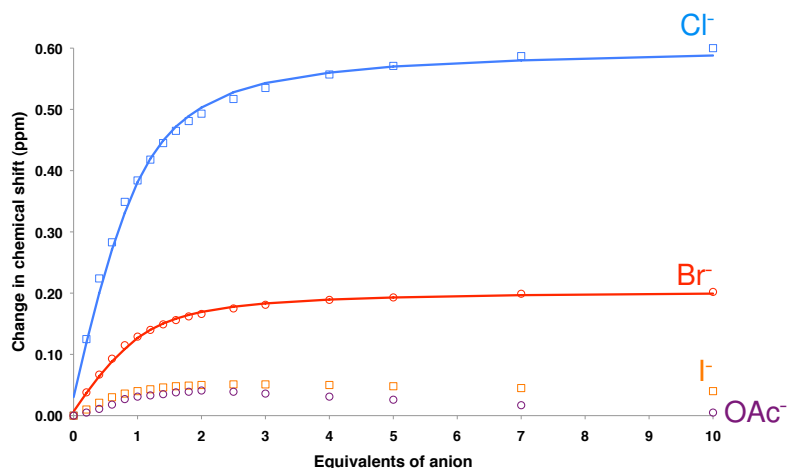


Figure 4.27: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **67**·PF₆ following triazolium resonance (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

Table 4.8: Association of **67**·PF₆ with anions.

Anion	K_a (M ⁻¹) ^a
Cl ⁻	2035(50)
Br ⁻	1948(15)
I ⁻	— ^b
OAc ⁻	— ^b
H ₂ PO ₄ ⁻	— ^{b,c}

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (1:1 CDCl₃:CD₃OD, 293 K). ^bVery small shifts observed, see discussion in text. ^cTitration carried out with an initial host concentration of 1.0 mM due to a lack of material.

to shift upfield. In the case of acetate anion, the triazolium resonance is in almost the same position after ten equivalents of anion as it is before any acetate has been added. Oxoanions typically cause large shifts upon complexation due to their high basicity, hence the very small magnitude of the perturbations suggests no binding is occurring.

It is noteworthy that **67**·PF₆ binds chloride and bromide anions more strongly than any of the triazolium containing rotaxanes reported in this Chapter, due to the additional amide hydrogen bond donor in the axle component. The strong anion complexation that is achieved in competitive 1:1 CDCl₃:CD₃OD solvent mixture demonstrates the potent anion recognition that can be achieved by incorporating triazolium groups into interlocked anion receptors.

Small single crystals of **67**·Br were obtained, suitable for synchrotron X-ray structural analysis. The bromide anion is held within the interlocked cavity (Figure 4.28) by

hydrogen bonds from triazolium, amide and phenylene protons. Hydrogen bonds from the axle triazolium and amide groups are of moderate strength ($\%VdW_{H,Br} = 91$ for both interactions), while the anion sits asymmetrically within the macrocycle, with one strong and one weak hydrogen bond to amide donors ($\%VdW_{H,Br} = 85, 96$). Donor–acceptor interactions are observed between one of the macrocycle’s hydroquinone rings and the central phenylene ring of the axle component [centroid··centroid = 3.660(17) Å] and between the cycle’s other hydroquinone ring and the triazolium group [centroid··centroid = 3.813(9) Å] .

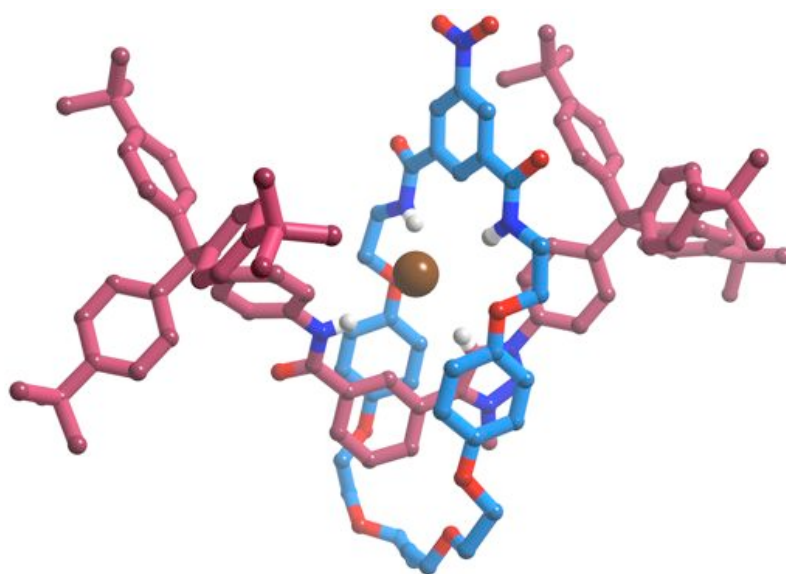


Figure 4.28: Structure of **67**·Br in the crystal. Minor component of macrocycle disorder and most hydrogen atoms omitted for clarity.

4.5 Conclusions

4.5.1 Summary

Two new rotaxanes were prepared containing mono- or bis-aryl substituted triazolium axle components. Anion binding studies revealed that these rotaxanes displayed significantly higher halide anion binding affinities than a previously reported analogue containing an alkyl-substituted triazolium motif.²⁴⁵ All three of these triazolium rotaxanes exhibit impressive selectivity for halide anions over basic acetate, and the aryl-substituted receptors show a modest preference for chloride and bromide over iodide. Titration

experiments demonstrate that the three axle components have similar halide recognition strengths, suggesting that the increase in binding affinity for the aryl-substituted rotaxanes is a result of increased inter-component preorganization afforded by the smaller, more rigid axle components.

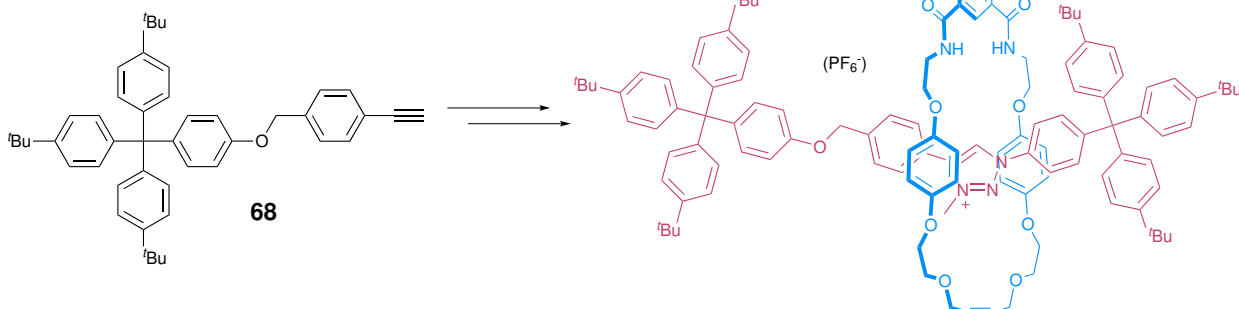
As an extension of this work, a smaller macrocycle precursor was synthesized and used to prepare two new rotaxanes. The anion recognition strength of both of these rotaxanes was reduced compared to their analogues containing larger macrocycles. This was attributed to the macrocycle's smaller size requiring it to buckle in order to bind anions, removing the possibility of favourable donor–acceptor interactions between the macrocycle's hydroquinone groups and the triazolium axle component.

A new axle component was prepared incorporating both amide and triazolium functionality, and this axle incorporated into a novel rotaxane. The interlocked species is a potent receptor for chloride and bromide anions, complexing these guests more strongly than any of the other triazolium rotaxanes in this Chapter.

4.5.2 Future work

Further evidence for the important role of inter-component preorganization in the recognition properties of interlocked host molecules could be provided by preparing a triazolium rotaxane containing a bis-aryl substituted triazolium motif in a larger, less preorganized axle component. The aryl alkyne-appended stopper group **68** has been reported by Leigh and co-workers;³⁷² incorporation of this into a triazolium rotaxane host framework (Scheme 4.12) would give such a system. Preparation of this rotaxane would offer further insight into the role of inter-component preorganization in the host–guest chemistry of interlocked molecules.

To increase anion recognition strength, and possibly selectivity, systems should be designed with increased non-covalent interactions between axle and macrocycle components, in order to enforce a fixed co-conformation on the interlocked host. A covalently tethered receptor, where the axle and macrocycle are chemically bonded to one another could also be conceived, although the synthesis of such a molecule would potentially be challenging. The design of receptors based on hydrogen bonding



Scheme 4.12: Possible synthesis of a rotaxane incorporating a longer axle component featuring a bis-aryl substituted triazolium motif.

that effectively discriminate between the halide anions in protic solvents is intrinsically complicated by the geometric flexibility of hydrogen bonds. The recently developed paradigm of solution halogen bonding may offer the answer to this challenge, due to the stringent linearity of this interaction, and indeed, some success has recently been reported using this approach.^{40,148}

Anion recognition strength may also be increased by synthesizing multiply charged hosts, and taking advantage of the resulting increased electrostatic attraction for negatively charged species. This approach to stronger anion binding will be detailed in Chapter 5.

Chapter 5

Poly-triazolium anion receptors

5.1 Introduction

In Chapter Three, it was demonstrated that the incorporation of triazole motifs into interlocked architectures gave anion receptors with interesting selectivity properties. Chapter Four showed that triazolium containing rotaxanes exhibited potent anion binding, particularly when inter-component preorganization was optimized. This Chapter will discuss the incorporation of two or more triazolium groups into anion receptors, in an attempt to give multiply-charged hosts capable of anion recognition in aqueous solvent media.

With a few notable exceptions,^{116,117,137,373–376} the design of anion receptors that function in competitive aqueous media has relied on the integration of positive charge into the host structural framework.^{114,142,143,377} Surprisingly, the use of the triazolium motif to introduce this charge has remained largely unexplored,^{109,241,245,277–279,288,378} and only one triazolium,²⁴¹ and one iodotriazolium³⁹ containing receptor that function in solvent mixtures containing water have been reported.

5.1.1 Chapter objectives

This chapter will detail the synthesis of macrocyclic, interpenetrated and interlocked anion receptor systems containing two or more triazolium groups. It is expected that the integration of these alkylated heterocycles into various host structural frameworks will allow strong anion recognition *via* hydrogen bonding from the polarized C–H bonds and electrostatic attraction from the positive charges.

5.2 Tetra-triazolium macrocycles

5.2.1 Introduction

In 2005, Beer and co-workers reported a series of tetra-imidazolium and tetra-benzimidazolium macrocycles (Figure 5.1), which exhibit a selectivity preference for fluoride over other halides and benzoate in 9:1 CD₃CN:D₂O mixtures.³⁷⁹ A series of tetra-triazole macrocycles was targeted, with the aim of subsequent alkylation affording

cyclic tetra-triazolium receptors, analogous to these imidazolium and benzimidazolium hosts.

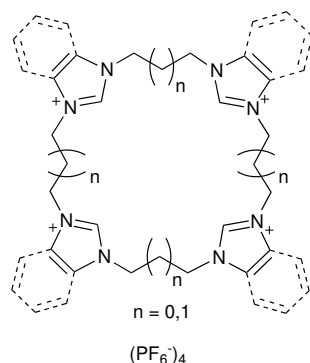


Figure 5.1: Previously reported fluoride selective imidazolium and benzimidazolium macrocycles.³⁷⁹

We reasoned that rigid tetra-triazole aryl macrocycles, such as those reported by Flood,^{45,106,291} would be problematic to fully alkylate, both in terms of the difficulty of completely alkylating a highly conjugated system, and of the possibility of yielding highly insoluble products. Therefore we targeted the less rigid macrocycles, **69**, **70** and **71** (Figure 5.2), in the hope that anion binding affinity lost by the diminished degree of preorganization would be compensated by the increased binding strength resulting from greater electrostatic interactions upon subsequent alkylation.

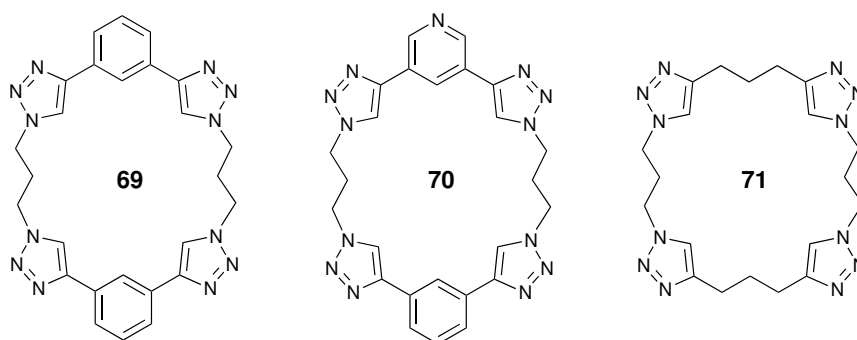


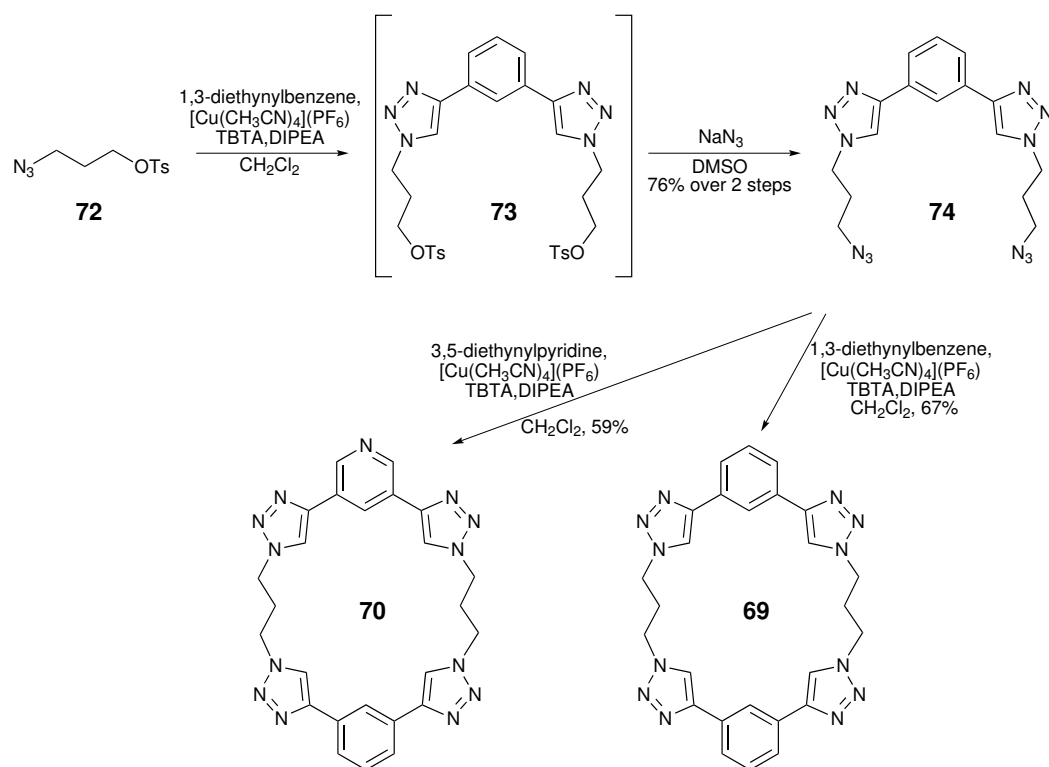
Figure 5.2: Targeted tetra-triazole macrocycles.

A general strategy was used to synthesize the macrocycles: reacting a simple bis-alkyne with 3-azidopropoxytosylate **72**,³⁴⁵ in dichloromethane under CuAAC conditions gave bis-triazole tosylates. Nucleophilic substitution reaction with sodium azide in dimethylsulfoxide gave bis-triazole azides. These could then be cyclized with another equivalent of bis-alkyne to give tetra-triazole macrocycles (Schemes 5.1 and 5.3). While

the macrocycles reported herein are reasonably simple symmetric structures, the synthetic route described potentially allows access to far more complicated systems, as the nature of either of the dialkynes or the azido-tosylate can be altered.

5.2.2 Synthesis of aryl-substituted macrocycles

The azide-substituted tosylate **72** was prepared from 3-bromopropan-1-ol as previously described.³⁴⁵ The reaction of **72** with 1,3-diethynylbenzene under CuAAC conditions in dichloromethane gave the bis-triazole tosylate **73**, which was purified by column chromatography and then reacted immediately with sodium azide in dimethylsulfoxide to give the bis-triazole azide **74** in good yield (76% over two steps from 1,3-diethynylbenzene) after chromatographic purification. This bis-azide was cyclized with either 1,3-diethynylbenzene or 3,5-diethynylpyridine at high dilution in dichloromethane (1.0 mmol L⁻¹) using catalytic [Cu(CH₃CN)₄](PF₆), TBTA and DIPEA. Purification by column chromatography gave **69** and **70** as white powders in good yields (67 and 59% respectively, Scheme 5.1).



Scheme 5.1: Synthesis of tetra-triazole macrocycles **69** and **70**.

The new macrocycles were characterized by ^1H and ^{13}C NMR spectroscopy and by high resolution ESI mass spectrometry. The structure of **69** was also determined in the solid state by X-ray crystallography. Single crystals were grown from two solvent systems: either by diffusion of dichloromethane vapour into a dimethylsulfoxide solution of **69**, or by the slow evaporation of a very dilute methanol/water solution (Figure 5.3). Crystallization from dimethylsulfoxide/dichloromethane gave solventless crystals, while the methanol/water mix afforded **69** $\cdot$ 3H $_2$ O. The solventless crystal has an open structure, while **69** $\cdot$ 3H $_2$ O exhibits a very bunched conformation, presumably due to solvophobic effects.

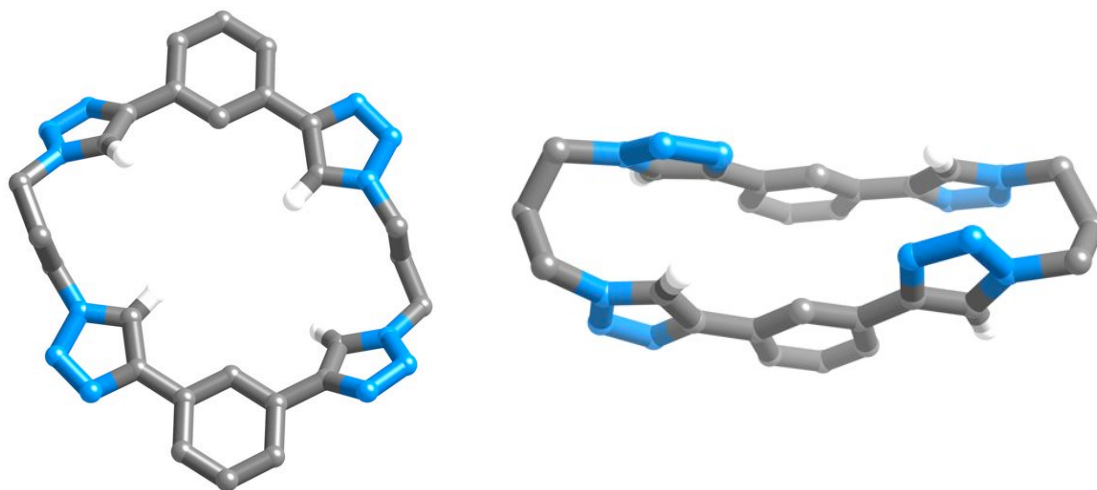
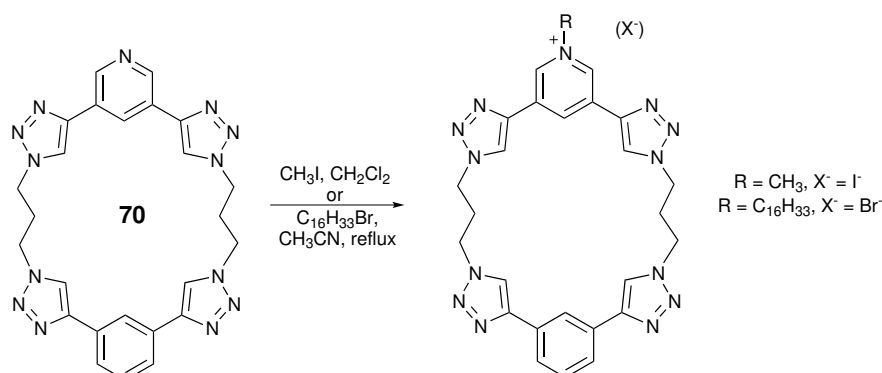


Figure 5.3: Solid state structures of **69** when grown from DMSO/ CH_2Cl_2 (left) and methanol/water (right). Solvent molecules and most hydrogen atoms are omitted for clarity.

Attempts to alkylate **69** and **70** were hampered by their low solubility in common solvents, which ruled out the use of trimethyloxonium tetrafluoroborate. Instead, **69** was heated to 120 $^\circ\text{C}$ for two hours in benzyl bromide using microwave irradiation, giving a mixture of unreacted starting material, mono-alkylated and two doubly-alkylated macrocycles as evidenced by TLC and mass spectrometry. Unfortunately, these products could not be separated chromatographically, and attempts to alkylate further using higher temperatures appeared to cause decomposition of the triazole groups.

Initial investigations suggested that it is possible to selectively alkylate **70** at the pyridine nitrogen using methyl iodide in dichloromethane, but the resulting cationic macrocycle proved to be extremely insoluble in common solvents. Alkylation with

hexadecyl bromide was also attempted, using ten equivalents of the alkyl bromide in refluxing acetonitrile, in the hope that the long alkyl chain would solubilize the charged product. TLC, ESI mass spectrometry, and ^1H NMR spectroscopy of the crude reaction mixture suggested successful selective alkylation at the pyridine nitrogen atom (Scheme 5.2), but the product had low solubility in common solvents, hampering chromatographic purification. Attempts to ease purification by anion-exchanging the crude reaction mixture to the potentially more soluble hexafluorophosphate salt were also unsuccessful.



Scheme 5.2: Attempted alkylation of **70** using methyl iodide and bromohexadecyl bromide.

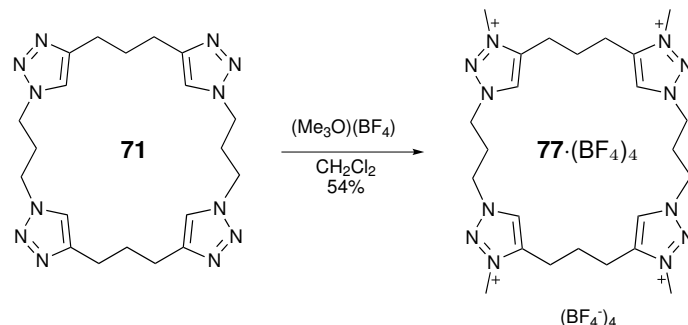
5.2.3 Synthesis of an alkyl-substituted macrocycle

The azidosylate **72** was reacted with 1,6-heptadiyne in dichloromethane under CuAAC conditions to give the bis-triazole tosylate **75**, which was used immediately after purification due to concerns over its stability. The nucleophilic substitution reaction with sodium azide in dimethylsulfoxide was very sluggish at room temperature, and so the reaction was heated to 60 °C to increase its rate. While this resulted in complete consumption of starting material, several byproducts were formed and the yield was much lower than for the corresponding reaction with the phenyl-linked bis-triazole **74** (30% from 1,6-heptadiyne). The cyclization of **76** and another equivalent of 1,6-heptadiyne under analogous conditions to those used for the synthesis of **69** and **70** gave **71** in moderate yield (49%) as a white powder following purification by column chromatography (Scheme 5.3).

Macrocycle **71** was characterized by ^1H and ^{13}C NMR spectroscopy, and by high resolution ESI mass spectrometry. Single crystals were obtained by

5.2.4 Synthesis of a tetra-triazolium macrocycle

Macrocycle **71** has good solubility in a range of organic solvents, allowing facile alkylation in dry dichloromethane containing five equivalents (*i.e.* 1.25 equivalents per triazole group) of trimethyloxonium tetrafluoroborate. The resulting crude solid was recrystallized from ethanol/acetonitrile to give the tetra-cationic product **77**·(BF₄)₄, as white crystals in 54% yield (Scheme 5.4). This was characterized by ¹H, ¹³C and ¹⁹F NMR spectroscopy, and by ESI mass spectrometry and single crystal X-ray crystallography (Figure 5.5). One of the two independent tetrafluoroborate anions in the asymmetric unit cell sits centrally in the macrocycle, slightly above the plane of the receptor with another symmetry-generated anion sitting below the plane of the macrocycle: this anion is involved in weak hydrogen bonds to the two triazolium groups in the asymmetric unit [C–H···F = 3.213(3), 3.247(3) Å; ∠C–H···F = 147, 153°; %VdW_{H,F} = 93, 93]. Close anion···π contacts are also observed [centroid···F distances = 2.866(2), 3.010(2) Å], although given the very weak nature of such interactions in solution,²⁷ these are thought unlikely to affect the host's association with anionic guest species in aqueous solvent mixtures.



Scheme 5.4: Synthesis of **77**·(BF₄)₄.

5.2.5 Anion Recognition Studies

5.2.5.1 Neutral tetra-triazole macrocycles

Receptors **69** and **70** are insoluble in common organic solvents, but have sufficient solubility in d₆-DMSO to allow investigation of their anion binding properties *via* ¹H NMR titration experiments. Addition of aliquots of TBA·Cl to a solution of either **69** or **70** caused perturbation in the triazole signals, as well as smaller shifts in the phenylene

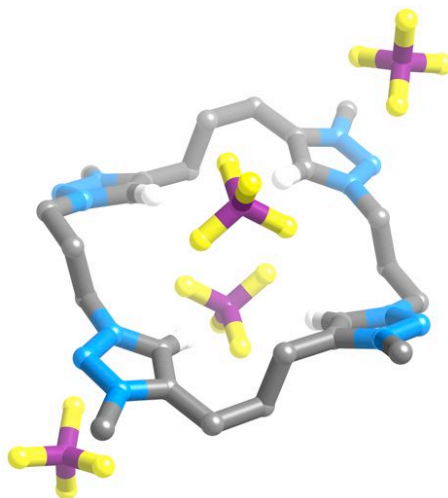


Figure 5.5: Solid state structure of **77**·(BF₄)₄. Acetonitrile solvate and some hydrogen atoms are omitted for clarity.

and/or pyridyl protons. Stoichiometric 1:1 anion association constants were determined using WINEQNMR2,³²⁸ monitoring the triazole proton. As shown in Table 5.1, both macrocycles, **69** and **70** bind chloride in this competitive solvent with the bis-phenylene receptor **69** displaying stronger halide association than the pyridyl-substituted host **70**. Association of cyclic tetra-alkyl receptor **71** and chloride is negligible in d₆-DMSO, and in less competitive 1:1 CDCl₃:CD₃CN. Even in CD₂Cl₂, the affinity of **71** for a range of anions (Cl⁻, I⁻, BzO⁻, SO₄²⁻) is extremely weak ($K_a < 60 \text{ M}^{-1}$).

Table 5.1: Association constants, $K_a \text{ (M}^{-1}\text{)}^a$ for tetra-triazole macrocycles with chloride anion.

Solvent	69	70	71
d ₆ -DMSO	77(5)	37(3)	< 10
1:1 CDCl ₃ :CD ₃ CN	—	—	< 10

^aChloride added as TBA salt, standard errors are given in parentheses. Association constants calculated using WINEQNMR2³²⁸ (293 K).

5.2.5.2 Tetra-triazolium macrocycle

Macrocycle **77**·(BF₄)₄ is insoluble in the 9:1 CD₃CN:D₂O solvent mixture used in the previous studies of tetra-imidazolium macrocycles,³⁷⁹ so fluoride and chloride binding studies were instead conducted in 9:1 d₆-DMSO:D₂O, monitoring the four equivalent triazolium protons. Analysis of the titration data using WINEQNMR2³²⁸ showed very strong 1:1 stoichiometric binding of both halides ($K_a > 10^4 \text{ M}^{-1}$), and so further titration

experiments were undertaken in the more competitive 1:1 d₆-DMSO:D₂O aqueous mixture. The macrocycle displays a preference for the larger halides bromide and iodide (Table 5.2 and Figure 5.6), presumably due to the relatively lower energies of solvation of these anions. All halides associate more strongly than the acetate oxoanion, while the sulfate dianion is bound extremely strongly, due to its doubly negative charge.

Interestingly, the anion binding trend displayed by **77**·(BF₄)₄ (sulfate >> iodide > bromide > other monobasic anions) is similar to the trends reported by Kubik *et al.* for their neutral cyclic pseudo-peptide systems in methanol-water mixtures,^{116,117,373} where the observed selectivity is attributed to complementary host/guest size.

Table 5.2: Association constants, K_a (M⁻¹)^a for **77**·(BF₄)₄ and various anions.

Anion	9:1 d ₆ -DMSO:D ₂ O	1:1 d ₆ -DMSO:D ₂ O
F ⁻	> 10 ⁴	226(28)
Cl ⁻	> 10 ⁴	228(5)
Br ⁻	—	388(29)
I ⁻	—	463(24)
OAc ⁻	—	148(30)
SO ₄ ²⁻	—	> 10 ⁴

^aChloride added as TBA salt, estimated standard errors are given in parentheses. Association constants calculated using WINEQMR2³²⁸ (293 K).

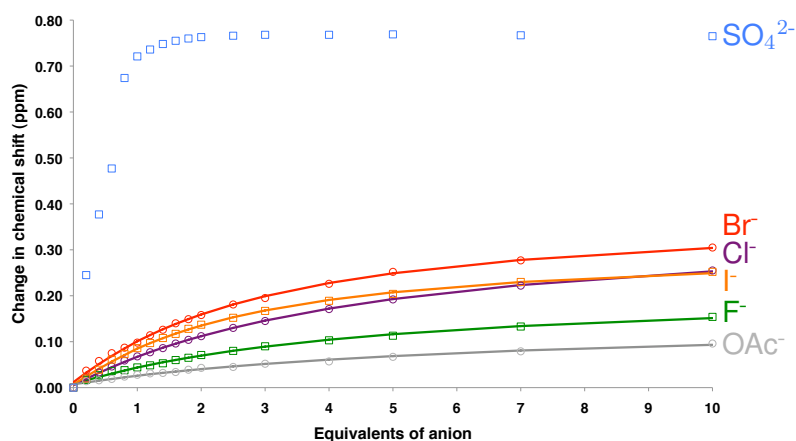


Figure 5.6: Experimental titration data (solid points) and fitted binding isotherms (lines) for addition of TBA·X to **77**·(BF₄)₄ monitoring triazolium resonance. Sulfate binding was too strong to quantify ($K_a > 10^4$ M⁻¹) using WINEQMR2³²⁸ (1:1 d₆-DMSO:D₂O, 293 K, 500 MHz).

It is noteworthy that amongst the halides, the selectivity trend of **77**·(BF₄)₄ is different from that of tetra-imidazolium and tetra-benzimidazolium analogues.³⁷⁹ These receptors

exhibit a pronounced selectivity for fluoride in 9:1 CD₃CN:D₂O, with other anions being bound only weakly, whereas **77**·(BF₄)₄ preferentially binds bromide and iodide.³⁸⁰

5.2.6 Molecular modelling of anion complexes of **77**⁴⁺

The following modelling studies were carried out by Dr. Sílvia Carvalho and Prof. Vítor Félix at the University of Aveiro, Portugal.

The halide and sulfate anion binding affinities of **77**⁴⁺ in competitive 1:1 DMSO:H₂O solvent mixture were investigated by classical molecular dynamics (MD) simulations followed by quantum mechanics/molecular mechanics (QM/MM) simulations as described in the Appendix. Representative snapshots taken from the QM/MD simulations showing the solvated chloride, bromide, iodide and sulfate complexes are presented in Figure 5.7 (the behaviour of the fluoride complex is less straightforward, and is discussed in more detail in Section 5.2.6.1).

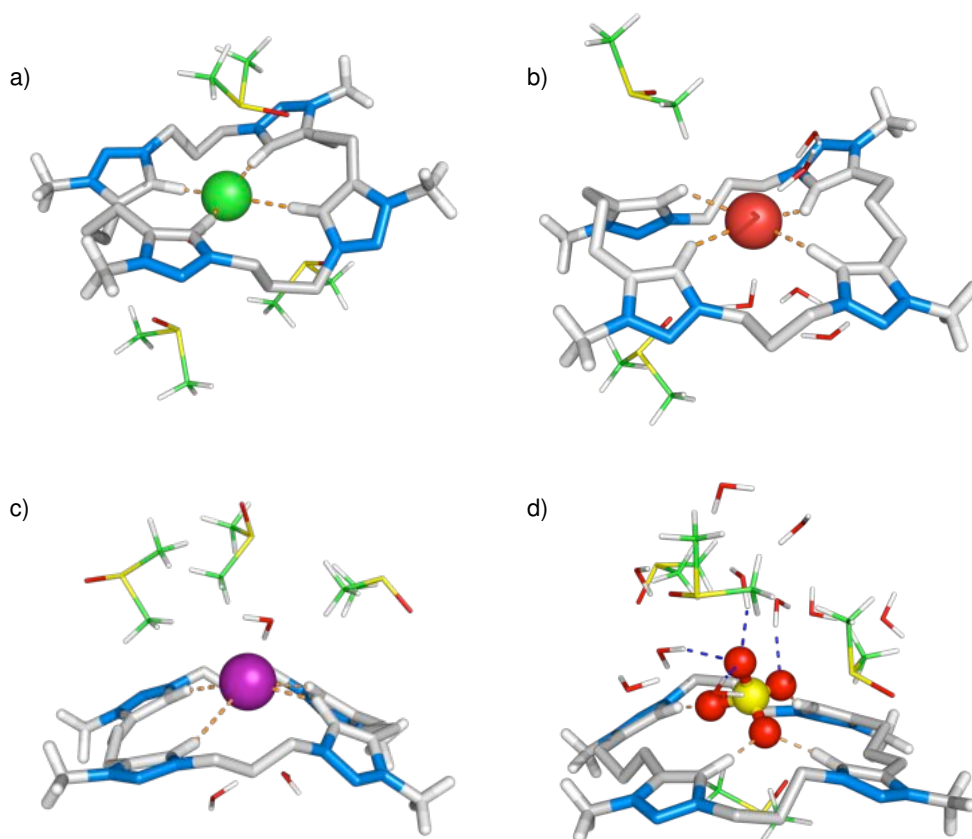


Figure 5.7: Illustrative snapshots (QM/MD) of a) **77**·Cl; b) **77**·Br; c) **77**·I; and d) **77**·SO₄ showing the primary and secondary anion solvent shell.

In the chloride and bromide complexes of **77**⁴⁺, the macrocycle is approximately planar and the anion is encapsulated within the host cavity, while in the case of the larger anions, iodide and sulfate, the macrocycle takes on a “bowl-like” shape, with the anion sitting slightly above the macrocycle. In all of these complexes, four intermittent C–H ···X[−] hydrogen bonds are present between receptor and anion (Table 5.3). The larger standard deviations estimated for H ···I[−] and H ···SO₄^{2−} distances indicate that the charge assisted hydrogen bonding interactions are more often interrupted in these complexes than in the chloride and bromide complexes. They also reflect the prominent exposure of iodide and sulfate anions to the water solvent molecules, with these anions recurrently above the macrocycle cavity throughout the course of the QM/MM simulation. In contrast, the smaller standard deviations for H ···Br[−] distances suggest that among these three monoatomic anions, bromide is the most tightly bound by **77**⁴⁺. To understand the observed binding preference of the macrocycle for iodide, other structural parameters were investigated, as described below.

Table 5.3: Average H ···A distances (Å) with their standard deviations^a between the anions and the four C–H triazolium groups.

Anion	H ₁ ··· A	H ₂ ··· A	H ₃ ··· A	H ₄ ··· A
F [−] ^b	1.71 ± 0.08 <i>1.73 ± 0.07</i>	1.69 ± 0.06 <i>1.72 ± 0.06</i>	4.40 ± 0.58 ^c <i>1.73 ± 0.08</i>	1.71 ± 0.07 <i>1.73 ± 0.07</i>
Cl [−]	2.22 ± 0.52	2.17 ± 0.38	2.28 ± 0.48	2.36 ± 0.55
Br [−]	2.64 ± 0.27	2.68 ± 0.31	2.64 ± 0.28	2.63 ± 0.25
I [−]	3.31 ± 0.75	3.31 ± 0.79	3.12 ± 0.53	3.18 ± 0.76
SO ₄ ^{2−} O ₁ ^d	3.40 ± 0.75	3.71 ± 1.16	3.32 ± 0.84	2.94 ± 0.97
SO ₄ ^{2−} O ₂ ^d	3.13 ± 1.00	2.97 ± 1.18	3.20 ± 1.01	3.74 ± 0.47
SO ₄ ^{2−} O ₃ ^d	3.46 ± 0.95	3.90 ± 0.96	3.69 ± 0.68	3.36 ± 0.99
SO ₄ ^{2−} O ₄ ^d	3.15 ± 0.97	3.21 ± 1.04	3.00 ± 1.00	3.11 ± 0.98

^aThe standard deviations were calculated for $N = 2000$ with the exception of the values quoted for **77**·F, which were calculated with $N = 898$ for the first 898 ps of simulation and $N=1102$ for the remaining simulation length. ^bThe values in italics are for the folded binding arrangement, see Section 5.2.6.1. ^cThe large standard deviation for this measurement indicates that H₃ is not involved in hydrogen bonding interactions. ^dThe H ···O distances listed for sulfate were calculated between each C–H triazolium group and the four oxygen atoms.

5.2.6.1 Conformation of fluoride complex of $\mathbf{77^{4+}}$

Conformational changes in the macrocycle $\mathbf{77^{4+}}$ were investigated by measuring the distances between opposite triazolium C–H protons ($\text{H}_t \cdots \text{H}_t$) during the course of the QM/MM simulations (Table 5.4).

Table 5.4: Average $\text{H}_t \cdots \text{H}_t$ distances (Å) with their standard deviations.^a

Anion	$\text{H}_1 \cdots \text{H}_3$	$\text{H}_2 \cdots \text{H}_4$
$\mathbf{77^{4+}}$	6.18 ± 0.78	6.59 ± 0.86
F^- ^b	5.96 ± 0.63 <i>3.30 ± 0.19</i>	2.96 ± 0.20 <i>3.37 ± 0.11</i>
Cl^-	4.36 ± 0.68	4.34 ± 0.64
Br^-	5.11 ± 0.39	5.14 ± 0.41
I^-	5.84 ± 0.65	5.88 ± 0.73
SO_4^{2-}	5.29 ± 0.34	5.35 ± 0.62

^aThe standard deviations were calculated for $N=2000$ with the exception of the values quoted for $\mathbf{77 \cdot F}$, which were calculated with $N=898$ for the first 898 ps of simulation and $N=1102$ for the remaining simulation length. ^bThe values in italics are for the folded binding arrangement.

In contrast to the chloride, bromide and iodide complexes, in which small variations in both $\text{H}_t \cdots \text{H}_t$ distances were observed, the fluoride complex has a drastic change in one of these distances as shown in Figure 5.8, where they are plotted together with the four $\text{H} \cdots \text{F}^-$ distances. During the first 898 ps of QM/MM simulation, the macrocycle exhibits an almost flattened conformation forming three uninterrupted hydrogen bonds with fluoride with identical average distances of 1.71, 1.69 and 1.71 Å (Table 5.3). Subsequently, the complex undergoes a significant conformational change with $\mathbf{77^{4+}}$ encapsulating the fluoride anion in a folded fashion until the end of the simulation. This binding event is accompanied by a decrease of one $\text{H}_t \cdots \text{H}_t$ distance (Table 5.4) and a concomitant increase of the number of $\text{C-H} \cdots \text{F}^-$ hydrogen bonding interactions from three to four. These structural findings show that the cavity provided by the flattened macrocyclic conformation is too large to accommodate the fluoride anion. Accordingly, $\mathbf{77^{4+}}$ undertakes a conformational change with a substantial decrease of the macrocyclic cavity size in order to bind the smallest halide anion efficiently in a binding arrangement where all four $\text{H} \cdots \text{F}^-$ distances have small standard deviations (Table 5.3). This

conformational rearrangement is illustrated in Figure 5.9 with three sequential snapshots taken from the QM/MM simulation.

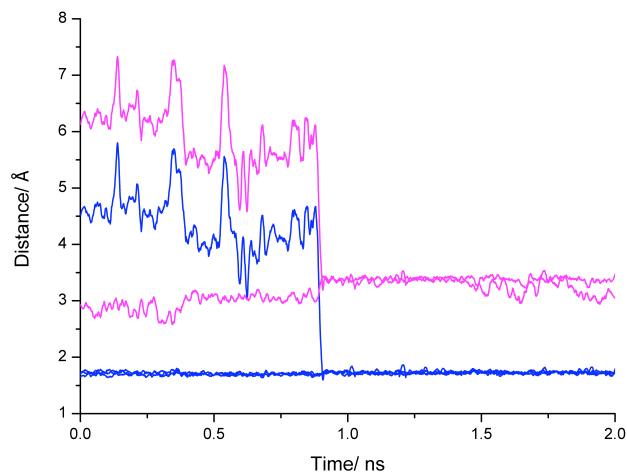


Figure 5.8: Evolution of C-H $\cdots$ F $^-$ hydrogen bond (blue) distances and H $_t\cdots$ H $_t$ (magenta) distances along the QM/MM simulation of the fluoride complex.

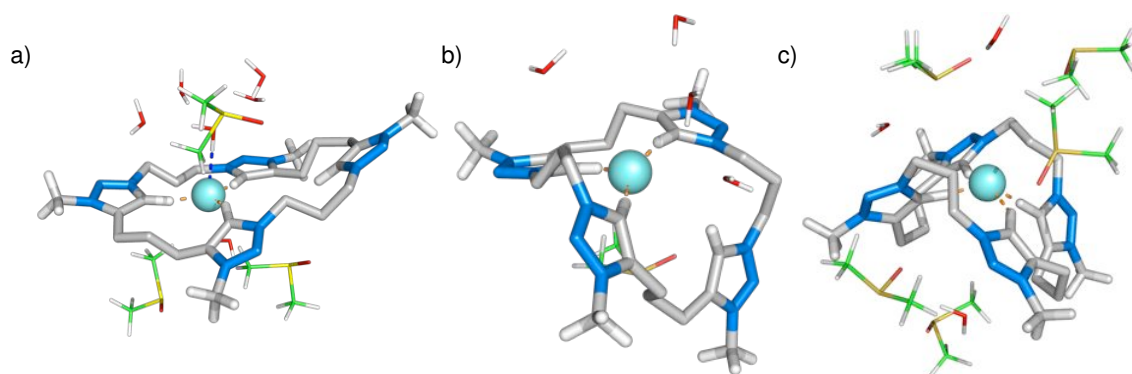


Figure 5.9: Three representative snapshots of fluoride complex taken during the QM/MM simulation: a) 0.160 ns; b) 0.899 ns; and c) 2 ns.

5.2.6.2 Conformational changes

Further understanding of the binding selectivity of **77** $^{4+}$ for halide anions was obtained by comparison of the H $_t\cdots$ H $_t$ distances for the tetra-triazolium macrocycle in complexes and in its free form. The H $_t\cdots$ H $_t$ average values listed in Table 5.4 for the free macrocycle are notably different from those reported for the chloride and fluoride complexes. This is particularly evident for the latter complex, in which the macrocycle adopts a folded conformation to accommodate the smallest anion. In contrast, in the iodide complex, H $_t\cdots$ H $_t$ distances are much closer to the distances reported for the free macrocycle. This

comparison suggests that the energetic cost associated with the conformational change of the macrocycle to bind the iodide is less than for the other halides, leading to a more stable complex.

Solvent Effects

The impact of the competitive 1:1 dimethylsulfoxide:water solvent mixture on the binding affinity of **77**⁴⁺ for halides and sulfate anions was ascertained by calculating the number of water and dimethylsulfoxide molecules around each anion during the QM/MM simulations (Table 5.5).

Table 5.5: Average number of solvent molecules enclosing the anions within the 1st and 2nd shells with *radii* of 3.4 and 5.0 Å respectively.^a

	DMSO		H ₂ O	
	1st	2nd	1st	2nd
F ⁻	0.6 (0–3)	2.1	0.5 (0–3)	3.6
Cl ⁻	0.8 (0–3)	2.1	0.7 (0–3)	3.8
Br ⁻	0.7 (0–3)	2.5	1.7 (0–4)	4.7
I ⁻	0.7 (0–3)	3.0	1.5 (0–5)	3.8
SO ₄ ²⁻	0.5 (0–3)	1.6	5.9 (2–10)	9.3

^aThe maximum and minimum number found in both coordination spheres are given in parentheses.

It is clear that in **77**·Br, **77**·I, and **77**·SO₄, the anion is preferentially solvated by water molecules in the first solvation shell while in **77**·F and **77**·Cl, the anion is surrounded by an equivalent smaller number of water and dimethylsulfoxide solvent molecules. This fact is understandable considering that the two smaller anions are sheltered from both solvent molecules by the macrocycle. Indeed, the chloride anion is co-planar with the flattened macrocycle, while the fluoride anion is wrapped by the folded macrocyclic conformation during most of the simulation. In contrast, iodide and sulfate anions are positioned above the macrocycle, and hence are exposed to water molecules, particularly the polyatomic anion. Nonetheless, the average number of water molecules within the first solvation shell of bromide (1.7) is slightly higher than for iodide (1.5), despite the fact that bromide is largely co-planar with the macrocycle, while iodide perches above the host. This surprising result corroborates the experimental binding preference of **77**⁴⁺ for iodide over bromide (Table 5.2).

As expected, in all complexes the extent of anion solvation increases in the second coordination sphere, which is preferentially composed of water molecules. The significant number of dimethylsulfoxide molecules surrounding the anions, in particular in the case of halide complexes, reflects the solvation of the tetra-triazolium macrocycle by a large number of these molecules. This is particularly evident for the iodide complex with an average of three dimethylsulfoxide molecules protecting the iodide anion from extensive solvation by coordinating water molecules. The sulfate anion is widely solvated by water molecules in both solvation shells and consequently, the experimental binding preference of **77**⁴⁺ for the sulfate anion seems to be dictated by the strength of the electrostatic interactions between tetra-cationic **77**⁴⁺ and di-anionic sulfate.

Overall, these modelling studies show that the impressive anion affinity of **77**⁴⁺ occurs due to multiple charged assisted C–H ···X[−] hydrogen bonds, with the anion selectivity preference of the host due to a number of factors including preorganization, electrostatic and solvation effects.

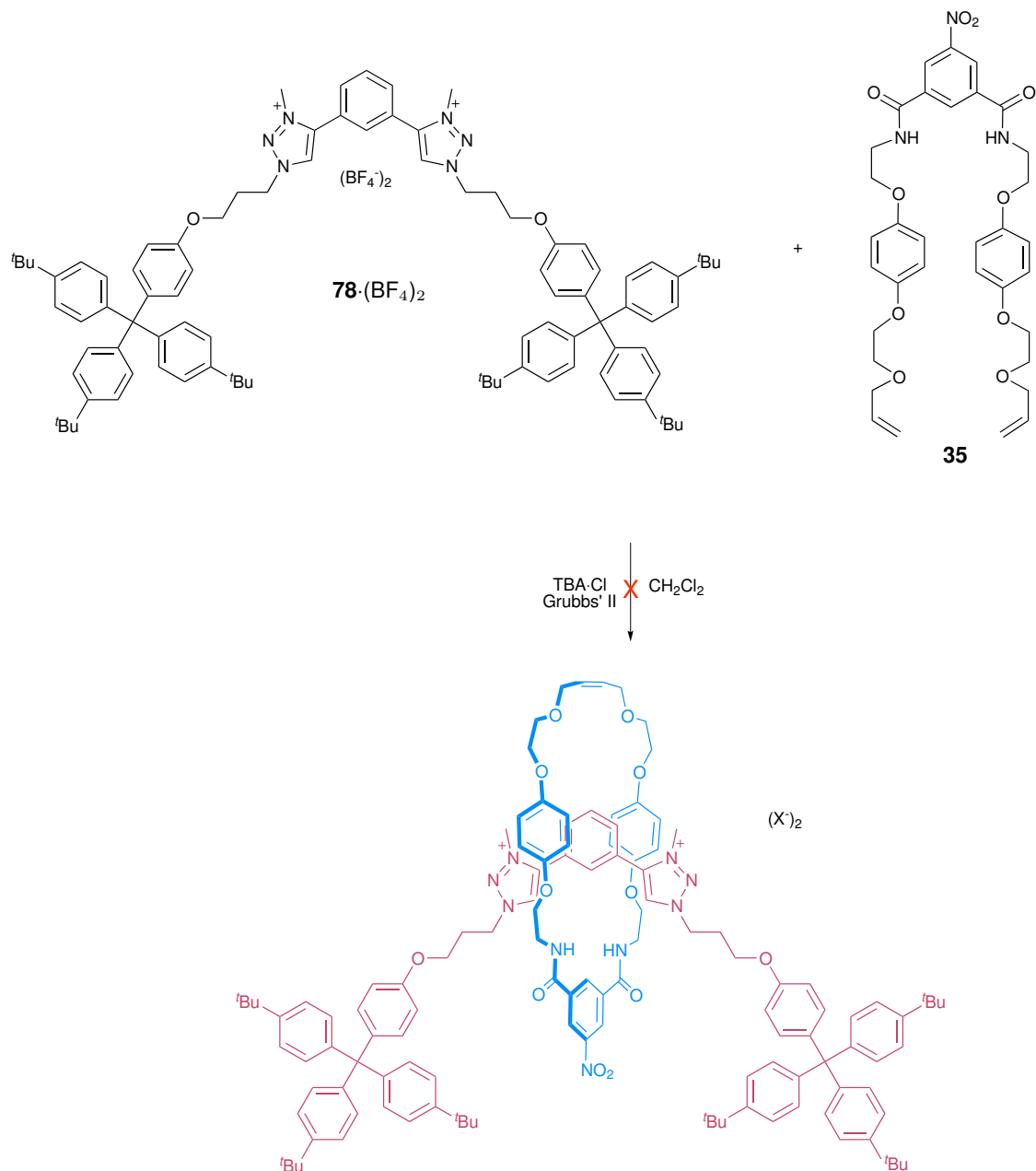
5.3 Rotaxane hosts incorporating a bis-triazolium axle component

5.3.1 Introduction

In Chapter 3, it was demonstrated that selective anion recognition in competitive organic solvents could be achieved using mono-triazolium [2]rotaxanes, while Section 5.2.5.2 demonstrated the efficacy of a tetra-triazolium macrocycle to complex anions in aqueous media. Therefore the synthesis of rotaxanes containing two or more triazolium heterocycles was targeted in an effort to combine the *selectivity* of an interlocked host, and the *strength* of a multiply cationic poly-triazolium system.

Initial investigations targeted a bis-triazolium rotaxane, and investigations into the possibility of synthesizing such a system had previously been conducted in Beer’s research group.³⁷¹ The bis-triazolium axle component **78**·(BF₄)₂ was synthesized, and rotaxane synthesis attempted by chloride anion templated Grubbs’ II-catalyzed RCM of **35** and this axle component, however no evidence of rotaxane formation was observed (Scheme 5.5).

Subsequent investigations showed that the bis-triazolium axle component does complex anions with a 1:1 stoichiometry, but no evidence of association between the axle component **78**²⁺ and macrocycle precursor **35** was obtained in the presence of chloride or bromide anion in CD₂Cl₂ solution. It was decided to investigate this further, with the aim of synthesizing rotaxanes incorporating a bis-triazolium containing axle component.

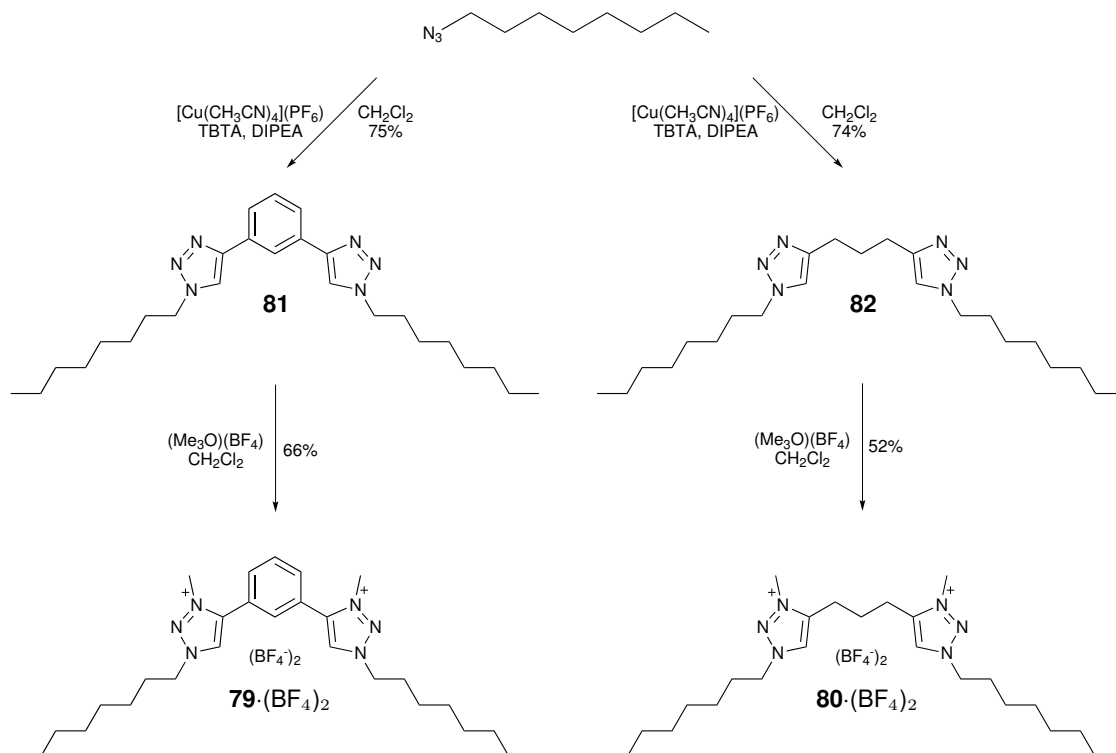


Scheme 5.5: Attempted synthesis of a bis-triazolium rotaxane.³⁷¹

5.3.2 Anion recognition and pseudorotaxane formation properties of acyclic bis-triazolium receptors

An initial investigation of the anion recognition properties of the bis-triazolium motif was conducted using simple acyclic systems. Two acyclic bis-triazolium receptors **79**·(BF₄)₂ and **80**·(BF₄)₂ were synthesized containing two triazolium groups joined by either a phenyl or propyl linker. The propyl containing system was targeted as it was thought that the smaller, more flexible triazolium–propyl–triazolium motif may prove less sterically demanding for rotaxane formation.

Octyl azide was prepared from octyl bromide using sodium azide in dimethylsulfoxide, and this was reacted with 1,3-diethynylbenzene and 1,6-heptadiyne under CuAAC conditions using [Cu(CH₃CN)₄](PF₆), TBTA and DIPEA in dichloromethane to give the neutral bis-triazole molecules **81** and **82** in good yields (75 and 74% respectively). Alkylation using trimethyloxonium tetrafluoroborate in dry dichloromethane, followed by purification using preparative TLC gave the bis-triazolium compounds **79**·(BF₄)₂ and **80**·(BF₄)₂ in reasonable yields (66 and 52% respectively, Scheme 5.6).



Scheme 5.6: Synthesis of bis-triazolium threading components **79**·(BF₄)₂ and **80**·(BF₄)₂.

Anion recognition studies were conducted using ^1H NMR titration experiments in d_6 -acetone: addition of halide anions caused large downfield shifts in the triazolium protons of both receptors, as well as smaller shifts in the triazolium-methyl resonances. In the case of phenyl-linked $\mathbf{79}^{2+}$, the central phenylene proton also underwent a significant downfield perturbation.

Quantitative 1:1 stoichiometric association constants were determined using WINEQNMR2,³²⁸ monitoring the triazolium resonance (Figure 5.10 and Table 5.6). Both receptors bind chloride anion more strongly than bromide anion, presumably due to the more basic nature of the smaller halide. Furthermore, the alkyl-substituted host $\mathbf{80} \cdot (\text{BF}_4)_2$ has a significantly higher affinity for both halide anions than $\mathbf{79} \cdot (\text{BF}_4)_2$. While perhaps initially surprising, this result can be explained by the charge delocalization arguments used to rationalize the anion recognition trends of alkyl- and aryl-substituted rotaxane axle components in Chapter Four. Namely, while aryl-substituted receptor $\mathbf{79}^{2+}$ has more acidic triazolium protons, its cationic charge can be partially delocalized onto the phenyl ring, hence reducing electrostatic attraction for the anion.

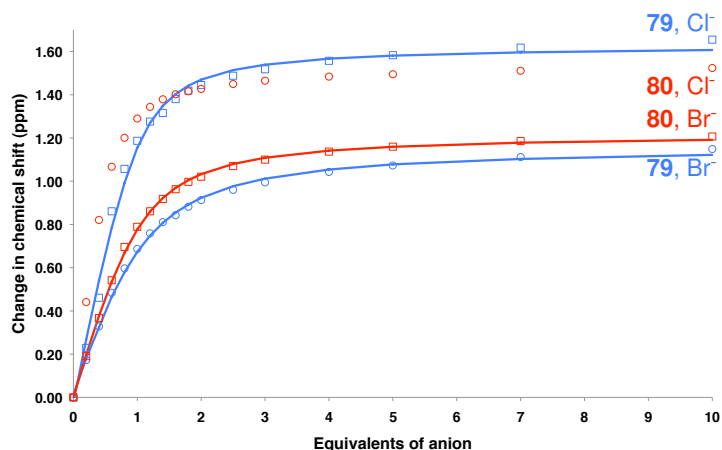


Figure 5.10: Experimental titration data (solid points) and fitted binding isotherms (lines) for addition of TBA-X to acyclic bis-triazolium receptors, monitoring triazolium resonance. Association of chloride anion with $\mathbf{80} \cdot (\text{BF}_4)_2$ was too strong to quantify ($K_a > 10^4 \text{ M}^{-1}$) using WINEQNMR2³²⁸ (d_6 -acetone, 293 K, 500 MHz).

Table 5.6: Association constants, K_a (M^{-1})^a for **79**·(BF₄)₂ and **80**·(BF₄)₂ with halide anions.

	Cl ⁻	Br ⁻
79 ·(BF ₄) ₂	4365(257)	1593(49)
80 ·(BF ₄) ₂	>10 ⁴	2421(124)

^aAssociation constants calculated using WINEQNMR2, estimated standard errors are given in parentheses. Anions added as TBA salts (d₆-acetone, 293 K).³²⁸

Having demonstrated the ability of both bis-triazolium receptors **79**·(BF₄)₂ and **80**·(BF₄)₂ to form stable 1:1 stoichiometric complexes with halide anions, attention was turned to investigating the ability of these compounds to form anion templated pseudorotaxanes with an isophthalamide containing macrocycle in d₆-acetone. Addition of **79**·(BF₄)₂ or **80**·(BF₄)₂ and one equivalent of TBA·Cl or TBA·Br to macrocycle **16** resulted in upfield movement of the macrocycle’s hydroquinone resonances, indicative of donor–acceptor interactions between these electron-rich rings and the electron-deficient bis-triazolium motifs in an interpenetrated assembly. The magnitude of the shifts was much larger when aryl-substituted **79**²⁺ was used than was the case for **80**²⁺, presumably due to the larger aromatic portion of the molecule that can undergo donor–acceptor interactions with the macrocycle hydroquinone rings (Figure 5.11). Downfield shifts were also observed in the macrocycle’s isophthalamide resonances *1*, *2* and *3*, consistent with hydrogen bonding interactions with the halide anion.

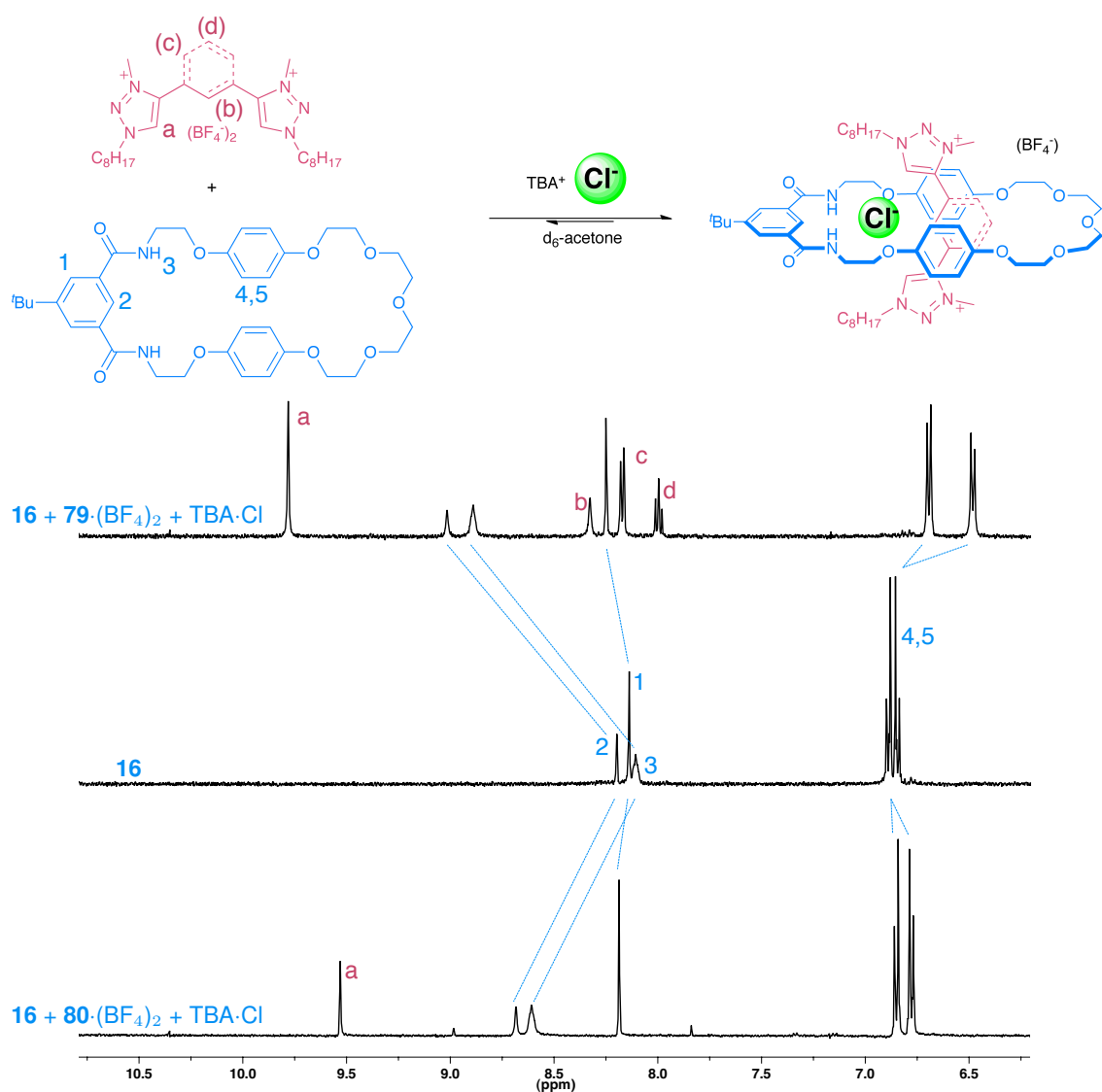


Figure 5.11: Truncated ^1H NMR spectra of **16** (centre), and **16** and one equivalent each of **79**·(BF_4)₂ and TBA·Cl (top), and one equivalent each of **80**·(BF_4)₂ and TBA·Cl (bottom) (500 MHz, 293 K, d_6 -acetone).

Quantitative analysis of the hydroquinone shifts using WINEQNMR2³²⁸ showed that stable halide templated pseudorotaxanes are formed between both threads and **16** with either a chloride or bromide anion template (Table 5.7, Figure 5.12). Significantly stronger assemblies are observed with phenyl-substituted threading component **79**²⁺ than with **80**²⁺, and when chloride anion is used as template instead of bromide. The ability of **79**²⁺ to form anion templated pseudorotaxanes with isophthalamide macrocycle **16** contrasts with the previously reported failure of the analogous axle component **78**²⁺ to undergo anion templated association with **35**.³⁷¹

Table 5.7: Apparent association constants K_{app} (M^{-1}) for halide templated pseudorotaxane formation between **16** and bis-triazolium threading components.^a

Thread	Cl^-	Br^-
79 ²⁺	3214(317)	544(35)
80 ²⁺	465(9)	154(12)

^aEquimolar mixtures of threads as the bis-tetrafluoroborate salts and TBA·halide were added. Association constants calculated using WINEQNMR2, estimated standard errors are given in parentheses (d_6 -acetone, 293 K).³²⁸

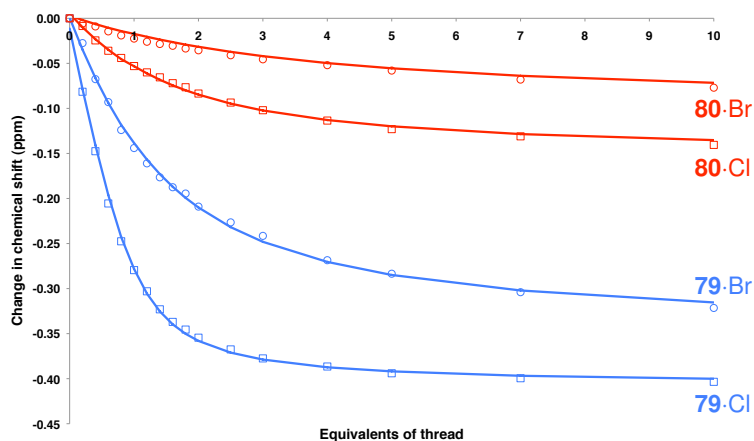


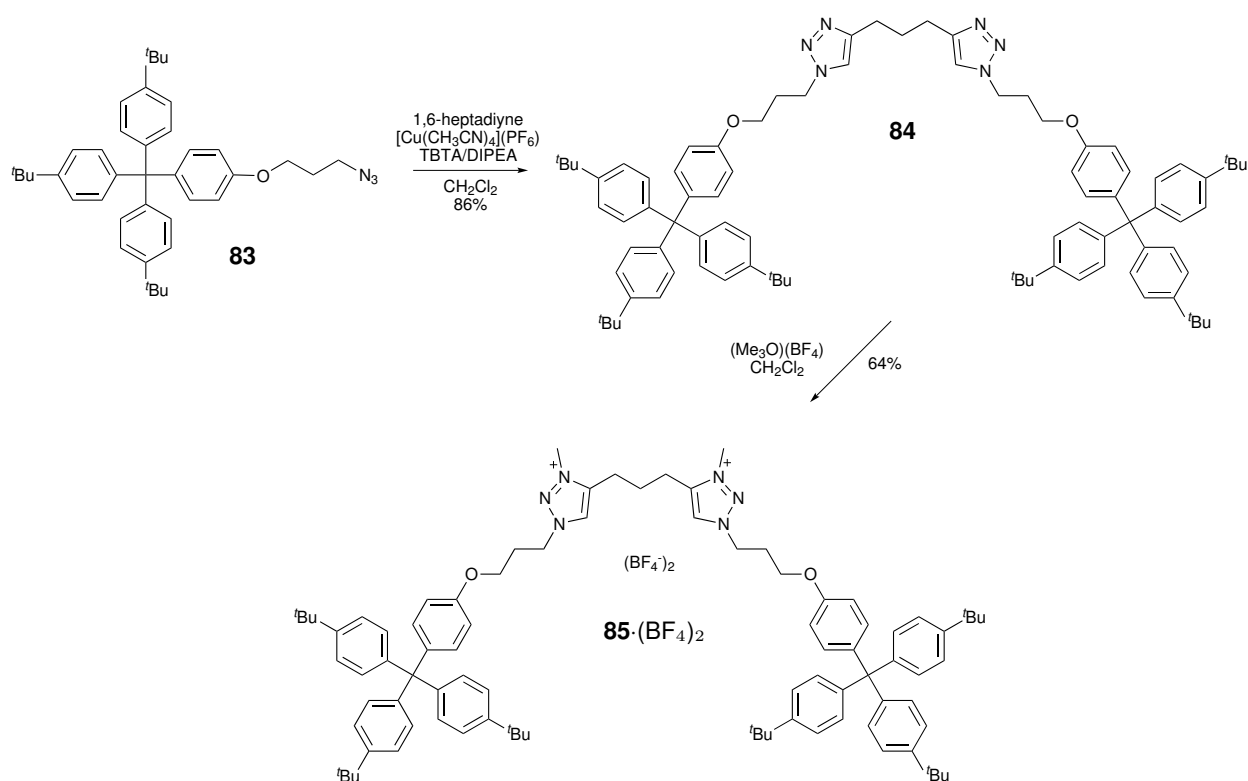
Figure 5.12: Experimental titration data (points) and fitted binding isotherms (lines) for addition of threading components **79**·(BF_4)₂ and **80**·(BF_4)₂, and chloride and bromide anion to **16** (d_6 -acetone, 293 K, 500 MHz).

5.3.3 Synthesis of bis-triazolium rotaxanes by clipping

With the objective of preparing a bis-triazolium axle containing rotaxane, the new bis-triazolium axle **85**·(BF_4)₂ was synthesized. It was thought that this smaller, more flexible motif may be more likely to associate with macrocycle precursor **35** in the presence of an anion template.

Alkyl-azide appended stopper group **83** was prepared in 34% yield over four steps from commercially available materials, as previously described.^{282,370} Two equivalents of **83** were then reacted with 1,6-heptadiyne in dichloromethane under CuAAC conditions, using $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$, TBTA and DIPEA to give the stoppered bis-triazole axle **84** in 86% yield. Alkylation using trimethyloxonium tetrafluoroborate gave the bis-triazolium axle component **85**·(BF_4)₂ in 64% yield after purification by preparative TLC (Scheme 5.7).

The chloride anion templated association of the new axle component **85**·(BF_4)₂ and macrocycle precursor **35** was investigated *via* ^1H NMR spectroscopy in CD_2Cl_2 . Addition



Scheme 5.7: Synthesis of propyl-linked bis-triazolium axle component **85**·(BF₄)₂.

of TBA·Cl to a 1:1 mixture of these components caused small upfield shifts in the hydroquinone resonance of **35**, suggesting some association in solution, and the possibility of rotaxane synthesis *via* an anion templated clipping methodology.

Chloride anion templated rotaxane formation was attempted using Grubbs' II catalyzed RCM reaction of axle component **85**·(BF₄)₂, TBA·Cl and **35**, however no evidence was obtained of any interlocked product formation. Furthermore, the ¹H NMR spectrum of the crude reaction mixture suggested that no alkene metathesis had occurred. An analogous reaction was undertaken using the triazolium–phenyl–triazolium axle component **78**²⁺, as described by Mercurio,³⁷¹ but again no evidence of alkene metathesis was observed.

It is speculated that the Grubbs' II catalyst (itself a ruthenium carbene complex) may be forming some kind of non-catalytically active carbene complex with the bis-triazolium axle component, and thus preventing metathesis from occurring. The ability of the triazolium group to form carbenes with transition metals is well documented,³⁸¹ and a range of metal-carbene complexes derived from precursors similar to **78**²⁺ have been

reported (Figure 5.13). Notably, Zhong and co-workers³⁸² have described a ruthenium complex of a bis-carbene formed from a phenyl-1,3-bis(imidazolium) precursor where the ruthenium is chelated by two carbenes and a cyclometallated phenyl ring (Figure 5.13a), while Crudden has reported that phenyl-1,3-bis(triazolium) compounds form bis-carbenes with silver(I) or rhodium(I), although in this case, the metals are not chelated, possibly due to the steric bulk of the rest of the ligand (Figure 5.13b).³⁸³ It is noteworthy that good donor groups, such as pyridine have been observed to have an inhibitory effect on Grubbs' catalyst.²³⁶

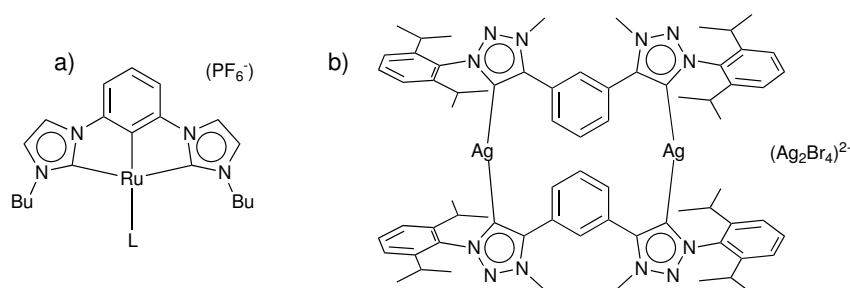
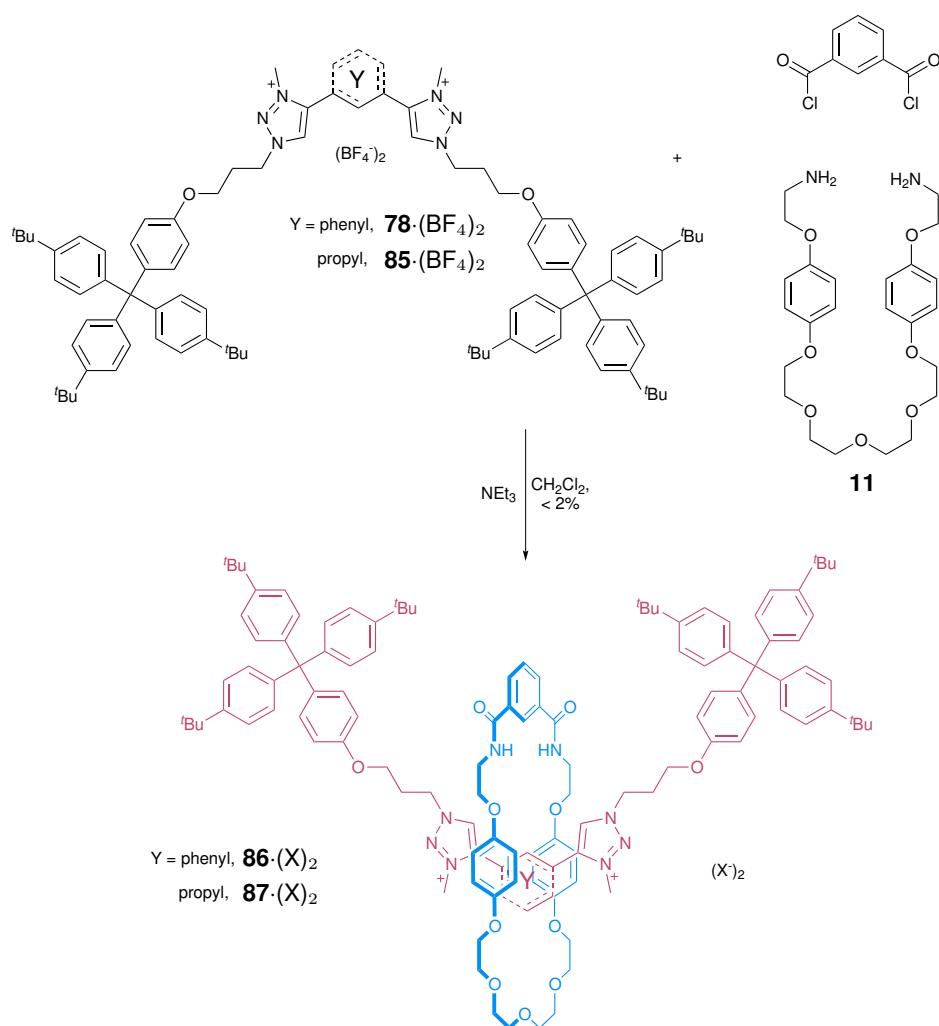


Figure 5.13: Literature metal carbene complexes.^{382,383}

5.3.4 Attempted synthesis of bis-triazolium rotaxanes by amide condensation

As discussed in Section 3.5.1, the synthesis of rotaxanes containing a pyridinium bis-amide axle component can be achieved in good yield by the condensation of a bis-acid chloride and bis-amine in the presence of the pyridinium containing axle. Given the failure of a RCM clipping approach, this route was investigated as a possible alternative method for preparing rotaxanes containing bis-triazolium axle components, as shown in Scheme 5.8. Bis-amine **11** and isophthaloyl dichloride were added to a solution of bis-triazolium axles **78**²⁺ or **85**²⁺ in dichloromethane containing triethylamine. In both cases, the reaction was shown to contain the target rotaxane products **86**²⁺ and **87**²⁺, as evidenced by high resolution ESI mass spectrometry and an upfield-shifted hydroquinone environment in the ¹H NMR spectrum of the respective crude reaction mixture. Initial purification followed by integration of the ¹H NMR spectrum suggested a yield of no more than 2% interlocked product in both cases, and so further purification was not attempted.



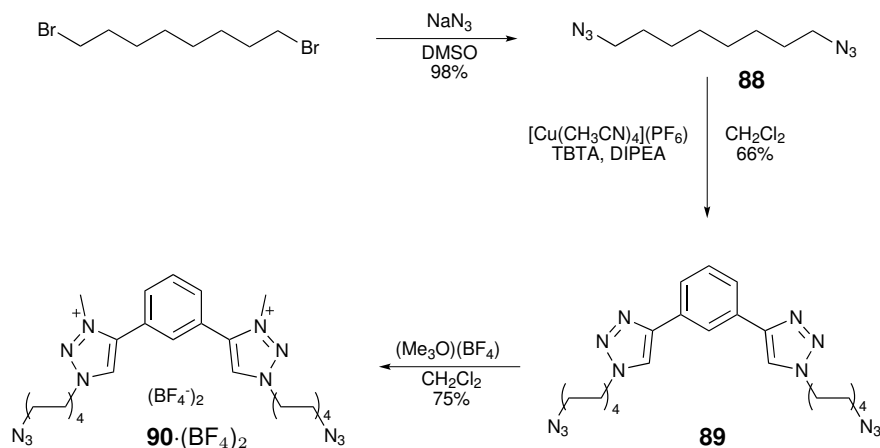
Scheme 5.8: Attempted synthesis of bis-triazolium rotaxanes by amide condensation.

5.3.5 Stoppering synthesis of bis-triazolium rotaxanes

As a final method for the synthesis of bis-triazolium rotaxanes, a stoppering approach was attempted. Previous work by the Beer group has demonstrated that anion templated pseudorotaxanes with suitably appended functionality can be stoppered using the CuAAC reaction to give interlocked host molecules.^{287,384} To facilitate this approach, a bis-azide-appended analogue of bis-triazolium threading component **79**·(BF₄)₂ was prepared, as shown in Scheme 5.9.

The bis-azide **88** was prepared from the corresponding dibromide. Reaction of a large excess of this compound with 1,3-diethynylbenzene under CuAAC conditions gave

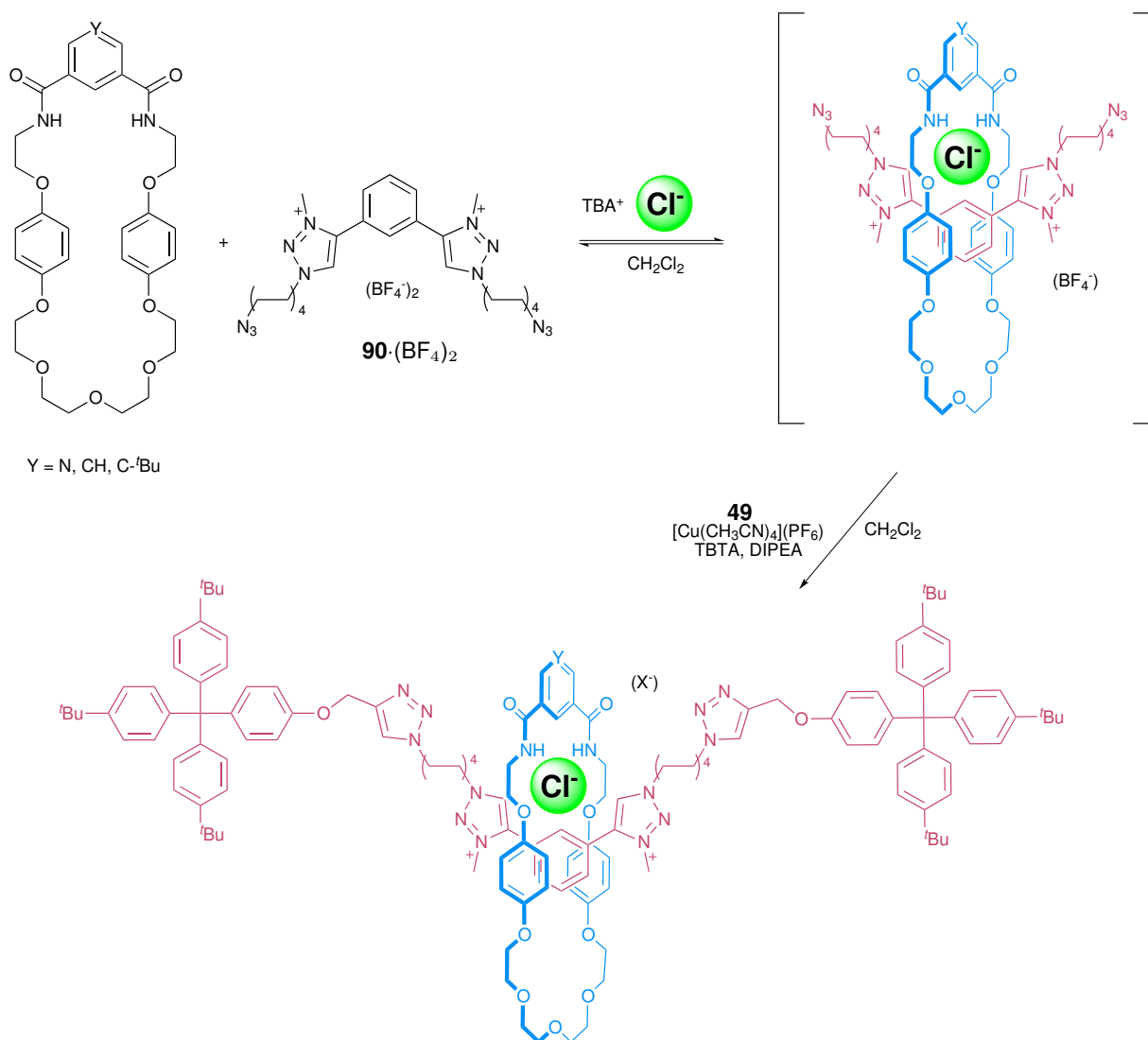
89 in 66% yield, following purification by column chromatography. Alkylation with trimethyloxonium tetrafluoroborate gave the bis-triazolium azide **90**·(BF₄)₂ in 75% yield.



Scheme 5.9: Synthesis of azide-appended threading component **90**·(BF₄)₂.

Stoppering rotaxane formation was attempted as shown in Scheme 5.10. A pseudorotaxane was prepared by mixing one molar equivalent each of an isophthalamide macrocycle, azide-appended threading component **90**·(BF₄)₂ and TBA·Cl in dichloromethane. Two equivalents of the bulky alkyne **49**, [Cu(CH₃CN)₄](PF₆), TBTA and DIPEA were added to effect the stoppering reaction.

The reaction was attempted with three different macrocycles, **16**, **20** and **91** (Y = N in Scheme 5.10): in each case initial purification by preparative TLC gave a band that was shown by ¹H NMR spectroscopy to contain a mixture of rotaxane and stoppered axle component. Integration of the respective ¹H NMR spectrum indicated that the rotaxane was being formed in approximately 25% yield with each macrocycle employed. Numerous attempts were made to separate any of these three rotaxanes from their axle components to give a pure sample of rotaxane: in all cases, a combination of chromatographic, anion exchange, and recrystallization techniques gave samples of increasing purity, but with diminishing yields. Despite these attempts, it was not possible to isolate satisfactorily pure interlocked product. It was thought that this may be due to the octyl chains in the threading/axle component causing problems with purification because of their lipophilicity and lack of crystallinity. Therefore, a new azide-appended threading component **92**·(BF₄)₂ was designed, having *para*-xylyl groups in place of octyl chains (Figure 5.14).



Scheme 5.10: Attempted syntheses of bis-triazolium rotaxanes *via* stoppering.

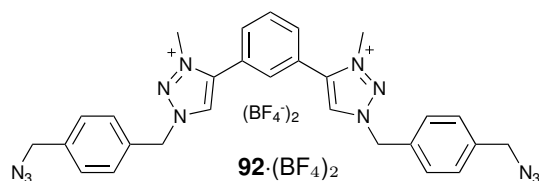
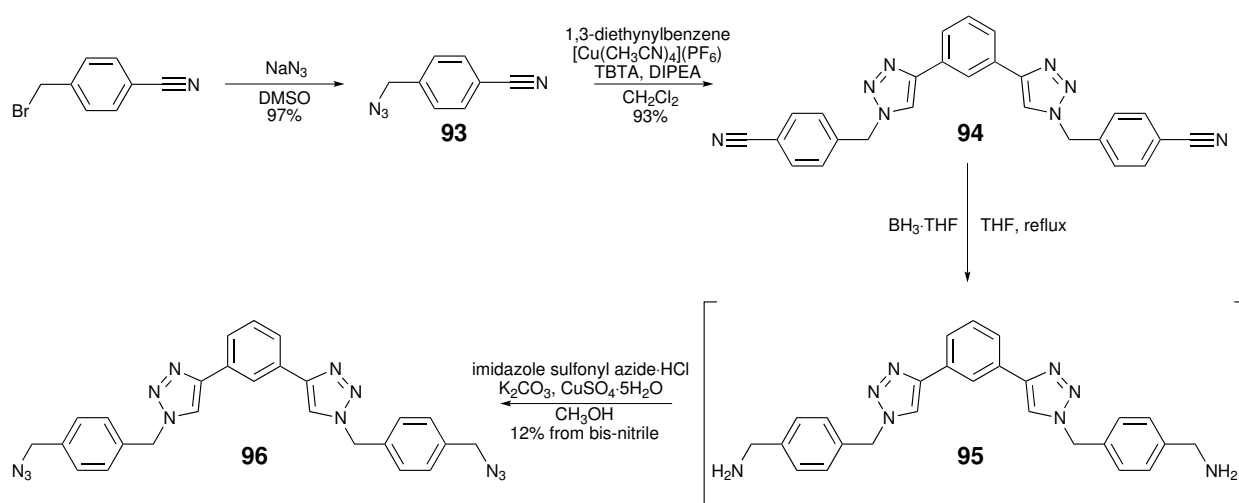


Figure 5.14: Targeted new threading component **92**·(BF₄)₂.

Initial attempts to synthesize **92**·(BF₄)₂ by CuAAC reaction of a large excess of *para*-bis(azidomethyl)benzene and 1,3-diethynylbenzene followed by alkylation proved problematic, with the neutral bis-triazole compound difficult to isolate from oligomeric and macrocyclic by-products. Therefore a new multi-step synthetic route was designed, which avoids the need for statistical reactions (Scheme 5.11). Commercially available

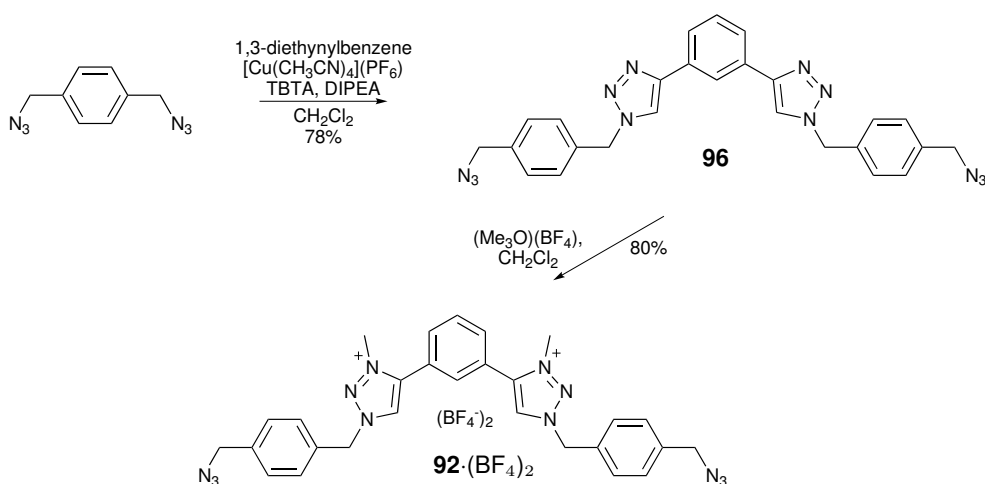
4-bromomethyl benzonitrile was reacted with sodium azide to give **93** in near quantitative yield. Two equivalents of this azide were reacted with 1,3-diethynylbenzene under CuAAC conditions to give bis-triazole nitrile **94** in 93% yield. Reduction of the nitrile to amine **95** using the THF adduct of borane was complicated by the extremely low solubility of the product in all common solvents. It was found that reacting this mixture, without purification, with the hydrochloride salt of imidazole sulfonyl azide gave the desired bis-azide **96** after purification by column chromatography, albeit in a low yield of 12% from **94**.



Scheme 5.11: Synthesis of bis-azide appended bis-triazole compound **96**.

Given the low yield of this route to the bis-azide **96**, it was decided to re-attempt the statistical synthesis of this material from *para*-bis(azidomethyl)benzene and 1,3-diethynylbenzene now that a pure sample of the product was in hand for TLC comparison analysis. Reaction of one equivalent of 1,3-diethynylbenzene with fifteen molar equivalents of *para*-bis(azidomethyl)benzene under CuAAC conditions gave **96** in 78% yield following purification by column chromatography (Scheme 5.12). Alkylation using trimethyloxonium tetrafluoroborate gave azide appended bis-triazolium threading component **92**·(BF_4)₂ in 80% yield.

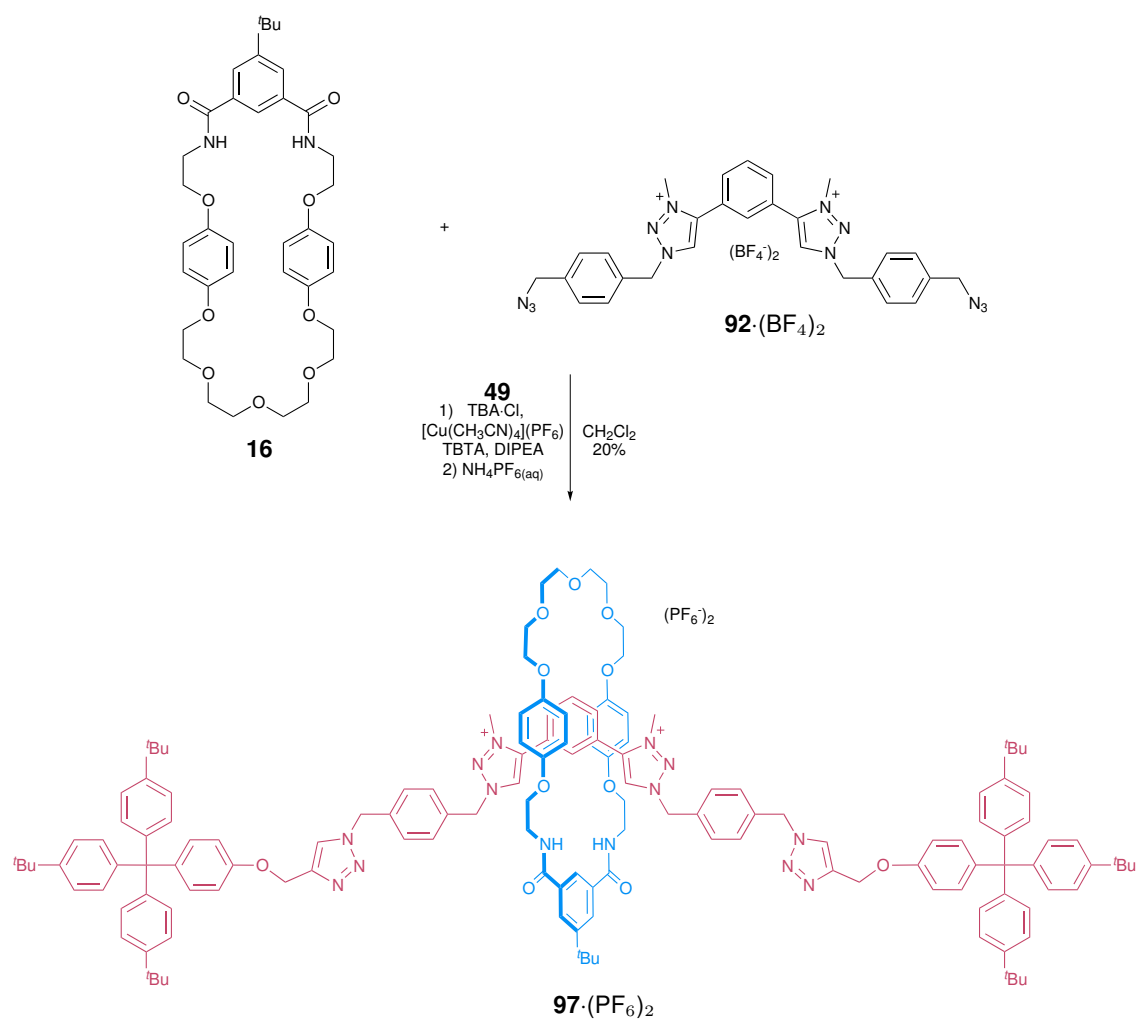
CuAAC stoppering reactions were undertaken with this threading component and isophthalamide macrocycles, as described for octyl containing threading component **90**²⁺. After partial purification using preparative TLC, bands were obtained containing a mixture of the rotaxane and axle component, with integration of the ^1H NMR spectra indicating



Scheme 5.12: Synthesis of bis-azide appended threading component **92·(BF₄)₂**.

a yield of formation of 25–30%. These rotaxanes were still difficult to purify, but in the case of the rotaxane containing *t*butyl-substituted macrocycle **16**, it was possible to isolate pure interlocked product, although when **20** or **91** were used, this was not the case. Purification by preparative TLC and recrystallization followed by anion exchange using aqueous ammonium hexafluorophosphate gave **97·(PF₆)₂** in 20% yield (Scheme 5.13).

The new rotaxane **97·(PF₆)₂** was characterized by ¹H, ¹³C, ¹⁹F and ³¹P NMR spectroscopy, as well as by high resolution ESI mass spectrometry. The interlocked nature of the product was confirmed by 2D ROESY NMR spectroscopy, which revealed several inter-component couplings, consistent with formation of the target rotaxane (Figure 5.15).



Scheme 5.13: Synthesis of bis-triazolium rotaxane **97**·(PF₆)₂.

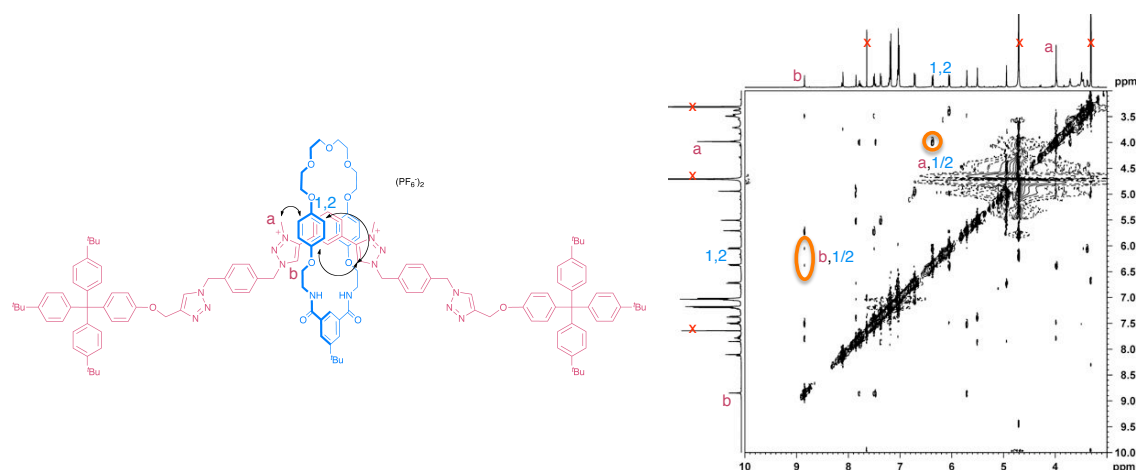


Figure 5.15: Truncated 2D ROESY NMR spectrum of **97**·(PF₆)₂ showing selected inter-component couplings. Further couplings involving the macrocycle alkyl protons are not depicted due to the overlap of these signals in the ¹H NMR spectrum (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

5.3.6 Anion recognition properties of bis-triazolium rotaxane **97**·(PF₆)₂

Addition of chloride anion to rotaxane **97**·(PF₆)₂ in 1:1 CDCl₃:CD₃OD caused downfield shifts of the axle component's triazolium and axle phenylene protons (Figure 5.16), indicative of hydrogen bonding between these groups and the halide anion. Concomitant upfield movement of the hydroquinone resonances was also observed, caused by enhanced donor–acceptor interactions upon anion complexation.

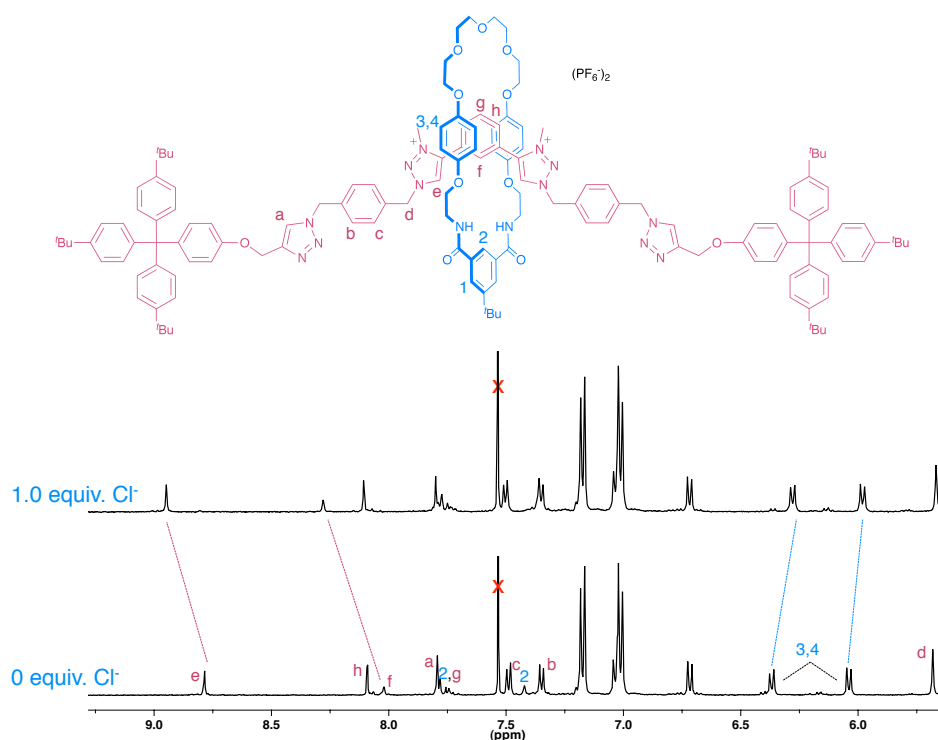


Figure 5.16: Truncated NMR spectra of **97**·(PF₆)₂ upon addition of chloride anion. Peak labelled x corresponds to residual chloroform solvent signal, unlabelled resonances belong to bulky stopper protons (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

Quantitative 1:1 stoichiometric anion association constants were determined using WINEQNMR2³²⁸ (Table 5.8, Figure 5.17), with the rotaxane host exhibiting a selectivity preference for the halide anions over more basic dihydrogen phosphate, but interestingly not over acetate. Within the halide anions, a modest preference for bromide over chloride and iodide is observed. A possible reason for the lack of selectivity for halide anions over acetate is provided by monitoring the hydroquinone resonance: addition of chloride anion causes a significant upfield shift in the hydroquinone resonance (midpoint of

hydroquinone resonances shifts 0.075 ppm upfield after one equivalent of anion) suggesting that chloride is complexed in the host’s cavity and strengthens donor–acceptor interactions between the macrocycle’s hydroquinone rings and the positively-charged core of the axle component. When acetate anion is bound, only a very minor downfield shift in the hydroquinone resonance is observed (0.014 ppm after one equivalent of anion, suggesting little strengthening of these interactions, possibly due to acetate associating primarily with the axle component, with little or no interaction with the macrocycle.

Table 5.8: Association constants, K_a (M^{-1})^a for **97**·(PF₆)₂ and various anions.

Anion	K_a (M^{-1})
Cl [−]	283(20)
Br [−]	407(21)
I [−]	293(23)
OAc [−]	428(70) ^b
H ₂ PO ₄ [−]	131(12)

^aAnions added as TBA salts, association constants calculated using WINEQNMR2,³²⁸ monitoring triazolium resonance. Estimated standard errors are given in parentheses (1:1 CDCl₃:CD₃OD, 293 K). ^bThe triazolium peak disappeared during the titration due to deuterium/hydrogen exchange, and so this value was obtained by monitoring the axle component’s interior phenylene resonance.

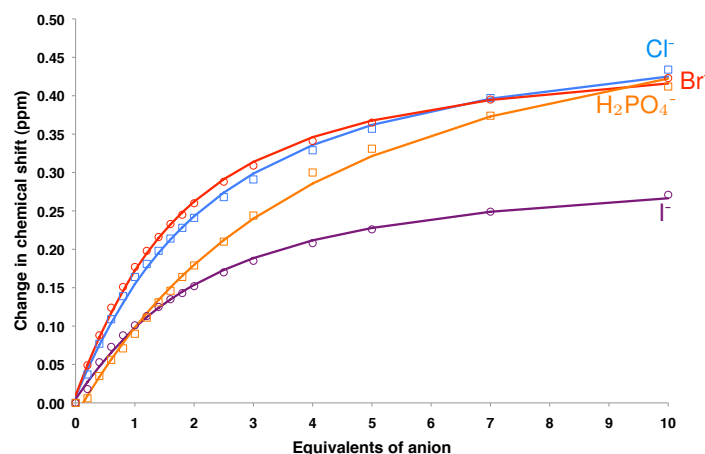


Figure 5.17: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **97**·(PF₆)₂ monitoring triazolium resonance. Movement of triazolium resonance upon addition of acetate anion could not be monitored due to deuterium exchange (1:1 CDCl₃:CD₃OD, 293 K, 500 MHz).

The anion recognition properties of **97**·(PF₆)₂ are surprisingly modest, with this host exhibiting weaker halide binding in 1:1 CDCl₃:CD₃OD than any of the mono-triazolium rotaxanes discussed in Chapter Three, despite the greater positive charge of **97**²⁺ and

the additional triazolium hydrogen bond donor group. This relatively weak anion binding affinity of the interlocked host is probably attributable to the lack of preorganization of the large rotaxane, with the axle component significantly longer than in any of the rotaxanes in Chapter Three.

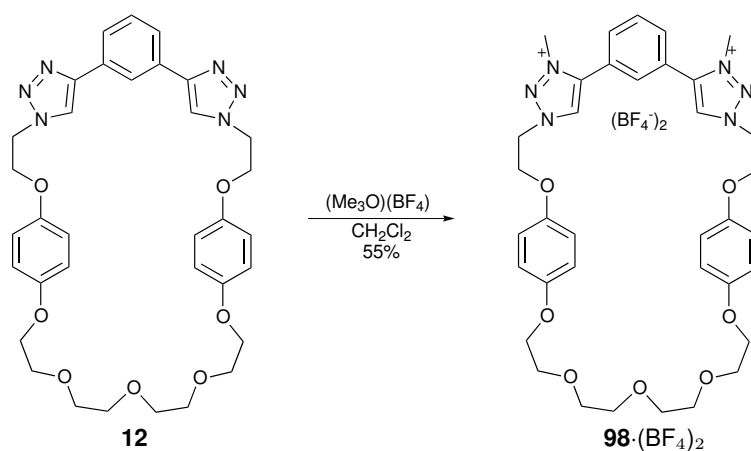
5.4 Interlocked hosts incorporating a bis-triazolium macrocyclic component

The work in this section was conducted in conjunction with Henry Lovett, a Part II student working under my supervision.

5.4.1 Synthesis of a bis-triazolium macrocycle

Given the weak anion recognition properties of bis-triazolium rotaxane **97**·(PF₆)₂, the synthesis of more highly charged, and more preorganized anion receptors was attempted. To this end, a bis-triazolium macrocycle was targeted, to allow formation of tetra-triazolium pseudorotaxanes, rotaxanes and catenanes.

The bis-triazolium macrocycle **98**·(BF₄)₂ was prepared by alkylation of bis-triazole macrocycle **12** with trimethyloxonium tetrafluoroborate, as shown in Scheme 5.14. Purification by recrystallization gave **98**·(BF₄)₂, which was characterized by ¹H, ¹³C and ¹⁹F NMR spectroscopy, and by high resolution ESI mass spectrometry.



Scheme 5.14: Synthesis of **98**·(BF₄)₂.

Single crystals were also obtained, allowing for structural analysis using X-ray crystallography (Figure 5.18). One of the tetrafluoroborate anions is encapsulated within the macrocycle, and two moderate hydrogen bonds are formed between the triazolium protons and one of the anion's fluorine atom [$\text{C-H}\cdots\text{F} = 3.232(7), 3.271(7) \text{ \AA}$, $\angle\text{C-H}\cdots\text{F} = 161, 169^\circ$, $\% \text{VdW}_{\text{H,F}} = 91, 92$]. A strong anion- π interaction is also present between the other tetrafluoroborate anion and one of the triazolium rings [$\text{F}\cdots\text{centroid} = 2.803(6) \text{ \AA}$]

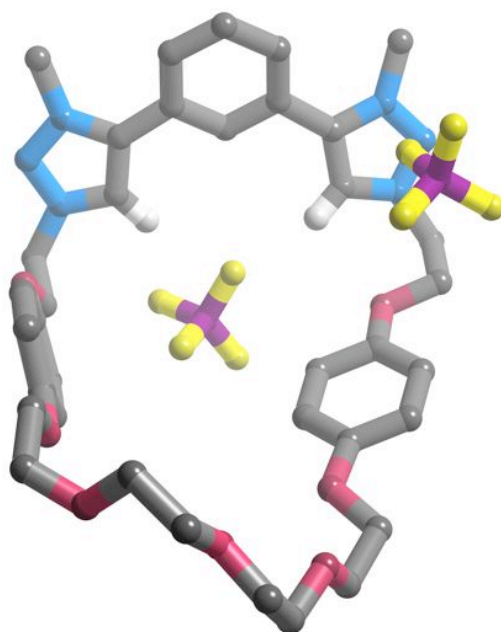


Figure 5.18: Solid state structure of **98**·(BF_4)₂. Acetonitrile solvates, and most hydrogen atoms omitted for clarity.

5.4.2 Anion recognition properties of **98**·(PF_6)₂

The anion recognition properties of **98**·(BF_4)₂ were investigated *via* ^1H NMR titration experiments in CD_3CN . As shown in Figure 5.19, addition of chloride anion causes significant downfield shifts in triazolium proton *e* and interior phenylene proton *c*. Hydroquinone protons *h* and *i* also split due to the increased inequivalence of these environments upon addition of chloride anion.

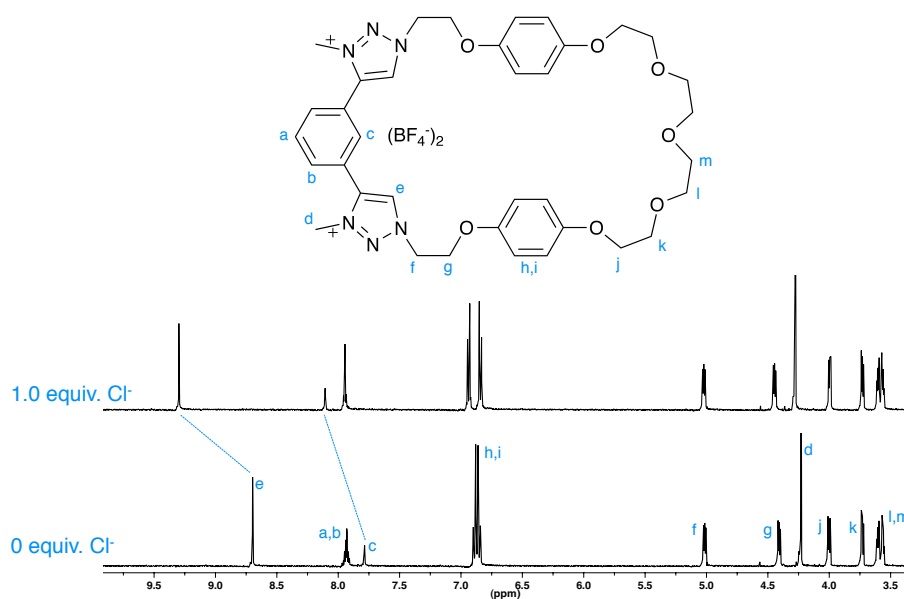


Figure 5.19: Truncated ^1H NMR spectra of **98**·(BF_4) $_2$ upon addition of TBA·Cl (CD_3CN , 293 K, 500 MHz).

Quantitative 1:1 stoichiometric anion association constants were determined using WINEQNMR2,³²⁸ monitoring the macrocycle's triazolium resonance. As shown in Figure 5.20 and Table 5.9, **98**·(BF_4) $_2$ binds a range of anions in CD_3CN , with anion binding affinity generally following anion basicity trends. The exception is basic fluoride, which is bound only weakly, presumably due to its high energy of solvation. Addition of dihydrogen phosphate or sulfate anions caused rapid precipitation, preventing determination of quantitative data.

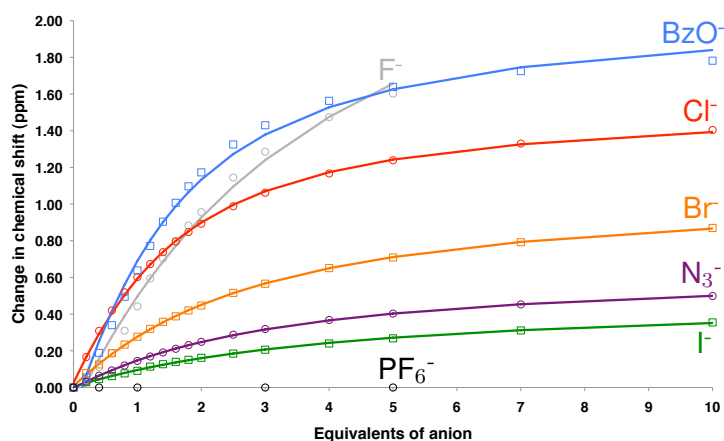


Figure 5.20: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **98**·(BF_4) $_2$ monitoring triazolium resonance (CD_3CN , 293 K, 500 MHz).

Table 5.9: Association of anions with **98**·(BF₄)₂.

Anion	K_a (M ⁻¹) ^a
F ⁻	141(37) ^b
Cl ⁻	457(17)
Br ⁻	210(5)
I ⁻	129(6)
N ₃ ⁻	187(3)
BzO ⁻	467(62)
PF ₆ ⁻	0 ^c
H ₂ PO ₄ ⁻	precipitation
SO ₄ ²⁻	precipitation

^aAnions added as TBA salts, estimated standard errors are given in parentheses. Association constants calculated using WINEQNMR2.³²⁸ (CD₃CN, 293 K). ^bAddition of fluoride cause precipitation after approximately 5 equivalents of anion. An association constant could still be determined, albeit with a large error. ^cNo movement of the triazolium resonance was observed implying no binding event.

The binding of sulfate was investigated further in competitive d₆-DMSO, addition of this anion to **98**·(BF₄)₂ resulted in very large shifts in the macrocycle's interior phenylene proton and triazolium signals (Figure 5.21). The hydroquinone resonance also splits significantly, indicating an inequivalence in the chemical environments of these aromatic rings.

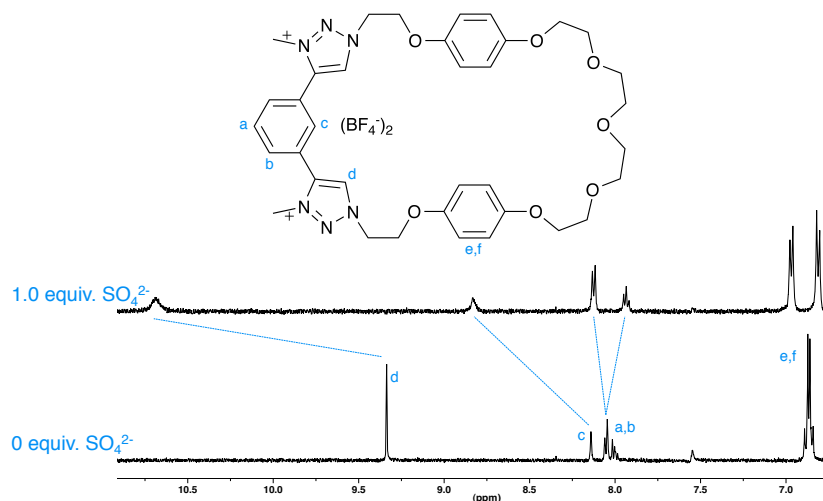


Figure 5.21: Truncated ¹H NMR spectra of **98**·(BF₄)₂ upon addition of TBA₂·SO₄ (d₆-DMSO, 293 K, 500 MHz).

Association of sulfate with **98**·(BF₄)₂ in d₆-DMSO was too strong for WINEQNMR2³²⁸ to calculate a binding constant, despite the competitive nature of the solvent (Figure 5.22).

For comparison, association of chloride anion with **98**·(BF₄)₂ was 44(4) M⁻¹ in this solvent, compared with 457(17) M⁻¹ in CD₃CN . Even in highly competitive 9:1 d₆-DMSO:D₂O, significant sulfate binding was observed, with an association constant of 113(1) M⁻¹.

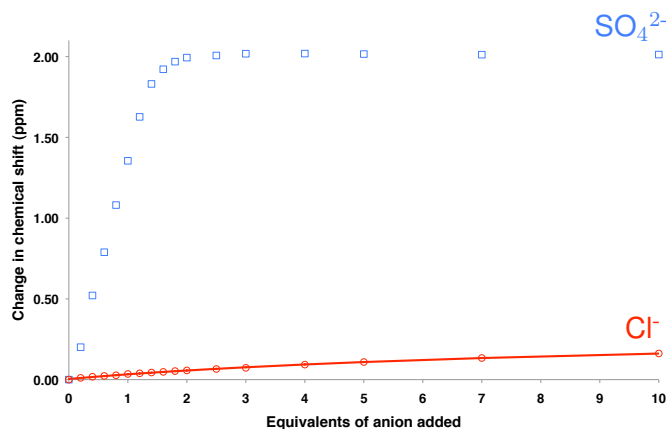


Figure 5.22: Experimental titration data (points) and fitted binding isotherms (lines) for addition of anions to **98**·(BF₄)₂ monitoring triazolium resonance; association of sulfate was too strong ($K_a > 10^4$ M⁻¹) for WINEQNM2³²⁸ to calculate a binding constant (d₆-DMSO, 293 K, 500 MHz).

Single crystals of the chloride, azide and iodide salts of **98**²⁺ were obtained, suitable for X-ray diffraction studies (Figure 5.23), in each case one anion associates within the macrocycle cavity, while the other is located peripherally. In the case of the halide anion salts, the anion located in the cavity forms a strong hydrogen bond to one triazolium group, but is not involved in hydrogen bonding to the other triazolium heterocycle or the macrocycle's interior phenylene proton [C–H···Cl = 3.298(7) Å, ∠C–H···Cl = 173°, %VdW_{H,Cl} = 84; C–H···I = 3.699(8) Å, ∠C–H···I = 165°, %VdW_{H,I} = 91]. The other halide anion forms weak hydrogen bonds to solvent molecules and a methyl proton from the triazolium-methyl group. In the structure of **98**·(N₃)₂, an unusual hydrogen bonding arrangement is formed where the azide within the macrocycle hydrogen bonds to both triazolium groups, with one C–H···N interaction involving a terminal nitrogen atom, and the other the central nitrogen. Both hydrogen bonds are moderately strong (%VdW_{H,N} = 92 and 93 for interactions involving the central and terminal nitrogen atom respectively). The azide located outside the macrocycle cavity forms a very strong hydrogen bond to a water solvate [O–H···N = 2.827(11) Å, ∠O–H···N = 179°, %VdW_{H,N} = 78].

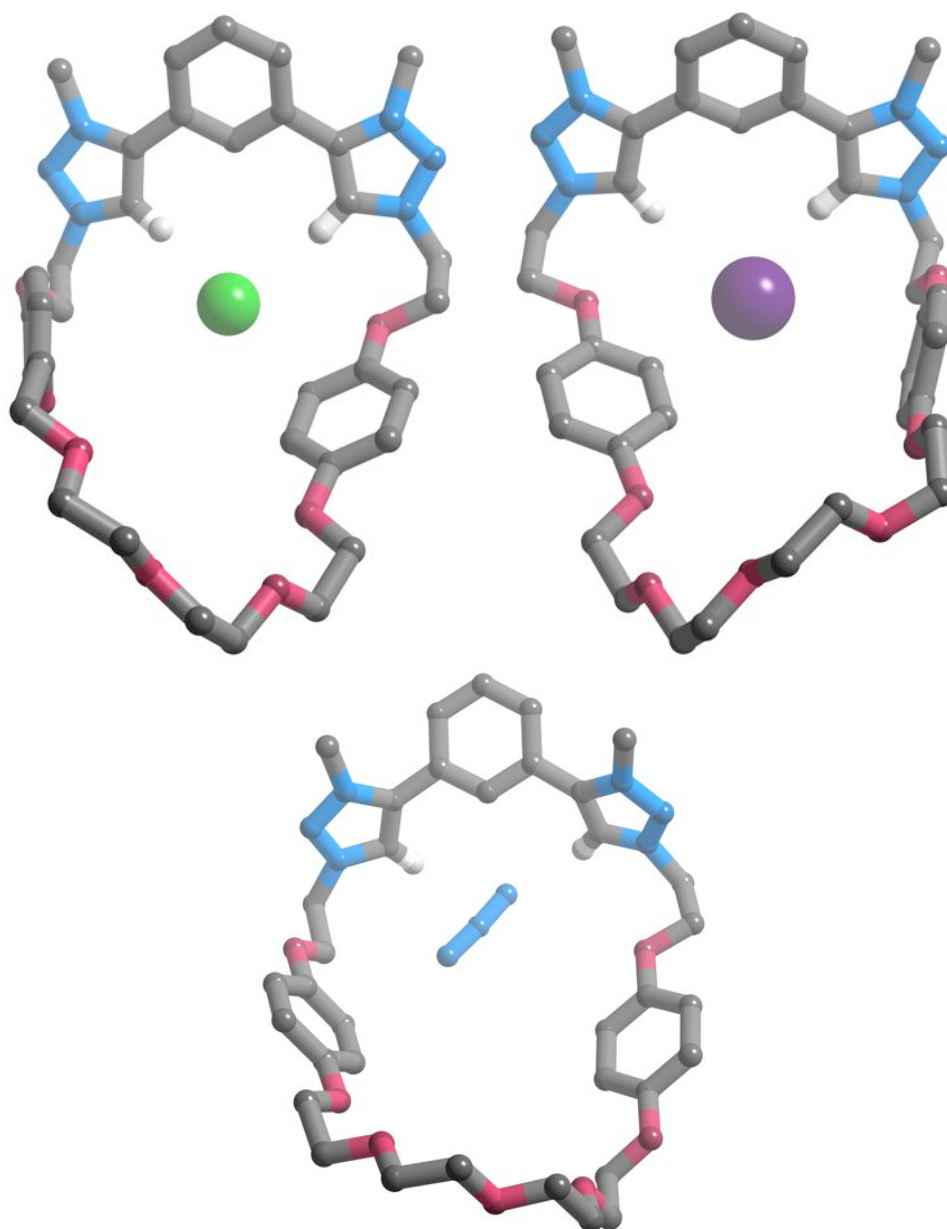


Figure 5.23: Structures of chloride, iodide and azide salts of **98**²⁺ in the crystal. Peripherally-associated anions, solvent molecules and most hydrogen atoms omitted for clarity.

Very poor quality crystals of **98**·SO₄ were obtained. While the quality of the data do not permit a detailed discussion of non-covalent interactions, the gross structure of the complex is clear (Figure 5.24). Each triazolium group donates one hydrogen bond to a sulfate anion, so that the macrocycles form dimers bridged by two sulfate anions. While the accuracy of the measurement of this distance is limited by the poor data, it appears that the hydrogen bonding interactions are strong (%VdW_{H,O} ~ 81–88).

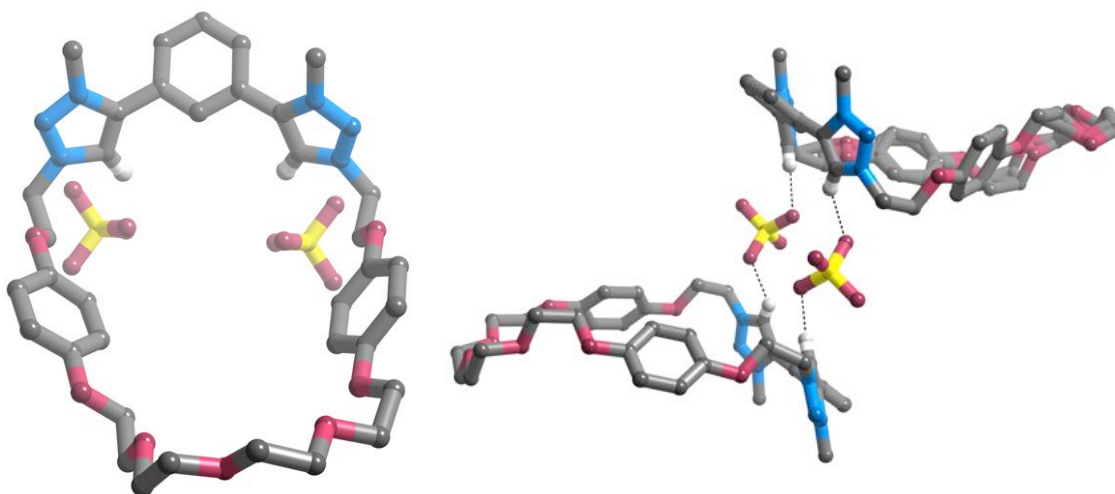


Figure 5.24: Structure of **98**·SO₄ in the crystal showing one macrocycle (left) and the dimeric packing arrangement (right). Most hydrogen atoms are omitted for clarity.

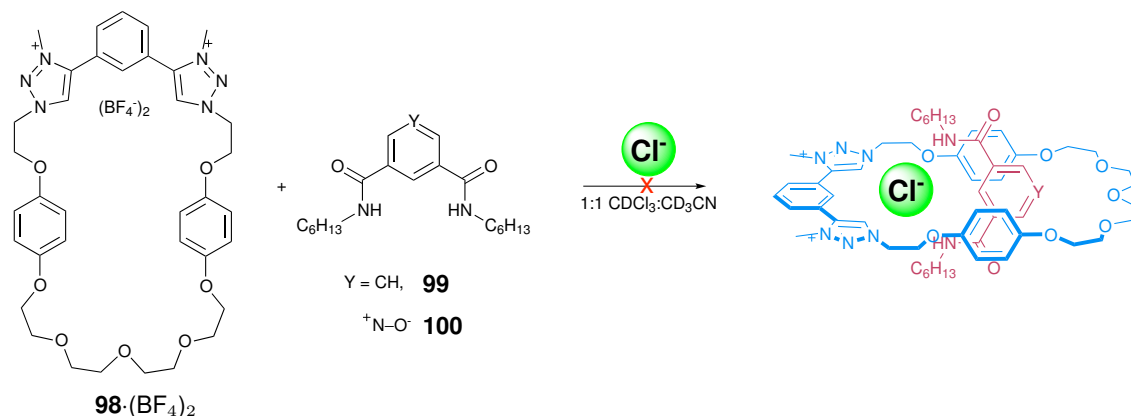
5.4.3 Assembly of poly-triazolium interpenetrated and interlocked architectures

5.4.3.1 Pseudorotaxane formation

The assembly of interpenetrated poly-triazolium systems was investigated using bis-triazolium macrocycle **98**²⁺ and bis-triazolium threading component **79**²⁺. Addition of chloride anion to a 1:1 mixture of **98**·(BF₄)₂ and **79**·(BF₄)₂ in CD₃CN did not result in upfield shifts of the macrocycle's hydroquinone resonance, suggesting no anion templated interpenetration. Given that the macrocycle and threading component complex chloride anion only moderately strongly in this solvent [*K*_a = 457(17) and 313(16) M⁻¹, respectively], it would appear that the favourability of chloride binding is not sufficient to overcome the electrostatic repulsion between the two dicationic components.

The chloride templated association of **98**·(BF₄)₂ with neutral isophthalamide threading component **99** or pyridine-*N*-oxide thread **100** (generously supplied by Dr. Laura Hancock) was investigated to see if reducing the net positive charge of the system would make pseudorotaxane formation more favourable (Scheme 5.15). No significant upfield movement of the hydroquinone resonances was observed when **99** and one equivalent of TBA·Cl, **100** and one equivalent of TBA·Cl or **100** alone were added to **98**·(BF₄)₂ in 1:1 CDCl₃:CD₃CN, suggesting no interpenetration. It is noteworthy that a similar

pseudorotaxane containing an isophthalamide macrocycle and bis-triazolium threading component (that is, the “reversed” form of **98**²⁺ and **99**) does form a stable anion templated pseudorotaxane, albeit in the less competitive solvent d₆-acetone (Section 5.3.2), demonstrating again the critical role played by “secondary” interactions in such systems.



Scheme 5.15: Attempted pseudorotaxane formation between **98·(BF₄)₂** and **99** or **100** (1:1 CDCl₃:CD₃CN, 293 K, 500 MHz).

Given the greater negative charge of the sulfate anion, as well as its strong association with **98**²⁺, and a previous demonstration of its ability to template pseudorotaxane formation,²⁴² it was decided to investigate the use of this anion to template pseudorotaxane assembly between **79·(BF₄)₂** and **98·(BF₄)₂**. As addition of TBA₂·SO₄ to **98·(BF₄)₂** in CD₃CN caused the macrocycle to precipitate from solution, these investigations were carried out in d₆-DMSO. Addition of sulfate anion to a 1:1 mixture of **79·(BF₄)₂** and **98·(BF₄)₂** in this solvent resulted in large downfield shifts of the interior phenylene and triazolium proton signals of both components, consistent with hydrogen bonding from macrocycle and thread to the anion (Figure 5.25). Significant upfield movement of the macrocycle’s hydroquinone resonances suggest the threading component is penetrating the annulus of the macrocycle, with the resulting donor–acceptor interactions causing these shifts.

A qualitative study was undertaken to determine if any other anions could template interpenetration in d₆-DMSO. Addition of F⁻, Cl⁻, Br⁻, I⁻, OAc⁻, ClO₄⁻, H₂PO₄⁻, HSO₄⁻ or C₂O₄²⁻ to a 1:1 mixture of **79·(BF₄)₂** and **98·(BF₄)₂** did not result in upfield shifts of the

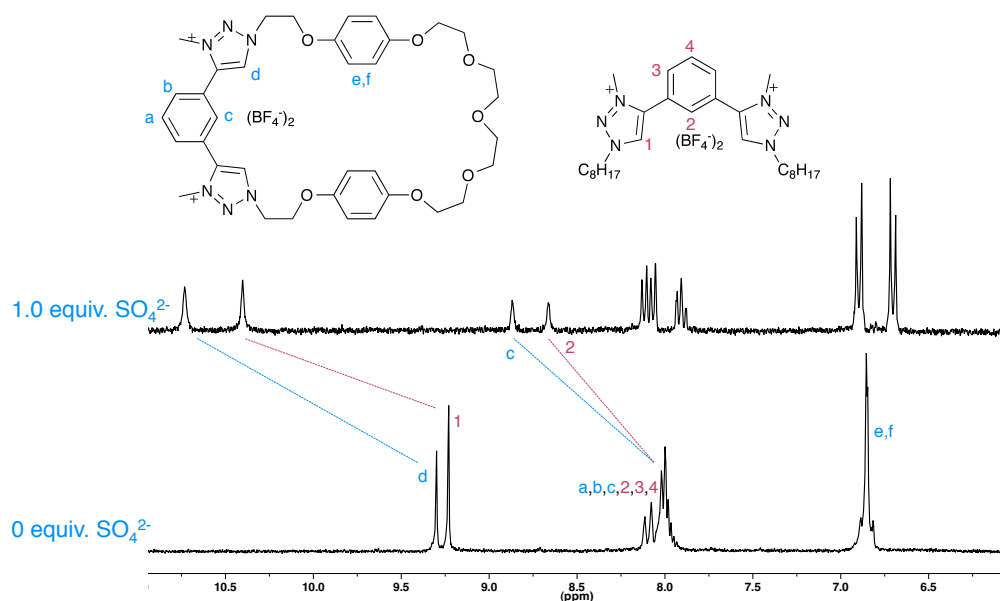


Figure 5.25: Truncated ^1H NMR spectra of **98**·(BF_4) $_2$ and **79**·(BF_4) $_2$ upon addition of $\text{TBA}_2\cdot\text{SO}_4$ (d_6 -DMSO, 293 K, 500 MHz).

macrocycle's hydroquinone resonance suggesting that only sulfate templates formation of the interweaved assembly.

The stability of the pseudorotaxane assembly was investigated using quantitative ^1H NMR titration experiments in d_6 -DMSO. Aliquots of an equimolar solution of **79**·(BF_4) $_2$ and $\text{TBA}_2\cdot\text{SO}_4$ were added to the macrocycle **98**·(BF_4) $_2$. While the threading component and anion appeared to completely dissolve, integration of the ^1H NMR spectra showed that the threading component solution was not as concentrated as expected, suggesting micro-precipitation. Numerous repetitions of the titration experiment produced the same result. The titration curve obtained is shown in Figure 5.26, with the number of equivalents of threading component on the x -axis based on integration of the ^1H NMR spectra.

The movement of the hydroquinone resonance suggests very strong pseudorotaxane formation, and this was investigated further by 2D ROESY NMR of a 1:1:1 stoichiometric mixture of **79**·(BF_4) $_2$, **98**·(BF_4) $_2$ and $\text{TBA}_2\cdot\text{SO}_4$ (Figure 5.27). Several inter-component couplings are observed, consistent with the formation of a stable pseudorotaxane in solution.

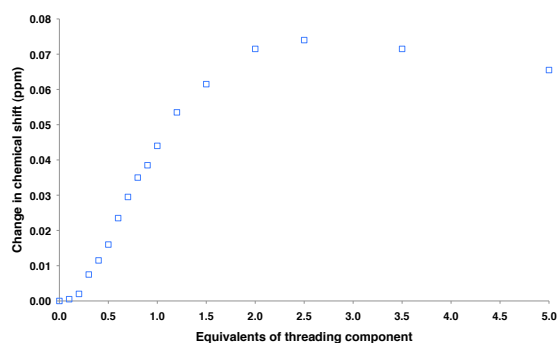


Figure 5.26: Movement of hydroquinone resonance of **98**·(BF₄)₂ upon addition of a 1:1 mixture of **79**·(BF₄)₂ and TBA₂·SO₄ (d₆-DMSO, 293 K, 500 MHz).

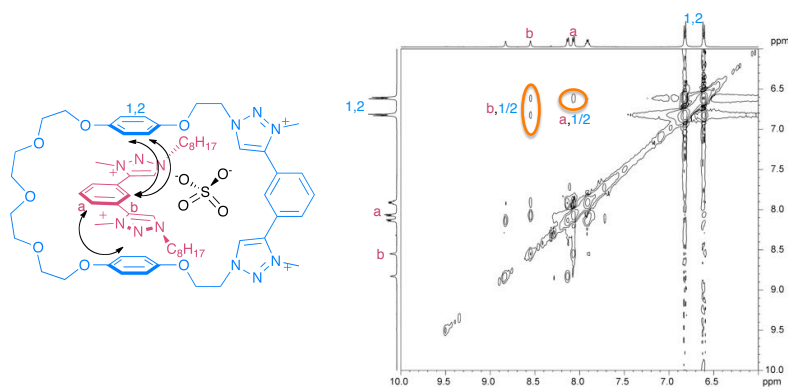


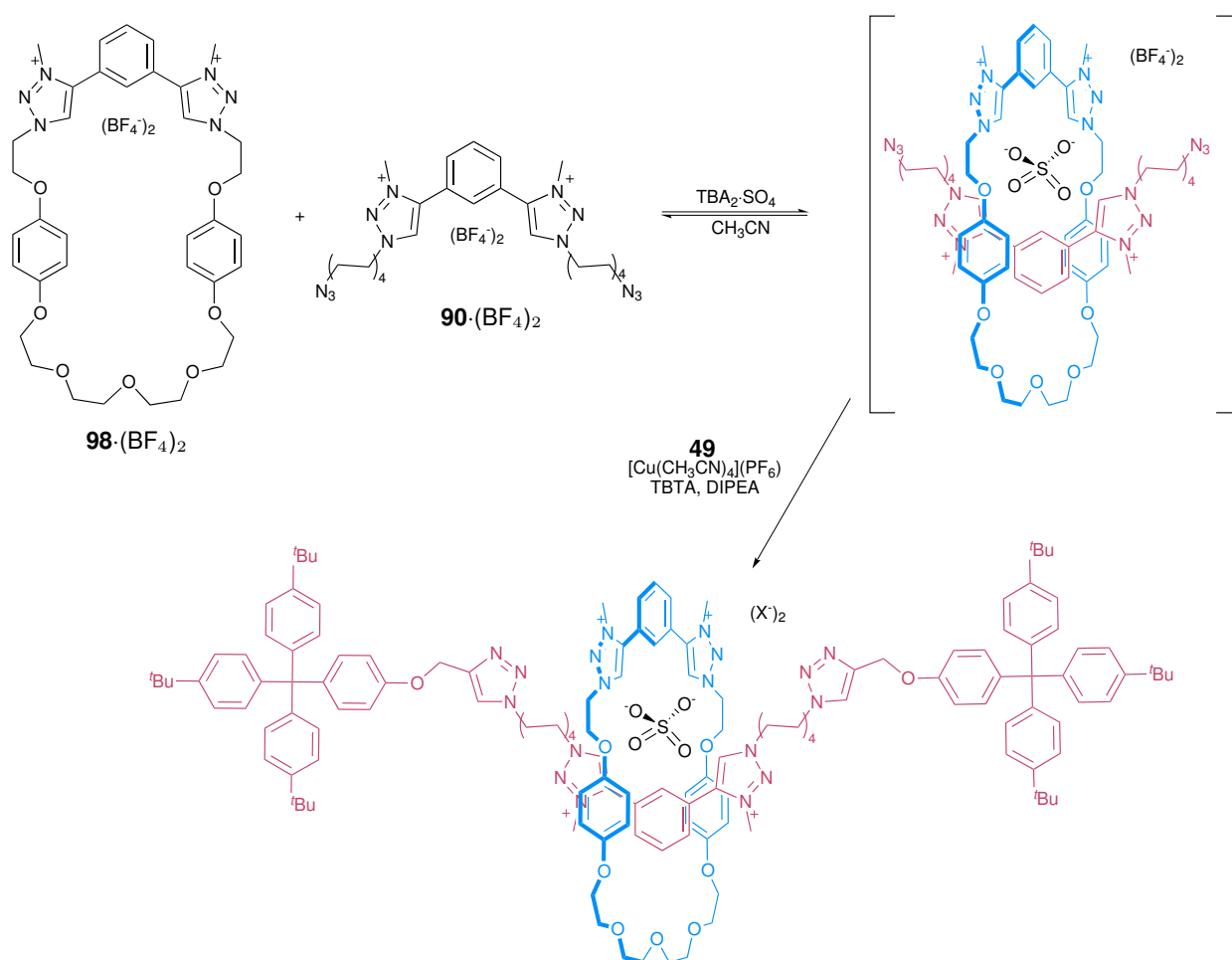
Figure 5.27: Truncated 2D ROESY NMR spectrum of a 1:1:1 stoichiometric mixture of **79**·(BF₄)₂, **98**·(BF₄)₂, TBA₂·SO₄, showing selected inter-component couplings. (d₆-DMSO, 293 K, 500 MHz).

Subsequent attempts to repeat this work using a different batch of TBA₂·SO₄ were unsuccessful. While the reasons for this are not immediately clear, it is suspected that different amounts of moisture in the respective TBA₂·SO₄ samples may be to blame.*

5.4.3.2 Formation of poly-triazolium containing interlocked receptors

The bis-triazolium macrocycle **98**·(BF₄)₂ is completely insoluble in chlorinated solvents in the presence of sulfate anion, and so the sulfate templated formation of interlocked architectures was attempted in acetonitrile. As Grubbs' II catalyst is not effective in this solvent, the synthesis of mechanically interlocked molecules was attempted using CuAAC chemistry. Initially, the synthesis of a tetra-triazolium rotaxane was targeted, as shown in Scheme 5.16.

*Solid TBA₂·SO₄ is prepared by thoroughly drying a commercially available 50% weight solution in water, and the resulting solid is appreciably hygroscopic.

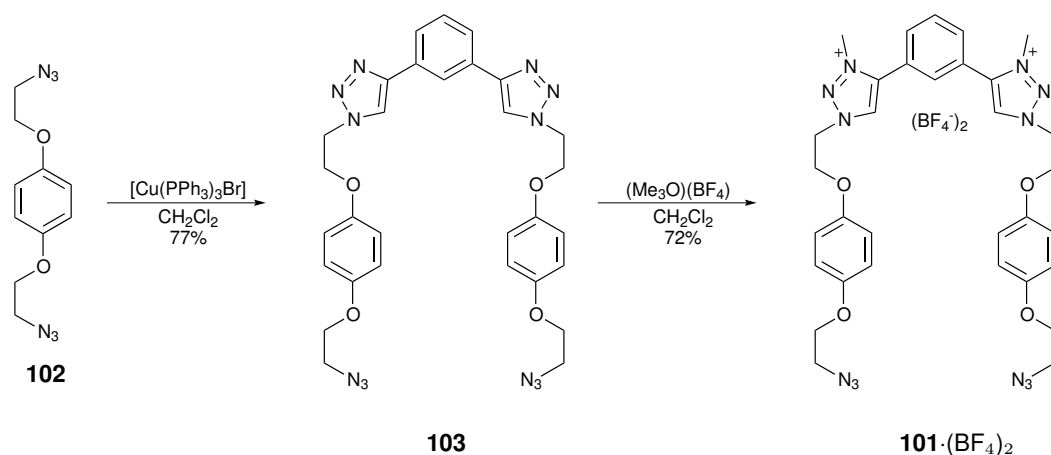


Scheme 5.16: Attempted synthesis of a tetra-triazolium rotaxane.

Bis-azide appended threading component **90**·(BF₄)₂, macrocycle **98**·(BF₄)₂ and TBA₂·SO₄ were dissolved in acetonitrile, and stopper **49**, [Cu(CH₃CN)₄](PF₆), DIPEA and TBTA added. Analysis of the crude reaction mixture using ¹H NMR spectroscopy suggested that trace amounts of rotaxane had been formed (as evidenced by upfield shifted hydroquinone resonances), but the majority of the mixture corresponded to unreacted starting material. This is almost certainly due to the very limited solubility of stopper **49** in acetonitrile. While it may well be possible to overcome this by preparing an alkyne-appended stopper that is more soluble in polar organic solvents, it was decided instead to focus on synthesis of a tetra-triazolium catenane, as this negates the need to solubilize the lipophilic stopper groups.

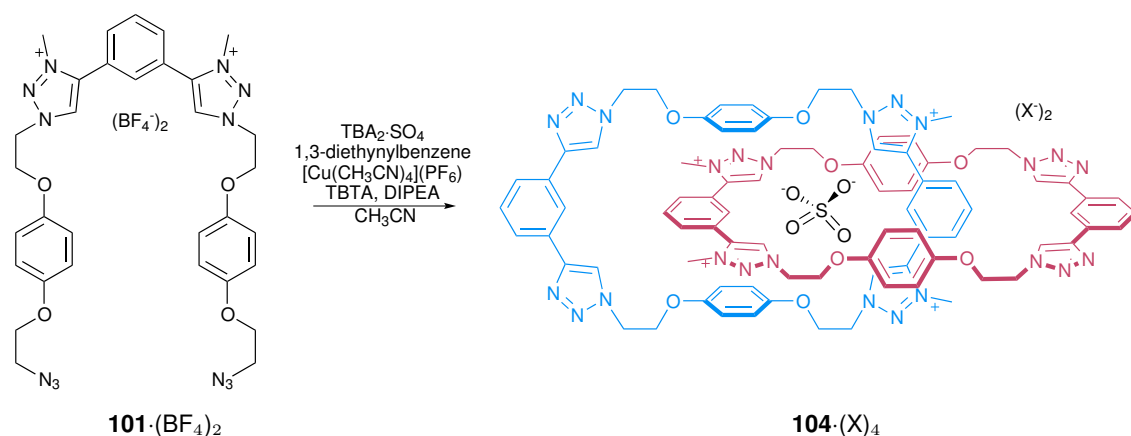
A bis-azide appended macrocycle precursor **101**·(BF₄)₂ suitable for catenane formation was synthesized as shown in Scheme 5.17: the bis-azide **102** was prepared in 83%

yield over two steps from commercially available hydroquinone bis(2-hydroxyethyl)ether as previously described.³⁸⁵ Attempting to couple this with 1,3-diethynylbenzene under CuAAC conditions using $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$, TBTA, and DIPEA gave a product that was difficult to separate from the TBTA ligand, and so $[\text{Cu}(\text{PPh}_3)_3\text{Br}]$ ³⁸⁶ was used as catalyst instead, giving bis-triazole azide **103** in 77% yield. Alkylation using trimethyloxonium tetrafluoroborate gave the bis-triazolium compound **101**· BF_4 in 72% yield after purification by preparative TLC.



Scheme 5.17: Synthesis of **101**· $(\text{BF}_4)_2$.

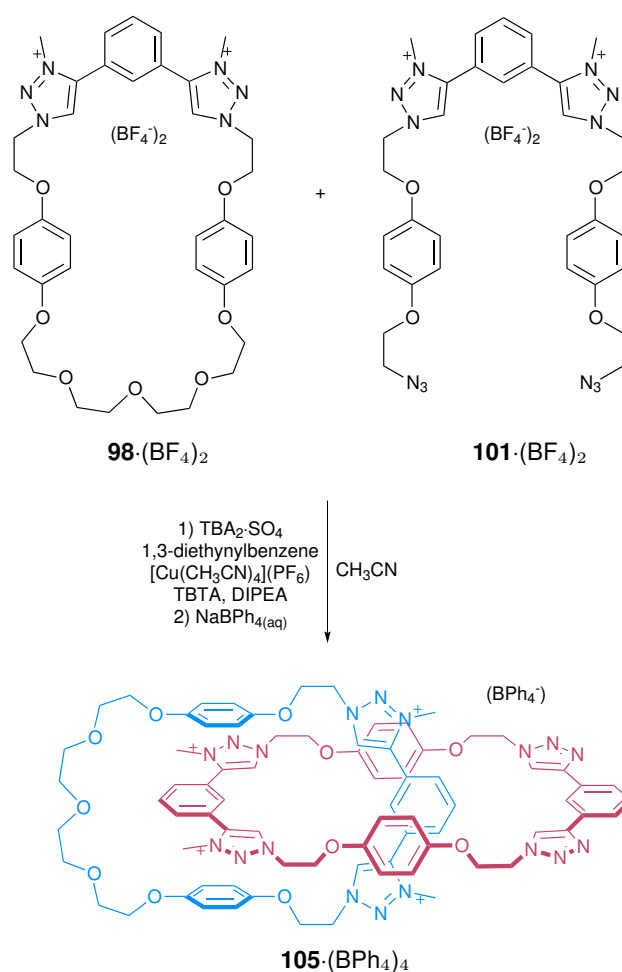
The synthesis of a *homo*-[2]catenane **104**⁴⁺ was initially attempted, as this would provide the most direct route to the interlocked host (only five steps from commercially available materials). The macrocycle precursor **101**· $(\text{BF}_4)_2$ was dissolved in acetonitrile and half a molar equivalent of $\text{TBA}_2\cdot\text{SO}_4$ was added to template pseudorotaxane formation as well as $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$, TBTA, and DIPEA to effect the CuAAC reaction (Scheme 5.18). Initial purification by preparative TLC to remove the catalyst, base and ligand, followed by ^1H NMR analysis of the crude product indicated that macrocycle and catenane were the only two significant products being formed, in an approximate ratio of 4:1. Despite repeated attempts using a variety of eluents, it was not possible to separate these two compounds using chromatography, and purification by recrystallization was similarly unsuccessful.



Scheme 5.18: Attempted synthesis of *homo*-catenane **104**·(X)₄.

The synthesis of the *hetero*-catenane **105**⁴⁺ was also attempted (Scheme 5.19). The CuAAC reaction of one molar equivalent each of **98**·(BF₄)₂ and **101**·(BF₄)₂ in the presence of one equivalent of TBA₂·SO₄ in acetonitrile gave a crude reaction mixture, which was shown by ¹H NMR analysis to contain significant amounts of the target catenane.

At least partial separation of the catenane and macrocyclic impurities could be achieved using preparative TLC, eluting with 17:2:1 acetonitrile:H₂O:KNO_{3(aq)}, however separating the resulting **105**·(NO₃)₄ from the inorganic salts in the eluent proved problematic. Typically when this eluent is used, the product is isolated from the aqueous nitrate solution by precipitation with NH₄PF₆; however, as **105**·(PF₆)₄ has significant solubility in water, this was ineffective. Instead, the catenane was eluted with a modified 17:2:1 acetonitrile:H₂O:NaNO_{3(aq)} mixture; removal of the acetonitrile under reduced pressure followed by addition of sodium tetraphenylborate precipitated crude **105**·(BPh₄)₄. By repeating this purification procedure, a very small amount of a reasonably pure sample of the target compound was prepared.



Scheme 5.19: Synthesis of *hetero*-catenane $\mathbf{105} \cdot (\text{BPh}_4)_4$.

This was characterized by high resolution ESI mass spectrometry and ^1H NMR spectroscopy (Figure 5.28). Due to the similar chemical environments of a number of signals, it is not possible to distinguish between them (for example, it is not possible to say which of the two triazolium resonances ϵ belongs to which macrocycle). Despite this, and despite the slight impurities present, all proton resonances can be sensibly assigned, confirming the identity of the tetra-triazolium catenane.

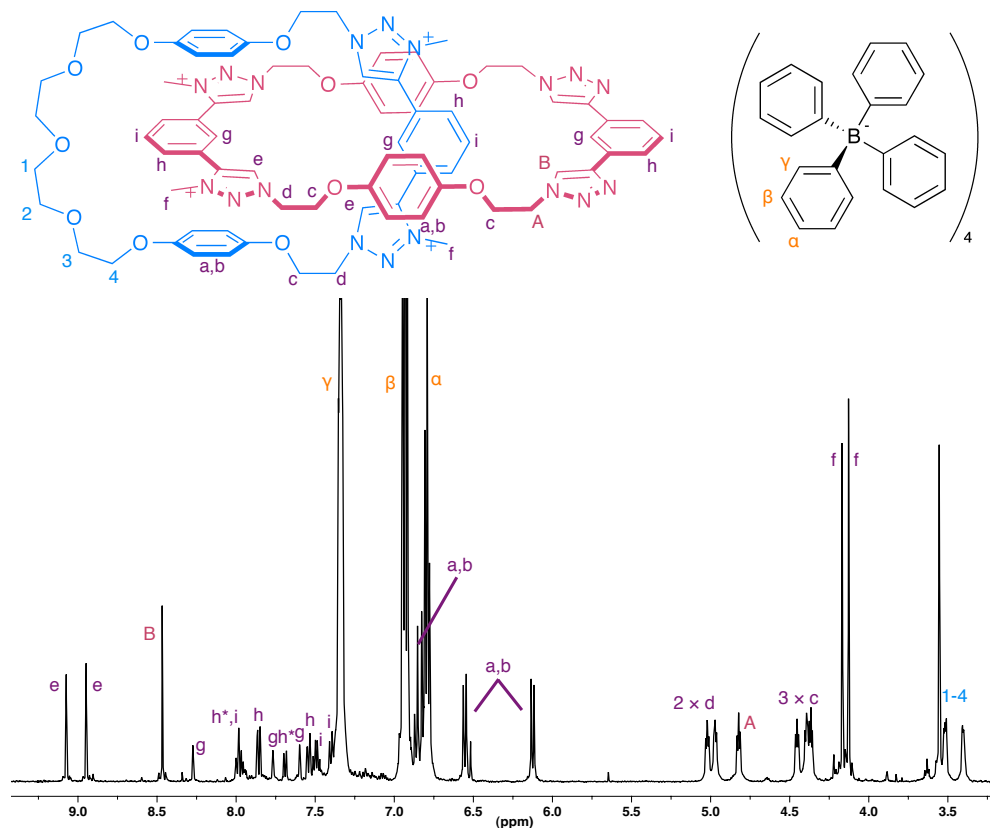


Figure 5.28: Truncated ^1H NMR spectrum of **105**·(BPh_4) $_4$. Peaks that could belong to either macrocyclic component are labelled in purple, in one case the two h environments appear to be inequivalent, these have been labelled h^* (d_6 -acetone, 293 K, 500 MHz).

In an effort to overcome the inherent difficulties with purifying highly charged tetra-cationic systems, the synthesis of catenanes incorporating the mono-cationic triazole-phenyl-triazolium motif was investigated. Bis-azide **103** was mono-alkylated using methyl iodide in dichloromethane at 50 °C as shown in Scheme 5.20. Anion exchange by repeated washing with aqueous ammonium hexafluorophosphate solution gave **106**· PF_6 in 27% yield.



$\text{106} \cdot \text{PF}_6^-$

TBA·Cl or TBA₂·SO₄
 1,3-diethynylbenzene,
 [Cu(CH₃CN)₄](PF₆)
 TBTA, DIPEA
 $\xrightarrow{\text{CH}_2\text{Cl}_2}$

$(\text{X}^-)_2$

Scheme 5.21: Attempted synthesis of bis-triazolium *homo*-catenane.

5.5 Conclusions

5.5.1 Summary

The CuAAC reaction was used to synthesize three tetra-triazole macrocycles, one of which could be alkylated to give the tetra-triazolium receptor. This tetra-cationic system displays impressive anion recognition in 1:1 d₆-DMSO:D₂O: sulfate is bound very strongly, while amongst the mono-anionic species, iodide and bromide are bound significantly more strongly than chloride, fluoride or acetate. Extensive solution phase modelling suggests that this is due to both preorganization and solvation effects.

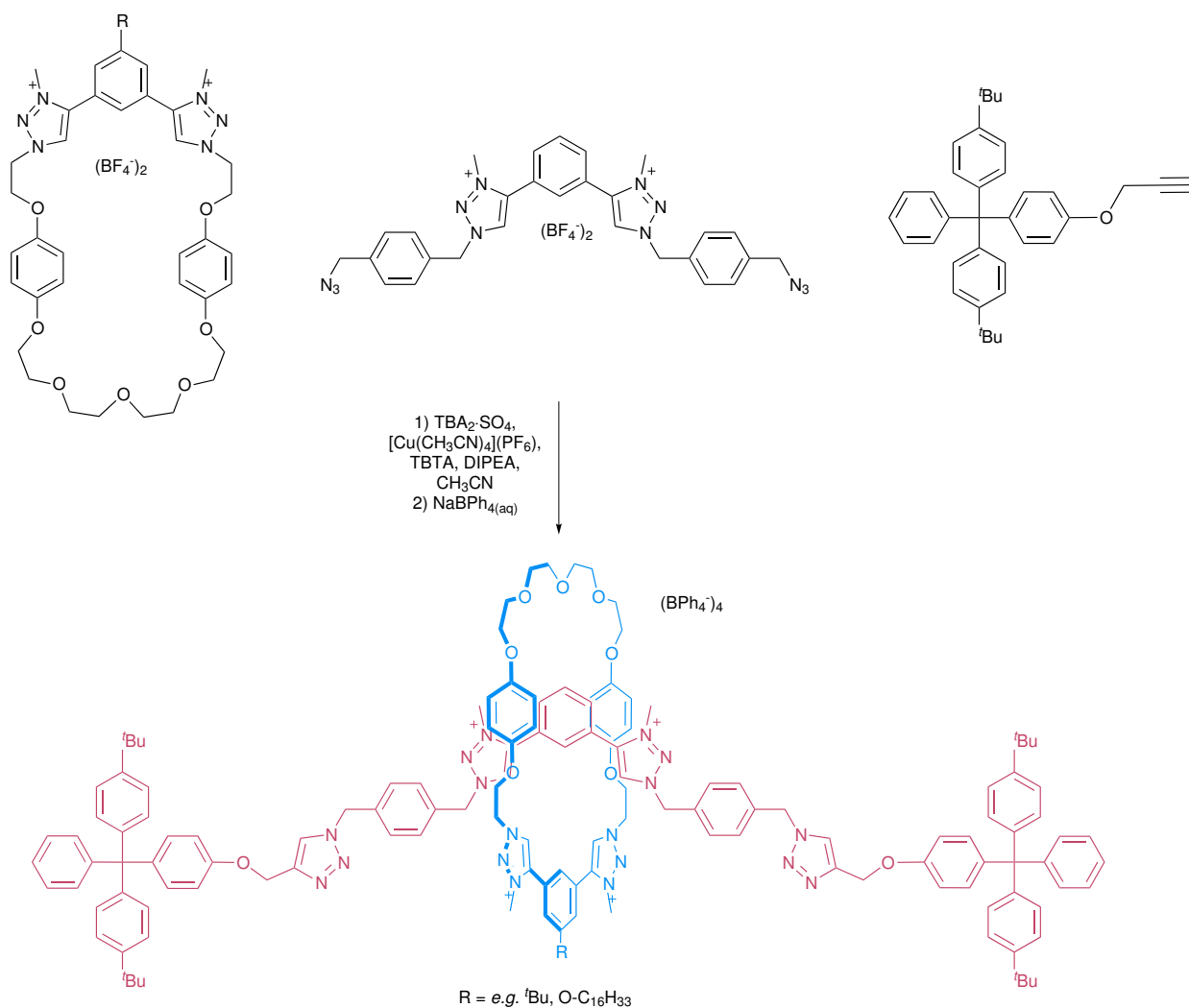
The synthesis of interlocked poly-triazolium receptors was attempted, initially using a bis-triazolium axle component. Neither Grubbs' II-catalyzed RCM nor amide condensation strategies yielded the target rotaxane, and so a stoppering route was used to prepare an interlocked architecture incorporating the bis-triazolium motif. The anion binding affinities of this host were surprisingly weak, which was attributed to the poor preorganization features of the rotaxane.

To increase the anion recognition strength of the receptor, the introduction of additional positive charge into the host framework was attempted: a bis-triazolium macrocycle was synthesized, which formed a stable sulfate templated pseudorotaxane with a bis-triazolium threading component. The CuAAC reaction could be used to prepare a *hetero*-tetra-triazolium catenane from this interweaved assembly in reasonable yield, however this interlocked product proved extremely difficult to purify.

5.5.2 Future work

In order to synthesize highly charged interlocked anion receptors for *strong* and *selective* anion recognition, a more lipophilic host should be designed, to facilitate purification using chromatographic techniques. It is suggested that a rotaxane would be preferable, as the bulky stopper groups would help to solubilize the interlocked host architecture. The synthesis of such a molecule was attempted using a sulfate anion templated stoppering strategy (Section 5.4.3.2), but this was not successful as the tris-*t*butyl substituted stopper group was insoluble in the acetonitrile solvent used for the reaction. Since this work was

conducted, the bis-*t*-butyl substituted stopper has been observed to be soluble in this solvent, which may allow for synthesis of the rotaxane host. If this route were used, it would also allow facile incorporation of further solubilising groups on the macrocyclic component (Scheme 5.22). It is expected that such a tetra-triazolium rotaxane would display a marked selectivity for the templating sulfate anion, with larger anions being excluded based on their size, and halide anions binding weakly relative to sulfate due to their lesser monoanionic charge.



Scheme 5.22: Postulated synthesis of a more tractable tetra-triazolium interlocked anion receptor.

The incorporation of bromo- or iodo-triazolium heterocycles into macrocycles and interlocked structures would allow potent and selective anion recognition using halogen bonding. The synthesis of the halogen bonding analogue of **98**²⁺ was not attempted,

as it was thought that the phenyl-1,3-bis(halotriazolium) motif would be too small to allow convergent binding of an anion. However, Huber has recently demonstrated that convergent binding of halides using similar molecules is indeed possible,³⁸⁷ as discussed in the Conclusions to Chapter Three. A tetra-halotriazolium rotaxane, for example, the iodotriazolium analogue of the rotaxane shown in Scheme 5.22, would potentially allow extremely strong anion recognition in competitive solvent mixtures.

Chapter 6

Experimental

6.1 Titration Protocols

Spectra for ^1H NMR titrations were recorded at 293 K on a Varian Unity Plus 500 spectrometer with ^1H operating at 500 MHz. Initial sample volumes were 0.50 mL and concentrations were 2.0 mM of host. Solutions (100 mM) of anions as their tetrabutylammonium salts, metals as their hexafluorophosphate salts or threading components were added in aliquots, the samples thoroughly shaken and spectra recorded. Spectra were recorded at 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 equivalents. In all cases where association constants were calculated, bound and unbound species were found to be in fast exchange on the NMR timescale. Stability constants were obtained by analysis of the resulting data using the WinEQNMR2³²⁸ computer program.

Binding stoichiometries were investigated by visual analysis of the titration data, and using approximations of Job plots. A graph of $\Delta\delta \cdot \chi_{\text{H}}$ against χ_{H} was plotted, with a 1:1 binding stoichiometry corresponding to a maximum $\delta \cdot \chi_{\text{H}} \sim 0.5$ (χ_{H} = mole fraction of host, $\Delta\delta$ = change in chemical shift relative to free host).

Estimates for the association constant and the limiting chemical shifts were added to the program's input file. The parameters were refined by non-linear least-squares analysis using WINEQNMR2³²⁸ to achieve the best fit between observed and calculated chemical shifts. The input parameters for the final chemical shift and association constant were adjusted based on the program output until convergence was reached. Comparison of the calculated and experimental binding isotherms demonstrated that an appropriate model with an appropriate stoichiometry was being used.

WINEQNMR2 also provides an estimate of the standard error of the measurement, which is included with all data. To avoid introduction of inaccuracies by rounding, the absolute values of an association constant and its error are given in the text: for example 566(23) M^{-1} rather than 570(20) or $5.7(2) \times 10^2 \text{ M}^{-1}$. This has the disadvantage that values are often given to more significant figures than is statistically valid, but this is taken into account when discussing the similarities and differences between association constants. It should also be noted that these estimated errors only account for the fitting of a binding isotherm to the titration data, they do not consider systematic error behind such data, for example an incorrect concentration of the titrant solution. While the relative concentrations of solutions were checked by integration of the ^1H NMR spectra, the magnitude of the errors provided by WINEQNMR2 are probably underestimated.

6.2 X-ray Crystallography

Single crystal X-ray diffraction data were collected using either Mo K α radiation, Cu K α radiation, or synchrotron radiation, as described below. Full crystallographic data in CIF format are provided in the Appendix.

6.2.1 Data collected using Mo K α radiation

Data were collected using graphite monochromated Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$) on a Nonius Kappa CCD diffractometer equipped with a Cryostream N2 open-flow cooling device,³⁸⁸ at 150 K. Series of scans were performed in such a way as to collect a complete set of unique reflections to a maximum of $0.77 \text{ \AA}$ or to the limit of diffraction. Raw frame data (including data reduction, inter-frame scaling, unit cell refinement and absorption corrections) were processed using the DENZO-SMN package.³⁸⁹

6.2.2 Data collected using Cu K α radiation

Data were collected using graphite monochromated Cu K α radiation ($\lambda = 1.54184 \text{ \AA}$) on an Oxford Diffraction SuperNova diffractometer equipped with a Cryostream N2 open-flow cooling device,³⁸⁸ at 150 K. Series of scans were performed in such a way as to collect a complete set of unique reflections to a maximum of $0.80 \text{ \AA}$ or to the limit of diffraction. Raw frame data (including data reduction, inter-frame scaling, unit cell refinement and absorption corrections) were processed using CrysAlis Pro.³⁹⁰

6.2.3 Data collected using synchrotron radiation

Data were collected using Si-111 double-crystal monochromated synchrotron radiation ($\lambda = 0.6889$ or $1.1949 \text{ \AA}$) on Beamline I19 at Diamond Light Source.³⁹¹ A Cryostream N2 open-flow cooling device,³⁸⁸ was used to cool samples to either 100 or 150 K. Series of scans were performed in such a way as to collect a complete set of unique reflections to a maximum of $0.65 \text{ \AA}$ or to the limit of diffraction. Raw frame data (including data reduction, inter-frame scaling, unit cell refinement and absorption corrections) were processed using either CrystalClear³⁹² or CrysAlis Pro.³⁹⁰

6.2.4 Structure solution and refinement

Structures were solved using either SIR92³⁹³ or SUPERFLIP³⁹⁴ and refined using full-matrix least-squares on F^2 within the CRYSTALS suite.³⁹⁵ All non-hydrogen atoms were refined with anisotropic displacement parameters. After the construction of a stable, chemically reasonable model (using bond length, bond angle and thermal ellipsoid parameter restraints where necessary), the weights were optimized,^{396,397} outlying reflections were omitted, and, in the case of poorly diffracting samples, data beyond the diffraction limit were removed using the Wilson plot as a guide.

Where positional disorder was present, it was modeled by having multiple positions for the affected atoms. The occupancy of each position was optimized and then fixed. Several of the larger structures presented contained regions of diffuse electron density, which could not be sensibly modeled. In these cases, the SQUEEZE program³⁹⁸ within the PLATON suite³⁹⁹ was used to include this electron density in the refinement. Where crystals were found to be twinned:

appropriate twin laws were determined using the ROTAX package⁴⁰⁰ within the CRYSTALS suite.³⁹⁵ The relative fraction of each twin component was refined.

6.2.5 Treatment of hydrogen atoms

Hydrogen atoms were generally visible in the difference map and were initially refined with restraints on bond lengths and angles, after which the positions were used as the basis for a riding model.⁴⁰¹ Occasionally this led to unstable refinements (typically for hydrogen atoms attached to atoms with large thermal ellipsoids in structures based on low quality data), in which case the offending hydrogen atoms were placed at geometric positions. Where amide hydrogen atoms were not visible in the map, they were inserted at geometric positions and refined using riding constraints. Where alcohol hydrogen atoms were not visible in the map, they were inserted at idealized hydrogen bonding positions and refined using riding constraints.

6.2.5.1 Errors associated with hydrogen bonding distances and angles

Errors can be obtained for distances and angles using standard crystallography programs. Even for a poor quality dataset, these estimated errors are small (typically around 0.01 Å for H···A distances, 0.2° for D–H···A angles, 0.4% for %VdW_{H,A} values), while for high quality datasets, they are considerably smaller (typically around 0.002 Å for H···A distances, 0.05° for D–H···A angles, 0.15% for %VdW_{H,A} values). Due to the weak scattering of X-rays by hydrogen atoms, these values have little or no chemical significance, therefore, errors are not reported in the text. Instead values are given to a small number of significant figures, and the error is expected to be significantly less than the range the value reflects. It should also be noted that the inter-nuclear distance for D–H bonds is underestimated by X-rays, the “real” value of this distance will be larger, and the corresponding H···X and %VdW_{H,X} distances shorter.⁴⁰²

6.3 Synthesis and characterization

6.3.1 Safety note

CAUTION: Low molecular weight organic azides, sodium azide and 1,2,3-triazole and triazolium groups are potentially explosive. While no problems were encountered in the course of this work, they should be handled in small quantities and with appropriate care.

In an addendum to the communication reporting its preparation,³³⁶ the authors reported that the hydrochloride salt of imidazolesulfonyl azide is hygroscopic, and potentially explosive when wet. A recent paper has suggested that the H_2SO_4 or HBF_4 adducts are equally good diazo transfer agents and can be handled far more safely.⁴⁰³ **The use of these salts is therefore recommended in preference to the hydrochloride adduct.**

6.3.2 Reactants and reagents

Unless otherwise specified, reagents were bought from commercial suppliers and used as received. Where solvents are specified as “dry,” they were purged with nitrogen and passed through an MBraun MPSP-800 column. Water was de-ionized and microfiltered using a Milli-Q Millipore machine. TBA salts, Grubbs’ II catalyst, $\text{Pd}_2(\text{dba})_3$, $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$, TBTA and AgPF_6 were stored in a vacuum desiccator. Column chromatography was performed on silica gel (particle size: 40–63 μm), preparative TLC was performed on 20 $\times$ 20 cm plates, with a silica layer of thickness 1 mm. NEt_3 was distilled from, and stored over, KOH pellets. Amberlite[®] was “loaded” by washing the resin with $\text{NaOH}_{(\text{aq})}$ (10%), water, and either $\text{NH}_4\text{Cl}_{(\text{aq})}$ (1 M) or $\text{NH}_4\text{PF}_6_{(\text{aq})}$ (0.1 M), followed by further water, and the solvent to be used in the anion exchange.

Brine refers to a saturated aqueous solution of NaCl, $\text{NH}_4\text{OH}_{(\text{aq})}$ refers to a 28–30% solution of NH_3 in water. Aqueous NH_4OH /EDTA refers to an aqueous solution containing 1 M $\text{NH}_4\text{OH}_{(\text{aq})}$ and 0.02 M ethylenediaminetetraacetic acid. Petrol refers to the fraction of petroleum ether boiling between 40 and 60 °C.

Literature routes followed to prepare known compounds are generally given in the text. TBTA⁴⁰⁴ and imidazolesulfonyl azide·HCl³³⁶ were prepared as previously described.

6.3.3 Characterization

6.3.3.1 NMR spectroscopy

Routine NMR spectra were recorded on a Varian Mercury 300 spectrometer with ^1H NMR operating at 300 MHz, ^{13}C at 75.5 MHz, ^{19}F at 283 MHz, and ^{31}P at 122 MHz. Some compounds were too poorly-soluble, or not enough compound was synthesized to allow ^{13}C NMR spectra to be recorded on the 300 MHz spectrometer. In these cases, the spectra were collected on a Bruker AVII 500 spectrometer with a 5 mm $^{13}\text{C}(^1\text{H})$ dual cryoprobe with ^{13}C operating at 126 MHz.

Proton-proton coupling constants are vicinal, 3-bond (^3J) unless otherwise indicated. All spectra were referenced to the residual solvent peak,⁴⁰⁵ when mixed solvents were used, the spectra were referenced to the component of the mixture having the most deuterium atoms (*e.g.* a 1:1 mixture of $\text{CDCl}_3:\text{CD}_3\text{OD}$ would be referenced to the residual methanol signal).

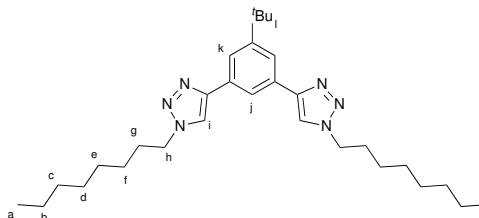
Where the expected number of ^{13}C resonances are not visible, due to these peaks overlapping, or being too weak to be detected, the number of “missing” peaks is noted. When appropriate, 2D COSY and/or ROESY NMR spectroscopies were used to aid assignment of ^1H NMR spectra; however, in many cases, even 2D techniques could not definitively assign all resonances, and so peak assignments should be considered a guide only.

6.3.3.2 Mass spectrometry

High resolution ESI mass spectra were recorded on a Bruker μTOF spectrometer. High resolution EI mass spectra were recorded on a Waters GCT Classic spectrometer. Low resolution ESI mass spectra were recorded on a Waters LCT premier spectrometer.

6.4 Synthesis of compounds from Chapter 2

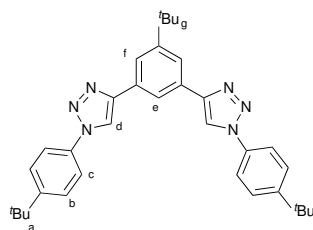
C-linked alkyl substituted bis-triazole receptor **3**



5-*t*-Butyl-1,3-diethynylbenzene (0.182 g, 1.00 mmol) was dissolved in 4:1 DMF:H₂O (15 mL). NaN₃ (0.156 g, 2.40 mmol), Na₂CO₃ (0.106 g, 1.00 mmol), CuSO₄·5H₂O (0.050 g, 0.20 mmol), ascorbic acid (0.176 g, 1.00 mmol) and bromooctane (0.38 mL, 0.43 g, 2.2 mmol) were added and the mixture heated to 80 °C under a nitrogen atmosphere for 16 hours. The reaction was then cooled to room temperature and partitioned between aqueous NH₄OH/EDTA (50 mL), and Et₂O (50 mL). The aqueous layer was extracted further with Et₂O (50 mL), and the combined organic fractions were washed with H₂O (50 mL), brine (50 mL) and dried (MgSO₄). Purification by column chromatography (4% CH₃OH in CHCl₃) gave **3** as a yellow oil. Yield: 0.470 g (95%).

¹H NMR (CDCl₃): 8.06 (s, 1H, *H*_j), 7.89 (s, 2H, 2 × *H*_i), 7.85 (s, 2H, 2 × *H*_k), 4.41 (t, *J*_{g,h} = 7.2 Hz, 4H, 4 × *H*_h), 1.91–2.00 (m, 4H, 4 × *H*_g), 1.41 (s, 9H, 9 × *H*_l), 1.22–1.38 (m, 20H, 4 × *H*_b, 4 × *H*_c, 4 × *H*_d, 4 × *H*_e, 4 × *H*_f), 0.87 (t, *J*_{a,b} = 6.9 Hz, 6H, 6 × *H*_a). ¹³C NMR (CDCl₃): 152.6, 147.9, 131.0, 122.5, 120.4, 119.8, 50.5, 40.4, 31.8, 31.4, 30.4, 29.1, 29.0, 26.5, 22.7, 14.1. HRESI-MS (pos.): 515.3816, calc. for [C₃₀H₄₈N₆·Na]⁺ = 515.3833.

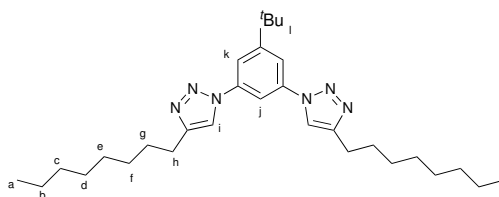
C-linked aryl substituted bis-triazole receptor **4**



NaN₃ (0.098 g, 1.5 mmol), L-proline (0.035 g, 0.30 mmol), Na₂CO₃ (0.032 g, 0.30 mmol), sodium ascorbate (0.099 g, 0.50 mmol) and CuSO₄·5H₂O (0.037 g, 0.15 mmol) were placed in a microwave vial. 5-*t*-butyl-1,3-Diethynylbenzene (0.091 g, 0.50 mmol), 4-*t*-butyl-iodobenzene (0.20 mL, 0.29 g, 1.1 mmol) were combined in 9:1 DMSO:H₂O (2 mL) and added to the dry reagents. The mixture was deoxygenated with nitrogen, the vial sealed and the reaction heated to 65 °C for 16 hours. It was cooled to room temperature and partitioned between aqueous NH₄OH/EDTA (30 mL) and EtOAc (30 mL). The aqueous layer was extracted with further EtOAc (2 × 30 mL), the combined organic phases washed with brine (60 mL), dried (MgSO₄) and taken to dryness under reduced pressure. Purification by column chromatography (1% CH₃OH in CH₂Cl₂) gave a yellow oil, which ¹H NMR showed to be slightly impure **4**. This was taken up in CH₃OH (5 mL) and cooled in a freezer causing the precipitation of clean **4** as yellow crystals, which were isolated by filtration. Yield: 0.047 g (18%).

^1H NMR (CDCl_3): 8.30 (s, 2H, $2 \times H_d$), 8.22 (t, $^4J_{e,f} = 1.4$ Hz, 1H, H_e), 8.00 (d, $^4J_{e,f} = 1.4$ Hz, 2H, $2 \times H_f$), 7.75 (d, $J_{b,c} = 8.6$ Hz, 4H, $4 \times H_c$), 7.58 (d, $J_{b,c} = 8.6$ Hz, 4H, $4 \times H_b$), 1.46 (s, 9H, $9 \times H_g$), 1.39 (s, 18H, $18 \times H_a$). ^{13}C NMR (CDCl_3): 152.9, 152.3, 148.4, 134.8, 130.8, 126.8, 123.1, 120.7, 120.4, 118.1, 35.2, 35.0, 31.5, 31.4. HRESI-MS (pos.): 555.3209, calc. for $[\text{C}_{34}\text{H}_{40}\text{N}_6\cdot\text{Na}]^+ = 555.3207$.

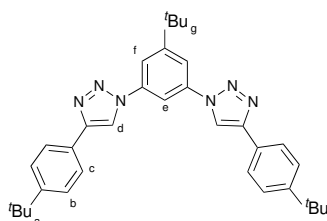
N-linked alkyl substituted bis-triazole receptor 5



5-*t*-Butyl-1,3-diiodobenzene (0.193 g, 0.500 mmol) and decyne (0.190 mL, 0.145 g, 1.05 mmol) were placed in a small vial. L-proline (0.023 g, 0.20 mmol), Na_2CO_3 (0.021 g, 0.20 mmol), sodium ascorbate (0.040 g, 0.20 mmol), NaN_3 (0.078 g, 1.2 mmol), $\text{CuSO}_4\cdot 5\text{H}_2\text{O}$ (0.025 g, 0.10 mmol) and 9:1 DMSO: H_2O (2 mL) were added, the suspension deoxygenated with nitrogen, the vial sealed and heated to 65 °C for 16 hours. It was cooled to room temperature, poured into $\text{NH}_4\text{OH}_{(\text{aq})}$ (1 M, 30 mL) and then extracted with EtOAc (3×20 mL). The combined organic fractions were washed with brine (2×20 mL), dried (MgSO_4) and taken to dryness under reduced pressure. Purification by column chromatography (gradient: 15:1 – 10:1 CH_2Cl_2 :acetone) gave **5** as a golden oil. Yield: 0.195 g (79%).

^1H NMR (CDCl_3): 7.89 (t, $J_{j,k} = 2.0$ Hz, 1H, H_j), 7.80–7.82 (m, 4H, $2 \times H_i$, $2 \times H_k$), 2.80 (t, $J_{g,h} = 7.7$ Hz, 4H, $4 \times H_h$), 1.68–1.78 (m, 4H, $4 \times H_g$), 1.22–1.44 (m, 29H, $4 \times H_b$, $4 \times H_c$, $4 \times H_d$, $4 \times H_e$, $4 \times H_f$, $9 \times H_l$), 0.87 (t, $J_{a,b} = 6.9$ Hz, 6H, $6 \times H_a$). ^{13}C NMR (CDCl_3): 155.6, 149.7, 138.1, 119.0, 117.3, 109.7, 35.6, 32.0, 31.3, 29.5, 29.5, 29.4, 29.3, 25.8, 22.8, 14.2. HRESI-MS (pos.): 515.3833, calc. for $[\text{C}_{30}\text{H}_{48}\text{N}_6\cdot\text{Na}]^+ = 515.3833$.

N-linked aryl substituted bis-triazole receptor 6

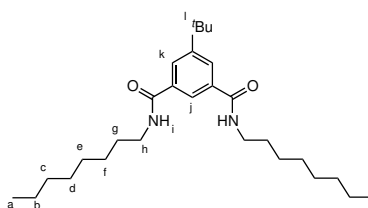


5-*t*-Butyl-1,3-diiodobenzene (0.193 g, 0.50 mmol), 4-*t*-butyl-ethynylbenzene (0.20 mL, 0.17 g, 1.1 mmol), L-proline (0.035 g, 0.30 mmol), Na_2CO_3 (0.032 g, 0.30 mmol), NaN_3 (0.098 g, 1.5 mmol), sodium ascorbate (0.099 g, 0.50 mmol) and $\text{CuSO}_4\cdot 5\text{H}_2\text{O}$ (0.037 g, 0.15 mmol) were placed in a microwave vial. 9:1 DMSO: H_2O (2 mL) was added, and the mixture deoxygenated with nitrogen. The vial was sealed and heated to 60 °C for 4 days. It was then cooled to room temperature and partitioned between aqueous NH_4OH /EDTA (30 mL) and EtOAc (30 mL). The aqueous layer was extracted with further EtOAc (2×30 mL), and the combined organic fractions were washed with

brine (60 mL), dried (MgSO₄), and taken to dryness under reduced pressure to give a yellow oil. This was taken up in hot CH₃OH (5 mL), and left to stand in a freezer overnight, resulting in the precipitation of **6** as pale yellow crystals, which were isolated by filtration and washed with cold CH₃OH (2 mL). Yield: 0.019 g (14%).

¹H NMR (CDCl₃): 8.29 (s, 2H, 2 × *H*_d), 8.05 (t, ⁴*J*_{e,f} = 1.4 Hz, 1H, *H*_e), 7.93 (d, ⁴*J*_{e,f} = 1.4 Hz, 2H, 2 × *H*_f), 7.88 (d, *J*_{b,c} = 8.2 Hz, 4H, 4 × *H*_c), 7.51 (d, *J*_{b,c} = 8.2 Hz, 4H, 4 × *H*_b), 1.47 (s, 9H, 9 × *H*_g), 1.37 (s, 18H, 18 × *H*_a). ¹³C NMR (CDCl₃): 155.9, 151.9, 148.9, 138.0, 127.2, 126.0, 125.8, 117.7, 117.5, 109.9, 35.8, 34.9, 31.4, 31.3. HRESI-MS (pos.): 555.2308, calc. for [C₃₄H₄₀N₆·Na]⁺ = 555.2307.

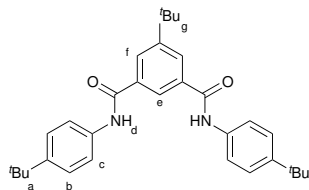
Alkyl substituted bis-amide receptor **7**



5-*t*-Butyl-isophthalic acid (0.222 g, 1.00 mmol) was suspended in SOCl₂ (10 mL). Pyridine (2 drops) was added cautiously and the colourless suspension heated to reflux for 16 hours under a nitrogen atmosphere. It was cooled to room temperature, and unreacted SOCl₂ removed under reduced pressure, before the resulting yellow solid was dried further under high vacuum. It was taken up in dry CH₂Cl₂ (30 mL), and NEt₃ (0.42 mL, 0.30 g, 3.0 mmol) was added, followed by a solution of octyl amine (0.40 mL, 0.31 g, 2.4 mmol) in dry CH₂Cl₂ (10 mL). The reaction was stirred at room temperature under a nitrogen atmosphere for 2 hours and then washed with HCl_(aq) (10%, 2 × 40 mL) and H₂O (40 mL), dried (MgSO₄) and taken to dryness under reduced pressure. Purification by column chromatography (5% CH₃OH in CH₂Cl₂) gave **7** as an off-white foam. Yield: 0.396 g (89%).

¹H NMR (CDCl₃): 7.89–7.92 (m, 3H, 2 × *H*_k, *H*_j), 6.71 (t, *J*_{h,i} = 5.6 Hz, 2H, 2 × *H*_i), 3.33–3.40 (m, 4H, 4 × *H*_h), 1.51–1.60 (m, 4H, 4 × *H*_g), 1.18–1.35 (m, 20H, 4 × *H*_b, 4 × *H*_c, 4 × *H*_d, 4 × *H*_e, 4 × *H*_f), 0.85 (t, *J*_{a,b} = 6.7 Hz, 6H, 6 × *H*_a). ¹³C NMR (CDCl₃): 167.4, 152.4, 134.8, 127.2, 122.1, 40.4, 35.1, 31.9, 31.2, 29.7, 29.4, 29.3, 27.1, 22.7, 14.2. HRESI-MS (pos.): 467.3603, calc. for [C₂₈H₄₈N₂O₂·Na]⁺ = 467.3608.

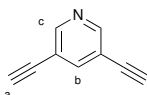
Aryl substituted bis-amide receptor **8**



5-*t*-Butyl-isophthalic acid (0.222 g, 1.00 mmol) was suspended in SOCl_2 (10 mL). Pyridine (2 drops) was added cautiously and the colourless suspension was heated to reflux for 16 hours under a nitrogen atmosphere. The reaction mixture was cooled to room temperature, and unreacted SOCl_2 removed under reduced pressure, before the resulting yellow solid was dried further under high vacuum. It was taken up in dry CH_2Cl_2 (30 mL) and NEt_3 (0.42 mL, 0.30 g, 3.0 mmol) was added, followed by 4-*t*-butyl-aniline (0.35 mL, 0.33 g, 2.2 mmol) in further dry CH_2Cl_2 (10 mL). The reaction was stirred at room temperature under a nitrogen atmosphere for 5 hours and then washed with $\text{HCl}_{(\text{aq})}$ (1 M, 2×40 mL) and H_2O (40 mL), dried (MgSO_4) and taken to dryness under reduced pressure. The crude product was filtered through a short pad of silica (eluting with 5% CH_3OH in CH_2Cl_2) and then recrystallized from boiling CH_3OH (15 mL) to give **8** as large, slightly off-white crystals. Yield: 0.355 g (73%).

^1H NMR (CDCl_3): 8.28 (br. s, 2H, $2 \times H_d$), 7.96–8.01 (m, 3H, H_e , $2 \times H_f$), 7.58 (d, $J_{b,c} = 8.6$ Hz, 4H, $4 \times H_c$), 7.37 (d, $J_{b,c} = 8.6$ Hz, 4H, $4 \times H_b$), 1.32 (s, 27H, $18 \times H_a$, $9 \times H_g$). ^{13}C NMR (d_6 -acetone): 165.9, 152.8, 147.4, 137.7, 136.5, 128.3, 126.3, 124.5, 120.8, 35.7, 34.9, 31.7, 31.5. HRESI-MS (pos.): 507.2973, calc. for $[\text{C}_{32}\text{H}_{40}\text{N}_2\text{O}_2\cdot\text{Na}]^+ = 507.2982$.

3,5-Diethynyl pyridine **9**

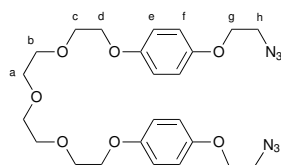


Prepared by a modification of literature procedures.^{334,335}

A vial was loaded with 3,5-dibromopyridine (0.711 g, 3.00 mmol), $\text{Pd}_2(\text{dba})_3$ (0.046 g, 0.050 mmol), CuI (0.029 g, 0.15 mmol) and triphenylphosphine (0.131 g, 0.500 mmol). NEt_3 (15 mL) was added and the vial de-oxygenated with nitrogen. TMS-acetylene (1.06 mL, 0.737 g, 7.50 mmol) was added, the vial sealed and heated to 75 °C for 16 hours. The reaction mixture was cooled to room temperature, and filtered through cotton wool, with the solid residue being washed thoroughly with Et_2O (5×20 mL). The resulting yellow solution was taken to dryness under reduced pressure to give a yellow oil, which was taken up in CH_3OH (20 mL). Potassium hydroxide (0.56 g, 10 mmol) in H_2O (2 mL) was added, and the yellow solution stirred for 30 minutes. It was extracted with pentane (7×20 mL) and filtered through cotton wool into a shallow dish. The pentane was allowed to evaporate at ambient temperature and pressure to give a crude yellow solid. This was purified by sublimation (100 °C, ambient pressure) to give **9** as feathery white crystals. Yield: 0.170 g (45%).

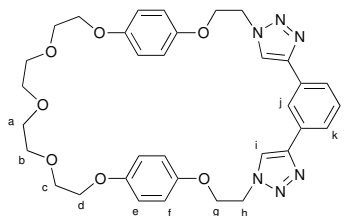
^1H NMR (CDCl_3): 8.65 (d, $^4J_{b,c} = 1.9$ Hz, 2H, $2 \times H_c$), 7.85 (t, $^4J_{b,c} = 1.9$ Hz, 1H, H_b), 3.24 (s, 2H, $2 \times H_a$). ^{13}C NMR (CDCl_3): 152.1, 142.0, 119.1, 81.6, 79.5.

Bis-azide macrocycle precursor 10



The bis-amine **11** (2.32 g, 5.00 mmol), K_2CO_3 (3.50 g, 25.0 mmol) imidazolesulfonyl azide-HCl (2.52 g, 12.0 mmol) and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.025 g, 0.10 mmol) were dissolved in CH_3OH (75 mL), and the colourless solution stirred at room temperature under a nitrogen atmosphere for 16 hours. The mixture was concentrated to ~ 10 mL under reduced pressure, diluted with H_2O (50 mL), acidified with conc. $\text{HCl}_{(\text{aq})}$ (10 mL) and extracted with EtOAc (3×50 mL). The organic layer was dried (MgSO_4) and taken to dryness under reduced pressure. It was filtered through a short pad of silica gel (eluting with 4% CH_3OH in CH_2Cl_2) and again taken to dryness to give a pale yellow oil. This was triturated with ice-cold Et_2O (12 mL). The resulting fine white powder was isolated by filtration, washed with cold Et_2O (2×2 mL) and dried *in vacuo*. Yield: 1.80 g (70%). ^1H NMR(CDCl_3): 6.84 (app. s, 8H, $4 \times H_e$, $4 \times H_f$), 4.05–4.10 (m, 8H, $4 \times H_d$, $4 \times H_g$), 3.83 (t, $J_{c,d} = 4.6$ Hz, 4H, $4 \times H_c$), 3.67–3.74 (m, 8H, $4 \times H_a$, $4 \times H_b$), 3.56 (t, $J_{g,h} = 4.5$ Hz, 4H, $4 \times H_h$). ^{13}C NMR(CDCl_3): 153.6, 152.6, 115.8, 115.7, 70.9, 70.8, 70.0, 68.2, 67.8, 50.4. HRESI-MS(pos): 555.1965, calc. for $[\text{C}_{24}\text{H}_{32}\text{N}_6\text{O}_7\cdot\text{K}]^+ = 555.1964$.

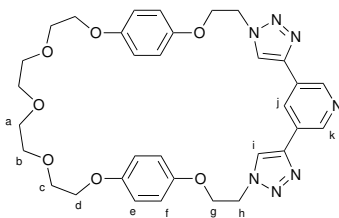
Phenyl bis-triazole macrocycle 12



The bis-azide **10** (0.103 g, 0.200 mmol) and 1,3-diethynylbenzene (0.0266 mL, 0.0252 g, 0.200 mmol) were dissolved in CH_2Cl_2 (200 mL). DIPEA (0.045 mL, 0.032 g, 0.250 mmol), TBTA (0.023 g, 0.040 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.015 g, 0.040 mmol) were added and the pale yellow solution stirred under a nitrogen atmosphere for 2 days at room temperature. This was taken to dryness under reduced pressure and purified by preparative TLC (6% CH_3OH in CH_2Cl_2) to give **12** as a white powder. Yield: 0.058 g (45%).

^1H NMR (d_6 -acetone): 8.54 (s, 2H, $2 \times H_i$), 8.23 (t, $^4J_{j,k} = 1.7$ Hz, 1H, H_j), 7.97 (dd, $J_{k,l} = 7.7$ Hz, $^4J_{j,k} = 1.7$ Hz, 2H, $2 \times H_k$), 7.51 (t, $J_{k,l} = 7.7$ Hz, 1H, H_l), 6.80–6.91 (m, 8H, $4 \times H_e$, $4 \times H_f$), 4.87 (t, $J_{g,h} = 4.8$ Hz, 4H, $4 \times H_h$), 4.42 (t, $J_{g,h} = 4.8$ Hz, 4H, $4 \times H_g$), 4.01 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_d$), 3.75 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_c$), 3.58–3.62 (m, 8H, $4 \times H_a$, $4 \times H_b$). ^{13}C NMR (CDCl_3): 153.8, 152.2, 147.7, 131.3, 129.7, 125.6, 123.2, 121.3, 115.9, 115.8, 70.9, 70.9, 69.8, 68.2, 67.6, 50.3. HRESI-MS (pos.): 665.2696, calc. for $[\text{C}_{34}\text{H}_{38}\text{N}_6\text{O}_7\cdot\text{Na}]^+ = 665.2694$.

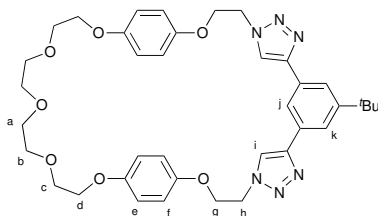
Pyridine bis-triazole macrocycle **13**



The bis-azide **10** (0.155 g, 0.300 mmol) and 3,5-diethynylpyridine (0.038 g, 0.30 mmol) were dissolved in CH_2Cl_2 (300 mL). DIPEA (0.17 mL, 0.13 g, 1.0 mmol), TBTA (0.032 g, 0.060 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.022 g, 0.060 mmol) were added and the pale yellow solution stirred under a nitrogen atmosphere for 4 days at room temperature. It was concentrated under reduced pressure to a volume of 50 mL, filtered through cotton wool, and then taken to dryness under reduced pressure. Purification by preparative TLC (4% CH_3OH in CHCl_3) gave **13** as a white crystalline solid. Yield: 0.082 g (43%).

^1H NMR (CDCl_3): 9.12 (d, $^4J_{j,k} = 2.0$ Hz, 2H, $2 \times H_k$), 8.32 (t, $^4J_{j,k} = 2.0$ Hz, 1H, H_j), 8.10 (s, 2H, $2 \times H_i$), 6.72–6.81 (m, 8H, $4 \times H_e$, $4 \times H_f$), 4.83 (t, $J_{g,h} = 4.7$ Hz, 4H, $4 \times H_h$), 4.33 (t, $J_{g,h} = 4.7$ Hz, 4H, $4 \times H_g$), 4.02 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_d$), 3.78 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_c$), 3.63–3.69 (m, 8H, $4 \times H_a$, $4 \times H_b$). ^{13}C NMR (d_6 -DMSO): 152.9, 152.0, 145.1, 143.5, 129.4, 128.8, 123.3, 115.7, 115.2, 70.0, 69.9, 68.9, 67.5, 67.0, 49.8. HRESI-MS (pos.): 666.2647, calc. for $[\text{C}_{33}\text{H}_{37}\text{N}_7\text{O}_7\cdot\text{Na}]^+ = 666.2647$.

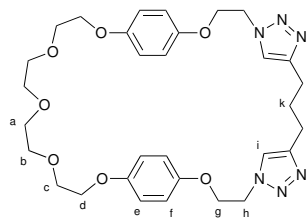
t-Butylphenyl bis-triazole macrocycle **14**



The bis-azide **10** (0.155 g, 0.300 mmol) and 5-*t*-butyl-1,3-diethynylbenzene (0.0547 g, 0.300 mmol) were dissolved in CH_2Cl_2 (300 mL). DIPEA (0.17 mL, 0.13 g, 1.0 mmol), TBTA (0.032 g, 0.060 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.022 g, 0.060 mmol) were added and the pale yellow solution stirred under a nitrogen atmosphere for 3 days at room temperature. It was taken to dryness under reduced pressure, and then purified by preparative TLC (3% CH_3OH in CH_2Cl_2) to give **14** as a white powder. Yield: 0.076 g (36%).

^1H NMR (CDCl_3): 8.04 (s, 2H, $2 \times H_i$), 8.02 (d, $^4J_{j,k} = 1.5$ Hz, 2H, $2 \times H_k$), 7.75 (t, $^4J_{j,k} = 1.5$ Hz, 1H, H_j), 6.74–6.81 (m, 8H, $4 \times H_e$, $4 \times H_f$), 4.79 (t, $J_{g,h} = 4.7$ Hz, 4H, $4 \times H_h$), 4.31 (t, $J_{g,h} = 4.7$ Hz, 4H, $4 \times H_g$), 4.02 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_d$), 3.80 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_c$), 3.64–3.73 (m, 8H, $4 \times H_a$, $4 \times H_b$), 1.42 (s, 9H, $9 \times H_l$). ^{13}C NMR (CDCl_3): 153.8, 152.9, 152.2, 148.1, 130.9, 122.9, 121.3, 120.7, 115.8, 110.1, 70.9, 70.9, 69.8, 68.2, 67.6, 50.3, 35.2, 31.5. HRESI-MS (pos.): 721.3314, calc. for $[\text{C}_{38}\text{H}_{46}\text{N}_6\text{O}_7\cdot\text{Na}]^+ = 721.3320$.

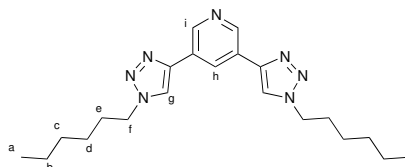
Propyl bis-triazole macrocycle **15**



The bis-azide **10** (0.155 g, 0.300 mmol) and 1,6-heptadiyne (0.038 g, 0.30 mmol) were dissolved in CH_2Cl_2 (300 mL). DIPEA (0.17 mL, 0.13 g, 1.0 mmol), TBTA (0.032 g, 0.060 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.022 g, 0.060 mmol) were added and the pale yellow solution stirred under a nitrogen atmosphere for 4 days at room temperature. It was taken to dryness under reduced pressure and purified by preparative TLC (5% CH_3OH in CH_2Cl_2) to give **15** as a crystalline white solid. Yield: 0.047 g (25%).

^1H NMR (CDCl_3): 7.46 (s, 2H, $2 \times H_i$), 6.71–6.81 (m, 8H, $4 \times H_e$, $4 \times H_f$), 4.68 (t, $J_{g,h} = 4.9$ Hz, 4H, $4 \times H_h$), 4.25 (t, $J_{g,h} = 4.9$ Hz, 4H, $4 \times H_g$), 4.01 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_d$), 3.80 (t, $J_{c,d} = 4.8$ Hz, 4H, $4 \times H_c$), 3.64–3.71 (m, 8H, $4 \times H_a$, $4 \times H_b$), 2.77 (t, $J_{j,k} = 7.5$ Hz, 4H, $4 \times H_j$), 2.06 (qn, $J_{j,k} = 7.5$ Hz, 2H, $2 \times H_k$). ^{13}C NMR (CDCl_3): 153.8, 152.2, 147.7, 122.3, 115.9, 115.7, 70.9, 70.9, 69.8, 68.3, 67.5, 49.9, 29.0, 24.9. HRESI-MS (pos.): 609.3019, calc. for $[\text{C}_{31}\text{H}_{40}\text{N}_6\text{O}_7\cdot\text{H}]^+ = 609.3031$.

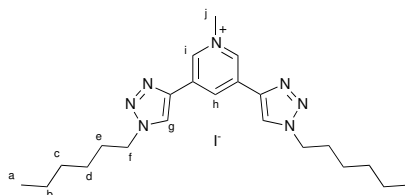
Pyridine bis-triazole precursor **17**



NaN_3 (0.156 g, 2.40 mmol), Na_2CO_3 (0.106 g, 1.00 mmol), ascorbic acid (0.176 g, 1.00 mmol) and $\text{CuSO}_4\cdot 5\text{H}_2\text{O}$ (0.015 g, 0.060 mmol) were added to a solution of 3,5-diethynylpyridine (0.127 g, 1.00 mmol) in 4:1 DMF: H_2O (15 mL). Bromohexane (0.31 mL, 0.36 g, 2.2 mmol) was added and the yellow solution heated to 80 °C under a nitrogen atmosphere over the weekend. The reaction was cooled to room temperature and partitioned between EtOAc (50 mL) and aqueous NH_4OH /EDTA (50 mL). The aqueous layer was extracted with further EtOAc (50 mL) and the combined organic fractions washed with H_2O (50 mL), brine (50 mL) and dried (MgSO_4). The pale yellow solution was taken to dryness under reduced pressure, and purified by column chromatography (3% CH_3OH in CH_2Cl_2) to yield **17** as a white powder. Yield: 0.301 g (79%).

^1H NMR (d_6 -acetone): 9.02 (d, $^4J_{h,i} = 2.1$ Hz, 2H, $2 \times H_i$), 8.69 (t, $^4J_{h,i} = 2.1$ Hz, 1H, H_h), 8.59 (s, 2H, H_g), 4.51 (t, $J_{e,f} = 7.1$ Hz, 4H, $4 \times H_f$), 1.92–2.06 (m, 4H, $4 \times H_e$), 1.25–1.45 (m, 12H, $4 \times H_b$, $4 \times H_c$, $4 \times H_d$), 0.88 (t, $J_{a,b} = 7.0$ Hz, 6H, $6 \times H_a$). ^{13}C NMR (CDCl_3): 146.3, 144.6, 129.8, 127.0, 120.3, 50.8, 31.3, 30.4, 26.3, 22.5, 14.1. HRESI-MS (pos.): 404.2530, calc. for $[\text{C}_{21}\text{H}_{31}\text{N}_7\cdot\text{Na}]^+ = 404.2533$.

Pyridinium bis-triazole threading component 18.I



The pyridine bis-triazole thread **17** (0.057 g, 0.15 mmol) was dissolved in dry CH₂Cl₂ (10 mL). CH₃I (0.23 mL, 0.53 g, 3.8 mmol) was added and the reaction stirred for 3 days under a nitrogen atmosphere. It was taken to dryness and purified by preparative TLC (3% CH₃OH in CH₂Cl₂) to give **18-I** as a golden yellow powder. Yield: 0.064 g (81%).

¹H NMR (d₆-acetone): 9.64 (d, ⁴J_{h,i} = 1.3 Hz, 2H, 2 × H_i), 9.57 (t, ⁴J_{h,i} = 1.3 Hz, 1H, H_h), 9.41 (s, 2H, 2 × H_g), 4.79 (s, 3H, 3 × H_j), 4.56 (t, J_{e,f} = 7.1 Hz, 4H, 4 × H_f), 1.95—obscured by acetone solvent signal (4 × H_e), 1.25–1.43 (m, 12H, 4 × H_b, 4 × H_c, 4 × H_d), 0.88 (t, J_{a,b} = 6.9 Hz, 6H, 6 × H_a). ¹³C NMR (CDCl₃): 140.1, 138.9, 136.3, 133.0, 126.0, 51.2, 49.7, 31.2, 30.1, 26.2, 22.6, 14.1. HRESI-MS (pos.): 396.2859, calc. for [C₂₂H₃₄N₇]⁺ = 396.2870.

Pyridinium bis-triazole threading component 18.Cl

The iodide salt **18**-I (0.042 g, 0.080 mmol) was dissolved in CH₂Cl₂ (10 mL) and the solution stirred vigorously with NH₄Cl_(aq) (1 M, 10 mL) for 30 minutes. The organic layer was washed with further NH₄Cl_(aq) (1 M, 5 × 10 mL), brine (10 mL), dried (MgSO₄), and taken to dryness to give **18**-Cl as a brown powder. Yield: 0.034 g (98%).

¹H NMR (d₆-acetone): 9.97 (t, ⁴J_{h,i} = 1.5 Hz, 1H, H_h), 9.78–9.80 (m, 4H, 2 × H_g, 2 × H_i), 4.78 (s, 3H, 3 × H_j), 4.52 (t, J_{e,f} = 7.1 Hz, 4H, 4 × H_f), 1.95—obscured by acetone solvent signal (4 × H_e), 1.29–1.42 (m, 12H, 4 × H_b, 4 × H_c, 4 × H_d), 0.88 (t, J_{a,b} = 7.1 Hz, 6H, 6 × H_a). LRESI-MS (pos.): 396.32, calc. for [C₂₂H₃₄N₇]⁺ = 396.29.

Pyridinium bis-triazole threading component 18·PF₆

The iodide salt **18-I** (0.105 g, 0.200 mmol) was dissolved in CH₂Cl₂ (25 mL), and the solution stirred vigorously with aqueous ammonium hexafluorophosphate (0.1 M, 25 mL) for 30 minutes, during which time the biphasic mixture changed colour from bright yellow to essentially colourless. The organic layer was washed with further aqueous ammonium hexafluorophosphate (0.1 M, 6 × 10 mL), and then H₂O (2 × 10 mL), and taken to dryness under reduced pressure to give **18-PF₆** as a very pale yellow powder. Yield: 0.096 g (89%).

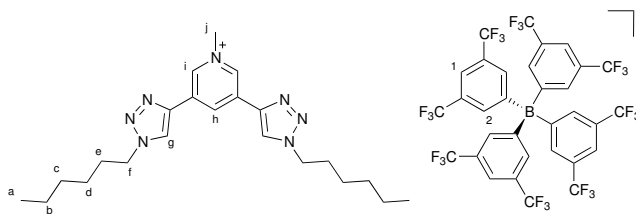
¹H NMR (d₆-acetone): 9.55 (d, ⁴J_{h,i} = 1.4 Hz, 2H, 2 × H_i), 9.38 (t, ⁴J_{h,i} = 1.4 Hz, 1H, H_h), 8.92 (s, 2H, 2 × H_g), 4.80 (s, 3H, 3 × H_j), 4.60 (t, J_{e,f} = 7.1 Hz, 4H, 4 × H_f), 1.97–2.03 (m, 4H, 4 × H_e), 1.27–1.41 (m, 12H, 4 × H_b, 4 × H_c, 4 × H_d), 0.86 (t, J_{a,b} = 7.1 Hz, 6H, 6 × H_a). LRESI-MS (pos.): 396.28, calc. for [C₂₂H₃₄N₇]⁺ = 396.29; 937.60, calc. for [(C₂₂H₃₄N₇)₂·PF₆]⁺ = 937.54.

Pyridinium bis-triazole threading component **18**·NO₃

The chloride salt of **18**⁺ (0.0086 g, 0.0020 mmol) and AgNO₃ (0.0051 g, 0.0030 mmol) were heated to reflux for an hour in acetone, during which time a fine precipitate developed. The suspension was cooled to room temperature, and solvents removed under reduced pressure. The resulting crude solid was suspended in 9:1 CH₃OH:CH₂Cl₂ (10 mL) and filtered through a short pad of silica, with the pad being washed with further 9:1 CH₃OH:CH₂Cl₂ (50 mL). The combined filtrates were taken to dryness under reduced pressure to give **18**·NO₃ as a white powder. Yield: 0.0052 g (57%).

¹H NMR (d₆-acetone): 9.55 (s, 2H, 2 × *H*_i), 9.46 (s, 1H, *H*_h), 9.17 (s, 2H, 2 × *H*_g), 4.75 (s, 3H, 3 × *H*_j), 4.56 (t, *J*_{e,f} = 7.0 Hz, 4H, 4 × *H*_f), 1.95–? (m, partially obscured by residual acetone signal, 4 × *H*_e), 1.24–1.40 (m, 12H, 4 × *H*_b, 4 × *H*_c, 4 × *H*_d), 0.87 (t, *J*_{a,b} = 7.0 Hz, 6H, 6 × *H*_a). LRESI-MS (pos.): 396.27, calc. for calc. for [C₂₂H₃₄N₇]⁺ = 396.29.

Pyridinium bis-triazole receptor **18**·BAR^F₄



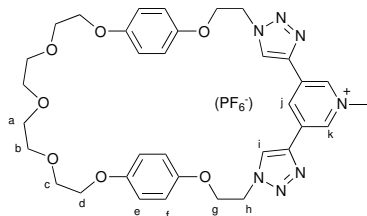
Sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (0.044 g, 0.050 mmol) was suspended in refluxing 1:1 CH₂Cl₂:toluene. The iodide salt of **18**⁺ (0.031 g, 0.060 mmol) in CH₂Cl₂ (3 mL) was added, and the mixture stirred at reflux temperature for 10 minutes. It was cooled to room temperature, and filtered, the precipitate being washed with toluene (2 × 10 mL) and CH₂Cl₂ (2 × 10 mL). The resulting pale yellow solution was taken to dryness under reduced pressure and purified by preparative TLC (3% CH₃OH in CH₂Cl₂) to give pure **18**·BAR^F₄ as an orange oil, which crystallized on standing. Yield: 0.060 g (95%).

¹H NMR (CDCl₃): 8.98 (s, 1H, *H*_h), 8.93 (s, 2H, *H*_i), 8.03 (s, 2H, *H*_g), 7.68 (s, 8H, *H*₂), 7.49 (s, 4H, *H*₁), 4.43 (t, *J*_{e,f} = 7.2 Hz, 4H, *H*_f), 4.32 (s, 3H, *H*_j), 1.94 (app. t, *J*_{d,e} = *J*_{e,f} = 7.2 Hz, 4H, 4 × *H*_e), 1.23–1.35 (m, 12H, 4 × *H*_b, 4 × *H*_c, 4 × *H*_d), 0.85 (t, *J*_{a,b} = 6.9 Hz, 6H, 6 × *H*_a). ¹⁹F NMR (CDCl₃): -62.4 (s). ¹³C NMR (CDCl₃): 161.6* (app. q, *J*_{11B-C} = 50 Hz), 139.1, 138.3, 136.0, 134.7* (br. s), 133.9, 128.8–129.9* (m), 126.3, 122.6* (app. d, *J*_{F-C} = 14 Hz), 117.3–117.6* (m), 51.3, 49.3, 30.9, 30.0, 25.9, 22.3, 13.7.* LRESI-MS (pos.): 396.27, calc. for [C₂₂H₃₄N₇]⁺ = 396.29; 1655.59, calc. for [C₇₆H₈₀BN₁₄F₂₄]⁺, ie [M₂L]⁺ = 1655.64. LRESI-MS (neg.): 862.94, calc. for [C₃₂H₁₂BF₂₄]⁻ = 863.07.

*The ¹³C NMR spectrum is significantly complicated by ¹⁰B-¹³C, ¹¹B-¹³C couplings, as well as short-range and long-range ¹⁹F-¹³C couplings. Peaks attributed to the BAR^F₄ anion are denoted with asterisks and described as they appear. A full analysis of the ¹³C NMR spectrum of sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate is given in the supporting information of Filippou *et al.*, Angew. Chem. Int. Ed., 2004, 43(47), 6512–6516.

6.5 Synthesis of compounds from Chapter 3

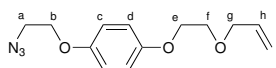
Pyridinium bis-triazole macrocycle **21**·PF₆



The neutral macrocycle **13** (0.064 g, 0.10 mmol) was suspended in dry CH₂Cl₂ (50 mL). CH₃I (0.19 mL, 0.43 g, 3.0 mmol) was added and the suspension stirred at room temperature under a nitrogen atmosphere for 6 days. It was purified by column chromatography (gradient: 10–20% CH₃OH in CH₂Cl₂), and then dissolved in 7:3 acetone:H₂O (15 mL) and passed down a PF₆superscript--loaded Amberlite[®] anion exchange column to give **21**·PF₆ as an essentially pure pale yellow powder. Yield: 0.051 g (63%). A pure sample was obtained by recrystallization from 4:1 CHCl₃/acetone (25 mL).

¹H NMR (d₆-acetone): 9.45 (d, ⁴J_{j,k} = 1.3 Hz, 2H, 2 × H_k), 9.28 (t, ⁴J_{j,k} = 1.3 Hz, 1H, H_j), 8.95 (s, 2H, 2 × H_i), 6.79–6.87 (m, 8H, 4 × H_e, 4 × H_f), 4.96 (t, J_{g,h} = 4.7 Hz, 4H, 4 × H_h), 4.73 (s, 3H, 3 × H_l), 4.40 (t, J_{g,h} = 4.7 Hz, 4H, 4 × H_g), 4.00 (t, J_{c,d} = 4.7 Hz, 4H, 4 × H_d), 3.74 (t, J_{c,d} = 4.7 Hz, 4H, 4 × H_c), 3.58–3.62 (m, 8H, 4 × H_a, 4 × H_b). ¹³C NMR (d₆-DMSO): 153.2, 152.1, 140.9, 140.4, 136.2, 131.1, 125.4, 115.9, 115.4, 70.2, 70.1, 69.1, 67.7, 67.1, 50.2, 48.7. ¹⁹F NMR (d₆-acetone): -72.5 (d, J_{P,F} = 708 Hz). ³¹P NMR (d₆-acetone): -144.3 (septet, J_{P,F} = 708 Hz). HRESI-MS (pos.): 658.2979, calc. for [C₃₄H₄₀N₇O₇]⁺ = 658.2984.

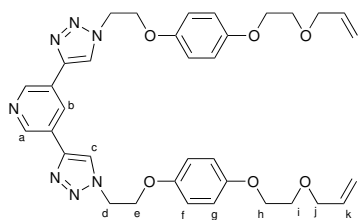
Vinyl-appended azide **23**



The vinyl-appended amine **22** (1.42 g, 6.00 mmol) was dissolved in CH₃OH (60 mL). The hydrochloride salt of imidazolesulfonyl azide (1.95 g, 7.20 mmol), K₂CO₃ (2.07 g, 15.0 mmol) and CuSO₄·5H₂O (0.015 g, 0.060 mmol) were added and the white suspension stirred at room temperature under a nitrogen atmosphere for 16 hours. It was cautiously concentrated to ~ 5 mL under reduced pressure, diluted with HCl_(aq) (10 %, 100 mL) and extracted with EtOAc (3 × 100 mL). The combined organic fractions were washed with brine (100 mL), dried (MgSO₄), taken to dryness under reduced pressure, and purified by column chromatography (2:1 petrol:EtOAc) to give **23** as a colourless oil. Yield: 1.36 g (86%).

¹H NMR (CDCl₃): 6.86 (s, 8H, 4 × H_c, 4 × H_d), 5.85–6.04 (m, 1H, H_h), 5.17–5.36 (m, 2H, H_i), 4.07–4.13 (m, 6H, 2 × H_b, 2 × H_e, 2 × H_g), 3.78 (t, J_{e,f} = 4.9 Hz, 2H, 2 × H_f), 3.56 (t, J_{a,b} = 5.0 Hz, 2H, 2 × H_a). ¹³C NMR (CDCl₃): 152.5, 134.6, 129.9, 128.0, 117.4, 115.7, 72.4, 68.6, 68.1, 67.6, 50.2. HRESI-MS (pos.): 286.1183, calc. for [C₁₃H₁₇N₃O₃·Na]⁺ = 286.1182.

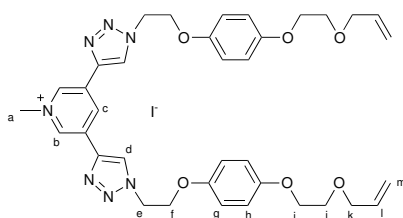
Pyridine bis-triazole macrocycle precursor **24**



The vinyl-appended azide **23** (0.663 g, 2.52 mmol) and 3,5-diethynyl pyridine (0.153 g, 1.20 mmol) were dissolved in CH_2Cl_2 (15 mL). DIPEA (0.54 mL, 0.39 g, 3.0 mmol) was added, followed by $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.089 g, 0.24 mmol) and the mixture heated to 50 °C for 4 days in a sealed vial. Aqueous $\text{NH}_4\text{OH}_{(\text{aq})}$ (20 mL) was added, the organic layer taken and the aqueous layer extracted with further CH_2Cl_2 (2×20 mL). The combined organic fractions were washed with brine (30 mL), dried (MgSO_4), taken to dryness under reduced pressure. The residue was purified by column chromatography (3% CH_3OH in CH_2Cl_2) to give **24** as a white powder. Yield: 0.640 g (82%).

^1H NMR (CDCl_3): 9.01 (d, $^4J_{\text{a,b}} = 2.0$ Hz, 2H, $2 \times H_{\text{a}}$), 8.59 (t, $^4J_{\text{a,b}} = 2.0$ Hz, 1H, H_{b}), 8.12 (s, 2H, $2 \times H_{\text{c}}$), 6.78–6.86 (m, 8H, $4 \times H_{\text{f}}$, $4 \times H_{\text{g}}$), 5.85–5.98 (m, 2H, $2 \times H_{\text{k}}$), 5.16–5.31 (m, 4H, $4 \times H_{\text{l}}$), 4.80 (t, $J_{\text{d,e}} = 4.8$ Hz, 4H, $4 \times H_{\text{d}}$), 4.34 (t, $J_{\text{d,e}} = 4.8$ Hz, 4H, $4 \times H_{\text{e}}$), 4.03–4.07 (m, 8H, $4 \times H_{\text{h}}$, $4 \times H_{\text{j}}$), 3.75 (t, $J_{\text{h,i}} = 4.8$ Hz, 4H, $4 \times H_{\text{i}}$). ^{13}C NMR (CDCl_3): 153.9, 152.1, 146.3, 144.6, 134.7, 130.1, 127.0, 121.8, 117.5, 115.9, 115.8, 72.5, 68.7, 68.2, 67.2, 50.3. HRESI-MS (pos.): 676.2839, calc. for $[\text{C}_{35}\text{H}_{39}\text{N}_7\text{O}_6\cdot\text{Na}]^+ = 676.2854$.

Pyridinium bis-triazole macrocycle precursor **25-I**



The pyridine containing compound **24** (0.261 g, 0.400 mmol) was dissolved in dry CH_2Cl_2 (15 mL) in a vial. CH_3I (0.62 mL, 1.4 g, 10 mmol) was added, the vial sealed and the colourless solution stirred at room temperature for 7 days, during which time a yellow precipitate developed. The mixture was diluted with CH_3OH (15 mL), taken to dryness under reduced pressure, and purified by column chromatography (5–12% CH_3OH in CHCl_3) to give **25-I** as a lemon yellow powder. Yield: 0.289 g (91%).

^1H NMR (CDCl_3): 9.49 (br. s, 2H, H_{b}), 9.46 (br. s, 1H, H_{c}), 9.33 (s, 2H, H_{d}), 6.80–6.92 (m, 8H, $4 \times H_{\text{g}}$, $4 \times H_{\text{h}}$), 5.86–5.99 (m, 2H, $2 \times H_{\text{l}}$), 5.16–5.33 (m, 4H, $4 \times H_{\text{m}}$), 4.81 (t, $H_{\text{e,f}} = 4.8$ Hz, 4H, $4 \times H_{\text{e}}$), 4.59 (s, 3H, $3 \times H_{\text{a}}$), 4.39 (t, $H_{\text{e,f}} = 4.8$ Hz, 4H, $4 \times H_{\text{f}}$), 4.02–4.09 (m, 8H, $4 \times H_{\text{i}}$, $4 \times H_{\text{k}}$), 3.75 (t, $J_{\text{i,j}} = 4.8$ Hz, 4H, $4 \times H_{\text{j}}$). ^{13}C NMR (CDCl_3): 153.8, 152.2, 140.4, 139.4, 136.2, 134.7, 132.5, 126.6, 117.5, 116.1, 115.7, 72.5, 68.7, 68.1, 66.8, 50.7, 29.8. HRESI-MS (pos.): 668.3192, calc. for $[\text{C}_{36}\text{H}_{42}\text{N}_7\text{O}_6]^+ = 668.3191$.

Pyridinium bis-triazole macrocycle precursor **25·Cl**

The iodide salt of **25**⁺ (0.080 g, 0.10 mmol) was dissolved in 4:1 acetone:H₂O (50 mL). The solution was repeatedly passed down a Cl[−]-loaded Amberlite® anion exchange column, and the column then washed with more of the same solvent. All solvent was removed under reduced pressure, and the resulting waxy solid taken up in 5% CH₃OH in CH₂Cl₂ (50 mL), it was dried (MgSO₄), filtered and taken to dryness under reduced pressure to give **25·Cl** as a pale yellow powder. Yield: 0.063 g (89%).

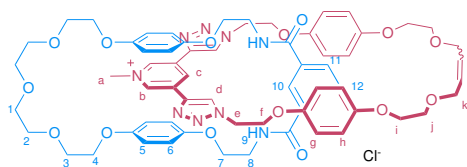
¹H NMR (CDCl₃): 9.61 (br. s, 2H, 2 × *H*_b), 9.53 (br. s, 1H, *H*_c), 9.22 (s, 2H, 2 × *H*_d), 6.78–6.85 (m, 8H, 4 × *H*_g, 4 × *H*_h), 5.83–5.96 (m, 2H, 2 × *H*_l), 5.15–5.30 (m, 4H, 4 × *H*_m), 4.87 (app. br. s, 4H, 4 × *H*_e), 4.58 (s, 3H, 3 × *H*_a), 4.37 (app. br. s, 4H, 4 × *H*_f), 4.01–4.05 (m, 8H, 4 × *H*_i, 4 × *H*_k), 3.73 (t, *J*_{i,j} = 4.7 Hz, 4H, 4 × *H*_j). LRESI-MS (pos.): 668.30, calc. for [C₃₆H₄₂N₇O₆]⁺ = 668.32.

Pyridinium bis-triazole macrocycle precursor **25·PF₆**

The iodide salt of **25**⁺ (0.056 g, 0.070 mmol) was taken up in 5% CH₃OH in CH₂Cl₂ (20 mL). It was washed with 0.1 M NH₄PF₆(aq) (6 × 20 mL) and H₂O (2 × 20 mL), dried (MgSO₄) and taken to dryness to give **25·PF₆** as a pale yellow solid. Yield: 0.054 g (95%).

¹H NMR (CDCl₃): 9.06 (br. s, 2H, 2 × *H*_b), 9.01 (br. s, 1H, *H*_c), 8.60 (s, 2H, 2 × *H*_d), 6.77–6.84 (m, 8H, 4 × *H*_g, 4 × *H*_h), 5.86–5.99 (m, 2H, 2 × *H*_l), 5.17–5.32 (m, 4H, 4 × *H*_m), 4.77 (t, *J*_{e,f} = 4.4 Hz, 4H, 4 × *H*_e), 4.43 (s, 3H, 3 × *H*_a), 4.33 (t, *J*_{e,f} = 4.4 Hz, 4H, 4 × *H*_f), 4.00–4.08 (m, 8H, 4 × *H*_i, 4 × *H*_k), 3.74 (t, *J*_{i,j} = 4.7 Hz, 4H, 4 × *H*_j). LRESI-MS (pos.): 668.30, calc. for [C₃₆H₄₂N₇O₆]⁺ = 668.32, 1481.61, calc. for [C₇₂H₈₄N₁₄O₁₂PF₆]⁺, *i.e.* [M₂·PF₆]⁺ = 1481.60.

Pyridinium bis-triazole catenane **26·Cl**



The isophthalamide macrocycle **20** (0.018 g, 0.030 mmol) and chloride salt of **25**⁺ (0.025 g, 0.036 mmol) were dissolved in dry CH₂Cl₂ (6 mL). Grubbs' II catalyst (0.0025 g, 10% by weight) was added and the mixture stirred at room temperature under a nitrogen atmosphere for 4 days. It was taken to dryness, and then purified by preparative TLC (5% CH₃OH in CH₂Cl₂) to give **26·Cl** as a pale yellow powder. Yield: 0.024 g (64%).

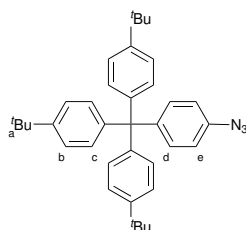
¹H NMR (CDCl₃): 9.71 (s, 1H, *H*_c), 9.44 (s, 2H, 2 × *H*_b), 9.15 (br. s, 2H, 2 × *H*_g), 8.73 (s, 1H, *H*₁₀), 8.65 (s, 2H, 2 × *H*_d), 8.33 (d, *J*_{11,12} = 7.8 Hz, 2H, 2 × *H*₁₁), 7.62 (t, *J*_{11,12} = 7.8 Hz, 1H, *H*₁₂), 6.77 (app. s, 8H, 4 × *H*_g, 4 × *H*_h), 5.73–5.90 (m, 10H, 4 × *H*₅, 4 × *H*₆, 2 × *H*_l), 4.57 (s, 3H, 3 × *H*_a), 4.47 (t, *J*_{e,f} = 4.2 Hz, 4H, 4 × *H*_e), 4.18 (t, *J*_{e,f} = 4.2 Hz, 4H, 4 × *H*_f), 3.97–4.01 (m, 8H, 4 × *H*₇, 4 × *H*_i), 3.68–3.83 (m, 24H, 4 × *H*₁, 4 × *H*₂, 4 × *H*₃, 4 × *H*₄, 4 × *H*_j, 4 × *H*_k). HRESI-MS (pos.): 1234.5432, calc. for [C₆₆H₇₆N₉O₁₅]⁺ = 1234.5455.

Pyridinium bis-triazole catenane **26**·PF₆

The chloride salt of **26**⁺ (0.019 g, 0.015 mmol) was taken up in CH₂Cl₂ (20 mL). The solution was washed with NH₄PF_{6(aq)} (0.1 M, 7 × 20 mL) and H₂O (3 × 20 mL), and taken to dryness under reduced pressure. Thorough drying *in vacuo* gave **26**·PF₆ as a white powder. Yield: 0.015 g (71%).

¹H NMR (CDCl₃): 8.74 (s, 2H, 2 × *H*_b), 8.34–8.46 (m, 3H, 2 × *H*_d, *H*_c), 8.25 (d, *J*_{11,12} = 7.8 Hz, 2H, 2 × *H*₁₁), 7.77 (br. s, 1H, *H*₁₀), 7.65 (t, *J*_{11,12} = 7.8 Hz, 1H, *H*₁₂), 7.18 (br. s, 2H, 2 × *H*₉), 6.75 (s, 8H, 4 × *H*_g, 4 × *H*_h), 5.95 (s, 8H, 4 × *H*₅, 4 × *H*₆), 5.70 (br. s, 2H, *H*_i), 4.73 (br. s, 4H, 4 × *H*_e), 4.48 (s, 3H, *H*_a), 4.28 (br. s, 4H, 4 × *H*_f) 3.91–3.96 (m, 8H, 4 × *H*₄, 4 × *H*_i), 3.73–3.80 (m, 8H, 4 × *H*₄, 4 × *H*₇), 3.63–3.66 (m, 12H, 4 × *H*₂, 4 × *H*₃, 4 × *H*_j), 3.44–3.60 (m, 8H, 4 × *H*₁, 4 × *H*_k). ¹³C NMR (CDCl₃): 167.2, 153.7, 152.9, 152.2, 152.1, 141.1, 139.2, 134.5, 133.8, 132.1, 130.7, 129.6, 129.2, 124.5, 123.5, 115.9, 115.4, 115.0, 114.2, 71.2, 70.9, 70.8, 70.1, 68.8, 68.2, 67.7, 66.5, 50.8, 49.0, 40.4 (*one resonance not observed*). ¹⁹F NMR (CDCl₃): -70.6 (d, *J*_{P,F} = 714 Hz). ³¹P NMR (CDCl₃): -143.9 (septet, *J*_{P,F} = 714 Hz). LRESI-MS (pos.): 1234.54, calc. for [C₆₆H₇₆N₉O₁₅]⁺ = 1234.55.

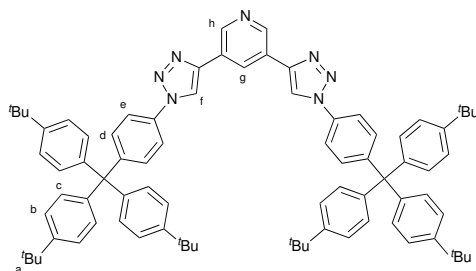
Aryl azide stopper **31**



Aniline stopper **30** (1.01 g, 2.00 mmol) was suspended in 9:1 EtOH:conc. HCl_(aq) (500 mL), and the mixture warmed, causing all material to dissolve. Further conc. HCl_(aq) (25 mL) was added and the colourless solution cooled to 0 °C. NaNO₂ (0.276 g, 4.00 mmol) was added, followed by NaN₃ (0.260 g, 4.00 mmol). The reaction was stirred under a nitrogen atmosphere for 1 hour in an ice bath, before being allowed to warm to room temperature overnight. The EtOH was removed under reduced pressure, the resulting aqueous suspension diluted with H₂O (200 mL), and extracted with Et₂O (2 × 200 mL). The combined organic fractions were washed with saturated Na₂CO_{3(aq)} (2 × 150 mL) and brine (150 mL), dried (MgSO₄) and taken to dryness under reduced pressure. The resulting white powder was taken up in 1:1 petrol:CH₂Cl₂ and filtered through a short pad of silica, washing through with further 1:1 petrol:CH₂Cl₂. Evaporation of the solvent gave **31** as a white powder. Yield: 0.876 g (83%).

¹H NMR (CDCl₃): 7.24 (d, *J*_{b,c} = 8.6 Hz, 6H, 6 × *H*_b), 7.17 (d, *J*_{d,e} = 8.8 Hz, 2H, 2 × *H*_d), 7.07 (d, *J*_{b,c} = 8.6 Hz, 6H, 6 × *H*_c), 6.90 (d, *J*_{d,e} = 8.8 Hz, 2H, 2 × *H*_e), 1.30 (s, 27H, 27 × *H*_a). ¹³C NMR (CDCl₃): 148.7, 144.5, 143.8, 137.4, 132.7, 130.8, 124.3, 117.9, 63.4, 34.5, 31.5. HR-MS (EI): 529.3448, calc. for [C₃₇H₄₃N₃]⁺ = 529.3457.

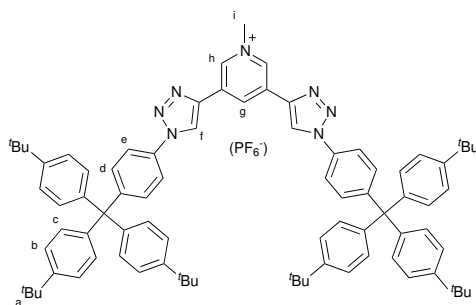
Pyridine bis-triazole axle **32**



The aryl azide **31** (0.233 g, 0.440 mmol) and 3,5-diethynylpyridine (0.025 g, 0.20 mmol) were dissolved in CH_2Cl_2 (25 mL). DIPEA (0.090 mL, 0.065 g, 0.50 mmol), TBTA (0.021 g, 0.040 mmol), and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.015 g, 0.040 mmol) were added and the resulting yellow solution stirred at room temperature under a nitrogen atmosphere for 5 days. The reaction mixture was taken to dryness under reduced pressure and purified by column chromatography (3% CH_3OH in CHCl_3) to give **32** as a white powder. Yield: 0.197 g (83%).

^1H NMR (CDCl_3): 9.13 (d, $^4J_{g,h} = 1.9$ Hz, 2H, $2 \times H_h$), 8.76 (t, $^4J_{g,h} = 1.9$ Hz, 1H, H_g), 8.34 (s, 2H, $2 \times H_f$), 7.66–7.69 (m, 4H, $4 \times H_e$), 7.42–7.45 (m, 4H, $4 \times H_d$), 7.25–7.29 (m, 12H, $12 \times H_b$), 7.11–7.14 (m, 12H, $12 \times H_c$), 1.32 (s, 54H, $54 \times H_a$). ^{13}C NMR (CDCl_3): 149.1, 148.9, 146.8, 145.1, 143.4, 134.5, 132.8, 130.8, 130.1, 126.7, 124.5, 119.6, 118.6, 63.8, 34.5, 31.5. HRESI-MS (pos.): 1208.7231, calc. for $[\text{C}_{83}\text{H}_{91}\text{N}_7\cdot\text{Na}]^+ = 1208.7228$.

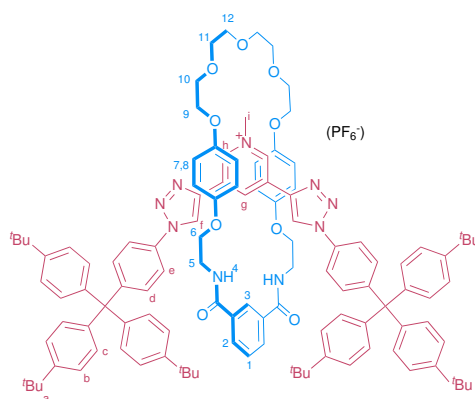
Pyridinium bis-triazole axle **33**· PF_6



The neutral axle component **32** (0.297 g, 2.50 mmol) was dissolved in dry CH_2Cl_2 (20 mL) in a vial. CH_3I (0.37 mL, 0.85 g, 6.0 mmol) was added, and the vial sealed. It was stirred at room temperature for 7 days and then purified by column chromatography (2% CH_3OH in CHCl_3) to give the product as its iodide salt. It was suspended in 7:3 acetone: H_2O (100 mL) and stirred for 16 hours with PF_6 superscript--loaded Amberlite[®] anion exchange beads. The suspension was separated from the beads by decanting, and the acetone removed under reduced pressure. The remaining aqueous suspension was extracted with CH_2Cl_2 (4×50 mL) and the combined organic fractions washed with $\text{NH}_4\text{PF}_6(\text{aq})$ (2×75 mL) and H_2O (2×75 mL), and then dried (MgSO_4) to give **33**· PF_6 as an off-white powder. Yield: 0.211 g (63%).

^1H NMR (CDCl_3): 9.21 (t, $^4J_{\text{g,h}} = 1.2$ Hz, 1H, H_{g}), 9.18 (d, $^4J_{\text{g,h}} = 1.2$ Hz, 2H, $2 \times H_{\text{h}}$), 8.83 (s, 2H, $2 \times H_{\text{f}}$), 7.63–7.68 (m, 4H, $4 \times H_{\text{e}}$), 7.39–7.44 (m, 4H, $4 \times H_{\text{d}}$), 7.23–7.29 (m, 12H, $12 \times H_{\text{b}}$), 7.10–7.15 (m, 12H, $12 \times H_{\text{c}}$), 4.48 (s, 3H, $3 \times H_{\text{i}}$), 1.30 (s, 54H, $54 \times H_{\text{a}}$). ^{13}C NMR (d_6 -DMSO): 148.5, 148.1, 143.3, 141.3, 135.3, 134.3, 133.8, 131.9, 130.6, 129.9, 124.7, 122.8, 119.8, 63.3, 48.7, 34.1, 31.1. ^{19}F NMR (d_6 -DMSO): -71.2 (d, $J_{\text{P,F}} = 711$ Hz). ^{31}P NMR (d_6 -DMSO): -144.3 (septet, $J_{\text{P,F}} = 711$ Hz). HRESI-MS (pos.): 1200.7586, calc. for $[\text{C}_{84}\text{H}_{94}\text{N}_7]^+ = 1200.7565$.

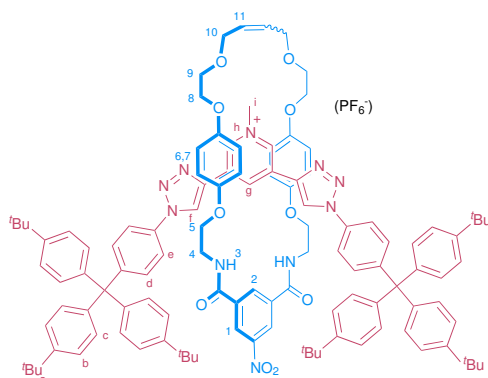
Pyridinium bis-triazole rotaxane **34**· PF_6



The axle component **33**· PF_6 (0.040 g, 0.030 mmol) was dissolved in dry CH_2Cl_2 (50 mL). NEt_3 (0.010 mL, 0.0076 g, 0.075 mmol) was added, followed by bis-amine **11** (0.014 g, 0.030 mmol) and isophthaloyl dichloride (0.0061 g, 0.030 mmol) in dry CH_2Cl_2 (2 mL). The reaction was stirred at room temperature under a nitrogen atmosphere for 2 hours, washed with $\text{HCl}_{(\text{aq})}$ (10%, 2×30 mL), brine (30 mL), dried (MgSO_4), and taken to dryness under reduced pressure. Integration of the crude ^1H NMR spectrum suggested the rotaxane was formed in approximately 20% yield. The crude solid was purified by preparative TLC (3% CH_3OH in CH_2Cl_2), then taken up in CH_2Cl_2 (20 mL) and washed with $\text{NH}_4\text{PF}_6_{(\text{aq})}$ (0.1 M, 6×20 mL) and H_2O (2×20 mL). Drying thoroughly *in vacuo* gave **34**· PF_6 as a white powder, which was shown by ^1H NMR spectroscopy to contain minor impurities. Yield: 0.0062 g (11%). A pure sample was obtained by recrystallization from $\text{CH}_3\text{OH}/\text{CHCl}_3$ (4:1).

^1H NMR (1:1 CDCl_3 : CD_3OD): 9.03 (s, 2H, $2 \times H_{\text{h}}$), 8.93 (s, 2H, $2 \times H_{\text{f}}$), 8.68 (s, 1H, H_{g}), 8.51 (s, 1H, H_3), 8.01–8.06 (m, 3H, H_1 , $2 \times H_2$), 7.68 (d, $J_{\text{d,e}} = 8.8$ Hz, 4H, $4 \times H_{\text{e}}$), 7.43 (d, $J_{\text{d,e}} = 8.8$ Hz, 4H, $4 \times H_{\text{d}}$), 7.31–7.34 (m, 12H, $12 \times H_{\text{b}}$), 7.12–7.15 (m, 12H, $12 \times H_{\text{c}}$), 6.36 (d, $J_{7,8} = 9.1$ Hz, 4H, $4 \times H_{7/8}$), 6.17 (d, $J_{7,8} = 9.1$ Hz, 4H, $4 \times H_{7/8}$), 4.43 (s, 3H, $3 \times H_{\text{i}}$), 3.88 (t, $J_{5,6} = 4.8$ Hz, 4H, $4 \times H_5$), 3.82–3.84 (m, 4H, $4 \times H_6$), 3.73–3.75 (m, 4H, $4 \times H_9$), 3.64–3.71 (m, 8H, $4 \times H_{10}$, $4 \times H_{11}$), 3.51–3.53 (m, 4H, $4 \times H_{12}$), 1.30 (s, 54H, $54 \times H_{\text{a}}$). ^{19}F NMR (CDCl_3): -73.4 (d, $J_{\text{P,F}} = 711$ Hz). HRESI-MS (pos.): 1911.0968, calc. for $[\text{C}_{122}\text{H}_{144}\text{N}_9\text{O}_{11}]^+ = 1911.0980$.

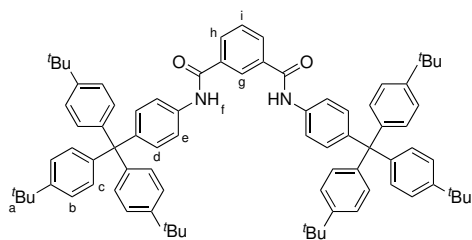
Pyridinium bis-triazole rotaxane **36**·PF₆



The pyridinium bis-triazole axle component **33**⁺ (0.034 g, 0.025 mmol) was dissolved in dry CH₂Cl₂ (70 mL), and the solution reduced in volume to 20 mL under reduced pressure. The macrocycle precursor **35** (0.024 g, 0.038 mmol), TBA·Cl (0.0069 g, 0.025 mmol) and Grubbs' II catalyst (0.0024 g, 10% by weight) were added, and the mixture stirred at room temperature under a nitrogen atmosphere for 3 days. It was taken to dryness and purified by preparative TLC (2% CH₃OH in CH₂Cl₂) to give a crude product containing a mixture of rotaxane and ring-closed macrocycle (accounting for the presence of macrocycle impurity, the yield at this point was estimated to be 65% on the basis of ¹H NMR analysis). This material was taken up in CH₂Cl₂ (20 mL), washed with NH₄PF₆(aq) (0.1 M, 7 × 20 mL), and H₂O (3 × 20 mL) and taken to dryness. Recrystallization from CH₃OH/CHCl₃ (5 mL, ~ 4:1) gave pure **36**·PF₆ as a pale yellow powder. Yield: 0.022 g (44%).

¹H NMR (1:1 CDCl₃:CD₃OD): 9.15 (s, 1H, *H*_g), 9.03 (s, 2H, 2 × *H*_h), 8.84–8.87 (m, 3H, *H*₂, 2 × *H*_f), 8.78 (s, 2H, 2 × *H*₁), 8.53 (br. s, 2H, 2 × *H*₃), 7.70 (d, *J*_{d,e} = 8.8 Hz, 4H, 4 × *H*_e), 7.45 (d, *J*_{d,e} = 8.8 Hz, 4H, 4 × *H*_d), 7.28 (d, *J*_{b,c} = 8.6 Hz, 12H, 12 × *H*_b), 7.12 (d, *J*_{b,c} = 8.6 Hz, 12H, 12 × *H*_c), 6.14–6.27 (m, 8H, 4 × *H*₆, 4 × *H*₇), 5.99 (br. s, 2H, 2 × *H*₁₁), 4.39 (s, 3H, 3 × *H*_i), 4.03–4.06 (m, 4H, 4 × *H*₄), 3.65–3.86 (m, 16H, 4 × *H*₅, 4 × *H*₈, 4 × *H*₉, 4 × *H*₁₀), 1.30 (s, 54H, 27 × *H*_a). ¹³C NMR (1:1 CDCl₃:CD₃OD): 166.7, 153.5, 153.3, 150.2, 149.5, 149.3, 144.1, 141.7, 140.2, 137.0, 135.4, 134.6, 133.3, 132.5, 132.1, 131.3, 130.5, 126.1, 125.1, 122.4, 119.7, 115.5, 115.1, 78.5, 71.5, 69.9, 68.4, 67.3, 64.4, 40.8, 34.9, 31.7. ¹⁹F NMR (1:1 CDCl₃:CD₃OD): -72.6 (d, *J*_{P,F} = 712 Hz). ³¹P NMR (1:1 CDCl₃:CD₃OD): -144.3 (septet, *J*_{P,F} = 712 Hz). HRESI-MS (pos.): 1821.9881, calc. for [C₁₁₆H₁₂₉N₁₀O₁₀]⁺ = 1821.9888.

Isophthalamide axle component **38**

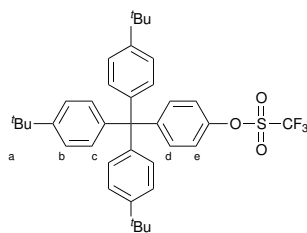


Isophthaloyl dichloride (0.028 g, 0.14 mmol) was dissolved in dry CH_2Cl_2 (5 mL) containing NEt_3 (0.069 mL, 0.051 g, 0.50 mmol). The aniline stopper **30** (0.155 g, 0.308 mmol) in dry CH_2Cl_2 (10 mL) was added and the reaction stirred at room temperature under a nitrogen atmosphere for 4 hours. It was washed with $\text{HCl}_{(\text{aq})}$ (10%, 2×20 mL) and brine (20 mL), dried (MgSO_4), and purified by column chromatography (gradient: 0–4% CH_3OH in CHCl_3) to give **38** as a white powder. Yield: 0.127 g (79%).

^1H NMR (CDCl_3): 8.32 (s, 1H, H_g), 8.07 (s, 2H, $2 \times H_f$), 7.99 (d, $J_{h,i} = 7.8$ Hz, 2H, $2 \times H_h$), 7.47–7.56 (m, 5H, $4 \times H_e$, H_i), 7.19–7.26 (m, 16H, $12 \times H_b$, $4 \times H_d$), 7.11 (d, $J_{b,c} = 8.5$ Hz, 12H, $12 \times H_c$), 1.31 (s, 54H, $54 \times H_a$). ^{13}C NMR (CDCl_3): 164.9, 148.6, 144.3, 143.9, 135.8, 135.3, 132.1, 130.8, 130.4, 129.6, 125.6, 124.3, 119.2, 63.5, 34.5, 31.5. HRESI-MS (pos.): 1159.7025, calc. for $[\text{C}_{82}\text{H}_{92}\text{N}_2\text{O}_2 \cdot \text{Na}]^+ = 1159.7051$.

6.6 Synthesis of compounds from Chapter 4

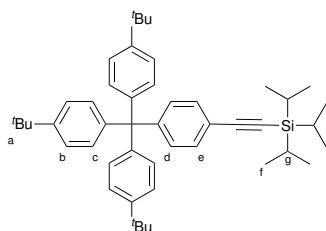
Aryl triflate stopper **45**



The aryl alcohol **44** (1.51 g, 3.00 mmol) was suspended in dry CH_2Cl_2 (30 mL). NEt_3 (0.83 mL, 0.61 g, 6.0 mmol) was added, causing all material to dissolve, followed by trifluoromethanesulfonic anhydride (0.61 mL, 1.0 g, 3.6 mmol) in dry CH_2Cl_2 (5 mL). The reaction was stirred at room temperature under a nitrogen atmosphere for 1 hour. It was then diluted with Et_2O (100 mL) and washed sequentially with $\text{HCl}_{(\text{aq})}$ (1 M, 100 mL), $\text{NaHCO}_{3(\text{aq})}$ (100 mL) and brine (100 mL), and dried (MgSO_4). Column chromatography (1:1 petrol: CH_2Cl_2) gave **45** as a white crystalline solid. Yield: 1.71 g (90%).

^1H NMR (CDCl_3): 7.21–7.29 (m, 8H, $6 \times H_d$, $2 \times H_e$), 7.09–7.16 (m, 2H, $2 \times H_b$), 7.01–7.08 (m, 6H, $6 \times H_c$), 1.30 (s, 27H, $27 \times H_a$). ^{13}C NMR (CDCl_3): 149.0, 148.1, 147.6, 143.3, 133.1, 130.8, 124.5, 120.0, 63.6, 34.5, 31.5. ^{19}F NMR (CDCl_3): 73.0 (s). HR-MS (EI): 636.2885, calc. for $[\text{C}_{38}\text{H}_{43}\text{O}_3\text{F}_3\text{S}]^+ = 636.2883$.

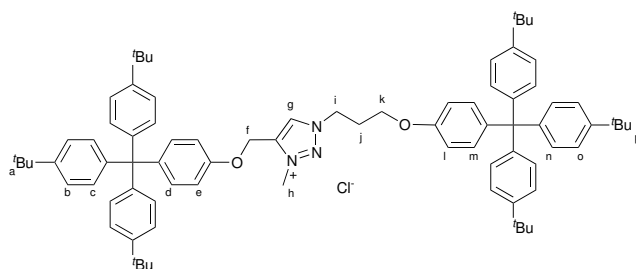
Aryl TIPS-alkyne stopper **43**



The aryl triflate **45** (1.27 g, 2.00 mmol), CuI (0.076 g, 0.40 mmol) and [Pd(PPh₃)₄] (0.232 g, 0.200 mmol) were placed in a microwave vial. DMF (20 mL), NEt₃ (1.67 mL, 1.21 g, 12.0 mmol) and TIPS-acetylene (0.54 mL, 0.44 g, 2.4 mmol) were added, the suspension deoxygenated by bubbling nitrogen through it, and the vial sealed. It was heated to 75 °C for 16 hours, cooled to room temperature and filtered through cotton wool, washing the residue thoroughly with toluene. The combined filtrates were taken to dryness under reduced pressure. The resulting brown oil was taken up in toluene (50 mL), and washed with HCl_{aq} (1 M, 2 × 50 mL) and brine (50 mL), and dried (MgSO₄). Purification by column chromatography (24:1 petrol:CH₂Cl₂) gave **43** as a white powder. Yield: 0.815 g (61%).

¹H NMR (CDCl₃): 7.33–7.38 (m, 2H, 2 × *H_e*), 7.21–7.25 (m, 6H, 6 × *H_b*), 7.13–7.17 (m, 2H, 2 × *H_d*), 7.06–7.11 (m, 6H, 6 × *H_c*), 1.30 (s, 27H, 27 × *H_a*), 1.11 (app. s, 18H, 18 × *H_f*), 1.10 (app. s, 3H, 3 × *H_g*). ¹³C NMR (CDCl₃): 148.6, 148.1, 143.7, 131.2, 131.1, 130.8, 124.4, 120.8, 107.4, 90.3, 63.9, 34.5, 31.5, 18.8, 11.5. MS (EI): 668.462, calc. for [C₄₈H₆₄Si]⁺ = 668.478.

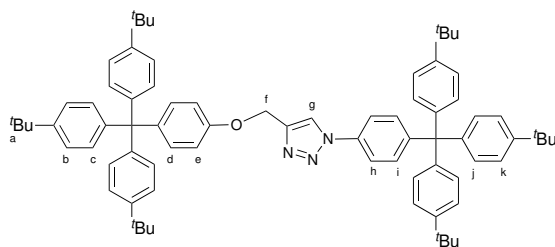
Alkyl triazolium axle·Cl **52**



The tetrafluoroborate salt of **52**⁺ (0.062 g, 0.050 mmol) was dissolved in CH₂Cl₂ (20 mL). The solution was washed with NH₄Cl_(aq) (8 × 20 mL) and H₂O (2 × 20 mL), dried (MgSO₄) and taken to dryness under reduced pressure to give **52**·Cl as a pale yellow powder. Yield: 0.052 g (89%).

¹H NMR (CDCl₃): 10.02 (s, 1H, *H_g*), 7.02–7.22 (m, 28H, 6 × *H_b*, 6 × *H_c*, 2 × *H_d*, 2 × *H_m*, 6 × *H_n*, 6 × *H_o*), 6.82 (d, *J_{d,e}* = 8.7 Hz, 2H, 2 × *H_e*), 6.60 (d, *J_{l,m}* = 8.8 Hz, 2H, 2 × *H_l*), 5.44 (s, 2H, 2 × *H_f*), 4.99 (app. br. s, 2H, 2 × *H_i*), 4.23 (s, 3H, *H_h*), 4.07 (app. br. s, 2H, 2 × *H_k*), 2.56 (app. br. s, 2H, 2 × *H_j*), 1.29 (s, 27H, 27 × *H_p*), 1.28 (s, 27H, 27 × *H_a*). LRESI-MS. (pos): 1144.73, calc. for [C₈₁H₉₈N₃O₂]⁺ = 1144.77

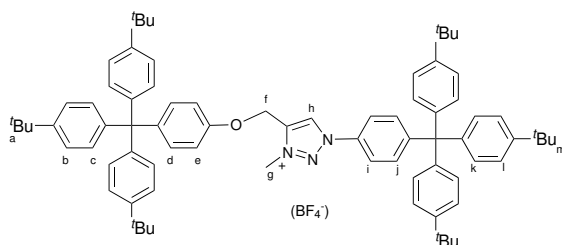
Mono-aryl triazole axle 47



The azide **31** (0.159 g, 0.300 mmol) and alkyne **49** (0.179 g, 0.330 mmol) were dissolved in CH_2Cl_2 (25 mL). DIPEA (0.17 mL, 0.13 g, 1.0 mmol), TBTA (0.016 g, 0.030 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.011 g, 0.030 mmol) were added and the clear yellow solution stirred under a nitrogen atmosphere for 4 days. The reaction mixture was taken to dryness under pressure and purified by column chromatography (gradient: 3:2 CH_2Cl_2 :petrol to CH_2Cl_2 to 3% CH_3OH in CH_2Cl_2) to give **47** as a white powder. Yield: 0.286 g (89%).

^1H NMR (CDCl_3): 7.99 (s, 1H, H_g), 7.59 (d, $J_{h,i} = 8.5$ Hz, 2H, $2 \times H_h$), 7.37 (d, $J_{h,i} = 8.5$ Hz, 2H, $2 \times H_i$), 7.21–7.27 (m, 12H, $6 \times H_b$, $6 \times H_k$), 7.05–7.11 (m, 14H, $6 \times H_c$, $2 \times H_d$, $6 \times H_j$), 6.87 (d, $J_{d,e} = 8.1$ Hz, 2H, $2 \times H_e$), 5.26 (s, 2H, $2 \times H_f$), 1.30 (s, 54H, $27 \times H_a$, $27 \times H_l$). ^{13}C NMR (CDCl_3): 156.2, 148.9, 148.8, 148.5, 145.2, 144.2, 143.4, 140.4, 134.7, 132.6, 132.5, 130.9, 130.8, 124.5, 124.2, 121.0, 119.6, 113.4, 63.7, 63.2, 62.2, 34.5, 34.4, 31.5, 31.5. HRESI-MS (pos.): 1094.6909, calc. for $[\text{C}_{77}\text{H}_{89}\text{N}_3\text{O} \cdot \text{Na}]^+ = 1094.6898$.

Mono-aryl triazolium axle 41·BF₄



The neutral axle component **47** (0.215 g, 0.200 mmol) was dissolved in dry CH_2Cl_2 (40 mL). $(\text{Me}_3\text{O})(\text{BF}_4)$ (0.032 g, 0.22 mmol) was added, causing the clear colourless solution to immediately turn yellow. It was stirred at room temperature under a nitrogen atmosphere for 16 hours, and then CH_3OH (1 mL) was added to quench the alkylating agent, causing the reaction to lose its colour. It was taken to dryness under reduced pressure and purified by column chromatography (4% CH_3OH in CHCl_3) to give **41·BF₄** as a white powder. Yield: 0.223 g (95%).

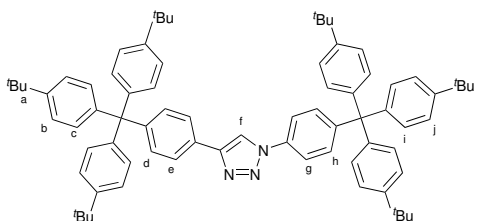
^1H NMR (CDCl_3): 8.94 (s, 1H, H_h), 7.70 (d, $J_{i,j} = 8.9$ Hz, 2H, $2 \times H_i$), 7.49 (d, $J_{i,j} = 8.9$ Hz, 2H, $2 \times H_j$), 7.21–7.28 (m, 12H, $6 \times H_b$, $6 \times H_l$), 7.15 (d, $J_{d,e} = 8.9$ Hz, 2H, $2 \times H_d$), 7.03–7.08 (m, 12H, $6 \times H_c$, $6 \times H_k$), 6.85 (d, $J_{d,e} = 8.9$ Hz, 2H, $2 \times H_e$), 5.47 (s, 2H, $2 \times H_f$), 4.45 (s, 3H, $3 \times H_g$), 1.30 (s, 27H, $27 \times H_m$), 1.29 (s, 27H, $27 \times H_a$). ^{13}C NMR (CDCl_3): 154.7, 152.9, 149.2, 148.6, 143.9, 142.0, 141.1, 133.4, 132.9, 130.8, 130.7, 124.7, 124.3, 120.4, 113.3, 77.4, 63.9, 63.2, 39.3, 34.5, 34.5, 31.5, 31.5 (3 resonances not observed). ^{19}F NMR (CDCl_3): -152.9 (m). HRESI-MS (pos.) 1086.7223, calc. for $[\text{C}_{78}\text{H}_{92}\text{N}_3\text{O}]^+ = 1086.7235$.

Mono-aryl triazolium axle 41·Cl

The tetrafluoroborate salt of **41**⁺ (0.047 g, 0.040 mmol) was dissolved in 4:1 acetone:H₂O and the solution was passed down a Cl⁻-loaded Amberlite® anion exchange column. The acetone was removed under reduced pressure and the resulting aqueous suspension extracted with CH₂Cl₂ (3 × 20 mL). The combined organic fractions were dried (MgSO₄) and taken to dryness to give **41**·Cl as a white powder. Yield: 0.039 g (86%).

¹H NMR (CDCl₃): 10.59 (s, 1H, H_h), 7.88 (d, $J_{ij} = 8.8$ Hz, 2H, $2 \times H_i$), 7.50 (d, $J_{ij} = 8.8$ Hz, 2H, $2 \times H_j$), 7.22–7.28 (m, 12H, $6 \times H_b$, $6 \times H_l$), 7.16 (d, $J_{d,e} = 8.9$ Hz, 2H, $2 \times H_d$), 7.04–7.08 (m, 12H, $6 \times H_c$, $6 \times H_k$), 6.93 (d, $J_{d,e} = 8.9$ Hz, 2H, $2 \times H_d$), 5.70 (s, 2H, $2 \times H_f$), 4.51 (s, 3H, $3 \times H_g$), 1.31 (s, 27H, $27 \times H_m$), 1.29 (s, 27H, $27 \times H_a$). LR-ESI MS (pos.): 1086.71, calc. for $[\text{C}_{78}\text{H}_{92}\text{N}_3\text{O}]^+ = 1086.72$.

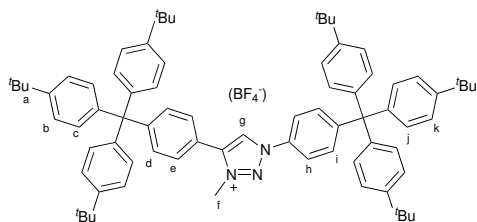
Bis-aryl triazole axle 48



The aryl azide **31** (0.265 g, 0.500 mmol) and the protected alkyne **43** (0.368 g, 0.550 mmol) were dissolved in dry CH₂Cl₂ (25 mL). DIPEA (0.17 mL, 0.13 g, 1.0 mmol), TBTA (0.265 g, 0.500 mmol) and [Cu(CH₃CN)₄](PF₆) (0.186 g, 0.500 mmol) were added, and the yellow solution deoxygenated with nitrogen. TBA-F (1.0 M in tetrahydrofuran, 1.5 mL) was added and the solution stirred at room temperature under a nitrogen atmosphere for 2 days. It was taken to dryness under reduced pressure, suspended in aqueous NH₄OH/EDTA solution (50 mL) and extracted with CH₂Cl₂ (3 × 50 mL). The combined organic layers were dried (MgSO₄) and purified by column chromatography (2:3 CH₂Cl₂:petrol) to give **48** as a white powder. Yield: 0.444 g (85%).

¹H NMR (CDCl₃): 8.10 (s, 1H, *H*_f), 7.76 (d, *J*_{g,h} = 8.4 Hz, 2H, 2 × *H*_g), 7.64 (d, *J*_{d,e} = 8.6 Hz, 2H, 2 × *H*_e), 7.39 (d, *J*_{g,h} = 8.4 Hz, 2H, 2 × *H*_h), 7.21–7.32 (m, 14H, 6 × *H*_c, 2 × *H*_d, 6 × *H*_i), 7.10–7.14 (m, 12H, 6 × *H*_b, 6 × *H*_j), 1.31 (s, 54H, 27 × *H*_a, 27 × *H*_k). ¹³C NMR (CDCl₃): 148.9, 148.6, 148.3, 148.0, 143.8, 143.5, 134.8, 132.6, 131.9, 130.9, 130.8, 127.7, 124.9, 124.5, 124.4, 124.3, 119.4, 117.5, 63.8, 63.7, 34.5, 34.5, 31.5, 31.5. HRESI-MS (pos.): 1064.6781, calc. for [C₇₆H₈₇N₃·Na]⁺ = 1064.6792.

Bis-aryl triazolium axle **42**·BF₄



The triazole axle **48** (0.261 g, 0.250 mmol) was dissolved in dry CH₂Cl₂ (30 mL). (Me₃O)(BF₄) (0.044 g, 0.30 mmol) was added and the colourless solution stirred at room temperature under a nitrogen atmosphere for 16 hours. It was quenched by the addition of CH₃OH (1 mL), taken to dryness under reduced pressure and purified by column chromatography (2% CH₃OH in CHCl₃) to give **42**·BF₄ as a white powder. Yield: 0.242 g (89%).

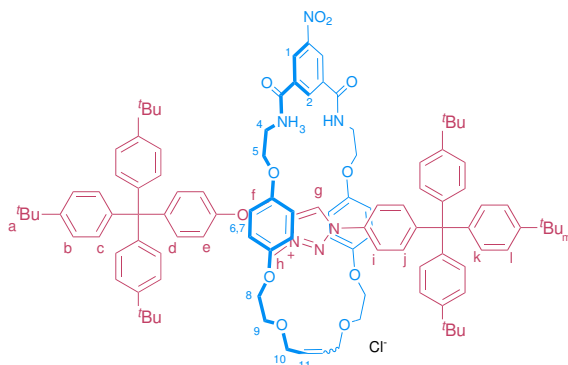
¹H NMR (CDCl₃): 8.74 (s, 1H, *H_g*), 7.78–7.81 (m, 2H, 2 × *H_h*), 7.60–7.63 (m, 2H, 2 × *H_e*), 7.47–7.52 (m, 4H, 2 × *H_d*, 2 × *H_i*), 7.25–7.29 (m, 12H, 6 × *H_b*, 6 × *H_k*), 7.06–7.11 (m, 12H, 6 × *H_c*, 6 × *H_j*), 4.37 (s, 3H, 3 × *H_f*), 1.31 (s, 54H, 27 × *H_a*, 27 × *H_l*). ¹³C NMR (CDCl₃): 152.6, 152.5, 149.1, 149.0, 143.0, 142.9, 133.2, 132.7, 132.5, 130.8, 130.7, 128.6, 126.2, 124.7, 124.6, 121.0, 118.9, 64.0, 63.9, 39.1, 34.5, 31.5 (3 resonances not observed). ¹⁹F NMR (CDCl₃): -153.9 (m). HRESI-MS (pos.): 1056.7147, calc. for [C₇₇H₉₀N₃]⁺ = 1056.7129.

Bis-aryl triazolium axle **42**·Cl

The tetrafluoroborate salt of **42**⁺ (0.057 g, 0.050 mmol) was dissolved in 4:1 acetone:H₂O and repeatedly passed down a Cl⁻-loaded Amberlite[®] anion exchange column. The acetone was removed under reduced pressure, the aqueous phase extracted with CH₂Cl₂ (3 × 20 mL), the combined organic fractions dried (MgSO₄) and taken to dryness to give **42**·Cl as a white powder. Yield: 0.055 g (100%).

¹H NMR (CDCl₃): 11.06 (s, 1H, *H_g*), 8.31 (d, *J_{h,i}* = 8.8 Hz, 2H, 2 × *H_h*), 7.89 (d, *J_{d,e}* = 8.4 Hz, 2H, 2 × *H_e*), 7.50–7.55 (m, 4H, 2 × *H_d*, 2 × *H_i*), 7.22–7.27 (m, 12H, 6 × *H_b*, 6 × *H_k*), 7.05–7.10 (m, 12H, 6 × *H_c*, 6 × *H_j*), 4.44 (s, 3H, 3 × *H_f*), 1.30 (s, 54H, 27 × *H_a*, 27 × *H_l*). LRESI-MS (pos.): 1056.67, calc. for [C₇₇H₉₀N₃]⁺ = 1056.71. LRESI-MS (neg.): 1126.65, calc. for [C₇₇H₉₀N₃·2Cl]⁻ = 1126.66.

Mono-aryl triazolium rotaxane **50·Cl**



The alkylated axle **41·Cl** (0.034 g, 0.030 mmol) and macrocycle precursor **35** (0.029 g, 0.045 mmol) were dissolved in dry CH_2Cl_2 (10 mL). Grubbs' II catalyst (0.0029 g, 10% by weight) was added and the mixture stirred under a nitrogen atmosphere for 7 days. Purification by preparative TLC (3% CH_3OH in CH_2Cl_2) gave slightly impure rotaxane. This was recrystallized from boiling $\text{CH}_3\text{OH}/\text{CH}_2\text{Cl}_2$ (10 mL, $\sim 9:1$) to give **50·Cl** as a white powder. Yield: 0.027 g (51%).

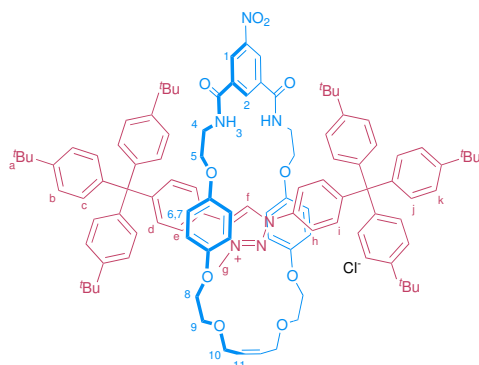
^1H NMR (CDCl_3): 10.12 (br. s, 1H, H_g), 9.86 (br. s, 1H, H_2), 9.16 (br. s, 2H, $2 \times H_3$), 8.86 (s, 2H, $2 \times H_1$), 7.71 (br. s, 2H, $2 \times H_i$), 7.23–7.30 (m, 18H, $6 \times H_b$, $2 \times H_d$, $2 \times H_e$, $6 \times H_j$, $2 \times H_l$), 7.09 (d, $J_{k,l} = 8.0$ Hz, 6H, $6 \times H_k$), 6.97 (d, $J_{b,c} = 8.0$ Hz, 6H, $6 \times H_c$), 6.21 (br. s, 8H, $4 \times H_6$, $4 \times H_7$), 5.81 (br. s, 2H, $2 \times H_{11}$), 4.74 (s, 2H, $2 \times H_f$), 4.30 (s, 3H, $3 \times H_h$), 3.53–4.11 (m, 20H, $4 \times H_4$, $4 \times H_5$, $4 \times H_8$, $4 \times H_9$, $4 \times H_{10}$), 1.35 (s, 27H, $27 \times H_a$), 1.30 (s, 27H, $27 \times H_m$). LRESI-MS (pos.) 1707.78, calc. for $[\text{C}_{110}\text{H}_{127}\text{N}_6\text{O}_{11}]^+ = 1707.96$.

Mono-aryl triazolium rotaxane **50·PF₆**

The rotaxane **50·Cl** (0.017 g, 0.010 mmol) was taken up in CH_2Cl_2 (20 mL) and the solution was washed with $\text{NH}_4\text{PF}_6(\text{aq})$ (0.1 M, 7×20 mL) and H_2O (2×20 mL). It was dried thoroughly *in vacuo* to give **50·PF₆** as a white powder. Yield: 0.018 g (100%).

^1H NMR (CDCl_3): 8.90 (s, 2H, $2 \times H_1$), 8.43 (s, 1H, H_g), 8.25 (s, 1H, H_2), 7.53 (d, $J_{i,j} = 8.6$ Hz, 2H, $2 \times H_i$), 7.36 (d, $J_{i,j} = 8.6$ Hz, 2H, $2 \times H_j$), 7.19–7.26 (m, 12H, $6 \times H_b$, $6 \times H_l$), 7.01–7.07 (m, 14H, $6 \times H_c$, $2 \times H_d$, $6 \times H_k$), 6.85 (d, $J_{d,e} = 8.8$ Hz, 2H, $2 \times H_e$), 6.41 (d, $J_{6,7} = 8.8$ Hz, 4H, $4 \times H_{6/7}$), 6.16 (d, $J_{6,7} = 8.8$ Hz, 4H, $4 \times H_{6/7}$), 5.49 (br. s, 2H, $2 \times H_{11}$), 4.63 (s, 2H, $2 \times H_f$), 4.21–4.28 (m, 4H, $4 \times H_4$), 3.56–3.96 (m, 19H, $3 \times H_h$, $4 \times H_5$, $4 \times H_8$, $4 \times H_9$, $4 \times H_{10}$), 1.33 (s, 27H, $27 \times H_m$), 1.30 (s, 27H, $27 \times H_a$). ^{13}C NMR (CDCl_3): 164.6, 154.8, 153.3, 152.8, 152.2, 149.3, 149.0, 148.7, 144.0, 142.9, 142.3, 139.9, 136.5, 132.9, 132.7, 132.0, 130.8, 130.7, 130.5, 130.5, 129.7, 126.9, 124.8, 124.4, 120.4, 115.3, 114.2, 113.5, 70.7, 69.3, 67.7, 66.4, 64.0, 63.3, 40.6, 34.6, 34.5, 31.5, 31.5, 29.9. ^{19}F NMR (CDCl_3): -69.8 (d, $J_{\text{P,F}} = 716$ Hz). HRESI-MS (pos): 1707.9565, calc. for $[\text{C}_{110}\text{H}_{127}\text{N}_6\text{O}_{11}]^+ = 1707.9567$.

Bis-aryl triazolium rotaxane 51·Cl



The axle **42**·Cl (0.044 g, 0.040 mmol) and macrocycle precursor **35** (0.039 g, 0.060 mmol) were dissolved in dry CH_2Cl_2 (10 mL). Grubbs' II catalyst (0.0039 g, 10% by weight) was added and the mixture stirred at room temperature under a nitrogen atmosphere for 3 days. Purification by preparative TLC (2% CH_3OH in CH_2Cl_2) gave slightly impure rotaxane. This was recrystallized from boiling $\text{CH}_3\text{OH}/\text{CHCl}_3$ (25 mL, $\sim 4:1$), and the resulting white powder isolated by filtration and washed with cold CH_3OH (8 mL) to give pure **51**·Cl. Yield: 0.039 g (57%).

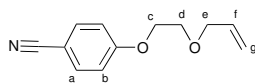
^1H NMR (CDCl_3): 10.46 (s, 1H, H_f), 9.82 (s, 1H, H_2), 9.16 (s, 2H, $2 \times H_3$), 8.76 (s, 2H, $2 \times H_1$), 8.09 (d, $J_{d,e} = 8.8$ Hz, 2H, $2 \times H_e$), 7.53 (d, $J_{h,i} = 8.6$ Hz, 2H, $2 \times H_h$), 7.39 (d, $J_{h,i} = 8.6$ Hz, 2H, $2 \times H_i$), 7.22–7.32 (m, 14H, $6 \times H_b$, $2 \times H_d$, $6 \times H_k$), 7.12 (d, $J_{b,c} = 8.6$ Hz, 6H, $6 \times H_c$), 6.93 (d, $J_{j,k} = 8.6$ Hz, 6H, $6 \times H_j$), 6.16 (d, $J_{6,7} = 9.1$ Hz, 4H, $4 \times H_{6/7}$), 6.05 (d, $J_{6,7} = 9.1$ Hz, 4H, $4 \times H_{6/7}$), 5.90 (br. s, 2H, $2 \times H_{11}$), 4.24 (s, 3H, $3 \times H_g$), 3.54–3.99 (m, 20H, $4 \times H_4$, $4 \times H_5$, $4 \times H_8$, $4 \times H_9$, $4 \times H_{10}$), 1.35 (s, 27H, $27 \times H_1$), 1.33 (s, 27H, $27 \times H_a$). LRESI-MS (pos.): 1677.89, calc. for $[\text{C}_{109}\text{H}_{125}\text{N}_6\text{O}_{10}]^+ = 1677.95$.

Bis-aryl triazolium rotaxane 51·PF₆

The rotaxane **51**·Cl (0.031 g, 0.018 mmol) was taken up in CH_2Cl_2 (20 mL), and the solution was washed with $\text{NH}_4\text{PF}_6(\text{aq})$ (0.1 M, 7×20 mL) and H_2O (2×20 mL). It was dried thoroughly to give **51**·PF₆ as a white powder. Yield: 0.035 g (100%).

^1H NMR (d_6 -DMSO): 9.12 (s, 1H, H_2), 9.07 (s, 1H, H_f), 8.80 (s, 2H, $2 \times H_1$), 7.44–7.47 (m, 4H, $2 \times H_e$, $2 \times H_h$), 7.32–7.39 (m, 14H, $6 \times H_c$, $2 \times H_d$, $6 \times H_k$), 7.24 (d, $H_{h,i} = 8.7$ Hz, 2H, $2 \times H_i$), 7.11 (d, $J_{b,c} = 8.5$ Hz, 6H, $6 \times H_b$), 7.03 (d, $J_{j,k} = 8.5$ Hz, 6H, $6 \times H_j$), 6.35 (d, $J_{6,7} = 9.0$ Hz, 4H, $4 \times H_{6/7}$), 6.20 (d, $J_{6,7} = 9.0$ Hz, 4H, $4 \times H_{6/7}$), 5.65 (br. s, 2H, $2 \times H_{11}$), 4.24 (s, 3H, $3 \times H_g$), 3.81–3.88 (m, 8H, $4 \times H_4$, $4 \times H_{10}$), 3.52–3.68 (m, 12H, $4 \times H_5$, $4 \times H_8$, $4 \times H_9$), 1.27 (s, 54H, $27 \times H_a$, $27 \times H_1$). ^{13}C NMR (d_6 -DMSO): 163.7, 152.1, 152.0, 148.2, 148.2, 147.8, 143.1, 143.0, 142.5, 135.6, 131.6, 131.3, 131.1, 129.9, 128.6, 128.2, 125.4, 124.7, 124.7, 124.3, 119.9, 118.9, 114.9, 114.4, 70.0, 68.3, 67.3, 67.0, 66.5, 63.4, 63.3, 34.1, 34.1, 31.1, 31.1 (*5 resonances not observed*). ^{19}F NMR (CDCl_3): -70.2 (d, $J_{\text{P,F}} = 717$ Hz). ^{31}P NMR (CDCl_3): -144.0 (septet, $J_{\text{P,F}} = 717$ Hz). HRESI-MS (pos.): 1677.9542, calc. for $[\text{C}_{109}\text{H}_{125}\text{N}_6\text{O}_{10}]^+ = 1677.9542$.

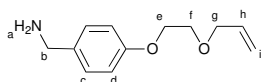
Vinyl-appended nitrile **56**



The mesylate derived from 2-allyloxy(ethanol) (4.15 g, 23.0 mmol) and 4-cyanophenol (3.29 g, 27.6 mmol) were suspended in dry CH₃CN (100 mL). K₂CO₃ (6.36 g, 46.0 mmol) was added and the suspension heated to reflux under a nitrogen atmosphere for 3 days. The reaction mixture was taken to dryness under reduced pressure, the crude product dissolved in CH₂Cl₂ (100 mL) and washed with HCl_{aq} (1 M, 2 × 100 mL), brine (100 mL), dried (MgSO₄) and taken to dryness under reduced pressure. The crude oil was purified by column chromatography (1:1 petrol:CH₂Cl₂) to give **56** as a colourless oil. Yield: 4.16 g (89%).

¹H NMR (CDCl₃): 7.55–7.60 (m, 2H, 2 × *H*_a), 6.95–7.00 (m, 2H, 2 × *H*_b), 5.86–6.00 (m, 1H, *H*_f), 5.20–5.34 (m, 2H, 2 × *H*_g), 4.18 (t, *J*_{c,d} = 4.7 Hz, 2H, 2 × *H*_c), 4.07–4.10 (m, 2H, 2 × *H*_e), 3.82 (t, *J*_{c,d} = 4.7 Hz, 2H, 2 × *H*_d). ¹³C NMR (CDCl₃): 162.2, 134.4, 134.0, 119.3, 117.7, 115.4, 104.2, 72.5, 68.2, 67.9. HRESI-MS (pos.): 226.0837, calc. for [C₁₂H₁₃NO₂·Na]⁺ = 226.0838.

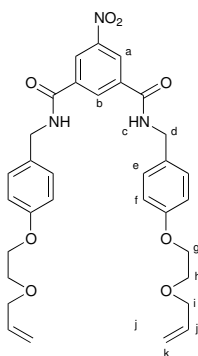
Vinyl-appended amine **57**



The nitrile **56** (2.03 g, 10.0 mmol) was dissolved in dry Et₂O (50 mL) and added dropwise to a suspension of LiAlH₄ (0.76 g, 20 mmol) in dry Et₂O (50 mL). Once addition was complete, the suspension was heated to reflux under a nitrogen atmosphere for 3 hours. It was then cooled in an ice bath, and quenched by the addition of MgSO₄·10H₂O (3.22 g, 10.0 mmol). After bubbling had ceased, the suspension was filtered and the colourless filtrate taken to dryness under reduced pressure. It was dissolved in 225:24:1 CH₂Cl₂:CH₃OH:NEt₃ and the solution was passed through a short pad of silica, and then evaporated to dryness under reduced pressure. Thorough drying *in vacuo* gave **57** as a colourless oil that solidified on standing. Yield: 1.67 g (81%).

¹H NMR (CDCl₃): 7.19–7.24 (m, 2H, 2 × *H*_c), 6.87–6.92 (m, 2H, 2 × *H*_d), 5.88–6.01 (m, 1H, *H*_h), 5.18–5.34 (m, 2H, 2 × *H*_i), 4.07–4.14 (m, 4H, 2 × *H*_e, 2 × *H*_g), 3.78–3.81 (m, 4H, 2 × *H*_b, 2 × *H*_f). ¹³C NMR (CDCl₃): 157.8, 135.9, 134.7, 128.3, 117.5, 114.8, 72.5, 68.7, 67.6, 46.0. HRMS (EI): 207.1294, calc. for [C₁₂H₁₇NO₂]⁺ = 207.1259.

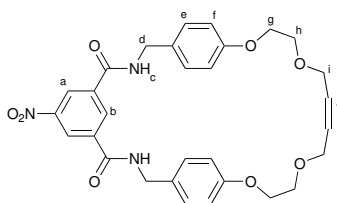
Vinyl-appended macrocycle precursor **55**



5-Nitroisophthalic acid (0.422 g, 2.00 mmol) was suspended in SOCl_2 (10 mL). Pyridine (5 drops) was added and the colourless suspension heated to reflux under a nitrogen atmosphere for 16 hours. Excess SOCl_2 was removed under reduced pressure and the crude acid chloride taken up in dry CH_2Cl_2 (30 mL). NEt_3 (0.83 mL, 0.61 g, 6.0 mmol) was added, followed by **57** (0.871 g, 4.20 mmol) in dry CH_2Cl_2 (10 mL). The reaction was stirred at room temperature under a nitrogen atmosphere for 3 hours, and then washed with $\text{HCl}_{(\text{aq})}$ (10%, 2×40 mL) and brine (40 mL). It was dried (MgSO_4) and purified by column chromatography (3% CH_3OH in CHCl_3) to give **55** as an off-white solid. Yield: 1.08 g (91%).

^1H NMR (CDCl_3): 8.66 (d, $^4J_{\text{a,b}} = 1.4$ Hz, 2H, $2 \times H_{\text{a}}$), 8.52 (t, $^4J_{\text{a,b}} = 1.4$ Hz, 1H, H_{b}), 7.42 (t, $H_{\text{c,d}} = 5.4$ Hz, 2H, $2 \times H_{\text{c}}$), 7.11 (d, $J_{\text{e,f}} = 8.6$ Hz, 4H, $4 \times H_{\text{e}}$), 6.69 (d, $J_{\text{e,f}} = 8.6$ Hz, 4H, $4 \times H_{\text{f}}$), 5.84–5.98 (m, 2H, $2 \times H_{\text{j}}$), 5.17–5.33 (m, 4H, $4 \times H_{\text{k}}$), 4.43 (d, $J_{\text{c,d}} = 5.4$ Hz, 4H, $4 \times H_{\text{d}}$), 4.03–4.06 (m, 4H, $4 \times H_{\text{i}}$), 3.98 (t, $H_{\text{g,h}} = 4.7$ Hz, 4H, $4 \times H_{\text{g}}$), 3.73 (t, $H_{\text{g,h}} = 4.7$ Hz, 4H, $4 \times H_{\text{h}}$). ^{13}C NMR (CDCl_3): 164.4, 158.3, 148.3, 136.2, 134.4, 131.2, 129.8, 129.4, 124.9, 117.9, 114.7, 72.5, 68.6, 67.4, 44.0. HRESI-MS (pos.): 612.2321, calc. for $[\text{C}_{32}\text{H}_{35}\text{N}_3\text{O}_8\cdot\text{Na}]^+ = 612.2316$.

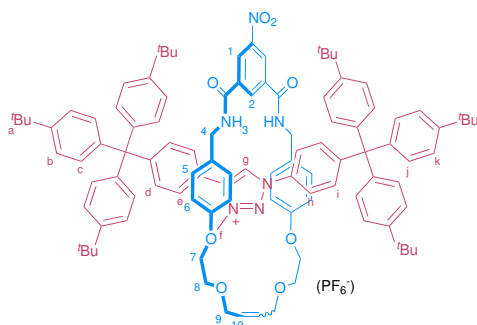
Small alkene macrocycle **58**



Small quantities of this macrocycle were isolated as by-products of reactions to form rotaxanes.

^1H NMR (9:1 $\text{CDCl}_3\text{:CD}_3\text{OD}$): 8.71 (d, $^4J_{\text{a,b}} = 1.5$ Hz, 2H, $2 \times H_{\text{a}}$), 8.27 (t, $^4J_{\text{a,b}} = 1.5$ Hz, 1H, H_{b}), 7.09 (d, $J_{\text{e,f}} = 8.6$ Hz, 4H, $4 \times H_{\text{e}}$), 6.67 (d, $J_{\text{e,f}} = 8.6$ Hz, 4H, $4 \times H_{\text{f}}$), 5.75–5.77 (m, 2H, $2 \times H_{\text{j}}$), 4.37 (s, 4H, $4 \times H_{\text{d}}$), 3.93–3.98 (m, 8H, $4 \times H_{\text{g}}$, $4 \times H_{\text{i}}$), 3.69 (t, $J_{\text{g,h}} = 4.4$ Hz, 4H, $4 \times H_{\text{h}}$). ^{13}C NMR (9:1 $\text{CDCl}_3\text{:CD}_3\text{OD}$): 164.8, 158.2, 148.6, 136.0, 129.7, 129.6, 129.0, 125.5, 114.5, 71.0, 68.7, 67.4, 43.9 (*one resonance not observed*). HRESI-MS (pos.): 584.1891, calc. for $[\text{C}_{30}\text{H}_{31}\text{N}_3\text{O}_8\cdot\text{Na}]^+ = 584.2003$.

Bis-aryl triazolium rotaxane **59**·Cl



The axle component **42**·Cl (0.033 g, 0.030 mmol) and macrocycle precursor **55** (0.027 g, 0.045 mmol) were dissolved in dry CH₂Cl₂ (5 mL). Grubbs' II catalyst (5.4 mg 20% by weight) was added, and the mixture stirred at room temperature under a nitrogen atmosphere for 3 days. It was taken to dryness and purified by preparative TLC (3% CH₃OH in CH₂Cl₂) to give slightly impure rotaxane. This was recrystallized from boiling CH₃OH (4 mL) to give a white solid, which was isolated by filtration, and washed with cold CH₃OH (2 × 1 mL) to give pure **59**·Cl as a white powder. Yield: 0.020 g (40%).

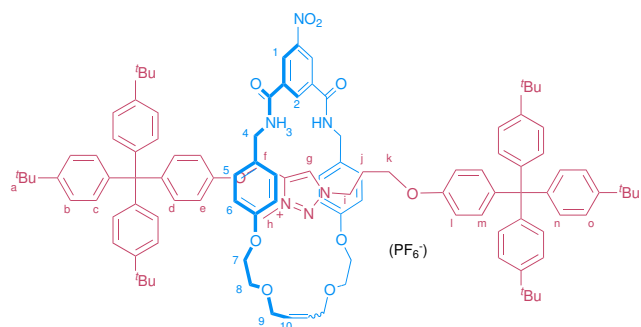
¹H NMR (1:1 CDCl₃:CD₃OD): 9.33 (t, $J_{3,4} = 5.8$ Hz, 2H, 2 × H_3), 9.22 (s, 1H, H_g), 8.90 (s, 1H, H_2), 8.80 (s, 2H, 2 × H_1), 7.69 (d, $H_{h,i} = 8.8$ Hz, 2H, 2 × H_h), 7.42 (d, $H_{d,e} = 8.8$ Hz, 2H, 2 × H_e), 7.26–7.32 (m, 14H, 6 × H_b , 6 × H_k , 2 × H_i), 7.21 (d, $J_{d,e} = 8.8$ Hz, 2H, 2 × H_d), 7.07–7.14 (m, 12H, 6 × H_c , 6 × H_j), 6.80 (d, $J_{5,6} = 8.6$ Hz, 4H, 4 × H_5), 5.92 (d, $J_{5,6} = 8.6$ Hz, 4H, 4 × H_6), 5.70 (br. s, 2H, 2 × H_{10}), 4.42 (app. t, $J_{3,4} = 5.8$ Hz, 4H, 4 × H_4), 4.12 (s, 3H, 3 × H_f), 3.86 (br. s, 4H, 4 × H_9), 3.64 (br. s, 4H, 4 × H_7), 3.53 (br. s, 4H, 4 × H_8), 1.30 (s, 27H, 27 × H_1), 1.29 (s, 27H, 27 × H_a). HRESI-MS (pos.): 1617.9253, calc. for [C₁₀₇H₁₂₁N₆O₈]⁺ = 1617.9240.

Bis-aryl triazolium rotaxane **59**·PF₆

The chloride salt of **59**⁺ (0.013 g, 0.0080 mmol) was taken up in CH₂Cl₂ (20 mL) and the solution washed with NH₄PF₆(aq) (0.1 M, 7 × 20 mL) and H₂O (3 × 20 mL). Thorough drying *in vacuo* gave **59**·PF₆ as a white powder. Yield: 0.011 g (79%).

¹H NMR (1:1 CDCl₃:CD₃OD): 9.03 (s, 1H, H_g), 8.80 (s, 2H, 2 × H_1), 8.31 (s, 1H, H_2), 7.40 (d, $H_{h,i} = 8.4$ Hz, 2H, 2 × H_h), 7.28–7.32 (m, 14H, 6 × H_b , 2 × H_e , 6 × H_k), 7.13–7.16 (m, 16H, 6 × H_c , 2 × H_d , 6 × H_j , 2 × H_i), 6.85 (d, $J_{5,6} = 8.5$ Hz, 4H, 4 × H_5), 6.02 (d, $J_{5,6} = 8.5$ Hz, 4H, 4 × H_6), 5.45 (br. s, 2H, 2 × H_{10}), 4.28–4.42 (m, 4H, 4 × H_4), 3.88 (s, 3H, 3 × H_f), 3.50–3.72 (m, 12H, 4 × H_7 , 4 × H_8 , 4 × H_9), 1.29 (s, 54H, 27 × H_a , 27 × H_1). ¹³C NMR (1:1 CDCl₃:CD₃OD): 165.5, 157.9, 153.3, 153.0, 149.7, 149.6, 149.4, 143.9, 143.8, 143.6, 137.1, 133.1, 132.6, 132.5, 132.1, 131.0, 130.9, 130.3, 130.1, 128.7, 127.7, 125.7, 125.4, 125.3, 125.0, 121.0, 119.4, 114.0, 71.3, 69.8, 67.7, 64.8, 64.7, 43.7, 39.2, 34.9, 34.9, 31.7, 31.6. ¹⁹F NMR (1:1 CDCl₃:CD₃OD): -73.7 (d, $J_{P,F} = 711$ Hz). ³¹P NMR (1:1 CDCl₃:CD₃OD): -144.5 (septet, $J_{P,F} = 711$ Hz). LRESI-MS (pos.): 1617.88, calc. for [C₁₀₇H₁₂₁N₆O₈]⁺ = 1617.92.

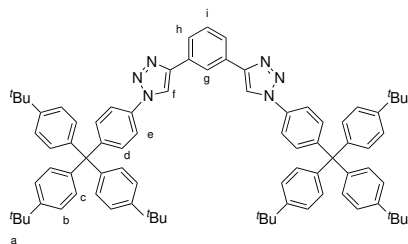
Alkyl triazolium rotaxane **60**·PF₆



Axle component **52**·Cl (0.024 g, 0.020 mmol) and **35** (0.018 g, 0.030 mmol) were dissolved in dry CH₂Cl₂ (5 mL). Grubbs' II catalyst (0.0035 g, 20% by weight) was added and the reaction stirred at room temperature under a nitrogen atmosphere for 3 days. It was taken to dryness under reduced pressure and purified by preparative TLC (1:1 CH₂Cl₂:CH₃CN). The product was taken up in CH₂Cl₂ (10 mL), washed with NH₄PF₆(aq) (0.1 M, 7 × 10 mL) and water (3 × 10 mL) and dried thoroughly to give **60**·PF₆ as a white powder. Yield: 0.0025 g (9%).

¹H NMR (1:1 CDCl₃:CD₃OD): 8.78 (d, ⁴J_{1,2} = 1.5 Hz, 2H, 2 × H₁), 8.37 (s, 1H, H_g), 8.32 (t, ⁴J_{1,2} = 1.5 Hz, 1H, H₂), 7.20–7.23 (m, 12H, 6 × H_c, 6 × H_o), 7.00–7.10 (m, 20H, 4 × H₅, 6 × H_b, 2 × H_d, 2 × H_m, 6 × H_n), 6.65 (d, J_{d,e} = 9.0 Hz, 2H, 2 × H_e), 6.59 (d, J_{l,m} = 9.0 Hz, 2H, 2 × H_l), 6.39 (d, J_{5,6}, 4H, 4 × H₆), 5.68 (br. s, 2H, 2 × H₁₀), 4.68 (s, 2H, 2 × H_f), 4.34–4.46 (m, 6H, 4 × H₄, 2 × H_i), 3.87 (s, 3H, 3 × H_h), 3.73–3.81 (m, 12H, 4 × H_k, 4 × H₇, 4 × H₈), 3.56 (m, 4H, 4 × H₉), 2.08 (qn, J_{i,j} = J_{j,k} = 6.2 Hz, 2H, 2 × H_j), 1.28 (s, 27H, 27 × H_a), 1.27 (s, 27H, 27 × H_p). ¹³C NMR (1:1 CDCl₃:CD₃OD): 165.7, 158.3, 156.5, 155.2, 149.3, 149.2, 149.0, 144.8, 144.6, 142.5, 141.2, 139.9, 137.1, 133.0, 132.9, 132.1, 131.6, 131.3, 131.2, 131.1, 130.7, 130.2, 130.1, 125.5, 124.8, 114.5, 113.9, 113.6, 71.4, 69.8, 67.9, 64.2, 63.8, 63.7, 51.9, 43.8, 38.7, 35.8, 35.3, 34.8, 34.8, 31.7 (*one resonance not observed*). ¹⁹F (CDCl₃): -71.5 (d, J_{P,F} = 716 Hz). HRESI-MS (pos.): 1705.9746, calc. for [C₁₁₁H₁₂₉N₆O₁₀]⁺ = 1705.9765.

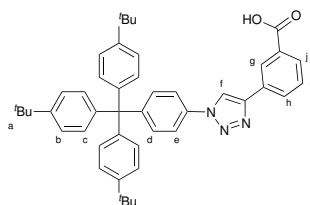
Bis-triazole axle component **64**



The aryl azide **31** (0.222 g, 0.420 mmol) and 1,3-diethynylbenzene (0.0266 mL, 0.0252 g, 0.200 mmol) were dissolved in CH_2Cl_2 (20 mL). DIPEA (0.090 mL, 0.065 g, 0.50 mmol), TBTA (0.021 g, 0.040 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.015 g, 0.040 mmol) were added and the yellow solution stirred at room temperature under a nitrogen atmosphere for 4 days. It was then stirred vigorously with aqueous NH_4OH /EDTA (20 mL); the organic layer was taken, and the aqueous phase extracted further with dichloromethane (20 mL). The combined organic fractions were dried (MgSO_4) and taken to dryness under reduced pressure. Column chromatography (1% CH_3OH in CH_2Cl_2) gave **64** as a white powder. Yield: 0.225 g (95%).

^1H NMR (CDCl_3): 8.44 (t, $^4J_{g,h} = 1.6$ Hz, 1H, H_g), 8.28 (s, 2H, $2 \times H_f$), 7.93 (dd, $J_{h,i} = 7.7$ Hz, $^4J_{g,h} = 1.6$ Hz, 2H, $2 \times H_h$), 7.68 (t, $J_{d,e} = 8.8$ Hz, 4H, $4 \times H_e$), 7.56 (t, $J_{h,i} = 7.7$ Hz, 1H, H_i), 7.42 (t, $J_{d,e} = 8.8$ Hz, 4H, $4 \times H_d$), 7.25–7.30 (m, 12H, $12 \times H_b$), 7.10–7.15 (m, 12H, $12 \times H_c$), 1.32 (s, 54H, $54 \times H_a$). ^1H NMR (CDCl_3): 148.9, 148.8, 148.0, 143.5, 134.7, 132.7, 132.7, 130.8, 129.8, 125.8, 124.4, 123.2, 119.5, 118.1, 63.7, 34.5, 31.5. LRESI-MS (pos.): 1207.78, calc. for $[\text{C}_{84}\text{H}_{96}\text{N}_3 \cdot \text{Na}]^+ = 1207.73$.

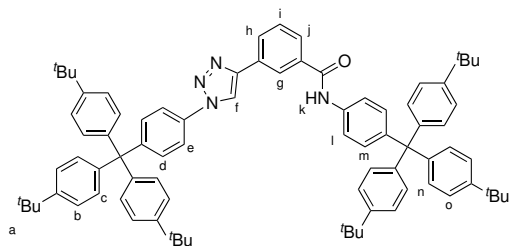
Triazole axle component precursor **65**



The aryl azide **31** (0.106 g, 0.200 mmol) and 3-ethynylbenzoic acid (0.037 g, 0.25 mmol) were dissolved in CH_2Cl_2 (10 mL). DIPEA (0.090 mL, 0.065 g, 0.50 mmol), TBTA (0.011 g, 0.020 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.0075 g, 0.020 mmol) were added and the yellow solution stirred at room temperature under a nitrogen atmosphere over the weekend. The reaction was diluted with further CH_2Cl_2 (10 mL), washed with $\text{HCl}_{(\text{aq})}$ (1 M, 2×20 mL) and brine (20 mL), dried (MgSO_4), and taken to dryness under reduced pressure. Column chromatography (5% CH_3OH in CH_2Cl_2) gave **65** as a white powder. Yield: 0.093 g (69%).

^1H NMR (d_6 -DMSO): 9.36 (s, 1H, H_f), 8.51 (s, 1H, H_g), 8.16 (d, $J_{i,j} = 7.8$ Hz, 1H, H_j), 7.94 (d, $J_{h,i} = 7.8$ Hz, 1H, H_h), 7.88 (d, $J_{d,e} = 8.7$ Hz, 2H, $2 \times H_e$), 7.62 (app. t, $J_{h,i} = J_{i,j} = 7.8$ Hz, 1H, H_i), 7.33–7.41 (m, 8H, $6 \times H_b$, $2 \times H_d$), 7.15 (d, $J_{b,c} = 8.5$ Hz, 6H, $6 \times H_c$), 1.26 (s, 27H, $27 \times H_a$). ^{13}C (d_6 -DMSO): 148.1, 147.7, 146.5, 143.4, 134.2, 131.7, 130.6, 130.0, 129.4, 129.4, 129.0, 129.0, 126.0, 124.7, 120.1, 119.5, 63.2, 34.1, 31.1 (one resonance not observed). HRESI-MS (neg.): 674.3757, calc. for $[\text{C}_{46}\text{H}_{48}\text{N}_3\text{O}_2]^- = 674.3752$.

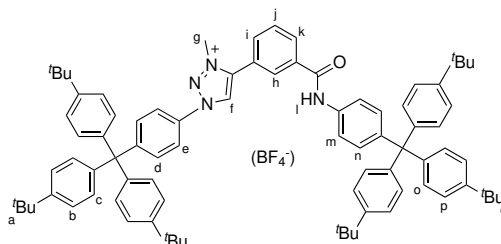
Amide triazole axle component **66**



The carboxylic acid **65** (0.068 g, 0.10 mmol) was suspended in SOCl_2 (2 mL). A drop of pyridine was added, and the suspension was heated to reflux under a nitrogen atmosphere for 16 hours, during which time all material dissolved. The SOCl_2 was removed under reduced pressure and the resulting yellow solid taken up in dry CH_2Cl_2 (10 mL). NEt_3 (0.056 mL, 0.040 g, 0.40 mmol) was added followed by the aryl amine **30** in dry CH_2Cl_2 (10 mL), and the resulting clear yellow solution was stirred at room temperature under a nitrogen atmosphere for 16 hours. It was washed with 10% $\text{HCl}_{(\text{aq})}$ (2×20 mL) and brine (20 mL), dried (MgSO_4), and taken to dryness under reduced pressure. Column chromatography (CH_2Cl_2) gave **66** as a white powder. Yield: 0.080 g (69%).

^1H NMR (CDCl_3): 8.39 (s, 1H, H_k), 8.25 (s, 1H, H_f), 8.07 (d, $J_{h,i} = 8.0$ Hz, 1H, H_h), 8.01 (s, 1H, H_g), 7.86 (d, $J_{i,j} = 7.7$ Hz, 1H, H_j), 7.65 (d, $J_{d,e} = 8.8$ Hz, 2H, $2 \times H_e$), 7.54–7.59 (m, 3H, H_i , $2 \times H_l$), 7.42 (d, $J_{d,e} = 8.8$ Hz, 2H, $2 \times H_d$), 7.21–7.29 (m, 14H, $6 \times H_b$, $2 \times H_m$, $6 \times H_o$), 7.10–7.14 (m, 12H, $6 \times H_c$, $6 \times H_n$), 1.32 (s, 27H, $27 \times H_a$), 1.31 (s, 27H, $27 \times H_p$). ^{13}C NMR (CDCl_3): 165.4, 148.9, 148.5, 144.0, 143.4, 135.9, 135.6, 134.5, 132.7, 132.0, 131.0, 130.8, 130.6, 129.6, 129.1, 127.2, 124.8, 124.8, 124.5, 124.3, 119.5, 119.1, 118.3, 118.3, 63.7, 63.5, 34.5, 34.5, 31.5 (*one resonance not observed*). HR-ESI MS (pos.): 1183.7157, calc. for $[\text{C}_{83}\text{H}_{92}\text{NO}_4 \cdot \text{Na}]^+ = 1183.7163$.

Amide triazolium axle component **63·BF₄**



The triazole axle component **66** (0.058 g, 0.050 mmol) was dissolved in dry CH_2Cl_2 (10 mL). $(\text{Me}_3\text{O})(\text{BF}_4)$ (0.0088 g, 0.060 mmol) was added and the mixture stirred at room temperature under a nitrogen atmosphere. The alkylating agent was quenched by addition of CH_3OH (1 mL), and the colourless solution taken to dryness under reduced pressure. Column chromatography (5% CH_3OH in CH_2Cl_2) gave **63·BF₄** as a white powder. Yield: 0.042 g (67%).

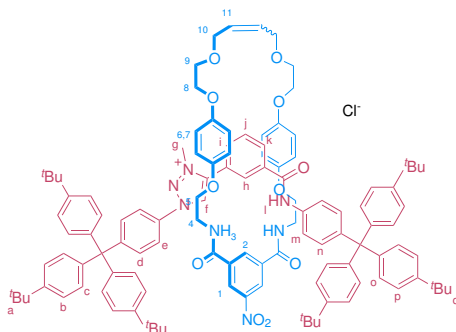
^1H NMR (CDCl_3): 9.15 (s, 1H, H_i), 9.07 (s, 1H, H_f), 8.21 (s, 1H, H_h), 8.01 (d, $J_{i,j} = 7.9$ Hz, 1H, H_i), 7.61–7.73 (m, 5H, $2 \times H_e$, $2 \times H_m$, H_k), 7.49 (d, $J_{d,e} = 8.9$ Hz, 2H, $2 \times H_d$), 7.40 (app. t, $J_{i,j} = J_{j,k} = 7.9$ Hz, 1H, H_j), 7.09–7.30 (m, 26H, $6 \times H_b$, $6 \times H_c$, $2 \times H_n$, $6 \times H_o$, $6 \times H_p$), 4.27 (s, 3H, H_g), 1.31 (s, 27H, $27 \times H_a$), 1.29 (s, 27H, $27 \times H_q$). ^{13}C NMR (d_6 -DMSO): 164.4, 151.0, 148.3, 147.8, 143.8, 143.0, 142.6, 142.4, 136.4, 136.1, 132.3, 132.2, 132.1, 130.6, 130.4, 130.0, 129.9, 129.7, 129.1, 127.7, 124.8, 124.5, 122.9, 120.9, 119.7, 63.4, 62.9, 34.1, 34.1, 31.3, 31.3 (*one peak obscured by DMSO signal*). ^{19}F NMR (d_6 -DMSO): -148.3 (m). HR-ESI MS: 1175.7475, calc. for $[\text{C}_{84}\text{H}_{95}\text{N}_4\text{O}]^+ = 1175.7500$.

Amide triazolium axle component **63**·Cl

The tetrafluoroborate salt of **63** (0.032 g, 0.025 mmol) was taken up in 9:1 $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (50 mL, required gentle heating). It was repeatedly passed down a Cl^- -loaded Amberlite[®] anion exchange column. The CH_3CN was removed under reduced pressure and the remaining aqueous suspension extracted with CH_2Cl_2 (3×20 mL). The combined organic fractions were washed with brine (20 mL), dried (MgSO_4), and taken to dryness under reduced pressure to give **63**·Cl as a white powder. Yield: 0.029 g (94%).

^1H NMR (5:1 $\text{CDCl}_3:\text{CD}_3\text{OD}$): 9.79 (s, 1H, H_f), 8.49 (s, 1H, H_h), 8.20 (d, $J_{i,j} = 7.8$ Hz, 1H, H_i), 7.82–7.89 (m, 3H, $2 \times H_e$, H_k), 7.68–7.75 (m, 3H, $2 \times H_m$, H_j), 7.53 (d, $J_{d,e} = 8.9$ Hz, 2H, $2 \times H_d$), 7.15–7.27 (m, 14H, $6 \times H_b$, $2 \times H_n$, $6 \times H_p$), 7.04–7.10 (m, 12H, $6 \times H_c$, $6 \times H_o$), 4.44 (s, 3H, $3 \times H_g$), 1.27 (s, 27H, $27 \times H_a$), 1.26 (s, 27H, $27 \times H_q$). LRESI-MS (pos.): 1175.77, calc. for $[\text{C}_{84}\text{H}_{95}\text{N}_4\text{O}]^+ = 1175.75$.

Amide triazolium rotaxane **67**·Cl



The chloride salt of **63**⁺ (0.024 g, 0.020 mmol) and the bis-vinyl precursor **35** (0.020 g, 0.030 mmol) were dissolved in dry CH₂Cl₂ (5 mL, required gentle heating). Grubbs' II catalyst (0.0020 g, 10% by weight) was added and the reaction stirred at room temperature under a nitrogen atmosphere for 3 days. It was taken to dryness under reduced pressure and purified by preparative TLC (2% CH₃OH in CH₂Cl₂) to give slightly impure **67**⁺ (yield at this point, 0.021 g, 57%). It was taken up in hot CH₃OH/CH₂Cl₂ (10 mL 4:1 CH₃OH:CH₂Cl₂, and the total volume reduced to ~ 5 mL by boiling. Cooling the solution resulted in the precipitation of a white powder, which was by filtration and washed with ice-cold CH₃OH (2 × 1 mL) to give **67**·Cl. Yield: 0.017 g (47%).

¹H NMR (1:1 CDCl₃:CD₃OD): 10.10 (s, 1H, *H*_l), 9.96 (s, 1H, *H*_f), 9.53 (s, 1H, *H*_h), 8.92 (s, 1H, *H*₂), 8.72 (s, 2H, 2 × *H*₁), 8.14 (d, *J*_{i,j} = 7.4 Hz, 1H, *H*_i), 7.63–7.87 (m, 8H, 2 × *H*₃, 2 × *H*_e, *H*_j, *H*_k, 2 × *H*_m), 7.16–7.30 (m, 20H, 8 × *H*_b, 2 × *H*_d, 2 × *H*_n, 8 × *H*_p), 7.09 (d, *J*_{b,c} = 8.5 Hz, 6H, 6 × *H*_c), 6.95 (d, *J*_{o,p} = 8.5 Hz, 6H, 6 × *H*_o), 6.14–6.22 (m, 8H, 4 × *H*₆, 4 × *H*₇), 5.95 (br. s, 2H, 2 × *H*₁₁), 4.32 (s, 3H, 3 × *H*_g), 3.61–4.16 (m, 20H, 4 × *H*₄, 4 × *H*₅, 4 × *H*₈, 4 × *H*₉, 4 × *H*₁₀), 1.33 (s, 27H, 27 × *H*_a), 1.27 (s, 27 × *H*_q). HRESI-MS (pos.): 1796.9870, calc. for [C₁₁₆H₁₃₀N₇O₁₁]⁺ = 1796.8923.

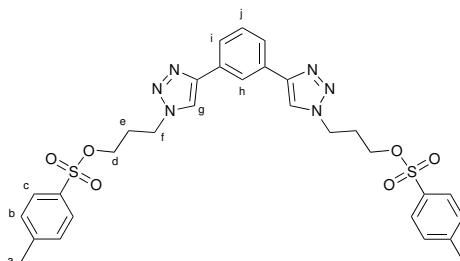
Amide triazolium rotaxane **67**·PF₆

The chloride salt of **67**⁺ (0.014 g, 0.0075 mmol) was taken up in CH₂Cl₂ (20 mL). The solution was washed with NH₄PF₆(aq) (0.1 M, 7 × 20 mL) and H₂O (3 × 20 mL). Thorough drying *in vacuo* gave **67**·PF₆ as a white powder. Yield: 0.012 g (79%).

¹H NMR (1:1 CDCl₃:CD₃OD): 9.40 (s, 1H, *H*_f), 8.94 (s, 1H, *H*_h), 8.75 (d, ⁴*J*_{1,2} = 1.5 Hz, 2H, 2 × *H*₁), 8.04 (d, *J*_{i,j} = 7.9 Hz, 1H, *H*_i), 7.81 (d, *J*_{d,e} = 8.8 Hz, 2H, 2 × *H*_e), 7.74 (s, ⁴*J*_{1,2} = 1.5 Hz, 1H, *H*₂), ~ 7.59 (obscured by CHCl₃ residual peak, 1H, *H*_k), 7.55 (app. t, *J*_{i,j} = *J*_{j,k} = 7.9 Hz, 1H, *H*_j), 7.43 (d, *J*_{d,e} = 8.8 Hz, 2H, 2 × *H*_d), 7.30 (d, *J*_{b,c} = 8.7 Hz, 6H, 6 × *H*_b), 7.24 (d, *J*_{o,p} = 8.9 Hz, 6H, 6 × *H*_p), 7.20 (d, *J*_{m,n} = 8.9 Hz, 2H, 2 × *H*_m), 7.07–7.10 (m, 14H, 6 × *H*_c, 2 × *H*_n, 6 × *H*_o), 6.21–6.33 (m, 8H, 4 × *H*₆, 4 × *H*₇), 5.83 (br. s, 2H, 2 × *H*₁₁), 4.19 (s, 3H, 3 × *H*_g), 3.43–4.00 (m, 20H, 4 × *H*₄, 4 × *H*₅, 4 × *H*₈, 4 × *H*₉, 4 × *H*₁₀), 1.32 (s, 27H, 27 × *H*_a), 1.29 (s, 27H, 27 × *H*_q). ¹³C NMR (1:1 CDCl₃:CD₃OD): 165.9, 165.7, 153.3, 153.1, 149.8, 149.2, 149.1, 145.1, 144.6, 143.5, 143.3, 136.6, 136.5, 136.1, 133.5, 132.7, 132.2, 131.7, 131.2, 131.0, 130.2, 130.1, 129.7, 127.0, 126.1, 125.3, 124.8, 122.4, 120.7, 120.2, 115.6, 115.0, 71.4, 69.8, 68.4, 66.9, 64.6, 64.1, 40.6, 40.1, 34.9, 34.8, 31.7, 31.6 (3 resonances not observed). ¹⁹F NMR (1:1 CDCl₃:CD₃OD): -73.4 (d, *J*_{P,F} = 711 Hz). ³¹P NMR (1:1 CDCl₃:CD₃OD): -144.5 (d, *J*_{P,F} = 711 Hz). LRESI-MS (pos.): 1796.88, calc. for [C₁₁₆H₁₃₀N₇O₁₁]⁺ = 1796.98.

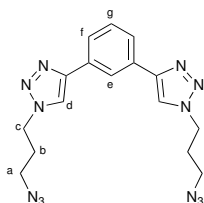
6.7 Synthesis of compounds from Chapter 5

Bis-triazole tosylate **73**



1,3-Diethynylbenzene (0.359 mL, 0.341 g, 2.70 mmol) and tosyl-protected azide **72** (1.45 g, 5.67 mmol, 2.1 equiv) were dissolved in dry CH_2Cl_2 (60 mL). DIPEA (1.1 mL, 0.78 g, 6.0 mmol), TBTA (0.287 g, 0.540 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4(\text{PF}_6)]$ (0.202 g, 0.540 mmol) were added and the resulting pale yellow solution stirred at room temperature under a nitrogen atmosphere for 4 days. It was taken to dryness under reduced pressure and purified by column chromatography (3% CH_3OH in CH_2Cl_2) to give **73** as a pale yellow foam. This was used immediately to prepare **74**. ^1H NMR (CDCl_3): 8.20 (s, 2H, $2 \times H_g$), 7.75–7.83 (m, 7H, $4 \times H_c$, H_h , $2 \times H_i$), 7.50 (t, $J_{i,j} = 7.7$ Hz, 1H, H_j), 7.33 (d, $J_{b,c} = 8.0$ Hz, 4H, $4 \times H_b$), 4.51 (t, $J_{e,f} = 6.6$ Hz, 4H, $4 \times H_f$), 4.06 (t, $J_{d,e} = 5.7$ Hz, 4H, $4 \times H_d$), 2.31–2.43 (m, 10H, $6 \times H_a$, $4 \times H_e$). LRESI-MS (pos.): 659.26, calc. for $[\text{C}_{30}\text{H}_{32}\text{N}_6\text{O}_6\text{S}_2 \cdot \text{Na}]^+ = 659.17$.

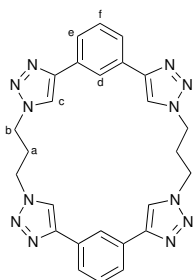
Bis-triazole azide **74**



The ditosylate **73** (all of previous reaction) was dissolved in DMSO (25 mL). NaN_3 (0.478 g, 7.35 mmol) was added and the mixture heated at 60 °C under a nitrogen atmosphere over the weekend. It was cooled to room temperature, and partitioned between H_2O and CH_2Cl_2 (100 mL each). The organic layer was taken and the aqueous layer extracted further with CH_2Cl_2 (100 mL). The combined organic fractions were washed with H_2O (100 mL), brine (100 mL) and dried (MgSO_4), taken to dryness under reduced pressure. Purification by column chromatography (2% CH_3OH in CH_2Cl_2) gave **74** as a pale yellow foamy solid. Yield: 0.773 g (76% over 2 steps from 1,3-diethynylbenzene).

^1H NMR (CDCl_3): 8.29 (s, 2H, $2 \times H_d$), 7.82–7.87 (m, 3H, H_e , $2 \times H_f$), 7.51 (t, $J_{f,g} = 7.7$ Hz, 1H, H_g), 4.53 (t, $J_{b,c} = 6.7$ Hz, 4H, $4 \times H_c$), 3.41 (t, $J_{a,b} = 6.3$ Hz, 4H, $4 \times H_a$), 2.17–2.31 (m, 4H, $4 \times H_b$). ^{13}C NMR (CDCl_3): 147.3, 131.1, 129.5, 125.3, 122.8, 120.4, 48.0, 47.3, 29.4. HRESI-MS (pos.): 401.1667, calc for $[\text{C}_{16}\text{H}_{18}\text{N}_{12} \cdot \text{Na}]^+ = 401.1670$.

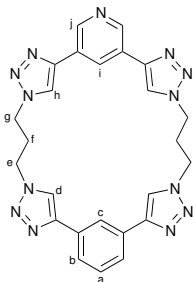
Phenyl tetra-triazole macrocycle **69**



The bis-azide **74** (0.151 g, 0.400 mmol) and 1,3-diethynylbenzene (0.053 mL, 0.051 g, 0.40 mmol) were dissolved in CH_2Cl_2 (400 mL). DIPEA (0.17 mL, 0.13 g, 1.0 mmol), TBTA (0.042 g, 0.080 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.030 g, 0.080 mmol) were added and the pale yellow solution stirred for 4 days under a nitrogen atmosphere, during which time a fluffy yellow precipitate developed. The reaction mixture was taken to dryness under reduced pressure and purified by column chromatography (gradient: 5–10% CH_3OH in CH_2Cl_2) to give **69** as a white powder. Yield: 0.136 g (67%).

^1H NMR (d_6 -DMSO): 8.11 (s, 4H, $4 \times H_c$), 7.98 (t, $^4J_{d,e} = 1.4$ Hz, 2H, $2 \times H_d$), 7.56 (dd, $J_{e,f} = 7.5$ Hz, $^4J_{d,e} = 1.4$ Hz, 4H, $4 \times H_e$), 7.30 (t, $J_{e,f} = 7.5$ Hz, 2H, $2 \times H_f$), 4.53 (t, $J_{a,b} = 5.3$ Hz, 8H, $8 \times H_b$), 2.68 (qn, $J_{a,b} = 5.3$ Hz, 4H, $4 \times H_a$). ^{13}C NMR (d_6 -DMSO): 146.1, 130.8, 128.9, 123.9, 122.4, 121.3, 47.9, 29.2. HRESI-MS (neg.): 539.1936, calc. for $[\text{C}_{26}\text{H}_{24}\text{N}_{12}\cdot\text{Cl}]^- = 539.1941$.

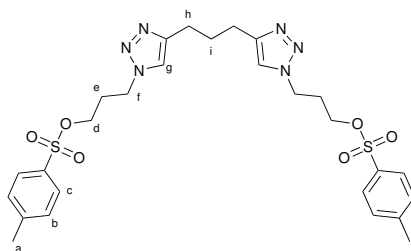
Pyridine tetra-triazole macrocycle **70**



The bis-azide **74** (0.265 g, 0.700 mmol) and 3,5-diethynylpyridine (0.089 g, 0.70 mmol) were dissolved in CH_2Cl_2 (700 mL). DIPEA (0.31 mL, 0.24 g, 1.0 mmol), TBTA (0.074 g, 0.14 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.052 g, 0.14 mmol) were added and the pale yellow solution stirred for 3 days under a nitrogen atmosphere at room temperature, during which time a pale precipitate developed. It was taken to dryness under reduced pressure and purified by column chromatography (gradient: 9:1 – 6:1 CH_2Cl_2 : CH_3OH) to give **70** as a white powder. Yield: 0.208 g (59%).

^1H NMR (d_6 -DMSO): 8.56 (br. s, 2H, $2 \times H_j$), 8.10 (t, $^4J_{i,j} = 1.9$ Hz, 1H, H_i), 8.05 (s, 2H, $2 \times H_h$), 7.91 (s, 2H, $2 \times H_d$), 7.84 (t, $^4J_{b,c} = 1.5$ Hz, 1H, H_c), 7.36 (dd, $J_{a,b} = 7.7$ Hz, $^4J_{b,c} = 1.5$ Hz, 2H, $2 \times H_b$), 7.20 (t, $J_{a,b} = 7.7$ Hz, H_a), 4.58–4.64 (m, 8H, $4 \times H_e$, $4 \times H_g$), 2.66–2.76 (m, 4H, $4 \times H_f$). ^{13}C NMR (d_6 -DMSO): 146.0, 144.8, 143.2, 130.6, 128.7, 128.3, 126.2, 124.0, 121.6, 121.3, 120.9, 48.8, 48.6, 28.8. HRESI-MS (pos.): 528.2081, calc. for $[\text{C}_{25}\text{H}_{23}\text{N}_{13}\cdot\text{Na}]^+ = 528.2092$.

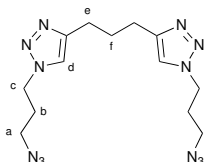
Bis-triazole tosylate **75**



1,6-Heptadiyne (0.103 mL, 0.083 g, 0.90 mmol) and tosyl-protected azide **75** (0.482 g, 1.89 mmol, 2.1 equiv) were dissolved in dry CH_2Cl_2 (25 mL). DIPEA (0.35 mL, 0.26 g, 2.00 mmol), TBTA (0.096 g, 0.18 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4(\text{PF}_6)]$ (0.067 g, 0.18 mmol) were added and the resulting pale yellow solution stirred at room temperature under a nitrogen atmosphere for 16 hours. It was taken to dryness under reduced pressure and purified by column chromatography (2% CH_3OH in CHCl_3) to give **75** as a yellow oil. This was used immediately to prepare **76**.

^1H NMR (CDCl_3): 7.75–7.79 (m, 4H, $4 \times H_c$), 7.33–7.37 (m, 4H, $4 \times H_b$), 7.29 (s, 2H, $2 \times H_g$), 4.40 (t, $J_{e,f} = 6.7$ Hz, 4H, $4 \times H_f$), 4.00 (t, $J_{d,e} = 5.7$ Hz, 4H, $4 \times H_d$), 2.73 (t, $J_{h,i} = 7.5$ Hz, 4H, $4 \times H_h$), 2.44 (s, 6H, $6 \times H_a$), 2.23–2.32 (m, 4H, $4 \times H_e$), 1.97–2.07 (m, 2H, $2 \times H_i$). ^{13}C NMR (CDCl_3): 147.6, 145.4, 132.6, 130.2, 128.1, 121.8, 66.8, 46.1, 29.7, 29.1, 24.9, 21.8. LRESI-MS (pos.): 625.23, calc. for $[\text{C}_{27}\text{H}_{34}\text{N}_6\text{O}_6\text{S}_2\cdot\text{Na}]^+ = 625.19$.

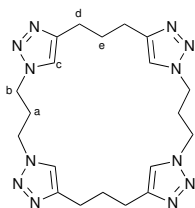
Bis-triazole azide **76**



The ditosylate **75** (all of previous reaction) was dissolved in DMSO (10 mL). NaN_3 (0.234 g, 3.60 mmol) was added and the mixture heated at 60 °C under a nitrogen atmosphere over the weekend. It was cooled to room temperature, and partitioned between H_2O and Et_2O (100 mL each). The organic layer was taken and the aqueous layer extracted further with Et_2O (100 mL). The combined organic fractions were dried (MgSO_4), taken to dryness under reduced pressure and purified by column chromatography (1.5% CH_3OH in CH_2Cl_2) to give **76** as a pale yellow oil. Yield: 0.093 g (30% over 2 steps from 1,6-heptadiyne).

^1H NMR (CDCl_3): 7.37 (s, 2H, $2 \times H_d$), 4.47 (t, $J_{b,c} = 6.6$ Hz, 4H, $4 \times H_c$), 3.41 (t, $J_{a,b} = 6.4$ Hz, 4H, $4 \times H_a$), 2.73 (t, $J_{e,f} = 8.8$ Hz, 4H, $4 \times H_e$), 1.95–2.25 (m, 6H, $4 \times H_b$, $2 \times H_f$). ^{13}C NMR (CDCl_3): 147.8, 121.5, 48.2, 47.1, 29.6, 29.2, 25.0. HRESI-MS (pos.): 367.1826, calc. for $[\text{C}_{13}\text{H}_{20}\text{N}_{12}\cdot\text{Na}]^+ = 367.1826$.

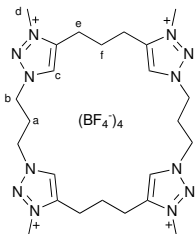
Propyl tetra-triazole macrocycle **71**



The bis-azide **76** (0.069 g, 0.20 mmol) and 1,6-heptadiyne (0.023 mL, 0.018 g, 0.20 mmol) were dissolved in CH_2Cl_2 (200 mL). DIPEA (0.035 mL, 0.026 g, 0.20 mmol), TBTA (0.021 g, 0.040 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.015 g, 0.040 mmol) were added and the yellow solution stirred at room temperature under a nitrogen atmosphere for 3 days. It was concentrated to ~ 50 mL under reduced pressure and filtered, with the precipitate washed thoroughly with 10% CH_3OH in CH_2Cl_2 . The combined filtrates were taken to dryness under reduced pressure and purified by column chromatography (5–15% CH_3OH in CHCl_3) to give **71** as a white powder. Yield: 0.043 g (49%).

^1H NMR (CDCl_3): 7.41 (s, 4H, $4 \times H_c$), 4.29 (t, $J_{a,b} = 6.2$ Hz, 8H, $8 \times H_b$), 2.64–2.73 (m, 12H, $4 \times H_a$, $8 \times H_d$), 2.09 (qn, $J_{d,e} = 6.9$ Hz, 4H, $4 \times H_e$). ^{13}C NMR (CDCl_3): 147.3, 122.9, 46.5, 29.5, 28.3, 23.9. HRESI-MS (pos.): 459.2455, calc. for $[\text{C}_{20}\text{H}_{28}\text{N}_{12} \cdot \text{Na}]^+ = 459.2452$.

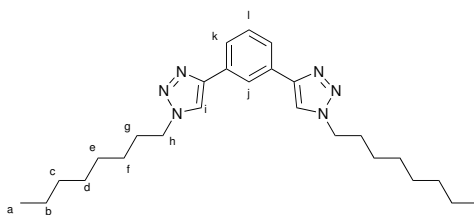
Propyl tetra-triazolium macrocycle **77**·(BF_4)₄



The neutral macrocycle **71** (0.022 g, 0.050 mmol) was dissolved in dry CH_2Cl_2 (20 mL). $(\text{Me}_3\text{O})(\text{BF}_4)$ (0.037 g, 0.25 mmol) was added and the mixture stirred at room temperature under a nitrogen atmosphere for 2 days. CH_3OH (1 mL) was added and the solution taken to dryness under reduced pressure. The crude solid was stirred in CH_2Cl_2 (15 mL); the supernatant fluid was decanted and the resulting white powder washed with further CH_2Cl_2 (10 mL). The solid was recrystallized from boiling 6:1 $\text{EtOH}:\text{CH}_3\text{CN}$ to give **77**·(BF_4)₄ as large white needles. Yield: 0.023 g (54%).

^1H NMR (d_6 -DMSO): 8.47 (s, 4H, $4 \times H_c$), 4.69 (t, $J_{a,b} = 7.0$ Hz, 8H, $8 \times H_b$), 4.22 (s, 12H, $12 \times H_d$), 2.96 (t, $J_{e,f} = 7.0$ Hz, 8H, $8 \times H_e$), 2.48–2.54 (m, obscured by residual DMSO solvent peak, $4 \times H_a$), 2.02–2.08 (m, 4H, $4 \times H_f$). ^{13}C NMR (d_6 -DMSO): 143.8, 128.0, 49.5, 37.5, 28.8, 23.8, 21.6. ^{19}F NMR (d_6 -DMSO): -148.4 (m). HRESI-MS (pos.): 757.3593, calc. for $[\text{C}_{24}\text{H}_{40}\text{N}_{12} \cdot 3(\text{BF}_4)]^+ = 757.3581$.

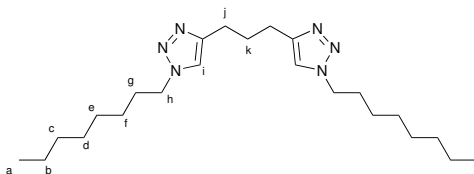
Bis-triazole precursor 81



Diethynylbenzene (0.133 mL, 0.126 g, 1.00 mmol) and octyl azide (0.342 g, 2.20 mmol) were dissolved in CH_2Cl_2 (30 mL). DIPEA (0.51 mL, 0.39 g, 3.0 mmol), TBTA (0.12 g, 0.22 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.075 g, 0.20 mmol) were added and the reaction stirred under a nitrogen atmosphere for 4 days. The reaction was taken to dryness under reduced pressure and then purified by column chromatography (gradient: 0–6% acetone in CH_2Cl_2) to give **81** as a white powder. Yield: 0.329 g (75%).

^1H NMR (d_6 -acetone): 8.44 (s, 2H, $2 \times H_i$), 8.43 (t, $^4J_{j,k} = 1.7$ Hz, 1H, H_j), 7.84 (dd, $J_{k,l} = 7.9$ Hz, $^4J_{j,k} = 1.7$ Hz, 2H, $2 \times H_k$), 7.49 (t, $J_{k,l} = 7.9$ Hz, 1H, H_l), 4.48 (t, $J_{g,h} = 7.1$ Hz, 4H, $4 \times H_h$), 1.99–? (obscured by residual acetone solvent peak, $4 \times H_g$), 1.24–1.41 (m, 20H, $4 \times H_b$, $4 \times H_c$, $4 \times H_d$, $4 \times H_e$, $4 \times H_f$), 0.86 (t, $J_{a,b} = 6.8$ Hz, 6H, $6 \times H_a$). ^{13}C NMR (CDCl_3): 147.5, 131.4, 129.5, 125.3, 122.9, 119.9, 50.6, 31.8, 30.5, 29.2, 29.1, 26.6, 22.7, 14.2. HRESI-MS (pos.): 459.3216, calc. for $[\text{C}_{26}\text{H}_{40}\text{N}_6\cdot\text{Na}]^+ = 459.3207$

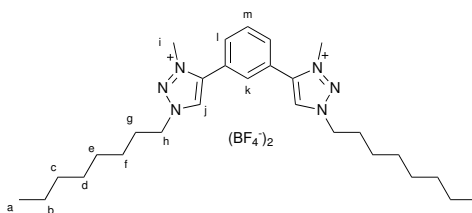
Bis-triazole precursor 82



1,6-Heptadiyne (0.11 mL, 0.092 g, 1.00 mmol) and octyl azide (0.342 g, 2.20 mmol) were dissolved in dry CH_2Cl_2 (30 mL). TBTA (0.234 g, 0.440 mmol), DIPEA (0.51 mL, 0.39 g, 3.00 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.15 g, 0.40 mmol) were added and the mixture stirred at room temperature under a nitrogen atmosphere for 6 days. It was stirred vigorously with aqueous NH_4OH /EDTA (20 mL) and the aqueous layer extracted with CH_2Cl_2 (20 mL). The combined organic layers were washed with H_2O (2×30 mL), dried (MgSO_4) and taken to dryness. Column chromatography (3:2 acetone:petrol) gave **82** as a white powder. Yield: 0.299 g (74%).

^1H NMR (CDCl_3): 7.31 (s, 2H, $2 \times H_i$), 4.30 (t, $J_{g,h} = 7.3$ Hz, 4H, $4 \times H_h$), 2.77 (t, $J_{j,k} = 7.5$ Hz, 4H, $4 \times H_j$), 2.00–2.10 (m, 4H, $4 \times H_g$), 1.87 (qn, $J_{j,k} = 7.5$ Hz, 2H, $2 \times H_k$), 1.20–1.37 (m, 20H, $4 \times H_b$, $4 \times H_c$, $4 \times H_d$, $4 \times H_e$, $4 \times H_f$), 0.86 (t, $J_{a,b} = 6.7$ Hz, 6H, $6 \times H_a$). ^{13}C NMR (CDCl_3): 147.5, 120.8, 50.3, 31.8, 30.4, 29.3, 29.1, 29.0, 26.6, 25.0, 22.7, 14.1. HRESI-MS (pos.): 425.3366, calc. for $[\text{C}_{23}\text{H}_{42}\text{N}_6\cdot\text{Na}]^+ = 425.3363$.

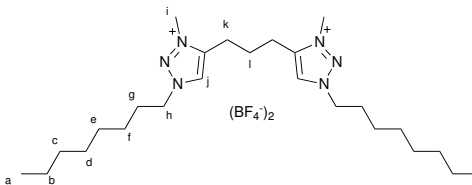
Bis-triazolium threading component **79**·(BF₄)₂



The bis(triazole) thread **81** (0.175 g, 0.400 mmol) was dissolved in dry CH₂Cl₂ (30 mL). (Me₃O)(BF₄) (0.129 g, 0.88 mmol) was added and the reaction stirred under a nitrogen atmosphere for 4 days. It was quenched by the addition of CH₃OH (1 mL), and taken to dryness under reduced pressure. Preparative TLC (4% CH₃OH in CH₂Cl₂) gave **79**·(BF₄)₂ as a white powder. Yield: 0.168 g (66%).

¹H NMR (d₆-acetone): 9.00 (s, 2H, 2 × *H_j*), 8.21 (t, ⁴*J_{k,l}* = 1.5 Hz, 1H, *H_k*), 8.09 (dd, *J_{l,m}* = 7.9 Hz, ⁴*J_{k,l}* = 1.5 Hz, 2H, 2 × *H_l*), 7.91 (t, *J_{l,m}* = 7.9 Hz, 1H, *H_m*), 4.76 (t, *J_{g,h}* = 7.3 Hz, 4H, 4 × *H_h*), 4.43 (s, 6H, 6 × *H_i*), 2.07–2.16 (m, 4H, 4 × *H_g*), 1.29–1.52 (m, 20H, 4 × *H_b*, 4 × *H_c*, 4 × *H_d*, 4 × *H_e*, 4 × *H_f*), 0.88 (t, *J_{a,b}* = 6.8 Hz, 6H, 6 × *H_a*). ¹³C NMR (CDCl₃): 141.9, 132.4, 131.0, 130.6, 129.2, 123.8, 54.5, 38.9, 31.8, 29.1, 29.1, 28.9, 26.3, 22.7, 14.2. ¹⁹F NMR (d₆-acetone): –151.5 (m). HRESI-MS (pos.): 233.1887, calc. for [C₂₈H₄₆N₆]²⁺ = 233.1886.

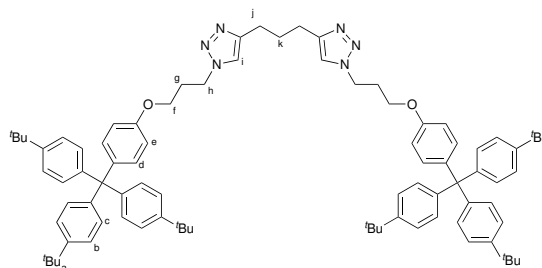
Bis-triazolium threading component **80**·(BF₄)₂



The bis(triazole) thread **82** (0.201 g, 0.500 mmol) was dissolved in dry CH₂Cl₂ (40 mL). (Me₃O)(BF₄) (0.221 g, 1.50 mmol) was added and the reaction stirred at room temperature under a nitrogen atmosphere for 2 days. CH₃OH (1 mL) was added, and the reaction taken to dryness under reduced pressure. Purification by preparative TLC (10% CH₃OH in CH₂Cl₂) gave **80**·(BF₄)₂ as a pale yellow oil. Yield: 0.158 g (52%).

¹H NMR (d₆-acetone): 8.80 (s, 2H, 2 × *H_j*), 4.71 (t, *J_{g,h}* = 7.3 Hz, 4H, 4 × *H_h*), 4.38 (s, 6H, 6 × *H_i*), 3.22 (t, *J_{k,l}* = 7.8 Hz, 4H, 4 × *H_k*), 2.32–2.38 (m, 4H, 4 × *H_g*), 2.17 (qn, *J_{k,l}* = 7.8 Hz, 2H, 2 × *H_l*), 1.22–1.43 (m, 20H, 4 × *H_b*, 4 × *H_c*, 4 × *H_d*, 4 × *H_e*, 4 × *H_f*), 0.86 (t, *J_{a,b}* = 7.0 Hz, 6H, 6 × *H_a*). ¹³C NMR (CDCl₃): 143.9, 128.5, 54.1, 37.6, 31.8, 29.2, 29.0, 28.9, 26.2, 23.8, 22.7, 22.0, 14.2. ¹⁹F NMR (d₆-acetone): –151.4 (m). HRESI-MS (pos.): 519.3969, calc. for [C₂₅H₄₈N₆·BF₄]⁺ = 519.3964.

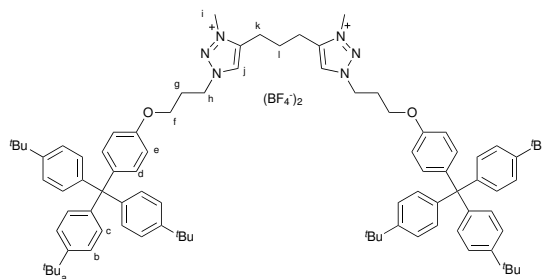
Bis-triazole axle component **84**



1,6-Heptadiyne (0.057 mL, 0.046 g, 0.50 mmol) and azide **83** (0.647 g, 1.10 mmol) were dissolved in dry CH_2Cl_2 (40 mL). TBTA (0.318 g, 0.600 mmol), DIPEA (0.27 mL, 0.19 g, 1.5 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.205 g, 0.550 mmol) were added and the resulting solution stirred under a nitrogen atmosphere for 4 days. The solvent was removed under reduced pressure, and the resulting off-white solid purified by column chromatography (2% CH_3OH in CH_2Cl_2) to give **84** as a white powder. Yield: 0.547 g (86%).

^1H NMR (d_6 -acetone): 7.73 (s, 2H, $2 \times H_i$), 7.31–7.34 (m, 12H, $12 \times H_c$), 7.09–7.15 (m, 16H, $12 \times H_b$, $4 \times H_d$), 6.81–6.85 (m, 4H, $4 \times H_e$), 4.57 (t, $J_{g,h} = 6.9$ Hz, 4H, $4 \times H_h$), 3.99 (t, $J_{f,g} = 6.0$ Hz, 4H, $4 \times H_f$), 2.68 (t, $J_{j,k} = 6.9$ Hz, 4H, $4 \times H_j$), 2.32–2.37 (m, 4H, $4 \times H_g$), 1.96 (qn, $J_{j,k} = 6.9$ Hz, 2H, $2 \times H_k$). ^{13}C NMR (CDCl_3): 156.4, 148.5, 144.2, 140.2, 132.5, 130.8, 129.2, 124.2, 113.0, 64.1, 63.2, 47.1, 34.4, 31.5, 30.2, 29.2, 25.0 (*one resonance not observed*). HRESI-MS (pos.): 1267.8429, calc. for $[\text{C}_{87}\text{H}_{106}\text{O}_2\text{N}_6 \cdot \text{H}]^+ = 1267.8450$.

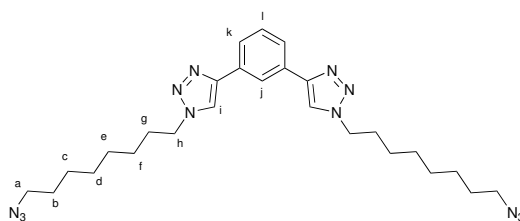
Bis-triazolium axle component **85**·(BF_4)₂



The axle component **84** (0.254 g, 0.200 mmol) was dissolved in dry CH_2Cl_2 (40 mL). $(\text{Me}_3\text{O})(\text{BF}_4)$ (0.074 g, 0.50 mmol) was added and the reaction mixture stirred at room temperature under a nitrogen atmosphere for 16 hours. The reaction was quenched by the addition of CH_3OH (1 mL), taken to dryness and purified by preparative TLC (89:10:1 CH_2Cl_2 : CH_3OH : $\text{NH}_4\text{OH}_{(\text{aq})}$) to give the bis(triazolium) axle **85**·(BF_4)₂ as a white powder. Yield: 0.188 g (64%).

^1H NMR (d_6 -acetone): 8.84 (s, 2H, $2 \times H_j$), 7.32–7.36 (m, 12H, $12 \times H_c$), 7.12–7.16 (m, 16H, $12 \times H_b$, $4 \times H_d$), 6.82–6.84 (m, 4H, $4 \times H_e$), 4.94 (t, $J_{g,h} = 7.0$ Hz, 4H, $4 \times H_h$), 4.32 (s, 6H, $6 \times H_i$), 4.14 (t, $J_{f,g} = 5.8$ Hz, 4H, $4 \times H_f$), 3.23 (t, $J_{k,l} = 7.7$ Hz, 4H, $4 \times H_k$), 2.51–2.56 (m, 4H, $4 \times H_g$), 2.39 (qn, $J_{k,l} = 7.7$ Hz, 2H, $2 \times H_l$), 1.29 (s, 54H, $54 \times H_a$). ^{13}C NMR (d_6 -DMSO): 155.8, 147.8, 143.9, 143.1, 139.3, 131.5, 130.0, 128.5, 124.2, 113.3, 64.1, 62.6, 50.7, 37.4, 34.1, 31.2, 28.5, 23.5, 21.6. ^{19}F NMR (CDCl_3): −151.7 (m). HRESI-MS (pos.): 1383.8914, calc. for $[\text{C}_{89}\text{H}_{112}\text{N}_6\text{O}_2 \cdot \text{BF}_4]^+ = 1383.8884$.

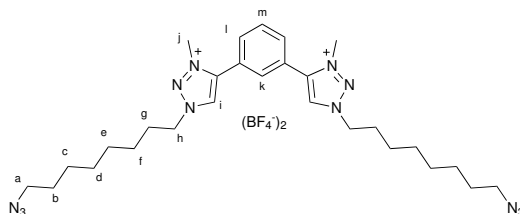
Azide-appended bis-triazole precursor **89**



1,8-Diazidooctane (1.37 g, 7.00 mmol) and 1,3-diethynylbenzene (0.093 mL, 0.088 g, 0.70 mmol) were dissolved in CH_2Cl_2 (50 mL). DIPEA (0.25 mL, 0.18 g, 1.4 mmol), TBTA (0.074 g, 0.14 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.052 g, 0.14 mmol) were added and the resulting yellow solution stirred at room temperature under a nitrogen atmosphere for 16 hours. It was carefully concentrated under reduced pressure and then purified by column chromatography (2% CH_3OH in CHCl_3) to give **89** (0.24 g, 66%) as a slightly off-white waxy solid.

^1H NMR (CDCl_3): 8.30 (t, $^4J_{j,k} = 1.6$ Hz, 1H, H_j), 7.85 (s, 2H, $2 \times H_i$), 7.83 (dd, $J_{k,l} = 7.7$ Hz, $^4J_{j,k} = 1.6$ Hz, 2H, $2 \times H_k$), 7.49 (t, $J_{k,l} = 7.7$ Hz, 1H, H_l), 4.42 (t, $J_{g,h} = 7.1$ Hz, 4H, $4 \times H_h$), 3.25 (t, $J_{a,b} = 6.9$ Hz, 4H, $4 \times H_a$), 1.92–2.01 (m, 4H, $4 \times H_g$), 1.54–1.63 (m, 4H, $4 \times H_b$), 1.30–1.41 (m, 16H, $4 \times H_c$, $4 \times H_d$, $4 \times H_e$, $4 \times H_f$). ^{13}C NMR (CDCl_3): 147.4, 131.3, 129.5, 125.3, 122.8, 119.9, 51.4, 50.5, 30.3, 28.9, 28.9, 28.8, 26.6, 26.4. HRESI-MS (pos.): 541.3235, calc. for $[\text{C}_{26}\text{H}_{38}\text{N}_{12} \cdot \text{Na}]^+ = 541.3235$.

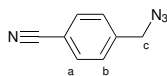
Azide-appended bis-triazolium threading component **90**·(BF_4)₂



The bis(triazole) thread **89** (0.156 g, 0.300 mmol) was dissolved in dry CH_2Cl_2 (25 mL). $(\text{Me}_3\text{O})(\text{BF}_4)$ (0.097 g, 0.66 mmol) was added and the mixture stirred at room temperature under a nitrogen atmosphere over the weekend. The reaction was quenched by the addition of CH_3OH (1 mL), and then taken to dryness under reduced pressure. Purification by preparative TLC (10% CH_3OH in CH_2Cl_2) gave **90**·(BF_4)₂ as a very pale yellow oil. Yield: 0.163 g (75%).

^1H NMR (d_6 -acetone): 9.11 (s, 2H, $2 \times H_i$), 8.30 (s, 1H, H_k), 8.13 (d, $J_{l,m} = 8.3$ Hz, 2H, $2 \times H_l$), 7.98 (t, $J_{l,m} = 8.3$ Hz, 1H, H_m), 4.83 (t, $J_{g,h} = 7.3$ Hz, 4H, $4 \times H_h$), 4.50 (s, 6H, $6 \times H_j$), 3.32 (t, $J_{a,b} = 6.9$ Hz, 4H, $4 \times H_a$), 2.10–2.19 (m, 4H, $4 \times H_g$), 1.55–1.63 (m, 4H, $4 \times H_b$), 1.34–1.51 (m, 16H, $4 \times H_c$, $4 \times H_d$, $4 \times H_e$, $4 \times H_f$). ^{13}C NMR (CDCl_3): 141.8, 132.3, 130.8, 130.5, 129.0, 123.7, 54.2, 51.3, 38.7, 28.9, 28.7, 28.6, 26.5, 25.9 (one resonance not observed). ^{19}F NMR (d_6 -acetone): −151.4 (m). HRESI-MS (pos.): 274.1903, calc. for $[\text{C}_{28}\text{H}_{44}\text{N}_{12}]^{2+} = 274.1900$.

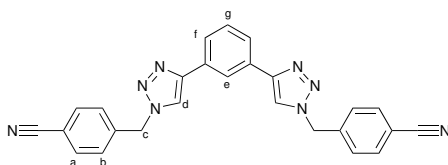
4-Cyanobenzyl azide **93**



NaN₃ (0.715 g, 11.0 mmol) was added to a solution of 4-cyanobenzyl bromide (1.96 g, 10.0 mmol) in DMSO (22 mL) and the colourless solution stirred at room temperature under a nitrogen atmosphere for 5 hours. Water (100 mL) was added and the solution extracted with Et₂O (100 mL, then 50 mL). The combined organic phases were washed with H₂O (2 × 100 mL), brine (100 mL), dried (MgSO₄) and taken to dryness under reduced pressure to give **93** as a colourless oil. Yield: 1.54 g (97%).

¹H NMR (CDCl₃): 7.68 (d, *J*_{a,b} = 8.5 Hz, 2H, 2 × *H*_a), 7.43 (d, *J*_{a,b} = 8.5 Hz, 2H, 2 × *H*_b), 4.45 (s, 2H, 2 × *H*_c). ¹³C NMR (CDCl₃): 141.0, 132.8, 128.7, 118.6, 112.4, 54.2.

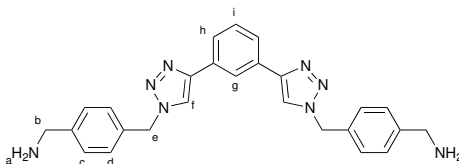
Bis-triazole bis-nitrile **94**



To a solution of 1,3-diethynylbenzene (0.598 mL, 0.568 g, 4.50 mmol) and 4-cyanobenzyl azide (1.50 g, 9.50 mmol) in CH₂Cl₂ (30 mL) was added DIPEA (0.80 mL, 0.58 g, 4.5 mmol), TBTA (0.239 g, 0.450 mmol) and [Cu(CH₃CN)₄](PF₆) (0.168 g, 0.450 mmol), and the resulting solution stirred at room temperature under a nitrogen atmosphere for 3 days. It was taken to dryness under reduced pressure and purified by column chromatography (3% CH₃OH in CHCl₃) to give **94** as a white powder. Yield: 1.84 g (93%).

¹H NMR (CDCl₃): 8.26 (t, ⁴*J*_{e,f} = 1.7 Hz, 1H, *H*_e), 7.78–7.81 (m, 4H, 2 × *H*_d, 2 × *H*_f), 7.69 (d, *J*_{a,b} = 8.2 Hz, 4H, 4 × *H*_a), 7.47 (t, *J*_{f,g} = 7.8 Hz, 1H, *H*_g), 7.40 (d, *J*_{a,b} = 8.2 Hz, 4H, 4 × *H*_b), 5.66 (s, 4H, 4 × *H*_c). ¹³C NMR (CDCl₃): 148.3, 139.9, 133.1, 130.9, 129.7, 128.6, 125.8, 123.1, 120.1, 118.2, 113.1, 53.7. HRESI-MS (pos.): 465.1536, calc. for [C₂₆H₁₈N₈·Na]⁺ = 465.1547.

Bis-triazole bis-amine **95**

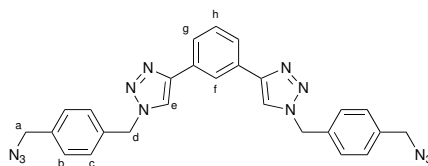


The nitrile **94** (0.442 g, 1.00 mmol) was suspended in dry THF (15 mL). A solution of borane in THF (1.0 M, 5 mL) was added dropwise and the suspension heated to reflux under a nitrogen atmosphere for 3 hours, during which time all material dissolved and then a white precipitate developed. The suspension was cooled to 0 °C and CH₃OH (5 mL) added dropwise to quench unreacted borane. The suspension was reduced in volume to ~ 5 mL and then 20 mL H₂O added.

The gummy white solid was isolated by filtration. ^1H NMR analysis at this point showed that the product contained several impurities, however due to its low solubility, it could not be effectively purified at this point, and so was immediately reacted on to prepare **96**.

^1H NMR ($\text{d}_6\text{-DMSO}$): 8.67 (s, 2H, $2 \times H_f$), 8.32 (t, $^4J_{g,h} = 1.5$ Hz, 1H, H_g), 7.79 (dd, $J_{h,i} = 7.8$ Hz, $^4J_{g,h} = 1.5$ Hz, 2H, $2 \times H_h$), 7.49 (t, $J_{h,i} = 7.8$ Hz, 1H, H_i), 7.29–7.36 (m, 8H, $4 \times H_c$, $4 \times H_d$), 5.62 (s, 4H, $4 \times H_e$), 3.69 (s, 4H, $4 \times H_b$). ^{13}C NMR ($\text{d}_6\text{-DMSO}$): 146.4, 144.0, 133.8, 131.3, 129.5, 127.9, 127.5, 124.6, 121.7, 109.5, 53.0, 45.2. HRESI-MS (pos.): 451.2359, calc. for $[\text{C}_{26}\text{H}_{26}\text{N}_8\cdot\text{H}]^+ = 451.2353$.

Bis-triazole bis-azide **96**



Method A:

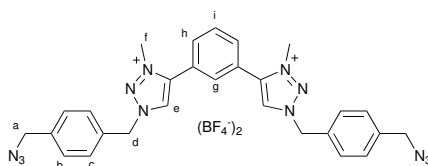
The amine **95** (all of the previous reaction) was suspended in CH_3OH (50 mL). Imidazolesulfonyl azide-HCl (0.503 g, 2.40 mmol), K_2CO_3 (0.699 g, 5.00 mmol) and $\text{CuSO}_4\cdot 5\text{H}_2\text{O}$ (0.012 g, 0.050 mmol) were added and the reaction stirred at room temperature under a nitrogen atmosphere for 7 days. It was concentrated to ~ 5 mL under reduced pressure, diluted with $\text{HCl}_{(\text{aq})}$ (1 M, 50 mL) and extracted with EtOAc (3×30 mL). The combined organic fractions were washed with brine (50 mL), dried (MgSO_4) and taken to dryness under reduced pressure. Column chromatography (3% CH_3OH in CHCl_3) followed by preparative TLC (3% CH_3OH in CH_2Cl_2) gave **96** as a white powder. Yield: 0.062 g (12% from **94**).

Method B:

To a solution of 1,3-diethynylbenzene (0.067 mL, 0.063 g, 0.50 mmol) and 1,4-bis(azidomethyl)benzene (1.41 g, 7.50 mmol) in CH_2Cl_2 (50 mL) was added DIPEA (0.27 mL, 0.19 g, 1.5 mmol), TBTA (0.053 g, 0.10 mmol) and $[\text{Cu}(\text{CH}_3\text{CN})_4](\text{PF}_6)$ (0.037 g, 0.10 mmol). The solution was stirred at room temperature under a nitrogen atmosphere for 6 days, taken to dryness under reduced pressure and purified by column chromatography (1% CH_3OH in CHCl_3) to give **96** as a white powder. Yield: 0.20 g (78%).

^1H NMR (CDCl_3): 8.19 (t, $^4J_{f,g} = 1.7$ Hz, 1H, H_f), 7.78 (dd, $J_{g,h} = 7.7$ Hz, $^4J_{f,g} = 1.7$ Hz, 2H, $2 \times H_g$), 7.74 (s, 2H, $2 \times H_e$), 7.44 (t, $J_{g,h} = 7.7$ Hz, 1H, H_h), 7.31–7.37 (m, 8H, $4 \times H_b$, $4 \times H_c$), 5.58 (s, 4H, $4 \times H_d$), 4.36 (s, 4H, $4 \times H_a$). ^{13}C NMR (CDCl_3): 148.0, 136.4, 134.8, 131.1, 129.6, 129.1, 128.7, 125.5, 123.0, 120.0, 54.4, 54.0. HRESI-MS (pos.): 525.1988, calc. for $[\text{C}_{26}\text{H}_{22}\text{N}_{12}\cdot\text{Na}]^+ = 525.1983$.

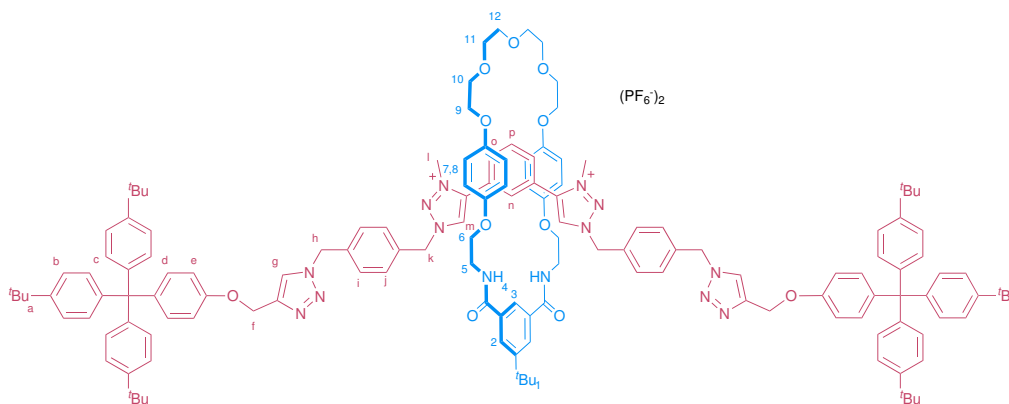
Azide-appended bis-triazolium threading component **92**·(BF₄)₂



The bis-azide **96** (0.101 g, 0.200 mmol) was dissolved in dry CH₂Cl₂ (10 mL). (Me₃O)(BF₄) (0.065 g, 0.44 mmol) was added and the reaction stirred at room temperature under a nitrogen atmosphere for 16 hours. CH₃OH (1 mL) was added, and the reaction taken to dryness under reduced pressure. Purification by preparative TLC (10% CH₃OH in CH₂Cl₂) gave **92**·(BF₄)₂ as a pale yellow foam. Yield: 0.113 g (80%).

¹H NMR (d₆-acetone): 9.11 (s, 2H, 2 × *H_e*), 8.23 (t, ⁴*J_{g,h}* = 1.6 Hz, 1H, *H_g*), 8.09 (dd, *J_{h,i}* = 7.8 Hz, ⁴*J_{g,h}* = 1.6 Hz, 2H, 2 × *H_h*), 7.92 (t, *J_{h,i}* = 7.8 Hz, 1H, *H_i*), 7.67 (d, *J_{b,c}* = 8.2 Hz, 4H, 4 × *H_c*), 7.50 (d, *J_{b,c}* = 8.2 Hz, 4H, 4 × *H_b*), 6.03 (s, 4H, 4 × *H_d*), 4.51 (s, 4H, 4 × *H_a*), 4.46 (s, 6H, 6 × *H_f*). ¹³C NMR (CDCl₃): 143.2, 138.5, 133.5, 133.3, 131.7, 131.5, 130.6, 130.3, 130.0, 125.1, 57.6, 54.5, 39.6. ¹⁹F NMR (d₆-acetone): -151.4 (m). HRESI-MS (pos.): 619.2591, calc. for [C₂₈H₂₈N₁₂·BF₄]⁺ = 619.2584.

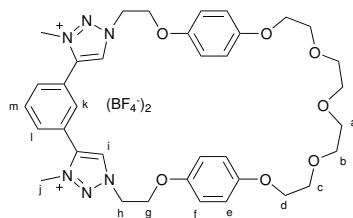
Bis-triazolium rotaxane **97**·(PF₆)₂



The bis-triazolium threading component **92**·BF₄ (0.03 g, 0.050 mmol) and macrocycle **16** (0.033 g, 0.050 mmol) were dissolved in dry CH₂Cl₂ (50 mL). TBA·Cl (0.014 g, 0.050 mmol) was added, followed by alkyne **49** (0.060 g, 0.11 mmol), DIPEA (0.017 mL, 0.013 g, 0.1 mmol), TBTA (0.0053 g, 0.010 mmol) and [Cu(CH₃CN)₄](PF₆) (0.0037 g, 0.010 mmol), and the clear yellow solution stirred at room temperature under a nitrogen atmosphere for 7 days. It was taken to dryness under reduced pressure and purified by preparative TLC (6% CH₃OH in CH₂Cl₂) to give essentially pure rotaxane. This was taken up in CH₂Cl₂ (10 mL), and stirred vigorously with NH₄PF₆(aq) (0.1 M, 10 mL) for 30 minutes. The organic phase was taken and washed with further NH₄PF₆(aq) (0.1 M, 6 × 10 mL) and H₂O (3 × 10 mL) and then thoroughly dried *in vacuo*. The white powder was dissolved in hot CH₃OH:CH₂Cl₂ (19:1, 20 mL), and the volume of the solution reduced to ~ 10 mL by boiling. Cooling the solution caused precipitation of **97**·(PF₆)₂ as a white powder. Yield: 0.026 g (20%).

^1H NMR (1:1 $\text{CDCl}_3\text{:CD}_3\text{OD}$): 8.85 (s, 2H, $2 \times H_m$), 8.13 (br. s, 1H, H_n), 8.10 (d, $^4J_{o,p} = 1.5$ Hz, 2H, $2 \times H_o$), 7.85 (s, 2H, $2 \times H_g$), 7.73–7.80 (m, 3H, $2 \times H_2$, H_p), 7.47–7.51 (m, 5H, H_3 , $4 \times H_j$), 7.37 (d, $J_{i,j} = 8.2$ Hz, 4H, $4 \times H_i$), 7.17–7.20 (m, 12H, $12 \times H_b$), 7.01–7.05 (m, 16H, $12 \times H_c$, $4 \times H_d$), 6.72 (d, $J_{d,e} = 9.0$ Hz, 4H, $4 \times H_e$), 6.37 (d, $J_{7,8} = 9.1$ Hz, 4H, $4 \times H_{7/8}$), 6.05 (d, $J_{7,8} = 9.1$ Hz, 4H, $4 \times H_{7/8}$), 5.71 (s, 4H, $4 \times H_k$), 5.51 (s, 4H, $4 \times H_h$), 4.94 (s, 4H, $4 \times H_f$), 3.97–4.00 (m, 10H, $4 \times H_5$, $6 \times H_l$), 3.71 (t, $J_{9,10} = 4.8$ Hz, 4H, $4 \times H_9$), 3.36–3.50 (m, 16H, $4 \times H_6$, $4 \times H_{10}$, $4 \times H_{11}$, $4 \times H_{12}$), 1.26 (s, 54H, $54 \times H_a$). ^{13}C NMR (1:1 $\text{CDCl}_3\text{:CD}_3\text{OD}$): 169.1, 156.8, 153.7, 153.3, 152.9, 149.1, 145.0, 144.9, 142.3, 141.1, 137.8, 134.9, 133.0, 132.5, 131.5, 131.4, 131.3, 131.0, 130.4, 130.1, 129.9, 128.9, 125.0, 124.7, 124.3, 122.6, 115.8, 115.2, 113.9, 71.4, 71.1, 70.5, 68.3, 67.0, 63.8, 61.9, 57.7, 54.1, 40.6, 39.3, 35.7, 34.8, 31.7, 31.5. ^{19}F NMR (1:1 $\text{CDCl}_3\text{:CD}_3\text{OD}$): -71.6 (d, $J_{\text{P,F}} = 712$ Hz). ^{31}P NMR (1:1 $\text{CDCl}_3\text{:CD}_3\text{OD}$): -144.7 (septet, $J_{\text{P,F}} = 712$ Hz). HRESI-MS (pos.): 1133.6386, calc. for $[\text{C}_{144}\text{H}_{166}\text{N}_{14}\text{O}_{11}]^{2+} = 1133.6425$.

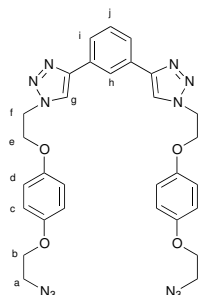
Bis-triazolium macrocycle **98**·(BF_4)₂



The neutral macrocycle **12** (0.193 g, 0.300 mmol) was dissolved in dry CH_2Cl_2 (40 mL) and $(\text{Me}_3\text{O})(\text{BF}_4)$ (0.098 g, 0.66 mmol) was added. This solution was stirred under a nitrogen atmosphere at room temperature for 16 hours. The reaction was quenched by addition of CH_3OH (1 mL), and taken to dryness under reduced pressure. The resulting crude solid was stirred for 2 hours in CH_2Cl_2 (10 mL), then filtered and washed with further CH_2Cl_2 (2 mL). Purification by recrystallization from hot 49:1 $\text{CHCl}_3\text{:CH}_3\text{OH}$ (50 mL) gave **98**·(BF_4)₂ as white crystals. Yield: 0.141 g (55%).

^1H NMR (CD_3CN): 8.67 (s, 2H, $2 \times H_i$), 7.88–7.91 (m, 2H, $2 \times H_l$), 7.74–7.75 (m, 1H, H_m), 7.59 (s, 1H, H_k), 6.80–6.88 (m, 8H, $4 \times H_e$, $4 \times H_f$), 5.00 (t, $J_{g,h} = 4.6$ Hz, 4H, $4 \times H_h$), 4.39 (t, $J_{g,h} = 4.6$ Hz, 4H, $4 \times H_g$), 4.22 (s, 6H, $6 \times H_j$), 3.98–4.01 (m, 4H, $4 \times H_d$), 3.71–3.74 (m, 4H, $4 \times H_c$), 3.54–3.61 (m, 8H, $4 \times H_a$, $4 \times H_b$). ^{13}C NMR (CD_3CN): 154.8; 152.8; 142.9; 133.5; 131.8; 130.8; 124.8; 116.7; 116.3; 111.0; 71.4; 71.3; 70.4; 68.9; 66.7; 54.8; 39.7. ^{19}F NMR (CD_3CN): -151.5 (br. s). HRESI-MS (pos.): 759.3294, calc. for $[(\text{C}_{36}\text{H}_{44}\text{N}_6\text{O}_7) \cdot (\text{BF}_4)]^+ = 759.3301$.

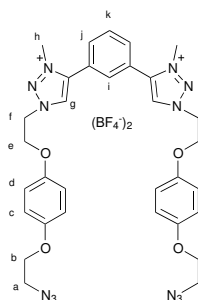
Azide-appended bis-triazole macrocycle precursor **103**



The bis-azide **102** (7.45 g, 30.0 mmol) and 1,3-diethynylbenzene (0.319 mL, 0.303 g, 2.40 mmol) were dissolved in CH_2Cl_2 (75 mL). $[\text{Cu}(\text{PPh}_3)_3]\text{Br}$ (0.223 g, 0.240 mmol) was added and the yellow solution stirred at room temperature under a nitrogen atmosphere for 3 days. It was taken to dryness under reduced pressure and purified by column chromatography (gradient: 0–2% CH_3OH in CHCl_3) to give **103** as a slightly impure off-white solid, which was reacted on without further purification. Yield: 1.15 g (77%).

^1H NMR (CDCl_3): 8.29 (t, $^4J_{\text{h,i}} = 1.6$ Hz, 1H, H_{h}), 8.05 (s, 2H, $2 \times H_{\text{g}}$), 7.84 (dd, $J_{\text{i,j}} = 7.8$ Hz, $^4J_{\text{h,i}} = 1.6$ Hz, 2H, H_{i}), 7.50 (t, $J_{\text{i,j}} = 7.8$ Hz, 1H, H_{j}), 6.85 (app. s, 8H, $4 \times H_{\text{c}}$, $4 \times H_{\text{d}}$), 4.81 (t, $J_{\text{e,f}} = 4.8$ Hz, 4H, $4 \times H_{\text{f}}$), 4.37 (t, $J_{\text{e,f}} = 4.8$ Hz, 4H, $4 \times H_{\text{e}}$), 4.09 (t, $J_{\text{a,b}} = 5.1$ Hz, 4H, $4 \times H_{\text{b}}$), 3.56 (t, $J_{\text{a,b}} = 5.1$ Hz, 4H, $4 \times H_{\text{a}}$). ^{13}C NMR (CDCl_3): 153.3, 152.6, 147.7, 131.3, 129.6, 125.6, 123.1, 121.2, 115.9, 115.9, 67.7, 67.3, 50.3, 50.2. HRESI-MS (pos.): 645.2405, calc. for $[\text{C}_{30}\text{H}_{30}\text{N}_{12}\text{O}_4 \cdot \text{Na}]^+ = 645.2405$.

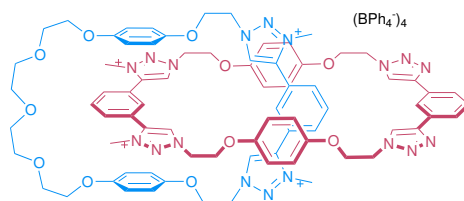
Azide-appended bis-triazolium macrocycle precursor **101**·(BF_4)₂



The bis-triazole bis-azide **103** (0.093 g, 0.15 mmol) was dissolved in dry CH_2Cl_2 (40 mL). $(\text{Me}_3\text{O})(\text{BF}_4)$ (0.049 g, 0.33 mmol) was added and the reaction stirred at room temperature under a nitrogen atmosphere for 16 hours. The reaction was quenched by the addition of CH_3OH (1 mL), taken to dryness under reduced pressure, and purified by preparative TLC (16:3:1 CH_2Cl_2 :acetone: CH_3OH) to give **101**·(BF_4)₂ as a waxy yellow solid. Yield: 0.090 g (72%).

^1H NMR (CD_3CN): 8.67 (s, 2H, $2 \times H_{\text{g}}$), 7.87–7.91 (m, 3H, H_{i} , $2 \times H_{\text{j}}$), 7.78–7.80 (m, 1H, H_{k}), 6.87–6.95 (m, 8H, $4 \times H_{\text{c}}$, $4 \times H_{\text{d}}$), 5.00 (t, $J_{\text{e,f}} = 4.8$ Hz, 4H, $4 \times H_{\text{f}}$), 4.45 (t, $J_{\text{e,f}} = 4.8$ Hz, 4H, $4 \times H_{\text{e}}$), 4.22 (s, 6H, $6 \times H_{\text{h}}$), 4.10 (t, $J_{\text{a,b}} = 5.1$ Hz, 4H, $4 \times H_{\text{b}}$), 3.56 (t, $J_{\text{a,b}} = 5.1$ Hz, 4H, $4 \times H_{\text{a}}$). ^{13}C NMR (CD_3CN): 154.3, 153.2, 142.9, 133.7, 131.8, 131.3, 130.7, 124.8, 116.9, 116.6, 68.6, 66.7, 54.7, 51.0, 39.6. ^{19}F NMR (CD_3CN): –151.6 (m). HRESI-MS (pos.): 362.1476, calc. for $[\text{C}_{32}\text{H}_{36}\text{N}_{12}\text{O}_4]^{2+} = 362.1486$.

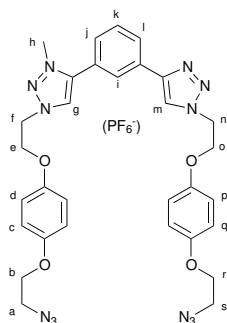
Tetra-triazolium catenane, **105**·(BPh₄)₄



The bis-triazolium macrocycle **98**·(BF₄)₂ (0.042 g, 0.050 mmol), bis-triazolium bis-azide precursor **101**·(BF₄)₂ (0.041 g, 0.050 mmol) and TBA₂·SO₄ (0.029 g, 0.050 mmol) were dissolved in dry CH₃CN (200 mL) and the solution stirred under a nitrogen atmosphere for 20 minutes. To this was added 1,3-diethynylbenzene (0.0063 g, 0.0067 mL, 0.050 mmol), DIPEA (0.0078 g, 0.010 mL, 0.0060 mmol), and TBTA (0.0021 g, 0.0040 mmol) and the solution deoxygenated with bubbling nitrogen for 2 minutes. [Cu(CH₃CN)₄](PF₆) (0.0015 g, 0.0040 mmol) was added and the solution stirred under a nitrogen atmosphere for 8 days. The reaction mixture was taken to dryness under reduced pressure, and purified by iterative preparative TLC (17:2:1 CH₃CN:H₂O:sat. aq. NaNO₃). The CH₃CN was removed under reduced pressure and the remaining solution stirred with NaBPh₄ (0.086 g, 0.25 mmol) in H₂O (1 mL). The resulting white precipitate was isolated by filtration and washed with cold H₂O (5 × 2 mL). The solid was dried thoroughly to give slightly impure **105**·(BPh₄)₄ as a white solid. Yield: 0.007 g (~ 5%).

¹H NMR (d₆-acetone): 9.07 (s, 2H), 8.95 (s, 2H), 8.47 (s, 2H), 8.27 (s, 1H), 7.94–8.01 (m, 2H), 7.85–7.87 (m, 2H), 7.77 (s, 1H); 7.68–7.70 (m, 2H), 7.60 (s, 1H); 7.53–7.55 (m, 2H), 7.47–7.51 (m, 1H), 7.32–7.41 (m, 33H), 6.92–6.95 (m, 24H), 6.77–6.87 (m, 16H), 6.55 (d, *J* = 9.1 Hz, 4H), 6.13 (d, *J* = 9.1 Hz, 4H), 5.02 (t, *J* = 4.7 Hz), 4.97 (t, *J* = 4.7 Hz), 4.82 (t, *J* = 4.7 Hz), 4.45 (t, *J* = 4.7 Hz), 4.39 (t, *J* = 4.7 Hz), 4.37 (t, *J* = 4.7 Hz), 4.17 (s, 6H), 4.13 (s, 6H), 3.39–3.58 (m, 16H). See Figure 5.28 for assignment of signals. HRESI-MS (pos.): 362.6665, calc. for [C₇₈H₈₆N₁₈O₁₁]⁴⁺ = 362.6675.

Azide-appended mono-triazolium macrocycle precursor **106**·PF₆



The bis-azide **103** (0.187 g, 0.300 mmol) was placed in a vial; dry CH₂Cl₂ (10 mL) and methyl iodide (1.9 mL, 4.2 g, 30 mmol) were added, the vial sealed and heated to 50 °C for 7 days. The reaction mixture was taken to dryness and purified by preparative TLC (5% CH₃OH in CH₂Cl₂) to give **106**·I. This was taken up in CH₂Cl₂ (10 mL) and stirred vigorously with NH₄PF₆(aq) (0.1 M, 10 mL) for half an hour. It was then washed with further NH₄PF₆(aq) (0.1 M, 4 × 10 mL), and H₂O (2 × 10 mL), and taken to dryness to give **106**·PF₆ as a waxy yellow solid. Yield: 0.063 g (27%).

¹H NMR (CDCl₃): 8.50 (s, 1H, *H_g*), 8.21 (s, 1H, *H_m*), 8.08–8.12 (m, 1H, *H_j*), 7.96 (app. t, ⁴*J_{i,j}* = ⁴*J_{i,l}* = 1.6 Hz, 1H, *H_i*), 7.52 (app. t, *J_{j,k}* = *J_{k,l}* = 7.8 Hz, 1H, *H_k*), 7.37–7.41 (m, 1H, *H_l*), 6.76–6.84 (m, 8H, 2 × *H_c*, 2 × *H_d*, 2 × *H_p*, 2 × *H_q*), 4.90 (t, *J_{e,f}* = 4.7 Hz, 2H, 2 × *H_f*), 4.71 (t, *J_{n,o}* = 5.0 Hz, 2H, 2 × *H_n*), 4.40 (t, *J_{e,f}* = 4.7 Hz, 2H, 2 × *H_e*), 4.30 (t, *J_{n,o}* = 5.0 Hz, 2H, 2 × *H_o*), 4.20 (s, 3H, 3 × *H_h*), 3.99–4.01 (m, 2 × *H_b*, 2 × *H_r*), 3.49–3.53 (m, 4H, 2 × *H_a*, 2 × *H_s*). ¹³C NMR (CDCl₃): 153.5, 153.1, 152.6, 152.0, 145.9, 143.4, 132.7, 130.4, 129.0, 128.1, 126.7, 122.4, 122.3, 116.1, 116.0, 115.9, 67.7, 66.9, 65.4, 53.9, 53.6, 50.3, 50.2, 38.7, 31.1 (*two resonances not observed*). ¹⁹F NMR (CDCl₃): -72.7 (d, *J_{P,F}* = 713 Hz). HRESI-MS (pos.): 637.2762, calc. for [C₃₁H₃₃N₁₂O₄]⁺ = 637.2742.

Chapter 7

Conclusions

Conclusions

Chapters Two and Three describe systems incorporating the *triazole* motif. The investigation of the anion recognition properties of simple acyclic phenyl-1,3-bis(triazole) and pyridinium-3,5-bis(triazole) receptors demonstrated that these triazole containing compounds displayed far weaker anion complexation than their pyridinium-3,5-bis(amide) analogues. Nevertheless, incorporation of the triazole motif into interpenetrated and interlocked structures gave rise to host molecules that exhibited comparable anion binding affinities to equivalent all-amide receptors, and importantly, offered superior selectivity properties.

These results suggested that the anion binding properties of an interlocked host depend on more than simply those of their components, a topic that was explored further in Chapter Four by the investigation of a series of closely related *triazolium* containing rotaxanes. It was found that by increasing the degree of preorganisation within the interlocked receptor, significant enhancements in anion recognition strength could be achieved.

The use of the triazolium heterocycle as a method of preparing highly charged anion receptors to function in aqueous media was explored in Chapter Five. A tetra-triazolium macrocycle was prepared and exhibited impressive anion recognition in competitive d_6 -DMSO/ D_2O mixtures, although a bis-triazolium rotaxane displayed surprisingly weak anion binding properties, which was attributed to the poorly preorganised nature of the interlocked host. Attempts to combine the *strength* of anion recognition provided by the tetra-triazolium motif with the *selectivity* of an interlocked receptor were hampered by difficulties in purifying highly charged systems.

Overall, the results described herein clearly demonstrate the significant effect that inter-component preorganisation can have on the anion recognition properties of an interlocked host, with these factors affecting both the strength and selectivity of anion binding.

Future research could investigate the recognition properties of the halogen bonding analogues of the systems reported in this work, with the aim of using the stringent linearity of halogen bonds to achieve strong and selective anion recognition.

Chapter 8

References

References

- [1] J.-M. Lehn, *Science*, 1985, **227**, 849–856.
- [2] J. W. Steed and J. L. Atwood, *Supramolecular Chemistry*, John Wiley & Sons, Ltd., 2000.
- [3] E. Arunan, G. R. Desiraju, R. A. Klein, J. Sadlej, S. Scheiner, I. Alkorta, D. C. Clary, R. H. Crabtree, J. J. Dannenburg, P. Hobza, H. G. Kjaergaard, A. C. Legon, B. Mennucci and D. J. Nesbitt, *Pure Appl. Chem.*, 2011, **83**, 1637–1641.
- [4] J. W. Pflugrath and F. A. Quirocho, *Nature*, 1985, **314**, 257–260.
- [5] C. A. Hunter and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1990, **112**, 5525–5534.
- [6] S. K. Burley and G. A. Petsko, *Science*, 1985, **229**, 23–28.
- [7] S. Grimme, *Angew. Chem. Int. Ed.*, 2008, **47**, 3430–3434.
- [8] C. R. Martinez and B. L. Iverson, *Chem. Sci.*, 2012, **3**, 2191–2201.
- [9] J. W. G. Bloom and S. E. Wheeler, *Angew. Chem. Int. Ed.*, 2011, **50**, 7847–7849.
- [10] S. E. Wheeler and K. N. Houk, *J. Am. Chem. Soc.*, 2008, **130**, 10854–10855.
- [11] S. E. Wheeler, *J. Am. Chem. Soc.*, 2011, **133**, 10262–10274.
- [12] M. S. Cubberly and B. L. Iverson, *J. Am. Chem. Soc.*, 2001, **123**, 7560–7563.
- [13] W. R. Carroll, P. Pellechia and K. D. Shimizu, *Org. Lett.*, 2008, **10**, 3547–3550.
- [14] W. Blokziyl and J. B. F. N. Engberts, *Angew. Chem. Int. Ed. Engl.*, 1993, **32**, 1545–1579.
- [15] Y. S. Djikaev and E. Ruckenstein, *J. Phys. Chem. B*, 2012, **116**, 2820–2830.
- [16] I. A. Sedov, M. A. Stolov and B. N. Solomonov, *J. Phys. Org. Chem.*, 2011, **24**, 1088–1094.
- [17] J. C. Ma and D. A. Dougherty, *Chem. Rev.*, 1997, **97**, 1303–1324.
- [18] G. W. Gokel, L. J. Barbour, R. Ferdani and J. Hu, *Acc. Chem. Res.*, 2002, **35**, 878–886.
- [19] L. M. Salonen, C. Bucher, D. W. Banner, W. Haap, J.-L. Mary, J. Benz, O. Kuster, P. Seiler, W. B. Schweizer and F. Diederich, *Angew. Chem. Int. Ed.*, 2009, **48**, 811–814.
- [20] L. M. Salonen, M. Ellermann and F. Diederich, *Angew. Chem. Int. Ed.*, 2011, **50**, 4808–4842.
- [21] B. L. Schottel, H. T. Chifotides and K. R. Dunbar, *Chem. Soc. Rev.*, 2008, **37**, 68–83.
- [22] D. Quiñonero, C. Garau, C. Rotger, A. Frontera, P. Ballester, A. Costa and P. M. Deyà, *Angew. Chem. Int. Ed.*, 2002, **41**, 3389–3392.
- [23] T. J. Mooibroek, C. A. Black, P. Gamez and J. Reedijk, *Cryst. Growth Des.*, 2008, **8**, 1082–1093.
- [24] Y. S. Rosokha, S. V. Lindeman, S. V. Rosokha and J. K. Kochi, *Angew. Chem. Int. Ed.*, 2004, **43**, 4650–4652.
- [25] G. Gil-Ramírez, E. C. Escudero-Adán, J. Benet-Buchholz and P. Ballester, *Angew. Chem. Int. Ed.*, 2008, **47**, 4114–4118.
- [26] D.-X. Wang, Q.-Y. Zheng, Q.-Q. Wang and M.-X. Wang, *Angew. Chem. Int. Ed.*, 2008, **47**, 7485–7488.
- [27] O. B. Berryman and D. W. Johnson, *Chem. Commun.*, 2009, 3143–3153.
- [28] H. T. Chifotides, B. L. Schottel and K. R. Dunbar, *Angew. Chem. Int. Ed.*, 2010, **49**, 7202–7207.
- [29] F. Inokuchi, Y. Miyahara, T. Inazu and S. Shinkai, *Angew. Chem. Int. Ed. Engl.*, 1995, **34**, 1364–1366.
- [30] In the X-ray crystal structures of this host, the calix cavity contained a halide anion and a water molecule. This is omitted from the figure for clarity.
- [31] P. Metrangolo and G. Resnati, *Science*, 2008, **321**, 918–919.
- [32] T. Clark, M. Hennemann, J. S. Murray and P. Politzer, *J. Mol. Model.*, 2007, **13**, 291–296.
- [33] M. G. Sarwar, B. Dragisic, L. J. Salsberg, C. Gouliaras and M. S. Taylor, *J. Am. Chem. Soc.*, 2010, **132**, 1646–1653.
- [34] M. G. Sarwar, B. Dragisic, S. Sagoo and M. S. Taylor, *Angew. Chem. Int. Ed.*, 2010, **49**, 1674–1677.
- [35] K. Rissanen, *CrystEngComm*, 2008, **10**, 1107–1113.
- [36] C. J. Serpell, N. L. Kilah, P. J. Costa, V. Félix and P. D. Beer, *Angew. Chem. Int. Ed.*, 2010, **49**, 5322–5326.

- [37] T. M. Beale, M. G. Chudzinski, M. G. Sarwar and M. S. Taylor, *Chem. Soc. Rev.*, 2012, DOI: 10.1039/c2cs35213c.
- [38] C. B. Aakeröy, M. Fasulo, N. Schultheiss, J. Desper and C. Moore, *J. Am. Chem. Soc.*, 2007, **129**, 13772–13773.
- [39] 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.
- [40] A. Caballero, N. G. White and P. D. Beer, *Angew. Chem. Int. Ed.*, 2011, **50**, 1845–1849.
- [41] J. S. Murray, P. Lane, T. Clark and P. Politzer, *J. Mol. Model.*, 2007, **13**, 1033–1038.
- [42] J. S. Murray, P. Lane and P. Politzer, *Int. J. Quantum. Chem.*, 2007, **12**, 2286–2292.
- [43] J. W. Wielandt, N. L. Kilah, A. C. Willis and S. B. Wild, *Chem. Commun.*, 2006, 3679–3690.
- [44] J.-M. Lehn, *Angew. Chem. Int. Ed.*, 1988, **27**, 89–112.
- [45] Y. Li and A. H. Flood, *J. Am. Chem. Soc.*, 2008, **130**, 12111–12222.
- [46] D. E. Koshland, *Angew. Chem. Int. Ed. Engl.*, 1994, **33**, 2375–2378.
- [47] D. E. Koshland, *Proc. Nat. Acad. Sci. U.S.A.*, 1958, **44**, 98–104.
- [48] I. Bandyopadhyay, K. Raghavachari and A. H. Flood, *ChemPhysChem.*, 2009, **10**, 2535–2540.
- [49] D. J. Cram, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1009–112.
- [50] R. D. Hancock, *J. Chem. Ed.*, 1992, **69**, 615–621.
- [51] A. E. Martell, R. D. Hancock and R. J. Motekaitis, *Coord. Chem. Rev.*, 1994, **133**, 39–65.
- [52] K. Choi and A. Hamilton, *J. Am. Chem. Soc.*, 2001, **123**, 2456–2457.
- [53] A. Metzger, V. M. Lynch and E. V. Anslyn, *Angew. Chem. Int. Ed.*, 1997, **36**, 862–865.
- [54] M. T. Albelda, J. C. Frías, E. García-España and H.-J. Schneider, *Chem. Soc. Rev.*, 2012, **41**, 3859–3877.
- [55] C. J. Pedersen, *J. Am. Chem. Soc.*, 1967, **89**, 2495–2496.
- [56] C. J. Pedersen, *J. Am. Chem. Soc.*, 1967, **89**, 7017–7036.
- [57] J.-M. Lehn, *Acc. Chem. Res.*, 1978, **11**, 49–57.
- [58] D. J. Cram, T. Kaneda, R. C. Helgeson and G. M. Lein, *J. Am. Chem. Soc.*, 1979, **101**, 6752–6754.
- [59] H. K. Frensdorff, *J. Am. Chem. Soc.*, 1971, **93**, 600–606.
- [60] B. C. Pressman, *Annu. Rev. Biochem.*, 1976, **45**, 501–530.
- [61] J. Rebek, *Acc. Chem. Res.*, 2009, **42**, 1660–1668.
- [62] T. Heinz, D. M. Rudkevich and J. Rebek, *Nature*, 1998, **394**, 764–766.
- [63] T. Benzing, T. Tjivikua, J. Wolfe and J. Rebek, *Science*, 1988, **242**, 266–268.
- [64] Y. Kato, M. M. Conn and J. Rebek, *Proc. Nat. Acad. Sci. U.S.A.*, 1995, **92**, 1208–1212.
- [65] Y. Ferrand, M. P. Crump and A. P. Davis, *Science*, 2007, **318**, 619–622.
- [66] W. Meng, B. Breiner, K. Rissanen, J. D. Thoburn, J. K. Clegg and J. R. Nitschke, *Angew. Chem. Int. Ed.*, 2011, **50**, 3749–3483.
- [67] P. Mal, B. Breiner, K. Rissanen and J. R. Nitschke, *Science*, 2009, **324**, 1697–1699.
- [68] J. E. M. Lewis, E. L. Gavey, S. A. Cameron and J. D. Crowley, *Chem. Sci.*, 2012, **3**, 778–784.
- [69] P. Beer and P. Gale, *Angew. Chem. Int. Ed. Engl.*, 2001, **40**, 486–516.
- [70] A. P. Davis, D. N. Sheppard and B. D. Smith, *Chem. Soc. Rev.*, 2007, **36**, 348–357.
- [71] G. J. C. G. M. Bosman, K. Renkawek, F. P. A. van Workum, I. G. P. Bartholomeus and W. J. de Grip, *Gerontology*, 1997, **43**, 67–78.
- [72] M. H. Ward, T. M. de Kok, P. Levallois, J. Brender, G. Gulis, B. T. Nolan and J. van der Slice, *Environ. Health Perspect.*, 2005, **113**, 1607–1614.
- [73] R. D. Shannon, *Acta. Crystallogr.*, 1976, **A32**, 751–757.
- [74] C. Caltagirone, G. W. Bates, P. A. Gale and M. E. Light, *Chem. Commun.*, 2008, 61–63.
- [75] J. L. Cook, C. A. Hunter, C. M. R. Low, A. Perez-Velasco and J. G. Vinter, *Angew. Chem. Int. Ed.*, 2008, **47**, 6275–6277.
- [76] A. Brown and P. D. Beer, *Dalton Trans.*, 2012, **41**, 118–129.
- [77] J. L. Sessler, P. A. Gale and W.-S. Cho, *Anion Receptor Chemistry*, Royal Society of Chemistry, 2006.
- [78] S. Alunni, A. Pero and G. Reichenbach, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1747–1750.
- [79] H. Juwarker, J. M. Lenhardt, J. C. Castillo, E. Zhao, S. Krishnamurthy, R. M. Jamiolkowski, K. H. Kim and S. L. Craig, *J. Org. Chem.*, 2009, **74**, 8924–8934.
- [80] A. J. McConnell and P. D. Beer, *Chem. Eur. J.*, 2011, **9**, 2724–2733.
- [81] Y. Hua, R. O. Ramabhadran, E. O. Uduchi, J. A. Karty, K. Raghavachari and A. H. Flood, *Chem. Eur. J.*, 2011, **17**, 312–321.
- [82] Y. Hua, R. O. Ramabhadran, J. A. Karty, K. Raghavachari and A. H. Flood, *Chem. Commun.*, 2011, **47**, 5979–5981.
- [83] 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.

- [84] C. H. Park and H. E. Simmons, *J. Am. Chem. Soc.*, 1968, **90**, 2431–2432.
- [85] N. Gavrushenko, H. L. Carrell, W. C. Stallings and J. P. Glusker, *Acta. Crystallogr.*, 1977, **B33**, 3936–3939.
- [86] Y. Huse and Y. Iitaka, *Acta. Crystallogr.*, 1969, **B25**, 498–509.
- [87] C. Nakai and W. Glinsmann, *Biochemistry*, 1977, **16**, 5636–5641.
- [88] J. S. Mendy, M. L. Pilate, T. Horne, V. W. Day and M. A. Hossain, *Chem. Commun.*, 2010, **46**, 6084–6086.
- [89] J.-M. Lehn, E. Sonveaux and A. K. Willard, *J. Am. Chem. Soc.*, 1978, **100**, 4914–4916.
- [90] E. Graf and J.-M. Lehn, *J. Am. Chem. Soc.*, 1976, **98**, 6403–6405.
- [91] J. L. Sessler, M. J. Cyr, V. Lynch, E. McGhee and J. A. Ibers, *J. Am. Chem. Soc.*, 1990, **112**, 2810–2812.
- [92] F. P. Schmidtchen, *Angew. Chem. Int. Ed. Engl.*, 1977, **16**, 720–721.
- [93] K. Worm and F. P. Schmidtchen, *Angew. Chem. Int. Ed. Engl.*, 1995, **34**, 65–66.
- [94] A. Ursu and F. P. Schmidtchen, *Angew. Chem. Int. Ed.*, 2012, **51**, 242–246.
- [95] For example, Lehn has reported that the binding affinity of a hexaprotonated cryptand decreases above pH = 5.5. J.-M. Lehn, R. Méric, J.-P. Vigneron, I. Bkouche-Waksman and C. Pascard, *Chem. Commun.*, 1991, 62–64.
- [96] T. H. Wirth and N. Davidson, *J. Am. Chem. Soc.*, 1964, **86**, 4325–4329.
- [97] G. Müller, J. Riede and F. P. Schmidtchen, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1516–1518.
- [98] A. Echavarren, A. Galán, J.-M. Lehn and J. de Mendoza, *J. Am. Chem. Soc.*, 1989, **111**, 4995–4997.
- [99] A. G. Avent, P. A. Chaloner, M. P. Day, K. R. Seddon and T. Welton, *J. Chem. Soc., Dalton Trans.*, 1994, 3405–3413.
- [100] E. Alcade, C. Alvarez-Rúa, S. García-Granda, E. García-Rodríguez, N. Mesquida and L. Pérez-García, *Chem. Commun.*, 1999, 295–296.
- [101] K. Chellappan, N. J. Singh, I.-C. Hwang, J. W. Lee and K. S. Kim, *Angew. Chem. Int. Ed.*, 2005, **44**, 2899–2903.
- [102] K. Sato, S. Arai and T. Yamagishi, *Tetrahedron Lett.*, 1999, **40**, 5219–5222.
- [103] H. Ihm, S. Yun, H. G. Kim, J. K. Kim and K. S. Kim, *Org. Lett.*, 2002, **4**, 2897–2900.
- [104] W. J. Belcher, M. Fabre, T. Harhan and J. W. Steed, *Org. Biomol. Chem.*, 2006, **4**, 781–786.
- [105] A. L. Cresswell, M.-O. M. Piepenbrock and J. W. Steed, *Chem. Commun.*, 2010, **46**, 2787–2789.
- [106] Y. Li and A. H. Flood, *Angew. Chem. Int. Ed.*, 2008, **47**, 2649–2652.
- [107] H. Juwarker, J. M. Lenhardt, D. M. Pham and S. L. Craig, *Angew. Chem. Int. Ed.*, 2008, **47**, 3740–3743.
- [108] R. M. Meudtner and S. Hecht, *Angew. Chem., Int. Ed.*, 2008, **47**, 4926–4930.
- [109] A. Kumar and P. S. Pandey, *Org. Lett.*, 2008, **10**, 165–168.
- [110] R. A. Pascal, J. Spergel and D. van Engen, *Tetrahedron Lett.*, 1986, **27**, 4099–4102.
- [111] K. Kavallieratos, S. R. de Gala, D. J. Austin and R. H. Crabtree, *J. Am. Chem. Soc.*, 1997, **119**, 2325–2326.
- [112] K. Kavallieratos, C. M. Bertao and R. H. Crabtree, *J. Org. Chem.*, 1999, **64**, 1675–1683.
- [113] S. O. Kang, R. A. Begum and K. Bowman-James, *Angew. Chem. Int. Ed.*, 2006, **45**, 7882–7894.
- [114] S. Kubik, *Chem. Soc. Rev.*, 2010, **39**, 3648–3663.
- [115] A. P. Bisson, V. M. Lynch, M.-K. C. Monahan and E. V. Anslyn, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 2340–2342.
- [116] S. Kubik, R. Goddard, R. Kirchner, D. Nolting and J. Seidel, *Angew. Chem. Int. Ed.*, 2001, **40**, 2648–2651.
- [117] S. Kubik and R. Goddard, *Proc. Nat. Acad. Sci. U.S.A.*, 2002, **99**, 5127–5132.
- [118] A.-F. Li, J.-H. Wang, F. Wang and Y.-B. Jiang, *Chem. Soc. Rev.*, 2010, **39**, 3729–3745.
- [119] V. Amendola, L. Fabbri and L. Mosca, *Chem. Soc. Rev.*, 2010, **39**, 3889–3915.
- [120] S. J. Brooks, P. A. Gale and M. E. Light, *Chem. Commun.*, 2005, 4696–4698.
- [121] C. Pérez-Casas and A. K. Yatsimirsky, *J. Org. Chem.*, 2008, **73**, 2275–2284.
- [122] P. A. Gale, J. L. Sessler, V. Král and V. Lynch, *J. Am. Chem. Soc.*, 1996, **118**, 5140–5141.
- [123] P. A. Gale, *Chem. Commun.*, 2008, 4525–4540.
- [124] C.-H. Lee, J.-S. Lee, H.-K. Na, D.-W. Yoon, H. Miyaji, W.-S. Cho and J. L. Sessler, *J. Org. Chem.*, 2005, **70**, 2067–2074.
- [125] D.-W. Yoon, D. E. Gross, V. M. Lynch, C.-H. Lee, P. C. Bennett and J. L. Sessler, *Chem. Commun.*, 2009, 1109–1111.
- [126] J. L. Sessler, P. Anzenbacher, J. A. Shriver, K. Jursiková, V. M. Lynch and M. Marquez, *J. Am. Chem. Soc.*, 2000, **122**, 12061–12062.
- [127] G. Cafeo, F. H. Kohnke, G. L. La Torre, A. J. P. White and D. J. Williams, *Chem. Commun.*, 2000, 1207–1208.

- [128] G. Cafeo, F. H. Kohnke, M. F. Parisi, R. P. Nascone, G. L. La Torre and D. J. Williams, *Org. Lett.*, 2002, **4**, 2695–2697.
- [129] J. L. Sessler, W.-S. Cho, D. E. Gross, J. A. Shriver, V. M. Lynch and M. Marquez, *J. Org. Chem.*, 2005, **70**, 5982–5986.
- [130] J. L. Sessler, D. An, W.-S. Cho and V. Lynch, *Angew. Chem. Int. Ed.*, 2003, **42**, 2278–2281.
- [131] J. L. Sessler, D. An, W.-S. Cho, V. Lynch and M. Marquez, *Chem. Commun.*, 2005, 540–542.
- [132] S. Camiolo, S. J. Coles, P. A. Gale, M. B. Hursthouse and J. L. Sessler, *Acta. Crystallogr.*, 2001, **E57**, o816–o818.
- [133] J. L. Sessler, D.-G. Cho and V. Lynch, *J. Am. Chem. Soc.*, 2006, **128**, 16518–16519.
- [134] J.-M. Suk and K.-S. Jeong, *J. Am. Chem. Soc.*, 2008, **130**, 11868–11869.
- [135] D. Curiel, A. Cowley and P. D. Beer, *Chem. Commun.*, 2005, 236–238.
- [136] P. Dydio, D. Lichosyt and J. Jurczak, *Chem. Soc. Rev.*, 2011, **40**, 2971–2985.
- [137] I. E. Drubi Vega, S. Camiolo, P. A. Gale, M. B. Hursthouse and M. E. Light, *Chem. Commun.*, 2003, 1686–1687.
- [138] T. W. Hudnall, C.-W. Chiu and F. P. Gabbaï, *Acc. Chem. Res.*, 2009, **42**, 388–397.
- [139] M. Newcomb, J. H. Horner and M. T. Blanda, *J. Am. Chem. Soc.*, 1987, **109**, 7878–7879.
- [140] T. J. Wedge and M. F. Hawthorne, *Coord. Chem. Rev.*, 2003, **240**, 111–128.
- [141] E. J. O’Neil and B. D. Smith, *Coord. Chem. Rev.*, 2006, **250**, 3068–3080.
- [142] R. Vilar, *Eur. J. Inorg. Chem.*, 2008, 357–367.
- [143] D. Mercer and S. Loeb, *Chem. Soc. Rev.*, 2010, **39**, 3612–3620.
- [144] M. Melaimi and F. P. Gabbaï, *J. Am. Chem. Soc.*, 2005, **127**, 9680–9681.
- [145] J. V. Carolan, S. J. Butler and K. A. Joliffe, *J. Org. Chem.*, 2009, **74**, 2992–2996.
- [146] M. Cametti, K. Raatikainen, P. Metrangolo, T. Pilati, G. Terraneo and G. Resnati, *Org. Biomol. Chem.*, 2012, **10**, 1329–1333.
- [147] S. M. Walter, F. Kniep, L. Rout, F. P. Schmidtchen, E. Herdtweck and S. M. Huber, *J. Am. Chem. Soc.*, 2012, **134**, 8507–8512.
- [148] F. Zapata, A. Caballero, N. G. White, T. D. W. Claridge, P. J. Costa, V. Félix and P. D. Beer, *J. Am. Chem. Soc.*, 2012, **134**, 11533–11541.
- [149] M. G. Chudzinski, C. A. McClary and M. S. Taylor, *J. Am. Chem. Soc.*, 2011, **133**, 10559–10567.
- [150] A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher and T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515–1566.
- [151] C. Suksai and T. Tuntulani, *Chem. Soc. Rev.*, 2003, **32**, 192–202.
- [152] P. D. Beer, P. A. Gale and G. Z. Chen, *Coord. Chem. Rev.*, 1999, **185–186**, 3–36.
- [153] S. L. Wiskur, H. Ait-Haddou, J. J. Lavigne and E. V. Anslyn, *Acc. Chem. Res.*, 2001, **34**, 963–972.
- [154] X. Lou, D. Ou, Q. Li and Z. Li, *Chem. Commun.*, 2012, **48**, 8462–8477.
- [155] P. Bühlmann, E. Pretsch and E. Bakker, *Chem. Rev.*, 1998, **98**, 1593–1687.
- [156] M. M. G. Antonisse and D. Reinhoudt, *Electroanalysis*, 1999, **11**, 1035–1048.
- [157] J. V. Ros-Lis, R. Martínez-Máñez and J. Soto, *Chem. Commun.*, 2002, 2248–2249.
- [158] K. Kaur, R. Saini, A. Kumar, V. Luxami, N. Kaur, P. Singh and S. Kumar, *Coord. Chem. Rev.*, 2012, **256**, 1992–2028.
- [159] Y. Willener, K. M. Joly, C. J. Moody and J. H. R. Tucker, *J. Org. Chem.*, 2008, **73**, 1225–1233.
- [160] F. Otón, A. Tárraga and P. Molina, *Org. Lett.*, 2006, **8**, 2107–2110.
- [161] N. H. Evans, C. J. Serpell and P. D. Beer, *Chem. Commun.*, 2011, **47**, 8775–8777.
- [162] N. H. Evans, C. J. Serpell, N. G. White and P. D. Beer, *Chem. Eur. J.*, 2011, **17**, 12347–12354.
- [163] N. H. Evans, H. Rahman, A. V. Leontiev, N. D. Greenham, G. A. Orlowski, Q. Zeng, R. M. J. Jacobs, C. J. Serpell, N. L. Kilah, J. J. Davis and P. D. Beer, *Chem. Sci.*, 2012, **3**, 1080–1089.
- [164] M. C. Thompson and D. H. Busch, *J. Am. Chem. Soc.*, 1962, **84**, 1762–1763.
- [165] M. C. Thompson and D. H. Busch, *J. Am. Chem. Soc.*, 1964, **86**, 213–217.
- [166] M. C. Thompson and D. H. Busch, *J. Am. Chem. Soc.*, 1964, **86**, 3651–3656.
- [167] D. H. Busch and N. A. Stephenson, *Coord. Chem. Rev.*, 1990, **100**, 119–154.
- [168] S. Anderson, H. L. Anderson and J. K. M. Sanders, *Acc. Chem. Res.*, 1993, **26**, 469–475.
- [169] M.-T. Youinou, N. Rahmouni, J. Fischer and J. A. Osborn, *Angew. Chem. Int. Ed. Engl.*, 1992, **31**, 733–735.
- [170] P. N. W. Baxter, J.-M. Lehn, J. Fischer and M.-T. Youinou, *Angew. Chem. Int. Ed. Engl.*, 1994, **33**, 2284–2287.
- [171] A.-M. Stadler, *Eur. J. Inorg. Chem.*, 2009, 4751–4770.
- [172] 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.
- [173] Q.-F. Sun, J. Iwasa, D. Ogawa, Y. Ishido, S. Sato, T. Ozeki, Y. Sei, K. Yamaguchi and M. Fujita, *Science*, 2010, **328**, 1144–1147.

- [174] Q.-F. Sun, S. Sato and M. Fujita, *Nature Chem.*, 2012, **4**, 330–333.
- [175] Q.-F. Sun, T. Murase, S. Sato and M. Fujita, *Angew. Chem. Int. Ed.*, 2011, **50**, 10318–10321.
- [176] B. Hasenknopf, J.-M. Lehn, B. O. Kneisel, G. Baum and D. Fenske, *Angew. Chem. Int. Ed. Engl.*, 1996, **35**, 1838–1840.
- [177] B. Hasenknopf, J.-M. Lehn, N. Boumediene, A. Dupont-Gervais, A. van Dorsselaer, B. Kneisel and D. Fenske, *J. Am. Chem. Soc.*, 1997, **119**, 10956–10962.
- [178] C. S. Campos-Fernández, B. L. Schottel, H. T. Chifotides, J. K. Bera, J. Bacsá, J. M. Koomen, D. H. Russell and K. R. Dunbar, *J. Am. Chem. Soc.*, 2005, **127**, 12909–12923.
- [179] M. Bru, I. Alfonso, M. I. Burguette and S. V. Luis, *Angew. Chem. Int. Ed.*, 2006, **45**, 6155–6159.
- [180] A. Moure, S. V. Luis and I. Alfonso, *Chem. Eur. J.*, 2012, **18**, 5496–5500.
- [181] V. Martí-Centelles, M. I. Burguette and S. V. Luis, *Chem. Eur. J.*, 2012, **18**, 2409–2422.
- [182] P. R. Ashton, M. Bělohradský, D. Philp and J. F. Stoddart, *Chem. Commun.*, 1993, 1269–1274.
- [183] There is some controversy in the literature whether rotaxanes formed by slippage are “true” rotaxanes, or simply kinetically-stable pseudorotaxanes.
- [184] I. Yoone, M. Narita, T. Shimizu and M. Asakawa, *J. Am. Chem. Soc.*, 2004, **126**, 16740–16741.
- [185] S.-Y. Hsueh, J.-L. Ko, C.-C. Lai, Y.-H. Liu, S.-M. Peng and S.-H. Chiu, *Angew. Chem. Int. Ed.*, 2011, **50**, 6643–6646.
- [186] C.-W. Chiu, C.-C. Lai and S.-H. Chiu, *J. Am. Chem. Soc.*, 2007, **129**, 3500–3501.
- [187] E. Wasserman, *J. Am. Chem. Soc.*, 1960, **82**, 4433–4434.
- [188] I. T. Harrison and S. Harrison, *J. Am. Chem. Soc.*, 1967, **89**, 5723–5724.
- [189] G. Agam, D. Graiver and A. Zilkha, *J. Am. Chem. Soc.*, 1976, **98**, 5206–5214.
- [190] G. Agam and A. Zilkha, *J. Am. Chem. Soc.*, 1976, **98**, 5214–5216.
- [191] G. Schill and A. Lüttringhaus, *Angew. Chem. Int. Ed. Engl.*, 1964, **3**, 546–547.
- [192] C. O. Dietrich-Buchecker, J.-P. Sauvage and J. P. Kintzinger, *Tetrahedron Lett.*, 1983, **24**, 5095–5098.
- [193] C. O. Dietrich-Buchecker, J.-P. Sauvage and J. P. Kintzinger, *J. Am. Chem. Soc.*, 1984, **106**, 3043–3045.
- [194] J. F. Stoddart, *Chem. Soc. Rev.*, 2009, **38**, 1521–1529.
- [195] M. Cesario, C. O. Dietrich-Buchecker, J. Guilhem, C. Pascard and J.-P. Sauvage, *J. Chem. Soc., Chem. Commun.*, 1985, 244–247.
- [196] J.-P. Sauvage and J. Weiss, *J. Am. Chem. Soc.*, 1985, **107**, 6108–6110.
- [197] C. O. Dietrich-Buchecker, A. Khemiss and J.-P. Sauvage, *J. Chem. Soc., Chem. Commun.*, 1986, 1376–1378.
- [198] C. O. Dietrich-Buchecker and J.-P. Sauvage, *Angew. Chem. Int. Ed.*, 1989, **28**, 189–192.
- [199] S. M. Goldup, D. A. Leigh, P. J. Lusby, R. T. McBurney and A. M. Z. Slawin, *Angew. Chem. Int. Ed.*, 2008, **47**, 6999–7003.
- [200] A. I. Prikhod'ko and J.-P. Sauvage, *J. Am. Chem. Soc.*, 2009, **131**, 6794–6807.
- [201] A. Joosten, Y. Trolez, J.-P. Collin, V. Heitz and J.-P. Sauvage, *J. Am. Chem. Soc.*, 2012, **134**, 1802–1809.
- [202] J.-P. Collin, F. Durola, J. Frey, V. Heitz, F. Reviriego, J.-P. Sauvage, Y. Trolez and K. Rissanen, *J. Am. Chem. Soc.*, 2010, **132**, 6840–6850.
- [203] C. Roche, A. Sour and J.-P. Sauvage, *Chem. Eur. J.*, 2012, **18**, 8366–8376.
- [204] J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, K. Rissanen and D. Schultz, *Nature Chem.*, 2012, **4**, 15–20.
- [205] 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.
- [206] J. D. Crowley, S. M. Goldup, A.-L. Lee, D. A. Leigh and R. T. McBurney, *Chem. Soc. Rev.*, 2009, **38**, 1530–1541.
- [207] J. M. Timko, R. C. Helgeson, M. Newcomb, G. W. Gokel and D. J. Cram, *J. Am. Chem. Soc.*, 1974, **96**, 7097–7099.
- [208] W. Jiang, D. Sattler, K. Rissanen and C. A. Schalley, *Org. Lett.*, 2011, **13**, 4502–4505.
- [209] M.-V. Martínez-Díaz, N. Spencer and J. F. Stoddart, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 1904–1907.
- [210] S.-Y. Hsueh, K.-W. Cheng, C.-C. Lai and S.-H. Chiu, *Angew. Chem. Int. Ed.*, 2008, **47**, 4436–4439.
- [211] E. N. Guidry, S. J. Cantrill, J. F. Stoddart and R. H. Grubbs, *Org. Lett.*, 2005, **7**, 2129–2132.
- [212] 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.
- [213] B. L. Allwood, N. Spencer, H. Shahriari-Zavareh, J. F. Stoddart and D. J. Williams, *Chem. Commun.*, 1987, 1064–1066.
- [214] B. Odell, M. V. Reddington, A. M. Z. Slawin, N. Spencer, J. F. Stoddart and D. J. Williams, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1547–1550.

- [215] P. R. Ashton, B. Odell, M. V. Reddington, A. M. Z. Slawin, J. F. Stoddart and D. J. Williams, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1550–1553.
- [216] P.-L. Anelli, N. Spencer and J. F. Stoddart, *J. Am. Chem. Soc.*, 1991, **113**, 5131–5133.
- [217] P. R. Ashton, T. T. Goodnow, A. E. Kaifer, M. V. Reddington, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, C. Vicent and D. J. Williams, *Angew. Chem. Int. Ed. Engl.*, 1989, **28**, 1396–1399.
- [218] C. A. Hunter, *J. Am. Chem. Soc.*, 1992, **114**, 5303–5311.
- [219] A. G. Johnston, D. A. Leigh, R. J. Pritchard and M. D. Deegan, *Angew. Chem. Int. Ed. Engl.*, 1995, **34**, 1209–1212.
- [220] A. G. Johnston, D. A. Leigh, L. Nezhat, J. P. Smart and M. D. Deegan, *Angew. Chem. Int. Ed. Engl.*, 1995, **34**, 1212–1216.
- [221] 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.
- [222] R. Ahmed, A. Altieri, D. M. D'Souza, D. A. Leigh, K. M. Mullen, M. Papmeyer, A. M. Z. Slawin, J. K. Y. Wong and J. D. Woollins, *J. Am. Chem. Soc.*, 2011, **133**, 12304–12310.
- [223] H. Y. Au-Yeung, G. D. Pantos and J. K. M. Sanders, *Proc. Nat. Acad. Sci. U.S.A.*, 2009, **106**, 10466–10470.
- [224] F. B. L. Cougnon, H. Y. Au-Yeung, G. D. Pantos and J. K. M. Sanders, *J. Am. Chem. Soc.*, 2011, **133**, 3198–3207.
- [225] F. B. L. Cougnon, N. A. Jenkins, G. D. Pantos and J. K. M. Sanders, *Angew. Chem. Int. Ed.*, 2012, **51**, 1443–1447.
- [226] E. J. F. Klotz, T. D. W. Claridge and H. L. Anderson, *J. Am. Chem. Soc.*, 2006, **128**, 15374–15375.
- [227] G. M. Hübner, J. Gläser, C. Seel and F. Vögtle, *Angew. Chem. Int. Ed.*, 1999, **38**, 383–386.
- [228] P. Ghosh, O. Mermagen and C. A. Schalley, *Chem. Commun.*, 2002, 2628–2629.
- [229] E. Arunkumar, C. C. Forbes, B. C. Noll and B. D. Smith, *J. Am. Chem. Soc.*, 2005, **127**, 3288–3289.
- [230] J. J. Gassensmith, J. M. Baumes and B. D. Smith, *Chem. Commun.*, 2009, 6329–6338.
- [231] J.-J. Lee, J. M. Baumes, R. D. Connell, A. G. Oliver and B. D. Smith, *Chem. Commun.*, 2011, **47**, 7188–7190.
- [232] J. A. Wisner, P. D. Beer and M. G. B. Drew, *Angew. Chem. Int. Ed.*, 2001, **40**, 3606–3609.
- [233] J. A. Wisner, P. D. Beer, M. G. B. Drew and M. R. Sambrook, *J. Am. Chem. Soc.*, 2002, **124**, 12469–12476.
- [234] M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul and A. R. Cowley, *J. Am. Chem. Soc.*, 2004, **126**, 15364–15365.
- [235] M. D. Lankshear and P. D. Beer, *Acc. Chem. Res.*, 2007, **40**, 657–668.
- [236] L. M. Hancock, L. C. Gilday, S. Carvalho, P. J. Costa, V. Félix, C. J. Serpell, N. L. Kilah and P. D. Beer, *Chem. Eur. J.*, 2010, **16**, 13082.
- [237] Y. Li, K. M. Mullen, T. D. W. Claridge, P. J. Costa, V. Félix and P. D. Beer, *Chem. Commun.*, 2009, 7134–7136.
- [238] N. H. Evans, C. J. Serpell and P. D. Beer, *Angew. Chem. Int. Ed.*, 2011, **50**, 2507–2510.
- [239] D. Curiel, P. D. Beer, R. L. Paul, A. Cowley, M. R. Sambrook and F. Szemes, *Chem. Commun.*, 2004, 1162–1163.
- [240] A. Caballero, F. Zapata, N. G. White, P. J. Costa, V. Félix and P. D. Beer, *Angew. Chem. Int. Ed.*, 2012, **51**, 1876–1880.
- [241] L. C. Gilday, N. G. White and P. D. Beer, *Dalton Trans.*, 2012, **41**, 7092–7097.
- [242] M. J. Chmielewski, L. Zhao, A. Brown, D. Curiel, M. R. Sambrook, A. L. Thompson, S. M. Santos, V. Felix, J. J. Davis and P. D. Beer, *Chem. Commun.*, 2008, 3154–3156.
- [243] A. Brown, K. M. Mullen, J. Ryu, M. J. Chmielewski, S. M. Santos, V. Félix, A. L. Thompson, J. E. Warren, S. I. Pascu and P. D. Beer, *J. Am. Chem. Soc.*, 2009, **131**, 4937–4952.
- [244] G. T. Spence, C. J. Serpell, J. Sardinha, P. J. Costa, V. Félix and P. D. Beer, *Chem. Eur. J.*, 2011, **17**, 12955–12966.
- [245] K. M. Mullen, J. Mercurio, C. J. Serpell and P. D. Beer, *Angew. Chem. Int. Ed.*, 2009, **48**, 4781–4784.
- [246] L. M. Hancock, L. C. Gilday, N. L. Kilah, C. J. Serpell and P. D. Beer, *Chem. Commun.*, 2011, **47**, 1725–1727.
- [247] J. E. Walker, *Angew. Chem. Int. Ed.*, 1998, **37**, 2308–2329.
- [248] N. Hirokawa, *Science*, 1998, **279**, 519–526.
- [249] P. R. Ashton, R. Ballardini, V. Balzani, I. Baxter, A. Credi, M. C. T. Fyfe, M. T. Gandolfi, M. Gómez-López, M.-V. Martínez-Díaz, A. Piersanti, N. Spencer, J. F. Stoddart, M. Venturi, A. J. P. White and D. J. Williams, *J. Am. Chem. Soc.*, 1998, **120**, 11932–11942.
- [250] D. A. Leigh, J. K. Y. Wong, F. Dehez and F. Zerbetto, *Nature*, 2003, **424**, 174–179.
- [251] J. Berná, D. A. Leigh, M. Lubomska, S. M. Mendoza, E. M. Pérez, P. Rudolf, G. Teobaldi and F. Zerbetto, *Nature Mater.*, 2005, **4**, 704–710.

- [252] M. C. Jiménez, C. Dietrich-Buchecker and J.-P. Sauvage, *Angew. Chem. Int. Ed.*, 2000, **39**, 3284–3287.
- [253] M. R. Craig, M. G. Hutchings, T. D. W. Claridge and H. L. Anderson, *Angew. Chem. Int. Ed.*, 2001, **40**, 1071–1074.
- [254] A. Fernandes, A. Viterisi, F. Coutrot, S. Potok, D. A. Leigh, V. Aucagne and S. Papot, *Angew. Chem. Int. Ed.*, 2009, **48**, 6443–6447.
- [255] R. T. S. Lam, A. Belenguer, S. L. Roberts, C. Naumann, T. Jarrosson, S. Otto and J. K. M. Sanders, *Science*, 2005, **308**, 667–669.
- [256] M. K. Chae, J.-M. Suk and K.-S. Jeong, *Tetrahedron Lett.*, 2010, **51**, 4240–4242.
- [257] Y. Zhao, Y. Li, Y. Li, H. Zheng, X. Yin and H. Liu, *Chem. Asian J.*, 2010, **46**, 5698–5700.
- [258] D.-W. Yoon, D. E. Gross, V. M. Lynch, J. L. Sessler, B. P. Hay and C.-H. Lee, *Angew. Chem. Int. Ed.*, 2008, **47**, 5038–5042.
- [259] S. S. Zhu, H. Staats, K. Brandhorst, J. Grunenberg, F. Gruppi, E. Dalcanele, A. Lützen, K. Rissanen and C. A. Schalley, *Angew. Chem. Int. Ed.*, 2008, **47**, 788–792.
- [260] H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2001, **40**, 2004–2021.
- [261] V. Rostovtsev, L. Green, V. Fokin and K. Sharpless, *Angew. Chem. Int. Ed.*, 2002, **41**, 2596–2599.
- [262] C. W. Tornøe, C. Christensen and M. Meldal, *J. Org. Chem.*, 2002, **67**, 3057–3064.
- [263] J. E. Hein and V. V. Fokin, *Chem. Soc. Rev.*, 2010, **39**, 1302–1315.
- [264] M. Meldal and C. W. Tornøe, *Chem. Rev.*, 2008, **108**, 2952–3015.
- [265] K. D. Hänni and D. A. Leigh, *Chem. Soc. Rev.*, 2010, **39**, 1240–1251.
- [266] A. C. Fahrenbach and J. F. Stoddart, *Chem. Asian J.*, 2011, **6**, 2660–2669.
- [267] W. B. Farnham, D. C. Roe, D. A. Dixon, J. C. Calabrese and R. L. Harlow, *J. Am. Chem. Soc.*, 1990, **112**, 7707–7718.
- [268] One further report of an ion selective electrode using a polyfluorinated macrocycle very similar to Farnham and Dixon's was reported in the interim. D. Siswanta, J. Takenaka, T. Suzuki, H. Sasakura, H. Hisamoto and K. Suzuki, *Chem. Lett.*, 1997, 195–196.
- [269] D.-W. Yoon, H. Hwang and C.-H. Lee, *Angew. Chem. Int. Ed.*, 2002, **41**, 1757–1759.
- [270] S. Lee, Y. Hua and A. H. Flood, *Org. Lett.*, 2010, **12**, 2100–2102.
- [271] Q.-Y. Cao, T. Pradhan, S. Kim and J. Kim, *Org. Lett.*, 2011, **13**, 4386–4389.
- [272] Y. Wang, J. Xiang and H. Jiang, *Chem. Eur. J.*, 2011, **17**, 613–619.
- [273] K. P. McDonald, R. O. Ramabhadran, S. Lee, K. Raghavachari and A. H. Flood, *Org. Lett.*, 2011, **13**, 6260–6263.
- [274] E. M. Zahran, Y. Hua, Y. Li, A. H. Flood and L. G. Bachas, *Anal. Chem.*, 2010, **82**, 368–375.
- [275] E. M. Zahran, Y. Hua, S. Lee, A. H. Flood and L. G. Bachas, *Anal. Chem.*, 2011, **83**, 3455–3461.
- [276] Y. Hua and A. H. Flood, *J. Am. Chem. Soc.*, 2010, **132**, 12838–12840.
- [277] B. Schulze, C. Friebe, M. D. Hager, W. Günther, U. Köhn, B. O. Jahn, H. Görls and U. Schubert, *Org. Lett.*, 2010, **12**, 2710–2713.
- [278] K. Ohmatsu, M. Kiyokawa and T. Ooi, *J. Am. Chem. Soc.*, 2011, **133**, 1307–1309.
- [279] R. Chhatra, A. Kumar and P. S. Pandey, *J. Org. Chem.*, 2011, **76**, 9086–9089.
- [280] F. Coutrot and E. Busseron, *Chem. Eur. J.*, 2008, **14**, 4784–4787.
- [281] F. Coutrot and E. Busseron, *Chem. Eur. J.*, 2009, **15**, 5186–5190.
- [282] H. Zheng, W. Zhou, J. Lv, X. Yin, Y. Li, H. Liu and Y. Li, *Chem. Eur. J.*, 2009, **15**, 13253–13262.
- [283] E. Busseron, C. Romauld and F. Coutrot, *Chem. Eur. J.*, 2010, **16**, 10062–10073.
- [284] Y. Zhao, Y. Li, S.-W. Lai, J. Yang, C. Liu, H. Liu, C.-M. Che and Y. Li, *Org. Biomol. Chem.*, 2011, **9**, 7500–7503.
- [285] F. Coutrot, C. Romauld and E. Busseron, *Org. Lett.*, 2008, **10**, 3741–3744.
- [286] C. Romauld, E. Busseron and F. Coutrot, *J. Org. Chem.*, 2010, **75**, 6516–6531.
- [287] C. J. Serpell, R. Chall, A. L. Thompson and P. D. Beer, *Dalton Trans.*, 2011, **40**, 12052–12055.
- [288] G. T. Spence, M. B. Pitak and P. D. Beer, *Chem. Eur. J.*, 2012, **18**, 7100–7108.
- [289] Y. Li, M. Pink, J. A. Karty and A. H. Flood, *J. Am. Chem. Soc.*, 2008, **130**, 17293–17295.
- [290] Y. Wang, F. Bie and H. Jiang, *Org. Lett.*, 2010, **12**, 3630–3633.
- [291] R. O. Ramabhadran, Y. Hua, Y. Li, A. H. Flood and K. Raghavachari, *Chem. Eur. J.*, 2011, **17**, 9123–9129.
- [292] V. Haridas, S. Sahu and P. Venugopalan, *Tetrahedron*, 2011, **67**, 727–733.
- [293] M. R. Krause, R. Goddard and S. Kubik, *J. Org. Chem.*, 2011, 7084–7095.
- [294] Y. Lau, P. Rutledge, M. Watkinson and M. Todd, *Chem. Soc. Rev.*, 2011, **40**, 2848–2866.
- [295] C.-H. Lee, S. Lee, H. Yoon and W.-D. Jang, *Chem. Eur. J.*, 2011, **17**, 13898–13903.
- [296] N. G. Angelo and P. S. Arora, *J. Am. Chem. Soc.*, 2005, **127**, 17134–17135.
- [297] N. G. Angelo and P. S. Arora, *J. Org. Chem.*, 2007, **72**, 7963–7967.
- [298] W. S. Horne, C. D. Stout and M. R. Ghadiri, *J. Am. Chem. Soc.*, 2003, **125**, 9372–9376.

- [299] W. S. Horne, M. K. Yadav, C. D. Stout and M. R. Ghadiri, *J. Am. Chem. Soc.*, 2004, **126**, 15366–15367.
- [300] H. Luecke and F. A. Quirocho, *Nature*, 1990, **347**, 402–406.
- [301] M. R. Sambrook, P. D. Beer, M. D. Lankshear, R. F. Ludlow and J. A. Wisner, *Org. Biomol. Chem.*, 2006, **4**, 1529–1538.
- [302] M. R. Sambrook, P. D. Beer, J. A. Wisner, R. L. Paul, A. R. Cowley, F. Szemes and M. G. B. Drew, *J. Am. Chem. Soc.*, 2005, **127**, 2292–2302.
- [303] M. R. Krause, R. Goddard and S. Kubik, *Chem. Commun.*, 2010, **46**, 3307.
- [304] J. G. Haasnoot, *Coord. Chem. Rev.*, 2000, **200–202**, 131–185.
- [305] M. H. Klingele and S. Brooker, *Coord. Chem. Rev.*, 2003, **241**, 119–132.
- [306] J. A. Kitchen and S. Brooker, *Coord. Chem. Rev.*, 2008, **252**, 2072–2092.
- [307] H. Struthers, T. L. Mindt and R. Schibli, *Dalton Trans.*, 2010, **39**, 675–696.
- [308] Y. Li, J. C. Huffman and A. H. Flood, *Chem. Commun.*, 2007, 2692–2694.
- [309] R. M. Meudtner, M. Ostermeier, R. Goddard, C. Limberg and S. Hecht, *Chem. Eur. J.*, 2007, **13**, 9834–9840.
- [310] M. Ostermeier, M.-A. Berlin, R. M. Meudtner, S. Demeshko, F. Meyer, C. Limberg and S. Hecht, *Chem. Eur. J.*, 2010, **16**, 10202–10213.
- [311] R. Bronisz, *Inorg. Chem.*, 2005, **44**, 4463–4465.
- [312] B. M. J. M. Suijkerbuijk, B. N. H. Aerts, H. P. Dijkstra, M. Lutz, A. L. Spek, G. van Koten and R. J. M. K. Gebbink, *Dalton Trans.*, 2007, 1273–1276.
- [313] S. Badèche, J.-C. Daran, J. Ruiz and D. Astruc, *Inorg. Chem.*, 2008, **47**, 4903–4908.
- [314] M. L. Gower and J. D. Crowley, *Dalton Trans.*, 2010, **39**, 2371–2378.
- [315] G. F. Manbeck, W. W. Brennessel, C. M. Evans and R. Eisenberg, *Inorg. Chem.*, 2010, **49**, 2834–2843.
- [316] B. Colasson, N. L. Poul, Y. L. Mest and O. Reinaud, *Inorg. Chem.*, 2011, **50**, 10985–10993.
- [317] B. S. Uppal, R. K. Booth, N. Ali, C. Lockwood, C. R. Rice and P. I. P. Elliott, *Dalton Trans.*, 2011, **40**, 7610–7616.
- [318] J. Kusz, R. Bronisz, M. Zubko and G. Bednarek, *Chem. Eur. J.*, 2011, **17**, 6807–6820.
- [319] J. D. Crowley and E. L. Gavey, *Dalton Trans.*, 2010, **39**, 4035–4037.
- [320] A. K. Feldman, B. Colasson and V. V. Fokin, *Org. Lett.*, 2004, **6**, 3897.
- [321] J. D. Crowley and P. Bandeen, *Dalton Trans.*, 2010, **39**, 612.
- [322] W. Zhu and D. Ma, *Chem. Commun.*, 2004, 888–889.
- [323] Y. Miura, Y. Ushitani, K. Inui, Y. Teki, T. Takui and K. Itoh, *Macromolecules*, 1993, **26**, 3698.
- [324] K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett.*, 1975, **16**, 4467.
- [325] D. A. Shultz, H. Lee, R. K. Kumar and K. P. Gwaltney, *J. Org. Chem.*, 1999, **64**, 9124–9136.
- [326] Y. Tobe, J. Kishi, I. Ohki and M. Sonoda, *J. Org. Chem.*, 2003, **68**, 3330–3332.
- [327] Acetone was used as solvent because it is only weakly competitive, and does not have the difficulties of TBA[−]anion pairing associated with even less competitive chlorinated solvents.
- [328] M. J. Hynes, *J. Chem. Soc., Dalton Trans.*, 1993, 311–312.
- [329] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **80**, 420–427.
- [330] S. Binauld, C. J. Hawker, E. Fleury and E. Drockenmüller, *Angew. Chem. Int. Ed.*, 2009, **48**, 6654.
- [331] A. R. Kelly, J. Wei, S. Kesavan, J.-C. Marié, N. Windmon, D. W. Young and L. A. Marcaurelle, *Org. Lett.*, 2009, **11**, 2257.
- [332] G. Chouhan and K. James, *Org. Lett.*, 2011, **13**, 2754.
- [333] K.-Y. Ng, V. Félix, S. M. Santos, N. H. Rees and P. D. Beer, *Chem. Commun.*, 2008, 1281–1283.
- [334] H. Goto, J. Heemstra, D. Hill and J. Moore, *Org. Lett.*, 2004, **6**, 889–892.
- [335] T. X. Neenan and G. M. Whitesides, *J. Org. Chem.*, 1988, **53**, 2489–2496.
- [336] E. D. Goddard-Borger and R. V. Stick, *Org. Lett.*, 2007, **9**, 3797–3800.
- [337] C. J. Serpell, O. Thomas, B. Odell, T. D. W. Claridge, R. Chall, A. L. Thompson and P. D. Beer, *CrystEngComm*, 2011, **13**, 4586–4591.
- [338] These values were obtained by averaging the values from all bis-triazole macrocycle structures, and all macrocycles in Ref. 337 having a *syn-syn* amide arrangement.
- [339] L. M. Hancock and P. D. Beer, *Chem. Eur. J.*, 2009, **15**, 42.
- [340] These nitrogen atoms are observed to preferentially coordinate to metal cations in previous reports of triazoles acting as ligands.
- [341] A similar arrangement has been observed by Eisenberg and co-workers, Ref. 315.
- [342] Unfortunately no crystals were obtained when AgPF₆ was used instead of Ag(CF₃SO₃).
- [343] R. Fernández-Galán, B. R. Manzano, A. Otero, M. Lanfranchi and M. A. Pellinghelli, *Inorg. Chem.*, 1994, **33**, 2309–2312.
- [344] A. J. Tasiopoulos, N. C. Harden, K. A. Abboud and G. Christou, *Polyhedron*, 2003, **22**, 133–143.

- [345] V. Aucagne, K. D. Hanni, D. A. Leigh, P. J. Lusby and D. B. Walker, *J. Am. Chem. Soc.*, 2006, **128**, 2186–2187.
- [346] A. Bondi, *J. Phys. Chem.*, 1964, **68**, 441–451.
- [347] R. S. Rowland and R. Taylor, *J. Phys. Chem.*, 1996, **100**, 7384–7391.
- [348] S. S. Andersen, M. Jensen, A. Sørensen, E. Miyazaki, K. Takimiya, B. W. Laursen, A. H. Flood and J. O. Jeppesen, *Chem. Commun.*, 2012, **48**, 5157–5159.
- [349] A. G. Massey and A. J. Parl, *J. Organometal. Chem.*, 1964, **2**, 245–250.
- [350] This salt was kindly provided by Prof. Andrew Weller's research group (University of Oxford).
- [351] R. Díaz-Torres and S. Alvarez, *Dalton Trans.*, 2011, **40**, 10742–10750.
- [352] J. A. Wisner, P. D. Beer, N. G. Berry and B. Tomapatanaget, *Proc. Nat. Acad. Sci. U.S.A.*, 2002, **99**, 4983–4986.
- [353] L. Zhao, K. M. Mullen, M. J. Chmielewski, A. Brown, N. Bampos, P. D. Beer and J. J. Davis, *New J. Chem.*, 2009, **33**, 760–768.
- [354] K. M. Mullen, J. J. Davis and P. D. Beer, *New J. Chem.*, 2009, **33**, 769–776.
- [355] N. L. Kilah, M. D. Wise and P. D. Beer, *Cryst. Growth Des.*, 2011, **11**, 4565–4571.
- [356] G. T. Spence, N. G. White and P. D. Beer, *Org. Biomol. Chem.*, 2012, **10**, 7282–7291.
- [357] While the pseudorotaxane was not directly observed, Jeong has reported a catenane containing neutral components, which was formed using anion templation, Ref. 256.
- [358] M. C. T. Fyfe, P. T. Glink, S. Menzer, J. F. Stoddart, A. J. P. White and D. J. Williams, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 2068–2070.
- [359] B. A. Blight, K. A. van Noortwyk, J. A. Wisner and M. C. Jennings, *Angew. Chem. Int. Ed.*, 2005, **44**, 1499–1504.
- [360] B. A. Blight, J. A. Wisner and M. C. Jennings, *Inorg. Chem.*, 2009, **48**, 1920–1927.
- [361] H.-Y. Gong, B. M. Rambo, E. Karnas, V. M. Lynch and J. L. Sessler, *Nature Chem.*, 2010, **2**, 406–409.
- [362] H.-Y. Gong, B. M. Rambo, E. Karnas, V. M. Lynch, K. M. Keller and J. L. Sessler, *J. Am. Chem. Soc.*, 2011, **133**, 1526–1533.
- [363] H.-Y. Gong, B. M. Rambo, V. M. Lynch, K. M. Keller and J. L. Sessler, *Chem. Eur. J.*, 2012, **18**, 7803–7809.
- [364] Y. Yamada, M. Okamoto, K. Furukawa, T. Kato and K. Tanaka, *Angew. Chem. Int. Ed.*, 2012, **51**, 709–713.
- [365] J. D. Megiatto and D. I. Schuster, *J. Am. Chem. Soc.*, 2008, **130**, 12872–12873.
- [366] H. Lahlali, K. Jobe, M. Watkinson and S. M. Goldup, *Angew. Chem. Int. Ed.*, 2011, **50**, 4151–4155.
- [367] S. Mecozzi and J. Rebek, *Chem. Eur. J.*, 1998, **4**, 1016–1022.
- [368] K.-Y. Ng, A. R. Cowley and P. D. Beer, *Chem. Commun.*, 2006, 3676–3678.
- [369] N. H. Evans, E. S. H. Allinson, M. D. Lankshear, K.-Y. Ng, A. R. Cowley, C. J. Serpell, S. M. Santos, P. J. Costa, V. Félix and P. D. Beer, *RSC Adv.*, 2011, **1**, 995–1003.
- [370] H. W. Gibson, S. H. Lee, P. T. Engen, P. Le Cavalier, J. Sze, Y. X. Shen and M. Bheda, *J. Org. Chem.*, 1993, **58**, 3748–3756.
- [371] J. M. Mercurio, *Part II Thesis, University of Oxford*, 2009.
- [372] V. Aucagne, J. Bernaá, J. D. Crowley, S. M. Goldup, K. D. Hänni, D. A. Leigh, P. J. Lusby, V. E. Ronaldson, A. M. Z. Slawin, A. Viterisi and D. B. Walker, *J. Am. Chem. Soc.*, 2007, **129**, 11950–11963.
- [373] S. Kubik, R. Kirchner, D. Nolting and J. Seidel, *J. Am. Chem. Soc.*, 2002, **124**, 12752–12760.
- [374] Z. Rodriguez-Docampo, S. Pascu, S. Kubik and S. Otto, *J. Am. Chem. Soc.*, 2006, **128**, 11206–11210.
- [375] R. Yang, W.-X. Liu, H. Shen, H.-H. Huang and Y.-B. Jiang, *J. Phys. Chem. B*, 2008, **112**, 5105–5110.
- [376] C. Caltagirone, J. R. Hiscock, M. B. Hursthouse, M. E. Light and P. A. Gale, *Chem. Eur. J.*, 2008, **14**, 10236–10243.
- [377] P. Ballester, *Chem. Soc. Rev.*, 2010, **39**, 3810–3830.
- [378] N. G. White and P. D. Beer, *Beilstein J. Org. Chem.*, 2012, **8**, 246–252.
- [379] W. W. H. Wong, M. S. Vickers, A. R. Cowley, R. L. Paul and P. D. Beer, *Org. Biomol. Chem.*, 2005, **3**, 4201–4208.
- [380] Kim has recently reported a larger tetra-imidazolium receptor, which binds iodide in preference to the smaller halides or acetate in 9:1 CD₃CN:D₂O. V. Suresh, N. Ahmed, I. S. Youn and K. S. Kim, *Chem. Asian J.*, 2012, **7**, 658–663.
- [381] P. Mathew, A. Neels and M. Albrecht, *J. Am. Chem. Soc.*, 2008, **130**, 13534–13535.
- [382] Y.-M. Zhang, J.-Y. Shao, C.-J. Yao and Y.-W. Zhong, *Dalton Trans.*, 2012, **41**, 9280–9282.
- [383] E. C. Keske, O. V. Zenkina, R. Wang and C. M. Crudden, *Organometallics*, 2012, **31**, 456–461.
- [384] A. V. Leontiev, C. A. Jemmett and P. D. Beer, *Chem. Eur. J.*, 2011, **17**, 816–825.
- [385] D. E. Phipps and P. D. Beer, *Tetrahedron Lett.*, 2009, **50**, 3454–3457.

- [386] S. Lal and S. Díez-González, *J. Org. Chem.*, 2011, **76**, 2367–2373.
- [387] F. Kniep, L. Rout, S. M. Walter, H. K. V. Bensch, S. H. Jungbauer, E. Herdtweck and S. M. Huber, *Chem. Commun.*, 2012, **48**, 9299–9301.
- [388] J. Cosier and A. M. Glazer, *J. Appl. Crystallogr.*, 1986, **19**, 105–107.
- [389] Z. Otwinowski and W. Minor, in *Methods Enzymol.*, ed. C. W. Carter and R. M. Sweet, Academic Press, 1997, ch. 276.
- [390] Agilent Technologies, *CrysAlisPro*, 2011.
- [391] H. Nowell, S. A. Barnett, K. E. Christensen, S. J. Teat and D. R. Allan, *J. Synchrotron Rad.*, 2012, **19**, 435–441.
- [392] CrystalClear: An Integrated Program for the Collection and Processing of Area Detector Data, Rigaku Corporation, 1997–2002.
- [393] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori and M. Camalli, *J. Appl. Crystallogr.*, 1994, **27**, 435.
- [394] L. Palatinus and G. Chapuis, *J. Appl. Crystallogr.*, 2007, **40**, 786–790.
- [395] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout and D. J. Watkin, *J. Appl. Crystallogr.*, 2003, **36**, 1487.
- [396] E. Prince, *Mathematical Techniques in Crystallography and Materials Science*, Springer-Verlag, New York, 1982.
- [397] J. R. Carruthers and D. J. Watkin, *Acta. Crystallogr.*, 1979, **A35**, 698–699.
- [398] P. van der Sluis and A. L. Spek, *Acta. Crystallogr.*, 1990, **A46**, 194–201.
- [399] A. Spek, *J. Appl. Crystallogr.*, 2003, **36**, 7–13.
- [400] R. I. Cooper, R. O. Gould, S. Parsons and D. J. Watkin, *J. Appl. Crystallogr.*, 2002, **35**, 168–174.
- [401] R. I. Cooper, A. L. Thompson and D. J. Watkin, *J. Appl. Crystallogr.*, 2010, **43**, 1017–1022.
- [402] R. Taylor and O. Kennard, *Acc. Chem. Res.*, 1984, **17**, 320–326.
- [403] N. Fischer, E. D. Goddard-Borger, R. Greiner, T. M. Klapötke, B. W. Skelton and J. Stierstorger, *J. Org. Chem.*, 2012, **77**, 1760–1764.
- [404] B.-Y. Lee, S. R. Park, H. B. Jeon and K. S. Kim, *Tetrahedron Lett.*, 2006, **47**, 5105–5109.
- [405] H. E. Gottlieb, V. Kotlyar and A. Nudelman, *J. Org. Chem.*, 1997, **62**, 7512–7515.