Rotaxane Synthesis *via* the 'Threading Followed by Stoppering' Approach.

by

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Declaration

All of the work carried out in this thesis is original research carried out at The University of Warwick between October 2008 and December 2011. I declare that the material described that is not original has been identified and appropriately referenced. I certify that the material within this thesis has not been submitted for a degree at any other university.

Abstract

The development of template directed synthesis towards the formation of interlocked architectures has allowed for the synthesis of a variety of rotaxanes. Chapter 1 covers the history of rotaxanes including their nomenclature and methods of formation. An overview of the intermolecular interactions used to facilitate the synthesis of these architectures is described and examples of template directed synthesis and properties of rotaxanes are discussed.

In Chapter 2 the use of the Diels-Alder reaction towards formation of rotaxanes in a 'threading followed by stoppering' protocol is covered. The synthesis of [n]rotaxanes is described with secondary ammonium ions, a novel perimidine benzimidazole and *bis*pyridinium binding templates integrated into threads.

In Chapter 3 a novel binding template was developed, incorporating a triazole into a dibenzylammonium binding motif. Binding studies were carried out and [n]rotaxanes were synthesised using this motif with the groups Diels-Alder 'threading followed by stoppering' protocol.

Chapter 4 discusses the modification of the DB24C8 macrocycle with the aim to enhance binding interactions with a variety of binding motifs. Two macrocycles were successfully synthesised and their binding affinities calculated with known and novel binding templates investigated in the previous chapters.

The work in this thesis shows a Diels-Alder stoppering reaction can be successfully used to synthesise [n]rotaxanes with a variety of binding templates including novel templates discovered during this project. During the work it was also revealed that modifications to

known binding templates can provide an enhancement in binding interactions in comparison to their unmodified predecessors.

Abbreviations

δ	Chemical shift
aq.	aqueous
BOP	Benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate
BPX26C6	bis-*p*-xylyl[26]crown-6
br	broad
Calc	Calculated
cat	catalytic amount
$CBPQT^{4+}$	cyclobis(paraqut-*p*-phenylene)
CH_2Cl_2	Dichloromethane
CuAAC	Cu(I)-catalysed terminal alkyne-azide cycloaddition
d	doublet
dd	double doublet
DB24C8	Dibenzo-24-crown-8
DCC	*N*,*N*'-dicyclohexylcarbodiimide
DEAD	Diethylazodicarboxylate
Decomp.	Decomposition
DMAc	Dimethylacetamide
DMAP	4-Dimethylaminopyridine
DMF	*N,N'*-Dimethylformamide
DMSO	Dimethylsulphoxide
DNP	1,5-Dimethoxynaphthalene
EDAC	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
EtOAc	Ethyl Acetate
Et_2O	Diethyl ether

Equiv.	Equivalents
ESI	Electrospray Ionisation
g	Grams
HBTU	O-Benzotriazole-N,N,N',N'-tetramethyl-uronium-hexafluorophosphonium
$HClO_4$	Perchloric Acid
HOBt	Hydroxybenzotriazole
HRMS	High resolution mass spectrometry
J	Coupling constant
m	multiplet
MeOH	Methanol
mg	Milligrams
MHz	Megahertz
mmol	Millimoles
m.p.	Melting Point
MS	Mass Spectrometry
m/z	Mass-to-charge ratio
NaAsc	Sodium Ascorbate
PPh_3	Triphenyl phosphine
ppm	parts per million
q	quartet
quant.	Quantitative
RCM	Ring closing metathesis
RT	Room temperature
s	singlet
t	triplet
THF	Tetrahydrofuran
TFA	Trifluoroacetic acid
TFAA	Trifluoroacetic anhydride

TLC	Thin layer chromatography
TTF	Tetrathiafulvalene
TMeAB	3,5,3’,5’-Tetramethylazobenzene

Chapter 1 Introduction

1. Supramolecular Chemistry

Supramolecular chemistry is an area which has expanded and diversified over recent years. It concerns the self assembly of molecules using weak and reversible, non-covalent bonding interactions into larger more complex structures. Two or more molecules can interact to give a supramolecular structure when there is selective recognition or 'complementarity' between them. Some examples that use this concept include molecular recognition and self assembly, host-guest chemistry, protein folding and the synthesis of mechanically interlocked structures.

Supramolecular chemistry was first recognised in the late 1800's when Emil Fischer described the binding of enzyme-substrate complexes in the 'lock and key' terminology, introducing ideas such as molecular recognition and host-guest chemistry.[1] It wasn't until the late 1900's that any major breakthroughs came to light. In 1987 the chemists Pedersen, Cram and Lehn won the Nobel Prize for their work in the area, helping to define the importance and principals of supramolecular chemistry.[2]

Weak intermolecular interactions are of great importance in biological structures. One famous example is in the formation of the DNA double helix held together by complimentary hydrogen bonding between the two inter-coiled strands.

There are a number of key weak intermolecular forces used in the formation of supramolecular structures. These include hydrogen bonding,[3-4] Van der Waals forces,[5] π-π interactions,[6-8] electrostatic interactions,[9] ion-dipole interactions,[10-11] hydrophobic forces[12-14] and metal coordination.[15-17] In comparison to covalent bonds, these interactions are much weaker, but when multiple weaker interactions are collated it can allow binding that is both strong and selective to drive the self assembly process.

Using self assembly, highly complex, novel structures can be created from relatively simple starting materials highlighted by examples of interlocked complexes such as catenanes,[18-20] rotaxanes[21] and knots.[22-26]

1.2 Rotaxanes

The word rotaxane is derived from the Latin words rota and axis, which mean 'wheel' and 'axle'.[27] They are molecules consisting of an axle which is threaded through a macrocycle; it is prevented from slipping off the axle using large end groups to act as bulky stoppers. The end groups of the axle are selected to be adequately large enough to prevent the macrocycle slipping off and the components of such compounds are mechanically interlocked. Pseudorotaxanes have no bulky stoppers and the macrocycle is free to slip off the axle. It is weak non covalent interactions between the thread and macrocycle that direct the threading process.

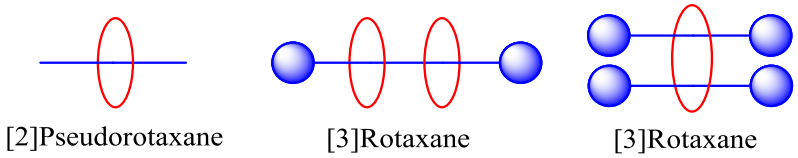


Figure 1.1 Nomenclature of pseudorotaxanes and rotaxanes.

The nomenclature of rotaxanes provides information on the number of components that are non-covalently interlinked by the use of the prefix [n], which is followed by the complex name; pseudorotaxane or rotaxane (Figure 1.1). For example a [2]pseudorotaxane would be composed of a macrocycle on an axle, which is free to slip off whereas a [3]rotaxane would consist of two macrocycles on an axle with bulky stoppers preventing the macrocycle from unthreading. Alternatively a [3]rotaxane can be comprised of two stoppered axles through a single macrocycle.[28]

1.3 Early Methods of Synthesis

Early methods of rotaxane synthesis were based on a statistical approach. Harrison[29] reported the first synthesis of a rotaxane based upon the statistical probability of

pseudorotaxane formation then the addition of stoppers to trap the macrocycle onto the thread. This was carried out by attaching the macrocycle to a solid support phase, then treating the supported macrocycle with the thread and reactive groups that can form stoppers. Even with more than 60 threading and stoppering cycles performed on the support, yields of the rotaxane, of only 6% were obtained. Even so, these experiments were the first to produced evidence for the formation of these mechanically interlocked architectures. Up until the early 80's, attempts at rotaxane formation were still relying on the chance interaction of thread and crown. This was clearly not an efficient way to synthesise rotaxanes and in the last three decades there has been much more emphasis on 'directed' synthesis of these supramolecular complexes.

1.4 Self Assembly Approaches to Rotaxane Synthesis

The development of both directed and self assembly approaches to rotaxanes, led to improved yields and interest grew in their potential applications. There are three general methods to forming rotaxanes *via* the self assembly approach; these include threading followed by stoppering, clipping and slipping (Figure 1.2).[30]

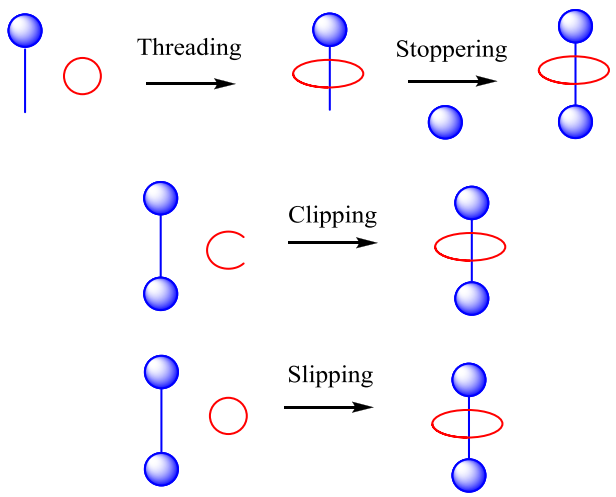


Figure 1.2 Schematic representations of self assembly methods toward the synthesis of rotaxanes.

In the first approach, the macrocycle is threaded onto the axle and bulky stoppers are attached to prevent the macrocycle from unthreading. The clipping approach utilises a

preformed stoppered axle and a macrocycle precursor is ‘clipped’ around it. In the slipping approach the axle and macrocycle are preformed and heat is applied to distort the macrocycle so that it can pass over one of the stoppers. Once cooled the macrocycle is trapped on the thread.

The slippage approach requires the precise tuning of the macrocycle cavity and stopper size. Enough thermal energy needs to be added to the system to allow the macrocycle to squeeze it over the stoppers. On cooling the macrocycle can’t surmount the steric barrier of the stopper.

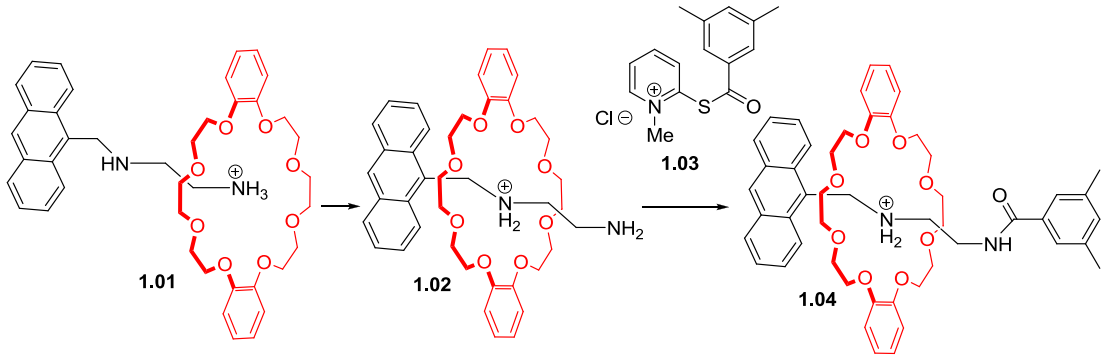
1.5 Non-Metal Templates

The use and manipulation of intermolecular forces has provided an abundance of mechanically interlocked molecules. There are many examples of metal ligand interactions used to template the synthesis of rotaxanes and catenanes. This thesis focuses on the assembly of rotaxanes using the interactions between crown ethers and ammonium or pyridinium templates.

1.5.1 Hydrogen bonding

Hydrogen bonding is an important interaction found in nature and is used to assemble DNA double helix and the secondary structure of peptides. Synthetic chemists have used hydrogen bonding to construct rotaxanes and catenanes. One of the more widely used templates for rotaxane formation is the secondary ammonium ion binding site which interacts with crown ether type macrocycles primarily through hydrogen bonding. This binding template was first investigated by both Busch[31] and Stoddart.[21,32] Busch has developed a thread with an anthracene moiety at one terminal end and a primary amine on the other. Incorporated in the thread is a secondary ammonium ion available for binding with dibenzo-24-crown-8 (DB24C8). The macrocycle is trapped onto the axle in an acylating reaction to give rotaxane **1.04** shown in Scheme 1.1. The solid state structure of the rotaxane showed the hydrogen

bonding between the ammonium ion hydrogen's and crown ether oxygen atoms that template the interlocking of the two components.



Scheme 1.1 Interfacial synthesis of rotaxane **1.04**, facilitated by hydrogen bonding in a 'threading followed by stoppering' protocol.[31]

Stoddart[32-33] incorporated both one and two ammonium binding sites into axles. In a 'threading followed by stoppering' protocol with DB24C8 the group successfully synthesised both [2] and [3]rotaxanes using this binding motif Figure 1.3.

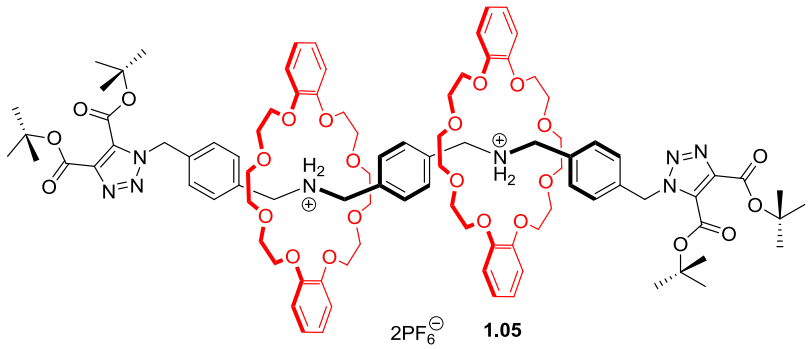
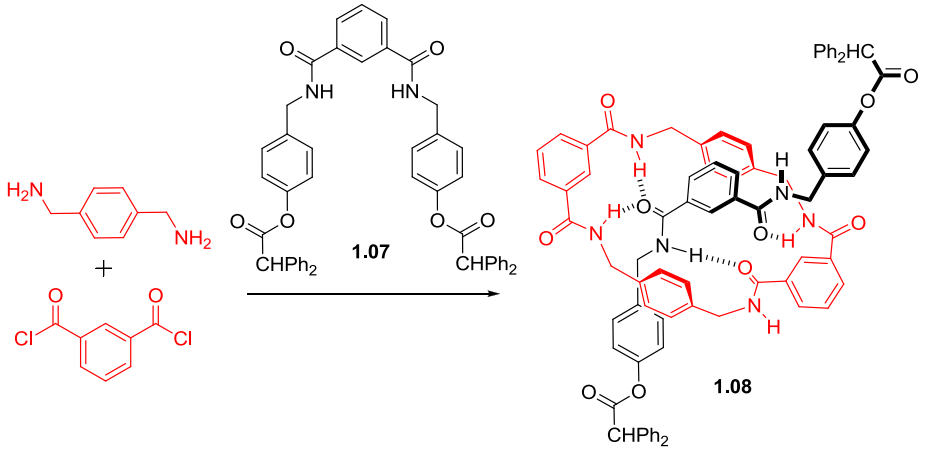


Figure 1.3 [3]Rotaxane containing two secondary ammonium ion binding sites.

Hydrogen bonding is also a valuable interaction in the synthesis of amide containing rotaxanes. Tetralactam macrocycles were originally developed by Hunter[34] and Vögtle[35] towards the synthesis of catenanes. Leigh[36] discovered a catenane synthesis from two simple reagents and initially exploited this approach in a clipping strategy where the amide groups are used to both construct the macrocycle and direct rotaxane formation with an amide template.[37] *p*-Xylylenediamine and isophthaloyl dichloride provide the macrocycle. The

presence of an amide containing thread in the reaction solution acts as an auxiliary for the macrocycle to form around and provides an axle for rotaxane formation all mediated by hydrogen bonding (Scheme 1.2).



Scheme 1.2 Leigh's use of hydrogen bonding to synthesise [2]rotaxane **1.08**.

Further development of the amide binding template towards the synthesis of higher order rotaxanes has been realised by Vögtle. Synthesis of a [3]rotaxane composed of two tetralactam macrocycles and a thread with two amide stations was successfully achieved however yields of the [3]rotaxane were very low.[38] More recently the group has created complex architectures utilising threads with amide binding site and sulfonamide wheels where the wheels are capable of bridging to one another when more than one is present.[39]

1.5.2 π-π Interactions

The use of π-π interactions to form rotaxanes has been employed by a number of groups. This relies on using a π electron deficient component and a complimentary π electron rich component. A recent review by Stoddart has discussed the importance of this intermolecular interaction in the formation of mechanically interlocked structures.[40] Work carried out by Stoddart in the early 90's has shown how utilisation of these interactions can form rotaxanes.[41] The cavity of the electron deficient cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) macrocycle **1.09** has been shown to bind with the electron rich 1,5-dimethoxynaphthalene (DNP). There are both face to face and edge to face π-π interactions observed in the solid state structure of the pseudorotaxane. As well as binding with dihydroxynaphthalenes the

CBPQT^{4+} macrocycle **1.09** has also been shown to bind with biphenyl[42] and the π-electron donor tetrathiafulvalene (TTF) unit.[43] Stoddart has successfully produced a number of rotaxanes using this macrocycle including [2]rotaxane **1.10** shown in Figure 1.4.[44]

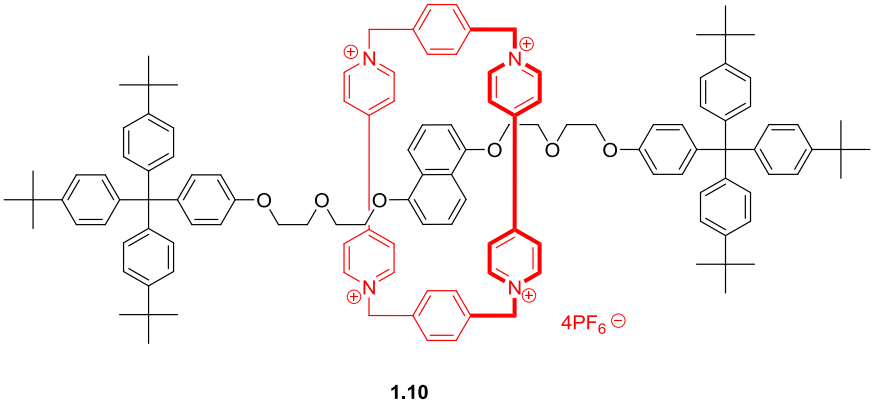


Figure 1.4 Stoddart [2]rotaxane **1.10** with a DNP binding site and CBPQT^{4+} macrocycle.

The Becher[45] group have also used CBPQT^{4+} macrocycle to synthesise [2]rotaxanes with multiple TTF binding sites as shown in Figure 1.5. The CBPQT^{4+} macrocycle can 'shuttle' from one TTF site to the other. Threads with up to three stations were synthesised containing TTF binding sites.

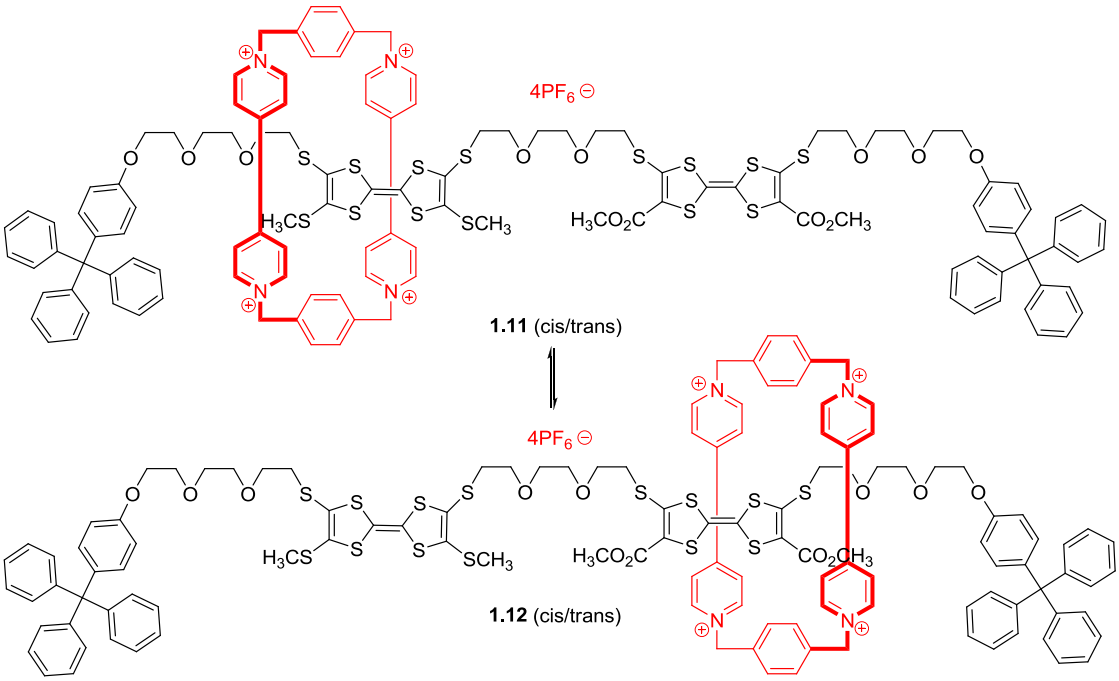


Figure 1.5 Becher group [2]rotaxane with two TTF units and a CBPQT^{4+} macrocycle.

Other groups have exploited the use of π-π interactions in the formation of interlocked structures. Loeb and co-workers[46] developed the *bis*pyridinium template which has been shown to have excellent binding *via* both π stacking and hydrogen bonding interactions with crown ether type macrocycles. This binding motif has been successfully used to synthesise a number of mechanically interlocked architectures. Loeb and co-workers have also used the *bis*pyridinium template to design more intricate supramolecular structures. Using functionalised DB24C8 he was able to synthesise a variety of branched higher order [n]rotaxanes (n = 2-4) and an example (**1.13**) is shown in Figure 1.6.[47]

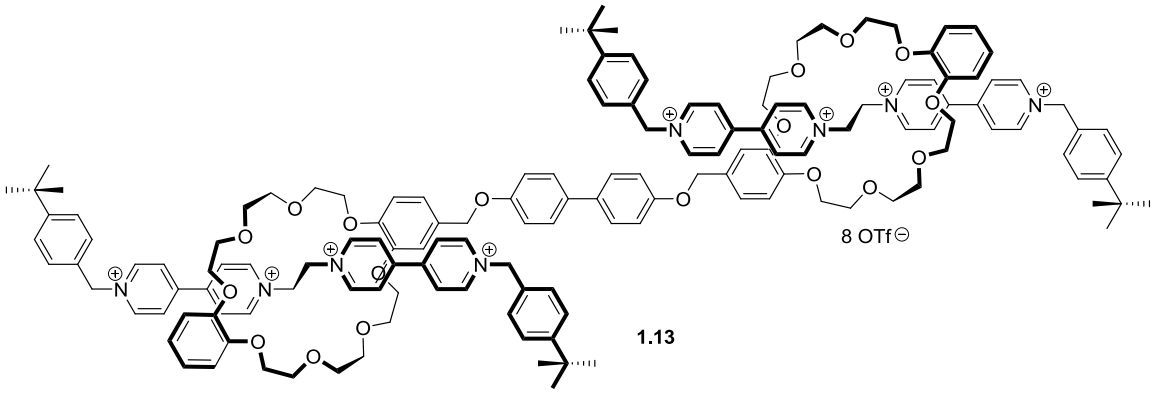
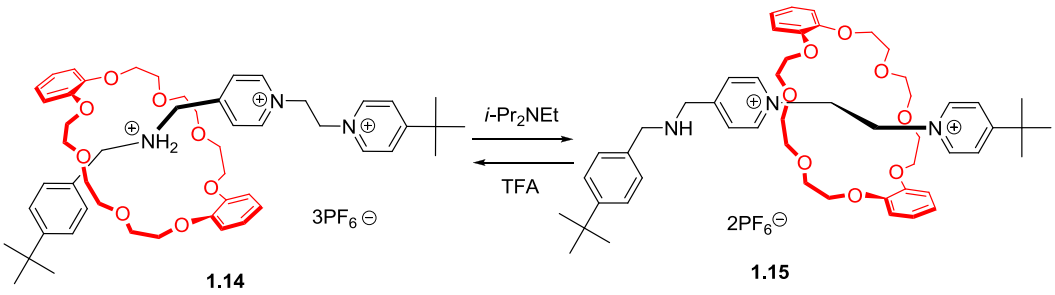


Figure 1.6 Loeb branched [n]rotaxane.

Other groups have utilised the *bis*pyridinium template in order to synthesise a molecular shuttle. Stoddart and co workers[48] have synthesised an axle with two binding sites; a 1,2-*bis*-(pyridinium)ethane site and a secondary dialkylammonium site. DB24C8 is known to bind both of these motifs and with the use of pH they were able to exert some control over the position of the macrocycle on the axle shown in Scheme 1.3. The two sites have different binding affinities with DB24C8 with the K_a of the secondary dibenzylammonium hexafluorophosphate site at 420 M^{-1} and the 1,2-*bis*-(pyridinium)ethane hexafluorophosphate site at 167 M^{-1}. When both sites are charged, the DB24C8 resides predominantly over the ammonium binding site. The ammonium site can be deprotonated with Hunig's base then the macrocycle favours the 1,2-*bis*-(pyridinium)ethane site.

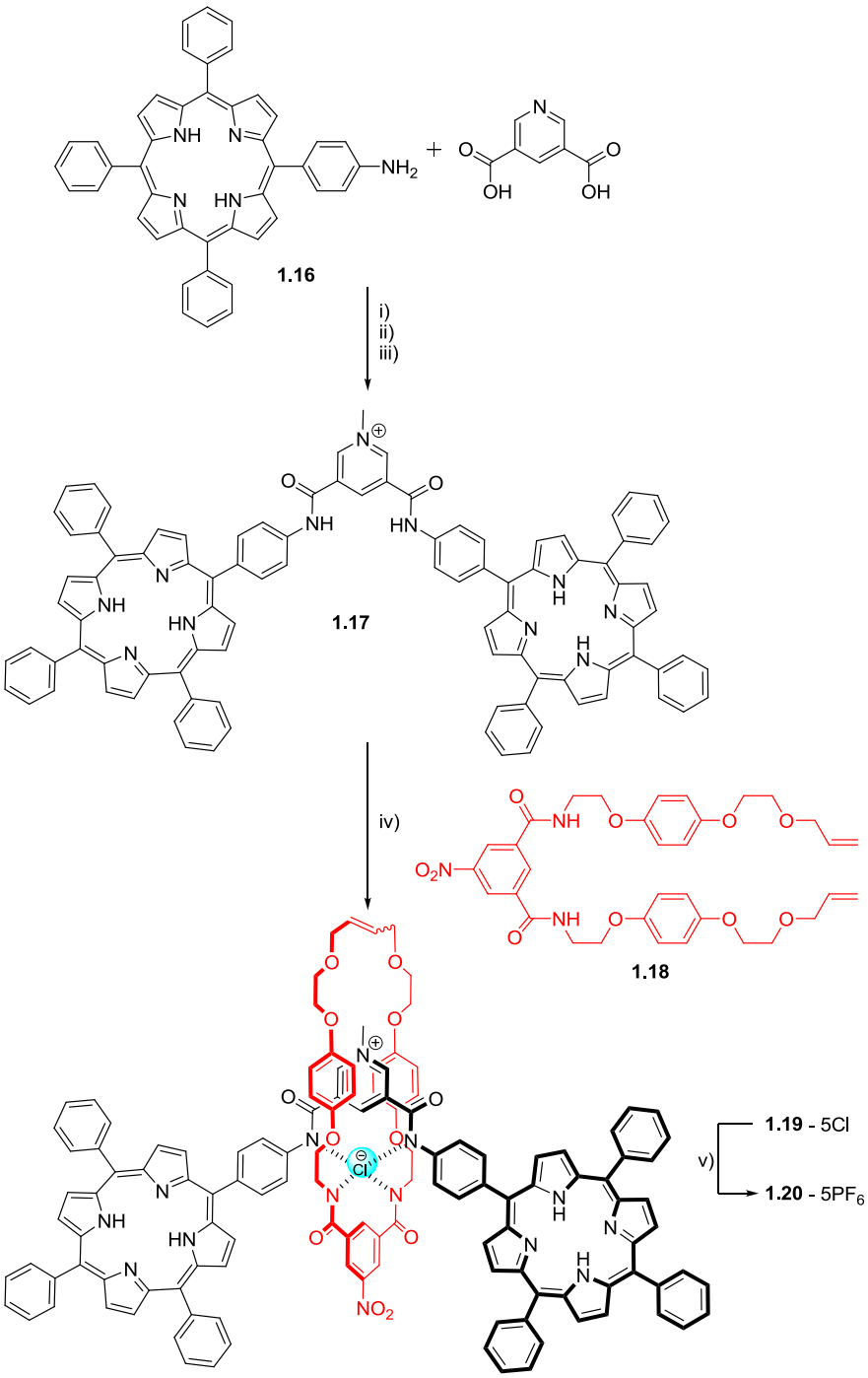
Reprotonation of the ammonium site can be carried out with TFA causing the crown ether to sit predominantly back at the ammonium site as monitored by ^{1}H NMR.



Scheme 1.3 A pH switchable rotaxane.[48]

1.5.3 Anion Template

Anion binding templates can also be used in order to synthesise mechanically interlocked structures. Recent work by P. D. Beer[49] has shown rotaxane formation *via* a chloride anion recognition template using a clipping method. This was performed by taking a stoppered pyridinium chloride ion pair 'thread' with two porphyrin ring stoppers. Carrying out ring closing metathesis (RCM) of the acyclic *bis*-vinyl-functionalised isophthalamide produced the rotaxane **1.20** in a 30% yield. The chloride template in the interlocked system can be exchanged for other ions. With this system the group has successfully developed a number of [2]rotaxanes with porphryin incorporated into the thread and the macrocycle. The Beer group have also used this anion template approach to synthesise a variety of [2] catenanes[50-51] and [2]rotaxanes.[52-53] Further work using anion templates allowed groups to synthesise molecular shuttles[54] and molecular machines.[55] Developing supramolecular structures templated by anions is an interesting area as ions play an essential role in many biological and medical processes.



Scheme 1.4 Beer porphyrin stoppered [2]rotaxane **1.20** formed by anion templation. Reagents and conditions: i) 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDAC), Hydroxybenzotriazole (HOBt), 4-Dimethylaminopyridine (DMAP), CH_2Cl_2, 0˚C, 10 min, RT, 48h, 59%; ii) MeI, dimethylformamide (DMF), 70˚C, 40 mins; iii) NaCl, CH_2Cl_2/H_2O, 95%; iv) Grubbs' 2nd generation catalyst, CH_2Cl_2, RT, 24h, 30%; v) NH_4PF_6, CH_2Cl_2/H_2O, 100%.[49]

1.5.4 Hydrophobic Interactions

Hydrophobic interactions comprise a further weak force that can be exploited in the synthesis of rotaxanes. One of the most notable macrocyclic structures that takes advantage of these interactions are cyclodextrins. They consist of a hydrophobic cavity and a hydrophilic exterior. The first report of cyclodextrins used in the synthesis of rotaxanes using hydrophobic effects as the driving force was by Ogino[56]. Taking either α or β cyclodextrin, the macrocycle was threaded over a 1,10 diaminododecane chain and end capped with a *bis*(ethylenediamine)cobalt(III) complex to provide the bulky stopper groups forming a [2]rotaxane.

Cyclodextrin containing rotaxanes have a wide variety of applications including their use as long lasting dyes. This is a result of the dye functionalised axle being 'protected' by the macrocycle surrounding it, blocking interactions with other molecules giving it an enhanced stability. An example of rotaxanes used as dyes has been reported by Anderson *et al*. [57] Cyanine dyes have potential applications such as their use in photographic sensitizers, laser dyes and biological fluorescence probes, but they suffer from a low photochemical stability. To overcome this limitation, a rotaxane was developed in which the chromophore was trapped inside a cyclodextrin cavity. These rotaxanes showed enhanced fluorescence and photostability in several different solvents.

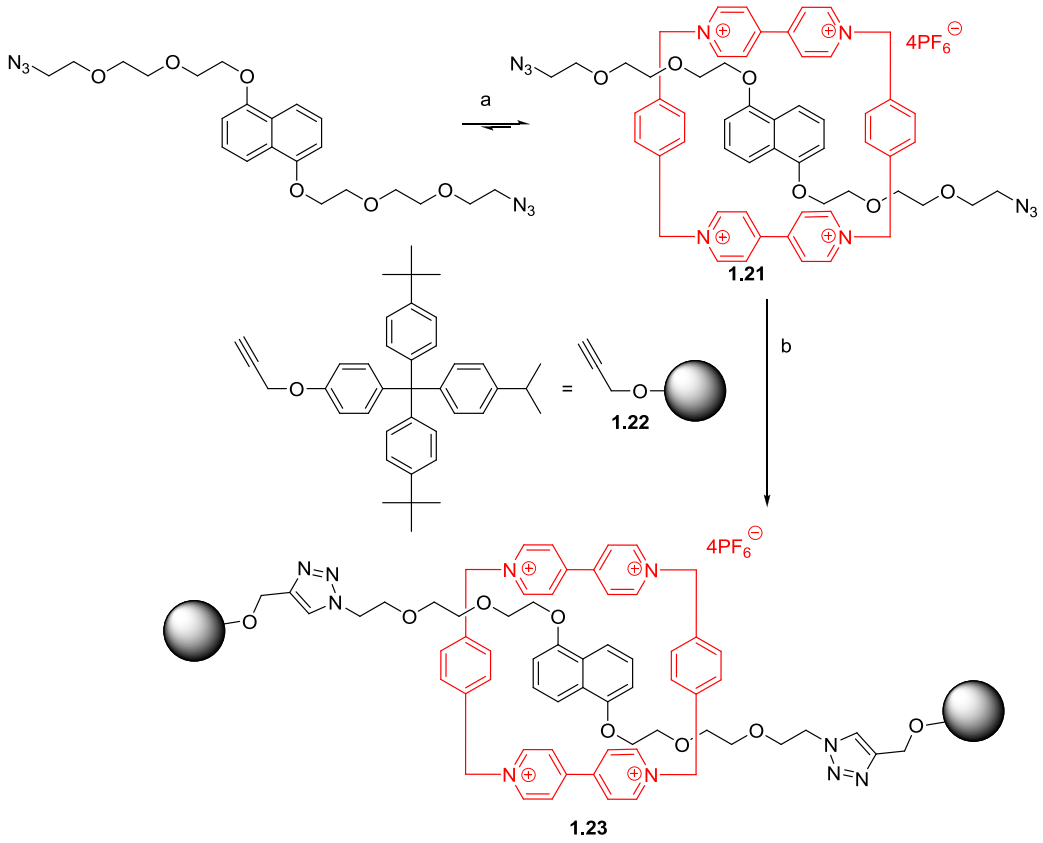
Further work by Anderson *et al*, also addressed some key questions to improve the understanding of such complexes.[58] This included studies on the binding of the dye and the chromophore lifetime when encapsulated within cyclodextrin. In this instance, a chlorotriazine-functionalised azo dye was synthesised and used for the experiments. When encapsulated, it was found that it had increased stability to bleaching but there was no prevention of the dye binding to a cellulose surface (cotton cloth).

1.6 Methods of Formation

Template-directed synthetic methods to produce rotaxanes have been developed to enhance yields of these mechanically interlocked structures. They use specific non-covalent interactions between the components holding them in the appropriate orientation to produce the rotaxane. Both covalent and non-covalent approaches have been used as the concluding step in rotaxanes synthesis. As discussed earlier there are three general methods towards the synthesis of rotaxanes. After reviewing some of the different interactions that are required to form these structures, we now look into more detail at the synthetic protocols that provide us with such mechanically interlocked architectures.

1.6.1 Template Directed Synthesis *via* the 'Threading Followed by Stoppering' Approach

One of the more successful and widely used approaches to the synthesis of rotaxanes, is 'threading followed by stoppering'. It involves a kinetically controlled reaction, where the axle and macrocycle are synthesised separately and the macrocycle is then threaded onto the axle exploiting intermolecular forces to produce an intermediate pseudorotaxane. This is then transformed into a rotaxane by the covalent attachment of bulky stopper groups, onto the ends of the axle.[59] We have seen an example of this previously by Stoddart and Fyfe[33] involving the threading of DB24C8, onto an axle containing a secondary dialkylammonium moiety. The crown is held in place as a result of the weak, non-covalent hydrogen bonds with the axle. The pseudorotaxane is stoppered when the azido terminating ends are reacted with acetylenedicarboxylate in a 1,3-dipolar cycloaddition to give rotaxane **1.05**. Stoddart has also used the Cu(I) catalysed 1,3-dipolar cycloaddition reaction 'CuAAC click chemistry' in order to generate stoppers.[60] [2]Pseudorotaxane **1.21** was formed from a thread containing a DNP binding site and the $CBPQT^{4+}$ macrocycle. Addition of a propargyl functionalised bulky stopper group **1.22** in the presence of ascorbic acid and $CuSO_4.5H_2O$ in DMF allowed the 'click' reaction to proceed providing [2]rotaxane **1.23** in an 82% yield.

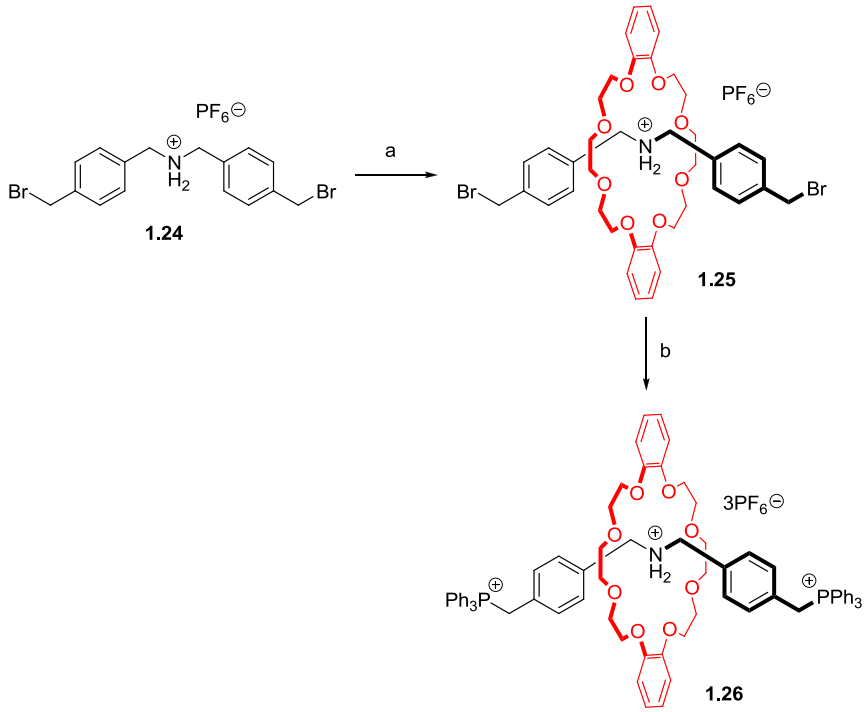


Scheme 1.5 Synthesis of [2]rotaxane **1.23** *via* the 'threading followed by stoppering' protocol. a) DMF, $CBPQT^{4+}$, -10˚C; b) $CuSO_4.5H_2O$, DMF, -10˚C, 82%.

There have been numerous reports of rotaxanes synthesised using the 'threading followed by stoppering' approach, but there are still a restricted number of chemical reactions that can be used to create the stopper. This is because many reaction conditions that could be used to introduce stopper groups include the use of polar solvents, high temperatures, the presence of a strong base or produce competitive hydrogen bonding counter ions. This makes them unsuitable as these may lead to dissociation of the pseudorotaxane complex, producing low yields of rotaxanes.[61]

Triphenylphosphine (PPh_3) can also be utilised as the bulky stopper group in a 'threading followed by stoppering' as shown by Stoddart.[62] A dibenzyl ammonium binding motif containing aryl *p*-bromomethyl groups incorporated can be threaded with DB24C8 in acetonitrile. Once the pseudorotaxane **1.25** was formed the stopper forming reaction was

carried out by the addition of PPh_3 which attacks the bromomethyl groups of the interlocked axle (Scheme 1.6).

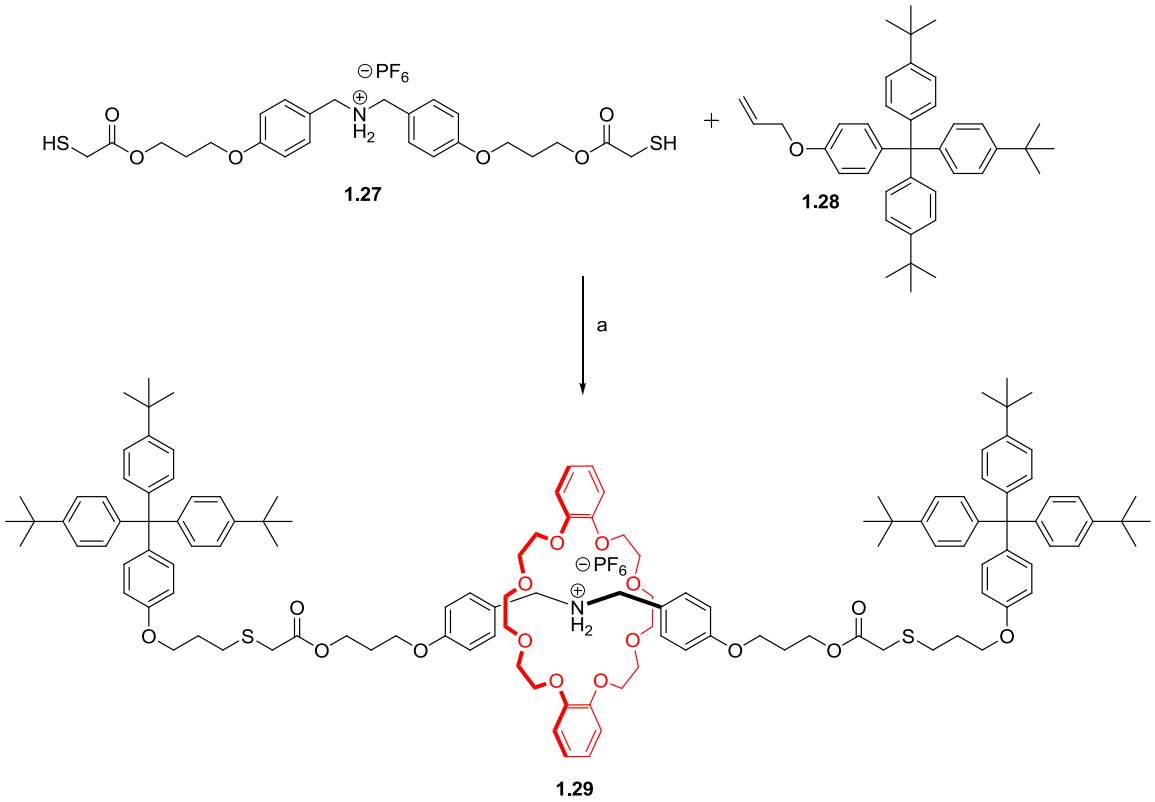


Scheme 1.6 Stoddart synthesis of [2]rotaxane using triphosphonium 'stoppers' *via* the 'threading followed by stoppering' protocol. Reagents and conditions; a) CH_2Cl_2, CH_3CN, DB24C8; b) PPh_3, NH_4PF_6, H_2O, 55%.

Stoddart has further exploited this method to synthesise dendrimers with rotaxane like branches.[63] In this case after the original 'stoppering reaction' with PPh_3, a 'stopper exchange' reaction was then performed utilising a bulky aldehyde in a Wittig reaction and gave the new rotaxane in high yield.

Zheng and co-workers[64] have also taken advantage of the 'threading followed by stoppering' protocol utilising an ammonium ion binding motif and the DB24C8 macrocycle. The thiol-ene coupling reaction was used to attach bulky stopper groups to the terminating ends of the axle trapping the macrocycle into place. A similar approach was first used by Takata[65] in 1999, however, low yields were observed due to the high temperature requirement of the reaction which was found to destabilise the delicate intermolecular forces between components. In Zheng's work,[64] the bulky stoppers were added to the thiols of the

pseudorotaxane in CH_2Cl_2 after irradiation with a UV lamp (λ_{ex} = 365nm) at room temperature under inert conditions to give the [2]rotaxane in a 75% yield (Scheme 1.7).

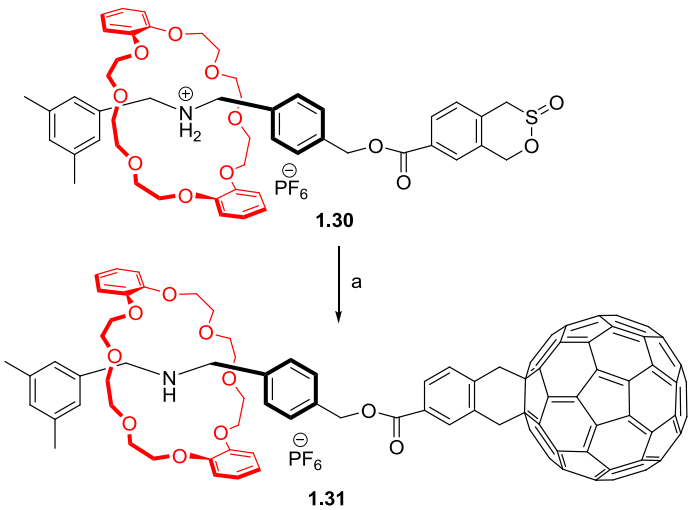


Scheme 1.7 Synthesis of [2]rotaxane **1.29** *via* a thiol-ene stoppering reaction. Reagents and conditions: a) CH_2Cl_2, DB24C8, UV Irradiation (λ_{ex}=365nm), RT, 1h, 75%.

Cycloaddition reactions have been shown to be useful in the synthesis of rotaxanes especially when incorporating stoppers onto pseudorotaxanes in the 'threading followed by stoppering' protocol. We have seen Stoddart[66] report the copper catalysed azide-alkyne reaction now commonly referred to as 'click chemistry' to stopper ammonium centred rotaxanes. Bohmer[67] has also used a cycloaddition reaction to create rotaxanes. He was able to heat a pseudorotaxane containing maleimide end groups with a functionalised anthracene to trap the interlocked complex as its Diels-Alder product in toluene at 100˚C.

Takata[68-69] *et al* have utilised the Diels-Alder reaction to incorporate C_{60} onto rotaxanes producing a variety of C_{60} containing interlocked compounds. The fullerene could be added to both the wheel and axle of the rotaxane. The LUMO level of C_{60} is low enough to

undergo the Diels-Alder reaction so it can be introduced onto the pseudorotaxane according to the 'threading followed by stoppering' approach. The sulfolene can act as a masked diene on the ammonium ion axle trapping the crown wheel by a Diels-Alder reaction with C_{60} at 80°C to afford the C_{60} rotaxane **1.31** in a 33% yield (Scheme 1.8).[68]



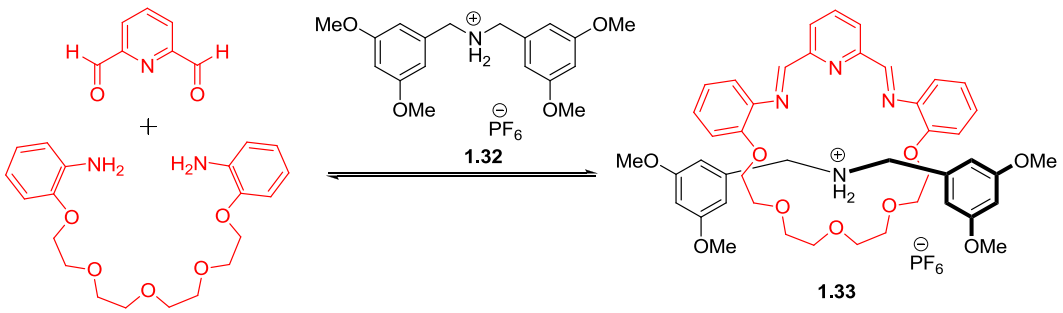
Scheme 1.8 Synthesis of [2]rotaxane **1.31**. Reagents and conditions: a) 1,2-Dichlorobenzene, C_{60}, 80˚C, 33%.

1.6.2 Template-Directed Synthesis *via* the Clipping Approach

In 2001, Stoddart[70] reported the template directed synthesis of a [2]rotaxane in a clipping approach under thermodynamic control. The kinetically stable [2]rotaxane was isolated and characterised (Scheme 1.9). The procedure involved synthesising a macrocycle from two components in a condensation reaction, while encompassing a templating NH_2^+ group of a dialkylammonium ion with bulky stoppers at each end of the axle. This provided a rotaxane consisting of a dumbbell-shaped template surrounded by a macrocyclic diimine. These imino bonds can also be reduced giving a robust diamine macrocycle.

From analysis, it was found that the [2]rotaxane was the thermodynamic product, but did revert gradually back to its original components when removed from the reaction mixture. The dumbbell-shaped axle interacts with the centre of the macrocycle stabilised by N-H···O and N-H···N hydrogen bonding and π-π stacking interactions. This is an excellent example of

a template directed approach using clipping, producing a [2]rotaxane under thermodynamic control. Stoddart has used this approach to synthesise [n]rotaxanes where 'n' is up to 11.[30]



Scheme 1.9 Synthesis of [2]rotaxane **1.34** *via* the 'clipping' approach.

1.6.3 Self-Assembly Approach *via* Slipping

A further protocol for the synthesis of [n]rotaxanes is a relatively simple self assembly approach, known as 'slipping'.[71-72] The macrocycle cavity must be large enough to allow the stoppered ends of an axle to pass through, once an appropriate amount of thermal energy has been introduced to the system. Raymo and Stoddart,[73] have described the synthesis of [n]rotaxanes (up to n = 4) using this method, as well as describing the kinetics of the process. Upon heating together a stoppered axle with a macrocycle in solution, the macrocycle can 'slip'[74] over the bulky terminal end group to produce the molecular assembly. Once cooled, the macrocycle is trapped on the thread as it doesn't have the thermal energy to surmount the steric barrier provided by the stoppers (Figure 1.7). The rotaxane formed is both kinetically and thermodynamically stable at the lower temperature. Lowering the stability of the rotaxane, for example by changing the polarity of the solvent, can make the free components more favourable so now the addition of enough thermal energy favours the 'slipping off' direction.

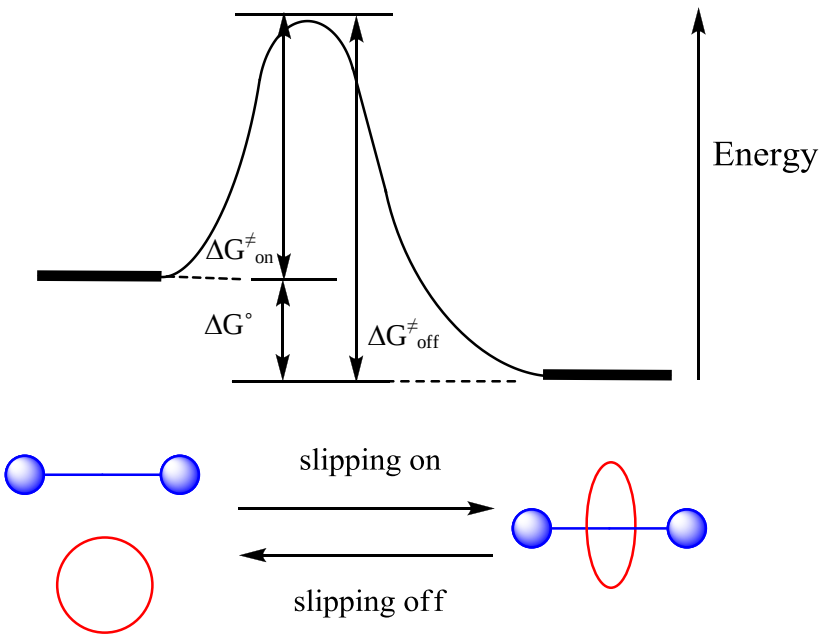
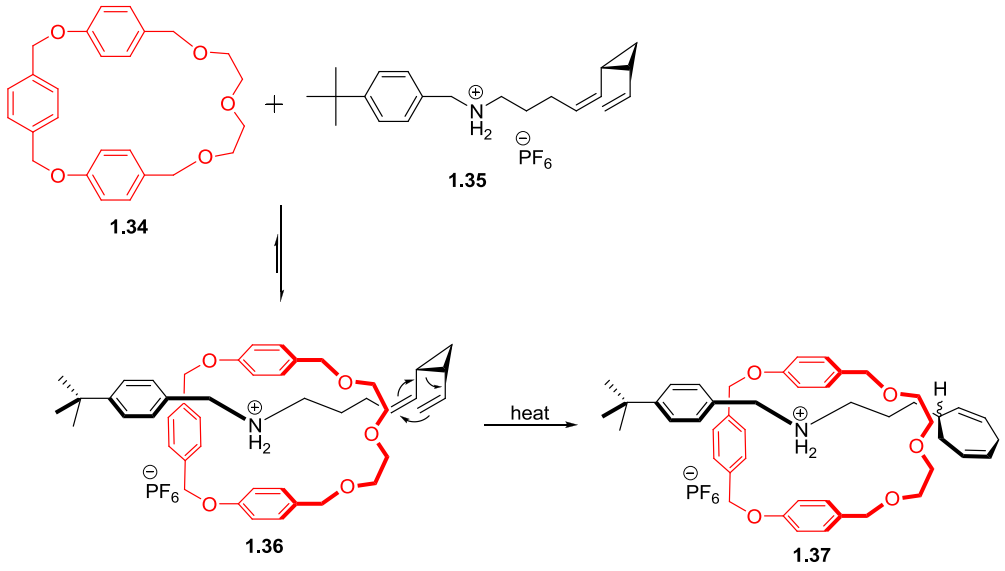


Figure 1.7 Schematic of the 'slipping' protocol.

1.6.4 Threading Followed by Swelling Approach

Chiu *et al*[75] have described a novel method of stopper forming reactions in rotaxane synthesis. The 'threading followed by swelling' approach involves swelling of the terminal group on the axle of a pseudorotaxane complex, enlarging it sufficiently to prevent the macrocycle from slipping off. This approach has some unique features including the enlargement of the terminal group is attained without any additional atoms or functional groups having to be added during rotaxane formation. The macrocycle must be able to pass over the terminal end of the axle before, but not after swelling, and the swelling process should be conducted under controllable conditions. Using a cis-1-[(Z)-alk-1'-enyl]-2-vinylcyclopropane moiety for the swelling reaction, the thread (**1.36**) containing a dibenzylammonium ion was threaded by a macrocycle **1.35**. The [2]pseudorotaxane **1.37** was then converted to a [2]rotaxane **1.38** by heating the complex converting the cis-1-[(Z)-alk-1'-enyl]-2-vinylcyclopropane moiety into a bulky cycloheptadiene group through a Cope rearrangement under relatively mild reaction condition and good yields (Scheme 1.10).



Scheme 1.10 Synthesis of [2]rotaxane **1.38** *via* the 'threading followed by swelling' approach.

1.7 Potential Uses and Scientific Interest

In recent years, there has been a significant development in supramolecular chemistry. The emergence of molecular machinery and highly complex self-assembled structures are becoming more apparent. As a result of such research, a number of advances have materialised in the use of such structures in nanotechnology. Interlocked compounds such as catenanes and rotaxanes are one such area of importance.[76] Rotaxanes in particular are receiving much interest in new research as they have the ability to act as molecular machines and switches,[77] valves, insulated wires,[78] drug delivery vehicles,[79] wheels,[80] scaffolds[81] and in nanoelectronics.[82] Exploiting the week intermolecular forces we have seen many examples of the synthesis of these structures come to light over the last three decades.

1.7.1 Valves

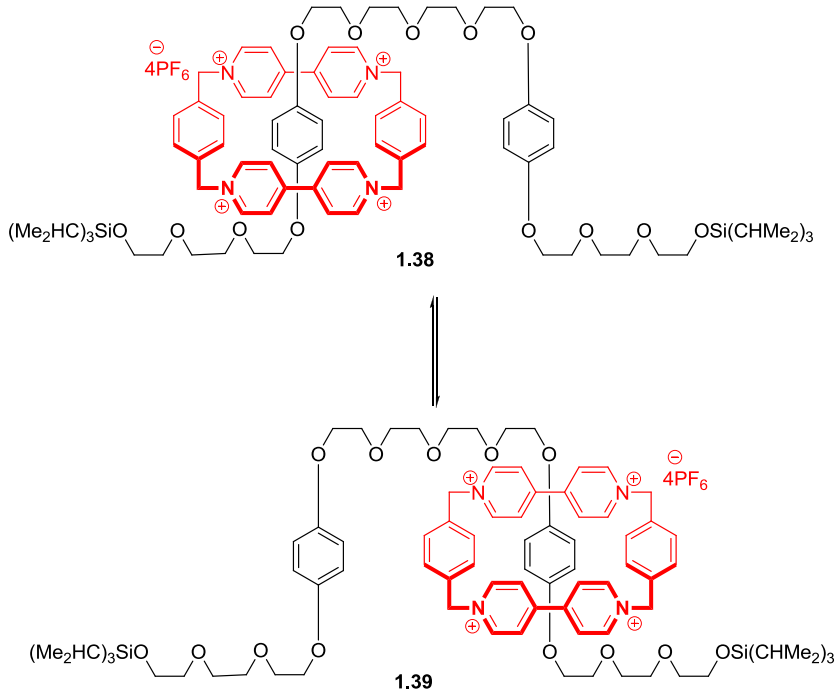
Stoddart[78], has developed rotaxanes that are able to act as valves, trapping and releasing molecules under chemical and light control. These then have applications in sensors and controlled drug release. Using pH stimulation and competitive binding in order to control 'gatekeeper supermolecules', the openings of nanosized pores on silica particles were able to be regulated.

1.7.2 Wheels

Investigating configurational entropy of protein-ligand interactions to measure complex stability, Smithrud[80] used host-guest complexes, rather than the traditional lock-and-key or induced-fit model. Rotaxane axles act as the synthetic hosts, with bulky calixarenes and cyclophanes used as 'stoppers'. Attaching functional groups to the macrocycle (wheel) allowed guest recognition. The host-guest association was measured in both water and DMSO. The binding sites were arranged over several parts of the axle to create a relationship between guest association and conformational changes that occur as the wheel moves between each site. The hosts use several conformations to bind guests so are excellent models of protein binding domains. From these studies, an increase in entropy of binding has been observed on addition of the wheel to the host. Increasing motion of the wheel is thought to be where this originates from, showing favourable configurational entropy which aids complex formation.

1.7.3 Molecular Switches

The relative movement of the interlocked components of a rotaxane can be modulated in a controlled manner in the development of molecular switches and shuttles. There is great interest is such complexes with research into several methods of stimulation including chemical, electrochemical and photochemical processes. Stoddart *et al*[83] reported one of the first [2]rotaxanes to act as a 'molecular shuttle'. They described the complex as a tetracationic "bead" that shuttles between two identical "stations". It consisted of a $CBPQT^{4+}$ macrocycle acting as the "bead" on a polyether thread with hydroquinol units to act as the "stations". The ends of the rotaxane were stoppered by large triisopropylsilyl groups preventing the macrocycle from slipping off. (Scheme 1.11) The shuttling motion was temperature dependant with a large free energy of activation (13 kcal mol^{-1}). Changes in the rate of the macrocycle shuttling were measured using variable temperature ^{1}H NMR.



Scheme 1.11 Stoddart's first example of a molecular shuttle.

A molecular shuttle has recently been reported by Li and co-workers[84] to drive a multilevel fluorescence switch. It is a [2]rotaxane prepared by a thermodynamically controlled, template induced clipping method. The thread has two recognition sites which are separated by a phenyl unit, these are $-NH_2^+-$ and an amide. When protonated, the macrocycle binds to the $-NH_2^+-$ region through a variety of non-covalent interactions. When the ammonium ion is deprotonated, the macrocycle prefers to hydrogen bond to the amide region. Addition of either Li^+ or Zn^{2+} ions to the system then controls the movement from one recognition site to the other. All three processes result in a fluorescent response (Figure 1.8) and it is pH dependant and reversible.

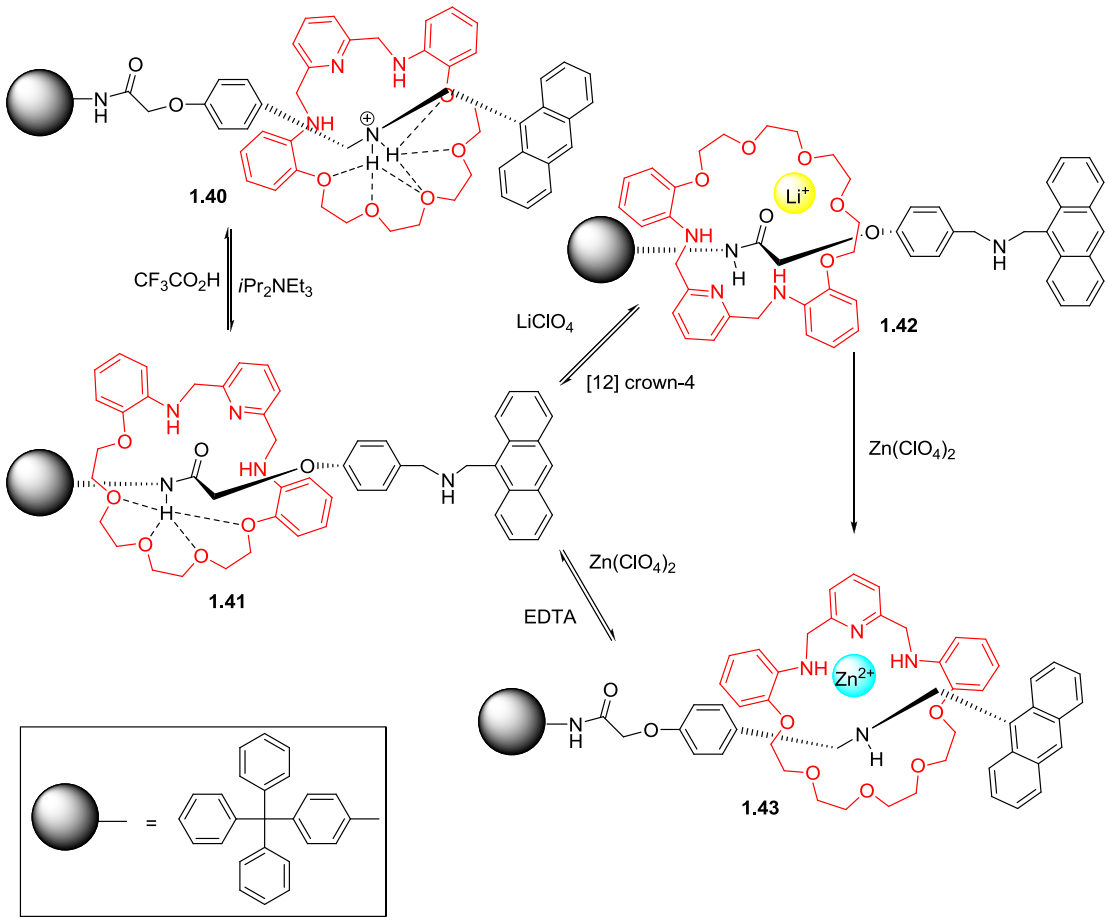
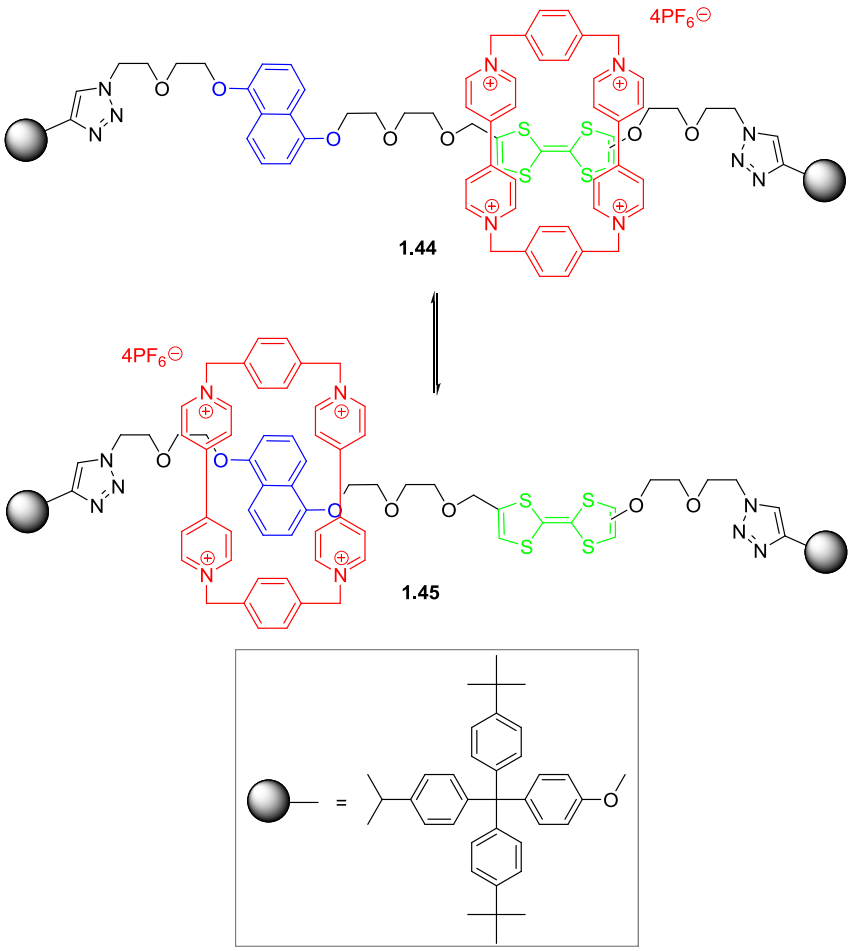


Figure 1.8 A pH switchable molecular switch.

The Stoddart group have successfully synthesised a bistable [2]rotaxane which can be controlled thermodynamically. The macrocyclic ring structure is the π electron deficient $CBPQT^{4+}$ ring and the axle contains two different π electron accepting moieties which are a TTF and DNP units. The $CBPQT^{4+}$ macrocycle was threaded onto an axle with two terminating azide groups. The bulky stoppers were attached in a 'CuAAC' reaction to give the bistable [2]rotaxane. The position of the macrocycle could be controlled *via* oxidation and reduction of the TTF unit (Scheme 1.12).[85]



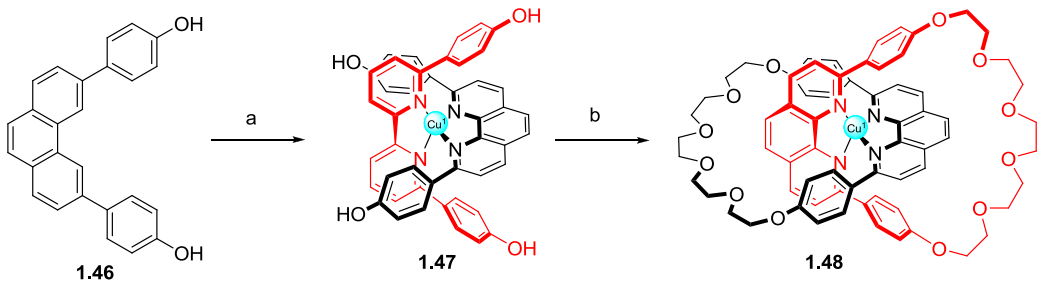
Scheme 1.12 Schematic of a bistable [2]rotaxane.

A more recent example of this molecular switch has been created by Stoddart.[86] They have further developed the bistable [2]rotaxane with a $CBPQT^{4+}$ π electron deficient macrocycle and the axle again containing the TTF and DNP units. Located in the central part of the axle is a 3,5,3',5'-tetramethylazobenzene (TMeAB) unit which is photoactive and can change between its cis and trans conformations. In the axle's neutral form the $CBPQT^{4+}$ macrocycle resides over the more π electron rich TTF unit. Upon oxidation the $CBPQT^{4+}$ is 'switched' to the DNP moiety. The 'switching' process is also controlled by the photo induced isomerisation of TMeAB unit. When in the trans configuration the $CBPQT^{4+}$ macrocycle can move freely between stations. Once in the cis configuration the macrocycle now has a much larger energy barrier to overcome due to steric hindrance which provides further control of the macrocycle position.

1.8 Transition Metal Strategy

Metal templating strategies have been a key area in synthesising interlocked architectures. Using transition metals towards templating the synthesis of supramolecular molecules has been advantageous. Early work by Sauvage and co-workers[87] utilised a transition metal to orientate ligands in an exact position to facilitate the formation of a macrocycle by covalent bond formation leading to the construction of a catenane.

There has been much work using copper (I) as the templating metal due to its preferred tetrahedral co-ordination geometry. It holds the two components in an appropriate orientation to allow further reactions to occur forming the desired interlocked structures. An early example shown by Sauvage[88] has taken two diphenol ligands around the metal ion Cu^+ and reacting with 1,14-diiodo-3,6,9,12-tetraoxatetradecane to give a metallocatanene in a 27% yield (Scheme 1.13). A final demetallation with tetramethylammonium cyanide gives the two interlocked macrocycles. The same method has also been successfully used towards the synthesis of [n]rotaxanes[89-90] and other catenane systems.[91-92] Further development in this area has seen these interlocked structures synthesised in much higher yields.[93] A variety of transition metals can be used in the formation of these supramolecular structures including palladium[94] and ruthenium.[95]



Scheme 1.13 Reagents and conditions: a) $Cu(MeCN)_4.BF_4$; b) DMF, 1,14-diiodo-3,6,9,12-tetraoxatetradecane, 26%.

Other groups have used the transition metal template strategy to synthesise molecular architectures. In 2006 the Leigh group developed the active template approach where the

metal acts as both the template and catalyst.[96-97] For the reaction to proceed, it requires a catalytically active metal centre incorporated into a macrocycle that will allow covalent bond formation to occur in the cavity of the ring. A schematic representation of the reaction is shown in Figure 1.9. In this case a stoichiometric quantity of the metal can be added to 'stitch' the components together. A covalent bond forming step takes place followed by demetallation to give the interlocked structure. This reaction has also been achieved using catalytic amounts of metal. A range of reactions are able to be exploited to synthesise rotaxanes in the active template metal approach. These include the CuAAC click reaction,[96] Cu mediated alkyne homocouplings (Glaser reaction)[98-99] and palladium catalysed cross coupling reactions.[100] There has also been success synthesising catenanes using the active metal template approach using the CuAAC reaction[101] and Glaser homocoupling reaction.[102]

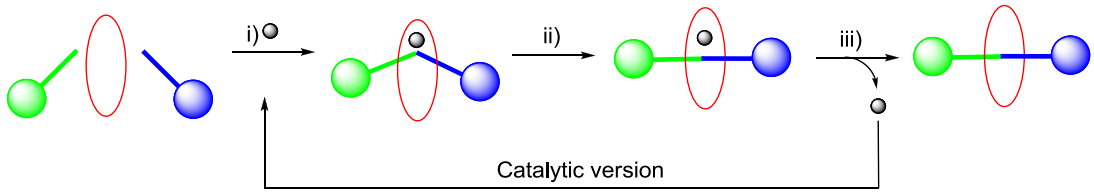
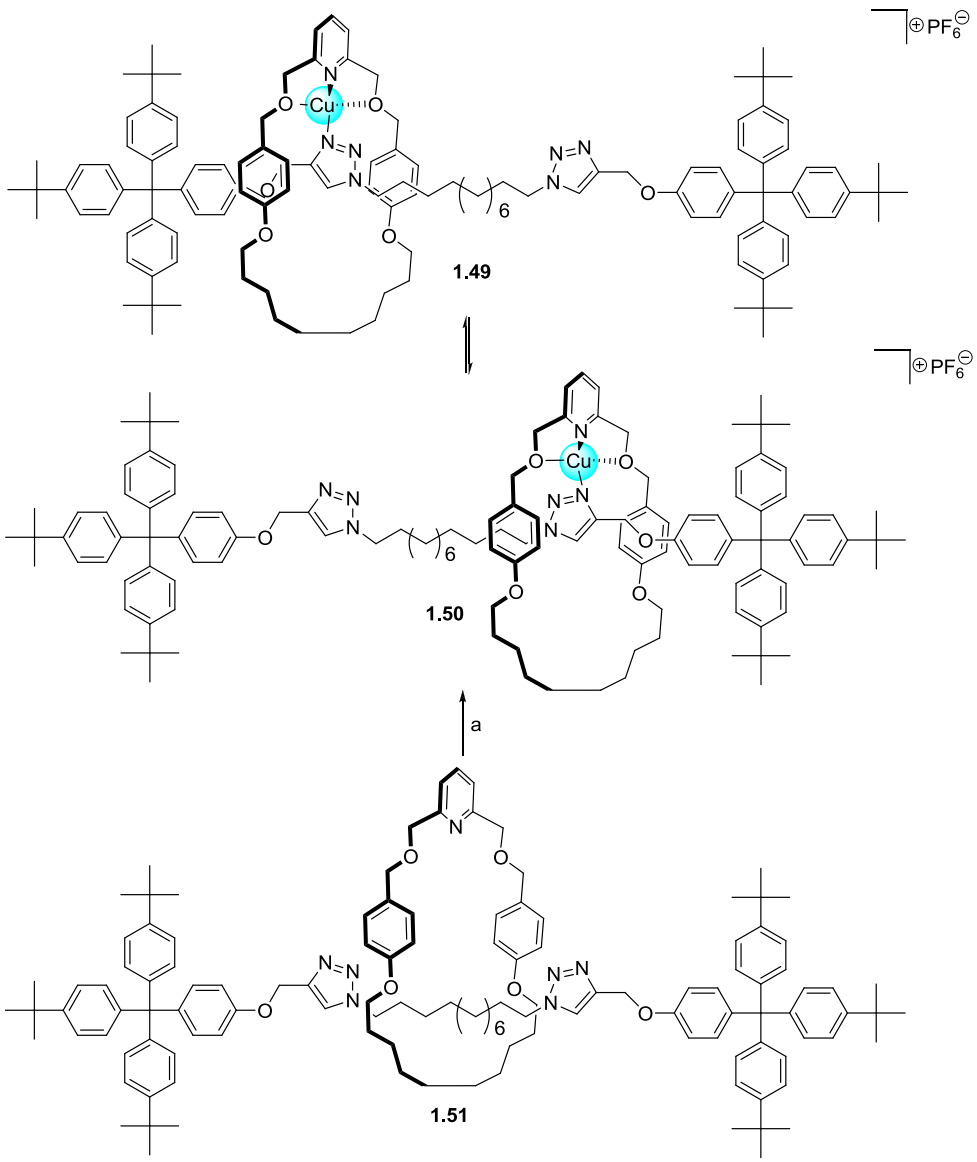


Figure 1.9 Schematic representation of the active metal template protocol. i) Metal addition; ii) Complexation and covalent bond formation; iii) Demetallation and [2]rotaxane formation.

More recently Goldup[103] has also used the active template approach towards synthesising rotaxanes first pioneered by Leigh.[96,104] Using the widely exploited CuAAC reaction and applying it to the active template approach the group have used the copper(I) catalysed azide-alkyne click active template reaction (CuAAC-AT) to synthesise a variety of molecular architectures in high yields. This method has been successful varying the chain length and stopper size and the macrocycle cavity to produce supramolecular structures.

More complex architectures such as molecular shuttles[105] can be synthesised using a metal template protocol. In 2007 Leigh has shown how 'CuAAC click chemistry' can be used to create these structures. In this approach a 2,6-*bis*[alkyloxy)methyl]pyridine macrocycle was

used as the ligand with a $Cu(MeCN)_4PF_6$ metal catalyst and a diazide. The two cycloaddition reactions that occur provide a *bis*triazole thread with an encompassing macrocycle giving [2]rotaxane **1.52** in a 74% yield. Demetallation is performed with KCN and the macrocycle is free to move along the length of the thread. This was confirmed by ^{1}H NMR where shielding was observed on several proton signals of the thread. Reintroducing Cu(I) to the system provided fast shuttling between the two triazole stations (Scheme 1.14). However addition of $PdCl_2$ shows two distinct peaks for the triazole indicating the macrocycle is in a fixed position on the thread and can no longer shuttle between the sites.



Scheme 1.14 Reagents and conditions: a) $Cu(MeCN)_4PF_6$ (1 equiv), CD_2Cl_2(90%)/CD_3CN(10%), 25˚C, 5 min, >99%.

1.9 Summary and Outlook

Over the last few decades we have seen significant developments in the synthesis of supramolecular structures. It has been shown how you can take advantage of intermolecular interactions to enhance binding by using a combination of these interactions. Further exploitation of intermolecular forces allows us to produce a variety of molecules where controlling the position of components can be manipulated by stimulating the system to provide a response. Due to these advances much more complex architectures have been synthesised including molecular machines, wheels and valves. There is great importance in understanding and further developing this area of chemistry as many structures in nature make use of intermolecular interactions including DNA, protein tertiary structures and enzyme-substrate binding.

We have seen there are several routes towards the synthesis of rotaxanes including self assembly methods and template directed synthesis showing varying degrees of success. In this thesis a novel route to synthesising rotaxanes *via* the 'threading followed by stoppering' protocol using the Diels-Alder reaction is explored. We have successfully created a variety of molecular architectures using this reaction which is desirable due to its benign reaction conditions. We also want to develop ways to enhance the binding interactions between axles and macrocycles. Synthesising novel binding templates containing a combination of intermolecular interactions will also be investigated as well as synthesis of novel macrocycles. Merging these ideas we would like to create a library of threads and macrocycles with the ability to construct a variety of molecular machines and switches.

Chapter 2 - Synthesis of [2] and [3]Rotaxanes Using a 'Diels-Alder Approach to Threading Followed by Stoppering'.

2. Synopsis

The introduction in Chapter 1 covers a general overview of rotaxanes and their synthesis. In particular focus is on the different intermolecular interactions and methods used to self assemble rotaxanes. This chapter describes the use of the Diels-Alder reaction in order to synthesise rotaxanes via the 'threading followed by stoppering' approach. A protected maleimide unit was incorporating into an axle containing the well known ammonium ion template. The retro Diels-Alder reaction was performed to deprotect the maleimide allowing DB24C8 to thread onto the axle and bind with the ammonium template. The stopper forming reaction was carried out on addition of cyclopentadiene trapping DB24C8 onto the axle. The presence of the bridgehead group was found to be critical for the moiety to act as an effective stopper. Investigations with the flat phthalimide analogue have shown that unthreading can occur under more extreme conditions.

As well as applying the Diels-Alder approach to 'threading followed by stoppering' with ammonium ion motifs, the group has previously developed a novel bisbenzimidazole binding template that shows significant binding with DB24C8. A modified binding template is reported with better binding activity and additional functional potential suitable for incorporation into molecular machines simply by substituting one of the benzimidazoles for a perimidine group (Figure 2.1). An improved binding interaction was found with this template in comparison to the bisbenzimidazole and we were successfully able to synthesise a [2]rotaxane with this binding site as the axle.

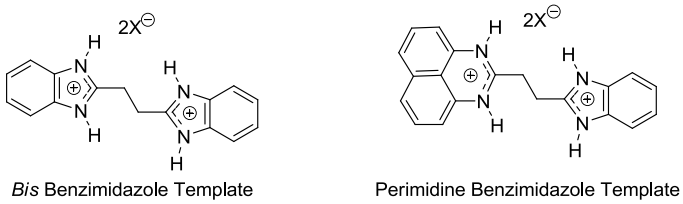
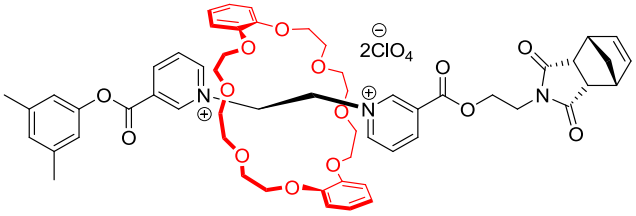


Figure 2.1 *Bis*benzimidazole and perimidine benzimidazole binding templates.

The bispyridinium ethane binding template developed by Loeb and an unreported bispyridinium methane unit which also binds DB24C8 were successfully transformed into rotaxanes using the Diels-Alder approach to synthesise [2]rotaxanes (Figure 2.2).[46]



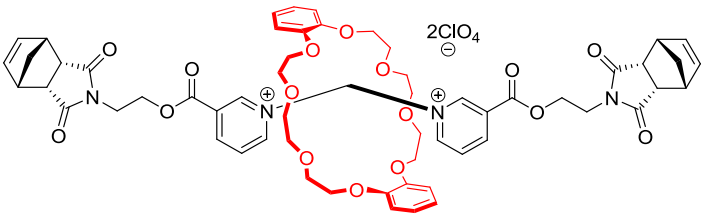


Figure 2.2 Unsymmetrical [2]rotaxane **2.01** and symmetrical [2]rotaxane **2.02**.

2.1 Introduction

As discussed in the original introduction, cycloaddition reactions are ideal for stopper formation as they can occur under mild conditions, spontaneously without catalyst, so not interfering with the weak interactions holding the pseudorotaxane together. There are several examples of cycloaddition reactions in the production of rotaxanes and other interlocked compounds. The thermal azide/alkyne click reaction,[33] the Cu catalysed click reaction,[106] the nitrile N-oxides of Takata[107] and the nitrone of Philp[108] are examples of the breadth of the chemistry possible for stopper formation using this approach. By the very nature of 1,3-diopoles these approaches introduce a level of asymmetry into the thread and hence rotaxane, making analysis more complex. Additionally, conditions to form the 1,3-dipoles and/or catalysts for their addition can complicate the yields and isolation of the interlocked compounds.

The Diels-Alder reaction discovered in 1928[109] has found wide synthetic application.[110] It is a [4+2] cycloaddition reaction that occurs between an alkene or alkyne acting as the dienophile, and a conjugated diene to form an unsaturated six membered ring. It has all the advantages highlighted for the other cycloaddition reactions but the possibility of symmetrical systems making analysis simpler. Additionally, the Diels-Alder reaction can be reversible at room temperature offering the potential of rotaxane synthesis under thermodynamic control. We envisioned that the Diels-Alder reaction of a maleimide with a cyclic diene would be a suitable starting point. As well as having a plane of symmetry, these adducts produce a 3-dimensional stopper molecule from 2-dimensional precursors. The hybridization of the orbitals changes from sp^2 to sp^3 (Figure 2.3) and additional steric bulk is produced by formation of a bridged skeleton.

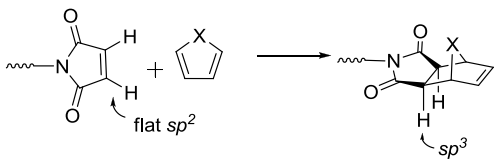


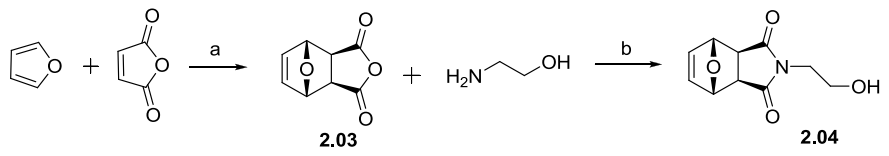
Figure 2.3 The Diels-Alder 'stopper formation' reaction.

The Diels-Alder approach to 'threading followed by stoppering' has been successfully used by Takata introducing buckminsterfullerene (C_{60}) as a bulky stopper, trapping a dibenzo-24-crown-8 (DB24C8) macrocycle on an ammonium ion template though at rather high temperatures. It has also been exploited by Bohmer in the synthesis of interlocked capsules, but remains under utilised as a facile synthesis of rotaxanes by a 'threading followed by Diels-Alder stopper formation'.

A simple but efficient binding motif for the synthesis of rotaxanes is *via* the interaction of DB24C8 with a secondary ammonium ion. Initially investigated by Busch, it binds primarily through hydrogen bonding between the crown oxygens and the NH's.[31] This binding motif has been further developed by Stoddart and has been used to synthesise a range of rotaxanes[21,32] and towards the synthesis of a variety of molecular architectures.[111-113] Herein we report the use of threads incorporating a secondary ammonium binding motif and a protected Diels-Alder maleimide unit in the synthesis of rotaxanes.

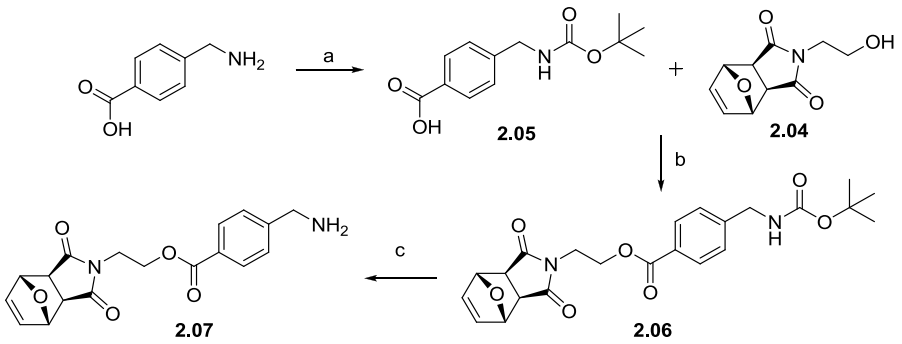
2.2 Synthesis of [n]rotaxanes with Ammonium Ion Binding Motifs

The group has developed a Diels-Alder motif in order to synthesise rotaxanes in a 'threading followed by stoppering' protocol. To carry this out, a maleimide dieneophile must be incorporated onto the terminating end of a suitable axle. To insert the sensitive maleimide into the thread, a pre-stopper approach was developed where the maleimide was introduced in a protected form as the furan Diels-Alder adduct, the synthesis of which was carried out as shown in Scheme 2.1. The *exo* anhydride from the Diels-Alder reaction of furan and maleic anhydride (**2.03**) was reacted in EtOH at 0˚C, with ethanolamine, to give alcohol **2.04** in an 84% yield.



Scheme 2.1 Synthesis of the Diels-Alder adduct. Reagents and conditions: a) Et_2O, RT, 48h, 72%; b) EtOH, NEt_3, 0→70°C; 24h, 84%.

We then wanted to apply the Diels-Alder 'threading followed by stoppering' strategy towards the synthesis of rotaxanes with a secondary ammonium ion binding motif. Beginning with 4-(aminomethyl)benzoic acid, the amine was protected using di-*tert*-butyl dicarbonate providing compound **2.05**. An esterification reaction was then carried out with the Diels-Alder 'gate' using PyBOP (Figure 2.4) as a coupling agent in CH_2Cl_2 with triethylamine to give new compound **2.06**. Finally the amine was deprotected using trifluoroacetic acid (TFA) furnishing the amine **2.07** (Scheme 2.2).



Scheme 2.2 Reagents and conditions: a) Di-*tert*-butyl dicarbonate, dioxane, aq. NaOH 1M, 0°C, 48 h; b) CH_2Cl_2, NEt_3, PyBOP, RT, 24h, 65%; c) CH_2Cl_2, TFA, RT, 24 h, 92%.

PyBOP was used as the coupling reagent in the esterification but is more commonly used to synthesise peptides.[114] Other useful coupling agents including phosphonium reagents such as benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (BOP) and benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP), and uronium reagents such as *o*-benzotriazole-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU) and carbodiimides such as *N,N'*-dicyclohexylcarbodiimide (DCC) (Figure 2.4) were also screened but PyBOP provided the best yields and the simplest work up in the esterification shown in Scheme 2.2.

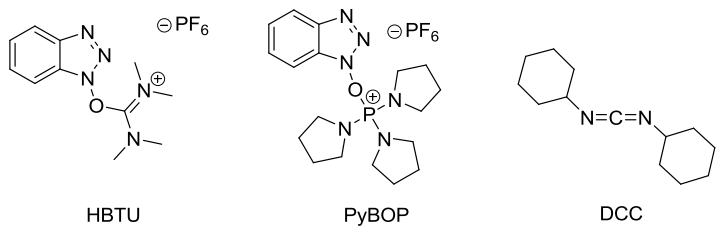
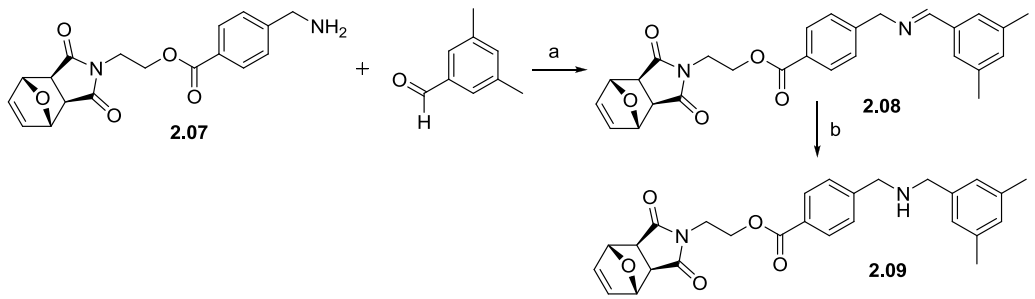


Figure 2.4 Coupling reagents that can be used in esterification reactions.

Reductive amination of the amine **2.07** was then carried out on reaction with 3,5-dimethylbenzaldehyde to give the intermediate imine **2.08** which was reduced using sodium cyanoborohydride giving the neutral thread **2.09** in the final step with 93% yield (Scheme 2.3).

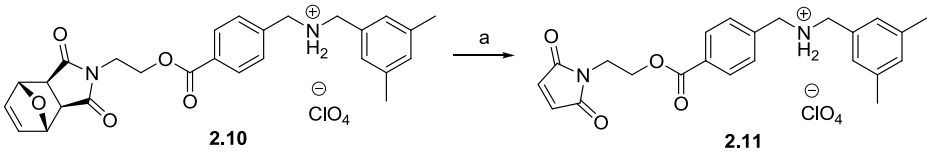


Scheme 2.3 Reagents and conditions: a) MeOH, RT, 24h, 98%; b) MeOH, AcOH, $NaBH_3CN$ (1.1 equiv), RT, 2h, 93%.

To generate the template to induce binding between crown and thread, the amine was converted into the ammonium salt. A weakly or non-coordinating counter-ion such as ClO_4^-, PF_6^- and BF_4^- are key to enhance the interaction between macrocycle and axle.[115] Using a stronger coordinating ion, for instance Cl^- competes with the macrocycle to interact with the cationic thread thus inhibiting pseudorotaxane formation as Cl^- is a good hydrogen bond acceptor. A weakly co-ordinating counter ion does not compete with the hydrogen bonding interactions that template the threading. π-π Stacking interactions between the thread and the macrocycle also take part in pseudorotaxane formation. Although not the best non-competing counter ion the ClO_4^- is more thermally stable than PF_6^- which is important during the thermal retro Diels-Alder reaction to reveal the maleimide pre-stopper.[116-117] The ClO_4^- salt of the thread was generated by protonating the amine with perchloric acid ($HClO_4$)

to give compound **2.10**. The formation of the ClO_4^- salt was confirmed by a shift in the benzylic CH_2's on formation of the dibenzyl ammonium ion and a peak observed at 1094 cm^{-1} in the IR corresponding to the ClO_4.[118]

The retro Diels-Alder reaction of the furan adduct, opened the 'gate' to reveal the maleimide so the DB24C8 can thread onto the ammonium ion template. The maleimide end of the thread is sufficiently sized to slip through the cavity of the macrocycle. Microwave heating the ClO_4^- salt thread **2.10** in acetonitrile was the most efficient method to produce furan and the maleimide thread **2.11** shown in Scheme 2.4.

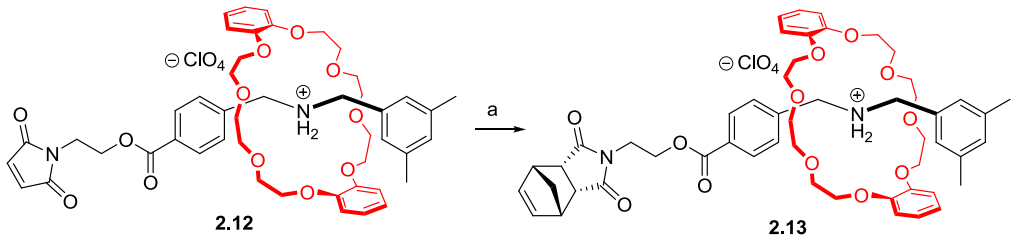


Scheme 2.4 Reagents and conditions: a) CH_3CN, MW, 150W, 110 ˚C, 3h, 78 %.

The choice of solvent is important to consider when creating a pseudorotaxane. Acetonitrile was the preferred solvent as it can dissolve the thread easily and is not too polar so that it interferes with the weak interactions between the crown and thread.[61] To form the pseudorotaxane (**2.12**), two equivalents of DB24C8 were added to push the equilibrium towards complex formation and after 48 hours no free thread (**2.11**) was observed by ^1H NMR. Once the DB24C8 has threaded onto the axle, bulky stoppers must be attached to prevent it from slipping back off. The Diels-Alder reaction was implemented using cyclopentadiene which forms a stopper on the maleimide end of the thread once the macrocycle is in place. Cyclopentadiene is used to create this bulky stopper as it reacts quickly, produces only one of the possible isomers and forms the bulky bridged adduct.[119]

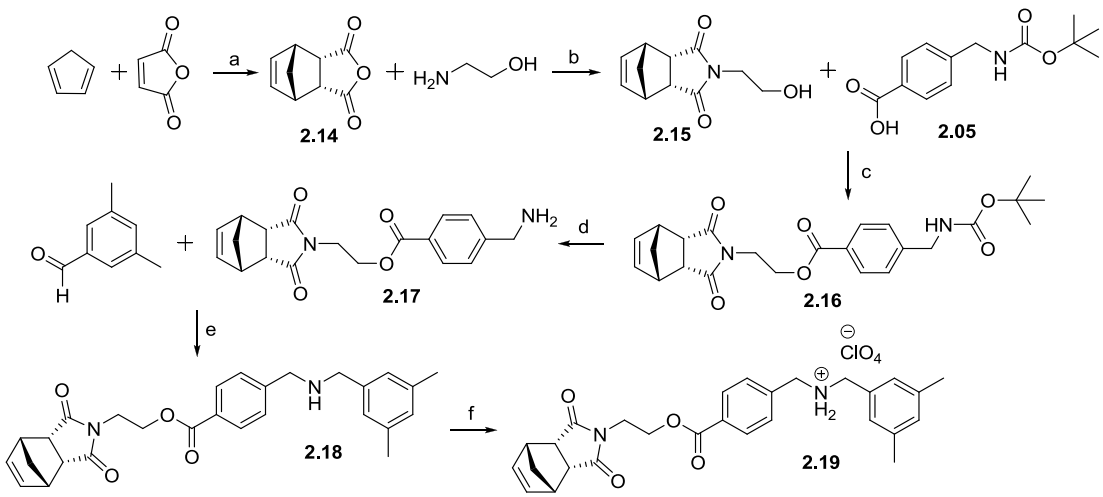
Dicyclopentadiene was heated to crack the dimer into the monomer cyclopentadiene. This was then added to the pseudorotaxane **2.12** at room temperature to perform the Diels-Alder reaction producing only the *endo* complex **2.13** (Scheme 2.5). Excess cyclopentadiene was

removed *in vacuo*. The rotaxane was characterised by high field NMR and HRMS with the [**2.13**-ClO_4]$^+$ ion peak appearing at *m/z* 907.4378.



Scheme 2.5 Synthesis of [2]rotaxane **2.13**. Reagents and conditions: a) CH_3CN, cyclopentadiene, RT, 50%.

Confirmation of the *endo* stereochemistry was provided by independent synthesis of the thread from the known *endo* adduct of maleic anhydride with cyclopentadiene to give **2.14**. Only the *endo* conformation is observed as this is the kinetic product whereas in the reaction of furan and maleic anhydride only the thermodynamic *exo* product precipitates from the reaction medium. The synthesis of a comparison thread from the [2]rotaxane (**2.13**) is shown in Scheme 2.6. Reacting the cyclopentadiene maleimide adduct with ethanolamine gave the *endo* imide alcohol (**2.15**). An esterification reaction between the alcohol **2.15** and acid **2.05** gave the resulting compound **2.16**. Deprotection of the amine was carried out using TFA to form **2.17**. The imine **2.18** was synthesised in MeOH with 3,5-dimethylbenzaldehyde and reduced using sodium cyanoborohydride. Finally the ClO_4^- salt **2.19** was formed by protonating the amine with $HClO_4$.



Scheme 2.6 Synthesis of comparison thread **2.19**. Reagents and conditions: a) EtOAc, Pet. Ether (60-80˚C), 0˚C, 3h, 71%; b) EtOH, NEt_3, 0˚C→70˚C, 37%; c) CH_2Cl_2, NEt_3, DMAP, PyBOP, 0˚C→RT, 48h, 45%; d) CH_2Cl_2, TFA, RT, 24h, 85%; e) MeOH, $NaBH_3CN$, HOAc, RT, 81%; f) $HClO_4$, RT, 97%.

A stacking diagram comparing the ^{1}H NMR of the free thread **2.19** and DB24C8 with the [2]rotaxane **2.13** is shown in Figure 2.5. In rotaxane **2.13** the aromatic hydrogens of both crown and thread are shifted upfield as they become shielded due to the proximity of their π systems. The CH_2's adjacent to the ammonium ion of the thread show a shift downfield due to hydrogen bonding with the oxygens of the crown ether. They also become more complex multiplets due to coupling with the NH_2^+. Now that the thread is encompassed within the crown, the hydrogens of the NH_2^+ undergo a slow exchange on the NMR timescale and are able to express the coupling with the adjacent hydrogens.[32] The imide and dimethylphenyl stopper portions of the thread are relatively unaffected in the rotaxane indicating the DB24C8 macrocycle is situated predominantly over the ammonium region of the thread.

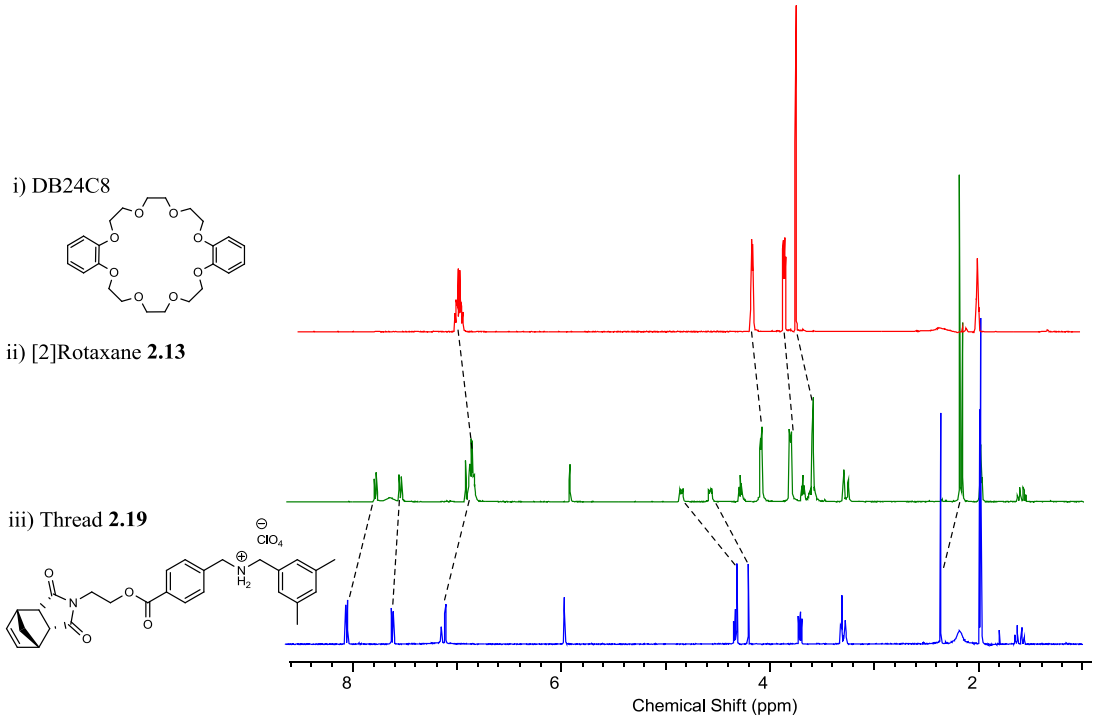
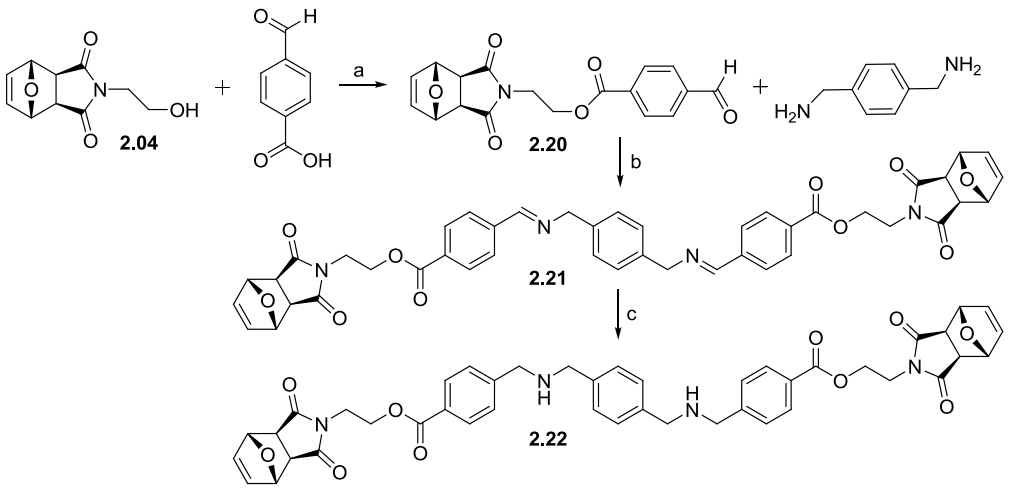


Figure 2.5 ^{1}H NMR (400 MHz, CD_3CN, 300K) stacking plot of i) DB24C8; ii) [2]Rotaxane **2.13** and iii) Comparison thread **2.19**.

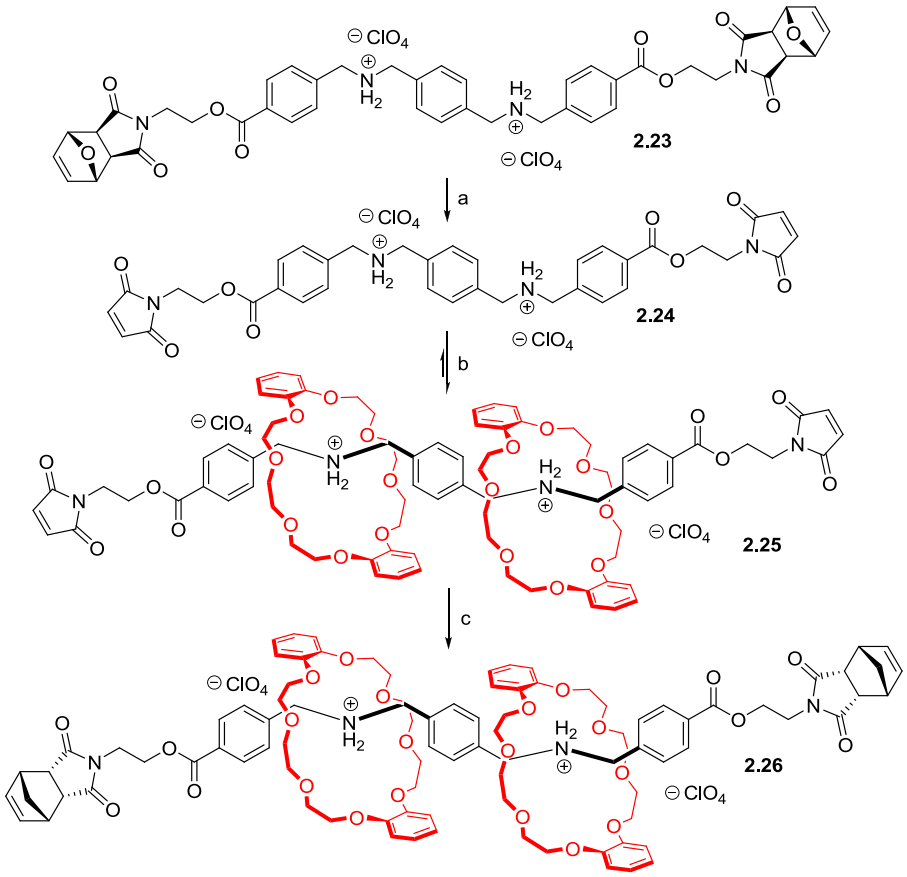
2.2.1 Higher Order Rotaxanes

To exploit the simplicity of the Diels-Alder 'threading followed by stoppering' approach the synthesis of higher order rotaxanes containing two ammonium ion templates was explored. This was done by taking the Diels-Alder adduct (**2.04**) in an esterification reaction with 4-carboxybenzaldehyde providing compound **2.20**. Taking two equivalents of this and reacting with *p*-xylylenediamine, the diimine was obtained (**2.21**). This was reduced using sodium cyanoborohydride giving the new diamine **2.22** seen in Scheme 2.7.



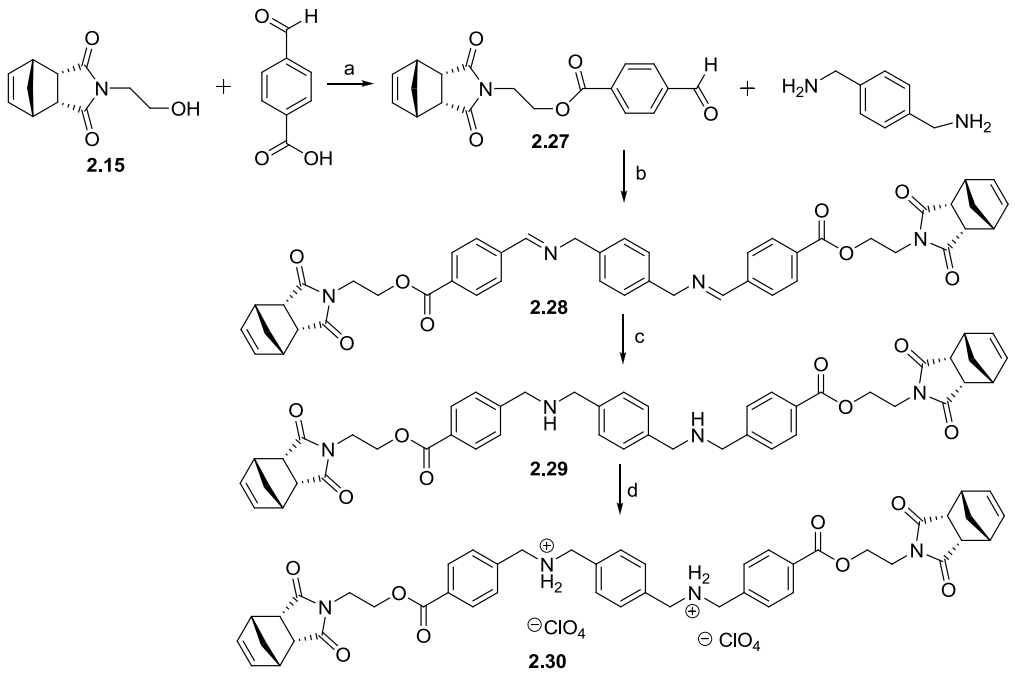
Scheme 2.7 Synthesis of neutral thread. Reagents and conditions: a) CH_2Cl_2, *N,N,N',N'*-tetramethylchloroformamidinium hexafluorophosphate, NEt_3, DMAP, RT, 48h, 64%; b) MeOH, RT, 24h, 92%; c) MeOH, $NaBH_3CN$, HOAc, RT, 78%.

The neutral thread was converted to its ClO_4^- salt (**2.23**) using $HClO_4$ and the retro Diels-Alder reaction was carried out under microwave irradiation in acetonitrile revealing both maleimides and generating axle **2.24** in a quantitative yield. Five equivalents of DB24C8 were added to the axle dissolved in deuterated acetonitrile to drive the reaction towards [3]pseudorotaxane formation. After 48 hours the [3]pseudorotaxane formation had reached completion as determined by ^{1}H NMR with no free thread observed. The [3]pseudorotaxane could also be observed *via* ESI-mass spectrometry with a peak seen at *m/z* 774.7 which relates to the [**2.25**-2ClO_4]$^{2+}$ ion. The macrocycles were trapped onto the axle with the addition of cyclopentadiene to the system providing the [3]rotaxane **2.26** in a 73% yield as shown in Scheme 2.8.



Scheme 2.8 Synthesis of [3]rotaxane **2.26**. Reagents and conditions: a) CH_3CN, MW, 150W, 110 ˚C, 3h, 100%; b) CD_3CN, DB24C8 (5 equiv), RT, 48h; c) CH_3CN, cyclopentadiene, RT, 73%.

Again the comparison thread was synthesised *via* the same synthetic pathway using the cyclopentadiene maleimide Diels-Alder alcohol **2.15**. Reacting this with 4-carboxybenzaldehyde gave intermediate aldehyde **2.27** and the imine **2.28** was formed with *p*-xylylenediamine in MeOH. Reduction of the imine was carried out and finally protonation with $HClO_4$ gave ClO_4^- salt **2.30** (Scheme 2.9).



Scheme 2.9 Synthesis of comparison thread **2.30**. Reagents and conditions: a) CH_2Cl_2, N,N,N',N'-tetramethylchloroformamidinium-hexafluorophosphate, NEt_3, DMAP, RT, 72h, 75%; b) MeOH, RT, 2h, 83%; c) MeOH, $CHCl_3$, $NaBH_3CN$, HOAc, RT, 24h, 92%; d) CH_2Cl_2, $HClO_4$, RT, 79%.

The ^{1}H NMR stacking plot of [3]rotaxane **2.26**, thread **2.30** and DB24C8 is shown in Figure 2.6. In the rotaxane the aromatic protons including the central phenyl ring of the thread are shifted upfield due to the close proximity of the aromatic rings of the crown. For the same reason the crown aromatic protons are also shifted upfield. The crown ether CH_2's are recorded as complex multiplets as each interlocked crown now has two distinct faces in the [3]rotaxane. Shielding effects are seen on these crown CH_2 protons. The $CH_2NH_2^+CH_2$ recognition unit of the thread is shifted downfield and take on the characteristic splitting pattern[32] whilst the Diels-Alder stopper portion of the thread remains relatively unaffected.

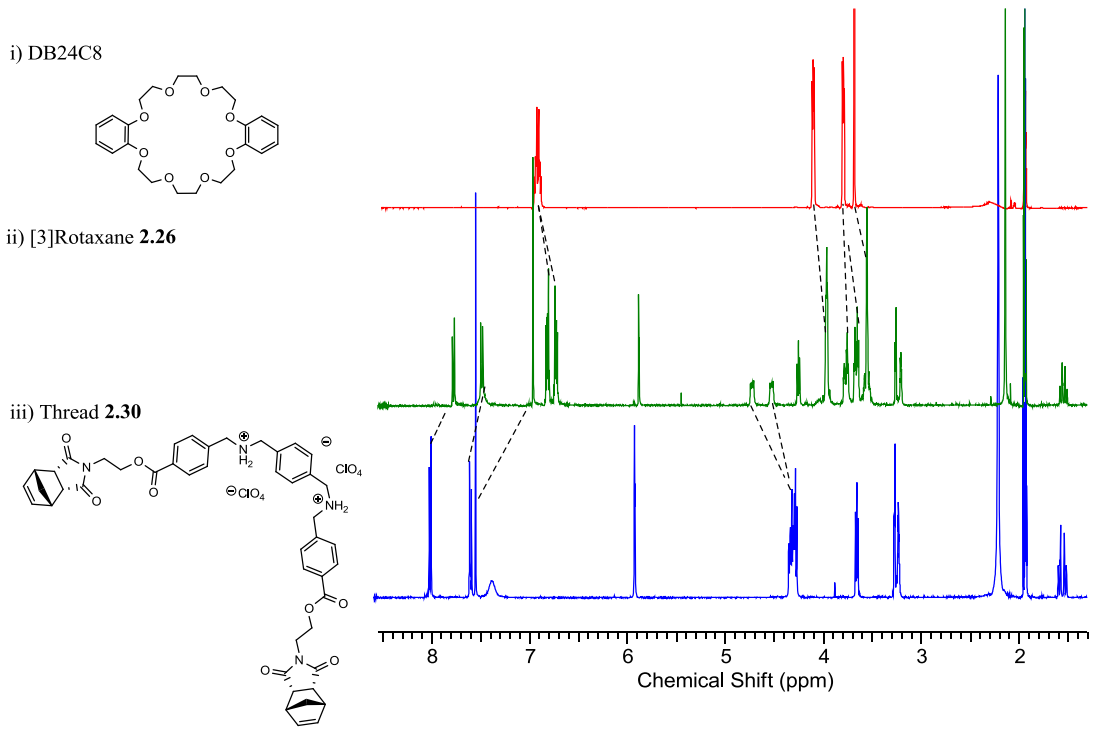
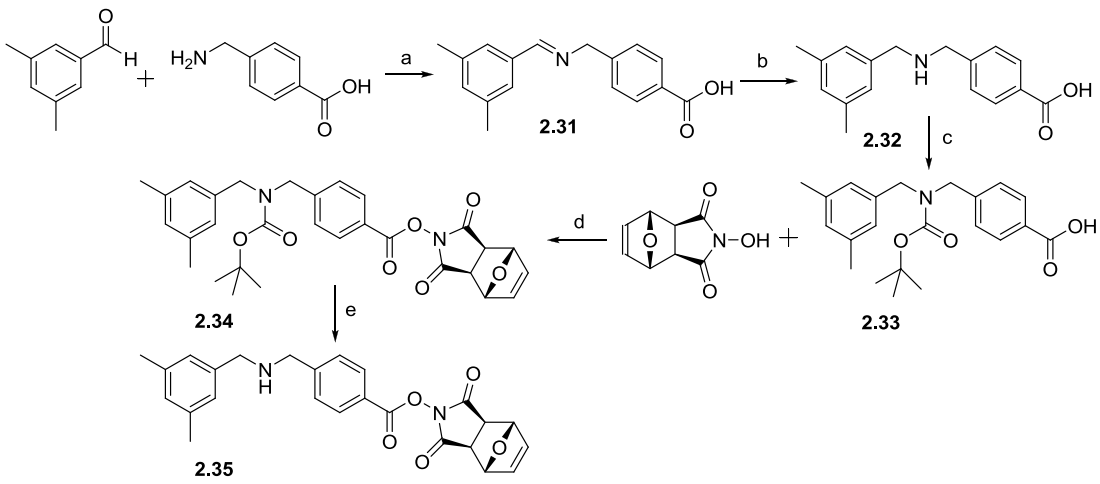


Figure 2.6 ^{1}H NMR (400 MHz, CD_3CN, 300K) stacking plot of i) DB24C8; ii) [3]Rotaxane **2.26** and iii) Comparison thread **2.30**.

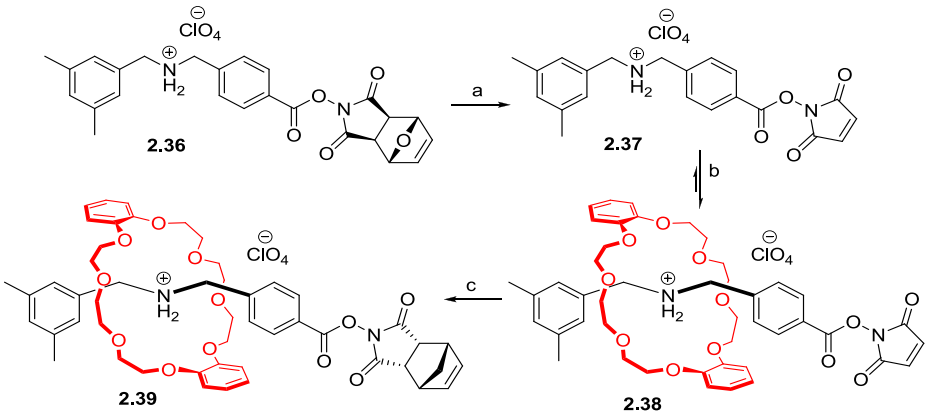
2.2.2 Synthesis of a Short Diels-Alder Stopper Rotaxane

Shortening the chain length between the recognition unit and maleimide pre stopper was investigated to determine how this would affect both yield and rate of rotaxane formation. A [2]rotaxane was synthesised incorporating a Diels-Alder gate with no alkyl spacer between the ester and imide. In this case the thread was synthesised from benzaldehyde and 4-(aminomethyl)benzoic acid, and the imine formed (**2.31**) was reduced using sodium borohydride (Scheme 2.10). As the maleimide group had not been included in the molecule at this stage, it was possible to use sodium borohydride to reduce the imine. The reaction could also be performed using sodium cyanoborohydride and worked with no significant differences in yields of reaction.



Scheme 2.10 Synthesis of neutral thread **2.35**. Reagents and conditions: a) MeOH, RT, 48h, 93%; b) MeOH, THF, $NaBH_4$, 0˚C→RT, 24h, 33%; c) THF, di-*tert*-butyl dicarbonate, reflux, 24h, 94%; d) CH_2Cl_2, *N,N,N',N'*-tetramethylchloroformamidinium hexafluorophosphate, NEt_3, DMAP, 0˚C→RT, 7%; e) CH_2Cl_2, TFA, RT, 2h, 98%.

The amine was protected using di-*tert*-butyl dicarbonate (**2.33**) and the esterification could then be performed with the commercially available short Diels-Alder stopper alcohol *exo-N*-hydroxy-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide. It was then necessary to deprotect amine **2.34** and this was carried out using TFA to provide the neutral axle **2.35** shown in Scheme 2.10 in a 98% yield.



Scheme 2.11 Synthesis of [2]rotaxane **2.39**. Reagents and conditions: a) CH_3CN, MW, 150W, 110˚C, 3h, 34 %; b) CD_3CN, DB24C8, 60 ˚C, 1 month; c) CH_3CN, cyclopentadiene, RT, 85%.

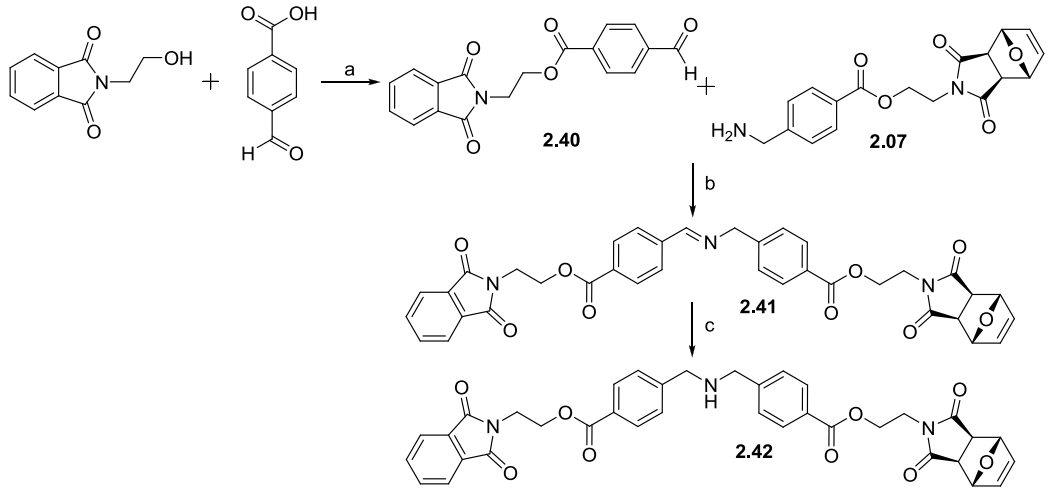
The neutral axle was converted to the ClO_4^- ammonium ion (**2.36**) with $HClO_4$ and the retro Diels-Alder reaction was performed under microwave conditions to give the open gate axle

2.37. Two equivalents of DB24C8 were added to the axle in deuterated acetonitrile to push equilibrium towards pseudorotaxane formation (**2.38**). The threading rate of this axle was much slower than the axle with the alkyl chain between the ester and maleimide (**2.11)** at similar concentration. The close proximity of the three carbonyl groups probably presents a greater barrier to the threading of the DB24C8. In this case the reaction required heating in order to generate the pseudorotaxane so the macrocycle could surmount the steric barrier. Once pseudorotaxane formation was ≥ 95%, the macrocycle was trapped onto the axle using cyclopentadiene in a Diels-Alder reaction giving the [2]rotaxane **2.39** shown in Scheme 2.11. The comparison thread was not obtained due to low reaction yields and difficulties in purification in the esterification of acid **2.33** and alcohol *endo-N*-hydroxy-5-norbornene-2,3-dicarboximide. However the [2]rotaxane was successfully characterised by IR and ESI-MS giving the expected [**2.39**-ClO_4]$^+$ peak at *m/z* 879.4068. Also observing the ^{1}H NMR the two methylenes of the CH_2NH$_2^+$CH_2 unit were seen to shift downfield to 4.88 and 4.54 ppm from 4.34 and 4.19 ppm and undertake the characteristic splitting patterns of the encompassed thread.[32] Other notable shifts were observed in the ^{1}H NMR spectra in comparison to free maleimide axle **2.37** including shielding upfield of the aromatic portions of both axle and DB24C8 and a complicated splitting pattern of the crown ether CH_2‘s.

2.2.3 Investigating the Stopper Size

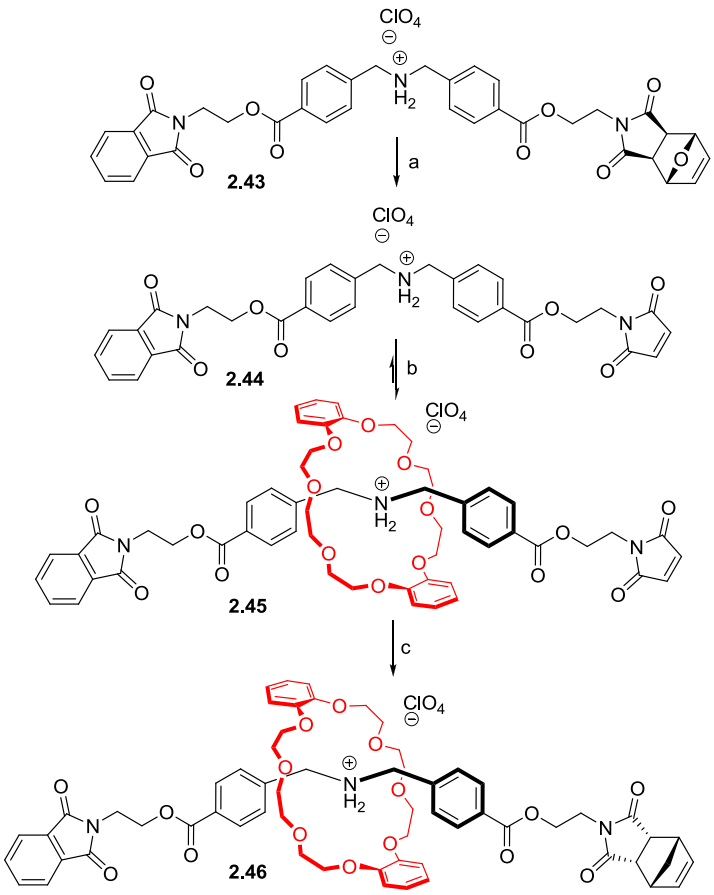
In previous studies it has been found that the threading of DB24C8 over the maleimide stopper was not instantaneous but required time to reach equilibrium. This suggests DB24C8 is only just able to thread over the maleimide end of the axle. It is likely that the two carbonyls of the imide provide both a steric and electronic barrier to the threading of the macrocycle. It was postulated that the bridging CH_2 and sp^3 hybridisation provided by the Diels-Alder reaction of the maleimide with cyclopentadiene might not be required and simpler (smaller) substituents would be just as effective as stoppers. Therefore a stopper functionalised with a phthalimide moiety was investigated to see if this was also able to act

as a stopper. It is known that macrocycles with 24 atom cavities have the ability to fit over the benzene ring so it's possible to see if it's the presence of the carbonyls alongside the phenyl group that allow it to act as a stopper. *N*-(2-Hydroxyethyl)phthalimide was reacted with 4-carboxybenzaldehyde to provide the aldehyde **2.40**. Aldehyde **2.40** was then reacted with amine **2.07** giving the imine **2.41** which was reduced carefully with sodium cyanoborohydride followed to completion by thin layer chromatography (TLC). This gave the neutral unsymmetrical thread **2.42** shown in Scheme 2.12 and no over-reduction of the carbonyl imide was observed.



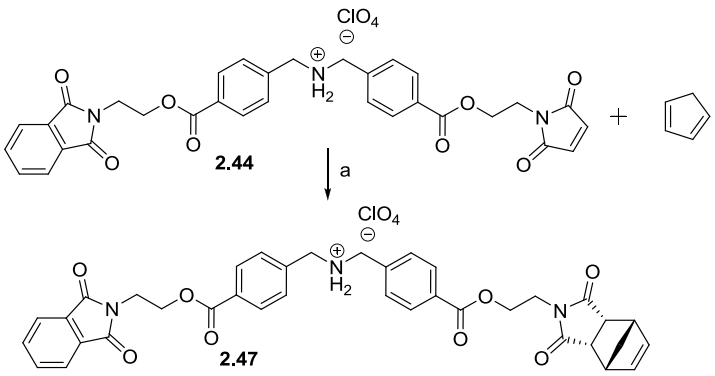
Scheme 2.12 Reagents and conditions: a) CH_2Cl_2, N,N,N',N'-tetramethylchloroformamidinium hexafluorophosphate, NEt_3, DMAP, 0˚C→RT, 24h, 75%; b) MeOH, RT, 24h, 100%; c) MeOH, CH_2Cl_2, $NaBH_3CN$, RT, 1h, 78%.

The thread was converted to the ClO_4^- salt (**2.43**) and the retro Diels-Alder reaction performed by refluxing in a mixture of acetonitrile and toluene to give **2.44**. The [2]pseudorotaxane **2.45** was again made by adding two equivalents of DB24C8 to push pseudorotaxane formation followed by ^{1}H NMR. The stoppering Diels-Alder reaction was carried out with cyclopentadiene to trap the macrocycle onto the axle (Scheme 2.13). The [2]rotaxane (**2.46**) was left to stand in deuterated acetonitrile for two weeks and no dissociation of the complex was observed. The reaction was then heated to 60˚C and after one month there was still no decomplexation observed indicating the [2]rotaxane is stable in this solvent.



Scheme 2.13 Synthesis of [2]rotaxane **2.46**. Reagents and conditions: a) CH_3CN, toluene, reflux, 96h, 86%; b) CD_3CN, DB24C8 (2 equiv), 48h; c) CH_3CN, cyclopentadiene, RT, 85%

The comparison axle was synthesised taking the deprotected maleimide thread (**2.44**) and cyclopentadiene in a Diels-Alder reaction to give new thread **2.47** in a 72% yield (Scheme 2.14). We were then able to compare this thread's ^{1}H NMR shifts to the interlocked [2]rotaxane spectra. Significant shifts in both the aromatic and aliphatic regions of the thread were observed. The methylenes of the $CH_2NH_2^+CH_2$ unit are shifted downfield by 0.42 ppm due to hydrogen bonding with the crown ether oxygens and appear as a multiplet from coupling with hydrogens of the ammonium NH_2^+. The signal for the aromatic hydrogens of both axle and DB24C8 are shifted upfield due to interactions with each other and the crown ether CH_2's become complex multiplets.



Scheme 2.14 Synthesis of thread **2.47**. Reagents and conditions: a) CH_3CN, compound **2.44**, cyclopentadiene, RT, 72%.

The stability of the [2]rotaxane was further examined by recording the ^{1}H NMR spectra in a more polar solvent that would disrupt the intermolecular interactions between the two components. The [2]rotaxane **2.46** was dissolved in DMSO-d_6 and monitored by ^{1}H NMR at room temperature. After 5 days there was no change observed in the spectra. The reaction was then warmed to 40˚C and in this instance unthreading of the macrocycle was observed by ^{1}H NMR. After one month of heating, the macrocycle had completely dissociated from the axle. The ^{1}H NMR spectra can be seen in Figure 2.7. It is apparent that in a polar solvent the disruption of the delicate intermolecular interactions between macrocycle and axle is sufficient to enable decomplexation. In DMSO-d_6, the disruption of the binding interaction between the ammonium ion and the crown favours the free components, though the very slow rate of unthreading highlights the considerable barrier that the macrocycle encounters when threading/dethreading over the phthalimide moiety.

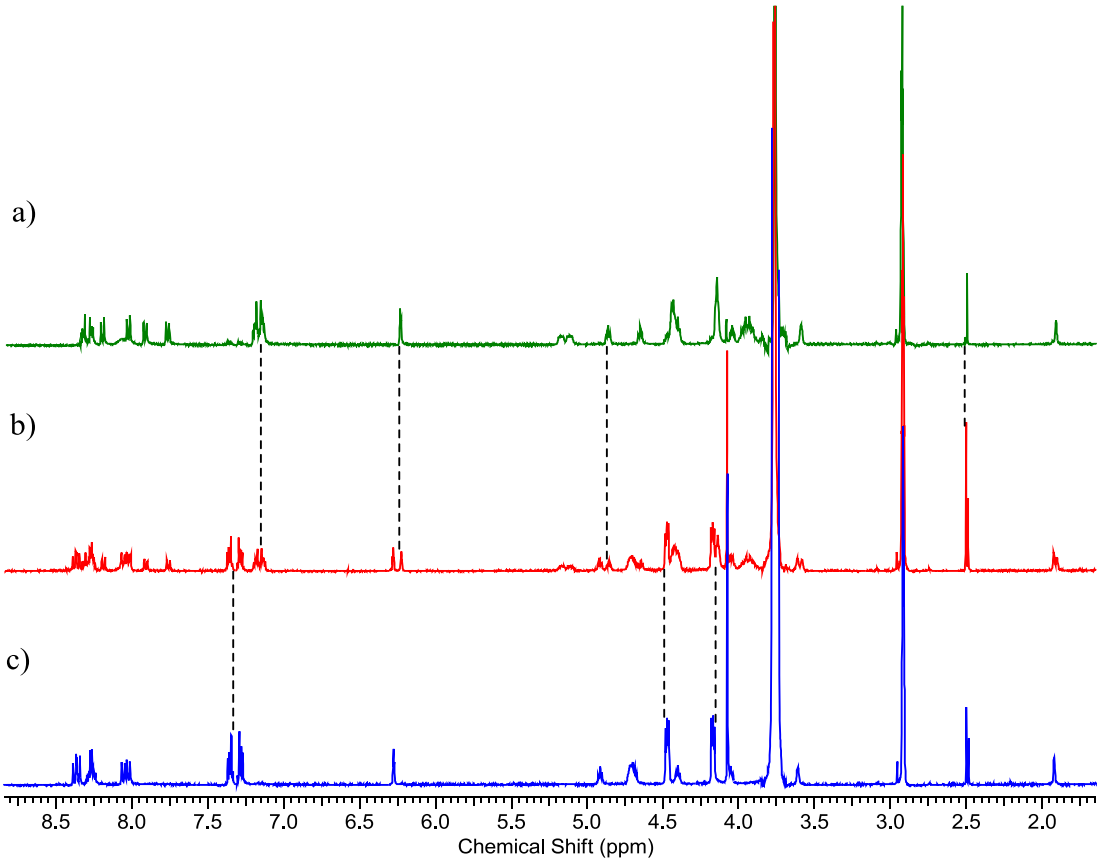
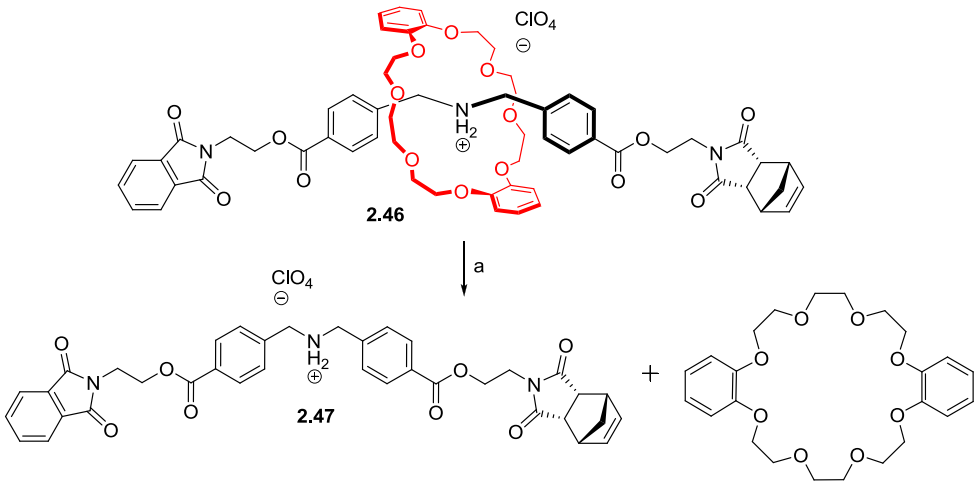


Figure 2.7 ^{1}H NMR spectra of a) [2]pseudorotaxane **2.46** in DMSO-d_6, RT; b) [2]pseudorotaxane **2.46** in DMSO-d_6, 40˚C, 2 weeks; c) [2]pseudorotaxane **2.46** in DMSO-d_6, 40˚C, 1 month.

In Figure 2.7, spectrum a) shows [2]pseudorotaxane **2.46** dissolved in DMSO-d_6. Characteristic peaks indicating complex formation are observed. Most notably the CH_2's situated next to the NH_2 have shifted downfield with their distinctive splitting pattern, and the CH_2's of DB24C8 have taken on the very complex splitting pattern. The DMSO-d_6 solvent disrupts the hydrogen bonding interaction between the crown and thread meaning the crown no longer predominantly resides over the $CH_2NH_2^+CH_2$ unit but spends longer residence time over all the thread. This is exemplified by small shifts of the peaks associated with the stopper region of the thread. You can see in spectrum b) after two weeks of heating at 40˚C in DMSO-d_6, a second set of peaks have appeared which correspond to the free thread and DB24C8. Finally in spectrum c) the [2]pseudorotaxane **2.46** has completely dissociated after one month in DMSO-d_6 at 40˚C to give a spectra of the free thread and DB24C8. The shifts of the free thread in this spectra are identical to *endo* thread **2.47** made

for comparison purposes and show that no maleimide **2.44** from the retro Diels-Alder reaction could be detected. The dethreading is shown in Scheme 2.15.



Scheme 2.15 Reagents and conditions: a) DMSO-d_6, 1 month, 40˚C.

Finally the ClO_4^- thread **2.47** and DB24C8 were dissolved in deuterated acetonitrile and the reaction monitored at 40˚C by ^{1}H NMR. After following the reaction for several weeks, no threading occurred indicating that a retro Diels-Alder reaction is not responsible for the unthreading and that the phthalimide group presents a formidable barrier to threading/dethreading of DB24C8. As DB24C8 is known to thread over a benzene ring and we have shown it can thread over a maleimide, the presence of the two carbonyl groups and the benzene ring presents a considerable barrier to the passage of the macrocycle.

2.3 Perimidine Benzimidazole Binding Motif

The development of new templates for rotaxane formation can yield both a better understanding of the threading process and new components for incorporation into rotaxane based molecular machines. Many interlocking structures have been reported utilising both secondary ammonium ions and quarternised pyridines. A *bis*benzimidazole template (Figure 2.8) has been previously disclosed that combines the π-stacking abilities of the electron deficient pyridinium and hydrogen bonding capabilities of the ammonium ions. This template has shown significant binding to DB24C8 *via* these interactions.[120]

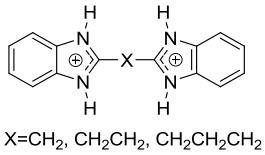
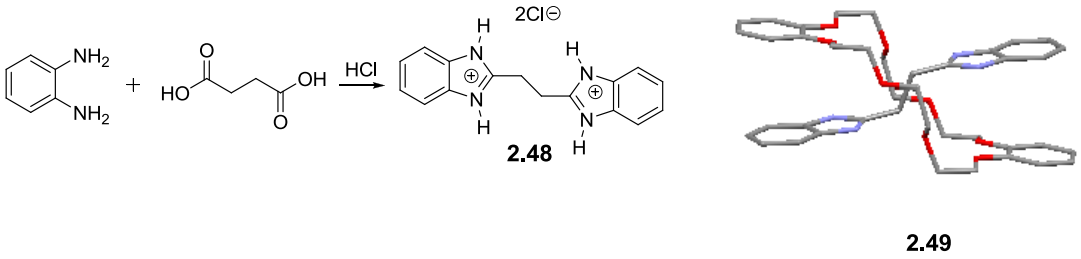


Figure 2.8 The *bis*benzimidazole template.

Work by Li[120] has shown that unfunctionalised *bis*benzimidazole templates can be synthesised readily from the acid catalyzed condensation of 1,2-phenylenediamine and succinic acid, as shown in Scheme 2.16. With the thread having two recognition sites joined by a short linker, the *bis*benzimidazolium cation can interact with both electron rich aromatic rings of the DB24C8 crown, as well as hydrogen bonding to either face of the macrocycle to position the thread within its cavity as shown by the solid state structure of pseudorotaxane **2.49**.



Scheme 2.16 Synthesis of the *bis*benzimidazole template and X-Ray crystallography structure.

Previous work has also found that introducing an electron withdrawing group onto the benzimidazole such as an ester can increase the binding interaction. The ester group offers the possibility of modification to create a wide variety of stopper groups acting as the terminating end of the axle for the synthesis of rotaxanes. Routes towards functionalised threads starting from suitably functionalised *o*-phenyldiamine has proved to be challenging due to the difficulty of finding a functionalised benzimidazole which can withstand the harsh synthetic conditions of the reaction to make the benzimidazole ring. A milder and asymmetric route has been discovered where the functionalised benzimidazole groups are introduced consecutively yielding [2]rotaxanes using this binding motif.[119]

To further explore the *bis*benzimidazole motif, one of the benzimidazole moieties was replaced with a perimidine group (Figure 2.9). Perimidines and their derivatives were discovered in the early 1900s by Sachs.[121] They are useful as dye intermediates[122-123] and can also be found in a number of biologically active compounds.[124-125] Paragamian and co workers have also spent time optimising the synthesis of these structures and investigated their pharmacological activity.[126]

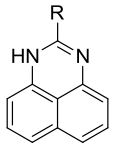


Figure 2.9 The perimidine template.

One of the key reasons we were interested in incorporating this novel moiety into the binding motif, is the redox ability of this molecular system as demonstrated for hydrogen bonded charge transfer complexes. Nakasuji *et al*[127-128] has explored this ability in order to develop new conducting organic molecular based materials. The 1,3 diazanaphthalene system is isoelectronic with the phenalenyl anion. The phenalenyl has three states shown in Figure 2.10. It is an odd-alternate hydrocarbon π-electron system and has high thermodynamic stability.

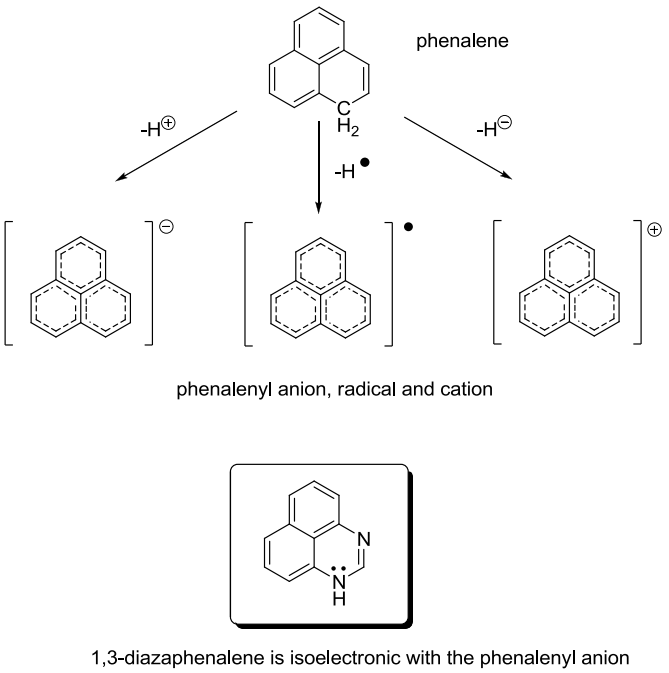


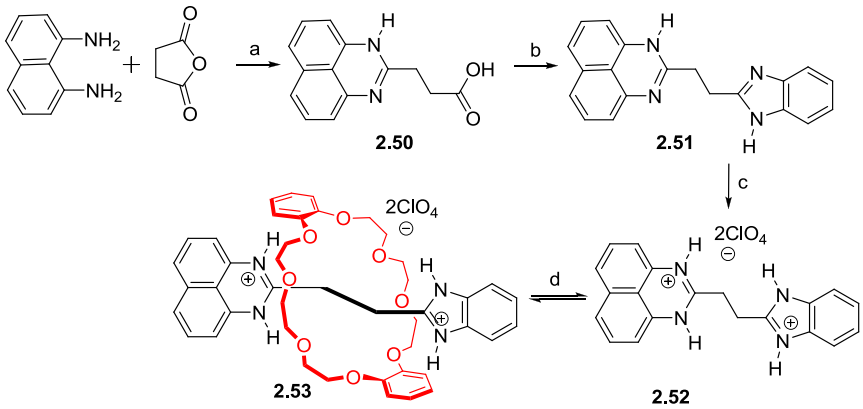
Figure 2.10 The three phenalenyl redox species and the isoelectronic 1,3-diazaphenalene compound.

As well as these electronic characteristics, the perimidine has both proton donor and proton acceptor functionalities and can form hydrogen bonds. Due to these characteristics, its similarity to the functionality in a benzimidazole and the possibility to act as a stopper, we were interested in incorporating this system into the binding motif of a rotaxane with the potential of controlling the interaction between the macrocycle and the axle using its redox activity. This also gives the opportunity to exploit the Diels-Alder 'threading followed by stoppering' approach to form rotaxanes with this binding motif.

2.3.1 Synthesis of Perimidine Pseudorotaxanes and Rotaxanes

The simple perimidine modified template has been synthesised within the group. The unfunctionalised perimidine benzimidazole thread is formed by reacting 1,8-diaminonaphthalene with succinic anhydride in HOAc to provide the resulting acid **2.50** in a 95% yield. Further reaction with trifluoroacetic anhydride (TFAA) in CH_2Cl_2 provided an intermediate lactam which was immediately reacted with the 1,2-phenylenediamine giving the neutral thread **2.51**. Conversion of this to the ClO_4^- salt **2.52** provided a template with an increased π surface and novel hydrogen donor in the form of the perimidinyl cation. The

binding template was characterised using NMR and HRMS with the mass ion occurring at 313.1444 corresponding to the [**2.52**-H.2ClO$_4$]$^+$. The IR spectra also shows an absorption at 1053 cm^{-1} which is characteristic for the ClO$_4^-$ counterion.



Scheme 2.17 Reagents and conditions: a) HOAc, 70˚C, 24 h, 95%; b) i) CH_2Cl_2, TFAA, RT, 24h; ii) HOAc, *o*-phenylenediamine, 70˚C, 48h, 74%; c) MeOH, $HClO_4$, 46%; d) CH_3CN, DB24C8 (1 equiv).

Equimolar quantities of the thread **2.52** and DB24C8 were dissolved in deuterated acetonitrile and the pseudorotaxane was formed. Formation of the pseudorotaxane **2.53** was confirmed by ^{1}H NMR and ESI-mass spectrometry. The binding constant was measured using the single point method[129] at 2 mmol and found to be 1055 M^{-1}, a two fold increase from the simple *bis*benzimidazole thread (490 M^{-1}). This showed that the perimidine thread had a much stronger interaction with the DB24C8 than its simple counterpart suggesting heightened π-stacking and hydrogen bonding capabilities. Over time, suitable crystals for X-ray crystallography grew from the NMR sample and the solid state structure of [2]pseudorotaxane **2.53** was obtained and is shown in Figure 2.11. The structure obviously differs from the solid state structure of the *bis*benzimidazole pseudorotaxane **2.49** but it was surprising to see the uneven nature of the interaction of the two hydrogen bond donating units with the crown. The benzimidozolium ion has only one NH interaction with the crown. Both NH's of the perimidinium ion have short contacts to the crown oxygens. Additionally, the dioxybenzene of the crown is almost parallel to the plane of the perimidine π system. The benzimidazole and crown π systems are slightly orientated away from each other

suggesting a weaker π stacking interaction and the NH of the benzimidazolium cation is hydrogen bonded to a ClO_4 counter ion (not shown in image).

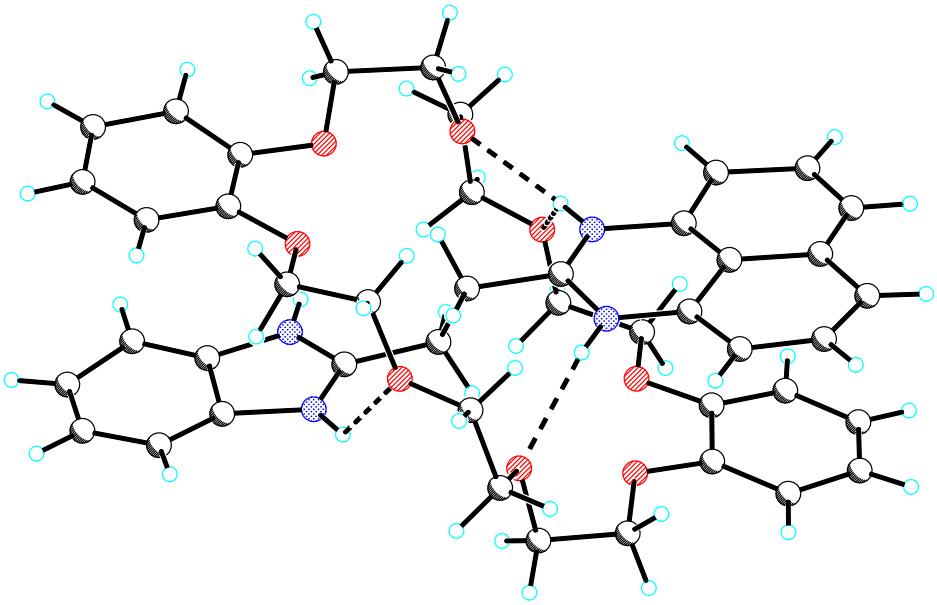
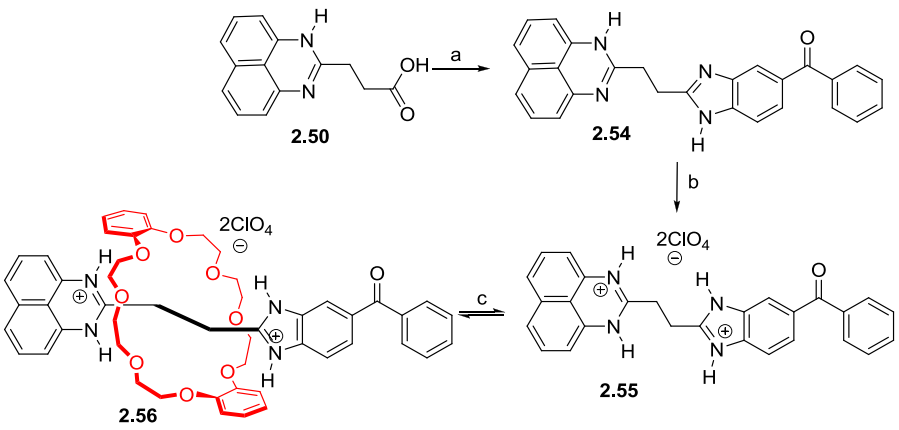


Figure 2.11 Solid state structure side on view of [2]pseudorotaxane **2.53** showing hydrogen bonding between the thread NHs and crown ether oxygens. C white; O red; N blue; H pale blue. ClO_4 counter ions have been removed for clarity.

As a simple modification to increase the hydrogen bonding ability of the benzimidazole, thread **2.54** was constructed. Acid **2.50** was again reacted at room temperature with TFAA in CH_2Cl_2 to give an intermediate lactam, followed by addition of 3,4-diaminobenzophenone in HOAc providing the neutral thread (**2.54**). Reacting this with $HClO_4$ in MeOH provided the ClO_4^- salt **2.55**. The [2]pseudorotaxane **2.56** was then generated taking equimolar quantities of thread and DB24C8 in deuterated acetonitrile at 2 mmol. The binding constant was found to be 995 M^{-1} calculated using the single point method at 2 mmol.[129] It seems there is little effect on binding by the substitution of electron withdrawing groups on the benzimidazole moiety.



Scheme 2.18 Reagents and conditions: a) i) CH_2Cl_2, TFAA, RT, 24h, 65%; ii) HOAc, 3,4-diaminobenzophenone, 70˚C, 48h, 65%; b) MeOH, $HClO_4$, 50%; c) CH_3CN, DB24C8 (1 equiv), RT.

The formation of the [2]pseudorotaxane **2.56** was confirmed by ^{1}H NMR, ESI-mass spectrometry and an x-ray crystal structure was obtained (Figure 2.12). In contrast to the solid state structure of **2.53** (Figure 2.11), the hydrogen bonding pattern between thread and crown in the solid state more closely resembles that of the symmetrical *bis*benzimidozolium threads[120] with one NH on each heterocycle forming a bifurcated hydrogen bond to the crown oxygens and the other interacting with the ClO_4^- counter ion. Differences between the two cationic units of the thread are apparent in the π stacking interaction with the crown. The perimidine and dioxybenzene of the crown have planar π systems whereas the benzimidazole and dioxybenzene are again slightly orientated away. This picture is complicated by the benzophenone substituent not being parallel to the benzimidazole which could be interfering with the π stacking interactions. In an effort to further investigate the effect of substitution the modification of this template into a maleimide functionalised thread for rotaxane formation was an obvious avenue for exploration.

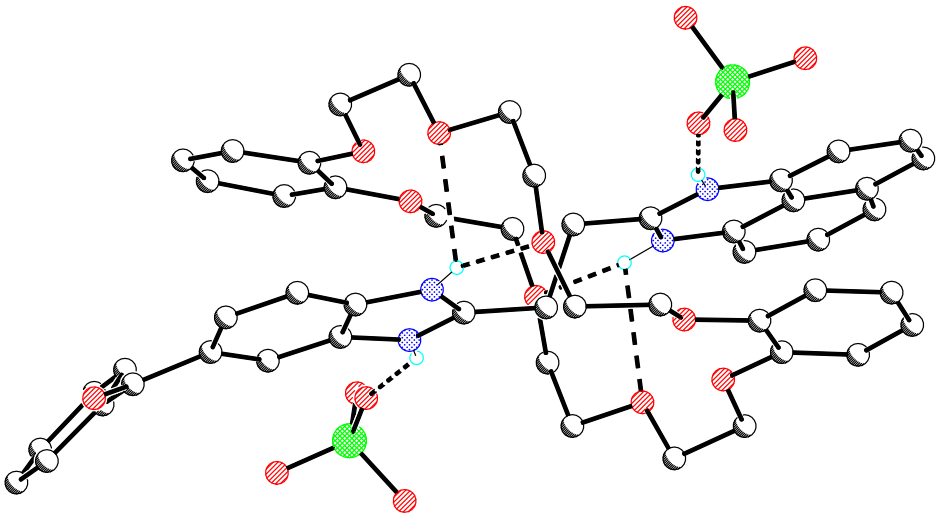
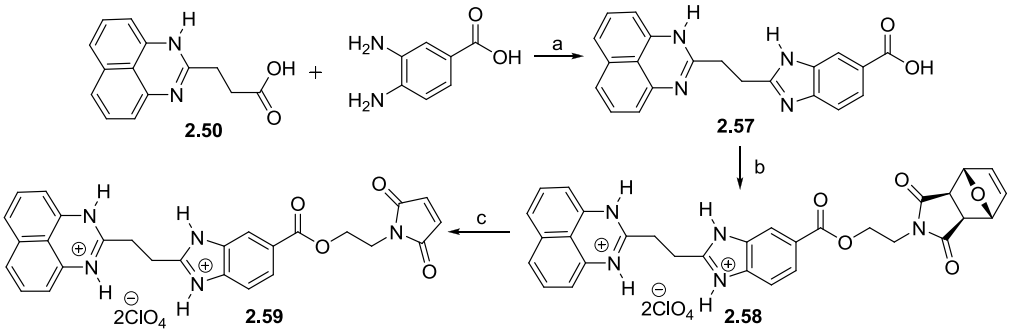


Figure 2.12 Solid state structure of [2]pseudorotaxane **2.56** showing the interlocked nature of crown and thread. Hydrogens have been omitted for clarity except the NH's involved in hydrogen bonding interactions with the crown and ClO_4 counter ions. C white; O red; N blue; Cl green.

The synthesis of a thread suitable the Diels-Alder strategy was carried out to generate rotaxanes *via* the 'threading followed by stoppering' approach. Again started by reaction of acid **2.50** with TFAA in CH_2Cl_2, a further reaction with 3,4-diaminobenzoic acid provided the new acid functionalised binding motif **2.57**. At this stage, incorporation of the Diels-Alder adduct was undertaken in an esterification reaction with the acid. Using the coupling agent HBTU in a solution of CH_2Cl_2 and NEt_3 the neutral thread was synthesised. Although chromatography and several methods of purification were attempted, we were unable to isolate the neutral thread for characterisation. The most significant problem encountered in the ester synthesis was the solubility of acid **2.57**. A variety of reaction conditions were investigated in order to improve efficiency of this reaction. The acid **2.57** was found to be soluble in solvents such as DMAc and DMF but formation of the ester either did not occur or yields of product were very low under these conditions. Using a mixture of CH_2Cl_2 and NEt_3 was found to be the best solvent/base system for the reaction. Stirring these with the acid **2.57**, 4-dimethylaminopyridine (DMAP) and coupling agent HBTU overnight then addition of alcohol **2.04** gave the most efficient synthesis of the axle. Conversion of the

crude material into the ClO_4^- salt was carried out immediately in MeOH with the addition of $HClO_4$ to give thread **2.58** (Scheme 2.19). To enable the DB24C8 to thread, a retro Diels-Alder reaction to remove the furan was necessary. This was undertaken using microwave heating to generate **2.58** in a 55% yield after purification *via* recrystallisation.



Scheme 2.19 Reagents and conditions: a) i) CH_2Cl_2, TFAA, RT, 12h; ii) HOAc, 70˚C, 48h, 43%; b) i) CH_2Cl_2, NEt_3, Alcohol **2.04**, DMAP, HBTU, RT, 72h; ii) MeOH, $HClO_4$, RT, 12%; c) CH_3CN, MW, 150W, 110 ˚C, 3h, 55%.

The DB24C8 was now able access the binding motif of the axle by threading over the maleimide functional group to provide us with the intermediate pseudorotaxane structure **2.60**. After 48 hours using two equivalents of DB24C8 the reaction had reached equilibrium in favour of pseudorotaxane formation observed by ^{1}H NMR. A stoppering reaction was then performed in order to prevent the macrocycle from slipping off the axle. This was done using cyclopentadiene at room temperature to give only the kinetically preferred *endo* isomer of the [2]rotaxane **2.61** (Scheme 2.20). Isolation of the [2]rotaxane proved difficult and the stability of the material was poor although there is proof of the interlocked structure by both appropriate shifts in ^{1}H NMR and ESI-MS with a peak seen at *m/z* 994.4233 relating to the expected [**2.61**-ClO_4]$^+$ species. Synthesis of the comparison thread was hampered by the low solubility and reactivity of this system.

During isolation of the [2]rotaxane **2.61** by column chromatography, ^{1}H NMR analysis of a pure fraction gave a spectra rather more complex than expected. There was a doubling of the peaks associated with the benzimidazole group. From previous work on the

*bis*benzimidazole rotaxane[119] it was found that the basicity of the *bis*benzimidazole rotaxane is much less than the ammonium rotaxanes where there is an enhanced pKa due to the stability of the ammonium ion buried in the rotaxane complex. The *bis*benzimidazole has the NH's exposed outside either face of the crown and additionally the heterocyclic ring is not as basic as a secondary amine. In simple substituted benzimidazoles, the tautomerism of the hydrogen can be slow on the ^{1}H NMR timescale leading to a broadening or doubling of signals (Figure 2.13).[130] This inter-conversion of the benzimidazole inside the cavity of a crown slows this tautomerism even further.

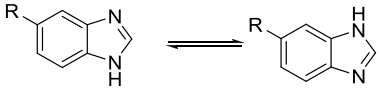
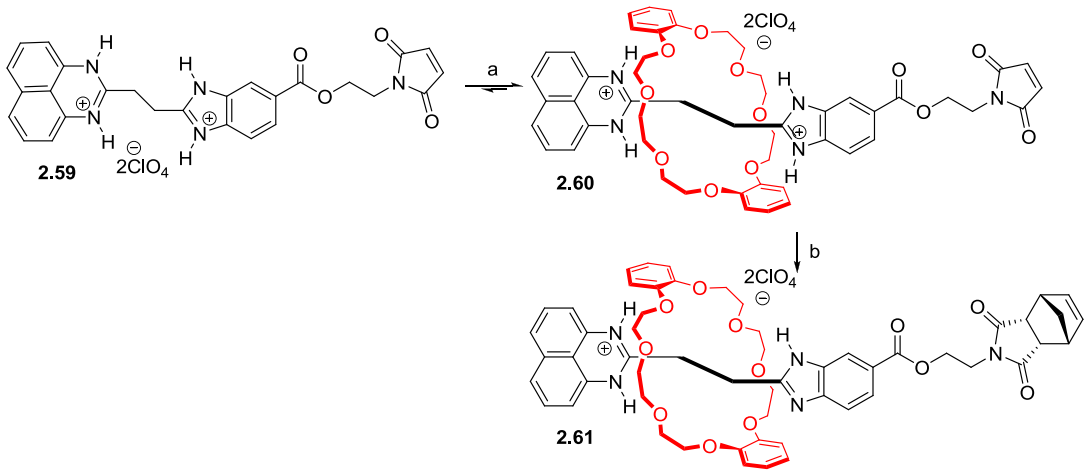


Figure 2.13 Tautomerism of functionalised benzimidazole.

Rotaxane **2.60** must have been neutralised following silica gel column chromatography. VT-NMR was carried out on the [2]rotaxane but it did not provide any better resolution of these peaks and affected the stability of the compound. However addition of TFA to the sample reprotonates this moiety and once again we see a single set of sharp peaks corresponding to the charged benzimidazole disalt of the [2]rotaxane.



Scheme 2.20 Reagents and conditions: a) CH_3CN, DB24C8 (2 equiv), RT; b) CH_3CN, cyclopentadiene, RT, 34%.

Due to the problems associated with the synthesis and purification of these materials, the focus of the work shifted to exploiting the 'threading followed by Diels-Alder stoppering approach' to rotaxane formation with other systems.

2.4 *Bis*Pyridinium Functionalised Rotaxanes

As we have previously seen, development of novel templates can lead to a greater understanding of the interlocking process and provide new and improved applications for rotaxanes. In Chapter 1 the Loeb groups development of a *bis*pyridinium template (Figure 2.14) which has been shown to have excellent binding with crown ether macrocycles was discussed.[46] The axle and macrocycle bind through N^+…. O interactions and C-H…. O hydrogen bonding. The interaction can be enhanced by the addition of π-π stacking interactions by the incorporation of a benzene ring into the macrocycle i.e. benzo-24-crown-8 (B24C8) and DB24C8. Varying substituents on the *bis*pyridinium template also has an impact on binding. Adding an electron withdrawing group such as CO_2Et at the 3 or 4 position of the pyridinium causes the binding interaction between template and macrocycle to increase greatly (Figure 2.14). This is a result of removing electron density from the pyridinium ring making it more electron poor thus enhancing its interaction with the electron rich catechol ring of the macrocycle and increasing the hydrogen binding ability of the pyridinium α-CH's.

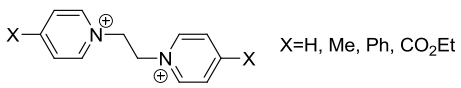
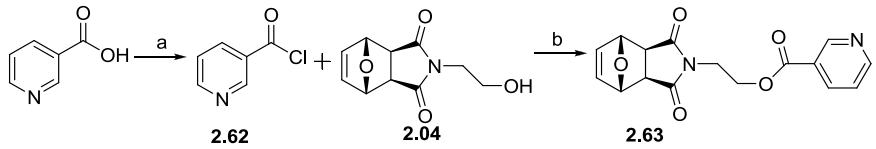


Figure 2.14 1,2-*bis*(pyridinium)ethane binding template.

Since the initial discovery of the binding motif, it has been used to synthesise a variety of supramolecular complexes including pseudorotaxanes,[131-132] rotaxanes,[133-136] metal organic frameworks[137] and molecular shuttles.[138]

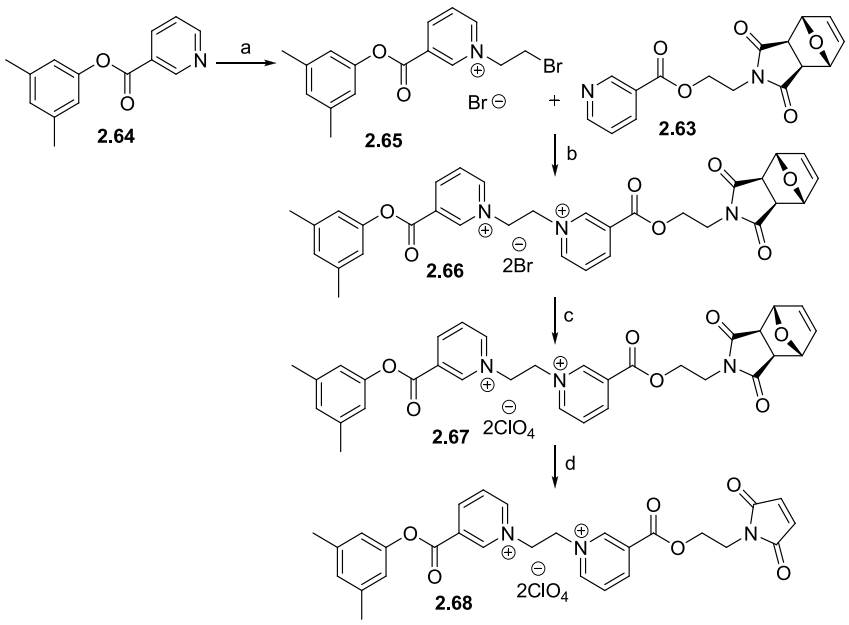
2.4.1 Synthesis of Rotaxanes Incorporating *Bis*pyridinium Binding Motifs

As we have seen, the *bis*pyridinium functionality has been successfully used as a binding motif by Loeb and others and we wanted to use this binding motif to showcase the groups' Diels-Alder 'threading followed by stoppering' approach in rotaxane synthesis. Nicotinic acid was converted to its acid chloride **2.62** and reacted with the Diels-Alder stopper under basic conditions to give ester **2.63** (Scheme 2.21). The ester was observed by both NMR and IR showing a peak at 1688 cm^{-1} corresponding to an ester carbonyl. The ESI-HRMS also provided evidence of synthesis of this ester showing *m/z* 315.0978 for the [**2.63**+H]$^+$ ion.



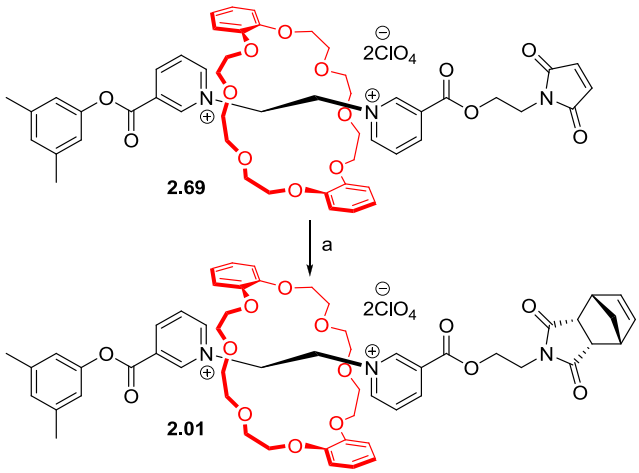
Scheme 2.21 Reagents and conditions: a) $SOCl_2$, DMF, RT, 24h, quant; b) CH_2Cl_2, NEt_3, 0˚C→RT, 48h, 58%.

Using 1,2-dibromoethane, synthesis of unsymmetrical *bis*pyridinium thread was successfully performed. Introduction of a stopper by reacting nicotinic acid chloride with 3,5-dimethyl phenol provided ester **2.64**. Subsequent reactions in acetonitrile with 1,2-dibromoethane at 60˚C produced the bromide salt **2.65**. Reacting this with pyridinium ester **2.63** in acetonitrile provided the dibromide salt **2.66** shown in Scheme 2.22. Conversion to the ClO_4^- salt **2.67** *via* an ion exchange reaction was successful using sodium perchlorate and finally the retro Diels-Alder reaction was carried out by refluxing **2.67** in acetonitrile unmasking the maleimide moiety to give axle **2.68**.



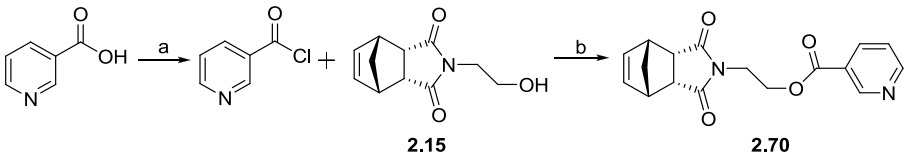
Scheme 2.22 Reagents and conditions: a) CH_3CN, 1,2-dibromoethane, 60 ˚C, 72h, 24%; b) CH_3CN, 60 ˚C, 72 h, 48%; c) H_2O, $NaClO_4$, RT, 73%; d) CH_3CN, reflux, 24h, 36%.

The axle **2.68** was dissolved in deuterated acetonitrile and two equivalents of DB24C8 were added forming pseudorotaxane **2.69**. The effects of the macrocycle encompassing the axle can be seen clearly in the ^{1}H NMR with several significant shifts in peaks observed. The final stage is to trap the macrocycle onto the axle in a 'stoppering' reaction giving rotaxane **2.70** shown in Scheme 2.23. Freshly distilled cyclopentadiene was added to the pseudorotaxane **2.69** in acetonitrile generating the bulky stopper. This provided us with new [2]rotaxane **2.01** in a 58% yield.



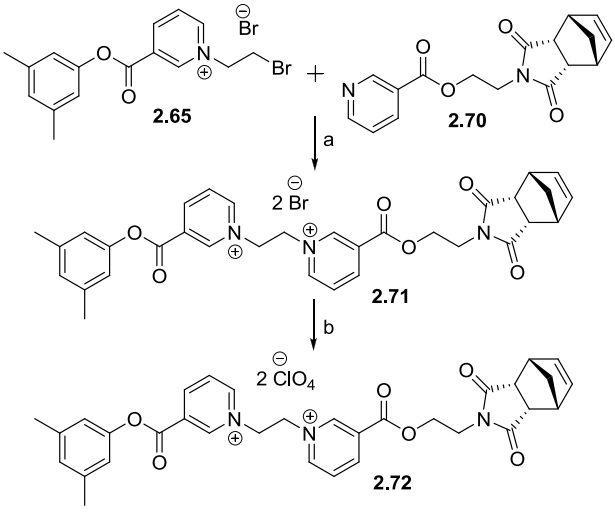
Scheme 2.23 Reactants and reagents: a) CH_3CN, cyclopentadiene, 58%.

A comparison thread with the *endo* conformation from the known *endo* alcohol **2.15**[139] was also synthesised by reacting with nicotinic acid chloride shown in Scheme 2.24. The product formation was confirmed by NMR and ESI-HRMS with a single peak at 313.1182 in concordance with the [**2.70**+H]$^+$ species.



Scheme 2.24 Reagents and conditions: a) $SOCl_2$, DMF, 24h, RT, quant; b) CH_2Cl_2, NEt_3, 0˚C→RT, 48h, 18%.

The comparison thread was successfully synthesised reacting the bromide salt **2.65** with pyridinium **2.70** to form new dibromide salt **2.71**. Conversion to the ClO_4^- salt was carried out in an ion exchange reaction using a concentrated aqueous solution of sodium perchlorate to give the thread **2.72**.



Scheme 2.25 Reagents and conditions: a) CH_3CN, 60 ˚C, 72h, 55%; b) H_2O, $NaClO_4$, RT, 47%.

Comparison of the ^{1}H NMR spectra of the [2]rotaxane **2.01** is shown in Figure 2.15, the peaks associated with the dimethylphenyl and the Diels-Alder stopper portions of the thread are relatively unaffected by the presence of the macrocycle encompassing the axle. The α-aromatic protons of the *bis*pyridinium motif are seen to shift downfield due to hydrogen bonding between these and the crown ether oxygens. The aromatic protons of DB24C8 are shifted upfield and separate into two multiplets and the ethylene CH_2's of the macrocycle are

seen to form two broad singlets. The ethylene spacer situated in the binding motif shows a considerable shift downfield due to hydrogen bonding with the crown ether oxygens. The shift of the two triplets corresponding to the ester chain of the stopper are relatively unaffected by the axle being encompassed by the macrocycle.

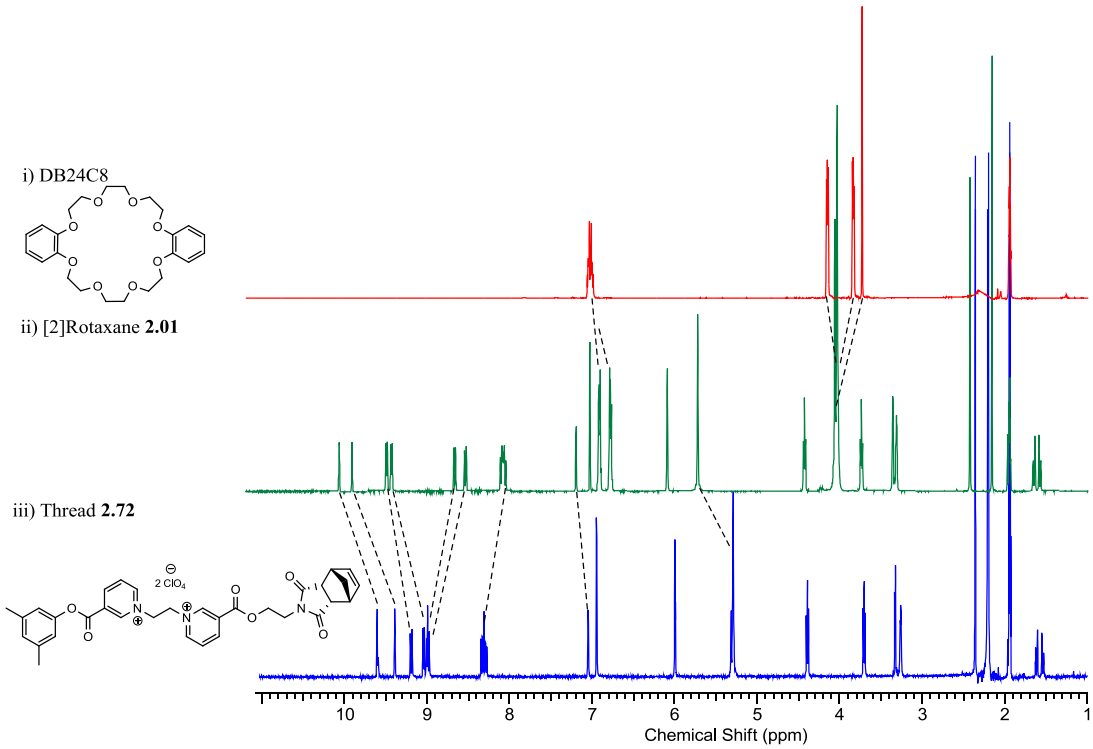


Figure 2.15 ^{1}H NMR (400 MHz, CD_3CN, 300K) stacking plot of i) DB24C8 ii) [2]rotaxane **2.01** and iii) comparison thread **2.72**.

The solid state structure was also obtained of the [2]rotaxane **2.01** shown in Figure 2.16. The structure confirms the *endo* conformation of the Diels-Alder stopper portion of the thread and highlights how the thread **2.72** and DB24C8 take on a conformation to provide π stacking between the two interlocked components in the solid state.

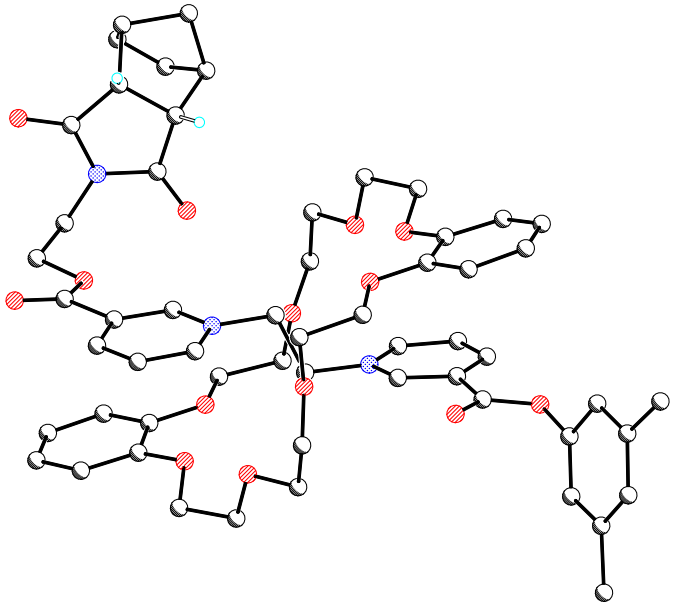
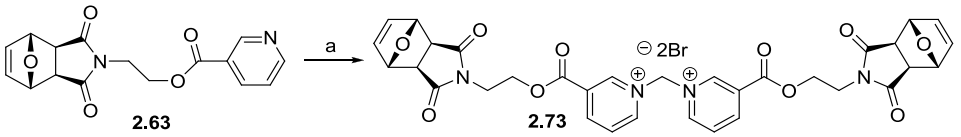


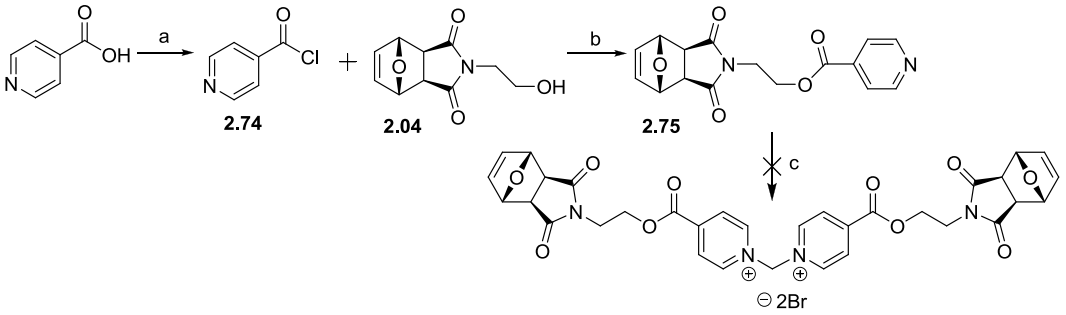
Figure 2.16 Solid state structure of [2]rotaxane **2.01** in an orientation to highlight the pi stacking interactions and the *endo* stereochemistry of the imide stopper. Only the hydrogens of the Diels-Alder stopper are retained to emphasise the stereochemistry. C white; N blue; O red; H pale blue. ClO_4 counter ions have been removed for clarity.

After successfully synthesising a [2]rotaxane with a *bis*pyridinium ethane binding motif using the groups' Diels-Alder 'gate' in a 'threading followed by stoppering' protocol, we wanted to take further advantage of this strategy. A *bis*pyridinium methane template has been developed by the group[140] based on a simple modification of the Loeb *bis*pyridinium ethane motif.[46] Taking the previously synthesised ester pyridinium **2.63** in an S_N2 reaction with an excess of dibromomethane in DMF provided a *bis*pyridinium bromine salt **2.73** symmetrically functionalised with Diels-Alder gates. The pyridinium protons are shifted downfield due to the nitrogen becoming charged. The central CH_2 appears at 7.61 due to its location between the two quarternised nitrogens.



Scheme 2.26 Reagents and conditions: a) CH_2Br_2, DMF, 60˚C, 48h, 55%.

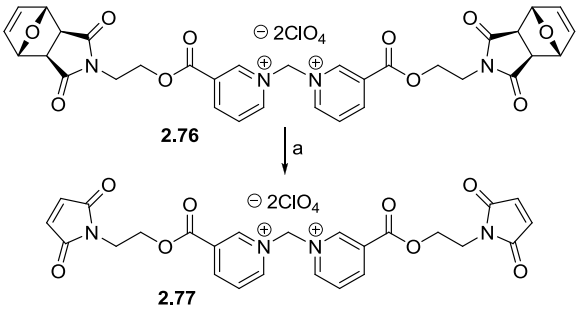
Attempts at forming the thread using the isonicotinic ester **2.75** were also carried out but proved unsuccessful when reacted with dibromomethane. This lack of reactivity is probably because the pyrimidine nitrogen is less nucleophilic due to the presence of the ester in the 4-position of **2.75** (Scheme 2.27).



Scheme 2.27 Reagents and conditions: a) $SOCl_2$, DMF, RT, quant; b) CH_2Cl_2, NEt_3, 0˚C→RT, 48h, 58%; c) CH_2Br_2, DMF, 60 ˚C, 48h.

To enhance binding of the macrocycle to the thread, the *bis*pyridinium moiety was converted into a salt with a weakly co-ordinating counter ion. The ClO_4^- salt of the nicotinate axle **2.73** was generated in an ion exchange reaction by mixing a saturated solution of sodium perchlorate with a saturated solution of thread **2.73** to precipitate **2.76** from solution.

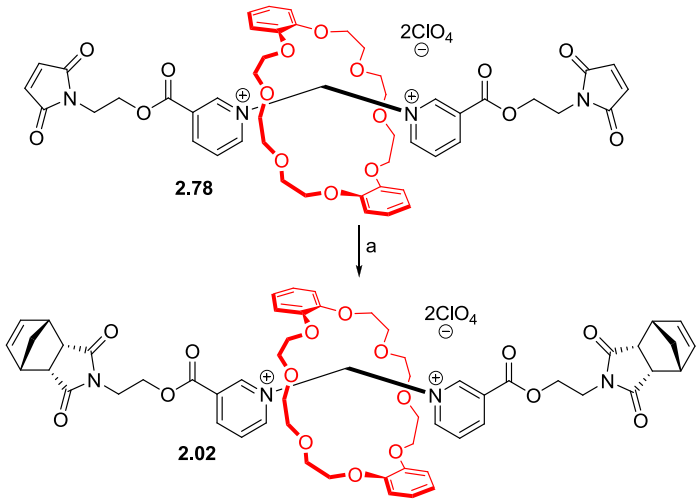
The 'gate' is opened by generating the maleimide pre-stopper *via* a retro Diels-Alder reaction making the terminating end of the thread sufficiently sized to slip through the cavity of the macrocycle. This was done simply by heating the ClO_4^- salt thread **2.76** in acetonitrile at reflux to produce the maleimide thread **2.77** and furan as a by-product (Scheme 2.28).



Scheme 2.28 Retro Diels-Alder reaction of the *bis*pyridinium ClO_4^- thread **2.76**. Reagents and conditions: a) CH_3CN, 110˚C, 150W, 3h, 46%.

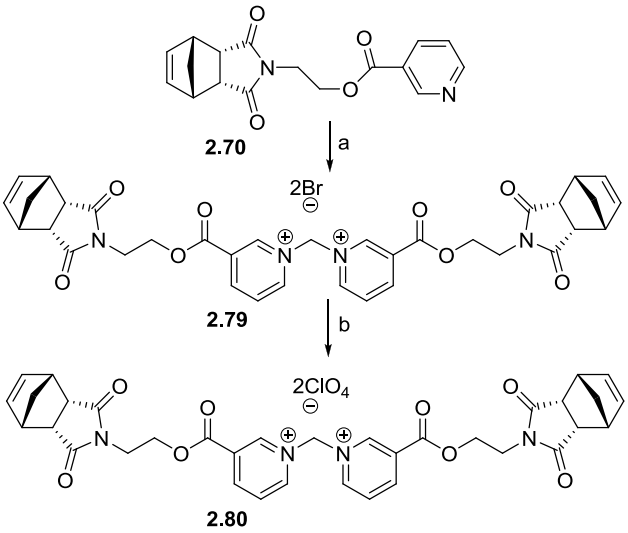
Originally the unmasking of the maleimide was carried out by refluxing the perchlorate thread **2.77** in acetonitrile. Problems were encountered when undergoing the retro Diels-Alder reaction. Hydrolysis of the axle occurred regenerating the initial pyridine ester **2.63**. This problem was partially overcome by carrying out the reaction in a microwave at 110˚C in a greatly reduced time of 3 hours in acetonitrile. The solvent and furan generated were removed *in vacuo*. The increase in the retro Diels-Alder rate by microwave heating reduced the amount of hydrolysis observed.

The thread was then dissolved in deuterated acetonitrile with two equivalents of DB24C8 to push the threading of the crown to > 90% (by ^{1}H NMR) to produce pseudorotaxane **2.78**. Once the DB24C8 was threaded onto the axle, the Diels-Alder reaction was implemented using freshly cracked cyclopentadiene forming the bulky stopper to trap the macrocycle onto the axle to give rotaxane **2.02** (Scheme 2.29). Excess cyclopentadiene was removed in *vacuo*. Purifying the [2]rotaxane proved difficult due to the instability of the compound and only a small amount was isolated with some minor impurities visible in ^{1}H NMR (Figure 2.17). Rotaxane formation was also confirmed by ESI-HRMS with the [**2.02**-2ClO_4]$^{2+}$ ion occuring at 543.2285.



Scheme 2.29 Reagents and conditions; a) CH_3CN, cyclopentadiene, RT, 57%

Again the comparison thread was synthesised from the cyclopentadiene stoppered pyridinium **2.70**. Reacting this with dibromomethane gives thread **2.79** and this is converted to the ClO_4^- salt **2.80** on reacting with aqueous sodium perchlorate (Scheme 2.30) to the give disalt in a 29% yield.



Scheme 2.30 Reagents and conditions: a) CH_2Br_2, DMF, 60˚C, 48h, 13%; b) H_2O, $NaClO_4$, RT, 29%.

A stacking plot of the ^{1}H NMR of crown, thread and rotaxane is shown in Figure 2.17. Once the axle is encompassed by the macrocycle the α pyridyl protons are shifted downfield as they hydrogen bond with the crown oxygens. There is a shielding effect on the aromatic protons of the crown caused by its close proximity to the π system of the thread. The central

CH_2 is also shifted downfield. There is little or no effect observed for the stopper portion of the thread showing that the crown mainly resides over the *bis*pyridinium template.

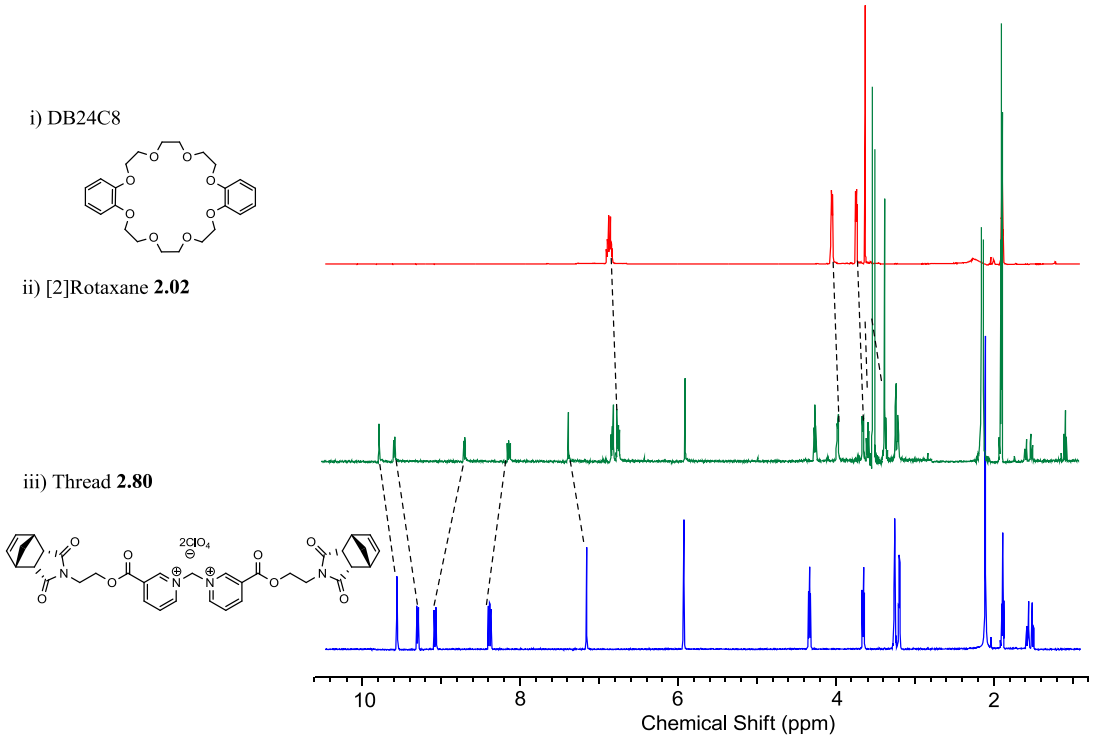
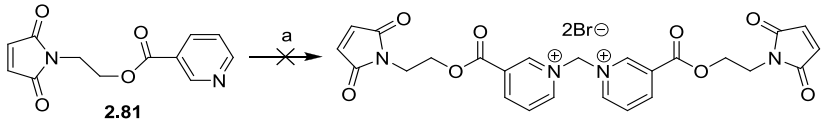


Figure 2.17 ^{1}H NMR (400 MHz, CD_3CN, 300K) stacking plot of i) DB24C8 ii) [2]Rotaxane **2.02** and iii) Comparison thread **2.79**.

Due to the low yields and hydrolysis problems encountered during the retro Diels-Alder reaction, the stability of the Br^- and ClO_4^- threads were investigated. The Br^- thread was dissolved in D_2O and left to stand at room temperature monitoring by ^{1}H NMR. After one day the hydrolysed pyridine begins to form highlighting the instability of this compound in water. The stability of the ClO_4^- salt was also examined. It was dissolved in deuterated acetonitrile and after a week at room temperature only a trace of thread hydrolysis was observed. The ClO_4^- salt is relatively stable at room temperature but breaks down during the thermal retro Diels-Alder reaction probably due to residual water in the reaction system.

Attempts to improve the synthesis by undertaking the retro Diels-Alder reaction before formation of the salt by reaction of maleimide **2.81** in dibromomethane and DMF were unsuccessful (Scheme 2.31). Only small amounts of starting material were recovered on

analysis. This failed presumably because the maleimide is prone to Michael addition and polymerization.



Scheme 2.31 Attempted synthesis of the retro Diels-Alder thread. Reagents and conditions: a) CH_2Br_2, DMF, 60˚C.

2.5 Conclusion

The Diels-Alder reaction has been successfully exploited to synthesise a number of rotaxanes in a 'threading followed by stoppering' protocol with a variety of binding motifs. The ammonium ion template has been used with promising results to synthesise [2] and [3]rotaxanes using this approach. We have found that removing the alkyl spacer between the maleimide and ester unit significantly reduces the threading rate of the macrocycle. It has also been found that replacing the bridged six membered ring, with the flat sp^2 hybridized phthalimide moiety compromises its ability to act as a stopper for DB24C8 macrocycle under relatively harsh conditions. Unfortunately when dissolving the [2]rotaxane in DMSO and heating to 40 ˚C this disrupts the intermolecular interactions and unthreading of the macrocycle occurs.

Synthesis of a novel binding motif has also been achieved which has been shown to have promising binding affinities with crown ether macrocycles. Substituting a perimidine moiety into the *bis*benzimidazole template gave a two fold increase in the binding interaction between the two components from 490 M^{-1} to 1055 M^{-1}. Addition of the electron withdrawing benzophenone functional group to the benzimidazole side of the template did not make a significant difference in binding interaction between the thread and DB24C8. Using the perimidine template, a [2]rotaxane **2.61** was successfully synthesised with a Diels-Alder 'gate' incorporated into the axle. Several sets of reaction conditions were attempted to synthesise this axle but yields of the esterification reaction were still very low. As a result,

only small amounts of the rotaxane were obtained and so far we have not been able to synthesise enough material to investigate its properties.

The Diels-Alder reaction has also been applied to achieve rotaxanes incorporating with *bis*pyridinium binding motifs in a 'threading followed by stoppering' approach. It was found that when there was only one CH_2 connecting the two pyridine nitrogens, problems occurred during the retro Diels-Alder reaction when considerable hydrolysis of thread **2.76** was observed. Using the known 1,2-pyridinium ethane motif, the rotaxane synthesis was more successful and no hydrolysis was observed during rotaxane formation and isolation. The rotaxane was synthesised and the solid state crystal structure was obtained proving the *endo* conformation of the cyclopentadiene functionalised maleimide adduct.

2.6 General Experimental

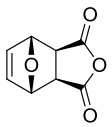
All experiments were carried out in fume hoods, adhering to general laboratory safety protocols and risk assessments (COSHH). Reagents and chemicals were purchased from Sigma Aldrich, Lancaster, TCI or Alfa Aesar and used without further purification. Solutions used to generate the appropriate ammonium salts were made up by diluting commercial samples of the appropriate acid. Approximately 10% $HClO_4$ solution was made by carefully adding 10 mL $HClO_4$ to 70 mL water. Approximately 10% hexafluorophosphoric acid was made by carefully adding 6.5 mL of acid to 65 mL water.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DRX 400 MHz fourier transform machine at room temperature (298 K) unless otherwise stated. Chemical shifts are quoted in parts per million downfield of tetramethylsilane. Solvents were used as an internal standard when assigning NMR spectra (δH: $CDCl_3$ 7.26 ppm, CD_3CN 1.94 ppm, CD_3OD 3.31 ppm, DMSO-d_6 2.50 ppm, D_2O 4.79 ppm; δC: $CDCl_3$ 77.1 ppm, CD_3CN 118.7 ppm, CD_3OD 49.0 ppm, DMSO-d_6 39.5 ppm. Coupling constants, *J*, are given in Hz. ^{13}C NMR spectra were recorded with broadband proton decoupling and spectra assigned on the basis of pendant, 3D COSY , HMQC and HMBC spectra. Infra-red spectra were recorded on an

Avatar 320. Thin Layer Chromatography (TLC) was performed using silica (0.25 mm) coated alumina 149 plates. ESI mass spectra were obtained on a Bruker Esquire 2000 mass spectrometer coupled with an Agilent 1100 HPLC (without a column) as the delivery system. Accurate mass spectra were obtained using a Bruker micro-TOF ESI attached to a time of flight (TOF) analyser. CHN elemental analyses were carried out by Warwick Analytical Services. Melting points were determined using a Stuart SMP10 melting point machine.

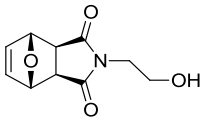
2.6.1 Experimental Section

2.03



Synthesised according to a modified literature procedure.[141] Maleic anhydride (10 g, 102 mmol) was dissolved in Et_2O (50 mL) until a clear solution was obtained. Furan (7.4 mL, 102 mmol) was added to the mixture and it was left to stand at room temperature for 48 h. A white precipitate formed which was filtered and washed with petroleum ether to provide white crystals (12.14 g, 73.1 mmol, 72%). ^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ_H 6.59 (br s, 2H, C*H*=C*H*), 5.48 (br s, 2H, 2 C*H*O), 3.20 (br s, 2H, 2 C*H*CO); ^{13}C NMR (75 MHz, 298 K, $CDCl_3$) δ_C 170.3 (*C*=O), 137.3 (*C*H=*C*H), 81.6 (*C*HO), 48.1 (*C*HCO); IR ν cm^{-1} 3033 (saturated C-H), 1779 (anhydride C=O), 1211 (C-O).

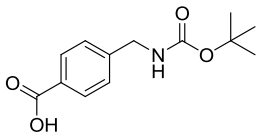
2.04



Synthesised according to a modified literature procedure.[142] Anhydride **2.03** (5 g, 28 mmol) was dissolved in EtOH (50 mL). The solution was cooled to 0°C and a solution of

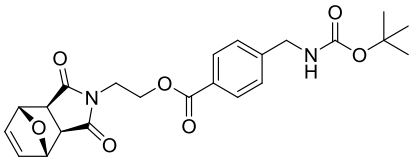
ethanolamine (1.8 mL, 30 mmol) and NEt_3 (4.2 mL, 30 mmol) in EtOH (10 mL) was added dropwise to the solution and left to stir for 30 minutes. It was then heated overnight at 70°C. Solvent was partially removed *in vacuo* until the product began to precipitate. It was then cooled to 0°C for 5 minutes and filtered and washed with ice cold EtOH to provide a light pink solid (5.43 g, 26 mmol, 84%). ^{1}H NMR (300 MHz, 298 K, CD_3CN) δ_H 6.51 (br s,2H, C*H*=C*H*), 5.12 (s, 2H, 2 C*H*O), 3.51 (t, 2H, *J* = 6.0 Hz, CH_2CH_2O), 3.54 (t, 2H, *J* = 6.0 Hz, CH_2CH_2N), 2.90 (br s, 2H, 2 C*H*CO), 2.24 (br s, 1H, O*H*); ^{13}C NMR (75 MHz, 298 K, CD_3CN) δ_C 171.0 (*C*=O),136.1 (*C*H=*C*H), 80.5 (*C*HO), 58.0 (CH_2CH_2O), 47.1 (*C*HCO), 40.5 (CH_2CH_2N); IR ν cm^{-1} 3472 (OH), 1682 (imide C=O); MS (ESI$^+$): *m/z* 231.9 [**2.04**+Na]$^+$.

2.05



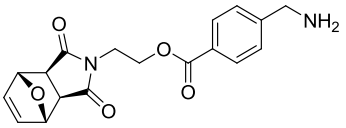
Synthesised according to a modified literature procedure.[143] To an ice cooled solution 4-aminomethylbenzoic acid (1 g, 6.62 mmol) in dioxane (15 mL) and aqueous sodium hydroxide 1M (15 mL) was added a solution of di-*tert*-butyl dicarbonate (2.17 g, 10 mmol) dissolved in dioxane (5 mL). The mixture was stirred for 48 h, acidified to pH 4 with HCl 4M and extracted with CH_2Cl_2 (2 x 20 mL). The organic layers were collected, washed with brine (15 mL) and dried over $MgSO_4$. The solution was filtered and concentrated *in vacuo* to provide a white solid (750 mg, 3.00 mmol, 45%). m.p. 162-163°C; ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 7.90 (d, *J* = 8.2 Hz, 2H, 2 ArC*H*), 7.35 (d, *J* = 8.2Hz, 2H, 2 ArC*H*), 4.20 (br s, 2H, CH_2), 1.41 (s, 9H, 3 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 167.2 (*C*OOH), 155.8 (NH*C*OO), 145.3 (Ar*C*), 129.3 (Ar*C*H), 129.1 (Ar*C*), 126.9 (Ar*C*H), 77.9 ($C(CH_3)_3$), 43.2 (CH_2), 28.2 (CH_3); IR ν cm^{-1} 3349 (NH), 2980 (saturated CH), 1679 (ester C=O), 1611 (imide C=O); MS (ESI$^+$): *m/z* 274.1 [**2.05**+Na]$^+$.

2.06



Amine **2.05** (700 mg, 2.78 mmol) was dissolved in dry CH_2Cl_2 with alcohol **2.04** (583 mg, 2.78 mmol), PyBOP (1.74g, 3.34mmol) and NEt_3 (0.8 L, 5.57mmol). The mixture was stirred overnight at room temperature, and then washed with water (15 mL), saturated citric acid (15 mL), saturated sodium carbonate (15 mL), water (15 mL) and brine (15 mL). The organic layer was dried with $MgSO_4$, filtered off and concentrated *in vacuo* and the white solid recyrstallised from EtOAc (797 mg, 1.80 mmol, 65%). m.p. 93-94 ˚C; ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 7.96 (d, *J* = 8.2 Hz, 2H, 2 ArC*H*), 7.35 (d, *J* = 8.2Hz, 2H, 2 ArC*H*), 6.52 (s, 2H, C*H*=C*H*), 5.26 (s, 2H, 2 C*H*O), 4.46 (t, *J* = 6.3Hz, 2H, CH_2CH_2O), 3.37 (m, 2H, CH_2-NHBoc), 3.92 (t, *J* = 6.3Hz, 2H, CH_2CH_2N), 2.88 (s, 2H, 2 C*H*CO), 1.49 (s, 9H, 3 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 176.0 (imide *C*=O), 166.0 (*C*OO), 155.7 (Ar*C*), 144.5 (Ar*C*), 136.5 (*C*H=*C*H), 130.1 (Ar*C*H), 127.2 (Ar*C*H), 128.8 (Ar*C*), 80.9 ($C(CH_3)_3$), 77.4 (*C*HO), 61.3 (CH_2CH_2O), 47.5 (*C*HCO), 44.3 (CH_2NHBoc), 37.8 (CH_2CH_2N), 28.4 (CH_3); IR ν cm^{-1} 3311 (NH), 1700 (imide and ester C=O), 1677 (carbamate C=O); CHN Analysis Calc. for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C 57.92; H 4.86; N 11.26%.

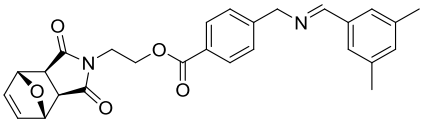
2.07



2.06 (535mg, 1.21 mmol) was stirred overnight in a 1:1 solution of CH_2Cl_2:TFA (5 mL). The solvent was removed *in vacuo*; the residue was diluted with CH_2Cl_2 and washed with saturated sodium bicarbonate (2 x10 mL) and brine (10 mL). The organic layer was dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford a white precipitate (380 mg, 1.11 mmol, 92%). m.p. 144-145 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.88 (d, 2H, *J* = 8.2

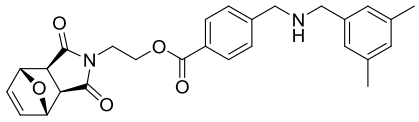
Hz, 2 ArC*H*), 7.30 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*), 6.43 (s, 2H, C*H*=C*H*), 5.17 (s, 2H, 2 C*H*O), 4.37 (t, 2H, *J* = 5.4 Hz, CH_2CH_2O), 3.86 (s, 2H, CH_2NH_2), 3.83 (t, 2H, *J* = 5.4Hz, CH_2CH_2N), 2.79 (s, 2H, 2 C*H*CO), 1.95 (br s, 2H, NH_2); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide *C*=O), 166.0 (*C*OO), 148.2 (Ar*C*), 136.6 (*C*H=*C*H), 130.1 (Ar*C*H), 128.4 (Ar*C*), 127.0 (Ar*C*H), 80.9 (*C*HO), 61.2 (CH_2CH_2O), 47.5 (*C*HCO), 46.0 (CH_2NH_2), 37.9 (CH_2CH_2N); IR ν cm^{-1} 3403 (NH_2), 1718 (imide C=O), 1605 (C-O); HRMS (ESI$^+$): *m/z* found 343.1285 calc for $C_{18}H_{19}N_2O_5$ 343.1288 [**2.07**+H]$^+$.

2.08



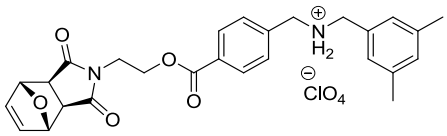
2.07 (130 mg, 0.38 mmol) was dissolved in hot MeOH (5 mL). 3,5-dimethylbenzaldehyde (50 mg, 0.37 mmol) was added and the solution allowed to cool and stirred at room temperature for 24 h. The reaction was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered and solvent removed *in vacuo* to provide a pale yellow solid (170 mg, 0.37 mmol, 98%). m.p. 140-141°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.18 (s, 1H, C*H*-N=C), 7.80 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*), 7.24 (s, 2H, 2 ArC*H*), 7.23 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*), 6.92 (s, 1H, ArC*H*), 6.32 (s, 2H, C*H*=C*H*), 5.07 (s, 2H, 2 C*H*O), 4.67 (s, 2H, CH_2-N=C), 4.27 (t, 2H, *J* = 5.4 Hz, CH_2CH_2O), 3.74 (t, 2H, *J* = 5.4 Hz, CH_2CH_2N), 2.69 (s, 2H, 2 C*H*CO), 2.19 (s, 6H, 2 CH_3);^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 175.4 (imide *C*=O), 165.6 (*C*OO), 162.6 (*C*H=N), 144.3 (Ar*C*), 137.7 (Ar*C*), 135.9 (*C*H=*C*H), 135.2 (Ar*C*), 132.1 (Ar*C*H), 129.3 (Ar*C*H), 127.7 (Ar*C*), 127.2 (Ar*C*H), 125.5 (Ar*C*H), 80.3 (*C*HO), 64.0 (CH_2-N=C), 60.6 (CH_2CH_2O), 46.8 (*C*HCO), 37.2 (CH_2CH_2N), 21.1 (CH_3); IR ν cm^{-1} 3001 (saturated C-H), 1695 (imide and ester C=O), 1644 (C=N); MS (ESI$^+$): *m/z* 459.1 [**2.08**+H]$^+$; CHN analysis found, C 70.65, H 5.84, N 5.57 calc for $C_{27}H_{26}N_2O_5$ C 70.73, H 5.72, N 6.11%.

2.09



To the imine **2.08** (200 mg, 0.44 mmol) dissolved in MeOH (2 mL), sodium cyanoborohydride (30 mg, 0.48 mmol) was added and one drop of HOAc. The reaction was monitored by TLC. The reaction mixture was partitioned between CH_2Cl_2 (10 mL) and water (10 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to provide a yellow solid used without further purification (190 mg, 0.41 mmol, 93%). m.p. 115-116°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.89 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*), 7.32 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*), 6.86 (s, 2H, 2 ArC*H*), 6.83 (s, 1H, ArC*H*), 6.41 (s, 2H, C*H*=C*H*), 5.16 (s, 2H, 2 C*H*O), 4.36 (t, 2H, *J* = 5.4 Hz, CH_2CH_2O), 4.17 (br s, 1H, N*H*), 3.82 (t, 2H, *J* = 5.4 Hz, CH_2CH_2N), 3.78 (s, 2H, CH_2NH), 3.66 (s, 2H, CH_2NH), 2.78 (s, 2H, 2 C*H*CO), 2.23 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide C=O), 166.1 (*C*OO), 144.7 (Ar*C*), 138.7 (Ar*C*), 138.1 (Ar*C*), 136.5 (*C*H=*C*H), 129.9 (Ar*C*H), 129.0 (Ar*C*H), 128.7 (Ar*C*), 128.3 (Ar*C*H), 126.2 (Ar*C*H), 80.9 (*C*HO), 61.2 (CH_2CH_2O), 52.6 (CH_2NH), 52.2 (CH_2NH), 47.5 (*C*HCO), 37.9 (CH_2CH_2N), 21.3 (CH_3); IR ν cm^{-1} 2965 (saturated C-H), 1699 (imide and ester C=O), 1607 (C-O stretching).

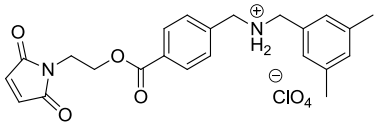
2.10



The amine **2.09** (100 mg, 0.22 mmol) was dissolved in CH_2Cl_2 (10 mL) and washed with an aqueous solution of $HClO_4$ (10%) (2 x 10 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the ClO_4^- salt (120 mg, 0.21 mmol, 97 %). m.p. 92-93 °C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.02 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*), 7.61 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*), 7.13 (m, 3H, 3 ArC*H*), 6.52 (s, 2H, C*H*=C*H*), 5.11 (s, 2H, 2 C*H*O), 4.39 (t, 2H, *J* = 5.4 Hz, CH_2CH_2O), 4.33 (s, 2H, $CH_2NH_2^+$), 4.23 (s, 2H, $CH_2NH_2^+$),

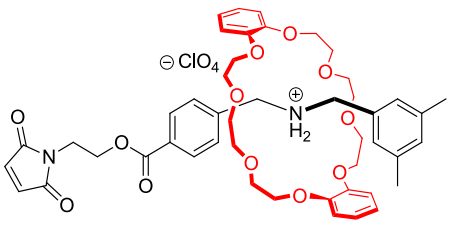
3.82 (t, 2H, J = 5.4 Hz, CH_2CH_2N), 2.90 (s, 2H, 2 C*H*CO), 2.35 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.3 (imide *C*=O), 166.2 (*C*OO), 138.5 (Ar*C*), 136.3 (Ar*C*), 136.1 (*C*H=*C*H), 135.1 (Ar*C*), 130.8 (Ar*C*H), 130.0 (Ar*C*H), 129.8 (Ar*C*), 129.5 (Ar*C*H), 127.5 (Ar*C*H), 80.6 (*C*HO), 61.1 (CH_2CH_2O), 51.4 ($CH_2NH_2^+$), 50.5 ($CH_2NH_2^+$), 47.1 (*C*HCO), 36.9 (CH_2CH_2N), 19.9 (CH_3); IR ν cm^{-1} 3093 (saturated C-H), 1694 (imide and ester C=O), 1094 (ClO_4); HRMS (ESI^+): *m/z* found, 461.2082 calc for $C_{27}H_{29}N_2O_5$ 461.2071 [**2.10**-ClO_4]$^+$.

2.11



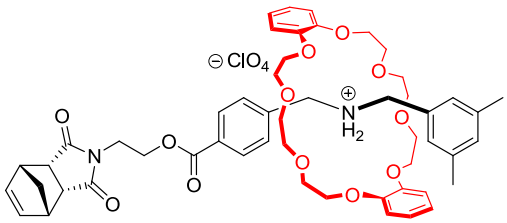
The ClO_4^- salt **2.10** (50 mg, 0.11 mmol) was heated under microwave irradiation in acetonitrile (1 mL) (150W, 110 °C, 3 h). The solvent was removed *in vacuo* to provide an off-white solid used without further purification (42 mg, 0.085 mmol, 78 %). m.p. 64-65°C; ^1H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.03 (d, 2H, J = 8.3 Hz, 2 ArC*H*), 7.60 (d, 2H, J = 8.3 Hz, 2 ArC*H*), 7.15 (s, 1H, ArC*H*), 7.11 (s, 2H, 2 ArC*H*), 6.81 (s, 2H, C*H*=C*H*), 4.44 (t, 2H, J = 5.3 Hz, CH_2CH_2O), 4.31 (s, 2H, $CH_2NH_2^+$), 4.21 (s, 2H, $CH_2NH_2^+$), 3.88 (t, 2H, J = 5.3 Hz, CH_2CH_2N), 2.36 (s, 6H, 2 CH_3), 2.23 (br s, 2H, NH_2^+); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.6 (imide *C*=O), 165.1 (*C*OO), 138.5 (Ar*C*), 136.1 (Ar*C*), 134.1 (*C*H=*C*H), 130.8 (Ar*C*H), 130.2 (Ar*C*), 130.1 (Ar*C*H), 129.7 (Ar*C*), 129.5 (Ar*C*H), 127.6 (Ar*C*H), 62.2 (CH_2CH_2O), 51.3 ($CH_2NH_2^+$), 50.4 ($CH_2NH_2^+$), 36.2 (CH_2CH_2N), 19.9 (CH_3); IR ν cm^{-1} 3502 (NH_2), 1746 (imide and ester C=O), 1051 (ClO_4); HRMS (ESI^+): *m/z* found, 393.1817 calc for $C_{23}H_{25}N_2O_4$ 393.1809 [**2.11**-ClO_4]$^+$.

2.12



Thread **2.11** (10 mg, 0.02 mmol) and DB24C8 (18 mg, 0.04 mmol) were dissolved in deuterated acetonitrile (0.5 mL). The reaction was followed by ^{1}H NMR until pseudorotaxane formation reached completion. **Pseudorotaxane 2.12** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.69 (d, 2H, *J* = 8.5Hz, ⊂ 2 ArC*H*), 7.46 (d, 2H, *J* = 8.5Hz, ⊂ 2 ArC*H*), 7.94-6.78 (m, 13H, ⊂ 2 C*H*=CH, ⊂ 3 ArC*H*, ⊂ 8 crown ArC*H*), 4.81-4.78 (m, 2H, ⊂ $CH_2NH_2^+$), 4.57-4.54 (m, 2H, ⊂ $CH_2NH_2^+$), 4.36 (t, 2H, *J* = 5.3Hz, ⊂ CH_2CH_2O), 4.06-4.03 (m, 8H, ⊂ 4 OCH_2), 3.84-3.76 (m, 10H, ⊂ 4 OCH_2 and CH_2CH_2N), 3.56 (s, 8H, ⊂ 4 OCH_2), 2.19 (s, 6H, ⊂ 2 CH_3); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93-6.90 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); HRMS (ESI$^+$): *m/z* found, 841.3964 calc for $C_{47}H_{57}N_2O_{12}$ 841.3906 [**2.12**-ClO_4]$^+$.

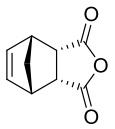
2.13



To the pseudorotaxane **2.12** (19 mg, 0.02mmol) in acetonitrile (2 mL), freshly distilled cyclopentadiene (0.1 mL, excess) was added. Excess cyclopentadiene and solvent was removed *in vacuo*. Purification *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2/MeOH 9:1) gave a white foam (10 mg, 0.01 mmol, 50 %). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.75 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*), 7.64 (br s, 2H, ⊂ $^+NH_2$), 7.52 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*), 6.92 (s, 2H, ⊂ 2 ArC*H*), 6.85-6.79 (m, 9H, ⊂ ArC*H* and ⊂ 8 crown ArC*H*), 5.88 (br s, 2H, ⊂ C*H*=C*H*), 4.81 (m, 2H, ⊂ $CH_2NH_2^+$), 4.53 (m, 2H, ⊂ $CH_2NH_2^+$), 4.27 (t, 2H, *J* = 5.3 Hz, ⊂ CH_2CH_2O), 4.05 (m, 8H, ⊂ 4 OCH_2), 3.61 (m, 8H, ⊂ 4 OCH_2), 3.69 (t, 2H, *J* = 5.3 Hz, ⊂ CH_2CH_2N), 3.59 (br s, 8H, ⊂ 4 OCH_2), 3.29 (br s, 2H, ⊂ 2 C*H*CO), 3.25 (br s, 2H, ⊂ 2 C*H*CH_2), 2.15 (s, 6H, ⊂ 2 CH_3), 1.61 (d, 1H, *J* = 9.0 Hz, C*H*H), 1.57 (d, 1H, *J* = 9.0 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 178.9 (imide *C*=O), 166.6 (ester *C*=O),

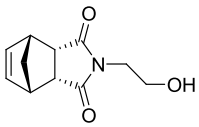
148.7 (Ar*C*), 139.7 (Ar*C*), 138.7 (Ar*C*), 135.6 (*C*H=*C*H), 133.0 (Ar*C*), 131.7 (Ar*C*H), 131.6 (Ar*C*), 131.0 (Ar*C*H), 130.8 (Ar*C*H), 128.2 (Ar*C*H), 122.6 (Ar*C*H), 113.8 (Ar*C*H), 71.9 (O*C*H_2), 71.5 (O*C*H_2), 69.3 (O*C*H_2), 63.0 (CH_2*C*H_2O), 54.1 (*C*$H_2NH_2^+$), 53.3 (bridgehead *C*H_2), 53.1 (*C*$H_2NH_2^+$), 46.9 (*C*HCH_2*C*H), 46.1 (*C*HO), 38.2 (CH_2*C*H_2N), 21.6 (*C*H_3); IR ν cm^{-1} 2874 (saturated C-H), 1698 (ester and imide C=O), 1253 (C-O), 1084 (ClO_4); HRMS (ESI^+): *m/z* found, 907.4378 calc for $C_{52}H_{63}N_2O_{12}$ 907.4376 [**2.13**-ClO_4]$^+$.

2.14



Synthesised according to a modified literature procedure.[144] Maleic anhydride, (16 g, 163 mmol) was dissolved in EtOAc (50 mL) and petroleum ether (60-80˚C) (50 mL) and the solution cooled to 0°C. Cyclopentadiene (12 g, 187 mmol) was added carefully to the solution and stirred for 3 h. The precipitate formed was filtered and washed with petroleum ether (60-80°C) to provide white crystals (19.10 g, 116 mmol, 71%). ^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ_H 6.30 (br s, 2H, C*H*=C*H*), 3.57 (br s, 2H, 2 C*H*CO), 3.49 (br s, 2H, 2 C*H*CH_2), 1.76 (d, 1H, *J* = 9.0 Hz, C*H*H), 1.56 (d, 1H, *J* = 9.0 Hz, CH*H*); ^{13}C NMR (75 MHz, 298 K, $CDCl_3$) δ_C 170.8 (imide *C*=O), 134.9 (*C*H=*C*H), 52.1 (bridgehead *C*H_2), 46.5 (*C*HCH_2), 45.4 (*C*HCO); MS (ESI^+): *m/z* 165.0 [**2.14**+H]$^+$.

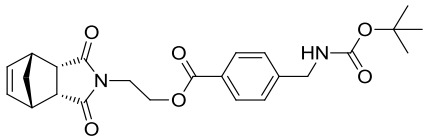
2.15



Synthesised according to a modified literature procedure.[139] **2.14** (5g, 30 mmol) was dissolved in EtOH (25 mL) and cooled to 0˚C. Ethanolamine (1.8 mL, 30 mmol) and NEt_3 (4.2 mL, 30 mmol) in EtOH (25 mL) were added dropwise to the stirring solution. The resulting mixture was heated to 70˚C overnight. The EtOH was removed *in vacuo* to provide

an oil which was taken up in $CHCl_3$ (30 mL) and partitioned with water (10 mL). It was washed with HCl 1M (3 x 20 mL). The organic layer was dried over $MgSO_4$, filtered and the product was obtained by precipitation on the addition of Et_2O. The white crystals were filtered (2.25 g, 10.9 mmol, 37%). ^{1}H NMR (300 MHz, 298 K, CD_3CN) δ_H 6.05 (s, 2H, C*H*=C*H*), 3.44 (t, 2H, *J* = 5.5 Hz, CH_2CH_2OH), 3.36 (t, 2H, *J* = 5.5 Hz, CH_2CH_2N), 3.27 (br s, 4H, 2 C*H*CH_2 and 2 C*H*CO), 1.62 (d, 1H, *J* = 8.5 Hz, CH*H*), 1.56 (d, 1H, *J* = 8.5 Hz, C*H*H); ^{13}C NMR (75 MHz, 298 K, CD_3CN) δ_C 177.8 (imide *C*=O), 134.3 (*C*H=*C*H), 58.5 (CH_2CH_2OH), 51.5 (bridgehead CH_2), 45.4 (*C*HCH_2), 44.5 (*C*HCO), 40.2 (CH_2CH_2N); IR ν cm^{-1} 3508 (OH), 3015 (saturated C-H), 1756 (imide C=O); HRMS (ESI$^+$): found, 230.0791, calc. for $C_{11}H_{13}NO_3Na$ 230.0788 [**2.15**+Na]$^+$.

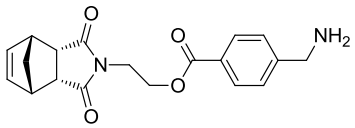
2.16



The alcohol **2.15** (165 mg, 0.8 mmol) and acid **2.05** (200 mg, 0.8 mmol) were dissolved in CH_2Cl_2 (10 mL). The reaction was cooled to 0°C then PyBOP (499 mg, 1 mmol) and NEt_3 (0.22 mL, 1.6 mmol) were added. The reaction was warmed to room temperature and stirred for 48 h. The reaction was diluted with CH_2Cl_2 (15 mL) and washed with water (15 mL), saturated citric acid (15 mL), saturated sodium carbonate (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$, filtered and solvent removed *in vacuo*. The crude product was purified *via* flash chromatography (SiO_2: EtOAc) to give a colourless oil (160 mg, 0.36 mmol, 45 %). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) 7.94 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.34 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 5.96 (s, 2H, C*H*=C*H*), 4.35 (br s, 2H, CH_2NH), 4.30 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 3.76 (t, 2H, , *J* = 5.3 Hz, CH_2CH_2N), 3.35 (br s, 2H, 2 C*H*CO), 3.26 (br s, 2H, 2 C*H*CH_2), 1.67 (d, 1H, *J* = 8.5 Hz, C*H*H), 1.51 (d, 1H, *J* = 8.5 Hz, CH*H*), 1.44 (s, 9H, 3 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 177.3 (imide *C*=O), 165.9 (*C*OO), 155.9 (carbamate *C*=O), 144.5 (Ar*C*H), 135.1 (Ar*C*), 134.3 (*C*H=*C*H), 129.9 (Ar*C*H), 128.6 (Ar*C*), 127.1 (ArCH), 61.6 (CH_2CH_2O), 52.1 (bridgehead CH_2), 45.7

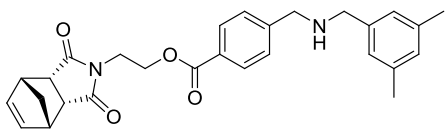
($CHCH_2$), 44.8 ($CHCO$), 44.2 (CH_2NH), 37.1 (CH_2CH_2N), 28.3 (CH_3); IR ν cm^{-1} 2975 (saturated C-H), 1694 (imide and ester C=O), 1270 (C-O); HRMS (ESI^+): *m/z* found, 463.1835 calc for $C_{24}H_{28}N_2NaO_6$ 463.1840 [**2.16**+Na]$^+$.

2.17



2.16 (150 mg, 0.34 mmol) was dissolved in CH_2Cl_2 (2 mL) and TFA (1 mL) and stirred at room temperature for 24 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with a saturated aq. sodium carbonate (2 x 15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$, filtered and solvent removed *in vacuo* to give the product as a colourless oil (100 mg, 0.29 mmol, 85 %). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) 7.94 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.38 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 5.96 (s, 2H, C*H*=C*H*), 4.10 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.92 (s, 2H, CH_2NH_2), 3.75 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.33 (s, 2H, 2 C*H*CO), 3.25 (s, 2H, 2 C*H*CH_2), 2.33 (br s, 2H, NH_2), 1.66 (d, 1H, *J* = 8.5 Hz, C*H*H), 1.50 (d, 1H, *J* = 8.5 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 177.4 (imide *C*=O), 165.9 (*C*OO), 147.7 (Ar*C*), 134.2 (*C*H=*C*H), 129.9 (Ar*C*H), 128.3 (Ar*C*), 127.1 (Ar*C*H), 61.6 (CH_2CH_2O), 52.1 (bridgehead CH_2), 45.8 (CH_2NH_2), 45.7 ($CHCH_2$), 44.8 ($CHCO$), 37.1 (CH_2CH_2N); IR ν cm^{-1} 2993 (saturated C-H), 1692 (ester C=O), 1271 (C-O); HRMS (ESI^+): *m/z* found, 341.1490 calc for $C_{19}H_{21}N_2O_4$ 341.1496 [**2.17**+H]$^+$.

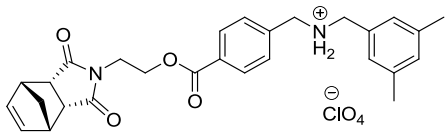
2.18



Amine **2.17** (120 mg, 0.35 mmol) and 3,5-dimethylbenzaldehyde (0.49 ml, 0.36 mmol) were dissolved in MeOH (5 mL) and stirred at room temperature for 24 h. Sodium cyanoborohydride (24 mg, 0.4 mmol) and HOAc (0.1 mL) were added and the reaction stirred at room temperature for a further 24 h. The reaction was diluted with water (15 mL) and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic extracts were dried over

$MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 95:5) to give a colourless oil (130 mg, 0.28 mmol, 81 %). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.96 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 7.46 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 6.97 (s, 2H, 2 ArC*H*), 6.95 (s, 1H, ArC*H*), 6.29 (s, 1H, N*H*), 5.98 (s, 2H, C*H*=C*H*), 4.31 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 3.94 (s, 2H, CH_2NH), 3.83 (s, 2H, CH_2NH), 3.75 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N), 3.34 (s, 2H, 2 C*H*CO), 3.27(s, 2H, 2 C*H*CH_2), 2.30 (s, 6H, 2 CH_3), 1.69 (d, 1H, *J* = 8.5 Hz, C*H*H), 1.52 (d, 1H, *J* = 8.5 Hz, C*H*H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 177.4 (imide *C*=O), 165.7 (*C*OO), 140.2 (Ar*C*), 138.5 (Ar*C*), 134.2 (*C*H=*C*H), 130.1 (Ar*C*H), 130.0 (Ar*C*H), 129.6(0) (Ar*C*), 129.5(7) (ArC), 129.1 (Ar*C*H), 126.9 (Ar*C*H), 61.7 (CH_2CH_2O), 52.1 (CH_2NH), 51.6 (bridgehead CH_2), 50.9 (CH_2NH), 45.8 ($CHCH_2$), 44.9 (*C*HCO), 37.1 (CH_2CH_2N), 21.2 (CH_3); IR ν cm^{-1} 2940 (saturated C-H), 1697 (imide and ester C=O), 1253 (C-O); HRMS (ESI$^+$): *m/z* found, 459.2274 calc for $C_{28}H_{31}N_2O_4$ 459.2278 [**2.18**+H]$^+$.

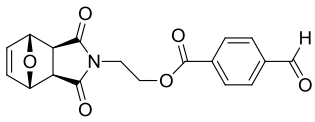
2.19



The thread **2.18** (25 mg, 0.05 mmol) was dissolved in CH_2Cl_2 (5 mL) and washed with a 10% aqueous solution of $HClO_4$ (2 x 10 mL). The organic layer was dried over $MgSO_4$, filtered and solvent removed *in vacuo* to provide the product as a white solid (27 mg, 0.048 mmol, 97 %). m.p. 84-87°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.01 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.57 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 7.10 (s, 1H, ArC*H*), 7.06 (s, 2H, 2 ArC*H*), 5.92 (s, 2H, C*H*=C*H*), 4.28 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 4.27 (s, 2H, $CH_2NH_2^+$), 4.16 (s, 2H, $CH_2NH_2^+$), 3.66 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N), 3.27 (s, 2H, 2 C*H*CO), 3.23 (br s, 2H, 2 C*H*CH_2), 2.31 (s, 6H, 2 CH_3), 1.58 (d, 1H, *J* = 8.5 Hz, C*H*H), 1.52 (d, 1H, *J* = 8.5 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 175.1 (imide *C*=O), 166.7 (*C*OO), 140.3 (Ar*C*), 136.8 (Ar*C*), 136.5 (Ar*C*), 135.7 (*C*H=*C*H), 132.4 (Ar*C*H), 131.8 (Ar*C*H), 131.5 (Ar*C*), 131.3 (Ar*C*H), 129.1 (Ar*C*H), 63.3 (CH_2CH_2O), 53.1 ($CH_2NH_2^+$), 53.0 (bridgehead

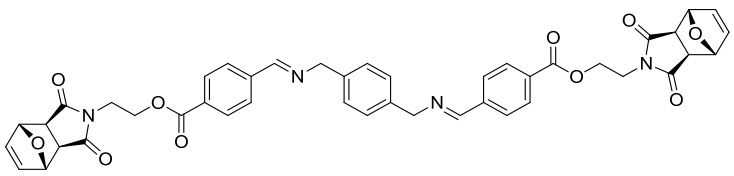
CH_2), 52.1 (*C*$H_2NH_2^+$), 47.0 (*C*HCH_2), 46.0 (*C*HCO), 38.2 (CH_2*C*H_2N), 21.6 (*C*H_3); IR ν cm^{-1} 2979 (saturated C-H), 1699 (ester and imide C=O), 1244 (C-O); HRMS (ESI^+): *m/z* found, 459.2279 calc for $C_{28}H_{31}N_2O_4$ 459.2278 [**2.19**+H]$^+$.

2.20



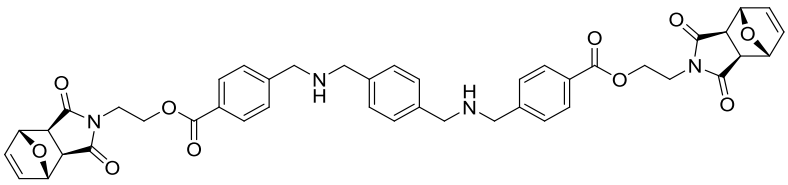
The Diels-Alder adduct **2.04** (2.95g, 14.1 mmol) and 4-carboxybenzaldehyde (2g, 13.3 mmol) were dissolved in CH_2Cl_2 (50 mL). The *N,N,N',N'*-tetramethylchloroformamidinium-hexafluorophosphate (4.28g, 14.1 mmol) was added to the stirring solution along with NEt_3 (4 mL) and DMAP (10mg, cat.). The solution was stirred at room temperature for 48 h. The organic layer was washed with water (20 mL), saturated sodium bicarbonate solution (20 mL), saturated citric acid (20 mL), water (20 mL) and brine (20 mL). The solution was dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The crude pale yellow solid was recrystallised from EtOAc to give a white powder (2.88 g, 8.44 mmol, 64 %). m.p. 139 - 140°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 10.12 (s, 1H, CO*H*), 8.18 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 7.97 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 6.53 (s, 2H, C*H*=C*H*), 5.26 (s, 2H, 2 C*H*O), 4.52 (t, 2H, *J* = 5.3 Hz, CH_2C*H*$_2$O), 3.96 (t, 2H, *J* = 5.3 Hz CH_2C*H*$_2$N), 2.90 (s, 2H, 2 C*H*CO); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 191.5 (*C*OH), 176.0 (imide *C*=O), 166.1 (*C*OO), 136.6 (Ar*C*), 134.8 (Ar*C*), 130.3 (Ar*C*H), 129.5 (Ar*C*H), 80.9 (C*H*O), 61.8 (CH_2*C*H_2O), 47.5 (*C*HCO), 37.8 (CH_2*C*H_2N); IR ν cm^{-1} 2976 (saturated C-H), 1689.5 (ester and imide C=O); HRMS (ESI^+): *m/z* 364.0792 calc for $C_{18}H_{15}NO_6Na$ 364.0792 [**2.20**+Na]$^+$; CHN Analysis Found: C 63.10; H 4.46; N 4.15. Calc. for $C_{18}H_{15}NO_6$: C 63.34; H 4.43; N 4.10%.

2.21



2.20 (800 mg, 2.35 mmol) was stirred in hot MeOH (8 mL) with *p*-xylylenediamine (150 mg, 1.10 mmol) for 2 h. A white precipitate was collected and washed in ice cold MeOH (800mg, 1.01 mmol, 92 %). m.p. 148-149°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.42 (s, 2H, 2 C*H*=N), 8.02 (d, *J* = 8.4 Hz, 4H, 4 ArC*H*), 7.96 (d, *J* = 8.4 Hz, 4H, 4 ArC*H*), 7.33 (s, 4H, 4 ArC*H*), 6.49 (s, 4H, 2 C*H*=C*H*), 5.23 (s, 4H, 4 C*H*O), 4.84 (s, 4H, 2 CH_2-N=C), 4.46 (d, *J* = 5.3Hz, 4H, 2 CH_2CH_2O), 3.91 (t, *J* = 5.3Hz, 2H, 2 CH_2CH_2N), 2.86 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.1 (imide *C*=O), 165.9 (*C*OO), 161.2 (*C*H=N), 140.0 (Ar*C*), 137.6 (Ar*C*), 136.5 (*C*H=*C*H), 131.5 (Ar*C*), 130.0 (Ar*C*H), 128.3 (Ar*C*H), 128.2 (Ar*C*H), 80.9 (*C*HO), 64.8 (CH_2-N=C), 61.4 (CH_2CH_2O), 47.5 (*C*HC), 37.8 (CH_2CH_2N); IR ν cm^{-1} 2845 (saturated C-H), 1701 (imide and ester C=O), 1639 (C=N); MS (ESI$^+$): *m/z* 805.1 [**2.21**+Na]$^+$.

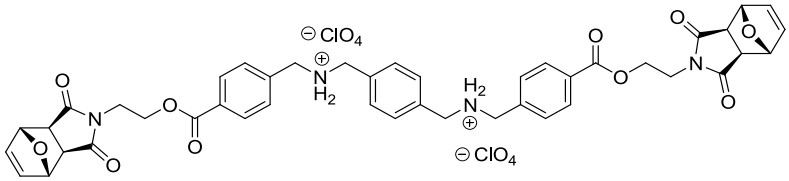
2.22



The imine **2.21** (700 mg, 0.9 mmol) was dissolved in $CHCl_3$ (7.5 mL) and MeOH (7.5 mL). Sodium cyanoborohydride (62 mg, 1 mmol) was added to the stirring solution along with 3 drops of HOAc. The solution was left to stir at room temperature for 24 h. Water (20 mL) was added and the solution extracted with $CHCl_3$ (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed to produce a white foam (550 mg, 0.70 mmol, 78 %). m.p. 137-138°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.96 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.42 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.31 (s, 4H, 4 ArC*H*), 6.50 (s, 4H, 4 C*H*=CH), 5.25 (s, 4H, 4 C*H*O), 4.45 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 3.91 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N), 3.86 (s, 4H, 2 CH_2NH), 3.80 (s, 4H, 2 CH_2NH), 2.87 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 175.9 (imide *C*=O), 166.1 (*C*OO), 145.6 (Ar*C*), 138.7 (Ar*C*), 136.5 (*C*H=*C*H), 129.8 (Ar*C*H), 128.4 (Ar*C*), 128.3 (Ar*C*H), 128.0 (Ar*C*H), 80.9 (*C*HO), 61.7 (CH_2CH_2O), 52.8 (CH_2NH), 52.6 (CH_2NH), 47.4 (*C*HCO), 37.8

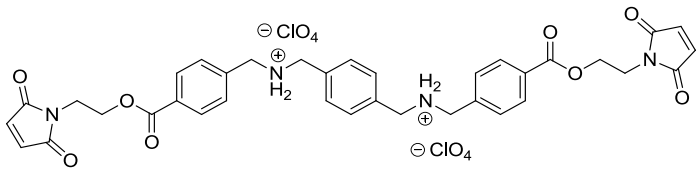
(CH_2CH_2N); IR ν cm^{-1} 3339 (NH stretching), 2957 (saturated C-H), 1694 (ester and imide C=O); HRMS (ESI^+) *m/z*: found, 787.300 calc for $C_{44}H_{43}N_4O_{10}$ 787.2974 [**2.22**+H]$^+$.

2.23



2.22 (450 mg, 0.57 mmol) was dissolved in CH_2Cl_2 (10 mL). The organic layer was washed with a 10% aqueous solution of $HClO_4$. A white precipitate formed in the aqueous layer which was filtered and washed with water (250 mg, 0.25 mmol, 44 %). m.p. 129-130°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.99 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.59 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.54 (s, 4H, 4 ArC*H*), 7.39 (br s, 4H, 2 NH_2), 6.49 (s, 4H, C*H*=C*H*), 5.08 (s, 4H, 4 C*H*O), 4.38 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 4.33 (8H, m, 2 CH_2NH_2 and 2 CH_2CH_2N), 3.80 (s, 4H, 2 $CH_2NH_2^+$), 2.87 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 177.9 (imide *C*=O), 166.7 (*C*OO), 137.8 (*C*H=*C*H), 136.5 (Ar*C*), 133.3 (Ar*C*), 132.6 (Ar*C*), 132.2 (Ar*C*H), 131.8 (Ar*C*H), 131.3 (Ar*C*H), 82.3 (*C*HO), 62.8 (CH_2CH_2O), 52.42 (2 $CH_2NH_2^+CH_2$), 48.8 (*C*HCO), 38.6 (CH_2CH_2N); IR ν cm^{-1} 3013 (saturated CH), 1722 (ester and imide C=O), 1612 (C-O), 1078 (ClO_4); HRMS (ESI^+): *m/z* found, 787.2967 calc for $C_{44}H_{43}N_4O_{10}$ 787.2974 [**2.23**-$HClO_4$]$^+$; CHN Analysis Found: C 53.12; H 4.42; N 5.66. Calc. for $C_{44}H_{44}N_4O_{18}Cl_2$: C, 53.30; H, 4.49; N, 5.67%.

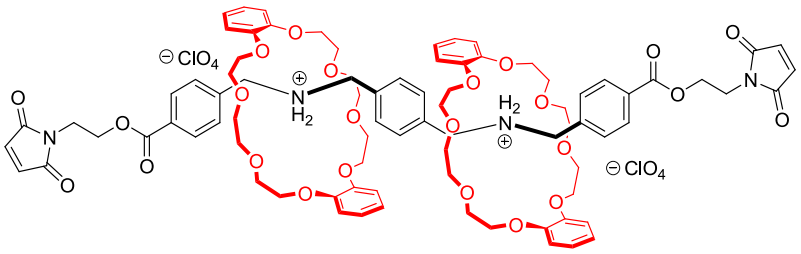
2.24



The thread **2.23** (100 mg, 0.10 mmol) was dissolved in acetonitrile (2 mL) and heated under microwave irradiation (150W, 3 h, 110˚C). The solvent was removed *in vacuo* to give a beige solid (85 mg, 0.1 mmol, 100 %). m.p. 235-237 °C (decomp.); ^{1}H NMR (400 MHz, 298

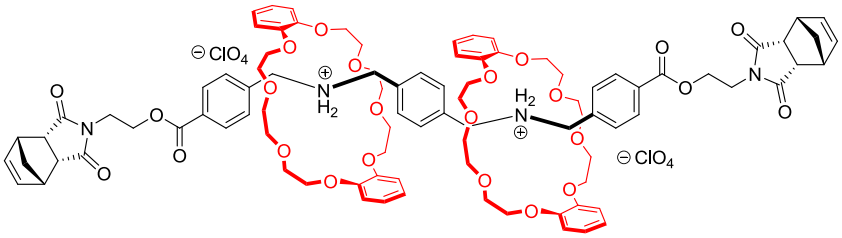
K, CD_3CN) δ_H 8.02 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.63 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.58 (s, 4H, 4 ArC*H*), 6.80 (s, 4H, 2 C*H*=C*H*), 4.42 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 4.35 (4H, m, 2 $CH_2NH_2^+$), 4.32 (m, 4H, 2 $CH_2NH_2^+$), 3.87 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 172.3 (imide *C*=O), 166.8 (*C*OO), 136.6 (Ar*C*), 135.8 (*C*H=*C*H), 133.3 (Ar*C*), 132.5 (Ar*C*), 132.2 (Ar*C*H), 131.8 (Ar*C*H), 131.3 (Ar*C*H), 63.9 (CH_2CH_2O), 52.4 ($CH_2NH_2^+$), 52.3 ($CH_2NH_2^+$), 37.9 (CH_2CH_2N); IR ν cm^{-1} 3099 (saturated C-H), 1708 (ester and imide C=O), 1574 (NH_2); HRMS (ESI^+): *m/z* found, 651.2456 calc for $C_{36}H_{35}N_4O_8$ 651.2449 [**2.24**-H.2ClO_4]$^+$.

2.25



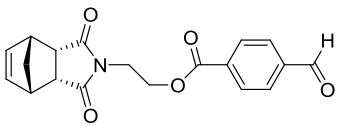
The thread **2.24** (10 mg, 0.012 mmol) was dissolved in deuterated acetonitrile. DB24C8 (21 mg, 0.05 mmol, 4 equiv.) was added to the solution and the extent of threading followed by ^1H NMR. **Pseudorotaxane 2.25** ^1H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.71 (d, 4H, *J* = 8.0 Hz, ⊂ 4 ArC*H*), 7.43 (d, 4H, *J* = 8.0 Hz, ⊂ 4 ArC*H*), 7.03 (s, 4H, ⊂ 4 ArC*H*), 6.80-6.69 (m, 20H, ⊂ 16 crown ArC*H* and ⊂ 4 C*H*=C*H*), 4.70 (m, 4H, ⊂ 2 $CH_2NH_2^+$), 4.56 (m, 4H, ⊂ 2 $CH_2NH_2^+$), 4.36 (t, 4H, *J* = 5.0 Hz, ⊂ 2 CH_2CH_2O), 3.96 (m, 16H, ⊂ 8 OCH_2), 3.82-3.64 (m, 18H, ⊂ 7 OCH_2 and ⊂ 2 CH_2CH_2N), 3.56 (s, 18H, ⊂ 9 OCH_2); Also contains unthreaded **DB24C8** ^1H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); MS (ESI^+): *m/z* found 774.7 calc for $C_{84}H_{100}N_4O_{24}^{2+}$ 774.4 [**2.25**-2ClO_4]$^{2+}$.

2.26



To the pseudorotaxane **2.25** in acetonitrile (2 mL), freshly distilled cyclopentadiene (0.1 mL, excess) was added. The solvent and excess cyclopentadiene were immediately removed *in vacuo*. The solid was extracted with hot benzene (5 x 2 mL) to leave the rotaxane **2.26** (15 mg, 0.008 mmol, 73 %). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.77 (d, 4H, *J* = 8.5 Hz, ⊂ 4 ArC*H*), 7.49 (d, 4H, *J* = 8.0 Hz, ⊂ 4 ArC*H*), 6.97 (s, 4H, ⊂ 4 ArC*H*), 6.83-6.72 (m, 16H, ⊂ 16 crown ArC*H*), 5.88 (m, 4H, ⊂ 4 C*H*=C*H*), 4.72 (m, 4H, ⊂ 2 C$H_2NH_2^+$), 4.52 (m, 4H, ⊂ 2 C$H_2NH_2^+$), 4.25 (t, 4H, *J* = 5.0 Hz, ⊂ 2 CH_2CH_2O), 4.03-3.95 (m, 16 H, ⊂ 6 OCH_2 and ⊂ 2 CH_2CH_2N), 3.77 (m, 8H, ⊂ 4 OCH_2), 3.66 (m, 12H, ⊂ 6 OCH_2), 3.59-3.53 (m, 16H, ⊂ 8 OCH_2), 3.26 (m, 4H, ⊂ 4 C*H*CO), 3.20 (m, 4H, ⊂ 4 C*H*CH_2), 1.56 (d, 2H, *J* = 8.5 Hz, ⊂ 2 C*H*H), 1.51 (d, 2H, *J* = 8.5 Hz, ⊂ 2 CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 178.9 (imide *C*=O), 166.6 (*C*OO), 148.7 (Ar*C*), 138.4 (Ar*C*), 135.6 (*C*H=*C*H), 133.8 (Ar*C*), 131.8 (Ar*C*), 131.0 (Ar*C*H), 130.9 (Ar*C*H), 130.8 (Ar*C*H), 122.6 (Ar*C*H), 113.8 (Ar*C*H), 72.0 (O*C*H_2), 71.5 (O*C*H_2), 69.2 (O*C*H_2), 63.0 (CH_2*C*H_2O), 53.4 (*C*$H_2NH_2^+$), 53.3 (bridgehead *C*H_2), 53.1 (*C*$H_2NH_2^+$), 46.9 (*C*H*C*H_2*C*H), 46.1 (*C*HCO), 38.2 (CH_2*C*H_2N); IR ν cm^{-1} 2979 (saturated C-H), 1699 (ester and imide C=O), 1609 (C-O), 1073 (ClO_4); HRMS (ESI$^+$): *m/z* 840.3835 calc for $C_{94}H_{112}N_4O_{24}$ 840.3828 [**2.26**-2ClO_4]$^{2+}$.

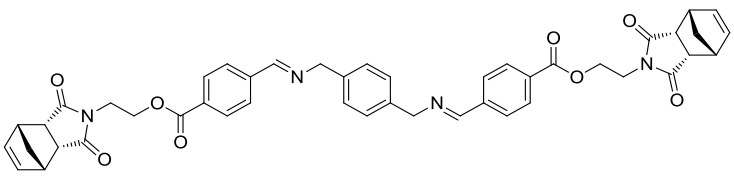
2.27



2.15 (0.74 g, 3.6 mmol) was dissolved in CH_2Cl_2 (20 mL). 4-Carboxybenzaldehyde (500 mg, 3.3 mmol) was added along with the *N*,*N*,*N'*,*N'*-tetramethylchloroformamidinium hexafluorophosphate (1.07 g, 3.8 mmol), NEt_3 (1 mL) and DMAP (40mg, 0.33 mmol). The

solution was stirred for 72 h then washed with water (15 mL), saturated sodium carbonate solution (15 mL), saturated citric acid (15 mL), water (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The resulting yellow solid was taken up in Et_2O and filtered to leave the product as a white solid (0.9 g, 2.7 mmol, 75 %). m.p. 120-122°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 10.10 (s, 1H, CO*H*), 8.15 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.96 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 5.97 (s, 2H, C*H*=C*H*), 4.36 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 3.79 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N), 3.36 (s, 2H, 2 C*H*CO), 3.28 (s, 2H, 2 C*H*CH_2), 1.62 (d, 1H, *J* = 8.5 Hz, C*H*H), 1.58 (d, 1H, *J* = 8.5 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 191.6 (*C*OH), 177.4 (imide *C*=O), 165.2 (*C*OO), 139.3 (Ar*C*), 134.7 (Ar*C*), 134.4 (*C*H=*C*H), 130.3 (Ar*C*H), 129.6 (Ar*C*H), 62.4 (CH_2CH_2O), 52.3 (bridgehead CH_2), 45.9 (*C*HCH_2*C*H), 44.9 (*C*HCO), 37.1 (CH_2CH_2N); IR ν cm^{-1} 2947 (saturated C-H), 1723 (aldehyde C=O), 1688 (imide and ester C=O); HRMS (ESI$^+$): found 362.0999 calc for $C_{19}H_{17}NO_5Na$ 362.1003 [**2.27**+Na]$^+$.

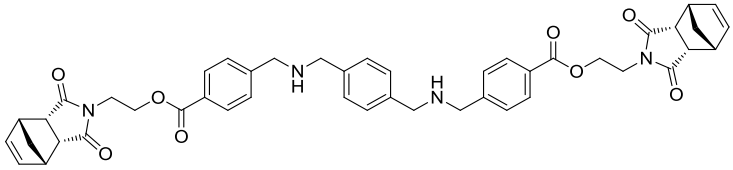
2.28



The aldehyde **2.27** (200 mg, 0.59 mmol) was stirred in hot MeOH (8 mL) with *p*-xylylenediamine (37.5 mg, 0.28 mmol) for 2 h. A white precipitate was collected and washed in ice cold MeOH (180 mg, 0.23 mmol, 83 %). m.p.: 159-162°C; ^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ_H 8.44 (s, 2H, 2 C*H*=N), 8.04 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*), 7.85 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*), 7.34 (s, 4H, 4 ArC*H*), 5.97 (s, 4H, 2 C*H*=C*H*), 4.86 (s, 4H, 2 CH_2N=CH), 4.34 (t, 4H, *J* = 5.5 Hz, 2 CH_2CH_2O), 3.97 (t, 4H, *J* = 5.5 Hz, 2 CH_2CH_2N), 3.36 (br s, 4H, 4 C*H*CO), 3.28 (br s, 4H, 4 C*H*CH_2), 1.71 (d, 2H, *J* = 9.0 Hz, 2 C*H*H), 1.52 (d, 2H, *J* = 9.0 Hz, 2 CH*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 177.7 (imide *C*=O), 166.1 (*C*OO), 161.2 (*C*H=N), 140.5 (Ar*C*), 138.0 (Ar*C*), 134.6 (*C*H=*C*H), 131.7 (Ar*C*), 130.3 (Ar*C*H), 128.6 (Ar*C*H), 128.5 (Ar*C*H), 65.2 (CH_2N=C), 62.2 (CH_2CH_2O), 52.5 (bridgehead CH_2), 46.1 (*C*HCH_2*C*H), 45.3 (*C*HCO), 37.5 (CH_2CH_2N); IR ν cm^{-1} 2985

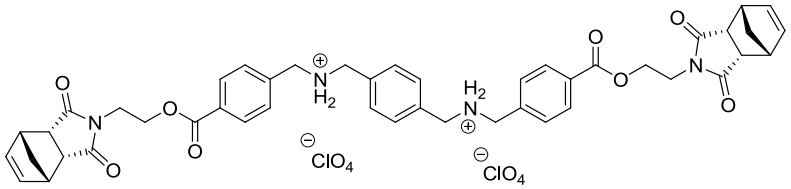
(saturated C-H), 1693 (ester and imide C=O), 1640 (C=N); HRMS (ESI$^+$): *m/z* 779.3095 calc for $C_{46}H_{43}N_4O_8$ 779.3075 [**2.28**+H]$^+$.

2.29



The imine **2.28** (100 mg, 0.13 mmol) was dissolved in MeOH (5 mL) and $CHCl_3$ (5 mL). Sodium cyanoborohydride (9 mg, 0.14 mmol) and a few drops of HOAc were added to the solution. The reaction was stirred at room temperature for 24 h then diluted with water (20 mL) and extracted with $CHCl_3$ (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to provide the product as an oil (90 mg, 0.12 mmol, 92 %). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.96 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.44 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.31 (s, 4H, 4 ArC*H*), 5.98 (s, 4H, 2 C*H*=C*H*), 4.31 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 3.90 (s, 4H, 2 CH_2NH), 3.83 (s, 4H, 2 CH_2NH), 3.76 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N), 3.35 (s, 4H, 4 C*H*CO), 3.27 (s, 4H, 4 C*H*CH_2), 1.76 (d, 2H, *J* = 8.5 Hz, 2 C*H*H), 1.51 (d, 2H, *J* = 8.5 Hz, 2 CH*H*); ^{13}C NMR (175 MHz, 298 K, $CDCl_3$) δ_C 177.6 (imide *C*=O), 166.3 (*C*OO), 146.0 (Ar*C*), 139.0 (Ar*C*), 134.5 (*C*H=*C*H), 130.0 (Ar*C*H), 128.6 (Ar*C*H), 128.5 (Ar*C*H), 128.3 (Ar*C*), 61.8 (CH_2CH_2O), 53.1 (CH_2NH), 52.9 (CH_2NH), 52.4 (bridgehead CH_2), 46.0 ($CHCH_2CH$), 45.1 (*C*HCO), 37.4 (CH_2CH_2N); IR ν cm^{-1} 2941 (saturated C-H), `1693 (ester and imide C=O), 1260 (C-O); HR MS (ESI$^+$): *m/z* found, 783.3395 calc for $C_{46}H_{47}N_4O_8$ 783.3388 [**2.29**+H]$^+$.

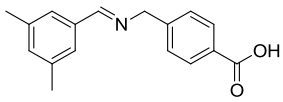
2.30



The thread **2.29** (30 mg, 0.038 mmol) was dissolved in MeOH (1 mL) and $HClO_4$ (70%) was added (0.1 mL). Water (5 mL) was added and the mixture extracted with CH_2Cl_2 (3 x 5 mL).

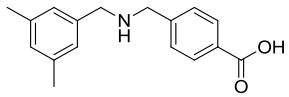
The organic layer was dried over $MgSO_4$, filtered and solvent removed *in vacuo* providing a white solid which was recrystallised from acetonitrile/Et_2O (29 mg, 0.03 mmol, 79 %). m.p. 69-71°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.02 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*), 7.61 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*), 7.55 (s, 4H, 4 ArC*H*), 7.39 (br s, 4H, 2 NH_2^+), 5.94 (s, 4H, 2 C*H*=C*H*), 4.36-4.28 (m, 12H, 2 CH_2CH_2O and 4 $CH_2NH_2^+$), 3.66 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N), 3.27 (s, 4H, 4 C*H*CO), 3.24 (s, 4H, 4 C*H*CH_2), 1.59 (d, 2H, *J* = 8.5 Hz, 2 C*H*H), 1.53 (d, 2H, *J* = 8.5 Hz, 2 CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 179.1 (imide *C*=O), 166.7 (*C*OO), 136.7 (Ar*C*), 135.7 (*C*H=*C*H), 133.3 (Ar*C*), 132.6 (Ar*C*), 132.2 (Ar*C*H), 131.9 (Ar*C*H), 131.3 (Ar*C*H), 63.3 (CH_2CH_2O), 53.1 (bridgehead CH_2), 52.5 ($CH_2NH_2^+$), 52.4 ($CH_2NH_2^+$), 47.0 (*C*HCH_2*C*H), 46.0 (*C*HCO), 38.2 (CH_2CH_2N); IR ν cm^{-1} 2982 (saturated C-H), 1685 (ester and imide C=O), 1095 (ClO_4); HRMS (ESI$^+$): found, *m/z* 392.1727 calc for $C_{46}H_{48}N_4O_8$ 392.1731 [**2.30**-2ClO_4]$^{2+}$.

2.31



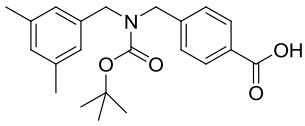
Synthesised according to a modified literature procedure.[145] 4-Aminomethylbenzoic acid (0.25 g, 1.66 mmol) was dissolved in hot MeOH (10 mL). 3,5-Dimethylbenzaldehyde (0.225 mL, 1.66 mmol) was added and the solution was stirred for 72 h. A white precipitate developed and was filtered and washed with ice cold MeOH (410 mg, 1.54 mmol, 93%). m.p. 194-195°C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H 8.44 (s, 1H, N=C*H*), 7.91 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.43 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.39 (s, 2H, 2 ArC*H*), 7.10 (s, 1H, ArC*H*), 4.81 (s, 2H, CH_2), 2.30 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ_C 167.4 (*C*OO), 162.6 (N=*C*H), 144.6 (Ar*C*), 137.8 (Ar*C*), 135.9 (Ar*C*), 132.3 (Ar*C*H), 129.8 (ArC), 129.4 (Ar*C*H), 127.8 (Ar*C*H), 125.8 (Ar*C*H), 63.5 (CH_2), 20.7 (CH_3); IR ν cm^{-1} 2915 (saturated C-H), 1698 (C=N stretching), 1638 (acid C=O); HRMS (ESI$^+$): *m/z* 268.1352 calc for $C_{17}H_{18}NO_2$ 268.1332 [**2.31**+H]$^+$.

2.32



Synthesised according to a modified literature procedure.[145] The imine **2.31** (300 mg, 1.12 mmol) was dissolved in a solution of THF (5 mL) and MeOH (5 mL). The solution was cooled to 0°C and sodium borohydride (47 mg, 1.23 mmol) was added portion wise. After 24 h the reaction was diluted with water (10 mL) and extracted with EtOAc (2 x 20 mL). The organic layers were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to leave a white solid (100 mg, 0.37 mmol, 33%). m.p. 226-229°C; ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 8.00 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.38 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 6.97 (s, 2H, 2 ArC*H*), 6.95 (s, 1H, ArC*H*), 3.88 (s, 2H, CH_2NH), 3.78 (s, 2H, CH_2NH), 2.29 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 166.5 (*C*OO), 141.5 (Ar*C*), 139.5 (Ar*C*), 138.4 (Ar*C*), 130.9 (Ar*C*H), 130.4 (Ar*C*H), 129.5 (Ar*C*H), 128.0 (ArC), 127.8 (Ar*C*H), 53.3 (*C*H_2NH), 53.0 (*C*H_2NH), 21.5 (*C*H_3); HRMS (ESI$^+$): *m/z* found, 270.1490 calc for $C_{17}H_{20}NO_2$ 270.1489 [**2.32**-ClO_4]$^+$.

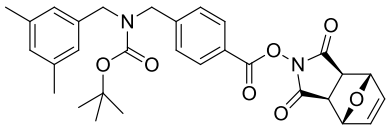
2.33



The acid **2.32** (440 mg, 1.6 mmol) was heated in THF (20 mL) and di-*tert*-butyl dicarbonate (392 mg, 1.8 mmol) was added. The reaction was heated to reflux and followed by TLC (EtOAc:MeOH; 9:1). The THF was removed *in vacuo* and the crude oil partitioned between CH_2Cl_2 (10 mL) and water (10 mL). The aqueous layer was extracted with a further portion of CH_2Cl_2 (10 mL) and the combined organic extracts were dried over $MgSO_4$, filtered and solvent removed *in vacuo* to provide a colourless oil used without further purification (540 mg, 1.5 mmol, 94 %). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.15 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.40 (br m, 2H, 2 ArC*H*), 6.96 (br s, 1H, ArC*H*), 6.86 (br m, 2H, 2 ArC*H*), 4.54-4.36 (m, 4H, CH_2NCH_2), 2.32 (br s, 6H, 2 CH_3), 1.55 (br s, 9H, 3 CH_3); ^{13}C NMR (100

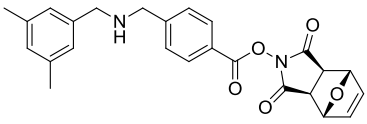
MHz, 298 K, $CDCl_3$) δ_C 171.0 (*C*OOH), 156.0 (N*C*OO), 138.2 (Ar*C*), 138.1 (Ar*C*), 138.0 (Ar*C*), 130.7 (Ar*C*H), 130.3 (Ar*C*H), 129.8 (Ar*C*H), 128.4 (Ar*C*), 127.7 (rotamer Ar*C*H), 127.1 (rotamer Ar*C*H), 125.8 (rotamer Ar*C*H), 125.2 (rotamer Ar*C*H), 80.4 ($C(CH_3)_3$), 49.7 (CH_2N), 49.6 (CH_2N), 28.3 (boc-CH_3), 21.2 (Ar-CH_3); IR ν cm^{-1} 2985 (saturated C-H), 1785 (carbamate C=O), 1686 (ester C=O); HRMS (ESI^+): *m/z* found 392.1833 calc for $C_{22}H_{27}NO_4Na$ 392.1832 [**2.33**+Na]$^+$.

2.34



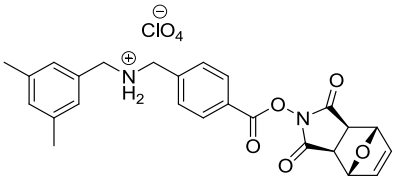
Compound **2.33** (640 mg, 1.7 mmol) was dissolved in CH_2Cl_2 (10 mL), then *N,N,N',N'*-tetramethylchloroformamidinium hexafluorophosphate (584 mg, 2.04 mmol), NEt_3 (0.437 mL, 3.4 mmol) and DMAP (21 mg, 0.17 mmol) were added at 0˚C over 1 h. Alcohol *exo-N*-hydroxy-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide (314 mg, 1.7 mmol) was added and stirred for a further 24 h. The solution was diluted with CH_2Cl_2 (20 mL) and washed with water (15 mL), saturated citric acid (15 mL), saturated sodium bicarbonate (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The solid was washed with Et_2O and filtered to provide the product (60 mg, 0.11 mmol, 7%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.09 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 7.35-7.31 (br d, 2H, 2 ArC*H*), 6.92 (s, 1H, ArC*H*), 6.84-6.79 (m, 2H, 2 ArC*H*), 6.57 (s, 2H, C*H*=C*H*), 5.40 (s, 2H, 2 C*H*O), 4.49-4.29 (m, 4H, $CH_2NH_2^+CH_2$), 2.97 (s, 2H, 2 C*H*C=O), 2.30 (s, 6H, 2 CH_3), 1.50 (m, 9H, 3 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 169.2 (imide *C*=O), 169.1 (*C*OO), 155.6 (N*C*OO), 144.6 (Ar*C*), 138.4 (Ar*C*), 137.6 (Ar*C*), 136.5 (*C*H=*C*H), 131.1 (Ar*C*H), 129.3 (Ar*C*H), 128.4 (rotamer Ar*C*H), 127.6 (rotamer Ar*C*H), 126.1 (rotamer Ar*C*H), 125.5 (rotamer Ar*C*H), 124.1 (Ar*C*), 80.8 (*C*HO), 80.7 ($C(CH_3)_3$), 50.0 (broad signal, CH_2NCH_2), 44.7 (*C*HCO) 28.7 (Boc-CH_3), 21.6 (CH_3); IR ν cm^{-1} 2870 (saturated C-H), 1690 (ester C=O), 1611 (imide C=O), 1240 (C-O); HRMS (ESI^+): *m/z* found, 555.2104 calc for $C_{30}H_{32}N_2O_7Na$ 555.2102 [**2.34**+Na]$^+$.

2.35



Thread **2.34** (50 mg, 0.094 mmol) was dissolved in TFA (3 mL) and CH_2Cl_2 (3 mL) and the reaction was followed by TLC (CH_2Cl_2;MeOH; 9:1). The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated sodium bicarbonate (2 x 10 mL) and water (2 x 10 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo* providing a white solid (40 mg, 0.092 mmol, 98%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.09 (d, 2H, *J* =8.0 Hz, 2 ArC*H*), 7.51 (d, 2H, *J* =8.0 Hz, 2 ArC*H*), 6.95 (s, 2H, 2 ArC*H*), 6.92 (s, 1H, ArC*H*), 6.57 (s, 4H, C*H*=C*H*), 5.40 (br s, 2H, 2 C*H*O), 3.91 (s, 2H, CH_2NH), 3.74 (s, 2H, CH_2NH), 2.97 (br s, 2H, 2 C*H*CO), 2.32 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 168.9 (imide *C*=O), 164.9 (*C*OO), 148.3 (Ar*C*), 138.0 (Ar*C*), 138.0 (Ar*C*), 136.3 (*C*H=*C*H), 130.7 (Ar*C*H), 128.8 (Ar*C*H), 128.5 (Ar*C*H), 126.1 (Ar*C*H), 123.7 (Ar*C*), 80.5 (*C*HO), 52.8 (*C*H_2NH), 52.4 (*C*H_2NH), 44.5 (*C*HCO), 21.2 (*C*H_3); HRMS (ESI$^+$): *m/z* found, 433.1762 calc for $C_{25}H_{25}N_2O_5$ 433.1758 [**2.35**+H]$^+$.

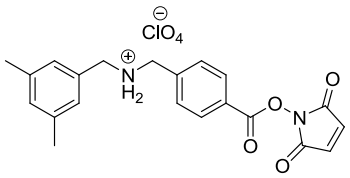
2.36



Neutral thread **2.35** (40 mg, 0.092 mmol) was dissolved in CH_2Cl_2 (5 mL) and washed with a 10% aqueous solution of $HClO_4$ (3 x 5 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The resulting solid was recrystallised from acetonitrile/Et_2O to provide the ClO_4^- salt (10 mg, 0.19 mmol, 20%). m.p. 190-191°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.19 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 7.66 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*), 7.12 (s, 1H, ArC*H*), 7.08 (s, 2H, 2 ArC*H*), 6.57 (s, 2H, C*H*=C*H*), 5.27 (s, 2H, 2 C*H*O), 4.34 (s, 2H, C$H_2NH_2^+$), 4.19 (s, 2H, C$H_2NH_2^+$), 3.05 (br s, 2H, 2 C*H*CO), 2.33 (s, 6H, 2 CH_3); ^{13}C NMR (150 MHz, 298 K, CD_3CN) δ_C 170.9 (imide

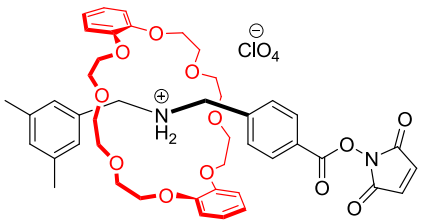
C=O), 166.3 (*C*OO), 140.3 (Ar*C*), 139.0 (Ar*C*), 137.6 (*C*H=*C*H), 132.6 (Ar*C*H), 132.4 (Ar*C*H), 132.1 (Ar*C*H), 131.4 (Ar*C*), 129.2 (Ar*C*H), 127.4 (Ar*C*), 81.2 (*C*HO), 53.0 ($CH_2NH_2^+$), 52.0 ($CH_2NH_2^+$), 46.0 (*C*HCO), 21.6 (CH_3); IR ν cm^{-1} 3054 (saturated C-H), 1741 (ester C=O), 1661 (imide C=O), 1056 (ClO_4); HRMS (ESI^+): *m/z* found, 433.1755 calc for $C_{25}H_{25}N_2O_5$ 433.1758 [**2.36**-ClO_4]$^+$.

2.37



The ClO_4^- salt **2.36** (10 mg, 0.019 mmol) was dissolved in acetonitrile (5 mL) and heated to reflux for 72 h. The solvent was removed *in vacuo* and the crude product recrystallised from acetonitrile/Et_2O to provide a pale white solid (6 mg, 0.012 mmol, 68%). m.p. 202-203°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.21 (d, 2H, *J* =8.0 Hz, 2 ArC*H*), 7.69 (d, 2H, *J* =8.0 Hz, 2 ArC*H*), 7.12 (s, 1H, ArC*H*), 7.08 (s, 2H, 2 ArC*H*), 6.98 (s, 2H, C*H*=C*H*), 4.34 (s, 2H, $CH_2NH_2^+$), 4.19 (s, 2H, $CH_2NH_2^+$), 2.33 (s, 6 H, 2 CH_3); IR ν cm^{-1} 3093 (saturated C-H), 1748 (ester C=O), 1613 (imide (C=O), 1051 (ClO_4); MS (ESI^+): *m/z* 365.1 [**2.37**-ClO_4]$^+$.

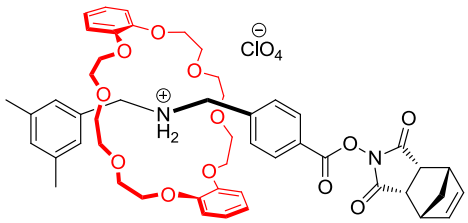
2.38



Thread **2.37** (3 mg, 0.006 mmol) and DB24C8 (6 mg, 0.012 mmol) were dissolved in deuterated acetonitrile and heated to 60°C. The threading was followed by ^{1}H NMR until the pseudorotaxane formed. **Pseudorotaxane 2.38** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.74 (d, 2H, *J* =8.0 Hz, ⊂ 2 ArC*H*), 7.52 (d, 2H, *J* =8.0 Hz, ⊂ 2 ArC*H*), 6.96-6.88 (m, 13H, ⊂ 3 ArCH, ⊂ C*H*=C*H* and ⊂ 8 crown ArC*H*), 4.91-4.88 (m, 2H, ⊂ CH_2NH_2), 4.58-4.54 (m, 2H,

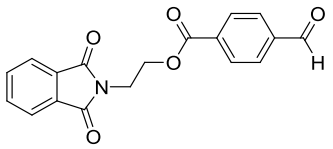
⊂ C*H*$_2$NH$_2$), 4.07-3.97 (m, 8H, ⊂ 4 OC*H*$_2$), 3.66 (m, 16H, ⊂ 8 OC*H*$_2$), 2.31 (s, 2H, ⊂ 2 C*H*$_3$); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OC*H*$_2$), 3.83 (m, 8H, 4 OC*H*$_2$), 3.72 (s, 8H, 4 OC*H*$_2$).

2.39



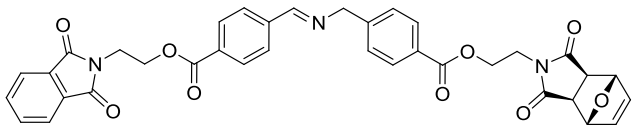
To the [2]pseudorotaxane **2.38** (5.5 mg, 0.006 mmol) a drop of freshly distilled cyclopentadiene (0.1 mL, excess) was added to the solution. The solvent and excess cyclopentadiene were removed *in vacuo*. The excess DB24C8 was removed by extracting the solid with benzene to give [2]rotaxane **2.39** (5 mg, 0.005 mmol, 85%). ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 7.70 (d, 2H, *J* = 8.5 Hz, ⊂ 2 ArC*H*), 7.50 (d, 2H, *J* = 8.5Hz, ⊂ 2 ArC*H*), 6.79 (s, 2H, ⊂ 2 ArC*H*), 6.93 (s, 1H, ⊂ ArC*H*), 6.83-6.74 (m, 8H, ⊂ 8 crown ArC*H*), 6.20 (s, 2H, ⊂ C*H*=C*H*), 4.86 (m, 2H, ⊂ C*H*$_2$NH$_2^+$), 4.54 (m, 2H, ⊂ C*H*$_2$NH$_2^+$), 4.90-3.97 (m, 8H, ⊂ 4 OC*H*$_2$), 3.78 (t, 8H, *J* = 3.8 Hz, ⊂ 4 OC*H*$_2$), 3.96-3.57 (m, 8H, ⊂ 4 OC*H*$_2$), 3.46 (br s, 2H, ⊂ 2 C*H*CO), 3.39 (br s, 2H, ⊂ 2 C*H*CH$_2$), 2.18 (s, 6H, ⊂ 2 C*H*$_3$), 1.73 (d, 1H, *J* = 8.5 Hz, ⊂ C*H*H), 1.59 (d, 1H, *J* = 9.5 Hz, ⊂ CH*H*); ^{13}C NMR (150 MHz, 298 K, CD$_3$CN) δ_C 171.7 (imide *C*=O), 159.8 (*C*OO), 148.4 (Ar*C*), 140.6 (Ar*C*), 136.2 (*C*H=*C*H), 133.0 (Ar*C*), 131.8 (Ar*C*H), 131.4 (Ar*C*H), 129.1 (Ar*C*H), 128.2 (Ar*C*H), 122.6 (Ar*C*H), 113.6 (Ar*C*H), 72.0 (O*C*H$_2$), 71.5 (O*C*H$_2$), 69.1 (O*C*H$_2$), 54.1 (*C*H$_2$NH$_2^+$), 53.1 (bridgehead *C*H$_2$), 52.1 (*C*H$_2$NH$_2^+$), 45.9 (*C*HCH$_2$*C*H), 42.8 (*C*HCO), 21.6 (*C*H$_3$); All quaternary ArC not observed. IR ν cm^{-1} 2920 (saturated C-H), 1735 (ester and imide C=O), 1097 (ClO$_4$); HRMS (ESI$^+$): *m/z* found, 879.4068 calc for C$_{50}$H$_{59}$N$_2$O$_{12}$ 879.4063 [**2.39**-ClO$_4$]$^+$.

2.40



4-Carboxybenzaldehyde (432 mg, 2.9 mmol) and *N*-(2-hydroxyethyl)phthalimide (500 mg, 2.6 mmol) were dissolved in CH_2Cl_2 (10 mL). The *N,N,N',N'*-tetramethylchloroformamidinium hexafluorophosphate (882 mg, 3.1 mmol) and NEt_3 (0.44 mL, 3.1 mmol) were added and the solution was stirred at room temperature for 48 h. The solution was diluted with CH_2Cl_2 (15 mL) and washed with water (20 mL), saturated citric acid (20 mL), saturated sodium bicarbonate (20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The yellow solid was washed with Et_2O and filtered to provide a pale yellow solid (700 mg, 2.17 mmol, 75%). m.p. 160-161˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 10.09 (s, 1H, CO*H*), 8.15 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.93 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.87-7.85 (m, 2H, 2 Phthalimide-ArC*H*), 7.75-7.72 (m, 2H, 2 Phthalimide-ArC*H*), 4.58 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 4.14 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 191.6 (*C*OH), 168.1 (imide *C*=O), 165.3 (*C*OO), 139.2 (Ar*C*), 134.6 (Ar*C*), 134.2 (Ar*C*H), 131.9 (Ar*C*), 130.4 (Ar*C*H), 129.6 (Ar*C*H), 123.5 (Ar*C*H), 62.9 (CH_2CH_2O), 36.9 (CH_2CH_2N); IR ν cm^{-1} 1770.1 (aldehyde C=O), 1698 (imide and ester C=O); HRMS (ESI$^+$): *m/z* found, 346.0684 calc for $C_{18}H_{13}NO_5Na$ 346.0686 [**2.40**+Na]$^+$.

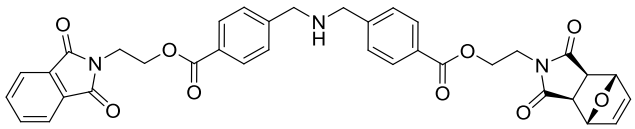
2.41



Amine **2.07** (200mg, 0.59 mmol) and aldehyde **2.40** (189 mg, 0.59 mmol) were dissolved in a mixture of MeOH (5 mL) and CH_2Cl_2 (5 mL) and stirred at room temperature. After 3 h the solvent was removed to give the imine as a yellow solid (381 mg, 0.59 mmol, 100%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.44 (s, 1H, C*H*=N), 8.04 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.98 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 7.85 (m, 2H, 2 Phthalimide-ArC*H*), 7.83 (d, 2H, *J* = 8.0 Hz, 2 ArCH), 7.73 (m, 2H, 2 Phthalimide-ArC*H*), 7.40 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*), 6.49 (s, 2H, C*H*=C*H*), 5.24 (s, 2H, 2 C*H*O), 4.88 (br s, 2H, CH_2N=C), 4.56 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 4.45 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 4.13 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N), 3.91 (t,

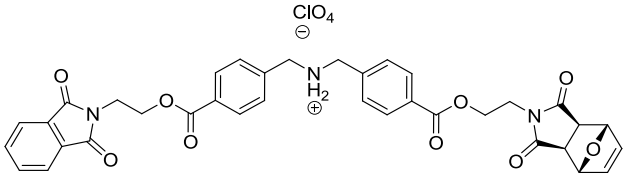
2H, J = 5.3 Hz, CH_2CH_2N), 2.86 (s, 2H, 2 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.3 (imide *C*=O), 168.4 (imide *C*=O), 166.4 (*C*OO), 166.1 (*C*OO), 161.8 (*C*H=N), 144.7 (Ar*C*), 140.2 (Ar*C*), 136.8 (*C*H=*C*H), 134.4 (Ar*C*H), 132.6 (Ar*C*), 131.9 (Ar*C*), 130.4 (Ar*C*H), 130.3 (Ar*C*H), 128.8 (Ar*C*), 128.5 (Ar*C*H), 128.1 (Ar*C*H), 123.7 (Ar*C*H), 81.2 (*C*HO), 64.9 (CH_2CH_2O), 62.8 (CH_2CH_2O), 61.5 (CH_2N=C), 47.8 (*C*HCO), 38.1 (CH_2CH_2N), 37.2 (CH_2CH_2N); HRMS (ESI$^+$): *m/z* found, 648.2001 calc for $C_{36}H_{30}N_3O_9Na$ 648.1977 [**2.41**+Na]$^+$.

2.42



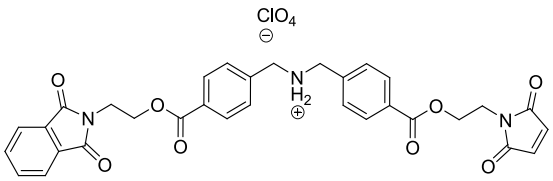
The imine **2.41** (381 mg, 0.59 mmol) was dissolved in MeOH (5 mL) and CH_2Cl_2 (5 mL). Sodium cyanoborohydride (45 mg, 0.73 mmol) and HOAc (5 drops) were added and the solution was stirred at room temperature for 4 h. The solvent was removed *in vacuo* and the residue dissolved in water (10 mL) and extracted with EtOAc (2 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to provide an off-white solid (300 mg, 0.46 mmol, 78 %). m.p. 121-122˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.97 (d, 4H, J = 7.5 Hz, 4 ArC*H*), 7.87 (m, 2H, 2 Phthalimide-ArC*H*), 7.74 (m, 2H, 2 Phthalimide-ArC*H*), 7.40 (d, 4H, J = 7.5 Hz, 4 ArC*H*), 6.51 (s, 2H, C*H*=C*H*), 5.25 (s, 2H, 2 C*H*O), 4.55 (t, 2H, J = 5.3 Hz, CH_2CH_2O), 4.45 (t, 2H, J = 5.3 Hz, CH_2CH_2O), 4.13 (t, 2H, J = 5.3 Hz, CH_2CH_2N), 4.01 (br s, 1H, N*H*), 3.91 (t, 2H, J = 5.3 Hz, CH_2CH_2N), 3.97 (s, 4H, CH_2NHCH_2), 2.88 (s, 2H, 2 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.1 (imide *C*=O), 168.1 (imide *C*=O), 166.0 (*C*OO), 165.9 (*C*OO), 136.5 (*C*H=*C*H), 134.1 (Ar*C*H), 131.9 (Ar*C*), 130.1 (Ar*C*H), 130.0 (Ar*C*H), 129.2 (Ar*C*), 129.1 (Ar*C*), 128.6 (Ar*C*H), 128.5 (Ar*C*H), 123.5 (Ar*C*H), 80.9 (*C*HO), 62.4 (CH_2CH_2O), 61.4 (CH_2CH_2O), 51.8 (CH_2NHCH_2), 47.5 (*C*HCO), 37.9 (CH_2CH_2N), 37.0 (CH_2CH_2N); IR ν cm^{-1} 3451 (NH), 1694 (ester C=O), 1628 (imide C=O); HRMS (ESI$^+$): *m/z* found, 650.2146 calc for $C_{36}H_{32}N_3O_9$ 650.2133 [**2.42**+H]$^+$.

2.43



The neutral thread **2.42** (150 mg, 0.23 mmol) was dissolved in CH_2Cl_2 (5 mL). The organic layer was washed with an 10% aqueous solution of $HClO_4$ (2 x 10 mL). The organic layer was dried over $MgSO_4$ and solvent remove *in vacuo*. The crude solid was recrystallised from acetonitrile/Et_2O to give a pale greenish solid (100 mg, 0.134 mmol, 58%). m.p. 78-80 ˚C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.99 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.83-7.77 (m, 4H, 4 Phthalimide-ArC*H*), 7.59-7.55 (m, 4H, 4 ArC*H*), 6.49 (s, 2H, C*H*=C*H*), 5.08 (s, 2H, 2 C*H*O), 4.51 (t, 2H, *J* =5.3 Hz, CH_2CH_2O), 4.38 (t, 2H, *J* =5.3 Hz, CH_2CH_2O), 4.32 (s, 4H, $CH_2NH_2^+CH_2$), 4.02 (t, 2H, *J* =5.3 Hz, CH_2CH_2N), 3.80 (t, 2H, *J* =5.3 Hz, CH_2CH_2N), 2.87 (s, 2H, 2 C*H*CO); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.6 (imide *C*=O), 168.2 (imide *C*=O), 165.5 (*C*OO), 165.3 (*C*OO), 136.4 (*C*H=*C*H), 135.3 (Ar*C*), 135.2 (Ar*C*), 134.3 (Ar*C*H), 132.1 (Ar*C*), 131.3 (Ar*C*), 131.3 (Ar*C*), 130.5 (Ar*C*H), 130.4 (Ar*C*H), 129.9 (Ar*C*H), 129.9 (Ar*C*H), 122.9 (Ar*C*H), 80.9 (*C*HO), 62.6 (CH_2CH_2O), 61.5 (CH_2CH_2O), 51.1 ($CH_2NH_2^+CH_2$), 47.5 (*C*HCO), 37.3 (CH_2CH_2N), 36.8 (CH_2CH_2N); IR ν cm^{-1} 3066 (NH), 1772 (Phthalimide C=O), 1694 (ester C=O), 1100 (ClO_4); HRMS (ESI$^+$): *m/z* found, 650.2130 calc for $C_{36}H_{32}N_3O_9$ 650.2133 [**2.43**+H]$^+$.

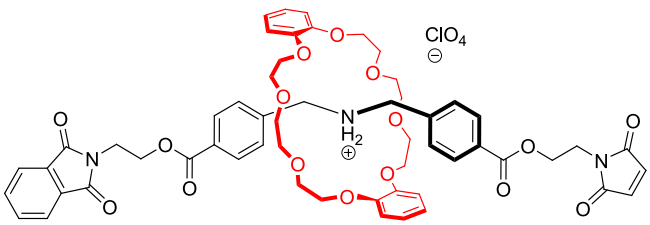
2.44



The thread **2.43** (50 mg, 0.07 mmol) was dissolved in acetonitrile (3 mL) and toluene (3 mL) and heated to reflux for 96 h. The solvent was removed *in vacuo* to provide a white powder (40 mg, 0.06 mmol, 86%). m.p. 102-104˚C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.01-7.98 (m, 4H, 4 ArC*H*), 7.83-7.77 (m, 4H, 4 Phthalimide-ArC*H*), 7.58-7.55 (m, 4H, 4 ArC*H*),

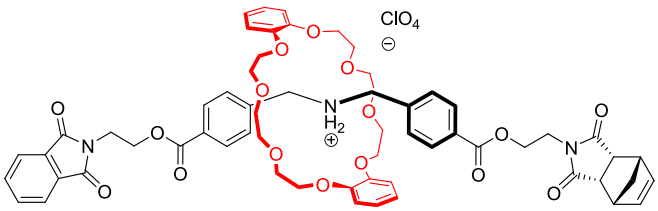
6.77 (s, 2H, C*H*=C*H*), 4.51 (t, 2H, *J* =5.3 Hz, CH_2CH_2O), 4.40 (t, 2H, *J* =5.3 Hz, CH_2CH_2O), 4.31 (s, 4H, $CH_2NH_2^+CH_2$), 4.02 (t, 2H, *J* =5.0 Hz, CH_2CH_2N), 3.84 (t, 2H, *J* =5.3 Hz, CH_2CH_2N); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.9 (imide *C*=O), 168.2 (imide *C*=O), 165.5 (*C*OO), 165.4 (*C*OO), 135.4 (Ar*C*), 135.5 (Ar*C*), 134.4 (*C*H=*C*H), 134.3 (Ar*C*H), 132.1 (Ar*C*), 131.2 (Ar*C*), 131.1 (Ar*C*), 130.4(1) (Ar*C*H), 130.3(7) (ArCH), 129.9 (Ar*C*H), 129.8 (Ar*C*H), 122.9 (Ar*C*H), 62.6 (CH_2CH_2O), 62.5 (CH_2CH_2O), 51.1 ($CH_2NH_2^+CH_2$), 36.9 (CH_2CH_2N), 36.6 (CH_2CH_2N); IR ν cm^{-1} 3100 (NH), 1695 (imide and ester C=O), 1102 (ClO_4); HRMS (ESI^+): *m/z* found, 604.1697 calc for $C_{32}H_{27}N_3O_8Na$ 604.1690 [**2.44**+Na]$^+$.

2.45



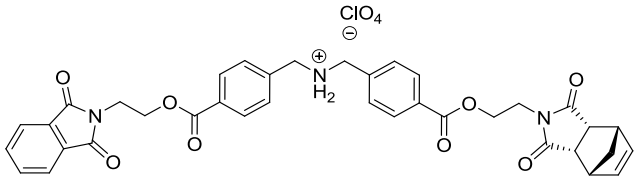
Thread **2.44** (15 mg, 0.02 mmol) was dissolved in deuterated acetonitrile (0.5 mL) and DB24C8 (20 mg, 0.04 mmol) was added. The threading was monitored by ^1H NMR. Threading was completed after 72 h to give the pseudorotaxane. **Pseudorotaxane 2.45** ^1H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.84-7.82 (m, 2H, ⊂ 2 ArC*H*), 7.83-7.77 (m, 2H, ⊂ 2 ArC*H*), 7.73-7.71 (m, 2H, ⊂ 2 Phthalimide-ArC*H*), 7.67-7.65 (m, 2H, ⊂ 2 Phthalimide-ArC*H*), 7.45-7.43 (m, 2H, ⊂ 2 ArC*H*), 7.40-7.38 (m, 2H, ⊂ 2 ArC*H*), 6.78 (s, 2H, ⊂ C*H*=C*H*), 6.73-6.68 (m, 8H, ⊂ 8 crown ArC*H*), 4.78-4.75 (m, 4H, ⊂ 2 CH_2NH_2), 4.46 (t, 2H, *J* = 5.3 Hz, ⊂ CH_2CH_2O), 4.36 (t, 2H, *J* = 5.3 Hz, ⊂ CH_2CH_2O), 4.00-3.98 (m, 10H, ⊂ 4 OCH_2 and ⊂ CH_2CH_2N), 3.83-3.81 (m, 2H, ⊂ CH_2CH_2N), 3.76-3.75 (m, 8H, ⊂ 4 OCH_2), 3.58 (s, 8H, ⊂ 4 OCH_2); Also contains unthreaded **DB24C8** ^1H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); HRMS (ESI^+): *m/z* found, 1030.4006 calc for $C_{56}H_{60}N_3O_{16}$ 1030.3968 [**2.45**-ClO_4]$^+$.

2.46



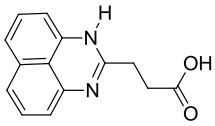
To the [2]pseudorotaxane **2.45** (23 mg, 0.02 mmol) in acetonitrile, cyclopentadiene (0.1 mL, excess) was added and mixed. The solvent and excess cyclopentadiene was immediately removed *in vacuo*. The excess DB24C8 was removed by extracting with benzene to provide a beige solid (20 mg, 0.017 mmol, 85%) m.p. 102-104˚C; ^{1}H NMR (500 MHz, 298 K, CD_3CN) δ_H 7.85 (m, 2H, ⊂ 2 ArC*H*), 7.80-7.78 (m, 4H, ⊂ 4 Phthalimide-ArC*H*), 7.70 (br s, 2H, ⊂ NH_2), 7.64 (d, 2H, *J* = 8.2 Hz, ⊂ 2 ArC*H*), 7.50 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*), 7.38 (d, 2H, *J* = 8.2 Hz, ⊂ 2 ArC*H*), 6.72 (m, 8H, ⊂ 8 crown ArC*H*), 5.89 (s, 2H, ⊂ C*H*=C*H*), 4.82-4.75 (m, 4H, ⊂ CH_2NH$_2^+$CH_2), 4.46 (t, 2H, *J* = 4.4 Hz, ⊂ CH$_2$CH_2O), 4.26 (t, 2H, *J* = 5.7 Hz, ⊂ CH$_2$CH_2O), 4.02-3.99 (m, 10H, ⊂ 4 OCH_2 and ⊂ CH$_2$CH_2N), 3.78-3.76 (m, 8H, ⊂ 4 OCH_2), 3.65 (t, 2H, *J* = 5.7 Hz, ⊂ CH$_2$CH_2N), 3.62-3.56 (m, 8H, ⊂ 4 OCH_2), 3.26 (m, 2H, ⊂ C*H*CO), 3.21 (m, 2H, ⊂ C*H*CH$_2$), 1.60 (d, 1H, *J* = 8.5 Hz, ⊂ C*H*H), 1.55 (d, 1H, *J* = 8.5 Hz, ⊂ CH*H*); ^{13}C NMR (125 MHz, 298 K, CD_3CN) δ_C 178.9 (imide *C*=O), 169.5 (imide *C*=O), 166.6 (*C*OO), 166.5 (*C*OO), 148.5 (Ar*C*), 138.4 (Ar*C*), 138.0 (Ar*C*), 135.7 (Ar*C*H), 135.6 (*C*H=*C*H), 133.5 (Ar*C*), 131.8 (Ar*C*), 131.6 (Ar*C*), 131.0 (ArCH), 130.8 (Ar*C*H), 130.7 (Ar*C*H), 130.7 (Ar*C*H), 124.3 (Ar*C*H), 122.5 (Ar*C*H), 113.7 (Ar*C*H), 72.0 (O*C*H$_2$), 71.6 (O*C*H$_2$), 69.1 (O*C*H$_2$), 63.5 (O*C*H$_2$CH$_2$N), 63.1 (O*C*H$_2$CH$_2$N), 53.5 (*C*H$_2$NH$_2^+$), 53.4 (bridgehead CH_2), 53.1 (*C*H$_2$NH$_2^+$), 47.0 (*C*HCH$_2$), 46.1 (*C*HCO), 38.2 (OCH$_2$*C*H$_2$N), 38.2' (OCH$_2$*C*H$_2$N); IR ν cm^{-1} 2947 (saturated C-H), 1742 (phalamide C=O), 1696 (ester and imide C=O), 1081 (C-O); HRMS (ESI$^+$): *m/z* found, 1096.4444 calc for $C_{61}H_{66}N_3O_1$ 1096.4438 [**2.46**-ClO$_4$]$^+$.

2.47



Thread **2.44** (10 mg, 0.015 mmol) was dissolved in acetonitrile (1 mL) and cyclopentadiene (0.1 mL, excess) was added. The solvent and excess cyclopentadiene were removed *in vacuo* and the solid recrystallised from acetonitrile/Et_2O to provide the thread (8 mg, 0.011 mmol, 72%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.03-7.99 (m, 4H, 4 ArC*H*), 7.84-7.78 (m, 4H, 4 Phthalimide-ArC*H*), 7.61-7.56 (m, 4H, 4 ArC*H*), 5.94 (s, 2H, C*H*=C*H*), 4.51 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 4.32-4.28 (m, 6H, CH_2CH_2O and $CH_2NH_2^+CH_2$), 4.03 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N), 3.67 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.28 (br s, 2H, 2 C*H*CO), 3.24 (br s, 2H, 2 C*H*CH_2), 1.59 (d, 1H, *J* =8.5 Hz, CH*H*), 1.56 (d, 1H, *J* =8.5 Hz, C*H*H); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 179.0 (imide *C*=O), 169.6 (imide *C*=O), 166.7 (*C*OO), 166.6 (*C*OO), 136.7 (Ar*C*), 136.6 (Ar*C*), 135.7 (*C*H=*C*H), 135.6 (Ar*C*H), 133.5 (Ar*C*), 132.6 (Ar*C*), 132.6 (Ar*C*), 131.8 (Ar*C*H), 131.7 (Ar*C*H), 131.3 (Ar*C*H), 131.2 (Ar*C*H), 124.3 (Ar*C*H), 62.9 (CH_2CH_2O), 63.3 (CH_2CH_2O), 53.1 (bridgehead CH_2), 52.5 ($CH_2NH_2^+CH_2$), 47.0 ($CHCH_2CH$), 46.1 (*C*HCO), 38.3 (CH_2CH_2N), 38.2 (CH_2CH_2N); IR ν cm^{-1} 2978 (saturated C-H), 1694 (ester and imide C=O), 1099 (ClO_4); HRMS (ESI$^+$): *m/z* found, 648.2345 calc for $C_{37}H_{34}N_3O_8$ 648.2340 [**2.47**-ClO_4]$^+$.

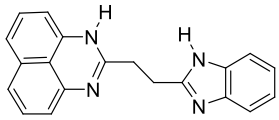
2.50



1,8-Diaminonaphthalene (2 g, 12.6 mmol) was dissolved in HOAc (50 mL) and heated to 70°C. To the stirring solution, succinic anhydride (1.33 g, 13.3 mmol) was added and stirred for 24 h. On cooling, a precipitate formed which was filtered and the solid washed with ice cold acetone (2.91 g, 12.1 mmol, 95%). m.p. 243-244˚C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H 11.39 (br s, 2H, N*H* and O*H*), 7.12 (dd, 2H, *J* = 8.0 and *J* = 7.0 Hz,

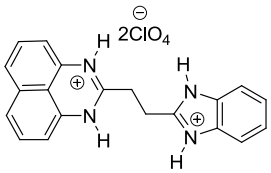
Hz, 2 PerimidineC*H*), 6.99 (d, 2H, *J* = 8.0 Hz, 2 PerimidineC*H*), 6.40 (d, 2H, *J* = 7.0 Hz, 2 PerimidineC*H*), 2.65 (t, 2H, *J* = 6.5 Hz, CH_2CH_2), 2.52 (t, 2H, *J* = 6.5 Hz, CH_2CH_2); ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ_C 173.8 (*C*OOH), 159.9 (Ar*C*), 156.4 (Ar*C*), 135.3 (Ar*C*), 128.6 (Perimidine*C*H), 128.6' (Perimidine*C*H), 121.6 (Ar*C*), 118.2 (Perimidine*C*H), 30.0 (CH_2CH_2), 29.2 (CH_2CH_2); IR ν cm^{-1} 2920 (br signal, OH), 1654 (acid C=O); HRMS (ESI^+): *m/z* found, 241.0970 Calc for $C_{14}H_{13}N_2O_2^+$ 241.0977 [**2.50**+H]$^+$.

2.51



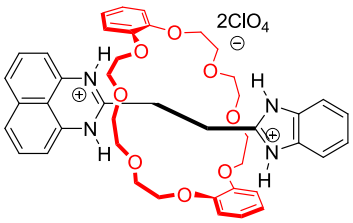
To the acid **2.50** (250 mg, 1.04 mmol) in CH_2Cl_2 (10 mL) was added TFAA (1 mL) and the solid slowly dissolved to give a dark green solution. The solution was stirred at room temperature for 2 h and the solvent was removed *in vacuo*. The remaining TFAA was removed *in vacuo* using benzene as an azeotrope to give a black solid. The intermediate was dissolved in HOAc (20 mL) and *o*-phenylenediamine (124 mg, 1.15 mmol) was added. The resulting mixture was stirred at 70˚C for 24 h. The solution was cooled and HOAc removed *in vacuo*. The crude solid was recrystallised from CH_2Cl_2/petroleum ether to provide a yellow solid (240 mg, 0.77 mmol, 74%). m.p. 205-206˚C; ^1H NMR (500 MHz, 298 K, CD_3OD) δ_H 7.67 (d, 2H, *J* = 6.0 Hz, 2 ArC*H*), 7.43 (d, 2H, *J* = 6.0 Hz, 2 ArC*H*), 7.37 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 7.30 (dd, 2H, *J* = 8.0 + 7.5 Hz, 2 PerimidineC*H*), 6.72 (d, 2H, *J* = 7.5 Hz, 2 PerimidineC*H*), 3.61 (t, 2H, *J* = 7.5 Hz, CH_2CH_2), 3.18 (t, 2H, *J* = 7.5 Hz, CH_2CH_2); ^{13}C NMR (125 MHz, 298 K, CD_3OD) δ_C 161.5 (Ar*C*), 153.2 (Ar*C*), 136.7 (Ar*C*), 136.1 (Ar*C*), 135.0 (Ar*C*), 129.9 (Perimidine*C*H), 126.1 (Ar*C*H), 124.2 (Perimidine*C*H), 122.4 (Ar*C*), 115.6 (2 Ar*C*H), 109.6 (Perimidine*C*H), 31.2 (CH_2CH_2), 25.7 (CH_2CH_2); IR ν cm^{-1} 2911 (saturated C-H), 1651 (C=N); HRMS (ESI^+): *m/z* found, 313.1443 Calc for $C_{20}H_{17}N_4$ 313.1448 [**2.51**+H]$^+$.

2.52



Thread **2.51** (50 mg, 0.160 mmol) was dissolved in MeOH (0.5 mL) and $HClO_4$ (70%) was added cautiously until a precipitate formed. The precipitate was filtered and washed with EtOAc to provide a pale green solid (38 mg, 0.074 mmol, 46%). m.p. 270-271°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 12.34 (br s, 2H, 2 N*H*), 10.56 (br s, 2H, 2 N*H*), 7.83 (m, 2H, 2 ArC*H*), 7.64 (m, 2H, ArC*H*), 7.47 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 7.37 (dd, 2H, *J* = 8.5 + 7.5 Hz, 2 PerimidineC*H*), 6.82 (d, 2H, *J* = 7.5 Hz, 2 PerimidineC*H*), 3.71 (t, 2H, *J* = 7.5 Hz, CH_2CH_2), 3.17 (t, 2H, *J* = 7.5 Hz, CH_2CH_2); ^{13}C NMR (175 MHz, 298 K, CD_3CN) δ_C 160.8 (Ar*C*), 151.5 (Ar*C*), 135.9 (Ar*C*), 133.0 (Ar*C*), 131.9 (Ar*C*), 130.0 (Perimidine*C*H), 128.2 (Ar*C*H), 124.9 (Perimidine*C*H), 121.8 (Ar*C*), 115.4 (Ar*C*H), 110.1 (Perimidine*C*H), 30.4 (CH_2CH_2), 24.5 (CH_2CH_2); IR ν cm^{-1} 3209 (br NH), 1646 (C=N), 1053 (ClO_4); HRMS (ESI$^+$): *m/z* found, 313.1444 calc for $C_{20}H_{17}N_4$ 313.1448 [**2.52**-H.2ClO_4]$^+$.

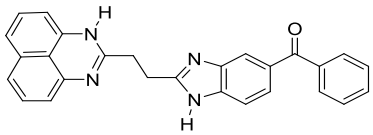
2.53



Thread **2.52** (10.3 mg, 0.2 mmol) and DB24C8 (9 mg, 0.2 mmol) were dissolved in deuterated acetonitrile (10 mL). Binding constant = **755 M^{-1}** was calculated from the single point method[129] by measuring the integration of ArC*H* protons for the free and bound crown at 6.93 ppm and 6.46 ppm respectively. **Pseudorotaxane 2.53** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 10.67 (br s, 4H, ⊂ 2 N*H*), 7.72 (m, 2H, ⊂ 2 ArC*H*), 7.56 (m, 2H, ⊂ 2 ArC*H*), 7.12-7.04 (m, 4H, ⊂ 4 PerimidineC*H*), 6.53 (m, 2H, ⊂ 2 PerimidineC*H*), 6.46 (s, 8H, ⊂ 8 crown ArC*H*), 4.15-4.09 (m, 4H, ⊂ 2 OCH_2), 4.07-4.02 (m, 4H, ⊂ 2 OCH_2), 4.00-3.96 (m,

6H, ⊂ 3 OCH_2), 3.92-3.88 (m, 12H, ⊂ 5 O-CH_2 and ⊂ CH_2CH$_2$), 3.38 (m, 2H, ⊂ CH$_2$CH_2); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); and **Thread 2.52** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 7.83 (m, 2H, 2 ArC*H*), 7.65-7.62 (m, 2H, ArC*H*), 7.47 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 7.37 (dd, 2H, *J* = 8.5 Hz, *J* = 7.5 Hz, 2 PerimidineC*H*), 6.82 (d, 2H, *J* = 7.5 Hz, 2 PerimidineC*H*), 3.71 (t, 2H, *J* = 7.5 Hz, CH_2CH$_2$), 3.17 (t, 2H, *J* = 7.5 Hz, CH$_2$CH_2); HRMS (ESI$^+$): *m/z* 761.3541 calc for $C_{44}H_{49}N_4O_8$ 761.3545 [**2.53**-H.2ClO$_4$]$^+$.

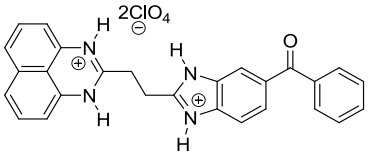
2.54



To a slurry of **2.50** (1 g, 4.2 mmol) in CH$_2$Cl$_2$ was added TFAA (1 mL). The solid gradually dissolved and the solution turned dark and was stirred overnight at room temperature. The solvent and TFAA were removed *in vacuo* and the oil provided was taken up in HOAc. 3,4-Diaminobenzophenone (0.88 g, 4.2 mmol) was added to the solution and it was heated at 70°C for 48 h. The HOAc was removed *in vacuo* and the crude product washed with hot water (3 x 10mL). The crude product was then dissolved in boiling MeOH, filtered and the solvent removed *in vacuo* to provide a pale green solid (1.12g, 2.7 mmol, 65%). m.p. 196-197˚C; ^{1}H NMR (400 MHz, 298 K, DMSO- d$_6$) δ_H 8.04 (s, 1H, BenzimidazoleC*H*), 7.66 (m, 5H, 5 ArC*H*), 7.76 (d, 2H, *J* = 7.5 Hz, 2 ArC*H*), 7.54 (d, 2H, *J* = 7.5 Hz, 2 ArC*H*), 7.41 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 7.33 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 6.77 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 3.61 (t, 2H, *J* = 7.5 Hz, CH_2CH$_2$), 3.23 (t, 2H, *J* = 7.5 Hz, CH$_2$CH_2); ^{13}C NMR (100 MHz, 298 K, DMSO-d$_6$) δ_C 198.3 (C=O), 162.1 (Ar*C*), 156.1 (Ar*C*), 141.4 (Ar*C*), 139.3 (Ar*C*), 138.5 (Ar*C*), 136.2 (Ar*C*), 133.9 (Ar*C*), 133.8 (Ar*C*), 133.6 (Ar*C*H), 130.0 (Perimidine*C*H), 129.7 (Ar*C*H), 129.5 (Ar*C*H), 126.5 (Ar*C*H), 124.2 (Ar*C*H), 121.8 (Ar*C*), 119.0 (Perimidine*C*H), 115.3 (Ar*C*H), 109.3 (Perimidine*C*H), 30.8

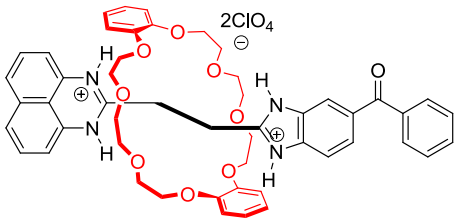
(CH_2CH_2), 26.1 (CH_2CH_2); IR ν cm^{-1} 2801 (saturated C-H), 1654.6 (ketone C=O); MS (ESI^+): *m/z* 417.2 [**2.54**+H]$^+$.

2.55



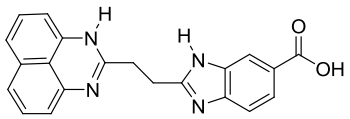
2.54 (50 mg, 0.12 mmol) was dissolved in the minimum amount of MeOH. $HClO_4$ (70%) was added cautiously dropwise to the solution until a black precipitate appeared. The liquid was decanted off whilst warm and left to cool and crystallise. The grey precipitate was filtered and washed with ice cold MeOH (36 mg, 0.06 mmol, 50%). m.p. 179-180°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 12.74 (br s, 2H, 2 N*H*), 10.70 (br s, 2H, 2 N*H*), 8.18 (s, 1H, BenzimidazoleC*H*), 8.01 (d, 1H, *J* = 8.6 Hz, BenzimidazoleC*H*), 7.93 (d, 1H, *J* = 8.6 Hz, BenzimidazoleC*H*), 7.80 (d, 2H, *J* = 7.0 Hz, 2 ArC*H*), 7.71 (t, 1H, *J* = 7.5 Hz, ArC*H*), 7.58 (t, 2H, *J* = 7.5 Hz, 2 ArC*H*), 7.45 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 7.36 (m, 2H, 2 PerimidineC*H*), 6.83 (d, 2H, *J* = 8.0 Hz, 2 PerimidineC*H*), 3.78 (t, 2H, *J* = 8.0 Hz, CH_2CH_2), 3.22 (t, 2H, *J* = 8.0 Hz, CH_2CH_2); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 160.7 (*C*=O), 153.9 (Ar*C*), 138.3 (Ar*C*), 137.4 (Ar*C*), 135.9 (Ar*C*), 134.4 (Ar*C*H), 134.3 (Ar*C*), 133.0 (Ar*C*), 131.6 (Ar*C*), 131.3 (Ar*C*H), 130.0 (Perimidine*C*H), 129.9 (Ar*C*H), 129.5 (Ar*C*H), 124.9 (Ar*C*H), 123.9 (Ar*C*), 121.8 (Ar*C*), 117.7 (Perimidine*C*H), 115.6 (Ar*C*H), 110.1 (Perimidine*C*H), 30.3 (CH_2CH_2), 24.7 (CH_2CH_2); IR ν cm^{-1} 3200 (NH), 1648 (ketone C=O), 1070 (ClO_4); HRMS (ESI^+): *m/z* found, 417.1706 calc for $C_{27}H_{21}N_4O$ 417.1710 [**2.55**-H.2ClO_4]$^+$.

2.56



Thread **2.55** (12.3 mg, 0.02mmol) and DB24C8 (8.9 mg, 0.02mmol) were dissolved in deuterated acetonitrile (10mL) and pseudorotaxane formation was observed by ^{1}H NMR. Binding constant = **995 M^{-1}** was calculated from the single point method[129] by measuring the integration of ArC*H* protons for the free and bound crown at 6.93 ppm and 6.48 ppm respectively. **Pseudorotaxane 2.56** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 12.52 (br s, 1H, ⊂ N*H*H), 12.36 (br s, 1H, ⊂ NH*H*), 7.99 (m, 1H, ⊂ BenzimidazoleC*H*), 7.90 (m, 1H, ⊂ BenzimidazoleC*H*), 7.82-7.70 (m, 3H, ⊂ 3 ArC*H*), 7.63-7.57 (m, 3H, ⊂ 3 ArC*H*), 7.16-7.15 (m, 4H, ⊂ 4 PerimidineC*H*), 6.60 (m, 2H, ⊂ 2 PerimidineC*H*), 6.48 (s, 8H, ⊂ 8 crown ArC*H*), 4.15-3.92 (m, 26 H, ⊂ 12 OCH_2 and ⊂ CH_2CH$_2$), 3.43-3.39 (m, 2H, ⊂ CH_2CH$_2$); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); and **Thread 2.55** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 12.74 (br s, 2H, 2 N*H*), 10.70 (br s, 2H, 2 N*H*), 8.18 (s, 1H, BenzimidazoleC*H*), 8.01 (d, 1H, *J* = 8.6 Hz, BenzimidazoleC*H*), 7.93 (d, 1H, *J* = 8.6 Hz, BenzimidazoleC*H*), 7.80 (d, 2H, *J* = 7.0 Hz, 2 ArC*H*), 7.71 (t, 1H, *J* = 7.5 Hz, ArC*H*), 7.58 (t, 2H, *J* = 7.5 Hz, 2 ArC*H*), 7.45 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 7.36 (m, 2H, 2 PerimidineC*H*), 6.83 (d, 2H, *J* = 8.0 Hz, 2 PerimidineC*H*), 3.78 (t, 2H, *J* = 8.0 Hz, CH_2CH$_2$), 3.22 (t, 2H, *J* = 8.0 Hz, CH_2CH$_2$); HRMS (ESI$^+$): *m/z* found, 865.3812 calc for $C_{51}H_{53}N_4O_9$ 865.3807 [**2.56**-H.2ClO$_4$]$^+$.

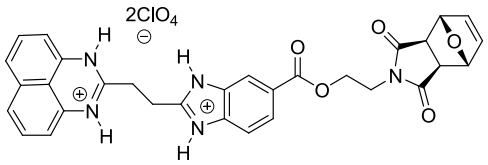
2.57



Acid **2.50** (2 g, 8.3 mmol) was dissolved in CH_2Cl_2 (20 mL) and TFAA (2 mL) and stirred at room temperature for 12 h. The CH_2Cl_2 and excess TFAA were removed *in vacuo*. The residue was dissolved in HOAc (40 mL) and 3,4-diaminobenzoic acid (1.33g, 8.7 mmol) was added. The solution was heated at 70°C for 48 h. The solution was cooled and the precipitate filtered and washed in HOAc and acetone. The green solid was recrystallised from MeOH/water (1.25g, 3.5 mmol, 43%). m.p. 237-238°C; ^{1}H NMR (400 MHz, 298 K,

DMSO-d_6) δ_H 8.15 (s, 1H, BenzimidazoleC*H*), 7.85, (d, 1H, *J* = 8.5 Hz, BenzimidazoleC*H*), 7.63 (d, 1H, *J* = 8.5 Hz, BenzimidazoleC*H*), 7.36 (m, 4H, 4 PerimidineC*H*), 6.77 (d, 2H, *J* = 8.0 Hz, 2 PerimidineC*H*), 3.50 (t, 2H, *J* = 7.5 Hz, CH_2CH$_2$), 3.18 (t, 2H, *J* = 7.5 Hz, CH$_2$CH_2); ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ_C 167.8 (*C*OOH), 163.0 (Ar*C*), 160.1 (Ar*C*), 155.4 (Ar*C*), 138.1 (Ar*C*), 134.9 (Ar*C*), 134.4 (Ar*C*), 128.6 (Perimidine*C*H), 124.4 (Ar*C*), 123.3 (Ar*C*H), 121.2 (Perimidine*C*H), 120.4 (Ar*C*), 116.6 (Ar*C*H), 114.1 (Ar*C*H), 107.7 (Perimidine*C*H), 29.64 (*C*H$_2$CH$_2$), 24.74 (CH$_2$*C*H$_2$); IR ν cm^{-1} 2778 (saturated C-H), 1652 (acid C=O); HRMS (ESI$^+$): *m/z* found, 357.1348 calc for $C_{21}H_{17}N_4O_2$ 357.1352 [**2.57**+H]$^+$.

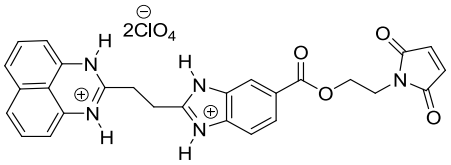
2.58



To a mixture of the acid **2.57** (200 mg, 0.56 mmol) in CH$_2$Cl$_2$ (5 mL) was added NEt$_3$ (2 mL, excess). The HBTU (255 mg, 0.67 mmol) was added and the reaction stirred for 24 h. The alcohol **2.04** (117 mg, 0.56 mmol) and DMAP (7 mg, 0.056 mmol) were added and stirred for a further 48 h. The reaction was followed by TLC (EtOAc:MeOH:H$_2$O; 40:15:3). CH$_2$Cl$_2$ (20 mL) was added and the solution was washed with water (3 x 20 mL). The organic layer was dried over MgSO$_4$, filtered and the solvent removed *in vacuo*. The residue was dissolved in CH$_2$Cl$_2$ and Et$_2$O was added to form a precipitate and was filtered and washed with EtOAc. The solid was dissolved in MeOH and HClO$_4$ (70%) (0.5 mL) was added cautiously. Water was added drop-wise to induce precipitation and the solid was filtered and washed with water (3mL) to provide a pale green solid (50 mg, 0.07 mmol, 12%). m.p. 118-119°C; ^{1}H NMR (700 MHz, 298 K, CD$_3$CN) δ_H 8.33 (s, 1H, BenzimidazoleC*H*), 8.15 (d, 1H, *J* = 8.5 Hz, BenzimidazoleC*H*), 7.88 (d, 1H, *J* = 8.5 Hz, BenzimidazoleC*H*), 7.44 (d, 2H, *J* = 8.5 Hz, 2 PerimidineC*H*), 7.35 (dd, 2H, *J* = 8.5 Hz, *J* = 8.0 Hz and 2 PerimidineC*H*), 6.82 (d, 2H, *J* = 8.0 Hz, 2 PerimidineC*H*), 6.48 (s, 2H, C*H*=C*H*), 5.09 (s, 2H, 2 C*H*O), 4.43 (t, 2H, *J* = 5.0 Hz, CH$_2$CH_2O), 3.83 (t, 2H, *J* = 5.0 Hz,

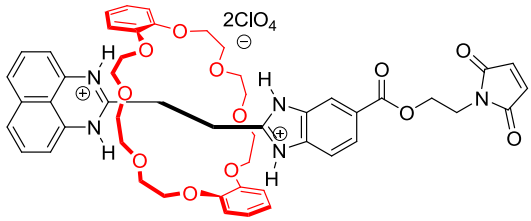
CH_2CH_2N), 3.77 (t, 2H, *J* = 8.0 Hz, CH_2CH_2), 3.23 (t, 2H, *J* = 8.0 Hz, CH_2CH_2), 2.89 (s, 2H, 2 C*H*CO); ^{13}C NMR (175 MHz, 298 K, CD_3CN) δ_C 176.7 (imide *C*=O), 164.7 (*C*OO), 159.3 (Ar*C*), 152.6 (Ar*C*), 136.5 (*C*H=*C*H), 134.6 (Ar*C*), 133.5 (Ar*C*), 131.6 (Ar*C*), 130.4 (Ar*C*), 128.8 (Ar*C*), 128.7 (PerimidineCH), 127.6 (Ar*C*H), 123.6 (PerimidineCH), 120.4 (Ar*C*), 115.9 (Ar*C*H), 114.3 (Ar*C*H), 108.8 (PerimidineCH), 80.9 (*C*HO), 61.9 (CH_2CH_2O), 47.5 (*C*HCO), 37.2 (CH_2CH_2N), 28.9 (CH_2CH_2), 23.2 (CH_2CH_2); IR ν cm^{-1} 3488 (br NH), 1697 (ester and imide C=O), 1092 (ClO_4); HRMS (ESI$^+$): *m/z* found, 548.1929 calc. for $C_{31}H_{26}N_5O_5$ 548.1928 [**2.58**-H.2ClO_4]$^+$.

2.59



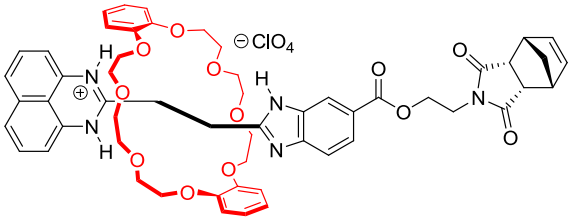
Perchlorate thread **2.58** (30 mg, 0.04 mmol) was dissolved in acetonitrile and heated under microwave irradiation (3h, 150W, 110°C) and the reaction followed by TLC. The solvent was removed *in vacuo* and the yellow solid recrystallised from MeOH/water (15mg, 0.022 mmol, 55%). m.p. 216-217°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.36 (s, 1H, ArC*H*), 8.13 (d, 1H, *J* = 8.0 Hz, ArC*H*), 7.87 (d, 1H, *J* = 8.0 Hz, ArC*H*), 7.45 (d, 2H, *J* = 7.5 Hz, 2 PerimidineC*H*), 7.36 (t, 2H, *J* = 7.5 Hz, 2 PerimidineC*H*), 6.81 (d, 2H, *J* = 7.5 Hz, PerimidineC*H*), 6.78 (s, 2H, C*H*=C*H*), 4.45 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.88 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.74 (t, 2H, *J* = 7.5 Hz, CH_2CH_2), 3.22 (t, 2H, *J* = 7.5 Hz, CH_2CH_2); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 169.8 (imide *C*=O), 165.4 (*C*OO), 159.3 (Ar*C*), 157.5 (Ar*C*), 147.6 (Ar*C*), 143.9 (Ar*C*), 135.9 (Ar*C*), 135.8 (*C*H=*C*H), 132.9 (Ar*C*), 130.1 (PerimidineCH), 128.9 (Ar*C*H), 128.0 (Ar*C*), 125.0 (PerimidineCH), 123.6 (Ar*C*), 117.3 (Ar*C*H), 115.7 (Ar*C*H), 110.1 (PerimidineCH), 64.4 (CH_2CH_2O), 36.0 (CH_2CH_2N), 30.2 (CH_2CH_2), 24.6 (CH_2CH_2); IR ν cm^{-1} 3216 (N-H), 1707 (imide and ester C=O), 1093 (ClO_4); HRMS (ESI$^+$): *m/z* found, 480.1663 calc for $C_{27}H_{22}N_5O_4$ 480.1666 [**2.59**-H.2ClO_4]$^+$.

2.60



Thread **2.59** (10 mg, 0.015 mmol) was dissolved in deuterated acetonitrile and DB24C8 (13 mg, 0.03 mmol, 2 equiv) was added. Pseudorotaxane formation was monitored by ^{1}H NMR. **Pseudorotaxane 2.60** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 10.73 (br s, 2H, ⊂ N*H*$_2$), 8.23 (s, 1H, ⊂ BenzimidazoleC*H*), 8.06 (t, 1H, *J* = 8.5 Hz, ⊂ PerimidineC*H*), 7.74 (d, 1H, *J* = 8.5 Hz, ⊂ BenzimidazoleC*H*), 7.40 (m, 1H, ⊂ BenzimidazoleC*H*), 7.15 (m, 2H, 2 ⊂ PerimidineC*H*), 6.81 (s, 2H, ⊂ C*H*=C*H*), 6.61 (m, 2H, ⊂ 2 PerimidineC*H*), 6.48 (s, 8H, ⊂ 8 crown ArC*H*), 4.47 (t, 2H, *J* = 5.0 Hz, ⊂ CH_2CH_2O), 4.19-3.92 (m, 30 H, ⊂ 12 OC*H*$_2$ and ⊂ 2 C*H*$_2$CH$_2$), 3.45 (m, 2H, ⊂ CH_2CH_2); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OC*H*$_2$), 3.83 (m, 8H, 4 OC*H*$_2$), 3.72 (s, 8H, 4 OC*H*$_2$); MS (ESI$^+$): *m/z* 930.0 [**2.60**-H.2ClO_4]$^+$.

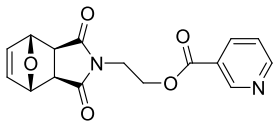
2.61



To the pseudorotaxane **2.60** (16.5 mg, 0.015 mmol) in acetonitrile, freshly distilled cyclopentadiene (0.1 mL, excess) was added at room temperature and the solvent and excess cyclopentadiene removed immediately *in vacuo*. The resulting residue was purified *via* flash chromatography (SiO_2: CH_2Cl_2:Acetone; 95:5 to CH_2Cl_2:MeOH; 95:5) to give a yellow oil (6 mg, 0.005 mmol, 34 %). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 10.77 (br s, ⊂ N*H*), 8.24 (br s, 1H, ⊂ isomer BenzimidazoleC*H*), 8.12 (br s, 1H, ⊂ isomer BenzimidazoleC*H*), 7.87 (br m, 1H, ⊂ isomer BenzimidazoleC*H*), 7.66 (br s, 1H, ⊂ isomer BenzimidazoleC*H*), 7.55

(br s, ⊂ isomer BenzimidazoleC*H*), 7.05 (dd, 2H, *J* = 7.0 + 8.0 Hz, ⊂ 2 PerimidineC*H*), 6.97 (d, 2H, *J* = 8.0 Hz, ⊂ 2 PerimidineC*H*), 6.52 (d, 2H, *J* = 7.0 Hz, ⊂ 2 PerimidineC*H*), 6.47 (s, 8H, ⊂ 8 crown ArC*H*), 5.99 (s, 2H, ⊂ C*H*=C*H*), 4.31 (t, 2H, *J* = 5.0 Hz, ⊂ CH_2CH_2O), 4.17-4.13 (m, 4H, ⊂ CCH_2CH_2C and OCH_2), 4.06-4.00 (m, 8H, ⊂ 4 OCH_2), 3.87-3.77 (m, 10H, ⊂ 5 OCH_2), 3.70 (m, 2H, ⊂ CH_2CH_2N), 3.63 (m, 4H, ⊂ 2 OCH_2), 3.41-3.37 (m, 2H, ⊂ CCH_2CH_2C), 3.29 (br s, 2H, ⊂ 2 C*H*CO), 3.25 (br s, 2H, ⊂ 2 C*H*CH_2), 1.59 (d, 1H, *J* = 9.0 Hz, ⊂ C*H*H), 1.54 (d, 1H, *J* = 9.0 Hz, ⊂ CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 177.7 (imide *C*=O), 147.2 (*C*OO), 134.3 (*C*H=*C*H), 134.2 (Ar*C*), 131.7 (Ar*C*), 131.7' (Ar*C*), 127.7 (Perimidine*C*H), 122.0 (Ar*C*H), 121.4 (Ar*C*H), 121.3 (Ar*C*H), 120.5 (Perimidine*C*H), 119.5 (Ar*C*), 114.2 (Ar*C*H), 114.01 (Ar*C*), 111.6 (Ar*C*H), 107.2 (Perimidine*C*H), 100.0 (Ar*C*), 70.6 (OCH_2), 70.3 (OCH_2), 69.3 (CH_2CH_2), 68.6 (CH_2CH_2), 68.4 (OCH_2), 60.6 (CH_2CH_2O), 51.7 (bridgehead CH_2), 45.7 ($CHCH_2CH$), 44.7 (*C*HCO), 37.1 (CH_2CH_2N), 29.3 (CH_2CH_2), 24.3 (CH_2CH_2) ArC quaternary carbons not observed; IR ν cm^{-1} 3222 (NH), 2923 (saturated C-H), 1699 (ester C=O), 1655 (imide C=O), 1098 (ClO_4); HRMS (ESI^+): *m/z* found, 994.4235 calc for $C_{56}H_{60}N_5O_{12}$ 994.4233 [**2.61**-ClO_4]$^+$.

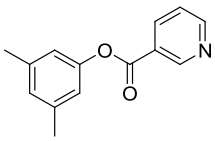
2.63



To a mixture of nicotinic acid (2.0 g, 16 mmol) in thionyl chloride (20.0 mL, excess) was carefully added 3 drops of DMF. The mixture was stirred at room temperature overnight then the thionyl chloride was removed *in vacuo* while heating was maintained with an oil bath (40°C) to give a white powder that was used without further purification. To the nicotinoyl chloride in CH_2Cl_2 (20 mL), a solution of Diels-Alder alcohol **2.04** (3.74 g, 17.9 mmol) and NEt_3 (5 mL, 35.9 mmol) in CH_2Cl_2 (15 mL) was added dropwise over 10 minutes. The mixture was stirred for 48 h. To the reaction mixture, a saturated solution of sodium carbonate (50 mL) was added and allowed to stir for 20 minutes. The mixture was

separated and the organic layer was washed with sodium carbonate (2 x 50 mL), dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to provide a white solid which was recrystallised from CH_2Cl_2/Et_2O (2.97 g, 9.46 mmol, 58%). m.p. 83-84°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 9.14 (s, 1H, PyrC*H*-N), 8.87 (d, 1H, *J* = 7.0 Hz, PyrC*H*-N), 8.23 (d, 1H, *J* = 7.0 Hz, PyrC*H*-C), 7.35 (t, 1H, *J* = 7.0 Hz, PyrC*H*), 6.50 (s, 2H, C*H*=C*H*), 5.22 (s, 2H, 2 C*H*O), 4.48 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.90 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 2.86 (s, 2H, 2 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide *C*=O), 165.0 (*C*OO), 153.6 (Pyr*C*H), 151.1 (Pyr*C*H), 137.1 (Pyr*C*H) 136.5 (*C*H=*C*H), 125.7 (Ar*C*), 123.3 (Pyr*C*H), 80.9 (*C*HO), 61.6 (CH_2CH_2O), 47.5 (*C*HCO), 37.7 (CH_2CH_2N); IR ν cm^{-1} 3021 (saturated C-H), 1688 (ester and imide C=O); HRMS (ESI$^+$): *m/z* found, 315.0978 calculated for $C_{16}H_{15}N_4O_5$ 315.0981 [**2.63**+H]$^+$;

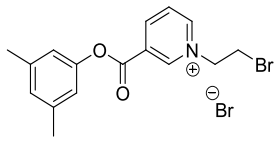
2.64



To a mixture of nicotinic acid (2.0 g, 16 mmol) in thionyl chloride (10.0 mL, excess) was carefully added 3 drops of DMF. The mixture was stirred at room temperature overnight then the thionyl chloride was removed *in vacuo* while heating was maintained with an oil bath (40˚C) to give a white powder that was used without further purification. To the nicotinoyl chloride in CH_2Cl_2 (20 mL), 3,5-dimethylphenol (2.4 g, 20 mmol) was added and the solution cooled to 0˚C. NEt_3 (5.5 mL, 54 mmol) was diluted in CH_2Cl_2 (10 mL) and added to the cooled mixture over 30 minutes. The reaction mixture was warmed to room temperature and stirred overnight. Water (10 mL) was added to the solution and stirred for 30 minutes then extracted with CH_2Cl_2 (2 x 10 mL). The organic layers were combined and washed with a 2M sodium hydroxide solution (3 x 20 mL). The organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to provide a yellow oil, which slowly crystallised on standing at room temperature (2.8 g, 12.5 mmol, 78 %). m.p. 53-54˚C;

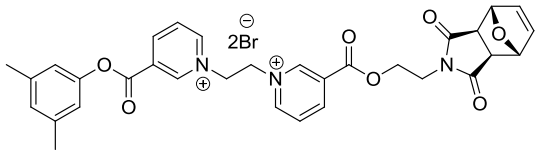
^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 9.38 (s, 1H, PyrC*H*-N), 8.84 (d, 1H, *J* = 5.0 Hz, PyrC*H*-N), 8.43 (d, 1H, *J* = 8.0 Hz, PyrC*H*-C), 7.48 (m, 1H, PyrC*H*), 6.92 (br s, 1H, ArC*H*), 6.84 (br s, 2H, 2 ArC*H*), 2.35 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 164.1 (*C*OO), 153.9 (Ar*C*H), 151.3 (Ar*C*H), 150.4 (Ar*C*), 139.5 (Ar*C*H), 137.5 (Ar*C*H), 127.9 (Ar*C*), 125.8 (Ar*C*H), 123.4 (Ar*C*H), 119.1 (Ar*C*H), 21.3 (CH_3); IR ν cm^{-1} 2915 (saturated C-H), 1728 (ester C=O), 1258 (C-O); HRMS (ESI$^+$): found, 250.0838 calc for $C_{14}H_{13}NO_2Na$ 250.0838 [**2.64**+Na]$^+$; CHN Analysis Found: C 73.87; H 5.73; N 6.11. Calc. for $C_{14}H_{13}NO_2$: C 73.99; H 5.77; N 6.16.

2.65



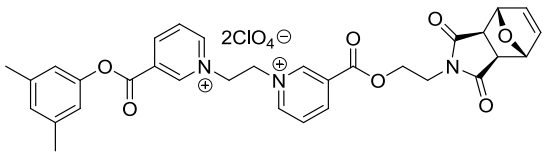
Compound **2.64** (1 g, 4.4 mmol) was dissolved in 1,2 dibromoethane (1 mL, excess) and acetonitrile (1 mL). It was heated at 60˚C for 72 h. The solution was cooled and the solvent removed *in vacuo*. EtOAc (20 mL) was added and the solution filtered to remove *bis*pyridinium product. The liquors were left crystallise. The solution was filtered to provide a white solid (420 mg, 1.06 mmol, 24%). m.p. 192-193˚C; ^{1}H NMR (400 MHz, 298 K, D_2O) δ_H 9.75 (s, 1H, PyrC*H*-N), 9.30 (d, 1H, *J* = 8.0 Hz, PyrC*H*), 9.25 (d, 1H, *J* = 6.0 Hz, PyrC*H*), 8.38 (t, 1H, *J* = 8.0 + 6.0 Hz, PyrC*H*), 7.15 (s, 1H, ArC*H*), 7.00 (s, 2H, ArC*H*), 5.22 (t, 2H, *J* = 5.5 Hz, CH_2N^+), 4.09 (t, 2H, *J* = 5.5 Hz, CH_2Br), 2.38 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, D_2O) δ_C 161.9 (*C*OO), 149.7 (Ar*C*), 148.2 (Ar*C*H), 146.9 (Ar*C*H), 146.4 (Ar*C*H), 140.6 (Ar*C*), 130.4 (Ar*C*), 128.7 (Ar*C*H), 128.6 (Ar*C*H), 118.5 (Ar*C*H), 62.6 (CH_2N^+), 29.9 (CH_2Br), 20.3 (CH_3); IR ν cm^{-1} 3013 (saturated C-H), 1741 (ester C=O), 1279 (C-O); HRMS (ESI$^+$): *m/z* found, 334.0441 calc for $C_{16}H_{17}NO_2Br^{79}$ 334.0437 [**2.65**-Br]$^+$; CHN Analysis Found: C 46.51; H 4.09; N 3.37. Calc. for $C_{16}H_{17}Br_2NO_2$: C 46.29; H 4.13; N 3.37%.

2.66



The bromide salt **2.65** (30 mg, 0.072 mmol) and nicotinate ester **2.63** (25 mg, 0.08 mmol) were dissolved in acetonitrile (2 mL) and heated to 60˚C for 72 h. The reaction was cooled and a precipitate formed which was filtered and washed with cold acetonitrile. The solid was collected and used without further purification (25 mg, 0.034 mmol, 48%). ^{1}H NMR (400 MHz, 298 K, DMSO-d$_6$) δ_H 9.92 (s, 1H, PyrC*H*-N), 9.70 (s, 1H, PyrC*H*-N), 9.35 (dd, 2H, *J* = 7.5 Hz and 6.5 Hz, 2 PyrC*H*), 9.23 (d, 1H, *J* = 8.5 Hz PyrC*H*), 8.88 (d, 1H, *J* = 8.5 Hz PyrC*H*), 8.42 (dd, 2H, *J* = 8.2 Hz and 7.5 Hz, 2 PyrC*H*), 7.03 (s, 1H, ArC*H*), 6.96 (s, 2H, 2 ArC*H*), 6.54 (s, 2H, C*H*=C*H*), 5.38 (4H, 2 CH_2-N$^+$), 5.11 (s, 2H, 2 C*H*CO), 4.48 (t, 2H, *J* = 5.5 Hz, CH$_2$CH_2O), 3.80 (t, 2H, *J* = 5.5 Hz, CH$_2$CH_2N), 2.97 (s, 2H, 2 C*H*CO), 2.33 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD$_3$CN) δ_C 176.8 (imide *C*=O), 161.5 (*C*OO), 160.7 (*C*OO), 150.1 (Ar*C*), 149.2 (Ar*C*H), 149.1 (Ar*C*H), 147.7 (Ar*C*H), 147.2 (Ar*C*H), 146.8 (Ar*C*H), 145.9 (Ar*C*H), 139.5 (Ar*C*), 136.7 (*C*H=*C*H), 130.1 (Ar*C*), 130.0 (Ar*C*), 128.9 (Ar*C*H), 128.8 (Ar*C*H), 128.4 (Ar*C*H), 119.0 (Ar*C*H), 80.6 (*C*HO), 64.5 (N$^+$-CH$_2$*C*H$_2$-N$^+$), 64.4 (N$^+$-*C*H$_2$CH$_2$-N$^+$), 62.9 (CH$_2$*C*H$_2$O), 47.4 (*C*HCO), 36.7 (CH$_2$*C*H$_2$N), 21.0 (*C*H$_3$).

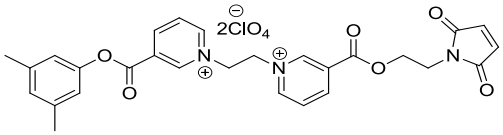
2.67



Bromide salt **2.66** (20 mg, 0.03 mmol) was dissolved in water (0.5 mL) and a saturated aqueous solution of sodium perchlorate (1 mL) was added. The white precipitate formed was filtered and washed with water and dried in the desiccator (17 mg, 0.022 mmol, 73 %).^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 9.57 (s, 1H, PyrC*H*-N), 9.36 (s, 1H, PyrC*H*-N), 9.18 (d, 1H, *J* = 8.0 Hz, PyrC*H*), 8.99-8.96 (m, 3H, 3 PyrC*H*), 8.33-8.25 (m, 2H, 2 PyrC*H*), 7.04 (s, 1H, ArC*H*), 6.95 (s, 2H, 2 ArC*H*), 6.69 (s, 2H, C*H*=C*H*), 5.27 (s, 4H, 2 CH_2-N$^+$), 5.12 (s,

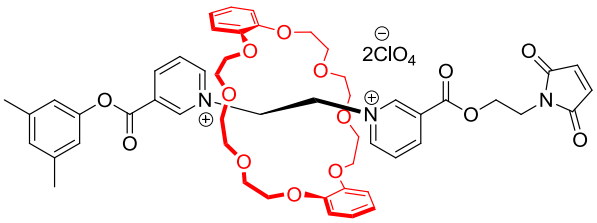
2H, 2 C*H*CO), 4.54 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 3.84 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N), 2.92 (s, 2H, 2 C*H*CO), 2.36 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 178.2 (imide *C*=O), 162.1 (*C*OO), 161.6 (*C*OO), 151.6 (Ar*C*), 149.9 (Ar*C*H), 149.8 (Ar*C*H), 148.9 (Ar*C*H), 148.5 (Ar*C*H), 148.3 (Ar*C*H), 148.2 (Ar*C*H), 141.4 (Ar*C*), 137.9 (*C*H=*C*H), 132.8(4) (Ar*C*), 132.8(1) (Ar*C*), 131.0 (Ar*C*H), 130.9 (Ar*C*H), 129.7 (Ar*C*H), 120.0 (Ar*C*H), 82.3 (*C*HO), 64.5 (N^+-CH_2CH_2-N^+), 64.4 (N^+-CH_2CH_2-N^+), 61.0 (CH_2CH_2O), 48.9 (*C*HCO), 38.4 (CH_2CH_2N), 21.6 (CH_3); CHN: Found C 49.07; H 3.79; N 5.44; Calc. for $C_{32}H_{31}Cl_2N_3O_{15}.H_2O$: C 48.87; H 4.23; N 5.34%.

2.68



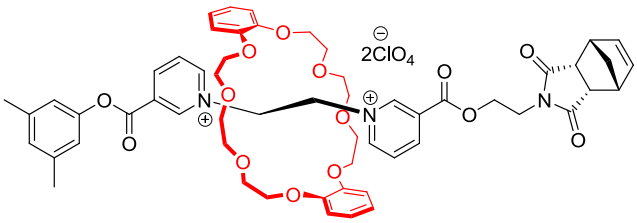
The ClO_4^- salt **2.67** (30 mg, 0.04 mmol) was dissolved in acetonitrile and heated to reflux for 24 h. The solvent was removed *in vacuo* to provide a pale yellow solid recrystallised from CH_3CN/Et_2O (10 mg, 0.014 mmol, 36%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.57 (s, 1H, PyrC*H*-N), 9.36 (s, 1H, PyrC*H*-N), 9.18 (d, 1H, *J* = 8.2 Hz, PyrC*H*), 8.90-9.00 (m, 3H, 3 PyrC*H*), 8.25-8.34 (m, 2 H, 2 PyrC*H*), 7.05 (s, 1H, ArC*H*), 6.93 (s, 2H, 2 ArC*H*), 6.80 (s, 2H, C*H*=C*H*), 5.26 (br s, 4H, 2 CH_2N^+), 4.51 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.88 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 2.36 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.8 (imide *C*=O), 160.6 (*C*OO), 159.9 (*C*OO), 149.8 (Ar*C*), 148.3 (Ar*C*H), 148.1 (Ar*C*H), 147.3 (Ar*C*H), 146.8 (Ar*C*H), 146.5 (Ar*C*H), 139.5 (Ar*C*), 136.2 (Ar*C*H), 134.2 (*C*H=*C*H), 131.3 (Ar*C*), 131.2 (Ar*C*), 129.3 (Ar*C*H), 129.2(8) (Ar*C*H), 128.1 (Ar*C*H), 118.3 (Ar*C*H), 64.3 (CH_2CH_2O), 59.3 (N^+-CH_2CH_2-N^+), 59.2 (N^+-CH_2CH_2-N^+), 36.0 (CH_2CH_2N), 19.9 (CH_3).

2.69



Thread **2.68** (10 mg, 0.014 mmol) and DB24C8 (12.5 mg, 0.028 mmol) were dissolved in deuterated acetonitrile (0.5 mL). The reaction was monitored by ^{1}H NMR to follow pseudorotaxane formation. **Pseudorotaxane 2.69** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.91 (s, 1H, ⊂ PyrC*H*-N), 9.72 (s, 1H, ⊂ PyrC*H*-N), 9.34 (d, 1H, *J* = 6.0 Hz, ⊂ PyrC*H*), 9.27 (d, 1H, *J* = 6.0 Hz, ⊂ PyrC*H*), 8.56 (d, 1H, *J* = 8.0 Hz, ⊂ PyrC*H*), 8.35 (d, 1H, *J* = 8.0 Hz, ⊂ PyrC*H*), 7.99 (t, 1H, *J* = 7.0 Hz, ⊂ PyrC*H*), 7.92 (t, 1H, *J* = 6.5 Hz, ⊂ PyrC*H*), 7.08 (s, 1H, ⊂ ArC*H*), 6.90 (m, 2H, ⊂ 2 ArCH), 6.85 (s, 2H, ⊂ C*H*=C*H*), 6.82 (m, 4H, 4 ⊂ crown ArC*H*), 6.71 (m, 4H, ⊂ 4 crown ArC*H*), 5.63 (br s, 4H, ⊂ 2 CH_2N^+), 4.49 (t, 2H, *J* = 5.0 Hz, ⊂ CH_2CH_2O), 4.00-3.98 (br m, 24H, ⊂ 12 OCH_2), 3.88 (t, 2H, *J* = 5.3 Hz, ⊂ CH_2CH_2N), 2.41 (s, 6H, ⊂ 2 CH_3); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2).

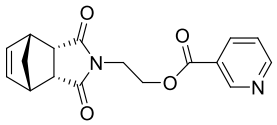
2.01



To pseudorotaxane **2.69** in acetonitrile (0.5 mL), freshly distilled cyclopentadiene (0.1 mL, excess) was added at room temperature. The excess cyclopentadiene and solvent were removed immediately *in vacuo* and the crude solid purified by precipitation in acetonitrile/Et_2O to give the rotaxane (10 mg, 0.008 mmol, 58%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.91 (s, 1H, ⊂ PyrC*H*-N), 9.75 (s, 1H, ⊂ PyrC*H*-N), 9.34 (d, 1H, *J* = 6.0 Hz, ⊂ PyrC*H*), 9.28 (d, 1H, *J* = 6.0 Hz, ⊂ PyrC*H*), 8.53 (d, 1H, *J* = 8.0 Hz, ⊂ PyrC*H*), 8.41 (d, 1H, *J* = 8.0 Hz, ⊂ PyrC*H*), 7.99-7.93 (m, 2H, ⊂ 2 PyrC*H*), 7.08 (s, 1H, ⊂ ArC*H*), 6.93 (s, 2H, ⊂ 2 ArCH), 6.82 (m, 4H, ⊂ 4 crown ArC*H*), 6.68 (m, 4H, ⊂ 4 crown ArC*H*), 6.01 (s, 2H, ⊂ C*H*=C*H*), 5.65 (br s, 4H, ⊂ 2 CH_2N^+), 4.38 (t, 2H, *J* = 5.0 Hz, ⊂ CH_2CH_2O), 4.02-3.99 (br m, 24H, ⊂ 12 OCH_2), 3.70 (t, 2H, *J* = 5.3 Hz, ⊂ CH_2CH_2N), 3.33 (br s, 2H, ⊂ 2

C*H*CO), 3.29 (br s, 2H, ⊂ 2 C*H*CH_2), 2.41 (s, 6H, ⊂ 2 CH_3), 1.65 (dd, 1H, *J* = 9.0 Hz, ⊂ CH*H*), 1.58 (dd, 1H, *J* = 9.0 Hz, ⊂ C*H*H); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 179.0 (imide *C*=O), 162.5 (*C*OO), 161.7 (*C*OO), 151.3 (Ar*C*), 151.0 (Ar*C*H), 150.6 (Ar*C*H), 148.9 (Ar*C*H),148.4 (Ar*C*H), 148.1 (Ar*C*), 146.8 (Ar*C*H), 146.5 (Ar*C*H), 141.6 (Ar*C*), 135.8 (*C*H=*C*H), 131.0 (Ar*C*), 130.6 (Ar*C*), 129.9 (Ar*C*H), 129.5 (Ar*C*H), 129.2 (Ar*C*H), 122.6 (Ar*C*H), 120.1 (Ar*C*H), 113.9 (Ar*C*H), 71.8 (O*C*H_2), 71.4 (O*C*H_2), 68.9 (O*C*H_2), 65.1 (CH_2*C*H_2O), 60.1 (N^+-CH_2*C*H_2-N^+), 60.0 (N^+-*C*H_2CH_2-N^+), 53.2 (bridgehead *C*H_2), 47.1 (*C*HCH_2*C*H), 46.1 (*C*HCO), 37.9 (CH_2*C*H_2N), 21.7 (*C*H_3).

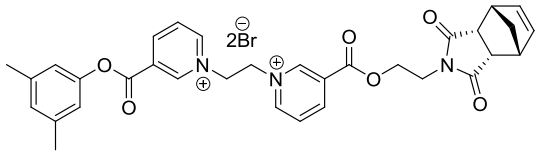
2.70



To a mixture of nicotinic acid (1.0 g, 8 mmol) in thionyl chloride (10.0 mL, excess) was carefully added 3 drops of DMF. The mixture was stirred at room temperature overnight then the thionyl chloride was removed at *in vacuo* while heating was maintained with an oil bath (40˚C) to give a white powder that was used without further purification. To the nicotinoyl chloride in CH_2Cl_2 (20 mL), a solution of **12** (1.85g, 9.5 mmol) and NEt_3 (2.5 mL, 35.9 mmol) in CH_2Cl_2 (15 mL) was added dropwise over 10 minutes. The mixture was stirred for 48 h at room temperature. To the reaction mixture, a saturated solution of sodium hydrogen carbonate (25 mL) was added and allowed to stir for 20 minutes. The mixture was separated and the organic layer was washed with aqueous sodium bicarbonate solution (2 x 30 mL), dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to provide a white solid which was recrystallised from CH_2Cl_2/Et_2O (0.45 g, 1.44 mmol, 18%). m.p. 101-102˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 9.16 (s, 1H, PyrC*H*-N), 8.76 (d, 1H, *J* = 5.0 Hz, PyrC*H*), 8.24 (d, 1H, *J* = 8.0 Hz, PyrC*H*), 7.38 (dd, 1H, *J* = 8.0 + 5.0 Hz, PyrC*H*), 6.00 (s, 2H, C*H*=C*H*), 4.36 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.77 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.36 (s, 2H, 2 C*H*CO), 3.28 (s, 2H, 2 C*H*CH_2), 1.69 (d, 1H, *J* = 9.0 Hz, C*H*H), 1.53 (d, 1H, *J*

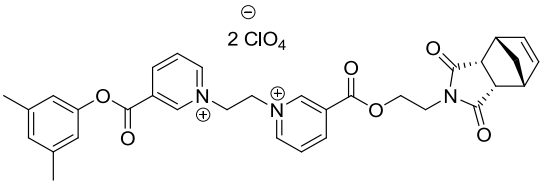
= 9.0 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 177.4 (imide *C*=O), 164.5 (*C*OO), 153.6 (Ar*C*H), 151.0 (Ar*C*H), 137.1 (Ar*C*H), 134.4 (*C*H=*C*H), 125.7 (Ar*C*), 123.4 (Ar*C*H), 62.2 (CH_2*C*H_2O), 52.3 (bridgehead *C*H_2), 45.8 (*C*HCH_2*C*H), 44.9 (*C*HCO), 37.1 (CH_2*C*H_2N); IR ν cm^{-1} 2985 (saturated C-H), 1719 (imide C=O), 1686 (ester C=O); HRMS (ESI^+): *m/z* found, 313.1182 calc for $C_{17}H_{17}N_2O_4$ 313.1183 [**2.70**+H]$^+$.

2.71



Bromine salt **2.70** (50 mg, 0.12 mmol) and ester (42 mg, 0.13 mmol) were dissolved in acetonitrile and heated to 60˚C for 72 h. A pale brown precipitate forms which is filtered and washed in acetonitrile (48 mg, 0.07 mmol, 55 %). ^{1}H NMR (400 MHz, 298 K, D_2O) δ_H 9.65 (s, 1H, PyrC*H*-N), 9.45 (s, 1H, PyrC*H*-N), 9.30-9.21 (m, 3H, 3 PyrC*H*), 9.05 (d, 1H, *J* = 8.5 Hz, PyrC*H*), 8.39-8.31 (m, 2H, 2 ArC*H*), 7.07 (s, 1H, ArC*H*), 6.89 (s, 2H, 2 ArC*H*), 5.89 (br s, 2H, C*H*=C*H*), 5.48 (br s, 4H, 2 CH_2N^+), 4.39 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.73 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.38 (br s, 2H, C*H*CO), 3.22 (m, 2H, C*H*CH_2), 2.29 (s, 6H, 2 CH_3), 1.59 (d, 1H, , *J* = 9.0 Hz, CH*H*), 1.49 (d, 1H, *J* = 9.0 Hz, C*H*H).

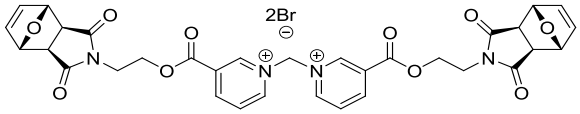
2.72



Bromide thread **2.71** (40 mg, 0.055 mmol) was dissolved in the minimum amount of water. A saturated solution of sodium perchlorate (0.5 mL) was added and a precipitate formed which was filtered and washed with water (20 mg, 0.026 mmol, 47%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.60 (s, 1H, PyrC*H*-N), 9.39 (s, 1H, PyrC*H*-N), 9.19 (d, 1H, *J* = 8.0 Hz, PyrC*H*), 9.03 (d, 1H, *J* = 6.0 Hz, PyrC*H*), 9.00-8.97 (m, 2H, 2 PyrC*H*), 8.34-8.27 (m, 2H, 2 PyrC*H*), 7.04 (s, 1H, ArC*H*), 6.94 (s, 2H, 2 ArC*H*), 6.00 (br s, 2H, C*H*=C*H*), 5.29 (br s, 4H, 2 CH_2N^+), 4.39 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 3.70 (t, 2H, *J* = 5.3 Hz, CH_2CH_2N), 3.33-3.32

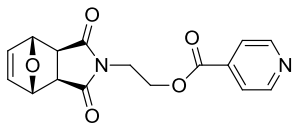
(br s, 2H, C*H*CO), 3.26 (m, 2H, C*H*CH_2), 2.35 (s, 6H, 2 CH_3), 1.61 (d, 1H, *J* = 9.0 Hz, CH*H*), 1.52 (d, 1H, *J* = 9.0 Hz, C*H*H); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 178.1 (imide *C*=O), 160.8 (*C*OO), 160.7 (*C*OO), 150.2 (Ar*C*), 148.7 (Ar*C*H), 148.5 (Ar*C*H), 147.6 (Ar*C*H), 146.9 (Ar*C*H), 146.8 (Ar*C*H), 140.1 (Ar*C*), 134.4 (*C*H=*C*H), 131.5(3) (Ar*C*), 131.5(0) (Ar*C*), 129.7 (Ar*C*H), 129.6 (Ar*C*H), 128.4 (Ar*C*H), 118.7 (Ar*C*H), 64.1 (CH_2CH_2O), 59.7 (N^+-CH_2CH_2-N^+), 51.9 (bridgehead CH_2), 45.8 ($CHCH_2$), 44.8 (*C*HCO), 36.6 (CH_2CH_2N), 20.3 (CH_3).

2.73



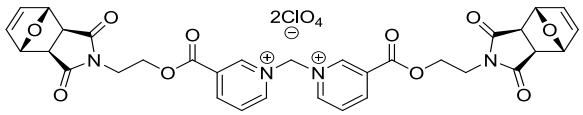
Compound **2.63** (500 mg, 1.6 mmol) was dissolved in dibromomethane (3 mL, excess) and DMF (1.5 mL) and was heated to 60°C for 48 h. The solution was cooled to room temperature and EtOAc (10 mL) was added to form a precipitate (355 mg, 0.442 mmol, 55%). m.p. 190-191˚C (decomp.); ^{1}H NMR (400 MHz, 298 K, D_2O) δ_H 9.91 (s, 2H, 2 PyrC*H*-N), 9.62 (d, 2H, *J* = 6.0 Hz, 2 PyrC*H*-N), 9.23 (d, 2H, *J* = 8.0 Hz, 2 PyrC*H*-C), 8.51 (t, 2H, *J* = 6.0 + 8.0 Hz, 2 PyrC*H*), 7.61 (s, 2H, CH_2) 6.58 (s, 4H, 2 C*H*=C*H*), 5.16 (s, 4H, 4 C*H*O), 4.70 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 4.00 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N), 3.12 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, D_2O) δ_C 179.2 (imide *C*=O), 161.3 (*C*OO), 149.6 (Pyr*C*H), 148.6 (Pyr*C*H), 146.9 (Pyr*C*H), 136.4 (*C*H=*C*H), 131.54 (Ar*C*), 130.1 (Pyr*C*H), 80.9 (*C*HO), 78.3 (CH_2), 63.5 (CH_2CH_2O), 47.4 (*C*HCO), 37.6 (CH_2CH_2N); IR ν cm^{-1} 2997 (C-H), 1742 (imide C=O), 1698 (ester C=O); HRMS (ESI^+): *m/z* found 641.1910 calc for $C_{33}H_{29}N_4O_{10}$ 641.1878 [**2.73**-2Br+H]$^+$.

2.75



To a stirred mixture of isonicotinic acid (2.0 g, 16 mmol) and thionyl chloride (20.0 mL, excess) 3 drops of DMF were added. The mixture was stirred at room temperature overnight then the thionyl chloride was removed *in vacuo* while heating was maintained with an oil bath (40°C) to give a white powder that was used without further purification. To the isonicotinoyl chloride in CH_2Cl_2 (20 mL), a solution of **2.04** (3.74 g, 17.9 mmol) and NEt_3 (5 mL, 35.9 mmol) in CH_2Cl_2 (15 mL) was added dropwise over 10 minutes. The mixture was stirred for 48 h. To the reaction mixture, a saturated solution of sodium hydrogen carbonate (50 mL) was added and allowed to stir for 20 minutes. The mixture was separated and the organic layer washed with saturated sodium bicarbonate (2 x 50 mL), dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to provide a white solid which was recrystallised from CH_2Cl_2/isopropyl alcohol (3.17 g, 10.1 mmol, 62%). m.p. 146-147˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.71 (d, 2H, *J* = 4.5 Hz, 2 PyrC*H*-N), 7.74 (d, 2H, *J* = 4.5 Hz, 2 PyrC*H*-C), 6.44 (s, 2H, C*H*=C*H*), 5.16 (s, 2H, 2 C*H*O), 4.43 (t, 2H, *J* = 5.5 Hz, CH_2CH_2O), 3.86 (t, 2H, *J* = 5.5 Hz, CH_2CH_2N), 2.81 (s, 2H, 2 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide *C*=O), 164.8 (*C*OO), 150.6 (PyrCH), 137.0 (Ar*C*), 136.5 (*C*H=*C*H), 122.9 (Pyr*C*H), 81.0 (*C*HO), 62.0 (CH_2CH_2O), 47.5 (*C*HCO), 37.6 (CH_2CH_2N); IR ν cm^{-1} 1726 (ester C=O), 1694 (imide C=O); HRMS (ESI$^+$): *m/z*: found 315.0974 calc for $C_{16}H_{15}N_4O_5$ 315.0981 [**2.75**+H]$^+$.

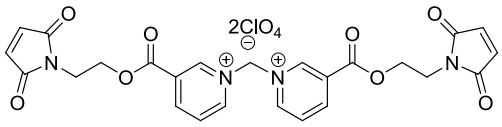
2.76



Compound **2.74** (50 mg, 0.062 mmol) was dissolved in water (0.5 mL). It was added to a solution of saturated sodium perchlorate (1 mL). A beige precipitate formed and was filtered and washed with water (20 mg, 0.024 mmol, 38 %). m.p. 173-174°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.56 (s, 2H, 2 PyrC*H*-N), 9.33 (d, 2H, *J* = 6.0 Hz, 2 PyrC*H*-N), 9.10 (d, 2H, *J* = 8.0 Hz, 2 PyrC*H*-C), 8.38 (t, 2H, *J* = 6.0 + 8.0 Hz, 2 PyrC*H*), 7.17 (s,

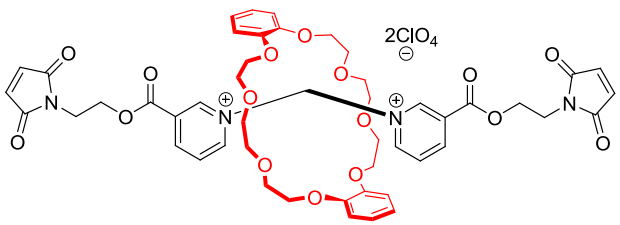
2H, $N^+CH_2N^+$), 6.50 (s, 4H, 2 C*H*=C*H*), 5.09 (s, 4H, 4 C*H*O), 4.54 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 3.84 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N), 2.88 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.5 (imide *C*=O), 159.9 (*C*OO), 148.9 (Pyr*C*H), 148.3 (Pyr*C*H), 146.6 (Pyr*C*H), 135.9 (*C*H=*C*H), 131.2 (Ar*C*), 129.5 (Pyr*C*H), 80.4 (*C*HO), 77.5 (CH_2), 62.9 (CH_2CH_2O), 47.0 (*C*HCO), 36.5 (CH_2CH_2N); IR ν cm^{-1} 3079 (saturated C-H), 1692 (ester and imide C=O), 1077 (ClO_4).

2.77



2.76 (20 mg, 0.024 mmol) heated at 80˚C in a solution of acetonitrile and propionitrile under microwave irradiation (150 W, 110˚C, 3h) to give a beige precipitate, filtered and used without further purification (8 mg, 0.011 mmol, 46 %). ^1H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.57 (s, 2H, 2 PyrC*H*-N), 9.31 (d, 2H, *J* = 6.0 Hz, 2 PyrC*H*-N), 9.11 (d, 2H, *J* = 8.0 Hz, 2 PyrC*H*-C), 8.40 (dd, 2H, *J* = 6.0 + 8.0 Hz, 2 PyrC*H*), 7.21 (s, 2H, $N^+CH_2N^+$), 6.79 (s, 4H, 2 C*H*=C*H*), 4.50 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 3.88 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N).

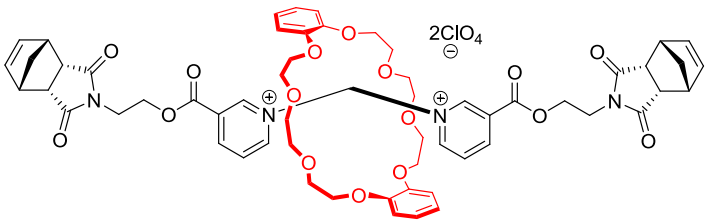
2.78



Thread **2.77** (8 mg, 0.011 mmol) in deuterated acetonitrile, DB24C8 (9.8 mg, 0.022 mmol) was added and pseudorotaxane formation monitored by ^1H NMR. **Pseudorotaxane 2.78** ^1H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.85 (s, 2H, ⊂ 2 PyrC*H*-N), 9.66 (d, 2H, *J* = 6.0 Hz , ⊂ 2 PyrC*H*-N), 8.80 (d, 2H, *J* = 8.0 Hz , ⊂ PyrC*H*-C), 8.20 (dd, 2H, *J* = 6.0 Hz, *J* = 8.0 Hz , ⊂ 2 PyrC*H*), 7.45 (s, 2H, ⊂ $N^+CH_2N^+$), 6.69 (br m, 4H, 4 ⊂ crown ArC*H*), 6.81 (br m, 4H, 4 ⊂

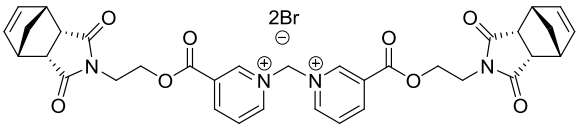
crown ArC*H*), 6.76 (s, 4H, ⊂ 2 C*H*=C*H*), 4.43 (t, 4H, *J* = 5.0 Hz, ⊂ 2 CH_2CH_2O), 4.01 (m, 8H, ⊂ 4 OCH_2), 3.83 (t, 4H, *J* = 5.0 Hz, ⊂ 2 CH_2CH_2N), 3.72-3.70 (m, 8H, ⊂ 4 OCH_2), 3.41 (m, 8H, ⊂ 4 OCH_2). Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2).

2.02



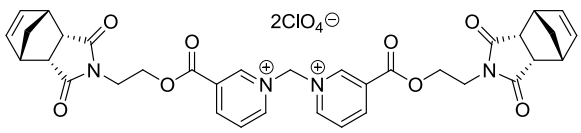
To a solution of pseudorotaxane **2.78** in acetonitrile, freshly cracked cyclopentadiene (0.1 mL, excess) was added. After 5 minutes, the solvent and excess cyclopentadiene were removed *in vacuo* to provide the rotaxane. The rotaxane was isolated by dissolving in acetonitrile and precipitating out the pure material with EtOAc (8 mg, 0.006 mmol, 57%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.88 (s, 2H, 2 PyrC*H*-N), 9.69 (d, 2H, *J* = 6.0 Hz, ⊂ 2 PyrC*H*-N), 8.79 (d, 2H, *J* = 8.0 Hz, ⊂ 2 PyrC*H*-C), 8.22 (dd, 2H, *J* = 8.0 + 6.0 Hz, ⊂ 2 PyrC*H*), 7.47 (s, 1H, ⊂ $N^+CH_2N^+$), 6.85 (s, 8H, ⊂ 8 crown ArC*H*), 5.98 (s, 4H, ⊂ 2 C*H*=C*H*), 4.32 (t, 4H, *J* = 5.5 Hz, ⊂ 2 CH_2CH_2O), 4.04 (m, 8H, ⊂ 4 OCH_2), 3.73 (m, 8H, ⊂ 4 OCH_2), 3.66 (t, 4H, *J* = 5.5 Hz, ⊂ 2 CH_2CH_2N), 3.60 (s, 4H, ⊂ 4 C*H*O), 3.43 (s, 4H, ⊂ 4 C*H*CH_2), 3.49 (m, 8H, ⊂ 4 OCH_2), 1.61 (d, 2H, *J* = 8.5 Hz, ⊂ C*H*H), 1.56 (d, 2H, *J* = 8.5 Hz, ⊂ CH*H*); HRMS (ESI$^+$): *m/z* found, 543.2285 calc for $C_{59}H_{66}N_4O_{16}$ 543.2287 [**2.02**-$2ClO_4$]$^{2+}$.

2.79



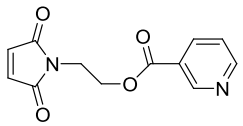
Compound **2.70** (500 mg, 1.6 mmol) was dissolved in dibromomethane (3 mL, excess) and DMF (1.5 mL) and heated to 60˚C for 48 h. The solution was cooled and EtOAc (10 mL) was added to form a precipitate (150 mg, 0.208 mmol, 13%). ^{1}H NMR (400 MHz, 298 K, D_2O) δ_H 9.98 (s, 2H, PyrC*H*-N), 9.69 (d, 2H, *J* = 6.0 Hz, PyrC*H*-N), 9.30 (d, 2H, *J* = 8.0 Hz, PyrC*H*), 8.56 (dd, 2H, *J* = 8.0 + 6.0 Hz, PyrC*H*), 7.68 (s, 2H, $N^+CH_2N^+$), 6.00 (s, 4H, 2 C*H*=C*H*), 4.54 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 3.87 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N), 3.50 (s, 4H, 4 C*H*CO), 3.30 (s, 4H, 4 C*H*CH_2), 1.70 (d, 2H, *J* = 8.5 Hz, C*H*H), 1.63 (d, 2H, *J* = 8.5 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, D_2O) δ_C 181.4 (imide *C*=O), 161.3 (*C*OO), 149.7 (Pyr*C*H), 148.7 (Pyr*C*H), 148.6 (Pyr*C*H), 134.3 (*C*H=*C*H), 131.6 (Ar*C*), 130.2 (Pyr*C*H), 64.7 (CH_2CH_2O), 52.2 (bridgehead CH_2), 45.8 (*C*HCH_2*C*H), 44.8 (*C*HCO), 37.1 (CH_2CH_2N). Central CH_2 not observed in pendant ^{13}C.

2.80



Dibromide thread **2.79** (100 mg, 0.13 mmol) was dissolved in the minimum amount of water. A saturated solution of sodium perchlorate (1 mL) was added to the solution allowed to precipitate, filtered and washed with water to provide white crystals (30 mg, 0.038 mmol, 29%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.60 (s, 2H, PyrC*H*-N), 9.34 (d, 2H, *J* = 6.0 Hz, PyrC*H*), 9.12 (d, 2H, *J* = 8.0 Hz, PyrC*H*), 8.43 (dd, 2H, *J* = 8.0 + 6.0 Hz, PyrC*H*), 7.21 (s, 2H, CH_2), 5.98 (s, 4H, 2 C*H*=C*H*), 4.39 (t, 4H, *J* = 5.0 Hz, CH_2CH_2O), 3.70 (t, 4H, *J* = 5.0 Hz, CH_2CH_2N), 3.30 (br s, 4H, 4 C*H*CO), 3.24 (br s, 4H, 4 C*H*CH_2), 1.16 (d, 2H, *J* = 8.5 Hz, 2 C*H*H), 1.57 (d, 2H, *J* = 8.5 Hz, 2 CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 177.7 (imide *C*=O), 159.5 (*C*OO), 149.1 (Ar*C*H), 148.1 (Ar*C*H), 146.8 (Ar*C*H), 134.1 (*C*H=*C*H), 131.5 (Ar*C*), 129.8 (Ar*C*H), 78.2 (CH_2), 64.1 (CH_2CH_2O), 51.5 (bridgehead CH_2), 45.4 (*C*HCH_2), 44.4 (*C*HCO), 36.2 (CH_2CH_2N); HRMS (ESI$^+$): *m/z* found 319.1182 calc for $C_{35}H_{34}N_4O_8$ 319.1183 [**2.80**-2ClO_4]$^{2+}$.

2.81



Compound **2.63** (0.5 g, 1.6 mmol) was heated in toluene at 90˚C for 5 days. The reaction was monitored by TLC (40:5:1; EtOAc:MeOH:H_2O). The solvent was removed *in vacuo* to provide a beige solid (315 mg, 1.28 mmol, 80%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 9.15 (s, 1H, PyrC*H*-N), 8.76 (d, 1H, *J* = 5.0 Hz, PyrC*H*), 8.25 (d, 1H, *J* = 8.0 Hz, PyrC*H*), 7.38 (dd, 1H, *J* = 5.0 + 8.0 Hz, PyrC*H*), 6.74 (s, 2H, C*H*=C*H*), 4.49 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.95 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 170.4 (imide *C*=O), 165.1 (*C*OO), 153.6 (Pyr*C*H), 151.1 (Pyr*C*H), 137.2 (Pyr*C*H), 134.3 (*C*H=*C*H), 125.6 (Ar*C*), 123.4 (Pyr*C*H), 62.6 (CH_2CH_2O), 36.8 (CH_2CH_2N); MS (ESI$^+$): *m/z* 247.0 [**2.82**+H]$^+$.

Chapter 3 - Synthesis of [n]Rotaxanes using CuAAC 'Click Chemistry' and the Diels-Alder Approach to 'Threading followed by Stoppering'.

3. Synopsis

In Chapter 2 the use of incorporating our Diels-Alder 'stopper' to synthesise rotaxanes in a 'threading followed by stoppering' protocol has been discussed with a variety of binding motifs. Thus far this method has been used on existing templates such as the bispyridinium and dibenzylammonium binding templates and on the new perimidine benzimidazole template. A novel ammonium template with a triazole incorporated into the binding site (Figure 3.1) has now been developed. The presence of the triazole enhances the binding between the axle and macrocycle in comparison to a simple dibenzylammonium template.

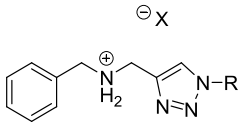


Figure 3.1 Benyzlammonium triazole binding motif.

Using this template a variety of [n]pseudorotaxanes and [n]rotaxanes have been synthesised. These were again created via the Diels-Alder 'threading followed by stoppering' protocol using click chemistry to incorporate the masked maleimide into the axle. Rotaxanes were also successfully synthesised simply using 'CuAAC' click conditions reported by Coutrot[106] *for stopper formation providing [n]rotaxanes with the new triazole binding motif in the axle.*

3.1 Introduction

3.1.1 The Cu(I)-Catalysed Terminal Alkyne-Azide 1,3-Dipolar Cycloaddition (CuAAC Reaction).

Huisgen[146-148] first investigated 1,3-dipolar cycloadditions in the early 60's between 1,3 dipolar compounds and a dipolarophile in order to synthesise five membered rings. Sharpless[149] and Meldal[150] further developed this idea using copper(I)-catalysed conditions more famously known as 'CuAAC click chemistry', which forms a triazole unit regioselectively between the two components. The 'click chemistry' concept is now widely used in synthetic chemistry to fabricate a wide variety of molecules as it is an effective way for the efficient coupling of two components. The reaction is commonly performed using alcohol and water solvent systems with a catalytic system generated from a Cu(II) salt and a reducing agent which in many cases is sodium ascorbate. This generates the required Cu(I) salt in situ catalysing the cycloaddition. The postulated catalytic cycle for this reaction is shown in Figure 3.2.

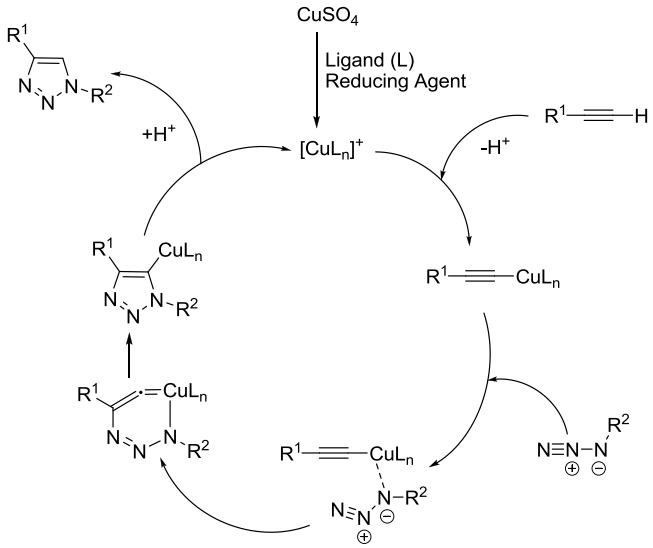


Figure 3.2 Hypothesized Catalytic Cycle for 'CuAAC' Reaction.[151]

The reactive intermediate in this mechanism is still under investigation. DFT calculation suggest a second copper centre is required for the reaction to proceed where the second copper forms a π-activated Cu acetylene.[152] Recently Heaney proposed the reaction

progresses *via* a dinuclear alkynylcopper(I) ladderane complex.[153] Further postulated transition states includes the alkyne and azide co-ordinated by different copper atoms.[154-155] There is the possibility that all of these pathways can feature in the 'CuAAC' mechanism with the transition state depending on a variety of factors including choice of solvents, ligands and reactants playing a part.

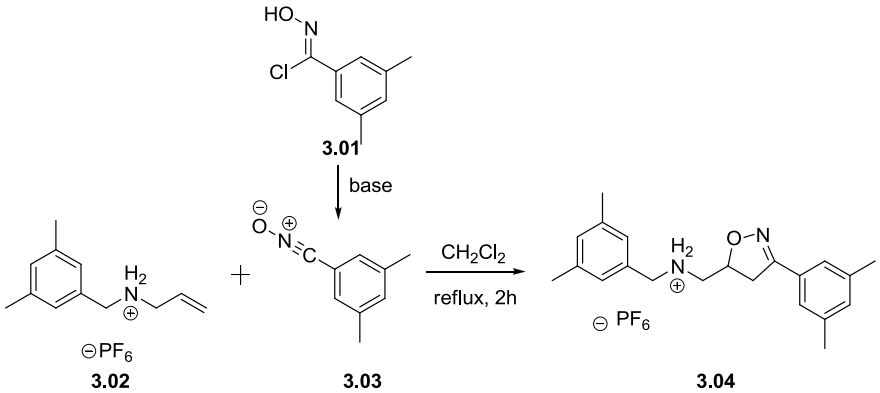
3.1.2 'CuAAC' in Rotaxane Formation

There have been several examples of using the 'CuAAC click' reaction to attach the stopper groups in the synthesis of rotaxanes. Coutrot *et al*,[106,156] have used this to synthesise a mannosyl [2]rotaxane molecular machine as well as a dimannosyl[c2]daisy chain molecular machine.[156] Stoddart *et al*[157] have also used 'CuAAC click chemistry' towards the synthesis of molecular machines. Early reports by Mock[158-159] to facilitate the 1,3 dipolar cycloaddition of an ammonium functionalised azide and alkyne by confinement inside a macrocycle cavity have also been realised to synthesise [2]rotaxanes. It was found in this case that cucurbituril can enhance the reaction rate by acting as a catalyst providing the regiospecific triazole. Synthesis of rotaxanes consisting of multiple components can prove challenging but using 'CuAAC click chemistry' has several advantages.

Click chemistry is not only useful towards the synthesis of threads; it has also shown potential to be used to generate triazole recognition sites on axles in order to bind with crown macrocycles. The Coutrot group were one of the first to show an alkylated triazole acting as a recognition site for a crown macrocycle.[160] This group has synthesised molecular machines with the macrocycle shuttling between an alkylated triazole and an ammonium ion in a pH dependent manner. Li *et al*[161] have also incorporated a triazole as a station for a molecular machine. It is thought that for the triazole to act as a recognition site for a crown like macrocycle it must be positively charged. When the ammonium ion template of the thread was neutralised, the macrocycle shuttled across to the neutral triazole station where it

participates in hydrogen bonding. The neutral triazole has a weaker interaction with the crown than the ammonium ion but better than the amine.

Takata[107] has also used the click concept in order to synthesise rotaxanes. This time taking the nitrile *N*-oxide as a replacement for the azide, they were able to perform click reactions not only with alkynes but also alkenes under mild conditions (Scheme 3.1). They successfully used this method to end cap several pseudorotaxanes in high yields as well as in the synthesis of a molecular shuttle.



Scheme 3.1 Synthesis of the nitrile *N*-oxide thread for rotaxane synthesis.[107]

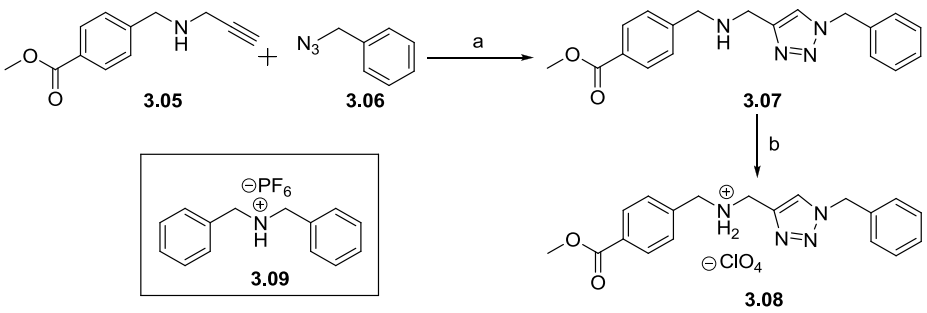
3.2 Results and Discussion

3.2.1 Synthesis of Pseudorotaxanes Using 'CuAAC Click Chemistry'.

As discussed previously, there have already been examples of using triazole subunits incorporated into ammonium salt threads for the synthesis of rotaxanes and we have seen Coutrot[156] use this approach to synthesise molecular shuttles. Development of a 'clickable' unit containing a rotaxane forming template (ammonium ion) using the Diels-Alder gate could transform any azide into a suitable thread using the orthogonality of 'CuAAC'.

The effect of incorporating a triazole subunit adjacent to the ammonium ion was investigated. The benzyl azide, **3.06** was synthesised from benzyl chloride and sodium azide in EtOH. Reacting with alkyne **3.05** using 'CuAAC click chemistry' with $CuSO_4.5H_2O$ and a sodium ascorbate as reducing agent was then executed providing the neutral thread (**3.07**)

with a secondary amine and a triazole in the vicinity of the binding motif. This was then converted to the ClO_4^- salt on the addition of $HClO_4$ (**3.08**) as shown in Scheme 3.2 providing the new binding template that could interact with crown ether type macrocycles. Appropriate shifts of the benzyl CH_2's was observed in ^{1}H NMR and an IR stretching frequency at 1060 cm^{-1} show the amine has been converted to the ClO_4^- salt.



Scheme 3.2 Reagents and conditions: a) EtOH, THF, H_2O, $CuSO_4.5H_2O$, Sodium Ascorbate (NaAsc), RT, 24h, 93%; b) MeOH, $HClO_4$, RT, 54%.

The thread **3.08** was then used as a binding motif for DB24C8 to generate pseudorotaxane **3.10** (Figure 3.3). Pseudorotaxane formation was observed by ^{1}H NMR and ESI-MS with the mass ion at 785.3 corresponding to [**3.10**-ClO_4]$^+$. Equimolar amounts of the thread and DB24C8 were added together at a 2 mmol concentration to provide a binding constant of 820 M^{-1} measured *via* a single point method.[129] The binding constant for the dibenzyl ammonium thread (**3.09**) with DB24C8 at 2 mmol is reported as 237 M^{-1}.[162] It was pleasing to find that this simple click derived ammonium ion thread gives almost a fourfold increase in the binding interaction with DB24C8 in comparison to the dibenzyl ammonium motif.

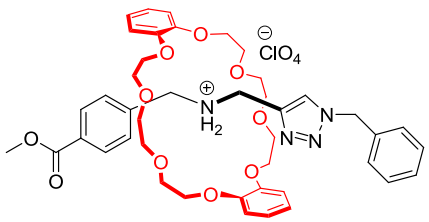
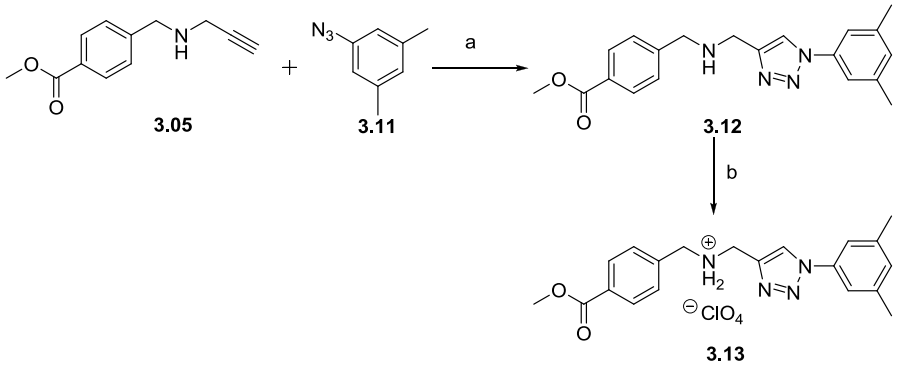


Figure 3.3 [2]pseudorotaxane 3.10.

Following the indication that incorporating triazoles into these threads increases binding affinity, the effect of having the triazole directly linked to the benzene ring was investigated

as it would then be conjugated with the aromatic system. This binding motif was created from propargyl amine **3.05** and 3,5-dimethyl phenyl azide (**3.11**), its formation was supported by ^{1}H and ^{13}C NMR and HRMS with peak seen at *m/z* 351.1808 corresponding with the [**3.12**+H]$^{+}$ ion. The neutral thread (**3.12**) was converted to its ClO_4^- salt using $HClO_4$ (**3.13**) Scheme 3.3.



Scheme 3.3 Reagents and conditions: a) EtOH, THF, H_2O, $CuSO_4.5H_2O$, NaAsc, RT, 24h, 45%; b) MeOH, $HClO_4$, 100%.

Addition of DB24C8 in deuterated acetonitrile provided pseudorotaxane **3.14 (**Figure 3.4) as well as unbound thread **3.13** and unbound DB24C8. Pseudorotaxane **3.14** was characterised by both ^{1}H NMR and HRMS with the mass ion observed at *m/z* 799.3934 relating to [**3.14**-ClO_4]$^{+}$. The binding constant was calculated from equimolar amounts of thread and crown at 2 mmol concentration *via* the single point method.[129] For this complex it was found to be 1060 M^{-1} giving a 20% increase in binding compared to the un-conjugated triazole thread (**3.08**).

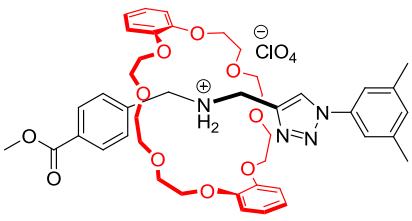
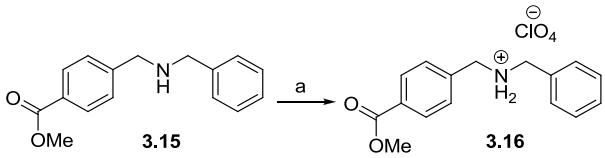


Figure 3.4 [2]pseudorotaxane **3.14**.

A mono ester functionalised dibenzylammonium ClO_4^- thread **3.16** (Scheme 3.4) was also synthesised as a better reference model for a truer comparison of binding constants with

these 'click' threads. Having an electron withdrawing group attached to the aromatic rings has previously been shown to enhance binding between DB24C8 and axles so the unfunctionalised dibenzylammonium thread **3.09** is not a fair representation of the enhancement in binding.[46]



Scheme 3.4 Synthesis of compound **3.16**. Reagents and conditions a) CH_2Cl_2, $HClO_4$, RT, 40%.

The binding constant was measured between perchlorate thread **3.16** and DB24C8 at 2 mmol with one equivalent of DB24C8 and was found to be 687 M^{-1}. The [2]pseudorotaxane **3.17** formed is shown in Figure 3.5.

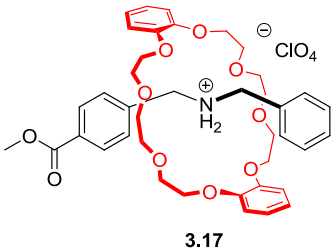


Figure 3.5 [2]pseudorotaxane **3.17**.

The binding value observed was lower than that of the benzyl azide derived thread **3.08** and phenyl azide derived thread **3.13** again validating that the presence of the triazole does in fact enhance the binding interaction between axle and the crown ether macrocycle. Binding constant results for all pseudorotaxanes are shown in Table 3.1. Enhancement in the binding interaction is thought to be a result of improved hydrogen bonding between the two interlocked components. The triazole may increase the CH acidity of the adjacent CH_2 and additionally the triazole hydrogen is able to take part in hydrogen bonding with DB24C8 oxygens. It could also be postulated that incorporating this five membered aromatic ring in the binding site provides a better 'fit' in the cavity of the crown ether. Conjugating the two aromatic systems in the case of the phenyl azide derived thread **3.13** would provide a more

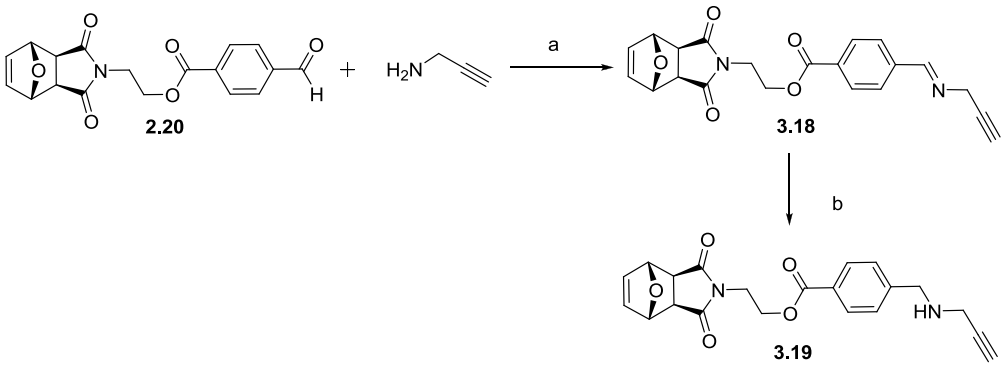
electron deficient triazole ring increasing the π stacking interaction with the catechol rings of the crown and making the triazole CH a better H bond donor.

Pseudorotaxane	**Binding Constant in Acetonitrile at 2 mmol concentration (M^{-1})**
Dibenzylammonium methyl ester **3.16**	687
Benzyl azide derived thread **3.08**	820
Phenyl azide derived thread **3.13**	1060

Table 3.1 Binding constant comparison of dibenzylammonium methyl ester thread **3.16**, click threads **3.08** and **3.13** (errors estimated at < 10%).

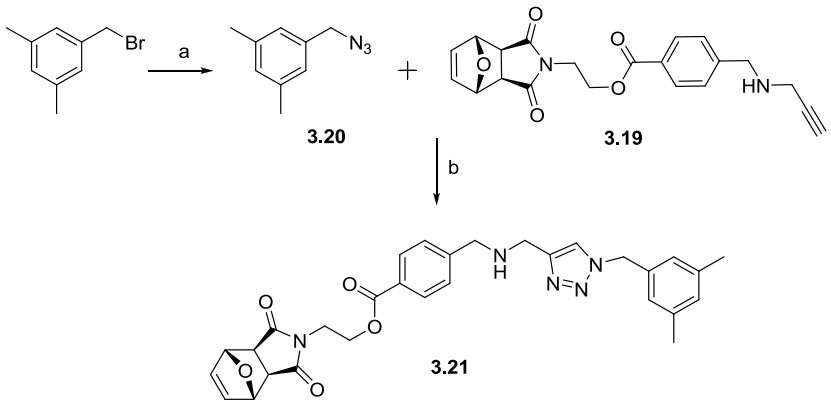
3.3 Synthesis of Rotaxanes Using 'CuAAC Click Chemistry' and the Diels-Alder Reaction

Having shown the advantages of the triazole derived threads, incorporating these templates into rotaxanes using the Diels-Alder 'threading followed by stoppering' approach was investigated. Synthesis of the rotaxane was carried out by reacting ester **2.20** with propargyl amine providing imine **3.18**. Reduction of the imine **3.18** was first attempted using sodium borohydride but this lead to a mixture of products and it was believed that some over reduction occurred, reducing one of the carbonyls of the imide.[163] Several sets of reaction conditions using sodium borohydride were attempted but reduction of the carbonyl was unavoidable. Using sodium cyanoborohydride overcame this predicament and after a few hours TLC analysis showed the disappearance of **3.18** and a new single spot. The amine (**3.19**) was isolated in a 76% yield with no evidence of side products (Scheme 3.5).



Scheme 3.5 Reagents and conditions: a) MeOH, RT, 24h, 81%; b) MeOH, $NaBH_3CN$, HOAc, RT, 1h, 76%.

It was then required to attach a bulky stopper forming group to the propargyl end of the axle using the 'CuAAC' approach. The bulky stopper group was synthesised from 3,5-dimethylbenzybromide with sodium azide to provide the resulting azide **3.20**. The propargyl (**3.19**) and azide (**3.20**) were reacted together using 'CuAAC click chemistry' conditions with $CuSO_4.5H_2O$ and sodium ascorbate in a mixture of *tert*-butanol, THF and water to provide the neutral thread **3.21** (Scheme 3.6) in a 56% yield.

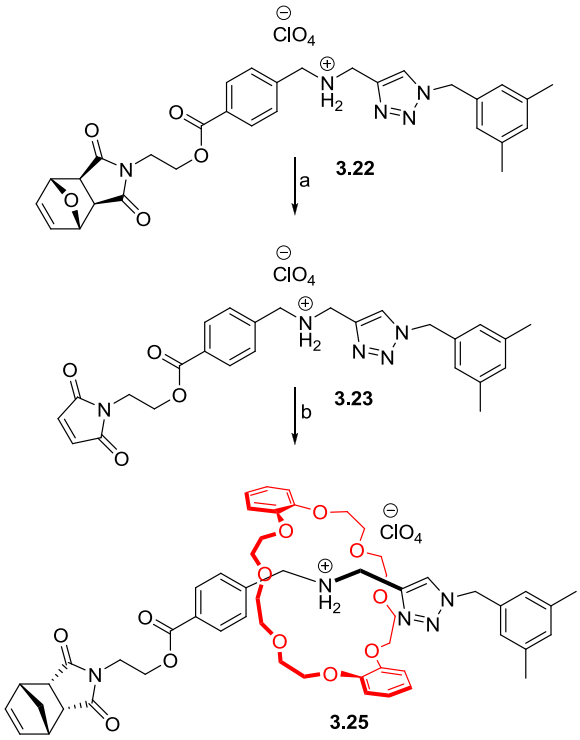


Scheme 3.6 Reagents and conditions: a) EtOH, NaN_3, RT, 24h, 65%; b) *tert*-Butanol, THF, H_2O, $CuSO_4.5H_2O$, NaAsc, RT, 24h, 56%.

Conversion to an ammonium salt was required in order for the macrocycle to bind with the axle. The neutral thread (**3.21**) was converted into ClO_4^- salt **3.22** by treatment with $HClO_4$ and the retro Diels-Alder reaction was carried out to open the maleimide gate so as to allow the macrocycle to thread onto the axle. Microwave heating was used to induce the retro Diels-Alder reaction on the ClO_4^- salt thread (**3.22**) in acetonitrile.

Treatment of a solution of maleimide thread (**3.23**) with two equivalents of DB24C8 in deuterated acetonitrile produced pseudorotaxane **3.24**. The excess of crown is required in order to push the equilibrium in favour of pseudorotaxane formation as monitored by ^1H NMR and confirmation of pseudorotaxane formation observed by HRMS with the mass ion found at 922.4253 relating to the [**3.24**-ClO_4]$^+$ species. The final step to generate the rotaxane (**3.25**) required a few drops of freshly distilled cyclopentadiene and the excess was removed *in vacuo* giving only the kinetic *endo* isomer.

Solvent choice was again important to consider when creating a pseudorotaxane. Acetonitrile is commonly used as it can dissolve the ionic thread easily, but is not so polar as to it interfere with the weak interactions between the crown and thread and this was again the solvent used in the synthesis of pseudorotaxanes and rotaxanes.[61]

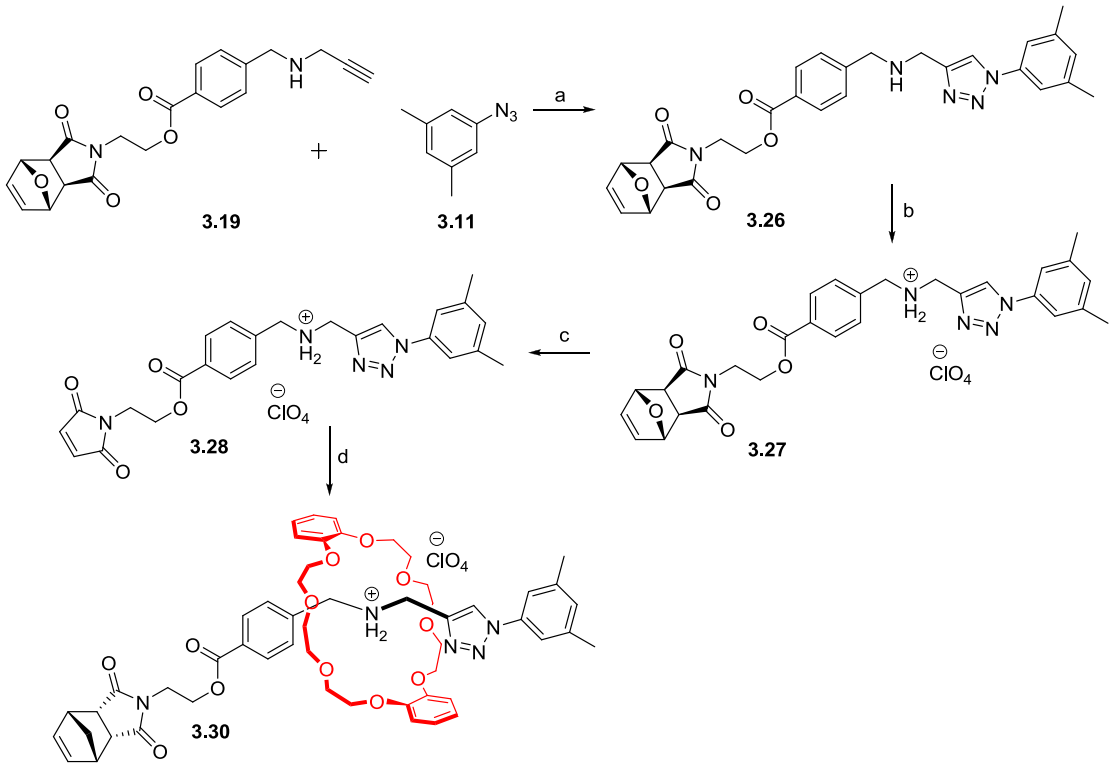


Scheme 3.7 Reagents and conditions: a) CH_3CN, MW, 110˚C, 3h, 86%; b) i) CD_3CN, DB24C8 (excess), RT, 48h; ii) CH_3CN, cyclopentadiene, 37%.

A similar approach provided the rotaxane formed from the thread derived from phenyl azide synthesised using the same reaction conditions. Reacting azide **3.11** with the propargyl amine **3.19** under 'CuAAC click chemistry' conditions to produce thread **3.26** was carried out. Conversion to ClO_4^- salt **3.27** by treatment with $HClO_4$ gave the resulting ammonium imide in a 68% yield and the retro Diels-Alder conducted under microwave conditions (Scheme 3.8) opened the maleimide 'gate' to give thread **3.28**.

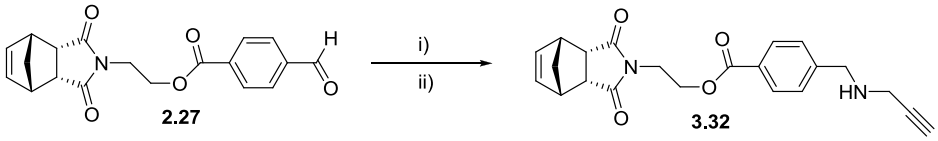
The pseudorotaxane **3.29** was assembled using two equivalents of DB24C8 and rotaxane **3.30** was generated on addition of freshly cracked cyclopentadiene. Excess cyclopentadiene was removed *in vacuo* and following purification, rotaxane **3.30** was isolated in a 62% yield. The characteristic shifts in the ^{1}H NMR spectra in comparison to the free thread **3.36** and

DB24C8 indicated rotaxane formation with additional confirmation from HRMS finding a peak at 974.4550 corresponding to the expected [**3.30**-ClO_4]$^+$. IR spectroscopy of the rotaxane shows significant peaks at 1697 cm^{-1} indicating the presence of carbonyl groups and 1093 cm^{-1} relating to the ClO_4.



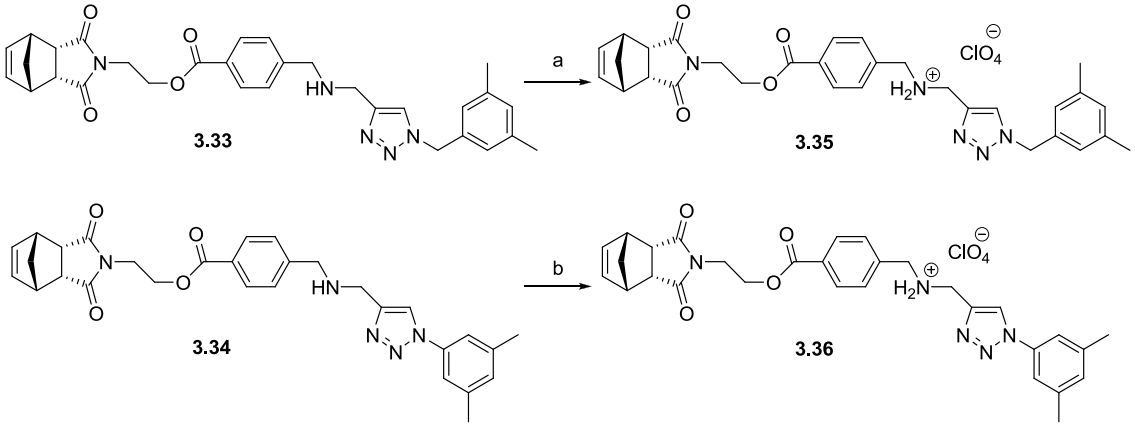
Scheme 3.8 Reagents and conditions: a) *tert*-Butanol, THF, H_2O, $CuSO_4.5H_2O$, NaAsc, RT, 24h, 80%; b) CH_2Cl_2, $HClO_4$, RT, 68%; c) CH_3CN, MW, 110 ˚C, 3h, 92%; d) i) CD_3CN, DB24C8 (excess), 48 h; ii) CH_3CN, cyclopentadiene, 62%.

The comparison ClO_4^- threads were synthesised starting with the *endo* adduct of maleic anhydride and cyclopentadiene (**2.14**). Reacting with ethanolamine gave intermediate alcohol **2.15** and an esterification with 4-carboxybenzaldehyde formed the functionalised aldehyde **2.27**. Synthesis of the imine (**3.31**) and reduction to the amine (**3.32**) were synthesised according to the same procedures as the furan alkyne **3.19** counterpart and this is shown in Scheme 3.9.



Scheme 3.9 Reagents and conditions: i) MeOH, propargyl amine, RT, 24h; ii) $NaBH_3CN$, HOAc, 24h, 85%**.**

The new propargyl compound **3.32** was reacted with the azides **3.20** and **3.11** under 'CuAAC' click conditions to provide neutral threads **3.33** and **3.34**. Conversion to the ClO_4^- salt using $HClO_4$ gave threads **3.35** and **3.36** in 59% and 66% yields respectively (Scheme 3.10).



Scheme 3.10 Reagents and conditions: a) $HClO_4$, RT, 59%; b) $HClO_4$, RT, 66%.

Comparison of the ^{1}H NMR of rotaxane (**3.30**), thread (**3.36**) and DB24C8 is shown in Figure 3.6. The aromatic hydrogens of the thread are shifted upfield due to the shielding effect from the close proximity of the aromatic ring currents of the benzo group of DB24C8. A reciprocal interaction with the π systems of the thread means the crown aromatic hydrogens are also shifted upfield. The crown ether CH_2's are recorded as complex multiplets as the interlocked crown now has two distinct faces due to the asymmetry of the thread. Both shielding and desheilding effects are observed on these protons. The $CH_2NH_2^+CH_2$ protons of the thread show a shift downfield as they are hydrogen bonding with the crown ether oxygen's. They also become a complicated multiplet due to coupling with the NH_2^+, a further indication of being encompassed by the crown ether macrocycle.[32] The shift of protons associated with the imide stopper portion of the thread are relatively

unaffected in the rotaxane indicating the DB24C8 macrocycle is situated predominantly over the ammonium portion of the thread.

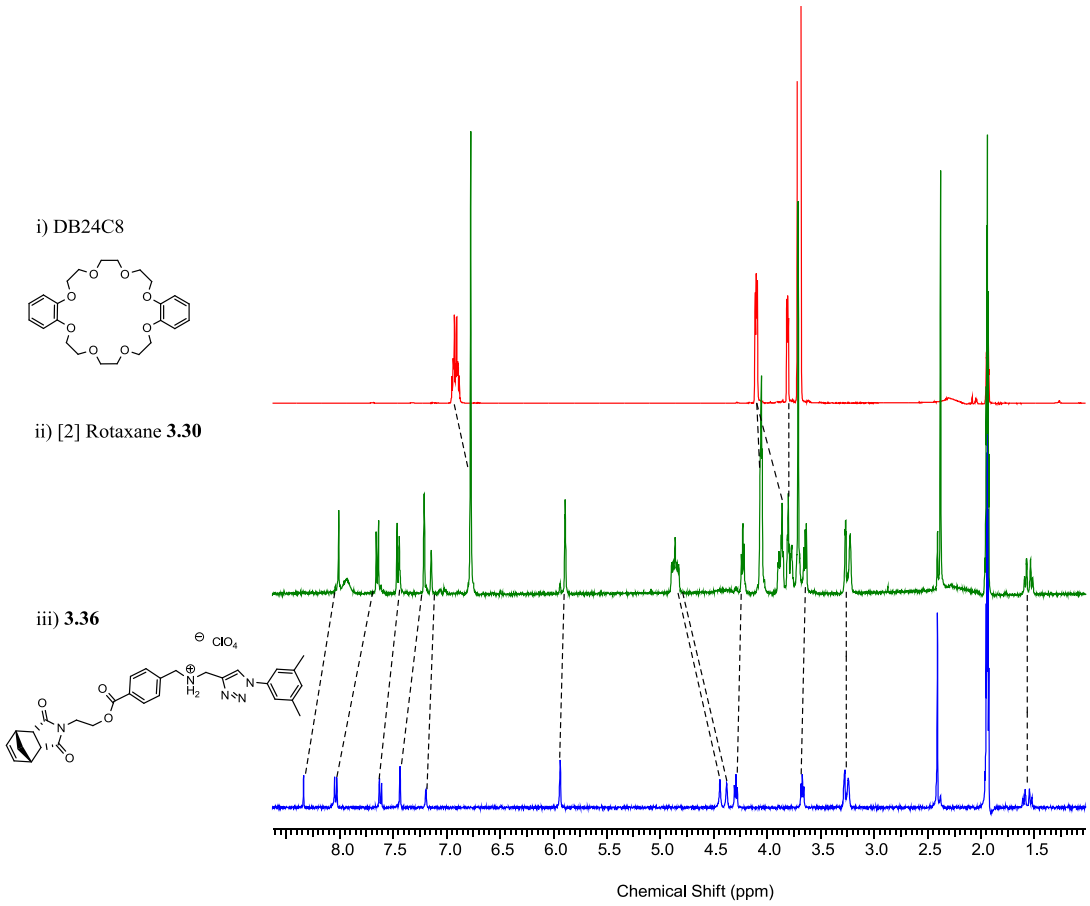
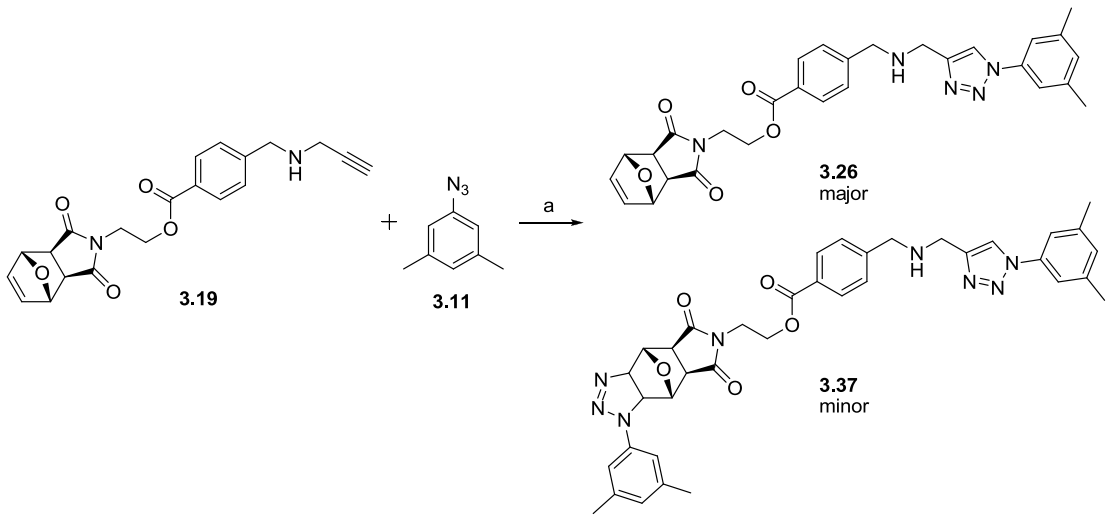


Figure 3.6 ^{1}H NMR spectra (400 MHz, CD_3CN, 300K) stacking plot of; i) DB24C8; ii) [2]Rotaxane **3.30** and iii) Comparison thread **3.36**.

When first synthesising the neutral axles **3.21** and **3.26** *via* 'CuAAC click chemistry' the yields produced from the reaction were very low. 'CuAAC click chemistry' is reported to be high yielding without difficult purification steps so a detailed study of the reaction was undertaken in an attempt to improve the yield and gain information as to why yields were low. The investigation was primarily performed on the conjugated triazole thread **3.26**. Using a variety of solvent systems and with varying equivalents of catalyst and reagents the yield of click thread **3.26** was successfully improved from 33% to 80% by using an excess of propargyl amine **3.19**.

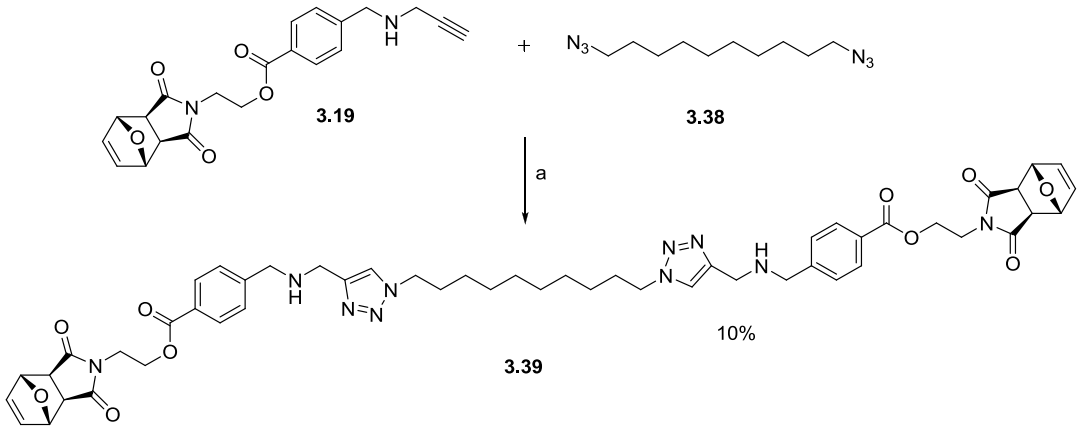
During this investigation it was found that an extra set of peaks were observed in the ^{1}H NMR indicating there was a side reaction occurring. Isolation and characterisation of this new product was achieved *via* column chromatography. It became apparent that the azide **3.11** was not only reacting with the propargyl moiety of compound **3.19** but it was also reacting with the strained double bond situated on the [2.2.1] bridged system of the protected maleimide shown in Scheme 3.11. A similar reaction has previously been reported by Reymond, but in this case it is suggested heating is required for the reaction to occur.[164-165] However Philp[166] has also reported the reaction occurring at 30˚C in $CDCl_3$ between an azide and a maleimide. From investigation with a variety of azides and [2.2.1] bridge imide systems this reaction was found to be occurring at room temperature in $CDCl_3$ both with and without a copper catalyst present. Time periods of up to a month at room temperature were required before the product formation reached 100%. It was possible to overcome this problem, using an excess of the propargyl compound **3.19** and purification *via* column chromatography provided the required thread **3.26** only and no side product **3.37** was observed. So far assigning the relative stereochemistry of the new ring junction of thread **3.37** has not been achieved.



Scheme 3.11 Reagents and conditions: a) *tert*-butanol, THF, H_2O, $CuSO_4.5H_2O$, NaAsc, RT, 24h.

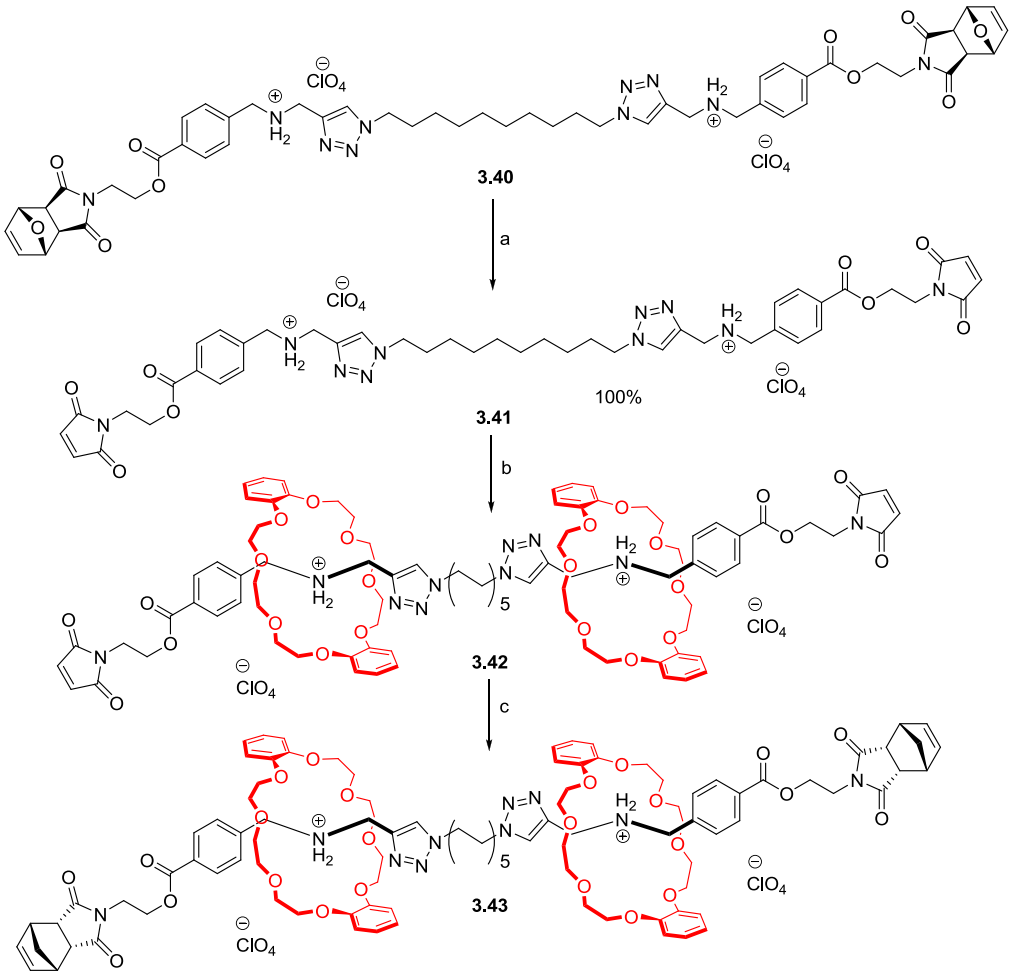
3.4 Synthesis of Higher Order Rotaxanes Using 'CuAAC Click Chemistry'

After showing the successful application of the chemistry to synthesise [2]rotaxanes, the synthesis of higher order rotaxanes was investigated. Taking the propargyl amine compound (**3.17**) with 1,10-diazidodecane **3.38** under 'CuAAC' click conditions, the neutral thread **3.39** with two triazole ammonium binding motifs separated by a C_{10} chain was synthesised (Scheme 3.12). In this case using the previous solvent systems did not provide significant product formation and a two phase solvent system of CH_2Cl_2 and water was required.



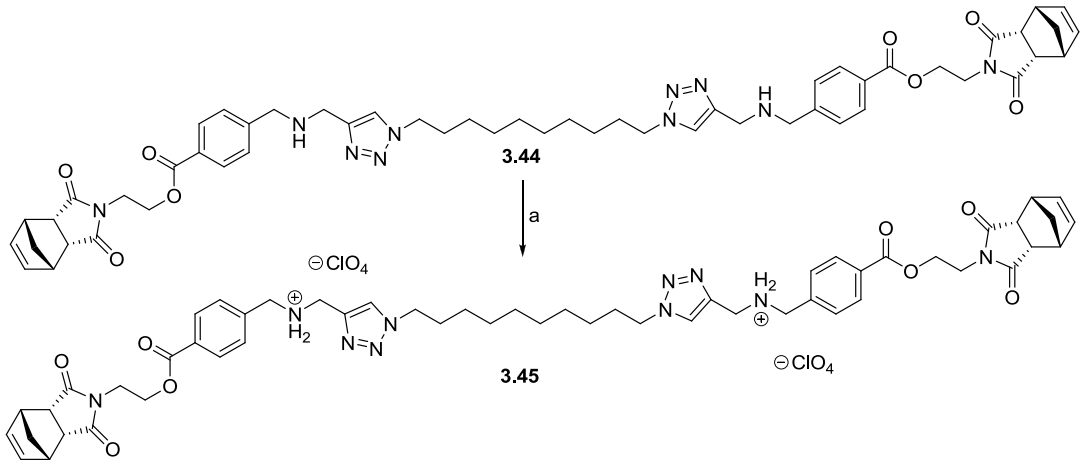
Scheme 3.12 Reagents and conditions: a) CH_2Cl_2, H_2O, $CuSO_4.5H_2O$, NaAsc, RT, 24h, 10%.

The thread was converted to the ClO_4^- salt **3.40** by washing with $HClO_4$ followed by the retro Diels-Alder reaction to deprotect the maleimide under microwave conditions. After following the reaction to completion by TLC, thread **3.41** was obtained in a quantitative yield. The [3]pseudorotaxane **3.42** was synthesised in deuterated acetonitrile this time by adding in four equivalents of DB24C8 to push equilibrium towards [3]pseudorotaxane formation. The threading was followed by ^{1}H NMR until no further change in the spectra was observed. Cyclopentadiene was added to the pseudorotaxane performing the Diels-Alder reaction with the maleimide double bond giving the *endo* Diels-Alder thread and trapping the macrocycles onto the axle. The [3]rotaxane **3.43** was successfully isolated in a 58% yield and the mass ion relating to [**3.43**-2ClO_4]$^{2+}$ was observed at 939.9640 using ESI-HRMS.



Scheme 3.13 Reagents and conditions: a) CH_3CN, MW, 110˚C, 3h, 100%; b) CD_3CN, DB24C8 (4 equiv), 48 h; c) CH_3CN, cyclopentadiene, RT, 58%.

Comparison thread **3.45** was also successfully synthesised from the cyclopentadiene stoppered propargyl amine **3.32**. Reacting with diazide **3.38** provided the neutral thread **3.44** and conversion to the ClO_4^- salt washing with $HClO_4$ gave thread **3.45** in a 30% yield.



Scheme 3.14 Synthesis of comparison thread **3.45**. Reagents and conditions a) CH_2Cl_2, $HClO_4$, 30%

The ^{1}H NMR of the [3]rotaxane **3.43** was carried out and revealed the characteristic shifts for rotaxane formation including the $CH_2NH_2^+CH_2$ shifts upfield in their distinctive splitting pattern.[32] The aromatic protons of both axle and DB24C8 are shifted downfield as a result of shielding. The ethylene oxy units of the crown became complex multiplets as shown in Figure 3.7. Protons associated with the Diels-Alder stopper or the central alkyne chain of the thread remained relatively unaffected indicating the crown ethers are situated over the ammonium ion portions of the axle.

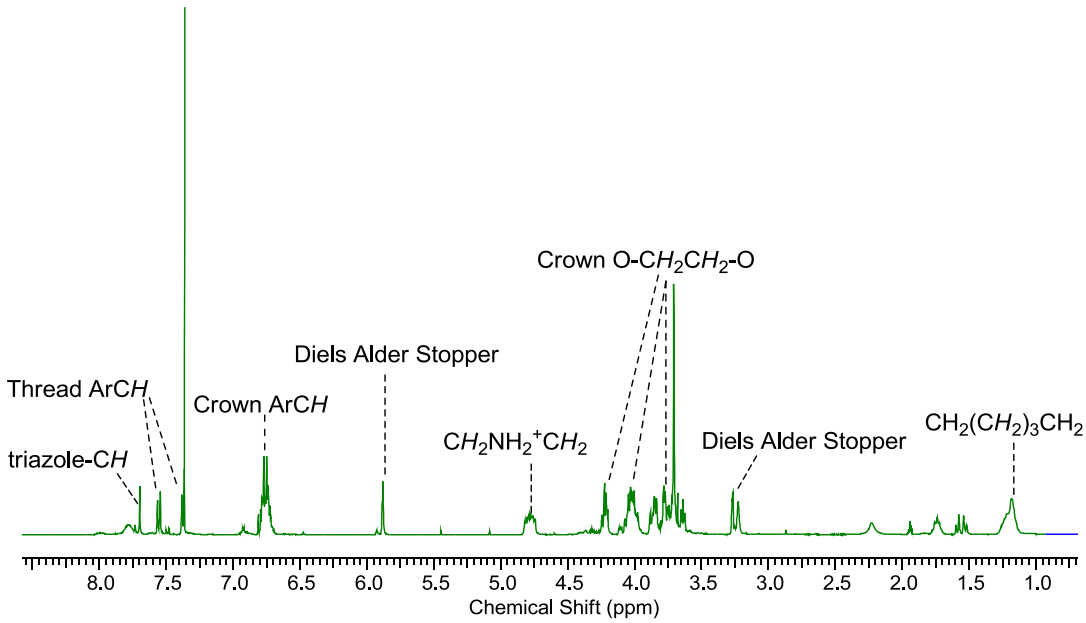
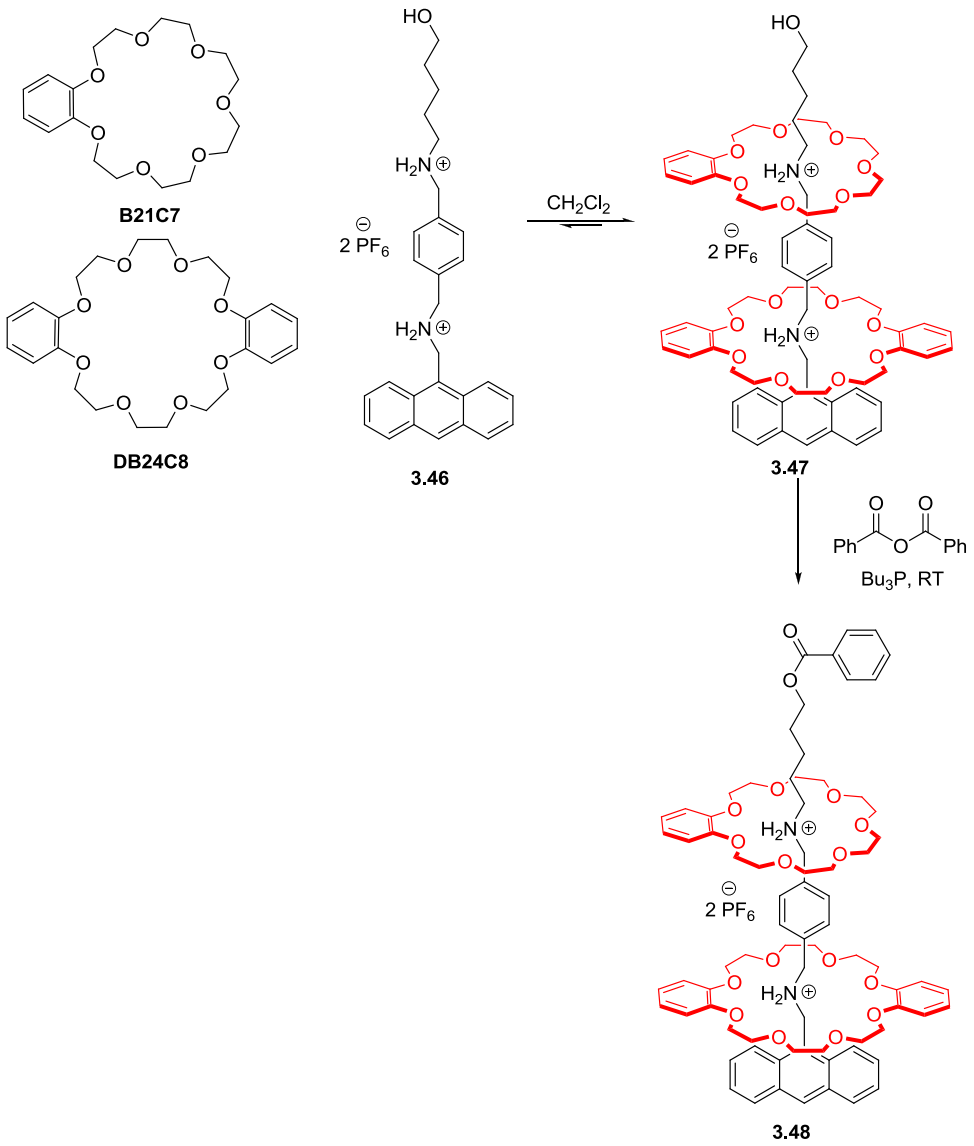


Figure 3.7 ^{1}H NMR spectra (400 MHz, $CDCl_3$, 300K) [3]Rotaxane **3.43**.

3.5 Research into the Synthesis of Multiple Component Rotaxanes

Nature exploits weak supramolecular interactions to construct complex functional systems from simple starting materials. It was shown that by using a combination of 'CuAAC click chemistry' and the Diels-Alder threading followed by stoppering protocol, a [3]rotaxane was assembled. This approach was then used to synthesise a more complex interlocked system consisting of two different binding sites and two different macrocycles. Synthesis of higher order rotaxanes has proved challenging but it has been possible to synthesise rotaxanes with as many as 11 components.[70] There has been some recent work by both Chiu[167] and Schalley[168] where higher order rotaxanes containing different macrocycle components have been assembled by "self sorting". Additionally, Schalley[169] has reported a hetero [3]rotaxane where the stopper size is such that it can only inhibit the dethreading of the smallest crown but the design of the thread is such that this crown/small stopper assembly acts to lock the larger crown on the thread (Scheme 3.15).



Scheme 3.15 Schalley's hetero [3]rotaxane formed in a self sorting protocol.

'CuAAC click chemistry' was then used in order to synthesise a thread providing a template with three potential binding sites for a higher order rotaxane. Synthesis of the following thread (Figure 3.8) which would contain a π-electron rich DNP recognition motif shown to have an excellent binding affinity for the Stoddart[170] $CBPQT^{4+}$ macrocycle **1.09** and two ammonium benzyl triazole units for hydrogen bonding with DB24C8 was attempted. Stopper formation of the terminal maleimide gates with cyclopentadiene will give the [2.2.1] *endo* Diels-Alder adduct. This is unlikely to act as a stopper for the $CBPQT^{4+}$ macrocycle but will trap DB24C8. The crown/Diels-Alder adduct was considered to be a large enough

mechanically interlocked assembly to block the passage of the larger $CBPQT^{4+}$ macrocycle so acting as 'mechanical stoppers'.

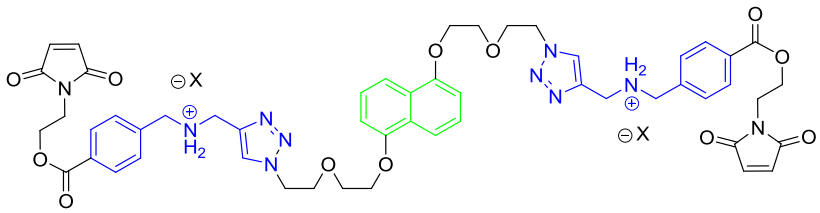
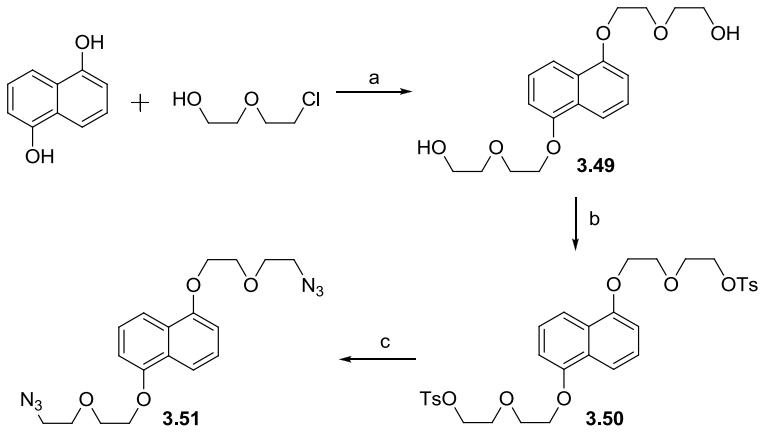


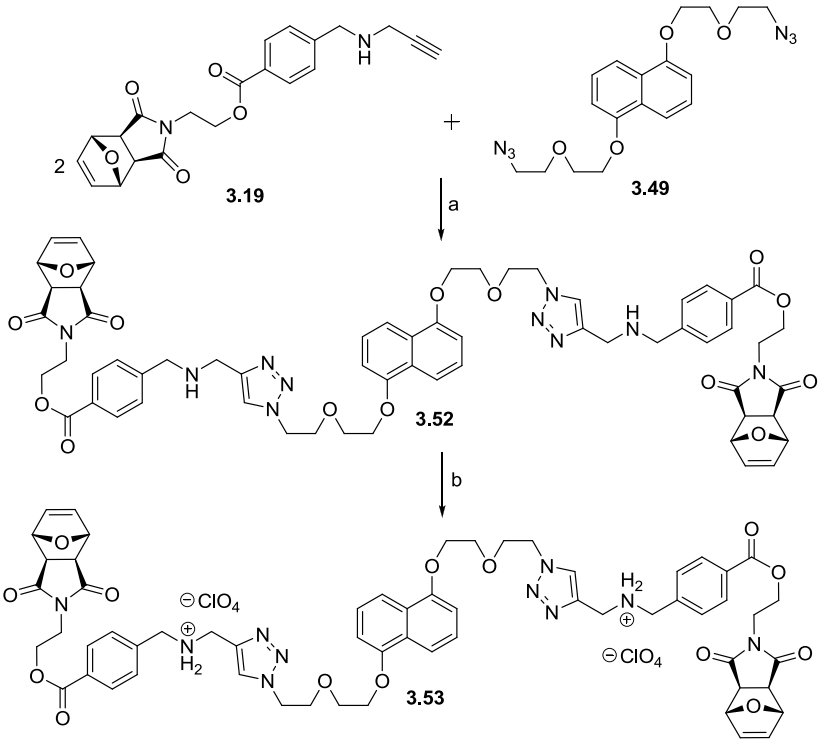
Figure 3.8 Thread with two separate binding sites incorporated.

The synthesis of the thread first started with the *bis* oxy naphthalene core. Naphthalene-1,5-diol was reacted with 2-(2-chloroethoxy)ethanol in acetonitrile with potassium carbonate to produce the diol (**3.49**). Diol **3.49** was converted to the ditosylate in CH_2Cl_2 with tosyl chloride (**3.50**).[171] Finally conversion of the ditosylate to the diazide (**3.51**) was carried out in DMF at 60°C and the product was purified *via* recrystallisation (Scheme 3.16).



Scheme 3.16 Reagents and conditions: a) CH_3CN, K_2CO_3, reflux, 48h, 62%; b) CH_2Cl_2, NEt_3, TsCl, DMAP, 0˚C→RT, 55%; c) DMF, NaN_3, 60˚C, 69%.

The axle was synthesised taking the propargyl amine compound **3.19** and reacting under 'CuAAC click conditions' giving neutral thread **3.52**. The previous solvent systems used in earlier 'click' reactions were again found to be unsuitable for the synthesis of this thread and in this case a two phase mixture of CH_2Cl_2 and water were used to give the product in a 34% yield. The synthesis of the ClO_4^- salt **3.53** was done by washing the neutral thread in CH_2Cl_2 with an aqueous solution of $HClO_4$ shown in Scheme 3.17.



Scheme 3.17 Reagents and conditions: a) CH_2Cl_2, H_2O, $CuSO_4.5H_2O$, NaAsc, RT, 34%; b) CH_2Cl_2, $HClO_4$, RT, 54%.

The retro Diels-Alder reaction was performed using the perchlorate thread **3.53** to produce the 'open gate' **3.54** (Figure 3.9). Finally threading of the axle with the $CBPQT^{4+}$ macrocycle was investigated to form the pseudorotaxane as the first stage in synthesising the multi component rotaxane.

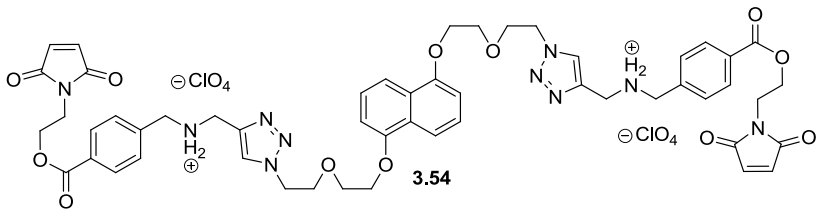
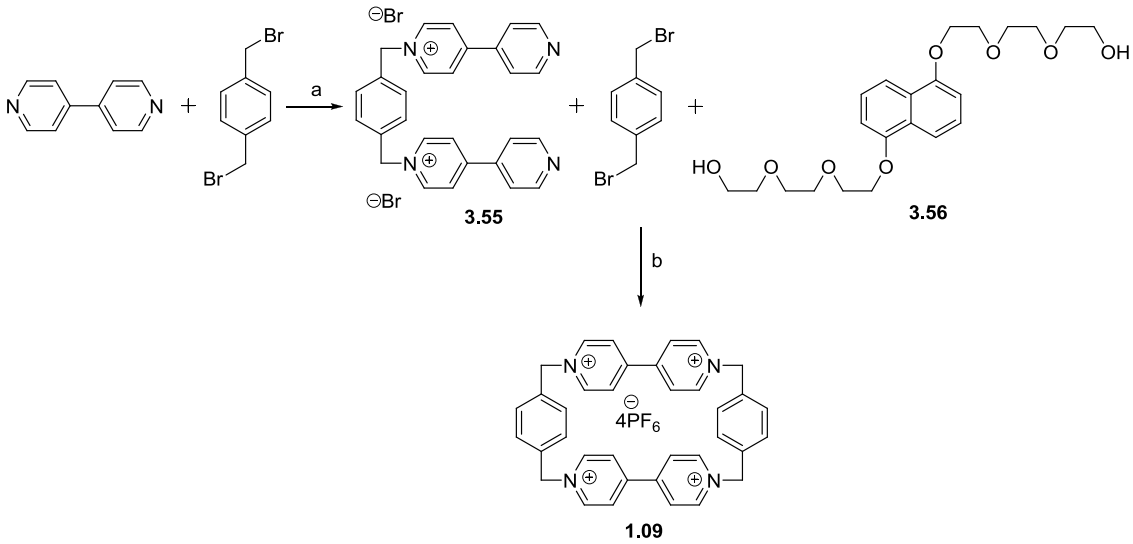


Figure 3.9 Open gate axle **3.52**.

The $CBPQT^{4+}$ macrocycle (**1.09**) was synthesised according to the Stoddart group literature procedures.[170,172] Taking 4,4-bipyridine, 1,4-bis(bromomethyl)benzene and refluxing in acetonitrile, intermediate **3.55** was obtained. The final stage was to perform template directed synthesis of the macrocycle. Diol **3.56**, intermediate **3.55**, 1,4-bis(bromomethyl)benzene were heated in DMF to provide the $CBPQT^{4+}$ macrocycle **1.09**

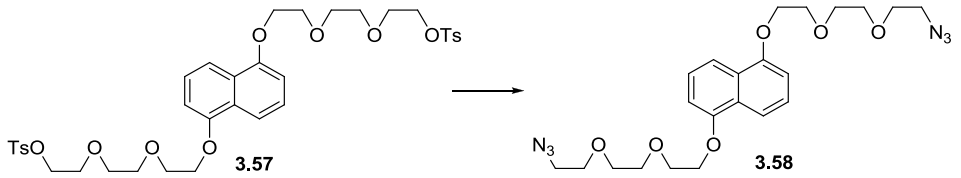
after an ion exchange with ammonium hexafluorophosphate. Characterisation of the product was consistent with literature values.



Scheme 3.18 Reagents and conditions: a) CH_3CN, 2h, reflux-RT, 70%; b) DMF, 40˚C, 5 d, NH_4PF_6, 31%.

One equivalent of thread **3.54** and two equivalents of CBPQT^{4+} **1.09** were dissolved in deuterated acetonitrile to form the pseudorotaxane. The CBPQT^{4+} **1.09** was able to thread over the axle and distinctive shifts were seen in the ^{1}H NMR indicating pseudorotaxane formation, however pushing the equilibrium towards pseudorotaxane formation ≥ 99% proved difficult. No such problems were associated with threading of the neutral thread **3.52** with macrocycle **1.09** therefore the problem must lie with the presence of the ammonium salts located on both sides of the naphthalene moiety. The 4^+ charge on the macrocycle is repelled by the 1^+ charge on the ammonium ion making it difficult to slip over the group therefore threading was slow but it was also believed that their proximity to the DNP binding unit destabilised the pseudorotaxane.[173-175] A thread with longer ether chains that sandwich the naphthalene group so moving the ammonium ion salt further away from the macrocycle binding site was synthesised. Longer ether chains are also known to enhance the binding interaction between thread and CBPQT^{4+} **1.09** by increasing the C-H···O hydrogen bonding between the α-bipyridinium hydrogen and the ether chain oxygen.[176] Li *et al* have shown that increasing the ether chain length decreases the effect of the positively charged

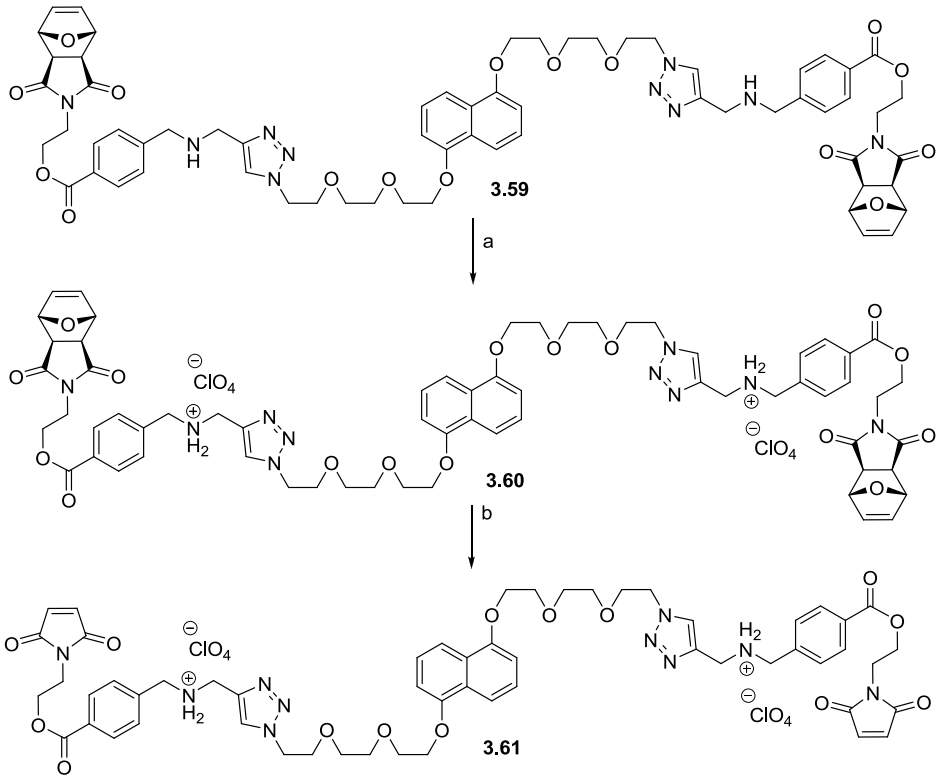
ion on the encompassing CBPQT^{4+} **1.09** giving a reduction in the electrostatic repulsion.[174] Taking diol **3.56** and reacting with tosyl chloride provided the ditosylate compound **3.57**. A further reaction with sodium azide in DMF at 60˚C produced the diazide **3.58** in a 71% yield (Scheme 3.19).



Scheme 3.19 Reagents and conditions: a) DMF, NaN_3, 60˚C, 24h, 71%.

The thread **3.59** was synthesised from the diazide **3.58** and the propargyl compound **3.19** under 'CuAAC' conditions. Conversion to the ClO_4^- salt was carried out by treating the neutral thread with $HClO_4$ (**3.60**) and finally the retro Diels-Alder reaction was performed under microwave conditions giving axle **3.61**.

Again synthesis of the [2]pseudorotaxane using the multi binding site axle with CBPQT^{4+} **1.09** was attempted. This new thread **3.61** was dissolved in deuterated acetonitrile with just one equivalent of the CBPQT^{4+} **1.09**. Again [2]pseudorotaxane formation was observed by ^{1}H NMR but even with adding additional CBPQT^{4+} **1.09** the equilibrium could not be pushed towards generation of a favourable amount of pseudorotaxane.

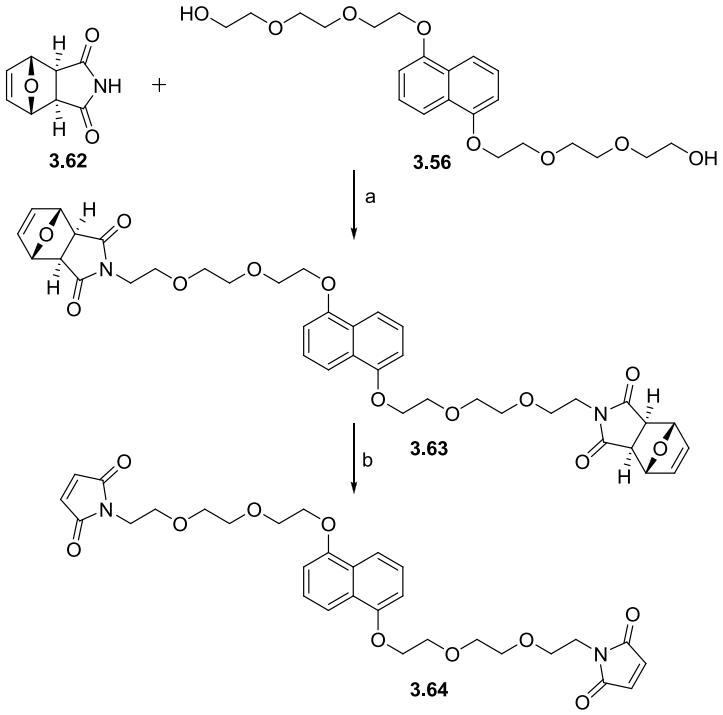


Scheme 3.20 Reagents and conditions: a) $HClO_4$, RT, 67%; b) CH_3CN, (MW, 100W, 110˚C, 4 h), 95%.

A secondary effect observed when trying to synthesise the pseudorotaxane was an ion exchange reaction between the thread **3.61** and $CBPQT^{4+}$ **1.09**. The macrocycle (**1.09**) with ClO_4^- counter ion precipitated out of the solution as proved by x-ray analysis. The ClO_4^- salt macrocycle was extremely insoluble in solvents suitable for pseudorotaxane synthesis meaning that it could not be used in place of the PF_6^- macrocycle **1.09**.

A different strategy was then attempted to synthesise the pseudorotaxane. Instead of using $HClO_4$ to generate the ClO_4^- counter ion, hexafluorophosphate was used in its place. Unfortunately this did not produce a suitable thread in sufficient purity to carry on with the synthesis. Carrying out the retro Diels-Alder reaction on the neutral threads **3.52** and **3.59** was also investigated but again problems were encountered with this stage due to revealing the maleimides in the presence of the free amines which led to a mixture of polymeric material. Due to a lack of time, the attempted synthesis of a multicomponent [4]rotaxane was curtailed.

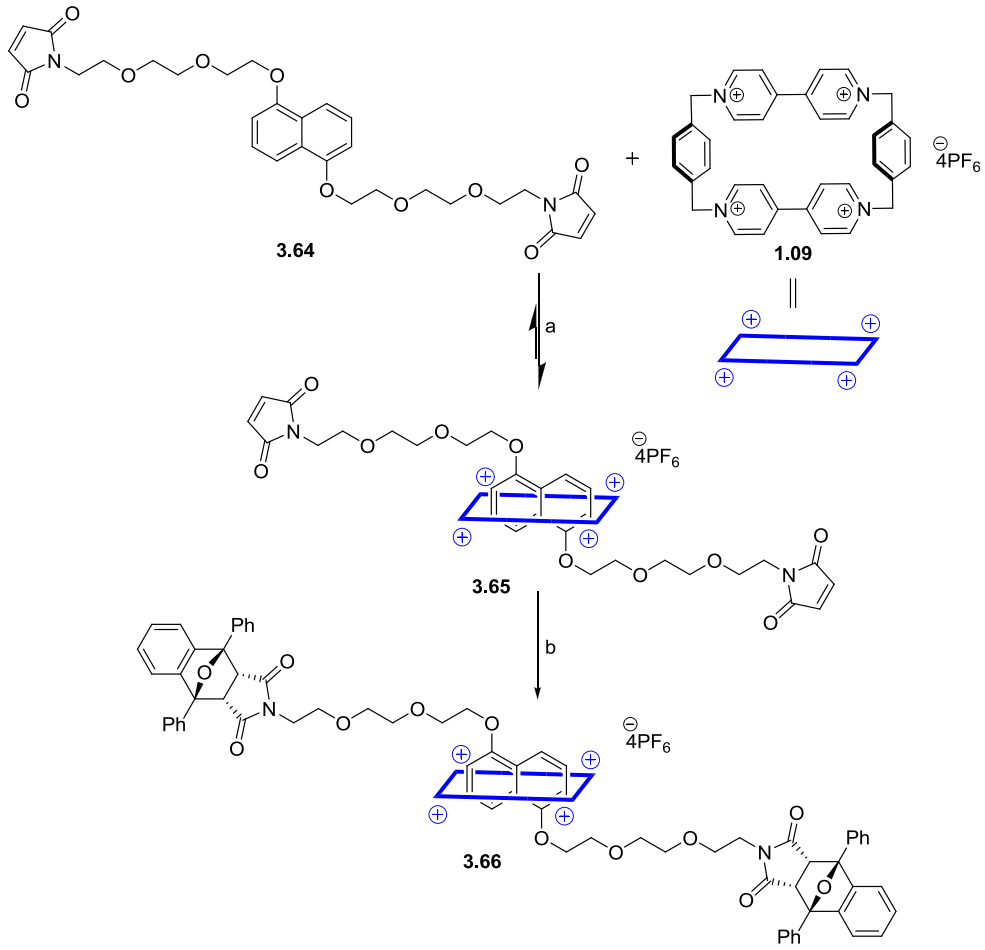
A different approach to incorporate the Diels-Alder 'threading followed by stoppering' protocol in the synthesis of rotaxanes derived from the CPBQT^{4+} **1.09** was then exploited. A simple DNP functionalised thread was synthesised from the diol **3.56**, by reacting with the Diels-Alder adduct **3.62** under Mitsonubu conditions. This provided the symmetrical thread **3.63** incorporating two Diels-Alder gates. The retro Diels-Alder reaction was carried out under microwave conditions to unmask the maleimide units to give axle **3.64** in an 81% yield.



Scheme 3.21 Reagents and conditions: a) THF, DEAD, PPh_3, 0˚C→RT, 14%; b) CH_3CN, (MW, 100W, 110˚C, 3h), 81%

Two equivalents of CBPQT^{4+} **1.09** to thread **3.64** were then dissolved in deuterated acetonitrile to provide the intermediate pseudorotaxane **3.65**. On addition of the macrocycle to the axle in acetonitrile, the reaction immediately changes from colourless to a deep purple solution. This is due to the charge transfer interaction between the π-electron deficient *bis*pyridinium of the macrocycle and the π-electron rich DNP unit of the thread.[177] The pseudorotaxane **3.65** formation was observed by ^{1}H NMR with no unbound thread **3.64** observed in the spectra. The naphthalene hydrogen's were seen to shift both upfield and

downfield due to shielding and deshielding effects as a result of their close proximity to the macrocycle aromatic π-system. The aromatic protons of the macrocycle **1.09** are also shifted both upfield and downfield by a reciprocal effect.

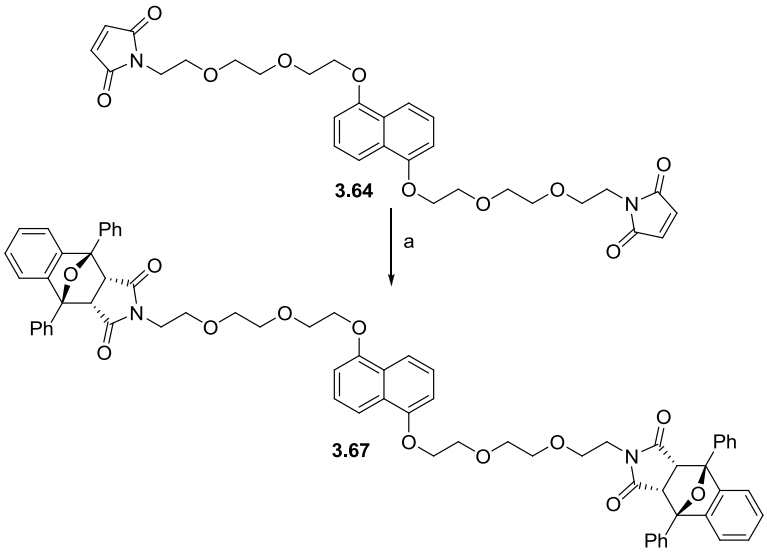


Scheme 3.22 Reagents and conditions: a) CD_3CN, RT; b) CD_3CN, 1,3 diphenylisobenzofuran (2 equiv), RT, 70%.

To trap the macrocycle onto the axle, cyclopentadiene is not bulky enough to use as a stopper. An initial experiment with thread **3.63** and $CBPQT^{4+}$ (**1.09**) provided evidence of pseudorotaxane formation and it was required to substitute cyclopentadiene for a larger diene. 1,3-Diphenylisobenzofuran reacts with the maleimide giving the *endo* isomer incorporating the [2.2.1] bicyclic bridge substituted at the bridge head with two phenyl groups. It was envisioned that this would then be large enough to prevent the macrocycle **1.09** from slipping back off the axle. This stoppering step was carried out in acetonitrile at room temperature with the reaction occurring faster than the ^1H NMR spectra could be

recorded. After purification the [2]rotaxane **3.66** was afforded in a 70% yield simply by two successive crystallisations.

Comparison thread **3.67** was also synthesised taking the deprotected maleimide thread and carrying out the Diels-Alder reaction with 1,3-diphenylisobenzofuran giving the *endo* Diels-Alder adduct shown in Scheme 3.23.



Scheme 3.23 Reagents and conditions: a) CH_3CN, 1,3 diphenylisobenzofuran (2 equiv), RT, 62%.

Comparison of the thread **3.67**, macrocycle **1.09** and rotaxane **3.66** are shown in Figure 3.10. From the ^{1}H NMR, you can observe that the aromatic protons of the thread derived from the diphenylisobenzofuran portion are relatively unaffected. The naphthalene protons are significantly affected by the presence of the macrocycle. The naphthalene protons in C4 and C8 are shifted from 7.76 ppm downfield to 2.24 ppm. The naphthalene protons in the C2 and C6 position are shifted from 6.90 ppm to 6.30 ppm and the C3 and C7 are also shifted by a similar magnitude from 7.33 ppm to 6.02 ppm. Some of the ethylene protons of the thread undergo slight shifts. The protons of the macrocycle become very broad as they undergo a rocking/precessing motion relative to the thread axis that is slower than the NMR time scale.[178] The rotaxane was also characterised *via* HRMS with the *m/z* found to be 547.5626 corresponding to the [**3.66**-4PF_6]$^{3+}$ ion.

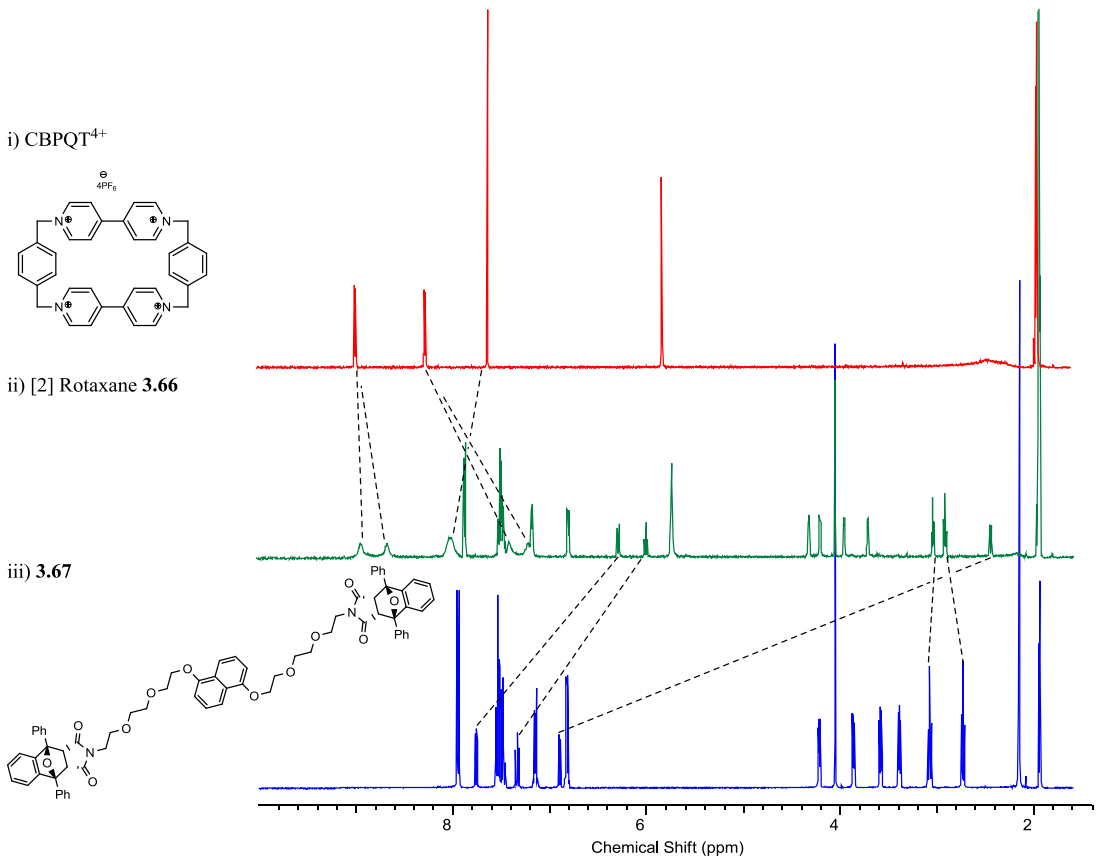


Figure 3.10 ^{1}H NMR (400MHz, CD_3CN, 300K) stacking plot of i) $CBPQT^{4+}$; ii) [2]rotaxane **3.66** and iii) comparison thread **3.67**.

The solid state structure of the [2]rotaxane **3.66** was also obtained and is shown in Figure 3.11. You can observe that the Diels-Alder reaction with 1,3-diphenylisobenzofuran provides the *endo* isomer. This stereochemistry has a shielding effect on the hydrogens of the first ethylene glycol unit directly attached to the maleimide moiety in the ^{1}H NMR. The protons associated with this ethylene oxy unit are shifted upfield by 3.19 ppm due to a shielding effect from the close proximity to the π system of the newly created benzene rings of the stopper group.

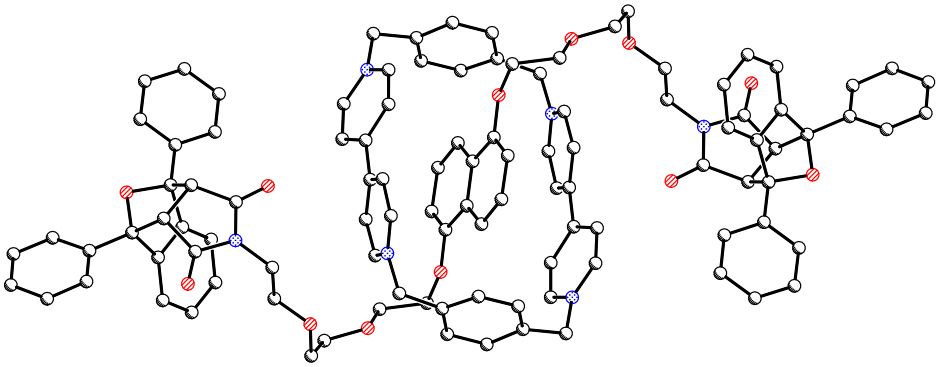


Figure 3.11 A view of the solid state structure of **3.66** highlighting the interlocked nature of the [2]rotaxane and the *endo* stereochemistry of the Diels-Alder stopper adduct. Hydrogens and minor disordered components have been removed for clarity. C white; O red, N blue.

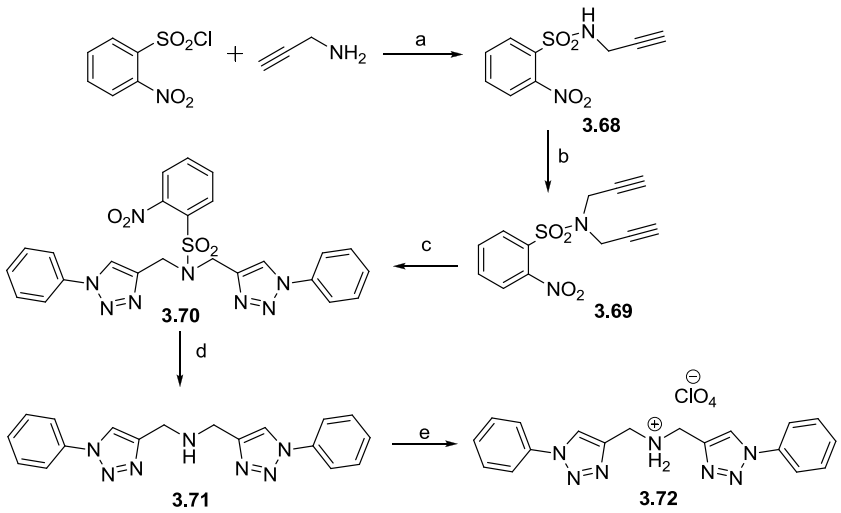
The relative orientation of the macrocycle and DNP unit of the thread are similar to other solid state structures reported by Stoddart.[175] π Stacking interactions between the π electron deficient $CBPQT^{4+}$ **1.09** and π electron rich DNP moiety are revealed in the solid state structure.

To sharpen up the ^{1}H NMR signals of the macrocycle, a sample in DMSO was heated to 80˚C. Unfortunately, dethreading of the macrocycle was observed. We are presently unable to ascertain if this dethreading is due to slippage as the stopper is too small or opening and closing of the stopper gate by a retro Diels-Alder mechanism. The macrocycle **1.09** does not surmount the end group of thread **3.67** at room temperature as revealed by ^{1}H NMR by following a mixture of two equivalents of macrocycle **1.09** and one equivalent of thread **3.67** in acetonitrile over a period of a week. Unfortunately there was not the time to investigate this further and work focussed on completing the ammonium templates containing a triazole.

3.6 Synthesis of *Bis*triazole Ammonium Threads Using 'Click Chemistry'

With the success of the mono triazole functionalised ammonium thread, incorporating two triazoles into the binding site was investigated to observe the effect it would have on the binding interaction between crown ether macrocycles and the axle. The synthesis of this new binding template was carried out beginning with 2-nitrobenzenesulphonyl chloride and

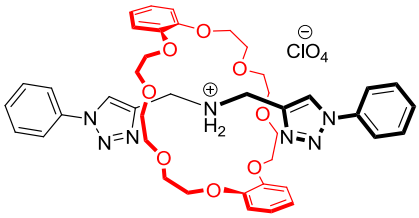
propargyl amine providing compound **3.68**. The 2-nitrobenzenesulphonyl group can act both as a protecting group for the amine but also activates the group towards base catalysed alkylation.[179-180] A further reaction with propargyl bromide produces the dipropargyl sulphonamide **3.69**. This was followed by a 'CuAAC' reaction with two equivalents of benzyl azide providing the amine protected thread **3.70**. Deprotection was carried out using thiophenol and potassium carbonate in acetonitrile at 60˚C. For the macrocycle to bind with the template it was again converted to an ammonium ion with a weakly co-ordinating counter ion. As in previous examples neutral thread **3.71** was converted to the ClO_4^- salt using $HClO_4$ producing the *bis*triazole ammonium template thread **3.72** in a 66% yield.



Scheme 3.24 Reagents and conditions: a) i) aq. $NaHCO_3$, THF, RT, 24h, conc. HCl, 0˚C, 69%; b) CH_3CN, K_2CO_3, propargyl bromide, RT, 48h, 64%; c) EtOH, THF, H_2O, $CuSO_4.5H_2O$, NaAsc, phenyl azide, RT, 48h, 51%; d) CH_3CN, PhSH, K_2CO_3, 60˚C, 24h, 86%; e) CH_2Cl_2, $HClO_4$, RT, 66%.

Binding between the new thread and macrocycle was assessed using equimolar quantities of DB24C8 and the ClO_4^- salt thread **3.72** at 2 mmol concentration. Pseudorotaxane (**3.73**) formation was observed by complexation induced shifts in the ^{1}H NMR and HRMS which included a peak at 780.3715 corresponding to the expected [**3.73**-ClO_4]$^+$. The binding constant was found to be 864 M^{-1} calculated from the single point method.[129] Incorporation of two triazoles into the ammonium binding motif gives a four times increase in the binding interaction between the thread and crown compared to the value of the binding interaction between dibenzylammonium thread and DB24C8 (237 M^{-1}). The introduction of the two

triazole rings may increase the CH hydrogen binding ability of the benzylic CH_2's and provide enhanced π stacking interactions between aromatic moieties on crown and thread. It is possible that the crown cavity also has a better 'fit' over the binding motif with the five membered ring triazoles in the macrocycle cavity compared to the larger six membered benzene ring. The triazole C-H may also be involved in hydrogen bonding with the crown ether oxygens further stabilising the [2]pseudorotaxane complex.[161,181]



3.73

Figure 3.12 [2]pseudorotaxane **3.73**.

Shown in Figure 3.13 is the ^{1}H NMR stacking plot of [2]pseudorotaxane **3.73** with DB24C8 and ClO_4^- salt **3.72**. Observing the chemical shifts of the macrocycle, the aromatic protons are shifted slightly upfield due to shielding of these hydrogens. The first ethylene oxy group of the crown chain shifts upfield as a result of their close contact with the π system of the thread. The $CH_2NH_2^+CH_2$ protons of the thread are shifted upfield due to hydrogen bonding with the crown ether oxygens. They are also split into a multiplet as they now show coupling with the $^+NH_2$ protons of the thread.[32] When considering the aromatic protons of the thread **3.72**, the phenyl ring protons are generally unaffected by the presence of the macrocycle encompassing the axle. The triazole proton however is shifted downfield by 0.4 ppm due to π stacking interactions of the conjugated system with the aromatics of the DB24C8.

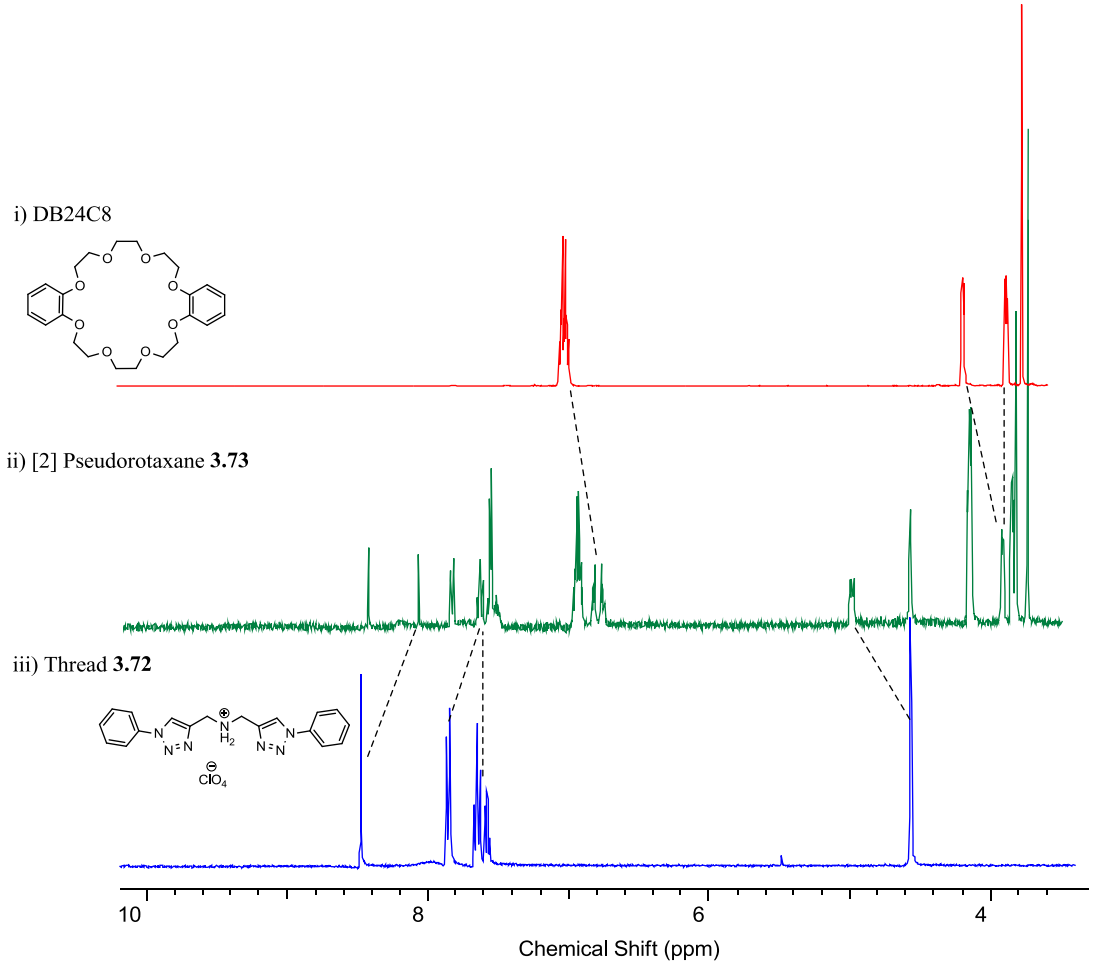
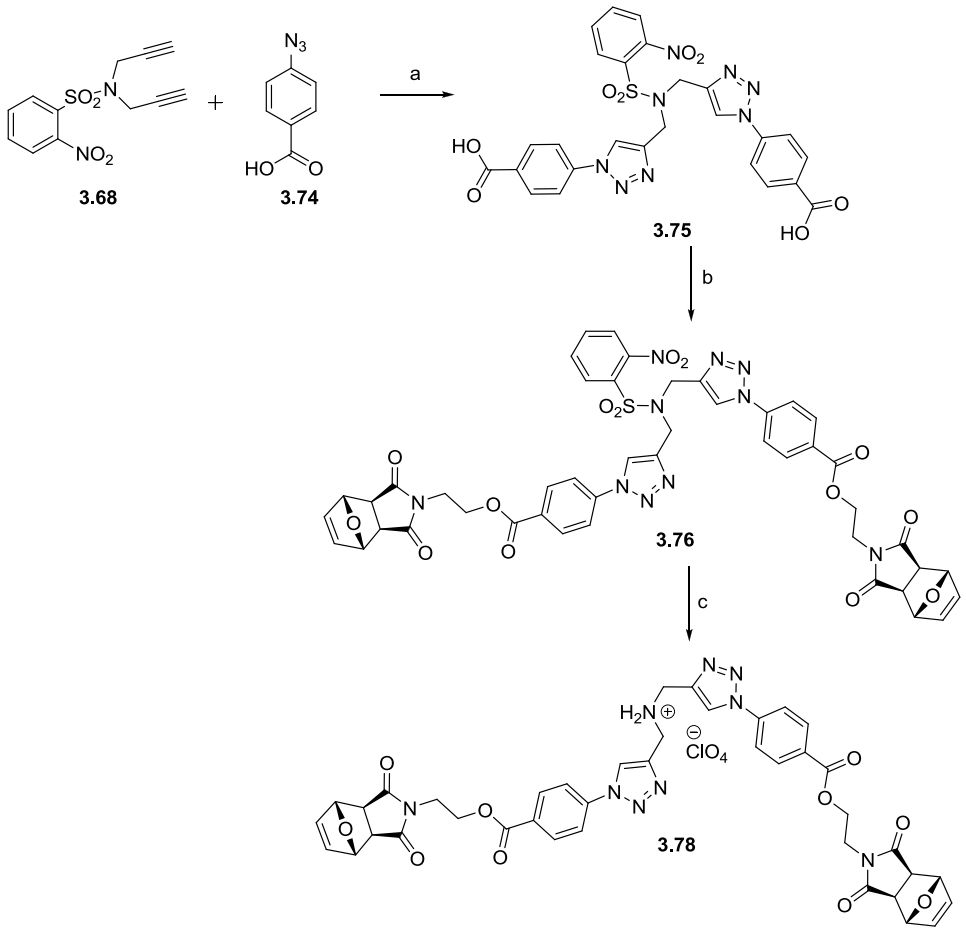


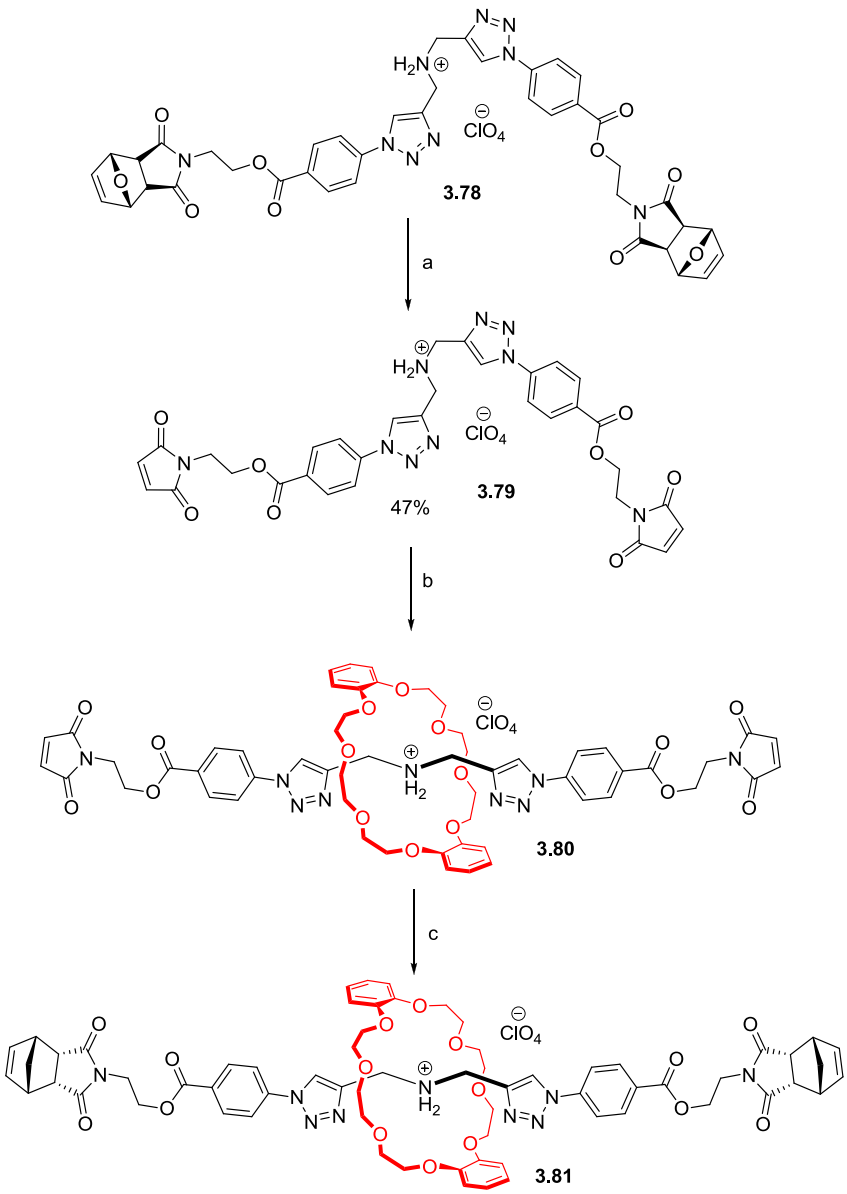
Figure 3.13 Partial ^{1}H NMR (400 MHz, CD_3CN, 300K) stacking plot of i) DB24C8; ii) [2]pseudorotaxane **3.73** and iii) Comparison thread **3.72**.

Incorporation of the *bis* triazole ammonium binding template into an axle with our 'Diels-Alder gates' to synthesise a rotaxane in the threading followed by stoppering protocol was then carried out. Taking the dipropargyl **3.69** and reacting with the acid azide **3.74** under 'CuAAC click chemistry' conditions new compound **3.75** was obtained. This was followed by an esterification reaction with the Diels-Alder alcohol **2.04** giving the neutral thread containing the protected amine **3.76**. Deprotection was performed with thiophenol and potassium carbonate in acetonitrile to provide neutral thread **3.77**. This was converted to ClO_4^- ammonium salt **3.78** using $HClO_4$ to give the salt which had rather low solubility in acetonitrile.



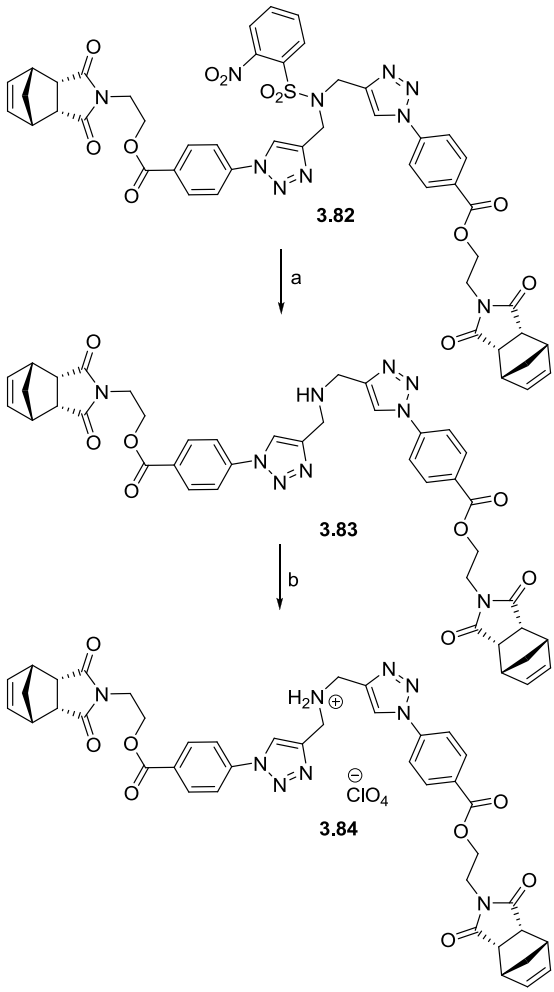
Scheme 3.25 Reagents and conditions: a) EtOH, THF, H_2O, $CuSO_4.5H_2O$, NaAsc, RT, 24h, 73%; b) CH_2Cl_2, Alcohol **2.04**, NEt_3, *N,N,N',N'*-tetramethylchloroformamidinium hexafluorophosphate, RT, 48h, 52%; c) i) CH_3CN, PhSH, K_2CO_3, 60˚C, 24h, 54%; ii) CH_2Cl_2, $HClO_4$, RT, 100%.

The retro Diels-Alder reaction was carried out under microwave conditions to deprotect the maleimide this time in a mixture of acetonitrile and nitromethane. The retro Diels-Alder thread **3.79** had improved solubility in deuterated acetonitrile and adding 2.3 equivalents of DB24C8 induces the formation of the [2]pseudorotaxane **3.80**. Once pseudorotaxane formation was complete when observing by ^{1}H NMR, the macrocycle was trapped onto the thread with the addition of freshly cracked cyclopentadiene. [2]rotaxane **3.81** was obtained in a 57% yield following purification.



Scheme 3.26 Reagents and conditions: a) CH_3CN, CH_3NO_2, MW (4h, 150W, 100°C), 96%; b) CD_3CN, DB24C8 (2.3 equiv.), RT, 48h; c) CH_3CN, cyclopentadiene (excess), RT, 57%.

Thread **3.84** was synthesised as a comparison to see the effect of the macrocycle encompassing the axle on the ^{1}H NMR shifts. The reaction synthesis is shown in Scheme 3.27 showing the protected amine **3.82** synthesised from the diacid **3.74** reacting it with alcohol **2.15**. The deprotection was carried out using thiophenol and potassium carbonate to give neutral thread **3.83**. Finally conversion to the ClO_4^- salt was performed using $HClO_4$ to produce thread **3.84**.



Scheme 3.27 Reagents and conditions: a) CH_3CN, K_2CO_3, PhSH, 60˚C, 24h, 74%; b) CH_2Cl_2, $HClO_4$, 100%

The ^{1}H NMR comparison of DB24C8, [2]rotaxane **3.81** and thread **3.84** is shown in Figure 3.14. The $CH_2NH_2^+CH_2$ are shifted downfield and are coupled with the ammonium hydrogens. Aromatic hydrogens of the thread are also deshielded and shift upfield. The Diels-Alder stopper portion of the axle is once again unaffected by the presence of the encompassing macrocycle.

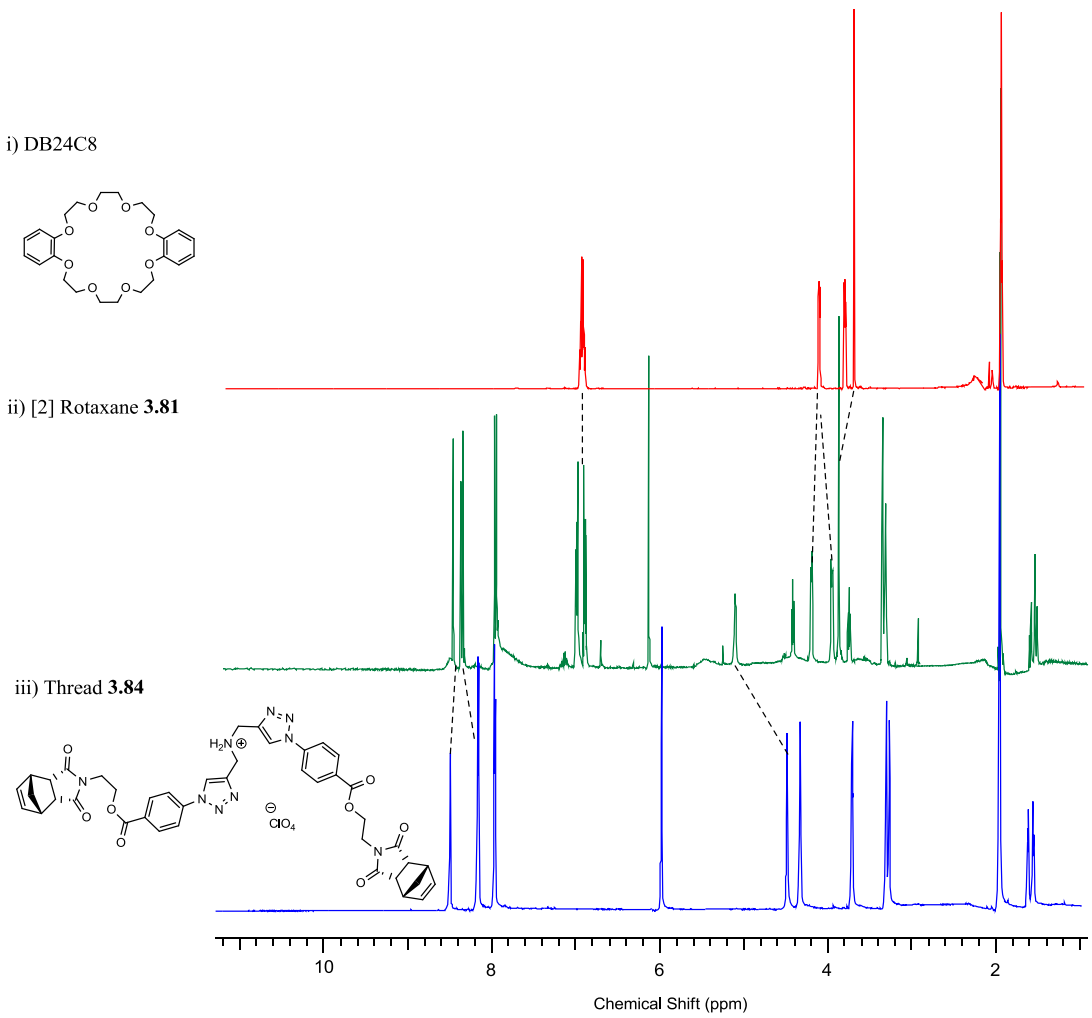
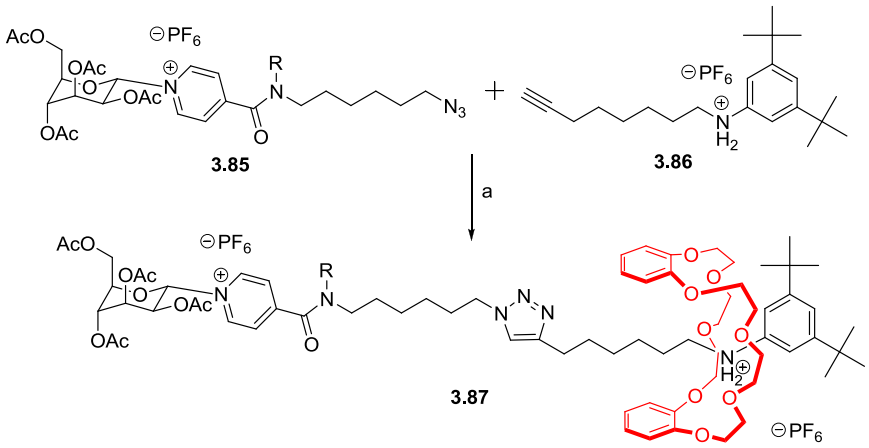


Figure 3.14 ^{1}H NMR (400 MHz, CD_3CN, 300K) i) DB24C8; ii) [2]Rotaxane **3.81** and iii) ClO_4^- thread **3.84**.

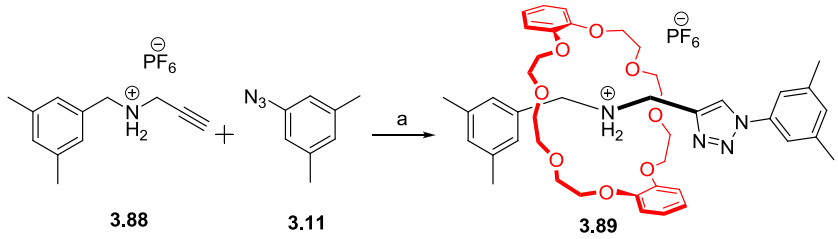
3.7 Synthesis of Rotaxanes in a One Pot Method Using 'CuAAC Click Chemistry'

It has been reported that the click reaction using copper (I) salt $Cu(MeCN)_4PF_6$ can occur quantitatively in solvents compatible with crown rotaxane formation.[106] The propargyl **3.86** as an ammonium hexafluorophosphate salt and the azide with a pyridinium hexafluorophosphate salt **3.85** were 'clicked' in dry CH_2Cl_2 under nitrogen using 2,6-lutidine as a base. This lead to the successful synthesis of a [2]rotaxane reported by Coutrot shown in Scheme 3.28.



Scheme 3.28 Synthesis of a [2]rotaxane molecular shuttle using 'CuAAC click chemistry'.[106] Reagents and conditions: a) DB24C8, $[Cu(CH_3CN)_4]PF_6$, 2,6-lutidine, CH_2Cl_2, 75%.

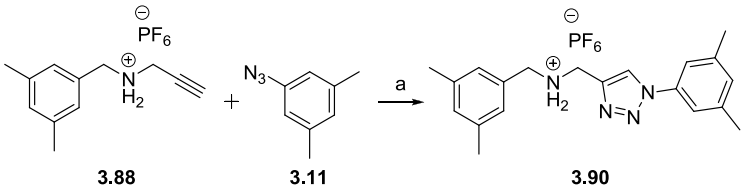
As discussed earlier, Takata[107] had shown rotaxane formation using N-oxide click chemistry with the ammonium ion binding site very close to the reacting unit. The pseudorotaxane was trapped as the rotaxane when the click reaction was carried out under mild enough conditions giving high yields of the resulting rotaxanes. Synthesis of rotaxanes generating the ammonium triazole binding site during rotaxane formation was therefore investigated. The ammonium hexafluorophosphate propargyl unit (**3.88**), 3,5-dimethylbenzyl azide and DB24C8 were dissolved in dry CH_2Cl_2 and after 24 hours a new spot was visualised on the TLC. On purification *via* column chromatography the [2]rotaxane **3.89** was isolated in 30% yield. Some free thread was also isolated during the purification stage.



Scheme 3.29 Reagents and conditions: a) CH_2Cl_2, DB24C8 (2 equiv), $Cu(MeCN)_4PF_6$, 2,6-lutidine, N_2, 24 h, RT, 30%

The free thread (**3.90**) was also synthesised using the same reaction conditions for comparison with the rotaxane. In this case, it was found beneficial to neutralise the reaction

before purification *via* flash chromatography then converting the isolated thread back to the PF_6^- salt using hexafluorophosphoric acid.



Scheme 3.30 Reagents and conditions: a) CH_2Cl_2, $Cu(MeCN)_4PF_6$, 2,6-lutidine, N_2, 24 h, RT, 29%

The ^{1}H NMR of DB24C8, thread **3.90** and [2]rotaxane **3.89** is shown in Figure 3.15. The $CH_2NH_2^+CH_2$ hydrogens of the thread are shifted downfield and sharpen up taking on the usual coupling patterns associated with forming a rotaxane with the DB24C8.[32] The signal for the ethylene oxy units of the crown ether become complex due to the unsymmetrical axle they are encompassing and are shifted slightly downfield.[182] There are also complexation induced shifts in the aromatic hydrogen of the thread with all of these peaks seen to shift upfield due to shielding from the close proximity of the aromatic systems of DB24C8.

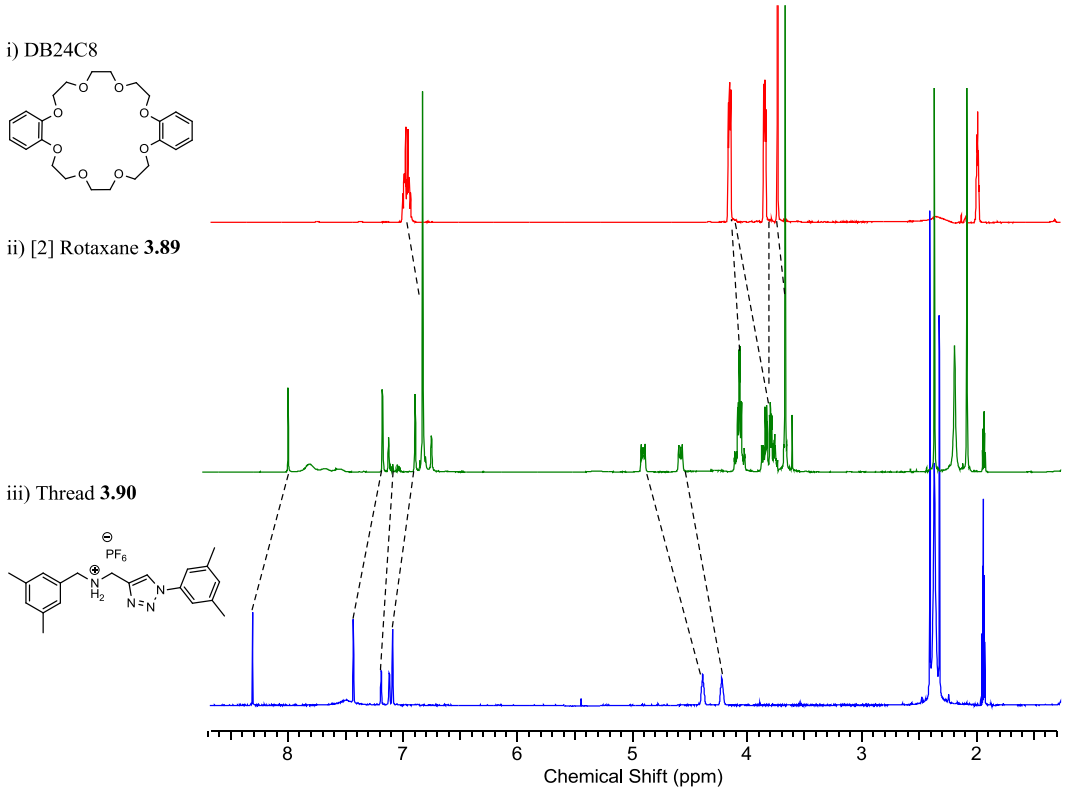
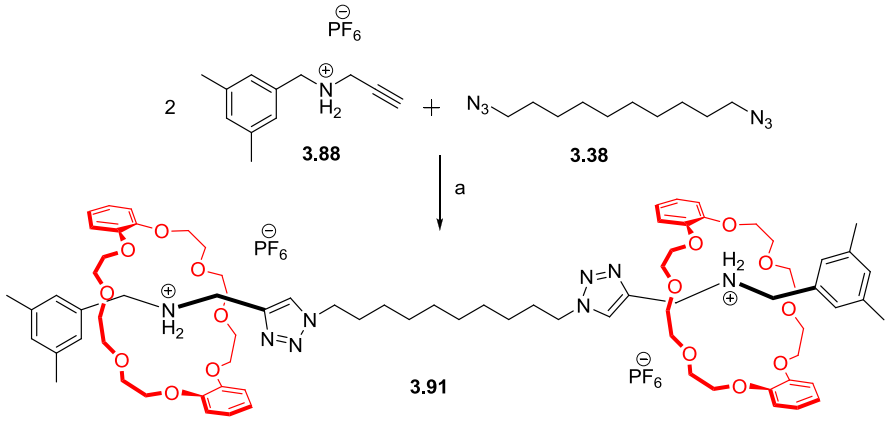


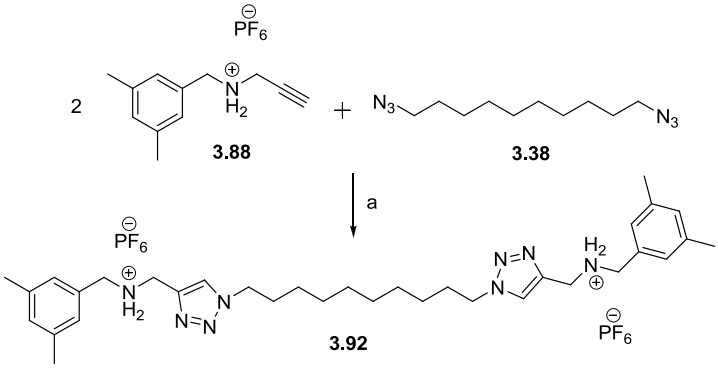
Figure 3.15 ^{1}H NMR (400 MHz, CD_3CN, 300K) stacking plot of i) DB24C8 ii) [2]rotaxane **3.89** and iii) Comparison thread **3.90**.

The possibility of using this approach to synthesise higher order rotaxanes was explored. In this case starting with two equivalents of the PF_6^- salt **3.88** was reacted with the simple diazide **3.38** in the presence of four equivalents of DB24C8. The [3]rotaxane **3.91** shown in Scheme 3.31 was successfully synthesised using the same 'CuAAC' click conditions shown in the previous examples.



Scheme 3.31 Reagents and conditions: a) i) CH_2Cl_2, DB24C8 (4 equiv), $Cu(MeCN)_4PF_6$, 2,6-lutidine, N_2, RT, 24 h, RT; ii) HPF_6, 19%.

The comparison thread was synthesised taking two equivalents of the PF_6^- salt **3.88** and one equivalent of the diazide **3.38** under the same 'CuAAC click' conditions as before. The thread was again neutralised before column chromatography, then reprotonation was carried out with hexafluorophosphoric acid. This provided us with the new PF_6^- salt **3.91** in a 26% yield shown in Scheme 3.32.



Scheme 3.32 Reagents and conditions: a) CH_2Cl_2, $Cu(MeCN)_4PF_6$, 2,6-lutidine, N_2, 24h, RT; ii) HPF_6, RT, 26%.

Again from comparing the ^1H NMR of the free thread and DB24C8 with the rotaxane, a number of shifts indicative of rotaxane formation were observed. The encompassed

$CH_2NH_2^+CH_2$ protons see a characteristic shift downfield due to hydrogen bonding interaction with the crown ether oxygens and become complex multiplet *via* coupling with the hydrogens of the ammonium salt (Figure 3.16). The crown ethylene oxy signals also become complex multiplets due to their asymmetric environment on the interlocked thread.

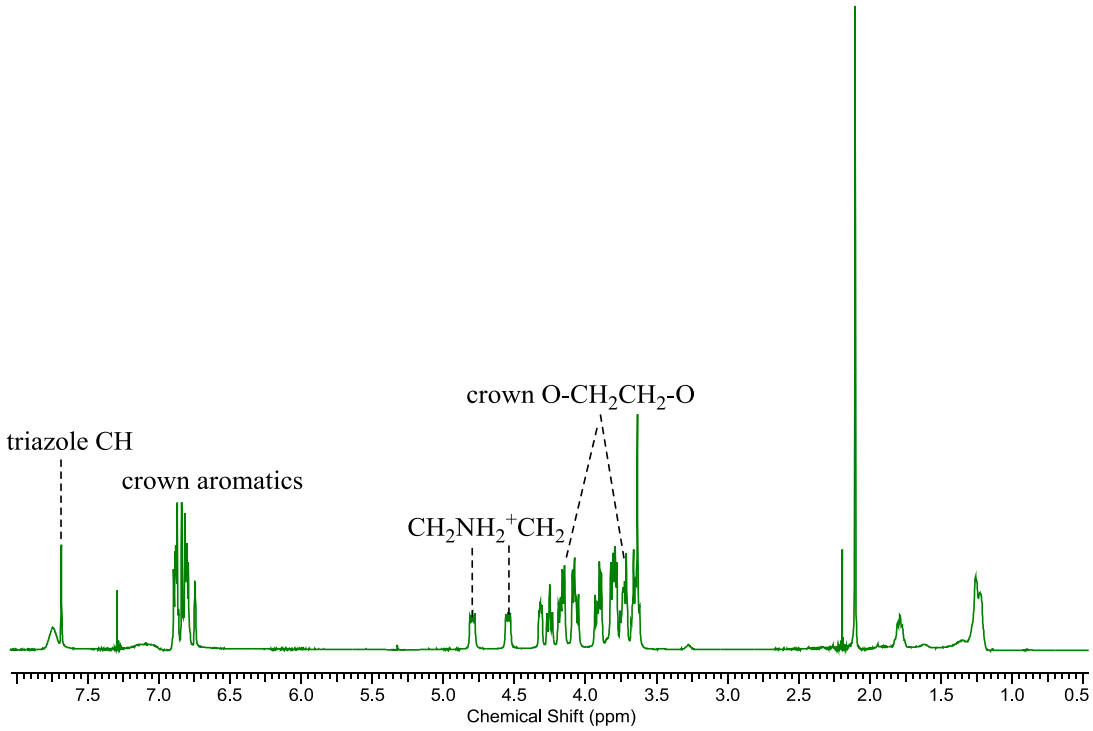
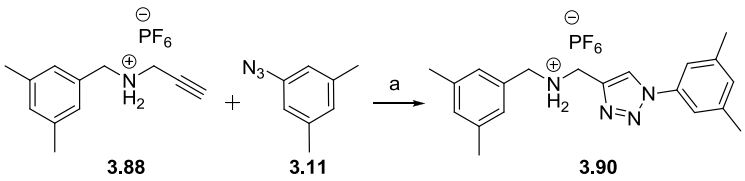


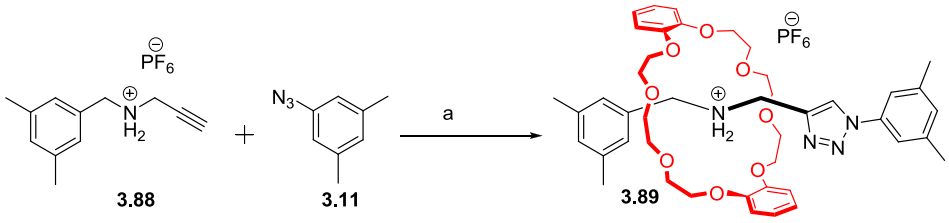
Figure 3.16 ^{1}H NMR of [3]rotaxane 3.91 (400MHz, $CDCl_3$, 300K).

In an attempt to increase the yields of the isolated rotaxanes different copper salt catalysts to perform the 'CuAAC click' reaction were investigated. There is literature precedent for 'CuAAC click' reactions using $CuBr(PPh_3)_3$.[183-184] This particular reagent is also commercially available and other groups have had success using it in rotaxane formation. Synthesis of the thread **3.90** was performed taking one equivalent of the PF_6^- salt **3.88**, one equivalent of azide **3.11** and a catalytic quantity of $CuBr(PPh_3)_3$ (0.1 equiv.) in acetonitrile. After 24 hours the reaction was worked up and purified to give the thread in an 8% yield (Scheme 3.33). The reaction seemed to occur using this copper complex but the yields were very low and no other products or starting materials could be isolated from the reaction. The synthesis was also attempted with longer reaction times with no improvement in yield of product.



Scheme 3.33 Reagents and conditions: a) CH_2Cl_2, $CuBr(PPh_3)_3$ (0.1 equiv.), N_2, RT, 8%

Even though we obtained a low yield of the thread using these conditions, the synthesis of the rotaxane was attempted for completeness. Using the same reaction conditions but with the two equivalents of DB24C8 added to the system, a small amount of [2]rotaxane formation was detected by TLC but the product was not able to be isolated. Examining the crude ^{1}H NMR it appears that the yield is in fact < 5%. Following from this a full equivalent of the $CuBr(PPh_3)_3$ salt was tried as it seemed that using only a catalytic amount may have been a factor in producing the low yield. Unfortunately in this case no rotaxane formation was detected and the ^{1}H NMR spectra showed only a mixture of starting materials and reagents. It is postulated that the presence of bromine may be having an effect on the formation of the rotaxane. This ion exchange may also influence the reactivity of the copper catalyst as no 'click' reaction was detected. There may also be some steric factors influencing the reaction as the large PPh_3 ligands may inhibit rotaxane formation during the catalytic cycle. As a result this particular reagent was not pursued to undertake the 'CuAAC click chemistry' reactions.



Scheme 3.34 Reagents and conditions: a) CH_2Cl_2, DB24C8 (2 equiv.), $CuBr(PPh_3)_3$ (0.1 equiv.), N_2, RT, <5% or a) CH_2Cl_2, DB24C8 (2 equiv.), $CuBr(PPh_3)_3$ (1 equiv.), N_2, RT, no product formed.

3.8 Conclusion

A simple but useful modification to the known dibenzylammonium binding motif for interactions with DB24C8 has been developed. The introduction of the triazole into the

binding site was found to enhance the interaction between axle and the DB24C8 macrocycle. A further increase in binding interaction was seen when the triazole was conjugated to a benzene ring. In comparison to the mono ester functionalised dibenzylammonium template **3.13**, there was almost a two fold increase in the binding constant observed at 2 mmol concentration. Synthesis of [2] and [3]rotaxanes were successfully carried out incorporating this binding template into axles and using the Diels-Alder approach to 'threading followed by stoppering'.

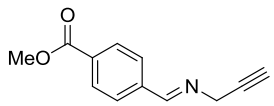
Synthesis of the desired multicomponent [4]rotaxane was unsuccessful so exploiting this chemistry could not be carried out due to a number of limiting factors. These included the proximity of the ammonium cations to the DNP binding site and solubility problems due to counter ion exchange. A synthesis including only PF_6^- salts or conducting the retro Diels-Alder reaction on the free amine caused side reactions to occur.

A binding motif with two triazoles incorporated either side of the ammonium ion was also successfully synthesised. It was found to enhance the binding interaction between the thread and DB24C8 even further. This new binding motif was introduced into an axle with two Diels-Alder type gates attached allowing us to synthesise a symmetrical [2]rotaxane.

Finally generating the triazole binding motif in rotaxanes during the stopper formation was completed using the 'CuAAC' reaction conditions that have been employed by Coutrot.[106] Synthesis of a [2]rotaxane and a [3]rotaxane as well as free threads was achieved using this method.

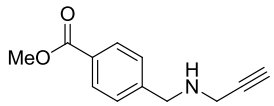
3.9 Experimental

3.93



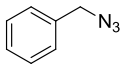
Methyl 4-formylbenzoate (1g, 6.10 mmol) was dissolved in MeOH and propargyl amine (0.42 mL, 6.70 mmol) was added. The solution was stirred at room temperature for 24 h. A precipitate formed which was filtered and washed with cold MeOH (800 mg, 3.98 mmol, 66%). m.p. 124-125°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.65 (s, 1H, C*H*=N), 8.10 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*CCO_2), 7.84 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*CCH), 4.57 (s, 2H, CH_2N), 3.94 (s, 3H, OCH_3), 2.56 (s, 1H, C≡C*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 166.6 (*C*OO), 161.4 (*C*H=CN), 139.6 (Ar*C*), 132.1 (Ar*C*), 129.9 (Ar*C*HCCO_2), 128.2 (Ar*C*HCC=N), 78.5 (C≡*C*H), 76.0 (*C*≡CH), 52.3 (O*C*H_3), 47.2 (*C*H_2); IR ν cm^{-1} 3182 (alkyne C-H), 2945 (saturated C-H), 1718 (ester C=O), 1651 (C=N); HRMS (ESI$^+$): *m/z* found, 202.0865 calc for $C_{12}H_{12}NO_2$ 202.0863 [**3.93**+H]$^+$.

3.05



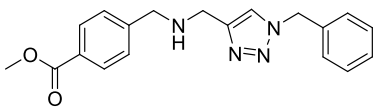
Known compound data consistent with literature.[185] The imine **3.91** (750 mg, 3.73 mmol) was dissolved in MeOH (10 mL). Sodium cyanoborohydride (258 mg, 4.1 mmol) and a few drops of HOAc were added to the stirring solution. The reaction was followed by TLC until completion (EtOAc). The MeOH was removed *in vacuo* and the residue diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The solvent was removed to provide a pale yellow solid (700 mg, 3.47 mmol, 93 %). m.p. 45-47°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.00 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO_2), 7.45 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH_2), 3.95 (s, 2H, CCH_2NH), 3.92 (s, 3H, OCH_3), 3.45 (s, 2H, CH_2C≡CH), 2.28 (s, 1H, C≡C*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 167.0 (*C*=O), 144.7 (Ar*C*), 130.0 (Ar*C*HCCO_2), 129.0 (Ar*C*), 128.3 (ArC*H*CCH_2), 81.8 (*C*≡CH), 71.8 (C≡*C*H), 52.7 (O*C*H_3), 51.8 (C*C*H_2NH), 37.4 (*C*H_2C≡CH); IR ν cm^{-1} 3270 (alkyne C-H), 2917 (saturated C-H), 1707 (ester C=O); HRMS (ESI$^+$): *m/z* found, 204.1017 calc for $C_{12}H_{14}NO_2$ 204.1019 [**3.05**+H]$^+$.

3.06



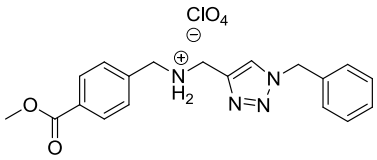
Known compound data consistent with literature.[186] Benzyl chloride (0.5 mL, 4.9 mmol) was dissolved in EtOH (5 mL), sodium azide (355 mg, 5.4 mmol) was added and the solution stirred at room temperature overnight. Water (10 mL) was added to the mixture and it was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent removed *in vacuo* providing the product as a clear oil (400 mg, 3.00 mmol, 61%); ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.37 (m, 5H, 5 ArC*H*), 4.38 (s, 2H, CH_2); ^{13}C NMR (75 MHz, 298 K, $CDCl_3$) δ_C 137.4 (Ar*C*), 128.8 (Ar*C*H), 128.6 (Ar*C*H), 128.1 (Ar*C*H), 54.8 (CH_2); IR ν cm^{-1} 3030 (saturated C-H), 2097 (N_3).

3.07



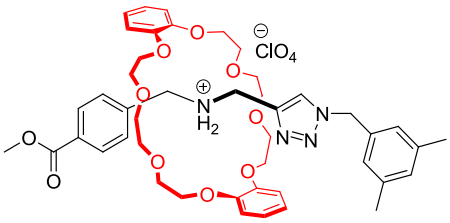
To a solution of azide **3.06** (51 mg, 0.375 mmol) and alkyne **3.05** (76 mg, 0.375 mmol) in 1:1 EtOH/water (5 mL) was added $CuSO_4$.5 H_2O (10 mg, 0.0375 mmol) and sodium ascorbate (25 mg, 0.113 mmol) in one portion. The resulting yellowish cloudy suspension was stirred at room temperature for 36 h. The mixture was partitioned between water (10 mL) and EtOAc (10 mL), and the aqueous layer extracted with additional EtOAc (2 x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The yellow oil purified *via* column chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 95:5) (75 mg, 0.255 mmol, 60 %). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.97 (d, 2H, J = 8.0 Hz, 2 ArC*H*CCO), 7.39-7.34 (m, 6H, 2 ArC*H*CH_2, 3 ArC*H* and triazole-C*H*), 7.26 (m, 2H, 2 ArC*H*), 5.50 (s, 2H, CH_2N-triazole), 3.90 (s, 3H, OCH_3), 3.89 (br s, 2H, CH_2NH), 3.87 (br s, 2H, CH_2NH), 1.99 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 166.9 (*C*=O), 146.8 (Ar*C*), 145.0 (Ar*C*), 134.6 (Ar*C*), 129.8 (Ar*C*H), 129.7 (Ar*C*H), 129.1 (Ar*C*H), 128.9 (Ar*C*), 128.1 (Ar*C*H), 128.0 (Ar*C*H), 121.5 (triazole-*C*H), 54.1 (*C*H_2N-triazole), 52.9 (*C*H_2NH), 52.0 (O*C*H_3), 44.1 (*C*H_2NH); IR ν cm^{-1} 2953 (saturated C-H), 1713 (ester C=O), 1434 (N=N); HRMS (ESI$^+$): *m/z* found 337.1657 cal for $C_{19}H_{21}N_4O_2$ 337.1659 [**3.06**+H]$^+$.

3.08



Compound **3.07** (50 mg, 0.13 mmol) was dissolved in MeOH (0.5 mL). A few drops of $HClO_4$ (70%) were added to the solution followed by water to induce precipitation. The white solid formed was filtered and washed with water (31 mg, 0.07 mmol, 54%). m.p. 140-141°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.05 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.95 (s, 1H, triazole-C*H*), 7.58 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.35 (m, 5H, 5 ArC*H*), 5.60 (s, 2H, C*H*$_2$N-triazole), 4.35 (broad s, 4H, C*H*$_2$NH$_2$C*H*$_2$) 3.89 (s, 3H, OC*H*$_3$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 165.8 (*C*OO), 137.1 (Ar*C*), 135.1 (Ar*C*), 134.7 (Ar*C*), 131.1 (Ar*C*), 130.1 (Ar*C*H), 129.5 (Ar*C*H), 129.12 (Ar*C*H), 128.6 (Ar*C*H), 128.2 (Ar*C*H), 127.8 (Ar*C*H), 127.7 (Ar*C*H), 125.3 (triazole-*C*H), 53.3 (*C*H$_2$N-triazole), 51.7 (O*C*H$_3$), 50.0 (*C*H$_2$NH$_2$), 41.84 (*C*H$_2$NH$_2$); IR ν cm^{-1} 3146 (NH$_2$), 1721 (ester C=O), 1060 (ClO_4); HRMS (ESI$^+$): *m/z* found, 337.1656 calc. for $C_{19}H_{21}N_4O_2$ 337.1659 [**3.08**-ClO_4]$^+$.

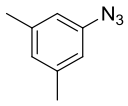
3.10



The thread **3.08** (10 mg, 0.02 mmol) and DB24C8 (10 mg, 0.02 mmol) were dissolved in deuterated acetonitrile (10 mL) and a new set of signals for pseudorotaxane formation was observed. Binding constant = **820 M^{-1}** was calculated from the single point method[129] by measuring the integration of triazole-C*H* protons for the free and bound thread at 8.05 ppm and 7.73 ppm respectively. **Pseudorotaxane 3.10** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.73 (s, 1H, ⊂ triazole-C*H*), 7.58 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCO), 7.35 (m, 7 H ⊂ 2 ArC*H*CCH$_2$ and ⊂ 5 ArC*H*), 6.77 (m, 4H, ⊂ 4 crown ArC*H*), 6.72 (m, 4H, ⊂ 4 crown ArC*H*), 5.46 (s, 2H, ⊂ C*H*$_2$N-triazole), 4.75 (m, 4H, ⊂ C*H*$_2$NH$_2^+$C*H*$_2$), 4.13-3.58 (m, ⊂ 12

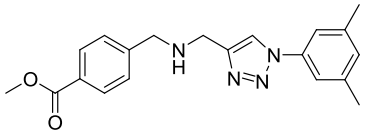
OCH_2, ⊂ OCH_3); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); and unthreaded **Thread 3.08** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.05 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.95 (s, 1H, triazole-C*H*), 7.58 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH_2), 7.35 (m, 5H, 5 ArC*H*), 5.60 (s, 2H, CH_2N-triazole), 4.35 (br s, 4H, CH_2NH$_2^+$CH_2) 3.89 (s, 3H, OCH_3); MS (ESI$^+$): *m/z* 785.3 [**3.10**-ClO_4]$^+$.

3.11



Known compound synthesised according to a modified literature procedure.[187] 3,5-Dimethylaniline (0.5 g, 4.1 mmol) was dissolved in 5M HCl (10 mL) and cooled to 0°C. Sodium nitrite (314 mg, 4.5 mmol) dissolved in water (10 mL) was added drop wise over 30 minutes. Sodium azide (1.07 g, 16.5 mmol) was added portion wise over 30 minutes with some slight effervescence. The solution was stirred for 1 h, basified to pH 8 with the addition of sodium bicarbonate and extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with water (20 mL) and dried over $MgSO_4$. The solvent was removed to provide an orange oil (390 mg, 2.63 mmol, 65%); ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.81 (s, 1H, ArC*H*), 6.69 (s, 2H, 2 ArC*H*), 2.34 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 139.7 (Ar*C*), 139.6 (Ar*C*), 126.8 (Ar*C*H), 116.7 (Ar*C*H), 21.3 (*C*H_3); IR ν cm^{-1} 2919 (saturated C-H), 2099 (N_3).

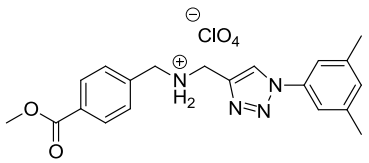
3.12



The propargyl **3.05** (83 mg, 0.41 mmol) was dissolved in *tert*-butanol (5 mL), water (5 mL) and THF (5 mL). The azide **3.11** (60 mg, 0.41 mmol) was added along with $CuSO_4.5H_2O$ (10 mg, 0.041 mmol) and sodium ascorbate (24 mg, 0.12 mmol). The solution was stirred at

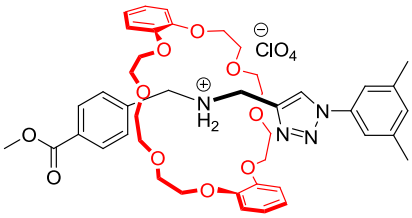
room temperature for 24 h. The solution was diluted with water (15 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$, the solvent removed *in vacuo* and the crude product purified *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2/MeOH 9:1) to provide an orange oil (65 mg, 0.19 mmol, 45%); ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.04 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO$_2$), 7.89 (s, 1H, triazole-C*H*), 7.48 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.35 (s, 2H, 2 ArC*H*), 7.09 (s, 1H, ArC*H*), 3.93 (broad s, 7H, C*H*$_2$NHC*H*$_2$ and OC*H*$_3$), 2.42 (s, 6H, 2 C*H*$_3$); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 167.3 (*C*OO), 147.0 (Ar*C*), 145.2 (Ar*C*), 139.7 (Ar*C*), 137.0 (Ar*C*), 130.3 (Ar*C*H), 129.8 (Ar*C*H), 129.0 (Ar*C*), 128.1 (Ar*C*H), 120.0 (triazole-*C*H), 118.3 (Ar*C*H), 52.9 (*C*H$_2$NH), 52.1 (O*C*H$_3$), 44.1 (*C*H$_2$NH), 21.3 (*C*H$_3$); IR ν cm^{-1} 2953 (saturated C-H), 1715 (ester C=O), 1614 (C-O); HRMS (ESI$^+$): *m/z* found 351.1808 calc. for $C_{20}H_{23}N_4O_2$ 351.1816 [**3.12**+H]$^+$.

3.13



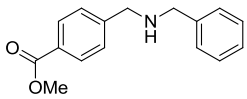
Compound **3.12** (45 mg, 0.13 mmol) was dissolved in CH_2Cl_2 (5 mL). The organic layer was washed with a 10% aqueous solution of $HClO_4$ (3 x 10 mL). The organic layer was separated and dried by passing through filter paper and the solvent removed to provide a pale brown solid which was recrystallised from acetonitrile/Et_2O to provide a white solid (57 mg, 0.13 mmol, 100 %). m.p. 223-224°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.33 (s, 1H, triazole-C*H*), 8.07 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO$_2$), 7.61 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.43 (s, 2H, 2 ArC*H*), 7.19 (s, 1H, ArC*H*), 4.43 (s, 2H, C*H*$_2$NH$_2^+$), 4.37 (s, 2H, $^+$NH$_2$C*H*$_2$), 3.88 (s, 3H, OC*H*$_3$), 2.41 (s, 6H, 2 C*H*$_3$); ^{13}C NMR (150 MHz, 298 K, CD_3CN) δ_C 165.8 (*C*=O), 139.8 (Ar*C*), 137.6 (Ar*C*), 136.3 (Ar*C*), 134.9 (Ar*C*), 131.2 (Ar*C*), 130.3 (Ar*C*H), 130.1 (Ar*C*H), 129.6 (Ar*C*H), 123.5 (triazole-*C*H), 117.9 (Ar*C*H), 51.7 (O*C*H$_3$), 50.0 (*C*H$_2$NH$_2$), 41.7(*C*H$_2$NH$_2$), 20.0 (C*C*H$_3$); IR ν cm^{-1} 1687 (ester C=O), 1106 (ClO_4); HRMS (ESI$^+$): *m/z* found 351.1812 calc for $C_{20}H_{23}N_4O_2$ 351.1816 [**3.13**-ClO_4]$^+$.

3.14



The thread **3.13** (9 mg, 0.02 mmol) and DB24C8 (8.9 mg, 0.02 mmol) were dissolved in deuterated acetonitrile (10 mL). Binding constant = **1060 M^{-1}** was calculated from the single point method[129] by measuring the integration of triazole-C*H* protons for the free and bound thread at 8.33 ppm and 8.04 ppm respectively. The peaks of the pseudorotaxane are partially obscured by free DB24C8 and thread **3.13**. **Pseudorotaxane 3.14** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.04 (m, 1H, ⊂ triazole-C*H*), 7.62 (m, 2H, ⊂ 2 ArC*H*CCO_2), 7.42 (m, 2H, ⊂ 2 ArC*H*CCH_2), 7.23 (s, 2H, ⊂ 2 ArC*H*), 7.15 (s, 1H, ⊂ ArC*H*), 6.92 (m, 4H, ⊂ 4 crown ArC*H*), 6.76 (m, 4H, ⊂ 4 crown ArC*H*), 4.85 (m, 4H, ⊂ $CH_2NH_2^+CH_2$), 4.12-3.68 (m, 27H, ⊂ 12 OCH_2, ⊂ OCH_3) 2.38 (s, 6H, ⊂ 2 CH_3); Also observed for comparison **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); and **Thread 3.13** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.33 (s, 1H, triazole-C*H*), 8.07 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO_2), 7.61 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH_2), 7.43 (s, 2H, 2 ArC*H*), 7.19 (s, 1H, ArC*H*), 4.43 (s, 2H, CH_2NH_2), 4.37 (s, 2H, NH_2CH_2), 3.88 (s, 3H, OCH_3), 2.41 (s, 6H, 2 CH_3); HRMS (ESI$^+$): *m/z* found, 799.3934 calc for $C_{44}H_{55}N_4O_{10}$ 799.3913 [**3.14**-ClO_4]$^+$.

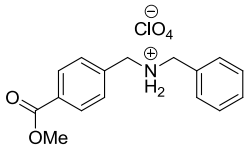
3.15



Known compound synthesised according to a modified literature procedure.[188] Methyl 4-(aminomethyl)benzoate (50 mg, 0.48 mmol) and benzaldehyde (0.031 mL, 0.48 mmol) were dissolved in MeOH (5 mL) and stirred at room temperature. After 24 h sodium borohydride (22 mg, 0.57 mmol) was added and stirred at room temperature for 1 h. The reaction was diluted with water (15 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic

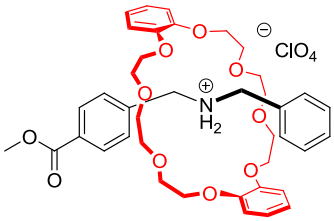
extracts were dried over $MgSO_4$ and the solvent removed *in vacuo* and purified *via* column chromatography (SiO_2: EtOAc) to give a clear oil (100 mg, 0.39 mmol, 82%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.94 (d, 2H, *J* = 8.5 Hz, 2 Ar*C*HCCO$_2$), 7.36 (d, 2H, *J* = 8.5 Hz, 2 Ar*C*HCCH$_2$), 7.28-7.27 (m, 4H, 4 Ar*C*H), 7.21 (m, 1H, Ar*C*H), 3.84 (s, 3H, OC*H*$_3$), 3.80 (s, 2H, C*H*$_2$NH), 3.74 (s, 2H, C*H*$_2$NH); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 167.0 (*C*OO), 144.9 (Ar*C*), 139.2 (Ar*C*), 129.8 (Ar*C*H), 129.0 (Ar*C*), 128.5 (Ar*C*H), 128.3 (Ar*C*H), 128.2 (Ar*C*H), 127.3 (Ar*C*H), 52.9 (*C*H$_2$NH), 52.4 (*C*H$_2$NH), 52.0 (O*C*H$_3$); HRMS (ESI$^+$): *m/z* found, 256.1329 calc for $C_{16}H_{18}NO_2$ 256.1332 [**3.15**+H]$^+$.

3.16



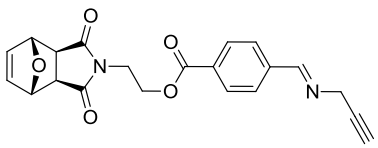
The neutral thread **3.15** (100 mg, 0.78 mmol) was dissolved in CH_2Cl_2 (10 mL) and washed with a 10% aqueous solution of $HClO_4$ (3 x 10 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was recrystallised from acetonitrile/Et_2O to give a white solid (110 mg, 0.31 mmol, 40 %). m.p. 179-180˚C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.05 (d, 2H, *J* = 8.0 Hz, 2 Ar*C*HCCO$_2$), 7.60 (d, 2H, *J* = 8.0 Hz, 2 Ar*C*HCCH$_2$), 7.50-7.45 (m, 5H, 5 Ar*C*H), 4.32 (s, 2H, C*H*$_2$NH$_2^+$), 4.27 (s, 2H, C*H*$_2$NH$_2^+$), 3.88 (s, 2H, OC*H*$_3$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 165.8 (*C*OO), 135.3 (Ar*C*), 131.4 (Ar*C*), 130.5 (Ar*C*H), 130.4 (Ar*C*), 130.3 (Ar*C*H), 129.9 (Ar*C*H), 129.8 (Ar*C*H), 129.1 (Ar*C*H), 52.0 (O*C*H$_3$), 51.6 (*C*H$_2$NH$_2^+$), 50.9 (*C*H$_2$NH$_2^+$); IR ν cm^{-1} 3596 (NH$_2$), 1689 (ester C=O), 1278 (CH$_2$), 1071 (ClO$_4$); HRMS (ESI$^+$): *m/z* found, 256.1332 calc for $C_{16}H_{18}NO_2$ 256.1332 [**3.16**-ClO$_4$]$^+$.

3.17



Thread **3.16** (7.1 mg, 2 mmol) and DB24C8 (8.9 mg, 2 mmol) were dissolved in deuterated acetonitrile (10 mL). Binding constant = **688 M^{-1}** was calculated from the single point method[129] by measuring the integration of ArC*H* protons for the free and bound crown at 6.93 ppm and 6.77 ppm respectively. **Pseudorotaxane 3.17** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.66 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCO_2), 7.47 (s, 5H, ⊂ 2 ArC*H*CCH_2), 7.41-7.40 (m, 3H, ⊂ 3 ArC*H*), 7.28-7.27 (m, 2H, ⊂ 2 ArC*H*), 6.77 (m, 8H, ⊂ 8 crown ArC*H*), 4.81 (m, 2H, ⊂ C$H_2NH_2^+$), 4.66 (m, 2H, ⊂ C$H_2NH_2^+$), 4.06-3.98 (m, 8H, ⊂ 4 OCH_2), 3.93 (s, 3H, ⊂ OCH_3), 3.69 (s, 8H, ⊂ 4 OCH_2), 3.62-3.52 (m, 8H, ⊂ 4 OCH_2); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); and **Thread 3.16** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.05 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO_2), 7.60 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH_2), 7.50-7.45 (m, 5H, 5 ArC*H*), 4.32 (s, 2H, C$H_2NH_2^+$), 4.27 (s, 2H, C$H_2NH_2^+$), 3.88 (s, 2H, OCH_3); MS (ESI$^+$): *m/z* 704.1 [**3.17**-ClO_4]$^+$.

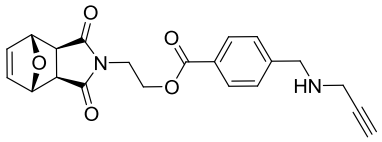
3.18



Aldehyde **2.20** (300mg, 0.9 mmol) was dissolved in MeOH (5 mL) and propargyl amine (0.069 mL, 1.2 mmol) and stirred overnight at room temperature. A precipitate formed which was filtered and washed with MeOH to provide a white solid (276 mg, 0.73 mmol, 81%). m.p. 146-147°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.63 (s, 1H, *H*C=N), 8.03 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*CCO_2), 7.83 (d, 2H, *J* = 8.2 Hz, 2 ArC*H*CC=N), 6.49 (s, 2H, C*H*=C*H*), 5.23 (s, 2H, 2 C*H*O), 4.57 (s, 2H, CH_2N), 4.46 (t, 2H, *J* = 5.2 Hz, CH_2CH_2O), 3.91 (t, 2H, *J* = 5.2 Hz, CH_2CH_2N), 2.86 (s, 2H, C*H*CO), 2.55 (s, 1H, C≡C*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 174.9 (imide *C*=O), 164.7 (*C*OO), 160.3 (H*C*=N), 138.7 (*C*H=*C*H), 135.5 (Ar*C*), 130.7 (Ar*C*H), 129.0 (Ar*C*), 127.1 (Ar*C*H), 79.9 (C*H*O), 77.5 (*C*≡CH), 74.9 (C≡*C*H), 60.8 (CH_2CH_2O), 46.4 (*C*HCO), 46.2 (CH_2N), 36.7 (CH_2CH_2N); IR ν cm^{-1} 3182 (alkyne C-H), 1718 (imide C=O), 1692 (ester C=O); MS (ESI$^+$) : *m/z* 397.1 [**3.18**+H]$^+$; CHN

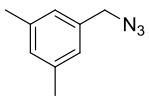
Analysis Found: C 66.40; H 4.81; N 7.33. Calc. for $C_{21}H_{18}N_2O_5$: C, 66.66; H, 4.79; N, 7.40%.

3.19



The imine **3.18** (300 mg, 0.75 mmol) was dissolved in MeOH (5 mL). Sodium cyanoborohydride (88 mg, 1.4 mmol) was added and on addition of a few drops of HOAc the solution clears. The reaction was followed by TLC (EtOAc). After 1 h the imine had been consumed and the product obtained by adding water (20 mL) and extracting with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent removed to provide a yellow oil used without further purification (216 mg, 0.57 mmol, 76%). m.p. 93-95°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.90 (d, 2H, *J* = 8.1 Hz, 2 ArC*H*CCO$_2$), 7.37 (d, 2H, *J* = 8.1 Hz, 2 ArC*H*CCH$_2$), 6.45 (s, 2H, C*H*=C*H*), 5.19 (s, 2H, 2 C*H*O), 4.40 (t, 2H, *J* = 5.5 Hz, CH$_2$C*H*$_2$O), 3.87 (m, 4H, ArC*H*$_2$NH and CH$_2$C*H*$_2$N), 3.39 (s, 2H, NHC*H*$_2$C ≡), 2.82 (s, 2H, 2 C*H*CO), 2.26 (s, 1H, ≡C*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.0 (imide *C*=O), 166.1 (*C*OO), 144.7 (Ar*C*), 136.5 (*C*H=*C*H), 129.9 (Ar*C*H), 128.6 (Ar*C*), 128.3 (Ar*C*H), 81.6 (*C*≡CH), 80.9 (C*H*O), 72.0 (C≡*C*H), 61.2 (CH$_2$*C*H$_2$O), 51.7 (*C*H$_2$NH), 47.4 (*C*HCO), 37.8 (*C*H$_2$NH), 37.2 (CH$_2$*C*H$_2$N); IR ν cm^{-1} 3294 (alkyne C-H), 1698 (ester and imide C=O), 1257 (C-O); HRMS (ESI$^+$): *m/z* found, 381.1445, calc for $C_{21}H_{21}N_2O_5$ 381.1450 [**3.19**+H]$^+$.

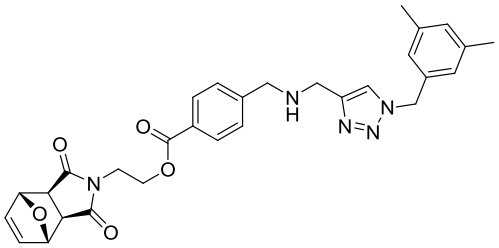
3.20



Known compound data consistent with literature.[189] 3,5 Dimethylbenzyl bromide (250 mg, 1.26 mmol) was dissolved in EtOH (5 mL) and sodium azide (123 mg, 1.89 mmol) was added. It was stirred overnight and a white precipitate formed which was filtered. The liquors were diluted with water (25 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The

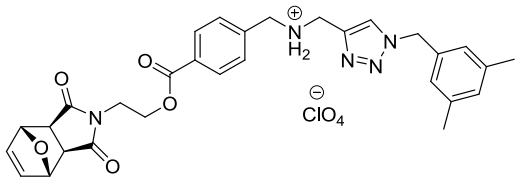
combined organic extracts were dried over $MgSO_4$ and solvent removed *in vacuo* to provide a clear oil (155 mg, 0.96 mmol, 78%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.00 (s, 1H, ArC*H*), 6.95 (s, 2H, 2 ArC*H*), 4.28 (s, 2H, CH_2), 2.35 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 138.5 (Ar*C*), 135.2 (Ar*C*), 129.9 (Ar*C*H), 126.0 (Ar*C*H), 54.9 (CH_2), 21.27 (CH_3); IR ν cm^{-1} 2922 (saturated C-H), 1460 (N=N stretching).

3.21



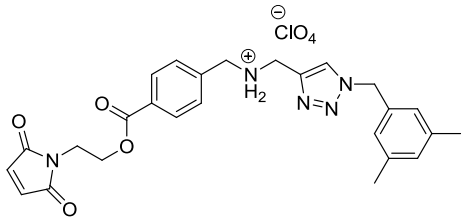
$CuSO_4.5H_2O$ (6.5 mg, 0.026 mmol) and sodium ascorbate (15 mg, 0.078 mmol) were dissolved in THF (3 mL), *t*-Butanol (3 mL) and water (3 mL). The propargyl amine (**3.19**) (100 mg, 0.26 mmol) and the azide (**3.20**) (42 mg, 0.23 mmol) were added and the solution stirred at room temperature for 24 h. The solution was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent removed *in vacuo* to give a pale orange oil purified *via* flash chromatography (SiO_2: EtOAc to EtOAc:MeOH; 4:1) (70 mg, 0.13 mmol, 56%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.95 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.39 (m, 3H, triazole-C*H* and 2 ArC*H*CCH_2), 6.98 (s, 1H, ArC*H*), 6.89 (s, 2H, 2 ArC*H*), 6.49 (s, 2H, C*H*=C*H*), 5.42 (s, 2H, CH_2N-triazole), 5.23 (s, 2H, 2 C*H*O), 4.43 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.80 (br m, 6H, CH_2NHCH_2 and CH_2CH_2N), 2.87 (s, 2H, 2 C*H*CO), 2.30 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide *C*=O), 166.1 (*C*OO), 146.8 (Ar*C*), 145.4 (Ar*C*), 138.8 (Ar*C*), 136.5 (*C*H=*C*H), 134.5 (Ar*C*), 130.3 (Ar*C*H), 129.8 (Ar*C*H), 128.6 (Ar*C*), 128.1 (Ar*C*H), 125.4 (Ar*C*H), 121.6 (triazole-*C*H), 81.2 (C*H*O), 61.1 (CH_2CH_2O), 54.1 (CH_2N-triazole), 52.9 (CH_2NH), 47.5 (*C*HCO), 44.2 (CH_2NH), 37.8 (CH_2CH_2N), 21.2 (CH_3); IR ν cm^{-1} 2918 (saturated C-H), 1698 (imide C=O), 1690 (ester C=O), 1270 (C-O); HRMS (ESI$^+$): *m/z* found, 542.2403 calc for $C_{30}H_{32}N_5O_5$ 542.2398 [**3.21**+H]$^+$.

3.22



Compound **3.21** (50 mg, 0.98 mmol) was dissolved in a 10% aqueous solution of $HClO_4$ (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with an aqueous solution of the $HClO_4$ (5 mL). The organic layer was dried through filter paper and the solvent removed *in vacuo*. The crude yellow solid obtained was purified by precipitation from acetonitrile/Et_2O to provide a pale yellow solid (35 mg, 0.55 mmol, 59%). m.p. 95-97˚C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.98 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO_2), 7.96 (s, 1H, triazole-C*H*), 7.57 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH_2), 7.38 (broad s, 2H, NH_2), 7.01 (s, 1H, ArC*H*), 6.94 (s, 2H, 2 ArC*H*), 6.49 (s, 2H, C*H*=C*H*), 5.50 (s, 2H, CH_2N-triazole), 5.08 (s, 2H, 2 C*H*O), 4.37 (m, 6H, C$H_2NH_2^+CH_2$ and CH_2CH_2O), 3.80 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 2.87 (s, 2H, 2 C*H*CO), 2.27 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.6 (imide *C*=O), 165.3 (*C*OO), 138.7 (Ar*C*), 136.5 (*C*H=*C*H), 135.3 (Ar*C*), 135.4 (Ar*C*), 135.2 (Ar*C*), 131.27 (Ar*C*), 130.4 (Ar*C*H), 129.9 (Ar*C*H), 129.6 (Ar*C*H), 127.9 (*C*H-triazole), 125.4 (Ar*C*H), 80.9 (C*H*O), 61.5 (CH_2CH_2O), 53.7 (CH_2N-triazole), 50.4 ($CH_2NH_2^+$), 47.5 (*C*HCO), 42.2 ($CH_2NH_2^+$), 37.3 (CH_2CH_2N), 20.2 (CH_3); IR ν cm^{-1} 3010 (saturated C-H), 1698 (imide and ester C=O), 1272 (C-O); HRMS (ESI$^+$): *m/z* found, 542.2395 calc for $C_{30}H_{32}N_5O_5$ 542.2398 [**3.22**-ClO_4]$^+$.

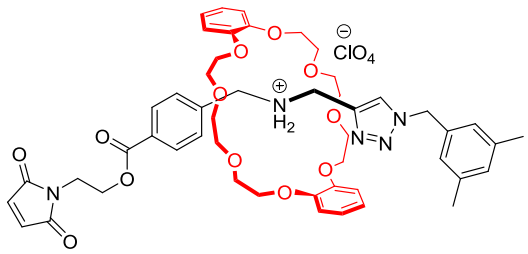
3.23



Compound **3.22** (40 mg, 0.06 mmol) was dissolved in acetonitrile (3 mL). The solution was subjected to microwave irradiation (150 W, 3 h, 110°C) the solvent was removed to provide

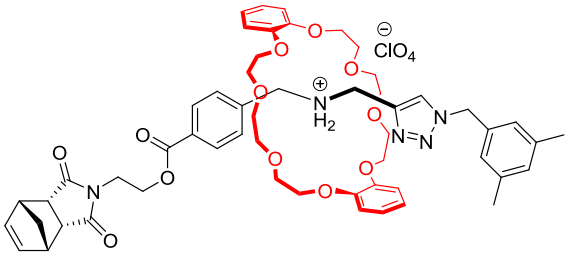
the retro Diels-Alder product as a pale yellow solid which was recrystallised from acetonitrile/Et_2O (31 mg, 0.05 mmol, 86%). m.p. 204-205°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.97 (m, 3H, triazole-C*H* and 2 ArC*H*CCO), 7.59 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.51 (br s, 2H, N*H*$_2$), 7.00 (s, 1H, ArC*H*), 6.93 (s, 2H, 2 ArC*H*), 6.77 (s, 2H, C*H*=C*H*), 5.49 (s, 2H, C*H*$_2$N-triazole), 4.38 (m, 6H, C*H*$_2$NH$_2$C*H*$_2$ and CH$_2$C*H*$_2$O), 3.84 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$N), 2.26 (s, 6H, 2 C*H*$_3$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.6 (imide *C*=O), 165.1 (*C*OO), 138.4 (Ar*C*), 137.1 (Ar*C*), 136.1 (*C*H=*C*H), 135.0 (Ar*C*), 134.9 (Ar*C*), 134.1 (Ar*C*H), 130.9 (Ar*C*), 130.2 (Ar*C*H), 129.6 (Ar*C*H), 125.4 (Ar*C*H), 125.3 (triazole *C*H), 62.2 (CH$_2$*C*H$_2$O), 53.3 (*C*H$_2$N-triazole), 47. 1 (*C*H$_2$NH$_2$), 41.9 (*C*H$_2$NH$_2$), 36.2 (CH$_2$*C*H$_2$N), 19.9 (*C*H$_3$); IR ν cm^{-1} 3100 (NH$_2$), 1710 (imide C=O), 1063 (ClO$_4$); HRMS (ESI$^+$): *m/z* found, 474.2134 calc. for $C_{26}H_{28}N_5O_4$ 474.2136 [**3.23**-ClO$_4$]$^+$.

3.24



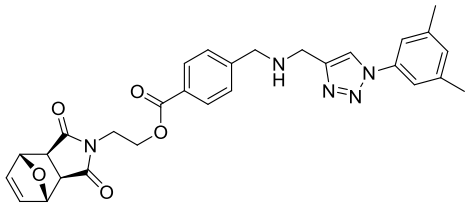
Compound **3.23** (20 mg, 0.035 mmol) was dissolved in deuterated acetonitrile (1 mL) and DB24C8 (63 mg, 0.14 mmol, 4 equiv) was added. After 72 h threading was in favour of pseudorotaxane formation (35.7 mg, 0.035 mmol). **Pseudorotaxane 3.24** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.01 (br s, 2H, NH$_2$), 7.71 (s, 1H, ⊂ C*H*-triazole), 7.48 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCO$_2$), 7.29 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCH$_2$), 6.98 (s, 1H, ⊂ ArC*H*), 6.94 (s, 2H, ⊂ 2 ArC*H*), 6.81 (s, 2H, ⊂ C*H*=C*H*), 6.75 (m, 4H, ⊂ 4 crown ArC*H*), 6.69 (m, 4H, ⊂ 4 crown ArC*H*), 5.37 (s, 2H, ⊂ C*H*$_2$N-triazole), 4.75 (m, 4 H, ⊂ C*H*$_2$NH$_2^+$C*H*$_2$), 4.31 (t, 2H, ⊂ CH$_2$C*H*$_2$O), 4.02-3.56 (m, 26 H, ⊂ CH$_2$C*H*$_2$N and 12 OC*H*$_2$), 2.23 (s, 6H, ⊂ 2 C*H*$_3$); Also contains unbound **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OC*H*$_2$), 3.83 (m, 8H, 4 OC*H*$_2$), 3.72 (s, 8H, 4 OC*H*$_2$); HRMS (ESI$^+$): *m/z* found, 922.4253 calc for $C_{50}H_{60}N_5O_{12}$ 922.4233 [**3.24**-ClO$_4$]$^+$.

3.25



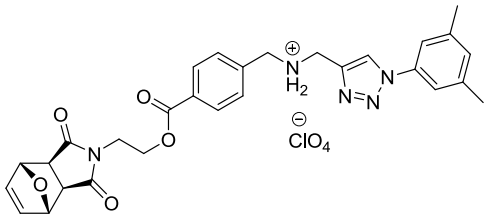
To a solution of pseudorotaxane **3.24** in acetonitrile a few drops of freshly distilled cyclopentadiene were added. The solution was stirred and the solvent and excess cyclopentadiene were removed immediately *in vacuo*. The crude reaction was purified *via* flash chromatography (SiO_2: CH_2Cl_2:acetone 95:5 to CH_2Cl_2:MeOH 95:5) to give the [2]rotaxane (14 mg, 0.013 mmol, 37 %). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.69 (s, 1H, ⊂ triazole-C*H*), 7.53 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCO), 7.31 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCH$_2$), 6.98 (s, 1H, ⊂ ArC*H*), 6.94 (s, 2H, ⊂ 2 ArC*H*), 6.80-6.71 (m, 8H, ⊂ 8 crown ArC*H*), 5.88 (s, 2H, ⊂ C*H*=C*H*), 5.36 (s, 2H, ⊂ C*H*$_2$N-triazole), 4.74 (m, 4 H, ⊂ C*H*$_2$NH$_2^+$C*H*$_2$), 4.31 (t, 2H, *J* = 5.3 Hz ⊂ CH$_2$C*H*$_2$O), 4.29-4.15 (m, 8H, ⊂ 4 OC*H*$_2$), 3.80-3.53 (m, 18H, ⊂ CH$_2$C*H*$_2$N and 8 OC*H*$_2$), 3.27 (broad s, 2H, 2 C*H*CO), 3.23 (broad s, 2H, 2 C*H*CH$_2$), 2.23 (s, 6H, ⊂ 2 C*H*$_3$), 1.58 (d, 1H, *J* = 8.5 Hz, ⊂ C*H*H), 1.55 (d, 1H, *J* = 8.5 Hz, ⊂ CH*H*); ^{13}C NMR (125 MHz, 298 K, CD_3CN) δ_C 177.4 (imide *C*=O), 165.4 (*C*OO), 147.2 (Ar*C*), 138.3 (Ar*C*), 138.1 (Ar*C*), 137.1 (Ar*C*), 135.3 (Ar*C*), 134.3 (*C*H=*C*H), 130.0 (Ar*C*H), 129.8 (Ar*C*), 129.7 (Ar*C*H), 129.4 (Ar*C*H), 126.1 (Ar*C*H), 125.8 (Ar*C*H), 121.5 (triazole-*C*H), 112.5 (Ar*C*H), 70.9 (O*C*H$_2$), 70.3 (O*C*H$_2$), 67.8 (O*C*H$_2$), 61.8 (CH$_2$*C*H$_2$O), 54.0 (*C*H$_2$N-triazole), 52.2 (bridgehead *C*H$_2$), 51.8 (*C*H$_2$NH$_2^+$), 45.8 (*C*HCH$_2$), 45.0 (*C*HCO), 43.9 (*C*H$_2$NH$_2^+$), 37.1 (CH$_2$*C*H$_2$N), 21.2 (*C*H$_3$); IR ν cm^{-1} 2918 (saturated C-H), 1698 (imide and ester C=O), 1252 (C-O), 1091 (ClO_4); HRMS (ESI$^+$): *m/z* found, 988.4726 calc for $C_{55}H_{66}N_5O_{12}$ 988.4702 [**3.25**-ClO_4]$^+$.

3.26



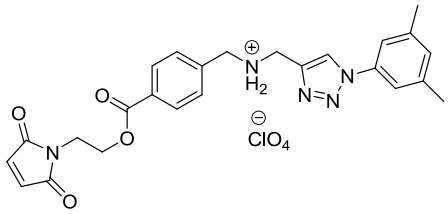
$CuSO_4.5H_2O$ (6.5 mg, 0.03 mmol) and sodium ascorbate (15 mg, 0.08 mmol) were dissolved in *tert*-butanol (5 mL), water (5 mL) and THF (5 mL). The propargyl **3.19** (100 mg, 0.26 mmol) and azide **3.11** (35 mg, 0.23 mmol) were added and stirred at room temperature for 24 h. The reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude reaction mixture was purified *via* flash chromatography (SiO_2: EtOAc to EtOAc:MeOH; 85:15) to give a colourless oil (97 mg, 0.18 mmol, 80%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.97 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.87 (s, 1H, triazole-C*H*), 7.44 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.34 (broad s, 2H, 2 ArC*H*), 7.09 (s, 1H, ArC*H*), 6.50 (s, 2H, C*H*=C*H*), 5.25 (s, 2H, 2 C*H*O), 4.45 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$O), 3.91 (broad m, 6H, C*H*$_2$NH$_2$C*H*$_2$ and CH$_2$C*H*$_2$N), 2.89 (s, 2H, 2 C*H*CO), 2.41 (s, 6H, 2 C*H*$_3$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 175.9 (imide *C*=O), 166.1 (*C*OO), 147.1 (Ar*C*), 145.4 (Ar*C*), 139.7 (Ar*C*), 137.0 (Ar*C*), 136.5 (*C*H=*C*H), 130.3 (Ar*C*H), 130.0 (Ar*C*H), 128.6 (Ar*C*), 128.1 (Ar*C*H), 120.0 (triazole-*C*H), 118.3 (Ar*C*H), 80.9 (*C*HO), 61.2 (CH$_2$*C*H$_2$O), 52.9 (*C*H$_2$NH), 47.5 (*C*HCO), 44.1 (*C*H$_2$NH), 37.8 (CH$_2$*C*H$_2$N), 21.3 (*C*H$_3$); IR ν cm^{-1} 2914 (saturated C-H), 1698 (imide and ester C=O), 1271 (C-O); HRMS (ESI$^+$) : *m/z* found, 528.2238 calc for $C_{29}H_{30}N_5O_5$ 528.2241 [**3.26**+H]$^+$.

3.27



Compound **3.26** (100 mg, 0.2 mmol), was dissolved in CH_2Cl_2 (5 mL) and washed with a 10% aqueous solution of $HClO_4$ (2 x 10 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude solid was recrystallised from acetonitrile/Et_2O to provide a yellow solid (80 mg, 0.13 mmol, 68%). m.p. 150-151°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.35 (s, 1H, triazole C*H*), 8.02 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO$_2$), 7.60 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.43 (broad s, 4H, N*H*$_2$ and 2 ArC*H*), 7.19 (s, 1H, ArC*H*), 6.49 (s, 2H, C*H*=C*H*), 5.09 (s, 2H, 2 C*H*O), 4.45 (broad s, 2H, C*H*$_2$NH$_2$), 4.38 (m, 4H, C*H*$_2$NH$_2$ and CH$_2$C*H*$_2$O), 3.80 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$N), 2.87 (s, 2H, 2 C*H*CO), 2.41 (s, 6H, 2 C*H*$_3$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.3 (imide *C*=O), 165.0 (*C*OO), 139.8 (Ar*C*), 137.6 (Ar*C*), 136.3 (Ar*C*), 136.1 (Ar*C*) 135.0 (*C*H=*C*H), 134.1 (Ar*C*), 130.8 (Ar*C*H), 130.0 (Ar*C*H), 129.6 (Ar*C*H), 123.4 (triazole-*C*H), 117.9 (Ar*C*H), 80.6 (C*H*O), 61.6 (CH$_2$*C*H$_2$O), 49.9 (*C*H$_2$NH$_2$), 47.1 (*C*HCO), 41.7 (*C*H$_2$NH$_2$), 36.9 (CH$_2$*C*H$_2$N), 20.0 (C*H*$_3$); IR ν cm^{-1} 3163 (NH stretching), 1700 (imide C=O stretching), 1061 (ClO_4); HRMS (ESI$^+$): *m/z* found, 528.2239 calc for $C_{29}H_{30}N_5O_5^+$ 528.2241 [**3.27**-ClO_4]$^+$.

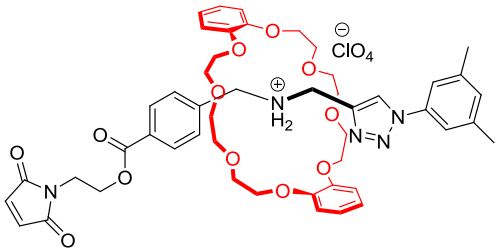
3.28



Compound **3.27** (50 mg, 0.08 mmol) was dissolved in acetonitrile (1 mL) and reacted under microwave irradiation (150W, 110 °C, 3 h). The solvent and furan were removed *in vacuo* to provide a beige solid (41 mg, 0.073 mmol, 92%). m.p 204-205°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.36 (s, 1H, triazole-C*H*), 8.01 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.61 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.43 (s, 2H, 2 ArC*H*), 7.18 (s, 1H, ArC*H*), 6.77 (s, 2H, C*H*=C*H*), 4.45 (broad s, 2H, C*H*$_2$NH$_2^+$), 4.39 (m, 4H, C*H*$_2$NH$_2^+$ and CH$_2$C*H*$_2$O), 3.84 (t, 2H, *J* = 5.3 Hz, CH$_2$C*H*$_2$N), 2.41 (s, 6H, 2 C*H*$_3$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.9 (imide *C*=O), 165.4 (*C*OO), 140.1 (Ar*C*), 137.9 (Ar*C*), 136.6 (Ar*C*), 136.5 (*C*H=*C*H), 135.3 (Ar*C*),

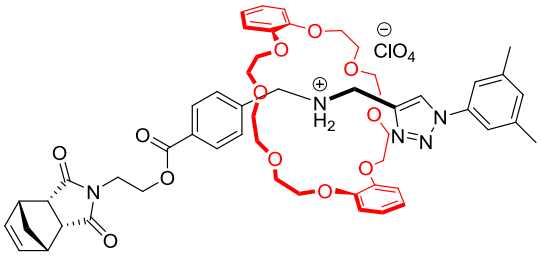
131.2 (Ar*C*), 130.7 (Ar*C*H), 130.5 (ArC*H*), 130.2 (Ar*C*H), 123.8 (triazole *C*H), 118.3 (Ar*C*H), 62.5 (CH_2CH_2O), 50.4 ($CH_2NH_2^+$), 42.1 ($CH_2NH_2^+$), 36.6 (CH_2CH_2N), 20.3 (CH_3); IR ν cm^{-1} 3092 (saturated C-H), 1723 (imide C=O), 1072 (ClO_4); HRMS (ESI^+): found, 460.1990 calc for $C_{25}H_{26}N_5O_4$ 460.1979 [**3.28**-ClO_4]$^+$; CHN Analysis Found: C 53.13; H 4.65; N 12.10. Calc. for $C_{25}H_{26}N_5O_8Cl$: C, 53.62; H, 4.68; N, 12.51%.

3.29



Thread **3.28** (10mg, 0.018 mmol) was dissolved in deuterated acetonitrile. DB24C8 (40 mg, 4 equivalents, 0.072 mmol) was added to the mixture. Pseudorotaxane formation was monitored by ^{1}H NMR. **Pseudorotaxane 3.29** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.05 (s, 1H, ⊂ triazole-C*H*), 7.91 (broad s, ⊂ NH_2), 7.59 (m, 2H, ⊂ 2 ArC*H*CCO), 7.40 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCH_2), 7.23 (s, 2H, ⊂ 2 ArC*H*), 7.14 (s, 1H, ⊂ ArC*H*), 6.80 (s, 2H, ⊂ C*H*=C*H*), 6.75 (m, 8H, ⊂ 8 crown ArC*H*), 4.89 (m, 2H, ⊂ $CH_2NH_2^+$), 4.82 (m, 2H, ⊂ CH_2NH_2), 4.34 (t, 2H, *J* = 5.0 Hz, ⊂ CH_2CH_2O), 4.09-4.06 (m, 8H, ⊂ 4 OCH_2), 3.94 -3.86 (m, 10H, ⊂ 4 OCH_2, ⊂ CH_2CH_2N), 3.76 (s, 8H, ⊂ 4 OCH_2), 2.38 (s, 6H, ⊂ 2 CH_3); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2).

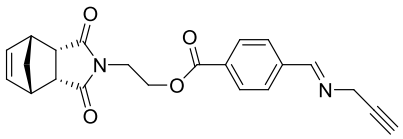
3.30



To the pseudorotaxane **3.29** in acetonitrile was added a few drops of freshly distilled cyclopentadiene. Excess cyclopentadiene and acetonitrile were removed *in vacuo*. The solid

was extracted with hot benzene (3 x 5 mL) to remove excess crown leaving [2]rotaxane (12 mg, 0.11 mmol, 62 %). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.05 (s, 1H, ⊂ triazole-C*H*), 7.97 (broad s, 2H, ⊂ NH_2), 7.68 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCO), 7.49 (d, 2H, *J* = 8.0 Hz, ⊂ 2 ArC*H*CCH_2), 7.25 (s, 2H, ⊂ 2 ArC*H*), 7.18 (s, 1H, ⊂ ArC*H*), 6.81 (s, 8H, ⊂ 8 crown ArC*H*), 5.93 (s, 2H, ⊂ C*H*=C*H*), 4.90 (m, 4H, ⊂ C$H_2NH_2^+CH_2$), 4.27 (t, 2H, ⊂ CH_2CH_2O), 4.09 (m, 8H, ⊂ 4 OCH_2), 3.90 (m, 4H, ⊂ 2 OCH_2), 3.84 (m, 4H, ⊂ 2 OCH_2), 3.75 (s, 8H, ⊂ 4 OCH_2), 3.68 (t, 2H, ⊂ CH_2CH_2N), 3.30 (s, 2H, ⊂ 2 C*H*CO), 3.26 (s, 2H, ⊂ 2 C*H*CH_2), 2.24 (s, 6H, ⊂ 2 CH_3), 1.60 (d, 1H, *J* = 9.0 Hz, ⊂ C*H*H), 1.57 (d, 1H, *J* = 9.0 Hz, ⊂ CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 178.9 (imide *C*=O), 166.5 (*C*OO), 148.6 (Ar*C*), 141.2 (Ar*C*), 140.9 (Ar*C*), 138.1 (Ar*C*), 137.8 (Ar*C*), 135.6 (*C*H=*C*H), 131.8 (ArCH), 131.5 (Ar*C*), 131.3 (Ar*C*H), 130.7 (Ar*C*H), 123.9 (Ar*C*H), 122.5 (triazole-*C*H), 119.6 (Ar*C*H), 113.7 (Ar*C*H), 72.1 (O*C*H_2), 71.6 (O*C*H_2), 69.0 (O*C*H_2), 62.9 (CH_2*C*H_2O), 53.4 (bridgehead *C*H_2), 53.1 (*C*$H_2NH_2^+$), 47.0 (*C*HCH_2), 46.1 (*C*HCO), 44.9 (*C*$H_2NH_2^+$), 38.2 (CH_2*C*H_2N), 21.6 (*C*H_3); IR ν cm^{-1} 2924 (saturated C-H), 1697 (imide and ester C=O), 1251 (C-O), 1093 (ClO_4); HRMS (ESI$^+$): *m/z* found, 974.4550 calc for, $C_{54}H_{64}N_5O_{12}$ 974.4546 [**3.30**-ClO_4]$^+$.

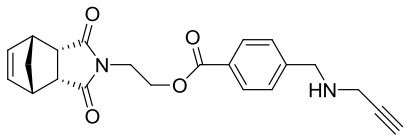
3.31



To **2.27** (100 mg, 0.29 mmol) in MeOH (5 mL), propargyl amine (0.023 mL, mmol) was added. The solution was stirred at room temperature overnight. The reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent removed *in vacuo* to provide a yellow oil used without further purification (95 mg, 0.25 mmol, 86%). ^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ_H 8.63 (s, 1H, C*H*=N), 8.03 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.84 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH), 5.96 (s, 2H, C*H*=C*H*), 4.56 (s, 2H, CH_2N), 4.33 (t, 2H, *J* = 5.0 Hz, CH_2CH_2O), 3.77 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.34 (s, 2H, 2 C*H*CO), 3.27 (broad s, 2H, 2

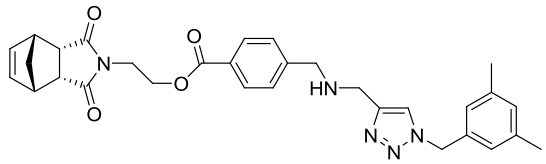
C*H*CH$_2$), 2.56 (s, 1H, C≡C*H*), 1.66 (d, 1H, *J* = 9.0 Hz, CH*H*), 1.52 (d, 1H, *J* = 9.0 Hz, C*H*H); ^{13}C NMR (100 MHz, 298 K, CDCl$_3$) δ_C 177.9 (imide *C*=O), 165.5 (*C*OO), 161.1 (*C*H=N), 139.6 (Ar*C*), 134.1 (*C*H=*C*H), 131.4 (Ar*C*), 129.8 (Ar*C*H), 128.1 (Ar*C*H), 78.5 (*C*≡CH), 76.1 (C≡*C*H), 61.9 (CH$_2$*C*H$_2$O), 52.2 (bridgehead *C*H$_2$), 47.2 (*C*H$_2$N), 45.8 (*C*HCH$_2$), 44.9 (*C*HCO), 37.1 (CH$_2$*C*H$_2$N); IR ν cm^{-1} 2946 (saturated C-H), 1693 (imide and ester C=O), 1647 (C=N), 1268 (C-O); MS (ESI$^+$): *m/z* 377.2 [**3.31**+H]$^+$.

3.32



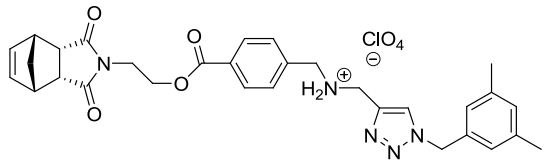
To the imine **3.31** (100mg, 0.27 mmol) in MeOH (3 mL), sodium cyanoborohydride (20 mg, 0.3 mmol) and HOAc (2 drops) were added. The solution was stirred at room temperature for 2 h. The mixture was diluted with water (10 mL) and extracted with CH$_2$Cl$_2$ (3 x 10 mL). The combined organic extracts were dried over MgSO$_4$ and the solvent removed *in vacuo*. The crude product was purified *via* flash chromatography (SiO$_2$: CH$_2$Cl$_2$:MeOH; 95:5) to provide a yellow oil (87 mg, 0.23 mmol, 85%). ^{1}H NMR (400 MHz, 298 K, CDCl$_3$) δ_H 7.93 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.40 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH), 5.96 (s, 2H, 2 C*H*=CH), 4.29 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$O), 3.92 (s, 2H, C*H*$_2$NH), 3.75 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$N), 3.41 (s, 2H, C*H*$_2$C≡CH), 3.33 (s, 2H, 2 C*H*CO), 3.25 (broad s, 2H, 2 C*H*CH$_2$), 2.27 (s, 1H, C≡C*H*), 1.65 (d, 1H, *J* = 9.0 Hz, C*H*H), 1.49 (d, 1H, *J* = 9.0 Hz, C*H*H); ^{13}C NMR (100 MHz, 298 K, CDCl$_3$) δ_C 177.5 (imide *C*=O), 166.1 (*C*OO), 144.7 (Ar*C*), 134.5 (*C*H=*C*H), 129.8 (Ar*C*), 128.9 (Ar*C*H), 128.7 (Ar*C*H), 81.5 (*C*≡CH), 72.05 (C≡*C*H), 61.7 (CH$_2$*C*H$_2$O), 53.5 (bridgehead *C*H$_2$), 52.2 (*C*H$_2$C≡CH), 51.7 (*C*H$_2$NH), 45.8 (*C*HCH), 44.8 (*C*HCO), 37.26 (CH$_2$*C*H$_2$N); IR ν cm^{-1} 3267 (N-H), 2987 (saturated C-H), 1692 (imide and ester C=O); HRMS (ESI$^+$): *m/z* found, 379.1648 calc for C$_{22}$H$_{23}$N$_2$O$_4$ 379.1652 [**3.32**+H]$^+$.

3.33



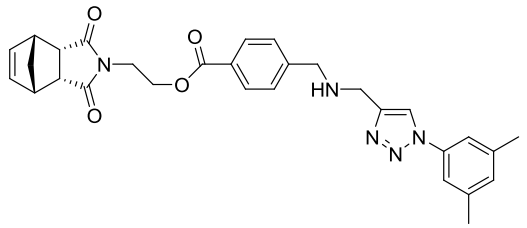
$CuSO_4.5H_2O$ (6 mg, 0.02 mmol) and sodium ascorbate (14 mg, 0.08 mmol) were dissolved in *tert*-butanol (5 mL), THF (5 mL) and water (5 mL). The propargyl amine **3.32** (90 mg, 0.24 mmol) and azide **3.06** (38 mg, 0.24 mmol) were added and the solution stirred at room temperature for 48 h. The solution was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified *via* column chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 95:5) to give a yellow oil (80 mg, 0.15 mmol, 63%). ^{1}H NMR (400 MHz, 298 K, CD_3Cl) δ_H 7.97 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.41 (m, 3H, 2 ArC*H*CCH$_2$ and triazole-C*H*), 7.01 (s, 1H, ArC*H*), 6.92 (s, 2H, 2 ArC*H*), 6.01 (s, 2H, C*H*=C*H*), 5.45 (s, 2H, C*H*$_2$N-triazole), 4.34 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$O), 3.91-3.90 (broad m, 4H, C*H*$_2$NHC*H*$_2$), 3.80 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$N), 3.39 (s, 2H, 2 C*H*CO), 3.30 (s, 2H, 2 C*H*CH$_2$), 2.32 (s, 6H, 2 C*H*$_3$), 1.72 (d, 1H, *J* = 9.0 Hz, CH*H*), 1.54 (d, 1H, *J* = 9.0 Hz, C*H*H); ^{13}C NMR (100 MHz, 298 K, CD_3Cl) δ_C 177.4 (imide *C*=O), 166.1 (*C*OO), 146.8 (Ar*C*), 145.4 (Ar*C*), 138.8 (Ar*C*), 134.5 (Ar*C*), 134.3 (*C*H=*C*H), 130.4 (Ar*C*H), 129.9 (Ar*C*H), 128.5 (Ar*C*), 128.2 (Ar*C*H), 126.0 (Ar*C*H), 121.6 (triazole-*C*H), 61.7 (CH$_2$*C*H$_2$O), 54.2 (*C*H$_2$N-triazole), 53.0 (*C*H$_2$NH), 52.2 (bridgehead *C*H$_2$), 45.8 (*C*HCH$_2$), 45.0 (*C*HCO), 44.2 (*C*H$_2$NH), 37.2 (CH$_2$*C*H$_2$N), 21.2 (*C*H$_3$); IR ν cm^{-1} 2994 (saturated C-H), 1694 (imide and ester C=O), 1609 (C-O); HRMS (ESI$^+$): *m/z* 540.2608 calc for $C_{31}H_{34}N_5O_4$ 540.2605 [**3.33**+H]$^+$.

3.35



The neutral thread (50 mg, 0.093 mmol) was dissolved in CH_2Cl_2 (5 mL). The organic layer was washed with a 10% aqueous solution of $HClO_4$ (3 x 10 mL) and dried through filter paper. The solvent was removed and the crude solid recrystallised from acetonitrile/Et_2O to give an off white solid (30 mg, 0.055 mmol, 59%). m.p. 144-146°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.02 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.97 (s, 1H, triazole-C*H*), 7.59 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.40 (br s, 2H, N*H*$_2$), 7.01 (s, 1H, ArC*H*), 6.94 (s, 2H, 2 ArC*H*), 5.93 (s, 2H, C*H*=C*H*), 5.50 (s, 2H, C*H*$_2$N-triazole), 4.36 (br m, 4H, C*H*$_2$NH$_2^+$C*H*$_2$), 4.29 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$O), 3.67 (t, 2H, *J* = 5.0 Hz, CH$_2$C*H*$_2$N), 3.28 (s, 2H, 2 C*H*CO), 3.24 (s, 2H, 2 C*H*CH$_2$), 2.27 (s, 6H, 2 C*H*$_3$), 1.59 (d, 1H, *J* = 8.5 Hz, C*H*H), 1.56 (d, 1H, *J* = 8.5 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 177.8 (imide *C*=O), 165.0 (*C*OO), 138.4 (Ar*C*), 137.1 (Ar*C*), 135.0 (Ar*C*), 134.9 (Ar*C*), 133.9 (*C*H=*C*H), 131.2 (Ar*C*), 130.1 (Ar*C*H), 129.6 (Ar*C*H), 125.3 (Ar*C*H), 125.1 (Ar*C*H), 120.1 (triazole-*C*H), 61.7 (CH$_2$*C*H$_2$O), 53.3 (*C*H$_2$N-triazole), 51.5(bridgehead *C*H$_2$), 50.0 (*C*H$_2$NH$_2^+$), 45.3 (*C*HCH$_2$), 44.3 (*C*HCO), 41.8 (*C*H$_2$NH$_2^+$), 36.6 (CH$_2$*C*H$_2$N), 19.9 (*C*H$_3$); IR ν cm^{-1} 3151 (saturated C-H), 1701 (ester and imide C=O), 1102 (ClO_4); HRMS (ESI$^+$): *m/z* found, 540.2607 calc for, $C_{31}H_{34}N_5O_4$ 540.2605 [**3.35**-ClO_4]$^+$.

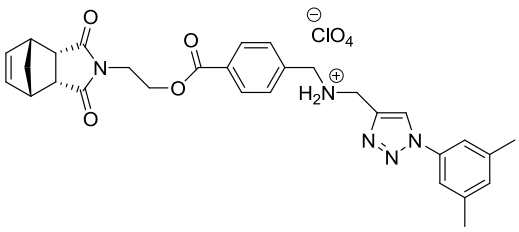
3.34



$CuSO_4.5H_2O$ (21 mg, 0.08 mmol) and sodium ascorbate (51 mg, 0.25 mmol) were dissolved in *tert*-butanol (5 mL), THF (5 mL) and water (5 mL). The propargyl amine **3.32** (300 mg, 0.8 mmol) and azide **3.11** (114 mg, 0.8 mmol) were added and the solution stirred at room temperature for 48 h. The solution was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was subjected to column chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 95:5) to give a yellow oil (150 mg, 0.29 mmol, 36%). ^{1}H NMR

(400 MHz, 298 K, $CDCl_3$) δ_H 7.98 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO_2), 7.90 (s, 1H, triazole-C*H*), 7.46 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH_2), 7.35 (s, 2H, 2 ArC*H*), 7.07 (s, 1H, ArC*H*), 6.06 (s, 2H, C*H*=C*H*), 4.33 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 4.02 (br s, 2H, CH_2NH), 3.96 (br s, 2H, CH_2NH), 3.79 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.37 (s, 2H, 2 C*H*CO), 3.28 (s, 2H, 2 C*H*CH_2), 2.41 (s, 6H, 2 CH_3), 1.69 (d, 1H, *J* = 9.0 Hz, C*H*H), 1.55 (d, 1H, *J* = 9.0 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 177.4 (imide *C*=O), 166.0 (*C*OO), 145.6 (Ar*C*), 137.7 (Ar*C*), 139.6 (Ar*C*), 136.9 (Ar*C*), 134.4 (*C*H=*C*H), 134.3 (Ar*C*H), 130.3 (Ar*C*H), 129.9 (Ar*C*H), 128.7 (Ar*C*), 128.4 (Ar*C*H), 118.3 (triazole-*C*H), 61.6 (CH_2CH_2O), 53.1 (CH_2NH), 52.1 (bridgehead CH_2), 45.8 ($CHCH_2$), 44.9 (*C*HCO), 41.2 (CH_2NH), 37.2 (CH_2CH_2N), 21.3 (CH_3); IR ν cm^{-1} 2943 (saturated C-H), 1700 (ester and imide C=O), 1613 (C≡C); HRMS (ESI^+): *m/z* found, 526.2448 calc for $C_{30}H_{32}N_5O_4$ 526.2449 [**3.34**+H]$^+$.

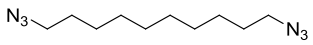
3.36



The neutral thread (50 mg, 0.095 mmol) was dissolved in CH_2Cl_2 (5 mL). The organic layer was washed with a 10% aqueous solution of $HClO_4$ 10% (3 x 10 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* and the crude product recrystallised from acetonitrile/Et_2O to give a cream solid (40 mg, 0.06 mmol, 67%). m.p. 145-146°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.34 (s, 1H, C*H*-triazole), 8.04 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO_2), 7.62 (d, 2H, *J* = 8.5 Hz, 2 ArC*H*CCH_2), 7.43 (s, 2H, 2 ArC*H*), 7.19 (s, 1H, ArC*H*), 5.94 (s, 2H, C*H*=C*H*), 4.44 (br s, 2H, $CH_2NH_2^+$), 4.38 (br s, 2H, $CH_2NH_2^+$), 4.29 (t, 2H, *J* = 5.3 Hz, CH_2CH_2O), 3.67 (t, 2H, *J* = 5.0 Hz, CH_2CH_2N), 3.27 (s, 2H, 2 C*H*CO), 3.24 (s, 2H, 2 C*H*CH_2), 2.41 (s, 6H, 2 CH_3), 1.60 (d, 2H, *J* = 8.5 Hz, C*H*H), 1.57 (d, 2H, *J* = 8.5 Hz, CH*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 177.7 (imide *C*=O), 165.4 (*C*OO), 140.1 (Ar*C*), 136.6 (Ar*C*), 135.4 (Ar*C*), 134.3 (*C*H=*C*H), 131.2 (Ar*C*), 130.7 (Ar*C*H), 130.5 (Ar*C*H), 130.0 (Ar*C*H), 128.0 (Ar*C*), 123.8 (triazole-*C*H), 118.3 (Ar*C*H), 62.0 (CH_2CH_2O),

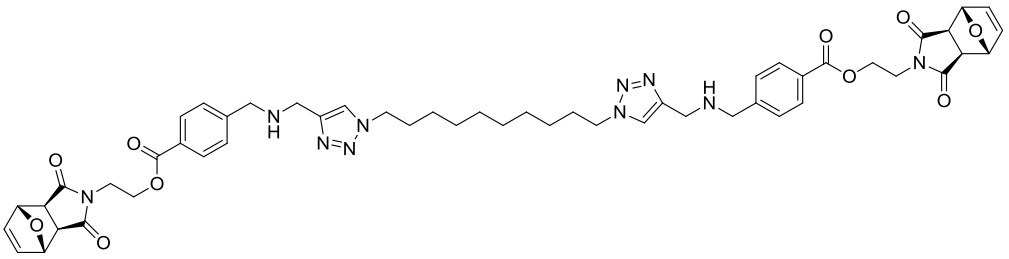
51.8 (bridgehead CH_2), 50.3 ($CH_2NH_2^+$), 45.6 ($CHCH_2$), 44.7 ($CHCO$), 42.0 ($CH_2NH_2^+$), 36.9 (CH_2CH_2N), 20.3 (CH_3); IR ν cm^{-1} 3305 (NH), 1686 (imide and ester C=O); HRMS (ESI^+): *m/z* found, 526.2450 calc for, 526.2449 [**3.36**-ClO_4]$^+$.

3.38



Known compound data consistent with literature.[190] 1,10-dibromodecane (2.5 g, 8.42 mmol) was dissolved in DMF (25 mL). Sodium azide (2.9 g, 44.6 mmol) was added and the solution heated to 60°C for 24 h. The DMF was removed *in vacuo* and the residue diluted with water (20 mL). The solution was extracted with CH_2Cl_2 (3 x 20 mL), the combined organic extracts were washed with water and dried over $MgSO_4$ and the oil purified *via* flash chromatography (SiO_2: petroleum ether/EtOAc 95:5) to provide a clear liquid (1.88 g, 8.40 mmol, 100%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 3.27 (t, 4H, J = 7.0 Hz, 2 CH_2N_3), 1.60 (m, 4H, 2 CH_2), 1.39-1.31 (m, 12H, $CH_2(CH_2)_6CH_2$); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 51.4 (CH_2N_3), 29.3 (CH_2), 29.0 (CH_2), 28.8 (CH_2), 26.6 (CH_2); IR ν cm^{-1} 2927 (C-H stretching), 2087 (-N_3).

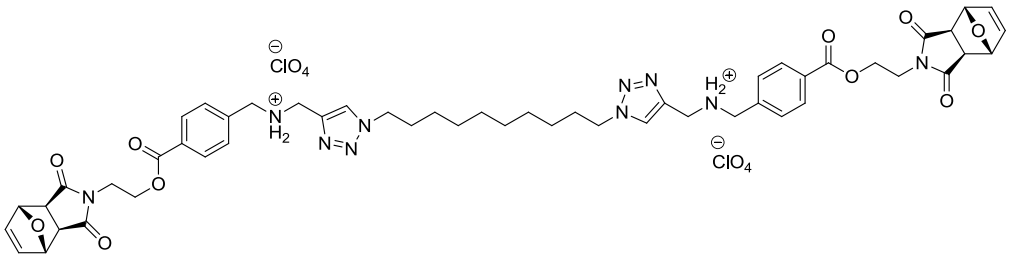
3.39



Propargyl amine **3.19** (650 mg, 1.7 mmol) and 1,10-diazidodecane **3.38** (250 mg, 1.02 mmol) were dissolved in a two phase solution of CH_2Cl_2 (10 mL) and water (10 mL). Sodium ascorbate (75 mg, 0.37 mmol) and $CuSO_4.5H_2O$ (28 mg, 0.11 mmol) were added and the solution was stirred at room temperature for 24 h. The organic layer was removed and the aqueous was further extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The crude residue was purified *via* flash chromatography (SiO_2: gradient elution CH_2Cl_2:MeOH; 100:0

to 90:10) to give a pale orange solid (100 mg, 0.07 mmol, 10%). m.p. 124-125 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.95 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCO$_2$), 7.46 (s, 2H, 2 triazole-C*H*), 7.39 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH$_2$), 6.49 (s, 4H, 2 C*H*=C*H*), 5.23 (s, 4H, 4 C*H*O), 4.43 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$O), 4.32 (t, 4H, *J* = 7.0 Hz, 2 C*H*$_2$N-triazole), 3.91-3.88 (m, 12H, 2 CH$_2$C*H*$_2$N and 2 C*H*$_2$NHC*H*$_2$), 2.99 (br s, 2H, 2 N*H*), 2.86 (s, 4H, 4 C*H*CO), 1.87 (br m, 4H, 2 triazole-NCH$_2$C*H*$_2$), 1.29-1.25 (br m, 12H, CH$_2$(C*H*$_2$)$_6$CH$_2$); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide *C*=O), 166.1 (*C*OO), 146.0 (Ar*C*), 144.9 (Ar*C*), 136.6 (*C*H=*C*H), 129.9 (Ar*C*H), 128.7 (Ar*C*), 127.8 (Ar*C*H), 121.7 (triazole-*C*H), 80.9 (*C*HO), 61.2 (CH$_2$*C*H$_2$O), 53.4 (*C*H$_2$NH), 50.7 (*C*H$_2$N-triazole), 47.5 (*C*HCO), 43.9 (*C*H$_2$NH), 37.8 (CH$_2$*C*H$_2$N), 30.2 (*C*H$_2$), 29.2 (*C*H$_2$), 28.9 (*C*H$_2$), 26.4 (*C*H$_2$); IR ν cm^{-1} 2957 (saturated C-H), 1699 (imide C=O), 1431 (C-O); HRMS (ESI$^+$): *m/z* 985.4603 calc for $C_{52}H_{61}N_{10}O_{10}$ 985.4567 [**3.39**+H]$^+$.

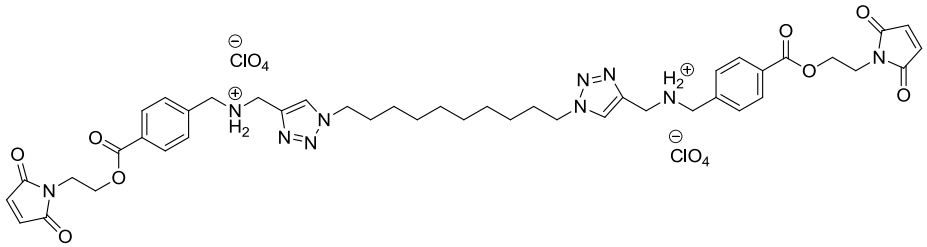
3.40



The neutral thread **3.39** (100 mg, 0.1 mmol) was dissolved in CH_2Cl_2 (5 mL). The organic layer was washed with a 10% aqueous solution of $HClO_4$ (3 x 10 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* and the crude solid recrystallised from acetonitrile/Et_2O to provide a white solid (120 mg, 0.1 mmol, 100 %). m.p.176-177°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.01 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCO$_2$), 7.93 (s, 2H, 2 triazole-C*H*), 7.78 (br s, 4H, 2 N*H*$_2$), 7.62 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH$_2$), 6.49 (s, 4H, 2 C*H*=C*H*), 5.08 (s, 4H, 4 C*H*-O), 4.66-4.60 (m, 8H, 2 C*H*$_2$N-triazole, 2 C*H*$_2$NH$_2^+$), 4.45 (broad s, 4H, 2 C*H*$_2$NH$_2^+$), 4.38 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$O), 3.80 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$N), 2.87 (s, 4H, 4 C*H*CO), 1.95 (br m, 4H, 2 NCH$_2$C*H*$_2$), 1.32-1.28 (br m, 12H, CH$_2$(C*H*$_2$)$_6$CH$_2$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.3 (imide

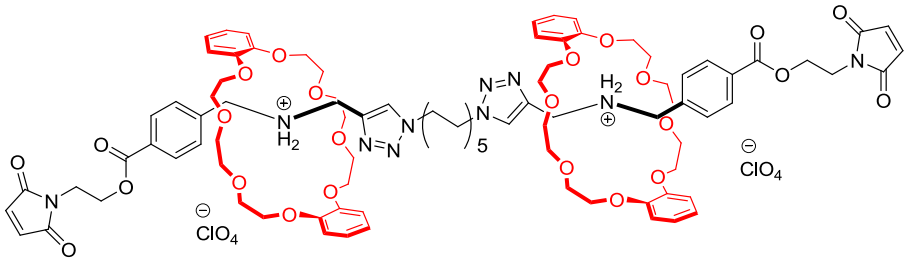
C=O), 164.9 (*C*OO), 136.5 (*C*H=*C*H), 134.5 (Ar*C*), 133.3 (Ar*C*), 131.5 (Ar*C*), 130.7 (triazole-*C*H), 130.4 (Ar*C*HCCO$_2$), 130.1 (Ar*C*), 80.9 (C*H*O), 61.5 (CH_2*C*H_2O), 54.1 (*C*$H_2NH_2^+$), 51.5 (*C*$H_2NH_2^+$), 47.5 (*C*HCO), 39.3 (triazole-N*C*H_2), 37.3 (CH_2*C*H_2N), 28.9 (*C*H_2), 28.7 (*C*H_2), 28.4 (*C*H_2), 25.5 (*C*H_2); IR ν cm^{-1} 1694 (imide and ester C=O), 1276 (C-O), 1057 (ClO_4).

3.41



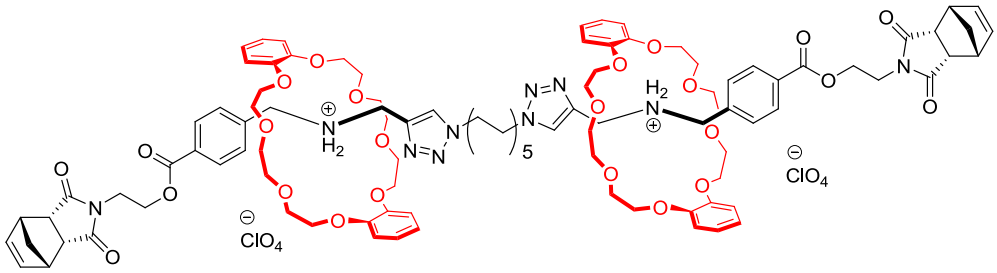
The perchlorate salt **3.40** (120 mg, 0.10 mmol) was dissolved in acetonitrile (3 mL) and reacted under microwave irradiation (150 W, 180 minutes, 110°C). The solvent and furan were removed under reduced pressure to provide a yellow solid (98 mg, 0.10 mmol, 100 %). m.p. 72-73°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.02-8.00 (m, 6H, 4 ArC*H*CCO$_2$ and 2 triazole-C*H*), 7.64 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH$_2$), 6.81 (s, 4H, 2 C*H*=C*H*), 4.46-4.37 (m, 16H, 2 C*H*$_2$NH$_2^+$C*H*$_2$, 2 CH$_2$C*H*$_2$O and 2 C*H*$_2$N-triazole), 3.87 (t, 4H, *J* = 5.3 Hz, 2 CH$_2$C*H*$_2$N), 1.86 (br m, 4H, 2 NCH$_2$C*H*$_2$), 1.30-1.25 (br m, 12H, CH$_2$(C*H*$_2$)$_6$CH$_2$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.6 (imide *C*=O), 165.1 (*C*OO), 134.9 (Ar*C*), 134.1 (*C*H=*C*H), 130.9 (Ar*C*), 130.2 (Ar*C*H), 129.6 (Ar*C*H), 127.3 (Ar*C*), 125.0 (triazole-*C*H), 62.2 (CH_2*C*H_2O), 50.0 (*C*$H_2NH_2^+$), 49.9 (*C*$H_2NH_2^+$), 41.9 (*C*H$_2$N-triazole), 36.2 (CH_2*C*H_2N), 29.5 (*C*H_2), 28.5 (*C*H_2), 28.1 (*C*H_2), 25.6 (*C*H_2); IR ν cm^{-1} 2930 (saturated C-H), 1704 (imide and ester C=O), 1273 (C-O), 1071 (ClO_4); HRMS (ESI$^+$) : *m/z* 425.2053 calc for $C_{44}H_{54}N_{10}O_8$ 425.2058 [**3.41**-2ClO_4]$^{2+}$.

3.42



Thread **3.41** (10 mg, 0.01 mmol) was dissolved in deuterated acetonitrile along with DB24C8 (36 mg, 0.08 mmol). Pseudorotaxane formation was monitored by ^{1}H NMR. **Pseudorotaxane 3.42** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.74 (s, 2H, ⊂ 2 triazole-C*H*), 7.49 (d, 4H, *J* = 8.0 Hz, ⊂ 4 ArC*H*CCO$_2$), 7.33 (d, 4H, *J* = 8.0 Hz, ⊂ 4 ArC*H*CCH$_2$), 6.81 (s, 4H, ⊂ 2 C*H*=C*H*), 6.93-6.88 (m, 16H, ⊂ 16 crown ArC*H*), 4.80-4.79 (m, 8H, ⊂ 2 C*H*$_2$NH$_2^+$C*H*$_2$), 4.32 (t, 4H, *J* = 5.3 Hz, ⊂ 2 CH$_2$C*H*$_2$O), 4.25 (t, 4H, *J* = 7.0 Hz, ⊂ 2 C*H*$_2$N-triazole), 4.04-3.95 (m, 16H, ⊂ 8 OC*H*$_2$), 3.88-3.68 (m, 36H, ⊂ 16 OC*H*$_2$ and ⊂ 2 CH$_2$C*H*$_2$N), 1.75 (m, 4H, ⊂ 2 triazole-NCH$_2$C*H*$_2$), 1.21-1.17 (m, 12H, ⊂ CH$_2$(C*H*$_2$)$_6$CH$_2$); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OC*H*$_2$), 3.83 (m, 8H, 4 OC*H*$_2$), 3.72 (s, 8H, 4 OC*H*$_2$).

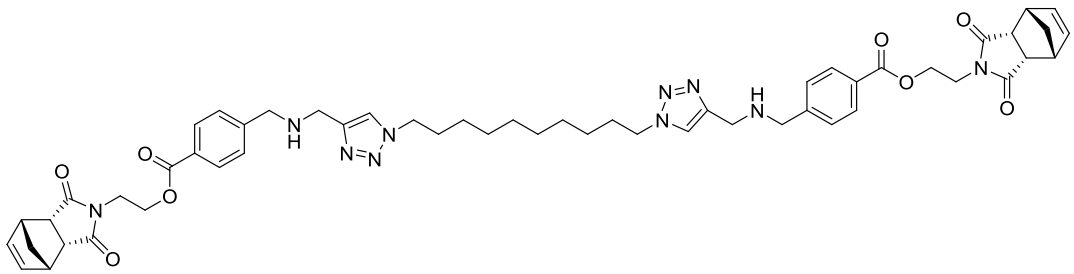
3.43



To the pseudorotaxane **3.42** (19 mg, 0.01 mmol) in acetonitrile, 2 drops of freshly distilled cyclopentadiene were added and the solvent immediately removed *in vacuo*. The orange oil was extracted with hot benzene (5 x 2 mL) to leave a white solid (12 mg, 0.006 mmol, 58%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.79 (br s, 4H, ⊂ 2 NH$_2^+$), 7.71 (s, 2H, ⊂ 2 triazole-C*H*), 7.56 (d, 4H, *J* = 8.0 Hz, ⊂ 4 ArC*H*CCO), 7.39 (d, 4H, *J* = 8.0 Hz, ⊂ 4 ArC*H*CCH$_2$), 6.82-6.73 (m, 16H, ⊂ 16 crown ArC*H*), 5.89 (s, 4H, ⊂ 2 C*H*=C*H*), 4.83-4.75 (m, 8H, ⊂ 2

C*H*$_2$NH$_2^+$C*H*$_2$), 4.25-4.21 (m, 8H, ⊂ 2 CH$_2$C*H*$_2$O and ⊂ 2 C*H*$_2$N-triazole), 4.08-3.98 (m, 16H, ⊂ 8 OC*H*$_2$), 3.75 (m, 32H, ⊂ 16 OC*H*$_2$), 3.64 (t, 4H, *J* = 5.3 Hz, ⊂ 2 CH$_2$C*H*$_2$N), 3.27 (br s, 4H, ⊂ 4 C*H*CH$_2$), 3.23 (br s, 4H, ⊂ 4 C*H*CO), 1.75 (m, 4H, ⊂ 2 NCH$_2$C*H*$_2$), 1.59 (d, 2H, *J* = 9.0 Hz, ⊂ 2 C*H*H), 1.54 (d, 2H, *J* = 9.0 Hz, ⊂ 2 CH*H*), 1.23-1.19 (m, 12H, ⊂ CH$_2$(C*H*$_2$)$_6$CH$_2$); ^{13}C NMR (100 MHz, 298 K, CD$_3$CN) δ_C 177.2 (imide *C*=O), 164.8 (*C*OO), 146.8 (Ar*C*), 138.4 (Ar*C*), 136.4 (*C*H=*C*H), 130.2 (Ar*C*), 129.6 (Ar*C*H), 128.8 (Ar*C*H), 128.0 (Ar*C*H), 123.8 (Ar*C*H), 121.0 (triazole-*C*H), 111.9 (Ar*C*H), 70.3 (O*C*H$_2$), 69.8 (O*C*H$_2$), 67.3 (O*C*H$_2$), 61.7 (CH$_2$*C*H$_2$O), 51.6 (bridgehead *C*H$_2$), 51.4 (*C*H$_2$NH$_2^+$), 49.6 (*C*H$_2$NH$_2^+$), 45.3 (*C*HCH$_2$), 44.4 (*C*HO), 43.4 (*C*H$_2$N-triazole), 36.5 (CH$_2$*C*H$_2$N), 29.5 (*C*H$_2$), 28.7 (*C*H$_2$), 28.2 (*C*H$_2$), 25.7 (*C*H$_2$); HRMS (ESI$^+$): *m/z* found, 939.9640 calc for C$_{102}$H$_{130}$N$_{10}$O$_{24}$ 939.9640 [**3.43**-2ClO$_4$]$^{2+}$.

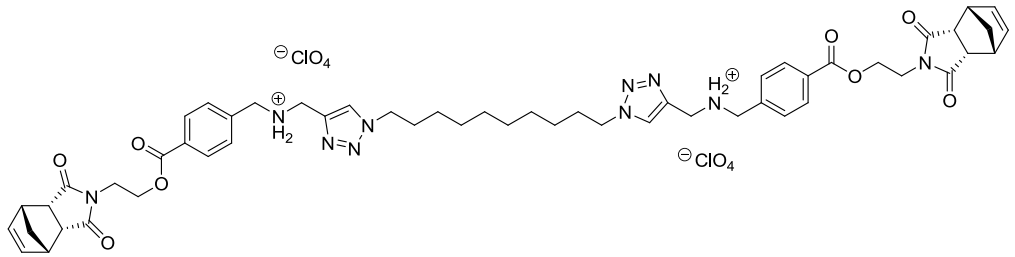
3.44



CuSO$_4$.5H$_2$O (6 mg, 0.06 mmol) and sodium ascorbate (15 mg, 0.08 mmol) were dissolved in CH$_2$Cl$_2$ (10 mL) and water (10 mL). The propargyl amine **3.19** (135 mg, 0.36 mmol) and azide **3.38** (36 mg, 0.16 mmol) were added and the reaction stirred at room temperature for 24 h. The reaction was diluted with water (20 mL) and extracted with CH$_2$Cl$_2$ (3 x 20 mL). The combined organic layers were dried over MgSO$_4$ and solvent removed *in vacuo*. The crude was purified *via* flash chromatography (SiO$_2$: CH$_2$Cl$_2$ to CH$_2$Cl$_2$ /MeOH 9:1) to give a viscous oil (60 mg, 0.06 mmol, 38%). ^{1}H NMR (400 MHz, 298 K, CDCl$_3$) δ_H 7.94 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*COO$_2$), 7.45 (s, 2H, 2 triazole-C*H*), 7.41 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH$_2$), 5.95 (s, 4H, 2 C*H*=C*H*), 4.33-4.29 (m, 8H, 2 CH$_2$C*H*$_2$O and 2 C*H*$_2$N-triazole), 3.89 (m, 8H, 2 C*H*$_2$NHC*H*$_2$), 3.79 (t, 4H, *J* = 8.0 Hz, 2 CH$_2$C*H*$_2$N), 3.34 (br s, 4H, 4 C*H*CH$_2$), 3.26 (br s, 4H, 4 C*H*CO), 2.45 (br s, 2H, 2 N*H*), 1.87 (m, 4H, 2 triazole-N-

CH_2CH_2), 1.68 (d, 2H, *J* = 9.0 Hz, 2 C*H*H), 1.50 (d, 2H, *J* = 9.0 Hz, 2 CH*H*), 1.29-1.24 (m, 12H, $CH_2(CH_2)_6CH_2$); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 177.4 (imide *C*=O), 166.1 (*C*OO), 146.3 (Ar*C*), 145.3 (Ar*C*), 134.3 (*C*H=*C*H), 129.9 (Ar*C*H), 128.5 (Ar*C*), 126.2 (Ar*C*H), 121.5 (triazole-*C*H), 61.6 (CH_2CH_2O), 52.9 (CH_2NH), 52.2 (bridgehead CH_2), 50.3 (CH_2), 45.8 ($CHCH_2$), 44.9 (*C*HCO), 44.1 (CH_2N-triazole), 37.2 (CH_2CH_2N), 30.3 (CH_2), 29.2 (CH_2NH), 28.9 (CH_2), 26.4 (CH_2); IR ν cm^{-1} 2931 (saturated C-H), 1694 (ester and imide C=O), 1270 (C-O).

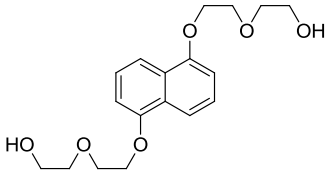
3.45



The neutral thread **3.44** (70 mg, 0.07 mmol) was dissolved in MeOH (1 mL) and a few drops of 70% $HClO_4$ were added, the reaction mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo* providing a white solid recrystallised from acetonitrile/Et_2O (25 mg, 0.021 mmol, 30%). m.p. 89-90°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.02 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCO_2), 7.94 (s, 2H, 2 triazole-C*H*), 7.62 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH_2), 5.94 (t, 4H, *J* = 1.8 Hz, 2 C*H*=C*H*), 4.39-4.36 (m, 12H, 2 CH_2N-triazole and 2 $CH_2NH_2^+CH_2$), 4.29 (t, 4H, *J* = 5.0 Hz, CH_2CH_2O), 3.68 (t, 4H, *J* = 5.0 Hz, CH_2CH_2N), 3.29 (br s, 4H, 4 C*H*CO), 3.24 (br s, 4H, 4 C*H*CH_2), 1.86 (m, 4H, 2 triazole-NCH_2CH_2), 1.60 (d, 2H, *J* = 9.0 Hz, C*H*H), 1.54 (d, 2H, *J* = 9.0 Hz, CH*H*), 1.28-1.25 (m, 12H, $CH_2(CH_2)_6CH_2$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 179.0 (imide *C*=O), 168.0 (*C*OO), 136.7 (Ar*C*), 136.7 (Ar*C*), 134.0 (*C*H=*C*H), 132.5 (Ar*C*), 131.8 (Ar*C*H), 131.3 (Ar*C*H), 126.7 (triazole-*C*H), 62.1 (CH_2CH_2O), 53.1 ($CH_2NH_2^+$), 51.7 (bridgehead CH_2), 51.5 ($CH_2NH_2^+$), 47.0 ($CHCH_2$), 46.0 (*C*HCO), 43.6 (CH_2N-triazole), 38.2 (CH_2CH_2N), 31.2 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 27.2 (CH_2); IR ν cm^{-1} 2932 (saturated C-H), 1693 (imide and

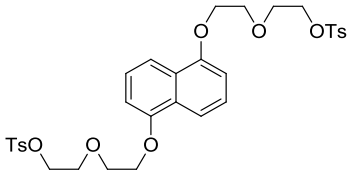
ester C=O), 1273 (C-O), 1096 (ClO_4); HRMS (ESI^+): *m/z* found, 491.2529 calc for $C_{54}H_{66}N_{10}O_8$ 491.2527 [**3.45**-2ClO_4]$^{2+}$.

3.49



Known compound synthesised according to literature procedure.[171] Naphthalene-1,5-diol (4.0 g, 25 mmol) and potassium carbonate (34.5 g, 25.2 mmol) were dissolved in acetonitrile (200 mL). 2-(2-Chloroethoxy)ethanol (5.05 mL, 50 mmol) was dissolved in acetonitrile (40 mL) and added dropwise to the suspension over 30 minutes. The resulting solution was heated to reflux overnight, allowed to cool and filtered through celite. The solvent was removed and the resulting brown solid recyrstallised from toluene to provide pale brown crystals (5.2 g, 15.3 mmol, 62 %). m.p. 95-97°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.87 (d, 2H, *J* = 8.0 Hz, 2 NaphthC*H*), 7.36 (t, 2H, *J* = 8.0 Hz, 2 NaphthC*H*), 6.84 (d, 2H, *J* = 8.0 Hz, 2 NaphthC*H*), 4.30 (t, 4H, *J* = 5.0 Hz, OCH_2), 4.00 (t, 4H, *J* = 5.0 Hz, OCH_2), 3.75 (br s, 8H, OCH_2), 2.12 (br s, 2H, 2 O*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 153.9 (Ar*C*), 126.4 (Ar*C*), 124.8 (Naphth*C*H), 114.3 (Naphth*C*H), 105.5 (Naphth*C*H), 72.3 (O*C*H_2), 69.4 (O*C*H_2), 67.6 (O*C*H_2), 61.5 (O*C*H_2); IR ν cm^{-1} 3505 (O-H), 2931 (saturated C-H); MS (ESI^+): *m/z* 359.1 [**3.49**+Na]$^+$.

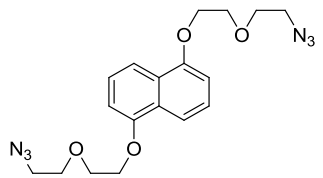
3.50



Known compound synthesised according to literature procedure.[171] Tosyl chloride (2.54 g, 5.8 mmol), NEt_3 (1.07 mL, 7.7 mmol) and DMAP (20 mg, cat.) were dissolved in CH_2Cl_2 (10 mL) and added dropwise to a stirring solution of **3.49** (1 g, 2.9 mmol) at 0°C over 30 minutes. The solution was allowed to warm to room temperature and stirred for 24 h. The

organic layer was washed in dilute HCl (50 mL), concentrated sodium carbonate (2 x 50 mL) and water (2 x 50 mL). The organic layer was dried over $MgSO_4$, filtered over silica and washed with CH_2Cl_2. The solvent was removed and the crude product recrystallised from CH_2Cl_2/petroleum ether to provide a pale beige solid (1 g, 1.55 mmol, 55%). m.p. 122-126°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.83 (d, 2H, *J* = 8.0 Hz, NaphthC*H*), 7.78 (d, 4H, *J* = 8.0 Hz, ArC*H*SO_2), 7.35 (t, 2H, *J* = 8.0 Hz, NaphthC*H*), 7.24 (d, 4H, *J* = 8.0 Hz, ArC*H*CH_3), 6.82 (d, 2H, *J* = 8.0 Hz, NaphthC*H*), 4.21 (br s, 8H, 4 OCH_2), 3.92 (t, 4H, *J* = 4.5 Hz, 2 OCH_2), 3.83 (t, 4H, *J* = 4.5 Hz, 2 OCH_2), 2.36 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 154.2 (Ar*C*O), 144.8 (Ar*C*), 138.1 (Ar*C*), 129.8 (ArC*H*), 127.9 (ArC*H*), 126.8 (Ar*C*), 125.2 (NaphthC*H*), 114.7 (NaphthC*H*), 105.8 (NaphthC*H*), 70.0 (CH_2), 69.4 (CH_2), 69.0 (CH_2), 67.9 (CH_2), 21.6 (CH_3); IR ν cm^{-1} 1596 (ether C-O), 1348 (SO_2), 1086 (ether C-O); HRMS (ESI$^+$): found, 667.1642 calc for. $C_{32}H_{36}NaO_{10}S_2$ 667.1648 [**3.50**+Na]$^+$.

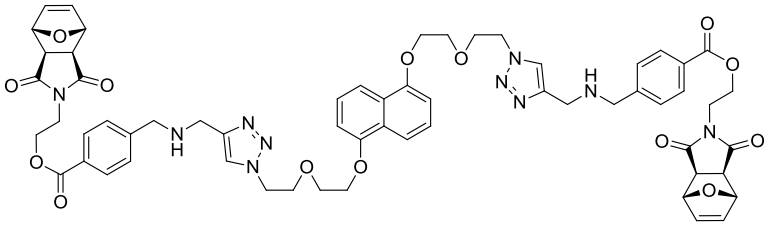
3.51



The ditosylate **3.50** (200 mg, 0.3 mmol) was dissolved in DMF (3mL). Sodium azide (355 mg, 5.5 mmol) was added and the solution heated to 60°C for 48 h followed by TLC (Et_2O). The solution was cooled and partitioned between water (30 mL) and Et_2O (20 mL). The aqueous layer was extracted with Et_2O (2 x 20 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The brown oil was recrystallised from MeOH/water to provide a cream solid (80 mg, 0.21 mmol, 69%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.90 (s, 2H, *J* = 8.0 Hz, 2 NaphthC*H*), 7.39 (dd, 2H, *J* = 8.0 Hz + *J* = 7.5 Hz, 2 NaphthC*H*), 6.89 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 4.35 (4H, t, *J* = 5.0 Hz, 2 CH_2CH_2), 4.05 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2), 3.86 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2), 3.47 (t, 4H, *J* = 5.0 Hz, 2 N_3-CH_2CH_2); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 154.3 (Ar*C*), 126.8 (Ar*C*), 125.1 (Naphth*C*H), 114.7 (Naphth*C*H), 105.8 (Naphth*C*H), 70.4 (CH_2CH_2),

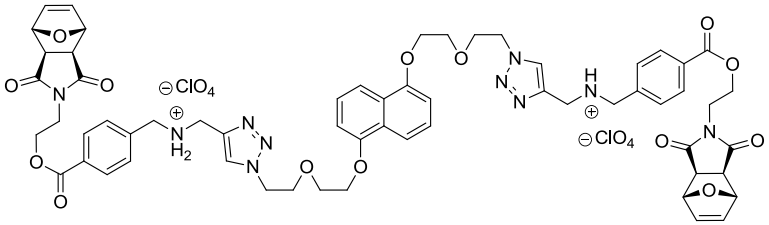
69.9 (CH_2CH_2), 68.0 (CH_2CH_2), 50.9 (CH_2CH_2); IR ν cm^{-1} 2157 ($-N_3$); HRMS (ESI^+): found, 409.1595 calc for $C_{18}H_{22}N_6NaO_4$ 409.1600 [**3.51**+Na]$^+$.

3.52



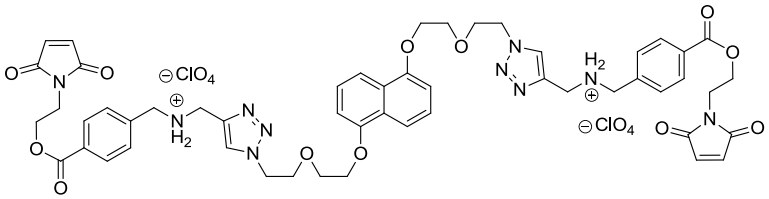
Propargyl amine **3.19** (500 mg, 1.32 mmol) and azide **3.51** (200 mg, 0.51 mmol) were dissolved in CH_2Cl_2 (10 mL). Sodium ascorbate (51 mg, 0.26 mmol) and $CuSO_4.5H_2O$ (26 mg, 0.10 mmol) were dissolved in water (10 mL) added to the solution and stirred at room temperature for 48 h. The organic layer was collected and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL), the combined organic extracts were dried over $MgSO_4$ and the solvent removed *in vacuo* to provide a pale orange solid. The crude product was purified *via* column chromatography (SiO_2: EtOAc to CH_2Cl_2:MeOH; 95:5) providing the thread as a pale yellow oil (200mg, 0.17 mmol, 34%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.93 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCO$_2$), 7.80 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.64 (s, 2H, 2 triazole-C*H*), 7.35-7.29 (m, 6H, 4 ArC*H*CCH$_2$ and 2 NaphthC*H*), 6.84 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.49 (s, 4H, 2 C*H*=C*H*), 5.24 (s, 4H, 4 C*H*O), 4.58 (t, 4H, *J* = 4.8 Hz, CH$_2$C*H*$_2$N-triazole), 4.45 (t, 4H, *J* = 5.3 Hz, CH$_2$C*H*$_2$O), 4.27 (t, 4H, *J* = 4.5 Hz, OCH$_2$C*H*$_2$O), 4.02 (t, 4H, *J* = 4.8 Hz, NCH$_2$C*H*$_2$O), 3.97 (br t, 4H, *J* = 4.5 Hz, OCH$_2$C*H*$_2$O), 3.91 (t, 4H, *J* = 5.3 Hz, CH$_2$C*H*$_2$N-imide), 3.78 (broad s, 4H, 2 N*H*$_2$), 2.86 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 175.6 (imide *C*=O), 165.8 (*C*OO), 153.9 (Ar*C*), 145.8 (Ar*C*), 144.9 (Ar*C*), 136.1 (*C*H=*C*H), 129.5 (Ar*C*H), 128.1 (Ar*C*), 127.7 (Ar*C*H), 126.3 (Ar*C*), 124.9 (Naphth*C*H), 122.5 (triazole-*C*H), 114.1 (Naphth*C*H), 105.4 (Naphth*C*H), 80.5 (*C*HO), 69.5 (*C*H$_2$), 69.4 (*C*H$_2$), 67.3 (*C*H$_2$), 60.8 (CH$_2$*C*H$_2$O), 52.3 (*C*H$_2$), 50.0 (*C*H$_2$), 47.1 (C*H*CO), 43.5 (*C*H$_2$), 37.5 (CH$_2$*C*H$_2$N-imide); HRMS (ESI^+): *m/z* found, 574.2301 calc for $C_{60}H_{64}N_{10}O_{14}$ 547.2296 [**3.52**+2H]$^{2+}$.

3.53



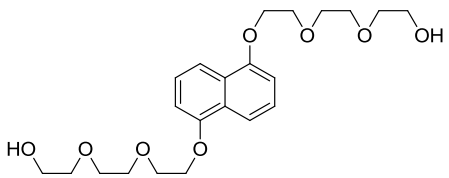
Neutral thread **3.52** (100 mg, 0.087 mmol) was dissolved in CH_2Cl_2 (5 mL) and washed with a 10% aqueous solution of $HClO_4$ (2 x 10 mL). A precipitate appeared in the aqueous phase which was filtered and recrystallised from acetonitrile/Et_2O to provide the product as a pale grey solid (70 mg, 0.05 mmol, 60%). m.p. 128-129°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.74 (s, 2H, 2 triazole-C*H*), 7.98 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCOO), 7.86 (broad s, 4H, 2 NH_2), 7.72 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.59 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCH$_2$), 7.38 (dd, 2H, *J* = 8.5 Hz + *J* = 7.5 Hz, 2 NaphthC*H*), 6.94 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.49 (s, 4H, 2 C*H*=C*H*), 5.10 (s, 4H, 4 C*H*O), 4.89 (t, 4H, *J* = 5.0 Hz, 2 OCH$_2$C*H*$_2$N-triazole), 4.56 (t, 4H, *J* = 5.5 Hz, 2 CH$_2$C*H*$_2$O), 4.42-4.37 (m, 8H, 2 C*H*$_2$NH$_2^+$C*H*$_2$), 4.37 (m, 4H, 2 NCH$_2$C*H*$_2$O), 4.28 (t, 4H, *J* = 5.0 Hz, 2 OC*H*$_2$CH$_2$N-triazole), 4.14 (t, 4H, *J* = 5.0 Hz, 2 OC*H*$_2$CH$_2$O), 3.99 (t, 4H, *J* = 5.0 Hz, 2 OC*H*$_2$CH$_2$O), 3.81 (t, 4H, *J* = 5.5 Hz, 2 OCH$_2$C*H*$_2$N-imide), 2.89 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 177.9 (imide *C*O), 166.7 (*C*OO), 155.5 (Ar*C*), 137.8 (*C*H=*C*H), 137.5 (Ar*C*), 132.6 (Ar*C*), 131.1 (Ar*C*H), 131.3 (Ar*C*H), 128.4 (triazole-*C*H), 127.7 (Ar*C*), 126.9 (Naphth*C*H), 115.4 (Naphth*C*H), 107.2 (Naphth*C*H), 82.3 (*C*HO), 70.6 (*C*H$_2$), 70.2 (*C*H$_2$), 69.2 (*C*H$_2$), 62.8 (CH$_2$*C*H$_2$O), 52.4 (*C*H$_2$), 51.8 (*C*H$_2$NH$_2^+$), 48.4 (*C*HCO), 42.7 (*C*H$_2$NH$_2^+$), 38.6 (CH$_2$*C*H$_2$N-imide); IR ν cm^{-1} 3537 (NH), 1697 (ester and imide C=O), 1072 (ClO_4); HRMS (ESI$^+$): *m/z* found, 574.2303 calc for $C_{60}H_{64}N_{10}O_{14}$ 574.2296 [**3.53**-2ClO_4]$^{2+}$.

3.54



Thread **3.53** (60 mg, 0.045 mmol) was dissolved in acetonitrile (2 mL) and reacted under microwave irradiation (150W, 110 °C, 3 h). The solvent and furan were removed *in vacuo* to provide the retro Diels-Alder thread (53 mg, mmol, 98%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.04 (s, 2H, 2 triazole-C*H*), 7.94 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCOO), 7.66 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.51 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCH$_2$), 7.31 (dd, 2H , *J* = 8.5 + 7.5 Hz, 2 NaphthC*H*), 6.87 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.75 (s, 4H, 2 C*H*=C*H*), 4.61 (t, 4H, *J* = 4.8 Hz, 2 OCH$_2$C*H*$_2$N), 4.38 (t, 4H, *J* = 5.3 Hz, 2 CH$_2$C*H*$_2$O), 4.24 (broad 2, 4H, 2 C*H*$_2$NH$_2$), 4.21-4.18 (m, 8H, 2 C*H*$_2$NH$_2$ and 2 OC*H*$_2$CH$_2$N), 4.01 (t, 4H, *J* = 4.8 Hz, 2 OC*H*$_2$CH$_2$O), 3.92 (t, 4H, *J* = 4.8 Hz, 2 OC*H*$_2$CH$_2$O), 3.82 (t, 4H, *J* = 5.3 Hz, 2 CH$_2$C*H*$_2$N-imide); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.6 (imide *C*=O), 165.1 (*C*OO), 153.8 (Ar*C*), 136.5 (Ar*C*), 134.9 (Ar*C*), 134.1 (*C*H=*C*H), 130.7 (Ar*C*), 130.1 (4 Ar*C*H) , 129.6 (ArC*H*), 126.1 (triazole-*C*H), 126.0 (Ar*C*), 125.2 (Naphth*C*H), 113.7 (Naphth*C*H), 105.5 (Naphth*C*H), 68.9 (*C*H$_2$), 68.6 (*C*H$_2$), 67.4 (*C*H$_2$), 62.2 (imide-NCH$_2$*C*H$_2$O), 50.2 (*C*H$_2$), 50.0 (*C*H$_2$NH$_2$), 41.5 (*C*H$_2$NH$_2$), 36.2 (OCH$_2$*C*H$_2$N-imide); HRMS (ESI$^+$): *m/z* found, 506.2032 calc for $C_{52}H_{56}N_{10}O_{12}$ 506. 2034 [**3.53**-2ClO$_4$]$^{2+}$.

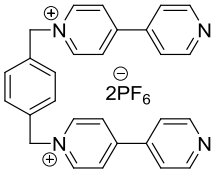
3.56



Known compound synthesised according to literature procedure.[191] 1,5-Dihydroxynaphthalene (4.0 g, 25 mmol) and potassium carbonate (3.45 g, 25.2 mmol) were dissolved in acetonitrile (200 mL). 2-(2-[2-Chloroethoxy]ethoxy)ethanol (7.97 mL, 55 mmol) was dissolved in acetonitrile (40 mL) and added drop wise to the suspension over 30 minutes. The resulting solution was heated to reflux overnight; allowed to cool and filtered through celite. The solvent was removed and the resulting brown oil was purified *via* flash chromatography (SiO_2: Et_2O to Et_2O:MeOH; 9:1) to provide the diol **3.56** (2.5 g, 5.8 mmol, 24%). m.p. 67-69 °C ; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.84 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.32 (dd, 2H, *J* = 8.5 + 7.5 Hz, 2 NaphthC*H*), 6.79 (d, 2H, *J* = 7.5 Hz, 2

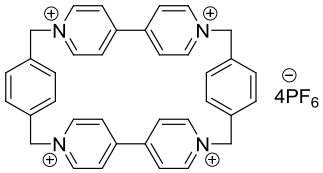
NaphthC*H*), 4.23 (t, 4H, *J* = 5.0 Hz, OCH_2CH$_2$O), 3.92 (t, 4H, *J* = 4.5 Hz, OCH$_2$CH_2O), 3.74 (t, 4H, *J* = 5.0 Hz, OCH_2CH$_2$O), 3.68-3.62 (m, 8H, 4 OCH_2CH$_2$O), 3.55 (t, 4H, *J* = 5.0 Hz, OCH_2CH$_2$O), 3.04 (broad s, 2H, 2 O*H*); ^{13}C NMR (100 MHz, 298 K, CDCl$_3$) δ_C 154.3 (Ar*C*), 126.7 (Ar*C*), 125.4 (Naphth*C*H), 114.9 (Naphth*C*H), 105.7 (Naphth*C*H), 72.6 (O*C*H$_2$CH$_2$OH), 70.9 (*C*H$_2$), 70.3 (*C*H$_2$), 69.8 (*C*H$_2$), 67.8 (*C*H$_2$), 61.6 (*C*H$_2$OH); IR ν cm^{-1} 3508 (OH), 2930 (saturated C-H); HRMS (ESI$^+$) : *m/z* 425.2177 calc for $C_{22}H_{33}O_8$ 425.2170 [**3.56**+H]$^+$.

3.55



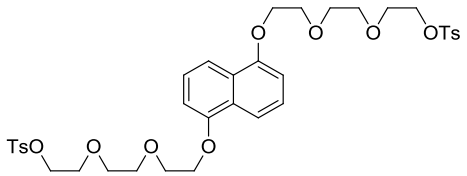
Known compound synthesised according to literature procedure.[172] 4,4'-Bipyridine (3.12 g, 20 mmol) was dissolved in dry acetonitrile (40 mL) and added drop wise to a refluxing solution of 1,4-bis(bromomethyl)benzene (2.2 g, 8.33 mmol) overnight. It was refluxed for a further 2 h then cooled to room temperature. The suspension was filtered and partitioned between CH$_2$Cl$_2$ (20 mL) and water (20 mL). The layers were separated and to the aqueous layer a saturated solution of aqueous NH$_4$PF$_6$ was added until no further precipitate was seen. The precipitate was filtered and washed with water (10 mL) and the yellow solid recrystallised from acetonitrile/Et$_2$O to provide an off white solid (4.09 g, 5.8 mmol, 70%). m.p. 132-133˚C; ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 8.83 (m, 4H, 4 PyrC*H*N$^+$ and 4 PyrC*H*N), 8.33 (d, 4H, *J* = 7.0 Hz, 4 PyrC*H*), 7.79 (m, 4H, 4 PyrC*H*), 7.56 (s, 4H, 4 ArC*H*), 5.78 (s, 4H, 2 CH_2); ^{13}C NMR (100 MHz, 298 K, CD$_3$CN) δ_C 154.5 (Ar*C*), 150.9 (ArCH), 144.7 (Ar*C*H), 140.8 (Ar*C*), 134.3 (Ar*C*), 130.0 (Ar*C*H), 126.0 (Ar*C*H), 121.4 (Ar*C*H), 63.1 (*C*H$_2$).

1.09



Known compound synthesised according to literature procedure.[170] **3.55** (706 mg, 1 mmol), 1,4-bisbromomethylbenzene (264 mg, 1 mmol) and **3.56** (1092 mg, 3.3 mmol) were dissolved in anhydrous DMF (30 mL) and stirred at room temperature under N_2 for 5 days. The DMF was removed *in vacuo* and the purple solid obtained, dissolved in a concentrated aqueous solution of NH_4Cl (100 mL) and extracted for 72 h with CH_2Cl_2 (200 mL). The aqueous layer was reduced *in vacuo* and the crude solid purified *via* flash chromatography (SiO_2: MeOH:H_2O:NH_4Cl; 60:30:10). The combined fractions containing product were reduced *in vacuo* and the solid dissolved in water (20 mL). An aqueous solution of NH_4PF_6 was added carefully added until precipitation ceased. The solid was filtered and washed with water to provide the macrocycle as a white solid (345 mg, 0.31 mmol, 31%). m.p. 272-273˚C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.85 (m, 8H, 8 PyrC*H*N$^+$), 8.19 (m, 8H, 8 PyrC*H*), 7.54 (s, 8H, 8 ArC*H*), 5.77 (s, 8H, 4 CH_2); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 149.1 (Ar*C*), 144.9 (Ar*C*H), 135.7 (Ar*C*), 130.1 (Ar*C*H), 127.0 (Ar*C*H), 64.4 (CH_2).

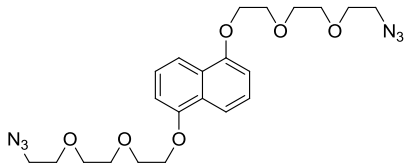
3.57



Known compound synthesised according to literature procedure.[191] The diol **3.56** (1 g, 2.36 mmol) was dissolved in CH_2Cl_2 (10 mL), *p*-toluenesulphonyl chloride (742 mg, 3.91 mmol) was added to the stirring solution and it was cooled to 0°C. DMAP (20 mg, cat.) and NEt_3 (0.72 ml, 5.19 mmol) in CH_2Cl_2 (10 mL) were added drop wise and the solution was stirred for 48 h. The solution was diluted with CH_2Cl_2 (20 mL) and the organic layer washed with water (3 x 20 mL) dried over $MgSO_4$ and concentrated *in vacuo*. The crude material was

purified *via* flash chromatography (SiO_2: Hexane/Et_2O, 100:0, 90:10, 0:100) providing a white solid (1.5 g, 2.05 mmol, 87%). m.p. 74-75°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.87 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.80 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CSO$_2$), 7.37 (dd, 2H, *J* = 8.5 Hz + 8.0 Hz, 2 NaphthC*H*), 7.32 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH$_3$), 6.86 (d, 2H, *J* = 8.0 Hz, 2 NaphthC*H*), 4.30 (t, 4H, *J* = 5.5 Hz, 2 OC*H*$_2$CH$_2$O), 4.17 (t, 4H, *J* = 5.0 Hz, OCH$_2$C*H*$_2$O), 3.98 (t, 4H, *J* = 5.0 Hz, 2 OC*H*$_2$CH$_2$O), 3.77-3.71 (m, 8H, 4 OC*H*$_2$CH$_2$O), 3.65 (t, 4H, *J* = 5.0 Hz, 2 OC*H*$_2$CH$_2$O), 2.42 (s, 6H, 2 C*H*$_3$); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 154.3 (Ar*C*), 144.8 (Ar*C*), 133.0 (Ar*C*), 129.8 (Ar*C*HCCH$_3$), 127.9 (Ar*C*HCS), 126.8 (Ar*C*), 125.1 (Naphth*C*H), 114.6 (Naphth*C*H), 105.7 (Naphth*C*H), 70.9 (*C*H$_2$), 69.9 (*C*H$_2$), 69.2 (*C*H$_2$), 68.7 (*C*H$_2$), 67.9 (*C*H$_2$), 65.9 (*C*H$_2$), 21.6 (*C*H$_3$); IR ν cm^{-1} 2889 (saturated C-H), 1594 (C-O), 1349 (-SO$_2$-O-); HRMS (ESI$^+$): *m/z* found, 755.2166 calc for $C_{36}H_{44}O_{12}S_2Na$ 755.2166 [**3.57**+Na]$^+$.

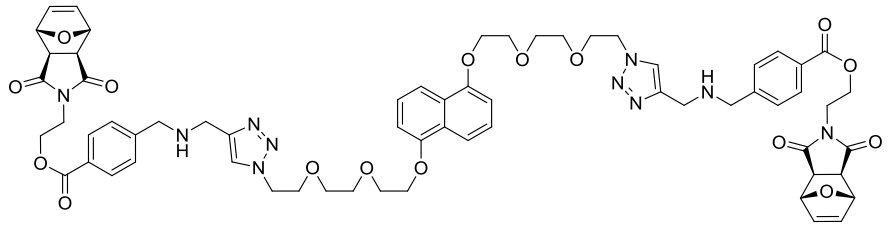
3.58



Known compound synthesised according to literature procedure.[192] The ditosylate **3.57** (1.1 g, 1.50 mmol) was dissolved in DMF (10 mL) and sodium azide (2.6 g, excess) was added. The solution was heated to 60˚C for 24 h and the reaction followed by TLC (CH_2Cl_2:Et_2O; 7:3). The solution was cooled, diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were washed with brine (2 x 20 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* and purified *via* flash chromatography (SiO_2: CH_2Cl_2/Et_2O; 7:3) giving a pale solid. (500mg, 1.06 mmol, 71%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.88 (d, 2H, *J* = 8.0 Hz, 2 NaphthC*H*), 7.36 (dd, 2H, *J* = 8.0 + 7.5 Hz, 2 NaphthC*H*), 6.86 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 4.32 (t, 4H, *J* = 4.8 Hz, 2 OC*H*$_2$CH$_2$O), 4.02 (t, 4H, *J* = 5.0 Hz, 2 N$_3$-CH$_2$C*H*$_2$O) 3.83 (t, 4H, *J* = 4.8 Hz, 2 OCH$_2$C*H*$_2$O), 3.73-3.68 (m, 8H, 4 OC*H*$_2$CH$_2$O), 3.38 (t, 4H, *J* = 5.0 Hz, 2 N$_3$-C*H*$_2$CH$_2$O); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 154.3 (Ar*C*), 126.8 (Ar*C*), 125.1 (Naphth*C*H), 114.6 (Naphth*C*H), 105.7

(Naphth*C*H), 71.1 (*C*H_2CH_2), 70.8 (*C*H_2CH_2), 70.1 (*C*H_2CH_2), 69.9 (*C*H_2CH_2), 67.9 (*C*H_2CH_2), 50.7 (CH_2*C*H_2); IR ν cm^{-1} 2896 (saturated C-H), 2097 (-N_3), 1593 (C-O), 1264 (C-O); HRMS (ESI^+): *m/z* found, 497.2135 calc for $C_{22}H_{30}N_6O_6Na$ 497.2119 [**3.58**+H]$^{2+}$.

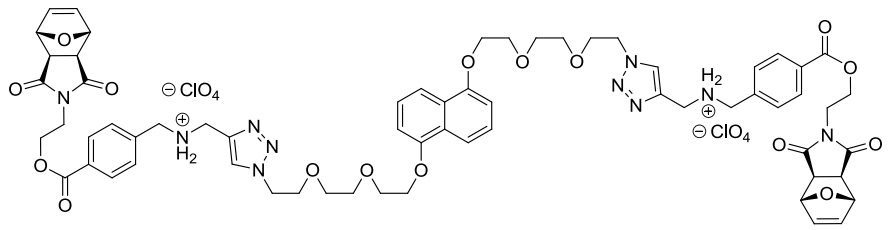
3.59



The propargyl amine **3.19** (842 mg, 2.23 mmol) and diazide **3.58** (350 mg, 0.74 mmol) were dissolved in CH_2Cl_2 (10 mL). Sodium ascorbate (139 mg, 0.70 mmol), $CuSO_4.5H_2O$ (52 mg, 0.21 mmol) were dissolved in water (10 mL) and added to the organic layer. The solution was stirred for 72 h. The organic layer was collected and the aqueous extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The crude orange solid obtained was purified *via* flash chromatography (SiO_2: EtOAc to CH_2Cl_2/MeOH 95:5) to give a pale yellow solid (455 mg, 0.37 mmol, 50%). m.p. 50-5˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.89 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCO_2), 7.81 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.59 (s, 2H, 2 triazole-*CH)*, 7.34 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH_2), 7.30 (dd, 2H, *J* = 8.5 + 7.5 Hz, 2 NaphthC*H*), 6.79 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.43 (s, 4H, 2 C*H*=C*H*), 5.18 (s, 4H, 4 C*H*O), 4.46 (t, 4H, *J* = 4.8 Hz, 2 CH_2CH_2O), 4.39 (t, 4H, *J* = 5.3 Hz, 2 imide-NCH_2CH_2O), 4.23 (t, 4H, *J* = 4.3 Hz, 2 CH_2CH_2), 3.91 (t, 4H, *J* = 4.3 Hz, 2 CH_2CH_2), 3.86-3.71 (m, 20H, 6 CH_2CH_2 and 2 CH_2NHCH_2), 3.62 (t, 4H, *J* = 4.8 Hz, 2 CH_2CH_2), 2.80 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide *C*=O), 165.6 (*C*OO), 153.7 (Ar*C*), 145.7 (Ar*C*), 145.0 (Ar*C*), 136.0 (*C*H=*C*H), 129.3 (Ar*C*H), 127.9 (Ar*C*), 127.5 (Ar*C*H), 126.1 (Ar*C*), 124.6 (Naphth*C*H), 122.3 (triazole-*C*H), 114.0 (Naphth*C*H), 105.1 (Naphth*C*H), 80.3 (*C*HO), 70.8 (*C*H_2), 70.6 (*C*H_2), 69.8 (*C*H_2), 69.5 (*C*H_2), 67.9 (*C*H_2), 61.2 (imide-NCH_2*C*H_2O), 52.8 (*C*H_2), 50.1 (*C*H_2NH), 47.4 (*C*HCO), 44.0 (*C*H_2NH), 37.8 (CH_2*C*H_2N-imide); IR ν cm^{-1}

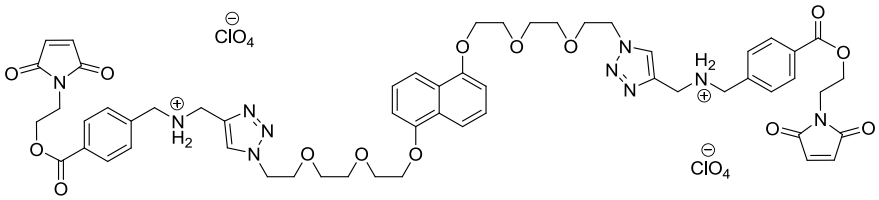
2873 (saturated CH), 1697 (imide and ester C=O), 1266 (C-O); HRMS (ESI$^+$): *m/z* found 618.2593 calc for $C_{64}H_{72}N_{10}O_{16}$ 618.2558 [**3.59**+H]$^{2+}$.

3.60



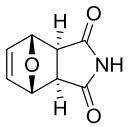
Thread **3.59** (100 mg, 0.081 mmol) was dissolved in CH_2Cl_2 (10 mL) and washed with a 10% aqueous solution of $HClO_4$ (3 x 10 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to give a pale yellow solid (77 mg, 0.054 mmol, 67%). m.p. 52-53°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.90 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCO$_2$), 7.86 (s, 2H, 2 triazole-C*H*), 7.73 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.39 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCH$_2$), 7.34 (dd, 2H, *J* = 8.5 + 7.5 Hz, 2 NaphthC*H*), 6.89 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.47 (s, 4H, 2 C*H*=C*H*), 5.07 (s, 4H, 4 C*H*O), 4.50 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$), 4.36 (t, 4H, *J* = 5.3 Hz, 2 imide-NCH$_2$C*H*$_2$O), 4.21 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$), 4.01 (broad s, 4H, 2 N*H*$_2$), 3.88-3.83 (m, 8H, 2 C*H*$_2$NH$_2^+$C*H*$_2$), 3.79 (t, 4H, *J* = 5.3 Hz, OCH$_2$C*H*$_2$N-imide), 3.69-3.66 (m, 4H, 2 CH$_2$C*H*$_2$), 3.62 (m, 4H, 2 CH$_2$C*H*$_2$), 2.85 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 176.6 (imide *C*=O), 168.8 (*C*OO), 154.3 (Ar*C*), 141.1 (Ar*C*), 138.4 (Ar*C*), 136.5 (*C*H=*C*H), 129.9 (Ar*C*H), 129.7 (Ar*C*H), 127.9 (Ar*C*), 126.5 (triazole-*C*H), 125.5 (Naphth*C*H), 124.3 (Ar*C*), 114.1 (Naphth*C*H), 106.0 (Naphth*C*H), 80.9 (*C*HO), 70.3 (*C*H$_2$), 70.1 (*C*H$_2$), 69.4 (*C*H$_2$), 68.9 (*C*H$_2$), 68.1 (*C*H$_2$), 61.4 (imide-NCH$_2$*C*H$_2$O), 52.7 (*C*H$_2$), 50.2 (*C*H$_2$NH$_2^+$), 47.5 (*C*HCO), 43.6 (*C*H$_2$NH$_2^+$), 37.3 (CH$_2$*C*H$_2$N-imide); IR ν cm^{-1} 3499 (NH), 2926 (saturated CH), 1694 (imide and ester C=O stretching), 1067 (ClO_4); HRMS (ESI$^+$): *m/z* found, 618.2565 calc for $C_{64}H_{72}N_{10}O_{16}$ 618.2558 [**3.60**-2HClO$_4$]$^{2+}$.

3.61



Thread **3.60** (60 mg, 0.042 mmol) was dissolved in acetonitrile (2 mL) and reacted under microwave irradiation (150 W, 4h, 110˚C) followed by TLC (EtOAc:MeOH; 9:1). The solvent was removed *in vacuo* to provide the retro Diels-Alder thread (52 mg, 0.040 mmol, 95%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.09 (s, 2H, 2 triazole-C*H*), 7.91 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCO$_2$), 7.75 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.51 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCH$_2$), 7.34 (dd, 2H, *J* = 8.5 + 7.5 Hz, 2 NaphthC*H*), 6.91 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.78 (s, 4H, 2 C*H*=C*H*), 4.60 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$), 4.46 (t, 4H, *J* = 5.3 Hz, imide-NCH$_2$C*H*$_2$O), 4.32 (br s, 8H, 2 C*H*$_2$NH$_2^+$C*H*$_2$), 4.24 (m, 4H, 2 CH$_2$C*H*$_2$), 3.90 (t, 4H, *J* = 5.3 Hz, 2 CH$_2$C*H*$_2$N-imide), 3.70 (m, 4H, 2 CH$_2$C*H*$_2$), 3.63 (m, 4H, 2 CH$_2$C*H*$_2$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 170.6 (imide *C*=O), 165.1 (*C*OO), 153.9 (Ar*C*), 136.6 (Ar*C*), 134.9 (Ar*C*), 134.1 (*C*H=*C*H), 130.7 (Ar*C*), 130.1 (Ar*C*H), 129.6 (Ar*C*H), 126.1 (Ar*C*), 125.9 (Ar*C*H), 125.1 (triazole-*C*H), 113.7 (Ar*C*H), 105.6 (Ar*C*H), 69.9 (*C*H$_2$), 69.7 (*C*H$_2$), 69.5 (*C*H$_2$), 69.0 (*C*H$_2$), 65.4 (*C*H$_2$), 62.2 (imide-NCH$_2$*C*H$_2$O), 54.0 (*C*H$_2$NH$_2^+$), 50.0 (*C*H$_2$N), 41.6 (*C*H$_2$NH$_2^+$), 36.2 (OCH$_2$*C*H$_2$N-imide); HRMS (ESI$^+$): *m/z* found, 550.2305 calc for $C_{56}H_{64}N_{10}O_{14}$ 550.2296 [**3.61**-2HClO$_4$]$^{2+}$.

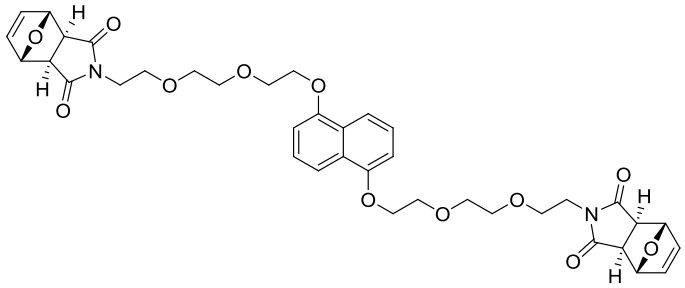
3.62



Known compound synthesised according to literature procedure.[193] Maleimide (286 mg, 2.9 mmol) and furan (0.37 mL, 5.1 mmol) were dissolved in water (3 mL) and subjected to microwave irradiation (1h, 100W, 90°C). On cooling a white precipitate formed which is filtered and washed with water (2 x 5 mL). The white solid was dried in the desiccator

overnight (200 mg, 1.21 mmol, 42%). m.p. 164-166°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.53 (s, 2H, C*H*=C*H*), 5.33 (m, 2H, 2 C*H*O), 2.90 (s, 2H, 2 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 175.9 (*C*=O), 136.6 (*C*H=*C*H), 81.0 (*C*HO), 48.7 (*C*HCO); MS (ESI$^+$): *m/z* 188.1 [**3.62**+Na]$^+$.

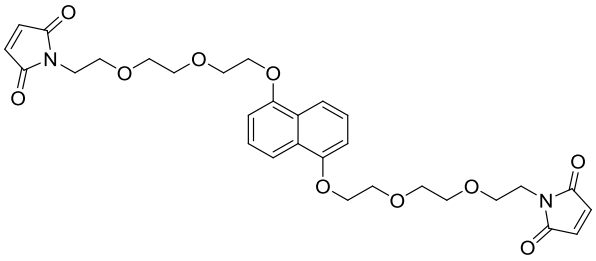
3.63



The imide **3.62** (100 mg, 0.6 mmol), naphthyl diol **3.58** (123 mg, 0.29 mmol) and PPh_3 (168 mg) were dissolved in dry THF (10 mL) and cooled to 0°C. DEAD (0.1 mL, 0.6 mmol) was dissolved in dry THF (5 mL) and added dropwise over 10 minutes. The solution was allowed to warm to room temperature and stirred for 48 h. The THF was removed *in vacuo* and the residue partitioned between EtO_2 and water. The aqueous layer was extracted with $CHCl_3$ (3 x 15 mL) and the combined organic extracts dried over $MgSO_4$, and solvent removed *in vacuo*. The crude product purified *via* silica gel flash chromatography (SiO_2: Petroleum ether:EtOAc 1:1 to EtOAc:MeOH; 95:5) to give the product as a yellow oil (30 mg, 0.04 mmol, 14%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.86 (d, 2H, *J* = 8.0 Hz, NaphthC*H*), 7.35 (t, 2H, *J* = 8.0 Hz, NaphthC*H*), 6.87 (d, 2H, *J* = 8.0 Hz, NaphthC*H*), 6.35 (s, 4H, 2 C*H*=C*H*), 5.20 (m, 4H, 4 C*H*O), 4.28 (t, 4H, *J* = 5.0 Hz, 2 NCH_2CH_2O), 3.97 (t, 4H, *J* = 4.5 Hz, 2 OCH_2CH_2O), 3.76-3.64 (m, 16H, 6 OCH_2CH_2O and 2 OCH_2CH_2N), 2.73 (s, 4H, C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.1 (imide C=O), 154.3 (Ar*C*), 136.4 (*C*H=*C*H), 126.7 (Ar*C*), 125.1 (Naphth*C*H), 114.6 (Naphth*C*H), 105.7 (Naphth*C*H), 80.8 (*C*HO), 70.9 (CH_2CH_2O), 70.2 (CH_2CH_2O), 69.8 (CH_2CH_2O), 67.9 (CH_2CH_2O), 67.1 (CH_2CH_2O), 47.4 (*C*HCO), 38.2 (OCH_2CH_2N); IR ν cm^{-1} 2987 (saturated C-H), 1698 (imide

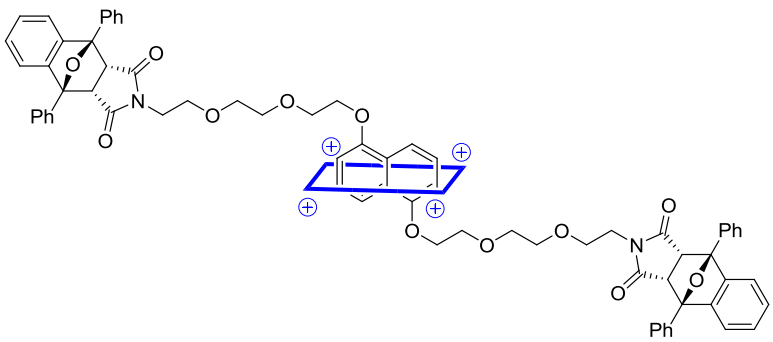
C=O), 1227 (C-O); HRMS (ESI$^+$): *m/z* found, 741.2628 calc for $C_{38}H_{42}N_2NaO_{12}$ 741.2630 [**3.63**+Na]$^+$.

3.64



Thread **3.63** (30 mg, 0.042 mmol) was dissolved in acetonitrile (3 mL) and subjected to microwave irradiation (100W, 110°C, 3 h). The solvent was removed *in vacuo* to provide the product as beige solid used without further purification (20 mg, 0.034 mmol, 81%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.79 (d, 2H, *J* = 8.0 Hz, 2 NaphthC*H*), 7.39 (dd, 2H, *J* = 8.0 Hz + 7.5 Hz, 2 NaphthC*H*), 6.94 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.69 (s, 4H, 2 C*H*=C*H*), 4.24 (t, 4H, *J* = 5.5 Hz, 2 NCH_2CH_2O), 3.88 (t, 4H, *J* = 4.5 Hz, 2 OCH_2CH_2O), 3.96-3.55 (m, 16H, 6 OCH_2CH_2O and 2 OCH_2CH_2N); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 172.3 (imide *C*=O), 155.7 (Ar*C*), 135.6 (*C*H=*C*H), 127.9 (Ar*C*), 126.8 (Naphth*C*H), 115.5 (Naphth*C*H), 107.3 (Naphth*C*H), 71.7 (CH_2CH_2), 71.4 (CH_2CH_2), 70.7 (CH_2CH_2), 69.4 (CH_2CH_2), 68.8 (CH_2CH_2), 38.5 (OCH_2CH_2N); IR ν cm^{-1} 2913 (saturated C-H), 1728 (imide C=O), 1272 (C-O); HRMS (ESI$^+$): *m/z* found, 605.2113 calc for $C_{30}H_{34}N_2NaO_{10}$ 605.2106 [**3.64**+Na]$^+$.

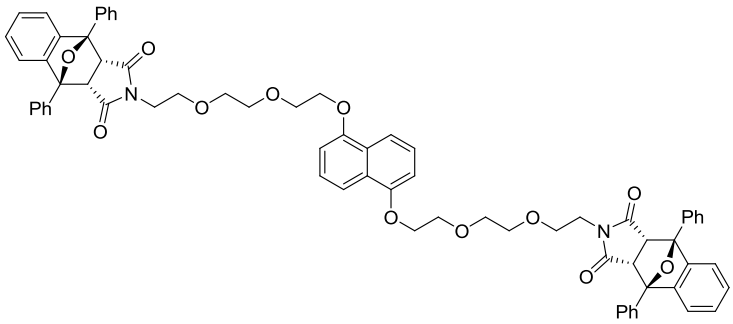
3.66



CBPQT^{4+} **1.09** (10 mg, 0.009 mmol) and thread **3.64** (6 mg, 0.01 mmol) were dissolved in acetonitrile to form the intermediate pseudorotaxane **3.77**. 1,3-Diphenylisobenzofuran (5.4

mg, 0.02 mmol) was added and the reaction stirred for 30 minutes. The solvent was removed *in vacuo* and the crude solid extracted with $CHCl_3$ (3 x 5 mL) and CH_2Cl_2 (3 x 5 mL) to leave a purple solid. This was recrystallised twice from acetonitrile to give the [2]rotaxane as a purple solid (14 mg, 0.006 mmol, 70%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.95 (br s, 4H, ⊂ 4 PyrC*H*N$^+$), 8.68 (br s, 4H, ⊂ 4 PyrC*H*N$^+$), 8.10 (br s, 8H, ⊂ 8 macro ArC*H*), 7.87 (d, 8H, *J* = 6.5 Hz, ⊂ 8 thread ArC*H*), 7.52-7.43 (m, 16 H, ⊂ 4 macro PyrC*H* and ⊂ 12 thread ArC*H*), 7.25 (br s, 4H, ⊂ 4 macro PyrC*H*), 7.20 (m, 4H, ⊂ 4 thread ArC*H*), 6.80 (m, 4H, ⊂ 4 thread ArC*H*), 6.30 (d, 2H, *J* = 8.0 Hz, ⊂ 2 NaphthC*H*), 6.02 (t, 2H, *J* = 8.0 Hz, ⊂ 2 NaphthC*H*), 5.74 (br s, 8H, ⊂ 4 CH_2), 4.30 (m, 4H, ⊂ 2 CH_2O), 4.20 (m, 4H, ⊂ 2 CH_2O), 4.04 (s, 4H, ⊂ 4 C*H*CO), 3.95 (m, 4H, ⊂ 2 CH_2O), 3.71 (m, 4H, ⊂ 2 CH_2O), 3.03 (t, 4H, *J* = 6.5 Hz, ⊂ 2 NCH$_2$CH_2O), 2.88 (t, 4H, *J* = 6.5 Hz, ⊂ 2 NCH_2CH$_2$O), 2.44 (d, 2H, *J* = 8.0 Hz, ⊂ 2 NaphthC*H*); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 175.5 (imide *C*=O), 152.4 (Ar*C*), 146.6 (Ar*C*), 145.6 (Ar*C*), 137.9 (Ar*C*), 137.8 (Ar*C*), 136.5 (Ar*C*H), 135.6 (Ar*C*H), 132.7 (Ar*C*H), 130.1 (Ar*C*H), 129.9 (Ar*C*H), 129.5 (Ar*C*H), 128.5 (Ar*C*H), 127.6 (Ar*C*H), 125.7 (Ar*C*), 121.7 (Ar*C*H), 109.7 (Ar*C*H), 105.7 (Ar*C*H), 91.4 (Ar-*C*O), 72.2 (*C*H$_2$), 71.8 (*C*H$_2$), 71.1 (*C*H$_2$), 69.7 (*C*H$_2$), 67.9 (*C*H$_2$), 66.6 (*C*H$_2$), 55.2 (*C*HCO), 38.7 (*C*H$_2$); HRMS (ESI$^+$): *m/z* found, 547.5626 calc for $C_{106}H_{93}N_6O_{12}$ 547.5623 [**3.66**-4PF$_6$]$^{3+}$.

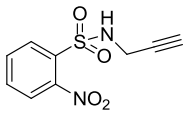
3.67



Retro Diels-Alder thread **3.64** (30 mg, 0.05 mmol) was dissolved in acetonitrile (2 mL) and 1,3 diphenylisobenzofuran (29 mg, 0.11 mmol) was added. The reaction was stirred for 30 minutes then the solvent removed *in vacuo*. The crude mixture was purified *via* flash chromatography (SiO_2: Petroleum ether to petroleum ether:EtOAc; 1:1 to EtOAc) to give the

product as a yellow solid (35 mg, 0.031 mmol, 62%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.98 (m, 8H, 8 ArC*H*), 7.76 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.56-7.46 (m, 12H, 12 ArC*H*), 7.33 (dd, 2H, *J* = 8.5 + 7.5 Hz, 2 NaphthC*H*), 7.15 (m, 4H, 4 ArC*H*), 6.90 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 6.82 (m, 4H, 4 ArC*H*), 4.21 (t, 4H, *J* = 5.3 Hz, 2 CH_2CH_2), 4.05 (s, 4H, 4 *C*HCO), 3.86 (t, 4H, *J* = 5.3 Hz, 2 CH_2CH_2), 3.38 (t, 4H, *J* = 5.5 Hz, 2 CH_2CH_2), 3.58 (t, 4H, *J* = 5.5 Hz, 2 CH_2CH_2), 3.08 (t, 4H, *J* = 6.8 Hz, 2 NCH_2CH_2O), 2.37 (t, 4H, *J* = 6.8 Hz, 2 OCH_2CH_2N); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 175.4 (imide *C*=O), 155.7 (Ar*C*), 145.6 (Ar*C*), 138.1 (Ar*C*), 130.1 (Ar*C*H), 129.9 (Ar*C*H), 129.5 (Ar*C*H), 128.5 (Ar*C*H), 127.9 (Ar*C*), 126.8 (Ar*C*H), 121.8 (Ar*C*H), 115.5 (Ar*C*H), 107.3 (Ar*C*H), 91.4 (Ar-*C*O), 71.6 (CH_2), 71.3 (CH_2), 70.7 (CH_2), 69.4 (CH_2), 67.5 (CH_2), 55.3 (*C*HCO), 38.6 (OCH_2CH_2N); IR ν cm^{-1} 3061 (saturated C-H), 1698 (imide C=O), 1265 (C-O); HRMS (ESI^+): *m/z* found, 1145.4196 calc for $C_{70}H_{62}N_2O_{12}$ 1145.4195 [**3.67**+H]$^+$.

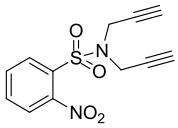
3.68



Known compound synthesised according to a modified literature procedure.[194] 2-Nitrobenzenesulphonyl chloride (150 mg, 0.67 mmol) and propargyl amine (0.05 mL, 0.78 mmol) were dissolved in a saturated aqueous sodium bicarbonate solution (3 mL). THF (0.5 mL) was added to the stirring solution and the mixture stirred at room temperature for 24 h. The solution was cooled to 0°C and acidified to pH 1 with concentrated HCl. A precipitate formed which was filtered and washed with water to provide a pale yellow solid (110mg, 0.46 mmol, 69%). m.p. 95-97˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.21 (m, 1H, ArC*H*), 7.93 (m, 1H, ArC*H*), 7.78-7.76 (m, 2H, 2 ArC*H*), 5.70 (br s, 1H, N*H*), 4.03 (dd, 2H, *J* = 6.5 + 2.5 Hz, CH_2), 1.96 (d, 1H, *J* = 2.5 Hz, C≡C*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 147.9 (Ar*C*), 133.6 (Ar*C*), 133.5 (Ar*C*H), 132.6 (Ar*C*H), 131.3 (Ar*C*H), 125.2 (Ar*C*H), 76.9 (C≡*C*H), 72.9 (*C*≡CH), 33.1 (CH_2); IR ν cm^{-1} 3343 (NH), 3294 (alkyne C-H),

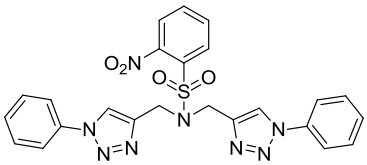
2126 (C≡C), 1525 (NO), 1340 (SO_2); HRMS (ESI^+): *m/z* found 263.0097 calc for $C_9H_8N_2O_4SNa$ 263.0102 [**3.68**+Na]$^+$.

3.69



Propargyl sulphonamide **3.68** (320 mg, 1.3 mmol) was dissolved in acetonitrile (2 mL). Potassium carbonate (202 mg, 1.5 mmol) and propargyl bromide (0.162 mL, 1.5 mmol) were added. The solution was stirred at room temperature for 48 h and the reaction followed by TLC (CH_2Cl_2:MeOH; 9:1). The mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and solvent removed *in vacuo* to give a pale orange oil (230 mg, 0.83 mmol, 64%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.06 (d, 1H, *J* = 7.5 Hz, ArC*H*), 7.76-7.66 (m, 3 H, 3 ArC*H*), 4.30 (d, 4H, *J* = 2.0 Hz, CH_2NCH_2), 2.24 (t, 2H, *J* = 2.0 Hz, 2 C≡C*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 146.3 (Ar*C*), 132.3 (Ar*C*H), 130.4 (Ar*C*), 130.0 (Ar*C*H), 129.4 (Ar*C*H), 122.5 (Ar*C*H), 74.4 (C≡*C*H), 72.3 (*C*≡CH), 34.7 (N*C*H_2); IR ν cm^{-1} 3293 (alkyne C-H), 2123 (C≡C), 1543 (NO), 1360 (SO_2); HRMS (ESI^+): *m/z* found, 301.0265 calc for $C_{12}H_{10}N_2O_4S$ 301.0264 [**3.69**+H]$^+$.

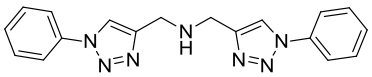
3.70



The propargyl **3.69** (100 mg, 0.036 mmol) and phenyl azide (90 mg, 0.075 mmol) were dissolved in EtOH (3 mL) and THF (3 mL). Sodium ascorbate (43 mg, 0.022 mmol) and $CuSO_4.5H_2O$ (18 mg, 0.007 mmol) were dissolved in water (3mL) and added to the stirring solution. The reaction was stirred at room temperature for 48 h then diluted with CH_2Cl_2 (10 mL) and washed with water (10 mL), 1M HCl (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude product was taken up in

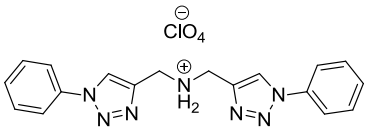
MeOH and filtered to provide a yellow solid (95 mg, 0.018 mmol, 51%). m.p. 178-179˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.27 (d, 1H, *J* = 7.0 Hz, ArC*H*), 8.18 (s, 2H, triazole-C*H*), 7.73-7.76 (m, 7H, 7 ArC*H*), 7.55-7.44 (m, 6H, 6 ArC*H*), 4.75 (s, 4H, C*H*$_2$NC*H*$_2$); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 165.5 (Ar*C*), 156.9 (Ar*C*), 136.8 (Ar*C*), 133.7 (Ar*C*H), 133.5 (Ar*C*), 132.2 (Ar*C*H), 131.3 (Ar*C*H), 129.8 (Ar*C*H), 124.2 (Ar*C*H), 122.2 (triazole-*C*H), 121.0 (Ar*C*H), 120.6 (Ar*C*H), 50.9 (*C*H$_2$N*C*H$_2$); IR ν cm^{-1} 3142 (saturated C-H), 1548 (C-NO$_2$); HRMS (ESI$^+$): *m/z* found, 517.1405 calc for $C_{24}H_{21}N_8O_4S$ 517.1401 [**3.70**+H]$^+$.

3.71



The ditriazole **3.70** (70 mg, 0.14 mmol) was dissolved in acetonitrile (2 mL). Potassium carbonate (83 mg, 0.6 mmol) and thiophenol (0.05 mL, 0.46 mmol) was added and the solution heated to 50°C and followed by TLC (CH_2Cl_2:MeOH; 19:1) to completion. The crude reaction mixture was purified *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 19:1) to provide the amine (40 mg, 0.12 mmol, 86%). m.p. 136-137°C; ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 8.47 (s, 2H, 2 triazole-C*H*), 7.87-7.84 (m, 4H, 4 ArC*H*), 7.62-7.48 (m, 6H, 6 ArC*H*), 4.05 (broad s, 4H, C*H*$_2$NHC*H*$_2$); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 147.7 (Ar*C*), 140.6 (Ar*C*), 130.8 (Ar*C*H), 129.9 (Ar*C*H), 122.5 (triazole-*C*H), 121.4 (Ar*C*H), 44.0 (*C*H$_2$NH*C*H$_2$); IR ν cm^{-1} 3276 (N-H), 3125 (saturated C-H), 1501 (C=C); HRMS (ESI$^+$): *m/z* found, 332.1612 calc for $C_{18}H_{18}N_7$ 332.1618 [**3.71**+H]$^+$.

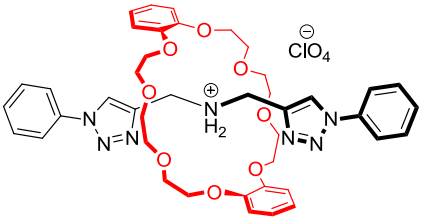
3.72



Neutral thread **3.71** (30 mg, 0.091 mmol) was dissolved in CH_2Cl_2 (5 mL) and washed with an aqueous solution of $HClO_4$ (10%) (3 x 10 mL). A precipitate formed in the aqueous layer which was filtered and recrystallised from acetonitrile/Et_2O to provide a white solid (26 mg, 0.06 mmol, 66%). m.p. 198-199˚C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.44 (s, 2H, 2 triazole-C*H*), 7.82 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.63-7.52 (m, 6H, 6 ArC*H*), 4.53 (s, 4H,

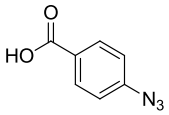
$CH_2NH_2^+CH_2$); ^{13}C NMR (150 MHz, 298 K, CD_3CN) δ_C 138.0 (Ar*C*), 136.7 (Ar*C*), 129.9 (Ar*C*H), 129.3 (Ar*C*H), 124.0 (triazole-*C*H), 120.7 (Ar*C*H), 41.7 ($CH_2NH_2CH_2$); IR ν cm^{-1} 3142 (saturated C-H), 1427 (N=N), 1056 (ClO_4), HRMS (ESI$^+$): *m/z* found, 332.1619 calc for $C_{18}H_{18}N_7$ 332.1618 [**3.72**-ClO_4]$^+$.

3.73



Thread **3.72** (8.6 mg, 2 mmol) and DB24C8 (9 mg, 2 mmol) were dissolved in deuterated acetonitrile (10 mL). Binding constant = **864 M^{-1}** was calculated from the single point method[129] by measuring the integration of triazole-C*H* protons for the free and bound thread at 8.44 ppm and 8.05 ppm respectively. **Pseudorotaxane** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.05 (s, 2H, ⊂ 2 triazole-C*H*), 7.54-7.45 (m, 10H, ⊂ 10 ArC*H*), 6.81-6.73 (m, 8H, ⊂ 8 crown ArC*H*), 4.95 (m, 4H, ⊂ $CH_2NH_2CH_2$), 4.10 (m, 8H, ⊂ 4 OCH_2), 3.87 (m, 8H, ⊂ 4 OCH_2), 3.77 (s, 8H, ⊂ 4 OCH_2); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); and **Thread 3.72** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.44 (s, 2H, 2 triazole-C*H*), 7.82 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.63-7.52 (m, 6H, 6 ArC*H*), 4.53 (s, 4H, CH_2NCH_2); HRMS (ESI$^+$): *m/z* found, 780.3715 calc for $C_{42}H_{50}N_7O_8$ 780.3715 [**3.73**-ClO_4]$^+$.

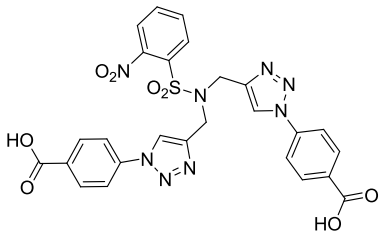
3.74



Known compound synthesised according to literature procedure.[195] 4-Aminobenzoic acid (0.3g, 2.19 mmol) was dissolved in TFA (10 mL) and cooled to 0°C. Sodium nitrite (298 mg, 4.4 mmol) was added portion wise over 5 minutes and the solution was stirred for a

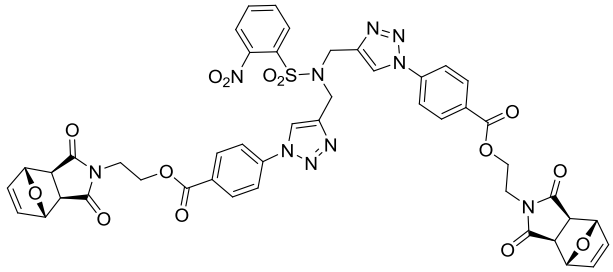
further 30 minutes. After this time sodium azide (1.43 g, 21.9 mmol) was added carefully in portions over 5 minutes then Et_2O (5 mL) and stirring continued for 1 h. The solution was partitioned between Et_2O (15 mL) and water (15 mL) and the organic layer dried over $MgSO_4$ and the solvent removed *in vacuo*. The excess TFA was removed by azeotrope with benzene to give a white powder (230 mg, 1.4 mmol, 64%). ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 8.03 (d, 2H, *J* =8.5 Hz, 2 ArC*H*CCO$_2$), 7.15 (d, 2H, *J* =8.5 Hz, 2 ArC*H*CN$_3$); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 167.6 (*C*OO), 144.8 (Ar*C*), 131.3 (Ar*C*H), 127.1 (Ar*C*), 118.5 (Ar*C*H); IR ν cm^{-1} 2941 (saturated C-H), 2100 (N_3), 1668 (acid C=O).

3.75



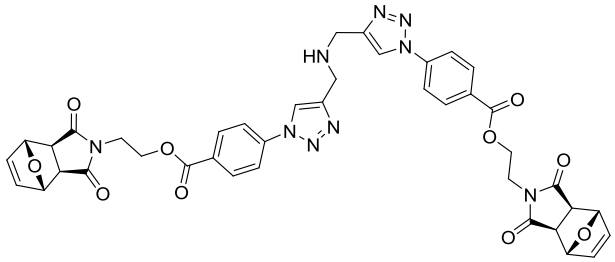
The propargyl **3.69** (243.7 mg, 0.88 mmol) and azide **3.74** (300 mg, 1.8 mmol) were dissolved in THF (3 mL) and EtOH (3 mL). To the stirring solution $CuSO_4.5H_2O$ (22 mg, 0.09 mmol) and sodium ascorbate (53 mg, 0.26 mmol) in water (3 mL) was added. The solution was stirred at room temperature for 48 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 x 10 mL). A precipitate was found in the CH_2Cl_2 layer which was filtered and washed with CH_2Cl_2 to provide a pale green solid (350 mg, 0.65 mmol, 73%). m.p. 240-241°C (decomp.); ^{1}H NMR (400 MHz, 298 K, DMSO-d$_6$) δ_H 8.77 (s, 2H, 2 triazole-C*H*), 8.12-8.07 (m, 5H, 5 ArC*H*), 7.99-7.94 (m, 5H, 5 ArC*H*), 7.83 (t, 1H, *J* = 7.5 Hz, ArC*H*), 7.77 (t, 1H, *J* = 7.5 Hz, ArC*H*), 4.78 (broad s, 4H, C*H*$_2$NC*H*$_2$); ^{13}C NMR (100 MHz, 298 K, DMSO-d$_6$) δ_C 168.2 (COOH), 147.9 (Ar*C*), 143.6 (Ar*C*), 139.7 (Ar*C*), 135.0 (Ar*C*H), 132.8 (Ar*C*H), 132.7 (Ar*C*), 132.5 (Ar*C*), 130.6 (Ar*C*H), 124.8 (Ar*C*H), 124.7 (Ar*C*H), 123.0 (triazole-*C*H), 121.1 (Ar*C*H), 42.5 (*C*H$_2$N*C*H$_2$); IR ν cm^{-1} 2991 (saturated C-H), 1683 (acid C=O), 1540 (NO), 1430 (weak N=N), 1341 (SO_2); HRMS (ESI$^+$): *m/z* found, 605.1205 calc for $C_{27}H_{27}NO_{13}S$ 605.1198 [**3.75**+H]$^+$.

3.76



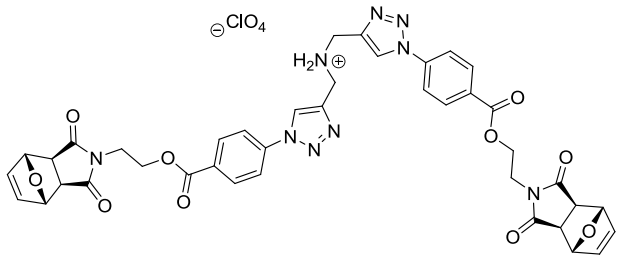
Acid **3.75** (230 mg, 0.43 mmol) was dissolved in CH_2Cl_2 (3 mL). NEt_3 (0.18 mL, 1.3 mmol) was added to solubilise **3.75**. The alcohol **2.04** (187 mg, 0.89 mmol) was added along with the *N*,*N*,*N'*,*N'*-tetramethylchloroformamidinium hexafluorophosphate (299 mg, 1.1 mmol) and DMAP (13 mg, 0.11 mmol). The solution was stirred at room temperature for 48 h. The reaction was followed by TLC (EtOAc:MeOH:H_2O; 40:15:3) to completion. The reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with water (10 mL), citric acid (10 mL), sodium bicarbonate (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo* to provide an orange solid (210 mg, 0.22 mmol, 52%). m.p. 73-74°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.26-8.23 (m, 3H, 2 triazole-C*H* and ArC*H*), 8.16 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CCO$_2$), 7.81 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*CN), 7.75-7.70 (m, 3H, 3 ArC*H*), 6.52 (s, 4H, 2 C*H*=C*H*), 5.25 (s, 4H, 4 C*H*O), 4.75 (s, 4H, C*H*$_2$NC*H*$_2$), 4.50 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$O), 3.94 (t, 4H, *J* = 5.0 Hz, 2 CH$_2$C*H*$_2$N), 2.90 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 176.1 (imide *C*=O), 164.9 (*C*OO), 143.5 (Ar*C*), 142.9 (Ar*C*), 139.7 (Ar*C*), 136.5 (*C*H=*C*H), 133.9 (Ar*C*H), 133.4 (Ar*C*), 132.2 (Ar*C*H), 131.6 (Ar*C*H), 131.2 (Ar*C*H), 130.1 (Ar*C*), 124.3 (Ar*C*H), 122.0 (triazole-*C*H), 119.9 (Ar*C*H), 80.9 (*C*HO), 61.7 (CH$_2$*C*H$_2$O), 47.5 (*C*HCO), 41.7 (*C*H$_2$N*C*H$_2$), 37.8 (CH$_2$*C*H$_2$N); IR ν cm^{-1} 2948 (saturated C-H), 1695 (imide and ester C=O), 1541 (NO), 1337 (SO$_2$).

3.77



Thread **3.76** (150 mg, 0.16 mmol) was dissolved in acetonitrile (5 mL). Potassium carbonate (88 mg, 0.64 mmol) and thiophenol (0.05 mL, 0.49 mmol) were added. The solution was heated to 50°C and the reaction followed by TLC ($MeOH:CH_2Cl_2$; 1:9) to completion. The crude material was purified *via* flash chromatography. (SiO_2: $MeOH:CH_2Cl_2$; 1:9) to provide a pale yellow solid (70 mg, 0.087 mmol, 54%). ^{1}H NMR (700 MHz, 298 K, $CDCl_3$) δ_H 8.16 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCO_2), 8.06 (broad s, 2H, 2 triazole-C*H*), 7.84 (broad d, 4H, , *J* = 8.5 Hz, 4 ArC*H*CN), 6.51 (s, 4H, 2 C*H*=C*H*), 5.25 (s, 4H, 4 C*H*O), 4.50 (t, 4H, *J* = 5.5 Hz, 2 CH_2CH_2O), 4.10 (broad s, 4H, CH_2NHCH_2), 3.94 (t, 4H, *J* = 5.5 Hz, 2 CH_2CH_2N), 2.89 (s, 4H, 4 C*H*CO); ^{13}C NMR (175 MHz, 298 K, $CDCl_3$) δ_C 176.0 (imide *C*=O), 165.0 (*C*OO), 147.3 (ArC), 140.1 (ArC), 136.5 (*C*H=*C*H), 131.5 (Ar*C*HCCO_2), 129.8 (Ar*C*), 120.1 (triazole-*C*H), 119.8 (ArC*H*CN), 80.9 (*C*HO), 61.7 (CH_2CH_2O), 47.5 (*C*HCO), 43.6 (CH_2NHCH_2), 37.8 (CH_2CH_2N); HRMS (ESI$^+$): *m/z* found, 802.2588 calc for $C_{40}H_{36}N_9O_{10}$ 802.2580 [**3.77**+H]$^+$.

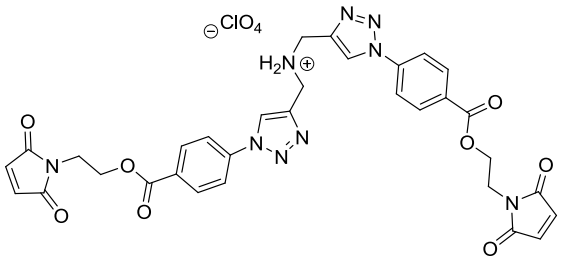
3.78



Thread **3.77** (40 mg, 0.05 mmol) was dissolved in CH_2Cl_2 (5 mL) and washed with a concentrated aqueous solution of $HClO_4$ (10%) (2 x 10 mL). The organic layer was dried over $MgSO_4$ and solvent removed *in vacuo* to give a white solid (46 mg, 0.5 mmol, 100%). m.p. 221-222°C; ^{1}H NMR (400 MHz, 298 K, CD_3NO_2) δ_H 8.50 (s, 2H, 2 triazole-C*H*), 8.08

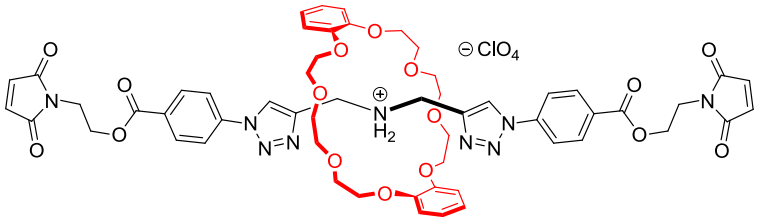
(d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCO$_2$), 7.87 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CN), 6.43 (s, 4H, 2 C*H*=C*H*), 5.03 (s, 4H, 4 C*H*O), 4.67 (s, 4H, C*H*$_2$NH$_2^+$C*H*$_2$), 4.35 (t, 4H, *J* = 5.5 Hz, 2 CH$_2$C*H*$_2$O), 3.78 (t, 4H, *J* = 5.5 Hz, 2 CH$_2$C*H*$_2$N), 2.83 (s, 4H, 4 C*H*CO); ^{13}C NMR (100 MHz, 298 K, DMSO-d$_6$) δ_C 176.5 (imide *C*=O), 164.5 (*C*OO), 150.9 (ArC), 139.5 (Ar*C*), 136.4 (*C*H=*C*H), 131.2 (Ar*C*H), 129.7 (Ar*C*), 124.2 (Ar*C*H), 120.1 (Ar*C*H), 80.4 (*C*HO), 61.4 (CH$_2$*C*H$_2$O), 47.2 (*C*HCO), 40.6 (*C*H$_2$NH$_2^+$*C*H$_2$), 37.0 (CH$_2$*C*H$_2$N); IR ν cm^{-1} 3072 (saturated C-H), 1699 (imide and ester C=O), 1607 (C-O), 1097 (ClO$_4$); HRMS (ESI$^+$): *m/z* found, 802.2573 calc for $C_{40}H_{36}N_9O_{10}$ 802.2580 [**3.78**-ClO$_4$]$^+$.

3.79



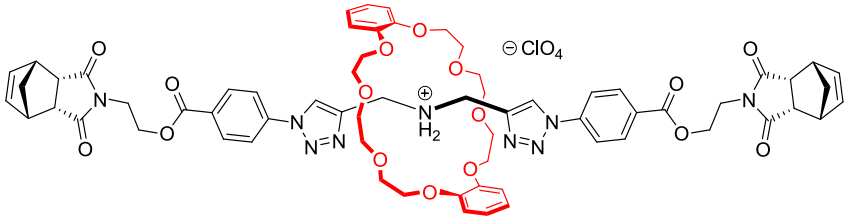
Perchlorate thread **3.78** (25 mg, 0.028 mmol) was dissolved in acetonitrile (3 mL) and nitromethane (1 mL) and subjected to microwave irradiation (4h, 150W, 100 °C) and the reaction followed by TLC (CH$_2$Cl$_2$:MeOH; 9:1). The solvent was removed *in vacuo* to give the retro Diels-Alder thread as a white solid (21 mg, 0.027 mmol, 96%). ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 8.53 (s, 2H, 2 triazole-C*H*), 8.14 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCO$_2$), 7.94 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CN), 6.78 (s, 4H, 2 C*H*=C*H*), 4.54 (s, 4H, C*H*$_2$NH$_2^+$C*H*$_2$), 4.43 (t, 4H, *J* = 5.5 Hz, 2 CH$_2$C*H*$_2$O), 3.87 (t, 4H, *J* = 5.5 Hz, 2 CH$_2$C*H*$_2$N); ^{13}C NMR (150 MHz, 298 K, , CD$_3$CN) δ_C 172.3 (imide *C*=O), 166.3 (*C*OO), 141.2 (Ar*C*), 139.7 (Ar*C*), 135.8 (*C*H=*C*H), 132.6 (Ar*C*H), 131.9 (Ar*C*), 125.4 (Ar*C*H), 121.8 (triazole-*C*H), 64.0 (CH$_2$*C*H$_2$O), 42.9 (*C*H$_2$NH$_2^+$*C*H$_2$), 37.9 (CH$_2$*C*H$_2$N); IR ν cm^{-1} 1711 (imide and ester C=O), 1608 (C-O), 1276 (C-O), 1109 (ClO$_4$); HRMS (ESI$^+$): *m/z* found, 666.2059 calc for $C_{32}H_{28}N_9O_8$ 666.2055 [**3.79**-ClO$_4$]$^+$.

3.80



Perchlorate thread **3.79** (10 mg, 0.013 mmol) and DB24C8 (15 mg, 0.039 mmol) were dissolved in deuterated acetonitrile (1 mL). The reaction was followed by ^{1}H NMR until no change in the spectrum was observed. **Pseudorotaxane** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.25 (broad s, 2H, ⊂ NH_2), 8.18 (s, 2H, ⊂ 2 triazole-C*H*), 8.11 (d, 4H, *J* = 8.5 Hz, ⊂ 4 ArC*H*CCO_2), 7.70 (d, 4H, *J* = 8.5 Hz, ⊂ 4 ArC*H*CN), 6.83 (s, 4H, ⊂ 2 C*H*=C*H*), 6.82-6.72 (m, 8H, ⊂ 8 crown ArC*H*), 5.00 (m, 4H, ⊂ C$H_2$$NH_2^+CH_2$), 4.47 (t, 4H, *J* = 6.0 Hz, ⊂ 2 CH_2CH_2O), 4.10-4.08 (m, 8H, ⊂ 4 OCH_2), 3.91 (m, 12H, ⊂ 2 CH_2CH_2N and 4 OCH_2), 3.72-3.70 (m, 8H, ⊂ 4 OCH_2); Also contains unthreaded **DB24C8** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.93 (m, 8H, 8 ArC*H*), 4.14 (m, 8H, 4 OCH_2), 3.83 (m, 8H, 4 OCH_2), 3.72 (s, 8H, 4 OCH_2); HRMS (ESI$^+$): *m/z* found, 1114.4167 calc for $C_{56}H_{60}N_9O_{16}$ 1114.4153 [**3.80**-ClO_4]$^+$.

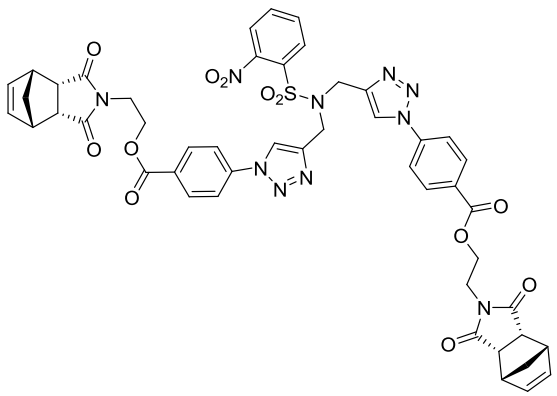
3.81



To the pseudorotaxane **3.80** in acetonitrile, freshly distilled cyclopentadiene (0.1 mL, excess) was added. The solvent and excess cyclopentadiene were removed *in vacuo*. The solid obtained was extracted with hot benzene (3 x 5 mL) providing [2]rotaxane **3.81** (10 mg, 0.007 mmol, 57 %). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.19 (s, 2H, ⊂ 2 triazole C*H*), 8.09 (d, 4H, *J* = 8.5 Hz, ⊂ 4 ArC*H*CCO_2), 7.71 (d, 4H, *J* = 8.5 Hz, ⊂ 4 ArC*H*CN), 6.78 (m, 4H, ⊂ 4 crown ArC*H*), 6.68 (m, 4H, ⊂ 4 crown ArC*H*), 5.96 (s, 4H, ⊂ 2 C*H*=C*H*), 4.98 (m, 4H, ⊂ C$H_2$$NH_2^+CH_2$), 4.32 (t, 4H, *J* = 5.5 Hz, ⊂ 2 CH_2CH_2O), 4.10-4.09 (m, 8H, ⊂ 4

OCH_2), 3.89-3.87 (m, 8H, ⊂ 4 OCH_2), 3.81 (s, 8H, ⊂ 4 OCH_2), 3.70 (t, 4H, J = 5.5 Hz, ⊂ CH_2CH_2N), 3.29 (m, 4H, ⊂ 4 C*H*CO), 3.26 (m, 4H, ⊂ 4 C*H*CH_2), 1.61 (d, 2H, J = 9.0 Hz, ⊂ C*H*H), 1.55 (d, 2H, J = 9.0 Hz, ⊂ CH*H*); ^{13}C NMR (175 MHz, 298 K, CD_3CN) δ_C 179.1 (imide *C*=O), 166.3 (*C*OO), 148.5 (Ar*C*), 141.2 (Ar*C*), 140.9 (Ar*C*), 135.6 (*C*H=*C*H), 132.3 (Ar*C*H), 131.5 (Ar*C*), 124.2 (Ar*C*H), 122.5 (Ar*C*H), 121.7 (Ar*C*H), 113.5 (Ar*C*H), 72.0 (O*C*H_2), 71.5 (O*C*H_2), 68.9 (O*C*H_2), 63.4 (CH_2*C*H_2O), 53.1 (bridgehead *C*H_2), 46.9 (*C*HCH_2), 46.0 (*C*HCO), 44.5 (*C*$H_2NH_2^+$*C*H_2), 38.2 (CH_2*C*H_2N); HRMS (ESI$^+$): *m/z* found, 1246.5090 calc for $C_{66}H_{72}N_9O_{16}$ 1246.5092 [**3.81**-ClO_4]$^+$.

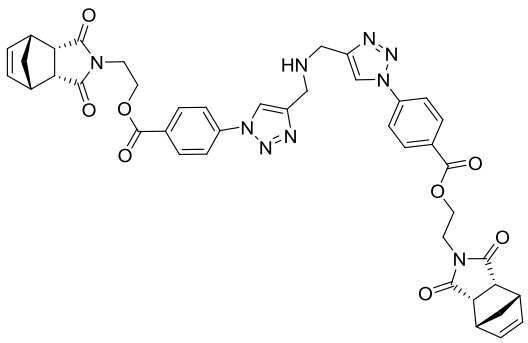
3.82



Diacid **3.69** (100 mg, 0.17 mmol) was dissolved in CH_2Cl_2 (10 mL). The alcohol **2.15** (72 mg, 0.35mmol) was added along with *N*,*N*,*N'*,*N'*-tetramethylchloroformamidinium hexafluorophosphate (105 mg, 0.37 mmol), DMAP (4 mg, 0.04 mmol) and NEt_3 (0.07 mL, 0.5 mmol). The solution was stirred at room temperature for 48 h. CH_2Cl_2 (10 mL) was added to the mixture, and the organic layer was washed with water (10 mL), citric acid (10 mL), sodium bicarbonate (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude yellow solid was recrystallised from CH_2Cl_2/Et_2O to provide a pale yellow solid (90 mg, 0.09 mmol, 54%). m.p. 108-109°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 8.28-8.15 (m, 6H, 6 ArC*H*), 7.86-7.11 (m, 8H, 8 ArC*H*), 6.01 (s, 4H, 2 C*H*=C*H*), 4.79 (br s, 4H, 2 CH_2NCH_2), 4.38 (t, 4H, J = 5.3 Hz, 2 CH_2CH_2O), 3.82 (t, 4H, J = 5.3 Hz, 2 CH_2CH_2N), 3.39 (br s, 4H, 4 C*H*CO), 3.31 (br s, 4H, 4 C*H*CH_2), 1.72 (d, 2H, J = 8.7 Hz, 2 C*H*H), 1.55 (d, 2H, J = 8.7 Hz, 2 CH*H*); ^{13}C NMR (100 MHz, 298

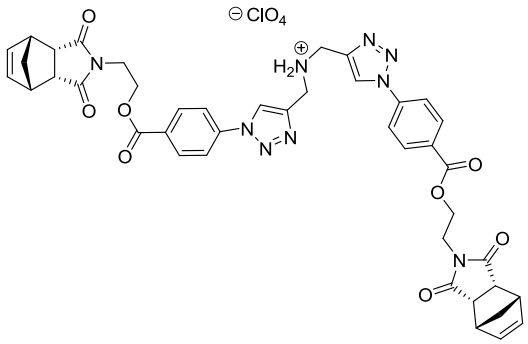
K, $CDCl_3$) δ_C 177.4 (imide *C*=O), 164.9 (*C*OO), 152.5 (Ar*C*), 143.5 (Ar*C*), 139.9 (Ar*C*), 134.3 (*C*H=*C*H), 133.9 (Ar*C*H), 132.1 (Ar*C*H), 131.5 (Ar*C*H), 131.2 (Ar*C*H), 130.0 (Ar*C*), 124.3 (Ar*C*H), 122.0 (ArCH), 120.0 (Ar*C*H), 62.3 (CH_2*C*H_2O), 52.3 (bridgehead *C*H_2), 45.8 (*C*HCH_2), 44.9 (*C*HCO), 41.7 (*C*H_2N*C*H_2), 37.2 (CH_2*C*H_2N); IR ν cm^{-1} 1694 (imide and ester C=O), 1542 (C-O), 1272 (C-O); HRMS (ESI^+): *m/z* found, 1005.2638 calc for $C_{48}H_{42}N_{10}O_{12}SNa$ 1005.2597 [**3.82**+Na]$^+$.

3.83



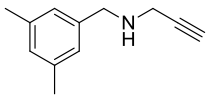
Thread **3.82** (50 mg, 0.05 mmol) was dissolved in acetonitrile (5 mL). Thiophenol (0.016 mL, 0.15 mmol) and potassium carbonate (28 mgs, 0.2 mmol) were added and the reaction mixture was heated to 60°C and stirred for 24 h. The crude reaction mixture was purified *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 9:1) to provide a pale yellow solid (30 mgs, 0.04 mmol, 74%). m.p. 85-86°C (decomp.); ^{1}H NMR (700 MHz, 298 K, $CDCl_3$) δ_H 8.18 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CCO_2), 8.08 (s, 2H, 2 triazole-C*H*), 7.86 (d, 4H, *J* = 8.5 Hz, 4 ArC*H*CN), 6.01 (s, 4H, 2 C*H*=C*H*), 4.38 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2O), 4.11 (br s, 4H, CH_2NHCH_2), 3.81 (t, 4H, *J* = 5.0 Hz, 2 CH_2CH_2N), 3.39 (br s, 4H, 4 C*H*CH_2), 3.30 (br s, 4H, 4 C*H*CO), 1.73-1.54 (m, 4H, 2 x bridgehead CH_2); ^{13}C NMR (175 MHz, 298 K, $CDCl_3$) δ_C 177.4 (imide *C*=O), 165.0 (*C*OO), 147.2 (Ar*C*), 140.2 (Ar*C*), 134.3 (*C*H=*C*H), 131.5 (Ar*C*H), 129.8 (Ar*C*), 120.1 (triazole-*C*H), 119.9 (Ar*C*H), 62.3 (CH_2*C*H_2O), 52.3 (bridgehead *C*H_2), 45.9 (C*H*CH_2), 45.0 (C*H*CO), 45.3 (*C*H_2NH*C*H_2), 37.2 (CH_2*C*H_2N); IR ν cm^{-1} 1728 (imide and ester C=O stretching), 1613 (C-O).

3.84



Neutral thread **3.83** (10 mg, 0.013 mmol) was dissolved in CH_2Cl_2 (10 mL) and washed with an aqueous solution of $HClO_4$ (10%) (2 x 10 mL). The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. The crude solid was recrystallised from acetonitrile/Et_2O to give a white solid (12 mg, 0.013 mmol, 100%). m.p. 151-152°C; ^{1}H NMR (700 MHz, 298 K, CD_3CN) δ_H 8.48 (s, 2H, 2 triazole C*H*), 8.14 (d, 4H, *J* = 8.4 Hz, 4 ArC*H*CCO$_2$), 7.95 (d, 4H, *J* = 8.4 Hz, 4 ArC*H*CN), 5.96 (s, 4H, 2 C*H*=C*H*), 4.47 (s, 4H, C*H*$_2$NH$_2^+$C*H*$_2$), 4.32 (t, 4H, *J* = 5.6 Hz, 2 CH$_2$C*H*$_2$O), 3.69 (t, 4H, *J* = 4.8 Hz, 2 CH$_2$C*H*$_2$N), 3.29 (s, 4H, 4 C*H*CO), 3.25 (s, 4H, 4 C*H*CH$_2$), 1.61 (d, 2H, *J* = 8.8 Hz, 2 CH*H*), 1.55 (d, 2H, *J* = 8.8 Hz, 2 C*H*H); ^{13}C NMR (175 MHz, 298 K, CD_3CN) δ_C 177.7 (imide *C*=O), 164.8 (*C*OO), 139.9 (Ar*C*), 139.8 (Ar*C*), 134.3 (*C*H=*C*H), 131.2 (Ar*C*H), 130.4 (Ar*C*), 123.5 (triazole *C*H), 120.4 (Ar*C*H), 62.1 (CH$_2$*C*H$_2$O), 51.8 (bridgehead *C*H$_2$), 45.7 (*C*HCH$_2$), 44.7 (*C*HCO), 41.8 (*C*H$_2$NH$_2^+$*C*H$_2$), 36.9 (CH$_2$*C*H$_2$N); IR ν cm^{-1} 3052 (saturated C-H), 1685 (ester and imide C=O), 1092 (ClO_4); HRMS (ESI$^+$): *m/z* found, 798.3013 calc for $C_{42}H_{40}N_9O_8$ 798.2994 [**3.93**-ClO_4]$^+$.

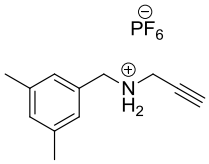
3.94



Known compound synthesised according to literature procedure.[107] 3,5-Dimethylbenzaldehyde (250 mg, 1.9 mmol) and propargyl amine (0.12 mL, 1.9 mmol) were heated to reflux in $CHCl_3$ (3 mL) for 1 h. The solution was cooled to room temperature and solvent removed *in vacuo*. The crude oil was dissolved in MeOH (5 mL) and cooled to 0°C,

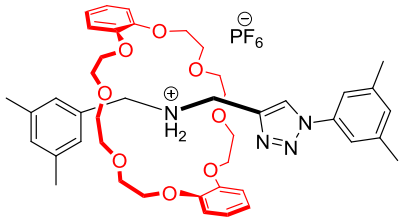
sodium borohydride (72 mg, 1.9 mmol) was added and the solution stirred for 1 h. Water (10 mL) was added to quench the reaction and solvent removed *in vacuo*. THF (10 mL) was added and the precipitate formed was removed by filtration. The liquors were reduced *in vacuo* to give a pale yellowish oil used without further purification (303 mg, 1.75 mmol, 92%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.98 (s, 2H, 2 ArC*H*), 6.92 (s, 1H, ArC*H*), 3.83 (d, 2H, *J* = 7.0 Hz, ArCH_2NH), 3.44 (dd, 2H, *J* = 6.0 Hz, *J* = 2.5 Hz, C≡CCH_2NH), 2.32 (s, 6H, 2 CH_3), 2.27 (t, 1H, *J* = 2.5 Hz, C≡C*H*); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 139.3 (Ar*C*), 138.0 (Ar*C*), 128.8 (Ar*C*H), 126.6 (Ar*C*H), 124.8 (C≡*C*H), 71.6 (*C*≡CH), 52.3 (Ar*C*H_2NH), 37.4 (C≡C*C*H_2NH), 21.3 (*C*H_3); HRMS (ESI$^+$): *m/z* found, 174.1276 calc for $C_{12}H_{16}N$ 174.1277 [**3.94**+H]$^+$.

3.88



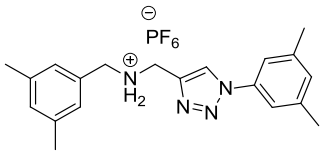
Known compound synthesised according to literature procedure.[107] The propargyl compound **3.92** (303 mg, 1.75 mmol) was dissolved in acetonitrile (5 mL). NH_4PF_6 (304 mg, 2.1 mmol) was added to the solution and it was stirred at room temperature overnight. The crude reaction mixture was reduced *in vacuo* and the residue taken up in THF. Et_2O was added to the solution and left to precipitate out excess NH_4PF_6, then filtered. The liquors were concentrated *in vacuo* providing an off white solid (550 mg, 1.72 mmol, 98%). ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 7.04 (broad s, 3H, 3 ArC*H*), 4.05 (broad s, 2H, ArC$H_2NH_2^+$), 3.72 (d, 2H, *J* = 3.0 Hz, C≡CCH_2NH_2), 3.05 (t, 1H, *J* = 3.0 Hz, C≡C*H*), 2.32 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 139.8 (Ar*C*), 131.4 (Ar*C*), 128.2 (Ar*C*H), 128.1 (Ar*C*H), 122.6 (C≡*C*H), 77.6 (*C*≡CH), 51.7 (Ar*C*$H_2NH_2^+$), 36.9 (C≡C*C*$H_2NH_2^+$), 21.2 (*C*H_3); HRMS (ESI$^+$): *m/z* found, 174.1275 calc for $C_{12}H_{16}N$ 174.1277 [**3.88**-PF_6]$^+$.

3.89



The propargyl **3.88** (100 mg, 0.31 mmol) and the 3,5-dimethylphenyl azide **3.11** (51 mg, 0.35mmol) were dissolved in CH_2Cl_2 (10 mL). DB24C8 (281 mg, 0.63 mmol) was added followed by $Cu(MeCN)_4PF_6$ (117 mg, 0.31 mmol) and 2,6-lutidine (0.004 mL, 0.013 mmol) and the solution stirred at room temperature for 48 h. The solution was reduced *in vacuo* and the crude mixture purified *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:acetone 5:1) to give the rotaxane as an oil. (85 mg, 0.093 mmol, 30%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.94 (s, 1H, ⊂ triazole C*H*), 7.86 (s, 2H, ⊂ NH_2), 7.20 (s, 2H, ⊂ 2 ArC*H*), 7.03 (s, 1H, ⊂ ArC*H*), 6.89 (s, 2H, ⊂ 2 ArC*H*), 6.85-6.76 (m, 9H, ⊂ 8 crown ArC*H* and ⊂ ArC*H*), 4.86 (m, 2H, ⊂ ArC$H_2NH_2^+$), 4.60 (m, 2H, ⊂ triazole-C$H_2NH_2^+$), 4.18-4.14 (m, 4H, ⊂ 2 CH_2O), 4.08-4.04 (m, 4H, ⊂ 2 CH_2O), 3.94-3.90 (m, 4H, ⊂ 2 CH_2O), 3.82-3.72 (m, 8H, ⊂ 4 CH_2O), 3.65-3.60 (m, 4H, ⊂ 2 CH_2O), 2.38 (s, 6H, ⊂ 2 CH_3), 2.12 (s, 6H, ⊂ 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 147.4 (Ar*C*), 139.7 (Ar*C*), 138.0 (Ar*C*), 136.2 (Ar*C*), 135.1 (Ar*C*), 131.3 (Ar*C*), 130.4 (Ar*C*H), 127.3 (Ar*C*H), 123.5 (triazole-*C*H), 121.7 (Ar*C*H), 121.5 (Ar*C*H), 117.8 (Ar*C*H), 112.4 (Ar*C*H), 70.8 (*C*H_2O), 70.2 (*C*H_2O), 67.9 (*C*H_2O), 52.7 (*C*$H_2NH_2^+$), 43.4 (*C*$H_2NH_2^+$), 21.2 (*C*H_3), 21.1 (*C*H_3); IR ν cm^{-1} 2926 (saturated C-H), 1725 (ether C-O), 1250 (ether C-O), 838 (PF_6); HRMS (ESI$^+$): *m/z* found, 769.4174 calc for $C_{44}H_{57}N_4O_8$ 769.4171 [**3.89**-PF_6]$^+$.

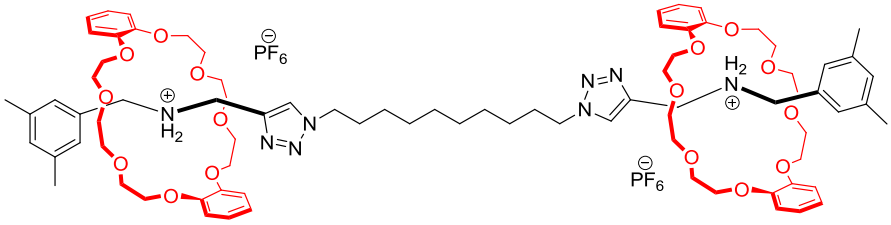
3.90



Propargyl amine **3.88** (100 mg, 0.31 mmol) and 3,5-dimethyl azide **3.11** (52 mg, 0.35 mmol) were dissolved in dry CH_2Cl_2 (10 mL). $Cu(MeCN)_4PF_6$ (117 mg, mmol) and 2,6-lutidine

(0.004 mL, 0.03 mmol) were added and the reaction stirred at room temperature for 24 h under N_2. The reaction was diluted with CH_2Cl_2 (20 mL) and washed with ammonia (2 x 20 mL), water (20 mL), and brine (20 mL) and aqueous hexafluorophosphoric acid (10%) (20 mL). The organic layer was dried over $MgSO_4$ and solvent removed *in vacuo* (40 mg, 0.09 mmol, 29 %). m.p. 214-215°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.22 (s, 1H, triazole-C*H*), 7.39 (s, 2H, 2 ArC*H*), 7.15 (s, 1H, ArC*H*), 7.04 (s, 1H, ArC*H*), 7.02 (s, 2H, 2 ArC*H*), 4.74 (br s, 2H, NH_2), 4.20 (br s, 4H, CH_2NH$_2^+$CH_2), 2.38 (s, 6H, 2 CH_3), 2.28 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 141.4 (Ar*C*), 140.0 (Ar*C*), 138.0 (Ar*C*), 131.8 (Ar*C*H), 131.7 (Ar*C*H), 128.6 (Ar*C*H), 124.2 (triazole-*C*H), 119.5 (Ar*C*H), 52.3 (*C*H$_2$NH$_2^+$), 43.1 (*C*H$_2$NH$_2^+$), 21.7 (*C*H$_3$), 21.6 (*C*H$_3$); IR ν cm^{-1} 2919 (saturated C-H), 1602 (NH$_2$), 1435 (N=N), 840 (PF$_6$); HRMS (ESI$^+$): *m/z* found, 321.2072 calc. for $C_{20}H_{25}N_4$ 321.2074 [**3.90**-PF$_6$]$^+$.

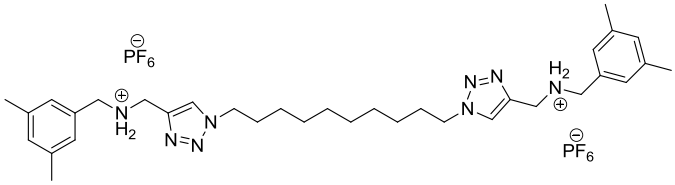
3.91



The propargyl amine **3.88** (160 mg, 0.50 mmol) was dissolved in dry CH_2Cl_2 (10 mL) with DB24C8 (430 mg, 0.96 mmol). After 5 minutes the Cu(MeCN$_4$)PF$_6$ (178 mg, 4.80 mmol) and 2,6-lutidine (0.01 mL, 0.048 mmol) were added followed by diazide **3.38** (54 mg, 0.240 mmol). The solution was stirred for 72 h. The solvent was removed and the crude mixture purified *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 97:3) to give a pale oil (82 mg, 0.047 mmol, 19%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.72 (br s, 4H, ⊂ 2 NH$_2$), 7.66 (s 2H, ⊂ 2 triazole-C*H*), 6.87-6.77 (m, 20H, ⊂ 16 crown ArC*H* and ⊂ 4 ArC*H*), 6.72 (s, 2H, ⊂ 2 ArC*H*), 4.78 (m, 4H, ⊂ 2 triazole-CH_2NH$_2$CH$_2$), 4.52 (m, 4H, ⊂ 2 triazole-CH$_2$NH$_2$CH_2), 4.31-4.28 (m, 4H, ⊂ 2 OCH$_2$), 4.23 (t, 4H, *J* = 7.3 Hz, ⊂ CH_2N-triazole), 4.17-4.13 (m, 4H, ⊂ 2 OCH_2), 4.07-4.03 (m, 8H, ⊂ 4 OCH_2), 3.91-3.87 (m, 8H, ⊂ 4 OCH_2),

3.80-3.76 (m, 8H, ⊂ 4 OCH_2), 3.73-3.69 (m, 8 H, ⊂ 4 OCH_2), 3.66-3.60 (m, 8H, ⊂ 4 OCH_2), 1.78-1.75 (m, 4H, ⊂ 2 $CH_2CH_2CH_2$), 1.23-1.20 (br m, 12H, ⊂ $CH_2(CH_2)_6CH_2$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 140.4 (Ar*C*), 139.4 (Ar*C*), 132.7 (Ar*C*), 131.5 (Ar*C*H), 128.7 (Ar*C*H), 122.9 (Ar*C*H), 122.6 (Ar*C*H), 120.8 (Ar*C*), 113.7 (Ar*C*H), 70.7 (OCH_2), 70.2 (OCH_2), 67.8 (OCH_2), 53.8 ($CH_2NH_2^+$), 51.3 (CH_2N-triazole), 44.8 ($CH_2NH_2^+$), 31.9 (CH_2), 30.4 (CH_2), 29.9 (CH_2), 27.5 (CH_2), 21.6 (CH_3); IR ν cm^{-1} 2914 (saturated C-H), 2848 (saturated C-H), 1728 (ether C-O), 1254 (C-O), 841 (PF_6); HRMS (ESI$^+$): *m/z* found, 734.4247 calc for $C_{82}H_{116}N_8O_{16}$ 734.4249 [**3.91**-2PF_6]$^{2+}$.

3.92



Propargyl amine **3.88** (178 mg, 0.56 mmol) and diazide **3.38** (50 mg, 0.22 mmol) were dissolved in dry CH_2Cl_2. The Cu(MeCN)$_4PF_6$ (166 mg, 0.45 mmol) and 2,6-lutidine (14 mg, 0.045 mmol) were added, the system flushed with N_2 and stirred at room temperature for 24 h. The reaction was diluted with CH_2Cl_2 (20 mL) and washed with ammonia (3 x 15 mL), water (20 mL) and brine (20 mL). The crude oil was purified *via* flash chromatography (SiO_2: CH_2Cl_2 to CH_2Cl_2:MeOH; 9:1). The combined fractions were reduced *in vacuo*, dissolved in CH_2Cl_2 (10 mL) and washed with and aqueous solution of hexafluorophosphoric acid (10%) (3 x 10 mL). The organic layer was dried over $MgSO_4$ and solvent removed *in vacuo* to provide a white solid (50 mg, 0.058 mmol, 26%). m.p. 148-149°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.86 (s, 2H, 2 triazole-C*H*), 7.45 (br s, 4H, 2 NH_2), 7.11 (s, 2H, 2 ArC*H*), 7.06 (s, 4H, 4 ArC*H*), 4.36 (t, 4H, *J* = 7.0 Hz, 2 CH_2N-triazole), 4.29 (s, 4H, 2 C$H_2NH_2^+$), 4.16 (s, 4H, 2 C$H_2NH_2^+$), 2.32 (s, 12H, 4 CH_3), 1.85 (m, 4H, 2 CH_2CH_2N), 1.28-1.26 (m, 12H, $CH_2(CH_2)_6CH_2$); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 140.3 (Ar*C*), 138.5 (Ar*C*), 132.5 (Ar*C*H), 131.5 (Ar*C*), 129.1 (Ar*C*H), 126.5 (triazole-*C*H), 52.2 (NH_2CH_2), 51.5 (CH_2-N), 43.1 (CH_2NH_2), 31.2 (CH_2), 30.3 (CH_2), 29.9 (CH_2) 27.3

(CH_2), 21.6 (CH_3); IR ν cm^{-1} 2924 (saturated C-H), 1458 (N=N), 821 (PF_6); HRMS (ESI^+): *m/z* found 571.4233 calc for $C_{34}H_{51}N_8$ 571.4231 [**3.92-** $H.2PF_6]^+$.

Chapter 4 - Synthesis of [2]Pseudorotaxanes and [2]Rotaxanes Using Novel Macrocycles.

4. Synopsis

In the previous chapters, work focussed on using the Diels-Alder approach to 'threading followed by stoppering' to synthesise novel rotaxanes. Both existing and new templates were transformed into rotaxanes using this approach. In this chapter modifications to the DB24C8 macrocycle in order to enhance the binding interactions were investigated. DB24C8 is a crown ether macrocycle that has been shown to have excellent binding affinities to templates such as dibenzylammonium and bispyridinium ethane. Modifications to this macrocycle and the effects on binding and their transformation into rotaxanes was explored.

Replacement of one of the ethylene oxy units in DB24C8 with an acetal provided two novel macrocycles (Figure 4.1). These macrocycles were subjected to binding studies with a variety of templates in order to see the effects of reducing macrocycle size but retaining the oxygen H bond acceptors. The results of which are discussed within the chapter.

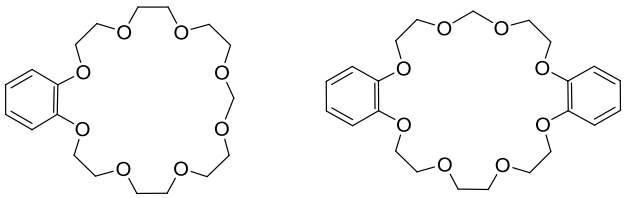


Figure 4.1 Macrocycle **4.01** and **4.02**.

4.1 Introduction

There are a variety of possible templates that can form axles to interact with crown macrocycles for rotaxane formation.[31-33,46,120] These enhancements can include changing the macrocycle cavity size or incorporating additional functionality into a macrocycle in order to modify the binding interaction. Herein we look at how changes to the macrocycle can also play a role in effecting the binding affinity to axle templates.

There are many examples of crown ethers threading over a variety of axles with various recognition sites including secondary dialkylammonium salts[196-197] and *bis*pydridiniums.[46] Previously it was assumed that macrocycles required a minimum of 24 atoms to encompass a simple alkyl chain into its central cavity.[21,32,198] There have been many examples of DB24C8 showing excellent binding with secondary dialkylammonium salts.[31,61,199] However Huang *et al*[200] have reported the threading of benzo-21-crown-7 **4.03** over secondary dialkylammonium salts giving improved binding to provide [2]pseudorotaxanes and [2]rotaxane complexes. The interaction of the macrocycle with a series of secondary dialkyl ammonium salts was followed by ^{1}H NMR and the two complexes formed with threads **4.04** and **4.05** had slow exchange on the NMR time scale (Figure 4.2). The cavity of macrocycle **4.03** was found to be unable to thread over dibenzylammonium thread **3.09** and no pseudorotaxane formation was seen in this case. The binding constants for threads **4.04** and **4.05** were calculated in acetone and both showed a higher binding with macrocycle **4.03** than DB24C8. Pseudorotaxane formation was also characterised by the use of ESI mass spectrometry. It was reported that benzo-21-crown-7 **4.03** is the smallest cavity a secondary dialkylammonium salt is able to thread through as similar investigations with benzo-18-crown-6 showed no complex formed.

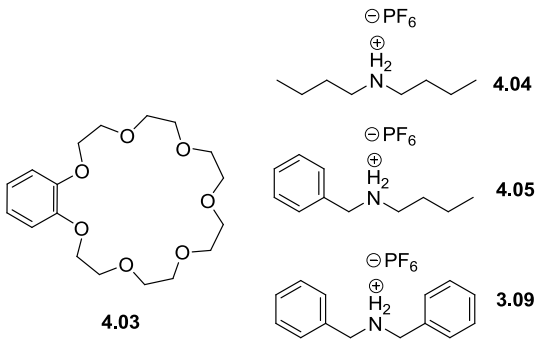


Figure 4.2 Benzo-21-crown-7 binding studies with three ammonium binding templates.

Huang *et al* have also synthesised [2]pseudorotaxanes with secondary dialkylammonium ions using pyrido-21-crown-7 (Figure 4.3).[201] It has been found that crowns containing pyridine show an enhanced complexation with threads due to the pyridyl nitrogen being a better hydrogen bond acceptor than the aliphatic or phenolic ether oxygens. Likewise, this pyrido macrocycle was complexed with the threads shown in Figure 4.2. The pseudorotaxanes were again in a slow-exchange in the ^{1}H NMR time scale enabling the binding constant to be calculated using the single point method.[129] The K_a values were found to be higher with each thread than those with the benzo-21-crown-7 macrocycle in acetone. [2]rotaxanes were obtained using the threading followed by stoppering approach with phenyl groups acting as stoppers (Figure 4.3). The rotaxane architecture was characterised by x-ray crystallography and ESI-MS as well as NMR.

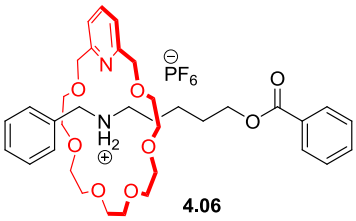


Figure 4.3 [2]rotaxane formed from a secondary dialkylammonium and a pyrido-21-crown-7.

More recently Wu *et al* have synthesised a [2]rotaxane with just 20 atoms in the macrocycle surrounding an ammonium ion.[202] In this case a trifluoromethyl group is utilised to both enhance the templating effect and act as a stopper. Using a clipping strategy a diolefin polyether cyclised by a ring closing metathesis (RCM) step provided the [2]rotaxane **4.07** in a 54% yield (Figure 4.4).

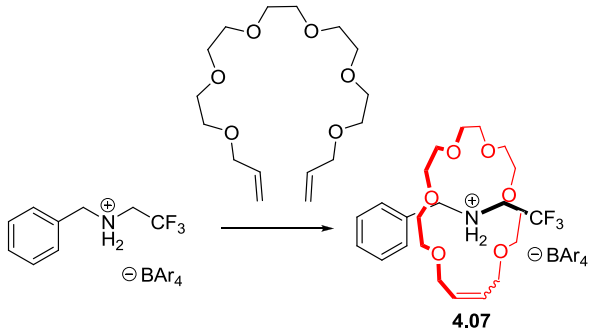


Figure 4.4 Synthesis of [2]rotaxane **4.07** *via* a RCM clipping strategy.

Synthesis of interlocked molecules can prove challenging as they usually rely on supramolecular assistance from weak interactions such as π-stacking, ion-dipole and hydrogen bonding. The electrostatic attraction between oppositely charged ions is a stronger more robust interaction. Loeb reported the use of these electrostatic interactions in the formation of [2]pseudorotaxanes (Figure 4.5).[131] These were prepared using a positively charged 1,2-*bis*(pyridinium)ethane axle and a negatively charged DB24C8 ether macrocycle with sulphonic (SO_3^-) groups attached to each aromatic moiety (Figure 4.5). The interactions between the axle and macrocycle providing the [2]pseudorotaxane **4.08** were driven by hydrogen bonds, π-stacking and ion-dipole interactions as well as the electrostatic ion-ion interactions. It was found that the interaction of the sulphonated crown macrocycle were greater than for the neutral crown in polar solvents such as MeOH. Comparing K_a values of the neutral and charged crown highlighted the significance of this added electrostatic interaction in providing an overall stronger attraction between the wheel and axle.

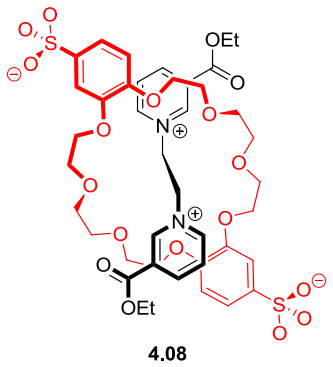


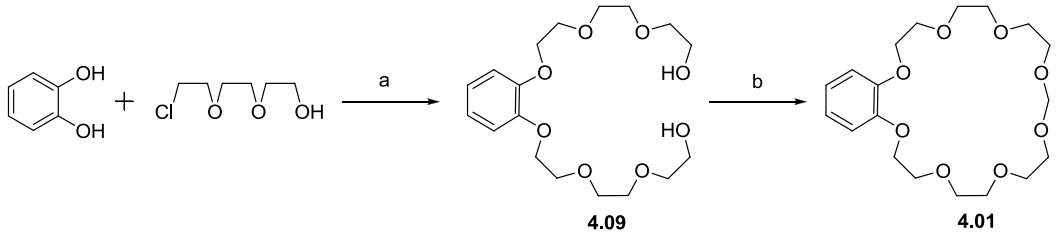
Figure 4.5 Loeb's [2]pseudorotaxane **4.08** containing additional ionic interactions.

Other groups have investigated the effect of increasing macrocycle size on the binding interactions between crown and axle. Chiu *et al* have taken bis-*p*-xylyl[26]crown-6 (BPX26C6) with a larger macrocycle cavity than DB24C8 and shown it can bind with *bis*pyridinium cations.[203] Taking equimolar quantities of this crown and *N,N'*-dimethyl-4,4'-bipyridinium it was seen to form [3]rotaxanes with a stoichiometry of 2:1. Chiu has also successfully incorporated this macrocycle towards the synthesis of molecular shuttles in one pot reactions with *bis*pyridinium binding templates.[203-204]

4.2 Synthesis of Novel 23 Atom Cavity Macrocycles.

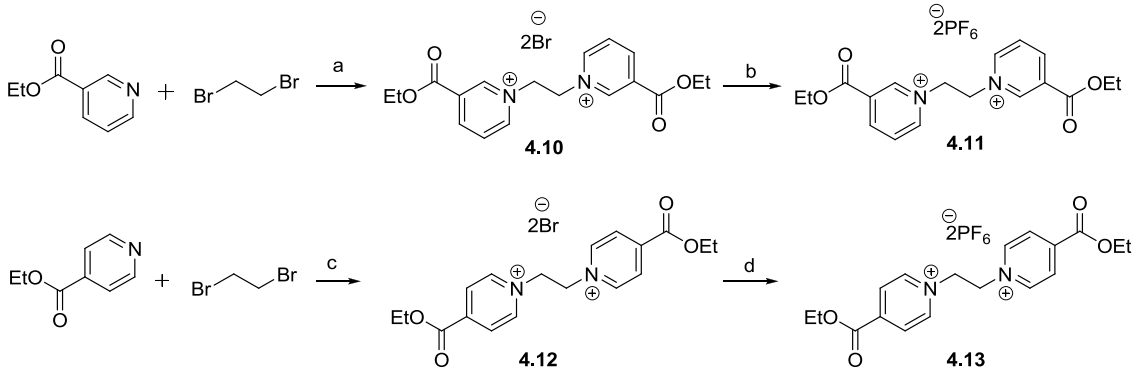
As shown, there are many examples of modifying macrocycle size as well as changing functionality to moderate the interactions between macrocycle and axle.[131,200-201] Herein we report on modifications to the DB24C8 macrocycle with a reduction of the crown ether macrocycle cavity size first investigated. To achieve this, an ethyl oxy bridge (OCH_2CH_2O) was replaced with an acetal moiety (OCH_2O). This reduced the macrocycle from a 24 atom cavity to a 23 atom cavity but retained the number of oxygen acceptors. Introduction of the acetal would also allow us to introduce functionality to the macrocycle whilst retaining a degree of symmetry of the macrocycle. Previous examples by Loeb had shown that lowering the symmetry of the crown makes analysis of resulting pseudorotaxanes and rotaxanes more challenging.[131]

A macrocycle with a cavity of 23 atoms was successfully synthesised by initially reacting catechol and triethylene glycol chlorohydrin to give the corresponding diol **4.09**. The diol was then reacted in high dilution in CH_2Cl_2 with sodium hydroxide to provide the macrocycle **4.01** in a 39% yield shown in Scheme 4.1.[205]



Scheme 4.1 Reagents and conditions: a) DMF, K_2CO_3, N_2, 100˚C, 24h, 47%; b) CH_2Cl_2, NaOH (excess), RT, 5d, 39%.

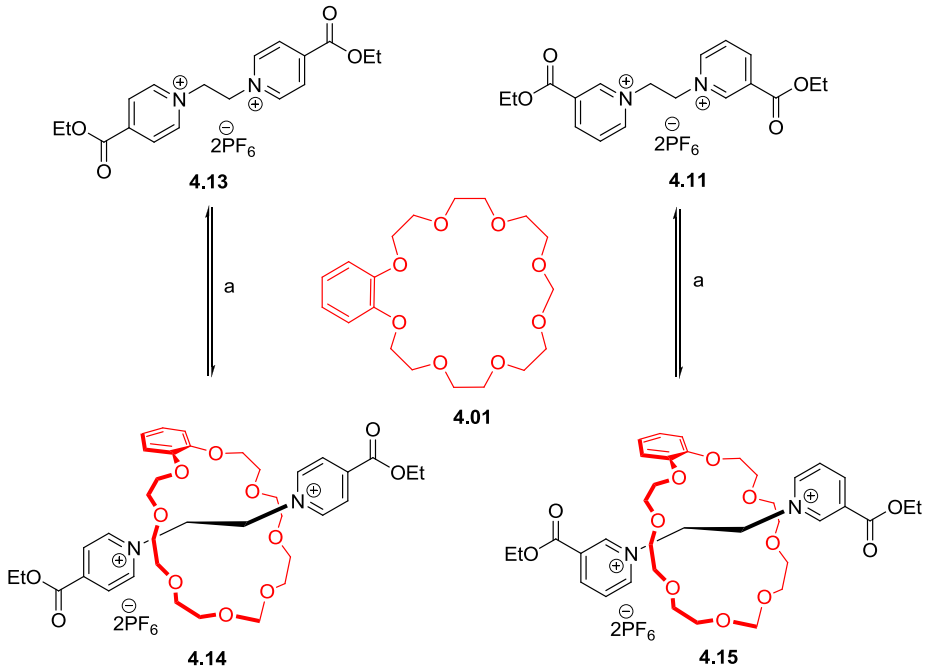
The binding ability of this macrocycle was then investigated with known and novel binding templates that have shown interactions with crown ether type macrocycles. Loeb has previously reported that *bis*pyridinium salts have excellent binding with DB24C8 macrocycles and this was the first binding template investigated.[46] The known *bis*pyridnium salts were synthesised from ethyl isonicotinate and ethyl nicotinate as starting materials. This was carried out in an excess of dibromoethane heating at 100°C overnight to give the corresponding bromide salts **4.10** and **4.12**. Ion exchange by treatment with ammonium hexafluorophosphate gave the two *bis* pyridinium PF_6 salts **4.11** and **4.13** shown in Scheme 4.2.



Scheme 4.2 Reagents and conditions: a) 100˚C, 24h, 44%; b) MeOH, NH_4PF_6, RT, 36%; c) 100˚C, 24h, 40%; d) MeOH, NH_4PF_6, RT, 40%.

The binding of the new macrocycle was examined in comparison to the known DB24C8 values. Initially performing these binding experiments at 2 mmol was attempted but at this concentration there was only a small extent of pseudorotaxane formation observed. All binding studies were then carried out with these novel macrocycles performed at a 15 mmol

concentration. Taking an equimolar solution of the *bis*pyridinium threads (**4.11** and **4.13**) and novel macrocycle **4.01** in deuterated acetonitrile a slow exchange in the ^{1}H NMR timescale was observed. The binding constants were able to be calculated by the single point method for each of the complexes.[129] These were found to be 11 M^{-1} for the interactions of isonicotinate thread **4.13** and crown **4.01** to give pseudorotaxane **4.14** and 55 M^{-1} for nicotinate thread **4.11** and crown **4.01** to give pseudorotaxane **4.15**. These binding constants are vastly different to the observed binding constants reported by Loeb[131] with DB24C8 which are 1940 M^{-1} and 4750 M^{-1} respectively. The reasons for this two orders of magnitude difference probably include the loss of a benzene ring meaning there is a decrease in the π-stacking interactions as well as a detrimental change of hydrogen bonding capabilities from the change of the -OCH_2CH_2O- unit. Previously the *bis*pyridinium threads have been found to rely predominantly on π-stacking interaction in pseudorotaxane formation so the loss of the benzene ring from the macrocycle was expected to have a detrimental effect on the interaction.[46] It was hoped however that the reduction in ring size would provide a better fit between thread and crown and maximise the H-bonding capabilities between the two components.[200]



Scheme 4.3 Reagents and conditions: a) CD_3CN, RT.

Comparison of the ^{1}H NMR spectra of free thread **4.11** and macrocycle **4.01** and rotaxane (**4.15**) is shown in Figure 4.6. The α-pyridinium hydrogen's of the thread are seen to shift downfield due to hydrogen bonding with the crown ether oxygens. The other hydrogens of the pyridinium are shifted upfield as are the aromatic's of the macrocycle due to shielding effects of the interacting π system. The central ethylene group situated in the *bis*pyridinium binding motif are seen also to shift downfield due to hydrogen bonding with the crown ether oxygen's. The signals for the crown ether CH_2's become complicated multiplets shifting both upfield and downfield as a result of their proximity to the thread **4.11**. An NOE interaction was observed between the crown and thread confirming the interlocked nature of pseudorotaxane **4.15**. On irradiation of the two encompassed CH_2N^+ hydrogen's at 5.60 ppm, an enhancement of the signal from the ethylene units of the crown was observed confirming these hydrogen's are close in space. There is also an NOE observed between the α-pyridinium protons and the crown ethoxy methylenes.

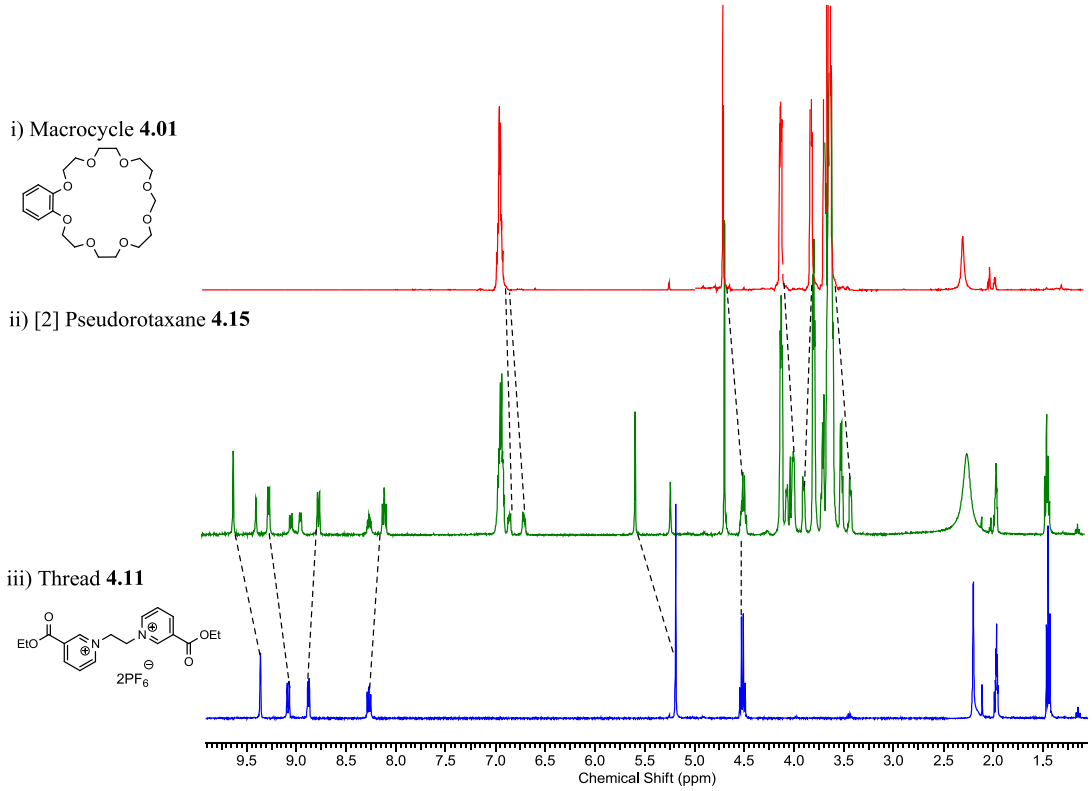


Figure 4.6 ^{1}H NMR Spectra (400 MHz, CD_3CN, 300K) stacking plot i) Macrocycle **4.01**; ii) [2]Pseudorotaxane **4.15**; iii) *Bis*pyridinium thread **4.11**.

The ^{1}H NMR of pseudorotaxane **4.14** shown in Figure 4.7 exhibits very similar shifts to the isonicotinic pseudorotaxane **4.15** with the α-pyridinium hydrogen's again shifted downfield and β aromatic protons shifted upfield due to shielding and deshielding effects of the encompassing macrocycle. Again the central ethylene group of the *bis*pyridinium binding motif are seen to shift downfield as a result of hydrogen bonding with the oxygens of macrocycle **4.01**. The aromatic protons of the macrocycle shift upfield and the CH_2's of the bound crown ether become a complex set of multiplets further indicating the presence of the interlocked structure.

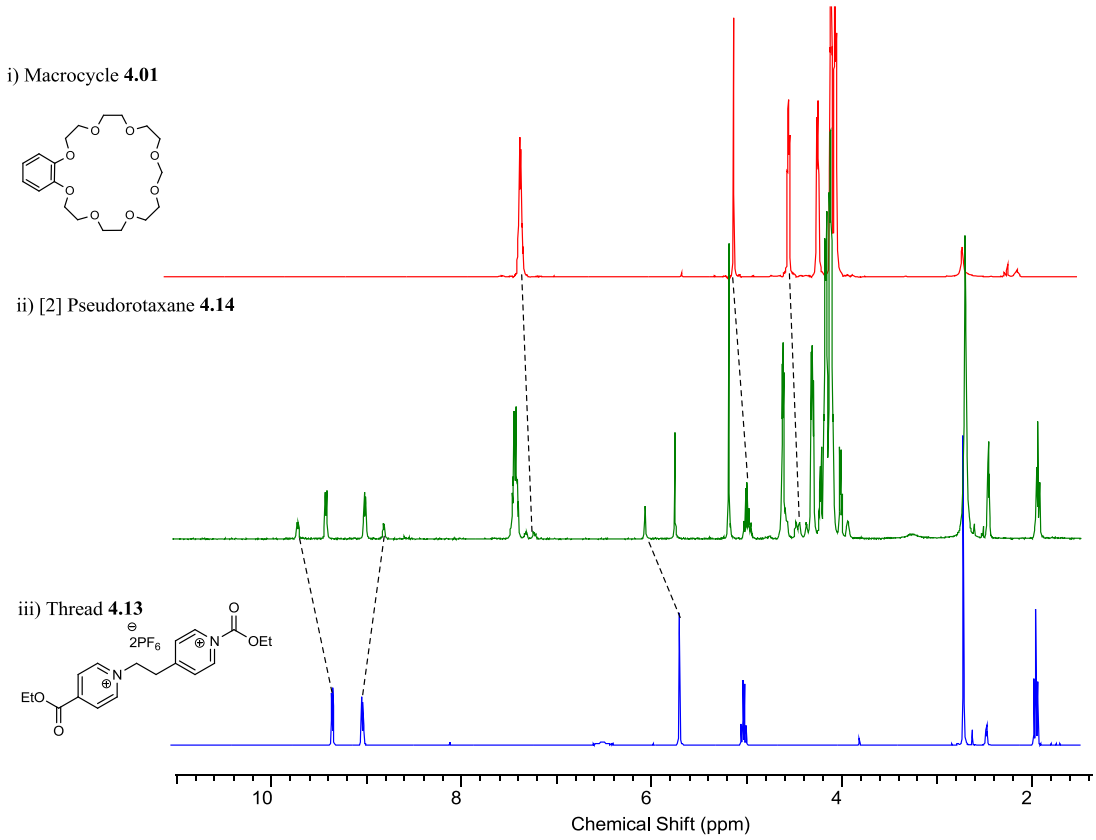


Figure 4.7 ^{1}H NMR Spectra (400 MHz, CD_3CN, 300K) stacking plot i) Macrocycle **4.01**; ii) [2]Pseudorotaxane **4.14**; iii) *Bis*pyridinium thread **4.13**.

4.3 Threading of the 23 Atom Macrocycle with Dialkylammonium Salts

As there was some success with the ability to form pseudorotaxanes with *bis*pyridinium threads **4.11** and **4.13**, binding of the benzo-23-crown macrocycle **4.01** with dialkylammonium salts was also investigated. This was carried out by synthesising the

dibenzylammonium hexafluorophosphate salt **3.09**. Equimolar quantities of macrocycle **4.01** and thread **3.09** were dissolved in deuterated acetonitrile at 15 mmol. A new set of peaks were observed in the ^{1}H NMR due to slow exchange on the NMR timescale allowing calculation of the binding constant by the single point method.[129] The aromatic hydrogens of the thread are shifted slightly upfield and the central ethylene C*H*$_2$NH$_2^+$ hydrogens show a shift downfield because of hydrogen bonding with the crown ether oxygen's (Figure 4.8). The aromatic protons of the crown also show a slight shift upfield due to π-stacking interactions with the thread. The pseudorotaxane **4.16** was also observed by ESI-MS with a peak at 584.4 corresponding to the [**4.16**-PF$_6$]$^+$ complex.

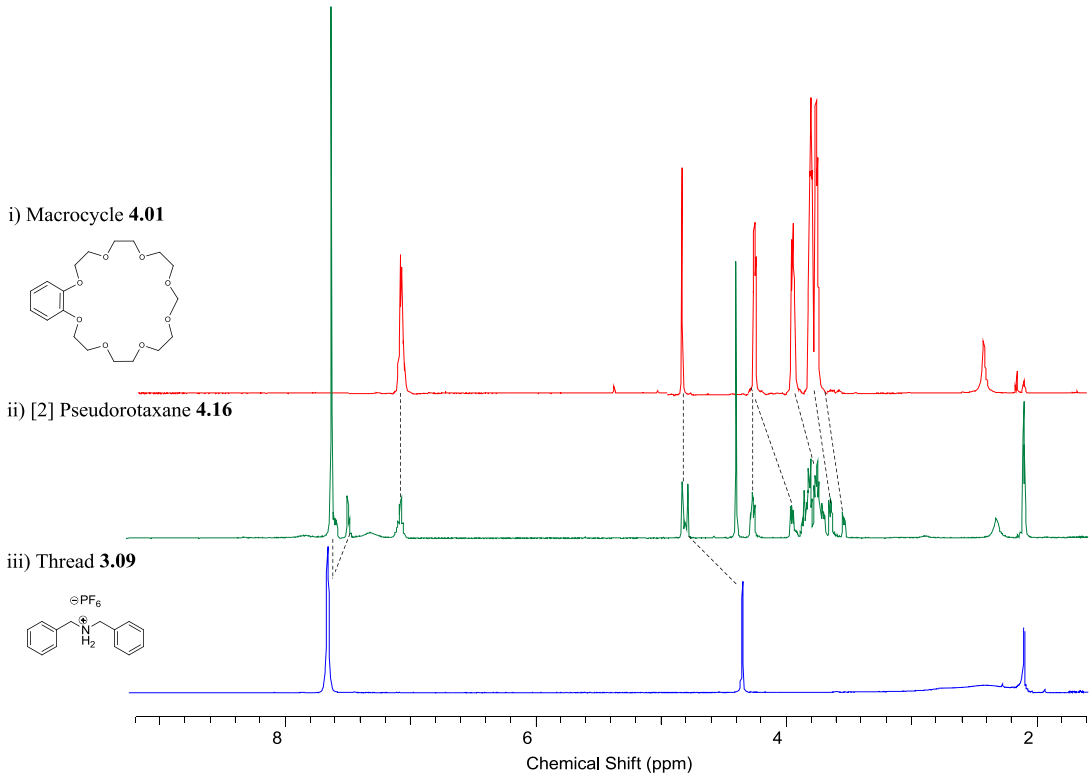
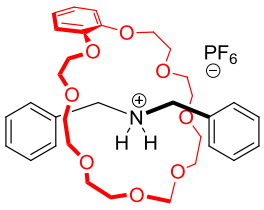


Figure 4.8 ^{1}H NMR Spectra (400 MHz, CD$_3$CN, 300K) stacking plot i) Macrocycle **4.01**; ii) [2]Pseudorotaxane **4.16**; iii) Dibenzylammonium hexafluorophosphate thread **4.16**.

The binding constant of pseudorotaxane **4.16** was found to be 27 M^{-1} in comparison to 200 M^{-1} for the same dialkylammonium salt with DB24C8.[162] In this case there is only one order of magnitude difference between the two values as these recognition sites rely mainly on the hydrogen bonding between crown and axle. However the large decrease in binding suggested the H-bonding capabilities of the crown ether have been compromised.



4.16

Figure 4.9 [2]Pseudorotaxane **4.16**.

The solid state structure of pseudorotaxane **4.16** shown in Figure 4.10 was obtained from crystals grown from an acetonitrile solution of crown **4.01** and thread **3.09** slowly saturated with diethyl ether. Several of the ethylene oxy groups and the acetal of the crown are disordered over two positions in a ratio of 55:45. This variable orientation adopted by about half of the crown chain highlights the lack of any dominant interactions and a poor fit between the thread and the oxygen acceptors of the crown in the solid state and by implication in solution.

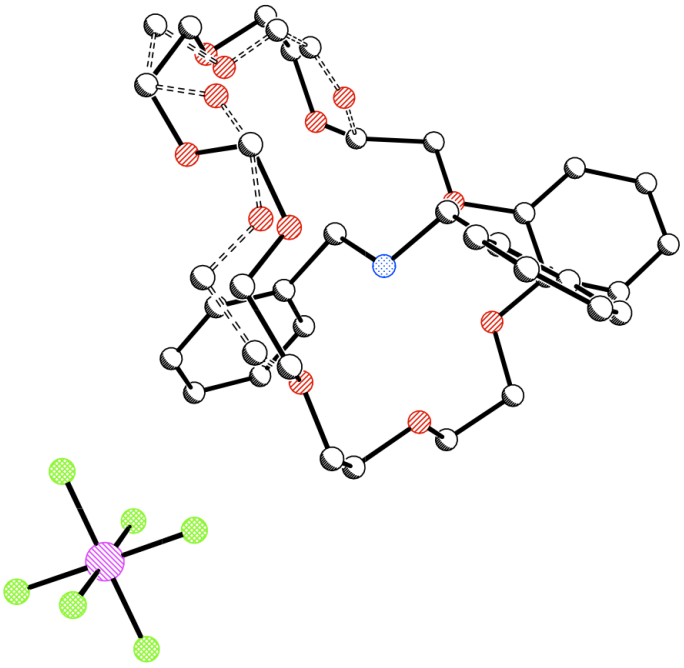


Figure 4.10 Solid state structure of [2]pseudorotaxane **4.16** showing the disordered conformation of the crown chain about the dibenzylammonium ion **3.09**. The two disordered components are in a 55:45 ratio with the bonds of the minor component of the disorder chain shown in dotted lines. Hydrogen atoms have been removed for clarity.

The removal of one -OCH_2CH_2O- and replacement with -OCH_2O- does not affect the smaller crowns ability to thread over the templates. It does however dramatically alter the 'ideal' positioning of the polyethylene oxy chains and their oxygen acceptors around the ammonium ion recognition motif giving a poor fit and reduced complementarity (Figure 4.11). The advantages of this 'ideal' orientation of the oxygens provided by the -OCH_2CH_2O- motif is also prevalent in the binding of metal ions by crowns.[162,206]

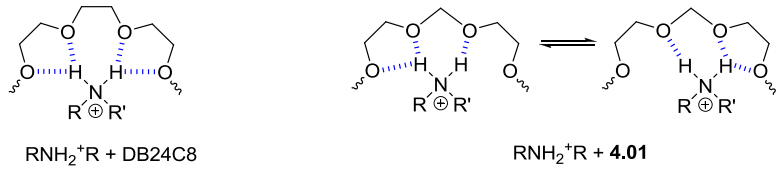
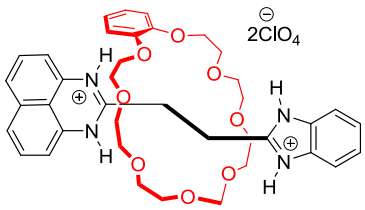


Figure 4.11 A cartoon representation of the 'ideal' H bonding situation of the polyethylene oxy chain of DB24C8 with an ammonium ion and the poorer fit of the methylene acetal containing chain in the solid state structure of pseudorotaxane **4.16**.

The binding constant of the benzo-23-crown macrocycle **4.01** was also investigated with the novel perimidine benzimidazole thread **2.52**. This thread has shown an enhanced binding interaction with DB24C8 presumably by increased π stacking ability and better H bonding. Taking equimolar quantities of thread **2.52** and macrocycle **4.01** in deuterated acetonitrile the binding interaction between the two components was measured at a 15 mmol concentration. The value was found to be 44 M^{-1} which is greatly reduced when comparing to DB24C8 which gave a binding constant of 755 M^{-1} (Figure 4.12). It is however larger than the interaction with the dibenzyl ammonium thread **3.09** so the more favourable binding interaction seen for DB24C8 is mirrored to a lesser extent in its interaction with **4.01**. The binding constants observed are summarised in Table 4.1. In comparison with DB24C8 the greatest difference in binding with macrocycle **4.01** is seen for the *bis*pyridinium threads where the interaction is known to rely heavily on π stacking.



4.17

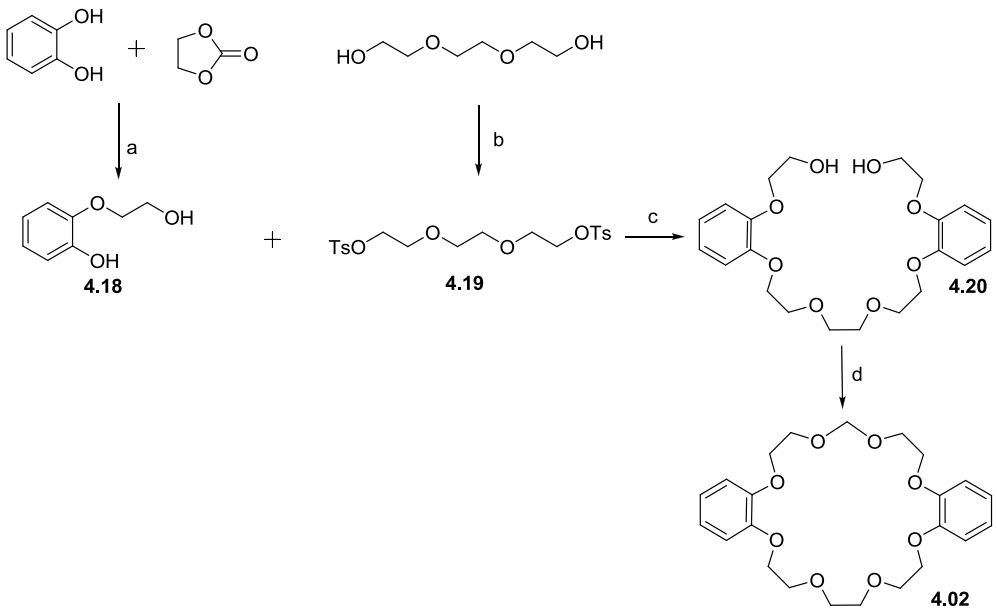
Figure 4.12 [2]Pseudorotaxane **4.17**.

[2]Pseudorotaxanes	23 atom cavity crown Binding constant (15 mM)	DB24C8 binding constant (2 mM)
Dibenzylammonium **4.16**	27 M^{-1}	200 M^{-1}
Perimidine benzimidazole **4.17**	44 M^{-1}	755 M^{-1}
Nicotinate *bis* pyridinium **4.15**	55 M^{-1}	4750 M^{-1}
Isonicotinate *bis*pyridinium **4.14**	11 M^{-1}	1940 M^{-1}

Table 4.1 Summary of binding constants of benzo-23-crown macrocycle **4.01** and DB24C8 with various binding motifs.[46,162]

4.4 Synthesis of Dibenzo-23-crown Macrocycle.

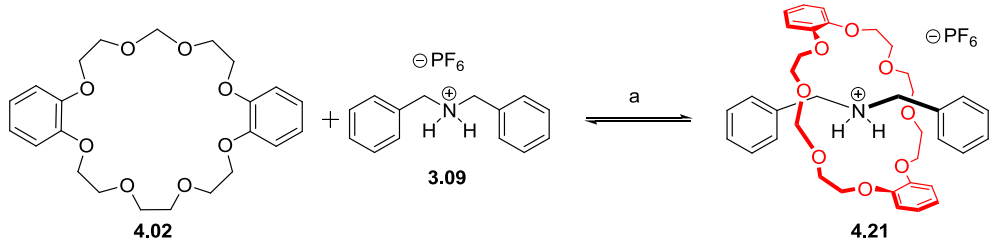
A 23 atom macrocycle was then designed that still contains the 8 oxygen acceptors and retained a similar π stacking ability to DB24C8. This was achieved taking triethylene glycol and activating the alcohols with tosyl groups to provide **4.19**. A second reaction heating catechol and ethylene carbonate to 160°C provided the diol (**4.18**). These two compounds were heated together at reflux in acetonitrile with potassium carbonate under N_2 to provide **4.20**. Finally the macrocycle (**4.02**) was synthesised in CH_2Cl_2 with an excess of sodium hydroxide and purified *via* column chromatography (Scheme 4.4). Confirmation of the structure was provided by ESI-MS with a peak at 452.1 corresponding to the [**4.02**+NH_4]$^+$ ion.



Scheme 4.4 Reagents and conditions: a) TBAI, 160˚C, 18h, 52%; b) THF, aq. NaOH, H_2O, TsCl, 24h, 77%; c) Acetone, K_2CO_3, N_2, reflux; 24h, 29%; d) CH_2Cl_2, NaOH (excess), RT, 5d, 41%.

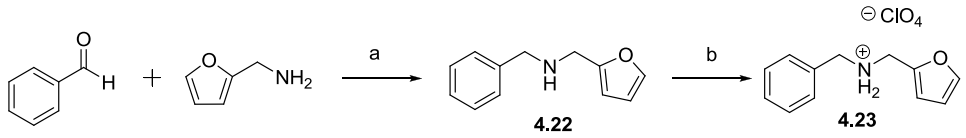
This new dibenzo-23-crown macrocycle **4.02** was then investigated in the assembly of pseudorotaxanes. Binding with both the *bis*pyridinium threads **4.11**, **4.13** and equimolar quantities of macrocycle **4.02** in deuterated acetonitrile was first attempted at 15 mmol concentration. Unfortunately no pseudorotaxane formation was seen after several days of observation at room temperature. Heating the samples to 40˚C for 72 hours was carried out but still no threading of the macrocycle occurred. It was then attempted to assemble the pseudorotaxane using the macrocycle **4.02** with dibenzyl ammonium thread **3.09** and in this case a very small amount of pseudorotaxane **4.21** formation was detected. This took several days before reaching equilibrium as observed *via* ^{1}H NMR. The pseudorotaxane **4.21** was also identified by HRMS with peak seen at 632.3222 for the expected [**4.21**-PF_6]$^+$ species. In this case the binding constant was calculated to be 9 M^{-1}, even lower than with the previous benzo-23-crown macrocycle **4.01** (Scheme 4.5) which was 27 M^{-1}. It is found that incorporation of the second benzene ring into the macrocycle has a detrimental effect on both the threading and binding with typical axles. Pseudorotaxane formation was also observed with the perimidine benzimidazole thread **3.09** which suggests that the lack of complete binding with *bis*pyridinium threads **4.11** and **4.13** may be a result of the change in

shape of the macrocycle cavity. Threading appears to be hindered by the presence of the ester units on these two threads.



Scheme 4.5 Synthesis of [2]rotaxane **4.21**. Reagents and conditions: a) CD_3CN, RT.

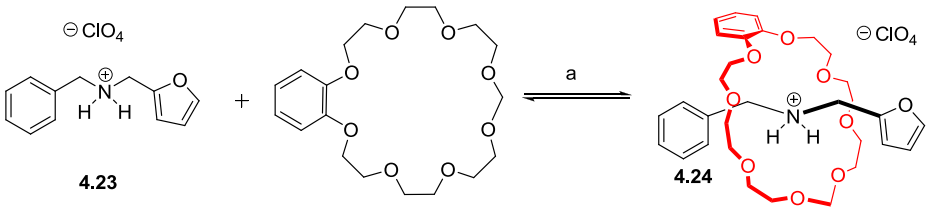
To gain a fair comparison of the binding of the dibenzo-23 atom cavity macrocycle **4.02** with that of the benzo-23-crown macrocycle **4.01** a different binding template was investigated. It was observed in Chapter 3 that incorporating a five membered triazole ring into the binding template can enhance the interaction between the axle and DB24C8. A dibenzyl ammonium thread was synthesised where one of the aromatic rings was a five membered heterocycle. The reduced ring size allows threading through both macrocycle cavities to enable comparison of the two crown ethers. Reaction of benzaldehyde and furfurylamine provided the intermediate imine. Reduction of the imine with one equivalent of sodium borohydride provided the neutral thread **4.22**, which was converted to the ClO_4^- salt on treating with $HClO_4$ (Scheme 4.6).



Scheme 4.6 Reagents and conditions: a) i) MeOH, RT, 24 h; ii) MeOH, $NaBH_4$, 0˚C, 67%; c) $HClO_4$, 51%.

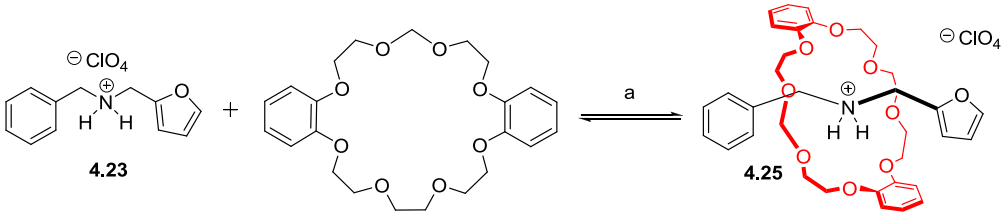
The binding interaction between new thread **4.23** and the two novel macrocycles was then compared. Equimolar quantities of macrocycle **4.01** and thread **4.23** were dissolved in deuterated acetonitrile at 15 mmol. Formation of pseudorotaxane **4.24** (Scheme 4.7) was observed by ^{1}H NMR and ESI-MS at 574.1 for the expected [**4.24**-ClO_4]$^+$. The binding constant between these two components was found to be 114 M^{-1}, the highest binding

interaction we had seen using this macrocycle. This enhancement is thought to be a result of a better 'fit' between the two components.



Scheme 4.7 Reagents and conditions a) CD_3CN, RT.

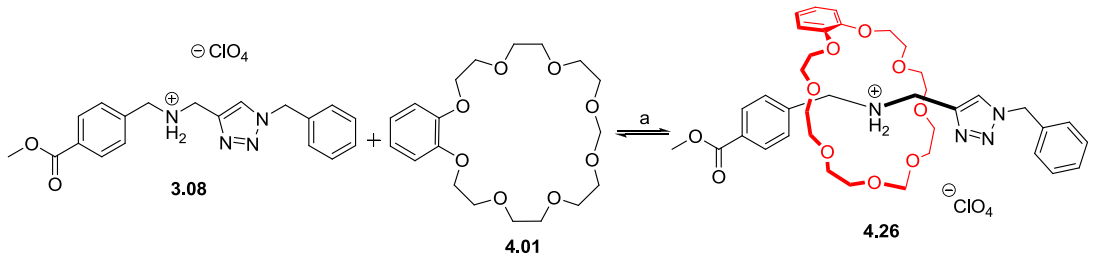
With these encouraging results the binding interaction was next measured between thread **4.23** and the dibenzo-23 macrocycle **4.02**. Again equimolar amounts of thread **4.23** and macrocycle **4.02** were dissolved in deuterated acetonitrile at 15 mmol concentration giving pseudorotaxane **4.25** (Scheme 4.8). In this case the binding was found to be 10 M^{-1}, one order of magnitude less than pseudorotaxane **4.24**. This was surprising as it was expected that the binding would be increased for the dibenzo-23-crown **4.02** as it has the added benzene ring able to take part in π-stacking interactions. Again this provided evidence that addition of a second benzene ring does in fact have a detrimental effect on the binding with ammonium axles. It is thought that the additional benzene moiety adds extra rigidity to the crown ether removing its ability to adapt an ideal binding conformation. Also there is an increase in the number of weaker H bond accepting aromatic ethers compromising the hydrogen bond accepting capability of the macrocycle.[207] Unfortunately a solid state structure was not obtained of this macrocycle or any pseudorotaxane so the unfavourable effects that are operating in the dibenzo-23 crown **4.02** are difficult to clarify.



Scheme 4.8 Reagents and conditions a) CD_3CN, RT.

4.5 Pseudorotaxane Formation with Novel 23 Atom Macrocycles and Triazole Binding Templates

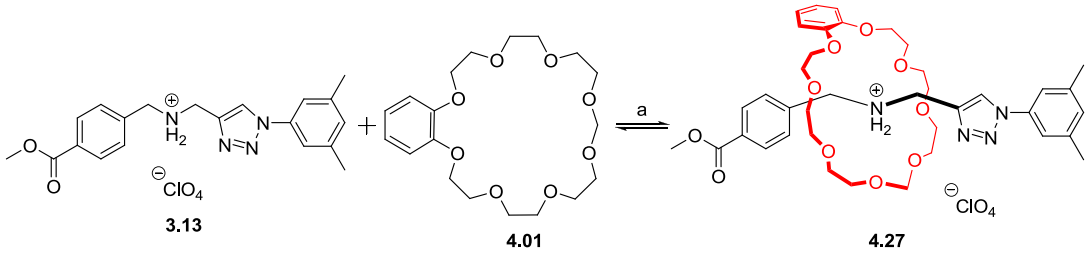
From the results obtained in binding investigations with the novel macrocycles and a variety of threads, the binding interaction was found to be best with the furfuryl ammonium thread **4.23**. Having discovered the beneficial effect of incorporating a triazole into a dibenzylammonium binding motif enhancing the binding interaction between threads **3.08** and **3.13** and DB24C8, investigating interactions between this novel binding motif and the 23 atom cavity macrocycle (**4.01**) was performed. The binding between the benzyl azide derived thread **3.08** and the benzo-23-crown macrocycle **4.01** was first investigated. Taking equimolar quantities of these two compounds at 15 mmol concentration it was pleasing to see the presence of a new set of peaks corresponding to pseudorotaxane (**4.26**) formation *via* ^{1}H NMR (Scheme 4.9). Once the reaction had reached equilibrium the binding constant was measured between the components. It was found to be 112 M^{-1} comparable with the binding between macrocycle **4.01** and furfuryl thread **4.23** which was 114 M^{-1}. Incorporation if this five membered ring system again had a positive effect on the interaction with the 23 atom cavity macrocycles. Pseudorotaxane formation was also observed by HRMS seeing a peak at 723.3559 corresponding to the expected [**4.26**-ClO_4]$^{+}$ species.



Scheme 4.9 Reagents and conditions: a) CD_3CN, RT, 4 d.

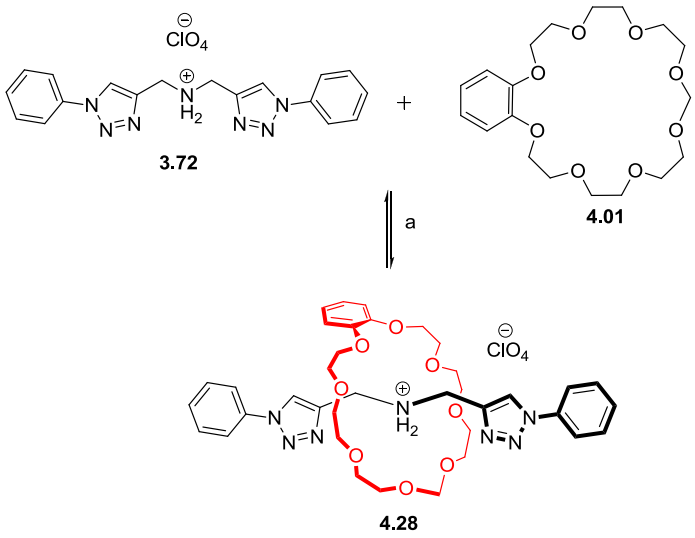
After gaining these promising results, the interaction between macrocycle **4.01** and the phenyl azide derived thread **3.13** was next considered. Taking the thread **3.13** with equimolar quantity of macrocycle **4.01** at 15 mmol, a new set of peaks appeared in the ^{1}H NMR indicating pseudorotaxane (**4.27**) formation (Scheme 4.10). This was confirmed by a

peak seen at 737.3757 in the HRMS relating to the expected [**4.27**-ClO_4]$^+$. The reaction took 4 days to reach equilibrium at which point the binding constant was calculated and found to be 122 M^{-1}. This value is very similar to the previous benzyl azide derived pseudorotaxane **4.26** and it appears that the conjugated system does not have a great effect on the binding between these novel macrocycles and axles. Having a five membered ring system such as the triazole or the furfuryl group is the greatest factor in enhancing the binding of these two components suggesting the cavity shape is the limiting factor. It is thought the 23 atom macrocycles 'fit' better around the reduced bulk of this binding template rather than an enhancement of the hydrogen bonding ability of the thread.



Scheme 4.10 Reagents and conditions: a) CD_3CN, RT, 4 d.

As it was found that insertion of a five membered ring can enhance the binding interactions between ammonium containing axles and novel benzo-23 macrocycle **4.01** incorporating two triazoles in the binding site was investigated to observe any enhancements to these delicate interactions. Taking ditriazole thread **3.72** discussed in Chapter 3 with one equivalent of macrocycle **4.01** at 15 mmol in deuterated acetonitrile the reaction took four days to reach equilibrium. Pseudorotaxane (**4.28)** formation was monitored *via* ^{1}H NMR (Scheme 4.11). The binding constant was calculated to be 151 M^{-1}, a slight increase in the interaction between this thread compared to the pseudorotaxane **4.27** which gave a binding constant of 122 M^{-1}. This indicates that incorporating two triazoles in the binding template of an axle provides an even better fit with this 23 atom cavity macrocycle **4.01**. This enhances the intermolecular interactions between these components and the binding appears to be more sensitive to the size of the groups adjacent to the ammonium ion centre.



Scheme 4.11 Reagents and conditions: a) CD_3CN, RT.

Axles with triazoles incorporated have shown the best binding interactions with these novel 23 atom macrocycles. Synthesis of rotaxanes using this novel binding template was carried out using the Coutrot[106] 'CuAAC click chemistry' conditions previously seen in Chapter 3. A [2]rotaxane **4.29** was synthesised containing the mono triazole binding motif and benzo-23-crown macrocycle **4.01**. Taking one equivalent of the PF_6^- salt **3.88** and four equivalents of macrocycle **4.01** in CH_2Cl_2 with $Cu(MeCN_4)PF_6$, 2,6-lutidine and azide **3.11** rotaxane formation was observed by TLC. Purification *via* column chromatography afforded the final product **4.29** in a 12% yield. The rotaxane was characterised by ^{1}H and ^{13}C NMR and HRMS with peak seen at 707.4024 relating to the [**4.29**-PF_6]$^+$ species.

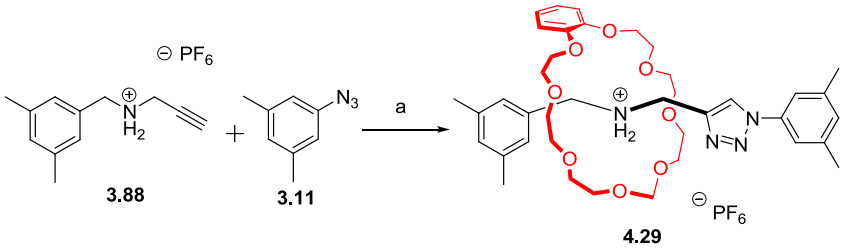


Figure 4.13 Synthesis of [2]pseudorotaxane **4.29**. Reagents and conditions a) CH_2Cl_2, $Cu(MeCN_4)PF_6$, 2,6-lutidine, RT, 24h, **4.01** (4 equiv).

The ^{1}H NMR spectra is shown in Figure 4.14. The two $CH_2NH_2^+$ exhibit the familiar shift downfield due to hydrogen bonding with the macrocycle **4.01** crown ether oxygens and

show coupling with the ammonium ion hydrogens.[32] The acetal CH_2 of the macrocycle is shifted slightly downfield and these hydrogens become diastereotopic due to the asymmetry of the thread and couple with each other to appear as two doublets. The macrocycle ethylene CH_2's become very complex as a result of encompassing the asymmetric thread. The aromatic hydrogen's are only slightly affected on being encompassed by the macrocycle suggesting the π stacking interactions are not as great as they are with DB24C8 macrocycle.

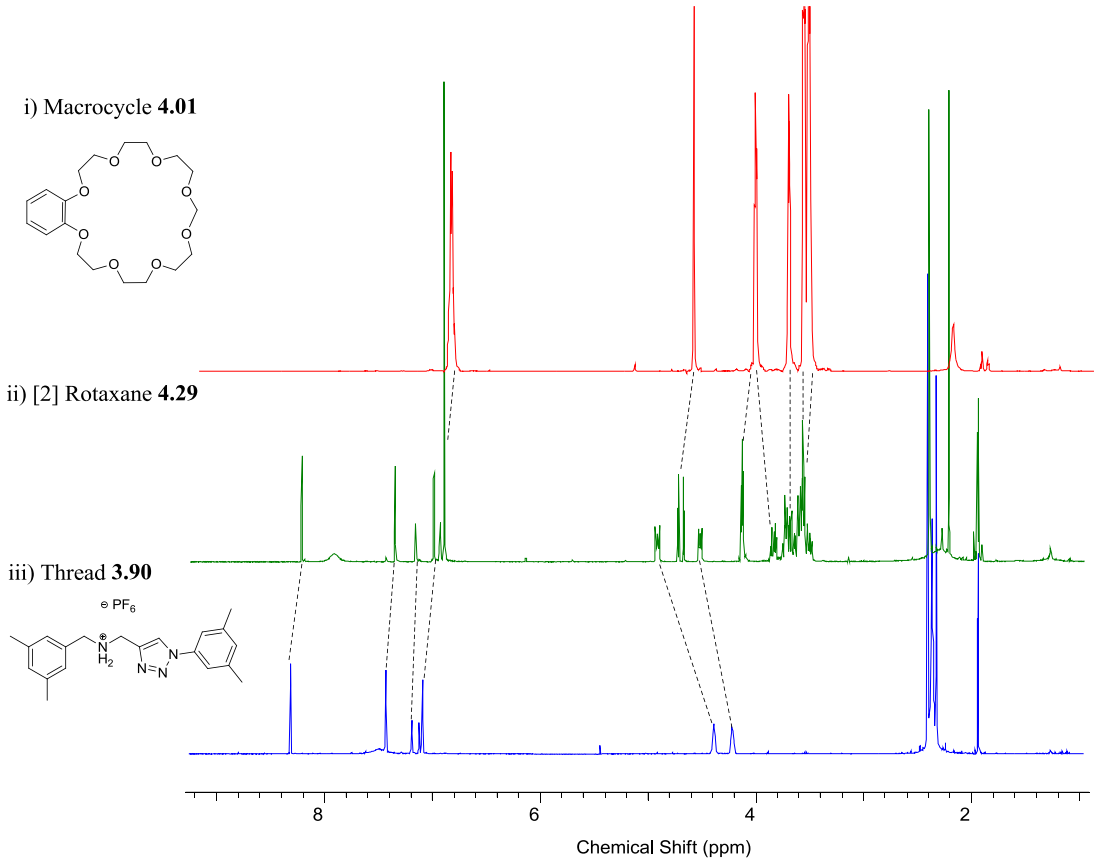


Figure 4.14 ^{1}H NMR (400 MHz, CD_3CN, 300K) stacking plot of i) Macrocycle **4.01**; ii) [2]Rotaxane **4.29**; ii) thread **3.90**.

Finally attempts were made to synthesise a [2]rotaxane with this thread and the dibenzo-23 macrocycle **4.02**. A very small amount of [2]rotaxane was formed as observed by ^{1}H NMR and also by ESI-MS with a peak at 755.2 that indicated the presence [**4.30**-PF_6]$^+$ ion. Due to the low extent of threading we were however unable to isolate and purify the [2]rotaxane but the findings were encouraging.

4.7 Conclusion

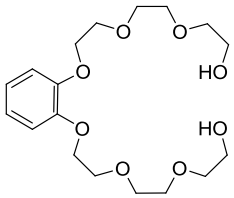
Two novel macrocycles have been successfully synthesised with cavities of 23 atoms and used to create a variety of pseudorotaxanes and a [2]rotaxane. We found that when comparing binding interactions between these new macrocycles with typical templates for rotaxane formation, a large decrease in binding affinity was found with respect to similar interactions with DB24C8.

The study of benzo-23-crown **4.01** and *bis*pyridinium threads **4.11** and **4.13** showed the binding interaction was vastly different in comparison to the reported interactions with DB24C8. Some of this loss in binding interaction was accounted for as these templates rely heavily on π stacking interactions and one benzene ring was lost, but when modifying the macrocycle to contain two benzene rings (**4.02**) the macrocycle was no longer capable of threading onto the axle.

The binding studies were also carried out between these macrocycles and a dibenzyl ammonium axle **3.09** and perimidine benzimidazole axle **2.52**. Again values obtained were very low in comparison to the same threads binding with DB24C8. However some improvement was found when incorporating a five membered ring system into the binding template. Values of binding interactions with benzo-23-crown **4.01** were found to be as high as 150 M^{-1} with the ditriazole thread **3.72** but the dibenzo-23-crown **4.02** did not show any significant improvement in binding. It appears the change in shape of the cavity and replacing an ethylene unit with an acetal reduces its ability to form strong intermolecular interactions with typical rotaxane forming templates. Although the 23 atom cavity macrocycles showed reduced binding with known and novel templates, a [2]rotaxane **4.29** was successfully isolated and characterised using the Coutrot click conditions.[106]

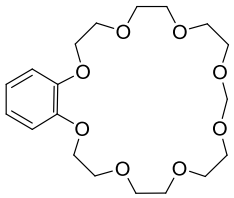
4.8 Experimental

4.09



Known compound synthesised according to literature procedure.[208] A solution of catechol (1.5 g, 13.6mmol) and triethylene glycol chlorohydrin (4.3 mL, 25 mmol) in DMF (30 mL), along with potassium carbonate (6 g, 60 mmol) was stirred at 100°C for 12 h under N_2. After cooling to room temperature, the solution was filtered and concentrated under reduced pressure. The residue was diluted in water (10 mL) and extracted with $CHCl_3$ (3 x 20 mL). The extracts were dried over $MgSO_4$, filtered and solvent removed *in vacuo*. The crude product was purified *via* flash chromatography (EtOAc:CH_2Cl_2; 2:1) to provide a colourless oil (2.4 g, 6.4 mmol, 47%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.68 (m, 4H, 4 ArC*H*), 4.13 (m, 4H, 2 OCH_2CH_2O-Ar), 3.85 (m, 4H, 2 OCH_2CH_2O-Ar), 3.80 (m, 4H, 2 CH_2O), 3.71 (m, 4H, 2 CH_2O), 3.64 (m, 4H, 2 CH_2CH_2OH), 3.58 (m, 4H, 2 CH_2CH_2OH); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 148.9 (Ar*C*), 121.7 (Ar*C*H), 114.9 (Ar*C*H), 72.6 (CH_2O), 70.8 (CH_2O), 70.4 (CH_2O), 69.8 (CH_2O), 68.9 (CH_2OH), 61.6 (CH_2O); IR ν cm^{-1} 3438 (OH), 2874 (saturated C-H), 1503 (ether C-O); HRMS (ESI$^+$): *m/z* found, 397.1830 calc for $C_{18}H_{30}NaO_8$ 397.1833 [**3.09**+Na]$^+$.

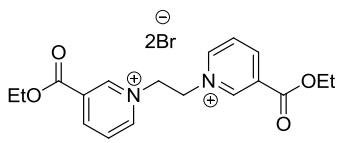
4.01



4.09 (500 mg, 1.34 mmol) was dissolved in CH_2Cl_2 (25 mL) and added dropwise to a rapidly stirred mixture of sodium hydroxide (25 mg, 0.6 mmol) in CH_2Cl_2 (250 mL). The reaction was followed by TLC (EtOAc:MeOH:H_2O; 40:5:1) until completion. The solution was concentrated *in vacuo* to around 30 mL then washed with water (3 x 20 mL). The organic

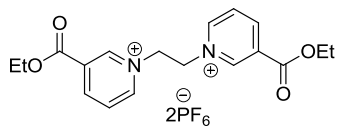
layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The product was then purified *via* flash chromatography (SiO_2: EtOAc to EtOAc:MeOH 9:1) providing a colourless oil (0.4g, 1.04 mmol, 78%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.89 (br s, 4H, 4 ArC*H*), 4.73 (s, 2H, OCH_2O), 4.15 (t, 4H, *J* = 5.0 Hz, 2 Ar-OCH_2CH$_2$O), 3.90 (t, 4H, *J* = 5.0 Hz, 2 Ar-OCH$_2$CH_2O), 3.78-3.71 (m, 16H, 8 OCH_2); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 148.6 (Ar*C*), 121.2 (Ar*C*H), 114.1 (Ar*C*H), 95.3 (acetal *C*H$_2$), 71.1 (O-*C*H$_2$), 71.1' (O-*C*H$_2$), 70.6 (O-*C*H$_2$), 69.9 (O-*C*H$_2$), 69.1 (O-*C*H$_2$), 66.9 (O-*C*H$_2$); HRMS (ESI$^+$): *m/z* found, 409.1834 calc for $C_{19}H_{30}NaO_8$ 409.1833 [**4.01**+Na]$^+$; IR ν cm^{-1} 2870 (saturated C-H), 1500 (ether C-O).

4.10



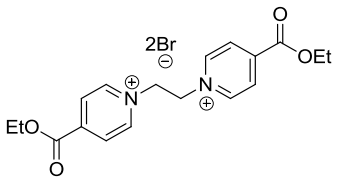
Known compound synthesised according to modified literature procedure.[132] Ethyl nicotinate (2 mL, 14.7 mmol) was dissolved in dibromoethane (10 mL) and heated to 100 °C for 24 h. The solution was cooled, filtered and the solid washed with acetone (3 mL) to give a white solid (3.2 g, 6.53 mmol, 44%). m.p. 250-251°C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 9.82 (s, 2H, 2 PyrC*H*N), 9.43 (d, 2H, *J* = 6.5 Hz, 2 PyrC*H*), 9.18 (d, 2H, *J* = 8.0 Hz, 2 PyrC*H*), 8.35 (dd, 2H, *J* = 6.5 + 8.0 Hz, 2 PyrC*H*), 5.50 (s, 4H, NCH_2CH_2N), 4.55 (q, 4H, *J* = 7.5 Hz, 2 OCH_2CH$_3$), 1.47 (t, 6H, *J* = 7.5 Hz, 2 OCH$_2$CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 162.8 (*C*=O), 149.9 (Pyr*C*H), 148.7 (Pyr*C*H), 148.4 (Pyr*C*H), 133.5 (Pyr*C*), 130.6 (Pyr*C*H), 64.8 (O*C*H$_2$CH$_3$), 61.4 (N*C*H$_2$*C*H$_2$N), 14.8 (OCH$_2$*C*H$_3$); MS (ESI$^+$): *m/z* 308.0 [**4.10**-Br]$^+$; IR ν cm^{-1} 2990 (saturated C-H), 1723 (ester C=O).

4.11



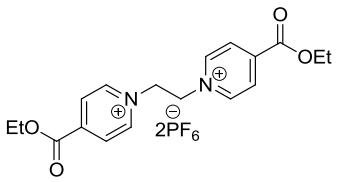
Known compound synthesised according to modified literature procedure.[132] Dibromide salt **4.10** (1g, 2.04 mmol) was dissolved in MeOH (1 mL). A concentrated solution of ammonium hexafluorophosphate in MeOH (2.5 mL) was added followed by the dropwise addition of water to induce precipitation. The solid was filtered and recrystallised from acetonitrile/Et_2O to provide a light brown solid (460 mg, 0.74 mmol, 36%). m.p. 238-239°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.34 (s, 2H, 2 PyrC*H*N), 9.06 (d, 2H, *J* = 8.0 Hz, 2 PyrC*H*), 8.85 (d, 2H, *J* = 6.0 Hz, 2 PyrC*H*), 8.25 (dd, 2H, *J* = 8.0 + 6.0 Hz, 2 PyrC*H*), 5.17 (s, 4H, NCH_2CH_2N), 4.49 (q, 4H, *J* = 7.3 Hz, 2 OCH_2CH$_3$), 1.42 (t, 6H, *J* = 7.3 Hz, 2 OCH$_2$CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 162.4 (*C*=O), 149.4 (Pyr*C*H), 148.5 (Pyr*C*H), 147.9 (Pyr*C*H), 133.3 (*C*CO), 130.9 (Pyr*C*H), 64.8 (O*C*H$_2$CH$_3$), 60.9 (N*C*H$_2$*C*H$_2$N), 14.7 (OCH$_2$*C*H$_3$); MS (ESI$^+$): *m/z* 475.0 [**4.11**-PF$_6$]$^+$; IR ν cm^{-1} 3094 (saturated C-H), 1732 (ester C=O), 822 (P-F).

4.12



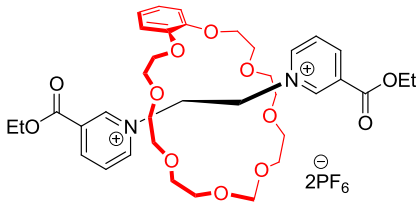
Known compound synthesised according to modified literature procedure.[132] Ethyl isonicotinate (2 mL, 13 mmol) was dissolved in dibromoethane (10 mL, excess) and heated at 70°C for 24 h. Acetone (50 mL) was added to the hot stirring solution and it was then allowed to cool. The white solid precipitate (1.2g, 2.45 mmol, 40%) was filtered and washed with acetone (3 mL). m.p. 237-238°C (decomp.); ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 9.20 (d, 4H, *J* = 6.7 Hz, 4 α-PyrC*H*), 8.67 (d, 4H, *J* = 6.7 Hz, 4 PyrC*H*), 5.52 (s, 4H, NCH_2CH_2N), 4.57 (q, 4H, *J* = 7.0 Hz, 2 OCH_2CH$_3$), 1.47 (t, 6H, *J* = 7.0 Hz, 2 OCH$_2$CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 162.8 (*C*=O), 146.7 (*C*CO), 146.3 (Pyr*C*H), 128.5 (Pyr*C*H), 64.4 (O*C*H$_2$CH$_3$), 60.0 (N*C*H$_2$*C*H$_2$N), 13.2 (OCH$_2$*C*H$_3$); IR ν cm^{-1} 3018 (saturated C-H), 1723 (ester C=O).

4.13



Known compound synthesised according to literature procedure.[132] Dibromide salt **4.12** (100 mg, 0.20 mmol) was dissolved in MeOH (1 mL) and a concentrated MeOH solution of ammonium hexafluorophosphate (1 mL) was added. A precipitate formed which was filtered and washed with water (3 mL) (50 mg, 0.08 mmol, 40%). m.p. 208-209 °C (decomp.); ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.34 (d, 4H, *J* = 7.0 Hz, 4 α-PyrC*H*), 9.02 (d, 4H, *J* = 7.0 Hz, 4 PyrC*H*), 5.69 (s, 4H, NCH_2CH_2N), 5.02 (q, 4H, *J* = 7.0 Hz, OCH_2CH_3), 1.94 (t, 6H, *J* = 7.0 Hz, 2 OCH_2CH_3); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 162.4 (*C*=O), 148.0 (*C*CO), 147.8 (PyrCH), 129.8 (PyrCH), 65.0 (OCH_2CH_3), 61.2 (NCH_2CH_2N), 14.5 (OCH_2CH_3); MS (ESI$^+$): *m/z* 164.1 [**4.13**-2PF_6]$^{2+}$; IR ν cm^{-1} 3084 (saturated C-H), 1732 (ester C=O), 817 (P-F).

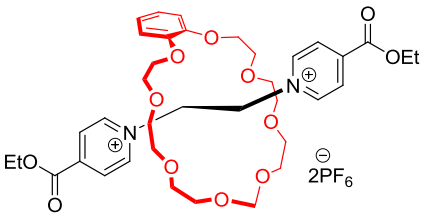
4.15



Thread **4.11** (18 mg, 0.03 mmol) and crown **4.01** (12 mg, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL) and pseudorotaxane formation observed by ^{1}H NMR. Binding constant = **55 M^{-1}** was calculated from the single point method[129] by measuring the integration of α-PyrCC*H*N protons for the free and bound thread at 9.34 ppm and 9.60 ppm respectively. **Pseudorotaxane 4.15** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.60 (s, 2H, ⊂ 2 PyrC*H*N), 9.25 (d, 2H, *J* = 6.0 Hz, ⊂ 2 PyrC*H*), 8.75 d, 2H, *J* = 8.0 Hz, ⊂ 2 PyrC*H*), 8.09 (dd, 2H, *J* = 6.0 + 8.0 Hz, ⊂ 2 PyrC*H*), 6.83 (m, 2H, crown ⊂ 2 ArC*H*), 6.69 (m, 2H, crown ⊂ 2 ArC*H*), 5.57 (s, 4H, ⊂ NCH_2CH_2N), 4.50-4.45 (m, 6H, ⊂ O-CH_2-O and ⊂ 2 OCH_2CH_3),

4.05-3.98 (m, 8H, ⊂ 4 crown OCH_2), 3.89-3.88 (m, 4H, ⊂ 2 crown OCH_2), 3.72-3.70 (m, 4H, ⊂ 2 crown OCH_2), 3.50-3.48 (m, 4H, ⊂ 2 crown OCH_2), 3.41-3.40 (m, 4H, ⊂ 2 crown OCH_2), 1.43 (m, 6H, ⊂ 2 OCH_2CH_3); Also contains for comparison **Crown 4.01** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-CH_2-O), 4.15 (t, 4H, *J* = 5.0 Hz, Ar-O-CH_2CH$_2$-O), 3.90 (t, 4H, *J* = 5.0 Hz, Ar-O-CH$_2$CH_2-O), 3.77 (m, 16H, 8 CH_2); and **Thread 4.11** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.34 (s, 2H, 2 PyrC*H*N), 9.06 (d, 2H, *J* = 8.0 Hz, 2 PyrC*H*), 8.85 (d, 2H, *J* = 6.0 Hz, 2 PyrC*H*), 8.25 (dd, 2H, *J* = 8.0 Hz + 6.0 Hz, 2 PyrC*H*), 5.17 (s, 4H, CH_2CH_2), 4.49 (q, 4H, *J* = 7.0 Hz, 2 OCH_2CH$_3$), 1.42 (t, 6H, *J* = 7.0 Hz, 2 OCH_2CH_3); MS (ESI$^+$): *m/z* 861.1 [**4.15**-PF_6]$^+$, 358.2 [**4.15**-2PF_6]$^{2+}$.

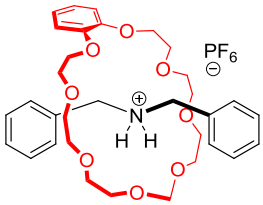
4.14



Thread **4.13** (18 mg, 0.03 mmol) and crown **4.01** (12 mg, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL) and pseudorotaxane formation observed by ^{1}H NMR. Binding constant = **11 M^{-1}** was calculated from the single point method[129] by measuring the integration of α-PyrC*H*N protons for the free and bound thread at 8.90 ppm and 9.20 ppm respectively. **Pseudorotaxane 4.14** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 9.20 (d, 4H, *J* = 6.0 Hz, ⊂ 4 α-PyrC*H*N), 8.30 (d, 4H, *J* = 6.0 Hz, ⊂ 4 PyrC*H*), 6.81-6.80 (m, 2H, ⊂ 2 crown ArC*H*), 6.73 (m, 2H, ⊂ 2 crown ArC*H*), 5.55 (s, 4H, ⊂ CH_2CH_2), 4.65 (s, 2H, ⊂ O-CH_2-O), 4.47 (m, 4H ⊂ 2 CH_2CH$_3$), 4.11-4.05 (m, 8H, ⊂ 4 crown OCH_2), 3.97-3.92 (m, 8H, ⊂ 4 crown OCH_2), 3.72-3.70 (m, 4H, ⊂ 2 crown OCH_2), 3.43-3.42 (m, 4H, ⊂ 2 crown OCH_2), 1.43 (m, 6H, ⊂ 2 CH$_2$CH_3); Also for comparison **Crown 4.01** ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-CH_2-O), 4.15 (t, 4H, *J* = 5.0 Hz, Ar-O-CH_2CH$_2$O), 3.90 (t, 4H, *J* = 5.0 Hz, Ar-OCH$_2$CH_2O), 3.77 (m, 16H, 8 CH_2); **Thread 4.13** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.90 (d, 4H, *J* = 7.0 Hz, 4 α-PyrC*H*N), 8.51 (d, 4H, *J* =

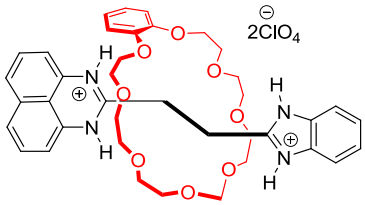
7.0 Hz, 4 PyrC*H*), 5.23 (s, 4H, CH_2CH_2), 4.49 (q, 4H, *J* = 7.0 Hz, 2 OCH_2CH$_3$), 1.42 (t, 6H, *J* = 7.0 Hz, 2 OCH$_2$CH_3); MS (ESI$^+$): 358.1 [**4.14**-2PF$_6$]$^{2+}$.

4.16



Thread **3.09** (15 mg, 0.03 mmol) and crown **4.01** (12 mg, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL) and pseudorotaxane formation observed by ^{1}H NMR. Binding constant = **27 M^{-1}** was calculated from the single point method[129] by measuring the integration of the 10 ArC*H* protons for the free and bound thread at 7.47 ppm for free thread 7.45-7.43 and 7.34 ppm for the bound thread. **Pseudorotaxane 4.16** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 7.45-7.43 (m, 4H, ⊂ 4 thread ArC*H*), 7.34 (m, 6H, ⊂ 6 thread ArC*H*), 6.94-6.96 (m, 4H, ⊂ 4 crown ArC*H*), 4.67-4.63 (m, 6H, ⊂ CH_2NH$_2^+$CH_2 and ⊂ O-CH_2-O), 4.13-4.10 (m, 4H, ⊂ 2 OCH_2), 3.55-3.33 (m, 8H, ⊂ 4 OCH_2), 3.49-3.47 (m, 8H, ⊂ 4 OCH_2), 3.39-3.37 (m, 4H, ⊂ 2 OCH_2); Also for comparison **Crown 4.01** ^{1}H NMR (400 MHz, 298 K, CDCl$_3$) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-CH_2-O), 4.15 (t, 4H, *J* = 5.0 Hz, Ar-O-CH_2CH$_2$-O), 3.90 (t, 4H, *J* = 5.0 Hz, Ar-O-CH$_2$CH_2-O), 3.77 (m, 16H, 8 CH_2); **Thread 3.09** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 7.47 (m, 10H, 10 ArC*H*), 4.24 (s, 4H, CH_2NH$_2^+$CH_2); MS (ESI$^+$): *m/z* 584.4 [**4.16**-PF$_6$]$^+$.

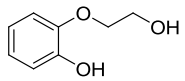
4.17



Thread **2.52** (15 mg, 0.03 mmol) and crown **4.01** (12 mg, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL) and the binding constant was measured. Binding constant = **44 M^{-1}** was calculated from the single point method[129] by measuring the integration of acetal

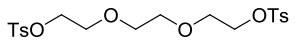
CH_2 protons for the free and bound crown at 4.73 ppm for free crown and 4.44 and 4.36 ppm for bound. **Pseudorotaxane 4.17** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.92-7.84 (m, 2H, ⊂ 2 thread ArC*H*), 7.69-7.67 (m, 2H, ⊂ 2 thread ArC*H*), 7.27-7.22 (m, 4H, ⊂ 4 NaphthC*H*), 6.71-6.69 (m, 2H, ⊂ 2 NaphthC*H*), 6.56 (br s, 4H, ⊂ 4 crown ArC*H*), 4.44 (d, 1H, *J* = 4.0 Hz, ⊂ acetal C*H*H), 4.36 (d, 1H, *J* = 4.0 Hz, ⊂ acetal CH*H*), 4.24-4.19 (m, 2H, ⊂ OCH_2), 4.11-4.09 (m, 8H, ⊂ 4 OCH_2), 4.02-3.96 (m, 4H, ⊂ 2 OCH_2), 3.94-3.90 (m, 4H, ⊂ OCH_2 and ⊂ C-CH_2CH_2-C), 3.56-3.53 (m, 8H, ⊂ 4 OCH_2), 3.46-3.42 (m, 2H, ⊂ C-CH_2CH_2-C); Also for comparison **Crown 4.01** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-CH_2-O), 4.15 (t, 4H, *J* = 5.0 Hz, Ar-O-C$H_2$$CH_2$-O), 3.90 (t, 4H, *J* = 5.0 Hz, Ar-O-CH_2CH_2-O), 3.77 (m, 16H, 8 CH_2); **Thread 2.52** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 12.34 (br s, 2H, 2 N*H*), 10.56 (br s, 2H, 2 N*H*), 7.84-7.82 (m, 2H, 2 ArC*H*), 7.65-7.62 (m, 2H, ArC*H*), 7.47 (d, 2H, *J* = 8.5 Hz, 2 NaphthC*H*), 7.37 (dd, 2H, *J* = 8.5 + 7.5 Hz, 2 NaphthC*H*), 6.82 (d, 2H, *J* = 7.5 Hz, 2 NaphthC*H*), 3.71 (t, 2H, *J* = 7.5 Hz, C$H_2$$CH_2$), 3.17 (t, 2H, *J* = 7.5 Hz, CH_2CH_2); MS (ESI$^+$): *m/z* 700.7 [**4.17**-ClO_4]$^+$.

4.18



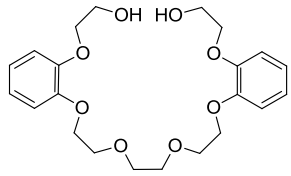
Known compound synthesised according to literature procedure.[209] Catechol (5.5 g, 50 mmol), ethylene carbonate (4.4g, 55 mmol) and tetrabutylammonium iodide (0.6 g, 1.9 mmol) were heated to 160°C for 24 h. The reaction was followed by TLC (EtOAc) until completion. The reaction was purified *via* flash chromatography (SiO_2: CH_2Cl_2/EtOAc; 3:1) to give a brown solid (4g, 25.9 mmol, 52%). m.p. 98-99°C; ^{1}H NMR (400 MHz, 298 K, CD_3OD) δ_H 6.90 (d, 1H, *J* = 7.0 Hz, ArC*H*COH), 6.81-6.74 (m, 3H, 3 ArC*H*), 4.04 (t, 2H, *J* = 6.5 Hz, C$H_2$$CH_2$OH), 3.88 (t, 2H, *J* = 6.5 Hz, CH_2CH_2OH); ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ_C 148.1 (Ar*C*), 147.9 (Ar*C*), 122.7 (Ar*C*H), 120.9 (Ar*C*H), 116.6 (Ar*C*H), 114.2 (Ar*C*H), 71.4 (*C*$H_2$$CH_2$OH), 59.5 ($CH_2$*C*$H_2$OH); IR ν cm^{-1} 3275 (O-H), 2946 (saturated C-H), 1609 (ether C-O); HRMS (ESI$^+$): *m/z* found, 177.0513 calc for $C_8H_{10}NaO_3$ 177.0522 [**4.18**+Na]$^+$.

4.19



Known compound synthesised according to literature procedure.[210] Triethylene glycol (10mL, 60.6 mmol) was dissolved in THF (15 mL) and distilled water (15 mL). The solution was cooled to 0°C and sodium hydroxide (4.68g, 121 mmol) was added. To the cooled solution toluene-*p*-sulphonyl chloride (24 g, 126 mmol) in THF (80 mL) was added dropwise over 1.5 h. The solution was warmed to room temperature, and stirred for a further 24 h. THF was removed *in vacuo* and the residue diluted with water (30 mL) and extracted with $CHCl_3$ (3 x 40 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified *via* flash chromatography (SiO_2: EtOAc) to give a white solid (15.7 g, 46.7 mmol, 77%). m.p. 82-83˚C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.79 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 7.34 (d, 4H, *J* = 8.0 Hz, 4 ArC*H*), 4.14 (t, 4H, *J* = 4.5 Hz, 2 $OCH_2CH_2OSO_2$), 3.65 (t, 4H, *J* = 4.5 Hz, 2 $OCH_2CH_2OSO_2$), 3.52 (s, 4H, 2 CH_2), 2.44 (s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 144.9 (Ar*C*), 132.9 (Ar*C*), 129.8 (Ar*C*H), 127.9 (Ar*C*H), 70.7 (CH_2), 69.2 (CH_2), 68.7 (CH_2), 21.6 (CH_3); IR ν cm^{-1} 1624 (ether C-O), 1173 (-SO_2-O-); MS (ESI$^+$): *m/z* 359.1 [**4.19**+Na]$^+$; CHN Analysis Found: C 52.33; H 5.66. Calc. for $C_{20}H_{26}O_8S_2$: C, 52.39; H, 5.72%.

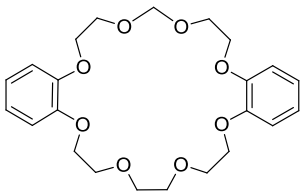
4.20



Known compound synthesised according to literature procedure.[211] The diol **4.18** (200 mg, 1.3 mmol) and ditosylate **4.19** (270 mg, 0.6 mmol) were dissolved in acetone (30 mL) and potassium carbonate (2 g, 15.6mmol) was added. The solution was stirred at reflux under N_2 for 48 h. The solution was cooled, filtered and washed with acetone (10 mL). The solvent was removed and the residue dissolved in CH_2Cl_2 (20 mL). The solution was washed with concentrated aqueous sodium hydroxide solution (3 x 15 mL), dried over $MgSO_4$ and the

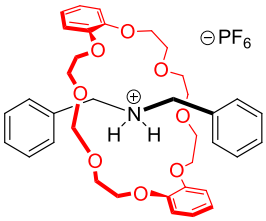
solvent removed *in vacuo*. The product was purified *via* flash chromatography (SiO_2: 9:1, EtOAc:MeOH) to provide a pale brown oil (160 mg, 0.38 mmol, 29%). m.p. 76-77°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.91 (s, 8H, 8 ArC*H*), 4.14 (t, 4H, *J* = 5.0 Hz, 2 O-C*H*$_2$CH$_2$-O), 4.07 (t, 4H, *J* = 5.0 Hz, 2 O-C*H*$_2$CH$_2$-O), 3.90-3.88 (m, 8H, 4 O-C*H*$_2$CH$_2$-O), 3.77 (br s, 4H, O-C*H*$_2$C*H*$_2$-O); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 149.0 (Ar*C*), 148.9 (Ar*C*), 123.8 (Ar*C*H), 121.8 (Ar*C*H), 116.3 (Ar*C*HCO), 115.7 (Ar*C*HCO), 71.6 (O*C*H$_2$), 70.0 (O*C*H$_2$), 68.8 (O*C*H$_2$), 68.0 (O*C*H$_2$), 61.5 (O*C*H$_2$); IR ν cm^{-1} 3563 (O-H), 2916 (saturated C-H), 1252 (ether C-O); HRMS (ESI$^+$): *m/z* found, 445.1854 calc for $C_{22}H_{30}NaO_8$ 445.1833 [**4.20**+Na]$^+$.

4.02



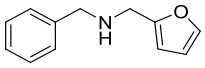
To a stirring mixture of sodium hydroxide (36 mg, 0.9 mmol) in CH_2Cl_2 (250 mL), **4.20** (150 mg, 0.35 mmol) in CH_2Cl_2 (25 mL) was added dropwise over 2 h. The reaction was followed by TLC (EtOAc). The solution was concentrated to around 30 mL and washed with water (3 x 20 mL). The product was purified *via* flash chromatography (SiO_2: EtOAc) to provide a white solid (65 mg, 0.15 mmol, 41%). m.p. 113-114°C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 6.89 (m, 8H, 8 ArC*H*), 4.95 (s, 2H, O-C*H*$_2$-O), 4.18 (m, 4H, 2 Ar-O-C*H*$_2$CH$_2$), 4.15 (m, 4H, 2 Ar-O-C*H*$_2$CH$_2$-O), 3.97 (m, 4H, 2 O-C*H*$_2$CH$_2$-O), 3.91 (m, 4H, 2 O-C*H*$_2$CH$_2$-O), 3.83 (br s, 4H, O-C*H*$_2$C*H*$_2$-O); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 149.2 (Ar*C*), 148.7 (Ar*C*), 121.7 (Ar*C*H), 114.5 (Ar*C*H), 95.9 (O-*C*H$_2$-O), 71.4 (O-*C*H$_2$CH$_2$-O), 69.8 (O-*C*H$_2$CH$_2$-O), 69.3 (O-*C*H$_2$CH$_2$-O), 68.8 (O-*C*H$_2$CH$_2$-O), 66.1 (O-*C*H$_2$CH$_2$-O); HRMS (ESI$^+$): *m/z* found, 457.1831 calc for $C_{23}H_{30}NaO_8$, 457.1838 [**4.02**+Na]$^+$; IR ν cm^{-1} 3073 (saturated C-H).

4.21



Crown **4.02** (13 mg, 0.03 mmol) and thread **3.09** (10 mg, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL) and pseudorotaxane formation monitored by ^{1}H NMR. Binding constant = **9 M^{-1}** was calculated from the single point method[129] by measuring the integration of the 10 ArC*H* protons for the free and bound thread at 7.47 ppm for the free and 7.38-7.35 ppm and 7.19-7.18 ppm for the bound. **Pseudorotaxane 4.21** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.38-7.35 (m, 4H, ⊂ 4 thread ArC*H*), 7.19-7.18 (m, 6H, ⊂ 6 thread ArC*H*), 6.95-6.87 (m 8H, ⊂ 8 crown ArC*H*), 4.79-4.76 (m, 4H, ⊂ $CH_2NH_2^+CH_2$), 4.75 (s, 2H, ⊂ O-CH_2-O), 4.20-4.29 (m, 4H, ⊂ 2 O-CH_2CH_2-O), 4.05-4.02 (m, 8H, ⊂ 4 O-CH_2CH_2-O), 3.95-3.93 (m, 4H, ⊂ 2 O-CH_2CH_2-O), 3.85-3.81 (m, 4H, ⊂ 2 O-CH_2CH_2-O), 3.74-3.71 (m, 4H, ⊂ 2 O-CH_2CH_2-O); Also contains for comparison **Crown 4.02** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.89 (m, 8H, 8 ArC*H*), 4.95 (s, 2H, O-CH_2-O), 4.18 (m, 4H, 2 Ar-O-CH_2CH_2-O), 4.15 (m, 4H, 2 Ar-O-CH_2CH_2-O), 3.97 (m, 4H, 2 O-CH_2CH_2-O), 3.91 (m, 4H, 2 O-CH_2CH_2-O), 3.83 (br s, 4H, 2 O-CH_2CH_2-O); **Thread 3.09** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.47 (m, 10H, 10 ArC*H*), 4.24 (s, 4H, $CH_2NH_2^+CH_2$); HRMS (ESI$^+$): *m/z* found, 632.3222 calc for $C_{37}H_{46}N_2NO_8$ 632.3218 [**4.21**-PF_6]$^+$.

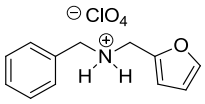
4.22



Known compound synthesised according to literature procedure.[212] Furfurylamine (0.87 mL, 9.8 mmol) and benzaldehyde (1 mL, 9.8 mmol) were dissolved in MeOH (10 mL) and stirred at room temperature for 24 h. The reaction was cooled to 0˚C and sodium borohydride (400 mg, 10 mmol, 1 equiv.) was added portion wise and the solution stirred for 15 minutes. The solution was allowed to warm to room temperature, stirred for 12 h, diluted

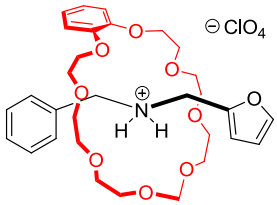
with water (50 mL) and acidified to pH 1 with 4M HCl. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL) then basified to pH 10 with 2M sodium hydroxide. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic extracts were dried over $MgSO_4$, filtered and solvent removed *in vacuo* (1.2 g, 7.27 mmol, 67%). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ_H 7.43 (m, 1H, Fufuryl-C*H*), 7.40 (m, 5H, 5 ArC*H*), 6.38 (m, 1H, Fufuryl-C*H*), 6.25 (m, 1H, Fufuryl-C*H*) , 3.85 (br s, 4H, CH_2NHCH_2); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ_C 154.0 (Ar*C*), 141.9 (Furfuryl-*C*H), 140.1 (Ar*C*), 128.5 (Ar*C*H), 128.3 (Ar*C*H), 127.1 (Ar*C*H), 110.2 (Furfuryl-*C*H), 107.0 (Furfuryl-*C*H), 52.8 (*C*H_2NH), 45.4 (*C*H_2NH); IR ν cm^{-1} 3031 (saturated C-H); MS (ESI$^+$): *m/z* 188.0 [**4.22**+Na]$^+$.

4.23



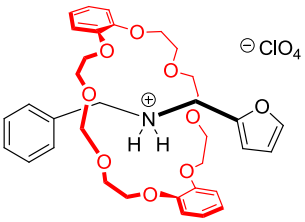
Furfurylbenzyl amine (0.25 g, 1.34 mmol) was dissolved in MeOH (0.5 mL). A 70% aqueous solution of $HClO_4$ (0.25 mL) was added cautiously to the solution. Distilled water was then added dropwise to the solution to induce precipitation. This was filtered and washed with cold water (3 mL) and dried in a desiccator overnight (200 mg, 0.70 mmol, 51%). m.p. 125-126°C; ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.60 (m, 1H, Furfuryl-C*H*), 7.47 (br s, 5H, ArC*H*), 6.64 (m, 1H, Furfuryl-C*H*), 6.50 (m, 1H, Furfuryl-C*H*), 4.28 (s, 2H, C$H_2NH_2^+$), 4.21 (s, 2H, C$H_2NH_2^+$), 2.17 (br s, 2H, NH_2); ^{13}C NMR (100 MHz, 298 K, CD_3CN) δ_C 146.2 (Furfuryl-*C*H), 136.5 (Ar*C*), 131.6 (Ar*C*), 131.5 (Ar*C*H), 131.2 (Ar*C*H), 130.5 (Ar*C*H), 114.7 (Furfuryl-*C*H), 112.6 (Furfuryl-*C*H), 52.3 (*C*H_2), 44.6 (*C*H_2); HRMS (ESI+): *m/z* found, 188.1070 calc for $C_{12}H_{14}NO$ 188.1070 [**4.23**-ClO_4]$^+$; IR ν cm^{-1} 3103 (saturated C-H), 1418 (CH deformations), 1064 (ClO_4).

4.24



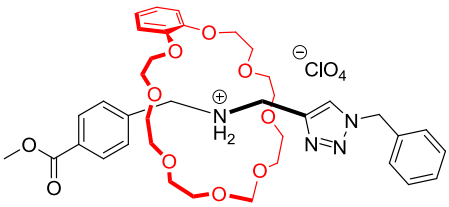
Crown **4.01** (12 mg, 0.03 mmol) and thread **4.23** (8.6 g, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL) and the binding constant measured. Binding constant = **114 M^{-1}** was calculated from the single point method[129] by measuring the integration of furfuryl-C*H* protons for the free and bound thread at 6.64 ppm and 6.44 ppm respectively. **Pseudorotaxane 4.23 - Some peaks obscured by free crown:** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.84 (br s, 2H, ⊂ N*H*$_2$), 7.47-7.44 (m, 1H, ⊂ Furfuryl-C*H*), 7.42-7.40 (m, 2H, ⊂ 2 ArC*H*), 7.34-7.31 (m, 3H, ⊂ 3 ArC*H*), 6.99-6.88 (m, 4H, ⊂ 4 crown ArC*H*), 6.44 (d, 1H, *J* = 3.0 Hz, ⊂ Furfuryl-C*H*), 6.37 (dd, 1H, *J* = 3.0 + 2.0 Hz, ⊂ Furfuryl-C*H*), 4.70 (m, 2H, ⊂ C*H*$_2$NH$_2^+$), 4.69 (m, obscured by free crown, 1H, ⊂ acetal CH*H*), 4.63 (d, 1H, *J* = 4.5 Hz, ⊂ acetal C*H*H), 4.55-4.52 (m, 2H, ⊂ C*H*$_2$NH$_2^+$), 4.10-4.09 (m, 4H, ⊂ 2 OC*H*$_2$), 3.61-3.58 (m, 8H, ⊂ 4 OC*H*$_2$), 3.55-3.48 (m, 12H, ⊂ 6 OC*H*$_2$); Also for comparison **Crown 4.01** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-C*H*$_2$-O), 4.15 (t, 4H, *J* = 5.0 Hz, Ar-O-C*H*$_2$CH$_2$-O), 3.90 (t, 4H, *J* = 5.0 Hz, Ar-O-CH$_2$C*H*$_2$-O), 3.77 (m, 16H, 8 C*H*$_2$); and **Thread 4.23** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.60 (m, 1H, Furfuryl-C*H*), 7.47 (br s, 5H, ArC*H*), 6.64 (m, 1H, Furfuryl-C*H*), 6.50 (m, 1H, Furfuryl-C*H*), 4.28 (s, 2H, C*H*$_2$NH$_2^+$), 4.21 (s, 2H, C*H*$_2$NH$_2^+$), 2.17 (br s, 2H, N*H*$_2$); MS (ESI$^+$): *m/z* 574.1 [**4.24**-ClO$_4$]$^+$.

4.25



Crown **4.02** (12 mg, 0.03 mmol) and thread **4.23** (8.6g, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL) and the binding constant measured. Binding constant = **10 M^{-1}** was calculated from the single point method[129] by measuring the integration of furfuryl-C*H* protons for the free and bound thread at 6.64 ppm and 6.41 ppm respectively. **Pseudorotaxane 4.25** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.35-7.33 (m, 2H, ⊂ 2 ArC*H*), 7.27 (br s, 1H, ⊂ Furfuryl-C*H*), 7.16-7.15 (m, 3H, ⊂ 3 ArC*H*), 6.41 (m, 1H, ⊂ Furfuryl-C*H*), 6.23 (m, 1H, ⊂ Furfuryl-C*H*), 4.74 (s, 2H, ⊂ O-CH_2-O), 4.87 (m 2H, ⊂ CH_2NH$_2^+$), 4.64 (m, 2H, ⊂ CH_2NH$_2^+$), 4.07-4.04 (m, 8H, ⊂ 4 OCH_2), 3.97 (d, 4H, *J* = 4.0 Hz, ⊂ 2 OCH_2), 3.84-3.82 (m, 4H, ⊂ 2 OCH_2), 3.74-3.70 (m, 8H, ⊂ 4 OCH_2); Also for comparison **Crown 4.02** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 6.89 (m, 8H, 8 ArC*H*), 4.95 (s, 2H, O-CH_2-O), 4.18 (m, 4H, 2 Ar-O-CH_2CH$_2$-O), 4.15 (m, 4H, 2 Ar-O-CH_2CH$_2$-O), 3.97 (m, 4H, 2 O-CH_2CH$_2$-O), 3.91 (m, 4H, 2 O-CH_2CH$_2$-O), 3.83 (br s, 4H, 2 O-CH_2CH$_2$-O); and **Thread 4.23** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 7.60 (m, 1H, Furfuryl-C*H*), 7.47 (br s, 5H, ArC*H*), 6.64 (m, 1H, Furfuryl-C*H*), 6.50 (m, 1H, Furfuryl-C*H*), 4.28 (s, 2H, CH_2NH$_2^+$), 4.21 (s, 2H, CH_2NH$_2^+$), 2.17 (br s, 2H, NH_2); MS (ESI$^+$): *m/z* 622.1 [**4.25**-ClO_4]$^+$.

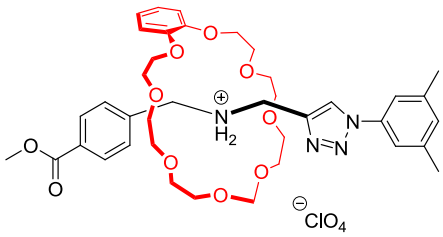
4.26



Thread **3.08** (13 mg, 0.03 mmol) and crown **4.01** (12 mg, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL). Pseudorotaxane formation was monitored by ^{1}H NMR over 4 days. Binding constant = **112 M^{-1}** was calculated from the single point method[129] by measuring the integration of CH_2NH$_2^+$CH_2 protons for the free and bound thread at 4.35 ppm for free and 4.90 and 4.75 ppm for bound. **Pseudorotaxane 4.26** ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.34 (s, 1H, ⊂ triazole-C*H*), 7.94-7.89 (m, 2H, ⊂ 2 ArC*H*), 7.60-7.54 (m, 2H, ⊂ 2 ArC*H*), 7.48-7.42 (m, 3H, ⊂ 3 ArC*H*), 7.19-7.17 (m, 2H, ⊂ 2 ArC*H*), 6.92-6.83 (m, 4H, ⊂ 4 crown ArC*H*), 5.53 (s, 2H, ⊂ CH_2N-triazole), 4.90 (m, 2H, ⊂ CH_2NH$_2^+$), 4.75 (m, 2H, ⊂

C*H*$_2$NH$_2^+$), 4.64 (d, 1H, J_{HH} = 4.0, ⊂ acetal C*H*H), 4.55 (d, 1H, J_{HH} = 4.0, ⊂ acetal CH*H*), 3.86 (s, 3H, ⊂ OC*H*$_3$), 3.62-3.59 (m, 16H, ⊂ 8 crown O-C*H*$_2$CH$_2$-O), 3.50-3.49 (m, 8H, ⊂ 8 crown O-C*H*$_2$CH$_2$-O). Also contains for comparison **Macrocycle 4.01** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-C*H*$_2$-O), 4.15 (t, 4H, *J* = 5.0 Hz, O-C*H*$_2$CH$_2$-O), 3.90 (t, 4H, *J* = 5.0 Hz, 2 O-C*H*$_2$CH$_2$-O), 3.77 (m, 16H, 8 O-C*H*$_2$CH$_2$-O); **Thread 3.08** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 8.05 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCO), 7.95 (s, 1H, triazole-C*H*), 7.58 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.35 (m, 5H, 5 ArC*H*), 5.60 (s, 2H, C*H*$_2$N-triazole), 4.35 (br s, 4H, C*H*$_2$NH$_2^+$C*H*$_2$) 3.89 (s, 3H, OC*H*$_3$); HRMS (ESI$^+$): found, 723.3559 calc for $C_{38}H_{51}N_4O_{10}$ 723.3600 [**4.26**-ClO$_4$]$^+$.

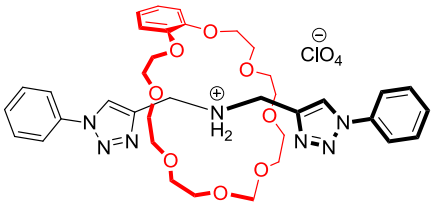
4.27



Thread **3.13** (14 mg, 0.03 mmol) and crown **4.01** (12 mg, 0.03 mmol) were dissolved in deuterated acetonitrile (2 mL). Pseudorotaxane formation was observed using ^{1}H NMR. After 4 days the reaction reached equilibrium. Binding constant = **122 M^{-1}** was calculated from the single point method[129] by measuring the integration of C*H*$_2$NH$_2^+$ protons for the free and bound thread at 4.43 ppm and 4.97 ppm respectively. **Pseudorotaxane 4.27 – Some peaks obscured by free thread and macrocycle.** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) 8.16 (s, 1H, ⊂ triazole-C*H*), 7.89 (d, 2H, *J* = 7.5 Hz, ⊂ 2 ArC*H*CCOO), 7.55 (d, 2H, *J* = 7.5 Hz, ⊂ 2 ArC*H*CCH$_2$), 7.33 (s, 2H, ⊂ 2 ArC*H*), 7.19 (s, 1H, ⊂ ArC*H*), 6.95-6.88 (br s, 4H, ⊂ 4 crown ArC*H*), 4.89 (m, 2H, ⊂ C*H*$_2$NH$_2^+$), 4.77 (m, 2H, ⊂ C*H*$_2$NH$_2^+$), 4.72 (s, 2H, ⊂ O-C*H*$_2$-O), 3.87 (s, 3H, ⊂ OC*H*$_3$), 3.86-3.58 (m, 20H, ⊂ 10 crown O-C*H*$_2$CH$_2$-O), 3.55-3.47 (m, 4H, ⊂ 2 crown O-C*H*$_2$CH$_2$-O), 2.40 (s, 6H, ⊂ 2 CC*H*$_3$); Also contains for comparison **Macrocycle 4.01** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-C*H*$_2$-O), 4.15 (t, 4H, *J* = 5.0 Hz, 2 O-C*H*$_2$CH$_2$-O), 3.90 (t, 4H, *J* = 5.0 Hz, 2 O-

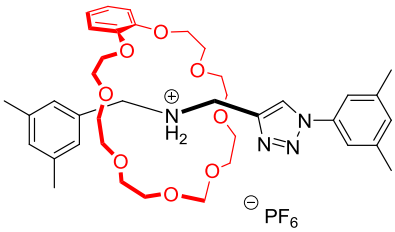
C*H*$_2$CH$_2$-O), 3.77 (m, 16H, 8 O-C*H*$_2$CH$_2$-O); and **Thread 3.13** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 8.33 (s, 1H, triazole-C*H*), 8.07 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCOO), 7.61 (d, 2H, *J* = 8.0 Hz, 2 ArC*H*CCH$_2$), 7.43 (s, 2H, 2 ArC*H*), 7.19 (s, 1H, ArC*H*), 4.43 (s, 2H, C*H*$_2$NH$_2^+$), 4.37 (s, 2H, C*H*$_2$NH$_2^+$), 3.88 (s, 3H, OC*H*$_3$), 2.41 (s, 6H, 2 C*H*$_3$); HRMS (ESI$^+$): found, 737.3757 calc for $C_{39}H_{53}N_4O_{10}$ 737.3756 [**4.27**-ClO$_4$]$^+$.

4.28



Crown **4.02** (12 mg, 0.03 mmol) and thread **3.72** (13 mg, 0.03mmol) were dissolved in deuterated acetonitrile (2 mL). Pseudorotaxane formation was monitored using ^{1}H NMR. Binding constant = **151 M^{-1}** was calculated from the single point method[129] by measuring the integration of triazole-C*H* protons for the free and bound thread at 8.44 ppm and 8.23 ppm respectively. **Pseudorotaxane 4.28** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 8.36 (br s, 2H, ⊂ NH$_2$), 8.23 (s, 2H, ⊂ 2 triazole-C*H*), 7.64-7.50 (m, 10H, ⊂ 10 ArC*H*), 6.96-6.80 (m, 4H, ⊂ 4 crown ArC*H*), 4.96-4.90 (m, 4H, ⊂ C*H*$_2$NH$_2^+$C*H*$_2$), 4.68 (s, 2H, ⊂ O-C*H*$_2$-O), 4.11-4.10 (m, 4H, ⊂ 2 crown OC*H*$_2$), 3.81-3.79 (m, 4H, ⊂ 2 crown OC*H*$_2$), 3.72-3.70 (m, 4H, ⊂ 2 crown OC*H*$_2$), 3.68-3.59 (m, 12H, ⊂ 8 crown OC*H*$_2$); Also contains for comparison **Macrocycle 4.01** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 6.89 (br s, 4H, ArC*H*), 4.73 (s, 2H, O-C*H*$_2$-O), 4.15 (t, 4H, *J* = 5.0 Hz, O-C*H*$_2$CH$_2$-O), 3.90 (t, 4H, *J* = 5.0 Hz, O-C*H*$_2$CH$_2$-O), 3.77 (m, 16H, O-C*H*$_2$CH$_2$-O); and **Thread 3.72** ^{1}H NMR (400 MHz, 298 K, CD$_3$CN) δ_H 8.44 (s, 2H, 2 triazole-C*H*), 7.82 (d, 4H, *J* =8.0 Hz, 4 ArC*H*), 7.63-7.52 (m, 6H, 6 ArC*H*), 4.53 (s, 4H, C*H*$_2$NH$_2^+$C*H*$_2$).

4.29



Thread **3.88** (50 mg, 0.16 mmol) and crown **4.01** (247 mg, 0.64 mmol) were dissolved in CH_2Cl_2 (5 mL) and stirred at room temperature for 5 minutes. The 3,5-dimethylphenylazide **3.11** (26 mg, 0.18 mmol), $Cu(MeCN_4)PF_6$ (60 mg, 0.16 mmol) and 2,6-lutidine (0.02 mL, 0.02 mmol) were added and the reaction was stirred under N_2 for 24 h. The crude reaction mixture was concentrated *in vacuo* and purified *via* flash chromatography (SiO_2: EtOAc to EtOAc:MeOH; 9:1 to CH_2Cl_2:MeOH; 9:1) to provide the rotaxane as a clear oil (15 mg, 0.02 mmol, 12%). ^{1}H NMR (400 MHz, 298 K, CD_3CN) δ_H 8.21 (s, 1H, ⊂ triazole C*H*), 7.91 (br s, 2H, ⊂ NH_2), 7.34 (s, 2H, ⊂ 2 ArC*H*), 7.16 (s, 1H, ⊂ ArC*H*), 6.99 (s, 2H, ⊂ 2 ArC*H*), 6.93 (s, 1H, ⊂ ArC*H*), 6.89 (s, 4H, ⊂ 4 crown ArC*H*), 4.92 (m, 2H, ⊂ C$H_2NH_2^+$), 4.72 (d, 1H, *J* = 4.5Hz, ⊂ acetal C*H*H), 4.67 (d, 1H, *J* = 4.5Hz, ⊂ acetal CH*H*), 4.52 (m, 2H, ⊂ C$H_2NH_2^+$), 4.13 (t, 4H, *J* = 3.8Hz, ⊂ 2 OCH_2), 3.86-3.81 (m, 2H, ⊂ 2 OCH_2), 3.76-3.67 (m, 6H, ⊂ 3 OCH_2), 3.65-3.48 (m, 12H, ⊂ 6 OCH_2), 2.39 (s, 6H, ⊂ 2 CH_3), 2.21 (s, 6H, ⊂ 2 CH_3); ^{13}C NMR (150 MHz, 298 K, CD_3CN) δ_C 148.5 (Ar*C*), 141.4 (Ar*C*), 141.2 (Ar*C*), 139.8 (Ar*C*), 137.9 (Ar*C*), 133.0 (Ar*C*), 131.9 (Ar*C*H), 131.8 (Ar*C*H), 128.9 (Ar*C*H), 124.3 (Ar*C*H), 122.8 (triazole-*C*H), 119.6 (Ar*C*H), 113.8 (Ar*C*H), 97.2 (O-*C*H_2-O), 72.3 (O*C*H_2), 72.0 (O*C*H_2), 71.7 (O*C*H_2), 71.5 (O*C*H_2), 69.8 (O*C*H_2), 68.4 (O*C*H_2), 53.5 (*C*$H_2NH_2^+$), 44.1 (*C*$H_2NH_2^+$), 21.6 (*C*H_3), 21.5 (*C*H_3); HRMS (ESI$^+$): *m/z* found, 707.4024 calc for $C_{39}H_{55}N_4O_8$ 707.4014 [**4.29**-PF_6]$^+$.

Chapter 5

5.1 Conclusion

Using the Diels-Alder reaction [n]rotaxanes have been successfully synthesised *via* the 'threading followed by stoppering' protocol. This has been performed with a variety of binding motifs incorporated into the axles. Using known ammonium ion and *bis*pyridinium templates, [2] and [3]rotaxanes were constructed utilising this approach. Using the 1,2-pyridinium ethane motif, a [2]rotaxane was synthesised and the solid state crystal structure was obtained proving the *endo* conformation of the cyclopentadiene functionalised maleimide Diels-Alder adduct.

Investigation of the Diels-Alder stopper size was also performed. Replacing the bridged six membered ring, with the flat sp^2 hybridised phthalimide moiety the ability to act as a stopper for a DB24C8 macrocycle was removed. When subjected to unfavourable conditions that disrupted the delicate binding interactions between the two components the macrocycle was able to unthread from the axle.

Synthesis of novel binding motifs has also been shown which demonstrate promising binding affinities with crown ether macrocycles. Substituting a perimidine moiety into the *bis*benzimidazole template gave a two fold increase in the binding interaction between the axle and crown ether macrocycle. Introduction of both one and two triazoles into the dibenzylammonium binding site was also found to enhance the interaction between axle and the DB24C8 macrocycle demonstrating how simple modifications can improve binding interactions between components. Synthesis of [n]rotaxanes was carried out using these novel binding templates in the Diels-Alder approach to 'threading followed by stoppering'.

Novel macrocycles were also synthesised with cavities of 23 atoms and used to create a variety of interlocked architectures using known and novel binding motifs. In this case the modification of a crown ether macrocycle has shown a detrimental effect on the binding interaction between the interlocked components. The change in shape of the cavity by replacing an ethylene unit with an acetal reduced its ability to form strong intermolecular interactions with typical binding motifs for rotaxane formation. Although the binding was not as desirable as expected a number of [2]pseudorotaxanes were synthesised as well as a [2]rotaxane using the Coutrot click conditions.[106]

Future work within the group would include the focus on development and synthesis of known and novel binding motifs in order to further enhance binding interactions between these complexes. This would enable the synthesis of more intricate intermolecular complexes including multicomponent rotaxanes as well as the synthesis of molecular machines using the novel binding motifs developed.

Chapter 6

6.1 References

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Appendix

Determination of Association Constants

Peaks are observed for both complexed and uncomplexed species in all pseudorotaxanes described in this thesis. As chemical exchange is slow on the NMR timescale association constants were determined by integration of a 1:1 mixture using ^{1}H NMR calculated *via* the single point method.

$$K_a = \frac{[Pseudorotaxane]}{[Unbound\ Thread][Unbound\ Crown]}$$