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Abstract

The aim of my PhD is to study rotaxanes. This study is intended to contribute to the understanding of rotaxanes and to provide some insights into the possibilities of their application, and is divided in two parts accordingly.

In the first part of my thesis I develop and analyze new hydrogen-bond templates that contain phosphorus and can be used to improve the existing rotaxane formation processes and to synthesize new rotaxanes. The second part of my research is based on the fact that the form of rotaxanes restricts the macrocycle movements to two options only: rotational and translational movement. Thus, in the second part I focus on improving the potential practical application of rotaxanes and on developing and implementing rotational and translational molecular machines, whereby a rotational machine is critical for creating and implementing a translational machine.

In the course of this work two different types of a molecular machine (a molecular accelerator and a molecular shuttle) have been created. The results achieved demonstrate that hydrogen bond-based templates containing phosphorus can be used to template the rotaxane formation, and that both movements of macrocycle, translational and rotational, can indeed be used to improve the molecular machines.
Declaration

I, Andrea Altieri, hereby declare that this PhD thesis has been composed by me. Chapters 1 and 2 are entirely my own, have been composed by me and have not been published to-date. Chapters 3 and 4 are based on the papers that present the results of my research done in co-operation with my colleagues from David Leigh Group and are referred to as specified. This work has not been submitted for any other degree or professional qualification.

The scientific work described in this thesis was carried out in the Department of Chemistry at University of Warwick between July 1999 and September 2001 and in the Department of Chemistry at the University of Edinburgh between October 2001 and November 2002.

Andrea Altieri

Date: 14/10/2004

Signature:
Attended Lectures and Meetings

1- NMR Spectroscopy and Mass Spectrometry Courses, October 2000, University of Warwick.

2- RSC lectures, University of Warwick.

3- Organic Research Seminars, University of Edinburgh.

4- FATEC (Future Advanced Technology Educational Course), University of Warwick.


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Special thanks are due to all members of Dave Leigh’s Group, and especially to Dr Angeles Farran, Dr Gianni Bottari, Dr Francesco Gatti and Dott. Alessio Altieri.
List of Abbreviations

DCM dichloromethane

DMF \(N,N'\)-dimethylformamide

DMSO dimethylsulphoxide

EDCI 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride

Et Ethyl

THF tetrahydrofuran

TFA trifluoroacetic acid

Me Methyl

NMR Nuclear Magnetic Resonance

ppm part per million

\(\delta\) chemical shift

\(E\ trans\) isomer

\(Z\ cis\) isomer

mp melting point

TLC thin Layer Chromatography

FAB Fast Atom Bombardment

rt room temperature

mL milliliters
g grams

HRMS High Resolution Mass Spectrometry

Calcd. calculated

VT variable temperature

SPT-IR Spin Polarisation Transfert by Selective Inversion Recovery

$\Delta G^\circ$ Gibbs energy
Preface

PhD Thesis Structure: A Brief Outline

The aim and purpose of my PhD is to study the rotaxanes. This study is intended to contribute to the theoretical understanding of rotaxanes and to provide some insights into the possibilities of their practical application, and is accordingly divided in two parts.

In the first part of my thesis I develop and analyze new hydrogen-bond templates containing phosphorus that can be used to improve the existing rotaxane formation processes and to synthesize new rotaxanes. The practical part of my research is based on the fact that the form of the rotaxanes restricts the macrocycle movements to the only two possibilities: rotational and translational movement. In the second part I focus on improving the potential practical application of rotaxanes and developing and implementing rotational and translational molecular machines while a rotational machine is indispensable for creating and implementing a translational machine.

The overall practical application of this research is quite extensive:

a) I will create new templates that can add to the range of templates available in rotaxane chemistry which will give to the synthetic chemist more flexibility in designing rotaxanes. Also, the new templates serve as a foundation for the creation of a set of new rotaxanes containing heteroatoms. They can potentially be used in creating and designing new molecular shuttles or new phosphorus-based catalysts. However, both application possibilities are beyond the scope of the present research.
b) Generally, rotaxanes serve as a basis for molecular level machines. In my research I focus on how rotaxanes can be used to develop a more flexible molecular machine which, being one of the smallest possible machines, can be beneficially used in nanotechnology, a leading cross-scientific field of research.

My PhD thesis is structured in accordance with the above-stated goals.

In Chapter 1 I give some overall historical background of the research into interlocked molecules and outline their development, from the origins to the creation of catenanes and rotaxanes.

I also draw on the research on rotaxanes done and on the strategies used for synthesizing rotaxanes to-date.

I will then specifically focus on the latter, especially on benzylamidic rotaxanes. Also, in this chapter I will describe the existing varieties of molecular shuttles and the way they operate.

I demonstrate that not only are benzylamidic rotaxanes aesthetically beautiful and have a very special theoretical value, but that they can also be used extensively in devising molecular machines.

In Chapter 2, I focus on the practical application of the properties of the new class of phosphine oxide-based templates giving special attention to how they operate and produce new rotaxanes. I prove experimentally that new templates containing phosphorous can be used to create rotaxanes, and thus confirm the validity of this kind of chemistry.

In Chapter 3, based on the rotational movement of a macrocycle, I implement a rotational movement-based molecular machine: a light-induced acceleration of large amplitude rotational motion(2). My main contribution to this work has been the
conducting thermical isomerization of the molecules described in the supporting information of that chapter.

In Chapter 4 I use the rotational molecular accelerator created using the methods described in Chapter 3 as a model to create a translational molecular machine: a molecular Shuttle. My major contribution to this work has been the design of the tetramide molecular shuttle (E-2, E-6, Z-2, Z-6, , Z-7, S1, S2, S8, S9, S11, S12, S13, S14)

The results achieved through the experiments outlined in Chapter 4 demonstrate that in this thesis I have developed an unprecedented reversible Light and Heat-Switchable Hydrogen Bonded Molecular Shuttle with a large amplitude of movements.

NOTES


Introduction: From Catenanes and Rotaxanes Towards Molecular Shuttles

1.1 Rotaxane and Catenane

Recently, there has been an increased interest on a class of molecules, which are characterized by their particular interwoven and interlocked(1) structures. Its examples are catenanes, rotaxanes, knots(2) and the helices(3) (Figure 1.1). Such attention is caused not only by an extraordinary beauty of these structures, but also by their potential applications.

Catenanes (from Latin: catena = chain) are molecules formed by two or more interlocked macrocycles like one could find in a macroscopic chain. The only way to separate the two elements is to physically break one of its macrocyclic components. Rotaxanes (from Latin: rota = wheel and axis = axle), indeed, consist of a
macrocycle encircling a thread on which it is trapped by the attachment of two bulky stoppers at either end of the thread. A rotaxane without one or both “stoppers” is referred to as a *pseudorotaxane*. Anyway, the demarcation line between a rotaxane and a pseudorotaxane has not been clearly defined yet. In fact, under some conditions, the rotaxanes, which demonstrate a certain complementarity among the dimensions of the macrocycle and the stoppers, may behave as pseudorotaxanes, thus they can dissociate to their components if exposed to the appropriate conditions. and it is possible to induce the rotaxane-pseudorotaxane passage simply by changing the temperature or the solvent.

In order to name these compounds chemists have developed a special nomenclature where the number of interlocked species is shown in square brackets in front of the name of the species in question. For example, when we speak about a [2]rotaxane or [2]catenane, we mean that the rotaxane is composed of an interlocked thread and macrocycle and the catenane by two interlocked macrocycles.

### 1.1.1 Toward new materials: Topological Polymers

The presence of a topological bond allows the possibility of multi-linking the interlocking units in a many different ways. Example of such polymeric systems based on rotaxanes and catenanes(4) are showed in Figure 1.2. These systems are particularly interesting, because they represent characteristics which are totally diverse and new unlike conventional polymers.
The first fundamental difference is evidently the nature of the bonding which knits them together. In fact, in polyrotaxanes and polycatenanes the covalent bond is partially integrated by the mechanical-type bond (topological bond). It stands to reason that such a difference must show itself in some way also in the chemical-physical properties of these "polymers". For example, both polyethylene glycol (linear polyether) and \(\alpha\)-cyclodextrin are soluble in water, while pseudorotaxane which is obtained by threading rings of \(\alpha\)-cyclodextrin into the ethylenic polyglycol thread, is not soluble in water(4).
1.1.2 Synthesis of catenanes and rotaxanes

In this paragraph the argument will simply be introduced to illustrate the history of these compounds and reveal how the synthetic methods used nowadays are notably evolved unlike the early ones.

1.1.3 Statistical methods

The casual formation of a macrocycle, while being threaded towards another one, is called the statistical approach. It was absolutely the first method used for the production of a [2]catenane. It was carried into practice by Wasserman in 1960 and resulted in a poor yield, less than 1% (Scheme 1.1).

Scheme 1.1. Example of the statistical synthesis of the catenanes

The statistical method was applied to the rotaxanes for the first time in 1967 by I. T. Harrison and S. Harrison. The rotaxane which they synthesized was named "hooplane" (from "hoop" and "plane"). Even in this case the yield of this method was very low. In fact, a yield of 6% was achieved after repeating the reaction for 70 times on the surface of the resin (Scheme 1.2).
Scheme 1.2. Example of statistical synthesis of the rotaxanes

Afterwards I. T. Harrison(7) introduced a new statistical method for the synthesis of the same rotaxane defined as "statistical slipping" (Scheme 1.3).
Scheme 1.3. Statistical Slipping (the reaction was repeated with macrocycles with a number of carbon atoms variable from 11 to 39).

This method consists of making the stoppers-fitted thread react in the presence of a macrocycles of different size and waiting for the macrocycles to literally slip inside the two stoppers. In practice, it is not a real “chemical reaction”, because no covalent bond is broken or created.

The statistical methods are not actually of any particular interest because of the arrival of the new methods of “templated” synthesis.
1.1.4 Direct methods

It is evident that the use of statistical methods is extremely limiting due to the low yield obtained in synthesising interlocked molecules. Thus it is necessary to use a template or “auxiliary bonds”. Figure 1.3 demonstrates the principle which this approach is based upon.

![Diagram showing the principle of direct synthesis](image)

**Figure 1.3.** Schematic representation of "Direct" synthesis

The components of a ring which are to become incorporated in a [2]catenane or a [3]catenane, are exposed to the reaction condition with an appropriate orientation, that is the position which will lead us to the interlocked structure. It is clear that the templating effect can be achieved by using covalent bonds, coordinating bonds or “non-covalent” bonds. We describe as direct methods(8), when the templating effect is achieved by means of covalent bonds. In substance, this method implicates a synthesis with more stages of precatenanes and prerotaxanes, where the future interconnected components are bonded with the temporary covalent
bonds. The breaking of these bonds leads us to a molecular structure where the interlocked components are held together by the mechanical bonds only.

It is important to draw attention to the fact that the direct methods implicate a particularly long and complicated synthetic way. For specific examples please refer to the literature.\(^{(1,2)}\)

### 1.1.5 Supramolecular chemistry and templated synthesis

In the last century a new branch of Chemical science is born: the supramolecular chemistry.\(^{(9-11)}\) The origin can be traced back to the early sixties from the pioneering work of C.J. Pedersen.\(^{(12)}\) His goal was to make multidentate ligands for copper and vanadium. While he was working on the synthesis of these compounds he came across one of the first compounds which has been essential to the development of supramolecular chemistry, the crown ethers (Fig 1.4).

![Figure 1.4. A crown ether](image)

But what do we exactly mean by “supramolecular chemistry”?

Supramolecular chemistry as defined by Jean-Marie Lehn is the chemistry beyond the single molecule\(^{(11)}\), that is, the chemistry that will create new molecules
by using molecules created by conventional chemistry or the chemistry of non-covalent bonds.

The driving force of such chemistry is based on "supramolecular glue" (10). This is the attractive forces due to the main non-covalent interaction, such as, electrostatic interactions, hydrogen bonding, \(\pi-\pi\) stacking interactions, induction forces or hydrophobic effects.

With the arrival of the supramolecular chemistry (9-11), application of non-covalent processes of the "host-guest" complexes allows assembly with the geometry of pseudorotaxanes (Figure 1.5) to become available.

![Figure 1.5. Self-assembly of a pseudorotaxane](image)

### 1.1.6 Metallic ions as templates

The metals mostly used for this method are transition metals. The most used of them, especially by J.-P. Sauvage and his colleagues (13) is copper(I). The method developed by Sauvage is essentially based on the tetrahedron coordination geometry of copper(I), especially when two molecules of 2,9-disubstituted 1,10-phenanthroline are used as bonds.
As it is clearly seen from the Scheme 1.4, the complex of copper(I) with 2,9-dianisyl-1,10-phenanthroline has an ideal geometry for a catenane assembly (Scheme 1.5).

Scheme 1.4. Cu(I) as a template

Scheme 1.5. Assembly of copper(I) based catenane(13)
A similar synthetic procedure(1) can be applied for the synthesis of other interlocked structures as rotaxanes, knots, or for the synthesis of double helices, similar by their structure to the DNA structure.

1.1.7 \( \pi \)-Electron-Accepting and \( \pi \)-Electron-Donating Interactions as templates

Other possibility for the template synthesis is to exploit the \( \pi \)-electron-accepting and \( \pi \)-electron-donating interactions. Rotaxanes and catenanes which exhibit this type of interaction have been synthesized especially by the research group of Stoddart.

In Scheme 1.6 we see the formation of a pseudorotaxane, using \textit{paraquat} (a pesticide) as a \( \pi \)-acceptor and the bis-p-phenylene-34-crown-10(14) as a \( \pi \)-donator.
Scheme 1.6. Formation of a pseudorotaxane using a *paraquat* based template

Scheme 1.6 helps to understand that using paraquat opportunely makes it possible to create rotaxanes or catenanes on the usual schemes.

### 1.1.8 Hydrophobic interactions as templates

An example of this technique was developed by Ognino in 1981 to create a rotaxane which had a cyclodextrin as the macrocycle and used diaminodecane chain(15) as a thread (Figure 1.6).
1.1.9 Hydrogen bonding as templates

This part will be examined more in details in the paragraph dedicated to the benzylic amide rotaxane and catenane. The principle which subtends to this method is always the molecular recognition: the components of the future rotaxane or catenane must exhibit, in the complementary manner, a site to be the hydrogen bond-accepting site, and another one to be the hydrogen bond-donating site.

1.1.10 Threading, slipping or clipping?

We examined that there are different methods to execute the synthesis of the interconnected molecules. Among these methods, the first ones to be used were the statistical ones and direct ones which presented the inconvenience of low yields for the first method and of numerous "steps" for the second one. During the last twenty years various methods have been developed based on molecular recognition, which permitted the inconveniences of the first ones to be overcome. We examined that in
quality of the template groups one can use transition metals, $\pi$-accepting-donating interactions, hydrophobic interactions and, finally, hydrogen bonding.

To-date, the template methodology has proved to be the most effective one for producing interlocked structures, such as catenanes and rotaxanes. However, this method can be applied through different strategies\textsuperscript{(16)}. There are three main strategies of using this method, known as \textit{threading}\textsuperscript{(17)}, \textit{slipping}\textsuperscript{(18)}, and \textit{clipping}\textsuperscript{(19)}; illustrated by Figure 1.7 respectively.

![Figure 1.7. Synthetic strategy for rotaxanes](image)

The synthesis of the rotaxanes through the "clipping" methodology is a priori a more difficult process as compared with "threading" and "slipping": in fact, it requires a major number of the components to be organized and oriented in such a manner to obtain the desired product (catenane or rotaxane). Anyway, the "clipping"
has an insurmountable advantage towards the other strategies: it is the a more direct methodology as it does not require the preformation of a macrocycle.

1.2 **Hydrogen Bond Template Direct Synthesis of Benzylic Amide Catenanes and Rotaxanes.**

1.2.1 **Benzylic Amide Catenanes**

The formation of hydrogen bonds in synthesis is one of the most effective ways to synthesize benzylic amide catenanes and rotaxanes.\(^{(20-22)}\) The formation of benzylic amide \([2]\)catenanes was serendipitously discovered by D. Leigh’s group\(^{(20)}\) in 1995 during the synthesis of a macrocycle \(1\) that was designed to be a chemical sensor for \(\text{CO}_2\) \(^{(2)}\). The synthetic approach adopted is depicted in Scheme 1.7 and consisted of the direct condensation \([2+2]\) of equimolar amounts of isophthaloyl chloride and \(p\)-xylylenediamine.
As soon as the addition of the reagents started, a precipitate immediately started to form. After 24 hours the precipitate was removed by filtration and when the filtrate was characterized it was identified at first as the macrocycle 1 by $^1$H and $^{13}$C NMR spectroscopy. However, during the complexation experiments it was not possible to detect any traces of bound CO$_2$. X-Ray diffraction of a single crystal of the presumed macrocycle clearly showed why the synthesized compound did not bind any CO$_2$: molecules. The isolated compound was not macrocycle 1, but the interlocked structure known as *catenane* 3, which originates from two macrocycle 1 molecules held together by H-bonds. This structure was formed by a self assembly-process during the condensation reaction (Scheme 1.8). At this stage, macrocycle 1 could not be isolated since it remained in the precipitate creating many purification problems due to its poor solubility in nearly all of organic solvents.
Scheme 1.8. Proposed mechanism for the formation of benzylic amid catenanes

As shown above, it is clear that the synthesis of this catenane is really very simple (the starting materials are commercially available and the purification procedure does not imply the use of chromatographic techniques) and, besides, it is very versatile, since it is possible to vary the substituents of isophthaloyl chloride or to use instead other acid chlorides, such as, pyridines or thiophenes. The yield of a forementioned reaction is 20%, which is rather high taking into consideration that the catenane is the product of a simultaneous 8 molecule condensation. The X-Ray structure of catenane 3 (Figure 1.8) reveals that the “driving force” for the formation of the catenane is a web of bifurcated hydrogen bonds which are established among the amide hydrogens of a ring and two carbonyls of an isophthalic group of another ring in the “transoid” conformation.
1.2.2 Benzylic Amide Rotaxanes

Following the discovery of benzylic amide catenane, D. Leigh’s group went a step forward, and thought about using the same synthetic approach to obtain [2]rotaxanes. Using what we would refer as “clipping” methodology (Paragraph 1.1.10), a [2]benzylic amide rotaxane(23) was synthesized being the templating unit the 1,3-benzylicamide derivative (thread) (Scheme 1.9), with a yield of nearly 28%.

Scheme 1.9. Synthesizing a rotaxane using the clipping methodology
The choice of templating group was made by extrapolation of the benzylic amide catenane (20,23), where two carbonyls, as shown by the X-Ray crystal structure, are distant from one another 6.2 Å in the transoid conformation.

The spatial arrangement of the amide bonds of the 1,3-benzylic amide thread, may be found in the residual aminoacids which are adjacent to the peptidic chains. Thus, the most simple dipeptide glycine-glycine (gly-gly) was incorporated into the thread 4 (Scheme 1.10). (24) Then, using the “clipping methodology”, equimolar amounts of isophthaloyl chloride and p-xylylenediamine were slowly added to the solution of the dipeptidic thread in anhydrous, ethanol free CHCl₃. After the addition of 5 equivalents was completed, rotaxane 5 was obtained in a 62% yield and in a 34% for rotaxane 6.

The difference in yields observed when using different isophthaloyl chlorides can be explained on two grounds. 1) the intercarbonyl distance in the glycine-glycine dipeptide is 4.8 Å and proves to be optimal to maximize the H-bond interactions with the macrocycle 2) Due to the Zwiterionic character of the peptide bond, the amide group is reorganized in a transoid conformation, in which two carbonyls are located trans to each other.
1.2.3 Fumaramide rotaxanes

Taking into consideration the factors that are crucial in the effective formation of interlocked molecules (such as, intercarbonyl distance, locking in the transoid conformation etc.), a new template group was introduced, the fumaric amide moiety. The use of a fumarilamide derivative as the templating
thread (Scheme 1.11a) offers the advantage of having approximately the same intercarbonylic distance as the Gly-Gly unit and in addition introduces an element of rigidity that is due to the presence of the double bond, situated between two carbonyls groups, locking the unit in the transoid conformation and therefore reducing the conformational entropy of the system.

As hypothesized, the templating ability of the fumaric thread is better in comparison to that of the peptidic system, because two carbonylic systems are retained in a transoid configuration because of the rigidity of the double bond.

Indeed, as we will see later in this chapter, the fumaramide group permits a drastic increase in the yield of rotaxane formation up to 97% (22,25-26).

The thread designed for this purpose is shown in Figure 3.6, where the 2,2-diphenylethylamine groups play the part of “stoppers”. The synthesis of the thread is trivial and consists of a simple condensation reaction between 2 equivalents of 2,2-diphenylethylene amine with 1 equivalent of fumaryl acid chloride in the presence of triethylamine (Scheme 1.11b).
Scheme 1.11. a) Fumaramide group b) Synthesis of the N,N'-Bis(2,2-diphenyl)fumaramide thread.

Up to date, the furamide template has shown to be the most effective in the synthesis of [2] rotaxanes

1.3 Molecular shuttles

1.3.1 Introduction: molecular machines

In the previous century, the average person would have had a hard time trying to understand how cars and airplanes worked, and computers existed only in theory. By the next turn of the century, we may have submicroscopic molecular devices.
Hard to imagine? No, thanks to molecular nanotechnology a hybrid of chemistry and engineering that would let us manufacture anything with atomic precision. In fact, in many spheres of the technology, the miniaturization of the components of the equipment has become a necessity.

Recent advances in nanotechnology have encouraged scientists to develop molecular machines.

A molecular machine can be defined as an assembly of a discrete number of molecular components designed to perform mechanical-like movements(27). These kind of molecular devices can be grouped in two different categories: i) systems with rotating moving parts and ii) systems with translating moving parts.

Valid representatives of this category are the Tryptycene-based molecular gears(28) which are an example of nanoscale gears that can be build (Figure 1.9). However in this paragraph the rotating nanomachines are just briefly described, for more detail refer to the specialized literature(28)
These molecular gears work in a simple way: each phenyl unit of the tryptycene fits perfectly in other two adjacent phenyl units of the other brunch, exactly in same way as a teeth of a wheel gear fits with the other two teeth of the nearby wheel. To this end the movements along the bond ax C-O (whatever is its own origin: heat, Brownian movements, etc) will condition the movements of the other components.

Most of the work in this thesis is devoted to the translation movements at molecular level, focusing on what is known as molecular shuttles.(29)
1.3.2 Molecular shuttle

Up to this stage we have described how to obtain interlocked molecules, we will now focused on the study of their properties. It is an undeniable fact that in a certain way their so “exotic” structure impresses us. At this point one should ask whether these molecules are purely an academic curiosity or if on the contrary they could be used in the construction of potential molecular machines.

Speaking about practical applications, the rotaxanes have an very useful property due to their interlocked nature: the macrocycle’s degrees of freedom with respect to the thread are restricted to only two. Only rotational and translational movements are allowed (Figure 1.10). This particularity makes them ideal for the design of novel molecular machines.

![Fig 1.10. Cartoon with schematic representation of the restricted degrees of freedom of the macrocycle movement.](image)

As a matter of fact, if we introduce a second recognition site in the thread, we create a second site of recognition for the macrocycle. Then if one applies an
“external stimulus”, one can *modulate* the affinity of the macrocycle for the recognition sites.

In order to make the concept clearer, one can visualize the situation in Figure 1.11; in which the rotaxane is composed of a thread with two recognition sites and a macrocycle ring that has different affinities for each of them. Thus, the ring in “normal” conditions will be stationed exclusively (or principally) on such a site. In case that we, introducing an *external stimulus*, are able to change the things in favor of the non-occupied site, the macrocycle will be *moving* towards it, bringing us to a *translational isomer* of the initial rotaxane. Further, if the process is reversible, the removal of the external stimulus will bring the macrocycle back to the initial recognition site.

A rotaxane that performs the situation described above is known as “*molecular shuttle*”. (29)

![Figure 1.11. Molecular Shuttle](image-url)
1.3.3 Thermodynamic considerations on molecular shuttle

When speaking of "molecular shuttles" we have to consider that the shuttle must be reversible and after the stimuli have been applied the macrocycle must lie prevalently on one station. But what do we mean exactly by prevalently?

To understand this concept more clearly we need to do some thermodynamic considerations.

Consider the situation where:

S\(_1\) is the first station,

S\(_2\) is the second station,

M is the macrocycle without bonding to anything,

S\(_1\)M is the complex of the macrocycle with station 1, and K\(_1\) is the relative bonding constant,

S\(_2\)M is the complex of the macrocycle with station 2 and K\(_2\) is the relative bonding constant.
So:

1) \[ S_1 + M \xrightleftharpoons{K_1} S_1M \]  \[ K_1 = \frac{[S_1M]}{[S_1][M]} \]  \hspace{1cm} \text{(Eq. 1)}

2) \[ S_2 + M \xrightleftharpoons{K_2} S_2M \]  \[ K_2 = \frac{[S_2M]}{[S_2][M]} \]  \hspace{1cm} \text{(Eq. 2)}

At this point we can subtract the first relation from the second, so:

\[ S_1 - S_2 \rightleftharpoons S_1M - S_2M \]

Now rearranging it in a way that will make sense chemically:

\[ S_1 + S_2M \rightleftharpoons S_1M + S_2 \]

And if we consider the constant that is associated with this equilibrium:

\[ K_e = \frac{[S_1M][S_2]}{[S_1][S_2M]} = \frac{K_1}{K_2} \]  \hspace{1cm} \text{(Eq. 3)}

And then we should consider that:

\[ [S_1M] = [S_2] \]  \hspace{1cm} \text{and}  \hspace{1cm} \[ [S_2M] = [S_1] \]

so we can simplify the relation written before in this way:

\[ \frac{[S_1M]^2}{[S_2M]^2} = \frac{K_1}{K_2} \]  \hspace{1cm} \text{(Eq. 4)}

If now we consider the dissociation degree for \( S_1M \) it can be defined as:
\[ \alpha_{S_{1M}} = \frac{[S_{1M}]}{[S_{1M}] + [S_{2M}]} \]  
(Eq. 5)

Where \([S_{1M}] + [S_{2M}]\) represents the total amount of rotaxane.

If from eq. 4 we solve \([S_{2M}]\):

\[ [S_{2M}] = \sqrt{\frac{K_1}{K_2}} [S_{1M}] \]  
(Eq. 6)

Then we can substitute it into eq. 5, so:

\[ \alpha_{S_{1M}} = \frac{[S_{1M}]}{[S_{1M}] + \sqrt{\frac{K_1}{K_2}} [S_{1M}]} = \frac{1}{1 + \sqrt{\frac{K_1}{K_2}}} \]  
(Eq. 7)

And rearranging it:

\[ \alpha_{S_{1M}} \left[ 1 + \sqrt{\frac{K_1}{K_2}} \right] = 1 \]

\[ \alpha_{S_{1M}} + \alpha_{S_{1M}} \sqrt{\frac{K_1}{K_2}} = 1 \]  
(Eq. 8)

And solving it in a way that we can express \(K_2\) as a function of \(K_1\):

\[ K_2 = \frac{(\alpha_{S_{1M}})^2}{(1 - \alpha_{S_{1M}})^2} K_1 \]  
(Eq. 10)
Now with eq. 10 we can fix the dissociation degree for $S_1 M$ and we can get an idea of what effect the difference in magnitude of the equilibrium constants has on the extent of population on the two station.

<table>
<thead>
<tr>
<th>$\alpha_{S_1 M}$</th>
<th>$K_1 = nK_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>90%</td>
<td>81</td>
</tr>
<tr>
<td>95%</td>
<td>361</td>
</tr>
<tr>
<td>99%</td>
<td>9801</td>
</tr>
</tbody>
</table>

1.3.4 Brief history of the molecular shuttle

The first example of the molecular shuttle was done by Stoddart who in 1994 created a rotaxane, based on electrostatic $\pi$-accepting-donating interactions (29), and which could be driven both electrochemically and through the change of pH (Figure 1.12.).
In this rotaxane, the macrocycle is a $\pi$-electron-accepting cyclophane which can be positioned on the two $\pi$-electron-donating stations, both present on the thread, consisting of a biphenol and a benzidine units. In normal conditions the cyclophane resides on the benzidine unit, which is more $\pi$-donating than the biphenol one, but for the same reason it is easier to oxidize it. Thus, once the benzidine is oxidized, the macrocycle moves to the biphenol station. The same mechanism can be activated by the protonation of the benzidine.
Another very interesting and efficient example is proposed by Sauvage and collaborators (30) (Figure 1.13).

Figure 1.13. Sauvage Shuttle

The macrocycle contains a phenanthroline group (phen), while the thread contains both a phen group and a terpyridine group (terpy). The ion Cu(I) prefers a tetrahedral coordination which is organized much better by the phen bonds (one on the thread and another on the macrocycle). The oxidation of tetrahedral Cu(I) brings the formation of the unstable species which has a Cu(II) ion in a tetrahedral coordination site. Thus, there is a slow movement of the macrocycle towards the terpy station which permits the complex to adopt the pentacoordinated geometry,
preferred by Cu(II). Reducing the rotaxane to Cu(I) leads us back to the initial situation.

It is possible to induce a "shuttling" also by changing the polarity of the solvent in which the rotaxane is dissolved. An example was proposed by Leigh and collaborators(31) (Figure 1.14).

![Figure 1.14. Solvent based molecular shuttle](image)

In practice, it concerns a rotaxane assembled towards the hydrogen bonds. In non-polar solvents the macrocycle oscillates between two peptidic stations. When a drop of ethanol is added the polarity increases and a concomitant translational movement of the macrocycle occurs. The subsequent growth of polarity (changing the solvent to dimethylsulfoxide) forces the macrocycle to reside exclusively on the hydrophobic chain.
A step forward in the development of these charming molecular devices, is the choice of external stimuli that does not damage the molecule; in other words reversible external stimuli would be ideal.

One option would be to use a photochemical stimulus that brings about a chemical or conformational change, such as cis-trans isomerisation. In this thesis, we will discuss the properties of such a system, that is the rotaxane formed with a fumaric amide moiety. This unit has the advantage that the double bond can be isomerized to the cis form by irradiating the molecules with light of an appropriate frequency. Also, the double bond can be isomerized back to the trans thermally. The cis-trans isomerization causes a conformational change and therefore pushing the macrocycle towards a different recognition site. In Figure 1.15 an example is shown(32).

![Figure 1.15. Photochemistry based molecular shuttle](image-url)
An outstanding example is also the benzylic amide [2]rotaxane molecular shuttle reported by Leigh and co-workers in the 2001(33), Figure 1.16.

Figure 1.16. Photoelectronic molecular shuttle

The principle underlying is very elegant, the thread of rotaxane a has two different stations. One with high affinity for the macrocycle: the succinicamide (good hydrogen bond acceptor), and another with low affinity: the naphthalamide (a poor hydrogen bond acceptor).

So in equilibrium conditions at RT, the macrocycle is spending most of its time on the succinamide portion of the thread.

However, if this system is perturbed by irradiating it with a laser pulse at 355 nm, what happen is that the naphthalamide is photoreduced to an anion radical species, which has and excellent ability to accept hydrogen bonds. Therefore the
macrocyle, of rotaxane b, prefers to spend most of its time, not on the succinamide station but rather on the radical naphthalenic anion station.

A part of this thesis work has been dedicated to the realization of a translational shuttle, similar to this one- see chapter IV.

References


Chapter 2

Exploring Phosphorus and Sulfur Based Templates for the Tetrabenzylicamide [2]Rotaxane Formation

ABSTRACT

In the recent years there has been an outstanding achievement in the strategy to synthesize tetrabenzylic amide [2]rotaxanes. The usual way of synthesizing tetrabenzylic amide[2]rotaxanes has been the 5 molecule self-assembly using as templates dipeptides or diamides(1) motifs that enable the interlocking of the benzylic amide macrocycle precursor around “dumbbell-shaped” thread. The purpose of this study is to go further and explore the templating capability of groups containing different heteroatoms such as Phosphorus or Sulfur. The new systems may benefit from being better H-bond acceptors, which enables them to obtain higher yields of [2]rotaxanes, as well as to be able to process different chemical reactivities adding functionality to the original peptido derived templates.
Recently there has been a remarkable achievement in the development of synthetic strategies to produce interlocked species such as, knots, catenanes and rotaxanes (2).

One of the most effective is the template synthesis which uses the ability of two or more precursor units to self-assemble into the target molecule (2b). As Leigh et al. and others have shown (1) a very well validated synthetic pathway for producing benzylic amide [2]rotaxanes is to exploit peptido derived amide motifs that template the interlocking of benzylic amide macrocycles around a "dumbbell-shaped" thread in order to form [2]rotaxane (1).

Different kinds of amide templates have been used and the best results were obtained from succinamide (3), diglycinic (1a) and fumaramide (1c) templates (Figure 2.1); the latter results in an almost quantitative yield.

![Amide based templating groups](image)

**Figure 2.1.** Amide based templating groups
There has been recent interest in developing alternative hydrogen bonding motifs as templates(4).

The new systems may benefit from being better H-bond acceptors, which enables them to obtain higher yields of [2]rotaxanes, as well as to process different chemical reactivities into the original peptido-derived templates.

Furthermore, having a wider range of H-Bonded templates, enables the supramolecular chemist to have more flexibility in order to design new interlocked architectures(3,5) creating more chances for a possible practical application of these otherwise only aesthetical chemical structures.

The research for novel non-amide templates is not new, in fact a remarkable result (70% yield) has been achieved in the past by the Leigh group using N-oxide based templates (1b,1c).
Results and Discussion

This work described in this chapter focuses mainly on Phosphine-oxide based H-bonding templates which have the advantage of possessing a large dipole on the P=O bond, which makes them good hydrogen bond acceptors(6).

As first approach, a set of bis diphenylphosphine oxide based threads (Figure 2.2) was chosen to test their ability to template the [2]rotaxane formation around them.

Figure 2.2. Bis diphenylphoshines threads 1-5

These threads can be easily synthesized starting from commercially available bis diphenylphoshines simply by oxidation with hydrogen peroxide.

Every bis diphenylphosphine oxide thread (1-5) was subjected to the rotaxane formation reaction conditions (slow addition, by syringe pump, of two separate chloroform solutions; one of the p-xylylendiamine and triethylamine and the other of isophthaloyl dichloride to a stirred chloroform solution of the thread.).
Unfortunately in none of the reactions tested it was possible to detect any measurable trace of [2]rotaxane. Instead, column chromatography of the crude reaction product yielded the starting thread.

However, thanks to its large dipole moment, the phosphine oxide moiety is a better hydrogen bond acceptor than the carboxylic group, which should enable it to hydrogen bond the U-shape precursor of the macrocycle.

Yet, although it does indeed form hydrogen bonding, it is not so efficient in orienting the two extremities of the U-shape precursor of the macrocycle to a position required for the macrocycle formation around the thread (1a, 7).

The inability to template the [2]rotaxane formation from bisphosphineoxide-based templates could also be attributed to the steric hindrance of the two phenyl groups directly bonded to the phosphorus, which does not encourage the self-assemble process.

Yet another, and possibly the most critical reason for the inability of these threads to template the rotaxane formation is the lack of a hydrogen bond donor element in the phosphine oxide moiety, whereas it is present in the traditional amide-based templates. Among other reasons, template planar geometry may be considered. The phosphine oxide tetrahedral geometry might be in part responsible for the misorientation of the two U-shape endings.

Moreover, the planar orientation in the amide-based template has the advantage of extending the π system. An extended π system improves the interaction between the U-shape precursor and the template, thus enabling π–π interaction between the π system of the template and the π system of the benzylic rings of the macrocycle U-shape.
When a thread (Scheme 2.1, thread 6) where one of the two bisphosphine moieties was replaced by an ester moiety, was used, rotaxane was formed, albeit in a small quantity (Yield 1.5% scheme 3).

This fact reinforces the importance of planar geometry. The ester is known to be a weak hydrogen bond acceptor, however, it has a carbon atom with a \( sp^2 \) hybridization. This \( \pi \) element allowed the phosphine-oxide ester-based template to preorganize the macrocycle precursors in a suitable position for its ring closure around the thread.

Scheme 2.1. Synthesis of Rotaxane 7. The macrocycle is represented by a blue circle for practical reasons.¹

From here, the teramide macrocycle will be represented as a blue circle as depicted on the right.
Another remarkable example is the yield of 3% in rotaxane formation achieved with a bis ester thread (1b) (Figure 2.4) where only weak hydrogen bond acceptors and no hydrogen bond donors are present. In this case, the presence of the fumaric double bond emphasizes the importance of pre-organizing the U-shape around the thread for a better yield (1b,1c).
In order to improve the yield in rotaxane formation, a hydrogen bond donor group was introduced in the phosphine oxide based template. A series of amide-phosphine oxide template-based [2]rotaxane with different methylene spacer groups between the amide and the phosphine oxide moiety was studied and fully characterized by $^1$H, $^{13}$C, and $^{31}$P NMR spectroscopy, MS and elemental microanalysis.

They ensure a simple synthetic route (Scheme 2.2) and a reasonable yield in [2]rotaxanes (42% for n=2).

Scheme 2.2. Synthetic route for producing phosphine oxide-amide based rotaxanes 9-14  i) Ph$_3$P, CH$_3$CN Reflux, 90-95%; ii) NaOH, H$_2$O Reflux, 70-85%; iii) 2,2-Diphenyl-ethylamine, EDCI, 4-DMAP, DCM, RT, 70-80%; iv) isophthaloyl dichloride, p-xylylenediamine, Et$_3$N, CHCl$_3$, RT, 10-42%.
Preparation of the thread with only one methylene spacer group, following
the synthetic scheme 1 mentioned above, was problematic. In fact, when the
phosphonium salt undergoes hydrolysis (step ii) it loses the alkyl group instead of
losing the phenyl group (Scheme 2.3).

![Chemical反应](attachment:chemical_image.png)

**Figure 2.4. Representation of the de-alkylation of the phosphonium salt 7a**

Building thread n=1 from the diphenylamide stopper rather than starting with
the diphosphine oxide stopper enabled us to bypass the synthetic problem.

![Synthetic route](attachment:synthetic_route.png)

**Scheme 2.4. Synthetic route applied for producing rotaxanes 8** i) Et₃N, DCM, 0°C, 80%; ii) Ph₂POMe,
Toluene, Reflux, 60%; iii) isophthaloyl dichloride, p-xylylenediamine, Et₃N, CHCl₃, RT, <1%.
The resulting rotaxane yields, under the rotaxane formation conditions (see the supporting information), obtained from this set of threads were compared to the rotaxane yields obtained from the analogous diamide threads (8); as shown in Table 2.1.

![Image of rotaxane structures]

<table>
<thead>
<tr>
<th>Compound</th>
<th>n = Number of methylene units</th>
<th>Yields obtained (%)</th>
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<td>Phosphine Oxide-Based Template a)</td>
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<td>14</td>
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Table 2.1. Comparison of the resulting rotaxane yields, under the rotaxane formation conditions obtained from phosphine oxide based thread a) to the rotaxane yields obtained from the analogous diamide threads b).

The lowest rotaxane yield was obtained in case "n=1". This is clearly due to the lack of room between the two stoppers. Also, the phosphine-oxide based template presents a lower yield as compared to the diamide-based thread: it is shorter than the latter, and the two phenyl groups directly bonded to the phosphorus do not help to accommodate the U-shape precursor during the self assembly process.
The lack of space in the resulting phosphine oxide-based rotaxane with only one methylene group as spacer constrains the macrocycle to adopt a distorted conformation (Figure 2.5) and the number of resulting hydrogen bonds between the macrocycle and the thread is reduced to only three.

![Figure 2.5. X-ray crystal structure of rotaxane 8 (for clarity carbon atoms of macrocycle are shown in blue and the carbon atom of the thread in yellow, oxygen atoms, nitrogen atoms dark blue, phosphorous atom-pink and selected hydrogen atoms white)](image)

The best yield was obtained in case “n=2” as in this case the hydrogen bond between the thread and the macrocycle fits better than in other cases, however the yield is slightly lower compared to the diamide analogue. Again, this is due to a lack of space in the phosphine oxide-based template compared to the diamide based template.
Interestingly, when there is a sufficient number of methylene spacers, (more than three), the situation is different: the threads with the phosphine oxide based-templates are formed in higher yield compared to the diamide templates. Therefore, the phosphine oxide moiety should have an active role in the rotaxane formation reaction, even though by itself it cannot work as a template, unlike in the cases of the bis diphenylphosphine-oxide threads. One may suppose that in the above mentioned case the phosphine oxide is auxiliary to the amide moiety in templating the rotaxane formation.
For rotaxane 10 and 12 (cases n=3 and n=5), it was possible to obtain suitable crystals for the x-ray investigation. These structures are represented below:

Figure 2.7. X-ray crystal structures of rotaxanes 10 (left) and 12 (right) (for clarity carbon atoms of macrocycle are shown in blue and the carbon atom of the thread in yellow; oxygen atoms, nitrogen atoms dark blue, phosphorous atoms pink and selected hydrogen atoms white).

Furthermore, when the thread is long enough, as is the case in n=7 and n=11 (rotaxanes 13 and 14), it is clear that the macrocycle tends to spend most time in the proximity of the amide region rather than in the phosphine-oxide area as is shown by the NMR (Figure 2.8). This is emphasized by the fact that the anisotropic current of the aryl groups of macrocycle affects much more the CH$_2$ protons next to the amide rather the protons nearby the phosphine-oxide moiety (Figure 2.8).
An alternative to the amide phosphine oxide-based templates are templates containing the phosphineamide moiety. They have the advantage that an hydrogen bond donor such as the NH is directly bonded to the phosphorus, which makes their use more promising.

The phosphonamides are excellent hydrogen bond acceptors(9). However, their tetrahedral geometry at phosphorus makes them different from the amides. The tetrahedral nature of phosphorous not only introduces a new dimension (both chemically and sterically) into the thread, but also means the stopper will be much closer to the phosphonamide P=O than it is in the amide C=O case.
Two different phosphineamide threads have been synthesized: one containing a mix phosphineamide amide-based template (thread 15) and the other containing a bis phosphineamide based template (19).

The thread with the phosphineamide and amide moiety has been prepared following Scheme 2.5. This thread has been effective and was able to yield [2]rotaxane 16 in higher yields compared to the previous templates so far discussed here. This confirms that a hydrogen bond donor element has a pivotal role in obtaining the actual rotaxane in a reasonable yield.

From the X-ray analysis of a crystal from the phosphineamide amide based rotaxane 16 obtained from thread 15, it is clearly possible to see that the macrocycle is situated on the amidic part (Figure 2.9). While the ester moiety, which is a weak hydrogen bond acceptor does not interact at all with the macrocycle. Also it is evident that the phosphineamide moiety creates steric hindrance and cannot fit inside the macrocycle. However, being such a good hydrogen bond donor it fights to create
a bond with the amide of the macrocycle and it constrains the macrocycle to adopt a distorted conformation.

Figure 2.9. X-ray crystal structure of rotaxane 16 (for clarity carbon atoms of macrocycle are shown in blue and the carbon atom of the thread in yellow; oxygen atoms, nitrogen atoms dark blue, phosphorus atom pink and selected hydrogen atoms white).

A team of the University of St Andrews led by Prof Derek J. Woollins has also synthesized analogues, where the oxygen of phosphine amide moiety was replaced with Se and S atoms(10). However, this synthesis produced lower yields of rotaxane.

In Figure 2.10 the X-ray crystal structures of rotaxane 17 and 18 are reported. These rotaxanes are the first examples where a hydrogen bonding acceptor other than C=O groups of an amide has been used as a template for macrocyclization of Leigh’s macrocycle and led to rotaxane formation. It is noteworthy that in the corresponding rotaxane from PO, the yield was 55%, in the rotaxane P=S and P=Se the yields are 18 and 20% respectively. This can only be attributed to the
electronegativity and hence polarity of the double bond between the heteroatoms atoms (Se, S) and the phosphorus.

As mentioned above, a remarkable result was obtained by St Andrews group using bis phosphineamide thread(10).

The results of the St Andrew Laboratory was gained by exposing the phosphine amidic thread, which was easily prepared by a reaction between diethylamine and diphenylphosphonic chloride, to rotaxane formation conditions. A yield of 20% of rotaxane formation was obtained, which is not that low given the fact that we operated with a template containing no amidic unity.

Crystals of this rotaxane suitable for X-ray diffraction were obtained (Figure 2.11). Interestingly, the macrocycle forms two sets of bifurcated hydrogen bonds and adopts a boat conformation; which is absolutely symmetrical, unlike in the previous cases. This again suggests that using two methylene groups as spacers and two donor acceptors groups may be an ideal solution.
Figure 2.11. X-ray crystal structure of rotaxane 19 showing hydrogen bonding characteristics. Intramolecular hydrogen bond distances and angles: O31A-HN2A/O31-HIN2 2.19 Å, 162.2°; O31A-HNI1A/O31-HN11 2.35 Å, 170.8°. For clarity carbon atoms of macrocycle are shown in blue and the carbon atom of the thread in yellow; oxygen atoms are red, nitrogen atoms dark blue, phosphorous atoms pink and selected hydrogen atoms white.

Other promising hydrogen bond acceptors alternative to CO amides may be found in sulfoxide moiety.

Vötgle group has already prepared rotaxanes containing sulfonamide moieties in both the thread and the macrocycle (4a). The yields are lower than the amide analogues. Unfortunately, he was unable to prepare catenanes containing only sulphonamide based template groups (4b); the result of this work prompts us to conclude that in the rotaxanes formation process the sulfonamides play no part.

This is supported by binding studies (11), which have proven that sulfonamide are poor hydrogen bond acceptors. Therefore it was decided that to prepare a rotaxane with a sulfonamide group in the thread would not be beneficial to rotaxane formation.
Alternatively, sulfoxides have large local dipoles and are therefore strong hydrogen-bond acceptor(12).

A bis-sulfoxide thread 19b was synthesized by the Leigh group in the past(13). Thread 19b was obtained as a mixture of both enantiomers and the meso isomer. No attempt was made to separate these products and this mixture was used directly in the rotaxane forming reaction. But still no rotaxane was isolated.

![Chemical structure of 19b](image)

Better results were obtained with a sulfoxide-amide template based thread 20 prepared following Scheme 2.6(13).
Scheme 2.6. i) 89%. ii) DCC, N-hydroxysuccinimide, THF, 0°C, 97%. iii) Et$_3$N, glycine ethyl ester hydrochloride, CHCl$_3$, RT, 61%. iv) diphenyl ethanol, and bis (chlorodibutyltin) oxide, toluene, reflux, 88%. v) isophthaloyl dichloride, p-xylylenediamine, Et$_3$N, CHCl$_3$, RT, 12%. vi) m-chloroperbenzoic acid, CHCl$_3$, Ar, –20 °C, 98%. vii) isophthaloyl dichloride, p-xylylenediamine, Et$_3$N, CHCl$_3$, RT, 43%. viii) m-chloroperbenzoic acid, CHCl$_3$, Ar, –20 °C, 98%. ix) isophthaloyl dichloride, p-xylylenediamine, Et$_3$N, CHCl$_3$, RT, 10%. x) m-chloroperbenzoic acid, CHCl$_3$, Ar, –20 °C, 97%. xi) Lawesson's reagent, THF, –20°C, 87%. xii) m-chloroperbenzoic acid, CHCl$_3$, Ar, –20 °C, 95%.

Studying the oxidation cycles and reductions whilst using the relevant reagents (Scheme 2.6) it was possible to raise the sulfur of the sulfoxide moiety to its lowest oxidation level. From here, the whole reaction was reverted and sulfur was oxidised to the highest oxidation state possible: all this was done on a selective basis with no interaction with other functional groups. The reduction of rotaxane 22 into 21 was problematic.

For each of the three rotaxanes containing sulfur (21-23) in different states of oxidation it was possible to obtain crystals for a suitable X-ray investigation (Figure 2.12).
This work leads to a conclusion that phosphorus and sulfur based templates can be used to produce benzylamide [2]rotaxane.
References


10. R. Ahmed PhD thesis. Prof. Derek J Woollins, School of Chemistry University of St Andrews, North Haugh, St Andrews, Fife, KY 16 9ST, UK


Exploring Phosphorus and Sulfur Based Templates for the
Tetrabenzylicamide [2]Rotaxane Formation

General Methods

Reagents and anhydrous solvents used for the reactions were purchased from Aldrich and were in general used without further purification. isophthaloyl dichloride was routinely recrystallized from hexane and para-xylylenediamine was distilled under reduced pressure. Anhydrous chloroform used for the rotaxane formation reactions was stabilized with amylene

$^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer ($^1$H NMR are reported as follows: br = broad, s = singlet, d = doublet, dd = doublet of doublets, t = triplet, dt doublet of triplets, q = quartet, m = multiplet, $J$ = coupling constant). Column chromatography was carried out using Kieselgel C60 (Merck). TLC analysis was performed on Merck precoated silica gel 60 F-254. Spots were visualized with UV light first and H$_2$SO$_4$ (1%) in ethanol later.

Abbreviations: TFA = trifluoroacetic acid, DMSO = dimethylsulfoxide, 4-DMAP = 4-dimethylaminopyridine, EDCI·HCl = 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride, rt = room temperature, calcd = calculated.
General procedure for the preparation of Bisdiphenylphosphinoylalkane: To a refluxed solution of Bisdiphenylphosphinoylalkane (1 equiv.) in toluene (30 mL) was added H$_2$O$_2$ in excess. The solution was allowed to reflux for 1h. After that it was let cool down and the white precipitate was filtered off and dried in the oven overnight. The powder was considered pure enough for the next step.

General procedure for the preparation of the (ω-Carboxy-alkyl)-triphenyl-phosphoniumbromides: To a solution of ω-bromoalkyl acid (1.1 equiv.) and CH$_3$CN (25 mL) was added Ph$_3$P (1 equiv.). The resulting mixture was stirred at 80 °C for 24 h and then concentrated. The residue was taken up with chloroform (2.5 mL) and the product was precipitated from the solution with Et$_2$O. The white precipitate was filtered, recrystallized in acetonitrile and dried in oven to give the corresponding (ω-carboxy-alkyl)-triphenyl-phosphonium-bromides as white solid.

General procedure for the preparation of the ω-(Diphenyl-phosphinoyl)-alkanoic acid: To a water solution (20 mL) of (ω-carboxy-alkyl)-triphenyl-phosphoniumbromides (1 equiv.), was added NaOH in pellets (5 equiv.) and the reaction mixture was refluxed for 12 h with removal of benzene from reaction environment by distillation. The obtained mixture was acidified with HCl 2N (pH paper) and the acidic aqueous layers were extracted with CHCl$_3$ (3 × 20 mL). The organic layers were unificated and dried over anhydrous MgSO$_4$. The solvent was removed under reduced pressure. The oil obtained was taken up in CH$_2$Cl$_2$ (5 mL) and the product was precipitated with Et$_2$O as a white solid that was dried in oven overnight.
General procedure for the preparation of the \( N-(2,2\text{-diphenylethyl})-\omega\)-(diphenyl-phosphinoyl)-alkanoylamide (thread): To a stirred solution of 2,2-diphenylethylamine (1.1 equiv.), 4-DMAP (0.610 g, 4.992 mmol) and \( \omega\)-(Diphenylphosphinoyl)-alkanoic acid (1 equiv.) in \( \text{CH}_2\text{Cl}_2 \) was added EDCI (1.2 equiv.) at 0 °C. The reaction mixture was left overnight. The organic layer was washed with NaOH IN (2 x 10 mL), HCl IN (2 x 10 mL) and H₂O (1 x 10 mL). The residual water from the resulting organic layer was removed treating the solution with dry MgSO₄. The solvent was removed under reduced pressure. The oil obtained was taken up in \( \text{CH}_2\text{Cl}_2 \) (5 mL) and the product was precipitated with Et₂O as a white solid that was dried in oven overnight.

General procedure for the preparation of benzylic amide [2]Rotaxanes: The thread (1 equiv.) and Et₃N (24 equiv.) were dissolved in anhydrous CHCl₃ (stabilised with amylene not ethanol, 100 mL) and stirred vigorously whilst solutions of para-xylylenediamine (12 equiv.) in anhydrous CHCl₃ (40 mL) and isophthaloyl dichloride (12 equiv.) in anhydrous CHCl₃ (40 mL) were simultaneously added over a period of 2 h using motor-driven syringe pumps. After a further 2 h the resulting suspension was filtered and the filtrate concentrated under reduced pressure to afford the crude product.
trans-Bisdiphenyphosphinoylethane (1). [Dondi, Stefano; Nardelli, Mario; Pelizzi, Corrado; Pelizzi, Gioancarlo; Predieri, Giovanni; J. Chem. Soc. Dalton Trans. ; EN; 1985; 487-492] Compound 1 was synthesized using the general procedure for the preparation of Bisdiphenyphosphinoylalkane from Bisdiphenylethane (1 g, 2.33 mmol) (95% yield, white powder). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.81-7.43 (m, 22H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.4 (dd, $^1$J(C,P) = 87.1 Hz, 2C, -CH=CH-), 132.3 (br d, $^4$J(C,P) = 2.2, 4C, ArCH (para)), 131.3 (d, $^1$J(C,P) = 106.8 Hz, 4C, ArC-(ipso)), 131.2 (d, $^2$J(C,P) = 10.3 Hz, 8C, ArCH (ortho)) and 128.8 (d, $^3$J(C,P) = 12.4 Hz, 8C, ArCH (meta)).

Bisdiphenyphosphinoylethane (2). [Harrison, Philip G.; Sharpe, Nelson W.; Pelizzi, Corrado; Pelizzi, Giancarlo; Tarasconi, Pieralberto; J. Chem Soc. Dalton Trans.; EN; 1983; 921-926] Compound 2 was synthesized using the general procedure for the preparation of Bisdiphenyphosphinoylalkane from Bisdiphenylethane (1 g, 2.51 mmol) (98% yield, white powder). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.74-7.68 (m, 8H, ArH (meta)), 7.53-7.40 (m, 12H, ArH (ortho and
and 2.58 (d, 4H, $^2J(H,P) = 2.5$ Hz, CH$_2$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 132.3 (s, 4C, ArCH (para)), 130.9 (d, $^1J(C,P) = 103.2$ Hz, 4C, ArC-P (ipso)), 130.8 (d, $^2J(C,P) = 9.5$ Hz, 8C, ArCH (ortho)), 128.9 (d, $^3J(C,P) = 11.7$ Hz, 8C, ArCH (meta)) and 21.3 (d, $^4J(C,P) = 66.6$ Hz, 2C, -CH$_2$-).

Bisdiphenyphosphinoylbutane (3). [Quin; Andeson; J. Org. Chem.; 29, 1964; 1859. S. Tarlok, H., S. Cheema, S. S. Sandhu; J. Chem. Soc. Dalton Trans.; EN; 1983; 2039-2042] The oxidation of the bisdiphenylbutane (1 g, 2.18 mmol) by the general procedure for the preparation of Bisdiphenyphosphinoylalkane from Bisdiphenyletafle yield compound 3 in 95% yield. mp 259-260. $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.72-7.65 (m, 8H, ArH (meta)), 7.54-7.41 (m 12H, ArH (ortho and para)), 2.28-2.18 (m, 4H, Ph$_2$PO-CH$_2$-) and 1.76-1.64 ((m, 4H, Ph$_2$PO-CH$_2$-CH$_2$-); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 132.8 (d, $^1J(C,P) = 98.8$ Hz, 4C, ArC- (ipso)), 131.7 (d, $^4J(C,P) = 2.9$ Hz, 4C, ArCH (para)), 130.7 (d, $^2J(C,P) = 9.5$ Hz, 8C, ArCH (ortho)), 128.7 (d, $^3J(C,P) = 11.7$ Hz, 8C, ArCH (meta)), 29.5 (d, $^1J(C,P) = 71..8$ Hz, 2C, Ph$_2$PO-CH$_2$-) and 22.9 (d, $^2J(C,P) = 19.8$ Hz, 2C, Ph$_2$PO-CH$_2$-CH$_2$-).
Bisdiphenyphosphinoypentane (4). [P. Calcagno, B. M. Kariuki, S.J. Kitchin, J. M. A. Robinson, D. Philp, K. D. M. Douglas; Chem. Europ. J.; EN; 6; 13; 2000; 2338-2349; for melting point: Kosolapoff, Struck, J. Chem. Soc.; 1959; 3950] Compound 4 was synthesized using the general procedure for the preparation of Bisdiphenylphosphinoylalkane from Bisdiphenylethane (1 g, 2.12 mmol). Yield 80%, mp 124-126 °C NMR (400 MHz, CDCl₃): δ = 7.73-7.64 (m, 8H, ArH (meta)), 7.52-7.39 (m, 12H, ArH (ortho and para)), 2.26-2.16 (m, 4H, Ph₂PO-CH₂-) and 1.66-1.46 (m, 6H, Ph₂PO-CH₂-CH₂- and Ph₂PO-CH₂-CH₂-CH₂-); ¹³C NMR (100 MHz, CDCl₃): δ = 132.4 (d, ¹J(C,P) = 98.8 Hz, 4C, ArC- (ipso)), 131.7 (d, ⁴J(C,P) = 2.2 Hz, 4C, ArCH (para)), 130.6 (d, ²J(C,P) = 9.5 Hz, 8C, ArCH (ortho)), 128.6 (d, ³J(C,P) = 11.7 Hz, 8C, ArCH (meta)), 31.6 (d, ⁵J(C,P) = 13.9 Hz, 1C, Ph₂PO-CH₂-CH₂-CH₂-), 29.0 (d, ¹J(C,P) = 71.7 Hz, 2C, Ph₂PO-CH₂-) and 20.61 (d, ²J(C,P) = 3.6 Hz, 2C, Ph₂PO-CH₂-CH₂-).

Bisdiphenyphosphinoylhexane (5). The oxidation of the bisdiphenylbutane (1 g, 2.05 mmol) by the general procedure for the preparation of
Bisdiphenyphosphinoylalkane from Bisdiphenyletane yield compound 5 in 85% yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) 7.75-7.66 (m, 8H, ArH (meta)), 7.53-7.41 (m, 12H, ArH (ortho and para)), 2.26-2.17 (m, 4H, Ph\(_2\)PO-CH\(_2\)-), 1.64-1.52 (m, 4H, Ph\(_2\)PO-CH\(_2\)-CH\(_2\)-) and 1.43-1.34 (m, 4H, Ph\(_2\)PO-CH\(_2\)-CH\(_2\)-CH\(_2\)-); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta \) = 132.7 (d, \(^1\)J(C,P) = 98.1 Hz, 4C, ArC- (ipso)), 131.8 (d, \(^4\)J(C,P) = 2.9 Hz, 4C, ArCH (para)), 130.7 (d, \(^2\)J(C,P) = 9.5 Hz, 8C, ArCH (ortho)), 128.7 (d, \(^3\)J(C,P) = 11.7 Hz, 8C, ArCH (meta)), 30.2 (d, \(^3\)J(C,P) = 13.9 Hz, 2C, Ph\(_2\)PO-CH\(_2\)-CH\(_2\)-CH\(_2\)-), 29.4 (d, \(^1\)J(C,P) = 71.7 Hz, 2C, Ph\(_2\)PO-CH\(_2\)-) and 20.6 (d, \(^2\)J(C,P) = 3.7 Hz, 2C, Ph\(_2\)PO-CH\(_2\)-CH\(_2\)-).

![Chemical structure](attachment:image.png)

(2-Carboxyethyl)-triphenylphosphoniumbromide (5a). Compound 5a was obtained using the general procedure for the preparation of the (ω-Carboxy-alkyl)-trimphenyl-phosphoniumbromides starting from 3-bromopropionic acid (10.00 g, 65.00 mmol). The white solid obtained was recrystallized in CH\(_2\)Cl\(_2\); the crystals were dried in oven to give 20.11 g of 5a (92% yield, white solid). mp 196-198 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) = 10.34 (br s, 1 H, -COOH), 7.79-7.60 (m, 15 H, ArH), 3.72 (dt, \(^2\)J(H,P) = 12.6 Hz, \(^3\)J(H,H) = 7.20 Hz, 2H, Ph\(_3\)P-CH\(_2\)-) and 2.93 (dt, \(^3\)J(H,H) = 7.2 Hz, \(^3\)J(H,P) = 7.2 Hz, 2H, -CH\(_2\)-CO-); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta \) = 171.6 (d, \(^3\)J(C,P) = 13.8 Hz, -CO-), 135.8 (d, \(^4\)J(C,P) = 3.1 Hz, 3C, ArCH (para)), 134.0 (d, \(^2\)J(C,P) = 10.7 Hz, 6C, ArCH (ortho)), 131.0 (d, \(^3\)J(C,P) = 13.0 Hz, 6C,
ArCH (meta)), 117.8 (d, \( ^1J(C,P) = 86.6 \) Hz, 3C, ArC-P (ipso)), 28.4 (s, -CH\(_2\)-CO-) and 19.2 (d, \( ^1J(C,P) = 55.2 \) Hz, Ph\(_3\)P-CH\(_2\)-), \( ^{31}\)P NMR (CDCl\(_3\)): \( \delta = 25.88 \); MS (FAB, mNBA): \( m/z = 336 \) [(M-Br)]. Anal. Calcd for C\(_{21}\)H\(_{21}\)O\(_2\)PBr: C 60.45, H 5.31, Br 19.15, O 7.67, P 7.42. Found C 60.39, H 5.42.

![3-(Diphenyl-phosphinoyl)-propionic acid (5b).](image)

3-(Diphenyl-phosphinoyl)-propionic acid (5b). [Larpent, Chantal; Patin, Henri; Tetrahedron; EN; 44; 19; 1988; 6107-6118]. Compound 5b (3.071 g after recrystallisation in CHCl\(_3\), yield 93%) had been prepared using the general procedure for the preparation of the \( \omega \)-(Diphenyl-phosphinoyl)-alkanoic acid from compound 5a (5.00 g, 12.04 mmol). mp 108-109 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 10.13 \) (br s, -COOH), 7.72 (dd, \( J = 11.8 \) Hz, \( J = 8.0 \) Hz, 4H, ArH (meta)), 7.56-7.41 (iii, 6H, ArH (para and ortho)) and 2.66 (m, 4H, Ph\(_2\)PO-CH\(_2\)-CH\(_2\)-); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 174.4 \) (d, \( ^3J(C,P) = 14.6 \) Hz, -COOH), 132.7 (d, \( ^4J(C,P) = 3.1 \) Hz, 2C, ArCH (para)), 131.5 (d, \( ^1J(C,P) = 101.2 \) Hz, 2C, ArC-PO (ipso)), 131.2 (d, \( ^2J(C,P) = 10.0 \) Hz, 4C, ArCH (ortho)), 129.3 (d, \( ^3J(C,P) = 12.3 \) Hz, 4C, ArCH (meta)), 27.0 (d, \( ^2J(C,P) = 2.3 \) Hz, -CH\(_2\)-COOH) and 25.1 (d, \( ^1J(C,P) = 72.8 \) Hz, Ph\(_2\)PO-CH\(_2\)-); \( ^{31}\)P NMR (CDCl\(_3\)): \( \delta = 36.98 \); MS (FAB, mNBA): \( m/z = 275 \) [(M+H)]\. Anal. Calcd for C\(_{15}\)H\(_{15}\)O\(_3\)P: C 65.69, H 5.51, O 17.50, P 11.29. Found C 65.38, H 5.55.
3-(Diphenylphosphinoyl)-propionic acid 2,2-diphenylethyl ester (6). To a stirred solution of 2,2-diphenylethanol (234 mg, 1.21 mmol), 4-DMAP (0.196 g, 1.54 mmol) and 5b (0.50 g, 1.1 mmol) in CH₂Cl₂ was added EDCI-HCl (251 mg, 1.32 mmol) at rt. The reaction mixture was left overnight. The organic layer was washed with NaOH aq 1N (2 x 10 mL), HCl aq 1N (2 x 10 mL) and H₂O (1 x 10 mL). The residual water from the resulting organic layer was removed treating the solution with dry MgSO₄. The solvent was removed under reduced pressure. The oil obtained was taken up in CH₂Cl₂ (5 mL) and the product was precipitated with Et₂O as a white solid that was dried in oven overnight (6, 450 mg, yield 90%) mp 95-98 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.69-7.58 (m, 4H, ArH (ortho, Ph₂PO)), 7.52-7.37 (m, 6H, ArH (meta and para, Ph₂PO)), 7.28-7.11 (m, 10H, ArH (Ph₂CH)), 4.55 (d, 3J(H,H) = 7.6 Hz, 2H, Ph₂CH-CH₂-), 4.27 (t, 3J(H,H) = 7.6 Hz, 1H, Ph₂CH-) and 2.59-2.27 (m, 4H, Ph₂PO-(CH₂)₂-). ¹³C NMR (100 MHz, CDCl₃): δ = 172.2 (d, 3J(C,P) = 17.5 Hz, -CO-), 140.8 (s, 2C, ArC-CH (ipso)), 132.1 (d, 1J(C,P) = 100.1 Hz, 2C, ArC-PO (ipso)), 131.9 (d, 4J(C,P) = 2.7 Hz, 2C, ArCH (para, Ph₂PO)), 130.7 (d, 2J(C,P) = 9.4 Hz, 4C, ArCH (ortho, Ph₂PO)), 128.7 (d, 3J(C,P) = 11.7 Hz, 4C, ArCH (meta, Ph₂PO)), 128.5 (s, 4C, ArCH (meta, Ph₂CH)), 128.1 (s, 4C, ArCH (ortho, Ph₂CH)), 126.8 (s, 2C, ArCH (para, Ph₂CH)), 67.0 (s, Ph₂CH-CH₂-), 49.7 (s, Ph₂CH-), 26.4 (d, 2J(C,P) = 1.4 Hz, Ph₂PO-CH₂-CH₂-) and 24.9 (d, 1J(C,P) = 73.2
Hz, Ph$_2$PO-CH$_2$-); MS(454.50). Anal. Calcd for C$_{29}$H$_{27}$O$_3$P: C, 76.64; H, 5.99; O, 10.56; P, 6.81. Found C 76.65, H 6.06.

[2]-(1, 4, 7, 14, 17, 20, -Hexaaza - 2, 6, 15, 19 - tetraoxo - 3, 5, 9, 12, 16, 18, 22, 25 -terabenzocyclohexacosane)-(3)-(Diphenyl-phosphinoyl)-propionic acid 2,2-diphenyl-ethyl ester)-rotaxane (7).

Rotaxane 7 was synthesized using the general procedure for the preparation of benzylic amide [2]rotaxanes from thread 6 (0.500 g, 1.1 mmol). The crude product obtained was subjected to column chromatography on silica gel using a gradient of CHCl$_3$ to CHCl$_3$/MeOH (95/5) as eluent to obtain the desired compound as white solid (7, 65 mg, 6%). mp 112-115 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.33$ (dd, $^3J$(H$_B$,H$_A$) = 7.8 Hz, $^4J$(H$_B$,H$_C$) = 1.6 Hz, 4H, ArH$_B$), 8.12 (br t, $^4J$(H$_C$,H$_B$) = 1.6 Hz, 2H, ArH$_C$), 7.72 (t, $^3J$(H$_A$,H$_B$) = 7.8 Hz, 2H, ArH$_A$), 7.63-7.55 (m, 2H, ArH (para, Ph$_2$PO)), 7.53-7.43 (m, 4H, ArH (ortho, Ph$_2$PO)), 7.34-7.23 (m, 8H, NH$_D$ and ArH (meta, Ph$_2$PO)), 7.21-7.13 (m, 6H, ArH (meta and para, Ph$_2$CH)), 7.06-6.98 (m, 4H, ArH (ortho, Ph$_2$CH)), 6.55 (s, 8H, ArH$_F$), 4.52 (dd, $^2J$(H$_E$,H$_E'$) = 14.2 Hz, $^3J$(H$_E$ or H$_E'$,H$_D$) = 5.8 Hz, 4H, CH$_E$ or CH$_E'$), 4.32 (d, $^3J$(H,H) = 7.6 Hz, 2H, Ph$_2$CH-CH$_2$-).
4.27 (dd, $^2J(H_E, H_E') = 14.2$ Hz, $^3J(H_E$ or $E', H_D) = 5.5$ Hz, 4H, CH$_E$ or CH$_E'$), 4.09 (t, $^3J(H, H) = 7.6$ Hz, 1H, Ph$_2$CH -), 1.36-1.16 (m, 2H, Ph$_2$PO-CH$_2$-) and 1.07-0.93 (m, 2H, Ph$_2$PO-CH$_2$-CH$_2$-); 13C NMR (100 MHz, CDCl$_3$): $\delta = 174.0$ (s, -COO-), 166.2 (s, 4C, -CONH-), 140.2 (s, 2C, Ar$\cdot$CH (ipso)), 137.8 (s, 4C, ArC-CH$_2$NH-), 134.3 (s, 4C, Ar-C-O-), 132.6 (s, 2C, ArCH (para, Ph$_2$PO)), 132.1 (s, 4C, ArCH$_B$), 132.0 (d, $^1J(C, P) = 100.0$ Hz, 2C, ArC-PO (ipso)), 130.0 (d, $^2J(C, P) = 10.0$ Hz, 4C, ArCH (ortho, Ph$_2$PO)), 129.7 (s, 2C, ArCH$_A$), 129.2 (d, $^3J(C, P) = 12.0$ Hz, 4C, ArCH (meta, Ph$_2$PO)), 129.0 (s, 8C, ArCH$_F$), 128.8 (s, 4C, ArCH (meta, Ph$_2$CH), 127.7 (s, 4C, ArCH (ortho, Ph$_2$CH)), 127.5 (s, 2C, ArCH (para, Ph$_2$CH)), 122.4 (s, 2C, ArCH$_C$), 69.0 (s, -O-CH$_2$-), 49.5 (s, Ph$_2$CH-), 43.5 (s, 4C, CH$_E$), 26.1 (s, -CH$_2$-COO- ) and 22.8 (d, $^1J(C, P) = 73.2$ Hz, Ph$_2$PO-CH$_2$-); MS (FAB, mNBA): $m/z = 987$ [(M+H$^+$)]. Anal. Calcd for C$_{61}$H$_{55}$N$_4$O$_7$P: C, 74.22; H, 5.62; N, 5.68; O, 11.35; P, 3.14. Found C, 74.34; H, 5.79; N, 5.77.

Carboxymethyl-triphenylphosphoniumbromide (7a). [Griffin, C.E.; Gordon, M. J. Organomet. Chem.; EN; 3; 1965; 414-419.] Compound 7a was obtained using the general procedure for the preparation of the (ω-Carboxy-alkyl)-triphenylphosphonium-bromides using a solution of 2-bromoacetic acid (5.00 g, 35.98 mmol) in CH$_3$CN (25 ml). The white precipitate obtained from precipitation from Et$_2$O was filtered, recrystallized in acetonitrile and dried in oven to give 13.71 g of 7a (95% yield, white solid). mp 313-318 °C (decomp). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.85
(dd, $J = 13.1$ Hz, $J = 7.5$ Hz, 6H, ArH (ortho)), 7.68 (t, $J = 7.5$ Hz, 3H, ArH (para)),
7.55 (td, $J = 7.5$ Hz, $J = 3.3$ Hz, 6H, ArH (meta)) and 6.80 (d, $^2J(HP) = 10.8$ Hz, 2H,
-CH$_2$-); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 196.4$ (s, -CO-), 134.9 (s, 3C, ArCH
(para)), 134.6 (d, $^2J(C,P) = 5.4$ Hz, 6C, ArCH (ortho)), 130.4 (d, $^3J(C,P) = 6.90$ Hz,
6C, ArCH (meta)), 119.0 (d, $^1J(C,P) = 89.7$ Hz, 3C, ArC-P (ipso)) and 41.5 (d,
$^1J(C,P) = 66.7$ Hz, -CH$_2$-); $^{31}$P NMR (CDCl$_3$): $\delta = 20.76$; MS (FAB, mNBA): $m/z = 322$
[(M-Br)$^+$]. Anal. Cald for C$_{20}$H$_{17}$O$_2$P·HBr: C, 59.87; H, 4.52; Br, 19.91; O, 7.97;
P, 7.72. Found C, 60.05; H, 4.50.

2-Bromo-N-(2,2-diphenylethyl)-acetamide (7b). [Liu, Gang; Kozmina, Natasha S.;
Winn, Martin; Geldern, Opgenorth, Terry J.; J. Med. Chem.; EN; 42; 18; 1999;
3679-3689.] The 2,2-diphenylethylamine (5.00 g, 25.38 mmol) was dissolved in 20
mL of CH$_2$Cl$_2$. To this solution at 0 °C were added 3.56 mL of Et$_3$N (2.57 g, 25.38
mmol) and then, dropwise, a solution of bromoacetyl bromide (6.15 g, 30.46 mmol)
in 20 mL of CH$_2$Cl$_2$. The reaction mixture was stirred at 0 °C for 10 min, then at rt
for 2h. The obtained mixture was washed first with sat. NaHCO$_3$ (1 $\times$ 25 mL), then
with a solution of 1N HCl (1 $\times$ 25 mL). The resulting organic layer was dried over
MgSO$_4$. The solvent was removed under reduced pressure to give 7.75 g of 7b (96%,
white solid). mp 96-100 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.34$-$7.23$ (m, 10H,
ArH), 6.4 (br t, $^3J(H,H) = 5.8$ Hz, 1H, -CONH-), 4.23 (t, $^3J(H,H) = 8.0$ Hz, 1H,
Ph₂CH-), 3.96 (dd, ³J(H,H) = 8.0 Hz, ³J(H,H) = 5.8 Hz, 2H, Ph₂CH-CH₂-) and 3.82 (s, 2H, -CH₂-Br); ¹³C NMR (100 MHz, CDCl₃): δ = 165.7 (-CO-), 141.8 (2C, ArC-CH (ipso)), 129.2 (4C, ArCH (meta)), 128.4 (4C, ArCH (ortho)), 127.4 (2C, ArCH (para)), 50.7 (Ph₂CH-), 44.8 (-CH₂-NH-) and 29.6 (-CO-CH₂); MS (FAB, mNBA): m/z = 319 [(M+H)⁺]. Anal. Calcd for C₁₆H₁₆BrNO: C, 60.39; H, 5.07; Br, 25.11; N, 4.40; O, 5.03. Found C, 60.41; H, 5.02; N, 4.44.

N-(2,2-Diphenylethyl)-2-(diphenylphosphinoyl)-acetamide (7c). To a solution of 7b (6.134 g, 19.29 mmol) in toluene (50 mL) was added diphenylmethoxyphosphine (5.00 g, 23.15 mmol). The solution was refluxed overnight. The solvent was removed under reduced pressure and the oil was taken up with CHCl₃ (30 mL). The resulting organic solution was washed with 1N NaOH (1 × 10 mL) and 1N HCl (1 × 10 mL) then dried over anhydrous MgSO₄. The resulting solution was concentrated, under reduced pressure, to 2 mL and the product was precipitated with Et₂O, then recrystallized in MeOH to give 4.66 g of 7c (55%, white solid). mp 259-266 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.68-7.40 (m, 11H, ArH (Ph₂PO) and -NIH-), 7.32-7.18 (m, 10H, ArH (Ph₂CH)), 4.17 (t, ³J(H,H) = 8.0 Hz, 1H, Ph₂CH-CH₂-), 3.89 (dd, ³J(H,H) = 8.0 Hz, ³J(H,H) = 5.8 Hz, 2H, -CH₂-NH-) and 3.24 (d, ²J(H,P) = 12.6 Hz, 2H, Ph₂PO-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ = 165.1 (d, ²J(C,P) = 4.6 Hz, -CO-
142.2 (s, 2C, ArC-CH (ipso)), 132.8 (d, $^1J(C,P) = 102.7$ Hz, 2C, ArC-PO (ipso)), 132.7 (d, $^4J(C,P) = 3.1$ Hz, 2C, ArCH (para Ph$_2$PO)), 131.1 (d, $^2J(C,P) = 10.0$ Hz, 4C, ArCH (ortho Ph$_2$PO)), 129.2 (d, $^3J(C,P) = 12.3$ Hz, 4C, ArCH (meta Ph$_2$PO)), 129.0 (s, 4C, ArCH (meta Ph$_2$CH)), 128.4 (s, 4C, ArCH (ortho Ph$_2$CH)), 127.1 (s, 2C, ArCH (para Ph$_2$CH)), 50.9 (s, 2C, Ph$_2$CH-), 44.7 (s, -CH$_2$-NH-), and 38.8 (d, $^1J(C,P) = 60.6$ Hz, Ph$_2$PO-CH$_2$-); $^{31}$P NMR (CDCl$_3$): $\delta = 30.31$; MS (FAB, mNBA): m/z = 440 [(M+H)$^+$]. Anal. Calcd for C$_{28}$H$_{26}$NO$_2$P: C, 76.52; H, 5.96; N, 3.19; O, 7.28; P, 7.05. Found C, 76.40; H, 6.01; N, 3.20.

[2] - (1, 4, 7, 14, 17, 20, - Hexaaza - 2, 6, 15, 19 – tetraoxo - 3, 5, 9, 12, 16, 18, 22, 25 - terabenzocyclohexacosane) - (N - (2, 2 - diphenylethyl) – 2 - (diphenylphosphinoyl) - acetamide) - Rotaxane (8). Rotaxane 8 was obtained using the general procedure for the preparation of benzylic amide [2]rotaxanes using thread 7c (0.500 g, 1.136 mmol). The crude material was subjected to column chromatography on silica gel using a gradient of CHCl$_3$ to CHCl$_3$/MeOH (95/5) give 10 mg of 7c (1%, white solid). mp 345-348 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.56$ (br t, $^4J(H_c,H_b) = 1.6$ Hz, ArH$_c$), 8.26 (dd, $^3J(H_b,H_a) = 7.7$ Hz, $^4J(H_b,H_c) = 1.6$ Hz, 4H, ArH$_b$), 7.66 (br m, 6H, NH$_D$ (4H) and ArH$_A$ (2H)), 7.65-7.42 (br m, 10H,
ArH (Ph2PO)), 7.15 -7.03 (m, 6H, ArH (Ph2CH)), 6.61-6.54 (m, 4H, ArH (Ph2CH)), 6.34 (s, 8H, ArH), 5.77 (br t, 3j(H,H) = 5.8 Hz, 1H, -CONH-), 4.64 (dd, 2j(H,E,H,E') = 14.3 Hz, 3j(H or H', H') = 7.0 Hz, 4H, CH or CH'), 4.03 (dd, 2j(H,E,H,E') = 14.3 Hz, 3j(H or H', H') = 4.5 Hz, 4H, CH or CH'), 3.25 (t, 3j(H,H) = 8.0 Hz, 1H, Ph2CH), 2.67 (dd, 3j(H,H) = 8.0 Hz, 3j(H,H) = 5.8 Hz, 2H, -CH2-NH-) and 1.68 (d, 2j(H,P) = 12.9 Hz, 2H, Ph2PO-CH2-); 13C NMR (100 MHz, CDCl3): δ = 167.1 (s, -CO- (macrocycle)), 165.0 (d, 3j(C,P) = 4.6 Hz, -CO- (thread)), 142.4 (s, 2C, ArC-CH (ipso)), 138.4 (s, 4C, ArC-CH2NH-), 135.0 (s, 4C, ArC-CO-), 132.6 (d, 4j(C,P) = 3.1 Hz, 2C, ArC (para Ph2PO)), 132.1 (d, 4j(C,P) = 102.7 Hz, 2C, ArC-PO (ipso)), 131.3 (s, 2C, CHB), 130.46 (d, 3j(C,P) = 10.0 Hz, 4C, ArC (ortho, Ph2PO)), 129.6 (s, 2C, Cc), 129.30 (s, 8C, Cc), 129.1 (d, 3j(C,P) = 12.3 Hz, 4C, ArC (meta, Ph2PO)), 129.0 (s, 4C, ArC (meta, Ph2CH)), 128.4 (s, 4C, ArC (ortho, Ph2CH)), 127.5 (s, 2C, ArC (para, Ph2CH)), 125.5 (s, 2C, Cc), 50.1 (s, Ph2CH), 45.8 (s, -CONH-CH2-), 44.4 (s, 4C, CHB) and 36.0 (d, 1j(C,P) = 60.8 Hz, Ph2PO-CH2-); 31P NMR (CDCl3): δ = 27.67; MS (FAB, mNBA): m/z = 972 [(M+H)+]. Anal. Calcd for C60H54N5O6P: C, 74.14; H, 5.60; N, 7.20; O, 9.88; P, 3.19. Found C, 74.53; H, 5.72; N, 7.26.

X-ray crystallographic data for compound 8. C64H58Cl12N5O6P, M = 1449.52, colourless block, crystal size 0.46 × 0.27 × 0.27 mm, monoclinic, P21/n, a = 14.042(4), b = 19.369(5), c = 26.468(7) Å, β = 103.504(4)°, V = 7000(3) Å³, Z = 4, ρcalcd = 1.375 Mg m⁻³, MoKα radiation (graphite monochromator, λ = 0.71073 Å), μ = 0.549 mm⁻¹, T = 150(2) K. 33336 data (7342 unique, Rint = 0.0491, 1.32 < θ < 25.00°), R1 = 0.0473 (I > 2σI), wR2 = 0.1067. The structure was solved by direct methods and refined by full-matrix least-squares on F². The non-H atoms were refined anisotropically. The molecule consists of a macrocycle containing a phosphorus atom with three nitrogen atoms and one oxygen atom, and four chlorine atoms. The macrocycle is connected to two Ph2PO groups by two nitrogen atoms. The crystal packing is stabilized by hydrogen bonding.
20.88°), were collected on a Siemens SMART CCD diffractometer using narrow frames (0.3° in ω), and were corrected semiempirically for absorption and incident beam decay. The structure was solved by direct methods and refined by full-matrix least-squares on $F^2$ values of all data (G. M. Sheldrick, SHELXTL manual, Siemens Analytical X-ray Instruments, Madison WI, USA, 1994, version 5) to give $wR = \left\{ \Sigma [w(F^2_o - F^2) / \Sigma [w(F^2)]] \right\}^{1/2} = 0.3152$, conventional $R = 0.1108$ for $F$ values of 7342 reflections with $F^2_o > 2\sigma(F^2)$, $S = 1.048$ for 813 parameters. Residual electron density extremes were 1.878 and -1.346 eÅ⁻³. Amide hydrogen atoms were refined isotropically with the remainder constrained; anisotropic displacement parameters were used for all non-hydrogen atoms.

![Structural diagram]

N-(2,2-Diphenylethyl)-3-(diphenylphosphinoyl)-propionamide (8a). Thread 8a had been made from compound 5b (1.140 g, 4.160 mmol) using the general procedure for the preparation of the $N$-(2,2-diphenylethyl)-ω-(diphenylphosphinoyl)-alkanoylamide. The white solid obtained was subjected to column chromatography on silica gel using a gradient of CHCl₃ to CHCl₃/MeOH (95/5) as eluent to obtain the desired compound as a white powder (8a, 1.300 g, yield 71%). mp 197-200 °C. $^1H$ NMR (400 MHz, CDCl₃): δ = 7.61-7.55 (m, 4H, ArH (meta Ph₂CH)), 7.48-7.35 (m, 6H, ArH (ortho and para Ph₂PO)), 7.21-7.07 (m, 10H, ArH (Ph₂CH)), 6.60 (br t, $^3J(H,H) = 5.8$ Hz, 1H, NH), 4.10 (t, $^3J(H,H) = 8.0$ Hz, 1H, PhPh)}
Ph₂CH⁻), 3.75 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.8 Hz, 2H, -CH₂-NH⁻), 2.44-2.35 (m, 2H, Ph₂PO-CH₂⁻) and 2.35-2.26 (m, 2H, -CH₂-CO⁻), ¹³C NMR (100 MHz, CDCl₃): δ = 171.7 (d, 3J(C,P) = 12.3 Hz, -CO⁻), 142.3 (s, 2C, ArC-CH (ipso)), 132.5 (s, 2C, ArCH (para, Ph₂CH)), 132.3 (d, 1J(C,P) = 99.7 Hz, 2C, ArC-PO (ipso)), 131.1 (d, 2J(C,P) = 9.2 Hz, 4C ArCH (ortho, Ph₂PO)), 129.2 (d, 3J(C,P) = 11.5 Hz, 4C, ArCH (meta, Ph₂PO)), 129.0 (s, 4C, ArCH (meta, Ph₂CH)), 128.4 (s, 4C, ArCH (ortho, Ph₂CH)), 127.1 (s, 2C, ArCH (para, Ph₂CH)), 50.9 (s, Ph₂CH⁻), 44.3 (s, CONH-CH₂⁻), 28.6 (s, -CH₂-CO⁻) and 25.6 (d, 1J(C,P) = 72.8 Hz, Ph₂PO-CH₂⁻); ³¹P NMR (CDCl₃): δ = 34.59; MS (FAB, mNBA): m/z = 441 [(M+H)⁺]. Anal. Calcd for C₂₉H₂₈NO₂P: C, 76.80; H, 6.22; N, 3.09; O, 7.06; P, 6.83. Found C, 76.81; H, 6.20; N, 3.12.

[2] - (1, 4, 7, 14, 17, 20, 25 -Hexaaza - 2, 6, 15, 19 - tetraoxo - 3, 5, 9, 12, 16, 18, 22, -tetrabenzocyclohexacosane) - ( N - (2, 2 - diphenylethyl ) - 3 - (diphenylphosphinoyl ) -propionamide)-rotaxane (9). Rotaxane 9 was obtained using the general procedure for the preparation of benzylic amide [2]rotaxanes using thread 8a (0.550 g, 1.214 mmol). The crude material was subjected to column chromatography on silica gel using a gradient of CHCl₃ to CHCl₃/MeOH (95/5) as
eluent to obtain the desired compound as a colourless solid (9, 42%, white solid). mp 157-158 °C. \( ^1H \) NMR (400 MHz, CDCl3): \( \delta = 8.33 \) (br t, \( ^4J(H_c,H_b) = 1.5 \) Hz, ArHc), 8.19 (dd, \( ^3J(H_b,H_a) = 7.8 \) Hz, \( ^4J(H_b,H_c) = 1.5 \) Hz, 4H, ArHb), 7.79 (br t, \( ^3J(H,H) = 5.0 \) Hz, 4H, ArHd), 7.66 (t, \( ^3J(H_a,H_b) = 7.8 \) Hz, 2H, ArH), 7.49 (t, \( ^3J(H,H) = 7.4 \) Hz, 2H, ArH (para, Ph2PO)), 7.37-7.19 (m, 14H, ArH (Ph2CH and meta from Ph2PO)), 6.92 (dd, \( ^1J(H,P) = 11.54 \) Hz, \( ^3J(H,H) = 7.3 \) Hz, 4H, ArH (ortho, Ph2PO)), 6.85 (br t, \( ^3J(H,H) = 5.0 \) Hz, 1H, -CH2-CONH-CH2-), 4.40 (m, 8H, CHE and CHE'), 6.55 (s, 8H, ArHf), 4.22 (t, \( ^3J(H,H) = 8.0 \) Hz, 1H, Ph2CH-), 3.66 (dd, \( ^3J(H,H) = 8.0 \) Hz, \( ^3J(H,H) = 5.0 \) Hz, 2H, -CH2-NHCO-), 0.93 (br m, 2H, Ph2PO-CH2-) and 0.78 (br m, 2H, -CH2-CONH-); \(^13C\) NMR (100 MHz, CDCl3): \( \delta = 173.4 \) (d, \( ^3J(C,P) = 18.40 \) Hz, -CO- (thread)), 167.1 (s, -CO- (macrocycle)), 142.4 (s, 2C, ArC-CH (ipso)), 138.3 (s, 4C, ArC-CH2NH-), 135.0 (s, 4C, ArC-CO-), 132.2 (d, \( ^4J(C,P) = 2.3 \) Hz, 2C, ArCH (para, Ph2PO)), 132.2 (d, \( ^1J(C,P) = 100.5 \) Hz, 2C, ArC-PO (ipso)), 131.3 (s, 4C, ArCH3), 130.5 (d, \( ^2J(C,P) = 10.0 \) Hz, 4C, ArCH (ortho, Ph2PO)), 129.6 (s, 2C, ArCH3), 129.3 (s, 8C, ArCHF), 129.1 (d, \( ^3J(C,P) = 11.5 \) Hz, 4C, ArCH (meta, Ph2PO)), 128.9 (s, 4C, ArCH (meta, Ph2CH), 128.4 (s, 4C, ArCH (ortho, Ph2CH)), 127.6 (s, 2C, ArCH (para, Ph2CH)), 125.5 (s, 2C, CHC), 50.2 (s, Ph2CH-), 45.8 (s, -CONH-CH2-), 44.2 (s, 4C, CHB), 26.9 (s, -CH2-CONH-) and 23.4 (d, \( ^1J(C,P) = 72.1 \) Hz, Ph2PO-CH2-); \(^31P\) NMR (CDCl3): \( \delta = 31.38 \) MS (FAB, mNBA): \( m/z = 987 ((M+H)^+) \). Anal. Calcd for C61H56N5O6P: C, 74.30; H, 5.72; N, 7.10; O, 9.73; P, 3.14. Found C, 74.21; H, 5.69; N, 7.15.
(3-Carboxypropyl)-triphenylphosphonium bromide (9a). Compound S9a was obtained using the general procedure for the preparation of the (ω-Carboxy-alkyl)-triphenylphosphonium bromides using 4-bromobutyric acid (5.00 g, 29.94 mmol). The white precipitate obtained from precipitation from Et₂O was filtered, recrystallized in CH₃CN and dried in oven to afford a white solid (9a, 92% yield).

mp 240-243 °C. ¹H NMR (400 MHz, d₆-DMSO): δ = 12.36 (br s, 1H, -COOH), 7.97-7.77 (m, 15H, ArH), 3.64 (m, 2H, -CH₂-PPh₃), 2.52 (t, 3/HH = 7.4 Hz, 2H, -CH₂-COOH) and 1.76 (m, 2H, -CH₂-CH₂-COOH); ¹³C NMR (400 MHz, d₆-DMSO): δ = 173.7 (s, -COOH), 135.3 (d, 4/JP(C,P) = 3.1 Hz, 3C ArCH (para)), 133.9 (d, 2/JP(C,P) = 10.0 Hz, 6C, ArCH (ortho)), 130.6 (d, 3/JP(C,P) = 13.0 Hz, 6C, ArCH (meta)), 118.7 (d, 1/JP(C,P) = 88.2 Hz, 3C, ArC-P (ipso)), 34.0 (d, 3/JP(C,P) = 16.9 Hz, -CH₂-COOH), 20.2 (d, 1/JP(C,P) = 51.4 Hz, Ph₂PO-CH₂-) and 18.1 (s, -CH₂-CH₂-COOH); ³¹P NMR (d₆-DMSO): δ = 25.03; MS (FAB, mNBA): m/z = 350 [(M-Br)⁻]. Anal. Calcd for C₂₂H₂₂O₂P·HBr: C 61.27, H 5.61, Br 18.53, O 7.42, P 7.18. Found C 61.18, H 5.70.
4-(Diphenylphosphinoyl)-butyric acid (9b). Compound 9b was prepared using the general procedure for the preparation of the ω-(Diphenylphosphinoyl)-alkanoic acid from compound 9a (5.00 g, 11.59 mmol). With those procedure had been obtained a white solid that was recrystallized in CH$_3$CN (9b, 2.51 g, yield 75%). mp 126-128 °C. $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.77-7.70 (m, 4H, ArH (meta)), 7.52-7.42 (m, 6H, ArH (ortho and para)), 2.43-2.38 (m, 4H, -CH$_2$-COOH and Ph$_2$PO-CH$_2$-) and 1.93 (m, 2H, -CH$_2$-CH$_2$-COOH); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 175.5 (s, -CO-), 132.5 (s, 2C, ArCH (para)), 132.2 (d, $^1$J(C,P) = 100.5 Hz, 2C, ArC-P (ipso)), 131.2 (d, $^2$J(C,P) = 10.0 Hz, 4C, ArCH (ortho)), 129.2 (d, $^3$J(C,P) = 12.3 Hz, 4C, ArCH (meta)), 35.0 (d, $^4$J(C,P) = 16.9 Hz, -CH$_2$-COOH), 28.8 (d, $^5$J(C,P) = 72.1 Hz, Ph$_2$PO-CH$_2$-) and 17.9 (d, $^6$J(C,P) = 3.1 Hz, -CH$_2$-CH$_2$-COOH); $^{31}$P NMR (CDCl$_3$): δ = 36.77; MS (FAB, mNBA): m/z = 289 [(M+H)$^+$]. Anal. Calcd for C$_{16}$H$_{17}$O$_3$P: C 66.66, H 5.94, O 16.65, P 10.74. Found C 66.54, H 6.00.
**N-(2,2-Diphenylethyl)-4-(diphenylphosphinoyl)-butyramide (9c).** Compound 9c had been prepared from compound 9b (1.000 g, 3.472 mmol) using the general procedure for the preparation of the **N-(2,2-diphenylethyl)-ω-(diphenylphosphinoyl)-alkanoylamide.** The white solid obtained was subjected to column chromatography on silica gel using a gradient of CH₂Cl₂ to CH₂Cl₂/EtOAc (70/30) as eluent to obtain the desired compound as a white powder (9c, 1.200 g, yield 73.9%).

mp 148-150 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.70-7.63 (m, 4H, Ph₂PO), 7.55-7.43 (m, 6H, Ph₂PO), 7.24-7.19 (m, 8H, ArH (ortho and meta of Ph₂CH)), 7.17-7.11 (m, 2H, ArH (para Ph₂CH)), 6.36 (br t, 3J(H,H) = 5.4 Hz, 1H, -NH-), 4.21 (t, 3J(H,H) = 8.0 Hz, 1H, Ph₂CH-), 3.89 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.4 Hz, 2H, Ph₂CH-CH₂-), 2.25 (t, 3J(H,H) = 6.7 Hz, 2H, -CH₂-CONH-), 2.06 (dt, 2J(H,P) = 10.8 Hz, 3J(H,H) = 7.4 Hz, 2H, Ph₂PO-CH₂-), 1.84 (m, 2H, -CH₂-CH₂-CONH-); ¹³C NMR (100 MHz, CDCl₃): δ = 172.5 (s, -CO-), 142.4 (s, 2C, ArC-CH (ipso)), 133.0 (d, 3J(C,P) = 98.2 Hz, 2C, ArC-PO (ipso)), 132.2 (d, 4J(C,P) = 3.1 Hz, 2C, ArCH (para, Ph₂PO)), 131.1 (d, 2J(C,P) = 9.2 Hz, 4C, ArCH (ortho, Ph₂PO)), 129.1 (d, 3J(C,P) = 11.5 Hz, 4C, ArCH (meta, Ph₂PO)), 128.5 (s, 4C, ArCH (ortho, Ph₂CH)), 127.1 (s, 2C, ArCH (para, Ph₂CH)), 51.1 (s, Ph₂CH-), 44.1 (s, Ph₂CH₂-CH₂-), 37.6 (d, 3J(C,P) = 9.2 Hz, -CH₂-CONH-), 27.9 (d, 3J(C,P) = 11.5 Hz, Ph₂PO-CH₂-), 18.8 (d, 2J(C,P) = 3.8 Hz, -CH₂-CH₂-CONH-);
$^{31}$P NMR (400 MHz, CDCl$_3$): $\delta = 34.54$; MS (FAB, mNBA): $m/z = 468 [(M+H)$]$^+$. Anal. Calcd for C$_{30}$H$_{30}$NO$_2$P: C 77.07, H 6.47, N 3.00, O 6.84, P 6.62. Found C, 76.98; H, 6.39; N, 3.09.

[2] - (1, 4, 7, 14, 17, 20, - Hexaaza - 2, 6, 15, 19 – tetraoxo - 3, 5, 9, 12, 16, 18, 22, 25 -terabenzocyclohexacosane) - (N - (2,2-Diphenylethyl)-4-(diphenylphosphinoyl)-butyramide)-rotaxane (10). Rotaxane 10 was obtained using the general procedure for the preparation of benzylic amide [2]rotaxanes using thread 9c (0.500 g, 1.070 mmol). The crude obtained was subjected to column chromatography on silica gel using a gradient of CHCl$_3$ to CHCl$_3$/MeOH (95/5) as eluent to obtain the desired compound as white solid (10, 331 mg, 31%). mp 285-288 $^\circ$C (decomp). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.34$ (s, 2H, ArH$_c$), 8.27 (d, $^3$J(H$_B$,H$_A$) = 7.8 Hz, 4H, ArH$_b$), 7.78 (br t, $^3$J(H$_D$,H$_{E}$) = 5.5 Hz, 4H, NH$_D$), 7.64 (t, $^3$J(H$_A$,H$_B$) = 7.8 Hz, 2H, ArH$_A$), 7.61-7.55 (m, 2H, ArH (para, Ph$_2$PO)), 7.54-7.44 (m, 8H, ArH (ortho and meta, Ph$_2$PO)), 7.2-7.13 (m, 6H, ArH (Ph$_2$CH)), 7.02-7.08 (m, 4H, ArH (Ph$_2$CH)), 6.76 (s, 8H, ArH$_F$), 5.11 (br t, $^3$J(H$_H$) = 5.0 Hz, 1H, -CONH$-$), 4.61 (dd, $^2$J(H$_E$,H$_E'$) = 14.3 Hz, $^3$J(H$_E$ or H$_{E'}$,H$_D$) = 6.0 Hz, 4H, CH$_E$ or CH$_{E'}$), 4.16 (dd, $^2$J(H$_E$,H$_E'$) = 14.3 Hz, $^3$J(H$_E$ or H$_{E'}$,H$_D$) = 5.0 Hz, 4H, CH$_E$ or CH$_{E'}$),
3.91 (t, \( \delta = 8.0 \) Hz, 1H, Ph\(_2\)CH\(-\), 3.56 (dd, \( \delta = 8.0 \) Hz, \( \delta = 5.0 \) Hz, 2H, Ph\(_2\)CH-CH\(-\)), 1.50 (Ph\(_2\)PO-CH\(-\)), 0.86 (br m, 2H, -CH\(_2\)-CH\(-\)-CONH\(-\)) and 0.74 (br m, 2H, -CH\(_2\)-CONH\(-\) (thread)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta = 173.7 \) (s, -CO- (thread)), 166.7 (s, -CO- (macrocycle)), 141.4 (s, 2C, ArC-CH (ipso)), 138.3 (s, 4C, ArC-CH\(_2\)NH\(-\)), 134.5 (s, 4C, ArC-CO\(-\)), 132.9 (d, \( \delta (C,P) = 1.5 \) Hz, 2C, ArCH (para, Ph\(_2\)PO)), 132.8 (d, \( \delta (C,P) = 98.2 \) Hz, 2C, ArC-PO (ipso)), 132.2 (s, 4C, ArCH\(_3\)), 130.4, (d, \( \delta (C,P) = 9.2 \) Hz, 4C, ArCH (ortho, Ph\(_2\)PO)), 129.7 (s, 2C, ArCH\(_4\)), 129.6 (d, \( \delta (C,P) = 11.5 \) Hz, 4C, ArCH (meta, Ph\(_2\)PO)), 129.4 (s, 4C, ArCH (meta, Ph\(_2\)CH)), 129.3 (s, 8C, ArCH\(_{3}\)), 128.0 (s, 4C, ArCH (ortho, Ph\(_2\)CH)), 127.7 (s, 2C, ArCH (para, Ph\(_2\)CH)), 124.10 (s, 2C, ArCH\(_3\)), 50.4 (s, Ph\(_2\)CH\(-\)), 44.7 (s, Ph\(_2\)CH-CH\(-\)), 43.9 (s, 4C, CH\(_2\)), 35.6 (d, \( \delta (C,P) = 5.4 \) Hz, -CH\(_2\)-CONH\(-\)), 28.0 (d, \( \delta (C,P) = 71.3 \) Hz, Ph\(_2\)PO-CH\(-\)) and 16.9 (d, \( \delta (C,P) = 4.6 \) Hz, CH\(_2\)-CH\(_2\)-CONH\(-\)); \(^{31}\)P NMR (CDCl\(_3\)) \( \delta = 35.76 \); MS (FAB, mNBA): \( m/z = 1000 [(M+H)^+] \). Anal. Calcd for C\(_{62}\)H\(_{58}\)N\(_5\)O\(_6\)P: C, 74.46; H, 5.85; N 7.00, O 9.60, P 3.10. Found C, 74.50; H 6.00; N, 7.11.

**X-ray crystallographic data for compound 10.** C\(_{64}\)H\(_{62}\)N\(_5\)O\(_6\)P, \( M = 1028.16, \) colourless block, crystal size 0.16 × 0.08 × 0.08 mm, monoclinic, \( P2_1/c, a = 14.515(3), b = 21.621(5), c = 17.856(4) \) Å, \( \beta = 108.008(3)^\circ, V = 5329(2) \) Å\(^3\), \( Z = 4, \) \( \rho_{calcd} = 1.281 \) Mg m\(^{-3}\), Mo\(_{K\alpha}\) radiation (graphite monochromator, \( \lambda = 0.71073 \) Å), \( \mu = 0.111 \) mm\(^{-1}\), \( T = 150(2) \) K. 25935 data (5650 unique, \( R_{int} = 0.1581, 1.48 < \theta < 20.93^\circ \)), were collected on a Siemens SMART CCD diffractometer using narrow frames (0.3° in \( \omega \)), and were corrected semiempirically for absorption and incident
beam decay. The structure was solved by direct methods and refined by full-matrix least-squares on $F^2$ values of all data (G. M. Sheldrick, SHELXTL manual, Siemens Analytical X-ray Instruments, Madison WI, USA, 1994, version 5) to give $wR = \{\Sigma[w(F_o^2-F_e^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2} = 0.2182$, conventional $R = 0.0885$ for $F$ values of 5650 reflections with $F_o^2 > 2\sigma(F_o^2)$, $S = 1.047$ for 705 parameters. Residual electron density extremes were 0.391 and -0.353 eÅ$^{-3}$. Amide hydrogen atoms were refined isotropically with the remainder constrained; anisotropic displacement parameters were used for all non-hydrogen atoms.

(4-Carboxybutyl)triphenylphosphonium bromide (10a). [J. Org. Chem., Vol. 64, No. 9, 1999 Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. J. Am. Chem. Soc. 1969, 91, 5675]. The phosphonium bromide salt 10a was obtained using the general procedure for the preparation of the ($\omega$-Carboxyalkyl)-triphenylphosphonium bromides using 5-bromovaleric acid (10.00 g, 55.25 mmol). The white material obtained was recrystallized in CH$_2$Cl$_2$ and dried in oven to afford the desired compound as white solid (10a, 23.55 g, 96%). mp 200-201 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.83-7.75$ (m, 9H, ArH), 7.74-7.67 (m, 6H, ArH), 3.65 (m, 2H, Ph$_3$P-C$_6$H$_5$), 2.73 (t, $^3J$(H,H) = 6.9 Hz, 2H, -C$_6$H$_2$-COOH), 1.95 (tt, $^3J$(H,H) =
$^3\!J(H,H) = 6.9\ \text{Hz},\ 2\text{H},\ -\text{CH}_2\text{-CH}_2\text{-COOH}$ and 1.72 (dt,$^3\!J(H,P) = 7.8\ \text{Hz},\ ^3\!J(H,H) = \\
^3\!J(H,H) = 6.9\ \text{Hz},\ 2\text{H},\ \text{Ph}_3\text{P-CH}_2\text{-CH}_2\text{-}$); $^{13}\!\text{C}\ \text{NMR} (100\ \text{MHz, CDCl}_3): \delta = 175.4\ (s,\ \text{-CO-}),\ 135.6\ (d,\ ^4\!J(C,P) = 2.3\ \text{Hz},\ 3\text{C},\ \text{ArCH (para)}),\ 134.0\ (d,\ ^2\!J(C,P) = 10.0\ \text{Hz},\ 6\text{C},\ \text{ArCH (ortho)}),\ 131.0\ (d, \ ^3\!J(C,P) = 13.0\ \text{Hz},\ 6\text{C},\ \text{ArCH (meta)}),\ 118.4\ (d,\ ^1\!J(C,P) = 86.7\ \text{Hz},\ 3\text{C},\ \text{ArC-P (ipso)}),\ 34.2\ (s,\ \text{-CH}_2\text{-COOH}),\ 25.9\ (d,\ ^3\!J(C,P) = 16.9\ \text{Hz},\ \text{-CH}_2\text{-CH}_2\text{-COOH}),\ 22.2\ (d,\ ^1\!J(C,P) = 51.4\ \text{Hz},\ \text{Ph}_3\text{P-CH}_2\text{- and }\ \text{-CH}_2\text{-COOH})\ \text{and 22.0 (s, Ph}_3\text{P-CH}_2\text{-CH}_2\text{-});\ ^{31}\!\text{P}\ \text{NMR (CDCl}_3): \delta = 25.51;\ \text{MS (FAB, mNBA): } m/z = 364\ [(\text{M-Br})^+].$ Anal. Cacld for $\text{C}_{22}\text{H}_{23}\text{O}_2\text{P-HBr: C 61.27, H 5.61, Br 18.53, O 7.42, P 7.18. Found C 61.10, H 5.88.}$

$^{5}\!(\text{Diphenylphosphinoyl})$-pentanoic\ acid (10b). Compound 10b was prepared using the general procedure for the preparation of the $\omega$-(Diphenylphosphinoyl)-alkanoic acid from the phosphonium bromide salt 10a (6.00 g, 13.54 mmol). The white material obtained was ricrystallized in CH$_3$CN. (10b, 4.10 g, yield 100 %). mp 140-145 °C. $^{1}\!\text{H}\ \text{NMR (400 MHz, CDCl}_3): \delta = 11.58\ (br\ s,\ 1\text{H, -COOH}),\ 7.77-7.69\ (m,\ 4\text{H, ArH}),\ 7.54-7.45\ (m,\ 6\text{H, ArH}),\ 2.39-2.25\ (m,\ 4\text{H, Ph}_2\text{PO-CH}_2\text{- and }\ \text{-CH}_2\text{-COOH})\ \text{and 1.79-1.56 (m, 4H, Ph}_2\text{PO-CH}_2\text{-CH}_2\text{-COOH});\ ^{13}\!\text{C}\ \text{NMR (100 MHz, CDCl}_3): \delta = 176.3\ (s,\ \text{-CO-}),\ 132.4\ (d,\ ^1\!J(C,P) = 99.7\ \text{Hz},\ 2\text{C, ArC-PO (ipso)}),\ 132.4\ (d,\ ^4\!J(C,P) = 2.3\ \text{Hz},\ 2\text{C, ArCH (para)}),\ 131.2\ (d,\ ^2\!J(C,P) = 10.0\ \text{Hz},\ 4\text{C, ArCH (ortho)}),\ 129.2\ (d,\ ^3\!J(C,P) = 11.5\ \text{Hz},\ 4\text{C, ArCH (meta)}),\ 34.2\ (s,\ \text{-CH}_2\text{-COOH}),\ 29.5\ (d,\ ^1\!J(C,P) =}$
71.3 Hz, Ph$_2$PO-CH$_2$-), 25.5 (d, $^3$J(C,P) = 15.4 Hz, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-) and 21.4 (d, $^2$J(C,P) = 3.1 Hz, Ph$_2$PO-CH$_2$-CH$_2$-); $^{31}$P NMR (CDCl$_3$): $\delta$ = 36.47; MS (FAB, mNBA): $m/z$ = 303 [(M+H)$^+$]. Anal. Calcd for C$_{17}$H$_{19}$O$_3$P: C 67.54, H 6.33, O 15.88, P 10.25. Found C 67.54, H 6.20.

$N$-(2,2-Diphenylethy1)-5-(diphenylphosphinoyl)-valericamide (10c). Thread 10c had been prepared from compound 10b (1.000 g, 3.311 mmol) using the general procedure for the preparation of the $N$-(2,2-diphenylethy1)-$\omega$-(diphenylphosphinoyl)-alkanoylamide. The white solid obtained was crystallized from CH$_3$Cl (10c, 1.2 g, yield 72.9%) mp 130-135 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.74-7.66 (m, 4H, ArH (Ph$_2$PO)), 7.54-7.43 (m, 6H, ArH (Ph$_2$PO)), 7.31-7.25 (m, 4H, ArH (Ph$_2$CH)), 7.23-7.17 (m, 6H, ArH (Ph$_2$CH)), 5.64 (br t, $^3$J(H,H) = 5.8 Hz, 1H, NH), 4.14 (t, $^3$J(H,H) = 8.0 Hz, 1H, Ph$_2$CH-), 3.84 (dd, $^3$J(H,H) = 8.0 Hz, $^3$J(H,H) = 5.8 Hz, 2H, Ph$_2$CH-CH$_2$-), 2.23-2.19 (m, 2H, Ph$_2$PO-CH$_2$-), 2.05 (t, $^3$J(H,H) = 7.4 Hz, 2H, -CH$_2$COOH) and 1.71-1.49 (m, 4H, Ph$_2$PO-CH$_2$-(CH$_2$)$_2$-); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 172.8 (s, -CO-), 142.3 (s, 2C, ArC-CH (ipso)), 133.4 (d, $^1$J(C,P) = 98.2 Hz, 2C, ArC-PO (ipso)), 132.1 (d, $^4$J(C,P) = 2.3 Hz, 2C, ArCH (para, Ph$_2$PO)), 131.1 (d, $^2$J(C,P) = 9.2 Hz, 4C, ArCH (ortho, Ph$_2$PO)), 129.1 (d, $^2$J(C,P) = 10.7 Hz, 4C, ArCH (meta, Ph$_2$PO)), 129.0 (s, 4C, ArCH (meta, Ph$_2$CH)), 128.4 (s, 4C, ArCH
(ortho, Ph₂CH), 127.1 (s, 2C, ArCH (para, Ph₂CH)), 51.0 (s, Ph₂CH-), 44.1 (s, Ph₂CH-CH₂-), 36.4 (s, -CH₂-COOH), 29.7 (d, J(C,P) = 72.1 Hz, Ph₂PO-CH₂-), 27.2 (d, J(C,P) = 14.6 Hz, Ph₂PO-(CH₂)₂-CH₂-) and 21.5 (d, J(C,P) = 3.8 Hz, Ph₂PO-CH₂-CH₂-); ³¹P NMR (CDCl₃): δ = 33.71; MS (FAB, mNBA): m/z = 482 [(M+H)⁺].

Anal. Cald for C₃₁H₃₂NO₂P: C 77.32, H 6.70, N 2.81, O 6.64, P 6.43. Found C 77.52, H 6.77, N 2.91.

[21-(1, 4, 7, 14, 17, 20, -Hexaaza-2, 6, 15, 19-tetraoxo-3, 5, 9, 12, 16, 18, 22, 25-terabenzocyclohexacosane)-(5-(Diphenylphosphinoyl)-pentanoic acid (2,2-diphenylethyl)-amide)-rotaxane (11). Rotaxane 11 was synthesized using the general procedure for the preparation of benzylic amide [2]rotaxanes from thread 10c (0.500 g, 1.038 mmol). The crude obtained was subjected to column chromatography on silica gel using a gradient of CHCl₃ to CHCl₃/MeOH (95/5) as eluent to obtain the desired compound as white solid (11, 27%, 275 mg). mp >350 deomp °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.20 (t, J(H₃,H₄) = 1.3 Hz, 2H, ArHc), 8.17 (dd, J(H₄,H₅) = 7.8 Hz, J(H₅,H₆) = 1.3 Hz, 4H, ArH₃), 7.75 (t, J(H₆,H₇) = 5.8 Hz, 4H, ArHd), 7.59-7.45 (m, 12H, ArH (Ph₂PO and ArH₃)), 7.27-7.10 (m, 10 H, ArH (Ph₂CH)), 6.93 (s, 8H, ArHE), 5.60 (br t, J(H₄,H₅) = 5.4 Hz, 1H, NH (thread)), 4.46 (dd, J(H₉,H₁₀) = 14.1 Hz, J(H₉ or H₁₀,H₁₁) = 5.5 Hz, 4H, CHE or CHF), 4.35 (dd,
\(^2(J(H_E,H_E')) = 14.1 \text{ Hz, } ^3(J(H_E \text{ or } H_F,H_D)) = 6.0 \text{ Hz, } 4H, \text{ CH}_E \text{ or } \text{ CH}_F, \) 3.93 \((t, \ ^3(J(H,H)) = 7.9 \text{ Hz, } 1H, \text{ Ph}_2\text{CH}-), 3.57 \((dd, \ ^3(J(H,H)) = 7.9 \text{ Hz, } ^3(J(H,H)) = 5.4 \text{ Hz, } 2H, \text{ Ph}_2\text{CH}-\text{CH}_2-), 1.69-1.59 \((m, 2H, \text{ Ph}_2\text{PO}-\text{CH}_2-), 0.74-0.62 \((m, 4H, -\text{CH}_2-\text{COOH} \text{ and } \text{ Ph}_2\text{PO}-\text{CH}_2-\text{CH}_2-\text{COOH}), ^{13}\text{C NMR (100 MHz, CDCl}_3): \delta = 174.6 \((s, -\text{CO- (thread)}), 167.0 \((s, 4C, -\text{CO- (macrocycle)}), 142.0 \((s, 2C, \text{ ArC-CH (ipso)}), 138.5 \((s, 4C, \text{ ArC-CH}_2\text{NH-}), 134.5 \((s, 4C, \text{ ArC-CO-}), 132.7 \((s, 2C, \text{ ArCH (para, Ph}_2\text{PO))}, 132.4 \((d, \ ^1J(C,P) = 98.8 \text{ Hz, } 2C, \text{ ArC-PO (ipso)}), 131.9 \((s, 4C, \text{ ArCH}_B), 131.3 \((s, 2C, \text{ ArCH}_A), 130.6 \((d, \ ^2J(C,P) = 9.2 \text{ Hz, } 4C, \text{ ArCH (ortho, Ph}_2\text{PO)}), 129.5 \((d, \ ^3J(C,P) = 12.3 \text{ Hz, } 4C, \text{ ArCH (meta, Ph}_2\text{PO)}), 129.3 \((s, 8C, \text{ ArCH}_E), 129.3 \((s, 4C, \text{ ArCH (meta Ph}_2\text{CH)}), 128.16 \((s, 4C, \text{ ArCH (ortho, Ph}_2\text{CH)}), 127.5 \((s, 2C, \text{ ArCH (para, Ph}_2\text{CH)}), 124.5 \((s, 2C, \text{ ArCH}_C), 50.7 \((s, \text{ Ph}_2\text{CH-}), 44.7 \((s, \text{ NH-CH}_2- \text{ (thread)}), 44.0 \((s, 4C, \text{ CH}_E), 34.5 \((s, -\text{CH}_2-\text{CONH-}), 27.9 \((d, \ ^1J(C,P) = 71.3 \text{ Hz, Ph}_2\text{PO-CH}_2-\text{CH}_2-), 25.1 \((d, \ ^3J(C,P) = 12.3 \text{ Hz, Ph}_2\text{PO-(CH}_2)_2-\text{CH}_2-\text{CH}_2-\text{COOH} \text{ and } 20.7 \((d, \ ^2J(C,P) = 3.1 \text{ Hz, Ph}_2\text{PO-CH}_2-\text{CH}_2-\text{COOH}), ^{31}\text{P NMR (CDCl}_3): \delta = 35.30; \text{ MS (FAB, mNBA): } m/z = 1015 [(M+H)^+] \text{.} \text{ Anal. Calcd for C}_{63}H_{60}N_5O_{10}P: C 74.61, H 5.96, N 6.91, O 9.47, P 3.05. Found C 74.52, H 6.27, N 6.85.}

(5-Carboxypentyl)-triphenylphosphonium bromide (11a). Compound 11a was obtained using the general procedure for the preparation of the (ω-Carboxyalkyl)-triphenylphosphonium bromides from 6-Bromohexanoic acid (10.00 g, 51.27 mmol).
The solid obtained was washed with benzene, hexanes, and Et₂O and dried to give 20.55 g of 11a, (44.74 mmol, 96%, white solid). mp 195-199 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.82-7.67 (m, 15H, ArH), 3.65-3.55 (m, 2H, Ph₃P-CH₂-), 2.35 (t, 3J(H,H) = 7.0 Hz, 2H, -CH₂-COOH) and 1.69-1.61 (m, 6H, Ph₃P-CH₂-(CH₂)₂-); ¹³C NMR (100 MHz, CDCl₃): δ = 175.8 (s, -COOH), 135.1 (d, 4J(C,P) = 2.5 Hz, 3C, ArCH (para)), 133.6, (d, 2J(C,P) = 10.0 Hz, 6C, ArCH (ortho)), 130.5 (d, 3J(C,P) = 12.3 Hz, 6C, ArCH (meta)), 118.1, (d, 1J(C,P) = 85.9 Hz, 3C, ArC-P (ipso)), 34.2 (s, -CH₂-COOH), 29.5 (d, 3J(C,P) = 16.1 Hz, Ph₃P-(CH₂)₂-CH₂-), 24.0 (s, -CH₂-CH₂-COOH), 22.5 (d, 1J(C,P) = 50.6 Hz, Ph₃P-CH₂-) and 21.9 (d, 2J(C,P) = 4.1 Hz, Ph₃P-CH₂-CH₂-); ³¹P NMR (CDCl₃): δ = 25.39; MS (FAB, mNBA): m/z = 378 [(M-Br)⁺]. Anal. Calcd for C₂₄H₂₅O₂P·HBr: C 62.75, H 6.14, Br 17.39, O 6.97, P 6.74. Found C 62.70, H 5.99.

6-(Diphenylphosphinoyl)-hexanoic acid (11b). Compound 11b was prepared using the general procedure for the preparation of the ω-(Diphenylphosphinoyl)-alkanoic acid from the phosphonium bromide salt 11a (5.00 g, 10.94 mmol). The material obtained was recrystallized in CHCl₃ (11b, 3.4 g, yield 98%). mp 155-160 °C. ¹H NMR (400 MHz, CDCl₃): δ = 11.54 (br s, 1H, -COOH), 7.69 (dd, 3J(H,P) = 11.1 Hz, 3J(H,H) = 7.5 Hz, 4H, ArH (ortho)), 7.49-7.38 (m, 6H, ArH (meta and para)), 2.31-2.19 (m, 4H, Ph₁PO-CH₂- and -CH₂-COOH), 1.64-1.51 (m, 4H, Ph₂PO-CH₂-CH₂- and -CH₂-CH₂-COOH) and 1.39 (tt, 3J(H,H) = 3J(H,H) = 7.0 Hz, 2H, Ph₂PO-(CH₂)₂-
6-(Diphenylphosphinoyl)-hexanoic acid (2,2-diphenylethyl)-amide (11c). Thread 11c had been prepared from compound 11b (2.000 g, 6.329 mmol) using the general procedure for the preparation of the \( N-(2,2\text{-diphenylethyl})-\omega-(\text{diphenylphosphinoyl})\)-alkanoylamide. The white material obtained was subjected to column chromatography on silica gel using a gradient of CHCl$_3$ to CHCl$_3$/MeOH (95/5) as eluent to obtain the desired compound as white solid (11c, 2.2 g, yield 70.13%). mp 126-128 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.74-7.68$ (m, 4H, ArH (ortho, Ph$_2$PO)), 7.54-7.43 (m, 6H, ArH (meta and para, Ph$_2$PO)), 7.31-7.26 (m, 4H, ArH (meta, Ph$_2$CH)), 7.24-7.17 (m, 6H, ArH (ortho and para, Ph$_2$CH)), 5.51 (br t, $^3$J(H,H) = 5.5 Hz, -NH-), 4.18 (t, $^3$J(H,H) = 8.0 Hz, 1H, Ph$_2$CH-), 3.87 (dd, $^3$J(H,H) = 8.0 Hz, 2C, ArCH (meta)).
Hz, $^3J(H,H) = 5.5$ Hz, 2H, Ph$_2$CH-CH$_2$-), 2.23-2.15 (m, 2H, Ph$_3$PO-CH$_2$-), 2.01 (t, $^3J(H,H) = 7.5$ Hz, 2H, -CH$_2$-CH$_2$-CONH-), 1.62-1.47 (m, 4H, Ph$_2$PO-CH$_2$-CH$_2$- and -CH$_2$-CH$_2$-CONH-) and 1.32 (tt, $^3J(H,H) = 7.5$ Hz, 2H, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 172.7$ (s, -CO-), 141.9 (s, 2C, ArC-CH (ipso)), 133.0 (d, $^1J(C,P) = 98.2$ Hz, 2C, ArC-PO (ipso)), 131.6 (d, $^4J(C,P) = 2.3$ Hz, 2C, ArCH (para, Ph$_2$PO)), 130.7 (d, $^2J(C,P) = 9.2$ Hz, 4C, ArCH (ortho, Ph$_2$PO)), 128.6 (s, 4C, ArCH (meta, Ph$_2$CH)), 128.6 (d, $^3J(C,P) = 11.5$ Hz, 4C, ArCH (meta, Ph$_2$PO)), 128.0 (s, 4C, ArCH (ortho, Ph$_2$CH)), 126.7 (s, 2C, ArCH (para, Ph$_2$CH)), 50.5 (s, Ph$_2$CH-), 43.6 (s, Ph$_2$CH-CH$_2$-), 36.1 (s, Ph$_2$PO-(CH$_2$)$_4$-CH$_2$-), 30.0 (d, $^3J(C,P) = 13.8$ Hz, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-), 29.3 (d, $^1J(C,P) = 72.1$ Hz, Ph$_2$PO-CH$_2$-), 24.9 (s, -CH$_2$-CH$_2$-CONH-) and 20.9 (d, $^2J(C,P) = 3.1$ Hz, Ph$_2$PO-CH$_2$-CH$_2$-), $^{31}$P NMR (CDCl$_3$): $\delta = 33.70$; MS (FAB, mNBA): m/z = 496 [(M+H)$^+$]. Anal. Calcd for C$_{32}$H$_{34}$NO$_2$P: C 77.55, H 6.91, N 2.83, O 6.46, P 6.25. Found C 77.56, H 7.01.

[2]-[1, 4, 7, 14, 17, 20, -Hexaaza- 2, 6, 15, 19 -tetraoxo- 3, 5, 9, 12, 16, 18, 22, 25-terabenzocyclohexacosane)-(6-(Diphenylphosphinoyl)-hexanoic acid (2.2-
diphenylethyl)-amide)-rotaxane (12). Compound 12 was synthesized using the general procedure for the preparation of benzylic amide [2]rotaxanes from thread 11c (0.500 g, 1.010 mmol). The crude obtained was subjected to column chromatography on silica gel using a gradient of CHCl₃ to CHCl₃/MeOH (95/5) as eluent to obtain the desired compound as white solid (12, 207 mg, 20%). mp 200-202 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.13 (dd, 3J(H₆,H₇) = 7.5 Hz, 4J(H₆,H₇) = 1.0 Hz, 4H, ArH₆), 8.04 (s, 2H, ArH₇), 7.79 (br t, 3J(H,H) = 5.5 Hz, 4H, NHₓ), 7.68-7.49 (m, 10H, ArH (Ph₂PO)), 7.19-7.35 (m, 12H, ArH (Ph₂CH and ArH₆)), 7.04 (s, 8H, ArH₇), 6.32 (br t, 3J(H,H) = 5.5 Hz, 1H, Ph₂CH-CH₂-NH-), 4.66 (dd, 2J(H₆,H₇) = 14.1 Hz, 3J(H₆,H₇) = 5.0 Hz, 4H, CHE or CH₂E), 4.34 (dd, 2J(H₆,H₇) = 14.1 Hz, 3J(H₆,H₇) = 5.5 Hz, 2H, Ph₂CH-CCH₂-NH-), 3.89 (t, 3J(H,H) = 7.5 Hz, 1H, Ph₂CHE⁻⁻), 3.42 (dd, 3J(H,H) = 7.5 Hz, 3J(H,H) = 5.5 Hz, 2H, Ph₂CH-CH₂-NH⁻⁻), 1.46-1.37 (m br, 2H, Ph₂PO-CH₂⁻⁻), 0.65-0.56 (br m, 4H, -(CH)₂-(CH₂)₂-CO-NH⁻⁻) and 0.55-0.44 (br m, 4H, -(CH₂)₂-CO-NH⁻⁻); ¹³C NMR (100 MHz, CDCl₃): δ = 174.1 (s, -CO-(thread)), 166.5 (s, 4C, -CO- (macrocycle)), 142.3 (s, 2C, ArC-CH (ipso)), 137.6 (s, 4C, ArC-CH₂NH⁻⁻), 133.8 (s, 4C, ArC-CO-), 132.5 (d, 1J(C,P) = 98.9 Hz, 2C, ArC-PO (ipso)), 132.2 (d, 4J(C,P) = 2.3 Hz, 2C, ArCH (para, Ph₂PO)), 131.6 (s, 4C, ArCH₆), 130.4 (s, 2C, ArCH₆), 130.4 (d, 2J(C,P) = 9.2 Hz, 4C, ArCH (ortho, Ph₂PO)), 129.0 (d, 3J(C,P) = 12.3 Hz, 4C, ArCH (meta, Ph₂PO)), 128.9 (s, 8C, ArCH₇), 128.7 (s, 4C, ArCH (meta, Ph₂CH)), 128.2 (s, 4C, ArCH (ortho, Ph₂CH)), 126.8 (s, 2C, ArCH (para, Ph₂CH)), 124.6 (s, 2C, ArCH₆), 50.0 (s, Ph₂CH⁻⁻), 44.5 (s, -CONH-CH₂⁻⁻ (thread)), 43.9 (s, 4C, CH₇), 33.5 (s, Ph₂PO-(CH₂)₄-CH₂⁻⁻), 29.1 (d, 3J(C,P) = 13.0 Hz, Ph₂PO-(CH₂)₂-CH₂⁻⁻), 28.8 (d, 1J(C,P) = 71.5 Hz, Ph₂PO-CH₂⁻⁻), 24.9 (s, -CH₂-CH₂-CONH⁻⁻) and 20.9 (d, 2J(C,P) = 3.1 Hz, Ph₂PO-CH₂-CH₂⁻⁻); ³¹P
NMR (CDCl₃): δ = 34.63; MS (FAB, mNBA): m/z = 1028 [(M+H⁺)]. Anal. Calcd for C₆₄H₆₂N₅O₆P: C, 74.76; H, 6.08; N 6.81, O 9.34, P 3.01. Found C, 74.80; H 6.11; N, 7.01.

(5-Carboxyheptyl)-triphenylphosphonium; bromide (12a). [Dawson, M.I.; Vasser, M.; J. Org. Chem.; EN; 42; 1977; 2783-2785] The bromide salt 12a was obtained using the general procedure for the preparation of the (ω-Carboxyalkyl)-triphenylphosphonium-bromides using 8-Bromo-octanoic acid acid (5.00 g, 22.41 mmol). The white material obtained was recrystallized in CHCl₃ to afford colorless needles (12a, 9.70 g, 98%). mp 188-192 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.80-7.74 (m, 9H, ArH), 7.72-7.66 (m, 6H, ArH), 3.60-3.52 (m, 2H, Ph₃P-C₃H₂-), 2.34 (t, J(H,H) = 7.0 Hz, 2H, -CH₂-COOH), 1.63-1.48 (m, 6H, Ph₃P-CH₂-(CH₂)₂- and Ph₃P-(CH₂)₅-C₃H₂-) and 1.33-1.15 (m, 4H, Ph₃P-(CH₂)₃-(CH₂)₂-); ¹³C NMR (100 MHz, CDCl₃): δ = 176.7 (s, -CO-), 135.0 (d, J(C,P) = 3.1 Hz, 3C, ArCH (para)), 133.5 (d, J(C,P) = 10.0 Hz, 6C, ArCH (ortho)), 130.5 (d, J(C,P) = 12.3 Hz, 6C, ArCH (meta)), 118.1 (d, J(C,P) = 85.9 Hz, 3C, ArC-P (ipso)), 34.3 (s, -CH₂-COOH), 29.8 (d, J(C,P) = 16.1 Hz, Ph₃P-(CH₂)₃-CH₂-), 28.1 (s, Ph₃P-(CH₂)₃-CH₂-), 28.0 (s, Ph₃P-(CH₂)₄-CH₂-), 24.4 (s, Ph₃P-(CH₂)₃-CH₂-), 22.5 (d, J(C,P) = 50.6 Hz, Ph₃P-CH₂-)
and 22.2 (d, $^2J(C,P) = 4.1$ Hz, Ph$_3$P-CH$_2$-CH$_2$-); $^{31}$P NMR (CDCl$_3$): $\delta = 25.33$; MS (FAB, mNBA): $m/z = 406 [(M-Br)^+]$. Anal. Calcld for C$_{26}$H$_{31}$O$_2$P-HBr: C, 64.07; H, 6.62; Br, 16.39; O 6.56, P 6.35. Found C, 63.99; H 6.60.

8-(Diphenylphosphinoyl)-octanoic acid (12b). Compound 12b was prepared using the general procedure for the preparation of the $\omega$-(Diphenylphosphinoyl)-alkanoic acid from 12a (5.00 g, 10.31 mmol). The material obtained was recrystallized in CH$_2$Cl$_2$ (3.4 g, yield 90%). mp 182-183 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.76$-7.69 (m, 4H, ArH (ortho)), 7.55-7.42 (m, 6H, ArH (meta and para)), 2.32-2.24 (m, 4H, Ph$_2$PO-CH$_2$- and -CH$_2$-COOH), 1.64-1.53 (m, 4H, Ph$_2$PO-CH$_2$-CH$_3$-(CH$_2$)$_3$-CH$_2$-), 1.43-1.34 (m, 2H, Ph$_2$PO-(CH$_2$)$_3$-CH$_2$-) and 1.31-1.24 (m, 4H, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-CH$_2$-CH$_2$-); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 177.2 (s, -CO-), 132.4 (d, $^1J(C,P) = 98.9$ Hz, 2C, ArC-PO (ipso)), 131.8 (d, $^2J(C,P) = 2.3$ Hz, 2C, ArCH (para)), 130.8 (d, $^2J(C,P) = 10.0$ Hz, 4C, ArCH (ortho)), 128.7 (d, $^3J(C,P) = 11.5$ Hz, 4C, ArCH (meta)), 34.1 (s, -CH$_2$-COOH), 30.5 (d, $^4J(C,P) = 14.6$ Hz, Ph$_2$PO-(CH$_2$)$_3$-CH$_2$-), 29.3 (d, $^1J(C,P) = 71.3$ Hz, Ph$_2$PO-CH$_2$-), 28.6 (d, $^3J(C,P) = 10.0$ Hz, Ph$_2$PO-CH$_2$-CH$_2$-), 28.6 (s, Ph$_2$PO-(CH$_2$)$_4$-CH$_2$-), 24.7 (s, Ph$_2$PO-(CH$_2$)$_5$-CH$_2$-) and 21.2 (d, $^2J(C,P) = 3.8$ Hz, Ph$_2$PO-CH$_2$-CH$_2$-); $^{31}$P NMR (CDCl$_3$): $\delta = 35.96$; MS (FAB,

8-(Diphenylphosphinoyl)-octanoic acid (2,2-diphenylethyl)-amide (12c).

Compound 12c had been prepared from 12b (2.0 g, 5.81 mmol) using the general procedure for the preparation of the $N$-(2,2-diphenylethyl)-ω-(diphenylphosphinoyl)-alkanoylamide. The white solid obtained was subjected to column chromatography on silica gel using a gradient of CHCl$_3$ to CHCl$_3$/MeOH (95/5) as eluent to obtain the desired compound as white solid (12c, 2.58 g, yield 85%); mp 100-105 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.79-7.72$ (m, 4H, ArH (ortho, Ph$_2$PO)), 7.57-7.46 (m, 6H, ArH (meta and para, Ph$_2$PO)), 7.35-7.29 (m, 4H, ArH (meta, Ph$_2$CH)), 7.27-7.20 (m, 6H, ArH (ortho and para, Ph$_2$CH)), 5.51 (br t, $^3J(H,H) = 5.5$ Hz, 1H, -NH-), 4.21 (t, $^3J(H,H) = 8.0$ Hz, 1H, Ph$_2$CH-), 3.90 (dd, $^3J(H,H) = 8.0$, $^3J(H,H) = 5.5$ Hz, 2H, Ph$_2$CH-CH$_2$-), 2.29-2.21 (m, 2H, Ph$_2$PO-CH$_2$-), 2.04 (t, $^3J(H,H) = 7.5$ Hz, 2H, -CH$_2$-CONH-), 1.66-1.55 (m, 2H, Ph$_2$PO-CH$_2$-CH$_2$-), 1.50 (tt, $^3J(H,H) = 7.5$ Hz, 2H, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-), 1.37 (tt, $^3J(H,H) = 7.5$ Hz, 2H, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-), 1.28-1.13 (m, 4H, Ph$_2$PO-(CH$_2$)$_3$-(CH$_2$)$_2$-); $^{13}$C NMR (400 MHz, CDCl$_3$): $\delta = 172.9$ (s, -CO-), 141.9 (s, 2C, Ar-C-CH (ipso)), 133.2
(d, $^1J(C,P) = 97.4$ Hz, 2C, ArC-PO (ipso)), 131.6 (d, $^4J(C,P) = 2.3$ Hz, 2C, ArCH (para, Ph$_2$PO)), 130.7 (d, $^2J(C,P) = 9.2$ Hz, 4C, ArCH (ortho, Ph$_2$PO)), 128.6 (s, 4C, ArCH (meta, Ph$_2$CH)), 128.6 (d, $^3J(C,P) = 11.5$ Hz, 4C, ArCH (meta, Ph$_2$PO)), 128.0 (s, 4C, ArCH (ortho, Ph$_2$CH)), 126.7 (s, 2C, ArCH (para, Ph$_2$CH)), 50.5 (s, Ph$_2$CH-), 43.6 (s, Ph$_2$CH-CH$_2$-), 36.5 (s, -CH$_2$-CONH-), 30.6 (d, $^3J(C,P) = 13.8$ Hz, Ph$_2$PO-(CH$_2$)$_3$-CH$_2$-), 29.9 (s, Ph$_2$PO-(CH$_2$)$_4$-CH$_2$-), 29.6 (d, $^1J(C,P) = 72.1$ Hz, Ph$_2$PO-CH$_2$-), 28.6 (d, $^4J(C,P) = 6.1$ Hz, Ph$_2$PO-(CH$_2$)$_3$-CH$_2$-), 25.4 (s, Ph$_2$PO-(CH$_2$)$_5$-CH$_2$-); $^31$P NMR (CDCl$_3$): $\delta = 33.69$; MS (FAB, mNBA): $m/z = 524$ [(M+H)$^+$]. Anal. Calcd for C$_{34}$H$_{38}$NO$_2$P: C, 77.99; H, 7.31; N, 2.67; O, 6.11; P 5.91. Found C, 78.12; H, 7.29; N, 2.75.

[2]-[1, 4, 7, 14, 17, 20, -Hexaaza-2, 6, 15, 19-tetraoxo-3, 5, 9, 12, 16, 18, 22, 25-terabenzocyclohexacosane) - (8 - (Diphenylphosphinoyl) - octanoic acid (2,2-diphenylethyl)-amide)-rotaxane (13). Rotaxane 13 was synthesized using the general procedure for the preparation of benzylic amide [2]rotaxanes from thread 12c (0.500 g, 0.955 mmol). The crude obtained was subjected to column chromatography on silica gel using a gradient of CHCl$_3$ to CHCl$_3$/MeOH (95/5) as eluent to obtain
the desired compound as white solid (13, 161 mg, 16%) mp 233-235 °C.  
$^1$H NMR (400 MHz, CDCl$_3$): \( \delta = 8.19 \) (d, \( ^3J(H_B,H_A) = 7.5 \) Hz, 4H, ArH$_B$), 8.13 (br s, 2H, ArH$_C$), 7.88 (br t, \( ^3J(H,H) = 5.5 \) Hz, 4H, ArH$_D$), 7.77-7.69 (m, 4H, ArH (ortho, Ph$_2$PO)), 7.61-7.48 (m, 6H, ArH (meta and para, Ph$_2$PO)), 7.38-7.29 (m, 6H, 4H, ArH (meta, Ph$_2$CH) and ArH$_A$), 7.27-7.21 (m, 6H, ArH (ortho and para, Ph$_2$CH)), 7.00 (s, 8H, ArH$_F$), 6.63 (br t, \( ^3J(H,H) = 5.8 \) Hz, 1H, Ph$_2$CH-CH$_2$-NH$_2$)}, 4.67 (dd, \( ^2J(H_E,H_E') = 14.1 \) Hz, \( ^3J(H_E \text{ or } E',H_D) = 7.2 \) Hz, 4H, CH$_E$ or CH$_E'$), 4.30 (dd, \( ^2J(H_E,H_E') = 14.1 \) Hz, \( ^3J(H_E \text{ or } E',H_D) = 3.8 \) Hz, 4H, CH$_E$ or CH$_E'$), 4.08 (t, \( ^3J(H,H) = 7.8 \) Hz, 1H, Ph$_2$CH-), 3.45 (dd, \( ^3J(H,H) = 7.8 \) Hz, \( ^3J(H,H) = 5.8 \) Hz, 2H, Ph$_2$CH-CH$_2$-), 2.01-1.91 (br m, Ph$_2$PO-CH$_2$-), 1.01-0.90 (br m, 2H, Ph$_2$PO-CH$_2$-CH$_2$-), 0.87-0.75 (br m, 2H, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-), 0.53-0.42 (br, m, 4H, -(CH$_2$)$_2$-CONH-), 0.38-0.29 (br m, 2H, Ph$_2$PO-(CH$_2$)$_3$-CH$_2$- and 0.26-0.16 (br m, 2H, Ph$_2$PO-(CH$_2$)$_4$-CH$_2$-);  
$^{13}$C NMR (100 MHz, CDCl$_3$): \( \delta = 174.7 \) (s, -CO- (thread)), 166.3 (s, 4C, -CO- (macrocycle)), 142.5 (s, 2C, ArC-CH (ipso, Ph$_2$CH)), 137.8 (s, 4C, ArC-CH$_2$NH$_2$-), 133.8 (s, 4C, ArC-CO-), 132.3 (d, \( ^1J(C,P) = 98.9 \) Hz, 2C, ArC-PO (ipso)), 132.2 (d, \( ^4J(C,P) = 2.3 \) Hz, 2C, ArCH (para, Ph$_2$PO)), 131.3 (s, 4C, ArCH$_B$), 130.4 (d, \( ^{2}J(C,P) = 9.2 \) Hz, 4C, ArCH (ortho, Ph$_2$PO)), 129.0 (d, \( ^3J(C,P) = 11.5 \) Hz, 4C, ArCH (meta, Ph$_2$PO)), 128.8 (s, 2C, ArCH$_A$), 128.6 (s, 12C, ArCH$_F$ and ArCH (meta, Ph$_2$CH)), 128.2 (s, 4C, ArCH (ortho, Ph$_2$CH)), 126.7 (s, 2C, ArCH (para, Ph$_2$CH)), 124.8 (s, 2C, ArCH$_C$), 49.8 (s, Ph$_2$CH-), 44.7 (s, Ph$_2$CH-CH$_2$-), 43.9 (s, 4C, CH$_E$), 34.1 (s, -CH$_2$-CONH- (thread)), 28.9 (d, \( ^1J(C,P) = 72.8 \) Hz, Ph$_2$PO-CH$_2$-), 28.7 (d, \( ^3J(C,P) = 14.6 \) Hz, Ph$_2$PO-(CH$_2$)$_2$-CH$_2$-), 27.0 (s, Ph$_2$PO-(CH$_2$)$_4$-CH$_2$-), 26.7 (s, Ph$_2$PO-(CH$_2$)$_3$-CH$_2$-), 22.9 (s, Ph$_2$PO-(CH$_2$)$_5$-CH$_2$- and 20.3 (d, \( ^2J(C,P) = 3.1 \) Hz, Ph$_2$PO-CH$_2$-CH$_2$-);  
$^{31}$P NMR (CDCl$_3$): \( \delta = 35.37 \); MS (FAB, mNBA): \( m/z = 1056 \) [(M+H)$^+$]. Anal.
Calcd for C$_{66}$H$_{66}$N$_5$O$_6$P: C, 75.05; H, 6.30; N, 6.63; O, 9.09; P 2.93. Found C, 74.96; H, 6.22; N, 6.71.

(11-Carboxyundecyl)-triphenylphosphonium bromide (13a). The phosphonium bromide salt 13a was obtained using the general procedure for the preparation of the (ω-Carboxyalkyl)-triphenylphosphonium bromides using 11-bromoundecanoic acid (10.00 g, 37.71 mmol). The white material obtained was recrystallized in CH$_2$Cl$_2$ and dried in oven to afford the desiderated compound as white solid (13a, 19.56 g, 98%).

mp 170-172 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.87-7.76 (m, 9H, ArH (ortho and para)), 7.74-7.66 (m, 6H, ArH (meta)), 3.70 (br m, 2H, Ph$_3$P-CH$_2$-), 2.37 (t, $^3$J(H,H) = 7.8 Hz, 2H, -CH$_2$-COOH), 1.66-1.53 (m, 6H, -CH$_2$- (chain)), 1.33-1.14 (br m, 10H, -CH$_2$- (chain)); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 176.9 (-ÇO-), 134.8 (d, $^3$J(C,P) = 2.9 Hz, 3C, ArCH (para)), 133.1 (d, $^2$J(C,P) = 9.5 Hz, 6C, ArCH (ortho)), 130.2 (d, $^3$J(C,P) = 12.4 Hz, 6C, ArCH (meta)), 117.7 (d, $^1$J(C,P) = 86.4 Hz, 3C, ArH (para)), 34.0 (-CH$_2$-COOH), 29.9 (d, $^3$J(C,P) = 16.1 Hz, Ph$_3$P-(CH$_2$)$_2$-CH$_2$-), 28.7 (s), 28.6 (s), 28.5 (s), 28.4 (s), 24.3 (s), 22.2 (d, $^1$J$_{CP}$ = 50.5 Hz, Ph$_3$P-CH$_2$-), 22.1 (d, $^2$J(C,P) = 4.4 Hz, Ph$_3$P-CH$_2$-CH$_2$-); $^{31}$P NMR (CDCl$_3$): $\delta$ = 25.40; MS (FAB, mNBA): $m/z$ = 448 [(M-Br)$^+$]. Anal. Calcd for C$_{29}$H$_{37}$O$_3$P·HBr: C, 65.78; H, 7.23; Br, 15.09; O, 6.04; P 5.85. Found C, 65.81; H, 7.15.
11-(Diphenylphosphinoyl)-undecanoic acid (13b). Compound 13b was prepared using the general procedure for the preparation of the \( \omega \)-(Diphenylphosphinoyl)-alkanoic acid from 13a (10.0 g, 18.88 mmol). The material obtained was re-crystallized in CH\(_2\)Cl\(_2\) (13b, 6.57 g, yield 90%). mp 208-210 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.77-7.70 \) (m, 4H, ArH (meta)), 7.55-7.42 (m, 6H, ArH (ortho and para)), 2.35-2.23 (m, 4H, -NHCO-CH\(_2\)- and Ph\(_2\)PO-CH\(_2\)-), 1.67-1.53 (m, 4H, -NHCO-CH\(_2\)-CH\(_2\)- and Ph\(_2\)PO-CH\(_2\)-CH\(_2\)-), 1.43-1.16 (m, 12H, CH\(_2\) alkyl chain); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta 177.6 \) (-CO-), 132.4 (d, \(^1\)J(C,P) = 98.8, 2C, ArC- (ipso)), 131.8 (d, \(^4\)J(C,P) = 2.9 Hz, 2C, ArCH (para)), 130.8 (d, \(^2\)J(C,P) = 9.5 Hz, 4C, ArCH (ortho)), 128.7 (d, \(^3\)J(C,P) = 11.7 Hz, 4C, ArCH (meta)), 34.3 (s, -CH\(_2\)-COOH), 30.7 (d, \(^3\)J(C,P) = 14.6 Hz, Ph\(_2\)PO-(CH\(_2\))\(_3\)-CH\(_2\)-), 29.4 (d, \(^1\)J(C,P) = 71.7 Hz, Ph\(_2\)PO-CH\(_2\)-), 29.0, 28.9-28.8, 28.7, 24.8 (-CH\(_2\)-CH\(_2\)-CONH-), 21.2 (d, \(^2\)J(C,P) = 4.4 Hz, Ph\(_2\)PO-CH\(_2\)-CH\(_2\)-). \(^{31}\)P NMR (CDCl\(_3\)): \( \delta = 35.84 \); MS (FAB, mNBA): \( m/z = 387 \) [(M+H)+].

Anal. Calcd for C\(_{23}\)H\(_{31}\)O\(_3\)P: C, 71.48; H, 8.09; O, 12.42; P 8.01. Found C, 71.55; H, 8.00.
Thread 13c had been prepared from 13b (2.000 g, 5.17 mmol) using the general procedure for the preparation of the N-(2,2-diphenylethyl)-ω-(diphenylphosphinoyl)-alkanoylamide. The white solid obtained was subjected to column chromatography on silica gel using a gradient of CHCl₃ to CHCl₃/MeOH (95/5) as eluent to obtain the desired compound as white solid (13c, 2.16 g, 3.83 mmol yield 74%) mp 70-75 °C. $^1$H NMR (400 MHz, CDCl₃): δ = 7.75-7.68 (m, 4H, ArH (meta, Ph₂PO)), 7.53-7.41 (m, 6H, ArH (ortho and para, Ph₂PO)), 7.32-7.25 (m, 4H, ArH (Ph₂CH)), 7.24-7.16 (m, 6H, ArH (Ph₂CH)), 5.58 (br t, $^3$J(H,H) = 5.2 Hz, 1H, -NH-), 4.18 (t, $^3$J(H,H) = 8.0 Hz, 1H, Ph₂CH-), 3.87 (dd, $^3$J(H,H) = 8.0 Hz, $^3$J(H,H) = 5.7 Hz, 2H, -CH₂-NHCO-), 2.27-2.19 (m, 2H, -CH₂-PO-), 2.02 (t, $^3$J(H,H) = 7.2 Hz, 2H, -HNCO-CH₂-), 1.65-1.53 (m, 2H, -CH-PO-), 1.52-1.42 (m, 2H, -CH₂-CH₂-, 1.40-1.31 (m, 2H, -CH₂-(CH₂)₂-PO-), 1.27-1.11 (m, 10H, -(CH₂)₆- aliphatic chain), $^{13}$C NMR (100 MHz, CDCl₃): δ = 173.1 (-CO-), 141.9 (s, 2C, Ph₂CH-, (ipso)), 133.2 (d, $^1$J(C,P) = 98.1 Hz, 2C, Ph₃PO- (ipso)), 131.6 (d, $^4$J(C,P) = 2.2 Hz, 2C, ArCH (para, Ph₂PO-)), 130.8 (d, $^2$J(C,P) = 9.5 Hz, 4C, ArCH (ortho, Ph₂PO)), 128.7 (s, 4C, ArCH (meta, Ph₂CH)), 128.6 (d, $^3$J(C,P) = 12.4 Hz, 4C, ArCH Ph₃PO-(meta)), 128.1 (s, 4C, ArCH (ortho, Ph₂CH)), 126.8 (s, 2C, ArCH (para, Ph₂CH)), 50.6 (s, Ph₂CH-), 43.7 (s, Ph₂CH-CH₂-), 36.7 (s, -CH₂-CNH-), 30.9 (d, $^3$J(C,P) =
14.6 Hz, -CH$_2$-(CH$_2$)$_2$-PO-), 29.7 (d, $^1$J(C,P) = 72.5 Hz, -CH$_2$-PO-), 29.3, 29.25, 29.2, 29.1, 29.0, 25.6 (s, -CH$_2$-CH$_2$-CONH-) and 21.4 (d, $^2$J(C,P) = 3.7 Hz, -CH$_2$-CH$_2$-PO-); $^{31}$P NMR (CDCl$_3$): $\delta$ = 33.66; MS (FAB, mNBA): $m/z$ = 566 [(M+H)$^+$].

Anal. Calcd for C$_{37}$H$_{44}$NO$_2$P: C, 78.55; H, 7.84; N, 2.48; O, 5.66; P 5.47. Found C, 78.70; H, 7.96; N, 2.50.

[(21)-(1, 4, 7, 14, 17, 20, -Hexaaza-2, 6, 15, 19 -tetraoxo- 3, 5, 9, 12, 16, 18, 22, 25 -terabenzocyclohexacosane)-(11-(Diphenylphosphinoyl)-undecanoic acid (2,2-diphenylethyl)-amide)-rotaxane (14). Rotaxane 14 was synthesized using the general procedure for the preparation of benzylic amide [2]rotaxanes from thread 13c (0.500 g, 0.884 mmol). The crude obtained was subjected to column chromatography on silica gel using a gradient of CHCl$_3$ to CHCl$_3$/MeOH (95/5) as eluent to obtain the desired compound as white solid (14, 97.1 mg, 10%); mp120-123. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.24 (dd, $^3$J(H,H) = 7.8 Hz, $^3$J(H,H) = 1.5 Hz, 4H, ArH$_B$), 8.19, (br t, $^3$J(H,H) = 1.5 Hz, 2H, ArH$_C$), 7.81 (br t, $^3$J(H,H) = 5.4 Hz, 4H, NH$_D$), 7.78-7.71 (m, 4H, ArH (ortho, Ph$_2$PO)), 7.59-7.44 (m, 8H, ArH$_A$ and ArH (meta and para, Ph$_2$PO)), 7.32-7.19 (m, 10H, ArH (Ph$_2$CH)), 6.99 (s, 8H, ArH$_E$), 6.93 (br t, $^3$J(H,H) =
5.0 Hz, 1H, NH), 4.58 (dd, ²J(H₆',H₉) = 14.1 Hz, ³J(H₆,or E',H₁²D) = 6.1 Hz, 4H, CH₆' or CH₉), 4.39 (dd, ²J(H₆',H₉) = 14.1 Hz, ³J(H₆,or E',H₁²D) = 4.6 Hz, 4H, CH₆' or CH₉),
4.08 (t, ³J(H_H) = 7.8 Hz, 1H, Ph₂CH⁻), 3.37 (dd, ³J(H_H) = 7.8 Hz, ³J(H_H) = 5.0 Hz, 2H, Ph₂CH⁻CH₂⁻), 2.26-2.18 (m, 2H, Ph₂PO-CH₂⁻CH₂⁻), 1.53-1.42 (m, 2H, Ph₂PO-CH₂⁻CH₂⁻), 1.32-1.23 (m, 2H, Ph₂PO-(CH₂)₃⁻CH₂⁻), 0.79-0.66 (m, 4H, -CH₂⁻), 0.57-0.51 (m, 4H, -(CH₂)₂⁻CONH⁻), 0.46-0.32 (m, 4H, -(CH₂)₂⁻(CH₂)₂⁻CONH⁻); ¹³C NMR (100 MHz, CDCl₃): δ = 174.7 (-CO- (thread)), 166.2 (4C, -CO- (macrocycle)), 142.7 (s, 2C, ArC-CH (ipso, Ph₂CH)), 137.7 (s, 4C, ArC-CH₂NH⁻), 133.8 (s, 4C, ArC-CO⁻), 133.2 (d, ¹J(C,P) = 98.0 Hz, 2C, ArC-PO (ipso, Ph₂PO)), 132.1 (d, ⁴J(C,P) = 2.9 Hz, 2C, ArCH (para, Ph₂PO)), 131.2 (s, 4C, ArCH₂), 130.5 (d, ²J(C,P) = 9.5 Hz, 4C, ArCH (ortho, Ph₂PO)), 128.95 (s, 2C, ArCH₃), 128.9 (d, ³J(C,P) = 11.7 Hz, 4C, ArCH (meta, Ph₂PO)), 128.6 (s, 12C, ArCH₆ and ArCH (meta, Ph₂CH)), 128.3 (s, 4C, ArCH (ortho, Ph₂CH)), 126.6 (s, 2C, ArCH (para, Ph₂CH)), 124.9 (s, 2C, ArCH₂), 49.5 (s, Ph₂CH⁻), 44.9 (s, CONHCH₂ (thread)), 44.2 (s, 4C, CH₆ (macrocycle)), 34.38 (s, CH₂-CO⁻), 27.9-27.3 (broad), 23.5 and 20.6 (d, ²J(C,P) = 4.4 Hz, Ph₂PO-CH₂⁻CH₂⁻). ³¹P NMR (CDCl₃): δ = 35.05; MS (FAB, mNBA): m/z = 1099 [(M+H)⁺]. Anal. Calcd for C₆₀H₇₂N₅O₆P: C, 75.46; H, 6.61; N, 6.38; O, 8.74; P 2.82. Found C, 75.59; H, 6.77; N, 6.44.
Ethyl N-diphenylphosphinyl glycyglycinate (14a). Diphenylphosphonic chloride (0.85 mL, 1.0 g, 4.23 mmol) was added to a solution of glycyglycine ethyl ester hydrochloride salt (0.831 g, 4.23 mmol) in chloroform (40 mL) containing triethylamine (2.4 mL, 1.71 g, 8.46 mmol). The reaction mixture was allowed to stir at room temperature for 40 minutes then washed with water. The organic layer was dried over magnesium sulfate and the solvent removed under reduced pressure. Column chromatography (1/99 methanol/chloroform) lead to one main fraction as a colourless oil (14a, 1.27 g, 84 %); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.17$ (t, $J = 5.0$ Hz, 1H, CONH), 7.93-7.39 (m, 10H, ArH), 4.22 (qt, $J = 7.2$ Hz, 1H, PNH), 4.05 (d, $J = 5.0$ Hz, 2H, CH$_2$CO), 3.94 (qt, $J = 7.0$ Hz, 2H, CH$_2$CH$_3$), 3.70 (dd, $J = 7.0$ and 13 Hz, 2H, PNHCH$_2$) and 1.29 (t, 3H, $J = 7.0$ Hz, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 171.6$ (-CO-), 170.2 (-CO-), 132.4 (ArCH), 129.1 (ArCH), 129.0 (ArCH), 61.6 (CH$_2$CH$_3$), 44.6 (NHCH$_2$), 41.7(NHCH$_2$) and 14.4 (CH$_3$); FAB MS m/z = 361 (M+H)$^+$; HRMS 361.1323 Calculated for C$_{18}$H$_{21}$N$_2$O$_4$P (+H) = 361.1317.
2,2-Diphenylethyl N-diphenylphosphinylglycylglycinate (15). Ethyl diphenylphosphonic glycylglycinate 14a (1.11 g, 3.09 mmol), 2,2-diphenylethanol (0.613 g, 3.09 mmol) and bis(chlorodibutyltin) oxide (10 mg) were heated to reflux for eight hours in toluene with the continual distillation of the ethanol byproduct. The solvent was removed from the reaction mixture under reduced pressure and the crude product purified by column chromatography (chloroform solvent) to give one main fraction as a colorless oil (1.02 g, 65 %); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.15$ (t, $J = 6.0$ Hz, 1H, -CO-NH), 7.91-7.22 (m, 20H, ArH), 4.70 (d, $J = 8.0$ Hz, 2H, Ph$_2$CHCH$_2$), 4.37 (t, $J = 8.0$ Hz, 1H, Ph$_2$CH), 3.98 (d, $J = 6.0$ Hz, 2H, NHCH$_2$CO), 3.60 (dd, $J = 8.0$, $^2J$(H,P) = 14.0 Hz, 2H, PO-NHCH$_2$CO) and 3.51 (dt, $J = 8.0$, $^2J$(H,P) = 14.0 Hz, 1H, PO-NH); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 171.5$ (-CO-), 170.1 (-CO-), 141.2 (ArC-CH (ipso)), 132.5 (ArCH), 132.4 (ArCH), 132.3(ArCH), 130.6 (q, ArC), 129.2 (ArCH), 129.1 (ArCH), 129.0 (ArCH), 67.6 (Ph$_2$CHCH$_2$), 50.1 (Ph$_2$CH), 44.9 (NHCH$_2$) and 41.7 (NHCH$_2$); FAB MS m/z = 513 (M+H)$^+$; HRMS 513.1949 Calculated for C$_{30}$H$_{29}$N$_2$O$_4$P (+H) = 513.1943.
Rotaxane 16 was synthesized using the general procedure for the preparation of benzylic amide [2]rotaxanes from thread 15 (1.13 g, 2.20 mmol). Column chromatography (CHCl₃) lead to a white solid. (16, 138mg, 60%); mp 155 – 156 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.83 (s, 2H, ArHc), 8.36 (d, J = 8.0 Hz, 4H, ArHb), 7.92 (bt, 4H, NH₂), 7.79 (bt, 1H, NH-CH₂-COO⁻), 7.70 (t, J = 8.0 Hz, 2H, ArHb), 7.66-7.15 (m, 16H, ArH), 7.00 (d, J = 11.2 Hz, 4H, ArH), 6.74 (s, 8H, ArHb), 4.88 (dd, 2J(Hₑ,Hₑ') = 14.0 Hz, 3J(Hₑ or E',Hₑ) = 7.0 Hz, 4H, CHₑ or CHₑ'), 4.36 (d, 2J(Hₑ,Hₑ') = 14.0 Hz, 3J(Hₑ or E',Hₑ) = 4.0 Hz, 4H, CHₑ or CHₑ'), 3.24 (dd, 2J(Hₑ,Hₑ') = 14.0 Hz, 3J(Hₑ or E',Hₑ) = 4.0 Hz, 4H, CHₑ or CHₑ'), 3.05 (m, 1H, PO-NH), FAB MS m/z = 1045 (M + H)⁺, 513 (Thread); HRMS 1045.4065 Calculated for C₆₂H₅₇N₆O₈P (+ H) = 1045.4053.
3- Benzhydrylmercaptopropionic acid (17). 3-Mercaptopropionic acid (1.1 g, 10.4 mmol) was added slowly to bromodiphenylmethane (2.5 g, 10.4 mmol) with the vigorous evolution of HBr. When the reaction subsided the reaction mixture was heated to 100 °C until there was no further evolution of HBr. The reaction mixture was allowed to cool to room temperature and extracted with sodium bicarbonate solution. The aqueous layer was acidified with 1M HCl and extracted with CHCl₃. The organic layer was dried over magnesium sulfate and the solvent removed under reduced pressure. Recrystallisation from aqueous ethanol yields a colorless solid (17, 2.64 g, 89%) mp 90 - 91 °C, ¹H NMR (300MHz, CDCl₃): δ = 7.43-7.20 (m, 10H, Ar-H), 5.19 (s, 1H, Ar₂CH), 2.65 (m, 2H, CH₂COOH) and 2.56 (m, 2H, CH₂S); ¹³C NMR (75 MHz, CDCl₃): δ = 177.8 (q, -CO-), 141.0 (q, Ar-C), 128.9 (Ar-CH), 128.5 (Ar-CH), 127.6 (Ar-CH), 54.3 (Ar₂CH), 34.2 (CH₂COOH) and 26.8 (SCH₂). Anal. Calc. for C₁₆H₁₆O₂S: C, 70.6; H, 5.9; Found C, 70.3; H, 6.1.
3-Benzhydrylsulfanylpropionic acid succinimide ester (18)

\(N, N'-\text{Dicyclohexylcarbodiimide} (2.3 \text{ g}, 11.0 \text{ mmol})\) was added to a solution of 17 (3 g, 11.0 mmol) and \(N\)-hydroxysuccinimide (1.30 g, 11.0 mmol) in THF (20 mL) at 0°C. The reaction mixture was left at 0°C for eight hours then filtered and the solvent removed under reduced pressure. Further urea byproduct was removed by recrystallisation from ethyl acetate and the solvent was removed under reduced pressure to yield a colorless solid (18, 3.96 g, 97%) mp 109 - 110 °C, \(^1\text{H NMR} (300\text{ MHz, CDCl}_3): \delta = 7.45-7.21 \text{ (m, 10H, ArCH), 5.23 \text{ (s, 1H, Ar}_2\text{CII) and 2.85-2.72} \text{ (m, 8H, 4xCCH)}; \ ^{13}\text{C NMR} (100\text{MHz, CDCl}_3): \delta = 169.3 \text{ (-CO-), 167.5 \text{ (-CO-), 141(2C, ArC-CH (ipso))}, 129.1 \text{ (ArCH), 128.7 (ArCH), 127.8 (ArCH), 54.9 (Ar}_{2}\text{CH), 31.9 (SCH}_2\text{CH}_2, 27.0 \text{ (N-CO-CH})) and 26.0 (SCH}_2\text{CH}_2); FAB MS m/z = 368 (M+H)}^+;\) Anal. Calc. for \(\text{C}_{20}\text{H}_{10}\text{O}_4\text{SN}: \text{C, 65.0; H, 5.2; Found C, 65.1; H, 5.4.}\)
Triethylamine (0.6 mL), was added to a slurry of glycine ethyl ester hydrochloride (0.64 g) in chloroform (10 mL) and the reaction mixture allowed to stir for five minutes then 3-Benzhydrylsulfanylpropionic acid N-hydroxysuccinimide ester 18 was (1.65 g) added and the reaction mixture allowed to stir for 30 min. The reaction mixture was washed with water and the organic layer dried over magnesium sulfate and the solvent removed under reduced pressure to give a colorless solid (1.59 g, 61%) mp 46 - 47 °C; \(^1H\) NMR (200 MHz, CDCl\(_3\)): \(\delta = 7.49-7.28\) (m, 10H, ArH), 6.13 (bt, 1H, NHCH\(_2\)), 5.23 (s, 1H, Ar\(_2\)CH), 4.22 (qt, \(J = 7.0\) Hz, 2H, CH\(_2\)CH\(_3\)), 4.04 (d, \(J = 7.0\) Hz, 2H, NH-CH\(_2\)-CO-), 2.77 (t, \(J = 7.0\) Hz, 2H, SCH\(_2\)CH\(_2\)), 2.45 (t, \(J = 7.0\) Hz, 2H, SCH\(_2\)CH\(_2\)) and 1.32 (t, \(J = 7.0\) Hz, 3H, CH\(_3\)CH\(_3\)); \(^13C\) NMR (100 MHz, CDCl\(_3\)): \(\delta = 171.6\) (-CO-), 170.3 (-CO-), 141.6 (q, ArC), 129.0 (ArCH), 128.7 (ArCH), 127.7 (ArCH), 62.0 (OCH\(_2\)CH\(_3\)), 55.1 (ArCH), 41.8 (NHCH\(_2\)CO), 36.3 (SCH\(_2\)CH\(_2\)), 28.3 (SCH\(_2\)CH\(_2\)) and 14.5 (CH\(_3\)); FAB MS m/z = 357 (M\(^+\)); HRMS 357.1406 Calculated for C\(_{20}\)H\(_{23}\)O\(_3\)NS 357.13985
(3-Benzhydrylsulfanylpropionylamino)acetic acid 2,2-diphenyl ethyl ester (18b)

(3-Benzhydrylsulfanylpropionylamino) acetic acid ethyl ester (18a) (966 mg, 2.70 mmoles), diphenyl ethanol (536 mg, 2.70 mmoles), and bis (chlorodibutyltin) oxide (10 mg) were heated to reflux in toluene for * h with the continual distillation of the solvent to remove the ethanol byproduct. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography to give a colorless oil 18b (1.21 g, 88 %) 

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.46$-7.28 (m, 20H, ArCH), 6.00 (t, $J = 7.0$ Hz, 1H, NHCH$_2$), 5.21 (s, 1H, Ph$_2$CH), 4.74 (d, $J = 7.0$ Hz, 2H, CH$_2$CHAR$_2$), 4.40 (t, $J = 7.0$ Hz, 1H, CH$_2$CHAR$_2$), 3.95 (d, $J = 7.0$ Hz, 2H, NHCH$_2$), 2.72 (t, $J = 7.0$ Hz, 2H, SCH$_2$CH$_2$) and 2.39 (t, $J = 7.0$ Hz, 2H, SCH$_2$CH$_2$);

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 170.9$ (-CO-), 170.0 (-CO-), 135.6 (q, ArC), 135.3 (q, ArC), 129.8 (ArCH), 129.7 (ArCH), 129.4 (ArCH), 129.2 (ArCH), 129.1 (ArCH), 129.0 (ArCH), 73.2 (CHS), 67.8 (OCH$_2$CHAR), 50.1 (CHCH$_2$), 41.7 (NHCH$_2$-CO-), 36.2 (SCH$_2$CH$_2$) and 28.3 (SCH$_2$CH$_2$); FAB MS m/z = 510 (M+H)$^+$; HRMS 510.2097 Calculated for C$_{32}$H$_{31}$NO$_3$S (+H) 510.2103.
(+,-) 3-(Benzhydrylmethanesulfinyl)propionylaminoacetic acid 2,2-diphenylethyl ester (20)

To a solution of 18b (1.17 g, 2.29 mmol) in chloroform (10 mL) under an argon atmosphere at -20°C was added a solution of m-chloroperbenzoic acid (45.5 mg, 2.29 mmoles) in chloroform (5 mL) over 10 min. The reaction mixture was stirred at -20°C for 90 min then diluted with chloroform (30 mL) and allowed to warm to room temperature. The reaction mixture was washed three times with 5% sodium bicarbonate solution (30 mL) and three times with water (30 mL) then the organic layer dried over magnesium sulfate and the solvent removed under reduced pressure to give a colorless solid (84.5 mg, 70 %) mp 110-111 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.51-7.29$ (m, 20H ArH), 6.53 (t, 1H, NHCH$_2$), 4.89 (s, 1H, Ar$_2$CHS), 4.71 (d, $J = 7.0$ Hz, 2H, CH$_2$CHAr$_2$), 4.38 (t, $J = 7.0$ Hz, 1H, CH$_2$CHAr$_2$), 3.89 (dd, $J = 6.0$ Hz, $J = 18.0$ Hz, 2H, NHCH$_2$) and 2.93-2.67 (m, 4H, SCH$_2$CH$_2$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 170.9$ (-CO-), 170.0 (-CO-), 135.6 (q, ArC), 135.3 (q, ArC), 129.4 (ArCH), 129.1 (ArCH), 129.0 (ArCH), 128.8 (ArCH), 128.6 (ArCH), 127.3 (ArCH), 73.2 (CHS), 67.8 (OCH$_2$CHAr), 50.1 (CHCH$_2$), 46.0 (SCH$_2$CH$_2$), 41.7 (NHCH$_2$CO) and 29.1 (SCH$_2$CH$_2$); FAB MS m/z = 526 (M+H)$^+$; HRMS 526.2047 Calculated for C$_{33}$H$_{31}$O$_4$NS 526.2052
3-(Benzhydrylmethanesulfonyl)propionylaminoacetic acid 2,2-diphenyl ethyl ester (20a).

To a solution of 20 (2.66 g, 5.06 mmoles) in chloroform (10 mL) under an argon atmosphere at -20 °C was added a solution of m-chloroperbenzoic acid (0.873 g, 5.06 mmoles) in chloroform (8 mL). The reaction mixture was allowed to stir at -20 °C for 90 min then allowed to warm to room temperature. The reaction mixture was diluted with chloroform and washed with sodium bicarbonate (5%) three times then water three times. The organic layer was dried over magnesium sulfate and the solvent removed under reduced pressure to give a colorless solid (2.68 g, 98 %), mp 138 – 139 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.48-7.23 (m, 10H, ArH), 6.17 (t, J = 5.0 Hz, 1H, NH), 5.43 (s, 1H, Ph₂CH-SO₂), 4.72 (d, J = 7.0 Hz, 2H, Ph₂CHCH₂), 4.39 (t, J = 7.0 Hz, 1H, Ph₂CHCH₂), 3.92 (d, J = 5.0 Hz, 2H, NHCH₂), 3.23 (t, J = 7.0 Hz, 2H, SCH₂CH₂) and 2.70 (t, J = 7.0 Hz, 2H, SCH₂CH₂); ¹³C NMR (75 MHz, CDCl₃): δ = 170.9 (-CO-), 170.0 (-CO-), 135.6 (q, ArC), 135.3 (q, ArC), 129.4 (ArCH), 129.1 (ArCH), 129.0 (ArCH), 128.8 (ArCH), 128.6 (ArCH), 127.3 (ArCH), 74.2 (CHS), 67.0 (OCH₂CHAr), 50.1 (CHCH₂), 47.8 (SCH₂CH₂), 41.9 (NHCH₂CO) and 28.1 (SCH₂CH₂); FAB MS m/z = 542 (M+H); HRMS 542.2005 Calculated for C₃₂H₃₁NO₅S (+H) 542.2001.
(+,−) [2]−(1, 4, 7, 14, 17, 20, − Hexaaza−2, 6, 15, 19−tetraoxo−3, 5, 9, 12, 16, 18, 22, 25−terabenzocyclohexacosane) − ((benzhydrylmethanesulfinyl)-propionylaminoacetic acid 2,2-diphenylethyl ester) - rotaxane (21).

Rotaxane 21 was synthesized using a) the general procedure for the preparation of benzylic amide [2]rotaxanes from thread 20 (0.441 g, 0.84 mmol). Column chromatography (CHCl₃) gave one main fraction as a white solid. (21, 379 mg, 43%). b) a solution of rotaxane 23 (25 mg, 0.024 mmol) in CHCl₃ (1 mL) under an argon atmosphere at −20 °C; which was added a solution of m-chloroperbenzoic acid (4.14 mg, 0.024 mmol) in CHCl₃ (0.5 mL). The reaction mixture was allowed to stir at −20 °C for 90 minutes then allowed to warm to RT. The reaction mixture was diluted with CHCl₃ and washed with sodium bicarbonate (5%) 3 times then water 3 times. The organic layer was dried over MgSO₄ and the solvent removed under reduced pressure to give a colourless solid (21, 24.13 mg, 95%), mp 127−128 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.22 (t, J = 8.0 Hz, 4H, ArH₈), 7.97 (s, 2H, ArH₆), 7.63 (t, J = 8.0, 4H, Hz, NH₉), 7.33-7.27 (m, 28H, ArH), 7.24 (bt, 2H, ArH₆), 4.60
(m, 8H, CH₆), 4.38 (s, 1H, Ph₂CH-SO), 4.30 (t, J = 8.0 Hz, 1H, Ph₂CH-CH₂), 3.70 (t, 
J = 5.0 Hz, 2H, COOC₂H₅) and 1.29-0.92 (m, 4H, SO-CH₂-CH₂); FAB MS m/z = 
1059 (M+H)⁺, 533 (mac); HRMS 1058.4154 Calculated for C₆₄H₅₉O₈N₅S 1058.4162.

[2]-{1, 4, 7, 14, 17, 20, - Hexaaza - 2, 6, 15, 19 - tetraoxo - 3, 5, 9, 12, 16, 18, 22, 25 
-terabenzocyclohexacosane) - ((3-benzhydrylsulfonylpropionylamino) acetic 
acid 2,2 diphenylethyl ester) - rotaxane (22).

Method a): Rotaxane 22 was synthesized using a) the general procedure for the 
preparation of benzylic amide [2]rotaxanes from thread 20a (0.500 g, 0.92 mmol). 
The crude obtained was subjected to column chromatography on silica gel using 
CHCl₃ as eluent to obtain the desired compound as colorless solid (22, 99 mg, 10%).

Method b): To a solution of rotaxane 21 (100 mg, 0.094 mmol) in CHCl₃ (2 mL) 
under an Ar atmosphere at −20 °C was added a solution of m-chloroperbenzoic acid 
(16.3 mg, 0.094 mmol) in CHCl₃ (0.5 mL). The reaction mixture was allowed to stir 
at −20 °C for 90 minutes then allowed to warm to RT. The reaction mixture was 
diluted with chloroform and washed with sodium bicarbonate (5%) three times then 
water three times. The organic layer was dried over magnesium sulfate and the
solvent removed under reduced pressure to give a colorless solid (22, 94 mg, 97 %),
mp 110-111 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.11\) (d, 4H, \(J = 8.0\) Hz, ArH\(_D\)),
7.91 (s, 2H, ArH\(_C\)), 7.62 (t, \(J = 6.0\) Hz, 1H, CH\(_2\)CON\(\text{H}\)CH\(_2\)COO), 7.56 (bt, 2H,
ArH\(_A\)), 7.42 (t, \(J = 4.0\) Hz, 4H, NH\(_D\)), 7.32-7.02 (m, 28H, ArH), 4.86 (s, 1H, Ph\(_2\)CH-
SO\(_2\)-), 4.66 (d, \(J = 8.0\) Hz, 2H, COOCH\(_2\)), 4.56 (m, 8H, CH\(_E\)), 4.32 (t, 1H, \(J = 8.0\)
Hz, Ph\(_2\)CHCH\(_2\)O), 3.57 (d, \(J = 6.0\) Hz, 2H, NHCH\(_2\)COO), 2.00 (t, 2H, \(J = 7\) Hz,
SO\(_2\)CH\(_2\)CH\(_2\) or SO\(_2\)CH\(_2\)CH\(_2\) and 1.57 (t, \(J = 7.0\) Hz, 2H, SO\(_2\)CH\(_2\)CH\(_2\) or
SO\(_2\)CH\(_2\)CH\(_2\)); FAB MS m/z = 1074 (M+H)\(^+\) 533 (mac); HRMS 1074.4106
Calculated for C\(_{64}\)H\(_{59}\)N\(_5\)O\(_9\)S (+H) 1074.4111.

[2]-(1, 4, 7, 14, 17, 20, - Hexaaza - 2, 6, 15, 19 - tetraoxo - 3, 5, 9, 12, 16, 18, 22, 25
-terabenzocyclohexacosane) - ( 3 - Benzhydrylsulfanylpropionylamino) acetic
acid 2,2-diphenylethyl ester) - rotaxane (23).

Method a): Rotaxane 23 was synthesized using the general procedure for the
preparation of benzylic amide [2]rotaxanes from thread 18b (0.503 g, 0.98 mmol).
The crude obtained was subjected to column chromatography on silica gel using
CHCl₃ as eluent to obtain the desired compound as a colorless solid (23, 118 mg, 12%)

Method b): to a solution of rotaxane 21 (37 mg, 0.035 mmol) in THF (2 mL) at -20 °C was added Lawessons reagent (14.2 mg, 0.035 mmol). The reaction mixture was allowed to stir at room temperature for 1 hour then the solvent removed under reduced pressure. The crude product was purified by column chromatography (95/5; CHCl₃/MeOH) to give the desired product as a colorless solid (23, 31.7 mg, 87 %); mp 115-116 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.21 (d, J = 7.0 Hz, 4H, CH₃b), 8.11 (br t, 2H, CH₃c), 7.67 (t, J = 7.0 Hz, 2H, CH₃a), 7.31 (br t, 4H, CH₃d), 7.29–7.12 (m, 28H, ArH), 6.43 (br t, 1H, CH₂CONHCH₂COO), 4.66 (s, 1H, Ph₂CHS), 4.57 (d, J = 7.0 Hz, 2H, COOC₃), 4.53 (AA’BB’ system, 8H, J = 5.0 and 14.0 Hz, 8H, CH₃e), 4.27 (t, J = 7.0 Hz, 1H, Ph₂CHCH₂O), 3.31 (d, J = 6.0 Hz, 2H, CH₂COO), 1.72 (t, J = 8.0 Hz, 4H, S-CH₂-CH₂ or S-CH₂-CH₂) and 1.43 (t, J = 8.0 Hz, 4H, S-CH₂-CH₂ or S-CH₂-CH₂); FAB MS 1080 (M+K)⁺; HRMS 1042.4210 Calculated for C₆₄H₅₉O₇N₅S (+H) 1042.4213.
Chapter 3

Photoisomerization of a Rotaxane Hydrogen Bonding Template:
Light-induced Acceleration of a Large Amplitude Rotational Motion

Abstract

Establishing methods for controlling aspects of large amplitude submolecular movements is a prerequisite for the development of artificial devices that function through rotary motion at the molecular level. Here we demonstrate that the rate of rotation of the interlocked components of fumaramide-derived [2]rotaxanes can be accelerated - by more than six orders of magnitude – by isomerizing them to the corresponding maleamide [2]rotaxanes using light.

Data deposition

Crystallographic data for E-5 and Z-5 (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-149672 and 149673. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: teched@chemcrys.cam.ac.uk).
Photoisomerization of a Rotaxane Hydrogen Bonding Template: Light-induced Acceleration of a Large Amplitude Rotational Motion

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Key words

Rotaxanes, Molecular Machines, Rotational Motion, Dynamics, Hydrogen Bonding.
Main Text

Large amplitude internal rotations which resemble to some degree processes found in authentic machinery have recently inspired analogic molecular versions of gears(1), turnstiles(2), brakes(3), ratchets(4, 5), rotors(6) and unidirectional spinning motors(7-10), and are an inherent characteristic of many catenanes and rotaxanes(11-13). Establishing methods for controlling aspects of such movements is a prerequisite for the development of artificial devices that function through rotary motion at the molecular level. In this regard, we recently reported the unexpected discovery that the rate of rotation of the interlocked components of benzylic amide macrocycle-containing nitrone and fumaramide [2]rotaxanes can be slowed ("dampened") by 2-3 orders of magnitude by applying a modest (∼1Vcm⁻¹) external oscillating electric field(14). Here we demonstrate that the rate of rotation of the interlocked components of the olefin-based rotaxanes can also be accelerated - by more than six orders of magnitude – using another broadly useful stimulus, light.

For wonderful examples of using submolecular rotational motion to bring about a macroscopic change in a material see (22) and (23). Examples of controlling the frequency of large amplitude internal rotary motions include the redox-mediated acceleration/deceleration of the spinning of porphyrin ligands in cerium and zirconium sandwich complexes(24), the environment-dependent rate of circumrotation in hydrogen bonded [2]catenanes(25), and the electrochemically-induced pirouetting of a macrocycle in a rotaxane(26).
Fumaramide threads template the assembly of benzylic amide macrocycles around them to form rotaxanes in high yields (15). This cheap and simple preparative procedure (suitable threads are prepared in a single step from fumaryl chloride and a bulky primary or secondary amine) is particularly efficient because the \textit{trans}-olefin fixes the two hydrogen bond-accepting groups of the thread in an arrangement which is complementary to the geometry of the hydrogen bond-donating sites of the forming macrocycle.

\begin{align*}
E-1: & R^1 = R^2 = \text{CH}_2\text{CO}_2\text{CH}_2\text{Ph} \\
E-2: & R^1 = \text{Me}, R^2 = \text{CH}_2\text{CHPh}_2 \\
E-3: & R^1 = \text{H}, R^2 = \text{CH}_2\text{CHPh}_2 \\
Z-1: & \text{R} \\
Z-2: & \text{R} \\
Z-3: & \text{R} \\
Z-4: & \text{R} \\
Z-5: & \text{R} \\
Z-6: & \text{R} \\
\end{align*}

Scheme 1. Synthesis and dynamics of [2]rotaxanes E/Z-4-6. (i) 4 equivs. isophthahoyl dichloride, 4 equivs. \( p \)-xylylene diamine, Et3N, 4 h, high dilution; CHCl\(_3\) for E-4 (67%) and E-5 (33%), 1/9 MeCN/CHCl\(_3\) for E-6 (97%). Direct irradiation (254 nm, 30 min.) of a solution of an E-rotaxane (0.1 M, RT, CH\(_2\)Cl\(_2\) [1:9 MeOH/CHCl\(_3\) for E-6]) yields the “accelerated” Z-isomer (45-50% single experiment; >90% from 4 successive cycles). Heating a 0.02 M solution of a Z-rotaxane at 400K reforms the “dampened” E-isomer (E-4: C\(_2\)D\(_2\)Cl\(_2\), 7 days, 84% or d6-DMSO, 4 days, 100%).
However, the feature of the fumaramide unit that makes it such an effective template also provides an opportunity to enforce a geometrical change in the thread after rotaxane formation, thus altering the nature and strength of the interactions between the interlocked components. Isomerization of the olefin from \( E \)- to \( Z \)- must necessarily disrupt the near-ideal hydrogen bonding motif between macrocycle and thread and therefore also change any internal dynamics governed by those interactions.

To test this idea, the photochemical isomerization of three fumaramide-based threads (\( E-1-3 \)) and rotaxanes (\( E-4-6 \)) was investigated. The synthesis of rotaxanes \( E-4 \) and \( E-6 \) has previously been described(15) and \( E-5 \) was prepared in analogous fashion from the corresponding thread, \( E-2 \), isophthaloyl dichloride and \( p \)-xylylene diamine (Scheme 1).**

** The modest yield (33%) of \( E-5 \) is probably a consequence of the \{\( E,E \}\} and/or \{\( E,Z \}\} tertiary amide rotamers being sterically mismatched with the forming macrocycle. Interestingly, a small amount (2%) of rotaxane \( E-6 \), presumably arising from \( p \)-xylylene diamine-catalyzed isomerization of the thread, was isolated from the reaction of pristine \( Z-3 \), again indicating the extraordinary efficiency of the \( E-3 \) template for rotaxane formation.
Under the same reaction conditions the cis-olefin (maleamide) threads, Z-1-3, did not give detectable quantities of the corresponding Z-rotaxanes.

Single crystals suitable for investigation by X-ray crystallography were obtained for each of the three E-rotaxanes. In each case the solid-state structure shows two sets of bifurcated hydrogen bonds between the amide groups of the macrocycle and the carbonyl groups of the fumaramide system. The crystal structure of E-5 is typical (Figure 1), and shows the macrocycle in a chair conformation forming short, close-to-linear, hydrogen bonds orthogonal to the lone pairs of the fumaramide carbonyl groups. Of the three different tertiary amide rotamers present in solution (as observed by NMR) only the {ZZ}amide rotamer of E-5 is found in the crystal.

Figure 1. X-Ray crystal structure of [2]rotaxane E-5 (for clarity carbon atoms of the macrocycle are shown in blue and the carbon atoms of the thread in yellow, oxygen atoms are depicted in red, nitrogen atoms dark blue and selected hydrogen atoms white). Intramolecular hydrogen bond distances (Å): O40–HN2/O43–HN20 = 2.22, O40–HN1/043–HN29 = 1.94.
All three fumaramide rotaxanes $E$-$1$-$3$ and threads $E$-$4$-$6$ smoothly undergo photoisomerization (16) (254 nm; 0.1 M solution in CH$_2$Cl$_2$ or, for solubility reasons in the case of $E$-$6$, 1:9 MeOH/CHCl$_3$; 30 min.) to the corresponding maleamide ($Z$-olefin) systems. The yields for the rotaxanes, 45-50%, are remarkably good considering the confined cavity that the molecular rearrangement has to occur in and that the intercomponent hydrogen bonding between the thread and macrocycle is complementary to the positions of the amide groups only in the $E$-olefin. Unanticipated enhanced solubility of the $Z$-rotaxanes in nonpolar solvents allowed the separation of the $E/Z$ photochemical reaction mixtures into the individual isomers by simple trituration (PhMe/CH$_2$Cl$_2$, 1:1). The photoisomerization reaction produces few byproducts so $E$-rotaxanes recovered in this way could be recycled leading to >90% overall conversion to the $Z$-isomer from a series of irradiation experiments.

The $^1$H NMR spectra of each pair of $E$- and $Z$-olefin rotaxanes gives insight regarding their structure and relative dynamic properties in nonpolar solvents. The trends are similar in all cases but the clearest information is provided by $E/Z$-$4$.††

†† The spectra of $Z$-$6$ are complicated because intracomponent hydrogen bonding of the maleamide group desymmetrizes the rotaxane (the macrocycle methylene groups appear as an ABX system because the two faces of the macrocycle experience different environments). Similarly, the temperature-dependent equilibrium between the populations of the different amide rotamers present in the methylated rotaxanes $E/Z$-$5$ makes their study nontrivial, whereas the symmetrical tertiary amides means $E/Z$-$4$ suffers no such complication. For a discussion of the effect of the different
The variable temperature $^1$H NMR spectra of $E$-4 and $Z$-4 in CD$_2$Cl$_2$ (223-273K) and C$_2$D$_2$Cl$_4$ (339-393K) are shown in Figure 2 (the wide temperature range strengths of intercomponent hydrogen bonding in $E$-4 and $Z$-4 on the dynamics of amide rotamerization see Supporting Information.
involved meant different non-hydrogen bond-disrupting solvents were required to monitor the dynamic processes at high and low temperatures). Pirouetting, a 180° rotation of the macrocycle about the axis of the arrow plus formal chair-chair flip of the macrocycle, is the simplest process that must occur in order to translate the equatorial macrocycle methylene, H\textsubscript{E2}, protons onto the axial, H\textsubscript{E1}, sites. In the fumaramide system the H\textsubscript{E} protons coalesce at 273K and are fully resolved into the H\textsubscript{E1} and H\textsubscript{E2} resonances at 223K (Fig. 2a). The coupling constants confirm the axial and equatorial assignments of H\textsubscript{E1} and H\textsubscript{E2}. Spin polarization transfer by selective inversion recovery (SPT-SIR) experiments provided a direct measure of the rate of the exchange process I (i.e. half circumrotation of the macrocycle) at 298K corresponding to an energy barrier ΔG\textsuperscript{‡} = 13.4±0.1 kcal mol\textsuperscript{-1} which extrapolates to a rate of macrocycle rotation of ~1 s\textsuperscript{-1} at 223K(15). In contrast, the macrocycle methylene protons (H\textsubscript{E}) in Z-4 remain sharp and well resolved throughout this temperature range and only begin to broaden significantly at 223K (Fig. 2b); remarkably, the broadening of H\textsubscript{E} in Z-4 at 223K is comparable to that in E-4 at 359K – a 136° temperature difference between the two rotaxane isomers! Exchange is so fast in Z-4 that it is not possible to resolve the signals and prove unequivocally by experiment that the process responsible for the broadening at this temperature is, in fact, macrocycle pirouetting (it could be occurring at even lower temperatures). However, making the assumption (vide infra) that this is the process responsible for broadening, line shape analysis gives an energy barrier of 6.8 ±0.8 kcal mol\textsuperscript{-1}, i.e. a macrocycle spinning rate > 1.2 x 10\textsuperscript{6} s\textsuperscript{-1} at 223K.
Remarkably, it was possible to obtain an X-ray crystal structure of one of these rotaxanes with a 'switched off' recognition motif. Small crystals of Z-5 suitable for investigation using a synchrotron source were grown from slow evaporation of a saturated solution in chloroform/methanol. In contrast to the crystal structure of E-5, two of the three tertiary amide rotamers, \( i.e. \{ZE\} \) and \( \{EE\} \) rotamers are present in the unit cell of Z-5 (Figure 3a and 3b, respectively). Both forms are consistent with the dramatic increase in the rate of rotation in solution for the cis-rotaxanes observed experimentally by \(^1\)H NMR spectroscopy; the consequence of isomerizing the double bond is that the amide groups of the thread are held in positions such that they can hydrogen bond to only one of the two isophthalamide groups of the macrocycle. It is interesting to note that the energy barrier for the trans-rotaxane with four intercomponent hydrogen bonds (13.4 kcal mol\(^{-1}\)) is almost exactly twice the value for the cis-rotaxane with two intercomponent hydrogen bonds (~6.8 kcal mol\(^{-1}\)).
In order to obtain a more detailed understanding of the dynamic properties of these systems and, in particular, to confirm that the low energy dynamic process measured by NMR in the maleamide rotaxane was circumrotation, we carried out simulations of the dynamic processes present in both \( E \)- and \( Z \)-4.
Using a computational procedure which employs the MM3 forcefield(17) and the TINKER program(18), and has previously proved successful in describing the circumrotation pathway in catenanes(19), macrocycle pirouetting in rotaxanes(13) and other properties in mechanically-interlocked molecules(20, 21), it was possible to locate the saddle points for macrocycle circumrotation in $E$-4 and $Z$-4. Figure 4 shows the transition states, the arrows indicating the initial motion that macrocycle and thread would undergo away from the saddle point. The calculated activation energies (13.51 kcal mol$^{-1}$ for $E$-4 and 6.53 kcal mol$^{-1}$ for $Z$-4) compare well with the NMR determined $\Delta G$'s of 13.4±0.1 and 6.8±0.8 kcal mol$^{-1}$, respectively, and thus confirm that macrocycle pirouetting is probably a major contributor to the broadening of resonances observed in the low temperature NMR spectra of $Z$-4. The good agreement of calculations and experiments also allows one to take a closer look at the contributions of various kinds of interactions to the dynamic process of
pirouetting. Table 1 shows the different energy contributions to the $E$-4 and $Z$-4 minima and transition states. Interestingly, from the calculations the $\sim 7$ kcal mol$^{-1}$ difference between the activation barriers of circumrotation in the two molecules can be ascribed to contributions from all the energy components, not just H-bonding.

<table>
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<th>$E_v$</th>
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<th>$E_{\pi\text{-stacking}}$</th>
<th>$E_{vdW}$</th>
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<td>-13.75</td>
<td>-12.65</td>
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<td>(6.39)</td>
<td>(2.71)</td>
<td>(0.51)</td>
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<tr>
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<td>-30.97</td>
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<tr>
<td>$Z$-4$^b$</td>
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<td>-15.99</td>
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<td>-29.99</td>
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<td></td>
<td>(6.55)</td>
<td>(0.85)</td>
<td>(-1.84)</td>
<td>(0.98)</td>
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(a) energy minimum (b) transition state energy

Table 1. Molecular energy contributions (kcal mol$^{-1}$) divided into four components: (i) a valence term, $E_v$, which includes stretchings and in-plane and out-of-plane bendings, (ii) a hydrogen bond contribution, $E_{H\text{-bonding}}$, (iii) $\pi-\pi$ stacking energy, $E_{\pi\text{-stacking}}$, and (iv) the remaining van der Waals components, $E_{vdW}$. The energy differences between the minima and the transition states are given in parentheses.

Preliminary studies show that it is possible to reverse the photo-isomerization process thermally. Heating each of $Z$-4-6 ($C_2D_2Cl_4$ or $d_6$-DMSO, 400K, 4-7 days) resulted in re-conversion to the more thermodynamically stable $E$-rotaxanes in good-to-excellent (80-100%) yields. Other simple cis-trans olefin interconversion reactions are currently being investigated.$^{11}$

$^{11}$ Attempts to grow crystals of $Z$-6 resulted in significant yields of crystalline $E$-6 although no $E$-6 could be detected at any stage in solution! It appears that the
The post-assembly photoconversion of a precise hydrogen bond recognition rotaxane-forming template to a motif that does not template the formation of mechanical bonds is unprecedented. The resulting mis-match in recognition sites between macrocycle and thread dramatically reduces the energy barrier to macrocycle pirouetting in the rotaxane. Such control could be useful in the construction of future synthetic molecular machines that utilize large amplitude internal rotary motions.

growing crystal surface of E-6 is able to catalyse the cis-trans isomerization process. Such a phenomenon is not unprecedented (27).
Experimental Section


The rotaxanes $E$-$4$-$6$ (0.60 g) were dissolved in CH$_2$Cl$_2$ [except for solubility reasons $E$-$6$, MeOH/CHCl$_3$ (1/9)] in a quartz vessel. The solutions were directly irradiated at 254 nm using a multilamp photoreactor model MLU18 manufactured by Photochemical Reactors Ltd, Reading UK. The progress of photoisomerization was monitored by TLC (silica, CHCl$_3$/EtOAc 4:1) or $^1$H NMR. The different photostationary states were reached in a range of times not exceeding 30 min after which the reaction mixture was concentrated under reduced pressure to afford the crude products ($Z$-$4$-$6$). The unconverted tran$\text{s}$ isomers were isolated by triturating the solids with toluene/dichloromethane (1:1, ~20 mL) and, because the photoisomerization process produces few byproducts, could be recycled eventually leading to >90% conversion of each rotaxane to the corresponding cis-isomer. The solutions were then passed through a pad of silica (CHCl$_3$/EtOAc, 4:1) to afford the cis isomers $E$-$4$-$6$ in 50, 47 and 45% yields, respectively, from a single photoisomerization experiment.

Experimental procedures for the synthesis of $Z$-$5$, X-ray crystallography of $E$- and $Z$-$5$ and selected characterization data for $Z$-$5$ and $E$-$4$-$6$ are provided as Supporting Information.
References


Supporting Information

Photoisomerization of a Rotaxane Hydrogen Bonding Template: 
Light-induced Acceleration of a Large Amplitude Rotational Motion

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Preparation of thread (E)-N,N'-dimethyl-bis(2,2-diphenylethyl)-butendiamide (E-2).

To a stirred ice-cooled solution of bis-(2,2-diphenylethyl) fumaramide (1g, 2.10 mmol) in dry THF (20 mL) under nitrogen was added NaH (0.2 g, 60% dispersion in oil, excess) portion-wise under nitrogen. After the effervescence had subsided, methyl iodide (0.3 mL, excess) was added in one portion. The reaction was allowed to warm to room temperature and stirred overnight and water (20 mL) and ammonia solution (10 mL) added drop-wise to quench the reaction. Most of the solvent was removed under reduced pressure, and the remainder partitioned between water and CH₂Cl₂ (3 x 20 mL). The organic extracts were washed with sodium hydroxide (1N, 20 mL) and dried over anhydrous magnesium sulfate. The filtered solution was concentrated under reduced pressure to give an oil that slowly solidified. Recrystallization from CH₂Cl₂/diisopropyl ether afforded colorless needles (E-2, 0.87g, 83%); m.p. 134-136°C; ¹H NMR (400 MHz, C₂D₂Cl₄ at 363K): δ = 7.34-7.19 (m, 20H, ArCH), 6.99 (s, 2H, CH₆ₐ), 4.37 (t, 3J(H,H) = 8.8 Hz, 2H, CH₆), 4.04 (d, 3J(H,H) = 8.8 Hz, 4H, CH₆), 2.79 (s, 6H, CH₃); ¹³C NMR (100 MHz, C₂D₂Cl₄ at 393K): δ = 166.7, 143.0, 132.1, 129.7, 128.9, 127.2, 55.5, 51.0, 37.5; MS (FAB, mNBA): m/z = 502 [(M+H)+]; Anal. Calcd. for C₃₄H₃₄N₂O₂: C 81.24, H 6.82, N 5.57. Found: C 81.61, H 6.68, N 5.43.

The threads $E$-1-3 (1.00 mmol) and Et$_3$N (2.1 mL, 15.7 mmol) were dissolved in CHCl$_3$ (100 mL) or, in the case of $E$-3, 1/9 CH$_3$CN/CHCl$_3$, and stirred vigorously whilst solutions of the diamine (1.09 g, 4 equivs.) in CHCl$_3$ (45 mL) and the acid chloride (1.62 g, 4 equivs.) in CHCl$_3$ (45 mL) were simultaneously added over a period of 2 hours using motor-driven syringe pumps. After a further two hours the resulting suspension was filtered and concentrated under reduced pressure. The rotaxanes $E$-4 and $E$-5 were purified by trituration of the respective solids in CH$_2$Cl$_2$ (to remove the polar impurities - catenane, macrocycles, Et$_3$HN$^+$Cl$^-$ etc), and subsequently separating the rotaxane from unreacted thread through trituration in hot toluene. Rotaxane $E$-6 was obtained by spontaneous crystallization from the reaction mixture as previously described.$^{15}$
Selected data for ([2](1,7,14,20-tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-((E)-N,N'-(dimethyl)-bis[2',2'-diphenylethyl]-butendiamide)-rotaxane (E-5): 

(E-5, 0.34 g, 33%); m.p. 320-323°C; $^1$H NMR (400 MHz, $d_6$-DMSO at 403K): $\delta =$ 8.51 (br s, 2H, ArCH$_c$), 8.09 (dd, $^3$J(H,H) = 7.8 Hz, 4H, ArCH$_b$), 7.78 (br t, 4H, NH$_d$), 7.60 (t, $^3$J(H,H) = 7.8 Hz, 2H, ArCH$_A$), 7.35-7.11 (m, 20H, ArCH), 6.96 (s, 8H, ArCH$_E$), 5.92 (br s, 2H, CH$_A$), 4.40 (br d, $^3$J(H,H) = 5.4 Hz, 8H, CH$_E$), 4.26 (br t, 2H, CH$_A$), 3.91 (br d, 4H, CH$_c$), $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 166.9-166.0, 142.9, 138.9, 134.9, 129.3-127.6, 125.1, 53.9-53.1, 49.8, 44.6-44.1, 36.3-36.1; FAB-MS (mNBA matrix): m/z = 1036 [(M+H$^+$)]; Anal. Calcd. for C$_{65}$H$_{62}$N$_6$O$_6$: C 76.57, H 6.04, N 8.12. Found: C 76.88, H 6.20, N 8.30.

The rotaxanes \textit{E-4-6} (0.60 g) were dissolved in CH$_2$Cl$_2$ [except for solubility reasons \textit{E-6}, MeOH/CHCl$_3$ (1/9)] in a quartz vessel. The solutions were directly irradiated at 254 nm using a multilamp photoreactor model MLU18 manufactured by Photochemical Reactors Ltd, Reading UK. The progress of photoisomerization was monitored by TLC (silica, CHCl$_3$/EtOAc 4/1) or $^1$H NMR. The different photostationary states were reached in a range of times not exceeding 30 mins after which the reaction mixture was concentrated under reduced pressure to afford the crude products (Z-4-6). The unconverted \textit{trans} isomers were isolated by triturating the solids with PhMe/CH$_2$Cl$_2$ (1:1, ~20 mL) and, because the photoisomerization process produces few byproducts, could be recycled eventually leading to >90% conversion of each rotaxane to the corresponding \textit{cis}-isomer. The solutions were then passed through a pad of silica (CHCl$_3$/EtOAc 4:1) to afford the \textit{cis} isomers \textit{E-4-6} in 50, 47 and 45% yields, respectively, from a single photoisomerization experiment.

(Z-4, 0.3 g, 50%); m.p. 243-244°C; $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta = 8.92$ (dd, 4J(H,H) = 1.7 Hz, 3J(H,H) = 7.8 Hz, 4H, ArCH$_B$), 7.60 (t, 4J(H,H) = 1.7 Hz, 2H, ArCH$_C$), 7.40 (t, 3J(H,H) = 7.8 Hz, 2H, ArCH$_A$), 7.30 (t, 3J(H,H) = 5.1 Hz, 4H, NH$_D$), 7.23-7.11 (m, 20H, ArCH), 7.03 (s, 8H, ArCH$_F$), 4.89 (s, 4H, CH$_{b2}$), 4.83 (s, 2H, CH$_d$), 4.78 (s, 4H, CH$_{b1}$), 4.36 (s, 3J(H,H) = 5.1 Hz, 8H, CH$_E$), 3.63 (s, 4H, CH$_{a2}$), 3.58 (s, 4H, CH$_{a1}$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.4, 167.6, 166.6, 166.2, 137.3, 135.9, 134.5, 134.4, 132.5, 129.9-128.6, 123.4, 68.8, 68.3, 50.9, 50.6; LSIMS, $m/z = 1239 [(M+H)^+]$, 1262 [(M+Na)$^+$]. Anal. Calcd. for C$_{72}$H$_{66}$N$_6$O$_{14}$: C 69.78, H 5.37, N 6.78. Found: C 69.56, H 5.32, N 6.68.
Selected data for [(1)(7,14,20-tetraaza-2,6,15,19-tetraoxo-5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-((Z)-N,N'-((dimethyl)s{2',2'-diphenylethyl}-
butendiamide)-rotaxane (Z-5):

\[(Z-5, 0.28 \text{ g, 47%}); \text{ m.p. } > 300 \degree \text{C (decompose)}; ^1\text{H NMR (400 MHz, } \text{C}_2\text{D}_2\text{Cl}_4 \text{ at 403K): } \delta = 8.13 \text{ (dd, } ^3\text{J(H,H) = 7.8 Hz, 4H, ArCH}_B\text{)}, 7.91 \text{ (br s, 2H, ArCH}_A\text{)}, 7.63 \text{ (t, } ^3\text{J(H,H) = 7.8 Hz, 2H, ArCH}_A\text{)}, 7.35-7.11 \text{ (m, 24H, ArCH + NH}_D\text{)}, 6.98 \text{ (s, 8H, ArCH}_E\text{)}, 4.92 \text{ (br s, 2H, } \text{CH}_D\text{)}, 4.40 \text{ (br d, } ^3\text{J(H,H) = 5.4 Hz, 8H, CH}_E\text{)}, 4.07 \text{ (b t, 2H, CH}_A\text{)}, 3.51 \text{ (br d, 4H, CH}_B\text{)}, 2.21 \text{ (s, 6H, CH}_D\text{); } ^13\text{C NMR (100 MHz, } \text{CDCl}_3): \delta = 166.9-166.0, 142.9, 138.2, 134.9, 129.3-127.6, 125.1, 53.9-53.1, 49.8, 44.6-44.1, 36.3-36.1; \text{ FAB-MS (mNBA matrix): } m/z = 1036 \text{ [(M+H)\text{]}]; Anal. Calcd. for } C_{66}H_{62}N_{10}O_6: C 76.57, H 6.04, N 8.12. \text{ Found: C 76.98, H 6.30, N 8.23.} \]
Selected data for ([2](1,7,14,20-tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-((Z)-N,N’-(dimethyl)-bis{2’,2’-diphenylethyl}-butendiamide)-rotaxane (Z-6):

(Z-6, 0.27 g, 45%); m.p. >300 °C (decompose); $^1$H NMR (400 MHz, CDC$_3$) $\delta =$ 8.22 (d, $^3$J$_{H,H}$ = 7.8 Hz, 4H, ArCH$_{B}$), 8.13 (s, 2H, ArCH$_{C}$), 7.73 (t, $^3$J$_{H,H}$ = 5.4 Hz, 4H, NH$_D$), 7.62 (t, $^3$J$_{H,H}$ = 7.8 Hz, 2H, ArCH$_{A}$), 7.27-7.11 (m, 18H, ArCH + NH), 6.98 (d, $^3$J$_{H,H}$ = 7.5 Hz, 4H, ArCH), 6.83 (s, 8H, ArCH$_F$), 5.11 (s, 2H, CH$_D$), 4.38 (d, $^3$J$_{H,H}$ = 5.4 Hz, 8H, CH$_E$), 3.87 (t, 2H, CH$_{A'}$), 3.41 (d, 4H, CH$_B$); $^{13}$C NMR (100 MHz, CDC$_3$): $\delta =$ 166.8, 165.5, 141.8, 137.4, 134.3, 131.9, 131.2, 129.9, 129.3, 129.2, 128.0, 127.5, 124.8, 50.3, 44.9, 44.8; MS (FAB, mNBA): $m/z =$ 1029 [(M+Na)$^+$]. Anal. Calcd. for C$_{64}$H$_{58}$N$_6$O$_6$: C 76.32, H 5.80, N 8.34. Found: C 76.39, H 5.91, N 8.19.
X-Ray Crystallographic Structure Determinations:

E-5: C₆₄H₈₈N₆O₆, \( M = 1039.22 \), crystal size \( 0.18 \times 0.04 \times 0.02 \) mm, triclinic P-1, \( a = 13.4337(13), b = 16.2778(16), c = 29.964(3) \) Å, \( \alpha = 75.716(2), \beta = 87.934(2), \gamma = 71.880(2) \)°, \( V = 6028.9(10) \) Å³, \( Z = 4 \), \( \rho_{\text{calcld}} = 1.145 \) Mg m⁻³; synchrotron radiation (CLRC Daresbury Laboratory Station 9.8, silicon monochromator, \( \lambda = 0.69290 \) Å), \( \mu = 0.107 \) mm⁻¹, \( T = 150(2) \) K. 23260 data (12003 unique, \( R_{\text{int}} = 0.0466, 1.73 < \theta < 20.00 \)°), were collected on a Siemens SMART CCD diffractometer using narrow frames (0.3° in \( \omega \)), and were corrected semi-empirically for absorption and incident beam decay (transmission 0.20-1.00). The structure was solved with SIR97 (Altomare A., Burla M.C., Camalli M., Cascarano G.L., Giacovazzo C., Guagliardi A., Moliterni A.G.G., Polidori G., Spagna R. J. Appl. Cryst. 32, 115-119 (1999)) and refined by full-matrix least-squares on \( F^2 \) values of all data (G.M.Sheldrick, SHELXTL manual, Siemens Analytical X-ray Instruments, Madison WI, USA, 1994, version 5) to give \( wR = \left( \frac{\sum w(F_o^2 - F_c^2)^2}{\sum w(F_o^2)} \right)^{1/2} = 0.2771 \), conventional \( R = 0.0952 \) for \( F \) values of 12003 reflections with \( F_o^2 > 2\sigma(F_o^2) \), \( S = 1.050 \) for 1480 parameters. Residual electron density extremes were 1.093 and -0.420 Å⁻³.

Z-5: C₆₆H₆₂N₆O₆, \( M = 1035.22 \), crystal size 0.30×0.14×0.08 mm, monoclinic, P2₁/c, \( a = 10.5696(3), b = 27.7157(9), c = 10.7503(3) \) Å, \( \beta = 115.2530(10), V = 2848.27(15) \) Å³, \( Z = 2 \), \( \rho_{\text{calcld}} = 1.207 \) Mg m⁻³; MoKα radiation (graphite monochromator, \( \lambda = 0.71073 \) Å), \( \mu = 0.078 \) mm⁻¹, \( T = 293(2) \) K. 13437 data (4049 unique, \( R_{\text{int}} = 0.1701, 1.47 < \theta < 23.29 \)°), were collected on a Siemens SMART CCD diffractometer using narrow frames (0.3° in \( \omega \)), and were corrected semi-empirically for absorption and
incident beam decay (transmission 0.20-1.00). The structure was solved by direct methods and refined by full-matrix least-squares on $F^2$ values of all data (G.M. Sheldrick, SHELXTL manual, Siemens Analytical X-ray Instruments, Madison WI, USA, 1994, version 5) to give $wR = \{ \Sigma [w(F_o^2 - F_c^2)^2] / \Sigma [w(F_o^2)^2] \}^{1/2} = 0.2136$, conventional $R = 0.0811$ for $F$ values of 4049 reflections with $F_o^2 > 2\sigma(F_o^2)$, $S = 0.754$ for 361 parameters. Residual electron density extremes were 0.355 and -0.337 Å$^{-3}$. Amide hydrogen atoms were refined isotropically subject to a distance constraint N-H = 0.98 Å, with the remainder constrained; anisotropic displacement parameters were used for all non-hydrogen atoms.

Crystallographic data for $E$-5 and $Z$-5 (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-149672 and 149673 ($E$-5 and $Z$-5). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: teched@chemcrys.cam.ac.uk).
The Effect of Olefin Stereochemistry on Amide Bond Rotamerization in E/Z-4.

The energy barrier for amide bond rotamerization in tertiary amide rotaxanes increases if intercomponent hydrogen bonding occurs to stabilise the R₂N⁺=C-O⁻ resonance contribution of the tertiary amide group [W. Clegg, C. Gimenez-Saiz, D. A. Leigh, A. Murphy, A. M. Z. Slawin, S. J. Teat, J. Am. Chem. Soc., 1999, 121, 4124-4129]. In Fig. 2a, slow amide bond rotamerization is responsible for the magnetically distinct environments observed for Hₐ₁ and Hₐ₂ (and H₉₁/H₉₂). Even though the coalescence temperature for their interconversion cannot be reached in C₂D₂Cl₄, their exchange rate can be measured directly by SPT-SIR and gives an energy barrier of 21.1 kcal mol⁻¹ at 383K (cf. 17.2 kcal mol⁻¹ at 383K for rotamerization in the trans thread, obtained by ¹H line shape analysis). In contrast, it is clear from the broadening of the Hₐ₁/Hₐ₂ resonances in Fig. 2b that the same process is occurring with a lower energy barrier in the cis-rotaxane. Indeed, ¹³C line shape analysis (¹H line shape analysis was not possible because the diastereotopic methylene protons in the cis thread are accidentally isochronous) experiments give the energy barrier of 20.0 kcal mol⁻¹ for Z-4 at 383K (cf. 17.4 kcal mol⁻¹ at 383K for rotamerization of the cis thread).
References


Chapter 4

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Remarkable Positional Discrimination in Bistable, Light and Heat-Switchable, Hydrogen Bonded Molecular Shuttles[**]

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**Keywords:** photoinduced isomerization, rotaxanes, molecular shuttles, molecular machines.
Stimuli-responsive molecular ‘shuttles’, mechanically interlocked molecules where a macrocycle can be translocated between different sites in response to an external signal, all operate through the same basic principle. The external stimulus does not induce directional motion of the macrocycle per se, rather it alters the equilibrium between different translational co-conformers (a Boltzmann distribution determined by the difference in binding affinities of the macrocycle for the two sites at a given temperature), either by increasing the binding strength of the less populated station or destabilizing the initially preferred binding site. The motion of the components arises from the background thermal energy, the net result being a change in the position of the macrocycle through biased Brownian motion (Figure 1).

**Figure 1.** Macrocycle translation in a rotaxane-based stimuli-responsive molecular shuttle. Stimulus A induces a blue-to-green transformation, stimulus B a green-to-blue transformation. The equilibrium distribution of the macrocycle between two stations is determined by the difference in their binding energies and the temperature.
Trying to design synthetic systems where photons initiate such processes is fraught with technical difficulties. It took more than 15 years to develop light-mediated shuttles from transition metal-coordinated interlocked molecules and over a decade from paraquat-based systems. A major problem is finding a way of generating sufficiently large, long lived, binding energy differences between the two positional isomers by modifying only non-covalent – i.e. intrinsically weak - binding modes. One solution is to use photochemistry to sterically block what are essentially ‘one station’ rotaxanes, systems where the macrocycle is only able to sit on an azobenzene or stilbene unit in the $E$- diastereomer of the rotaxane and so must reside elsewhere in the $Z$-form. Another is to compromise on the timescales involved; the binding strength of poorly hydrogen bonding groups can be dramatically increased by photo-production of an excited state if it is a better hydrogen bonding motif than the ground state or can be chemically reduced to one. However, such processes are transient (or require a sacrificial chemical reductant) and in the rotaxanes described to date the macrocycle returns to its original position over millisecond and nanosecond timescales, respectively. Here we describe a new class of hydrogen bonded shuttles (1-3) where each translational form is stable until a particular stimulus is applied. The macrocycle moves over a relatively large distance (~1.5 nm) between two discrete stations with almost complete positional integrity (even at room temperature), despite the fact that the discrimination between the binding sites is caused only by ‘matched’ and ‘mis-matched’ hydrogen bonding motifs.
The basis for this bistable shuttling mechanism lies in the photochemical and thermal interconversion of fumaramide and maleamide groups. The trans-olefin bis-amide acts as an excellent template for the formation of benzylic amide macrocycle-based rotaxanes (e.g. E-4) because the amide groups of the thread are rigidly held in positions that fit the hydrogen bond-donating sites of the forming macrocycle (an arrangement maintained even in crystals of E-4 obtained from DMSO, Figure 2a). Somewhat remarkably however, given the tight encapsulated binding site and that only the trans-olefin has hydrogen bonding sites complementary to the macrocycle, photoisomerization (254 nm, CHCl₃/MeOH (9/1), 30 min, 45%) of a fumaramide rotaxane produces the corresponding maleamide rotaxane in which the numbers of intercomponent hydrogen bonds is reduced from four to two (Figure 2b), considerably reducing the strength of binding between thread and macrocycle[¹H NMR experiments show that the macrocycle spins >10^6 times faster in the Z-form of the rotaxane than the E-form in CD₂Cl₂ at 233K!]. By incorporating a second binding site ('station') into the thread, of macrocycle binding affinity in between those of the fumaramide and maleamide groups, we reasoned it should be possible to generate photoinduced, thermally reversible, translation of the macrocycle along the thread.
Figure 2. X-ray structures of model single binding site [2]rotaxanes showing hydrogen bonding characteristics of predicted (a) 'strong', (b) 'weak', and (c)-(g) 'intermediate strength' hydrogen bonding stations. (a) fumaramide rotaxane E-4 crystallized from DMSO; (b) \( \text{N}_2\text{N}'\)-dimethyl derivative of the corresponding maleamide (Z) rotaxane; (c) succinamide analogue of E-4; (d) glucosamide analogue of E-4; (e) succinic amide ester analogue of E-4; (f) \( \text{N}_2\text{N}'\)-dimethyl derivative of E-4; (g) \( \text{N}_2\text{N}'\)-diphenyl analogue of E-4. Intramolecular hydrogen bond distances and angles: (a) \( \text{O}40\text{H}-\text{N}2/\text{O}40\text{A}-\text{H}N2\text{A} \) 2.13 Å, 173.7 °; \( \text{O}40\text{H}-\text{H}N2/\text{O}40\text{A}-\text{H}N1\text{A} \) 1.89 Å, 169.3 °; (b) \( \text{O}40\text{H}-\text{N}1\text{A} \) 2.08 Å, 139.3 °; \( \text{O}43\text{H}-\text{N}2 \) 2.00 Å, 142.1 °; (c) \( \text{O}40\text{H}-\text{O}43\text{H}-\text{N}20 \) 1.88 Å, 165.3 °; (d) \( \text{O}40\text{H}-\text{N}45\text{H}-\text{N}28 \) 2.00 Å, 168.8 °; (e) \( \text{O}40\text{H}-\text{O}43\text{H}-\text{N}29 \) 1.89 Å, 156.1 °; (f) \( \text{O}40\text{H}-\text{O}43\text{H}-\text{N}20 \) 2.22 Å, 157.4 °; \( \text{O}40\text{H}-\text{O}11\text{H}-\text{O}43\text{H}-\text{N}29 \) 1.94 Å, 154.8 °; (g) \( \text{O}38\text{H}-\text{O}41\text{H}-\text{N}20 \) 2.21 Å, 152.9 °; \( \text{O}38\text{H}-\text{O}41\text{H}-\text{N}29 \) 2.43 Å, 152.9 °. For clarity the carbon atoms of the macrocycles are shown in blue and the carbon atoms of the threads in yellow; oxygen atoms are red, nitrogen atoms dark blue and selected hydrogen atoms white. \( \uparrow \) stoppers = \( \text{CH}_2\text{CHPh}_2 \); \( \downarrow \) stoppers = \( \text{CH}_3\text{Ph} \).
The design of a non-photoactive second station which would be sufficiently different in binding affinity to both the fumaramide and maleamide groups to produce discrete translational isomerism in both states requires subtle choices. Too strong a binding site would cause poor positional discrimination in the fumaramide form of the shuttle; too weak would lead to the same problem in the maleamide isomer. Since the transition state of the rotaxane-forming reaction is similar in structure to the final rotaxane, it seemed likely that the binding affinity of a given station for the macrocycle should be closely related to its ability to template the formation of the rotaxane. Several factors affect both the template efficacy and the nature of the intercomponent hydrogen bonding interactions (NH-O-C distances, angles etc) including; the hydrogen bond basicity of the functional groups (e.g. amides are better than esters), preorganisation (e.g. fumaramide is better than succinamide), distance between the binding sites (succinamide better than adipamide), steric hinderance (fumaramide better than N,N-dimethylfumaramide), and the presence of additional noncovalent binding interactions (N,N-diphenylfumaramide better than N,N-dimethylfumaramide).

We prepared a series of three molecular shuttles (1-3, Scheme 1), each containing a fumaramide/maleamide site plus a non-photoactive second station of predicted intermediate macrocycle binding affinity. Where the solid state hydrogen bonding characteristics of the stations were not known (1 and 3) we also prepared the model 'one station' [2]rotaxanes and determined their structures by X-ray crystallography.
(Figure 2). The synthetic routes to 1-3 are worthy of note: Although E-1 was prepared from the corresponding thread, E-5, in good yield (CHCl₃/CH₃CN (9/1), Et₃N, RT, 4 h, 57%), the other E-threads were insufficiently insoluble in non-hydrogen bond-disrupting solvents to be used in this way. Therefore rotaxanes 2 and 3 were prepared from the corresponding Z-threads (CHCl₃, Et₃N, RT, 4 h, 40 and 20%, respectively, the lower yields a consequence of the lack of a fumaramide template in the thread) and the Z-rotaxanes converted to the E-isomers thermally (120 °C, 7 days, C₂H₂Cl₄, 80%). Pleasingly, in fact, the E-isomers of each molecular shuttle could be converted to the Z-form with light (E→Z, direct radiation at 254 nm, CH₂Cl₂, 30 min, 39-54% or with catalytic benzophenone sensitizer at 350 nm, CH₂Cl₂, 5 min, 60-65%) and the Z-forms converted to the corresponding E-isomers with heat (as described above, 80% E-1) or reversible Michael addition (catalytic ethylenediamine, 60 °C, 4 h, 75-85%).
Scheme 1. Synthesis of bistable molecular shuttles 1-3. (i) succinic anhydride, Et₃N, CH₂Cl₂, 90%. (ii) H₂N(CH₂)₅NHBOc, 4-dimethylaminopyridine (DMAP), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI.HCl), CH₂Cl₂, 68%. (iii) trifluoroacetic acid, CHCl₃, quantitative. (iv) fumaric acid monoethyl ester, DMAP, EDCI.HCl, CH₂Cl₂, 85%. (v) NaOH in H₂O, EtOH, 91%. (vi) DMAP, EDCI.HCl, DMF, E-5, 76%. (vii) isophthaloyl dichloride, p-xylene diamine, Et₃N, CHCl₃, E-1, 57%. (viii) hv at 254 nm for 30 min., CH₂Cl₂, E-1, 54%; E-2, 48%; E-3, 39%. (ix) C₂H₂Cl₄ at 120 °C for 7 days, Z-1, 80%; Z-2, 80%; Z-3, 80%. (x) maleic anhydride, anhydrous THF, 75%. (xi) succinic anhydride, anhydrous THF, 95%. (xii) SOCl₂, 1,12 diaminododecane, CH₂Cl₂, 35%. (xiii) adipic acid monoethyl ester, DMAP, EDCI.HCl, CH₂Cl₂, 86%. (xiv) KOH in H₂O, EtOH, 95%. (xv) H₂N(CH₂)₁₂NHBOc, DMAP, EDCI.HCl, CHCl₃, 92%. (xvi) trifluoroacetic acid, CHCl₃, quantitative. (xvii) DMAP, EDCI.HCl, CHCl₃, Z-5, 70%; Z-6, 70%; Z-7, 70%; (xviii) isophthaloyl dichloride, p-xylene diamine, Et₃N, CHCl₃, Z-1, 2%; Z-2, 40% and Z-3, 20%. Full experimental procedures can be found in Supporting Information.
Since the xylylene rings of the macrocycle shield encapsulated regions of the thread, for each pair of rotaxane diastereomers the position of the macrocycle in CDCl₃ could be determined by comparing the chemical shift of the protons of each station in the rotaxane with those of the corresponding thread (or suitable model compounds in the case of E-2 and E-3). The spectra of E/Z-1 and E/Z-5 in CDCl₃ (400 MHz, 298K, Figure 3 and 4) show that, remarkably, the macrocycle is held by hydrogen bonding over a particular station with almost complete positional integrity in each rotaxane diastereomer even at room temperature! The H₁ and H₂ protons of the fumaramide group are shielded in the rotaxane E-1 compared to the thread E-5 by 1.09 and 1.02 ppm, respectively, whereas the chemical shifts of the H₃ and H₄ protons of the succinamide group are identical in both compounds (Figure 3). Furthermore, the H₄ and H₅ fumaramide amide protons are deshielded by ~1.7 ppm in the rotaxane, indicating their involvement in hydrogen bonding to the macrocycle in some co-conformers of E-1. The slight downshift of H₆ is probably a result of intramolecular hydrogen bonding indicating some folding in the E-rotaxane.
Figure 3. 400 MHz $^1$H NMR spectra of (a) thread $E$-5 and (b) rotaxane $E$-1 in CDCl$_3$ at 298K. The assignments correspond to the lettering shown in Scheme 1.
The $^1$H NMR spectra in Figure 4 show that the position of the macrocycle on the thread is completely reversed in the maleamide isomer. The Z-olefin protons ($H_{1'}$ and $H_{1''}$) occur at almost identical chemical shifts in the rotaxane and thread, whereas the succinamide methylene groups ($H_c$ and $H_d$, located by $C,H$ correlation experiments) are each shielded by $>1.3$ ppm.

A similar series of shifts occurs in the $^1$H NMR spectra of the other molecular shuttle diastereomer pairs, although the alternative second stations (which are both better templates for rotaxane formation) compete with the fumaramide station for the macrocycle more effectively than the succinic amide-ester group. From the relative
chemical shift differences the discrimination of the macrocycle for the different 
stations in CDCl₃ is remarkable, even at 298K.

20:1 (E-1) → <1:40* (Z-1); [* limit of the NMR method];

~12:1 (E-2) → <1:40* (Z-2);

20:1 (E-3) → ~1:8 (Z-3).

It is interesting to note that our estimates of relative station binding affinities from 
either rotaxane yield or hydrogen bond distances/angles are not completely accurate.
The maleamide station is significantly populated with the macrocycle in Z-3 (Figure 
5) yet the same station does not compete at all with the succinic amide ester site in Z-
1 (Figure 4), even though the yields and X-ray structure suggest the adipamide group
should be the better station.
Overall the discrimination for the macrocycle for the different stations is excellent and, at temperatures which require substantial energy differences to significantly bias the population 8 distribution, somewhat remarkable (most notably between the fumaramide and succinamide stations in E-2 which offer virtually identical hydrogen bonding surfaces to the macrocycle). To probe this further, molecular modelling\cite{16,17,21,24} was carried out by simulated annealing followed by geometrical optimization using the TINKER program with the MM3 forcefield. The difference in co-conformer stability for each pair of rotaxane diastereomers was calculated by
comparing the energies (including zero point energies) of the occupied and unoccupied stations in each coconformer to give: $\Delta A G = 3.6$ kcal mol$^{-1}$ (fumaramide cf. succinic amide ester occupancy) in $E-1$; $\Delta A G = 2.9$ kcal mol$^{-1}$ (succinic amide ester cf. maleamide occupancy) in $Z-1$; $\Delta A G = 3.6$ kcal mol$^{-1}$ (fumaramide cf. succinamide occupancy) in $E-2$; $\Delta A G = 3.0$ kcal mol$^{-1}$ (succinamide cf. maleamide occupancy) in $Z-2$; $\Delta A G = 3.9$ kcal mol$^{-1}$ (fumaramide cf. adipamide occupancy) in $E-3$; $\Delta A G = 3.1$ kcal mol$^{-1}$ (adipamide cf. maleamide occupancy) in $Z-3$. Whilst in each case there is probably overbinding as a result of solvation and folding not being included in the model, the calculations are broadly in line with the experimental results (i.e. $\Delta A G$'s $\geq 2$ kcal mol$^{-1}$), although at this level they do not reproduce the anomalously poor binding of the adipamide station in $Z-3(20)$. However, the calculations do offer a simple explanation for why the positional discrimination is so good in these rotaxane systems: when it's not occupied, each station – except fumaramide – can intramolecularly hydrogen bond to itself and so the positional isomer which has that station occupied has at least one hydrogen bond less than the positional isomer with the fumaramide station occupied (Figure 6). The use of 'self-binding' to compensate for the lack of station occupancy could prove a useful concept for driving submolecular motion in molecular machines that rely only on weak, noncovalent, interactions.

![Figure 6](image)

**Figure 6.** Translational isomerism in fumaramide-succinamide shuttle $E-2$. 163
Keywords: photoinduced isomerization, rotaxanes, molecular shuttles, molecular machines.

References


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Supporting Information

*Synthesis and X-ray structure determinations of molecular shuttles 1-3 and [2]rotaxane model compounds for the various individual binding stations*

**Remarkable Positional Discrimination in Bistable, Light and Heat-Switchable, Hydrogen Bonded Molecular Shuttes**

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Details of X-Ray Crystal Structure Determination: Crystallographic data for E-4, S2, S4 and S7 (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-157383 and 157381. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: teched@chemcrys.cam.ac.uk).

General procedure for the preparation of benzylic amide macrocycle containing [2]rotaxanes and shuttles
The thread (1 equiv.) and Et₃N (24 equiv.) in anhydrous CHCl₃ [or for E-4 and E-1, CH₃CN/CHCl₃ (1/9)] (100 mL) were stirred vigorously whilst solutions of para-xylylene diamine (12 equiv.) in anhydrous CHCl₃ (40 mL) and isophthaloyl dichloride (12 equiv.) in anhydrous CHCl₃ (40 mL) were simultaneously added over a period of 2 h using motor-driven syringe pumps. After a further 2 h the resulting suspension was filtered and the solvent removed under reduced pressure. The resulting solid was subjected to column chromatography (silica gel) to yield, typically, unconsumed thread, [2]rotaxane, [2]catenane and, in some cases, [3]rotaxane.

General procedure for the photoisomerization of fumaramide derivatives:
The fumaramide derivative (0.05 mmol) was dissolved in CH₂Cl₂ (30 mL) [except for solubility reasons E-4 and S7, MeOH/CHCl₃ (1/9)] in a quartz vessel. The solution was directly irradiated at 254 nm using a multilamp photo-reactor. The
progress of the photoisomerization was monitored by TLC [CHCl₃/EtOAc (4/1)] or ¹H NMR. Different photostationary states were reached in a range of times not exceeding 30 min, after which the reaction mixture was concentrated under reduced pressure to afford the crude product.

General procedure for the thermal-isomerization of maleamide derivatives:
The maleamide derivative (0.02 mmol) was dissolved in C₂D₂Cl₄ or d₆-DMSO and heated at 400K for 4-7 days, resulting in the conversion to the more thermodynamically stable fumaramide derivative in good-to-excellent (80-100%) yields as indicated by ¹H NMR.
Rotaxane $E$-1 was obtained using the general procedure for the preparation of benzylic amide macrocycle containing [2]rotaxanes using thread $E$-5 (0.19 g, 0.25 mmol). The crude material was subjected to column chromatography on silica gel using a gradient of CH$_2$Cl$_2$ to CH$_2$Cl$_2$/EtOAc (80/20) as eluent to obtain the desired compound as a colourless powder ($E$-1, 0.19 g, 57%).

Rotaxane $E$-1 was also obtained using the general procedure for the thermal-isomerization from compound $Z$-1 (70%, C$_{21}$H$_{42}$O$_4$). mp 186-187 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.31$ (br t, $^4J$(H$_c$,H$_b$) = 1.2 Hz, 2H, ArH$_c$), 8.08 (dd, $^3J$(H$_b$,H$_a$) =
7.8 Hz, $^4 J(H_B,H_C) = 1.2$ Hz, $4J(H, NH_B)$, $7.68$ (br t, $^3 J(H,H) = 5.4$ Hz, $4H$, NH$_D$), $7.60$ (br t, $^3 J(H,H) = 5.7$ Hz, $1H$, NH$_B$), $7.56$ (t, $^3 J(H_A,H_B) = 7.8$ Hz, $2H$, ArH$_A$), $7.45$ (br t, $^3 J(H,H) = 5.7$ Hz, $1H$, NH$_D$), $7.31-7.14$ (m, $20H$, ArH), $6.95$ (s, $8H$, ArH$_F$), $5.86$ (br t, $^3 J(H,H) = 5.7$ Hz, $1H$, NH$_D$), $5.77$ (d, $^3 J(H,H) = 14.8$ Hz, $1H$, CH$_i$ or CH$_j$), $5.69$ (d, $^3 J(H,H) = 14.8$ Hz, $1H$, CH$_i$ or CH$_j$), $4.59$ (d, $^3 J(H,H) = 7.7$ Hz, $2H$, CH$_b$), $4.42$ (br d, $^3 J(H,H) = 5.4$ Hz, $8H$, CH$_E$), $4.32$ (t, $^3 J(H,H) = 7.7$ Hz, $1H$, CH$_a$), $4.24$ (t, $^3 J(H,H) = 8.0$ Hz, $1H$, CH$_m$), $3.84$ (dd, $^3 J(H,H) = 8.0$ Hz, $^3 J(H,H) = 5.8$ Hz, $2H$, CH$_b$), $3.17-3.07$ (m, $4H$, H$_f$ and CH$_g$), $2.47$ (br t, $^3 J(H,H) = 7.0$ Hz, $2H$, CH$_d$), $2.23$ (br t, $^3 J(H,H) = 7.0$ Hz, $2H$, CH$_d$), $1.51-1.36$ (m, $4H$, -CH$_2$-CH$_f$ and -CH$_2$-CH$_g$) and $1.31-1.10$ (m, $16H$, -CH$_2$- (alkyl chain)); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 173.0$ (-CO-O (succinic)), $171.3$ (-CO-NH (succinic)), $166.6$ (4C, -CO- (macrocycle)), $165.5$ (-CO- (fumaric)), $165.2$ (-CO- (fumaric)), $141.4$ (2C, ArC-CH (ipso thread)), $141.0$ (2C, ArC-CH (ipso thread)), $137.0$ (4C, ArC-CH$_2$NH-), $134.6$ (4C, ArC-CO-), $131.3$ (4C, C$_b$), $130.3$ (C$_i$ or C$_j$), $129.8$ (C$_j$ or C$_i$), $129.1$ (2C, C$_A$), $129.0$ (8C, C$_F$), $128.9$ (4C, ArCH (meta thread)), $128.6$ (4C, ArCH (meta thread)), $128.2$ (4C, ArCH (ortho thread)), $127.8$ (4C, ArCH (ortho thread)), $127.2$ (2C, ArCH (para thread)), $126.8$ (2C, ArCH (para thread)), $124.5$ (2C, C$_C$), $67.0$ (C$_a$), $50.3$ (C$_a$), $49.8$ (C$_m$), $44.8$ (C$_i$), $44.2$ (4C, C$_E$), $40.1$ (C$_r$ or C$_g$), $39.6$ (C$_g$ or C$_r$), $30.8$ (-CH$_2$-), $29.6$ (-CH$_2$-), $29.5$ (-CH$_2$-), $29.3$ (-CH$_2$-), $29.1$ (-CH$_2$-), $26.9$ (-CH$_2$-), $26.8$ (-CH$_2$-); MS (FAB): $m/z = 1290$ [(M + H)$^+$]; Anal. calcd for C$_{80}$H$_{87}$N$_7$O$_9$: C 74.45, H 6.79, N 7.60. Found C 74.53, H 6.92, N 7.66.

Rotaxane $E$-2 was obtained using the general procedure for thermal-isomerization from rotaxane $Z$-2 (80%, C$_2$D$_2$Cl$_4$, isolated by preparative TLC on silica gel).

mp 186-187°C. $^1$H NMR (400 MHz, CDCl$_3$, 320K): $\delta = 8.39$ (br t, $^4$J(H$_C$,H$_B$) = 1.2 Hz, 2H, ArH$_C$), 8.11 (dd, $^3$J(H$_B$,H$_A$) = 7.6 Hz, $^4$J(H$_B$,H$_C$) = 1.2 Hz, 4H, ArH$_B$), 7.63 (br t, $^3$J(H,H) = 5.4 Hz, 4H, ArH$_D$), 7.71 (t, $^3$J(H$_A$,H$_B$) = 7.6 Hz, 2H, ArH$_A$), 7.30-7.14 (m, 21H, ArH (thread) and NH$_1$), 6.93 (s, 8H, H$_E$), 6.86 (br t, $^3$J(H,H) = 5.7 Hz, 1H, NH$_2$), 6.27 (br t, $^3$J(H,H) = 5.7 Hz, 1H, NH$_3$).
5.89 (d, $^{3}J(H,H) = 15.1$ Hz, 1H, CH$_1$ or CH$_m$), 5.72 (d, $^{3}J(H,H) = 15.1$ Hz, 1H, CH$_m$
 or CH$_i$), 4.42 (br d, $^{3}J(H,H) = 5.4$ Hz, 8H, CH$_e$), 4.20 (t, $^{3}J(H,H) = 7.8$ Hz, 1H, CH$_p$
 or CH$_k$), 4.15 (t, $^{3}J(H,H) = 7.7$ Hz, 1H, CH$_p$ or CH$_a$), 3.85-3.78 (m, 4H, CH$_b$ and
 CH$_o$), 3.14-3.06 (m, 4H, CH$_e$ and CH$_j$), 2.08 (br s, 4H, CH$_d$ and CH$_a$), 1.50-1.39 (m,
 4H, CH$_h$ and CH$_i$) and 1.30-1.15 (m, 16H, -CH$_2$- (alkyl chain)); $^{13}$C NMR (100 MHz,
 CDCl$_3$) $\delta$ 172.4 (-CO- (succinic)), 172.2 (-CO- (succinic)), 166.7 (4C, -CO-
 (macrocycle)), 165.6 (-CO- (fumaric)), 165.3 (-CO- (fumaric)), 141.9 (2C, ArC-CH-
 (ipso, thread)), 141.6 (2C, ArC-CH- (ipso, thread)), 136.9 (4C, ArC-CH$_2$NH-), 133.6
 (4C, ArC-CO-), 131.3 (4C, C$_b$), 130.7 (C$_k$ or C$_i$), 128.9 (C$_l$ or C$_k$), 129.1 (8C, C$_f$),
 129.0 (2C, C$_h$), 128.9 (4C, ArCH (meta thread)), 128.7 (4C, ArCH (meta thread)),
 127.9 (4C, ArCH (ortho thread)), 127.8 (4C, ArCH (ortho thread)), 127.1 (2C, ArCH
 (para thread), 126.8 (2C, ArCH (para thread), 124.6 (2C, C$_c$), 50.5 (C$_p$ or C$_a$), 50.4
 (C$_a$ or C$_p$), 44.8 (C$_b$ or C$_o$), 44.2 (8C, C$_e$), 43.9 (C$_o$ or C$_b$), 40.0 (C$_g$ or C$_j$), 39.6 (C$_j$
 or C$_g$), 31.8 (-CH$_2$-), 31.7 (-CH$_2$-), 29.7 (-CH$_2$-), 29.4 (-CH$_2$-), 29.3 (-CH$_2$-), 29.2
 (-CH$_2$-), 29.1 (-CH$_2$-), 29.0 (-CH$_2$-), 26.9 (-CH$_2$-) and 26.7 (-CH$_2$-); MS(FAB): $m/z =
 1289 [(M + H)$$]^{+}$; Anal. calcd for C$_{80}$H$_{88}$N$_8$O$_8$: C 74.51, H 6.88, N 8.69. Found C
 74.62, H 7.01, N 8.63.
\((E)\), \(N\)-\{12-\(3\)-(2,2-Diphenylethylcarbamoyl)–acyrloylamino\}-dodecyl\}-sucinamic acid 2,2-diphenylethyl ester, \(E-5\).

To a stirred solution of \(S10\) (0.52 g, 0.89 mmol) in anhydrous \(CHCl_3\) (30 mL) was added trifluoroacetic acid (5 mL) and the solution allowed to stir for 2 hours. The solution was reduced in volume and the excess trifluoroacetic acid removed \textit{in vacuo} over 16 h. The resulting oil was taken up in anhydrous DMF (40 mL) and \(S12\) (0.36 g, 1.21 mmol), 4-DMAP (0.20 g, 1.65 mmol) and EDCI-HCl (0.42 g, 2.17 mmol) added sequentially under argon at 0°C with stirring. After 16 h the solution was reduced in volume and the resulting oil taken up with \(CHCl_3\) and washed with 0.5N HCl (3 x 100 mL). The organic layer was dried over anhydrous MgSO\(_4\), filtered and the filtrate reduced in volume to obtain a compound that was purified by column chromatography (\(CH_2Cl_2/EtOAc\)) (\(E-5\), 0.51 g, 76%).

Rotaxane \(E-5\) was also obtained using the general procedure for the thermal-isomerization from thread \(Z-5\) (75%, \(C_2D_2Cl_4\)). mp 151-152°C. \(^1\)H NMR (400 MHz, \(CDCl_3\)): \(\delta = 7.34\text{--}7.18\) (m, 20H, ArH), 6.86 (d, \(3J(H,H) = 14.8\) Hz, 1H, CH\(_a\) or CH\(_b\)), 6.71 (d, \(3J(H,H) = 14.8\) Hz, 1H, CH\(_a\) or CH\(_b\)), 6.05 (br t, \(3J(H,H) = 5.7\) Hz, 1H, NH\(_a\)), 5.91 (br t, \(3J(H,H) = 5.7\) Hz, 1H, NH\(_b\)), 5.59 (br t, \(3J(H,H) = 5.7\) Hz, 1H, NH\(_c\)), 4.64
(d, $^3J(\text{H,H}) = 7.7 \text{ Hz}, 2\text{H, CH}_b), 4.34 \text{ (t, } ^3J(\text{H,H}) = 8.0 \text{ Hz, } 1\text{H, CH}_a), 4.21 \text{ (t, } ^3J(\text{H,H}) = 8.0 \text{ Hz, } 1\text{H, CH}_m); 3.98 \text{ (dd, } ^3J(\text{H,H}) = 8.0 \text{ Hz, } ^3J(\text{H,H}) = 5.7 \text{ Hz, } 2\text{H, CH}_i), 3.30 \text{ (td, } ^3J(\text{H,H}) = 7.0 \text{ Hz, } ^3J(\text{H,H}) = 5.7 \text{ Hz, } 2\text{H, CH}_e), 2.58 \text{ (t, } ^3J(\text{H,H}) = 7.0 \text{ Hz, } 2\text{H, CH}_e), 2.34 \text{ (t, } ^3J(\text{H,H}) = 7.0 \text{ Hz, } 2\text{H, CH}_d), 1.55-1.38 \text{ (m, } 4\text{H, } -\text{CH}_2-\text{CH}_f \text{ and } -\text{CH}_2-\text{CH}_g) \text{ and } 1.34-1.17 \text{ (m, } 16\text{H, } -\text{CH}_2- \text{ (alkyl chain))}; ^{13} \text{C NMR (100 MHz, CDCl}_3): } \delta = 173.1 \text{ (-CO-O (succinic)), 171.7 (-CO-NH (succinic)), 165.2 (-CO- (fumaric)), 164.9 (-CO- (fumaric)), 141.8 (2C, ArC- (ipso)), 140.9 (2C, ArC- (ipso)), 132.8 (C}_i \text{ or } C}_j, 132.0 \text{ (C}_j \text{ or } C}_i), 128.5 \text{ (4C, ArCH (meta)), 128.4 \text{ (4C, ArCH (meta))}, 128.0 \text{ (4C, ArCH (ortho)), 127.9 \text{ (4C, ArCH (ortho))}, 126.7 \text{ (2C, ArCH (para))}, 126.6 \text{ (2C, ArCH (para))}, 66.9 \text{ (C}_b), 50.2 \text{ (C}_m \text{ or } C}_a), 49.7 \text{ (C}_m \text{ or } C}_a), 44.2 \text{ (C}_i), 39.7 \text{ (C}_g \text{ or } C}_i), 39.4 \text{ (C}_g \text{ or } C}_i), 30.6 \text{ (C}_c), 29.5 \text{ (C}_d), 29.3-29.0 \text{ (8C, } -\text{CH}_2- \text{), 28.9 (-CH}_2- \text{) and 26.8 (-CH}_2- \text{)); MS (FAB): } m/z = 758 [(M + H)^+]; \text{ Anal. calcd for C}_{48} \text{H}_{59} \text{N}_3 \text{O}_5: C 76.06, H 7.85, N 5.54. \text{ Found C 76.21, H 8.08, N 5.49.}

**(E)**- But-2-enedioic acid (2,2-diphenylethyl) - amide \{12 - [3 - (2,2 - diphenylethylcarbamoyl)-propionylamino]-dodecyl\}-amide, **E-6.**

![Chemical Structure](image)

To a stirred solution of S12 (0.50 g, 1.69 mmol) in CH$_2$Cl$_2$ was added thionyl chloride (0.124 mL, 1.69 mmol). The solution was heated until complete dissolution of S12 had occurred and the resulting solution was added dropwise to a solution of
S14 (0.81 g, 1.69 mmol) and Et$_3$N (0.17 g, 1.69 mmol) in CH$_2$Cl$_2$ at 0 °C and allowed to stir for 30 min. The solution was then filtered and the solid recrystallized from hot DMSO to give a colorless solid (E-6, 0.56 g, 44%). mp 213-214 °C. $^1$H NMR (400 MHz, $d_6$-DMSO, 400K): $\delta$ = 8.12 (br t, $^3$J(H,H) = 5.7 Hz, 1H, NH$_b$), 8.01 (br t, $^3$J(H,H) = 5.7 Hz, 1H, NH$_k$), 7.52 (br t, $^3$J(H,H) = 5.7 Hz, 1H, NH$_o$), 7.40 (br t, $^3$J(H,H) = 5.7 Hz, 1H, CH$_l$ or CH$_m$), 6.71 (d, $^3$J(H,H) = 15.3 Hz, 1H, CH$_l$ or CH$_m$), 4.26 (t, $^3$J(H,H) = 8.0 Hz, 1H, CH$_p$), 4.20 (t, $^3$J(H,H) = 8.0 Hz, 1H, CH$_q$), 3.82 (dd, $^3$J(H,H) = 8.0 Hz, 1H, CH$_s$), 3.70 (dd, $^3$J(H,H) = 8.0 Hz, 1H, CH$_h$), 3.12 (td, $^3$J(H,H) = 7.0 Hz, $^3$J(H,H) = 5.7 Hz, 2H, CH$_i$), 3.00 (td, $^3$J(H,H) = 7.0 Hz, $^3$J(H,H) = 5.7 Hz, 2H, CH$_i$) and 1.32-1.20 (br m, 16H, -CH$_2$- (alkyl chain)); $^{13}$C NMR was not possible to be recorded for the low solubility of the compound; MS (FAB): $m/z$ (%) = 757 [(M + H)$^+$]; Anal. calcd for C$_{48}$H$_{60}$N$_4$O$_4$: C 76.16, H 7.99, N 7.40. Found C 75.89, H 8.04, N 7.65.

(E) - Hexanedioic acid (2,2 - diphenylethyl ) - amide \{12 - [ 3 - (2,2-diphenylcarbamoyl)-acryloylamino]-dodecyl\}-amide, E-7.

A solution of S12 (0.053 g, 0.18 mmol), S18 (0.1 g, 0.20 mmol) and 4-DMAP (0.02 g, 0.18 mmol) in CHCl$_3$ (10 mL) was stirred at 0 °C for 10 minutes. EDCI·HCl (0.034 g, 0.18 mmol) was added and the reaction mixture allowed to stir for 16 h at rt. The reaction was diluted with CHCl$_3$ (10 mL) and the combined organic phase washed with 1N HCl (3 x 10 mL), saturated NaHCO$_3$ (3 x 10 mL) and brine (1 x 10 mL). The organic layer was dried over anhydrous MgSO$_4$, filtered and concentrated to give the product as a colourless solid (E-7, 69 mg, 45%). $^1$H NMR (400 MHz, $d_6$-DMSO at 400K): $\delta$ = 8.47 (br t, 1H, NH$_p$), 8.34 (br t, 1H, NH$_m$), 7.82 (br t, 1H, NH$_c$), 7.22 (s, 4H, CH$_d$ and CH$_e$), 1.48-1.34 (m, 4H, CH$_h$ and CH$_i$) and 1.32-1.20 (br m, 16H, -CH$_2$- (alkyl chain)); $^{13}$C NMR was not possible to be recorded for the low solubility of the compound; MS (FAB): $m/z$ (%) = 757 [(M + H)$^+$]; Anal. calcd for C$_{48}$H$_{60}$N$_4$O$_4$: C 76.16, H 7.99, N 7.40. Found C 75.89, H 8.04, N 7.65.
7.69 (br t, 1H, NH₆), 7.31-7.19 (m, 20H, ArH), 6.80 (d, J(H,H) = 15.3 Hz, 1H, CH₃ or CH₆), 6.73 (d, J(H,H) = 15.3 Hz, 1H, CH₃ or CH₆), 4.24 (t, J(H,H) = 8.0 Hz, 1H, CH₃), 4.19 (t, J(H,H) = 8.0 Hz, 1H, CH₃), 3.82 (dd, J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₃), 3.69 (dd, J(H,H) = 8.0 Hz, J(H,H) = 5.7 Hz, 2H, CH₃), 1.96 (m, 4H, CH₄ and CH₆), 1.35 (m, 8H, CH₂, CH₃ and CH₄), 1.25 (m, 16H, CH₂ (alkyl chain)). ¹³C NMR was not possible to be recorded for the low solubility of the compound. MS(FAB): m/z = 785 [(M + H)⁺]; Anal. calcd for C₅₀H₆₄N₄O₄: C 76.50, H 8.22, N 7.14. Found C 76.75, H 8.35, N 7.24.


Compound Z-1 was obtained using the general procedure for photo-isomerization from rotaxane E-1. The crude product was subjected to column chromatography using a solvent gradient of CH₂Cl₂ to CH₂Cl₂/EtOAc (70/30) to obtain the desired compound as a colorless solid (Z-1, 35 mg, 54%). mp 152-154 °C. ¹H NMR (400
METHZ, CDCl₃): δ = 8.55 (br t, J(H,H) = 5.7 Hz, 1H, NH₉), 8.28 (br t, J(H_C,H_B) = 1.2 Hz, 2H, ArH_B), 8.18 (dd, J(H_B,H_A) = 7.8 Hz, 4J(H_B,H_C) = 1.2 Hz, 4H, ArH_B), 7.82 (br t, J(H,H) = 5.7 Hz, 1H, NH₉), 7.60 (t, J(H_A,H_B) = 7.8 Hz, 2H, ArH_A), 7.38 (br t, J(H,H) = 5.4 Hz, 4H, NH₉), 7.32-7.10 (m, 20H, ArH), 7.00 (s, 8H, ArH_B), 6.36 (t, J(H,H) = 5.7 Hz, 1H, CH_i or CH_j), 5.90 (d, J(H,H) = 13.4 Hz, 1H, CH_i or CH_j), 5.82 (d, J(H,H) = 13.4 Hz, 1H, CH_i or CH_j), 4.55 (dd, J(H,H) = 14.1 Hz, 3J(H,H) = 5.8 Hz, 4H, CH₃ or CH₄), 4.44 (d, J(H,H) = 7.7 Hz, 2H, CH_b), 4.40 (dd, J(H,H) = 14.1 Hz, J(H,H) = 5.0 Hz, 4H, CH₃ or CH₄); 3.88 (dd, J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH_i), 3.04 (td, J(H,H) = 7.0 Hz, J(H,H) = 5.7 Hz, 2H, CH_g), 2.94 (td, J(H,H) = 7.0 Hz, J(H,H) = 5.7 Hz, 2H, CH_f), 1.47 (m, 2H, CH_i), 1.16 (m, 2H, CH_i), 1.43-1.34 (m, 4H, CH₂-CH₁ and CH₂-CH₂) and 1.30-1.13 (m, 18H, CH₂-alkyl chain); ¹³C NMR (100 MHz, CD₂Cl₂): δ = 174.7 (-CO-O (succinic)), 172.6, (-CO-NH (succinic)), 166.9 (4C, -COO-(macrocycle)), 166.0 (-CO- (maleic)), 165.4 (-CO- (maleic)), 142.7 (2C, ArC-CH-(ipso, thread)), 141.9 (2C, ArC-CH-(ipso, thread)), 138.5 (4C, ArC-CH₂NH-), 135.0 (4C, ArC-CO-), 134.2 (C_i or C_j), 132.1(C_i or C_j), 132.0 (4C, C_b), 130.0 (2C, C_A), 129.8 (8C, C_b), 129.5 (4C, ArCH (meta thread)), 129.4 (4C, ArCH (meta thread)), 128.8 (4C, ArCH (ortho thread)), 128.6 (4C, ArCH (ortho thread)), 127.8 (2C, ArCH (para thread)), 127.6 (2C, ArCH (para thread)), 124.8 (2C, C_C), 68.1 (C_b), 51.2 (C_a or C_m), 50.5 (C_a or C_m), 44.9 (C_i), 44.8 (4C, C_b), 40.7 (C_f or C_g), 40.6 (C_f or C_g), 30.2 (C_a), 30.1(C_d), 29.9 (-CH₂-), 29.8-29.6 (8C, -CH₂-), 29.5 (-CH₂-), 29.4 (-CH₂-), 27.5 (-CH₂-) and 27.3 (-CH₂-); MS (FAB): m/z = 1291 [(M + H)⁺]; Anal. calcd for C₈₀H₇₇N₇O₉: C 74.45, H 6.79, N 7.60. Found C 74.62, H 6.68, N 7.49.
Rotaxane Z-2 was obtained using the general procedure for the preparation of the benzylc amide macrocycle containing-[2]rotaxanes from the thread Z-6 (0.50 g, 0.66 mmol). Column chromatography of the crude product using a solvent gradient of CHCl₃ to CHCl₃/MeOH (95/5) gave a colorless solid (Z-2, 0.34 g, 40%).

Rotaxane Z-2 was also obtained using the general procedure for photo-isomerization from rotaxane E-2 (48%). mp 171-172 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.67 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₄), 8.31 (br t, 4J(H₅,Ha) = 1.2 Hz, 2H, ArH), 8.16 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₄), 8.14 (dd, 3J(H₅,Ha) = 7.8 Hz, 4J(H₅,He) = 1.2 Hz, 4H, ArH), 7.67 (br t, 3J(H₆,He) = 5.4 Hz, 4H, NH₄), 7.56 (t, 3J(H₅,He) = 7.8 Hz, 2H, ArH), 7.31-7.10 (m, 20H, ArH (thread)), 7.02 (s, 8H, ArH), 6.53 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₄), 6.15 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₄), 5.92 (d, 3J(H,H) = 13.6 Hz, 1H, CH₃ or CH₃), 5.83 (d, 3J(H,H) = 13.6 Hz, 1H, CH₃ or CH₃), 4.50 (dd, 2J(H₃,He) = 14.1 Hz, 3J(H₃ or Hₑ⁻, Hₑ⁻) = 5.4 Hz, 4H, CH₃ or CH₃), 4.43 (dd, 2J(H₃,He) = 14.1 Hz, 3J(H₃ or Hₑ⁻, Hₑ⁻) = 5.4 Hz, 4H, CH₃ or CH₃).
Hz, $^3J(\mathrm{H}_E \text{ or } \mathrm{H}_E', \mathrm{H}_D) = 5.4 \text{ Hz}, 4 \mathrm{H}, \mathrm{CH}_E \text{ or } \mathrm{CH}_E'$), 4.23 (t, $^3J(\mathrm{H}, \mathrm{H}) = 8.0 \text{ Hz}, 1 \mathrm{H}, \mathrm{CH}_p$), 4.06 (t, $^3J(\mathrm{H}, \mathrm{H}) = 8.0 \text{ Hz}, 1 \mathrm{H}, \mathrm{CH}_a$), 3.90 (dd, $^3J(\mathrm{H}, \mathrm{H}) = 8.0 \text{ Hz}, ^3J(\mathrm{H}, \mathrm{H}) = 5.7 \text{ Hz}, 2 \mathrm{H}, \mathrm{CH}_o$), 3.67 (dd, $^3J(\mathrm{H}, \mathrm{H}) = 8.0 \text{ Hz}, ^3J(\mathrm{H}, \mathrm{H}) = 5.7 \text{ Hz}, 2 \mathrm{H}, \mathrm{CH}_b$), 3.15 (td, $^3J(\mathrm{H}, \mathrm{H}) = 7.0 \text{ Hz}, ^3J(\mathrm{H}, \mathrm{H}) = 5.7 \text{ Hz}, 2 \mathrm{H}, \mathrm{CH}_j$), 2.99 (td, $^3J(\mathrm{H}, \mathrm{H}) = 7.0 \text{ Hz}, ^3J(\mathrm{H}, \mathrm{H}) = 5.7 \text{ Hz}, 2 \mathrm{H}, \mathrm{CH}_b$), 1.48 (m, 2H, CH), 1.38 (m, 2H, CH$_a$), 1.33-1.16 (m, 16H, CH$_2$ (chain)) and 1.07 (m, 4H, CH$_a$ and CH$_o$); $^{13}$C NMR (100 MHz, CDC$_3$): $\delta$ = 173.0 (-CO- (succinic)), 172.9 (-CO- (succinic)), 166.6 (4C, -CO- (macrocycle)), 165.0 (-CO- (maleic)), 164.7 (-CO- (maleic)), 141.7 (2C, ArC-CH- (ipso thread)), 141.6 (2C, ArC-CH- (ipso thread)), 137.5 (4C, ArC-CH$_2$NH-), 133.8 (4C, ArC-CO-), 133.1 (C$_l$ or C$_m$), 131.5 (4C, C$_B$), 131.4 (C$_l$ or C$_m$), 129.2 (8C, C$_r$), 129.1 (2C, C$_A$), 128.8 (4C, ArCH (meta thread)), 128.7 (4C, ArCH (meta thread)), 127.9 (4C, ArCH (ortho thread)), 127.8 (4C, ArCH (ortho thread)), 127.1 (2C, ArCH (para thread)), 126.8 (2C, ArCH (para thread)), 124.0 (2C, C$_o$), 50.5 (C$_p$), 50.3 (C$_a$), 44.2 (C$_o$), 44.1 (C$_b$), 44.0 (4C, C$_E$), 39.7 (2C, C$_l$ and C$_g$), 29.8 (C$_d$ or C$_o$), 29.4 (C$_a$ or C$_d$), 29.3 (-CH$_2$-), 29.2 (-CH$_2$-), 29.1 (2C, -CH$_2$-), 29.0 (2C, -CH$_2$-), 28.8 (-CH$_2$-) and 28.7 (-CH$_2$-); MS (FAB): $m/z = 1289 [(\text{M + H})^+]$; Anal. calcd for C$_{80}$H$_{88}$N$_8$O$_6$: C 74.51, H 6.88, N 8.69. Found C 74.69, H 6.94, N 8.76.
Rotaxane Z-3 was made using the general procedure for the formation of the benzylic amide macrocycle containing [2]rotaxanes from thread Z-7 (1.5 g, 1.9 mmol). Column chromatography of the crude product (silica gel, 3:97, MeOH/CHCl₃) gave the product as a colorless solid (Z-3, 0.5 g, 20%).

¹H NMR (400 MHz, CDCl₃): δ = 8.82 (brt, ³J(H,H) = 5.7 Hz, 1H, NHₐ), 8.24 (brs, 3H, ArCHc & NHₗ), 8.13 (dd, ³J(Hₐ,Hₐ) = 7.8 Hz, 4J(Hₐ,Hₖ) = 1.5 Hz, 4H, ArCHₖ), 7.63 (t, ³J(Hₖ,Hₖ) = 5.3 Hz, 4H, CH₂ₙ), 7.53 (t, ³J(Hₙ,Hₙ) = 7.8 Hz, 2H, ArCH₅), 7.32-7.15 (m, 20H, ArH), 7.05 (s, 8H, ArCH₆), 6.20 (brt, ³J(H,H) = 5.6 Hz, 1H, NHcentration), 6.03 (brt, ³J(H,H) = 5.1 Hz, 1H, NHb), 5.79 (d, ³J(H,H) = 13.4 Hz, 1H, CHₕ or CHₘ), 5.71 (d, ³J(H,H) = 13.4 Hz, 1H, CHₕ or CHₘ), 4.55 (dd, ²J(Hₕ,Hₕ) = 14.4 Hz, 3J(Hₕ or Hₕ, HD) = 5.3 Hz, 4H, CHₖ or CHₖ'), 4.45 (dd, ²J(Hₕ,Hₕ) = 14.4 Hz, 3J(Hₕ or Hₕ, HD) = 5.3 Hz, 4H, CHₖ or CHₖ'), 4.19 (t, ³J(H,H) = 7.8 Hz, 1H, CHₖ), 4.13 (t, ³J(H,H) = 7.8 Hz, 1H, CHₖ), 3.87 (2d, ³J(H,H) = 7.8 Hz, 2H, CHₙ), 3.66 (2d, ³J(H,H) = 7.8 Hz, 2H, CHₙ), 2.94 (m, 4H, CHₙ and CHₙ), 1.41 (brm, 2H, -CH₂-, (alkyl chain)), 1.33 (brm, 4H, CHₙ and CHₙ), 1.25-1.18 (m, 22H, -CH₂- (alkyl chain)), 0.76 (brm, 4H, CHₙ and CHₙ), ¹³C NMR (100 MHz, CDCl₃): δ = 173.4 (⁻CO- (adipamide)), 173.3 (⁻CO- (adipamide)), 166.4 (4C, -CO- (macrocycle)), 165.4 (⁻CO- (maleic)), 181
164.6 (-CO- (maleic)), 142.1 (2C, ArC- (ipso thread)), 141.5 (2C, ArC- (ipso thread)), 137.6 (4C, ArC-CH2NH-), 133.9 (4C, ArC-CO-), 133.2 (C_6 or C_8), 131.9 (C_6 or C_8), 131.8 (C_4C, C_3F), 129.2 (2C, C_3A), 128.4 (8C, ArCH (meta thread)), 128.0 (8C, ArCH (ortho thread)), 126.91 (4C, ArCH (para thread)), 124.4 (2C, C_6), 50.7 (C_6), 50.2 (C_3A), 44.4 (C_3A), 44.3 (C_3B), 44.0 (4C, C_3E), 40.1 (C_3I), 39.7 (C_3I), 35.5 (C_4D or C_4G), 34.5 (C_4D or C_4G), 29.4 (-CH_2-), 29.3 (-CH_2-), 29.2 (-CH_2-), 29.1 (-CH_2-), 29.0 (-CH_2-), 28.9 (-CH_2-), 28.6 (-CH_2-), 26.8 (-CH_2-), 26.7 (-CH_2-), 24.7 (-CH_2-) and 24.5 (-CH_2-). HRMS (FAB, NBA matrix): m/z = 1317.70829 [(M+H)^+]
(Nal. Calcd. For C_{82}H_{93}N_{8}O_{8}: m/z = 1317.71164)

(Z),N-{12-[3-(2,2-Diphenylethylcarbamoyl)-acryloylamino]-dodecyl}-succinamic acid 2,2-diphenylethyl ester, Z-5.

To a stirred solution of S10 (0.25 g, 0.43 mmol) in anhydrous CHCl_3 (30 mL) was added trifluoroacetic acid (5 mL) and the solution stirred for 2 h. The solution was reduced in volume and the excess trifluoroacetic acid removed in vacuo over 16 h. The resulting oil was taken up in anhydrous CHCl_3 (200 mL) and Et_3N (1 mL), S8 (0.14 g, 0.47 mmol) and EDCI-HCl (0.10 g, 0.51 mmol) added sequentially under cooling with an ice bath. After 16 h the solution was reduced in volume and the resulting oil taken up with CHCl_3 and washed with 0.5N HCl (3 x 100 mL). The organic layer was dried over anhydrous MgSO_4, filtered and the filtrate reduced in volume to give a colourless solid that was purified by column chromatography CHCl_3/MeOH (90/10) (Z-5, 0.23 g, 70%).
Compound Z-5 was also obtained using the general procedure for photo-
isomerization from the thread E-5 (57% by 1H NMR). mp 54-56 °C; 1H NMR (400 MHz, CDCl₃): δ = 8.45 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₆), 7.91 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₆), 7.28-7.08 (m, 20H, ArH), 5.90 (d, 3J(H,H) = 13.4 Hz, 1H, CH₁ or CH₂), 5.82 (d, 3J(H,H) = 13.4 Hz, 1H, CH₁ or CH₂), 5.53 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₆), 4.55 (d, 3J(H,H) = 7.7 Hz, 2H, CH₆), 4.27 (t, 3J(H,H) = 7.7 Hz, 1H, CH₃), 3.87 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 8.0 Hz, 1H, CH₃), 3.16 (td, 3J(H,H) = 7.0 Hz, 3J(H,H) = 7.0 Hz, 1H, CH₃), 2.48 (t, 3J(H,H) = 7.0 Hz, 2H, CH₂), 2.24 (t, 3J(H,H) = 7.0 Hz, 2H, CH₂), 1.51-1.40 (m, 2H, CH₂-CH₂), 1.40-1.31 (m, 2H, CH₂-CH₂), 1.30-1.12 (m, 16H, CH₂, (alkyl chain)); 13C NMR (100 MHz, CDCl₃): δ = 173.3 (-CO-O (succinic)), 171.6 (-CO-NH (succinic)), 165.4 (-CO- (maleic)), 165.0 (-CO- (maleic)), 142.2 (2C, ArC- (ipso)), 141.4 (2C, ArC- (ipso)), 133.9 (Cₚ or Cₗ), 131.7 (Cₚ or Cₗ), 129.1 (4C, ArCₚ- (meta)), 129.0 (4C, ArCₗ- (meta)), 128.6 (4C, ArCₚ- (ortho)), 128.4 (4C, ArCₗ- (ortho)), 127.2 (4C, ArCₚ- (para + para)), 67.3 (Cₖ), 50.7 (Cₗ), 50.2 (Cₖ), 44.6 (Cₗ), 40.2 (Cₘ or Cₙ), 40.0 (Cₙ or Cₘ), 31.4 (Cₖ or Cₗ), 30.1 (Cₗ or Cₖ), 29.9 (-CH₂-), 29.8-29.7 (4C, -CH₂-), 29.6 (-CH₂-), 29.5 (-CH₂-), 27.4 (-CH₂-), 27.3 (-CH₂-); MS(FAB): m/z = 758 [(M + H)⁺]; Anal. calcd for C₄₈H₅₉N₃O₅: C 76.06, H 7.85, N 5.54. Found C 76.09, H 8.11, N 5.63.
(Z), But-2-enedioic acid (2,2-diphenylethyl) - amide 112 - [3 - (2,2-

To a stirred solution of S14 (0.50 g, 1.04 mmol) in anhydrous CHCl₃ (50 mL) at 0 °C was added S8 (0.34 g, 1.15 mmol), 4-DMAP (0.15 g, 1.25 mmol) and EDCI·HCl (0.24 g, 1.25 mmol) and the resulting reaction mixture stirred for 16 hours at rt. The solution was then washed with a solution of 1N NaOH (3 x 100 mL), 1N HCl (3 x 100 mL) and H₂O (1 x 100 mL). The organic layer was dried over anhydrous MgSO₄, filtered and the solvent removed under reduced pressure to obtain a colorless solid that was subjected to column chromatography using a solvent gradient of CH₂Cl₂ to CH₂Cl₂/MeOH (95/5) (Z-6, 0.63 g, 70%). mp 68-69 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.40 (br t, 3 J(H,H) = 5.7 Hz, 1H, NH₆), 7.80 (br t, 3 J(H,H) = 5.7 Hz, 1H, NH₂), 7.25-7.09 (m, 20H, ArH), 5.91-6.00 (br m, 2H, NH and NH₂), 5.90 (d, 3 J(H,H) = 13.3 Hz, 1H, CH₁ or CH₆), 5.83 (d, 3 J(H,H) = 13.3 Hz, 1H, CH₆ or CH₁), 4.18 (t, 3 J(H,H) = 8.0 Hz, 1H, CH₂), 4.09 (t, 3 J(H,H) = 8.0 Hz, 1H, CH₁), 3.79 (dd, 3 J(H,H) = 8.0 Hz, 3 J(H,H) = 5.7 Hz, 2H, CH₂), 3.16 (td, 3 J(H,H) = 7.0 Hz, 3 J(H,H) = 5.7 Hz, 2H, CH₂), 2.29 (s, 4H, CH₂ and CH₆), 1.45 (m, 2H, CH₂), 1.37 (m, 2H, CH₆) and 1.12-1.29 (m, 16H, -C₁₂- (alkyl chain)). ¹³C NMR (100 MHz, CDCl₃): δ = 172.6 (-CO- (succinic)), 172.4 (-CO- (succinic)), 165.4 (-CO- (maleic)), 164.9 (-CO- (maleic)), 142.2 (2C, ArC- (ipso)), 142.17 (2C, ArC- (ipso)), 133.96 (C₁ or C₆), 131.61 (C₆ or C₁), 129.1 (8C, ArCH (meta)), 128.4 (8C, ArCH (ortho)), 127.2 (4C, ArCH (para)), 51.0 (C₆), 50.7 (C₆), 44.6 (C₆), 44.2 (C₆), 40.2 (C₆)
or C₈), 40.0 (C₈ or C₁), 32.2 (C₉ or C₁₀), 32.1 (C₁₀ or C₁₁), 29.9-29.8 (-CH₂-(alkyl chain)), 29.6-29.5 (-CH₂-(alkyl chain)), 27.3 (-CH₂-(alkyl chain)) and 27.2 (-CH₂-(alkyl chain)); MS (FAB): m/z (%) = 757 [(M + H)⁺]; Anal. calcd for C₄₈H₆₀N₄O₄: C 76.16, H 7.99, N 7.40. Found C 75.98, H 8.10, N 7.45.

(Z)-Hexanedioic acid (2,2-diphenylethyl) - amide {12 - [3 - (2,2-diphenylethylcarbamoyl)-acryloylaminol-dodecyl]-amide, Z-7.

A solution of S8 (0.16 g, 0.54 mmol), S18 (0.3 g, 0.59 mmol) and 4-DMAP (0.07 g, 0.54 mmol) in CHCl₃ (10 mL) was stirred at 0 °C for 10 minutes followed by addition of EDCI-HCl (0.10 g, 0.537 mmol). The reaction mixture was stirred for 16 h at rt. The solution was diluted with CHCl₃ (10 mL) and the combined organic phase washed with 1N HCl (3 x 10 mL), saturated NaHCO₃ (3 x 10 mL) and brine (1 x 10 mL). The organic layer was dried over anhydrous MgSO₄, filtered and the filtrate concentrated to give the product as a colorless solid (Z-7, 295 mg, 70%). ¹H NMR (400 MHz, CDCl₃): δ = 8.45 (br t, ³J(H,H) = 5.7 Hz, 1H, NHₐ), 7.88 (br t, ³J(H,H) = 5.7 Hz, 1H, NHₐ), 7.33-7.20 (m, 20H, ArH), 6.02 (d, ³J(H,H) = 13.3 Hz, 1H, CH₉ or CH₁₀), 5.92 (d, ³J(H,H) = 13.3 Hz, 1H, CH₉ or CH₁₀), 5.72 (br m, 2H, NH and NEt), 4.26 (t, ³J(H,H) = 8.0 Hz, 1H, CH₁), 4.20 (t, ³J(H,H) = 8.0 Hz, 1H, CH₁), 3.96 (dd, ³J(H,H) =8.0 Hz, ³J(H,H) = 5.7 Hz, 2H, CH₂), 3.89 (dd, ³J(H,H) =8.0 Hz, ³J(H,H) = 5.7 Hz, 2H, CH₂), 3.23 (m, 4H, CH₁ and CH₁), 2.10 (t, ³J(H,H) = 7.3 Hz, 2H, CH₉ or CH₁₀), 2.07 (t, ³J(H,H) = 7.3 Hz, 2H, CH₉ or CH₁₀), 1.55-1.47 (m, 8H, CH₂, CH₂, CH₂ and CH₂), 1.32-1.27 (m, 16H, -CH₂-(alkyl chain)); ¹³C NMR (100 MHz, CDCl₃): δ = 172.8 (-CO-(adipamide)), 172.6 (-CO-(adipamide)), 165.0 (-CO-(maleic)), 164.6 (-CO-(maleic)), 141.9 (2C, ArC- (ipso)), 141.8 (2C, ArC- (ipso)), 141.8 (2C, ArC- (ipso)),
133.4 (C or C), 131.4 (C or C), 128.7 (4C, ArCH (meta)), 128.6 (4C, ArCH (meta)), 128.0 (8C, ArCH (ortho)), 126.8 (4C, ArCH (para)), 50.6 (C), 50.3 (C), 44.2 (C), 43.8 (C), 39.8 (C), 39.5 (C), 36.2 (C or C), 36.1 (C or C), 29.5 (-CH2-), 29.3 (-CH2-), 29.1 (-CH2-), 29.0 (-CH2-), 26.9 (-CH2-), 26.8 (-CH2-) and 24.9 (-CH2-). MS (FAB): m/z = 785 [(M + H)+]; Anal. Calcd for C50H64N4O4: C 76.50, H 8.22, N 7.14. Found C 76.83, H 8.33, N 7.12.

N,N'-bis-(2,2-Diphenyl-ethyl)-succinamide, S1.

To a stirred solution of 2,2-diphenylethylamine (0.50 g, 2.54 mmol) and Et3N (0.26 g, 2.54 mmol) in CH2Cl2 (20 mL) at 0 °C was added dropwise a solution of succinyl dichloride (0.2 g, 1.27 mmol) in CH2Cl2. The obtained solution was allowed to stir for 3 h and then washed with 1N HCl (2 x 20 mL), 1N NaOH (2 x 20 mL) and H2O (1 x 20 mL). The organic layer was dried over anhydrous MgSO4, filtered and the solvent removed under reduced pressure to obtain a solid that was recrystallized from acetone to give colourless needles (S1, 0.59 g, 97%). mp 168-169 °C; 1H NMR (400 MHz, CDCl3): δ = 7.34-7.18 (m, 20H, ArH), 5.84 (br t, 3J(H,H) = 5.7 Hz, 2H, NH), 4.14 (t, 3J(H,H) = 8.0 Hz, 2H, CHa), 3.83 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, 4H, CM); 13C NMR (100 MHz, CDCl3): δ = 172.0 (2C, -CO-), 141.8 (4C, ArC-CH- (ipso)), 128.9 (8C, ArCH (meta)), 128.0 (8C, ArCH (ortho)), 126.8 (4C, ArCH (para)), 50.5 (2C, C), 43.8 (2C, C) and 31.6 (2C, C); MS (FAB): m/z = 477 [(M + H)+]; Anal. calcd for C32H32N2O2: C 80.64, H 6.77, N 5.88. Found C 81.03, H 6.92, N 6.09.
Rotaxane S2 was obtained using the general procedure for the preparation of benzylic amide macrocycle containing [2]rotaxanes from the thread S1 (0.50 g, 1.05 mmol). The crude product was subjected to column chromatography on silica gel [CH$_3$Cl/MeOH (5/95)] to obtain a colorless solid (S2, 0.55 g, 52%). mp 230-232 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.31$ (br t, $^4J(H_c,H_b) = 1.3$ Hz, 2H, ArH$_c$), 8.19 (dd, $^3J(H_b,H_a) = 7.7$ Hz, $^4J(H_b,H_c) = 1.3$ Hz, 4H, ArH$_b$), 7.62 (t, $^3J(H_a,H_b) = 7.7$ Hz, 2H, ArH$_a$), 7.47 (br t, $^3J(H,H) = 5.4$ Hz, 4H, NH$_2$), 7.30-7.15 (m, 12H, ArH (para and meta thread)), 7.12 (d, $^3J(H,H) = 7.1$ Hz, 8H, ArH (ortho thread)), 6.85 (s, 8H, ArH$_f$), 5.87 (br t, $^3J(H,H) = 5.6$ Hz, 2H, NH$_2$), 4.43 (d, $^3J(H,H) = 5.4$ Hz, 8H, CH$_b$), 4.04 (t, $^3J(H,H) = 7.8$ Hz, 2H, CH$_d$), 3.65 (dd, $^3J(H,H) = 7.8$ Hz, $^3J(H,H) = 5.6$ Hz, 4H, CH$_b$) and 0.89 (s, 4H, CH$_d$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 172.8$ (2C, -CO- (thread)), 166.5 (4C, -CO- (macrocycle)), 141.4 (4C, ArC-CH- (ipso thread)), 137.6 (4C, ArC-CH$_2$NH-), 134.0 (4C, ArC-CO-), 130.8 (4C, C$_b$), 129.3 (8C, C$_f$), 129.0 (2C, C$_A$), 128.9 (8C, ArCH (meta)), 127.8 (8C, ArCH (ortho)), 127.2 (4, ArCH (para)), 125.4 (2C, C$_c$), 49.4 (2C, C$_a$), 44.3 (2C, C$_b$), 43.9 (4C, C$_E$) and
28.4 (2C, Cδ); MS(FAB): \textit{m/z} = 1009 \ [(M + H)^+]; \textit{Anal. calcd} for C_{64}H_{60}N_{6}O_{6}; \textit{C} 76.17, \textit{H} 5.99, \textit{N} 8.33. \textit{Found} \textit{C} 76.28, \textit{H} 5.85, \textit{N} 8.16.

\textit{X-ray crystallographic data for compound S2.}

\textit{C}_{76}\textit{H}_{88}\textit{N}_{10}\textit{O}_{10}, M=1301.56, \textit{crystal size} 0.24\times0.06\times0.06\textit{mm}, \textit{triclinic} \textit{P}-1, \alpha=9.8887(5), \beta=13.1481(6), \gamma=15.3131(7) \text{Å}, \alpha=108.0300(10), \beta=106.0530(10), \gamma=101.9480(10) ^\circ, V=1723.58(14) \text{Å}^3, Z=1, \rho_{\text{calcld}}=1.254 \text{Mg m}^{-3}; \text{MoK}_{\alpha} \text{radiation (graphite monochromator,} \lambda=0.71073 \text{Å), } \mu=0.084 \text{mm}^{-1}, T=293(2)\text{K. 8463 data (4770 unique, } R_{\text{int}}=0.0628, 1.50<\theta<23.31^\circ), \text{were collected on a Siemens SMART CCD diffractometer using narrow frames (0.3} ^\circ \text{in } \omega), \text{and were corrected semi-empirically for absorption and incident beam decay (transmission 0.70-1.00). The structure was solved by direct methods and refined by full-matrix least-squares on } F^2 \text{values of all data (G.M.Sheldrick, SHELXTL manual, Siemens Analytical X-ray Instruments, Madison WI, USA, 1994, version 5) to give} wR=\{\Sigma[w(F_0^2-F_c^2)^2]/\Sigma[w(F_0^2)^2]\}^{1/2} = 0.2659, \text{conventional} \ R = 0.0866 \text{for } F \text{values of 4770 reflections with } F_0^2>2\sigma(F_0^2), S = 1.027 \text{for 446 parameters. Residual electron density extremes were 0.356 and -0.250 } \text{Å}^3. \text{Amide hydrogen atoms were refined isotropically with the remainder constrained; anisotropic displacement parameters were used for all non-hydrogen atoms.}
Hexanedioic acid bis-[(2,2-diphenylethyl)-amide], S3.

To a solution of 2,2-diphenylethylamine (0.42 g, 2.1 mmol) in CH₂Cl₂ (10 mL) was added Et₃N (0.25 g, 2.5 mmol) followed by dropwise addition of hexanedionyl dichloride (0.18 g, 1 mmol) in CH₂Cl₂ (5 mL) over 10 min at 0 °C. The reaction mixture was allowed to stir for 16 h at rt and then washed with 1N HCl (2 x 10 mL), saturated aqueous NaHCO₃ (2 x 10 mL) and brine (10 mL). The organic layer was dried over anhydrous MgSO₄, filtered and the solution concentrated under reduced pressure to give a colorless solid that was recrystallized in CH₂Cl₂/MeOH to afford colorless needles (S3, 2.2 g, 79%). ¹H NMR (400 MHz, CDCl₃): δ = 7.35-7.22 (m, 20H, ArH), 5.60 (br t, 3J(H,H) = 5.7 Hz, 2H, NH₂), 4.21 (t, 3J(H,H) = 8.0 Hz, 2H, CH₆), 3.91 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, CH₇), 2.03 (m, 4H, CH₈) and 1.47 (m, 4H, CH₉). ¹³C NMR (100 MHz, CDCl₃): δ = 172.6 (2C, -CO-), 141.9 (4C, ArC-CH- (ipso)), 128.7 (8C, ArCH (meta)), 128.0 (8C, ArCH (ortho)), 126.8 (4C, ArCH (para)), 50.6 (2C, C₉), 43.74 (2C, C₈), 36.05 (2C, C₇) and 24.72 (2C, C₆). MS (FAB, mTHIOPG): m/z = 505 [(M+H)⁺]. Anal. calcd for C₃₄H₃₆N₂O₂: C 80.92, H 7.19, N 5.55. Found C 81.08, H 7.25, N 5.60.
Rotaxane S4 was prepared from thread S3 (0.50 g, 0.99 mmol) according to the general procedure for the preparation of benzylic amide macrocycle containing [2]rotaxanes. The crude product was purified by column chromatography (CHCl₃/MeOH (97/3)) to give S4, 0.08 g, 8%; ¹H NMR (400 MHz, CDCl₃): δ = 8.16 (br s, 4H, ArHb), 8.14 (br s, 2H, ArHc), 7.59 (t, 3J(H,H) = 7.8 Hz, 2H, ArHa), 7.49 (br t, 4H, NHd), 7.40-7.25 (m, 20H, AM (thread)), 7.06 (s, 8H, ArHF), 5.99 (br t, 2H, NH), 4.55 (d, 3J(H,H) = 5.6 Hz, 8H, CHb), 4.12 (t, 3J(H,H) = 7.8 Hz, 2H, CHa), 3.65 (dd, 3J(H,F) = 7.8 Hz, 4H, CHb), 0.91 (m, 4H, CH₂) and 0.50 (m, 4H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ = 173.5 (2C, -CO- (thread)), 166.5 (4C, -CO- (macrocycle)), 142.0 (4C, Ar-C-CH- (ipso thread)), 137.8 (4C, Ar-C-CH₂-), 134.1 (4C, Ar-C-CO-), 131.1 (4C, Cb), 129.3 (2C, Ca), 128.8 (8C, Cf), 128.7 (8C, ArCH (meta thread)), 128.0 (8C, ArCH (ortho thread)), 126.9 (4C, ArCH (para thread)), 124.5 (2C, Cc), 50.2 (2C, Ca), 44.2 (2C, Cb), 43.8 (4C, Cc), 34.7 (2C, Cc) and 23.8 (2C, Cc); HRMS: m/z = 1037.49395 [(rotaxane+H)⁺]. Anal. calcd for C₆₆H₆₄N₆O₆: C 76.42, H 6.22, N 8.10. Found C 76.30, H 6.23, N 8.05.
X-ray crystallographic data for compound S4.

Crystals of rotaxane grown in CHCl₃/MeOH: C₆₈H₇₂N₆O₆, M=1101.32, crystal size mm, monoclinic, C2/c, a=30.939(6), b=11.3129(18), c=18.568(3) Å, β=118.147(17)°, V=5730.5(17) Å³, Z=4, ρ_calc=1.277 Mg m⁻³; synchrotron radiation (CLRC Daresbury Laboratory Station 9.8, silicon monochromator, λ=0.69230 Å), μ=0.084 mm⁻¹, T=150(2)K. 18920 data (7604 unique, R_mnt =0.0348, 2.42<θ<29.30 °), were collected on a Siemens SMART CCD diffractometer using narrow frames (0.3° in ω), and were corrected semi-empirically for absorption and incident beam decay (transmission). The structure was solved by direct methods and refined by full-matrix least-squares on F² values of all data (G.M.Sheldrick, SHELXTL manual, Siemens Analytical X-ray Instruments, Madison WI, USA, 1994, version 5) to give wR=Σ[w(Fo²-Fc²)²]/Σ[w(Fo²)]¹/²=0.1361, conventional R=0.0541 for F values of 7604 reflections with Fo²>2σ(Fo²), S=1.070 for 384 parameters. Residual electron density extremes were 0.429 and -0.411 Å⁻³. Amide hydrogen atoms were refined isotropically with the remainder constrained; anisotropic displacement parameters were used for all non-hydrogen atoms.

(2,2-Diphenylethyl)-succinic acid mono ester, S5.

To a stirred solution of 2,2-diphenylethanol (3.00 g, 15.0 mmol) in CH₂Cl₂ (150 mL) was added one drop of Et₃N and a solution of succinic anhydride (1.66 g, 16.7 mmol) in CH₂Cl₂ (25 mL) added slowly over 30 mins. After 16 h the solution was reduced in volume and recrystallized from CH₂Cl₂ (10 mL) to obtain a colorless solid (S5, 4.00 g, 90%). mp 103-104 °C. ¹H NMR (400 MHz, d₆-DMSO): δ = 7.38-7.21 (m,
10H, ArH), 4.61 (d, $^3J(H,H) = 7.7$ Hz, 2H, CH$_b$), 4.35 (t, $^3J(H,H) = 7.7$ Hz, 1H, CH$_a$) and 2.40 (m, 4H, CH$_c$ and CH$_d$); $^{13}$C NMR (100 MHz, $d_{6}$-DMSO): $\delta = 173.9$ (-CO-), 172.4 (-CO-), 141.8 (2C, Ar-CH- (ipso)), 128.8 (4C, Ar-CH (meta)), 128.3 (4C, Ar-CH (ortho)), 127.0 (2C, Ar-CH (para)), 66.5 (C$_b$), 49.6 (C$_a$), 29.1 (C$_c$ or C$_d$) and 28.9 (C$_d$ or C$_e$); MS (FAB): $m/z = 299$ [(M + H)$^+$]; Anal. calcd for C$_{18}$H$_{18}$O$_4$: C 72.47, H 6.08, O 21.45. Found C 73.01, H 6.22.

$N$-(2,2-Diphenylethyl)-succinamic acid 2,2-diphenylethyl ester, S6.

![](image)

To a stirred solution of S5 (1.0 g, 3.40 mmol), 2,2-diphenylethylamine (0.66 g, 3.40 mmol) and 4-DMAP (0.49 g, 4 mmol) in CH$_2$Cl$_2$ (350 mL) cooled in an ice bath was added EDCI.HCl (0.71 g, 3.68 mmol) and the solution allowed to stir for 16 h. The reaction mixture was washed with a saturated solution of citric acid (3 x 50 mL) and H$_2$O (3 x 50 mL). The organic layer was dried over anhydrous MgSO$_4$, filtered and the filtrate reduced in volume and the resulting solid purified by chromatography on silica gel using a gradient of CH$_2$Cl$_2$ to CH$_2$Cl$_2$/EtOAc (80/20) to obtain the desired compound as a colorless powder (S6, 1.16 g, 71%). mp 150-153 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.42$-7.22 (m, 20H, ArH), 5.60 (br, 1H, NH$_a$), 4.64 (d, $^3J(H,H) = 7.8$ Hz, 2H, CH$_b$), 4.38 (t, $^3J(H,H) = 7.8$ Hz, 1H, CH$_a$), 4.21 (t, $^3J(H,H) = 8.0$ Hz, 1H, CH$_c$), 3.90 (dt, $^3J(H,H) = 8.0$ Hz, 1H, CH$_d$), 2.55 (t, $^3J(H,H) = 7.0$ Hz, 2H, CH$_e$) and 2.27 (t, $^3J(H,H) = 7.0$ Hz, 2H, CH$_f$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 173.1$ (-CO-O), 171.6 (-CO-NH), 142.3 (2C, Ar$_C$-CH- (ipso)), 141.5 (2C, Ar$_C$-CH- (ipso)), 129.2 (4C, ArCH (meta)), 129.0 (4C, ArCH (meta)), 128.6 (4C, ArCH (ortho)), 128.5 (4C, ArCH (ortho)), 127.3 (4C, ArCH (para)), 67.3 (C$_b$), 51.0 (C$_a$), 50.0 (C$_e$),...
44.3 (Cδ), 31.3 (Cε) and 29.9 (Cζ); FABMS: m/z 478 [M+H]+; Anal. calcd for C_{32}H_{31}NO_{3}: C 80.48, H 6.54, N 2.93. Found C 80.70, H 6.68, N 3.02.


Rotaxane S7 was obtained using the general procedure for the preparation of benzylic amide macrocycle containing [2]rotaxanes from thread S6 (1.16 g, 2.4 mmol). The crude solid was subjected to column chromatography on silica gel using CH$_2$Cl$_2$/EtOAc (75/15) as eluent to obtain the desired compound as a colorless powder (S7, 95 mg, 4%). mp 204-205 °C. $^1$H NMR (400 MHz, CDCl$_3$): δ = 8.21 (dd, $^3$J(H$_b$,H$_a$) = 7.8 Hz, $^4$J(H$_b$,H$_c$) = 1.5 Hz, 4H, ArH$_b$), 8.17 (br t, $^4$J(H$_c$,H$_b$) = 1.5 Hz, 2H, ArH$_c$), 7.66 (t, $^3$J(H$_a$,H$_b$) = 7.8 Hz, 2H, ArH$_a$), 7.31-7.08 (m, 24H, ArH(thread) and ArH$_D$), 6.84 (s, 8H, ArH$_F$), 7.33 (br t, $^3$J(H,H) = 5.6 Hz, 1H, NH$_2$), 4.46 (dd, $^2$J(H,H) = 14.4 Hz, $^3$J(H,H) = 5.6 Hz, 4H, ArH$_E$ or ArH$_E'$), 4.40 (dd, $^2$J(H,H) = 14.4 Hz, $^3$J(H,H) = 5.3 Hz, 4H, ArH$_E$ or ArH$_E'$), 4.34 (d, $^3$J(H,H) = 7.3 Hz, 2H, CH$_b$), 4.14 (t, $^3$J(H,H) = 7.3 Hz, 1H, CH$_a$), 4.05 (t, $^3$J(H,H) = 7.8 Hz, 1H, CH$_g$), 3.57 (dd,
$^3J(H,H) = 7.8 \text{ Hz}, \quad ^3J(H,H) = 5.6 \text{ Hz}, \quad \text{H}, \text{CH}_3$, 1.26 (br t, $^3J(H,H) = 7.5 \text{ Hz}, \quad \text{H}, \text{CH}_3$) and 0.86 (br t, $^3J(H,H) = 7.5 \text{ Hz}, \quad \text{H}, \text{CH}_3$), $^{13}$C NMR (100 MHz, $d_6$-DMSO): $\delta = 173.1$ (-CO-O), 171.9 (-CO-NH), 166.1 (4C, -CO- (macrocycle)), 143.2 (2C, ArC-CH (ipso thread)), 141.6 (2C, ArC-CH (ipso thread)), 137.6 (4C, ArC-CH$_2$NH-), 134.9 (4C, ArC-CO-), 130.7 (4C, C$_B$), 129.1 (2C, C$_A$), 128.8 (8C, C$_F$), 128.7 (8C, ArC-CH (meta thread)), 128.0 (8C, ArC-CH (ortho thread)), 126.9 (2C, ArC-CH (para thread)), 126.7 (2C, ArC-CH (para thread)), 125.8 (2C, C$_C$), 66.3 (C$_b$), 50.4 (C$_A$ or C$_g$), 49.3 (C$_A$ or C$_g$), 43.6 (C$_F$), 43.5 (4C, C$_F$), 28.8 (C$_E$ or C$_d$) and 28.1 (C$_E$ or C$_d$); MS (FAB): $m/z = 1010$ [M+H$^+$]; Anal. calcd for $C_{64}H_{59}N_5O_7$: C 76.09, H 5.89, N 6.93. Found C 76.31, H 5.78, N 6.79.

X-ray crystallographic data for compound S7.

$C_{72}H_{82}N_5O_{11}S_4$, $M=1321.67$, crystal size 0.15x0.10x0.08mm, triclinic P-1, $a=9.9959(4), \quad b=12.8280(4), \quad c=15.1241(6) \text{ Å}, \quad \alpha=107.0330(10), \quad \beta=105.5420(10), \quad \gamma=99.0490(10) \degree, \quad V=1726.95(11) \text{ Å}^3, \quad Z=1, \quad \rho_{\text{calc}}=1.271 \text{ Mg m}^{-3}; \quad \text{MoK$_\alpha$ radiation (graphite monochromator, } \lambda=0.71073 \text{ Å), } \mu=0.201 \text{ mm}^{-1}, \quad T=180(2)K. \quad 11064 \text{ data (7963 unique, } R_{\text{int}}=0.0510, \quad 1.72<\theta<28.97 \degree), \quad \text{were collected on a Siemens SMART CCD diffractometer using narrow frames (0.3° in } \omega), \quad \text{and were corrected semi-empirically for absorption and incident beam decay (transmission 0.45-1.00). The structure was solved by direct methods and refined by full-matrix least-squares on } F^2 \quad \text{values of all data (G.M.Sheldrick, SHELXL manual, Siemens Analytical X-ray Instruments, Madison WI, USA, 1994, version 5) to give } \text{wR}=(\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2])^{1/2}=0.2697, \quad \text{conventional } R=0.0963 \text{ for } F \text{ values of } 7963 \text{ reflections with } F_o^2>2\sigma(F_o^2), \quad S=0.873 \text{ for 438 parameters. Residual electron density extremes were 0.998 and -0.719 Å}^{-3}. \quad \text{Amide hydrogen atoms were refined isotropically with the remainder constrained; anisotropic displacement parameters were used for all non-hydrogen atoms.}
To a stirred solution of 2,2-diphenylethylamine (5.00 g, 25.3 mmol) in anhydrous THF (25 mL) at 0 °C, was added dropwise a solution of maleic anhydride (2.50 g, 25.5 mmol) in anhydrous THF (10 mL). The mixture obtained was allowed to stir at rt for 16 h then reduced in volume and the resulting oil taken up in CHCl₃ (50 mL) and washed with a solution of 1N NaOH (3 x 20 mL) and H₂O (1 x 20 mL). The organic layer was dried over anhydrous MgSO₄, filtered and the solvent removed under reduced pressure to obtain a colorless solid which was recrystallized from CH₂Cl₂. (S₈, 5.62 g, 75%). m.p. 209 °C. \(^\text{1}^H\) NMR (400 MHz, CDCl₃): \(\delta = 7.29-7.23\) (m, 4H, ArH (meta)), 7.20-7.14 (m, 6H, ArH (ortho and para)), 6.43 (br t, \(^3J(H,H) = 5.7 \text{ Hz}\), 1H, NH), 6.19 (d, \(^3J(H,H) = 12.6 \text{ Hz}\), 1H, CH₂), 6.02 (d, \(^3J(H,H) = 12.6 \text{ Hz}\), 1H, CH₂), 4.18 (t, \(^3J(H,H) = 8.0 \text{ Hz}\), 1H, CH₃) and 3.95 (dd, \(^3J(H,H) = 8.0 \text{ Hz}, \ ^5J(H,H) = 5.7 \text{ Hz}\), 2H, CH₂); \(^{13}C\) NMR (100 MHz, CDCl₃): \(\delta = 166.0\) (-CO-OH), 164.5 (-CO-NH), 140.7 (2C, Ar-CH (ipso)), 137.1 (C₆), 130.2 (C₅), 129.0 (4C, ArCH (meta)), 127.9 (4C, ArCH (ortho)), 127.4 (2C, ArCH (para)), 50.0 (C₆) and 44.6 (C₅); HRMS: \(m/z = 296.12884\) [(M + H)\(^+\)]; Anal. calcd for C\(_{18}\)H\(_{17}\)NO\(_3\): C 73.20, H 5.80, N 4.74. Found C 73.13, H 5.85, N 4.61.
(12-Aminododecyl)-carbamic acid tert-butyl ester, S9.

To a stirred solution of 1,12-diaminododecane (20.00 g, 100 mmol) in CHCl₃ (500 mL) was added di-tert-butyl dicarbonate (11 g, 50 mmol). The reaction was allowed to stir for 16 h at rt after which time the solvent was removed under reduced pressure and the residual oil subjected to column chromatography using a solvent gradient of CHCl₃/MeOH (95/5) to CHCl₃/MeOH/NH₄OH (89/10/1) to obtain a colorless solid (S9, 9 g, 60%). mp 96-97 °C. ¹H NMR (400 MHz, CDCl₃): δ = 4.50 (br t, J(H,H) = 5.7 Hz, 1H, NHb), 3.10 (td, J(H,H) = 7.0 Hz, J(H,H) = 5.7 Hz, 2H, CH2), 2.67 (t, J(H,H) = 7.0 Hz, 2H, CH2), 1.49-1.36 (br, 13H, CHa, CHb and CH2) and 1.33-1.20 (br, 16H, -CH2- (alkyl chain)); ¹³C NMR (100 MHz, CDCl₃): δ = 156.3 (-CO-), 79.2 (-CH3), 42.6 (C6), 40.9 (C5), 34.2 (-CH2-), 30.4 (-CH2-), 30.0 (-CH2-), 29.9 (-CH2-), 29.7 (-CH2-), 29.6 (-CH2-), 29.2 (-CH2-), 28.9 (-CH2-), 28.8 (3C, C6), 27.2 (-CH2-), 27.1 (-CH2-); MS (FAB): m/z = 301 [M +H]+; Anal. calcd for C17H36N2O2: C 67.95, H 12.08, N 9.32. Found C 67.73, H 11.94, N 9.31.
N-(12-tert-Butoxycarbonylaminododecyl)-succinamic acid 2,2-diphenylethyl ester, S10.

To a stirred solution of S5 (0.40 g, 1.30 mmol), S9 (0.40 g, 1.30 mmol) and 4-DMAP (0.20 g, 1.60 mmol) in anhydrous CH₂Cl₂ (200 mL) cooled in an ice bath, was added EDCI-HCl (0.28 g, 1.50 mmol) and the reaction allowed to stir for 48 h at rt. The solution was washed with a saturated solution of citric acid (2 x 50 mL) and H₂O (2 x 50 mL) and the organic layer dried over anhydrous MgSO₄, filtered and the filtrate reduced in volume. The solid obtained was subjected to column chromatography using a solvent gradient of CHCl₃ to CHCl₃/MeOH (90/10) to obtain a colorless solid (S10, 0.52 g, 68%). mp 88-89 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.22-7.18 (m, 4H, ArH (meta)) 7.17-7.09 (m, 6H, ArH (ortho and para)), 5.52 (t br, 3J(H,H) = 5.7 Hz, 1H, NH₂), 4.56 (d, 3J(H,H) = 7.7 Hz, 2H, CH₄), 4.47 (br, 1H, NH), 4.28 (t, 3J(H,H) = 7.7 Hz, 1H, CH₃), 3.10 (td, 3J(H,H) = 7.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₂), 3.02 (br, 2H, CH₂), 2.50 (t, 3J(H,H) = 7.0 Hz, 2H, CH₂), 2.25 (t, 3J(H,H) = 7.0 Hz, 2H, CH₂), 1.42-1.30 (m, 13H, CH₂, CH₃ and CH₄) and 1.25-1.13 (m, 16H, -CH₂-(alkyl chain)); ¹³C NMR (100 MHz, CDCl₃): δ = 173.2 (-CO-O (succinic)), 171.6 (-CO-NH (succinic)), 156.3 (-CO-), 141.4 (2C, ArC- (ipso)), 128.9 (4C, ArCH (meta)), 128.6 (4C, ArCH (ortho)), 127.2 (2C, ArCH (para)), 79.4 (-C(CH₃)₃), 67.3 (C₆), 50.2 (C₅), 41.0 (C₄), 40.0 (C₃), 32.4 (C₂), 31.0 (C₁), 30.4 (-CH₂-), 30.1 (-CH₂-), 30.0-29.9 (3C, -CH₂-), 29.6 (-CH₂-), 29.5 (-CH₂-), 29.4 (-CH₂-), 28.8 (3C, C₆), 27.3 (-CH₂-) and 27.2 (-CH₂-); MS (FAB): m/z = 581 [(M + H)+]; Anal. calcd for C₃₅H₅₂N₂O₅: C 72.38, H 9.02, N 4.82. Found C 72.62, H 9.40, N 5.02.
To a stirred solution of 2,2-diphenylethylamine (0.50 g, 2.50 mmol), fumaric acid monoethylester (0.37 g, 2.50 mmol) and 4-DMAP (0.33 g, 2.70 mmol) in anhydrous CH₂Cl₂ (200 mL) cooled in an ice bath was added EDCI·HCl (0.52 g, 2.7 mmol). After 24 h the solution was washed with a saturated solution of citric acid (3 x 50 mL) and H₂O (3 x 50 mL) and the organic layer dried over anhydrous MgSO₄, filtered and the filtrate reduced in volume to obtain a colorless solid that was recrystallized from EtOAc (S11, 0.70 g, 85%). mp 112-113 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.34-7.27 (m, 4H, ArH (meta)), 7.26-7.19 (m, 6H, ArH (ortho and para)), 6.77 (d, ³J(H,H) = 14.4 Hz, 1H, CH₆), 6.72 (d, ³J(H,H) = 14.4 Hz, 1H, CH₆), 5.90 (br t, ³J(H,H) = 5.7 Hz, 1H, NH), 4.25-4.15 (m, 3H, CHa and CHb), 3.98 (dd, ³J(H,H) = 8.0 Hz, ³J(H,H) = 5.7 Hz, 2H, CHb) and 1.28 (t, ³J(H,H) = 7.0 Hz, 3H, CHg); ¹³C NMR (100 MHz, CDCl₃): δ = 165.6 (-CO-OEt), 163.6 (-CO-NH), 141.5 (2C, ArC- (ipso)), 136.0 (C₆), 130.6 (C₆), 128.9 (4C, ArCH (meta)), 128.1 (4C, ArCH (ortho)), 127.0 (2C, ArCH (para)), 61.2 (C₆), 50.3 (C₆), 44.1 (C₆) and 14.1 (C₆); MS (FAB): m/z = 324 [(M + H)⁺]; Anal. calcd for C₂₀H₂₁NO₃: C 74.28, H 6.55, N 4.33. Found C 74.83, H 6.91, N 4.38.
**N-(2,2-Diphenylethyl)-fumaricamide acid, S12.**

![Chemical Structure](image)

To a stirred solution of **S11** (0.70 g, 2.20 mmol) in EtOH (50 mL) was added dropwise a solution of NaOH (0.10 g, 2.40 mmol) in H₂O (2.5 mL). After 16 h the solution was reduced in volume and washed several times with Et₂O to obtain a colorless powder which was recrystallized from CHCl₃ (S12, 0.58 g, 91%). mp >270 °C (decomp). ¹H NMR (400 MHz, d₆-DMSO): δ = 12.83 (br s, 1H, -COOH), 8.57 (br t, 3J(H,H) = 5.7 Hz, 1H, NH), 7.33-7.15 (m, 10H, ArH), 6.87 (d, 3J(H,H) = 15.4 Hz, 1H, CH₆), 6.47 (d, 3J(H,H) = 15.4 Hz, 1H, CH₆), 4.22 (t, 3J(H,H) = 8.0 Hz, 1H, CH₂) and 3.81 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₂); ¹³C NMR (100 MHz, d₆-DMSO) δ 168.0 (-CO-OH), 164.5 (-CO-NH), 143.1 (2C, ArC- (ipso)), 134.3 (C₀), 134.0 (C₀), 128.8 (4C, ArCH (meta)), 128.2 (4C, ArCH (ortho)), 126.7 (2C, ArCH (para)), 50.3 (C₀) and 43.7 (C₀); MS (FAB): m/z = 296 [(M + H)⁺]; Anal. calcd for C₁₈H₁₇NO₃: C 73.20, H 5.80, N 4.70. Found C 73.10, H 5.20, N 4.73

**N-(2,2-Diphenylethyl)-succinic acid, S13.**

![Chemical Structure](image)

To a stirred solution of succinic anhydride (2.53 g, 25.3 mmol) in anhydrous THF (25 mL) was added at rt dropwise a solution of 2,2-diphenylethylamine (5.00 g, 25.3 mmol) in anhydrous THF (25 mL). After 16 h the solvent was removed under
reduced pressure and the resulting oil recrystallized from CH₂Cl₂ to obtain a colorless solid. (S13, 7.16 g, 95%). mp 153-154 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.34-7.28 (m, 4H, ArH (meta)), 7.26-7.19 (m, 6H, ArH (ortho and para)), 5.63 (br t, ³J(H,H) = 5.7 Hz, 1H, NH), 4.18 (t, ³J(H,H) = 8.0 Hz, 1H, CH₃), 3.90 (dd, ³J(H,H) = 8.0 Hz, ³J(H,H) = 5.7 Hz, 2H, CH₂), 2.63 (t, ³J(H,H) = 6.5 Hz, 2H, CH₂), 2.39 (t, ³J(H,H) = 6.5 Hz, 2H, CH₂); ¹³C NMR (100 MHz, CDCl₃): δ = 176.2 (-CO-OH), 172.1 (-CO-NH), 141.5 (2C, ArC- (ipso)), 128.8 (4C, ArCH (meta)), 128.0 (4C, ArCH (ortho)), 127.0 (2C, ArCH (para)), 50.4 (C₆), 44.0 (C₆), 30.6 (C₆) and 29.6 (C₆); MS (FAB): m/z = 298 [(M + H)⁺]; Anal. calcd for C₁₈H₁₉NO₃: C 72.71, H 6.44, N 4.71. Found C 72.83, H 6.57, N 4.80.


To a stirred solution of S13 (0.50 g, 1.68 mmol) in CH₂Cl₂ was added thionyl chloride (0.12 mL, 1.68 mmol). The solution was heated until complete dissolution of S13 and the resulting solution added dropwise to a solution of 1,12-diaminododecane (1.68 g, 8.40 mmol) and Et₃N (0.17 g, 1.68 mmol) in CH₂Cl₂ at 0 °C. After 30 min the reaction mixture was washed with 1N NaOH (1 x 100 mL) and H₂O (1 x 100 mL). The organic layer was dried over anhydrous MgSO₄, filtered and the filtrate reduced in volume to obtain a solid that was subjected to column chromatography using a solvent gradient of CHCl₃ to CHCl₃/MeOH (90/10) to obtain a colorless solid (S14, 0.28 g, 35%). mp 78-79 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.36-7.29 (m, 4H, ArH (meta)), 7.28-7.21 (m, 6H, ArH (ortho and para)), 6.14 (br t, ³J(H,H) = 5.7 Hz, 1H, NH₂), 6.09 (br t, ³J(H,H) = 5.7 Hz, 1H, NH₂), 4.19 (t, ³J(H,H)
= 8.0 Hz, 1H, CH₃), 3.89 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₆), 3.19 (td, 3J(H,H) = 7.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₂), 2.69 (t, 3J(H,H) = 7.0 Hz, 2H, CH₂), 2.41 (m, 4H, CH₄ and CH₂), 1.40-1.54 (m, 4H, CH₂ and CH₃) and 1.20-1.40 (m, 16H, -CH₂- (alkyl chain)); ¹³C NMR (100 MHz, CDCl₃): δ = 172.6 (-CO-), 172.3 (-CO-), 142.3 (2C, ArC- (ipso)), 129.1 (4C, ArCH (meta)), 128.4 (4C, ArCH (ortho)), 127.2 (2C, ArCH (para)), 51.0 (C₆), 44.2 (C₁), 42.7 (C₄), 40.0 (C₇), 34.3 (C₅), 32.2 (C₈ or C₉), 32.1 (C₆ or C₇), 30.0 (-CH₂-), 29.9 (2C, -CH₂-), 29.8 (-CH₂-), 29.7 (-CH₂-), 27.3 (-CH₂-) and 27.2 (-CH₂-); MS (FAB): m/z = 480 [(M + H)⁺].


5-(2,2-Diphenylethylcarbamoyl)-pentanoic acid ethyl ester, S15.

A solution of adipic acid monoethyl ester (4.01 g, 23 mmol), 2,2-diphenylethylamine (5.00 g, 25 mmol) and 4-DMAP (2.81 g, 23 mmol) in CH₂Cl₂ (250 mL) was stirred at 0 °C for ten minutes followed by addition of EDCI-HCl (4.42 g, 23 mmol). After 16 h the organic phase was washed with 1N HCl (3 x 70 mL), saturated aqueous NaHCO₃ (3 x 70 mL) and brine (1 x 70 mL). The organic layer was dried over anhydrous MgSO₄, filtered and the filtrate concentrated to give the product as a colorless solid. (S5, 7.03 g, 86%). ¹H NMR (400 MHz, CDCl₃): δ = 7.34-7.21 (m, 10H, ArH₆), 5.70 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₃), 4.23 (t, 3J(H,H) = 8.0 Hz, 1H, CH₆), 4.13 (q, 3J(H,H) = 7.0 Hz, 2H, CH₂), 3.91 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₂), 2.26 (t, 3J(H,H) = 7.0 Hz, 2H, CH₂ or CH₃), 2.09 (t, 3J(H,H) = 7.0 Hz, 2H, CH₂ or CH₃), 1.56 (m, 4H, CH₄ and CH₂), 1.27 (t, 3J(H,H) = 7.0 Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ = 173.8 (-CO-OEt), 172.9 (-CO-NH), 142.3 (2C, 131.2 (ArC-), 129.1 (ArC- (meta)), 127.9 (ArC- (para)), 50.0 (C₆), 45.2 (C₁), 42.6 (C₄), 40.0 (C₇), 34.3 (C₅), 32.2 (C₈ or C₉), 32.1 (C₆ or C₇), 30.0 (-CH₂-), 29.9 (2C, -CH₂-), 29.8 (-CH₂-), 29.7 (-CH₂-), 27.3 (-CH₂-) and 27.2 (-CH₂-); MS (FAB): m/z = 480 [(M + H)⁺].

ArC- (ipso)), 129.1 (4C, ArCH (meta)), 128.5 (4C, ArCH (ortho)), 127.2 (2C, ArCH (para)), 60.7 (C₈), 51.0 (C₆), 44.17 (C₇), 36.55 (C₄ or C₉), 34.31 (C₄ or C₉), 25.41 (Cᵫ or Cᵪ), 24.7 (Cᵪ or Cᵫ) and 14.66 (Cᵪ); MS(FAB): \( m/z = 354 \) [(M + H)⁺]; Anal. calcd for C₂₂H₂₇NO₃: C 74.76, H 7.70, N 3.96. Found C 74.88, H 7.95, N 4.04.

5-(2,2-Diphenylethylcarbamoyl)-pentanoic acid, S16.

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\begin{array}{c}
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\text{NH} \\
\text{O} \\
\text{Ph} \\
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To a solution of S15 (7.03 g, 19.9 mmol) in EtOH (50 mL) was added aqueous KOH (5.58 g in 9 mL of H₂O, 99.4 mmol) and the resulting solution stirred for 2 h at 78 °C. The yellow solution was cooled to rt, poured into water and acidified with dropwise addition of concentrated HCl resulting in a colorless precipitate that was filtered and dried \textit{in vacuo} to give the product as a colorless solid (S16, 6.12 g, 95%).

\(^1\text{H} \text{NMR} (400 \text{ MHz}, \text{CDCl}_3): δ = 7.36-7.23 \text{ (m, 10H, ArH)}, 5.55 \text{ (br t, } ^3\text{J(H,H)} = 5.7 \text{ Hz, 1H, NH}_2), 4.21 \text{ (t, } ^3\text{J(H,H)} = 8.0 \text{ Hz, 1H, CH}_2), 3.92 \text{ (dd, } ^3\text{J(H,H)} = 8.0 \text{ Hz, } ^3\text{J(H,H)} = 5.7 \text{ Hz, 2H, CH}_2), 2.33 \text{ (t, } ^3\text{J(H,H)} = 7.0 \text{ Hz, 2H, CH}_2), 2.12 \text{ (t, } ^3\text{J(H,H)} = 7.0 \text{ Hz, 2H, CH}_2), 1.59 \text{ (m, 4H, CH}_3 \text{ and CH}_2); ^{13}\text{C NMR (100 MHz, CDCl}_3): δ = 178.2 \text{ (-CO-OH), 172.8 \text{ (-CO-NH), 141.7 \text{ (2C, ArC- (ipso))}, 128.74 \text{ (4C, ArC- (meta))}, 128.0 \text{ (4C, ArC- (ortho))}, 126.9 \text{ (2C, ArC- (para))}, 50.6 \text{ (C}_6), 43.79 \text{ (C}_9), 36.2 \text{ (C}_8), 33.5 \text{ (C}_4), 24.9 \text{ (C}_8 \text{ or C}_9) \text{ and 24.0 \text{ (C}_4 \text{ or C}_9); MS(FAB): } m/z = 326 \text{ [(M + H)}^+\text{]}; \text{HRMS: } m/z = 326.1763 \text{ [(M + H)}^+\text{]} \text{ (Anal. calcd for C}_{20}\text{H}_{24}\text{O}_3: m/z = 326.41550). \text{Anal. calcd for C}_{20}\text{H}_{23}\text{O}_3: C 73.82, H 7.12, N 4.30. \text{Found C 73.82, H 7.10, N 4.17.}
(12-[5-(2,2-Diphenylethylcarbamoyl)-pentanoylamino]-dodecyl]-carbamic acid tert-butyl ester, S17.

A solution of S16 (0.50 g, 1.54 mmol), S9 (0.51 g, 1.69 mmol) and 4-DMAP (0.19 g, 1.54 mmol) in CHCl₃ (20 mL) was stirred at 0 °C for 10 minutes followed by addition of EDCI·HCl (0.29 g, 1.54 mmol). After 16 h the reaction mixture was diluted with CHCl₃ (10 mL) and the organic phase washed with 1N HCl (3 x 10 mL), saturated NaHCO₃ (3 x 10 mL) and brine (1 x 10 mL). The organic layer was dried over anhydrous MgSO₄, filtered and the filtrate concentrated to give the product as a colorless solid (S17, 0.85 g, 92%). ¹H NMR (400 MHz, CDCl₃): δ = 7.33-7.20 (m, 1OH, ArH), 5.84 (br t, ³J(H,H) = 5.7 Hz, 1H, NH₈), 5.79 (br t, ³J(H,H) = 5.7 Hz, 1H, NH₈), 4.57 (br t, ³J(H,H) = 5.7 Hz, 1H, NH₈), 4.22 (t, ³J(H,H) = 8.0 Hz, 1H, CH₆), 3.90 (dd, ³J(H,H) = 8.0 Hz, ³J(H,H) = 5.7 Hz, 2H, CH₆), 3.23 (td, ³J(H,H) = 7.0 Hz, ³J(H,H) = 5.7 Hz, Hz, 2H, CH₆), 3.11 (m, 2H, CH₆), 2.11 (t, ³J(H,H) = 7.3 Hz, 2H, CH₆ or CH₆), 2.09 (t, ³J(H,H) = 7.3 Hz, 2H, CH₆ or CH₆), 1.56 (m, 4H, CH₆ and CH₆), 1.46 (s, 13H, CH₆, CH₆ and CH₆), 1.27 (br s, 16H, CH₆ (alkyl chain)); ¹³C NMR (100 MHz, CDCl₃): δ = 172.7 (-CO-), 172.5 (-CO-), 157.6 (-CO-O), 141.9 (2C, ArC- (ipso)), 128.7 (4C, ArCH (meta)), 128.0 (4C, ArCH (ortho)), 126.8 (2C, ArCH (para)), 79.4 (-C(CH₃)₃), 50.6 (Ca), 43.7 (Cb), 40.6 (Ci), 39.6 (Ci), 36.2 (Cd or

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C₉, 36.1 (C₆ or C₇), 30.0 (-CH₂-), 29.6 (-CH₂-), 29.5 (-CH₂-), 29.3 (-CH₂-), 29.4 (-CH₂-), 26.9 (-CH₂-), 26.8 (-CH₂-), 26.9 (-CH₂-), 26.8 (-CH₂-), 24.9 (-CH₂-), 24.8 (-CH₂-); MS(FAB): m/z = 608 [(M + H)⁺]; HRMS: m/z = 608.44148 [(M + H)⁺]; Anal. calcd for C₃₇H₅₇N₃O₄: C 73.11, H 9.45, N 6.91. Found C 72.97, H 9.50, N 6.85.

Hexanedioic acid (12-aminododecyl)-amide (2, 2-diphenylethyl)-amide, S18.

A solution of S17 (0.4 g, 6.58 mmol) in trifluoroacetic acid (15 mL) was stirred at rt for 30 minutes. The reaction mixture was concentrated under reduced pressure and CH₂Cl₂ (20 mL) added. The organic phase was washed with 1N NaOH (2 x 10 mL), brine (1 x 10 mL), dried over anhydrous MgSO₄, filtered and concentrated to give the product as a colorless solid (S18, 0.22 g, 66%). ¹H NMR (400 MHz, CDCl₃): δ = 7.35-7.22 (m, 10H, ArH), 5.77 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₂ or NH₃), 5.75 (br t, 3J(H,H) = 5.7 Hz, 1H, NH₂ or NH₃), 4.22 (t, 3J(H,H) = 8.0 Hz, 1H, CH₂), 3.91 (dd, 3J(H,H) = 8.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₂), 3.24 (td, 3J(H,H) = 7.0 Hz, 3J(H,H) = 5.7 Hz, 2H, CH₂), 2.69 (m, 2H, CH₂), 2.11 (t, 3J(H,H) = 7.3 Hz, 2H, CH₂ or CH₃), 2.09 (t, 3J(H,H) = 7.3 Hz, 2H, CH₂ or CH₃), 1.58 (m, 4H, CH₂ and CH₃), 1.51 (m, 2H, CH₂), 1.45 (m, 2H, CH₂), 1.28 (brs, 16H, -CH₃, alkyl); ¹³C NMR (100 MHz, CDCl₃): δ = 172.7 (-CO-), 172.6 (-CO-), 141.9 (2C, ArC- (ipso)), 128.7 (4C, ArCH (meta)), 128.0 (4C, ArCH (ortho)), 126.8 (2C, ArCH (para)), 50.6 (Ca), 43.7 (Cb), 42.2 (Cc), 39.5 (C₁), 36.2 (C₄ or C₅), 36.1 (C₆ or C₇), 33.7 (-CH₂-), 29.6-29.5 (4C, -CH₂-), 29.4 (-CH₂-), 29.2 (-CH₂-), 26.9 (-CH₂-), 26.8 (-CH₂-), 24.9 (-CH₂-), 24.8 (-CH₂-); MS(FAB): m/z = 508 [(M + H)⁺]; HRMS: m/z = 508.391143 [(M + H)⁺]; Anal. calcd for C₃₂H₄₉N₃O₂: C 75.70, H 9.73, N 8.28. Found C 75.09, H 9.76, N 8.20.
Appendix: List of Publications

