

Unidirectional Rotation in Catenanes

In this work, two different catenane based molecular motors were reviewed. These motor molecules consist of two interlocked rings, one of which has binding sites for the other ring. The smaller ring without the binding sites can rotate over the other macrocycle when the affinities of the binding sites are changed. If the rotation is unidirectional the molecule could in principle perform work. In the two systems investigated, unidirectionality was achieved but it was not shown that the molecules could indeed perform work. The molecular motors showed good unidirectionality, but the speed of rotation was quite poor. Therefore, these motors are still far from ideal. In the last section some possible improvements are suggested.

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1. Introduction

The invention of the steam engine marked the start of the industrial revolution. Since then machines have become more and more complex. Modern day machines are able to do almost any task required. Nanoscience might just trigger its own industrial revolution when artificial molecular machines become powerful enough to perform technological relevant tasks. In principle molecular based machines can be created to do many of the task current day machines can do. This might seem unlikely at first glance, but nature provides numerous examples of molecular machinery performing visible macroscopic work. An important example is the system of flagellar proteins some bacteria use to propel themselves through liquid water. A more impressive example is nature's motor that controls muscle movement. Muscle contraction is caused by the guided movement of myosin proteins along actin filaments. The concerted action of many of these proteins is capable of doing a lot of useful macroscopic work.¹ Even though the numerous examples provided by nature, it is very difficult to make artificial molecular machines. The biological machinery itself is not suited for the use in artificial systems, for several reasons. First of all the stability of different molecules is limited outside a biological cell. *In vivo*, the conditions remain within certain parameters, within which the machines function properly, by the numerous feedback mechanisms of the cell. Also, many repair mechanisms exist through which damaged machinery is repaired. To replicate the cells feedback and repair mechanism is beyond the limits of current day nanotechnology.²

1.1. Artificial molecular machines

In order to create molecular machines that do not rely on the living cell for its operation, it is more feasible to create completely synthetic molecular machines. These machines are potentially able to operate under a wide range of conditions. The tasks these molecular machines can perform can be very diverse. It is most likely that the main applications will be those in which nanoscale precision is required. Manipulation on these scales is very difficult with conventional machines, although some techniques like STM and AFM are also capable of manipulation on the nanoscale. At this point in time no useful perspective can be given since the field of artificial machines is still in its infancy. The design of molecular machines is not straight forward. This is because molecular machines operate within a very different set of parameters compared to conventional machines. It is important to keep in mind that downscaling of conventional machines to the molecular level, or a top-down approach, is not possible. Important building blocks of macroscopic machines, such as engines or gears, cannot be build out of a collection of molecules in a one to one fashion. This is because of the fundamentally different properties of macroscopic and microscopic system, as will be discussed later. Instead, a bottom-up approach has to be used. In this kind of approach one tries to exploit the known properties of microscopic building blocks in order to create a functional device.

The current stage of the development of molecular machines is manly that of design, synthesis and characterisation of subunits. These subunits are often compounds that can move under influence of external stimuli. If the design is right, these compounds are in principle able to do some amount of work. Already many different kinds of molecules are reported which show various kinds of controlled motion. Examples include molecular switches³, elevator⁴, muscle like molecules⁵ and molecular scissors⁶. However, actually making these molecules do work is an entirely different story. So far only a limited number of artificial molecular machines were shown to be capable of macroscopic work. Three important examples are shown in Figure 1, Figure 2 and Figure 3. The first example shows how a glass rod is rotated under the combined influence of molecular motors added to a liquid crystalline material. The molecular motor will rotate unidirectionally under irradiation with UV light. The fact that the rod moves is proof of the statement that the molecular motor can be used to perform work.⁷ The second example shows the uphill movement of a droplet during irradiation with UV light. The reason for the movement is a change in wettability induced by the shuttling of a rotaxane ring from one station to another.⁸ The last example shows the bending of a cantilever as a result of the contraction of many surface mounted muscle like molecules. These artificial muscle molecules are [3]rotaxanes. The change in structure of these molecules is also shown.⁹

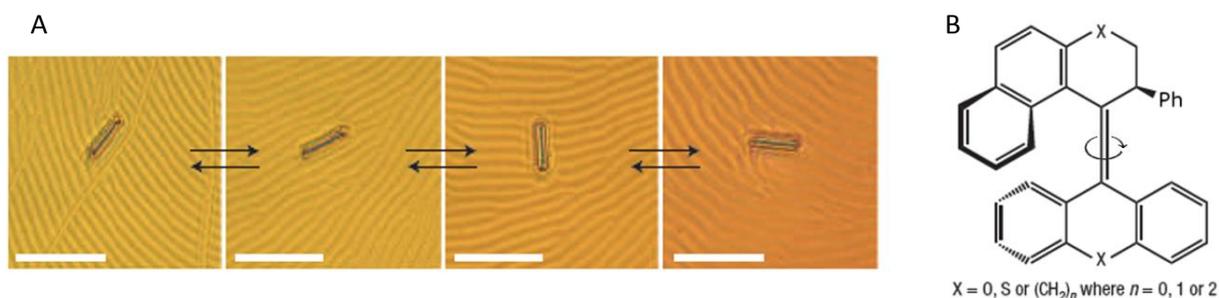


Figure 1: The motion of a glass rod on a liquid crystal doped with a molecular motor. (A) Photographs taken at 15s intervals during irradiation with UV light. Scale bar 50 μ m. (B) The general structure of the motor compound used. Images adapted from (2)

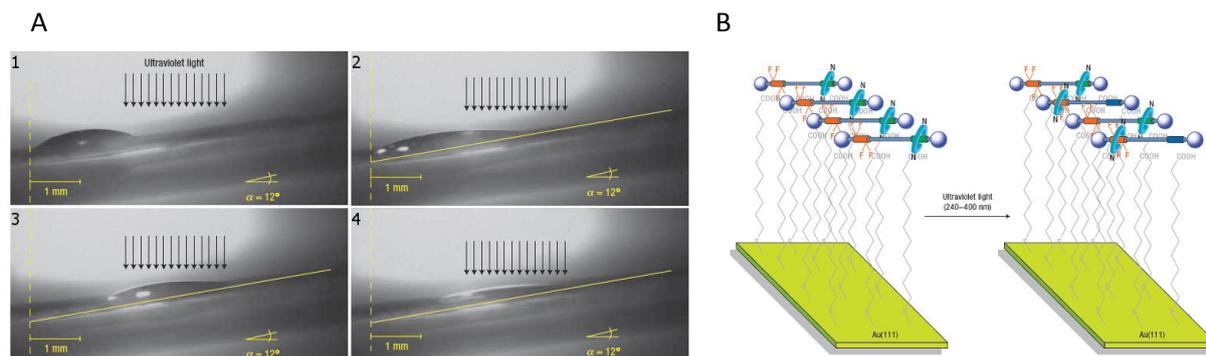


Figure 2: The movement of a diiodomethane droplet on a surface coated with a molecular motor. (A) Photographs taken (1) before and after (2) 160s, (3) 245s and (4) 640s of irradiation. (B) a schematic representation of the system used. Images adapted from (8)

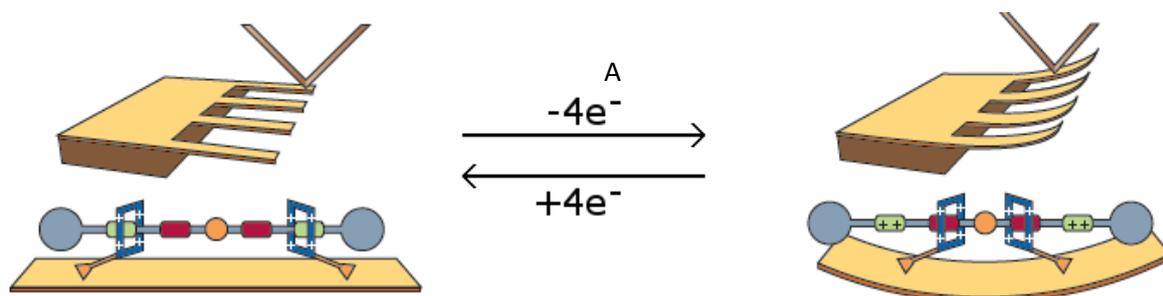


Figure 3: Deflection of a cantilever caused by the contraction and expansion of a surface mounted [3]rotaxane. Image adapted from (2)

1.2. Definition of molecular rotors and motors

The definition of both a rotor and a motor become somewhat ambiguous at the nanoscale. Different definitions are given in various works. Often the dictionary definitions for macroscopic quantities are not applicable at the molecular level. In the following, the definitions adopted for this work will be given. These are the definitions given by Kottas et. al. from 2005¹⁰. Also, some of the controversies will be outlined.

The terms rotator and rotor have very similar meanings in macroscopic machines, where the latter is more specifically used for motors and dynamos. According the Oxford English Dictionary, a rotator is “A thing, apparatus, part, etc., which has a rotatory motion or action” and a rotor is “The rotating part of a dynamo or motor”. The complementary stationary part of a motor or dynamo is usually called the stator. However, for molecular motors, rotor and rotator are given separate meanings. A molecular rotor is “a molecular system in which a molecule or part of a molecule rotates against another part of the molecule or against a macroscopic entity such as a surface or a solid”. A rotator is then defined as the “part of the molecule or system that rotates against the rest” and a stator as “the stationary part of the system with respect to which the rotator turns”. Therefore, the stator and the rotator together make up the molecular rotor. In conventional motors the definitions for stator and rotator will not lead to confusion.

However, molecules are always in motion, and this motion includes rotation around many different axes. Therefore the terms rotor and stator are used only for the parts of the system that undergo large amplitude rotations. Another complication is met when trying to assign the terms rotor and stator to different parts of the molecule. Unless one part of the molecule is attached to some macroscopic object, in which the free part can be seen as the rotator and the fixed part as the stator, the distinction is not unambiguous. In the case of a free rotor, the part with the lower moment of inertia is usually considered the rotator, and the part with the higher moment the stator.

For macroscopic systems it is easy to define a motor. According to the Oxford English Dictionary, a motor is “*a machine or mechanical agency which imparts motion*”. In other terms, a motor is something that consumes a fuel of some kind to produce work. In molecular systems, it is often difficult to convert the energy put into the system in actual work. This is comparable with an ordinary motor operating in idle. Therefore, a molecule is said to be a molecular motor if it is “*a molecular rotor capable of produce useful work*”. This definition clearly distinguishes molecular motors from molecular rotors, although in practice the distinction is not always clear. This is because it is hard to say that a molecular rotor is capable of doing work if rotation is only observed without an opposing force. The definition of a molecular motor given only includes rotary motors, but in principle they apply just as well to linear molecular motors.

1.3. Brownian motion

The properties of macroscopic and microscopic systems are fundamentally different. In the world of the molecular motor, Van der Waals and Coulomb forces are the most important forces. These forces govern the interactions between all species present. Forces that are important in the macroscopic regime, such as gravity, play a very limited role. Gravity is not important because the molecules have very low mass, and any effect is negligible compared to other forces. Also, effects that have to do with inertia of the components are neglectable. However, the most important factor at the nanoscale is temperature, or Brownian motion. Because of temperature, everything is moving on its own. This motion is not directed in any sense, but is completely random. Therefore the challenge is not to make objects move, but to control the movement. In other words, if one wants to make a molecular motor, some degree of directionality must be built in into the system. Directed motion, unlike random thermal motion, can be used to do work. In order to do work, an energy input is also necessary to obey the rules of thermodynamics. This amount of energy can be quite low compared to the thermal energy of the surrounding.¹¹

In principle there are two ways of gaining control over the microscopic motion. One can either try to overcome the inherent Brownian motion, or use it to their advantage. In order to overcome Brownian motion in a molecular motor it is necessary to make the barrier for the intended motion higher than the energy available from ambient thermal energy. Good examples of molecular motors that work by stopping the interference of Brownian motion with the function are those that use a carbon-carbon double bond as a rotation axis. At ambient temperatures, there is not enough energy to do a cis/trans isomerisation of the double bond. However, when energy is put into the system by irradiation with light of the appropriate wavelength, the first isomerisation is triggered. Isomerisation back to the ground state is thermally activated and, because of chirality, in the same direction. The motor will not be rotating without an external energy input, but with an energy input full 360° unidirectional rotation is achieved.⁷ This is analogous to a macroscopic motor, which will only work if fuel of some kind is consumed. Note that only the isomerisation of the double bond is prevented by a high energy barrier. Other rotational, vibrational or translational movements are unaffected, but these are not relevant for the function of the molecule.

The other possibility is making use of the Brownian motion to make a molecular motor work. In these kind of motors, an external energy input is needed to provide a driving force for the movement. The movement itself is governed by Brownian motion. This kind of transport is called fluctuation driven transport, and the molecular machines in this category are often referred to as Brownian ratchets or Brownian motors. Three components are typically needed. The first is a randomizing element, this is the thermal energy of the system.

The second is an energy input, which is needed to obey the second law of thermodynamics as work needs to be done by the motor. The last is an asymmetry in the potential to make the molecule move in the specified direction. This kind of mechanisms can account for the working principles of biological motors, which are generally driven by thermal motion. A good illustration of the workings of the Brownian ratchet is given by the flashing ratchet mechanism¹². A series of potential energy curves associated with such a system is shown in Figure 4. It consists of a periodic series of two different potential minima and two different potential maxima. In the ground state, the particle will reside in the lowest minimum. Now, all minima and maxima are simultaneously raised and lowered, such that the energy difference between the minima and that between the maxima changes sign. This corresponds to event 1. The molecule will be in a non-equilibrium situation. The randomising element, Brownian motion, will cause the particle to go to the new global minimum. This corresponds to event 2. The direction of movement will be dictated by the lowest energy barrier. If subsequently the minima and maxima are changed back to their original values, the same situation will occur. This is event 3. Again the particle will move in the same direction, as in event 4. Repeating the cycle will cause a net unidirectional movement. The step to change the equilibrium of the system is the step that requires energy input, not the thermally driven motion to the new global minimum. Therefore, no motion would be possible without Brownian motion, in contradiction to the motor compounds described above.

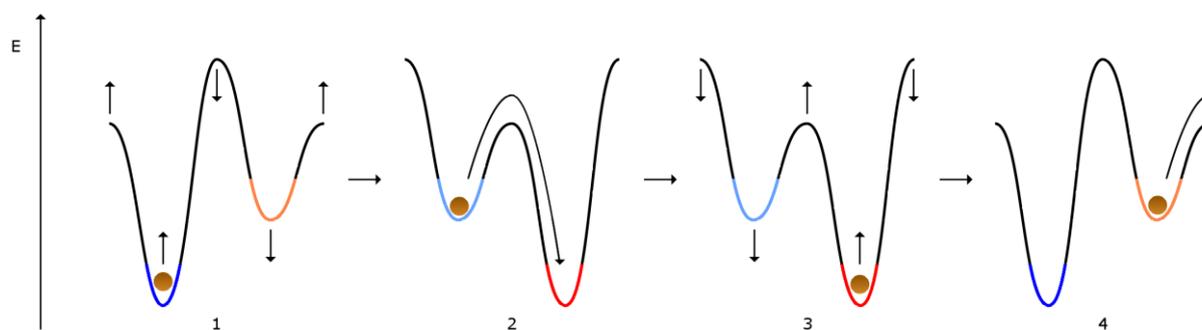


Figure 4: A series of potential energy surfaces associated with the flashing ratchet mechanism that shows unidirectional Brownian particle transport

1.4. Interlocked molecules

Interlocked molecules are molecules that consist of two or more fragments that are not covalently linked. However, it does take the breaking of at least one covalent bond to separate the different fragments. Because of this fact, these molecules are strictly not supramolecular complexes, but they are often assigned to this class of compounds. Since the fragments are interlocked, many degrees of freedom are severely restricted. However, other degrees of freedom are still open, and allow large amplitude motions. The amplitudes are typically much larger than for example rotation of a side group of a molecule around a single bond.

Two of the most important classes of interlocked compounds are those of the rotaxanes and the catenanes. Schematic representations of the simplest form of both are shown in Figure 5. A rotaxane consists of a ring mounted on a bar shaped molecule. At the ends of the bar, large stopper groups are located to prevent the ring from unthreading. There are two principal modes of motions in this system. First, the movement of the ring back and forth on the rod, often referred to as shuttling. Second, the rotation of the ring around the bar, often referred to as pirouetting. A catenane consists of two rings interlocked with each other. In this kind of molecule, the only mode of motion is the rotation of one ring around the other. If the two rings are not the same, the two indicated rotations are different. In principle, all these modes of motion can be exploited in molecular machines, if the motion can be controlled by some external influence.

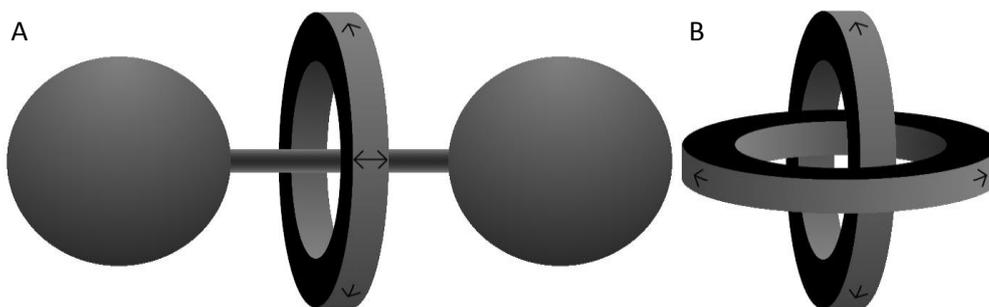


Figure 5: Schematic representations of (A) a rotaxane and (B) a catenane. The arrows on the ring indicate possible movements

There are already numerous examples of molecular rotors based upon rotaxanes. All these examples are linear motors based upon the shuttling of the ring. The complexity of these rotaxane based molecular motors is already quite high. For example, molecules resembling the function of an elevator⁴ and a muscle⁵ have already been reported. These are shown in Figure 6. The elevator molecule has three parallel rotaxane units. These can each be switched with addition or abstraction of protons. The net effect is that the inner part goes up and down with respect to the outer part. The muscle molecule consists of two identical parts that can slide along each other. When the molecules complexes with copper ions it will be in the extended form, and when it complexes with zinc ions it will be in the contracted form. Note that this rotaxane muscle is different than the one in Figure 3. It can be seen that the complexity is already far beyond a simple rotaxane, instead they consists of multiple rotaxane parts linked together. Even rotaxane systems that make macroscopic work possible have been demonstrated, as seen in Figure 2 and Figure 3.

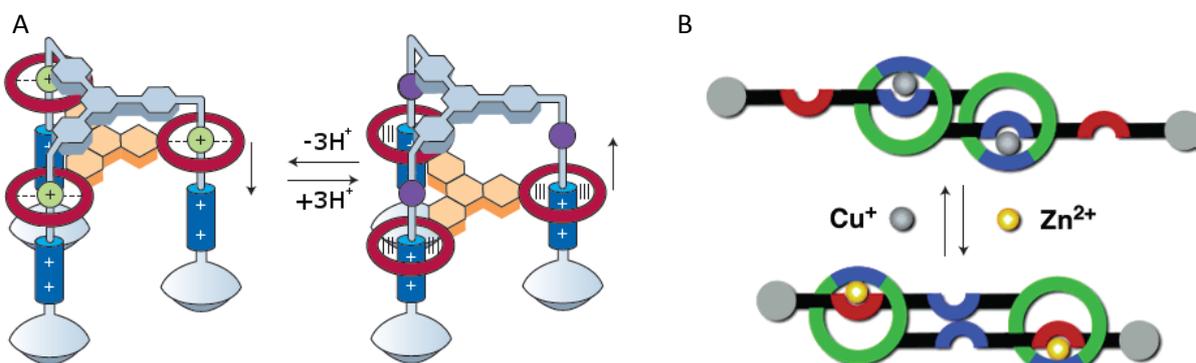


Figure 6: Schematic representations of (A) a molecular elevator and (B) a muscle. Images adapted from (2) and (1)

The reason for the success of rotaxanes as molecular motors is the fact that the motion of the ring is easy to control. The ring can only move back and forth along the rod. There is only one possible route between the different ends. Therefore, controlling the position along the ring is sufficient to control the complete movement. Control over the position is achieved by incorporating two different fragments in the rod where the ring can bind. These fragments are called stations. In the ground state the ring will be bound to the station with the highest affinity. The affinity of at least one station can be changed by some external influence. In Figure 6 these external influences are pH and cation concentrations respectively. If this is done, the other station becomes the most favourable and the macrocycle will move to that station under influence of Brownian motion. It is clear that this kind of mechanism falls in the category of motors making use of Brownian motion.

For the class of catenanes, although very similar to rotaxanes, there are very few successful attempts to make rotors that are in principle able to do work. The reason for this is the fact that one ring can rotate in two directions around the other ring. There is no inherent mechanism that blocks the rotation in only one particular direction and designing systems that do have this property is not easy. There are only two catenane systems realized in which unidirectionality is possible^{13,14}. These are schematically shown in Figure 7.

Both catenanes were realized in the same research group, that of David A. Leigh. Both systems are also quite similar in the structure of the various components. However, as will be discussed later, the mode of operation is quite different. The basic idea for both unidirectional motions is the selective blocking of the motion in one direction by transient barriers of some sort. In the first system, the barrier is a third ring. The barriers in the second system are two different blocking groups.

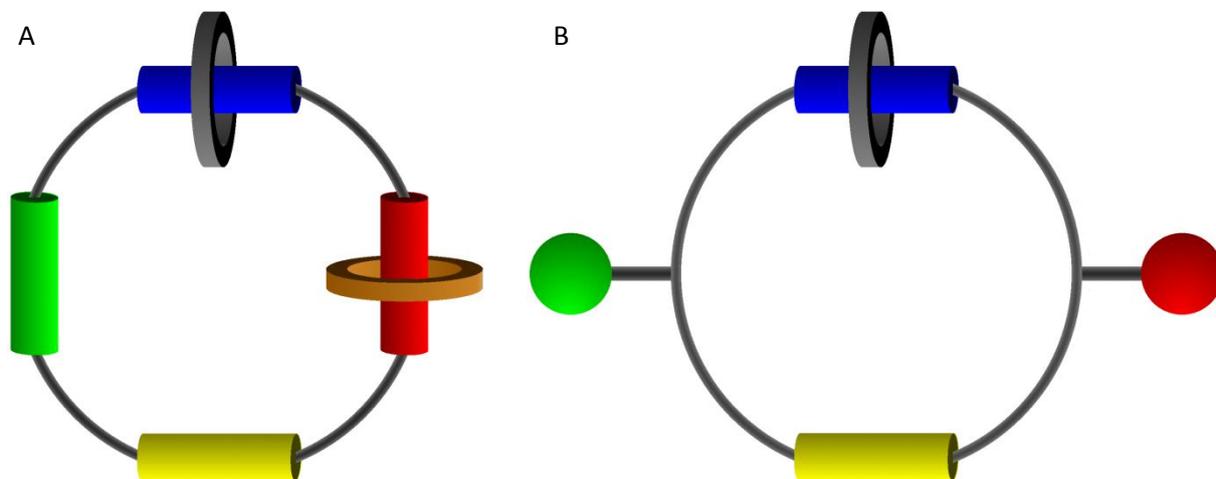


Figure 7: Schematic representations of the two catenane systems that show unidirectional rotation

1.5. Outline of this work

In this work, the two motor catenanes shown in Figure 7 will be reviewed in detail. These two interlocked molecules are the only examples of catenane motors so far. For this reason, catenane motors were not extensively reviewed. Only certain general reviews of molecular motors mention one or both of these systems. The present review will go in depth into the catenanes systems to gain insight into the feasibility of catenane motors.

In the next section, the synthesis of catenanes in general and some details about the synthesis of the present systems will be outlined. This is not the main focus of this review, so the synthesis will not be dealt with in depth. In the third section, the difficulties of making a molecular motor out of catenanes are addressed in more detail. Afterwards the systems of interest are dealt with in detail. Finally, some possibilities for future catenane motors are given. Note that other catenane based compounds, such as molecular switches, are not discussed here since they are not capable of doing work.

2. Catenane synthesis

As mentioned in the introduction, a catenane is a molecule consisting of interlocked rings. The number of rings can be anything, but the synthesis of interlocked molecules becomes more difficult with increasing order of the interlocked system. Molecules with two interlocking rings are referred to as [2]catenanes, with three rings as [3]catenanes and so on. The rings can be the same, but typically they are different. This is often more convenient for synthetic reasons as well as for the required functions of the molecules. Catenanes are very interesting molecules in the fact that the two rings are severely restricted in their motions along some degrees of freedom, whereas they can exhibit large amplitude motions in other degrees of freedom. These kinds of properties are quite rare among non-interlocked molecules. On the other hand, the fact that the two fragments are not covalently linked provides a large synthetic challenge. The chances of two rings becoming interlocked in an ordinary ring forming reaction are neglectable. Some basic strategies for the synthesis of catenanes are outlined in the first part of this section. The synthesis of the catenanes motor molecules discussed in this work is discussed afterwards.

2.1. General approach

In order to make interlocked structures a synthetic strategy must be used that promotes the formation of these structures as compared to regular ring formation reactions. The general strategy usually has three important steps. These steps are schematically depicted in Figure 8. First, one of the rings is synthesised by regular chemistry. The exact chemistry of this macrocycle is not very important, as long as it has one important property. It must have some functionalities through which it can interact through non-covalent interactions. This is represented by the red part in the figure. The second step is the addition of part of the second ring. This part must have functionalities that can form complementary non-covalent bonds with the first macrocycle. There is a finite probability that this fragment threads through one of the macrocycles present. The non-covalent interactions between the two molecules must be such that it prevents the fragment from unthreading. The third step is the closing of the second ring through any compatible chemical reaction, as illustrated by the complementary yellow parts attached to the black ring. The yield of catenanes will depend on the ability of the non-covalent interactions to keep the molecules together in the threaded state.

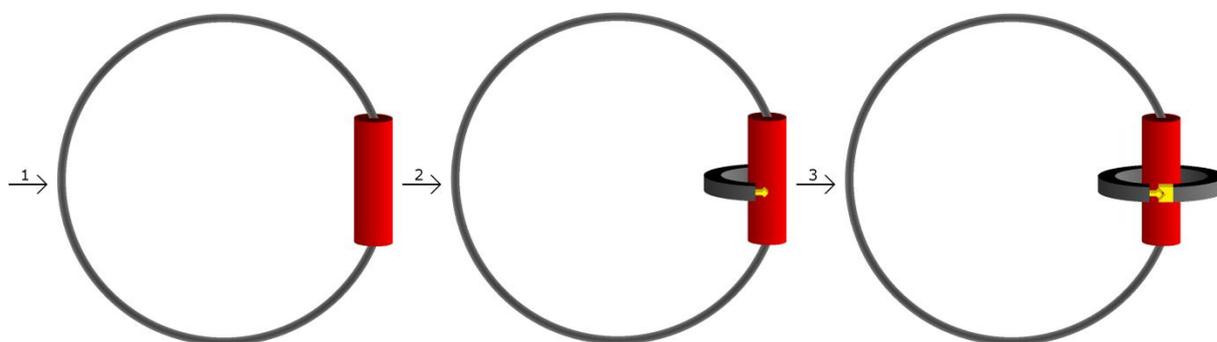


Figure 8: Schematic representation of the synthesis of catenanes. The difference in size between the macrocycles is exaggerated

Different kinds of interactions are shown to provide viable ways to synthesise catenanes. The first kind of interaction utilized was that of coordination of ligands to metal cations¹⁵. Often, both rings or ring precursors have a group that is a bidentate or tridentate ligand such as phenanthroline units. These ligands can effectively bind to metal ions such as copper(I). Upon ligand coordination in a tetrahedral fashion, the orientation of the ligands is perpendicular with respect to each other. The rigidity of the coordination compounds formed and the favourable geometry of the complex make these systems ideal for catenane formation. Once the catenane is formed the metal ion can be removed leading to a true interlocked molecule in good yield. In later work on catenane synthesis, other interactions were successfully used, including hydrogen bonding¹⁶, π - π interactions and charge transfer interactions¹⁷. All these different methods can be used to synthesize catenanes with various properties in a good yield.

This general strategy is not strictly followed in many cases. There are also synthetic strategies that rely on different schemes. For example, in the case of metal coordinated synthesis methods it is often sufficient to use two ring precursors instead of one complete ring and one precursor. This is because the metal coordination is very robust and can be highly directed towards catenane formation. Also in other systems it is possible to have efficient catenane synthesis straight from commercial building blocks¹⁶. The opposite is also possible, there are strategies possible that allow two fully formed rings to form catenanes^{18,19}. These strategies involve bond breaking in one of the rings and reformation after threading into the other ring.

The synthesis of higher interlocked structures is more difficult. The same reaction strategies can be used, because there is no principle difference between a [2] and a [3]catenane other than the number of rings involved. The only differences in actual synthesis are the facts that the macrocycles used must be larger to allow multiple molecules to be threaded through and the complexity of these molecules because of the increased number of binding sites required. These provide some synthetic challenges but these are not insurmountable.

A larger problem in the synthesis of higher interlocked molecules is the statistics. The chances that a [3]catenane forms is already notably lower than the chance of a [2]catenane forming. Therefore lower yields are expected for increasingly complex interlocked molecules. Again, there are methods developed to synthesise [3]catenanes in high yield, even with three different macrocycles^{18,20,21}.

2.2. Benzylic amide catenanes

The catenanes described in the papers discussed are all formed using the same synthetic procedure. First the larger macrocycle is synthesised. These macrocycles are different for the two motor molecules because they are adapted for their intended function. The synthetic steps taken to create these molecules are therefore very different. This synthesis will not be discussed here but the final products are shown in Figure 9. The subsequent formation of the second ring is done in a single step. This step directly gives the required catenanes in good yield. Note that this catenane formation is the basically same for both articles discussed.

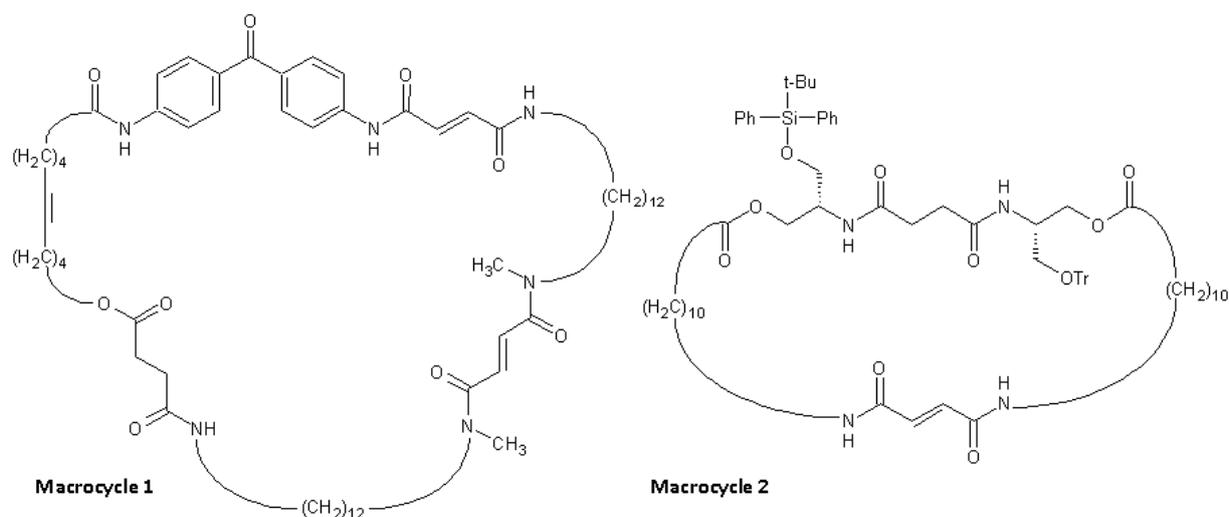


Figure 9: The two different macrocycles used in catenane synthesis, macrocycles 1 and 2. The chirality in macrocycle 2 is present only for synthetic convenience

The most important step in the synthesis is the actual catenane formation. The type of catenane forming reaction used was first reported in 1995¹⁶ and was also shown to be quite versatile²². The reaction scheme of the first catenane forming reaction found is shown in Figure 10. It can be seen that the catenane is formed from only two different simple reagents, isophthaloyl dichloride and *p*-xylylenediamine. In fact, these reagents are commercially available. The condensation of these units results first in the formation of amide groups. It is known that amides are very good hydrogen bonding agents. It is exactly this hydrogen bond formation between a formed diamide and the carbonyl groups of the acid chloride or other intermediates that is thought to be the driving force of catenane formation. The stacking of the electron-rich and electron-poor aromatic rings is also likely to contribute to this process. In a subsequent paper it was shown that a large number of different reagents, with different aromatic rings, can be used to form this kind of catenanes. The yield of the [2]catenane is typically around 20%. It is interesting to note that the aim of the researchers was not to synthesise a [2]catenane, but rather a normal macrocycle that was thought to be a possible sensor molecule for carbon dioxide.

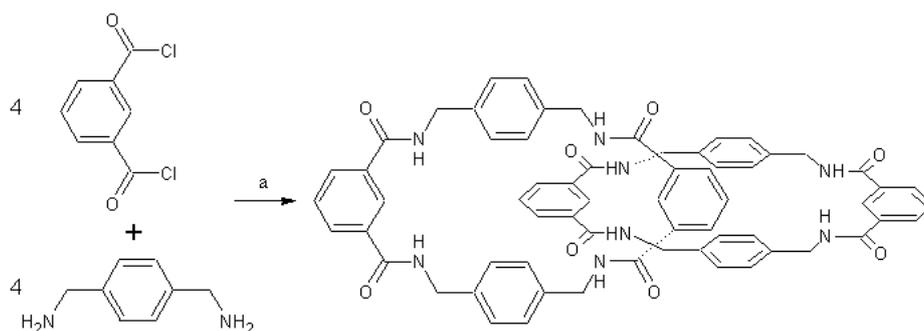


Figure 10: The synthetic procedure for the formation of a benzylic amide [2]catenane. The reaction conditions are in (a) Et_3N , anhydrous CHCl_3 . The yield of [2]catenane is 20.1%

Macrocycles **1** and **2** have three and two diamide units in the backbone respectively. Therefore they are equally suited for the catenane formation reaction described above. Adding these macrocycles to a mixture of the reactants described above will give the required catenanes in good yield. These reactions are shown in Figure 11 and Figure 12. The reaction of compound **1** gives a mixture of [2],[3] and [4]catenanes with different yields. The reaction of compound **2** gives mainly the [2]catenane. An excess of isophthaloyl dichloride and *p*-xylylenediamine is used because the reaction in Figure 10 will also take place. Note that the second step, step b, in Figure 12 is only a conversion of the side group.

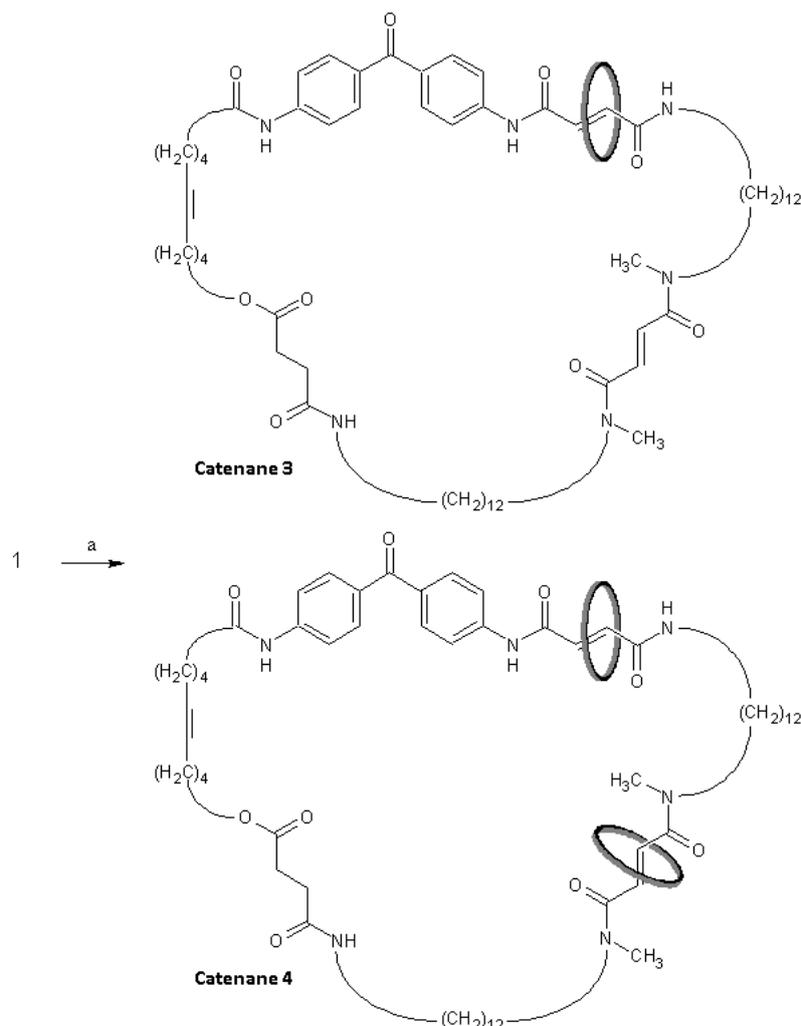


Figure 11: Formation of the [2] and [3]catenanes from macrocycle **1**. The [2] and [3] catenanes are catenanes **3** and **4** respectively. A small amount of [4]catenane is also formed. Reaction conditions are in (a) isophthaloyl dichloride, *p*-xylylenediamine, Et_3N , 1/9 $\text{MeCN}/\text{CHCl}_3$, 2 h. The yields of [2]catenane and [3]catenane are 50% and 21% respectively. The benzylic amide rings are represented by the black cylinders for clarity

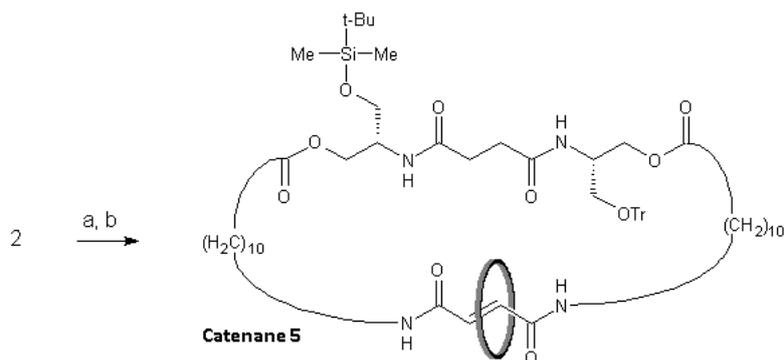


Figure 12: Formation of the [2]catenane from macrocycle 2. The [2]catenane is compound 5. Reaction conditions are in (a) isophthaloyl dichloride (8 eq.), *p*-xylylenediamine (8 eq.), Et₃N, CHCl₃, 3 h and in (b) TBAF, 20 min, then cool to -10°C, add 2,4,6-collidine, TBDMSOTf, 40 min. The yield of [2]catenane is 52%. The benzylic amide ring is represented by the black cylinder for clarity

3. Unidirectional rotation in catenanes

In order to use catenanes as molecular motors, it is important to gain control over the intramolecular motion in these systems. It is possible to do this by interlocking one large macrocycle, functionalized with different stations, with a smaller ring that can dock at those stations. In these kinds of catenane rotors, the larger ring with the stations is considered the stator and the smaller ring as the rotators. The approach is similar to that used in rotaxane motors, except the stations are arranged in a circular rather than in a linear fashion. Any number of binding sites can be added to the larger macrocycle. In general more than one is needed to be able to control motion. Also, the different stations should all have different binding affinities to ensure selectivity. The addition of different stations will restrict the rotation of the rotor around the larger ring. Control over the motion is obtained if the potential minimum of the system can be shifted selectively to and from different stations. In other words, it must be possible to change the stations of highest affinity by some external influence, such as irradiation, temperature or chemicals. If these conditions are fulfilled, the small ring can be selectively moved between different binding sites.

3.1. Controlled rotation in a [2]catenane

The first example of the system described above was published in 2003¹³. In this work, a macrocycle with four different potential binding sites was synthesised first. This is macrocycle 1 in Figure 11. The structure of the four stations is shown in Figure 13. Station **A** is a secondary (2°) amide fumaramide group. This group can form hydrogen bonds with the small ring through the amide groups. The affinity of the small ring is expected to be large because the amide groups are kept in almost ideal conformation by the *E*-olefin to form the intercomponent hydrogen bonds. Station **B** is a tertiary (3°) amide fumaramide group. This station is similar to station **A**, only the amide nitrogen atoms bare an extra methyl group. The effect of these groups is to increase the steric hindrance. Therefore the affinity of the small ring towards this binding site will be less. The third station, station **C**, is a succinic amide ester. Here, one of the amide functionalities is replaced by an ester group. This significantly reduces the affinity of the small ring since an ester is a poor hydrogen bond acceptor. Also, no double bond between the functional groups is present. This makes the station more flexible, further lowering the affinity. The last station, station **D**, is a simple amide group. This group can form fewer hydrogen bonds than the other three stations and will therefore be the least favourable station. In fact, in catenane 3, the fourth station does not affect the behaviour of the system. The energetics of the system are such that the small ring binds selectively to the current lowest energy site.

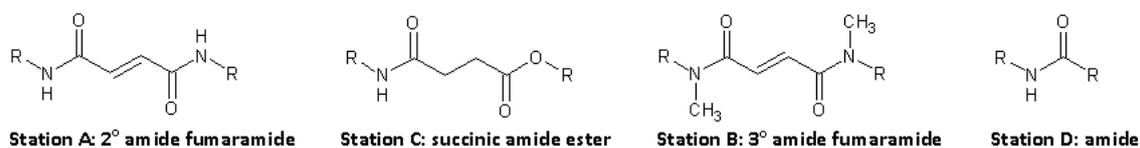


Figure 13: The structure of stations A-D. R denotes the rest of the macrocycle 1

The stations used also grant good control over the affinities by external stimuli. Both stations **A** and **B** can be isomerised from the trans form to the cis form by irradiation. Stations in the cis form are referred to as stations **A'** and **B'**. The cis form of both stations have a far lower affinity for the small macrocycle because fewer hydrogen bonds can be formed in this conformation. Also the steric match is poor. Even binding to station **D** is more favourable. Both station **A** and **B** can be switched by light of 254 nm, but to be able to selectively isomerise station **A** it is attached to a benzophenone unit. This group acts as a sensitizer, enabling switching of station **A** with light of 350 nm. The reverse reaction of both stations is done chemically or thermally. Different protocols can be used, but the transformation of both stations occur in the same step. The structures of both conformations of stations **A** and **B**, as well as the reaction conditions required to switch between them are shown in Figure 14. The structure of the sensitizer is also shown. In short, three states of the larger macrocycle are possible. The ground state, with both stations in the trans conformation is referred to as the trans,trans state. If station **A** is isomerised to the cis conformation it is in the cis,trans state and with both stations isomerised it is in the cis,cis state. The binding constants follow the order $k_b(\mathbf{A}) > k_b(\mathbf{B}) > k_b(\mathbf{C}) > k_b(\mathbf{D}) > k_b(\mathbf{A}') > k_b(\mathbf{B}')$.

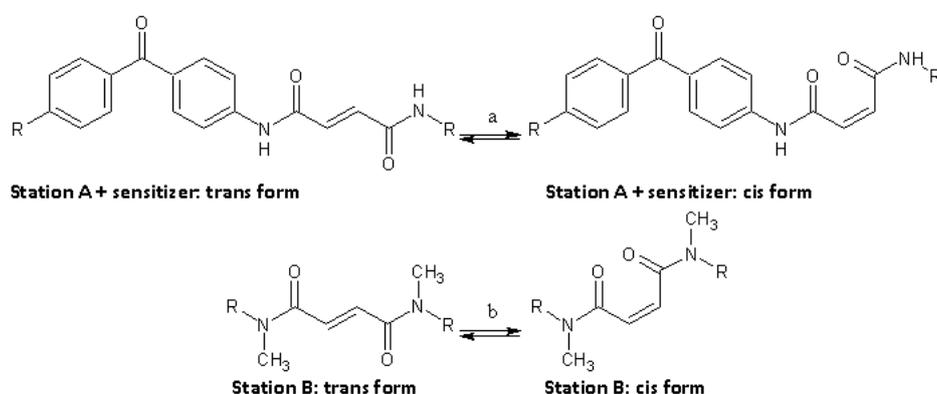


Figure 14: The interconversions of station **A** and **B** under irradiation. Reaction condition for the forward reaction are in (a) 350 nm, CH_2Cl_2 , 5 min, yield 65-67% and in (b) 254 nm, CH_2Cl_2 , 20 min, 48-51%. For the reverse reactions the conditions are both in (a) and (b) 100°C $\text{C}_2\text{H}_2\text{Cl}_4$, 24 h, ~100% or cat. ethylene diamide 50°C , 48 h, yield 50-74%. R denotes the rest of the macrocycle 1

With these tools, catenane **3** can be selectively changed between three states. This is shown schematically in Figure 15. The benzylic amide ring resides on station **A** in the ground state. Irradiation of the sample at 350 nm moves the ring to station **B** because this station has the highest affinity now. After subsequent irradiation at 245 nm the ring moves to station **C**. Finally, heating will return the ring to station **A**. Station **D** is drawn in Figure 15 but does not participate because it is never the station with the highest affinity. This catenane may seem like an ideal candidate for a molecular motor. However, the direction of the movement of the small ring is arbitrary. The ring makes just as many rotations clockwise as anti-clockwise. This means no net work can be performed by such a simple system.

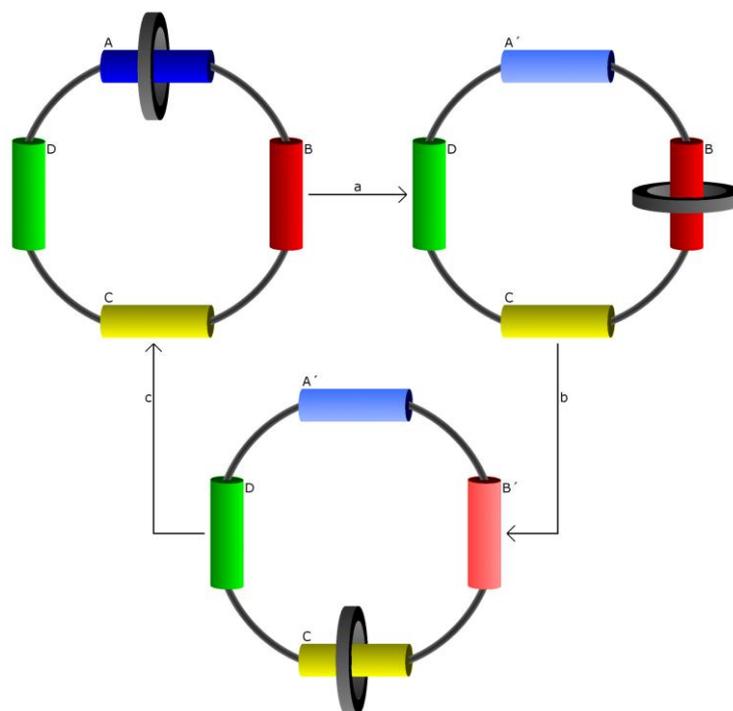


Figure 15: Stimuli induced rotation of the small benzylic amide ring in catenane **3**. The transformations are in (a) $A \rightarrow A'$ (yield 67%), in (b) $B \rightarrow B'$ (yield 48-51%) and in (c) $A' \rightarrow A$ and $B' \rightarrow B$ (yield ~100%). Note that the small ring does not reside on station D because it is never the most favourable station. The colored cylinders are the stations A, B, C, D, A' and B' as indicated, the large circle is macrocycle 1 and the small cylinder is the benzylic amide ring

3.2. Unidirectional rotation in a [3]catenane

If the catenane system could be modified such that the rotation becomes biased in one direction, it would be possible to make catenane based molecular motors. In other words either clockwise, or counter clockwise must be the only possible rotation direction. However, making such a modification is more difficult than it may seem at first sight. Since the small ring needs to travel a full circle, just adding a blocker on one site is not an option. This will only make the small ring go back and forth. So, it is also important that the barrier for rotation is transient. There has to be a way to remove the barrier temporarily to let the ring pass in one direction only.

It turns out that the [3]catenane variant on the previous example, or catenane **4**, provides one possible solution to the directionality problem. The same article from 2003¹³ also shows this first example of unidirectional rotation in catenanes. Instead of one benzylic amide ring, two are present on the larger macrocycle. This second ring can block the path of the first ring in certain steps, and vice versa. The reaction sequence is shown in Figure 16. The basic reaction steps are the same as those for catenane **3**. However, for full rotation it is necessary to do the reaction sequence twice. In each step, one or both rings move but in every case one path is effectively blocked by the other ring. In each series of three steps the rings effectively interchange positions, but the path each ring takes is difficult to make up from this image. Therefore, the paths are schematically illustrated in Figure 17. From this it is clear that both rings make a full 360° rotation after completing the three reaction steps twice. Both rings make a net rotation in the same direction. Thus, it can be concluded that the benzylic amide rings in this system undergo unidirectional rotation. The direction of rotation cannot be reversed in this system, because the direction is dictated by the location of the stations itself. Synthesis of a molecule with station **B** and **D** interchanged could in principle show rotation in the reverse direction. Note that this is not the same as taking the mirror image of the large macrocycle because of the precise structure of the molecule.

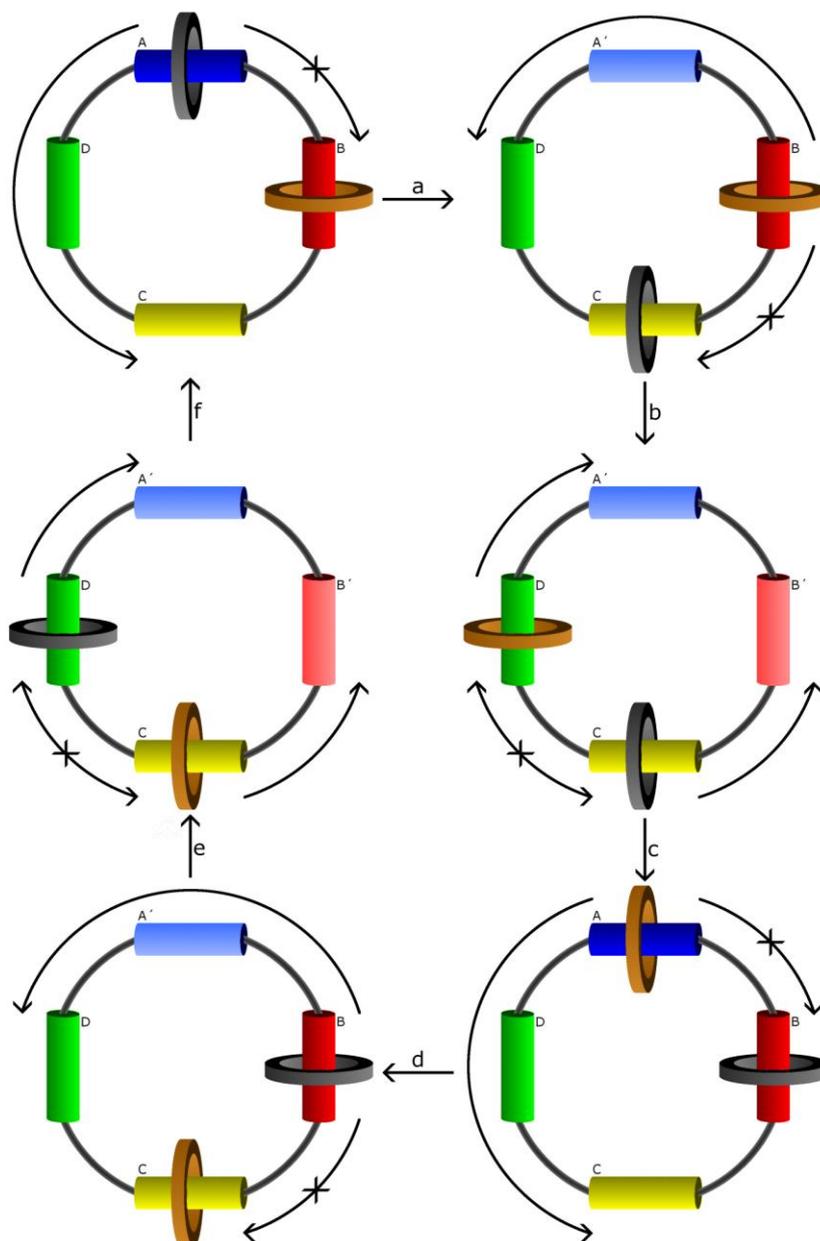


Figure 16: Stimuli induced rotation of the benzylic amide rings in catenane 4. The transformations are in (a) and (d) $A \rightarrow A'$ (yield 67%), in (b) and (e) $B \rightarrow B'$ (yield 48-51%) and in (c) and (f) $A' \rightarrow A$ and $B' \rightarrow B$ (yield ~100%). The brown and the black are identical benzylic amide rings but have different colour to differentiate them. This helps interpreting the movements of both rings

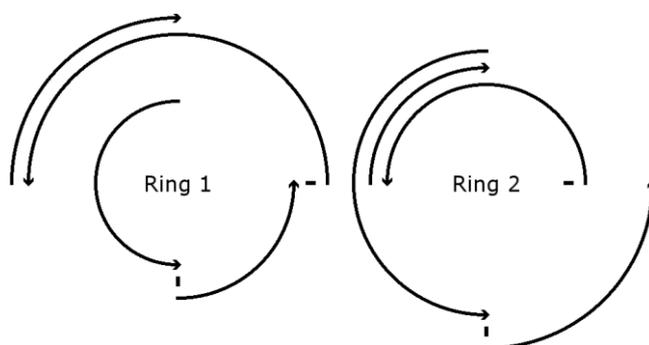


Figure 17: Visualisation of the movement of the benzylic amide rings of catenane 4. Ring 1 is the black ring in Figure 15 and ring 2 is the brown ring. Reaction steps a-f are shown from the center outward. Note that the motion in steps a-c for ring 1 are the same as the steps d-f for ring 2 and vice versa. This agrees with the fact that the positions of the rings interchange after each sequence of three reaction steps

Because the motion of benzylic amide rings is unidirectional, it is in principle possible to do work with this system. Therefore, according to the definition of a molecular motor adopted, this [3]catenane is in fact a molecular motor. Energy is put in the molecule by the chemical reactions in each stage of rotation because the molecule goes from an equilibrium conformation to a non-equilibrium conformation. The small ring is then driven to the new equilibrium position by means of Brownian motion. Note that this is the case for both catenane **3** and **4**. The difference in binding energy of the initial station and the final station in each reaction step is the energy released by the motion. This energy is necessarily different in each step. The maximum amount of energy available to do useful work depends on the exact energy differences between all stations, and it is therefore not possible to capture in a simple formula. However, it is important to note that the amount of this energy actually available to do useful work in the molecular machine depends on the degree of directionality of the system. In other words, the directionality partially determines the efficiency of the motor. The directionality of the rotation is dictated by kinetics, which is different in both systems. In catenane **3** the directionality is zero, so indeed no work can be done with this system. In catenane **4** the directionality is non-zero so indeed this system can convert some energy into work.

An estimation of the directionality in catenane **4** can give more insight in the potential of this molecular motor. The first obvious loss of efficiency is the fact that both rings inherently move in the wrong direction once in the series of six chemical transformations. An energy equal to the difference in binding energy of station **D** and **A** is wasted twice every rotation. Since station **D** is a station with low affinity, and station **A** the station with the highest affinity, this is quite a significant amount of energy. Another issue is the fact that the light driven reactions are not very efficient. Only about 67% and 50% conversion is achieved for the transformation of station **A** and **B** respectively. If only one of the reactions occurs in a certain molecule one of the rings does not move and hence the other ring can only go back and forth. The energy used for this motion cannot be used to do work.

The two effects described above are inherent to the method used, but losses can also occur due to random thermal motion. In principle, any routes taken by the benzylic amide macrocycles differently than those in Figure 16 must be regarded as losses due to thermal motion. Assuming the rings will always end up in the equilibrium position, possible losses include for example the movement of the brown ring from station **B** to **C** and the black ring from **A** to **B** simultaneously instead of the black ring from **A** to **C**. This will result in the net loss of half a rotation. The extent of these losses were estimated in the supporting information of the reference by studying model rotaxanes with variable temperature $^1\text{H-NMR}$. The use of these model compounds is required because the less favourable stations are insufficiently populated, due to the large difference in binding constants of the different stations. This makes it impossible to study kinetics in the catenanes directly. However, to be able to convert the results of these model systems to the catenanes under investigation it is necessary to assume that the rate of decomplexation of a small ring with a certain station is independent of the station it shuttles to. In other words, the rate is only determined by the characteristics of the initial station and the distance between two stations. Now, the barrier for the movement between two stations in five different symmetric rotaxanes were determined. The rotaxanes used are shown in Figure 18. In the first three, the stations **A**, **C** and **D** are present. Whether station **B** is assumed to have the same barrier or that it was actually also measured is not clear from the supplementary information. In any case, the barrier obtained for station **A** and **B** is both $16.2 \pm 0.4 \text{ kcal} \cdot \text{mol}^{-1}$. This is odd, as the stations were chosen in order to have significantly different affinities for the small macrocycle. The barriers obtained for stations **C** and **D** were 11.3 ± 0.2 and $< 8 \text{ kcal} \cdot \text{mol}^{-1}$ respectively. The fourth model rotaxane is that of the cis form of station **A**. Again, both the barrier of **A'** and **B'** were determined to be the same, $< 8 \text{ kcal} \cdot \text{mol}^{-1}$, using this system. Finally, the effect of the benzophenone unit was found to be small from the final model compound. It did not slow the movement down significantly.

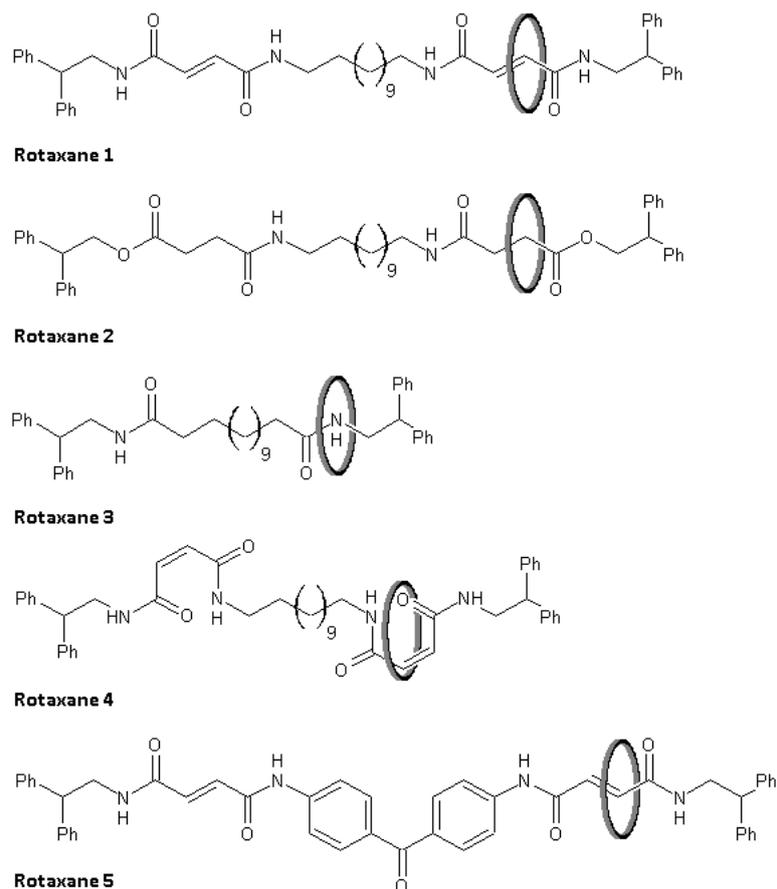


Figure 18: The rotaxanes used in the determination of the energy barrier associated with the movement between stations. The benzylic amide rings are represented by the black cylinders for clarity

From the obtained barriers and the appropriate thermodynamical relations it is clear that at 298 K in CDCl_3 the stations **A** and **B** decomplex $4 \cdot 10^3$ times faster than station **C** and $>10^6$ times faster than stations **D**, **A'** and **B'**. It is also possible to estimate the chance of wrong movement in each of the three reaction steps. In step one, the movement of the black ring in Figure 16 from station **A** to **C** after transformation of **A** to **A'** is at least a million times more likely than the other ring moving to **C** and the black ring from **A** to **B**. In step 2 and 3, the intended motion occurs $>10^3$ times more often than other motions. For the third step it is important to note that the observed rates for stations **A** and **B** are the same. According to the authors, this is sufficient to assure that the system will undergo only the desired motion in the third step. However, at the microscopic level the reactions take place in a stochastic fashion. Even though the macroscopic reaction rates are the same, this does not mean that for every molecule the stations are transformed at the same time. Therefore, the rate of faulty movement might be higher than assumed in the article. The effect will be larger if the overall reaction rate of both stations is lower. The energy barriers are determined in model compounds, and effect of the final state cannot be excluded. Also some other uncertainties exist still in the reasoning. Nevertheless, the numbers found suggest a very good directionality of the system.

Another factor is the degree of movement without external induced stimuli. The extent of this motion can be estimated by using the barriers found earlier to find the effective barrier for random rotation. The barrier for random rotation was found by numerical calculations to be about $23.5 \text{ kcal} \cdot \text{mol}^{-1}$. This is significantly higher than the barriers for stimuli induced motion, which are <8 and $11.3 \text{ kcal} \cdot \text{mol}^{-1}$. At room temperature, this means the frequency of random rotation is about once every 8 hours. Every 10°C reduction in temperature approximately halves this frequency. For the simplest reaction scheme, that is simply using heating to convert the stations **A** and **B** back to the trans form, the six reaction steps take over two days. During most of this time the sample is heated up to 100°C . There will be many background rotations under these conditions.

However, using different reaction conditions can dramatically improve this. Performing the isomerisation of the stations **A** and **B** to the trans form at -78°C catalysed by bromine radicals reduces the time of the complete reaction cycle to 70 min. Moreover, the frequency of background rotation and the rate at which rings take less kinetically favoured pathways to the new equilibrium will be reduced to a minimum. In any case, the rotation speed is very low.

3.3. Unidirectional rotation in a [2]catenane

A second example of unidirectional rotation in catenanes was published in 2004¹⁴ by the same group. The unidirectionality in this system is again governed by selective blocking of one path for the circumrotation of a small ring around the larger macrocycle. However, the way in which it was realized is quite different. The molecular rotor investigated in this reference is a much simpler molecule. It is only a [2]catenane with two different stations, specifically catenane **5** in Figure 12. One station is the same as station **A** in the previous system. The other station, here referred to as station **E**, is the same but the double bond is absent. This makes the station more flexible, and thus the affinity of the benzylic amide ring will be less for this station. Also, this station cannot be switched between cis and trans states. Unidirectional rotation is governed by two blocker groups. These are the *t*-butyldimethylsilyl ether and trityl ether groups in Figure 12. These are large side groups of the larger macrocycle, which the benzylic amide ring cannot pass. With these groups attached no rotation is possible. If these blocking groups are removed, the small macrocycles can pass and rotation is possible. These linking and unlinking reactions are shown in Figure 19. The total rotation sequence is shown in Figure 20. It can be seen that a total of six steps are necessary to complete a full rotation. In the first step station **A** is isomerised to the cis form. This is the same initial step as in the previous rotors. However, now both pathways to the other station **E**, which is now the station with the highest affinity, are blocked by the bulky side groups. In steps two and three one of the barriers is selectively removed and added again respectively. During the time between step two and three, when the barrier is absent, the small ring can travel to station **E** by biased Brownian motion. Once the barrier is back in place there is no way back. The fourth step is to transform station **A** back to the trans form. The same story as in step one holds, the other station is more favourable but it is kinetically inaccessible due to the large blocking groups on the large macrocycle. In the final steps the other barrier is removed temporarily. The small ring can now follow the other path back to station **A** restoring the initial situation. Because the paths taken to and from station **E** are different, a net rotation takes place in each sequence.



Figure 19: The linking and unlinking reactions of the blocking groups in catenane 5. Reaction conditions in (a) for the forward reaction are TBAF 20 min and for the reverse reaction 2,4,6-collidine, TBDMSOTf, -78°C , 1 h (overall yield 72%). Reaction conditions in (b) for the forward reaction are $\text{Me}_2\text{S}\cdot\text{BCl}_3$, -10°C , 15 min and for the reverse reaction 2,4,6-collidine, TrOTf, -78°C , 5 h (overall yield 63%). R denotes the rest of the macrocycle 2

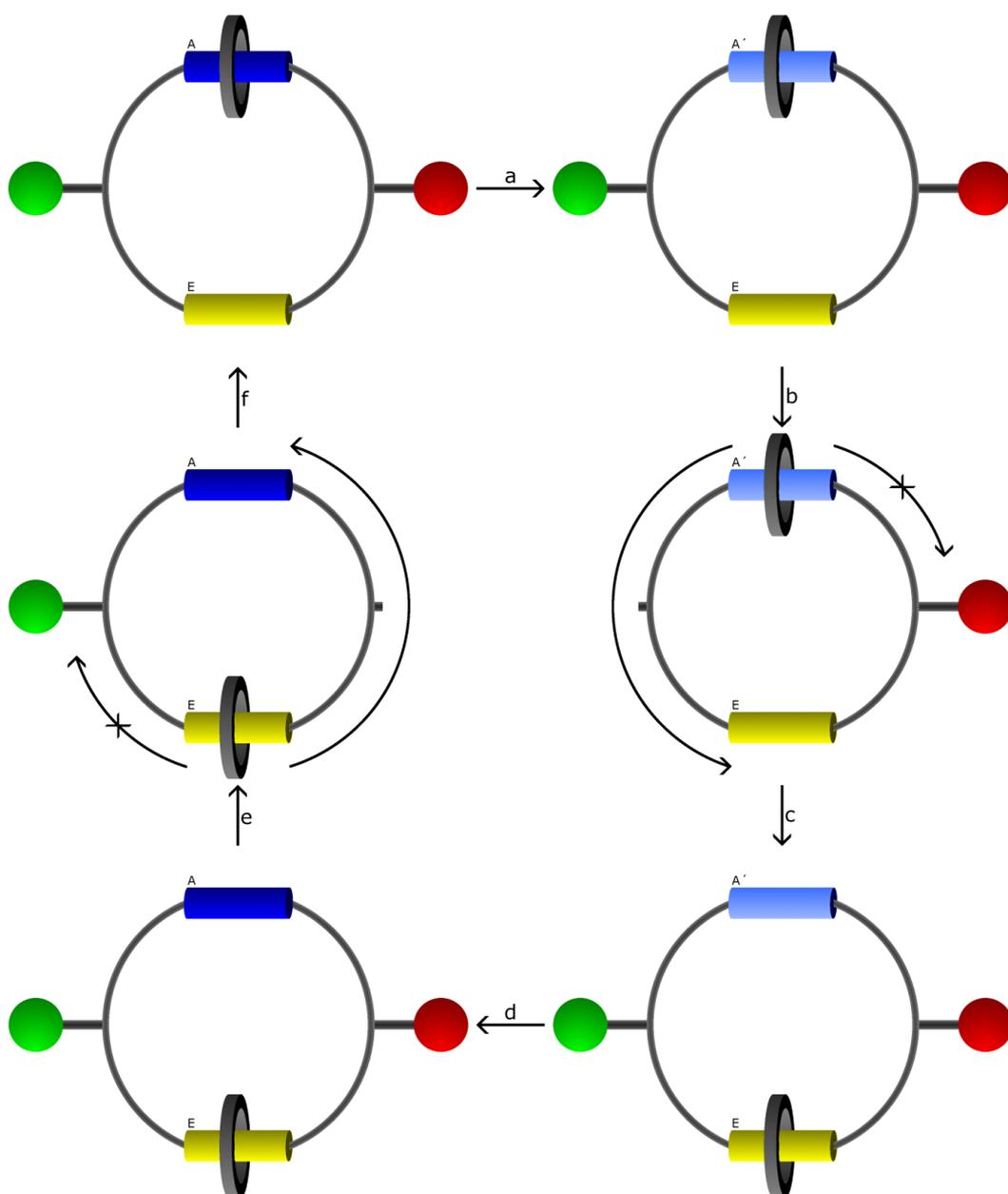


Figure 20: Stimuli induced rotation of the small benzylic amide rings in catenane 5. The transformations are in (a) $A \rightarrow A'$, in (b) linking and (c) unlinking reactions of the green blocking group which allows the benzylic amide ring to move to station E, in (d) $A' \rightarrow A$ and in (e) linking and (f) unlinking reactions of the red blocking group which allows the benzylic amide ring to move back to station A

The main improvement of this system with respect to previously reported molecular motors is the fact that this is the first artificial molecular motor that can selectively rotate either clockwise or counter clockwise. Interchanging the steps b and c with e and f will result in the same motion but with opposite directionality. All previous molecular motors could only rotate in one specific direction. Note that molecular rotors can generally rotate in both directions but there is no selectivity in these systems, meaning the net rotation is always averaged out to zero.

This [2]catenane molecular motor is also very useful in the fact that it can provide insight in the mechanisms and the fundamental role each part of the molecule plays in the operation. In contrast, biological motors are much more complex and the function of each individual amino acid residue cannot be deduced. In the catenane under study, there are two sets of chemical transformations that have distinguished different functions. The first set, the linking and unlinking reactions of both of the blocking groups or reactions b, c, e and f in Figure 20, modulates whether or not the small ring can shuttle between the two different binding sites.

In other words, these reactions control the kinetics of the movement. The other set, the balance breaking reactions that transform station **A** from the trans to the cis form and back, provides a driving force for the redistribution of the small ring. In other words, these reactions control the thermodynamics of the movement. It is thus apparent that the kinetics and the thermodynamics of the rotation are effectively decoupled in this molecular motor.

The mechanism of motion of this molecular system is essentially the same as that of the flashing ratchet transport mechanism described in the introduction and Figure 4. This transport mechanism corresponds to a periodical series of two different energy minima and two different energy maxima. A particle is moved along this potential in a directional fashion by repeated raising and lowering of the different minima and maxima. The similarity between this mechanism and that found for the molecular rotor discussed here can be seen when comparing it to the potential energy curves of catenane **5**. These curves are shown in Figure 21. Events 1 and 5 in Figure 21 correspond to the balance braking reactions, events 2, 4, 6 and 8 correspond to the linking/unlinking reactions and finally events 3 and 7 correspond to the actual movement of the benzylic amide ring. In both the flashing ratchet mechanism and this mechanism, there are two different minima and two different maxima. Also one particle, in this case the smaller macrocycle, is transported in an unidirectional fashion along this potential. There are some differences in the details of the mechanisms. First of all the flashing ratchet describes a linear motion along a periodic potential while in this case the system is cyclic with only two minima and two maxima. Also, only one of the energy minima is varied and not both, but the effect is the same because the energy difference changes sign twice. Finally, the steps that change minima depths and maxima heights are separated in this system. Regardless of the differences, this system can be considered a flashing ratchet.

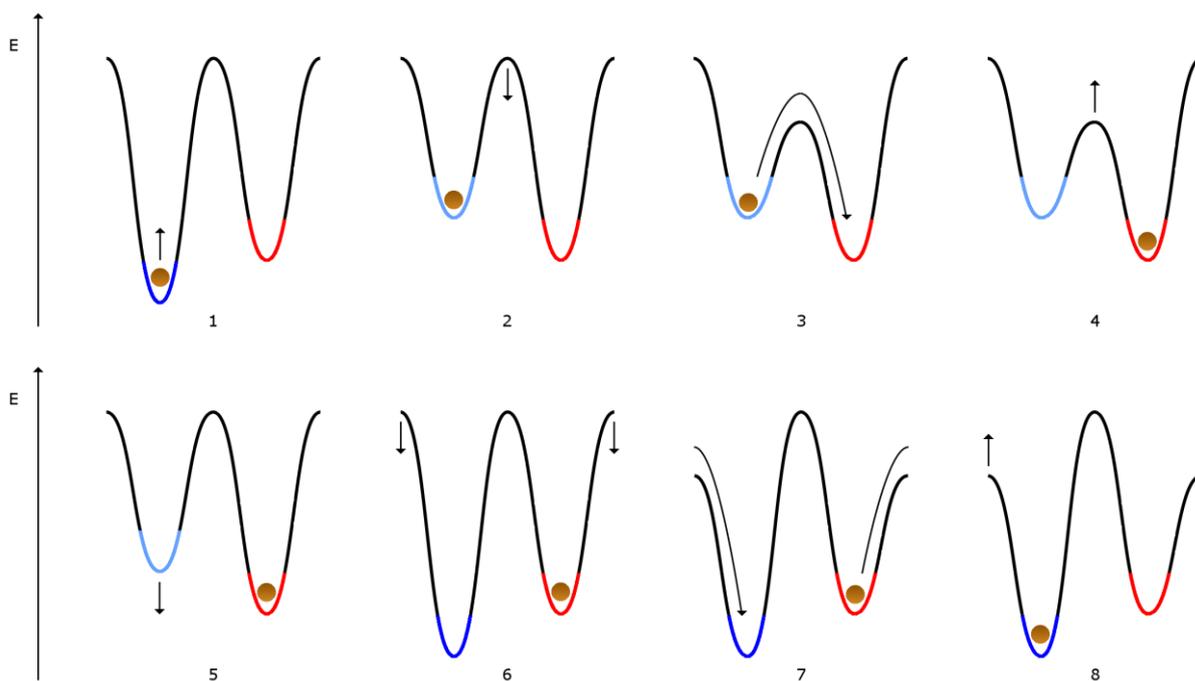


Figure 21: A series of potential energy surfaces associated with the rotation mechanism of catenane **5**

Looking at the thermodynamics of the system it is clear that the amount of energy available to do work is approximately the difference in binding energy of the small ring on station **A** in the trans and cis states. The binding energy of the intermediate station does not play a role because it does not change during the reaction sequence. However, it is also interesting to discuss the thermodynamics of the system rotating stationary. In that case, there is no opposing force on the benzylic amide ring and no work will be done. It can be seen that the system ends up in the same state as it started, and because there is no opposing force, no energy is dissipated in the rotation.

Therefore, the energy put into the system in the trans to cis isomerisation is not consumed, but rather returned to the surroundings upon the isomerisation back to the trans form. This makes sense because the motion itself is only driven by Brownian motion. On the other hand this raises the question of whether or not the balance breaking reactions are necessary. The answer can be found when considering the situation where all small rings start on the same station, and the different linking and unlinking reactions are carried out in sequence. In this case it is assumed the two binding stations have equal affinity for the small ring. After one sequence, a quarter of the small rings did a full rotation, half of them did half a rotation in either direction and the final quarter did not do a net rotation. Therefore there was some degree of unidirectional motion. In successive steps the initial population is half on station **A** and half on station **E**, so all rotation is balanced out and net rotation is no longer possible. The effect of the balance breaking reactions is to change the relative populations on the different stations in each step. Although no net energy consumption is needed for this, some energy must be processed in these steps to allow subsequent unidirectional rotations.

The performance of this molecular motor is not very good. This is already apparent from the yields of every step indicated in Figure 20. This means that not nearly all molecules complete the unidirectional rotation. However, there is always an imbalance between the amount of molecules with the small ring on one station and the amount with the small ring on the other station. Therefore, net unidirectional rotation will always be the result of this reaction sequence. These yields shown apply to isolated compounds after each step. The total time used to take a full rotation is about 18 h 35 min and 7 h 20 min respectively for both directions, excluding time to purify. So, just as the case with the [3]catenane, this is a slow and inefficient reaction sequence. An alternative approach can be used, in which the reaction sequence is carried out without the complete intermediate cleaning steps. The excess reactants and side products are either neutralized or removed using resins. This reduces the time needed to purify the sample, with only a small reduction in yields. With this approach, it was estimated that about 28% of the molecules undergo full unidirectional rotation each cycle. The chances of mistakes in the rotation due to random thermal motion was not determined, but it can be assumed to be very low since it requires the small rings to pass the very bulky side groups of the larger macrocycle.

4. Catenanes as molecular motors

Two different catenanes that could in principle perform work have been discussed in this work. These two first examples are a proof of the principle that catenane systems can indeed be used as molecular motors. It is still questionable if catenane based molecular motors are indeed suitable candidates for future molecular machines. They do offer some advantages over other molecular motor compounds that rely on rotation around single or double bonds. On the other hand there are also drawbacks associated with catenane motors.

4.1. Advantages and disadvantages of the current catenane motors

Catenane based motor compounds surely offer some advantages compared to other molecular motors. First of all, the rotation amplitude is much larger. This extra amplitude might be crucial for actual machines, where these kinds of rotors could be used to selectively bring certain chemical species from A to B along a predefined track even against an opposing force. This is something most non-catenane motors cannot do, except maybe the linear motors of the rotaxane type. Also, because the molecules are relatively large, the possibilities for functionalisation are excellent compared to other molecular motors. Moreover, the two examples given here both have a distinct property that sets them apart from conventional motor compounds. The [3]catenane motor has two potential rotating handles that can be used for transportation of other species or functionalisation. The [2]catenane motor compound has the unique capability of rotating controllably in both directions.

However both systems suffer as yet from some very large drawbacks. In both systems a series of chemical conversions is required to move the rings. Not all of these transformations can be carried out by using light. Therefore, other components of future molecular machines have to be able to withstand these conditions or different conditions must be found.

Especially for the catenane **5** motor this might be problematic because of the many different chemicals involved the linking and unlinking steps. Moreover, the speed of these reactions is very low. It is not unthinkable that molecular machines based on catenane motors will actually be limited by those very catenanes. For now, other molecular motors offer the benefits of continuous and fast operation while only needing photons as an energy source. If these drawbacks of catenanes are not overcome, their applicability in molecular factories will be very limited. Since these motors are only the first two examples of its kind, and the entire field of molecular machines is still in its early development, it is very likely that much better catenane based motors will be found.

4.2. Suggestions for future catenane based motor systems

It is interesting to imagine what such improvements might look like. It might be that a catenane such as that schematically shown in Figure 22 might be a big improvement. This system is very similar to catenane **4** reviewed here but it has two different types of binding sites. For example two binding sites are based upon hydrogen bonding similar to stations **A-E** here, while the other two in between are based upon π - π stacking interactions. The two small rings are also different, one only binds at the hydrogen binding stations while the other binds selectively through π - π interactions. Moving one ring can only go via one route because the other route is blocked. If subsequently the hydrogen bonded and the π bonded ring are moved back and forth the net effect will be that the rings follow each other. If all four movements can happen separately the efficiency will be improved significantly compared to catenane **4**. This is because now only four reactions are needed for a full rotation and no movement in the wrong direction is inherent in the system. If the reversion step has to be done using the same conditions, for example heating, there will be a chance the motion will go in the wrong direction because if the wrong ring moves first both rings are forced to rotate in the wrong direction. This leads to a zero net rotation for that run. The chance of this event will depend on the relative conversion rates and are different for clockwise and counter-clockwise rotation. But even in this case the system can be more efficient because still only three steps are required for a rotation. Moreover, the system can undergo rotation in both directions selectively, just like catenane **5**. The direction depends on which ring is moved first from the overall ground state of the system.

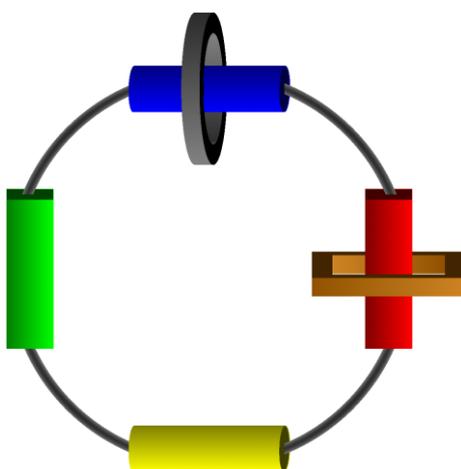


Figure 22: A schematic representation of a theoretical [3]catenane based on two different types of station-ring systems. This system could in principle show unidirectional rotation in either direction

A possible improvement on the theme of catenane **5** is proposed in Figure 23. The mechanism to bias the rotation is entropy based rather than physically blocking all movement. For the rotation in the requested direction to be possible a barrier has to be overcome that is made of a fragment with a favourable geometry. Therefore many initial conformations can lead to crossing of the barrier, or in other words, the approach to the barrier in a potential energy surface is very wide so it is entropically favourable to cross such a barrier. In the reverse direction, many conformations would result in the ring getting stuck on the barrier, which leaves the only possibility of going back. In the entropic picture, this means the approach to the barrier is relatively small and hard to cross.

The barrier might look something like that shown in Figure 24. This kind of barrier fulfils the two main requirements, it is rigid and it is biasing in one direction. Such a system with a double bond might even enable reversion of the rotation direction by cis/trans isomerisation. A more continuous operation might be possible in such a system because only two steps are required, the two balance breaking steps. If one is powered by irradiation and the other by heat, mild irradiation and heating might result in a continuous operation in which the average switching times are larger than the time taken to travel between the two stations. The idea might be tested first in a much simpler rotaxane configuration. In such a system, two identical stations could be separated by the proposed barrier. If the barrier indeed biased the motion, a difference in occupancy of the stations should be observed.

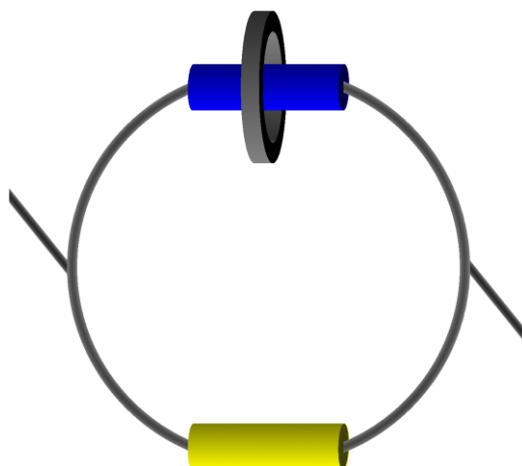


Figure 23: A schematic representation of a theoretical [2]catenane based on the unidirectional motor catenane **5**. This system could in principle show continuous unidirectional rotation in a single direction

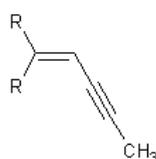


Figure 24: The chemical structure that could constitute the barrier in Figure 23

4.3. Suggestions for future surface mounted catenane based motor systems

Besides imagining the kind of improvements possible on current catenane motors, one can also imagine how these motors can be integrated into molecular machines. From a functional perspective, it is likely that the motors need to be fixed on, for example, a surface. This helps defining the absolute direction of motion. Also this will make it easier to integrate multiple components into one functional machine. The part that would be best to stick to the surface would be the large macrocycle, since that is most compatible with the idea of using the small ring to transport different species from A to B. However, the problem is that the connection to the surface will form a barrier that is most likely insurmountable for the small molecule. In other words, the motor function of the molecule will be lost. If the barriers are transient, for example a collection of many non covalent interactions, the motor function might still be possible but it will be even much less efficient as before. Most likely this kind of surface attachment will not be feasible, unless the barriers are actually used to govern the unidirectionality of the system. One could take a surface coated with two different molecules, which can both react with different groups on the larger macrocycle. In such a system control over the movement of the small ring could be the same as or similar to that for catenane **5**. If one can also assure the rings stick to the surface right side up, the rotation as observed from an external point will have uniform directionality. Chirality in the attachment of the blocking groups, as already present in catenane **5**, might already be sufficient. Such a system might actually be a next step in the development of molecular machines.

It would also be possible to attach the small ring to the surface instead of the larger one. This way, no barriers to the intended rotation will be formed. The large macrocycle will then be the moving part of the system. From fundamental point of view it is irrelevant which part of the motor is actually moving, so the motor function will not be compromised. However, this method does not comply with the idea of moving species from A to B so well. Putting molecules on the large macrocycle will give the same problem as above, namely that these molecules will form a barrier to the rotation of the catenane. It could be used to move certain species away from the surface, for example using the drag forces created if the ring can move fast enough. Using a system similar to catenane **4** will not directly improve the situation. The second benzylic amide macrocycle will only move back and forth as seen by an external observer. The larger macrocycle still makes a net full rotation. However, when viewed from a different perspective, this will be an interesting system. The large macrocycle together with the surface mounted ring can be considered the motor, and the other small ring as something like a scoop. This is shown in Figure 25. Then this system will behave like a large motor moving a scoop back and forth. The scoop might then pick material up on one side and deposit it on the other side. The scoop is going back and forth in any two consecutive steps of the reaction sequence, so the efficiency of such a system is already three times higher than that of the motor itself.

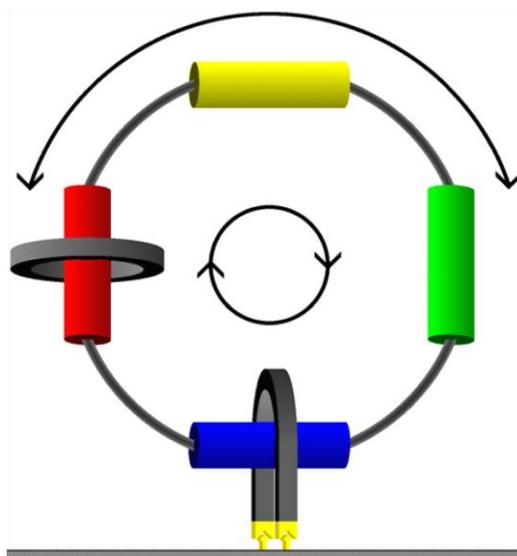


Figure 25: A schematic representation of a theoretical surface mounted [3]catenane based on the unidirectional motor catenane **4**. This system could in principle show unidirectional rotation of the larger macrocycle, as indicated by the central arrows. The effect of this rotation on the free benzylic amide group would be as indicated. The benzylic amide ring could be functionalized such that it could move something from left to right.

5. Conclusion

In this work, two different catenane based molecular motors were reviewed. The motor function of these catenane molecules is based upon the unidirectional rotation of a small ring around a larger macrocycle bearing different stations. These stations are designed to bind the small ring to different extent. Some stations can also be modified to change the affinity of the small ring and hence controlling movement in the system. It has been shown that the two different catenanes **4** and **5** display unidirectional rotation to quite a high degree. In catenane **5** the rotation can even go in both directions selectively. It was not yet shown that this type of rotors can do useful work but they are in principle able to do so. The downside of these catenane based motor molecules is that the speed of rotation is very low, and at least some form of purification is required at certain steps. In other words, continuous operation by, for example, constant irradiation is not possible. On the other hand, traits like high amplitudes of motion and the versatility of this kind of systems give it some advantages over other types of rotary motors. Some possible improvements on the given systems were discussed also. These hypothetical systems do not have some of the drawbacks the present systems have.

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