ChemPubSoc Europe

DOI: 10.1002/chem.201xxxxxx

CHEMISTRY
A European Journal
Full Paper

Supramolecular Chemistry

Slippage of a porphyrin macrocycle over threads of varying bulkiness. Implications for the mechanism of threading polymers through a macrocyclic ring

Alexander B. C. Deutman, Shaji Varghese, Mohamed Moalin, Johannes A. A. W. Elemans, Alan E. Rowan*, and Roeland J. M. Nolte*[a]

Abstract: The threading of a polymer through a macrocyclic ring may occur directly, i.e. by finding the end of the polymer chain, or via a process in which the polymer chain first folds and then threads through the macrocyclic ring in a hairpin-like conformation. We present kinetic and thermodynamic studies on the threading of a macrocyclic porphyrin receptor (**$H_2$1**) onto molecular threads that are blocked on one side and are open on the other side. The open side is modified by groups that vary in ease of folding and in bulkiness. Additionally, the threads contain a viologen binding site for the macrocyclic receptor, which is located close to the blocking group. The rates of threading of **$H_2$1** were measured under various conditions, by recording as a function of time the quenching of the fluorescence of the porphyrin, which occurs when receptor **$H_2$1** reaches the viologen binding site. The kinetic data suggest that threading is impossible if the receptor encounters an open side that is sterically encumbered in a similar way as a folded polymer chain. This indicates that threading of polymers through macrocyclic compounds via a folded chain mechanism is unlikely.

Introduction

The process of biopolymer translocation through pores formed by toroidal proteins is fundamental to numerous biological processes, including the transport of proteins across cell membranes, the infection of a host cell by viral DNA, and the packing of DNA into viral capsids.[1] Understanding the way in which biopolymers migrate through pores is very important, as it may open the possibility of developing novel, powerful analytical methods, such as the rapid sequencing of DNA molecules, gene therapy, and the controlled delivery of drugs.[2] In addition, the mechanisms by which natural systems convert chemical energy into directed motion is also connected to transport phenomena through pores and studying their mechanisms will provide in-depth information on the underlying principles of operation of these systems.[3] this in turn could avail researchers to design artificial motors systems and machines that can perform different tasks.[4]

[a] *Dr. A. B. C. Deutman, Dr. S. Varghese, Mohamed Moalin, Dr. J. A. A. W. Elemans, Prof. A. E. Rowan, Prof. R. J. M. Nolte*
Institute for Molecules and Materials
Radboud University Nijmegen
Heyendaalseweg 135, 6525 AJ Nijmegen (The Netherlands)
Fax: (+31)24-3652929
E-mail: A.Rowan@science.ru.nl
R.Nolte@science.ru.nl

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Previously, we have reported on a rotaxane catalyst that operates in a similar way as the naturally occurring DNA polymerases.[5] It is composed of a toroidally shaped cage compound containing a metalloporphyrin roof, which forms inclusion complexes with various substrate molecules. The manganese(III) porphyrin complex of this macrocyclic host (**$H_2$1**, Chart 1) was able to thread onto polymers e.g. polybutadiene and epoxidize the double bonds of this polymer in a "processive" manner, i.e. by carrying out several rounds of catalysis without detaching from the polymer chain. Our previous studies on the mechanism of threading and transport of **$H_2$1** on polymers revealed that the host compound initially binds to the outside of the polymer chain after which the polymer folds back and fills the cavity of the host (entron effect). The host subsequently moves along the polymer via a hopping process. This looping mechanism leads to accelerated threading and also to unidirectional motion.[7] There is some similarity with the conventional transport of proteins through pores of membranes in biological systems, namely, the "secretion (Sec)" pathway.[6] In this mechanism the biopolymer first binds to a site close to the open pore in the membrane and subsequently threads through it. In a similar fashion the end of the synthetic polymer may interact with the macrocyclic compound by binding to it and subsequently threading through it [7] (Figure1 and Figure 2a). The second type of transport of biopolymers through pores in membranes in biological systems is the twin-arginine translocation (Tat) pathway,

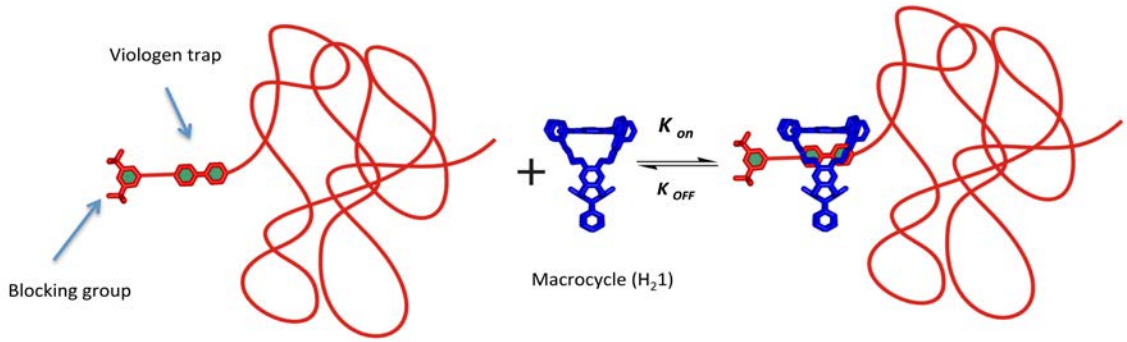


Figure 1. Reversible formation of a complex between a polymer and macrocyclic host **H₂1.** The polymer is blocked on one side and open on the other side. After threading the macrocycle is trapped at a viologen binding site, which is close to the blocked side.

which involves the process of translocating a fully folded protein across the cytoplasmic membranes of prokaryotes and the thylakoid membrane of plant chloroplasts. [6]

The intriguing question which we would like to answer is, "can a polymer chain thread through porphyrin macrocycle **H₂1** in a folded conformation or not?" It is known that a flexible polymer can adopt back-folded[8] and helical geometries,[9-14] while it is bound inside a host compound, hence it is not unlikely that **H₂1** can bind to a folded polymer chain and thread over it (Figure. 2b). This mechanism might be more favourable because the macrocycle does not have to find the open end of the polymer chain (Figure 2a), but can start the threading process at any position on the polymer chain.

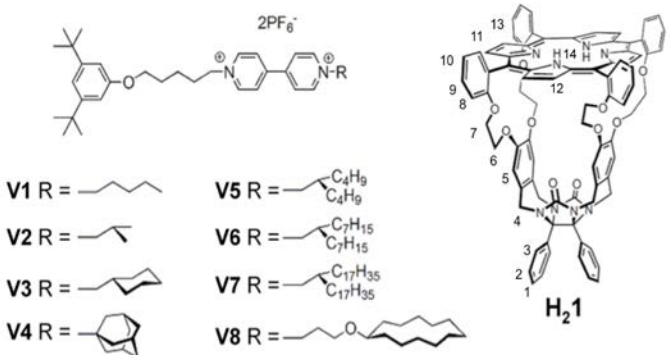


Chart 1. Porphyrin macrocycle **H₂1** and viologen derivatives **V1-V8.**

In order to answer this question we decided to study the kinetics of pseudo-rotaxane formation between porphyrin macrocycle **H₂1** and linear guest molecules that have a sterically crowded blocking group at one side and an open end at the other side (Chart 1). Close to the blocked side a viologen moiety is present to which **H₂1** strongly binds. Binding can only occur via the open side either by directly finding this end or via a folded chain mechanism. This approach was also chosen in our previous studies on the threading of **H₂1** onto polymers of different length.[7] To this end, viologen derivatives **V1-V8**, containing the same blocking group appended on one side and a variety of terminal groups appended on the other side, among which a cyclododecane moiety and a variety of appended iso-alkyl moieties, were synthesized (Chart 1). One of the main advantages of the use of porphyrin macrocycle **H₂1** in threading studies is its high affinity for viologen derivatives ($K_{assoc} \approx 10^5$-10^7 M^{-1}). When the porphyrin is bound to the viologen trap its fluorescence is quenched, hence measuring the fluorescence as a function of time allows the study of the threading process and complex formation at sub-micromolar concentrations. We decided to synthesize viologen derivatives with substituents that increase in size, with a bulkiness that is equal in size to a hairpin-folded conformation of the polymer. By studying the kinetic process of complex formation between **H₂1** and viologen derivatives **V1-V8**, not only the feasibility of the threading of **H₂1** over a folded polymer chain can be determined, but also the effect of the bulkiness of the end group on the process of threading can be estimated.

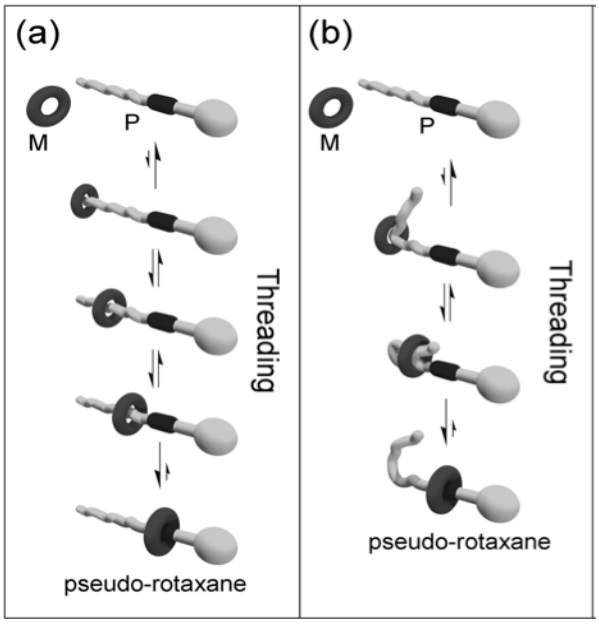
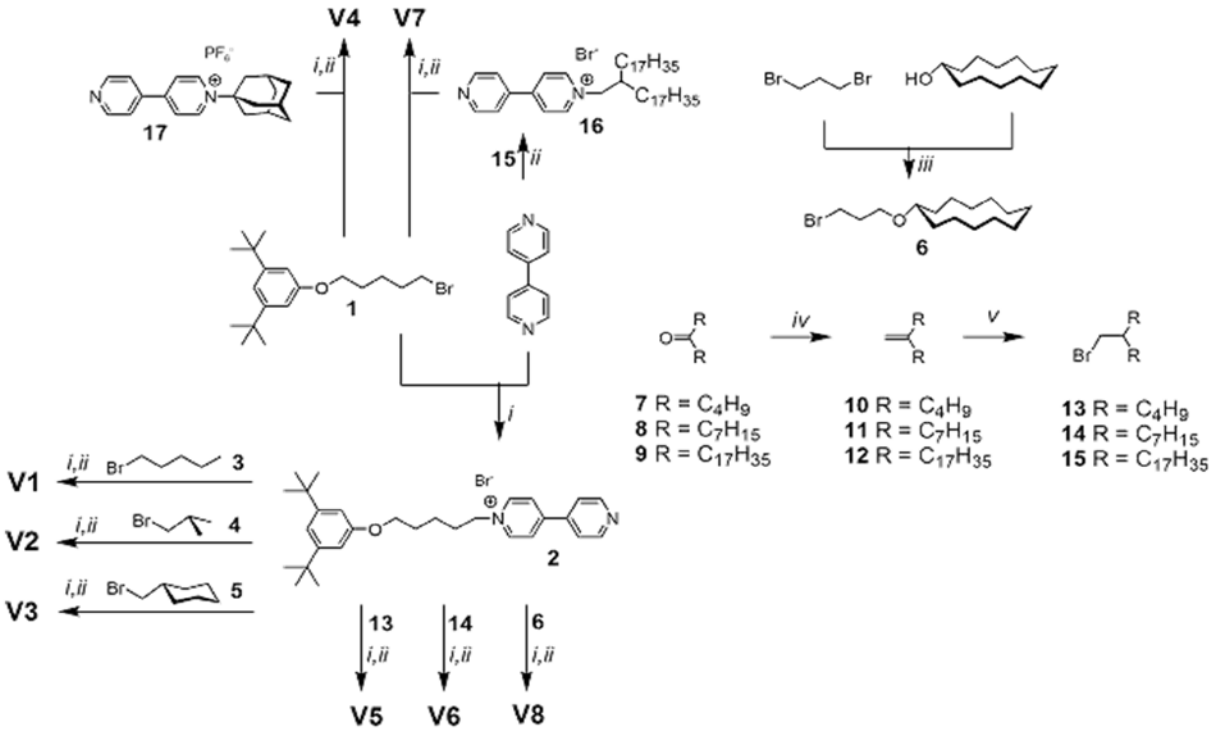


Figure 2. Schematic representation of pseudo-rotaxane formation via binding and threading. a) Threading mechanism in which the macrocycle threads onto the open end of the polymer chain and moves to the viologen trap in a random walk along a single chain. b) Threading mechanism in which the macrocycle binds to and moves over a folded chain eventually reaching the viologen trap.



Scheme 1. Synthesis of viologen derivatives **V1**-**V8**. Reagents and conditions: (*i*) DMF, 90°C, 1-5 d. (*ii*) NH_4PF_6 (aq). (*iii*) NaH, THF. (*iv*) KOtBu, Ph_3PCH_3Br, toluene. (v) 1. BH_3SMe_3, NaOH (aq), H_2O_2 (aq), THF; 2. Br_2Ph_3P, pyridine, CH_2Cl_2.

Results and Discussion

Synthesis of viologen derivatives

Macrocyclic host **H₂1** was synthesized as published previously.[22,23] Viologen derivatives **V1**-**V8** can be readily synthesized by substitution reactions of 4,4'-bipyridine (BiPy) with primary halides.[16] Reactions of an excess of BiPy with primary halides can statistically provide monoalkylated bipyridinium compounds. Two main approaches were chosen to synthesize viologens **V1**-**V8** (Scheme 1). In the first approach, blocking group-containing monoalkylated bipyridinium **2** was synthesized from BiPy and bromide **1**[5b] after which the terminal groups were appended by a second substitution reaction using primary bromides **3**, **4**, **5**, **6**, **13** and **14**, providing viologen derivatives **V1**-**V3, V5, V6** and **V8** after ion exchange with NH_4PF_6. In the second approach the terminal group-containing pyridinium salts **16** and **17** were first synthesized, after which the blocking groups were appended by nucleophilic substitution reactions with **1** providing viologen derivatives **V4** and **V7** after ion exchange with NH_4PF_6. (3-Bromo-propoxy)-cyclododecane **6** was synthesized by reacting 1,3-dibromopropane with cyclododecanol in the presence of NaH.[17] In addition to **6**, the terminal alkene elimination product of **6** was also formed in significant amounts and this product could unfortunately not be separated from **6**. This mixture of compounds was used as such in the synthesis of **V8**. Bromides **13**, **14** and **15** were synthesized via Wittig reactions[18a] of ketones **7**, **8**, and **9** followed by anti-Markovnikov bromination[19a] of the resulting alkenes **10**, **11** and **12**. Bipyridinium salt **17** was synthesized according to a literature procedure.[20]

^{1}H-NMR investigations

First, pseudo-rotaxane formation of **H₂1** with viologens **V1**-**V8** was investigated with the help of ^{1}H-NMR spectroscopy. Chloroform/acetonitrile solutions (1:1 (v/v)) containing **H₂1** (6.8 mM) and a slight excess of the different viologen guests were prepared. Immediate complex formation was observed in the case of the least bulky terminal group-containing viologen derivatives **V1**, **V2** and **V3**. The 400 MHz ^{1}H-NMR spectra revealed only proton resonances of the pseudo-rotaxane complexes between **H₂1** and **V1**, **V2** and **V3**, respectively, and resonances of the protons of unbound guests, because the exchange (hence the slippage) between **H₂1** and the different guests (**V1**-**V3**) is slow on the NMR timescale and no significant coordination between the outside of **H₂1** and the viologen derivatives occurred. The ^{1}H-NMR spectra of the solutions containing mixtures of **H₂1** and **V4** and **V5**, respectively, revealed slow formation of the pseudo-rotaxane complexes (Figure 3). Over time the proton resonances of uncomplexed **H₂1** and viologens **V4** and **V5** decreased in intensity at the benefit of the intensity of proton resonances of the respective pseudo-rotaxane complexes. The slippage over the adamantane group of **V4** is significantly faster than the slippage over the isononyl group of **V5**. Where full complexation was reached within the hour at room temperature in the slippage experiment using **V4**, for **V5** this was only achieved after 3 days of standing at room temperature. The ^{1}H-NMR experiments with **H₂1** and **V6**-**V8** revealed no pseudo-rotaxane formation, even after prolonged standing of the samples at elevated temperatures (50°C).

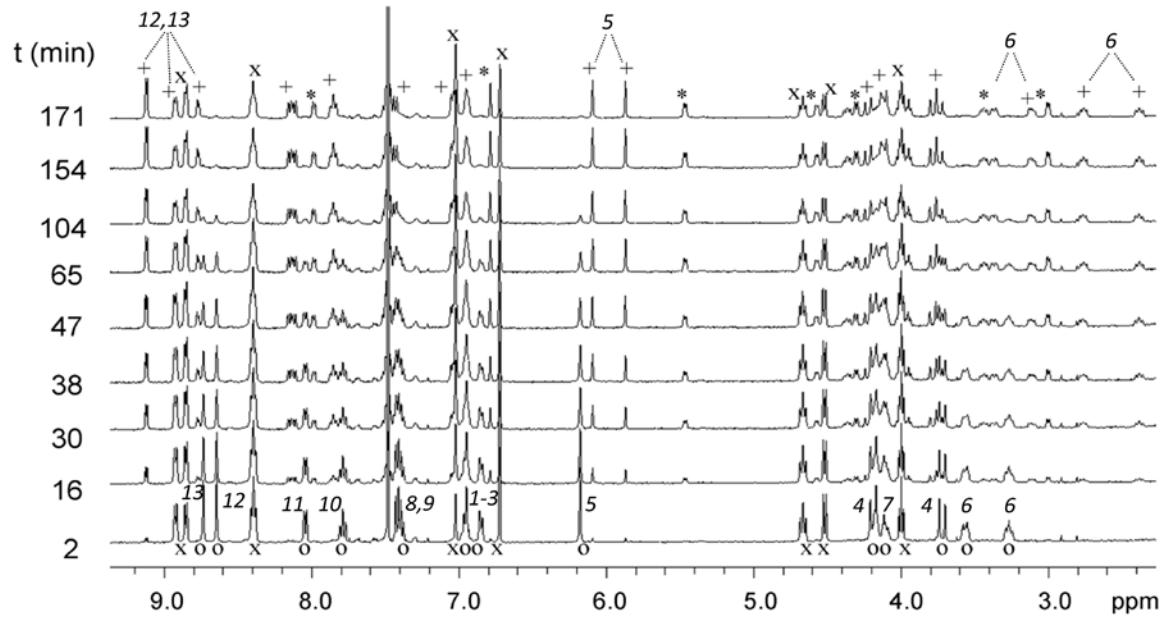


Figure 3. ^{1}H-NMR spectral changes (400 MHz, $CDCl_3/CD_3CN$ 1:1 (v/v)) during the threading experiment of **H₂1** (0.68 mM) and **V5** (1.4 mM, 2 equiv) as a function of time (from bottom to top) at 45°C, revealing the total disappearance of the resonances of **H₂1** and **V5** at the benefit of the formation of the non-symmetrical (pseudo-)rotaxane complex between **H₂1** and **V5**. The signals belonging to free **H₂1** (^{o}) and free **V5** (^{X}), and to **H₂1** ($^+$) and **V5** (*) in the rotaxane self-assembled structure are indicated. In the first and final spectrum, some of the proton signals of **H₂1** are assigned (see Chart 1 for numbering).

Thermodynamics and kinetics of pseudo-rotaxane formation.

The evolution of macrocycle A, guest B and pseudo-rotaxane C in time in the threading process can be completely described by Equations 1-3. The association constant (K_{assoc}) between the macrocycle and the guest is given by equation 4. Equation 1 is the universal formula for the threading process and can be employed independent of the relative ratios of macrocycle ($[A]_o$) and guest ($[B]_o$) or the initial amount of pseudo-rotaxane complex present at t = 0 ($[C]_o$). It is therefore not necessary to mix equimolar amounts of macrocycle and guest to calculate accurate rate constants. Equations 1-3 can also be employed to calculate rate constants in dethreading processes in which $k_{off} = k_{on}/K_{assoc}$.

$$A + B \underset{k_{off}}{\overset{k_{on}}{\rightleftharpoons}} C$$

$$[C] = p\frac{\left(1-\frac{q}{p}\frac{p-[C]_o}{q-[C]_o}e^{k_{on}(p-q)t}\right)}{\left(1-\frac{p-[C]_o}{q-[C]_o}e^{k_{on}(p-q)t}\right)} \quad (1)$$

$$p = [C]_{eq} \quad (2)$$

$$q = \frac{[A]_o[B]_o}{[C]_{eq}} \quad (3)$$

$$K_{assoc} = \frac{[C]_{eq}}{\left([A]_o - [C]_{eq}\right)\cdot\left([B]_o - [C]_{eq}\right)} \quad (4)$$

In the ^{1}H-NMR experiments in which the threading equilibrium is not immediately reached (i.e. in the case of viologen derivatives **V4** and **V5**), the ratios of **H₂1**, viologen and pseudo-rotaxane in time could be easily determined from the relative intensities of the ^{1}H-NMR signals associated with each species. By monitoring the decrease in the relative intensities of **H₂1** and viologen derivatives **V4** and **V5**, respectively, with respect to their concomitant appearance in the complexes as a function of time, the rate constants for the slippage processes, k_{on}, could be calculated by using equations 1-3. At equilibrium, no free **H₂1** could be observed at the used concentrations of this host and viologen guests **V4** or **V5**, which makes it impossible to derive accurate values for K_{assoc}. Only a lower limit for these association constants could be calculated from the experiments (Table 1).

The process of the slippage of **H₂1** with **V4** was slightly too fast to calculate satisfactorily accurate rate constants with the help of ^{1}H-NMR techniques (over 50% of pseudo-rotaxane had already been formed after recording the first spectrum). Therefore, it was decided to monitor pseudo-rotaxane formation by UV-vis spectroscopy. Solutions containing **H₂1** (2 x 10^{-5} M) and **V4** (6 x 10^{-4} M, 40 equivalents) were prepared in chloroform/acetonitrile 1:1 (v/v) and after the addition of the solution of **V4** to the solution of **H₂1** the spectral changes of the porphyrin Soret band were monitored in time. The concentrations of **V4** were chosen such that at equilibrium **H₂1** would be nearly completely occupied by **V4**, hence the total change in absorption at any wavelength simply represented the change in the amount of free **H₂1** with respect to the pseudo-rotaxane complex between **H₂1** and **V4**. The concentration of pseudo-rotaxane in time, $[C]_t$, in the experiment is therefore given by: $[C]_t = [A]_o\{A_t-A_o\}/\{A_{eq}-A_o\}$, in which A_o, A_t and A_{eq} are the absorbance at t = 0, t, and t = ∞,

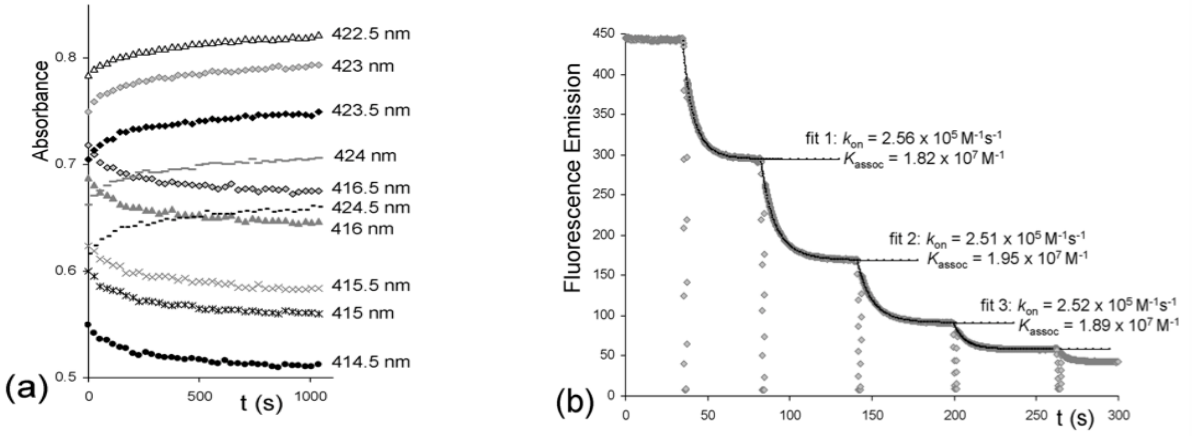


Figure 4. a) Evolution of the absorbance of the porphyrin Soret band of **H₂1** (1.6 x 10^{-4} M) at different wavelengths in time after the addition of 50 equiv. of **V4** in $CHCl_3/CH_3CN$ (1:1, v/v) at 25°C. b) Fluorescence emission (grey dots) of **H₂1** after the addition of increasing amounts of **V3** in time in $CHCl_3/CH_3CN$ (1:1, v/v) at 1°C. While mixing, the cuvettes were removed from the spectrometer which results in the local drops in fluorescence. The black lines indicate the fits that are obtained by using equations 1-4. The constants k_{on} and K_{assoc}, calculated from the individual threading curves, are all in the same order of magnitude, which stresses the accuracy of the data analysis.

respectively. A small red shift of the porphyrin Soret band and an isosbestic point were observed upon formation of the pseudo-rotaxane complex. The evolution of the absorbances at different wavelengths in time (Figure 4a) could be fitted with the help of equations 1-3. In fact, such an excess of **V4** was used that the kinetics of the threading could also be fitted with (pseudo) first order binding isotherms, and the calculated averaged rate constant for the threading of **H₂1** with **V4**, k_{on} = 7.9 $M^{-1}s^{-1}$), was in good agreement with the rate constant determined by ^{1}H-NMR spectroscopy (k_{on} = 8.5 $M^{-1}s^{-1}$).

In order to derive the rate constants for the threading of **H₂1** over the least bulky terminal groups of the viologens, i.e. those of **V1**-**V3**, threading experiments were performed at low concentrations (10^{-6} M) of **H₂1** and these guests in a 1:1 (v/v) mixture of chloroform and acetonitrile. Since upon the binding of viologen derivatives the porphyrin fluorescence emission is fully quenched, the kinetics and thermodynamics of complex formation could be easily monitored by recording this fluorescence emission in time. The pseudo-rotaxane concentration [C] is given by $[C]_t = [A]_o\{E_o\text{-}E_t\}/E_o$, in which E_o and E_t are the fluorescence emissions at t = 0 and t, respectively. In order to obtain as many data as possible in a short time span, it was decided to perform titration experiments in which solutions containing low concentrations (2-4 x 10^{-7} M^{-1}) of the viologen derivatives were added to a solution containing **H₂1**. After each addition, the fluorescence emission slowly reached a new equilibrium position, and at that point a following batch of viologen-containing solution was added (see Figure 4b for complexation between **H₂1** and **V3**). The fluorescence emission curves in time could be fitted with the use of equations 1-4, providing the values of k_{on} and K_{assoc} in plural, thereby significantly minimizing the error both in k_{on} and K_{assoc}.

In order to investigate the effect of the temperature on the kinetics of the process, the slippage of **H₂1** over the terminal groups of **V1**-**V5** was monitored at at least three different temperatures using either of the above described methods. The enthalpic ($\Delta H^{\neq}_{on}$) and entropic ($\Delta S^{\neq}_{on}$) contributions to the total free energy of activation ($\Delta G^{\neq}_{on}$) were determined from the straight lines of the Eyring Plots (Figure 5a). In addition, the enthalpic (ΔH^o) and entropic (ΔS^o) contributions to the total free binding energy (ΔG^o) of pseudo-rotaxane formation between **H₂1** and **V2** or **V3** could be determined with the help of Van 't Hoff plots (Figure 5b). All the thermodynamic and kinetic data are listed in Table1.

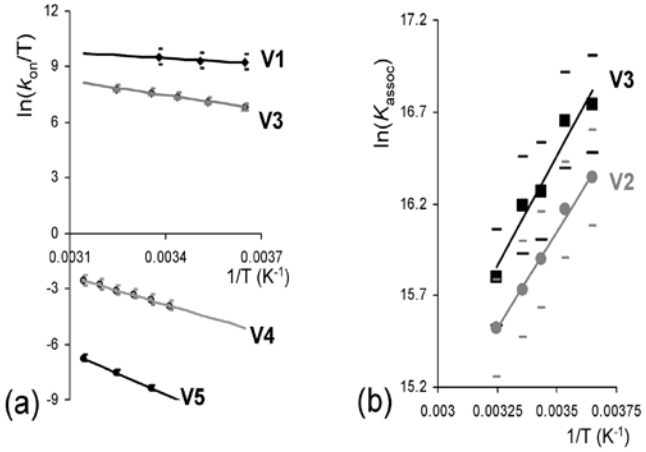


Figure 5. a) Eyring plots for the threading of **H₂1** over **V1**, **V3**, **V4** and **V5**. b) Van 't Hoff plots for the complexation of **H₂1** with **V2** and **V3.** (Error bars are indicated by the horizontal lines.)

Kinetic data

Earlier reports in the literature have shown that very subtle changes in terminal groups of a thread, such as going from on ethyl to an isopropyl[21] or from a cyclohexane to a cycloheptane substituent,[15j] result in an all-or-nothing effect for the slippage of a macrocycle over these terminal groups. A small increase in

Table 1. Rate constants (k_{on}) for the threading of **H₂1** over **V1-V8** and the activation parameters ($\Delta G^{\neq}_{on}$, $\Delta H^{\neq}_{on}$, $\Delta S^{\neq}_{on}$) obtained from an evolution of the kinetic data using Eyring plots, the association constants (K_{assoc}) and free energies of association (ΔG^{o}) of the formed complexes, and the thermodynamic complexation parameters (ΔH^{o}, ΔS^{o}) obtained from an evolution of the thermodynamic data using Van't Hoff plots.

Guest	k_{on} ($M^{-1}s^{-1}$) [g]	$\Delta G^{\neq}_{on}$ (kJ mol^{-1}) [i]	$\Delta H^{\neq}_{on}$ [j] (kJ mol^{-1})	$\Delta S^{\neq}_{on}$ [j] (J mol^{-1}K^{-1})	K_{assoc} (M^{-1}) [h]	ΔG^{o} (kJ mol^{-1}) [i]	ΔH^{o} (kJ mol^{-1}) [j]	ΔS^{o} (J mol^{-1} K^{-1}) [j]
V1[a]	5 x 10^{6}	35	15	-67	1.3 x 10^{7}	-41	[e]	[e]
V2[a]	3 x 10^{6}	36	[d]	[d]	6.8 x 10^{6}	-39	-18	72
V3[a]	6.0 x 10^{5}	40	21	-64	1.1 x 10^{7}	-40	-20	68
V4[b]	7.9	68	42	-87	> 10^{6} [e]	[e]	[e]	[e]
V5[c]	7.0 x 10^{-2}	80	63	-56	> 10^{6} [e]	[e]	[e]	[e]
V6-V8	[f]	[f]	[f]	[f]	[f]	[f]	[f]	[f]

[a] Determined by fluorescence titrations in $CHCl_3/CH_3CN$ 1:1, (v/v). [b] Determined by UV vis titrations in $CHCl_3/CH_3CN$ 1:1, (v/v). [c] Determined by ^{1}HNMR experiments in $CDCl_3/CD_3CN$ 1:1, (v/v). [d] Threading rate was too high to be measured accurately at the used experimental conditions. [e] Association constant was too high to be calculated accurately at the used experimental concentrations. [f] No complex formation was observed. [g] Estimated error < 15%. [h] Estimated error < 35%. [i] Estimated error 1 kJ mol^{-1}. [j] Estimated error 2 kJ mol^{-1}.

terminal group bulkiness can increase the steric hindrance to the level that the barrier for slippage becomes insurmountable. A similar and perhaps even more subtle all-or-nothing effect was observed in the present study. While a very low value for the rate constant was observed for the threading of **H₂1** over **V5**, indicating that **H₂1** can only just slip over the isononyl group, threading over the longer substituents of **V6**, **V7** and over the cyclododecyl moiety of **V8** appeared to be not possible. Obviously, the cavity of **H₂1** is not large enough to allow slippage of the cyclododecyl terminal group of **V8**. The all-or-nothing effect observed between **V5** and **V6** clearly indicates that very subtle differences in steric bulk govern whether threading is possible or not. It moreover provides a clear hint on the mechanism by which the isononyl of **V5** group is traversed. Two plausible mechanisms for this process can be rationalised. A first one, in which the macrocycle threads onto a single n-butyl chain, after which it moves in a second step over both the second chain and part of the viologen moiety (Figure 6b), similar to the mechanism reported for the slippage of bis-p-phenylene-34-crown-10 over 4-*R*-phenyl-bis(4-*tert*-butyl-phenyl)methane-based stoppers.[15i] Assuming this mechanism, the bottle-neck of the slippage lies for **V5** in traversing the part where **H₂1** needs to overcome the steric bulk of the second part of the chain and the viologen group. A second possible mechanism is that the two isononyl chain ends are 'tweezed' together in close proximity and the threading occurs over a double chain, as presented in Figure 6a. The first mechanism can be considered unlikely due to the need for a presumably highly unfavourable back-folding of the alkyl chain onto the viologen moiety, in which this chain gets in close proximity to the repelling positive charge on the viologen. ^{1}H-NMR studies do not suggest such a back-folding of the alkyl chain. Also the second mechanism is at first sight not very likely, since it needs an organization of the highly flexible alkyl chains in a very specifically tweezed geometry, which would in principle be entropically highly unfavourable, although the same entropic argument can also be applied to the first mechanism. In order to determine which of the two mechanisms is the most likely one, the circumferences of the Van der Waals surfaces of the different transition state conformations (the most bulky part of the terminal groups in their least bulky conformations) were estimated with the help of Corey-Pauling-Koltun (CPK) models. Although for **V5** and **V6** the differences in substituent bulkiness are very marginal (within 8%, see Figure 6), the transition state conformations of the second mechanism were less 'bulky' than those of the first. A measurement of the largest inner circumference of **H₂1** (19.8 Å, see Figure 7), moreover, revealed that only the transition state conformation of the isononyl group in the second mechanism (Figure 6a, 19.4 Å) is within the dimensions of the cavity. These results tentatively suggest that **H₂1** threads over the isononyl group of **V5** according to the second mechanism, in which the chain ends of the terminal group are tweezed together (Figure 6a). The slightly more bulky terminal group of **V6** just exceeds the dimensions of the cavity, resulting in no threading.

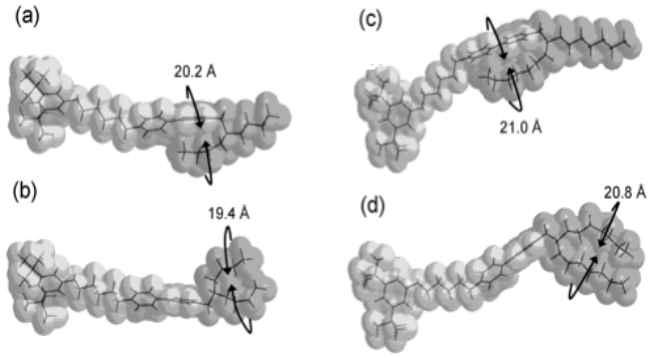


Figure 6. Space filling molecular models of proposed slippage transition state conformations of the terminal groups of **V5** (left) and **V6** (right) for the tweezed double chain mechanism ((a) and (c)) and the back-folding mechanism ((b) and (d)). The maximum circumferences of the Van der Waals surfaces in the transition state geometries are indicated to stress that conformation (a) is the least bulky.

(Figure 7b). The plot clearly shows that when the circumferences of the terminal groups approach the inner circumference of the macrocycle, the rate constant for threading tends to zero. This is another good indication that indeed the steric interactions between terminal group and the macrocycle determine the relative rates and feasibility of the threading process. The enthalpic contributions to the activation energy ($\Delta H^{\neq}_{on}$), obtained by evaluation of the threading at different temperatures, point in the same direction: a clear increase in enthalpy of activation is observed upon increasing the terminal group bulkiness (Table 1),

which is in line with the idea that the steric repulsion is enthalpic of origin.

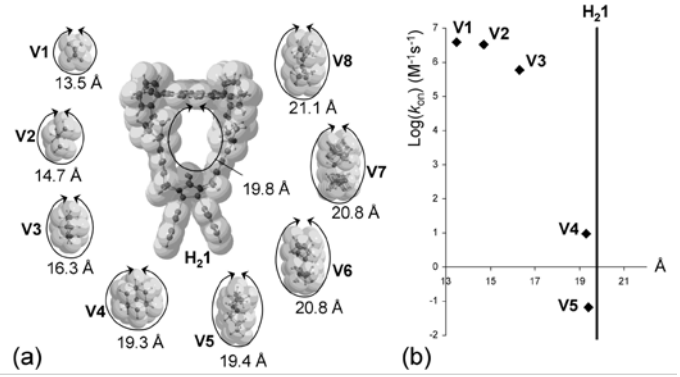


Figure 7. a) Circumferences of the terminal groups of **V1**-**V8** that **H21** has to surmount before complex formation can occur and the inner circumference of the cavity of **H21**, all based on Van der Waals surfaces. b) Rate constants for the slippage of **H21** over the different terminal groups plotted against the circumference of these groups and the inner circumference of the cavity of **H21**.

Although in all cases the slippage is entropically unfavourable, no trend could be observed in the values of the entropy of activation ($\Delta S^{\neq}_{on}$). The differences in the obtained activation parameters observed for the threading over the adamantane group of **V4** and the isononyl group of **V5** are intriguing. The rate constant for slippage over the adamantane is more than two orders of magnitude higher than the rate constant for the slippage over the isononyl group. While the adamantane group has a fixed and nearly spherical geometry and is therefore readily organized for the threading of **H21**, the isononyl group can be expected to be very flexible and needs to preorganize in its least bulky conformation to allow threading of **H21**. Based on these differences in flexibility one would therefore expect a more negative value for the entropy of activation ($\Delta S^{\neq}_{on}$) for slippage over the isononyl terminal group than over the adamantane group. However, the contrary was derived from the variable temperature experiments, suggesting that other factors than the flexibility of the terminal groups, like for instance differences in terminal group solvation, enthalpy-entropy compensation, or the flexibility of the receptor also play a crucial role in the threading process. It can also be argued that the isononyl group already is preferentially organised in the 'tweezed' conformation in the rather polar solvent mixture. Irrespective of what exactly causes the experimentally obtained activation parameters, the main difference between the threading over the terminal groups of **V4** and **V5** is reflected in the enthalpy of activation ($\Delta H^{\neq}_{on}$). This difference is most probably caused by a less favourable fit of the isononyl group of **V5** inside the cavity of **H21** compared to the adamantane group of **V4**, which stresses once more that steric hindrance is the main rate determining factor in the threading process.

Thermodynamic data

The binding free energy of the pseudo-rotaxane complexes of **H21** with **V2** and **V3** are a result of both favourable enthalpic (ΔH^{o}) and entropic contributions (ΔS^{o}), as can be concluded from the data in Table 1. In addition to stabilizing non-covalent binding interactions (such as π-π interactions, Van der Waals interactions and dipole-dipole interactions) between **H21** and the viologen derivatives, which are most likely enthalpic of origin, there is also a strong entropic driving force for complex formation. This is most probably the result of desolvation of the viologen moieties and the cavity of **H21** upon formation of the pseudo-rotaxane complexes. The association constant of **H21** with **V3** is larger than that of **H21** with **V2** (Table 1). This observation is in line with our previous findings that an increase in the size of the viologen substituents results in stronger complex formation with **H21**.[5b] Although the electronic properties of the viologen derivatives with different substituents are expected to be slightly different, and hence also the viologen-macrocycle interactions, this effect is proposed to be mainly the result of extra stabilizing (Van der Waals interactions between the macrocyle and the substituents in the formed host-guest complexes. For this reason, the cyclohexyl group of **V3** can provide more of these stabilizing interactions in the complex with **H21** than the isopropyl group of **V2**. The validity of this hypothesis is emphasized by the different enthalpic contributions (ΔH^{o}) to the binding free energy (ΔG^{o}), which reveal a more favourable enthalpy of binding in the complex between **H21** and **V3** than in the complex between **H21** and **V2**. The results suggest, on the other hand, that it is entropically more favourable to form the complex between **H21** and **V2** than the complex between **H21** and **V3**. This might be the result of a relatively better solvation of **V3** compared to **V2** in the used solvent system, because of the larger nonpolar cyclohexyl substituents compared to the isopropyl substituents, which reduces the relative 'need' for **V3** to form a complex with **H21** compared to **V2**. It is also possible that the extra stabilization of the complex between **H21** and **V3** by the cyclohexyl group is entropically more demanding.

Conclusion

The present study indicates that the ease of threading porphyrin macrocycle **H21** over viologen-containing guests with different terminal groups strongly depends on the size complementarities and subsequent steric interactions between the Van der Waals surfaces of the macrocycle and the terminal group. The rate constants of threading decrease upon increasing the bulkiness of the terminal group, and when the dimensions of its Van der Waals surface exceeds that of the inner Van der Waals surface of the macrocycle, the barrier for the threading becomes insurmountable, resulting in an all-or-nothing effect. The results strongly suggest that movement of **H21** over a looped polymeric chain, as proposed previously, is highly unfavourable, if not impossible. The experiments revealed that no threading occurred over the terminal groups of **V6**, **V7** and **V8**, and a very low rate constant for the threading over the terminal group of **V5**. The observed rate constant for the threading over the isononyl terminal group of **V5** is more than 5 orders of magnitude lower than the previously reported rate constant for the movement of **H21** over a poly-THF terminal group of 54 nm length.[7b] It can thus be concluded that in the threading of polymeric substrates, **H21** first binds onto the open end of the polymer chain after which it traverses the complete polymer chain before it reaches the

viologen binding site, and that threading over a folded polymer chain is unlikely.

Experimental Section

Materials and methods. Chloroform and acetonitrile used in the titration experiments were distilled from $CaCl_2$. Tetrahydrofuran was distilled under nitrogen from sodium and benzophenone. Dichloromethane was distilled under nitrogen from $CaCl_2$. Toluene was distilled under nitrogen from sodium. All other solvents and chemicals were commercial products and used as received. Fluorescence experiments were performed on a Perkin-Elmer LS50B luminescence spectrometer equipped with a thermostatted cuvette holder. UV-vis spectra were recorded on a Cary 100 Conc (Varian, Middelburg) UV-Vis spectrometer. MALDI-TOF mass spectroscopy was performed on a Bruker Biflex III spectrometer. High-resolution mass spectra (HRMS) were measured on a JEOL JMS-T100CS AccuTOF. NMR spectra were taken on a Varian Inova 400 (400 MHz, 1H and 2D spectra) instrument or on a Bruker DMX 300 (75 MHz, 13C spectra) machine and were calibrated to an internal standard of tetramethylsilane (0.00 ppm). Porphyrin macrocycle **$H_2$1** was synthesized according to a literature procedure.[22,23]

(3-Bromo-propoxy)-cyclododecane (6):

To a 0 °C suspension of NaH (0.11 g of 60 % NaH in mineral oil, 2.8 mmol) in dry THF (3 ml) was added dropwise a solution of cyclododecanol (0.26 g, 1.1 mmol) in dry THF (4 ml) over a period of 10 minutes under argon atmosphere. The reaction mixture was allowed to warm to room temperature, stirred for 1 hour, cooled to 0 °C after which 1,3-dibromopropane (2.2 ml, 24 mmol) was added slowly. The reaction mixture was allowed to warm to room temperature again, stirred for 1 hour, cooled to 0 °C, mixed with diethyl ether (14 ml), neutralized with aqueous 1.0 M HCl (14 ml) and then stirred for 1 hour at room temperature. The ether layer was washed with aqueous 1.0 M HCl (1x), brine (2x) and dried over $MgSO_4$. The drying agent was filtered off, the solvents were evaporated and the remaining 1,3-dibromopropane was distilled off to give 70 mg of a mixture of 6 and its alkene derivative as a white solid in a molar ratio of circa 1 to 2. This mixture was directly used for the synthesis of V8.

^{1}H-NMR (400 MHz, $CDCl_3$) alkene characteristics: δ (ppm) 5.92 (m, 1H, H_2C=C*H*), 5.27 (m, 1H, CH_2CH=CH_{trans}), 5.15 (m, 1H, CH_2CH=CH_{cis}), 3.98 (dt, 2H, C=CHCH_2, J = 5.6, J = 1.2 Hz), 3.47 (m, 1H, cyclododecaneC*H*), 1.28-1.36 (m, 22H, cyclododecane(CH_2)$_{11}$). Bromide characteristics: δ 3.55 (t, 2H, OCH_2, J = 6 Hz), 3.53 (t, 2H, BrCH_2, J = 6.8 Hz), 2.07 (q, 2H, BrCH$_2$CH_2, J = 5.2 Hz), 3.42 (m, 1H, cyclododecaneC*H*), 1.28-1.36 (m, 22H, cyclododecane(CH_2)$_{11}$).

General synthesis of the methylene compounds 10, 11, 12: [18a]

At room temperature, KOtBu (1.2 g, 11 mmol) was added in four portions to a solution of methyltriphenylphosphonium bromide (3.3 g, 9.3 mmol) in dry toluene (70 ml). The mixture was refluxed for 1 hour under argon atmosphere and then cooled to room temperature. A mixture of the corresponding ketone in dry toluene was added dropwise and then stirred for 30 minutes. A saturated aqueous NH_4Cl solution (30 ml) was added to the reaction mixture, which was then extracted with diethyl ether (3x). The combined organic phases were washed with brine (2x) and then dried over $MgSO_4$. The drying agent was filtered off and the filtrate was evaporated in the presence of an excess of silica to avoid stopping of the column by the remaining organic salts. The silica mixture was put on a flash silica column and the product eluted to obtain the corresponding methylene product.

5-Methylene-nonane (10): [18b]

Ketone mixture: 7 (1.0 g, 7.0 mmol) in 5 ml of toluene. Eluent: n-pentane. Yield = 0.63 g as a colourless liquid (4.5 mmol, 64 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.69 (q, 2H, C=CH_2, J = 0.8 Hz), 2.00 (t, 4H,CH_2=CCH_2, J = 8.0 Hz), 1.40 (m, 8H, CH_2=CCH_2CH_2CH_2), 0.91 (t, 6H, CH_3, J = 7.2 Hz).

8-Methylene-pentadecane (11): [18c]

Ketone mixture: 8 (2.1 g, 9.2 mmol) in 5 ml of toluene. Eluent: n-heptane. Yield = 1.5 g as a white solid (6.7 mmol, 72 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.68 (q, 2H, C=CH_2, J = 1.2 Hz), 1.99 (t, 4H,CH_2=CCH_2, J = 8.0 Hz), 1.41 (q, 4H, CH_2=CCH_2CH_2, J = 6.8 Hz), 1.28 (m, 16H, CH_2=CCH_2CH_2CH_2CH_2CH_2), 0.88 (t, 6H, CH_3, J = 7.2 Hz).

18-Methylene-pentatriacontane (12): [18d]

Ketone mixture: 9 (4.6 g, 9.2 mmol) in 10 ml of toluene. Eluent: n-heptane. Yield = 1.34 g as a white solid (2.66 mmol, 30 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.68 (m, 2H, C=CH_2), 1.99 (t, 4H,CH_2=CCH_2, J = 7.2 Hz), 1.40 (dd, 4H, CH_2=CCH_2CH_2, J = 6.8 Hz), 1.26 (m, 56H, CH_2=CCH_2CH_2 (CH_2)$_{14}$), 0.88 (t, 6H, CH_3, J = 7.2 Hz).

Synthesis of the primary bromides 13, 14, and 15:[19a]

(Alcohol synthesis) A 0 °C solution of the corresponding methylene compound (10, 11 or 12 respectively) in dry THF was treated dropwise with a 2.0 M solution of borane methyl sulfide in toluene. After 2 hours of stirring at 0 °C, the reaction mixture was warmed to room temperature, stirred for an additional 2.5 hours, cooled to 0 °C, neutralized with ethanol, aqueous 3.0 M NaOH and 35 % aqueous H_2O_2. After 30 minutes of stirring, the reaction mixture was allowed to warm to room temperature and stirred overnight. The basic mixture was treated with aqueous 1 M HCl, the organic layer was separated and the aqueous layer was extracted with diethyl ether (3x). The combined organic phases were washed with brine (2x) and then dried over $MgSO_4$. The drying agent was filtered off and the filtrate was evaporated. The crude mixture was subjected to a flash silica column to obtain the corresponding primary alcohol.

2-Butylhexan-1-ol: [19b]

Methylene solution: 10 (0.40 g, 2.9 mmol) in 30 ml of THF. Borane solution: 0.90 ml, 1.8 mmol. Neutralization solutions: ethanol (6 ml), aqueous 3.0 M NaOH (35 ml) and aqueous 35 % H_2O_2 (35 ml). Eluent: n-pentane/diethyl ether, 9:1 (v/v). Yield = 0.32 g as a colourless liquid (2.0 mmol, 69 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.54 (t, 2H, HOCH_2, J = 5.6 Hz), 1.45 (m, 1H, HOCH$_2$C*H*), 1.38-1.22 (m, 12H, HOCH$_2$-CHCH_2CH_2CH_2), 1.18 (t, 1H, O*H*, J = 5.6 Hz), 0.90 (t, 6H, CH_3, J = 7.2 Hz).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 65.14, 40.00, 30.14, 28.62, 22.61, 13.57.

2-Heptylnonan-1-ol: [19c]

Methylene solution: 11 (1.5 g, 6.7 mmol) in 50 ml of THF. Borane solution: 2.3 ml, 4.6 mmol. Neutralization solutions: ethanol (12 ml), aqueous 3.0 M NaOH (75 ml) and aqueous 35 % H_2O_2 (75 ml). Eluent: n-heptane/diethyl ether, 1:1 (v/v). Yield = 1.5 g as a white solid (6.2 mmol, 93 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.54 (m, 2H, HOCH_2), 1.45 (m, 1H, HOCH$_2$C*H*), 1.36-1.20 (m, 24H, HOCH$_2$-CH(CH_2)$_6$), 1.20 (s, 1H, O*H*), 0.88 (t, 6H, CH_3, J = 7.2 Hz).

2-Heptadecylnonadecan-1-ol:

Methylene solution: 12 (1.3 g, 2.7 mmol) in 30 ml of THF. Borane solution: 0.9 ml, 1.8 mmol). Neutralization solutions: ethanol (5 ml), aqueous 3.0 M NaOH (30 ml) and aqueous 35 % H_2O_2 (30 ml). Eluent: n-heptane/diethyl ether, 1:1 (v/v). Yield = 1.0 g as a white solid (1.9 mmol, 72 %).

^{1}H-NMR (400 MHz, CD_3CN:$CDCl_3$, 1:1 (v/v)): δ 3.43 (t, 2H, HOCH_2, J = 5.6 Hz), 2.18 (m, 1H, HOCH$_2$C*H*), 2.13-2.04 (m, HOCH$_2$-CHCH_2chain), 1.35-1.10 (m, CH_3CH_2chain), 1.25 (t, , 1H, O*H*), 0.88 (t, 6H, CH_3, J = 7.2 Hz).

(Bromination reaction) To a 0 °C suspension of triphenylphosphine dibromide in dry DCM was added a solution of the corresponding alcohol and pyridine in dry DCM. The reaction mixture was stirred at 0 °C for 15 minutes and for 1 hour at room temperature, and was subsequently neutralized with 10 % of aqueous sodium bisulfite. The organic layer was separated and the aqueous layer extracted with dichloromethane (2x) and diethyl ether (1x). The combined organic phases were dried over $MgSO_4$, filtered and then evaporated in the presence of an excess of silica to avoid stopping of the column by the remaining organic salts. The product was purified on a flash silica column and the eluent was evaporated to obtain the corresponding primary bromide.

5-(Bromomethyl)-nonane (13): [19b]

The triphenylphosphine dibromide suspension was prepared from triphenylphosphine (0.55 g, 2.1 mmol) and bromine (0.11 ml, 2.1 mmol) in 9 ml of DCM. Alcohol solution: 2-butylhexan-1-ol (0.25 g, 1.6 mmol) and pyridine (0.40 ml, 5.0 mmol) in 2 ml of DCM. Eluent: n-pentane. Yield = 0.22 g as a colourless liquid (0.99 mmol, 62 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.45 (d, 2H, BrCH_2, J = 4.8 Hz), 1.60 (m, 1H, BrCH$_2$C*H*), 1.44-1.17 (m, 12H, CH_2), 0.91 (t, 6H, CH_3, J = 7.2 Hz).

8-(Bromomethyl)-pentadecane (14):

The triphenylphosphine dibromide suspension was prepared from triphenylphosphine (1.4 g, 5.4 mmol) and bromine (0.28 ml, 5.5 mmol) in 20 ml of DCM. Alcohol solution: 2-heptylnonan-1-ol (1.0 g, 4.1 mmol) and pyridine (0.90 ml, 11 mmol) in 4 ml of DCM. Eluent: n-heptane. Yield = 1.0 g as a white solid (3.3 mmol, 80 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.45 (d, 2H, BrCH_2, J = 4.8 Hz), 1.59 (m, 1H, BrCH$_2$C*H*), 1.43-1.19 (m, 24H, CH_2), 0.89 (t, 6H, CH_3, J = 7.2 Hz).

18-(Bromomethyl)-pentatriacontane (15):

The triphenylphosphine dibromide suspension was prepared from triphenylphosphine (0.66 g, 2.5 mmol) and bromine (0.13 ml, 2.5 mmol) in 10 ml of DCM. Alcohol solution: 2-Heptadecylnonadecan-1-ol (1.0 g, 1.9 mmol) and pyridine (0.40 ml, 5.0 mmol) in 2 ml of DCM. Eluent: n-heptane. Yield = 0.90 g as a white solid (1.5 mmol, 79 %).

^{1}H-NMR (400 MHz, $CDCl_3$) δ = 3.45 (d, 2H, BrCH_2, J = 4.8 Hz), 1.58 (m, 1H, BrCH$_2$C*H*), 1.43-1.19 (m, 24H, CH_2), 0.88 (t, 6H, CH_3, J = 7.2 Hz).

1-Adamantyl-4-(pyridin-4-yl)pyridinium hexafluorophosphate (17):
This compound was synthesized according to a literature procedure.[20]
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 9.04 (d, 2H, Bipy*H*, J = 6.8 Hz), 8.85 (d, 2H, Bipy*H*, J = 6.4 Hz), 8.33 (d, 2H, Bipy*H*, J = 6.4 Hz), 7.82 (d, 2H, Bipy*H*, J = 6.4 Hz), 2.39 (m, 3H, adamantaneC*H*), 2.32 (m, 6H, amantaneCH_2), 1.84 (m, 6H, adamantaneCH_2).
1-(Pentatriacontan-18-yl)-4-(pyridin-4-yl)pyridinium bromide (16):
Bromide 15 (450 mg, 0.77 mmol) and 4,4'-bipyridine (1.4 g, 9.4 mmol) were dissolved in 20 ml of dry MeCN and the mixture was gently refluxed for 7 days under an argon atmosphere. After cooling to room temperature, the mixture was precipitated from diethyl ether (2x), toluene (2x) and then dried in vacuo to obtain 16 as a white solid in a yield of 300 mg (0.41 mmol, 53 %). In addition to 16, also iso-C33 and iso-C31 derivatives, which must be the result of impurities in the commercially available ketone, were found to be present in the product.
^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.39 (d, 2H, Bipy*H*, J = 6.8 Hz), 8.88 (d, 2H, Bipy*H*, J = 6.0 Hz), 8.36 (d, 2H, Bipy*H*, J = 7.2 Hz), 7.71 (d, 2H, Bipy*H*, J = 6.0 Hz), 4.87 (d, 2H, NCH_2, J = 7.6 Hz), 2.06 (m, 1H, C*H*), 1.44-1.16 (m, 64H, CH_2), 0.88 (t, 6H, CH_3, J = 6.8 Hz).
^{13}C-NMR (75 MHz, $CDCl_3$): δ 153.24, 151.02, 145.47, 140.27, 125.08, 120.95, 65.23, 40.01, 31.44, 29.97, 29.22, 25.58, 22.20, 13.63.
MALDI-TOF MS (m/z): 661.50 (M-Br)$^+$, 633.46 (M-Br iso-C33)$^+$, 605.43 (M-Br iso-C31)$^+$.
General synthesis of viologen derivatives V1, V2, V3, V5 and V6:
A 25 ml flask, closed with a septum, containing a solution of 2 and primary bromide (3, 4, 5, 6, 13 or 14) in DMF was stirred for 3 days at 95 °C. After cooling, Et_2O was added and the precipitate was filtered off and washed with 20 ml of Et_2O. The resulting solid was mixed with 2 ml of acetone followed by the addition of an excess of NH_4PF_6 (s) and the product was precipitated by the addition of 10 ml of water. The precipitate was filtered off, washed with 40 ml of water followed by 10 ml of Et_2O and then dried to obtain the corresponding viologen.
1-(5-(3,5-Di-tert-butylphenoxy)pentyl)-1'-pentyl-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V1): [7a]
Bromide solution: 3 (182 mg, 0.36 mmol) and 2 (540 mg, 3.6 mmol) in 2 ml of DMF. Yield = 1.9 g as a white solid (2.4 mmol, 67 %).
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 8.93 (d, 2H, Bipy*H*, J = 6.8 Hz), 8.91 (d, 2H, Bipy*H*, J = 6.8 Hz), 8.40 (m, 4H, Bipy*H*), 7.02 (s, 1H, Ar*H*), 6.73 (d, 2H, ortho-Ar*H*, J = 0.8 Hz), 4.67 (t, 2H, NCH_2, J = 7.6 Hz), 4.62 (t, 2H, NCH_2, J = 7.2 Hz), 4.00 (t, 2H, OCH_2, J = 6.4 Hz), 2.14 (dd, 2H, CH_2, J = 8 Hz), 2.04 (dd, 2H, CH_2, J = 7 Hz), 1.86 (dd, 2H, Ar-OCH$_2$-CH_2, J = 7.6 Hz), 1.61 (dd, 2H, CH_2, J = 7.2 Hz), 1.40 (m, 4H, CH_2) 1.30 (s, 18H, CH_3), 0.93 (t, 3H, CH_3, J = 6.8 Hz).
^{13}C-NMR (75 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 158.17, 151.71, 149.44, 149.38, 145.10, 126.82, 114.34, 108.35, 66.60, 61.84, 61.73, 34.33, 30.62, 30.43, 30.34, 28.11, 27.29, 22.10, 21.38, 12.94.
MALDI-TOF MS (m/z): 502.43 (M-2PF$_6$)$^+$.
1-(5-(3,5-Di-tert-butylphenoxy)pentyl)-1'-isobutyl-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V2):
Bromide solution: 2 (91 mg, 0.18 mmol) and 4 (26 mg, 0.19 mmol) in 1 ml of DMF. Yield = 20 mg as a white solid (0.026 mmol, 14 %).
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 8.93 (d, 2H, Bipy*H*, J = 6.4 Hz), 8.87 (d, 2H, Bipy*H*, J = 6.4 Hz), 8.40 (m, 4H, Bipy*H*), 7.02 (s, 1H, para-Ar*H*), 6.73 (d, 2H, ortho-Ar*H*, J = 1.2 Hz), 4.67 (t, 2H, NCH_2, J = 7.2 Hz), 4.47 (d, 2H, NCH_2, J = 7.2 Hz), 4.00 (t, 2H, OCH_2, J = 6.4 Hz), 2.32 (m, 1H, C*H*), 2.15 (m, under water peak, 2H, CH_2), 1.86 (dd, 2H, CH_2, J = 7.6 Hz), 1.61 (dd, 2H, CH_2, J = 7.2 Hz), 1.30 (s, 18H, CH_3), 1.02 (d, 6H, CH_3, J = 6.4 Hz).
^{13}C-NMR (75 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 158.18, 151.74, 145.19, 145.13, 126.82, 126.79, 114.37, 108.32, 67.94, 66.59, 61.68, 34.29, 30.51, 28.08, 22.09, 18.04.
MALDI-TOF MS (m/z): 488.18 (M-2PF$_6$)$^+$.
HRMS (ESI): m/z calcd for $C_{33}H_{48}F_6N_2O_1P_1$ 633.3408 (M-PF$_6$)$^+$ found 633.3396.
1-(Cyclohexylmethyl)-1'-(5-(3,5-di-tert-butylphenoxy)pentyl)-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V3):
Bromide solution: 2 (91 mg, 0.18 mmol) and 5 (33 mg, 0.19 mmol) in 1 ml DMF. Yield = 50 mg as a white solid (0.061 mmol, 34 %).
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 8.94 (d, 2H, Bipy*H*, J = 7.2 Hz), 8.85 (d, 2H, Bipy*H*, J = 7.2 Hz), 8.42 (d, 2H, Bipy*H*, J = 3.6 Hz), 8.41 (d, 2H, Bipy*H*, J = 3.2 Hz), 7.02 (t, 1H, para-Ar*H*, J = 1.6 Hz), 6.73 (d, 2H, ortho-Ar*H*, J = 1.6 Hz), 4.67 (t, 2H, NCH_2, J = 7.6 Hz), 4.48 (d, 2H, NCH_2, J = 7.6 Hz), 4.00 (t, 2H, OCH_2, J = 6.4 Hz), 2.12 (dd, 2H, CH_2, J = 7.6 Hz), 2.00 (m, 1H, C*H*), 1.86 (dd, 2H, CH_2, J = 7.6 Hz), 1.78 (m, 2H), 1.71 (m, 1H), 1.64 (m, 2H), 1.61 (m, 2H, CH_2), 1.30 (s, 18H, CH_3), 1.26 (m, 3H), 1.13 (m, 2H).
^{13}C-NMR (75 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 158.15, 151.72, 149.42, 145.13, 126.83, 126.72, 114.35, 108.32, 67.11, 66.57, 61.72, 39.04, 34.33, 30.61, 30.45, 28.94, 28.11, 25.19, 24.72, 22.12.
MALDI-TOF MS (m/z): 528.21 (M-2PF$_6$)$^+$.
HRMS (ESI): m/z calcd for $C_{36}H_{52}F_6N_2O_1P_1$ 673.3721 (M-PF$_6$)$^+$, found 673.3715.
1-(2-Butylhexyl)-1'-(5-(3,5-di-tert-butylphenoxy)pentyl)-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V5):
Bromide solution: 2 (91 mg, 0.18 mmol) and 13 (220 mg, 1.0 mmol) in 1 ml DMF. Yield = 17 mg as a white solid (0.020 mmol, 11 %).
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 8.95 (d, 2H, Bipy*H*, J = 6 Hz), 8.88 (d, 2H, Bipy*H*, J = 6.4 Hz), 8.45 (m, 4H, Bipy*H*), 7.01 (s, 1H, para-Ar*H*), 6.73 (d, 2H, ortho-Ar*H*, J = 1.2 Hz), 4.68 (t, 2H, NCH_2, J = 7.6 Hz), 4.53 (d, 2H, NCH_2, J = 7.2 Hz), 4.00 (t, 2H, OCH_2, J = 6.4 Hz), 2.15 (m, under water peak, 2H, CH_2), 2.08 (m, 1H, C*H*), 1.86 (dd, 2H, CH_2, J = 7.6 Hz), 1.62 (dd, 2H, CH_2, J = 7.2 Hz), 1.40-1.20 (m, 12H, CH_2), 1.30 (s, 18H, CH_3), 0.90 (t, 6H, CH_3, J = 6.8 Hz).
^{13}C-NMR (75 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 158.15, 151.70, 149.51, 149.35, 145.33, 145.11, 126.86, 126.76, 114.34, 108.34, 66.59, 65.45, 61.77, 39.51, 34.35, 30.67, 30.45, 29.33, 28.13, 27.38, 22.16, 13.18.
MALDI-TOF MS (m/z): 572.10 (M-2PF$_6$)$^+$.
HRMS (ESI): m/z calcd for $C_{39}H_{60}F_6N_2O_1P_1$ 717.4347 (M-PF$_6$)$^+$, found 717.4344.
1-(5-(3,5-Di-tert-butylphenoxy)pentyl)-1'-(2-heptylnonyl)-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V6):
Bromide solution: 2 (91 mg, 0.18 mmol) and 14 (520 mg, 1.7 mmol) in 1 ml DMF. Yield = 33 mg as a white solid (0.035 mmol, 19 %).
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 8.95 (d, 2H, Bipy*H*, J = 5.6 Hz), 8.86 (d, 2H, Bipy*H*, J = 6 Hz), 8.45 (bs, 4H, Bipy*H*), 7.02 (s, 1H, para-Ar*H*), 6.73 (s, 2H, ortho-Ar*H*), 4.68 (t, 2H, NCH_2, J = 7.6 Hz), 4.51 (d, 2H, NCH_2, J = 7.6 Hz), 4.00 (t, 2H, OCH_2, J = 6 Hz), 2.14 (m, 2H, CH_2), 2.08 (m, under water peak, 1H, C*H*), 1.86 (dd, 2H, CH_2, J = 6.8 Hz), 1.63 (dd, 2H, CH_2, J = 7.2 Hz), 1.45-1.15 (m, 24H, CH_2), 1.30 (s, 18H, CH_3), 0.88 (t, 6H, CH_3, J = 6.8 Hz).
^{13}C-NMR (75 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 151.73, 145.33, 145.12, 126.89, 126.77, 114.39, 108.29, 66.53, 65.54, 61.90, 61.82, 39.64, 34.37, 31.19, 30.72, 30.50, 29.66, 29.07, 28.56, 28.14, 25.28, 22.04, 13.40.
MALDI-TOF MS (m/z): 656.18 (M-2PF$_6$)$^+$.
HRMS (ESI): m/z calcd for $C_{45}H_{72}F_6N_2O_1P_1$ 801.5286 (M-PF$_6$)$^+$, found 801.5291.
1-(5-(3,5-Di-tert-butylphenoxy)pentyl)-1'-adamantyl-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V4):
A 25 ml flask, closed with a septum, containing a solution of 1 (53 mg, 0.15 mmol) and 17 (50 mg, 0.11 mmol) in DMF (1 ml) was stirred for 4 days at 90 °C. After cooling, Et_2O was added and the precipitate was filtered off and washed with 20 ml of Et_2O. The resulting solid was mixed with 2 ml of acetone followed by the addition of an excess of NH_4PF_6 (s) and the product was precipitated by the addition of 10 ml of water. The precipitate was filtered off, washed with 40 ml of water followed by 10 ml of Et_2O and then dried to obtain V4 in a yield of 11 mg as a white solid (0.013 mmol, 12 %).
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 9.18 (d, 2H, Bipy*H*, J = 6.8 Hz), 8.93 (d, 2H, Bipy*H*, J = 6.4 Hz), 8.43 (m, 4H, Bipy*H*), 7.02 (s, 1H, para-Ar*H*), 6.73 (s, 2H, ortho-Ar*H*), 4.67 (t, 2H, NCH_2, J = 7.6 Hz), 4.00 (t, 2H, OCH_2, J = 6.4 Hz), 2.43 (m, 3H, C*H*), 2.34 (m, 6H, CH_2), 2.15 (m, under water peak, 2H, CH_2), 1.86 (m, under adamantane proton peaks, 2H, CH_2), 1.85 (m, 6H, CH_2), 1.61 (dd, 2H, CH_2, J = 7.2 Hz), 1.30 (s, 18H, CH_3).
^{13}C-NMR (75 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 151.73, 148.90, 145.09, 142.07, 126.85, 126.48, 114.39, 108.30, 66.58, 61.72, 41.51, 34.21, 30.60, 29.68, 28.11, 22.15.
MALDI-TOF MS (m/z): 566.30 (M-2PF$_6$)$^+$.
HRMS (ESI): m/z calcd for $C_{39}H_{54}F_6N_2O_1P_1$ 711.3877 (M-PF$_6$)$^+$, found 711.3859.
1-(5-(3,5-Di-tert-butylphenoxy)pentyl)-1'-(2-heptadecylnonadecyl)-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V7):
A 25 ml flask, closed with a septum, containing a solution of 1 (1.4 g, 4.0 mmol) and 16 (250 mg, 0.34 mmol) in DMF (4 ml) was stirred for 6 days at 90 °C. After cooling, Et_2O was added and the precipitate was filtered off and washed with 20 ml of Et_2O and toluene. The resulting solid was mixed with 2 ml of acetone followed by the addition of an excess of NH_4PF_6 (s) and the product was precipitated by the addition of 10 ml of water. The precipitate was filtered, washed with 40 ml of water followed by 10 ml of Et_2O and then dried to obtain V7 as a white solid in a yield of 306 mg(0.25 mmol, 73 %).
^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 8.95 (d, 2H, Bipy*H*, J = 6.8 Hz), 8.86 (d, 2H, Bipy*H*, J = 6.8 Hz), 8.42 (t, 4H, Bipy*H*, J = 6.4 Hz), 7.02 (t, 1H, para-Ar*H*, J = 1.6 Hz), 6.73 (d, 2H, ortho-Ar*H*, J = 1.6 Hz), 4.68 (t, 2H, NCH_2, J = 7.6 Hz), 4.51 (d, 2H, NCH_2, J = 7.6 Hz), 4.00 (t, 2H, OCH_2, J = 6 Hz), 2.11 (m, under water peak, 2H, CH_2), 2.04 (m, under water peak, 1H, C*H*), 1.86 (dd, 2H, CH_2, J = 7.2 Hz), 1.62 (dd, 2H, CH_2, J = 7.2 Hz), 1.45-1.15 (m, 64H, CH_2), 1.30 (s, 18H, CH_3), 0.88 (t, 6H, CH_3, J = 6.8 Hz).
^{13}C-NMR (75 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 158.14, 151.73, 149.44, 149.29, 145.34, 145.13, 126.84, 126.74, 114.37, 108.31, 66.57, 65.45, 61.74, 39.54, 34.33, 31.31, 30.61, 29.54, 29.07, 28.11, 25.19, 22.08, 13.34.
MALDI-TOF MS (m/z): 936.65 (M-2PF$_6$)$^+$, iso-C33: 908.60 (M-2PF$_6$)$^+$, iso-C33: 880.54 (M-2PF$_6$)$^+$.

HRMS (ESI): m/z calcd for $C_{65}H_{112}F_6N_2O_1P_1$ 1081.8416 $(M\text{-}PF_6)^+$, found 1081.8406.

1-(Cyclododecylmethyl)-1'-(5-(3,5-di-tert-butylphenoxy)pentyl)-4,4'-bipyridine-1,1'-diium dihexafluorophosphate (V8): [7a]

A 25 ml flask, closed with a septum, containing a solution of 2 (44 mg, 0.087 mmol) and ~62 mg of 6 (0.092 mmol) in DMF (1 ml) (108 mg of the mixture containing **6** and the elimination product of **6**) was stirred for 3 days at 95 °C. After cooling, Et_2O was added and a gel was formed; the gel was sonicated and the solvents were evaporated. The crude product was dissolved in MeCN, precipitated with diethylether, and the precipitate was filtered off and subsequently washed with 20 ml of diethylether. The resulting solid was mixed with 2 ml of acetone followed by the addition of an excess of NH_4PF_6 (s) and the product was precipitated by the addition of 10 ml of water. The white precipitate was filtered off, washed with 40 ml of water followed by 10 ml of Et_2O and then dried to obtain a yield of 8 mg (0.0085 mmol, 9.8 %). It was not possible to purify this compound to obtain an analytically pure sample.

^{1}H-NMR (400 MHz, $CD_3CN/CDCl_3$, 1:1 (v:v)): δ 8.94 (bd, 4H, Bipy*H*), 8.40 (bd, 4H, Bipy*H*), 7.02 (s, 1H, para-Ar*H*), 6.73 (d, 2H, ortho-Ar*H*, J = 1.6 Hz), 4.75 (t, 2H, NCH_2, J = 6.8 Hz), 4.68 (t, 2H, NCH_2, J = 7.2 Hz), 4.00 (t, 2H, OCH_2, J = 5.6 Hz), 3.53 (t, 2H, cyclododecaneOCH_2, J = 5.6 Hz), 3.37 (m, 1H, C*H*), 2.27 (dd, 2H, CH_2, J = 5.6 Hz), 2.12 (m, under water peak, 2H, CH_2), 1.87 (dd, 2H, CH_2, J = 7.6 Hz), 1.63 (m, 2H, CH_2), 1.30 (s, 18H, CH_3), 1.28-1.36 (m, 22H, cyclododecane(CH_2)$_{11}$).

Acknowledgements

This research was supported by the European Research Council in the form of an ERC Advanced grant to R.J.M.N. and S.V. (ALPROS-290886) and an ERC Starting grant to J.A.A.W.E (NANOCAT-259064). Further financial support was obtained from the Council for the Chemical Sciences of the Netherlands Organization for Scientific Research (CW-NWO) (Vidi grant for J.A.A.W.E and Vici grant for A.E.R) and from the Ministry of Education, Culture and Science (Gravity program 024.001.035).

Keywords: rotaxane • porphyrin • slippage • supramolecular chemistry • dynamic covalent chemistry

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Received: ((will be filled in by the editorial staff))
Revised: ((will be filled in by the editorial staff))
Published online: ((will be filled in by the editorial staff))

ChemPubSoc Europe

DOI: 10.1002/chem.201xxxxxx

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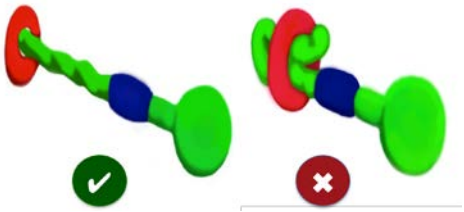
Kinetic and thermodynamic studies on the threading of a macrocyclic porphyrin receptor (**$H_2$1**) onto molecular threads that are blocked on one side and are open on the other side were performed. The results suggest that threading is impossible if the receptor encounters an open side that is sterically encumbered in a similar way as a folded polymer chain.



Supramolecular Chemistry

Alexander B. C. Deutman, Shaji Varghese, Mohamed Moalin, Johannes A. A. W. Elemans, Alan E. Rowan, and Roeland J. M. Nolte

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Slippage of a porphyrin macrocycle over threads of varying bulkiness. Implications for the mechanism of threading polymers through a macrocyclic ring