Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 3504

www.rsc.org/obc

PAPER

Template-directed synthesis of kinetically and thermodynamically stable molecular necklace using ring closing metathesis†

Suvankar Dasgupta and Jishan Wu*

Received 16th November 2010, Accepted 10th February 2011
DOI: 10.1039/c0ob01034k

We report the template-directed synthesis of a well-defined, kinetically stable [5]molecular necklace with dialkylammonium ion ($R_2NH_2^+$) as recognition site and DB24C8 as macrocycle. A thread containing four dialkylammonium ions with olefin at both ends was first synthesized and then subjected to threading with an excess amount of DB24C8 to form pseudo[5]rotaxane, which *in situ* undergoes ring closing metathesis at the termini with second generation Grubbs catalyst to yield the desired [5]molecular necklace. The successful synthesis of [5]molecular necklace is mainly attributed to the self-assembly and dynamic covalent chemistry which allows the formation of thermodynamically most stable product. The self-assembly of the DB24C8 ring onto the recognition site known as templating effect was driven by noncovalent stabilizing interactions like [N^+–H $\cdots$ O], [C–H $\cdots$ O] hydrogen bonds as well as [$\pi \cdots \pi$] interactions which is facilitated in non-polar solvents. The reversible nature of olefin metathesis reaction makes it suitable for dynamic covalent chemistry since proof-reading and error-checking operates until it generates thermodynamically the most stable interlocked molecule. Riding on the success of [5]molecular necklace, we went a step further and attempted to synthesize [7]molecular necklace using the same protocol. This led to the synthesis of another thread with olefin at both ends but having six dibenzylammonium ions along the thread. However, the extremely poor solubility of this thread containing six secondary ammonium ions limits the self-assembly process even after we replaced the typical PF_6^- counter anion with a more lipophilic BPh_4^- anion. Although the poor solubility of the thread remains the bottleneck for making higher order molecular necklaces yet this approach of "threading-followed-by-ring-closing-metathesis" for the first time produces kinetically and thermodynamically stable, well-defined, homogeneous molecular necklace which was well characterized by one-dimensional, two-dimensional, variable temperature proton NMR spectroscopy and ESI mass spectroscopy.

Introduction

The practical limitation of the "engineering down" approach[1] in the field of nanotechnology and the realization of the cumulative effects of weak noncovalent interactions existing in nature[2] gave chemists the impetus to emulate these interactions in chemical systems, giving rise to a new field of chemistry, known as supramolecular chemistry.[3] Molecular recognition and self-assembly[4] has remained the key to the development of supramolecular chemistry over years. Starting from simple host–guest chemistry,[5] supramolecular chemistry came a long way and made possible the synthesis of various kinds of mechanically interlocked molecules.[6] Mechanically interlocked molecule involves two or more molecules not connected by covalent bond but need to disrupt a covalent bond to separate the molecules. The various kinds of mechanically interlocked molecules include rotaxanes,[7] catenanes,[8] knots,[9] molecular necklaces,[10] suitane,[11] and Borromean ring[12] *etc*. The synthesis of such unorthodox molecule utilizes template-directed strategy[13] which functions on molecular recognition and self-assembly. Conventionally the molecular recognition and self-assembly process operating during the synthesis of interlocked molecules are thermodynamically controlled whereas the final and crucial step for the interlocking remains kinetically controlled which leads to the formation of undesirable unlocked oligomeric by-product. To address this acute problem dynamic covalent chemistry (DCC)[14] has been exploited.

DCC refers to the reversible chemical reactions involving making and breaking of chemical bonds under thermodynamic control. The reversibility aspect of DCC makes it suitable for the synthesis of interlocked molecules as there lays the scope for "error checking" and "proof-reading" which will eventually result in the formation of thermodynamically most stable and desirable interlocked molecules. Hence the template-directed approach is

Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore, 117543. E-mail: chmwuj@nus.edu.sg; Fax: (+65) 6779-1691

† Electronic supplementary information (ESI) available: NMR and mass spectra. See DOI: 10.1039/c0ob01034k

used in conjunction with DCC for the synthesis of various mechanically interlocked molecules. Reversible reactions like imine formation,[15] ester formation,[16] disulfide formation,[17] and olefin metathesis[18] have been particularly used for the synthesis of interlocked molecules.

Although there are ample literatures citing synthesis of rotaxane,[7] polyrotaxane[19] and catenane[8] yet there remains few limited literature[10] on molecular necklace which underlines the synthetic difficulty in making molecular necklace. A molecular necklace consists of three or more rings mechanically locked (threaded) onto a large ring. Molecular necklace are topological isomers of catenanes and uniquely defined for a given number of rings. It is denoted as [*n*]MN which means (*n* −1) rings are threaded onto a large ring. The smallest molecular necklace remains [4]MN having three rings threaded onto a large ring. [2]MN and [3]MN are essentially [2]catenane and [3]catenane. The molecular necklace happens to be a serendipitous scientific discovery. The first molecular necklace being accidently discovered by Sauvage and co-workers during the synthesis of [3]catenane.[10a] A mixture of [*n*]MN (*n* = 4–7) were observed and characterized by ESI mass spectroscopy. Stoddart and co-workers obtained [4]MN as a by-product during the synthesis of oligocatenanes[10b] and polyrotaxanes.[10e] Since then Kim and co-workers contributed immensely towards the synthesis of molecular necklaces. Using the metal coordination chemistry of copper(II) and platinum(II) along with self-assembly of macrocycle cucurbit[6]uril, they have successfully synthesized and characterized [4]MN[10c,f] and [5]MN.[10d,f] The striking difference between the accidental discoveries and intended synthesis of molecular necklaces lies in the crucial final step which takes place under kinetic control and thermodynamic control, respectively. The metal coordination driven synthesis provides two advantages over conventional synthesis, the first being the coordination geometry of the metal ion which can be suitably manoeuvred according to the MN of interest and the second being the involvement of reversible metal–ligand exchange process which gives the scope for "error checking" and "proof-reading", thus generating the most stable desired MN. Later Kim and co-workers report the synthesis of even higher molecular necklace [6]MN[10h] utilizing only self-assembly. This commendable work was facilitated by strong intermolecular charge-transfer interactions between identical guest molecules (having an electron donor and an electron acceptor connected by a rigid linker with a proper angle) inside the cavity of host cucurbit[8]uril. Harada and co-workers reported the formation of poly(catenane) (Molecular necklace)[10g] and poly(polyrotaxane) by photoreaction of 9-anthracene-capped polyrotaxane. Very recently Grubbs and co-workers reported the synthesis of [4]MN[10i] using self-assembly of diolefin crown ether-type fragment around dialkylammonium ion followed by olefin metathesis with Hoveyda–Grubbs 2nd generation catalyst.

Although the reported literatures on the synthesis of molecular necklace are appreciable yet there is a lack of general synthetic strategy to construct well-defined, homogeneous molecular necklace. The idiosyncratic coordination geometry of a particular metal ion limits the versatility of metal coordination chemistry in the synthesis of molecular necklace. Moreover, the obtained [*n*]MN by coordination chemistry is not kinetically stable as external stimuli (temperature, pH, and competitive ligand) can destroy the thermodynamically stable interlocked structures. This motivated us to develop a new synthetic strategy to construct molecular necklaces, in particular, both thermodynamically and kinetically stable molecular necklaces. In this paper, we introduce "threading-followed-by-ring-closing-metathesis" approach to successfully synthesize molecular necklace. Our strategy utilizes a well-known self-assembly process between macrocycle dibenzo-24-crown-8 (DB24C8) and dibenzylammonium ion[20] followed by reversible ring closing metathesis with Grubbs's 2nd generation catalyst. Although similar strategy has been utilised for making [n]catenanes (n = 2, 3),[8b] but for molecular necklace synthesis our strategy still remains unique.

Herein, we describe the attempt to make [5]MN and [7]MN from the two threads **1**·$(PF_6)_4$ and **2**·$(PF_6)_6$ (Fig. 1) respectively, which are having well defined dibenzylammonium ions along the thread and long alkyl chains with olefin at their termini. The major challenge for the synthesis of MN is to curb the formation of undesirable oligomeric/interlocked molecules which beckons for careful design of the thread. Therefore each segment of the thread was designed in a way to facilitate the formation of desired MN. *meta*-Substituted benzene moieties have been used for macrocyclization[21] and thus herein, the *meta*-substituted phenyl group is used as core to facilitate intramolecular cyclization. The polyethoxy backbone imparts flexibility to the thread in a manner that post self-assembly process there is not much strain involved in the system for the terminal olefinic bonds to remain in close proximity. In addition, the polyethoxy group increases the solubility of the thread overall. The well known self-assembly process of DB24C8 and dibenzylammonium ions influenced the inclusion of linearly attached dibenzylammonium ions next to each other along the thread. The long alkyl chain relieves the possible strain generated during ring closing metathesis of the self-assembled molecule. Solubility of the thread in non-polar solvent is also expected to be enhanced due to long alkoxy chains.

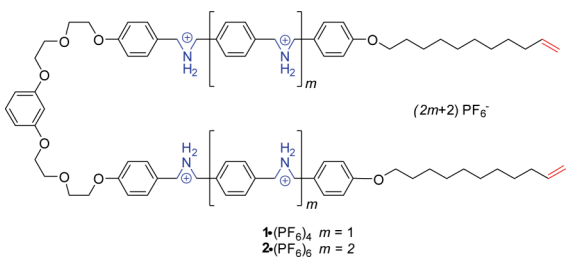
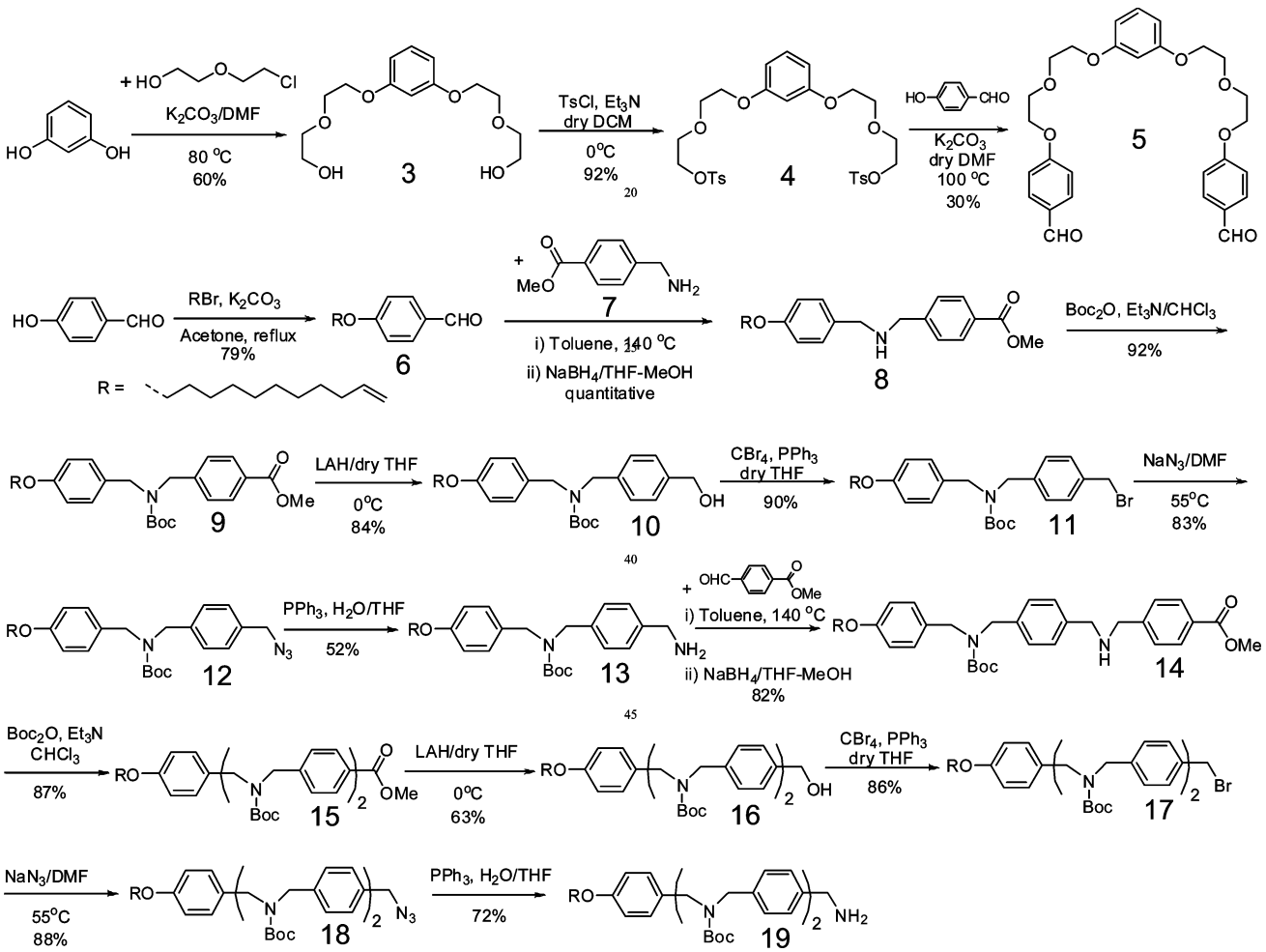


Fig. 1 Molecular structure of threads **1**·$(PF_6)_4$ and **2**·$(PF_6)_6$.

Results and discussion

Synthesis of key intermediates 5, 13 and 19

The synthetic route for key intermediates **5**, **13** and **19** is shown in Scheme 1. Resorcinol is reacted with 2-(2-chloroethoxy)ethanol to give dihydroxy compound **3** which is then ditosylated to yield compound **4** in 55% yield for two steps. 4-Hydroxybenzaldehyde undergoes O-alkylation with **4** to give the key intermediate **5** in a low yield (30%) mainly due to its poor solubility which made purification very difficult. Compound **6** is then obtained in 79% yield from 4- hydroxybenzaldehyde by O-alkylation with 11-bromoundec-1-ene. Methyl-4-(aminomethyl)-benzoate (**7**) is condensed with compound **6** in toluene to give the corresponding



Scheme 1 Synthetic route to key intermediates **5**, **13**, and **19**.

imine in quantitative yield which is then reduced by sodium borohydride in a mixture of THF and methanol to give the amine **8** in nearly quantitative yield. The secondary amine **8** is then converted in 92% yield to its *tert*-butyloxycarbonyl (Boc) protected form **9** which is then reduced with lithium aluminium hydride (LAH) to give the corresponding benzyl alcohol **10** in 84% yield. The alcohol is then transformed into the key intermediate **13** *via* high yielding steps, bromination (**11**), azidation (**12**), followed by the reduction of azide **12** in moderate yield. Following a similar synthetic approach, the key intermediate **19** which has two additional benzyl *N*-Boc unit compared with **13** can be prepared by similar sequential processes such as condensation, reduction by sodium borohydride, Boc-protection, reduction by LAH, bromination, azidation and reduction by PPh_3.

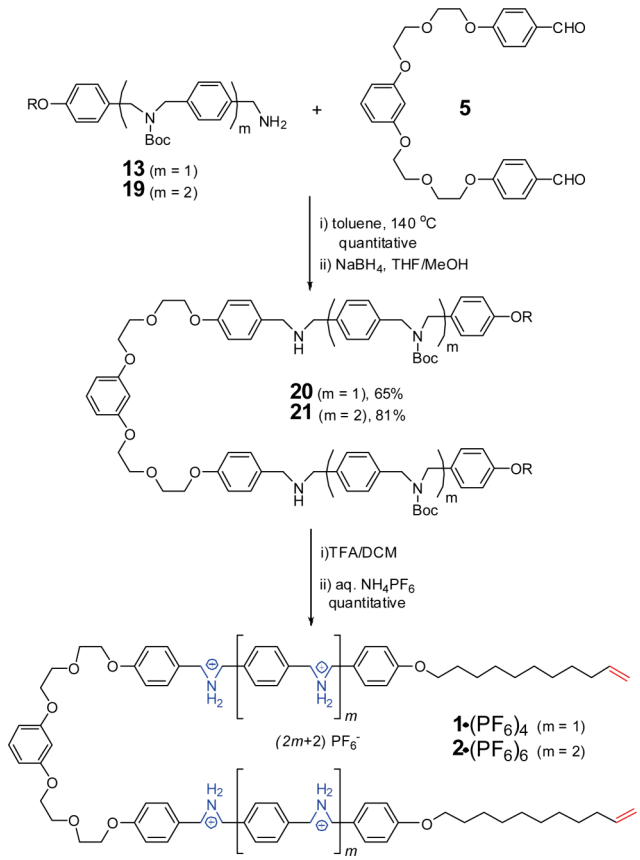
Synthesis of threads $1\cdot(PF_6)_4$ and $2\cdot(PF_6)_6$

As shown in Scheme 2, the intermediate **5** is condensed with 2 equivalents of **13** to give the corresponding imine in quantitative yield which is subsequently reduced to **20** by sodium borohydride in 65% yield. Similar reactions between **5** and **19** provide analogous **21** with two additional benzyl *N*-Boc units in 81% yield. Compounds **20** and **21** are subjected to Boc deprotection with trifluoroacetic acid (TFA) followed by counter ion exchange with aqueous NH_4PF_6 to yield the threads $\mathbf{1}\cdot(PF_6)_4$ and $\mathbf{2}\cdot(PF_6)_6$, respectively, both in quantitative yield. Counter ion exchange is done to ensure that the solubility of the salts increase in organic solvents.

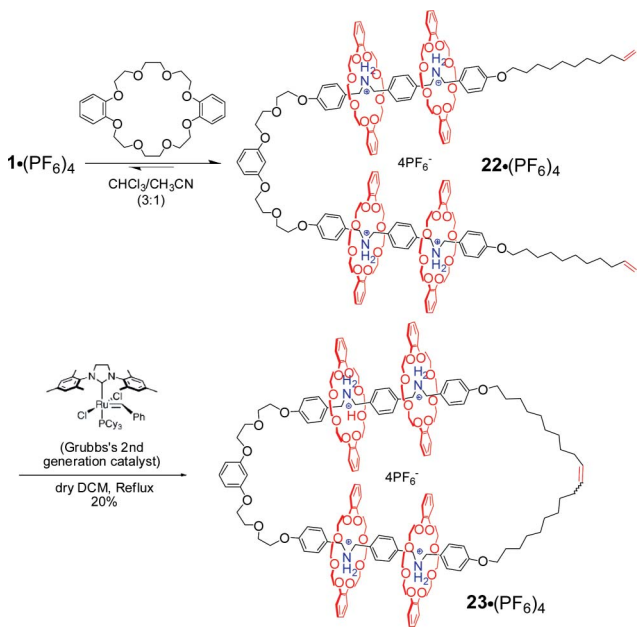
Synthesis of [5]molecular necklace $\mathbf{23}\cdot(PF_6)_4$

The thread $\mathbf{1}\cdot(PF_6)_4$ exhibits good solubility in acetonitrile however the solubility remains poor in chlorinated solvents such as chloroform and dichloromethane (DCM). The solubility of DB24C8 is just the other way. For the self-assembly process, the thread $\mathbf{1}\cdot(PF_6)_4$ and the macrocycle DB24C8 or their mixture needs to be soluble in a common medium. Even the mixture of $\mathbf{1}\cdot(PF_6)_4$ and DB24C8 was found to exhibit poor solubility in either of the solvents implying absence of self-assembly. To resolve this issue, a mixture of chloroform and acetonitrile solvents in 3 : 1 ratio[22] (henceforth will be referred as mixed solvent) was tried (Scheme 3). Interestingly the mixture of $\mathbf{1}\cdot(PF_6)_4$ and DB24C8 was soluble in the mixed solvent indicating self-assembly.[23] Therefore this mixed solvent was chosen for carrying out self-assembly process.

To ensure complete threading, we used 20 equivalents of DB24C8 for 1 equivalent of $\mathbf{1}\cdot(PF_6)_4$, making it 5 equivalent of DB24C8 for each dibenzylammonium ion. In the mixed solvent, a mixture of DB24C8 and $\mathbf{1}\cdot(PF_6)_4$, in the above mentioned ratio



Scheme 2 Synthetic route to threads **1**·$(PF_6)_4$ and **2**·$(PF_6)_6$.



Scheme 3 Synthetic route to **[5]MN 23**·$(PF_6)_4$.

was stirred. The clear solution indicated the completion of self-assembly process and formation of pseudorotaxane **22**·$(PF_6)_4$.[23] The clear solution was evaporated (under reduced pressure without heating avoiding any risk of disassembly) leaving a residue expected to have predominantly **22**·$(PF_6)_4$ and excess DB24C8. Although there exists a dynamic equilibrium between the threaded and dethreaded species yet equilibrium is expected to be shifted towards the threaded species in non-polar solvents given that threaded species is thermodynamically more stable in non-polar solvents. ^{1}H NMR spectrum of the residue in $CDCl_3$ clearly shows up-field resonance shift of the aromatic protons of the benzyl units on the thread **1**·$(PF_6)_4$, indicating a successful threading of the DB24C8 onto the dibenzylammonium sites under this mixed solvent condition. This was further supported by the fact that a clear solution was obtained by dissolving the residue in dichloromethane. In the final step, the clear dichloromethane solution suggesting only the presence of pseudorotaxane **22**·$(PF_6)_4$ was treated with Grubbs's 2nd generation catalyst under refluxing condition to obtain the desired [5]MN **23**·$(PF_6)_4$ in 20% yield (Scheme 3). Although the desired [5]MN **23**·$(PF_6)_4$ dominated the reaction mixture, yet there were trace amounts of [4]MN and [3]catenane, which could only be detected by ESI mass spectrometry of the crude reaction mixture. To ascertain the complete reversibility, successful ring closing metathesis and generation of thermodynamically most stable desired product, we performed the final ring closing metathesis reaction under strictly dry and extremely dilute condition (0.0003 M) with excess (20 equivalent) DB24C8 for 60 h so that we could exclusively get [5]MN **23**·$(PF_6)_4$ by eliminating the possibility for the formation of less stable interlocked molecules ([4]MN, [3]catenane, [2]rotaxane) and non-interlocked olefin oligomers. However even after 7 days the presence of [4]MN and [3]catenane could be traced. But the fact that [4]MN and [3]catenane were always present in trace amount could be testified by TLC progress. The [4]MN and [3]catenane never showed up in the TLC plate even when the TLC was run with high polarity eluent like 1 : 4 MeOH–$CHCl_3$ and 1 : 4 CH_3CN–$CHCl_3$. Therefore the crude reaction mixture mainly had the [5]MN **23**·$(PF_6)_4$ and excess unused DB24C8.

The purification of interlocked molecules is generally challenging due to high polarity, presence of side products and limited solubility. In our case we utilised dynamic covalent chemistry, the olefin metathesis as the final interlocking step to eliminate the undesirable side products. Although the [4]MN and [3]catenane formation could not be avoided however the amount is so little that effectively their presence can be ignored. So the trace amounts of [4]MN and [3]catenane did not complicate the purification and isolation of [5]MN **23**·$(PF_6)_4$. The column chromatographic purification however remained challenging due to the presence of excess amount of DB24C8 in the system which could not be eluted out with ease due to its poor solubility in both methanol–chloroform and acetonitrile–chloroform solvent system. The methanol–chloroform system was chosen over acetonitrile–chloroform system for purification of [5]MN **23**·$(PF_6)_4$ because the solubilising capability of the first system is better. The isolation of pure [5]MN **23**·$(PF_6)_4$ was rendered difficult due to the difficulty in removing the less polar DB24C8 from the system which is corroborated by the fact that during the purification, a large fraction containing the mixture of DB24C8 and the desired product [5]MN **23**·$(PF_6)_4$ is always obtained, which accounts for the low isolated yield (20%) of pure [5]MN **23**·$(PF_6)_4$ (Scheme 3). However the conversion ratio of pseudo [5]rotaxane **22**·$(PF_6)_4$ to [5]MN **23**·$(PF_6)_4$ is much higher than the isolated yield, which could also be perceived from the TLC plate.

Characterization of [5]molecular necklace 23·$(PF_6)_4$

The formation of [5]MN **23**·$(PF_6)_4$ is well supported by one-dimensional (1D), two-dimensional (2D), variable temperature proton NMR spectroscopy and ESI mass spectroscopy. The 2D COSY, NOESY NMR spectral data are discussed in details in the Supporting Information. Herein, we discuss the 1D NMR (Fig. 2), briefly 2D NOESY (Figure S2†), variable temperature NMR (Fig. 3) and ESI mass spectroscopy (Fig. 4).

In Fig. 2, the ^{1}H NMR spectra of **1**·$(PF_6)_4$ and **23**·$(PF_6)_4$, recorded in CD_3CN at an operating frequency of 500 MHz are compiled into a stacked form to appreciate the shift in resonance peaks affected due to the threading of DB24C8 rings onto the dibenzylammonium ions of **1**·$(PF_6)_4$. The threading of

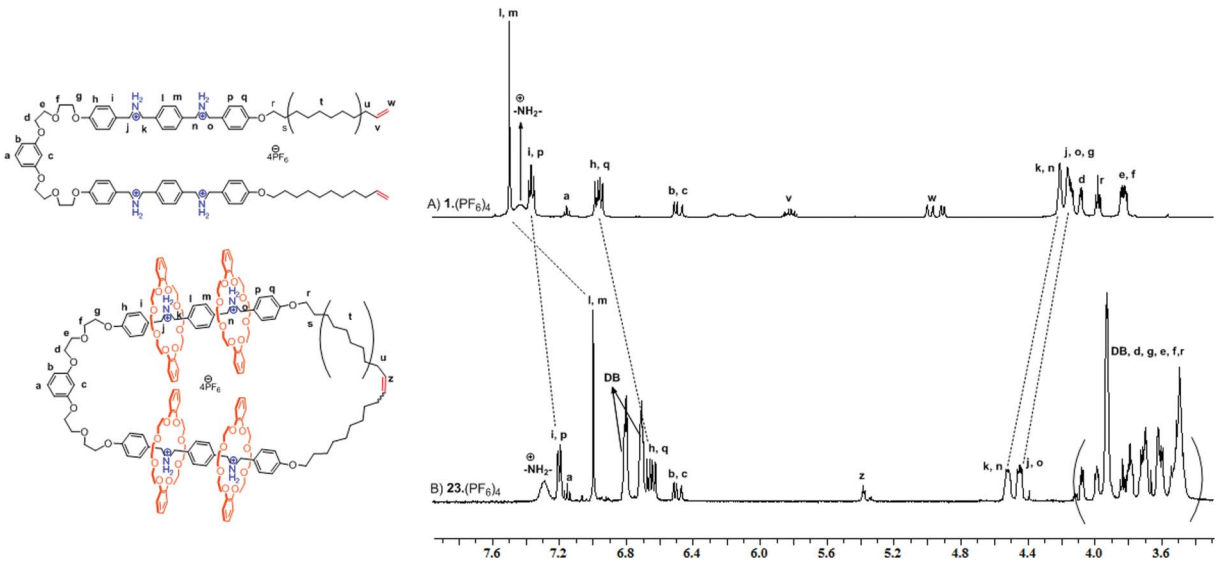


Fig. 2 ^{1}H NMR spectra of A) **1**·$(PF_6)_4$ (500 MHz, CD_3CN), B) [5]MN **23**·$(PF_6)_4$ (500 MHz, CD_3CN).

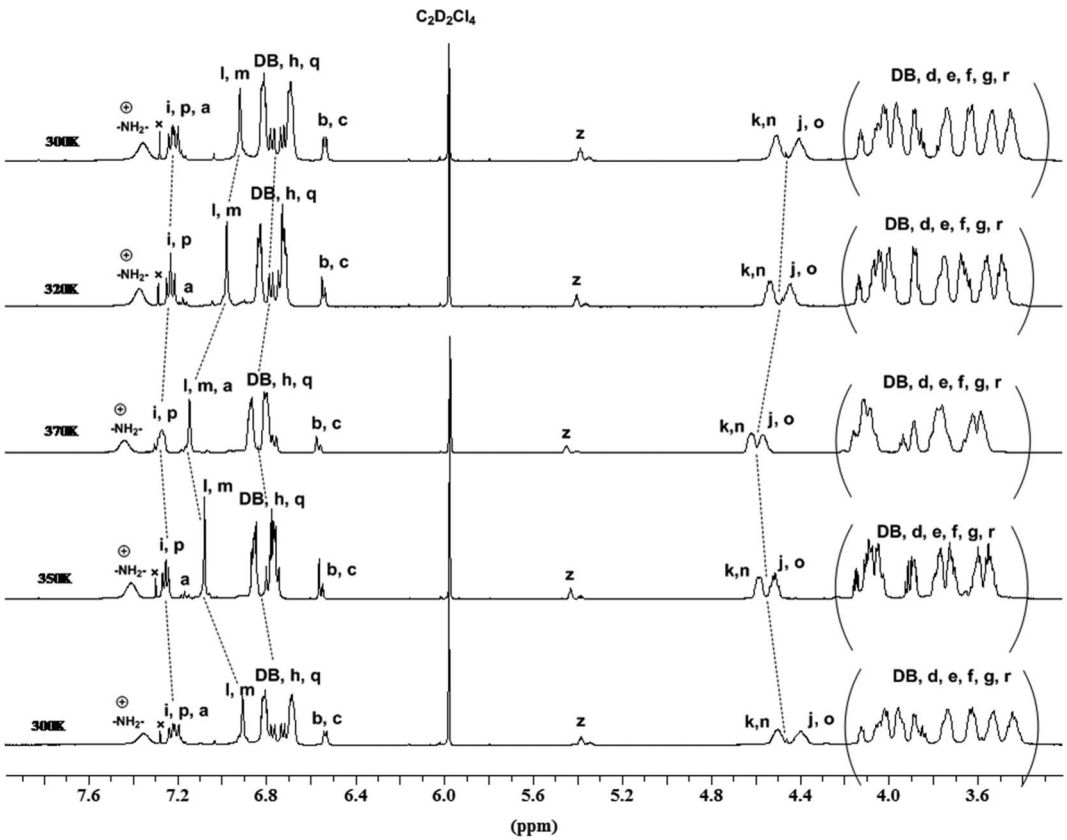


Fig. 3 ^{1}H NMR spectra (500 MHz, $C_2D_2Cl_4$) of [5]MN **23**·$(PF_6)_4$ at various temperatures.

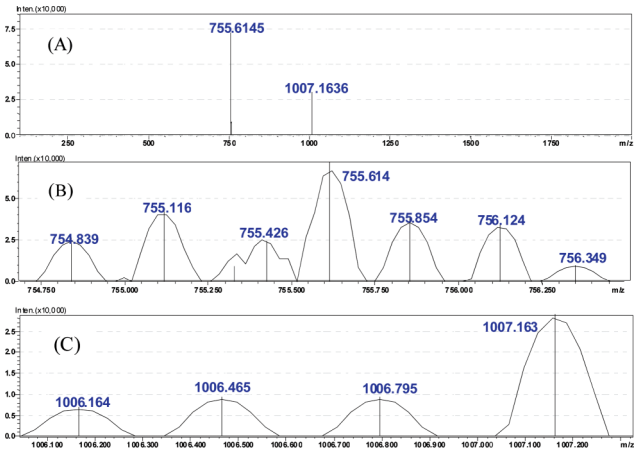


Fig. 4 ESI mass spectrum for [5]MN **23**·$(PF_6)_4$ (A) and the isotope distribution of the major peaks (B and C).

DB24C8 onto the dibenzylammonium ions shields the aromatic protons in its proximity due to which there will be an upfield shift in the resonance value for the shielded protons. For the thread **1**·$(PF_6)_4$, the aromatic protons (H_l, H_m) are expected to be most shielded due to threading. Other aromatic protons (H_i, H_p, H_h, H_q) will experience lesser shielding effect. The observed upfield shift for aromatic protons (H_l, H_m, H_i, H_p, H_h, H_q) and downfield shift for benzyl (methylene) protons (H_k, H_n, H_j, H_o) in **23**·$(PF_6)_4$ (compared with **1**·$(PF_6)_4$) accounts for the complete threading of DB24C8[20,22] onto all the four dibenzylammonium ions. Furthermore, the strong NOE cross-peaks (Figure S2†) observed for **23**·$(PF_6)_4$ indicates spatial interactions between the thread and DB24C8. DB24C8 (referred as DB in spectral assignment) show intramolecular NOE cross-peaks with the aromatic protons (H_l, H_m, H_i, H_p, H_h, H_q), benzyl (methylene) protons (H_k, H_n, H_j, H_o) and ammonium protons as expected from the structure elucidated for [5]MN **23**·$(PF_6)_4$. In addition, the absence of terminal olefin protons (H_v and H_w), presence of disubstituted olefin protons (H_z) and a distinct set of peaks observed for aromatic protons (H_l, H_m, H_i, H_p, H_h, H_q) indicate the compound **23**·$(PF_6)_4$ to be a molecular necklace resembling the structure proposed. The integration ratios of all the aromatic protons, olefin protons and benzyl protons agree well with this structure. Had it been a pseudorotaxane, signals corresponding to uncomplexed thread, eight possible partially complexed threads (2 isomeric pseudo[2]rotaxane, 4 isomeric pseudo[3]rotaxane and 2 isomeric pseudo[4]rotaxane) and uncomplexed crown ether would have been observed in addition to those attributed to the complexed species.[23] This is because for dibenzylammonium ion motif the threading and dethreading of DB24C8 are both slow on ^{1}H NMR time scale at room temperature[24] and we could have never observed a distinct set of peaks for the protons of interest. Moreover, the absence of peaks corresponding to uncomplexed DB24C8 eliminates the possibility for the exclusive formation of only pseudo[5]rotaxane in the presence of excess DB24C8.[23]

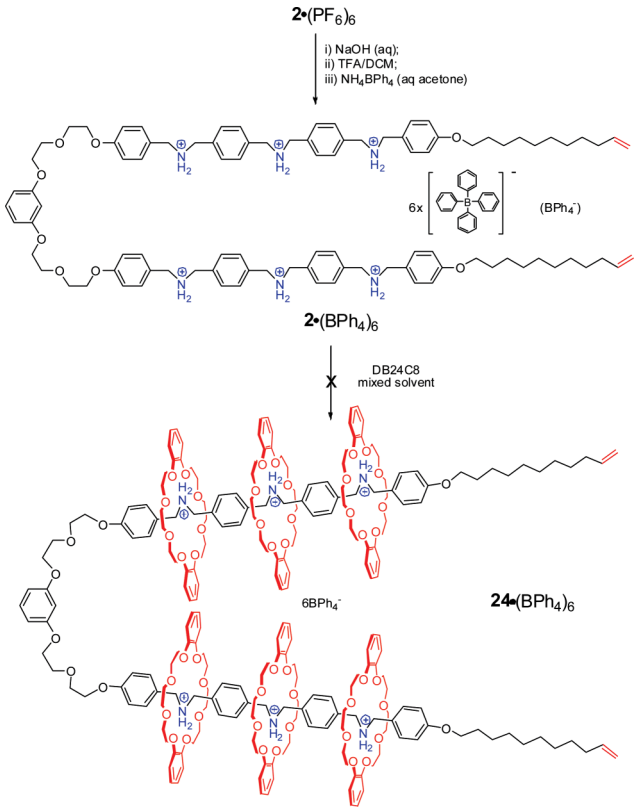
To further confirm the proposed structure of **23**·$(PF_6)_4$ and eliminate any possibility of this being a pseudorotaxane, we recorded the ^{1}H NMR spectra of **23**·$(PF_6)_4$ in $C_2D_2Cl_4$ at increasing and decreasing temperatures. Fig. 3 compares the shift in resonance peak value of **23**·$(PF_6)_4$ with temperature variations. As the temperature is increased from 300 K (room temperature) to 350 K, the resonance peak for aromatic protons (H_l, H_m) show a significant downfield shift from ~6.9 ppm to ~7.1 ppm with notable downfield shift for other aromatic protons of the system (H_i, H_p, H_{DB}). The downfield shift for the benzyl protons (H_k, H_n, H_j, H_o) of the system could also be observed. Increasing the temperature to 370 K caused further downfield shift for both the aromatic and the benzyl protons (H_l, H_m, H_i, H_p, H_{DB}, H_k, H_n, H_j, H_o) to varying extent. On cooling the system to 320 K, the protons (H_l, H_m, H_i, H_p, H_{DB}, H_k, H_n, H_j, H_o) displayed upfield shift in resonance peaks which shifted further upfield on lowering the temperature to 300 K. The observed shifts can only be explained for the structure proposed for **23**·$(PF_6)_4$. The toughness of mechanical bond holding the macrocycle DB24C8 to the dibenzylammonium ion in **23**·$(PF_6)_4$ relies on the strength of H-Bond formed which could be perturbed by the supply of energy. As we increase the temperature, the thermal energy of the system increases, causing disruption of H-bonds and shuttling of the freed macrocycle along the thread. The downfield shift observed is due to an increase in percentage of freed macrocycle making more of the dibenzylammonium ions deshielded. However even at 370 K the resonance peak for aromatic protons (H_l, H_m, H_i, H_p, supposedly the most affected due to heating) of **23**·$(PF_6)_4$ (Fig. 3) remain shifted to high field by a significant margin when compared with the corresponding resonance peak for open thread **1**·$(PF_6)_4$ aromatic protons (Fig. 2). This observed difference in resonance peak value accounts for the absence of dethreading process, excluding the possibility of **23**·$(PF_6)_4$ being a pseudorotaxane. Therefore the downfield shifts observed during heating process indicate temporal dislodgement of macrocycles from the recognition sites (causing deshielding) and shuttling of macrocycles along the thread. However, during the cooling process the resonance peak keeps shifting to high field and eventually returns to the initial state when cooled to 300 K which can only be explained by the H-bond driven regrouping of macrocycles (scattered along the thread) onto the dibenzylammonium ions. Thus both heating and cooling experiment confirms the formation of [5]MN.

The role of ESI mass spectroscopy in elucidating structure is always prominent in the field of supramolecular chemistry. The observation of m/z peaks corresponding to the charged molecular fragment of supramolecular species is typically observed by ESI technique. We employed LCMS-IT-TOF technology for our compound **23**·$(PF_6)_4$which detects mass in ESI mode. The LC-ESI-MS for [5]MN **23**·$(PF_6)_4$ in acetonitrile clearly showed two peaks 755.6145 and 1007.1636 that can be assigned to the $[M\text{-}4PF_6]^{4+}$ and $[M\text{-}3PF_6\text{-}HPF_6]^{3+}$ species respectively in which M is [5]MN **23**·$(PF_6)_4$ (Fig. 4). The absence of peak corresponding to the thread **1**·$(PF_6)_4$ ruled out the presence of any pseudorotaxane species. The lack of peaks corresponding to any undesirable interlocked/supramolecular species confirms the presence of only [5]molecular necklace whose molecular fragments are observed. Isotopic distribution of mass further proved the existence of species for the peaks assigned.

Attempted synthesis of [7]molecular necklace

The successful synthesis of [5]MN spurred us to make the higher homologue [7]MN utilising the same protocol. Accordingly the thread **2**·$(PF_6)_6$ was designed and synthesized using conventional

organic synthesis as shown above. The solubility of **2**·$(PF_6)_6$ is extremely poor in almost all organic solvents and it gets no better with excess DB24C8 in the mixed solvent. The six ammonium ion containing thread **2**·$(PF_6)_6$ seems to be extremely polar and hence to make it less polar, counter ion exchange was done with a more lipophilic salt NH_4BPh_4 to generate **2**·$(BPh_4)_6$ (Scheme 4). However, the solubility increases to an extent that it could only be soluble in methanol and not in acetonitrile or nitromethane. Keeping in mind about the limited solubility, we stirred **2**·$(BPh_4)_6$ along with excess DB24C8 in mixed solvent for a long time with occasional heating, but the solution never becomes clear which indicates threading does not take place to provide the desired pseudo [7]rotaxane **24**·$(BPh_4)_6$. Thus, the limited solubility of the six ammonium ion containing thread **2**·$(PF_6)_6$/**2**·$(BPh_4)_6$ impedes the threading of DB24C8, eluding the synthesis of [7]MN.



Scheme 4 Attempted threading of **2**·$(BPh_4)_6$.

Conclusion

In this paper, we report a new approach "threading-followed-by-ring-closing-metathesis" for the synthesis of molecular necklaces. This approach exploits the known self-assembly of DB24C8 with dibenzylammonium ion and the dynamic covalent chemistry in the form of olefin metathesis which is carried out by 2nd generation Grubbs catalyst. Utilizing the above mentioned approach, we could successfully synthesize a well-defined, well-characterized homogeneous [5]molecular necklace, which is both kinetically and thermodynamically stable. The "threading-followed-by-ring-closing-metathesis" approach could be generalised for synthesizing molecular necklaces since it does not involve metal coordination chemistry. Therefore, we attempted the synthesis of just the higher homologue [7]molecular necklace. Unfortunately we failed to get the desired [7]molecular necklace. The failure however is attributed to the poor solubility of the ammonium ion containing thread. Since this approach is not substrate specific, this idea can be extended to construct a variety of molecular necklaces based on different kind of recognition sites, lipophilic counteranions, and macrocycles.

Experimental

Materials and methods

All reagents and starting materials including DB24C8 were bought from commercial suppliers and used without further purification. Anhydrous solvents, *N*,*N*-dimethylformamide (DMF), dichloromethane were obtained from dry distillation of their analytical grade by CaH_2. Anhydrous tetrahydrofuran (THF) was obtained by distilling its analytical grade with sodium-benzophenone. Always freshly distilled dry solvents were used.

Column chromatography was performed on silica gel 60 (Merck 40–60 nm, 230–400 mesh). Deuterated solvents (Cambridge Isotope Laboratories) for NMR spectroscopic analyses were used as received. All NMR spectra were recorded on Bruker AMX500 at 500 MHz and Bruker ACF300 at 300 MHz spectrometers with tetramethylsilane (TMS) as the internal standard. The 2D COSY, NOESY NMR spectral data were recorded on Bruker AMX500 at 500 MHz. All chemical shifts are quoted in ppm with multiplicities being denoted by s (singlet), d (doublet), t (triplet), m (multiplet), and br (broad). Mass spectra were recorded on Finnigan LCQ quadrapole ion trap mass spectrometer and Shimadzu LCMS-IT-TOF, in ESI mode.

2,2′-(2,2′-(1,3-Phenylenebis(oxy))bis(ethane-2,1-diyl))bis(oxy)-diethanol (3). A mixture of resorcinol (2 g, 18.1 mmol), 2-(2-chloroethoxy)ethanol (11.36 g, 90.8 mmol), K_2CO_3 (15 g, 109 mmol), KI (0.15 g, 0.9 mmol) was heated to 80 °C in DMF (50 mL) under nitrogen atmosphere for 2 days. The mixture was filtered to remove undissolved excess K_2CO_3. The solvent was removed in vacuum to leave a residue which was extracted with $CHCl_3$. The organic layer was washed with water, dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum. The crude residue was purified by column chromatography (silica gel, acetone/hexane = 1 : 1) to give compound **3** (3.1 g, 60%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.16 (1 H, t, *J* = 8.2 Hz, Ar), 6.54 (2 H, br, Ar), 6.52 (1 H, d, *J* = 2.55 Hz, Ar), 4.12 (4 H, t, *J* = 4.4 Hz, CH_2), 3.85 (4 H, t, *J* = 5.05 Hz, CH_2), 3.75 (4 H, br, CH_2), 3.67 (4 H, m, CH_2), 2.20 (2 H, br, -OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.9, 129.9, 107.3, 102.0, 72.6, 69.7, 67.5, 61.8. ESI MS: *m*/*z* = 309.1 ([M + Na^+]); calculated exact mass: 286.14. HR ESI MS: *m*/*z* = 309.1323 ([M + Na^+]); calculated exact mass for $C_{14}H_{22}NaO_6$: 309.1309.

2,2′-(2,2′-(1,3-Phenylenebis(oxy))bis(ethane-2,1-diyl))bis(oxy)-bis(ethane-2,1-diyl) bis(4-methylbenzenesulfonate) (4). Compound **3** (2.45 g, 8.5 mmol) was dissolved in dry DCM (22 mL) under nitrogen atmosphere. To this was added triethylamine (3.47 g, 34.3 mmol) and the mixture was stirred under nitrogen atmosphere. The reaction mixture was cooled to 0 °C, and then toluene-4-sulfonyl chloride (4.9 g, 25.7 mmol) was added. The

reaction mixture was stirred for 36 h. The solvent was removed under vacuum leaving the crude residue which was purified by column chromatography (silica gel, acetone/hexane = 1 : 2) to give compound **4** (4.68 g, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (4 H, d, *J* = 8.2 Hz, Ar), 7.30 (4 H, d, *J* = 8.2 Hz, Ar), 7.15 (1 H, t, *J* = 8.2 Hz, Ar), 6.49 (2 H, dd, ^3J = 8.2 Hz, ^4J = 1.9 Hz, Ar), 6.44 (1 H, t, *J* = 2.55 Hz, Ar), 4.18 (4 H, t, *J* = 4.4 Hz, CH_2), 4.01 (4 H, t, *J* = 4.4 Hz, CH_2), 3.77 (8 H, m, CH_2), 2.40 (6 H, s, $PhCH_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.8, 144.8, 132.9, 129.9, 129.8, 127.9, 107.1, 101.8, 69.8, 69.2, 68.9, 67.4, 21.6. ESI MS: *m*/*z* = 617.0 ([M + Na^+]); calculated exact mass: 594.16. HR ESI MS: *m*/*z* = 617.1487 ([M + Na^+]); calculated exact mass for $C_{28}H_{34}NaO_{10}S_2$: 617.1486.

4,4′-(2,2′-(2,2′-(1,3-Phenylenebis(oxy))bis(ethane-2,1-diyl))bis-(oxy)bis(ethane-2,1-diyl))bis(oxy)dibenzaldehyde (5). A mixture of compound **4** (4.4 g, 7.4 mmol), 4- hydroxybenzaldehyde (1.98 g, 16.2 mmol) and K_2CO_3 (4.49 g, 32.5 mmol) was heated to 100 °C in dry DMF (25 mL) under nitrogen atmosphere for 3 days. The mixture was filtered to remove undissolved excess K_2CO_3. The solvent was removed in vacuum to leave a residue which was extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum. The crude residue was purified by column chromatography (silica gel, EA/hexane = 1 : 1) to give compound **5** (1.09 g, 30%). M.p.: 97–98 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.87 (1 H, s, CHO), 7.82 (4 H, d, *J* = 8.8 Hz, Ar), 7.15 (1 H, t, *J* = 8.2 Hz, Ar), 7.02 (4 H, d, *J* = 8.2 Hz, Ar), 6.51 (2 H, dd, ^3J = 8.2 Hz, ^4J = 1.9 Hz, Ar), 4.23 (4 H, t, *J* = 4.4 Hz, CH_2), 4.12 (4 H, t, *J* = 4.4 Hz, CH_2), 3.95 (4 H, t, *J* = 5.0 Hz, CH_2), 3.91 (4 H, t, *J* = 5.0 Hz, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.7, 163.8, 159.9, 131.9, 130.1, 129.9, 114.9, 107.2, 101.9, 70.0, 69.7, 67.8, 67.5. ESI MS: *m*/*z* = 517.1 ([M + Na^+]); calculated exact mass: 494.19. HR ESI MS: *m*/*z* = 517.1842 ([M + Na^+]); calculated exact mass for $C_{28}H_{30}NaO_8$ 517.1833.

4-(Undec-10-enyloxy)benzaldehyde (6). A mixture of 4-hydroxybenzaldehyde (5 g, 40.9 mmol), 11-bromoundec-1-ene (11.45 g, 49.1 mmol) and K_2CO_3 (16.97 g, 122.8 mmol) was refluxed in acetone (275 mL) for 2 days under nitrogen atmosphere. The mixture was filtered to remove undissolved excess K_2CO_3. The solvent was removed in vacuum to leave a residue which was extracted with $CHCl_3$. The organic layer was washed with water, dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum. The crude residue was purified by column chromatography (silica gel, EA/hexane = 1 : 4) to give compound **6** (8.8 g, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83 (2 H, d, *J* = 8.7 Hz, Ar), 7.00 (2 H, d, *J* = 8.7 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH═C(H_2)), 4.03 (2 H, t, *J* = 6.57 Hz, CH_2), 2.07 (2 H, m, CH_2), 1.85 (2 H, m, CH_2), 1.48 (12 H, br, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.7, 164.2, 139.0, 132.2, 131.9, 129.7, 114.7, 114.1, 68.3, 33.7, 29.4, 29.3, 29.2, 29.0, 28.9, 28.8, 25.9. ESI MS: *m*/*z* = 275.1 ([M + H^+]); calculated exact mass: 274.19. HR ESI MS: *m*/*z* = 297.1831 ([M + Na^+]); calculated exact mass for $C_{18}H_{26}NaO_2$: 297.1825.

Methyl 4-((4-(undec-10-enyloxy)benzylamino)methyl)benzoate (8). A mixture of compound **6** (8.16 g, 29.7 mmol) and methyl 4-(aminomethyl)benzoate (4.91 g, 29.7 mmol) in 1 : 1 molar ratio was heated in dry toluene (300 mL) to 140 °C for 16 h using a Dean–Stark apparatus under nitrogen atmosphere. The solvent was removed under vacuum, and the imine obtained was dissolved in THF (150 mL) and MeOH (150 mL) to which $NaBH_4$ (5.62 g, 148.6 mmol) was added in portions. After stirring for overnight, the solvent was removed under vacuum leaving a residue which was extracted by $CHCl_3$. The organic layer was washed by brine, dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum leaving the crude product **8** in quantitative yield which was used for the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.0 (2 H, d, *J* = 8.2 Hz, Ar), 7.43 (2 H, d, *J* = 8.2 Hz, Ar), 7.23 (2 H, d, *J* = 8.8 Hz, Ar), 6.86 (2 H, d, *J* = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH = C(H_2)), 3.94 (2 H, t, *J* = 6.3 Hz, CH_2), 3.91 (3 H, s, OCH_3), 3.84 (2 H, s, CH_2), 3.73 (2 H, s, CH_2), 2.06 (2 H, m, CH_2), 1.80 (2 H, m, CH_2), 1.47 (12 H, br, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.0, 158.3, 145.8, 139.2, 131.9, 129.7, 129.3, 128.8, 127.9, 114.5, 114.1, 68.0, 52.63, 52.61, 52.0, 33.8, 29.5, 29.39, 29.36, 29.3, 29.1, 28.9, 26.0. ESI MS: *m*/*z* = 423.9 ([M + H^+]); calculated exact mass: 423.28. HR ESI MS: *m*/*z* = 424.2858 ([M + H^+]); calculated exact mass for $C_{27}H_{38}NO_3$: 424.2846.

Methyl 4-((*tert*-butoxycarbonyl(4-(undec-10-enyloxy)benzyl)-amino)methyl)benzoate (9). Compound **8** (12.5 g, 29.5 mmol) was dissolved in $CHCl_3$ (250 mL) under nitrogen atmosphere. To this was added triethylamine (6.57 g, 64.9 mmol) and stirred for 5 min. This was followed by addition of Boc_2O (12.88 g, 59.0 mmol) and stirring of the reaction mixture for 24 h. The solvent was removed under vacuum leaving the crude residue which was purified by column chromatography (silica gel, EA/hexane = 1 : 9) to give compound **9** (14.2 g, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.0 (2 H, d, *J* = 8.2 Hz, Ar), 7.11 (8 H, br, Ar), 6.85 (2 H, d, *J* = 8.4 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH═C(H_2)), 4.35 (4 H, br, CH_2), 3.96 (2 H, br, CH_2), 3.91 (3 H, s, OCH_3), 2.07 (2 H, m, CH_2), 1.82 (2 H, m, CH_2) 1.52 (21 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.9, 158.5, 155.9, 139.1, 129.8, 129.4, 129.0, 128.8, 127.7, 127.0, 114.5, 114.1, 80.2, 68.0, 52.0, 49.0, 48.6, 33.7, 29.5, 29.4, 29.3, 29.2, 29.1, 28.9, 28.4, 27.4, 26.0. ESI MS: *m*/*z* = 546.1 ([M + Na^+]); calculated exact mass: 523.33. HR ESI MS: *m*/*z* = 546.3201 ([M + Na^+]); calculated exact mass for $C_{32}H_{45}NNaO_5$: 546.3190.

Tert-butyl 4-(hydroxymethyl)benzyl(4-(undec-10-enyloxy)benzyl)carbamate (10). Compound **9** (13.53 g, 25.8 mmol) was dissolved in dry THF (260 mL) under nitrogen atmosphere. The solution was cooled to 0 °C followed by addition of LAH (1.96 g, 51.6 mmol) in portions. The resulting suspension was gradually allowed to warm to room temperature and was stirred overnight. The excess LAH was quenched by slow addition of ground powder of $Na_2SO_4 \cdot 10H_2O$ and celite (1 : 1, w/w). The mixture was stirred for 30 min and filtered. The filtrate containing the desired compound was concentrated in vacuum, extracted with $CHCl_3$, washed with water, dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum leaving a residue which was purified by column chromatography (silica gel, EA/hexane = 3 : 7) to give compound **10** (7.9 g, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33 (2 H, d, *J* = 7.5 Hz, Ar), 7.18 (4 H, br, Ar), 6.85 (2 H, d, *J* = 8.8 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH═C(H_2)), 4.67 (2 H, s, CH_2), 4.37 (4 H, br, CH_2), 3.94 (2 H, t, *J* = 6.95 Hz, CH_2), 2.06 (2 H, m, CH_2), 1.97 (1 H, br, OH), 1.80 (2 H, m, CH_2), 1.49 (21 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz,

$CDCl_3$): δ = 158.4, 155.9, 139.9, 139.2, 137.5, 129.7, 129.3, 128.7, 128.1, 127.6, 127.2, 114.5, 114.1, 79.9, 68.0, 65.0, 48.6, 48.3, 33.7, 29.5, 29.4, 29.3, 29.2, 29.1, 28.9, 28.4, 26.0. ESI MS: m/z = 518.2 ([M + Na^+]); calculated exact mass: 495.33. HR ESI MS: m/z = 518.3254 ([M + Na^+]); calculated exact mass for $C_{31}H_{45}NNaO_4$: 518.3241.

Tert-butyl 4-(bromomethyl)benzyl(4-(undec-10-enyloxy)benzyl)carbamate (11). Compound **10** (8.72 g, 17.6 mmol) was dissolved in dry THF (118 mL) under nitrogen atmosphere. Triphenylphosphine (6.92 g, 26.3 mmol) was added and the solution was stirred for 5 min followed by addition of carbon tetrabromide (8.75 g, 26.3 mmol). After a while a white precipitate indicating the formation of triphenylphosphine oxide could be observed. The resulting mixture was stirred overnight under nitrogen atmosphere. The suspension was filtered and the filtrate was concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, EA/hexane = 1 : 9) to give compound **11** (8.8 g, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (2 H, d, J = 7.5 Hz, Ar), 7.14 (4 H, br, Ar), 6.85 (2 H, d, J = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH = C(H_2)), 4.49 (2 H, s, CH_2), 4.34 (4 H, br, CH_2), 3.94 (2 H, t, J = 6.3 Hz, CH_2), 2.05 (2 H, m, CH_2) 1.79 (2 H, m, CH_2), 1.49 (21 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.5, 155.9, 139.2, 136.6, 129.6, 129.3, 129.2, 128.7, 128.3, 127.7, 114.5, 114.1, 80.0, 68.0, 48.7, 48.5, 33.8, 33.3, 29.5, 29.4, 29.34, 29.26, 29.1, 28.9, 28.4, 26.0. ESI MS: m/z = 580.1 ([M + Na^+]); calculated exact mass: 557.25. HR ESI MS: m/z = 580.2411 ([M + Na^+]); calculated exact mass for $C_{31}H_{44}BrNNaO_3$: 580.2397.

Tert-butyl 4-(azidomethyl)benzyl(4-(undec-10-enyloxy)benzyl)carbamate (12). A mixture of compound **11** (8.15 g, 14.6 mmol) and sodium azide (1.9 g, 29.2 mmol) was heated to 55 °C in DMF (90 mL). After heating overnight, the solvent was removed under vacuum and the residue was extracted with $CHCl_3$. The organic layer was washed with water, dried over anhydrous Na_2SO_4, and the excess of solvent was then removed under vacuum to give crude compound **12** (6.3 g, 83%), which was used for the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (2 H, d, J = 8.2 Hz, Ar), 7.22 (4 H, br, Ar), 6.86 (2 H, d, J = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.97 (2 H, m, C(H) = C(H_2)), 4.35 (4 H, br, CH_2), 4.33 (2 H, s, CH_2), 3.94 (2 H, t, J = 6.9 Hz, CH_2), 2.07 (2 H, m, CH_2), 1.80 (2 H, m, CH_2), 1.49 (21 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.5, 155.9, 139.1, 138.4, 134.2, 129.6, 129.4, 128.7, 128.4, 127.8, 114.5, 114.1, 80.0, 68.0, 54.5, 48.8, 33.7, 29.5, 29.4, 29.3, 29.2, 29.0, 28.9, 28.4, 26.0. ESI MS: m/z = 543.2 ([M + Na^+]); calculated exact mass: 520.34. HR ESI MS: m/z = 543.3324 ([M + Na^+]); calculated exact mass for $C_{31}H_{44}N_4NaO_3$: 543.3306.

Tert-butyl 4-(aminomethyl)benzyl(4-(undec-10-enyloxy)benzyl)carbamate (13). Triphenylphosphine (6 g, 22.9 mmol) and deionised water (0.6 mL, 33.3 mmol) was added to the RBF containing compound **12** (5.97 g, 11.5 mmol). THF (55 mL) was added to dissolve the mixture which was stirred overnight under nitrogen atmosphere. The solvent was removed under vacuum to give a residue which was purified by column chromatography (silica gel, MeOH/$CHCl_3$ = 1 : 20) to give compound **13** (2.9 g, 52%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28 (2 H, br, Ar), 7.18 (4 H, br, Ar), 6.86 (2 H, d, J = 8.5 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH = C(H_2)), 4.31 (4 H, br, CH_2), 3.94 (2 H, t, J = 6.57 Hz, CH_2), 3.86 (2H, s, CH_2), 2.08 (2 H, m, CH_2), 1.82 (2 H, m, CH_2), 1.50 (21 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.4, 155.9, 142.2, 139.1, 136.6, 129.7, 128.7, 127.6, 127.2, 114.4, 114.1, 79.8, 67.9, 48.5, 46.1, 33.7, 29.4, 29.34, 29.3, 29.2, 29.0, 28.8, 28.4, 25.9. ESI MS: m/z = 495.0 ([M + H^+]); calculated exact mass: 494.35. HR ESI MS: m/z = 495.3590 ([M + H^+]); calculated exact mass for $C_{31}H_{47}N_2O_3$: 495.3581.

Methyl 4-((4-((*tert*-butoxycarbonyl(4-(undec-10-enyloxy)benzyl)amino)methyl)benzylamino)methyl)benzoate (14). Using the procedure for synthesizing compound **8**, compound **14** was obtained (4.25 g, 82%) from condensation of compound **13** (3.9 g, 8.0 mmol) with methyl 4-formylbenzoate (1.32 g, 8.0 mmol) followed by reduction with $NaBH_4$ (1.53 g, 40.4 mmol). Chromatographic purification was not done at this stage. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.01 (2 H, d, J = 8.2 Hz, Ar), 7.43 (2 H, d, J = 8.2 Hz, Ar), 7.30 (2 H, d, J = 7.5 Hz, Ar), 7.15 (4 H, br, Ar), 6.85 (2 H, d, J = 8.8 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.97 (2 H, m, CH = C(H_2)), 4.34 (4 H, br, CH_2), 3.94 (2 H, t, J = 6.3 Hz, CH_2), 3.90 (3 H, s, OCH_3), 3.86 (2 H, s, CH_2), 3.79 (2 H, s, CH_2), 2.06 (2 H, m, CH_2), 1.80 (2 H, m, CH_2), 1.50 (21 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.9, 158.4, 155.9, 145.7, 139.1, 138.9, 136.9, 129.8, 129.7, 129.3, 128.8, 128.3, 127.9, 127.6, 114.5, 114.1, 79.9, 67.9, 52.9, 52.7, 51.9, 48.6, 48.3, 33.7, 29.5, 29.4, 29.3, 29.2, 29.1, 28.9, 28.4, 26.0. ESI MS: m/z = 643.3 ([M + H^+]); calculated exact mass: 642.4. HR ESI MS: m/z = 643.4084 ([M + H^+]); calculated exact mass for $C_{40}H_{55}N_2O_5$: 643.4105.

Methyl 4-((*tert*-butoxycarbonyl(4-((*tert*-butoxycarbonyl(4-(undec-10-enyloxy)benzyl)amino)methyl)benzyl)amino)methyl)benzoate (15). Using the procedure for synthesizing compound **9**, compound **14** (4.13 g, 6.4 mmol) was reacted with Boc_2O (2.8 g, 12.8 mmol) and triethylamine (1.43 g, 14.1 mmol) to give compound **15** (4.1 g, 87%) after purification by column chromatography (silica gel, EA/hexane = 1 : 4). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00 (2 H, d, J = 7.5 Hz, Ar), 7.14 (8 H, br, Ar), 6.85 (2 H, d, J = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH = C(H_2)), 4.44 (8 H, br, CH_2), 3.94 (2 H, t, J = 6.95 Hz, CH_2), 3.90 (3 H, s, OCH_3), 2.06 (2 H, m, CH_2), 1.79 (2 H, m, CH_2), 1.50 (30 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.8, 158.4, 155.9, 155.8, 139.1, 137.3, 136.6, 129.8, 129.7, 129.3, 129.1, 128.7, 128.1, 127.7, 127.0, 114.4, 114.1, 80.3, 79.9, 67.9, 51.9, 49.4, 48.7, 48.4, 33.7, 29.4, 29.35, 29.31, 29.2, 29.0, 28.9, 28.4, 28.3, 25.9. ESI MS: m/z = 765.1 ([M + Na^+]); calculated exact mass: 742.46. HR ESI MS: m/z = 765.4468 ([M + Na^+]); calculated exact mass for $C_{45}H_{62}N_2NaO_7$: 765.4449.

Compound 16. Using the procedure for synthesizing compound **10**, compound **15** (4.13 g, 5.5 mmol) was reduced by LAH (0.42 g, 11.1 mmol) to give compound **16** (2.49 g, 63%) after purification by column chromatography (silica gel, EA/hexane = 3 : 7). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (2 H, d, J = 7.5 Hz, Ar), 7.15 (8 H, br, Ar), 6.86 (2 H, d, J = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.97 (2 H, m, CH = C(H_2)), 4.67 (2 H, s, CH_2), 4.40 (8 H, br, CH_2), 3.94 (2 H, t, J = 6.3 Hz, CH_2), 2.06 (2 H, m, CH_2), 1.80 (2 H, m, CH_2), 1.50 (30 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.4, 155.9, 140.0, 139.1, 137.3, 137.2, 137.0, 136.9, 129.7, 129.3, 128.8, 128.1, 127.6, 127.1, 114.5, 114.1,

80.1, 80.0, 68.0, 64.9, 49.1, 48.8, 48.4, 33.7, 29.5, 29.4, 29.3, 29.2, 29.1, 28.9, 28.44, 28.42, 26.0. ESI MS: m/z = 737.2 ([M + Na^+]); calculated exact mass: 714.46. HR ESI MS: m/z = 737.4502 ([M + Na^+]); calculated exact mass for $C_{44}H_{62}N_2NaO_6$: 737.4500.

Compound 17. Using the procedure for synthesizing compound **11**, compound **16** (2.48 g, 3.4 mmol) was brominated by CBr_4 (1.72 g, 5.2 mmol) and PPh_3 (1.36 g, 5.2 mmol) to give compound **17** (2.27 g, 86%) after purification by column chromatography (silica gel, EA/hexane = 1 : 4). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (2 H, d, J = 7.8 Hz, Ar), 7.17 (8 H, br, Ar), 6.87 (2 H, d, J = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.97 (2 H, m, CH = C(H_2)), 4.47 (2 H, s, CH_2), 4.41 (8 H, br, CH_2), 3.95 (2 H, t, J = 6.3 Hz, CH_2), 2.07 (2 H, m, CH_2), 1.81 (2 H, m, CH_2) 1.51 (30 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.3, 155.75, 155.73, 138.9, 138.3, 137.0, 136.6, 129.6, 129.2, 129.1, 128.6, 128.2, 127.9, 127.6, 127.5, 114.3, 114.0, 79.9, 79.7, 67.8, 48.6, 48.3, 33.6, 33.0 29.3, 29.23, 29.19, 29.12, 28.9, 28.7, 28.33, 28.28, 25.9. ESI MS: m/z = 799.0 ([M + Na^+]); calculated exact mass: 776.38. HR ESI MS: m/z = 799.3663 ([M + Na^+]); calculated exact mass for $C_{44}H_{61}BrN_2NaO_5$: 799.3656.

Compound 18. Using the procedure for synthesizing compound **12**, compound **17** (0.56 g, 0.72 mmol) was treated with sodium azide (0.09 g, 1.44 mmol) to give compound **18** (0.47 g, 88%). Chromatographic purification was not done at this stage. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (2 H, d, J = 7.5 Hz, Ar), 7.15 (8 H, br, Ar), 6.85 (2 H, d, J = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.97 (2 H, m, CH = C(H_2)), 4.41 (8 H, br, CH_2), 4.33 (2 H, s, CH_2), 3.94 (2 H, t, J = 6.95 Hz, CH_2), 2.06 (2 H, m, CH_2), 1.80 (2 H, m, CH_2), 1.49 (30 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.4, 155.9, 139.2, 136.8, 134.3, 129.7, 129.3, 128.8, 128.4, 128.1, 127.6, 114.5, 114.1, 80.2, 79.9, 68.0, 54.5, 49.0, 48.7, 33.8, 29.5, 29.4, 29.35, 29.27, 29.1, 28.9, 28.5, 28.4, 26.0. ESI MS: m/z = 762.2 ([M + Na^+]); calculated exact mass: 739.47. HR ESI MS: m/z = 762.4581 ([M + Na^+]); calculated exact mass for $C_{44}H_{61}N_5NaO_5$: 762.4565.

Compound 19. Using the procedure for synthesizing compound **13**, compound **18** (0.47 g, 0.63 mmol) was reduced by H_2O (0.029 g, 1.58 mmol) and PPh_3 (0.34 g, 1.27 mmol) to give compound **19** (0.32 g, 72%) after purification by column chromatography (silica gel, MeOH/$CHCl_3$ = 1 : 9). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (2 H, d, J = 8.2 Hz, Ar), 7.15 (8 H, br, Ar), 6.85 (2 H, d, J = 8.2 Hz, Ar), 5.81 (1 H, m, C(H) = CH_2), 4.96 (2 H, m, CH = C(H_2)), 4.39 (8 H, br, CH_2), 3.94 (2 H, t, J = 6.95 Hz, CH_2), 3.87 (2 H, s, CH_2), 2.06 (2 H, m, CH_2), 1.80 (4 H, br, CH_2 & NH_2), 1.50 (30 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.4, 155.96, 155.95, 142.0, 139.2, 137.1, 136.9, 136.6, 129.7, 129.3, 128.72, 128.67, 128.4, 128.1, 127.6, 127.3, 114.5, 114.1, 80.0, 79.9, 68.0, 48.9, 48.7, 48.4, 46.1, 33.8, 29.5, 29.38, 29.35, 29.27, 29.1, 28.9, 28.5, 28.4, 26.0. ESI MS: m/z = 714.1 ([M + H^+]); calculated exact mass: 713.48. HR ESI MS: m/z = 714.4848 ([M + H^+]); calculated exact mass for $C_{44}H_{64}N_3O_5$: 714.4840.

Tert-butyl (4,4′-(4,4′-(2,2′-(2,2′-(1,3-phenylenebis(oxy))bis(ethane-2,1-diyl))bis(oxy)bis(ethane-2,1-diyl))bis(oxy)bis(4,1-phenylene))bis(methylene)bis(azanediyl)bis(methylene)bis(4,1-phenylene))bis(methylene)bis(4-(undec-10-enyloxy)benzylcarbamate) (20). A mixture of compound **5** (0.71 g, 1.45 mmol) and compound **13** (1.44 g, 2.9 mmol) in 1 : 2 molar ratio was heated in dry toluene (100 mL) to 140 °C for 16 h using a Dean–Stark apparatus under nitrogen atmosphere. The solvent was removed under vacuum, and the imine obtained was dissolved in THF (20 mL) and MeOH (20 mL) to which $NaBH_4$ (0.27 g, 7.3 mmol) was added in portions. After stirring for overnight, the solvent was removed under vacuum leaving a residue which was extracted by $CHCl_3$. The organic layer was washed by brine, dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum leaving a residue which was purified by column chromatography (silica gel, MeOH/$CHCl_3$ = 1 : 19) to give compound **20** (1.37 g, 65%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21 (4 H, d, J = 8.2 Hz, Ar), 7.16 (4 H, d, J = 8.2 Hz, Ar), 7.08 (9 H, br, Ar), 6.81 (2 H, d, J = 8.8 Hz, Ar), 6.77 (4 H, d, J = 8.2 Hz, Ar), 6.44 (3 H, br, Ar), 5.73 (2 H, m, C(H) = CH_2), 4.88 (4 H, m, CH = C(H_2)), 4.29 (8 H, br, CH_2), 4.05 (8 H, m, CH_2), 3.86 (12 H, br, CH_2), 3.69 (4 H, s, CH_2), 3.65 (4 H, s, CH_2), 1.98 (4 H, m, CH_2), 1.75 (2 H, br, NH), 1.71 (4 H, m, CH_2), 1.41 (42 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.9, 158.4, 157.8, 155.9, 139.16, 139.13, 136.7, 132.5, 129.8, 129.3, 128.7, 128.3, 128.0, 127.5, 114.5, 114.4, 114.1, 107.1, 101.8, 79.9, 69.9, 69.8, 67.9, 67.5, 67.4, 52.7, 52.5, 48.5, 48.3, 33.7, 29.4, 29.34, 29.31, 29.2, 29.0, 28.8, 28.4, 25.9. ESI MS: m/z = 1451.4 ([M + H^+]), 726.5 ([M + 2H^+]); calculated exact mass: 1450.91. HR ESI MS: m/z = 1451.9158 ([M + H^+]); calculated exact mass for $C_{90}H_{123}N_4O_{12}$: 1451.9132.

Compound 21. A mixture of compound **5** (0.1 g, 0.21 mmol) and compound **19** (0.3 g, 0.42 mmol) in 1 : 2 molar ratio was heated in dry toluene (70 mL) to 140 °C for 16 h using a Dean–Stark apparatus under nitrogen atmosphere. The solvent was removed under vacuum, and the imine obtained was dissolved in THF (6 mL) and MeOH (6 mL) to which $NaBH_4$ (0.04 g, 1.06 mmol) was added in portions. After stirring for overnight, the solvent was removed under vacuum leaving a residue which was extracted by $CHCl_3$. The organic layer was washed by brine, dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum leaving a residue which was purified by column chromatography (silica gel, MeOH/$CHCl_3$ = 1 : 15) to give compound **21** (0.32 g, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (4 H, d, J = 7.6 Hz, Ar), 7.26 (4 H, d, J = 8.2 Hz, Ar), 7.18 (17 H, br, Ar), 6.91 (4 H, d, J = 8.8 Hz, Ar), 6.87 (4 H, d, J = 8.2 Hz, Ar), 6.54 (3 H, br, Ar), 5.82 (2 H, m, C(H) = CH_2), 4.97 (4 H, m, CH = C(H_2)), 4.42 (16 H, br, CH_2), 4.14 (8 H, m, CH_2), 3.95 (4 H, t, J = 6.3 Hz, CH_2), 3.92 (8 H, m, CH_2), 3.79 (4 H, s, CH_2), 3.75 (4 H, s, CH_2), 2.08 (4 H, m, CH_2), 1.96 (2 H, br, NH), 1.81 (4 H, m, CH_2), 1.52 (60 H, br, CH_2 & Boc). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.8, 158.3, 157.7, 155.82, 155.79, 139.2, 138.9, 136.9, 136.5, 132.4, 129.7, 129.1, 128.6, 128.3, 128.2, 127.9, 127.5, 114.44, 114.36, 114.0, 107.0, 101.7, 79.9, 79.8, 69.8, 69.7, 67.9, 67.4, 67.3, 52.6, 52.4, 48.8, 48.6, 48.3, 33.6, 29.3, 29.24, 29.21, 29.1, 28.9, 28.8, 28.33, 28.32, 25.9. ESI MS: m/z = 1890.5 ([M + H^+]), 946.3 ([M + 2H^+]); calculated exact mass: 1889.16. HR ESI MS: m/z = 945.5885 ([M + 2H^+]); calculated exact mass for $C_{116}H_{158}N_6O_{16}$: 945.5862.

Compound 1·$(PF_6)_4$. Compound **20** (1.3 g, 0.9 mmol) was dissolved in dry DCM (50 mL) under nitrogen atmosphere. Trifluoroacetic acid (2.04 g, 17.9 mmol) was added to this solution and stirred overnight. The solvent was removed in vacuum and the residue was dissolved in minimum amount of methanol-acetone

(2 : 1, v/v) mixture. To this was added a saturated aqueous NH_4PF_6 solution to yield compound **1**·$(PF_6)_4$ as a white precipitate. The solution was filtered through Buchner funnel and the residue collected was washed with water, dried in vacuum and used for next step. Compound **1**·$(PF_6)_4$ was obtained in quantitative yield. M.p.: Decomposed. ^{1}H NMR (500 MHz, CD_3CN): δ = 7.49 (8 H, br, Ar), 7.42 (8 H, br, NH_2^+), 7.38 (8 H, br, Ar), 7.15 (1 H, t, *J* = 8.2 Hz, Ar), 6.98 (4 H, d, *J* = 8.8 Hz, Ar), 6.95 (4 H, d, *J* = 8.8 Hz, Ar), 6.51 (2 H, dd, ^3J = 8.2 Hz, ^4J = 2.5 Hz, Ar), 6.46 (1 H, t, *J* = 1.9 Hz, Ar), 5.82 (2 H, m, C(H) = CH_2), 4.95 (4 H, m, CH = C(H_2)), 4.20 (8 H, br, CH_2), 4.16 (12 H, br, CH_2), 4.08 (4 H, t, *J* = 4.4 Hz, CH_2), 3.97 (4 H, t, *J* = 6.9 Hz, CH_2), 3.84 (8 H, m, CH_2), 2.04 (4 H, m, CH_2), 1.76 (4 H, m, CH_2), 1.42 (24 H, br, CH_2). ^{13}C NMR (125 MHz, CD_3CN): δ = 161.3, 161.1, 160.9, 140.3, 133.0, 132.9, 132.8, 131.7, 131.1, 123.4, 122.9, 115.99, 115.92, 114.7, 108.1, 102.3, 70.5, 70.4, 69.1, 68.7, 68.5, 52.12, 52.08, 51.5, 51.4, 34.4, 30.2, 30.1, 30.0, 29.9, 29.8, 29.7, 26.7. ESI MS: *m*/*z* = 1688.3 ([M-PF_6]$^+$), 1543.2 ([M-HPF_6-PF_6]$^+$), 1397.5 ([M-2HPF_6-PF_6]$^+$), 1251.3 ([M-3HPF_6-PF_6]$^+$), 722.1 ([M-2PF_6]$^{2+}$), 699.0 ([M-HPF_6-2PF_6]$^{2+}$), 626.5 ([M-2HPF_6-2PF_6]$^{2+}$); calculated exact mass: 1834.69. HR ESI MS: *m*/*z* = 626.4084 ([M-2HPF_6-2PF_6]$^{2+}$); calculated exact mass for $C_{80}H_{108}N_4O_8$: 626.4078.

Compound 23·$(PF_6)_4$ ([5]MN). Compound **1**·$(PF_6)_4$ (0.1 g, 0.056 mmol) and DB24C8 (0.5 g, 1.12 mmol) are dissolved in the mixed solvent (40 mL, $CHCl_3/CH_3CN$ = 3 : 1 (v/v)). The solution was stirred for 24 h and the solvent was then removed under vacuum without heating and then the residue was dissolved in dry DCM (200 mL, 0.0003 M) under nitrogen atmosphere. 2nd Generation Grubbs catalyst (0.02 g, 0.02 mmol) was added and the resulting mixture was refluxed for 3 days. The reaction mixture was cooled followed by quenching with ethyl vinyl ether. The excess solvent was removed in vacuum and the residue was subjected to column chromatography (silica gel, MeOH–$CHCl_3$ = 1 : 4 (v/v)) to give the desired product **23**·$(PF_6)_4$ (0.04 g, 20%). M.p.: Decomposed. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37 (8 H, br, NH_2^+), 7.24 (8 H, d, *J* = 8.0 Hz, Ar), 7.13 (1 H, t, *J* = 8.0 Hz, Ar), 6.94 (8 H, br, Ar), 6.77 (40 H, br, DB & Ar), 6.52 (2 H, br, Ar), 6.49 (1 H, br, Ar), 5.37 (2 H, br, C(H) = C(H)), 4.54 (8 H, br, C(H_2)NH_2^+), 4.36 (8 H, br, C(H_2)NH_2^+), 4.12–3.46 (116 H, br, DB & CH_2), 1.96 (4 H, br, CH_2), 1.76 (4 H, m, CH_2), 1.29 (24 H, br, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.9, 159.6, 159.3, 147.4, 132.3, 130.64, 130.58, 130.3, 129.8, 129.6, 124.1, 123.6, 121.3, 114.6, 114.4, 112.49, 112.46, 107.1, 101.9, 70.8, 70.2, 69.8, 69.7, 67.9, 67.5, 67.4, 52.0, 51.7, 32.5, 29.7, 29.5, 29.4, 29.3, 29.1, 25.9. ESI MS: *m*/*z* = 755.61 ([M-4PF_6^-]$^{4+}$), 1007.16 ([*M*-3PF_6^--HPF_6]$^{3+}$); calculated exact mass: 3599.50. EA: $C_{174}H_{234}F_{24}N_4O_{40}P_4$ requires C 58.03, H 6.55, N 1.56; found C 57.60, H 6.38, N 1.66.

Compound 2·$(PF_6)_6$. Compound **21** (0.32 g, 0.17 mmol) was dissolved in dry DCM (18 mL) under nitrogen atmosphere. Trifluoroacetic acid (0.77 g, 6.77 mmol) was added to this solution and stirred overnight. The solvent was removed in vacuum and the residue was dissolved in minimum amount of trifluoroacetic acid. To this was added a saturated aqueous NH_4PF_6 solution to yield compound **2**·$(PF_6)_6$ as a white precipitate. The solution was filtered through Buchner funnel and the residue collected was washed with water, dried in vacuum and used for next step. Compound **2**·$(PF_6)_6$ was obtained in quantitative yield. M.p.: Decomposed. ^{1}H NMR (500 MHz, CD_3SOCD_3): δ = 7.48 (16 H, br, Ar), 7.37 (8 H, br, Ar), 6.98 (8 H, br, Ar), 6.50 (3 H, br, Ar), 4.09 (br, -OCH_2 peaks overlap with broad solvent peak), 1.66 (4 H, br, CH_2), 1.27 (24 H, br, CH_2). ^{13}C NMR (125 MHz, CD_3SOCD_3): could not be observed even after scanning for long time, because of poor solubility. ESI MS obtained after neutralization of **2**·$(PF_6)_6$ with NaOH (aq), found: *m*/*z* = 1489.7 ([M + H$^+$]); calculated exact mass: 1488.95. EA: for neutral compound, $C_{96}H_{124}N_6O_8$ requires C 77.38, H 8.39, N 5.64; found C 77.24, H 8.51, N 5.95.

Compound 2·$(BPh_4)_6$. Compound **2**·$(PF_6)_6$ was neutralised with NaOH (aq) and extracted with $CHCl_3$. The solvent was removed and the residue obtained was dissolved in minimum amount of trifluoroacetic acid. To this was added equivalent amount of NH_4BPh_4 (in aqueous acetone) to yield **2**·$(BPh_4)_6$ as a white precipitate. The solution was filtered through Buchner funnel and the residue collected was dried in vacuum. Compound **2**·$(BPh_4)_6$ was obtained in quantitative yield. M.p.: Decomposed. ^{1}H NMR (500 MHz, CD_3OD): δ = 7.55 (br, BPh_4 peaks overlap with aromatic protons of thread), 7.38 (br, BPh_4 peaks overlap with aromatic protons of thread), 7.12 (1 H, br, Ar), 6.91 (8 H, br, Ar), 6.61 (3 H, br, Ar), 4.23 (44 H, br, CH_2), 1.70 (4 H, br, CH_2), 1.40 (24 H, br, CH_2). ^{13}C NMR (125 MHz, CD_3OD): δ = 163.4, 163.3, 163.2, 163.1, 163.0, 162.9, 161.6, 134.8, 134.4, 134.0, 133.8, 132.6, 131.85, 131.77, 131.1, 130.7, 130.4, 129.9, 129.8, 128.6, 120.5, 116.8, 116.5, 116.2, 116.1, 71.1, 70.9, 70.8, 69.1, 68.7, 68.6, 51.7, 51.6, 51.1, 40.2, 33.0, 30.7, 30.4, 30.2, 27.0, 26.8. ESI MS obtained after neutralization of **2**·$(BPh_4)_6$ with NaOH (aq), found: *m*/*z* = 1489.7 ([M + H$^+$]); calculated exact mass: 1488.95. EA: for neutral compound, $C_{96}H_{124}N_6O_8$ requires C 77.38, H 8.39, N 5.64; found C 77.24, H 8.51, N 5.95.

Acknowledgements

This work was financially supported by the AcRF Tier 1 grant (R-143-000-328-133) and the NUS Young Investigator Award (R-143-000-356-101).

Notes and references

1 A. L. Robinson, *Science*, 1984, **223**, 267–268.
2 H. Kuhn and J. Waser, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 500–520.
3 J. M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 89–112.
4 (*a*) D. Philp and J. F. Stoddart, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1155–1196; (*b*) T. Haino, Y. Matsumoto and Y. Fukazawa, *J. Am. Chem. Soc.*, 2005, **127**, 8936–8937; (*c*) J. J. McEwen and K. J. Wallace, *Chem. Commun.*, 2009, 6339–6351.
5 (*a*) D. J. Cram, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1009–1020; (*b*) X. Zhang, G. Gramlich, X. Wang and W. M. Nau, *J. Am. Chem. Soc.*, 2002, **124**, 254–263; (*c*) L. X. Song, H. M. Wang, X. Q. Guo and L. Bai, *J. Org. Chem.*, 2008, **73**, 8305–8316.
6 (*a*) D. B. Amabilino and J. F. Stoddart, *Chem. Rev.*, 1995, **95**, 2725–2828; (*b*) F. M. Raymo and J. F. Stoddart, *Chem. Rev.*, 1999, **99**, 1643–1663; (*c*) J.-P. Sauvage and C. Dietrich-Buchecker, *Molecular Catenanes, Rotaxanes and Knots*, ed., Wiley-VCH, Weinheim, 1999.
7 (*a*) P. L. Anelli, N. Spencer and J. F. Stoddart, *J. Am. Chem. Soc.*, 1991, **113**, 5131–5133; (*b*) R. A. Bissell, E. Cordova, A. E. Kaifer and J. F. Stoddart, *Nature*, 1994, **369**, 133–137; (*c*) M. Andersson, M. Linke, J. C. Chambron, J. Davidsson, V. Heitz, L. Hammarstrom and J. P. Sauvage, *J. Am. Chem. Soc.*, 2002, **124**, 4347–4362; (*d*) S. Nygaard, K. C. F. Leung, I. Aprahamian, T. Ikeda, S. Saha, B. W. Laursen, S. Y. Kim, S. W. Hansen, P. C. Stein, A. H. Flood, J. F. Stoddart and J. O. Jeppesen, *J. Am. Chem. Soc.*, 2007, **129**, 960–970; (*e*) N. Fu, J. M. Baumes, E. Arunkumar, B. C. Noll and B. D. Smith, *J. Org. Chem.*, 2009, **74**, 6462–6468.

8 (*a*) T. J. Kidd, D. A. Leigh and A. J. Wilson, *J. Am. Chem. Soc.*, 1999, **121**, 1599–1600; (*b*) H. Iwamoto, K. Itoh, H. Nagamiya and Y. Fukazawa, *Tetrahedron Lett.*, 2003, **44**, 5773–5776; (*c*) B. A. Blight, J. A. Wisner and M. C. Jennings, *Angew. Chem., Int. Ed.*, 2007, **46**, 2835–2838; (*d*) S. M. Goldup, D. A. Leigh, T. Long, P. R. McGonigal, M. D. Symes and J. Wu, *J. Am. Chem. Soc.*, 2009, **131**, 15924–15929.

9 (*a*) C. DietrichBuchecker, G. Rapenne and J. P. Sauvage, *Chem. Commun.*, 1997, 2053–2054; (*b*) H. Adams, E. Ashworth, G. A. Breault, J. Guo, C. A. Hunter and P. C. Mayers, *Nature*, 2001, **411**, 763–763; (*c*) R. F. Kelley, M. J. Tauber and M. R. Wasielewski, *Angew. Chem., Int. Ed.*, 2006, **45**, 7979–7982; (*d*) A. Böhmer, J. Brüggemann, A. Kaufmann, A. Yoneva, S. Müller, W. M. Müller, U. Müller, F. W. Vergeer, L. Chi, L. D. Cola, H. Fuchs, X. Chen, T. Kubota, Y. Okamoto and Fritz Vögtle, *Eur. J. Org. Chem.*, 2007, 45–52.

10 (*a*) F. Bitsch, C. O. Dietrichbuchecker, A. K. Khemiss, J. P. Sauvage and A. Vandorsselaer, *J. Am. Chem. Soc.*, 1991, **113**, 4023–4025; (*b*) D. B. Amabilino, P. R. Ashton, J. F. Stoddart, A. J. P. White and D. J. Williams, *Chem.–Eur. J.*, 1998, **4**, 460–468; (*c*) D. M. Whang, K. M. Park, J. Heo, P. Ashton and K. Kim, *J. Am. Chem. Soc.*, 1998, **120**, 4899–4900; (*d*) S. G. Roh, K. M. Park, G. J. Park, S. Sakamoto, K. Yamaguchi and K. Kim, *Angew. Chem., Int. Ed.*, 1999, **38**, 638–641; (*e*) S. H. Chiu, S. J. Rowan, S. J. Cantrill, L. Ridvan, P. R. Ashton, R. L. Garrell and J. F. Stoddart, *Tetrahedron*, 2002, **58**, 807–814; (*f*) K. M. Park, S. Y. Kim, J. Heo, D. Whang, S. Sakamoto, K. Yamaguchi and K. Kim, *J. Am. Chem. Soc.*, 2002, **124**, 2140–2147; (*g*) M. Okada and A. Harada, *Macromolecules*, 2003, **36**, 9701–9703; (*h*) Y. H. Ko, K. Kim, J. K. Kang, H. Chun, J. W. Lee, S. Sakamoto, K. Yamaguchi, J. C. Fettinger and K. Kim, *J. Am. Chem. Soc.*, 2004, **126**, 1932–1933; (*i*) P. G. Clark, E. N. Guidry, W. Y. Chan, W. E. Steinmetz and R. H. Grubbs, *J. Am. Chem. Soc.*, 2010, **132**, 3405–3412.

11 (*a*) A. R. Williams, B. H. Northrop, T. Chang, J. F. Stoddart, A. J. P. White and D. J. Williams, *Angew. Chem., Int. Ed.*, 2006, **45**, 6665–6669; (*b*) J. F. Stoddart, *Chem. Soc. Rev.*, 2009, **38**, 1802–1820.

12 (*a*) K. S. Chichak, S. J. Cantrill, A. R. Pease, S. H. Chiu, G. W. V. Cave, J. L. Atwood and J. F. Stoddart, *Science*, 2004, **304**, 1308–1312; (*b*) C. D. Meyer, R. S. Forgan, K. S. Chichak, A. J. Peters, N. Tangchaivang, G. W. V. Cave, S. I. Khan, S. J. Cantrill and J. F. Stoddart, *Chem.–Eur. J.*, 2010, **16**, 12570–12581.

13 (*a*) J. F. Stoddart and H. R. Tseng, *Proc. Natl. Acad. Sci. U. S. A.*, 2002, **99**, 4797–4800; (*b*) J. F. Stoddart and H. M. Colquhoun, *Tetrahedron*, 2008, **64**, 8231–8263.

14 (*a*) S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders and J. F. Stoddart, *Angew. Chem., Int. Ed.*, 2002, **41**, 898–952; (*b*) Y. Tokunaga, K. Akasaka, N. Hashimoto, S. Yamanaka, K. Hisada, Y. Shimomura and S. Kakuchi, *J. Org. Chem.*, 2009, **74**, 2374–2379; (*c*) J.-M. Han, J.-L. Pan, T. Lei, C. Liu and J. Pei, *Chem.–Eur. J.*, 2010, **16**, 13850–13861.

15 (*a*) P. T. Glink, A. I. Oliva, J. F. Stoddart, A. J. P. White and D. J. Williams, *Angew. Chem., Int. Ed.*, 2001, **40**, 1870–1875; (*b*) J. Wu, K. C. F. Leung and J. F. Stoddart, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 17266–17271; (*c*) L. M. Klivansky, G. Koshkakaryan, D. Cao and Y. Liu, *Angew. Chem., Int. Ed.*, 2009, **48**, 4185–4189; (*d*) G. Koshkakaryan, D. Cao, L. M. Klivansky, S. J. Teat, J. L. Tran and Y. Liu, *Org. Lett.*, 2010, **12**, 1528–1531.

16 (*a*) S. J. Rowan, P. A. Brady and J. K. M. Sanders, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 2143–2145; (*b*) P. A. Brady, R. P. BonarLaw, S. J. Rowan, C. J. Suckling and J. K. M. Sanders, *Chem. Commun.*, 1996, 319–320; (*c*) J. Berná, M. Alajarín and R.-A. Orenes, *J. Am. Chem. Soc.*, 2010, **132**, 10741–10747.

17 (*a*) M. F. Li, K. Yamato, J. S. Ferguson, K. K. Singarapu, T. Szyperski and B. Gong, *J. Am. Chem. Soc.*, 2008, **130**, 491–500; (*b*) B. M. Kiran and N. Jayaraman, *Macromolecules*, 2009, **42**, 7353–7359.

18 (*a*) E. N. Guidry, S. J. Cantrill, J. F. Stoddart and R. H. Grubbs, *Org. Lett.*, 2005, **7**, 2129–2132; (*b*) E. N. Guidry, J. Li, J. F. Stoddart and R. H. Grubbs, *J. Am. Chem. Soc.*, 2007, **129**, 8944–8945.

19 (*a*) A. Harada, J. Li and M. Kamachi, *Nature*, 1992, **356**, 325–327; (*b*) W. C. Hung, K. S. Liao, Y. H. Liu, S. M. Peng and S. H. Chiu, *Org. Lett.*, 2004, **6**, 4183–4186; (*c*) A. Harada, A. Hashidzume, H. Yamaguchi and Y. Takashima, *Chem. Rev.*, 2009, **109**, 5974–6023; (*d*) Y. Chen, Y.-M. Zhang and Y. Liu, *Chem. Commun.*, 2010, **46**, 5622–5633.

20 (*a*) P. R. Ashton, R. Ballardini, V. Balzani, M. GomezLopez, S. E. Lawrence, M. V. MartinezDiaz, M. Montalti, A. Piersanti, L. Prodi, J. F. Stoddart and D. J. Williams, *J. Am. Chem. Soc.*, 1997, **119**, 10641–10651; (*b*) P. R. Ashton, R. Ballardini, V. Balzani, I. Baxter, A. Credi, M. C. T. Fyfe, M. T. Gandolfi, M. Gomez-Lopez, M. V. Martinez-Diaz, A. Piersanti, N. Spencer, J. F. Stoddart, M. Venturi, A. J. P. White and D. J. Williams, *J. Am. Chem. Soc.*, 1998, **120**, 11932–11942; (*c*) H. W. Gibson, N. Yamaguchi, L. Hamilton and J. W. Jones, *J. Am. Chem. Soc.*, 2002, **124**, 4653–4665; (*d*) R. Ballardini, V. Balzani, M. Clemente-Leon, A. Credi, M. T. Gandolfi, E. Ishow, J. Perkins, J. F. Stoddart, H. R. Tseng and S. Wenger, *J. Am. Chem. Soc.*, 2002, **124**, 12786–12795; (*e*) K. Ghosh, H. B. Yang, B. H. Northrop, M. M. Lyndon, Y. R. Zheng, D. C. Muddiman and P. J. Stang, *J. Am. Chem. Soc.*, 2008, **130**, 5320–5334.

21 (*a*) S. Höger, A.-D. Meckenstock and S. Müller, *Chem.–Eur. J.*, 1998, **4**, 2423–2434; (*b*) J. B. Beil, N. G. Lemcoff and S. C. Zimmerman, *J. Am. Chem. Soc.*, 2004, **126**, 13576–13577; (*c*) T. Chen, G.-B. Pan, H. Wettach, M. Fritzsche, S. Höger, L.-J. Wan, H.-B. Yang, B. H. Northrop and Peter J. Stang, *J. Am. Chem. Soc.*, 2010, **132**, 1328–1333.

22 P. R. Ashton, I. Baxter, M. C. T. Fyfe, F. M. Raymo, N. Spencer, J. F. Stoddart, A. J. P. White and D. J. Williams, *J. Am. Chem. Soc.*, 1998, **120**, 2297–2307.

23 P. R. Ashton, M. C. T. Fyfe, P. T. Glink, S. Menzer, J. F. Stoddart, A. J. P. White and D. J. Williams, *J. Am. Chem. Soc.*, 1997, **119**, 12514–12524.

24 (*a*) P. R. Ashton, P. J. Campbell, E. J. T. Chrystal, P. T. Glink, S. Menzer, D. Philip, N. Spencer, J. F. Stoddart, P. A. Tasker and D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1865–1869; (*b*) P. R. Ashton, E. J. T. Chrystal, P. T. Glink, S. Menzer, C. Schiavo, N. Spencer, J. F. Stoddart, P. A. Tasker, A. J. P. White and D. J. Williams, *Chem.–Eur. J.*, 1996, **2**, 709–728.