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Making molecular-necklaces from rotaxanes

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Abstract—During an attempt to synthesize polyrotaxanes by Wittig step-growth polymerization between a dibenzylic bis(triphenylphosphonium)-stoppered [2]rotaxane, with an NH_2^+ recognition site encircled by a DB24C8 ring, and appropriate derivatives of terephthaldehyde carrying bulky groups, large macrocyclic compounds with the topologies of catenanes and molecular-necklaces, are formed.

1. Introduction

Interlocked molecules[1] are comprised of two or more mechanically bonded components that are not covalently linked to each other. The applications of the concept of self-assembly[2] and the fundamental principles of molecular recognition[3] in the context of supramolecular assistance to covalent synthesis[4] has led to highly efficient template-directed procedures[5] for constructing interlocked molecular compounds. Rotaxanes—molecules in which one or more[6] macrocyclic components are trapped around (a) recognition site(s) along the rod section of a dumbbell-shaped component by bulky terminal groups which are usually referred to as stoppers—represent one of the two major subsets[7] of such compounds. In recent times, [2]rotaxanes[6]—and indeed catenanes[7] as well—have aroused a lot of interest in the wider scientific community simply because the molecular recognition that exists between their two components can be turned off and on at will by chemical or electrochemical or photochemical means,[8] thus making it possible for the components to be stimulated to move relative to each other in a highly controlled manner. The fact that we have learned how to control the relative movements of the components in appropriately self-assembled [2]rotaxanes[6] by switching off and on noncovalent bonds between the macrocyclic and dumbbell-shaped components has inspired the design and synthesis of numerous artificial molecular machines.[9] Indeed, appropriately crafted [2]-rotaxanes have provided the basis for constructing molecular shuttles[10] and then subsequently turning them into molecular switches[11] that can ultimately be fabricated into molecular electronic devices.[12]

The successful performance of rotaxane molecules as switches and devices at the lower end of the nanometer scale prompts the obvious question—could such well-defined interlocking and the possibility of controlling component recognition and geometry also have a profound effect further up the nanometer scale in the macromolecular world? The only way to answer this question is to make interlocked macromolecules. Consequently, the progression from rotaxanes to polyrotaxanes[13] has been a rapid one, resulting in the design and construction of a diverse range of interlocked macromolecular compounds.[14]

The post-assembly modification of a triphenylphosphonium-stoppered [2]rotaxane,[15] using conventional Wittig chemistry, has been employed recently by us,[16] not only to convert this 'reactive' [2]rotaxane, without any loss of its mechanical integrity, into other 'inert' [2]rotaxanes, but also to construct, with complete supramolecular control, a degenerate molecular shuttle as well as a branched [4]rotaxane. The principle that is being exercised and exploited in this chemistry is shown schematically in Fig. 1 for the

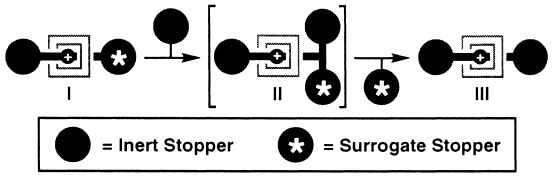

Figure 1. A schematic representation of the conversion of a 'reactive' [2]rotaxane into an 'inert' [2]rotaxane.

Keywords: molecular-necklaces; molecular recognition; rotaxanes; self-assembly; Wittig reaction.

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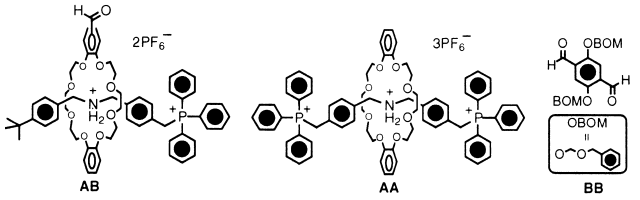


Figure 2. Monomers for the proposed syntheses of polyrotaxanes by Wittig step-growth polymerization. The **AB** monomer is designed to form daisy-chain polyrotaxanes whereas the **AA** and **BB** monomers should form linear polyrotaxanes carrying regularly spaced entrapped macrocycles.

conversion of a 'reactive' [2]rotaxane into an 'inert' one. Essentially, it involves the replacement of a surrogate stopper in the 'reactive' [2]rotaxane **I** to afford a new 'inert' [2]rotaxane **III**. The judicious selection of an appropriate exchange reaction—one, like the Wittig reaction, where a concerted mechanism operates—ensures the integrity of the mechanical bond throughout the transformation, i.e. in such a process, the intermediate **II** retains bulky stoppers at both ends of the dumbbell-shaped component. With the idea of extending the Wittig chemistry into a macromolecular setting, three monomers (Fig. 2) have been synthesized[15,17,18] that should allow access to at least two different polyrotaxane architectures. The **AB** monomer was designed to form daisy-chain[19] polyrotaxanes,[18] whereas the **AA** and **BB** monomers should form linear polyrotaxanes carrying regularly spaced, entrapped macrocycles. We were well aware of the possibility, however, particularly at relatively low monomer concentrations, of obtaining cyclic, as well as acyclic, products from the proposed reactions (Fig. 3). The reactions of **AB** monomers to give both cyclic and acyclic daisy-chain[19] oligomers have been described and discussed elsewhere.[17,18] Here, we report the outcome of reactions between the **AA** and **BB** monomers, showing that, while the major product is indeed polymeric material, at high monomer concentrations (typically 100 mM or greater), side products are also formed at lower monomer concentrations (10 mM or less, typically).

These observations demonstrate that a 'reactive' [2]rotaxane can be converted (Fig. 4) into a [3]catenane **IV** and mechanically-interlocked compounds, e.g. **V** and **VI**, reminiscent of molecular-necklaces.[20]

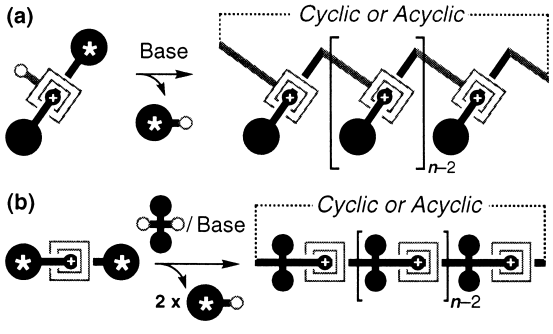


Figure 3. Schematic representations depicting the possible cyclic or acyclic components that can result upon Wittig step-growth polymerization of: (a) the **AB** monomer to give either cyclic or acyclic daisy-chains, and (b) the **AA** and **BB** monomers to give either: (i) catenanes and molecular-necklaces, or (ii) linear polyrotaxanes, bearing regularly spaced, entrapped macrocycles. Note that the NH_2^+ centers are generated in the products following acidic work-ups.

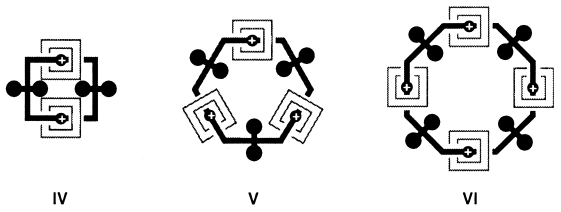


Figure 4. Schematic representations of the [3]catenane **IV** and the molecular-necklaces **V** and **VI** formed upon reaction of the **AA** and **BB** monomers at low concentrations.

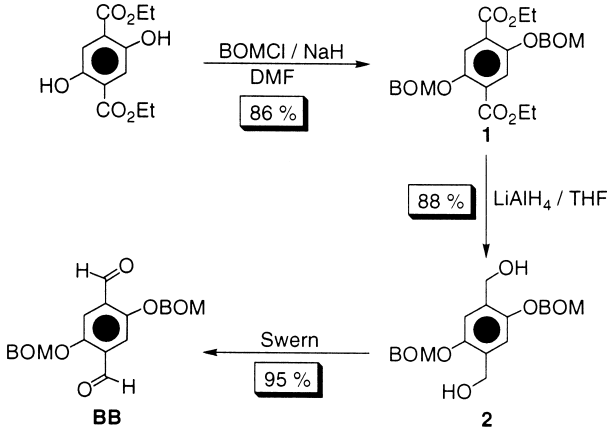
2. Results and discussion

2.1. Synthetic strategy

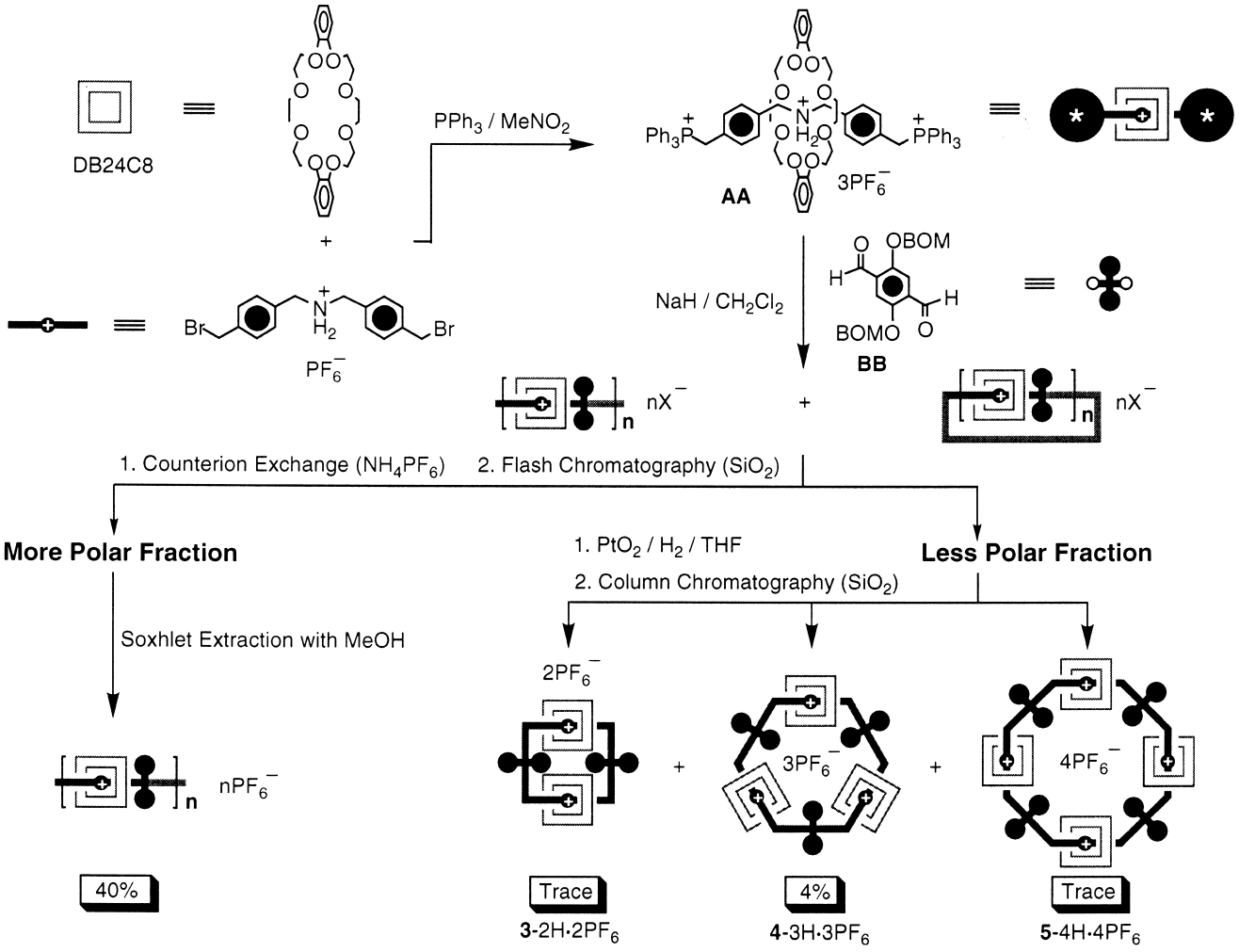
In our quest to synthesize polyrotaxanes by Wittig step-growth polymerization, we sought to identify a dialdehyde that would also act as a stopper following the first of the two consecutive Wittig reactions, otherwise the macrocycles would simply be released from the rods to become free in solution.[16,21] For reasons associated with its symmetry and steric bulk—and also the ability to be able to modify it in the products isolated at the end of the reaction—we chose to employ (Fig. 2) the benzyloxymethoxy (BOM) protected dialdehyde **BB** for reaction with the bis(triphenylphosphonium)-stoppered [2]rotaxane **AA** already reported by us.[15]

2.2. Isolation and characterization of a [4]molecular-necklace

The BOM-protected dialdehyde **BB** was prepared (Scheme 1) from diethyl 2,5-dihydroxyterephthalate in 72% overall yield in three steps: (i) protection (BOMCl/NaH/DMF) of the two phenolic hydroxyl groups to give **1**, (ii) reduction ($LiAlH_4$/THF) of **1** to afford the diol **2**, and (iii) Swern oxidation of **2** to yield the monomer **BB**. The presence of two BOM protecting groups in the monomer assisted greatly in both the separation and subsequent purification of the Wittig reaction products—and also in their eventual characterization where the appearance of two singlets for the benzylic methylene and dioxymethylene protons in ^1H NMR spectra is indicative or otherwise of the formation of cyclic products following reduction of the carbon–carbon double bonds formed during the Wittig olefinations. At a



Scheme 1. The synthesis of the **BB** monomer starting from diethyl 2,5-dihydroxyterephthalate.



Scheme 2. The synthesis and isolation procedure employed to separate the BOM-protected [4]molecular-necklace **4**·3H·3PF_6 from the polymeric material.

concentration of 9 mM, the monomer **BB** was added (Scheme 2) to a mixture of 1 equiv. of the **AA** monomer in CH_2Cl_2 in the presence of an excess of NaH as base. The reaction mixture was stirred at room temperature for one week. After work-up and counterion exchange (NH_4PF_6/H_2O), a yellow solid was obtained. Since it was not improbable that some macrocyclization might have accompanied polymerization, it was expected that the resulting product might contain [3]catenanes and molecular-necklaces, in addition to oligo- and polyrotaxanes, all as complex mixtures of diastereoisomers because of the existence of *E*/*Z* isomerism associated with all the newly formed carbon–carbon double bonds. Indeed, the identification of peaks at *m*/*z* 2235 and 3423 for $[M-PF_6]^+$ ions in the fast-atom bombardment (FAB) mass spectrum of this yellow solid suggested the presence of [3]catenanes and [4]molecular-necklaces, respectively. Isolation of these macrocycles directly from this reaction mixture by HPLC was impractical, not only because they are minor products, but also because of their existence in numerous diastereoisomeric forms. However, in principle, the isomeric mixtures can all be converted into single macrocycles by hydrogenation of their olefinic bonds. Hydrogenation employing H_2 and Pd/C in THF, however, was found to result in the concomitant hydrogenolysis of benzylic CH_2–NH_2^+ bonds, leading to cleavage of the backbones of the polyrotaxanes and also of the macrocycles associated with the [3]catenanes and molecular-necklaces. This competing reaction was evidenced by the large amount of free DB24C8 that could be isolated from reaction mixtures. Adams' catalyst (PtO_2) was much more selective. Hydrogenolysis did not become a serious competitor, unless samples were hydrogenated for long periods (>6 h) of time. Also, hydrogenation did not proceed well without chromatographic purification of the crude reaction mixture on silica gel. By employing FAB mass spectrometry in a screening capacity, we found that column chromatography on SiO_2 using MeOH/CH_2Cl_2 (2:98) as eluant is the most reliable way to separate cyclic products from most of the polymeric material. The less polar [3]catenanes and molecular-necklaces, and some oligomeric material, were isolated with this eluent. The more polar products, which were eluted with MeOH/MeCN (1:1) and then with pure MeCN, were found to contain none of the macrocycles. The yellow solid, which was isolated from the less polar fraction was dissolved in THF and hydrogenated over Adams' catalyst. Since the product at this stage was still a horrendous mixture of macrocycles and cyclic oligomers, the 'end-point' of the hydrogenation was not easy to recognize either by TLC or by ^1H NMR spectroscopy. We discovered, however, that provided

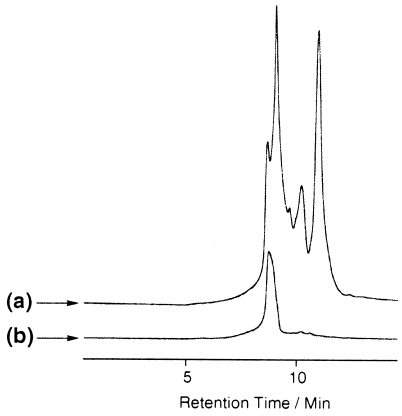


Figure 5. GPC Traces (Styragel column, CH_2Cl_2) of: (a) the less-polar fraction following hydrogenation (see Scheme 2) and (b) the BOM-protected [4]molecular-necklace **4**-3H·3PF$_6$ isolated after silica gel chromatography.

hydrogenation is terminated right after the solution turns colorless from its original bright yellow, then undesired hydrogenolysis is minimized. After work-up was complete, FAB mass spectrometry suggested that the BOM-protected [4]molecular-necklace was the major cyclic product. It was isolated as a pure compound in 4% yield[22] following chromatography on SiO_2 using MeCN/CH_2Cl_2 (1:9) as eluent. GPC traces of the less polar fraction, following hydrogenation, and the pure BOM-protected [4]molecular-necklace **4**-3H·3PF$_6$, isolated after column chromatography on silica gel are shown in Fig. 5. The less polar fraction, following flash chromatography on silica gel, contains compounds of a much smaller molecular weight than **4**-3H·3PF$_6$ and so this BOM-protected [4]molecular-necklace can be separated easily from the remainder of the less polar fraction by GPC since it is the first compound to be eluted from the column.

Although we devoted a lot of effort trying to isolate other cyclic homologues, only a trace amount of a compound, which was eluted from the silica gel column before **4**-3H·3PF$_6$ was isolated in just sufficient quantities ($<$1 mg) to obtain a ^{1}H NMR spectrum and a high resolution FAB mass spectrum. These data are consistent with this compound being the BOM-protected [3]catenane **3**-2H·2PF$_6$. Additionally, the presence of a triply charged peak at *m/z* 1447 for $[M-3PF_6]^{3+}$ in the electrospray mass spectrum of the crude hydrogenation product suggests the existence of some of the homologous [5]molecular-necklace **5**-4H·4PF$_6$. The amount present in the crude product was very small, however, and all our efforts to isolate it and characterize it have been unsuccessful.

The relative simplicity of the ^{1}H NMR spectrum (Fig. 6a) of **4**-3H·3PF$_6$ is consistent with the averaged D_{3h} symmetry of the BOM-protected [4]molecular-necklace.[23] As expected, the signals for the protons of the bismethylene groups that result from hydrogenation of olefinic double bonds appear as a symmetrical multiplet in the range δ 2.70–2.85. The multiplets for the α-, β- and γ-OCH_2 protons on the DB24C8 ring, which are centered on δ 3.90, 3.60, and 3.43, respectively, are shifted significantly upfield from

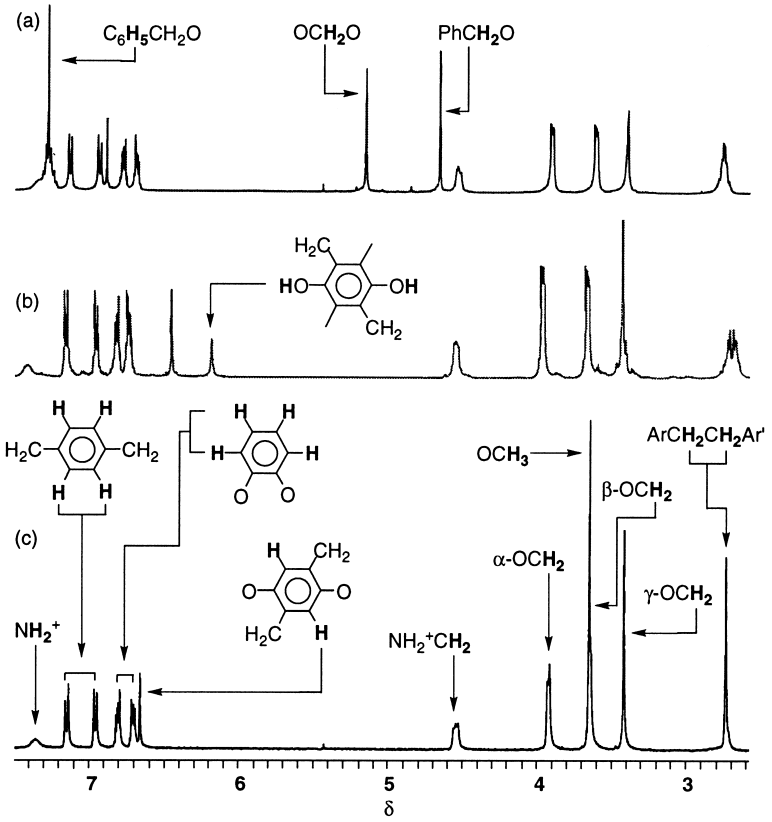
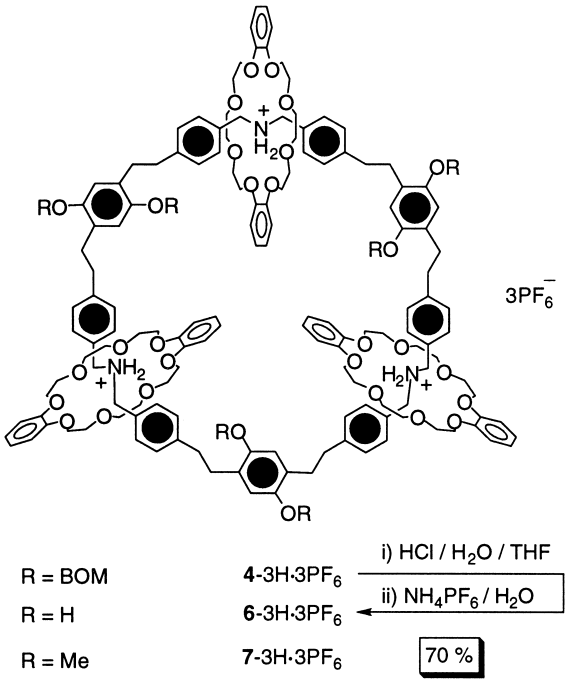


Figure 6. ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of: (a) the BOM-protected [4]molecular-necklace **4**-3H·3PF$_6$, (b) the [4]molecular-necklace **6**-3H·3PF$_6$, and (c) the permethylated [4]molecular-necklace **7**-3H·3PF$_6$.



Scheme 3. The deprotection of the BOM-protected [4]molecular-necklace **4**–3H·3PF$_6$ to give the [4]molecular-necklace **6**-3H·3PF$_6$-and the structural formula of the permethylated [4]molecular-necklace **7**-3H·3PF$_6$.

their δ values (4.24, 3.75, and 3.61, respectively) in free DB24C8, in keeping with the rings being mechanically interlocked around the NH_2^+ centers to which they are hydrogen bonded by means of [N^+–H···O], and, presumably also, [C–H···O] interactions.[24] Diagnostic of the fact that this recognition motif is operative[25] is the highly characteristic multiplet centered on δ 4.51 for the protons on the benzylic methylene groups on both (equivalent) sides of the NH_2^+ centers. The singlet resonating at δ 6.88 and the **AA′BB′** system with δ values of 6.93 and 7.13 arise from protons on the hydroquinone and *p*-xylyl units, respectively. The protons on the catechol units of the DB24C8 ring appear as an **AA′BB′** system in the range of δ from 6.60 through to 6.80. The BOM-protecting groups are contributing singlets at δ 4.85 and 5.44 for the benzylic methylene

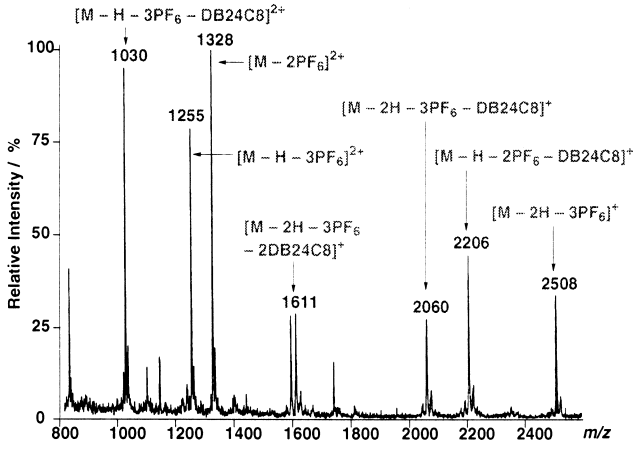


Figure 7. FAB mass spectrum of the permethylated [4]molecular-necklace **7**-3H·3PF$_6$.

and *O*-methylene protons, respectively—and in the range δ 7.21–7.31 for the phenyl ring protons.

The BOM protecting groups in **4**–3H·3PF$_6$ were cleaved (Scheme 3) by heating a solution of the [4]molecular-necklace in 5% $HCl_{(aq)}$/THF (5:95) under reflux overnight. The fully deprotected [4]molecular-necklace **6**-3H·3PF$_6$ was isolated (Scheme 3) in 70% yield after counterion exchange (NH_4PF_6/H_2O). The ^{1}H NMR spectrum (Fig. 6b) of **6**-3H·3PF$_6$ is similar to that (Fig. 6a) of the BOM-protected [4]molecular-necklace—particularly in relation to the signals for the DB24C8 rings and the dibenzylammonium subunits, suggesting little change if any around the recognition sites. Apart from the disappearance of signals for the BOM-protecting groups and the appearance of a broad singlet at δ 6.19 for the hydroxyl group protons, there is an upfield shift of the sharp singlet for the hydroquinone ring protons from δ 6.88 (protected) to 6.46 (deprotected), suggesting that deprotection occurs cleanly without damage to the molecules. However, the deprotected [4]molecular-necklace is not all that stable: freshly prepared **6**-3H·3PF$_6$ decomposes, even when not in solution, at ambient temperatures in a matter of days. The gradual appearance of signals for free DB24C8 in the ^{1}H NMR spectrum suggests that the large ammonium-ion-containing macrocycle is being cleaved during the decomposition process which we suspect might involve initially oxidation of the substituted hydroquinone rings. This process has not been investigated any further.

2.3. Synthesis of the permethylated [4]molecular-necklace and its characterization

In order to establish the generality of the synthetic approach, which we have discovered for making molecular-necklaces from rotaxanes, we decided to replace the BOM-protected dialdehyde in the synthesis with 2,5-dimethoxyterephthaldehyde. Using identical reaction conditions, the permethylated [4]molecular-necklace **7**-3H·3PF$_6$ was isolated in 2% yield after following the same purification procedure as before, i.e. subjecting the crude product to flash chromatography, followed by hydrogenation of the appropriate fraction and then using column chromatography to obtain **7**-3H·3PF$_6$ as a pure compound (Scheme 3). The ^{1}H NMR spectrum (Fig. 6c) of **7**-3H·3PF$_6$ is similar to that (Fig. 6a) of **4**-3H·3PF$_6$ except that signals for the BOM group protons are absent and replaced by a singlet for the methoxy protons at δ 3.66. There is also an upfield shift of the singlet (δ 6.67) for the hydroquinone ring protons relative to that at δ 6.88 in the spectrum of the BOM-protected [4]molecular-necklace. The FAB mass spectrum (Fig. 7) of **7**-3H·3PF$_6$ revealed intense peaks at *m/z* 2508, 1328, and 1255 corresponding to [M−2H−3PF$_6$]$^+$, [M−2PF$_6$]$^{2+}$, and [M−H− 3PF$_6$]$^{2+}$, respectively.

3. Conclusions

Although we set out to try and convert a [2]rotaxane with two potentially reactive benzylic triphenylphosphonium stoppers into polyrotaxanes using Wittig step-growth polymerizations with bulky aromatic dialdehydes, we ended up isolating small amounts of large interlocked macrocycles—

in particular, a protected [4]molecular-necklace derivative. While the overall yields of these large macrocycles containing localized catenated rings are small, the chemistry—rather complicated, as it is, from beginning to end—works amazingly well. At this stage, we can claim proof of principle for a synthetic procedure that involves recognition-directed assembly early on and retains molecular recognition features throughout for making molecular-necklaces out of rotaxanes.

4. Experimental

4.1. Methods and materials

All glassware, stirrer-bars, syringes, and needles were either oven- or flame-dried prior to use. Reactions were carried out under a N_2 or Ar atmosphere. All starting materials and reagents, unless otherwise indicated, were purchased from commercial sources. Anhydrous CH_2Cl_2 and MeCN were obtained by distillation from CaH_2 under N_2, and anhydrous THF by distillation from Na/Ph_2CO under N_2. Thin layer chromatography (TLC) was performed on Analtech 0.25-mm silica gel GHLF. Column chromatography was carried out using silica gel 60F (Merck 9385, 0.040–0.063 mm). GPC spectra were recorded using a Waters Styragel column HR3, 7.8×300 mm^2 with CH_2Cl_2 as the eluent at 25°C at a flow rate of 1.0 mL/min. ^{1}H NMR spectra were recorded at 360 or 400 MHz. The deuterated solvent was used as the lock while either TMS or the solvent's residual protons were employed as the internal standard. Chemical shifts are reported as δ values in parts per million. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (mutiplet), and br (broad). Coupling constants are in Hertz. ^{13}C NMR spectra were recorded at 90 or 100 MHz. Fast-atom bombardment (FAB) mass spectrometry was performed using either a Kr or Cs primary atom beam in conjunction with a *m*-nitrobenzyl alcohol matrix.

4.1.1. Diethyl 2,5-bis(benzyloxymethoxy)terephthalate (1). Diethyl 2,5-dihydroxyterephthalate (2.0 g, 7.9 mmol) and NaH (0.56 g, 23 mmol) were cooled down to 0°C in a round-bottomed flask. DMF (50 mL) was added slowly and the reaction mixture was stirred at 0°C for 1 h. Benzyloxymethyl chloride (3.6 mL) was added to the reaction mixture dropwise via syringe during 30 min. The solution was slowly warmed up to room temperature and stirred for 18 h. MeOH (3 mL) was added to quench the reaction. The mixture was partitioned between CH_2Cl_2 (200 mL) and H_2O (200 mL). The organic layer was separated and washed with 5% $HCl_{(aq)}$ (3×100 mL), dried ($MgSO_4$) and concentrated. Purification by column chromatography (SiO_2) using EtOAc/hexane (1:4) as eluent gave diethyl 2,5-bis(benzyloxymethoxy)terephthalate (**1**) (3.35 g, 86%). ^{1}H NMR (400 MHz, CD_3CN): δ 1.32 (t, J=7.1 Hz, 6H), 4.31 (q, J=7.1 Hz, 4H), 4.73 (s, 4H), 5.29 (s, 4H), 7.32 (s, 10H), 7.55 (s, 2H); ^{13}C NMR (100 MHz, CD_3CN): δ 14.6, 62.3, 71.1, 94.1, 120.4, 127.4, 128.8, 128.9, 129.3, 138.5, 151.1, 166.1; HRMS (FAB): calcd 494.1941 for $C_{28}H_{30}O_8$ found: 494.1940.

4.1.2. 2,5-Bis(benzyloxymethoxy)-1,4-bis(hydroxymethyl)-benzene (2). $LiAlH_4$ (1.1 g, 28.9 mmol) was added in small portions during 1 h to diethyl 2,5-bis(benzyloxymethoxy)-terephthalate (**1**) (1.45 g, 2.9 mmol) disssolved in THF (30 mL). The reaction mixture was heated under reflux for 3 h and stirred at room temperature for 18 h. After the reaction had been quenched by slowly adding H_2O (10 mL), anhydrous $MgSO_4$ (10 g) was added. The mixture was filtered and concentrated. Purification by column chromatography (SiO_2) using MeOH/CH_2Cl_2 (1:19) as eluent gave 2,5-bis(benzyloxymethoxy)-1,4-bis(hydroxymethyl)benzene (**2**) as a white solid (1.05 g, 88%). ^{1}H NMR (400 MHz, CD_3CN): δ 3.15 (t, J=5.9 Hz, 2H), 4.57 (d, J=5.9 Hz, 4H), 4.71 (s, 4H), 5.28 (s, 4H), 7.17 (s, 2H), 7.33 (s, 10H); ^{13}C NMR (100 MHz, CD_3CN): δ 60.0, 71.0, 94.2, 115.5, 128.7, 128.9, 129.4, 131.8, 138.9, 150.1; HRMS (FAB): calcd 410.1729 for $C_{24}H_{26}O_6$ found: 410.1736.

4.1.3. 2,5-Dibenzyloxymethoxyterephthaldehyde BB. To a round-bottomed flask charged with oxalyl chloride (0.74 mL, 8.47 mmol) and CH_2Cl_2 (25 mL) and cooled down to −78°C was added DMSO (1.0 mL, 14.0 mmol) and the reaction mixture was stirred at −78°C for 30 min. 2,5-Bis(benzyloxymethoxy)-1,4-bis(hydroxymethyl)benzene (**2**) (0.9 g, 2.2 mmol) in CH_2Cl_2 (15 mL) was added slowly into the reaction mixture using a syringe. The reaction mixture was stirred at −78°C for 40 min. Triethylamine (3.5 mL, 25 mmol) was then added to the reaction mixture and it was slowly warmed up to room temperature. The mixture was partitioned between CH_2Cl_2 (200 mL) and H_2O (200 mL). The organic layer was separated and washed with H_2O (3×100 mL), dried ($MgSO_4$) and concentrated. Purification by column chromatography (SiO_2) using EtOAc/hexane (3:17) as eluent gave 2,5-dibenzyloxymethoxyterephthaldehyde **BB** as a light yellow solid (0.85 g, 95%). ^{1}H NMR (400 MHz, CD_3CN): δ 4.74 (s, 4H), 5.44 (s, 4H), 7.29 (s, 10H), 7.60 (s, 2H), 10.37 (s, 2H); ^{13}C NMR (100 MHz, CD_3CN): δ 71.8, 94.3, 115.3, 128.8, 129.0, 129.4, 131.0, 138.5, 154.7, 190.0; HRMS (FAB): calcd 406.1416 for $C_{24}H_{22}O_6$ found: 406.1411.

4.1.4. BOM-protected interlocked molecular compounds 3-2H·2PF$_6$, 4-3H·3PF$_6$, 5-4H·4PF$_6$ and oligorotaxanes. CH_2Cl_2 (100 mL) was added to a round-bottom flask charged with the bis(triphenylphosphonium)-stoppered [2]rotaxane **AA** monomer (1.87 g, 1.15 mmol) and NaH (0.11 g, 4.58 mmol). 2,5-Bis(benzyloxymethoxy)terephthaldehyde, the **BB** monomer (0.45 g, 1.11 mmol), dissolved in CH_2Cl_2 (20 mL), was added via an addition funnel during 24 h to the reaction flask. The reaction mixture was stirred at room temperature for 7 days. It was quenched by the slow addition of MeOH (5 mL), and then the solution was concentrated under reduced pressure. The solid was suspended in MeCN and saturated aqueous NH_4PF_6 was added until the solid dissolved. The MeCN was then evaporated and the resulting precipitate was collected and washed with H_2O. The yellow residue was subjected to flash chromatography (SiO_2; MeOH/CH_2Cl_2 (2:98)) and the yellow, less polar fraction was collected and concentrated down to a yellow solid (259 mg). The more polar fraction was eluted with MeOH/CH_2Cl_2 (1:1) and was concentrated to give a yellow solid. Oligorotaxanes were obtained by Soxhlet extraction of the more polar yellow solid with MeOH for 3 days, before drying the solid under vacuum (0.68 g, ca. 40%). The less polar, yellow solid was then

dissolved in THF (10 mL), PtO_2 (30 mg) was added and H_2 gas was bubbled through the solution for 10 min. The mixture was then stirred under H_2 (balloon) until the solution became colorless, whereupon it was concentrated under reduced pressure. The solid was suspended in MeCN and saturated aqueous NH_4PF_6 was added until the solid dissolved. The MeCN was evaporated and the resulting precipitate was collected, washed with H_2O and purified by column chromatography (SiO_2; MeCN/CH_2Cl_2 (1:9)). The BOM-protected [4]molecular-necklace **4**-3H·3PF_6 was obtained as a white solid (49 mg, 4%); ^{1}H NMR (400 MHz, CD_3CN): δ=2.70–2.80 (m, 24H), 3.43 (s, 24H), 3.60 (m, 24H), 3.90 (m, 24H), 4.53 (m,12H), 4.85 (s, 12H), 5.44 (s, 12H), 6.60–6.70 (m, 12H), 6.70–6.80 (m, 12H), 6.88 (s, 6H), 6.93 (d, J=8 Hz, 12H), 7.12 (d, J=8 Hz, 12H), 7.20–7.40 (br, 36H); (400 MHz, CD_2Cl_2): δ 2.83 (s, 24H), 3.38 (s, 24H), 3.65 (s, 24H), 4.00 (s, 24H), 4.51 (s,12H), 4.70 (s, 12H), 5.20 (s, 12H), 6.65–6.75 (m, 12H), 6.75–6.85 (m, 12H), 6.91 (s, 6H), 7.01 (d, J=8 Hz, 12H), 7.13 (d, J=8 Hz, 12H), 7.30–7.50 (br, 36H); ^{13}C NMR (100 MHz, CD_3CN): δ 31.8, 35.9, 53.0, 68.8, 70.9, 71.0, 71.4, 94.7, 113.4, 122.2, 128.7, 129.4, 129.5, 130.3, 130.4, 130.5, 138.8, 143.8, 148.4, 151.0; (100 MHz, CD_2Cl_2): δ 31.6, 35.7, 52.7, 68.6, 70.5, 70.9, 71.0, 94.1, 113.0, 117.2, 121.9, 128.2, 128.8, 129.1, 129.6, 129.6, 129.8, 138.0, 143.5, 147.9, 150.5; HRMS (FAB): calcd 3437.4984 for $C_{192}H_{222}N_3O_{36}P_2F_{12}$ $[M-PF_6]^+$; found: 3437.4939. The BOM-protected [3]catenane **3**-2H·2PF_6 was isolated from the fraction that eluted before the [4]molecular-necklace. Data for **3**-2H·2PF_6: ^{1}H NMR (360 MHz, CD_3CN): δ 2.70–2.80 (br, 16H), 3.34 (s, 16H), 3.52 (m, 16H), 3.87 (m, 16H), 4.50 (m, 8H), 4.68 (s, 8H), 5.44 (s, 8H), 6.60–6.70 (m, 8H), 6.70–6.80 (m, 8H), 6.91 (s, 4H), 6.94 (d, J=8 Hz, 8H), 7.12 (d, J=8 Hz, 8H), 7.20–7.40 (br, 24H); HRMS (FAB): calcd 2243.0097 for $C_{128}H_{148}N_2O_{24}PF_6$ $[M-PF_6]^+$; found: 2243.0106. The existence of the [5]molecular-necklace **5**-4H·4PF_6 was confirmed by electrospray mass spectrometry of the hydrogenated less polar fraction. Data for **5**-4H·4PF_6: MS (Electrospray): 1447 for $[M-3PF_6]^{3+}$.

4.1.5. [4]Molecular-necklace 6-3H·3PF_6. The BOM-protected [4]molecular-necklace **4**-3H·3PF_6 (50 mg, 14 μmol) was dissolved in 5% $HCl_{(aq)}$/THF (1:19; 5 mL) and the solution was heated under reflux overnight. The mixture was partitioned between CH_2Cl_2 (50 mL) and H_2O (50 mL). The organic phase was dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2 (1:19)) and the [4]molecular-necklace **6**-3H·3PF_6 (30 mg, 70%) was recovered as a white solid; ^{1}H NMR (400 MHz, CD_3CN): δ 2.60–2.80 (m, 24H), 3.43 (m, 24H), 3.67 (m, 24H), 3.97 (m, 24H), 4.54 (m, 12H), 6.19 (s, 6H), 6.46 (s, 6H), 6.70–6.80 (m, 12H), 6.80–6.90 (m, 12H), 6.96 (d, J=8 Hz, 12H), 7.16 (d, J=8 Hz, 12H), 7.40–7.50 (br, 6H); ^{13}C NMR (100 MHz, CD_3CN): δ 31.6, 35.5, 53.1, 68.9, 71.0, 71.4, 113.5, 117.5, 122.2, 126.8,129.5, 130.3, 130.4, 143.9, 148.5, 148.6; MS (FAB): m/z 2716 $[M-PF_6]^+$, 2570 $[M-H-2PF_6]^+$.

4.1.6. Permethylated [4]molecular-necklace 7-3H·3PF_6. The permethylated [4]molecular-necklace **7**-3H·3PF_6 was isolated in 2% yield from the macrocyclization of [2]rotaxane **AA** and 2,5-dimethoxyterephthaldehyde under identical experimental conditions to those reported earlier for compound **4**-3H·3PF_6. Data for **7**-3H·3PF_6: ^{1}H NMR (400 MHz, CD_3CN): δ 2.75 (s, 24H), 3.43 (s, 24H), 3.67 (m, 42H), 3.93 (m, 24H), 4.54 (m, 12H), 6.67 (s, 6H), 6.67–6.73 (m, 12H), 6.75–6.85 (m, 12H), 6.96 (d, J=8 Hz, 12H), 7.15 (d, J=8 Hz, 12H), 7.35 (br, 6H); ^{13}C NMR (100 MHz, CD_3CN): δ 31.8, 35.6, 53.1, 56.7, 68.9, 71.0, 71.4, 113.5, 114.1, 122.2, 128.8, 129.5, 130.3, 130.4, 144.0, 148.5, 152.3; MS (FAB): m/z 2508 $[M-2H-3PF_6]^+$, 2206 $[M-H-2PF_6-DB24C8]^+$, 2060 $[M-2H-3PF_6-DB24C8]^+$, 1611 $[M-2H-3PF_6-2DB24C8]^+$, 1328 $[M-2PF_6]^{2+}$, 1255 $[M-H-3PF_6]^{2+}$, 1030 $[M-H-3PF_6-DB24C8]^{2+}$.

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21. We have shown (Ref. 16) that when unsubstituted terephthaldehyde is employed in Wittig-style covalent modifications on benzylic triphenylphosphonium-stoppered rotaxanes, the DB24C8 ring dissociates from what is effectively a semirotaxane because, not only is the NH_2^+ recognition site switched off, but also the formyl-terminated phenylene ring of the half-dumbbell component is not large enough to prevent dethreading.
22. At face value, a 4% overall yield of the BOM-protected [4]molecular-necklace, starting from the **AA** and **BB** monomers, is nothing to write home about. However, if we assume that a total of 12 reactions (five inter- and one intramolecular Wittig olefinations, followed by six carbon–carbon double bond hydrogenations) are involved, then a back-of-the-envelope calculation would suggest that an average yield of 76% is being attained in each of these dozen reactions. The challenge remains, however—how do we do better? The possibility that the proportions of macrocycles, as distinct from polymeric materials, could be increased by carrying out the multiple Wittig reactions at even lower reactant concentrations, but such conditions—namely, 7 and even 2 mM—were employed without there being an improvement in the yields of **3**-2H·2PF_6, **4**-3H·3PF_6, and **5**-4H·4PF_6. Also, when a reaction was carried out with the **AA** and **BB** monomers, using initial monomer concentrations of 100 mM each, FAB mass spectrometry of the crude reaction mixture indicated the presence of more high molecular weight components—presumably acyclic oligomers—and considerable less of the macrocycles. So far, all our numerous attempts to isolate high molecular weight polyrotaxanes of low polydispersities and uniform primary structures have been to no avail. So instead of trying to hydrogenate the olefinic double bonds with higher molecular weight fractions—for even a very small amount of concomitant hydrogenolysis of the repeating benzylic ammonium functions is going to be extremely detrimental to the polymer primary structure—we decided to try to simplify the situation by catalyzing the isomerization of any *cis* double bonds to *trans* ones using iodine as the catalyst. (For a recent example where this isomerization works well, following a Wittig step-growth polymerization, see: Star, A.; Stoddart, J. F.; Steuerman, D.; Diehl, M.; Boukai, A.; Wong, E. W.; Yang, X.; Chung, S.-W.; Choi, H.; Heath, J. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 1721–1725. However, the high molecular weight material was not soluble in the preferred solvents (PhMe or PhH) and in those solvents (e.g. CH_2Cl_2) or solvent mixtures (e.g. CH_2Cl_2/THF) where it was soluble, isomerization did not occur.
23. The ^{1}H NMR spectrum (also recorded in CD_3CN) of the BOM-protected [3]catenane **3**–2H·2PF_6 is almost identical with that (Fig. 6a) of the BOM-protected [4]molecular-necklace. The most significant differences are evident in the signals for the α-, β-, and γ-OCH_2 protons in the DB24C8 rings which resonate as multiplets centered on δ 3.87, 3.52 and 3.34—cf. the δ values of 3.90, 3.60 and 3.43 for **4**-3H·3PF_6. These chemical shift differences are important in so far as they tell us that the BOM-protected [4]molecular-necklace was isolated as a pure compound and is *not* contaminated with the BOM-protected [3]catenane.
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