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Towards mechanically linked polyrotaxanes by sequential deprotection–coupling steps of bifunctional rotaxanes

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The monomer rotaxane 13, bearing two protected functional groups, is used to obtain a dimer, following a new approach of sequential deprotection–coupling steps which can lead to mechanically linked polyrotaxanes.

Rotaxanes and catenanes as well as their polymer derivatives appear increasingly in the literature. In the field of polymers, a number of fascinating polyrotaxane structures have been presented.[1] It has been shown that the properties of these compounds are in many cases very different compared to the 'naked' polymers.[2]

In the vast majority of the compounds synthesized so far, a covalently connected polymer backbone is surrounded by 'cyclic' molecules, or alternatively, rotaxane subunits are connected to the polymer backbone as side groups.[1,2] The very attractive concept of synthesizing oligomers and/or polymers where the repeating units are connected to each other in a non-covalent way was proposed some years ago,[3] but progress towards this aim has been achieved only very recently.[4–6] Such polymers and/or oligomers with non-covalent connections are expected to give materials with new rheological and mechanical properties. Until now, this research has mainly been focused on polycatenanes.[4] Reports on mechanically linked polyrotaxanes have only described small assemblies[5] and polypseudorotaxanes.[6]

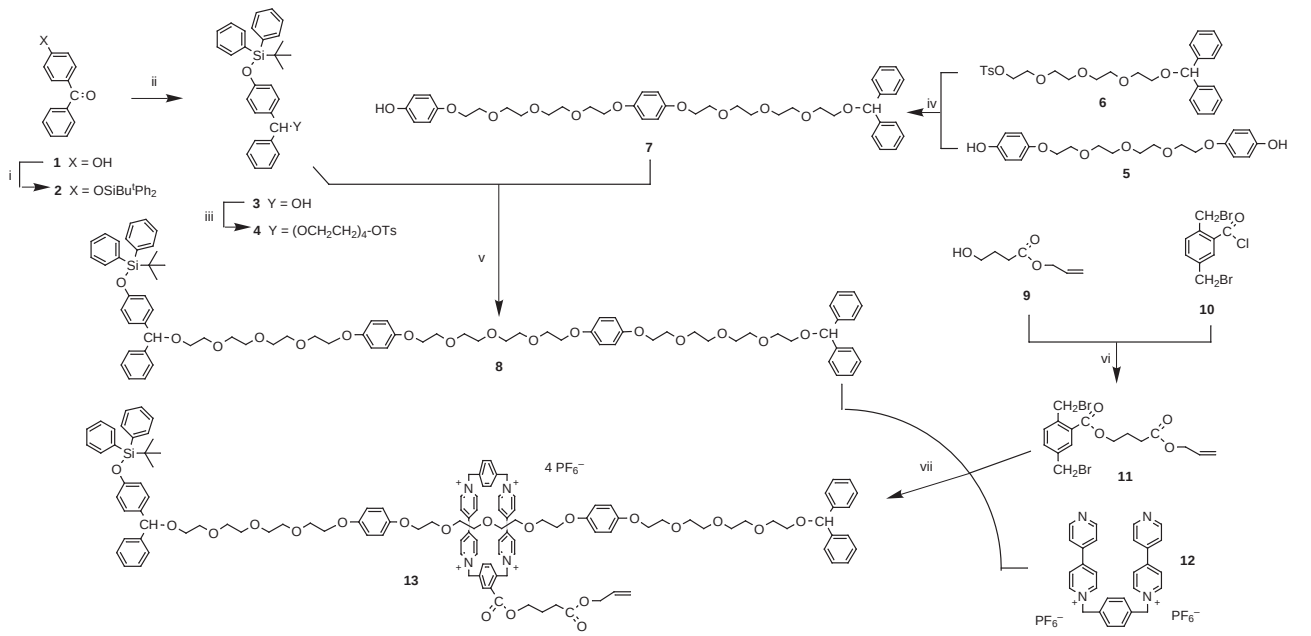
Here we present the synthesis of a new mechanically linked dimer rotaxane, where the repeating units are connected by non-covalent bonds. The synthesis is based on a new step-by-step approach consisting of sequential deprotection–coupling steps that can lead to well defined oligomers. A bisfunctionalized rotaxane is used as the starting monomer. The dimer synthesis and some preliminary studies are presented.

The rotaxane structure used as monomer (compound **13** on Scheme 1) is based on dialkoxybenzene units with a cyclophane containing two 4,4′-bipyridinium groups. Similar types of systems have been studied extensively by the group of Stoddart.[7]

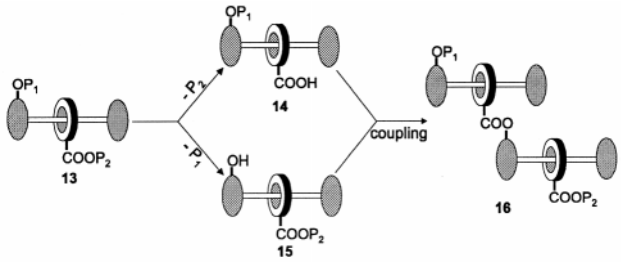
The synthesis of polyrotaxanes and polycatenanes has proven to be quite challenging. In the step-by-step approach, presented in Scheme 2, the initial monomer rotaxane **13** was designed to fulfil a number of requirements: (a) introduction of functional units so that polymerization is possible, (b) protection of these functional units for a step-by-step synthesis and (c) minimization of electronic and/or steric problems.

The positions of the two functional groups in the rotaxane were chosen in such a way that a dimerization and/or polymerization reaction could lead to oligomers with the repeating units connected non-covalently (Schemes 1 and 2). These groups are a phenol and a carboxylic acid. In general, between these two groups, a high-yield coupling reaction (esterification) can take place in only one synthetic step. This is important in order to minimize the number of reaction steps that involve the rotaxane molecule.

Although a number of protective groups are available for sequential removal, in our case the choice decreased significantly since selective deprotection of both groups is needed. In addition, the various sensitive groups in the rotaxane structure **13** should be inert to the deprotection conditions. This compound contains an ester bond and a bis(4,4′-bipyridinium) cyclophane derivative, which both show very limited stability in



Scheme 1 Synthesis of the bisprotected monomer **13**. *Reagents and conditions*: i, TBDPSCl, Et_3N, DMAP, Py, THF (71%); ii, $NaBH_4$, THF (79%); iii, NaH, $Ts(OCH_2CH_2)_4OTs$, THF (65%); iv, K_2CO_3, DMF (58%); v, NaH, THF (38%); vi, Pr^i_2EtN, CH_2Cl_2 (49%); vii, CH_3CN, $AgPF_6$ (4.8%).



Scheme 2 Schematic representation of the synthesis of the bisprotected dimer **16**.

alkaline pH. Furthermore, the two blocking groups are of the diphenylmethyl ether type and are unstable in acidic conditions. The hindered TBDPS protective group appears to be a good protective group for the phenol unit. It is stable under a variety of basic and acidic conditions[8] (necessary in steps ii, iii and v in the rotaxane synthesis), while it can be removed specifically with fluoride anions under very mild conditions. In the carboxylic acid case, our initial attempts were focused on the tetrahydropyranyl (THP) group. Unfortunately, despite encouraging results obtained with model compounds, it was found that this group was too labile, and was removed during simple work-up operations of the rotaxane **13**. In contrast, the allyl group was found to be suitable. The allyl ester bond is stable during steps vi and vii (Scheme 1) as well as during the reactions used in the synthesis of oligomers. At the same time, it can be selectively removed in the presence of other ester bonds by Pd catalysts under mild conditions.

The last point in the design of rotaxane **13** concerns the reactivity of the carboxylic acid group. It has been reported[9] that a carboxylic group directly connected to the bis(4,4′-bipyridinium) cyclophane is not active towards esterification. In preliminary experiments we found similar behaviour. Therefore, in molecule **13** the protected carboxylic group was moved to a position that is not in close proximity to the tetracationic cyclophane.

The synthesis of the rotaxane **13** was accomplished by reacting **8**, **11** and **12** in the presence of excess of $AgPF_6$ in 4.8% yield.† The low yield may be attributed[5] to the steric hindrance of the carboxylic ester group of **11**. Despite this low yield, at the end of the reaction most of the unreacted compound **8** can be recovered and used again in step vii. Compounds **5**, **6**, **10** and **12** were obtained according to literature procedures while molecule **9** was accessed by ring opening of γ-butyrolactone with allyl alcohol under acidic conditions. The procedures followed for the synthesis of molecule **8** are delineated in Scheme 1.

Selective deprotection of the two functional groups in two different batches was the first step towards the synthesis of the dimer. Thus, rotaxane **14** contained a free carboxylic acid group obtained by deprotection of **13** with $Pd(PPh_3)_4$, while rotaxane **15** contained a free phenol group, obtained by deprotection of **13** with Bu_4NF. In the last step, esterification (DCC/Py) between the acid **14** and the alcohol **15** gave the dimer **16** in a 30–40% yield. This compound also contains a protected phenol and a protected carboxylic acid, like the monomer **13**. Therefore, longer derivatives (tetramer, octamer *etc.*) can be obtained by sequential deprotection–esterification steps.

Both the monomer **13** and the dimer **16** were characterized by MALDI-TOF mass spectrometry and ^{1}H NMR and UV-VIS absorption spectroscopy. The ^{1}H NMR spectra of **13** and **16** in CD_3COCD_3 are consistent with the assigned structures.

The hexafluorophosphate salts of the rotaxanes **13** and **16** are red solids, insoluble in H_2O but soluble in acetone, CH_3CN and CH_2Cl_2. Also, they are insoluble in solvents of lower polarity such as Et_2O, $CHCl_3$ and hexane. The UV-VIS spectra of both **13** and **16** in CH_3CN and in CH_2Cl_2 show two absorption maxima; an intense peak at 265 nm and a very weak peak at 480 nm. The last one corresponds to the charge transfer interaction known in rotaxanes of similar structure.[10]

The MALDI-TOF mass spectrum of **16** with 2,5-dihydroxybenzoic acid as matrix [Fig. 1(*b*)] shows four peaks at 4303, 4159, 4015 and 3869 mass units (mu), corresponding to the ions $[M - 4PF_6]^+$, $[M - 5PF_6]^+$, $[M - 6PF_6]^+$ and $[M - 7PF_6]^+$, respectively. The peaks at lower masses can be easily identified as fragments of the molecular ion. By using 5-methoxysalicylic acid instead of 2,5-dihydroxybenzoic acid as matrix, a different series of ions can be identified $[M - 2PF_6]^+$, $[M - 3PF_6]^+$, $[M - 4PF_6]^+$ and $[M - 5PF_6]^+$. Similar results were found for the monomer **13**. The three peaks at 2299, 2154 and 2009 mass units (mu) correspond to the ions $[M - 2PF_6]^+$, $[M - 3PF_6]^+$ and $[M - 4PF_6]^+$, respectively [Fig. 1(*a*)].

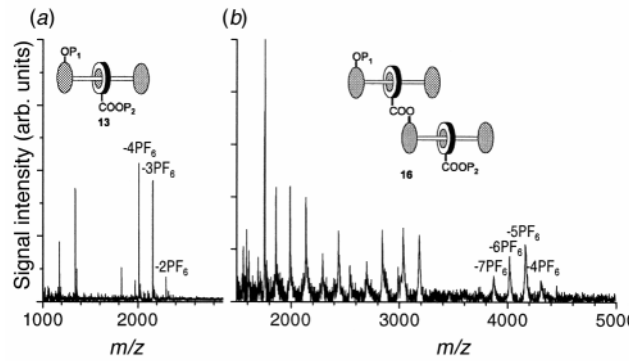


Fig. 1 MALDI-TOF spectra in 2,5-dihydroxybenzoic acid matrix: (*a*) monomer **13**, (*b*) dimer **16**.

In conclusion, we were able to synthesize the monomer rotaxane **13**, which bears two protected functional groups and can give oligomers in a controlled way for the first time, by sequential deprotection–coupling steps. Coupling between derivatives of **13** gives a dimer **16** which can be used for the synthesis of longer rotaxanes by applying the same approach. The connection of the repeating units in the dimer **16** provides a new way to obtain polyrotaxanes based on non-covalent bonds. Synthesis and study of the rheological properties of longer oligorotaxanes based on monomer **13** are in progress.

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Notes and references

† All new compounds have been characterized by mass and ^{1}H-NMR spectroscopy.

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