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Rotaxane-based Mechanically Linked Block Copolymer

Guillaume De Bo, Julien De Winter, Pascal Gerbaux and Charles-André Fustin*

((Dedication----optional))

Block copolymers constitute an extremely important class of materials thanks to their utility for countless applications.^[1] The development of controlled polymerization methods and the combined use of polymer and organic chemistries have enabled the production of complex architectures and highly functional polymers.^[2] Recently, block copolymers bearing an addressable junction have in particular attracted a lot of interest thanks to the added functionality and additional degrees of control on the properties and on the self-assembly behavior of such copolymers.^[3–8] Two main types of junction have been reported up to now: i) supramolecular junctions based for example on hydrogen bonds, metal-ligand coordination bond, or inclusion or host-guest complexes,^[3–5] and ii) covalent junctions responsive to various kinds of stimuli (light, pH, redox).^[6–8] Herein we report on the synthesis of a diblock copolymer where the two blocks are linked by a new type of junction: a mechanical bond of the rotaxane type (**1**, Figure 1).

Interlocked molecules such as catenanes and rotaxanes attract an ever-increasing amount of interest since the discovery in the late 1980's-early 1990's of efficient synthetic methods to prepare them. This interest stems in large part from the unique degrees of freedom associated to the mechanical (or topological) bond, i.e., it allows for controlled motions of large amplitude of the interlocked components, and for their relative positioning with respect to each other. These exceptional properties have made of catenanes and rotaxanes highly promising candidates for the design of molecular machines capable of performing well defined tasks in response to various stimuli.^[9] Moreover, they also show great potential for imparting unusual properties to polymers.^[10] Indeed, due to their unique flexibility and mobility, their incorporation into polymers is expected to strongly modify the rheological, mechanical, dynamic, and thermal properties of the latter. This promise of polymeric materials exhibiting new properties has thus generated an intense activity of research leading to the creation of polycatenanes and polyrotaxanes of diverse compositions and architectures.^[10] In all these previous

works the topological bonds were incorporated into the repeating units (in the main chain or as side groups) of the polymers. Contrary to those examples, here we use a single mechanical bond of the rotaxane type but strategically located at the junction between two polymer blocks (see Figure 1), giving rise to a new kind of diblock copolymers designated as A-rot-B. In this way, the blocks are linked by a bond which has the strength of a covalent bond, since the two interlocked components cannot be separated unless a covalent bond is broken, but which confers unique degrees of freedom to the polymer chains since the macrocycle bearing the B block can potentially move along the whole length of the A block acting as the thread. Copolymers of this type would thus enable motions of much larger amplitude than with conventional “small” rotaxanes, and constitute a first step toward large, fully synthetic, systems mimicking biological structures, where large amplitude motions are commonplaces.^[11]

Figure 1. Convergent synthetic strategy toward A-rot-B block copolymers

The chosen synthetic strategy is depicted in Figure 1. Among the different possible routes, we selected one that shows a highly convergent character, and where the key step (the rotaxation) is performed on a “small” molecule and not on a polymer chain-end. As template for the (pseudo)-rotaxane formation we selected a square-planar complex centred on a Pd(II) ion and built from one tridentate and one monodentate ligand. This is indeed a very efficient template that has been successfully used for the preparation of various catenanes^[12] and rotaxanes.^[13] Moreover, it is a neutral complex that can be used in a variety of organic solvents, and is robust enough to withstand chemical modifications performed on other parts of the molecule. Once available, the different building blocks will be assembled by two successive copper(I)-catalyzed

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azide-alkyne cycloaddition (CuAAC) “click” reactions, to yield the A-*rot*-B diblock copolymer.^[13] By following this strategy, a higher degree of control on the formation of the topological bond will be achieved, and its convergent nature allows an easy variation of the chemical structure of the polymer chains.

The first building block is the polymeric thread **4** end-capped at one end by a bulky stopper, and by an azide moiety at the other end. To this aim we synthesized the Atom Transfer Radical Polymerization (ATRP) initiator **2** bearing the bulky stopper (easily prepared from the corresponding phenol, see Supporting Information). This allows the facile synthesis of threads of different length and/or chemical nature without having to graft the bulky stopper in a subsequent step. As an example we chose to polymerize methyl acrylate. The ATRP polymerization of methyl acrylate from initiator **2** was performed in anisole with an equimolar CuBr/PMDETA (Pentamethyldiethylenetriamine) complex as catalytic system. A well-defined PMA (polydispersity index of 1.09) with a M_n of 5040 g/mol, and bearing a bulky stopper at one of its extremity was obtained in this way (**3**). The MALDI-MS characterization confirmed the presence of the expected end-groups (see Supporting Information). The bromide chain-end was then substituted with NaN_3 to quantitatively yield the azide terminated polymeric thread **4**.

Scheme 1. Synthesis of the polymeric thread **3** by ATRP from an initiator bearing a bulky stopper

The next step was to prepare the pseudo-rotaxane **8** bearing the second bulky stopper and an alkyne group to enable its “clicking” to the polymer thread **4**. As mentioned above we selected a square-planar complex centered on a Pd(II) ion as template for the pseudo-rotaxane. In order to efficiently template the rotaxane formation, this complex has to be built from a tridendate ligand, previously complexed with the palladium, and from a monodendate ligand.^[12-13] In our case, the tridendate ligand is the 2,6-pyridinedicarboxamide motif of the macrocycle **5**, and the monodendate ligand is the pyridine station present on the small thread **7** (Scheme 2). The pseudo-rotaxane **8** is then assembled by threading compound **7** through the cavity of macrocycle **6**, the pyridine station displacing the acetonitrile molecule present in **6**. The structure of the small thread **7** is inspired from previous studies^[13a,13b,13f] that showed that i) the presence of a bulky group on one side of the pyridine station, ii) the presence of a rigid arm (here the resorcinol fragment) on the other side of the pyridine, and iii) the 2,6 substitution of the pyridine ring, favor the threading through the cavity of the macrocycle and minimize the chance of an *exo* complexation, i.e., the non interlocked configuration. The small thread **7** is obtained in good yield in three steps starting from 2,6-bis(chloromethyl)pyridine and from the phenol form of the bulky stopper (see Supporting Information). The palladium complexed macrocycle **6** was obtained by adapting a reported procedure to chelidamic acid used as starting compound.^[13a] The pseudo-rotaxane **8** is formed in good yield by simply mixing the small thread **7** and

the macrocycle **6** at room temperature for one hour (Scheme 2), as unambiguously showed by ¹H NMR and mass spectrometry (see Supporting Information).

Scheme 2. Synthesis of pseudo-rotaxane **8** by slipping thread **7** through the cavity of the Pd-complexed macrocycle **6**

The building blocks being now available, the assembly of the A-*rot*-B copolymer can be performed. The first step is the clicking of the pseudo-rotaxane **8** onto the chain-end of the polymeric thread **4** by the CuAAC reaction to obtain the macro-rotaxane **9** (Scheme 3). This was performed at room temperature using CuBr/PMDETA as catalytic system. As shown by the mass spectrum of **9** in Figure 2, the clear mass shift to higher values compared to thread **4** and the very good agreement between experimental and isotope distributions confirm the efficiency of the coupling reaction. The Cl group present on the macrocycle was then substituted by an azide moiety by reacting the macro-rotaxane **9** with NaN_3 . It is worthwhile to note that the aromatic substitution of the Cl by the azide occurs smoothly in this case thanks to the presence of the two amide groups on the aromatic cycle and to the complexation of the pyridine nitrogen with the palladium.

Scheme 3. Synthesis of the macro-rotaxane **10** by “clicking” the pseudo-rotaxane **8** onto the chain-end of the polymeric thread **4**.

Scheme 4. Last step of the assembly of the PMA-rot-PEO copolymer by “clicking” the PEO chain **11** onto the macrocycle of macro-rotaxane **10**.

Figure 2. MALDI mass spectrum of macro-rotaxane **9**. The inset shows the very good agreement between the experimental (bottom) and theoretical isotope distributions (top).

The final step toward the A-rot-B copolymer is the clicking of the B block onto the macrocycle of the macro-rotaxane **10** by the CuAAC reaction. As B block we selected a poly(ethylene oxide), PEO, chain (M_n : 2000 g/mol, PDI: 1.05), end-capped with a propargyl group to allow its reaction with the azide on the macrocycle. The CuAAC reaction was conducted in refluxing chloroform with CuBr/PMDETA complex as catalyst. After purification to remove the residual homopolymers, the PMA-rot-PEO copolymer was obtained with satisfactory yield considering the complexity of the system.

Figure 3 shows a comparison of the size exclusion chromatography (SEC) traces of the polymeric thread **3**, of the macro-rotaxane **9** and of the PMA-rot-PEO copolymer **1**. A shift toward the shorter elution times is clearly visible between each of the three compounds, confirming the increase in molecular weight at each step of the assembly of the copolymer. Moreover, the ^1H NMR spectrum of copolymer **1** (see Supporting Information) confirms its structure since the integrations of the PMA and PEO signals match the expected composition of the copolymer.

Figure 3. SEC traces of the building blocks **3** (plain grey), **9** (dashed black), **11** (dashed grey) and of the PMA-rot-PEO copolymer **1** (plain black). (Eluent: DMF, flow rate: 1 mL/min, detector: RI).

To bring further evidence on the obtained structure, the PMA-rot-PEO copolymer **1** was analyzed by MALDI mass spectrometry. As presented in Figure 4, MALDI mass spectrum obtained for copolymer **1** is significantly less resolved than the spectrum of the macro-rotaxane **9**. Since compound **1** is a copolymer of PEO and PMA, the low mass difference between EO and MA units ($2 \times \text{EO} = 88$ u and $\text{MA} = 86$ u) leads to many isobaric ions, explaining the lesser resolution. Nevertheless, an interesting global shift of 2000 Th is observed, confirming the grafting of the PEO chain (M_n

= 2000 g/mol) onto the macro-rotaxane and therefore the structure of the PMA-rot-PEO copolymer **1**.

Figure 4. Comparison of the recorded MALDI mass spectra before and after clicking the PEO block onto the macro-rotaxane. In the bottom spectrum, low m/z signals correspond to PMA-containing fragment ions produced by decomposition of the copolymer (higher laser fluence conditions).

In conclusion, we have described the first synthesis of an original diblock copolymer where the two blocks are linked by a mechanical bond of the rotaxane type. The proposed strategy, by virtue of its modular and convergent character will allow the preparation of a series of copolymers with tunable composition. Moreover, it offers several possibilities of adaptation, for example by replacing the second click reaction by a polymerization step using a modified macro-rotaxane as macroinitiator. This would further broaden the accessible composition range and could give access to copolymers of high molecular weights. The type of copolymers reported here opens promising pathways to study the sliding motion of a macrocycle along a polymer chain. Gaining insight in such mechanisms is indeed very important for the development of synthetic molecular machines, for example systems mimicking processive enzymes.^[15]

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Polymer Architecture

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Rotaxane-based Mechanically Linked
Block Copolymer

A diblock copolymer, where the two blocks are linked by a mechanical bond of the rotaxane type, was prepared by a convergent approach consisting in assembling the building blocks by two successive copper(I)-catalyzed azide-alkyne cycloaddition “click” reactions.