

Reversible Switching between Macrocyclic and Polymeric States by Morphological Control in a Constitutional Dynamic System**

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Constitutional dynamic chemistry (CDC)^[1] explores the various facets of the chemistry of species whose constitution involves components linked through reversible covalent bonds or noncovalent interactions. Such species may undergo a constitutional modification by incorporation, removal, or exchange of components^[2] and result in a property change, or can be induced by property-driven selection.^[3] Structural information in chemistry is based on morphology and interaction sites, and endows molecular matter with molecular and supramolecular well-defined functions (recognition, reactivity, etc.), either static or dynamic. On the other hand, the implementation of reversible reactions allows for the generation of constitutional diversity on the molecular/covalent level through the recombination of components in a dynamic combinatorial fashion.^[4]

Component morphology may be expected to have a profound influence on the nature of the species generated in a constitutional dynamic system. As a consequence, a change in morphology should result in a change in constitution, and thus represents a potential constitutional switch. We describe here such a switch between a macrocycle state and polymer state in an effector-controlled system.

From the point of view of CDC, macrocycles and dynamic polymers (dynamers)^[1,5] formed by reversible covalent processes represent two correlated states that may in principle be interconverted by means of a suitably designed shape-switching process. The combination of reversible bonds and a morphologically controlled unit in a single system would make it possible to switch reversibly between a macrocycle and a polymer.

The template effect of metal ions has been used extensively to preorganize one or more reactants and to increase the efficiency of macrocycle formation,^[6] and it may lead to the stabilization of a given macrocycle among a virtual library of imine-based macrocycles.^[7] Previously we described motional dynamic molecular devices that display contraction/extension molecular motion upon binding and removal of a metal ion.^[8] We report now on a system that displays combined constitutional/morphological/motional dynamics in

which the morphological change triggered by a metal ion results in a reversible constitutional switch between macrocycle and polymer states (Figure 1).^[9] This process is based on

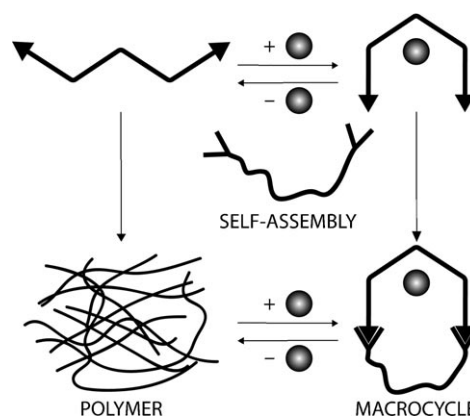


Figure 1. Principle of the switching process between a polymer and a metallomacrocycle on interconversion of ligand component between “W” and “U” shapes through binding and removal of a metal ion (see also Figure 2).

the ability to switch a tridentate terpyridine-type ligand molecule reversibly between an “extended” W-shaped state and a “compact” U-shaped state through the binding and removal of a metal ion. Such a type of morphological switch has been used in our research group to modulate physical and substrate-binding properties.^[10]

The system is based on a W-shaped dialdehyde **1**^[11] which may undergo polycondensation with a diamine to form a linear polymer. The binding of a metal ion to **1** should result in switching the W-shaped core into a U-shaped one in which the dialdehyde functions are held closer to each other (Figure 2), thus favoring the formation of a macrocycle on reaction with a suitable diamine. The system displays reversible switching between macrocycle and polymer states upon addition of a

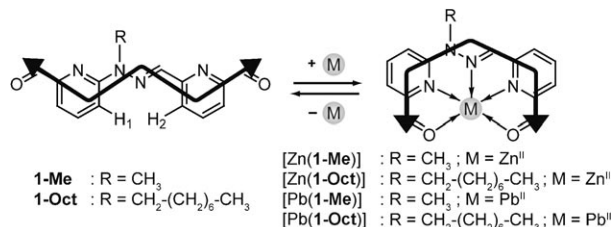


Figure 2. Structure of dialdehydes **1** and their reversible shape switching between “W” and “U” forms on binding and removal of a metal ion.

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metal ion or its removal by the addition of a competitive binder (Figure 1). For solubility reasons, the two dialdehydes **1-Me** and **1-Oct** were studied (Figure 2).

The pyridine-hydrazone-pyridine scaffold is an isomorphous form of 2,2',6',2''-terpyridine and, as for the latter, the "linear" bis-*transoid* form is expected to be much more stable than the corresponding bent bis-*cisoid* one.^[8] Therefore, the most favored conformation of dialdehyde **1** is the open bis-*transoid* W-shape with the two aldehyde functions pointing in opposite directions (Figure 2), as shown in the 2D ROESY NMR spectrum of **1-Me** by the NOE correlation between H1 and H2 (data not shown). The solid-state molecular structure of **1-Me** determined by X-ray crystallographic analysis of a single crystal obtained by slow evaporation of a CHCl₃ solution confirms that it has a bis-*transoid* conformation (Figure 3). This shape should favor the formation of a

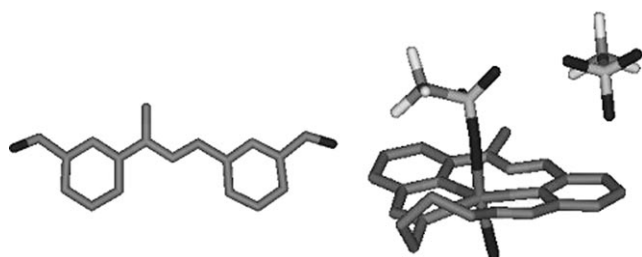
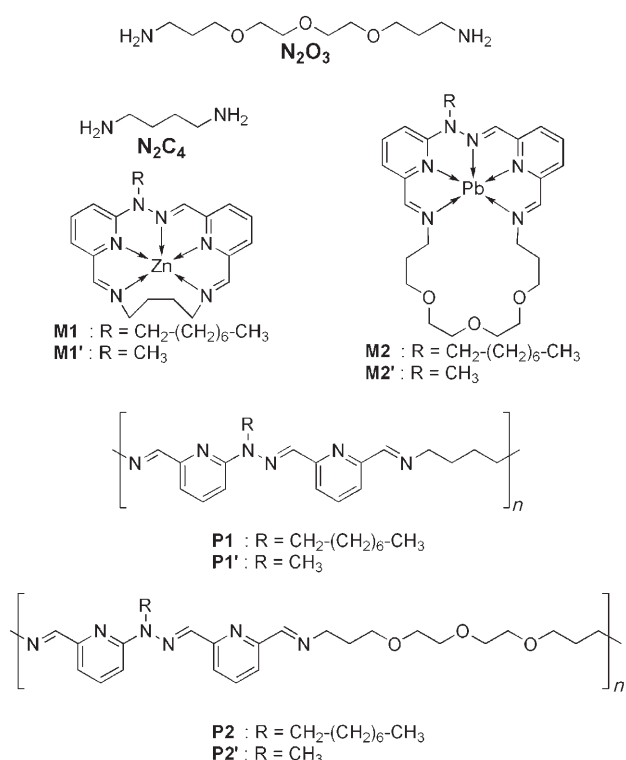


Figure 3. Solid-state molecular structure of the W-shaped dialdehyde **1-Me** (left) and the metallomacrocyclic complex **M1'** (right) obtained by condensation of [Zn(**1-Me**)] with **N₂C₄**.

polymer on polycondensation with a diamine. Indeed, the addition of one equivalent of the diamine **N₂C₄** or **N₂O₃** to **1-Oct** (50 mM each in CDCl₃/CD₃CN 8:2 or 6:4, respectively) results in the formation of a solution, the NMR spectrum of which shows that all the dialdehyde has reacted. The compound formed shows imine CH=N signals in the proton NMR spectrum (Figure 4 and Figure 5) and may be considered to consist of the corresponding polyimine polymers (**P1** and **P2**) formed by polycondensation (see below). The polymeric material **P1'** formed from **1-Me** and **N₂C₄** was insoluble in CDCl₃/CD₃CN mixtures and was thus not further studied.

The addition of zinc or lead triflate to **1-Me** leads to the formation of the ML complexes (M: metal ion; L: ligand) [Zn(**1-Me**)] and [Pb(**1-Me**)], respectively, as indicated by ¹H NMR titration experiments (data not shown). The formation of only the ML complex may be explained by the extra coordination provided by the two aldehyde functions, which prevent the formation of an ML₂-type complex. Ligand **1-Oct** yields the corresponding complexes [Zn(**1-Oct**)] and [Pb(**1-Oct**)].

The addition of one equivalent of **N₂C₄** to [Zn(**1-Oct**)] or of **N₂O₃** to [Pb(**1-Oct**)] (50 mM each in CDCl₃/CD₃CN 8:2 or 6:4, respectively) results in complete imine condensation. ¹H NMR spectroscopic analysis shows that all the aldehyde groups had reacted and that new signals had appeared, which are compatible with the formation of the bisimine macrocycles **M1** and **M2**, respectively (see Figure 4 and Figure 5).



MALDI-TOF analysis agreed with the formation of the [1+1] metallomacrocyclic in both cases. Single crystals could be obtained by slow diffusion of diisopropyl ether into a CHCl₃/CH₃CN solution of **M1'** which was obtained in similar fashion from **N₂C₄** and [Zn(**1-Me**)]. X-ray diffraction analysis confirms its structure as the zinc complex of the [1+1] macrocycle, with a coordination number of seven for the central zinc ion. The three nitrogen atoms of [Zn(**1-Me**)] and the two imine nitrogen atoms roll in a helical fashion around the metal ion, whereas one triflate and one water molecule lie perpendicular, thereby forming a distorted pentagonal bipyramid (Figure 3). Similar structural data have been obtained for the macrocycle **M2'** formed from [Pb(**1-Me**)] and **N₂O₃**.

The reversibility of the outcome—macrocycle or polymer—was then tested. The addition of one equivalent of hexacyclen, which strongly binds Zn^{II} ions,^[12] to the metallomacrocyclic **M1** removes the cation and converts the system into polymer **P1**, previously obtained with the starting free ligand **1-Oct**. Subsequent addition of one equivalent of zinc triflate results in the recovery of the macrocycle **M1**, as shown by ¹H NMR and MALDI-TOF analysis (Figure 4).

Similarly, the addition of [2.2.2]cryptand to the metallomacrocyclic **M2** removes the cation with concomitant formation of the highly stable lead cryptate,^[13] and regenerates the polymeric **P2** state (as obtained previously). The subsequent addition of one equivalent of lead triflate results in reformation of the initial macrocycle **M2** (Figure 5).

The imine exchange^[4,14] is the key step of the switching process. As described above, the outcome of the self-assembly by imine condensation depends on the morphology of the initial dialdehyde. Imine exchange is required to achieve a reversible switch between the polymeric state and the macro-

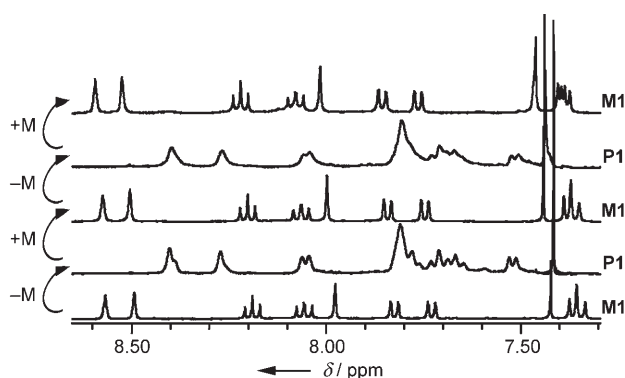


Figure 4. ^1H NMR spectra (400 MHz) showing the reversible switching process between the metallomacrocycle **M1** and polymer **P1** in $\text{CDCl}_3/\text{CD}_3\text{CN}$ (8:2) at 50 mm. +M refers to the addition of 1 equiv of $\text{Zn}(\text{OTf})_2$ and -M refers to the addition of 1 equiv of hexacyclen to remove the metal cation from the macrocyclic complex.

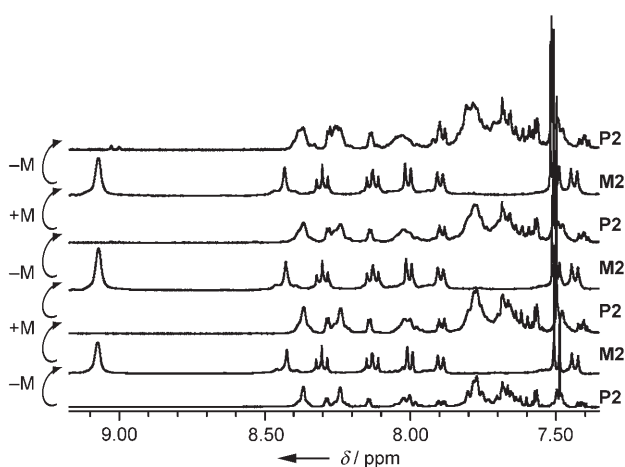


Figure 5. ^1H NMR spectra (400 MHz) showing the reversible switching process between the metallomacrocycle **M2** and polymer **P2** in $\text{CDCl}_3/\text{CD}_3\text{CN}$ (6:4) at 50 mm. +M refers to the addition of 1 equiv of $\text{Pb}(\text{OTf})_2$ and -M refers to the addition of 1 equiv of [2.2.2]cryptand to remove the metal cation from the macrocyclic complex.

cyclic state. This may proceed through hydrolysis by the residual water and recondensation, thus resulting in a two-step switching cycle which consists of a macrocyclization and a ring-opening polymerization under thermodynamic control.^[15]

The polymeric nature of the compounds formed from **1-Oct** and N_2C_4 or N_2O_3 is supported by the following data. When the same self-assembly based on imine condensation reactions are performed with reactants at lower concentrations (5 mm and 25 mm), ^1H NMR spectroscopic analysis shows that, as the concentration decreases, there is an increasing formation of macrocyclic compounds. These products were identified by MALDI-TOF mass spectrometry as the [1+1] and the [2+2] macrocycles, with some minor amounts of oligomeric assemblies (Figure 6).

Further support was obtained from DOSY measurements on the self-assembly between **1-Me** and N_2O_3 . At 5 mm, the

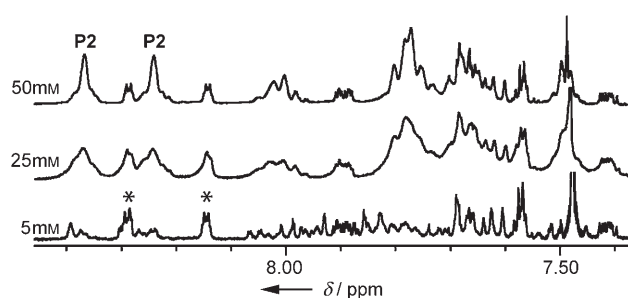


Figure 6. ^1H NMR spectra (400 MHz) showing the concentration-dependent constitution of the system resulting from the self-assembly between **1-Oct** and N_2O_3 . The asterisk indicates the macrocyclic entity, which is the major compound at 5 mm in $\text{CDCl}_3/\text{CD}_3\text{CN}$ (6:4), whereas the polymer **P2** becomes the major compound as the concentration is raised to 50 mm.

compounds formed have a diffusion coefficient of $D = 490 \mu\text{m}^2\text{s}^{-1}$, which corresponds to a diameter of 16.4 Å, when a spherical structure model is used. On the other hand, at a concentration of 50 mm, much larger objects of 200 Å diameter ($D = 40 \mu\text{m}^2\text{s}^{-1}$), compatible with a polymeric structure of **P2'**, are predominantly formed. Thus, an increase in the concentration of the partners from 5 to 50 mm leads to an increase in polymeric material at the expense of the macrocyclic compounds, until eventually a film (hard for **P1** and soft for **P2**) is formed in neat conditions (data not shown). It is worth noting that the complexes $[\text{Zn}(\mathbf{1})]$ and $[\text{Pb}(\mathbf{1})]$ self-assemble with the corresponding diamine to give the [1+1] metallomacrocycles **M1**, **M1'**, **M2**, and **M2'** over the 5–50 mm concentration range. This behavior as a function of concentration does indeed indicate the formation of polymer with a concomitant decrease in the macrocyclic compounds. It also shows that the structural information contained in the U-shaped metallomacrocycles $[\text{Zn}(\mathbf{1})]$ and $[\text{Pb}(\mathbf{1})]$ is characterized by a much higher effective molarity than in **1** itself.^[16] Furthermore, dilution and concentration experiments (data not shown) demonstrate the dynamic behavior of these imine-based dynamers. Thus, two independent tools—concentration and morphological state of the dialdehyde **1**—are available for controlling the constitution of the dynamic system.

In conclusion, the reactions undergone by the dialdehydes **1** show that a covalent self-assembly process and the constitution of its products can be reversibly steered by an allosteric switch. The study demonstrates that a morphologically controlled system, which incorporates reversible covalent connections, can be interconverted between macrocycles and polymers. In more general terms, it shows that a constitutional dynamic system can be switched between two different constitutional states by a controlled modulation of morphological information.^[17]

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