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ARTICLE

Copper(I)-Induced Amplification of a [2]catenane in a Virtual Dynamic Library of Macrocyclic Alkenes†

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Olefin cross-metathesis of diluted dichloromethane solutions (≤ 0.15 M) of the 28-membered macrocyclic alkene $\mathbf{C_1}$, featuring a 1,10-phenanthroline moiety in the backbone, as well as of catenand 1, composed of two identical interlocked $\mathbf{C_1}$ units, generates families of noninterlocked oligomers $\mathbf{C_i}$. The composition of the libraries is strongly dependent on monomer concentration, but independent of whether $\mathbf{C_1}$ or **1** is used as feedstock, as expected for truly equilibrated systems. Accordingly, the limiting value 0.022 M approached by the equilibrium concentration of $\mathbf{C_1}$ when the total monomer concentration approaches the critical value as predicted by the Jacobson-Stockmayer theory, provides a reliable estimate of the thermodynamic effective molarity. Catenand **1** behaves as a virtual component of the dynamic libraries, in that there is no detectable trace of its presence in the equilibrated mixtures, but becomes the major component – in the form of its copper (I) complex – when olefin cross-metathesis is carried out in the presence of a copper (I) salt.

Introduction

Dynamic combinatorial chemistry (DCC)[1] is a powerful tool for the synthesis of receptors under thermodynamic control. Efficient receptors may be selected among a family of interconverting members of a dynamic library (DL) upon the addition of a suitable template via repeatedly occurring bond dissociation-recombination processes. A major motivation for the intense work dedicated to this research field is the ability of the system to select and produce a good receptor, which sometimes is only virtually present,[2] i.e. not present at all in the initial reaction mixture.

[2]Catenanes are the most popular interlocked systems as witnessed by the high number of review articles[3] and book chapters[4] devoted to them. They consist of two distinct rings jointed together by a mechanical bond, topologically called Hopf link.[3c] The wide interest in [2]catenanes is motivated, inter alia, by their use in the construction of molecular switches and machines[5] for a great variety of functions.

Statistical syntheses of catenanes were of little practical significance,[6] but the pioneering work of Sauvage[7] nicely showed that synthetically useful quantities of simple catenanes and higher order interlocked macrocycles are easily obtained by metal templation. Since then, hundreds of new [2]catenanes have appeared in the literature. Although templating by metal ions is commonly used to achieve the synthesis of [2]catenanes, other kinds of intermolecular interactions have been exploited as well to direct the closure of the two interlocked cycles into the right topology.[8] Very recent developments in the field of DCC have opened the way for templated syntheses of [2]catenanes under equilibrium conditions. In a number of cases catenanes have been isolated as the response of systems to the addition of templates,[9] and even self-templated syntheses of catenanes under equilibrium conditions have also been reported.[10] Thus, DCC provides an alternative access to interlocked macrocycles that are generally obtained under kinetic control.

In our previous studies we have extensively investigated DLs of macrocycles generated by acid-catalyzed transacetalation of cyclophane formaldehyde acetals.[11] Many

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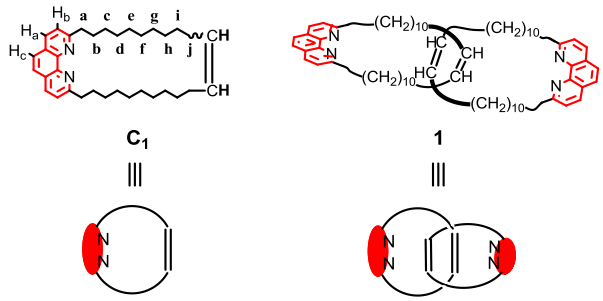
† Electronic Supplementary Information (ESI) available: ^{1}H NMR and ^{13}C NMR spectra of new compounds, 2D NMR spectra of **1** and **1**•Cu^+, stacks of spectra of the equilibration experiment at 5 mM c_{mon} (Figure ESI 1) and of selected equilibration experiments starting either from $\mathbf{C_1}$ or **1** (Figure ESI 2). See DOI: 10.1039/b000000x/

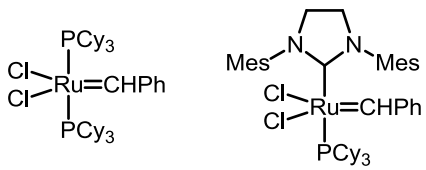
other types of reaction can be used for the production of DLs of macrocycles, among which olefin metathesis plays a most important role.[12]

Here, we report our investigations of the fully reversible ring-opening metathesis[13] of dilute dichloromethane solutions of the 28-membered macrocyclic alkene **C_1**, and the copper(I)-induced amplification of the [2]catenane dimer **1**. The latter is totally absent in the reaction mixtures equilibrated in the absence of copper(I).

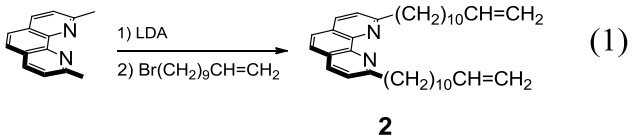


Results and discussion

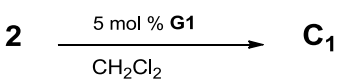
Synthesis of C_1 and 1



Treatment of 2,9-dimethyl-1,10-phenanthroline (neocuproine) with 2 mol equiv of lithium diisopropylamide (LDA), followed by alkylation with 11-bromoundecene gave building block **2** in 63% yield (eq 1). Ring-closing metathesis (RCM) of 10 mM **2** in CH_2Cl_2 in the presence of 5 mol % first generation Grubbs' catalyst **G1** afforded marcocycle **C_1** in 79 % yield (eq 2).

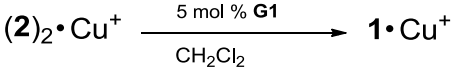


(1)

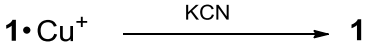


(2)

The copper(I) catenate **1**•Cu^+ was synthesized in 92% yield via a double RCM of 10 mM (**2**)$_2$•Cu^+ in CH_2Cl_2 in the presence of 5 mol % **G1** (eq 3). Cyanide-induced demetallation of **1**•Cu^+ afforded catenand **1** in quantitative yield (eq 4).



(3)



(4)

The ^{1}H NMR spectra of **1**•Cu^+ and **1** are shown in Fig. 1. Assignment of all methylene proton signals of both compounds were carried out on the basis of 1D-TOCSY, 2D-COSY and 2D-ROESY experiments (pages ESI 7-9 for **1**•Cu^+ and pages ESI 11-12 for **1**). The more resolved spectrum of **1**•Cu^+, in line with the expected mixture of E and Z configurations of the double bond,[14] shows two distinct sets of signals for protons **d**, **j**, =C**H** and H_a, each pair of signals being in the ratio of 7:1. Pairs of signals are also visible in the less resolved spectrum of **1** for protons **j**, =C**H**, H_b and H_c. Thus, it is likely that the synthesized catenanes are unresolved mixtures of the three diolefin isomers EE, EZ and ZZ.

The high-field shifts experienced by methylene protons **d**, **c**, **e**, **f** and **g** of **1**•Cu^+ (Fig. 1) are indicative for the shielding effect of the phenanthroline moiety of the other interlocked macrocycle. Also ROE interactions of methylene protons **e**-**j** with aromatic protons H_a and H_c (page ESI 8), provide strong indications of the existence of a catenane topology in compound **1**•Cu^+.

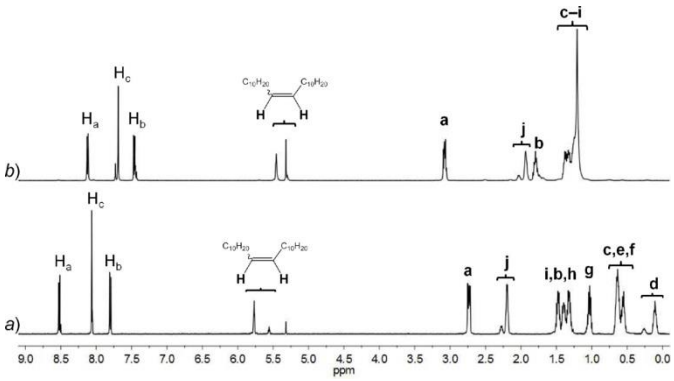


Fig. 1 ^{1}H NMR spectra of (*a*) **1**•Cu^+ and (*b*) **1** in CD_2Cl_2 at 25 °C.

X-ray analysis on crystals of **1**•Cu^+, as obtained by slow diffusion of methanol into a concentrated acetonitrile solution, was unfortunately not successful.

The confirmation of the interlocked structure of **1** was obtained from a series of Mass/Mass Collision-Induced Dissociation (MS/MS CID) experiments[15] carried out at increasing collision energy in our ESI-TOF equipment (Fig. 2). The sole fragment derived from the mass-selected ion, *m/z* 991 ($C_{68}H_{96}N_4$+Na^+), up to a collision potential as high as 70 V, is the one at *m/z* 507 ($C_{34}H_{48}N_2$+Na^+), corresponding to the Na^+ complex of the cyclic monomer **C_1**. The latter is most likely derived from the catenane by rupture of one covalent bond, followed by dethreading of the linear fragment of a labile pseudorotaxane assembly. This behavior is clearly inconsistent with the dimeric structure of **C_2**, an isomer of **1**, because its fragmentation could hardly produce a single ion fragment with an *m/z* value exactly corresponding to its half.

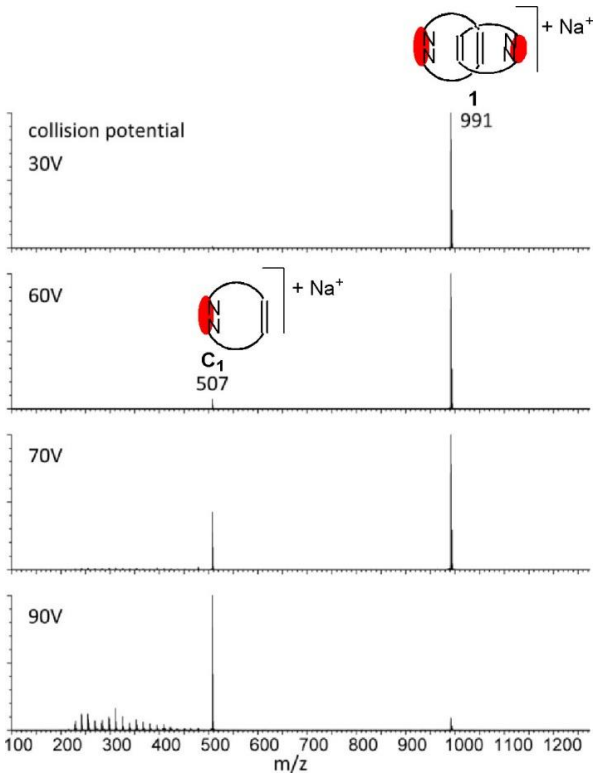
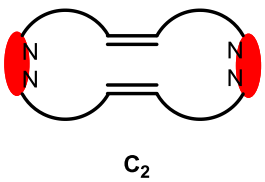


Fig. 2 CID experiments at increasing collision energy (from 30 to 90 V) carried out on selected peak **1**•Na^+ (m/z = 991). Peak at m/z = 507 corresponds to cyclic monomer $\mathbf{C_1}$•Na^+.



$\mathbf{C_2}$

Equilibration experiments under olefin metathesis conditions

In a first set of experiments, metathesis of a number of CD_2Cl_2 solutions of $\mathbf{C_1}$ in the concentration range from 10 to 150 mM was initiated by addition of 3 mol % second-generation Grubbs' catalyst **G2** at 30 °C. The more robust and catalytically active **G2** was preferred to **G1** for increasing the chance to achieve true equilibrium conditions.[16,17] Occasional monitoring of the ^{1}H NMR spectra of the reaction mixtures showed that after 24 hours equilibrium was reached in all cases. The ESI-TOF MS spectrum of a typical reaction mixture (Fig. 3) revealed the presence of a family of cyclic oligomers, whose intensities declined progressively with increasing ring size.

Catenand **1** (from 2.5 to 50 mM) was the reactant in a second set of metathesis experiments carried out under otherwise identical conditions. Interestingly, the most dilute solution afforded a quantitative transformation of **1** into its unthreaded macrocyclic component $\mathbf{C_1}$ (Fig. ESI 1), most likely via the open chain metal-alkylidene intermediate **3**, as schematically depicted in Scheme 1.

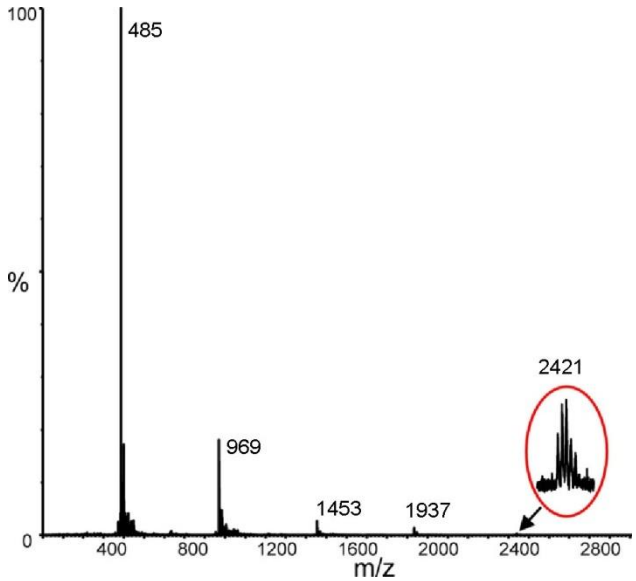
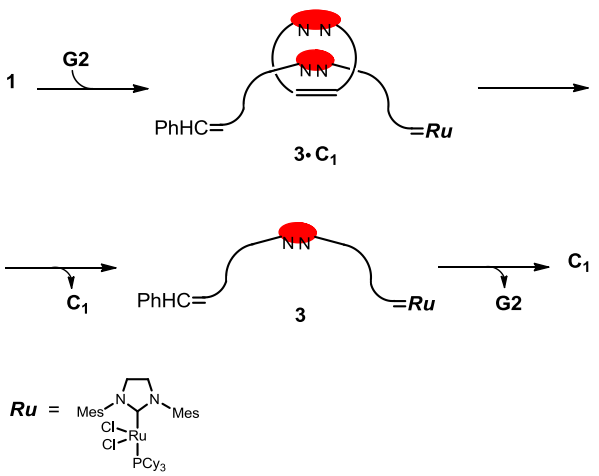


Fig. 3 ESI-TOF mass spectrum obtained from equilibrated reaction mixture of 60 mM c_{mon} starting from $\mathbf{C_1}$ (*m*/*z* of [$\mathbf{C_i}$ + H^+] = [i × 484] +1).



Scheme 1 Ring-opening of one of the two rings of **1** affords a labile pseudorotaxane intermediate (**3**•$\mathbf{C_1}$). Dissociation of the latter is followed by exclusive ring-closure of **3** in the extremely dilute solution (c_{mon} = 2×[**1**]$_0$ = 5 mM).

Mixtures of increasing complexity were obtained at higher concentrations, whose ^{1}H NMR spectra (Fig. ESI 2) turned out to be indistinguishable from those of the reaction mixtures derived from $\mathbf{C_1}$. This was expected for a truly reversible system, whose composition at equilibrium should be independent of the oligomer used as feedstock, but solely dependent on total concentration of monomer units, c_{mon}. No signal ascribable to catenand **1** was detected in the spectra of the equilibrates in the whole range of c_{mon} values (Fig. ESI 2), showing that catenand **1** is thermodynamically unstable with respect to the mixture of unlocked macrocyclic members of the DLs generated by metathesis of either $\mathbf{C_1}$ or **1**.

It is unfortunate that all attempts at analyzing the reaction mixtures by gel permeation chromatography failed and reversed-phase HPLC analysis was prevented by solubility problems. However, deconvolution and integration of the aromatic singlet at $\delta = 7.72$ (Fig. ESI 2) allowed at least the determination of the equilibrium concentration of $\mathbf{C_1}$ as a function of the concentration of monomer units c_{mon} (Table 1).

Table 1 Concentrations of $\mathbf{C_1}$ in the equilibrated mixtures obtained from $\mathbf{C_1}$ or catenand **1**.

Starting material	c_{mon} (mM)[a]	[$\mathbf{C_1}$] (mM)
1	5.0	5.0
1	10	9.1
$\mathbf{C_1}$	10	9.1
1	15	11.0
$\mathbf{C_1}$	30	16.8
$\mathbf{C_1}$	50	20.5
1	60	21.2
1	100	22.0
$\mathbf{C_1}$	150	22.1

[a] $c_{mon} = [\mathbf{C_1}]_0$ or $2\times[\mathbf{1}]_0$

The distribution of cyclic and linear polymers in ring-chain equilibria is ruled by the Jacobson-Stockmayer (J-S) theory.[18] Accordingly, the concentration of each cyclic species increases upon increasing c_{mon}, until a critical value c_{mon}* is reached. Such a critical concentration is a real cut-off point, below which the system is composed of cyclic species only, and above which the total monomer concentration of cyclic species remains constant, eq 5,[19] whereas the concentration of linear polymers $\mathbf{P_i}$ increases on increasing the total monomer concentration in excess to c_{mon}*, eq 6. The limiting value [$\mathbf{C_i}$*] coincides with the thermodynamic effective molarity EM_i of the given cyclic oligomer.[20]

$$\sum_i i[\boldsymbol{C}_i^*] = c_{mon}^* \quad (5)$$

$$\sum_i i[\boldsymbol{P}_i^*] = c_{mon} - c_{mon}^* \quad (6)$$

A plot of [$\mathbf{C_1}$] against c_{mon} indeed shows a negative curvature (Fig. 4) and a definite tendency to approach a limiting value in the high concentration region, in full agreement with the J-S theory. Incidentally, data points could be fitted to a good precision (rms = 0.17×10^{-3} M) to a simple exponential function, as found in analogous instances,[11b,c,21] although no theoretical explanation for such a behavior is available at present. In any event, it is worth noting that concentration data derived from two distinct sets of experiments could be fitted to a single, smooth curve thanks to the establishment of true equilibrium conditions.

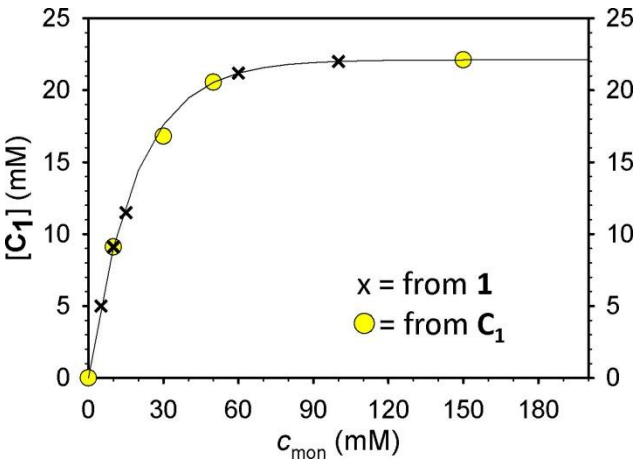
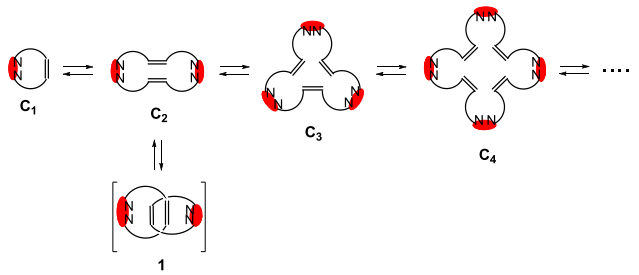


Fig. 4 Concentrations of $\mathbf{C_1}$ in the equilibrated reaction mixtures starting either from **1** (crosses) or $\mathbf{C_1}$ (yellow dots) (data from Table 1).

The concentration profile on Fig. 4 does not allow the c_{mon}* value to be obtained with any precision, because [$\mathbf{C_1}$] approaches asymptotically its limiting value. Nevertheless, the shape of the profile suggests that c_{mon}* should lie somewhere in the neighborhood of 0.15 M, a value that compares well with literature data related to macrocyclization equilibria based on olefin metathesis,[22] transacetalation,[11,21,23] transesterification,[24] and quadruple hydrogen bonding interactions,[25] for which c_{mon}* values in the range of 0.13 – 0.25 M were reported.

The thermodynamic effective molarity of $\mathbf{C_1}$, $EM_1 = 0.022$ M, compares well with a large body of EM values reported for the formation of large, strainless rings of similar size,[26] and this leads to the conclusion that the **G2** catalyzed transformation of $\mathbf{C_1}$ into a mixture of cyclic oligomers is a pure entropy driven reaction, or very nearly so.[27]

To sum up, well-behaved DLs composed of macrocyclic oligomers only were obtained upon treatment of either $\mathbf{C_1}$ or **1** with **G2** at c_{mon} values not exceeding the critical value c_{mon}* (Scheme 2). Catenand **1** is a virtual component of the DL, namely, one whose equilibrium concentration is too low to measure.



Scheme 2. DL of oligomeric macrocycles generated by ring-opening metathesis of either $\mathbf{C_1}$ or **1**.

A copper(I)-driven amplification experiment

An important feature of DLs is their ability to readjust the product distribution dictated by the initial conditions when the variables that rule the equilibrium change. Notably, addition of a template, e.g. a metal ion, that binds to the various members of the library with differential affinities, will strongly perturb the equilibrium composition.

The following two-step experiment was aimed to illustrate the adaptability of a DL to the equilibrium perturbation caused by the addition of copper(I), in view of its ability to form strong tetrahedral complexes of 1:2 stoichiometry with 1,10-phenanthroline ligands.[28]

In the first step a dilute solution of **1** in CD_2Cl_2 (2.5 mM) was treated with 3 mol % **G2** and left to stand at room temperature for 24 hours. The ^{1}H NMR spectrum of the final reaction mixture (Fig. 5*b*) revealed the presence of macrocycle $\mathbf{C_1}$ as the sole detectable product, as expected for the limiting composition of the DL in the very low concentration domain.

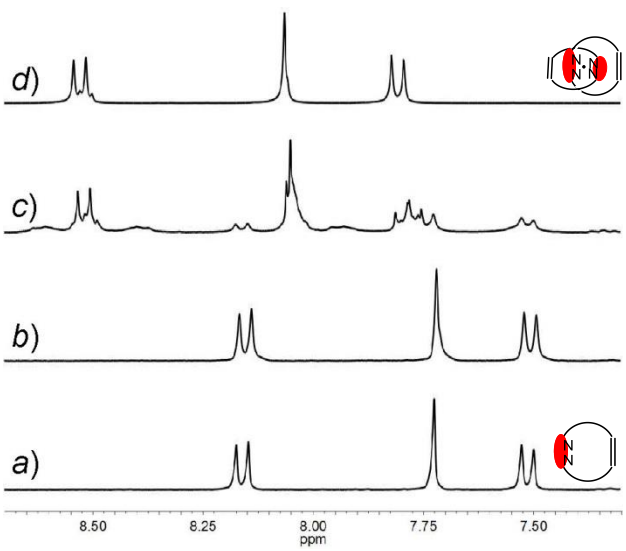
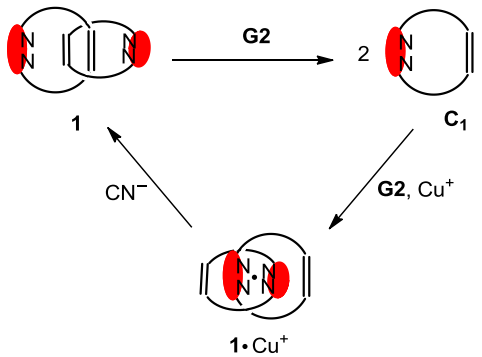


Fig. 5 Partial ^{1}H NMR spectrum of (*b*) product of the first step of the of the experiment (see text), (*c*) product of the second step of the experiment (see text). ^{1}H NMR spectra of pure $\mathbf{C_1}$ (*a*) and **1**•Cu^+ (*d*) are shown for comparison.

In the second step, $(CH_3CN)_4CuPF_6$ (2.5 mM) and a fresh portion of **G2** (3 mol %) were added to the above solution. The ^{1}H NMR spectrum, taken after 24 hours (Fig. 5*c*), showed a reaction mixture in which catenate **1**•Cu^+ was the major component (60%), accompanied by $\mathbf{C_1}$ (13%) and minor presumably copper(I)-complexed unidentified species (27%). It appears therefore that the dynamic system dramatically readjusted its composition in response to the presence of the copper(I) template. It is evident that catenand **1** is the best binder, most likely on account of the enforced proximity of the two phenanthroline units. The extra stabilization provided by metal coordination transforms a thermodynamically unstable, virtual component of the DL into the most stable metal-ligand species. Thanks to the adaptability of dynamic systems, the metal template performs the assembly of the optimal partner, whose concentration rises from a negligibly low value to 60% of the available monomeric units. Notably, a catenane structure is directly obtained from a macrocyclic monoolefin, rather than from an α,ω-diolefin precursor.[14]

Addition of a third step, namely, the cyanide induced demetallation of **1**•Cu^+ completes the cycle depicted in Scheme 3, in which any of the three species involved can be used as a starting point of a clockwise route.



Scheme 3. From catenane to unlocked macrocycle and back again. Only the clockwise route is allowed.

Conclusions

We have shown that ring-opening metathesis of dilute solutions of macrocyclic alkene $\mathbf{C_1}$, catalyzed by second-generation Grubbs' catalyst **G2**, yields well-behaved DLs of cyclic oligomers $\mathbf{C_i}$, that are indistinguishable from those obtained from catenand **1** under the same equilibrium conditions. As predicted by J-S theory, the equilibrium concentration of $\mathbf{C_1}$ increases upon increasing the total monomer concentration c_{mon}, and approaches a limiting value when c_{mon} approaches its critical value c_{mon}*. The limiting value of 0.022 M provides a genuine measure of the thermodynamic EM of $\mathbf{C_1}$. This value indicates that $\mathbf{C_1}$ is a strainless ring, or very nearly so. No visible traces of catenand **1** are found in the equilibrated mixtures. The thermodynamic sink featured by the strong complexation with copper (I) ion results in a tremendous amplification of **1** under copper (I) ion template action. These

results provide an additional illustration of the potential of well-behaved DLs, arising from their ability of "proof reading and editing" via repeated bond dissociations and recombinations, and of amplification of even a virtual component via strong interaction with a suitable template.

Experimental section

Instruments and General Methods

1D NMR spectra were recorded on either a 300- or 500-MHz spectrometer. 2D NMR spectra were recorded on a 500-MHz spectrometer. The spectra were internally referenced to the residual proton solvent signal. HR-ES mass spectra were obtained on either a ESI-TOF and MALDI-TOF spectrometer. UV-vis spectra were performed on a double-ray spectrophotometer using a standard quartz cell (light path = 1 cm) at 298 K.

Materials

All reagents and solvents were purchased at the highest commercial quality and were used without further purification, unless otherwise stated. Deuterated halogen solvents were flashed through basic alumina immediately prior to use.

General procedure for the untemplated olefin cross-metatheses

Either catenand **1** or cyclic monomer $\mathbf{C_1}$ were weighted in a NMR tube in order to prepare solutions in CD_2Cl_2 at the desired total monomer concentration c_{mon}. To such solutions, a calculated volume of a stock solution of 2nd generation Grubbs catalyst **G2** in CD_2Cl_2 was added to reach final catalyst concentrations of 3 mol %. Reaction runs were monitored by ^{1}H-NMR spectroscopy.

General procedure for the templated olefin cross-metatheses

Catenand **1** was weighted in a NMR tube in order to prepare solutions in CD_2Cl_2 at 5 mM c_{mon}. To such solutions, a calculated volume of a stock solution of 2nd generation Grubbs catalyst **G2** in CD_2Cl_2 was added to reach final catalyst concentrations of 3 mol %. After the equilibrium was reached, a weighted amount of solid $Cu(CH_3CN)_4PF_6$ was added to reach a final template concentration of 2.5 mM. Then, an additional portion of a stock solution of catalyst **G2** in CD_2Cl_2 was added (3 mol % again) to ensure the efficiency of the metathetical process. Reaction runs were monitored by ^{1}H-NMR spectroscopy.

2,9-di(dodec-11-en-1-yl)-1,10-phenanthroline (2). Neocuproine (6.5 g, 31.2 mmol) was dissolved in dry THF (260 mL) and the obtained solution was degassed and brought at -78 °C. A 1.5 M solution of LDA in cyclohexane (42 mL, 63 mmol) was slowly added to this solution at -78 °C. After 4 hours, the reaction mixture was brought from -78 °C to 10 °C, and then brought back to -45 °C. At this temperature, a degassed solution of $BrCH_2(CH_2)_9CH{=}CH_2$ (16.3 mL, 75 mmol) in dry THF (325 mL) was added in 30 minutes to the reaction mixture. The reaction mixture was kept at 0 °C for 12 hours, after which the reaction was quenched by adding water until no gas evolution was observed. THF was evaporated and the residue was dissolved in CH_2Cl_2/H_2O 1:1. The two phases were separated and the water phase was extracted three times with CH_2Cl_2. The organic phases were dried over Na_2SO_4, filtered and evaporated to obtain 19.3 g of crude product (yellow wax), which was subjected to column chromatography (neutral Al_2O_3, Hexane 100 %→Hexane/Ethyl acetate 5:1) to give **2** as a white solid, 10 g, 19.5 mmol, 62.5% yield, recrystallizable from hexane. mp 67.1-67.7 °C. ^{1}H-NMR (300 MHz, $CDCl_3$, δ): 1.26-1.43 (m, 28H), 1.80-1.88 (m, 4H), 1.99-2.06 (m, 4H), 3.17 (t, J = 8 Hz, 4H), 4.89-5.02 (m, 4H), 5.74-5.85 (m, 2H), 7.53 (d, J = 8 Hz, 2H), 7.72 (s, 2H), 8.18 (d, J = 8 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ): 28.89, 29.10, 29.45, 29.49, 29.52 (br), 29.54, 29.75, 33.78, 39.21, 114.04, 122.53, 125.48, 127.09, 136.51, 139.21, 144.76, 163.20. HRMS-ESI TOF (m/z): [M+H$^+$] calcd for $C_{36}H_{52}N_2$, 513.4209; found, 513.4158; [M_2+Na$^+$] calcd for $C_{72}H_{104}N_4$ 1047.8183; found, 1047.8129. UV-vis (CH_2Cl_2) λ_{max}, nm (ε): 234 (53340); 271 (31200); 283 sh (19290).

Cyclic monomer $\mathbf{C_1}$. Compound **2** (400 mg, 0.78 mmol) was dissolved in CH_2Cl_2 (78 mL) and the resulting solution was degassed. First generation Grubbs catalyst **G1** (32 mg, 0.04 mmol) was then added and the resulting mixture was kept under stirring at room temperature for one day (the reaction was monitored by ESI-TOF MS). The solution was filtered through a short path of silica gel and the solution evaporated to afford 440 mg of crude material, which was subjected to column chromatography (neutral Al_2O_3, Hexane/Ethyl acetate 20:1) to afford compound $\mathbf{C_1}$ (white wax, 300 mg, 0.62 mmol, 79% yield). mp 127.3-132.2 °C (mixture of *cis* and *trans* isomers). ^{1}H-NMR (300 MHz, CD_2Cl_2, δ): 1.18-1.56 (m, 28H), 1.83-2.04 (m, 8H), 3.12 (t, J = 8 Hz, 4H), 5.32-5.38 (m, 2H), 7.50 (d, J = 8 Hz, 2H), 7.72 (s, 2H), 8.16 (d, J = 8 Hz, 2H). ^{13}C-NMR (75 MHz, CD_2Cl_2, δ): 27.14, 28.66, 29.22, 29.24, 29.27, 29.29, 29.33, 29.36, 29.57, 29.64, 29.75, 30.07, 30.14, 32.41, 39.21, 39.26, 122.72, 122.84, 125.52, 127.19, 129.96, 130.59, 136.43, 162.91. HRMS-ESI TOF (m/z): [M+Na$^+$] calcd for $C_{34}H_{48}N_2$, 507.3715; found, 507.3703. UV-vis (CH_2Cl_2) λ_{max}, nm (ε): 234 (41657); 271 (24392); 283 sh (15970).

Bis[2,9-di(dodec-11-en-1-yl)-1,10-phenanthroline]copper (I) hexafluorophosphate ($(\mathbf{2})_2$•Cu$^+$). Compound **2** (1.5 g, 2.93 mmol) was dissolved in CH_2Cl_2 (50 mL) and the resulting solution was degassed by freeze-pump-thaw technique, and then a previously degassed solution of $[Cu(CH_3CN)_4]PF_6$ (550 mg, 1.46 mmol) in CH_3CN was added to it. The resulting mixture passed from colourless to red and was kept under stirring at room temperature for 24 hours, after which the solvent was evaporated. The red residue was filtered, washed with water and dried to afford complex $(\mathbf{2})_2$•Cu$^+$ (red solid, 1.8 g, 1.46 mmol, 100% yield). mp 57.3-58.1 °C. ^{1}H-NMR (300 MHz, CD_2Cl_2, δ): 0.53-0.69 (m, 16H), 0.74-0.95 (m, 16H), 1.05-1.27 (m, 16H), 1.31-1.39 (m, 16H), 2.02-2.09 (m, 8H), 2.74 (t, J = 8 Hz, 8H), 4.95-5.06 (m, 8H), 5.79-5.92 (m, 4H), 7.80 (d, J = 8 Hz, 4H), 8.06 (s, 4H), 8.53 (d, J = 8 Hz, 4H). ^{13}C-NMR (75 MHz, CD_2Cl_2, δ): 28.89, 28.99, 29.15, 29.28, 29.35,

29.37, 29.40, 29.43, 29.93, 33.87, 40.51, 113.99, 125.01, 126.18, 127.90, 137.46, 139.32, 143.32, 162.03. HRMS-ESI TOF (*m*/*z*): [M+Cu^+] calcd for $C_{72}H_{104}N_4$, 1087.7557; found, 1087.7584. UV-vis (CH_2Cl_2) λ_{max}, nm (ε): 229 (67490); 243 sh (34180); 276 (55086); 296 sh (31730); 459 (6807).

Catenate 1•Cu^+. Complex (**2**)$_2$•Cu^+ (1.05 g, 0.85 mmol) was dissolved in CH_2Cl_2 (85 mL) and the resulting solution was degassed. 1st generation Grubbs' catalyst **G1** (35 mg, 0.04 mmol) was then added and the resulting mixture was kept under stirring at room temperature for three days (the reaction was monitored by ESI-TOF MS). The solution was filtered through a short path of silica gel and the solution evaporated to afford complex **1** (orange solid, 920 mg, 0.76 mmol, 92% yield). mp 268.3-270.1 °C. ^{1}H-NMR (300 MHz, CD_2Cl_2, δ): 0.46-0.67 (m, 24H), 0.98-1.05 (m, 8H), 1.24-1.48 (m, 28H), 1.73-1.84 (m, 6H), 2.12-2.29 (m, 8H), 2.65-2.78 (m, 8H), 5.71-5.78 (m, 4H), 7.77 (d, *J* = 8 Hz, 4H), 8.03 (s, 4H), 8.49 (d, *J* = 8 Hz, 4H). ^{13}C-NMR (75 MHz, CD_2Cl_2, δ): 29.05, 29.39, 29.41, 29.63, 29.73, 29.76, 30.60, 32.07, 33.21, 40.47, 125.08, 126.37, 127.80, 131.03, 137.54, 143.25, 162.07. HRMS-ESI TOF (*m*/*z*): [M+Cu^+] calcd for $C_{68}H_{96}N_4$, 1031.6931; found, 1031.6919. HRMS-MALDI TOF (*m*/*z*): [M+Cu^+] calcd for $C_{68}H_{96}N_4Cu$, 1031.6931; found, 1031.6938. UV-vis (CH_2Cl_2) λ_{max}, nm (ε): 232 (59630); 244 sh (31110); 276 (49210); 293 sh (29310); 324 (4490); 467 (6030).

Catenand 1. Catenate **1**•Cu^+ (920 mg, 0.76 mmol) was dissolved in wet CH_3CN (200 mL). Excess KCN (33 g, 500 mmol) was added at room temperature. The heating was turned on and the refluxing suspension was kept under stirring for 4 hours, through which the colour passed from red to colourless. The solvent was removed and the residue dissolved in CH_2Cl_2. The organic phase was washed three times with an ammonia solution (0.1 M, 100 mL), dried over Na_2SO_4, filtered and evaporated to afford compound **1** (white wax, 735 mg, 0.76 mmol, 100% yield). mp 164.2-170.1° C. The ^{1}H-NMR spectrum shows additional signals related to chemical exchange in the NMR time scale due to protonation of **1**. ^{1}H-NMR (300 MHz, CD_2Cl_2, δ): 1.18-1.36 (m, 56H), 1.65-1.82 (m, 8H), 1.86-2.05 (m, 8H), 3.02-3.09 (m, 8H), 5.41-5.47 (m, 4H), 7.44 (d, *J* = 8 Hz, 4H), 7.67 (s, 4H), 8.10 (d, *J* = 8 Hz, 4H). ^{13}C-NMR (75 MHz, CD_2Cl_2, δ): 29.10, 29.24, 29.44, 29.49, 29.55, 29.70, 29.97, 30.49, 30.72, 32.82, 39.91, 40.21, 122.08, 122.25, 125.41, 127.08, 130.32, 135.96, 145.83, 162.81. HRMS-ESI TOF (*m*/*z*): [M+H^+] calcd for $C_{68}H_{96}N_4$, 969.7713; found, 969.7711; [M+Na^+] calcd for $C_{68}H_{96}N_4$, 991.7533; found, 991.7526. HRMS-MALDI TOF (*m*/*z*): [M+H^+] calcd for $C_{68}H_{96}N_4$, 969.7713; found, 969.7747. UV-vis (CH_2Cl_2) λ_{max}, nm (ε): 234 (97910); 271 (58420); 283 sh (37560).

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† Electronic Supplementary Information (ESI) available: ^{1}H NMR and ^{13}C NMR spectra of new compounds, 2D NMR spectra of **1** and **1**•Cu^+, stacks of spectra of the equilibration experiment at 5 mM c_{mon} (Fig. ESI 1) and of selected equilibration experiments starting either from $\mathbf{C_1}$ or **1** (Fig. ESI 2). See DOI: 10.1039/b000000x/

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$$SE = -RT \ln(0.022 / 0.061) = 0.6 \text{ kcal mol}^{-1}$$

Where 0.022 M is the given experimental EM_1 from Fig. 4 and 0.061 M is the ideal EM_1 predicted for a strainless ring whose ease of formation is solely determined by the conformational entropy loss upon cyclization of a chain precursor composed of 22 rotatable single bonds (see ref 26). Although too much emphasis cannot be placed on exact figures, the picture which emerges is one where the SE of $\mathbf{C_1}$, if any, should amount to a fraction of a kcal mol^{-1}.

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