



**Discoveries from a Phenanthroline-based Dynamic Combinatorial Library: Catenane from Copper(I) or Copper(II) Template?**

Journal:	<i>Inorganic Chemistry Frontiers</i>
Manuscript ID	QI-RES-10-2015-000227.R1
Article Type:	Research article
Date Submitted by the Author:	04-Dec-2015
Complete List of Authors:	Tong, King-Lung; University of Hong Kong, Department of Chemistry Yee, Chi-Chung; University of Hong Kong, Department of Chemistry Tse, Yuen Cheong; University of Hong Kong, Department of Chemistry Au-Yeung, Ho Yu; University of Hong Kong, Department of Chemistry



Journal Name

ARTICLE

## Discoveries from a Phenanthroline-based Dynamic Combinatorial Library: Catenane from Copper(I) or Copper(II) Template?

Received 00th January 20xx,  
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

King-Lung Tong<sup>†</sup>, Chi-Chung Yee<sup>†</sup>, Yuen Cheong Tse and Ho Yu Au-Yeung<sup>\*a</sup>

We report here a DCL study of a phenanthroline-based building block focusing on catenane formation with copper templates. Two [2]catenanes have been amplified by using Cu<sup>+</sup> as template from the DCLs that contains no interlocked compound in the absence of copper. In addition, an unexpected Cu<sup>2+</sup> template effect on the [2]catenane formation was discovered. The observed Cu<sup>2+</sup> template effect was found to be originated from the *in situ* reduction of the divalent metal to Cu<sup>+</sup>.

### Introduction

Dynamic combinatorial chemistry (DCC),<sup>1</sup> a selection approach of assembling molecular building blocks under thermodynamic control through reversible linkages, has been demonstrated as an efficient strategy for the discovery of unexpected yet successful molecular receptors,<sup>2</sup> biological ligands/inhibitors<sup>3</sup> or complex molecular topologies,<sup>4</sup> whose structures and syntheses could be unpredictable and/or unattainable. For example, Sanders and co-workers have recently reported a series of elegant examples of complex interlocked architectures including catenanes,<sup>5</sup> Solomon link<sup>6</sup> and trefoil knots,<sup>7</sup> that are otherwise unpredicted and extremely challenging to be synthesized, from aqueous disulfide dynamic combinatorial libraries (DCLs) using simple linear building blocks that can engage in aromatic donor-acceptor and hydrophobic interactions. If molecules having structures that are predesigned to favour catenane formation are used as building blocks in DCL, complex catenanes and other unexpected but potentially highly complicated molecular topologies could be obtained from this self-directing and self-selecting assembly approach. Since the orthogonal ligand arrangement from the tetrahedral phenanthroline-Cu<sup>I</sup> coordination is one of the most successful preorganization strategies for catenane assembly,<sup>8</sup> we propose the use of building blocks derived from the phenanthroline ligand will efficiently generate DCLs of interlocked structures plus other complex topologies when templated by Cu<sup>+</sup>, allowing the study of complex molecular topologies under thermodynamically-controlled conditions. We report here our initial study on the use of a phenanthroline-based dialdehyde building block for the generation of dynamic combinatorial libraries of catenanes<sup>9</sup> using hydrazone as

the exchange reaction. The DCL behaviour, amplification of two [2]catenanes by Cu<sup>+</sup> template and their characterisation are described. We also discovered an unexpected Cu<sup>2+</sup> template effect on the assembly of the [2]catenanes. Further experiments on the coordination chemistry of model systems revealed that the observed template effect from Cu<sup>2+</sup> is originated from the Cu<sup>+</sup> generated by the *in situ* reduction of the divalent metal ion. This unexpected template effect of Cu<sup>2+</sup> was also applied in the assembly of catenanes under non-DCL conditions. It is believed that the studies of the Cu<sup>+</sup>-phenanthroline coordination motif under DCL conditions could offer an unique opportunity for studying the assembly of catenane and other possible, but not necessarily predictable or imaginable, complex molecular topologies under thermodynamic control, and eventually unveil the rules governing the self-assembly process of these complicated molecular entities.

### Results and discussion

#### Building blocks designs and synthesis

The structure and synthesis of the phenanthroline-based building block **1** is depicted in Scheme 1. The bidentate phenanthroline **1** is designed to coordinate to Cu<sup>+</sup> in a tetrahedral geometry and that the terminal aldehydes are for hydrazone exchange with dihydrazide building blocks. Two dihydrazide building blocks were synthesized and studied. Dihydrazide **2** has a flexible tetraethyleneglycol linker, whereas **3** contains the  $\pi$ -rich dioxynaphthalene unit for possible recognition with complementary  $\pi$ -deficient aromatics.

#### DCL studies and Cu<sup>I</sup>-templated catenane formation

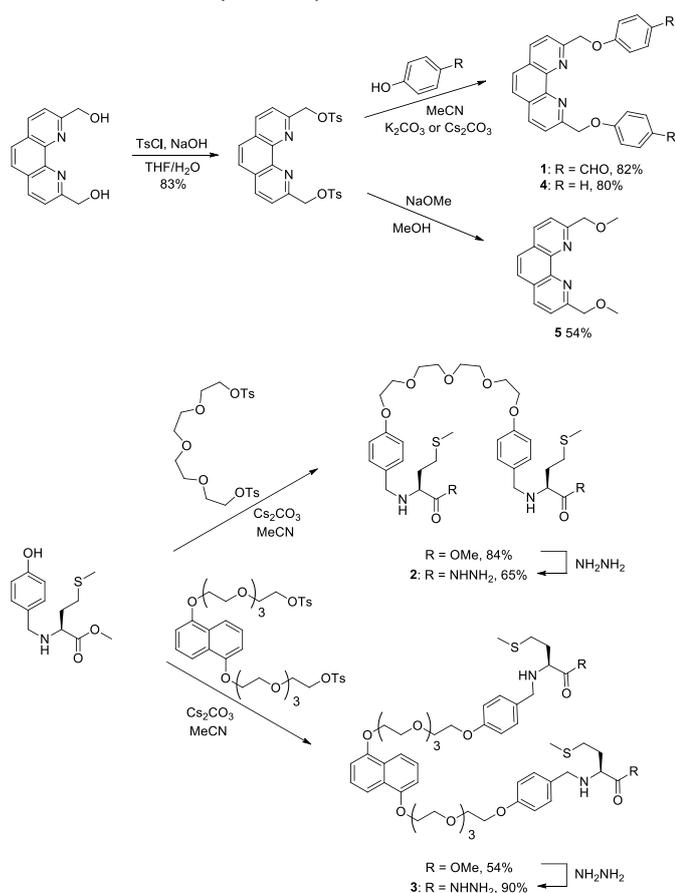
The first hydrazone DCL was prepared by dissolving 1 mM each of the building blocks **1** and **2** in CHCl<sub>3</sub>/MeOH/CF<sub>3</sub>COOH (10:10:1). The library solution was analysed by LCMS after 3 days. The HPLC chromatogram showed that the [1+1]macrocycle **M1** is the dominant species in the DCL, and it represents 96% of the library materials with the remaining 4% as the [2+2]macrocycles **M2** (Fig.

<sup>a</sup> Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, PR China.

<sup>†</sup> KLT and CCY contributed equally.

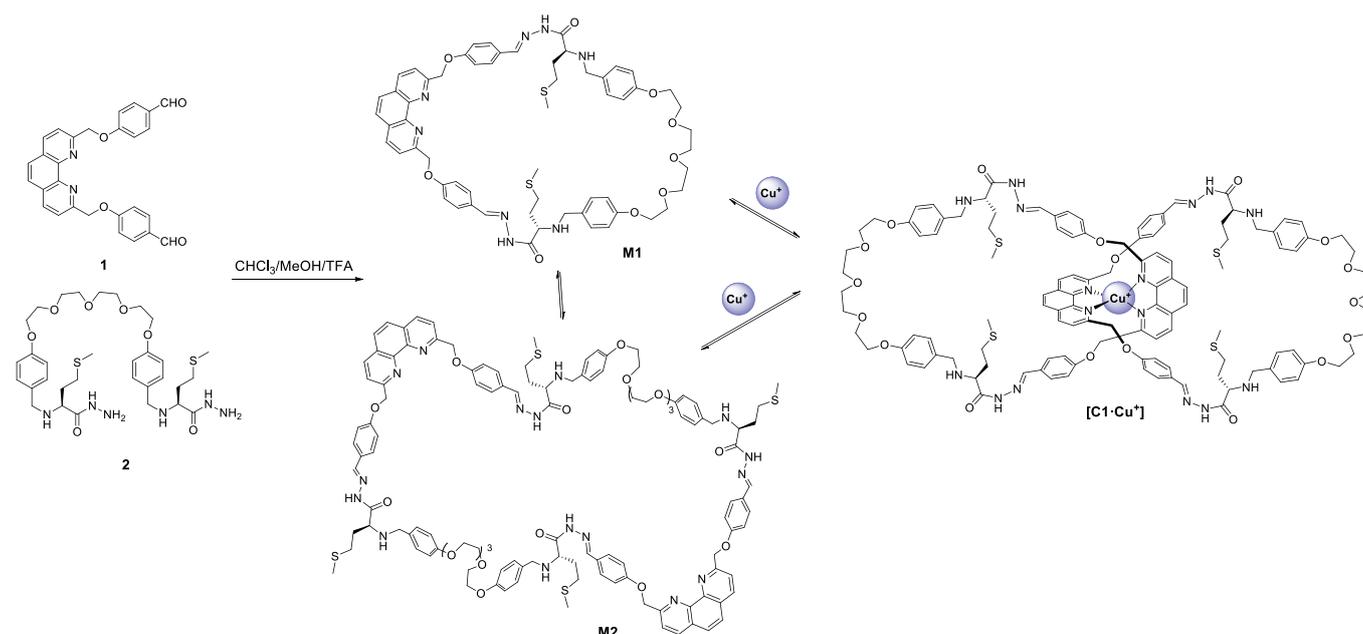
Electronic Supplementary Information (ESI) available: detailed synthesis, NMR, MS, HPLC, and X-ray crystallographic data. See DOI: 10.1039/x0xx00000x

1). Further analysis of the DCL at later time points (i.e. 5 and 7 days) revealed the same library composition, suggesting that the library has reached thermodynamic equilibrium.



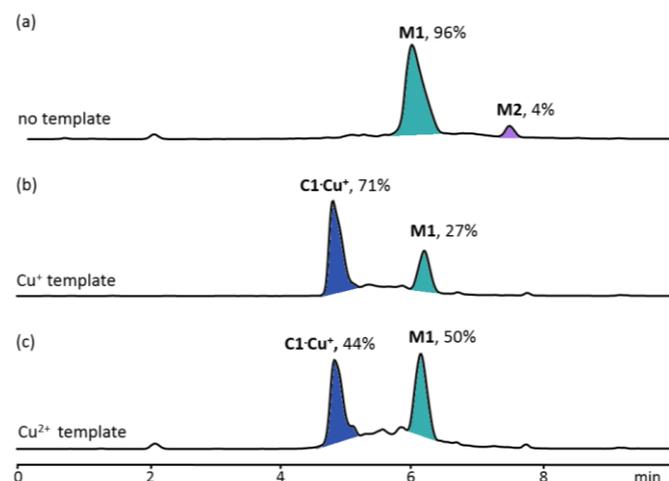
**Scheme 1.** Synthesis of the dialdehyde building block **1**, the dihydrazides **2** and **3**, and the phenanthroline derivatives **4** and **5**.

When the DCL was prepared in the presence of 0.5 mM  $\text{Cu}^+$ , a library of a different composition was obtained. Addition of  $\text{Cu}^+$  to the DCL templated the formation of a new species ( $\text{C1}\cdot\text{Cu}^+$ ), which was not detectable in the metal-free DCL, to 71% at the expense of other library members. Pure sample of  $\text{C1}\cdot\text{Cu}^+$  can be obtained by preparative HPLC or flash column chromatography for further analysis (see ESI for details). Results from ESI-MS, HRMS and MS/MS studies on  $\text{C1}\cdot\text{Cu}^+$  are consistent with an interlocked structure (Fig. 2). The mass spectrum of  $\text{C1}\cdot\text{Cu}^+$  shows peaks at  $m/z = 571.4$  [ $\text{C1}+\text{Cu}+3\text{H}$ ] $^{4+}$ , 761.5 [ $\text{C1}+\text{Cu}+2\text{H}$ ] $^{3+}$  and 1141.3 [ $\text{C1}+\text{Cu}+\text{H}$ ] $^{2+}$  that correspond to the tetra-, tri- and di-cation of  $\text{C1}\cdot\text{Cu}^+$  respectively. Fragmentation of the ion at  $m/z = 1141.3$  [ $\text{C1}+\text{Cu}+\text{H}$ ] $^{2+}$  directly resulted in daughter ions at  $m/z = 1109.3$  and 1171.3 that correspond to [ $\text{M1}+\text{H}$ ] $^+$  and [ $\text{M1}+\text{Cu}$ ] $^+$ . The observation that a [2+2] species directly fragment to a [1+1] and other smaller species without any other fragments with  $m/z$  larger than that of the [1+1] macrocycle is typical for a catenane, as other topologies such as a [2+2] macrocycle or a molecular figure-of-eight tied by  $\text{Cu}^+$  coordination should produce larger fragments such as those derived from the [2+2] or [2+1] building block combination in the MS/MS experiments.<sup>4a-c,5,10</sup> Furthermore, to further confirm the catenane topology, the metal-free **C1** obtained from treatment of  $\text{C1}\cdot\text{Cu}^+$  with NaCN was also analysed by MS and MS/MS. The mass spectrum of the sample showed a peak at  $m/z = 1132.3$  [ $\text{C1}+2\text{Na}$ ] $^{2+}$  that corresponds to the expected copper free **C1**. MS/MS analysis of **C1** again resulted in only **M1** ( $m/z = 1131.4$  [ $\text{M1}+\text{Na}$ ] $^+$ ) and its fragments ( $m/z = 1088.3, 1040.4, 1013.3$  and 987.3) as the only species observed in the MS/MS experiment (Fig. 2). No larger species than that derived from **M1** was observed in the tandem mass spectrum, further confirming the catenane topology of **C1** and that a [2]catenane was successfully amplified by the  $\text{Cu}^+$  template from the dynamic library upon the anticipated phenanthroline- $\text{Cu}^+$  coordination.  $^1\text{H}$  NMR studies on  $\text{C1}\cdot\text{Cu}^+$  revealed multiple sets of overlapped resonances in the aromatic region, suggesting the presence of different inequivalent conformations of the catenane.



**Scheme 2.** Generation of hydrazone DCL from dialdehyde **1** and dihydrazide **2**. The [2]catenane  $\text{C1}\cdot\text{Cu}^+$  was amplified by  $\text{Cu}^+$  template.

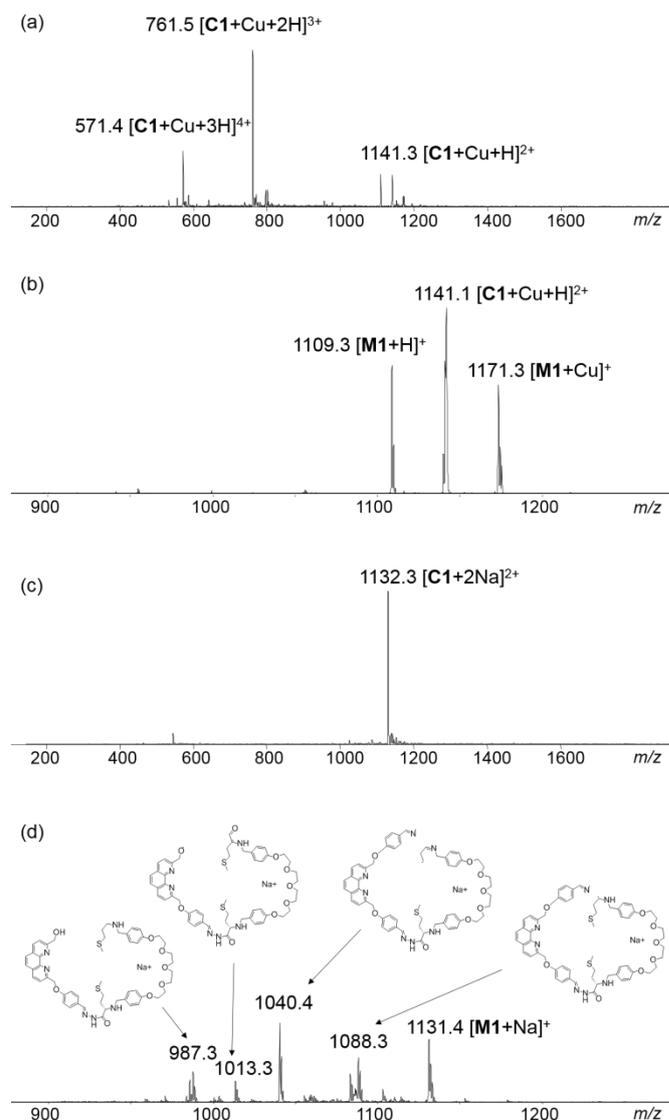
Indeed, the  $^1\text{H}$  NMR spectrum of **M1** does show at least six different sets of aromatic signals that are identified as the phenylene protons from the corresponding COSY spectrum (Fig. S19, S20), suggesting that both the *syn* and *anti* isomers of the hydrazone are present in **M1** (and also most likely in **C1** $\cdot\text{Cu}^+$ ) that lead to the inequivalent aromatic chemical environments.



**Fig. 1** HPLC analysis of a 1 mM DCLs of **1** and **2** (a) in the absence of template and in the presence of 0.5 mM of (b)  $\text{Cu}^+$  and (c)  $\text{Cu}^{2+}$ . Absorbance was monitored at 285 nm.

The dynamic nature of the catenane assembly was studied by a series of equilibration experiments. First, instead of adding the  $\text{Cu}^+$  template at the beginning of the DCL preparation, the metal ion was added to a DCL that has been equilibrated for 3 days. Concentration of **C1** $\cdot\text{Cu}^+$  in the DCL gradually increased from undetectable to *ca.* 70% with the remaining 30% as **M1**, which is almost the same as that of the DCL prepared when  $\text{Cu}^+$  was introduced at the beginning of the DCL evolution (Fig. S28). The observation that the same equilibrium position could be reached from two different starting points suggests that the library is dynamic and is under thermodynamic control.<sup>11</sup> Second, the effect of the building block concentration on the equilibrium position and yield of **C1** $\cdot\text{Cu}^+$  was studied. DCLs with different concentrations of **1** and **2** were setup and their equilibrium compositions were compared. In accord with the Le Châtelier's principle, an increase in the yield of **C1** $\cdot\text{Cu}^+$  was observed from 36% to 71% to 93% when the building block concentrations were increased from 0.1 mM to 1 mM to 5 mM at a building block/ $\text{Cu}^+$  ratio of 2:1 (Fig. S26). Third, effect of the  $\text{Cu}^+$  template to building block ratio was studied. DCLs with 0.1, 0.5, 1 and 2 eq. of  $\text{Cu}^+$  relative to **1** were prepared. From 0.1 eq. to 0.5 eq. of  $\text{Cu}^+$ , an increase in the yield of **C1** $\cdot\text{Cu}^+$  from 17% to 71% was observed. Further increasing the template concentration to 1 eq. and 2 eq. of  $\text{Cu}^+$  relative to **1**, on the other hand, lead to a decrease of the yield of **C1** $\cdot\text{Cu}^+$  to 68% to 48% respectively (Fig. S27). Presumably, at  $\text{Cu}^+$  concentration below 0.5 eq., increase in the concentration of  $\text{Cu}^+$  templates the formation of the 2:1

phenanthroline- $\text{Cu}^+$  complex and lead to a higher yield of **C1** $\cdot\text{Cu}^+$ . However, further increase in  $\text{Cu}^+$  concentration could shift the equilibrium towards the 1:1 phenanthroline- $\text{Cu}^+$  complex which favors the formation of the macrocycle instead of the [2]catenane.



**Fig. 2** ESI-MS analysis of **C1** $\cdot\text{Cu}^+$  and **C1**. (a) The MS and (b) MS/MS spectra of **C1** $\cdot\text{Cu}^+$ . The MS/MS spectrum was obtained from fragmenting the peak at  $m/z = 1141.3$ . (c) The MS of spectrum **C1**; and (d) the MS/MS spectrum from fragmentation of the peak at  $m/z = 1132.3$ .

A similar hydrazone DCL was also prepared from **1** and **3** under the same conditions (Scheme S4). The library mixture was analysed by LCMS which showed the [1+1]macrocycle **M3** as the only detectable library member. No [2+2]macrocycle similar to **M2** was found. Similar to the DCL of **1** and **2**, the presence of 0.5 mM  $\text{Cu}^+$  templates the formation of the [2]catenane **C2** $\cdot\text{Cu}^+$  to 90% (Fig. S26). The interlocked structure of **C2** $\cdot\text{Cu}^+$  and its metal-free form **C2** were also characterised by ESI-MS and MS/MS. Fragmentation behaviour

similar to that of **C1**·Cu<sup>+</sup> and **C1** was observed, confirming the catenane topology of **C2**·Cu<sup>+</sup> (Fig. S34, S35). Since building block **3** is designed with the  $\pi$ -rich dioxynaphthalene core for further molecular recognition with complementary  $\pi$ -deficient unit, we tested if the use of the  $\pi$ -deficient cyclobisparaquat(*p*-phenylene) (CBPQT<sup>4+</sup>)<sup>12</sup> macrocycle could amplify other interlocked compounds from the DCL. Due to the insolubility of CBPQT<sup>4+</sup> under the DCL condition, attempts to use the  $\pi$ -deficient macrocycle as template, in the form of a concentrated MeCN solution, were unsuccessful. LCMS analysis of the filtered library solution revealed the presence of only **C2**·Cu<sup>+</sup> and **M3**, in a distribution as if the macrocyclic template was not added (Fig. S29). No incorporation of the  $\pi$ -deficient unit to the  $\pi$ -rich library members was observed.

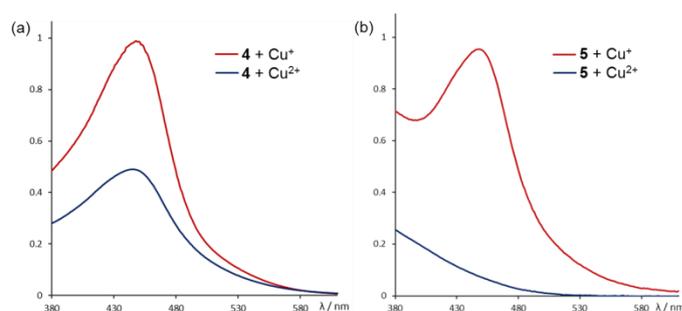
### Cu<sup>II</sup> templates catenane formation in DCL

In addition to Cu<sup>+</sup>, other metal ions including Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup>, Al<sup>3+</sup>, Mn<sup>2+</sup>, Fe<sup>2+</sup>, Fe<sup>3+</sup>, Co<sup>2+</sup>, Ni<sup>2+</sup>, Cd<sup>2+</sup>, Ce<sup>3+</sup> and Er<sup>3+</sup> were also tested as templates for the DCL of **1** and **2**. While these metal ions did not perturb the equilibrium position and the same library compositions as the metal-free DCL were observed (Fig. S25), **C1**·Cu<sup>+</sup> was amplified by addition of Cu<sup>2+</sup>. While the redox switching of Cu<sup>2+/+</sup> has been demonstrated to induce the circumrotation and conformation change of catenanes and other complex topologies with variable coordination geometry and coordination number,<sup>13</sup> templating [2]catenane assembly from two bidentate phenanthroline precursors by Cu<sup>2+</sup> is not known as far as we are concerned. Compared with the Cu<sup>+</sup> template, Cu<sup>2+</sup> only amplifies **C1**·Cu<sup>+</sup> to 44% of the library materials. The lower efficiency of Cu<sup>2+</sup> to template **C1** in the DCL may suggest that 1) Cu<sup>2+</sup> coordination to the [2]catenane is thermodynamically less stable than that of Cu<sup>+</sup> or 2) the mechanism of Cu<sup>2+</sup> template involves not only Cu<sup>2+</sup>-phenanthroline coordination.

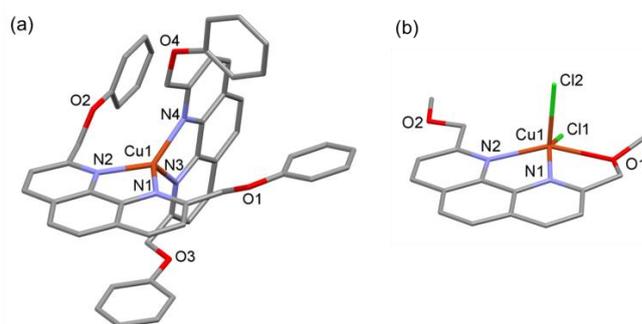
### In situ reduction of Cu<sup>II</sup> to Cu<sup>I</sup>

To elucidate the origin of Cu<sup>2+</sup> template effect on the [2]catenane assembly, the coordination chemistry of the phenanthroline derivative **4** and **5** to Cu<sup>2+</sup> was studied. Complexation of **4** to CuCl<sub>2</sub> in 2:1 ratio in CH<sub>2</sub>Cl<sub>2</sub>/MeOH at room temperature initially resulted in a yellow solution that gradually turned red. UV-Vis analysis showed that the red species has an absorption maximum at 445 nm which is consistent with the reported MLCT band of Cu<sup>I</sup>-phenanthroline (Fig. 3a).<sup>14</sup> The absorption spectrum also resembles to that of the independently synthesized [Cu(**4**)<sub>2</sub>][PF<sub>6</sub>], indicating a reduction of Cu<sup>2+</sup> to Cu<sup>+</sup> upon coordination of **4** under the experimental conditions. Similar Cu<sup>II</sup> to Cu<sup>I</sup> reduction has also been observed in cross-coupling reactions involving copper as the catalysts,<sup>15</sup> but such effect in molecular self-assembly involving the metal is not known. By comparing the relative absorbance, a ca. 60% conversion of Cu<sup>II</sup> to Cu<sup>I</sup> has been estimated, which correlates very well with the observed relative yields (71% vs. 44%) of **C1**·Cu<sup>+</sup> in the corresponding DCLs. The observed *in situ* reduction is also supported by <sup>1</sup>H NMR studies. The red solution obtained from a 2:1 mixture of **4** and CuCl<sub>2</sub> in CD<sub>3</sub>CN showed no paramagnetically shifted resonances due to the d<sup>9</sup> Cu<sup>II</sup>, and that the <sup>1</sup>H spectrum is consistent with the formation of [Cu(**4**)<sub>2</sub>]<sup>+</sup> (Fig. S24).

Presumably, the tetrahedral coordination geometry enforced by the two phenanthrolines modulates the reduction potential of Cu<sup>II/I</sup> such that Cu<sup>2+</sup> could be reduced to Cu<sup>+</sup>, possibly by protic reagents, upon coordination to the bidentate ligand under the experimental conditions.<sup>15,16</sup> X-ray structure of [Cu(**4**)<sub>2</sub>][PF<sub>6</sub>] revealed the expected tetrahedral coordination geometry around the metal (Fig. 4a). In addition, the observed  $\pi$ -stacking interaction between the phenanthroline and the aromatic substituents may also reinforce the stability of the tetrahedral coordination motif and facilitate the *in situ* reduction. Indeed, the complexation reaction of **5** to Cu<sup>2+</sup> resulted in a much less efficient reduction to Cu<sup>+</sup> as evident by both UV-Vis and <sup>1</sup>H NMR studies (Fig. 3b and S24). X-ray diffraction study of the crystalline product obtained from a 2:1 mixture of **5** and CuCl<sub>2</sub> showed only the 5-coordinated [Cu(**5**)Cl<sub>2</sub>] with a distorted square pyramidal structure (Fig 4b). The formation of such 1:1 complex suggests that Cu<sup>2+</sup>-phenanthroline coordination alone is not sufficient to explain the observed amplification of the [2]catenane in the DCL because the required preorganized ML<sub>2</sub> complex could not be formed. Together with the UV-Vis and NMR data, it is believed that the reduction of Cu<sup>2+</sup> to Cu<sup>+</sup>, and the subsequent formation of the tetrahedral ML<sub>2</sub> complex constitute the major part of the observed template effect.



**Fig. 3** UV-Vis spectra of a 2:1 complex mixture of the phenanthroline ligands (a) **4** and (b) **5** with Cu<sup>+</sup> (red) and Cu<sup>2+</sup> (blue). The absorption band at 445 nm is assigned as the Cu<sup>I</sup>-phenanthroline MLCT.<sup>13</sup>

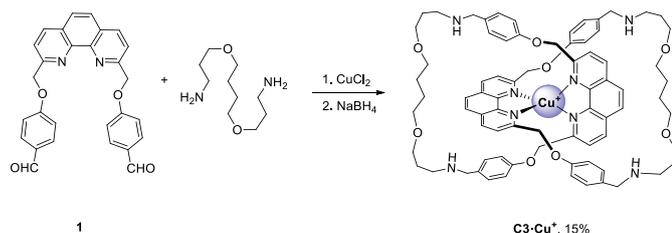


**Fig. 4** Molecular structures of (a) [Cu<sup>I</sup>(**4**)<sub>2</sub>]<sup>+</sup> (the PF<sub>6</sub><sup>-</sup> anion is omitted for clarity) and (b) [Cu<sup>II</sup>(**5**)Cl<sub>2</sub>]. Selected bond lengths (Å) and angles (deg) for [Cu<sup>I</sup>(**4**)<sub>2</sub>]<sup>+</sup>: Cu1–N1 2.029(2), Cu1–N2 2.038(3), Cu1–N3 2.048(3), Cu1–N4 2.032(3); N1–Cu1–N2 82.1(8), N3–Cu1–N4 82.2(7), N1–Cu1–N3 123.5(7), N2–Cu1–N4 132.8(8); for [Cu<sup>II</sup>(**5**)Cl<sub>2</sub>]: Cu1–N1

1.955(2), Cu1–N2 2.135(2), Cu1–O1 2.256(2); N1–Cu1–N2 80.7(9), N1–Cu1–O1 74.1(3), O1–Cu1–Cl1 90.3(9), N2–Cu1–Cl1 105.8(1).

### Templating another [2]catenane assembly by Cu<sup>2+</sup>

We also tested if the Cu<sup>2+</sup> template can be applied in the assembly of catenane in conditions other than that of the hydrazone DCL. We chose to study the assembly of catenane from **1** and 4,7-dioxadodecanediamine via a reductive amination reaction due to the wide applicability of imine formation in the synthesis of interlocked systems. Heating an equimolar solution of **1** and 4,7-dioxadodecanediamine (10 mM each) in the presence of 5 mM CuCl<sub>2</sub> for overnight in MeCN/CHCl<sub>3</sub> resulted in a red solution that is consistent with the previously observed Cu<sup>2+</sup> to Cu<sup>+</sup> reduction. To aid analysis, the dynamic imine was reduced to the corresponding secondary amine by NaBH<sub>4</sub>. Albeit in a lower yield than if Cu<sup>+</sup> is used as the template (58%), a [2]catenane **C3-Cu<sup>+</sup>** was successfully assembled in 15% (Scheme 3), demonstrating the feasibility of using Cu<sup>2+</sup> as the template for construction of molecular architectures with phenanthroline-based building blocks. The interlocked structure of **C3-Cu<sup>+</sup>** has been confirmed by NMR, ESI-MS and MS/MS (Fig. S22, S23, S36, S37).



**Scheme 3.** Self-assembly of **C3-Cu<sup>+</sup>** using CuCl<sub>2</sub> as template.

### Conclusions

In summary, the DCL behaviour of a phenanthroline-based dialdehyde building block for catenane assembly has been studied. Two [2]catenanes have been amplified in high yields by using Cu<sup>+</sup> as template. Unexpectedly, it is found that Cu<sup>2+</sup>, upon *in situ* reduction, could also lead to the formation of the interlocked compounds under both DCL and non-DCL conditions. The discovery of the Cu<sup>2+</sup>-template effect on catenane assembly not only suggests that a larger variety of copper salts could be used for molecular self assembly involving the versatile phenanthroline motif under different assembly conditions, but also highlights the relatively less explored application of DCC that it assists the discovery of alternative templates for an assembly event. Further studies of the dynamic combinatorial assembly of other complex interlocked structures using other building blocks, and diversifying the DCL composition by increasing the library complexity are currently underway.

### Acknowledgements

Financial supports from the URC, The University of Hong Kong under the Seed Funding programme for Basic Research (project code 201310159019) and the Croucher Foundation are gratefully acknowledged. We thank Dr. Lap Szeto and Mr. Kai Wang for technical assistance on X-ray crystallography and ESI-MS analysis, respectively. KLT and CCY also thank The University of Hong Kong for the provision of Postgraduate Scholarship. YCT is a recipient of the Summer Research Fellowship administered by the Faculty of Science, The University of Hong Kong.

### Notes and references

- (a) J.-M. Lehn, *Chem. Eur. J.*, 1999, **5**, 2455; (b) P. T. Corbett, J. Leclaire, L. Vial, K. R. West, J.-L. Wietor, J. K. M. Sanders and S. Otto, *Chem. Rev.*, 2006, **106**, 3652; (c) J.-M. Lehn, *Chem. Soc. Rev.*, 2007, **36**, 151; (d) S. Ladame, *Org. Biomol. Chem.*, 2008, **6**, 219; (e) F. B. L. Cougnon, J. K. M. Sanders, *Acc. Chem. Res.*, 2012, **45**, 2211.
- For recent examples: (a) L. I. James, J. E. Beaver, N. W. Rice and M. L. Waters, *J. Am. Chem. Soc.*, 2013, **135**, 6450; (b) S. Hamieh, V. Saggiomo, P. Nowak, E. Mattia, R. F. Ludlow and S. Otto, *Angew. Chem. Int. Ed.*, 2013, **52**, 12368; (c) N. K. Pinkin and M. L. Waters, *Org. Biomol. Chem.*, 2014, **12**, 7059; (d) J. E. Beaver, B. C. Peacor, J.V. Bain, L.I. James and M. L. Waters, *Org. Biomol. Chem.*, 2015, **13**, 3220; (e) J. Li, P. Nowak and S. Otto, *Angew. Chem. Int. Ed.*, 2015, **54**, 833.
- For recent examples: (a) M. Demetriades, I. K. H. Leung, R. Chowdhury, M. C. Chan, M. A. McDonough, K. K. Yeoh, Y.-M. Tian, T. D. W. Claridge, P. J. Ratcliffe, E. C. Y. Woon and C. J. Schofield, *Angew. Chem. Int. Ed.*, 2012, **51**, 6672; (b) M. Mondal, N. Radeva, H. Köster, A. Park, C. Potamitis, M. Zervou, G. Klebe and A. K. H. Hirsch, *Angew. Chem. Int. Ed.*, 2014, **53**, 3259; (c) Q.-Q. Jiang, W. Sicking, M. Ehlers and C. Schmuck, *Chem. Sci.*, 2015, **6**, 1792; (d) M. Mondal and A. K. H. Hirsch, *Chem. Soc. Rev.*, 2015, **44**, 2455.
- (a) R. T. S. Lam, A. Belenguer, S. L. Roberts, C. Naumann, T. Jarrosson, S. Otto and J. K. M. Sanders, *Science*, 2005, **308**, 667; (b) H. Y. Au-Yeung, G. Dan Pantoş and J. K. M. Sanders, *Proc. Natl. Acad. Sci. USA.*, 2009, **106**, 10466; (c) F. B. L. Cougnon, N. A. Jenkins, G. D. Pantoş and J. K. M. Sanders, *Angew. Chem. Int. Ed.*, 2012, **51**, 1443; (d) M.-K. Chung, S. J. Lee, M. L. Waters and M. R. Gagné, *J. Am. Chem. Soc.*, 2012, **134**, 11430; (e) J. Li, P. Nowak, H. Fanlo-Virgós and S. Otto, *Chem. Sci.*, 2014, **5**, 4968; (f) H. Wilson, S. Byrne and K. M. Mullen, *Chem. Asian J.*, 2015, **10**, 715.
- (a) H. Y. Au-Yeung, G. D. Pantoş and J. K. M. Sanders, *J. Am. Chem. Soc.*, 2009, **131**, 16030; (b) H. Y. Au-Yeung, G. D. Pantoş and J. K. M. Sanders, *J. Org. Chem.*, 2011, **76**, 1257; (c) F. B. L. Cougnon, H. Y. Au-Yeung, G. D. Pantoş and J. K. M. Sanders, *J. Am. Chem. Soc.*, 2011, **133**, 3198; (d) F. B. L. Cougnon, N. Ponnuswamy, N. A. Jenkins, G. D. Pantoş and J. K. M. Sanders, *J. Am. Chem. Soc.*, 2012, **134**, 19129.
- N. Ponnuswamy, F. B. L. Cougnon, G. D. Pantoş and J. K. M. Sanders, *J. Am. Chem. Soc.*, 2014, **136**, 8243.
- N. Ponnuswamy, F. B. L. Cougnon, J. M. Clough, G. D. Pantoş, J. K. M. Sanders, *Science*, 2012, **338**, 783.
- C. O. Dietrich-Buchecker and J.-P. Sauvage, *Chem. Rev.*, 1987, **87**, 795.
- J. A. Berrocal, M. M. L. Nieuwenhuizen, L. Mandolini, E. W. Meijer and S. D. Stefano, *Org. Biomol. Chem.*, 2014, **12**, 6167.
- (a) P. Bäuerle, M. Ammann, M. Wilde, G. Götz, E. Menz-Osteritz, A. Rang and C. A. Schalley, *Angew. Chem., Int. Ed.*, 2007, **46**, 363; (b) S.-A. Poulsen, P. J. Gates, G. R. L. Cousins

- and J. K. M. Sanders, *Rapid Commun. Mass Spectrom.*, 2000, **14**, 44.
- 11 Attempt to reverse the library composition from the catenane to the macrocycle by removal of the Cu<sup>+</sup> template was not tested because of the incompatibility of common demetallating reagents such as CN<sup>-</sup> with the acidic DCL condition.
- 12 For recent examples: (a) C. Wang, S. M. Dyar, D. Cao, A. C. Fahrenbach, N. Horwitz, M. T. Colvin, R. Carmieli, C. L. Stern, S. K. Dey, M. R. Wasielewski and J. F. Stoddart, *J. Am. Chem. Soc.*, 2012, **134**, 19136; (b) H. Liu, X.-Y. Li, X.-L. Zhao, Y. A. Liu, J.-S. Li, B. Jiang and K. Wen, *Org. Lett.*, 2014, **16**, 5894; (c) W.-B. Hu, W.-J. Hu, X.-L. Zhao, Y. A. Liu, J.-S. Li, B. Jiang and K. Wen, *Chem. Commun.*, 2015, **51**, 13882.
- 13 (a) A. Livoreil, C. O. Dietrich-Buchecker and J.-P. Sauvage, *J. Am. Chem. Soc.*, 1994, **116**, 9399; (b) F. Baumann, A. Livoreil, W. Kaim and J.-P. Sauvage, *Chem. Commun.*, 1997, 35; (c) A. Livoreil, J.-P. Sauvage, N. Armaroli, V. Balzani, L. Flamigni and B. Ventura, *J. Am. Chem. Soc.*, 1997, **119**, 12114; (d) D. J. Cárdenas, A. Livoreil and J.-P. Sauvage, *J. Am. Chem. Soc.*, 1996, **118**, 11980; (e) F. Niess, V. Duplan and J.-P. Sauvage, *J. Am. Chem. Soc.*, 2014, **136**, 5876; (f) F. Niess, V. Duplan, C. S. Diercks and J.-P. Sauvage, *Chem. Eur. J.*, 2015, **21**, 14393.
- 14 D. V. Scaltrito, D. W. Thompson, J. A. O'Callaghan, G. J. Meyer, *Coord. Chem. Rev.*, 2000, **208**, 243.
- 15 G. Franc and A. Jutand, *Dalton Trans.*, 2010, **39**, 7873.
- 16 E. A. Ambundo, M.-V. Deydier, A. J. Grall, N. Aguera-Vega, L. T. Dressel, T. H. Cooper, M. J. Heeg, L. A. Ochrymowycz and D. B. Rorabacher, *Inorg. Chem.*, 1999, **38**, 4233.