EDGE ARTICLE

Supramolecular reactions of metallo-architectures: Ag₂-double-helicate/Zn₄-grid, Pb₄-grid/Zn₄-grid interconversions, and Ag₂-double-helicate fusion†

Adrian-Mihail Stadler,*[ab] Juan Ramírez,[c] Jean-Marie Lehn[a] and Bruno Vincent[d]

Supramolecular reactions are of importance in many fields. We report herein three examples where complexes of hydrazone-based ligands are involved. A Ag₂-double-helicate was converted, by treatment with Zn(OTf)₂, into a Zn₄-grid (exchange of metal ions and change of the nature of the initial complex). A Pb₄-grid was converted, upon reaction with ZnCl₂ or ZnBr₂, into a Zn₄-grid (exchange of metal ions, but conservation of the nature of the initial complex). The reverse conversions were also achieved. The fusion of a Ag₂-double-helicate with another Ag₂-double-helicate was performed (exchange of ligands, but conservation of the nature of the complexes) and resulted in a mixture of three helicates (two homostranded ones and one heterostranded one).

Introduction

Like covalent molecules, supramolecular[1] assemblies may participate in various reactions. The understanding of supramolecular reactions is of much interest because they are involved in many areas such as complex chemical systems and networks,[2] adaptive[3] and stimuli-responsive[4] chemical systems, fabrication of nanodevices and materials,[4] biomolecular processes. Thus, in the complexity and diversity of supramolecular chemistry, the reactivity of supramolecules plays a crucial role. It includes the processes:

(a) of (self)assembly (*i.e.* formation of supramolecular architectures through assembly, but also their participation, as subunits, in more complex assemblies), and correlatively, partial or total disassembly;

(b) of partial or total reorganization or exchange (at the supramolecular and, additionally and possibly, at the covalent level), that involves the breaking of several or all of the initial supramolecular connections and formation of new ones;

(c) without breaking or formation of new supramolecular connections (*e.g.* covalent modifications after self-assembly[5]).

Amongst supramolecular architectures, double helices and helicates,[6] as well as grids[7] arouse much interest and work. For example, DNA[8] and the ion channel generated by gramicidine[9] have a double helical structure, and there are double helical complexes that act as molecular machines[10] or catalysts.[11] Grid-like complexes have been studied for their electrochemical and magnetic properties,[7] for their capacity to encapsulate ions[12] or as starting materials for building more complex architectures (*e.g.* a Solomon link[13]), amongst other things. However, supramolecular interconversions of grids and helicates have not, except several examples,[14,15] been much explored.

With these ideas in mind – and using principles such as the displacement of an equilibrium through precipitation, and the preference of Ag⁺ for tetrahedral and of Zn²⁺ for octahedral coordination – we designed, as reported herein, three supramolecular reactions[16] of reorganization and exchange (Fig. 1) involving grids and double helices. They are related through the ligands[17] (which are pyrimidine-bis-hydrazones;[18] Fig. 2)
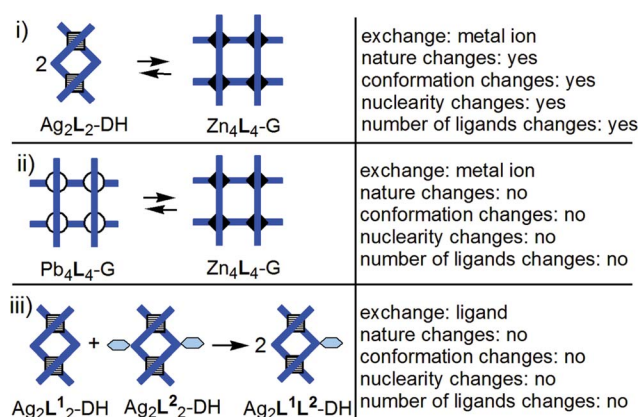
*a*Université de Strasbourg, CNRS, UMR 7006, ISIS, 8 Allée G. Monge, Strasbourg, France. E-mail: mstadler@unistra.fr

*b*Institute of Nanotechnology (INT), Karlsruhe Institute of Technolgoy (KIT), 76344, Eggenstein-Leopoldshafen, Germany

*c*Institut Pasteur Paris, 28 Rue du Docteur Roux, 75015 Paris, France

*d*Service de RMN, Faculté de Chimie, 1 Rue B. Pascal, Strasbourg, France

Fig. 1 Stylized representation of the three types of supramolecular reactions reported herein.
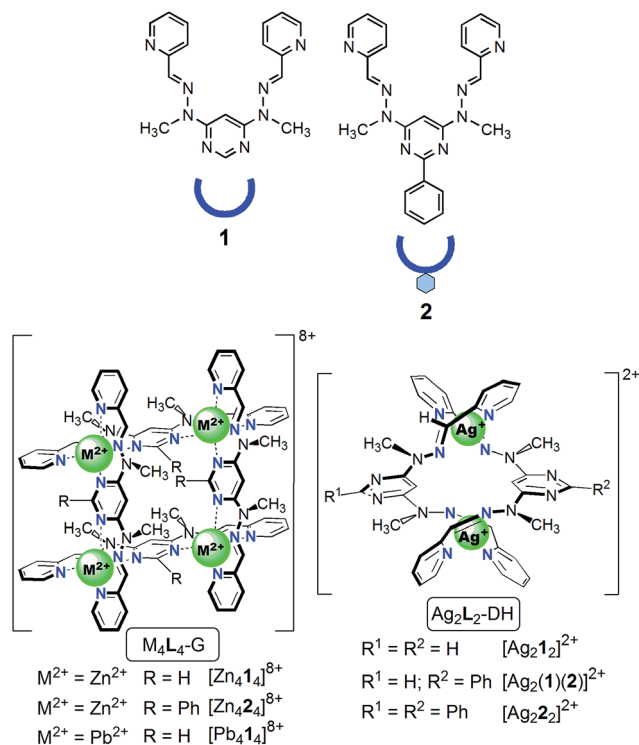
Fig. 2 Structural formulae and stylized representations of ligands **1** and **2**, and of grids and double helicates.

that produce the supramolecular complexes, as well as through the nature of complexes, and occur due to the dynamic character of the present metal–ligand connections. These reactions (Fig. 1) can be seen as:
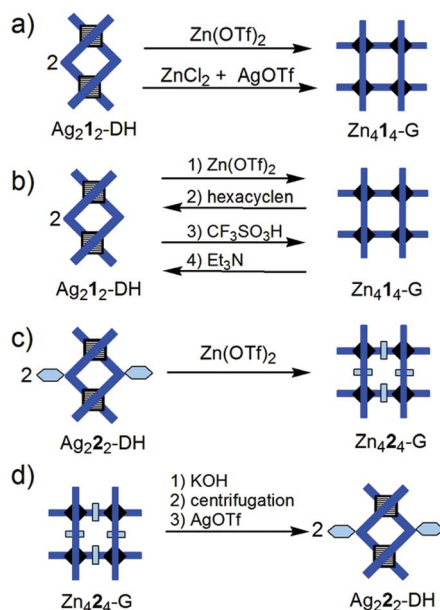

Fig. 3 Stylized representation of: (a) the conversion of Ag$_2$**1**$_2$-DH double helicate into the Zn$_4$**1**$_4$-G grid; (b) the interconversion Ag$_2$**1**$_2$-DH/Zn$_4$**1**$_4$-G; (c) the conversion of Ag$_2$**2**$_2$-DH double helicate into the Zn$_4$**2**$_4$-G grid; (d) the conversion of Zn$_4$**2**$_4$-G grid into Ag$_2$**2**$_2$-DH double helicate. Charges and stoichiometric coefficients are omitted for simplicity.
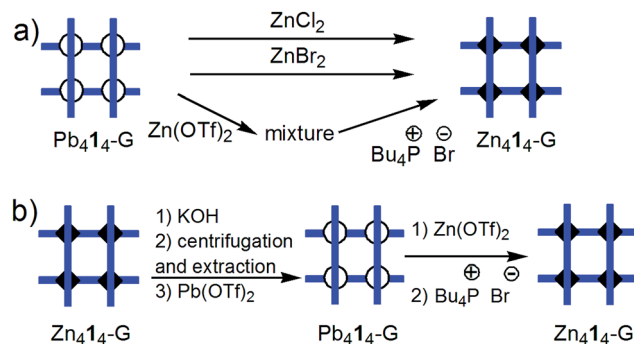

Fig. 4 Stylized representation of: (a) reaction of Pb$_4$**1**$_4$-G grid with ZnCl$_2$, ZnBr$_2$, and Zn(OTf)$_2$ and Bu$_4$P$^+$Br$^-$ (solvent CD$_3$CN); (b) Zn$_4$**1**$_4$-G/Pb$_4$**1**$_4$-G and Pb$_4$**1**$_4$-G/Zn$_4$**1**$_4$-G conversions. Charges and stoichiometric coefficients are omitted for simplicity.
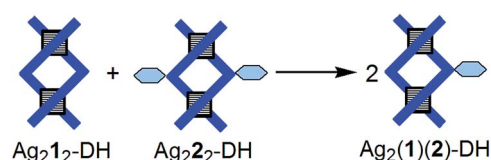

Fig. 5 Stylized representation of the fusion (conproportionation) reaction of double helicates Ag$_2$**1**$_2$-DH and Ag$_2$**2**$_2$-DH with formation of heterostranded species Ag$_2$(**1**)(**2**)-DH. Charges are omitted for simplicity.

(i) a change of the nature of the supramolecular architecture, from a Ag$^+$ dinuclear double helicate (DH) into a Zn^{2+} tetranuclear grid (G), induced by replacement of Ag$^+$ by Zn^{2+} (Fig. 3). In this reaction, not only the nature of the complex and that of the metal ion change, but also the conformation of the ligand (helical → unfolded), the charge ($2^+ \rightarrow 8^+$) and the nuclearity of the complex ($2 \rightarrow 4$) and the number of ligands per complex ($2 \rightarrow 4$). In regard to this last change, this process can be compared with the conversion or the equilibrium between supramolecular dimer and tetramer of bioactive proteins,[19] or between other homo-oligomers[20] with influence on the protein functions.

(ii) a substitution[21] (metal ion exchange or transmetallation), in a sole operation, of the four Pb^{2+} ions of a grid-like[22] complex by Zn^{2+} ions (Fig. 4);

(iii) a fusion (conproportionation)[23] between two Ag$^+$ double helicates[24] (Fig. 5).

While in case (ii) the equilibrium is shifted towards the Zn^{2+} grid through the precipitation of Pb^{2+} as its halides (chloride and bromide), in cases (i) and (iii), the conversions can be done without precipitation.

Results and discussion

(i) The conversion Ag$_2$**L**$_2$-DH → Zn$_4$**L**$_4$-G (**L** = **1**, **2**) through transmetallation is a dramatic reorganization of the nature of the metallo-supramolecular architecture induced by the replacement of Ag$^+$ by Zn^{2+} (Fig. 3a and c): 2 Ag$_2$**L**$_2$-DH + 4 Zn^{2+} → Zn$_4$**L**$_4$-G + 4 Ag$^+$. Ag$^+$ prefers a tetrahedral coordination geometry which is, in the case of ligands **1** and **2**, achieved from 2 two-Nsp^2-atom bidentate pyridine-hydrazone sites. In this

way, Ag^+ induces the formation of double helices with ligands **1** and **2**. Zn^{2+} prefers an octahedral coordination environment that results from **2** three-Nsp^2-atom tridentate sites of type pyridine-hydrazone-pyrimidine, thus generating a grid.

Reaction of 1 equiv. of Ag_2L_2-DH[15c] with 2 equiv. of $Zn(OTf)_2$ ($OTf^- = CF_3SO_3^-$) produces – without the need to precipitate Ag^+ as a halide – the corresponding grid Zn_4L_4-G[15b,22a] (solvent: CD_3NO_2 with 6–14% CD_3CN; ESI, pp. S9–S11†). Where $ZnCl_2$ is used in the reaction with $Ag_2\mathbf{1}_2$-DH, two equivalents of AgOTf per equiv. of DH are required according to the equation (ESI p. S8†):

$$2Ag_2\mathbf{1}_2\text{-DH} + 4ZnCl_2 + 4Ag^+ \rightarrow Zn_4\mathbf{1}_4\text{-G} + 8AgCl$$

On treatment of the double helice $Ag_2\mathbf{2}_2$-DH in CD_3NO_2 with 2 equiv. of $Zn(OTf)_2$ – added as a solution in a small volume of CD_3CN, or as a solid – the grid $Zn_4\mathbf{2}_4$-G was obtained. When the double helice $Ag_2\mathbf{1}_2$-DH in CD_3NO_2 was treated with 2 equiv. of $Zn(OTf)_2$, added as a solution in a small volume of CD_3CN (about 6–14% of the CD_3NO_2 volume), the grid $Zn_4\mathbf{1}_4$-G was obtained. When $Zn(OTf)_2$ was added as a solid, without CD_3CN, was obtained a mixture without the $Zn_4\mathbf{1}_4$-G grid; addition of a small volume of CH_3CN (about 6–14% of the CD_3NO_2 volume) to this mixture produced the expected grid $Zn_4\mathbf{1}_4$-G. A possible explanation could be that, in the case of the reaction $Ag_2\mathbf{1}_2$-DH $\rightarrow$ $Zn_4\mathbf{1}_4$-G, the CH_3CN acts as a coordinating species for the Ag^+ ions and so contributes to the displacement of the equilibrium from the double helix towards the grid. The grid $Zn_4\mathbf{2}_4$-G should be – due to the π-stacking aromatic interaction between a phenyl ring and the two ligands between which that phenyl is located within the grid – more stable than the grid $Zn_4\mathbf{1}_4$-G. This stability may be sufficient to make possible the formation of the grid $Zn_4\mathbf{2}_4$-G from the corresponding double helice without, unlike in the case of the grid $Zn_4\mathbf{1}_4$-G, the assistance of CH_3CN.

DOSY NMR was also used to study the conversion Ag_2L_2-DH $\rightarrow$ Zn_4L_4-G (L = **1**, **2**). As expected, the volume of the grid species obtained from double helices on treatment with $Zn(OTf)_2$ was found in agreement with that of the grid prepared from the free ligands **L** and $Zn(OTf)_2$.

The reverse conversion Zn_4L_4-G $\rightarrow$ Ag_2L_2-DH can be done as follows: after treatment of the grid with KOH, the solvent (CD_3CN or CD_3NO_2) is removed, and the ligand is extracted with $CDCl_3$ and separated from the solid residue (by centrifugation or filtration); after removal of $CDCl_3$, CD_3NO_2 is added, then AgOTf is added to form the helice. In order to simplify the procedure, we used ligand **2** and a mixture of $CDCl_3$ and CD_3NO_2 where ligand **2**, as well as the corresponding grid and double helice were soluble. After precipitation of Zn^{2+} with KOH, the mixture was centrifuged (the ligand **2** being soluble in the mixture of solvents), and to the recovered liquid phase AgOTf was added to produce the $Ag_2\mathbf{2}_2$-DH (ESI, p. S13†).

In a pH-dependent system (Fig. 3b), the interconversion between $Ag_2\mathbf{1}_2$-DH and $Zn_4\mathbf{1}_4$-G was achieved as follows (ESI, p. S10†): the grid was generated from the double helice by reaction with Zn^{2+}; then, Zn^{2+} was complexed with hexacyclen, and the double helice was regenerated; partial protonation of

hexacyclen with TfOH caused release of Zn^{2+} and formation of the grid (incomplete yield); finally, addition of triethylamine reactivated the hexacyclen that again encapsulated Zn^{2+} and resulted in the reformation of the double helice.

(ii) The $Pb_4\mathbf{1}_4$-G $\rightarrow$ $Zn_4\mathbf{1}_4$-G conversion (Fig. 4a) can formally be seen as a substitution of Pb^{2+} by Zn^{2+} ions, although the real mechanism, involving breaking and formation of supramolecular bonds, must be more complex. Reaction of $Pb_4\mathbf{1}_4$-G[15b] with 4 equiv. of $Zn(OTf)_2$ produces a mixture which no longer contains the grid-like species $Pb_4\mathbf{1}_4$-G or $Zn_4\mathbf{1}_4$-G (ESI p. S2†). This suggests that the affinity of Zn^{2+} for the ligand, as well as its preference for octahedral coordination are not sufficient to displace the equilibrium towards $Zn_4\mathbf{1}_4$-G. We considered that the involvement of Pb^{2+} ions in a weakly dissociating or sparingly soluble compound should displace the equilibrium. Indeed, addition of Br^- (as $Bu_4P^+Br^-$) to the above mixture, or treatment of $Pb_4\mathbf{1}_4$-G with four equivalents of $ZnBr_2$ or $ZnCl_2$ produced – along with the formation of PbX_2 (X = Br, Cl) which precipitates and, doing so, shifts the equilibrium – the expected $Zn_4\mathbf{1}_4$-G grid (solvent: CD_3CN; ESI pp. S3–S4†): $Pb_4\mathbf{1}_4$-G + 4 $ZnX_2 \rightarrow Zn_4\mathbf{1}_4$-G + 4 PbX_2.

The reverse conversion $Zn_4\mathbf{1}_4$-G $\rightarrow$ $Pb_4\mathbf{1}_4$-G grid was achieved in several steps (Fig. 4b). Treatment of $Zn_4\mathbf{1}_4$-G (in CD_3CN) with KOH led to the precipitation of Zn^{2+} (as $Zn(OH)_2$ or $K_2[Zn(OH)_4]$), as well as of the free ligand **1**. After removal of CD_3CN, the free ligand **1** was extracted with $CDCl_3$ and used further for the preparation of $Pb_4\mathbf{1}_4$-G (see ESI, p. S5†).

Thus, in addition to its self-assembly from Zn^{2+} and a ligand, the same Zn^{2+} grid, $Zn_4\mathbf{1}_4$-G, can be obtained, in reactions (i) and (ii), from a Ag^+ dinuclear double helice or from a Pb^{2+} tetranuclear grid (exchange of metal ions and reorganization of the architectures).

(iii) The fusion (conproportionation) reaction of double helice $Ag_2\mathbf{1}_2$-DH[15c] with 1 equiv. of $Ag_2\mathbf{2}_2$-DH (Fig. 5) according to the equation

$$Ag_2\mathbf{1}_2\text{-DH} + Ag_2\mathbf{2}_2\text{-DH} \rightarrow 2Ag_2(\mathbf{1})(\mathbf{2})\text{-DH}$$

produces a mixture that contains each of the three helices, namely two homoleptic (homostranded) ones and one heteroleptic (heterostranded) one. Ligands **1** and **2** equally participate to homo- and heteroleptic helices, and so the observed molar percentages are of approximately 25% for $Ag_2\mathbf{1}_2$-DH, 25% for $Ag_2\mathbf{2}_2$-DH, and 50% for $Ag_2(\mathbf{1})(\mathbf{2})$-DH. For characterization of the new compound $Ag_2\mathbf{2}_2$-DH, see ESI pp. S14–S20;† for ^1H, ^{13}C and DOSY of the mixture of three helices, see ESI pp. S25–S31.†

For the reactions described above it might appear necessary, in practice, to slightly (2–10%) increase the amounts of reagents with respect to those theoretically calculated.

Experimental

For experimental details, see the ESI.†

Conclusions

To summarize, three supramolecular reactions were investigated: (i) a Ag_2L_2-DH double-helice into Zn_4L_4-G grid

conversion, where the exchange of metal ions changes the nature of the metallo-supramolecular architecture, (ii) a $Zn_4\mathbf{1}_4$-G grid into $Pb_4\mathbf{1}_4$-G grid conversion driven by a halide-induced precipitation and where the nature of the metallo-supramolecular architecture is conserved, and (iii) a double exchange of ligands during the fusion of two double helicates.

The grid/grid and double-helicate/grid conversions were made reversible by precipitation of Zn^{2+} with KOH and subsequent reaction of the free ligand with Ag^+ or Pb^{2+}, or, for one DH/G interconversion, in a pH-dependent way.

In perspective, such ligands could be introduced in larger and more complex, suitably decorated, architectures where such supramolecular reactions can act as actuators of various properties (charge, volume, multivalency).

Acknowledgements

Notes and references

1 J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 89–121; J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 1304–1319.

2 R. F. Ludlow and S. Otto, *Chem. Soc. Rev.*, 2008, **37**, 101–108.

3 D. G. Kurth, *Sci. Technol. Adv. Mater.*, 2008, **9**, 014103.

4 J.-M. Lehn, *Angew. Chem., Int. Ed.*, 2013, **52**, 2836–2850.

5 K. C.-F. Leung, C.-P. Chak, C.-M. Lo, W.-Y. Wong, S. Xuan and C. H. K. Cheng, *Chem.–Asian J.*, 2009, **4**, 364–381; X. Yan, F. Wang, B. Zheng and F. Huang, *Chem. Soc. Rev.*, 2012, **41**, 6042–6065; A. J. McConnell, C. S. Wood, P. P. Neelakandan and J. R. Nitschke, *Chem. Rev.*, 2015, **115**, 7729–7793.

6 See, for example: M. Wang, W.-J. Lan, Y.-R. Zheng, T. R. Cook, H. S. White and P. J. Stang, *J. Am. Chem. Soc.*, 2011, **133**, 10752–10755.

7 For a selection of reviews, see: C. Piguet, G. Bernardinelli and G. Hopfgartner, *Chem. Rev.*, 1997, **97**, 2005–2062; C. Piguet, *J. Inclusion Phenom. Macrocyclic Chem.*, 1999, **34**, 361–391; M. Albrecht, *Chem. Rev.*, 2001, **101**, 3457–3497; M. J. Hannon and L. J. Childs, *Supramol. Chem.*, 2004, **16**, 7–22 For reviews, see: M. Ruben, J. Rojo, F. J. Romero-Salguero, L. H. Uppadine and J.-M. Lehn, *Angew. Chem., Int. Ed.*, 2004, **43**, 3644–3662; L. N. Dawe, T. S. M. Abedin and L. K. Thompson, *Dalton Trans.*, 2008, 1661–1675; L. N. Dawe, K. V. Shuvaev and L. K. Thompson, *Chem. Soc. Rev.*, 2009, **38**, 2334–2359; A.-M. Stadler, *Eur. J. Inorg. Chem.*, 2009, 4751–4770; J. Hardy, *Chem. Soc. Rev.*, 2013, **42**, 7881–7899.

8 J. D. Watson and F. H. Crick, *Nature*, 1953, **171**, 737–738.

9 B. M. Burkhart, N. Li, D. A. Langs, W. A. Pangborn and W. L. Duax, *Proc. Natl. Acad. Sci. U. S. A.*, 1998, **95**, 12950–12955.

10 K. Miwa, Y. Furusho and E. Yashima, *Nat. Chem.*, 2010, **2**, 444–449.

11 C.-T. Yeung, L.-H. Yeung, C.-S. Tsang, W.-Y. Wong and H.-L. Kwong, *Chem. Commun.*, 2007, 5203–5205.

12 B. R. Manzano, F. A. Jalón, I. M. Ortiz, M. L. Soriano, F. Gómez de la Torre, J. Elguero, M. A. Maestro, K. Mereiter and T. D. W. Claridge, *Inorg. Chem.*, 2008, **47**, 413–428.

13 J. E. Beves, J. J. Danon, D. A. Leigh, J.-F. Lemonnier and I. J. Vitorica-Yrezabal, *Angew. Chem., Int. Ed.*, 2015, **54**, 7555–7559.

14 For assembly/disassembly of double helicates, see: J.-P. Gisselbrecht, M. Gross, J.-M. Lehn, J.-P. Sauvage, R. Ziessel, C. Piccinni-Leopardi, J. M. Arrieta, G. Germain and M. V. Meersche, *Nouv. J. Chim.*, 1984, **8**, 661–667; Y. Yao, M. W. Perkovic, D. P. Rillema and C. Woods, *Inorg. Chem.*, 1992, **31**, 3956–3962; K. T. Potts, M. Keshavarz-K, F. S. Tham, H. D. Abruña and C. R. Arana, *Inorg. Chem.*, 1993, **32**, 4422–4435; V. Amendola, L. Fabbrizzi, L. Linati, C. Mangano, P. Pallavicini, V. Pedrazzini and M. Zema, *Chem.–Eur. J.*, 1999, **5**, 3679–3688; V. Amendola, L. Fabbrizzi, L. Gianelli, C. Maggi, C. Mangano, P. Pallavicini and M. Zema, *Inorg. Chem.*, 2001, **40**, 3579–3587; V. Amendola, L. Fabbrizzi, P. Pallavicini, E. Sartirana and A. Taglietti, *Inorg. Chem.*, 2003, **42**, 1632–1636; M. Boiocchi and L. Fabbrizzi, *Chem. Soc. Rev.*, 2014, **43**, 1835–1847. See also: M. Barboiu, G. Vaughan, N. Kyritsakas and J.-M. Lehn, *Chem.–Eur. J.*, 2003, **9**, 763–769.

15 (*a*) Grid/double-cross/stick: M. Barboiu, G. Vaughan, R. Graff and J.-M. Lehn, *J. Am. Chem. Soc.*, 2003, **34**, 10257–10265; (*b*) Grid/stick: A.-M. Stadler, N. Kyritsakas, R. Graff and J.-M. Lehn, *Chem.–Eur. J*, 2006, **12**, 4503–4522; (*c*) Double helicate/stick: A.-M. Stadler, N. Kyritsakas, G. Vaughan and J.-M. Lehn, *Chem.–Eur. J.*, 2007, **13**, 59–68; (*d*) Grid/pincer: J. Ramirez, A. M. Stadler, N. Kyritsakas and J.-M. Lehn, *Chem. Commun.*, 2007, 237–239; (*e*) Pincer/stick: J. Ramirez, A.-M. Stadler, L. Brelot and J.-M. Lehn, *Tetrahedron*, 2008, **64**, 8402–8410; (*f*) Double helicate/stick: D. J. Hutchinson, S. A. Cameron, L. R. Hanton and S. C. Moratti, *Inorg. Chem.*, 2012, **51**, 5070–5081; (*g*) Double-helicate/grid: A.-M. Stadler, C. Burg, J. Ramírez and J.-M. Lehn, *Chem. Commun.*, 2013, **49**, 5733–5735; (*h*) see also: P. N. W. Baxter, R. G. Khoury, J.-M. Lehn, G. Baum and D. Fenske, *Chem.–Eur. J.*, 2000, **6**, 4140–4148; (*i*) C. S. Campos-Fernandez, B. L. Schottel, H. T. Chifotides, J. K. Bera, J. Bacsa, J. M. Koomen, D. H. Russell and K. R. Dunbar, *J. Am. Chem. Soc.*, 2005, **127**, 12909–12923.

16 For examples of supramolecular interconversions, see: D. P. Funeriu, J.-M. Lehn, K. M. Fromm and D. Fenske, *Chem.–Eur. J.*, 2000, **6**, 2103–2111; K. Kumazawa, Y. Yamanoi, M. Yoshizawa, T. Kusukawa and M. Fujita, *Angew. Chem., Int. Ed.*, 2004, **43**, 5936–5940; A. M. Brown, M. V. Ovchinnikov, C. L. Stern and C. A. Mirkin, *J. Am. Chem. Soc.*, 2004, **126**, 14316–14317; O. Mamula, M. Lama, H. Stoeckli-Evans and S. Shova, *Angew. Chem., Int. Ed.*, 2006, **45**, 4940–4944; K. Harano, S. Hiraoka and M. Shionoya, *J. Am. Chem. Soc.*, 2007, **129**, 5300–5301; J. Heo, Y.-M. Jeon and C. A. Mirkin, *J. Am. Chem. Soc.*,

2007, **129**, 7712–7713; L. Zhao, B. H. Northrop and P. J. Stang, *J. Am. Chem. Soc.*, 2008, **130**, 11886–11888; S. Hiraoka, Y. Sakata and M. Shionoya, *J. Am. Chem. Soc.*, 2008, **130**, 10058–10059; H. Dong, J. Yang, X. Liu and S. Gou, *Inorg. Chem.*, 2008, **47**, 2913–2915; P. J. Lusby, P. Müller, S. J. Pike and A. M. Z. Slawin, *J. Am. Chem. Soc.*, 2009, **131**, 16398–16400; K. Parimal, E. H. Witlicki and A. H. Flood, *Angew. Chem., Int. Ed.*, 2010, **49**, 4628–4632; S. Chen, L.-J. Chen, H.-B. Yang, H. Tian and W. Zhu, *J. Am. Chem. Soc.*, 2012, **134**, 13596–13599; X. Yan, J.-F. Xu, T. R. Cook, F. Huang, Q.-Z. Yang, C.-H. Tung and P. J. Stang, *Proc. Natl. Acad. Sci. U. S. A.*, 2014, **111**, 8717–8722; X. Lu, X. Li, K. Guo, T.-Z. Xie, C. N. Moorefield, C. Wesdemiotis and G. R. Newkome, *J. Am. Chem. Soc.*, 2014, **136**, 18149–18155; Y.-F. Han, L. Zhang, L.-H. Weng and G.-X. Jin, *J. Am. Chem. Soc.*, 2014, **136**, 14608–14615; Y. Li, Z. Jiang, J. Yuan, D. Liu, T. Wu, C. N. Moorefield, G. R. Newkome and P. Wang, *Chem. Commun.*, 2015, **51**, 5766–5769; D. Preston, A. Fox-Charles, W. K. C. Lo and J. D. Crowley, *Chem. Commun.*, 2015, **51**, 9042–9045; M. Han, Y. Luo, B. Damaschke, L. Gýmez, X. Ribas, A. Jose, P. Peretzki, M. Seibt and G. H. Clever, *Angew. Chem., Int. Ed.*, 2016, **55**, 445–449.

17 J.-L. Schmitt, A.-M. Stadler, N. Kyritsakas and J.-M. Lehn, *Helv. Chim. Acta*, 2003, **86**, 1598–1624.

18 X. Su and I. Aprahamian, *Chem. Soc. Rev.*, 2014, **43**, 1963–1981.

19 See for example the cases of (*a*) spectrin: S.-C. Liu and J. Palek, *Nature*, 1980, **285**, 586–588; E. Ungewickell and W. Gratzer, *Eur. J. Biochem.*, 1978, **88**, 379–385. (*b*) the clock protein KaiB: T. Iida, R. Mutoh, K. Onai, M. Morishita, Y. Furukawa, K. Namba and M. Ishiura, *Genes Cells*, 2015, **20**, 173–190; (*c*) 6-phosphogluconate dehydrogenase, see: S. Hanau, L. Proietti d'Empaire, I. Capone, S. Alberighi, R. Montioli and F. Dallocchio,

Biochim. Biophys. Acta, 2013, **1834**, 2647–2652; (*d*) Bovine IF1, see: E. Cabezon, P. J. G. Butler, M. J. Runswick and J. E. Walker, *J. Biol. Chem.*, 2000, **275**, 25460–25464; (*e*) phosphofructokinase, see: J. Xu, T. Oshima and M. Yoshida, *J. Mol. Biol.*, 1990, **215**, 597–606.

20 For the case of (*a*) uracil phosphoribosyltransferase from *Escherichia coli*, see: K. F. Jensen and B. Mygind, *Eur. J. Biochem.*, 1996, **240**, 637–645; (*b*) mushroom tyrosinase, see: R. L. Jolley Jr, D. A. Robb and H. S. Mason, *J. Biol. Chem.*, 1969, **244**, 1593–1599; (*c*) D-amino acid oxidase, see: E. Antonini, M. Brunori, R. Bruzzesi, E. Chiancone and V. Massey, *J. Biol. Chem.*, 1966, **241**, 2358–2366 See also: (*d*) E. K. Jaffe, *Open Conf. Proc. J*, 2010, **1**, 1–6; T. Selwood and E. K. Jaffe, *Arch. Biochem. Biophys.*, 2012, **519**, 131–143.

21 For an example of supramolecular substitution reaction, see: J. Santamaría, T. Martín, G. Hilmersson, S. L. Craig and J. Rebek Jr, *Proc. Natl. Acad. Sci. U. S. A.*, 1999, **96**, 8344–8347.

22 Pb^{2+} or Zn^{2+} hydrazone-based grids: (*a*) M. Barboiu, M. Ruben, G. Blasen, N. Kyritsakas, E. Chacko, M. Dutta, O. Radekovich, K. Lenton, D. J. R. Brook and J.-M. Lehn, *Eur. J. Inorg. Chem.*, 2006, 784–789; (*b*) A. R. Stefankiewicz, G. Rogez, J. Harrowfield, M. Drillon and J.-M. Lehn, *Dalton Trans.*, 2009, 5787–5802; (*c*) M. Dutta, M. Movassat, D. J. R. Brook, A. Oliver and D. Ward, *Supramol. Chem.*, 2011, **23**, 630–640; (*d*) D. J. Hutchinson, L. R. Hanton and S. C. Moratti, *Inorg. Chem.*, 2011, **50**, 7637–7649.

23 M. L. Saha, S. Pramanik and M. Schmittel, *Chem. Commun.*, 2012, **48**, 9459–9461.

24 For other examples of Ag$^+$ hydrazone-based double helicates, see: D. J. Hutchinson, P. M. James, L. R. Hanton and S. C. Moratti, *Inorg. Chem.*, 2014, **53**, 2122–2132; D. J. Hutchinson, L. R. Hanton and S. C. Moratti, *Dalton Trans.*, 2014, **43**, 8205–8218.