

Constitutional Dynamic Chemistry

How to cite: *Angew. Chem. Int. Ed.* **2020**, 59, 12484–12492

International Edition: doi.org/10.1002/anie.202000818

German Edition: doi.org/10.1002/ange.202000818

Triple Self-Sorting in Constitutional Dynamic Networks: Parallel Generation of Imine-Based Cu^I, Fe^{II}, and Zn^{II} Complexes**

Jean-François Ayme, Sébastien Dhers, and Jean-Marie Lehn*

In memory of Professor Rolf Huisgen

Abstract: Three imine-based metal complexes, having no overlap in terms of their compositions, have been simultaneously generated from the self-sorting of a constitutional dynamic library (CDL) containing three amines, three aldehydes, and three metal salts. The hierarchical ordering of the stability of the three metal complexes assembled and the leveraging of the antagonistic and agonistic relationships existing between the constituents within the constitutional dynamic network corresponding to the CDL were pivotal in achieving the sorting. Examination of the process by NMR spectroscopy showed that the self-sorting of the Fe^{II} and Zn^{II} complexes depended on an interplay between the thermodynamic driving forces and a kinetic trap involved in their assembly. These results also exemplify the concept of “simplicity”—the fact that the output of a self-assembling system may be simplified by increasing its initial compositional complexity—as the two complexes could self-sort only in the presence of the third pair of organic components, those of the Cu^I complex.

Introduction

The construction of dynamic networks of molecules presenting a high level of structural and functional complexity requires the development of strategies to control the organization and interconnection of sets of chemical entities having a high compositional and interactional diversity.^[1] The application of the concepts of orthogonal self-assembly^[2] and self-

sorting^[3–7] within the context of constitutional dynamic chemistry (CDC) provides a basis for such strategies.^[11–n,8,9]

By operating through both reversible covalent bond formation and reversible supramolecular interactions, constitutional dynamic networks (CDNs) of molecules can be set up at both the molecular and supramolecular levels. Prime examples of such multilevel organization can be found in CDNs created by the dynamic binding of metal cations to imine-based ligand constituents generated by the reversible condensation of components containing amine and carbonyl groups (in particular 2-formylpyridine). Their high level of organization and their dynamic features have given access to architectures that would be otherwise inaccessible by traditional synthetic means and from which new properties have emerged.^[7e–i,9b–e,10,11]

The concomitant assembly of multiple constitutional dynamic architectures has further extended the range of properties accessible with CDC,^[1n,6d,9d,e,11a–d,q] thus highlighting the importance of fostering compositional diversity within such systems to access ever more complex features. However, increasing the compositional diversity of constitutional dynamic systems comes at an “informational cost”. As the system becomes more complex, more delicate structural and interactional information is required to prevent the crossover, within the different architectures, of components participating in dynamic processes that take place in the same domain. This cost grows rapidly as the number of architectures assembled through the same type of dynamic processes increases. For this reason, the majority of self-sorting systems involving constitutional dynamic metal-organic architectures known to date occur between architectures sharing one to two organic components and/or built around no more than two different types of metal cations.^[3,6,7] This limited compositional diversity reflects the need for strategies to simultaneously control the outcome of two (or more) dynamic processes over multiple architectures, namely reversible covalent imine bond formation and dynamic metal–ligand coordination.

Here we demonstrate how the careful design of amine- and 2-formylpyridine-containing components, satisfying (or not) the unique coordination preferences of Cu^I, Fe^{II}, and Zn^{II} ions, can enable the parallel generation of three imine-based metal complexes that do not overlap in terms of their composition. The present study of the mechanism and the driving forces underlying this self-sorting process provides insights into the self-assembly pathways of each individual species within the mixture and reveals a subtle interplay between the thermodynamic driving forces and the kinetic traps involved.

[*] Dr. J.-F. Ayme, Prof. Dr. J.-M. Lehn

Institute of Nanotechnology

Karlsruhe Institute of Technology

76344 Eggenstein-Leopoldshafen (Germany)

Dr. J.-F. Ayme, Dr. S. Dhers, Prof. Dr. J.-M. Lehn

Laboratoire de Chimie Supramoléculaire

Institut de Science et d'Ingénierie Supramoléculaires

Université de Strasbourg

8 allée Gaspard Monge, 67000 Strasbourg (France)

E-mail: lehn@unistra.fr

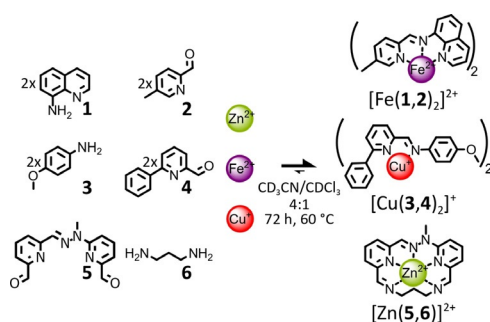
[**] A previous version of this manuscript has been deposited on a preprint server (<https://doi.org/10.26434/chemrxiv.9918479.v1>).Supporting information and the ORCID identification number for one of the authors of this article can be found under: <https://doi.org/10.1002/anie.202000818>.

© 2020 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution Non-Commercial NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial, and no modifications or adaptations are made.

Results and Discussion

Rationale

When a library of amine- and 2-formylpyridine-containing components is treated with different metal salts, all the complexes formed share the same dynamic features (i.e. reversible imine bonds and dynamic metal–ligand interactions). Consequently, the complexes are able to exchange building blocks and thus they will develop either antagonistic or agonistic relationships depending on whether or not they contain common building blocks. If they do share one or more components, the increase in the population of one of the complexes will occur at the expense of the population of the other one—these two complexes hence have an antagonistic relationship. If two complexes have no building block in common, they have an agonistic relationship: the formation of one complex in an agonistic pair will promote the formation of the other one by liberating, as it builds up, the unshared components that will form the agonistic complex. By exploiting these regulatory relationships, one can enforce the formation of a complex that would normally not be expressed, by trapping all components and metal cations in more stable complexes. Thus, to achieve the parallel self-assembly of three completely different imine-based metal complexes it may be sufficient that only one of these complexes is capable of self-assembling in the presence of the reactants of the two other ones. The work described herein demonstrates that this is the case. Indeed, if one complex is capable of selectively self-assembling from all the initial reactants, its formation will trap one type of metal cation and one pair of amine- and 2-formylpyridine-containing components in its structure. The next complex must then be able to form selectively from only the remaining two types of metal, amine, and aldehyde components. The self-assembly of the third complex does not even need to be selective, as its composition will be imposed by the reactants left in solution by the two other metal cations. We envisage that the three metal complexes $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$, $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$, and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ should present the appropriate hierarchical ordering of stabilities to allow for such self-sorting (Scheme 1); the notation (\mathbf{n},\mathbf{m}) refers to the imine-based constituent generated by the condensation of amine \mathbf{n} with aldehyde \mathbf{m} (in no specific order).



Scheme 1. Concomitant formation of complexes $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$, $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$, and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ through the hetero-self-sorting of their initial reactants.

We have previously shown that by exploiting the difference in coordination number between tetrahedral and octahedral coordination geometries and by manipulating the steric hindrance features of two derivatives of 2-formylpyridine, $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ could be selectively self-assembled from their initial reactants.^[12] The driving force of this self-sorting process was found to be the strong affinity of the Fe^{II} cations for the sterically unhindered tridentate coordination site formed by the condensation of the aminoquinoline $\mathbf{1}$ with the 2-formylpyridine $\mathbf{2}$. We also showed that the formation of the Cu^{I} complex $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ was compatible with the simultaneous formation of imine-containing Zn^{II} complexes.^[12] Given that Zn^{II} cations form a highly stable and selective macrocyclic complex $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ with dialdehyde $\mathbf{5}$ and diamine $\mathbf{6}$,^[9c,11s–u] we presumed that the presence of Cu^{I} cations and components $\mathbf{3}$ and $\mathbf{4}$ would not interfere with its formation. We also envisaged that the formation of the Fe^{II} complex $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ would be possible in the presence of Zn^{II} cations, dialdehyde $\mathbf{5}$, and diamine $\mathbf{6}$, as low-spin d^6 Fe^{II} cations are expected to favor the formation of an octahedral complex with two terpyridine-like ligands ($\mathbf{1},\mathbf{2}$) rather than a complex with the planar pentadentate macrocyclic ligand ($\mathbf{5},\mathbf{6}$). Furthermore, the inclusion of the terpyridine-like components $\mathbf{5}$ in a Fe^{II} complex should be disfavored due to the steric hindrance around its coordination site imposed by the substitution next to the nitrogen site in the pyridine groups. Finally, given that bis-terpyridine complexes of Fe^{II} are more stable than their Zn^{II} equivalents, the formation of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ should prevail over that of $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$.^[13]

On these grounds, it appeared likely that the three complexes would be able to self-sort from a mixture of their initial components upon addition of the three appropriate metal salts.

Parallel Self-Assembly of Three Imine-Containing Complexes by Hetero-Self-Sorting from an Initial Set of Nine Components

The self-sorting potential of a CDL composed of the six molecular components $\mathbf{1}$ – $\mathbf{6}$ in a 2:2:2:2:1:1 ratio and 1 equiv each of $\text{Fe}(\text{BF}_4)_2$, $\text{Cu}(\text{BF}_4)$, and $\text{Zn}(\text{BF}_4)_2$ was investigated by reacting the library in $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1) at 60 °C for 72 h. The ^1H NMR spectrum of the crude reaction mixture indicated the generation of the three anticipated metal complexes, as the diagnostic signals of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$, $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$, and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ dominated the spectrum of the reaction mixture (Figure 1E and see Figure S17 in the Supporting Information).

The initial pool of reactants was expected to yield the three complexes in a 1:1:1 ratio; however, $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$, $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$, and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ were obtained in a 0.95:0.8:1 ratio. The smaller amount of $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ in solution could be attributed to the partial hydrolysis of the ligand ($\mathbf{3},\mathbf{4}$) and to the presence of residual heteroleptic Fe^{II} complex $[\text{Fe}(\mathbf{1},\mathbf{2})-(\mathbf{1},\mathbf{4})]^{2+}$ (this heteroleptic complex has been shown to appear as a kinetic product during the formation of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ from their reactants).^[12] (More details on the composition of the mixture can be found in Section 3.1.2 in

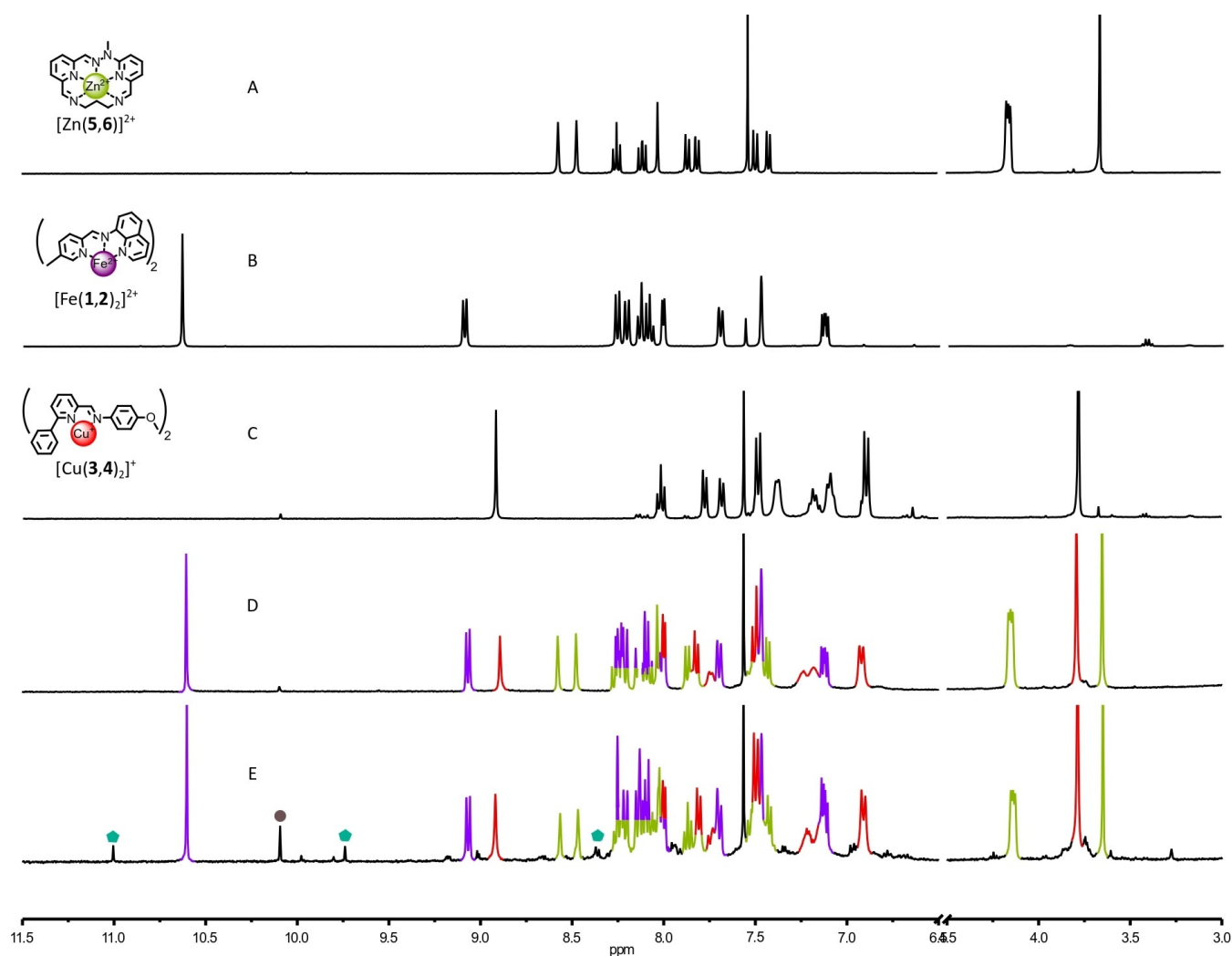


Figure 1. Partial ^1H NMR spectra (400 MHz, $\text{CD}_3\text{CN}/\text{CDCl}_3$ 4:1, 298 K) of: A) $[\text{Zn}(\mathbf{5,6})]^{2+}$, B) $[\text{Fe}(\mathbf{1,2})]^{2+}$, C) $[\text{Cu}(\mathbf{3,4})]^+$, D) an equimolar solution of preformed complexes $[\text{Fe}(\mathbf{1,2})]^{2+}$, $[\text{Cu}(\mathbf{3,4})]^+$, and $[\text{Zn}(\mathbf{5,6})]^{2+}$ after 18 h at 60°C , E) the reaction mixture obtained from mixing components $\mathbf{1}/\mathbf{2}/\mathbf{3}/\mathbf{4}/\mathbf{5}/\mathbf{6}/\text{Fe}(\text{BF}_4)_2/\text{Zn}(\text{BF}_4)_2/\text{Cu}(\text{BF}_4)$ in the molar ratio 2:2:2:2:1:1:1:1 at 60°C for 72 h. The diagnostic signals of the complexes are color coded: $[\text{Fe}(\mathbf{1,2})]^{2+}$ in purple, $[\text{Cu}(\mathbf{3,4})]^+$ in red, and $[\text{Zn}(\mathbf{5,6})]^{2+}$ in green; one of the diagnostic signals of the free aldehyde **4** is highlighted by a gray circle and some of the diagnostic signals of the heteroleptic complex $[\text{Fe}(\mathbf{1,2})(\mathbf{1,4})]^{2+}$ are highlighted by a green pentagon.

the Supporting Information.) Further heating of the reaction mixture at 60°C for up to 6 days helped to dissipate some of the residual heteroleptic complex $[\text{Fe}(\mathbf{1,2})(\mathbf{1,4})]^{2+}$, but resulted in an increased decomposition of complex $[\text{Cu}(\mathbf{3,4})]^+$ (Figure S17).

A mixture of the preformed complexes $[\text{Fe}(\mathbf{1,2})]^{2+}$, $[\text{Cu}(\mathbf{3,4})]^+$, and $[\text{Zn}(\mathbf{5,6})]^{2+}$ in a 1:1:1 ratio (Figure 1D) was heated at 60°C and followed by ^1H NMR spectroscopy for up to 72 h (Figures S18 and S19). The distribution of the three complexes mirrored the one obtained from the self-sorting experiment and remained unchanged throughout the experiment, indicating that this state is the thermodynamic end point of the self-sorting process under the conditions used.

Starting from the components themselves and under the same conditions, $\text{Ag}(\text{BF}_4)$ could be used as a substitute for $\text{Cu}(\text{BF}_4)$, which led to the formation of $[\text{Fe}(\mathbf{1,2})]^{2+}$, $[\text{Ag}(\mathbf{3,4})]^+$, and $[\text{Zn}(\mathbf{5,6})]^{2+}$ as the major products of the self-

sorting process (Figure S20). However, in this case, significantly more free aldehyde **4** was observed in the ^1H NMR spectrum of the reaction mixture compared to the system using Cu^I cations, and some unidentified side products were also observed alongside the three complexes.

Probing the Relative Selectivity in the Self-Assembly of the Three Complexes

To assess the relative stability of each complex with respect to the two other ones, their formation was studied in smaller systems of two complexes. The use of these subsystems also allowed the potential influence of the reagents of the third complex on the fidelity of the self-sorting of the two other ones to be probed.

The Fe^{II} complex $[\text{Fe}(\mathbf{1,2})]^{2+}$ and the Cu^I complex $[\text{Cu}(\mathbf{3,4})]^+$ were known to self-sort after 24 h at 60°C from

an equimolar mixture of their four initial components upon addition of 1 equiv Fe^{II} and 1 equiv Cu^{I} salts.^[12]

The selectivity in the self-assembly of $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ from their reactants was probed by mixing components **3**, **4**, **5**, and **6** in a 2:2:1:1 ratio in the presence of 1 equiv each of $\text{Cu}(\text{BF}_4)$ and $\text{Zn}(\text{BF}_4)_2$ (Figure 2A, see also Figures S21 and S22). After 72 h at 60 °C, most of the starting materials had been converted into a clean mixture of the two anticipated complexes $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$. Besides the diagnostic signals of the two complexes, the ^1H NMR spectrum of the crude reaction mixture revealed traces of the free components **3** and **4** as a result of hydrolysis of imine (**3,4**). The high fidelity of the self-sorting process of this system can be attributed to the strong differences in the coordination number and coordination geometries of the two metal cations.

To investigate the self-sorting potential of components **1**, **2**, **5**, and **6** in the presence of Fe^{II} cations and Zn^{II} cations, a 2:2:1:1 mixture of these components was allowed to react with 1 equiv $\text{Fe}(\text{BF}_4)_2$ and 1 equiv $\text{Zn}(\text{BF}_4)_2$ in $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1) at 60 °C (Figure 2B and Figure S23). After 18 h, three species were observable in the ^1H NMR spectrum of the crude reaction mixture (Figure S26). A significant amount of

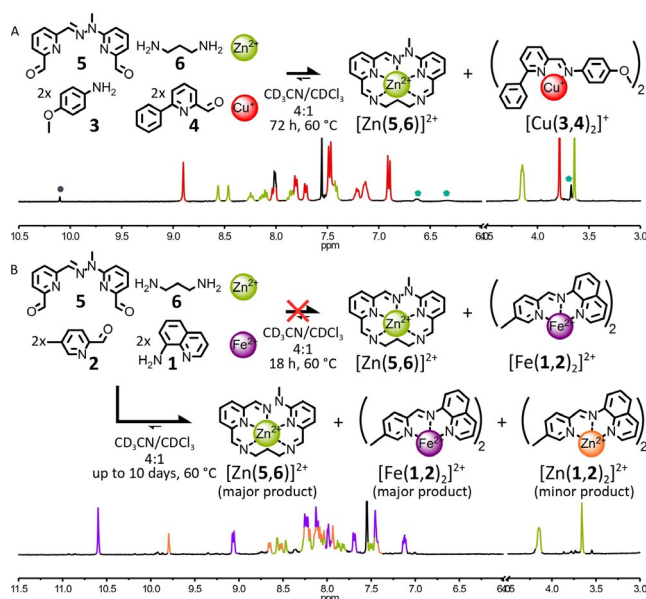


Figure 2. A) Parallel formation of complexes $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ through the self-sorting of their initial reactants. Reaction conditions: **3/4/5/6**/ $\text{Cu}(\text{BF}_4)$ / $\text{Zn}(\text{BF}_4)_2$ (2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60 °C, 72 h. Partial ^1H NMR spectrum (400 MHz, $\text{CD}_3\text{CN}:\text{CDCl}_3$ (4:1), 298 K) of the crude reaction mixture after 72 h at 60 °C, the diagnostic signals of the complexes are color coded: $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ in green and $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ in red; one of the diagnostic signals of the free aldehyde **4** is highlighted by a gray circle and diagnostic signals of the free aldehyde **3** are highlighted by turquoise pentagons. B) Simultaneous generation of complexes $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Fe}(\mathbf{1},\mathbf{2})]^{2+}$ through the self-sorting of their initial reactants. Reaction conditions: **1/2/5/6**/ $\text{Fe}(\text{BF}_4)_2$ / $\text{Zn}(\text{BF}_4)_2$ (2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60 °C, 10 days. Partial ^1H NMR spectrum (400 MHz, $\text{CD}_3\text{CN}:\text{CDCl}_3$ (4:1), 298 K) of the crude reaction mixture after 10 days at 60 °C, the diagnostic signals of the complexes are color coded: $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ in green, $[\text{Fe}(\mathbf{1},\mathbf{2})]^{2+}$ in purple, and $[\text{Zn}(\mathbf{1},\mathbf{2})]^{2+}$ in orange.

complex $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ could be seen besides the two anticipated complexes $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$. Scrutinizing the self-assembly process of the three complexes over time by ^1H NMR spectroscopy (Figure 3A, see also Figures S24–S26) revealed that $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ forms as a kinetic product. $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ appeared immediately upon mixing the reactants,

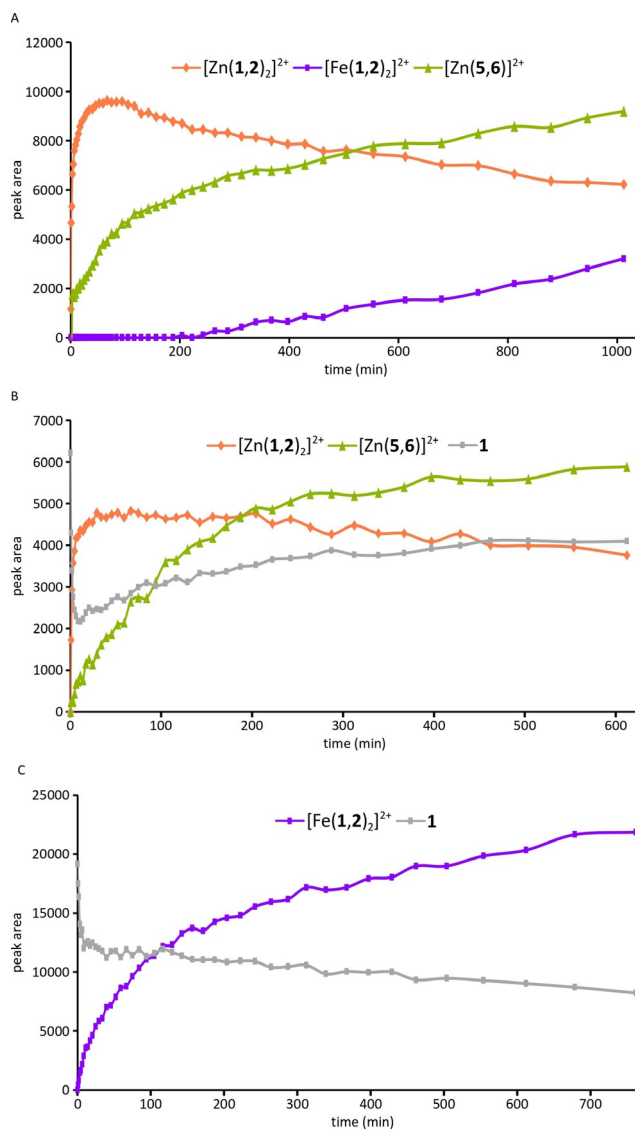


Figure 3. A) Formation as a function of time of thermodynamic products $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ (purple squares) and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ (green triangles) as well as kinetic product $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ (orange diamonds). Reaction conditions: **1/2/5/6**/ $\text{Fe}(\text{BF}_4)_2$ / $\text{Zn}(\text{BF}_4)_2$ (2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60 °C. B) Formation as a function of time of thermodynamic product $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ (green triangles) and kinetic product $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ (orange diamonds), as well as consumption as a function of time of component **1** (gray squares). Reaction conditions: **1/2/5/6**/ $\text{Zn}(\text{BF}_4)_2$ (2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60 °C. C) Formation as a function of time of thermodynamic product $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ (purple squares) and consumption as a function of time of component **1** (gray squares). Reaction conditions: **1/2/5/6**/ $\text{Fe}(\text{BF}_4)_2$ (2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60 °C. The ^1H NMR spectra of the reaction mixtures were recorded at increasing time increments. Peak areas of the imine signals for $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$, of the NCH_3 signal for $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$, and of the CH signal for **1** were obtained from the recorded ^1H NMR spectra.

and its concentration reached a maximum after heating for 90 mins at 60 °C. Then, the concentration of $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ slowly declined until the end of the experiment, while those of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ slowly increased. (A detailed discussion of the composition of the reaction mixture after 5 days at 60 °C and of the initial evolution of the reaction mixture can be found in Sections 3.4.2 and 3.4.4, respectively, of the Supporting Information.) The overall kinetics of the reorganization process of $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ into $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ are very slow, as a substantial amount of $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ was still observable in the ^1H NMR spectrum of the reaction mixture after 10 days at 60 °C (Figure 2 B).

To verify that $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ are the thermodynamic products of the reaction under the conditions used, the two complexes were prepared separately before being mixed in an approximately 1:1 ratio (Figure S27). After 5 days of heating at 60 °C, the ^1H NMR spectrum of the reaction mixture was a pristine superimposition of the spectra of the two individual complexes, indicating that $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ are indeed the thermodynamic products of the self-assembly process and that $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ is a kinetic product.

To gather more information on the driving forces governing the self-assembly of $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ as well as to evaluate the likelihood of reaching the thermodynamic end point of this self-sorting process, the formation of each of the two complexes was attempted by mixing 1 equiv of the corresponding metal salt with a 2:2:1:1 mixture of **1**, **2**, **5**, and **6**, respectively, in $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1) at 60 °C. The evolution of the composition of the two reaction mixtures was monitored by ^1H NMR spectroscopy over the course of 10 days.

First, the Zn^{II} system was investigated (Figure 3 B, see also Figures S28–S30). Immediately after the addition of Zn^{II} cations to the mixture of components, the characteristic signals of complex $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ appeared in the ^1H NMR spectrum of the reaction mixture (Figure 3 B). The amount of $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ in solution reached a maximum after 30 min, before slowly declining until the end of the experiment. Conversely, the formation of the macrocyclic complex $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ was slower but continuous throughout the experiment. After 5 days of heating at 60 °C, the signals of both complexes $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ were still observable in the ^1H NMR spectra of the reaction, and amounted to the consumption of 55 % and 45 %, respectively, of the initial Zn^{II} cations.^[14] (A detailed discussion of the composition of the reaction mixture after 5 days at 60 °C and of the initial evolution of the reaction mixture can be found in Section 3.4.6 of the Supporting Information.) The amount of the two complexes in solution did not change when the mixture was left to react for longer at 60 °C (up to 10 days). As $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ were obtained in almost a 1:1 ratio, the stability of both complexes must be similar, thus Zn^{II} cations alone cannot drive the $\text{Fe}^{\text{II}}/\text{Zn}^{\text{II}}$ system towards its thermodynamic end point.

Second, the Fe^{II} system was studied (Figure 3 C, see also Figures S31–S33). Minutes after the addition of Fe^{II} cations to the initial mixture of components, the characteristic signals of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ appeared in the ^1H NMR spectrum of the reaction

mixture (Figure 3 C). The concentration of the complex increased steadily throughout the experiment. After 5 days of heating at 60 °C, 85 % of the anticipated $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ had formed.^[14] (A detailed discussion on the composition of the reaction mixture after 5 days at 60 °C and of the initial evolution of the reaction mixture can be found in Section 3.4.7 of the Supporting Information.) Prolonged heating at 60 °C (up to 10 days) did not yield any additional $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ complex. Under these conditions, $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ appeared to be the thermodynamically most stable Fe^{II} complex obtained from the initial library of components. Thus, Fe^{II} cations should be able to drive the $\text{Fe}^{\text{II}}/\text{Zn}^{\text{II}}$ system towards its thermodynamic end point, given that $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ is more stable than $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$.

The stability of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ relative to $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ was probed by treating a solution of preformed complex $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ in $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1) with 1 equiv $\text{Zn}(\text{BF}_4)_2$ (Figure S34). After 4 days at 60 °C, the ^1H NMR spectrum of the mixture only contained the diagnostic signals of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$, indicating that it is more stable than $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$. The strong preference of the Fe^{II} cations for the N-N-N tridentate constituent (**1,2**) should theoretically lead the $\text{Fe}^{\text{II}}/\text{Zn}^{\text{II}}$ system towards the exclusive formation of $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$. However, the slow kinetics of the recombination process of $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ into $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ prevented the system from reaching its thermodynamic end point within a practical timeframe. In the $\text{Fe}^{\text{II}}/\text{Cu}^{\text{I}}/\text{Zn}^{\text{II}}$ system, some of the components of $[\text{Cu}(\mathbf{5},\mathbf{6})]^{2+}$ must speed up the rearrangement of $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ into $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$, as this problem was not encountered in the initial system with the three complexes.

Probing the Robustness of the Self-Assembly of the Three Complexes

To assess the affinity of each metal cation for its preferred pair of components, a solution of components **1–6** in a 2:2:2:2:1:1 ratio in $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1) was treated with only one of the three metal cations. The resulting mixtures were left to react at 60 °C for up to 3 days and the evolution of their compositions was followed by ^1H NMR spectroscopy.

When 1 equiv $\text{Fe}(\text{BF}_4)_2$ was added to the solution of the six organic components, the strong affinity of the Fe^{II} ions for the imine constituent (**1,2**) ensured the formation of most of the anticipated $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ complex (Figure 4 A and Figure S35).^[14] After 3 days at 60 °C, 85 % of the anticipated $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ had formed.^[14] (More details on the composition of the reaction mixture can be found in Section 3.5.1 of the Supporting Information.) This experiment confirmed that $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ is the thermodynamically most stable Fe^{II} complex obtainable from this library of components.

When the initial library of components was treated with 1 equiv $\text{Cu}(\text{BF}_4)_2$, no traces of $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$, could be detected by ^1H NMR spectroscopy (Figure 4 B and Figure S36). The affinity of Cu^{I} cations for the imine constituent (**3,4**) is too weak to allow the selective self-assembly of $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ from the initial components. This result confirms that the formation of $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ in the initial system is the product of the

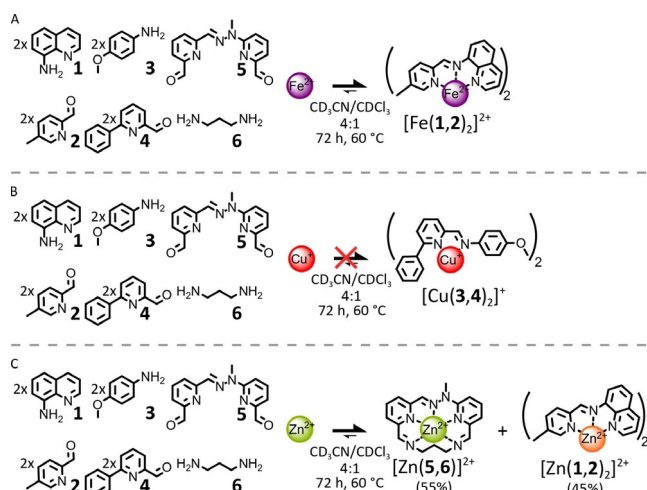


Figure 4. A) Formation of the complex $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ through self-sorting of its components from a mixture of components 1–6. Reaction conditions: 1/2/3/4/5/6/ $\text{Fe}(\text{BF}_4)_2$ (2:2:2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60°C , 72 h. B) Attempted generation of the complex $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ through self-sorting of its components from a mixture of components 1–6. Reaction conditions: 1–6 and $\text{Cu}(\text{BF}_4)$ (2:2:2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60°C , 72 h. C) Attempted generation of the complex $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ through self-sorting of its components from a mixture of components 1–6. Reaction conditions: 1–6 and $\text{Zn}(\text{BF}_4)_2$ (2:2:2:2:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60°C , 72 h.

antagonistic and agonistic regulatory relationships existing between the constituents of the CDN. Components 1, 2, 5, and 6 must be trapped into the more stable Fe^{II} and Zn^{II} complexes to allow for the formation of $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$. This example demonstrates how CDNs can be leveraged to enforce the formation of thermodynamically unfavorable products.^[9c,f]

When the initial organic components were treated with 1 equiv $\text{Zn}(\text{BF}_4)_2$, the affinity of the Zn^{II} cations for the imine-based macrocycle (5,6) was not strong enough to ensure the exclusive self-assembly of $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ (Figure 4C and Figure S37). After 3 days at 60°C , about 55% of the initial Zn^{II} ions were present as $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ and about 45% were present as $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$.^[14] (More details on the composition of the reaction mixture can be found in Section 3.5.3 of the Supporting Information.) The distribution of the Zn^{II} cations between $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ matched closely that obtained when Zn^{II} cations were added to a solution containing only components 1, 2, 5, and 6, thus suggesting that components 3 and 4 have no influence on the self-assembly of these two complexes.

Probing the Synergistic Behaviors during the Self-Assembly of the Three Complexes

To probe the synergistic behaviour of the metal cations and to evaluate the influence of an additional third pair of organic components on the self-assembly process, $\text{Fe}(\text{BF}_4)_2$, $\text{Cu}(\text{BF}_4)$, and $\text{Zn}(\text{BF}_4)_2$ were added in pairs (1 equiv each) to a solution of the components 1–6 in a 2:2:2:2:1:1 ratio in $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1). The resulting mixtures were heated at

60°C for up to 3 days and the evolution of their composition was followed by ^1H NMR spectroscopy.

When stoichiometric amounts of Fe^{II} and Cu^{I} salts were added to the solution of organic components (Figure 5A and Figure S38), the affinity of the Fe^{II} cations for the imine constituent (1,2) was strong enough to allow the selective self-assembly of $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$, with 95% of the anticipated Fe^{II} complex being formed after 3 days.^[14] In contrast, the Cu^{I} ions were not able to promote the formation of $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$, despite the trapping of components 1 and 2 in $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$. After 3 days, 65% of the initial component 4 still remained. From this result, one can conclude that components 5 and 6 likely compete with components 3 and 4 for the formation of an alternative, more stable, Cu^{I} or Cu^{II} complex (unfortunately this alternative complex could not be identified).

When Zn^{II} and Cu^{I} salts were allowed to react with the initial library of components (Figure 5B and Figure S39), the Cu^{I} complex $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ was unable to self-sort from the reacting mixture (unfortunately, no alternative copper complex could be identified). After 3 days, the only apparent complex in the ^1H NMR spectrum of the reaction mixture was $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$, accounting for 70% of the initial Zn^{II} cations. (More details on the composition of the reaction mixture can be found in Section 3.6.2 of the Supporting Information.) No signals corresponding to the complex $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ could be detected in the ^1H NMR spectrum of the reaction after 3 days. In this case, the strong binding of aminoquinoline 1 to Cu^{I} cations may explain both the absence of detectable Cu^{I} complexes and the absence of the complex $[\text{Zn}(\mathbf{1},\mathbf{2})_2]^{2+}$ —aminoquinoline 1 is known to bind to Cu^{I} cations and promote their oxidation to Cu^{II} .^[9e]

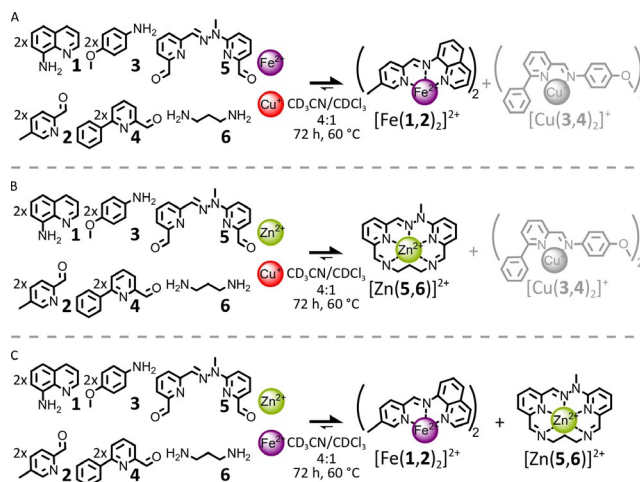


Figure 5. A) Attempted one-pot synthesis of the complexes $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ through self-sorting of their components from a mixture of components 1–6. Only $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ was observed. Reaction conditions: 1/2/3/4/5/6/ $\text{Fe}(\text{BF}_4)_2/\text{Cu}(\text{BF}_4)$ (2:2:2:2:1:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60°C , 72 h. B) Attempted one-pot synthesis of the complexes $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ and $[\text{Cu}(\mathbf{3},\mathbf{4})_2]^+$ through self-sorting of their components 1–6. Only $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ was observed. Reaction conditions: 1–6, $\text{Fe}(\text{BF}_4)_2$, and $\text{Cu}(\text{BF}_4)$ (2:2:2:2:1:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60°C , 72 h. C) One-pot synthesis of the complexes $[\text{Fe}(\mathbf{1},\mathbf{2})_2]^{2+}$ and $[\text{Zn}(\mathbf{5},\mathbf{6})]^{2+}$ through self-sorting of their components from a mixture of components 1–6. Reaction conditions: 1–6, $\text{Fe}(\text{BF}_4)_2$, $\text{Zn}(\text{BF}_4)_2$ (2:2:2:2:1:1:1:1), $\text{CD}_3\text{CN}/\text{CDCl}_3$ (4:1), 60°C , 72 h.

The addition of a stoichiometric amount of Fe^{II} and Zn^{II} salts to the solution of the six organic components led to the near quantitative self-assembly of complexes [Fe(1,2)₂]²⁺ and [Zn(5,6)]²⁺ (Figure 5C and Figure S40). 90% of the anticipated [Fe(1,2)₂]²⁺ complex and 98% of the anticipated [Zn(5,6)]²⁺ complex had formed after 3 days.^[14] (More details on the composition of the reaction mixture can be found in Section 3.6.3 of the Supporting Information.) In the absence of components **3** and **4**, complexes [Fe(1,2)₂]²⁺ and [Zn(5,6)]²⁺ were unable to selectively self-assemble from their reactants due to the persistence of the kinetic product [Zn(1,2)₂]²⁺ in the reaction mixture even after 10 days at 60 °C. In the presence of **3** and **4**, however, after only 3 days at 60 °C, no detectable amount of [Zn(1,2)₂]²⁺ could be observed in the ¹H NMR spectrum of the crude reaction mixture, thus indicating that the presence of components **3** and **4** must facilitate the rearrangement of [Zn(1,2)₂]²⁺ into [Fe(1,2)₂]²⁺ and [Zn(5,6)]²⁺. After further investigations, it was found that the *p*-anisidine **3** was the main contributor to the acceleration of the rearrangement (Figures S41–44). However, the presence of both components **3** and **4** provided a cleaner outcome.

From a more general perspective, the reduction in the diversity of metal complexes formed upon addition of Fe^{II} and Zn^{II} cations to the library of six components **1–6** compared to their addition to the library of four components **1, 2, 5, and 6** (see results and discussion above) exemplifies the concept of “simplicity”,^[9d–f] namely that an increase in the compositional complexity of a system (i.e. a larger number of components) may lead to a simplified output through dynamic competition.^[9e]

Conclusion

The above results demonstrate how the unique coordination preferences of Fe^{II}, Cu^I, and Zn^{II} cations can be exploited to achieve the parallel self-assembly of three completely different imine-containing metal complexes through the self-sorting of a library of six different amine- and 2-formylpyridine-containing components.

By selecting three metal complexes having a hierarchical ordering of their stability and by exploiting the regulatory relationships existing between the constituents of the CDN (i.e. antagonistic and agonistic relationships), it was possible to drastically reduce the amount of assembly instructions needed to achieve the selective self-assembly of the three different metal complexes. Only one of the three metal complexes needed to selectively self-assemble from the initial pool of reactants.

From the present study it appears important to not only consider the thermodynamic outcome of a self-sorting system when designing it, but also to consider, and aim to avoid, kinetic traps that may appear during its assembly, as they may keep an ordered output out of reach. To this end, increasing the initial complexity of the system, by using a larger number of components, may facilitate the assembly process by accelerating the reorganization of some of these kinetic traps, thereby resulting eventually in a simpler, more ordered output (i.e. a smaller number of products).

The development of synthetic strategies to simultaneously control the outcome of multiple dynamic processes shared by several entities is an indispensable step towards creating and exploiting complex dynamic networks of molecules that rival biological systems in terms of their complexity.

Acknowledgements

We acknowledge the financial support from the ERC (Advanced Research Grant SUPRADAPT 290585) and the University of Strasbourg Institute for Advanced Study (USIAS). J.-F.A. acknowledges the financial support from the European Union’s Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 749351. J.-F.A. gratefully acknowledges Prof. Jack Harrowfield, Dr. Jean-Louis Schmitt, and Dr. Christopher J. Campbell for extensive discussions.

Conflict of interest

The authors declare no conflict of interest.

Keywords: constitutional dynamic chemistry · metal-organic complexes · self-assembly · self-sorting · supramolecular chemistry

- [1] For selected resources on the self-organization of chemical systems, see a) G. M. Whitesides, R. F. Ismagilov, *Science* **1999**, *284*, 89–92; b) G. M. Whitesides, B. A. Grzybowski, *Science* **2002**, *295*, 2418–2421; c) J.-M. Lehn, *Science* **2002**, *295*, 2400–2403; d) J.-M. Lehn, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4763–4768; e) D. Newth, J. Finnigan, *Aust. J. Chem.* **2006**, *59*, 841–848; f) J.-M. Lehn, *Chem. Soc. Rev.* **2007**, *36*, 151–160; g) M. Schmittel, K. Mahata, *Angew. Chem. Int. Ed.* **2008**, *47*, 5284–5286; *Angew. Chem.* **2008**, *120*, 5364–5366; h) J. R. Nitschke, *Nature* **2009**, *462*, 736–738; i) M. D. Ward, P. R. Raithby, *Chem. Soc. Rev.* **2013**, *42*, 1619–1636; j) G. Ashkenasy, T. M. Hermans, S. Otto, A. F. Taylor, *Chem. Soc. Rev.* **2017**, *46*, 2543–2554; k) T. Kosikova, D. Philp, *Chem. Soc. Rev.* **2017**, *46*, 7274–7305; l) J.-M. Lehn, *Angew. Chem. Int. Ed.* **2013**, *52*, 2836–2850; *Angew. Chem.* **2013**, *125*, 2906–2921; m) J.-M. Lehn, *Angew. Chem. Int. Ed.* **2015**, *54*, 3276–3289; *Angew. Chem.* **2015**, *127*, 3326–3340; n) J.-F. Ayme, J.-M. Lehn, *Adv. Inorg. Chem.* **2018**, *71*, 3–78.
- [2] For selected general resources on orthogonal self-assembly, see a) W. T. S. Huck, R. Hulst, P. Timmerman, F. C. J. M. van Veggel, D. N. Reinhoudt, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1006–1008; *Angew. Chem.* **1997**, *109*, 1046–1049; b) V. Goral, M. I. Nelen, A. Eliseev, J.-M. Lehn, *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 1347–1352; c) M. L. Saha, S. De, S. Pramanik, M. Schmittel, *Chem. Soc. Rev.* **2013**, *42*, 6860–6909; d) X.-Y. Hu, T. Xiao, C. Lin, F. Huang, L. Wang, *Acc. Chem. Res.* **2014**, *47*, 2041–2051; e) A. Wilson, G. Gasparini, S. Matile, *Chem. Soc. Rev.* **2014**, *43*, 1948–1962; f) P. Wei, X. Yan, F. Huang, *Chem. Soc. Rev.* **2015**, *44*, 815–832.
- [3] For selected general resources on self-sorting, see a) R. Kramer, J.-M. Lehn, A. Marquis-Rigault, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 5394–5398; b) S. J. Rowan, D. G. Hamilton, P. A. Brady, J. K. M. Sanders, *J. Am. Chem. Soc.* **1997**, *119*, 2578–2579; c) A. Wu, L. Isaacs, *J. Am. Chem. Soc.* **2003**, *125*, 4831–

- 4835; d) K. Osowska, O. Š. Miljanić, *Synlett* **2011**, 1643–1648; e) M. M. Safont-Sempere, G. Fernández, F. Würthner, *Chem. Rev.* **2011**, *111*, 5784–5814; f) M. Lal Saha, M. Schmittel, *Org. Biomol. Chem.* **2012**, *10*, 4651–4684; g) Q. Ji, R. C. Lirag, O. Š. Miljanić, *Chem. Soc. Rev.* **2014**, *43*, 1873–1884; h) Z. He, W. Jiang, C. A. Schalley, *Chem. Soc. Rev.* **2015**, *44*, 779–789; i) W. Wang, Y.-X. Wang, H.-B. Yang, *Chem. Soc. Rev.* **2016**, *45*, 2656–2693; j) C.-W. Hsu, O. Š. Miljanić, in *Dynamic Covalent Chemistry: Principles, Reactions, and Applications* (Eds.: W. Zhang, Y. Jin), Wiley, Hoboken, **2017**; k) M. Schmittel, S. Saha, *Adv. Inorg. Chem.* **2018**, *71*, 135–176; l) S. Saha, I. Regeni, G. H. Clever, *Coord. Chem. Rev.* **2018**, *374*, 1–14.
- [4] For selected examples of self-sorting processes based on dynamic covalent bonds, see a) J. W. Sadownik, D. Philp, *Angew. Chem. Int. Ed.* **2008**, *47*, 9965–9970; *Angew. Chem.* **2008**, *120*, 10113–10118; b) B. İçli, N. Christinat, J. Tönnemann, C. Schüttler, R. Scopelliti, K. Severin, *J. Am. Chem. Soc.* **2009**, *131*, 3154–3155; c) P. Vongvilai, O. Ramström, *J. Am. Chem. Soc.* **2009**, *131*, 14419–14425; d) K. Osowska, O. Š. Miljanić, *J. Am. Chem. Soc.* **2011**, *133*, 724–727; e) Q. Ji, O. Š. Miljanić, *J. Org. Chem.* **2013**, *78*, 12710–12716; f) C. W. Hsu, O. Š. Miljanić, *Angew. Chem. Int. Ed.* **2015**, *54*, 2219–2222; *Angew. Chem.* **2015**, *127*, 2247–2250; g) S. Klotzbach, F. Beuerle, *Angew. Chem. Int. Ed.* **2015**, *54*, 10356–10360; *Angew. Chem.* **2015**, *127*, 10497–10502.
- [5] For selected examples of self-sorting processes based on metal complexes, see a) P. N. W. Baxter, J.-M. Lehn, A. DeCian, J. Fischer, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 69–72; *Angew. Chem.* **1993**, *105*, 92–95; b) D. L. Caulder, K. N. Raymond, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1440–1442; *Angew. Chem.* **1997**, *109*, 1508–1510; c) P. N. Taylor, H. L. Anderson, *J. Am. Chem. Soc.* **1999**, *121*, 11538–11545; d) C. Addicott, N. Das, P. J. Stang, *Inorg. Chem.* **2004**, *43*, 5335–5338; e) Y. R. Zheng, H. B. Yang, K. Ghosh, L. Zhao, P. J. Stang, *Chem. Eur. J.* **2009**, *15*, 7203–7214; f) A. M. Johnson, R. J. Hooley, *Inorg. Chem.* **2011**, *50*, 4671–4673; g) X. Lu, X. Li, K. Guo, T.-Z. Xie, C. N. Moorefield, C. Wesdemiotis, G. R. Newkome, *J. Am. Chem. Soc.* **2014**, *136*, 18149–18155; h) W. M. Bloch, J. J. Holstein, W. Hiller, G. H. Clever, *Angew. Chem. Int. Ed.* **2017**, *56*, 8285–8289; *Angew. Chem.* **2017**, *129*, 8399–8404.
- [6] For selected examples of self-sorting processes based on constitutional dynamic metal complexes, see a) D. Schultz, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2006**, *45*, 2453–2456; *Angew. Chem.* **2006**, *118*, 2513–2516; b) M. Schmittel, M. L. Saha, J. Fan, *Org. Lett.* **2011**, *13*, 3916–3919; c) C. J. Campbell, D. A. Leigh, I. J. Vitorica-Yrezabal, S. L. Woltering, *Angew. Chem. Int. Ed.* **2014**, *53*, 13771–13774; *Angew. Chem.* **2014**, *126*, 13991–13994; d) A. Jiménez, R. A. Bilbeisi, T. K. Ronson, S. Zarra, C. Woodhead, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2014**, *53*, 4556–4560; *Angew. Chem.* **2014**, *126*, 4644–4648; e) J.-F. Ayme, J. E. Beves, C. J. Campbell, D. A. Leigh, *Angew. Chem. Int. Ed.* **2014**, *53*, 7823–7827; *Angew. Chem.* **2014**, *126*, 7957–7961; f) L. R. Holloway, M. C. Young, G. J. Beran, R. J. Hooley, *Chem. Sci.* **2015**, *6*, 4801–4806; g) A. M. Johnson, C. A. Wiley, M. C. Young, X. Zhang, Y. Lyon, R. R. Julian, R. J. Hooley, *Angew. Chem. Int. Ed.* **2015**, *54*, 5641–5645; *Angew. Chem.* **2015**, *127*, 5733–5737; h) C. A. Wiley, L. R. Holloway, T. F. Miller, Y. Lyon, R. R. Julian, R. J. Hooley, *Inorg. Chem.* **2016**, *55*, 9805–9815; i) L. R. Holloway, P. M. Bogie, R. J. Hooley, *Dalton Trans.* **2017**, *46*, 14719–14723.
- [7] For selected examples on self-sorting processes involving supramolecular architectures built around more than one type of metal template, see a) X. Sun, D. W. Johnson, D. L. Caulder, R. E. Powers, K. N. Raymond, E. H. Wong, *Angew. Chem. Int. Ed.* **1999**, *38*, 1303–1307; *Angew. Chem.* **1999**, *111*, 1386–1390; b) F. Ibukuro, M. Fujita, K. Yamagushi, J.-P. Sauvage, *J. Am. Chem. Soc.* **1999**, *121*, 11014–11015; c) K. Mahata, M. Schmittel, *J. Am. Chem. Soc.* **2009**, *131*, 16544–16554; d) K. Mahata, M. L. Saha, M. Schmittel, *J. Am. Chem. Soc.* **2010**, *132*, 15933–15935; e) M. M. Smulders, A. Jiménez, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2012**, *51*, 6681–6685; *Angew. Chem.* **2012**, *124*, 6785–6789; f) M. L. Saha, M. Schmittel, *J. Am. Chem. Soc.* **2013**, *135*, 17743–17746; g) M. L. Saha, N. Mittal, J. W. Bats, M. Schmittel, *Chem. Commun.* **2014**, *50*, 12189–12192; h) W. J. Ramsay, F. T. Szczypinski, H. Weissman, T. K. Ronson, M. M. J. Smulders, B. Rybtchinski, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2015**, *54*, 5636–5640; *Angew. Chem.* **2015**, *127*, 5728–5732; i) F. J. Rizzuto, W. J. Ramsay, J. R. Nitschke, *J. Am. Chem. Soc.* **2018**, *140*, 11502–11509; j) M. D. Wise, J. J. Holstein, P. Pattison, C. Besnard, E. Solari, R. Scopelliti, G. Bricogne, K. Severin, *Chem. Sci.* **2015**, *6*, 1004–1010; k) H. Sepehrpour, M. L. Saha, P. J. Stang, *J. Am. Chem. Soc.* **2017**, *139*, 2553–2556; l) S. Gaikwad, M. L. Saha, D. Samanta, M. Schmittel, *Chem. Commun.* **2017**, *53*, 8034–8037.
- [8] For selected general resources on constitutional dynamic chemistry, see a) J.-M. Lehn, *Top. Curr. Chem.* **2012**, *322*, 1–32; b) *Constitutional Dynamic Chemistry, Topics in Current Chemistry, Vol. 322* (Ed.: M. Barboiu), Springer, Berlin, **2012**.
- [9] For selected recent examples of applications of constitutional dynamic chemistry, see a) N. Hafezi, J.-M. Lehn, *J. Am. Chem. Soc.* **2012**, *134*, 12861–12868; b) G. Vantomme, S. Jiang, J.-M. Lehn, *J. Am. Chem. Soc.* **2014**, *136*, 9509–9518; c) J. Holub, G. Vantomme, J.-M. Lehn, *J. Am. Chem. Soc.* **2016**, *138*, 11783–11791; d) S. Dhers, J. Holub, J.-M. Lehn, *Chem. Sci.* **2017**, *8*, 2125–2130; e) G. Men, J.-M. Lehn, *J. Am. Chem. Soc.* **2017**, *139*, 2474–2483; f) P. Kovaříček, A. C. Meister, K. Flidrová, R. Cabot, K. Kovaříčková, J.-M. Lehn, *Chem. Sci.* **2016**, *7*, 3215–3226; g) O. Shyshov, R.-C. Brachvogel, T. Bachmann, R. Srikantharajah, D. Segets, F. Hampel, R. Puchta, M. von Delius, *Angew. Chem. Int. Ed.* **2017**, *56*, 776–781; *Angew. Chem.* **2017**, *129*, 794–799; h) H. Löw, E. Mena-Osteritz, M. von Delius, *Chem. Sci.* **2018**, *9*, 4785–4793; i) A. Osypenko, S. Dhers, J.-M. Lehn, *J. Am. Chem. Soc.* **2019**, *141*, 12724–12737.
- [10] For selected examples of the complexity of the metallo-supramolecular architectures reachable from amine- and 2-formylpyridine-containing components, see a) K. S. Chichak, S. J. Cantrill, A. R. Pease, S.-H. Chiu, G. W. V. Cave, J. L. Atwood, J. F. Stoddart, *Science* **2004**, *304*, 1308–1312; b) J. R. Nitschke, *Acc. Chem. Res.* **2007**, *40*, 103–112; c) J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, K. Rissanen, D. Schultz, *Nat. Chem.* **2012**, *4*, 15–20; d) J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, D. Schultz, *J. Am. Chem. Soc.* **2012**, *134*, 9488–9497; e) J. E. Beves, C. J. Campbell, D. A. Leigh, R. G. Pritchard, *Angew. Chem. Int. Ed.* **2013**, *52*, 6464–6467; *Angew. Chem.* **2013**, *125*, 6592–6595; f) C. S. Wood, T. K. Ronson, A. M. Belenguer, J. J. Holstein, J. R. Nitschke, *Nat. Chem.* **2015**, *7*, 354–358.
- [11] For selected examples of the functional potential of metallo-supramolecular architectures built from amine- and 2-formylpyridine-containing components, see: *Potential for adaptation to stimuli*, see Ref. [9] and a) V. E. Campbell, X. de Hatten, N. Delsuc, B. Kauffmann, I. Huc, J. R. Nitschke, *Nat. Chem.* **2010**, *2*, 684–687; b) A. J. McConnell, C. S. Wood, P. P. Neelakandan, J. R. Nitschke, *Chem. Rev.* **2015**, *115*, 7729–7793; c) B. S. Pilgrim, D. A. Roberts, T. G. Lohr, T. K. Ronson, J. R. Nitschke, *Nat. Chem.* **2017**, *9*, 1276–1281; d) D. A. Roberts, B. S. Pilgrim, J. R. Nitschke, *Chem. Soc. Rev.* **2018**, *47*, 626–644; e) S. Pramanik, I. Aprahamian, *J. Am. Chem. Soc.* **2016**, *138*, 15142–15145; f) L. R. Holloway, H. H. McGarraugh, M. C. Young, W. Sontising, G. J. O. Beran, R. J. Hooley, *Chem. Sci.* **2016**, *7*, 4423–4427; g) D. A. Roberts, B. S. Pilgrim, G. Sirvinskaitė, T. K. Ronson, J. R. Nitschke, *J. Am. Chem. Soc.* **2018**, *140*, 9616–9623; *potential as molecular container*: h) P. Mal, B. Breiner, K. Rissanen, J. R. Nitschke, *Science* **2009**, *324*, 1697–

- 1699; i) T. K. Ronson, S. Zarra, S. P. Black, J. R. Nitschke, *Chem. Commun.* **2013**, 49, 2476–2490; j) A. G. Salles, Jr., S. Zarra, R. M. Turner, J. R. Nitschke, *J. Am. Chem. Soc.* **2013**, 135, 19143–19146; k) S. Zarra, D. M. Wood, D. A. Roberts, J. R. Nitschke, *Chem. Soc. Rev.* **2015**, 44, 419–432; *potential as biologically active molecules or as mimics of biological molecules*: l) A. C. G. Hotze, N. J. Hodges, R. E. Hayden, C. Sanchez-Cano, C. Paines, N. Male, M.-K. Tse, C. M. Bunce, J. K. Chipman, M. J. Hannon, *Chem. Biol.* **2008**, 15, 1258–1267; m) T. R. Cook, V. Vajpayee, M. H. Lee, P. S. Stang, K. W. Chi, *Acc. Chem. Res.* **2013**, 46, 2464–2474; n) A. D. Faulkner, R. A. Kaner, Q. M. A. Abdallah, G. Clarkson, D. J. Fox, P. Gurnani, S. E. Howson, R. M. Phillips, D. I. Roper, D. H. Simpson, P. Scott, *Nat. Chem.* **2014**, 6, 797–803; o) R. Kaner, S. Allison, A. Faulkner, R. Phillips, D. Roper, S. Shepherd, D. Simpson, N. Waterfield, P. Scott, *Chem. Sci.* **2016**, 7, 951–958; *potential in polymeric materials*: p) C.-F. Chow, S. Fujii, J.-M. Lehn, *Angew. Chem. Int. Ed.* **2007**, 46, 5007–5010; *Angew. Chem.* **2007**, 119, 5095–5098; q) C.-F. Chow, S. Fujii, J.-M. Lehn, *Chem. Asian J.* **2008**, 3, 1324–1335; r) G. Schaeffer, E. Buhler, S. J. Candau, J.-M. Lehn, *Macromolecules* **2013**, 46, 5664–5671; s) S. Ulrich, J.-M. Lehn, *Angew. Chem. Int. Ed.* **2008**, 47, 2240–2243; *Angew. Chem.* **2008**, 120, 2272–2275; t) S. Ulrich, E. Buhler, J.-M. Lehn, *New J. Chem.* **2009**, 33, 271–292; u) S. Ulrich, J.-M. Lehn, *J. Am. Chem. Soc.* **2009**, 131, 5546–5559; *potential as an anion binder*: v) I. A. Riddell, T. K. Ronson, J. K. Clegg, C. S. Wood, R. A. Bilbeisi, J. R. Nitschke, *J. Am. Chem. Soc.* **2014**, 136, 9491–9498; w) J.-F. Ayme, J. E. Beves, C. J. Campbell, G. Gil-Ramírez, D. A. Leigh, A. J. Stephens, *J. Am. Chem. Soc.* **2015**, 137, 9812–9815; x) R. A. Bilbeisi, T. Prakasam, M. Lusi, R. El-Khoury, C. Platas-Iglesias, L. J. Charbonnière, J.-C. Olsen, M. Elhabiri, A. Trabolzi, *Chem. Sci.* **2016**, 7, 2524–2532.
- [12] J.-F. Ayme, J.-M. Lehn, *Chem. Sci.* **2020**, 11, 1114–1121.
- [13] T. Vitvarová, J. Zedník, M. Bláha, J. Vohlídal, J. Svoboda, *Eur. J. Inorg. Chem.* **2012**, 3866–3874.
- [14] The amount of the different species in solution was determined by comparing the integrals of some of their characteristic ¹H NMR signals with the integral of HMDSO, which was used as an internal standard.

Manuscript received: January 16, 2020

Accepted manuscript online: April 14, 2020

Version of record online: June 3, 2020