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Supramolecular Complexes

Solvent-Free Ball-Milling Subcomponent Synthesis of Metallosupramolecular Complexes

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Abstract: Subcomponent self-assembly from components **A**, **B**, **C**, **D**, and Fe^{2+} under solvent-free conditions by self-sorting leads to the construction of three structurally different metallosupramolecular iron(II) complexes. Under carefully selected ball-milling conditions, tetranuclear $[Fe_4(\mathbf{AD}_2)_6]^{4-}$ 22-component cage **1**, dinuclear $[Fe_2(\mathbf{BD}_2)_3]^{2-}$ 11-component helicate **2**, and 5-component mononuclear $[Fe(\mathbf{CD}_3)]^{2+}$ complex **3** were prepared simultaneously in a one-pot reaction from 38 components. Through subcomponent substitution reaction by adding subcomponent **B**, the $[Fe_4(\mathbf{AD}_2)_6]^{4-}$ cage converts quantitatively to the $[Fe_2(\mathbf{BD}_2)_3]^{2-}$ helicate, which, in turn, upon addition of subcomponent **C**, transforms to $[Fe(\mathbf{CD}_3)]^{2+}$, following the hierarchical preference based on the thermodynamic stability of the complexes.

The subcomponent self-assembly[1] is an integral part of self-sorting reactions[2] in which ligands of the metallo-supramolecular complexes are formed in situ from their subcomponents. This concept has proved to offer a promising method for the synthesis of high-purity products from complex mixtures of starting materials.[3] The metal-ion-assisted subcomponent self-assembly of a rigid aromatic linear bisamine, pyridine-2-carboxaldehyde, and iron(II) resulting in tetrahedral $\mathbf{M}_4\mathbf{L}_6$ cage in water reported by the group of Nitschke and us opened a new page on supramolecular tetrahedral complexes.[4] Recently, by exploiting the same dynamic imine chemistry,[5] we have used this concept to prepare the smallest possible tetrahedral $\mathbf{M}_4\mathbf{L}_6$ cage complex[6] and for the anion-controlled formation of an aminal-(bis)imine Fe^{II}-complex.[7] In all the above-mentioned cases the dynamic behavior of the imine bond is the key factor to control the self-assembly process.[8]

In the last few years, mechanochemistry,[9] as a solvent-free synthesis method, has drawn great interest due to its advantages over traditional solution-based methods,[10a] including some self-assembling systems.[10b,c] The core benefit of mechanochemistry is to avoid traditional work-up.[11] This advantage has huge implications to green processes, shown to be economical, time efficient, and environmentally friendly. Quantitative conversion, less by-products, and no purification bring extra benefits to this method. The mechanochemical synthesis of small organic molecules is well explored,[12] also including multistep synthesis[11c] and the synthesis of small mononuclear Zn^{II}, Cu^{II}, and Ni^{II} salen/salophen complexes has been recently demonstrated by James and co-workers.[13]

However, unlike in solution, subcomponent synthesis of complex supramolecular assemblies in absence of any solvent is still rare. Herein we demonstrate that mechanochemistry, under one-pot solvent-free ball-milling conditions offers a very efficient route to prepare three distinct, structurally different, water-soluble metallosupramolecular iron complexes from their respective subcomponents by self-sorting from 38 components. These metallosupramolecular complexes are a tetrahedral $[Fe_4(\mathbf{AD}_2)_6]$ cage **1** (22 components), a dinuclear $[Fe_2(\mathbf{BD}_2)_3]$ triple helicate **2** (11 components), and a mononuclear $[Fe(\mathbf{CD}_3)]$ complex **3** (5 components) (Figure 1), in which $\mathbf{AD}_2$, $\mathbf{BD}_2$, and $\mathbf{CD}_3$ are the bis-, bis-, and tris-Schiff base ligands formed in situ during the one-pot reaction.

The one-pot solvent-free ball-milling reaction emulates the similar solution reaction[14] in which six equivalents of 4,4′-diaminobiphenyl-2,2′-disulfonic acid **A**, three equivalents of 6,6′-oxybis(3-ammoniobenzenesulfonate) **B**, one equivalent of tris(2-aminoethyl)amine **C**, 21 equivalents of 2-formyl pyridine **D**, 18 equivalents of sodium bicarbonate, together with seven equivalents of iron(II) sulfate heptahydrate are mixed together; however, here they were mechanically milled without any solvent in a ball mill (21 Hz) resulting in the same three metallosupramolecular complexes **1**, **2**, and **3** as in solution. This one-pot solvent-free reaction cannot be considered a true solid-state reaction as two of the components (**C** and **D**) are liquids. Individually, under the same ball-milling conditions, the supramolecular complexes **1**, **2**, and **3** were also produced from their respective subcomponents, **A**+**D** for **1**, **B**+**D** for **2** and **C**+**D** for **3**.

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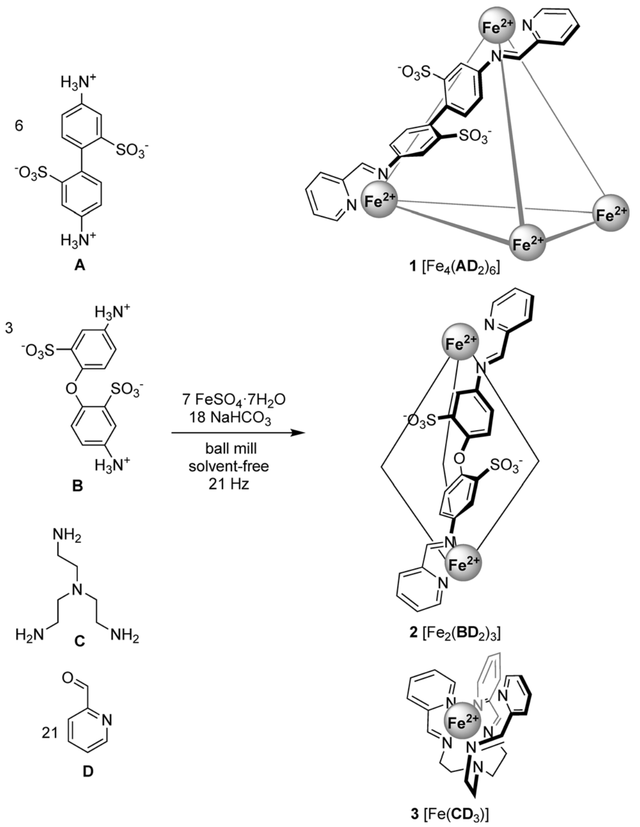

Figure 1. The one-pot solvent-free synthesis of 22-component $[Fe_4(\mathbf{AD}_2)_6]^{4-}$ **1**, 11-component $[Fe_2(\mathbf{BD}_2)_3]^{2-}$ **2**, and 5-component $[Fe(\mathbf{CD}_3)]^{2+}$ **3**. A slight excess of 2-formylpyridine (**D**) was used (1.1 equivalent).

The one-pot and individual reactions were performed under ambient conditions and monitored during the initial synthesis tests using ^{1}H NMR spectroscopy (Figure 2). During monitoring, the ball-milling apparatus was stopped, a small portion of the sample was extracted from the reaction chamber, and the ^{1}H NMR spectrum was recorded in D_2O. The final synthesis was done in a fixed time and the products were removed, placed on a paper filter, and washed with a minimum quantity of acetone to remove the excess pyridine-2-aldehyde (1.1 equiv). The complexes were characterized and their purity verified in comparison to the ^{1}H NMR spectra of a standard sample of the same complexes synthesized in water. The cage **1** was originally synthesized in water in 20 h at 50 °C;[14] however, in here the solvent-free ball-milling reaction times are 2 h for **1**, 1 h for **2**, and 0.5 h for **3**, respectively. The one-pot synthesis of **1**, **2**, and **3** took 2 h.

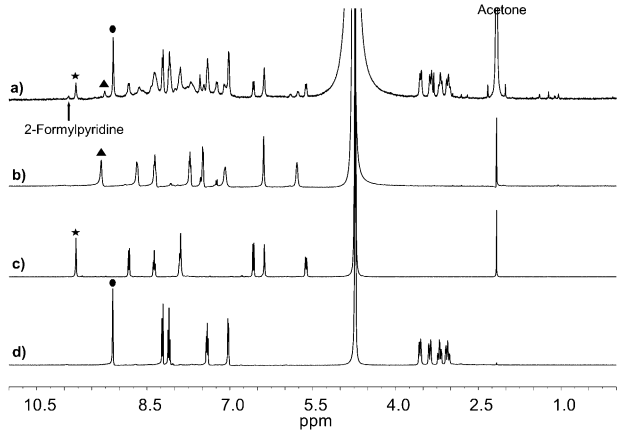

Figure 2. ^{1}H NMR spectra of the complexes obtained under solvent-free ball milling condition; a) **1**, **2**, and **3** from the one-pot reaction; individual reactions b) **1**, c) **2**, d) **3**.

The X-ray structures of the tetraanionic tetrahedral cage **1** as tetra-TMA (tetramethylammonium)$^+$ and di-Fe(H$_2$O)$^{2+}$ salts[4,16] and the mononuclear complex **3** as perchlorate,[17] tetrafluoroborate,[18] and hexafluorophosphate[19] salts have been reported previously. But the X-ray structure of the triple-helicate **2** has been unknown prior to this study. The negatively (overall 2−) charged triple-stranded helicate **2** is structurally very similar to the corresponding nonsulfonated diphenyl ether Ni- and Co-triple-helicates.[20] Whereas the Fe···Fe separation in **2** is 11.25 Å, the Ni- and Co-helicates have Ni···Ni and Co···Co distances of 11.41 and 11.37 Å, respectively (Figure 3). The triple-helicate **2** has tighter helix structure, with a C–H···centroid distance of the adjacent phenyl ring of 2.80 Å, when in the Ni- and Co-diphenyl ether triple-helicates the same distance is 3.00 Å.

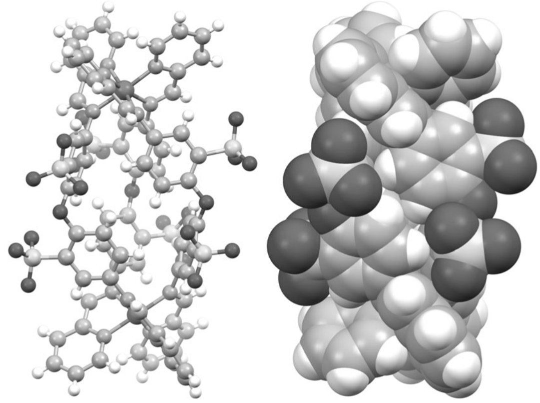

Figure 3. The X-ray structure of the Fe-triple-helicate **2**.

Previous studies in solution[14] have established that complexes **1**, **2**, and **3** can undergo transformation to a thermodynamically more stable structure upon an appropriate subcomponent substitution reaction. The role of the solvent has been considered to be crucial for the transformation from the thermodynamically less stable complex to the thermodynamically more stable complex, like **1**→**2**. However, under solvent-free conditions, due to restrictions of the molecular movements, the concept of dynamic chemistry has not been explored or defined. However, it has been anticipated that under ball-milling conditions the products formed are thermodynamically controlled.

The well-defined differences in the thermodynamical stability of **1**, **2**, and **3** enable post-assembly transformation (substitution) chemistry to progress in a predictable, hierarchical path also under solvent-free ball-milling conditions. The addition of the tris-amine subcomponent **C** to either **1** or **2** under ball-milling conditions yielded **3**, with ejection of diamine subcomponent **A** or **B**, respectively. Similarly adding **B** into **1** resulted in **2**, which could then subsequentially be transformed into **3** upon addition of **C** (Figure 4).

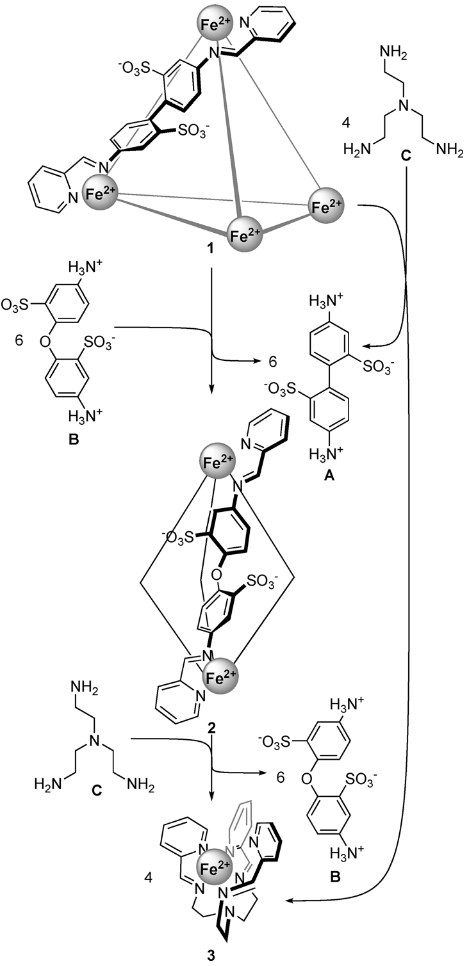

Figure 4. The solvent-free post-assembly transformation (substitution) reaction[15] of **1** and **2** leading to **3**.

Our focus on the competition among the iron complexes includes the flexibility/rigidity of their backbones and the entropy associated with degrees of freedom of mono-, di-, and tetra-iron(II) complexes. The geometries of **1**, **2**, and **3** derive from the flexibilities of their respective amine subcomponents: To maximize entropy, each imine ligand will generate the smallest self-assembled structure possible in which all iron(II) ions are hexacoordinate and all imine nitrogen atoms are coordinated to iron(II). As can be seen from the structural analysis of the iron complexes, the number of building blocks presents in the systems are 22, 11, and 5 for **1**, **2**, and **3**, respectively. Therefore the relative thermodynamic stability of the complexes could be as follows, $\mathbf{3} > \mathbf{2} > \mathbf{1}$. Thus the experimental outcome shown in Figure 4 may be justified.

Many self-sorting methodologies[2c,3b,21] are known in 'systems biology'.[22] However, the study of 'systems chemistry'[3c,23] provides primary insights into the self-sorting principles[24] of molecular networks which ultimately assist us to acquire new systems[25] with properties and functions unlike any conventional materials.[26] In other words, the dynamic self-sorting approach can enable easy access to certain materials of interests by changing inputs in either sub- or multicomponent systems.[27] To the best of our knowledge, this is the first example of a subcomponent self-assembly under solvent-free condition in which both cationic (**1** and **2**) and anionic (**3**) complexes were generated together.

In conclusion, an unprecedented example of self-sorting of three distinct iron(II) complexes under solvent-free mechanomilling condition has been demonstrated. The obtained three distinct structures were obtained from 38 subcomponents in one-pot reaction at room temperature. However, these complexes were transformed to their smaller and more stable counterparts upon subcomponent substitution under solvent-free conditions. Currently, in our laboratory, we are focusing on developing more complex supramolecular architectures whose molecular recognition can be reversibly controlled to facilitate control over product distribution of a particular system of interest.

Experimental Section

Detailed experimental procedures are given in the Supporting Information. All the complexes are known from literature and were characterized using NMR spectroscopy.

During the transformation reaction from **2** to **3**, silica gel (column chromatography grade, 100–200 mesh) was used to avoid stickiness at the milling ball. In absence of silica gel the reaction of **2** to **3** was unsuccessful.

One-pot ball-milling synthesis of 1, 2, and 3: Tris(2-ethylamino)-amine **A** (1.46 mg, 10.0 μmol), 4,4′-diaminobiphenyl ether-2,2′-disulfonic acid **B** (4.5 mg, 80%, balance water, 6.6 μmol), 4,4′-diaminobiphenyl-2,2′-disulfonic acid **C** (4.6 mg, 75%, balance water, 6.6 μmol), sodium bicarbonate (5.0 mg, 60 μmol), $FeSO_4{\cdot}7H_2O$ (6.5 mg, 23.3 μmol), and 2-formyl pyridine (6.7 μL, 70 μmol) were added in a 10 mL Teflon reaction chamber with a one 5 mm diameter steel ball. After reaction the mixture was washed with acetone and dissolved in 0.5 mL D_2O and ^1H NMR spectra recorded.

Crystal data for 2: $M = 2160.60$, violet block, $0.32 \times 0.26 \times 0.18$ mm^3, triclinic, space group $P\bar{1}$, $a = 15.8610(8)$ Å, $b = 15.9946(7)$ Å, $c = 22.5064(8)$ Å, $\alpha = 97.075(3)^\circ$, $\beta = 102.500(4)^\circ$, $\gamma = 97.641(4)^\circ$, $V = 5456.2(4)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.315$ g cm^{-3}, F000 = 2195, $\mu = 0.594$ mm^{-1}, $T = 120$ K, $2\theta_{max} = 50.6^\circ$, 19722 reflections used, 10748 with $I_o > 2\sigma(I_o)$, $R_{int} = 0.0965$, 1502 parameters, 175 restraints, GoF = 1.076, $R = 0.1361$ [$I_o > 2\sigma(I_o)$], wR = 0.3811 (all reflections), $1.122 < \Delta\rho < -1.097$ e Å^3. CCDC-1043159 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Keywords: ball mill · dynamic imine chemistry · mechanochemistry · multicomponent synthesis · self-sorting · supramolecular chemistry

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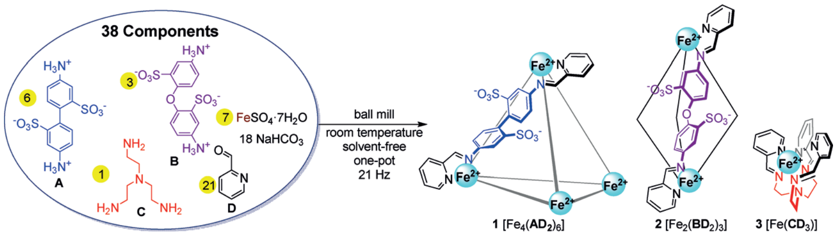

Four different subcomponents self-sorted around iron(II) templates to create Fe_4, Fe_2, and Fe_1 complexes under ball milling. Input-controlled clear hierarchical preferences were observed: the Fe_4 could be converted to Fe_2 or Fe_1. Similarly Fe_2 was switchable to Fe_1 depending on the input used.

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