Post-assembly error-checking in subphthalocyanine based M_3L_2 metallosupramolecular capsules†‡

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A kinetic mixture of self-assembled subphthalocyanine-based capsules was shown to gradually reorganize into its more stable symmetrical components by electrospray mass spectrometry.

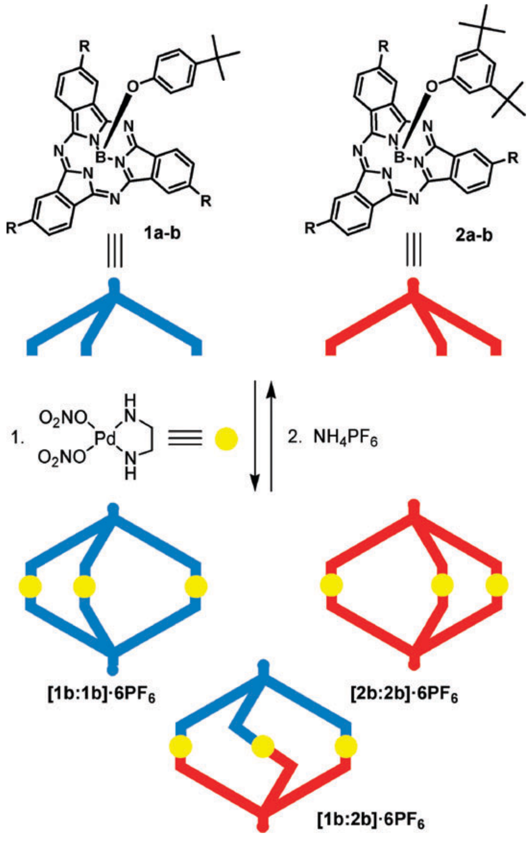
Metallo-supramolecular chemistry has undergone a remarkable expansion over the last decade.[1] Several works have dealt with the study of equilibrating systems of supramolecular assemblies. This field of chemistry has found applications in biological molecular recognition, dynamic materials, and catalysis.[2] Such systems rely on the reversible association between basic components, spontaneously generating supramolecular libraries that may evolve towards smaller sets of self-assembled structures in the presence or in the absence of a target molecule.

In order to explore processes of self-organization by selection, we describe here (i) the self-assembly of a set of three M_3L_2 capsules starting from two symmetrically distinct *tris*-3-pyridyl-substituted subphthalocyanine[3] derivatives **1b** and **2b** (Scheme 1) employing Pd(II) as metal ion followed by (ii) the kinetic study of their exchange by electrospray mass spectrometry.[4] It is worth mentioning that the C_3 symmetrical derivative of SubPc **1b** was shown to self-assemble into a mixture of two equilibrating diastereoisomeric cages[5] whereas C_1 symmetrical SubPc **2b** gave rise to only one out of the six possible diastereoisomeric cages.

Subphthalocyanines are 14 π-electron non-planar aromatic macrocycles comprising three diiminoisoindole units *N*-fused around a central boron atom.[3] Their cone-shaped aromatic structure makes them very appealing concave building blocks for their use in the self-assembly of dimeric hollow capsules and the subsequent molecular recognition of complementary convex π-conjugated molecules such as fullerenes.[5] Moreover, they show very attractive photophysical and electrochemical properties and have found applications as chromophores in nonlinear optics,[7] in OLEDs,[8] in photovoltaic devices[9] and in multicomponent donor–acceptor systems.[10]

With the purpose of studying the formation of the mixed cage $[\mathbf{1b}{:}\mathbf{2b}]\cdot6PF_6$ (Scheme 1) by mass spectrometry we took advantage of the readily functionalizable axial position on the boron atom of the subphthalocyanines.[11] Thus accordingly, 4-*tert*-butylphenol and 3,5-di-*tert*-butylphenol were incorporated into **1a–b** and **2a–b**, respectively, without altering the molecular recognition properties of the pyridyl derivatives in **1b** and **2b**.

4-*tert*-Butylphenoxy axially substituted SubPc **1a** was obtained (Scheme 1) in 81% yield by reacting 4-*tert*-butylphenol with the C_3 isomer of the corresponding chlorosubphthalocyanine in toluene at reflux for 16 h. Triple Sonogashira cross-coupling reaction between 3-ethynylpyridine and SubPc **1a** in the presence of catalytic amounts of CuI and $PdCl_2(PPh_3)_2$ in triethylamine as solvent gave C_3 symmetrical SubPc **1b** in 62% yield. SubPc **1b** was characterized by NMR spectroscopy, MALDI-TOF mass spectrometry and UV spectrophotometry. ^1H NMR spectroscopy of **1b** in $CDCl_3$ showed the expected



Scheme 1 Structural formula of subphthalocyanines **1** and **2** (**a**: R = I, **b**: R = 3-ethynylpyridine) and schematic representation of their self-assembly into M_3L_2 subphthalocyanine cages.

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pattern of signals in which one third of the protons account for all the signals corresponding to the C_3 symmetrical macrocycle. The UV-vis spectrum of **1b** shows the expected Q band at 583 nm and B or Soret band at 346 nm. MALDI-TOF mass spectrometry shows a peak at 848.4 corresponding to $[M + H]^+$ and a peak corresponding to the loss of the axial *tert*-butylphenoxy substituent at 698.2. SubPc **2b** was synthesized in a similar way according to a previously described procedure.[6]

Symmetrical M_3L_2 reference cages [**1b** : **1b**]·$6PF_6$ and [**2b** : **2b**]·$6PF_6$ of M_3L_2 subphthalocyanine cages were self-assembled individually.[5,6] The reactions were performed by mixing SubPc **1b** and **2b**, respectively, and stoichiometric amounts of $(en)Pd(NO_3)_2$ (1.5 eq.) in a 1 : 1 : 1 mixture of water, methanol and acetonitrile at 60 °C for 48 hours followed by anion exchange with a ten-fold excess of ammonium hexafluorophosphate. The formation of cage compound [**1b**:**1b**]·$6PF_6$ was supported by ESI-MS which showed prominent peaks at m/z = 1386.3 $[M - 2PF_6]^{2+}$, 875.8 $[M - 3PF_6]^{3+}$, 620.5 $[M - 4PF_6]^{4+}$, 467.5 $[M - 5PF_6]^{5+}$ and 365.4 $[M - 6PF_6]^{6+}$, respectively. The ^1H NMR spectrum of [**1b** : **1b**]·$6PF_6$ in CD_3CN showed the expected pattern of signals. Cage [**2b** : **2b**]·$6PF_6$ was previously described.[6]

A mixture of the three M_3L_2 cages [**1b** : **1b**]·$6PF_6$, [**1b** : **2b**]·$6PF_6$ and [**2b** : **2b**]·$6PF_6$ (see Fig. 1 for minimized PM3 structures) was obtained by combining together SubPcs **1b** and **2b** in a 3 to 2 ratio and by following virtually the same methodology described above except that it was performed at room temperature and for only one hour. ^1H NMR spectrum of the resulting product in CD_3CN showed an extremely complex pattern of signals in accordance with the presence of a mixture of various cage compounds. The presence of signals at *ca.* 9.0 ppm and the relative integral values of the various regions of the spectrum (*i.e.* aromatic *vs.* ethylenediamine protons) clearly demonstrated the presence of M_3L_2 cages in which the pyridine moieties are coordinated to Pd(II). Final evidence came from the ESI-MS spectra (Fig. 2) showing three sets of three peaks at 621.3, 468.3 and 365.9 for [**1b**:**1b**]·$6PF_6$, at 635.3, 479.5 and 375.5 for [**1b**:**2b**]·$6PF_6$ and at 649.5, 490.7 and 384.8 for [**2b** : **2b**]·$6PF_6$, corresponding to the three cages and the loss of four, five and six hexafluorophosphate anions, respectively.

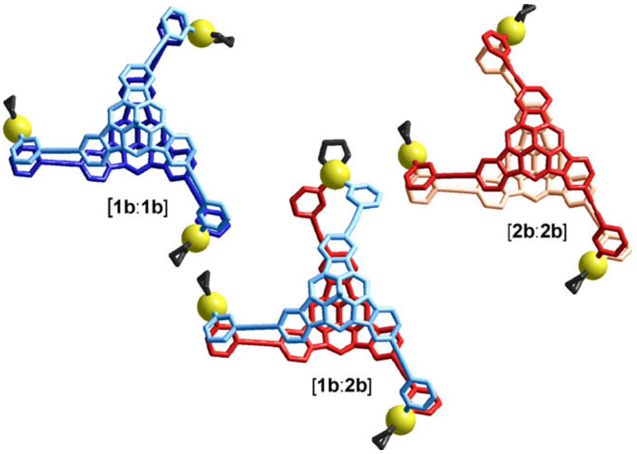

Fig. 1 Tubular representation of the minimized structures (PM3 semiempirical calculations) of M_3L_2 subphthalocyanine cages [**1b** : **1b**], [**2b** : **2b**] and [**1b** : **2b**] (Pd: yellow, ethylenediamine: black). Axial groups were omitted for clarity.

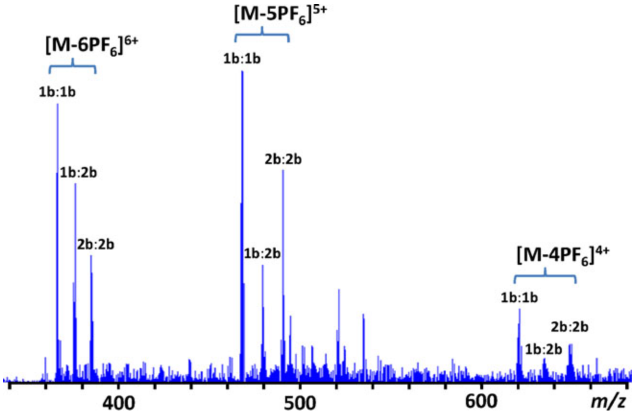

Fig. 2 Portion of the electrospray mass spectrum (at t = 190 min) showing the peaks corresponding to the loss of four, five and six PF_6^- anions of the M_3L_2 cages [**1b** : **1b**], [**2b** : **2b**] and [**1b** : **2b**].

Electrospray mass spectrometry analyses of the same mixture were performed at 30 min intervals starting from t = 100 min that corresponds to the minimum self-assembly and work-up duration. This kinetic study revealed a significant decrease of the relative ratio of [**1b** : **2b**]·$6PF_6$ (Fig. 3) and an increase of that of [**1b** : **1b**]·$6PF_6$ and [**2b** : **2b**]·$6PF_6$ over a 5 h period of time. These trends are consistent with the "immediate" formation of a statistical mixture (36/48/16) of the three cages [**1b** : **1b**]·$6PF_6$, [**1b** : **2b**]·$6PF_6$ and [**2b** : **2b**]·$6PF_6$, respectively, followed by slow equilibration towards the more stable symmetrical cages [**1b** : **1b**]·$6PF_6$ and [**1b** : **2b**]·$6PF_6$ in a 3 to 2 ratio reflecting the initial ratio of starting subphthalocyanines **1b** and **2b**.

In order to obtain quantitative data from this study, we made the assumption that the only relevant kinetic process is the irreversible conversion of the mixed cage [**1b** : **2b**]·$6PF_6$ into the symmetrical ones [**1b** : **1b**]·$6PF_6$ and [**2b** : **2b**]·$6PF_6$ according to the following equation:

$$2([\mathbf{1b}:\mathbf{2b}]\cdot 6PF_6) \xrightarrow{k} [\mathbf{1b}:\mathbf{1b}]\cdot 6PF_6 + [\mathbf{2b}:\mathbf{2b}]\cdot 6PF_6.$$

By fitting the experimental data according to this simple kinetic model (Fig. 3, R^2 = 0.98) we could derive the second

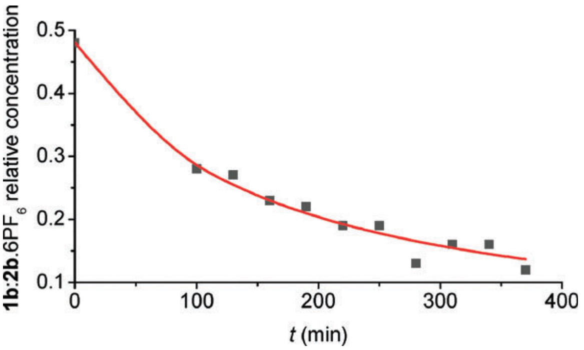

Fig. 3 Relative concentration of cage [**1b** : **2b**] with respect to the total concentration of cages as a function of time (filled squares). The red line shows the fitting curve (Origin 7.0) obtained employing a second order rate law.

order rate constant of the process: $k = 0.74\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ (see ESI‡).

These results demonstrate that after initial self-assembly of a statistical mixture of cages, the situation slowly equilibrates in a way similar to an error checking process towards the formation of the thermodynamically more stable symmetrical cages. It was shown that it was possible to follow quantitatively such dynamic process by electrospray mass spectrometry.

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