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Chiral Self-Discrimination in a M_3L_2 Subphthalocyanine Cage

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Subphthalocyanines[1] (SubPcs) are 14 π-electron aromatic macrocycles, combining three *N*-fused diiminoisoindole units around a boron atom (Figure 1, compounds **1**−**3**). Their curve-shaped structure,[2] their synthetic versatility,[1−3] and their attractive physical properties[4] make them ideal building blocks for the construction of functional homodimeric capsules. On the other hand, the C_{3v} symmetry of the SubPc core can be modified in accordance with the substitution pattern on the diiminoisoindole subunits. Thus, for example, SubPcs **1**−**3** (Figure 1) have C_3 symmetry and are inherently chiral; they possess two [M] and [P] enantiomers[5] that have the potential for chiral recognition in a C_3 environment.[6] In this sense, the formation of a SubPc molecular capsule may be accompanied by a self-recognition[7] or a self-discrimination[8] event that occurs when a given enantiomer within a racemic mixture specifically recognizes itself or its opposite, respectively. Very few examples of self-discrimination have been described thus far and to the best of our knowledge only one dealt with the partial self-discrimination in the formation of a cyclotriveratrilene-based cage compound.[9]

Since metal−pyridine coordination[10] has proved to be an excellent tool in self-assembly, we designed the SubPc-based tritopic receptor **3** (Figure 1) that combines both the preorganization of the rigid SubPc skeleton and three symmetrically located 3-pyridyl units. The only element of flexibility of the system resides in the torsional angle at the junction between the SubPc core and the pyridine ring.

In this communication we describe the synthesis and characterization of SubPc **3** and its dimerization into a heterochiral C_{3h} symmetric M_3L_2 cage[11] in the presence of a stoichiometric amount of $(en)Pd(NO_3)_2$.

Axially substituted SubPc **2** was obtained in 80% yield by reacting 3,5-di-*tert*-butylphenol with the C_3 isomer of SubPc **1**[5a] in toluene at reflux for 16 h. Stille cross-coupling reaction between dibutyl-3-pyridyl stannane[12] and **2** gave SubPc **3** in 42% yield. Cage compound **4**·6NO_3 was obtained by mixing at room temperature for 30 min **3** and 1.5 equiv of $(en)Pd(NO_3)_2$ in a 1:1:1 mixture of water, methanol. and acetonitrile. The complex was isolated in 91% yield as its hexafluorophosphate salt by adding a 10-fold excess of NH_4PF_6 to the reaction mixture.

The formation of the cage compound was supported by ESI-MS which showed prominent peaks for $[\mathbf{4}\cdot 4PF_6]^{2+}$, $[\mathbf{4}\cdot 3PF_6]^{3+}$, $[\mathbf{4}\cdot 2PF_6]^{4+}$, $[\mathbf{4}\cdot PF_6]^{5+}$, $[\mathbf{4}]^{6+}$ at m/z = 1371.3, 865.6, 613.0, 461.5, and 360.3, respectively.

The UV−vis spectra of precursor **3** and cage **4**·6PF_6 are virtually identical (λ_{max} = 574 nm) showing that the formation of the complex does not modify significantly the electronic structure of the subphthalocyanine.

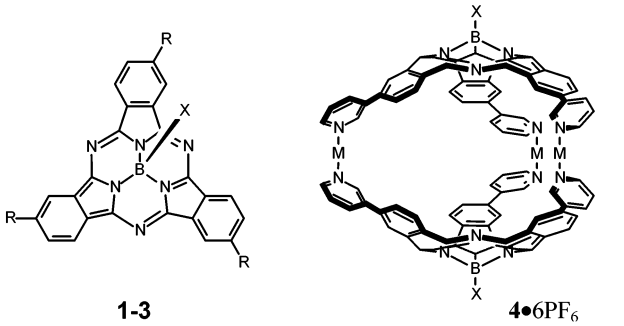

Figure 1. Subphthalocyanine **1** (X = Cl, R = I), SubPc **2** (X = 3,5-di-*tert*-butylphenoxy, R = I), SubPc **3** (X = 3,5-di-*tert*-butylphenoxy, R = 3-pyridyl), cage compound **4**·6PF_6 (same as **3** with M = Pd(en)).

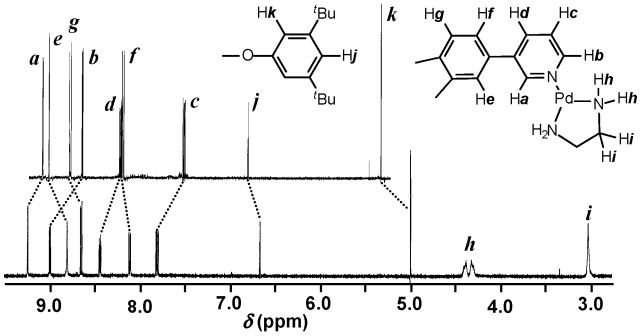

Figure 2. Portions of the ^{1}H NMR (500 MHz, 25 °C) spectra in CD_3CN of SubPc **3** (top) and cage compound **4**·6PF_6 (bottom).

The ^{1}H NMR spectrum of **4**·6PF_6 in CD_3CN revealed (Figure 2) a very symmetrical environment in which all six arms of the two SubPcs are magnetically equivalent. This well-resolved and highly symmetrical spectrum is consistent with an achiral C_{3h} symmetric compound and rules out the formation of a larger M_6L_4 complex. The assignment of the signals for **3** and **4**·6PF_6 was achieved on the basis of COSY experiments. Signals corresponding to the protons attached to the pyridine fragments (H_{a-d}) all undergo downfield shifts (ranging from 0.16 to 0.35 ppm) with respect to SubPc **3**, as a consequence of the Pd−N dative bond formation. On the other hand, the signals corresponding to the protons attached to the SubPc framework (H_{e-g}) experience upshield fields (ranging from −0.08 to −0.21 ppm), with respect to SubPc **3**, most probably as a consequence of the change in the torsional angle between the 3-pyridyl moiety and the adjacent SubPc aromatic unit as complexation occurs. Integrations of the signals corresponding to both the SubPc and the 1,2-ethanediamine moieties of the M_3L_2 complex are in perfect accordance with a 2 to 3 ratio, respectively. A NOESY experiment[13] performed at 25 °C in CD_3COCD_3 of **4**·6PF_6 confirmed the structure of the complex since strong cross-peaks

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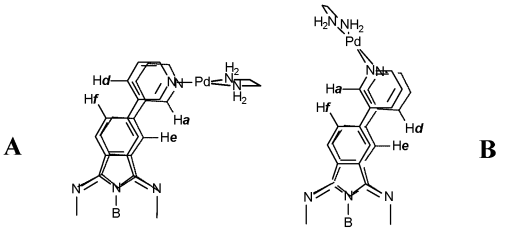

Figure 3. Schematical representation of the two possible arrangements of two Pd-coordinated 3-pyridyl subunits within **4**·6PF_6.

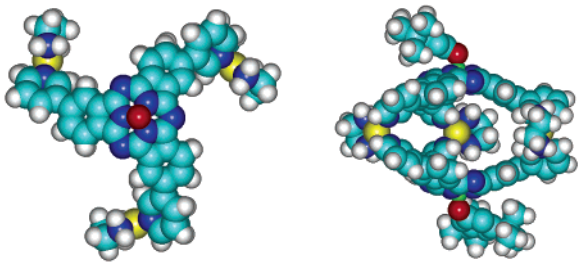

Figure 4. Top (right) and side (left) views of the **AAA** isomer of **4**·6PF_6 (generated by MM2 minimization). 3,5-Di-*tert*-butylphenoxy axial groups were removed for clarity in the top view.

were observed between the 3-pyridyl protons H_a and H_b and the ethanediamine protons H_h (Figure 2).

The homotopicities of (i) the methylene protons H_i belonging to the 1,2-ethanediamine ligands in **4**·6PF_6, that appear as a singlet at 3.06 ppm, and (ii) the amine protons (H_h) that give rise to a neat AB system upon irradiation of the methylene protons (H_i) are consistent with an achiral environment.[8] These results further confirmed that self-assembly of the cage takes place in a self-discriminatory manner between opposite enantiomers and yield a C_{3h} entity.

On the basis of the geometric restraints imposed by the Pd square planar coordination and the C_{3h} symmetry of **4**·6PF_6, the only two conceivable 3-pyridyl spatial arrangements within the complex are **A** and **B** schematically depicted in Figure 3. Hence, **4**·6PF_6 could potentially exist in solution as a mixture of 4 isomers **AAA**, **AAB**, **ABB**, and **BBB**. A situation in which all four isomers would exchange quickly on the NMR time scale is not likely since the **A** ↔ **B** exchange requires clearly a high amount of energy. Moreover, the high symmetry of the ^{1}H NMR spectrum of **4**·6PF_6 rules out the presence in solution of **AAB** and **ABB** and also indicates that **AAA** does not coexist with **BBB**.

NOESY experiments in CD_3COCD_3 at 25 °C revealed **4**·6PF_6 to adopt the **AAA** conformation (Figures 3 and 4). Indeed, cross-peaks between protons H_a and H_e and protons H_d and H_f are significantly stronger than those originated from protons H_a and H_f and protons H_d and H_e. These results were confirmed by monodimensional nOe experiments at 258 and 278 K by irradiating protons H_a, H_d, H_e, and H_f individually. The origin of this strong selectivity toward the **AAA** isomer is currently being investigated.

In conclusion, we have synthesized and fully characterized the first subphthalocyanine-based cage compound. We showed the cage to be C_{3h} symmetric as a consequence of chiral self-discrimination during its assembly. We point out that SubPcs, nonplanar aromatic compounds possessing interesting physical properties, may also be considered as chiral C_3 supramolecular building blocks that can be easily functionalized in both their peripheral (R in Figure 1) and axial (X in Figure 1) positions.

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Supporting Information Available: Experimental details, NMR, IR, UV, and MS data for compounds **2**, **3**, and **4**·6PF_6 (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Claessens, C. G.; González-Rodríguez, D.; Torres, T. *Chem. Rev.* **2002**, *102*, 835−853.
(2) (a) Claessens, C. G.; Torres, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 2561−2565. (b) Takamitsu, F.; Stork, J. R.; Potucek, R. J.; Olmstead, M. M.; Noll, B. C.; Kobayashi, N.; Durfee, W. S. *ibid.* **2002**, *41*, 2565−2568.
(3) Claessens, C. G.; Torres, T. *Eur. J. Org. Chem.* **2000**, 1603−1607.
(4) (a) González-Rodríguez, D.; Torres, T.; Guldi, D. M.; Rivera, J.; Echegoyen, L. *Org. Lett.* **2002**, *4*, 335−338. (b) del Rey, B.; Keller, U.; Torres, T.; Rojo, G.; Agulló-López, F.; Nonell, S.; Marti, C.; Brasselet, S.; Ledoux, I.; Zyss, J. *J. Am. Chem. Soc.* **1998**, *120*, 12808−12817.
(5) As a matter of fact [M] is [M,M,M] and [P] is [P,P,P], the key dihedric angles being the ones formed by Cl−B−N−C; see: (a) Claessens, C. G.; Torres, T. *Tetrahedron Lett.* **2000**, *41*, 6361−6365. (b) Kobayashi, N.; Nonomura, T. *Tetrahedron Lett.* **2002**, *43*, 4253−4255.
(6) (a) Collet, A. In *Comprehensive Supramolecular Chemistry: Molecular Recognition: Receptors for Molecular Guests*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vögtle, F., Eds.; Elsevier: New York, 1996; Vol. 2, pp 325−365. (b) Pieters, R. J.; Cuntze, J.; Bonnet, M.; Diederich, F. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1891−1900. (c) Moberg, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 248−268. (d) Kim, S.-G.; Kim, K.-H.; Jung, J.; Shin, S. K.; Ahn, K. H. *J. Am. Chem. Soc.* **2002**, *124*, 591−596. (e) Lesot, P.; Merlet, D.; Sarfati, M.; Courtieu, J.; Zimmermann, H.; Luz, Z. *J. Am. Chem. Soc.* **2002**, *124*, 10071−10082.
(7) (a) Enemark, E. J.; Stack, T. D. P. *Angew. Chem., Int. Ed.* **1998**, *37*, 932−935. (b) Albrecht, M.; Shneider, M.; Röttele, H. *Angew. Chem., Int. Ed.* **1999**, *38*, 557−559. (c) Ismagilov, R. F.; Schwartz, A.; Bowden, N.; Whitesides, G. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 652−654. (d) Kuhnle, A.; Linderoth, T. R.; Hammer, B.; Besenbacher, F. *Nature (London)* **2002**, *415*, 891−893. (e) Kim, H.-J.; Moon, D.; Soo Lah, M.; Hong, J.-I. *Angew. Chem., Int. Ed.* **2002**, *41*, 3174−3177.
(8) (a) Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028−4036. (b) Hasenknopf, B.; Lehn, J.-M.; Baum, G.; Fenske, D. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 1397−1400. (c) Kim, T. W.; Lah, M. S.; Hong, J.-I. *Chem. Commun.* **2001**, 743−744. (d) Alkorta, I.; Elguero, J. *J. Am. Chem. Soc.* **2002**, *124*, 1488−1493.
(9) Zhong, Z.; Ikeda, A.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *Org. Lett.* **2001**, *3*, 1085−1087.
(10) For recent reviews on the subject, see: (a) Caulder, D. L.; Raymond, K. N. *Acc. Chem. Res.* **1999**, *32*, 975−982. (b) Fujita M. In *Molecular Self-Assembly: Organic Versus Inorganic Approaches*; Fujita M., Ed.; Springer-Verlag: Berlin, 2000; pp 177−201. (c) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853−908. (d) Swiegers, G. F.; Malefetse, T. J. *Chem. Rev.* **2000**, *100*, 3483−3537. (e) Holliday, B. J.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2022−2043. (f) Hof, F.; Craig, S. L.; Nuckolls, C.; Rebek, J., Jr. *Angew. Chem., Int. Ed.* **2002**, *41*, 1488−1508. Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, ASAP article, August 21, 2002.
(11) Similar structures were described in: (a) Jacopozzi, P.; Dalcanale, E. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 613−615. (b) Fujita, M.; Fujita, N.; Ogura, K.; Yamaguchill, K. *Nature (London)* **1999**, *400*, 52−55. (c) Hiraoka, S.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 10239−10240. (d) Bretonniere, Y.; Mazzanti, M.; Wietzke, R.; Pecaut, J. *Chem. Commun.* **2000**, 1543−1544. (e) Radhakrishnan, U.; Schweiger, M.; Stang, P. J. *Org. Lett.* **2001**, *3*, 3141−3143. (f) Sun, W.-Y.; Fan, J.; Okamura, T.-A.; Xie, J.; Yu, K.-B.; Ueyama, N. *Chem. Eur. J.* **2001**, *7*, 2557−2562.
(12) Nicolaou, K. C.; Hepworth, D.; King, N. P.; Finlay, M. R. V.; Scarpelli, R.; Pereira, M. M. A.; Bigot, A.; Werschkun, B.; Winssinger, N. *Chem. Eur. J.* **2000**, *6*, 2783−2800.
(13) Pirkle, W. H.; Selness, S. R. *J. Org. Chem.* **1995**, *60*, 3252−3256.

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