Stereoselective self-assembly of atropoisomeric Pd(II) metallocycles induced by an aromatic guest†

Dolores Abella, Víctor Blanco, Elena Pía, Marcos Chas, Carlos Platas-Iglesias, Carlos Peinador* and José M. Quintela*

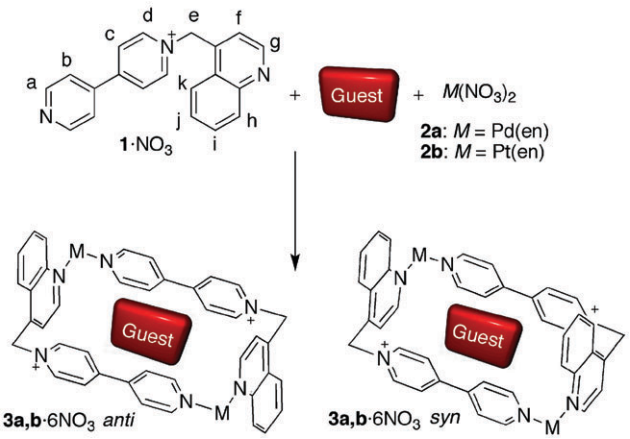
Received (in Cambridge, UK) 11th February 2008, Accepted 12th March 2008
First published as an Advance Article on the web 18th April 2008
DOI: 10.1039/b802213e

A new dinuclear Pd(II) metallocycle consisting of a 4,4′-bipyridin-1-ium ligand with a quinoline moiety was self-assembled in aqueous solution with the aid of template molecules; the situation found in solution in which both *syn* and *anti* or only the *anti* atropoisomers are observed strongly relies on the intermolecular host–guest interactions.

The facile obtention of macrocycles with cavities large enough to accommodate substrate molecules in complexation processes is of enormous importance in host–guest chemistry.[1] The structural characteristics of their cavities, including shape, size and flexibility, determinate the usefulness of the receptors towards target substrates. Metal-directed self-assembly has emerged as a powerful tool to obtain molecular hosts of defined shapes and sizes.[2] The design of receptors capable of adapting their structure to bind the guest in a manner reminiscent of Koshland's induced model[3] for substrate binding to enzymes has attracted much attention because such induced fit is the basis of many allosteric systems.[4]

In our previous reports, we have described different strategies and procedures towards the self-assembly of square and rectangular Pd(II) and Pt(II) metallocycles and related structures such as inclusion complexes and catenanes.[5] Here, we use 4-substituted quinoline moieties in the short sides of a molecular rectangle, which can rotate around the CH_2–N axis giving rise to the existence of two atropoisomers with different cavity characteristics. The advantage of this "flexible" receptor is that it can change its shape in order to maximize the intermolecular interactions with different guests (induced-fit).

Ligand **1**·NO_3 was easily obtained from 4,4′-bipyridine and 4-chloromethylquinoline[6] in moderate yield. The addition of one equivalent of hydroquinone (HQ) to an equimolecular 10 mM D_2O solution of ligand **1**·NO_3 and Pd(en)$(NO_3)_2$ results in the appearance of a reddish colour solution. The ^1H and ^{13}C NMR spectra showed an approximate 1 : 1 mixture of the *syn* and *anti* HQ⊂**3a**·6NO_3 atropoisomers (Scheme 1), as can be concluded from the two sets of signals and 2D NMR data (Fig. 1). The chemical shifts are compatible with the formation of the coordinative bonds ($\Delta\delta$ = 1.82 for H_h and $\Delta\delta$ = 0.58 ppm for H_g from those of **1**·NO_3). The upfield shift of the signal of HQ ($\Delta\delta$ = −1.10 ppm from those of the free HQ, for the aromatic protons of HQ) along with the upfield shift of the β protons of the bipyridine units ($H_{b,c}$) suggests that HQ is inserted into the cavity of metallocycle. Similar results have been obtained with resorcinol, cathecol, and phloroglucinol. It is noteworthy that the interconversion of the steroisomers is slow in the NMR timescale, probably as a result of the energy barrier for the rotation of the quinoline units, in addition to the steric and energetic impediments caused by the hydroquinone guest inside the cavity.



Scheme 1

Addition of $NaNO_3$ results in the slow crystallization of the inclusion complex. X-Ray analysis of these crystals shows the presence of the *anti* stereoisomer exclusively (Fig. 2).[7] Both components lie about a common inversion centre located at

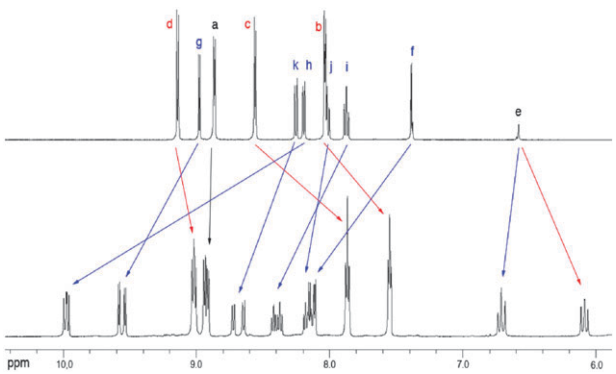


Fig. 1 Partial ^1H NMR spectra (500 MHz, D_2O, 298 K). Top: free ligand **1**·NO_3 (10 mM). Bottom: **1**·NO_3 (10 mM), Pd(en)$(NO_3)_2$ (10 mM), and HQ (5 mM). See Scheme 1 for proton assignments.

Departamento de Química Fundamental, Facultad de Ciencias, Universidade da Coruña, Campus A Zapateira, 15071 A Coruña, Spain. E-mail: capeveqo@udc.es; Fax: +34 81 167065; Tel: +34 81 167000

† Electronic supplementary information (ESI) available: Experimental, NMR spectra, theoretical calculations and crystallographic data in CIF format for CCDC 675724 & 675725. See DOI: 10.1039/b802213e

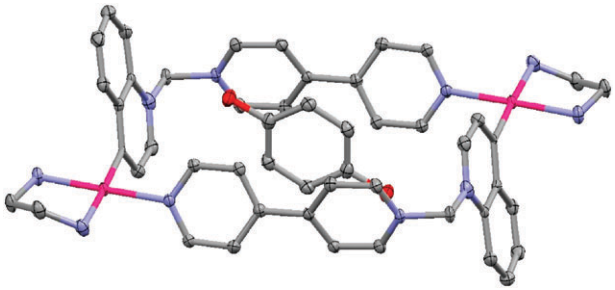


Fig. 2 Crystal structure of HQ⊂**3a**·6NO_3 showing the 50% probability thermal ellipsoids. Solvent molecules, counterions, and hydrogen atoms have been omitted for clarity.

the centroid defined by the guest. Immediately upon redissolution of the crystals in D_2O the ^{1}H NMR spectrum showed a 1 : 1 mixture of its *syn* and *anti* atropoisomers, indicating that the initial equilibrium is re-achieved in seconds. The fact that *anti* stereoisomer of HQ⊂**3b**·6NO_3 crystallizes out preferentially over the *syn* one suggests that crystal packing forces must play a significant role in determining the crystal structure.

To obtain more detailed information about the mechanism of interconversion between the *syn* and *anti* atropoisomers we prepared the corresponding platinum metallocycle. The reaction between ligand **1**·NO_3 and Pt(en)$(NO_3)_2$ was carried out at 100 °C to exploit the "molecular lock" strategy introduced by Fujita.[8] The reaction allowed the isolation of a 1 : 1 mixture of the *syn* and *anti* atropoisomers of **3b** as their hexafluorophosphate salts. The ^{1}H NMR spectrum of the mixture recorded in a CD_3NO_2 solution at room temperature is consistent with the presence of a 1 : 1 mixture of the *syn* and *anti* atropoisomers. Upon increasing the temperature the signals gradually broaden, reflecting conformational exchange processes. The coalescence method was used to calculate the $\Delta G^{\ddagger}_c$ (75.3 kJ mol^{-1}) value for the interconversion process.[9] Similar activation barriers have been determined for the rotation of Pt–N(quinoline) bonds in square planar Pt(II) complexes.[10]

To support that the interconversion between the *syn* and *anti* atropoisomers occurs by rotation around the Pt–N(quinoline)–CH_2 axis we performed DFT calculations at the B3LYP level. In these calculations we used the standard 6-31G(d) basis set for C, H and N ligand atoms, while the LanL2DZ valence and effective core potential functions were used for Pt. Our calculations provide two minimum energy conformations for the metallocycle that correspond to the expected *syn* and *anti* atropoisomers. According to the calculations the *syn* isomer is slightly more stable than the *anti* one in the gas phase, the relative free energy $\Delta G^{\circ}_{298} = G^{\circ}_{298(syn)} - G^{\circ}_{298(anti)}$ amounting only to −4.52 kJ mol^{-1}.[11] In the *anti* isomer the two quinoline units are parallel to each other, while in the *syn* form the metallocycle adopts a cone-like conformation with the least-squares planes defined by the two quinoline units forming an angle of 31.6° (Fig. S24, ESI†). The *syn* → *anti* interconversion process was studied *in vacuo* by using the synchronous transit-guided quasi-Newton method.[12] Our results show that the interconversion between the two isomers is a single-step process involving the rotation of one quinoline unit. Both the *syn* and *anti* isomers are characterised by dihedral angles of *ca.* 75° between the best plane of the metallocycle and the two planes described by the quinoline units. However, the structure of the transition state that connects the two minimum energy conformations presents a dihedral angle of *ca.* 75°, while the second one defined by the quinoline unit undergoing the rotation process amounts to *ca.* 6° (See ESI†). The computed Gibbs free energy barrier for the *syn* → *anti* interconversion process amounts to 69.9 kJ mol^{-1},[11] which is in reasonably good agreement with the experimental value obtained in CD_3NO_2 solution (75.3 kJ mol^{-1}). This relatively high energy barrier for the interconversion between the *syn* and *anti* isomers is related, at least in part, to the distortion of the Pt(II) coordination environment experienced by the molecule to reach the transition state. Indeed, the calculated bond distances between Pt and the nitrogen atoms of the bipyridine (Pt–N_b) and quinoline (Pt–N_q) moieties are 2.11–2.12 Å in both isomers, while in the transition state the Pt–N_b and Pt–N_q distances amount to 2.12 and 2.27 Å, respectively. The lengthening of the Pt–N_q distance in the transition state is a consequence of the steric hindrance caused by the ethylenediamine ligand on the quinoline unit undergoing the rotation process.

The inclusion complex with 1,5-bis[2-(2-hydroxyethoxy)-ethoxy]naphthalene (1,5-NPH) has also been studied. In this case, the *anti* stereoisomer is the only one present in solution, as shown by NMR analysis (Fig. S16†). The *anti* atropoisomer is the only one compatible with the presence of the inversion centre evidenced by the NMR spectrum.

As expected, the X-ray structure of 1,5-NPH⊂**3a**·6NO_3 (Fig. 3) shows the exclusive presence of the *anti* stereoisomer in the solid state.[13] Again, both components lie about a common inversion centre located at the centroid defined by the guest. The shorter distance between the centroids of the central C–C bonds of the two bipyridine moieties (0.14 Å shorter than in the hydroquinone inclusion complex) together with the almost coplanar arrangement of the pyridine rings (15° dihedral angle in comparison to the 28° dihedral angle found in HQ⊂**3a**·6NO_3) demonstrate enhanced host–guest interactions, undoubtedly due to the larger π-surface and the stronger π-donor character of the naphthalene guest.

Four C–H···π interactions between the guest (at positions C-3, C-4, C-7, and C-8) and the quinoline rings, resulting from the perfect host–guest fit, further contribute to the structure stabilization in solution and in solid phase.[14] In the *syn* isomer,

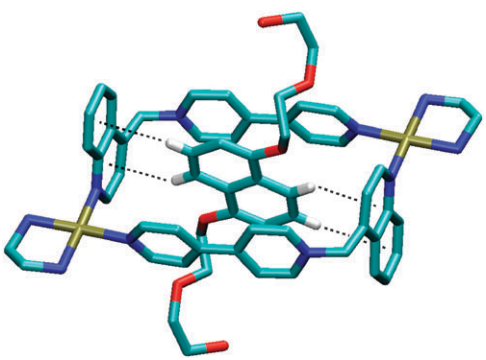


Fig. 3 Crystal structure of 1,5-NPH⊂**3a**·6NO_3 showing the four C–H···π interactions.[14] Solvent molecules and hydrogen atoms have been omitted for clarity.

only three of these interactions would be possible. Steric hindrance between the polyether chains and the quinoline could also contribute to the destabilization of the *syn* system. A third experiment was carried out trying to force the formation of the *syn* stereoisomer. This time, the template of choice, 1,3-bis[2-(2-hydroxyethoxy)ethoxy]naphthalene, is the result of shifting the unfavourable polyether chain at the C-5 position, that creates steric hindrance with the quinoline moiety in the *syn* stereoisomer, to the C-3 position, in which a similar impediment is introduced with the quinoline in the undesired *anti* isomer. The ^{1}H NMR spectrum of the resulting solution shows the presence of two isomers in an approximate 2 : 1 ratio. Although a specific assignment of the two sets of signals to a particular isomer (*syn* or *anti*) was not possible, these results clearly indicate that the nature of the aromatic guest plays an important role in the proportion of the two atropoisomers present in solution. The presence of two stereoisomers can probably be ascribed to the fact that, assuming a similar insertion mode for 1,3-NPH, only three C–H$\cdots\pi$ bonds (at positions C-4, C-7 and C-8) can be formed between 1,3-NPH and the quinoline systems in a *syn* conformation.

In conclusion, we have demonstrated that a judicious selection of the aromatic guest allows the stereoselective self-assembly of atropoisomeric Pd(II) metallocycles containing quinoline moieties.

This research was supported by Xunta de Galicia (PGIDIT06PXIB103224PR and PGIDIT04PXIC10307PN), Ministerio de Educación y Cultura and FEDER (CTQ2007-63839/BQU). V.B., D.A., and E.P. thank Ministerio de Educación y Ciencia (FPU Program) and Universidade da Coruña for predoctoral fellowships. The authors are also indebted to Centro de Supercomputación of Galicia (CESGA) for providing the computer facilities.

Notes and references

1. (*a*) *Comprehensive Supramolecular Chemistry*, ed. J.-M. Lehn, J. L. Atwood, J. E. D. Davis, D. D. MacNicol and F Vögtle, Pergamon, Oxford, UK, 1987–1996, vol. 1–11.
2. (*a*) G. F. Swiegers and T. J. Malefetse, *Chem. Rev.*, 2000, **100**, 3483–3537; (*b*) M. Fujita, M. Tominaga, A. Hori and B. Therrien, *Acc. Chem. Res.*, 2005, **38**, 369–378; (*c*) P. H. Dinolfo and J. T. Hupp, *Chem. Mater.*, 2001, **13**, 3113–3125; (*d*) P. J. Steel, *Acc. Chem. Res.*, 2005, **38**, 243–250; (*e*) M. Fujita, *Acc. Chem. Res.*, 1999, **32**, 53; (*f*) S. Leininger, B. Olenyuk and P. J. Stang, *Chem. Rev.*, 2000, **100**, 853–908; (*g*) B. Holliday and C. A. Mirkin, *Angew. Chem., Int. Ed.*, 2001, **40**, 2022–2043; (*h*) F. Würthner, C.-C. You and C. R. Saha-Möller, *Chem. Soc. Rev.*, 2004, 133–146; (*i*) R. M. Yeh, A. V. Davis and K. N. Raymond, in *Supramolecular Systems: Self-Assembly, Comprehensive Coordination Chemistry II*, ed. M Fujita, A Powell and C. A. Creutz, Pergamon, Oxford, 2004, vol. 7, pp. 327–355.
3. (*a*) D. E. Koshland, Jr, *Proc. Natl. Acad. Sci. U. S. A.*, 1958, **44**, 98; (*b*) D. E. Koshland, Jr, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2375–2378; (*c*) M. Gerstein, A. M. Lesk and C. Chothia, *Biochemistry*, 1994, **33**, 6739–6749.
4. (*a*) A. E. Rowan, J. Elemans and R. J. M. Nolte, *Acc. Chem. Res.*, 1999, **32**, 995–1006; (*b*) L. Kovbasyuk and R. Krämer, *Chem. Rev.*, 2004, **104**, 3161–3187; (*c*) S. Shinkai, M. Ikeda, A. Sugasaki and M. Takeuchi, *Acc. Chem. Res.*, 2001, **34**, 494–503.
5. (*a*) V. Blanco, M. Chas, D. Abella, C. Peinador and J. M. Quintela, *J. Am. Chem. Soc.*, 2007, **129**, 13978–13986; (*b*) M. Chas, D. Abella, V. Blanco, E. Pia, G. Blanco, A. Fernandez, C. Platas-Iglesias, C. Peinador and J. M. Quintela, *Chem.–Eur. J.*, 2007, **13**, 8572–8582; (*c*) V. Blanco, M. Chas, D. Abella, E. Pia, C. Platas-Iglesias, C. Peinador and J. M. Quintela, *Org. Lett.*, 2008, **10**, 409–412.
6. S. R. Ramadas and M. V. Krishna, *Curr. Sci.*, 1981, **50**, 120–122.
7. Crystal data for HQ$\subset$**3a**$\cdot$6$NO_3\cdot$10H_2O formula $C_{50}H_{74}N_{16}O_{30}Pd_2$, formula weight 1592.05, crystal system triclinic, space group $\bar{P}1$ centrosymmetric, a = 8.684(5), b = 13.421(5), c = 14.573(5) Å α = 95.949(5), β = 101.272(5), γ = 106.982(5)°, V = 1569.5(12) Å^3, Z = 1, reflections measured 21 542, unique reflections 7715 (R_{int} = 0.0194), T = 100 K, $R1$ ($I > 2\sigma(I)$) = 0.0406, w$R2$ (all data) = 0.1383.[15] CCDC 675724.†.
8. (*a*) M. Fujita, F. Ibukuro, K. Yamaguchi and K. Ogura, *J. Am. Chem. Soc.*, 1995, **117**, 4175; (*b*) A. Hori, H. Kataoka, T. Okano, S. Sakamoto, K. Yamaguchi and M. Fujita, *Chem. Commun.*, 2002, 182.
9. The coalescence method (I. O. Sutherland, *Annu. Rep. NMR Spectrosc.*, 1971, **4**, 71–235) uses the expression, $k_c = \pi(\Delta\nu)/(2)^{1/2}$ to approximate the rate constant at the coalescence temperature (T_c), where $\Delta\nu$ is the chemical shift difference (in Hertz) between the coalescing signals in the absence of exchange. The Eyring equation was subsequently employed to calculate $\Delta G^{\ddagger}_c$ value at T_c.
10. M. S. Davies, C. I. Diakos, B. A. Messerle and T. W. Hambley, *Inorg. Chem.*, 2001, **40**, 3048–3054.
11. Relative free energies include non-potential energy contributions (that is, zero point energy and thermal terms) obtained by frequency analysis.
12. (*a*) C. Peng, P. Y. Ayala, H. B. Schlegel and M. J. Frisch, *J. Comput. Chem.*, 1996, **17**, 49; (*b*) C. Peng and H. B. Schlegel, *Isr. J. Chem.*, 1994, **33**, 449.
13. One of the polyether chains of the guest in 1,5-NPH$\subset$**3a**$\cdot$6NO_3 is disordered. Crystal data for 1,5-NPH$\subset$**3a**$\cdot$6NO_3 formula $C_{54}H_{56}N_{16}O_{20}Pd_2$, formula weight 1461.95, crystal system triclinic, space group $\bar{P}1$ centrosymmetric, a = 11.818(2), b = 12.632(2), c = 12.814(2) Å, α = 109.691(3), β = 97.742(3), γ = 99.527(3)°, V = 1738.4(6) Å^3, Z = 1, reflections measured 23 236, unique reflections 8549 (R_{int} = 0.0879), T = 100 K, $R1$ ($I > 2\sigma(I)$) = 0.0626, w$R2$ (all data) = 0.1897.[15] CCDC 675725†.
14. The [H$\cdots\pi$] and [C–π] distances and [C–H$\cdots\pi$] angles are 2.75 Å, 2.94 Å, 3.56 Å, 3.80 Å, 146°, 153°.
15. G. M. Sheldrick, *SHELXL-97, Program for refinement of crystal structures*, University of Göttingen, Germany, 1997.