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Catenanes

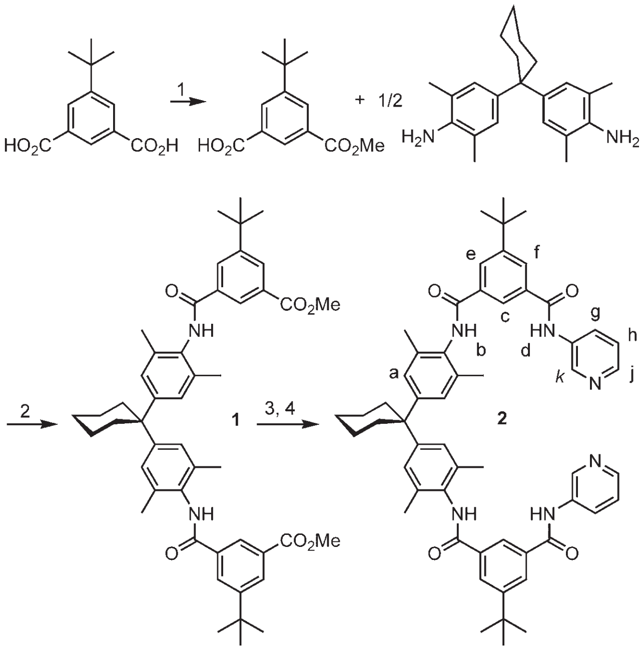
Reversible Formation of a [2]Catenane through First- and Second-Sphere Coordination**

Barry A. Blight, James A. Wisner, and Michael C. Jennings*

The synthesis of compounds containing catenated rings has received increasing attention because of their aesthetic appeal[1] as well as their potential in the areas of molecular machines and switches.[2] A particularly facile synthetic method in this context is the closure of one or more of the rings in the final products by using labile metal–ligand coordination as a linkage in the backbone under thermodynamic control.[3] However, the template used to generate the interlocked structures in the great majority of these cases operates independently from the aforementioned ring-closure reaction. Examples in which these two functions are associated with the same metal center(s) simultaneously are rare and involve either bridging ligands[4] or metal–metal interactions to achieve this result.[5] Herein, we report the one-step, high-yield synthesis and characterization of a new [2]catenane architecture that depends on the same metal center for both the macrocyclization and templated catenation stages of its self-assembly. The topology of the product is dependent on solvent polarity, the character of which can be used to switch reversibly between catenated and non-interlocked geometries.

Recently, we described the formation of a series of interpenetrated [2]pseudorotaxanes,[6] and a subsequent interlocked [2]rotaxane[7] from a known macrocyclic component[8] and *trans*-palladium dihalide complexes. The driving force for formation of the complexes rested mainly on the hydrogen-bond-donating interaction of amide groups in the macrocyclic framework with the residual hydrogen-bond-acceptor character of the halide ligands of the preformed metal complexes. The potential adaptation of this template to the formation of a [2]catenane superstructure led us, through examination of molecular models, to synthesize **2** as a bidentate ligand that could chelate a palladium dichloride metal center in a *trans* arrangement. Formation of the resulting product would yield a macrocycle incorporating both the desired metal center subunit (*trans*-{$PdCl_2L_2$}) in its backbone as well as the components for recognition of the subunit within the newly created cavity. Catenation of two macrocycles would further be templated through mutual recognition of the {$PdCl_2L_2$} subunit in one ring by its orthogonally disposed partner. Although we were reasonably confident that the macrocyclization reaction would occur, the viability of the catenation step was uncertain because of the requirement of dissociated acyclic intermediates, which might not conform to the intended template.

Bidentate ligand **2** was synthesized in 34% overall yield from *tert*-butylisophthalic acid and readily available or prepared starting materials[9] (Scheme 1; see also the Supporting Information). Partial esterification of the starting acid and subsequent DCC-mediated coupling produced intermediate diester **1**. Hydrolysis of **1** and a second DCC-mediated amide-forming reaction with 2 equivalents of 3-aminopyridine yielded **2**.



Scheme 1. Synthesis of **2**. 1) MeOH/THF, H_2SO_4; 2) DCC, HOBT, DMF; 3) 0.5 M LiOH, THF; 4) DCC, HOBT, 3-aminopyridine, DMF. DCC = *N*,*N'*-dicyclohexylcarbodiimide; HOBT = 1-hydroxy-1*H*-benzotriazole.

Self-assembly of the [2]catenane target (**3**) was attempted by combining equimolar amounts of $[Pd(PhCN)_2Cl_2]$[10] and **2** in a solvent mixture of 3:1 $CHCl_3$/MeCN and heating at reflux for 8 h. TLC of the final reaction solution indicated a sole product that did not match the R_f values of either starting material. Removal of the solvent and precipitation from dichloromethane with hexanes gave a pale yellow solid (87%

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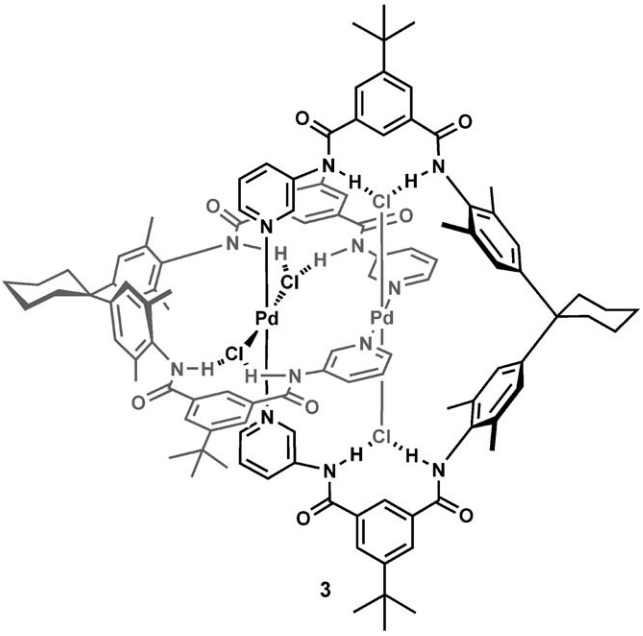

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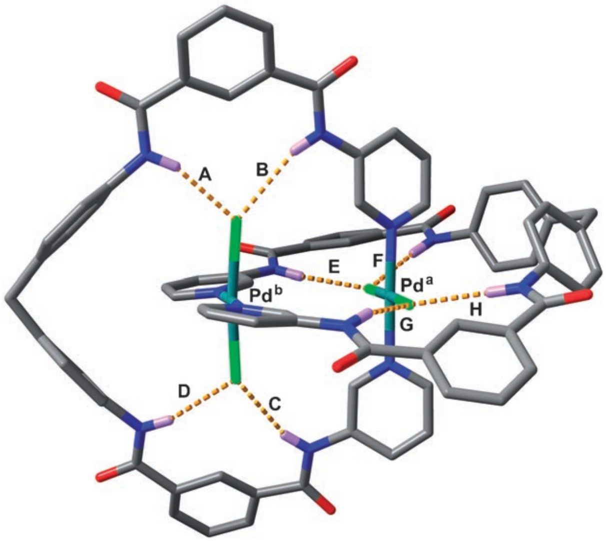

Figure 1. Stick representation of [2]catenane **3** in the solid state. All C–H hydrogen atoms, methyl, cyclohexyl, and *tert*-butyl groups have been removed for clarity. NH⋯Cl hydrogen bonds are indicated by orange dashed lines; O red, N blue, H light purple, Cl light green.

based on [2]catenane). Cold-spray-ionization mass spectrometry (CSI-MS)[11] of the product was consistent with the formation of the catenane; the only high-mass ($m/z > 300$) peaks observable were at m/z 1061.3 $[Pd_2(\mathbf{2})_2Cl_4+2H]^{2+}$ and m/z 2121.8 $[Pd_2(\mathbf{2})_2Cl_4+H]^{+}$. The isotopic ratios of the peaks corresponding to $[M{+}2H]^{2+}$ matched directly with those calculated for the catenane product. Poor resolution of the signals corresponding to the $[M{+}H]^{+}$ ion prevented a similar isotopic analysis. No peaks were observed in the regions in which either the non-interlocked macrocycle or the starting materials would be expected to appear.

Pale-yellow cube-shaped crystals of the putative [2]catenane were grown by slow diffusion of diisopropyl ether into a concentrated solution of **3** in 1,2-dichloroethane. Proof of the anticipated interlocked topology in the solid-state was obtained by single-crystal X-ray diffraction analysis (Figure 1).[12,13] **3** crystallized in space group $P\bar{1}$ containing two catenated macrocyclic rings, which adopt a nearly orthogonal orientation (84°), as measured from their intersecting least-squares planes.[14] Although each of the macrocycles (containing either Pd^{a} or Pd^{b}) adopt different gross conformations, the intended template is manifested in the interaction between both of the $\{PdCl_2\}$ subunits and their opposing macrocyclic cavities. $\{Pd^{a}Cl_2\}$ is hydrogen bonded to the four amide nitrogen atoms of macrocycle b (N⋯Cl = 3.53 (E), 3.41 (F), 3.44 (G), 3.36 Å (H), and N–H⋯Cl = 160 (E), 160 (F), 156 (G), 163° (H)). $\{Pd^{b}Cl_2\}$ is hydrogen bonded to the four amide nitrogen atoms of macrocycle a (N⋯Cl = 3.26 (A), 3.48 (B), 3.54 (C), 3.51 Å (D), and N–H⋯Cl = 153 (A), 163 (B), 151 (C), 156° (D)). The interlocked structure is further stabilized by two C–H⋯π interactions between a proton at the 6-position of one pyridyl ring in each macrocycle, and the diphenyl cyclohexyl sidewalls of the opposing cavity.

The [2]catenane is remarkably stable in view of the lability of the palladium metal centers that form the reversible links in the backbones of the component macrocycles. As a qualitative test of this stability, solutions of **3** (5 mmol) in $CDCl_3$ were diluted to 50 % v/v with a number of more competitive deuterated solvents ([D$_3$]MeCN, [D$_3$]MeNO$_2$, [D$_8$]THF, [D$_6$]acetone, [D$_4$]methanol) and heated at reflux for 24 h. The ^{1}H NMR spectra of the samples during dilution, before, and after reflux indicated no change in the integrity of the [2]catenane superstructure under these conditions. However, dissolution of **3** in a mixed solvent system of >1 M [D$_6$]DMSO/CDCl$_3$ results in the gradual appearance of a new set of resonances in the ^{1}H NMR spectra, consistent with the formation of free macrocycle **4**, and the concomitant disappearance of those corresponding to **3** (Figure 2). Although the number of protons and respective coupling patterns are the same in both sets of peaks, all of the aromatic and amide protons experience a change in chemical shift to different degrees upon the loss of the topological bond. In particular, the amide protons b and d are shifted downfield in the free macrocycle as a result of their exposure to the strongly hydrogen-bond-accepting solvent. The protons j at the 6-position of the pyridyl rings are more shielded in the catenated structure owing to their involvement in C–H⋯π bonding to the aryl sidewalls of the opposing macrocycle. Hence, they are shifted downfield in the non-interlocked macrocycle. Conversely, the sidewall protons a are shifted downfield in the catenane caused by their location within the deshielding regions of the pyridyl rings in the opposing macrocycle. CSI-MS of the NMR sample supported the presence of macrocycle **4** with observable high-mass peaks at m/z 1146.1 $[Pd(\mathbf{2})Cl_2+[D_6]DMSO+H]^{+}$ and m/z 1194.0 $[Pd(\mathbf{2})Cl+2[D_6]DMSO]^{+}$, the isotopic ratios of which displayed a direct match to the calculated patterns. Notably, no high-mass peaks that could be reasonably ascribed to **3** were observed.

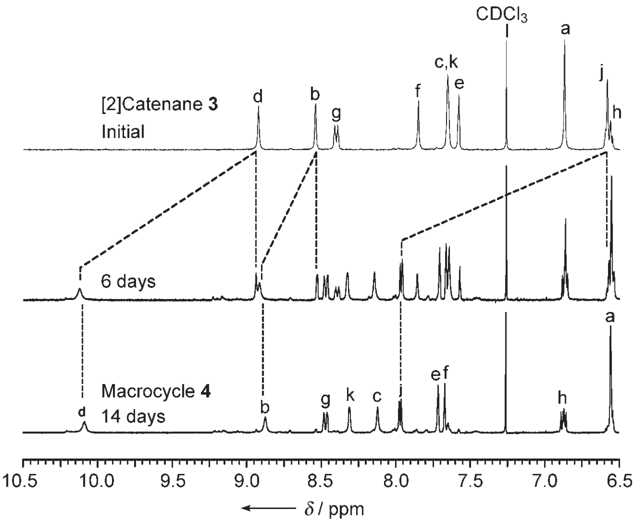

Figure 2. The aromatic region of ^{1}H NMR spectra (600 MHz, 298 K) monitoring the disassembly of [2]catenane **3** (top) into macrocycle **4** (bottom) in 4 M [D$_6$]DMSO/CDCl$_3$. Illustrated are the observed perturbations in chemical shift between interlocked and free components (dashed lines). ROESY experiments were performed to verify individual ^{1}H NMR assignments.

Diisopropyl ether was diffused into a two-week-old solution of **4** in 2 M DMSO/CHCl$_3$ to produce pale-yellow X-ray quality crystals. Single-crystal X-ray diffraction analysis provided confirmation of the change in topology in the solid state (Figure 3).[15] The disassembled material crystallizes in space group $P\bar{1}$ as centrosymmetric pairs of mutually hydrogen bonded but non-interlocked macrocycles. The influence of the DMSO cosolvent in nullifying the catenane template is apparent in the structure, as one of the two amide groups in each of the isophthalamide clefts is engaged in hydrogen bonding with included solvent molecules ($N\cdots OS(CH_3)_2 = 2.83$ (A), 2.98 Å (B), and $N{-}H\cdots OS(CH_3)_2 = 160$ (A), 153° (B)). The two remaining amides of each ring participate as intermacrocyclic hydrogen-bond donors with a chloride ligand ($N\cdots Cl = 3.54$ Å, $N\text{-}H\cdots Cl = 167°$(C)) and the carbonyl group of an amide in the opposing macrocycle ($N\cdots O = 2.93$ Å, $N{-}H\cdots O = 142°$ (D)) acting as acceptors.

The reversible nature of the catenane-forming step is revealed in the ^{1}H NMR spectra of **4** over a period of a week after dissolution in CDCl$_3$ (Figure 4). The resonances corresponding to the macrocycle are gradually replaced by those matching a separately prepared solution of catenane **3** in CDCl$_3$ (Figure 4). The identity of **3** was further confirmed by comparison with an authentic sample (TLC). The first-order rate constant k for loss of **4** (assembly of **3**) was determined to be 1.56×10^{-5} s^{-1} in CDCl$_3$ at 298 K by the method of initial rates. The rate of the re-formation of **3** may be increased substantially by either heating, the addition of a more-polar cosolvent (e.g. MeCN), or both, which nonetheless results in **3** being observed as the only product.

In conclusion, we have prepared a new [2]catenane by using first- and second-sphere coordination of the same metal center to form the interlocked topology. The catenation of the two rings is a fully reversible process and is dependent on the

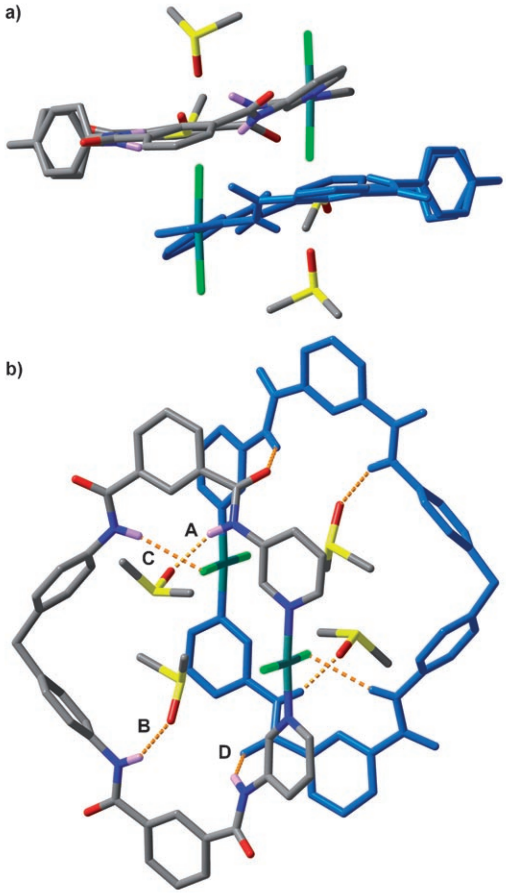

Figure 3. Stick representation of macrocycle **4** in the solid state; a) view in the plane of the dimer of macrocycles; b) view from above the plane of the macrocycles. All C–H hydrogen atoms, methyl, cyclohexyl, and *tert*-butyl groups have been removed for clarity. NH···Cl, NH···O=S, and NH···O=C hydrogen bonds are indicated by orange dashed lines; S yellow.

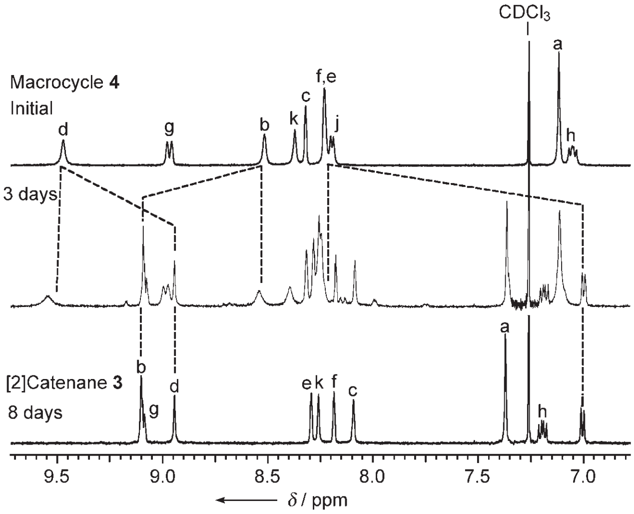

Figure 4. The aromatic region of ^{1}H NMR spectra (600 MHz, 298 K) monitoring the reassembly of macrocycle **4** (top) into [2]catenane **3** (bottom) in CDCl$_3$. Illustrated are the observed perturbations in chemical shift between free and interlocked components (dashed lines).

solvent used to dissolve the component macrocycle. We are currently exploring methods to expand this template further for the reversible formation of functional molecules such as molecular shuttles and switches.

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[1] P. D. Beer, M. R. Sambrook, D. Curiel, *Chem. Commun.* **2006**, 2105–2117; C. A. Schalley, W. Reckien, S. Peyerimhoff, B. Baytekin, F. Voegtle, *Chem. Eur. J.* **2004**, *10*, 4777–4789; Z. Cao, A. W. Roszak, L. J. Gourlay, G. J. Lindsay, N. W. Isaacs, *Structure* **2005**, *13*, 1661–1664; A. Hori, T. Sawada, K.-i. Yamashita, M. Fujita, *Angew. Chem.* **2005**, *117*, 4974–4977; *Angew. Chem. Int. Ed.* **2005**, *44*, 4896–4899; ; A.-M. Fuller, D. A. Leigh, P. J. Lusby, A. M. Z. Slawin, D. B. Walker, *J. Am. Chem. Soc.* **2005**, *127*, 12612–12619; Y. Liu, P. A. Bonvallet, S. A. Vignon, S. I. Khan, J. F. Stoddart, *Angew. Chem.* **2005**, *117*, 3110–3115; *Angew. Chem. Int. Ed.* **2005**, *44*, 3050–3055; ; E. N. Guidry, S. J. Cantrill, J. F. Stoddart, R. H. Grubbs, *Org. Lett.* **2005**, *7*, 2129–2132; R. T. S. Lam, A. Belenguer, S. L. Roberts, C. Naumann, T. Jarrosson, S. Otto, J. K. M. Sanders, *Science* **2005**, *308*, 667–669; L. Raehm, J.-M. Kern, J.-P. Sauvage, C. Hamann, S. Palacin, J.-P. Bourgoin, *Chem. Eur. J.* **2002**, *8*, 2153–2162; A. L. Hubbard, G. J. E. Davidson, R. H. Patel, J. A. Wisner, S. J. Loeb, *Chem. Commun.* **2004**, 138–139.

[2] J.-C. Chambron, J.-P. Collin, V. Heitz, D. Jouvenot, J.-M. Kern, P. Mobian, D. Pomeranc, J.-P. Sauvage, *Eur. J. Org. Chem.* **2004**, 1627–1638; W.-Q. Deng, A. H. Flood, J. F. Stoddart, W. A. Goddard, *J. Am. Chem. Soc.* **2005**, *127*, 15994–15995; A. H. Flood, A. J. Peters, S. A. Vignon, D. W. Steuerman, H.-R. Tseng, S. Kang, J. R. Heath, J. F. Stoddart, *Chem. Eur. J.* **2004**, *10*, 6558–6564; D. A. Leigh, P. J. Lusby, A. M. Z. Slawin, D. B. Walker, *Chem. Commun.* **2005**, 4919–4921; J. V. Hernandez, E. R. Kay, D. A. Leigh, *Science* **2004**, *306*, 1532–1537.

[3] M. Fujita, *Acc. Chem. Res.* **1999**, *32*, 53–61; M. Fujita, M. Tominaga, A. Hori, B. Therrien, *Acc. Chem. Res.* **2005**, *38*, 369–378; T. S. M. Abedin, L. K. Thompson, D. O. Miller, *Chem. Commun.* **2005**, 5512–5514; N. C. Habermehl, D. J. Eisler, C. W. Kirby, N. L.-S. Yue, R. J. Puddephatt, *Organometallics* **2006**, *25*, 2921–2928; M. Chas, E. Pia, R. Toba, C. Peinador, J. M. Quintela, *Inorg. Chem.* **2006**, *8*, 6117–6119; C. Dietrich-Buchecker, B. Colasson, M. Fujita, A. Hori, N. Geum, S. Sakamoto, K. Yamaguchi, J.-P. Sauvage, *J. Am. Chem. Soc.* **2003**, *125*, 5717–5725.

[4] M. E. Padilla-Tosta, O. D. Fox, M. G. B. Drew, P. D. Beer, *Angew. Chem.* **2001**, *113*, 4365–4369; *Angew. Chem. Int. Ed.* **2001**, *40*, 4235–4239; ; W. W. H. Wong, J. Cookson, A. A. L. Evans, E. J. L. McInnes, J. Wolowska, J. P. Maher, P. Bishop, P. D. Beer, *Chem. Commun.* **2005**, 2214–2216.

[5] N. C. Habermehl, F. Mohr, D. J. Eisler, M. C. Jennings, R. J. Puddephatt, *Can. J. Chem.* **2006**, *84*, 111–123.

[6] B. A. Blight, K. A. Van Noortwyk, J. A. Wisner, M. C. Jennings, *Angew. Chem.* **2005**, *117*, 1523–1528; *Angew. Chem. Int. Ed.* **2005**, *44*, 1499.

[7] B. A. Blight, J. A. Wisner, M. C. Jennings, *Chem. Commun.* **2006**, 4593.

[8] C. Fischer, M. Nieger, O. Mogck, V. Böhmer, R. Ungaro, F. Vögtle, *Eur. J. Org. Chem.* **1998**, 155.

[9] For the synthesis of 1,1-bis(4-amino-3,5-dimethylphenyl)cyclohexane, see: C. A. Hunter, *J. Am. Chem. Soc.* **1992**, *114*, 5303.

[10] P. Braunstein, R. Bender, J. Jud, *Inorg. Synth.* **1989**, *26*, 341.

[11] S. Sakamoto, M. Fujita, K. Kim, K. Yamaguchi, *Tetrahedron* **2000**, *56*, 955.

[12] The multiple conditions used in attaining X-ray diffraction quality crystals of **3** are listed in the Supporting Information.

[13] Crystal-structure data for [2]catenane **3**: $[(C_{56}H_{62}N_6O_4)PdCl_2]_2\cdot 2.5$(diisopropyl ether), $M = 2120.83$, triclinic, space group $P\bar{1}$, $a = 16.6067(5)$, $b = 20.0933(5)$, $c = 20.9225(6)$ Å, $\alpha = 96.87(0)$, $\beta = 109.83(0)$, $\gamma = 92.81(0)^\circ$, $V = 6490.43(346)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.08514\,g\,cm^{-3}$, $2\theta_{max} = 50.06^\circ$, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), $T = 123$ K. Pale-yellow crystal with dimensions $0.458 \times 0.33 \times 0.30\,mm^3$. 50966 total reflections, 22750 unique reflections [$R_{int} = 0.044$], $R_1 = 0.0992$, $wR_2 = 0.2920[I > 2\sigma I]$, $R_1 = 0.1404$, $wR_2 = 0.3295$, GOF(F^2) = 1.174, $N_o/N_v = 22750/1228$ with $I > 2\sigma(I)$. Please refer to the Supporting Information for a full description of the collection and refinement processes. CCDC-627518 contains 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.

[14] The least-squares planes were defined by the four carbonyl carbon atoms of each macrocyclic unit.

[15] Crystal structure data for macrocycle **4**: $[(C_{56}H_{62}N_6O_4)PdCl_2]\cdot 2\,CHCl_3\cdot 2.8\,DMSO\cdot 0.6$(diisopropyl ether), $M = 1565.91$, triclinic, space group $P\bar{1}$, $a = 12.3343(4)$, $b = 17.5097(8)$, $c = 18.9205(9)$ Å, $\alpha = 90.6(0)$, $\beta = 107.29(0)$, $\gamma = 104.19(0)^\circ$, $V = 3767.25(341)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.38037\,g\,cm^{-3}$, $2\theta_{max} = 50.06^\circ$, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), $T = 123$ K. Pale-yellow crystal with dimensions $0.50 \times 0.13 \times 0.05\,mm^3$. 31282 total reflections, 13238 unique reflections [$R_{int} = 0.051$], $R_1 = 0.0762$, $wR_2 = 0.2018[I > 2\sigma I]$, $R_1 = 0.1128$, $wR_2 = 0.2277$, GOF(F^2) = 1.046, $N_o/N_v = 13230/893$ with $I > 2\sigma(I)$. Please refer to the Supporting Information for a full description of the collection and refinement processes. CCDC-627517 contains 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.