Rotaxane Synthesis

A 3D Interlocked Structure from a 2D Template: Structural Requirements for the Assembly of a Square-Planar Metal-Coordinated [2]Rotaxane**

Anne-Marie Fuller, David A. Leigh, Paul J. Lusby, Iain D. H. Oswald, Simon Parsons, and D. Barney Walker*

The starting point for the revolution in catenane and rotaxane synthesis that occurred during the last part of the 20th century was the realization by Sauvage and co-workers that metal–ligand coordination geometries could fix molecular fragments in three-dimensional space such that they were predisposed to form mechanically interlocked architectures through macrocyclization or "stoppering" reactions.[1] Efficient synthetic methods to rotaxanes were subsequently developed based on four- (tetrahedral)[2], five- (trigonal bipyramidal and square pyramidal)[3] and, most recently, six-coordinate (octahedral)[4] metal templates (Figure 1).[5] One of the benefits of using specific coordination motifs for such assemblies is that the resulting interlocked ligands often do not permit other metal geometries in their binding site, which can consequently be exploited either to lock a metal in an unusual geometry for its oxidation state[6] or to bring about large-amplitude "shuttling" of the ligand components.[3,7] Here we show that three-dimensional interlocked architectures can also be assembled from two-dimensional coordination templates by using steric and electronic restrictions to direct the synthesis in the third

[*] A.-M. Fuller, Prof. D. A. Leigh, Dr. P. J. Lusby, I. D. H. Oswald, Dr. S. Parsons, D. B. Walker
School of Chemistry, University of Edinburgh
The King's Buildings, West Mains Road, Edinburgh EH9 3JJ (UK)
Fax: (+44) 131-667-9085
E-mail: David.Leigh@ed.ac.uk

[**] We thank E. R. Kay for assistance with the graphics and crystallography data. This work was supported by the European Union Future and Emerging Technology Program MechMol and the EPSRC.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

  DOI: 10.1002/ange.200353622

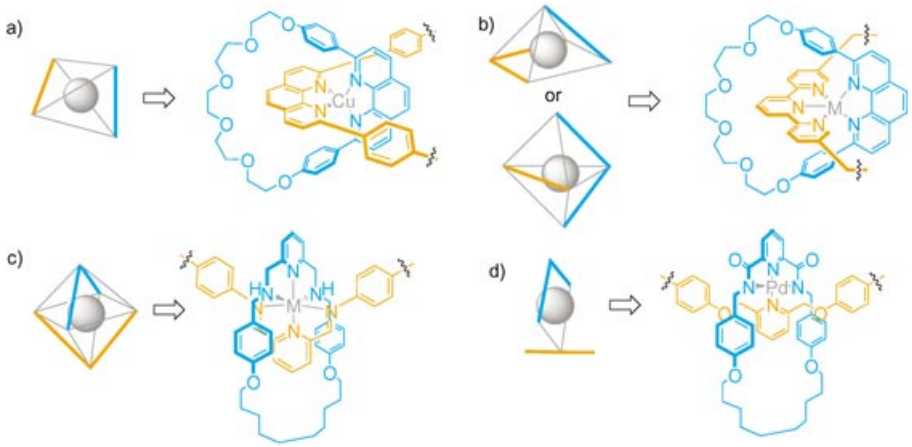
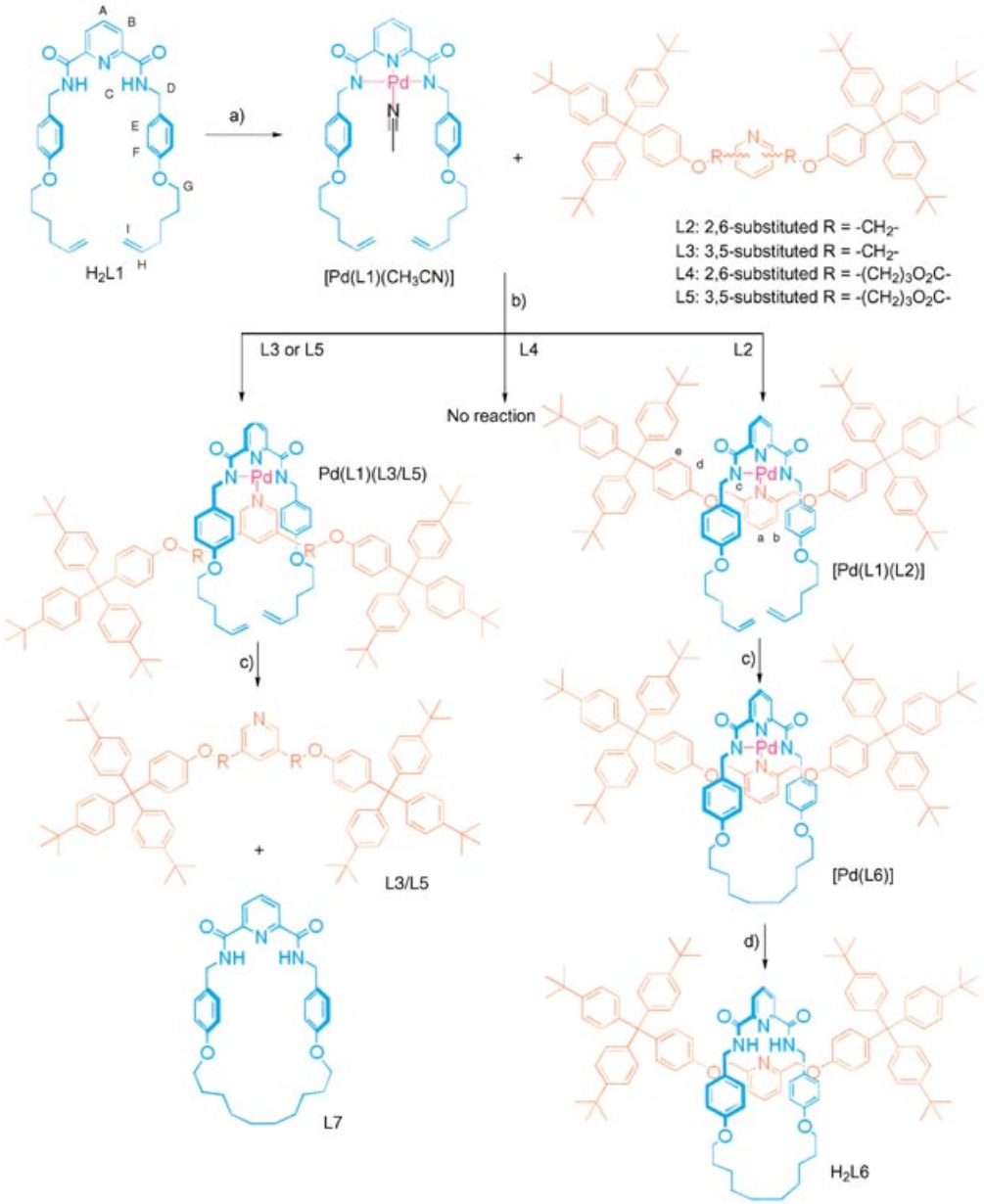


Figure 1. Exploiting transition-metal–ligand geometries in the synthesis of mechanically interlocked architectures: a) tetrahedral, b) square pyramidal and trigonal bipyrimidal, c) octahedral, and d) square-planar coordination motifs.



Scheme 1. Reagents and conditions: a) $Pd(OAc)_2$, CH_3CN, 76%; b) $CHCl_3$, 50 °C; L2: 63%, L3: 96%, L4: 0%, L5: 97%; c) 1. Grubbs catalyst (0.1 equiv), CH_2Cl_2; 2. H_2, Pd/C, THF, H_2L6: 98%, L3 + L7: 63%, L5 + L7: 69% (over 2 steps); d) KCN, MeOH, CH_2Cl_2, 20 °C, 1 h and then 40 °C, 0.5 h, 97%.

dimension. The resulting [2]rotaxane is the first example of a mechanically interlocked ligand that forms a four-coordinate square-planar metal complex.[8]

The square-planar [2]rotaxane ligand design consists of a tridentate benzylic amide macrocycle and a monodentate thread (Figure 1d). The macrocycle incorporates a 2,6-dicarboxyamidopyridine unit to exploit the palladium chemistry recently developed[9] by Hirao and co-workers. The thread contains a pyridine donor group substituted with appropriately bulky stoppers in either the 2,6- or 3,5-positions. It was envisioned that in the key intermediate, [Pd(L1)(L2–L5)] (see Scheme 1), the geometry of the precursor to the macrocycle (previously used to direct hydrogen bond assembly processes[10]) would promote intercomponent π-π stacking, thus encouraging the pyridine donor of the thread to bind the metal ion orthogonally to the N_3 ligand (complimenting the normally preferred orientation[11]) and directing the asssembly in the third dimension. A series of readily available threads L2–L5 was investigated during the study.

The rotaxane synthesis was carried out according to Scheme 1. Treatment of H_2L1 with $Pd(OAc)_2$ in acetonitrile smoothly generated a complex [Pd(L1)(CH_3CN)] in which the fourth coordination site of the metal is occupied by a normally labile acetonitrile molecule. Nevertheless, displacement of the acetonitrile by bis-ester pyridine ligand L4 was unsuccessful (see below). However, simple combination of L5 or either of the bis-ether pyridine threads (L2 and L3) with [Pd(L1)(CH_3CN)] in either dichloromethane or chloroform gave the desired complexes [Pd(L1)(L5/L2/L3)] in 97, 63 and 96% yields, respectively. The ^{1}H NMR spectrum of [Pd(L1)(L2)] is shown in Figure 2c. Comparison with the spectra of [Pd(L1)(CH_3CN)] and H_2L1 (Figure 2b and 2a, respectively) shows features clearly indicative of metal coordination (the absence of H_C and shifts in H_A and H_B) and the anticipated aromatic stacking between the tridentate and monodentate ligands (particularly H_E and H_F). Similar chemical shift differences were observed for [Pd(L1)(L3)] and [Pd(L1)(L5)], however, ring closing olefin metathesis (RCM) followed by hydrogenation (Scheme 1, step c) of the three complexes produced very different results. Whilst cyclization of [Pd(L1)(L2)] gave the corresponding [2]rotaxane [Pd(L6)] in 77% yield following hydrogenation of the olefin, no [2]rotaxane was produced from RCM of either [Pd(L1)(L3)] or [Pd(L1)(L5)], the only products in each case being the free macrocycle and thread. Why does only one of the four threads direct rotaxane synthesis in the desired manner?

The ^{1}H NMR spectra of the [2]rotaxane ([Pd(L6)], Figure 2d), mass spectrometric analysis, and the preserved association of the organic fragments upon demetalation, unambiguously confirmed the interlocked structure. In addition to the loss of the terminal alkene protons, some subtle differences in the ^{1}H NMR spectrum of [Pd(L6)] compared to [Pd(L1)(L2)] (Figure 2c) indicates that some rearrangement of the ligands does occur on formation of the rotaxane. Single crystals of [Pd(L6)] suitable for X-ray crystallography[12] were grown by slow cooling of a warm, saturated solution of the [2]rotaxane in acetonitrile. The solid-state structure (Figure 3) shows the interlocked architecture and the

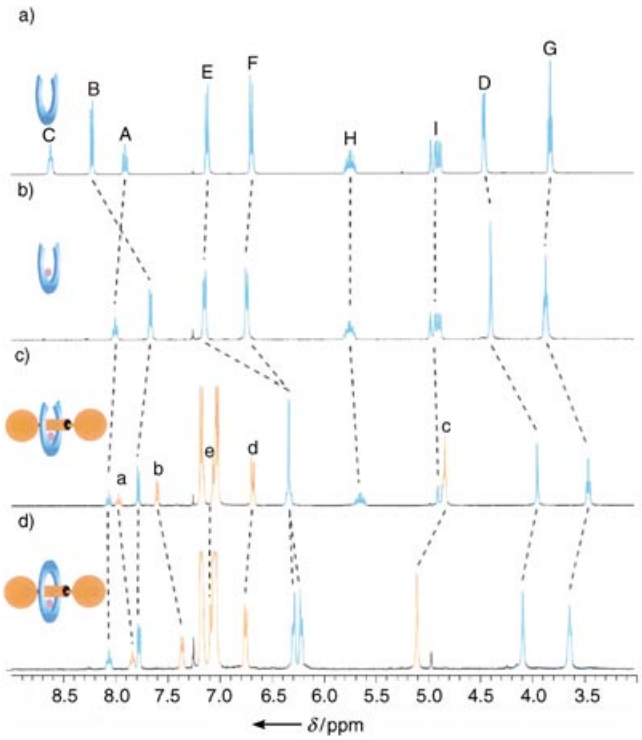


Figure 2. ^{1}H NMR spectra (400 MHz, 9:1 $CDCl_3$:CD_3CN, 298 K) of a) H_2L1; b) [Pd(L1)(CH_3CN)]; c) [Pd(L1)(L2)]; d) [2]rotaxane [Pd(L6)]. The lettering refers to the assignments in Scheme 1.

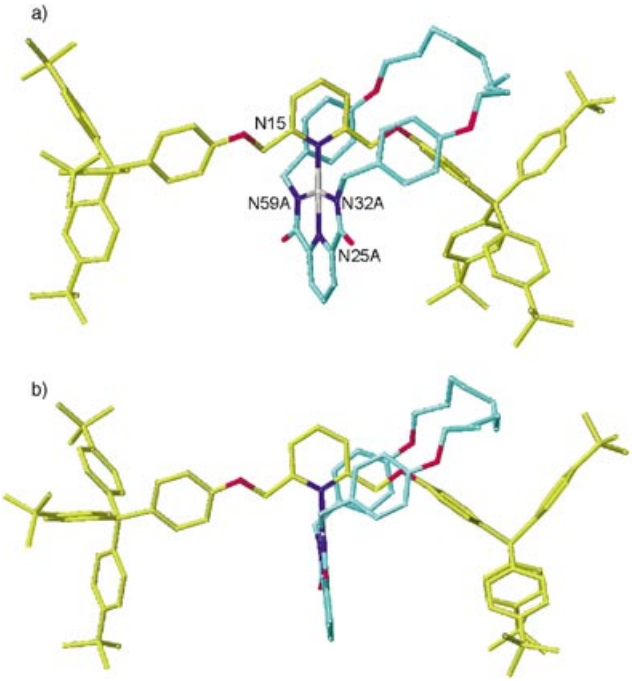


Figure 3. X-ray crystal structure of rotaxane [Pd(L6)] showing a) staggered and b) side-on views.[12] Carbon atoms of the macrocycle are shown in light blue and those of the thread in yellow; oxygen atoms are red, nitrogen dark blue, palladium gray. Selected bond lengths [Å]: Pd-N15 1.95, Pd-N25 1.86, Pd-N32 2.04, Pd-N59 2.02; other selected distance [Å]: N15-N25 3.81; macrocycle bite angle [°]: N59-Pd-N32 160.0. The macrocycle is disordered over two similar sites (50:50), but one is omitted for clarity together with the hydrogen atoms.

pseudo-square-planar geometry (the N_3 bite angle is 160.0°) around the palladium center. The π stacking between the macrocycle and the pyridine ring of the thread so apparent in solution from the ^{1}H NMR shifts is significantly offset in the solid state (see the side-on view, Figure 3b). The co-conformation adopted by the macrocycle and thread in the crystal structure of the rotaxane clearly illustrates why RCM of the complexes formed with the 3,5-disubstituted threads ([Pd(L1)(L3)] and [Pd(L1)(L5)]) can lead to uninterlocked products; even with both fragments attached to the metal, cyclization of L1 can readily occur without encircling a 3,5-substituted pyridine thread. Similarly, the conformation of the thread suggests a possible reason for the lack of reactivity of the 2,6-bis-ester thread L4 towards [Pd(L1)(CH_3CN)]. In the crystal structure the electron density of the ether oxygen atoms of the thread is directed away from the occupied d_{z^2} orbital lobes which lie above and below the plane of the square-planar geometry at the d^8 palladium center. Chelation of L4 to [Pd(L1)] has to occur orthogonally for steric reasons. Such an arrangement would force electron density from the ester carbonyl groups into this high-energy space.

Demetalation of [Pd(L6)] with potassium cyanide (Scheme 1, step d) generates the free [2]rotaxane H_2(L6) in 97% yield, thus confiming that the coordination bonds are not required to stabilize the interlocked architecture once it is formed. The ^{1}H NMR spectrum of H_2(L6) and its uninterlocked components in $CDCl_3$ are shown in Figure 4. The shielding of the benzyl groups in the rotaxane relative to the free macrocycle, together with the large ($\delta = 1.7$ ppm) downfield shift of the amide protons (H_C), indicate that specific hydrogen-bonding interactions between the thread and the macrocycle are "switched on" by the demetalation/protonation procedure. It appears that the amide groups of H_2L6 simultaneously hydrogen bond to the pyridine groups in both the macrocycle and thread.

In conclusion, we have described methodology for assembling a three-dimensional interlocked molecular architecture from a two-dimensional metal template. A combination of steric and electronic factors direct the synthesis in the third dimension, either promoting or preventing interlocking. The resulting [2]rotaxane is the first example derived from a square-planar-coordinated metal center and completes the series of mechanically interlocked ligands for common transition-metal geometries initiated by Sauvage and co-workers in 1983.

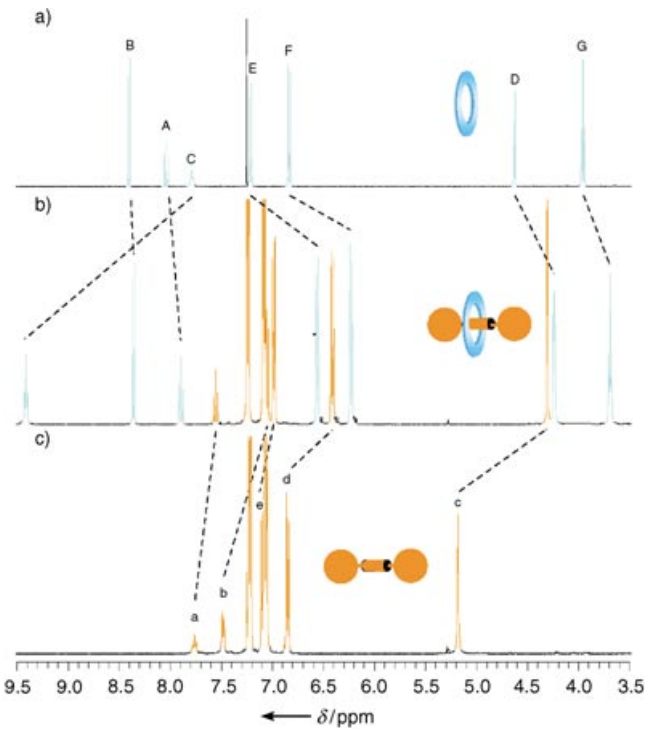


Figure 4. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of a) macrocycle; b) demetalated [2]rotaxane H_2L6; c) thread L2. The lettering refers to the assignments in Scheme 1.

Received: December 29, 2003 [Z53622]

Keywords: coordination modes · palladium · rotaxanes · template synthesis

[1] C. O. Dietrich-Buchecker, J.-P. Sauvage, J.-P. Kintzinger, *Tetrahedron Lett.* **1983**, *24*, 5095–5098.

[2] a) J.-P. Sauvage, C. Dietrich-Buchecker, G. Rapenne in *Molecular Catenanes, Rotaxanes and Knots* (Eds.: J.-P. Sauvage, C. Dietrich-Buchecker), Wiley-VCH, Weinheim, **1999**; b) J.-P. Collin, C. Dietrich-Buchecker, P. Gaviña, M. C. Jimenez-Molero, J.-P. Sauvage, *Acc. Chem. Res.* **2001**, *34*, 477–487.

[3] a) N. Armaroli, V. Balzani, J.-P. Collin, P. Gaviña, J.-P. Sauvage, B. Ventura, *J. Am. Chem. Soc.* **1999**, *121*, 4397–4408; b) L. Raehm, J.-M. Kern, J.-P. Sauvage, *Chem. Eur. J.* **1999**, *5*, 3310–3317.

[4] a) D. Pomeranc, D. Jouvenot, J.-C. Chambron, J.-P. Collin, V. Heitz, J.-P. Sauvage, *Chem. Eur. J.*, **2003**, *9*, 4247–4254; b) L. Hogg, D. A. Leigh, P. J. Lusby, A. Morelli, S. Parsons, J. K. Y. Wong, *Angew. Chem.* **2004**, *116*, 1238–1241; *Angew. Chem. Int. Ed.* **2004**, *43*, 1218–1221.

[5] For complexes in which metal coordination forms part of the macrocycle in a rotaxane, see a) K.-S. Jeong, J. S. Choi, S.-Y. Chang, H.-Y. Chang, *Angew. Chem.* **2000**, *112*, 1758–1761; *Angew. Chem. Int. Ed.* **2000**, *39*, 1692–1695; b) S.-Y. Chang, J. S. Choi, K.-S. Jeong, *Chem. Eur. J.* **2001**, *7*, 2687–2697; c) S.-Y. Chang, K.-S. Jeong, *J. Org. Chem.* **2003**, *68*, 4014–4019; d) S.-Y. Chang, H.-Y. Jang, K.-S. Jeong, *Chem. Eur. J.* **2003**, *9*, 1535–1541; for complexes in which metal coordination forms part of the thread in a rotaxane, see e) K.-M. Park, D. Whang, E. Lee, J. Heo, K. Kim, *Chem. Eur. J.* **2002**, *8*, 498–508; for complexes in which metal coordination forms the stoppers in a rotaxane, see f) R. B. Hannak, G. Färber, R. Konrat, B. Kräutler, *J. Am. Chem. Soc.* **1997**, *119*, 2313–2314; g) J.-C. Chambron, J.-P. Collin, J.-O. Dalbavie, C. O. Dietrich-Buchecker, V. Heitz, F. Odobel, N. Solladié, J.-P. Sauvage, *Coord. Chem. Rev.* **1998**, *178–180*, 1299–1312; h) A. J. Baer, D. H. Macartney, *Inorg. Chem.* **2000**, *39*, 1410–1417; i) G. J. E. Davidson, S. J. Loeb, N. A. Parekh, J. A. Wisner, *J. Chem. Soc. Dalton Trans.* **2001**, 3135–3136; for polyrotaxanes based on metal-coordination polymers, see j) S. R. Batten, R. Robson, *Angew. Chem.* **1998**, *110*, 1558–1595; *Angew. Chem. Int. Ed.* **1998**, *37*, 1460–1494; k) A. J. Blake, N. R. Champness, P. Hubberstey, W.-S. Li, M. A. Withersby, M. Schröder, *Coord. Chem. Rev.* **1999**, *183*, 117–138; l) K. Kim, *Chem. Soc. Rev.* **2002**, *31*, 96–107.

[6] N. Armaroli, L. De Cola, V. Balzani, J.-P. Sauvage, C. O. Dietrich-Buchecker, J.-M. Kern, A. Bailal, *J. Chem. Soc. Dalton Trans.* **1993**, 3241 – 3247.
[7] M. Consuelo Jiménez, C. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem.* **2000**, *112*, 3422 – 3425; *Angew. Chem. Int. Ed.* **2000**, *39*, 3284 – 3287.
[8] For a rotaxane which utilizes square-planar metal complexes as the stoppers, see S. J. Loeb, J. A. Wisner, *Chem. Commun.* **1998**, 2757 – 2758; for a pseudo-rotaxane based on a square-planar metal geometry, see C. Hamann, J.-M. Kern, J.-P. Sauvage, *Dalton Trans.* **2003**, 3770 – 3775.
[9] T. Moriuchi, S. Bandoh, M. Miyaishi, T. Hirao, *Eur. J. Inorg. Chem.* **2001**, 651 – 657.
[10] a) T. J. Kidd, D. A. Leigh, A. J. Wilson, *J. Am. Chem. Soc.* **1999**, *121*, 1599 – 1600; b) J. S. Hannam, T. J. Kidd, D. A. Leigh, A. J. Wilson, *Org. Lett.* **2003**, *5*, 1907 – 1910.
[11] a) J. E. Kickham, S. J. Loeb, *Inorg. Chem.* **1994**, *33*, 4351 – 4359; b) G. R. Newkome, T. Kawato, D. K. Kohli, W. E. Puckett, B. D. Olivier, G. Chiari, F. R. Fronczek, W. A. Deutsch, *J. Am. Chem. Soc.* **1981**, *103*, 3423 – 3429; c) this particular combination of metal coordination and π stacking to control the interaction of tridentate and monodentate ligands is very reminiscent of a series of metalloreceptors for DNA bases [J. E. Kickham, S. J. Loeb, S. L. Murphy, *Chem. Eur. J.* **1997**, *3*, 1203 – 1213].
[12] [Pd(L6)]: $C_{121}H_{141.5}N_{8.5}O_6Pd$, $M_r = 1917.33$, yellow block, crystal size $0.47 \times 0.31 \times 0.27\ mm^3$, triclinic, space group $P\bar{1}$, $a = 15.7840(10)$, $b = 15.9967(10)$, $c = 22.8029(14)$ Å, $\alpha = 84.9850(10)$, $\beta = 71.8430(10)$, $\gamma = 80.5460(10)°$, $V = 5392.5(6)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.193\ Mg\,m^{-3}$; $Mo_{K\alpha}$ radiation (graphite monochromator, $\lambda = 0.71073$ Å), $\mu = 0.231\ mm^{-1}$, $T = 150(2)$ K. 34043 data (15412 unique, $R_{int} = 0.0331$, $2.06 < \theta < 23.26°$), were collected on a Brucker SMART CCD diffractometer using narrow frames (0.5° in ω), and were corrected semiempirically for absorption and incident beam decay. Data beyond 0.9 Å were weak and were not used for refinement. The structure was solved by direct methods (SIR92)[13] and refined by full-matrix least-squares against F^2.[14] Phenyl groups were constrained to be rigid hexagons and hydrogen atoms were placed in calculated positions. The whole macrocyclic component, inclusive of the Pd atom, is disordered (50:50) over two positions. The alkyl chain is further disordered and the refinement of this portion of the structure was controlled by application of restraints to both 1,2 and 1,3 distances and use of a common isotropic displacement parameter for all C atoms forming the chain. The only disorder present in the thread is in two of the *tert*-butyl groups. That based on C244 is rotationally disordered (70:30) with the central carbon atom (C244) fully occupied and the two alternative sets of methyl positions related by a 60° rotation about the C244–C243 bond. All atoms in the groups were refined with anisotropic displacement parameters (adps), those of "opposite" C atoms being constrained to be equal. The *tert*-butyl group attached to C263 is disordered (70:30) over two positions and was refined isotropically. Similarity restraints were applied to chemically equivalent 1,2 and 1,3 distances in both disordered *tert*-butyl groups. In the latter stages of refinement there was still significant unassigned electron density associated with diffuse solvent. This density was modeled by using the procedure of van der Sluis and Spek,[15] comprising 199 electrons per unit cell, and corresponds to approximately 4.5 MeCN solvent molecules per asymmetric unit; values of M_r, $F(000)$, μ etc. have been calculated on this assumption. $wR = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2} = 0.2527$, conventional $R = 0.0806$ for F values of 15412 reflections with $F_o^2 > 2\sigma F_o^2$), $S = 1.115$ for 885 parameters. Residual electron density extremes were 1.03 and −0.94 e Å^{-3}. CCDC-229418 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).
[13] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, *J. Appl. Crystallogr.* **1993**, *26*, 343 – 350.
[14] G. M. Sheldrick, University of Göttingen, Germany, **1997**.
[15] P. van der Sluis, A. L. Spek, *Acta. Crystallogr. Sect. A* **1990**, *46*, 194 – 201.

