

Tetrameric Cyclic Double Helicates as a Scaffold for a Molecular Solomon Link**

Jonathon E. Beves, Christopher J. Campbell, David A. Leigh,* and Robin G. Pritchard

A Solomon link, colloquially termed a “Solomon knot” (a 4_1^2 link in Alexander–Briggs notation^[1]), is a topology of two interwoven rings that cross each other four times in the simplest representation (Figure 1).^[2] Such doubly-entwined

macrocyclization reactions that can be problematic when employing long linear helicates^[8] (Figure 1). A small-molecule pentafoil knot (five crossings) was recently prepared using a pentameric circular helicate scaffold.^[9] Here we report on the use of a tetrameric circular helicate as the basis for a Solomon link, illustrating the general utility of this approach for the assembly of complex molecular topologies.

The ligand used in our earlier synthesis of a pentafoil knot^[9] was based on a tris(bipyridine) motif employed^[7a,b,d] by Lehn to assemble penta- and hexameric cyclic helicates, but with both outer bipyridine units replaced by 2-formylpyridine groups that could condense with amines to form imines and generate tris(bidentate) ligand strands. As well as providing a convenient way of connecting metal binding components, imine bond formation is reversible, imparting an ‘error checking’ mechanism during the assembly process.^[10] Incorporating an additional oxygen atom in the ethylene spacer between each bipyridine group of Lehn’s tris(bipyridine) ligand led to cyclic tetrameric helicates.^[7b] Accordingly, in an attempt to generate the four crossings required for a Solomon link, we introduced a similar structural change to the ligand used in the pentafoil knot synthesis in the form of **1** (for the synthesis of **1** see the Supporting Information) and investigated its coordination chemistry with primary amines and Fe^{II} salts (Scheme 1).

The reaction of **1** with *n*-hexylamine and FeCl₂ (DMSO, 60 °C, 24 h, Scheme 1)^[8] produced an intensely colored purple solution typical of low-spin iron(II) tris(diimine) complexes. After 24 hours, the product was isolated in 47 % yield as the hexafluorophosphate salt **2** by precipitation with aqueous KPF₆. Electrospray ionization mass spectrometry (ESI-MS; see the Supporting Information, Figure S1) revealed that **2** was a metal–ligand tetramer with the formula [Fe₄L₄](PF₆)₈^[11] (L = bis(imine) ligand resulting from the condensation of **1** with two molecules of *n*-hexylamine). ¹H NMR spectroscopy (Figure 2a) indicated that **2** was highly symmetrical, with the splitting of the diastereotopic CH₂–O–CH₂ protons consistent with the chiral (racemic) helicate topology shown in Scheme 1. The yield of **2** was increased to 71 % (yield of isolated product) when employing 4.4 equivalents of the iron(II) salt (see the Supporting Information, Figure S9).

The formation of the tetrameric cyclic helicate was not limited to the use of FeCl₂ as the iron(II) salt (Scheme 1), both Fe(BF₄)₂ and Fe(ClO₄)₂ also produced **2**, although in significantly lower yields (see the Supporting Information, Figure S13) and contaminated with other polymeric and oligomeric by-products. When FeBr₂ was employed as the iron source, a different main product was obtained (Scheme 1), which was identified as the linear trinuclear triple helicate ([Fe₃L₃]⁶⁺) **3** by ¹H NMR spectroscopy (Figure 2b) and ESI-

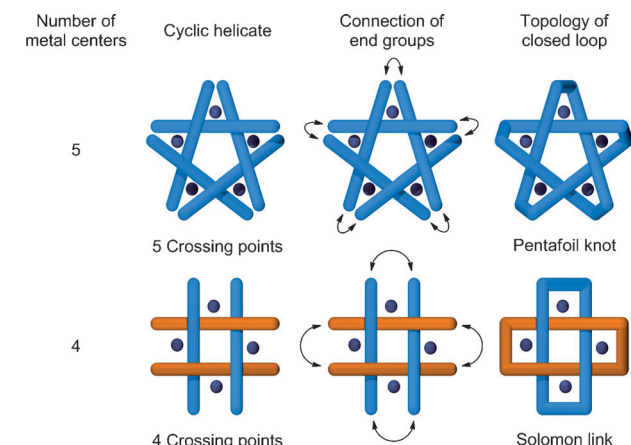


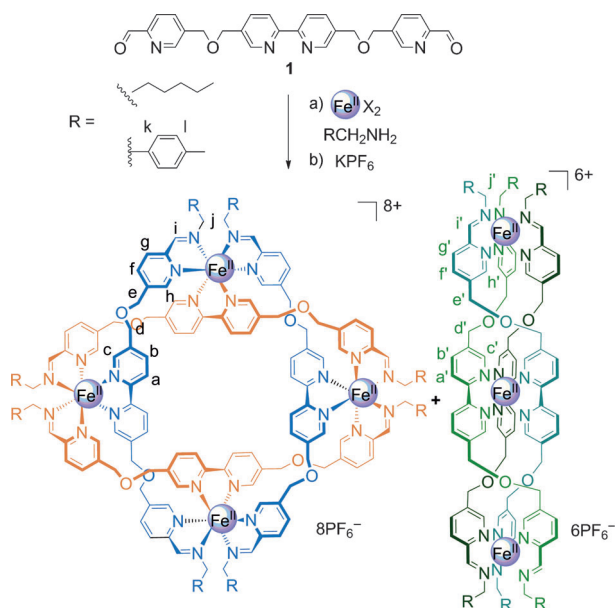
Figure 1. Ring-closing cyclic metal double helicates for the formation of topologically complex molecules. A pentameric circular double helicate is the scaffold (five crossings) required for a pentafoil knot,^[9] and a tetrameric circular double helicate (four crossings) the basis for a Solomon link.^[2b,d]

[2]catenanes are still rare,^[3–5] with only two small-molecule examples with wholly organic backbones reported^[4,5] to date. The Solomon link is the most complex topology to have been produced^[4] using Sauvage’s pioneering route^[6] of generating higher order interlocked structures through the connection of the termini of linear double-stranded metal helicates. In principle,^[2b,d] cyclic double helicates^[7] can provide the crossings required for a range of topologies, while simultaneously positioning connecting sites in close proximity to aid the

[*] Dr. J. E. Beves, C. J. Campbell, Prof. D. A. Leigh
School of Chemistry, University of Edinburgh
The King’s Buildings, West Mains Road, Edinburgh EH9 3JJ (UK)
Prof. D. A. Leigh, Dr. R. G. Pritchard
School of Chemistry, University of Manchester
Oxford Road, Manchester M13 9PL (UK)
E-mail: David.Laigh@manchester.ac.uk
Homepage: <http://www.catenane.net>

[**] We thank the Engineering and Physical Sciences Research Council (EPSRC) National Crystallography Service for data collection. This research was funded by the EPSRC. J.E.B. is a Swiss National Science Foundation postdoctoral fellow.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ange.201302634>.



Entry	R	FeX ₂ (equiv)	Cyclic helicate product (%)	Linear helicate product (%)
1	(CH ₂) ₄ CH ₃	FeCl ₂ (1.1)	2 (47)	-
2	(CH ₂) ₄ CH ₃	FeCl ₂ (4.4)	2 (71)	-
3	(CH ₂) ₄ CH ₃	FeBr ₂ (1.1)	2 (6)	3 (56)
4	<i>p</i> -C ₆ H ₄ CH ₃	FeCl ₂ (1.1)	4 (26)	5 (20)

Scheme 1. Synthesis of cyclic and linear iron(II) helicates. Reaction conditions: a) FeX₂, RCH₂NH₂, DMSO, 60 °C, 24 h; b) excess KPF₆ (aq). DMSO = dimethyl sulfoxide.

MS (see the Supporting Information, Figure S14). A linear triple helicate with a lifetime of a few minutes was previously observed as an intermediate during the formation of pentameric cyclic helicates using Lehn's tris(bipyridine) ligand.^[7d] While **3** is a much longer-lived species, it is not clear whether this is because the linear triple helicate is particularly stable as the bromide salt, or whether the assembly/disassembly/rearrangement of the various linear and circular helicates and oligomers is markedly slower using FeBr₂, perhaps as a result of their limited solubility.

Substituting *n*-hexylamine for 4-methylbenzylamine in the reaction of **1** with FeCl₂ gave a mixture of two species (Figure 2c), identified by ESI-MS (Supporting Information, Figures S3 and S5) as the cyclic tetramer **4** and the linear triple helicate ([Fe₃L₃]⁶⁺) **5** (Scheme 1). Using our standard reaction protocol with an initial concentration of **1** of 2.2 mM, the ratio of **4**/**5** was approximately 1:1, however the distribution of cyclic-double-helicate/linear-triple-helicate was significantly altered by small variations in concentration: using an initial concentration of 8.8 mM of **1**, more than 95% of the reaction product was the higher order (four ligands, four metal ions) circular helicate **4** after 24 hours, whereas starting with a concentration of 0.55 mM of **1**, the reaction produced more than 85% of the lower nuclearity (three ligands, three metal ions) linear helicate **5** over the same time period (Supporting Information, Figure S15).^[12] In contrast, the yield of the analogous *n*-hexylamine-derived cyclic tetramer **2** was essentially invariant over this concentration range and no linear triple helicate was observed, illustrating the influence

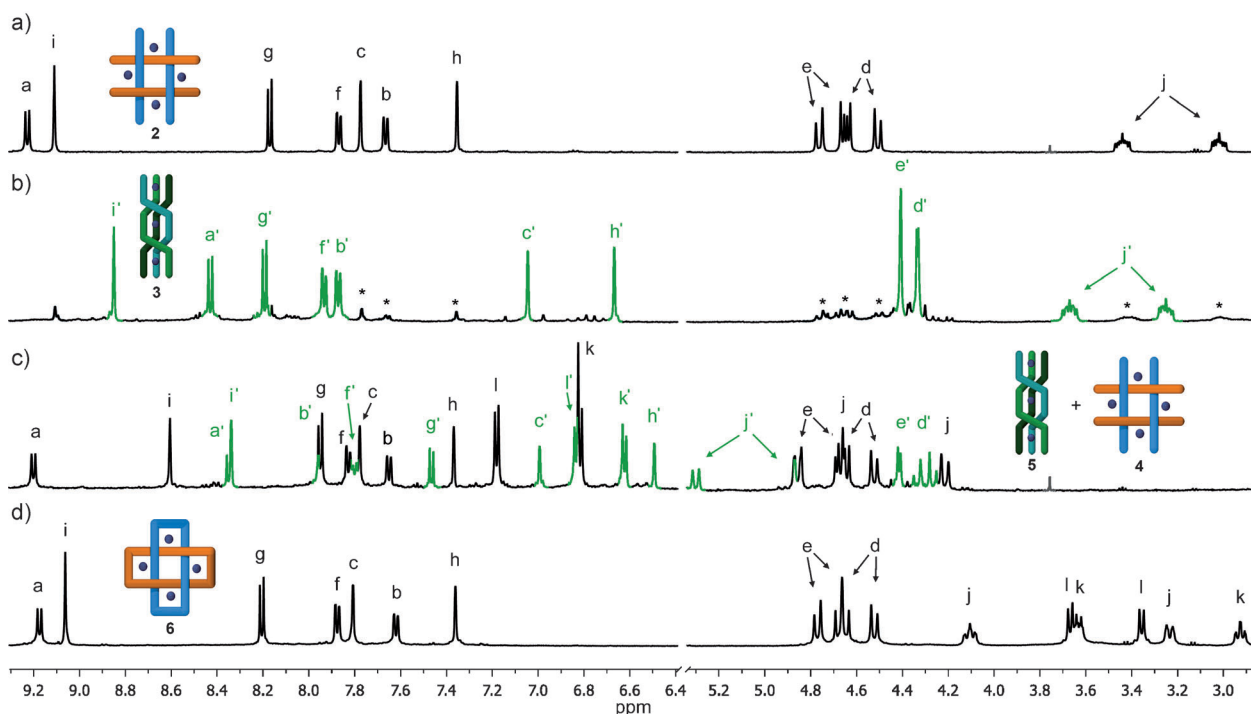
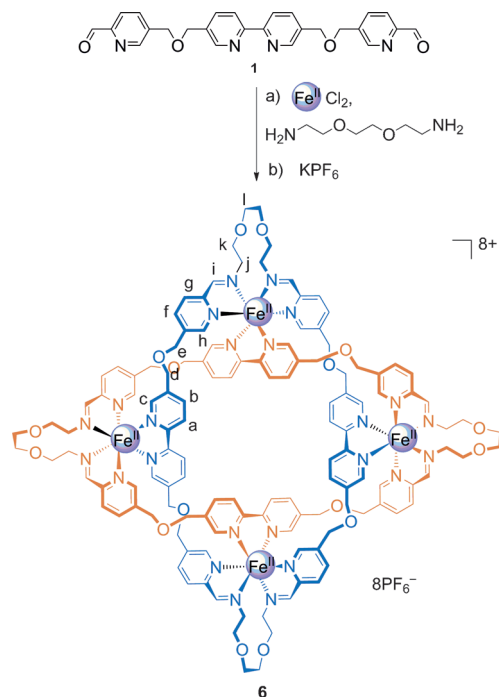


Figure 2. ¹H NMR spectra (CD₃CN, 500 MHz) for a) cyclic tetramer **2**, b) linear triple helicate **3** (green, signals marked * correspond to trace amounts of **2**), c) a 1:1 mixture of cyclic tetramer **4** (black) and linear triple helicate **5** (green), and d) Solomon link **6**. All spectra were recorded in the presence of AgPF₆ (0.1 equiv) to remove traces of chloride ions and sharpen the signal of H_a. For spectra collected in the absence of AgPF₆, see the Supporting Information, Figures S10–S12. Signal assignments refer to the lettering shown in Schemes 1 and 2.

that subtle changes in the ligands can have over the outcomes of the self-assembly reactions.

In order to link the end groups of the open cyclic helicate to generate a Solomon link, we employed 2,2'-(ethylenedioxy)bis(ethylamine), a diamine that is stereoelectronically predisposed to adopt low-energy turns.^[9] The reaction of **1** with the diamine and FeCl₂ in DMSO for 24 hours, with subsequent anion exchange with aqueous KPF₆, generated the Solomon link **6** in 75% yield of isolated product (Scheme 2).^[13]



Scheme 2. Synthesis of molecular Solomon link **6**. Reaction conditions: a) FeCl₂, 2,2'-(ethylenedioxy)bis(ethylamine), DMSO, 60 °C, 24 h; b) excess KPF₆ (aq), 75% (over two steps).

The ¹H NMR spectrum (CD₃CN, 500 MHz, Figure 2 d) of **6** is very similar to that of the tetrameric cyclic helicate **2** derived from *n*-hexylamine (Figure 2 a), including the splitting pattern for the diastereotopic CH₂-O-CH₂ protons. ESI-MS (Supporting Information, Figure S7) confirmed that **6** had a structural formula consistent with a Solomon link. Single crystals of **6** suitable for X-ray crystallography were grown by slow diffusion of diethyl ether into a nitromethane solution of **6**, and the structure was confirmed by X-ray crystallography (Figure 3). The solid-state structure shows the two organic macrocycles interlocked by the four crossings that define the topology of a Solomon link. The iron atoms are close-to-coplanar and lie on the vertices of a square with Fe–Fe distances of just over 1 nm. Despite the high yield, as for the related pentafoil knot,^[9] the octahedral coordination geometry of the iron(II) centers is amongst the most distorted [Fe(N-ligand)₆] structures in the Cambridge Structural Database^[14] (see the Supporting Information for details). The -OCH₂CH₂O- units in the linking group adopt close-to-gauche conformations (59–73°). Two PF₆[−] counter ions are

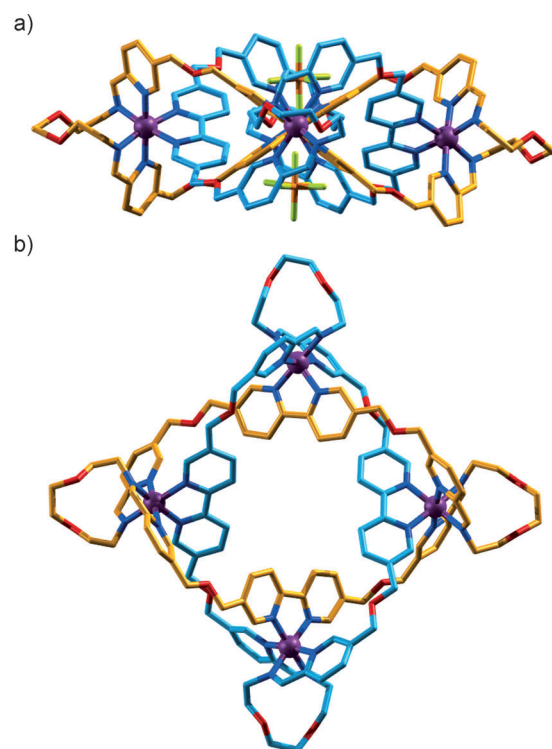


Figure 3. X-Ray crystal structure of Solomon link **6**. a) Viewed in the plane of Fe^{II} ions (all but two PF₆[−] anions omitted); b) viewed from above the center of the macrocycle cavities (all PF₆[−] anions omitted). The C atoms of one ring are colored orange and of the other ring light blue, N: dark blue, O: red, P: brown, F: green, Fe: purple. Solvent molecules, H atoms, and PF₆[−] anions (other than the two shown in view (a)) are omitted for clarity. Fe–Fe distances [Å]: 10.590(6), 10.677(7), 10.590(6), 10.709(7), and Fe–Fe–Fe angles [°]: 90.05(4), 89.85(4), 90.20(4), 89.66(4). O–C–C–O torsion angles [°]: 70(3), 59(3), 67(3), 73(3). CH₃...F distances [Å]: 2.72, 2.82, 2.74, 2.65, 2.78, 2.89, 2.99, 2.74, 2.96, 2.70, 2.86, 2.88, 2.85, 3.15, 2.95, 2.87.

positioned directly above and below the center of the helicate (Figure 3 a) and form bifurcated CH...F interactions with the eight H_a protons, which are particularly electron-poor because of the ligand coordination to the iron(II) dications (Supporting Information, Figures S16 and S17).

The one-pot synthesis of molecular Solomon link **6** assembles four iron(II) cations, four bis(aldehyde) and four bis(amine) building blocks to generate two interwoven 68-membered-ring macrocycles with four crossings in 75% isolated yield. The assembly process for the tetrameric cyclic double helicate forms the basis for the Solomon link synthesis and is sensitive to structural changes in the amine, the concentration and the anion used (even though the reaction product is not the result of an anion-template mechanism). The synthesis of Solomon link **6** and the earlier pentafoil knot^[9] show that cyclic helicates of different sizes can act as highly efficient and effective scaffolds for intricate molecular topologies.

Received: March 29, 2013

Published online: May 6, 2013

Keywords: catenanes · chemical topology · cyclic helicates · molecular knot · self-assembly

- [1] The principal number represents the number of crossings (four for the Solomon link). The superscript refers to the number of linked components. The subscript differentiates the topology from others with the same number of crossings and components. J. W. Alexander, G. B. Briggs, *Ann. Math.* **1926–1927**, 28, 562–586.
- [2] a) E. E. Fenlon, *Eur. J. Org. Chem.* **2008**, 5023–5035; b) J. E. Beves, B. A. Blight, C. J. Campbell, D. A. Leigh, R. T. McBurney, *Angew. Chem.* **2011**, 123, 9428–9499; *Angew. Chem. Int. Ed.* **2011**, 50, 9260–9327; c) R. S. Forgan, J.-P. Sauvage, J. F. Stoddart, *Chem. Rev.* **2011**, 111, 5434–5464; d) J.-F. Ayme, J. E. Beves, C. J. Campbell, D. A. Leigh, *Chem. Soc. Rev.* **2013**, 42, 1700–1712.
- [3] Solomon links in which metal ions are integral parts of the framework of each macrocycle have been prepared: a) F. Ibukuro, M. Fujita, K. Yamaguchi, J.-P. Sauvage, *J. Am. Chem. Soc.* **1999**, 121, 11014–11015; b) C. P. McArdle, J. J. Vittal, R. J. Puddephatt, *Angew. Chem.* **2000**, 112, 3977–3980; *Angew. Chem. Int. Ed.* **2000**, 39, 3819–3822; c) C. P. McArdle, M. C. Jennings, J. J. Vittal, R. J. Puddephatt, *Chem. Eur. J.* **2001**, 7, 3572–3583; d) C. Peinador, V. Blanco, J. M. Quintela, *J. Am. Chem. Soc.* **2009**, 131, 920–921; and a Solomon link formed from single-stranded DNA has also been described: e) T. Ciengshin, R. Sha, N. C. Seeman, *Angew. Chem.* **2011**, 123, 4511–4514; *Angew. Chem. Int. Ed.* **2011**, 50, 4419–4422; for the assembly of a related “Solomon cube” topology, see: f) T. K. Ronson, J. Fisher, L. P. Harding, P. J. Rizkallah, J. E. Warren, M. J. Hardie, *Nat. Chem.* **2009**, 1, 212–216.
- [4] a) J. F. Nierengarten, C. O. Dietrich-Buchecker, J. P. Sauvage, *J. Am. Chem. Soc.* **1994**, 116, 375–376; b) C. Dietrich-Buchecker, E. Leize, J.-F. Nierengarten, J.-P. Sauvage, A. Van Dorsselaer, *J. Chem. Soc. Chem. Commun.* **1994**, 2257–2258; c) C. Dietrich-Buchecker, J.-P. Sauvage, *Chem. Commun.* **1999**, 615–616.
- [5] a) C. D. Pentecost, K. S. Chichak, A. J. Peters, G. W. V. Cave, S. J. Cantrill, J. F. Stoddart, *Angew. Chem.* **2007**, 119, 222–226; *Angew. Chem. Int. Ed.* **2007**, 46, 218–222; b) C. D. Meyer, R. S. Forgan, K. S. Chichak, A. J. Peters, N. Tangchaivang, G. W. V. Cave, S. I. Khan, S. J. Cantrill, J. F. Stoddart, *Chem. Eur. J.* **2010**, 16, 12570–12581.
- [6] J.-P. Sauvage, *Acc. Chem. Res.* **1990**, 23, 319–327.
- [7] a) B. Hasenknopf, J.-M. Lehn, B. O. Kneisel, G. Baum, D. Fenske, *Angew. Chem.* **1996**, 108, 1987–1990; *Angew. Chem. Int. Ed. Engl.* **1996**, 35, 1838–1840; b) B. Hasenknopf, J.-M. Lehn, N. Boumediene, A. Dupont-Gervais, D. A. Van, B. Kneisel, D. Fenske, *J. Am. Chem. Soc.* **1997**, 119, 10956–10962; c) C. Provent, S. Hewage, G. Brand, L. J. Charbonnière, A. F. Williams, G. Bernardinelli, *Angew. Chem.* **1997**, 109, 1346–1348; *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 1287–1289; d) B. Hasenknopf, J.-M. Lehn, N. Boumediene, E. Leize, A. Van Dorsselaer, *Angew. Chem.* **1998**, 110, 3458–3460; *Angew. Chem. Int. Ed.* **1998**, 37, 3265–3268; e) O. Mamula, A. von Zelewsky, G. Bernardinelli, *Angew. Chem.* **1998**, 110, 302–305; *Angew. Chem. Int. Ed.* **1998**, 37, 289–293; f) C. Provent, E. Rivara-Minten, S. Hewage, G. Brunner, A. F. Williams, *Chem. Eur. J.* **1999**, 5, 3487–3494; g) C. S. Campos-Fernández, R. Clerac, J. M. Koomen, D. H. Russell, K. R. Dunbar, *J. Am. Chem. Soc.* **2001**, 123, 773–774; h) L. J. Childs, N. W. Alcock, M. J. Hannon, *Angew. Chem.* **2002**, 114, 4418–4421; *Angew. Chem. Int. Ed.* **2002**, 41, 4244–4247; i) L. J. Childs, M. Pasqu, A. J. Clarke, N. W. Alcock, M. J. Hannon, *Chem. Eur. J.* **2004**, 10, 4291–4300; j) C. S. Campos-Fernández, B. L. Schottel, H. T. Chifotides, J. K. Bera, J. Bacsá, J. M. Koomen, D. H. Russell, K. R. Dunbar, *J. Am. Chem. Soc.* **2005**, 127, 12909–12923; k) J.-M. Senegas, S. Koeller, G. Bernardinelli, C. Piguet, *Chem. Commun.* **2005**, 2235–2237; l) S. P. Argent, H. Adams, T. Riis-Johannessen, J. C. Jeffery, L. P. Harding, O. Mamula, M. D. Ward, *Inorg. Chem.* **2006**, 45, 3905–3919; m) J. Hamblin, F. Tuna, S. Bunce, L. J. Childs, A. Jackson, W. Errington, N. W. Alcock, H. Nierengarten, D. A. Van, E. Leize-Wagner, M. J. Hannon, *Chem. Eur. J.* **2007**, 13, 9286–9296; n) Y. Pang, S. Cui, B. Li, J. Zhang, Y. Wang, H. Zhang, *Inorg. Chem.* **2008**, 47, 10317–10324; o) K. E. Allen, R. A. Faulkner, L. P. Harding, C. R. Rice, T. Riis-Johannessen, M. L. Voss, M. Whitehead, *Angew. Chem.* **2010**, 122, 6805–6808; *Angew. Chem. Int. Ed.* **2010**, 49, 6655–6658; p) L. Bain, S. Bullock, L. Harding, T. Riis-Johannessen, G. Midgley, C. R. Rice, M. Whitehead, *Chem. Commun.* **2010**, 46, 3496–3498; q) H. B. Tanh Jeazet, K. Gloe, T. Doert, O. N. Kataeva, A. Jaeger, G. Geipel, G. Bernhard, B. Buechner, K. Gloe, *Chem. Commun.* **2010**, 46, 2373–2375; r) I. D. Giles, H. T. Chifotides, M. Shatruk, K. R. Dunbar, *Chem. Commun.* **2011**, 47, 12604–12606; s) Z.-S. Wu, J.-T. Hsu, C.-C. Hsieh, Y.-C. Horng, *Chem. Commun.* **2012**, 48, 3436–3438; alternatively, braided square grids (see e.g.: t) X.-H. Bu, H. Morishita, K. Tanaka, K. Biradha, S. Furusho, M. Shionoya, *Chem. Commun.* **2000**, 971–972) could potentially be used as the basis for Solomon links, see Ref. [2d].
- [8] C. Dietrich-Buchecker, B. Colasson, D. Jouvenot, J.-P. Sauvage, *Chem. Eur. J.* **2005**, 11, 4374–4386.
- [9] a) J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, K. Rissanen, D. Schultz, *Nat. Chem.* **2012**, 4, 15–20; b) M. J. Hardie, *Nat. Chem.* **2012**, 4, 7–8; c) J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, K. Rissanen, D. Schultz, *J. Am. Chem. Soc.* **2012**, 134, 9488–9497.
- [10] a) D. A. Leigh, P. J. Lusby, S. J. Teat, A. J. Wilson, J. K. Y. Wong, *Angew. Chem.* **2001**, 113, 1586–1591; *Angew. Chem. Int. Ed.* **2001**, 40, 1538–1543; 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; c) M. Hutin, C. A. Schalley, G. Bernardinelli, J. R. Nitschke, *Chem. Eur. J.* **2006**, 12, 4069–4076; d) J. R. Price, J. K. Clegg, R. R. Fenton, L. F. Lindoy, J. C. McMurtrie, G. V. Meehan, A. Parkin, D. Perkins, P. Turner, *Aust. J. Chem.* **2009**, 62, 1014–1019.
- [11] A small contamination of chloride-containing helicate was observed, indicating incomplete anion exchange. Neither recrystallization nor re-precipitation using KPF₆ removed this impurity.
- [12] For related concentration effects, see: a) X. Chi, A. J. Guerin, R. A. Haycock, C. A. Hunter, L. D. Sarson, *J. Chem. Soc. Chem. Commun.* **1995**, 2563–2565; b) E. C. Constable, C. E. Housecroft, T. Kulke, G. Baum, D. Fenske, *Chem. Commun.* **1999**, 195–196; c) P. N. W. Baxter, R. G. Khoury, J.-M. Lehn, G. Baum, D. Fenske, *Chem. Eur. J.* **2000**, 6, 4140–4148; d) M. Schweiger, S. R. Seidel, A. M. Arif, P. J. Stang, *Inorg. Chem.* **2002**, 41, 2556–2559; e) M. Ferrer, M. Mounir, O. Rossell, E. Ruiz, M. A. Maestro, *Inorg. Chem.* **2003**, 42, 5890–5899; f) T. Yamamoto, A. M. Arif, P. J. Stang, *J. Am. Chem. Soc.* **2003**, 125, 12309–12317; g) J. E. Beves, B. E. Chapman, P. W. Kuchel, L. F. Lindoy, J. McMurtrie, M. McPartlin, P. Thordarson, G. Wei, *Dalton Trans.* **2006**, 744–750; h) M. d. C. Rivera-Sánchez, I. Andújar-de-Sanctis, M. García-Arriaga, V. Gubala, G. Hobley, J. M. Rivera, *J. Am. Chem. Soc.* **2009**, 131, 10403–10405; i) C. Piguet, *Chem. Commun.* **2010**, 46, 6209–6231; j) M. Ferrer, A. Pedrosa, L. Rodríguez, O. Rossell, M. Vilaseca, *Inorg. Chem.* **2010**, 49, 9438–9449.
- [13] The use of other diamines led only to mixtures of oligomers and polymers.
- [14] F. H. Allen, *Acta Crystallogr. Sect. B* **2002**, 58, 380–388.
- [15] CCDC 931375 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.