

Lanthanide Template Synthesis of a Molecular Trefoil Knot

Jean-François Ayme, Guzmán Gil-Ramírez, David A. Leigh,* Jean-François Lemonnier, Augustinas Markevicius, Christopher A. Muryn, and Gen Zhang

School of Chemistry, University of Manchester, Oxford Road, Manchester M13 9PL, United Kingdom

Supporting Information

ABSTRACT: We report on a complex featuring three 2,6-pyridinedicarboxamide ligands entwined around a lanthanide (Ln^{3+}) ion. The ligand strands can be cyclized by ring-closing olefin metathesis to form a molecular trefoil knot in 58% yield. Demetalation with tetraethylammonium fluoride quantitatively generates the wholly organic 81-atom-loop trefoil knot.

Molecular knots¹ and entanglements are featured in cyclic DNA² and some proteins³ and are thought to play an important role in the chemical and physical properties of both natural and synthetic polymers.⁴ Sauvage and co-workers prepared the first synthetic molecular trefoil knot by connecting the end-groups of a linear two-metal-ion double helicate.⁵ However, the earliest published idea for a template synthesis of a trefoil knot is Sokolov's proposal⁶ for assembling three ligands around a metal center to generate the three crossings necessary⁷ in the cyclized product. Several groups have attempted to prepare trefoil knots using this strategy thus far without achieving the ultimate goal,⁸ although Hunter has succeeded in synthesizing a trefoil knot by folding a single ligand strand around a transition metal ion,⁹ and Siegel has made a 'trefoil knotted cyclophane'¹⁰ using a related triskelion approach featuring a covalently bonded scaffold.¹¹

Lanthanide complexes have found application for their luminescent properties,¹² as nanomaterials¹³ and as contrast agents for magnetic resonance imaging.¹⁴ However, their use in template synthesis has been limited compared to transition metals due to their lack of preferred coordination numbers and geometries.¹⁵ Pioneering work by Bünzli and Piguet in the 1990s¹⁶ used lanthanides in the assembly of triple linear helicates with varying lengths, compositions, and photophysical properties. More recently, the 2,6-dicarbonylpyridyl motif has emerged as a reliable tridentate ligand for lanthanide ions, with examples of well-defined 3:1 ligand/metal-ion complexes including luminescent bundles,¹⁷ cages,¹⁸ linear helicates,¹⁹ and catenanes.^{20,21} Here we utilize this motif as the basis for a simple and efficient Sokolov-like template synthesis of a molecular trefoil knot using lanthanide ions.

The end-groups of three ligands symmetrically entwined about a central metal ion can potentially be connected in different ways (Figure 1), leading to various architectures including a trefoil knot (3× connection a) or a topologically trivial "unknot" macrocycle (3× connection b).^{1e,g,22} The groups of Muller²³ and Gunnlaugsson²⁴ have found that aryl-substituted 2,6-diamidopyridyl ligands enhance the stability of 3:1 lanthanide ion complexes through interligand π - π stacking. We reasoned that

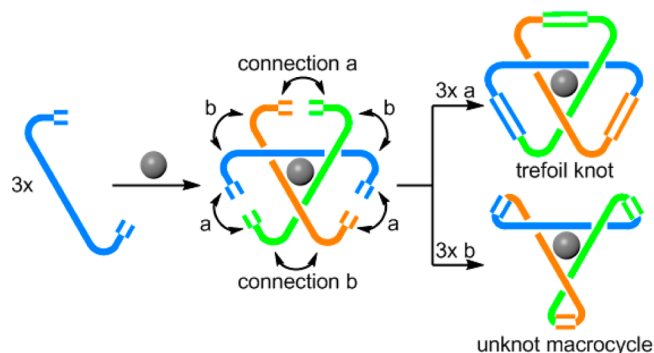


Figure 1. Three identical ligands held in a cyclic helical arrangement around a metal ion. Interligand olefin metathesis reactions can potentially lead to a trefoil knot (3× connection a) or an "unknot" macrocycle (3× connection b).²²

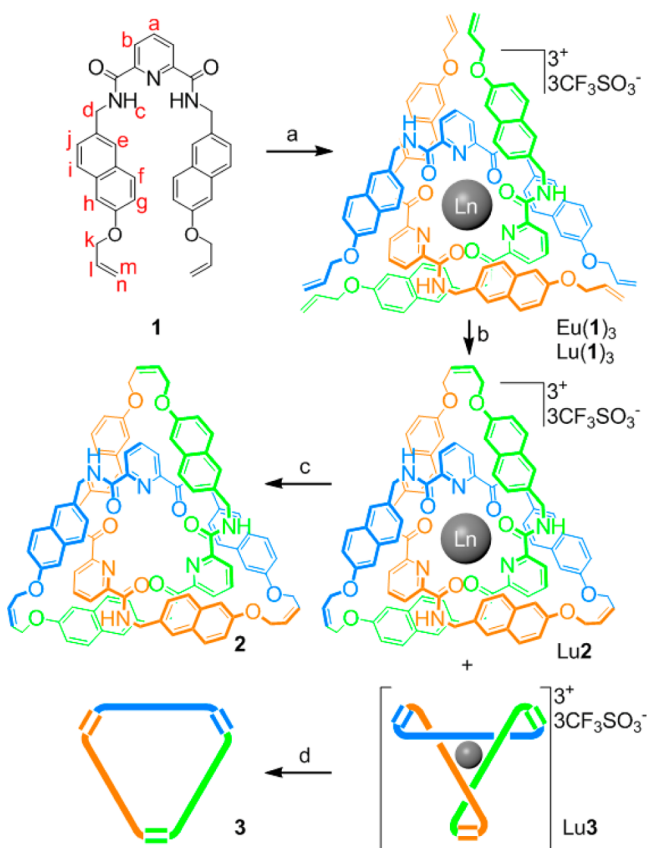
these interactions could be used to position the end-groups of appropriately designed ligands to favor ring-closure to form a molecular trefoil knot rather than the isomeric unknot macrocycle.

Ligand **1** (Scheme 1) was synthesized in three steps from commercially available 6-cyano-2-naphthol (see Supporting Information). Treatment of **1** with a $\text{Ln}(\text{CF}_3\text{SO}_3)_3$ salt ($\text{Ln} = \text{Eu}, \text{Lu}$) as a 20 mM solution in acetonitrile, followed by precipitation with dichloromethane, generated the corresponding $[\text{Ln}(\text{1})_3][\text{CF}_3\text{SO}_3]_3$ complexes in 85% (Eu) and 90% (Lu) yields (Scheme 1, step a). Electrospray ionization mass spectrometry (ESI-MS) confirmed the stoichiometry of the $\text{Lu}(\text{1})_3$ complex (peaks at 2145 ($[\text{Lu}(\text{1})_3][\text{CF}_3\text{SO}_3]_2^+$), 998 ($[\text{Lu}(\text{1})_3][\text{CF}_3\text{SO}_3]^{2+}$), and 615 ($[\text{Lu}(\text{1})_3]^{3+}$), together with well-matching isotope patterns, see Supporting Information). The ^1H NMR spectrum of $[\text{Lu}(\text{1})_3][\text{CF}_3\text{SO}_3]_3$ in CD_3CN (Figure 2b) shows the three coordinated ligands to be in equivalent environments and the AB system of the diastereotopic H_d methylene resonances confirm the helical nature of the cyclic trimeric arrangement of ligands. The upfield shift of the pyridine proton signals H_a and H_b ($\Delta\delta = 0.6$ and 0.5 ppm, respectively) compared to uncomplexed **1** (Figure 2a) are consistent with the anticipated interligand π - π stacking interactions. ^1H NMR and mass spectrometry of the corresponding $\text{Eu}(\text{1})_3$ complex indicated a similar structure (see Supporting Information).

Slow diffusion of diethyl ether into a saturated acetonitrile solution of the $[\text{Eu}(\text{1})_3][\text{CF}_3\text{SO}_3]_3$ complex afforded single crystals suitable for X-ray diffraction (see Supporting Informa-

Received: July 8, 2014

Published: September 8, 2014

Scheme 1. Synthesis of Molecular Trefoil Knot 2^a

^aReagents and conditions: (a) $\text{Eu}(\text{CF}_3\text{SO}_3)_3$, CH_3CN , r.t., 85%, or $\text{Lu}(\text{CF}_3\text{SO}_3)_3$, CH_3CN , r.t., 90%; (b) Hoveyda–Grubbs second generation catalyst (50 mol %), $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{NO}_2$, 323 K, 58% ($[\text{Lu}2][\text{CF}_3\text{SO}_3]_3$); (c) Et_4NF , $\text{DMSO}-d_6$, r.t., quantitative; (d) $\text{Na}_5\text{-DTPA}$, DMF, 17% (3; over two steps).

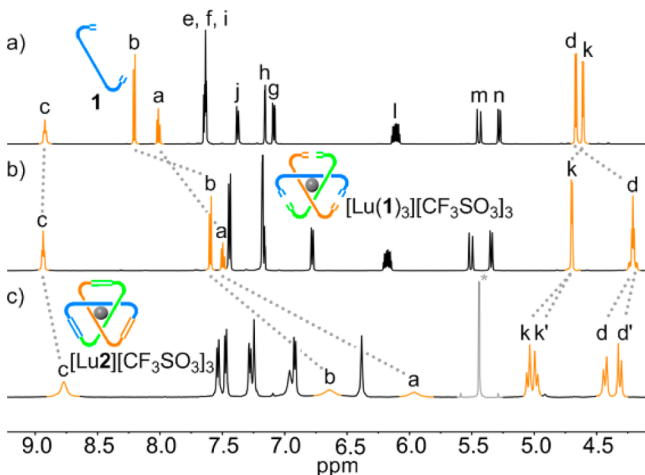


Figure 2. Selected regions of the ^1H NMR spectra (600 MHz, CD_3CN , 295 K (345 K for panel c)) of (a) ligand **1**; (b) cyclic trimeric helicate complex $[\text{Lu}(\mathbf{1})_3][\text{CF}_3\text{SO}_3]_3$; and (c) trefoil knot complex $[\text{Lu}2][\text{CF}_3\text{SO}_3]_3$ (345 K). *Residual solvent peak. The lettering in the figure refers to the proton assignments shown in Scheme 1

tion). In the solid state structure (Figure 3a) the three units of **1** are helically arranged around the europium ion in a nine-coordinate trigonal prism geometry (the $\text{Eu}-\text{O}$ and $\text{Eu}-\text{N}$ distances, 2.410(8)–2.439(9) and 2.54(1)–2.55(1) Å, respec-

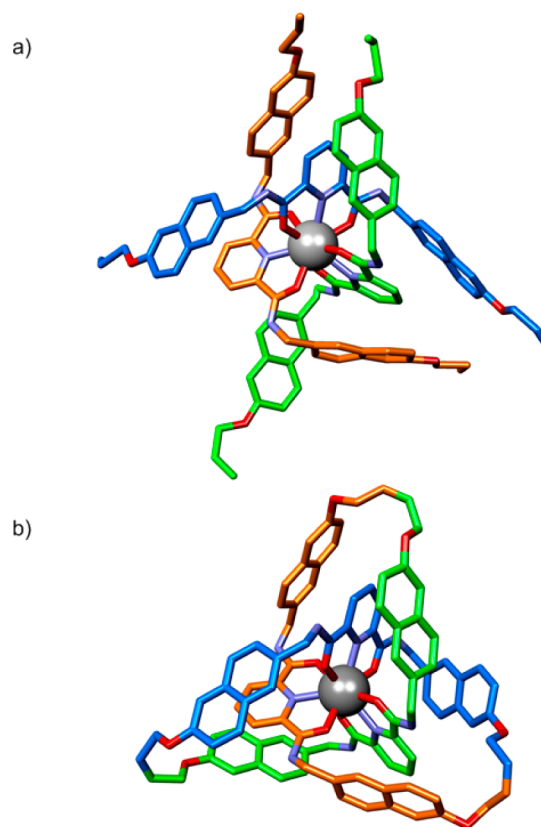


Figure 3. (a) X-ray crystal structure of complex $[\text{Eu}(\mathbf{1})_3][\text{CF}_3\text{SO}_3]_3$ shown in a framework representation. Hydrogen atoms, solvent molecules, and counteranions are omitted for clarity. The europium atom is shown in gray, nitrogen atoms in purple, oxygen atoms in red, and carbon atoms of the three ligands in blue, orange, and green. Selected metal–donor atom bond lengths (Å): $\text{Eu}-\text{O}$ 2.410(8), 2.419(8), 2.439(9), 2.434(8), 2.424(8), 2.425(8); and $\text{Eu}-\text{N}$ 2.54(1), 2.55(1), 2.543(9). (b) Hyperchem MM+ energy-minimized molecular model of molecular trefoil knot **Ln2**.

tively, are in the expected range of values for pyridine-2,6-dicarboxamide-based complexes).²⁵ Aromatic stacking interactions between each pyridine ring and one naphthalene group from each of the other ligand strands serve to orientate the ligand arms. In the crystal, the ligand end groups are positioned such that joining each of them to their nearest neighbor would generate a trefoil knot architecture. Indeed, comparison of the X-ray crystal structure of $[\text{Eu}(\mathbf{1})_3][\text{CF}_3\text{SO}_3]_3$ (Figure 3a) and the energy-minimized (MM+) structure of **Ln2** (Figure 3b) shows just how well interligand π -stacking preorganizes the complex for trefoil-knot-forming connections. In the crystal structure, the amide NH protons hydrogen bond with the triflate counterions (see Supporting Information). Lu and Eu complexes of related ligand systems are generally similar or isostructural with each other.²⁶ As europium is paramagnetic, $[\text{Lu}(\mathbf{1})_3][\text{CF}_3\text{SO}_3]_3$ was used in the subsequent ring closing reactions so that ^1H NMR spectroscopy could be used to help elucidate the structure of the products.

Complex $[\text{Lu}(\mathbf{1})_3][\text{CF}_3\text{SO}_3]_3$ was stirred overnight at 323 K with 50 mol % (17 mol % loading per connection) of second-generation Hoveyda–Grubbs catalyst (Scheme 1, step b). A 1:1 solvent mixture of dichloromethane and nitromethane was found to give good catalytic activity and product solubility.²⁷ The resulting reaction products were precipitated from dichloromethane and washed thoroughly to remove traces of the catalyst.

ESI-MS confirmed the loss of three ethene molecules per complex (m/z 588 and 956, corresponding to $[\text{Lu}2/3]^{3+}$ and $[\text{Lu}2/3][\text{CF}_3\text{SO}_3]^{2+}$, respectively) and ^1H NMR showed the absence of terminal alkene protons and the presence of two species in a $\sim 7:3$ ratio.

Treatment of a DMF solution of the mixture of products with the chelating agent pentasodium diethylenetriaminepentaacetate (Na_5DTPA ; Scheme 1, step d), followed by extraction into 1:1 acetonitrile/methanol, resulted in the major species (58% isolated yield) remaining in solution, still complexed to Lu^{3+} . The ^1H NMR of this compound (ultimately shown to be $[\text{Lu}2][\text{CF}_3\text{SO}_3]_3$ in CD_3CN was broad at room temperature, but sharpened at 345 K to the spectrum shown in Figure 2c.²⁸ The pyridine H_a and H_b protons are significantly shifted upfield ($\Delta\delta = 1.6$ and 0.8 ppm, respectively) compared to $[\text{Lu}(1)_3][\text{CF}_3\text{SO}_3]_3$ (Figure 2b), suggesting a more compact structure in the ring-closed complex that brings the naphthalene rings closer to the pyridine groups. Methylene groups H_d and H_k both appear as AB systems, indicating the protons within each methylene group are diastereotopic.

The colorless solid, **3**, precipitated during the Na_5DTPA extraction process was shown by ESI-MS to be a demetalated cyclized ligand (17% isolated yield; m/z 1611 $[\text{3} + \text{Na}]^+$). The solid was not soluble in CD_3CN , but its ^1H NMR spectrum in $\text{DMSO}-d_6$ (Figure 4b) is very similar to that of uncoordinated

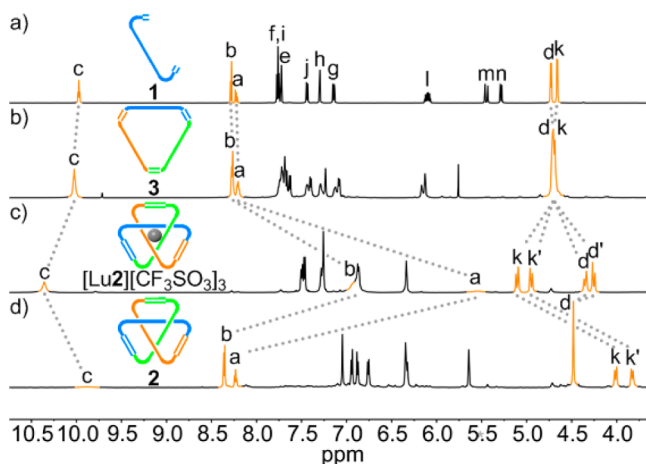


Figure 4. Selected regions of the ^1H NMR spectra (600 MHz, $\text{DMSO}-d_6$, 295 K (348 K for panels c and d)) of (a) ligand **1**; (b) macrocycle **3**; (c) trefoil knot complex $\text{Lu}2$ (348 K); and (d) demetalated trefoil knot **2** (348 K). The lettering in the figure refers to the proton assignments shown in Scheme 1

ligand **1** (Figure 4a), other than the absence of terminal alkene protons (H_m/H_n). In particular, there is no indication that the protons of methylene groups H_d or H_k of **3** are in diastereotopic environments.

The similarity of the ^1H NMR spectra of **1** and **3** in $\text{DMSO}-d_6$ (Figure 4a,b) meant that **3** (the minor product of the olefin metathesis reaction) could confidently be assigned as the unknot macrocycle; however, the shifts in the ^1H NMR spectra in CD_3CN (Figure 2c) of the major product (58%) suggested it was the trefoil knot complex $[\text{Lu}2][\text{CF}_3\text{SO}_3]_3$. Furthermore, the tightly entwined trefoil knot architecture could account for the exceptional stability of $[\text{Lu}2][\text{CF}_3\text{SO}_3]_3$ to demetalation with Na_5DTPA .

Lanthanide trications form stable complexes with fluoride,²⁹ and we reasoned that the small size of this anion might be

advantageous in extracting the metal ion through the narrow gaps in the knotted ligand. Indeed, we were delighted to find that treatment of $[\text{Lu}2][\text{CF}_3\text{SO}_3]_3$ with Et_4NF in $\text{DMSO}-d_6$ smoothly afforded the demetalated trefoil knot **2** (Scheme 1, step c).³⁰ Like its unknot isomer, **3**, the demetalated trefoil knot (**2**) is not soluble in CD_3CN , but the ^1H NMR spectrum of **2** in $\text{DMSO}-d_6$ (Figure 4d) shows considerable shielding of the naphthalene ring protons compared to either **1** or **3** (presumably resulting from $\pi-\pi$ stacking in the entwined structure similar to Figure 3). The H_k methylene groups of **2** appear as an AB system, indicating the protons are diastereotopic, which in the uncomplexed ligand can only result from the inherently chiral architecture of a trefoil knot.

In conclusion, we have demonstrated the lanthanide template synthesis of a molecular trefoil knot, in a manner reminiscent of the strategy first envisioned by Sokolov 41 years ago.⁶ Europium or lutetium trications form nine-coordinate trimeric circular helicates with 2,6-amidopyridine ligands in which the substitution pattern of pendent naphthalene groups and interligand aromatic stacking interactions position alkene end groups that can subsequently be joined to form the knotted architecture. The resulting 81-atom-loop trefoil knot is formed in 58% yield together with 17% of the topologically trivial unknot macrocycle isomer. The products are easily separated from each other as a result of the enhanced stability of the trefoil-knot-lanthanide complex.

The use of lanthanide ions as templates expands the chemical toolbox available for the synthesis of molecular knots. The well-expressed chiral environments of knotted ligands may offer an intriguing means of influencing the photophysical properties of encapsulated lanthanide ions.³¹

■ ASSOCIATED CONTENT

■ Supporting Information

Synthetic procedures, X-ray, NMR, and MS characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

david.leigh@manchester.ac.uk

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Engineering and Physical Sciences Research Council (EPSRC) for funding and the EPSRC National Mass Spectrometry Service Centre (Swansea, U.K.) for high-resolution mass spectrometry.

■ REFERENCES

- (1) For reviews on molecular knots see: (a) Dietrich-Buchecker, C.; Colasson, B. X.; Sauvage, J.-P. *Top. Curr. Chem.* **2005**, *249*, 261–283. (b) Lukin, O.; Vögtle, F. *Angew. Chem., Int. Ed.* **2005**, *44*, 1456–1477. (c) Fenlon, E. E. *Eur. J. Org. Chem.* **2008**, S023–S035. (d) Forgan, R. S.; Sauvage, J.-P.; Stoddart, J. F. *Chem. Rev.* **2011**, *111*, 5434–5464. (e) Beves, J. E.; Blight, B. A.; Campbell, C. J.; Leigh, D. A.; McBurney, R. T. *Angew. Chem., Int. Ed.* **2011**, *50*, 9260–9327. (f) Amabilino, D. B.; Sauvage, J.-P. *Top. Curr. Chem.* **2012**, *323*, 107–126. (g) Ayme, J.-F.; Beves, J. E.; Campbell, C. J.; Leigh, D. A. *Chem. Soc. Rev.* **2013**, *42*, 1700–1712.

- (2) (a) Depew, R. E.; Liu, L. F.; Wang, J. C. *Fed. Proc.* **1976**, *35*, 1493–1493. (b) Liu, L. F.; Liu, C. C.; Alberts, B. M. *Cell* **1980**, *19*, 697–707. (c) Krasnow, M. A.; Cozzarelli, N. R. *Cell* **1983**, *32*, 1313–1324.
- (3) (a) Nureki, O.; Shirouzu, M.; Hashimoto, K.; Ishitani, R.; Terada, T.; Tamakoshi, M.; Oshima, T.; Chijimatsu, M.; Takio, K.; Vassilyev, D. G.; Shibata, T.; Inoue, Y.; Kuramitsu, S.; Yokoyama, S. *Acta Crystallogr., Sect. D: Biol. Crystallogr.* **2002**, *58*, 1129–1137. (b) Taylor, W. R. *Nature* **2000**, *406*, 916–919. (c) Wagner, J. R.; Brunzelle, J. S.; Forest, K. T.; Vierstra, R. D. *Nature* **2005**, *438*, 325–331. (d) Taylor, W. R.; Lin, K. *Nature* **2003**, *421*, 25. (e) Taylor, W. R. *Comput. Biol. Chem.* **2007**, *31*, 151–162.
- (4) (a) Saitta, A. M.; Soper, P. D.; Wasserman, E.; Klein, M. L. *Nature* **1999**, *399*, 46–48. (b) Schappacher, M.; Deffieux, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 5930–5933. (c) Sayre, T. C.; Lee, T. M.; King, N. P.; Yeates, T. O. *Protein Eng. Des. Sel.* **2011**, *24*, 627–630.
- (5) (a) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Angew. Chem., Int. Ed.* **1989**, *28*, 189–192. (b) Dietrich-Buchecker, C. O.; Guilhem, J.; Pascard, C.; Sauvage, J.-P. *Angew. Chem., Int. Ed.* **1990**, *29*, 1154–1156.
- (6) Sokolov, V. I. *Russ. Chem. Rev.* **1973**, *42*, 452–463.
- (7) (a) Adams, C. C. *The Knot Book: An Elementary Introduction to the Mathematical Theory of Knots*; American Mathematical Society: Providence, RI, 2004. (b) Menasco, W. W.; Thistlethwaite, M. B., Eds. *Handbook of Knot Theory*; Elsevier: Amsterdam, The Netherlands, 2005; Vol. 44.
- (8) (a) Durola, F.; Russo, L.; Sauvage, J.-P.; Rissanen, K.; Wenger, O. S. *Chem.—Eur. J.* **2007**, *13*, 8749–8753. (b) Constable, E. C.; Housecroft, C. E.; Neuburger, M.; Rösel, P. J.; Schaffner, S.; Zampese, J. A. *Chem.—Eur. J.* **2009**, *15*, 11746–11757.
- (9) (a) Adams, H.; Ashworth, E.; Breault, G. A.; Guo, J.; Hunter, C. A.; Mayers, P. C. *Nature* **2001**, *411*, 763. (b) Guo, J.; Mayers, P. C.; Breault, G. A.; Hunter, C. A. *Nat. Chem.* **2010**, *2*, 218–222. (c) Fenlon, E. E. *Nat. Chem.* **2010**, *2*, 156–157.
- (10) (a) Woods, C. R.; Benaglia, M.; Toyota, S.; Hardcastle, K.; Siegel, J. S. *Angew. Chem., Int. Ed.* **2001**, *40*, 749–751. (b) Arias, K. I.; Zysman-Colman, E.; Loren, J. C.; Linden, A.; Siegel, J. S. *Chem. Commun.* **2011**, *47*, 9588–9590.
- (11) Molecular trefoil knots have been synthesized through other design strategies: (a) Mueller, J. E.; Du, S. M.; Seeman, N. C. *J. Am. Chem. Soc.* **1991**, *113*, 6306–6308. (b) Du, S. M.; Seeman, N. C. *J. Am. Chem. Soc.* **1992**, *114*, 9652–9655. (c) Du, S. M.; Seeman, N. C. *Biopolymers* **1994**, *34*, 31–37. (d) Ashton, P. R.; Matthews, O. A.; Menzer, S.; Raymo, F. M.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Liebigs Ann.* **1997**, 2485–2494. (e) Rapenne, G.; Dietrich-Buchecker, C.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1999**, *121*, 994–1001. (f) Barran, P. E.; Cole, H. L.; Goldup, S. M.; Leigh, D. A.; McGonigal, P. R.; Symes, M. D.; Wu, J. Y.; Zengerle, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 12280–12284. Or discovered as unexpected reaction products: (g) Safarowsky, O.; Nieger, M.; Fröhlich, R.; Vögtle, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 1616–1618. (h) Feigl, M.; Ladberg, R.; Engels, S.; Herbst-Irmer, R.; Fröhlich, R. *Angew. Chem., Int. Ed.* **2006**, *45*, 5698–5702. (i) Brüggemann, J.; Bitter, S.; Müller, S.; Müller, W. M.; Müller, U.; Maier, N. M.; Lindner, W.; Vögtle, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 254–259. (j) Ponnuswamy, N.; Cougnon, F. B. L.; Clough, J. M.; Pantoş, D. G.; Sanders, J. K. M. *Science* **2012**, *338*, 783–785. (k) Prakasam, T.; Lusi, M.; Elhabiri, M.; Platas-Iglesias, C.; Olsen, J.-C.; Asfari, Z.; Cianfèrari-Sanglier, S.; Debaene, F.; Charbonnière, L. J.; Trabolsi, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 9956–9960. (l) Ponnuswamy, N.; Cougnon, F. B. L.; Pantoş, D. G.; Sanders, J. K. M. *J. Am. Chem. Soc.* **2014**, *136*, 8243–8251. For other molecular knots and knot-like structures, see: (m) Fenlon, E. E.; Ito, B. R. *Eur. J. Org. Chem.* **2008**, 3065–3068. (n) Bourlier, J.; Jouaiti, A.; Kyritsakas-Gruber, N.; Allouche, L.; Planeix, J.-M.; Hosseini, M. W. *Chem. Commun.* **2008**, 6191–6193. (o) Ayme, J.-F.; Beves, J. E.; Leigh, D. A.; McBurney, R. T.; Rissanen, K.; Schultz, D. *Nat. Chem.* **2012**, *4*, 15–20. (p) Ayme, J.-F.; Beves, J. E.; Leigh, D. A.; McBurney, R. T.; Rissanen, K.; Schultz, D. *J. Am. Chem. Soc.* **2012**, *134*, 9488–9497. (q) Engelhard, D. M.; Freye, S.; Grohe, K.; John, M.; Clever, G. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 4747–4750. (r) Ayme, J.-F.; Beves, J. E.; Campbell, C. J.; Leigh, D. A. *Angew. Chem., Int. Ed.* **2014**, *53*, 7823–7827.
- (12) Bünzli, J.-C. G.; Piguet, C. *Chem. Soc. Rev.* **2005**, *34*, 1048–1077.
- (13) Binnemans, K. *Chem. Rev.* **2009**, *109*, 4283–4374.
- (14) (a) Werner, E. J.; Datta, A.; Jocher, C. J.; Raymond, K. N. *Angew. Chem., Int. Ed.* **2008**, *47*, 8568–8580. (b) Merbach, A. E.; Tóth, E. *The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging*; Wiley: Chichester, U.K., 2001.
- (15) Le Borgne, T.; Bénech, J. M.; Floquet, S.; Bernardinelli, G.; Aliprandini, C.; Bettens, P.; Piguet, C. *Dalton Trans.* **2003**, 3856–3868.
- (16) (a) Piguet, C.; Bünzli, J.-C. G.; Bernardinelli, G.; Hopfgartner, G.; Williams, A. F. *J. Am. Chem. Soc.* **1993**, *115*, 8197–8206. (b) Bünzli, J.-C. G.; Piguet, C. *Chem. Rev.* **2002**, *102*, 1897–1928.
- (17) Leonard, J. P.; Jensen, P.; McCabe, T.; O'Brien, J. E.; Peacock, R. D.; Kruger, P. E.; Gunnlaugsson, T. *J. Am. Chem. Soc.* **2007**, *129*, 10986–10987.
- (18) (a) El Aroussi, B.; Zebret, S.; Besnard, C.; Perrotet, P.; Hamacek, J. J. *J. Am. Chem. Soc.* **2011**, *133*, 10764–10767. (b) Hamacek, J.; Bernardinelli, G.; Filinchuk, Y. *Eur. J. Inorg. Chem.* **2008**, 3419–3422.
- (19) (a) Stomeo, F.; Lincheneau, C.; Leonard, J. P.; O'Brien, J. E.; Peacock, R. D.; McCoy, C. P.; Gunnlaugsson, T. *J. Am. Chem. Soc.* **2009**, *131*, 9636–9637. (b) Lincheneau, C.; Destribats, C.; Barry, D. E.; Kitchen, J. A.; Peacock, R. D.; Gunnlaugsson, T. *Dalton Trans.* **2011**, *40*, 12056–12059.
- (20) Lincheneau, C.; Jean-Denis, B.; Gunnlaugsson, T. *Chem. Commun.* **2014**, *50*, 2857–2860.
- (21) For rotaxanes assembled using lanthanide coordination, see: (a) Zapata, F.; Blackburn, O. A.; Langton, M. J.; Faulkner, S.; Beer, P. D. *Chem. Commun.* **2013**, *49*, 8157–8159. (b) Langton, M. J.; Blackburn, O. A.; Lang, T.; Faulkner, S.; Beer, P. D. *Angew. Chem., Int. Ed.* **2014**, DOI: 10.1002/anie.201405131.
- (22) The formation of catenanes through intraligand macrocyclizations can be ruled out by employing insufficiently long ligands.
- (23) (a) Hua, K. T.; Xu, J.; Quiroz, E. E.; Lopez, S.; Ingram, A. J.; Anne Johnson, V.; Tisch, A. R.; de Bettencourt-Dias, A.; Straus, D. A.; Muller, G. *Inorg. Chem.* **2012**, *51*, 647–660. (b) Bonsall, S. D.; Houcheime, M.; Straus, D. A.; Muller, G. *Chem. Commun.* **2007**, 3676–3678.
- (24) Kotova, O.; Kitchen, J. A.; Lincheneau, C.; Peacock, R. D.; Gunnlaugsson, T. *Chem.—Eur. J.* **2013**, *19*, 16181–16186.
- (25) For other examples of europium pyridine-2,6-dicarboxamide complexes, see (a) Tanase, S.; Gallego, P. M.; de Gelder, R.; Tian, F. W. *Inorg. Chim. Acta* **2007**, *360*, 102–108. (b) Renaud, F.; Piguet, C.; Bernardinelli, G.; Bünzli, J.-C. G.; Hopfgartner, G. *Chem.—Eur. J.* **1997**, *3*, 1646–1659. (c) Le Borgne, T.; Bénech, J.-M.; Floquet, S.; Bernardinelli, G.; Aliprandini, C.; Bettens, P.; Piguet, C. *Dalton Trans.* **2003**, 3856–3868.
- (26) Bradberry, S. J.; Savyasachi, A. J.; Martinez-Calvo, M.; Gunnlaugsson, T. *Coord. Chem. Rev.* **2014**, 273–274, 226–241.
- (27) Clark, P. G.; Guidry, E. N.; Chan, W. Y.; Steinmetz, W. E.; Grubbs, R. H. *J. Am. Chem. Soc.* **2010**, *132*, 3405–3412.
- (28) Similar temperature-dependent behavior is not observed for the ^1H NMR spectrum of unknot macrocycle 3.
- (29) Batsanova, L. R. *Russ. Chem. Rev.* **1971**, *40*, 465–484.
- (30) The metal-free trefoil knot 2 can be isolated by precipitation with D_2O (see Supporting Information).
- (31) While this manuscript was undergoing revision, we obtained a preliminary X-ray crystal of a derivative of $[\text{Eu}2][\text{CF}_3\text{SO}_3]_3$. The structure shows the connectivity and crossings of the trefoil knot and a similar arrangement of the ligands to that shown in Figure 3a,b (see Supporting Information).