Stereoselective Synthesis of Molecular Square and Granny Knots

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S1. ABBREVIATIONS

Abbreviations: ADMP 2-Azido-1,3-dimethylimidazolinium hexafluorophosphate; DBU 1,8-Diazabicyclo[5.4.0]undec-7-ene; DCM dichloromethane; DMF *N*,*N*-dimethylformamide; DMSO dimethylsulfoxide; DOSY Diffusion-Ordered Spectroscopy; MeCN acetonitrile; RT room temperature; TBS *tert*-butyldimethylsilyl; TBTA Tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine; THF tetrahydrofuran; TLC thin layer chromatography.

S2. General Experimental

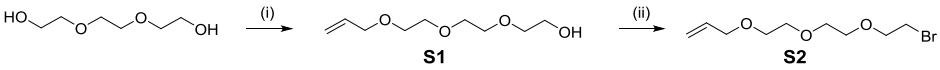
Unless stated otherwise, reagents were obtained from commercial sources and used without purification. Reactions were carried out in anhydrous solvents and under an N_2 atmosphere. Anhydrous solvents were obtained by passing the solvent through an activated alumina column on a Phoenix SDS (solvent drying system; JC Meyer Solvent Systems, CA, USA). Compounds **S1**[1], **S2**[2], **S3**[3] and **S4**-**S7**[4] were synthesized as previously described. ^{1}H NMR spectra were recorded on a Bruker Avance III instrument with an Oxford AS600 magnet equipped with a cryoprobe [5mm CPDCH ^{13}C-^{1}H/D] (600 MHz). Chemical shifts are reported in parts per million (ppm) from high to low frequency using the residual solvent peak as the internal reference ($CDCl_3$ = 7.26 ppm, CD_3OD = 3.31 ppm, $(CD_3)_2SO$ = 2.50 ppm and CD_3CN = 1.94 ppm). All ^{1}H resonances are reported to the nearest 0.01 ppm. The multiplicity of ^{1}H signals are indicated as: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; br = broad; app = apparent; or combinations of thereof. Coupling constants (*J*) are quoted in Hz and reported to the nearest 0.1 Hz. Where appropriate, averages of the signals from peaks displaying multiplicity were used to calculate the value of the coupling constant. ^{13}C NMR spectra were recorded on the same spectrometer with the central resonance of the solvent peak as the internal reference (CD_3CN = 118.26 ppm, $CDCl_3$ = 77.16 ppm, CD_3OD = 49.00 ppm and $(CD_3)_2SO$ = 39.52 ppm). All ^{13}C resonances are reported to the nearest 0.01 ppm. DEPT, COSY, HSQC and HMBC experiments were used to aid structural determination and spectral assignment. Fully characterized compounds were chromatographically homogeneous. Structural assignment of **L3**•$[Lu]_2$ and **1**•$[Lu]_2$ were done by direct comparison with **L1**•[Lu] and **L2**•[Lu]. DOSY experiments were carried out on the same spectrometer. DOSY measurements were performed using the standard Bruker pulse program dstebpgp3s. Smoothed square gradients were used with a total duration of 1.6 ms. The gradient recovery delay was 200 μs, and diffusion time Δ = 10 ms was used for the experiments. Ten gradient increments were acquired, ranging from 5.9–53.2 G•cm^{-1} in equal steps of gradient squared.

Flash column chromatography was carried out using Silica 60 Å (particle size 40–63 μm, Sigma Aldrich, UK) as the stationary phase. Size exclusion chromatography was carried out using Sephadex LH-20 support beads as the stationary phase. TLC was performed on precoated silica gel plates (0.25 mm thick, 60 F_{254}, Merck, Germany) and visualized using both short and long wave ultraviolet light in combination with standard laboratory stains (basic potassium permanganate, acidic ammonium molybdate and ninhydrin). Low resolution ESI mass spectrometry was performed with a Thermo Scientific LCQ Fleet Ion

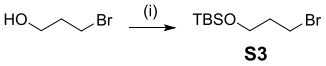
Trap Mass Spectrometer or an Agilent Technologies 1200 LC system with either an Agilent 6130 single quadrupole MS detector or an Advion Expression LCMS single quadrupole MS detector. CD and UV/Vis spectroscopy was measured on a Applied Photophysics Ltd Chirascan CD Spectrometer. High-resolution mass spectrometry (HR-MS) and MALDI-TOF (matrix assisted laser desorption/ionization time-of-flight) was carried out by staff at the Mass Spectrometry Service, School of Chemistry, The University of Manchester.

S3. REACTIONS SCHEMES

3.1. Synthesis of linkers

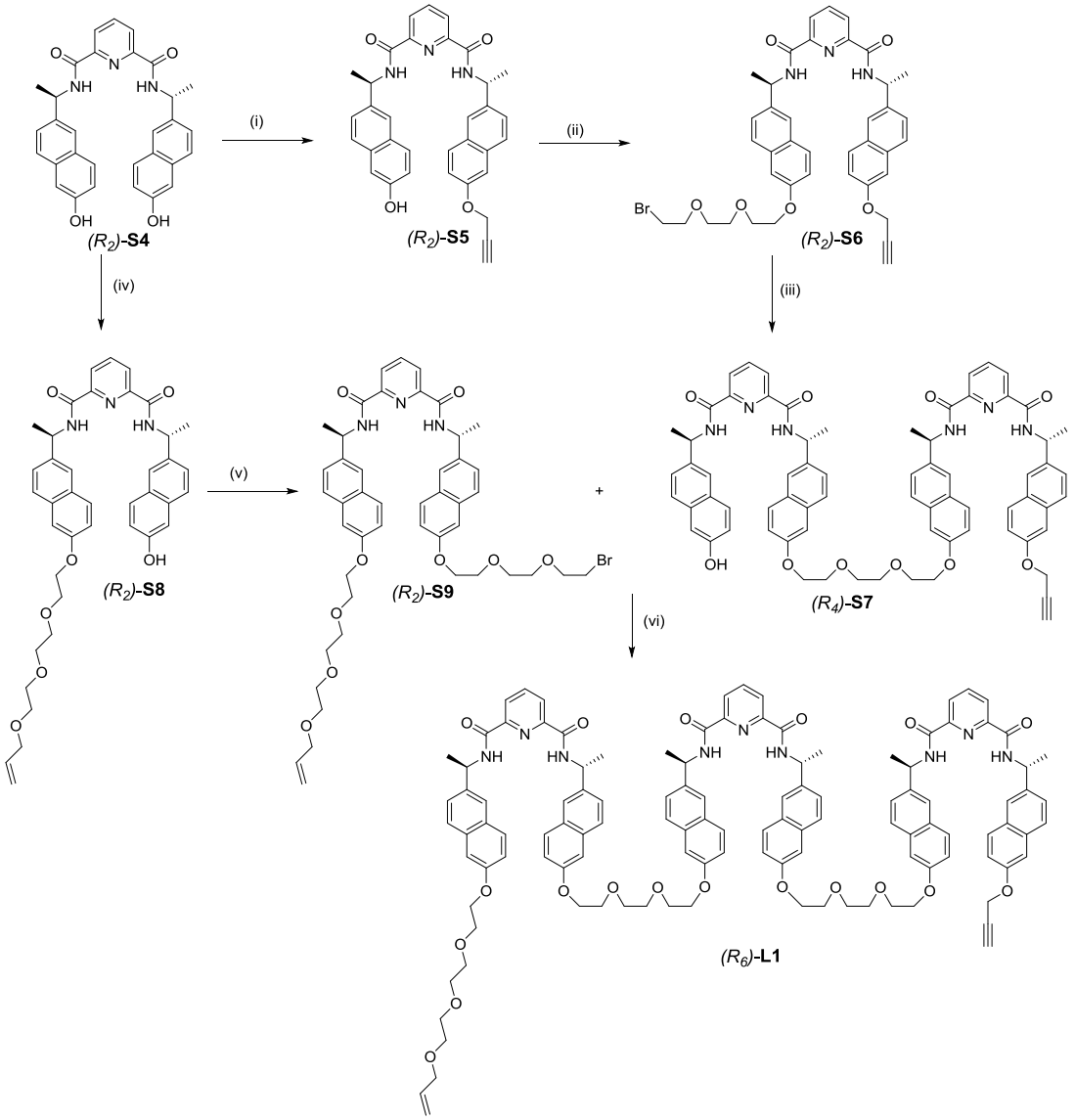


Scheme S1. Synthesis of linker **S2**. Reagents and conditions: (i) allyl bromide, NaOH, H_2O, 100 °C, 20 min, 56 %. (ii) CBr_4, PPh_3, CH_2Cl_2, RT, 2 h, 80 %.



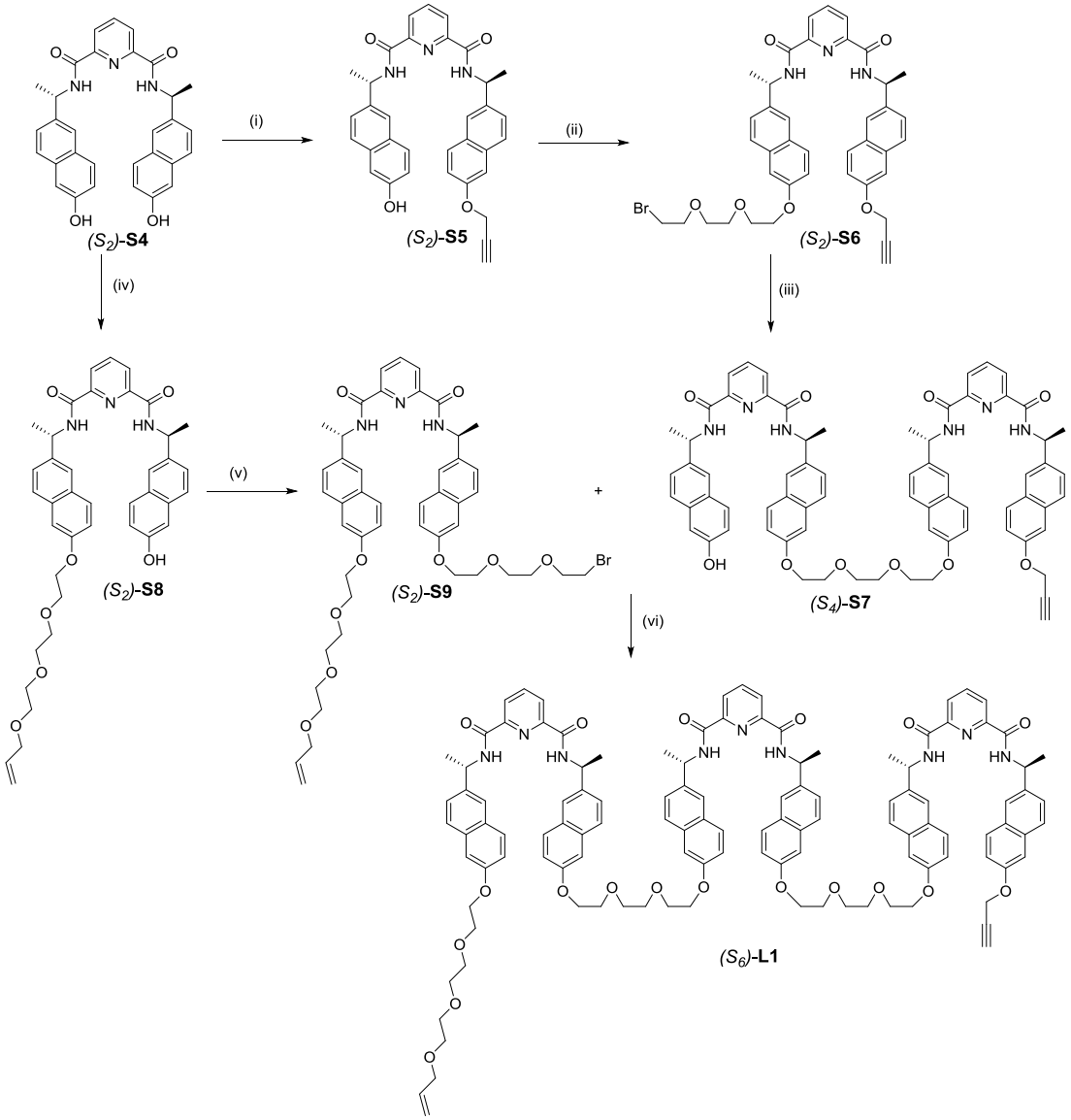
Scheme S2. Synthesis of linker **S3**. Reagents and conditions: (i) *tert*-butyl dimethylsilyl chloride, imidazole, CH_2Cl_2, RT, 3 h, 79 %

3.2 Synthesis of (R_6)-L1



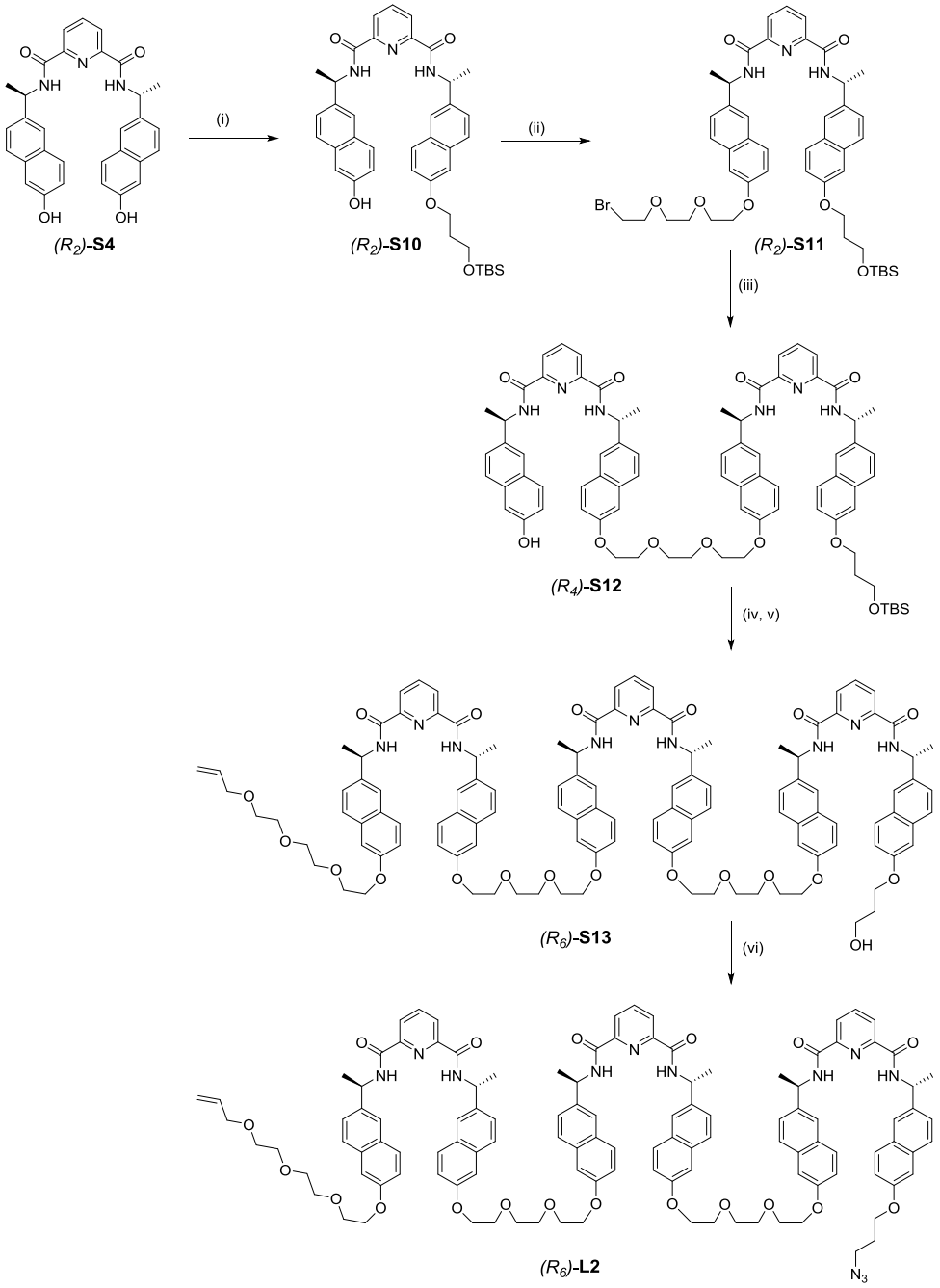
Scheme S3. Synthesis of (R_6)-**L1**. Reagents and conditions: (i) propargyl bromide, K_2CO_3, DMF, 80 °C, 2 h, 41 %. (ii) 1,2-bis(2-bromoethoxy)ethane, K_2CO_3, DMF, 80 °C, 1 h, 80 %. (iii) (R_2)-**S4**, K_2CO_3, DMF, 80 °C, 16 h, 32 %. (iv) **S2**, K_2CO_3, DMF, 80 °C, 16 h, 35 %. v) 1,2-bis(2-bromoethoxy)ethane, K_2CO_3, DMF, 80 °C, 2 h, 53 %. (vi) K_2CO_3, DMF, 80 °C, 16 h, 88 %.

3.3 Synthesis of (S_6)-L1



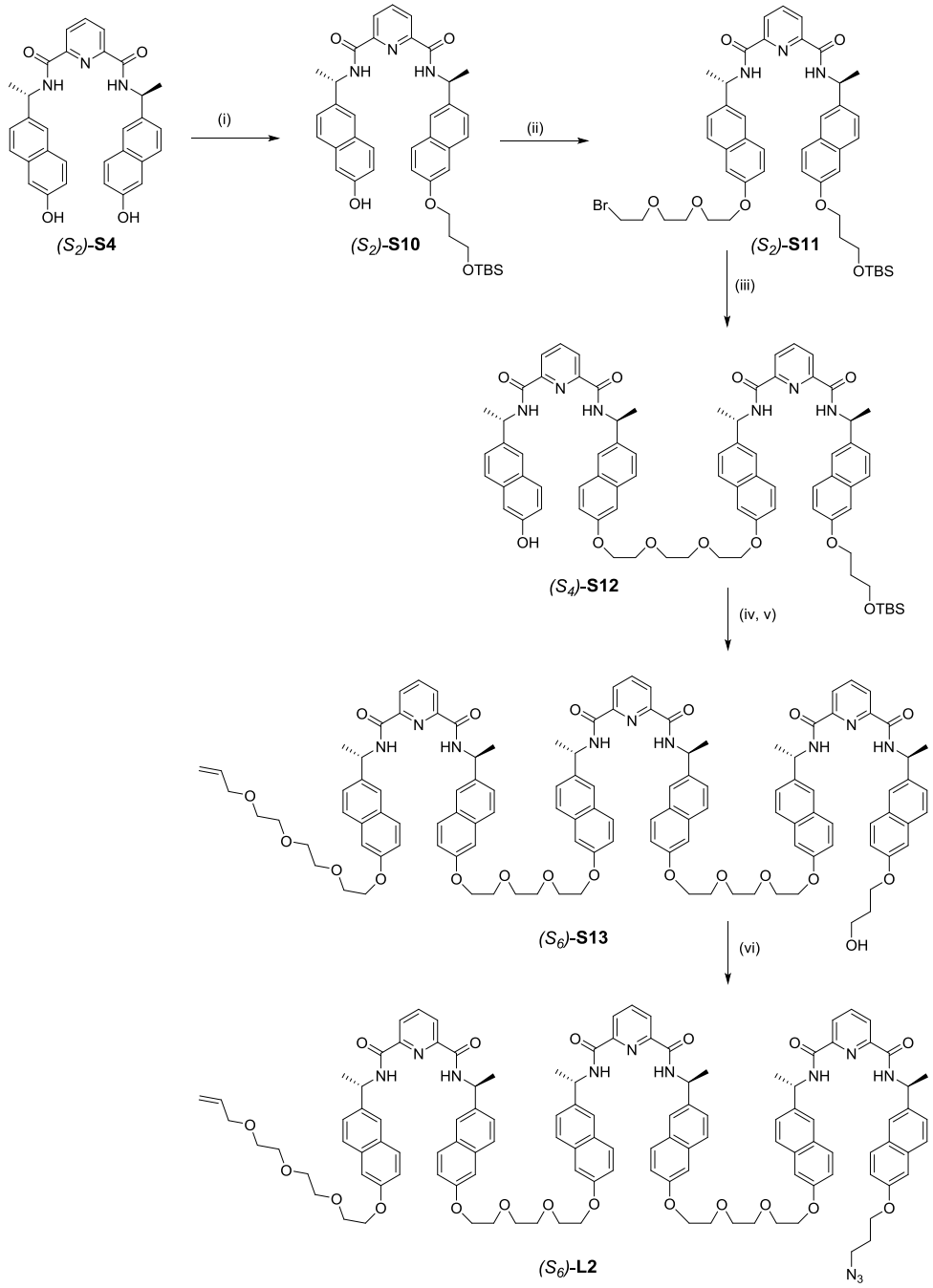
Scheme S4. Synthesis of (S_6)-**L1**. Reagents and conditions: (i) propargyl bromide, K_2CO_3, DMF, 80 °C, 2 h, 38 %. (ii) 1,2-bis(2-bromoethoxy)ethane, K_2CO_3, DMF, 80 °C, 2 h, 70 %. (iii) (S_2)-**S4**, K_2CO_3, DMF, 80 °C, 16 h, 33 %. (iv) **S2**, K_2CO_3, DMF, 80 °C, 16 h, 27 %. v) 1,2-bis(2-bromoethoxy)ethane, K_2CO_3, DMF, 80 °C, 3 h, 59 %. (vi) K_2CO_3, DMF, 80 °C, 16 h, 94 %.

3.4 Synthesis of (R_6)-L2



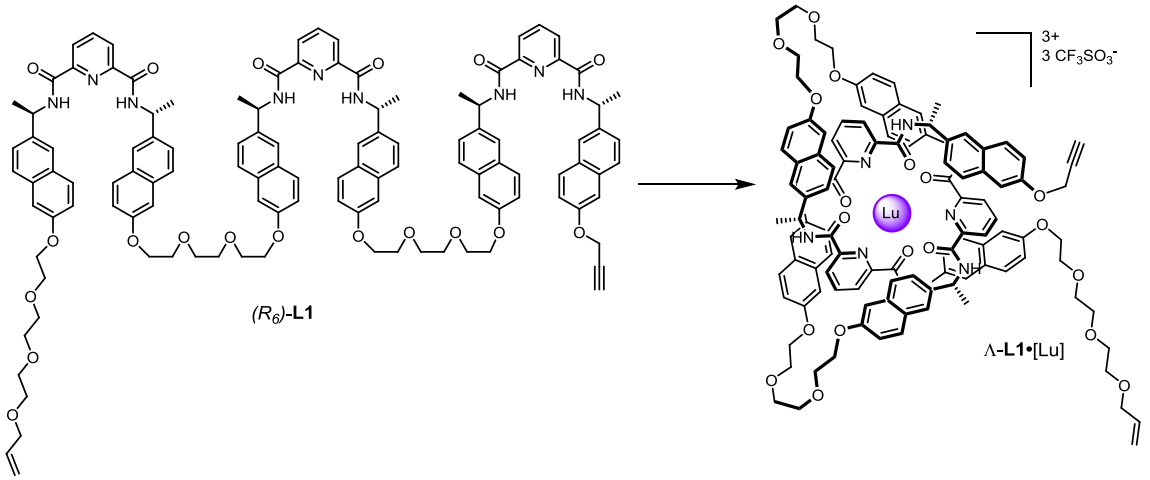
Scheme S5. Synthesis of (R_6)-**L2**. Reagents and conditions: (i) **S3**, K_2CO_3, DMF, 80 °C, 14 h, 33 %. (ii) 1,2-bis(2-bromoethoxy)ethane, K_2CO_3, DMF, 80 °C, 18 h, 66 %. (iii) (R_2)-**S4**, K_2CO_3, DMF, 80 °C, 17 h, 28 %. (iv) (R_2)-**S9**, K_2CO_3, DMF, 80 °C, 15 h. v) Tetrabutylammonium fluoride, THF, 0 °C to RT, 22 h, 42 % over two steps. (vi) ADMP, DBU, THF, 0 °C to RT, 24 h, 82 %.

3.5 Synthesis of (S_6)-L2

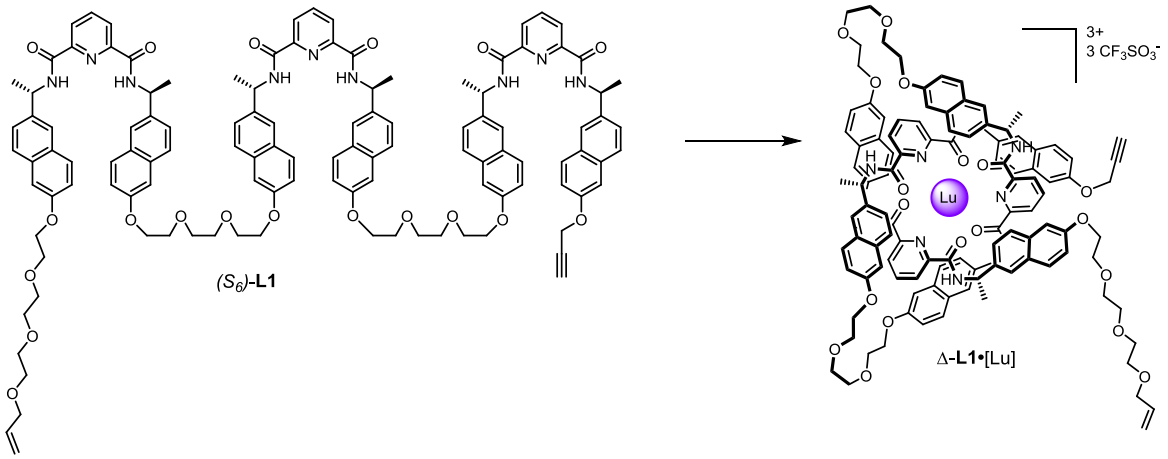


Scheme S6. Synthesis of (S_6)-**L2**. Reagents and conditions: (i) **S3**, K_2CO_3, DMF, 80 °C, 16 h, 40 %. (ii) 1,2-bis(2-bromoethoxy)ethane, K_2CO_3, DMF, RT, 16 h, 65 %. (iii) (S_2)-**S4**, K_2CO_3, DMF, 80 °C, 16 h, 37 %. (iv) (S_2)-**S9**, K_2CO_3, DMF, 80 °C, 16 h. v) Tetrabutylammonium fluoride, THF, 0 °C to RT, 4 h, 68 % over two steps. (vi) ADMP, DBU, THF, 0 °C to RT, 24 h, 88 %.

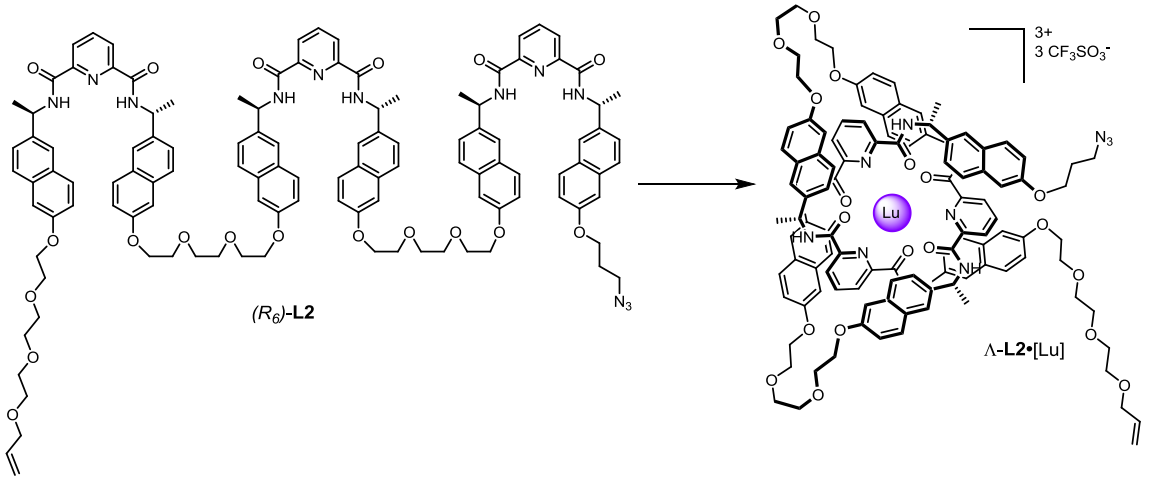
3.6 Synthesis of overhand knots



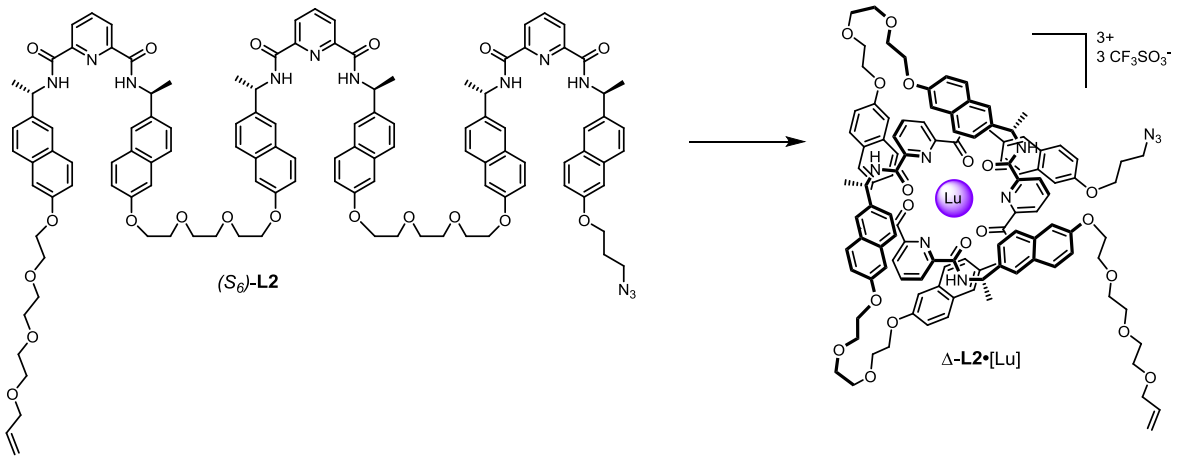
Scheme S7. Synthesis of Λ-**L1**•[Lu]. Reagents and conditions: $Lu(SO_3CF_3)_3$, MeCN, 80 °C, 16 h, 81 %.



Scheme S8. Synthesis of Δ-**L1**•[Lu]. Reagents and conditions: $Lu(SO_3CF_3)_3$, MeCN, 80 °C, 16 h, 82 %.

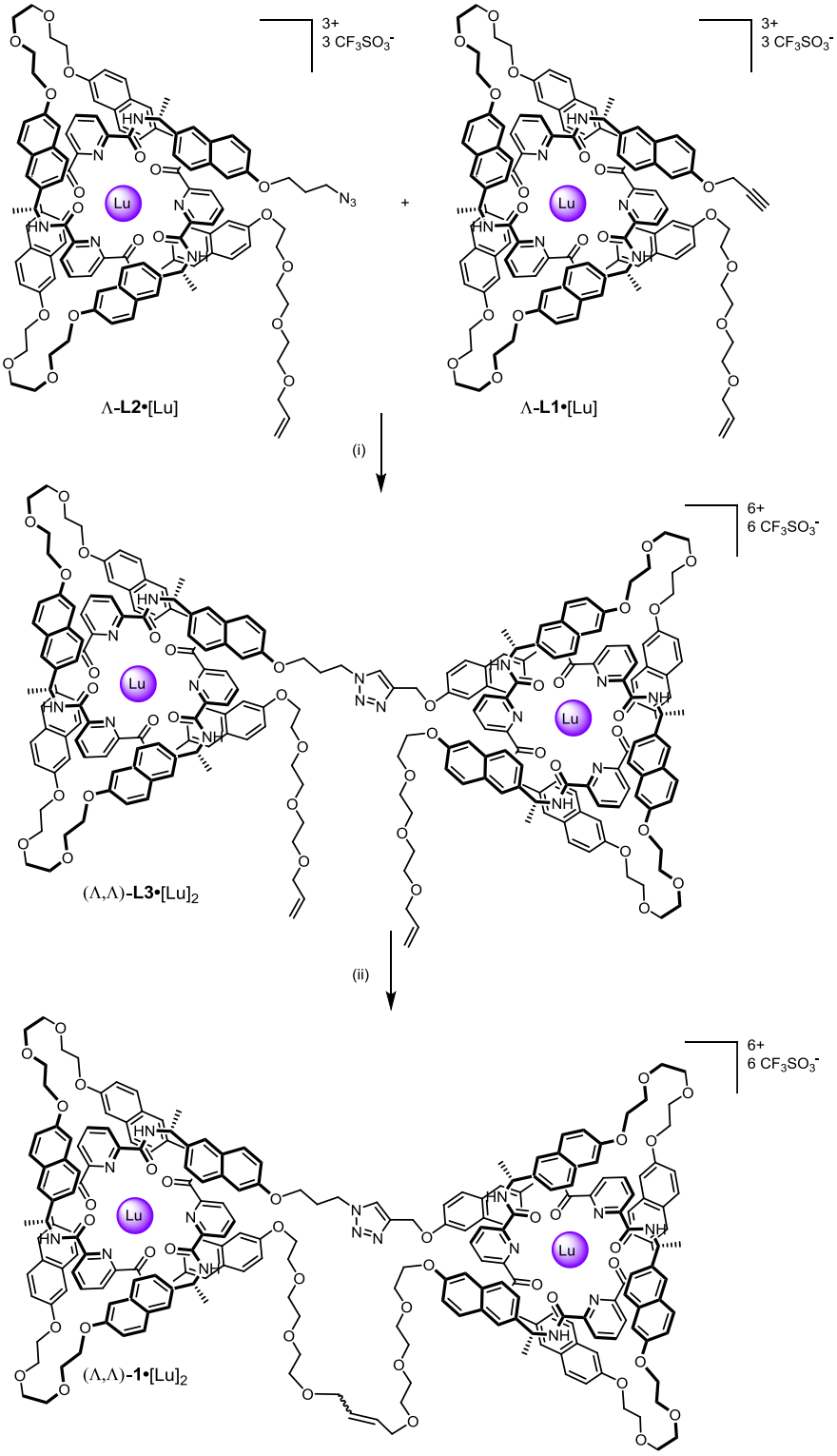


Scheme S9. Synthesis of Λ-**L2**•[Lu]. Reagents and conditions: $Lu(SO_3CF_3)_3$, MeCN, 80 °C, 16 h, 85 %.

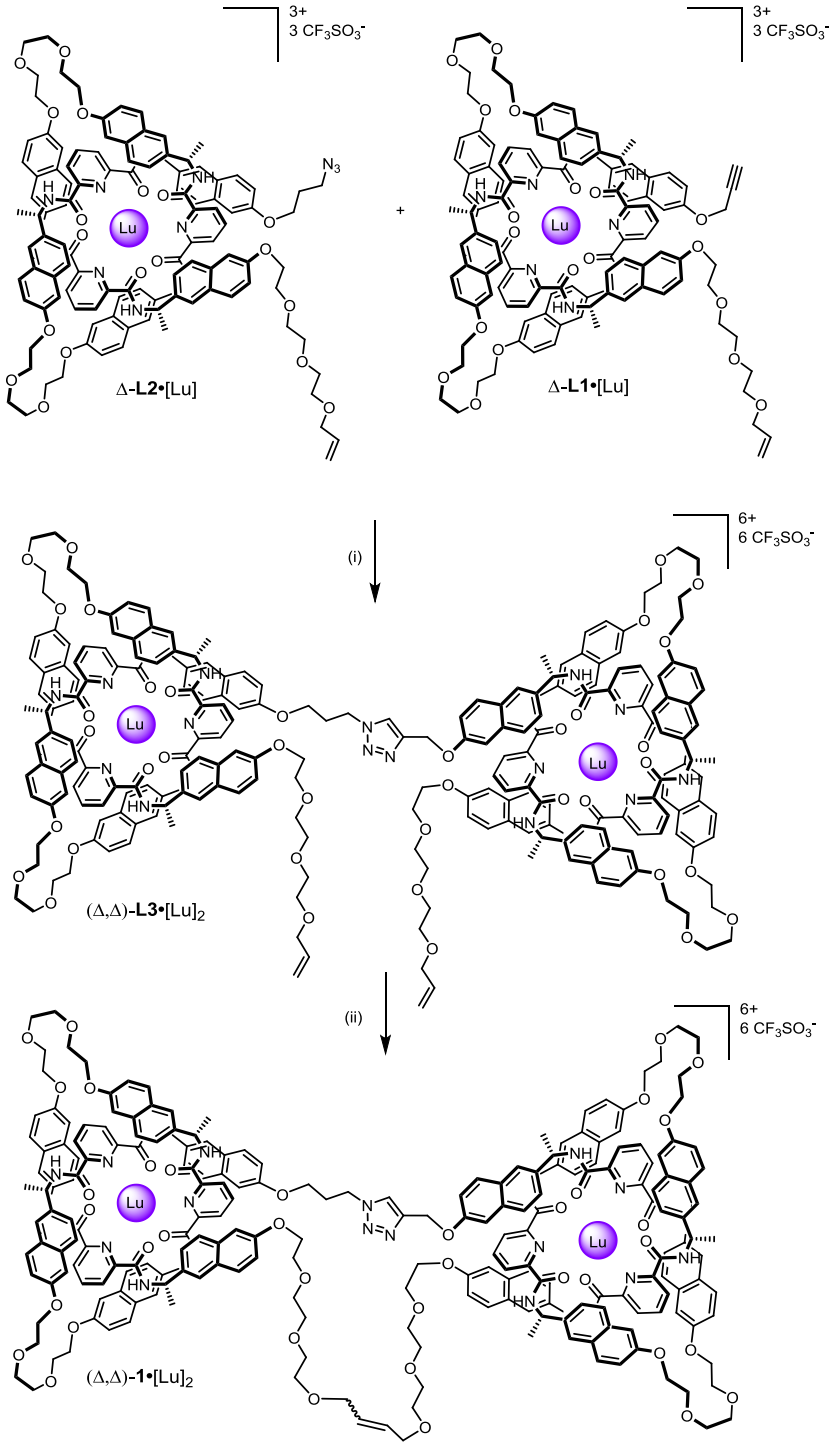


Scheme S10. Synthesis of Δ-**L2**•[Lu]. Reagents and conditions: $Lu(SO_3CF_3)_3$, MeCN, 80 °C, 16 h, 73 %.

3.7 Synthesis of granny knots

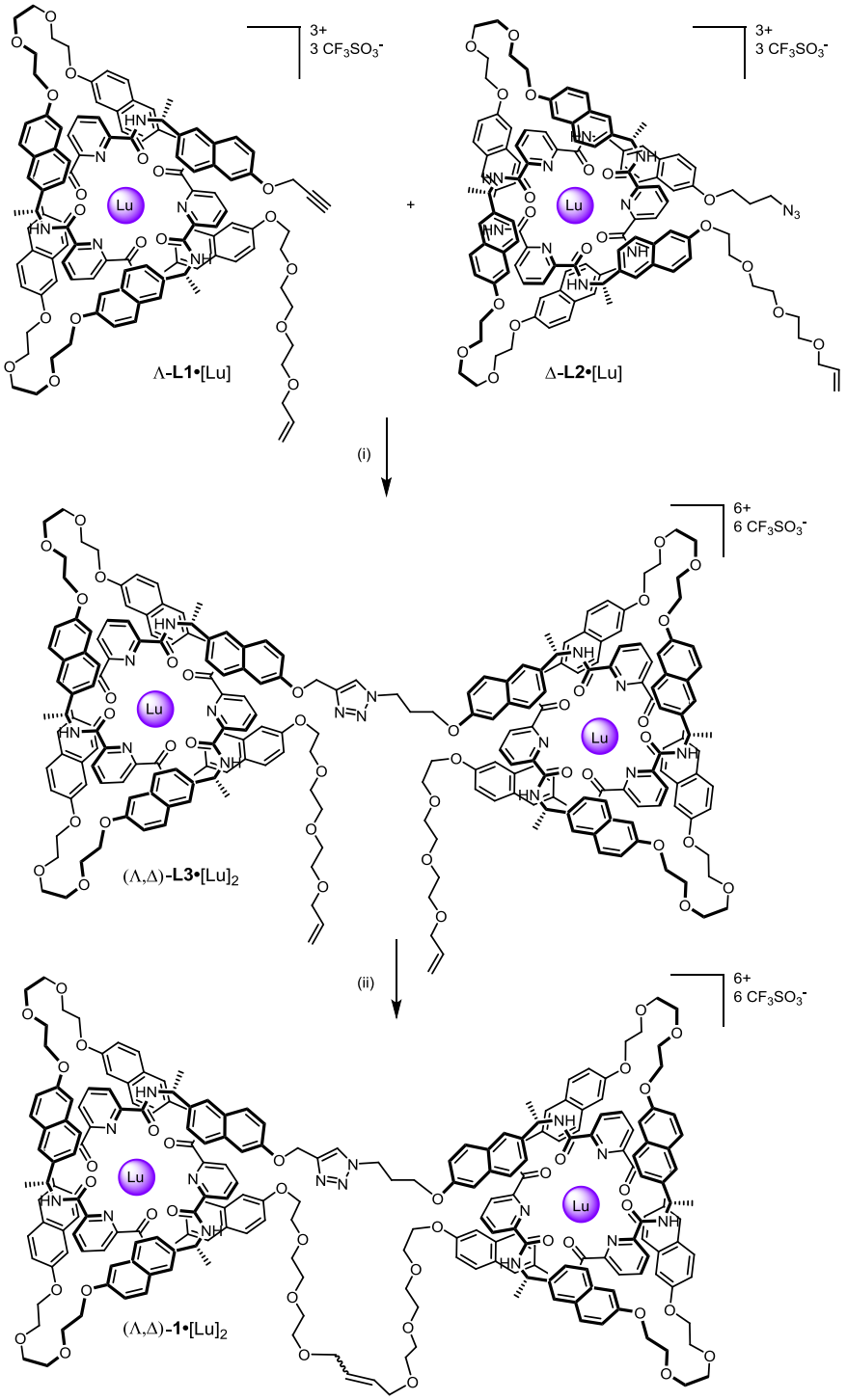


Scheme S11. Synthesis of (Λ,Λ)-**1**•$[Lu]_2$. Reagents and conditions: (i) $(MeCN)_4$•$Cu(CF_3SO_3)$, TentaGel TBTA, MeOH/MeCN (1:1), RT, 16 h, 79 %. (ii) Hoveyda-Grubbs 2nd Gen, CH_2Cl_2/$MeNO_2$ (1:1), 50 °C, 16 h, 33 %.



Scheme S12. Synthesis of (Δ,Δ)-**1**•$[Lu]_2$. Reagents and conditions: (i) $(MeCN)_4$•$Cu(CF_3SO_3)$, TentaGel TBTA, MeOH/MeCN (1:1), RT, 16 h, 52 %. (ii) Hoveyda-Grubbs 2nd Gen, CH_2Cl_2/$MeNO_2$ (1:1), 50 °C, 16 h, 31 %.

3.8 Synthesis of square knot

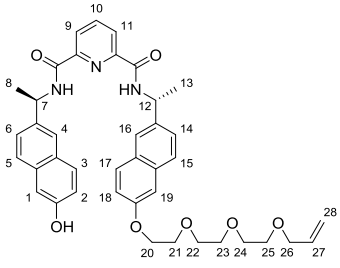


Scheme S13. Synthesis of (Λ,Δ)-**1**•$[Lu]_2$. Reagents and conditions: (i) $(MeCN)_4$•$Cu(CF_3SO_3)$, TentaGel TBTA, MeOH/MeCN (1:1), RT, 16 h, 70%. (ii) Hoveyda-Grubbs 2nd Gen, CH_2Cl_2/$MeNO_2$ (1:1), 50 °C, 16 h, 32 %.

S4. EXPERIMENTAL PROCEDURES

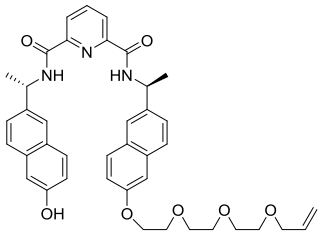
S4.1 Synthetic procedures and characterization details

(*R*$_2$)-S8



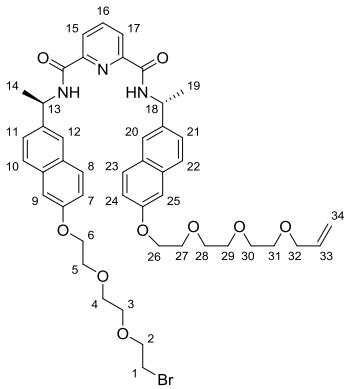
To a solution of (*R*$_2$)-**S4** (351 mg, 0.69 mmol) and potassium carbonate (95 mg, 0.69 mmol) in degassed DMF (65 mL) was added compound **S2** (163 mg, 0.69 mmol). The reaction was stirred for 16 hours at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. Further purification by flash column chromatography (DCM/MeOH 95:5) yielded (*R*$_2$)-**S8** (164 mg, 35 %) as a colorless solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 7.7, 4.6 Hz, 2H, $H_{9,11}$), 8.05 (t, *J* = 7.8 Hz, 1H, H_{10}), 7.78 (d, *J* = 7.4 Hz, 1H, *N-H*), 7.75 (d, *J* = 7.4 Hz, 1H, *N-H*), 7.65 (s, 1H, $H_{4/16}$), 7.62 (s, 1H, $H_{4/16}$), 7.56 (dd, *J* = 8.9, 4.7 Hz, 2H, $H_{3,17}$), 7.36–7.26 (m, 4H, $H_{5,6,14,15}$), 7.14–7.10 (m, 2H, $H_{2,18}$), 7.04 (d, *J* = 2.5 Hz, 1H, $H_{1/19}$), 7.01 (d, *J* = 2.5 Hz, 1H, $H_{1/19}$), 5.92–5.85 (m, 1H, H_{27}), 5.35–5.28 (m, 2H, $H_{7/12}$), 5.24 (dd, *J* = 10.4, 1.4 Hz, 1H, H_{28}), 5.14 (dd, *J* = 17.2, 1.7 Hz, 1H, H_{28}), 4.33–4.31 (m, 2H, H_{20}), 4.05–3.95 (m, 4H, $H_{21,26}$), 3.84 (t, *J* = 4.3 Hz, 2H, H_{22}), 3.77 (t, *J* = 2.5 Hz, 2H, H_{23}), 3.72–3.69 (m, 2H, H_{24}), 3.63–3.59 (m, 2H, H_{25}), 1.65 (d, *J* = 6.7 Hz, 6H, $H_{8,13}$); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.78, 162.76, 156.73, 154.64, 148.96, 148.95, 139.07, 137.33, 136.49, 134.40, 134.12, 133.79, 129.43, 129.30, 128.78, 128.23, 127.71, 127.14, 125.04, 124.96, 124.84, 124.66, 124.57, 124.41, 119.37, 118.80, 117.49, 109.34, 106.79, 72.26, 70.85, 70.60, 70.54, 69.70, 69.27, 67.09, 49.70, 49.55, 21.37, 21.35 ; **HRMS** (ESI$^+$): Calcd. for $C_{40}H_{43}O_7N_3K^+$: 716.2733, found 716.2703 $[M+K]^+$.

(*S*$_2$)-S8



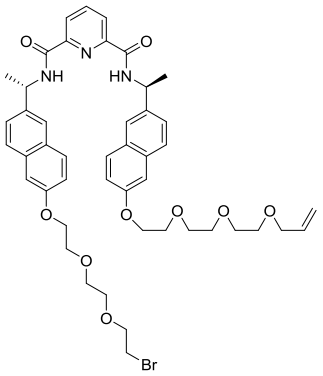
The compound was synthesized as described for (*R*$_2$)-**S8** but starting from (*S*$_2$)-**S4** (1.52 g, 3.0 mmol). Product (*S*$_2$)-**S8** was obtained as a colorless solid (542 mg, 27%). Analytical data was identical to its enantiomer.

(R_2)-S9



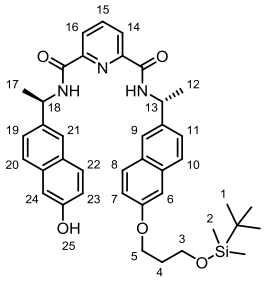
To a solution of (R_2)-**S8** (0.154 g, 0.23 mmol) and potassium carbonate (0.156 g, 1.15 mmol) in degassed DMF (10 mL) was added 1,2-bis(2-bromoethoxy)ethane (0.11 mL, 0.69 mmol). The reaction was stirred for 2 hours at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. Further purification by flash column chromatography (CH_2Cl_2/MeOH 98:2) gave (R_2)-**S9** (146 mg, 73 %) as a colorless solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.8 Hz, 2H, $H_{15,17}$), 8.02 (t, *J* = 7.8 Hz, 1H, H_{16}), 7.89 (d, *J* = 8.1 Hz, 2H, *N-H*), 7.72 (d, *J* = 1.9 Hz, 2H, $H_{12,20}$), 7.68–7.63 (m, 4H, $H_{8,10,22,23}$), 7.43 (dt, *J* = 8.5, 2.0 Hz, 2H, $H_{11,21}$), 7.19 (dt, *J* = 8.9, 2.3 Hz, 2H, $H_{7,24}$), 7.11 (app t, *J* = 3.1 Hz, 2H, $H_{9,25}$), 5.94–5.87 (m, 1H, H_{33}), 5.43 (quintet, *J* = 7.0 Hz, 2H, $H_{13,18}$), 5.26 (dq, *J* = 17.2, 1.7 Hz, 1H, H_{34}), 5.17 (dq, *J* = 10.4, 1.4 Hz, 1H, H_{34}), 4.26 (app q, *J* = 5.2 Hz, 4H, $H_{6,26}$), 4.01 (dt, *J* = 5.7, 1.4 Hz, 2H, H_{32}), 3.98–3.89 (m, 4H, $H_{5,27}$), 3.82 (t, *J* = 6.3 Hz, 2H, H_2), 3.77 (dd, *J* = 5.8, 3.5 Hz, 4H, $H_{4,28}$), 3.73 – 3.66 (m, 6H, $H_{29,30,31}$), 3.60 (d, *J* = 5.8 Hz, 2H, H_3), 3.47 (t, *J* = 6.3 Hz, 2H, H_1), 1.65 (d, *J* = 6.9 Hz, 6H, $H_{14,19}$). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.89, 157.34, 157.31, 149.11, 139.40, 138.24, 138.21, 135.06, 134.20, 129.69, 129.66, 129.17, 129.16, 127.88, 125.50, 125.25, 125.23, 124.90, 124.89, 119.91, 119.88, 117.49, 106.92, 106.89, 72.58, 71.59, 71.22, 71.21, 71.04, 71.03, 70.94, 70.16, 70.06, 69.75, 67.80, 49.35, 30.69, 21.95. Several carbon signals not determined due to overlapping peaks. **HRMS** (ESI^+): Calcd. for $C_{46}H_{54}N_3O_9BrK^+$: 910.2675, found 910.2640 $[M+K]^+$.

(S_2)-S9



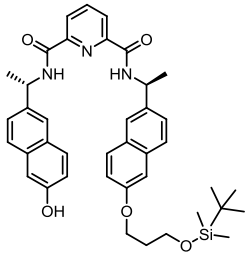
The compound was synthesized as described for (R_2)-**S9** but starting from (S_2)-**S8** (542 mg, 0.8 mmol). Product (S_2)-**S9** was obtained as a colorless solid (415 mg, 59%). Analytical data was identical to its enantiomer.

(R_2)-S10



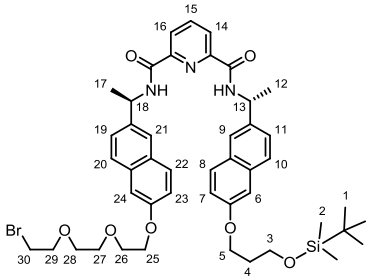
To a solution of (R_2)-**S4** (1.20 g, 2.37 mmol) and potassium carbonate (0.328 g, 2.37 mmol) in degassed DMF (240 mL) was added compound **S3** (0.601 g, 2.37 mmol). The reaction was stirred for 16 hours at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. Further purification by flash column chromatography (CH_2Cl_2/EtOAc 5:1) yielded (R_2)-**S10** (519 mg, 33 %) as a colorless solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 7.8, 2.0 Hz, 2H, $H_{14,16}$), 8.04 (t, br, *J* = 7.2 Hz, 2H, *N-H*), 7.96 (t, *J* = 7.8 Hz, 1H, H_{15}), 7.66 (s, 1H, $H_{9/21}$), 7.63–7.59 (m, 2H, $H_{9/21,8}$), 7.56 (d, *J* = 8.5 Hz, 1H, H_{10}), 7.51 (d, *J* = 8.6 Hz, 1H, H_{22}), 7.46 (d, *J* = 8.5 Hz, 1H, H_{20}), 7.38 (dd, *J* = 8.5, 1.8 Hz, 1H, H_{11}), 7.33 (dd, *J* = 8.6, 1.8 Hz, 1H, H_{19}), 7.12 (dd, *J* = 8.9, 2.4 Hz, 1H, H_7), 7.09–6.99 (m, 3H, $H_{6,23,24}$), 6.87 (s, br, 1H, H_{25}), 5.44–5.37 (m, 2H, $H_{13,18}$), 4.17 (app qt, *J* = 9.3, 4.6 Hz, 2H, H_5), 3.87 (t, *J* = 5.9 Hz, 2H, H_3), 2.06 (quintet, *J* = 6.2 Hz, 2H, H_4), 1.59 (app d, *J* = 6.8 Hz, 6H, $H_{12,17}$), 0.90 (s, 9H, H_1), 0.06 (s, 6H, H_2); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.84, 162.74, 157.17, 154.19, 148.72, 148.64, 139.06, 137.48, 137.13, 133.94, 133.91, 129.47, 129.17, 128.58, 128.34, 127.50, 127.03, 125.18, 124.80, 124.64, 124.58, 124.53, 119.49, 118.48, 109.34, 106.36, 64.53, 59.67, 49.11, 49.08, 32.26, 25.93, 21.54, 21.37, 18.36, -5.33; Several carbon signals not determined due to overlapping peaks. **HRMS** (ESI$^-$): Calcd. for $C_{40}H_{46}N_3O_5Si^-$: 676.3212, found 676.3180.

(S_2)-S10



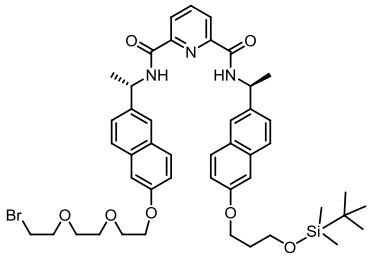
The compound was synthesized as described for (R_2)-**S10** but starting from (S_2)-**S4** (1.12 g, 2.21 mmol). Product (S_2)-**S10** was obtained as a colorless solid (581 mg, 40 %). Analytical data was identical to its enantiomer.

(R_2)-S11



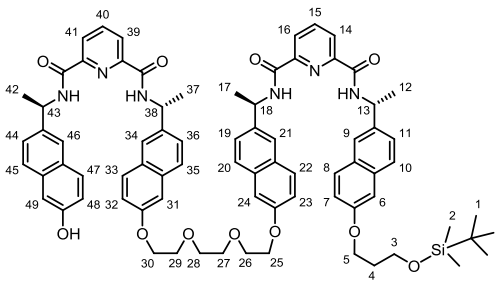
To a solution of (R_2)-**S10** (67.8 mg, 0.10 mmol) and potassium carbonate (55.3 mg, 0.40 mmol) in degassed DMF (1 mL) was added 1,2-bis(2-bromoethoxy)ethane (49.5 µL, 0.30 mmol). The reaction was stirred for 18 hours at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. Further purification by flash column chromatography (CH_2Cl_2, then CH_2Cl_2/EtOAc 3:1) gave (R_2)-**S11** (57.1 mg, 66 %) as a colorless solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.8 Hz, 2H, $H_{14,16}$), 7.99 (t, *J* = 7.8 Hz, 1H, H_{15}), 7.94 (d, *J* = 8.2 Hz, 2H, *N-H*), 7.70 (s, 2H, $H_{9,21}$), 7.67–7.62 (m, 4H, $H_{8,10,20,22}$), 7.42 (d, *J* = 8.2 Hz, 2H, $H_{11,19}$), 7.19 (dd, *J* = 8.9, 2.4 Hz, 1H, $H_{7/23}$), 7.15 (dd, *J* = 9.0, 2.3 Hz, 1H, $H_{7/23}$), 7.11 (app d, *J* = 7.9 Hz, 2H, $H_{6,24}$), 5.43 (quintet, *J* = 7.3 Hz, 2H, $H_{13,18}$), 4.26 (t, *J* = 4.8 Hz, 2H, H_{25}), 4.18 (t, *J* = 6.2 Hz, 2H, H_5), 3.95 (t, *J* = 4.8 Hz, 2H, H_{26}), 3.85 (t, *J* = 6.0 Hz, 2H, H_3), 3.82 (t, *J* = 6.3 Hz, 2H, H_{29}), 3.77 (dd, *J* = 5.9, 3.3 Hz, 2H, H_{27}), 3.72 (dd, *J* = 5.8, 3.3 Hz, 2H, H_{28}), 3.47 (t, *J* = 6.3 Hz, 2H, H_{30}), 2.05 (quintet, *J* = 6.2 Hz, 2H, H_4), 1.62 (d, *J* = 6.9 Hz, 6H, $H_{12,17}$), 0.89 (s, 9H, H_1), 0.05 (s, 6H, H_2) ; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.54, 157.22, 156.92, 148.73, 148.71, 138.98, 137.88, 137.67, 133.95, 133.80, 129.29, 129.21, 128.78, 128.63, 127.48, 127.46, 125.11, 124.90, 124.83, 124.50, 119.50, 119.49, 106.54, 106.37, 71.22, 70.84, 70.57, 69.79, 67.41, 64.44, 59.48, 48.93, 32.31, 30.32, 25.93, 25.91, 21.54, 18.31, -5.38; Due to the pseudo-symmetry, one carbon signal is not resolved due to overlapping peaks. **HRMS** (ESI^+): Calcd. for $C_{40}H_{44}N_3O_7SiNa^+$: 780.2255, found 780.2255 [M-TBS+Na^+], only the deprotected fragment ionized in the MS.

(S_2)-S11



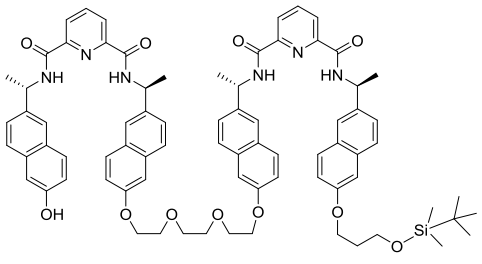
The compound was synthesized as described for (R_2)-**S11** but starting from (S_2)-**S10** (562 mg, 0.85 mmol). Product (S_2)-**S11** was obtained as a colorless solid (476 mg, 65 %). Analytical data was identical to its enantiomer.

(*R*$_4$)-S12



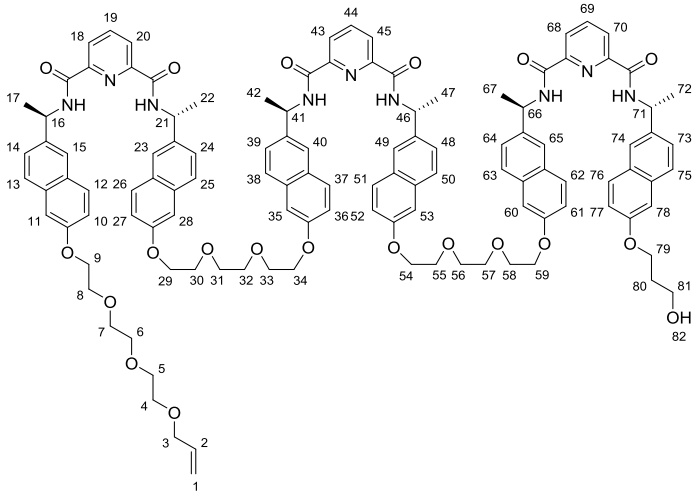
To a solution of (*R*$_2$)-**S4** (0.178 g, 0.35 mmol) and potassium carbonate (49 mg, 0.35 mmol) in degassed DMF (35 mL) was added (*R*$_2$)-**S11** (0.302 g, 0.35 mmol). The reaction was stirred for 17 hours at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. Further purification by flash column chromatography (CH_2Cl_2/EtOAc 1:4) gave (*R*$_4$)-**S12** (0.125 g, 28 %) as a colorless solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.7 Hz, 4H, $H_{14,16,39,41}$), 8.04–7.93 (m, 6H, $H_{15,40,N\text{-}H}$), 7.68–7.46 (m, 12H, $H_{8,9,11,19,21,22,33,34,36,44,46,47}$), 7.41–7.36 (m, 2H, $H_{10/20/35/45}$), 7.32–7.27 (m, 2H, $H_{7/23/32/48}$), 7.21 (d, *J* = 8.5 Hz, 1H, $H_{10/20/35/45}$), 7.14–7.05 (m, 5H, $H_{7/23/32/48,6/24/31/49}$), 7.02 (s, 2H, $H_{6/24/31/49}$), 5.43–5.28 (m, 4H, $H_{13,18,38,43}$), 4.25–4.15 (m, 6H, $H_{5,25,30}$), 3.98–3.90 (m, 4H, $H_{26,29}$), 3.86–3.82 (m, 6H, $H_{3,27,28}$), 2.04 (quintet, *J* = 6.0 Hz, 2H, H_4), 1.60–1.50 (m, 12H, $H_{12,17,37,42}$), 0.88 (s, 9H, H_1), 0.04 (s, 6H, H_2);**^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.82, 162.74, 162.70, 157.23, 156.88, 156.85, 154.42, 148.88, 148.84, 148.74, 148.69, 139.03, 139.01, 137.86, 137.66, 137.57, 136.85, 133.98, 133.96, 133.80, 133.78, 129.43, 129.27, 129.22, 128.77, 128.63, 128.27, 127.55, 127.48, 127.06, 125.20, 125.17, 125.11, 125.06, 124.97, 124.89, 124.70, 124,67, 124.57, 124.52, 124.49, 119.51, 119.41, 119.40, 118.71, 109.39, 106.80, 106.67, 106.39, 70.96, 70.88, 69.89, 69.84, 67.37, 67.32, 64.49, 59.53, 49.39, 49.28, 48.97, 48.95, 32.34, 25.95, 21.52, 21.47, 21.41, 21.24, 18.36, -5.33; Due to the pseudo-symmetry, several carbon signals could not be identified due to overlapping peaks. **HRMS** (ESI^-): Calcd. for $C_{77}H_{83}N_6O_{11}Si^-$: 1295.5895, found 1295.5916.

(*S*$_4$)-S12



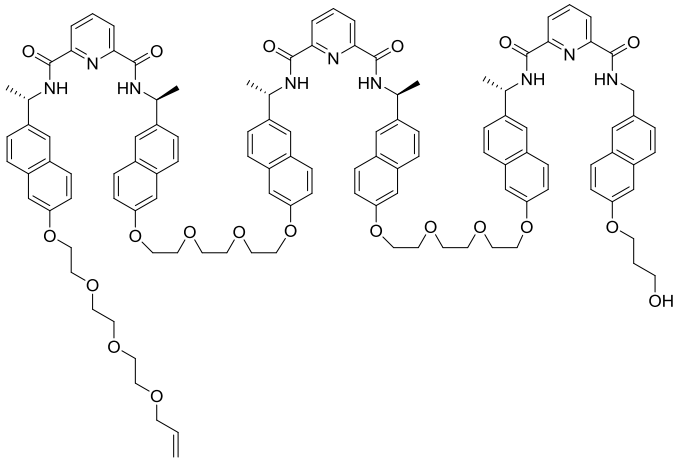
The compound was synthesized as described for (*R*$_2$)-**S12** but starting from (*S*$_2$)-**S11** (476 mg, 0.54 mmol) and (*S*$_2$)-**S4** (275 mg, 0.54 mmol). Product (*S*$_2$)-**S12** was obtained as a colorless solid (258 mg, 37 %). Analytical data was identical to its enantiomer.

(R_6)-S13



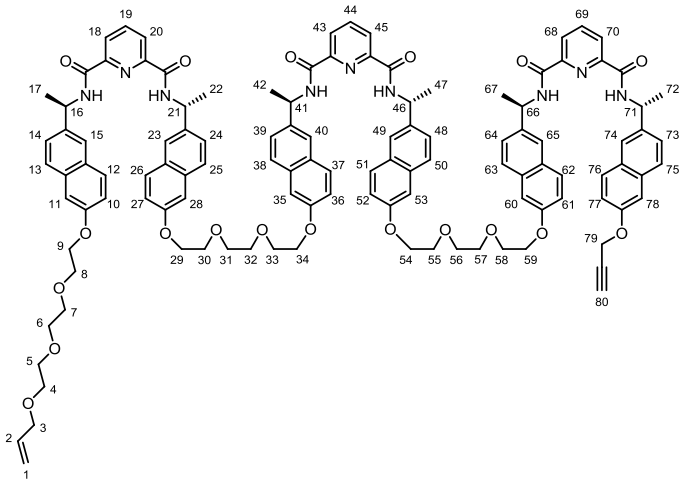
To a solution of (R_4)-**S12** (206 mg, 0.16 mmol) and potassium carbonate (72 mg, 0.51 mmol) in degassed DMF (15 mL) was added (R_2)-**S9** (152 mg, 0.17 mmol). The reaction was stirred for 16 hours at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. Flash column chromatography (EtOAc to CH_2Cl_2/MeOH 9:1) gave compound of moderate purity. This crude product was dissolved in THF (1 ml), cooled to 0° C, then treated with tetrabutylammonium fluoride (1 M solution in THF; 0.20 ml, 0.2 mmol). The sample was stirred at 0 °C for 1 h, then at RT for an additional 3 h until conversion was complete according to TLC. The reaction mixture was concentrated, and redissolved in CH_2Cl_2 (100 ml). The organic phase was washed with H_2O (100 ml) and brine (100 ml), dried with $MgSO_4$, filtered and concentrated. Further purification by passing the compound through a plug of silica (CH_2Cl_2/MeOH 19:1) yielded compound (R_6)-**S13** (141 mg, 42 %). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.50–9.46 (m, 6H, *N-H*), 8.27–8.23 (m, 6H, $H_{18,20,43,45,68,70}$), 8.22–8.17 (m, 3H, $H_{19,44,69}$), 7.88–7.77 (m, 18H, $H_{12,13,15,23,25,26,37,38,40,49,50,51,62,63,65,74,75,76}$), 7.62–7.57 (m, 6H, $H_{14,24,39,48,64,73}$), 7.35–7.30 (m, 6H, $H_{11,28,35,53,60,78}$), 7.20–7.15 (m, 6H, $H_{10,27,36,52,61,77}$), 5.88 (app ddt, J = 17.3, 10.6, 5.4 Hz, 1H, H_2), 5.47–5.39 (m, 6H, $H_{16,21,41,46,66,71}$), 5.25 (dd, J = 17.3, 1.9 Hz, 1H, H_1), 5.14 (dq, J = 10.4, 1.5 Hz, 1H, H_1), 4.62 (t, J = 5.2 Hz, 1H, H_{82}), 4.25–4.19 (m,10H, $H_{9,29,34,54,59}$), 4.16 (t, J = 6.4 Hz, 2H, H_{79}), 3.96–3.94 (m, 2H, H_3), 3.87–3.80 (m, 10H, $H_{8,30,33,55,58}$), 3.69–3.66 (m, 8H, $H_{31,32,56,57}$), 3.65–3.49 (m, 10H, $H_{4,5,6,7,81}$), 1.95 (quintet, J = 6.4 Hz, 2H, H_{80}) 1.72–1.67 (m, 18H, $H_{17,22,42,47,67,72}$); ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.79, 157.45, 157.21, 150.07, 140.36, 139.88, 139.78, 136.19, 134.30, 134.22, 130.17, 130.10, 129.14, 129.06, 127.85, 126.49, 126.45, 125.71, 124.99, 119.89, 119.82, 119.06, 117.23, 107.47, 107.35, 71.97, 70.93, 70.90, 70.79, 70.72, 69.93, 69.89, 68.09, 65.55, 58.28, 49.06, 32.10, 22.63. *Due to the high degree of apparent symmetry within **S13** many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{117}H_{123}N_9O_{20}Na^+$: 1996.8777, found 1996.8779 $[M+Na]^+$.

(S_6)-S13



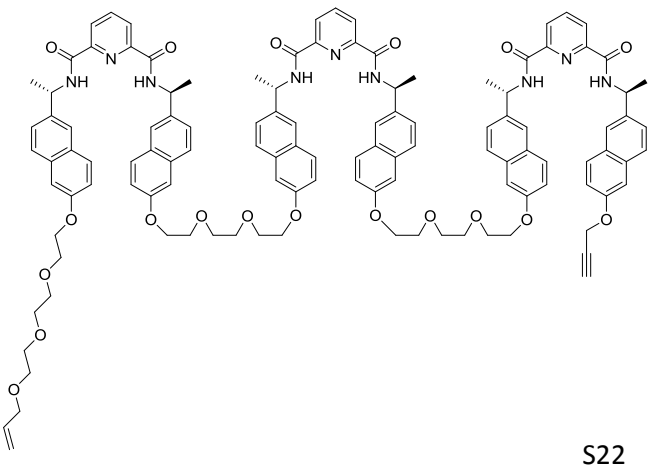
The compound was synthesized as described for (R_6)-**S13** but starting from (S_4)-**S12** (114 mg, 0.087 mmol) and (S_2)-**S9** (84 mg, 0.096 mmol). Product (S_6)-**S13** was obtained as a colorless solid (122 mg, 68 %). Analytical data was identical to its enantiomer.

(R_6)-L1



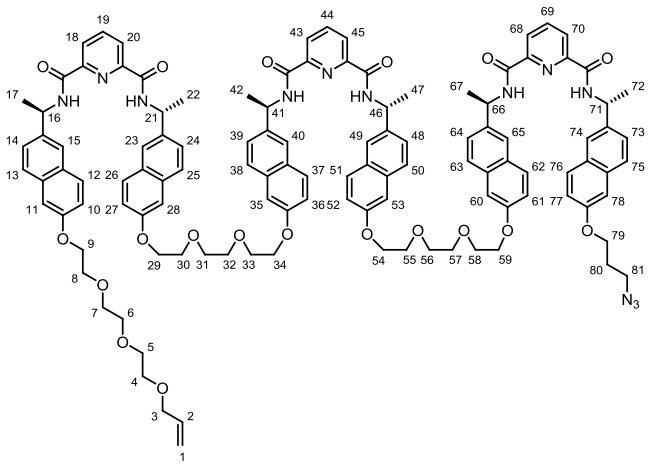
To a solution of (R_4)-**S7** (197 mg, 0.17 mmol) and potassium carbonate (118.3 mg, 0.86 mmol) in degassed DMF (24 mL) was added (R_2)-**S9** (147 mg, 0.17 mmol). The reaction was stirred for 16 hours at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. Further purification by flash column chromatography (EtOAc to CH_2Cl_2/MeOH 95:5) yielded (R_6)-**L1** as a colorless solid (290 mg, 87%). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.49–9.43 (m, 6H, *N-H*), 8.23–8.19 (m, 6H, $H_{18,20,43,45,68,70}$), 8.18–8.14 (m, 3H, $H_{19,44,69}$), 7.86–7.75 (m, 18H, $H_{12,13,15,23,25,26,37,38,40,49,50,51,62,63,65,74,75,76}$), 7.60–7.53 (m, 6H, $H_{14,24,39,48,64,73}$), 7.36 (d, J = 2.6 Hz, 1H, $H_{11/28/35/53/60/78}$), 7.31–7.27 (m, 5H, $H_{11/28/35/53/60/78}$), 7.19–7.12 (m, 6H, $H_{10,27,36,52,60,77}$), 5.84 (app ddd, J = 16.1, 10.5, 5.3 Hz, 1H, H_2), 5.39 (quintet, J = 6.6 Hz, 6H, $H_{16,21,41,46,66,71}$), 5.21 (dq, J = 17.3, 1.9 Hz, 1H, H_1), 5.10 (dd, J = 10.5, 1.9 Hz, 1H, H_1), 4.90 (d, J = 2.4 Hz, 2H, H_{79}), 4.21–4.16 (m, 10H, $H_{9,29,34,54,59}$), 3.91 (d, J = 5.4 Hz, 2H, H_3), 3.82–3.77 (m, 10H, $H_{8,30,33,55,58}$), 3.64 (s, 8H, $H_{31,32,56,57}$), 3.61–3.58 (m, 3H, $H_{7,80}$), 3.55-3.46 (m, 6H, $H_{4,5,6}$), 1.68–1.64 (m, 18H, $H_{17,22,42,47,67,72}$); ^{13}C NMR (151 MHz, DMSO-d_6) δ 162.87, 156.28, 154.98, 149.14, 139.43, 139.34, 138.96, 135.26, 133.29, 133.02, 129.35, 129.24, 128.49, 128.21, 127.02, 126.92, 125.70, 125.56, 124.78, 124.06, 118.89, 118.71, 116.31, 107.42, 106.54, 79.21, 78.38, 71.04, 70.00, 69.97, 69.86, 69.79, 69.00, 68.96, 68.93, 67.16, 55.49, 48.14, 21.70; *Due to the high degree of apparent symmetry within **L1** many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{117}H_{119}N_9O_{19}Na^+$: 1976.8514, found 1976.8531 $[M+Na]^+$.

(S_6)-L1



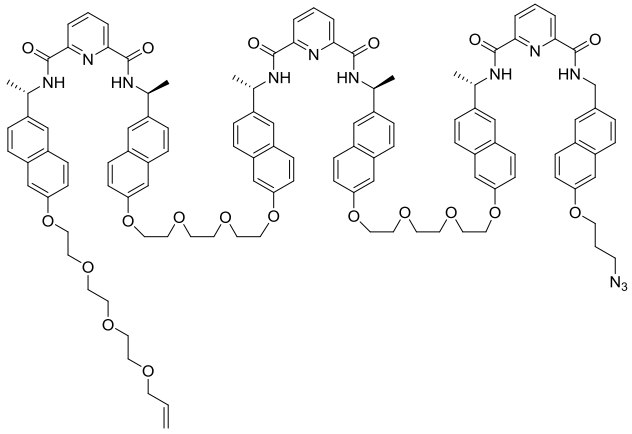
The compound was synthesized as described for (R_6)-**L1** but starting from (S_4)-**S7** (82.8 mg, 0.071 mmol) and (S_2)-**S9** (62.2 mg, 0.071 mmol). Product (S_6)-**L1** was obtained as a colorless solid (131 mg, 94 %). Analytical data was identical to its enantiomer.

(R_6)-L2



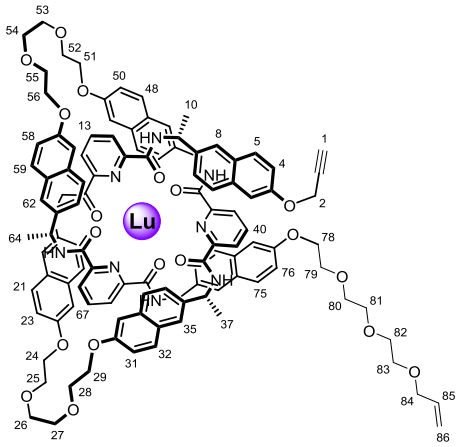
To a stirred suspension of (R_6)-**S13** (37.3 mg, 0.019 mmol) and ADMP (16.2 mg, 0.057 mmol) in anhydrous THF (0.2 mL) at 0 °C, DBU (8.5 µL, 0.057 mmol) was added dropwise. The reaction mixture was allowed to warm up to RT over 2 h and stirred at ambient temperature for 24 h. Upon full conversion, the reaction was quenched by addition of sat. aq. NH_4Cl solution (2 mL), then diluted with H_2O (10 mL) and CH_2Cl_2 (10 mL). The organic layer was separated and washed with H_2O (10 mL) and brine (10 mL), followed by drying with $MgSO_4$, filtration and concentration. Further purification by flash column chromatography (EtOAc, then CH_2Cl_2/MeOH 19:1) yielded the product as a colorless solid (31.0 mg, 82 %). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.50–9.45 (m, 6H, *N-H*), 8.27–8.22 (m, 6H, $H_{18,20,43,45,68,70}$), 8.22–8.17 (m, 3H, $H_{19,44,69}$), 7.88–7.78 (m, 18H, $H_{12,13,15,23,25,26,37,38,40,49,50,51,62,63,65,74,75,76}$), 7.62–7.56 (m, 6H, $H_{14,24,39,48,64,73}$), 7.36–7.30 (m, 6H, $H_{11,28,35,53,60,78}$), 7.20–7.15 (m, 6H, $H_{10,27,36,52,61,77}$), 5.88 (app ddt, J = 17.3, 10.6, 5.4 Hz, 1H, H_2), 5.48–5.38 (m, 6H, $H_{16,21,41,46,66,71}$), 5.25 (dq, J = 17.2, 1.8 Hz, 1H, H_1), 5.14 (dq, J = 10.4, 1.5 Hz, 1H, H_1), 4.24–4.18 (m, 10H, $H_{9,29,34,54,59}$), 4.17 (t, J = 6.4 Hz, 2H, H_{79}), 3.96–3.93 (m, 2H, H_3), 3.87–3.80 (m, 10H, $H_{8,30,33,55,58}$), 3.68 (s, 8H, $H_{31,32,56,57}$), 3.65–3.49 (m, 10H, $H_{4,5,6,7,81}$), 2.07 (quintet, J = 6.4 Hz, 2H, H_{80}) 1.73–1.66 (m, 18H, $H_{17,22,42,47,67,72}$); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 163.79, 157.20, 150.06, 140.35, 139.92, 139.87, 136.19, 134.22, 130.16, 129.17, 129.13, 127.85, 126.49, 125.70, 124.99, 119.82, 117.23, 107.50, 107.46, 71.96, 70.92, 70.89, 70.79, 70.71, 69.93, 69.89, 69.86, 68.08, 65.59, 60.72, 49.06, 48.69, 31.66, 29.06, 22.63, 21.73, 15.05. *Due to the high degree of apparent symmetry within **L2** many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{117}H_{122}N_{12}O_{19}Na^+$: 2021.8841, found 2021.8844 $[M+Na]^+$.

(S_6)-L2



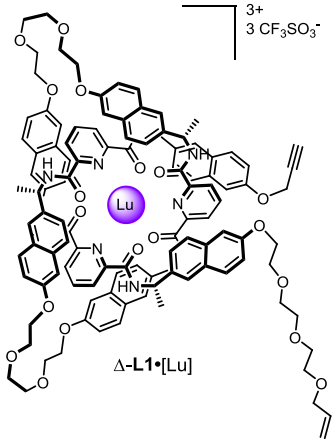
The compound was synthesized as described for (R_6)-**L2** but starting from (S_6)-**S13** (247 mg, 0.125 mmol). Product (S_6)-**L2** was obtained as a colorless solid (219 mg, 88 %). Analytical data was identical to its enantiomer.

Λ-L1•[Lu]



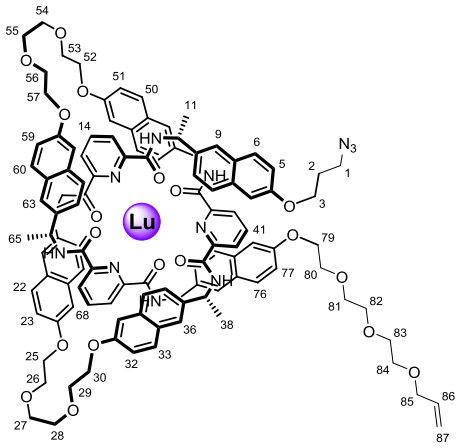
To a vigorously stirred solution of (R_6)-**L1** (0.14 g, 0.07 mmol) in MeCN (72 mL) was added a solution of lutetium trifluoromethanesulfonate (45 mg, 0.07 mmol). The reaction was stirred overnight at 80 °C. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. The solid was washed with dichloromethane and filtered to give Λ-**L1**•[Lu] (151 mg, 81 %) as an off-white powder. **^{1}H NMR** (600 MHz, MeCN-d_3) δ 8.49–8.43 (m, 4H, $H_{38,42,11/15/65/69}$), 8.35 (app dd, J = 8.3, 5.3 Hz, 2H, $H_{11/15/65/69}$), 7.69 (d, J = 9.0 Hz, 1H, $H_{5/75}$), 7.67 (d, J = 9.0 Hz, 1H, $H_{5/75}$), 7.58–7.53 (m, 5H, $H_{21,32,39/41,48,59}$), 7.50 (d, J = 8.5 Hz, 2H, $H_{6,74}$), 7.45 (d, J = 8.0 Hz, 1H, $H_{39/41}$), 7.36–7.19 (m, 14H, $H_{4,20,22,23,30,31,33,47,49,50,57,58,60,76}$), 7.17 (t, J = 8.0 Hz, 1H, H_{40}), 7.15–7.11 (m, 2H, $H_{35,45}$), 7.08 (app dd, J = 9.0, 2.5 Hz, 2H, $H_{3,77}$), 7.00 (s, 2H, $H_{8/62,18/72}$), 6.97–6.91 (m, 4H, $H_{12/14,66/68,8/62,18/72}$), 6.89–6.79 (m, 6H, $H_{12/14,66/68,7,19,61,73}$), 6.67 (dd, J = 8.4, 1.8 Hz, 1H, $H_{34/46}$), 6.64 (dd, J = 8.5, 1.8 Hz, 1H, $H_{34/46}$), 6.00 (app td, J = 7.9, 1.9 Hz, 2H, $H_{13,67}$), 5.94–5.86 (m, 1H, H_{85}), 5.25 (dt, J = 17.2, 1.8 Hz, 1H, H_{86}), 5.12 (dt, J = 10.5, 1.6 Hz, 1H, H_{86}), 4.99 (d, J = 2.1 Hz, 2H, H_2), 4.79–4.72 (m, 2H, $H_{9/16/36/43/63/70}$), 4.69–4.63 (m, 4H, $H_{9/16/36/43/63/70}$), 4.35–4.24 (m, 10H, $H_{24,29,51,56,78}$), 4.09–4.05 (m, 4H, $H_{25/28/52/55/79}$), 3.98–3.81 (m, 16H, $H_{25/28/52/55/79,26,27,53,54,84}$), 3.74–3.72 (m, 2H, H_{80}), 3.66–3.64 (m, 2H, H_{81}), 3.62–3.59 (m, 2H, H_{82}), 3.56–3.54 (m, 2H, H_{83}), 3.03 (t, J = 2.4 Hz, 1H, H_1), 1.60–1.42 (m, 18H, $H_{10,17,37,44,64,71}$); **^{13}C NMR** (151 MHz, MeCN-d_3) δ 167.56, 167.55, 167.28, 167.11, 167.05, 158.02, 157.95, 157.85, 157.83, 156.61, 145.30, 145.25, 144.61, 144.56, 144.56, 144.53, 141.82, 139.90, 139.50, 139.35, 139.33, 139.05, 136.20, 134.52, 134.30, 134.20, 134.02, 133.99, 130.24, 130.10, 130.00, 129.77, 129.75, 129.56, 129.28, 129.04, 129.01, 128.25, 128.13, 128.12, 127.89, 127.87, 125.19, 125.03, 124.54, 124.51, 124.08, 124.00, 123.97, 123.93, 123.88, 123.35, 123.34, 123.30, 12306, 123.03, 120.94, 120.40, 120.30, 120.21, 108.57, 107.99, 107.97, 107.94, 107.89, 79.73, 77.30, 72.38, 71.60, 71.55, 71.51, 71.50, 71.40, 71.17, 71.12, 70.29, 69.94, 69.26, 69.12, 69.10, 68.65, 56.72, 54.15, 54.09, 53.61, 53.58, 53.01, 52.81, 23.47, 23.30, 22.17, 22.10. *Due to the high degree of apparent symmetry within the compound many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{117}H_{119}N_9O_{19}Lu$ $[M\text{-}3(CF_3SO_3)]^{3+}$: 709.6004, found 709.5979

Δ-L1•[Lu]



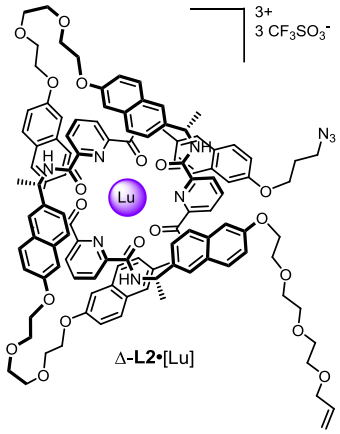
The compound was synthesized as described for Λ-**L1**•[Lu] but starting from (S_6)-**L1** (131 mg, 0.067 mmol). Product Δ-**L1**•[Lu] was obtained as a colorless solid (142 mg, 82 %). Analytical data was identical to its enantiomer.

Λ-L2•[Lu]



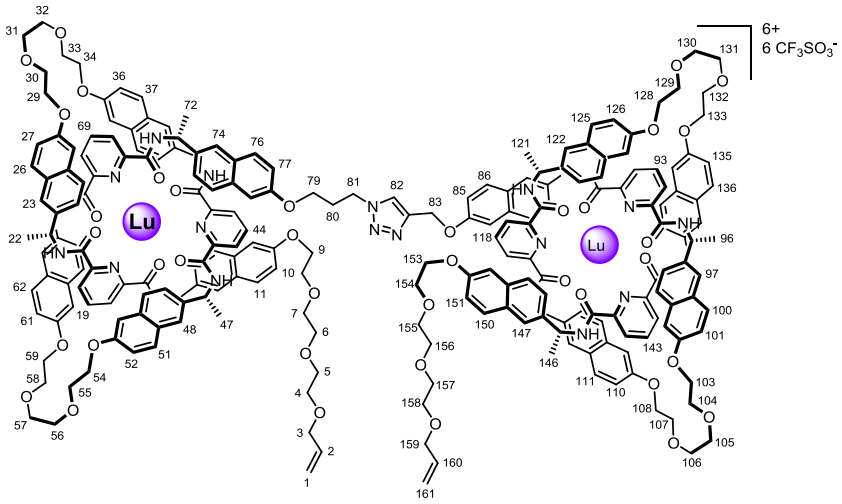
To a vigorously stirred solution of (R_6)-**L2** (55 mg, 0.028 mmol) in MeCN (28 mL) was added lutetium trifluoromethanesulfonate (17 mg, 0.028 mmol). The reaction was stirred for 16 h at 80 °C. The mixture was allowed to cool to room temperature, filtered and concentrated. The solid was washed with dichloromethane and filtered to give Λ-**L2**•[Lu] (61 mg, 86 %) as an off-white powder. **^{1}H NMR** (600 MHz, MeCN-d_3) δ 8.47–8.35 (m, 4H, $H_{39,43,12/16/66/70}$), 8.29 (app dd, J = 8.8, 5.3 Hz, 2H, $H_{12/16/66/70}$), 7.65 (d, J = 4.7 Hz, 1H, $H_{6/76}$), 7.64 (d, J = 4.7 Hz, 1H, $H_{6/76}$), 7.61–7.52 (m, 6H, $H_{22,33,40,42,49,60}$), 7.51–7.48 (m, 2H, $H_{7,75}$), 7.32–7.20 (m, 15H, $H_{5,21,23,24,30,31,32,34,48,50,51,58,59,61,77}$), 7.19 (t, J = 8.0 Hz, 1H, H_{41}), 7.17–7.14 (m, 3H, $H_{36,46,63}$), 7.09 (app d, J = 2.5 Hz, 2H, $H_{4,78}$), 7.02 (s, br, 2H, $H_{9/63,19/73}$), 6.97–6.91 (m, 4H, $H_{13/15,67/69,9/63,19/73}$), 6.89–6.80 (m, 6H, $H_{13/15,67/69,8,20,62,74}$), 6.69–6.65 (m, 2H, $H_{35,47}$), 6.07 (app td, J = 7.9, 4.2 Hz, 2H, $H_{14,68}$), 5.96–5.89 (m, 1H, H_{86}), 5.27 (app dd, J = 17.3, 1.8 Hz, 1H, H_{87}), 5.15 (app dd, J = 10.4, 1.9 Hz, 1H, H_{87}), 4.82–4.76 (m, 2H, $H_{10/17/37/44/64/71}$), 4.72–4.65 (m, 4H, $H_{10/17/37/44/64/71}$), 4.38–4.27 (m, 12H, $H_{3,25,30,52,57,79}$), 4.13–4.07 (m, 4H, $H_{26/29/53/56/80}$), 4.01–3.81 (m, 16H, $H_{26/29/53/56/80,27,28,54,55,85}$), 3.77–3.74 (m, 2H, H_{81}), 3.70–3.65 (m, 4H, $H_{1,82}$), 3.63–3.61 (m, 2H, H_{83}), 3.58–3.55 (m, 2H, H_{84}), 2.22 (quintet, J = 6.3 Hz, 2H, H_2, partial overlap with solvent peak), 1.70–1.38 (m, 18H, $H_{11,18,38,45,65,72}$); ^{13}C NMR (151 MHz, MeCN-d_3) δ 206.52, 166.66, 166.65, 166.37, 166.11, 166.09, 157.13, 157.09, 157.06, 156.92, 144.44, 144.40, 144.34, 143.70, 143.66, 143.61, 139.07, 138.40, 138.10, 137.98, 135.28, 133.65, 133.63, 133.62, 133.39, 133.38, 133.06, 129.22, 129.19, 129.08, 128.84, 128.83, 128.40, 128.36, 128.09, 127.23, 127.20, 126.95, 124.31, 124.22, 123.66, 123.52, 123.33, 123.32, 123.13, 123.07, 123.00, 122.96, 122.44, 122.38, 122.36, 122.33, 122.30, 122.29, 122.22, 122.18, 120.06, 119.49, 119.45, 119.43, 119.38, 107.05, 107.03, 107.02, 106.93, 106.91, 71.46, 70.69, 70.59, 70.50, 70.26, 70.20, 69.37, 69.02, 69.01, 68.36, 68.19, 67.73, 65.05, 53.24, 53.18, 52.73, 52.69, 51.91, 48.20, 29.91, 28.47, 22.58, 22.37, 21.18, 21.08, 14.64. Due to the high degree of apparent symmetry within the compound many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{117}H_{122}N_{12}O_{19}Lu$ $[M\text{-}3(CF_3SO_3)]^{3+}$: 724.6113, found 724.6085

Δ-L2•[Lu]



The compound was synthesized as described for Λ-**L2**•[Lu] but starting from (S_6)-**L2** (0.208 g, 0.104 mmol). Product Δ-**L2**•[Lu] was obtained as a colorless solid (0.198 g, 73%). Analytical data was identical to its enantiomer.

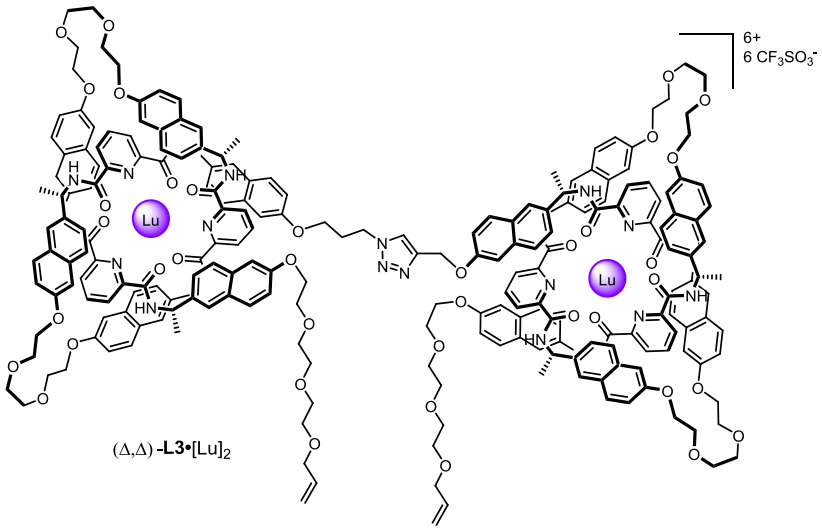
(Λ,Λ)-L3•[Lu]$_2$



To a solution of Λ-**L1**•[Lu] (25.2 mg, 0.01 mmol) and Λ-**L2**•[Lu] (25.6 mg, 0.01 mmol) in MeOH/MeCN (1:1 , deoxygenated, 2 mL) was added tetrakisacetonitrile copper(I) trifluoromethane sulfonate (3.7 mg, 0.01 mmol) and TentaGel TBTA (0.17 mmol/g loading, 58 mg, 0.01 mmol). The reaction was stirred for 16 h at RT, after which the resin was filtered off and the resulting solution concentrated under reduced pressure. The product was obtained with full conversion, and the crude mixture could be further purified by size exclusion chromatography (MeOH) to give (Λ,Λ)-**L3**•[Lu]$_2$ as a colorless solid (41.1 mg, 79 %). **^{1}H NMR** (600 MHz, MeCN-d_3) δ 8.78–8.32 (m, 12H, *N-H*), 7.66–7.47 (m, 20H, $H_{12,13,26,37,43,45,50,62,75,76,86,87,100,111,117,119,124,136,149,150}$), 7.33–7.04 (m, 39H, $H_{10,11,25,27,28,35,36,38,40,44,48,51\text{-}53,60,61,63,77,78,82,84,85,99,101,102,109,110,112,114,118,122,125\text{-}127,134,135,137,151,152,}$ due to the complexity of the molecule, these signals are clustered together), 7.01–6.75 (m, 24H, $H_{14,15,18,20,23,24,64,65,68,70,73,74,88,89,92,94,97,98,138,139,142,144,147,148}$), 6.64–6.58 (m, 4H, $H_{39,49,113,123}$), 6.04–5.94 (m, 4H, $H_{19,69,93,143}$), 5.91–5.83 (m, 2H, $H_{2,160}$), 5.26–5.18 (m, 2H, $H_{1,161}$), 5.13–5.06 (m, 2H, $H_{1,161}$), 4.81–4.59 (m, 14H, $H_{16,21,41,46,66,71,81,90,95,115,120,140,145}$), 4.35–4.21 (m, 22H, $H_{9,29,34,54,59,79,103,108,128,133,153}$), 4.09–4.03 (m, 8H, $H_{8/30/33/55/58/104/107/129/132/154}$), 3.99–3.78 (m, 34H, $H_{8/30/33/55/58/104/107/129/132/154,3,31,32,56,57,83,105,106,130,131,159}$), 3.75–3.49 (m, 16H, $H_{4,5,6,7,155,156,157,158}$), 2.55 (t, br, J = 4.8 Hz, 2H, H_{80}), 1.60–1.42 (m, 36H, $H_{17,22,42,47,67,72,91,96,116,121,141,146}$). **^{13}C NMR** (151 MHz, MeCN-d_3) δ 166.70, 166.67, 166.66, 166.37, 166.11, 162.93, 157.34, 157.12, 157.09, 157.05, 156.92, 156.72, 144.40, 143.70, 143.65, 143.63, 143.62, 139.02, 139.00, 138.41, 138.12, 135.28, 133.69, 133.66, 133.64, 133.53, 133.39, 133.07, 129.22, 129.19, 129.12, 129.09, 128.93, 128.84, 128.37, 128.09, 127.28, 127.23, 127.21, 127.16, 127.02, 126.95, 125.57, 124.78, 124.31, 124.25, 124.20, 123.66, 123.42, 123.16, 123.10, 123.00, 122.97, 122.41, 122.36, 122.19, 122.14, 120.06, 119.55, 119.49, 119.42, 119.39, 118.91, 117.94, 117.53, 117.34, 117.15, 115.91, 107.06, 107.03, 106.94, 106.92, 106.87, 72.20, 72.17, 71.46, 70.69, 70.63, 70.59, 70.49, 70.43, 70.39, 70.26, 70.20, 70.18, 70.07, 69.99, 69.97, 69.93, 69.89, 69.85, 69.39, 69.37, 69.34, 69.17, 69.02, 69.01, 68.36, 68.19, 67.72, 67.49, 65.23, 65.04, 64.81, 60.86, 58.31, 53.21, 53.17, 52.70, 52.67, 51.95, 51.89, 48.20, 39.48, 32.19, 31.48, 28.47, 22.57, 22.38, 21.22, 21.15, 21.14, 21.07. Due to the high degree of apparent symmetry within the compound

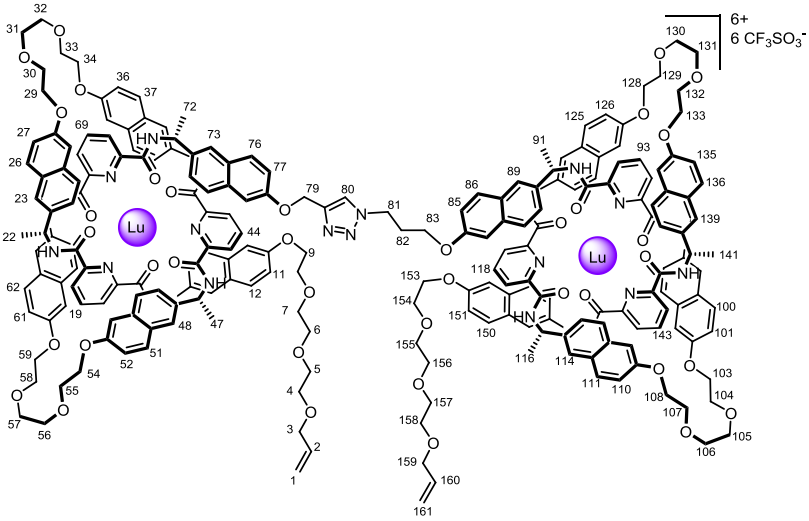
many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{233}H_{239}N_{21}O_{38}Lu_2$ [M-6(CF_3SO_3)]$^{6+}$:717.4403, found 717.4394.

(Δ,Δ)-L3•[Lu]$_2$



The compound was synthesized as described for (Λ,Λ)-**L3**•[Lu]$_2$ but starting from Δ-**L1**•[Lu] (9.8 mg, 3.8 μmol) and Δ-**L2**•[Lu] (10.0 mg, 3.8 μmol). Product (Δ,Δ)-**L3**•[Lu]$_2$ was obtained as a colorless solid (10.3 mg, 52%). Analytical data was identical to its enantiomer.

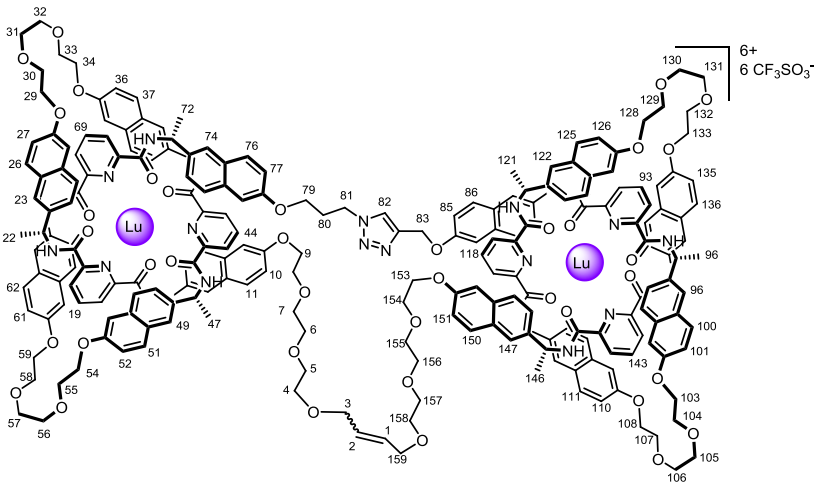
(Λ,Δ)-L3•[Lu]$_2$



To a solution of Λ-**L1**•[Lu] (9.8 mg, 3.8 μmol) and Δ-**L2**•[Lu] (10.0 mg, 3.8 μmol) in MeOH/MeCN (1:1 , deoxygenated, 0.8 mL) was added tetrakisacetonitrile copper(I) trifluoromethane sulfonate (2.8 mg, 7.6 μmol) and TentaGel TBTA (0.17 mmol/g loading, 45 mg, 7.6 μmol). The reaction was stirred for 16 h at RT, after which the resin was filtered off and the resulting solution concentrated under reduced pressure. The product was obtained with full conversion, and the crude mixture could be further purified by size exclusion chromatography (MeOH) to give (Λ,Δ)-**L3**•[Lu]$_2$ as a colorless solid (13.8 mg, 70 %). The product has minor (<3 wt%) contamination from polymers leaching from the TentaGel. **^{1}H NMR** (600 MHz, MeCN-d_3) δ 8.58–8.28 (m, 12H, *N-H*), 7.67–7.46 (m, 20H, $H_{12,13,26,37,43,45,50,62,75,76,86,87,100,111,117,119,124,136,149,150}$), 7.32–7.05 (m, 39H, $H_{10,11,25,27,28,35,36,38,40,44,48,51\text{-}53,60,61,63,77,78,80,84,85,99,101,102,109,110,112,114,118,122,125\text{-}127,134,135,137,151,152}$, due to the complexity of the molecule, these signals are clustered together), 7.01–6.75 (m, 24H, $H_{14,15,18,20,23,24,64,65,68,70,73,74,88,89,92,94,97,98,138,139,142,144,147,148}$), 6.65–6.59 (m, 4H, $H_{39,49,113,123}$), 6.06–5.95 (m, 4H, $H_{19,69,93,143}$), 5.93–5.81 (m, 2H, $H_{2,160}$), 5.30–5.17 (m, 2H, $H_{1,161}$), 5.16–5.06 (m, 2H, $H_{1,161}$), 4.82–4.60 (m, 14H, $H_{16,21,41,46,66,71,81,90,95,115,120,140,145}$), 4.35–4.19 (m, 22H, $H_{9,29,34,54,59,83,103,108,128,133,153}$), 4.09–4.03 (m, 8H, $H_{8/30/33/55/58/104/107/129/132/154}$), 3.98–3.79 (m, 34H, $H_{8/30/33/55/58/104/107/129/132/154,3,31,32,56,57,79,105,106,130,131,159}$), 3.74–3.50 (m, 16H, $H_{4,5,6,7,155,156,157,158}$), 2.55 (app s, br, 2H, H_{82}), 1.60–1.42 (m, 36H, $H_{17,22,42,47,67,72,91,96,116,121,141,146}$). **^{13}C NMR** (151 MHz, MeCN-d_3) δ 167.64, 167.61, 167.60, 167.27, 167.26, 167.07, 167.03, 158.02, 157.96, 157.94, 157.82, 157.81, 157.76, 157.66, 157.64, 157.50, 145.38, 145.34, 145.32, 144.62, 144.60, 144.51, 141.91, 139.86, 139.82, 139.37, 139.37, 139.33, 139.26, 139.23, 139.13, 139.04, 139.04, 136.17, 134.56, 134.45, 134.31, 133.98, 130.21, 130.17, 130.14, 130.11, 130.00, 129.73, 129.46, 129.34, 129.31, 129.28, 129.00, 128.84, 128.60, 128.19, 128.18, 128.17, 128.12, 128.07, 127.95, 127.86, 126.48, 125.42, 125.39, 125.21, 125.20, 124.62, 124.60, 124.49, 124.36, 124.21, 124.11, 124.04, 123.85, 123.39, 123.32, 123.30, 123.09, 122.98, 120.96, 120.40, 120.34, 120.30, 119.83, 118.84, 116.83, 116.75, 108.43, 107.98, 107.94, 107.85, 73.18, 73.16, 72.35, 71.60,

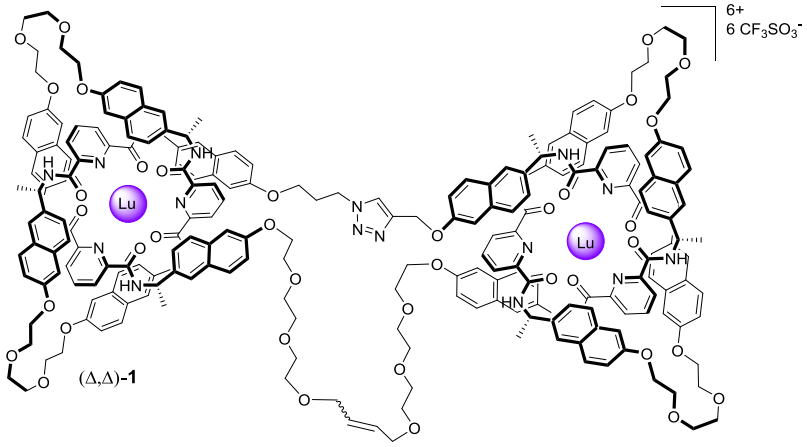
71.49, 71.36, 71.34, 71.32, 71.14, 71.11, 71.09, 71.07, 71.03, 71.01, 70.99, 70.97, 70.94, 70.88, 70.85, 70.26, 70.24, 69.93, 69.27, 69.09, 68.58, 68.40, 65.78, 62.53, 61.84, 61.82, 55.27, 54.12, 54.08, 53.55, 52.88, 52.79, 52.76, 49.81, 48.29, 40.43, 30.83, 30.71, 23.47, 23.31, 22.03, 21.98. Due to the high degree of apparent symmetry within the compound many ^{13}C signals overlap. **HRMS** (ESI^+): Calcd. for $C_{233}H_{239}N_{21}O_{38}Lu_2$ $[M\text{-}6(CF_3SO_3)]^{6+}$: 717.4403, found 717.4390.

(Λ,Λ)-1•[Lu]$_2$



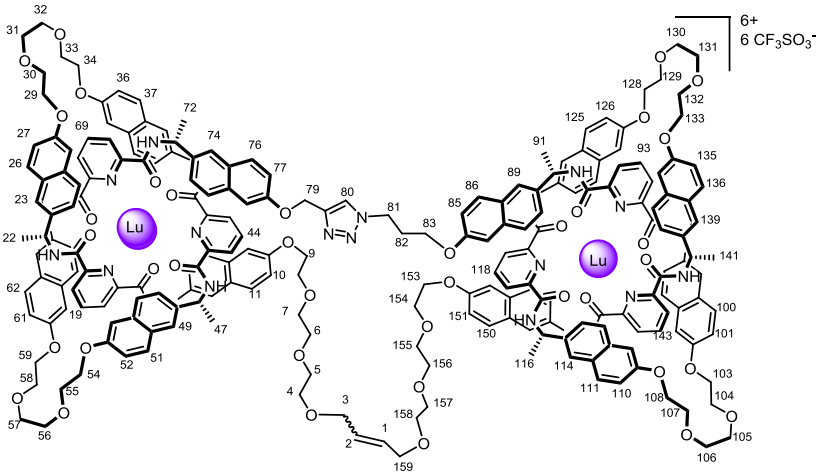
To a stirred solution of (Λ,Λ)-**L3**•[Lu]$_2$ (17.0 mg, 3.3 µmol) in $MeNO_2$ (freshly degassed, 1.6 mL) was added a solution of Hoveyda-Grubbs 2nd Generation catalyst (2.0 mg, 3.3 µmol) in CH_2Cl_2 (freshly degassed, 1.6 mL). The reaction was stirred for 20 h at 50 °C, after which ethyl vinyl ether (1 mL) was added. The quenched reaction was stirred for 1 h at RT, after which the mixture was concentrated under reduced pressure. The obtained solid was repeatedly triturated with CH_2Cl_2, followed by purification via size exclusion chromatography (MeOH) to give (Λ,Λ)-**1**•[Lu]$_2$ as a colorless solid (5.6 mg, 33 % yield). **^{1}H NMR** (600 MHz, MeCN-d_3) δ 7.70–7.45 (m, 20H, $H_{12,13,26,37,43,45,50,62,75,76,86,87,100,111,117,119,124,136,149,150}$), 7.34–6.83 (m, 63H, $H_{10,11,14,15,18,20,23\text{-}25,27,28,35,36,38,40,44,48,51\text{-}53,60,61,63\text{-}65,68,70,73,74,77,78,82,84,85,88,89,92,94,97\text{-}99,101,102,109,110,112,114,118,122,125\text{-}127,134,135,137\text{-}139,142,144,147,148,151,152}$, due to the complexity of the molecule, these signals are clustered together), 6.70–6.60 (m, 4H, $H_{39,49,113,123}$), 6.09–5.96 (m, 6H, $H_{1,2,19,69,93,143}$), 4.85–4.63 (m, 14H, $H_{16,21,41,46,66,71,81,90,95,115,120,140,145}$), 4.39–4.21 (m, 22H, $H_{9,29,34,54,59,79,103,108,128,133,153}$), 4.11–3.50 (m, 58H, $H_{3\text{-}8,30\text{-}33,55\text{-}58,83,104\text{-}107,129\text{-}132,154\text{-}159}$), 2.51 (app s, br, 2H, H_{80}), 1.64–1.45 (m, 36H, $H_{17,22,42,47,67,72,91,96,116,121,141,146}$). **^{13}C NMR** (151 MHz, MeCN-d_3) δ 166.73, 166.71, 166.38, 166.27, 166.20, 166.17, 166.14, 157.09, 157.00, 156.95, 156.89, 156.86, 156.76, 156.73, 143.72, 143.64, 143.61, 138.91, 138.44, 133.62, 133.49, 133.40, 133.07, 129.73, 129.17, 129.10, 128.85, 128.37, 128.09, 127.27, 127.22, 127.04, 126.96, 124.29, 122.40, 122.17, 120.05, 119.48, 119.37, 117.92, 107.09, 107.05, 106.95, 72.33, 70.69, 70.58, 70.18, 70.08, 69.86, 69.36, 69.21, 69.01, 68.35, 68.18, 67.66, 67.49, 61.00, 60.98, 53.17, 52.63, 51.86, 29.91, 29.34, 28.95, 28.78, 28.72, 22.56, 22.48, 22.41, 21.38. Due to the high degree of apparent symmetry within the compound many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{232}H_{237}N_{21}O_{38}Lu_2$ $[M\text{-}6(CF_3SO_3)]^{6+}$: 712.7685, found 712.7658.

(Δ,Δ)-1•[Lu]$_2$



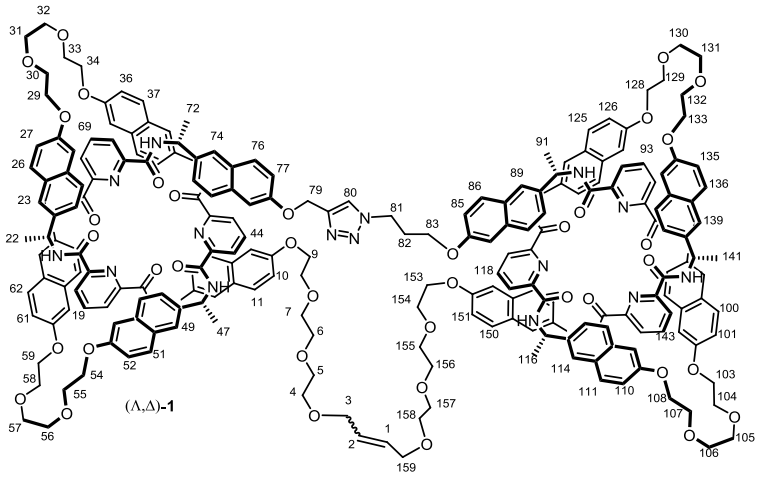
The compound was synthesized as described for (Λ,Λ)-**1**•[Lu]$_2$ but starting from (Δ,Δ)-**L3**•[Lu]$_2$ (4.7 mg, 0.9 μmol). Product (Δ,Δ)-**1**•[Lu]$_2$ was obtained as a colorless solid (1.5 mg, 32 %). Analytical data was identical to its enantiomer.

(Λ,Δ)-1•[Lu]$_2$



To a stirred solution of (Λ,Δ)-**L3**•[Lu]$_2$ (16.9 mg, 3.3 μmol) in $MeNO_2$ (freshly degassed, 1.6 mL) was added a solution of Hoveyda-Grubbs 2nd Generation catalyst (2.0 mg, 1.6 μmol) in CH_2Cl_2 (freshly degassed, 1.6 mL). The reaction was stirred for 20 h at 50 °C, after which ethyl vinyl ether (1 mL) was added. The quenched reaction was stirred for 1 h at RT, after which the mixture was concentrated under reduced pressure. The obtained solid was repeatedly triturated with CH_2Cl_2, followed by purification via size exclusion chromatography (MeOH) to give (Λ,Δ)-**1**•[Lu]$_2$ as a colorless solid (5.5 mg, 32 30%). **^{1}H NMR** (600 MHz, MeCN-d_3) **^{1}H NMR** (600 MHz, MeCN-d_3) δ 7.71–7.48 (m, 20H, $H_{12,13,26,37,43,45,50,62,75,76,86,87,100,111,117,119,124,136,149,150}$), 7.34–6.79 (m, 63H, $H_{10,11,14,15,18,20,23\text{-}25,27,28,35,36,38,40,44,48,51\text{-}53,60,61,63\text{-}65,68,70,73,74,77,78,80,84,85,88,89,92,94,97\text{-}99,101,102,109,110,112,114,118,122,125\text{-}127,134,135,137\text{-}139,142,144,147,148,151,152}$, due to the complexity of the molecule, these signals are clustered together), 6.73–6.62 (m, 4H, $H_{39,49,113,123}$), 6.10–5.99 (m, 6H, $H_{1,2,19,69,93,143}$), 4.84–4.61 (m, 14H, $H_{16,21,41,46,66,71,81,90,95,115,120,140,145}$), 4.39–4.22 (m, 22H, $H_{9,29,34,54,59,83,103,108,128,133,153}$), 4.13–4.04 (m, 8H, $H_{8/30/33/55/58/104/107/129/132/154}$), 4.02–3.76 (m, 34H, $H_{8/30/33/55/58/104/107/129/132/154,3,31,32,56,57,79,105,106,130,131,159}$), 3.72–3.44 (m, 16H, $H_{4,5,6,7,155,156,157,158}$), 2.50 (app s, br, 2H, H_{82}), 1.64–1.48 (m, 36H, $H_{17,22,42,47,67,72,91,96,116,121,141,146}$). δ **^{13}C NMR** (151 MHz, MeCN-d_3) δ 166.78, 166.38, 166.20, 157.09, 156.88, 149.24, 143.76, 143.63, 138.43, 136.91, 133.67, 133.38, 133.06, 130.21, 129.82, 129.77, 129.73, 129.25, 129.23, 129.18, 129.10, 128.98, 128.89, 128.85, 128.63, 128.50, 128.37, 128.15, 128.11, 127.29, 127.21, 127.20, 127.02, 126.96, 125.56, 124.78, 124.31, 124.21, 122.43, 122.19, 120.07, 119.48, 119.36, 118.90, 107.06, 107.03, 106.98, 72.33, 70.69, 70.59, 70.43, 70.19, 69.98, 69.94, 69.89, 69.33, 69.30, 69.02, 68.37, 68.20, 67.49, 67.30, 60.99, 60.96, 54.35, 53.19, 53.18, 52.68, 52.64, 52.57, 48.90, 35.14, 31.65, 31.64, 29.91, 29.63, 29.48, 29.46, 29.39, 29.38, 29.37, 29.20, 29.07, 29.06, 28.98, 28.97, 28.95, 28.87, 28.66, 26.79, 25.33, 25.26, 22.57, 22.41, 21.35. Due to the high degree of apparent symmetry within the compound many ^{13}C signals overlap. **HRMS** (ESI$^+$): Calcd. for $C_{232}H_{237}N_{21}O_{38}Lu_2$ [M-6(CF_3SO_3)]$^{6+}$: 712.7680, found 712.7677.

4.2. Demetallation and remetallation



Representative procedure for demetallation to produce wholly organic composite knots **1**: (Λ,Δ)-**1**•$[Lu]_2$ (5.3 mg, 1.0 μmol) was dissolved in MeCN (1 mL) and tetraethylammonium fluoride (1.5 mg, 10 μmol) in MeCN (0.5 mL) was added while stirring under air. After five minutes, the organic knot was fully precipitated. The filtrate was collected, washed repeatedly with MeCN and dried *in vacuo* to obtain the composite knot (Λ,Δ)-**1** (3.7 mg, 95% yield). A similar procedure was used to obtain (Λ,Λ)-**1** (2.1 mg obtained, starting from 3.0 mg of Λ,Λ)-**1**•$[Lu]_2$, 92% yield). The organic products could be identified with MALDI-MS (Figure S1) as well as ^{1}H NMR spectroscopy (Figure S2). The organic composite knots exhibited very similar ^{1}H NMR spectra, broadened due to reptation of the knotted strand. **^{1}H NMR** (600 MHz, $CDCl_3/CD_3OD$ 10:1) δ 8.29–8.15 (m, 12H, $H_{18,20,\ 43,45,68,70,92,94,117,119,142,144}$), 7.99–7.81 (m, 6H, $H_{19,69,44,93,118,143}$), 7.75–7.50 (m, 40H, $H_{11,13,14,15,23,\ 24,25,\ 26,37,39,40,\ 41,48,49,50,\ 51,80,86,87,\ 88,89,97,98,99,100,111,\ 112,113,114,122,\ 123,124,125,136,137,\ 138,139,147,\ 148,149,150}$), 7.44–7.32 (m, 12H, $H_{12,28,35,53,60,78,84,102,103,127,134,152}$), 7.14–6.95 (m, 12H, $H_{10,27,36,52,61,77,85,101,110,126,135,151}$), 5.80–5.75 (m, 2H, $H_{1,2}$), 5.40–5.29 (m, 12H, $H_{16,21,41,46,66,71,90,95,115,120,140,145}$), 4.21–4.1 (m, 24H, $H_{9,29,34,54,59,79,83,103,108,128,133,153}$), 3.90–3.81 (m, 22H, $H_{8,30,33,55,58,81,104,107,129,132,154}$), 3.70–3.27 (m, 36H, $H_{3,4,5,6,7,31,32,56,57,105,106,130,131,155,156,157,158,159}$), 2.27 (m, 2H, H_{82}, overlaps with solvent peak), 1.63–1.42 (m, 36H, $H_{17,22,42,47,67,72,91,96,116,121,141,146}$), **^{13}C NMR** (151 MHz, $CDCl_3/CD_3OD$ 10:1) δ 163.30, 163.29, 163.25, 163.22, 157.16, 149.06, 149.05, 139.28, 139.24, 138.22, 138.20, 134.05, 134.02, 129.59, 129.57, 129.05, 129.03, 127.69, 127.66, 125.46, 125.43, 125.35, 124.73, 124.72, 119.69, 119.67, 116.77, 106.88, 106.83, 106.76, 77.57, 71.16, 71.08, 70.91, 70.90, 70.78, 70.44, 70.06, 69.99, 69.69, 67.69, 31.22, 21.56, 21.51. Due to the high degree of symmetry and reptation, several signals in both the ^{1}H and ^{13}C NMR spectra were not resolved.

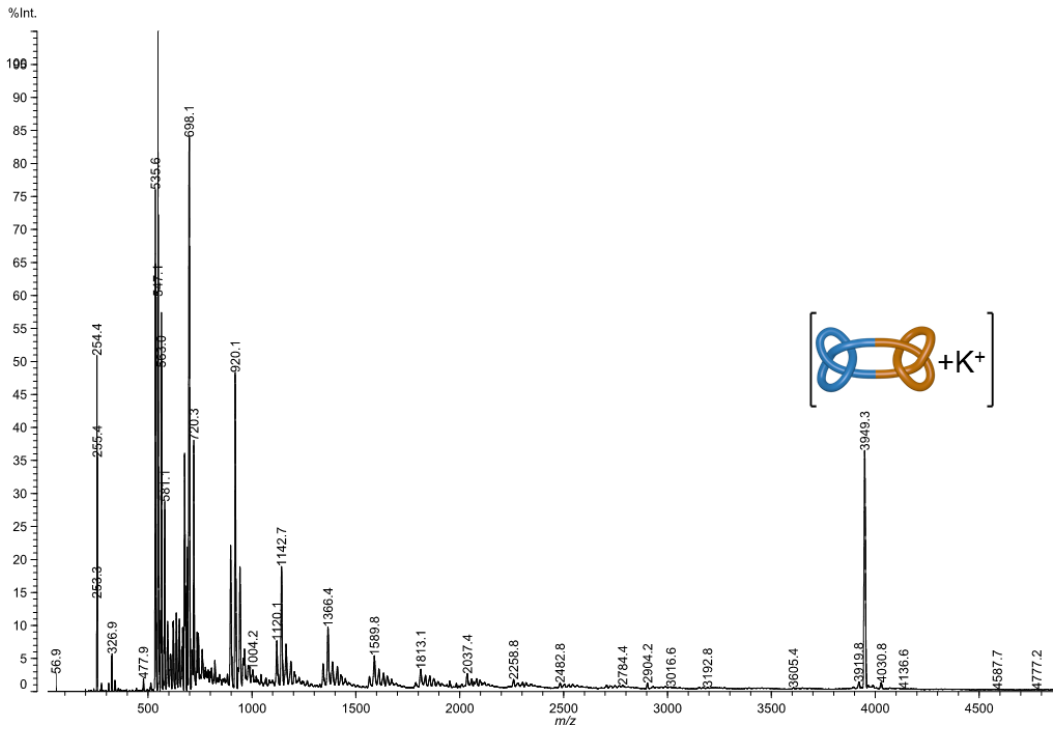


Figure S1. MALDI-TOF MS (positive mode) of demetallated square knot (Λ,Δ)-**1**. Peak observed as the $[M+K]^+$ adduct. Calculated peak (m/z): 3949.6.

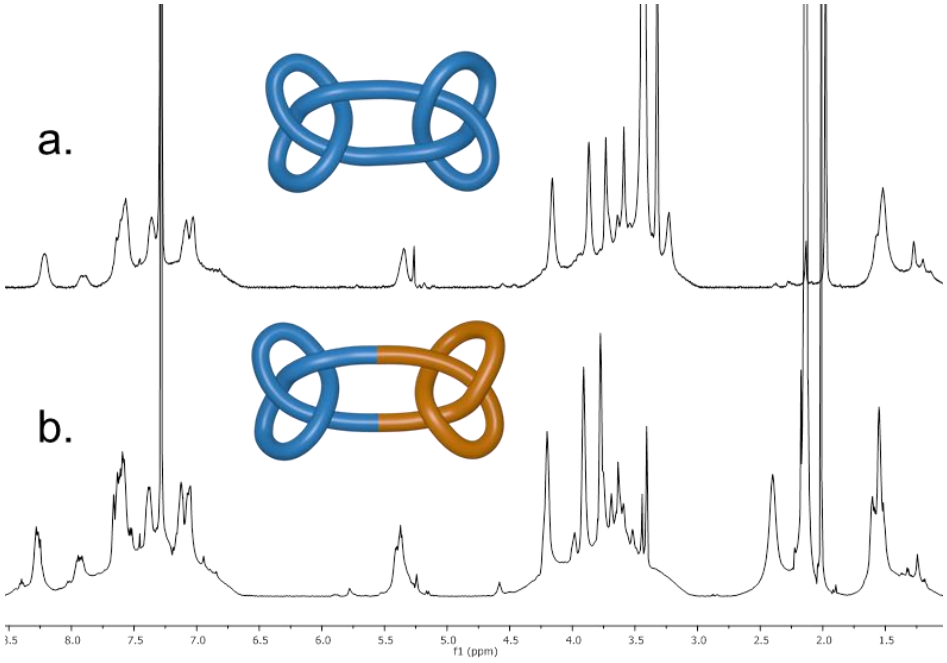


Figure S2. ^{1}H NMR (600 MHz, 298 K, $CDCl_3$/MeOD-*d_4 10:1*) of a) demetallated granny knot (Λ,Λ)-**1** (top) and b) demetallated square knot (Λ,Δ)-**1** (bottom).

To remetallate the wholly organic composite knot, the following procedure was used: To a stirred solution of (Λ,Λ)-**1** (2.1 mg, 0.5 μmol) in MeCN at 80°C was added lutetium trifluoromethanesulfonate (3.3 mg, 5 μmol) and the solution was stirred for 18 h. The solvent was then concentrated under reduced pressure, and the solid obtained was triturated with

$CHCl_3$ solution to reobtain (Λ,Λ)-**1**•$[Lu]_2$ with full mass balance. The doubly remetallated knot was confirmed by ESI-MS (Figure S3).

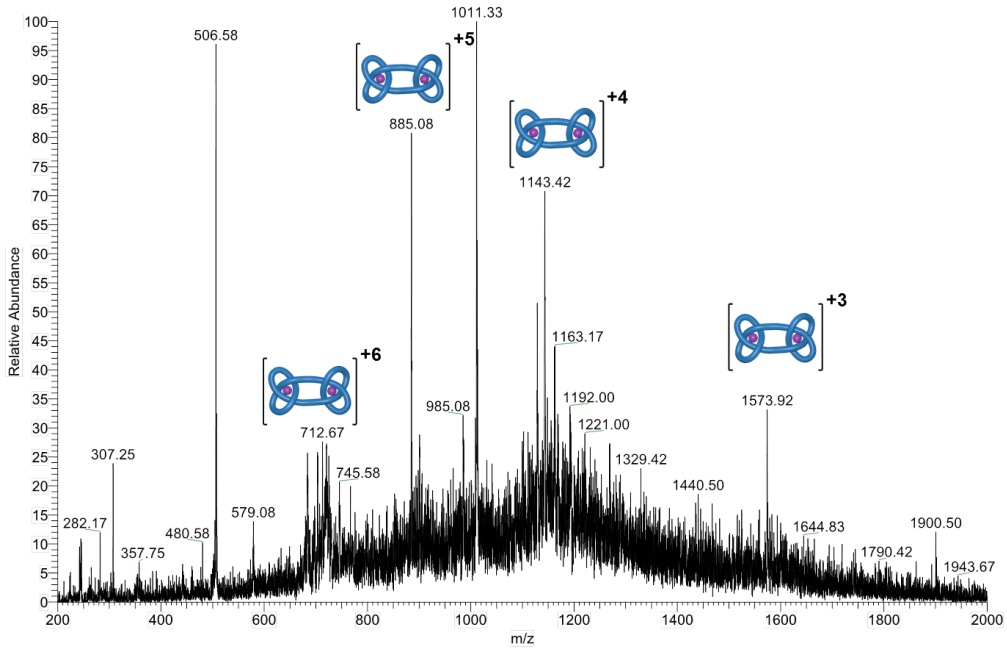
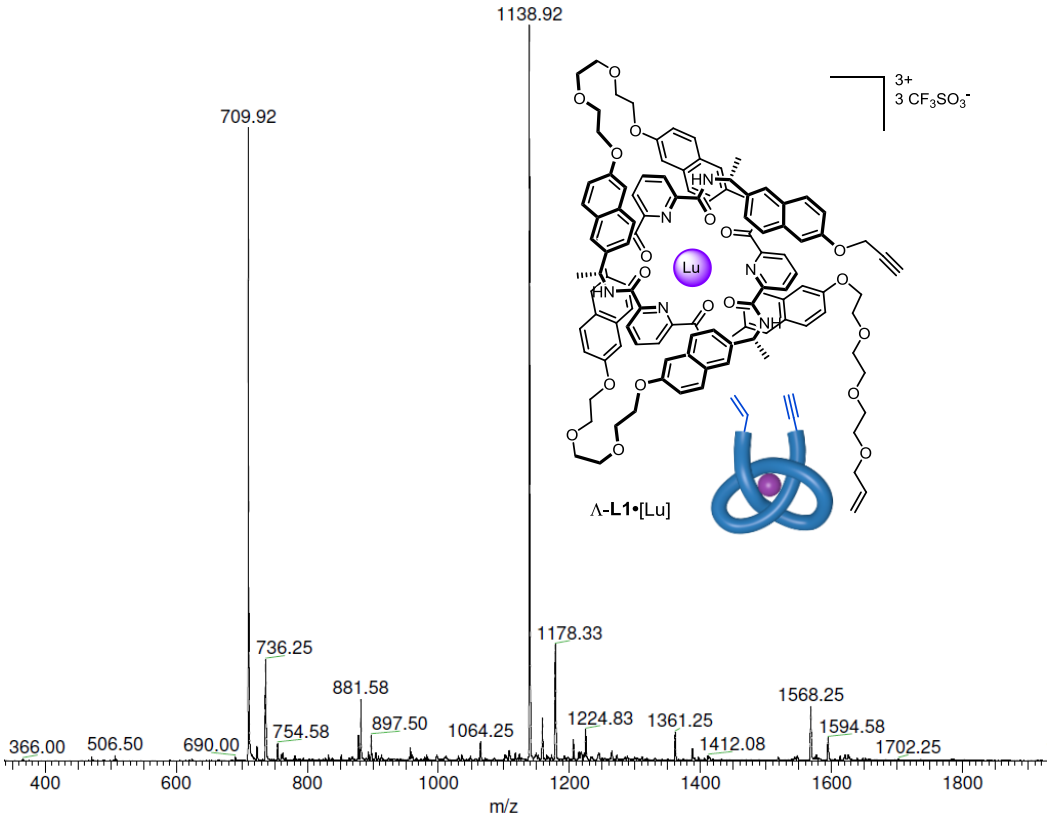


Figure S3. Low resolution ESI-MS (+ mode) of the crude remetallation mixture after mixing organic (Λ,Λ)-**1** knot with excess $Lu(CF_3SO_3)_3$ to obtain (Λ,Λ)-**1**•$[Lu]_2$ (all peaks observed as the $[(Λ,Λ)\text{-}\mathbf{1}\bullet[Lu]_2 - n(CF_3SO_3)]^{n+}$ adducts).

S5. MASS SPECTRA



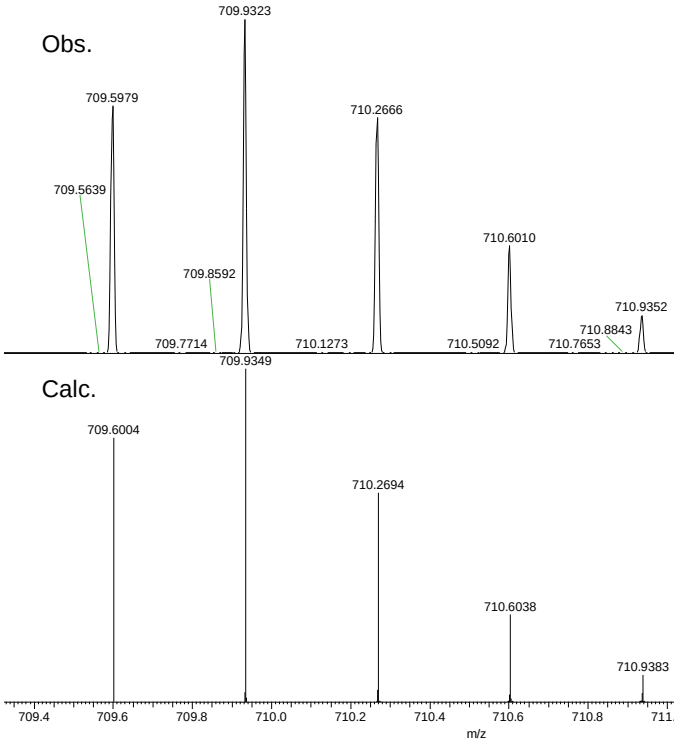
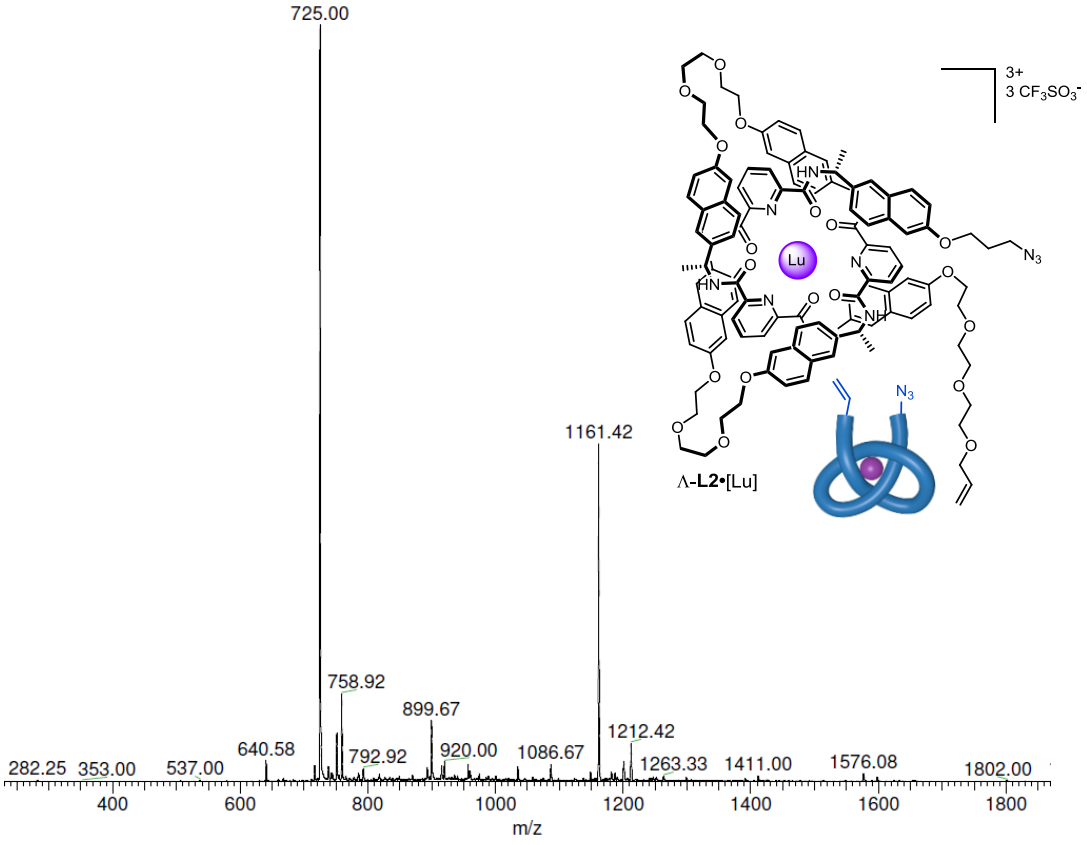


Figure S4. a) Low resolution ESI-MS (positive mode) of Λ-**L1**•[Lu] (all peaks observed as the [Λ-**L1**•[Lu] - n(CF_3SO_3)]$^{n+}$ adducts). b) High-resolution ESI-MS isotopic distribution of Λ-**L1**•[Lu] $[M]^{3+}$, observed (top) and predicted (bottom).



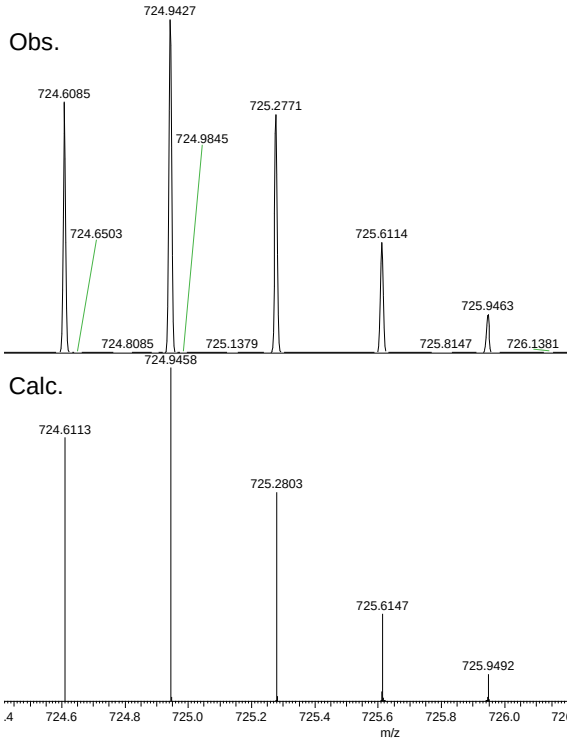


Figure S5. a) Low resolution ESI-MS (positive mode) of Λ-**L2**•[Lu] (all peaks observed as the [Λ-**L2**•[Lu] - n(CF_3SO_3)]$^{n+}$ adducts). b) High-resolution ESI-MS isotopic distribution of Λ-**L2**•[Lu] $[M]^{3+}$, observed (top) and predicted (bottom).

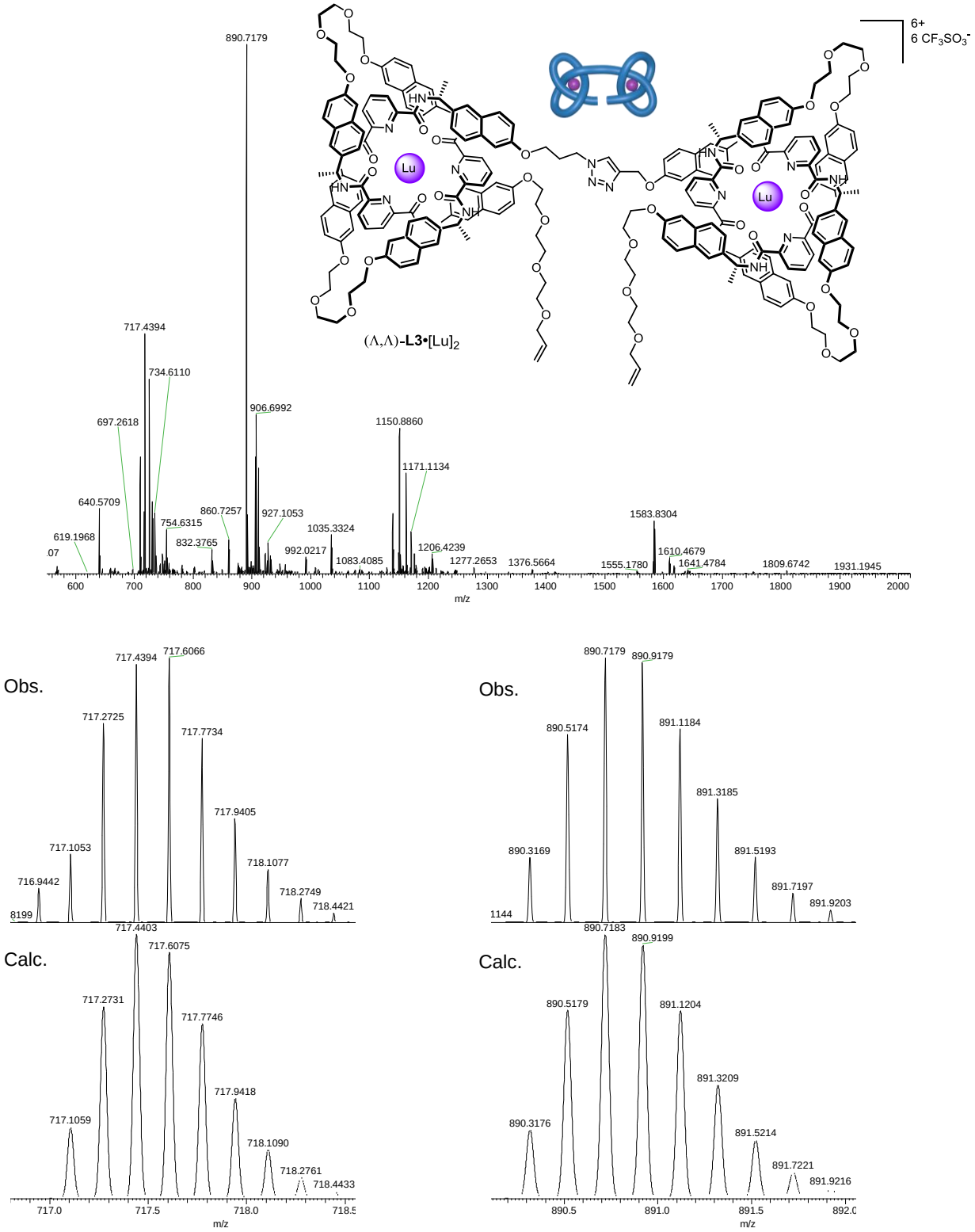


Figure S6. a) Low resolution ESI-MS (positive mode) of (Λ,Λ)-**L3**•$[Lu]_2$ (all peaks observed as the $[(Λ,Λ)\text{-}\mathbf{L3}\bullet[Lu]_2 - n(CF_3SO_3)]^{n+}$ adducts). b) High-resolution ESI-MS isotopic distribution of (Λ,Λ)-**L3**•$[Lu]_2$ $[M]^{6+}$ (left) and $[M+(CF_3SO_3)]^{5+}$ (right), with observed spectra above and predicted below.

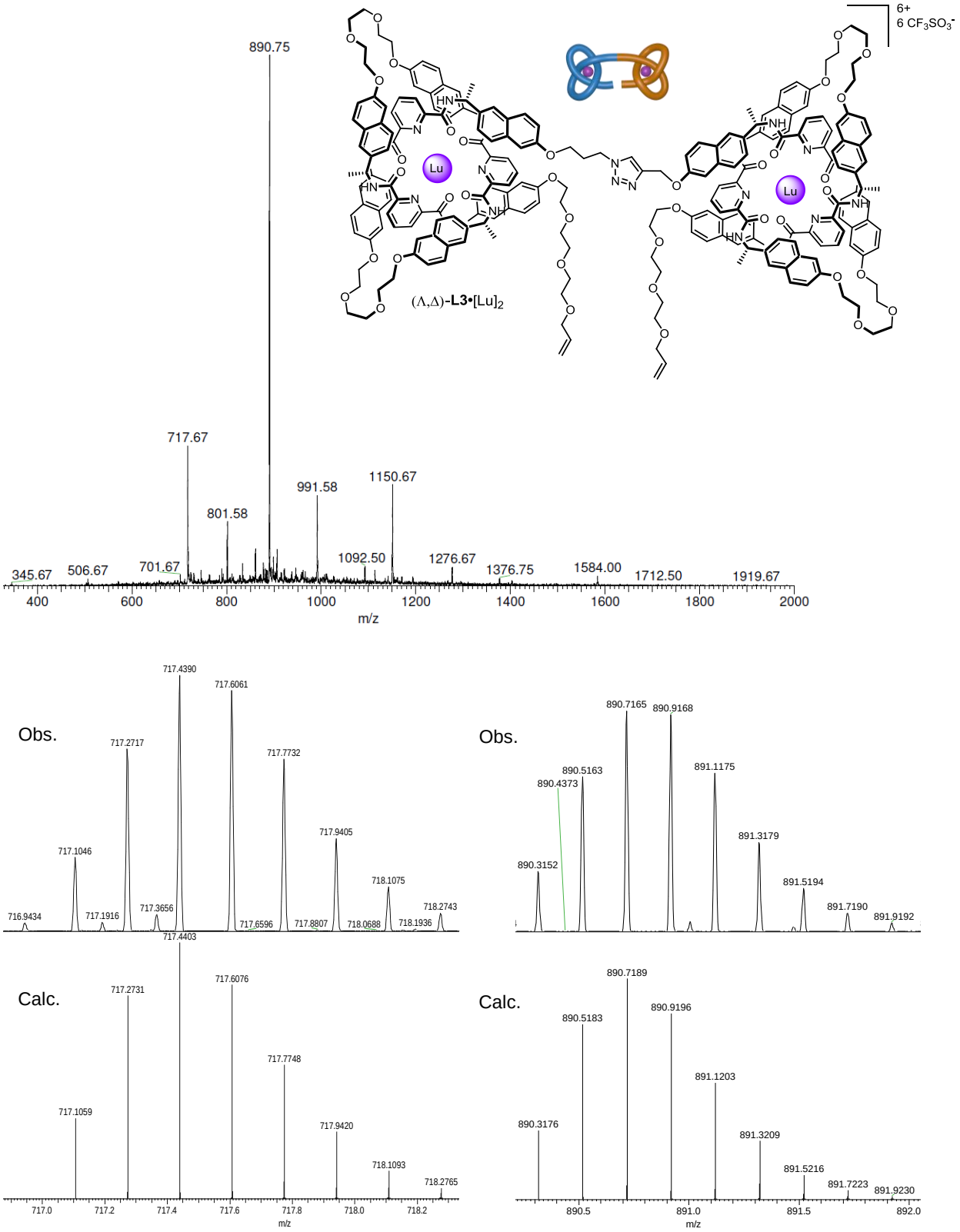


Figure S7. a) Low resolution ESI-MS (positive mode) of (Λ,Δ)-**L3**•$[Lu]_2$ (all peaks observed as the $[(Λ,Δ)\text{-}\mathbf{L3}\bullet[Lu]_2 - n(CF_3SO_3)]^{n+}$ adducts). b) High-resolution ESI-MS isotopic distribution of (Λ,Δ)-**L3**•$[Lu]_2$ $[M]^{6+}$ (left) and $[M+(CF_3SO_3)]^{5+}$ (right), with observed spectra above and predicted below.

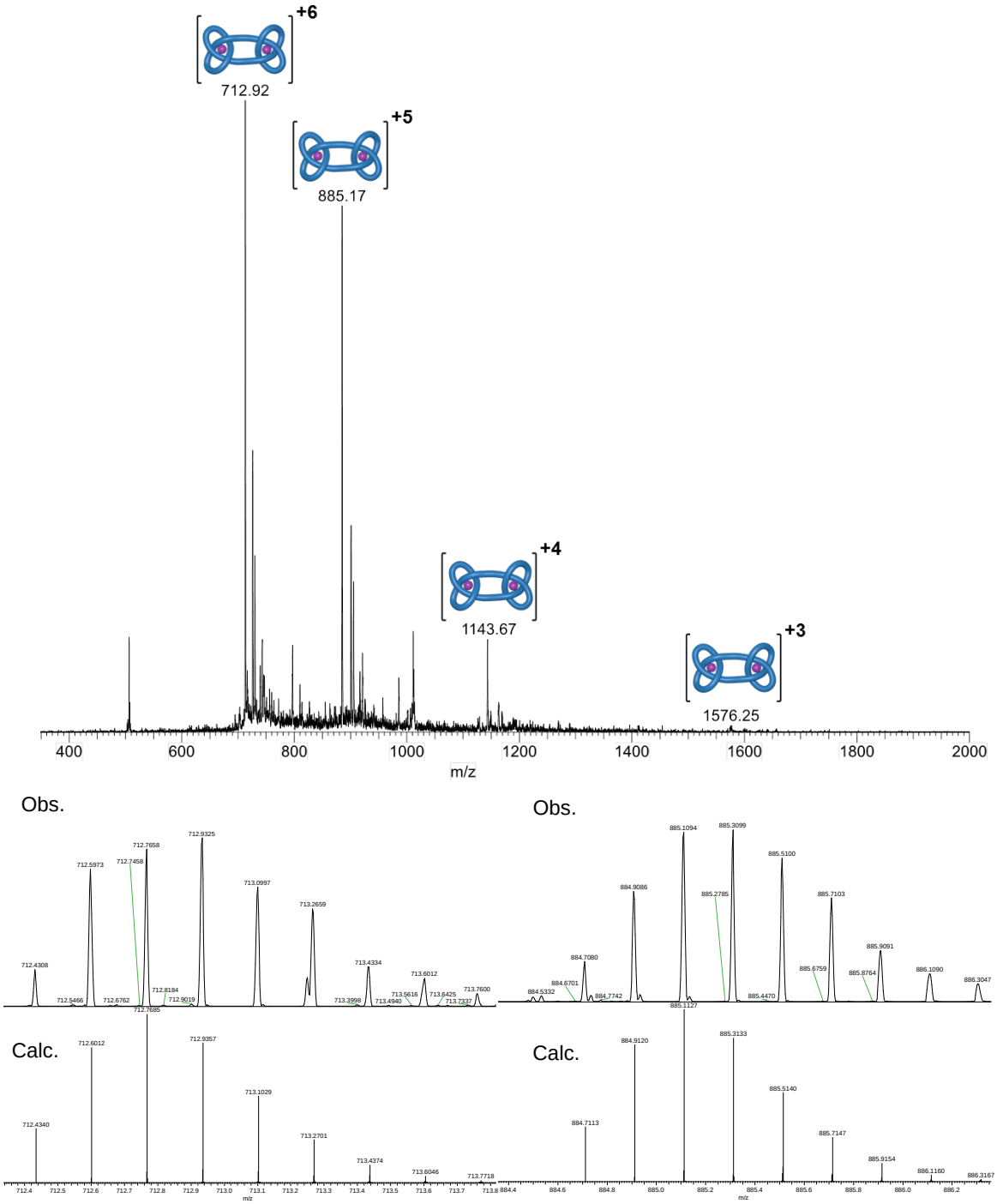


Figure S8. a) Low resolution ESI-MS (positive mode) of (Λ,Λ)-**1**•$[Lu]_2$ (all peaks observed as the $[(Λ,Λ)\text{-}\mathbf{1}\bullet[Lu]_2 - n(CF_3SO_3)]^{n+}$ adducts). b) High-resolution ESI-MS isotopic distribution of (Λ,Λ)-**1**•$[Lu]_2$ $[M]^{6+}$ (left) and $[M]^{5+}$ (right), with observed spectra above and predicted below.

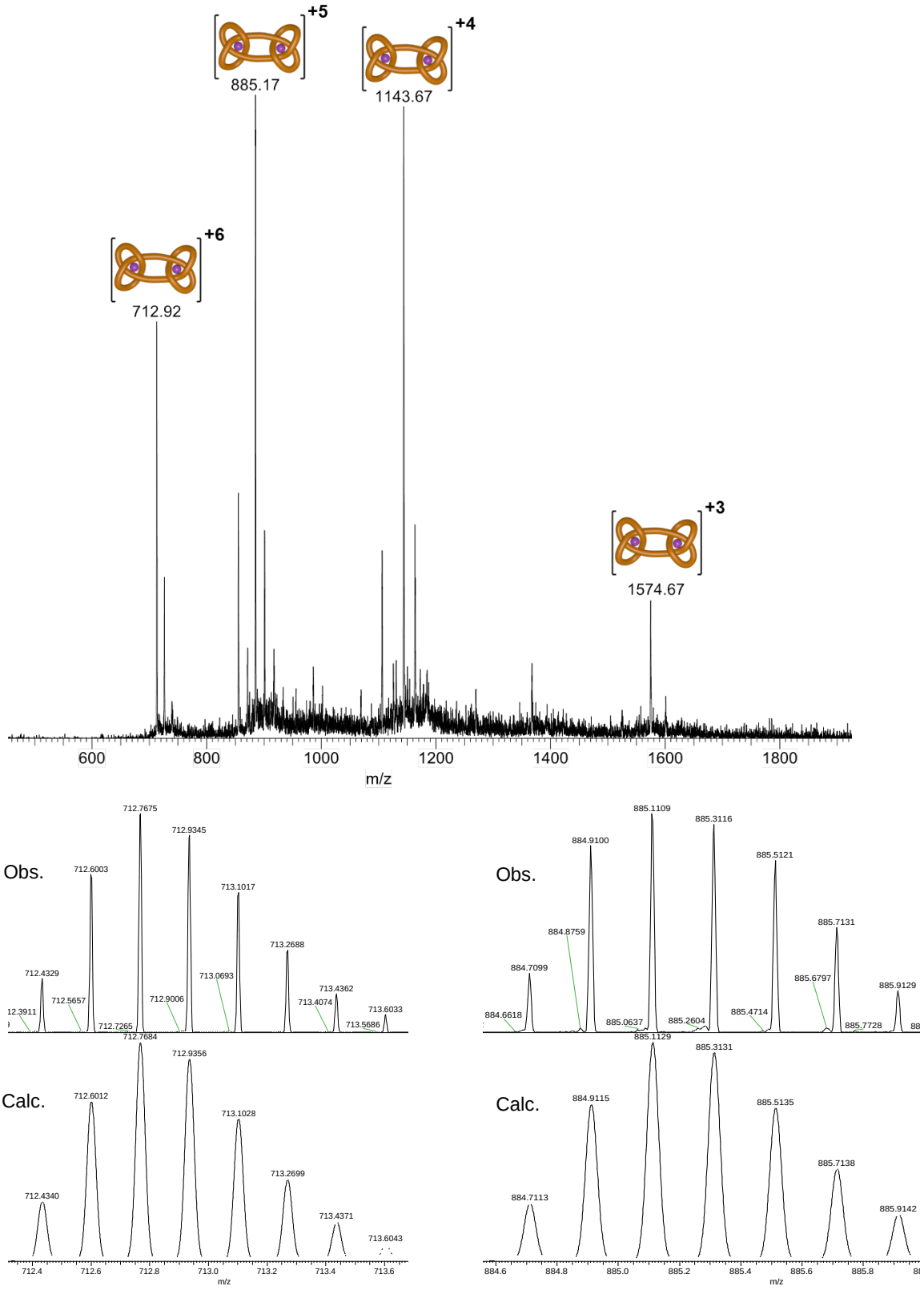


Figure S9. a) Low resolution ESI-MS (positive mode) of (Δ,Δ)-**1**•$[Lu]_2$ (all peaks observed as the $[(\Delta,\Delta)\text{-}\mathbf{1}\bullet[Lu]_2 - n(CF_3SO_3)]^{n+}$ adducts). b) High-resolution ESI-MS isotopic distribution of (Δ,Δ)-**1**•$[Lu]_2$ $[M]^{6+}$ (left) and $[M+(CF_3SO_3)]^{5+}$ (right), with observed spectra above and predicted below.

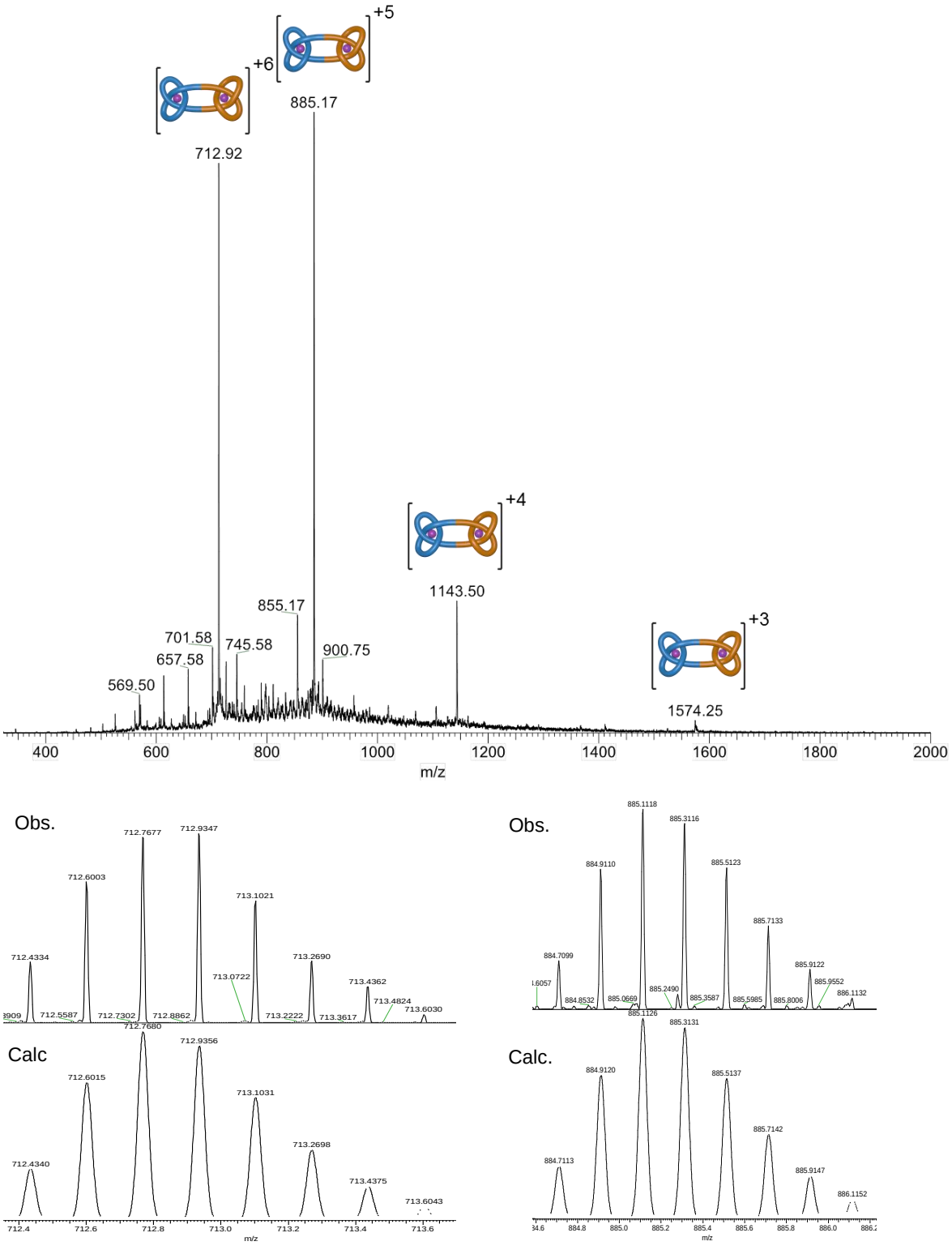
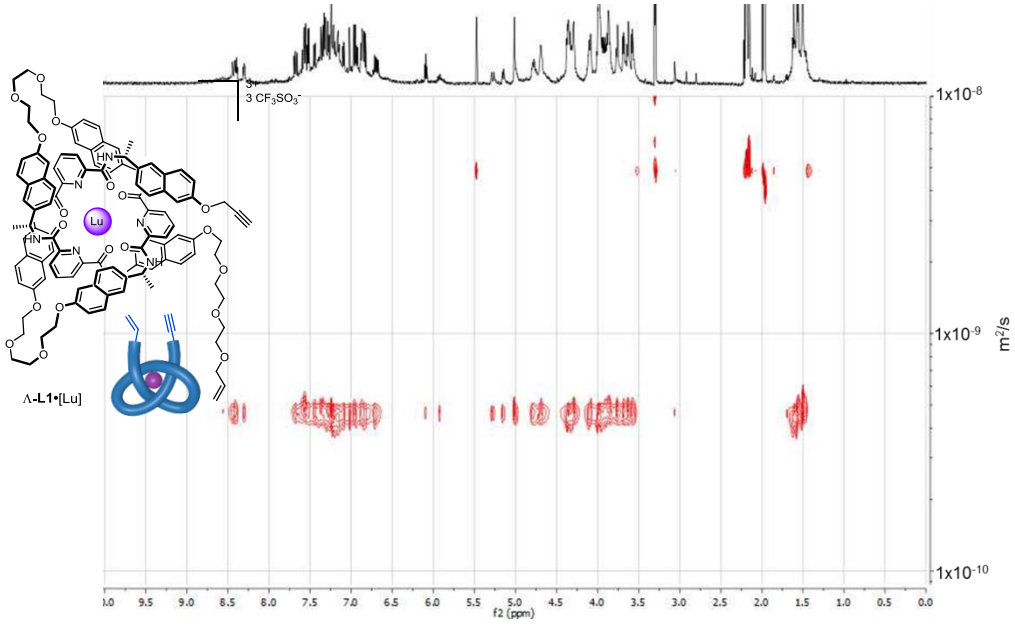
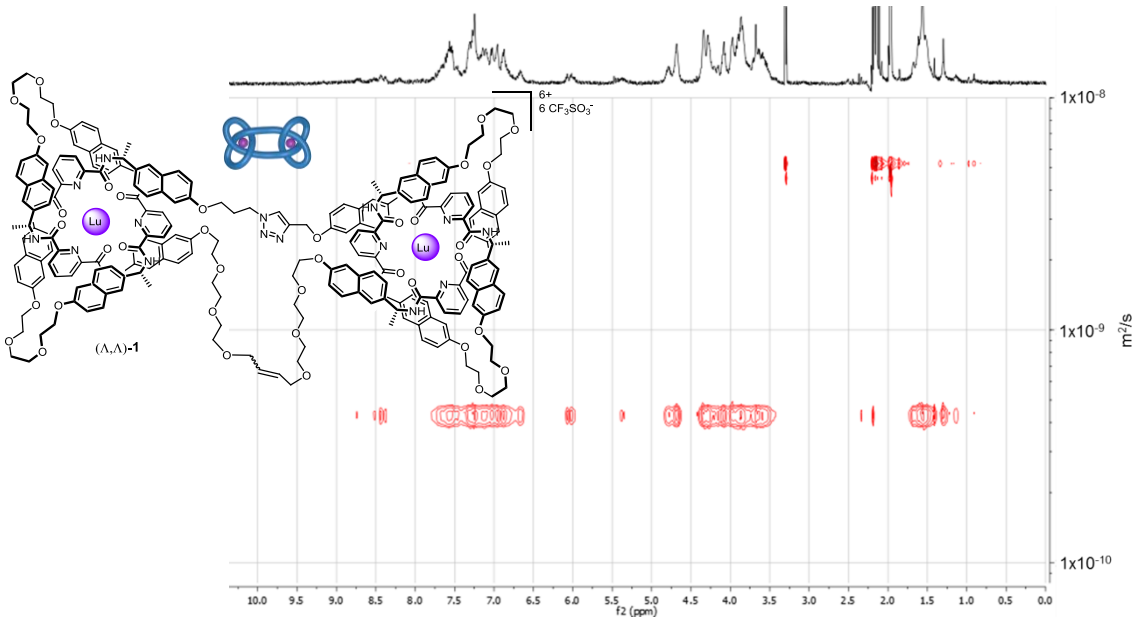


Figure S10. a) Low resolution ESI-MS (positive mode) of (Λ,Δ)-**1**•$[Lu]_2$ (all peaks observed as the $[(Λ,Δ)\text{-}\mathbf{1}\bullet[Lu]_2 - n(CF_3SO_3)]^{n+}$ adducts). b) High-resolution ESI-MS isotopic distribution of (Λ,Δ)-**1**•$[Lu]_2$ $[M]^{6+}$ (left) and $[M+(CF_3SO_3)]^{5+}$ (right), with observed spectra above and predicted below.

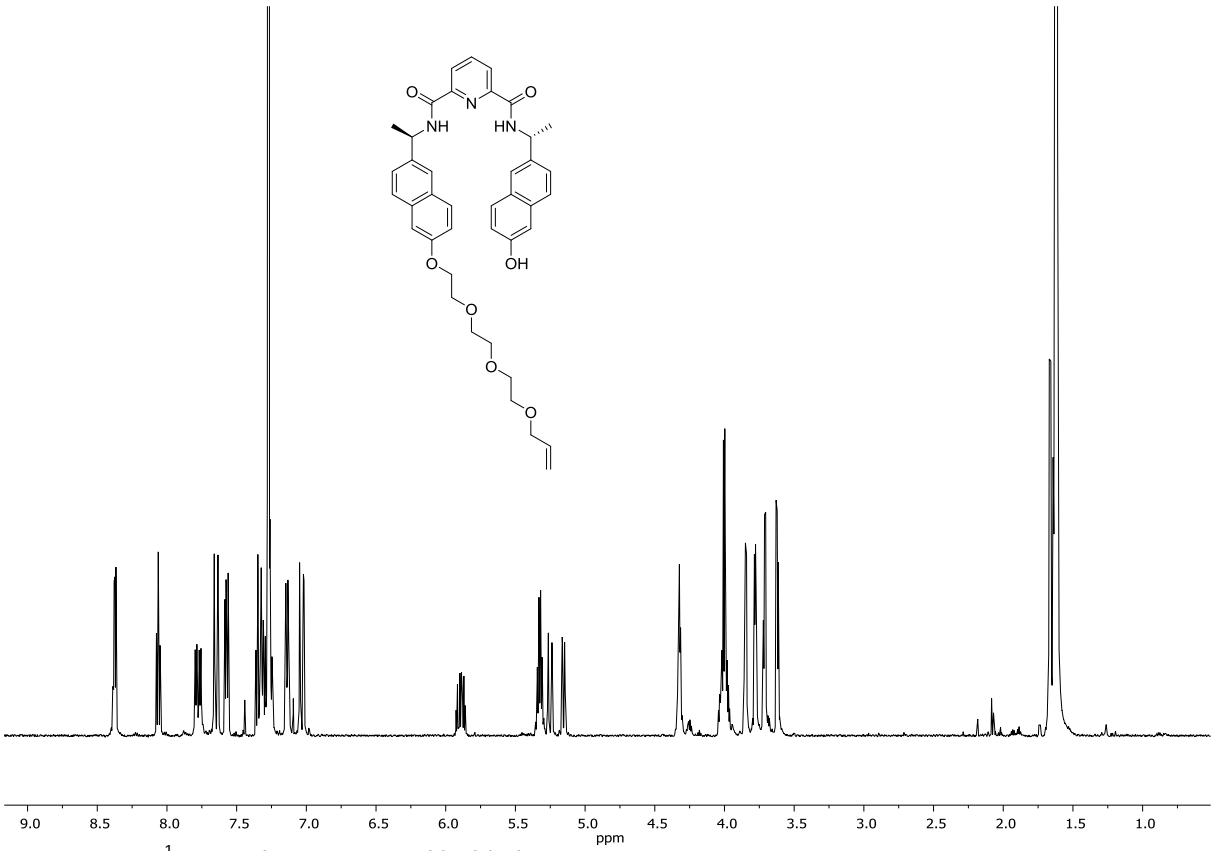
S6. NMR SPECTRA



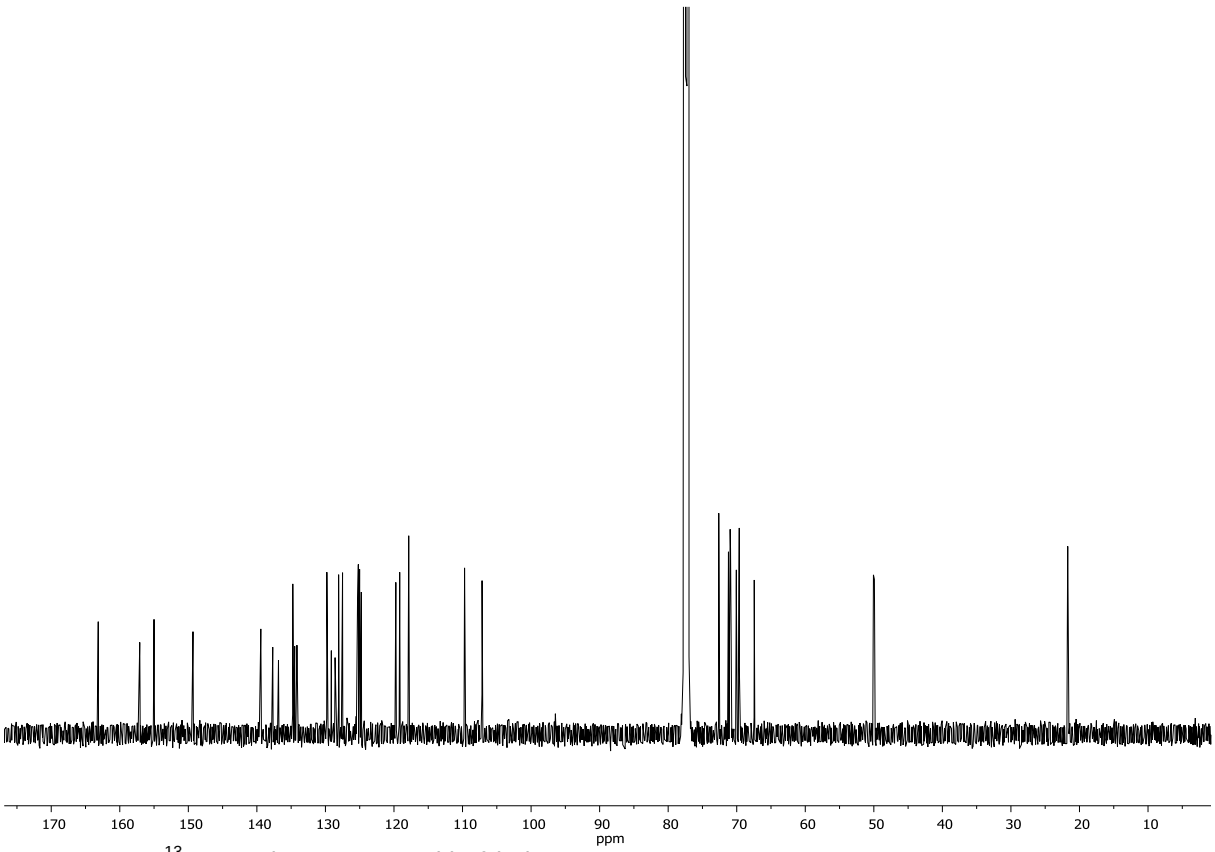
Spectrum S1. DOSY NMR (600 MHz, 298 K, MeCN-d_3) of Λ-**L1**•[Lu].



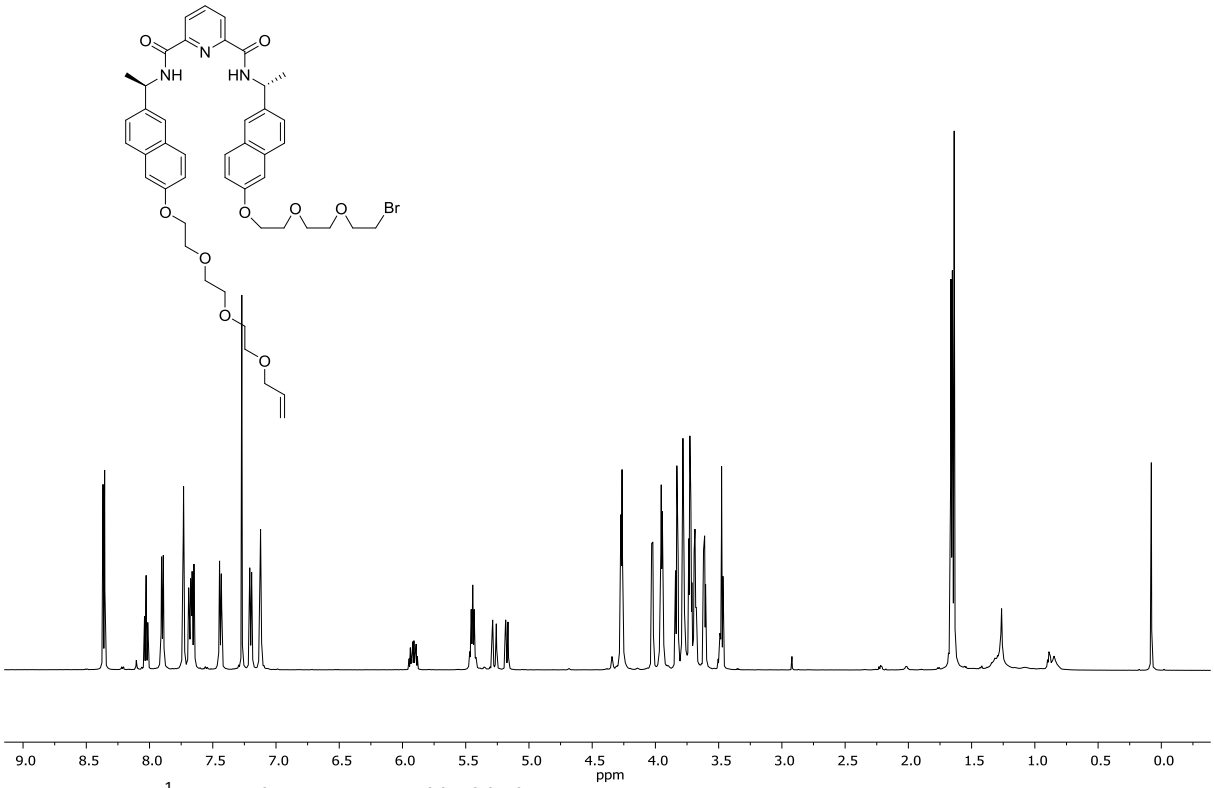
Spectrum S2. DOSY NMR (600 MHz, 298 K, MeCN-d_3) of (Λ,Λ)-**1**•$[Lu]_2$.



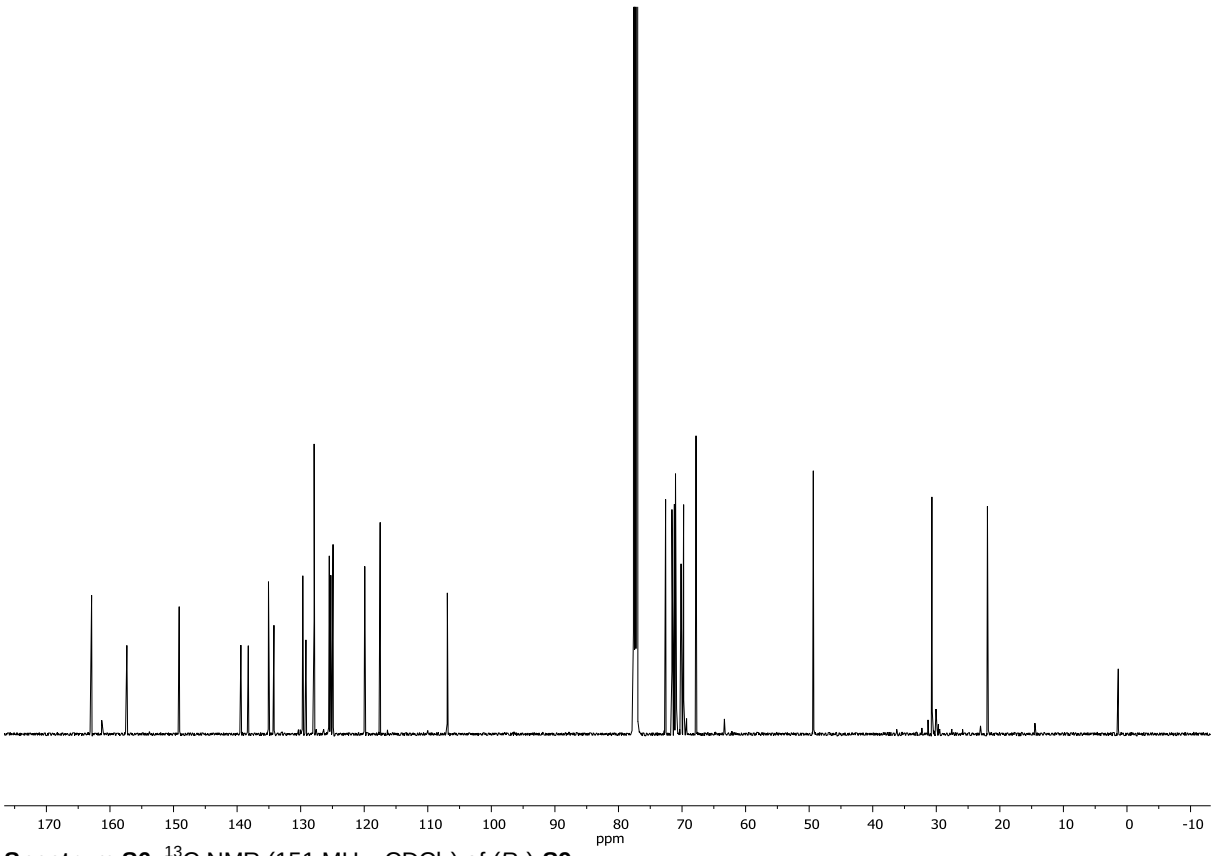
Spectrum S3. ^{1}H NMR (600 MHz, $CDCl_3$) of (R_2)-**S8**.



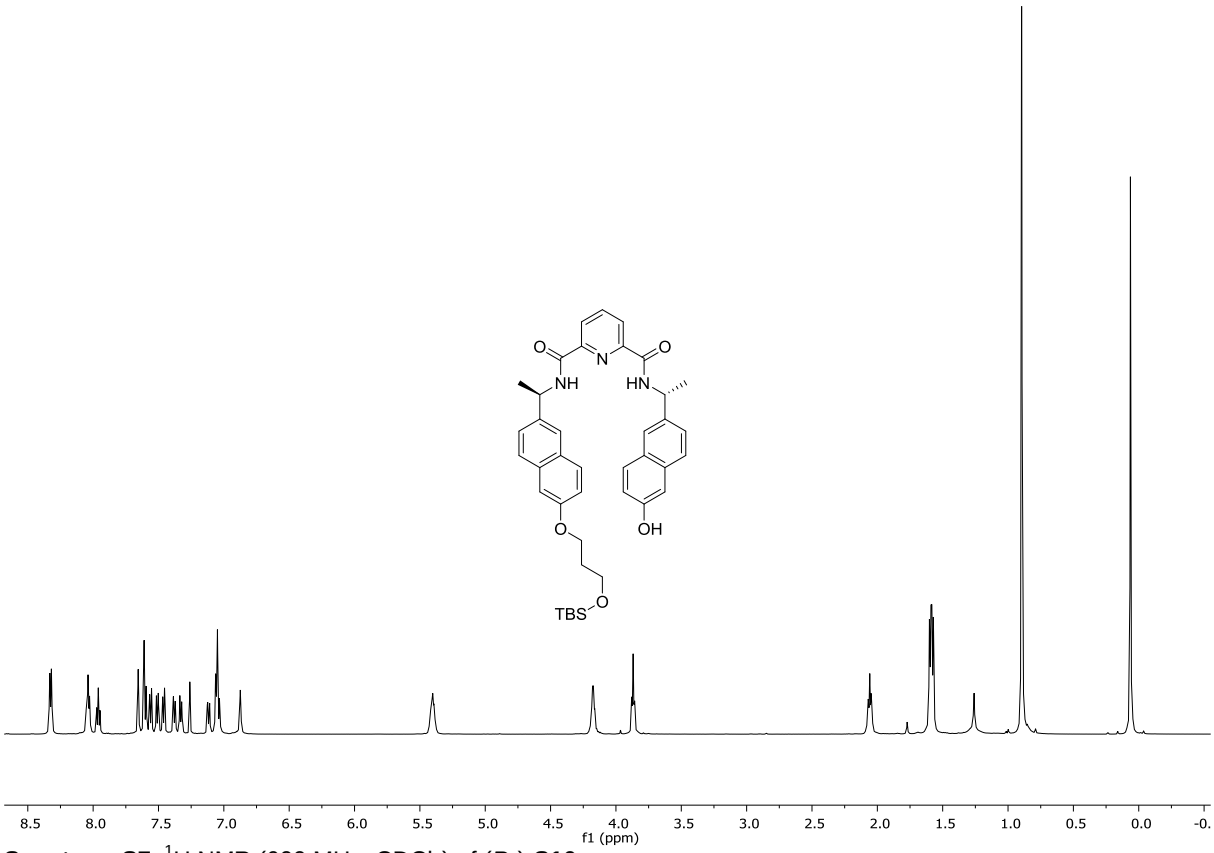
Spectrum S4. ^{13}C NMR (151 MHz, $CDCl_3$) of (R_2)-**S8**.



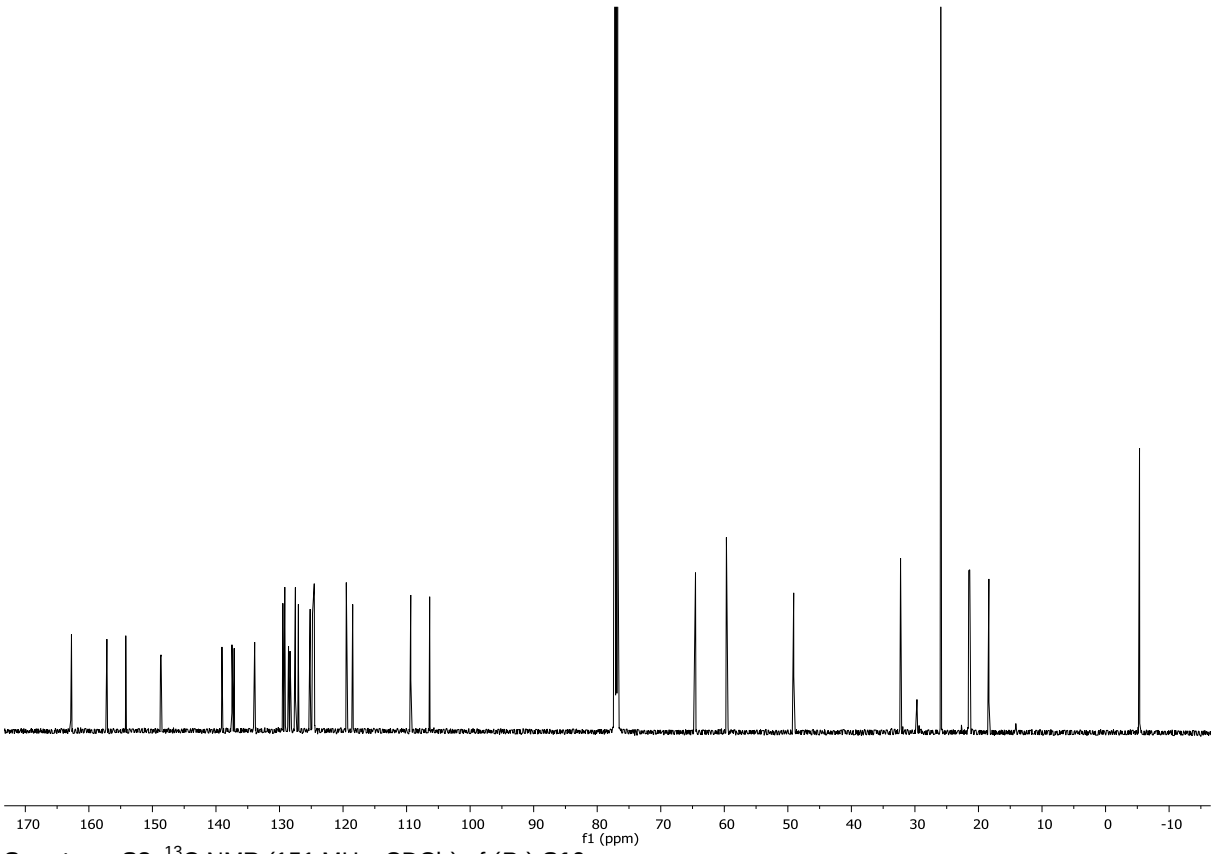
Spectrum S5. ^{1}H NMR (600 MHz, $CDCl_3$) of (R_2)-**S9**.



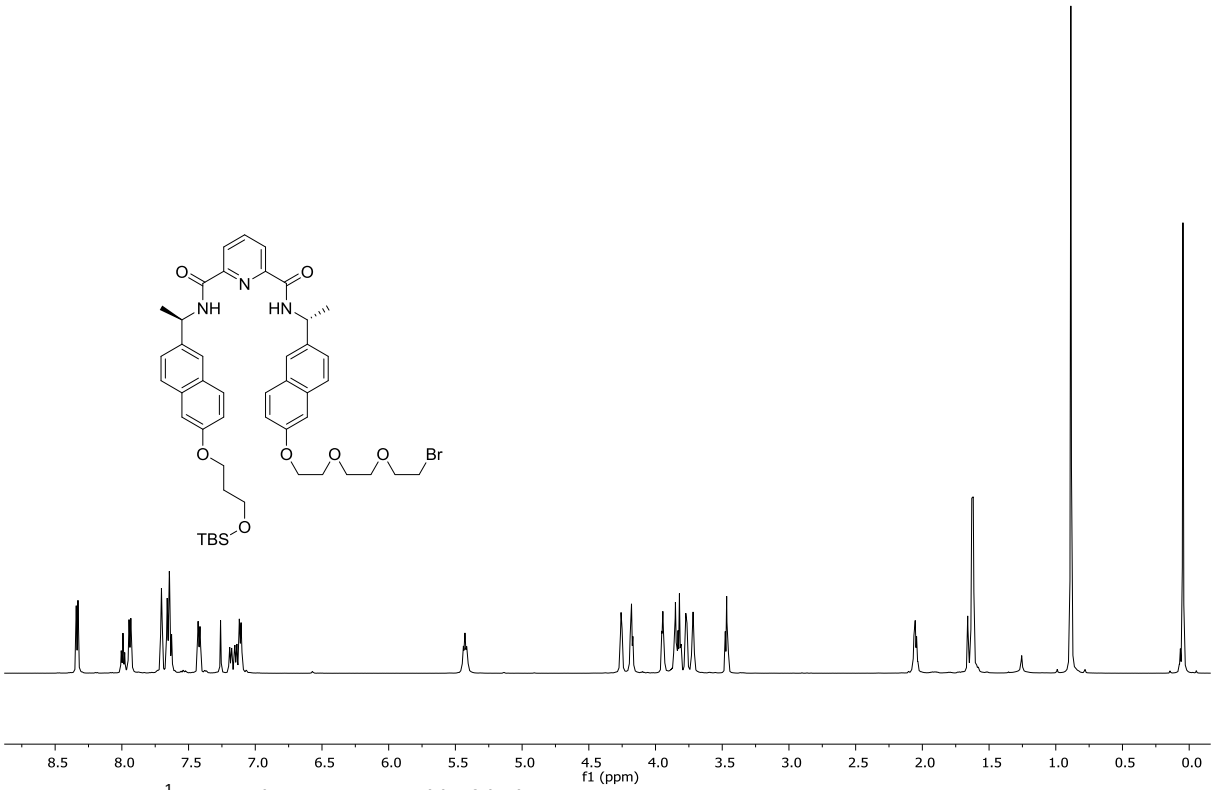
Spectrum S6. ^{13}C NMR (151 MHz, $CDCl_3$) of (R_2)-**S9**.



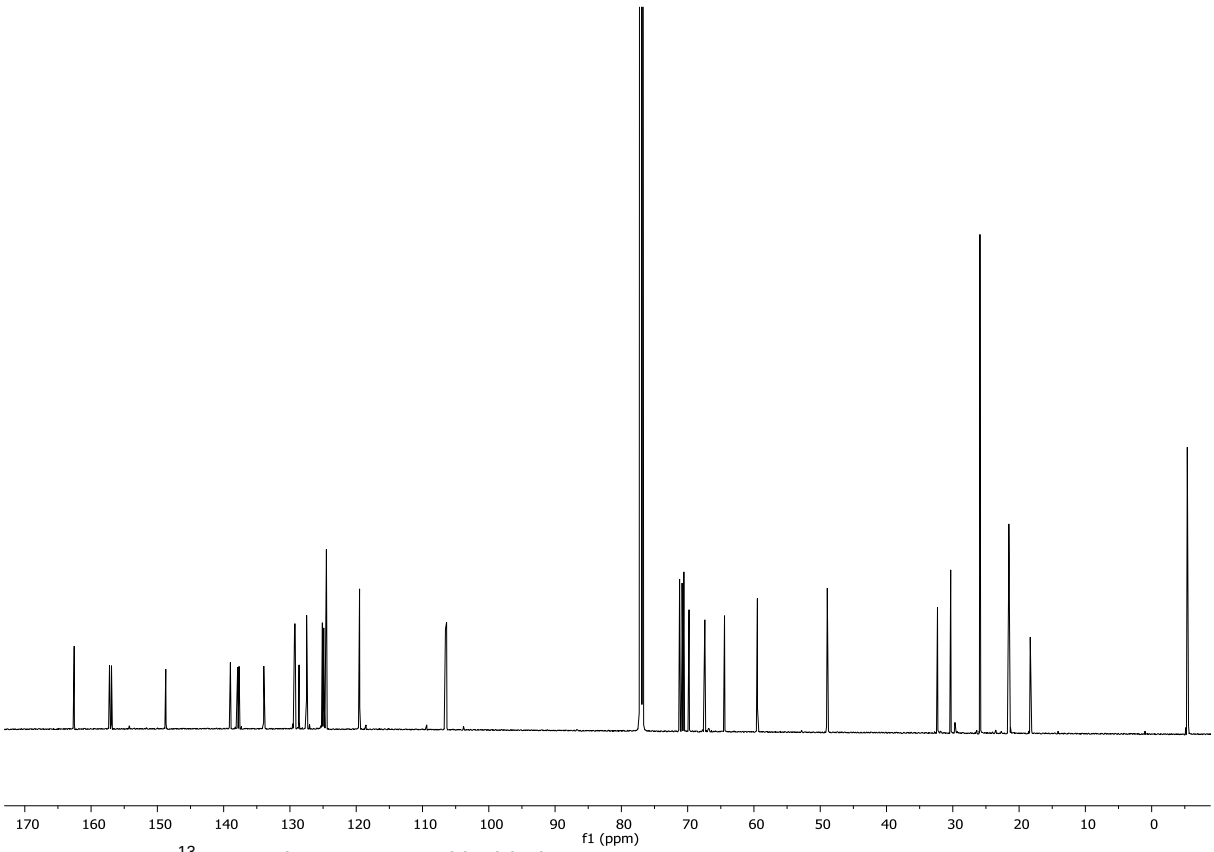
Spectrum S7. ^{1}H NMR (600 MHz, $CDCl_3$) of (R_2)-**S10**.



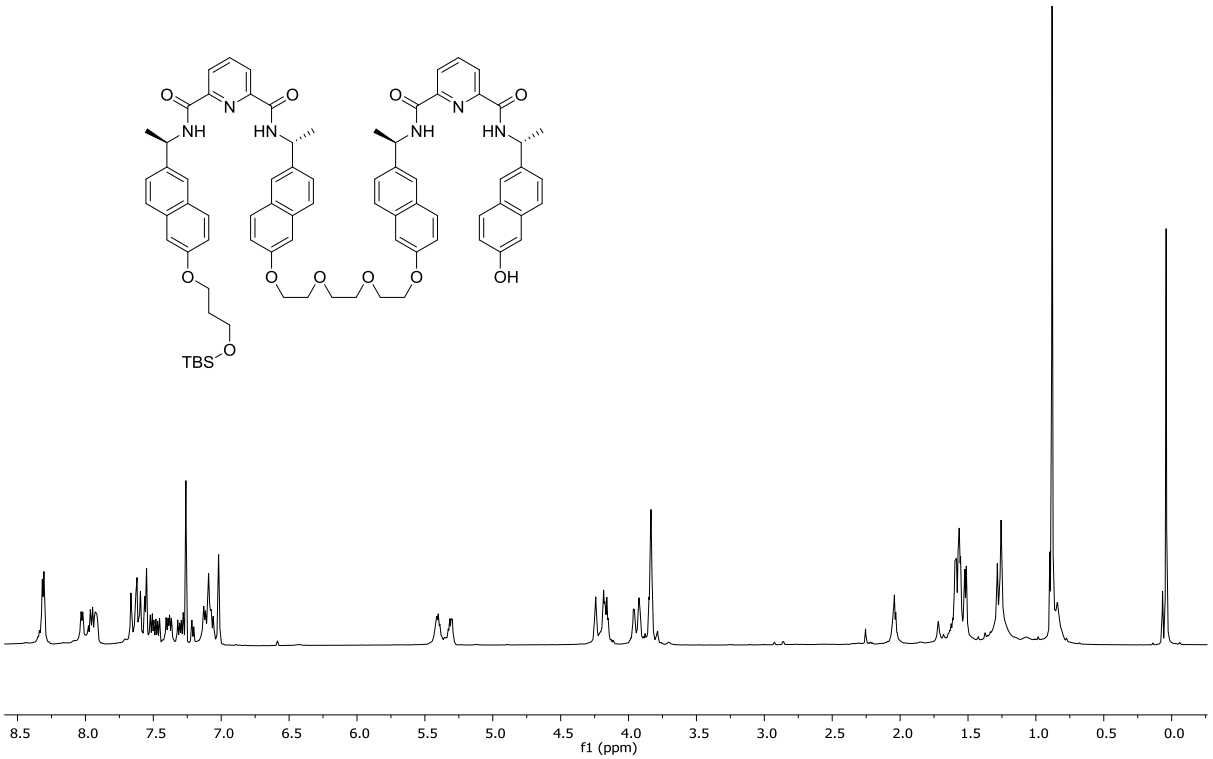
Spectrum S8. ^{13}C NMR (151 MHz, $CDCl_3$) of (R_2)-**S10**.



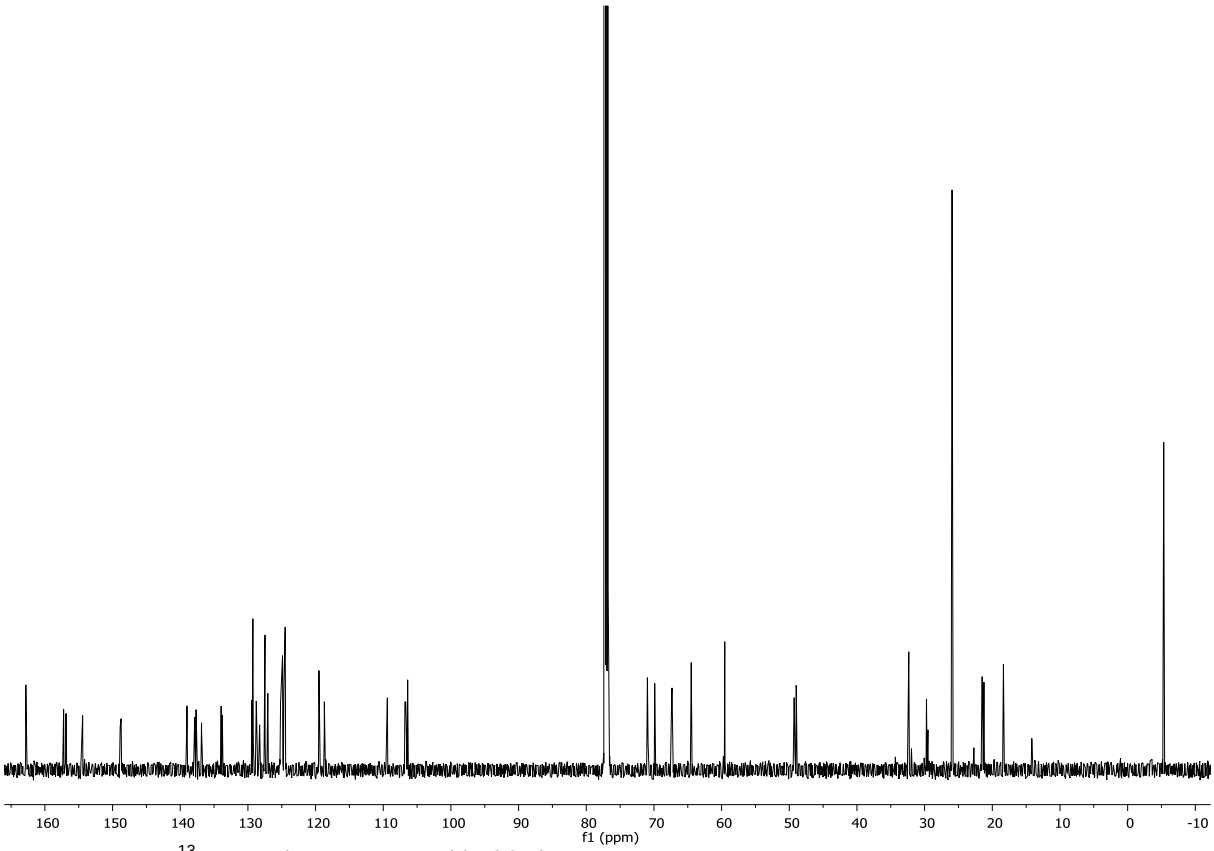
Spectrum S9. ^{1}H NMR (600 MHz, $CDCl_3$) of (R_2)-**S11**.



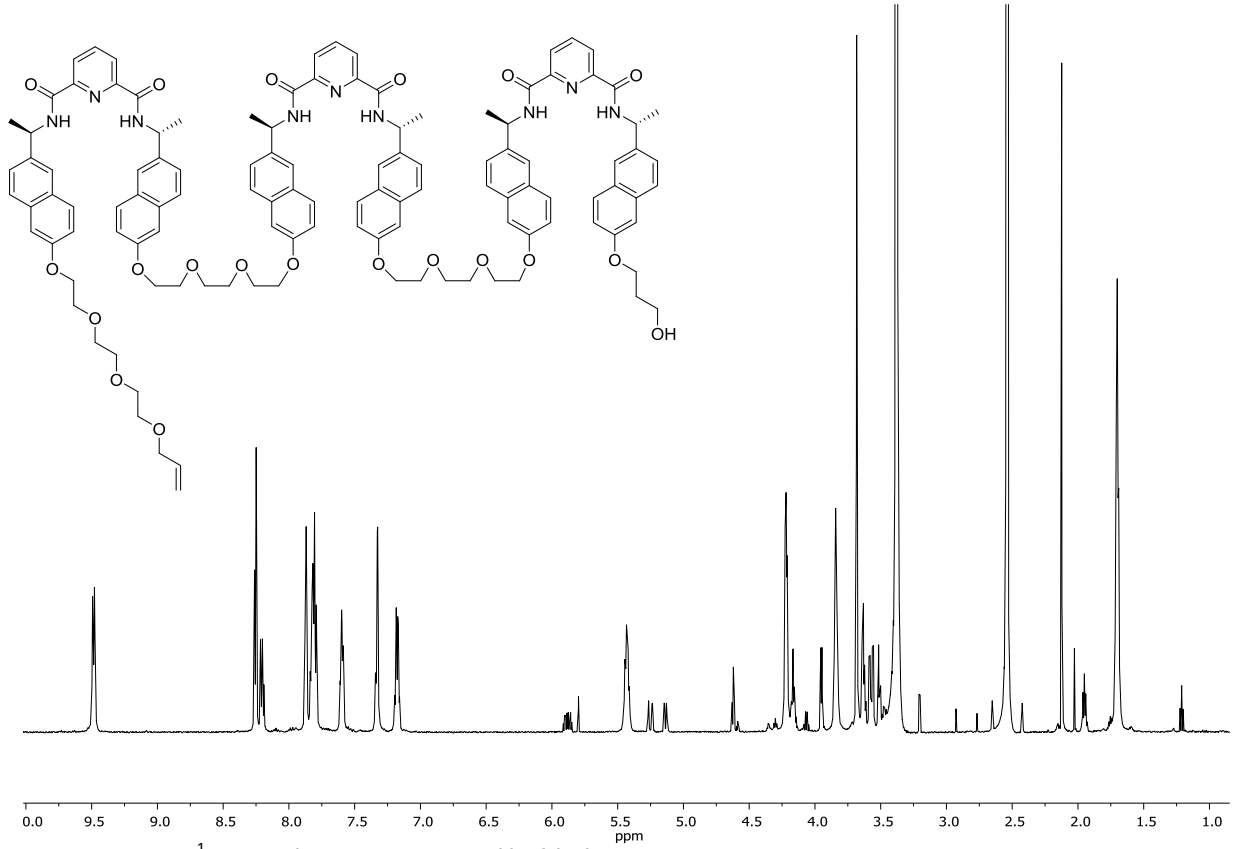
Spectrum S10. ^{13}C NMR (151 MHz, $CDCl_3$) of (R_2)-**S11**.



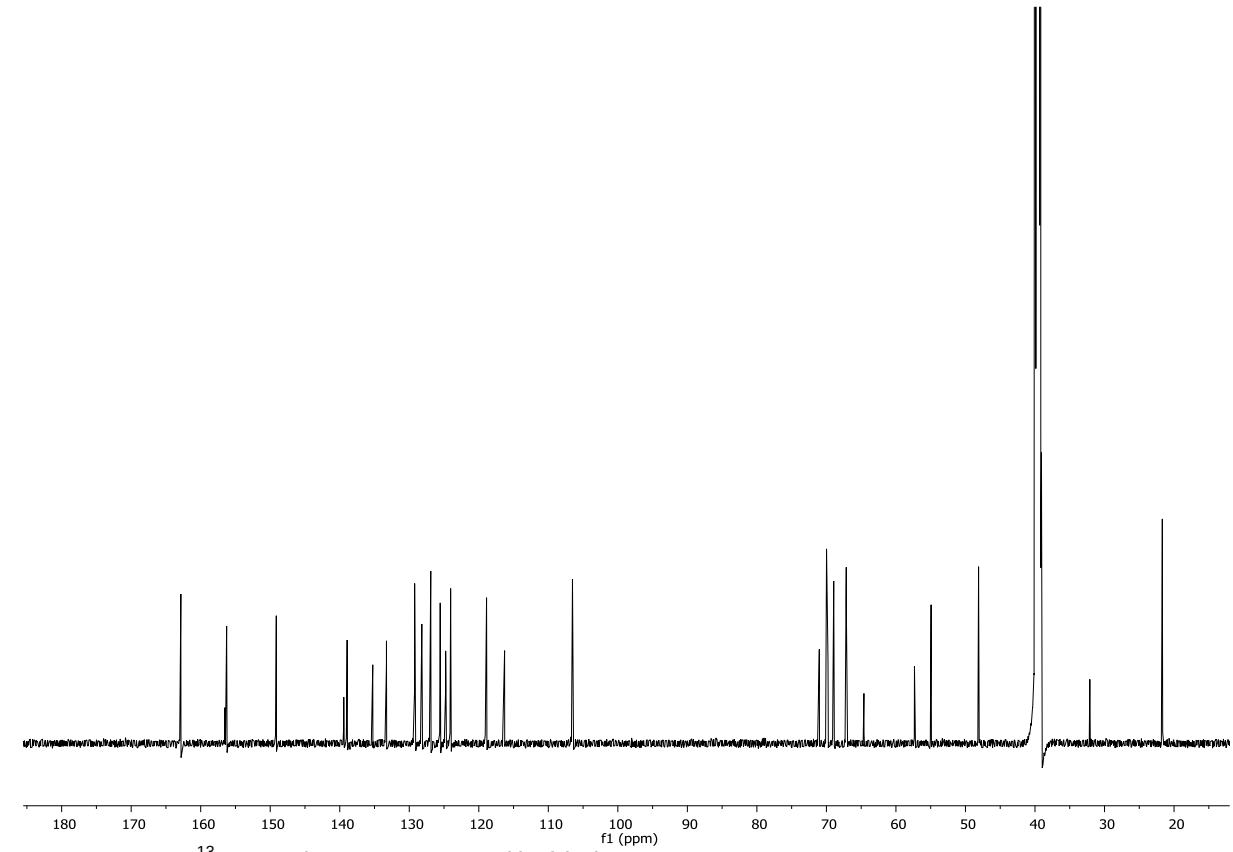
Spectrum S11. ^{1}H NMR (600 MHz, $CDCl_3$) of (R_4)-**S12**.



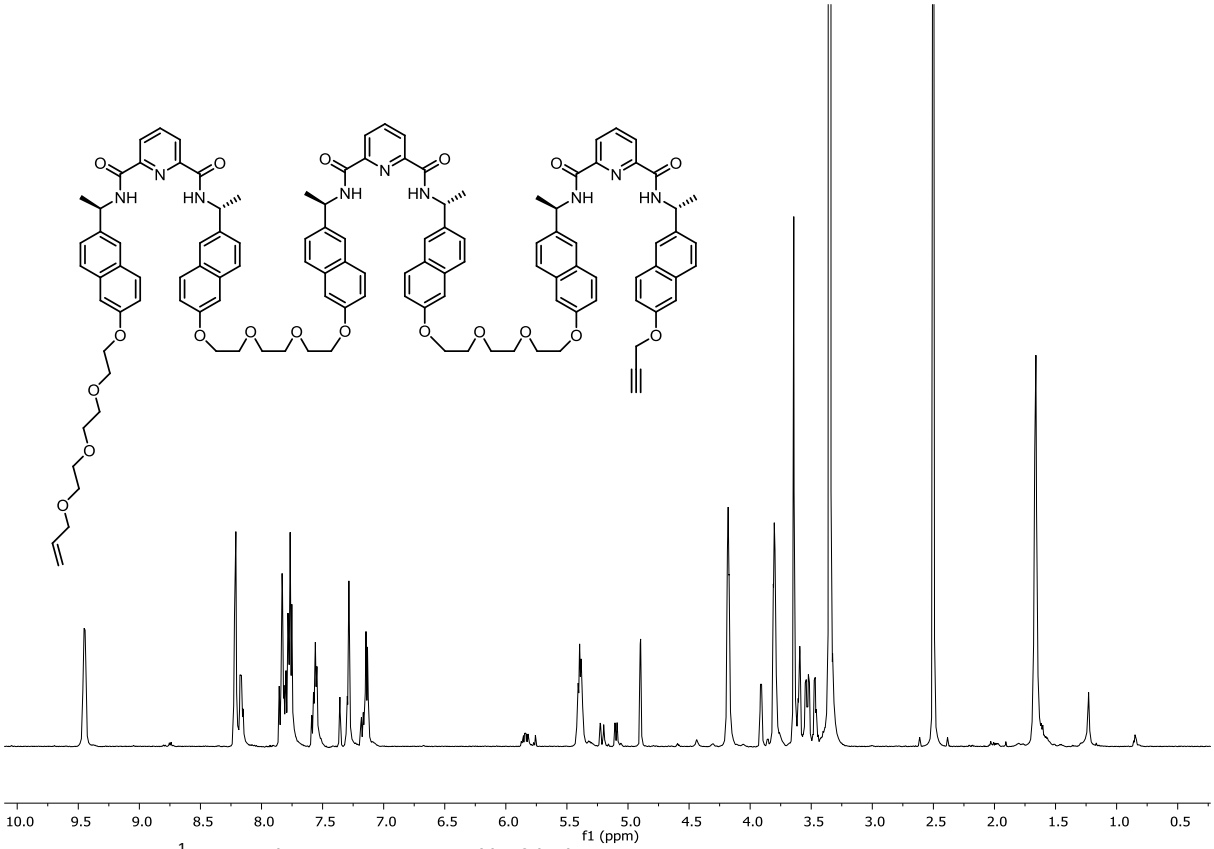
Spectrum S12. ^{13}C NMR (151 MHz, $CDCl_3$) of (R_4)-**S12**.



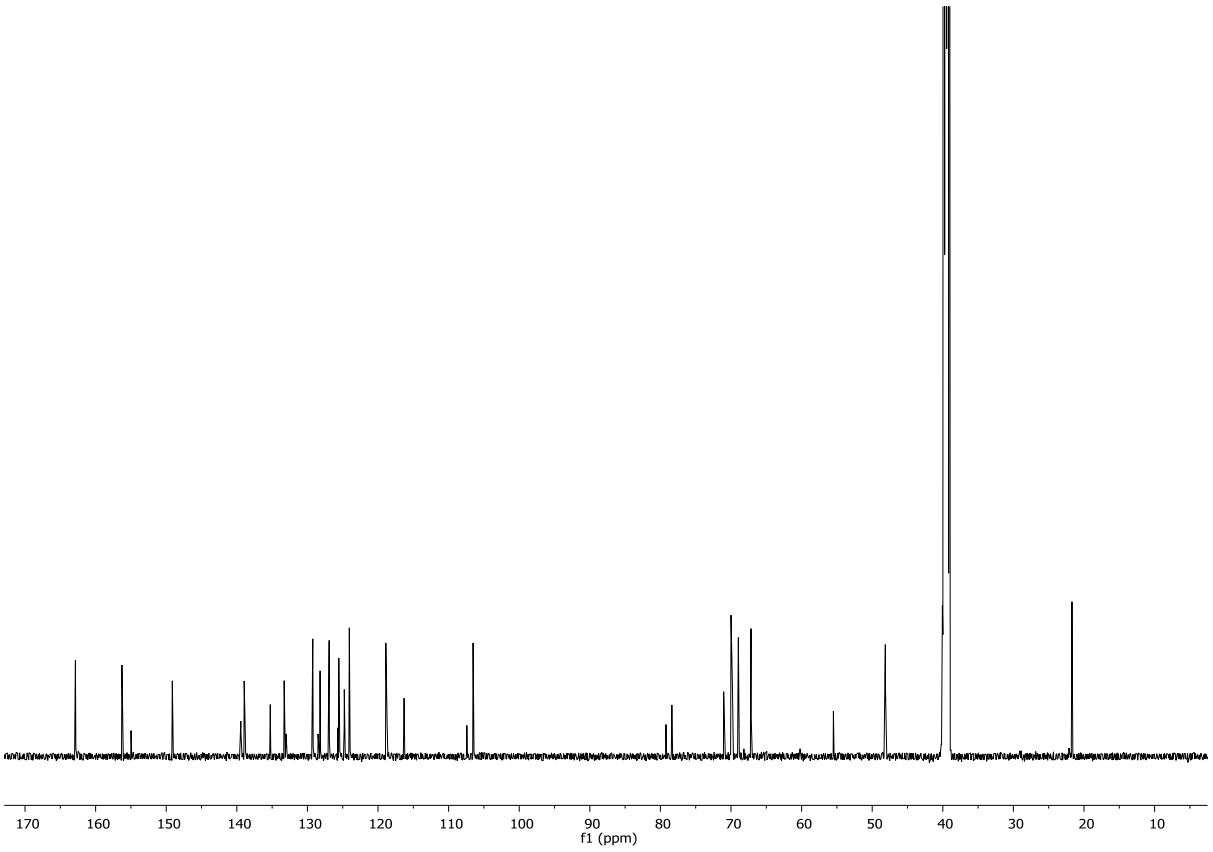
Spectrum S13. ^{1}H NMR (600 MHz, DMSO-d_6) of (R_6)-**S13**.



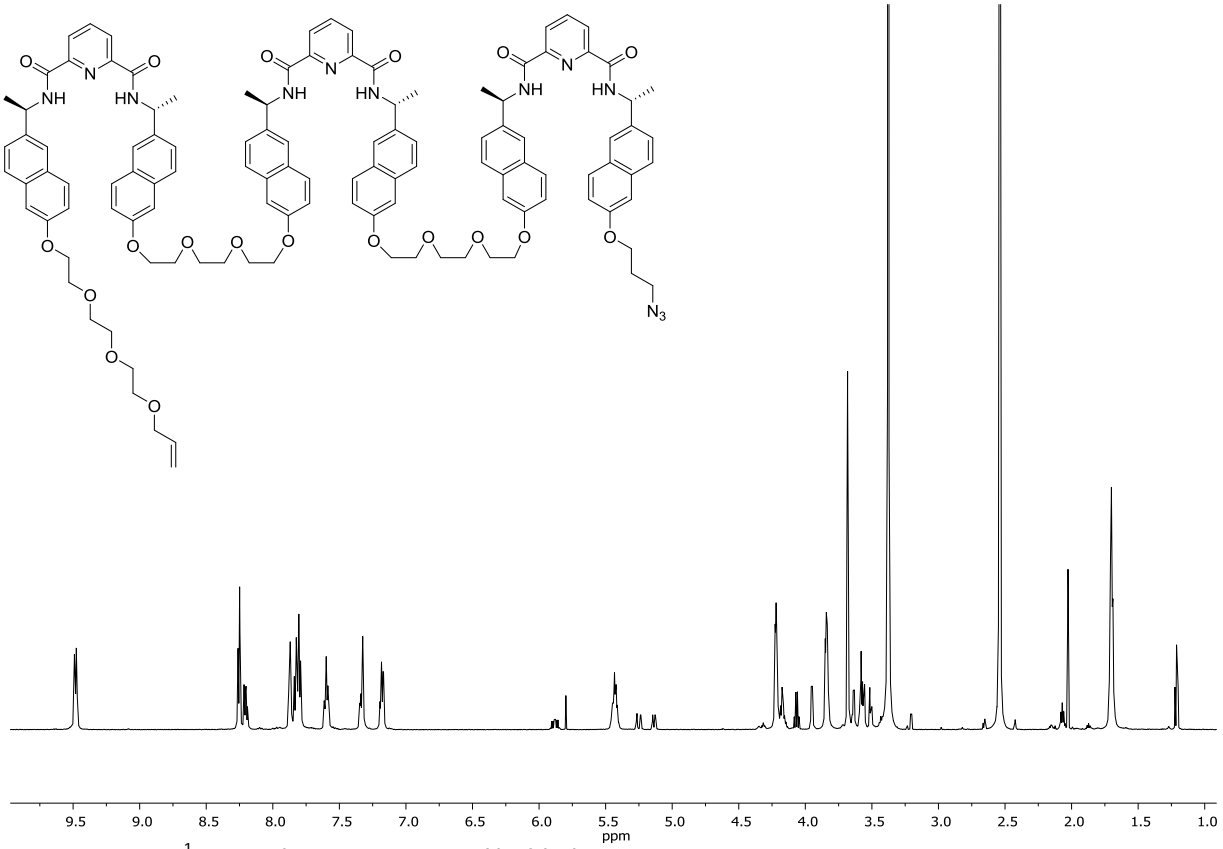
Spectrum S14. ^{13}C NMR (151 MHz, DMSO-d_6) of (R_6)-**S13**.



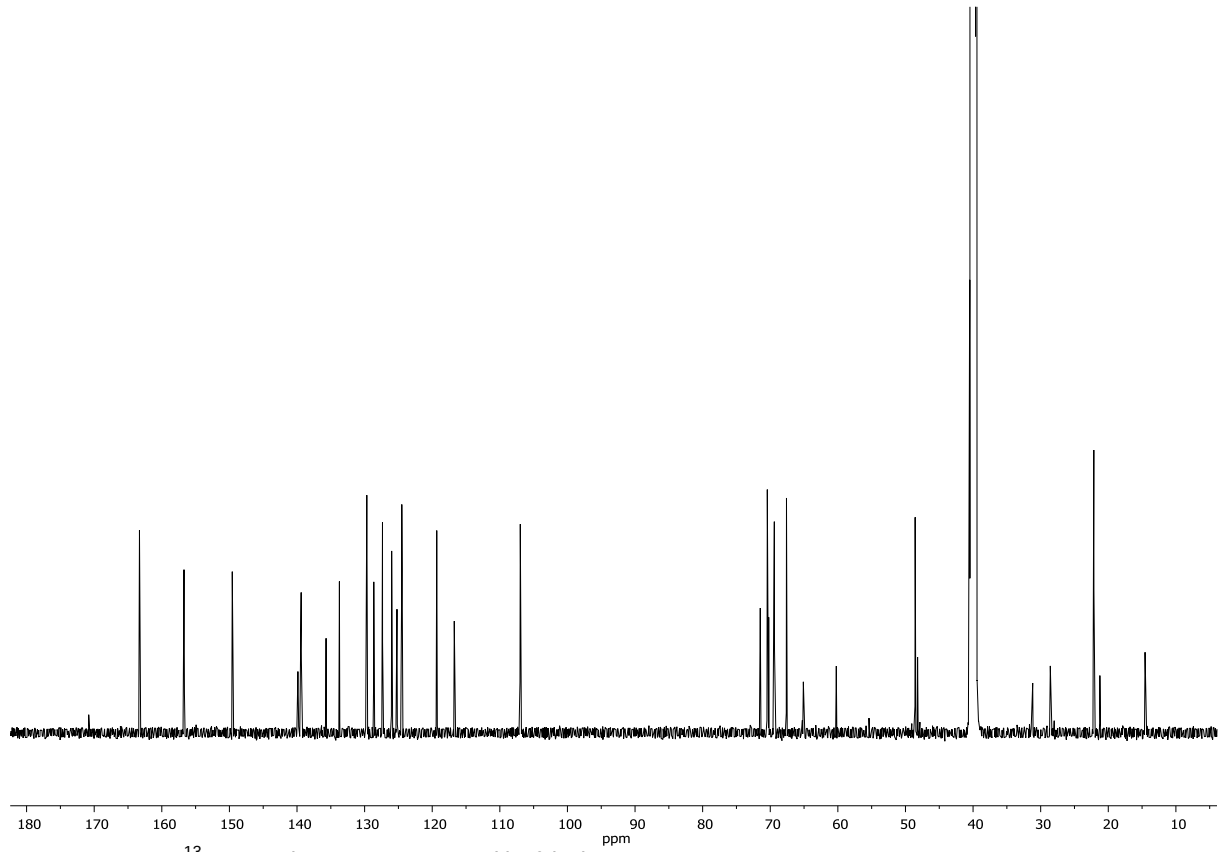
Spectrum S15. ^{1}H NMR (600 MHz, DMSO-d_6) of (R_6)-**L1**.



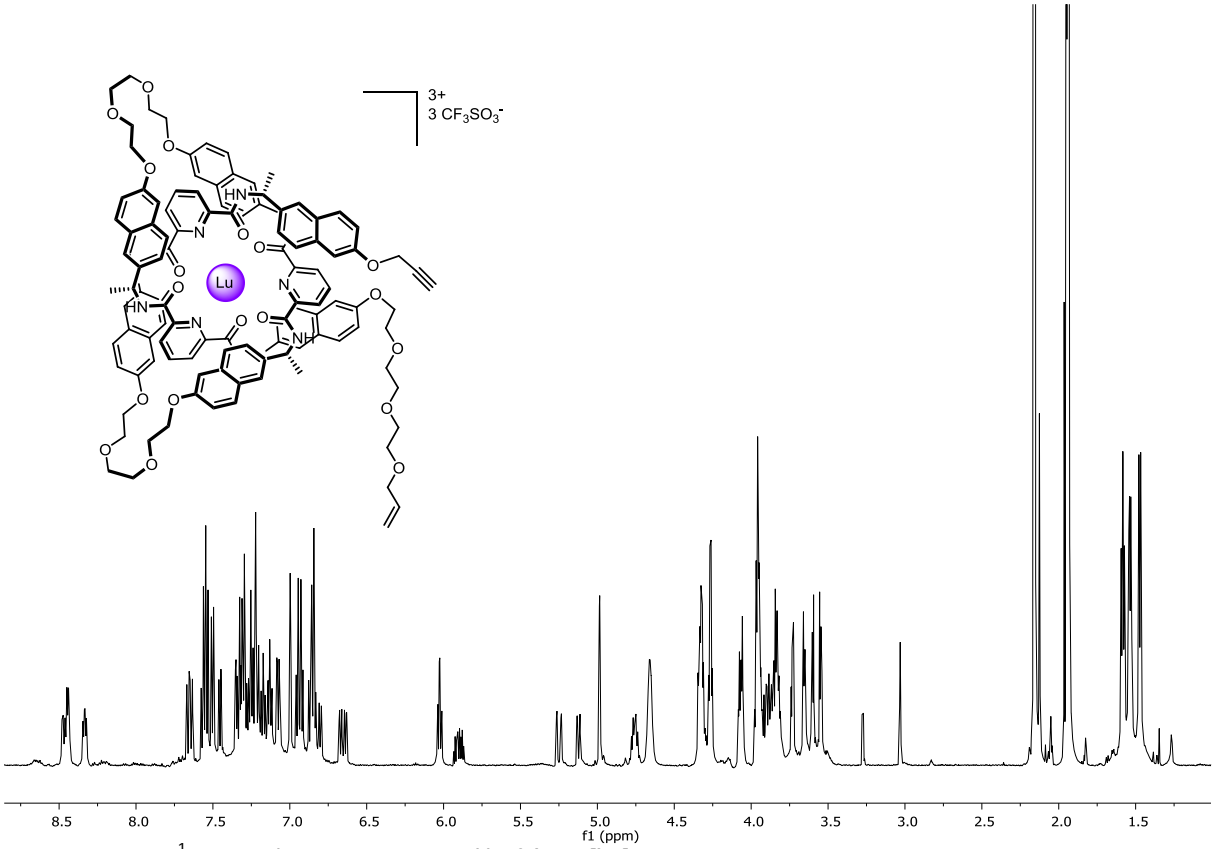
Spectrum S16. ^{13}C NMR (151 MHz, DMSO-d_6) of (R_6)-**L1**.



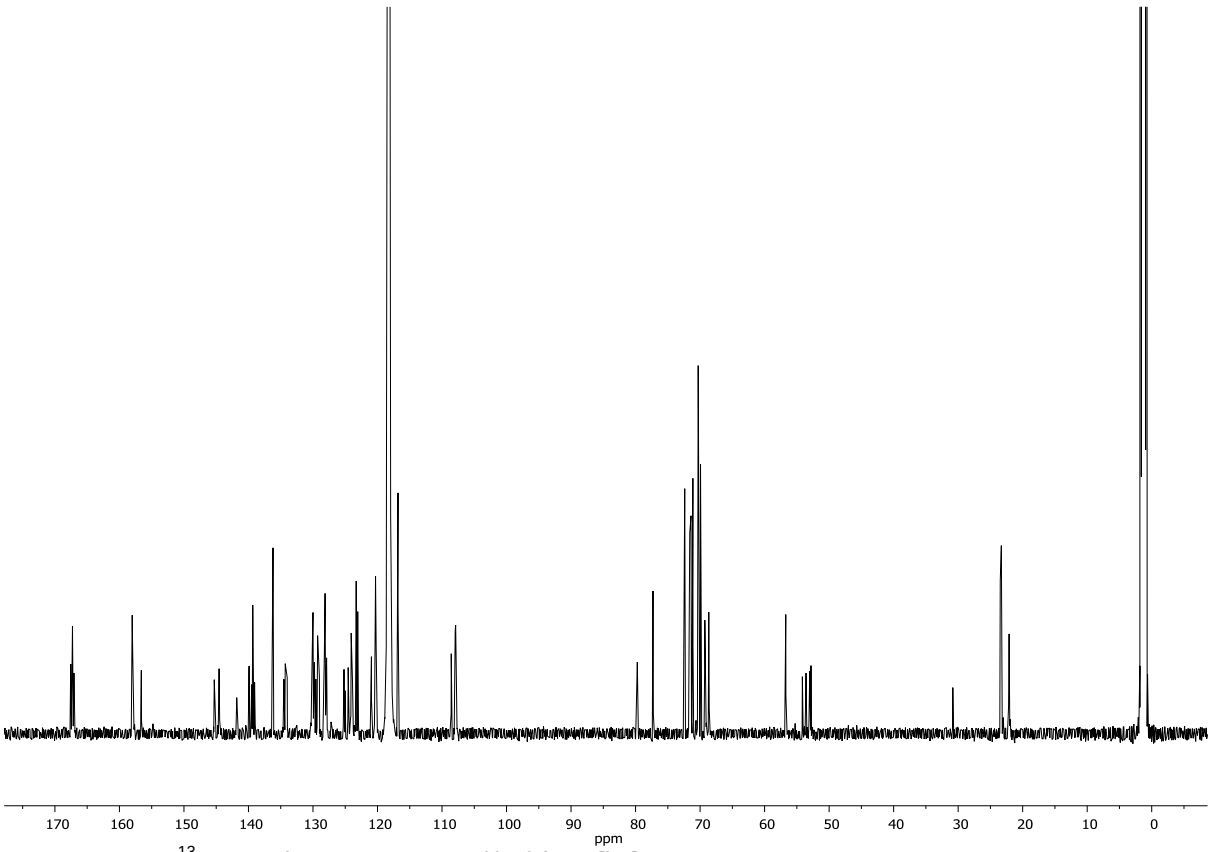
Spectrum S17. ^{1}H NMR (600 MHz, DMSO-d_6) of (R_6)-**L2**.



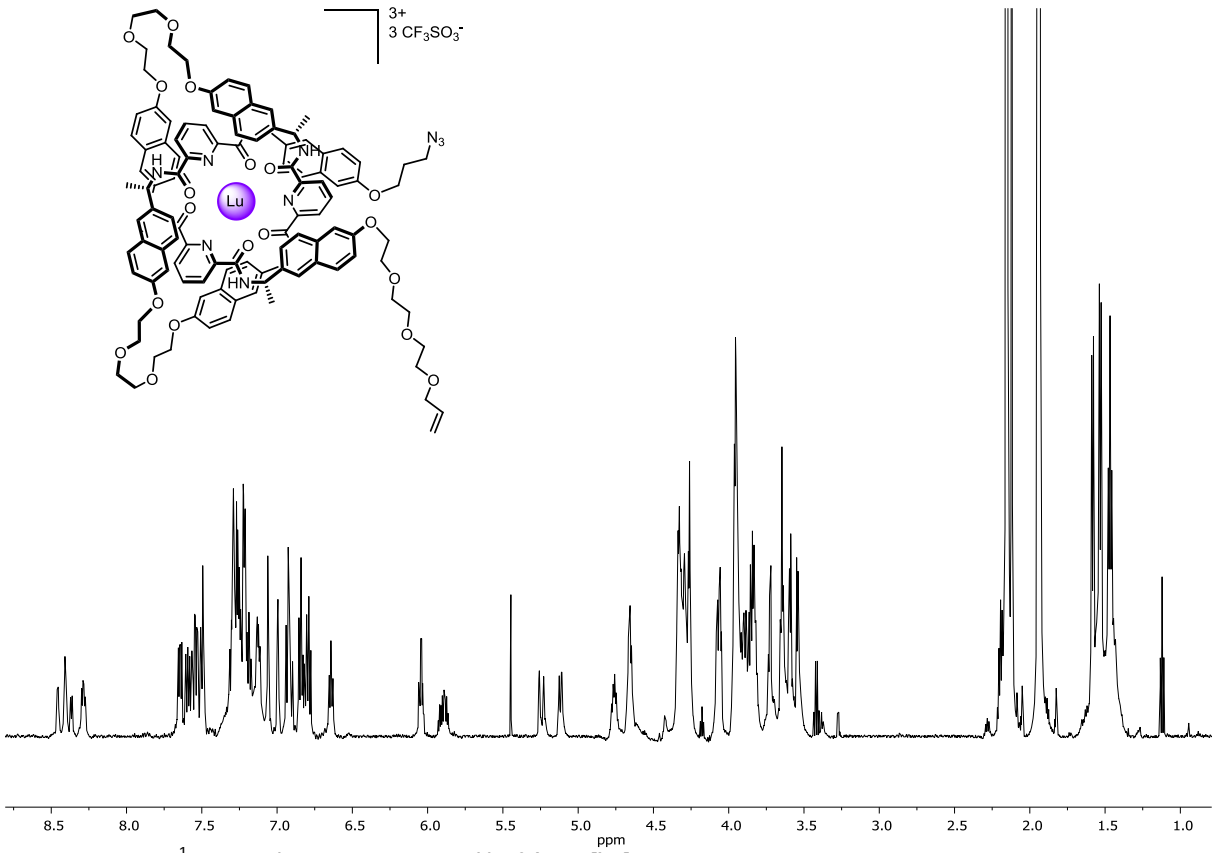
Spectrum S18. ^{13}C NMR (151 MHz, DMSO-d_6) of (R_6)-**L2**.



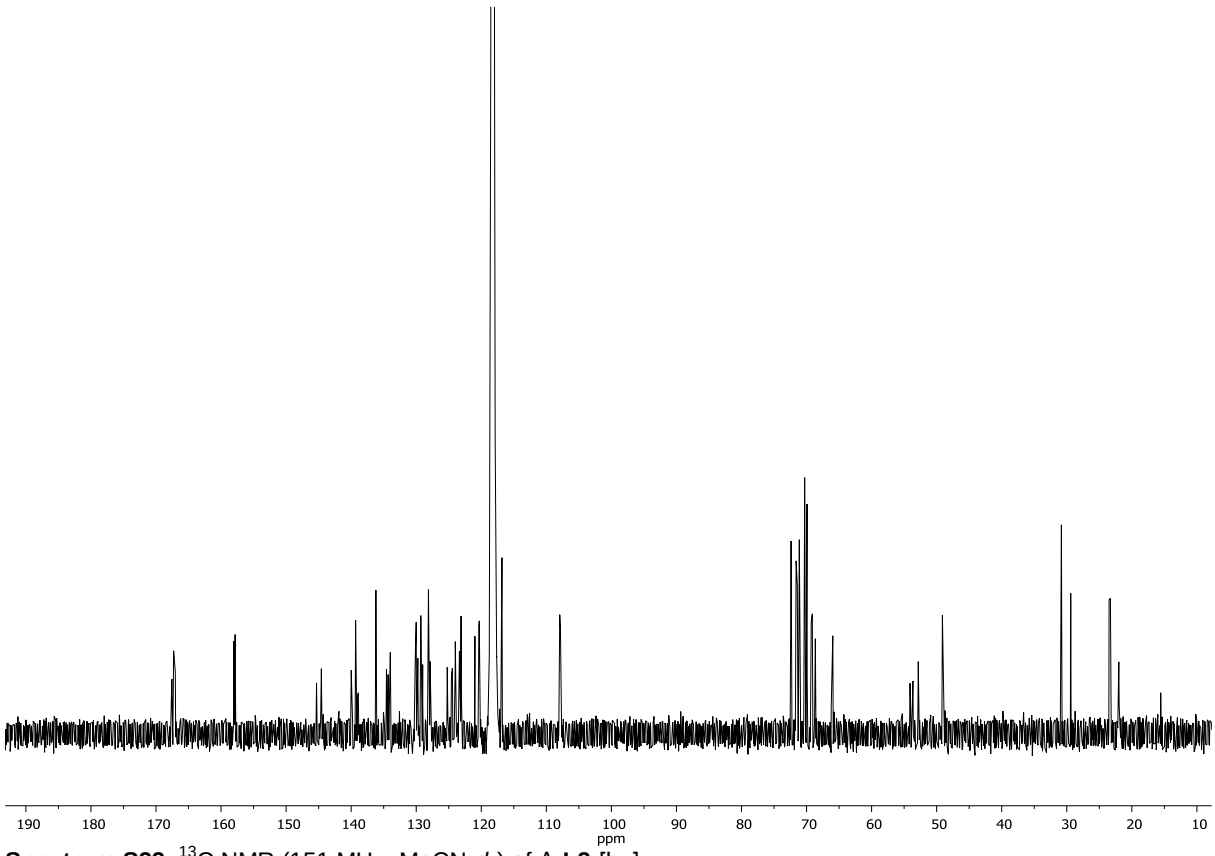
Spectrum S19. ^{1}H NMR (600 MHz, MeCN-d_3) of Λ-**L1**•[Lu].



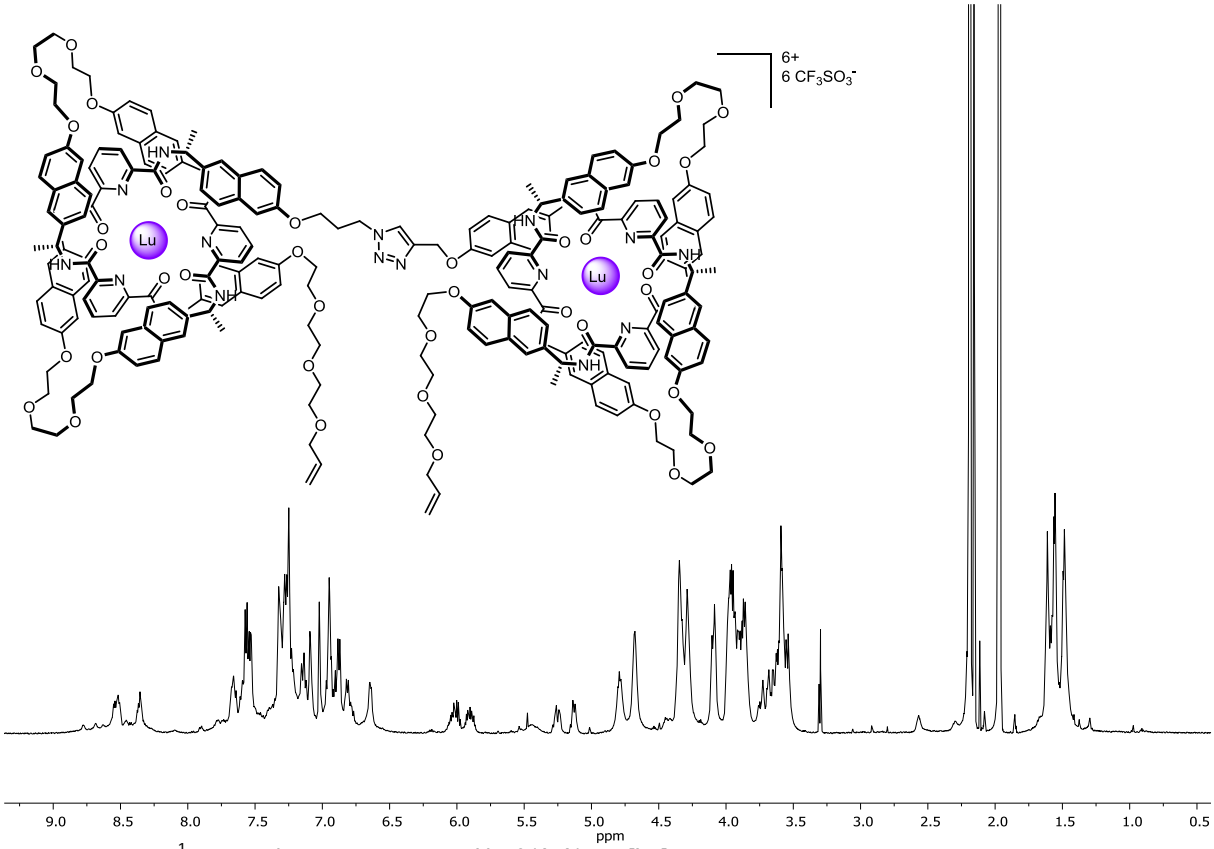
Spectrum S20. ^{13}C NMR (151 MHz, MeCN-d_3) of Λ-**L1**•[Lu].



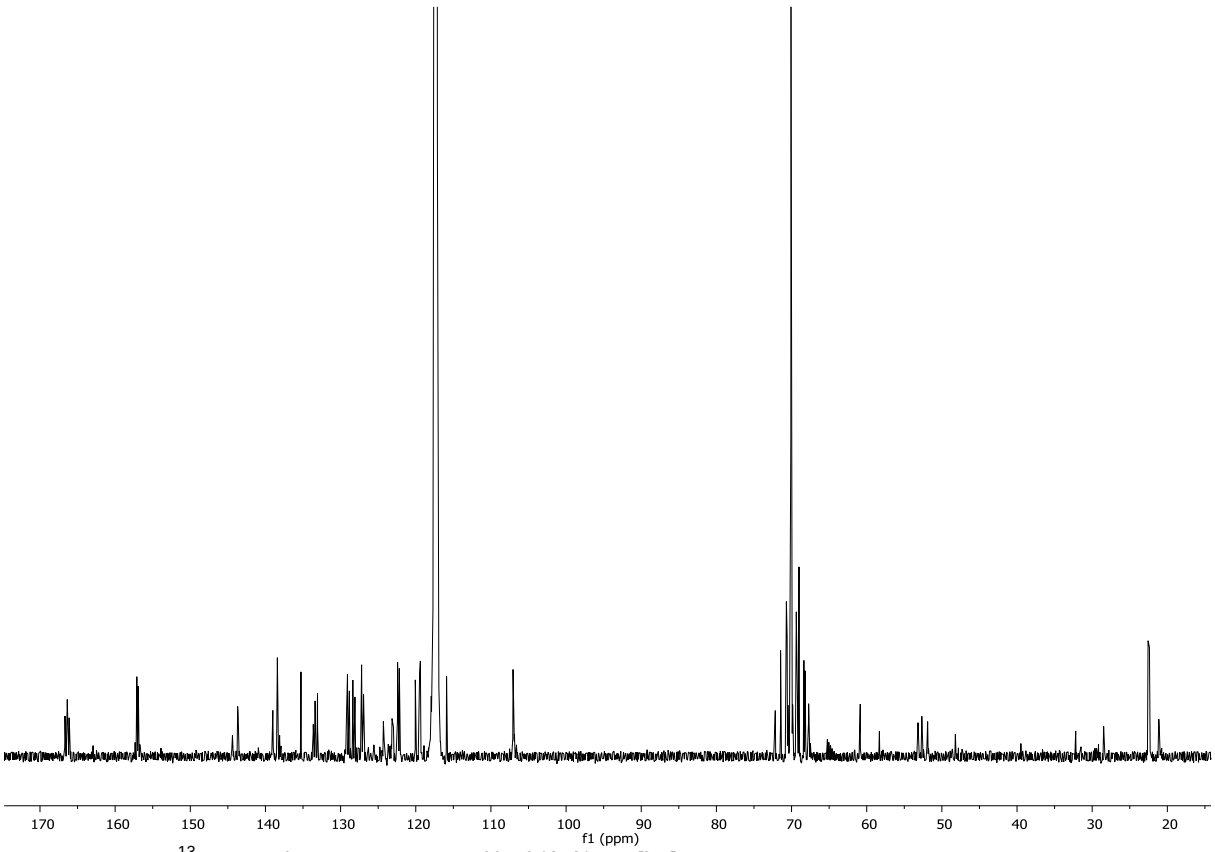
Spectrum S21. ^{1}H NMR (600 MHz, MeCN-d_3) of Δ-**L2**•[Lu].



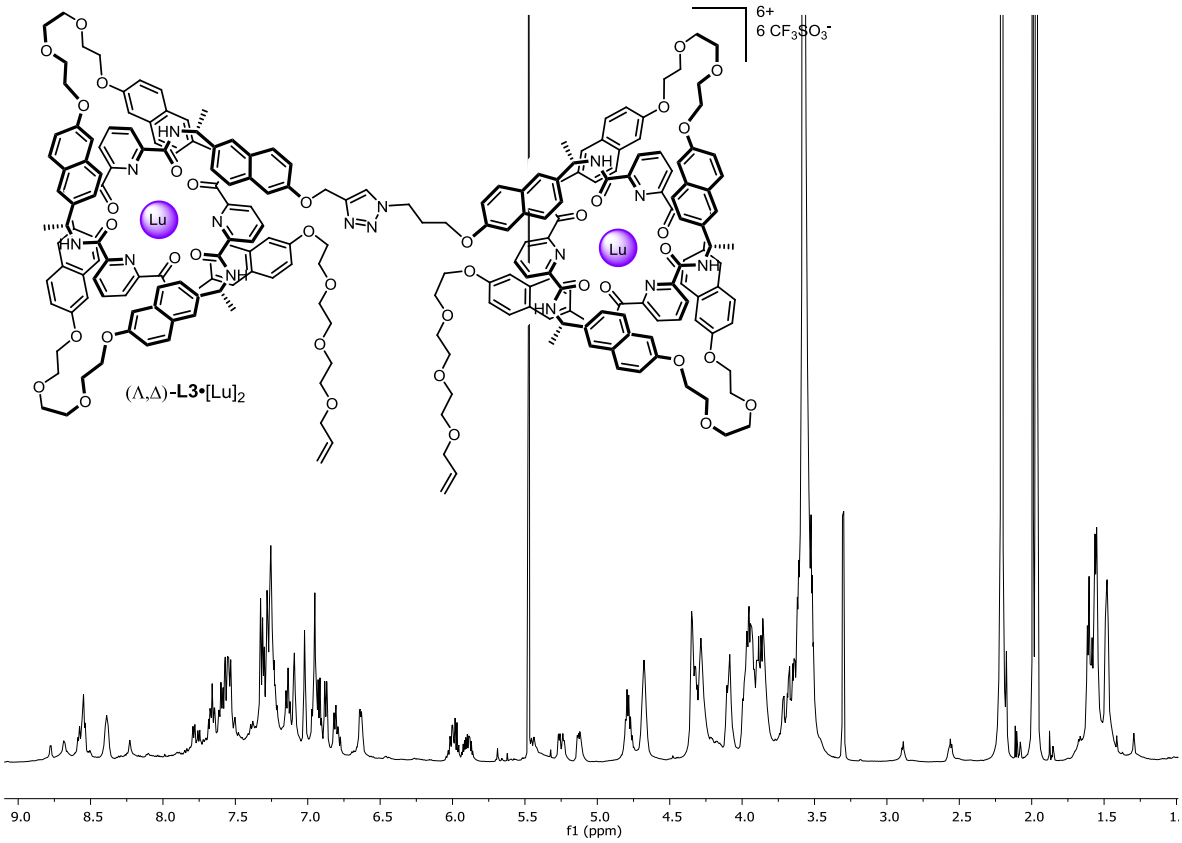
Spectrum S22. ^{13}C NMR (151 MHz, MeCN-d_3) of Λ-**L2**•[Lu].



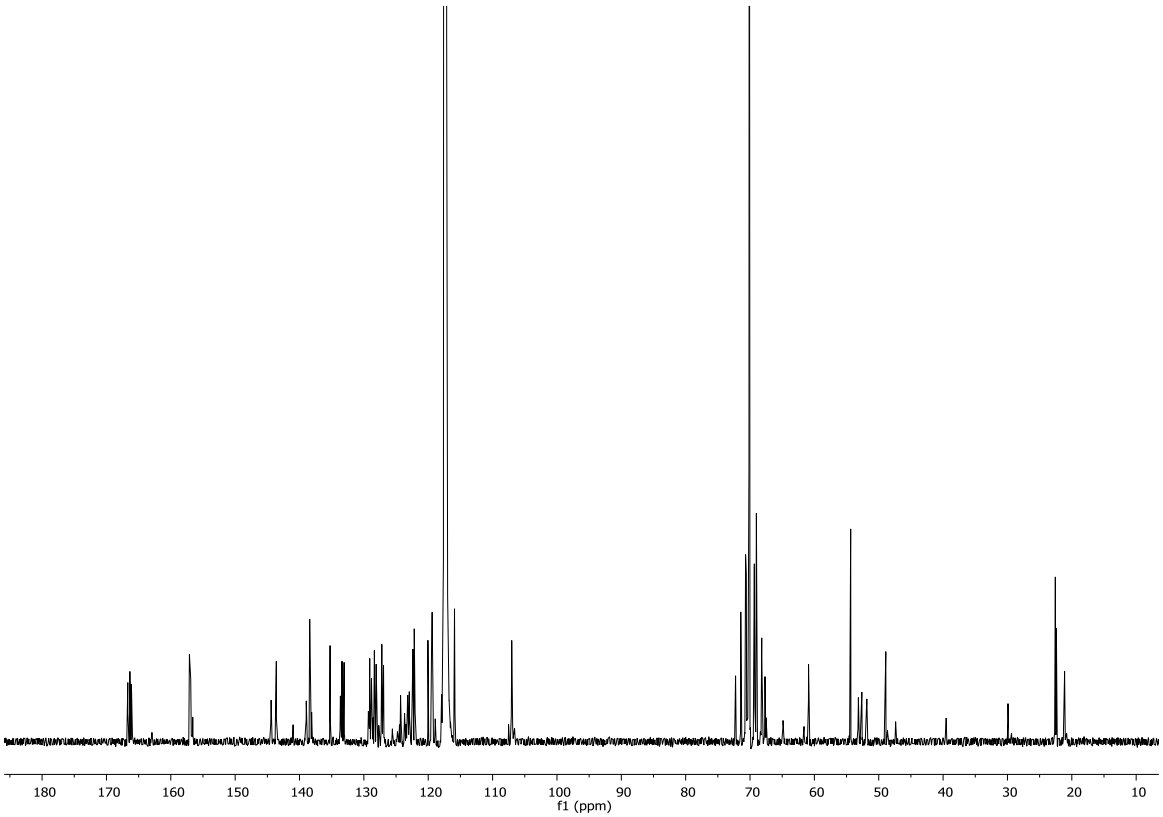
Spectrum S23. ^{1}H NMR (600 MHz, MeCN-d_3) of (Λ,Λ)-**L3**•[Lu]$_2$.



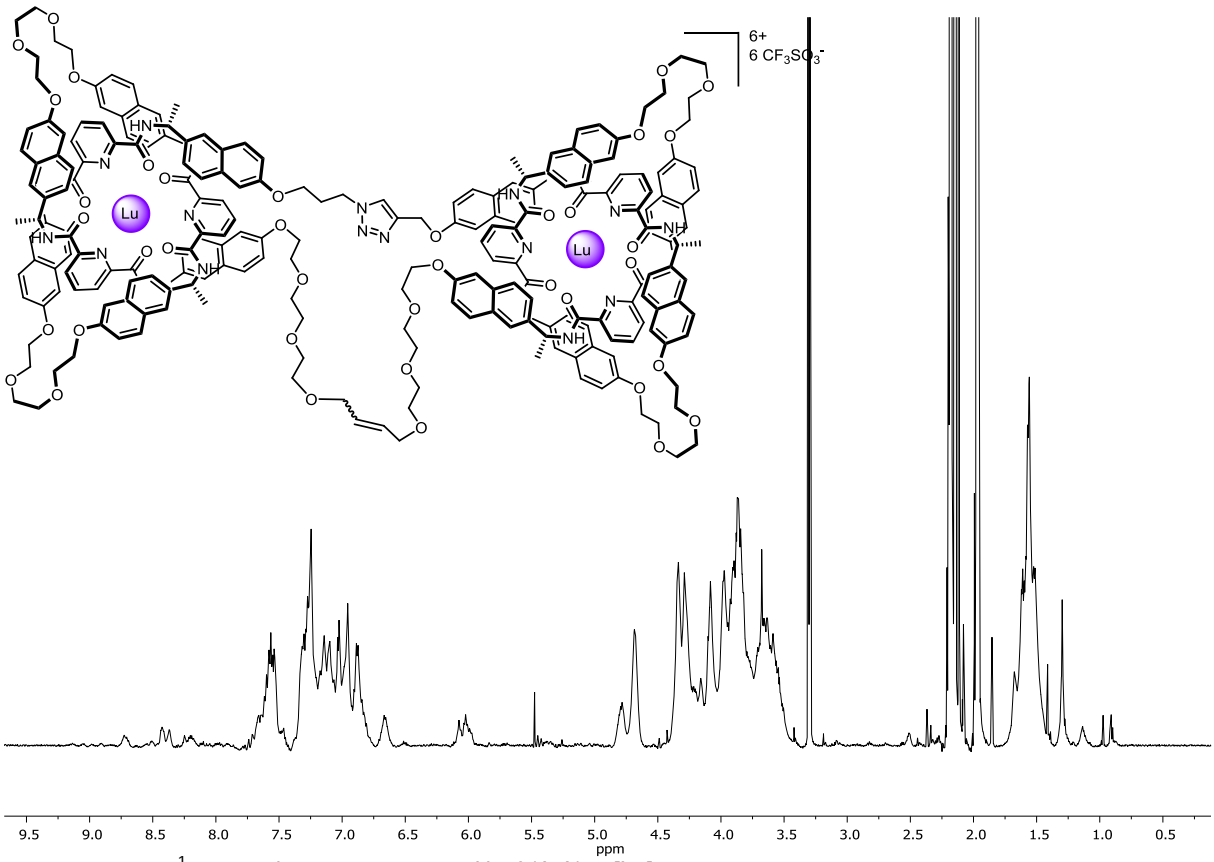
Spectrum S24. ^{13}C NMR (151 MHz, MeCN-d_3) of (Λ,Λ)-**L3**•[Lu]$_2$.



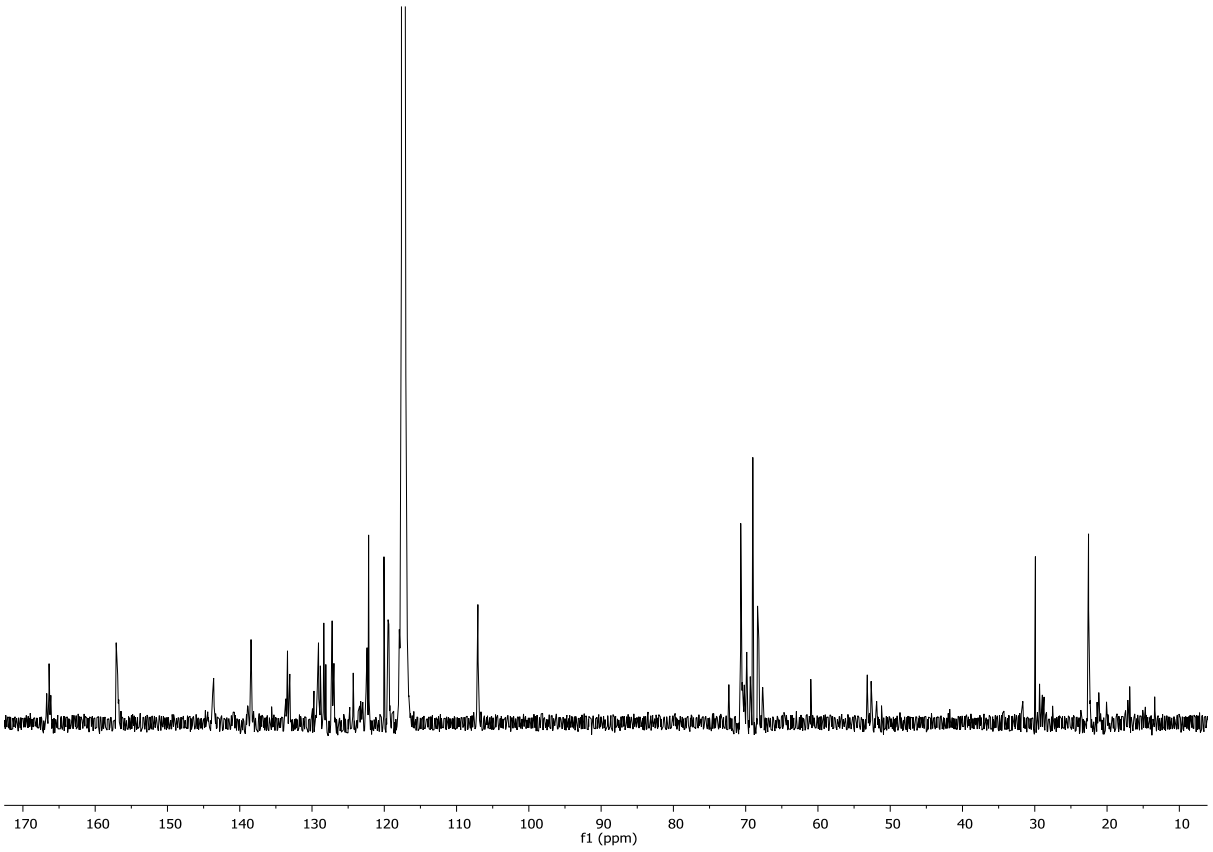
Spectrum S25. ^{1}H NMR (600 MHz, MeCN-d_3) of (Λ,Δ)-**L3**•[Lu]$_2$.



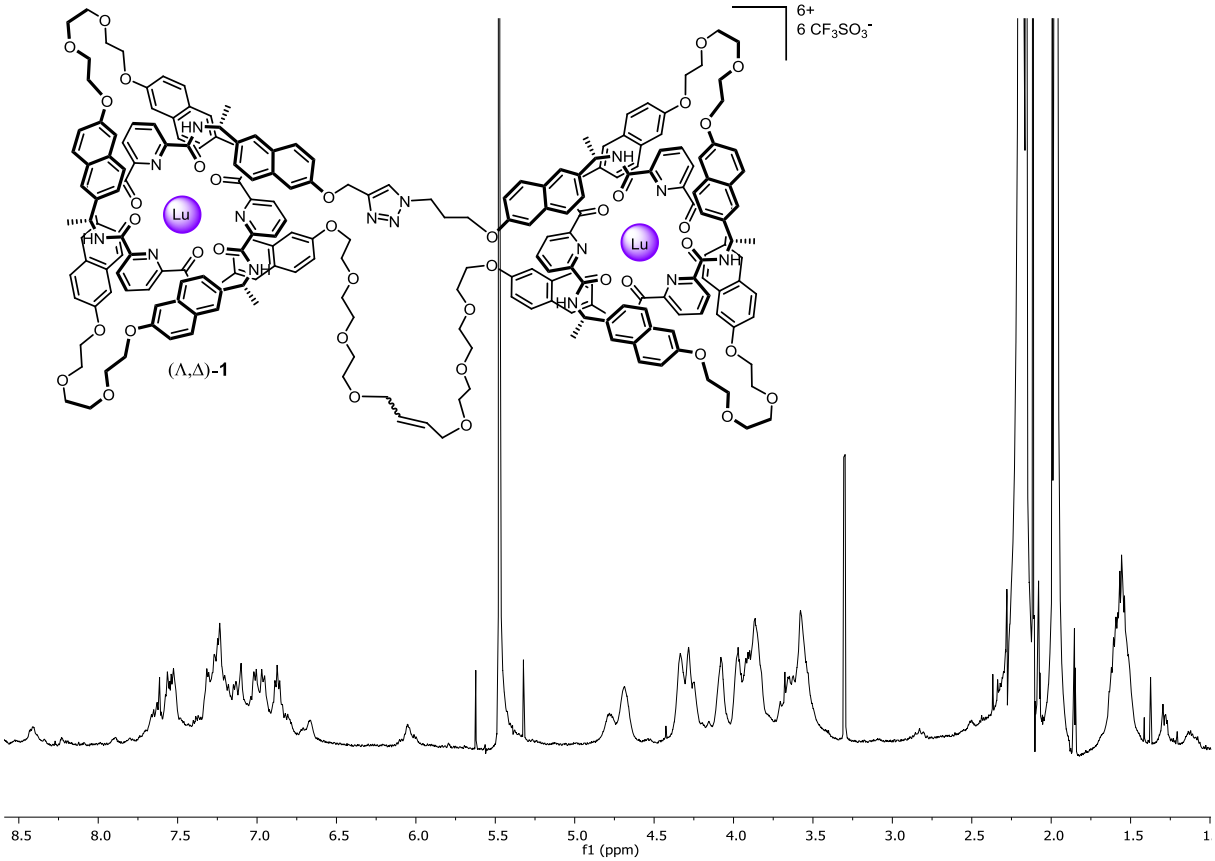
Spectrum S26. ^{13}C NMR (151 MHz, MeCN-d_3) of (Λ,Δ)-**L3**•[Lu]$_2$.



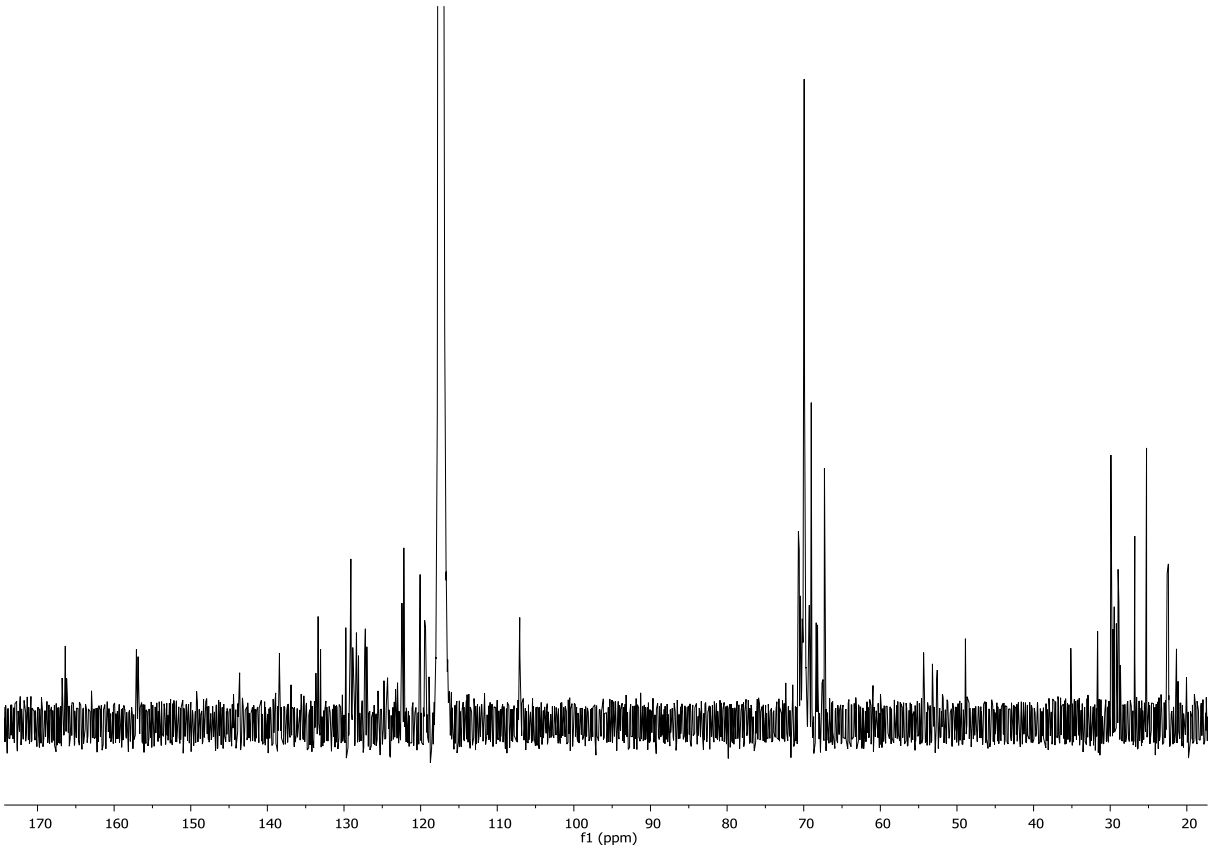
Spectrum S27. ^{1}H NMR (600 MHz, MeCN-d_3) of (Λ,Λ)-**1**•[Lu]$_2$.



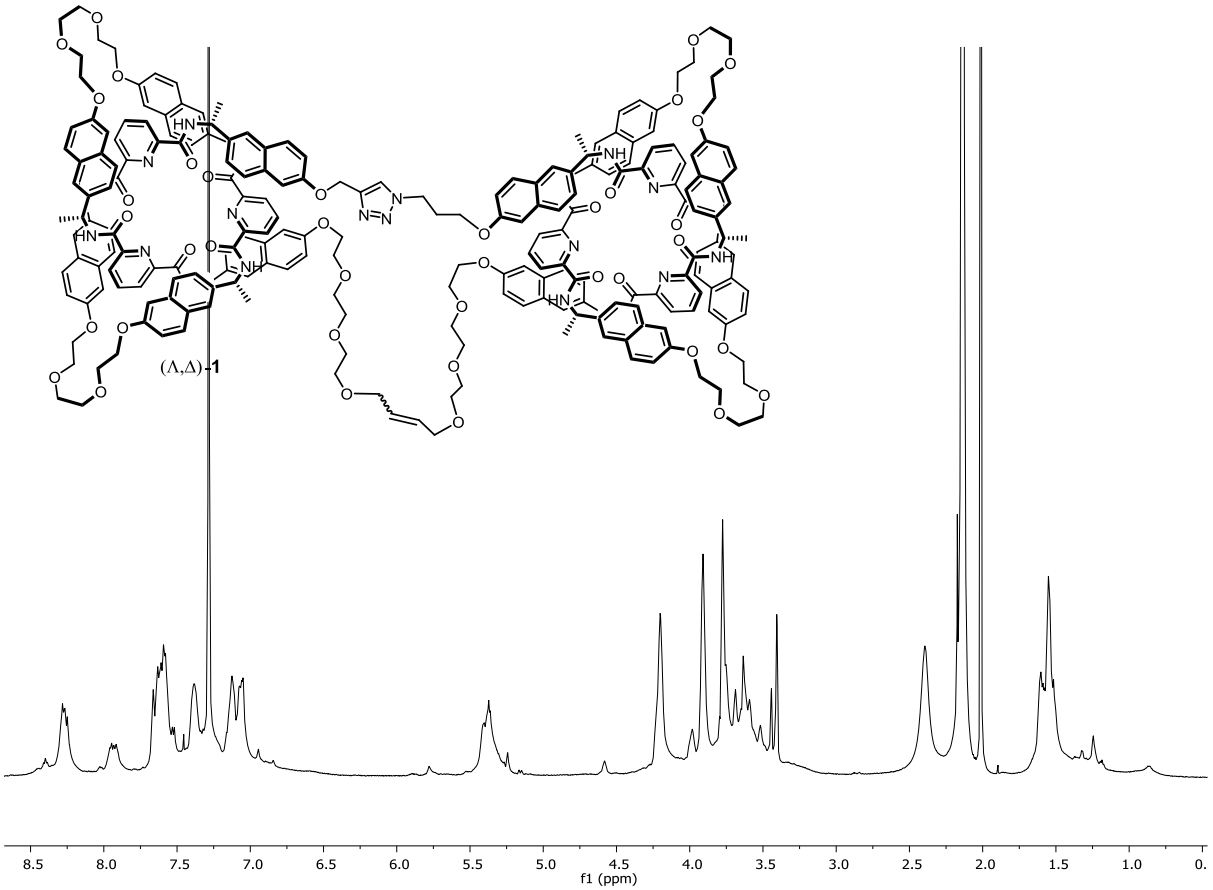
Spectrum S28. ^{13}C NMR (151 MHz, MeCN-d_3) of (Λ,Λ)-**1**•[Lu]$_2$.



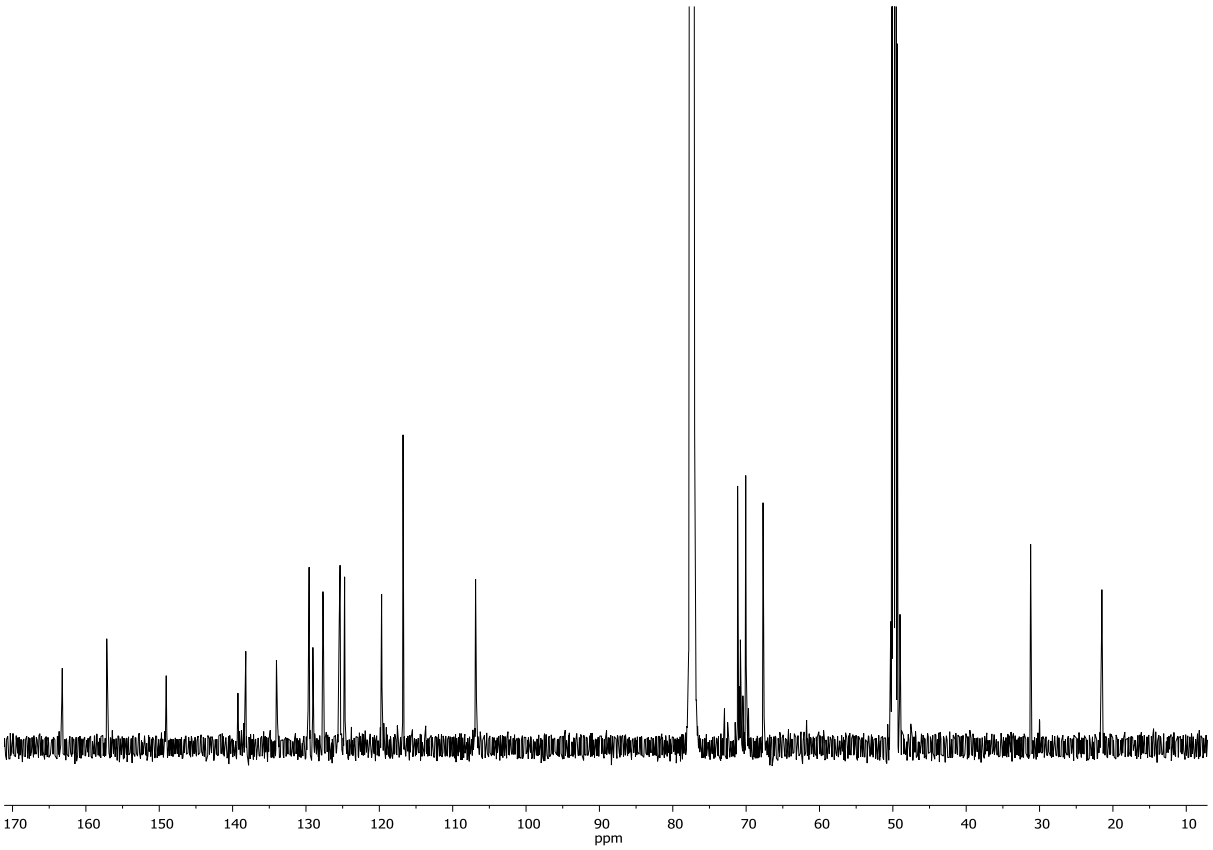
Spectrum S29. ^{1}H NMR (600 MHz, MeCN-d_3) of (Λ,Δ)-**1**•[Lu]$_2$.



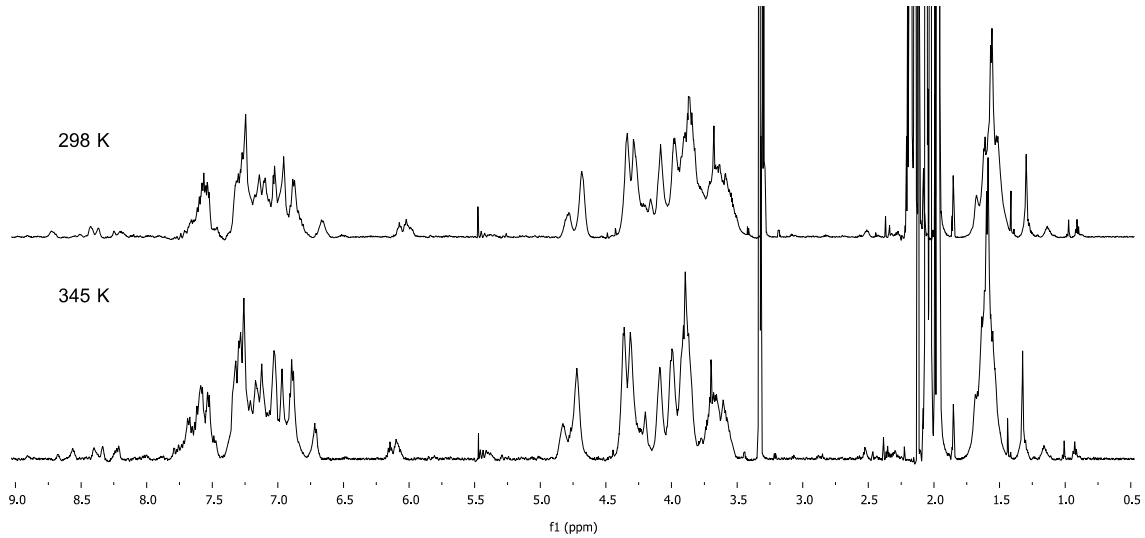
Spectrum S30. ^{13}C NMR (151 MHz, MeCN-d_3) of (Λ,Δ)-**1**•[Lu]$_2$.



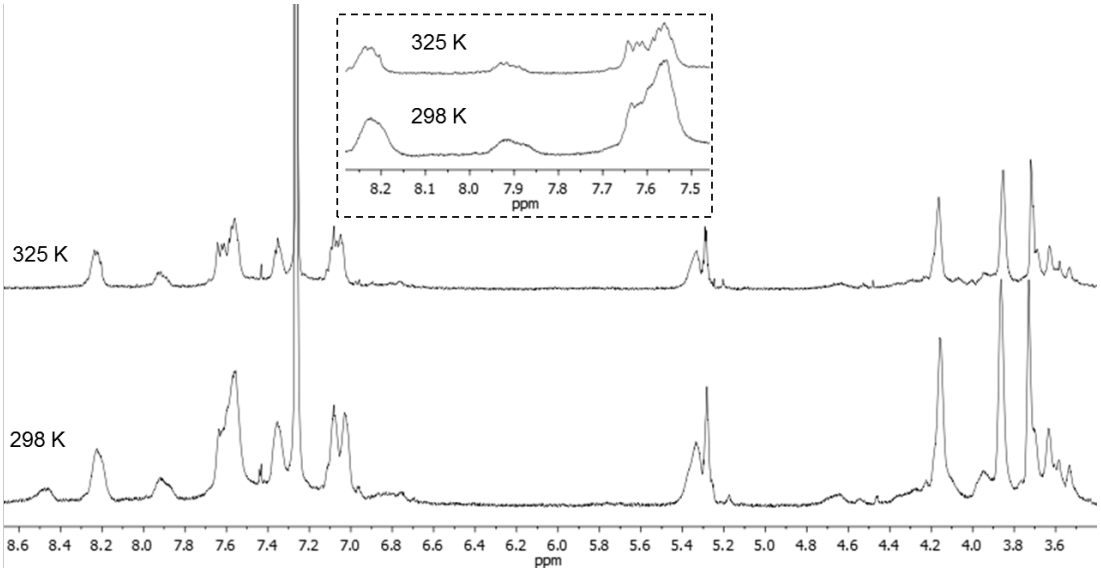
Spectrum S31. ^{1}H NMR (600 MHz, $CDCl_3/CD_3OD$ 10:1) of (Λ,Δ)-**1**.



Spectrum S32. ^{13}C NMR (151 MHz, $CDCl_3/CD_3OD$ 10:1) of (Λ,Δ)-**1**.

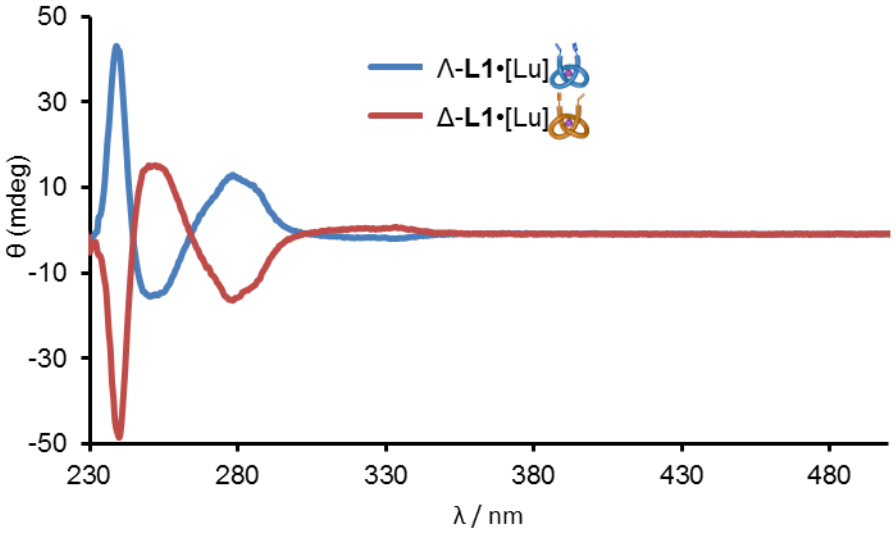


Spectrum S33. ^{1}H VT NMR (600 MHz, MeCN-d_3) of (Λ,Λ)-**1**•[Lu]$_2$ at 298 K (top) and 345 K (bottom).

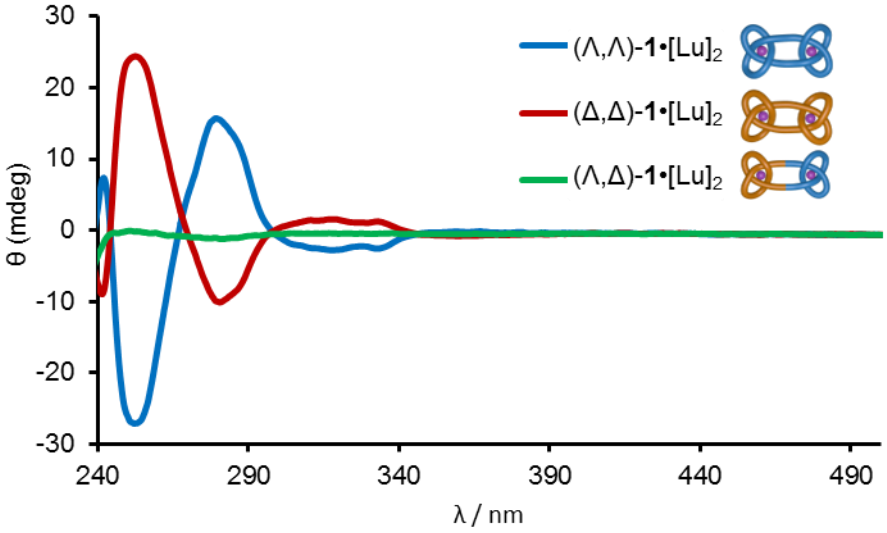


Spectrum S34. ^{1}H VT NMR (600 MHz, $CDCl_3$/MeOD-d_4 *10:1*) of (Λ,Λ)-**1** at 325 K (top) and 298 K (bottom). Expansion of aromatic region in inset shows slight sharpening of the signals at higher T.

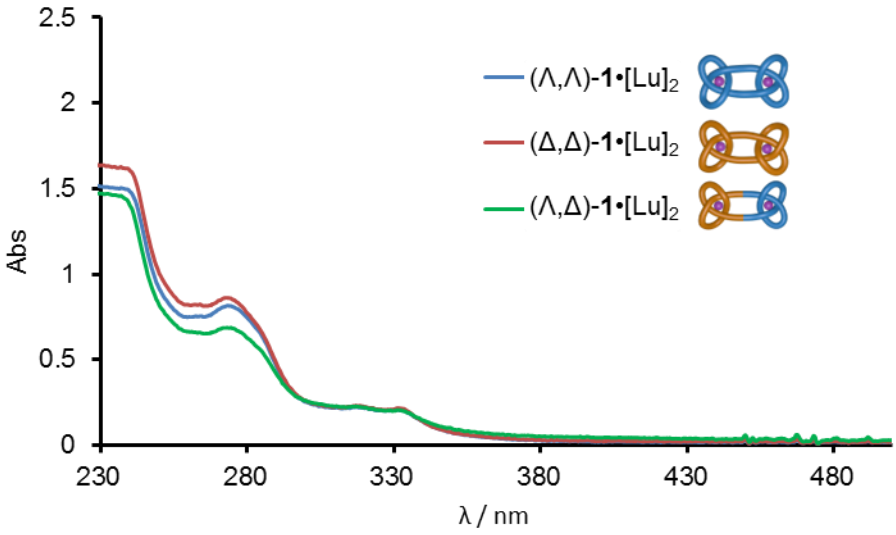
S7. CD AND ABSORPTION SPECTRA



Spectrum S35. CD spectra (1.0×10^{-4} M, MeCN, 298 K) of overhand knots Λ-**L1**•[Lu] (blue) and Δ-**L1**•[Lu] (red). Normalized for absorbance.



Spectrum S36. CD spectra (1.0×10^{-4} M, MeCN, 298 K) of granny knots (Λ,Λ)-**1**•$[Lu]_2$ (blue) and (Δ,Δ)-**1**•$[Lu]_2$ (red) as well as square knot (Λ,Δ)-**1**•$[Lu]_2$ (green). Normalized for absorbance.



Spectrum S37. UV/Vis spectra (1.0×10^{-4} M, MeCN, 298 K) of granny knots (Λ,Λ)-**1**•$[Lu]_2$ (blue) and (Δ,Δ)-**1**•$[Lu]_2$ (red) as well as square knot (Λ,Δ)-**1**•$[Lu]_2$ (green).

S8. MOLECULAR MODEL OF (Λ,Λ)-L3•[Lu]$_2$

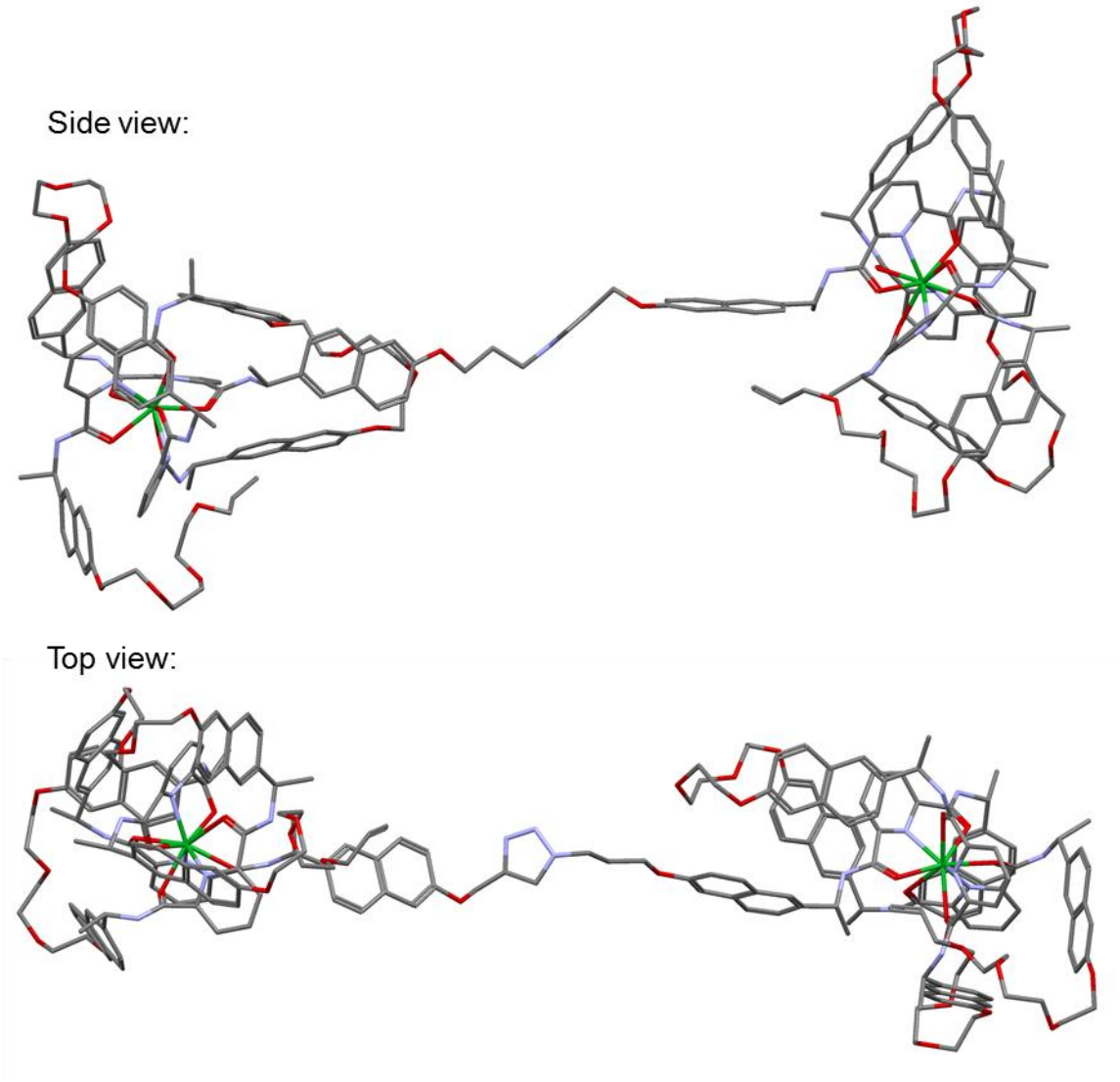


Figure S11. Molecular model of (Λ,Λ)-**L3**•[Lu]$_2$. Optimized by semi-empirical PM7 algorithm (vacuum). Hydrogens omitted for clarity.

S9. REFERENCES

[1] S. Combemale, J.-N. Assam-Evoung, S. Houaidji, R. Bibi, V. Barragan-Montero, *Molecules*, **2014**, *19*, 1120–1149.
[2] M. K. Chae, J.-m. Suk, K.-S. Jeong, *Tetrahedron Lett*. **2010**, *51*, 4240–4242.
[3] Y. Maeda,K. Saito, N. Akamatsu, Y. Chiba, S. Ohno, Y. Okui, M. Yamada, T. Hasegawa, M. Kako, T. Akasaka, *J. Am. Chem. Soc.* **2012**, *134*, 18101–18108.
[4] D. A. Leigh, L. Pirvu, F. Schaufelberger, D. J. Tetlow, L. Zhang, *Angew. Chem. Int. Ed.* **2018**, *57*, 10484–10488.