

Synthesis of Inert Homo- and Heterodinuclear Rare Earth Cryptates

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Supporting Information

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1 Synthesis

1.1 General

Chemicals were purchased from commercial suppliers and used as received unless stated otherwise. Deuterated solvents had deuterium contents > 99.8%D. CH₃CN for the synthesis of the cryptates was HPLC-grade. DMF used for the nickel-catalyzed coupling reaction was SPPS-grade. Tetrahydrofuran (THF) for the debromination reaction was dried by standard procedures (Na). Air-sensitive reactions were carried out under a dry, dioxygen-free atmosphere of N₂ using Schlenk technique. Column chromatography was performed with silica gel 60 (Merck, 0.063-0.200 mm). Analytical thin layer chromatography (TLC) was done on silica gel 60 F₂₅₄ plates (Merck, coated on aluminium sheets).

NMR spectra were measured on Bruker DPX-200 (¹H: 200 MHz, ¹³C: 50.3 MHz), DPX-250 (¹H: 250 MHz, ¹³C: 62.9 MHz), and DRX-400 (¹H: 400 MHz, ¹³C: 101 MHz). The chemical shifts (δ) are reported in ppm relative to TMS and the residual solvent signals have been used as internal reference.

ESI mass spectrometry was done using Bruker Daltonics Esquire6000. MALDI mass spectra were measured on a Bruker Ultraflex III TOF/TOF200 spectrometer. The samples were prepared using the double-layer preparation method on a ground steel target with cinnamic acid as matrix substance.

Analytical reversed-phase HPLC (Lichrospher RP-18e (Merck), 125×4mm-5μm, flow rate: 1 mL min⁻¹, UV detection at 300 nm) and semi-preparative reversed-phase HPLC (Lichrospher RP-18e (Merck), 250×10mm-10μm, flow rate: 3 mL min⁻¹, UV detection at 300 nm) was performed using the following program:

Mobile Phases: A: H₂O (+1% TFA, v/v) B: CH₃CN (HPLC gradient grade)

min	%A	%B
0	85	15
5	85	15
19	45	55
25	45	55
40	85	15
50	85	15

1.2 Synthetic Procedures

4,4',6,6'-Tetramethyl-2,2'-bipyrimidine (1)¹

Under N₂, NiCl₂ • 6 H₂O (8.33 g, 35.1 mmol, 1.0 equiv.) and PPh₃ (36.8 g, 140 mmol, 4.0 equivs.) were suspended in DMF (160 mL) and the mixture was degassed by two freeze-pump-thaw cycles. Zinc powder (3.21 g, 49.1 mmol, 1.4 equivs.) was added and the reaction mixture was degassed by one additional freeze-pump-thaw cycle. The suspension was stirred under N₂ for one hour at room temperature. 4,6-Dimethyl-2-chloropyrimidine² (5.00 g, 35.1 mmol, 1.0 eq) in degassed DMF (30 mL, three freeze-pump-thaw cycles) was added to the brown suspension and the reaction mixture was stirred at 70 °C (bath temperature) for 24 hours. The black suspension was allowed to come to ambient temperature and was poured into 4M aqueous ammonia (630 mL). After stirring for additional 30 minutes at ambient temperature, the precipitate was filtered off and the blue filtrate solution was extracted with CH₂Cl₂ (4 x 250 mL). The combined organic layers were dried over MgSO₄, volatiles were removed under reduced pressure, and the crude residue was purified by column chromatography (SiO₂, preloading of the crude material onto SiO₂, CH₂Cl₂/MeOH gradient: 100:1 → 24:1, detection: UV) to yield a slightly yellow solid (2.71 g, 72%, R_f = 0.16 (SiO₂, CH₂Cl₂/MeOH 24:1, detection: UV)).

¹H NMR (200 MHz, CDCl₃) δ = 7.15 (s, 2 H), 2.66 (s, 12 H) ppm. ¹³C NMR (50.3 MHz, CDCl₃) δ = 168.2, 162.1, 120.9, 24.4 ppm. MS (ESI, pos. mode): *m/z* (%) = 214.8 (52, [M+H]⁺), 236.8 (100, [M+Na]⁺).

4,4',6,6'-Tetrakis(dibromomethyl)-2,2'-bipyrimidine³

4,4',6,6'-Tetramethyl-2,2'-bipyrimidine (3.30 g, 15.4 mmol, 1.0 equiv.) was dissolved in acetic acid (250 mL) before Br₂ (6.63 mL, 20.7 g, 129 mmol, 8.4 equivs.) was added at ambient temperature. The reaction mixture was heated to 80 °C (bath temperature) overnight. The orange suspension was allowed to come to ambient temperature, volatiles were removed under reduced pressure, and the crude residue was treated with an aqueous saturated solution of NaHCO₃ until pH = 7. The resulting suspension was stirred with Et₂O (150 mL) for 15 minutes and after separation of the phases, the aqueous phase was extracted with additional Et₂O (2 x 150 mL). The combined organic layers were dried over MgSO₄, volatiles were removed under reduced pressure, and the crude residue was purified by column chromatography (SiO₂, preloading of the crude material onto SiO₂, CHCl₃, detection: UV) to yield a bright, yellow solid (742 mg, 6 %, R_f = 0.60 (SiO₂, CHCl₃, detection: UV)).

¹H NMR (200 MHz, CDCl₃) δ = 8.51 (s, 2 H), 6.73 (s, 4 H) ppm. ¹³C NMR (50.3 MHz, CDCl₃) δ = 170.2, 160.1, 118.1, 38.5 ppm. Anal. calcd. for C₁₂H₈Br₈N₄ (M_r = 845.44): C, 17.05; H, 0.72; N, 6.63. Found: C, 17.55; H, 0.77; N, 6.46.

4,4',6,6'-Tetrakis(bromomethyl)-2,2'-bipyrimidine (2)⁴

Under N₂, 4,4',6,6'-tetrakis(dibromomethyl)-2,2'-bipyrimidine (38 mg, 45 μmol, 1.0 equiv.) was dissolved in dry THF (1.5 mL) and the mixture was cooled in an ice bath. Diethyl phosphite (47 μL, 50 mg, 360 μmol, 8.0 equivs.) and freshly distilled *N,N*-diisopropylethylamine (63 μL, 47 mg, 360 μmol, 8.0 equivs.) were added by syringe. The slightly yellow solution was stirred at 0 °C for 1 h and additional 5 h at ambient temperature. The crude reaction mixture was poured onto crushed ice (2.2 g) and extracted with Et₂O (3 x 20 mL). The combined organic layers were washed with brine and dried over magnesium sulfate (MgSO₄). After concentration under reduced pressure, the crude yellow residue was subjected to column chromatography (SiO₂, CH₂Cl₂/MeOH gradient: 75:1 → 50:1, detection:

UV). The title compound was obtained as a white solid (14 mg, 58 %, R_f = 0.12 (SiO₂, CH₂Cl₂/MeOH 50:1, detection: UV)).

¹H NMR (200 MHz, CDCl₃) δ = 7.86 (s, 2 H), 4.64 (s, 8 H) ppm. ¹³C NMR (50.3 MHz, CDCl₃) δ = 167.7, 162.2, 120.2, 31.6 ppm.

Dinuclear sodium cryptate 4-Na/Na

Under N₂, the macrocycle **3**⁵ (74.0 mg, 189 μ mol, 2.0 equivs.), 4,4',6,6'-tetrakis(bromomethyl)-2,2'-bipyrimidine (**2**) (50.0 mg, 94.4 μ mol, 1.0 equiv.), and anhydrous Na₂CO₃ (200 mg, 1.89 mmol, 20.0 equivs.) were suspended in CH₃CN (280 mL, HPLC grade). The mixture was heated under reflux for 64 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was dry-loaded onto silica and purified by column chromatography (SiO₂, CH₂Cl₂/MeOH gradient: 24:1 \rightarrow 2:1, detection: UV + I₂ vapor) to yield a slightly yellow solid (25 mg, 22 %, R_f = 0.12 (SiO₂, CH₂Cl₂/MeOH 9:1, detection: UV)).

¹H NMR (250 MHz, CD₃OD) δ = 8.04 (d, J = 7.6 Hz, 8 H), 7.89 - 7.83 (m, 8 H), 7.53 (s, 2 H), 7.35 (d, J = 7.4 Hz, 8 H), 3.86 (s, 8 H), 3.82 (s, 16 H) ppm. ¹³C NMR (63 MHz, CD₃OD) δ = 170.7, 163.1, 159.9, 156.7, 139.5, 125.3, 122.5, 121.8, 60.3, 59.4 ppm. MS (ESI, pos. mode): m/z (%) = 520.1 (100, [M]²⁺).

Homodinuclear rare earth cryptate 4-Eu/Eu

4-Na/Na (16.6 mg, 13.9 μ mol, 1.0 eq) was dissolved in CH₃CN (21 mL, HPLC grade) before EuCl₃ • 6 H₂O (17.7 mg, 48.4 μ mol, 3.5 equivs.) was added. The reaction mixture was heated under reflux for 40 h. The white suspension was allowed to come to ambient temperature and volatiles were removed under reduced pressure. The crude residue was redissolved in a minimum amount of CH₃CN/H₂O/TFA (5/19/0.15; v/v/v) and purified by preparative HPLC to isolate the title compound as a colorless solid.

¹H NMR (400 MHz, CD₃OD): δ = 13.24 (br, 4 H), 8.71 (br, 16 H), 7.45 (br, 20 H), 6.88 (br, 8 H) ppm (Remark: 2 H obscured by the solvent signal at 4.70 ppm). MALDI-MS: (see Figure S4).

Heterodinuclear rare earth cryptate 4-Eu/Y

4-Na/Na (6.40 mg, 5.33 μ mol, 1.0 equiv.) was dissolved in CH₃CN (10 mL, HPLC grade) and EuCl₃ • 6 H₂O (2.93 mg, 7.99 μ mol, 1.5 equivs.) was added. The reaction mixture was heated under reflux for 66 h. The white suspension was allowed to come to ambient temperature and volatiles were removed under reduced pressure. The crude residue was redissolved in a minimum amount of CH₃CN/H₂O/TFA (5/19/0.15; v/v/v) and purified by preparative HPLC to isolate the title compound as a colorless solid (2.1 mg). This material (**4-Eu**) was used in the subsequent step.

4-Eu (1.05 mg, 656 nmol, 1.0 eq) and YCl₃ • 6 H₂O (259 μ g, 853 nmol, 1.3 equivs.) were suspended in acetonitrile (CH₃CN) (3.5 mL). Subsequently, the reaction mixture was heated to reflux for 19 h. The white suspension was allowed to come to ambient temperature and volatiles were removed under reduced pressure. The crude residue was redissolved in a minimum amount of CH₃CN/H₂O/TFA (5/19/0.15; v/v/v) and purified by preparative HPLC to isolate the title compound as a colorless solid. The obtained **4-Eu/Y** contained small amounts of **4-Eu** (10 %).

MALDI-MS: (see Figure S11).

1.3 HPLC Purification / MALDI MS /NMR

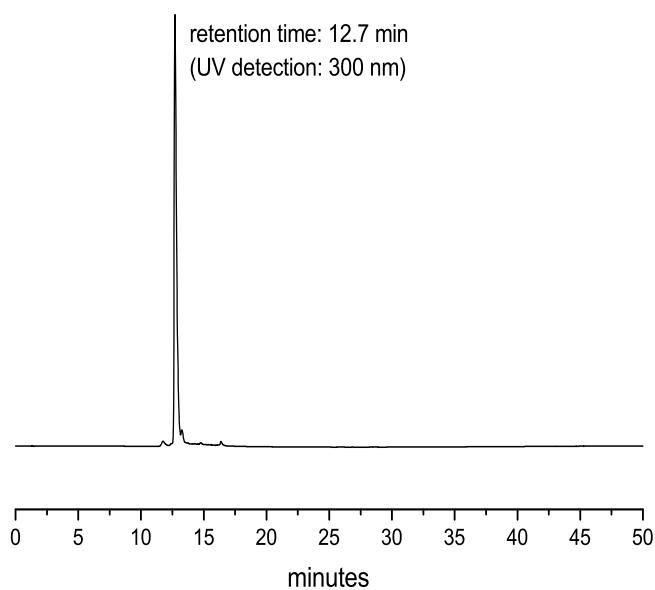


Figure S1. Analytical HPLC trace of the cryptate **4-Na/Na**.

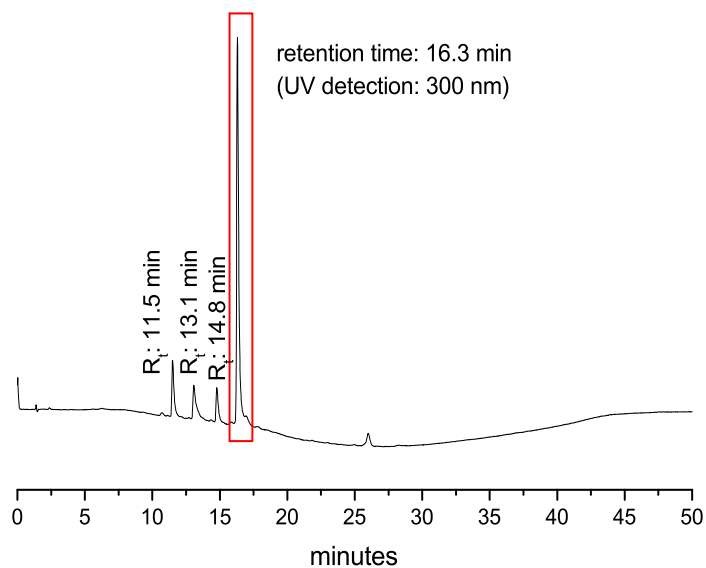


Figure S2. Analytical HPLC trace of the crude reaction mixture to obtain **4-Eu/Eu** (in red: fraction isolated by preparative HPLC).

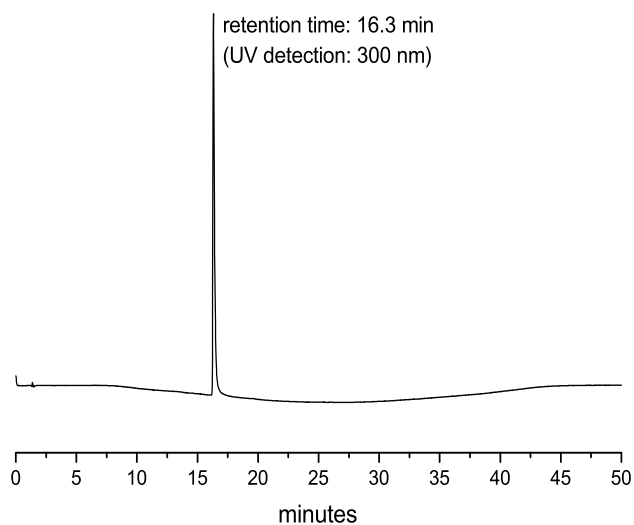


Figure S3. Analytical HPLC trace of the cryptate **4-Eu/Eu** (after HPLC purification, see Figure S2).

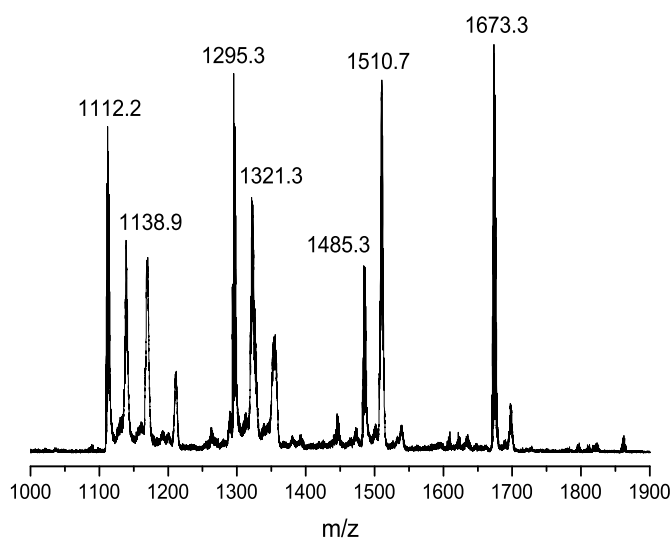


Figure S4. MALDI-MS spectrum (pos. mode) of **4-Eu/Eu** (after HPLC purification):

Assignments: $m/z =$

- 1295.3 $\{[\text{Eu}^{3+}] + \text{Cl}^- + \text{CF}_3\text{COO}^-\}^+$
- 1321.3 $\{[\text{Eu}^{3+}/\text{Na}^+] + 2 \text{Cl}^- + \text{Br}^-\}^+$
- 1485.4 $\{[\text{Eu}^{3+}/\text{Eu}^{2+}] + 3 \text{Cl}^- + \text{Br}^-\}^+$
- 1510.7 $\{[\text{Eu}^{3+}/\text{Na}^+] + 3 \text{CF}_3\text{COO}^-\}^+$
- 1673.3 $\{[\text{Eu}^{3+}/\text{Eu}^{2+}] + \text{Cl}^- + 3 \text{CF}_3\text{COO}^-\}^+$

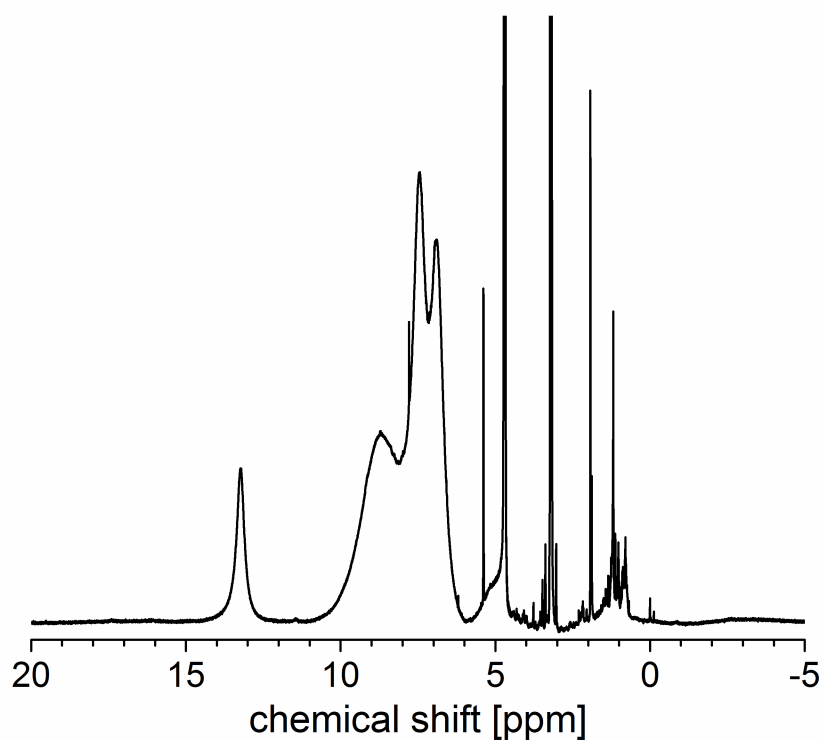


Figure S5. ^1H NMR (400 MHz, CD_3OD) of **4-Eu/Eu**.

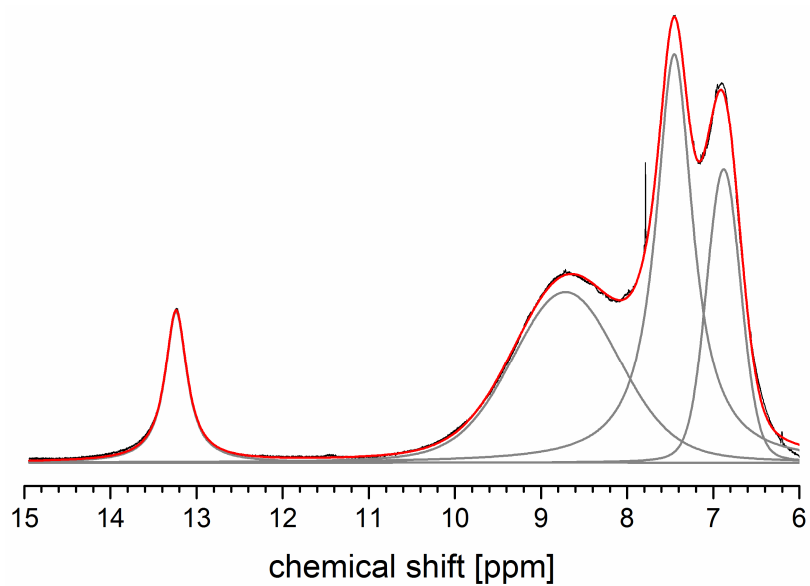


Figure 5a. Line fitting (Voigt, Levenberg-Marquardt) of the ^1H NMR spectrum **4-Eu/Eu** (see Figure S5; black: data; gray: individual Voigt functions ; red: cumulative fit function).

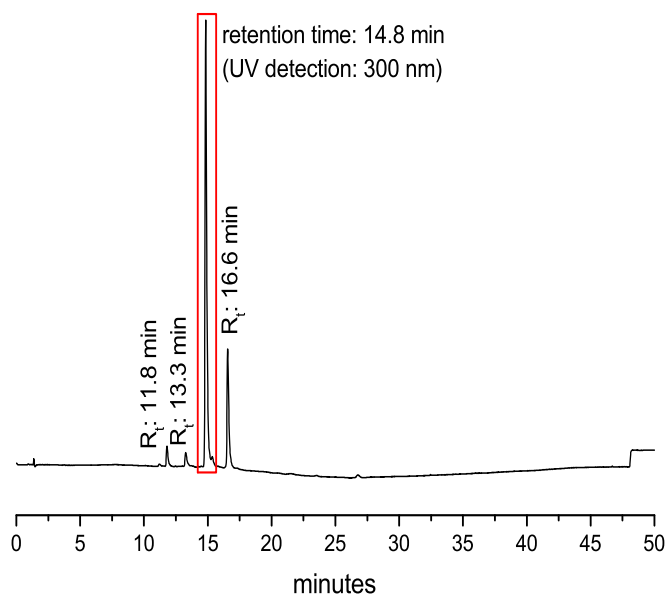


Figure S6. Analytical HPLC trace of the crude reaction mixture to obtain **4-Eu** (in red: fraction isolated by preparative HPLC).

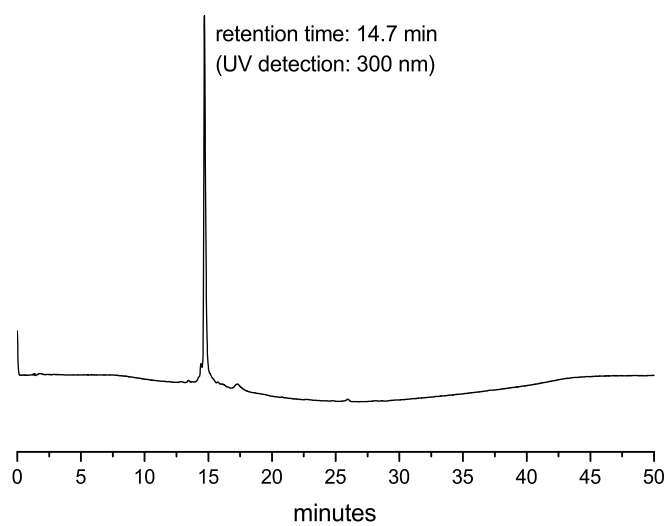


Figure S7. Analytical HPLC trace of the cryptate **4-Eu** (after HPLC purification, see figure S6).

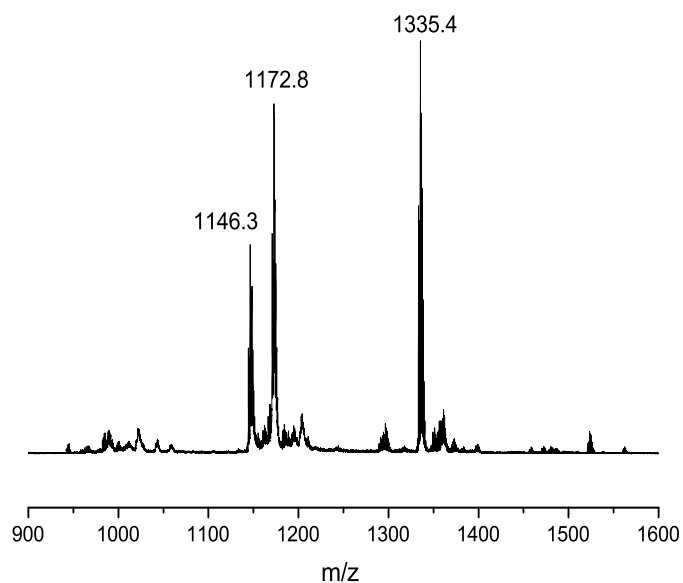


Figure S8. MALDI-MS spectrum (pos. mode) of **4-Eu** (after HPLC purification):
Assignments: $m/z = 1335.4$ ($[\text{Eu}^{2+}/\text{K}^+]\text{-cryptate} + \text{Cl}^- + \text{CF}_3\text{COO}^-$)⁺

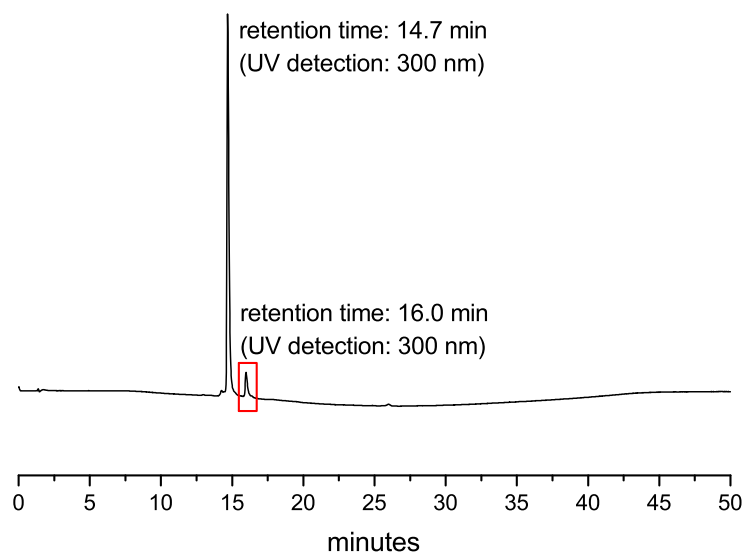


Figure S9. Analytical HPLC trace of the crude reaction mixture to obtain **4-Eu/Y** (in red: fraction isolated by preparative HPLC).

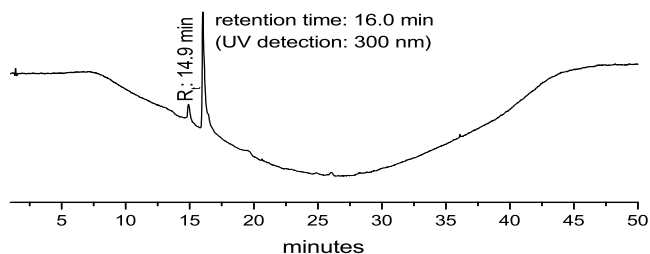


Figure S10. Analytical HPLC trace of the cryptate **4-Eu/Y** (after HPLC purification, see Figure S9). The obtained **4-Eu/Y** contained small amounts of the cryptate **4-Eu** (10 %).

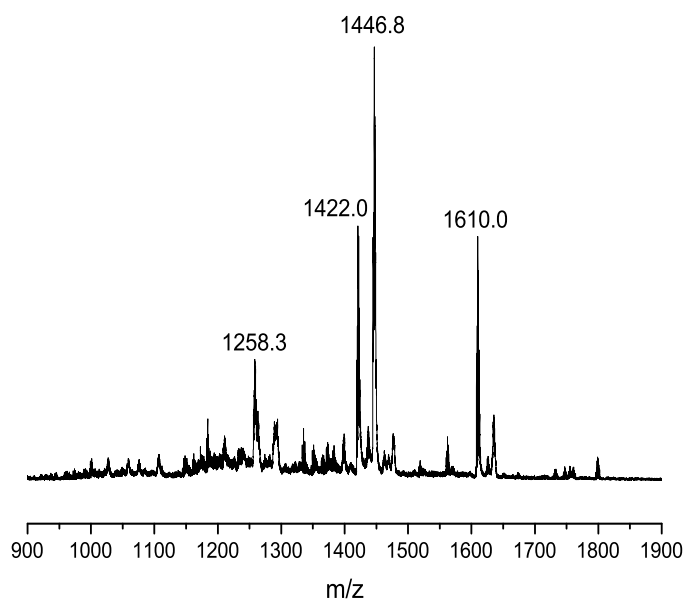


Figure S11. MALDI-MS spectrum (pos. mode) of **4-Eu/Y** (after HPLC purification):

Assignments: $m/z =$ 1422.0 $\{[\text{Eu}^{2+}/\text{Y}^{3+}] + 3 \text{Cl}^- + \text{Br}^-\}^+$
 1610.0 $\{[\text{Eu}^{2+}/\text{Y}^{3+}] + \text{Cl}^- + 3 \text{CF}_3\text{COO}^-\}^+$

2 Photophysical Properties – Experimental Details

2.1 UV/vis Absorption Spectra

UV/vis spectra of the dicryptates were recorded on a Jasco-V670 spectrophotometer using 1.0 cm quartz cuvettes.

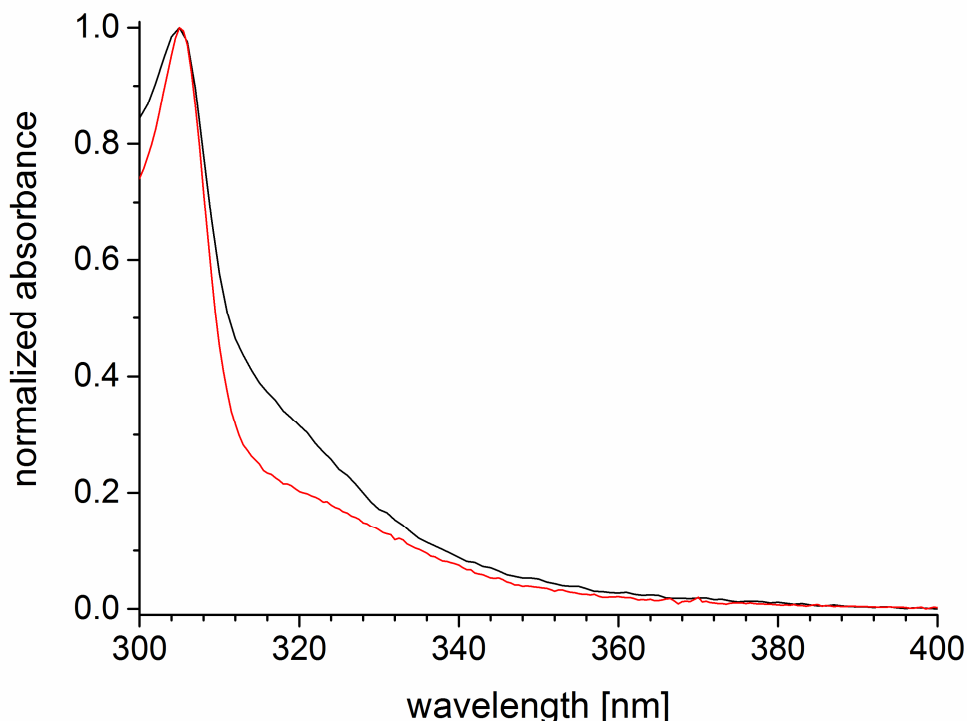


Figure S13. Normalized UV/vis absorption spectra of **4-Eu/Y** (black) and **4-Eu/Eu** (red) in CD_3OD .

2.2 Steady State Emission Spectra

Steady state emission spectra were acquired on a PTI Quantamaster QM4 spectrofluorimeter using 1.0 cm quartz cuvettes at RT. CD_3OD (NMR grade 99.8%D) was purchased from commercial suppliers and used as received without special drying procedures. The excitation light source was a 75 W continuous xenon short arc lamp. Emission was monitored at 90° using a PTI P1.7R detector module (Hamamatsu PMT R5509-72 with a Hamamatsu C9525 power supply operated at -1500 V and a Hamamatsu liquid N_2 cooling unit C9940 set to -80°C). Spectral selection was achieved by single grating monochromators (excitation: 1200 grooves/mm, blazed at 300 nm; emission: 1200 grooves/mm, blazed at 500 nm).

2.3 Luminescence Lifetime Measurements

Luminescence lifetimes were determined with the same instrumental setup as described in section 2.2 without the use of the long-pass filter. The light source for these measurements was a xenon flash lamp (Hamamatsu L4633: 10 Hz repetition rate, pulse width ca. $1.5\ \mu\text{s}$ FWHM). Lifetime data analysis (deconvolution, statistical parameters, etc.) was performed using the software package FeliX32 from PTI. Lifetimes were either determined by fitting the middle and tail portions of the decays or by deconvolution of the decay profiles with the instrument response function, which was determined using a dilute aqueous dispersion of colloidal silica (Ludox® AM-30). The estimated uncertainties in τ are $\pm 10\%$.

3 References

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