Controlled preparation of a heterobimetallic lanthanide complex containing different lanthanides in symmetrical binding pockets

Louise S. Natrajan, Aaron Joseph L. Villaraza, Alan M. Kenwright and Stephen Faulkner*

Supplementary Information

Experimental Procedures

General Methods

Cyclen was purchased from Strem Chemicals, while other reagents, solvents and starting materials were obtained from the Aldrich Chemical Company. All chemicals were used as supplied. 1,4,7-Tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane was synthesized according to a published procedure.[i]

Mass Spectra were obtained using positive electrospray in acetonitrile or methanol solutions on a Micromass Platform II spectrometer, or by MALDI using methanol solutions with an ALPHA maxtrix on a Micromass TOF Spec 2E spectrometer.

FT-IR spectra were recorded on an Equinox 55 FRA106/5 instrument using pressed KBr disks.

Elemental analyses were performed by the microanalytical services at the University of Manchester using a Carlo ERBA Instruments CHNS-O EA1108 elemental analyzer (C, H, N and S analysis) and a Fisons Horizon Elemental Analysis ICP-OED spectrometer for metals and halogens. All lanthanide complexes gave analyses that proved highly dependent upon atmospheric moisture and results are therefore not reported for these compounds.

Absorption spectra were recorded in H_2O on a T60U spectrometer (PG Instruments Ltd.) using fused quartz cells with a path length of 1cm.

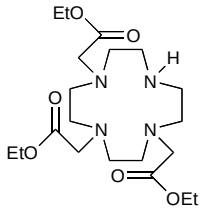
All NMR spectra of diamagnetic compounds were recorded on a Bruker Avance 400 spectrometer, operating frequency 400 MHz (^{1}H), 100 MHz (^{13}C), variable temperature unit set at 300 K, unless otherwise stated. Chemical shifts are reported in parts per million relative to TMS and referenced to the residual proton resonances in

$CDCl_3$ or D_2O. NMR spectra of paramagnetic compounds were recorded primarily on a Varian Inova 500, operating frequency 500 MHz (^1H) at 295 K.

Luminescence Measurements

Steady state and time-resolved luminescence properties of the terbium centre in TbYb**.1** were determined using a PerkinElmer LS55 fluorimeter operating in phosphorescence mode. In the case of the ytterbium complexes, the sample was excited using a pulsed nitrogen laser (337 nm) operating at 10 Hz. Light emitted at right angles to the excitation beam was focused onto the slits of a monochromator, which was used to select the appropriate emission wavelength. The growth and decay of the luminescence at selected wavelengths was detected using a liquid N_2 cooled germanium photodiode detector (Edinburgh Instruments, EI-P) and recorded using a digital oscilloscope (Tektronix TDS220) before being transferred to a PC for analysis. Luminescence lifetimes were obtained by iterative reconvolution of the detector response (obtained by using a scatterer) with exponential components for growth and decay of the metal centred luminescence, using a spreadsheet running in Microsoft Excel. The details of this approach have been discussed elsewhere. Fitting to a double exponential decay yielded no improvement in fit as judged by minimisation of residual squared and reduced chi squared.

Preparation of 1,4,7-tris-(ethoxy-carbonylmethyl)–1,4,7,10–tetraazacyclo-dodecane, sodium bromide salt (7)[ii]



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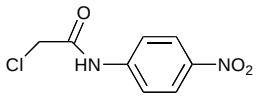
According to a known procedure, 1,4,7,10-tetraazacyclododecane (1.78 g, 10 mmol) and sodium hydrogen carbonate (2.78 g, 33 mmol) were added to 60 mL of acetonitrile stirring in an ice bath (~0°C). Ethyl-bromoacetate (3.44 mL, 31 mmol) was added dropwise very slowly to the mixture, and left to stir for 48 hours. Afterwards, the sodium hydrogen carbonate was filtered off and the solvent removed under reduced pressure. The resulting beige-colored solid was then redissolved in warm dichloromethane and cooled slowly to -18°C. The precipitated solid was then

filtered and washed with cold dichloromethane yielding a while solid powder (2.81 g, 63 %). ES^+ MS (MeCN): *m/z* 431 $\{M+H\}^+$ (100 %). ^1H NMR ($CDCl_3$) δ_H (ppm) 1.20 (9H, m, CH_3), 1.90 (br, 4H, H_2O), 2.83 (br, 4H, CH_2N), 3.24 (br, 2H, CH_2N), 3.41, 3.44, 3.49 (br, 10H, NCH_2CO_2, CH_2N), 3.82 (br, 2H, CH_2N), 4.06 (q, 4H, $C\underline{H}_2CH_3$), 4.20 (q, 2H, $C\underline{H}_2CH_3$), 4.38 (br, 2H, CH_2N), 4.50 (s, 2H, CH_2N), 10.60 (1H, br, NH); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ_C (ppm): 14.0, 14.1 (CH_3), 42.8, 43.3, 48.3, 50.7, 53.0, 53.3, 54.8 (NCH_2), 61.8, 62.7 ($CH_3C\underline{H}_2$), 166.3, 171.6 (C=O). CHN expected for $C_{20}H_{38}N_4O_6(HBr)_2(H_2O)_2$: C, 38.23; H, 7.06; N, 8.92; Br, 25.43; found: C, 38.05; H, 7.10; N, 8.68; Br, 25.97.

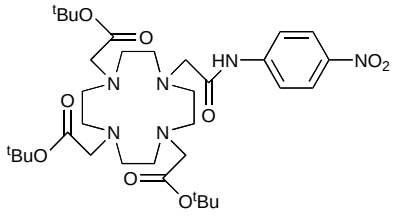
2-chloro-*N*-(4-nitro-phenyl)-acetamide (4)



4

4-nitroaniline (2.0 g, 14.5 mmol) was dissolved in acetonitrile (100 mL), sodium hydrogen carbonate was added (2.0 g, 24 mmol) and the mixture stirred in an ice bath. Chloroacetyl chloride (1.2 mL, 15.2 mmol) was added dropwise slowly to the solution, and the mixture allowed to stir overnight. Afterwards, the sodium hydrogen carbonate was filtered off, and the solvent removed under reduced pressure. The solid was redissolved in hot toluene and allowed to crystallise in the refrigerator overnight. The solid was then filtered and washed with cold toluene, to yield dark green crystals (2.78 g, 90%). ES^- MS (MeCN): *m/z* 213 $\{M-H\}^-$, 249 $\{M+Cl\}^-$, ^1H NMR (400 MHz, *d*-DMSO, 300 K) δ_H (ppm) 4.35 (2H, s, $OCCH_2Cl$), 7.84 (2H, d, $^3J_{HH}$ = 9.6 Hz, Ar-NHCO), 8.25 (2H, d, $^3J_{HH}$ = 9.2 Hz, Ar-NO_2), 10.90 (1H, s br., Ar-N$\underline{H}$CO); $^{13}C\{^1H\}$ NMR (400 MHz, *d*-DMSO, 300 K) δ_C (ppm) 43.54 (C-Cl), 119.07, 125.01 (Ar-H), 142.60 (C-NH), 144.55 (C-NO_2), 165.57 (C=O); IR (ATR) n (N=O asymmetric stretch) 1501.83 cm^{-1}, (N=O symmetric stretch) 1334.81 cm^{-1}; CHN expected for $C_8H_7N_2OCl$: C, 44.86; H, 3.27, N, 13.08, Cl, 16.35; found: C, 44.87; H, 3.10; N, 13.04; Cl, 16.41.

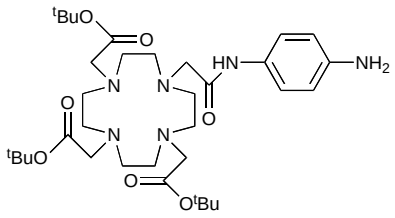
10-[1,4,7-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-*N*-(4-nitro-phenyl)-acetamide (5)



5

3 (1.0 g, 1.95 mmol) was dissolved in acetonitrile (100 mL), solid sodium carbonate (0.5 g, 4.71 mmol) was added and the solution stirred. **96** (0.46 g, 2.14 mmol) was added, the mixture heated under reflux for 24 hours. Afterwards, the sodium carbonate was filtered off and the solvent removed under reduced pressure. The residue was redissolved in hot toluene and left in the refrigerator overnight to precipitate out any unreacted starting material. The solids were filtered off, the filtrate evaporated under reduced pressure, and the residue purified by column chromatography using a silica plug. Initially, pure DCM was used as eluent into order to wash away trace amounts of **4**, then the polarity was increased to dichloromethane:methanol (9:1) to isolate the product from salts which remained at the top of the column. The pure fractions were collected, and the solvents removed under reduced pressure, yielding a pale yellow powder (0.19 g, 14.1%). ES^+ MS (MeCN): *m/z* 715 $\{M+Na\}^+$, ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ_H (ppm) 1.40 (27H, s, ^tBu), 2.25-3.65 (24H, m, CH_2N), 7.97 (2H, d, $^3J_{HH}$ = 9.2 Hz, Ar-NHCO), 8.08 (2H, d, $^3J_{HH}$ = 9.2 Hz, Ar-NO_2), 11.24 (1H, s, NHCO); $^{13}C\{^1H\}$ NMR (400 MHz, $CDCl_3$, 300 K) δ_C (ppm) 28.17, 28.28 ($C\underline{C}H_3$), 50.78, 51.78, 51.98, 54.63, 55.79, 57.01, 59.34 (CH_2N), 81.23, 81.33 ($\underline{C}CH_3$), 119.27, 125.03 (Ar-H), 143.15 ($\underline{C}$NHCO), 144.51 (C-NO_2), 169.92, 170.16, 170.23 (C=O); IR (ATR) n (C=O) 1723.35 cm^{-1}, (N=O asymmetric stretch) 1507.05 cm^{-1}, (N=O symmetric stretch) 1327.78 cm^{-1}, (C-C(C=O)-C asymmetric stretch) 1150.10 cm^{-1}, 1107.93 cm^{-1}; CHN expected for $C_{34}H_{56}N_6O_9$(NaCl): C, 54.36; H, 7.51; N, 11.18; found: C, 53.30; H, 7.40; N, 11.10; Accurate Mass MS (MeCN): composition $C_{34}H_{56}N_6O_9Na_1$, theoretical 715.4001, found 715.4014, error 1.8 ppm.

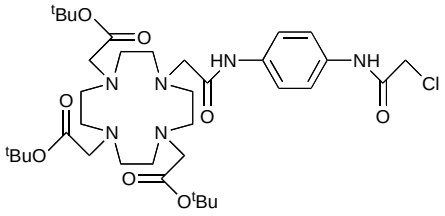
10-[1,4,7-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-*N*-(4-amino-phenyl)-acetamide (6)



6

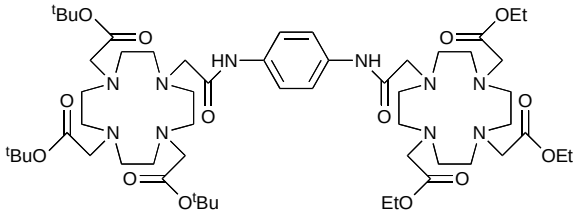
5 (500 mg, 0.72 mmol) was dissolved in ethanol (10 mL) and warmed to around 78 °C. Once warmed, 62 % hydrazine hydrate solution (2 mL) and Pd/C catalyst were added to the mixture, and the reaction stirred under reflux for three hours. Afterwards, the catalyst was filtered off into celite, the filtrate evaporated under reduced pressure, re-dissolved in chloroform and extracted with distilled water to remove most of the hydrazine. The organic portions were collected and dried over anhydrous $MgSO_4$, filtered, and the solvent removed under reduced pressure, purified through a silica column eluted with dichloromethane:methanol (9:1) to remove the last traces of hydrazine. Pure fractions were pooled together and the solvent removed under reduced pressure, yielding a pale beige powder (330 mg, 68%). ES^+ MS (MeCN): *m/z* 686 $\{M+H+Na\}^+$; ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ_H 1.38 (27H, s, ^tBu), 2.15-3.60 (16H, m, CH_2N), 6.48 (2H, d, $^3J_{HH}$ = 9.2 Hz, Ar-NH_2), 7.64 (2H, d, $^3J_{HH}$ = 9.2 Hz, Ar-NHCO), 10.24 (1H, s, NHCO); $^{13}C\{^1H\}$ NMR (400 MHz, $CDCl_3$, 300 K) d_C (ppm) 25.86, 25.91 (CCH_3), 53.03, 53.40, 53.68, 53.93, 54.71 (CH_2N), 79.79, 79.94 (CCH_3), 112.91, 119.58 (Ar-H), 129.16 (C-NH_2), 139.83 (CNHCO), 168.02, 170.12 (C=O); IR (ATR) n (br. N-H) 3227.01 cm^{-1}, (C=O) 1724.38 cm^{-1}, 1150 cm^{-1}, (C-C(C=O)-C asymmetric stretch) 1107.62 cm^{-1} (C-C(C=O)-C asymmetric stretch); CHN expected for $C_{34}H_{58}N_6O_7(NaBr)(H_2O)$: C, 52.10; H, 7.72; N, 10.72; found: C, 52.42; H, 7.99; N, 10.69.

10-[1,4,7-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-*N*-[4-(2-chloro-acetylamino-phenyl)]-acetamide.



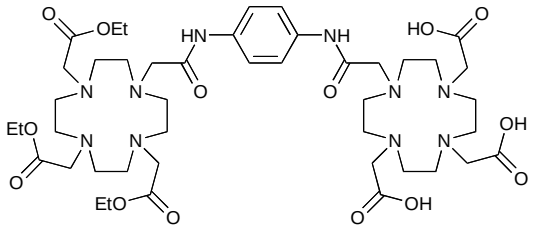
6 (0.46 g, 0.69 mmol) was dissolved in dicholoromethane (50 mL) containing 1.05 equivalents of diisopropylethylamine. This was added dropwise slowly to a solution of dichloromethane (5 mL) and 1.05 equivalents of chloroacetyl chloride stirred over an ice bath (~0°C). Once the addition was complete, the reaction was left to stir overnight. Afterwards, the reaction mixture was extracted with 10% $NaHCO_3$ solution, then with 0.1 M HCl, the organic portions collected and dried over anhydrous $MgSO_4$, then filtered. The solvent was removed under reduced pressure and the residue triturated with hexane to yield a beige powder (0.19 g, 37%). ES^+ MS (MeCN): *m/z* 761 $\{M+Na\}^+$; ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ_H (ppm) 1.37 (27H, s, ^{t}Bu), 2.10-4.29 (24 H, m, CH_2N), 5.23 (2H, s, $OCCH_2Cl$), 7.48 (2H, d, $^3J_{HH}$ = 8 Hz, Ar-NHCO), 7.71 (2H, d, $^3J_{HH}$ = 8 Hz, Ar-NHCO), 9.47 (1H, s, NHCO), 10.38 (1H, s, NHCO); $^{13}C\{^1H\}$ NMR (400 MHz, $CDCl_3$, 300 K) δ_C (ppm) 26.70, 26.89 (CCH_3), 42.46, 44.59, 46.96, 50.97, 54.46, 55.47 (CH_2N), 80.74, 80.95 (CCH_3), 119.08, 119.34 (Ar-H), 132.08, 134.57 (CNHCO), 163.62, 169.57, 171.31 (C=O); CHN expected for $C_{36}H_{59}N_6O_8Cl(NaCl)(H_2O)$: C, 53.00; H, 7.54; N, 10.30; Cl, 8.69; found: C, 52.54; H, 7.70; N, 9.11; Cl, 6.00.

10-[1,4,7-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-({acetylamino-phenylcarbamoyl}-methyl)-[1,4,7,10-tetraaza-cyclododec-1-yl]-acetic acid ethyl ester (2)



7, (0.11 g, 0.26 mmol) was dissolved in acetonitrile (50 mL) and sodium hydrogen carbonate (0.50 g) was added. The mixture was stirred and warmed to 80 °C. **10-[1,4,7-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-*N*-[4-(2-chloro-acetylamino-phenyl)]-acetamide**, (0.19 g, 0.26 mmol) was dissolved in a minimal amount of acetonitrile and added dropwise to the stirring solution. Once the addition was complete, the mixture heated to reflux temperature overnight. Afterwards, the sodium hydrogen carbonate was filtered off, and the solvent removed under reduced pressure. The residue was triturated with hexane to yield a pale beige coloured solid (0.20 g, 69 %). MALDI MS (alpha/MeOH): *m/z* 1135 $\{M+2H\}^+$, 1157 $\{M+Na+H\}^+$; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) δ_H (ppm) 1.20 (9H, m, $C\underline{H}_3CH_2$), 1.37, 1.41 (27H, s, ^{t}Bu), 1.85-3.58 (48H, m, CH_2N), 4.14 (6H, m, $CH_3C\underline{H}_2$), 7.69 (2H, d, $^3J_{HH}$ = 9.6 Hz, Ar$\underline{H}$), 7.73 (2H, d, $^3J_{HH}$ = 9.6 Hz, Ar$\underline{H}$), 10.20 (1H, s, NHCO), 10.37 (1H, s, NHCO); $^{13}C\{^1H\}$ NMR (400 MHz, $CDCl_3$, 300 K) δ_C (ppm) 11.85, 11.97 ($\underline{C}H_3CH_2$), 25.66, 25.71 ($C\underline{C}H_3$), 46.28, 47.23, 49.24, 50.30, 52.84, 53.41, 54.50, 54.74 (CH_2N), 59.02, 59.24 ($CH_3\underline{C}H_2$), 79.68, 79.93 ($\underline{C}CH_3$), 117.87, 118.09, 132.11, 132.52 (Ar), 156.63, 166.44, 168.09, 168.44, 168.09, 168.24, 169.90, 170.77 (C=O); CHN expected for $C_{56}H_{96}N_{10}O_{14}(NaBr)_4(H_2O)_3(MeCN)$: C, 47.73; H, 7.38; N, 10.74; Br 11.14, found: C, 47.97; H, 7.35; N, 10.72; Br ~11.

10-[1,4,7-tris(ethoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-({acetylamino-phenylcarbamoyl}-methyl)- 10-[1,4,7-tris(carbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl] acetic acid (8)

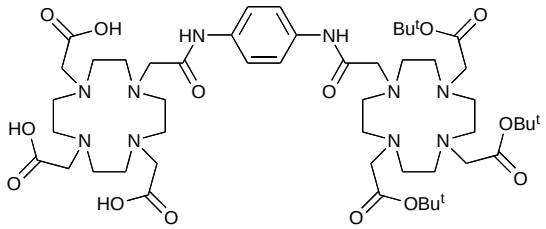


8

2, (0.061 g, 0.046 mmol) was dissolved in dichloromethane (5 mL) and trifluoroacetic acid (5mL) was added dropwise to the stirring solution. The reaction mixture was allowed to stir at room temperature for 24 hours. All volatiles were then removed under reduced pressure and the residue washed repeatedly with dichloromethane (3 x

10 mL) and methanol (3 x 10 mL). The resultant solid was then dissolved in methanol (5 mL) and precipitated by layering this solution with diethyl ether (15 mL). After diffusion was complete (5 days), the hygroscopic product was filtered, and washed with diethyl ether to afford a white solid (0.034 g, 58 %). MALDI MS (alpha/MeOH): *m/z* 966 $\{M+H\}^+$ (100 %), 989 $\{M+Na\}^+$ (83 %); UV-vis (H_2O) λ_{max} (ε/mol^{-1}dm^{3}cm) = 263 (27510); ^{1}H NMR (400 MHz, MeOD, 300 K) δ_H (ppm) 1.17 (9H, m, C<u>H</u>$_3$CH$_2$), 3.02-3.69 (48H, m, CH$_2$N), 4.09 (6H, m, CH$_3$C<u>H</u>$_2$), 7.43 (4H, m, Ar<u>H</u>); CHN expected for $C_{44}H_{72}N_{10}O_{14}(CF_3CO_2H)_3(H_2O)_4$: C, 43.54; H, 6.07; N, 10.16; found: C, 43.43; H, 5.98; N, 11.32.

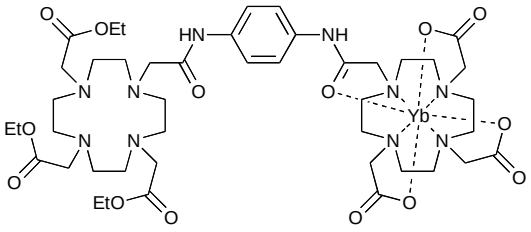
10-[1,4,7-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-({acetylamino-phenylcarbamoyl}-methyl)-10-[1,4,7-tris(carbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl] acetic acid (9)



9

To a stirred solution of **2**, (0.060 g, 0.046 mmol) in thf (10 mL) was added an aqueous solution of NaOH (0.006 g, 0.138 mmol, 10 mL). The reaction mixture was stirred at room temperature for 48 hours. After this time, the pH of the solution was adjusted to 6 with a 0.1 M solution of HCl and all volatiles removed under reduced pressure at room temperature or just above. 10 mL ethanol was then added to the residue and the solution left to stand at 4°C for several hours. The precipitated inorganic salts were removed by vacuum filtration and all volatiles removed under reduced pressure. The residue was then dissolved in 3 mL MeCN and filtered through a plug of glass wool. The product was precipitated by layering the acetonitrile solution with diethyl ether (10 mL). After diffusion was complete (5 days), the solid was filtered, washed with diethyl ether (5 x 10 mL) and dried. The complex was isolated as a white solid (0.034 g, 70 %). MALDI MS (alpha/MeOH): *m/z* 1046 $\{M+H\}^+$ (48 %); ^{1}H NMR (400 MHz, MeOD, 300 K) δ_H (ppm): 1.41, 1.35 (27H, s, CC<u>H</u>$_3$), 2.85-3.90 (48H, m, CH$_2$N), 7.41 (4H, m, Ar<u>H</u>).

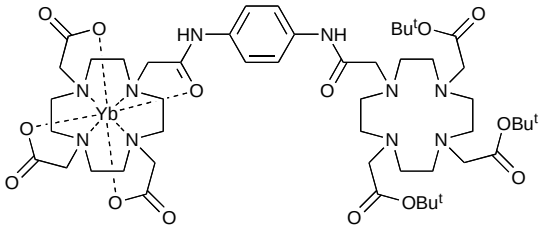
10-[1,4,7-tris(ethoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-({acetylamino-phenylcarbamoyl}-methyl)-[1,4,7,10-tetraaza-cyclododec-1-yl]-ytterbium (Yb.8)



Yb**.8**

To a solution of $YbOTf_3$ (0.016 g, 0.026 mmol) in methanol (2 mL) was added a methanolic solution of the ligand adduct **8** (0.030 g, 0.026 mmol) dropwise in methanol (3 mL). The reaction mixture was then warmed gently to 40°C for 48 h. All volatiles were removed under reduced pressure, and 5 mL H_2O added. The pH was adjusted to ~10 with 0.1 M NaOH to precipitate any uncomplexed Yb as the hydroxide, and the solution filtered through a pad of celite. The pH was then readjusted to 6 with 0.1 M HCl and all solvents removed under reduced pressure. 3 mL ethanol was added and the solution left to stand at 4°C for several hours before removing the insoluble sodium salts by filtration. All volatiles were then removed, 3 mL methanol added and the solution filtered through a plug of glass wool. The product was slowly precipitated by layering the methanol solution with diethyl ether (15 mL). After diffusion was complete (5 days), the solid was filtered, washed with diethyl ether (5 x 10 mL) and air dried. The complex was isolated as a white solid (0.023 g, 76 %). MALDI MS (alpha/MeOH): *m/z* broad cluster 1136 $\{M+H\}^+$ (78 %), 1158 $\{M+Na\}^+$ (75 %), 966 $\{M-Yb+H\}^+$ (100 %). UV-vis (H_2O) λ_{max} (ε/mol^{-1}dm^{3}cm) = 265 (17390); ^{1}H NMR (500 MHz, D_2O, 295 K) δ_H (ppm) (major species): 135.45, 124.01, 121.01, 117.77, 37.29, 29.16, 24.24, 18.68, 17.97, 17.49, 14.68, 14.39, 11.48, 11.21, 9.78, 9.22, 7.46, 6.59, 6.38, 5.88, 5.59, 4.80-1.30 (m), 0.79, 0.23, -0.85, -12.89, -20.67, -25.82, -44.67, -46.84, -61.50, -63.96, -75.34, -77.70.

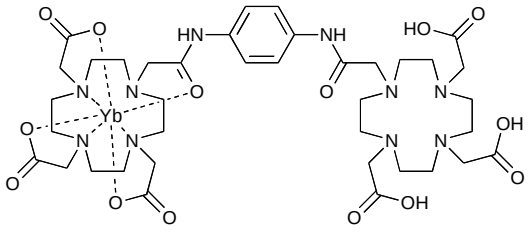
10-[1,4,7-tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-({acetylamino-phenylcarbamoyl}-methyl)-10-[1,4,7-tris(carbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl] ytterbium (Yb.9)



Yb.**9**

To a solution of $YbOTf_3$ (0.018 g, 0.029 mmol) in methanol (2 mL) was added a methanolic solution of the ligand adduct **9** (0.030 g, 0.029 mmol) dropwise in methanol (3 mL). The reaction mixture was then warmed gently to 40°C for 48 h. All volatiles were removed under reduced pressure and 3 mL H_2O added. The pH was adjusted to ~10 with 0.1 M NaOH to precipitate any uncomplexed Yb as the hydroxide, and the solution filtered through a pad of celite. The pH was then readjusted to 6 with 0.1 M HCl and all solvents removed under reduced pressure. 3 mL ethanol was added and the solution left to stand at 4°C for several hours before removing the insoluble sodium salts by filtration. All volatiles were then removed, 3 mL methanol added and the solution filtered through a plug of glass wool. The product was slowly precipitated by layering the methanol solution with diethyl ether (10 mL). After diffusion was complete (5 days), the solid was filtered, washed with diethyl ether (5 x 15 mL) and air dried. The complex was isolated as a white solid (0.017 g, 48 %). MALDI MS (alpha/MeOH): *m/z* broad cluster 1223 $\{M+H\}^+$ (11 %), 1052 $\{M-Yb+H\}^+$ (100 %). UV-vis (H_2O) λ_{max} (ε/mol^{-1}dm^{3}cm) = 266 (17716). ^{1}H NMR NMR (500 MHz, D_2O, 295 K) δ_H (ppm) (major species): 135.45, 124.01, 121.01, 117.77, 37.29, 29.16, 24.24, 18.68, 17.97, 17.49, 14.68, 14.39, 11.48, 11.21, 9.78, 9.22, 7.46, 6.59, 6.38, 5.88, 5.59, 4.80-1.30 (m), 0.79, 0.23, -0.85, -12.89, -20.67, -25.82, -44.67, -46.84, -61.50, -63.96, -75.34, -77.70.

10-[1,4,7-tris(carbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-ytterbium ({acetylamino-phenylcarbamoyl}-methyl)-10-[1,4,7-tris(carbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl] acetic acid (H_3Yb.1)



H_3Yb.**1**

Method 1. From Yb.8

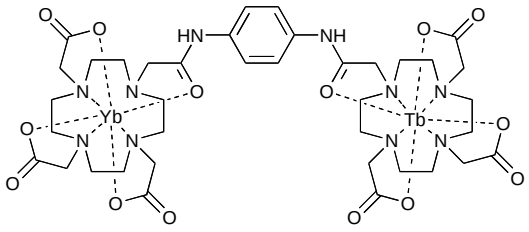
To a stirred solution of Yb.**8**, (0.023 g, 0.020 mmol) in thf (5 mL) was added an aqueous solution of NaOH (0.003 g, 0.060 mmol, 5 mL). The reaction mixture was stirred at room temperature for 48 hours. After this time, the pH of the solution was adjusted to 6 with a 0.1 M solution of HCl and all volatiles removed under reduced pressure at room temperature or just above. 5 mL ethanol was then added to the residue and the solution left to stand at 4°C for several hours. The precipitated inorganic salts were removed by vacuum filtration and all volatiles removed under reduced pressure. The residue was then dissolved in 3 mL MeOH and filtered through a plug of glass wool. The product was precipitated by layering the methanol solution with diethyl ether (15 mL). After diffusion was complete (5 days), the solid was filtered, washed with diethyl ether (5 x 10 mL) and dried. The complex was isolated as a white solid (0.012 g, 57 %). MALDI MS (alpha/MeOH): *m/z* 1052 $\{M\}^+$ (7 %). ^{1}H NMR (500 MHz, D_2O, 295 K); UV-vis (H_2O) λ_{max} (ε/mol^{-1}dm^{3}cm) = 267 (15110); δ_H (ppm) (major species): 127.89, 119.51, 114.06, 33.03, 26.76, 23.24, -16.23, -22.08, 18.24, 17.24, 15.70, 13.61, 13.02, 11.27, 8.93, 8.49, 8.29, 7.32, 7.10, 6.69, 2.22, 1.76, -25.24, -40.53, -43.24, -45.31, -56.62, -57.93, -70.16, -73.01, -73.64.

Method 2. From Yb.9

Yb.**9**, (0.027 g, 0.021 mmol) was dissolved in dichloromethane (5 mL) and trifluoroacetic acid (5mL) was added dropwise to the stirring solution. The reaction

mixture was allowed to stir at room temperature for 24 hours. All volatiles were then removed under reduced pressure and the residue washed repeatedly with dichloromethane (3 x 10 mL) and methanol (3 x 10 mL). The residue was then dissolved in methanol (3 mL) and precipitated by layering the solution with diethyl ether (15 mL). After diffusion was complete (5 days), the hygroscopic product was filtered, and washed with diethyl ether to afford a white solid (0.013 g, 50 %). MALDI MS (alpha/MeOH): *m/z* 1051 $\{M\}^+$ (10 %), 1073 $\{M+Na\}^+$ (6 %); UV-vis (H_2O) λ_{max} (ε/mol^{-1}dm^{3}cm) = 267 (15110); ^{1}H NMR (500 MHz, D_2O, 295 K) δ_H (ppm) (major species): 128.87, 128.29, 120.06, 119.54, 114.98, 114.50, 33.88, 33.45, 32.56, 27.45, 27.14, 26.60, 24.63, 24.00, 23.46, 18.82, 18.53, 17.63, 16.25, 15.93, 15.53, 15.10, 14.45, 13.79, 13.56, 11.45, 10.91, 10.24, 10.17, 7.33, -15.09, -15.55, -21.54, -22.66, -23.86, -24.82, -26.04, -40.32, -42.50, -43.32, -56.66, -57.75, -67.73, -68.79, -70.08, -72.69, -73.25. CHN expected for $C_{33}H_{58}N_{10}O_{14}(CF_3CO_2H)_{1.5}$: C, 34.05; H, 4.93; N, 11.51; found: C, 33.90; H, 4.67; N, 9.46.

10-[1,4,7-tris(carbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-ytterbium ({acetylamino-phenylcarbamoyl}-methyl)-10-[1,4,7-tris(carbonylmethyl)-1,4,7,10-tetraazacyclododecan-1-yl]-terbium (TbYb.1)



YbTb**.1**

To a solution of $TbOTf_3$ (0.012 g, 0.019 mmol) in methanol (2 mL) was added a methanolic solution of the ligand adduct (0.020 g, 0.019 mmol) dropwise in methanol (3 mL). The reaction mixture was then warmed gently to 40°C for 48 h. All volatiles were removed under reduced pressure and 3 mL H_2O added. The pH was raised to ~10 with 0.1 M NaOH to precipitate any uncomplexed Tb as the hydroxide, and the solution filtered through a pad of celite. The pH was then readjusted to 6 with 0.1 M HCl and all solvents removed under reduced pressure. 3 mL ethanol was added and the solution left to stand at 4°C for several hours before removing the insoluble sodium salts by filtration. All volatiles were then removed, 3 mL methanol added and the solution filtered through a plug of glass wool. The product was slowly precipitated by layering the methanol solution with diethyl ether (15 mL). After diffusion was

complete (5 days), the solid was filtered, washed with diethyl ether (5 x 10 mL) and air dried. The complex was isolated as a white solid (0.015 g, 65 %). MALDI MS (alpha/MeOH): *m/z* broad cluster 1205 $\{M\}^+$ (42 %), 1227 $\{M+Na\}^+$ (19 %). UV-vis (H_2O) λ_{max} (ε/mol^{-1}dm^{3}cm) = 267 (79410); ^{1}H NMR NMR (500 MHz, D_2O, 295 K) δ_H Tb^{3+} (ppm): 310.91, 253.18, 243.67, 219.55, -88.40, -100.56, -111.57, -122.24, -136.76, -143.48, -200.48, -250.20, -266.28, -328.92, -372.14, -404.95; δ_H Yb^{3+} (ppm): 128.93, 126.67, 120.53, 117.63, 115.07, 112.88, 111.54, 33.71, 31.94, 27.34, 25.59, 21.56, 20.09, 18.61, 17.73, 16.18, 15.57, 15.19, 14.46, 13.60, 11.22, 10.51, 8.37, -12.76, -14.99, -16.84, -21.46, -23.14, -23.80, -25.02, -26.12, -28.50, -29.43, -33.02, -40.52, -42.68, -45.51, -47.62, -50.03, -57.94, -59.80, -68.91, -74.61, -77.10.

Supplementary Figures

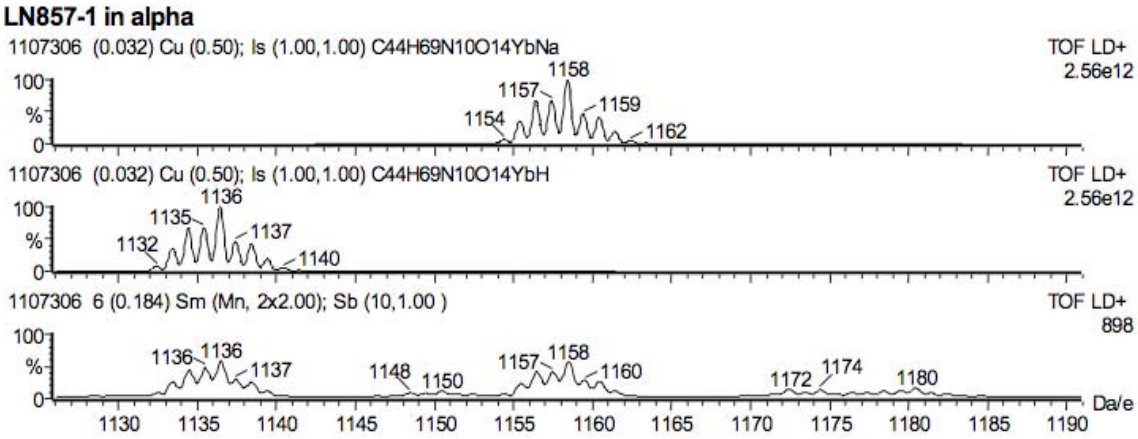


Figure S1. Calculated (top and middle trace) and observed (bottom trace) MALDI mass spectrum of Yb.**8**

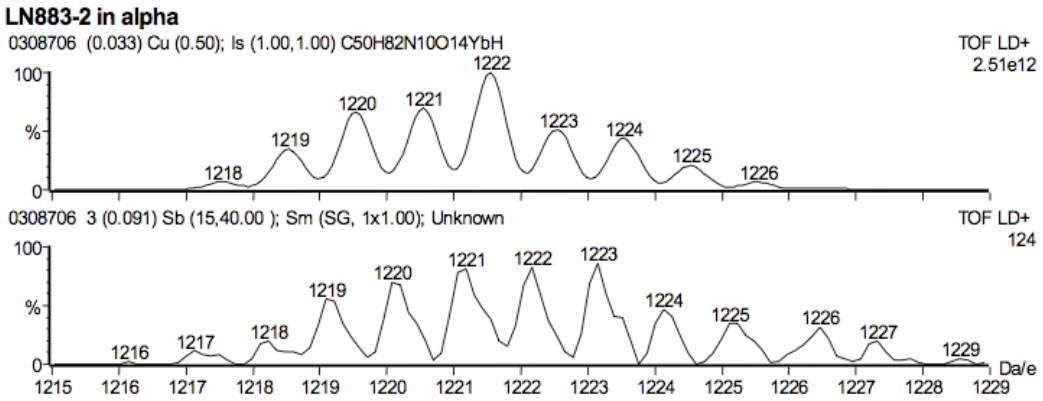


Figure S2. Calculated (top trace) and observed (bottom trace) MALDI mass spectrum of Yb.**9**

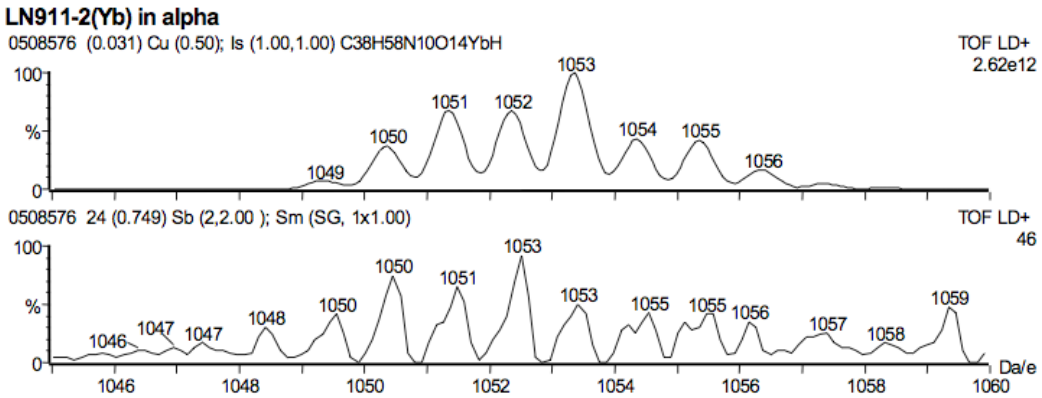


Figure S3. Calculated (top trace) and observed (bottom trace) MALDI mass spectrum of H_3Yb.**1** prepared from Yb.**8**

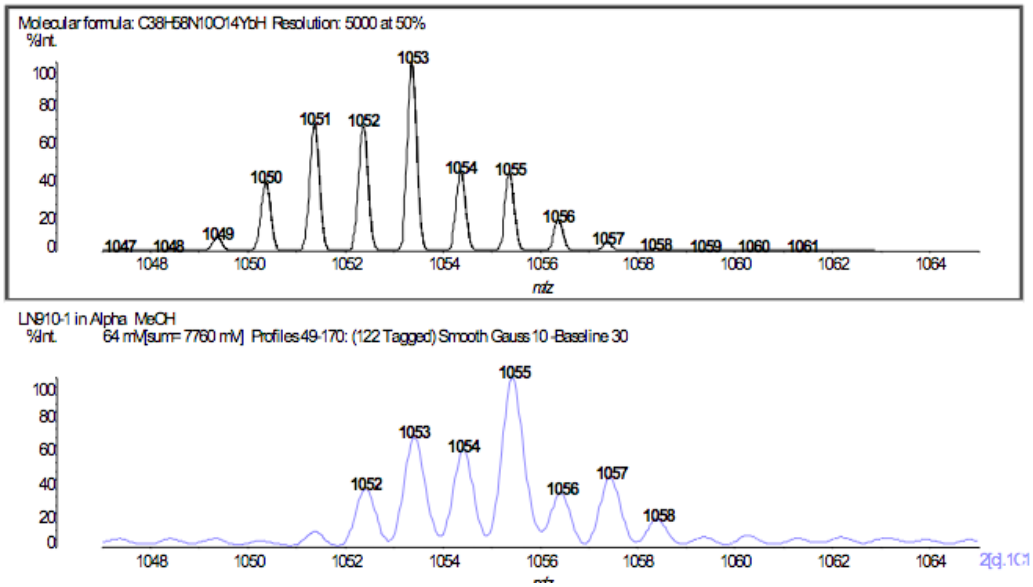


Figure S4. Calculated (top trace) and observed (bottom trace) MALDI mass spectrum of H_3Yb.**1** prepared from Yb.**9**

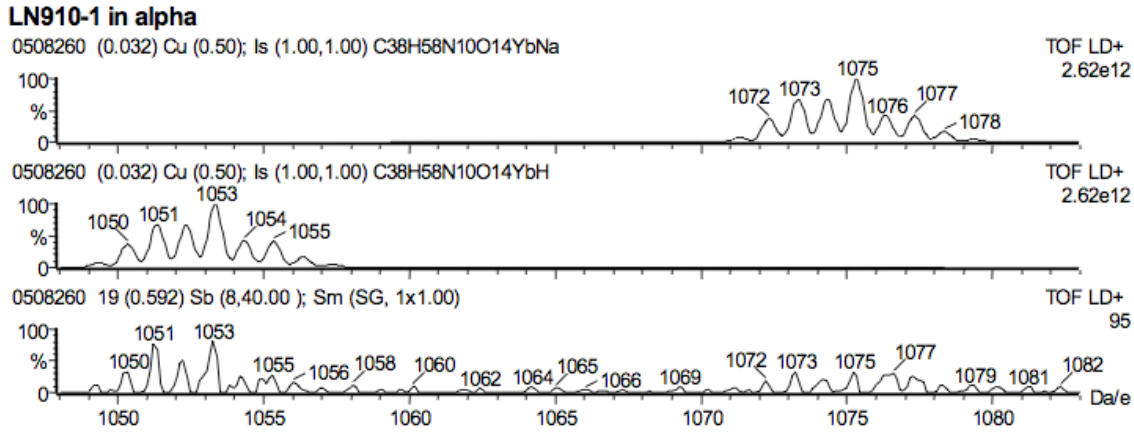


Figure S5. Calculated (top and middle trace) and observed (bottom trace) MALDI mass spectrum of H_3Yb.**1** prepared from Yb.**9**

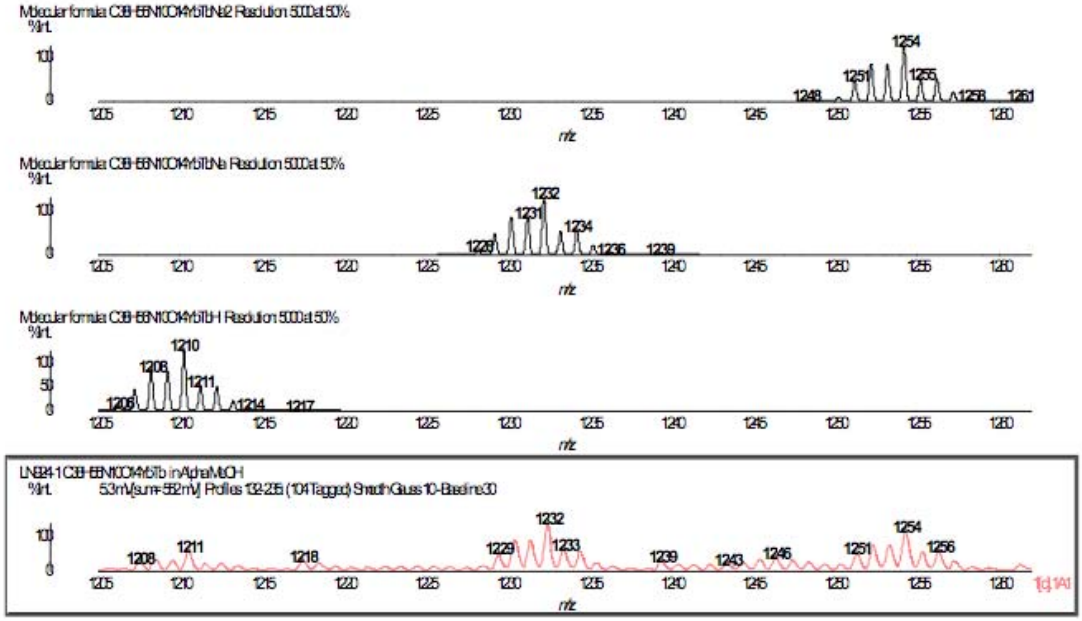


Figure S6. Calculated and observed (bottom trace) MALDI mass spectrum of YbTb.**1**

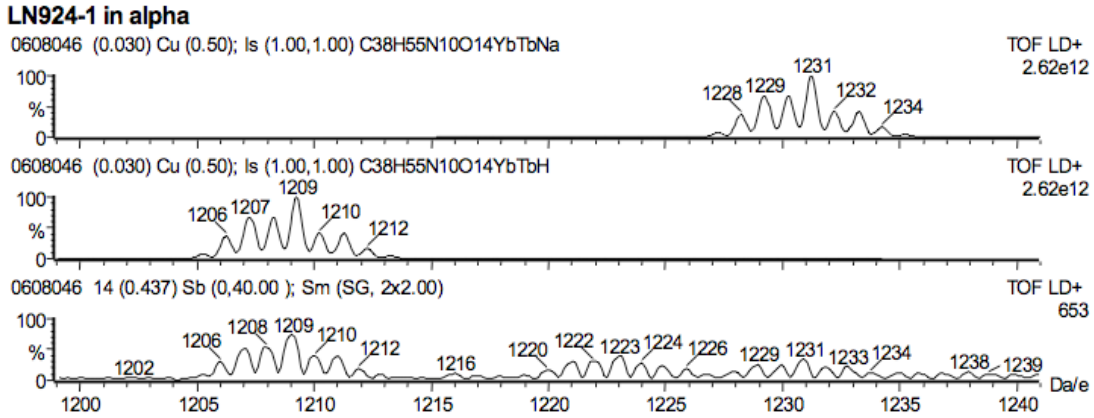


Figure S7. Calculated (top and middle trace) and observed (bottom trace) MALDI mass spectrum of YbTb.**1**

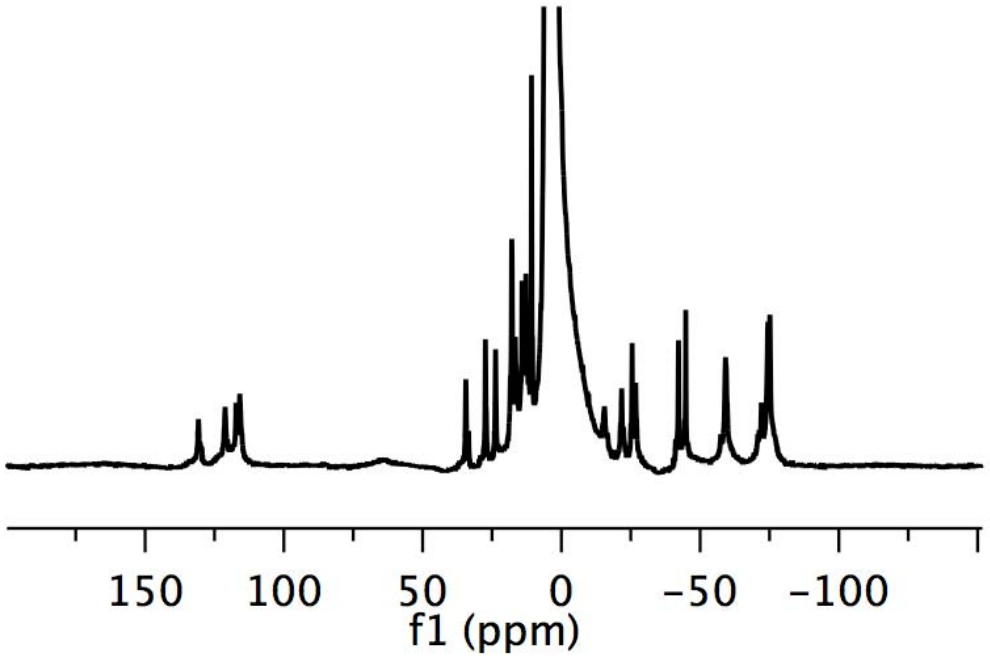


Figure S8. ^{1}H NMR spectrum of Yb.**8** (D_2O)

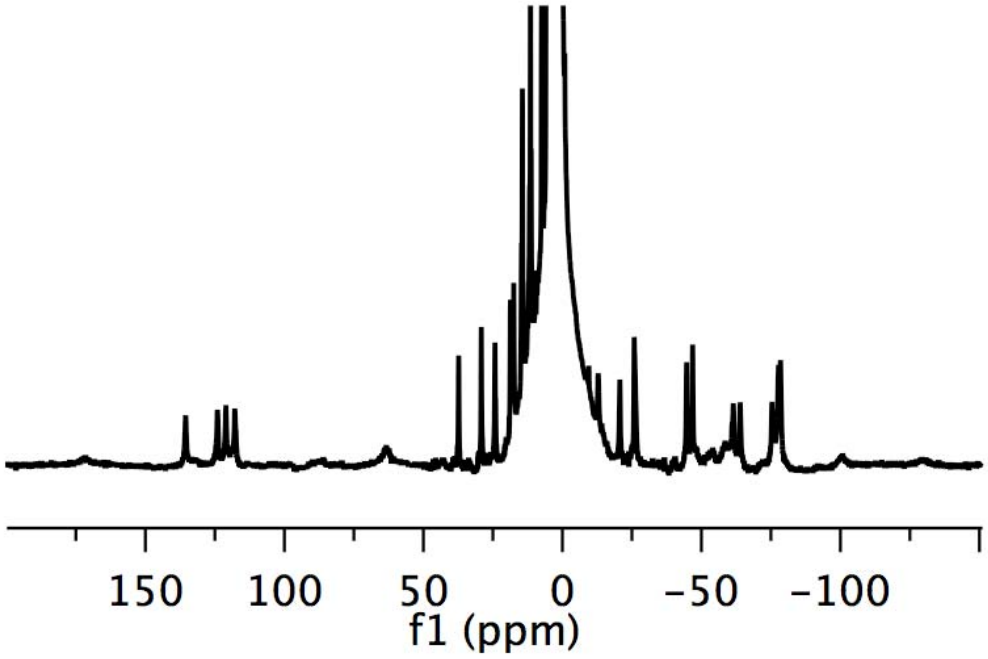


Figure S9. ^{1}H NMR spectrum of Yb.**9** (D_2O)

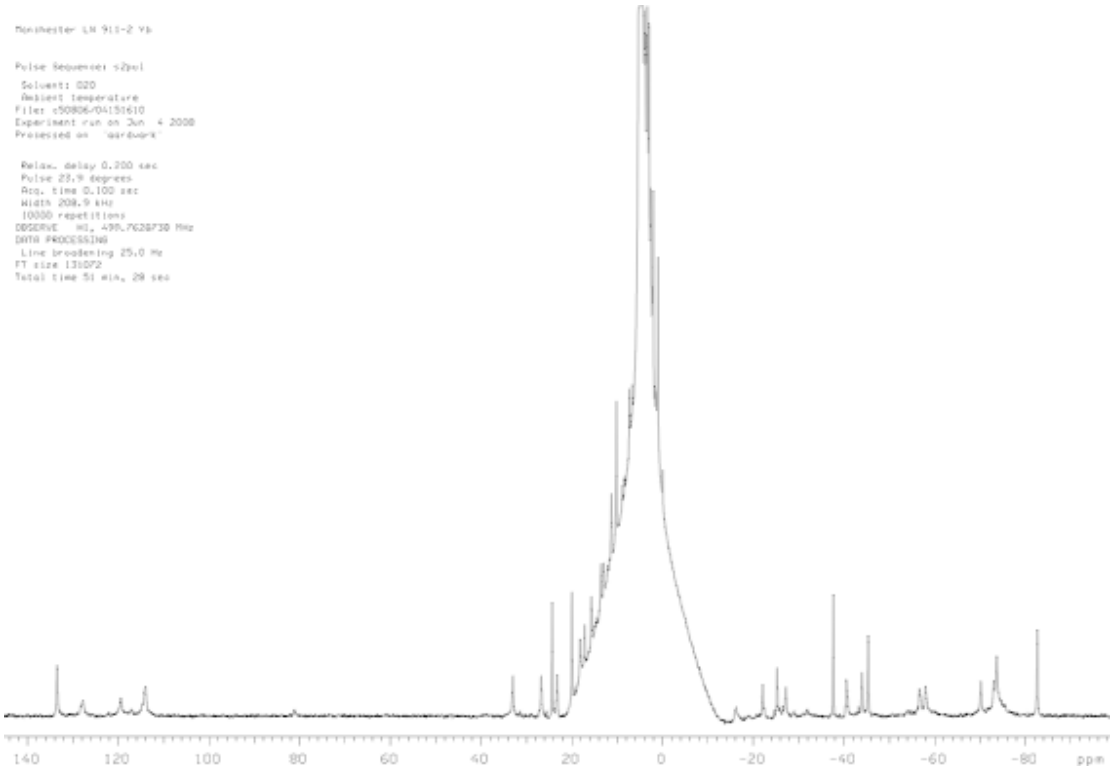


Figure S10. ^{1}H NMR spectrum of H_3Yb.**1** (D_2O) prepared from Yb.**8**

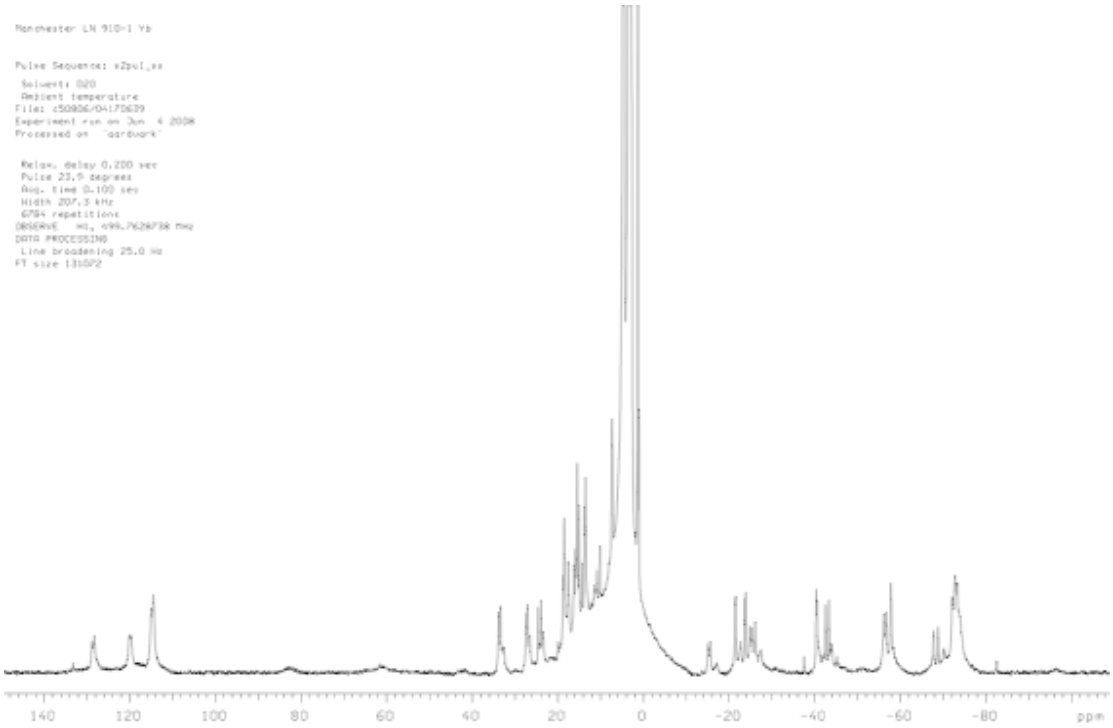


Figure S11. ^{1}H NMR spectrum of H_3Yb.**1** (D_2O) prepared from Yb.**9**

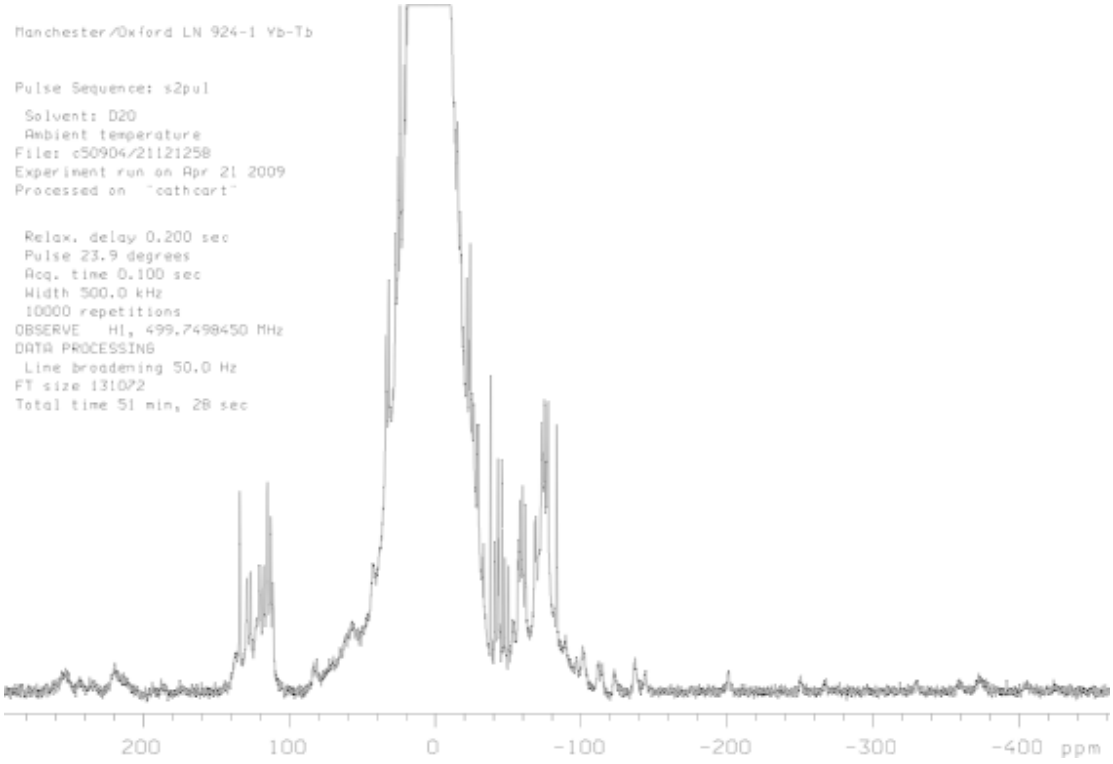


Figure S12. ^{1}H NMR spectrum of TbYb.**1** (D_2O)

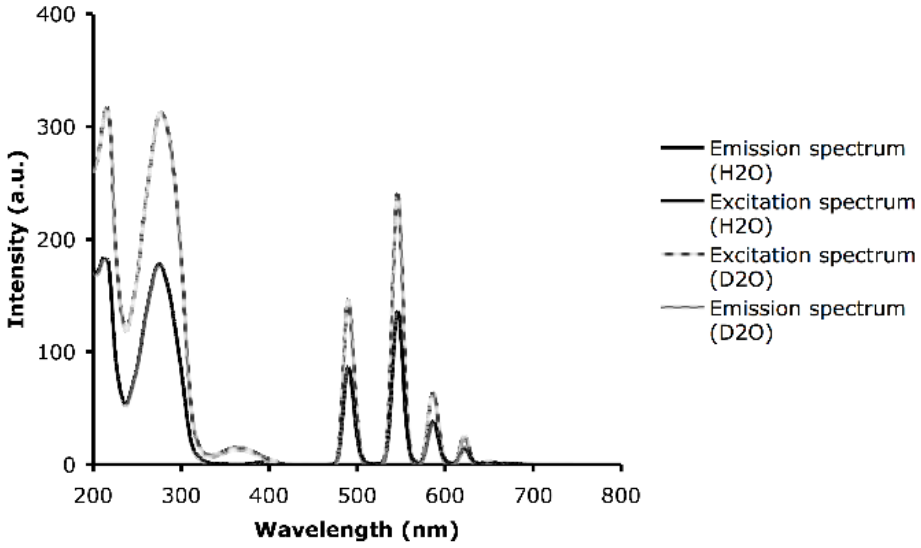


Figure S13. Steady state excitation (545 nm) and emission spectra of TbYb.**1** in H_2O (grey trace) and D_2O (black trace); λ_{exc} = 260 nm, λ_{em} = 545 nm, 10 nm slits, gate time = 0.1 ms, delay time = 0.1 ms

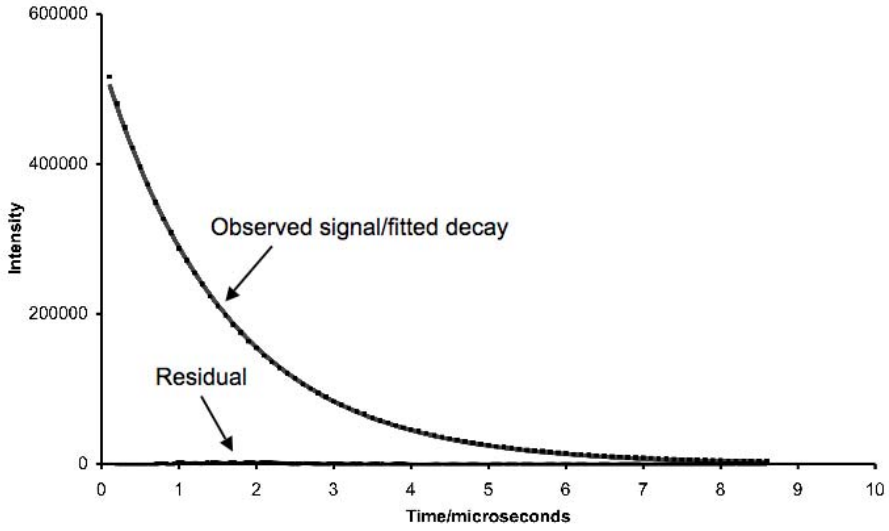


Figure S14. Fitted time resolved kinetic trace of TbYb.**1** (H_2O, λ_{exc} 260 nm, λ_{em} 545 nm)

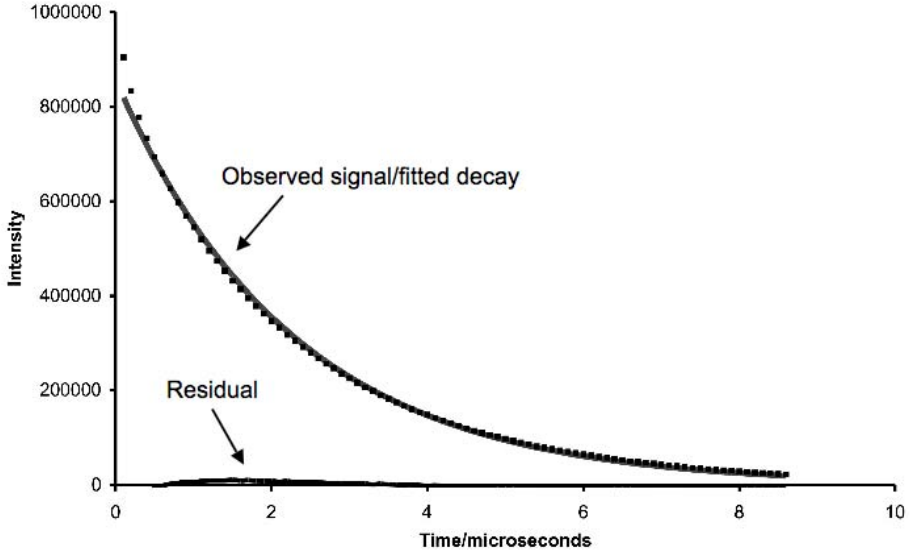


Figure S15. Fitted time resolved kinetic trace of TbYb.**1** (D_2O, λ_{exc} 260 nm, λ_{em} 545 nm)

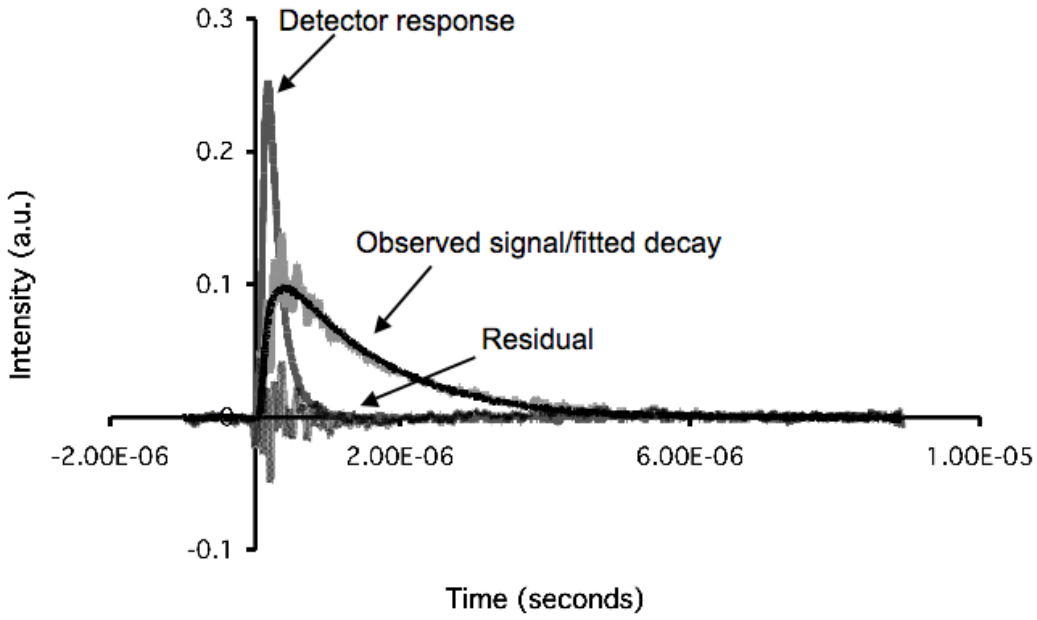


Figure S16. Fitted time resolved kinetic profile of TbYb.**1** (H_2O, λ_{exc} 337 nm, λ_{em} 980 nm)

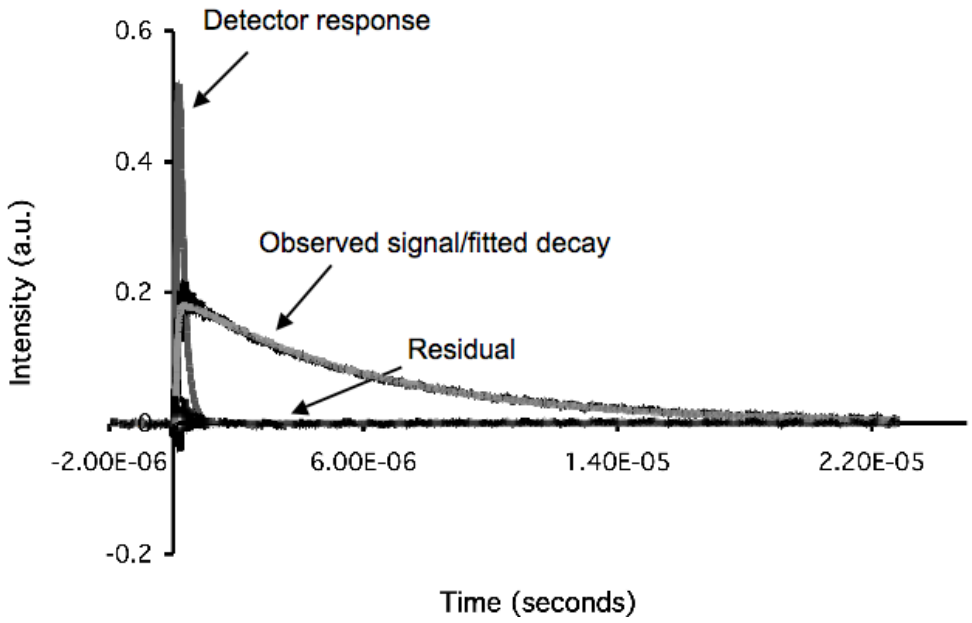


Figure S17. Fitted time resolved kinetic profile of TbYb.**1** (D_2O, λ_{exc} 337 nm, λ_{em} 980 nm)

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i. A. Dadabhoy, S. Faulkner and P.G. Sammes, *J. Chem. Soc. Perkin Trans 2*, 2000, 2359; A. Dadabhoy, S. Faulkner & P.G. Sammes , *J. Chem. Soc. Perkin Trans. 2*, 2002, 348.

ii. R. Aarons, PhD thesis, University of Manchester, 2004.