Luminescent probes based on water-soluble, dual-emissive lanthanide complexes: metal ion-induced modulation of near-IR emission

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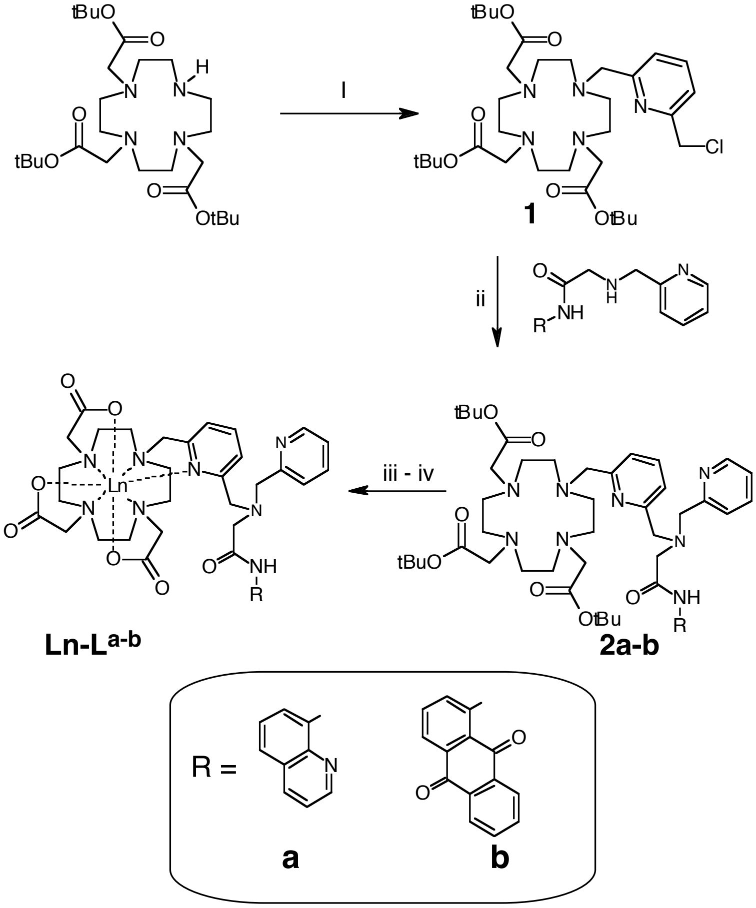
Experimental details for the precursors, ligands and complexes



General synthetic procedure for the synthesis of the chromophore-appended secondary amines(a-c)

The chloroacetamide (1 eq.) was dissolved in MeCN and the solution was added dropwise to a stirred mixture of 2-aminomethylpyridine (2 eq.), $NaHCO_3$ (2 eq.) and KI (1 eq.) at room temperature. The mixture was then heated to reflux and stirred overnight after which time it was left to cool, filtered over gravity and the solvent was removed *in vacuo*. The residue was purified by column chromatography using CH_2Cl_2 to CH_2Cl_2:CH_3OH (9:1) solvent gradient.

Compound 'a': 2-[(pyridin-2-ylmethyl)amino]-*N*-(quinolin-8-yl)acetamide was isolated as a red oil (73 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H = 3.42 (2H, s, NHCH_2-pyr), 3.92 (2H, s, COCH_2NH), 4.5 (1H br, s N*H*), 7.22 (1H, m, quin-H), 7.53 (1H, d J_{HH} = 7.6 Hz, pyr-H), 7.59 (1H, t J_{HH} = 7.2 Hz, pyr-H), 7.73 (1H, m, pyr-H, quin-H), 7.82 (1H, d J_{HH} = 0.8 Hz, pyr-H), 8.05 (2H, d J_{HH} = 6.8 Hz, quin-H), 8.45 (1H, d J_{HH} = 5.1 Hz, quin-H), 8.66 (1H, d J_{HH} = 2.4 Hz, quin-H) and 11.01 ppm (1H, s br, CON*H*). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ_C = 51.6, 53.5, 121.5, 121.7, 122.3, 126.1, 126.7, 127.1, 127.2, 127.9, 130.5, 135.9, 143.1, 144.0, 148.5, 156.6 and 169.4 ppm. ES+ MS: *m/z* = 293 {M+H}$^+$. UV-vis: λ_{max} (ε/mol^{-1}dm^{3}cm^{-1}); 211 (28800), 250 (34500), 322 (3600) and 332 (3200) nm. IR: ν_{max}($CHCl_3$); 1208, 1424, 1529, 1687, 2433 and 3013 cm^{-1}.

Compound 'b': *N*-(9,10-anthraquinocen-1-yl)-2-[(pyridin-2-ylmethyl)amino]acetamide was isolated as a yellow powder (53 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H = 3.54 (2H, s, NHCH_2-pyr), 4.04 (2H, s, COCH_2NH), 7.14 (1H, m, anth-H), 7.43 (1H, d J_{HH} = 7.6 Hz, pyr-H), 7.65 (1H, dt J_{HH} = 2 Hz and 7.6 Hz, pyr-H), 7.72 (3H, m, pyr-H, anth-H), 8.03 (1H, dd J_{HH} = 1.2 Hz and 7.6 Hz, pyr-H), 8.21 (2H, m, anth-H), 8.53 (1H, d J_{HH} = 4.0 Hz, anth-H), 9.18 (1H, dd J_{HH} = 1.2 Hz and 8.8 Hz, anth-H) and 16.16 ppm(1H, s br, CON*H*). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ_C = 53.59, 55.13, 118.40, 122.28, 122.62, 122.68, 126.37, 126.97, 127.35, 132.78, 134.18, 134.24, 135.52, 136.56, 141.29, 149.45, 158.90, 172.36 and 186.49 ppm. ES+ MS: *m/z* = 371 {M}$^{\cdot+}$. UV-vis: λ_{max} (ε/mol^{-1}dm^{3}cm^{-1}); 205 (7600), 223 (7100), 261 (9000), 329 (800) and 396 (1300) nm. IR: ν_{max}($CHCl_3$); 1017, 1211, 1423, 1520, 1579, 2434 and 3014 cm^{-1}.

General synthetic procedure for the reaction of the secondary amines (a-b) with macrocyclic precursor, 1

The amino (1 eq.) was added to a mixture of **1** (1 eq.), $NaHCO_3$ (2 eq.) and KI (1 eq.) in MeCN, which was then heated to reflux and stirred overnight. The mixture was then allowed to cool, filtered over gravity and the solvent was removed *in vacuo*. The residue was then dissolved in the minimum amount of hot toluene and left to cool at -5 ºC overnight. The solvent was then decanted to leave the pure product.

Compound 2a: isolated as a brown/red oil (0.220 g, 63 %). ^{1}H NMR (400 MHz, CDCl$_3$): □$_H$ = 1.36 (18H, s, C(CH_3)$_3$), 1.49 (9H, s, C(CH_3)$_3$), 2.07 – 2.41 (6H, br-m, NCH_2), 2.41 – 3.10 (16H, br-m, ring-CH_2), 2.97 (2H, br-s, ring-CH_2-pyr), 3.42 (2H, s, COCH_2N), 3.84 (2H, s, CH_2N), 3.88 (2H, s, NCH_2), 7.08 (2H, m, pyr-H, quin-H), 7.33 (1H, d J_{HH} = 7.7, link pyr-H), 7.48 (2H, m, pyr-H, link pyr-H), 7.56 (3H, m, pyr-H, quin-H), 7.73 (1H, d J_{HH} = 7.4 Hz, pyr-H), 7.97 (1H, d J_{HH} = 8.4 Hz, quin-H), 8.75 (1H, d J_{HH} = 4.6 Hz, pyr-H), 8.82 (1H, d J_{HH} = 2.4 Hz, quin-H), 9.01 (1H, d J_{HH} = 2.5 Hz, quin-H) and 11.33 ppm (1H, s br, CONH). ^{13}C{^{1}H} NMR (62.5 MHz, CDCl$_3$): □$_C$ = 28.05, 28.14, 40.49, 50.15, 55.93, 56.65, 58.13, 60.95, 82.16, 82.29, 122.52, 123.09, 123.24, 127.11, 127.72, 128.33, 128.80, 132.19, 137.62, 144.32, 144.88, 149.62, 157.25, 157.74, 158.99, 170.52, 172.33 and 172.94 ppm. ES+ MS: *m/z* 932 {M+Na}$^+$. UV-vis: □$_{max}$ (□/mol^{-1}dm^{3}cm^{-1}); 221 (21400), 250 (25600), 323 (3500) and 333 (3300) nm. IR: □$_{max}$(CHCl$_3$); 1211, 1424, 1522, 1674, 1725 and 3015 cm^{-1}.

Compound 2b: isolated as a yellow oil (0.125 g, 41 %). ^{1}H NMR (400 MHz, CDCl$_3$): □$_H$ = 1.30 (18H, s, C(CH_3)$_3$), 1.49 (9H, s, C(CH_3)$_3$), 2.17 (6H, br-m, NCH_2), 2.20 – 2.90 (16H, br-m, ring-CH_2), 2.98 (2H, br-s, ring-CH_2-pyr), 3.47 (2H, s, COCH_2N), 3.82 (2H, s, CH_2N), 3.89 (2H, s, NCH_2), 7.06 (1H, t J_{HH} = 4.0 Hz, pyr-H), 7.17 (1H, d J_{HH} = 7.8 Hz, pyr-H), 7.60 (1H, m, pyr-H), 7.67 (2H, m, pyr-H, anth-H), 7.80 (1H, dt J_{HH} = 1.4 Hz and 7.6 Hz, pyr-H), 7.88 (1H, m, anth-H), 7.94 (1H, d J_{HH} = 7.9 Hz, pyr-H), 8.00 (1H, dd J_{HH} = 1.1 Hz and 7.6 Hz, anth-H), 8.15 (1H, d J_{HH} = 7.8 Hz, anth-H), 8.24 (1H, dd J_{HH} = 7.3 Hz and 11.6 Hz, anth-H), 8.33 (1H, dd J_{HH} = 0.9 Hz and 7.8 Hz, anth-H), 8.40 (1H, d J_{HH} = 4.0 Hz, pyr-H), 9.03 (1H, dd J_{HH} = 1.1 and 8.6 Hz, anth-H) and 13.00 ppm (1H, s br, CONH). ^{13}C{^{1}H} NMR (62.5 MHz, CDCl$_3$): □$_C$ = 28.03, 28.21, 50.26, 56.75, 58.21, 62.02, 82.16, 82.43, 118.22, 122.70, 123.25, 126.11, 127.10, 134.04, 134.58, 134.73, 135.47, 136.74, 141.15, 149.01, 157.26, 157.88, 159.16, 171.12, 172.27, 172.86, 182.8 and

186.7 ppm. ES+ MS: *m/z* 989 {M+H}$^+$. UV-vis: λ_{max} (ε/mol^{-1}dm^{3}cm^{-1}); 224 (22700), 258 (24600), 334 (3000) and 401 (4100) nm. IR: ν_{max}(CHCl$_3$); 1228, 1311, 1417, 1509, 1593, 1650, 1725, 2253 and 2836 cm^{-1}.

General synthetic procedure for the deprotection of ligands

The protected ligand precursor was added to a 1:1 mixture of trifluoroacetic acid:CH_2Cl_2 and the mixture was stirred at room temperature overnight. The solvent was removed *in vacuo* and the residue was re-dissolved three times in MeOH and then rotary evaporated to eliminate excess acid. The residue was then dissolved in the minimum volume of MeOH or EtOH and added dropwise to a stirred Et_2O at 0 °C. The precipitate was filtered and dried to give the deprotected ligand.

Compound L^a: isolated as a brown solid. (0.120 g, 37 %). ^{1}H NMR (400 MHz, D_2O): δ_H = 2.95 (6H, br-m, ring-*H*), 3.03 – 3.56 (16H, br-m, ring-*H*), 4.03 (2H, s, NC*H*$_2$), 4.51 (2H, s, NC*H*$_2$), 4.55 (4H, br-s, N(C*H*$_2$)$_2$), 7.84 (4H, m; 2 pyr-H, 1 quin-H), 7.90 (1H, d J_{HH} = 8.1 Hz, pyr-H), 8.00 (3H, m, pyr-H, quin-H), 8.11 (2H, m, pyr-H, quin-H), 8.66 (1H, d J_{HH} = 5.8 Hz, pyr-H), 8.93 (1H, s, quin-H) and 9.35 ppm (1H, d J_{HH} = 2.2, quin-H). ES+ MS: *m/z* 804 {M+Cu}$^+$. HRMS (ESI$^+$) found *m/z* = 742.3671 {M + H}$^+$; $C_{38}H_{48}N_9O_7$ requires 742.3659. UV-vis: λ_{max} (ε/mol^{-1}dm^{3}cm^{-1}); 208 (20900), 250 (19700), 322 (2900) and 333 (2800) nm. Calculated for $C_{38}H_{47}N_9O_7(CF_3CO_2H)_5(H_2O)_5$: C, 41.12; H, 4.46; N, 8.99; Found C, 40.89; H, 5.27; N, 9.55 %.

Compound L^b: isolated as a brown solid (0.086 g, 44 %). ^{1}H NMR (400 MHz, D_2O): δ_H = 2.88 (6H, br-m, ring-*H*), 2.97 – 3.83 (16H, br-m, ring-*H*), 3.68 (2H, br-s, ring-NC*H*$_2$), 4.32 (2H, br-s, NC*H*$_2$), 4.41 (2H, br-s, NC*H*$_2$), 4.44 (2H, br-s, NC*H*$_2$), 7.44 (1H, t J_{HH} = 8.8 Hz, anth-H), 7.62 (1H, d J_{HH} = 7.2 Hz, pyr-H), 7.71 (1H, t J_{HH} = 8.8 Hz, pyr-H), 7.76 (1H, t J_{HH} = 8.3 Hz, anth-H), 7.80 (2H, t J_{HH} = 6.5 Hz, anth-H), 7.89 (2H, m, pyr-H, anth-H), 8.03 (1H, d J_{HH} = 7.8 Hz, pyr-H), 8.17 (1H, d J_{HH} = 8.1 Hz, anth-H), 8.26 (1H, d J_{HH} = 7.9 Hz, anth-H), 8.39 (1H, t J_{HH} = 8.1 Hz, anth-H), 8.57 (1H, d J_{HH} = 6.5 Hz, anth-H) and 8.70 ppm (1H, d J_{HH} = 6.0 Hz, pyr-H). ES+ MS: *m/z* 883 {M+Cu}$^+$. HRMS (ESI$^+$) found *m/z* = 821.3617 {M + H}$^+$; $C_{43}H_{49}N_8O_9$ requires 821.3611. UV-vis: λ_{max} (ε/mol^{-1}dm^{3}cm^{-1}); 206 (13400), 263 (11500), 316 (1000) and 396 (1400) nm. Calculated for $C_{43}H_{48}N_8O_9(CF_3CO_2H)_5(H_2O)_5$: C, 42.98; H, 4.29; N, 7.57; Found C, 42.71; H, 4.64; N, 8.05 %.

General synthetic procedure for the formation of the lanthanide complexes

A mixture of the ligand (approx. 0.020 g) and $Ln(OTf)_3$ was stirred in MeOH (10 mL) at 50 °C for 24h. The solution was reduced *in vacuo* then added dropwise to stirring diethyl ether at 0 °C. The precipitate was filtered, washed with diethyl ether and dried to give the desired lanthanide complex. The homogeneity of each isolated complex was assessed for absence of free metal (xylenol orange) and chromatographically for absence of free chromophoric ligand.

Compound Nd-L^a: was isolated as a dark brown powder (0.022, 92 %). ES+ MS: *m/z* 881 (M+H)$^+$. HRMS (ESI$^+$) found *m/z* = 881.2523 (M+H)$^+$; $C_{38}H_{45}N_9O_7Nd_1$ requires 881.2514. IR: ν_{max}(ATR, solid); 3500 and 1576 cm^{-1}.

Compound Eu-L^a: was isolated as a dark brown powder (0.022, 91 %). ES+ MS: *m/z* 892 (M+H)$^+$. HRMS (ESI$^+$) found *m/z* = 892.2653 (M+H)$^+$; $C_{38}H_{45}N_9O_7Eu_1$ requires 892.2653. IR: ν_{max}(ATR, solid); 3494, 1577, 1444 and 1406 cm^{-1}.

Compound Gd-L^a: was isolated as a dark brown powder (0.022, 95 %). ES+ MS: *m/z* 897 (M+H)$^+$. HRMS (ESI$^+$) found *m/z* = 897.2686 (M+H)$^+$; $C_{38}H_{45}N_9O_7Gd_1$ requires 897.2669. IR: ν_{max}(ATR, solid); 3490, 1576, 1445 and 1405 cm^{-1}.

Compound Yb-L^a: was isolated as a dark brown powder (0.024, 97 %). ES+ MS: *m/z* 913 (M+H)$^+$. HRMS (ESI$^+$) found *m/z* = 913.2831 (M+H)$^+$; $C_{38}H_{45}N_9O_7Yb_1$ requires 913.2821. IR: ν_{max}(ATR, solid); 3471, 1576, 1456 and 1400 cm^{-1}.

Compound Nd-L^b: was isolated as a brown powder (0.023, 98 %). ES+ MS: *m/z* 960 (M+H)$^+$. HRMS (ESI$^+$) found *m/z* = 960.2464 (M+H)$^+$; $C_{43}H_{46}N_8O_9Nd_1$

requires 960.2459. IR: □$_{max}$(ATR, solid); 3451, 1734, 1578, 1508, 1456 and 1408 cm^{-1}.

Compound Eu-L^b: was isolated as a brown powder (0.022, 93 %). ES+ MS: *m/z* 969 $(M+H)^+$. HRMS (ESI$^+$) found *m/z* = 969.2585 $(M+H)^+$; $C_{43}H_{46}N_8O_9Eu_1$ requires 969.2581. IR: □$_{max}$(ATR, solid); 3500, 1617, 1590 and 1477 cm^{-1}.

Compound Gd-L^b: was isolated as a brown powder (0.023, 97 %). ES+ MS: *m/z* 973 $(H+H)^+$. HRMS (ESI$^+$) found *m/z* = 973.2614 $(M+H)^+$; $C_{43}H_{46}N_8O_9Gd_1$ requires 973.2608. IR: □$_{max}$(ATR, solid); 3473, 1734, 576, 1507, 1456, 1442 and 1406 cm^{-1}.

Compound Yb-L^b: was isolated as a brown powder (0.022, 91 %). ES+ MS: *m/z* 992 $(H+H)^+$. HRMS (ESI$^+$) found *m/z* = 992.2670 $(M+H)^+$. IR: □$_{max}$(ATR, solid); 3491, 1734, 1590, 1516 and 1457 cm^{-1}.

General physical measurements

All photophysical data were obtained on a JobinYvon-Horiba Fluorolog spectrometer fitted with a JY TBX picosecond photodetection module and a Hamamatsu R5509-73 detector (cooled to –80 °C using a C9940 housing) for near-IR measurements. For the near-IR lifetimes the pulsed laser source was a Continuum Minilite Nd:YAG configured for 355 nm output. For the fluorescence lifetimes 372 and 459 nm NanoLEDs (operating at 1 MHz) were utilised. All lifetimes were obtained using the JY-Horiba FluoroHub single photon counting module. IR spectra were recorded on an ATR equipped Varian 7000 FT-IR. LR mass spectra were obtained using a Bruker MicroTOF LC. UV-vis data were recorded as solutions on a Jasco 570 spectrophotometer.

Additional spectroscopic data

Fig S1: Left: Room temperature excitation and emission spectra for Gd-L^a (blue), Gd-L^b (red). Right: Low temperature (77K) phosphorescence measurements on ethanol/methanol (2:1) glasses of Gd-L^a (□$_{ex}$ = 380 nm).

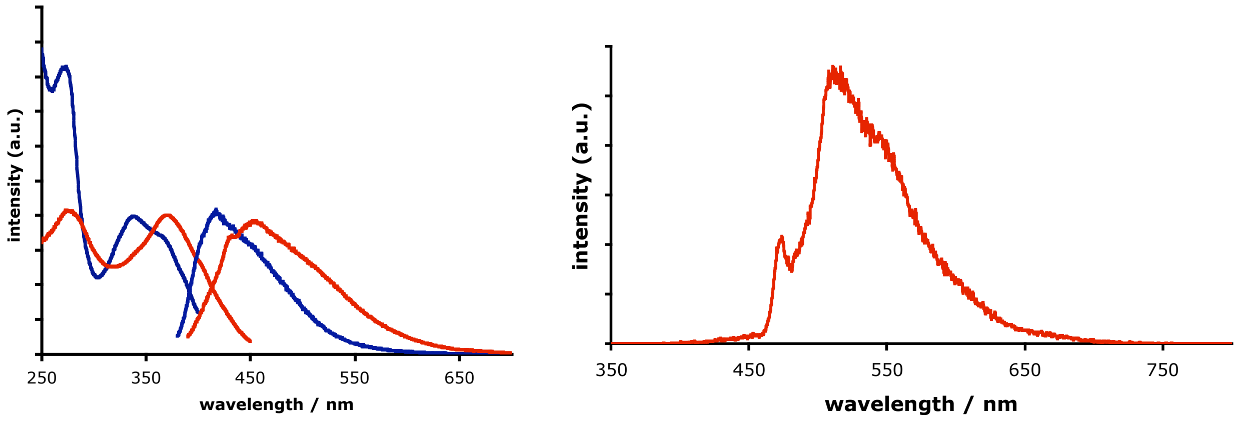


Fig S2: Steady state emission spectra for Eu-L^{a} (10^{-5} M) recorded in buffered water (HEPES, pH 7.4) (λ_{ex} = 280 nm) following addition of 1,2,5 and 10 eq. M(II)$(ClO_4)_2$.

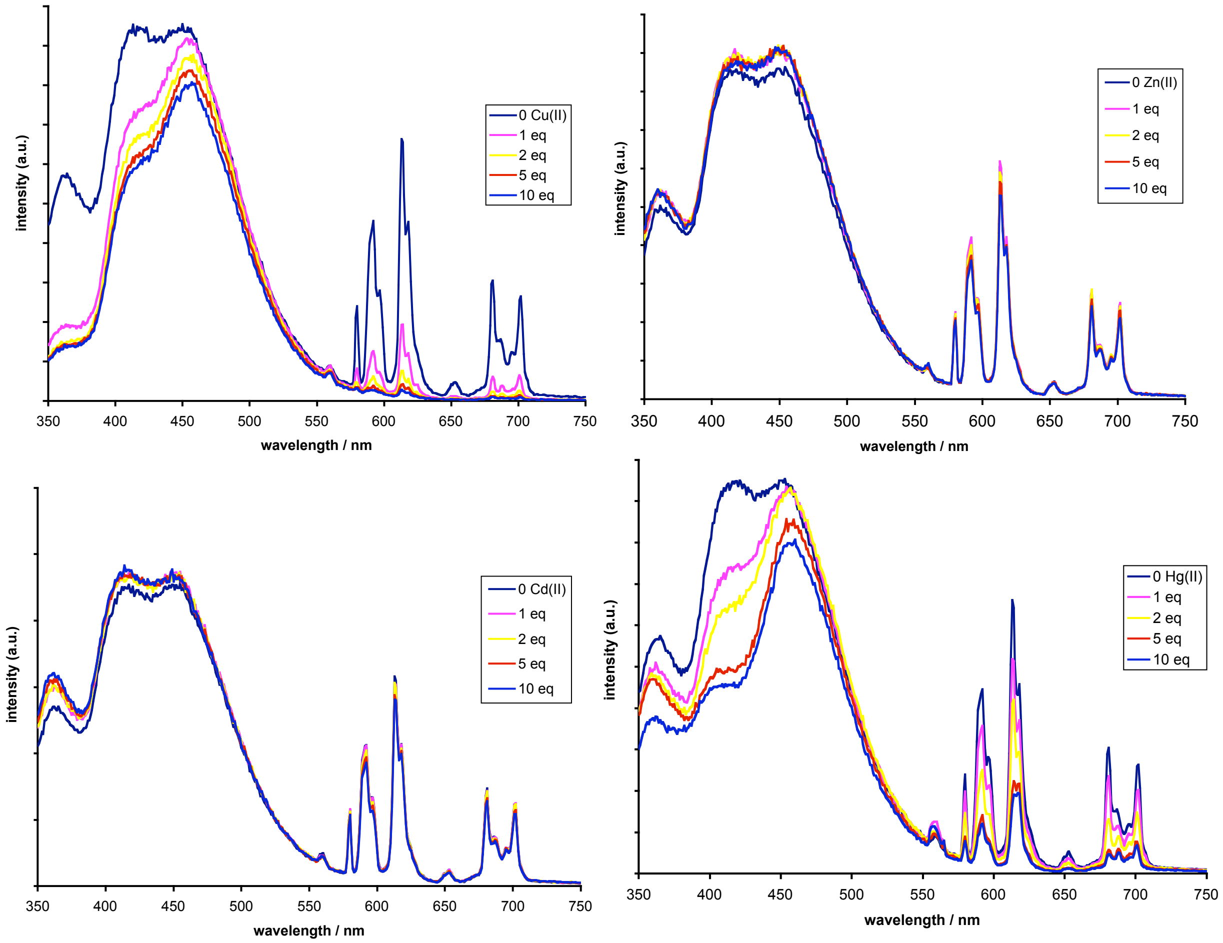


Fig S3: UV-vis absorption spectrum for Yb-L^b recorded in buffered water (HEPES, pH 7.4) following addition 10 eq. Hg(II)(ClO_4)$_2$.

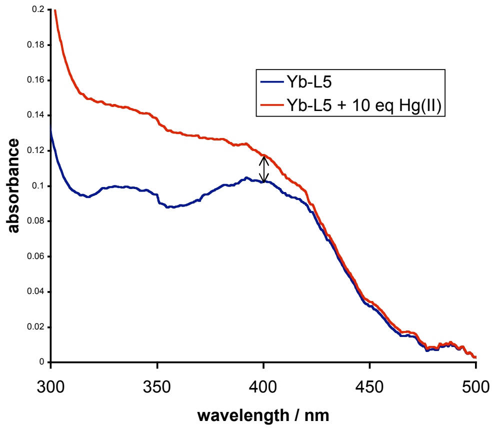


Fig S4: Steady state near-IR emission spectra (λ_{ex} = 400 nm) for ca. 2.5 × 10^{-4} M Nd-L^b recorded in buffered D_2O at pH 7.4.