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

Michael Andrews, Lindsay P. Harding and Simon J.A. Pope

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.), NaHCO₃ (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 CH₂Cl₂ to CH₂Cl₂:CH₃OH (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\(_3\)): \(\delta = 3.42\) (2H, s, NHCH\(_2\)-pyr), 3.92 (2H, s, COCH\(_2\)NH), 4.5 (1H br, s NH), 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, CONH). \(^{13}\)C{\(^1\)H} NMR (62.5 MHz, CDCl\(_3\)): \(\delta = 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: \(\lambda_{max} (\epsilon/mol^{-1}dm^3\cdot cm^{-1}); 211 (28800), 250 (34500), 322 (3600) and 332 (3200) nm. IR: \(\nu_{max}(CHCl_3); 1208, 1423, 1529, 1687, 2433 and 3013 cm^{-1}.\)

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\(_3\)): \(\delta = 3.54\) (2H, s, NHCH\(_2\)-pyr), 4.04 (2H, s, COCH\(_2\)NH), 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, CONH). \(^{13}\)C{\(^1\)H} NMR (62.5 MHz, CDCl\(_3\)): \(\delta = 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}\(^+\). UV-vis: \(\lambda_{max} (\epsilon/mol^{-1}dm^3\cdot cm^{-1}); 205 (7600), 223 (7100), 261 (9000), 329 (800) and 396 (1300) nm. IR: \(\nu_{max}(CHCl_3); 1017, 1211, 1423, 1520, 1579, 2434 and 3014 cm^{-1}.\)

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

The amino (1 eq.) was added to a mixture of I (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 °C 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\(_3\)): \(\delta_H = 1.36\) (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\(_2\)N), 3.84 (2H, s, CH\(_2\)N), 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). \(^1\)C\{\(^1\)H\} NMR (62.5 MHz, CDCl\(_3\)): \(\delta_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: \(\varepsilon_{\text{max}}\) (\(\text{mol}^{-1}\text{dm}^{3}\text{cm}^{-1}\)); 221 (21400), 250 (25600), 323 (3500) and 333 (3300) nm. IR: \(\varepsilon_{\text{max}}\) (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\(_3\)): \(\delta_H = 1.30\) (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\(_2\)N), 3.82 (2H, s, CH\(_2\)N), 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, d \(J_{HH} = 0.9\) 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). \(^1\)C\{\(^1\)H\} NMR (62.5 MHz, CDCl\(_3\)): \(\delta_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
General synthetic procedure for the deprotection of ligands

The protected ligand precursor was added to a 1:1 mixture of trifluoroacetic acid:CH₂Cl₂ 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 Et₂O at 0 °C. The precipitate was filtered and dried to give the deprotected ligand.

**Compound Lᵃ:** isolated as a brown solid (0.120 g, 37 %). ¹H NMR (400 MHz, D₂O): δ = 2.95 (6H, br-m, ring-H), 3.03 – 3.56 (16H, br-m, ring-H), 4.03 (2H, s, NCH₂), 4.51 (2H, s, NCH₂), 4.55 (4H, br-s, N(CH₂)₂), 7.84 (4H, m; 2 pyr-H, 1 quin-H), 7.90 (1H, d JHH = 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 JHH = 5.8 Hz, pyr-H), 8.93 (1H, s, quin-H) and 9.35 ppm (1H, d JHH = 2.2, quin-H). ES+ MS: m/z 804 {M+Cu}⁺. HRMS (ESI⁺) found m/z = 742.3671 {M + H}⁺; C₃₈H₄₈N₉O₇ requires 742.3659. UV-vis: \( \varepsilon_{\text{max}} \) (\{mol}⁻¹\text{dm}³\text{cm}⁻¹); 208 (20900), 250 (19700), 322 (2900) and 333 (2800) nm. Calculated for C₃₈H₄₇N₉O₇(CF₃CO₂H)₅(H₂O)₅: C, 41.12; H, 4.46; N, 8.99; Found C, 40.89; H, 5.27; N, 9.55 %.

**Compound Lᵇ:** isolated as a brown solid (0.086 g, 44 %). ¹H NMR (400 MHz, D₂O): δ = 2.88 (6H, br-m, ring-H), 2.97 – 3.83 (16H, br-m, ring-H), 3.68 (2H, br-s, ring-NCH₂), 4.32 (2H, br-s, NCH₂), 4.41 (2H, br-s, NCH₂), 4.44 (2H, br-s, NCH₂), 7.44 (1H, t JHH = 8.8 Hz, anth-H), 7.62 (1H, d JHH = 7.2 Hz, pyr-H), 7.71 (1H, t JHH = 8.8 Hz, pyr-H), 7.76 (1H, t JHH = 8.3 Hz, anth-H), 7.80 (2H, t JHH = 6.5 Hz, anth-H), 7.89 (2H, m, pyr-H, anth-H), 8.03 (1H, d JHH = 7.8 Hz, pyr-H), 8.17 (1H, d JHH = 8.1 Hz, anth-H), 8.26 (1H, d JHH = 7.9 Hz, anth-H), 8.39 (1H, t JHH = 8.1 Hz, anth-H),
8.57 (1H, d, \( J_{HH} = 6.5 \text{ Hz}, \text{anth-H} \)) and 8.70 ppm (1H, d, \( J_{HH} = 6.0 \text{ Hz}, \text{pyr-H} \)). 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: \( \lambda_{\text{max}} \) (\( \text{mol}^{-1}\text{dm}^3\text{cm}^{-1} \)); 206 (13400), 263 (11500), 316 (1000) and 396 (1400) nm. Calculated for \( C_{43}H_{48}N_8O_9(CF_3CO_2)H_2(H_2O)_2 \): 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-La**: 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: \( \lambda_{\text{max}} \) (ATR, solid); 3500 and 1576 cm\(^{-1}\).

**Compound Eu-La**: 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: \( \lambda_{\text{max}} \) (ATR, solid); 3494, 1577, 1444 and 1406 cm\(^{-1}\).

**Compound Gd-La**: 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: \( \lambda_{\text{max}} \) (ATR, solid); 3490, 1576, 1445 and 1405 cm\(^{-1}\).

**Compound Yb-La**: 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: \( \lambda_{\text{max}} \) (ATR, solid); 3471, 1576, 1456 and 1400 cm\(^{-1}\).

**Compound Nd-Lb**: 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)^+; \( C_{43}H_{46}N_8O_7Nd_1 \)
requires 960.2459. IR: $\tilde{\nu}_{\text{max}}$(ATR, solid); 3451, 1734, 1578, 1508, 1456 and 1408 cm$^{-1}$.

**Compound Eu-Lb** 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)$^+$; $C_{43}H_{46}N_8O_9$Eu$^+$ requires 969.2581. IR: $\tilde{\nu}_{\text{max}}$(ATR, solid); 3500, 1617, 1590 and 1477 cm$^{-1}$.

**Compound Gd-Lb** 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)$^+$; $C_{43}H_{46}N_8O_9$Gd$^+$ requires 973.2608. IR: $\tilde{\nu}_{\text{max}}$(ATR, solid); 3473, 1734, 576, 1507, 1456, 1442 and 1406 cm$^{-1}$.

**Compound Yb-Lb** 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: $\tilde{\nu}_{\text{max}}$(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$^a$ ($\lambda_{ex} = 380$ nm).
Fig S2: Steady state emission spectra for Eu-L² (10⁻⁵ M) recorded in buffered water (HEPES, pH 7.4) (λₑₓ = 280 nm) following addition of 1, 2, 5 and 10 eq. M(II)(ClO₄)₂.
Fig S3: UV-vis absorption spectrum for Yb-L\textsuperscript{b} recorded in buffered water (HEPES, pH 7.4) following addition 10 eq. Hg(II)(ClO\textsubscript{4})\textsubscript{2}. 

![Absorption Spectrum](image)

Fig S4: Steady state near-IR emission spectra (\(\lambda_{ex} = 400\) nm) for ca. 2.5 \(\times 10^{-4}\) M Nd-L\textsuperscript{b} recorded in buffered D\textsubscript{2}O at pH 7.4.

![Emission Spectra](image)