

Changing the local coordination environment in mono- and bi-metallic lanthanide complexes through “click” chemistry

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SUPPLEMENTARY INFORMATION

Synthesis of Ligands and Complexes

General:

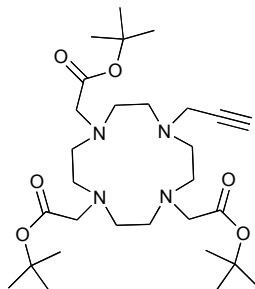
NMR spectroscopy

^1H (400.13 MHz) and ^{13}C (100.6 MHz) NMR spectra of the ligands were acquired on Bruker Advance 400 spectrometer. ^1H (500.0 MHz) NMR spectra of the lanthanide complexes were acquired on a Varian Inova NMR spectrometer.

Mass spectrometry

Electrospray (ES) spectra were measured on a Micromass LCT spectrometer using a methanol mobile phase. Matrix-assisted laser desorption (MALDI) spectra were obtained using a Bruker Biflex IV spectrometer with Flex software and an appropriate matrix.

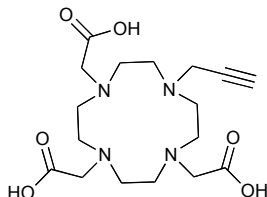
(4,7-Bis-*tert*-butoxycarbonylmethyl-10-prop-2-ynyl-1,4,7-tetraazacyclododec-1-yl)-acetic acid *tert*-butyl ester, **2**



1,4,7-tris-(*tert*-butylacetate)-1,4,7,10-tetraazacyclododecane (**1**, 2.0g, 3.88mmol) was dissolved in acetonitrile and caesium carbonate (11.38g, 34.95mmol) was added. The reaction mixture was stirred for 20 minutes at room temperature. Propargyl bromide (0.2g, 1.94 mmol) was added to the solution, and the mixture was stirred at room temperature overnight. The solids were filtered off, and the removal of the solvent yielded the product as a very pale oil (0.9g, 89%). ES⁺MS (MeCN): *m/z* 553 {*M* + *H*⁺}, 575 {*M* + *Na*⁺}; ^1H NMR (400MHz, CDCl_3 , 300K) δ_{H} = 1.38 (s, 27H, CCH_3), 2.15 (1H, s, CCH), 2.62 (4H, s, ring CH_2), 2.73 (12H, s, ring CH_2), 3.21 (6H, s, $\text{CH}_2\text{-CO}$), 3.38 (2H, s, $\text{CH}_2\text{-CCH}$); ^{13}C NMR (100MHz, CDCl_3 ,

300K) δ_C = 171.1 ($\underline{C=O}$), 80.7 ($\underline{CCH_3}$), 79.2 ($\underline{CCH}$), 72.6 ($\underline{CCH}$), 56.8 ($\underline{CH_2-CO}$), 56.8 ($\underline{CH_2-CO}$), 53.4 ($\underline{N-CH_2}$), 52.0 ($\underline{N-CH_2}$), 51.7 ($\underline{N-CH_2}$), 51.4 ($\underline{N-CH_2}$), 50.6 ($\underline{N-CH_2}$), 43.0 ($\underline{CH_2-CCH}$), 28.2 ($\underline{CCH_3}$)

(4,7-Bis-carboxymethyl-10-prop-2-ynyl-1,4,7,10-tetraazacyclododec-1-yl)-acetic acid, H_3L^1



(4,7-Bis-*tert*-butoxycarbonylmethyl-10-prop-2-ynyl-1,4,7-tetraazacyclododec-1-yl)-acetic acid *tert*-butyl ester (**2**, 0.7g, 1.26 mmol) was dissolved in a mixture of DCM (8 mL) and TFA (8 mL). The solution was stirred overnight at room temperature. The volatiles were removed by rotary evaporation, and the residue dissolved in the minimum amount of methanol. Addition of diethyl ether yielded the desired compound as a white solid in quantitative yield. MALDI MS (α -MeOH): m/z 385 $\{M + H^+\}$; 1H NMR (400MHz, D_2O , 300K) δ_H = 2.76 (1H, s, $\underline{CH}$), 2.84-3.91 (m, 24H, $\underline{CH_2}$), 4.46 (s, 1H, $\underline{CCH}$); ^{13}C NMR (100MHz, D_2O , 300K) δ_C = 31.38, 36.89, 43.61, 45.49, 48.86, 49.74, 51.78, 52.86, 53.10, 53.28, 54.44, 56.84 ($\underline{NCH_2}$), 72.62 ($\underline{CCH}$), 77.65 ($\underline{CCH}$), 171.98 ($\underline{C=O}$), 174.36 ($\underline{C=O}$). $C_{17}H_{29}N_4O_6 \cdot NaBr \cdot CF_3CO_2H \cdot H_2O$ requires C 36.79, H 5.20, N 9.03; found C 37.24, H 5.11, N 9.17.

Preparation of Lanthanide complexes, General Method

H_3L^1 (0.19g, 0.51 mmol) was dissolved in methanol and the appropriate lanthanide triflate salt (1.05 eq) added to the solution. The mixture was stirred at 50°C for two days and the solvent removed by rotary evaporation. The residue was re-dissolved in methanol and triturated with diethyl ether to yield the complex as a white solid.

EuL¹ Yield 0.2 g (67%), MALDI MS (α -MeOH): m/z 534 $\{M+H^+\}$, 555 $\{M+Na^+\}$, 1080 $\{M+2Na^+\}$, 1H NMR (400MHz, D_2O , 300K) δ_H = 35.34, 31.16, 28.02, 9.77, 8.47, -0.17, -0.29, -1.27, -3.46, -4.91, -6.48, -7.92, -9.48, -9.95, -10.64, -14.72, -15.02, -17.22, -17.94, -20.71.

TbL¹ Yield 0.24 g (80%), MALDI MS (α -MeOH): m/z 541 $\{M+H^+\}$, 579 $\{M+2Na^+\}$, 572 $\{2M-H^+\}$, 1H NMR (500MHz, D_2O , 295K) δ_H = only resolved peaks outside the range -50 to +50ppm are reported -407.3, -386.7, -371.1, -341.3, -183.2, -172.5, -114.0, -90.3, -87.4, -75.7, -66.8, 64.7, 88.4, 190.3, 228.7, 246.2, 409.9, 419.1.

Preparation of Eu.L²

Eu.L¹ (0.2 g, 0.37 mmol) and benzyl azide (66 mg, 0.5 mmol) were dissolved in a 1:1 mixture of water and *tert*-butanol (40 mL). sodium ascorbate (7 mg, 0.1 equiv.) and copper(II) sulfate pentahydrate (5 mg, 0.05 equiv.) were added to the

solution, and the mixture stirred at room temperature for 48 h. Excess benzyl azide was extracted into diethyl ether (4 x 30 mL), and the aqueous layer evaporated under reduced pressure. The crude product was re-dissolved in the minimum volume of methanol, and triturated with diethyl ether to yield a pale green solid (140 mg, 58%). MALDI MS (α -MeOH): m/z 667 $\{M+H^+\}$, 689 $\{M+Na^+\}$. 1H NMR (400MHz, D_2O , 300K) δ_H = 29.68, 27.31, 26.95, 26.29, 13.12, 11.34, 11.07, 10.17, 8.64, 7.93, 7.87, 7.24, 6.89, 6.16, 5.48, 4.34, 4.05, 3.87, 2.97, 1.56, 1.07, 0.64, -0.19, -4.98, -5.13, -6.07, -7.12, -7.71, -8.34, -8.54, -9.20, -11.45, -12.72, -13.79, -14.96, -16.77, -18.86, -19.51.

Preparation of Tb.L³

1,4-bis(bromomethyl)benzene (20mg, 0.074 mmol) was dissolved in DMF (5mL) and sodium azide (29 mg, 0.44 mmol) added to the stirring solution. Stirring was maintained for 16 h at room temperature. **OWING TO THE POTENTIALLY EXPLOSIVE NATURE OF THE PRODUCT, NO ATTEMPT WAS MADE TO ISOLATE THE DIAZIDE FORMED FROM THIS REACTION.** Instead, (Tb.L¹ (0.10g, 0.19 mmol) was added to the stirring solution, followed by sodium ascorbate (4.6 mg, 0.3 equiv.), copper(II) sulfate pentahydrate (5 mg, 0.25 equiv.) and TBTA (9.3 mg, 0.25 equiv) were added to the solution, and the mixture stirred at room temperature for 48 h. Excess azide was extracted into diethyl ether (4 x 30 mL), and the aqueous layer evaporated under reduced pressure. The crude product was re-dissolved in the minimum volume of methanol, and triturated with diethyl ether to yield a pale green solid. The product was then purified by HPLC using an Agilent 1200SL HPLC system and an ACE3 C18 column with 99% H_2O / 1% MeOH as eluant, to yield a white solid (43 mg, 45%). MALDI MS (α -MeOH): m/z 1268 $\{M^+\}$, 1315 $\{M-2H^++2Na^+\}$. 1H NMR (500MHz, D_2O , 295K) δ_H = only resolved peaks outside the range -40 to +30ppm for the major form are reported -386.5, -375.7, -366.2, -363.8, -142.4, -124.6, -112.5, -103.5, -91.7, -70.6, -65.1, -53.1, 36.7, 57.6, 87.8, 121.3, 142.9, 149.0, 159.1, 168.8, 245.3, 260.8, 336.6, 350.5

Luminescence spectroscopy

For the europium and terbium complexes, luminescence spectra were obtained using a Perkin-Elmer LS55 spectrometer. This was also used to determine the luminescence lifetimes by observing the intensity of emission at a variety of delay times while keeping the gate time constant.