Tuning the properties of cyclen based lanthanide complexes for phosphodiester hydrolysis; the role of basic cofactors

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Electronic Supplementary Information (ESI)

Synthesis

[2-(2-Chloro-acetylamino)-ethyl]-carbamic acid *tert*-butyl ester (5)

A solution of chloroacetyl chloride (1.37 g, 12.2 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 1 h to a solution of (2-amino-ethyl)carbamic acid *tert*-butyl ester (1.62 g, 10.2 mmol) and NEt_3 (1.53 g, 15.0 mmol) in CH_2Cl_2 (20 mL) at –20 ºC (acetone/ice bath). The resulting brown solution was left to stir at room temperature for 24 h. The inorganic salts that formed were filtered off and the filtrate washed with citric acid (3 x 20 mL) and then with water (2 x 20 mL). The organic layer was extracted and dried over K_2CO_3 and the solvent removed under reduced pressure to give a dark brown solid. Yield (1.82 g, 76%). M.p. 95-98 °C; Calculated for $C_9H_{17}ClN_2O_3$: C, 45.67; H, 7.24; N, 11.83, Found: C, 45.16; H, 6.86; N, 11.38; Calculated for $C_9H_{17}N_2O_3NaCl$: [$(M+Na)^+$ peak] *m/z* (ES^+) = 259.0825, Found: 259.0819 (−1.9 ppm); δ_H ($CDCl_3$, 400 MHz) 7.27 (br s, 1H, NH), 4.91 (br s, 1H, N<u>H</u>BOC), 4.05 (s, 2H, $ClCH_2CO$), 3.42 (q, *J* = 5.5 Hz, 2H, NHC<u>H</u>$_2$), 3.34 (q, *J* = 5.0 Hz, 2H, BOCNHC<u>H</u>$_2$), 1.46 (s, 9H, 3 x CH_3); δ_c ($CDCl_3$, 100 MHz) 166.3, 156.3, 79.4, 42.0, 40.7, 39.2, 27.8; *m/z* (ES^+) 259.10 $(M+Na)^+$; IR ν_{max}(cm^{-1}) 3363, 2984, 1693, 1647, 1528, 1446, 1367, 1278, 1175, 979, 869, 758.

[2-(2-{4,7,10-Tris-[(2-*tert*-butoxycarbonylamino-ethylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclododec-1-yl}-acetylamino)- ethyl]-carbamic acid *tert*-butyl ester (7)

A solution of **4** (0.62 g, 2.5 mmol) in dry MeCN (10 mL) was added to cyclen (0.1 g, 0.6 mmol), Cs_2CO_3 (1.69 g, 5.52 mmol) and KI (0.82 g, 2.5 mmol) in dry MeCN (10 mL). This was then heated at reflux under argon for 3 days. The mixture was filtered through celite and the solvent removed under reduced pressure. The residue was dissolved in $CHCl_3$ and washed with water and saturated KCl solution (3 x 20 mL). The organic layer was dried over K_2CO_3 and the solvent removed under reduced pressure to yield an

orange/brown hygroscopic powder (0.46 g, 87% yield). M.p. 168-171 °C; Calculated for $C_{44}C_{85}N_{12}O_{12}.CHCl_3$: C, 49.47; H, 7.84; N, 15.38, Found: C, 49.49; H, 7.62; N, 15.10; Calculated for $C_{44}C_{85}N_{12}O_{12}$: [$(M+H)^+$ peak] *m/z* (ES^+) = 973.6410, Found: 973.6456 (+4.7 ppm); δ_H ($CDCl_3$, 400 MHz) 7.73 (br s, 4H, NH), 5.58 (br s, 4H, NHBOC), 3.33 (d, *J* = 5.0 Hz, 8H, NCH_2CO), 3.21 (d, *J* = 5.5 Hz, 8H, $NHCH_2CH_2$), 3.05 (br s, 8H, NCH_2), 2.63 (s, 16H, NCH_2CH_2NH), 1.37 (s, 36H, BOC); δ_c ($CDCl_3$, 100 MHz) 171.3, 156.1, 78.7, 58.6, 52.8, 40.1, 39.0, 27.9; *m/z* (ES^+) 973.64 $(M+H)^+$; IR ν_{max} (cm^{-1}) 3329, 2976, 2820, 17018, 1528, 1366, 1251, 1171, 1001, 780.

Procedure 1; Deprotection of BOC group

The desired ligand was dissolved in EtOH (10 mL) and HCl (3 mL, neat) and left to stir for 1 h. CH_2Cl_2 was added (2 x 20 mL) and then removed under reduced pressure. This was then followed by addition of diethyl ether (2 x 20 mL) followed by subsequent removal under reduced pressure to give a hygroscopic solid. The product was stored in a dessicator.

***N*-(2-Amino-ethyl)-2-{4,7,10-tris-[(2-amino-ethylcarbamoyl)-methyl-1,4,7,10-tetraza-cyclodec-1-yl}-acetamide (1)**

Ligand **7** was prepared according to **Procedure 1,** using ligand **7** (0.23 g, 0.24 mmol). A pale yellow hygroscopic solid was obtained (0.13 g, 95% yield). M.p. decomposed above 220 °C; $C_{24}H_{53}N_{12}O_4$: [M+H peak] *m/z* (ES^+) = 573.4313, Found: 573.4294 (−1.9 ppm); δ_H (D_2O, 400 MHz) 3.42 (br s, 16H, NCH_2CO, $NHCH_2$), 3.23 (br s, 8H, NH_2CH_2), 3.05 (br s, 16H, NCH_2CH_2N); δ_c (D_2O, 100 MHz) 170.6, 54.07, 52.23, 38.53, 36.23; *m/z* (ES^+) 595.41 $(M+Na)^+$, 573.42 $(M+H)^+$, 315.24 $(M+2H)^{2+}$; IR ν_{max} (cm^{-1}) 3390, 2985, 2011, 1671, 1560, 1459, 1390, 1270, 1170, 1089, 1029, 921, 570.

Procedure 2; Synthesis of Lanthanide Complexes Using Lanthanide Triflate Salts

Lanthanide complexes were prepared by heating at reflux, under inert atmosphere, the ligand with 1.1 molar equivalents of the appropriate lanthanide triflate in dry MeOH (10 mL) for 16 h, unless otherwise stated. The complexes were isolated by precipitation in dry ether (100 mL) or CH_2Cl_2 (100 mL) and the precipitates collected by filtration. ^1H

NMR spectra of lanthanide complexes consisted of very broad signals and therefore were not fully characterised *i.e.* it was not possible to determine integration. The same properties prevent ^{13}C spectra from being obtained. For ^{1}H NMR spectra, spectral width was set at 100 ppm (i.e., –100 to 100).

_N_-(2-Amino-ethyl)-2-{4,7,10-tris-[(2-amino-ethylcarbamoyl)-methyl-1,4,7,10-tetraza-cyclodec-1-yl}-acetamide.La.3CF_3SO_3.2H_2O (La.1)

La.1 was prepared according to **Procedure 2**, using ligand **1** (28 mg, 0.04 mmol) and $La(CF_3SO_3)_3$ (30 mg, 0.043 mmol). A yellow solid was obtained (41 mg, 88% yield). M.p. 214-218 °C; Calculated for $C_{24}H_{52}N_{12}O_7La.CF_3SO_3$: [$(M+CF_3SO_3)^{2+}$ peak] *m/z* (ES^+) = 860.2818, Found: 860.2802 (−1.9 ppm); δ_H (D_2O, 400 MHz) 3.58, 3.47, 3.26, 3.15, 1.38, 1.18; *m/z* (ES^+) 430.14 $(M+CF_3SO_3)^{2+}$; IR $\nu_{max}(cm^{-1})$ 3288, 1637, 1571, 1480,1287, 1171, 1091, 1026, 973, 934, 862, 638.

_N_-(2-Amino-ethyl)-2-{4,7,10-tris-[(2-amino-ethylcarbamoyl)-methyl-1,4,7,10-tetraza-cyclodec-1-yl}-acetamide.Eu.3CF_3SO_3.H_2O (Eu.1)

Eu.1 was prepared according to **Procedure 2**, using **1** (97 mg, 0.17 mmol) and $Eu(CF_3SO_3)_3$ (111 mg, 0.19 mmol). A yellow solid was obtained (156 mg, 78% yield). M.p. 216-219 °C; Calculated for $C_{24}H_{52}N_{12}O_7Eu.CF_3SO_3$: [$(M+CF_3SO_3)^{2+}$ peak] *m/z* = 874.2967, Found: 874.2922 (−5.0 ppm); δ_H (D_2O, 400 MHz) 22.91, 3.54, 2.40, 1.03, -3.76, -9.36, -12.44; *m/z* 437.14 $(M+CF_3SO_3)^{2+}$, 362.16 $(M)^{2+}$; IR $\nu_{max}(cm^{-1})$ 2983, 1625, 1570, 1482, 1368, 1238, 1224, 1162, 1091, 1026, 970, 932, 836, 760.

[4-(2-Chloro-acetylamino)-propyl]-carbamic acid *tert*-butyl ester (5)

A solution of chloroacetyl chloride (1.43 g, 12.72 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 1 h to a solution of (3-amino-propyl)-carbamic acid tert-butyl ester (1.61 g, 10.6 mmol) and NEt_3 (1.61 g, 15.9 mmol) in CH_2Cl_2 (20 mL) at –20 ºC (acetone/ice bath). The resulting brown solution was left to stir at room temperature for 24 h. The inorganic salts formed were filtered off and the filtrate washed with citric acid (3 x 20 mL) and then with water (2 x 20 mL). The organic layer was extracted and dried over K_2CO_3 and solvent removed under reduced pressure to give a dark brown solid (1.23 g,

88% yield). M.p. 161-163 °C; Calculated for $C_{10}H_{19}ClN_2O_3$: C, 47.90; H, 7.64; N, 11.17, Found: C, 47.73; H, 7.43; N, 10.89; Calculated for $C_{10}H_{19}N_2O_3NaCl$: [$(M+Na)^+$ peak] *m/z* (ES^+) = 273.0982, Found: 273.0993 (+4.1 ppm); δ_H ($CDCl_3$, 400 MHz) 7.22 (br s, 1H, NH), 4.94 (br s, 1H, NHBOC), 4.05 (s, 2H, $ClCH_2CO$), 3.39 (q, *J* = 6.0 Hz, 2H, $NHCH_2$), 3.17 (q, *J* = 6.0 Hz, 2H, $BOCNHCH_2$), 1.70 (m, 2H, $CH_2CH_2CH_2$), 1.44 (s, 9H, 3 x CH_3); δ_c ($CDCl_3$, 100 MHz) 165.9, 156.1, 78.9, 42.1, 36.6, 36.0, 29.5, 27.9; *m/z* (ES^+) 273.09 $(M+Na)^+$; IR ν_{max}(cm^{-1}) 3363, 3327, 2984, 2879, 1677, 1647, 1532, 1437, 1366, 1285, 1167, 1131, 1010, 870, 765, 657.

[4-(-{4,7,10-Tris-[(4-*tert*-butoxycarbonylamino-propylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclododec-1-yl}-acetylamino)- propyl]-carbamic acid *tert*-butyl ester (8)

A solution of **5** (1.38 g, 5.52 mmol) in dry MeCN (10 mL) was added to cyclen (0.22 g, 1.28 mmol), Cs_2CO_3 (1.69 g, 5.52 mmol) and KI (0.92 g, 5.52 mmol) in dry MeCN (20 mL). This was then heated at reflux under argon for 2 days. The mixture was filtered through celite and the solvent removed under reduced pressure. The residue was dissolved in $CHCl_3$ and washed with water and saturated KCl solution (3 x 20 ml). The organic layer was dried over K_2CO_3 and the solvent removed under reduced pressure to yield a light brown hygroscopic powder (1.16 g, 88% yield). M.p. 98-100 °C; Calculated for $C_{48}C_{93}N_{12}O_{12}$: [$(M+H)^+$ peak] *m/z* (ES^+) = 1029.7036, Found: 1029.7037 (0.1 ppm); δ_H ($CDCl_3$, 400 MHz) 7.68 (br s, 4H, NH), 5.25 (br s, 4H, NHBOC), 3.30 (q, *J* = 6.0 Hz, 8H, NCH_2CO), 3.15 (d, *J* = 5.5 Hz, 8H, $NHCH_2CH_2$), 3.07 (br s, 8H, NCH_2), 2.71 (s, 16H, NCH_2CH_2NH), 1.64 (d, *J* = 5.5 Hz, 8H, $CH_2CH_2CH_2$), 1.44 (s, 36H, BOC); δ_c ($CDCl_3$, 100 MHz) 170.8, 156.0, 78.7, 58.6, 54.0, 36.8, 35.4, 29.7, 27.9; *m/z* (ES^+) 1029.70 $(M)^+$; IR ν_{max} (cm^{-1}) 3327, 2975, 1688, 1524, 1449, 1365, 1276, 1251, 1170, 1009, 779, 668.

***N*-(4-Amino-propyl)-2-{4,7,10-tris-[(4-amino-propylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclodec-1-yl}-acetamide (1)**

Ligand **1** was prepared according to **Procedure 1**, using ligand **8** (0.227 g, 0.22 mmol). A yellow hygroscopic solid was obtained (0.15 g, 90% yield). M.p. 161-156 °C; $C_{28}H_{60}N_{12}O_4Na$: [M+Na peak] *m/z* (ES^+) = 651.4758, Found: 651.4734 (−3.7 ppm); δ_H

(D_2O, 400 MHz) 3.23 (br s, 24H, NC<u>H</u>$_2$CO, NHC<u>H</u>$_2$, NH$_2$C<u>H</u>$_2$), 2.96 (t, *J* = 7.5 Hz, 16H, NC<u>H</u>$_2$C<u>H</u>$_2$N), 1.80 (q, *J* = 7.5 Hz, 8H, CH$_2$C<u>H</u>$_2$CH$_2$); δ_c (D_2O, 100 MHz) 54.1, 36.5, 36.3, 35.7, 26.0 *m/z* (ES^+) 651.47 $(M+Na)^+$, 315.24 $(M+2H)^{2+}$; IR ν_{max} (cm^{-1}) 3471, 3077, 1677, 1561, 1466, 1389, 1269, 1011.

_N_-(4-Amino-propyl)-2-{4,7,10-tris-[(4-amino-propylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclodec-1-yl}-acetamide.La.3CF_3SO_3.2H_2O (La.2)

La.2 was prepared according to **Procedure 2**, using ligand **2** (139 mg, 0.179 mmol) and $La(CF_3SO_3)_3$ (116 mg, 0.197 mmol). An orange/brown solid was obtained (185 mg, 76% yield). M.p. 167-170 °C; Calculated for $C_{28}H_{60}N_{12}O_4La.CF_3SO_3$: $[(M+CF_3SO_3)^{2+}$ peak] *m/z* (ES^+) = 916.3444, Found: 916.3440 (−0.5 ppm); δ_H (D_2O, 400 MHz) 3.45, 3.33, 3.22, 2.94, 1.84; *m/z* (ES^+) 458.15 $(M+CF_3SO_3)^{2+}$; IR ν_{max}(cm^{-1}) 3394, 3109, 1627, 1459, 1250, 1169, 1030, 610, 519.

_N_-(4-Amino-propyl)-2-{4,7,10-tris-[(4-amino-propylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclodec-1-yl}-acetamide.Eu.3CF_3SO_3.H_2O (Eu.2)

Eu.2 was prepared according to **Procedure 2**, using ligand **2** (65 mg, 0.084 mmol) and $Eu(CF_3SO_3)_3$ (55 mg, 0.092 mmol). An orange/brown solid was obtained (95 mg, 82% yield). M.p. decomposed above 160 °C; Calculated for $C_{28}H_{60}N_{12}O_4Eu.CF_3SO_3$: $[(M+CF_3SO_3)^{2+}$ peak] *m/z* = 930.3593, Found: 930.3552 (−4.4 ppm); δ_H (D_2O, 400 MHz) 25.17, 2.91, 2.50, 1.78, 0.77, −2.65, −5.10, −8.46, −10.36, −12.71; *m/z* 465.17 $(M+CF_3SO_3)^{2+}$, 390.20 $(M)^{2+}$, 260.46 $(M)^{3+}$; IR ν_{max}(cm^{-1}) 3421, 1629, 1252, 1170, 1030, 640.

[4-(2-Chloro-acetylamino)-butyl]-carbamic acid *tert*-butyl ester (6)

A solution of chloroacetyl chloride (0.639 g, 5.66 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 1 h to a solution of (4-amino-butyl)-carbamic acid *tert*-butyl ester (0.88 g, 4.7 mmol) and NEt_3 (0.72 g, 7.03 mmol) in CH_2Cl_2 (20 mL) at –20 ºC (acetone/ice bath). The resulting brown solution was left to stir at room temperature for 24 h. The inorganic salts formed were filtered off and the filtrate washed with citric acid (3 x 20 mL) and then with water (2 x 20 mL). The organic layer was extracted and dried over K_2CO_3 and

solvent removed under reduced pressure. Yield (0.916 g, 74%). M.p. 93-95 °C; Calculated for $C_{11}H_{21}ClN_2O_3$: C, 49.90; H, 8.00; N, 10.38, Found: C, 49.63; H, 7.46; N, 10.28; δ_H ($CDCl_3$, 400 MHz) 6.74 (br s, 1H, NH), 4.65 (br s, 1H, NHBOC), 4.05 (s, 2H, $ClCH_2CO$), 3.34 (dd, *J* = 7.0 & 6.0 Hz, 2H, $CONHCH_2$), 3.16 (d, *J* = 6.0 Hz, 2H, $BOCNHCH_2$), 1.56 (m, 4H, $NHCH_2CH_2CH_2$), 1.44 (s, 9H, 3 x CH_3); δ_c ($CDCl_3$, 100 MHz) 165.9, 156.0, 79.2, 42.6, 39.9, 39.4, 28.3, 27.4, 26.5; *m/z* 287.11 $(M+Na)^+$; IR $\nu_{max}(cm^{-1})$ 3376, 2979, 1686, 1647, 1546, 1522, 1446, 1367, 1304, 1262, 1172, 1017, 958, 715, 579.

[4-(-{4,7,10-Tris-[(4-*tert*-butoxycarbonylamino-butylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclododec-1-yl}-acetylamino)-butyl]-carbamic acid *tert*-butyl ester (9)

A solution of **6** (0.86 g, 3.34 mmol) in dry MeCN (10 mL) was added to cyclen (0.13 g, 0.74 mmol), Cs_2CO_3 (1.09 g, 3.34 mmol) and KI (0.55 g, 3.34 mmol) in dry MeCN (20 mL). This was then heated at reflux under argon for 5 days. The mixture was filtered through celite and the solvent removed under reduced pressure. The residue was dissolved in $CHCl_3$ and washed with water and a saturated KCl solution (3 x 20 mL). The organic layer was dried over K_2CO_3 and the solvent removed under reduced pressure to yield a light brown hygroscopic powder (0.752 g, 96% yield). M.p 69-72 ºC; Calculated for $C_{52}H_{100}N_{12}O_{12}.Na.H_2O$: C, 55.72; H, 9.35; N, 14.71, Found: C, 55.42; H, 9.14; N, 14.38; δ_H ($CDCl_3$, 400 MHz) 7.46 (br s, 4H, NH), 5.06 (br s, 4H, NHBOC), 3.26 (d, *J* = 5 Hz, 8H, $NHCH_2CH_2$), 3.08 (d, *J* = 14.5 Hz, 16H, NCH_2CO, $NHCH_2CH_2$), 2.70 (s, 16H, NCH_2CH_2N), 1.52 (s, 16H, 2 x $NHCH_2CH_2$), 1.43 (s, 36H, 3 x CH_3); δ_c ($CDCl_3$, 100 MHz) 170.4, 155.7, 78.6, 58.4, 52.8, 39.7, 38.4, 28.0, 27.2, 26.6; *m/z* (ES^+) 1084.32 $(M+H)^+$, 543.90 $(M+2H)^{2+}$; IR ν_{max} (cm^{-1}) 3322, 2975, 2935, 2866, 1701, 1658, 1529, 1452, 1365, 1274, 1171, 1043, 1005, 865, 736.

***N*-(4-Amino-butyl)-2-{4,7,10-tris-[(4-amino-butylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclodec-1-yl}-acetamide (3)**

Ligand **3** was prepared according to **Procedure 1**, using ligand **9** (0.4 g, 0.37 mmol). A yellow hygroscopic solid was obtained (0.31 g, 97% yield). M.p. decomposed above 150 °C; Calculated for $C_{32}H_{68}N_{12}O_4Na$: [M+Na peak] *m/z* (ES^+) = 707.5384, Found:

707.5397 (+1.8 ppm); δ_H (D_2O, 400 MHz) 3.14 (m, 24H, 3 x CH_2, NC<u>H</u>$_2$CO, NHC<u>H</u>$_2$, $NH_2C\underline{H}_2$), 2.90 (s, 16H, NC<u>H</u>$_2$C<u>H</u>$_2$N), 1.57 (m, 8H, $CH_2C\underline{H}_2CH_2$), 1.50 (m, 8H, $CH_2C\underline{H}_2CH_2$); δ_c (D_2O, 100 MHz) 164.2, 54.4, 49.3, 38.6, 38.2, 21.9, 23.7; *m/z* (ES^+) 707.54 $(M+Na)^+$, 685.63 $(M+H)^+$, 343.30 $(M+2H)^{2+}$, 229.20 $(M+3H)^{3+}$; IR ν_{max} (cm^{-1}) 3354, 3078, 2934, 1681, 1652, 155, 1466, 1399, 1290, 1164, 1088, 941.

_N_-(4-Amino-butyl)-2-{4,7,10-tris-[(4-amino-butylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclodec-1-yl}-acetamide.La.3CF_3SO_3.2H_2O (La.3)

La.3 was prepared according to **Procedure 2**, using ligand **9** (94 mg, 0.113 mmol) and $La(CF_3SO_3)_3$ (73 mg, 0.124 mmol). A light brown solid was obtained (113 mg, 71% yield). M.p. 220-224 °C; Calculated for $C_{32}H_{68}N_{12}O_4La.CF_3SO_3$: [$(M+CF_3SO_3)^{2+}$ peak] *m/z* (ES^+) = 927.4070, Found: 972.4058 (−1.3 ppm); δ_H (D_2O, 400 MHz) 3.23, 2.92, 1.58; *m/z* (ES^+) 486.20 $(M+CF_3SO_3)^{2+}$, 274.48 $(M)^{3+}$; IR ν_{max}(cm^{-1}) 3329, 1630, 1457, 1247, 1166, 1084, 1029, 640, 517.

_N_-(4-Amino-butyl)-2-{4,7,10-tris-[(4-amino-butylcarbamoyl)-methyl]-1,4,7,10-tetraaza-cyclodec-1-yl}-acetamide.Eu.3CF_3SO_3.H_2O (Eu.3)

Eu.3 was prepared according to **Procedure 2**, using ligand **9** (93 mg, 0.113 mmol) and $Eu(CF_3SO_3)_3$ (75 mg, 0.124 mmol). An orange/brown solid was obtained (73 mg, 45% yield). M.p. decomposed above 180 °C; Calculated for $C_{32}H_{68}N_{12}O_4Eu.CF_3SO_3$: [$(M+CF_3SO_3)^{2+}$ peak] *m/z* (ES^+) = 986.4219, Found: 986.4192 (−2.7 ppm); δ_H (D_2O, 400 MHz) 26.25, 3.48, 2.92, 1.81, 1.07, −2.35, −5.23, −7.99, −10.89, −12.76; *m/z* (ES^+) 493.20 $(M+CF_3SO_3)^{2+}$, 418.22 $(M)^{2+}$, 279.16 $(M)^{3+}$; IR ν_{max}(cm^{-1}) 3397, 1629, 1465, 1253, 1170, 1083, 1029, 640.

Figure 1. Second order rate constant determination for **La.1**

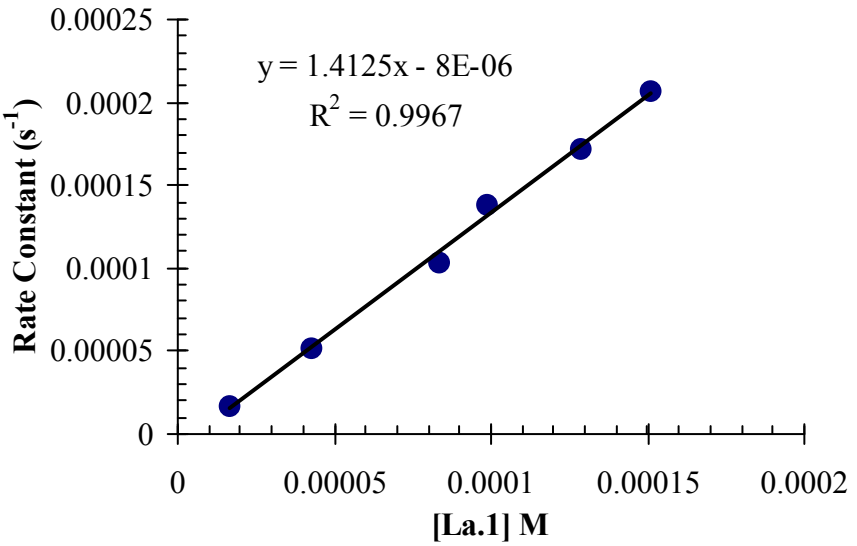

Figure 2. Typical titration curve of the protonated ligand **1** against NEt_4OH at 25 °C. [**1**] = 7.6 x 10^{-4} M, [H^+] = 7.75 x 10^{-3} M, [NEt_4OH] = 0.104 M, I = 0.10 M (NEt_4ClO_4), total volume = 10 cm^3.

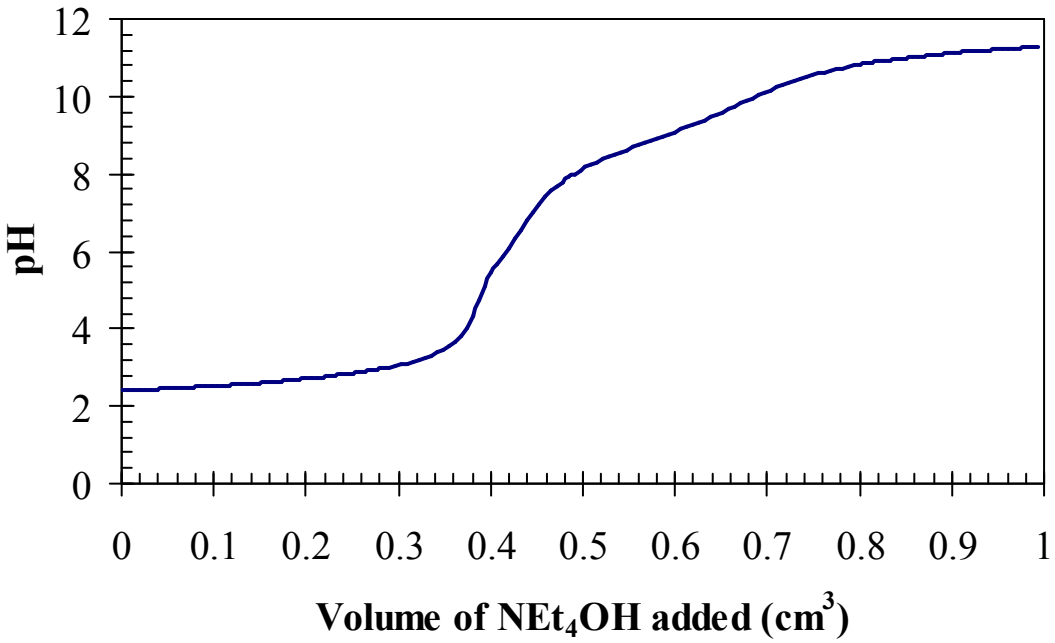

Figure 3. Speciation variation of ligand 135, showing the species present in H_2O at various pH in which $[\mathbf{1}]_{total}$ = 7.2 x 10^{-3} M, $[Eu(III)]_{total}$ = 7.0 x 10^{-3} M, I = 0.10 M (NEt_4ClO_4) at 25 °C. Speciation is shown relative to the total concentration of ligand **1**.

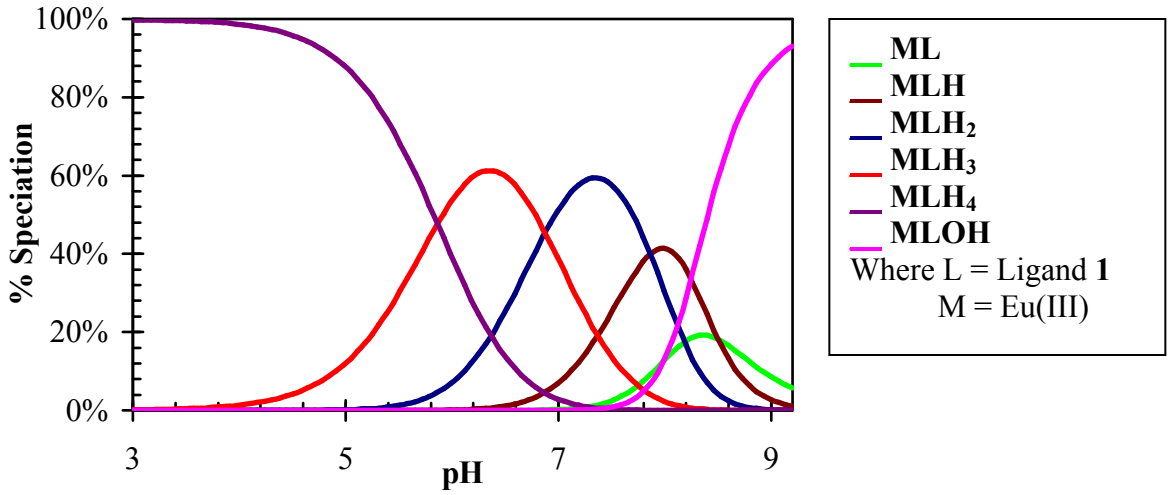

Figure 4. Typical titration curves of the protonated ligand **1** in the absence and presence of $La(ClO_4)_3$, $Eu(ClO_4)_3$, $Gd(ClO_4)_3$, $Tb(ClO_4)_3$ and $Yb(ClO_4)_3$ against NEt_4OH at 25 °C. $[\mathbf{1}]_{total}$ = 7.6 x 10^{-4} M, $[La(III)]_{total}$, $[Eu(III)]_{total}$, $[Gd(III)]_{total}$, $[Tb(III)]_{total}$ or $[Yb(III)]_{total}$ = 7.6 x 10^{-4} M, $[H^+]_{total}$ = 7.75 x 10^{-3} M, $[NEt_4OH]$ = 0.104 M, I = 0.10 M (NEt_4ClO_4), total volume = 10 cm^3.