Supplementary Information

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Supplementary Information

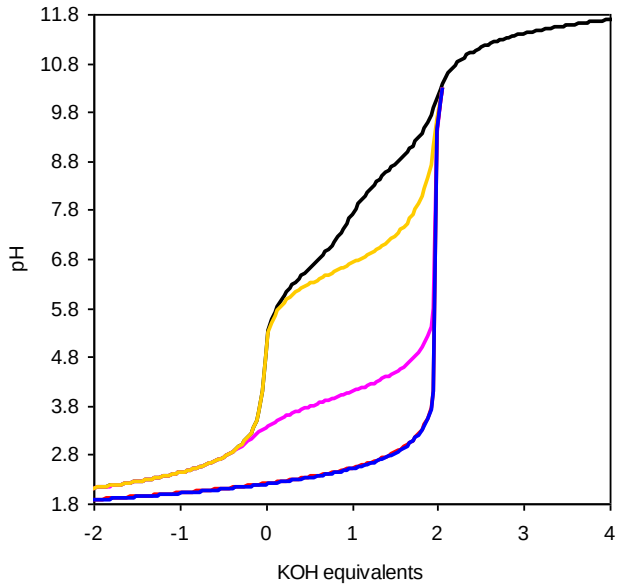

Figure S1 The pH-potentiometric titration of L^4 in the absence (black) and presence of an equivalent Mg^{2+} (yellow), Ca^{2+} (pink), Zn^{2+} (red) and Cu^{2+} (blue) (C_{tot} = 3.92 mM, V_{tot} = 10.00 cm^3, I = 1.0 KCl and t = 25 ^oC).

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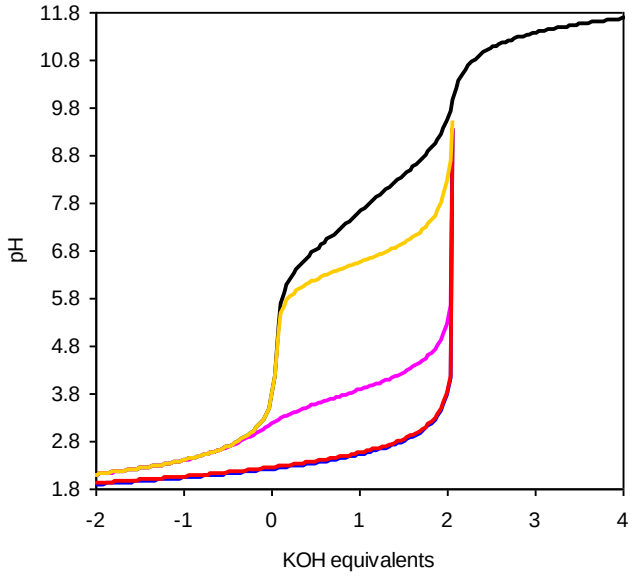

Figure S2 The pH-potentiometric titration of L^8 in the absence (black) and presence of an equivalent Mg^{2+} (yellow), Ca^{2+} (pink), Zn^{2+} (red) and Cu^{2+} (blue) (C_{tot} = 3.92 mM, V_{tot} = 10.00 cm^3, I = 1.0 KCl and t = 25 ^oC).

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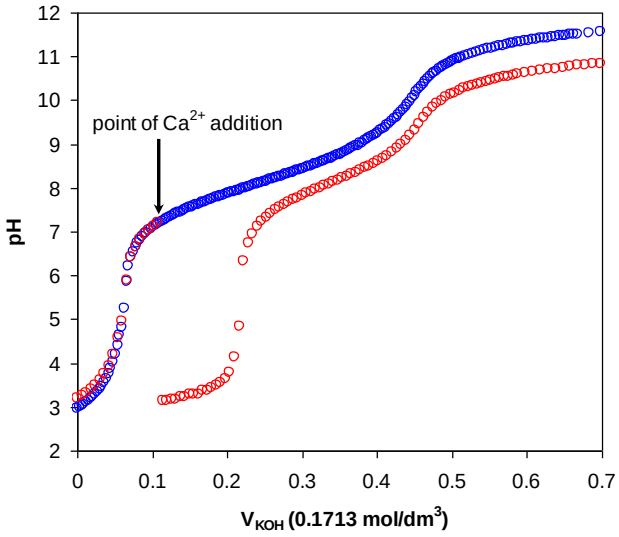

Figure S3. The pH-potentiometric titration of L^{12} in the absence (blue) and presence (red) of a large excess of $CaCl_2$ (C_{tot} = 1.35 mM I = 1.0 KCl, V_{tot} = 10.00 cm^3,). The samples were identical until the point of $CaCl_2$ addition.

Table S1. The protonation constants ($log\ K_i$) of L^{12} (I = 1.0 M KCl, 25°C).

	L^{12}
$log\ K_1^H$	9.21 ± 0.06
$log\ K_2^H$	8.48 ± 0.07
$log\ K_3^H$	8.27 ± 0.07
$log\ K_4^H$	7.60 ± 0.07
$log\ K_5^H$	7.47 ± 0.05
$log\ K_6^H$	2.63 ± 0.06

Supplementary Information S4

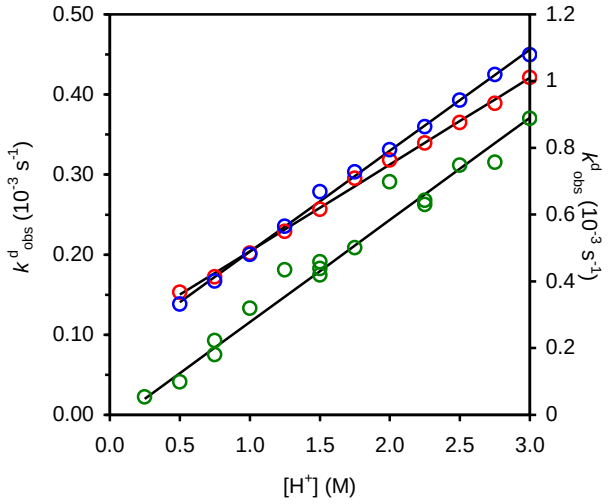

Figure S4. Plots of the observed acid-catalysed dissociation constants (k^d_{obs}) against acid concentration for CeL^4 (blue, left axis), CeL^8 (red, left axis) and CeL^{12} (green, right axis).

Table S2. Biodistribution of ligands labeled with ^{177}Lu in normal Balb/c mice (n = 4). Data are presented as %ID/organ ± standard deviation (s.d.)

		Time points (h)			
Complex	Tissue	0.5	1	4	24
^{177}LuL^1	Blood	2.70 ± 0.39	0.53 ± 0.16	0.01 ± 0.01	0.00 ± 0.00
	Lung	0.30 ± 0.04	0.10 ± 0.01	0.02 ± 0.01	0.01 ± 0.00
	Liver	0.79 ± 0.07	0.41 ± 0.08	0.29 ± 0.04	0.18 ± 0.04
	Spleen	0.05 ± 0.00	0.02 ± 0.01	0.01 ± 0.00	0.01 ± 0.00
	Kidney	1.01 ± 0.17	0.60 ± 0.04	0.60 ± 0.04	0.23 ± 0.05
	Heart	0.09 ± 0.01	0.03 ± 0.00	0.01 ± 0.00	0.01 ± 0.00
	Muscle	4.90 ± 0.93	3.96 ± 1.01	0.84 ± 0.46	0.13 ± 0.11
	Fat	0.89 ± 0.13	0.57 ± 0.43	0.11 ± 0.01	0.06 ± 0.04
	Bone	3.91 ± 3.76	1.64 ± 0.39	0.63 ± 0.29	0.23 ± 0.10
	Cumulative urine excretion (%ID) *	n.d.	n.d.	43.4	68.7
^{177}LuL^2	Blood	0.76 ± 0.35	0.12 ± 0.07	0.00 ± 0.00	0.01 ± 0.01
	Lung	0.16 ± 0.04	0.02 ± 0.01	0.02 ± 0.01	0.01 ± 0.00
	Liver	0.48 ± 0.15	0.10 ± 0.02	0.10 ± 0.02	0.05 ± 0.01
	Spleen	0.04 ± 0.01	0.01 ± 0.00	0.01 ± 0.00	0.03 ± 0.04
	Kidney	1.50 ± 0.49	0.53 ± 0.06	0.45 ± 0.07	0.23 ± 0.02
	Heart	0.05 ± 0.02	0.01 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	Muscle	12.14 ± 2.42	1.03 ± 0.24	0.58 ± 0.39	0.35 ± 0.22

	Fat	0.89 ± 0.26	0.21 ± 0.04	0.18 ± 0.11	0.10 ± 0.03
	Bone	0.16 ± 0.08	0.02 ± 0.01	0.02 ± 0.01	0.42 ± 0.26
	Cumulative urine excretion (%ID)	n.d.	n.d.	61.2	72.4
$^{177}LuL^{4}$	Blood	3.42 ± 0.53	0.47 ± 0.28	0.01 ± 0.01	0.00 ± 0.00
	Lung	0.30 ± 0.05	0.06 ± 0.02	0.01 ± 0.00	0.01 ± 0.01
	Liver	0.80 ± 0.13	0.29 ± 0.03	0.15 ± 0.03	0.20 ± 0.04
	Spleen	0.07 ± 0.01	0.02 ± 0.01	0.01 ± 0.00	0.00 ± 0.00
	Kidney	1.16 ± 0.21	0.53 ± 0.04	0.30 ± 0.04	0.36 ± 0.08
	Heart	0.09 ± 0.02	0.02 ± 0.00	0.01 ± 0.00	0.00 ± 0.00
	Muscle	5.78 ± 0.89	2.86 ± 1.52	0.28 ± 0.11	0.40 ± 0.19
	Fat	0.94 ± 0.21	1.00 ± 0.16	0.04 ± 0.03	0.02 ± 0.01
	Bone	3.68 ± 0.56	1.71 ± 0.99	0.34 ± 0.18	0.14 ± 0.08
	Cumulative urine excretion (%ID)	n.d.	n.d.	56.7	77.4
$^{177}LuL^{8}$	Blood	3.42 ± 0.57	0.29 ± 0.03	0.01 ± 0.01	0.01 ± 0.00
	Lung	0.30 ± 0.06	0.06 ± 0.01	0.03 ± 0.03	0.01 ± 0.00
	Liver	0.79 ± 0.11	0.25 ± 0.07	0.19 ± 0.07	0.08 ± 0.01
	Spleen	0.08 ± 0.04	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00
	Kidney	1.00 ± 0.13	0.50 ± 0.06	0.41 ± 0.08	0.34 ± 0.07
	Heart	0.10 ± 0.02	0.02 ± 0.01	0.00 ± 0.00	0.00 ± 0.00
	Muscle	5.49 ± 1.94	3.20 ± 1.58	0.24 ± 0.16	0.14 ± 0.04
	Fat	1.56 ± 1.13	0.39 ± 0.22	0.06 ± 0.02	0.12 ± 0.08
	Bone	3.20 ± 1.02	0.83 ± 0.35	0.30 ± 0.14	0.24 ± 0.03
	Cumulative urine excretion (%ID)	n.d.	n.d.	53.6	63.3
$^{177}LuL^{12}$	Blood	3.12 ± 0.99	0.27 ± 0.10	0.01 ± 0.01	0.02 ± 0.01
	Lung	0.32 ± 0.10	0.07 ± 0.04	0.01 ± 0.01	0.01 ± 0.00
	Liver	0.85 ± 0.26	0.21 ± 0.03	0.13 ± 0.01	0.15 ± 0.05
	Spleen	0.06 ± 0.02	0.01 ± 0.01	0.00 ± 0.00	0.01 ± 0.00
	Kidney	1.09 ± 0.27	0.42 ± 0.02	0.35 ± 0.01	0.17 ± 0.02
	Heart	0.09 ± 0.01	0.01 ± 0.01	0.00 ± 0.00	0.01 ± 0.00
	Muscle	16.20 ± 5.18	1.12 ± 0.69	0.24 ± 0.09	0.29 ± 0.13
	Fat	1.58 ± 0.59	0.25 ± 0.06	0.06 ± 0.05	0.10 ± 0.05
	Bone	3.06 ± 0.82	0.81 ± 0.41	0.25 ± 0.10	0.21 ± 0.10
	Cumulative urine excretion (%ID)	n.d.	n.d.	65.7	76.7

* Cumulative urine excretion was determined by housing a group of 4 mice in a metabolic mouse cage. The urine collected at each specific time point was counted along with a standard injection dose to calculate the percentage of urinary excretion.

n.d.: not determined.