

Dynamic Measurements of Aqueous Lanthanide Triflate-Catalyzed Reactions Using Luminescence Decay

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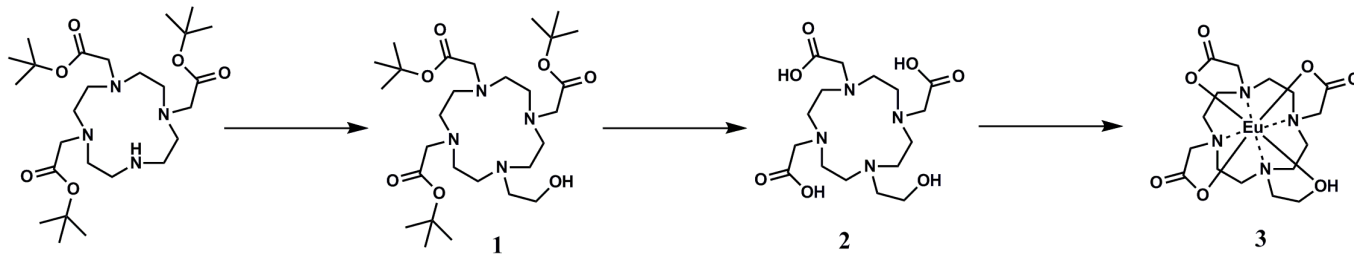
Experimental Procedures

Commercial chemicals were of reagent-grade purity or better and were used without further purification. Water was purified using a PURELAB Ultra Mk2 water purification system (ELGA).

Flash chromatography was performed using silica gel 60, 230–400 mesh (EMD Chemicals).¹ Analytical thin-layer chromatography (TLC) was carried out on ASTM TLC plates precoated with silica gel 60 F₂₅₄ (250 μm layer thickness). TLC visualization was accomplished using a UV lamp followed by charring with potassium permanganate stain (3 g KMnO₄, 20 g K₂CO₃, 5 mL 5% w/v aqueous NaOH, 300 mL H₂O).

¹H NMR spectra were obtained using a Varian Unity 300 (300 MHz) or a Varian Mercury 400 (400 MHz) spectrometer, and ¹³C NMR spectra were obtained using a Varian Mercury 400 (100 MHz) or a Varian Mercury 500 (125 MHz) spectrometer. Chemical shifts are reported relative to residual solvent signals unless otherwise noted (CDCl₃: ¹H: δ 7.27, ¹³C: δ 77.23; D₂O: ¹H: δ 4.79, ¹³C: δ 39.51 for an internal standard of dimethyl sulfoxide-*d*₆). ¹H NMR data are assumed to be first order with apparent singlets and multiplets reported as “s” and “m”. Italicized elements are those that are responsible for the shifts. High-resolution electrospray ionization mass spectra (HRESIMS) were obtained on an electrospray time of flight high-resolution Waters Micromass LCT Premier XE mass spectrometer. Liquid chromatography and mass spectrometry (LC–MS) analysis was performed on a Shimadzu LC–MS system equipped with a C18 column (Restek International, Viva C18, 5 μm, 250 × 4.6 mm) equilibrated with 0.4% v/v formic acid, using a binary gradient method (pump A: water; pump B: acetonitrile; 5–95% B over 70 min; flow rate: 1 mL/min).

2-(Hydroxyphenylmethyl)cyclohexanone was synthesized following a previously described procedure.²



***tert*-Butyl 2,2',2''-(10-(2-hydroxyethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetate (1):**

To a mixture of anhydrous acetonitrile (10 mL) and anhydrous K_2CO_3 (247 mg, 1.79 mmol, 5 equiv) under an atmosphere of N_2 was added *tert*-butyl 2,2',2''-(1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetate (184 mg, 0.358 mmol, 1 equiv) followed by 2-bromoethanol (127 μ L, 1.79 mmol, 5 equiv). The resulting mixture was stirred at 70 °C for 12 h. After cooling to ambient temperature and removing excess K_2CO_3 by filtration, the solvent was removed under reduced pressure. Purification was performed using silica gel chromatography (10:1 dichloromethane/methanol) to yield 198 mg (99%) of **1** as a light yellow oil. 1H NMR (400 MHz, $CDCl_3$, δ): 1.45 (s, CH_3 , 27H), 2.54–2.57 (m, CH_2 , 4H), 2.72–2.77 (m, CH_2 , 12H), 2.79–2.82 (m, CH_2 , 4H), 3.32 (s, $CH_2C=O$, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 28.8 (CH_3), 48.1 (CH_2), 51.3 (CH_2), 52.8 (CH_2), 57.8 (CH_2), 81.4 ($C(CH_3)_3$), 171.9 ($C=O$); TLC: R_f = 0.25 and 0.27 (18:1 dichloromethane/methanol); HRESIMS (m/z): $[M + H]^+$ calcd for $C_{28}H_{55}N_4O_7$, 559.4071; found, 559.4063.

2,2',2''-(10-(2-Hydroxyethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetic acid (2): A solution of **1** (180 mg, 0.322 mmol) in concentrated HCl (15 mL) was stirred at ambient temperature for 2 h. The reaction mixture was concentrated under reduced pressure, and the resulting residue was dissolved in H_2O (3 mL) and freeze dried to afford 124 mg (99%) of **2** as a white solid. 1H NMR (300 MHz, D_2O , δ): 3.13 (m, CH_2 , 8H), 3.49 (m, CH_2 , 10H), 3.63–3.65 (m, CH_2 , 4H), 3.98–4.01 (m, CH_2 , 4H); ^{13}C NMR (125 MHz, D_2O , δ): 49.5 (CH_2), 49.8 (CH_2), 52.1 (CH_2), 53.4 (CH_2), 54.5 (CH_2), 56.4 (CH_2), 56.5 (CH_2), 56.9 (CH_2), 60.9 (CH_2), 61.1 (CH_2), 64.1 (CH_2), 67.6 (CH_2), 68.1 (CH_2), 170.4 ($C=O$); 174.3 ($C=O$); 175.8 ($C=O$); HRESIMS (m/z): $[M - H]^-$ calcd for $C_{16}H_{29}N_4O_7$, 389.2036; found, 389.2042.

2,2',2''-(10-(2-Hydroxyethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetoeuropium(III)

(3): To a solution of **2** (18 mg, 47 μmol , 1 equiv) in H_2O (3 mL) was added EuCl_3 hexahydrate (35 mg, 96 μmol , 2 equiv), and the resulting reaction mixture was stirred at ambient temperature for 24 h while maintaining the pH between 6.9 and 7.1 by the addition of 0.1 M aqueous NH_4OH . The pH of the mixture was increased to 12 to precipitate excess Eu^{3+} as $\text{Eu}(\text{OH})_3$. After removing $\text{Eu}(\text{OH})_3$ by filtration through a 0.2 μm filter (Millipore, IC Millex-LG), the remaining filtrate was freeze dried. The resulting white solid was dissolved in H_2O (2 mL) and dialyzed against H_2O (cellulose ester, 100–500 Dalton molecular weight cut off, Spectra/Por Biotech). The entire dialysate volume was changed after 3, 7, and 17 h. After dialysis, the solution inside the membrane was freeze dried to yield 21 mg (85%) of **3** as a white solid. The purity of the product was confirmed by LC–MS characterization (page S15). HRESIMS (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{28}\text{N}_4\text{O}_7^{151}\text{Eu}$, 539.1173; found 539.1183.

Determination of q Values

Luminescence decay measurements were acquired using a HORIBA Jobin Yvon Fluoromax-4 spectrofluorometer in decay by delay scan mode using the phosphorescence life time setting. For luminescence decay measurements of control complex, **3**, an excitation wavelength of 395 nm and an emission wavelength of 594 nm were used. For measurements of $\text{Eu}(\text{OTf})_3$, an excitation wavelength of 394 nm and an emission wavelength of 591 nm were used. Other parameters were kept constant: excitation and emission slit width (5 nm), flash count (200), initial delay (0.01 ms), maximum delay (13 ms), and delay increment (0.01 ms). The natural log of the intensity of the scan was plotted against time, and the slope was used as the decay rate. This procedure was performed in H_2O and D_2O versions of each solvent. For each solvent, the decay rates in H_2O ($\tau_{\text{H}_2\text{O}}$) and D_2O ($\tau_{\text{D}_2\text{O}}$) were used in the eq 1, which was developed by Horrocks and coworkers,³ to determine the number of water molecules, q , coordinated to

the Eu^{3+} ion. For control complex, **3**, eq 2 was used because q is less than or equal to one for this complex.³

$$\text{eq 1: } q = 1.11 \left(\left| \tau_{\text{H}_2\text{O}}^{-1} - \tau_{\text{D}_2\text{O}}^{-1} \right| - 0.31 \right)$$

$$\text{eq 2: } q = 1.2 \left(\left| \tau_{\text{H}_2\text{O}}^{-1} - \tau_{\text{D}_2\text{O}}^{-1} \right| - 0.6666 \right)$$

$\text{Eu}(\text{OTf})_3$ solutions (1 mM) were prepared for each solvent (1–10, 20, 30, 40, 50, 60, 70, 80, 90, and 100% v/v of H_2O in THF) and used as the first reaction coordinate. The luminescence decay measurements for the second reaction coordinate were acquired using the $\text{Eu}(\text{OTf})_3$ solutions after addition of benzaldehyde in a 1:9 molar ratio of Eu^{3+} to benzaldehyde (9 mM benzaldehyde). The third reaction coordinate measurements were acquired after addition of 2-(hydroxyphenylmethyl)cyclohexanone to freshly prepared $\text{Eu}(\text{OTf})_3$ solutions in a 1:9 molar ratio of Eu^{3+} to 2-(hydroxyphenylmethyl)cyclohexanone. 2-(Hydroxyphenylmethyl)cyclohexanone was not soluble in $\text{H}_2\text{O}/\text{THF}$ ratios above 70%; thus, for 80–100% H_2O or D_2O in THF, a molar ratio of 1:1 (Eu^{3+} to 2-(hydroxyphenylmethyl)cyclohexanone) was used. The solutions composed of 100% H_2O or D_2O were sonicated for 10 min after the addition of 2-(hydroxyphenylmethyl)cyclohexanone. Control measurements were measured using complex **3** (1 mM) in each solvent studied. Finally, Figures S1 and S2 show representative decay curves, and Tables S1–S4 show results of the luminescence decay data for the control complex, **3**, and for the first, second, and third reaction coordinates of the catalytic cycle. Data reported in the tables is the result of single measurements for complex **3** and three to six replicates for each reaction coordinate.

References

- (1) Still, C. W.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
- (2) Kobayashi, S.; Hachiya, I. *J. Org. Chem.* **1994**, *59*, 3590–3596.
- (3) Supkowski, R. M.; Horrocks, W. D. *Inorg. Chim. Acta.* **2002**, *340*, 44–48.

Sample Luminescence Decay Curves

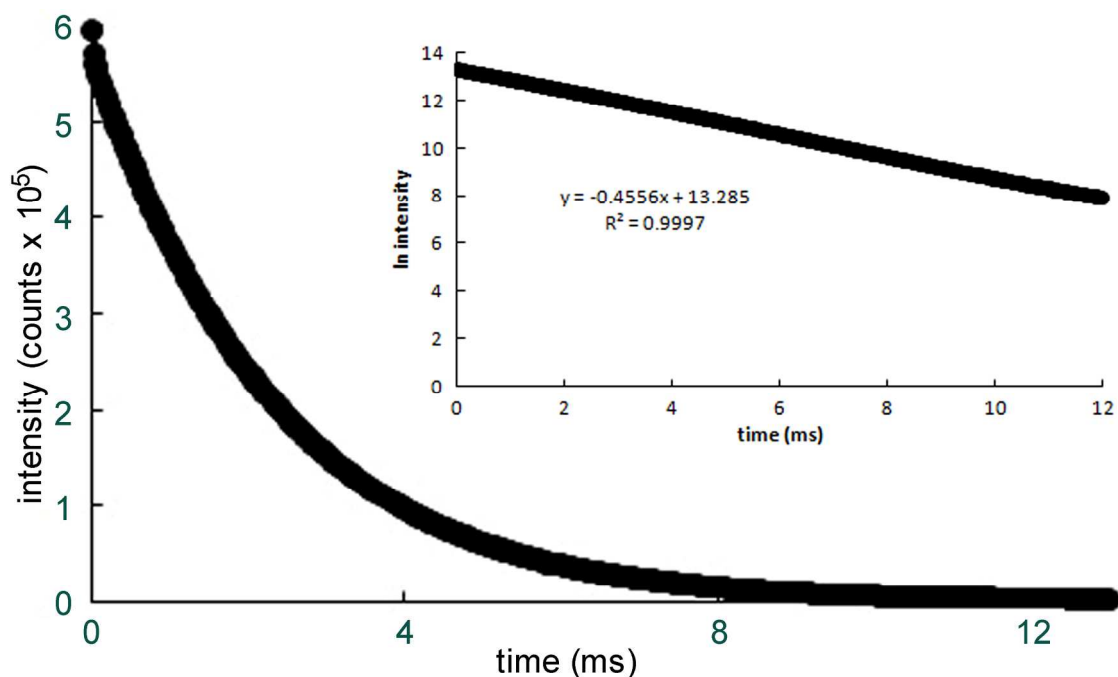


Figure S1. Luminescence decay curve of complex 3 in D₂O. The inset shows the natural log plot of the data, and the slope acquired from the natural log plot is the luminescence decay rate τ_{D_2O} .

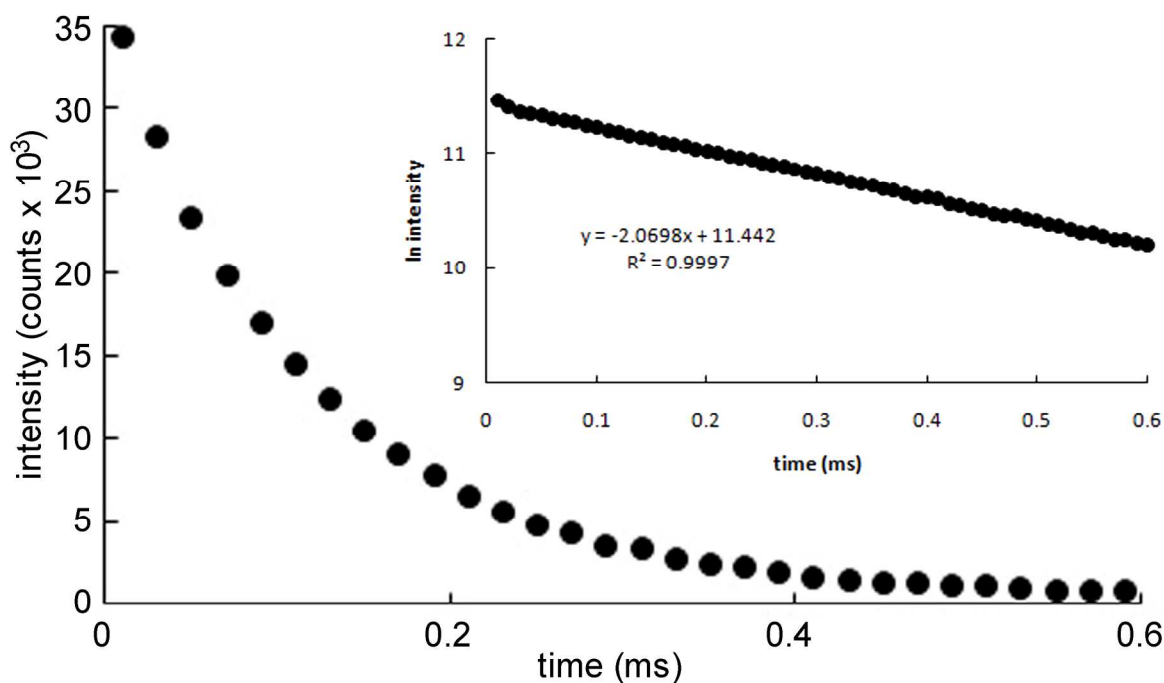


Figure S2. Luminescence decay curve of complex 3 in H₂O. The inset shows the natural log plot of the data, and the slope acquired from the natural log plot is the luminescence decay rate τ_{H_2O} .

Table S1. Number of H₂O molecules, q , coordinated to Eu³⁺ for the control complex, **3**.

% of solvent composed of H ₂ O	q
1	0.99
2	1.07
3	1.02
4	1.03
5	1.05
6	1.08
7	1.03
8	1.09
9	1.05
10	1.02
20	1.05
30	1.09
40	1.07
50	1.07
60	1.06
70	1.09
80	1.08
90	1.06
100	1.04

Table S2. Number of H₂O molecules, q , coordinated to Eu³⁺ in the first reaction coordinate of the catalytic cycle.

% of solvent composed of H ₂ O	q (mean)	standard error
1	5.08	0.03
2	5.45	0.03
3	7.29	0.04
4	7.27	0.03
5	7.20	0.03
6	7.39	0.03
7	7.38	0.04
8	7.35	0.04
9	7.35	0.02
10	7.55	0.03
20	7.85	0.03
30	7.82	0.03
40	7.79	0.06
50	7.82	0.03
60	7.91	0.03
70	7.95	0.03
80	7.92	0.05
90	8.04	0.03
100	8.28	0.03

Table S3. Number of H₂O molecules, q' , coordinated to Eu³⁺ in the second reaction coordinate of the catalytic cycle.

% of solvent composed of H ₂ O	q' (mean)	standard error
1	5.05	0.03
2	5.33	0.02
3	7.17	0.02
4	7.17	0.03
5	7.02	0.03
6	7.27	0.03
7	7.26	0.02
8	7.21	0.03
9	7.21	0.05
10	7.39	0.03
20	7.51	0.03
30	7.64	0.03
40	7.61	0.04
50	7.61	0.06
60	7.70	0.05
70	7.76	0.03
80	7.73	0.03
90	7.91	0.03
100	8.20*	0.03

* benzaldehyde was not completely dissolved.

Table S4. Number of H₂O molecules, q'' , coordinated to Eu³⁺ in the third reaction coordinate of the catalytic cycle.

% of solvent composed of H ₂ O	q'' (mean)	standard error
1	5.08	0.03
2	5.45	0.03
3	7.30	0.05
4	7.26	0.07
5	7.20	0.03
6	7.38	0.03
7	7.36	0.03
8	7.35	0.03
9	7.36	0.03
10	7.55	0.03
20	7.79	0.05
30	7.73	0.06
40	7.76	0.03
50	7.79	0.06
60	7.91	0.06
70	7.91	0.03
80	7.91*	0.03
90	8.01*	0.06
100	8.26**	0.05

* Eu³⁺:2-(hydroxyphenylmethyl)cyclohexanone ratio was 1:1.

** Eu³⁺:2-(hydroxyphenylmethyl)cyclohexanone ratio was 1:1, and the solution was sonicated.

