Lanthanide(III) complexes of monophosphinate/monophosphonate DOTA-analogues: effect of the substituents on formation rate and radiolabelling yield

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Figure S1. 2D coordination polymer motive found in the solid-state structure of Na[Eu(do3aP\text{III})(H\text{2}O)]·2NaCl·7.125H\text{2}O. The view perpendicular to O\text{6}/N\text{4}-planes of the coordination spheres (A) and the view along the y-axis (B). Hydrogen atoms are omitted for clarity.
Figure S2. Crystal packing of Na[Eu(do3aP^H)(H_2O)]·2NaCl·7.125H_2O. The view along the y-axis. Hydrogen atoms are omitted for clarity.
Isolation and structure of DO3A lactame – H$_2$do3a$_{\text{lac}}$

When old batches of H$_3$do3a were used for synthesis of H$_4$do3a$_{\text{P}}$ (especially when stored in semi-solid form obtained by evaporation from acid media after deesterification), some amount of lactam H$_2$do3a$_{\text{lac}}$ was isolated as a late fraction of the ion exchange workup of the reaction mixture. It is probably predominantly formed on prolonged standing of H$_3$do3a under acid conditions (after evaporation in CF$_3$COOH). Its $^1$H NMR spectra are rather complicated due to rigidity of the molecule and, thus, the X-ray diffraction study was performed to confirm identity of the compound (Figure S3).

Single-crystals of (H$_4$do3a$_{\text{lac}}$)Cl$_2$·2H$_2$O were grown by vapour diffusion of THF into the solution of the H$_4$do3a$_{\text{lac}}$ in 6 M aq. HCl. In the crystal structure of (H$_4$do3a$_{\text{lac}}$)Cl$_2$·2H$_2$O, no disorder was found. The thermal parameter of one water-belonging hydrogen atoms was kept using $U_{\text{eq}}(H) = 1.2 \ U_{\text{eq}}(O)$ as it became too large when freely refined.

The macrocycle of (H$_4$do3a$_{\text{lac}}$)$_2^+$ fragment is diprotonated. One of the protons is bound to the amine atom of the lactam ring, and the other is localized on the opposite nitrogen atom bearing one of the carboxylate pendants and is involved in the medium-strong intramolecular hydrogen bond ($d_{N\cdot\cdot\cdotO} =$ 2.88 Å) to the lactam oxygen atom. Both carboxylic acid pendant arms are protonated and involved in intermolecular hydrogen bonding with water molecules of crystallization and chloride counter anions.

Figure S3. Molecular structure of (H$_4$do3a$_{\text{lac}}$)$_2^+$ cation found in the crystal structure of (H$_4$do3a$_{\text{lac}}$)Cl$_2$·2H$_2$O. The intramolecular hydrogen bond is shown as a dashed line. Carbon-bound hydrogen atoms are omitted for clarity.
Table S1. Experimental data of the reported crystal structures.

| Compound | Formula | $M_r$ | Colour | Shape | Dimensions (mm) | Crystal system | Space group | $a$ (Å) | $b$ (Å) | $c$ (Å) | $\alpha$ (°) | $\beta$ (°) | $\gamma$ (°) | $V$ (Å$^3$) | $Z$ | $D_\text{c}$ (g cm$^{-3}$) | $\mu$ (mm$^{-1}$) | $F(000)$ | Reflections unique; observed ($I_o > 2\sigma(I)$) | Parameters | G-o-f on $F^2$ | $R; R'$ (all data) | $wR; wR'$ (all data) | Difference max; min (e Å$^{-3}$) |
|----------|---------|-------|--------|-------|----------------|---------------|-------------|--------|--------|--------|-----------|-----------|-----------|----------|----|-----------------|------------|-------------|-----------------|----------------|-------------------|-----------------|
| (H$_6$do3aP$^\text{H})$Cl$_2$-THF·3H$_2$O | C$_{19}$H$_{45}$N$_4$O$_{12}$P$_1$Cl$_2$ | 623.46 | colourless | prism | 0.30×0.25×0.20 | monoclinic | C2/c | 22.0543(3) | 11.19790(10) | 24.5815(4) | 90 | 96.4613(8) | 90 | 6032.13(14) | 8 | 1.373 | 0.329 | 2656 | 6889; 5601 | 432 | 1.078 | 0.0466; 0.0650 | 0.1291; 0.1449 | 0.474; –0.523 |
| Na[Eu(do3aP$^\text{H})$(H$_2$O)]·2NaCl·7.125H$_2$O | C$_{41.25}$H$_{41.25}$Cl$_2$Eu$_4$Na$_{2}$O$_{16.125}$P$_1$ | 858.57 | colourless | needle | 0.15×0.08×0.05 | monoclinic | C2/c | 32.1447(5) | 9.43790(10) | 23.5537(4) | 90 | 121.0061(8) | 90 | 6124.65(16) | 8 | 1.862 | 2.392 | 3466 | 7035; 6005 | 451 | 1.039 | 0.0299; 0.0406 | 0.0658; 0.0709 | 1.941; –1.169 |
| (H$_4$do3a$^\text{am}$)Cl$_2$·2H$_2$O | C$_{14}$H$_{30}$Cl$_2$N$_4$O$_7$ | 437.32 | colourless | prism | 0.50×0.20×0.20 | orthorhombic | P2$_1$2$_1$2$_1$ | 9.7430(4) | 10.3130(5) | 21.7340(10) | 90 | 90 | 90 | 2183.82(17) | 4 | 1.330 | 0.337 | 928 | 4220; 3435 | 276 | 1.066 | 0.0439; 0.0620 | 0.0987; 0.1088 | 0.321; –0.181 |
Table S2. Overall protonation constants log$\beta$ of ligands ($I = 0.1 \text{ m NMe}_4\text{Cl}$, 25 °C).

<table>
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<th>$H_5\text{do3aP}^{PIN}$</th>
<th>$H_4\text{do3aP}^{AM}$</th>
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<tr>
<td>$H_6$L</td>
<td>–</td>
<td>–</td>
<td>38.25(4)</td>
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Figure S4. Representative absorption spectra: Ce$^{III}$ aqua ion (black), out-of-cage (blue) and in-cage (red) Ce$^{III}$-do3aPIN complex ($c_M = c_L = 4.0 \cdot 10^{-4}$ M, 25 °C).

Figure S5. Representative absorption spectra of Ce$^{III}$ systems measured immediately after mixing at various pH (increasing pH). Changes of absorbance at absorption band maximum are shown in Figure S6. The arrow indicates increasing pH. Changes of absorbance at absorption band maximum are shown in Figure S6.
Figure S6. Formation of out-of-cage complexes: pH dependence of absorbance at absorption band maximum (298–305 nm) measured immediately after mixing of the components (25 °C) under the Ce$^{III}$ excess ($4.0 \cdot 10^{-3}$ M, $c_L = 4.0 \cdot 10^{-4}$ M) and under the ligand excess ($c_{Ce} = 4.0 \cdot 10^{-4}$ M, $c_L = 4.0 \cdot 10^{-3}$ M). The lines correspond to the best fits according to Equation 2.
Figure S7. Changes of absorption spectra in the course of complexation of $H_5$do3aP$^{\text{PIN}}$ and $H_4$do3aP$^{\text{AM}}$ (left, 25 °C) and time dependences of absorbance at absorption band maximum (~315 nm) of the in-cage complex (right). The curves represent the best fit according to Equation 1. 

A: $H_5$do3aP$^{\text{PIN}}$, $c_{\text{Ce}} = 4.0 \times 10^{-4}$ M, $c_{\text{L}} = 4.0 \times 10^{-3}$ M, pH = 5.4; B: $H_5$do3aP$^{\text{PIN}}$, $c_{\text{Ce}} = 4.0 \times 10^{-3}$ M, $c_{\text{L}} = 4.0 \times 10^{-4}$ M, pH = 5.4; C: $H_4$do3aP$^{\text{AM}}$, $c_{\text{Ce}} = 4.0 \times 10^{-4}$ M, $c_{\text{L}} = 4.0 \times 10^{-3}$ M, pH = 5.7; D: $H_4$do3aP$^{\text{AM}}$, $c_{\text{Ce}} = 4.0 \times 10^{-3}$ M, $c_{\text{L}} = 4.0 \times 10^{-4}$ M, pH = 5.7.
Figure S8. pH dependence of the formation rate constants (25 °C) under the Ce$^{III}$ excess ($c_{Ce} = 4.0 \cdot 10^{-3}$ M, $c_L = 4.0 \cdot 10^{-4}$ M, blue diamonds) and under the ligand excess ($c_{Ce} = 4.0 \cdot 10^{-4}$ M, $c_L = 4.0 \cdot 10^{-3}$ M, red squares). The lines correspond to the best fits according to Equation 3.