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Challenges of actinium coordination chemistry for nuclear medicine

Actinium-225 (225Ac) holds remarkable potential as radionuclide for targeted alpha-particle therapy (TAT) due to its advantageous properties, i.e. 10-day half-life and radioactive decay by emission of 4 alpha particles. To create a targeted alpha therapeutic comprising this radiometal, one must assemble two additional parts: a targeting moiety and a chelating ligand. Developing rationally designed 225Ac chelators for TAT applications is an ongoing challenge of primary importance. The chelating molecules must display fast kinetics of coordination under mild conditions and guarantee thermodynamic stability in vivo of the resulting complex. Part of this challenging task is the lack of fundamental knowledge of the coordination chemistry of actinium. In an effort to unravel the bonding interactions that govern actinium chemistry, we have prepared a set of macrocyclic ligands bearing pendant 1,2-hydroxypyridinone (HOPO) and catecholamide (CAM) moieties. To understand the suitability towards Ac chelation, we have performed spectroscopic experiments taking advantage of lanthanides as non-radioactive surrogates.

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