Abstract

Lanthanides have several specific properties which cannot be found for other elements in the periodic table. Among various applications of lanthanides, complexes of Ln^{III} ions are used in medicine, e.g., as contrast agents in MRI, as luminescent probes or as radiopharmaceuticals, where their specific properties are important. These complexes must be kinetically inert to prevent release of highly toxic "free" Ln^{III} ions. This requirement is fulfilled with pre-organized ligands such as analogues of H_4dota (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid). Many of important properties of Ln^{III} complexes of H_4dota, such as relaxivity, isomerism and fluxionality, depend on the solution dynamics of the complexes.

However, the knowledge of this solution dynamics is limited for Ln^{III} complexes of H_4dota derivatives with phosphonate or phosphinate pendant arms. Recently, a new dynamical process where phosphonate oxygen atoms interchange through a bidentate phosphonate intermediate ("a phosphonate rotation") has been proposed by DFT calculations but unconfirmed experimentally. To prove the process experimentally, solution dynamics of Ln^{III} complexes of monophosphonate and monophosphinate derivatives of H_4dota was investigated. Especially, to examine the "P-rotation", ^{17}O NMR spectroscopy was used along with the more common NMR techniques.

First, I prepared Ln^{III} complexes of monophosphorus acid H_4dota derivatives where the phosphonate monoester or methyl phosphinate groups were ^{17}O-enriched. Subsequently, the "P-rotation" was monitored for the entire lanthanide series by variable-temperature ^{17}O NMR to get kinetic parameters of the process confirming importance of ^{17}O NMR for investigations of the "P-rotation". Next, I investigated the mechanism of solution dynamics of Eu^{III} complexes of monophosphorus acid H_4dota derivatives by ^1H-^1H EXSY and 1D ^1H ESXY to determine kinetic parameters of multiple dynamic processes. The results (rate constants, activation parameters) were interpreted considering the size of the Ln^{III} ions and particular complex isomer.

The results show that, in addition to dynamic processes known for Ln^{III} complexes of H_4dota (arms rotation, macrocycle inversion and carboxylate rotation), phosphonate/phosphinate rotation also occurs in complexes of phosphorus acid derivatives of H_4dota. However, there are some special requirements for this rotation to occur. In complexes of both model ligands, the "P-rotation" occurs exclusively in isomers with the twisted-square antiprismatic (TSA) geometry. Furthermore, for both ligands, the rate of the "P-rotation" decreases with decreasing Ln^{III} size. Therefore, the process could not be detected in complexes of ions smaller than Tb^{III}.

The results experimentally confirmed that phosphinate/phosphonate group rotation occurs in solution of Ln^{III} complexes of phosphorus acid analogues of H_4dota (Ln = La–Tb) for isomers with TSA geometry. These results may be used to explain properties of analogous complexes and will help in design of new MRI contrast agents, radiotracers or even NMR shift reagents for proteins. Furthermore, these NMR experiments show the usefulness of ^{17}O NMR in studies of dynamical processes and may inspire its use while studying dynamics in many different areas of chemistry.

Keywords: metal complexes, derivatives of azamacrocycles, ligand synthesis, spectral methods, NMR