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Computational Insight into a Mechanistic Overview of Water Exchange Kinetics and Thermodynamic Stabilities of Bis and Tris-Aquated Complexes of Lanthanides

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Abstract : A thorough investigation of Ln3+ complexes with more than one inner-sphere water molecule is crucial for designing high relaxivity contrast agents (CAs) used in magnetic resonance imaging (MRI). This study accomplished a comparative stability analysis of two hexadentate (H3cbda and H3dpaa) and two heptadentate (H4peada and H3tpaa) ligands with Ln3+ ions. The higher stability of the hexadentate H3cbda and heptadentate H4peada ligands has been confirmed by the binding affinity and Gibbs free energy analysis in aqueous solution. In addition, energy decomposition analysis (EDA) reveals the higher binding affinity of the peada4− ligand than the cbda3− ligand towards Ln3+ ions due to the higher charge density of the peada4− ligand. Moreover, a mechanistic overview of water exchange kinetics has been carried out based on the strength of the metal–water bond. The strength of the metal–water bond follows the trend Gd–O47 (w) > Gd–O39 (w) > Gd–O36 (w) in the case of the tris-aquated [Gd(cbda)(H2O)3] and Gd–O43 (w) > Gd–O40 (w) for the bis-aquated [Gd(peada)(H2O)2]− complex, which was confirmed by bond length, electron density (ρ), and electron localization function (ELF) at the corresponding bond critical points. Our analysis also predicts that the activation energy barrier decreases with the decrease in bond strength; hence kex increases. The 17O and 1H hyperfine coupling constant values of all the coordinated water molecules were different, calculated by using the second-order Douglas–Kroll–Hess (DKH2) approach. Furthermore, the ionic nature of the bonding in the metal–ligand (M–L) bond was confirmed by the Quantum Theory of Atoms-In-Molecules (QTAIM) and ELF along with energy decomposition analysis (EDA). We hope that the results can be used as a basis for the design of highly efficient Gd(III)-based high relaxivity MRI contrast agents for medical applications.

Keywords : MRI contrast agents, lanthanide chemistry, thermodynamic stability, water exchange kinetics
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