Smart MRI Contrast Agents and Small Molecule Activation by Bioinspired Approach

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Smart MRI Probes: Our inorganic chemical biology projects are focusing MRI and optical imaging of intracellular nitric oxide (NO), L-cysteine, and pH environment of cancer cells. We have successfully designed and synthesized several Fe(II) complexes of macrocyclic ligands that are demonstrated as pH-responsive PARACEST MRI contrast agents (CAs). Very recently, our group has shown that the rhodamine appended high spin Fe(III)-O_6 complexes as dual-modal T1 MRI/optical imaging agents for the imaging of NO and acidic pH environments of tumour cells. The MRI unit has functioned through second-sphere water interactions. The functionalization of this MRI core Fe(III)-O_6 with C_{12}-alkyl chain conjugates and interaction with external marker IR780 dye forms an aggregated matrix. It functioned as a smart "MRI-ON-Fluorescence ON" imaging agent for imaging acidic pH environments of tumour cells. Further, the biotin group is conjugated to the MRI core Fe(III)-O_6 for delivering larger amounts of Fe(III) CA. The biotin attachment facilitated to increase the 'payload' of CA in the tumour environment by targeting biotin metabolism and provided better visualization of cancer cells. In addition, several other Fe(III) and Mn(II/III) complexes are synthesized as redox responsive T1-CAs. Specifically, a series of Mn(III) complexes of 1,4-diazepane based bisphenolate ligands are reported as redox-active CA and are found to be sensitive towards biological redox buffer molecule L-cysteine (Cys).

Small Molecule Activation by Bioinspired Approach: Our dioxygen activation project involves synthesis, reactivity, and mechanism of Fe(II) complexes as bioinspired models for healthcare-related Fe(II)-dependent cysteine dioxygenases (CDO) and diketo dioxygenases (DKDO), which converts L-cysteine to L-cysteine sulfinic acid (sulfur oxidation) and C-C bond breaking respectively using O_2. The active sites of these enzymes are unique and poorly understood among the non-heme iron(II) dioxygenases family, in fact, the aforementioned typical 2-His-1-carboxylate facial triad is not adopted. The catalytic mechanisms and key intermediates are probed using Fe(II) and Ni(II) model complexes at the molecular level by combining the spectroscopic and computational methods.

In addition, several bioinspired Cu(II) and Ni(II) complexes are reported as catalysts for the activation/ fixation of atmospheric CO_2 under mild conditions. The molecular structures of complexes and their CO_2-bound/ CO_3^{2-} key intermediates are studied by spectral and redox methods and single-crystal X-ray analysis. The CO_3^{2-} ion in these intermediates is originated from atmospheric CO_2 and the conversion occurred via geometrical and oxidation changes of metal centers. A series of Ni(II)/Cu(II) complexes of nitrogen-containing ligands are reported as the efficient and selective catalysts for the quantitative conversion of CO_2 into industrially important chemicals such as cyclic carbonates and carboxylic acids. The CO_2 fixation by our bioinspired complexes is found to be simultaneous and selective.

Selected References

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