Multifunctional metal complexes as probes toward theranostics: thiacalixarene–lanthanide(III) and diradical–Pt(II) complexes

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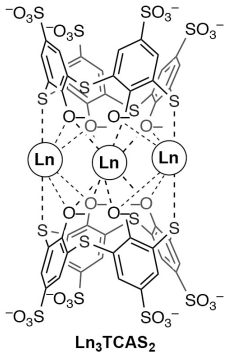
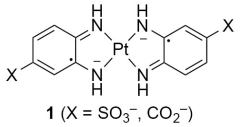
Abstract:
Modern medical diagnostics rely on imaging techniques such as X-ray, PET, and MRI enabling highly resolved visualization of organs locating deep inside the body. By contrast, molecular imaging using fluorescence and absorption in visual wavelength region is still in its infancy, suffering from scattered light, auto-fluorescence, and low ability to penetrate into tissues. To circumvent the problems, we have engaged in a study to use metal-ligand complexes exhibiting signaling such as long-lifetime emission which cannot be afforded by π*–π transition and signaling in near-infrared (NIR) region which is called the optical window of bio-tissues. In this talk, two metal complex systems will be presented to highlight the multifunctionality to lead to signaling suitable for medical diagnostics. Furthermore, extension to therapy and theranostics will be discussed.

Thiacalixarene–lanthanide(III) complex: Lanthanide(III) (Ln) and thiacalix[4]arene-*p*-tetrasulfonate (TCAS) self-assembled to form a 3:2 complex Ln_3TCAS_2.[1] It has many features such as the tri-Ln core, high kinetic inertness, and signaling functions. Tb_3TCAS_2 emits long-lived luminescence (τ = 1.1 ms), whereas Nd_3TCAS_2 ($\varphi = 1.7\times10^{-4}$) and Yb_3TCAS_2 ($\varphi = 2.7\times10^{-4}$) do NIR luminescence in water. Recently, we introduced different Ln species (Ln') into the 3:2 complex to afford heteronuclear complexes $Ln_{3-x}Ln'_xTCAS_2$ (x = 1, 2), which exhibited energy-transfer between Ln and Ln'.[2] As a result, down shifting (Tb→Yb) and upconversion (Tb←Yb, Er←Yb) luminescence were obtained, which should widen the modality to such as NIR light excitation–visual light imaging or NIR excitation–NIR imaging. For MRI, Gd_3TCAS_2 gave a 70% larger r_1 value than $[Gd(dota)]^-$ and $[Gd(dtpa)]^{2-}$ did.[3] Heteronuclear $Gd_{3-x}Ln_xTCAS_2$ (x = 1, 2) could be a probe for luminescent-magnetic bimodal imaging. Moreover, taking advantage of high neutron capture cross-section, application of Gd_3TCAS_2 to neutron capture therapy (NCT) is now underway. If $GdLnLn'TCAS_2$ has NCT effect, theranostics consisting of luminescence imaging, MRI, and NCT would be realized.

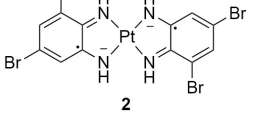


Ln_3TCAS_2

Diradical–Pt(II) complexes: Water-soluble *o*-phenylenediamine ligands afford diradical complexes (**1**), exhibiting a strong NIR absorption band ($\varepsilon \approx 10^5\ M^{-1}cm^{-1}$) resulted from ligand-to-ligand charge transfer.[4] The complex does not fluoresce, suggesting high photothermal effect. Hence, the complex can be a potential imaging probe for photoacoustic imaging. So far, we have successfully deliver a dibromo derivative **2** to MCF-7 cells to obtain a photoacoustic image. Recently, we found that MCF-7 cells containing **2** were killed by laser irradiation (730 nm, 157 mW, spot diameter: 1 mm) for 15 min, which would lead to photothermal therapy of cancer. Combination of photoacoustic imaging and photothermal therapy using the diradical–Pt(II) complex would provide a theranostic method.



1 (X = SO_3^-, CO_2^-)



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References and Notes:

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Bio-Sketch of the Speaker

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Nobuhiko IKI was born in 1966 in Sapporo, Japan and graduated from Tohoku University in 1988. During his postgraduate course (1989-1990), he studied coordination chemistry at the Department of Chemistry, Imperial College London, with Prof. D. F. Evans. He received his Ph.D. in analytical chemistry from Tohoku University under the direction of Prof. T. Yotsuyanagi in 1994. After his postdoctoral work at Ames Laboratory, Iowa State University, with Prof. E. S. Yeung, he joined Prof. S. Miyano's group at Tohoku University as a Research Associate to study thiacalixarene chemistry in 1996. He was promoted to an Associate Professor at the Graduate School of Environmental Studies, Tohoku University, in 2003, and then to a full Professor at the same school in 2014. Since 2015, he has been one of associate editors of the Analytical Sciences, a journal of Japan Society for Analytical Chemistry (JSAC). Since 2019, he has been one of directors for JSAC. His research interests focus on multifunctional metal complexes for bioimaging and therapy, capillary electrophoretic reactors for evaluating kinetic stability of metal and biomolecular complexes, and kinetic differentiation mode separation/detection systems for ultratrace metal ions.

Selected Publications

- Books

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