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PROGRAMME

The Final Oral Examination for the Degree of

DOCTOR OF PHILOSOPHY
(Department of Chemistry)

Kevin Allen

2008 University of Victoria BSc (Chemistry)

"Developing New Ligand Platforms for MRI Contrast Agents"

Tuesday, June, 17, 2014
1:00PM, ECS 130

Supervisory Committee:
Dr. David Berg, Department of Chemistry, UVic (Co-Supervisor)
Dr. Fraser Hof, Department of Chemistry, UVic (Co-Supervisor)
Dr. Lisa Rosenberg, Department of Chemistry, UVic (Member)
Dr. Stan Dosso, School of Earth and Ocean Sciences, UVic (Outside Member)

External Examiner:
Dr. Tim Storr, Faculty of Chemistry, Simon Fraser University

Chair of Oral Examination:
Dr. Peter Cook, Department of History, UVic

Abstract

Magnetic resonance imaging is an essential tool in the medical community as a non-invasive technique to diagnose a variety of medical ailments such as cancer, cardiovascular disease, and organ or tissue damage. As it detects minute differences in healthy and diseased tissues, it is often difficult to locate these small changes. However, image resolution can be improved through the administration of MRI contrast agents.

Contrast agents rely on a paramagnetic metal centre to alter the properties of water surrounding the agent, however, the metal core is toxic and must be bound by a ligand to render it safe for human use. Changes to the ligand design can greatly alter the properties of contrast agents making them more effective tools in disease detection.

Despite the great number of metal chelates available, current commercial contrast agents rely on the same ligand core with only small perturbations. In order to expand the understanding of contrast agent technology, three different classes of ligands have been designed and synthesized based on Kläui, oxazoline, and calix[4]arene ligands. Their properties were examined using a number of techniques to determine their potential as MRI contrast agents.

Awards

2012 - Chemistry department award for Excellence in Teaching, University of Victoria

Presentations

1. "New Insights into the Stability of Lanthanide-Kläui Complexes", Pacifichem, Honolulu, HI, Dec 2010 (Poster)

Publications

1. **Allen, K. J**. **H.**; Nicholls-Allison, E. C.; Johnson, K. R. D.; Nirwan, R. S.; Berg, D. J.; Wester, D.; Twamley, B. Lanthanide Complexes of the Kläui Metalloligand, $CpCo(P{=}O(OR)_2)_3$: An Examination of Ligand Exchange Kinetics between Isotopomers by Electrospray Mass Spectrometry. *Inorganic Chemistry* **2012**, *51*, 12436.

2. Tabet, S.; Douglas, S. F.; Daze, K. D.; Garnett, G. A. E.; **Allen, K. J. H**.; Abrioux, E. M. M.; Quon, T. T. H.; Wulff, J. E.; Hof, F. Synthetic trimethyllysine receptors that bind histone 3, trimethyllysine 27 (H3K27me3) and disrupt its interaction with the epigenetic reader protein CBX7. *Bioorganic & Medicinal Chemistry* **2013**, *21*, 7004.

3. **Allen, K. J. H**.; Reay, D.; Berg, D. J. Hof, F.; Lanthanide complexation via *p*-sulfonato calix[4]arenes for use in medical imaging. *Manuscript in preparation.* **(2014)**