Ligand Design in Medicinal Inorganic Chemistry

Medicinal inorganic chemistry is a thriving field of research and the impact of the ligands on the properties of metal complexes has been obvious since the discovery of the anticancer properties of a compound as simple as cisplatin and the number of analogues reported following its clinical approval. Even small modifications of the ligand structure often change the biological properties of the pharmacophore significantly. With the rise of targeted therapy, the use of other metals and expansion of their fields of application, the design strategies of metal complexes and the ligands bonded to them have become more sophisticated and are summarized in the book *Ligand Design in Medicinal Inorganic Chemistry* edited by Tim Storr.

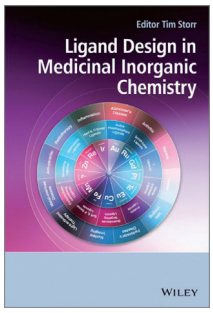
Chapter 1 gives a short introduction to medicinal inorganic chemistry, the roles of metal ions in biological systems and the importance of homeostasis, the development of the field and some of the major milestones achieved in recent years. The second chapter focuses on platinum anticancer agents and Hambley and Klein highlight some of the new developments in this area. In particular, the introduction of ligands to improve the selectivity of toxic platinum anticancer agents and also to track them through fluorescence measurements in biological systems is a hot topic. This chapter is followed by several chapters on the application of metal complexes and the roles of the ligands mainly in imaging. Radiopharmaceuticals and the high importance of ligand choice to obtain stable complexes is highlighted in Chapter 3, followed by the discussion of optical imaging agents, sensors and luminescent probes mainly used in cell systems and recent advances in terms of metal distribution studies in organelles and bioconjugation. Contrast agents in magnetic resonance imaging (MRI) are discussed in Chapter 12, together with the factors influencing the MRI response. The detailed background given will be surely helpful to the newcomer in this research area.

Carbohydrate transporters have been of interest for some time and in particular in tumor and inflammatory tissue, carbohydrate-derived radiotracers have been used for imaging purposes but similar strategies may also be applied for selective delivery of drug compounds, as pointed out by Mikata and Gottschaldt. The biological properties of the common class of Schiff base ligands appear to be dependent on the presence of metal ions. Several types of ligands are presented mainly for the treatment of cancer, such as well-known Triapine, with some discussion on their potential in imaging and against Chagas disease. Antimalarial treatments involving metal-containing compounds are discussed by Navarro and Biot (Chapter 8), highlighting the potential of compounds based on Au, Pt, Ru, etc. and especially ferrocene-based derivatives of chloroquine. Gold compounds have found application in the treatment of rheumatoid arthritis and more recently the design of new derivatives has led to potential cancer chemotherapeutics with DNA-independent modes of action and also to antiparasitic compounds (Chapter 9).

A range of metal ions have important roles for proper function of the brain, although sometimes present only in trace amounts. Ligand design to modulate metal–protein interactions in neurodegenerative diseases such as Alzheimer's and Parkinson's is discussed in Chapter 10, showing potential in medicinal inorganic chemistry in form of chelators. Chelating ligands are also important in the treatment of copper and iron overload, i.e., Wilson's disease and hemochromatosis, respectively, and this is what is discussed extensively in Chapter 11, summarizing classical, well-established therapeutics and the design of next-generation coordination compounds. Martin et al. show in Chapter 14 the potential of chelating ligands to inhibit metalloproteins, many of which have attracted attention as potential targets in diseases like cancer, hypertension and asthma.

Photoactivation of cancer chemotherapeutics may improve their selectivity and reduce side effects. This may occur through changes in the oxidation state or by inducing ligand exchange reactions, as discussed in Chapter 13 for Pt, Ru and other metal compounds, and potential applications beyond cancer treatment are demonstrated. Ru in cancer treatment and the use of biologically derived ligands is the focus of the last chapter of this book which includes besides the well-established ruthenium(III) complexes also more recent compounds, designed with targeting principles in mind.

In summary, the book is well written and gives a broad overview on ligand design in medicinal inorganic chemistry. One minor criticism would be that the chapters focusing on imaging could have been co-located and while some chapters are focused on the ligands, as implied by the book title, others take the metal as the shining star. Overall, this book fulfills its aim as an introduction to graduate students and newcomers in this research area and is a valuable source of information for established medicinal inorganic chemists.



Ligand Design in Medicinal Inorganic Chemistry
Edited by Tim Storr. John Wiley & Sons, Hoboken, 2014. 472 pp., hardcover, € 149.00.—ISBN 978-1118488522

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DOI: 10.1002/anie.201412260