

Spectroscopic and Crystallographic Evaluation of Ruthenium(II) Complexes Bearing Phenanthroline-Naphthalimide Ligands

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This Thesis predominantly focusses on the design, synthesis, and characterisation of novel, luminescent, Ru(II)-polypyridyl complexes bearing 1,8-naphthalimide (**Nap**) ligands, for use as DNA probes. In addition, a large X-ray crystallography sub-theme underpins this Thesis, where throughout the Chapters significant aspects are devoted to crystallographic studies of ligands and complexes and, where appropriate, relating these studies to broader themes such as their photophysical and biological properties.

Chapter 1 provides a broad overview of anti-cancer therapies including chemotherapeutics, photodynamic therapy (PDT), and, in particular, DNA targeting agents, before extensively exploring the photophysics underpinning ruthenium(II) polypyridyl complexes and the use of such complexes in a broad array of biomedical applications; particular emphasis here is placed on the interactions of these complexes with DNA. Following this, **Naps** are introduced and their photophysical and anti-cancer properties are described, before concluding the Chapter by broadening out the discussion to cover examples of photophysical and biological studies of metal-**Nap** conjugates.

Chapter 2 explores the synthesis and structural characterisation of two novel Ru(II)-polypyridyl complexes, bearing either two 1,10-phenanthroline ligands (**phen**) or two 1,4,5,8-tetraazaphenanthrene (**TAP**) ligands. Their coordination spheres are completed by *N*-(1,10-phenanthroline)-naphthalene-1,8-dicarboximide (**PhenNap**), **80**, giving the complexes [Ru(**phen**)₂(**PhenNap**)]²⁺ (**75**) and [Ru(**TAP**)₂(**PhenNap**)]²⁺ (**76**). A detailed crystallographic study is undertaken which includes the structurally similar **bpy** complex, [Ru(**bpy**)₂(**PhenNap**)]²⁺ (**89**), where **bpy** = 2,2'-bipyridine, demonstrating the role of the **PhenNap** in directing the crystallographic packing of the three complexes. The photophysical (UV-visible absorption spectroscopy; steady-state and time-resolved emission spectroscopy) and electrochemical (cyclic voltammetry) properties are described, followed by extensive DNA binding studies (monitored via UV-visible absorption, emission, linear dichroism, and circular dichroism spectroscopies, and thermal denaturation experiments) to determine the effect of **Nap** conjugation on the DNA binding properties of complexes **75** and **76**.

Chapter 3 develops the chemistry of the **PhenNaps**, incorporating different functional groups on the 4-position of the **Nap** (nitro, **91**, bromo, **92**, and chloro, **93**), and complexing them to generate a new family of Ru(II)-polypyridyl complexes (**94-96**). Additional efforts toward the synthesis of the amino substituted **PhenNap** ligand (**97**) and the corresponding complex (**99**) are described. Extensive crystallographic studies, as well as theoretical calculations, electrochemical and photophysical

measurements on the free ligands and on the complexes reveal the effects of substitution of these ligands. Analogous DNA binding studies to those described in Chapter 2 are also carried out.

Chapter 4 broadens out the chemistry of the **Nap**-based ligands, discussing attempts to generate **Nap** ligands with extended conjugation (106-108) or ditopic ligands capable of coordinating two metal centres (98 and 109), as well as detailing efforts to coordinate ligand 98 to Ru(II). The chapter concludes by exploring some Ir(III)-based chemistry analogous to that discussed for the Ru(II)-polypyridyl complexes in previous Chapters.

Chapter 5 builds on the crystallographic sub-themes of previous Chapters by discussing two dedicated crystallographic studies. The first study involves a large family of **Nap** molecules (C1-C8) bearing different substitutions on the imide *N*-terminus and/or the 4-position of the **Nap**. Particular care is given to highlighting trends in packing arrangements. The second study details efforts undertaken to resolve the structures of two enantiomers of a dinuclear, triple-stranded Eu(III)-based helicate (L1₃.Eu₂⁶⁺, C9, *S,S*, and L2₃.Eu₂⁶⁺, C10, *R,R*). The role of the counterions (CF₃SO₃³⁻ and ClO₄⁻) in crystallisation is discussed, followed by an in-depth analysis of the molecular structure and extended packing of the *S,S* helicate C9.

Chapter 6 concludes the Thesis, and provides a summary of the overall conclusions for each of the Chapters contained in this body of research, with specific reference to the potential of Ru(II)-**Nap** conjugates as photoreactive nucleic acid targeting agents.

Lastly, Chapter 7 summarises the experimental methods and techniques employed in this thesis, as well as detailed synthetic protocols and structural characterisation of the molecules synthesised as part of this thesis. An additional electronic document containing relevant experimental and crystallographic data is also included.