THE DEVELOPMENT OF ZINC (II) SELECTIVE FLUORESCENT LIGANDS

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ABSTRACT

This thesis describes the development of Zn^{2+} selective ligands suitable for use as fluorescent probes to monitor exchangeable Zn^{2+} in biological systems. A related aim was to develop fluorescent probes for other metal ions of biological concern, such as Al^{3+} and Pb^{2+}.

A series of prospective ligands were synthesised based on the phenyl substituted thiazoline substructure of 2-(2-*o*-hydroxyphenyl-2-thiazolin-4-yl)-3-methylthiazolidine-4-carboxylic acid (pyochelin), a naturally occurring fluorescent Zn^{2+} ligand. 2-(2-Hydroxyphenyl)-2-thiazoline-4-carboylic acid and the corresponding methyl ester were synthesised along with the methyl esters of the corresponding 2-methoxyphenyl and the phenyl substituted thiazolines. The ethyl esters of the analogous thiazole carboxylic acids were also synthesised.

The chelation of these ligands to Zn^{2+} was investigated using ultraviolet spectroscopy. The selectivity of the Zn^{2+} chelating ligands was investigated using a chosen series of metal ions and ultraviolet spectroscopy. The stability of the Zn^{2+} and other complexes formed was assessed by determining values for the stability constants of formation of the complexes, using a potentiometric titration technique. Fluorescence spectroscopy was utilised to establish the fluorescent nature of the complexes.

Only the ligands which contain the 2-hydroxyphenyl substituent chelated to Zn^{2+}. These appear suitable for use as Zn^{2+} probes, since they each form stable fluorescent Zn^{2+} complexes and do not form fluorescent complexes with biologically prevalent metal ions.

2-(2-Hydroxyphenyl)-2-thiazoline-4-carboxylic acid and the corresponding methyl ester both form highly fluorescent complexes with Al^{3+} making them suitable

for use as fluorescent Al^{3+} probes.

The 2-hydroxyphenyl substituted thiazolines provide a basis for further development of Pb^{2+} fluorescent ligands, since their Pb^{2+} complexes were of high stability, but were non fluorescent.

Ethyl 2-(2-hydroxyphenyl)-oxazole-4-carboxylate and methyl 2-(2-aminophenyl)-2-thiazoline-4-carboxylate were also synthesised and their Zn^{2+} chelation and selectivity along with the fluorescence of complexes formed by these ligands were assessed. Only the Zn^{2+} complex formed by the oxazole was fluorescent. This ligand appears suitable for use as a biological Zn^{2+} probe. The 2-aminophenyl substituted thiazoline did not form fluorescent complexes with any of the metal ions tested, indicating that the 2-hydroxyphenyl substituted thiazole derivatives are more suited as biological Zn^{2+} probes.