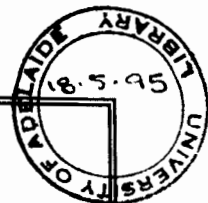


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**THE DEVELOPMENT OF  
ZINC (II) SELECTIVE  
FLUORESCENT LIGANDS**

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in

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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-carboxylic 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  $\text{Al}^{3+}$  probes.

The 2-hydroxyphenyl substituted thiazolines provide a basis for further development of  $\text{Pb}^{2+}$  fluorescent ligands, since their  $\text{Pb}^{2+}$  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  $\text{Zn}^{2+}$  chelation and selectivity along with the fluorescence of complexes formed by these ligands were assessed. Only the  $\text{Zn}^{2+}$  complex formed by the oxazole was fluorescent. This ligand appears suitable for use as a biological  $\text{Zn}^{2+}$  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  $\text{Zn}^{2+}$  probes.