

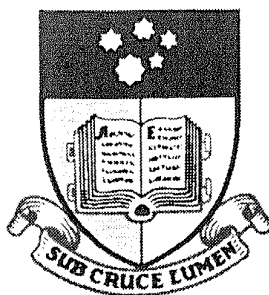
Synthetic Studies Towards Potential Lead(II) Specific Fluorescent Probes

A Thesis Submitted for the
Degree of Doctor of Philosophy

by

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Abstract

The adverse health effects of Pb^{2+} in children has prompted the demand for a fast, sensitive and inexpensive screening method for blood Pb^{2+} levels. In this regard, an investigation of potential Pb^{2+} specific fluorescent ligands as probes is reported in this thesis.

A series of flavones were synthesised and their chelation to Pb^{2+} , Zn^{2+} , Al^{3+} , Cd^{2+} , Ca^{2+} , Mg^{2+} , Co^{2+} , Cu^{2+} and Ni^{2+} was investigated using UV-visible absorption spectroscopy. These qualitative preliminary studies showed that of the flavones studied; 3-hydroxy-2'-methoxyflavone (**4**), 3-hydroxy-4'-methoxyflavone (**5**), 3-hydroxy-2'-methoxythioflavone (**6**) and 3-hydroxy-4'-methoxyflavone (**7**) were the only ligands which coordinated Pb^{2+} . Other flavones lacking the 3-hydroxy group did not coordinate Pb^{2+} and were not further studied. Stability constants (using UV-visible absorption spectroscopy) and fluorescence spectra of the Pb^{2+} , Zn^{2+} , Cd^{2+} and Al^{3+} complexes of **4** - **7** were measured under high and low acid concentration conditions. In the presence of a high acid concentration ($[\text{H}^+] = 10^{-2}$ M), ligands **4** and **5** only formed complexes with Al^{3+} and Pb^{2+} . Fluorescent studies showed that the Al^{3+} complexes of **4** and **5** were highly fluorescent while the Pb^{2+} complexes of **4** and **5** were weakly fluorescent (of equal fluorescence to the free ligands) making **4** and **5** suitable as Al^{3+} fluorescent probes under these conditions. Under a low acid concentration of $[\text{H}^+] = 10^{-5}$ M, ligands **4** and **5** coordinated all of the metal ions studied producing a relative stability order of $\text{Pb}^{2+} > \text{Al}^{3+} > \text{Zn}^{2+} > \text{Cd}^{2+}$. The complexes of **4** and **5** produced moderate to weak fluorescence levels with no selective fluorescence being observed for any particular metal ion.

Stability and fluorescence studies were conducted under the same high and low acid concentration conditions on the Pb^{2+} , Zn^{2+} and Cd^{2+} complexes of the thioflavones **6** and **7**. Neither ligand coordinated Al^{3+} . In the presence of a high acid concentration ligand **6** produced a stable, detectable complex only with Pb^{2+} , whereas under the low acid concentration conditions a relative stability order of $\text{Pb}^{2+} > \text{Zn}^{2+} > \text{Cd}^{2+}$ was determined. Under both conditions the complexes of **6** were either non-fluorescent or very weakly fluorescent. The stability constants of ligand **7** were not determined due to decomposition of the ligand in the presence of light, however, qualitative fluorescence studies were possible. Ligand **7** selectively produced a moderately fluorescent complex with Pb^{2+} under high acid

concentrations but moderate to weak fluorescent complexes with Pb^{2+} , Zn^{2+} and Cd^{2+} under low acid concentrations. Thus, Ligand **7** provides a basis for further development of Pb^{2+} fluorescent probes.

A further series of ligands were synthesised consisting of benzopyran-4-one thiazoles (**30** and **31**) and coumarin thiazoles (**32** and **33**). These ligands were assessed for their fluorescence in the presence of Pb^{2+} , Al^{3+} , Zn^{2+} , Cd^{2+} and Mg^{2+} . The unbound benzopyran-4-one thiazole ligands **30** and **31** produced very weak fluorescence, however, upon complexation with each of the metal ions, a slight enhancement of fluorescence was observed. As this fluorescence enhancement was not significant, these compounds were unsuitable as Pb^{2+} fluorescent probes. The coumarin thiazoles (**32** and **33**) exhibited intense fluorescence in the unbound state. The ester ethyl-2-(3-2-oxo-2H-1-benzopyran)-2-thiazole-4-carboxylate (**32**) did not produce any change in fluorescence in the presence of any of the metal ions studied, whereas the fluorescence emission of 2-(3-2-oxo-2H-1-benzopyran)-2-thiazole-4-carboxylic acid (**33**) was partially quenched in the presence of Pb^{2+} and the emission spectrum was altered in the presence of Al^{3+} . Ligand **33** provides the basis for further development of a Pb^{2+} selective fluorescent quenching probe.

C_8 -Substituted quinolines, quinoline-1-oxides and pyridine-1-oxides were also investigated. UV-visible absorption studies indicated that of these compounds only 8-mercaptoquinoline and 1-hydroxypyridine-2-thione coordinated the metal ions (Pb^{2+} , Zn^{2+} and Cd^{2+}). As the complexes were found to be highly unstable in solution due to oxidation of the ligand, 8-mercaptoquinoline and 1-hydroxypyridine-2-thione were not further studied.

*"I have not failed 10,000 times,
I have successfully found 10,000 ways that will not work".*

Thomas A. Edison