Photoactive Receptors for Metal ion Recognition

Subodh Kumar

Department of Chemistry, Guru Nanak Dev University,
Amritsar – 143 005.
MOLECULAR RECOGNITION IS BASIS OF LIFE

- RNA WORLD - PREBIOTIC PERIOD
- NUCLEIC ACID WORLD

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- Bridge between RNA world & present state

- The side chains of amino acids attached at C-5 of uracil.
- Limited metal ion selective pockets, poor recognition.
DNA - PROTEIN WORLD

- Adenine - Thymine       Guanine - cytosine       Cu(II) selective binding in protein
- Watson - Crick Model (1953)       Plastocyanin
Molecular Recognition & Asymmetric Synthesis

- Evans’ Bisoxazoline - Cu(II) Complexes

\[
\begin{align*}
\text{EtO} & \text{Me} \\
+ & \text{Methyl} \\
\text{SiBuOTMS} & \text{EtO} \text{Me OH} \\
\end{align*}
\]

1) 10 mol\% -78°C, CH₂Cl₂
2) 1N HCl / THF

Metal ions play the crucial role in organization of various moieties in Enzymatic and other catalytic reactions.

Development of receptors with selective metal ion binding features is necessitated for their estimations and other features.
Possible applications

Metal Ion selective receptor

- Devices for Qualitative & Quantitative estimation
- Biomimics for enzymes
- Organic Synthesis
- Asymmetric Synthesis

Chiral
Objectives

- *Photoactive Receptors* for Cu(II) and Ag(I)

- *Conventional Techniques: Atomic absorption spectroscopy, ion selective electrodes, Flame photometry etc.*

- *More recent Techniques: Chemosensors and their based ion-selective electrodes*

- more sensitive and accurate
Fluorescent Receptors

- Fluorescence Efficiency Before and after complexation (PET)

- -- nature of Fluorescent moiety (absorption and fluorescence wavelength and efficiency)
- -- interactions of ligating sites (N, S, O) of receptor with the guest species (enhancement)
- -- interactions of fluorophore moiety with the guest species (quenching)
- -- paramagnetic effect in case of some metal ions (quenching)
- -- placement of fluorescent moiety in the receptor (efficiency of above phenomena)
- (distance of ligating sites from fluorescent moiety)
Cu(II) Binding sites in enzymes
Tetragonal, Jahn-Teller effect

Type I
- $R = \text{Met (azurin, Plastocyanin)}$
- $R = \text{N/O donor (stellocyanin)}$

Type II
- $R = \text{N/O donor (stellocyanin)}$

Type III
- $R = \text{N/O donor (stellocyanin)}$

$\text{O}_2$
Various phenomena for the metal induced fluorescence enhancement / quenching (PET)

- Fluorescence quenching
- Fluorescence enhancement

Diagram: Molecular structures and interactions involving metal ions and fluorophores.
Anthracene based ionophores

• Synthesis

\[
\text{OH} + \text{OH} \rightarrow \text{N} \quad \text{CHCl}_3, \text{K}_2\text{CO}_3 \quad \text{stir, rt} \quad \text{R-CH}_2-\text{X}
\]

1(a-d)

\[
\begin{align*}
\text{Y} &= \text{OH} \\
\text{Y} &= \text{Cl} \\
\text{SOCl}_2
\end{align*}
\]

2(a-d) 3(a-d)

4(a-d)

\[
\begin{align*}
a & \quad R = \text{CH}_2\text{CHOH} \\
b & \quad R = \text{CH}_2\text{CH}_3 \\
c & \quad R = \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \\
d & \quad R = \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\end{align*}
\]

\[
\begin{align*}
\text{Cl} & \quad \text{NaH, THF, TBA HSO}_4 \\
\text{NaH, THF, TBA HSO}_4 & \quad \text{H}_3\text{CCH(CH}_3)_2
\end{align*}
\]

5a / 6a
Anthracene based ionophores

Fluorescence spectrum

UV-visible spectrum

Fluorescence intensity (a.u.)

Absorbance

wavelength (nm)

pH

fluorescence intensity (a.u.)
Anthracene based ionophores

\[ [4a] = 10^{-5}, \lambda_{ex} = 365 \text{ nm}, \lambda_{em} = 410 \text{ nm} \]

in CH\textsubscript{3}CN : H\textsubscript{2}O 4:1 at pH 7 (HEPES 10 mM)

Effect of metal ions

- Titration with Cu(II)

Anthracene based ionophores
Interference of other metal ions

conc. of Cu(II) added in the presence of 1000ppm of Mz+

*Cu(II)only
*Hg(II)+Cu(II)
*Ag(I)+Cu(II)
*Ni(II)+Cu(II)
*Cd(II)+Cu(II)
*Zn(II)+Cu(II)
• Effect of Cu(II) on UV-Vis spectrum

[4a] = 10^{-4} M, [Cu(II)] = 10^{-5} M
-10^{-6} M titration with Cu(II)
Anthracene based ionophores

- Interference of other metal ions
- Job plot
Anthracene based ionophores
Effect of appendage on UV-Vis spectrum

Absorption spectra of 4a-d (10^{-5} M)
on addition of Cu(II) (5 \times 10^{-5})
Anthracene based ionophores

Titration with Cu(II)

Interference of other metal ions
Synthesis of anthraquinone based Receptor

(a) $K_2CO_3$, DMF, tetrabutylammonium HSO$_4$, 18-Crown-6, 80°C, 48h

(b) $K_2CO_3$, DMF, TBA-HSO$_4$, 12h
Cu(I) Rusticyanin from Thiobacillus Ferroxidans

Structural basis for extreme stability
Disposition of ligands and spatially close side chains in the copper site

High density of aromatic rings immediately surrounding the Cu(II) site
Possible Models for Cu(II) Cavity
% ext. Ag⁺ = 97.6
Ag⁺ / Pb²⁺ sel. = 1085

% ext. Ag⁺ = 59
Ag⁺ / Pb²⁺ sel. = 212

% ext. Ag⁺ = 60
Ag⁺ / Pb²⁺ sel. = >2000

(0.01 M L, 0.01 M metal picrate)

% Ext. Ag⁺ = 7.48, Pb²⁺ 0.2
Ag⁺ / Pb²⁺ sel. 374

(0.001 M L; 0.001 M metal picrate)
Effect of pH on the fluorescence intensity of fluoroionophores

The effect of Cu$^{2+}$ on the Fluorescence of Fluoroionophore (5 µM)
9,10-anthracene based fluorescent Cu(II) sensor

Plot of conc. of Cu$^{2+}$ vs fluorescence of fluoroionophore

The estimation of Cu$^{2+}$ in the presence of Ni$^{2+}$, Cd$^{2+}$, Zn$^{2+}$, Hg$^{2+}$, Ag$^+$ and Pb$^{2+}$ (5000 μM)
9,10-anthracene based fluorescent Cu(II) sensor

The effect of Cu$^{2+}$ on the UV-vis spectrum of fluoroionophore

Plot of absorbance Vs concentration of Cu$^{2+}$ at 415 nm
- Estimation of Cu (II) in the presence of other competing metal ions (20mM)

Plot of abs. / quantum yield Vs. Eq. of Cu(II)
Change in the chemical shifts of carbon signals on addition of AgNO₃ (1 equiv.) to a solution of fluoroionophore in CD₃CN:CDCl₃ 1:1
8-Hydroxyquinoline based ionophores

- non-Fluorescent
- Fluorescent

- The most frequently used complexing agent after EDTA

- The proton transfer from O to N during excitation turns it non-fluorescent moiety

- undergoes colour changes during complexation
8-Hydroxyquinoline based ionophores

**Literature reports**

- Recognition is mainly dependent on ionophore core

![Chemical structures](image)

- Ionophores with only 8-hydroxyquinoline as ligating sites
8-Hydroxyquinoline based ionophores

Synthesis of Tripod and Podand Ionophores

\[
\text{OH} \quad + \quad \text{Br} \quad + \quad \text{Br} \quad + \quad \text{Br} \quad \xrightarrow{\text{X} = \text{H, Cl, NO}_2, \text{COPh}} \quad \text{CH}_3\text{CN} - \text{K}_2\text{CO}_3, \quad \text{TBA HSO}_4
\]

1. \( \text{X} = \text{H} \) (45%)
2. \( \text{X} = \text{Cl} \) (52%)
3. \( \text{X} = \text{NO}_2 \) (0%)
4. \( \text{X} = \text{COPh} \) (70%)
5. \( \text{X} = \text{CH(OH)}\text{Ph} \) (90%)

\[
\text{OH} \quad + \quad \text{Br} \quad \text{Br} \quad \xrightarrow{\text{CH}_3\text{CN} - \text{K}_2\text{CO}_3, \quad \text{TBA HSO}_4} \quad \text{6}
\]
$[1] = 1 \times 10^{-7} \text{M}, \quad \lambda_{\text{ex}} = 305 \text{nm}, \quad \lambda_{\text{em}} = 398 \text{nm}$

in CH$_3$CN:HO 4:1 (0.01M NaNO$_3$)
Interference of other metal ions

**Fluorescence Intensity vs. Conc. of Cu(II) (ppm) in the Presence of 1000ppm of Ni(II), Cd(II), Zn(II):**

- **Cu(II) only**
- **Ni(II) + Cu(II)**
- **Cd(II) + Cu(II)**
- **Zn(II) + Cu(II)**

**Fluorescence Intensity vs. Conc. of Cu(II) (ppm) in the Presence of 10ppm of Pb(II), Hg(II):**

- **Cu(II)**
- **Hg(II) + Cu(II)**
- **Pb(II) + Cu(II)**

**Absorbance vs. Wavelength (nm):**

**Absorbance vs. Eq. of Cu(II):**
• Energy minimized structures of tripod and its Cu(II) complex
• Planar Conformation = 66 Kcal / mol, tripodal conformation = 54 Kcal / mol, tripod : Cu(II) complex = 42 Kcal / mol
The diagrams illustrate the fluorescence intensity (a.u.) and absorbance as a function of pH and wavelength (nm) for three different compounds: CH(OH)Ph, Cl, and H.

- **CH(OH)Ph** (blue line): The fluorescence intensity increases with pH, peaking at around 407 nm.
- **Cl** (red line): The fluorescence intensity also increases with pH, peaking at around 398 nm.
- **H** (green line): The fluorescence intensity increases with pH, peaking at around 317 nm.

Each compound shows distinct absorbance peaks at different wavelengths, indicating their absorption characteristics.

The diagrams on the right show the relationship between pH and fluorescence intensity for the three compounds, with distinct symbols indicating different pH values.
The diagrams illustrate the fluorescence intensity (a.u.) for different complexes in the presence of 1000ppm of interfering metal ions. The complexes include Cu(II), Ag(I)+Cu(II), Cd(II)+Cu(II), Hg(II)+Cu(II), Ni(II)+Cu(II), Pb(II)+Cu(II), and Zn(II)+Cu(II). The x-axis represents the concentration of Cu(II) in ppm, while the y-axis shows the fluorescence intensity. The diagrams show a decrease in fluorescence intensity with increasing concentration of Cu(II) in the presence of interfering metal ions.
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