ABSTRACT

The formation of ternary complexes of metal-guanosine thymidine, uridine or adenosine have been studied by potentiometrically at 15°, 25°, 35° and 45°C and 0.1 M (KNO₃) ionic strength. The metal ions studied are Cu(II), Ni(II), Co(II), Zn(II), Mg(II) and Ca(II). The thermodynamic parameters, enthalpy and entropy changes for these ternary systems are calculated. The \( \Delta \Delta H \) values are highly negative and \( \Delta \Delta S \) are negative for these systems. The exothermic enthalpy for the mixed nucleoside complexes may be attributed to the energy of stacking interaction in these systems.

INTRODUCTION

Since mixed ligand complexes of nucleosides and nucleotides have attracted much attention in recent years because they serve as models for metalloenzyme reactions in biological systems\(^1\)\(^-\)\(^3\), and also they provide useful information in understanding the specific and selective interactions that take place in many biochemical process. In our laboratory much work\(^4\),\(^5\) has been carried out on the interaction of bivalent metal ions with these nucleosides and Bipyridyl, 1,10 phenanthroline and 1,5 sulphosalicylic acid, but very little is known about the interaction of metal ion with mixed nucleosides in solution. Recently we have reported\(^6\) the mixed nucleoside complexes of adenosine with bivalent metal ions. The present work is the extension of the earlier work.

METHODS AND MATERIALS

Potentiometric titration of each ligand with standard sodium hydroxide solution in the absence and in the presence of metal ions were carried out. Relatively low concentrations of ligands and metal ion were used presaturated. CO₂ free nitrogen was passed throughout each titration. Titrations were carried out at 15°, 25°, 35° and 45°C and at a constant ionic strength of 0.10 M (KNO₃). A digsun model DI-707 pH meter with a Toshniwal combination glass electrode was used to determine hydrogen ion concentration. The electrode system was calibrated by direct titration with acetic acid and the pH meter reading observed was compared with the actual hydrogen ion concentration as calculated for the data tabulated by Harned and Owen\(^7\). The pH region below 3.5 and above 10.5 we calibrated by measurements in HCl and NaOH solution respectively.

Reagent:

Guanosine, thymidine, uridine and adenosine were obtained from sigma chemical u.s.a all the ligands are chromatographically pure and are used as such. They are weighed
Calculations:

The acid dissociation constants of the ligands were calculated by a direct algebraic method, which involved setting up of suitable material balanced equations. For the stability constants of 1:1:1 metal guanosine-thymidine or uridine the equation (1) were considered.

\[
\begin{align*}
M + HA & \rightleftharpoons MHA \\
MHA + L & \rightleftharpoons MHAl
\end{align*}
\]

\[K_{MHAL} = \frac{[MHAl]}{[MHA][L]} \tag{1}\]

for 1:1:1 metal guanosine adenosine this following equilibrium (2) was considered

\[
\begin{align*}
M + HA + HL & \rightleftharpoons MLAH_2 \\
K_{MLAH_2}^M & = \frac{[MLAH_2]}{[M][HA][HL]} \tag{2}
\end{align*}
\]

The values of $\Delta H^\circ$, $\Delta G^\circ$, and $\Delta S^\circ$ were calculated using the usual relationships as described in an earlier paper

\[
\begin{align*}
\Delta H^\circ & = \frac{2.303RT_1(T_2 - T_1)}{T_2 - T_1} (\log K_2 - \log K_1) \\
\Delta G^\circ & = RT \ln K \\
\Delta S^\circ & = \frac{\Delta H^\circ - \Delta G^\circ}{T}
\end{align*}
\]

RESULTS

The titration curve for 1:1:1 Cu(II)-guanosine, thymidine or uridine system’s have shown an inflection at \( m = 1 \) similar titration curves were obtained for all other metal ions Ni(III), Co(II), Zn(II), Mg(II) and Ca(II), studied at different temperatures. The stability are calculated using equation (1) and are given in table 1, and the corresponding thermodynamic parameters are given in table 2 for the 1:1:1 Cu(II) guanosine-adenosine system, inflection was observed at \( m = 2 \), and similar titration curves were observed for other metal ions, studied. The stability constants and the corresponding thermodynamic parameters are given in table (1) and (2) respectively.

DISCUSSION

The stabilities are increasing with the increase in temperature for 1:1:1 metal guanosine uridine or thymidine systems, and follow the Irving Williams order of stability. The $\Delta \log$ values show that the ternary 1:1:1 metal guanosine uridine or thymidine systems are more stable than the corresponding, binary 1:1 systems. Ternary 1:1:1 metal guanosine uridine a thymidine systems the enthalpy change is less positive (less exothermic) than the corresponding binary systems. The less positive values are responsible for the higher stability of 1:1:1 metal mixed nucleosides complexes. The entropy values are however less positive than the binary systems.

The stability constants for 1:1:1 metal guanosine adenosine are more stable than the binary systems. The $\Delta \log K$ values are more positive than 1:1:1 metal-guanosine thymine or uradine systems.

Except Zn(II) Guanosine adenosine all the metal ion studied, the enthalpy values are negative (exotherms) and the entropy values are positive. The favourable enthalpy and entropy changes are the basis for the formation of mixed ligand complexes, similar trend was also observed for mixed ligand complexes of purine and pyrimidine bases with bivalent metal ions.
Table 1. Stability constants for 1:1:1 ternary systems

| Metal ion | 1:1:1 Metal-Guanosine-adenosine system | 1:1:1 Metal-guanosine-thymidine system | 1:1:1 Metal-guanosine-Cytidine system |
|-----------|---------------------------------------|----------------------------------------|--------------------------------------|
|           | 15° 25° 35° 45°                      | 15° 25° 35° 45°                          | 15° 25° 35° 45°                        |
| Cu(II)    | 6.63 6.57 6.50 6.38                  | 6.22 6.31 6.40 6.49                    | 5.88 5.97 6.01 6.04                   |
| Ni(II)    | 6.83 6.66 6.48 6.33                  | 3.89 3.% 4.06 4.12                     | 3.91 3.95 4.01 4.06                   |
| Co(II)    | 6.39 6.23 6.04 5.90                  | 3.71 3.76 3.82 3.88                    | 3.75 3.80 3.86 3.93                   |
| Zn(II)    | 6.10 5.93 5.81 5.64                  | 4.99 5.01 5.02 5.06                    | 4.73 4.77 4.82 4.88                   |
| Mg(II)    | 5.65 5.53 5.35 5.19                  | 3.58 3.69 3.80 3.91                    | 3.19 3.25 3.55 3.44                   |
| Ca(II)    | 5.59 5.47 5.30 5.13                  | 3.42 3.51 3.62 3.72                    | 3.17 3.23 3.32 3.38                   |

Values are accurate up to ± 0.06 log K units.

Table 2. Thermodynamic parameters associated with the interaction of metal ions with guanosine and adenosine, thymidine and uridine, $\mu = 0.1$ M (KNO$_3$)

| Metal ion | 1:1:1 Metal-Guanosine-adenosine | 1:1:1 Metal-Guanosine-thymidine | 1:1:1 Metal-Guanosine-uridine |
|-----------|---------------------------------|---------------------------------|-------------------------------|
|           | $\Delta$H$^\circ$ (Kcal/mole) | $\Delta$S$^\circ$ (e.u)        | $\Delta$H$^\circ$ (Kcal/mole) | $\Delta$S$^\circ$ (e.u)        | $\Delta$H$^\circ$ (Kcal/mole) | $\Delta$S$^\circ$ (e.u)        |
| Cu(II)    | -5.0 -9.9 +16                   | +2.1 -8.7 +36                   | +2.2 -8.2 +35                  |
| Ni(II)    | -4.9 -9.8 +16                   | +1.7 -5.5 +24                   | +2.1 -5.4 +25                  |
| Co(II)    | -4.5 -9.5 +17                   | +2.4 -5.1 +25                   | +2.5 -5.2 +26                  |
| Zn(II)    | +1.7 -9.2 +25                   | +1.0 -6.8 +26                   | +2.1 -6.5 +29                  |
| Mg(II)    | -1.1 -8.4 +25                   | +2.6 -5.1 +26                   | +3.5 -4.4 +17                  |
| Ca(II)    | -2.6 -7.4 +16                   | +1.7 -5.0 +23                   | +2.9 -4.4 +25                  |

$\Delta$H$^\circ$ Values are accurate up to ± 0.06 KCal/mole
$\Delta$S$^\circ$ Values are accurate up to ± 1 e.u.

Table 3. $\Delta$H, $\Delta$S values for metal-guanosine-adenosine, thymidine or uridine system $\mu = 0.1$ M (KNO$_3$)

| Metal ion | 1:1:1 Metal-Guanosine-adenosine | 1:1:1 Metal-Guanosine-thymidine | 1:1:1 Metal-guanosine-uridine |
|-----------|---------------------------------|---------------------------------|-------------------------------|
|           | $\Delta$H (KCal/mole)          | $\Delta$S (e.u)                | $\Delta$H (KCal/mole)        | $\Delta$S (e.u)                | $\Delta$H (KCal/mole)        | $\Delta$S (e.u)                |
| Cu(II)    | -2.4 -8.4                       | -1.66 -4.78                    | -0.63 +1.19                   |
| Ni(II)    | -2.4 -6.7                       | -0.27 -0.24                    | -0.85 -6.21                   |
| Co(II)    | -3.4 -7.9                       | -0.26 -1.19                    | -0.35 -1.19                   |
| Zn(II)    | -1.6 -1.4                       | -3.35 -11.95                   | -0.87 +2.15                   |
| Mg(II)    | -9.3 -23.7                      | -1.84 -0.24                    | -0.84 -3.52                   |
| Ca(II)    | -7.9 -18.2                      | -0.42 -2.63                    | -0.88 -3.58                   |
The $\Delta \log K$ values for 1:1:1 metal guanosine adenosine systems are higher than those of metal guanosine thymidine uridine system, indicating the higher stability of 1:1:1 metal guanosine adenosine system. The enhanced stabilities of ternary systems can be measured in terms of $\Delta \Delta H$ values. The $\Delta \Delta H$ values are highly exothermic and $\Delta \Delta S$ values are negative except Zn(II) guanosine uridine system Table 2. The $\Delta \Delta H$ values are negative for these 1:1:1 metal guanosine adenosine a thymidine a uridine systems and they vary from 1.0 to 2 KCal/mol.

The less exothermic enthalpy in the formation of 1:1:1 metal mixed ligand complexes may be attributed to the energy of stacking interaction in these systems, which is purely vanderwalls london type of interaction. The negative $\Delta \Delta H$ values favours mostly for the higher stability of these complexes.

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