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Binary and Ternary Metal Complexes of Guanine- Cytosine and Its Derivatives Stability and Thermodynamic Parameters

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Abstract

Stability constants data revealed the relative stability order of metal ligand binary and ternary complexes as M(II)-L-G>M(II)-G>M(II)-L. This is because of the lesser tendency of secondary ligand (G) towards $M(H_2O)_n^{2+}$ as compared to ML. comparable values of tability constants for various (1:1:1) systems also indicate the same coordination mode of ligands with metal ions.

Keywords: Guanine, Cytosine, Ternary Complexes.

Introduction

Guanine, a purine base found in both RNA and DNA where it pairs with cytosine by two hydrogen bonds. In 1846, first time it was reported in the guano birds. During 1879, it was established as one of the major constituents of nucleic acids. The accepted structure of the guanine molecule was proposed in 1875 and the compound was first synthesized in 1900. When combined with the sugar ribose in a glycosidiclingkage, guanine form a derivative called guanosine (a nucleoside), which in turn can be phosphorylate with phosphoric acid groups, yielding the three nucleotiodes GMP (guanosine monophosphate), GDP (guanosine diphosphate), GTP (guanosine triphosphate). The nucleotide derivatives of guanine perform important functions in cellular metabolism. GTP acts as a co enzyme in a carbohydrate metabolism and in the biosynthesis of proteins. It can readily donate one of its phosphate groups to adenosine diphosphate (ADP) and form adenosine triphosphate (ATP), and extremely important intermediate in the transfer of chemical energy in living systems. GTP is the source of the guanosine found in RNA and deoxyguanosine triphosphate (d GTP) is the source of the deoxyguanosine in DNA and thus guanine is intimately involved in the preservation and transfer of genetic information. Guanine is said to account for the iridescence of fish scales and the white, shiny appearance of the skin of many amphibians and reptiles. Sugiura and co-workers studied an inhibitory action of guanazolo on the growth of transplantable mammary adenocarcinoma in the mouse but no effect on spontaneous mammary cancer was observed.

The coordination sphere of central metal ion is homogeneous if all the donor atoms are identical, on the other hand if the donor atoms are different, the heterogeneous coordination sphere may be emphasized. In one the atomic numbers of the donor atoms may differ, e.g., N, O, S etc. While in the second case there may be a difference either in the oxidation state of the donor atoms, e.g., NH_3, NO_2, NCS etc., or in the adjacent or more remote environment of the donor atoms, e.g., NH_3, $NH_2CH_2CH_2NH_2$,$CH_3NHCH_2CH_2NH_2$,$CH_3CH\text{-}(NH_2)CH_2NH_2$.

Formation of such ternary complexes also depends on the electronic structure and ionic radius of the central atom. In addition to these most important requirements, the mutual polarizability of the central atom and the ligands. Acceptor ability of the ligands and the symmetry relations of the electronic orbital of central atom and the ligands affect the formation of ternary complexes considerably. Ternary complexes play an important role in biological processes as exemplified by many instances in which enzyme nucleic acids and other bio components are known to be activated by metal ions.Benoit and co-worker studied the protonation equilibria of purines and their derivatives by potentiometer, ^1H and ^{13}C NMR and UV spectroscopy. Cordula and coworkers performed the reactions of trans

-[$Pt(NH_3)_2$(tmade-N_3)Xn+(tmade = N_6, N_6, N_9-trimethyldenine, X=C1, n= 1; X= H_2O, n=2) with other nucleobases [9-ethylguanine (Hegua), 9-methyladenine (made) or 1-methylcytosine (mcyt)] in solution (D_2O) by using 1HNMR.Have studied the interaction of various metal ions with different type of nucleotides pH-metrically as well as spectrophotometrically. Potentiometer measurements for equilibrium determination at 25 + 0.1 C and ionic strength I=0.1M KNO_3 for the interaction of GMP, IMP and CMP primary ligands and biologically important zwitterionic buffer secondary ligands with some bivalent and trivalent metal ions and have suggested that at neutral pH, the affinity for the metal ion binding sites available in the nucleobases decreases along the series $N_7G>N_3C>N_7A>N_1A>N_3A,N_3G$.We studied the stability constants of binary complexes (1:1) of guanine (G) with metal ions viz., Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Ca(II), Sr(II) and Ba(II) the corresponding ternary complexes (1:1:1) With cytosine (C), cytidine (CD), 5bromocytosine (5BrC), 5-azacytosine (5AC) and 5-fluorocytosine (5FC) potentioemetrically at different temperatures. The experimental pH-titration data were analysed with the aid of the computer program in order to evaluate the formation constants of various intermediate species formed and their relative distribution in ternary systems.

Results

Potentiometer StudiesProton Ligand Dissociation Constants

The proton legend dissociation constants for guanine have been evaluated pH-metrically at 298,308 and 318+ 0.1 K temperatures and tanulated in Table the titration curve of the guanine legend shows two inflections, at a = 1 and 2 (Figure), indicated that two acidic groups of guanine which dissociated in two steps. The values for proton dissociation constant have been calculated by using following equations.

$H_2L = HL^- + H^+ ; K_1 = [HL^-][H^+] / [H_2L]$ (1)

$HL^- = L^{2-} + H^+ ; K_2 = [L^{2-}][H^+] / [HL^-]$ (2)

Metal Ligand Systems

Deprotonation constants of guanine were utilized for the evalution stability constants of binary (1:1) MG as well as ternary (1:1:1) MLG complexes at a constant ionic strength (I=0.1 M KNO_3) and 298,308 and 318 $\pm$ 1K temperatures. Here guanine acts as secondary ligand represented as G and primary ligand represented as L (Where L = cytosine, cytidine, 5-fluorocytosine, 5- azacytosine adn 5-bromocytosine).

THERMODYNAMIC STUDIES

The stability constants of the ternary complexes of cytosine, cytidine, 5-fluorocytosine, 5- azacytosine and 5- bromocytosine. with guanine along with the stability constants of corresponding binary (1:1) metal-guanine systems for the various metal ions under investigation at 298, 308 and 318 $\pm$ 0.1K temperatures are used to calculate thermodynamic parameters (i.e., enthalpy (ΔH^o_f) and entropy (ΔS^o_f) along with $\Delta\Delta H^o_f$ and $\Delta\Delta S^o_f$ values, which directly measure the extent of extra interaction in these systems. $\Delta\Delta H^0_f$ and $\Delta\Delta S^0_f$ are defined as

$$\Delta\Delta H^0_f = \Delta H_T^0 - \Delta H_B^0$$

$$\Delta\Delta S^0_f = \Delta S_T^0 - \Delta S_B^0$$

Here ΔH_T^0, ΔS_T^0 and ΔH_B^0, ΔS_B^0 are the enthalpy and entropy values associated with the ternary and binary complexes respectively.

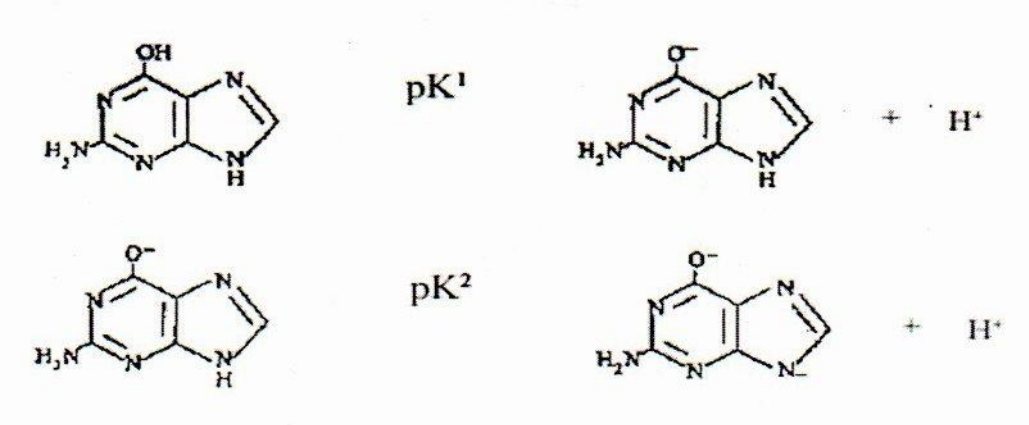
Discussion

Proton Ligand Systems

The proton ligand dissociation constants for guanine have been evaluated Ph- METRICALLY AT 298, 308 AND 318 + 0.1K Temperature and tabulated in Table 4.1, which are in good agreement with reported value. The formation curves of the protonation systems show that the equilibria (1) and (2) independently exist in the Ph range between 5.0 to 8.1 and 8.3 to above, respectively. Guanine exists in a mixture of the tautomeric forms A and B.

Metal Ligand Systems

When a solution contains two different ligands and a metal ion. There may exist equilibria in which either. (A) both the ligand may combine with the metal ion simultaneously. Or (B) The two ligands may combined one by one at different Ph.As it evident from the titration curves the addition of two ligands is stepwise in the buffer region at a = 1 and a=2 The formation of ternary complexes takes place according to the following equilibria (Charges are omitted for clarity)



M + HL
ML+ H:
k_3 = [ML] [H]/[M] [HL] (3)
ML + HG
MLG+H:
K_4 = [MLG] [H]/ [ML][HG] (4)

K_3 represents the formation constant of the binary complexes and K_4 represents the formation constant of the ternary complexes. Depending upon the chelation processes the formations of various stable complex species in the solution were altered. The Ph V.S.acurves for all metal ligand ternary systems studied, indicated several inflections and suggested about the formation of non protonated binary (ML/MG) or ternary (MLG) and mono hydroxo ternary species ($MLG(OH)^-$) in the solution.

Thermodynamic Studies

Since the value of Δlog K vary with temperature, there is need to measure the extra stability in ternary complexes by other parameters, such as $\Delta\Delta H_f$ and $\Delta\Delta S_f$ Hence thermodynamic parameters associated with metal ligand complexes are evaluated by studying stability constants of binary and ternary systems of guanine at three temperature viz., 298, 308 and 318 + 0.1K. In the case of all metal ligand binary (1:1) and ternary (1:1:1) systems, stability constants decrease with increase in temperature. The enthalpy change for the formation of 1:1 m(II)-legend (except Ca(II), Sr(II) and Ba(II) systems are exothermic and the entropy values are positive (Table 4,8). The complexes of ligands with alkaline earth metal ions, studied under investigations also exhibit large positive entropy values. The higher entropy values in all the metal-ligand systems further supported the bidentate nature of the ligand in the binary (1:1) complexes. The enthalpy changes for Ca(II), Sr(II), and Ba(II) complexes are in accord with the corresponding heats of hydration of the relative ions hence positive enthalpy value for Ca(II)-ligand systems are due to smaller ionic radius as compared to those of other alkaline earth metals.

TABLE (A) EQUILIBRIUM CONSTANT (log K ± 3σ) FOR REACTIONS OF METAL IONS WITH VARIOUS LIGANI (1:1:1) AT 298 ±0.1K TEMPERATURE AND IONIC STRENGTH I = 0.1mol dm^{-3} KNO_3 IN AQUEOUS SOLUTION.

S.N.	COMPLEX SPECIES	log K for Reactions				
		CYTOSINE	CYTIDINE	5-AZACYTOSINE	5-FLUOROCYTOSINE	5-BROMOCYTOSINE
				COBALT (II)		
1	ML	2.13±004	2.10±0.05	2.25±0.04	2.18±0.04	2.17±0.08
	MG	14.18±0.08	14.13±0.04	14.22±0.07	14.24±0.06	14.25±0.05
	MLG	18.05±0.05	17.96±0.08	18.23±0.06	18.11±0.05	18.12±0.06
	$MLG(H_2O)(OH)$	11.18±016	11.04±0.17	11.36±0.12	11.24±0.09	11.21±0.012
				NICKEL (II)		
2	ML	2.18±0.15	2.15±0.03	2.21±0.09	2.26±0.06	2.24±0.04
	MG	14.21±0.19	14.28±0.05	14.33±0.06	14.28±0.03	14.32±0.08
	MLG	18.41±0.16	18.33±0.03	18.45±0.05	18.38±0.16	18.47±0.12
	$MLG(H_2O)(OH)$	10.88±0.13	10.78±0.06	10.83±0.08	10.75±0.26	10.930±.012
				ZINC (II)		
3	ML	2.11±0.02	2.13±0.04	2.24±0.18	2.18±0.06	2.21±0.07
	MG	14.45±0.08	14.21±0.08	14.3±70.08	14.28±0.09	14.33±0.04
	MLG	18.22±0.06	18.12±0.04	18.38±0.04	18.31±0.014	18.45±0.16
	$MLG(H_2O)(OH)$	11.08±0.08	10.92±0.06	11.18±0.08	11.09±0.04	10.83±0.019
				CADMIUM (II)		
4	ML	2.18±0.07	2.11±0.15	2.28±0.10	2.15±0.12	2.21±0.02
	MG	14.18±0.20	14.06±0.09	14.31±0.13	14.21±0.19	14.27±0.07
	MLG	17.85±0.11	17.81±0.08	17.98±0.06	17.89±0.13	17.91±0.07
	$MLG(H_2O)(OH$	11.21±0.07	11.11±0.09	11.27±0.19	11.18±0.16	11.24±0.03

σ = Standard deviation

Reactions (1) M + HL ⇌ ML + H (2) M + GH ⇌ MG + H (3) MG + HL ⇌ MGL + H (4) $MLG(H_2O)_2$ ⇌ $MLG(H_2O)(OH)$ + H

TABLE FORMATION CONSTANT (log K ± 3σ) OF BINARY (1:1) AND TERNARY (1:1:1) METAL CYTOSINE COMPLEXES AND COMPARISON OF log K VALUES STRENGTH I=0.1mol dm^{-3} KNO_3 AT DIFFERENT TEMPERATURE IN AQUEOUS SOLUTION.

K	COBALT (II)	NICKEL (II)	ZINC (II)	CADMIUM (II)	COPPER (II)	CALCIUM (II)	STRONTIUM (II)	BARIUM (II)
METAL: GUANINE (log K_1)								
298	11.27±0.13	10.92±0.07	10.58±0.15	10.92±0.15	12.35±0.08	7.71±0.18	8.42±0.08	8.04±0.15
308	11.06±0.06	10.90±0.04	10.33±0.10	10.65±0.18	12.05±0.10	7.50±0.15	8.55±0.06	7.80±0.08
318	10.90±0.09	10.57±0.10	10.23±0.08	10.56±0.12	11.98±0.15	7.73±0.15	8.44±0.09	8.06±0.06
METAL: CYTOSINE (log K_2)								
298	9.59±0.20	7.98±0.19	8.26±0.05	9.85±0.12	11.20±0.15	7.75±0.12	8.15±0.09	8.16±0.02
308	9.55±0.21	7.81±0.12	8.10±0.04	8.40±0.15	11.75±0.10	7.80±0.12	8.58±0.15	6.40±0.18
318	9.32±0.15	7.78±0.19	8.05±0.08	9.47±0.11	10.93±0.15	7.90±0.05	8.62±0.14	6.50±0.16
METAL: CYTOSINE: GUANINE (log K_3)								
298	11.68±0.04	11.34±0.06	11.02±0.12	11.48±0.18	13.11±0.15	8.22±0.09	8.95±0.02	8.66±0.04
308	10.20±0.09	10.85±0.11	11.00±0.13	10.44±0.14	13.54±0.12	8.58±0.06	9.80±0.12	8.24±0.06
318	11.24±0.11	10.96±0.05	10.67±0.15	11.07±0.13	12.76±0.05	8.60±0.8	9.04±0.04	8.250±016
Δ log K (log $K_3 - K_1$)								
298	+0.41	+0.42	+0.44	+0.56	+0.76	+0.51	+0.54	+0.62
308	-0.86	-0.05	+0.67	-0.21	+1.49	+1.08	+1.25	+0.44
318	+0.34	+0.39	+0.44	+0.51	+0.78	+0.87	+0.60	+0.21
Δ log K (log $K_3 - K_2$)								
298	+2.09	+3.36	+2.76	+1.63	+1.13	+0.47	+0.80	+0.50
308	+0.65	+3.04	+2.90	+2.04	+1.79	+0.78	+1.22	+1.84
318	+1.92	+3.18	+2.62	+1.60	+1.83	+0.70	+0.42	+1.75

σ = Standard deviation

log K_1 and log K_2 are the formation constants of binary (1:1) M (II) Guanine and M (II) Cytosine complexes respectively and log K_3 is the ternary (1:1:1:) formation constant of M (II) Guanine Cytosine complex.

Materials and Methods

Doubly Distilled Water (Conductivity Water)

Doubly distilled water was prepared by redistilling distilled water in corning glass round bottom flask containing few crystals of potassium permanganate and potassium hydroxide to expel carbon dioxide and was cooled in stopper corning flasks. Doubly distilled water was stored in flask mad of corning glass.

Sodium Hydroxide, NaOH

Sodium hydroxide of Merck was used.

Oxalic Acid $C_2H_2O_4 . 2H_2O$

The solution of oxalic acid (Merck) was prepared directly by dissolving appropriate weighed amount of its sample in doubly distilled water. It is easily soluble in water.

Potassium Nitrate, KNO_3

The solution of potassium nitrate (Merck) was prepared directly by dissolving appropriate weighed amount of its sample in doubly distilled water.

Nitric Acid HNO_3.

(2.0 mol dm^{-3}) stock and standard solution of nitric acid (Merck) was prepared by dissolving appropriate volume of its sample (analytical reagent grade) slightly higher than that required. In doubly distilled water.

Metal Nitrates

Cobalt nitrate $Co(NO3)_2$. $6H_2O$ Nickel Nitrate Ni $(NO_3)_2$ $6H_2O$ Copper Nitrate, Cu $(NO_3)_2$ $3H_2O$ Zinc Nitrate Zn $(NO_3)_2$ $4H_2O$ Cadmium Nitrate Cd $(NO_3)_2$ Calcium Nitrate, Ca $(NO_3)_2$ $4H_2O$ Strontium nitrate Sr $(NO_3)_2$ Barium Nitrate Ba $(NO_3)_2$ (All Merck make) The solution of metal nitrate were prepared by dissolving appropriate weighed amount of their sample (analytical reagent grade)

Guanine (Ligand)

The stock and standard solution of guanine ($1.0x10^{-2}$ mol dm-3) was prepared by dissolving appropriate amount of its sample (SRL make) in known concentration of sodium hydroxide solution. The final concentration of sodium hydroxide was$5.0x10^{-2}$ mol dm-3 in guanine solution.

Others Ligands

Cytosine Cytidine (SRL make) 5-Azacytosine (Fluka make) 5-Fluorocytosine (Fluka make),5-Bromocytosine (Fluka make),5-Bromouracil (Fluka make) The stock and standard solution of legends ($1.0x10^{-2}$ mol dm^{-3}) were prepared by dissolving appropriate amount of their sample in minimum volume of doubly distilled water

Magnetic Susceptibility Measurements

Room temperature magnetic susceptibility was done on Cahn Faraday magnetic susceptibility balance suing cobalt mercury tetrathiocyanate as a calibrant and the experimental magnetic susceptibilities were corrected for diamagnetism using the procedure described by Figgis and Lweis.

CHN Analyzer

Carbon, hydrogen and nitrogen were analysed with a Vario EL III elemental analyser.

Determination of Stepwise Formation Constants

As the majority of organic completing legends used in analytical chemistry are moderately strong bases and become protonated in the Ph RANGE mostly applied in paratice (i.e. acidic Ph range), methods based on Ph measurement are often applicable for the determination of stability constants.

Reference

R. Phillips, Chem, Rev. 66 (1966) 501.

P.K Bhattacharya & C. Medhi; Indian J. Chem 43A (2004) 2043.

O. Eiigkvist, P. Astrand & G. Karlstom; Chem. Rev 100(2000) 4087.

L.F. Tan, X.J. Chen, J.L. Shen & X.L. Liang; J. Chem. Sci. 121 (2009) 397.

J.Liu, W.J. Mei, A.W. Xu, S. Shi, C.P. Tan&L.N.Ji; Antiviral Res. 62 (2004) 65.

H. Chao & L.N Jr; Bioinorg. Chem. Appl. 3 (2005) 15.
J.Z. Wu, L. Yuan &U Yu; Inorg. Chim. Acta. 359 (2006) 718.
A.A. Holder, S. Swavey &K.J. Brewer; Inorg Chem. 43 (2004) 303.
S. Dhar & A.R. Chakravarty; Inorg Chem. 42 (2003) 2483.
S. Chandra, L.K. Gupta and S. Agrawal, Trans. Met. Chem. 32(2007) 558.
R. Kumar and R, Singh, Russ, J. Coord. Chem. 32 (2006) 192.
S. Chandra, S.V. Verma and P. Meera, J. Indian Chem. Soc, 6 (2008) 896.
S. Neidle, Nat Prood Rep, (2001) 291.
J.Wang, Anal Chim Acta. 469 (2002) 63.
F.CR. Jelen Anal Chem.; 32(2002)261.
K. Rana, B.Kumar & B. Kumar; Indian J. Chem. 43B(2004) 1553.