Asian Journal of Chemistry Vol. 20, No. 2 (2008), 1095-1098

Stability Constant of Ce(III), Pr(III) and Tb(III) Chelates with Some Substituted Drugs

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The interaction of Ce(III), Pr(III) and Tb(III) metal ions with cefadroxyl or 8-[2-amino-2-(4-hydroxylphenyl)acetyl]-amino-4-methyl-7-oxo-2-thia-6-azobicyclo[4,2,0]oct-4-ene 5-carboxylic acid (**ligand-1**), deoxycycline or 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-1,11-dioxonaphthene-2-carboxamide (**ligand-2**) and dexamethasone or 9-fluro-11β, 17,21-trihydroxy-16a-methyl-pregna-14-diene-3,20-dione (**ligand-3**) have been investigated by pH-metric technique at 0.1 M ionic strength and at 27 ± 0.1 ºC in 70 % DMF-water mixture. The data obtained were used to estimate the values of proton-ligand stability constant (pK) and metal ligand stability constants (log K). It is 1:1 and 1:2 complexes with all the three ligands.

Key Words: Stability constant, Ce(III), Pr(III), Tb(III), Chelates, Substituted drugs.

INTRODUCTION

The substituted drugs forms colour complexes with metal ion in solid state. Narwade *et al.*[1] studied formation and stability constant of thorium(IV) complexes with some substituted pyrazolines. Kumar *et al.*[2] studied the physico chemical properties of Mn(II), Co(II), Zn(II) and Cu(II) complexes derived from 2-substituted benzaldehyde thiosemicarbazones. Parmar *et al.*[3] have been studied proton ligand stability constants of some substituted pyrazoles, isoxazoles, thioisoxazoles, pyrazolines and isoxazalines pH metrically at 0.1 M ionic strength. Seth *et al.*[4] have studied the some biological important ternary complexes of Ni(II) with 2-(2-hydroxyphenyl)benzimidazole and acids. Meshram *et al.*[5] have studied the stability constant of Co(II), Ni(II) and Cu(II) chelates with some substituted pyrazolines.

The detailed study of complexes under identical set of experimental condition is still lacking. It is therefore thought of interest to study the chelating properties of some substituted drugs under suitable condition pH metrically.

EXPERIMENTAL

Cerium(III), praseodymium(III) and terbium(III) nitrates (BDH) were dissolved in perchloric acid and their concentration were estimated by standard method[6]. The substituted drugs *viz.*, cefadroxyl or 8-[2-amino-2-(4-hydroxylphenyl)acetyl]-amino-4-methyl-7-oxo-2-thia-6-azobicyclo[4,2,0] oct-4-ene 5-carboxylic acid (**ligand-1**), deoxycycline or 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-penta-hydroxy-1,11-dioxo-naphthene-2-carboxamide (**ligand-2**) and dexamethasone or 9-fluro-11b, 17,21-trihydroxy-16a-methyl-pregna-14-diene-3,20-dione (**ligand-3**) are insoluble in water and hence 70 % DMF-water (v/v) was used as a solvent. The other solutions were prepared in double distilled water.

pH measurements were carried out with Elico-LI-10 pH meter (accuracy ± 0.05 unit) using glass electrode and calomel electrode at 27 ± 0.1 ºC. The B values (pH-meter reading in 70 % DMF-water mixture) were converted to (H^+) values by applying the correction proposed by Van-Uitert and Haas[7]. The overall 0.1 M ionic strength of solution was calculated by the expression, $\mu = \frac{1}{2}\sum C_i Z_i^2$ the contribution of the other ions in addition to Na^+ and ClO_4^- were also taken into consideration.

RESULTS AND DISCUSSION

Proton ligand stability constants

Substituted drugs may be considered as monobasic acids having only one replaceble H^+ ions from -OH group. The -OH group generally dissociates completely above pH 9.00 and can therefore be represented as HL *i.e.*

$$HL \rightleftharpoons H^+ + L^-$$

The titration data were used to construct the curves between volume of NaOH *vs.* pH. they are called acid-ligand and metal titration curves.

It is observed from titration curves for all the systems that ligand curves start deviating from the free acid ($HClO_4$) curves at about pH 5.5 and deviated continuously upto pH 11 the deviation shows that dissociation of -OH group in substituted drugs.

The average number of proton associated with the ligand ($\bar{n}_A$) was determined from acid and ligand titration curves employing the equation of Irving and Rossott[8]. The proton ligand formation curves were then obtained by plotting the values of $\bar{n}_A$ *vs.* pH. The values of pK were determined (half integral method) by noting the pH at which $\bar{n}_A = 0.5$. The values of pK were estimated by pointwise calculation method (Table-1).

pK values of **ligand 1** is greater than **ligand 2** and **ligand 3**. This may be due to the effect of stronger electron withdrawing group -COOH and >C=O group that reduces the pK values but increases the dissociation.

In case of simple drugs pK values is normally higher. This is due to the effect of -CH_3 electron releasing group that decreased the dissociation and increases the dissociation constant, pK values are found to increase in the following order of

ligand 1 > ligand 2 < ligand 3.

TABLE-1
DETERMINATION OF PROTON-LIGAND STABILITY CONSTANTS pK OF SOME SUBSTITUTED DRUGS AT 0.1 M IONIC STRENGTH

System	Constant pK	
	Half Integral	Pointwise calculation
Cefadroxyl	10.60	10.65 ± 0.05
Doxycycline	10.00	10.08 ± 0.06
Dexamethasone	10.50	10.55 ± 0.07

Metal ligand stability constants

Metal ligand stability constants of Ce(III), Pr(III) and Tb(III) complexes with some substituted drugs were determined by employing Bjerrum-calvin pH titration technique as adopted by Irving and Rossotti[8]. The formation of chelates between Ce(III), Pr(III) and Tb(III) with substituted drugs was indicated by (i) The significant departure starting from pH 4.5 for Ce(III), Pr(III) and Tb(III) for **ligand 1** (ii) The significant departure starting from pH 5.25 for Ce(III), Pr(III) and Tb(III) for **ligand 3** (iii) The change in colour from light yellow to light brown and then dark brown as pH was raised from 3.5 to 9.0.

Deviation between (acid+ligand+metal) titration curves from (acid + ligand) titration curves started from pH 4.5 which shows the commencement of complex formation. It could be seen from Table-2, the log K values follows the decreasing trend. This is due the effect of electron releasing group -CH_3 and electron withdrawing group –COOH *etc*.

The values of log K ($\log K_2 - \log K_1$) and $\log K_2/\log K_1$ are presented in Table-3.

It is observed that the smaller difference may be due to the trans-structure. The results shows that the ratio $\log K_2/\log K_1$ is positive in all cases. This implies that there is little or no steric hindrance to the addition of secondary ligand molecules.

Validity of log K = apK + b, relation

The linear relation of log K = apK + b, relation has been noted by some workers to hold for transition metal complexes of a series of closely related ligands. Similar plots of $\log K_1$ and $\log K_2$ against pK shows satisfactory linear relation giving slope values 1.105, 0.99, 0.95, respectively when the change in partial molal free energies of thermal ligand and proton ligand complex exactly compensate each other. The log K *vs.* pK plot is linear with the slopes of unity.

TABLE-2
DETERMINATION OF METAL-LIGAND STABILITY CONSTANTS (log K) OF Ce(III), Pr(III) AND Tb(III) COMPLEXES WITH SUBSTITUTED DRUGS AT 0.1 M IONIC STRENGTH

S. No.	System	Constant	
		log K_1 (PL_1)	log K_2 (PL_2)
I	Ce (III)-ligand-1	5.30	6.50
	Pr (III)-ligand-1	5.25	6.20
	Tb (III)-ligand-1	5.15	6.55
II	Ce (III)-ligand-2	5.65	6.35
	Pr (III)-ligand-2	4.40	5.90
	Tb (III)-ligand-2	4.80	5.50
III	Ce (III)-ligand-3	5.80	6.50
	Pr (III)-ligand-3	6.15	7.00
	Tb (III)-ligand-3	5.70	6.95

TABLE-3
METAL LIGAND STABILITY CONSTANTS AT 0.1 M IONIC STRENGTH

S. No.	System	Constant	
		log K_2–K_1	log K_2/log K_1
I	Ce (III)-ligand-1	1.20	1.22
	Pr (III)-ligand-1	0.95	1.14
	Tb (III)-ligand-1	1.40	1.27
II	Ce (III)-ligand-2	1.30	1.12
	Pr (III)-ligand-2	1.50	1.34
	Tb (III)-ligand-2	0.70	1.14
III	Ce (III)-ligand-3	0.70	1.12
	Pr (III)-ligand-3	0.85	1.13
	Tb (III)-ligand-3	1.25	1.21

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(*Received*: 19 January 2007; *Accepted*: 1 October 2007) AJC-5943