J. Chem. Eng. Data **2005,** *50,* 377−382

Solution Studies of Some Binary and Ternary Lanthanide Complexes

Shalu Tyagi, Rajeev Kumar, and Udai P. Singh*

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247667, India

---

The solution studies of some binary (1:1) and ternary (1:1:1) complexes of Eu(III), Gd(III), and Tb(III) with benzoic acid/its derivatives and uracil/its halo derivatives in dioxane−water (30:70 v/v) medium (ionic strength $I = 0.1$ mol·dm^{-3} $NaNO_3$) have been performed. The experimental pH titration data were analyzed with the help of the BEST computer program in order to evaluate the formation constants of various intermediate species formed. The stability constants of the binary (1:1) systems decrease in order of Tb(III) > Eu(III) > Gd(III). The formation constant of 1:1:1 mixed ligand complexes for Eu(III), Gd(III), and Tb(III) with benzoic acid/its derivatives as the primary ligand and uracil/its halo derivatives as the secondary ligand has also been studied. The available data suggested that the ternary complexes of Eu(III), Gd(III), and Tb(III) are more stable than the crossponding binary complexes.

Introduction

Uracil, a pyrimidine base, is preferentially utilized for nucleic acid biosynthesis in tumors. The replacement of the hydrogen atom by fluorine from position 5 of uracil resulted in the formation of a compound (5-flurouracil) very similar to it but with different chemical behavior. 5-Fluorouracil is the monofluorinated product of uracil, behaves as an antitumor agent, and has been used in the treatment of gastrointestinal malignancies and of breast, lung, ovary, and cervix carcinomas.[1] It interferes with thymidylate synthesis, and its major inhibitory effects occur after conversion to 5-fluoro-2′-deoxyuridine-5′-monophosphate in the cell. The later acts as an analogue of 2′-deoxyuridine-5′-monophosphate and binds very tightly to thymidylate synthetase in the presence of methylene tetrahydrofolate, forming a covalent complex with the enzyme that is unable to undergo the normal catalytic reaction.

Many of the organic substances that can affect the biological and ecological behavior of the lanthanide and actinide ions have aromatic carboxylate binding sites. Choppin et al.[2] studied lanthanide complexation by benzoic acid and isophthalic acid and suggested that in the latter ligand, steric effects prevent simultaneous binding to both carboxylate sites. Studies on complex formation by tripositive rare earth ions with biologically important ligands are in progress because of their role in biochemical processes, and some lanthanide complexes with nucleosides/nucleotides are also available in the literature.[3−5] To the best of our knowledge, no examples of the interaction of uracil and its halo derivatives with lanthanides in the presence of benzoic acid/its derivatives are known to date. The present paper reports studies on the interaction of uracil (Ur), 5-fluorouracil (FUr), 5-chlorouracil (ClUr), and 5-bromouracil (BrUr) as one ligand and benzoic acid (OBz), 4-nitrobenzoic acid (NBz), 4-fluorobenzoic acid (FBz), 4-chlorobenzoic acid (ClBz), and 4-bromobenzoic acid (BrBz) as another ligand with Eu(III), Gd(III), and Tb(III) in 1:1:1 ratio potentiometrically at (25 ± 0.1) °C. The experimental pH-titration data were analyzed with the help of the computer program BEST in order to evaluate the formation constants of various intermediate species formed and their relative distribution.

Experimental Section

Materials and Solutions. The ligands benzoic acid (C_6H_5COOH) and its different derivatives were purchased from SRL (Mumbai, India), whereas uracil ($C_4H_4N_2O_2$), 5-fluorouracil ($C_4H_3FN_2O_2$), 5-chlorouracil ($C_4H_3ClN_2O_2$), and 5-bromouracil ($C_4H_3BrN_2O_2$) were purchased from Fluka (Switzerland). Stock solutions of benzoic acids/derivatives (1.0×10^{-2} mol·dm^{-3}) were prepared by dissolving the required amount of ligands in the minimum volume of freshly double-distilled CO_2-free water with vigorous shaking at 40 °C and subsequently diluted to the final volume. Stock solutions of uracil/its halo derivatives were prepared by dissolving the required amount of ligands in the minimum volume of freshly distilled ethyl alcohol by heating it to about 40 °C with vigorous shaking, the volumes were made up by adding freshly double-distilled CO_2-free water.

Europium nitrate ($Eu(NO_3)_3{\cdot}6H_2O$), gadolinium nitrate ($Gd(NO_3)_3{\cdot}6H_2O$), and terbium nitrate ($Tb(NO_3)_3{\cdot}6H_2O$) (from Indian Rare Earth Ltd., Udyogamandal, S. India) were used to prepare metal solutions (1.0×10^{-2} mol·dm^{-3}) and were standardized by the EDTA titration method as discussed elsewhere in the literature.[6] HNO_3 and NaOH were from Merck. Stock solutions of NaOH (CO_2-free) and HNO_3 were prepared and standardized by a literature method.[7] All reagents used were of AR grade.

Apparatus and Procedure. The titrations were performed at (25 ± 0.1) °C in a double-walled cell fitted with a thermostat (Julabo F-10). In all titrations, oxygen-free N_2 gas was passed into the solution before and during the pH measurements. A Schott CG 841 pH meter using a glass electrode (Schott Gerate 6280) was used to monitor the pH changes. The titrant (CO_2-free standard NaOH) was added to the titration cell, and the pH changes were monitored through the pH meter. The pH meter was calibrated with standard buffer solutions (pH 4.0 and 10.0) before the pH measurements. The pH region below 3.5 and above 10.5

---

* Corresponding author. E-mail: udaipfcy@iitr.ernet.in.

10.1021/je0400097 CCC: $30.25

was calibrated using standard HCl and NaOH solutions, respectively. For the determination of the proton dissociation constants of the free ligands, the following mixtures (A, B, and C) were prepared and titrated separately with standard alkali soliution (0.2 mol·dm^{-3}):

(A) nitric acid (2.0 × 10^{-2} mol·dm^{-3}, 5.0 mL) + sodium nitrate (1.0 mol·dm^{-3}, 5.0 mL).

(B) mixture A + primary ligand solution (1.0 × 10^{-2} mol·dm^{-3}, 5.0 mL).

(C) mixture A + secondary ligand (1.0 × 10^{-2} mol·dm^{-3}, 5.0 mL).

For the study of binary (1:1) and ternary (1:1:1) complexes, the following mixtures (D, E, and F) were prepared and titrated as above:

(D) mixture B + metal nitrate (1.0 × 10^{-2} mol·dm^{-3}, 5.0 mL).

(E) Mixture C + metal nitrate (1.0 × 10^{-2} mol·dm^{-3}, 5.0 mL).

(F) Mixture D + secondary ligand (1.0 × 10^{-2} mol·dm^{-3}, 5.0 mL).

The total volume (i.e., 50 mL of 30:70 v/v dioxane−water mixture) and ionic strength (I) of all of the above titration mixtures were adjusted to 0.1 mol·dm^{-3} by adding double-distilled water and dioxane and an appropriate volume of 1.0 mol·dm^{-3} $NaNO_3$ solution, respectively. Nitric acid was used to lower the pH of the initial solution mixture. All of the pH-metric titrations were terminated when either the readings of the pH meter became unstable, showing a downward drift, or visual precipitation occurred. The proton-ligand dissociation constants for various ligands have been evaluated pH metrically at (25 ± 0.1) °C and a constant ionic strength (ionic strength I = 0.1 mol·dm^{-3}) by using Bjerrum−Calvin's pH titration technique,[8,9] as adopted by Irving and Rossotti.[10,11] Several complex equilibria were studied by using p^{KAS} and BEST computer programs.

Results and Discussion

The evaluated proton-ligand dissociation constants for various ligands in the present study are in good agreement with reported values. The pH-metric titration curves of the HL (where L = OBz, FBz, ClBz, BrBz, and NBz and curve b showing only one inflection point at a = 1 (Figure 1)), indicated that there is only one acidic group, whereas the curves for H_2U (where U = Ur, FUr, ClUr and BrUr and curve c clearly showing two inflection points at a = 1 and 2 (Figure 1)) indicate the dissociation of two protons from each ligand. The proton dissociation constants for HL and H_2U have been calculated by using the following equations.

$$\mathrm{HL} \rightleftharpoons \mathrm{L}^{1-} + \mathrm{H}^+ \qquad K^1 = \frac{[\mathrm{L}^{1-}][\mathrm{H}^+]}{[\mathrm{HL}]} \tag{i}$$

$$\mathrm{H_2U} \rightleftharpoons \mathrm{HU}^- + \mathrm{H}^+ \qquad K_a^1 = \frac{[\mathrm{HU}^-][\mathrm{H}^+]}{[\mathrm{H_2U}]} \tag{iia}$$

$$\mathrm{HU}^- \rightleftharpoons \mathrm{U}^{2-} + \mathrm{H}^+ \qquad K_a^2 = \frac{[\mathrm{U}^{2-}][\mathrm{H}^+]}{[\mathrm{HU}^-]} \tag{iib}$$

Ur involves enol tautomeric equilibria, but the diketo form (I) (Figure 2) is the most stable tautomer in condensed phases[12] as well as in the gas phase.[13] Nakanishi et al.[14] suggested that Ur is deprotonated at N_1 or N_3, leading to the anionic form of type II or III (Figure 2), respectively. The protonation of Ur occurs at C_2=O and C_4=O, leading to cationic forms of type IV and V and a dication of type VI (Figure 3). Poulter and Anderson[15] performed kinetic studies of the C_2- and C_4-hydroxyl protons of the 1,3-dimethyluracil dication and suggested that the monocation derived from protonation at C_4=O (V) is considerably more stable than its C_2=O protonated isomer (IV).

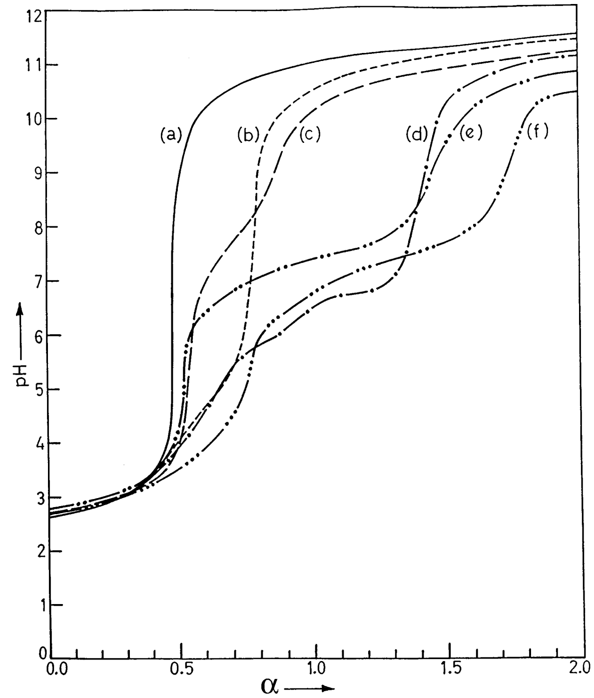
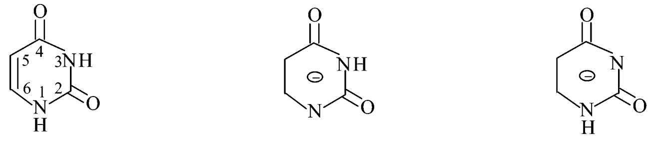
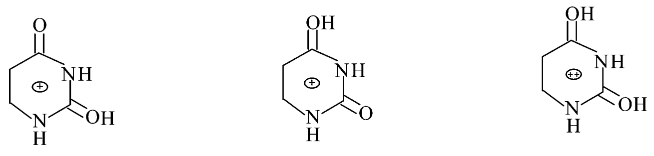


Figure 1. pH against a volume of 0.2 mol·dm^{-3} NaOH for the Tb(III) + 5FU + L system at (25 ± 0.1) °C and I = 0.1 mol·dm^{-3} $NaNO_3$: (a) 2.0 × 10^{-3} mol·dm^{-3} HNO_3; (b) 2.0 × 10^{-3} mol·dm^{-3} HNO_3 + 1.0 × 10^{-3} mol·dm^{-3} L; (c) 2.0 × 10^{-3} mol·dm^{-3} HNO_3 + 1.0 × 10^{-3} mol·dm^{-3} 5FU; (d) 2.0 × 10^{-3} mol·dm^{-3} HNO_3 + 1.0 × 10^{-3} mol·dm^{-3} L + 1.0 × 10^{-3} mol·dm^{-3} Tb(III); (e) 2.0 × 10^{-3} mol·dm^{-3} HNO_3 + 1.0 × 10^{-3} mol·dm^{-3} 5FU+ 1 × 10^{-3} mol·dm^{-3} Tb(III); (f) 2.0 × 10^{-3} mol·dm^{-3} HNO_3 + 1.0 × 10^{-3} mol·dm^{-3} L + 1.0 × 10^{-3} mol·dm^{-3} 5FU + 1× 10^{-3} mol·dm^{-3} Tb(III). a is the number of moles of alkali per mole of ligand.



(I) (II) (III)

Figure 2. Deprotonated structure of uracil.



(IV) (V) (VI)

Figure 3. Protonated structure of uracil.

The curves obtained between pH versus the volume of alkali added to the mixture (nitric acid + primary ligand) and (nitric acid + primary ligand + metal) at (25 ± 0.1) °C were utilized for the evaluation of the a value at different pH's. Additional pH versus a curves (Figure 1) were plotted for the binary systems, accounting for the metal−ligand association and equilibrium constant determination. The result suggested that various complex species were formed in solution. At various pH conditions, the important complex species formed are supposed to be nonprotonated (ML at a = 1) and nonprotonated-hydroxo

Table 1. Proton Dissociation Constants ($-\log K \pm 3\sigma^a$) at $t = (25 \pm 0.1)$ °C and at Ionic Strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in Dioxane−Water Medium

ligands	p$K^{1b,d}$	pK^{2c}
uracil	9.22 ± 0.05	12.65 ± 0.04
5-flurouracil	7.65 ± 0.03	10.60 ± 0.07
5-chlorouracil	8.00 ± 0.08	10.80 ± 0.10
5-bromouracil	8.20 ± 0.11	11.35 ± 0.06
benzoic acid	4.25 ± 0.05	
4-fluorobenzoic acid	3.75 ± 0.07	
4-chlorobenzoic acid	4.05 ± 0.04	
4-bromobenzoic acid	3.80 ± 0.04	
4-nitrobenzoic acid	3.40 ± 0.02	

[a] σ = standard deviation. [b] $pK^1 = -\log K^1$; $K^1 = [HU^-][H^+]/[H_2U]$. [c] $pK^2 = -\log K^2$; $K^2 = [U^{2-}][H^+]/[HU^-]$. [d] $pK^1 = -\log K^1$; $K^1 = [L^-][H^+]/[HL]$.

$(ML(OH)^-$ at $a = 2$. The equilibria involved in these pH regions (eqs iii and iv) can be given as

at $a = 1$;

$$M^{3+} + L^- \rightleftharpoons ML^{2+} \qquad K_1 = \frac{[ML^{2+}]}{[M^{3+}][L^-]} \qquad \text{(iii)}$$

$$M^{3+} + U^{2-} \rightleftharpoons MU^+ \qquad K_{1a} = \frac{[MU^+]}{[M^{3+}][U^{2-}]} \qquad \text{(iv)}$$

Concentrations of various species (i.e., $[M^{3+}]$ and $[ML^{2+}]$) were evaluated, and the corresponding equilibrium constant for each metal ion was determined and tabulated as log K in Tables 2 and 3.

In this region, metal−ligand systems show one more inflection along with the precipitation indicating the formation of hydroxo (ML(OH)) species as well as metal hydroxide in the corresponding systems. The equilibria involved in this region (eqs v, vi, vii, and viii) may be given as

$$M^{3+} + L^- + OH^- \rightleftharpoons ML(OH)^+ \quad K_2 = \frac{[ML(OH)^+]}{[M^{3+}][L^-][OH^-]} \qquad \text{(v)}$$

$$ML^{2+} + OH^- \rightleftharpoons ML(OH)^+ \qquad K_2' = \frac{[ML(OH)^+]}{[ML^{2+}][OH^-]} \qquad \text{(vi)}$$

$$M^{3+} + U^{2-} + OH^- \rightleftharpoons MU(OH)$$

$$K_{2a} = \frac{[MU(OH)]}{[M^{3+}][U^{2-}][OH^-]} \qquad \text{(vii)}$$

$$MU^+ + OH^- \rightleftharpoons MU(OH) \qquad K_{2a}' = \frac{[MU(OH)]}{[MU^+][OH^-]} \qquad \text{(viii)}$$

It is evident from the equilibrium study that the metalation of such ligands is strongly dependent on the pH of the solutions. Furthermore, there are various possible binding sites on Ur and 5·XUr for complex formation: (i) chelation between the 5-substituent and 4-carboxyl; (ii) complexing on N_1; and (iii) complexing on N_3. It is well known that the keto−enol tautomerism occurs more at N_3 than N_1 and complex formation is accompanied by the release of protons. The presence of a dissociable proton on N_3 in Ur as well as in substituted Ur makes N_3 the most likely complexing site.[16,17]

When a solution contains two different ligands and a metal ion, there may exist equilibria in which either (i) both ligands may combine with the metal ion simultaneously or (ii) the two ligands may combine one by one at different pH values. As 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 omitted for clarity):

$$M + HL \rightleftharpoons ML + H \qquad K^{M}_{ML} = \frac{[ML][H]}{[M][HL]} \qquad \text{(ix)}$$

$$ML + HU \rightleftharpoons MLU + H \qquad K^{ML}_{MLU} = \frac{[MLU][H]}{[ML][HU]} \qquad \text{(x)}$$

K^{ML}_{MLU} represents the formation constant of the ternary complexes.

Depending upon the chelation processes, the formation of various stable complex species in the solution was altered. The pH versus a curves for all metal−ligand ternary systems studied indicated several inflections and suggested the formation of nonprotonated binary (ML/MU) or ternary (MLU) and monohydroxo ternary species (MLU(OH)) in solution.

$$MLU(H_2O)_2 \rightleftharpoons MLU(OH)(H_2O) + H$$

$$K_{MLU(OH)(HO)} = \frac{[MLU(OH)(H_2O)][H]}{[MLU(H_2O)_2]} \qquad \text{(xi)}$$

The stability constants for various binary and ternary complexes have been calculated and are tabulated in Tables 4 and 5 as log K. Stability constant data also reveled the relative stability order of metal−ligand binary and ternary complexes as M(III)−L−U > M(III)−U > M(III)−L. This is in contrast to what has been observed for bivalent metal ions.[18] This may be explained on the basis of the difference in charge and coordination number of metal ions. The smaller size (higher charge) and higher coordination number of lanthanides permit their closer interaction with the ligands and at the same time allow minimum repulsion because of the expanded coordination number resulting in the formation of more stable complexes compared to those with bivalent metal ions.

K^{M}_{ML}, K^{ML}_{MLU}, and $K_{MLU(OH)(H_2O)}$ were calculated after the evaluation of various species concentrations (i.e., [ML], [MU], [MLU], and $[MLU(OH)(H_2O]$ as given in Table 6). A species distribution determination for various possible species in solution for all of the metal−ligand binary systems (Tables 2 and 3) and ternary systems (Table 6) has also been performed. This study enabled us to find the quantitative distribution of metal ions in two species (i.e., ML^{2+} and $ML(OH)^+$ in the case of HL and MU^+ and MU(OH) in the case of H_2U) along with free metal ions M(III) at all pH values. It is observed that at pH ∼2.0 free metals are present in (99 to 100) % amounts and the percentage of free metal ions decreases gradually on increasing the pH of the solution and attains almost a zero value at higher pH. This suggests that with increasing pH of the solution the metal ions distributed in ML^{2+} or MU^+ species are ∼(14 to 99)% for all metal−ligand systems in the pH range from ∼4.8 to 8.7, which further decreases with increasing pH of the solution starting with the converting into $ML(OH)^+$ or MU(OH) species. Finally, the total amount of metal distributed gets converted to $ML(OH)^+$ or MU(OH) species at pH ≥10.0, and the metal ion distribution observed is ∼99%.

An analysis of the species distribution curves for ternary (1:1:1) systems reveals the existence of the ternary species along with the neutral binary complex species for both primary and secondary ligands in the solution at various

Table 2. Equilibrium Constants (log $K \pm 3\sigma^a$) for Reactions^b of Ln (III) with Various Ligands (1:1) at $t = (25 \pm 0.1)$ °C and Ionic Strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in Dioxane−Water Medium

	Eu(III)		Gd(III)		Tb(III)	
	log *K* for reaction		log *K* for reaction		log *K* for reaction	
ligands	1^c	2^d	1^c	2^d	1^c	2^d
Bz	6.61 ± 0.07	0.67 ± 0.09	6.68 ± 0.03	2.93 ± 0.03	6.65 ± 0.06	1.02 ± 0.03
FBz	9.13 ± 0.04	2.96 ± 0.02	8.56 ± 0.09	3.98 ± 0.04	9.33 ± 0.05	1.86 ± 0.05
ClBz	10.36 ± 0.03	5.41 ± 0.02	10.06 ± 0.06	4.57 ± 0.05	10.44 ± 0.11	4.86 ± 0.06
BrBz	10.42 ± 0.03	5.89 ± 0.06	10.34 ± 0.06	5.67 ± 0.04	10.51 ± 0.04	5.7 ± 0.08
NBz	9.15 ± 0.05	2.05 ± 0.06	9.02 ± 0.02	2.85 ± 0.02	6.37 ± 0.05	0.83 ± 0.04

[a] σ = standard deviation. [b] Reactions for HL. [c] 1. $M^{3+} + L^- \rightleftharpoons ML^{2+}$. [d] 2. $M^{3+} + L^- + H_2O \rightleftharpoons ML(OH)^+ + H^+$.

Table 3. Equilibrium Constants (log $K \pm 3\sigma^a$) for Reactions^b of Ln(III) with Various Ligands (1:1) at $t = (25 \pm 0.1)$ °C and Ionic Strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in Dioxane−Water Medium

	Eu(III)		Gd(III)		Tb(III)	
	log *K* for reaction		log *K* for reaction		log *K* for reaction	
ligands	1^c	2^d	1^c	2^d	1^c	2^d
Ur	15.44 ± 0.09	6.89 ± 0.04	15.39 ± 0.04	6.29 ± 0.07	15.45 ± 0.03	6.58 ± 0.06
FUr	11.18 ± 0.05	3.25 ± 0.06	11.01 ± 0.06	3.18 ± 0.05	11.77 ± 0.04	3.31 ± 0.04
ClUr	11.48 ± 0.11	3.67 ± 0.05	11.44 ± 0.03	3.60 ± 0.09	11.61 ± 0.05	3.74 ± 0.02
BrUr	11.92 ± 0.05	4.95 ± 0.04	11.87 ± 0.05	4.47 ± 0.07	12.39 ± 0.04	5.51 ± 0.06

[a] σ = standard deviation. [b] Reactions for H_2U. [c] 1. $M^{3+} + U^{2-} \rightleftharpoons MU^+$. [d] 2. $M^{3+} + U^{2-} + H_2O \rightleftharpoons MU(OH) + H^+$.

Table 4. Formation Constants (log $K \pm 3\sigma^a$) of Binary (1:1) Metal Complexes at $t = (25 \pm 0.1)$ °C and Ionic Strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in Dioxane−Water Medium

	log K^{M}_{MU}		
ligand	Eu	Gd	Tb
Ur	10.65 ± 0.06	10.58 ± 0.04	10.86 ± 0.09
FUr	7.24 ± 0.08	7.14 ± 0.02	7.42 ± 0.05
ClUr	8.15 ± 0.08	8.15 ± 0.08	8.27 ± 0.03
BrUr	9.36 ± 0.05	9.15 ± 0.02	9.51 ± 0.06
		log K^{M}_{ML}	
OBz	3.33 ± 0.02	3.30 ± 0.07	3.34 ± 0.05
FBz	3.37 ± 0.04	3.38 ± 0.06	3.40 ± 0.03
ClBz	3.45 ± 0.02	3.42 ± 0.03	3.50 ± 0.06
BrBz	3.47 ± 0.03	3.44 ± 0.08	3.51 ± 0.07
NBz	3.31 ± 0.08	3.28 ± 0.05	3.32 ± 0.05

[a] σ = standard deviation.

pH values. For example, Figure 4 indicates the presence of free metal and 1:1 nonprotonated species M(III)−L and M(III)−U and 1:1:1 neutral M(III)−L−U complexes in solution around pH 2.0. The concentration of M(III)−L starts to decrease with increasing concentration of M(III)−U and M(III)−L−U and attains almost a zero value in a higher pH range (~6.0). The species distribution curves also suggest that monohydroxo species M(III)−L−U(OH) (i.e., 100% at pH 11.0) of the ternary complex are predominate over the neutral species that are being formed in comparatively small amounts in the lower pH range (~3.0). Because of differences between the p*K* values of the primary and secondary ligands, various complex species are formed in solution. At pH 2.0, free metals are completely converted to M(III)−L, M(III)−U, and M(III)−L−U. Also, in M(III)−L species, metal ions are distributed from (63 to 87)%. Furthermore, the association of H_2U with each metal ion and M(III)−L species starting

Table 5. Formation Constants (log $K \pm 3\sigma^a$) of a Ternary (1:1:1) System and Δ log *K* Values at $t = (25 \pm 0.1)$ °C and Ionic Strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in Dioxane−Water Medium

	log K^{MU}_{MUL}			$\Delta \log K = \log K^{MU}_{MUL} - \log K^{M}_{ML}$			$\Delta \log K' = \log K^{MU}_{MUL} - \log K^{M}_{MU}$		
	Eu	Gd	Tb	Eu	Gd	Tb	Eu	Gd	Tb
M/Ur/OBz	14.08 ± 0.13	13.42 ± 0.04	14.55 ± 0.05	10.75	10.12	11.21	3.43	2.84	3.69
M/Ur/FBz	13.00 ± 0.09	12.90 ± 0.03	13.40 ± 0.05	9.63	9.52	10.00	2.35	2.32	2.54
M/Ur/ClBz	13.30 ± 0.02	13.19 ± 0.06	13.40 ± 0.08	9.85	9.77	9.90	2.65	2.61	2.54
M/Ur/BrBz	13.47 ± 0.07	13.42 ± 0.04	13.85 ± 0.04	10.00	9.98	10.34	2.82	2.84	2.99
M/Ur/NBz	13.50 ± 0.05	13.33 ± 0.06	14.00 ± 0.11	10.19	10.05	10.68	2.85	2.75	3.14
M/FUr/OBz	11.10 ± 0.11	10.96 ± 0.03	11.50 ± 0.05	7.77	7.66	8.16	3.86	3.56	4.08
M/FUr/FBz	9.25 ± 0.03	9.55 ± 0.03	9.70 ± 0.06	5.88	6.17	6.30	2.01	2.41	2.28
M/FUr/ClBz	9.80 ± 0.09	9.64 ± 0.05	10.00 ± 0.04	6.35	6.22	6.50	2.56	2.50	2.58
M/FUr/BrBz	10.17 ± 0.06	9.96 ± 0.15	11.05 ± 0.05	6.70	6.52	7.54	2.93	2.82	3.63
M/FUr/NBz	10.90 ± 0.05	10.35 ± 0.02	11.15 ± 0.06	7.59	7.07	7.83	3.66	3.21	3.73
M/ClUr/OBz	12.15 ± 0.08	11.60 ± 0.04	12.30 ± 0.03	8.82	8.30	8.96	4.00	3.48	4.03
M/ClUr/FBz	10.20 ± 0.09	9.80 ± 0.03	10.45 ± 0.05	6.83	6.42	7.05	2.05	1.68	2.18
M/ClUr/ClBz	10.22 ± 0.02	9.90 ± 0.06	10.46 ± 0.08	6.77	6.48	6.96	2.07	1.78	2.19
M/ClUr/BrBz	10.40 ± 0.07	10.10 ± 0.04	10.52 ± 0.04	6.93	6.66	7.01	2.25	1.98	2.25
M/ClUr/NBz	10.43 ± 0.05	10.11 ± 0.06	10.58 ± 0.11	7.33	6.83	7.26	2.28	1.99	2.31
M/BrUr/OBz	12.23 ± 0.07	11.90 ± 0.04	12.42 ± 0.05	8.90	8.60	9.08	2.87	2.75	2.91
M/BrUr/FBz	10.20 ± 0.09	9.80 ± 0.03	10.45 ± 0.05	6.83	6.42	7.05	0.84	0.65	0.94
M/BrUr/ClBz	10.22 ± 0.02	9.90 ± 0.06	10.46 ± 0.08	6.77	6.48	6.96	0.86	0.75	0.95
M/BrUr/BrBz	10.40 ± 0.07	10.10 ± 0.04	10.52 ± 0.04	6.93	6.66	7.01	1.04	0.95	1.01
M/BrUr/NBz	10.43 ± 0.05	10.11 ± 0.06	10.58 ± 0.11	7.12	6.83	7.26	1.07	0.96	1.07

[a] σ = standard deviation.

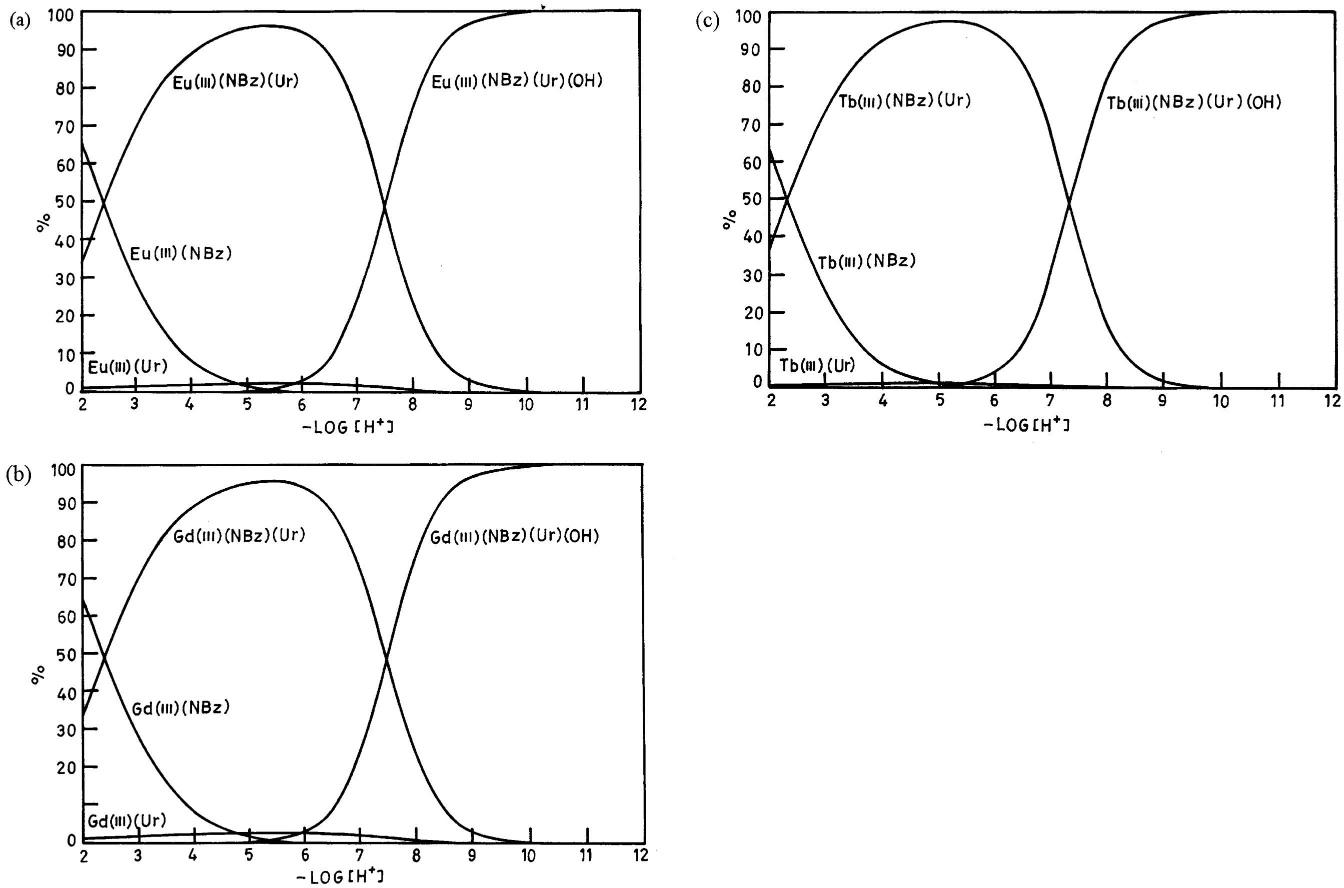


Figure 4. (a) Species distribution curve of the Eu(III) + U + NBz (1:1:1) ternary systems at (25 ± 0.1) °C and ionic strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in dioxane−water medium. (b) Species distribution curve of the Gd(III) + U + NBz (1:1:1) ternary systems at (25 ± 0.1) °C and ionic strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in dioxane−water medium. (c) Species distribution curve of the Tb(III) + U + NBz (1:1:1) ternary systems at (25 ± 0.1) °C and ionic strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in dioxane−water medium.

Table 6. Equilibrium Constants (log $K \pm 3\sigma$[a]) for Reactions[b] of Ln(III) with Various Ligands (1:1:1) at (25 ± 0.1) °C and Ionic Strength $I = 0.1$ mol·dm^{-3} $NaNO_3$ in Dioxane−Water Medium

	log *K* for reaction			
metal	1[c]	2[d]	3[e]	4[f]
		M/Ur/OBz		
Eu	7.48 ±0.06	17.64 ± 0.02	23.91 ± 0.13	16.37 ± 0.04
Gd	7.49 ± 0.04	17.60 ± 0.07	23.88 ± 0.04	16.34 ± 0.11
Tb	7.79 ± 0.09	17.96 ± 0.05	23.95 ± 0.05	16.47 ± 0.03
		M/Ur/FBz		
Eu	7.73 ± 0.02	18.94 ± 0.08	24.60 ± 0.05	17.28 ± 0.04
Gd	7.62 ± 0.07	18.77 ± 0.05	24.11 ± 0.06	17.10 ± 0.02
Tb	7.77 ± 0.03	19.23 ± 0.05	25.09 ± 0.11	17.37 ± 0.07
		M/Ur/ClBz		
Eu	7.86 ± 0.06	19.28 ± 0.04	24.58 ± 0.09	17.24 ± 0.06
Gd	7.81 ± 0.05	19.01 ± 0.06	24.65 ± 0.03	17.18 ± 0.06
Tb	7.90 ± 0.03	19.46 ± 0.03	24.89 ± 0.05	17.55 ± 0.03
		M/Ur/BrBz		
Eu	9.20 ±0.12	20.09 ± 0.02	25.34 ± 0.13	17.72 ± 0.02
Gd	9.01 ± 0.05	19.25 ± 0.07	25.04 ± 0.04	17.60 ± 0.08
Tb	9.24 ± 0.06	20.40 ± 0.05	25.60 ± 0.05	17.91 ± 0.03
		M/Ur/NBz		
Eu	7.04 ± 0.08	17.44 ± 0.03	23.74 ± 0.07	16.67 ± 0.04
Gd	6.91 ± 0.04	17.73 ± 0.08	23.70 ± 0.04	16.60 ± 0.05
Tb	7.14 ± 0.02	17.80 ± 0.07	23.74 ± 0.04	16.74 ± 0.09

[a] σ = standard deviation. [b] Reactions. [c] 1. $M^{3+} + L^- \rightleftharpoons ML^{2+}$. [d] 2. $M^{3+} + U^{2-} \rightleftharpoons MU^+$. [e] 3. $M^{3+} + L^- + U^{2-} \rightleftharpoons MLU$, $ML^{2+} + U^{2-} \rightleftharpoons MLU$. [f] 4. $M^{3+} + L^- + U^{2-} + H_2O \rightleftharpoons MLU(OH)^- + H^+$ or $MLU + H_2O \rightleftharpoons MLU(OH)^- + H^+$.

at pH ~2.0 and resulting in the formation of M(III)−U and M(III)−L−U species are (5 to 6)% and (90 to 98)% at pH ~3.5 to 5.5 and 4.8 to 5.6, respectively. Finally, the total number of metal ions distributed into ML, MU, and MLU species started converting to the hydroxo species after successive deprotonation of coordinated water molecules at pH >6.0. Here again the species distribution data clearly show that the ternary complexes are more stable than the binary complexes of primary and secondary ligands. Δ log *K* and Δ log *K*′ (Table 5) represent the difference between the stabilities of the binary and ternary metal ligand complexes with respect to both primary and secondary ligands. The positive values of Δ log *K* and Δ log *K*′ also indicate that the ternary complexes are more stable than the binary complexes.

The ordering of the formation constant for binary and ternary lanthanide complexes is Eu > Gd < Tb. The abnormal behavior of Gd can be explained on the basis of the fact that the formation constant increases from left to right in the periodic table because of the decreasing size of metal ions with subsequent increasing ionic potential. The decrease in the case of lanthanide ions is not uniform, and the smallest decrease in size of Gd(III) may be responsible for the above abnormal behavior.[19]

Conclusions

We have suggested that first proton dissociation from uracil/its halo derivatives is supposed to take place from N_3 and that the second proton dissociates either from N_1−H or from C_4−OH. From benzoic acid/its derivatives, the proton dissociation takes place from the carboxylic group. On the basis of stability constant data, it may be suggested that the coordination of uracil/its halo derivatives with lanthanides may take place through N_3−H and possibly through the C_4=O group, whereas benzoic acid/its derivatives may coordinate through the −COOH group. In the present paper, the stability constants for the binary (1:1) complexes were found to decrease in the order of Tb(III) > Eu(III) > Gd(III). Results also indicate that the ternary metal complexes of Eu(III), Gd(III), and Tb(III) are more stable than the binary complexes of the corresponding lanthanides.

Literature Cited

(1) Boccardo, F.; Canobbio, L. I. 5-Fluorouracil, twenty-five years later. An appraisal. *Chemioterapia* **1983**, *2*, 88−91.

(2) Choppin G. R.; Bertrand P. A.; Hasegawa Y.; Rizkalla E. N. Thermodynamics of Complexation of Lanthanides by Benzoic and Isophthalic Acids. *Inorg. Chem.* **1982**, *21*, 3722−3724.

(3) Reddy, P. R.; Malleswara, R. V. B. Rare Earth Complexes of Cytidine. *Inorg. Chim. Acta* **1986**, *125*, 191−195.

(4) Reddy, P. R.; Sudhakar, K. Ternary Complexes of Cytidine and Uridine- A Study with Bivalent and Trivalent Metal Ions in Solution. *Indian J. Chem.* **1990**, *29A*, 158−163.

(5) Ohyoshi, E.; Kohata, S. A Competitive Spectrophotometric Study of Eu(III) and Gd(III) Complexes with Adenosine 5′-Triphosphate by Use of a Sensitive Indicator Ligand. *J. Inorg. Biochem.* **1991**, *43*, 45−50.

(6) Meites L. *Handbook of Analytical Chemistry*, 1st ed.; McGraw-Hill: New York, 1963; p 187.

(7) Vogel, S. *Text Book of Quantitative Inorganic Analysis*, 4th ed.; Longman Group: Harlow, U.K., 1974; p 302.

(8) Bjerrum, J. *Metal Amine Complex Formation in Aqueous Solution*; Haase, Copenhagen, 1941.

(9) Calvine, M.; Wilson, K. W. Stability of Chelate Compounds. *J. Am. Chem. Soc.* **1945**, *67*, 2003−2007.

(10) Irving, H. M.; Rossotti, H. S. Methods for Computing Successive Stability Constants from Experimental Formation Curves. *J. Chem. Soc.* **1953**, 3397−3405.

(11) Irving, H. M.; Rossotti, H. S. The Calculation of Formation Curves of Metal Complexes from pH Titration Curves in Mixed Solvents. *J. Chem. Soc.* **1954**, 2904−2909.

(12) Becker, R. S.; Kogan, G. Photophysical Properties of Nucleic Acid Components. 1. The Pyrimidines: Thymine, Uracil, N,N-Dimethyl Derivatives, and Thymidine. *Photochem. Photobiol.* **1980**, *31*, 5−13.

(13) Szczesniak, M.; Nowak, M. J.; Rostkowska, H.; Szczepaniak, K.; Person, W. B.; Shugar, D. Matrix Isolation Studies of Nucleic Acid Constituents. 1. Infrared Spectra of Uracil Monomers. *J. Am. Chem. Soc.* **1983**, *105*, 5969−5976.

(14) Nakanishi, K.; Suzuki, N.; Yamazaki, F. Ultraviolet Spectra of N-Heterocyclic Systems. I. The Anions of Uracils. *Bull. Chem. Soc. Jpn.* **1961**, *34*, 53−57.

(15) Poulter, C. D.; Anderson, R. B. Direct Observation of Uracil Dication and Related Derivatives. *Tetrahedron Lett.* **1972**, 3823−3826.

(16) Tan, Y. L.; Beck, A. Complex Formation of Uracil, 2′-Deoxyuridine, and their 5-Halogenated Derivatives. *Biochim. Biophys. Acta*. **1973**, *299*, 500−506.

(17) Sekhon, B. S. Stability Constants of Mercury(II) and Beryllium-(II) Complexes with 5-Substituted-Uracils. *J. Indian Chem. Soc.* **1987**, *64*, 308−309.

(18) Reddy, P. R.; Malleswara, R. V. B. Metal Complexes of Uridine in Solution. *J. Chem. Soc., Dalton Trans* **1986**, 2331−2334.

(19) Flaschka, H. Microtitrations with Ethylenediaminetetraacetic Acid. XIV. Determination of Rare Earths. *Microchim. Acta* **1955**, 55−60.

Received for review June 15, 2004. Accepted November 17, 2004. This research was supported by UGC, New Delhi, in the form of a major research scheme [no. 12-107/2001(SR-I)].

JE0400097