

Pelagia Research Library

Der Chemica Sinica, 2012, 3(3):561-568



Complexation Behaviour and Thermodynamic Parametric Study of Lanthanone(iii) Ions with n, n-dimethylbiguanide

Jayesh Ramani, Jasmin Bhalodia, Mathurjya Neog and Sangita Sharma*

Department of Chemistry, Hemchandracharya North Gujarat University, Patan, Gujarat, India

ABSTRACT

The of complexation stability constants and thermodynamic parameters (ΔG , ΔH and ΔS) of binary Lanthanide(III) complexes where M = La(III) or Ce(III) or Pr(III) or Nd(III) or Sm(III) or Gd(III) or Dy(III) and L = N, N-dimethylbiguanide have been studied using Irving – Rossotti titration technique at ionic strength 0.2M in aqueous media at (30, 40, 50) $\pm 0.1^{\circ}$ C. The stability constant values $(log\beta_n)$ have been calculated by BEST program. The order of stability for complex is found as La(III) < Ce(III) < Pr(III) < Nd(III) < Sm(III) > Gd(III) < Dy(III). This order can be explained on the basis of basicity of ligand, electronic configuration of metal ions, size and ionic potential of tripositive ion, charge/size ratio of metal ions, gadolium break and species distribution diagrams. The mechanism through which protonation and complex formation takes place has also been discussed. Species distribution curves of complexes have been plotted using SPEPLOT program to visualize the presence of various species in thermodynamically equilibrium system.

Keywords :Binary complexes, N, N-dimethylbiguanide(DMBG), Thermodynamic parameters, Formation constants, Speciation.

INTRODUCTION

N, N-dimethylbiguanide has been introduced as an oral glucose-lowering agent for the treatment of non-insulin dependent diabetes mellitus. Like biguanide, it is a moderately strong base, forming well defined salts and possessing excellent capacity for coordination with transition metals, giving rise to highly colored bidentate chelate complexes. N, N-dimethylbiguanide lowers both basal and postprandial elevated blood glucose in patients with non-insulin-dependent diabetes(NIDDM) when hyperglycemia cannot be satisfactorily managed on diet alone [1-3]. N, N-dimethylbiguanide augments insulin-stimulated glucose uptake and metabolism by skeletal muscle and fat, and increases the suppression of hepatic gluconeogenesis by insulin.

Lanthanone(III) complexes are known for their important role in various biochemical reactions [4-9]. The compounds bearing $-NH_2$ group has a wide variety of applications in medicine[10,11], biology [12] and other fields of chemistry [13-17]. Lanthanides are typical hard acids. The low stability of lanthanide complexes can be increased by mean of chelate effect and much work has been directed towards elucidation of the stability of lanthanide chelates [18,19]. Nieboer [20] has discussed the matter in some detail and suggested that the characteristic variation in complex stability across the lanthanide series in solution state may be of diagnostic value in studying the binding sites of the ligand. The nature and interaction of various ligands with lanthanide ions has been the subject of numerous studies [21, 22].

Hence, in the present investigation, we have carried out a study on the stabilities Ln(III)N,N-dimethylbiguanide complexes and thermodynamic parameters of interest ΔG , ΔH and ΔS at 0.2M ionic strength (NaClO₄). The nature and distribution of complexes and other species formed in solution state has been explained by species distributed

curves. The stabilities of the lanthanide complexes were studied as a function of ionisation potential, ionic radius, atomic number, electronegativity of the metal ion, expansion of their coordination number, basic character of ligand and chelate effect. Gadolium break has been observed in this series of complexes.

MATERIALS AND METHODS

2.1 Chemicals

All chemicals used were analytical reagent grade. N, N-dimethylbiguanide and lanthanide nitrates (Aldrich-USA) were used without further purification. Lanthanide solutions were acidified with accurately known amounts of $HClO_4$ to prevent hydrolysis. The exact concentrations of the solutions of the lanthanide nitrates were determined by complexometric titration with disodium salt of EDTA, using EBT indicator [23]. All solutions were prepared in doubly distilled CO_2 -free water. Carbonate-free NaOH solution was standardized by reported method [24]. Perchloric acid was standardized with standard NaOH solution and constant ionic strength was maintained with an inert electrolyte sodium perchlorate (NaClO₄) (Reidol).

2.2 Apparatus and Procedure for Potentiometric Measurements

Potentiometric titrations were carried out with Systronics μ pH meter 361 having combined glass electrode and temperature probe with readability \pm 0.1°C. Temperature was maintained with High Precision Water Bath Cat. No. MSW-274 with readability \pm 0.1°C. Titrations were carried out in specially designed glass cell with magnetic stirrer in nitrogen atmosphere to avoid any side reactions. The Irving-Rossotti [25] titration method is used to evaluate the binary metal ligand stability constants at different temperatures, following sets of the solution were prepared for titration

- 1. acid [2 milimole]
- 2. acid [2 milimole] + N,N-dimethylbiguanide [0.5 milimole]
- 3. acid [2 milimole]+N,N-dimethylbiguanide [0.5milimole] + metal nitrate [0.05 milimole].

Total volume used in the cell was 50 ml, ionic strength was maintained at 0.2M (NaClO₄) and temperature at $30 \pm 0.1^{\circ}$ C in all sets. The metal to ligand ratio was mentioned as 1:10 so as to expect maximum coordination of ligands to metal ions. Titrations were carried out with carbonate free standardized 0.2M NaOH solution. All the titrations were repeated at 40 and 50^oC temperature under similar conditions.

RESULTS AND DISCUSSION

3.1 Protonation Constants of N, N-dimethylbiguanide

Protonation constants were calculated for N, N-dimethylbiguanide in the selected pH range with BEST program [26]. The values calculated are in good agreement with those given in litrature²³ and are given in (Table 1).

3.2 Stability Constants of Complexes

During complex formation, there is competition between protons and metal ion for ligand. Hydrogen ions also combine with the basic ligand or ligand ion in steps, for example the ligand, L gets protonated in the steps.

$L + H^+$ \longrightarrow LH^+	(1)
$LH^+ + H^+ $ LH_2^{2+}	(2)

Considering the concept of acid-base theory in a complex formation reaction, a ligand acts as base and a metal acts as an acid. So the stability of a complex so formed is governed by behavioural properties of both metal and ligand, considering other factors like, temperature, pressure, kinetic effect, thermodynamic effects constant. The stability constants of the binary complexes formed due to interaction of trivalent La(III) or Ce(III), or Pr(III) or Nd(III) or Sm(III) or Gd(III) or Dy(III) ion with N,N-dimethylbiguanide were calculated by measuring the magnitude of the proton liberated during the titration of the ligand in absence and in presence of metal against standard sodium hydroxide solution. The titration curves for La(III)-DMBG complexes are presented in (Figure 1). At temperature $30\pm0.1^{\circ}$ C and 0.2M dm⁻³ ionic strength (NaClO₄). The values of formation constant of [M(III)- DMBG] at three different temperature were calculated by BEST computer program [27] and are presented in (Table 2). The order of stability found is as:

La(III) < Ce(III) < Pr(III) < Nd(III) < Sm(III) > Gd(III) < Dy(III).

This order can be explain the basis of electronic configuration, size and ionic potential of tri positive ion, charge/size ratio and six membered ring formation with DMBG. This order shows Gadolium break. The stability of Ln^{3+}

Pelagia Research Library

complexes is greatest around the middle of the series (near Gadolium). This phenomenon has been called the "gadolinium Break"but its explanation is incompletely known. A similar effect has been seen with diglycollate as ligand [28].

3.3 Thermodynamic Parameters

The values of overall change in the free energy (ΔG), enthalpy (ΔH) and the entropy (ΔS) for the complexation reaction of N, N-dimethylbiguanide with Lantanone(III) ions are reported in the (Table 3). The data shows that the protonation constant of the ligand and their formation constants (log β) with metal ions decrease with increase in the temperature, indicating that formation equilibria are exothermic in nature. The negative values of the enthalpy (ΔH) and free energy (ΔG) indicate the complex formation reactions are favorable at ordinary temperature. The enthalpy changes accompanying the complexation of metal ions in the solution is the characteristic property of the heat of the reaction and measures energy difference between metal-ligand and the metal-water [M-H₂O] coordination bonds. The results obtained in the present study suggested that the metal-ligand bonds are fairly strong as evidenced by their negative enthalpy changes. For all the binary complexes studied, the negative ΔH and the positive ΔS values obtained indicate that the both enthalpy and entropy factors are favouring the complex formation. Enthalpy and Entropy factors are major driving force for the spontaneity of binary complexes and this probably has resulted from the coordination between the metal ions and nitrogen(–NH group) of the ligand. The positive entropy changes could be due to the displacement of water molecules from hydration shells of interacting ions which accompanies the essentially electrostatic interaction between positively charged metal ions and donor pair of electron of ligand.

3.4 Species Distribution and Stability Constants

Species distribution curves are plotted with the help of species SPEPLOT program and % of chemical species as function of pH for La(III)-DMBG complexes are presented in (Figure 2). For development of species distribution plots, the data was pruned for different set of models and for various expected stoichiometric species like HL, H₂L, ML, ML₂ and MLH₁. Perusal of species diagram reveals that 97-99% ML species lie in pH range 4-12 and 40-75% ML₂ species are formed in pH range of 8.5-12 in all systems. Stability constant values and species distribution diagrams reveal that ML and ML₂ are stable species formed in present set of experimental conditions. Hydroxy species, La-DMBG (OH) also appear above 8.4 pH.

3.5 Mechanism

On the basis of above study following mechanism has been proposed for protonation of N, N-dimethylbiguanide and complexation of Ln(III) with N,N-dimethylbiguanide.

Mechanism of protonation La(III)-DMBG





(IV)

 (\mathcal{O})

Formation of Ln(III) - N, N-dimethylbiguanide complex formation



ML₂ 1:2 complex

Pelagia Research Library

The cationic form of N, N-dimethylguanide is protonated at imino group and through this are an intramolecular N-H^{...}N hydrogen bond is formed which stabilized the conformation of cation in the structure. A complex of deprotonated form of N, N-dimethylguanide with Lanthanide(III) ion is produced in alkaline media. The deprotonation of ligand causes an increase in π -conjugation of C-N-C system reducing bond angle at the centre N atom to nearly to 120° making it more susceptible for complexation. Metal complexes of N, N-dimethylguanide as ligand are expected to be cationic in nature in solution state. It is proposed that this bidentate ligand can chelate to metal ion in octahedral configuration through four nitrogen atoms of two ligands in ML₂ type of complexes.

Table 1 Values of log β_i and pk_i for N,N-dimethylbiguanide and various observed parameters at temperature $30\pm0.1^{\circ}C$, μ = 0.2M dm⁻³ NaClO₄

pK ₁ ^H	11.30	11.52 ^a
pK_2^H	2.68	2.77 ^a
$\log \beta_1$	11.30	
$\log \beta_2$	13.98	
$L + H^+$	11.30	
$LH^{+} + H^{+}$	2.68	
No. data points	43	
No. of titration	2	
Concentration of ligand in millimoles	0.5	
pH range	1.52 - 9.23	5
Smin ^b	0.1614	

^a J.A. Dean [27] ^b A.E. Martell and R.J. Moteksites [26]

Table 2 Lanthanone(III)-N,N-dimethybiguanide Stability Constant values

Motel ligend	$\log K_1$				$logK_2$		$Log\beta_2$			
Wietai-iigaliu	30°C	40°C	50°C	30°C	40°C	50°C	30°C	40°C	50°C	
La(III)-DMBG	6.9848	6.900	6.8212	2.4903	2.4041	2.3800	9.4751	9.3041	9.2012	
No. of data pints	33	31	32	33	31	32	33	31	32	
No. of titration	2	2	2	2	2	2	2	2	2	
pH range	1.14-11.05	1.14-11.04	1.13-11.05	1.14-11.05	1.14-11.04	1.13-11.05	1.14-11.05	1.14-11.04	1.13-11.05	
Smin	0.151	0.151	0.150	0.151	0.151	0.150	0.151	0.151	0.150	
Ce(III)-DMBG	7.5307	7.4281	7.3401	2.5139	2.3801	2.3191	10.0446	9.8082	9.6591	
No. of data pints	38	37	38	38	37	38	38	37	38	
No. of titration	2	2	2	2	2	2	2	2	2	
pH range	1.51-11.23	1.50-11.22	1.50-11.23	1.50-11.23	1.50-11.22	1.50-11.23	1.50-11.23	1.50-11.22	1.50-11.23	
Smin	0.569	0.570	0.568	0.569	0.570	0.568	0.569	0.570	0.568	
Pr(III)-DMBG	7.9505	7.7066	7.6113	2.5801	2.5194	2.4995	10.5306	10.2200	10.1110	
No. of data pints	44	44	43	44	44	43	44	44	43	
No. of titration	2	2	2	2	2	2	2	2	2	
pH range	1.55-10.83	1.56-10.82	1.54-10.82	1.55-10.83	1.56-10.82	1.54-10.82	1.55-10.83	1.55-10.86	1.54-10.82	
Smin	0.426	0.425	0.423	0.426	0.425	0.423	0.426	0.425	0.423	
Nd(III)-DMBG	8.5160	8.4192	8.4082	2.6093	2.4108	2.4041	11.1253	10.8300	10.8120	
No. of data pints	40	40	41	40	40	41	40	40	41	
No. of titration	2	2	2	2	2	2	2	2	2	
pH range	1.54-11.0	1.53-10.98	1.53-10.96	1.54-11.0	1.53-10.98	1.53-10.96	1.54-11.0	1.53-10.98	1.53-10.96	
Smin	0.427	0.426	0.425	0.427	0.426	0.425	0.427	0.426	0.425	
Sm(III)-DMBG	8.6743	8.6038	8.5106	2.6813	2.4073	2.3530	11.3556	11.0110	10.9430	
No. of data pints	34	34	33	34	34	33	34	34	33	
No. of titration	2	2	2	2	2	2	2	2	2	
pH range	1.52-11.12	1.51-11.11	1.52-11.13	1.52-11.12	1.51-11.11	1.52-11.13	1.52-11.12	1.54-11.11	1.52-11.13	
Smin	0.107	0.105	0.106	0.107	0.105	0.106	0.107	0.105	0.106	
Gd(III)-DMBG	6.7664	6.6503	6.5106	2.5013	2.3901	2.3019	9.2677	8.9404	8.8125	
No. of data pints	34	33	34	34	33	34	34	33	34	
No. of titration	2	2	2	2	2	2	2	2	2	
pH range	1.16-11.10	1.14-11.09	1.15-11.08	1.16-11.10	1.14-11.09	1.15-11.08	1.16-11.10	1.14-11.09	1.15-11.08	
Smin	0.192	0.190	0.193	0.192	0.190	0.193	0.192	0.190	0.193	
Dy(III)-DMBG	7.0280	6.8108	6.7403	2.5314	2.3009	2.1711	9.5594	9.1117	8.9114	
No. of data pints	33	33	33	33	33	33	33	33	33	
No. of titration	2	2	2	2	2	2	2	2	2	
pH range	1.14-11.5	1.13-11.6	1.14-11.7	1.14-11.5	1.13-11.6	1.14-11.7	1.14-11.5	1.13-11.6	1.14-11.7	
Smin	0.155	0.158	0.155	0.155	0.158	0.155	0.155	0.158	0.155	

Table 3 Thermodynamic Parameters of Lathanone(III)-N,N-dimethybiguanide complexes

Metal Complex		ΔG	(K· Cal · m	ol ⁻¹)	$\Delta H (\mathbf{K} \cdot \mathbf{Ca})$	$1 \cdot mol^{-1}$	$\Delta S (\mathbf{K} \cdot \mathbf{Cal} \cdot \mathbf{mol}^{-1})$	
		30°C	40°C	50°C	40°C	50°C	40°C	50°C
La(III)-DMBG ^c	logK1	-9.684	-9.882	-10.082	-3.675	-3.640	0.01983	0.01994
	logK ₂	-13.039	-13.326	-13.599	-4.334	-4.754	0.05733	0.05776
Ce(III)-DMBG	logK ₁	-10.441	-10.639	-10.849	-4.446	-4.065	0.01978	0.02100
	logK ₂	-13.796	-14.048	-14.276	-6.145	-6.888	0.06581	0.06688
Pr(III)-DMBG	logK1	-11.023	-11.038	-11.250	-10.570	-4.403	0.00149	0.02119
	logK ₂	-14.377	-14.781	-15.092	-2.136	-5.045	0.05449	0.06334
Nd(III)-DMBG	logK1	-11.807	-12.058	-12.427	-4.195	-0.508	0.02512	0.03690
	logK ₂	-15.162	-15.511	-15.981	-4.563	-0.817	0.06509	0.05216
Sm(III)-DMBG	logK1	-12.027	-12.323	-12.579	-3.055	-4.306	0.02961	0.02561
	logK ₂	-15.381	-15.771	-16.174	-3.575	-3.141	0.06256	0.06042
Gd(III)-DMBG	logK ₁	-9.354	-9.525	-9.623	-4.165	-6.454	0.01713	0.00981
	logK ₂	-12.708	-12.805	-13.025	-9.764	-5.909	0.07416	0.05978
Dy(III)-DMBG	logK ₁	-9.744	-9.755	-9.962	-9.413	-3.257	0.00109	0.02076
	logK ₂	-13.099	-13.050	-13.171	-14.545	-9.254	0.09123	0.07250

^c Lathanone(III)-N,N-dimethybiguanide



Figure 1 Representative titration curves for formation of La(III)- N,N-dimethybiguanide complexes at $30 \pm 0.1^{\circ}$ C and 0.2M ionic strength in aqueous solution.



Figure 2 Species Distribution diagram of La(III)-N,N-dimethybiguanide complexes at $30 \pm 0.1^{\circ}$ C and 0.2M ionic strength in aqueous solution.

CONCLUSION

N, N-dimethylguanide forms ML and ML₂ type of binary complexes in solution state when ratio of metal to ligand taken was 1:10 and ionic strength maintained was 0.2M. The conformer protonated at imino group is most stabilized one due to intramolecular N-H^{...}N hydrogen bond formation in the structure. Deprotonation of ligand at higher pH causes an increase in π -conjugation of C-N-C system making it more susceptible for complexation. Thermodynamic studies have shown that reactions are exothermic in nature favored by enthalpy change. The positive values of Δ S indicate that complexation is entropically favored under this experimental condition. Species distribution studies explain for availability of lanthanide ion at lower pH and in complexed state at higher pH. This study can be useful to understand bioavailability of Lanthanide (III) ions in free or in combined state at a particular pH.

REFERENCES

- [1] D. Stepensky, M. Friedman, W. Srour, I. Raz, A. Hoffman, J. Control Rel., 2001, 71, 107.
- [2] G. Balan, P. Timmins, D. S. Green, P. H. Marather, J. Pharm. Sci., 2001, 9, 1176.
- [3] G. Gusler, J. Gorsline, G. Levy, S. Zhang, I. E. Weston, D. Naret, B. Berner, Clin. Pharm., 2001, 4, 655.
- [4] G. R. Choppin, A. J. Graffeo, J. Inorg. Chem., 1963, 4, 1254.
- [5] L. Feng, X. He, H. Xiao, Z. Li, F. Li, N. Liu, Z. Chai, Y. Zhao, Z. Zhang, Biol. Trace Ele. Res., 2007, 117, 89.
- [6] M. D. Lind, B. Lee, J. L. Hoard, J. Am. Chem. Soc., 1965, 87, 1612.
- [7] H. G. Brittain, F. S. Richardson, *Bioinorg. Chem.*, 1977, 7, 233.
- [8] S. M. Khetre, H. V. Jadhav, P. N. Jagadale, S. R. Kulal, S. R. Bamane, Adv. Appl. Sci. Res., 2011, 2(4), 503.
- [9] M. E. Mohamed, Der Chemica Sinica., 2011, 2(4), 274.
- [10] S. P. Fricker, Chem. Soc. Rev., 2006, 35, 524.
- [11] G. Otting, J. Biomol. NMR, 2008, 42, 1.
- [12] M. A. Kapadia, M. M. Patel, G. P. Patel, J. D. Joshi, Inter. J. Poly. Mater., 2007, 56, 549.
- [13] D. S. Pabreja, R. A. Patel, S. S. Sharma, J. J. Vora, J. D. Joshi, Asian J. Chem., 2001, 13, 357.
- [14] M. P. Brahmbhatt, S. S. Sharma, J. J. Vora, J. D. Joshi, Ultra Sci., 2002, 14, 262.
- [15] D. A. Robertis, D. C. Stefano, C. Rigano, S. Sammartano, J. Solution Chem., 1990, 19, 569.
- [16] R. C. Castro, R. C. Varela, R. Herrero, M. E. Sastre de Vicente, Talanta, 2003, 60, 93.
- [17] A. A. El-Sherif, M. M. Shoukry, R. V. Eldik, J. Chem. Soc. Dalton Trans., 2003, 8, 1425.
- [18] T. Moeller, D. F. Martin, L. C. Thompson, R. Ferrus, G. R. Feistel, W. J. Randall, Chem. Rev., 1965, 65, 1.
- [19] A. Tyagi, R. Sharma, H. Sharma, *Der Chemica Sinica*, **2011**, 2(6), 20.

- [21] C. Hong, D. Kim, K. Choi, C. Kim Y. Choi, Bull. Korean Chem. Soc., 1999, 20, 297.
- [22] R. Gupta, N. Agrawal, K. C. Gupta, Der Chemica Sinica, 2012, 3(1), 91.
- [23] H. A. Flaschka; EDTA Titrations, Pergamon, Oxford, 1964.
- [24] A. I. Vogel; A Text Book of Quantitative Inorganic Analysis, Longmans, London, 1978.
- [25] H. M. Irving, H. S. Rossotti, J. Chem. Soc., 1954, 2904.
- [26] A. E. Martell, R. J. Motekaitis; Determination and use of stability constants, VCH publishers, New York, 1992.
- [27] John, A. Dean; Lange's handbook of chemistry, 13th ed., McGraw-Hill Company, New York, **1987**.
- [28] C. H. Evans; Biochemistry of the Lanthanides, Plenum Press, London, 1990.

^[20] E. Nieboer, Struct. Bonding, 1975, 22, 1.