Mixed Chelates of Some Trivalent Lanthanide Ions Containing (*trans*-1,2-Cyclohexylenedinitrilo)tetra-acetate and Norleucinate

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Summary. Formation constants of mixed chelates with (*trans*-1,2-cyclohexylenedinitrilo)tetra-acetate (*DCTA*) as primary ligand and norleucinate (*nle*) as secondary ligand with metal ions La(III), Ce(III), Pr(III), Sm(III), Gd(III), Tb(III), Dy(III), Er(III), and Yb(III) have been determined by the modified potentiometric *pH* titration method of Irving-Rossotti in aqueous medium at (295 ± 1) K and fixed ionic strength of $\mu = 0.1\,M$ (NaClO$_4$). Formation constants of binary complexes of the metal ions with the secondary ligand have also been determined under identical conditions. The mixed chelates were found to be more stable than the binary ones. The order of stabilities in terms of metal ions is La(III) < Ce(III) < Pr(III) < Sm(III) > Gd(III) < Tb(III) < Dy(III) < Er(III) < Yb(III) for binary and ternary complexes with a prominent "Gadolinium break".

Keywords. *DCTA*; Lanthanides; Norleucinate; Mixed chelates.

Gemischte Chelate einiger dreiwertiger Lanthanidenionen mit (*trans*-1,2-Cyclohexylendinitril)tetraacetat und Norleucinat

Zusammenfassung. Es wurden die Komplexbildungskonstanten gemischter Chelate mit (*trans*-1,2-Cyclohexylendinitril)tetraacetat als Primärkomponente und Norleucinat als Sekundärkomponente mit den Metallionen La(III), Ce(III), Pr(III), Sm(III), Gd(III), Tb(III), Dy(III), Er(III) und Yb(III) mittels einer modifizierten potentiometrischen Titrationsmethode nach Irving-Rossotti in wäßrigem Medium bei (295 ± 1) K und einer konstanten Ionenstärke von $\mu = 0.1\,M$ (NaClO$_4$) bestimmt. Die Bildungskonstanten der binären Komplexe der Metallionen mit dem Sekundärliganden wurden ebenfalls unter identen Bedingungen bestimmt. Es wurde festgestellt, daß die gemischten Chelate stabiler sind als die binären. Die Stabilitätsreihenfolge bezüglich der Metallionen ist La(III) < Ce(III) < Pr(III) < Sm(III) > Gd(III) < Tb(III) < Dy(III) < Er(III) < Yb(III) für die binären und ternären Komplexe; es zeigt sich dabei bei Gd(III) ein deutlicher Bruch in der Reihenfolge.

Introduction

The polyaminocarboxylic acid, due to their high complexing ability have a variety of applications in analytical chemistry, nuclear medicine, chelation therapy and they interact in many biological systems [1–4]. (*Trans*-1,2-cyclohexylenedinitrilo)tetra-acetic acid (*DCTA*) is known to form stronger complexes with metal

ions as compared to the widely used *EDTA* (the stability constants are 10 to 1000 times larger than those of *EDTA* complexes) [5], due to the presence of the cyclohexane ring, which immobilizes the C – C bond between two nitrogens, thus causing an optimal orientation for coordination. It is well-known that the mixed chelate complexes play an important role in biological processes [6–16]. A literature survey shows that no work has been done on the mixed ligand formation of complexes of lanthanides containing (*trans*-1,2-cyclohexylenedinitrilo)tetra-acetate and norleucinate. Hence, it was intended to study the formation and stability of complexes of some lanthanide ions with the above two chelates and in this communication the stability constants of La(III), Ce(III), Pr(III), Sm(III), Gd(III), Tb(III), Dy(III), Er(III), and Yb(III) ions containing (*trans*-1,2-cyclohexylenedinitrilo)tetra-acetate and norleucinate are reported.

Experimental

Solutions of metal ions (0.001 *M*) were prepared by weighing out 'AnalaR' grade metal nitrates (Indian Rare Earths Limited) into doubly distilled water and the analyses of all the metals were carried out spectrophotometrically using a SICO UV-VIS spectrophotometer model DIGISPEC 110 D. The solutions of (*trans*-1,2-cyclohexylenedinitrilo)tetra-acetate (0.001 *M*) and norleucinate (0.001 *M*) were prepared by dissolving an appropriate amount of sodium salt of the *DCTA* or norleucine in doubly distilled water. The concentrations were estimated by potentiometric titrations. Pure sodium perchlorate monohydrate was used after repeated recrystallization from water. Perchloric acid (0.1 *M*) was prepared by diluting AnalaR sample in distilled water and its concentration was determined potentiometrically with standard NaOH solution. Carbonate free sodium hydroxide was prepared as described by Vogel [17] and standardized against 'AnalaR' potassium hydrogen phthalate, dried at 388 K.

A Systronics auto-calibrated microprocessor controlled *pH* meter model μ pH System-361 associated with combined glass and calomel electrode (precision ±0.01 *pH* unit) was used to measure the *pH*. The electrode was standardized using solutions of 0.05 *M* potassium hydrogen phthalate (*pH* = 4.008 at 298 K) and 0.01 *M* borax (*pH* = 9.180 at 298 K) [18]. Titrations were performed at 295.0 ± 1.0 K in a thermostated reaction vessel. For computation, a 80 386 base super AT computer was used and using FORTRAN 77 most of the calculations were performed.

Proton ligand and metal ligand formation constants have been determined using the Irving-Rossotti *pH* titration technique [19]. The mixture of solutions (a) 1 · 0.1 *M* perchloric acid; (b) 1 · 0.1 *M* perchloric acid + 25 · 0.001 *M* H*nle* solution and (c) 1 · 0.1 *M* perchloric acid + 25 · 0.001 *M* H*nle* solution + 5.0 · 0.001 *M* metal solution were prepared to study the binary complexes and (d) 1 · 0.1 *M* perchloric acid, (e) 1 · 0.1 *M* perchloric acid + 5 · 0.001 *M* H*nle* solution, (f) 1 · 0.1 *M* perchloric acid + 5 · 0.001 *M* *DCTA* + 5 · 0.001 *M* metal solution and (g) 1 · 0.1 *M* perchloric acid + 5 · 0.001 *M* *DCTA* + 5 · 0.001 *M* H*nle* + 5 · 0.001 *M* metal solution were prepared for the study of ternary complexes. The total volume was maintained 50 ml by addition of doubly distilled water. The ionic strength was maintained 0.1 *M* by adding appropriate amount of neutral sodium perchlorate to each set of the mixture solution. The ratio between the metal salt and ligand in binary complexes was such (1 : 5), that the maximum coordination number of the metal ion could be satisfied. For the study of ternary complexes the ratio of metal, primary ligand (*DCTA*), and secondary ligand (H*nle*) was maintained 1 : 1 : 1. A graph between *pH* meter reading (B) and the volume of sodium hydroxide added was plotted. The nature of the graphs were similar for all metal ions and the curves for binary and ternary complex of a representative metal ion, Sm(III), is shown in Fig. 1. The titration curves for the *M-nle* system were referred to as (*a*): acid titration curve, (*b*): secondary ligand titration curve, (*c*): binary complex titration curve; and the titration curves for the *M-(DCTA)-(nle)* system were referred to as (*d*): acid titration curve, (*e*): secondary ligand titration curve, (*f*): primary complex titration curve, and (*g*): ternary complex titration curve.
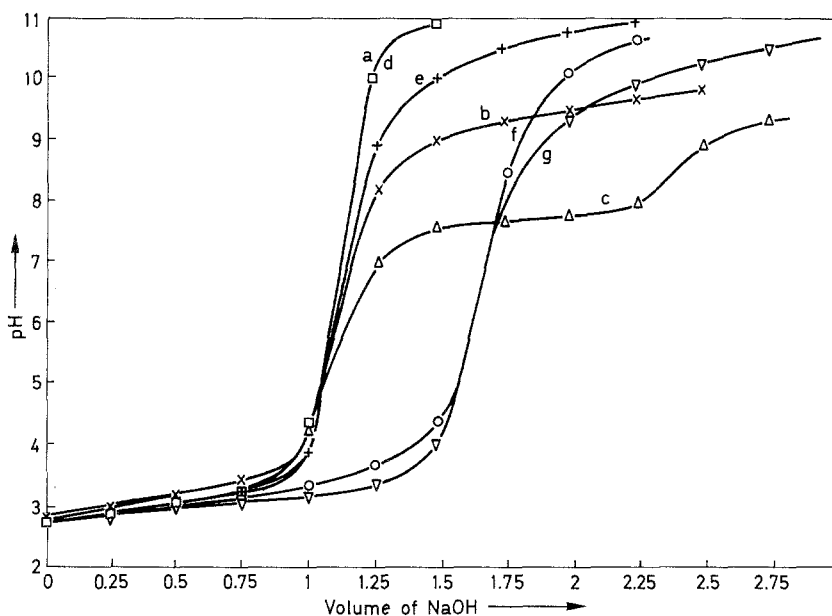
Fig. 1. Titration curves for the Sm-*nle* and Sm-*DCTA-nle* systems.
Binary complex curves: *a*: acid titration curve ($\square$), *b*: secondary ligand titration curve ($\times$), *c*: binary complex titration curve ($\triangle$). Ternary complex curves: *d*: acid titration curve (same as *a*) ($\square$), *e*: secondary ligand titration curve (+), *f*: primary complex titration curve ($\diamond$), *g*: ternary complex titration curve ($\triangledown$)

Results and Discussions

The practical proton ligand stability constant (K_n^H) for the norleucinate-metal system was calculated from *pH* titration data by various computational methods [19] at 295 ± 1 K and $\mu = 0.1$ (NaClO$_4$) using the relation

$$\log K_n^H = pH + \log \frac{\bar{n}_H - (n-1)}{n - \bar{n}_H}, \tag{1}$$
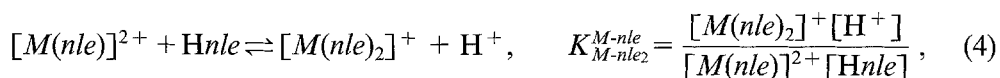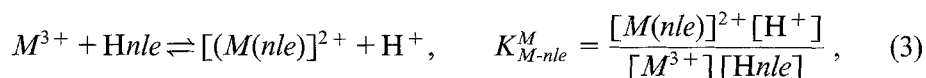
where $\bar{n}_H$ is the average number of protons bound per free ligand ion and n is the number of protons attached to the ligand in a ligand-proton complex. The value of $\bar{n}_H$ at various *pH* meter reading (B) was also plotted against B to obtain the value of pK_n^H. This was further corroborated by a straight line plot of $\log \bar{n}_H/(1 - \bar{n}_H)$ against B (not shown in Fig. 1). The curve obtained for $\bar{n}_H$ versus (B) was extended between 0 and 1 in the $\bar{n}_H$ scale of H*nle* indicating the dissociation of H*nle* as follows,

$$Hnle \rightleftharpoons nle^- + H^+. \tag{2}$$

The values of $\bar{n}$ lie between 0 to 2.5 for the *M-nle* system. The deviation of the formation curve (curve *c*) of the binary complex at lower *pH* from the free ligand curve (curve *b*) indicates the formation of the binary complex. The nature of the curve also reveals the stepwise formation of the complex,

Table 1. Stability constants of binary and ternary lanthanide(III) complexes [temp. 295 K; ionic strength 0.1 (mol dm^{-3}, NaClO$_4$)]

Formation constant	La(III) (4f⁰)	Ce(III) (4f¹)	Pr(III) (4f²)	Sm(III) (4f⁵)	Gd(III) (4f⁷)	Tb(III) (4f⁸)	Dy(III) (4f⁹)	Er(III) (4f¹¹)	Yb(III) (4f¹³)
$\log K^M_{M\text{-}nle}$	4.60	4.68	4.78	5.06	4.72	4.84	4.93	5.46	5.67
$\log K^{M\text{-}nle}_{M\text{-}nle_2}$	4.49	4.54	4.63	4.87	4.65	4.54	4.63	4.89	5.01
$\log K^{M\text{-}nle_2}_{M\text{-}nle_3}$	3.46	3.53	3.60	3.63	3.79	–	3.89	3.95	4.0
$\log K^M_{L\text{-}nle_3}$	12.55	12.75	13.01	13.56	13.16	–	13.45	14.30	14.68
$\log K^{M\text{-}DCTA}_{M\text{-}DCTA\text{-}nle}$	8.08	9.30	9.32	9.79	8.08	8.63	8.65	9.57	9.75
$\Delta \log K_1$	3.48	4.62	4.54	4.73	3.36	3.79	3.72	4.11	4.08
$\Delta \log K_2$	3.59	4.76	4.69	4.92	3.43	4.09	4.02	4.68	4.74
$\Delta \log K_3$	4.62	5.77	5.72	6.16	4.29	–	4.76	5.62	5.75

$$M^{3+} + Hnle \rightleftharpoons [(M(nle)]^{2+} + H^+, \qquad K^M_{M\text{-}nle} = \frac{[M(nle)]^{2+}[H^+]}{[M^{3+}][Hnle]}, \qquad (3)$$

$$[M(nle)]^{2+} + Hnle \rightleftharpoons [M(nle)_2]^+ + H^+, \qquad K^{M\text{-}nle}_{M\text{-}nle_2} = \frac{[M(nle)_2]^+[H^+]}{[M(nle)]^{2+}[Hnle]}, \qquad (4)$$

$$[M(nle)_2]^+ + Hnle \rightleftharpoons [M(nle)_3] + H^+ \qquad K^{M\text{-}nle_2}_{M\text{-}nle_3} = \frac{[M(nle)_3][H^+]}{[M(nle)_2]^+[Hnle]}. \qquad (5)$$

(The remaining coordination sites of the metal ions are assumed to be occupied by water molecules.)

The calculation of the stepwise metal ligand stability constants, $K^M_{M\text{-}nle}$, $K^{M\text{-}nle}_{M\text{-}nle_2}$ and $K^{M\text{-}nle_2}_{M\text{-}nle_3}$ was carried out by plotting a graph of $\bar{n}$ versus pL and then applying various computational methods [19]. The average values of logarithms of the stability constants are summarized in Table 1. Precipitation for all the binary complexes was obtained between pH 8.01 to 9.41.

The formation of ternary complexes was concluded initially from qualitative evidence. No precipitation was obtained up to pH 11 for mixed ligand systems. Further evidence was provided by comparing the ternary complex titration curve (curve g) with the composite curve (not shown in Fig. 1). The composite curve was drawn theoretically by graphical addition of the 1 : 1 M-$DCTA$ curve and the titration curve for the free ligand norleucine. If there is any interaction between M-$DCTA$ and nle, the composite curve should be displaced from the experimental curve (g). It was observed that for each mixed ligand system the composite curve was located on the left-hand side of the experimental curve (g) in the pH range 3.5–9.0. The nature of the complex equilibrium, whether stepwise or simultaneous, was investigated according to the method suggested by Carey and Martell [20]. It was observed (curve f of Fig. 1) that the chelate M-$DCTA$ is formed at lower pH and undergoes hydroxo complex formation at higher pH. The curve (g) deviates from curve (f) at lower pH indicating the formation of the M-$DCTA$-nle complex, and the deviation above pH 7 may be attributed to the formation of the hydroxo complex.

The stability constants for the ternary systems were computed from the titrations in which the concentrations of M(III): $DCTA$: $Hnle$ were kept in the ratio 1 : 1 : 1. Calculations were restricted to pH value below 8.0 in order to avoid the complication due to hydrolysis of various complex species at higher pH. The average number of secondary ligands attached per M(III)-$DCTA$ complex ion $\bar{n}_{mix}$ was calculated using the equation

$$\bar{n}_{mix} = \frac{(V_3 - V_2)(N + E_0)}{(V_0 + V_1)\bar{n}_H T_{cL}} , \tag{6}$$

where V_0 is the initial volume, V_1 is the volume of NaOH required in the titration of mixture (a), V_3 is the horizontal distance between curve (g) and (f), and V_2 is the horizontal distance between curve (e) and (d) in the same pH axis. $(V_3 - V_2)$ is equal to the amount of the secondary ligand attached to the M(III)-$DCTA$ ion; T_{cL} is the total ligand concentration, N the normality of alkali and E_0 is the initial concentration of the free acid. The value of $\bar{n}_H$ was taken from the M(III)-secondary ligand system. The value of pL was calculated using the equation

$$pL_{mix} = \log \frac{\sum\limits_{n=0}^{J} \beta_n^H [1/\text{antilog} pH]^n [V_0 + V_3]}{[T_{cL} - \bar{n}_{mix} \cdot T_{cM}] V_0} , \tag{7}$$

where β_n^H is the overall proton ligand stability constant and T_{cM} is the total metal concentration. The metal mixed ligand formation constants have been calculated by different computational methods [19], using the equation

$$\log K_{M\text{-}DCTA\text{-}nle}^{M\text{-}DCTA} = pL_{mix} + \log \frac{\bar{n}_{mix}}{1 - \bar{n}_{mix}} . \tag{8}$$

The average values for all the metals are shown in Table 1. The relative stability of mixed chelates is judged from the mixing constant (K_{mix}) or stabilization constant ($\Delta \log K$ or K_s) [21]. The mixing constant, K_{mix}, [21] for the formation of ternary complexes of the type MA_iB_j is defined as

$$K_{mix} = \beta_{ij} / \beta_{n0}^{i/n} \cdot \beta_{0n}^{j/n} , \tag{9}$$

where β_{ij}, β_{n0} and β_{0n} are the stability constants for MA_iB_j, MA_n, and MB_n complexes, respectively; $i + j = n$, the total number of ligands attached to the metal ion. The major contribution to the mixing constant arise from statistical arguments. However, the stabilization constant, K_s, [22] measures the extra stability (sometimes instability) of the ternary complex due to electrostatic forces, geometric factors, solvent effects, etc. in addition to the statistical factor which for ligands of equal denticity is given by

$$\log K_s = \log K_{mix} - \log \binom{n}{i} , \tag{10}$$

where $\binom{n}{i}$ is the binomial coefficient. $\Delta \log K$ is also a measure of catalytic activity of the metal ion [23]. However, when the ligands differ in denticity, it is possible to compare the mixed complexes with the binary complexes through parameter ΔK [21]. The $\Delta \log K$ values for binary and ternary complexes are defined below,

$$\Delta \log K_1 = \log K_{M\text{-}DCTA\text{-}nle}^{M\text{-}DCTA} - \log K_{M\text{-}nle}^{M} , \tag{11}$$

$$\Delta \log K_2 = \log K_{M\text{-}DCTA\text{-}nle}^{M\text{-}DCTA} - \log K_{M\text{-}nle2}^{M\text{-}nle} , \tag{12}$$

$$\Delta \log K_3 = \log K_{M\text{-}DCTA\text{-}nle}^{M\text{-}DCTA} - \log K_{M\text{-}nle3}^{M\text{-}nle2} . \tag{13}$$
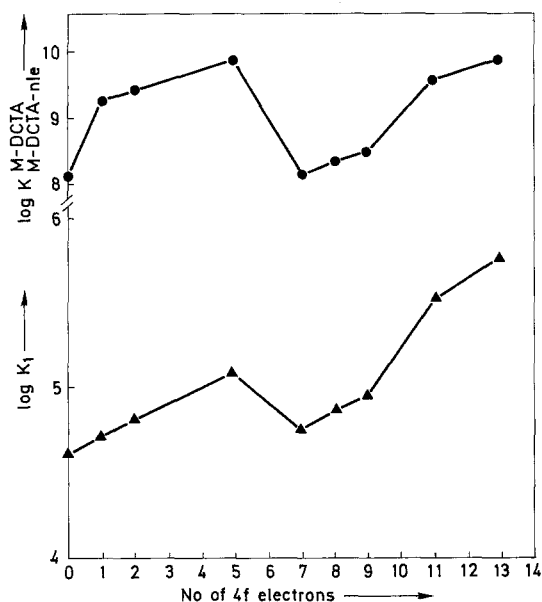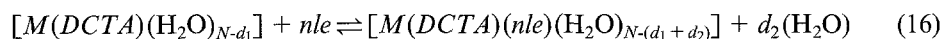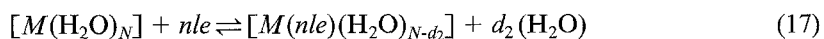
Fig. 2. Variation in the formation constants with the no. of $4f$-electrons of $Ln(III)$ ions [▲: $\log K^M_{M\text{-}nle}$, ●: $\log K^{M\text{-}DCTA}_{M\text{-}DCTA\text{-}nle}$]

It may be observed that successive addition of each ligand is less favourable than previous addition. There are many reasons, statistical, steric and electrostatic, for the observed decrease of successive stability constants. In general, addition of a secondary ligand to a metal chelate, $[M(DCTA)(H_2O)_{N\text{-}d_1}]$ is less favoured than the addition of a ligand to $[M(H_2O)_N]$, due to the effects mentioned above as may be seen from the reactions

$$[M(DCTA)(H_2O)_{N\text{-}d_1}] + nle \rightleftharpoons [M(DCTA)(nle)(H_2O)_{N\text{-}(d_1+d_2)}] + d_2(H_2O) \quad (16)$$

and

$$[M(H_2O)_N] + nle \rightleftharpoons [M(nle)(H_2O)_{N\text{-}d_2}] + d_2(H_2O) \quad (17)$$

(charges are omitted for simplicity), where N is the maximum coordination number of the metal ion, d_1 and d_2 are the denticities of $DCTA$ and nle, respectively. From statistical considerations it can be concluded that $\log K^M_{M\text{-}nle}$ should be larger than $\log K^{M\text{-}DCTA}_{M\text{-}DCTA\text{-}nle}$, as there is more electronic dipolar electronic repulsion between different ligand anions in the M-$DCTA$-nle system. $\Delta \log K$ should be negative. On the contrary, the $\Delta \log K_1$ (also $\Delta \log K_2$ and $\Delta \log K_3$) were found to be positive indicating that the ternary complexes are more stable than the binary ones. This is in agreement with the finding of Sigel [24–26], Martell [27], and Dey [28]. It is worthy to note here that $\Delta \log K_1$ values were found to be negative for some transition metal ions with the same ligand pair [29]. Since for transition metals $d_1 + d_2 > N$ ($N = 6$), there is no possibility of adding the ligand nle to $[M(DCTA)]$ without releasing some of the coordination groups of $DCTA$. In such case destabilization occurs and $\Delta \log K < 0$. However, for lanthanides the coordination number N is generally eight or nine and $d_1 + d_2 \leqslant N$. Hence, $\Delta \log K > 0$ and ternary complexes are relatively stabilized [21] as observed in the present study. The

cooperative effect between the primary and secondary ligand [30] may also account for the greater stability of ternary complexes.

A plot of log $K^{M\text{-}DCTA}_{M\text{-}DCTA\text{-}nle}$ (or log $K^{M}_{M\text{-}nle}$) versus $4f^n$ configuration (Fig. 2) indicate a gradual increase in log K with filling up $4f$ electrons, with a marked depression of Gd(III) which is a manifestation of the tetrad effect [31] and the "Gadolinium break" [32]. The discontinuity at gadolinium may be attributed to the discontinuity in the crystal radii of its ion or more plausibly, both may reflect small ligand field stabilization energies (LFSE) associated with the splitting of the partially filled f orbitals.

Acknowledgements

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