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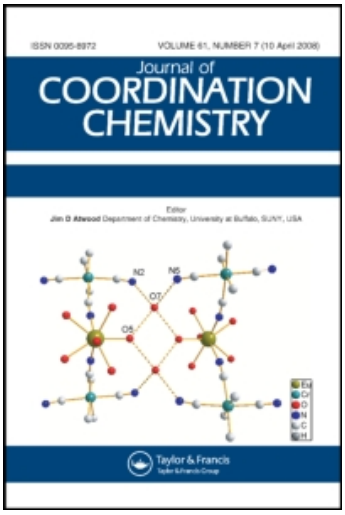

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Study on the interaction of lanthanum(III) with adrenaline

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Lanthanum(III) equilibria in the presence of adrenaline have been investigated by potentiometric titration under physiological conditions (37°C and an ionic strength of 0.15 M NaCl). The interaction of lanthanum(III) with adrenaline has also been studied using an ab initio method. The complex species in the lanthanum(III)–adrenaline system have been ascertained and the protonation constants for adrenaline and the stability constants for lanthanum(III) complexes with adrenaline have been obtained. Adrenaline can form stable lanthanum(III) complexes with the phenolic hydroxyl group of adrenaline as the binding site of lanthanum(III).

Keywords: Lanthanum(III); Adrenaline; Potentiometric titration; ab initio

1. Introduction

Rare earth compounds are applied extensively in agriculture in China [1], eliciting quite a significant improvement in yield for many kinds of crops, such as wheat, sugar beets, rice, corn and soy beans. However, the effect of rare earth metals on the environment and the human body remains unclear. Thus, studies on the biological effects of rare earth metals have attracted substantial attention in China [1,2]. Earlier work has revealed that rare earth metals show interesting biological effects, such as the enzyme effect [3]. For example, some enzymes (glutamine synthetase, phospholipase A2, etc.) can be activated by lanthanides. Meanwhile, some enzymes (aldolase, pyruvate kinase) can be inhibited by lanthanides. In recent years, we have studied the neural-endocrine effects of rare earth metals both in vitro and in vivo using various methods, showing for the first time that rare earth metals can influence the neural-endocrine system, and promote the secretion of hormones, such as tetraiodothyronine (T_4), and growth hormone (GH) [1]. To clarify the neural-endocrine effect of rare earth

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metals and mechanism further we studied the interaction of lanthanides with T_4 by pH potentiometry, NMR and spectroscopy [4]. Adrenaline or epinephrine (3,4-dihydroxy-α-(methylaminomethyl)benzyl alcohol, $(HO)_2C_6H_3CH(OH)CH_2NHCH_3$) is a kind of hormone. Some studies on complexes of metal ions with adrenaline have been reported [5–9]. However, so far, no research has been published concerning the interaction of lanthanum(III) with adrenaline. In particular, that group within the adrenaline molecule, which serves as a donor, has been a controversial subject for a long time. As a continuation of our studies on the interaction of lanthanides with hormones, we have investigated the interaction of lanthanum(III) with adrenaline by potentiometric titration and by a quantum chemical ab initio method and present the results below.

2. Experimental

2.1. *Reagents and solutions*

Lanthanum(III) chloride solution was prepared by dissolving lanthanum oxide (99.9%) in concentrated HCl. The resultant stock solution of lanthanum(III) chloride was adjusted to pH 3–4 using NaOH solution, and the concentration of lanthanum(III) was determined by titration with EDTA using xylenol orange as an indicator. Working solutions were made by diluting the stock solution. Adrenaline (3,4-dihydroxy-α-(methylaminomethyl)benzyl alcohol, biochemical reagent) was purchased from Sigma Chemical Co. After drying in a vacuum desiccator over P_2O_5, a weighted quantity of the reagent was dissolved in deionized water. A fresh adrenaline solution was used in these studies. Carbonate-free NaOH solutions were standardized with potassium biphthalate. Other chemicals were of analytical grade. Deionized water was used to prepare all solutions.

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2.2. *Potentiometric titration*

Potentiometric titrations were performed on a pHS-3C pH meter under physiological conditions (37°C and an ionic strength of 0.15 M NaCl) using titration techniques described previously [10,11]. The solutions to be titrated (40 cm^3) contained 5×10^{-4} M La(III) and 1×10^{-3} M adrenaline. 0.05 M NaOH was used as a titrant. The potentiometric data were treated on a Compaq 386/25e computer using the Program SCOGS2 [12] to obtain the protonation constants for adrenaline and the stability constants for lanthanum(III) complexes with adrenaline.

2.3. *Computational method*

Calculations were carried out using the Gaussian92 [13] package on a SUN SPARCsever 1000 workstation. All considered structures were partially optimized at the HF (Hartree–Fock) level with the LANL1DZ basis set. The fixed variables during optimization include the benzene ring (with C–C bond distance fixed at 1.395 Å, C–C–C and C–C–H bond angles at 120.0°) and X–H (X = C, N, O) bond distances (fixed at 1.0 Å). The convergence criteria are 4.5×10^{-4} Hartrees/Bohr for maximum force, 3.0×10^{-4} Hartrees/Bohr for rms force, 1.8×10^{-3} Bohr for maximum

displacement and 1.2×10^{-3} Bohr for rms displacement, with convergence not being reached until the four criteria are satisfied simultaneously.

3. Results and discussion

3.1. *Potentiometry study*

The equilibria in the La(III)–adrenaline system and the corresponding notations for the protonation constants of adrenaline and the stability constants of lanthanum(III) complexes with adrenaline are given below:

$$pLa + qL + rH = La_pL_qH_r$$

$$\beta_{pqr} = \frac{[La_pL_qH_r]}{[La]^p[L]^q[H]^r}$$

where p, q and r represent the chemical stoichiometric coefficients of the La(III) ion (La), ligand (L) and proton (H) in the complex molecule, respectively. The charges of the ions are omitted for the sake of clarity.

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The structure of adrenaline is comparatively complicated (figure 1) with an alcoholic hydroxyl group, a secondary amino group and two phenolic hydroxyl groups. It appears that adrenaline behaves as a tetraprotic ligand. However, ionization of the second phenolic hydroxyl group and the alcoholic hydroxyl group is very difficult. In fact, the titration curves of the ligand show only two ill-defined inflection points at one and two moles of base added per mole of ligand. From the pH titration results, adrenaline appears to act as a diprotic ligand under the experimental conditions. The protonation constants for the ligand adrenaline, obtained from the treatment of the potentiometric titration data, are presented in table 1. Various compounds containing both amine and phenolic groups are found in biological systems, such as tyrosine, adrenaline, and related compounds. The acidities of the phenolic and substituted ammonium groups are comparable so that their protonations often occur in almost the same pH region [14]. Thus, the adrenaline molecule exhibits two overlapping protonation constants. From the data in table 1, the protonation of the ligand, represented by β_{011}, is most likely due to the protonation of the secondary amino group while the second protonation of the ligand involves protonation of the first phenolic hydroxyl group [14]. Compared to the results reported previously [14], these protonation constants for adrenaline under physiological conditions are reasonable. The results were also confirmed by the quantum chemical ab initio study described below.

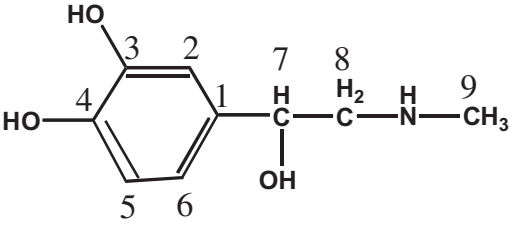

Figure 1. The numbering scheme for adrenaline.

Table 1. Protonation constants and stability constants for the lanthanum(III)–adrenaline system.

System	p	q	r	$\log \beta_{pqr}$	s.d.
L–H	0	1	1	9.76	0.03
	0	1	2	18.21	0.06
La–L–H	1	1	0	5.91	0.01
	1	2	0	10.73	0.04

The complex species in the La(III)–adrenaline system were ascertained by selection of several chemical models composed of computer-simulated LaL, LaL_2, LaLH, LaL_2H and $LaLH_{-1}$ (a complex containing a hydroxyl group) complexes. The stability constants for lanthanum(III) complexes with adrenaline were obtained by computer analysis of the potentiometric titration data, and are listed in table 1.

The protonation constants in table 1 show that the phenolic hydroxyl group is more acidic than the secondary amino group. Therefore, it is believed that the phenolic hydroxyl group of the ligand coordinates more easily to lanthanum(III). Also, rare earth ions behave as hard acids, interacting preferentially with hard bases, such as fluoride or oxygen donors, rather than with softer bases, such as nitrogen and sulfur donors [15]. Thus, the phenolic hydroxyl group is the donor for adrenaline. It could be considered that both the phenolic hydroxyl group and the secondary amino group are involved in coordination with lanthanum(III), resulting in the formation of a nine- (or eight-) membered chelate ring. However, such a chelate ring would be very unstable. As a result, the secondary amino group of the ligand is probably too far from the phenolic hydroxyl group for a stable chelate ring to be formed. It is thus reasonable to suggest that the phenolic hydroxyl group of adrenaline is the binding site for lanthanum(III). The results are in good agreement with those obtained by our quantum chemical ab initio study. It can be seen from table 1 that lanthanum(III) forms LaL and LaL_2 complexes. In rare earth complexes, the number and arrangement of the ligands are determined primarily by steric and electrostatic factors. Coordination numbers of eight and nine have been reported for rare earth complexes in solution [15]. The adrenaline molecule is coordinated to lanthanum(III) mainly through its phenolic hydroxyl group, so in the LaL complex the coordination potential of lanthanum(III) is far from saturated, resulting in the formation of the LaL_2 complex.

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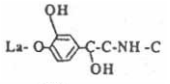
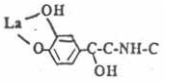
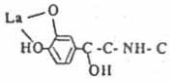
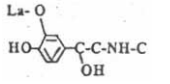
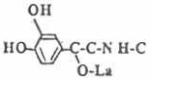
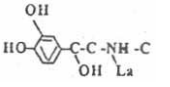
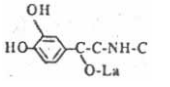
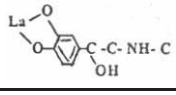
3.2. *Ab initio study*

The adrenaline molecule contains an alcoholic hydroxyl group, a secondary amino group and two phenolic hydroxyl groups; all of these groups are potential donors. The computational results of various coordination modes for the LaL complexes are listed in table 2. It can be seen from table 2 that the energies for coordination modes F, G and H are quite high, indicating that these three coordination modes are unstable. From an energetic point of view, coordination modes A, B, C, D and E, which are rather low in energy, are all possible coordination candidates. However, the calculated energy gaps decrease from coordination modes A to E, E having the smallest one. Meanwhile, coordination mode E is unreasonable, as seen from the potentiometric results. Thus, coordination mode E can be excluded. Therefore, it can be concluded that coordination modes A, B, C and D are viable; however, the energies are close to one another, which would theoretically result in the formation of a mixture of

Table 2. The computational results for coordination modes.

Coordination mode		Energy (au)	HOMO (au)	LUMO (au)	Gap (au)	Charge on La
A.		−619.971804	−0.521	−0.279	0.242	1.58
B.		−619.971499	−0.518	−0.279	0.239	1.58
C.		−619.970891	−0.505	−0.279	0.226	1.58
D.		−6.19.970844	−0.505	−0.279	0.226	1.58
E.		−619.969386	−0.456	−0.279	0.177	1.53
F.		−619.905324	−0.750	−0.446	0.304	1.74
G.		−619.893104	−0.542	−0.277	0.265	1.43
H.		−619.726069	−0.412	−0.131	0.281	1.16

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complexes with coordination modes A, B, C and D according to Boltzman distribution. The fractional populations of the coordination modes would decrease in the following order: A > B > C > D. In any case, adrenaline is coordinated to lanthanum(III) via its phenolic hydroxyl group (only one phenolic hydroxyl group is deprotonated), and the 4-phenolic hydroxyl group is the main binding site of lanthanum(III). The results are in good agreement with the potentiometric experiments.

It is quite interesting to ascertain which group in the adrenaline molecule serves as a donor for metal ions. It has been suggested that the ligand is coordinated to Cu(II), Co(II), Ni(II) [5], Mn(II) and Zn(II) [6] ions through its two phenolic hydroxyl groups. However, it is possible that for Ni(II) and Cu(II) complexes, the side chain (–CH(OH)–CH_2–NH–CH_3) is involved in bonding to the metal ions [6,7]. Chakrawarti *et al.* have proposed that in solid alkaline earth complexes the two phenolic hydroxyl groups serve as binding sites for the metal ions, but only one phenolic hydroxyl group is deprotonated [8]. Because the properties of lanthanum(III) are very similar to those of calcium(II), the results obtained by the ab initio method are quite reasonable in relation to Chakrawarti's results [8]. To summarize, the results for the LaL-type La(III) complex with adrenaline show that the ligand is coordinated to lanthanum(III) via its phenolic hydroxyl group (only one phenolic hydroxyl group is deprotonated). The 4-phenolic hydroxyl group of the adrenaline molecule is the main binding site for lanthanum(III).

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References

[1] J.Z. Ni, *Bioinorganic Chemistry of Rare Earth Elements*, Science Press, Beijing (1995).
[2] C.J. Niu, Y.Q. Jia, M.L. Liu, X.W. Liu, M.Z. Jin, *J. Inorg. Biochem.* **45**, 151 (1992).
[3] C.H. Evans, *Biochemistry of Lanthanide*, Plenum Press, New York (1990).
[4] F. Gao, C.J. Niu J.Z. Ni, *Chinese J. Inorg. Chem.* **13**(2), 19 (1997).
[5] A.C. Andrews, T.D. Lyons, T.D. O'Brien, *J. Chem. Soc.* **5**, 1776 (1962).
[6] R.F. Jameson, W.F.S. Neillie, *J. Inorg. Nucl. Chem.* **28**, 2667 (1966).
[7] R.F. Jameson, W.F.S. Neillie, *J. Inorg. Nucl. Chem.* **27**, 2623 (1965).
[8] P.B. Chakrawarti, B.L. Vijayvargiya, H.N. Sharma, *J. Indian Chem. Soc.* **60**, 89 (1983).
[9] L.T. Shen, D.H. Zhu, *Zhongguo Xitu Xuebao* **11**(2), 158 (1993).
[10] C.J. Niu, G.R. Choppin, *Inorg. Chim. Acta.* **131**, 277 (1987).
[11] E.N. Rizkalla, C.J. Niu, G.R. Choppin, *Inorg. Chim Acta* **146**, 135 (1983).
[12] D.J. Leggett, *Computational Methods for the Determination of Formation Constants*, Plenum Press, New York (1985).
[13] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.W. Wong, J.B. Foresman, M.A. Robb, M. Head-Gordon, E.S. Replogle, R. Gomperts, J.L. Andres, K. Raghavachari, J.S. Binkley, C. Gonzalez, R.L. Martin, D.J. Fox, D.J. Defrees, J. Baker, J.J.P. Stewart, J.A. Pople, Gaussian92/dft, Revision G.1 Gaussian Inc., Pittsburgh, PA (1993).
[14] R.B. Martin, *J. Phys. Chem.* **75**, 2657 (1971).
[15] G.R. Choppin, *J. Less-Common Metals* **93**, 323 (1983).

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