

Studies on Some Lanthanide(III) Complexes of (Substituted)-Oxaminoacetyl Thiazoles

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Proton-ligand dissociation constants of substituted oxaminoacetyl thiazoles and stability constants of their complexes with lanthanides have been determined pH-metrically, in 75-25% dioxane-water (v/v) mixture at 30°C and at ionic strength 0.1 M NaClO₄ using Calvin-Bjerrum titration technique. These compounds form complexes by deprotonation.

Key Words: Lanthanide(III) complexes, Substituted oxaminoacetyl thiazoles.

INTRODUCTION

Compounds containing thiazole ring system are known for their extensive activity in medicinal¹ chemistry. Vitamin B, sulphathiazole, promizole, aminotriazole, thiobendazole and tetramisole, all contain thiazole moiety in one form or the other. The Schiff bases having thiazole moiety are found to possess antitubercular activity². These are also active against Duning leukemia solids³. Revankar and Mahale⁴ have reported Co(II), Ni(II) and Cu(II) complexes with benzimidazole oximes to be biologically active. Their antibacterial and antifungal activities were found to increase substantially on complexation with lanthanides and transition metals. Recently lanthanide complexes have gained⁵ importance as radiopharmaceuticals.

Oximes are also well known for their versatile behaviour⁶ and high coordinating abilities. Rosenberg and Van Camp⁷ were the first to publish observations on antitumour effects of some platinum compounds in mouse sarcoma 180 and leukemia. Since then platinum complexes have been extensively used as anticancer agents in terminally ill patients⁸. But they have been found to be nephrotoxic and living systems have no effective mechanism for its rejection. It would, therefore, be necessary to hunt for the complexes of those metals, present in the body such as Cu and Fe. These complexes should not only possess antitumour properties but also the decomposition products should be easily removable.

The *trans*-bis(salicylaldoximate) Cu(II) and *trans*-bis(resorcyaldoximate) Cu(II) complexes have been found to possess the highest antitumour activity⁹. A carbohydrate molecule bearing amidoxime group¹⁰ is another compound showing antitumour activity with low toxicity. Salicylhydroxamic acid and its halogen derivatives have been reported to be antitubercular and antifungal in nature¹¹.

The oximes are also being increasingly used in analytical chemistry because

of their easy availability, sensitivity and selectivity for various methods and applications in gravimetry, colorimetry, spectrophotometry have been recently reviewed. Paria *et al.*¹² have reported that ninhydrin oxime in presence of pyridine could be used as an extractive spectrophotometric reagent for Pd(II). Mittal¹³ reported phenylazo-bis-benzaldoxime as a new gravimetric reagent for Pb(II), Co(II) and Ni(II).

It is thus clear from the literature survey that though there are a wealth of data on the metal complexes of oximes, a systematic study of their lanthanide complexes is lacking.

It was therefore decided to undertake a systematic study of lanthanide complexes of oxaminoacetyl thiazole and to determine the stability constants of the systems in solution using Calvin-Bjerrum titration technique¹⁴.

EXPERIMENTAL

2-Substituted amino-4-methyl-5-oxaminoacetyl thiazoles (Fig. 1) were prepared by Hantzsch¹⁵ method of cyclisation. The method has its own importance because the reaction can be carried out with great ease and with good yield.

The proton-ligand and metal-ligand stability constants of their lanthanide complexes were determined potentiometrically.

RESULTS AND DISCUSSION

Since the term pH is related to water, the readings, noted on pH-meter in 75% dioxane-25% water medium were referred to as B readings. The dissociation constants of the ligands and stability constants of their metal complexes were the practical constants. To convert these into thermodynamic ones, Van Uitert correction factor was applied. These thermodynamic pK and log K values are reported in Table-1.

TABLE-1

Ligand No.	Thermodynamic pK
(i) Without substituted	5.3018
(ii) Methyl-substituted	6.9747
(iii) Chloro-substituted	6.0353
(iv) Bromo-substituted	4.5502

The thermodynamic pK values of various ligands and log k values of their metal complexes were studied.

(a) The pK values of *o*-hydroxyacetophenone oxime, salicyl-doxime and 2-hydroxy naphthaldoxime are reported to be 13.76, 11.72 and 11.34 respectively³. However, in the present investigation the values are much lower indicating increased acid strength of the compounds. It may be due to various substituents

present in the ligand structure. This is in accordance with the earlier observation of a keto-oxygen, which facilitates deprotonation from oxime groups⁴⁻⁶.

(b) Though the substituents at position No. 2 influence the release of proton, the effect is more pronounced in ligand No. II since substituent is $-\text{CH}_3$ group, which is strong electron donating. Similarly, when ligands with chloro and bromo substituents are considered, chloro group, having higher electronegative character, is stabilising the anion character of ligand.

TABLE-2
METAL-LIGAND STABILITY CONSTANTS

Metal ion	Ligand I		Ligand II		Ligand III		Ligand IV	
	log k_1	log k_2	log k_1	log k_2	log k_1	log k_2	log k_1	log k_2
H ⁺	3.40	—	5.07	—	4.13	—	2.65	—
La ³⁺	4.17	3.39	2.55	3.62	3.19	2.77	2.00	2.61
Pr ³⁺	2.22	1.76	5.54	4.90	2.81	2.71	3.47	—
Nd ³⁺	1.32	1.47	3.14	2.89	3.04	2.37	—	3.30
Gd ³⁺	1.21	—	2.93	3.48	2.88	3.09	2.81	—
Dy ³⁺	4.13	3.45	2.54	2.95	4.33	4.59	3.17	2.91
Tb ³⁺	3.49	4.02	2.95	3.10	2.78	2.64	3.17	2.81
Ho ³⁺	—	3.52	3.00	3.26	2.75	2.95	2.55	2.91

Metal-Ligand Stability Constants

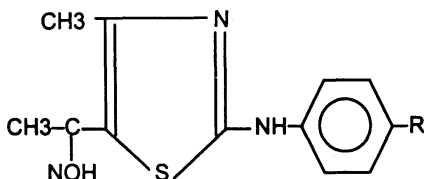
Since the ligands form a close series they were expected to have identical binding sites. It can be shown by plotting log k values vs. pK values⁷⁻⁸. A linear relationship is observed as it was expected.

For oxaminoacetyl thiazoles the difference between pK and log k is very small showing the tendency of back donation of electron¹⁶.

Mostly lanthanide complexes are ionic in nature due to shielding effect of 5s and 5p electrons. There is no direct interaction of ligand orbitals. Therefore orbitals of higher energy like 5d and 6s may involve showing covalency.

In the present investigation, when log k values of lanthanide⁹ complexes were plotted against e^2/r , a regular decrease in log k values was observed from La(III) to Gd(III). Then there was increase in log k . The Gd break was clearly seen. It means, in the first half the complexes are ionic and in the second half they are non-ionic.

Further, the thermodynamic parameters were determined and ΔG (free energy), when plotted against ΔH or ΔS , a linearity shows the validity of Hammett eqn.¹⁰.



2-(Phenylamino)-4-methyl-5-oxamino acetyl thiazole (R = H, CH₃, Cl, Br)

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