



Evaluation of Stability of Complexes of Inner Transition Metal Ions with 2-Oxo-1-pyrrolidine Acetamide and Role of Systematic Errors

SANGITA SHARMA*, JAYESH RAMANI,
DHARA PATEL, KETAN PATEL and MAHESH KADIYA

Department of Chemistry
Hemchandracharya North Gujarat University, Patan-384 265, India
smridhee2000@yahoo.co.in

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Abstract: BEST FIT models were used to study the complexation of inner transition metal ions like Y(III), La(III), Ce(III), Pr(III), Nd(III), Sm(III), Gd(III), Dy(III) and Th(IV) with 2-oxo-1-pyrrolidine acetamide at 30 °C in 10%, 20, 30, 40, 50% and 60% v/v dioxane-water mixture at 0.2 M ionic strength. Irving Rossotti titration method was used to get titration data. Calculations were carried out with PKAS and BEST Fortran IV computer programs. The expected species like L, LH⁺, ML, ML₂ and ML(OH)₃, were obtained with SPEPLOT. Stability of complexes has increased with increasing the dioxane content. The observed change in stability can be explained on the basis of electrostatic effects, non electrostatic effects, solvating power of solvent mixture, interaction between ions and interaction of ions with solvents. Effect of systematic errors like effect of dissolved carbon dioxide, concentration of alkali, concentration of acid, concentration of ligand and concentration of metal have also been explained here.

Keywords: Systematic errors, Inner transition metal ion, Stability of Complexes

Introduction

2-Oxo-1-pyrrolidine is well known drug used as cure for many clinical problems like to increase cognition and memory, slowing down brain ageing, increase in blood flow and oxygen to brain, add to stroke recovery, dementia and dyslexia¹⁻⁴. Inner transition metal complexes are also known for many bio medical applications⁵⁻⁶. A number of studies are being carried out to study the stability of metal complexes in solution state⁷⁻¹¹. But studies on inner transition metal complexes of 2-oxo-1-pyrrolidine acetamide in aqueous as well as in mixed equilibria are not reported. Effect of systematic errors on these complexes in solution state is also not reported.

So, we have carried out a study on binary complexes of inner transition metal ions with 2-oxo-1-pyrrolidine acetamide in solution state. BEST FIT models of inner transition metal ions 2-oxo-1-pyrrolidine acetamide were developed in different v/v dioxane-water mixtures at 30 ± 0.1 °C and ionic strength 0.2 M. Pessimistic errors are introduced in the form of dissolved carbon dioxide, alkali, ligand and metal content. Species distribution plots were generated with software to visualize the formation of various species in solution state and to see the effect of systemic errors on the percentage of various species formed.

Experimental

All chemicals used were of A. R. grade. All solutions were prepared in the conductivity water. Metal solution was prepared and standardized complexometrically¹². Perchloric acid was standardized with standard NaOH solution and constant ionic strength was maintained with an inert electrolyte sodium perchlorate (NaClO_4).

Apparatus

Titrimetric data were obtained with systronics μ pH meter 361 having combined glass electrode and temperature probe with readability ± 0.1 . The pH meter was calibrated with 0.05 mol dm^{-3} potassium hydrogen phthalate solution in acidic region and in 0.01 mol dm^{-3} borax solution in basic region. The glass electrode was in equilibration in well stirred dioxane-water mixture. The effects of variations in asymmetry potential, liquid junction potential, activity coefficient, sodium ion error and dissolved carbon dioxide on response of glass electrode were incorporated as correction factors¹³. The temperature was kept constant at 30 ± 0.1 °C throughout the experiment. High precision water bath Cat No. MSW-274 with readability ± 0.1 °C was used to maintain the temperature.

Procedure

Mixtures of dioxane–water solvents were treated like aqueous solutions for preparing solutions. pK_w values valid for 30 °C and 0.1 M ionic strength was computed via Debye-Huckel equation for 10%, 20%, 30%, 40%, 50%, 60% V/V dioxane -water mixtures¹⁴. The experimental procedure involved potentiometric titration of the following three sets of solutions.

I. Acid titration, II. Ligand titration, III. Metal+Ligand titration

Total volume used was 50.00 mL. The strength of acid and dissolved carbon dioxide was analyzed by using Gran's plot method¹⁵. The ratio of M: L maintained was 1:10 so as to expect maximum possible coordination of ligand to metal. The method of Bjerrum and Calvin as modified by Irving and Rossotti has been used¹⁶ for calculation of stability constants.

Calculation

For calculation of metal ligand stability constant, titration data was pruned using coordination of four ligand molecules to metal ion to make it as best fit model and data for Y(III)- 2-oxo-1-pyrrolidine acetamide complexes are given in Table 1. As the values of pK_3 and pK_4 for ML_3 and ML_4 respectively are small and the percentage of these species was also quite less, so ML and ML_2 types of complexes are used for the study and effect of systemic errors. Protonation constant is calculated by PKAS^{17} program and values are given in Table 2. Metal ligand stability constants of inner transition metal complexes with 2-oxo-1-pyrrolidine acetamide are calculated by BEST in different dioxane-water mixtures and are reported in Table 3. Stability constant values of complexes in presence of different systematic

errors are given in Table 4. Species distribution diagram of metal–ligand system were plotted using SPEPLOT program¹⁸. pH range between 0–7 is selected for calculation. 'S' minimum values for all the selected binary system are calculated. S_{\min} is the same statistical distribution as χ^2 with K degrees of freedom and with weights reported in accordant with Fletcher and Powell^{19–20}. S_{\min} can be equated to χ^2 .

Table 1. Results of BEST FIT model for complexes Y(III)-2-oxo-1-pyrrolidine acetamide temperature 30 ± 0.1 °C and ionic strength 0.2 mol dm^{-3} in 10% v/v dioxane-water mixture

$\log\beta_1$, pK ₁	$\log\beta_2$, pK ₂	$\log\beta_3$, pK ₃	$\log\beta_4$, pK ₄	pH scale	S_{\min}	No. of data points
4.291 (4.2391)	7.6811 (3.6693)	10.2455 (2.5644)	11.6889 (1.4434)	1.5 – 7.0 1.5 – 7.0	0.0445 -	38 -

Table 2. Protonation constant of 2-oxo-1-pyrrolidine acetamide in different solvent media at temperature 30 ± 0.1 °C and ionic strength 0.2 mol dm^{-3}

Protonation constant	Water	10% Dioxane v/v	20% Dioxane v/v	30% Dioxane v/v	40% Dioxane v/v	50% Dioxane v/v	60% Dioxane v/v
$\log\beta_H$	2.5126	2.6210	2.7199	2.8312	2.9412	3.0012	3.2413
Literature value	3.0801	-	-	-	-	-	-

Table 3. Parameters of BEST FIT model of inner transition metal ion with 2-oxo-1-pyrrolidine acetamide in dioxane-water mixture at temperature 30 ± 0.1 °C and ionic strength 0.2 mol dm^{-3}

logβ						
Dioxane % v/v	ML	ML ₂	ML (OH) ₃	S _{min}	pH scale	No. of data point
Y(III)						
10	4.2391	7.6811	-2.7314	0.0112	2-7	39
20	4.3109	7.7921	-2.8101	0.0411	2-7	39
30	4.4721	7.8241	-2.9019	0.0788	2-7	40
40	4.5213	7.9001	-3.0101	0.0933	2-7	38
50	4.6109	8.1124	-3.1141	0.0110	2-7	35
60	4.5911	7.9639	-2.9119	0.0870	2-7	37
La(III)						
10	4.4119	7.8209	-2.7401	0.0131	2-7	34
20	4.5390	7.9101	-2.8492	0.0141	2-7	39
30	4.6124	8.0090	-2.9009	0.0278	2-7	39
40	4.7229	8.2101	-2.9919	0.0193	2-7	39
50	4.8101	8.3441	-3.0011	0.1110	2-7	34
60	4.7992	8.2012	-2.8911	0.0170	2-7	38
Ce(III)						
10	4.6199	8.0141	-2.8114	0.0199	2-7	29
20	4.7279	8.1242	-2.7211	0.0001	2-7	41
30	4.8334	8.2247	-2.8001	0.9901	2-7	25
40	4.9019	8.3159	-2.8432	1.1030	2-7	34
50	5.0999	8.4237	-2.8929	0.1231	2-7	35
60	4.9121	8.1901	-2.7112	0.1241	2-7	29

Contd...

Pr(III)						
10	4.7221	8.2783	-2.8001	0.1210	2-7	32
20	4.8001	8.3224	-2.8211	0.4321	2-7	37
30	4.9328	8.4412	-2.7241	0.2131	2-7	34
40	5.0012	8.5009	-2.8001	0.2133	2-7	35
50	5.2243	8.6223	-2.7991	0.0491	2-7	34
60	5.0122	8.5105	-2.7801	0.0901	2-7	38
Nd(III)						
10	5.1209	8.5011	-2.8113	0.1101	2-7	34
20	5.2711	8.7201	-2.8421	0.0121	2-7	39
30	5.3409	8.8119	-2.8990	0.1219	2-7	39
40	5.4712	8.9001	-3.0001	0.7611	2-7	26
50	5.5509	8.9423	-3.1141	0.1907	2-7	34
60	5.4621	8.9102	-2.9412	0.1211	2-7	40
Sm(III)						
10	5.3214	8.7909	-2.8432	0.0013	2-7	33
20	5.4032	8.8114	-2.9092	0.0035	2-7	34
30	5.6227	8.9001	-2.9114	0.0032	2-7	40
40	5.8112	9.0321	-3.0012	0.0130	2-7	29
50	5.9009	9.1241	-3.0181	0.2101	2-7	35
60	5.8911	9.0981	-3.0001	0.0332	2-7	38
Gd(III)						
10	5.4121	8.9004	-2.8812	0.0199	2-7	36
20	5.6001	8.9339	-2.8921	0.2311	2-7	35
30	5.8231	9.1221	-2.9012	0.6199	2-7	39
40	5.9099	9.2478	-2.9114	0.2337	2-7	29
50	5.9909	9.3114	-2.9223	0.1411	2-7	35
60	5.8911	9.2024	-2.8114	0.1781	2-7	36
Dy(III)						
10	5.7114	9.1141	-2.9012	0.0111	2-7	36
20	5.8019	9.0224	-2.9121	0.1234	2-7	35
30	5.9229	9.1239	-2.9232	0.0154	2-7	39
40	6.0012	9.3333	-2.9344	0.1330	2-7	29
50	6.1214	9.4104	-2.9449	0.1210	2-7	35
60	5.9821	9.3992	-2.9229	0.1321	2-7	38
Th(IV)						
10	6.7101	10.1212	-2.9439	0.0111	2-7	36
20	6.8009	10.2321	-2.9813	0.1234	2-7	35
30	6.9234	10.3009	-2.9919	0.0154	2-7	39
40	6.9920	10.3447	-3.0141	0.1330	2-7	29
50	7.2141	10.4518	-3.1211	0.1210	2-7	35
60	7.1341	10.3999	-3.0421	0.1321	2-7	36

Table 4. Effect of systematic errors of La(III)-2-oxo-1-pyrrolidine acetamide Equilibrium in 10% v/v dioxane–water mixture

Component	% of error	$\log\beta_{ML}$	$\log\beta_{ML_2}$	$\log\beta_{ML(OH)_3}$
	0	4.4119	7.8209	-2.7401
Dissolved carbon dioxide	-5	4.1091	7.6012	-2.9912
	-1	4.3990	7.7992	-2.8001
	+1	4.3112	7.8442	-2.7121
	+5	4.6201	7.9012	-2.9001
Alkali	-5	4.0241	7.5812	-2.8449
	-1	4.3212	7.7142	-2.9114
	+1	4.2791	7.8019	-2.8621
	+5	4.5812	7.8345	-2.9103
Acid	-5	3.9012	7.5112	-2.8001
	-1	4.2212	7.6921	-2.7124
	+1	4.1733	7.6814	-2.5321
	+5	4.4121	7.7449	-2.6412
Ligand	-5	3.8713	7.4291	-2.7221
	-1	4.1234	7.7129	-2.6980
	+1	4.1102	7.6429	-2.5142
	+5	4.3990	7.6921	-2.6249
Metal	-5	4.4001	7.8219	-2.7421
	-1	4.4019	7.8201	-2.7319
	+1	4.4112	7.8191	-2.7299
	+5	4.4121	7.8001	-2.7301

Results and Discussion

As per Irving Rossotti technique, the ligands with one dissociable or protonable site have only one stability constant value for 1:1 metal to ligand ratio. In the present set of experimental condition with 1:10 metal to ligand ratio, the four β values are obtained, out of which two have not shown much difference and have less value. So it is anticipated that two 2-oxo-1-pyrrolidine acetamide are coordinated to inner transition metal ions. Small S_{min} values indicate that model is best studies for calculations. This is the BEST-FIT model which is used to calculated stability constant values for metal- 2-oxo-1-pyrrolidine acetamide species in dioxane-water mixtures.

Effect of solvent

The values of calculated protonation constants for 2-oxo-1-pyrrolidine acetamide in aqueous and dioxane–water mixtures are reported in Table 2. No such data is available in literature. It has been observed that up to 50% V/V of dioxane-water mixture pK_H value of 2-oxo-1-pyrrolidine acetamide varies linearly with increase in concentration of dioxane. The addition of dioxane to water decreases the dielectric constant of medium. The dielectric constant values for dioxane-water are taken from literature²¹.

Overall stability constant values *i.e.* $\log\beta_1$, $\log\beta_2$ also increase with increase in dioxane % in mixture. The regular linear trend is observed up to 50% v/v (Dioxane-water mixture). The cation solvating nature of cosolvent, specific solvent-water interaction, charge dispersion and interaction of cosolvent with solvent can account for small deviation from linear relationship between the stability of complexes and dielectric constant 1/D. Formation

of complexes in solution state is fair play and combined effect of many factors like solvent-solvent interaction, solvent-water interaction, interaction between solvated metal ions and ligand, relative thermodynamic and kinetic lability²². All these factors can be grouped as (1) electrostatic effect or (2) non electrostatic effect. According to Born²³ equation, the energy of electrostatic effect is related to dielectric constant of medium. Also interaction between the metal ion and ligand is also electrostatic in nature. So stability values showed increase with decrease in dielectric constant of medium. All other factors calculate to non electrostatic effects. Dioxane is less than that of water, non electrostatic effect many decrease proton accepting property of 2-oxo-1-pyrrolidine acetamide in dioxane rich medium. Also metal ions become more susceptible to react with 2-oxo-1-pyrrolidine acetamide, become addition of dioxane removes water molecules from coordination sphere of metal ion.

Effect of systematic error on BEST FIT model

An investigation is made by introducing pessimistic error in best fit model for critical evaluation of stability constant in present set of experimental conditions. BEST program does not have direct option for calculation of systematic error on the stability constants but small changes in various components can be explained as change in stability constants. The changes in concentration of dissolved carbon dioxide, alkali, acid, ligand and metal content are selected as sources of error. The calculated results are given in Table 4 and the order is dissolved carbon > alkali > acid > ligand. Variation in metal content shows insignificant effect in the values of stability constants. The reason may be that metal to ligand ratio is maintained at 1:10. The change in these systematic errors also affects formation and distribution of ML and ML₂ species in the equilibrium state, many times hydroxy species become predominant.

Conclusion

For critical evaluation of stability constant values for inner complexes of transition metals with 2-oxo-1-pyrrolidine acetamide, a best fit required in pretext to selected experimental conditions. Systematic errors plays important role in complexation tendency of metal to 2-oxo-1-pyrrolidine acetamide. Bioavailability of the metal ion, the 2-oxo-1-pyrrolidine acetamide and complexed of metal species is studies with species distribution diagrams.

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