

Formation Constants & Thermodynamic Parameters of Iron(II) Chelates with Quinoline-8-carboxylic & Quinoxaline-2-carboxylic Acids & Their Substituted Derivatives in Aqueous Ethanol Medium†

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The proton-ligand and metal-ligand stability constants of Fe(II) complexes with quinoline-8-carboxylic acid (8Q), 5-nitroquinoline-8-carboxylic acid (5NO₂8Q), 5-aminoquinoline-8-carboxylic acid (5NH₂8Q), quinoxaline-2-carboxylic acid (2Qx), 3-chloroquinoxaline-2-carboxylic acid (3Cl2Qx) and 3-hydroxyquinoxaline-2-carboxylic acid (3OH2Qx) have been studied with a view to understanding the effect of various substituents present in the ligands. The studies have been carried out potentiometrically in aqueous ethanol (50% v/v for 8Q and 5% v/v for 2Qx systems) medium using Calvin-Bjerrum titration technique as modified by Irving and Rossotti. Iron(II) forms 1:1 (metal-ligand) complexes with 2Qx systems and both 1:1 and 1:2 complexes with 8Q systems. Thermodynamic formation constants ($\log K_n^{m=0}$) and the values of ΔG^\ddagger , ΔH^\ddagger and ΔS^\ddagger have been evaluated and discussed. There is a regular and slow decrease in stability constants with increase in ionic strength. In case of 8Q systems, the order of metal-ligand stabilities has been found to be: 5NO₂8Q < 8Q < 5NH₂8Q and for 2Qx systems, 3Cl2Q < 3OH2Qx < 2Qx.

Quinoline-8-carboxylic acid (8Q) and quinoxaline-2-carboxylic acid (2Qx) have a wide range of applications¹⁻⁴. 2Qx plays an important biogenetic role in the synthesis of antibiotic peptide triostein⁵. Recently Yoshinori *et al.*⁶ synthesised and characterised complexes of 2Qx with some transition metal ions. In the present note we report proton-ligand and metal-ligand stability constants of 8Q, 5-nitroquinoline-8-carboxylic acid (5NO₂8Q), 5-aminoquinoline-8-carboxylic acid (5NH₂8Q), 2Qx, 3-chloroquinoxaline-2-carboxylic acid (3Cl2Qx) and 3-hydroxyquinoxaline-2-carboxylic acid (3OH2Qx) with Fe(II) in aqueous ethanol (50% v/v for 8Q and 5% v/v for 2Qx systems) medium at different temperatures and ionic strengths employing Calvin-Bjerrum^{7,8} pH titration technique as modified by Irving and Rossotti⁹. Stepwise and overall stability constants and the values of thermodynamic parameters accompanying the complex forming reactions have been evaluated and discussed.

All the chemicals used were either BDH (AR) or Merck (GR) reagents. The ligands employed were synthesised in our laboratory by known methods¹⁰⁻¹⁴

and their purities were checked on the basis of their IR spectra, melting points and neutralization equivalents. As the solubility of the ligands is low in water, the solutions were prepared in 50% (v/v) aqueous-ethanol medium for 8Q systems and in 5% (v/v) aq. ethanol for 2Qx systems. Redistilled water was employed for preparing all the other solutions. Ferrous nitrate solution was prepared freshly whenever required by the metathetical reaction of equimolar amounts of barium nitrate and ferrous sulphate solutions and filtering off the precipitate. Its strength was estimated volumetrically using potassium dichromate. During the titration the stability of Fe(II) was checked at regular intervals of time by removing an aliquot of reaction mixture from a duplicate set maintained under identical conditions and reacting it with ammonium thiocyanate solution; no red colouration was observed. Potassium nitrate was used as the supporting electrolyte for maintaining the total ionic strength (μ), and standard carbonate-free potassium hydroxide solution was used for titrations.

pH measurements were carried out on an Elico pH meter LI-10 fitted with glass and built-in saturated calomel electrodes. The instrument was standardised at constant temperature with known buffers and was calibrated with standard acid before use. A specially designed double-walled titration cell accommodating a micro-burette, a thermometer, calomel and glass electrodes and having an arrangement for bubbling nitrogen into the solution was used. The temperature of the reaction mixture was maintained constant throughout the titrations by circulating water from a thermostat into the outer jacket of the reaction cell.

The experimental procedure for 8Q systems involved the potentiometric titrations of the following solutions: (i) HNO₃ ($4.00 \times 10^{-3} M$); (ii) HNO₃ ($4.00 \times 10^{-3} M$) + ligand ($2.00 \times 10^{-3} M$); and (iii) HNO₃ ($4.00 \times 10^{-3} M$) + ligand ($2.00 \times 10^{-3} M$) + Fe(NO₃)₂ ($4.00 \times 10^{-4} M$) against standard potassium hydroxide (0.10 M). These concentrations were increased by two-fold for 2Qx systems. The initial total volume in each case was 50 ml and the ionic strength was maintained constant by adding requisite quantities of 1.0 M potassium nitrate solution. The pH and volume corrections for aquo-organic solvent mixture were made as suggested by van Uitert and Haas¹⁵.

From the titration curves, values of \bar{n}_A (the number of hydrogen ions bound to the ligand anion), \bar{n} (the metal-ligand formation number) and pL (free ligand exponent) were calculated by employing the relationships derived by Irving and Rossotti⁹.

In the initial stage of the titration the ligand curve shifted to the left (or above) the acid curve due to the basic property of the tertiary nitrogen (C=N) in 8Q systems which accepts a proton from the acid solution thereby indicating its involvement in the metal chelate formation. Such a trend was not observed in 2Qx systems as the complex formation occurred in the low pH region, but in the course of reactions colour formation was observed indicating the formation of complexes¹⁶ probably involving the heterocyclic nitrogen and adjacent carboxylic group of the ligand. The \bar{n}_A values were plotted against pH to obtain the formation curve for proton-ligand system. This curve extends between 0.2 and 0.8 indicating that only one proton is dissociating from each of the ligand. The approximate values of pK_a were directly read from the formation curves at $\bar{n}_A = 0.5$. The precise values of pK_a were obtained from the intercepts of plots of $\log \bar{n}_A / (1 - \bar{n}_A)$ versus pH.

The pH meter readings for hydrolysis of Fe(II) with 5NO₂8Q, 8Q and 5NH₂8Q were around 4.10, 5.50 and 6.30 respectively. The deviations of metal ligand complex titration curves for the above systems were noticed around pH meter readings 2.85, 3.10 and 3.75 respectively showing the complexation of the metal ion with these ligands. The \bar{n} values for 2Qx systems were in the range 0.25-0.85 indicating the formation of 1:1 metal-ligand complexes; the range extends upto 1.85 for 8Q systems showing the formation of 1:2 complexes in addition. From the plots of pL versus \bar{n} , the approximate stability constants were directly read at $\bar{n} = 0.5$ ($\log K_1$) and $\bar{n} = 1.5$ ($\log k_2$), i.e., by

employing Bjerrum's half \bar{n} method. In addition to this $\log K_1$ and $\log K_2$ values were also obtained by pointwise calculation method using Eqs 1 and 2.

$$\log K_1 = pL - \log [(1 - \bar{n})/\bar{n}] \quad \dots (1)$$

$$\log K_2 = pL - \log [(2 - \bar{n})/(\bar{n} - 1)] \quad \dots (2)$$

In the case of 8Q systems the proton-ligand and metal-ligand stability constant values were determined at 0.02, 0.05, 0.08 and 0.10 M ionic strengths at 30° (Table 1). Linear plots were obtained when $\log K_n$ values were plotted against $\sqrt{\mu}$. By extrapolating the above plots to zero ionic strength, thermodynamic stability constants were obtained. The variation in ionic strength, however, has no effect on the stability constants of 2Qx systems.

Changes in free energy (ΔG^\ddagger), enthalpy (ΔH^\ddagger) and entropy (ΔS^\ddagger) accompanying the metal-ligand complex formation reactions have been calculated at 20°, 30°, 40° and 50° and at 0.10 M ionic strength (μ) using Eqs 3-5.

$$\Delta G^\ddagger = -RT \ln K_n \quad \dots (3)$$

$$\frac{d(\log K_n)}{d(1/T)} = \frac{-\Delta H^\ddagger}{4.576} \quad \dots (4)$$

(equation of an isobaric reaction¹⁷).

$$\Delta S^\ddagger = \frac{\Delta H^\ddagger - \Delta G^\ddagger}{T} \quad \dots (5)$$

It is seen from Table 2 that there is a decrease in the values of proton-ligand stability constants with increase in temperature. The chelates of Fe(II) with all these ligands are formed spontaneously as is evidenced by the negative values of ΔG^\ddagger . The values of ΔH^\ddagger were calculated graphically using the above isobar equation, i.e., by plotting $\log K_n$ values at different temperatures as a function of $1/T$ and equating the gradient of this plot with $-\Delta H^\ddagger/4.576$. The decrease in metal-ligand stability constants of all the systems except 5NH₂8Q with increase in temperature and negative values of ΔH^\ddagger indicate that the reactions are exothermic and for 5NH₂8Q these are endothermic, i.e., higher temperatures favours complex formation as shown by the positive values of ΔH^\ddagger . The ΔS^\ddagger values are positive for all the chelates of 8Q system showing that entropy is favourable for the formation of these complexes. The relatively small ΔH^\ddagger values of 5NH₂8Q compared with the large values of ΔS^\ddagger indicate entropy as the principal driving force for the complex formation in aqueous ethanol solution. It was pointed out by Williams¹⁸ that usually a high entropy of reaction indicates a combination of positive and negative ions. The very low values of ΔS^\ddagger observed for 2Qx systems may be due to the interaction of undissociated ligands with metal ion, as evidenced by little effect of ionic strength on stabilities.

Table 1—Stepwise Stability Constants of Fe(II) Chelates in Aqueous Ethanol (50% v/v) Medium at Different Ionic Strengths and at 30°

Stability constant	Ionic Strength (μ)				
	0.00	0.02 M	0.05 M	0.08 M	0.10 M
Quinoline-8-carboxylic Acid					
$\log K^H$	6.85	6.70	6.62	6.55	6.52
$\log K_1$	6.24	6.16	6.11	6.08	6.06
$\log K_2$	4.34	4.20	4.11	4.06	4.02
$\log \beta_2$	10.58	10.36	10.22	10.14	10.08
5-Nitroquinoline-8-carboxylic Acid					
$\log K^H$	4.82	4.69	4.62	4.57	4.53
$\log K_1$	4.33	4.27	4.24	4.22	4.20
$\log K_2$	4.02	3.88	3.79	3.74	3.70
$\log \beta_2$	8.35	8.15	8.03	7.96	7.90
5-Aminoquinoline-8-carboxylic Acid					
$\log K^H$	8.74	8.61	8.53	8.48	8.45
$\log K_1$	7.65	7.58	7.54	7.52	7.50
$\log K_2$	5.80	5.67	5.59	5.54	5.50
$\log \beta_2$	13.45	13.25	13.13	13.06	13.00

Table 2—Stability Constants and Thermodynamic Parameters of Fe(II) Chelates in Aqueous Ethanol (50% v/v for 8Q and 5% v/v for 2Qx Systems) Medium at Different Temperatures and at 0.10 M Ionic Strength

Stability constant	Temperature				Thermodynamic parameters		
	20°	30°	40°	50°	−ΔG‡ (kcal mol ^{−1})	−ΔH‡ (kcal mol ^{−1})	ΔS‡ (e.u.)
Quinoline-8-carboxylic Acid							
log K ^H	6.62	6.52	6.44	6.35			
log K ₁	6.17	6.06	5.98	5.91	8.40*	3.73*	15.41*
log K ₂	4.11	4.02	3.95	3.90	(5.57)†	(3.10)†	(8.15)†
log β ₂	10.28	10.08	9.93	9.81			
5-Nitroquinoline-8-carboxylic Acid							
log K ^H	4.58	4.53	4.49	4.45			
log K ₁	4.26	4.20	4.17	4.14	5.82*	1.75*	13.43*
log K ₂	3.77	3.70	3.65	3.60	(5.13)†	(2.56)†	(8.48)†
log β ₂	8.03	7.90	7.82	7.74			
5-Aminoquinoline-8-carboxylic Acid							
log K ^H	8.55	8.45	8.37	8.30			
log K ₁	7.46	7.50	7.54	7.57	10.40*	−1.63*	39.70*
log K ₂	5.43	5.50	5.58	5.65	(7.63)†	(−3.16)†	(35.61)†
log β ₂	12.89	13.00	13.12	13.22			
Quinoxaline-2-carboxylic Acid							
log K ^H	2.92	2.80	2.72	2.61			
log β ₁	3.40	3.24	2.94	2.72	4.49*	11.85*	−24.25*
3-Chloroquinoxaline-2-carboxylic Acid							
log K ^H	1.98	1.85	1.71	1.62			
log β ₁	3.26	3.02	2.70	2.43	4.10*	9.14*	−16.05*
3-Hydroxyquinoxaline-2-carboxylic Acid							
log K ^H	2.81	2.60	2.48	2.35			
log β ₁	3.31	3.12	2.84	2.65	4.20*	10.30*	−20.14*

* Values for 1:1 complexes; † values for 1:2 complexes.

The overall stability constants (log β_n) of Fe(II) chelates follow the order: 5NO₂8Q < 8Q < 5NH₂8Q for 8Q systems and 3Cl2Qx < 3OH2Qx < 2Qx for 2Qx systems. The observed orders are in accordance with the electron withdrawing properties of nitro and chloro groups and electron releasing effect of amino group. In the case of 3-hydroxyquinoxaline-2-carboxylic acid we feel that the −OH group at 3-position has lower inductive effect which can be seen from its acid dissociation constant and, hence, a high value of log K is observed compared to the chloro-substituted complex.

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