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Potentiometric determination of stability constants of cobalt (II) with some substituted 1,2,4-triazoline-3-thione derivatives

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SUMMARY

In the present study, the protonation and stability constants of cobalt (II) complexes of some substituted 1,2,4-triazoline-3-thione derivatives were investigated. These compounds have previously been synthesised and their activities reported. The mole fractions of different species derived from ligand and complex were determined in relation to their pH values.

RIASSUNTO

In questo studio sono stati investigati la protonazione e le costanti di stabilità di complessi del cobalto (II) con derivati sostituiti del 1,2,4-triazolin-3-tione. Metodi di sintesi e attivita erano state riportate in precedenza. Le frazioni molari di differenti specie derivate da ligandi e complessi, sono state determinate in relazione ai loro valori di pH.

KEY WORDS: Cobalt (II) complexes; Stability constants; 1,2,4-Triazoline-3-thione

INTRODUCTION

The determination of protonation constants of ligands and the investigation of their stability, production and equilibrium constants are of a great importance in terms of pharmaceutical and analytical chemistry. Determination of protonation and stability constant of a given compound which gives a complex with ligand is a very important parameter as this would give an indication of its usage as a pharmaceutical agent. Of a series of 1,2,4-triazoline-3-thione derivatives, which were investigated as potential diuretic agents, the following compounds were selected as prototypes and these were synthesised according to literature [1] ie, 4-ethyl-5-phenyl-2,4-dihydro-3H-1,2,4-triazol-3-thion (2a), 4-ethyl-5-(4-hydroxyphenly)-2,4-dihydro-3H-1,2,4-triazol-3-thione (2b) and 4-ethyl-5-(4-pyridiyl)-2,4-dihydro-3H-1,2,4,-triazol-3-thione (2c). The protonation constants and pK_a values of these compounds were also determined by the method of Calvin-Bjerrum and Irwing-Rossotti using potentiometric technique [2,3,4]. In addition, the stability constants of the cobalt (II) complexes of these ligands were calculated using the same procedure. The mole fractions of different species were also determined in relation to their pH values [5].

EXPERIMENTAL

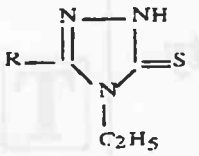
M.p.'s were determined with a Buchi (B-530) apparatus and were uncorrected. All compounds were routinely examined by TLC (HF_{254}).
The stock solution of metal ion was prepared from cobalt (II) nitrate. Other reagents used were sodium perchlorate, perchloric acid and sodium hydroxide. All chemicals were of analytical reagent grade. Metrohm 654 digital pH-meter, with a combined glass electrode assembly was used for pH-measurement "Metrohm Multi-Burette E-485" was used as the burette. The calculations on the pH-metric data were performed by computer.

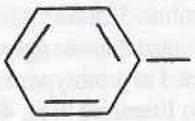
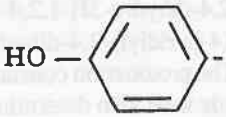
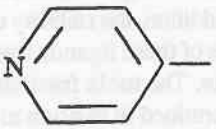
1. Synthesis of the derivatives

1.1. 1-Aroyl-4-ethylthiosemicarbazides (1a-c)
Equimolar amounts of aroylhydrazine (0,01 mol) and an appropriate isothiocyanate (0,01 mol) were refluxed in ethanol (50 mL) for 3h.
The solid which separated was filtered and recrystallized from C_2H_5OH/H_2O. M.p. 1a: 192°C, 1b: 204-205°C, 1c: 231°C (lit[1] m.p.1a: 192-193°C, 1b: 204-205°C, 1c: 230-231°C).

1.2. 4-Ethyl-5-substituted-2,4-dihydro-3H-1,2,4-triazol3-thiones (2a-c)
1a-c (0,05 mol) were refluxed in NaOH (15 mL, 2 mol/L) for 4h. The solution was allowed to cool, then acidified with HCl (37%). The precipiate thus formed was filtered and washed with H_2O and recrystallized from C_2H_5OH or C_2H_5OH/H_2O [6].

Table I. Some physico-chemical characteristic of 2a-c



Comp. No	R	M.P., °C (lit[1] m.p., °C)	Yield % (lit[1], yield %)	Molecular formular (m.w)
2a		141-142 (141-142)	84 (90)	$C_{10}H_{11}N_3S$ (205.28)
2b		211-213 (212-214)	76 (62)	$C_{10}H_{11}N_3OS$ (221.28)
2c		230-232 (231-233)	90 (89)	$C_9H_{10}N_4S$ (206.26)

2. The Determination of Protonation Constants

Ligands were dissolved in a dioxane-water (1:10, v/v) mixture. The ionic strength was kept at I = 0,20 using $NaClO_4$ during the experiment. In order to determine the protonation constants, solutions including $HClO_4$ and ligand+$HClO_4$ solutions were titrated potentiometrically using NaOH solution (0,100 M) (Fig.1). Average $\bar{n}_A$ values were calculated from the titration curves.
For this calculation, the following equation was used:

$$\bar{n}_A = y + \frac{(v_1 - v_2)(N + E^\circ)}{(V^\circ + v_1)T^\circ_L}$$

Where:

V°	= volume at the beginning	: 25,0 mL
N	= normality of base	: 0,100 M
T°_L	= concentration of total ligand (2a-c)	: $2{,}00.10^{-3}$M
E°	= concentration of acid	: $2{,}00.10^{-2}$M
y	= the number of protons given	
	for **2a**	: 1
	for **2b**	: 2
	for **2c**	: 1

The $\bar{n}_A$ values which corresponded to several pH values for **2a**, **2b**, **2c** by the use of v_1 and v_2 volumes from figure 1 were calculated. The figure of $\bar{n}_A = f$ (pH) was plotted by using the values obtained. From $\bar{n}_A = f$ (pH) figure plotted, the protonation constants which corresponded to $\bar{n}_A = 0{,}5$ and $\bar{n}_A = 1{,}5$ values and the corresponding acid constants were found. The results are given in Table II.

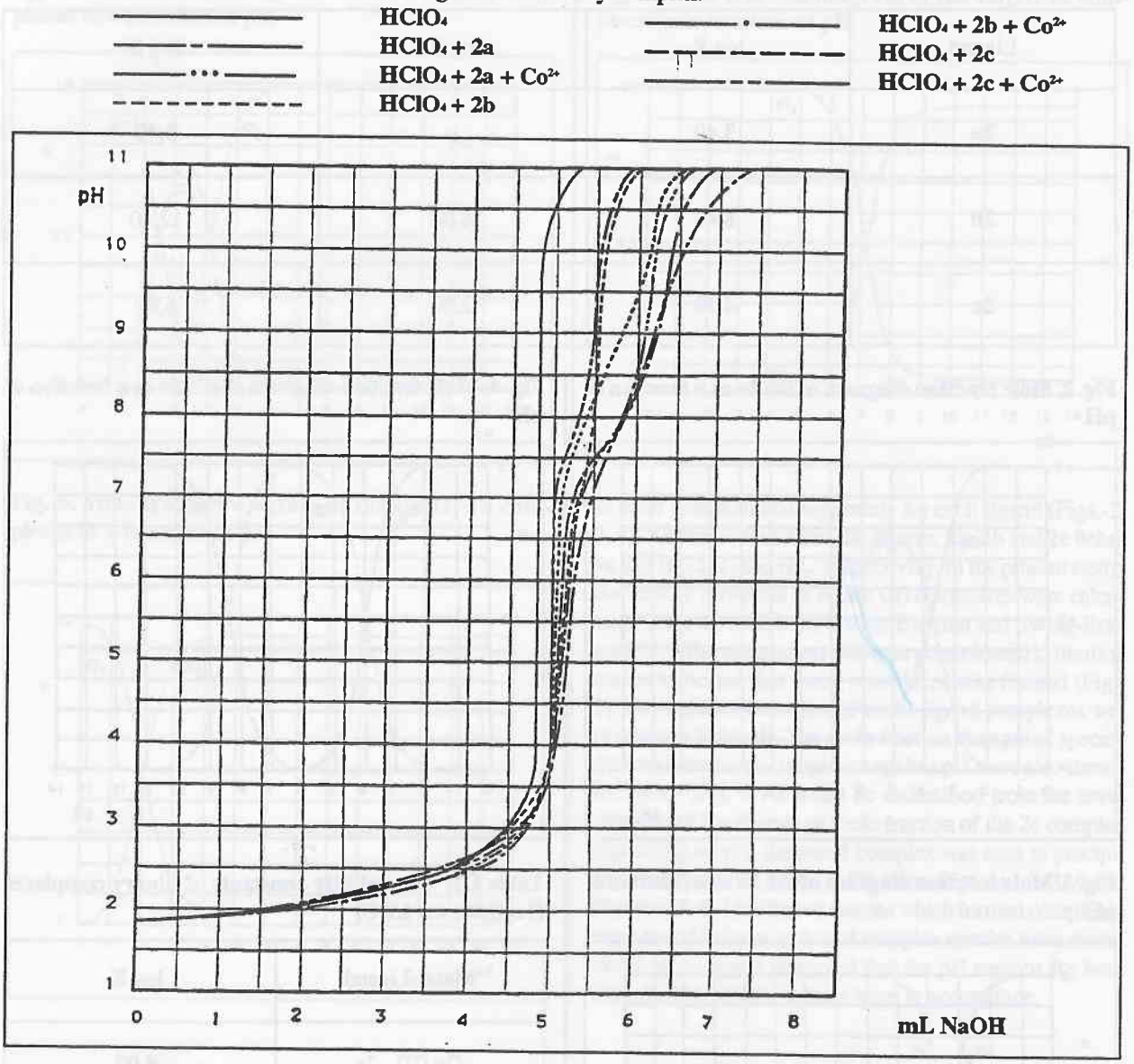
By the use of these protonation constants, the changes in mole fractions of the molecular and ionic species derived from these three ligands with the pH of the solution were calculated and their figures were plotted (Figs.-2, 3, 4).

3. The Determination of Stability Constants

The stability constants of binary complexes were determined potentiometrically using Irwing-Rossotti method. For the determination of the stability constants of the binary complexes of cobalt (II) with ligands, solutions (1:1, v/v) were separately prepared for each ligand.
Therefore, the mixtures which contain metal ions were titrated with 0,100 M NaOH potentiometrically and the titration curves were plotted (Fig.- 1). It was observed from the titration curves that the ligand and ligand+metal curves were significantly separated to give a complex. During the titration of mixtures containing metal, it was demonstrated that the colour changes appeared and a precipitation occured depending on the pH of the solution. For instance, the titration mixture had a yellow colour in the beginning; during the titration a solid precipitated at pH = 5,10 - 6.80 followed by a green precipitate in the end of the titration.
$\bar{n}_L$ values were calculated using $\bar{n}_A$ values, pL values were calculated using $\bar{n}_L$ values to calculate the stability constants of metal complexes. The following equation was used to calculate $\bar{n}_L$ values:

$$\bar{n}_L = \frac{(v_3 - v_2)[N + E^\circ + T^\circ_L(Y - \bar{n}_A)]}{(V^\circ + v_2)\bar{n}_A T^\circ_M}$$

Fig. 1. Potentiometric titration curves of ligands and binary complex.



Where:

V° = volume at the beginning : 25,0 mL
N = normality of base : 0,100 M
$T°_L$ = concentration of total ligand (2a-c) : $2{,}00.10^{-3}$M
E° = concentration of acid : $2{,}00.10^{-2}$M
y = the number of protons given
for 2a : 1
for 2b : 2
for 2c : 1
$T°_M$ = concentration of total metal : $2{,}00.10^{-3}$M

The following equation was used to calculate pL values:

$$pL = \log \frac{1 + \beta_1[H^+] + \beta_2[H^+]^2}{T°_L - \bar{n}_L T°_M}$$

for 2a;
$\beta = 2{,}51.10^3$
for 2b;
$\beta_1 = 2{,}51.10^8$
$\beta_2 = 2{,}51.10^8 . 1{,}00.10^4 = 2{,}51.10^{12}$
for 2c;
$\beta_1 = 1{,}58.10^4$
$\beta_2 = 1{,}58.10^4 . 3{,}98.10^2 = 6{,}29.10^6$

pL values were calculated using β values. $\bar{n}_L = f(pL)$ graphics were plotted using $\bar{n}_L$ and p_L values which were calculated for each metal ligand complex.

The stability constants of complexes were found from pL values which corresponded to $\bar{n}_L = 0{,}5$ value. The results are given in Table III.

In addition, the changes in mole fractions of the molecular and ionic species derived from binary complexes with the pH of the solution were calculated (Figs.- 5, 6, 7).

RESULTS AND DISCUSSION

In this study, the 1,2,4-triazoline-3-thione derivatives were used as ligands. The protonation constants and pK_a values of these compounds were also determined by the method of Calvin-Bjerrum and Irwing-Rossotti using potentiometric technique. The ionic strength was kept at I =

Table II. The protonation constants of ligands (I = 0,20; t = 25°C)

Ligand	log K_1	log K_2	log β
2a	3,40	–	3,40
2b	8,40	4,00	12,40
2c	4,20	2,60	6,80

Fig. 2. Mole fraction diagram of the 2a as a function of pH

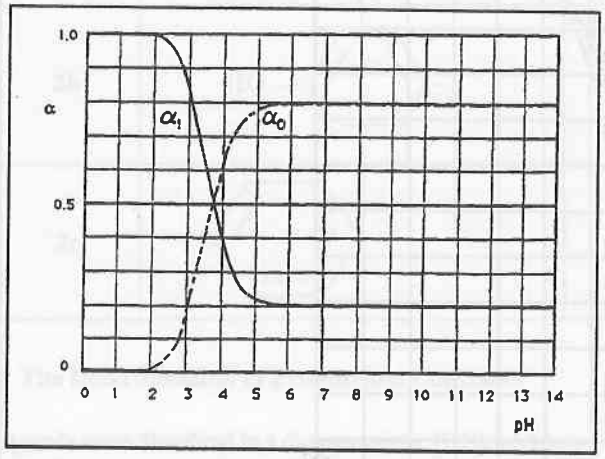
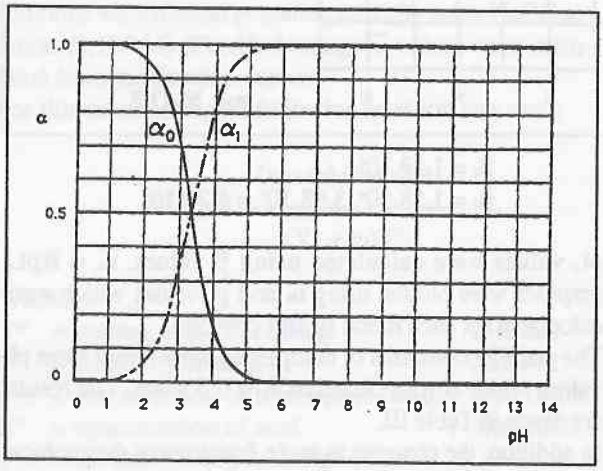


Fig. 3. Mole fraction diagram of the 2b as a function of pH



0,20 using $NaClO_4$ during the experiment. The experiments were carried out at 25°C. The protonation constants were calculated using potentiometric titration curves (Fig. 1) and these were given in Table II.

As can be seen in Table II, for ligand **2a**, only one protonation constant was found and this clearly demonstrates that this constant was related to the proton on the triazoline ring ligands 2b and 2c have pyridine and phenole rings which were different from 2a. The electron density on the triazoline ring increases with the mesomeric effect of the-

Fig. 4. Mole fraction diagram of the 2c as a function of pH

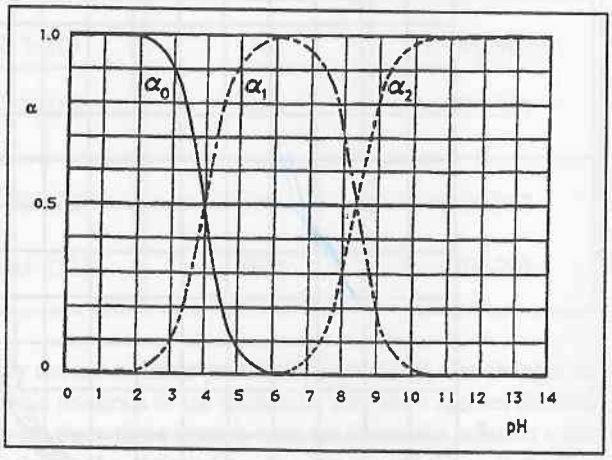


Table III. The stability constants of binary complexes (I = 0,20; t = 25°C)

Metal-Ligand	log K
Co (II) - 2a	4,00
Co (II) - 2b	3,95
Co (II) - 2c	3,30

se rings. Therefore the proton on the triazoline ring can not leave easily and finally the values of protonation constants slightly increase compared to ligand **2a**. In addition, the protonation constants related to pyridine and phenol rings, for ligands 2c and 2b were found respectively. This values were found slightly lower than literature values [7] because of the mesomeric effect of the triazoline ring. Because of the shift of electron density to the triazoline ring, the proton binding strengths of phenol oxygen and pyridine nitrogen decreased.

In addition, the changes of the mole fractions of species derived from ligands against pH were investigated and the-

Fig. 5. Mole fraction diagram of the Co(II)-2a complexes as a function of pH

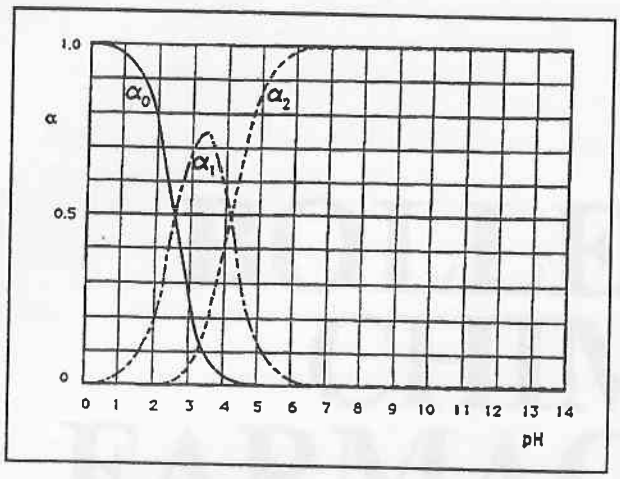


Fig. 6. Mole fraction diagram of the Co(II)-2b complexes as a function of pH

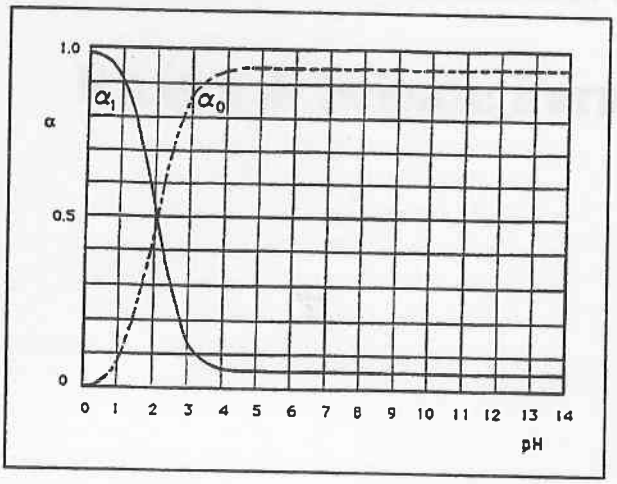
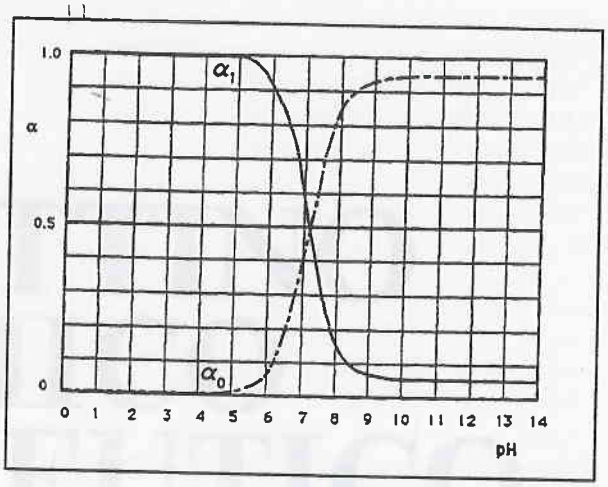


Fig. 7. Mole fraction diagram of the Co(II)-2c complexes as a function of pH



se were demonstrated separately for each ligand (Figs.-2, 3, 4). As can be seen from the figures, **2a**, **2b** and **2c** behave like HL, H_2L and H_2L^+ respectively. In the present study, the stabiliy constants of cobalt (II) complexes were calculated using the method of Calvin-Bjerrum and Irwing-Rossotti [2,3,4]. The separations between potentiometric titration curves indicates that metal complexes was formed (Fig.-1). The stability constants of metal-ligand complexes were given in Table III. The mole fraction changes of species derived from metal complexes against pH were also shown in figures 5, 6, 7. As it can be understood from the investigation of the change of mole fraction of the 2c complex depending on pH, the metal complex was seen to precipitate between pH = 5,00 - 6,00. From Figures - 2, 3, 4 and Figures - 5, 6, 7 the ligand species which formed complexes were found to be α_1 and α_2 if complex species were considered as α_0, it was observed that the pH regions for both ligand and complex species were in accordance.

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