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NEW BINARY AND TERNARY COMPLEXES OF FLUCLAXOCILLIN AND AMINO ACIDS WITH SOME TRANSITION METALS. SYNTHESIS, CHARACTERIZATION, AND CYCLIC VOLTAMMETRIC STUDIES

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NEW BINARY AND TERNARY COMPLEXES OF FLUCLAXOCILLIN AND AMINO ACIDS WITH SOME TRANSITION METALS. SYNTHESIS, CHARACTERIZATION, AND CYCLIC VOLTAMMETRIC STUDIES

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ABSTRACT

The new binary and ternary complexes of fluclaxocillin (HFluc) and amino acids (HAA) [glycine (HGly) and alanine (HAla)] with Fe(II), Fe(III), Co(II), Ni(II) and Cu(II) ions were prepared and characterized using various spectroscopic methods. According to the elemental analyses, the binary complexes were found to have the general formulas $[M(Fluc)(X)(H_2O)_x]\cdot yH_2O$ and $[Fe(Fluc)(Cl)_2(H_2O)_2]\cdot 4H_2O$ while the ternary complexes had the formulas $[M(Fluc)-(AA)(H_2O)_x]\cdot yH_2O$ and $[Fe(Fluc)(AA)(Cl)(H_2O)_x]\cdot yH_2O$

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where M = Fe(II), Co(II), Ni(II) and Cu(II), X = OAc in the case of Cu(II) and Cl in the case of Fe(II), Co(II) and Ni(II), $AA = Gly^-$ and Ala^- , x = 2-6 and y = 1-3. IR, magnetic and solid reflectance spectral studies were utilized to infer the structure of the complexes. Thermogravimetric analysis (TGA) was utilized to differentiate between coordinated and hydrated water molecules. The Fluc⁻, Gly⁻ and Ala⁻ molecules are decomposed in a second and subsequent steps. Cyclic voltametric investigations of these complexes were also carried out.

INTRODUCTION

Much interest had been shown in the chemistry of β -lactam antibiotics in relation to their useful biological activities.^[1–4] β -Lactam antibiotics, such as penicillins, cephalosporins, oxacephalosporins, represent the most important class of drugs against diseases caused by bacteria. Following the evidence of the important roles of calcium and magnesium in the transport of these drugs in blood plasma,^[5] it is suggested that copper can act as a cofactor of their antibiotic activity: first, the structural flexibility of copper binary complexes is expected to favor mixed-ligand coordination with bacterial nucleic acids; second, through formation of such ternary complexes, copper may induce the attack of free radicals known to damage these nucleic acids.^[6]

In continuation of our previous studies of the metal complexes of antibiotics,^[7–11] the present investigation reports studies of binary and ternary complexes of some metal ions with HFluc, HGly and HAla. The structures of these binary and ternary complexes are proposed based on elemental analyses, IR, magnetic and solid reflectance measurements. Thermal analyses were used to distinguish between the crystal and coordinated water molecules. The fragmentation of the ligand molecules (HFluc and AA) is also discussed. Various thermodynamic activation parameters were calculated. Cyclic voltammetric studies were also carried out to confirm the proposed structures.



Scheme. Structure of fluclaxocillin.

EXPERIMENTAL

Materials and Reagents

Fluclaxocillin is (6'R)-6-(3-2-chloro-6-flourophenyl)-5-methylisoxazole-4-carboxamido)pencillanic acid. It was obtained from the Nile Co., Egypt. The metal chlorides of Fe(II), Fe(III), Co(II) and Ni(II) were supplied from Aldrich. Copper acetate and the amino acids glycine and alanine were obtained from Sigma Chemical Co.

Instruments

IR spectra were recorded on a model 8001 Perkin-Elmer FT-IR spectrometer as KBr discs. Solid reflectance spectra were measured on a Shimadzu 3101 PC spectrophotometer. The molar magnetic susceptibilities were measured on powdered samples using the Faraday method. Diamagnetic corrections were made using Pascal's constants with Hg [Co(SCN)₄] as calibrant at room temperature. TGA was carried out in a dynamic nitrogen atmosphere (20 mL min⁻¹) with a heating rate of 10 $^{\circ}$ C min⁻¹ using a Shimadzu TGA-50H thermal analyzer in the temperature range from room temperature up to 1000 °C. Metal contents were determined by titration against standard EDTA solution after complete decomposition of the complexes with aqua regia in a Kjeldahl flask several times. Cyclic voltammetric polarization measurements were performed using a potentiometric Amel 5000 instrument which is a complete microprocessor-controlled electrochemical measurement system capable of satisfying all needs for simple or complex measurements. Amel Easyscan software was used in connection with a PC to control the system. The controlled potential ranges vary from +8 V to -8 V and the current range is up to 1 A. The measurements were carried out on solutions of the various complexes in 0.5 M HCl as a supporting electrolyte and 1×10^{-3} M concentrations were chosen for this study. The solutions were prepared by dissolving the appropriate weighed complex in 0.5 M HCl solution.

Preparation of Binary Metal Complexes

A solution of the metal chloride (Fe(II), Fe(III), Co(II) and Ni(II)) or Cu(II) acetate (1 mmol) in an ethanol-water mixture (1:1) (25 mL) was added to a solution of HFluc (1 mmol, 0.4525 g) in the same solvent (50 mL). The resulting mixture was stirred under reflux for a half-hour whereupon the complexes precipitated. They were removed by filtration, washed with a 1:1 ethanol-water mixture and dried in a vacuum desiccator over anhydrous calcium chloride. The analytical data are collected in Table I.

Preparation of Ternary Metal Complexes

A metal chloride (Fe(II), Fe(III), Co(II) and Ni(II)) or acetate (Cu(II)) solution (1 mmol) in ethanol-water mixture (1:1) (25 mL) was added to a solution of HFluc (1 mmol, 0.4525 g) and the amino acid (1 mmol, 0.075 g HGly or 0.088 g HAla) in the same solvent (50 mL) in the mole ratio 1:1:1 (metal salt:HFluc:HAA). The work-up was the same as mentioned above. The analytical data are collected in Table I.

RESULTS AND DISCUSSION

The main objective of this article is the preparation and chemical characterization of new binary complexes with HFluc and ternary complexes of HFluc and HGly or HAla with Fe(II), Fe(III), Co(II), Ni(II) and Cu(II) ions. As seen from Table I, 1:1 (M:Fluc) binary and 1:1:1 (M:Fluc: AA) ternary complexes were prepared with satisfactory elemental analyses results. The results indicate that HFluc and the amino acids (HGly and HAla) behave as uninegative, bidentate molecules. They lose the carboxylate hydrogen atom on coordination to the metal ions.

The formation of these binary and ternary complexes may proceed as follows:

 $MX_2 + HFluc \longrightarrow [M(Fluc)X] + HX$ (Binary complexes)

M = Fe(II), Co(II), Ni(II), Cu(II); X = CI in case of Fe(II), Co(II), Ni(II) and X = OAc in case of Cu(II).

 $FeCl_3 + HFluc \longrightarrow [Fe(Fluc)Cl_2] + HCl$ (Binary complexes)

 $MX_2 + HFluc + HAA \longrightarrow [M(Fluc)(AA)] + 2HX$ (Ternary complexes)

M = Fe(II), Co(II), Ni(II), Cu(II), X = CI in case of Fe(II), Co(II), Ni(II) and X = OAc in case of Cu(II).

 $FeCl_3 + HFluc + HAA \longrightarrow [Fe(Fluc)(AA)Cl] + 2HCl$ (Ternary complexes)

	Table I. Ana	lytical and Physical L	Data of Bin	ary and Te	rnary Coi	nplexes		
			,		Found (c	alcd.) %		
No.	Compound	Color (% yield)	M. p. (°C)	C	Н	z	М	$\mu_{eff}\left(B.M.\right)$
(E)	$[Fe(Fluc)(Cl)(H_2O)_3] \cdot 3H_2O$	Buff	>300	34.60	4.40	6.70	8.72	4.9
	$C_{19}H_{28}Cl_2FFeN_3O_{11}S$	(75)		(34.94)	(4.44)	(6.44)	(8.58)	
5	$[Fe(Fluc)(Cl)_2(H_2O)_2]\cdot 4H_2O$	Yellowish brown	>300	33.30	4.0	5.88	8.20	4.62
	$C_{19}H_{28}Cl_3FFeN_3O_{11}S$	(78)		(33.14)	(4.22)	(6.10)	(8.14)	
$\widehat{\mathbf{e}}$	$[Co(Fluc)(Cl)(H_2O)_3]$ ·3H ₂ O	Green	>300	34.53	4.19	6.80	8.60	5.5
	$C_{19}H_{28}Cl_2CoFN_3O_{11}S$	(20)		(34.78)	(4.42)	(6.41)	(0.0)	
<u>4</u>	$Ni(Fluc)(Cl)(H_2O)_3] \cdot 3H_2O$	Light green	>300	34.45	4.55	6.90	8.70	3.42
	$C_{19}H_{28}Cl_2FN_3NiO_{11}S$	(80)		(34.84)	(4.43)	(6.42)	(8.86)	
(2)	$[Cu(Fluc)(Oac)(H_2O)_3] \cdot 2H_2O$	Green	>300	37.80	4.70	6.40	9.65	2.04
	$C_{21}H_{29}CIC_{u}FN_{3}O_{12}S$	(85)		(37.92)	(4.67)	(6.32)	(9.56)	
و	$[Fe(Fluc)(Gly)] \cdot H_2O$	Buff	>300	36.86	4.17	8.70	8.95	4.5
	$C_{21}H_{22}CIFFeN_4O_8S$	(20)		(37.03)	(4.41)	(8.23)	(9.33)	
6	$[Fe(Fluc)(Gly)(Cl)(H_2O)]-4H_2O$	Buff	>300	35.30	4.0	8.20	7.53	4.5
	$C_{21}H_{30}Cl_2FFeN_4O_{12}S$	(82)		(35.57)	(4.20)	(7.90)	(7.90)	
8	$[Co(Fluc)(Gly)(H_2O)_2]$ ·5H ₂ O	Red	>300	42.10	3.50	9.50	9.13	5.2
	$C_{21}H_{34}CICoFN_4O_{14}S$	(78)		(41.93)	(3.99)	(9.32)	(9.32)	
6	$[Ni(Fluc)(Gly)(H_2O)_2]$ ·4H ₂ O	Light green	>300	35.55	4.88	7.43	8.55	3.75
	$C_{21}H_{32}CIFNiN_4O_{13}S$	(75)		(35.44)	(4.78)	(7.88)	(8.16)	
(10)	$[Cu(Fluc)(Gly)(H_2O)_2]$ ·3H ₂ O	Deep green	>300	36.30	4.52	8.32	8.10	1.95
	$C_{21}H_{30}CICuFN_4O_{12}S$	(65)		(36.31)	(4.61)	(8.07)	(8.50)	
(11)	[Fe(Fluc)(Ala)]·H ₂ O	Buff	>300	42.50	4.20	9.53	9.0	4.32
	$C_{22}H_{24}CIFFeN_4O_8S$	(85)		(42.93)	(3.90)	(9.11)	(9.11)	
								(continued)

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	- μ _{eff} (B.M.)	4.8	() 5.32	3)	3.7	(x)	1.97	(1
	Μ	8.75	(8.01 9.30	(9.13	10.05	(9.28)	9.0	(8.91
alcd.) %	z	8.53	(8.61) 8.90	(8.82)	9.0	(8.81)	8.20	(7.86)
Found (c	Н	3.90	(5.69) 4.70	(4.09)	3.80	(4.09)	4.60	(4.77)
	С	40.65	(40.58) 41.80	(41.57)	41.10	(41.51)	37.80	(37.55)
	M. p. (°C)	>300	>300		>300		>300	
	Color (% yield)	Light brown	(90) Brownish red	(73)	Yellowish green	(82)	Deep green	(89)
	Compound	$[Fe(Fluc)(Ala)(Cl)(H_2O)]$	C22H24CIFFeN4O85 [Co(Fluc)(Ala)(H2O)2]	$C_{22}H_{24}ClCoFN_4O_9S$	$[Ni(Fluc)(Ala)(H_2O)_2]$	$C_{22}H_{26}CIFNiN_4O_9S$	$[Cu(Fluc)(Ala)(H_2O)_2] \cdot 4H_2O$	$C_{22}H_{34}ClCuFN_4O_{13}S$
	No.	(12)	(13)		(14)		(15)	

Table I. Continued

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The structures of the prepared complexes were confirmed by using various tools of analyses, namely IR, magnetic, solid reflectance and thermal analysis measurements.

IR Spectra and Mode of Bonding

HFluc has various potential donor sites. A comparison between the IR spectra of HFluc and those of the transition metal complexes provides evidence regarding the bonding sites in the HFluc complexes. The IR spectra of all HFluc binary complexes show bands at 3450-3300 and $870-750 \text{ cm}^{-1}$ characteristic of water of crystallization and coordinated H₂O molecules, respectively.^[12,13] The IR spectrum of HFluc reveals bands at 1615 and 1430 cm⁻¹ due to $v_{asym}(COO^{-})$ and $v_{sym}(COO^{-})$.^[14,15] These bands decrease in intensity and shift to lower frequency on complexion, suggesting coordination via the carboxylate group.^[7,16] The band due to v(C–N) of the β -lactam ring (1355 cm⁻¹) in the free ligand is shifted to lower frequency and decreases in intensity on complexation, indicating coordination through the β-lactam nitrogen. The IR spectra of HGly and HAla exhibit a band at 2590 cm^{-1} assigned to $v(NH_3^+)$. In the spectra of the ternary complexes, the NH₃⁺ band has disappeared, a behavior which provides convincing evidence for coordination through the amino group.^[17] In addition, the ligand HFluc exhibits bands at 1760, 1645 and $1490 \,\mathrm{cm}^{-1}$ due to v(C=O) of β -lactam, amide, C=O stretch and $v(C=N)_{cvclic}$, respectively, and these remain unchanged on complexation. The spectra of the Cu complexes displays two intense bands at 1575 and 1400 cm⁻¹ due to $v(NH_3^+)$ and $v(NH_3^+)$ of the acetate group.^[12]

In the far-IR spectra, the bonding of nitrogen and oxygen is indicated by the presence of bands at 570–515 cm⁻¹ (M–N) and 430–375 cm⁻¹ (M–O).^[18] The metal complexes of HFluc contain chloride attached to the metal ions which is supported by the presence of a v(M–Cl)^[18] band at 330–290 cm⁻¹. The presence of acetate or chloride ions in the structural configuration of the complexes suggests that HFluc acts as a uninegative bidentate ligand on complexation with the metal ions. Also, it indicates that HFluc ligates with the metal ions through carboxylate and nitrogen in the β -lactam.

Electronic Spectra and Magnetic Properties

The solid reflectance spectrum of the [Cu(Fluc)(OAc)(H₂O)₃]·2H₂O complex shows a broad band at ~17,490 cm⁻¹, which is consistent with an octahedral environment.^[19] This band may be attributed to the ${}^{2}E_{g} \rightarrow {}^{3}T_{2g}$ transition in an octahedral environment. While, the μ_{eff} value of the

[Fe(Fluc)(Cl)H₂O)₃]·3H₂O binary complex (4.9 B.M.) is within the range of values corresponding to high-spin complexes of Fe(II) ions. The solid reflectance spectrum shows a doublet band at 10,300-8,020 cm⁻¹ and a shoulder at 20,550 cm⁻¹ assigned to ${}^{5}T_{2g}(D) \rightarrow {}^{5}E_{g}$ and $t_{2g} \rightarrow \pi^{*}$, respectively.^[20] Cotton and Meyers^[21] suggested that such doublet bands in sixcoordinated Fe(II) complexes could be due to Jahn-Teller distortion. The solid reflectance spectrum of the [Co(Fluc)(Gly)(H₂O)₂]·5H₂O complex exhibits three bands at 8,250, 14,250 and 20,570 cm⁻¹, which are assigned to ${}^{4}T_{1g} \rightarrow {}^{4}T_{2g}(F)(\nu_{1}), \ {}^{4}T_{1g} \rightarrow {}^{4}A_{2g}(\nu_{2}) \text{ and } {}^{4}T_{1g} \rightarrow {}^{4}T_{1g}(P)(\nu_{3}) \text{ transitions,}$ indicating an octahedral^[22] geometry of the Co(II) complex. This was further confirmed by the value of the magnetic moment (5.2 B.M.) in Table I. The solid reflectance spectrum of the [Ni(Fluc)(Gly)(H₂O)₂]·4H₂O ternary complex shows three bands at 8,060 (v_1), 12,097 cm⁻¹(v_2) and 22,946 cm⁻¹(v₃), which are assigned to the following transitions, ${}^{3}A_{2g} \rightarrow {}^{3}T_{2g}(v_1)$, ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(v_2)$ and ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(P)(v_3)$, respectively, consistent with octahedral geometry^[23] and is also confirmed by the magnetic moment value (3.75 B.M.) in Table I. The magnetic moment values of the ternary Fe(III) complexes with HGly and HAla have been found to be 4.5 B.M. and 4.8 B.M, respectively, which is within the range of values corresponding to high-spin octahedral complexes of Fe(III) ions. The μ_{eff} values of the [Fe(Fluc)(Gly)]·H₂O and [Fe(Fluc)(Ala)]·H₂O complexes are 4.5 B.M. and 4.32 B.M., respectively, which is in the range of values corresponding to tetrahedral complexes.

Redox Properties

When examined by cyclic voltammetry in HCl (Fig. 1a), it is observed that HFluc itself exhibits redox peaks at about +0.6 V (reduction) and +0.95 V vs. the normal hydrogen electrode (NHE). These peaks may be explained as a result of reduction and oxidation of the carboxylate group in the HFluc molecule. But on complexation with the various metal ions, these redox peaks vanished, which proves that this carboxylate group is participating in complex formation. It is observed in the voltammogram of all binary and ternary complexes for all metal ions except Cu(II), for which no redox peaks are obtained, which proves the relatively high stability of these complexes under the given experimental conditions.

In the case of the binary Cu(II) complexes, polarization usually started at thye potential of hydrogen evolution. As a result, Cu(II) ions could be chemically reduced by the evolved atomic hydrogen to Cu(I). In the positive scan the reduced Cu(I) ions are electrochemically oxidized^[24,25] to Cu(II), as confirmed by the oxidation peak at 0.62 V vs. the NHE reference electrode (Fig. 1b).



Figure 1. Cyclic voltammograms of Cu(II)-binary and ternary complexes (a) and Cu(II)-binary complex with repeated cycles (b). Scan rate 50 mVs^{-1} .

Thermal Analysis (TGA)

The TGA for the complexes was carried out within a temperature range from room temperature up to 1000 °C. The observed mass losses are based on the TG results and the calculated mass losses are based on the molecular weight of the proposed formulas. The observed temperature ranges, percent losses in mass, and thermal effects accompanying the changes in the solid complexes on heating are given in Table II, which reveals the following findings.

The thermograms of $[Fe(Fluc)(Cl(H_2O)_3]\cdot 3H_2$ (1), $[Fe(Fluc)-(Gly)]\cdot H_2O$ (6) and $[Fe(Fluc)(Ala)]\cdot H_2O$ (11) complexes show three decomposition steps within the temperature range from 25–900 °C. The first step of decomposition within the temperature range 25–130 °C corresponds to the loss of water molecules of hydration with a mass loss of 8.42% (calcd. for 3H₂O 8.28%), 2.83% (calcd. for H₂O 3.0%) and 2.69% (calcd. for H₂O 2.93%) for (1), (6) and (11), respectively. The energy of activation of this dehydration step is 56.91, 59.40 and 44.10 KJ mol⁻¹ for (1), (6) and (11), respectively. The second and third steps (from 130–900 °C) correspond to the removal of coordinated water, HCl, Fluc⁻, Gly⁻ and Ala⁻ molecules leaving metal oxide as residue. The overall weight loss amounts to 88.50%

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	Tabı	le II. Thermoan	alytical Results (TGA) of Fluclay	xocillin Metal Complexes
Complex	TG range (°C)	DTG _{max} (°C)	Mass loss; Total mass loss Found (Calcd. %)	Assignment
(1)	35-120	78	8.42 (8.28)	Loss of 3H ₂ O
~	125-445	208,419	35.94 (36.04)	Loss of $3H_2O$, HCl and C_7H_6ClF
	445-700	517	44.14 (44.63) 88.50 (88.95)	Loss of C ₁₂ H ₉ N ₃ O ₄ S leaving metal oxide
				residue.
(2)	30 - 100	65	7.65 (7.85)	Loss of $3H_2O$
	105 - 485	213	58.60 (58.25)	Loss of $3H_2O$ and $C_{17}H_{12}N_2O_3CIF$.
	485—665	550	15.52 (15.42) 81.77 (81.52)	Loss of C ₂ H ₄ NO ₂ S leaving metal chloride
				residue.
(3)	25 - 140	61	7.85 (8.25)	Loss of $3H_2O$
	140 - 400	306	37.46 (37.25)	Loss of $3H_2O$, HF, CH_4 , $\frac{1}{2}O_2$ and C_8H_8S .
	400 - 650	455	35.05 (34.81) 80.46 (80.31)	Loss of C ₁₀ H ₂ N ₃ O ₄ leaving metal chloride
				residue.
(4)	30 - 180	65	8.25 (8.25)	Loss of $3H_2O$
	185-445	328	37.46 (37.25)	Loss of $3H_2O$, HF, CH_4 , $\frac{1}{2}O_2$ and C_8H_8S .
	445—690	513	34.93 (34.81) 80.64 (80.31)	Loss of C ₁₀ H ₂ N ₃ O ₄ leaving metal chloride
				residue.
(5)	30 - 100	65	5.40 (5.27)	Loss of 2H ₂ O
	100 - 210	154	10.54 (10.26)	Loss of 3H ₂ O and CH ₄ .
	210-750	256,550,669	64.04 (64.09) 79.98 (79.62)	Loss of C ₁₉ H ₁₅ N ₂ O ₇ ClF leaving metal
				thiocyanate residue.
(9)	25-130	52	2.83 (3.0)	Loss of H_2O
	135-420	245	38.32 (38.85)	Loss of C ₂ H ₄ NO ₂ , C ₆ H ₃ ClF and C ₂ H ₆ .
	420 - 900	590	46.95 (46.09) 88.10 (87.94)	Loss of C ₁₁ H ₇ N ₃ O ₄ S leaving metal oxide
				residue.

(1)	30-150	09	9.95 (10.24)	Loss of 2H ₂ O and HCl.
	150-450	265	45.70 (45.52)	Loss of $3H_2O$, C_2H_4NO and $C_{10}H_6NOCIF$.
	450-720	560	33.15 (32.91) 88.80 (88.67)	Loss of C ₉ H ₉ N ₂ O _{3.5} S leaving metal oxide residue
(8)	20-125	81	7.67 (7.60)	Loss of 3H ₂ O
	125-490	230	51.51 (51.83)	Loss of 4H ₂ O, C ₂ H ₄ NO and C ₁₁ H ₆ NO ₂ ClF.
	490-745	580	24.29 (23.91) 83.47 (83.34)	Loss of C ₇ H ₁₀ N ₂ OS leaving metal carbonate
				residue.
(6)	25 - 130	86	7.85 (7.78)	Loss of 3H ₂ O
	130 - 500	245	50.24 (50.50)	Loss of 3H ₂ O, C ₂ H ₄ NO and C ₁₁ H ₆ NO ₂ ClF.
	505-760	615	31.0 (30.84) 89.09 (89.12)	Loss of C ₈ H ₁₀ N ₂ O ₃ S leaving metal oxide
				residue.
(10)	20 - 195	155	16.45(16.18)	Loss of 3H ₂ O, 2H ₂ O, and HF.
	195 - 410	259	34.77 (34.54)	Loss of C ₆ H ₇ O ₃ , HCl, NO and CH ₄ .
	410 - 1000	069	31.60 (32.75) 82.82 (83.47)	Loss of C ₁₃ H ₇ N ₃ O ₃ leaving metal thiocyanate
				residue.
(11)	25-105	59	2.69 (2.93)	Loss of H_2O .
	110-415	247	52.46 (52.93)	Loss of C ₁₁ H ₇ N ₂ O ₂ ClF and C ₃ H ₆ NO.
	420-570	465	35.41 (34.96) 90.74 (90.82)	Loss of C ₈ H ₉ NO ₃ S leaving metal oxide
				residue.
(12)	35 - 120	67	2.77 (2.46)	Loss of CH ₄ .
	125-425	257	48.66 (48.73)	Loss of HCl and C ₁₃ H ₁₀ N ₂ O ₂ ClF.
	430-650	510	30.19 (29.82) 81.62 (81.01)	Loss of C ₈ H ₉ N ₂ O ₆ leaving metal sulfide
				residue.
	625–990	755	38.18 (38.43) 88.34 (88.27)	Loss of C ₉ H ₁₀ N ₂ O ₄ S leaving metal oxide
				residue.
				(continued)

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			Table II. Continued	
Complex	TG range (°C)	DTG _{max} (°C)	Mass loss; Total mass loss Found (Calcd. %)	Assignment
(13)	25-120	65	2.97 (2.83)	Loss of H_2O .
	125-625	466	47.19 (47.01)	Loss H_2O and $C_{13}H_{10}N_2O_2CIF$.
(14)	20 - 150	87	5.92 (5.66)	Loss of 2H ₂ O
	155 - 490	237	60.74 (60.93)	Loss of $C_5H_{12}NO_2$, $C_{11}H_7N_2O_2CIF$ and $\frac{1}{5}O_2$.
	490 - 690	552	22.22 (21.54) 88.88 (88.13)	Loss of C ₆ H ₃ NOS leaving metal oxide residue.
(15)	20-125	68	5.64 (5.05)	Loss of 2H ₂ O.
	130 - 490	223	45.54 (45.27)	Loss 4H ₂ O, C ₁₁ H ₁₃ O ₃ , HCl and HF.
	490820	603	32.44 (32.71) 83.62 (83.03)	Loss of C ₁₀ H ₇ N ₃ O ₄ leaving metal thiocyanate
				residue.

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(calcd. 88.95%), 88.10% (calcd. 87.94%) and 90.74% (calcd. 90.82%) for (1), (6) and (11), respectively. According to the stereochemistry of these complexes suggested from electronic spectra, magnetic susceptibility measurements and from the mode of bonding based on the IR spectra, the proposed structure of these complexes is shown in Fig. 2.

The Fe(III) complexes with HFluc (2), HFluc-HGly (7) and HFluc-HAla (12) ligands give a three-stage decomposition pattern. The first stage (30–150 °C) represents the loss of three water molecules of hydration; two water molecules of hydration and HCl molecules; and CH₄ molecule from (2), (7) and (12), respectively, with mass losses being very close to the calculated mass loss (for water molecules of hydration, HCl and CH₄) as shown in Table II. The loss of Fluc⁻ and amino acid molecules take place within the temperature range of 105–750 °C leaving metal chloride [in the case of (2)], $\frac{1}{2}$ Fe₂O₃ [in the case of (7)] and $\frac{1}{2}$ Fe₂S₃ [in the case of (12)]. The structure of the Fe(III) complexes is suggested to be as shown in Fig. 3.



 $\mathbf{R} = \mathbf{R}\mathbf{e}$ maining part of fluclaxocillin molecule

Figure 2. Suggested structural formulas of binary and ternary Fe(II) complexes.



R = Remaining part of fluclaxocillin molecule

Figure 3. Suggested structural formula of binary and ternary Fe(III) complexes.

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The $[Co(Fluc)(Cl)(H_2O)_3]\cdot 3H_2O$ (3), $[Co(Fluc)(Gly)(H_2O)_2]\cdot 5H_2O$ (8) and $[Co(Fluc)(Ala)(H_2O)_2]$ (13) complexes exhibit three steps of decomposition on TGA analysis. The first decomposition step within the temperature range 25–130 °C corresponds to the loss of three water molecules of hydration (mass loss 7.85%; calcd. 8.25%), three water molecules of hydration (mass loss 7.67%; calcd. 7.60%), and one water molecule of hydration (mass loss 2.97%; calcd. 2.83%) for (3), (8) and (13), respectively. The energy of activation of this dehydration step is 44.65, 50.10 and 45.30 KJ mol⁻¹ for (3), (8) and (13), respectively. The loss of hydrated and coordinated water, Fluc⁻, Gly⁻ and Ala⁻ molecules takes place within the temperature range 130–990 °C with mass losses 72.51% (calcd. 72.06%), 75.80% (calcd. 75.74%) and 85.37% (calcd. 85.44%) for (3), (8) and (13), respectively. According to the IR, solid reflectance spectra and magnetic susceptibility measurements, the proposed structures of these complexes are shown in Fig. 4.

The TG curves of the $[Ni(Fluc)(Cl)(H_2O)_3]\cdot 3H_2O$ (4), $[Ni(Fluc)-(Gly)(H_2O)_2]\cdot 4H_2O$ (9) and $[Ni(Fluc)(Ala)(H_2O)_2]$ (14) complexes show three stages of decomposition within the temperature range of 20–760 °C. The first stage at 20–180 °C corresponds to the loss of water molecules of hydration, while the second and third stages involve the loss of Fluc⁻, Gly⁻, Ala⁻ and coordinated water molecules. The energy of activation of the dehydration step is 41.46, 53.21 and 30.85 KJ mol⁻¹ for (4), (9) and (14), respectively. The overall weight loss amounts to 80.64% (calcd. 80.31%), 89.09% (calcd. 89.12%) and 88.88% (calcd. 88.13%) for (4), (9) and (14), respectively. According to the elemental analyses and various spectroscopic methods, the proposed structures of these complexes are shown in Fig. 4.



(3) $[Co(Fluc)(Cl)(H_2O)_3] \cdot 3H_2O$ (4) $[Ni(Fluc)(Cl)(H_2O)_3] \cdot 3H_2O$ (5) $[Cu(Fluc)(OAc)(H_2O)_3] \cdot 2H_2O$

 $\begin{array}{ll} \textbf{(8)} & [\text{Co(Fluc)}(\text{Gly})(\text{H}_2\text{O})_2] \cdot 5\text{H}_2\text{O} & \textbf{(13)} & [\text{Co(Fluc)}(\text{Ala})(\text{H}_2\text{O})_2] \\ \textbf{(9)} & [\text{Ni}(\text{Fluc})(\text{Gly})(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O} & \textbf{(14)} & [\text{Ni}(\text{Fluc})(\text{Ala})(\text{H}_2\text{O})_2] \\ \textbf{(10)} & [\text{Cu}(\text{Fluc})(\text{Gly})(\text{H}_2\text{O})_2] \cdot 3\text{H}_2\text{O} & \textbf{(15)} & [\text{Cu}(\text{Fluc})(\text{Ala})(\text{H}_2\text{O})_2] \cdot 4\text{H}_2\text{O} \\ \end{array}$

R = Remaining part of fluclaxocillin molecule

Figure 4. Suggested structural formula of binary and ternary Ni(II), Co(II), and Cu(II) complexes.

Table III. Thermodynamic Data of the Thermal Decomposition of Binary and Ternary Metal Ions Complexes

Complex	Decomposition range, °C	E^* $KJ mol^{-1}$	$\operatorname*{A}_{\mathbf{S}^{-1}}$	$\frac{\Delta S^*}{JK^{-1}mol^{-1}}$	$\Delta H^* KJ mol^{-1}$	$\Delta G^* \ KJ mol^{-1}$
(1)	35-120	56.91	1.04×10^4	-23.45	56.28	58.05
	125-445	82.78	2.01×10^6	-23.81	81.03	86.02
	445-700	133.9	1.11×10^{5}	-23.07	129.3	142.1
(2)	30-100	30.27	2.58×10^{8}	-20.04	29.75	31.01
	105-485	26.44	8.96×10^{5}	-27.17	24.21	31.50
	485-665	102.1	1.09×10^{5}	-20.84	97.26	109.5
(3)	25-140	44.65	5.37×10^{6}	-19.29	44.14	45.31
	140-400	58.44	1.36×10^{5}	-19.96	55.93	61.95
	400-650	179.4	5.41×10^{8}	-32.81	175.6	190.5
(4)	30-180	41.46	7.10×10^{5}	-23.66	40.93	42.44
	185-445	54.99	3.16×10^{6}	-21.47	52.35	59.17
	445-690	183.0	3.04×10^{9}	-31.20	178.7	194.7
(5)	30-100	59.48	3.97×10^{6}	-24.33	58.89	60.59
	100-210	247.4	2.20×10^{11}	-71.75	246.0	257.0
	210-750	268.0	7.96×10^{4}	-79.30	246.0	286.8
(6)	25-130	59.40	3.12×10^{8}	-18.40	58.90	59.40
	135-420	79.71	1.91×10^{7}	-12.40	77.90	80.60
	420-900	177.0	4.34×10^{10}	-15.52	172.8	175.6
(7)	30-150	65.73	3.42×10^{7}	-11.98	66.32	75.56
	150-450	95.42	2.48×10^{5}	-25.69	50.75	89.46
	450-720	167.3	5.45×10^{8}	-19.75	112.3	143.0
(8)	20-125	50.10	3.30×10^{6}	-13.50	49.37	50.38
	125-490	82.40	3.94×10^{7}	-11.65	80.60	83.10
	490-745	183.0	1.24×10^{10}	-26.95	178.1	182.2
(9)	25-130	53.21	2.85×10^4	-10.68	46.53	46.46
	130-500	81.63	3.44×10^{6}	-14.86	81.76	85.37
	505-760	178.0	4.42×10^{9}	-22.79	166.9	189.4
(10)	20-195	78.20	4.9×10^{9}	-17.26	77.09	77.62
	195-410	76.64	2.40×10^{5}	-17.12	65.52	69.83
	410-1000	71.10	1.96×10^2	-25.20	64.93	83.50
(11)	25-105	44.10	1.06×10^{6}	-13.90	43.61	44.40
	110-415	77.60	1.10×10^{7}	-13.20	75.86	78.56
	420-570	372.8	3.73×10^{25}	-29.04	369.0	355.7
(12)	35-120	44.84	4.60×10^{5}	-15.16	44.14	45.41
	125-425	90.63	6.21×10^{8}	-18.88	88.92	90.75
	430-650	251.4	6.31×10^{15}	-16.36	247.0	243.7
(13)	25-120	45.30	1.03×10^{6}	-14.12	44.50	45.40
	125-625	85.65	5.91×10^{7}	-11.30	83.76	86.32
	625-900	122.6	2.74×10^{4}	-20.30	115.8	132.5

(continued)

Complex	Decomposition range, °C	E^* KJ mol ⁻¹	$\mathbf{\overset{A}{S^{-1}}}$	$\frac{\Delta S^*}{JK^{-1}mol^{-1}}$	$\Delta H^* \ KJ mol^{-1}$	$\Delta G^* \ KJ mol^{-1}$
(14)	20–150 155–490	30.85 104.0	$\begin{array}{c} 5.24 \times 10^{5} \\ 6.01 \times 10^{9} \end{array}$	$-14.90 \\ -16.70$	30.30 103.7	31.32 103.7
(15)	490–690 20–125 130–490 490–820	319.8 156.9 204.8 475.4	$\begin{array}{c} 3.30 \times 10^{19} \\ 7.90 \times 10^8 \\ 2.14 \times 10^8 \\ 3.10 \times 10^{10} \end{array}$	-14.95 -17.53 -10.43 -16.04	307.2 156.3 203.0 470.4	307.2 156.9 205.2 474.0

Table III. Continued

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the other hand, the $[Cu(Fluc)(OAc)(H_2O)_3] \cdot 2H_2O$ (5), On $[Cu(Fluc)(Gly)(H_2O)_2] \cdot 3H_2O$ (10) and $[Cu(Fluc)(Ala)(H_2O)_2] \cdot 4H_2O$ (15) complexes exhibit three distinct decomposition steps. The first step in the temperature range 30-100 °C (mass loss 5.40%; calcd. for 2H₂O: 5.27%), 20-195 °C (mass loss 16.54%; calcd. for 3H₂O, 2H₂O and HF: 16.8%), and 25-125 °C (mass loss 5.64%; calcd. for 2H₂O: 5.05%) may be accounted for the loss of two water molecules of hydration; four water molecules of hydration, two coordinated water molecule and HF gas, and loss of two water molecules of hydration for (5), (10) and (15), respectively, as shown in Table II. The energy of activation of the thermal dehydration of the complexes are 59.48, 78.20 and $156.90 \text{ KJ mol}^{-1}$ for (5), (10) and (15), respectively. The mass losses of the second and third steps amounted to 74.58% (calcd. 74.02%), 66.37% (calcd. 65.49%) and 77.98% (calcd. 77.69%) for (5), (10) and (15), respectively. They correspond to the removal of coordinated water, Fluc, Gly and Ala molecules leaving CuNCS^[11] as a residue in the of (5), (10) and (15), respectively. The structures of these complexes are given as shown in Fig. 4.

Kinetics of the Decomposition of the Complexes

Integral Method Using the Coats-Redfern Equation

For a first order process, the Coats-Redfern equation^[26] may be written in the following form:

$$\log\left[\frac{\log\{W_{\rm f}/(W_{\rm f}-W)\}}{T^2}\right] = \log\left[\frac{AR}{\theta E^*}\left(1-\frac{2RT}{E^*}\right)\right] - \frac{E^*}{2.303\,\rm RT} \tag{1}$$

where W_f is the mass loss at the completion of the reaction, W is the mass loss up to temperature T; R is the gas constant, E* is the activation energy in J. mol⁻¹, θ is the heating rate. Since, $1-(2RT/E^*) \cong 1$, a plot of the lefthand side of Eq. (1) against 1/T was drawn for all complexes from which E* was calculated from the slope and A (Arrhenius constant) was determined from the intercept. The calculated values of E*, A, ΔS^* , ΔH^* and ΔG^* for the decomposition steps are given in Table III. According to the kinetic data obtained from DTG curves, all of the complexes have a negative entropy which indicates that the activated complexes are in a more ordered states than the reactants. Based on the activation energy values, the Co(II) and Ni(II) complexes have nearly the same thermal stability since they are isostructural.

Further investigation to provide more convincing evidence for the structure of these complexes requires further studies including, *e.g.*, X-ray diffraction studies and other structural investigations.

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