Synthesis, Characterization, and Antibacterial Properties of mixed ligand Complexes of (L-leucine and 8-hydroxyquinoline) with Fe (III),Cr (III) La(III)) and Ru(III) ions

Taghreed H. Al- Noor
Shifaa Jameel Ibraheem
Ibtihaj Kadhim Malih
University of Baghdad-IRAQ

Abstract:

The research includes the synthesis and identification of the mixed ligands complexes of M^{+3} Ions in general composition ,$[M(Leu)_2(Q)]$

Where L-leucin ($C_6H_{13}NO_2$)symbolized as(Leu H) as a primary ligand and

8-hydroxyqinoline,(C_9H_7NO) symbolized as (8-HQ) as a secondary ligand .

The ligands and the metal chlorides were brought in to reaction at room temperature in ethanol as solvent. The reaction required the following molar ratio [(1:1:2)(metal): Q^-:$2Leu^-$] with M(III) ions, were

M(III) = Fe (III),Cr (III) La(III)) and Ru(III)

The reaction gave solid crystalline complexes which have been characterized us the following techniques: Thermal stability, Solubility, Molar conductivity, Determination the percentage of the metal in the complexes by (AAS). Spectroscopic Methods [FT-IR and UV-Vis], and. The proposed structure of the complexes using program, chem. office 3D(2006) .], Biological effects for some complexes were investigated .

Numerous papers have been published on metal complexation of amino acids and derivatives during the past ten years. Metal amino acid complexes have long been of interest as models for metal –Ligand systems and interaction which may occur in nature(1)Biological importance of several amino acids their complexes with transition metals is well documented(2-3)The amino acid L-leucin and various transition metals are important in the biological functions of humans, animals, and plants. L- leucine is one of the twenty major amino acids and is considered an essential amino acid (4)

8-hydroxyqinoline or 8-qinolineis an organic compound with the formula $C_9H_7NO_2$ is the name most commonly used ,while its trivial name is (oxine),which is conventionally used for the description of chelate compounds Oxinates ,as out of seven possible hydroxyqinoles, only 8-hydroxyqinoline forms chelate with metal ions . [5-6]

Ruthenium polypyridyl and phenanthroline complexes have been extensively investigated because of their interesting photochemical[7],catalytic [8], biological [9] and electrochemical [10,11] properties.

Lanthanide(III) carboxylates have been widely studied in recent years due to their physico-chemical properties, variety of structural types and potential uses as fluorescent sensors. The isomers of mono-,di- and trimethoxybenzoates of rare earth elements(III) have been examined. [12-13]

A series of ruthenium metal complexes involving mono-sulfonylated non-innocent o-phenylenediamine ligands have been characterized in detail using NMR, MS, FT-IR, X-Ray, UV-vis and electrochemical studies. [14]

In this paper we present the synthesis and study of Cr(III),Fe(III) La(III) and Ru(III) complexes with amino acid (L-leucin) as a primary ligand and 8-hydroxyqinoline as a secondary ligand have been used, respectively.

Experimental

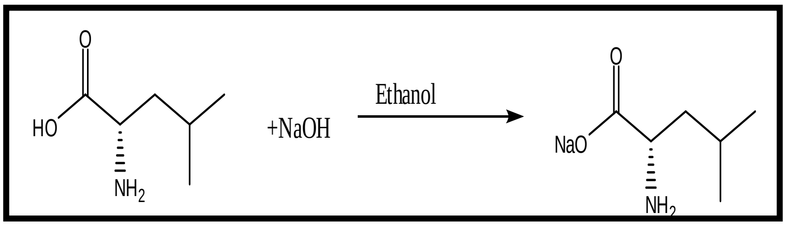
Materials and instruments

All chemicals were purchased from Merck / Aldrich. including $FeCl_3.6H_2O$, $RuCl_3.\ H_2O$, $CrCl_3.\ H_2O$, $LaCl_3.6H_2O$. The reagents were used without further purification . Double distilled water was used.

Instruments: FT-I.R spectra were recorded as K Br discs using Fourier transform Infrared Spectrophotometer Shimadzu 24 FT-I.R 8400s. Electronic spectra of the prepared complexes were measured in the region (200- 1100) nm for 10^{-3} M solutions in ethanol at 25ºC using shimadzu-U.V-160.A Ultra Violet Visible- Spectrophotometer with 1.000 ± 0.001 cm matched quartz cell. While metal contents of the complexes were determined by Atomic Absorption(A.A)Technique using Japan A.A-67G Shimadzu. Electrical conductivity measurements of the complexes were recorded at at room temperature for 10^{-3} M solutions of the samples in DMF using pw9527 Digital conductivity meter (Philips). Melting points were recorded by using Stuart melting point apparatus. chloride ion content were also evolution by (Mohr method),Magnetic susceptibility measurements were measured using Bruker magnet BM6 instrument at 298°K following the Farady's method. The proposed molecular structure of the complexes were determinated by using chem. office progrum, 3DX (2006**)**.

Synthesis of the complexes

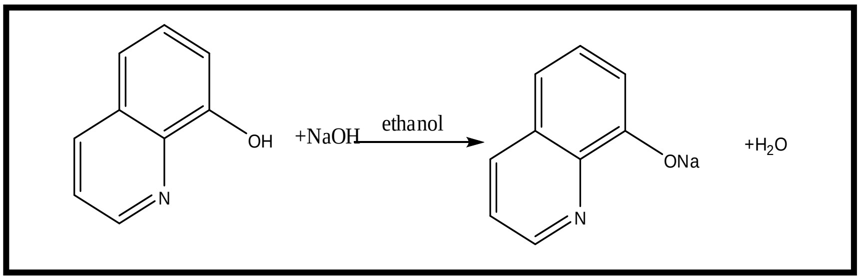
Sodium leucinate ($Na^+ Leu^-$):L-leucin [0.262 gm, 2 m mol] was dissolved in 10 ml ethanol and added to 10 ml of ethnolic solution containing [0.08 gm (2mmol)] of the sodium hydroxide , the solution was deprotonated according to the following reaction scheme (1)



Scheme (1): Synthesis of the Sodium leucinate (Na^+Leu^-)

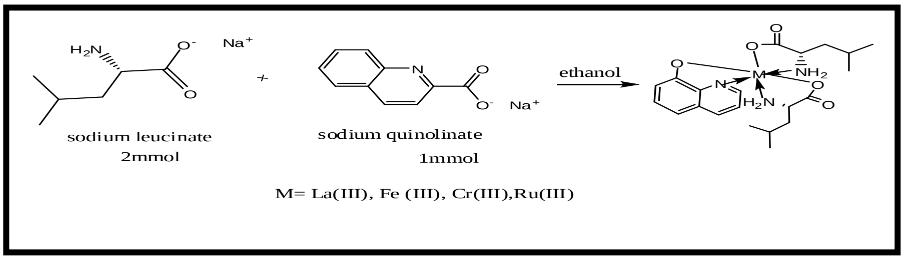
Sodium oxyqinolinate (Na^+Q^-): [0.145gm,1 m mol] 8-hydroxyquinoline (8-QH) with

[0.04gm(1mmol)] sodium hydroxide in ethanol was deprotonated according to the following reaction scheme (2)



Scheme (2) : Preparation of sodium-8-oxyqinolinate

Synthesis of complexes: An aqueous solution of the metal salt was added to the solution of the ligand in ethanol respectively using stoichiometric amounts [(1:2:1) [(metal: 2(Na^+ Leu): (Na^+ Q^-)] molar ratios, the mixture was stirred for (20 -30mint)at room temperature, crystalline precipitates observed. The solid products are filtered, washed with ethanol and dried in vacuum over anhydrous $CaCl_2$. according to the following reaction scheme (3)



Scheme (3) : Preparation of $[M(Leu)_2(Q)]$ complexes

Results and Discussion

All the complexes are colored, non-hygroscopic and thermally stable solids (Table 1), indicating a strong metal-ligand bond. The complexes are soluble in common organic solvents such as ethyl alcohol, acetone, chloroform etc. but are fairly soluble in, ethanol , DMF and DMSO .The observed molar conductance (Λ_M) ,(Table-1)values measured in ethanol in 10^{-3}M solution at room temperature showed fall in the range (1.93-7.50µS.cm^{2}.Mol^{-1}). These observed values of the molar conductance are well within the expected range for non- electrolytic nature [15]

The atomic absorption measurements and chloride content (Table-1) for all complexes gave approximated values for theoretical values .The analysis data (Table-1) of metal complexes are consistent with their general formulation as 1:2:1, mixed ligand complexes of the type [M (Leu)$_2$(Q)].

Fourier-transform infrared spectra and mode of coordination

The most important infrared spectral bands that provide conclusive structural evidence for the coordination of the ligands to the central metal ions .

The assignment of some of the most characteristic FT-IR band of the complexes are shown in Tables (2-4) together with those of two ligands recorded for comparative purposes and facilitate the spectral analysis .

Figure (1), Table (2), displays the (FT-IR) spectrum for the (L-leucin)exhibited a band around υ(3417)cm^{-1} that corresponds to the stretching vibration of υ(N-H) + υ (O-H), while another strong absorption band at υ (3070) cm^{-1} is due to the υ(N-H$_2$)sym while the bands at (1585) cm^{-1} and (1415)cm^{-1} were assigned to the υ(-COO)$_{asy}$ and

υ(-COO)$_{sym}$ respectively. υΔ (-COO)$_{asy\text{-}sym}$ =170 cm^{-1}. [16-17].The weak bands at (552cm^{-1}) and (478 cm^{-1}) refer to υ (Fe-N) and υ (Fe-O) bands respectively[16-17]The weak bands at (552cm^{-1}) and (439 cm^{-1}) refer to υ (Cr-N) and υ (Cr -O) bands respectively$^{)}$. The bands at (675cm^{-1}) and (525cm^{-1}) refer to υ (La-N) and υ (La-O) bands respectively [18] . The bands at (624cm^{-1}) and (489cm^{-1}) refer to υ (Ru-N) and υ (Ru-) bands respectively [14].

Magnetic Susceptibility

Magnetic susceptibility was determined at room temperature using solid sample by Gouy method. The magnetic moments of the complexes shown in Table (5) were calculated from the measured magnetic susceptibilities after employing diamagnetic corrections and revealed their diamagnetic nature as expected for La(III) with 4f ^{O} configuration. The magnetic moment shows the Cr(III) ion to be (3.20BM) with d^{3} (T$_2$g^{3} eg) configuration in a distorted octahedral environment. . The value of the measured magnetic moment for **Fe**(III) is (5.12 B.M.) in accordance with the presumption of high-spin d^{5} ferric ion in octahedral geometry**[19].**The value of the measured magnetic moment for Ru**(**III) is (5.56.M.) in accordance with the presumption of high-spin d^{5} Ru(III) ion in octahedral geometry[14,19].

Electronic spectral

The electronic spectra of Leucin show an absorption band at 305 nm ($32786 cm^{-1}$) in ethanol this band is attributed to ($\pi\rightarrow\pi^*$).The UV -Vis spectrum of the free ligand

8-ydroxyquinoline in ethanol solvent appeared a high intense absorption bands at **280** nm (**35714**cm^{-1})(ε_{max}=**1880 L. mol^{-}.cm^{-1}**) and at **301**nm (**33222**cm^{-1}) (ε_{max} =**2407 L. mol^{-}.cm^{-1}**)These bands are attributed to ($\pi\rightarrow\pi^*$)and ($n\rightarrow\pi^*$) transitions respectively

[Ru $(Leu)_2(Q)$]complex (Figure7.) is characterized by intense π-π * ligand transitions in the UV region (265-298 nm) [19] and metal-to-ligand charge transfer (MLCT) transition in the visible region. The broad MLCT absorption bands appear between 443-449 nm. Similar cases were observed between $[Ru(bpy)_2(dppz)]^{2+}$ (448 nm) and $[Ru(dppz)_3]^{2+}$ (455 nm) [14]and the band positions are similar to those observed for other octahedral ruthenium(III) complexes [19-24].

$Cr(Leu)_2(Q)]:d^3$ The spectrum of Pale-gray complex exhibited the following absorptions at υ1 (12453) cm^{-1} , υ2 (13003)cm^{-1} and υ3 (24875) cm^{-1} wave numbers these bands are characteristic of octahedral Cr(III) complex and were assigned to the transitions

${}^4A_2g(F) \rightarrow {}^4T_1g(P)$, ${}^4A_2g(F) \rightarrow {}^4T_1g(F)$,, ${}^4A_2g(F) \rightarrow {}^4T_2g(F)$ resbictivily.

12453 = transition energy =10Dq = $\Delta_{0,}$ υ1/ υ2=0.95 cm^{-1} , υ2/ υ1=0.52, B=1030 cm^{-1},

Δ/B=12.09.[22-25]

Preparation of Microorganism suspension

A) The micro- organism suspension was prepared by taking 2–4 colonies from all the studied micro- organism. Then it was inserted in the physiological solution in 0.85% concentration and was compared with Macferr land tube number 0.5 which is equal to 1.5×108 cell/mm. It is used for Petri dish preparation for the examination of biological activity against the under studied chemical compound.

B) Inhibition Activity Selection for the complexes in studied Micro-organism

The agar well diffusion method was used to see the effect of under studied chemical complexes on the micro-organism growth. This is done by using 20–25 ml from Nutrient agar medium for each Petri dish. The dish was incubated in incubator for 24 hours at (37°C) to make sure that no contamination would occur in the dish. The dish was wetted in 10 milliliters of micro-organism which was prepared as mentioned in the previous paragraph which include 1.5×108 cell/mm. Distributed evenly on the Nutrient Agar medium surface by using spreader. Bore was made on the cultured medium surface by using cork borer. The chemical complexes were made as 100 m ml per bore and left the central bore containing only DMF. The dishes were left for 1/2 hour in refrigerator at 4°C[26]. The biological activity for the complexes was defined by measuring the diameter of the inhibition area surrounding each bore in millimeters.

Antimicrobial activity

The in vitro antimicrobial screening results are given in Table 6. On the basis of observed zones of inhibition, All the metal-mixed ligand complexes are active against all tested organisms Escherichia coli , Candida albicans, Pseudomonas, Bacillus and Staphylococcus S.P+ .

which in fact is in agreement with the literature [27-28]. These mixed-ligand complexes have an advantage in that the respective bioactivities of the uncoordinated ligands and metal ions are combined which could make them more potent antimicrobial agents. [29]

REFERENCES

[1] Gleeson, B. Claffey, J. Hogan M., Müller- Bunz H., Wallis D., Tacke M., J. Organomet.Chem. 694,pp 1369–1374 (2009).
[2] H.sigel “ ***Metal Ions in Biological systems*** “ Dek Ker, New york, (1979).
[3] S.T Chow and C.A. Mcauliffe; J. Inorg .Nucl .Chem. Lett; 8, p913(1976).
[4] C.A Mcauliffe and W. Lavason; J. Inorg. Chem. Trans. Elem; 4, p 218(1976).
[5] J .S Shukia ,M Singh and R Rastogi, Indian J. Chem., 30 B(1983).
[6] J.P Philips , J.Chem. 56, p271(1956).
[7] W.T. Gao, Z. Zheng, J. *Molecules* 7,p511 (2002).
[8] S. Megha Deshpande, S. Avinash , *J. Chem. Sci.* 117,p153 (2005).
[9] E.D.A. Stemp, J.K. Barton, *Metal Ions in Biological systems* 33, p325 (1996).
[10] J. Annaraj, S. Srinivasan, K.M. Ponvel, PR. Athappan, *J. Inorg. Biochem.* 99 p669 (2005).
[11] C. Moucheron, A. Krish De Mesmaelcu, *Coord. J.Chem. Rev.* 168,p233 (1998).
[12] W. Ferenc, A. Walków-Dziewulska, J. Serb. Chem. Soc. 65,p789 (2000)
[13] W. Ferenc, A. Walków-Dziewulska, J. Them. Anal. Cal. 71,p375 (2003)
[14] Krainova, Julia, M.Sc. Ruthenium complexes of monosulfonylated benzoquinonediimine ligands, York University , p279 (2011).
[15] W. J. Geary, The Use of Conductivity Measurements in Organic Solvents for the Characterisation of Coordination Compounds. Coord. Chem. Rev. 7, 81-122.(1971).
[16] K. Nakamoto; “Infrared spectra of Inorganic and coordination compounds “4ED th ; J. Wiely and Sons, New york, (1996) .
[17] Y. Nishida., Niinuma. A., Abe. K., Inorg. Chem. Commun. 12,pp 198–200(2009).
[18] A .Ganesh. Thakur, V. Shrikant , Athlekarb, R.Sanjiv , Dharwadkr ,J. Acta Poloniae Pharmaceutica ,Drug Research, 64 No. 1,pp 9-15, (2007).
[19] A.Z. El-Sonbati, A.A, El-Bindary. A.A. and Mabrouk E.M.,J. Transition Met. Chem., 17,p 63 (1992).

[20] A.B.P. Lever, " ***Inorganic Electronic spectroscopy***", Elsevier, New York (1984).

[21] C.-W. Jiang, H. Chao, R.-H. Li, H. Li, L.-N. Ji, *Polyhedron* 20p2187 (2001).

[22] E. Amouyal, A. Homsi, J.-C. Chambron, J.-P. Sauvage, J. Chem. Soc., Dalton Trans.p1841 (1990).

[23] K. Natarajan, R.K. Podder, U. Agarwala, J. Inorg. Nucl. Chem. 39 p431 (1977).

[24] O.K. Medhi, U. Agarwala, *J. Inorg. Nucl. Chem.* 42 p1413 (1980).

[25] G. Muthusamy, K. Natarajan, Indian J. Chem. 30 A ,p 626(1991).

[26] Shriver & Atkins " *Inorganic Chemistry*", 3rd Ed., , Freeman, (1999).

[27] M.Vignolo; F.Suriant;; A.P ,Holgado,. and G.Oliver Antibacterial activity of Lado bacillus strains iso lated from dry fermented sausage; J. App. Bac. 75:pp 344-349, (1993).

[28] M.O.Agwara,; P.T.Ndifon,; M.K.Ndikontar,; M.A. Atamba Res. J. Chem. Environ. 12, p87, (2008).

[29] M.O. Agwara1, P.T. Ndifon1, N.B. Ndosiri1, A.G. Paboudam1, D.M. Yufanyi and A. Mohamadou, J. Bull. Chem. Soc. Ethiop., 24(3), pp383-389. (2010).

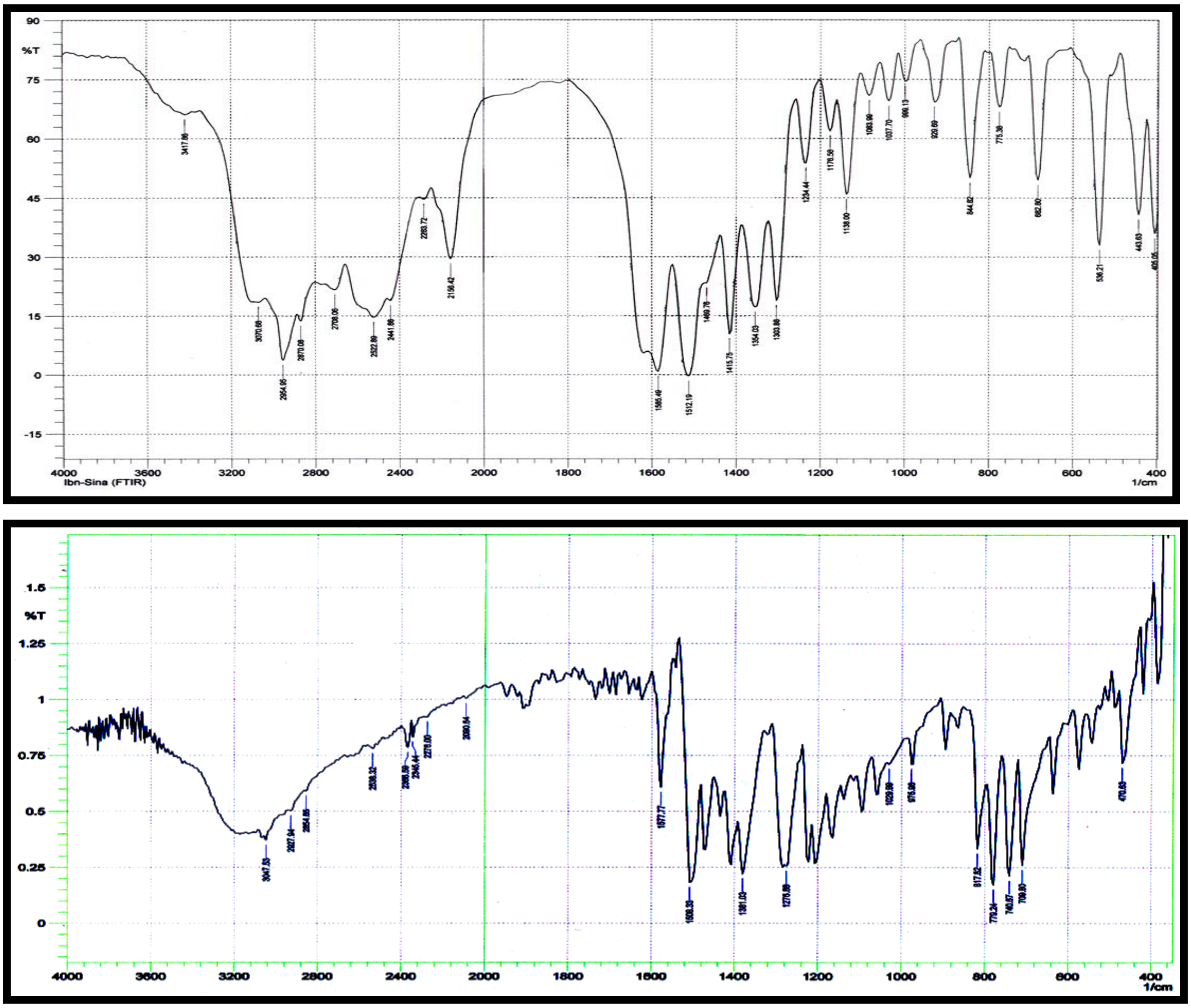
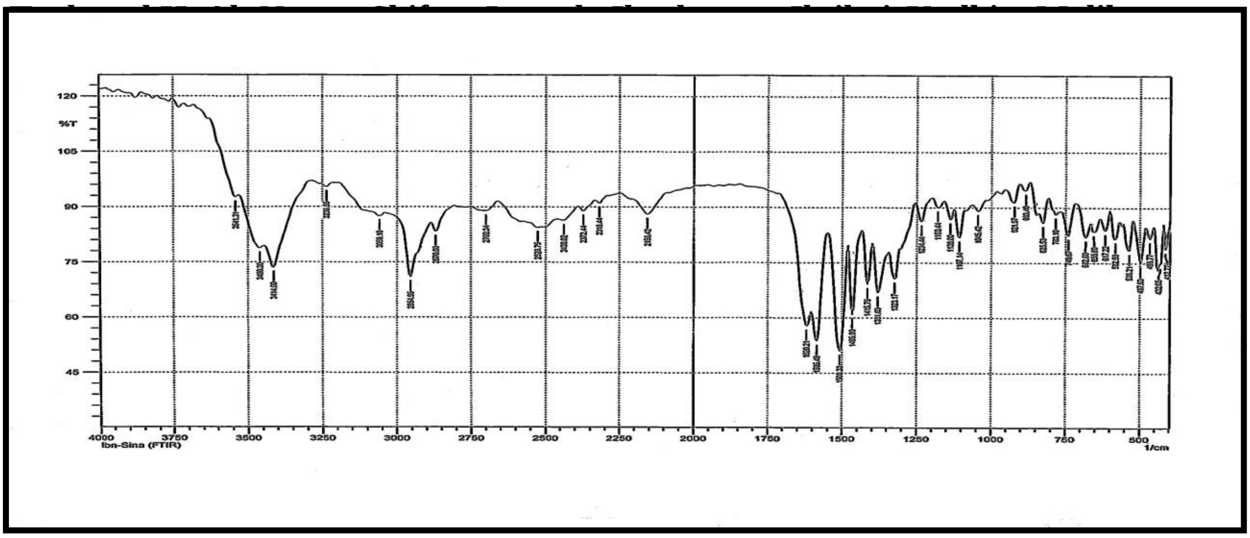


Figure (2) : FT-IR spectrum of (8-Hydroxyqinoline)



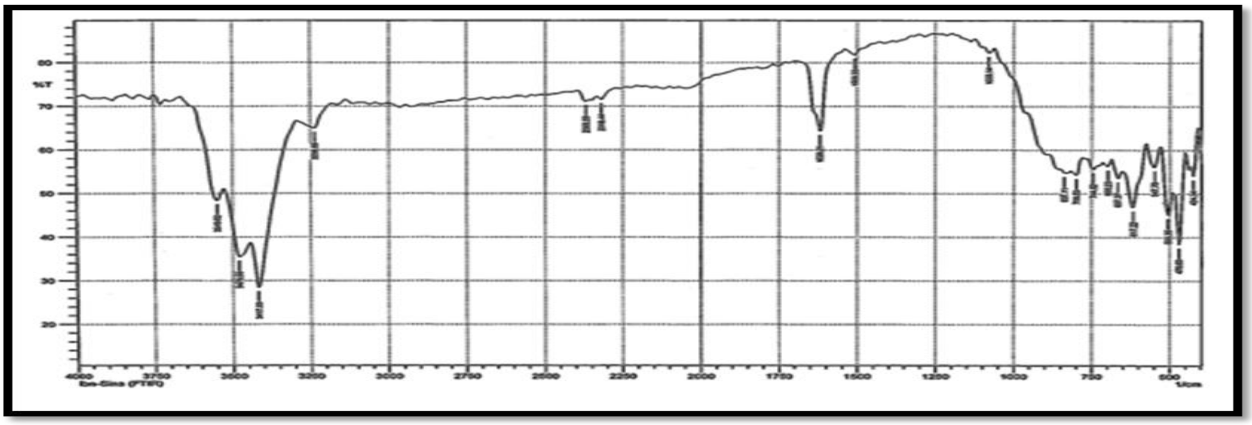


Figure (3) : FT-IR spectrum of [Fe (Leu)$_2$(Q)]
Figure (4) : FT-IR spectrum of [Ru (Leu)$_2$(Q)]

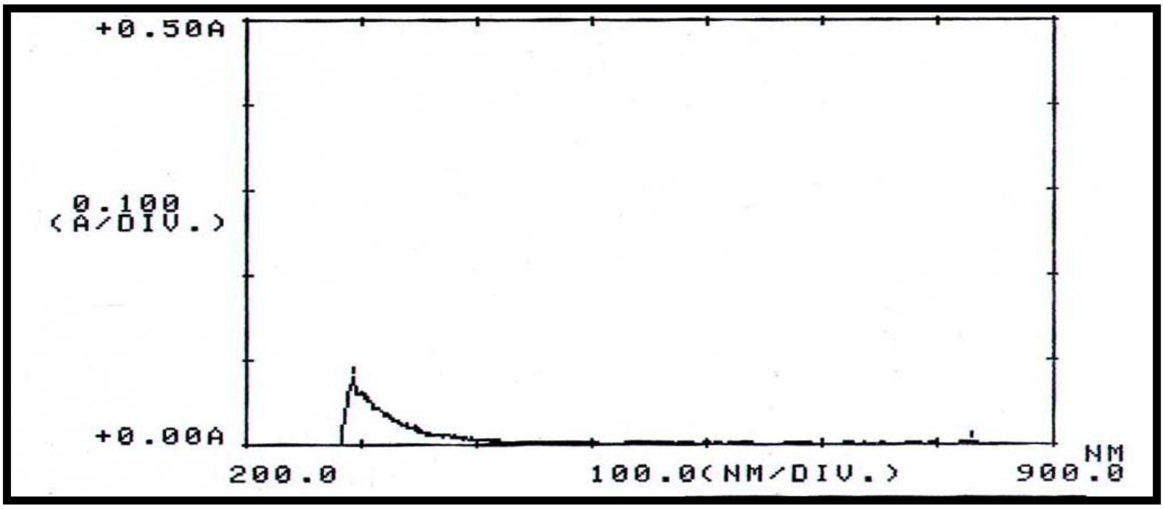


Figure (5)The (UV-Vis) Spectrum of L-leucin

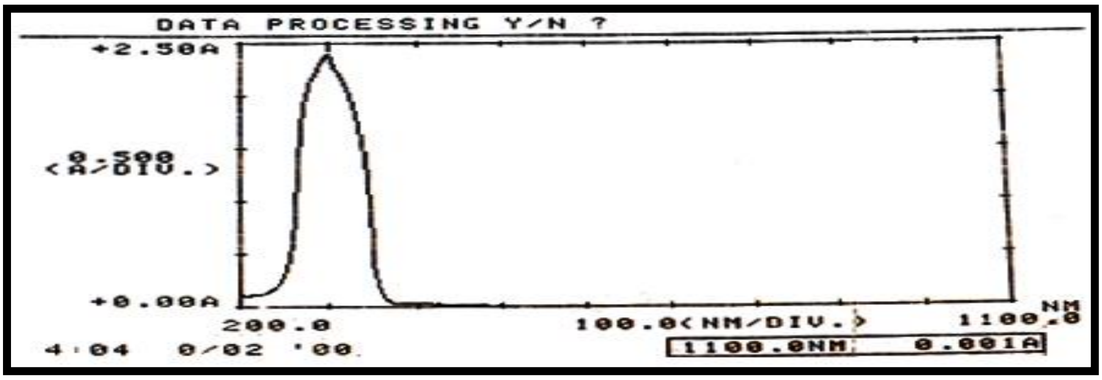


Figure (6) Electronic Spectrum of (8-hydroxyqinoline)

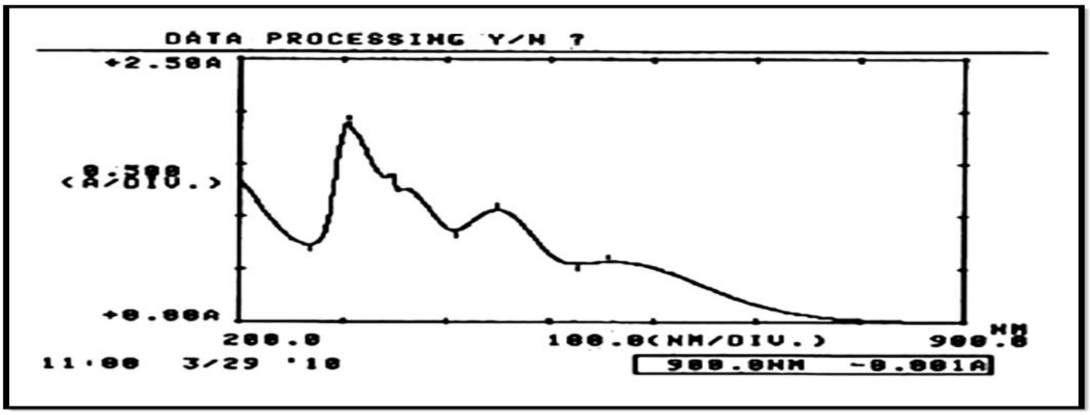


Figure (7) Electronic Spectrum of[Fe $(Leu)_2(Q)$]

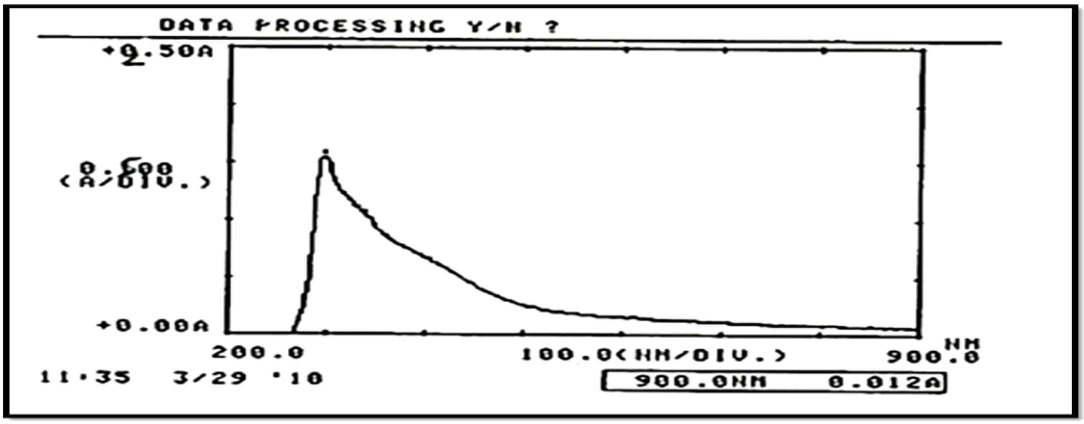


Figure (8) Electronic Spectrum of[Ru$(Leu)_2(Q)$]

Table 1-The physical properties of the compounds

Compounds	M. wt	Color	*Melting point* °c (de)	Λm μS.c $m^2.Mol^{-1}$	Metal %		l %
					heory	xp	
$C_6H_{13}NO_2$ (Leu)	131.17	White	289(dec)	1.24			
C_9H_6NO (8-HQ)	145.15	Browndark	277(dec)	1.77			
$[Cr(Leu)_2(Q)]$	456.48	Pale-gray	260	1.93	1.39	0.56	ill
$[Fe(Leu)_2(Q)]$	460.20	Brown	278de	2.10	2.13	1.1	ill
$[La(Leu)_2(Q)]$	543.39	Pale-yellow	>350	7.50	5.26	3.8	ill
$[Ru(Leu)_2(Q)]$	505.63	Pale-brown	320	2.27	9.99	----	ill

Λm = Molar Conductivity , Q = C_9H_5NO , Leu $C_6H_{12}NO_2$, $(Leu)_2(Q)= C_{21}H_{30}N_3O_5$, **Dec. = Decomposition temperature

Table 2-FT-R spectral data of the Leucin

Compound Leucin	υ(N-H)+ υ (O-H)	υ(N-H$_2$)$_{sym}$	υ	υ (C – H) aliphatic	υ(-COO)$_{asy}$	υ(-COO)$_{sym}$	υΔ (-COO)$_{asy-sym}$
$C_6H_{13}NO_2$	3417m	3070s	47	1580s	1585vs	1415vs	170

str: stretching, vs.: very strong, s: , am: amide, py: pyridine, Sym: symmetric, say: asymmetric, sh: shoulder. m: medium, w: week, strong,

Table 3 -FT-IR spectral data of the (8-Hydroxyquinoline)

Compound	υ(O-H)arom	υ(C-H)aro	υ(C=N)	υ(C=C)	υ(C-O)	δ(C-O)	δ(O-H) in plane δ(O-H)out plane
8-ydroxyquinoline	3240-3047br	3040 -2854s	1577vs	1508vs	1276vs	470s	1381vs 779s

Table (4) FT-IR spectral data of the compounds

Compounds	υ(N-H)+ υ (O-H	(NH$_2$)sym	CH$_{(py)}$str	(CH) cycil & ali	(C=N)	(C=C)	υ(C–O)	υ -COO) $_{asy}$	υ COO)$_{sym}$	M-O	M-N
$[Cr(Leu)_2(Q)]$	3429br-m	3074	2954s	2360s 2160m	1620s	1512vs	1234w	1558vs	1415s	36w	439
$[Fe(Leu)_2(Q)]$	460-3414s	3059	2954s	2372w 2156m	1620vs	1508vs	1234w	1585vs	1415s 1332	82w	497
$[La(Leu)_2(Q)]$	3444vs	3051	2958s	2329w	1631s	1566vs	1248m 1230m	1496vs 1458	1415m 1377vs	44m	489m
$[Ru(Leu)_2(Q)]$	3483vs 3414 vs	3232m	2962m	2376w 2152w	1616vs	1508 m	1234vw	1450m	1408w 1269w	24m	489s

, str: stretching, vs.: very strong, s: strong, am: amide, py: pyridine, Sym: symmetric, say: asymmetric, m: medium, w: week,

Table 5- Electronic Spectral data, magnetic moment, of the studied compounds

Compounds	**λ (nm)**	**υ′(cm^{-1})**	**Assignment**	**μ_{eff} (BM)**
$C_6H_{13}NO_2$ (leu)	305	32786	$\pi\rightarrow\pi^*$	--
8-Hydroxyqinoline	280 301	35714 33222	$\pi\rightarrow\pi$ $n\rightarrow\pi^*$	--
[Ru (Leu)$_2$(Q)]	297 443 449	33670 22573 22271	$\pi\rightarrow\pi^*$ MLCT MLCT	5.56
[Fe (Leu)$_2$(Q)]	304 448 557	32894 22321 17953	$\pi\rightarrow\pi^*$ $^6A_1g \rightarrow {}^4T_1g$ $^6A_1g \rightarrow {}^4Eg$	5.2
[Cr (Leu)$_2$(Q)]	249 402 769 803	34013 24875 13003 12453	$\pi\rightarrow\pi^*$ $^4A_2g(F) \rightarrow {}^4T_2g(F$ $^4A_2g(F) \rightarrow {}^4T_1g(F)$ $^4A_2g(F) \rightarrow {}^4T_1g(P)$	3.39
[La(Leu)$_2$(Q)]	316 718	31645 13927	C-T f-f	Dima

C.T= Charge transfer

Table (6) represent the antimicrobial activity of the ligands and their metal complexes

Compounds	***Escherichia coli***	***Candida albicans***	***Pseudomonas***	**Bacillus**	***Staphylococcus S.P+***
Control (D.M.F)	10	10	9	10	10
L- Leu	15	18	11	14	15
Q	20	25	12	22	20
[Cr(Leu)$_2$(Q)]	22	23	17	18	24
[Ru (Leu)$_2$(Q)]	15	16	17	11	-----
[Fe (Leu)$_2$(Q)]	14	22	10	28	20
[La(Leu)$_2$(Q)]	18	32	12	30	25

تحضير، تشخيص ودراسة الخواص الضديدة للبكتريا لمعقدات مختلطة الليكاند من (الليوسين و8-هيدروكسي كوينولين) مع الايونات ***Fe (III),Cr (III)*** و ***La(III))*** و***Ru(III)***

تغريد هاشم النور
جامعة بغداد / كلية التربية . ابن الهيثم
شفاء جميل إبراهيم
جامعة بغداد / كلية الطب
ابتهاج كاظم مالح
جامعة بغداد / كلية التمريض

الخلاصة

يتضمن البحث تحضير وتشخيص معقدات للايونات M^{+3} مختلطة الليكاند بالصيغة العامة : $[M(Leu)_2(Q)]$ باستعمال الحامض الاميني (الليوسين) ليكانداً أولي والليكاند 8– هيدروكسي كوينولين) ليكانداً ثاني إذ ان الليوسين ($C_6H_{13}NO_2$) بالرمز(LeuH) و8– هيدروكسي كوينولين (C_9H_7NO) بالرمز(8-HQ) وذلك بمفاعلة الليكاندين مع كلوريدات العناصر باستعمال الايثانول مذيباً وفي درجة حرارة المختبروبنسب مولية

$[(metal) : Q^- : 2Leu^-]$ (1:1:2) مع M(III) إذ إن:

M*(III) = Ru(III) , Cr(III),La(III)* و *Fe (III)*

المعقدات المحضرة بلورات صلبة درست من النواحي الآتية: الاستقرارية الحرارية، التوصيلية الكهربائية المولارية، الذوبانية، تقدير النسبة المئوية للأيون الفلزي في المعقدات بوساطة مطيافية الامتصاص الذري، الدراسات الطيفية: وتضمنت أطياف (الأشعة تحت الحمراء، الأشعة فوق البنفسجية– المرئية، الخواص المغناطيسية ومحتوى الكلور) مع

استعمال البرنامج (Chem. Office–Cs. chem– 3D progrum 2006) في رسم اشكال المعقدات. ودراسة التأثيرات الحياتية لبعض المعقدات .