المملكة العربية السعودية
وزارة التعليم العالى
جامعة أم القرى
معهد البحوث العلمية
مركز بحوث العلوم التطبيقية

سلسلة بحوث العلوم التطبيقية

متراكبات العناصر الانتقالية مختلطة الليجندات لأحماض الهيدروكساميك كمواد مضادة للميكروبات

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قسم الكيمياء - كلية العلوم التطبيقية
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١٤٢٤ هـ - ٢٠٠٣ م

الملخص

يتضمن البحث دراسة متراكبات العناصر الانتقالية مختلطة الليجندات لأحماض الهيدروكساميك . العناصر التي استخدمت في هذا البحث هي الحديد والكوبلت والنيكل والنحاس . وقد تم تحضير حمضين من أحماض الهيدروكساميك وهما بتروهيدروكساميك وهيدروكسي بتروهيدروكساميك بغرض استخدامهما كليجندات أولية ، أما الليجندات الثانوية التي استخدمت في ٨ ـ هيدروكسي كينولين ، ثنائي ايثيل ـ ثنائي ثيوفوسفات وازنسات البوتاسيوم . وقد تم تحضير المتراكبات الفلزية الثنائية للعنصر الانتقالية المذكورة آنفاً مع حمضي الهيدروكساميك ثم استخدمت هذه المتراكبات الثنائية لتحضير المتراكبات مختلط الليجندات . وتمت دراسة طريقة الترابط لك من الليجند الأولي والثانوي في المتراكبات عن طريق القياسات الطيفية في منطقتي فوق الأشعة البنفسجية ودون الحمراء حيث تبين أن أحماض الهيدروكساميك تعمل كليجندات ثنائية العطاء وأحادية القاعدة كما تعمل الليجندات الثانوية كثنائية العطاء . وقد فسرت الحزم الضوئية التي ظهرت في أطياف الأشعة دون الحمراء إلى النوع المناسب من الشد والاهتزاز الرابطي . كما تم تحديد التركيب الجزيئي للمتراكبات عن طريق التحاليل العنصرية وتمت دراسة ثبات المتراكبات حرارياً وكيفية تفككها عند درجات الحرارة العالية .

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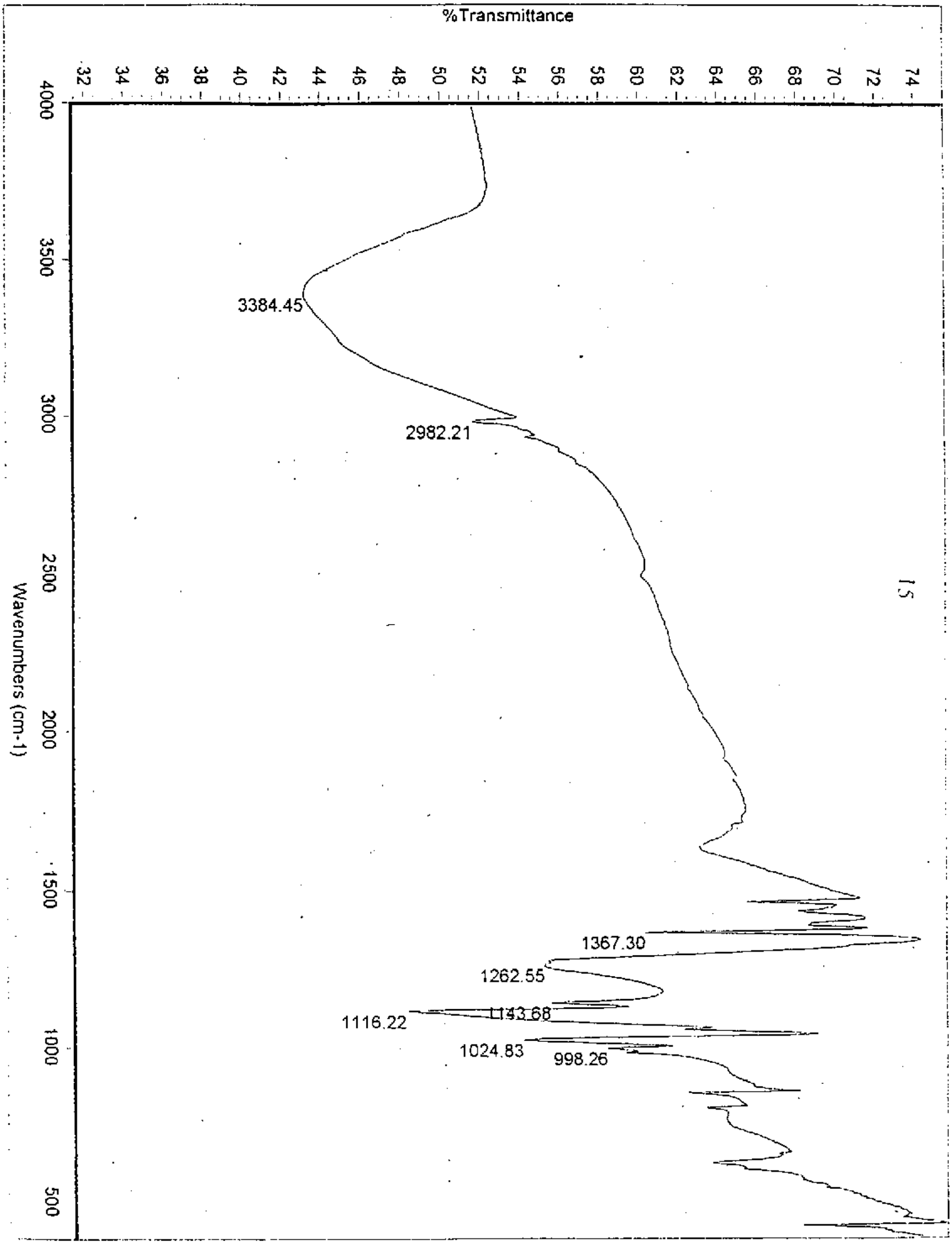
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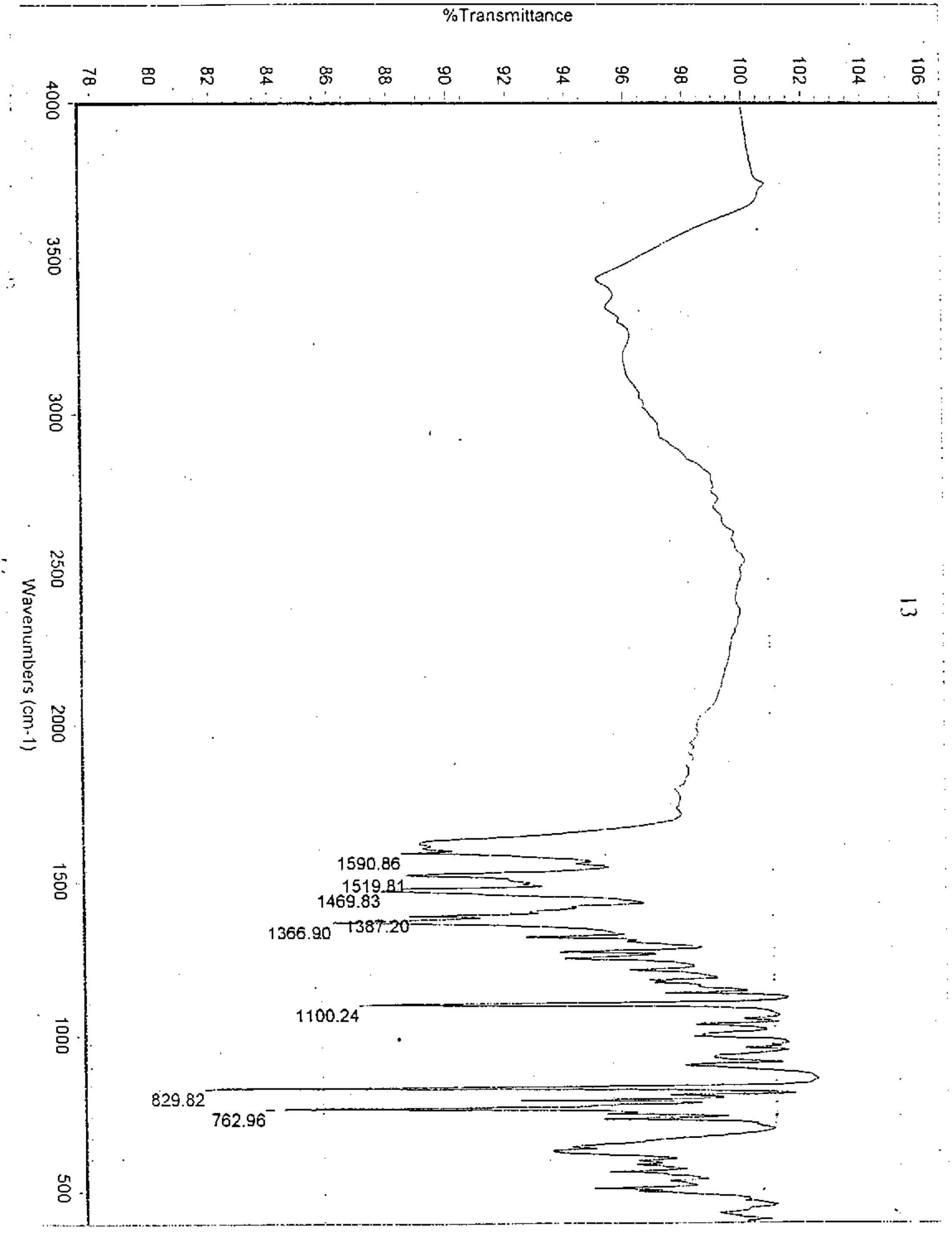
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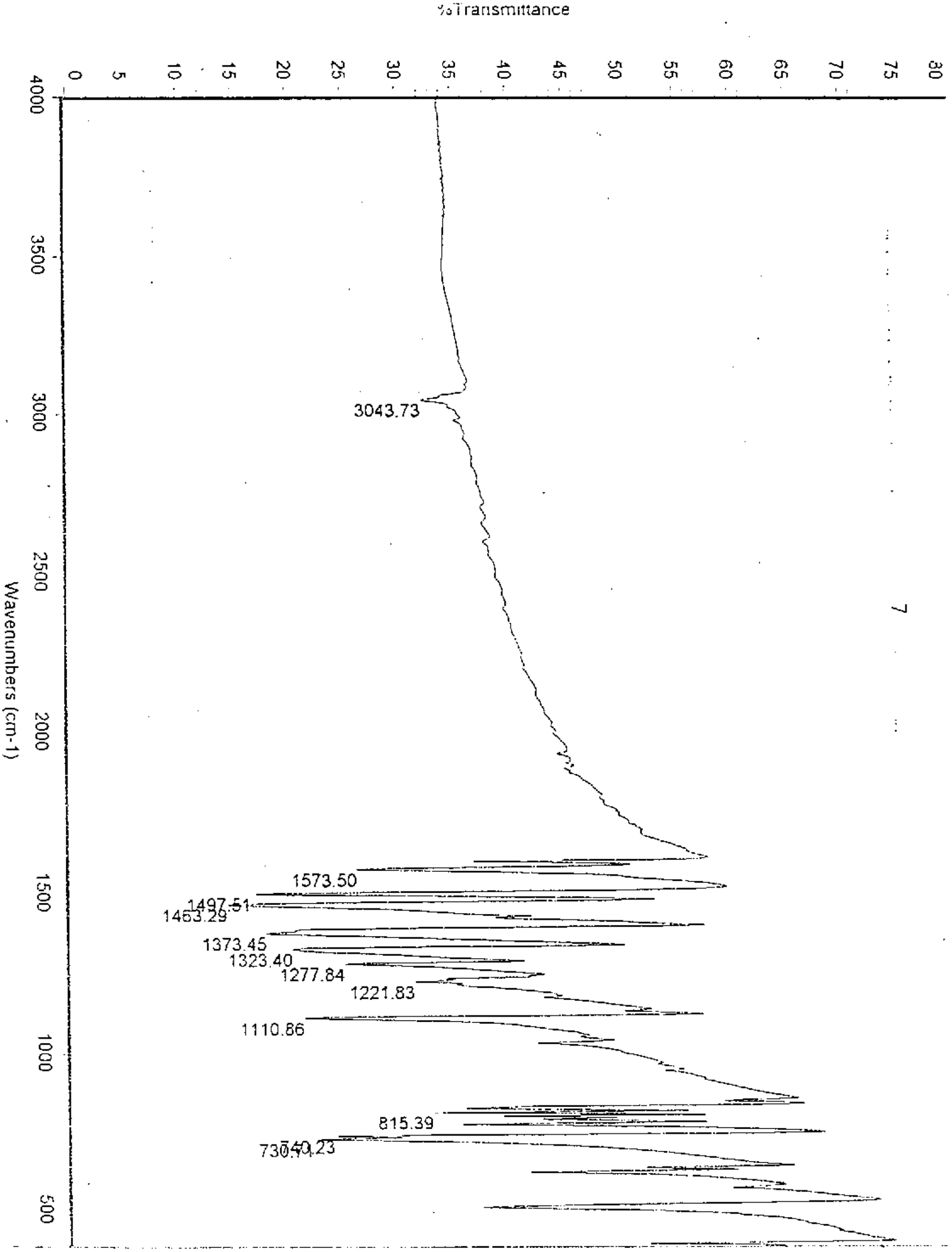
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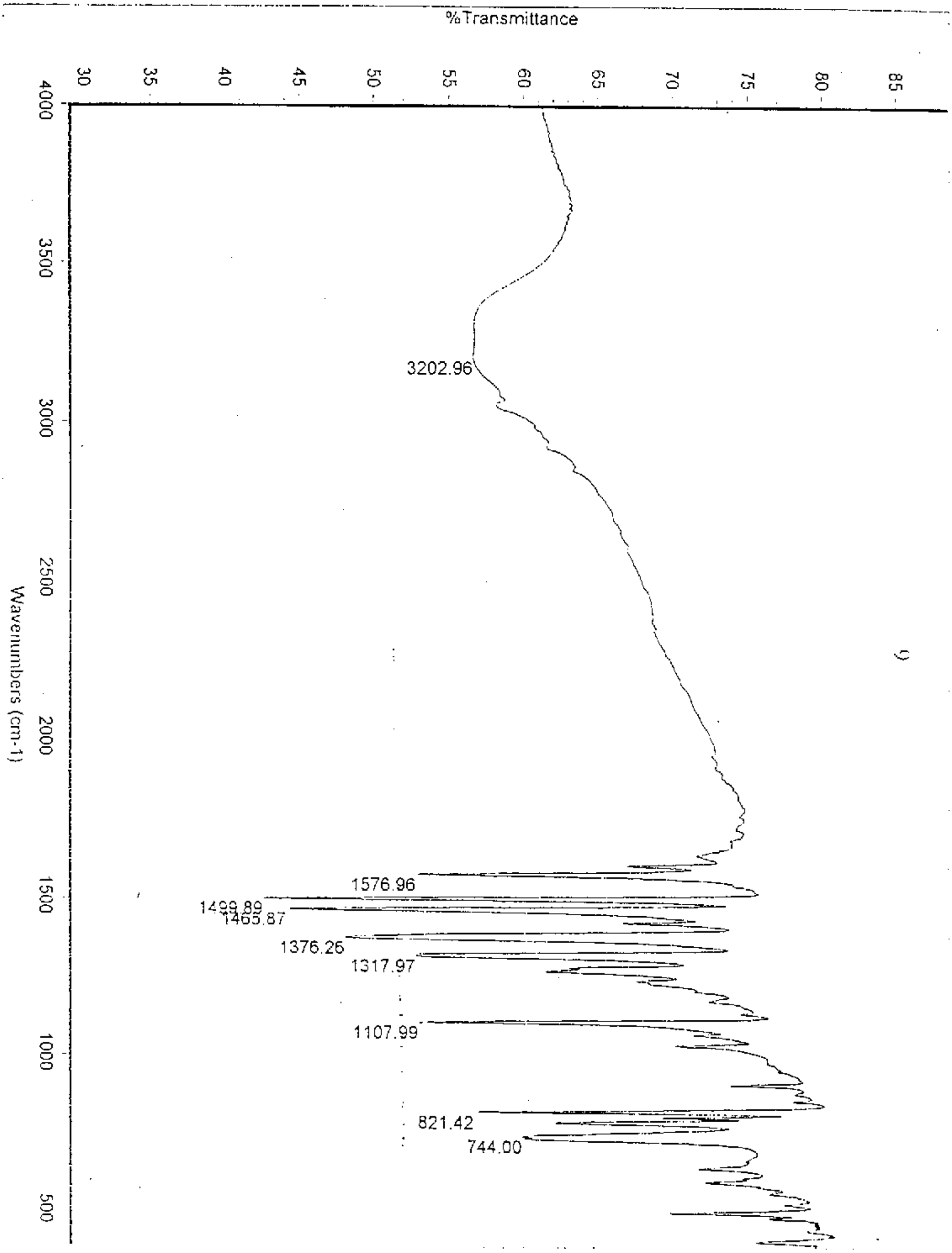
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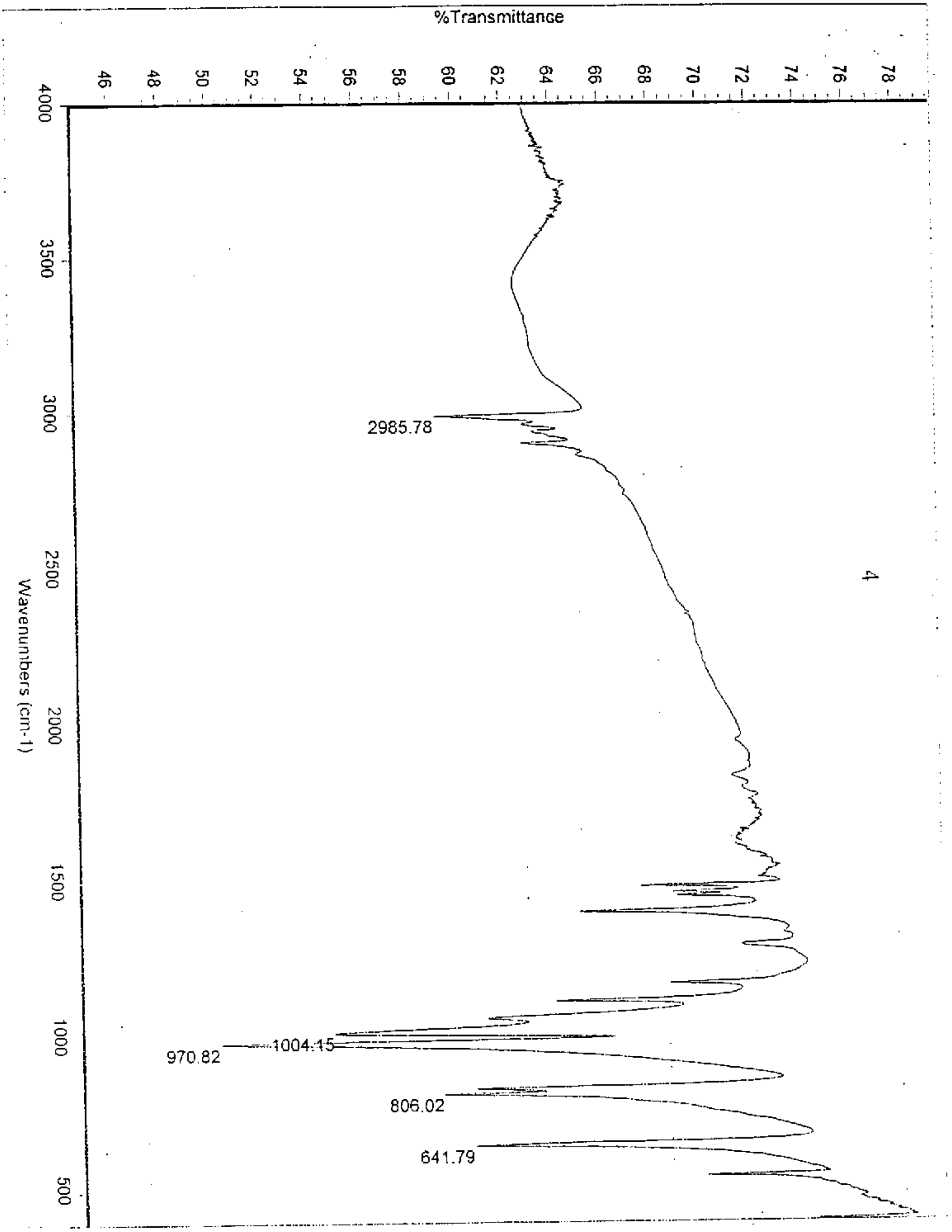
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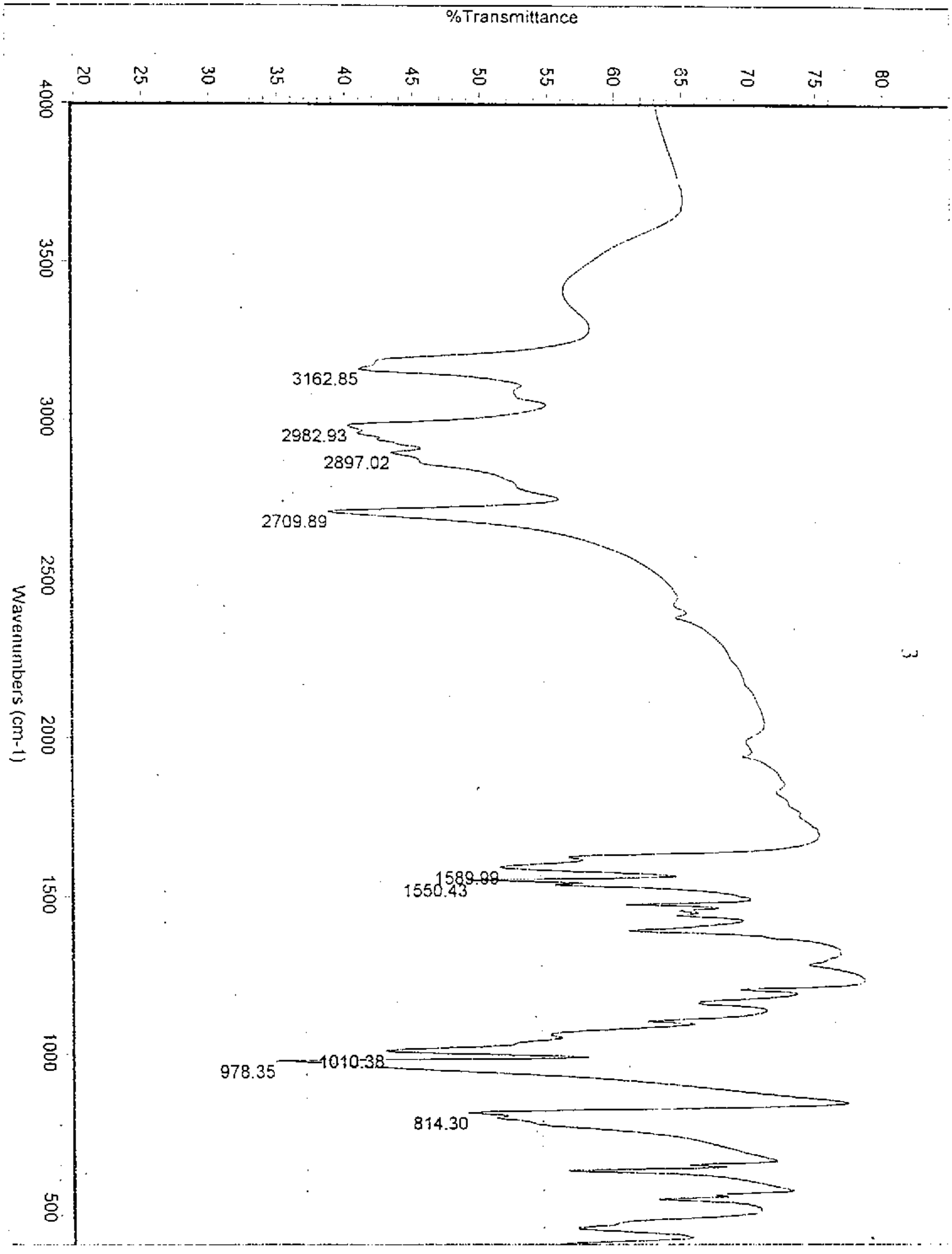
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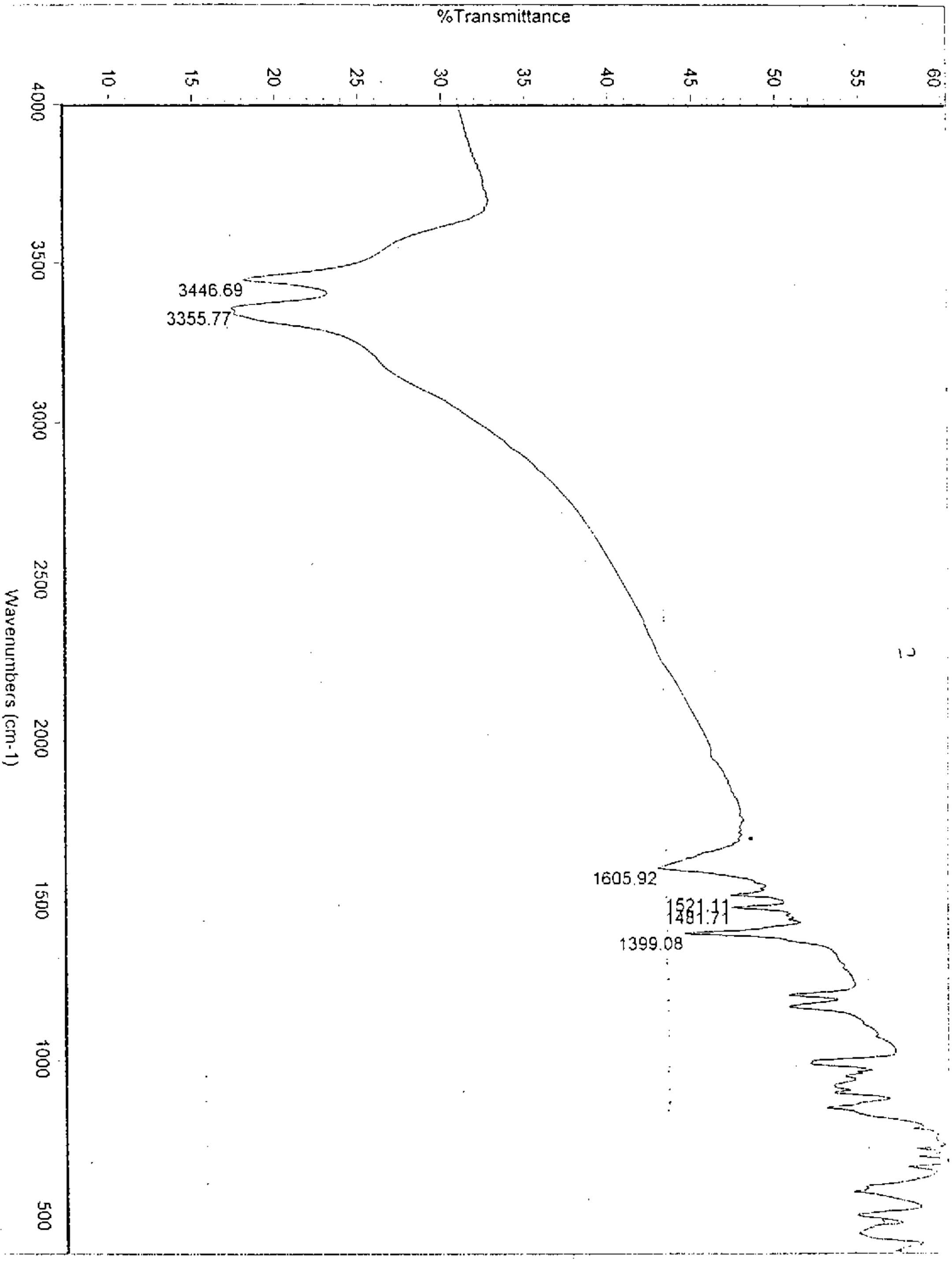
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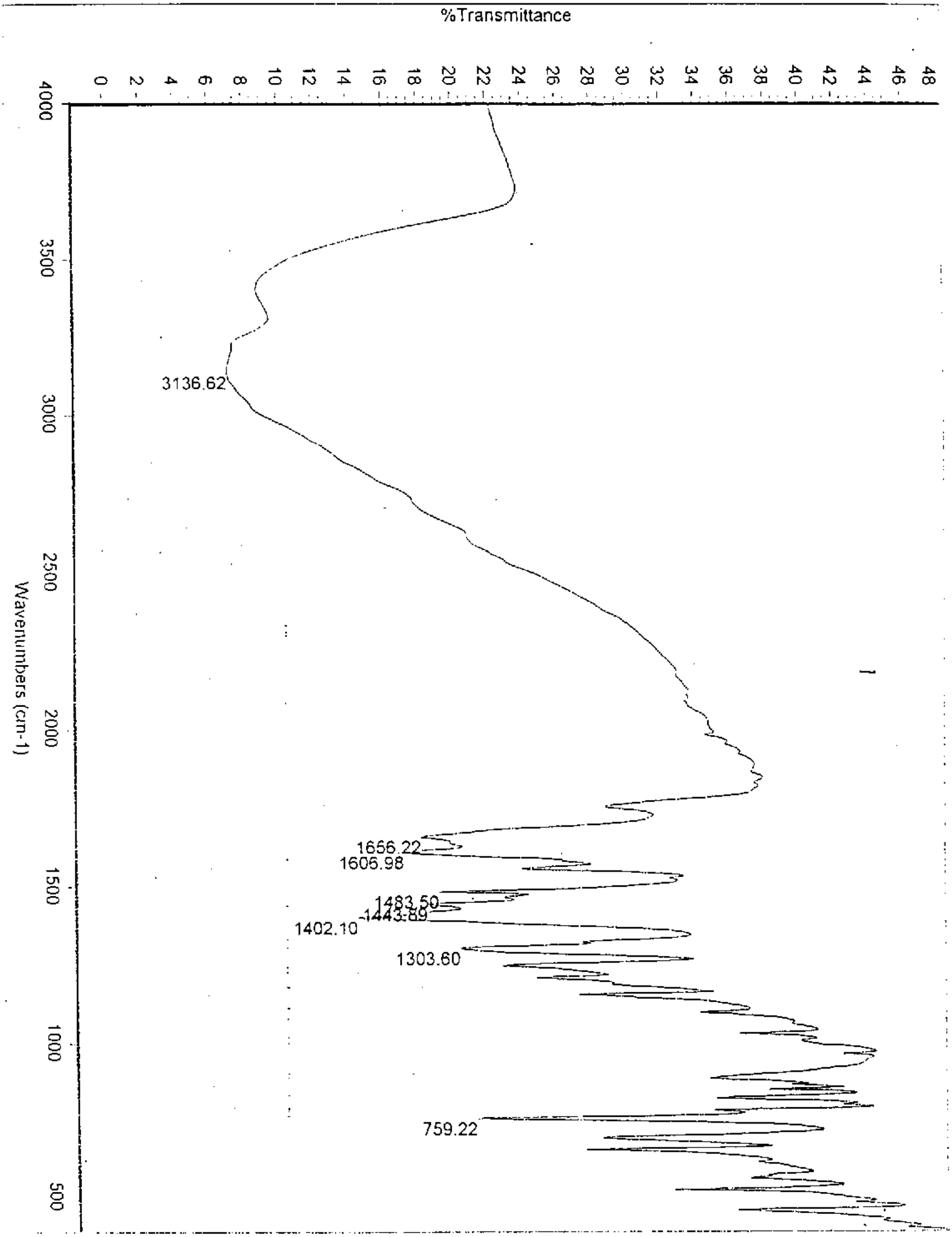
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1303.60
759.22

Table 4. Important IR Frequency of HBHA and its complexes.

Compounds / Frequency	Mixed ligands Complexes				Assignment
	7	9	13	15	
Free HBHA					
3260 3230	3043	3202	b	3384	νNH (Valence)
1650	1573	1576	1590	1580	νC=O (ketonic)
1570	1497	1498	1518	1530	NH planar deformation +νCN
1380	1373	1376	1366	1367	Out-of-planeNH deformation

Table 3. Important IR Frequencies of Benzohydroxamic and Its Complexes .

Compoun Frequency	Mixed Ligand Complexes				Assignment
	1	2	3	4	
Free BHA					
3200	3136	3446 3255	3162	2985	νNH (Valence)
1670	1656	1605	1580	1585	ν C=O 9ketonic)
1580	1603	1521	1550	1540	NH planar deformation +νCN
1400	1402	1399	1407	1400	out-of-plane NH deformation

Table 2 Antimicrobial Activity Data of the Complexes (inhibition zone, mm)

Compound / Organism	A	B	C	D	1	3	5	7	9	11	13	14	15
Bacteria:													
Serratia rhodii *	12	15	11	15	16	14	17	18	12	16	-	14	17
Bacillus Cereus *	13	12	13	16	13	11	20	13	15	18	12	15	11
Staphylococcus Citreus *	20	18	15	17	18	22	18	22cz	21	18	25pi	21	25cz
Pseudomonas aerag. *	11	-	12	18	11	18	22cz	18	14	-	17	13	18
Fungi													
Botryotrichum pilulif.	15	20	14	16	10	16	19	-	15	11	18	14	13
Candida albicans I	-	11	20	13	13	14	13	21	-	12	17	16	-
Candida albicans II	15	15	14	22cz	16	12	15	18	12	-	15	14	17
Emericella nidulans	20	18pi	15	18	19	20	21	19	13	16	18	13	18
Fusarium Solani	13	12	13	-	11	13	16	11	-	13	19	-	12
Geotrichum Candidum	18	24	17	20pi	13	-	12	15	12	17	11	19	13
Microsporum Canis *	21pi	18pi	20	19	17	18	20	20	18	22cz	19	16	18
M . Gypseum *	10	-	12	11	-	15	13	16	12	11	17	13	15
Penicillium Chrysog .	18	-	13	14	15	12	14	-	13	15	16	-	17
A. niger	16	11	16	12	17	17	16	15	17	14	-	15	11
Trichophyton gourv .	22pi	16	11	18	16	-	15	17	11	18	15	-	15
T. mmentagrophytes *	14	15	13	16	13	13	11	14	18	12	11	13	12
T.rubrum *	25cz	20pi	20	18	-	18	18	16	10	13	16	17	-

*** Pathogenic Species , Pi = Partial inlibition ; CZ = clear zone , - = inactive**

Table 1. Analytical data and conductance values of the prepared metal complexes

No.	Compound	Λ_m [(a)] (DMF)	% calculated (found)		
			C	H	N
1	$[Co(C_7H_6NO_2)_2(H_2O)_2]$	12.2	45.8 (46.1)	4.4 (4.5)	7.6 (8.0)
2	$[Ni(C_7H_6NO_2)_2]$	12.3	50.8 (51.3)	3.7 (4.0)	8.5 (8.9)
3	$[Cu(C_7H_6NO_2)_2]$	31.5	50.1 (49.80	3.6 (4.1)	8.3 (8.2)
4	$[Co(C_7H_6NO_3)_2(H_2O)_2]$	23.4	42.1 (41.8)	4.0 (3.7)	7.0 (6.8)
5	$[Ni(C_7H_6NO_3)_2]$	11.8	46.3 (46.8)	3.3 (3.6)	7.7 (8.3)
6	$[Cu(C_7H_6NO_3)_2]$	13.7	45.7 (46.2)	3.3 (3.7)	7.6 (8.0)
7	$[(C_{26}H_{24}P_2)Ni(C_7H_6NO_2)]$	12.1	66.8 (65.9)	5.1 (5.3)	2.4 (2.8)
8	$[(C_{26}H_{24}P_2)Ni(C_7H_6NO_3)_2]$	16.6	65.0 (65.7)	5.0 (5.3)	2.3 (2.9)
9	$[Co(C_7H_6NO_2)_2(C_9H_7NO)]$	26.3	60.9 (61.0)	3.7 (4.3)	8.2 (9.2)
10	$[Co(C_7H_6NO_3)_2(C_9H_7NO)]$	23.2	57.4 (54.8)	3.5 (4.2)	7.7 (3.5)
11	$[Co(C_7H_6NO_2)_2(C_{13}H_8O_3)_2]$	33.5	63.6 (64.2)	3.7 (4.1)	3.7 (3.9)
12	$[Co(C_7H_6NO_3)_2(C_{13}H_8O_3)_2]$	35.0	61.0 (59.7)	3.6 (4.0)	3.6 (4.1)
13	$[Cu(C_7H_6NO_2)_2(C_9H_7NO)]$	28.2	55.7 (56.1)	3.8 (4.2)	8.1 (7.9)
14	$[Cu(C_7H_6NO_3)_2(C_9H_7NO)]$	22.4	53.3 (54.0)	3.6 (3.7)	7.8 (8.2)
15	$[Cu(C_7H_6NO_2)_2(C_{13}H_8O_3)_2]$	21.5	63.5 (63.1)	3.6 (3.7)	2.2 (2.0)
16	$[Cu(C_7H_6NO_3)_2(C_{13}H_8O_3)_2]$	18.4	61.9 (62.4)	3.5 (3.1)	2.2 (2.3)

[(a)] $ohm^{-1}cm^2mol^{-1}$

BHA = $C_7H_6NO_2$

HBHA = $C_7H_9NO_3$

KH= $C_{13}H_8O_3$

HQ= C_9H_7NO

DEPE= $C_{26}H_{24}P_2$

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concentration of 5 mg sample (in DMF), per test using the basic assay method[57,58]. Nutrient agar medium with the following composition (gil beff extract 3, peptone 5, NaCl 5 and agar 20 were used for bacterial culture. Fung

containing (gil) glucose 40, peptone 10 and agar 20.

Inhabitation zones (in mm) around filter paper discs (3 mm in diameter) were measured and the average of three readings was taken. Tetracycline antibiotics were used as a standard reference. The obtained results are shown in Table 4. The compounds were tested against four bacteria (all pathogenic) and 13 fungi (four complexes were found to be, in general, more potent against the tested organisms than the binary complexes. The complexes showed enhanced potency against staphylococcus citrus (gm negative bacteria) and number of the tested fungi. On the other hand, it could be observed those Ni and Cu complexes are generally more potent against the used organisms than the other metal complexes[57,58]. It could be easily recognized that the change in the secondary ligands complexes. Xanthate and phosphate derived mixed ligand complexes are more active biologically against the tested organisms than those containing the 8-hydroxyquinohine moiety. They can be regarded to be related with the existence of sulphur atoms in the xanthate moiety and the phosphate moiety in the dithiophosphate scondary ligand.

Cobalt complexes (1,4 in Table 1) showed a weight loss corresponding to the removal of two water molecules at reatively high temperature (150 210 °C). This comes in confirmation to the results of elemental analysis data that the two water molecules in these complexes are coordinatively bonded to the Co (II) ions in their mixed-ligand complexes. On the other hand, the presence of two coordinated water molecules in these complexes completes the coordination number of Co(II) to six, which is favorable in the regard that Co(II) likely forms octahedral complexes[56].

At higher temperatures the complexes are decomposed in several steps confirming the presence of both the hydroxamic acid and the secondary ligands. The decomposition was formed to continue up the formation of metal oxide at temperatures higher than 600 °C.

Biological Activity

Hydroxamic acids exist in nature as trihydroxamic and dihyroxamic acids. They are found to be constituents of antibiotic growth factors, tumor inhibitors, cell-division factors and pigments. In addition, they also showed antitubeculous, antifungal and antileukaemic activities [2,6]. More hydroxamic acids have been used recently in attempts to design metal chelats as suitable oral sources of metals for mammals[7-9], and as suitable reagent for the treatment of metal-overload and related diseases[10,11]. These findings propagated us to study the biological activity of the prepared new mixed ligand complexes. For this purpose the antimicrobal activity of the synthesized binary and mixed ligand complexes has been tested at

This band was found to appear at lower frequency in the spectra of the mixed ligands complexes indicating the coordination of the enolic oxygen atom of the hydroxamic acids to the metal ions. This shift towards lower frequencies is consistent with the expected decrease in the band order of the carbonyl group upon complexation.

(c) The band appearing around 1570 cm^{-1} in free BHA in the HBHA can be attributed to the NH in-plane deformation CN valence frequency in the hydroxamic acid molecule [3]. This band acquired also a remarkable shift towards a lower frequency on complexatin confirming that the second coordination site for these hydroxamic acids is the NH-O$^-$ moiety. This behavior is in agreement with the previously proposed conclusion that structure 3 is the suitable for these hydroxamic acids as ligands.

(d) Free hydroxamic acids displayed a medium IR band in the range 1360 1410 cm^{-1} which could be due to NH out-of-plane deformation. This band showed a little change in its position upon complexatin. This behavior is usual for this kind of frequency as it is out of the field of the coordination metal ion.

Thermal Studies:

Thermagravimetric studies of the mixed ligands complexes were carried out with the aim to verify the presence of coordinated water molecules in these complexes. The thermograms of some comlexes showed a non stoichimetric weight loss at low temperatures (between 50 85 C). This weight loss was rgareded to represent the removal of water exusting as moisture in these complexes.

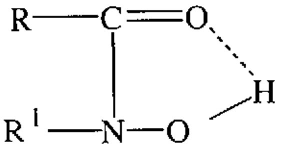
these secondary ligands can be summarized mainly in the following two points:

(i) The IR spectra of the mixed ligand complexes clearly features the characteristic bands of the secondary ligands (c.f. Figures 1- 8).

(ii) There are significant shifts in the main bands of either BHA or HBHA due to coordination of the secondary ligands to the binary complexes of these two ligands. The important changes can be described as follows:

(a) The NH frequency band appearing in the range 3200 3400 cm^{-1} , in the spectra of free BHA and HBHA, appears in the IR spectra of the mixed ligands complexes as a broad band or sometimes it splits to two bands. This behavior is due to the presence of coordination water molecules and/or molecules of water hydration. Further support for the presence of water molecules was achieved from the results of element analysis (Table 1) as well as from the thermogravimetric behavior as given herein after.

(b) The IR bands occurring in the range 1580 1680 cm^{-1} in the spectra of the free ligands as a broad bands is assignable to the stretching vibration of the ketonic carbonyl group of the compounds (BHA and HBHA). The broadening of this has been attributed to intermolecular H-bonding [54] within the hydroxamic acid molecules such as:



(HBHA) reveal the coordination of the two lignds to the metal ions in their monoionic bidentate mode. The molar conductivity values of some complexes, which could be dissolved in DMF, fall in the range 12 35 $Ohm^{-1}cm^{2}$ $mole^{-1}$. Since the reasonable range of 1: 1 electrolyte solutions in DMF is 65 90 $Ohm^{-1}cm^{2}$ $mole^{-1}$[53], all these complexes are non-electrolytes. This behavior is consistent with above-mentioned conclusion that both BHA and HBHA behave as mono-anionic bidentate ligands.

Elemental analysis data (cf. Table 1) indicate that the complexes were formed in molar ratio 2 : 1 (ligand : metal ion). Combination of the elemental analysis, conductivity measurements and thermal behavior suggests an octahedral six-coordination Co(II) complexes and square planar or tetrahedral four coordinate complexes in the case of using Ni(II) and Cu(II) ions.

On the other hand, the infrared spectra could provide ample evidence that both BHA and HBHA ligands are most likely coordinated through their mono-anionic form (structure 3 in scheme3) . The absence of distinct band due to $v_{C=N}$ ruled out the possibility of structure 2 (scheme 3) while structure 4 has been excluded due to the absence of OH group in the complexes that do not contain water molecules.

Tables 3 and 4 illustrate the most important infrared bands that could provide diagnostic evidence for the mode of attachment of BHA and HBHA ligand to the metal ions.

Since, we are concerned mainly with the mixed ligands, only infrared spectral bands of the mixed ligand complexes are included in Tables 3 and 4. The results showed there are significant changes in the spectra of the mixed ligand complexes relative to those of the free ligands. Such changes unambiguously indicated the coordination of

The resulting solution was stirred on an ice-bath for two hours whereby the solid complexes were precipitated. The solid was then filtered, washed with cold methanol and dried in vacuo over P_4O_{10}

(ii) *Mixed ligand complexes*

The precursors obtained in the previous step were used for preparation of the mixed ligand complexes. For this purpose (0.02 mole) of the binary complex was dissolved in about 50 ml of absolute ethanol, to which an ethanolic solution containing (0.02 mole) of secondary ligand was added while stirring. The stirring was continued for half hour and the mixture was left in the fridge for 2-3 hours to precipitate.

The prepared binary and mixed ligand complexes were analyzed for their C, H and N contents. The obtained results are given Table 1

Screening for antimicrobial activity

The antimicrobial activity of the mixed ligand complexes was tesed using the cup-plate technique [9,10]. The culture media used are nutrient agar media supplemented by 1 g yeast per liter. A final concentration of 10 ppm of the test compounds is used. The obtained results are in Table 2.

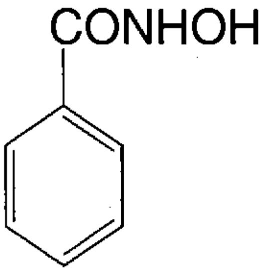
Results and Discussion

Hydroxamic acids, as derivatives of both hydroxylamine and carboxylic acids can exist in tautomeric forms as shown in scheme 3.

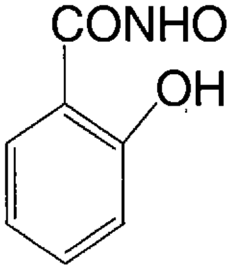
It is evident from scheme 3 that those compounds are potentially bidentate ligands either in neutral or monoionic forms. However, the elemental analysis and conductivity data of the complexes of benzohydroxamic (BHA) and hydroxybenzohydroxamic acids

Preparation of hydroxamic acids

Benzohydroxamic (BHA) and hydroxybenzohydroxamic (HBHA) acids were prepared by mixing ice-cold methanol solution of methyl ester of benzoic acid or salicylic acid (0.1 mole) and hydroxylamine (0.1 mole). The mixture was cooled for one hour in ice-bath whereby BHA or HBHA crystals were separated. These were filtered and washed with small portions of cold bidistilled water and dried in vacuum desiccator over preheated calcium chloride. The structure of the prepared hydroxamic acids is as follow:



BHA



HBHA

Synthesis of the Complexes

(i) *Binary hydroxamic acid metal complexes*

The Co(II), Ni(II), Cu(II) and Fe(II) complexes of either benzohydroxamic (BHA) or hydoxybenzohydroxamic (HBHA) acids have been prepared by mixing an aqueous solution of the metal salt (0.05 mole) to a methanolic solution of BHA or HBHA (0.1 mole).

a Ni(II) ion. The reasons for such behavior may drive from the different geometries of the parent complexes in the Bi (II) α-alaninehydroxamic acid and Ni(II)- B ligands. Square planar complexes are formed in the former system, while octahedral complexes are created in the latter case.

As discussed above, the hydroxamic group is very specific donor system able to effectively bind a variety of metal ions. The delocalization of the double bond system within the set of the hydroxamic group atoms makes its binding ability unique and metal coordination very strong. The presence of the amino group in the aminohydroxamic acid ligands increases the coordination effectiveness due to the possibility for [NH_2, N^-] chelate formation, which favours such metal ions as Cu(II) or Ni(II) in planar complexes. The presence of two different donor sites able to form chelate via the {N,N} or {O,O} donor sets very often leads to formation of stable oligonuclear complexes involving both the donor pairs.

Experimental

Materials

Organic solvents used in this project were of the Analar grade (B.D.H. products). Water used for preparation of aqueous solution was doubly distilled according to the recommended method. Metals salts, $CoCl_26H_2O$, $NiCl_22H_2O$, $CuCl_22H_2O$ and $(NH_4)Fe(SO_4)_212H_2O$ were of general purpose grade (G. P. R.). 8-Hydroxyquinoline, diethyl dithiophosphate and potassium xanthate used as secondary ligands were purchased from Sigma Chemical Co. and used without further purification.

research contain results on Mg (II) complexes hydroxamic axid and α-alaninehydrozamic acids [48,49]. Complexes of the latter metal ion werd found to rather weak and precipitation usually occurred at pH valuesaround 8. Aluminum (III) with alaninehydroxamic acid; the existence of mixed hydroxo complexes was proposed in the pH of 3-9, while above pH 9, [Al (OH)4] was found to be gthe only species in measurable concentration [49].

Ternary Complexes of Aminohydroxamic Acids

Taking into account the biological importance of aminohydroxamic acids (their possible applications of chemotherapy and in chemical modeling of the transport and storage of some metal ions [50]), the fact that ternary complexes are somewhat better models for complicated biological systems, the importance of the studies on ternary complexes containing aminohydroxamic acids is beyond doubt. Despite this intrinsic interest, study on ternary complexes of aminohydroxamic acids has been initiated recently [50-58]. El- Ezaby *et. al.,* studied the interaction of Ni(II) as Fe(III) with vitamin B_6 and glycine hydroxamic acid ligands. Based on kinetic results, the formation of intermediate ternary complexes was assumed [50,51]. More recently, results obtained for the modification of metal ion binding ability of α- alaninehydroxamic acid by different B ligands have been pulblished [50]. PH-metric and spectrophotometric measurements were preformed for Co (II) , Ni (II), Cu (II) and Zn (II) ions with α- alaninehuydroxamic acid and the B ligands were L- alanine, L-histidine, glycyglylcine and pyrocatecol. The results indicated that ternary complexes are not formed in systems containing pattern of the infrared spectra supported normal coordination via the ketonic oxygen and the oxygen atoms of the deprotonated NHO$^-$group [34,35]. The solid state magnetic moments and the electronic spectra provided further support for an octahedral structure, in the case of Fe(III), Co(II) and Ni(II) complexes and close to tetrahedral geometry for Cu(II) complexes [34].

In solution, equilibrium studies of monohydroxamic acids with Ni(II) [33,35,38]; Cu(II), Zn(II) [32,38] and Fe(II) [31,38-41] have shown the existence of different species. Expect for Cu(II), the acetohydroxamic, propionohydroxamic and benzohydroxamic acid ligands were assumed to form octahedral complexes, as found in the solid state. Analogous coordination, via two oxygen atoms occurs in Cu(II)- acetohydroxamic acid intersystem [38,40].

Aminohydroxamic Acids as ligands

The NH_2 group of α- aminohydroxamic acid is an α- position to the hydroxamic group. These compounds posses the ability to form two types five member chelate ring either via their nitrogen atoms or through the hydroxamate oxgen, and consequently the are good ligands for various metal ion.

Most published work dealing with complexes of aminjohydroxamic acids relates α- derivatives especialy to derivatives of simple aminoacids[38,42], such as glycine hydroxamic acid [43] and α- alaninehydroxamic axids [43,44]. Fe (II) was involved in most of the investigation because of the well-known biological importance of Fe (III)-hydroxamte complexes P43, 43, 45]. Complexes of Cu (II), Ni (II), and Zn (II) have also been investigated P46,47]. Few reported

These IR results are supported in several cases by NMR spectra. The NMR spectra of acetohydroxamic acid exhibit the signals of both NH and OH protons, while in the case of sodium acetohydroxamate, only the NH proton is observed in the spectrum [33]. This result supports the existence of the form (3). In contrast, the NMR spectra of Sn(II)-acetohydroxamic acid complex showed the presence of only OH proton [32,33]. Thus the NMR results seem to exclude structure (3) in complex system, while the IR spectra suggest the formation of structure (4) in complex species.

Hydroxamic Acid as Ligands

The singal hydroxamic acid group behaves as a typical bidentate donor towards various metal ions. Mono hydroxamic acid forms octahedral complexes with a number of metal ions coordinating via two oxygen atoms of the deprotonated hydroxamic acid group. This has been proved, e. g., in the X-ray studies of some complexes [36,37]. Brown *et.al.,* studied the solid state complexes of Fe (III), Co (II), Ni (II) and Cu (II) with monohydroxamic acids. In the case of the *bis* (acetohydro-xamic acid)nickel (II) dihydrate and *bis*(propionohydroxamic acid)- nickel (II) dihydrate, the infrared spectra showed shifts of about 40 60 cm^{-1} in the broad band at 1619 1583 cm^{-1} when compared with metal free ligand. This strongly suggested the complexation of ketonic oxygen atom. Bands in the 1445 cm^{-1} region can be assigned qualitatively to N-C stretching vibration with contribution from both C-O and C-R mode and those at about 1100 cm^{-1} to practically pure NO stretching mode. The general

The possibility of the existence of the several different monoionic forms depends on the ligand concerned. It was suggested, for example, that for hydroxamic acids, structures 3 and 4 occur in essentially equal concen-trations.

Exner and Simon concluded from IR and UV spectra that hydroxamic acids with common substituents form N-acids practically exclusively [29].

The existence of such forms in complex may depend on the metal ion [31,32]. The IR spectra of hydroxamic acids and their complexes are generally very complex, though some characteristic bands for different ligand structures were suggested [33-35]. For example, the band around 3200 cm^{-1} was assigned to NH valence frequency, while those in the 3080   3060 cm^{-1} region were attributed to the NH deformation and the CO valence vibrations. The broad band around 1610   1585 cm^{-1} observed in metal   free ligands is assigned to ketonic carbonyl vibration. Its broadening originates from the intermolecular hydrogen bonding and it undergoes an energy shift of 40   60 cm^{-1}when ketonic oxygen coordinates to the metal ion [35].

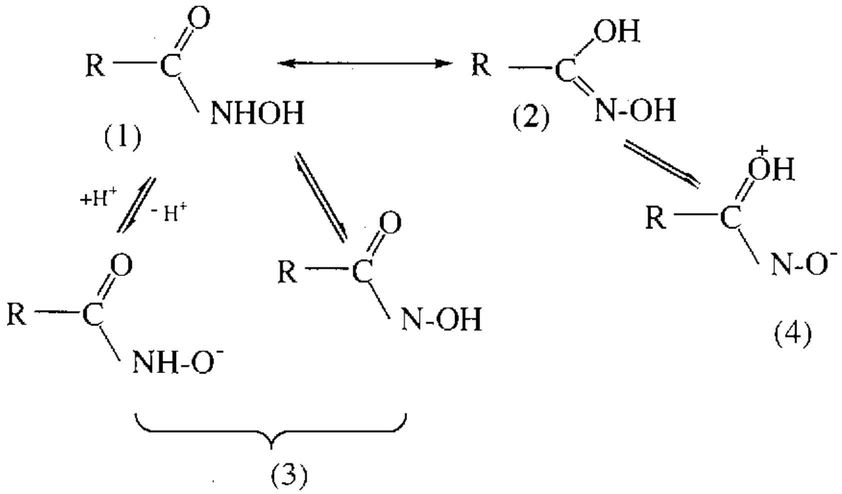
The band containing the NH planar deformation and CN valence frequency is centered at 1575 cm^{-1} [33]. There is also band around 1400   1440 cm^{-1} which is also assigned to the deformation of the NH moiety [33-35]. When hydroxamic acids are dissolved in an inert solvent, the band at 2770 cm^{-1} disappears and a new one is observed at 3420 cm^{-1} ; also band at 3280 cm^{-1} is shifted to 3220 cm^{-1} [33]. These variations suggest that there are considerable changes in the hydrogen bonding system during the dissolution process.

form has the lowest energy in case of both acetohydroxamic and formohydroxamic acids. However, on hydration, the (C) keto form becomes the more stable one due to hydrogen bonding [25].

The x-ray crystal of acetohydoxamic acid hemihydate revealed that, in its crystal, the (C) keto form is present [27].

Structure (A) in scheme 1 contains one easily replaceable proton (monobasic acid), while structure (B) may dissociated two protons, thus behaving as dibasic acid. This keto-enol tautomerism provides a number of sites, which are available for metal ion coordination. The keto form predominates in acidic solutions, while the enol is the dominant form in alkaline medium [28]. There are several possiblities for the mode of dissociation [29,30].

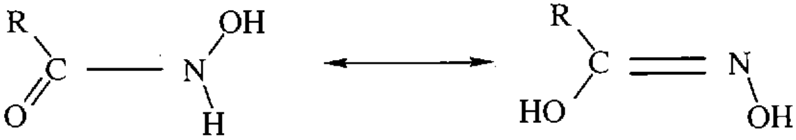
The mono-anions of these forms give rise to quite complex equlibira. Proton dissociation may follow the path shown in scheme 3.



Scheme 3

The Hydroxamic Acid Group and Its Metal Bonding Sites.

Hydroxamic acids may be regarded as derivatives of both hydroxyl-amine and carboxylic acids. The acyl portion of naturally occurring derivatives is usually simple and is often acetyl or originates biogentically form acetate. In solution, hydroxamic acid exists in the two tautomeric forms (A) and (B) as shown in scheme 1



(A) (B)

Scheme 1

If there is restricted rotation about the C-N bond, then both the (C) and (D) isomers of the keto form (scheme 2) exist [25].

(C) (D)

Scheme 2

NMR spectra confirm that both (C) and (D) forms are existing in solution, as do the enol forms [26]. The stabilities of the different forms of isolated and hydrated hydroxamic acids were examined using molecular orbital calculations, which showed that the isolated (D) keto

In 1978, a review of hydroxamic acid complexes finished the

s will

During the last years much more detailed information has been published, primarily involving the first transition metal series.

Introduction

Hydroxamic acid containing compounds is ubiquitous and intimately associated with iron-transport phenomena. The selectivity of this mechanism is critical since numerous other metal ions, which may not be essential or which may have a toxic effect on the organism, are present in the environment [1]. Hydroxamic acid is also known as constituent of growth factors, food additives, antibiotics, antibiotic antagonists, tumor inhibitors, antifungal agents and cell-division factors; several of them used as drugs [2-8]. Hydroxamic acids are also potent and specific inhibitors of urease activity [9], thrmolysin [10,11], elastase [12] and aminopetidases [13,14]. These enzymes are metalloproteinases and mechanism of inhibition appears to involve chelation of metal as their active sites [15].

Hydroxamic acids have also received considerable attention, as reagents in analytical chemistry for gravimetric analysis [16] and for solvent extraction and spectrophotometric determination of metals [17]. The reagents are also useful in the analysis of trace metals by flow injection analysis [18] and high performance liquid chromatography [19]. The properties and behavior of hydroxamic acid resins have been studied [20]. Discovery of oscillation phenomena in the florescence intensity of some aromatic hydroxamic acids suggest that they can undergo photochemical reactions [21-23].

With regard to the ability of these ligands to form chelates, one interesting question concerning the metal complexes is whether the nitrogen or oxygen atoms of the hydroxamic group (CONHOH) is involved in coordination to the metal ion.

Abstract

New mixed ligand complexes drived from benzohydroxamic and hydroxbenzo-hydrozamic acids as primary ligands and 8-hydrozyquinoline, diethyldithiophosophate and/or potassium zanthate as secondary ligands have been isolated and characterized. I.R. spectra data suggest that both primary and secondary ligands behave in bidentaet fashion towards metalions. Thermal analysis measurements of the solid complezes have also been conducted.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Prof. M. A. Al- Gurashi
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