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Research Article

SYNTHESIS OF NEW MACROCYCLIC SCHIFF BASES BASED ON 1,3-DOCARBONYL PHENYL DIHYDRAZIDE AND THEIR USE IN METAL CATIONS EXTRACTION

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Abstract

New Macrocyclic Hydrazone Schiff bases were synthesized by condensation of intermediate compounds: 1,7-bis (2-formylphenyl)-1,4,7-trioxaheptane (III) with dihydrazide of isophthalic acid. Identification of these macrocyclic Schiff bases ligands (VI). The Schiff bases were checked by different spectral technique (LC-MS, ^{1}H-NMR, IR, elemental analyses).Hydrazoic Schiff base have been studied by liquid-liquid extraction towards the metal ion Uo(II) from aqueous phase to organic phase. behave as good extractant ligand for uranyl ions Uo(II) from aqueous solution, and the study of conditions of extraction shows that the optimum pH values for extraction was (pH= 5.2), so the suitable concentration of Uo(II) ions in aqueous solution which is giving highest distribution ratio (D) was (1x10^{-4} M), in addition the optimum shaking time to reach the equilibria was (60 min.), as well as the stoichiometric study by using three methods shows the structure of Uo(II) ions complex with ligand was 1 : 1 (metal : ligand), in addition the study of organic solvent effect appear there is no straight line relation between the distribution ratio for extraction of Uo(II) ions and dielectric constant for organic solvents but this study demonstrate there is an effect for the structure of organic solvent used, thermodynamic study shows the complexation reaction an endothermic. The new Macrocyclic Hydrazone Schiff Bases were studied for antibacterial activities against (Bacillus subtilis and Staphylococcus aureus) are Gram positive and (Salmonella typhi and Escherichia coli) are Gram negative. The compounds ligands were exhibited a variable activity of inhibition on the growth of the bacteria.

Keywords: Macrocyclic Hydrazone, dihydrazide of isophthalic acid , spectral technique,liquid-liquid extraction, stoichiometric, thermodynamic antibacterial activity .

Introduction

Schiff bases are widely studied and used in the fields of organic synthesis and metal ion complexation [1,2] for a number of reasons: their physiological and pharmacological activities [3-5] their use in ion selective electrodes [6-11] in the determination of heavy metals ions in environmental samples [12] and in the extraction of metals ions [13,14] and their many catalytic applications (e.g. for epoxidation of olefins, alkene cyclopropanation [15,16] trimethylsilylcyanation of ketones [17] asymmetric oxidation of methyl phenyl sulfide enantioselectiveepoxidation of silylenol[18] and ring-opening Polymerization of lactide [19]. Hydrazones are special group of compounds in the Schiff bases family. They are characterized by the presence of (C=N-N=C). the presence of two inter-linked nitrogen atoms was separated from imines,oximes , etc. hydrazone Schiff bases of acyl, aroyl and heteroacroyl compounds have additional donor sites like C=O. The additional donor sites make them more flexible and versatile. This versatility has made hydrazones good polydentate chelating agents that can form a variety of complexes with various transition and inner transition metals and have attracted the attention of many researchers. Various hydrazones are obtained depending on the experimental conditions; which have application as biologically active compounds [20] and as analytical reagents [21]. As biologically active compounds, hydrazones find applications in the treatment of diseases such as anti-tumor [22] tuberculosis [22] leprosy and mental disorder [23]. Tuberculostatic activity is attributed to the formation of stable chelates with transition metals present in the cell. Thus many vital enzymatic reactions catalyzed by these transition metals cannot take place in the presence of hydrazones [24,25]. Hydrazones also act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators.

In the context of the above applications we have reported here the synthesis and characterization of novel macrocyclic hydrazone Schiff bases. All these compounds have been characterized by elementa analyses, LC-MS, IR, 1H NMR spectra data. A Survey of the literature reveal that no work has been carried out on the synthesis of mcrocyclic hydrazone Schiff bases derived from 1,3-Docarbonyl phenyl dihydrazide, and in the present study, we synthesized hydrazone Schiff bases and used it as an organic chelating agent to extract some metal cations from their aqueous to another organic phase. For the application to analysis, solvent extraction conditions such as solution pH, the types of organic solvents, the concentration of Schiff base and the effect of aqueous to organic phase, and used it in studying antibacterial activity.

2. Experimental

2.1.1.Reagents and Apparatus.

All the chemicals used were of AnalaR grade and procured from Sigma-Aldrich and Fluka. Metal salts were purchased from E. Merck and were used as received. Distilled water was used in the extraction experiments. The solvents were saturated with each other before use in order to prevent volume changes of the phases during extraction. The C, H, and N were analyzed on a Carlo-Erba 1106 elemental analyzer. The IR spectra was recorded on Jusco 300 instrument in KBr pellets. $^{1-}$H NMR spectra of ligands in $CDCl_3$ solution were recorded on a Bruker DT-400 MHz spectrometer, and chemical shifts are indicated in ppm relative to tetra methyl silane. Mass spectra were recorded using a KRATOS MS50TC spectrometer.TheUV–vis measurementswere recorded on a PerkinElmerʎ20UV–visSpectrometer.A pH meter (Metrohm–691pH Meter) was also used. All extraction experiments were performed by using a mechanical flask agitator in 50 cm^3 stoppered glass flasks, M.P Apparatus Digital (32-300 ^{0}C).

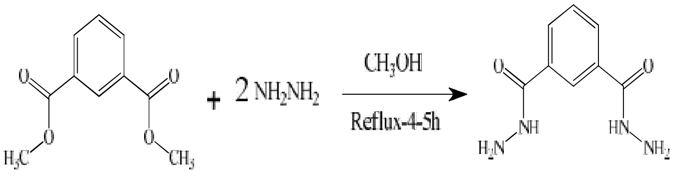
2.1.1.Synthesis of Dimethyl isophthalate(I).

Isophthalic acid (1.66 g, 0.1 mmol) in super dry methanol (60 mL) containing 2-3 drops of concentrated H_2SO_4 (AR) was refluxed till it dissolved. Then, the reaction mixture was poured onto ice cold water, immediately a solid started separating from the clear solution. To this a solution of sodium bicarbonate was added till the effervescence seized. The ester thus obtained was filtered and washed with water for several times (mp 64-67°C) [26].

2.1.2. Synthesis of dihydrazide of isophthalic acid(II).

A mixture of dimethyl ester of isophthalic acid (2.22 g) and hydrazine hydrate (98% 2 cc) in methanol was refluxed for 4-5h. The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured on to ice cold water. The dihydrazide of isophthalic acid thus obtained was filtered and recrystallized from ethanol.[27].

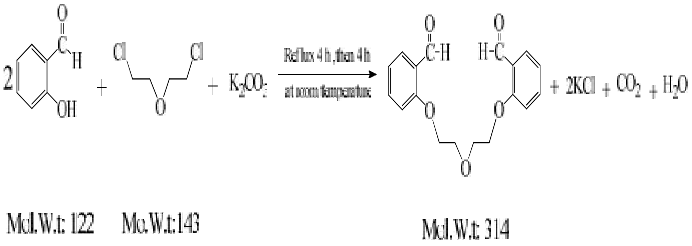
Yield:(85%), m.p=241 C^0, Empirical formula:($C_8H_{10}N_4O_2$),M.Wt:(194 g).



(II)

2.1.3. Synthesis of 1,7-bis (2-formylphenyl)-1,4,7-trioxaheptane:

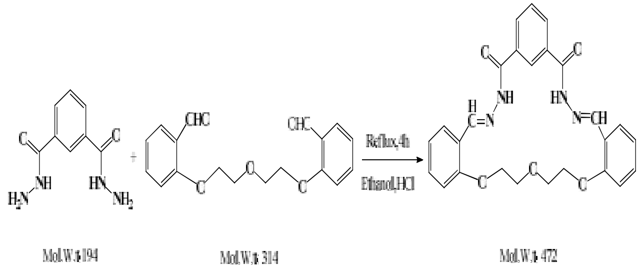
To a stirred solution of salicylaldehyde (2.44 g, 0.02 mol) and K_2CO_3 (1.38 g, 0.01mol) in DMF(50 mL), was added drop wise 1-chloro-2-(2-chloroethoxy)ethane (1.43 g, 0.01mol) in DMF (20 mL). The reaction was continued for 4 h at 150- 155°C and then for 4 hrs at room temperature. Then, 200 mL distilled water was added and the mixture was kept in refrigerator. After 1 h, the precipitate was filtered and washed with 500 ml water. It was dried in air and recrystalized from EtOH and filtered under vacuum. Yield: 81%, mp 75 °C, Empirical formula:($C_{18}H_{18}O_4$),M.Wt:(314 g).

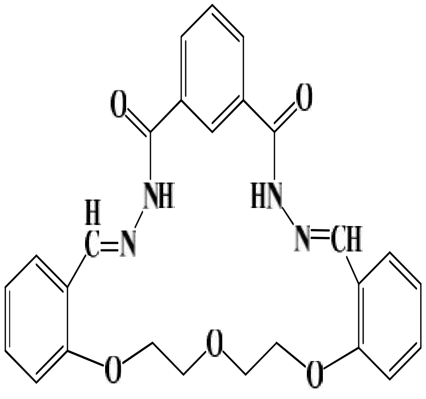


2.1.4. 1,2,8,9-tetraza-4,6; 11,12; 20,21-tribenzo–3,7-dicarbonyl-13, 16,19- trioxa- cyclodocosane-1,9-diene (IV):

The macrocyclic Schiff base (I) was prepared by dropwise addition of a solution of the dihydrazide of isophthalic acid(II) (0.388 g, 0.002 mol) in DMF (40 mL) to a stirred solution of 1,7-bis(2-formylphenyl) -1,4,7-trioxaheptane (i) (0.628 g, 0.002 mol) in DMF (60 mL) containing a few drops ofconcentrated HCl. The reaction mixture was heated to reflux for 5 h, where yellow precipitate was formed after cooling. On cooling, 200 ml distilled water was added and the mixture was kept in a refrigerator. After 2 h, the precipitate was filtered and washed with 200 mL water. The solid obtained was collected and recrystallized from mixture DMF ethanol as white crystals. A White colored precipitate was washed with water, ethanol, $CHCl_3$ and diethyl ether, respectively. Then dried in air.

Yield: 75 %. Mp>300 ^{0}C . Anal. Calc. for $C_{26}H_{24}N_4O_5$: C: 66.09, H: 5.12 , N: 11.86 , O: 16.93. Found: C: 65.99 , H:5.16 ,N:11.76 ,O:17.09 %,
Mass spectrum (LCMS):m/z= 472 ($[C_{26}H_{24}N_4O_5]$).
IR (KBr disk): 3167.12-3201.83 cm^{-1} (CO-NH-), 3008.95 – 3043.67 cm^{-1}(C-H), aromatic), 2854.65cm^{-1}(C-H), aliphatic), 1674.21cm^{-1}(C=O), 1635.64 cm^{-1}(C=N),1593.0 cm^{-1} (C=C, aromatic), 1300.02 cm^{-1}(C-O),aromatic).
^{1}H-NMR($CDCl_3$-400MHz) δ =12.513 (s,2H, CO-NH-), 11.117 (s,2H,CH=N) , 6.943 - 8.903 (m,12H, Ar-H), 2.508 – 3.361 (m,8 ,($-O-CH_2CH_2-O-)_2$.





2.2.Procedure of Extraction

The extraction properties of the Schiff base ligand (I) was investigated under liquid–liquid phase and neutral condition using transition metal picrates Cr(III), Co(II), Cd(II) as substrates and measuring by UV–vis measurements the amounts of metal picrate in the aqueous phase before and after treatment with the compounds. About 10 mm of 2×10^{-5} M aqueous picrate solution and 10 mm of 1×10^{-3} M solution of ligand in $CHCl_3$,CH_2Cl_2, C_6H_6 were vigorously agitated in a stoppered plastic tube with a mechanical shaker for 2 min, then magnetically stirred in a thermostated water bath at 25 ^{0}C for 1 h, and finally left standing for an additional 30 min. The concentration of the picrate ion remaining in the aqueous phasewas then determined spectrophotometrically. Blank experiments showed that no picrate extraction occurred in the absence of ligand. Transition metal picrates were prepared by successive addition of a 1×10^{-2}M metal nitrate solution to 2×10^{-5}M aqueous picric acid solution and shaken at 25 ^{0}C for 1 h.Thesemetal picrates Cr(III), Co(II), Cd(II) were measured by UV–vis using maximum wavelength 352 nm. For each combination of host and metal picrate, the picrate extraction was conducted on three different samples and the average value of percent picrate extracted, with a standard deviation, was calculated. In the absence of host, a blank experiment, no metal ion picrate extraction was detected. The extractability was calculated by using the equation below:

$$\text{Extractability (\%)} = \left(\frac{A_0 - A}{A_0}\right) \text{ x } 100$$

where A_0 is the absorbance in the absence of ligand. A denotes the absorbance in the aqueous phase after extraction.[Bülent .D., 2009].

2.3.Biological Activity

The prepared compounds were tested for their antimicrobial activity against four speices of bacteria (Bacillus subtilis, Escherichia coli , Staphylococcus aureus, Salmonella typhi) using filter paper disc method [38]The screened compounds were dissolved individually in DMSO (dimethyl sulfoxide) in order to make up a solution of 50, 100, and 200 µg/ml concentration for each of these compounds. Filter paper discs (Whitman No.1 filter paper,5mm diameter) were saturated with the solution of these compounds. The discs were placed on the surface of solidified Nutrient agar dishes seeded by the tested bacteria. The diameters of inhibition zones (mm) were measured at the end of an incubation period, which was 24 h at 37C for bacteria. Discs saturated with DMSO are used as solvent control. Ciprofloxacin 100 µg/ml was used as reference substance for bacteria**.[38].**

Results and Discussion

3.1.1. Synthesis

The prepared macrocyclic hydrazone (IV) was synthesized by condensation of intermediate compound: 1,7-bis (2-formylphenyl)-1,4,7-trioxaheptane (III) with dihydrazide of isophthalic acidin the molar ratio (1:1) in DMF. The reactions proceeded smoothly, producing the corresponding Schiff bases ligand in good yield. The ligand is soluble in common organic solvent but insoluble in water. The structures of the ligand was elucidated by elemental analyses, MS, FTIR, electronic absorption, and $^{1-}$H- NMR spectra, which help in elucidating their empirical formulaas in Table 1.

3.1.2. Elemental analyses of Schiff base

The results of elemental analyses Schiff base, as shown in Table (3.2), are in good agreement with those required by the proposed formulae

3.1.3. IR Spectra

IR spectra analysis

Compound(VI): A strong band at 1616.8 and 1637.2 cm^{-1} in the IR spectrum of the Schiff base**(figure 2)** are assigned to υ(C=N) of azomethine and carbonyl υ(C=O) vibrations, respectively. An intense band at 3414.3 - 3236.8 cm^{-1} is due to the -NH- vibrations of the hydrazine group The band in the spectra at 1599.3cm^{-1} is due to (C=C) of aromatic rings. while the band at 2939.3 – 2868 cm^{-1} are attributed to (C-H aliph) .Also, the band at 3072.2cm^{-1} are attributed to (C-H ar).[31-35]. However, in the IR spectra of Schiff bases this bands (C=O) disappears and a new vibration bands for azomethine (-HC=N-). Indicating that complete condensation takes place.All IR spectral data of the synthesized compound showed in theTable 3 [36-37].

3.1.3. $^{1-}$H-NMR Spectra of macrocyclic hydrazone (IV).

Compound (VI): The ^{1}H NMR spectrum**(figure 3)**of the Schiff base (VI), showed that in the region 2.223 - 1.873 ppm were assigned to protons of methyl groups in two differentenvironments [38]. The signals at 12.511 and 8.954ppm were assigned to the protons of amide CONH and imine -CH=N groups respectively. Signals in the region 8.391 - 7.121 ppm were assigned to the aromatic protons.While the singlet signal at 4.147 ppm assigned to the protons (**-**O-CH_2-) group.

The other obtained values for $^{1-}$H-NMR chemical shifts of the compounds are given in the experimental section.
The $^{1-}$HNMR spectral data of the new compoundsshowed in theTable 4. These data are in good agreement with those previously reported for similar compounds. These results strongly suggest that the proposed compounds have been formed**.[36-37]**

The complexation reaction between the ligand (I) and Cr(III), Co(II), Cd(II) ions to produce the ion pair complex have to extracted to the organic phase, this complexationreaction of necessity behave among many optimum condition to reach equilibria and giving stable ionpair complex .

3.2.1 Effect of pH:

Extracted of 10 ml of Cr(III), Co(II), Cd(II) ions in aqueous phase at different pH (3 –12) by using (10 ml) of (1×10^{-4} M) ligands dissolved in chloroform, after that shaking the two layers for suitable time and separate this two layers and determined the remainder of Cr(III), Co(II), Cd(II) ions in aqueous phase and Cr(III), Co(II), Cd(II) ions transfer to theorganic phase as complex by stripping method or by difference method according to general procedure, afterward determine the distribution ratio (D) and percentage of extraction (E) at each pH, the results in Table (4), and Fig. (5) shows the optimum of pHextraction was (pH_{ex} = 7). At pH less than optimum value effect to protonated ligand to Cr(III), Co(II), Cd(II) the pair of electron and then can't coordinate strongly with Cr(III), Co(II), Cd(II) ions and give less stable ion pair complex and minimize the distribution ratio (D) and percentage of extraction (E), also atpH values more than optimum value effect to decrease distribution ratio (D) and percentage ofextraction (E) by reason of formation ion pair complex contain anion (OH) this complex more soluble in aqueous phase and less extracted to organic phase and sovereignty the dissociation equilibria

3.2.2. Effect of Shaking Time:

Extraction of Cr(III), Co(II), Cd(II) ionS from (10 ml) aqueous phase at (pH = 7) by using (10 ml) of organic phase of (1×10^{-4} M) ligand dissolved in chloroform, after shaking the two phases at different times, separate the two phases and determine the concentration of Cr(III), Co(II), Cd(II) ions remainder in aqueous phase and the concentration of Cr(III), Co(II), Cd(II) ions transfer to organic phase as ion pair complex by previous spectrophotometricmethodand then determine distribution ratio (D) and percentage of extraction (E). the results in Table (5) and Fig. (6) demonstrate that the optimum shaking time was (60 min.) to reach the equlibria of complexation reaction and giving higher distribution ratio (D), the shaking time less than optimum shaking time not allow to reach for equilibria and giving low distribution ratio (D), but at shaking time more than optimum time effect to favor the dissociation step on the complexation and minimize the distribution ratio (D) depend on the kinetic energy of reaction

3.2.3.Stoichiometry by Slope Analysis Method:

To knowing the more probable structure of Cr(III), Co(II), Cd(II) ion pair complex produced, extracted (1×10^{-4} M) Cr(III), Co(II), Cd(II) ion from (10 ml) aqueous phase at (pH=7) by using (10 ml) of ligand solution dissolved in chloroform at different concentration ($2\ \text{x}10^{-5}$M – 3×10^{-4} M), after shaking the two layer for (60 min.), separate these layers and determine the remainder quantity of Cr(III), Co(II), Cd(II) ions in aqueous phase and transfer quantity of Cr(III), Co(II), Cd(II) ions to organic phase as complex, after that determine distribution ratio (D) and percentage of extraction (E) by previous method (spectrophotometric method). Afterward plot log D against log [Ligand]. The results in Table (6) and Fig. (7) shows from the slope of straight line that the more probable structure of ion pair complex extracted was 1:1(metal : ligand).

3.2.4. Organic Solvent Effect:

Solvent extraction method take care of organic extraction method; according to this concept extracted (1×10^{-4}M) Cr(III), Co(II), Cd(II) ions in (10 ml) aqueous phase at (pH=7) by (10 ml) organic phase contain ligand dissolved in different organic solvents at concentration of (1×10^{-4}M), after shaking for (60 min) separate the two layers and determine the remainder Cr(III), Co(II), Cd(II) ions in aqueous phase and Cr(III), Co(II), Cd(II) ions transfer to organic phase as Cr(III), Co(II), Cd(II) complex, according to previous method, afterward calculate the distribution ratio (D) and percentage of extraction (E). the results in Table (7) shows there is not any linear relation between distribution ratio (D) and dielectric for organic solvents used in extraction method of Cr(III), Co(II), Cd(II)ions, Fig(8) as well as this results reflect the effect of organic solvent structure on the extraction method and without any effect for polarity of organic solvent, and reflect the effect on ion pair complex extracted to be contact ion pair (tight ion pair) or solvent used separated ion pair (loose ion pair)

3.6Effect of Temperature:

Extraction of Cr(III), Co(II), Cd(II) ions in (10 ml) aqueous phase at (pH = 7) by using (10 ml) of (1×10^{-4} M) ligand dissolved in chloroform at different temperature (10 – 40ºC), after shaking the two layers for optimum time and separate the two layers, determine distribution ratio (D) according to the general procedure. The results in Table (8) and Fig. (9) illustrate the complexation reaction between ligand and Cr(III), Co(II), Cd(II) ions was Endothermic reaction, that is mean the coordination association between ligand and Cr(III), Co(II), Cd(II) ions increase with temperature increasing**.**
After calculated the thermodynamic data for extraction method to Cr(III), Co(II), Cd(II) ion byusing the below relation**:**

$$K_{ex} = \frac{D}{[M^{n+}]_{aq}[L]_{org}} \qquad (4.1)$$

Plot log K_{ex} against 1/T ºK and determine the slope of the straight line relation, calculate ΔH_{ex} as in the relation.

$$:\frac{\Delta \log K_{ex}}{\frac{\Delta 1}{T}} = \frac{-\Delta H}{2.303\ R} (4.2)$$

$$\text{Slope} = \frac{-\Delta H}{2.303\ R} (4.3)$$

$$\Delta G_{ext} = -RT \ln K_{ext} \mathbf{(4.4)}$$

$$\mathbf{(4.5)} \Delta G_{ext} = \Delta H_{ext} - T\Delta S_{ext}$$

After application of these relation, found the value of enthalpy for extraction of Cr(III), Co(II), Cd(II) ions were (ΔH_{ex} = 103.97, 57.79, 52.14 kJmol^{-1}) and Gibbs free energy was (ΔG_{ex} = -86.53, -47.76, -46.28 kJmol^{-1}) respectively, as well as the entropy was (ΔS_{ex} = 608.63, 337.86, 314.44 $\text{JK}^{-1}\text{mol}^{-1}$) these results shows from the value of ΔH_{ex} the ion pair complexes structure was 1 : 1 which is giving low value for ΔH_{ex}, but the high value for ΔS_{ex} reflect that complexation reaction was entropic in region [Arifien,et all.,2003]from other hand the endothermic reaction shows good association between Cr(III), Co(II), Cd(II) ions and ligand and may be produce contact ion pair (Tight ion pair).

3.3 Biological Activity

During the last two or three decades, attention has been increasingly paid to the synthesis of Schiff bases which exhibits various biological activities including antibacterial, fungicidal, tuberculostatic and plant growth regulative properties **[41]**. It was judicious to investigate the synthesis of various new types of Schiff base and studied their antibacterial activity against four strains of bacteria(Bacillus subtilis, Escherichia coli , Staphylococcus aureus, Salmonella typhi). The concentrations used for the screened compounds are 50, 100, and 200 µg/ml. Ciprofloxacin was used as reference standard while DMSO as control and inhibition zones are measured in mm. The new compounds were tested against one strain each of a gram positive and two gram negative. The test results presence in Table (3.11), a new compound was active against tested and another compounds are no active.

All compounds are no active where used 50, 100 μg/ml but active in the concentrations 200 μg/ml see table (3.4).

4. Conclusion

1- The (IV) compound is new and was prepared for the first time.

2- The new compound was identified by 1HNMR, IR, LC-MS spectral methods.

3-The compound showed a high draw ratio of copper ion at pH = 5.2 and the best organic stores is chloroform and that there is no linear relationship between the polarity of the shops and the distribution ratio(D).

4-That shaking a time more than a time best, which represents the time required to complete the process complexity and give a complex stable lead to lower values ratios distribution D and this would lead to the possibility of a reflection of interaction and increase the speed of interaction back and eventually dismantle the complex and perhaps a few Side reactions that maylead to the occurrence of the phenomenon of the three layers (Three layers) for the analysis of solutions and this is what requires us to comply with a time of shaking out the best

5-That the rate of ion correlation between copper and composite studied by Molar (cation: connected (1:1) between the ligand and the cation.

6-Calculated some parameters associated with extraction, such as constant extraction as well as parameters thermodynamic namely, enthalpy change(ΔH*),entropy change (ΔS*), and Gibbs free energy change (ΔG*).

7-proven data study the effect of different temperatures on the recovery operations that the formation of complexes between ligand and cation studied endothermic (Endothermic) , as indicated negative values of energy free to spontaneous reactions, as also indicated positive values of entropy system that many random.

8-The prepared compound has been biologically screened i.e. studying their effects against two gram-positive, two gram-negative bacteria. The results show that their activities were found to vary from moderate to very strong.

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Table 1. Physical and chemical properties of the synthesized compounds[IV]

Schiff base	**Color**	**M.Wt**	**Melting point ^{0}C**	Yield %	Crystallization Solvent
IV	White	472	> 300	75	DMF , EtOH

Table .2. Elemental analyses of macrocyclic hydrazone (IV).

Schiff base	Elemental analysis Calculated (Found %)				
	C	**H**	**N**	**S**	**O**
IV	65.99 (66.09)	5.16 (5.12)	11.76 (11.86)	-------	17.09 (16.93)

Table 3. IR spectral data of the synthesized compound[IV].

Schiff base	**v(C-O)**	**v(C=C)**	**v(HC=N)**	**v(C=O)**	**v(C-H) aliph**	**v(C-H) arom**	**v(N-H)**
I	1300.02	1593.0	1635.64	1674.21	2854.65	3043.67 - 3008.95	3201.83 - 3167.12

Table4.$^{1-}$H-NMR Spectra of the synthesized compound[IV].

Schiff base	**Chemical Shifts δ ppm**			
	-O-CH$_2$-	**C-H aromatic**	**CH=N**	**-CO-NH-**
IV	2.508 – 3.361 (m,8H)	8.395 - 6.943 (m,12 H)	8.903 (2,2H)	12.513 (s,2H)

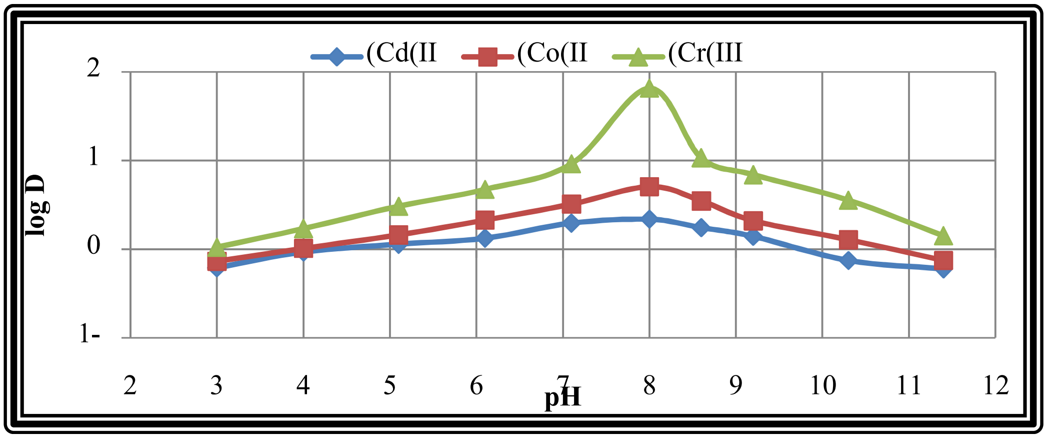

Fig. (5): pH effect on the extraction of Cr(III), Co(II), Cd(II) ions

Table (4): Effect of pH on the extraction of Cr(III), Co(II), Cd(II) ions

pH	**Cd^{+2}**			**Co^{+2}**			**Cr^{+3}**		
	log D	**D**	**E%**	**log D**	**D**	**E%**	**Log D**	**D**	**E%**
3	-0.207	0.621	**38.3±0.7**	**-0.135**	0.733	**42.3±0.7**	0.025	1.058	**51.4±0.9**
4.5	-0.031	0.931	**48.2±0.7**	0.010	1.024	**50.6±0.8**	0.233	1.710	**63.1±0.7**
5.4	0.056	1.137	**53.2**	0.162	1.451	**59.2±0.7**	0.486	3.065	**75.4±0.8**
6.3	0.124	1.331	**57.1±0.8**	0.329	2.135	**68.1±0.8**	0.676	4.747	**82.6±0.7**
7	0.296	1.976	**66.4±0.7**	0.510	3.237	**76.4±0.7**	0.964	9.204	**90.5±0.5**
8	0.339	2.185	**68.6±0.5**	**0.707**	**5.098**	**83.6±0.5**	**1.392**	**24.641**	**96.1±0.8**
8.5	0.246	1.761	**63.78±0.8**	0.545	3.505	**77.8±0.8**	1.031	10.74	**92.5**
9.4	0.147	1.404	**58.4±0.6**	0.321	2.094	**65.4±0.6**	0.841	6.934	**80.8±1.2**
10.3	-0.126	0.845	**45.8±0.9**	0.107	1.278	**56.1±0.5**	0.554	3.581	**69.3±0.6**
11.2	-0.22	0.603	**37.6**	-0.126	0.748	**42.8±0.9**	0.151	1.416	**58.6±0.7**

Table (5): Effect of shaking time on extraction of Cr(III), Co(II), Cd(II)ions

Shaking Time	**Cd(II)**			**Co(II)**			**Cr(III)**		
	Log D	**D**	**E%**	**Log D**	**D**	**E%**	**Log D**	**D**	**E%**
10	-0.209	0.618	38.2±0.6	-0.149	0.709	41.5 ± 0.8	0.075	1.188	54.3±0.06
20	-0.038	0.916	47.81 ±0.04	0.138	1.375	57.9 ± 0.09	0.280	1.907	65.6±0.05
30	0.021	1.050	51.22 ±0.5	0.182	1.519	60.3 ±0.7	0.464	2.91	74.4±0.9
40	0.101	1.262	55.8±0.5	0.331	2.145	68.2 ±0.2	0.686	4.848	82.9±0.7
50	0.321	2.096	67.7±0.5	0.484	3.048	71.7 ±0.5	**0.981**	**9.573**	**90.7±0.5**
60	**0.445**	**2.788**	**73.6±0.5**	**0.810**	**6.463**	**86.6±0.5**	**1.369**	**23.390**	**95.9±0.8**
70	**0.296**	**1.976**	**66.4±0.6**	**0.519**	**3.310**	**76.8±0.8**	**1.158**	**14.385**	**93.5**
80	**0.169**	**1.475**	59.6±0.04	0.345	2.215	68.9 ± 0.02	0.853	7.130	87.7±0.7
90	**0.043**	**1.105**	52.5±0.05	0.207	1.611	61.7 ± 0.09	0.565	3.673	78.6±0.8
100	**-0.042**	**0.908**	47.6±0.04	0.075	1.188	54.3±0.06	0.349	2.231	69.05 ±0.8
110	-0.168	0.679	40.46 ±0.04	-0.049	0.894	47.2 ±0.2	0.179	1.513	60.2±0.8
120	-0.218	0.605	37.7±0.05	**-0.183**	**0.656**	**39.6±0.5**	0.061	1.151	53.5±0.8

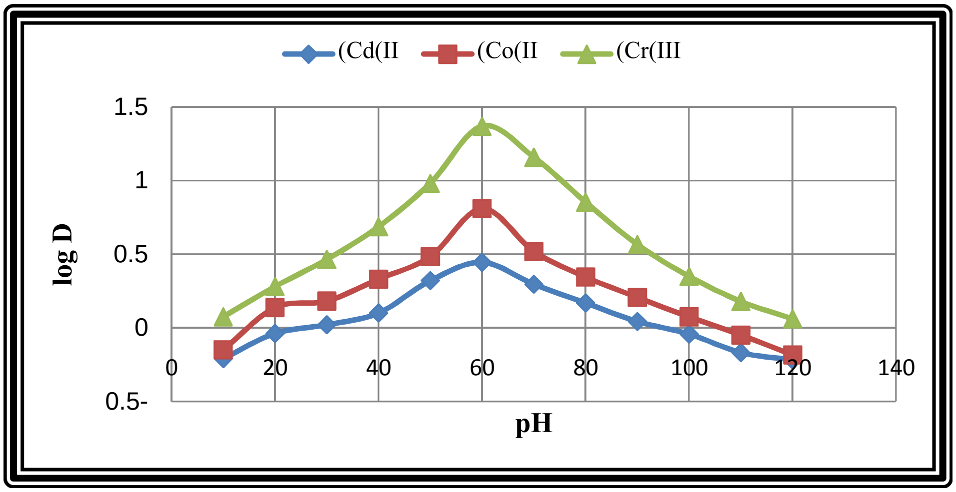

Fig. (6): Effect of shaking time on the extraction of Cr(III), Co(II), Cd(II) ions

Table (6): Slope analysis method for extraction of Cr(III), Co(II), Cd(II) ions

	Cd(II)				**Co(II)**				**Cr(III)**			
Log [L]	**Log D**	**D**	**E%**	**slope**	**Log D**	**D**	**E%**	**slope**	**Log D**	**D**	E%	**slope**
-4.698	-0.403	0.395	**28.3±0.7**	0.749	**-0.278**	0.527	**34.5±0.7**	0.858	0.138	1.374	**68.2±0.9**	1.25
-4.522	-0.179	0.662	**39.8±0.7**		-0.024	0.946	**44.1±0.8**		0.539	3.459	**74.9±0.7**	
-4.397	-0.121	0.757	**43.1±0.8**		0.092	1.236	**55.3±0.7**		0.756	5.701	**80.1±0.8**	
-4.301	0.009	1.02	**50.5±0.7**		0.207	1.611	**62.9±0.8**		0.857	7.195	**83.7±0.7**	
-4.097	0.205	1.603	**61.6±0.5**		0.389	2.449	**74.3±0.7**		1.103	12.677	**87.4±0.5**	
-4	0.451	2.825	**73.85±0.8**		0.697	4.98	**83.3±0.5**		1.571	37.24	**97.8±0.8**	
-3.698	0.438	2.742	**73.3±0.6**		0.683	4.82	**81.8±0.8**		1.561	36.39	**93.3**	
-3.522	0.439	2.748	**73.3±0.5**		0.678	4.76	**81.6±0.6**		1.521	35.81	**92.5±1.2**	

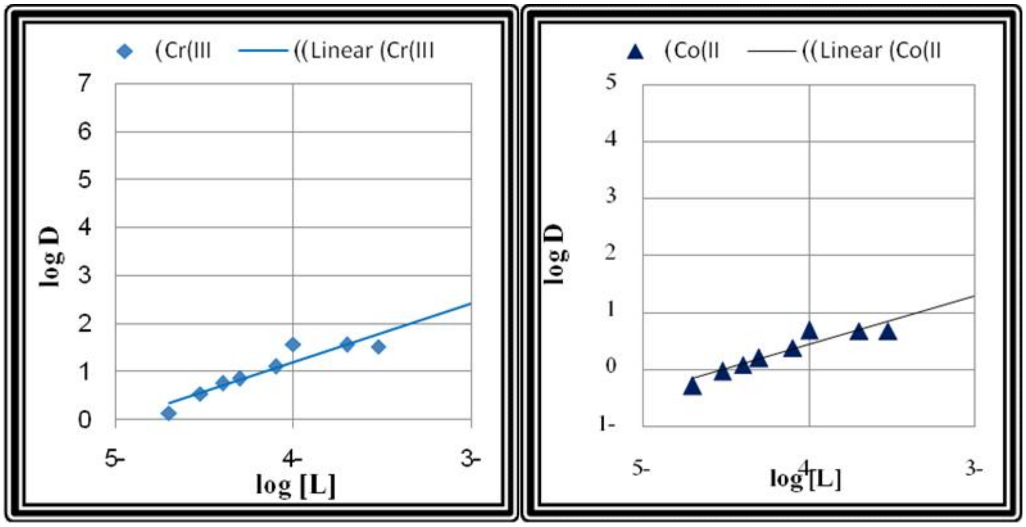

Fig. (7): Slope analysis method for extraction of Cr(III),Co(II) ions

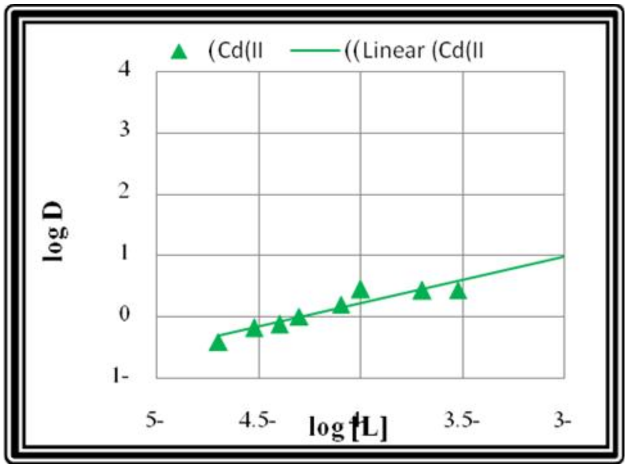

Fig. (8): Slope analysis method for extraction of Cd(II) ions

Table (7): Organic solvents effect on the extraction of Cr(III), Co(II), Cd(II) ions

Solvents	ε	Cd(II)			Co(II)			Cr(III)		
		Log (D)	D	E %	Log (D)	D	E %	Log (D)	D	E %
Dichloro methane	9.08	0.205	1.604	61.6 ±0.5	0.463	2.906	74.4 ±0.7	0.771	5.897	85.5 ±0.5
Chloroform	5.708	0.284	1.922	65.78±0.8	0.676	4.747	82.6 ±0.5	1.481	30.25	96.5 ±0.8
Benzene	2.804	0.042	1.101	52.4 ±0.6	0.173	1.488	59.8 ±0.8	0.421	2.636	72.5

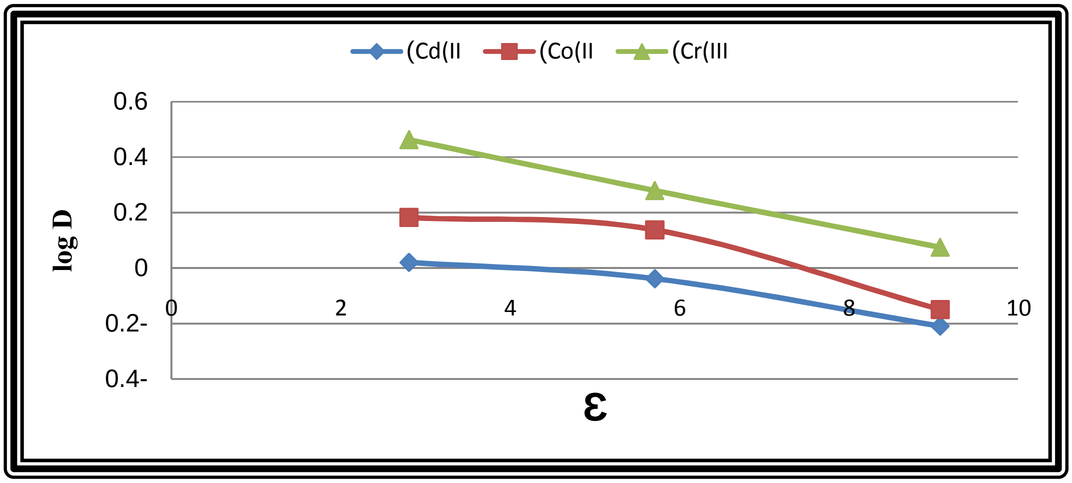

Fig. (8): Effect of solvents organic on the extraction of Cr(III), Co(II), Cd(II) ions

Table (8): Temperature effect on the extraction of Cr(III), Co(II), Cd(II) ions

T.C ^{0}	T.K^0	1/Tx10^{-3} K^0	Cd(II)			Co(II)			Cr(III)		
			Log (D)	D	E %	Log (D)	D	E %	Log (D)	D	E %
10	283	3.5	-0.137	0.729	41.26 ±0.3	-0.033	0.927	48.09±0.05	0.546	3.97	79.9
20	293	3.4	0.139	1.378	70.5±0.7	0.373	2.361	70.25±0.05	1.121	13.21	92.96 ±0.05
30	303	3.3	**0.402**	**2.523**	**73.8±0.5**	**0.712**	**5.152**	**84.8 ±0.5**	**1.691**	**49.09**	**98±0.8**
40	313	3.2	0.608	4.06	80.24 ±0.7	0.975	9.44	90.4 ±0.12	2.099	125.6	99.21

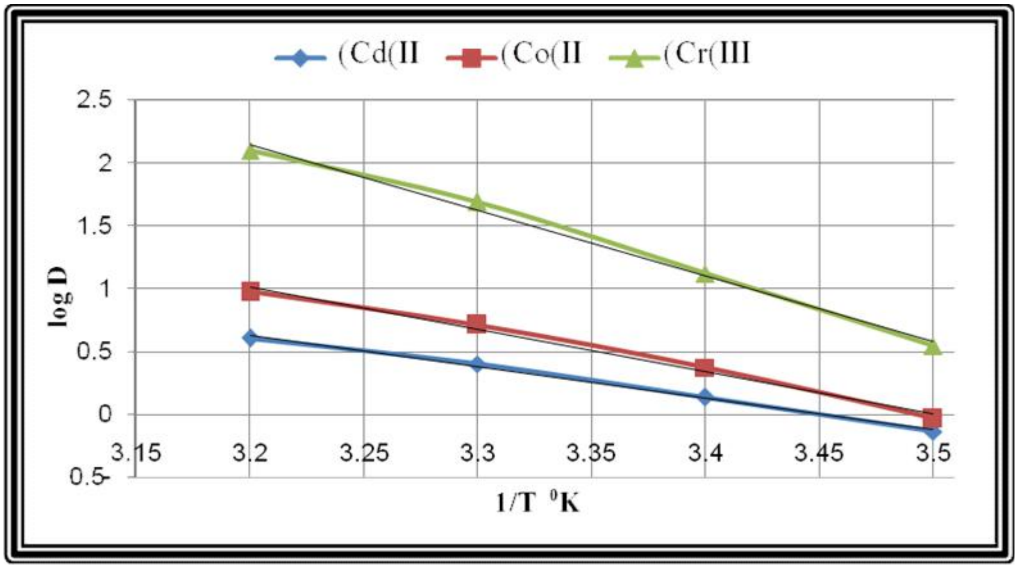

Fig. (9): Temperature effect on the extraction of Cr(III), Co(II), Cd(II) ions

Table (8): Thermodynamic parameters of Cr(III), Co(II), Cd(II)ions

Cation	K_{ext}	ΔS_{ext} $jK^{-1}mol^{-1}$	ΔG_{ext} $kjmol^{-1}$	ΔH_{ext} $kjmol^{-1}$
Cr(III)	158.9×10^{12}	588.53	-85.09	99.12
CO(II)	983.3×10^{5}	358.53	-47.89	64.33
Cd(II)	205.5×10^{5}	291.92	-43.82	47.55

Table 5. Antibacterial activity of the synthesized compounds[VI]-[IX]

Shiff base	**Bacteria**			
	Gram negative		**Gram positive**	
	B. subtilis	**S. aureus**	**E.coli**	**S. typhi**
I	**20 mm**	**18 mm**	**17 mm**	**19 mm**
Control	**00 mm**	**00 mm**	**00 mm**	**00 mm**
Ciprofloxacin	**20 mm**	**20 mm**	**20 mm**	**20 mm**

(-)No zones of inhibition were observed.
Moderately sensitive,(+)Inhibition zones of 7-10mm.
Sensitive,(++)Inhibition zones of 11-14mm.
High sensitive,(+++)Inhibition zones of 15-20mm

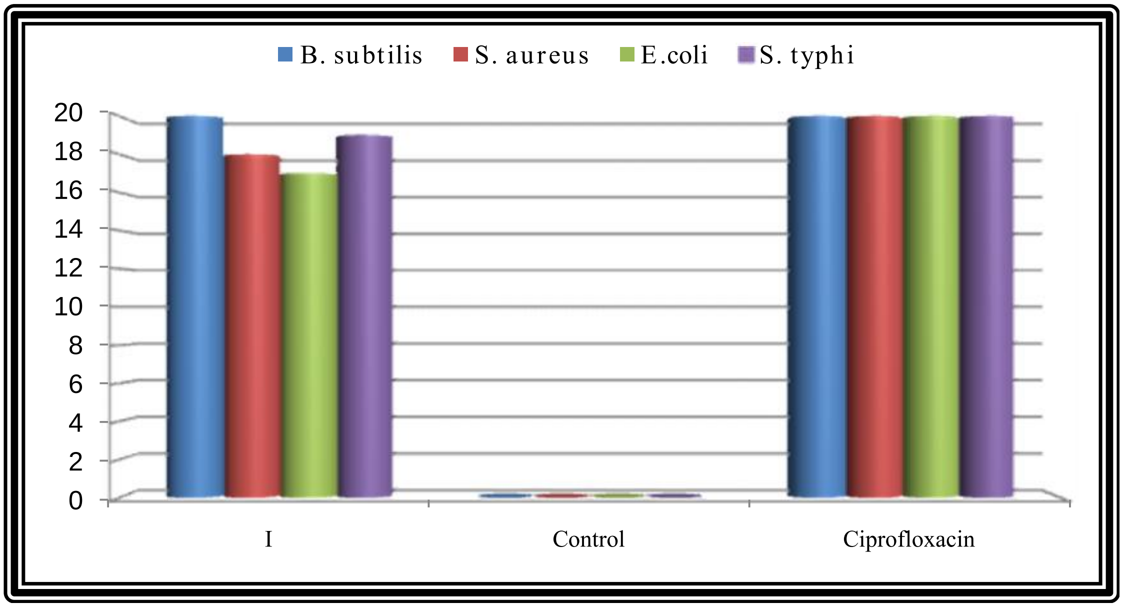

Figure 13.Antibacterial activity of synthesized compounds[IV].

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