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Synthesis Characterization and Antibacterial Activity of New Open and Macrocyclic Schiff Bases Ligands

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Abstract- In this work we focused on the synthesis of two new macrocyclic Schiff bases: (III) , (IV), (VI) containing nitrogen – oxygen donor atoms were synthesized by condensation of intermediate compounds: 1,6- bis (2- formylphenel) hexane (I)and α,α'-bis(2-carboxyaldehyde phenoxy) xylene(II) with 4,4'-Diamino-diphenylmethane and 4-Aminophenyl sulfone. Also new open Schiff bases (V) which were prepared by condensation of benzylhydrazidewith 1,6- bis (2- formylphenel) hexane (I). Identification of these macrocyclic Schiff bases: 1,16-di aza-3,4,13,14-tri phenyl-17,25 -di phenyl methane-5,12-di oxacyclo penta-icozane-1,15-diene(III), 1,16-di aza-3,4,7,10,13,14-tri phenyl-17,25 -di phenyl methan-5,8-di oxacyclo penta-icozane-1,15-diene. (IV).1,16-di aza-3,4,13,14-tri phenyl-17,25 -di phenyl sulphide-5,12-di oxacyclo penta-icozane-1,15-diene(V),and N',N'-(2,2'-(hexane-1,6-bis(oxy)) bis(2,1-phenylene))bis (methanylidene) dibenzhydrazide. (VI).The Schiff bases were checked by different spectral technique (LC-MS, ^{1}H-NMR, IR, elemental analyses). The new 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 ligands were exhibited a variable activity of inhibition on the growth of the bacteria.

Keywords: *macrocyclic schiff bases, open schiff bases spectral technique, antibacterial activity.*

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Synthesis Characterization and Antibacterial Activity of New Open and Macrocyclic Schiff Bases Ligands

Hamid Hussein Eissa

Abstract- In this work we focused on the synthesis of two new macrocyclic Schiff bases: (III) , (IV), (VI) containing nitrogen – oxygen donor atoms were synthesized by condensation of intermediate compounds: 1,6- bis (2- formylphenel) hexane (I)and α,α'-bis(2-carboxyaldehyde phenoxy) xylene(II) with 4,4'-Diamino-diphenylmethane and 4-Aminophenyl sulfone. Also new open Schiff bases (V) which were prepared by condensation of benzylhydrazidewith 1,6- bis (2- formylphenel) hexane (I). Identification of these macrocyclic Schiff bases: 1,16-di aza-3,4,13,14-tri phenyl-17,25 -di phenyl methane-5,12-di oxacyclo penta-icozane-1,15-diene(III), 1,16-di aza-3,4,7,10,13,14-tri phenyl-17,25 -di phenyl methan-5,8-di oxacyclo penta-icozane-1,15-diene. (IV).1,16-di aza-3,4,13,14-tri phenyl-17,25 -di phenyl sulphide-5,12-di oxacyclo penta-icozane-1,15-diene(V),and N',N'-(2,2'-(hexane-1,6-bis(oxy)) bis(2,1-phenylene))bis (methanylidene) dibenzhydrazide. (VI).The Schiff bases were checked by different spectral technique (LC-MS, ^{1}H-NMR, IR, elemental analyses). The new 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 ligands were exhibited a variable activity of inhibition on the growth of the bacteria.

Keywords: macrocyclic schiff bases, open schiff bases spectral technique, antibacterial activity.

I. Introduction

Polyazamacrocycles with large cavities have received recent interests as inorganic cation receptors [Kopolow et al,1973]. The cyclic arrangement of a large number of donor atoms and the flexibility of these ligands make them good hosts for ions [Lindoy et al.,1976]. They were also used as spectrophotometric analytical reagents [Lisowski et al.,1999]. Metal ions have enormous importance in many biological processes, especially heavy metal ions which are effective enzyme inhibitors exerting toxic effects on living system [Esteban et al.,1037]. Therefore, separation and determination of toxic metal ions such as mercury, lead, and cadmium in environmental sources play an important role for healthy life [Vance et al.,1997]. Although new paragraph macrocyclic compounds containing oxygen, sulfur, and nitrogen are knowing. Macrocyclic compounds used in solvent extraction were mostly the oxygen donor type [Ekstrom et al.,1980]. A number of methods for the preparation of the large polyazamacrocyclics have been reported. The most common synthetic procedure requires the use of N-tosyl groups to protect and activate the nitrogen atoms in the cyclization step [Ekstrom et al.,1979]. Ring closure occurs by a condensation reaction of *N*-tosylated polyamines with the appropriate ditosylate ester or dihalide in DMF in the presence of base [Anderegg et al.,1980]. These reactions allow the production of polyazamacrocycles in moderate yields [Adam et al.,1994], but removing the *N*- tosyl groups requires drastic conditions and is not always straightforward. Another cyclization process uses the template ring closure for formation of cyclic di- or tetra dentate Schiff bases. This is a simple process, but it is often difficult to choose the correct template metal ion or to predict certain ring contraction reactions were the template cation dose not coordinate with all of the ring nitrogen atoms [Fenton et al.,1981]. In some cases, reduction of the cyclic Schiff base and removal of the template ion have been difficult [Adam et al.,1981]. A non template method for the formation of macrocyclic poly Schiff bases has also been studied. This procedure often gave a polymeric material beside cyclization reaction, while there is no need to remove a metal ion [Henrick et al.,1984]. In the present work we used a non template method for the formation of four novel macrocyclic Schiff bases: (III), (IV), (V) and (V) then were used for removed of various metal ions from the aqueous phase into the organic phase in liquid – liquid extraction system.

II. Experimental

a) Materials and Method

Chloroform, dichloromethane, dimethylformamide, acetonitrile, methanol, K_2CO_3, were analytical grade reagents and were purchased from Merck. 4,4'-Diaminodiphenylmethane,4-Aminophenyl sulfone, benzylhydrazide, salicylaldehyde, 1,6- dibromohexane, α,α'-Dichlor-p-xylene were obtained from sigma- Aldrich. IR spectra were recorded on Jusco 300 FT-IR Spectrometer using KBr discs. Mass spectra of the ligands were carried out using a micro mass QuattroLC-

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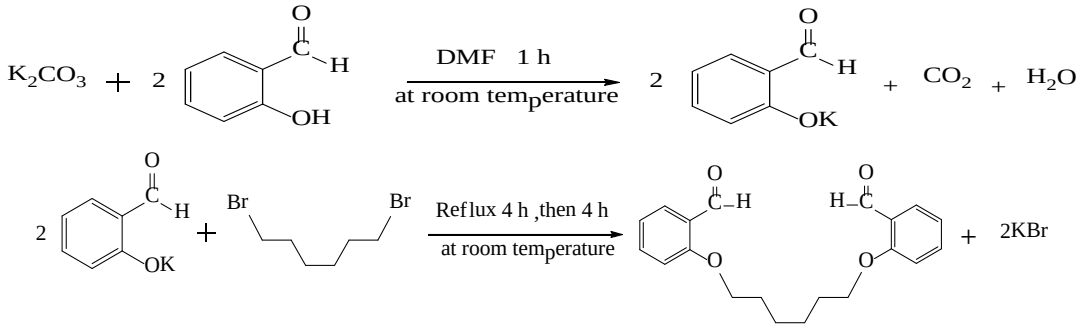
MS/MS Spectrometer. NMR spectra were recorded at ambient BRUKERRAVANCE PX-400 Spectrometer.

i. *Synthesis of 1,6- Bis (2- Formylphenel) Hexane (I)*

To a stirred solution of salicylaldehyde (2.44g, 0.02mol) and K_2CO_3 (1.38g, 0.01mol) in DMF (50ml) 1,6-dibromohexane (2.24 g, 0.01mol) in DMF (10ml) was added dropwise. The reaction was heated for 4h at 150-155 ^{0}C and then stirred at room temperature for 4h [Kenneth et al.,1995]. After the reaction was completed, 100 ml distilled water was added, left in a refrigerator for 1h, the precipitate was filtered, washed by 50 ml water, dried in air and recrystallized from ethanol. (scheme No.1)- (I)

Yield: 80% , colour: White, m.p: 75 0C.

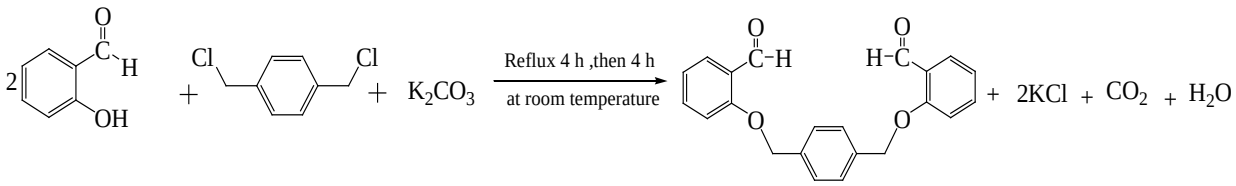


(Scheme No.1)- (I)

ii. *Synthesis of A,A'-Bis(2-Carboxyaldehyde Phenoxy) Xylene (II)*

To a stirred solution of salicylaldehyde (2.44g , 0.02mol) and K_2CO_3(1.38 g, 0.01mol) in DMF (50ml) α,α'-Dichlor-p-xylene (1.39g, 0.01 mol) in DMF(10ml) was added dropwise. The reaction was heated for 4h at 150-155^{0}C and then stirred at room temperature for 4h, after the reaction was completed, 100 ml distilled water was added, left in a refrigerator for 1h, the precipitate was filtered [Lindoy et al.,1976, Kenneth et al.,1995], washed by 50 ml water, dried in air and recrystallized from ethanol.(scheme No.2).

Yield: 85%, colour: White, m.p: 107 0C.



(Scheme No.2)- (II)

iii. *Synthesis of 1,16-Di Aza-3,4,13,14-Tri Phenyl-17,25 -Di Phenyl Methane-5,12-Di Oxacyclo Penta-Icozane-1,15-Diene(III)*

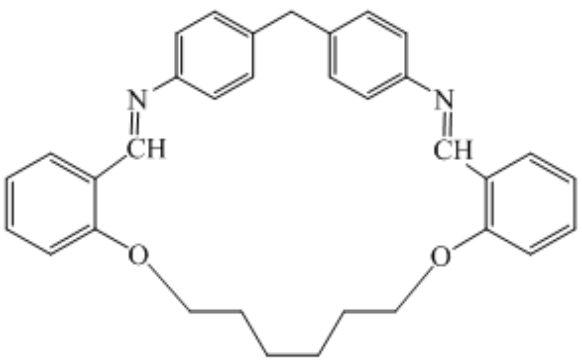
The macrocyclic compound (III) was prepared by dropwise addition of a solution of 4,4'-Diaminodiphenylmethane (0.40g, 0.002 mol) in methanol (40 ml) to a stirred solution of compound (I) (0.652g, 0.002 mol) in methanol (60 ml). The stirring was continued for 12h, a white powder[Salih et al.,2007] was precipitated which was filtered and washed with cold diethyl ether, and recrystallized from mixed (DMF , ethanol9:1). (scheme No.3).

Yield: 80%, colour: Yellow, m.p= 284 ^{0}C. formula: ($C_{33}H_{32}N_2O_2$), M.Wt:(488g).

IR (KBr disk): 3041.8 - 3083.3 cm^{-1} ((C-H), aromatic), 2870.6-2946.7 cm^{-1} (C-H), aliphatic), 1660.4cm^{-1} (C=N), 1573.7-1593.3 cm^{-1} (C=C, aromatic), 1243.5cm^{-1} (C-O).

^{1}H-NMR ($CDCl_3$-400MHz) δ=8.512 (s, 2H, CH=N), 6.954 - 7.766 (m, 16 H, Ar), 4.087-4.119 (s,4H ,O-CH_2-), 2.649 (s,2H, Ph-CH2-Ph), 1.625 – 1.927 (m, 8H,-CH_2-).

Elemental analysis found % C : 81.07 , H: 6.72 , N: 5.69 , O: 6.52 calculated for ($C_{33}H_{32}N_2O_2$) % C: 81.12, H: 6.60 , N: 5.73 ,O:6.55.



(Scheme No.3) (III)

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iv. *Synthesis of 1,16-Di Aza-3,4,7,10,13,14-Tri Phenyl-17,25 -Di Phenyl Methan-5,8-Di Oxacyclo Penta-Icozane-1,15-Diene. (IV).*

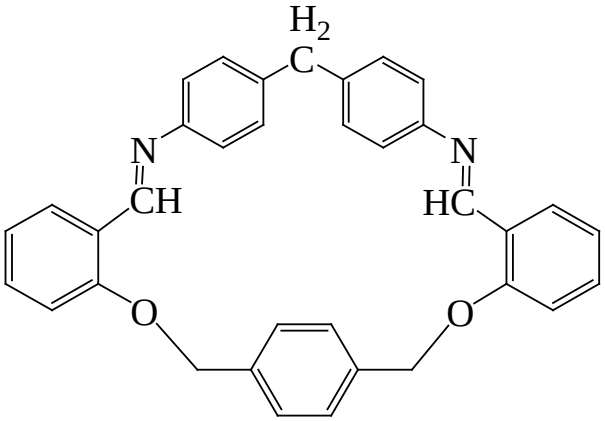
The macrocyclic compound (IV) was prepared by dropwise addition of a solution of 4,4'-Diaminodiphenylmethane (0.40g, 0.002 mol) in methanol (40 ml) to a stirred solution of compound (II) (0.692g, 0.002 mol) in methanol (60 ml). The stirring was continued for 12h, a white powder [Salih et al.,2007] was precipitated which was filtered and washed with cold diethyl ether, and recrystallized from mixed (DMF , ethanol.9:1).(scheme No.4).

Yield: 80%, colour: White, m.p> 300 0C dec. formula: ($C_{35}H_{28}N_2O_2$), M.Wt: (508g).

IR (KBr disk): 3056.6 cm^{-1} ((C-H), aromatic), 2870.7-2946.6 cm^{-1} ((C-H), aliphatic), 1660.8 cm^{-1} (C=N), 1575.2-1595.0 cm^{-1} (C=C, aromatic), 1243.2 cm^{-1} ((C-O).

^{1}H-NMR ($CDCl_3$-400MHz) δ=8.661(s,2H,CH=N), 6.965-8.160 (m,20 H, Ar), 5.073 (s, 4H- O-CH_2-Ph-), 3.994 (s,2H,-Ph-CH_2-Ph).

Elemental analysis found % C: 82.71, H: 5.48, N: 6.42, O: 5.39 calculated for ($C_{35}H_{28}N_2O_2$) % C: 82.65, H: 5.55, N: 5.51, O: 6.29.



(Scheme No.4)- (IV)

v. *Synthesis of 1,16-Di Aza-3,4,13,14-Tri Phenyl-17,25 -Di Phenyl Sulphide-5,12-Di Oxacyclo Penta-Icozane-1,15-Diene(V)*

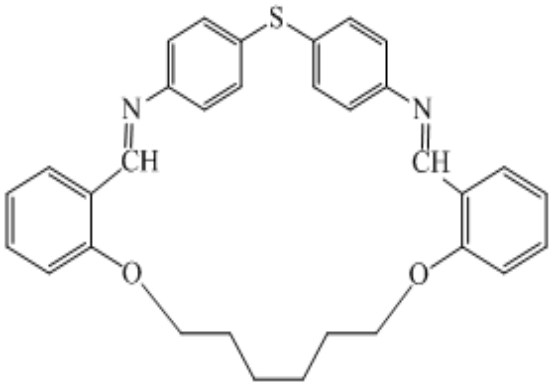
The macrocyclic compound (V) was prepared by dropwise addition of a solution of 4-Aminophenyl sulfone (0.432 g, 0.002 mol) in methanol (40 ml) to a stirred solution of compound (II) (0.692g, 0.002 mol) in methanol (60 ml). The stirring was continued for 12h, a white powder [Salih et al.,2007]was precipitated which was filtered and washed with cold diethyl ether, and recrystallized from mixed (DMF , ethanol. 9:1). (scheme No.5).

Yield: 65 %, colour: Yellow, m.p> 300 0C dec. formula: ($C_{32}H_{30}N_2O_2S$), M.Wt: (508g).

IR (KBr disk): 3047.6 cm^{-1} ((C-H), aromatic), 2864.7-2942.4 cm^{-1} (C-H), aliphatic), 1675.2cm^{-1} (C=N), 1594.2 cm^{-1} (C=C, aromatic), 1245.8cm^{-1} ((C-O).

^{1}H-NMR (CDCl3-400MHz) δ = 8.140 (s,2H,CH=N), 7.117-7.854 (m,16 H, Ar) , 3.729 (s,4H ,O-CH_2-), 1.164 - 1.642 (m, 8H,-CH_2-).

Elemental analysis found % C: 75.98, H: 5.86, N: 5.49, O: 6.44, S: 6.23 calculated for ($C_{32}H_{30}N_2O_2S$) % C: 75.86, H: 5.97, N: 5.53, O:6.32, S: 6.33.



(Scheme No.5)- (V)

vi. *Synthesis of N',N'-(2,2'-(Hexane-1,6-Bis(Oxy))Bis(2,1-Phenylene))Bis(Methanylidene) Dibenzhydrazide.(VI)*

The open Schiff base (VI) was prepared by dropwise addition of a solution of the benzhylhyrazide (2.72 g, 0.02 mol) in DMF (40 mL) to a stirred solution of 1,6-bis(2- formyl phenyl)-hexane (I) (3.26 g, 0.01mol) in DMF (60 mL) containing a few drops of concentrated HCl. The reaction mixture was heated to reflux for 5 hrs, where white precipitate was formed after cooling. On cooling, 200 ml distilled water was added and the mixture was kept in a refrigerator. After 2 hrs, the precipitate [Sultan et al.,2011] was filtered and washed with 200 mL water. The solid obtained was collected and recrystallized from mixture (DMF EtOH9:1) as yellow crystals. A white colored precipitate was washed with water, ethanol, CHCl3 and diethyl ether, respectively. Then dried in air. (scheme No.6).

Yield: 84%, colour: White, m.p= 263 ^{0}C dec. formula:($C_{35}H_{28}N_2O_2$), M.Wt: (562 g).

IR (KBr disk): 3217.27cm^{-1} (N-H), 3035.96 – 3062.96 cm^{-1}((C-H), aromatic, 2870.08 – 2939.52((C-H), aliphatic), 1647.21cm^{-1} (C=O), 1642.0 cm^{-1} (C=N).

^{1}H-NMR ($CDCl_3$-400MHz) δ =11.891 (s,2H, CO-NH-), 8.824 (s,2H,CH=N), 7.007 - 8.479 (m,18H, Ar), 1.065 – 1.820(m,8H,-CH_2-CH_2-CH_2-CH_2-), 2.512 - 3.353 (DMSO,H_2O).

Elemental analysis found % C: 72.81, H: 5.98, N: 10.04, O: 11.17 calculated for ($C_{34}H_{34}N_4O_4$) % C: 72.58; H: 6.09; N: 9.96; O: 11.37.

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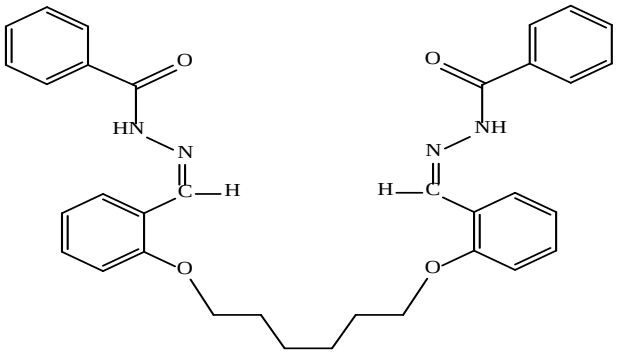

(Scheme No.6) (VI)

b) 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 [Ibrahim et al.,2006]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.[Ibrahim et al.,2006]

III. Result and Discussion

a) Synthesis

The prepared macrocyclic (III, IV, V, VI) were synthesized by the condensation of by condensation of intermediate compounds 1,6- bis (2- formylphenel) hexane (I) and α,α'-bis(2-carboxyaldehyde phenoxy) xylene (II) with both 4,4'-Diaminodiphenylmethane and 4-Aminophenyl sulfonein the molar ratio 1:1 in absolute methanol. Also new open Schiff bases (VI) which was prepared by condensation of benzylhydrazide with 1,6-bis (2- formylphenel) hexane in the molar ratio 2:1 in DMF. The reactions proceeded smoothly, producing the corresponding Schiff bases ligands in good yield. The ligands are soluble in common organic solvent but insoluble in water. The structures of the ligands were elucidated by elemental analyses, MS, FTIR, electronic absorption, and ^{1}H- NMR spectra, which help in elucidating their empirical formula Table 1.

Table 1 : Physical and chemical properties of the synthesized compounds[III]-[VI]

Schiff base	Color	M.Wt	Melting point ^{0}C	Yield %	Crystallization Solvent
III	White	448	248	80	DMF, EtOH (9:1)
IV	White	508	> 300	85	DMF, EtOH (9:1)
V	Yellow	506	> 300	65	DMF, EtOH (9:1)
VI	White	562	263 – 264	84	DMF, EtOH (9:1)

b) Elemental analyses of macrocyclic and open (III, IV, V, VI)

The results of elemental analyses macrocyclic and open (III, IV, V, VI), as shown in Table 2, are in good agreement with those required by the proposed formulae.

Table 2 : Elemental analysis data of the synthesized compounds[III]-[VI]

Schiff base	Elemental analysis Calculated (Found %)				
	C	H	N	S	O
III	81.07 (81.12)	6.72 (6.60)	5.69 (5.73)	--------	6.52 (6.55)
IV	82.71 (82.65)	5.48 (5.55)	6.42 (6.51)	--------	5.39 (5.29)
V	75.98 (75.86)	5.86 (5.97)	5.49 (5.53)	6.23 (6.33)	6.44 (6.32)
VI	72.81 (72.58)	5.98 (6.09)	10.04 (9.96)	--------	11.17 (11.37)

c) IR spectra analysis of macrocyclic Schiff bases (III, IV, V, VI)

i. *Compound (III)*

A strong band at 1660.4cm^{-1} in the IR spectrum of the macrocyclic Schiff base (Figure (1)) are assigned to υ(C=N) of azomethine vibrations. The band in the spectra at 1593.3 - 1573.7cm^{-1} is due to (C=C) of aromatic rings. The band in the spectra at 1243.5 cm^{-1} is due to (C-O). while the band at 2946.7 - 2870.6cm^{-1} is attributed to (C-H aliph). Also, the band at 3083.3 - 3041.8cm^{-1} is attributed to (C-H ar). [Salih et al.,2007, Sultan et al.,2011].

ii. *Compound (IV)*

A strong band at 1660.8 cm^{-1} in the IR spectrum of the macrocyclic Schiff base (Figure (2)) are assigned to υ(C=N) of azomethine vibrations. The band in the

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spectra at 1595.0 - 1575.2 cm^{-1} is due to (C=C) of aromatic rings. The band in the spectra at 1243.2 cm^{-1} is due to (C-O). while the band at 2946.6 - 2870.7 cm^{-1} is attributed to (C-H aliph). Also, the band at 3056.6 cm^{-1} is attributed to (C-H ar). [Salih et al.,2007, Sultan et al.,2011].

iii. *Compound (V)*

A strong band at 1675.2 cm^{-1} in the IR spectrum of the macrocyclic Schiff base (Figure (3)) are assigned to υ(C=N) of azomethine vibrations. The band in the spectra at 1594.2 cm^{-1} is due to (C=C) of aromatic rings. The band in the spectra at 1245.8 cm^{-1} is due to (C-O). while the band at 2942.4 - 2864.7 cm^{-1} is attributed to (C-H aliph). Also, the band at 3047.6 cm^{-1} is attributed to (C-H ar). [Salih et al.,2007, Sultan et al.,2011].

iv. *Compound (VI)*

A strong band at 1600.92 and 1647.21cm^{-1} in the IR spectrum of the Schiff base (Figure (4)) are assigned to υ(C=N) of azomethine and carbonyl υ(C=O) vibrations, respectively. An intense band at 3217.27 cm^{-1} is due to the -NH- vibrations of the hydrazine group. The band in the spectra at 1554.83 cm-1 is due to (C=C) of aromatic rings. The band in the spectra at 1249.86 cm^{-1} is due to (C-O). While the band at 2870.08 – 2939.52 cm-1 is attributed to (C-H aliph). Also, the band at 3035.96 – 3062.96 cm^{-1} is attributed to (C-H ar). [Salih et al.,2007, Sultan et al.,2011].

However, in the IR spectra of Schiff bases this band (C=O) disappears and a new vibration band for azo methane (-HC=N-), indicating that complete condensation takes place. [17-18].

Table 3 : IR spectral data of the synthesized compounds[III]-[VI]

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)
III	1243.5	1593.3 - 1573.7	1660.4	---------	2946.7 - 2870.6	3083.3 - 3041.8	---------
IV	1243.2	1595.0 - 1575.2	1660.8	---------	2946.6 - 2870.7	3056.6	---------
V	1245.8	1594.2	1675.2		2942.4 - 2864.7	3047.6	
VI	1249.86	1554.83	1600.92	1647.21	2870.08 – 2939.52	3035.96 – 3062.96	3217.27

d) ^{1}-H-NMR Spectra of macrocyclic Schiff bases (III, IV, V, VI).

i. *Compound (III)*

The ^{1}H NMR spectrum (Figure (5)) of the Schiff base (III), showed that in the signals at 8.512 ppm were assigned to the protons of imine -CH=N groups, The multiple signals in the region 1.927 - 1.625 ppm were assigned to protons of methylene groups in two different environments [Salih et al.,2007, Sultan et al.,2011]. The multiple signals in the region 7.766 - 6.954 ppm were assigned to the aromatic protons. While The signals at 4.119 - 4.087 ppm were assigned to the protons of (-O-CH_2-) group.

ii. *Compound (IV)*

The ^{1}H NMR spectrum (Figure (6)) of the Schiff base (IV), showed that in the signals at 8.661 ppm were assigned to the protons of imine -CH=N groups [Salih et al.,2007, Sultan et al.,2011].The multiple signals in the region 8.160 - 6.965 ppm were assigned to the aromatic protons. While the signals at 5.073 ppm were assigned to the protons of (-O-CH_2-) group.

iii. *Compound (V)*

The ^{1}H NMR spectrum (Figure (7)) of the Schiff base (V), showed that in the signals at 8.140 ppm were assigned to the protons of imine -CH=N groups, The multiple signals in the region 1.642 - 1.164 ppm were assigned to protons of methylene groups in two different environments [Salih et al.,2007, Sultan et al.,2011].The multiple signals in the region 7.854 - 7.117 ppm were assigned to the aromatic protons. While the signals at 3.729 ppm were assigned to the protons of (-O-CH2-) group. Also the signal at 11.891 ppm were assigned to the protons of amide (-CO-NH-) groups.

iv. *Compound (VI)*

The ^{1}H NMR spectrum (Figure (8)) of the Schiff base (VI), showed that in the signals at 8.824 ppm were assigned to the protons of imine -CH=N groups, The multiple signals in the region 1.065 – 1.820 ppm were assigned to protons of methylene groups in two different environments [Salih et al.,2007, Sultan et al.,2011].The multiple signals in the region 8.479 - 7.007 ppm were assigned to the aromatic protons. While the signals at 4.087 ppm were assigned to the protons of (-O-CH_2-) group. Also the signal at 11.891 ppm were assigned to the protons of amide (-CO-NH-) groups.

The other obtained values for ^{1}-H-NMR chemical shifts of the compounds are given in the experimental section. [Pathak et al.,2000, Rajaa.,2008].

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Table 4 : ^{1}H-NMR Spectra of the synthesized compounds[III]-[VI]

Schiff base	Chemical Shifts δ ppm				
	C-H aromatic	CH=N	-CO-NH-	-O-CH_2-	(-CH_2-CH_2-)$_n$
III	7.766 - 6.954 (m,16 H)	8.512 (s,2H)	----------	4.119 - 4.087 (s,4H)	1.927 - 1.625 (m,8H)
IV	8.160 - 6.965 (m,20 H)	8.661 (s,2H)	----------	5.073	----------
V	7.854 - 7.117 (m,16 H)	8.140 (s,2H)	11.891 (s,2H)	3.729 (m,8H)	1.642 - 1.164 (m,8H)
VI	8.479 - 7.007 (m,18H)	8.824 (s,2H)	11.891 (s,2H)	4.087 (s,2H)	1.065 – 1.820 (m,8H)

e) Biological Activity

During the last two or three decades, attention has been increasingly paid to the synthesis of macrocyclic and open (III, IV, V, VI) which exhibits various biological activities including antibacterial, fungicidal, tuberculostatic and plant growth regulative properties [19]. 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).

Table 5 : Antibacterial activity of the synthesized compounds[III]-[VI]

Shiff base	Bacteria			
	Gram negative		Gram positive	
	B. subtilis	S. aureus	E.coli	S. typhi
III	17 mm	18 mm	15 mm	18 mm
IV	18 mm	16 mm	16 mm	19 mm
V	20 mm	18 mm	17 mm	18 mm
VI	20 mm	18 mm	17 mm	18 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.

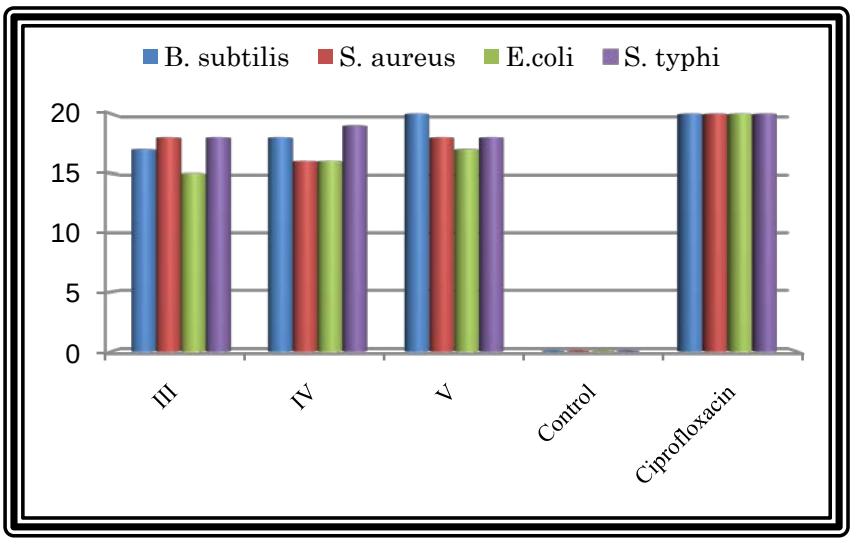

Figure 9 : Antibacterial activity of synthesized compounds[III]-[VI].

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IV. Conclusion

1. The compounds are new and were prepared for the first time.
2. The new compounds were identified by melting point, elemental analyses 1HNMR, IR, LC-MS, spectral methods.
3. The prepared compounds have 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.

V. Acknowledgment

The authors are grateful to the Department of Chemistry, Faculty of Science, University of Damascus, Damascus, Syria.

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Figures

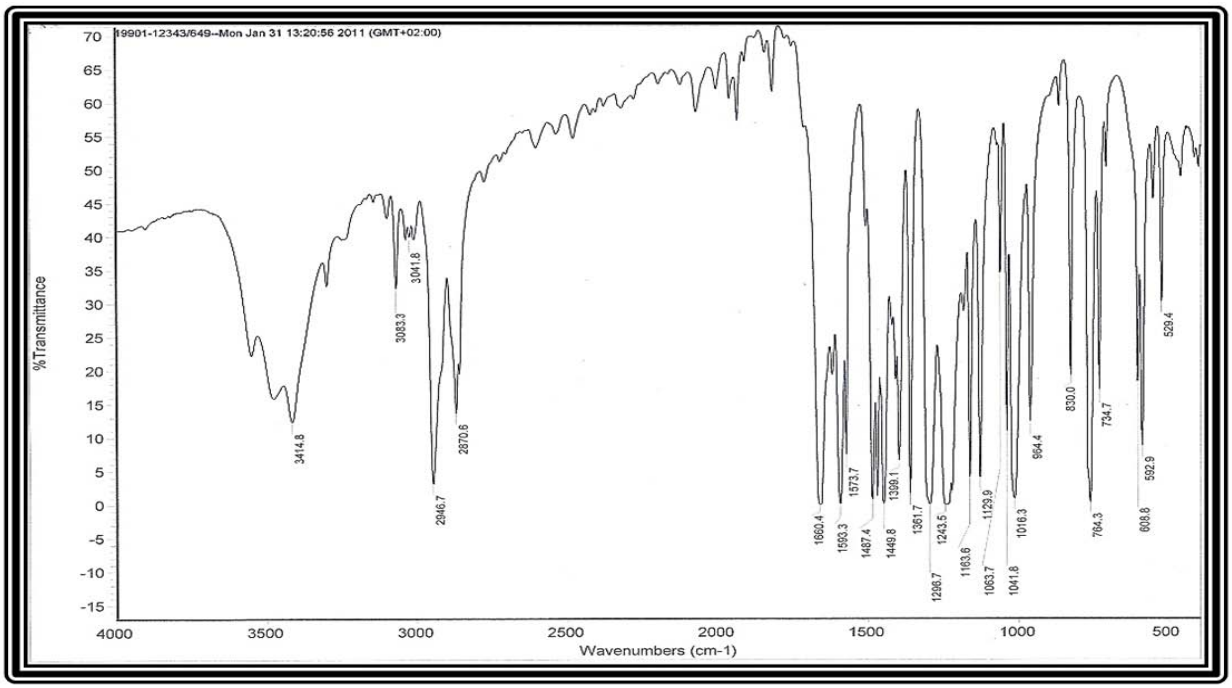

Figure 1 : IR spectrum of Macrocyclic Schiff base(III).

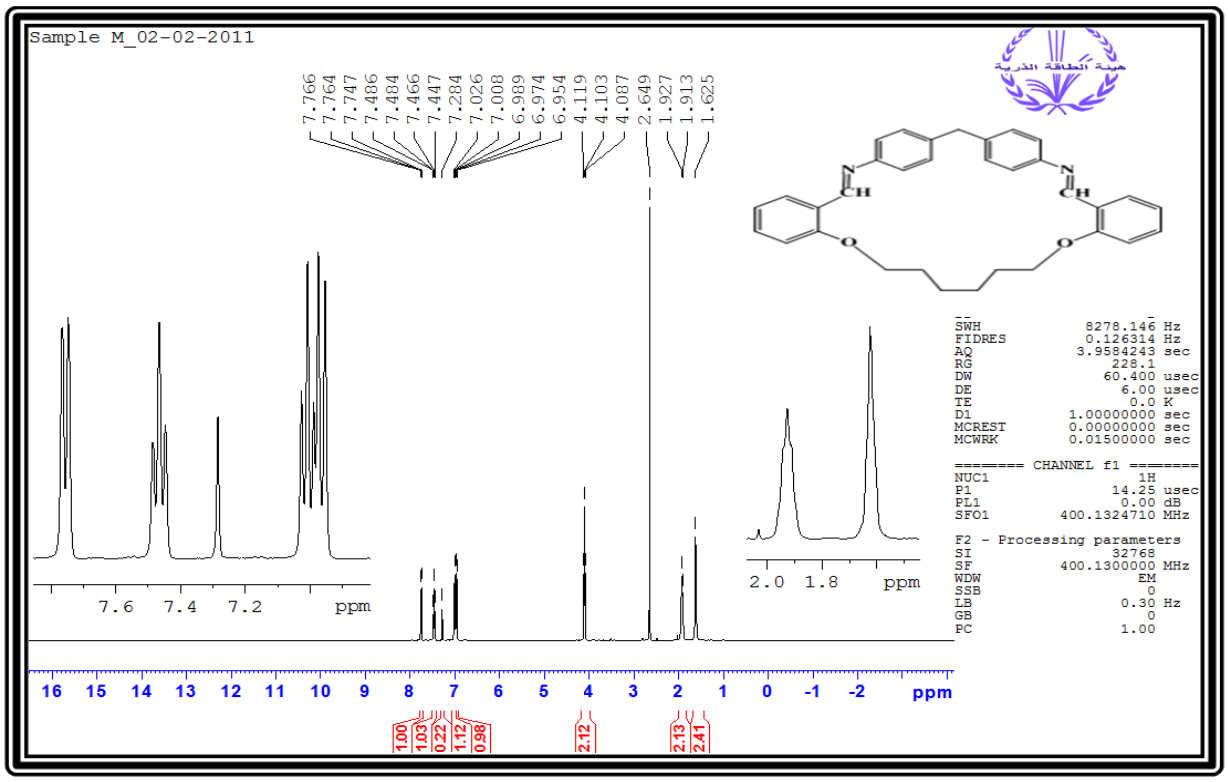

Figure 5 : ^{1}HNMR spectrum of Macrocyclic Schiff base(III)

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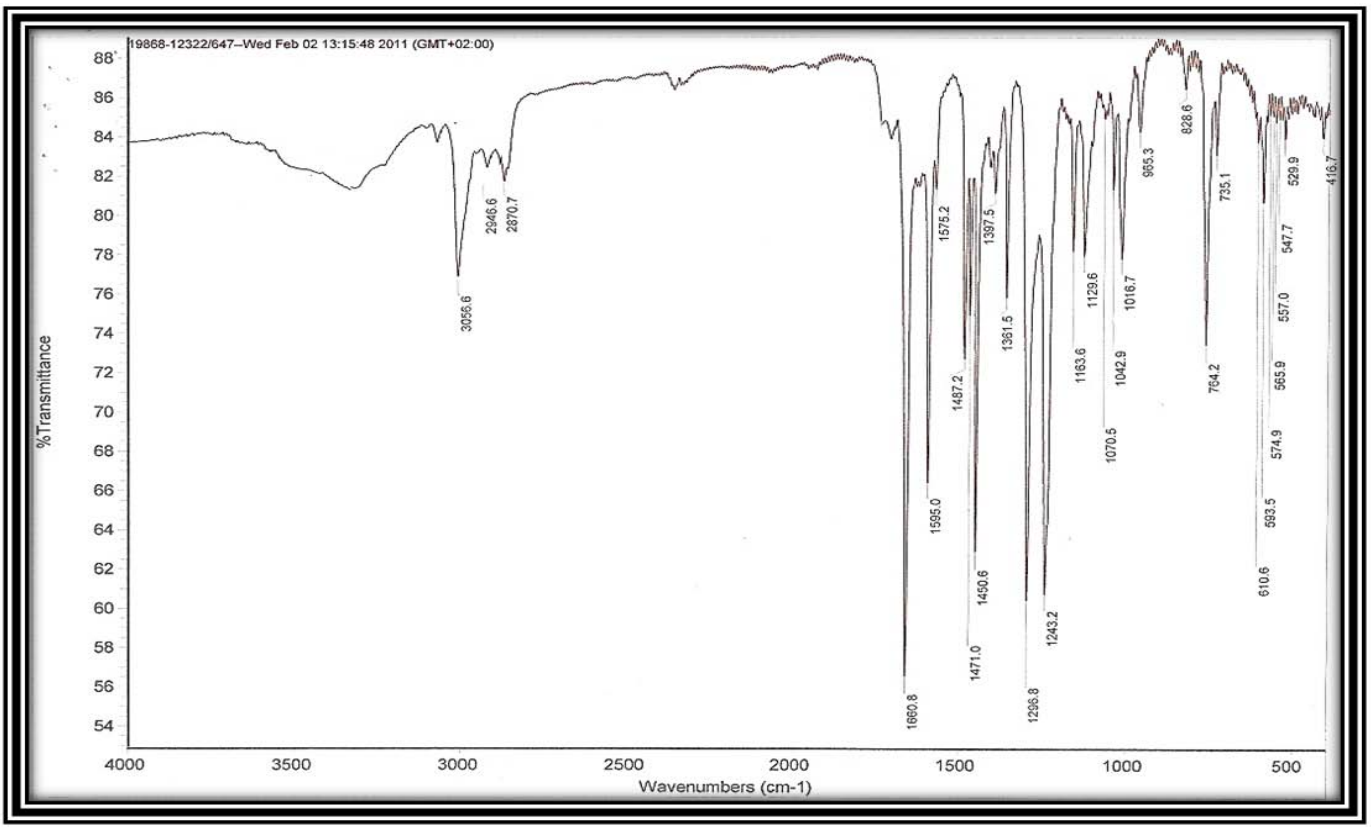

Figure 2 : IR of Macrocyclic Schiff base(IV)

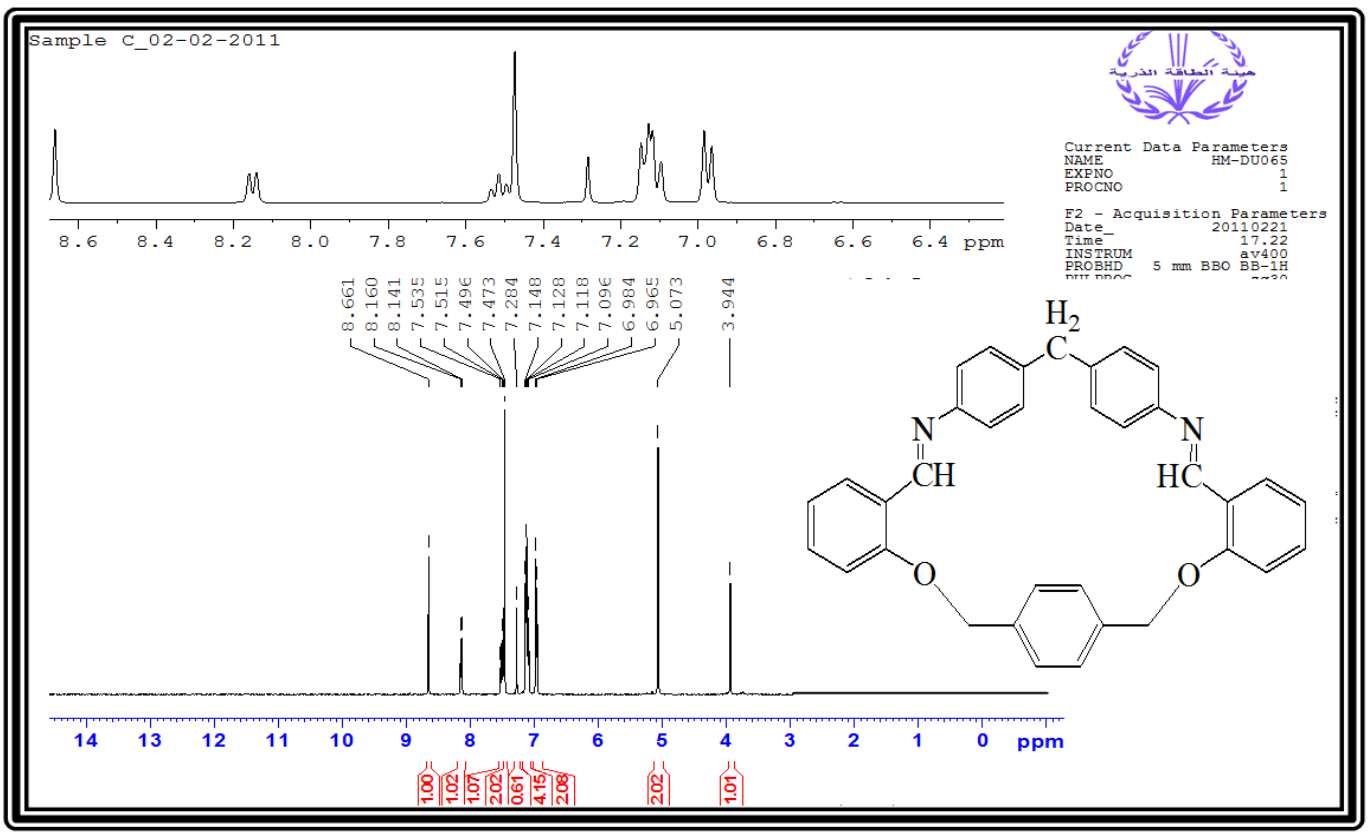

Figure 6 : [1-]HNMR spectrum of Macrocyclic- Schiff base(IV).

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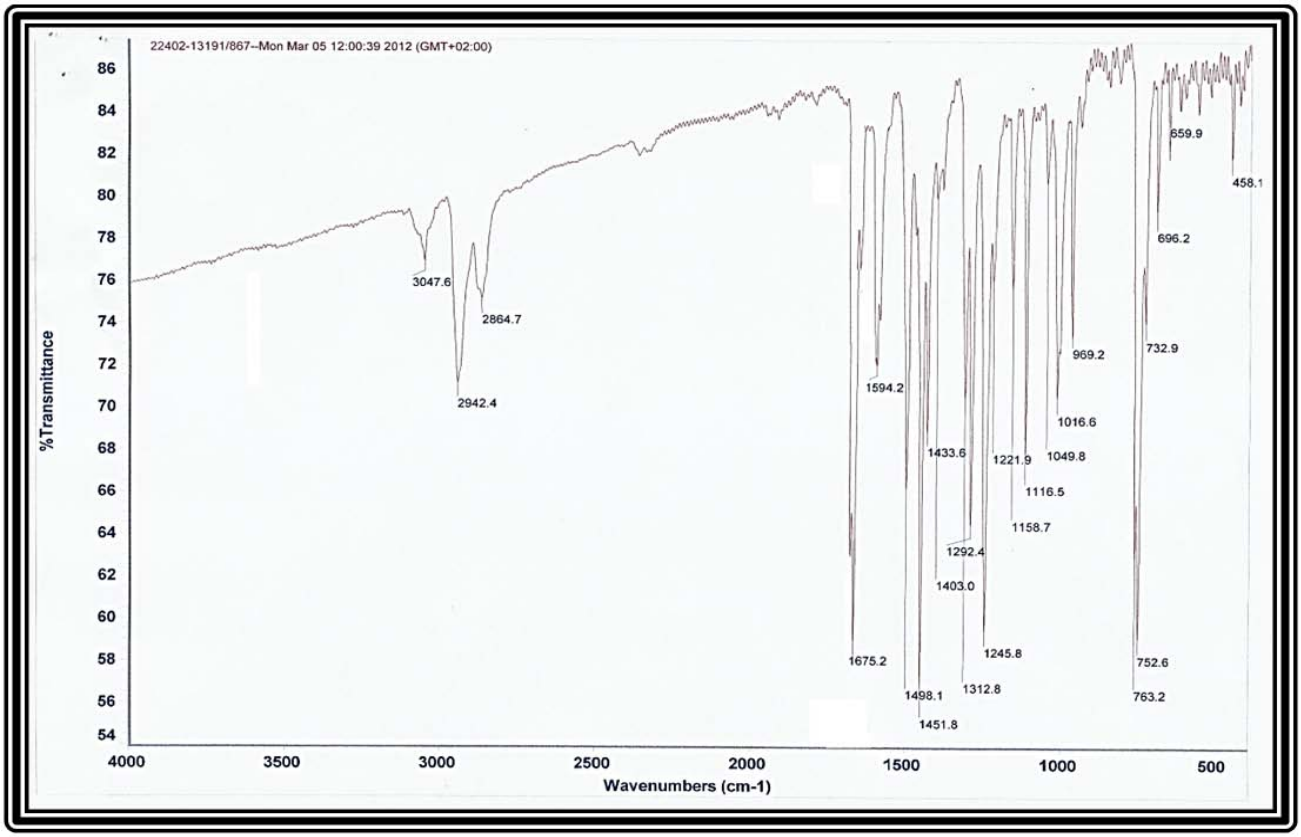

Figure 3 : IR of Macrocyclic Schiff base(IV)

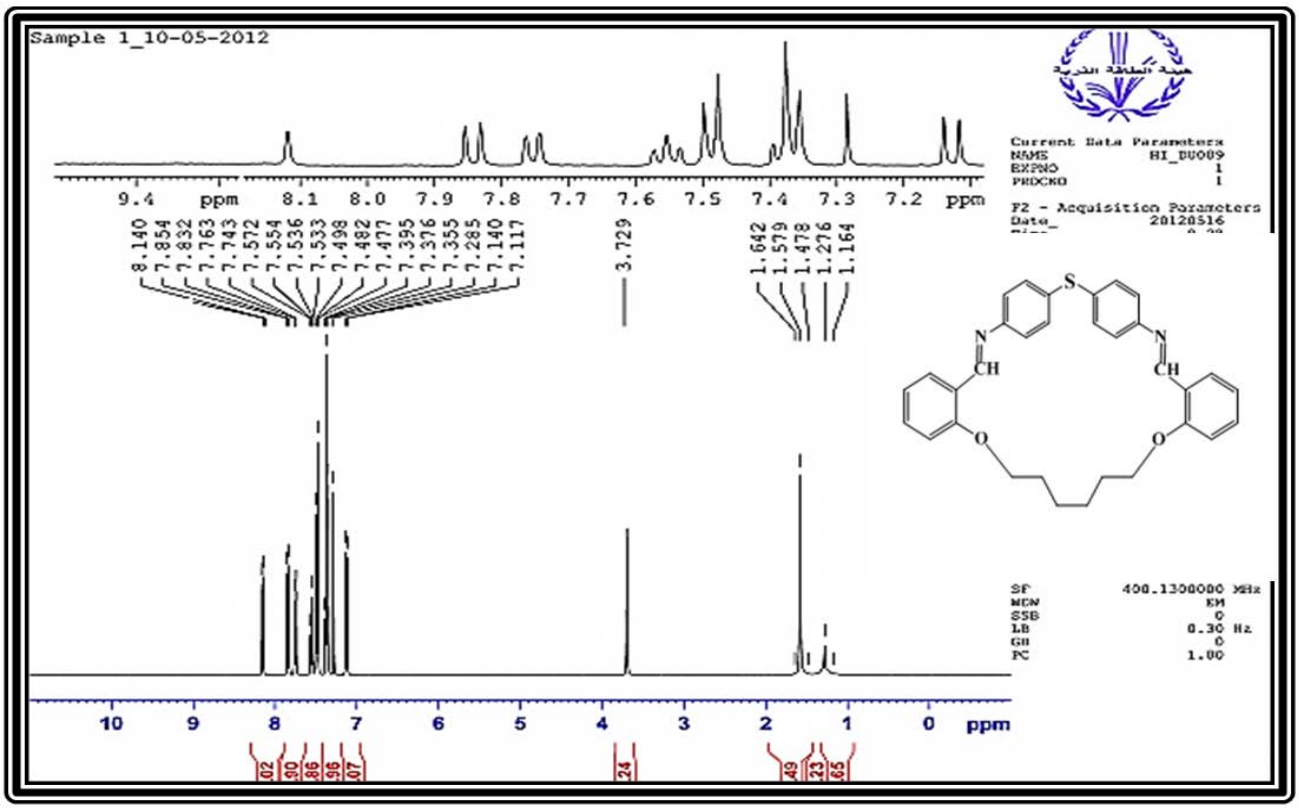

Figure 7 : [1-]HNMR spectrum of Macrocyclic- Schiff base(IV).

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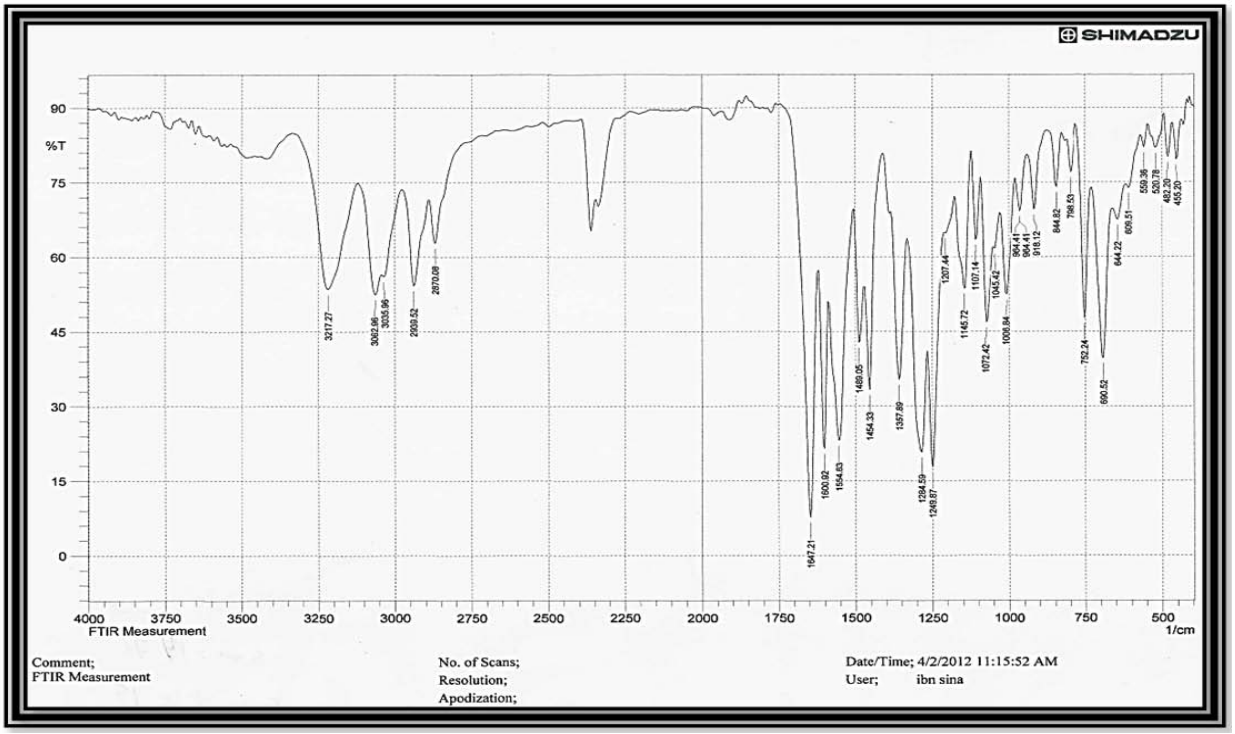

Figure 4 : IR spectrum of Schiff base(V).

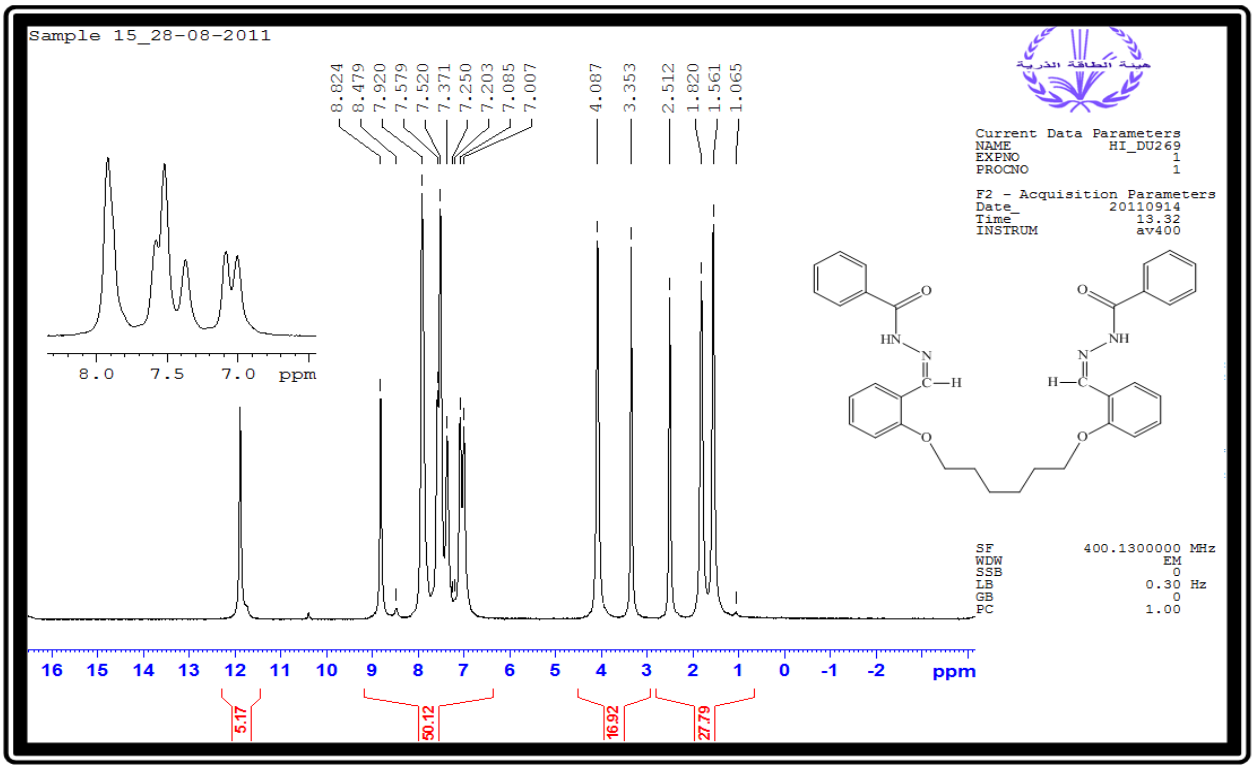

Figure 8 : [1]-HNMR spectrum of Schiff base(V).

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