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Synthesis of Novel Macrocyclic From Schiff Bases Based on acetylacetone and terephtaldialdehide

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ABSTRACT

A macrocyclic hydrazone Schiff base was synthesized by reaction of succinicdihydrazide, Adipicdihydrazide with acetylacetone, adipicdihydrazide with terephtaldialdehide and sebacicdihydrazide with terephtaldialdehide. The Schiff base have been characterized by IR , ^{1}H- NMR, Mass spectra.

Key words: Hydrazones, Schiff base, Macrocycles, Hiydrazides.

تحضير مركبات حلقية ضخمة جديدة من أسس شيف أساسها أسيتيل اسيتون وتير فتال ثنائي ألدهيد

وائل الزعبي و فاروق قنديل و محمد خالد الشيباني

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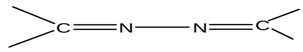
الملخص

صنعت الحلقات الضخمة لهيدرازونات أسس شيف بتفاعل سوكسنيل ثنائي هيدرازيد مع اسيتيل اسيتون وأديبيك ثنائي هيدرازيد مع الاسيتيل أسيتيون وتيرفتال ثنائي ألدهيد وسوبريك ثنائي هيدرازيد مع تير فتال ثنائي ألدهيد. وصفت أسس شيف المحضرة بـ MS و^{1}H-NMR و IR.

الكلمات المفتاحية: هدرازونات، أسس شيف، حلقات الضخمة،ثنائي الهيدرازيدات.

Introduction

Hydrazones are special group of compounds in Schiff base family. They are characterized by the presence of  .

The presence of two inter-linked nitrogen atoms was separated from imines, oximes, etc. Hydrazone Schiff bases of acyl, aroyl and heteroaroyl compounds have an addition donor sites. The additional donor sites make them more flexible and versatile. This versatility has made hydrazones good polydentate chelating agent that can form a variety of complexes with various transition and inner transition metals and have attracted the attention of many researchers. [1]

Bis-hydrazones derived from carbonyl compounds have long attracted researchers' attention due to their practical importance, primarily pronounced biological activity and strong complexing power. There are vast published data on bis-hydrazones derived from α-, β-, and γ-dicarbonyl compounds and their metal complexes. [2,3]In particular, antibacterial[14], antimicrobial, [5,6] anticancer,[7] and fungicidal activity [8] of these compounds was reported.

In analytical chemistry hydrazones found application by acting as multidentate ligands [9,10] with metals (usually from the transition group).

Various studies have also shown that the azomethine group having a lone pair of electrons in either π or sp^2 hybridized orbital on trigonally hybridized nitrogen has considerable biological importance[11].

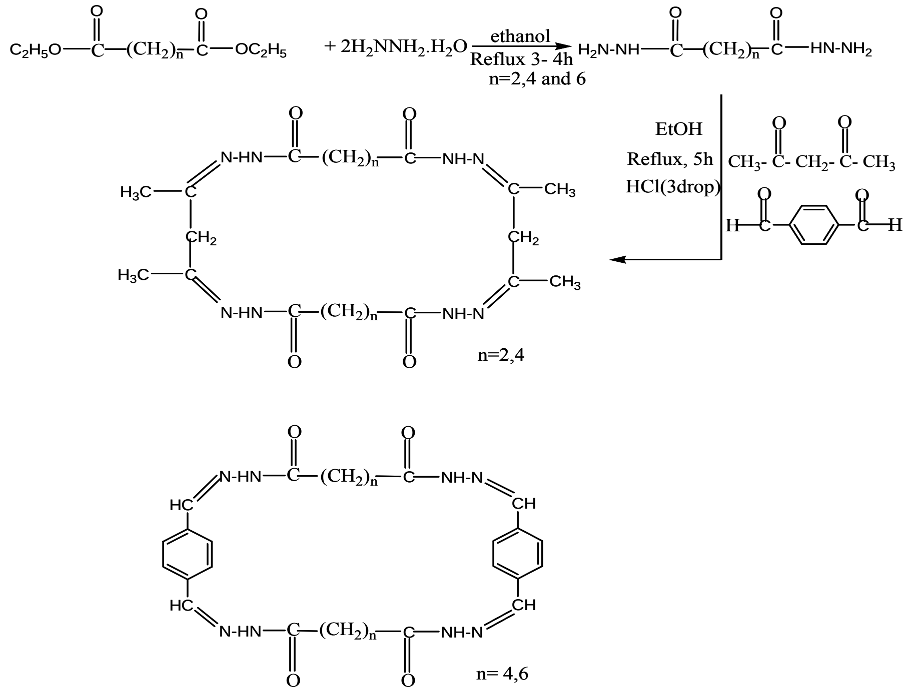
Five disymmetric tridentate Schiff base ligands containing a mixed donor set of ONN and ONO were prepared by the reaction of benzhydrazide with the appropriate salicylaldehyde and pyridine-2-carbaldehyde and characterized by FT-IR, ^{1}H and ^{13}C NMR. [12]

The synthesis and spectroscopic characterization of complexes of Ni(II), Cu(II), Zn(II), and Cd(II) containing hydrazones derived from 6-amino-5-formyl-1,3-dimethyluracil and nicotinic and isoicotinic acid hydrazides are reported. [13]

A macrocyclic hydrazone Schiff base was synthesized by reacting 1.4-dicarbonyl phenyl dihydrazide with 2,6-diformyl-4-methyl phenol and series of metal complexes with this new Schiff base were synthesized by reaction with Co(II), Ni(II) and Cu(II) metal salts. [1]

The Schiff base and its complexes have been characterized by element analyses, IR, ^{1}H-NMR, UV-vis, FAB mass, ESR spectra, fluorescence, thermal, magntic and molar conductance data.[14]

In view of the above application, in this present paper, we report the synthesis and characterization of macrocyclic ligands.



Experimental section

All chemicals and solvents used were of analar grade, and procured from Sigma–Aldrich, Fluka and Merck.

The IR spectra were recorded in KBr disks by FT-IR-600 spectrophotometer.^{1}H and spectra of ligands in $CDCl_3$ solution were recorded on a Bruker 400MHz spectrometer and chemical shifts are indicated in ppm relative to TMS. Mass spectra were recorded using a KRATOS MS50TC spectrometer.

Preparation of compounds

Synthesis of diester compounds

Synthesis of diethyl Succinate

Succinic acid(1.6 g) in absolute dry ethanol (60 mL) containing 2-3 drops of concentrated H_2SO_4 was refluxed till it dissolved. Then, the reaction mixture was poured onto ice cold water. To the last reaction mixture, sodium bicarbonate was added till the effervescence stopped. The ester thus obtained was extracted by diethyl ether.[1]

Synthesis of diethyl Adipate

Adipic acid (1.6 g) in super dry ethanol (60 mL) containing 2-3 drops of concentrated H2SO4(AR) was refluxed till it dissolved. Then, the reaction mixture was poured onto ice cold water. To the last reaction mixture, sodium bicarbonate was added till the effervescence stopped. The ester thus obtained was extraction by diethyl ether. [1]

Synthesis of diethyl Suberate

Suberic acid (1.6 g) in super dry ethanol (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. To the last reaction mixture, sodium bicarbonate was added till the effervescence stopped. The ester thus obtained was extraction by diethyl ether.[1]

Synthesis of dihydrazide compounds

Synthesis of dihydrazide of Succinic acid.

A mixture of diethyl ester of succinic acid (2.22 g) and hydrazine hydrate (98%2cc) in ethanol was refluxed for 4-5 h. The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. The dihydrazide of Succinic acid thus obtained was filtered and recrystallized from ethanol. [1,14]

Synthesis of dihydrazide of Adipic acid.

A mixture of diethyl ester of adipic acid (2.22 g) and hydrazine hydrate (98%2cc) in ethanol was refluxed for 4-5 h. The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. The dihydrazide of adipic acid thus obtained was filtered and recrystallized from ethanol. [1,14]

Synthesis of dihydrazide of Suberic acid.

A mixture of diethyl ester of suberic acid (2.22 g) and hydrazine hydrate (98%2cc) in ethanol was refluxed for 4-5 h. The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. The dihydrazide of suberic acid thus obtained was filtered and recrystallized from ethanol. [1,14]

Preparation of macrocyclic Schiff bases

Synthesis of macrocyclic Succinic acid hydrazone Schiff base (I)

The hot ethanolic solution (20 ml), of acetylacetone (2 mmole, 0.2 gr), and a hot ethnolic solution (20 ml), of dihydrazide of succinic acid (2 mmole, 0.292 gr) were mixed slowly with constant stirring. This mixture was refluxed at ~ 75° for 9h in the presence of concentrated hydrochloric acid (pH~3). The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. On cooling cream colored precipitate is separated out, filtered, washed with cold EtOH, and dried under vacuum over P_2O_5. Yield %50, mp >280ºC.

Synthesis of macrocyclic adipic acid hydrazone Schiff base (II).

The hot ethanolic solution (20 ml), of acetylacetone (2 mmole, 0.2 gr), and a hot ethanolic solution (20ml), of dihydrazide of a dipic acid (2 mmole, 0.348 gr) were mixed slowly with constant stirring. This mixture was refluxed at ~75º for 9 h in the presence of concentrated hydrochloric acid (pH~3). The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. On cooling cream colored precipitate is separated out, filtered, washed with cold EtOH, and dried under vacuum. Yield %55, mp > 280ºC.

Synthesis of macrocyclic adipic acid hydrazone Schiff base (III).

Terephtaldialdehide (2 mmole, 0.268 gr) in ehanol (20 ml) was added to an ethanolic solution of dihydrazide of adipic acid (2 mmole, 0.384 gr) containing a few drops of concentrated HCl. The reaction mixture was refluxed for 3 h. The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. On cooling cream colored precipitate is separated out, filtered, washed with cold EtOH and diethyl ether, and dried under vacuum. Yield %60, mp >290ºC.

Synthesis of macrocyclic Suberic acid hydrazone Schiff base (VI).

Terephtaldialdehide (2 mmole, 0.268 gr) in ehanol (20 ml) was added to an ethanolic solution of dihydrazide of Suberic acid (2 mmole, 0.404 gr) containing a few drops of concentrated HCl. The reaction mixture was refluxed for 3h. The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. On cooling cream colored precipitate is separated out, filtered, washed with cold EtOH and diethyl ether, and dried under vacuum. Yield %63, mp >290ºC. [1]

Results and discussion

All compounds are colored non-hygroscopic Solids, stable in air. They are sparingly soluble in organic solvents.

IR spectra

The IR spectra provide valuable information regarding the nature of functional groups of the Schiff bases.

Compound (I)

The IR spectrum of the Schiff base has been depicted in Fig 1. The spectrum showed a strong band at 1715 and 1587cm^{-1} in the spectrum of the Schiff base which are assigned to carbonyl υ (C=O) and υ(C=N) of azomethine vibrations, respectively. An intense band at 3111 cm^{-1} is due to the –NH- vibrations of the hydrazine group, a broad medium intense band was at 2930 cm^{-1} due to methylene groups. [15,16,17]

Compound (II)

The IR spectrum of the Schiff base has been depicted in Fig 4. The spectrum showed a strong band at 1717 and 1581 cm^{-1} in the spectrum of the Schiff base which are assigned to carbonyl υ (C=O) and υ(C=N) of azomethine vibrations, respectively.

Two a broad medium intense bands were at 2959 and 2873 cm^{-1} due to methyl groups and a band at 1183 cm^{-1} which is assigned to hydrazinic υ (N-N) of the Schiff base. [15,16,17]

Compound (III)

Two strong bands at 1668 and 1546 cm^{-1} in the spectrum of the Schiff base which are assigned to carbonyl υ (C=O) and υ (C=N) of azomethine vibrations, respectively. An intense band at 3208 cm^{-1} is due to the –NH- vibrations of the hydrazine group, a broad medium intense bands were at 2921 and 2851 cm^{-1} due to methyl groups and a band at 1181cm^{-1} is assigned to hydrazinic υ (N-N) of the Schiff base. [15,16,17]

Compound (VI)

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^{1}H NMR spectra

Compound (I)

The ^{1}H NMR spectrum of the Schiff base has been depicted in Fig. 3. The spectrum showed signals at δ 5.9 due to NH(4H) protons. It shows δ 2.24 corresponding to CH_3-C(12H), δ 2.54 attributable to –CH_2(4H), δ 3.55 corresponding to –CH_2–CO-(8H). [15,16,17]

Compound (II)

The ^{1}H NMR spectrum of the Schiff base has been depicted in Fig 6. The spectrum showed signals at δ 5.9 due to -NH(4H) protons. It shows δ 2.24 corresponding to CH3-C(12H), δ 3.17 attributable to -CO–CH2(4H), δ 1.8 corresponding to –CO–CH2–CH2(4H) and δ 2.54 corresponding to(-C=N–CH2–C=N-) (4H). [15,16,17]

Compound (III)

The Schiff base exhibits signals at δ 2.12 ppm due to NH protons.The other characteristic resonance due to azomethine proton in the Schiff base appears at δ 2.98-2.90. Signals in the region δ 6.5-8.0 due to aromatic protons. A signal in the region δ 1.6-0.85 is assigned to methyl protons. [15,16,17]

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Mass spectrum

Compound (I)

The electron impact spectrum of the ligand (I) confirms the probable formula by showing a peak (Fig 2) at 420 amu, corresponding to macrocyclic moiety [($C_{18}H_{28}N_8O_4$), calculated atomic mass 420]. The series of peaks in the range i.e. 40, 42, 44, 55, 56, 66, 67, 69, 81, 82, 96, 97, 122, 132, 150, 179, 322 and 420 amu, may be assigned to various fragments. Their intensity gives an idea of stability of fragments. [15,16,17]

Compound (II)

The electron impact spectrum of the ligand (II) confirms the probable formula by showing a peak (Fig 5) at 476 amu, corresponding to macrocyclic moiety [($C_{22}H_{36}N_8O_4$), calculated atomic mass 476]. The series of peaks in the range i.e 40, 41, 42, 43, 44, 54, 55, 56, 81, 83, 95, 96, 97, 111, 121, 129, 138, 150, 165, 179, 201, 206, 252, 302, 322 and 600 amu etc, may be assigned to various fragments. Their intensity gives an idea of stability of fragments. [15,16,17]

Compound (III)

The electron impact spectrum of the ligand (III) confirms the probable formula by showing a peak (Fig 7) at 545 amu, corresponding to macrocyclic moiety [(C28H32N8O4), calculated atomic mass 544]. The series of peaks in the range i.e 40, 41, 42, 43, 44, 51, 54, 55, 59, 60, 63, 65, 75, 77, 91, 97, 105, 112, 117, 141, 180 and 545 amu etc, may be assigned to various fragments. Their intensity gives an idea of stability of fragments. [15,16,17]

Compound (VI)

The electron impact spectrum of the ligand (V) confirms the probable formula by showing a peak (Fig 8) at 600 amu, corresponding to macrocyclic moiety [(C32H40N8O4), calculated atomic mass 600]. The series of peaks in the rang i.e 40, 44, 45, 51, 52, 97, 98, 99, 102, 118, 119, 134, 141, 148, 152, 158, 176, 180, 202, 286, 316, 318, 344, 378, 392, 552, 596 and 600 amu etc, may be assigned to various fragments. Their intensity gives an idea of stability of fragments. [15,16,17]

Conclusion

The new synthesized compounds act as hexadentate Schiff bases. In most cases these unsymmetrical compounds were obtained with yield more than %50 in some cases.

Four imines (Schiff bases) were synthesized. We think that these compounds prepared for the first time. This is confirmed by a precise review of the scientific background concerning this category of compounds. Their structures were identified by spectroscopic methods.

Prepared Schiff bases could by used later to extract cations of the transition elements from their aqueous phases to another organic phases, which they are not dissolved in and also to study their biological activities as antibiotics.

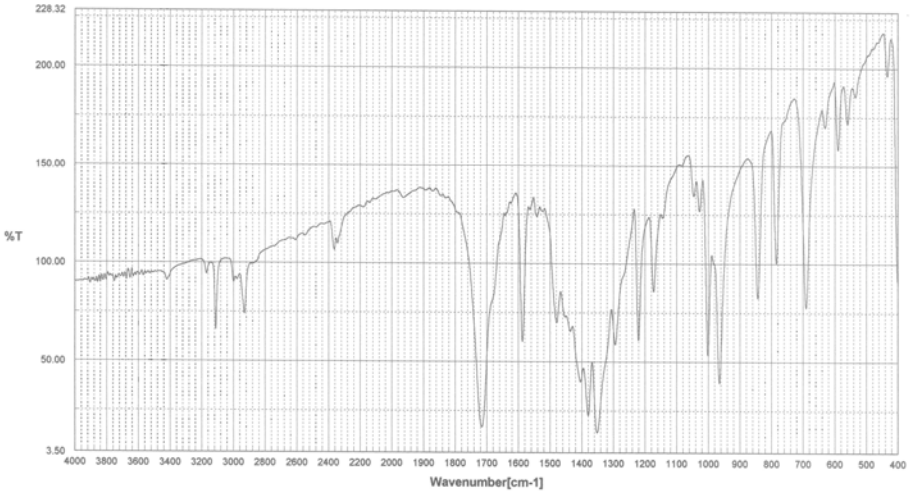

Fig 1. IR-spectra of Schiff base (I)

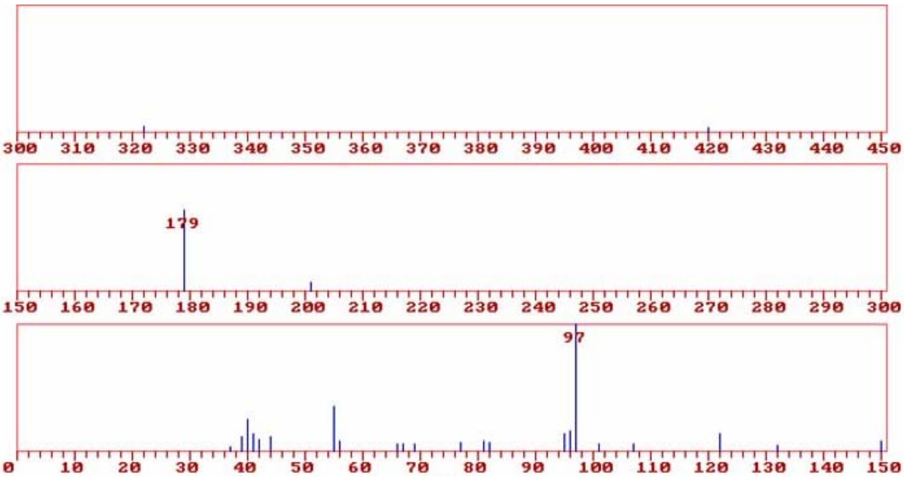

Fig 2. Electron impact mass spectrum of Schiff base (I)

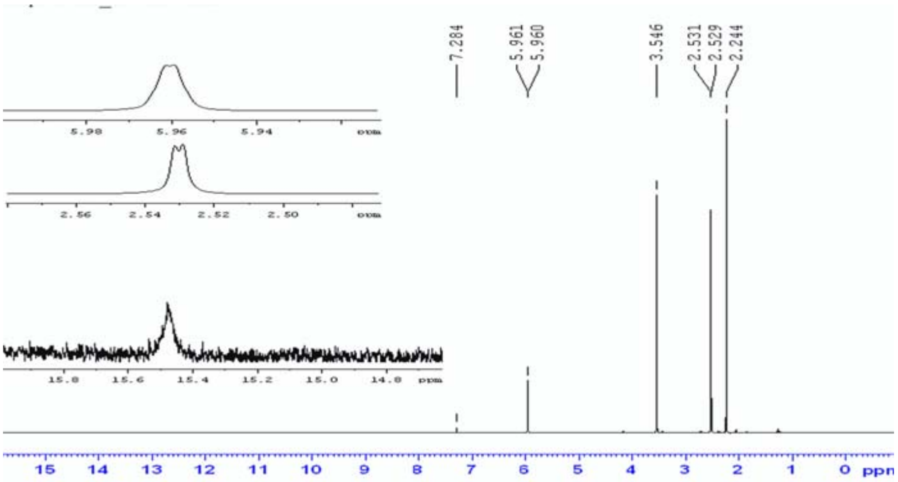

Figure 3. ^{1}H NMR spectra of Schiff base (I)

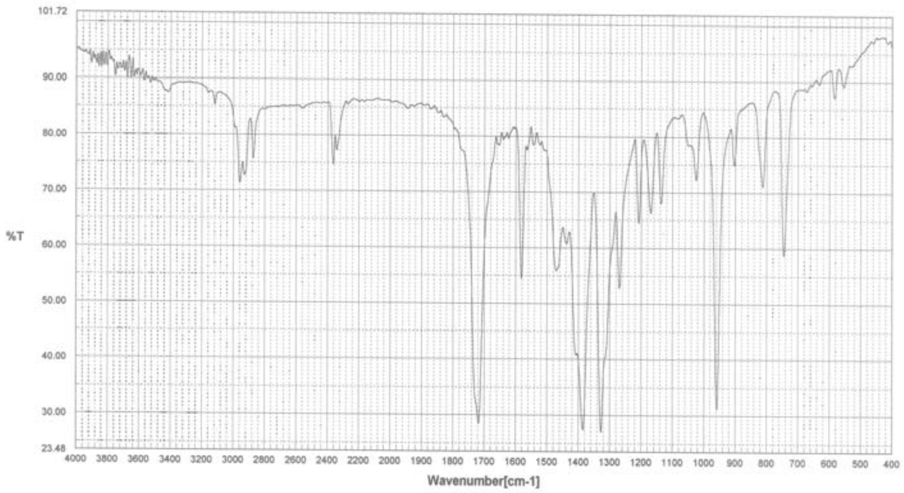

Fig 4. IR-spectra of Schiff base (II)

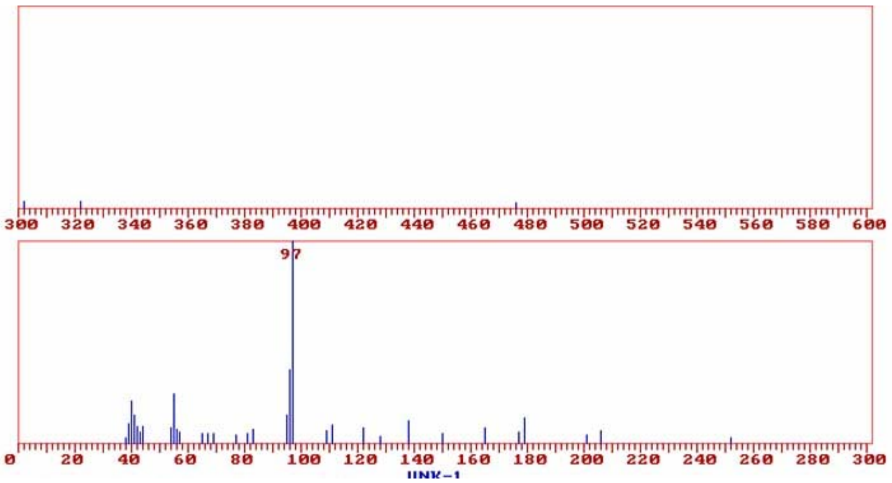

Fig 5. Electron impact mass spectrum of Schiff base (II)

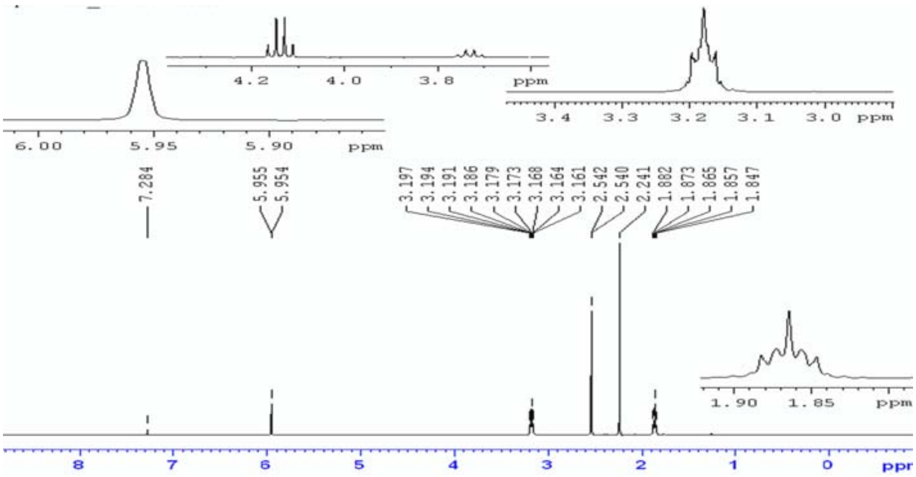

Figure 6. ^{1}H NMR spectra of Schiff base (II)

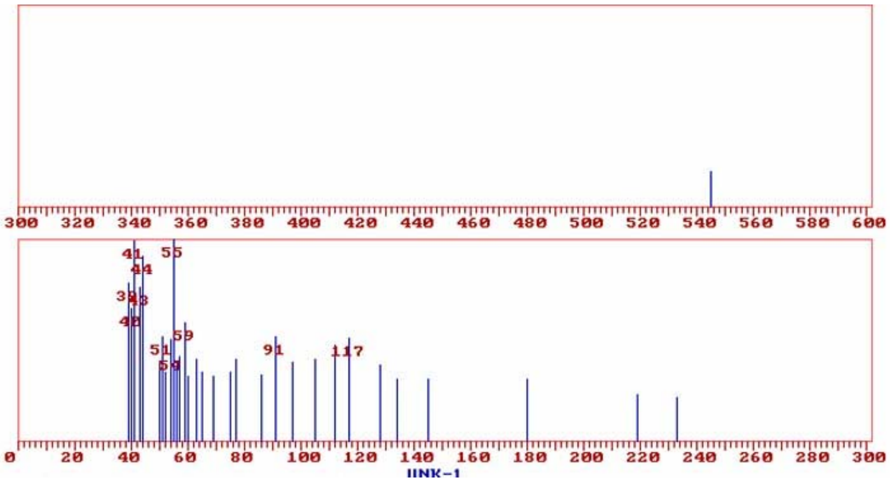

Fig 7. Electron impact mass spectrum of Schiff base (III)

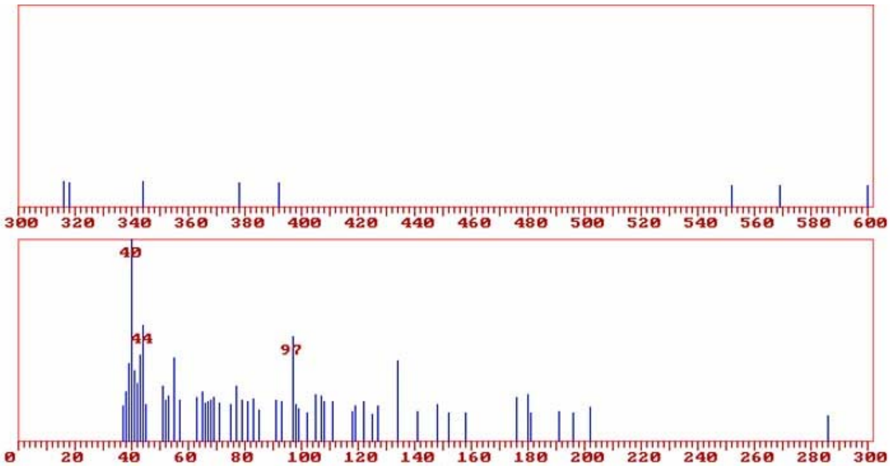

Fig 8. Electron impact mass spectrum of Schiff base (VI)

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