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RESEARCH PAPER

Synthesis and Characterization of Some Heterocyclic Compounds from Chalcone Derivatives and Studying of their Biological Activity

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Abstract

In this work a preliminary step was preparation of 1-(3-((1H-imidazol-2-yl)diazenyl)phenyl)ethan-1-one (1) via coupling of diazonium salt of m-amino acetophenone with imidazole in alkaline alcoholic media which is followed to condensation with different aromatic aldehydes (p-tolualdehyde ,4-dimethyl amino benzaldehyde) by aldol condensation in the presence of base in ethanol to give chalcones derivatives (2,3), that consider as excellent starting material for synthesis of many heterocyclic derivatives through its reaction with (hydrazine ,phenyl hydrazine ,2,4 dinitrophenyl hydrazine) to get pyrazol derivatives (4-9), likewise (2,3) react with hydroxylamine hydrochloride to get isoxazole (10,11), also (2,3) react with (urea, tiourea) to get oxazine and thiazine derivatives (12-15) , as well (2,3) react with (ethyl cyanoacetate, malononitrile) to get pyridine derivatives (16-19) ,too (2,3) react with guanidine hydrochloride to get pyrimidine derivatives (20,21). All these compounds characterized by means of FT-IR, ^{1}H-NMR, and 13C-NMR, and follow reaction by R_f- TLC and measurements melting points. After that we studied the biological activity for all prepared compounds to ward two types of bacteria.

Keywords: *Azo, Chalcone, Pyrazole, Isoxzazole , Oxazine, Thiazine, Pyridine , Pyrimidine, Biological activity.*

Introduction

Azo compound are characterized by the presence of (–N=N–) group in their structure, conjugated with two, identical or different, mono- or polycyclic aromatic systems. Azo compounds are excessively used as dyes and pigments, radical reaction initiators, food additives, therapeutic agents and indicators. Synthesis of azo dyes includes diazotization of a primary aromatic amine, then coupling with one or more nucleophiles. Furthermore azo compounds have biological activity as antibacterial [1-5].

Chalcones belong to the flavonoid class, its have important uses in medicinal field. These compounds are shown various biological activities like anti- malarial, antioxidant, anticancer, antitumor, and antimicrobial [6-9].

Pyrazoles are the significant members of heterocyclic compounds with two neighboring nitrogen's in a five-member ring system, pyrazole derivatives have given good pharmacological effects or have the biological activities, like, anti-inflammatory anti-bacterial, antitumor an antifungal [10-12].

Isoxazole derivatives well known for its medicinal importance, it's have variety of biological activity, Such as analgesic, antitumor, antibiotic, anti-inflammatory, analgesic, as well as antioxidant, antibacterial and antifungal (13-16).

Oxazines are heterocyclic compounds have one nitrogen and one oxygen, they constitute an important class of natural and non-natural products and exhibit useful biological activities like anticonvulsant, analgesic, antibacterial and anticancer activity (16-19).

Pyridines present wide group of compounds, its uses as polymers, antioxidants, dyes, pharmaceuticals and agrochemicals. Pyridine

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derivatives such as cyan pyridines have a wide range of biological activities as anti-hypertensive, anti-cancer; it's also use as important herbicides and insecticides due to their high bioactivity (20-22).

Thiazine a heterocyclic compound containing one nitrogen and four carbon atoms and sculpture atom at different positions in the six member ring, Thiazine derivatives have a vital function in many biological processes and in the synthesis of drugs, can be used for diabetes prevention or gastrointestinal disorders (23-25).

Pyrimidine derivatives have played an significant role in the field of medicinal chemistry, agricultural chemicals and drugs, Many Pyrimidine derivatives are used for thyroid drugs and leukemia, antimicrobial, anticancer, anticonvulsant, and analgesic activities (26-29).

Materials

(FTIR) Spectra (400-4000 cm^{-1}) in KBr disk were recorded on a SHIMADZU FTIR-8400S Fourier transform. Melting points were measured using Stuart, UK. ^{13}C-NMR and 1HNMR were recorded on Fourier transformation Bruker spectrometer operating at (400MHz) with (DMSO-d_6) measurements were made at Department of Chemistry, Esfahan University, Iran.

Synthesis Azo Derivative (1)

A diazonium solution was prepared by dissolve (1.35 g, 0.01 mol) of m-amino acetophenone in (40 mL) water and (4 mL)concentrated HCl this solution was cooled to 0 °C, treated with (0.69 g, 0.01 mol) NaNO2in (30mL) of water were added gradually with stirring for 20 min at (0 -5)°C to complete the diazotization . The mixture of diazonium chloride was then slowly added into the solution of (0.68 g, 0.01 mol) imidazol with 50ml of ethanol, which was dissolved in 5% Na OH (20 mL) at 5 °C. The mixture was keep cooled in the ice bath and stirred continuously for 1 hour, followed by adjusting the pH of solution to pH=6. The precipitate formed was filtered, recrystallized from ethanol, washed with water then dried in air. (30)

General Method of Synthesis Chalcone (2, 3)

A mixture of azo compound(1) (0.214 gm ,0.001 mol) and benzaldehyde derivatives (p-tolualdehyde, 4-(N,N-dim ethylamine benzaldehyde) (0.001mol) (0.11ml ,0.149gm) respectively was dissolved in 25 ml ethanol . after that was added drop wise to the above mixture 10ml of 10% NaOH solution followed for 30 minutes vigorous stirring. After that the mixture was let to stand for 12hrs, and then the precipitation occurred by neutralized with HCl (0.1-0.2) N. The precipitate obtained was filtered, dried in air and Re-crystallized by solvent ethanol. (31)

Synthesis of Pyrazole Derivatives (4, 5)

A mixture of of chalcone (2, 3) (0.001 mol) (0.3gm, 0.34 gm) with (0.05ml) of hydrazine hydrate was dissolved in ethanol (25 mL) after that allow to refluxed for (9,11)irrespectively. The reaction mixture was cooled then filtered, dried and re-crystallization from ethanol solvent (32).

Synthesis of Pyrazole Derivatives (6, 7, 8, 9)

A mixture of chalcone (2, 3) (0.001 mol) (0.3gm, 0.34gm) with (0.001mol) of (0.1ml,0.2g) of (phenyl hydrazine, 2,4-dinitrophenyl hydrazine)respectively then afew drops was added of glacial acetic acid, the mixture was dissolved in ethanol (25 mL) after that allow to refluxed for (11-15) hrs, the product were poured into ice water, then filtered, dried and re-crystallization from ethanol solvent (33).

Synthesis of Isoxazole Derivatives (10, 11)

chaconne (2,3) (0.001mol) (0.31 g, 0.34 g) respectively, hydroxylamine hydrochloride (0.001 mol) (0.07 gm) and aqueous sodium hydroxide (10%, 0.6 ml) were dissolved in (30 mL) ethanol then refluxed for (13-19) hrs and poured into ice cold water, Then filtered, washed and recrystallized for the precipitate obtained was from ethanol to give isoxazol derivatives (10 ,11) .(34)

Synthesis of Thiazine/Oxazine Derivatives (12, 13, 14, 15)

A mixture of chaconne (0.001mol)(0.3gm, 0.34gm), theorem/urea (0.001 mol) (0.076g, 0.06g) respectively were dissolved in (10 ml) ethanol sodium hydroxide solution then stirred for (15- 19) hrs, then it was poured into (20 ml) of cold water with continuous stirring for (1) hr then left overnight. The solid formed was filtered then washed and re-crystallized from ethanol. (35)

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Synthesis of Pyridine Derivatives (16, 17, 18, 19)

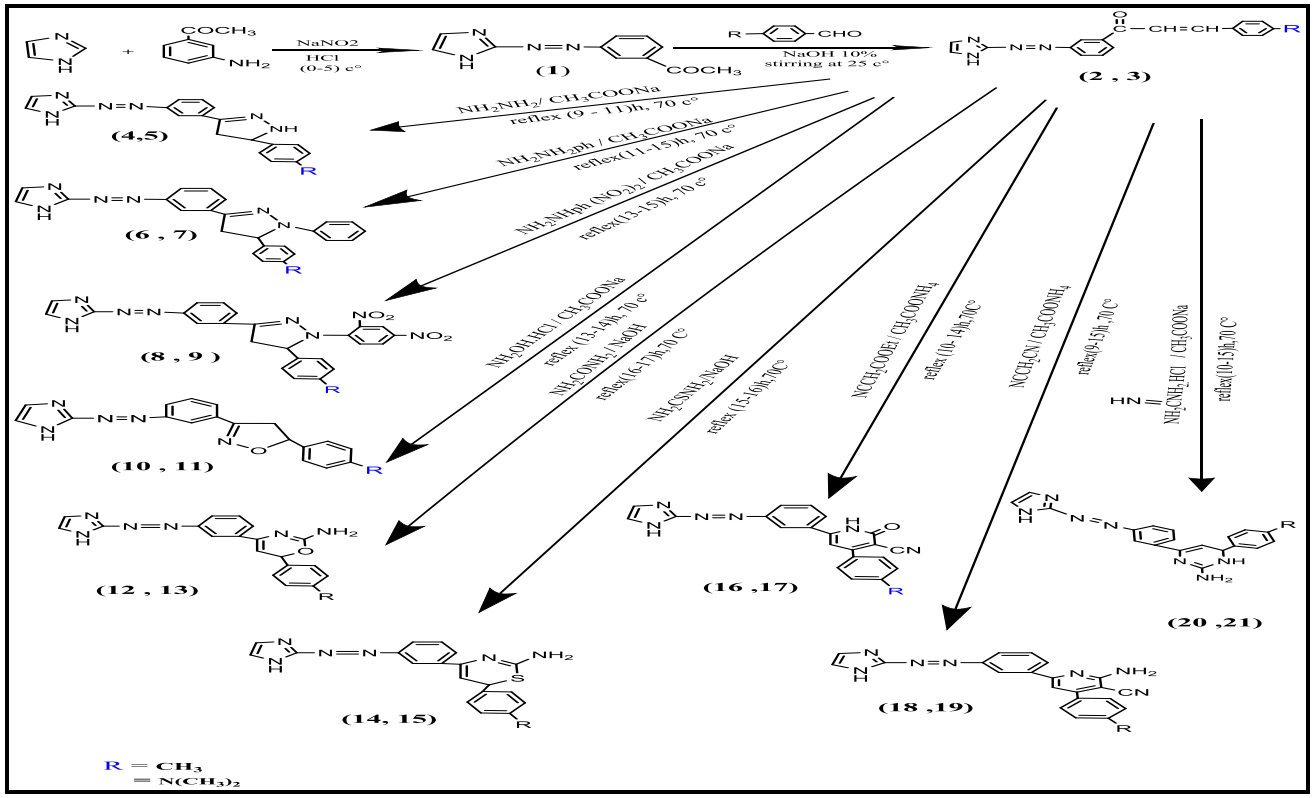
Compounds of chalcone (2, 3) (0.001 mol) (0.31 gm, 0.34 gm) respectively, ethylcyanoacetate/ malononitrile (0.001 mol) (0.1g,0.066g) respectively and (0.15g, 0.002 mol)ammonium acetate dissolved in (30ml) absolute ethanol then refluxed for (9-20) hrs .Then cooling and the product was filtration, washed with ethanol, dried and crystallized from the proper solvent to give the title compounds.(36)

Synthesis of Pyrimidine Derivative (20, 21)

A mixture of compounds (2, 3) (0.001 mol) and (0.095g, 0.001mol) guanidine hydrochloride then (0.08 g, 0.002 mole) sodium hydroxide in 30 ml ethanol then was added. The reaction mixture was refluxed for (10-21) hrs. After cooling, the precipitate was collected by filtration, dried and crystallized from the proper solvent to give the title compounds. (37)

Preparation of Microbiology Culture Media

38 g of nutrient agar is dissolved in (1L) of distillation water, then put in autoclave for (15) mins at 121 °C for sterilization. Pouring the media after becoming at 37 °C in Petri dishes made ready for streaking by bacteria It was getting (Escherichia coli) and (staphylococcus aurous) isolated bacteria from hospital. It was cultured and these plates were incubated at 37 °C for 24 h for both bacteria, DMSO was used as a solvent to prepare solutions of the various compounds were examined (0.02 g of compounds in 5mLDMSO) after that the inhibition zones were examined for all the compounds under test (38).



Scheme 1: Synthesis of some heterocyclic compounds derivatives

Results and Discussion

Compound (1):1-(3-((1H-imidazol-2-yl) diazeny l) phenyl) ethan-1-one

The infrared spectrum data of compound (1) showed band at (1685) cm^{-1} for (C=O), 3066 cm^{-1} for (Ar-H), 3402 cm^{-1} for (N-H) imidazole, 1593 cm^{-1} for (C=N) inside imidazole ring, 2923 $cm^{-1}$for (C-H) for (CH_3), 1419 cm^{-1} for (N=N) and 1558 cm^{-1} due to aromatic (C=C).The ^1H NMR (DMSO) spectrum data of compound (1) show δ:7.4-8 (m ,4H,Ar-H), 2.6 (S,3H,CH3),13.2 (S, 1H, NH imidazol ring),8.3 (S, 2H, CH imidazol ring).The C^{13}-NMR (DMSO) spectrum data of compound (1) show δ: 26.7 (C_{11}), 197.3 (C_{10}), 121.4 (C_2, C_3), 154.4 (C_1), 152 (C_8), 137 (C_5), 130 (C_7), 126.5 (C_6), 126.1 (C_9).

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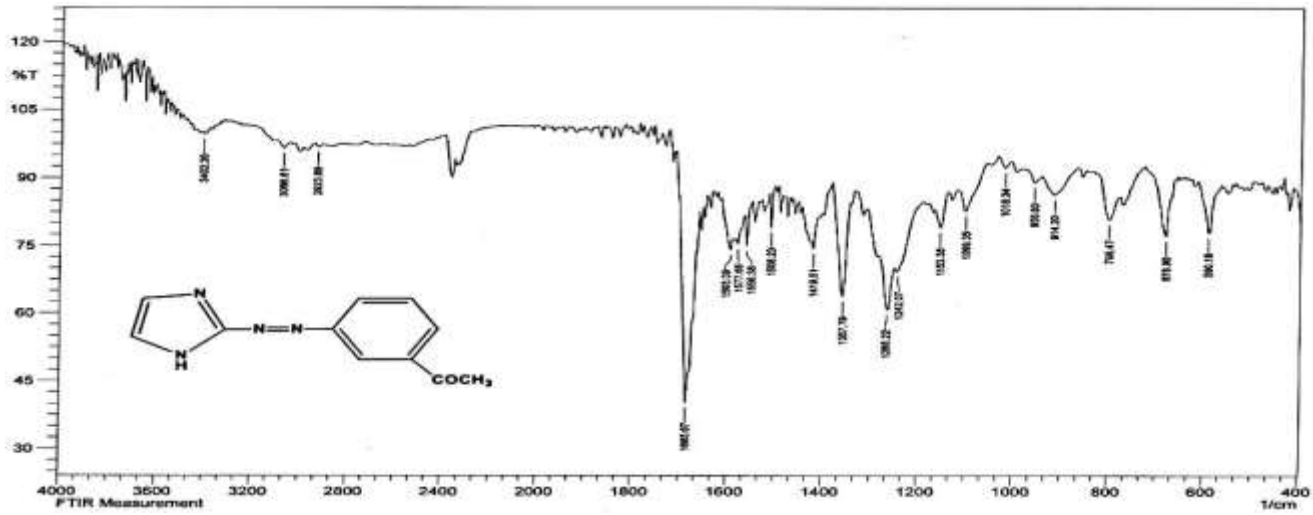

Fig 1: FT-IR spectra of compound (1)

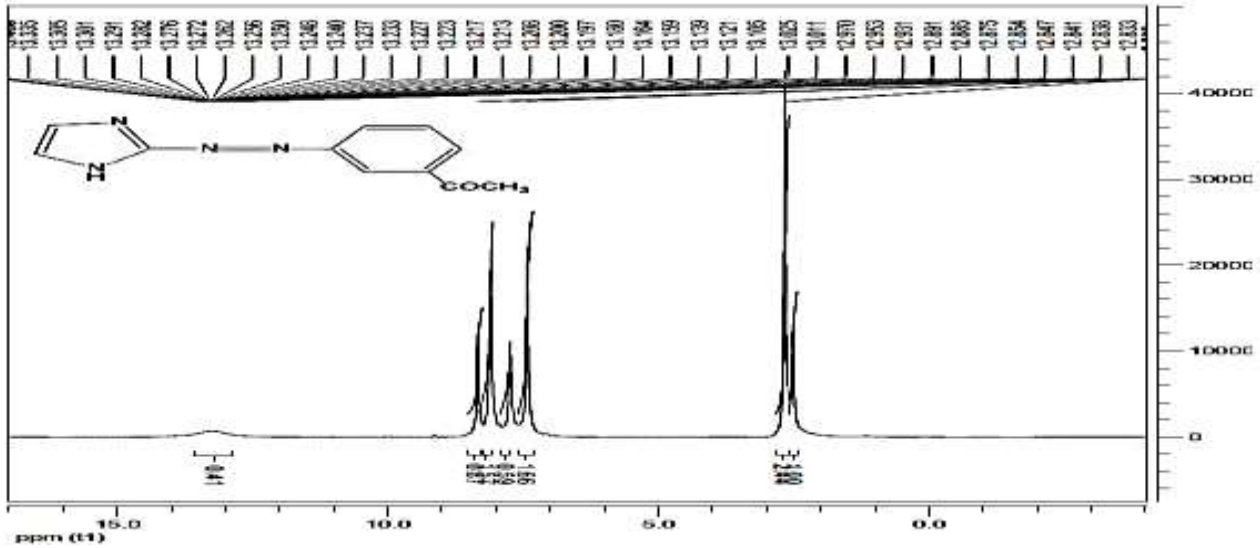

Fig. 2:[1]H NMR spectrum of compound (1)

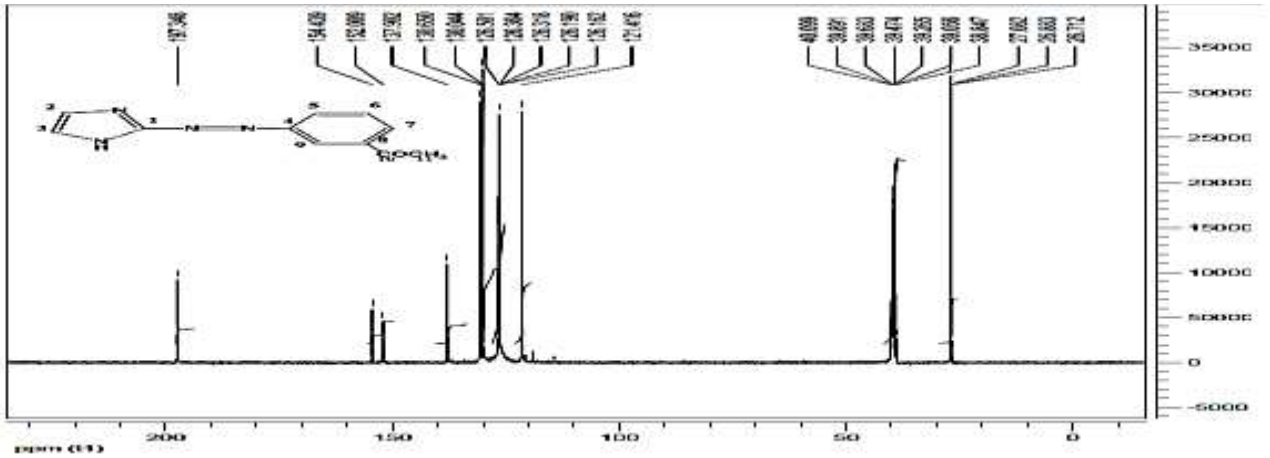

Fig. 3:[13]C-NMRspectrum of compound (1)

Compound (2):1-(3-((1H-imidazol-2-yl) diazenyl) Phenyl)-3-(p-Tolyl) Prop-2-en-1-One

The infrared spectrum data of compound (2) showed band at 1662 cm-1 for (C=O)chaconne, 3024 cm-1 for (Ar-H), 3421 cm-1 for (N-H) imidazole, 1596 cm-1 for (C=N) inside imidazole ring, 2920 cm-1 for (C-H) for (CH3), 1404 cm-1 for (N=N) , 1566 cm-1 due to aromatic (C=C) and 1512 cm-1 for aliphatic (C=C).The 1H NMR (DMSO) spectrum data of compound (2) show δ: 7.2-8.3 (m ,8H,Ar-H), 2(S,3H,CH3), 13.1 (S, 1H, NH imidazol ring),8.4 (S, 2H, CH imidazol ring), 3.5 (d, 1H, CO=CH), 3.3 (d, 1H, CH-Ar) .The C13-NMR (DMSO) spectrum data of compound (2) show δ: 38 (C19), 188 (C10), 120(C12), 137 (C13), 154 (C1), 152 (C8), 138 (C16), 121-131 (Caromatic).

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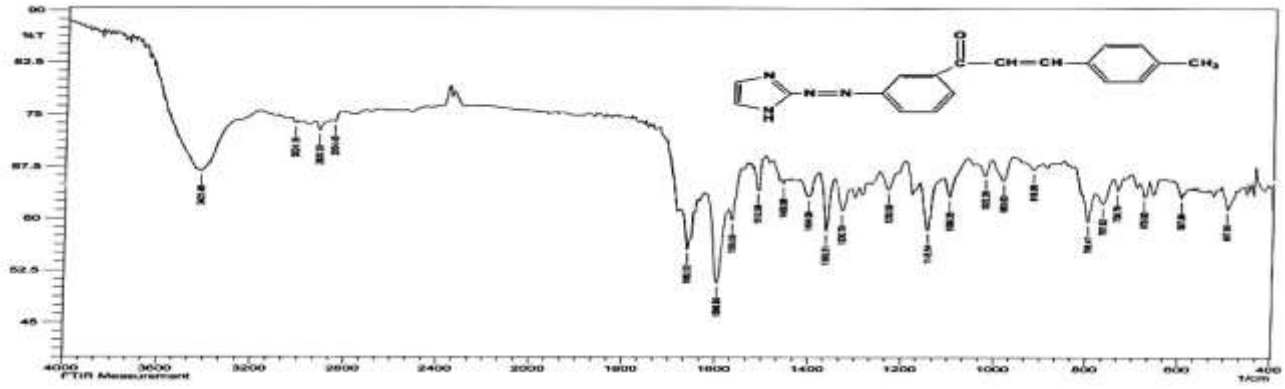

Fig 4: FT-IR spectra of compound (2)

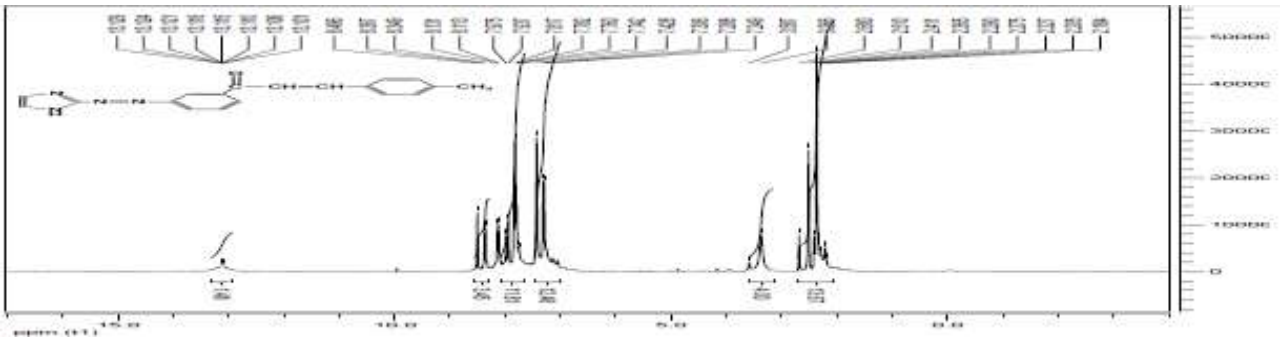

Fig. 5:^{1}H NMR spectrum of compound (2)

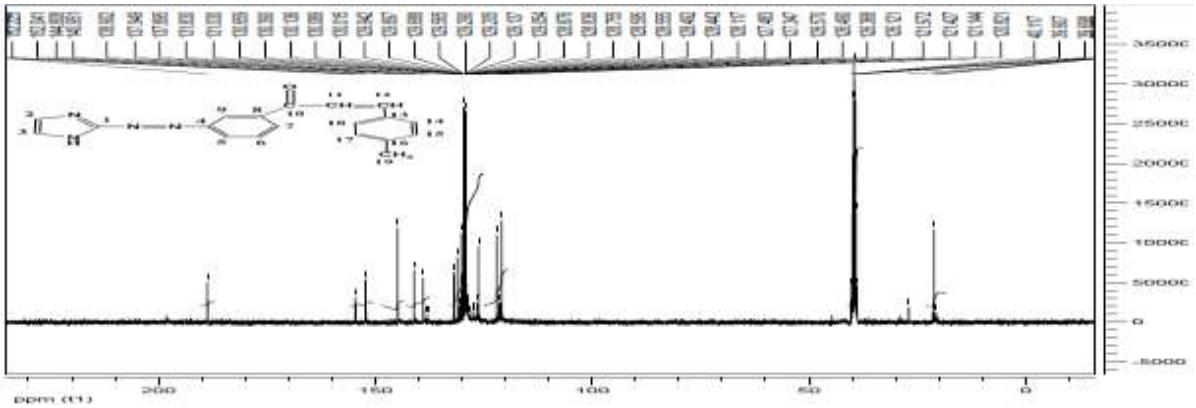

Fig. 6:^{13}C-NMRspectrum of compound (2)

***Compound (3)*: 1-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-3-(4-(dimethylamino) phenyl) prop-2-en-1-one**

The infrared spectrum data of compound (3) showed band at 1681 cm^{-1} for (C=O), 3078cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole, 1650 cm^{-1} for (C=N) inside imidazole ring, 2985 cm^{-1} for (C-H) for (CH_3), 1434 cm^{-1} for (N=N) , 1596cm^{-1} due to aromatic (C=C) and 1558cm^{-1} for aliphatic (C=C) . The ^{1}H NMR (DMSO) spectrum data of compound (3) show δ:6.5-8.4 (m ,8H,Ar-H), 3 (S,6H,CH3), 13.1 (S, 1H, NH imidazol ring),8.4(S, 2H, CH imidazol ring), 3.5 (d, 1H, CO=CH), 3.3 (d, 1H, CH-Ar) .The C^{13}-NMR (DMSO) spectrum data of compound (3) show δ: 189 (C_{10}), 121 (C_2, C_3),145(C_8), 137 (C_{12}),139 (C_{11}),137 (C_1), 154 (C_{16}), 25 (C_{19},C_{20}), 122-131 (C aromatic).

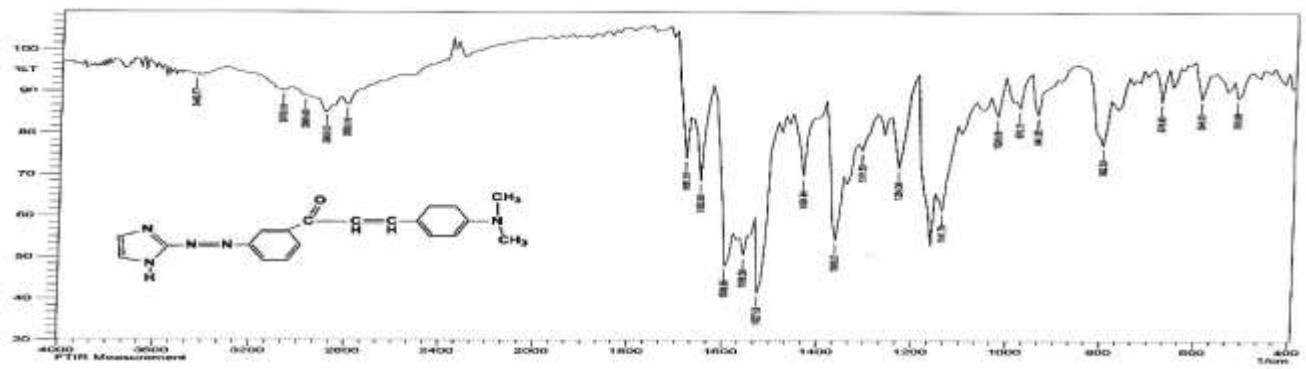

Fig 7:FT-IR spectra of compound (3)

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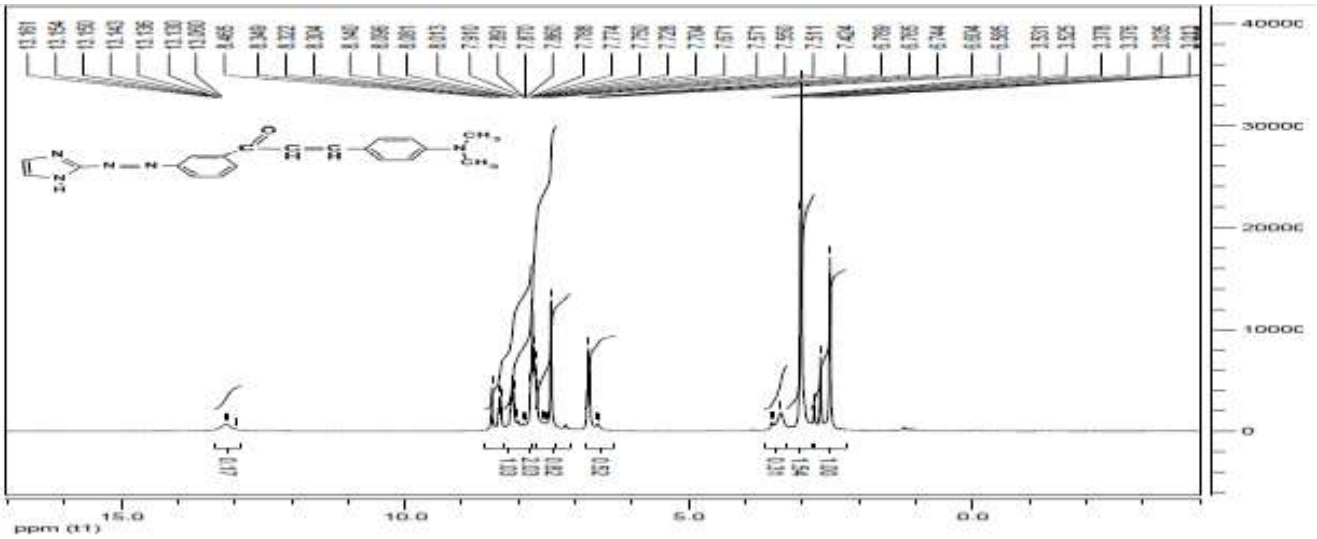

Fig. 8: 1H NMR spectrum of compound (3)

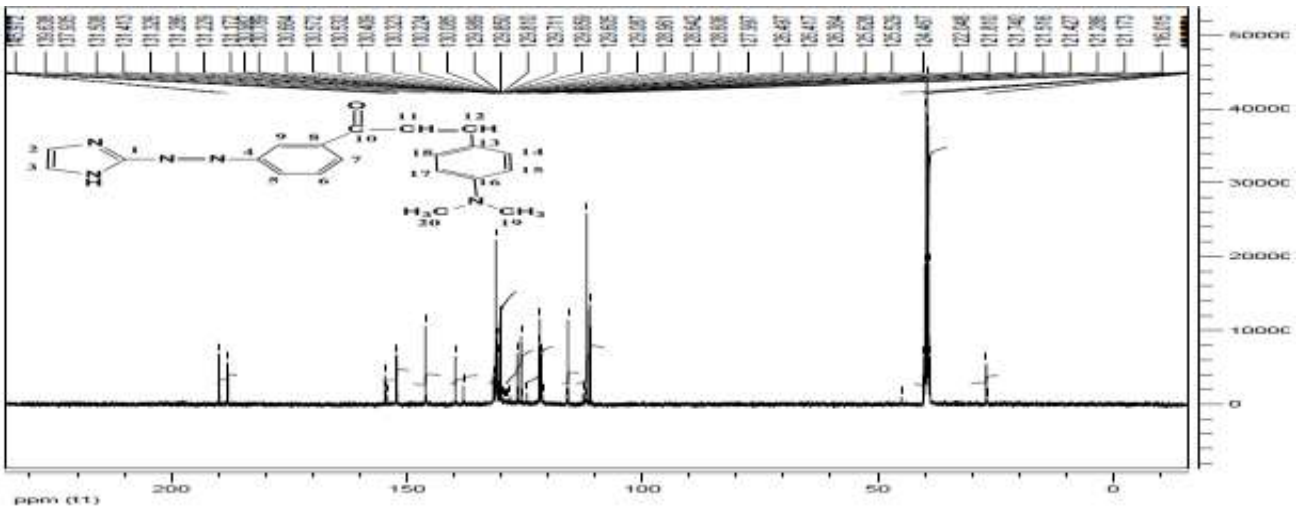

Fig 9:C^{13}-NMRspectrum of compound (3)

Compound (4): 3-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-5-(p-tolyl)-1H-pyrazole

The infrared spectrum data of compound (4) showed band at 1654 cm^{-1} for (C=N) pyrazol , 3004 cm^{-1} for (Ar-H), 3448 cm^{-1} for (N-H) imidazole overlapping with band for (N-H) pyrazol that show at 3398 cm^{-1} , 1596 cm^{-1} for (C=N) inside imidazole ring, 2981 cm^{-1} for (C-H) for (CH_3), 1411 cm^{-1} for (N=N) and 1558 cm^{-1} due to aromatic (C=C) . The ^{1}H NMR (DMSO) spectrum data of compound (4) show δ:6.8-8.4 (m ,8H,Ar-H), 2 (S,3H,CH3),13(S, 1H, NH imidazol ring),8.7 (S, 2H, CH imidazol ring),2.6 (d, 2H, CH_2 pyrazol ring),3.5 (t, 1H, CH pyrazol ring),5.2 (S, 1H, NH imidazol ring) .

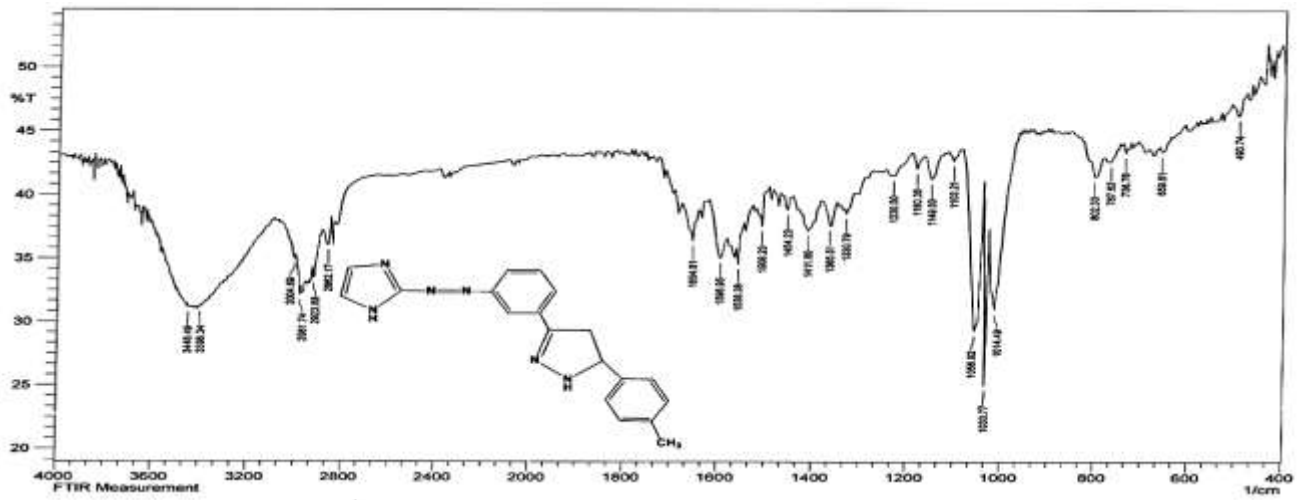

Fig 10: FT-IR spectra of compound [4]

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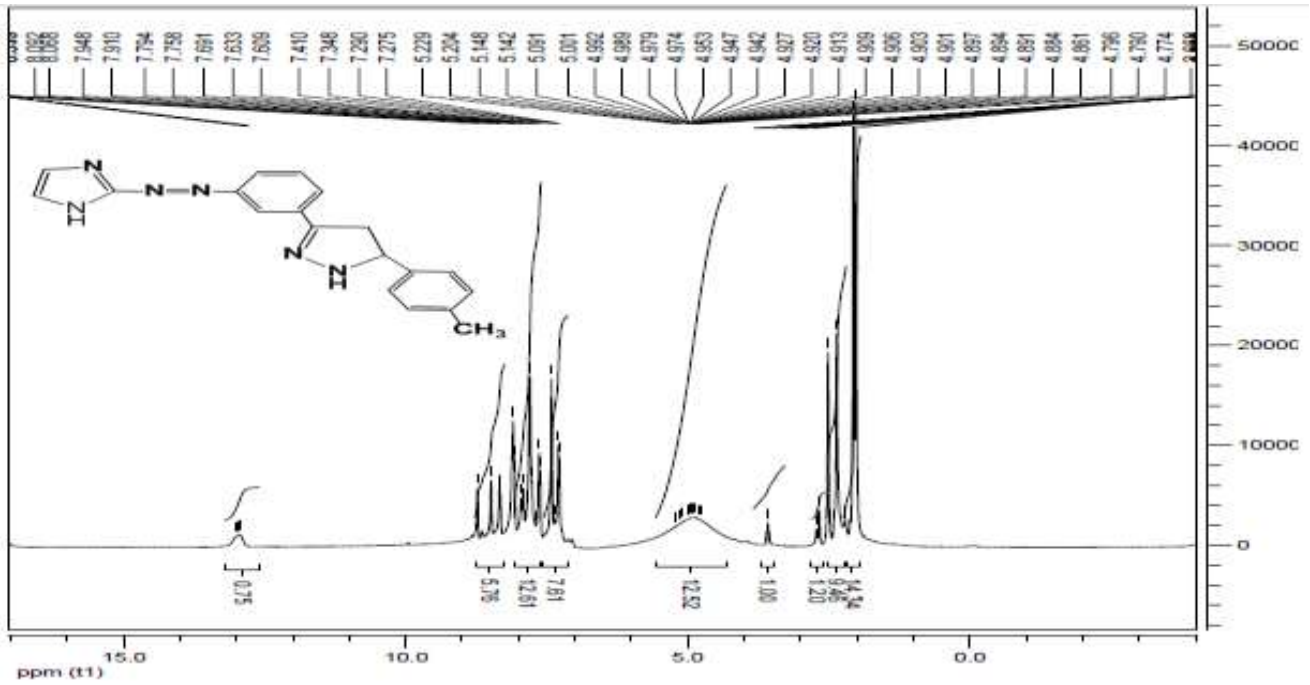

Fig. 11: 1H NMR spectrum of compound (4)

Compound (5):4-(3-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-1H-pyrazol-5-yl)-N, N-dimethylaniline

The infrared spectrum data of compound (5) showed band at 1650 cm^{-1} for (C=N) pyrazol, 3031 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (N-H) pyrazol that show at 3425 cm^{-1}, 1558 cm^{-1} for (C=N) inside imidazole ring, 2916 cm^{-1} for (C-H) for (CH_3), 1419 cm^{-1} for (N=N) and 1527 cm^{-1} due to aromatic (C=C).The ^1H NMR (DMSO) spectrum data of compound (5) show δ:6.8-8.4 (m ,8H,Ar-H), 2 (S,3H,CH_3), 13(S, 1H, NH imidazol ring),8.7 (S, 2H, CH imidazol ring), 2.6 (d, 2H, CH_2 pyrazol ring), 3.5 (t, 1H, CH pyrazol ring),5.2 (S, 1H, NH imidazol ring) .The C^{13}-NMR (DMSO) spectrum data of compound (5) show δ: 21($C_{19,20}$), 35 (C_{11}),38(C_{12}), 154(C_{16}), 152 (C_{10}),145 (C_1),131 (C_{13}), 139 (C_8), 111-139 (C aromatic).

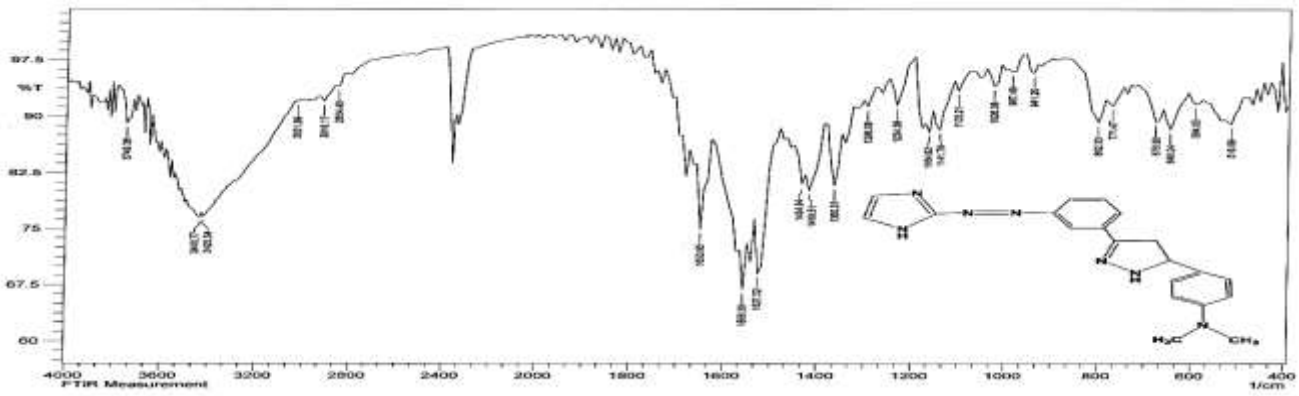

Fig 12: FT-IRspectra of compound [5]

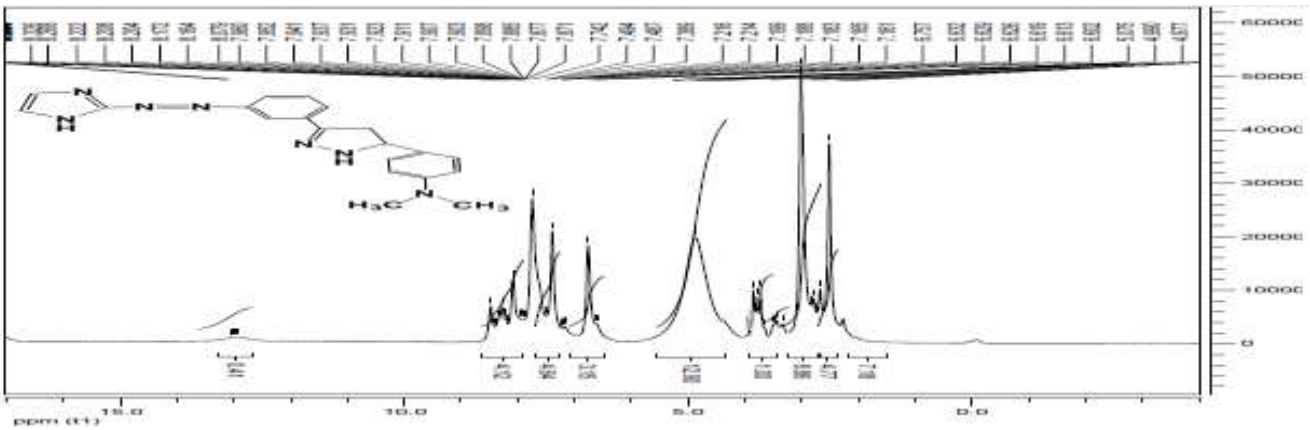

Fig. 13:^{1}H NMR spectrum of compound (5)

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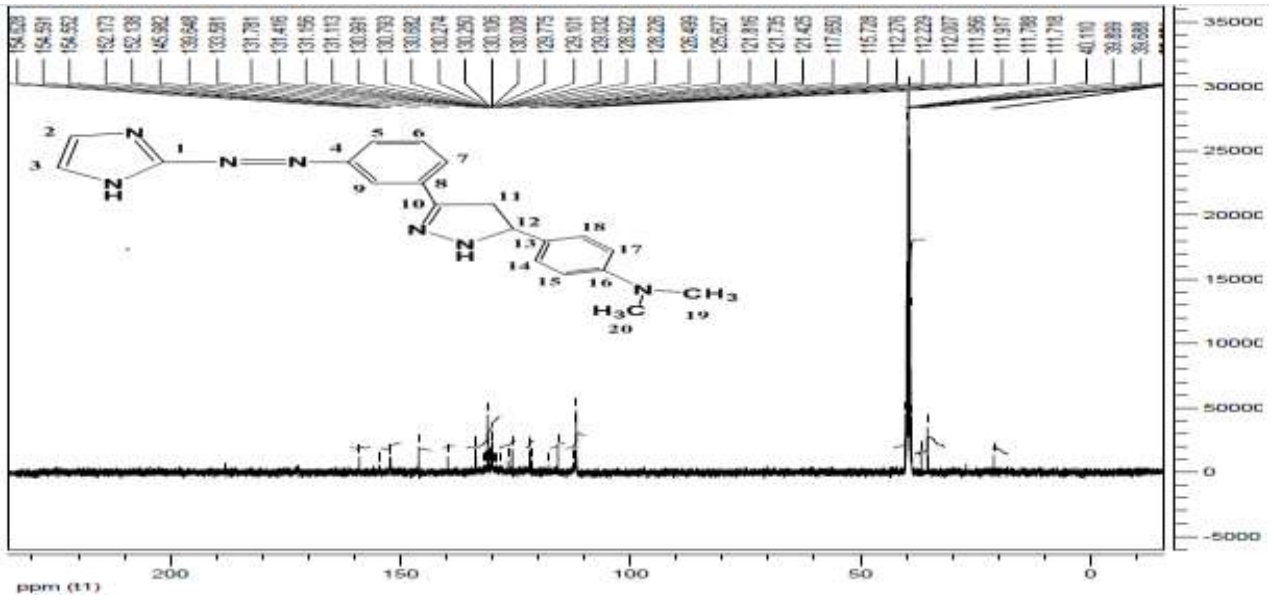

Fig.14:13C-NMRspectrum of compound (5)

***Compound* (6):5-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-1-phenyl-3-(p-tolyl)- 2, 3-1H-pyrazole**

The infrared spectrum data of compound (6) showed band at 3024 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (N-H) pyrazol that show at 3286 cm^{-1}, 1650 cm^{-1} for (C=N) inside pyrazol ring,1596 cm^{-1} for (C=N) inside imidazole ring, 2923 cm^{-1} for (C-H) for (CH_3), 1411 cm^{-1} for (N=N) and 1558 cm^{-1} due to aromatic (C=C).

The ^{1}H NMR (DMSO) spectrum data of compound (6) show δ: 6.8-8.4 (M, 13H, Ar-H), 1.9 (S, 3H, CH3), 13(S, 1H, NH imidazol ring), 8.5 (S, 2H, CH imidazol ring), 4.3 (d, 2H, CH_2 pyrazol ring), 5.3 (t, 1H, CH pyrazol ring).

The C^{13}-NMR (DMSO) spectrum data of compound (6) show δ: 21(C_{19}), 127 (C_2, C_3), 155(C_{10}), 39(C_{11}), 61 (C_{12}), 139 (C_{13}), 145 (C_{20}), 139 (C_8), 116-131 (C aromatic).

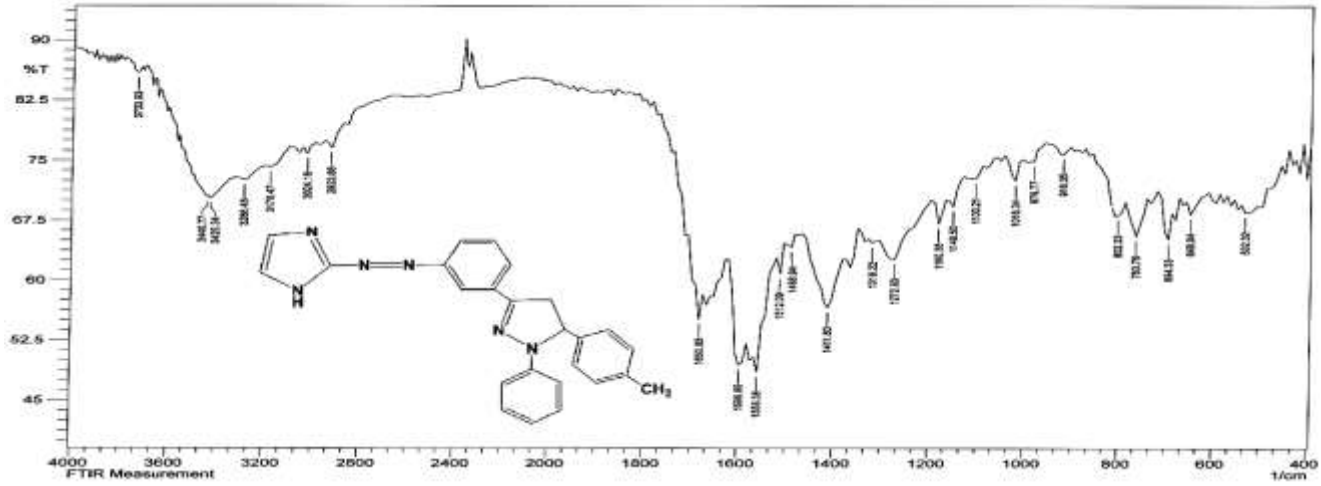

Fig 15: FT-IRspectra of compound [6]

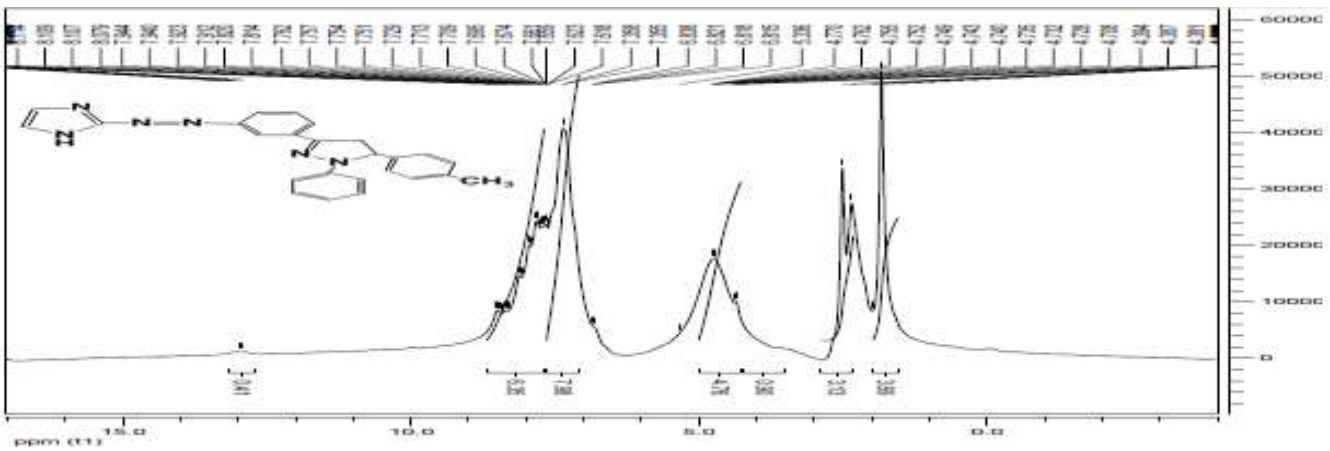

Fig. 16:^{1}H NMR spectrum of compound (6)

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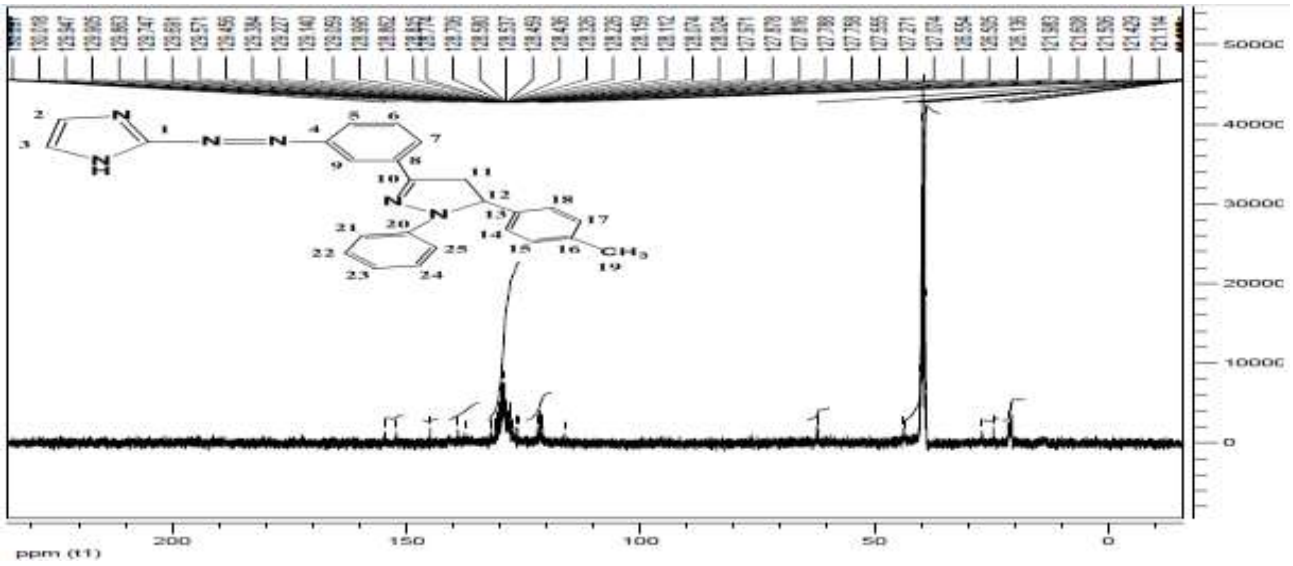

Fig. 17:^{13}C-NMRspectrum of compound (7)

Compound (7):4-(5-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-1-phenyl-1H-pyrazol-3-yl)-N, N-dimethylaniline

The infrared spectrum data of compound (7) showed band at 3031 cm^{-1} for (Ar-H), 3425 cm^{-1} for (N-H) imidazole, 1650cm^{-1} for (C=N) inside pyrazol ring,1589 cm^{-1} for (C=N) inside imidazole ring, 2916 cm^{-1} for (C-H) for (CH_3), 1419 cm^{-1} for (N=N) and 1558 cm^{-1} due to aromatic (C=C).The ^{1}H NMR (DMSO) spectrum data of compound (7) show δ: 7.3-8.4 (m ,13H,Ar-H), 2.4 (S,6H,CH3),13(S, 1H, NH imidazol ring),8.5 (S, 2H, CH imidazol ring),3.6 (d, 2H, CH_2 pyrazol ring),5 (t, 1H, CH pyrazol ring) .The C^{13}-NMR (DMSO) spectrum data of compound (7) show δ: 30($C_{19,20}$), 152 (C_{10}), 135(C_{13}), 173(C_{16}), 145 (C8),55 (C_{12}),39 (C_{11}), 111-129 (C aromatic).

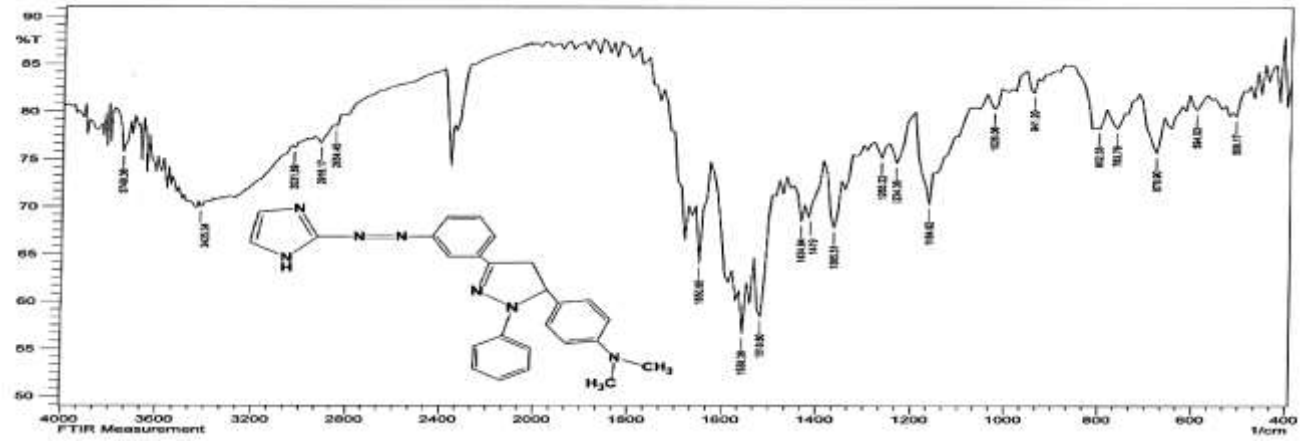

Fig 18:FT-IRspectra of compound [7]

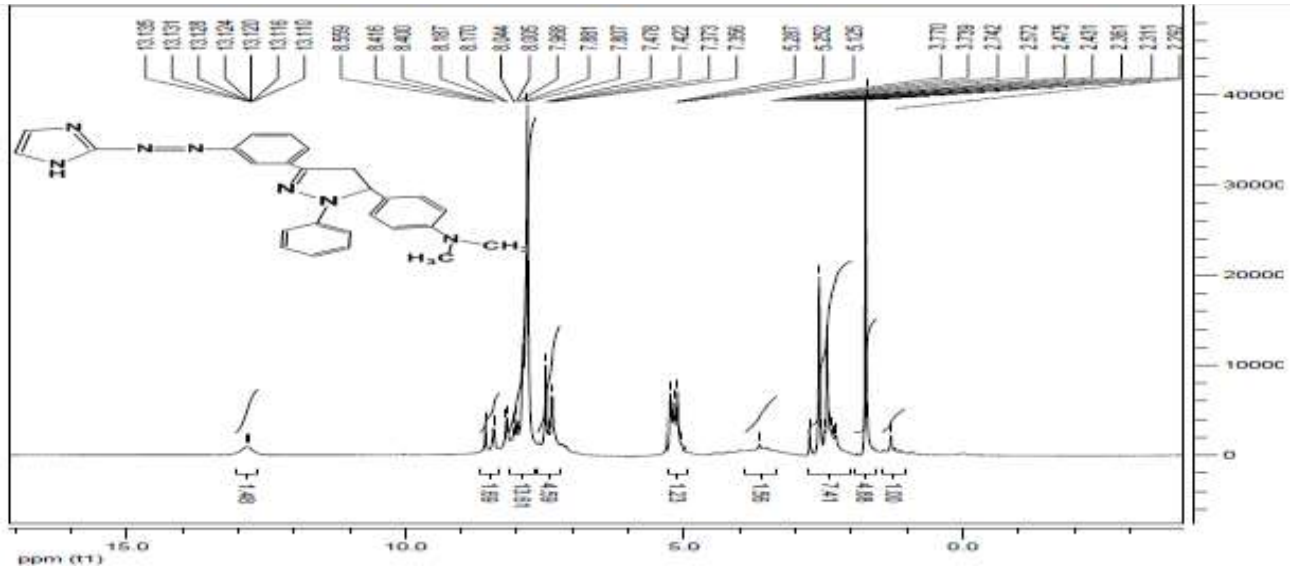

Fig. 19:^{1}H NMR spectrum of compound (7)

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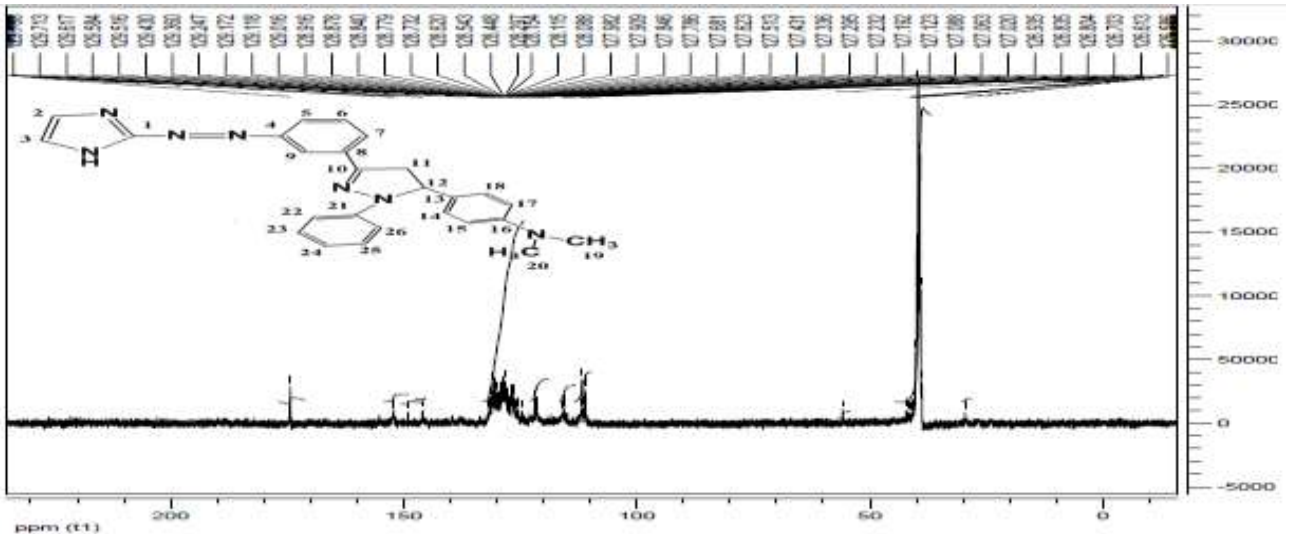

Fig. 20:^{13}C-NMRspectrum of compound (7)

Compound (8):5-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-1-(2, 4-dinitrophenyl)-3-(p-tolyl)-1H-pyrazole

The infrared spectrum data of compound (8)showed band at 3003 cm^{-1} for (Ar-H), 3448 cm^{-1} for (N-H) imidazole, 1620 cm^{-1} for (C=N)inside pyrazol ring, 1593cm^{-1} for (C=N)inside imidazole ring,2908 cm^{-1} for (C-H) for (CH_3), 1419 cm^{-1} for (N=N)and 1558 cm^{-1} due to aromatic (C=C).The ^{1}H NMR (DMSO) spectrum data of compound (8) show δ:7-8.7 (m ,11H,Ar-H), 1.7 (S,3H,CH3),13(S, 1H, NH imidazol ring),8.8 (S, 2H, CH imidazol ring),3.5 (d, 2H, CH_2 pyrazol ring),6.8 (t, 1H, CH pyrazol ring) .The C^{13}-NMR (DMSO) spectrum data of compound (8) show δ: 152($C_{23,25}$), 140 (C_1), 138(C_{20}), 145(C_{13}), 62(C_{12}),144.7 (C_{10}),137 (C8), 39 (C_{11}), 21 (C_{19}), 120-132 (C aromatic).

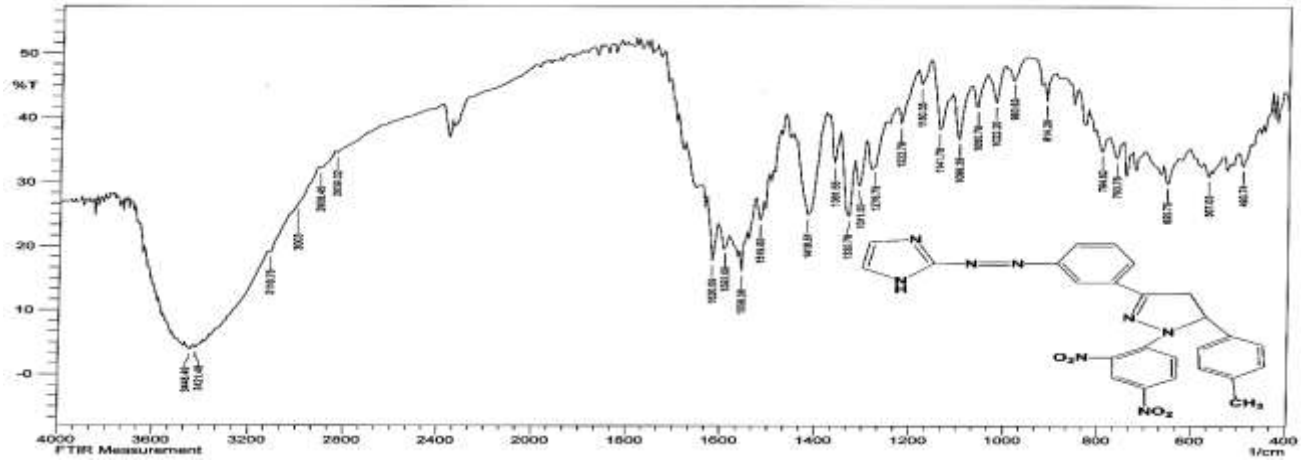

Fig 21: FT-IRspectra of compound [8]

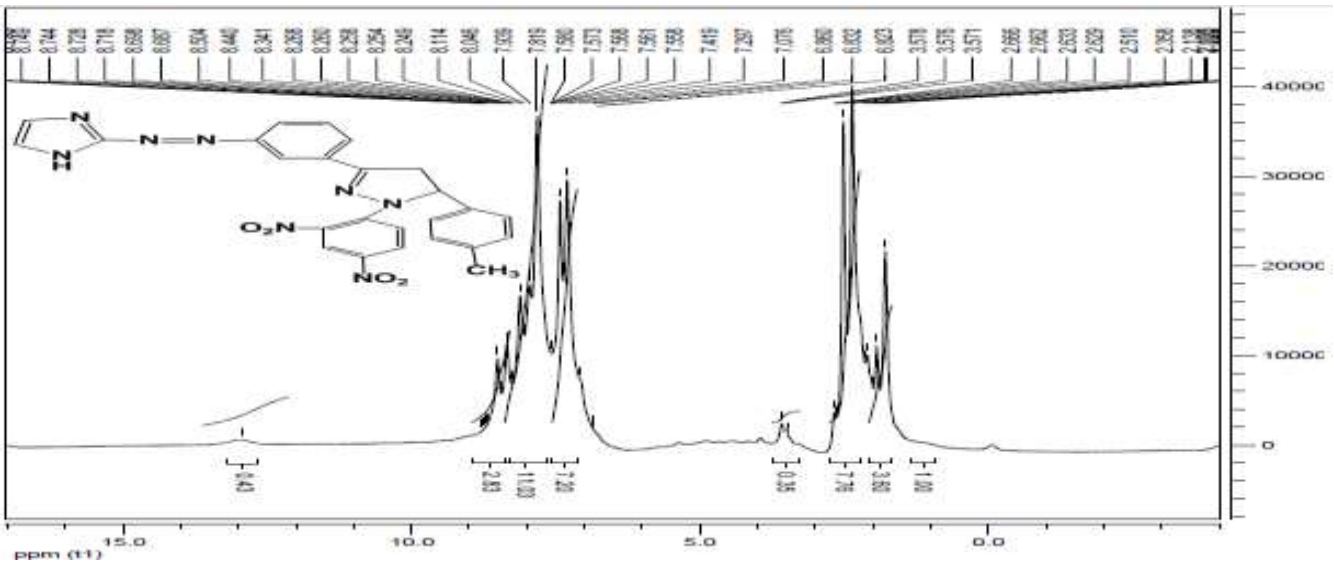

Fig. 22:^{1}H NMR spectrum of compound (8)

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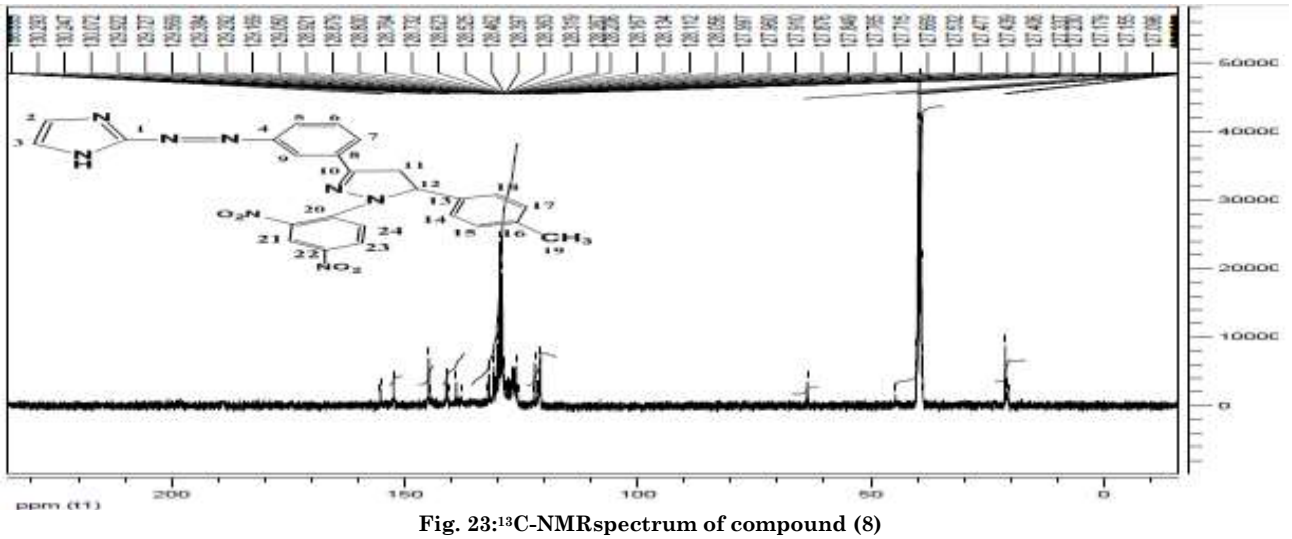

Fig. 23:^{13}C-NMRspectrum of compound (8)

Compound (9):4-(5-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-1-(2, 4-dinitrophenyl) - 1H-pyrazol-3-yl)-N, N-dimethylaniline

The infrared spectrum data of compound (9) showed band at 3031 cm^{-1} for (Ar-H), 3425 cm^{-1} for (N-H) imidazole, 1650 cm^{-1} for (C=N) inside pyrazol ring, 1620 cm^{-1} for (C=N) inside imidazole ring, 2923 cm^{-1} for (C-H) for (CH_3), 1419 cm^{-1} for (N=N) and 1596 cm^{-1} due to aromatic (C=C).The ^{1}H NMR (DMSO) spectrum data of compound (9) show δ: 6.7-8.6 (m ,11H,Ar-H), 3 (S,6H,CH_3), 13(S, 1H, NH imidazol ring),8.7 (S, 2H, CH imidazol ring), 3.5 (d, 2H, CH_2 pyrazol ring), 5 (t, 1H, CH pyrazol ring) .The C^{13}-NMR (DMSO) spectrum data of compound (9) show δ: 22($C_{19,20}$), 175 (C_{16}), 159(C_{22}), 157(C_{24}), 151(C10),62 (C_{12}),140 (C_1), 130(C_{19}), 131 (C_8), 30 (C_{11}), 111-128 (C aromatic).

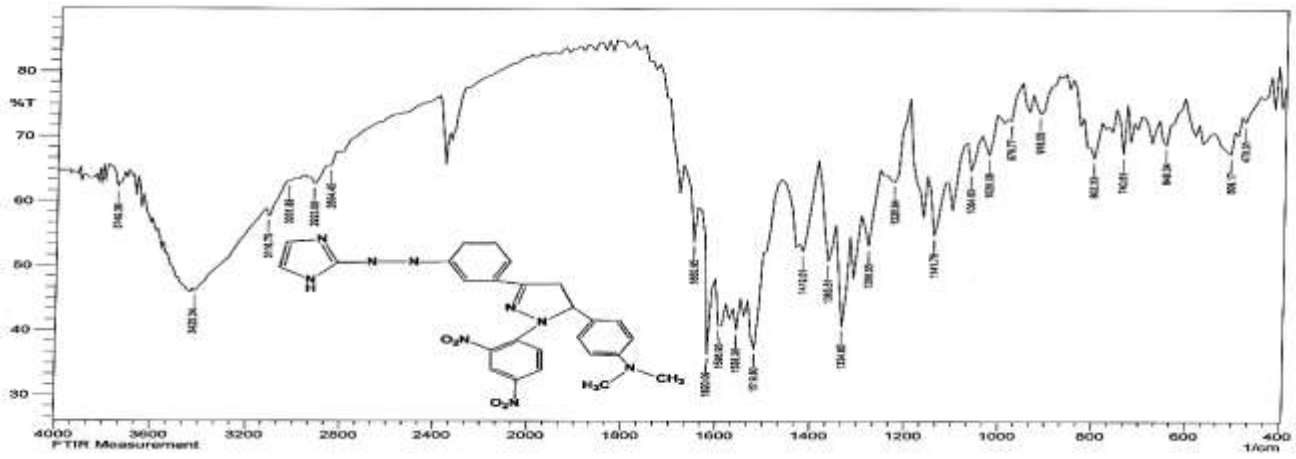

Fig 24:FT-IRspectra of compound [9]

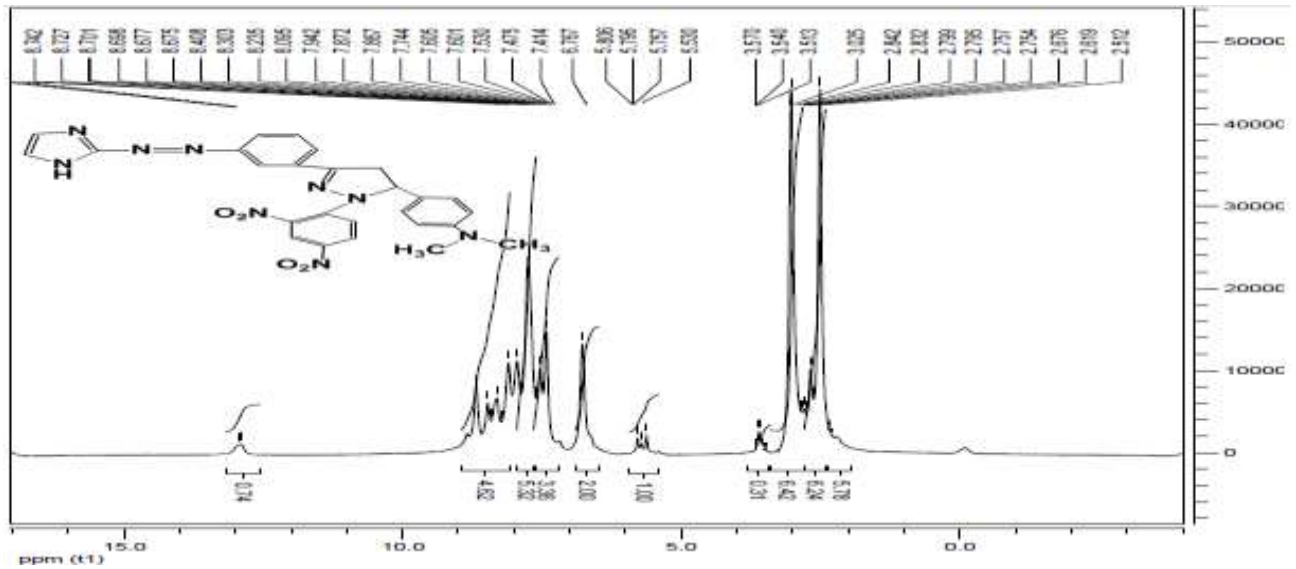

Fig. 25: ^{1}H NMR spectrum of compound (9)

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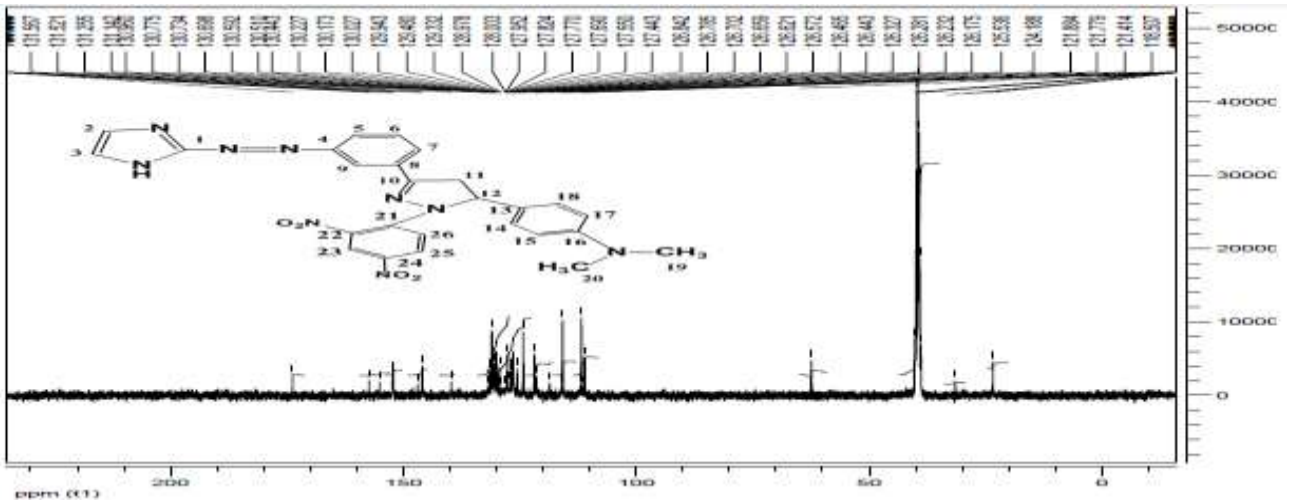

Fig. 26:^{13}C-NMRspectrum of compound (9)

Compound*(10)*:3-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-5-(p-tolyl) isoxazole

The infrared spectrum data of compound (10) showed band at 1654 cm^{-1} for (C=N) isoxazol, 3024 cm^{-1} for (Ar-H), 3421 cm^{-1} for (N-H) imidazole, 1596 cm^{-1} for (C=N) inside imidazole ring, 2977 cm^{-1} for (C-H) for (CH_3),1404 cm^{-1} for (N=N), 1558 cm^{-1} due to aromatic (C=C) and 1149 cm^{-1} (C-O) in isoxazolring.The^{1}H NMR (DMSO) spectrum data of compound (10) show δ:6.7-8.4 (m ,8H,Ar-H), 1.1(S,3H,CH_3), 13 (S, 1H, NH imidazol ring),11.8 (S, 2H, CH imidazol ring) , 4.3(d,2H,CH_2isoxazol ring), 4.4(t,1H,O-CH isoxazol ring) .The C^{13}-NMR (DMSO) spectrum data of compound (10) show δ:11.4 (C_{19}), 20 (C_{11}), 154(C_{10}), 144 (C_8),140 (C_{13}),131 (C_1), 130 (C_{16}),121 (C_2, C_3),120-129 (Caromatic).

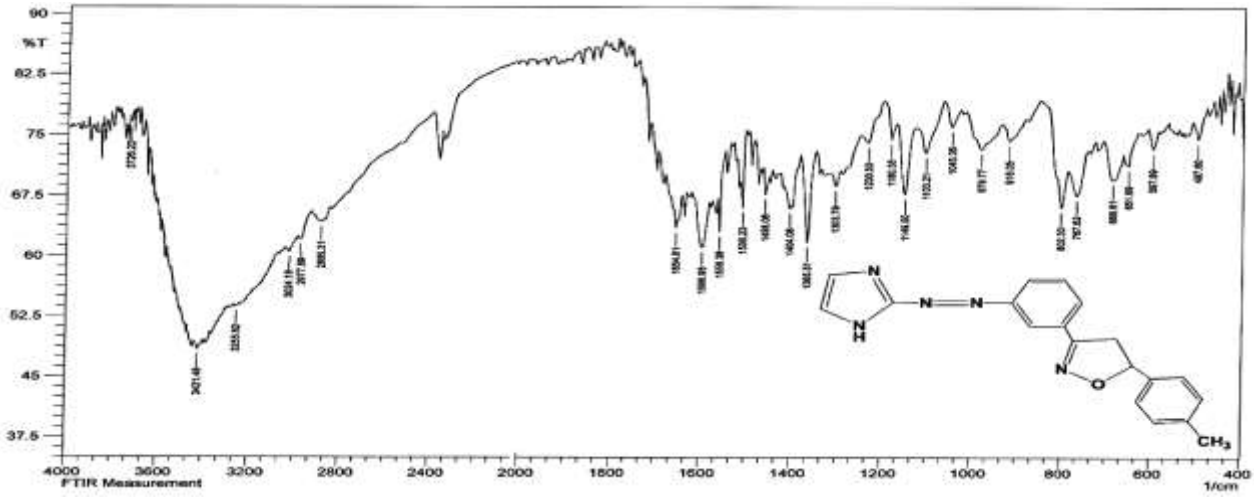

Fig 27:FT-IRspectra of compound [10]

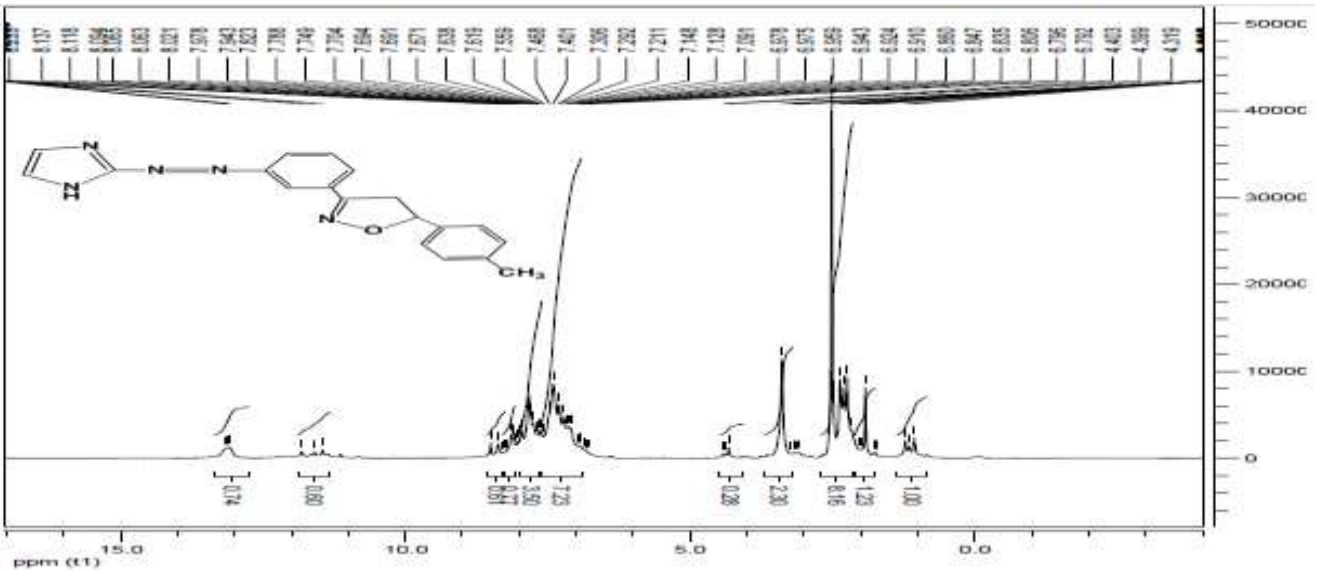

Fig. 28: ^{1}H NMR spectrum of compound (10)

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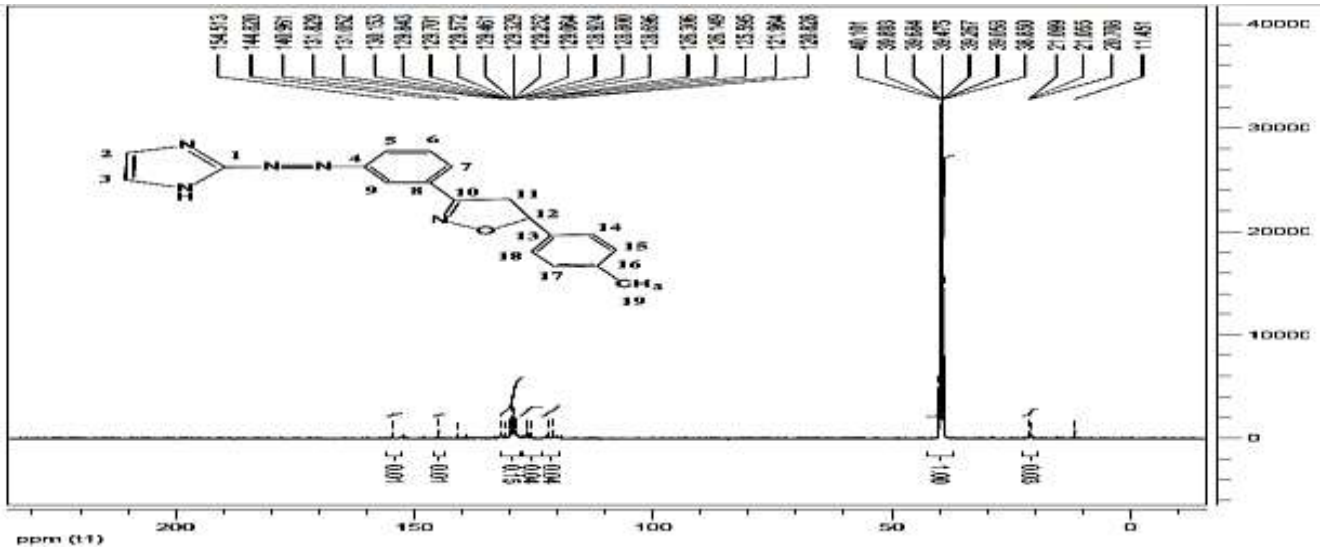

Fig. 29:[13]C-NMRspectrum of compound (10)

Compound *(11)*:4-(3-(3-((1H-imidazol-2-yl) diazenyl) phenyl) isoxazol-5-yl)-N, N-dimethylaniline

The infrared spectrum data of compound (11) showed band at 1650 cm^{-1} for (C=N)isoxazole, 3031 cm^{-1} for (Ar-H), 3417 cm^{-1} for (N-H) imidazole, 1604 cm^{-1} for (C=N) inside imidazole ring, 2916 cm^{-1} for (C-H) for (CH_3), 1434 cm^{-1} for (N=N) and 1558 cm^{-1} due to aromatic (C=C) and 1141 cm^{-1} (C-O) in isoxazolring.The[1]H NMR (DMSO) spectrum data of compound (11) show δ: 6.7-8.3 (m ,8H,Ar-H), 3(S, 6H,CH3),11.6 (S, 1H, NH imidazol ring),8.4 (S, 2H, CH imidazol ring), 3.9(d,2H,CH2isoxazol ring), 5.7(t,1H,O-CH isoxazol ring) .The C^{13}-NMR (DMSO) spectrum data of compound (3) show δ:48 ($C_{19,20}$), 45 (C_{11}), 154(C_{10}), 152 (C_8),131(C_{13}),148 (C_1), 169 (C_{16}),121 ($C_{2,}$ C_3),84(C_{12}),111-139 (Caromatic).

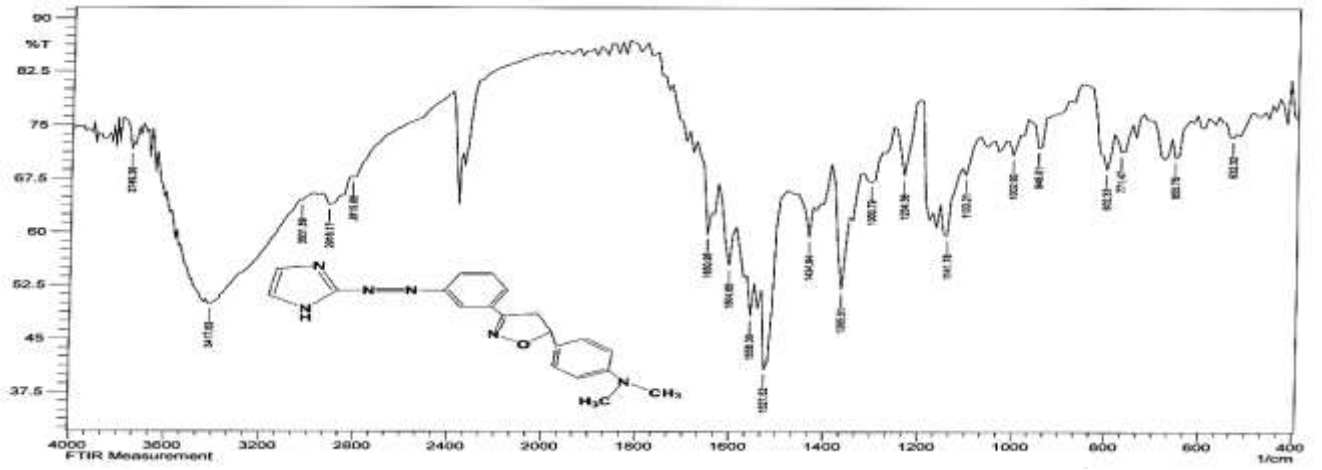

Fig 30: FT-IRspectra of compound [11]

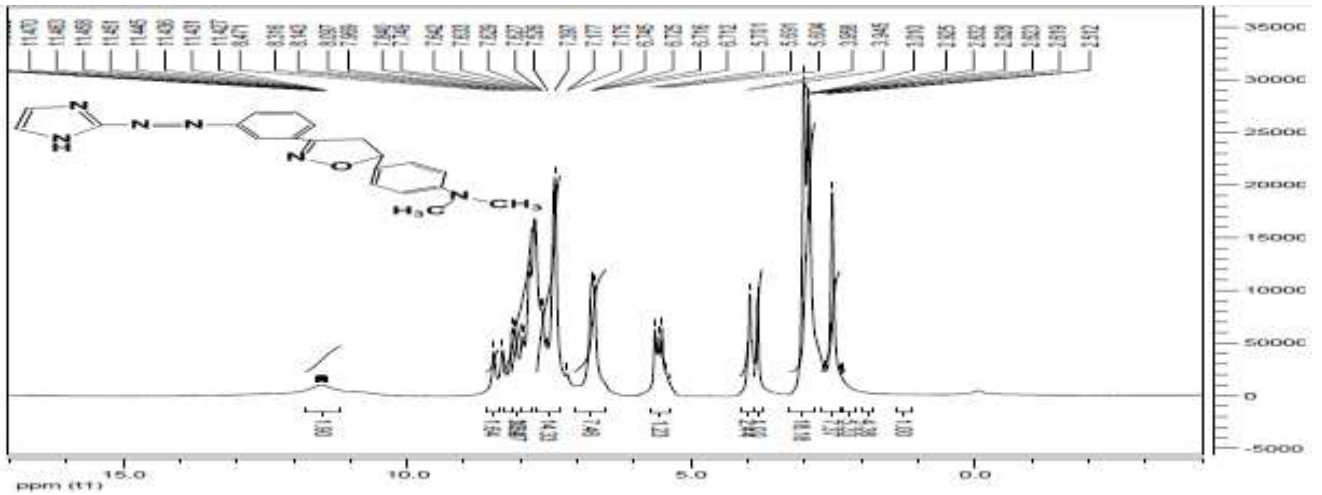

Fig. 31:[1]H NMR spectrum of compound (11)

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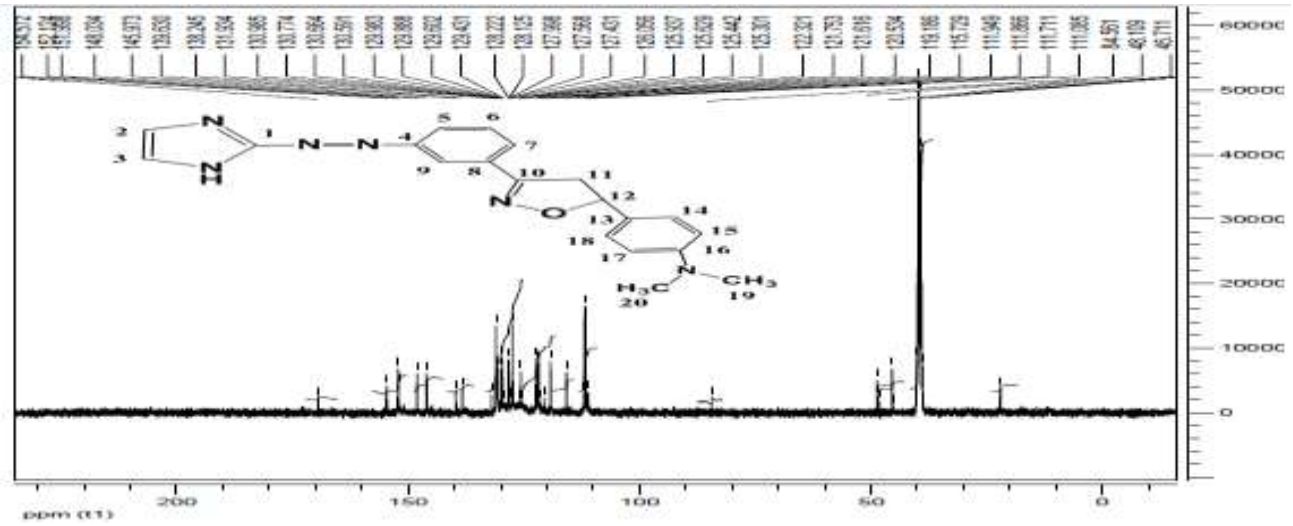

Fig. 32:^{13}C-NMRspectrum of compound (11)

***Compound (12)*:4-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-6-(p-tolyl)-6H-1,3-oxazin-2-amine**

The infrared spectrum data of compound (12) showed band at 1666 cm^{-1} (C=N) oxazine, 3001 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (NH_2) of oxazine that show at 3263 cm^{-1}, 1635 cm^{-1} for (C=N) inside imidazole ring, 2923 cm^{-1} for (C-H) for (CH_3), 1442 cm^{-1} for (N=N) and 1620 cm^{-1} due to aromatic (C=C) .The ^{1}H NMR (DMSO) spectrum data of compound (12) show δ:7.1-8.4 (m ,9H,Ar-H), 1.5(S,3H,CH_3), 13 (S,1H,NH imidazol ring),8.4(S, 2H, CH imidazol ring) , 5.6(S,1H,NH_2oxazine ring), 3.5 (d,1H,O-CHoxazine ring) .The C^{13}-NMR (DMSO) spectrum data of compound (12) show δ: 20 (C_{20}), 159 (C_{11}), 26(C_{12}), 130 (C_{10}),129.8 (C_1) ,127.7-129.5 (Caromatic).

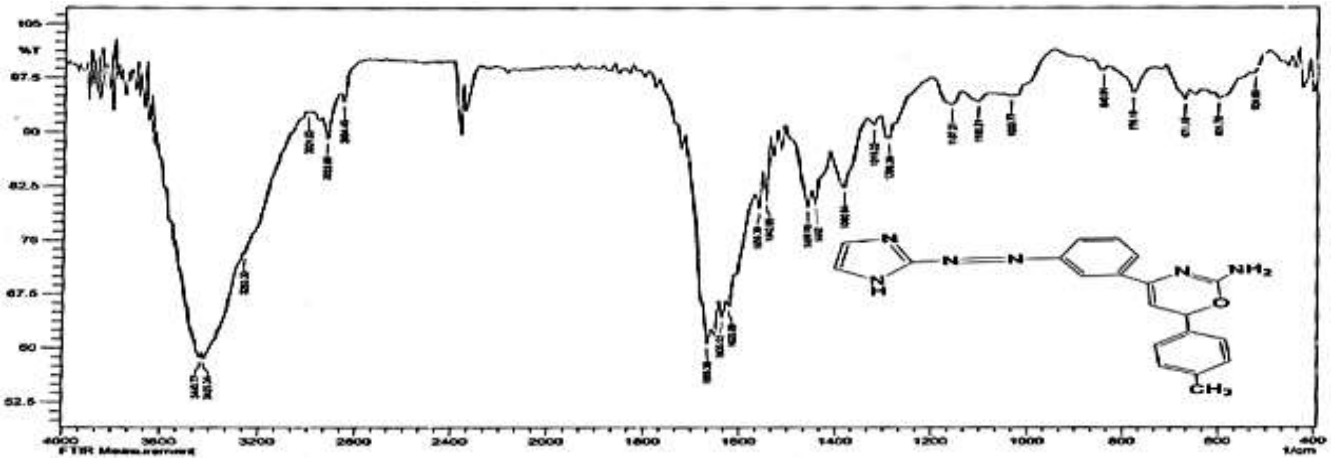

Fig 33:FT-IRspectra of compound [12]

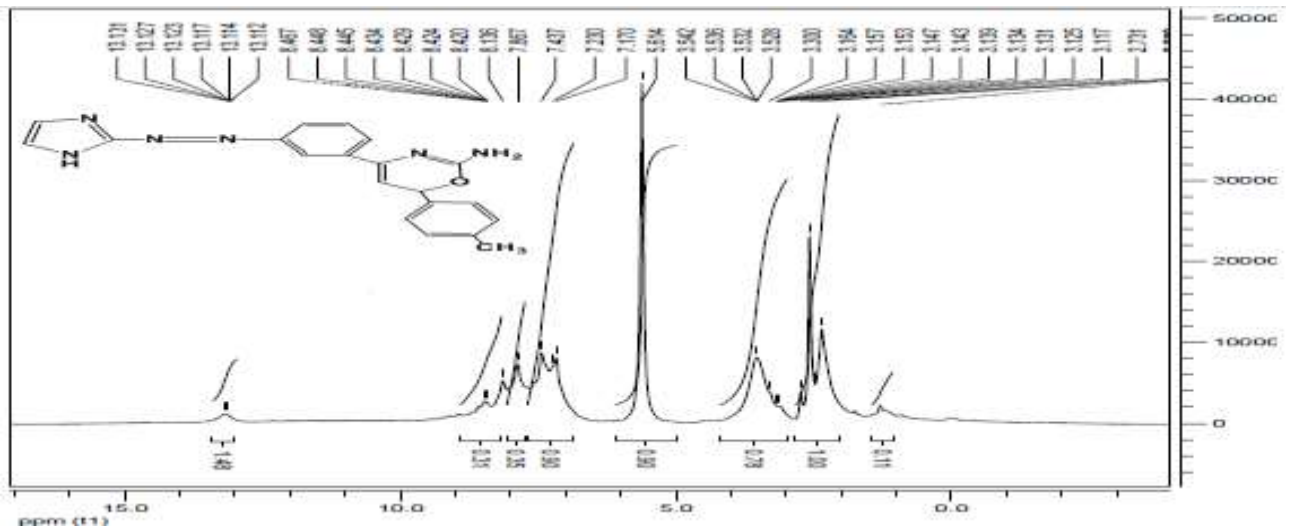

Fig. 34: 1H NMR spectrum of compound (12)

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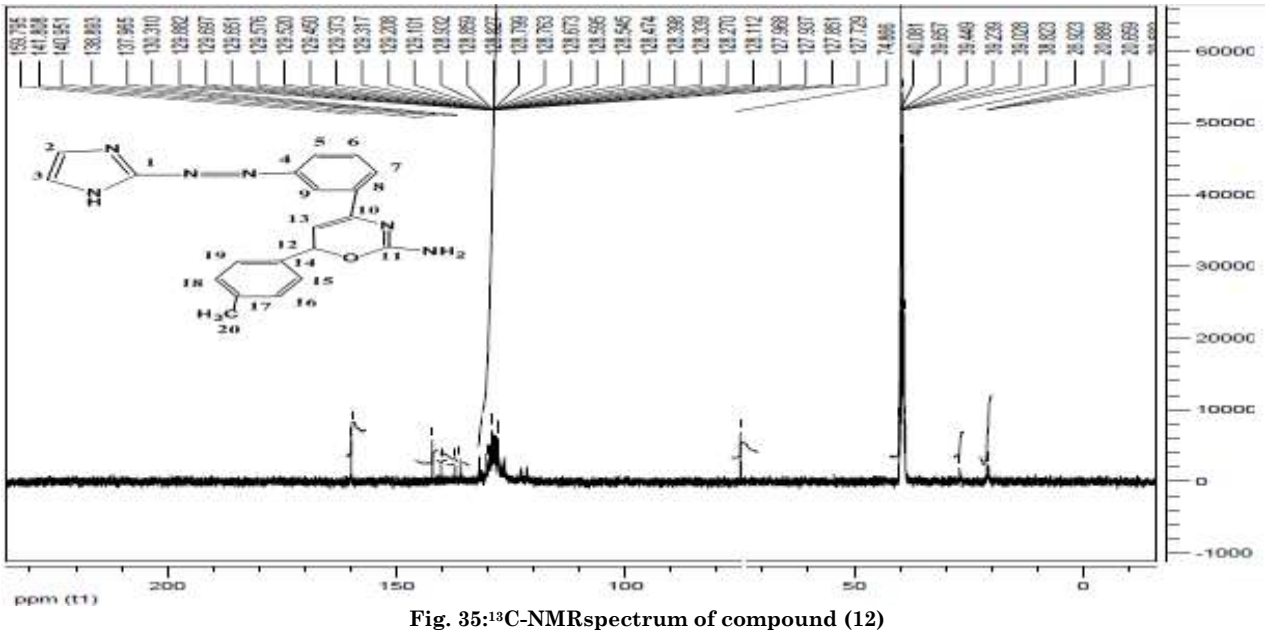

Fig. 35:^{13}C-NMRspectrum of compound (12)

Compound *(13)*:4-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-6-(4-(dimethylamino) phenyl)-6H-1, 3-oxazin-2-amineThe infrared spectrum data of compound (13) showed band at 1650 cm^{-1} for (C=N) oxazine , 3001cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (NH_2) of oxazine that show at 3363 cm^{-1}, 1596 cm^{-1} for (C=N) inside imidazole ring, 2923 cm^{-1} for (C-H) for (CH_3), 1442 cm^{-1} for (N=N) and 1558 cm^{-1} due to aromatic (C=C).The ^{1}H NMR (DMSO) spectrum data of compound (13) show δ: 6.6-8.4 (m ,9H,Ar-H), 2.8(S,6H,CH3),13 (S,1H,NH imidazol ring),8.4 (S, 2H, CH imidazol ring),5.5(S,2H,NH_2oxazine ring), 3(d,1H,O-CHoxazine ring) .The C^{13}-NMR (DMSO) spectrum data of compound (13) show δ: 20 ($C_{20,21}$), 159 (C_{11}), 26(C_{12}), 130 (C_{10}),129.8 (C_1) ,127.7-129.5 (Caromatic).

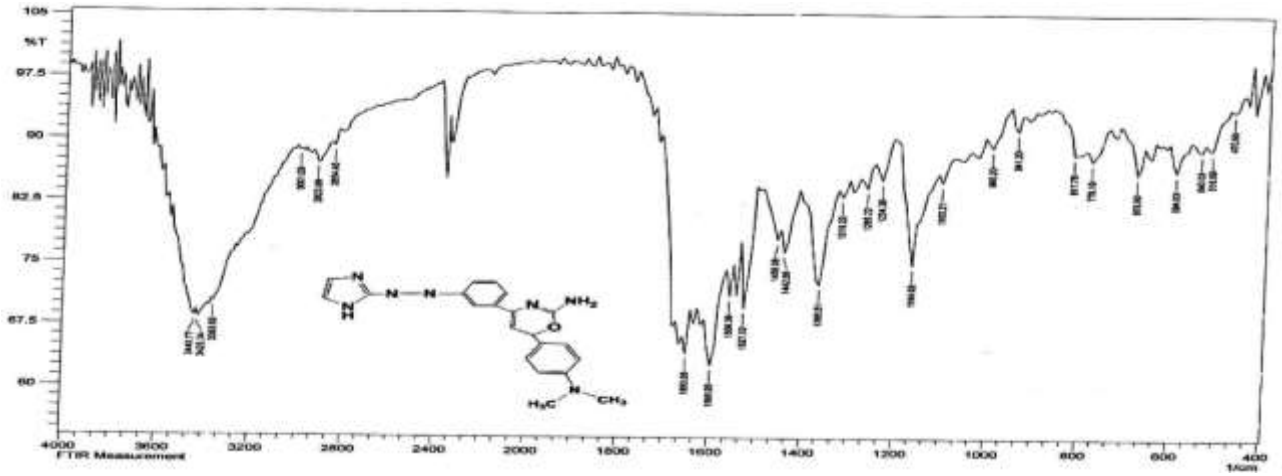

Fig 36:FT-IRspectra of compound [13]

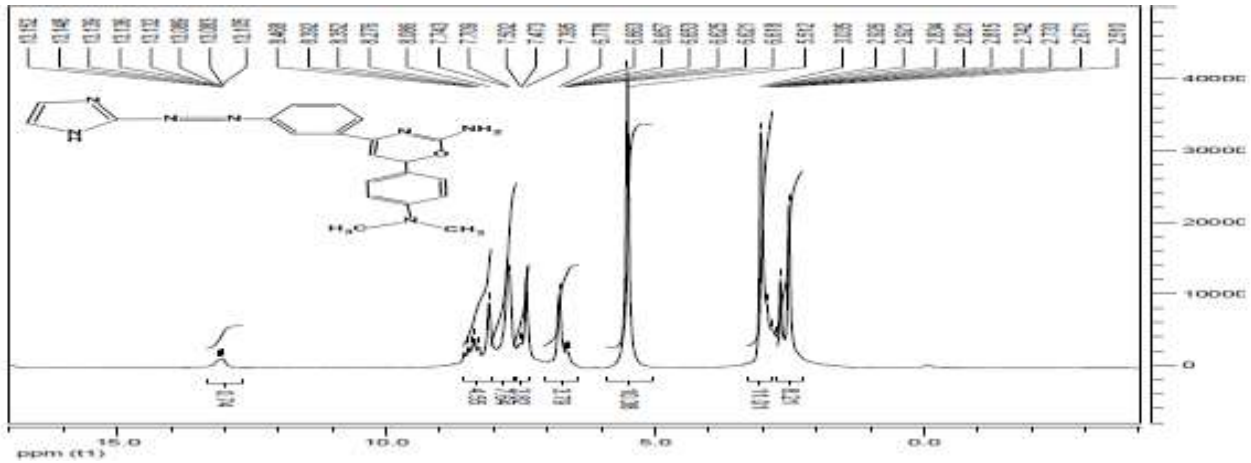

Fig. 37:^{1}H NMR spectrum of compound (13)

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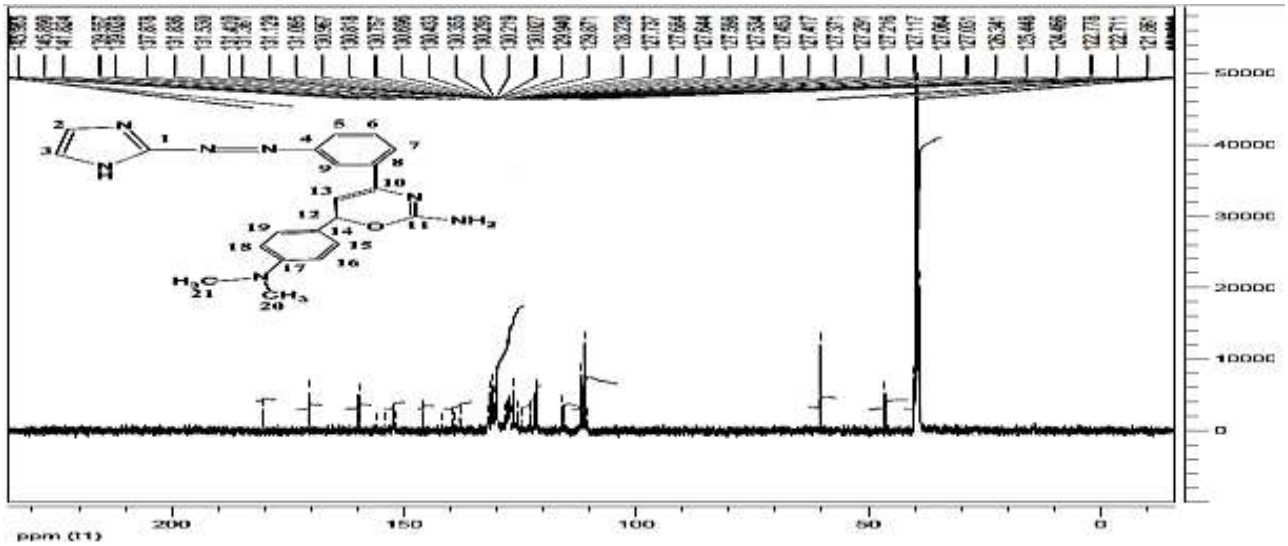

Fig. 38:[13]C-NMRspectrum of compound (13)

Compound*(14)*:4-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-6-(p-tolyl)-6H-1, 3-thiazin-2-amine

The infrared spectrum data of compound (14) showed band at1650cm^{-1}(C=N) thiazine,3024 cm^{-1} for (Ar-H),3440 cm^{-1} for (N-H) imidazole with band for (NH_2)of thiazine that show at 3425 cm^{-1}, 1635 cm^{-1} for (C=N) inside imidazole ring, 2923 cm^{-1} for (C-H) for(CH_3), 1458 cm^{-1} for (N=N) and 1558 cm^{-1} due to aromatic (C=C).The ^{1}H NMR (DMSO) spectrum data of compound (14) show δ:7.1-8.1 (m ,9H,Ar-H), 2.3(S,3H,CH3),12.9 (S,1H,NH imidazol ring),8.3(S, 2H, CH imidazol ring) , 5.5(S,2H,NH_2thiazine ring),4.5 (d,1H,S-CH thiazine ring) .The C^{13}-NMR (DMSO) spectrum data of compound (14) show δ:20 (C_{20}), 175 (C_{11}), 167(C_{10}), 147 (C_8),139 (C_{14}) 32 (C_{12}), 138 (C_{17}) ,111-129 (Caromatic).

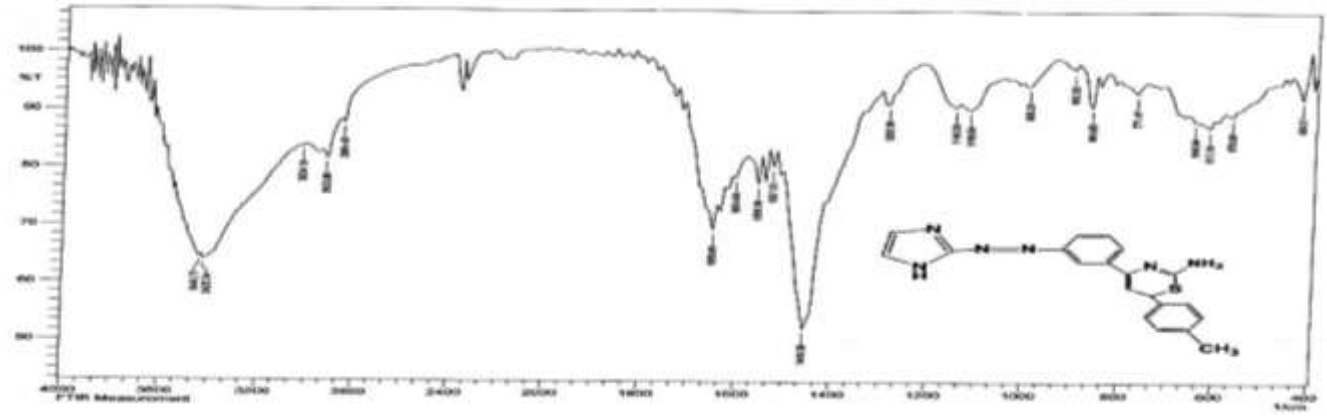

Fig 39:FT-IRspectra of compound [14]

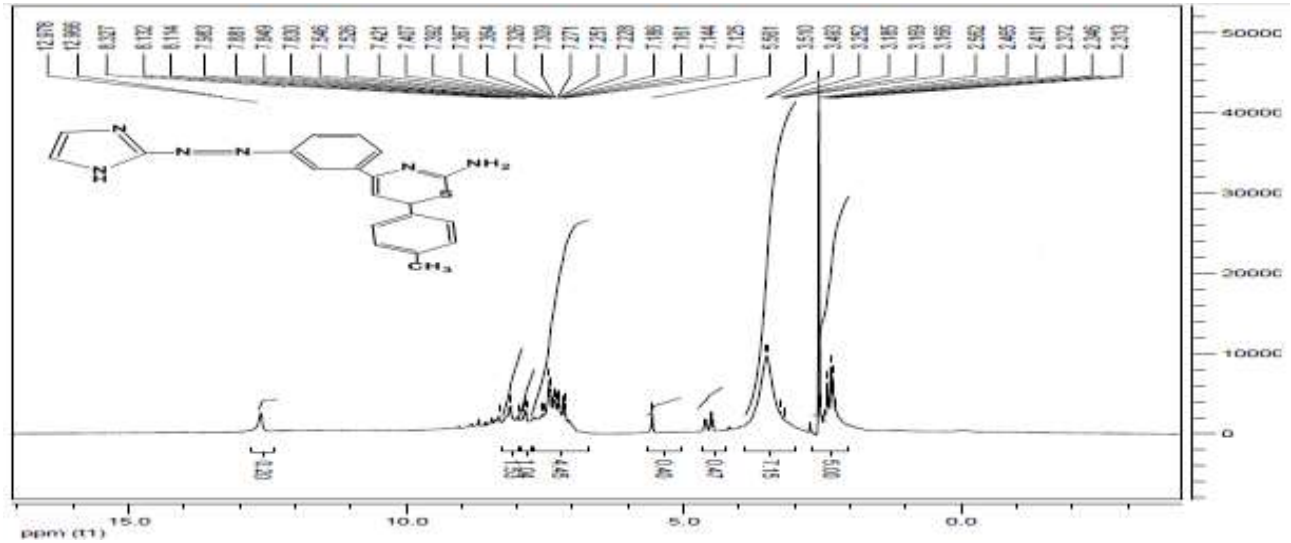

Fig. 39:[1]H NMR spectrum of compound (14)

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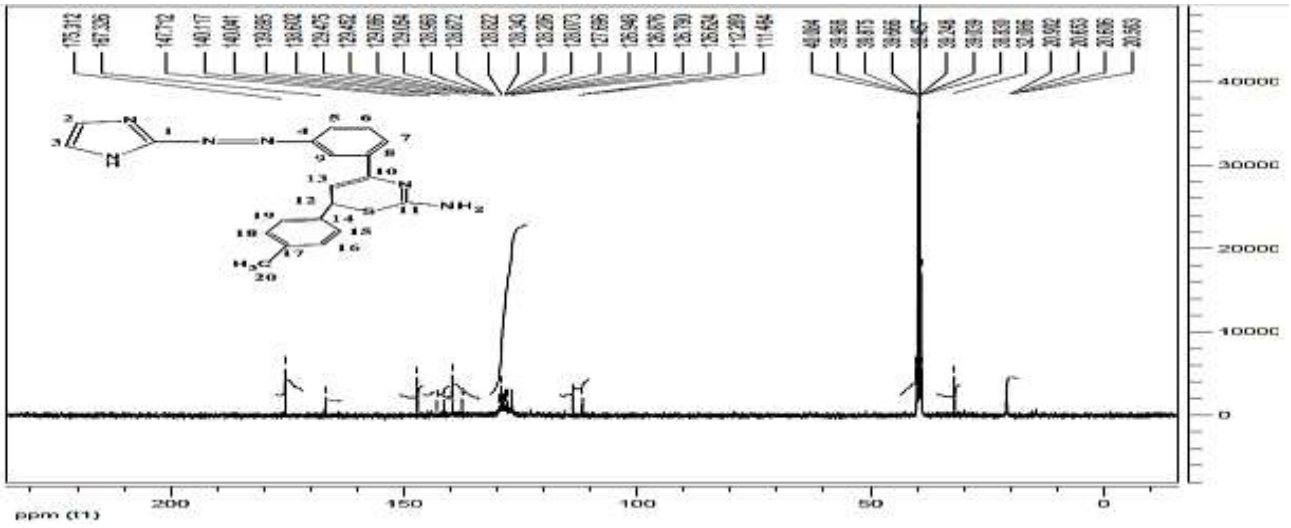

Fig. 40:^{13}C-NMRspectrum of compound (14)

***Compound (15)*:4-(3-((1H-imidazol-2-yl) diazenyl) phenyl) -6-(4 (dimethylamino) phenyl)-6H-1,3-thiazin-2-amine**

The infrared spectrum data of compound (15) showed band at 1650 cm^{-1} for (C=N) thiazine ,3031 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (NH_2)of thiazine that show at 3409 cm^{-1},1589 cm^{-1} for (C=N) inside imidazole ring, 2916 cm^{-1} for (C-H) for (CH_3),1450 cm^{-1} for (N=N) and 1527 cm^{-1} due to aromatic (C=C).The ^{1}H NMR (DMSO) spectrum data of compound (15) show δ :6.7-8 (m ,9H,Ar-H), 2.9(S,3H,CH3),13 (S,1H,NH imidazol ring),8.3 (S, 2H, CH imidazol ring) , 5.4(S,2H,NH_2thiazine ring),4.4 (d,1H,S-CH thiazine ring) .The C^{13}-NMR (DMSO) spectrum data of compound (15) show δ: 30 (C20,C21), 60 (C12), 152(C17), 145 (C10),163 (C11),136 (C8),115-133 (Chromatic).

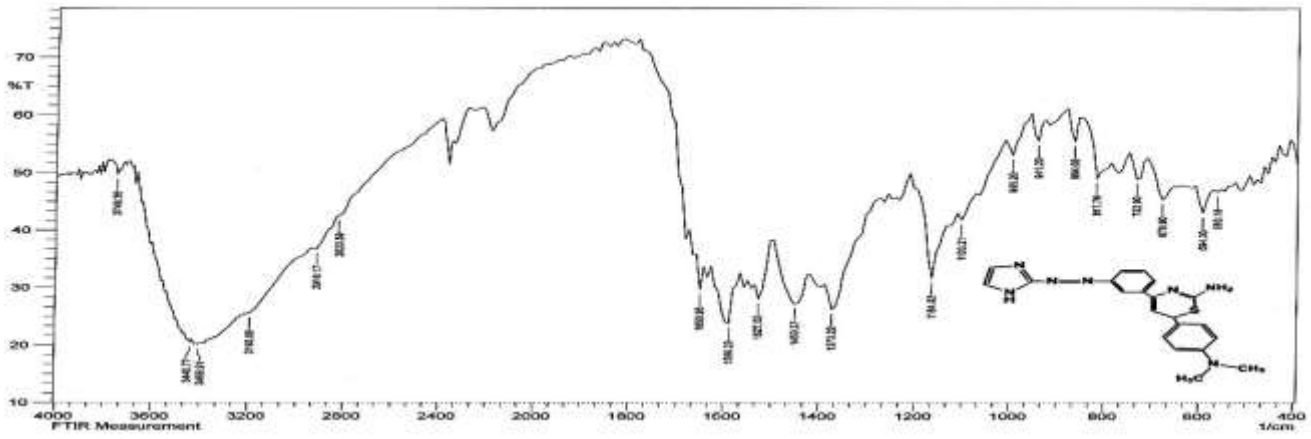

Fig 41:FT-IRspectra of compound [15]

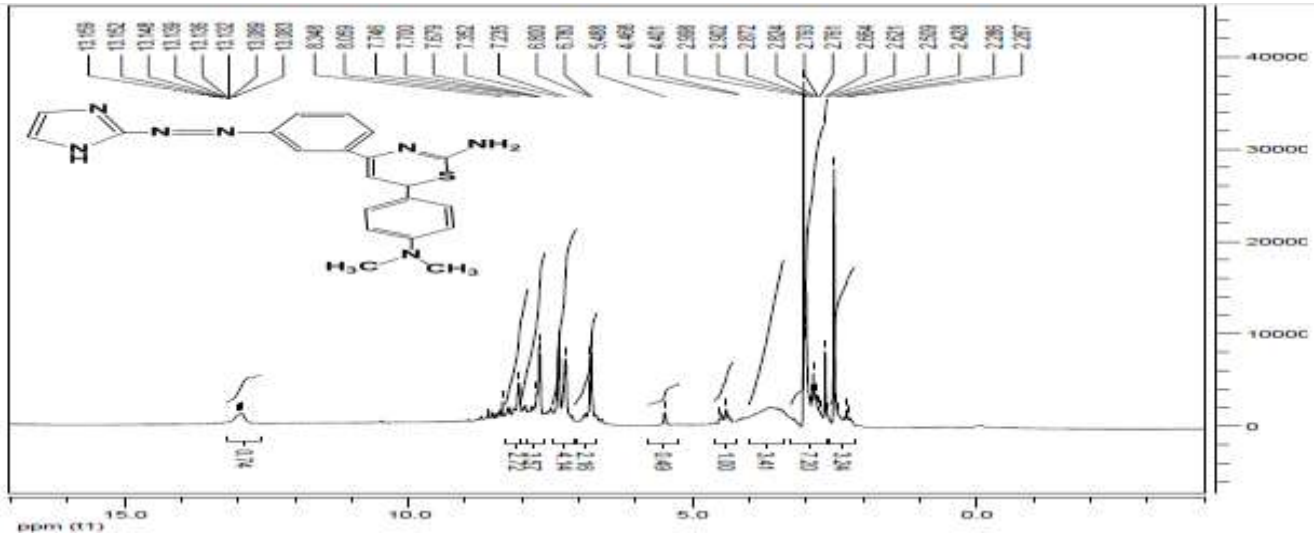

Fig. 42:^{1}H NMR spectrum of compound (15)

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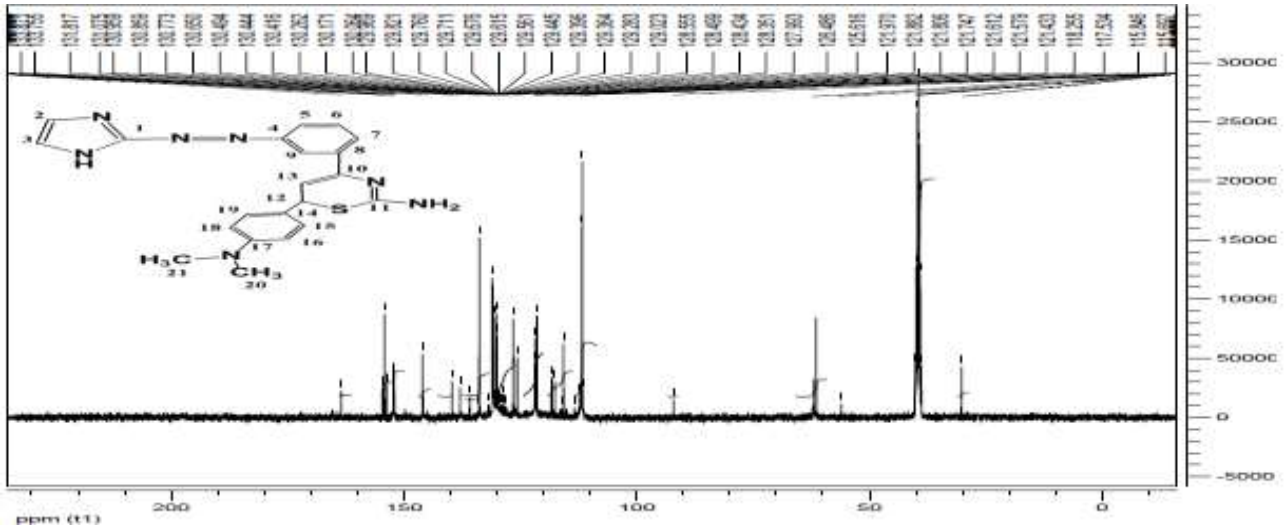

Fig. 43:[13]C-NMRspectrum of compound (15)

***Compound (16)*:6-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-2-oxo-4-(p-tolyl)-1, 2dihydropyridine-3-carbonitrile**

The infrared spectrum data of compound (16) showed band at 1743 cm^{-1} for (C=O), 3004 cm^{-1} for (Ar-H), 3444 cm^{-1} for (N-H) imidazole overlapping with band for (N-H)of pyridine that show at 3421 cm^{-1}, 1658 cm^{-1} for (C=N) inside imidazole ring, 2985 cm^{-1} for (C-H) for (CH_3), 1404 cm^{-1} for (N=N) , 1596 cm^{-1} due to aromatic (C=C) and 2217cm^{-1} for(C≡N). The ^{1}H NMR (DMSO) spectrum data of compound (16) show δ:6.8-8.4 (m ,9H,Ar-H), 3.4(S,3H,CH3),12(S,1H,NH imidazol ring),8.5(S, 2H, CH imidazol ring) ,4(S,1H,CH pyridine ring),10(S,1H,NH pyridine ring)..The C^{13}-NMR (DMSO) spectrum data of compound (16) show δ:140 (C_1), 115 (C_{21}), 21(C_{22}), 159 (C_{10}),155(C_{14}),135 (C_8), 120-133 (C aromatic).

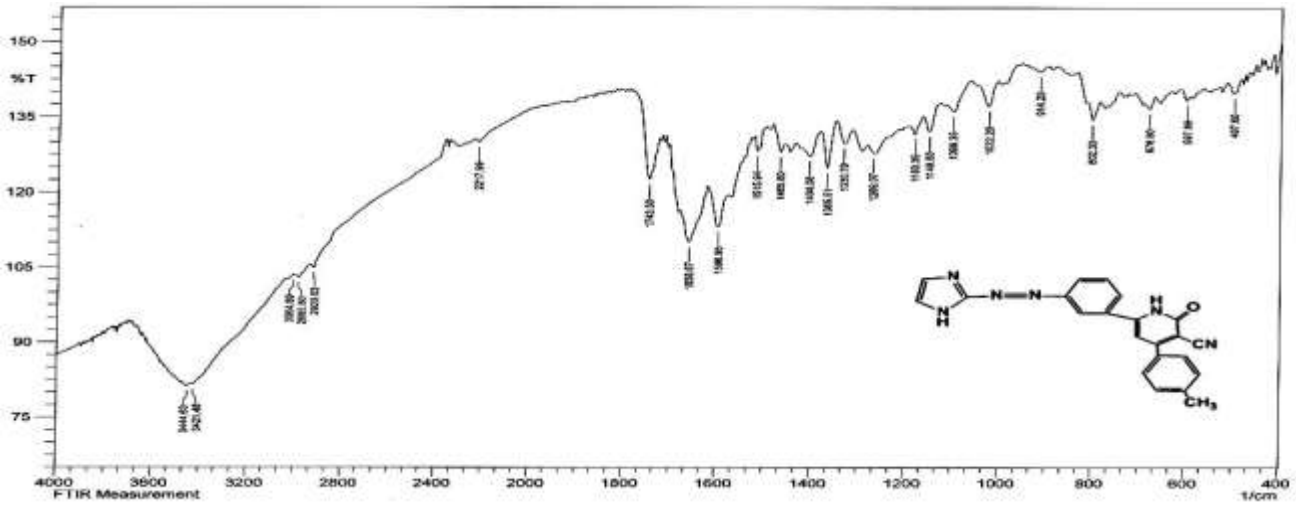

Fig 44: FT-IRspectra of compound [16]

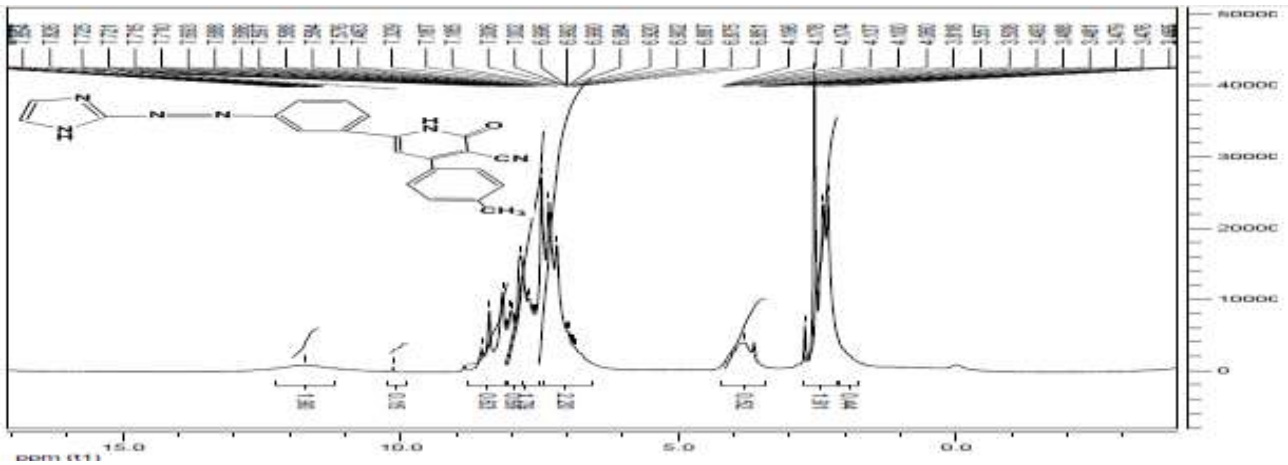

Fig. 45:[1]H NMR spectrum of compound (16)

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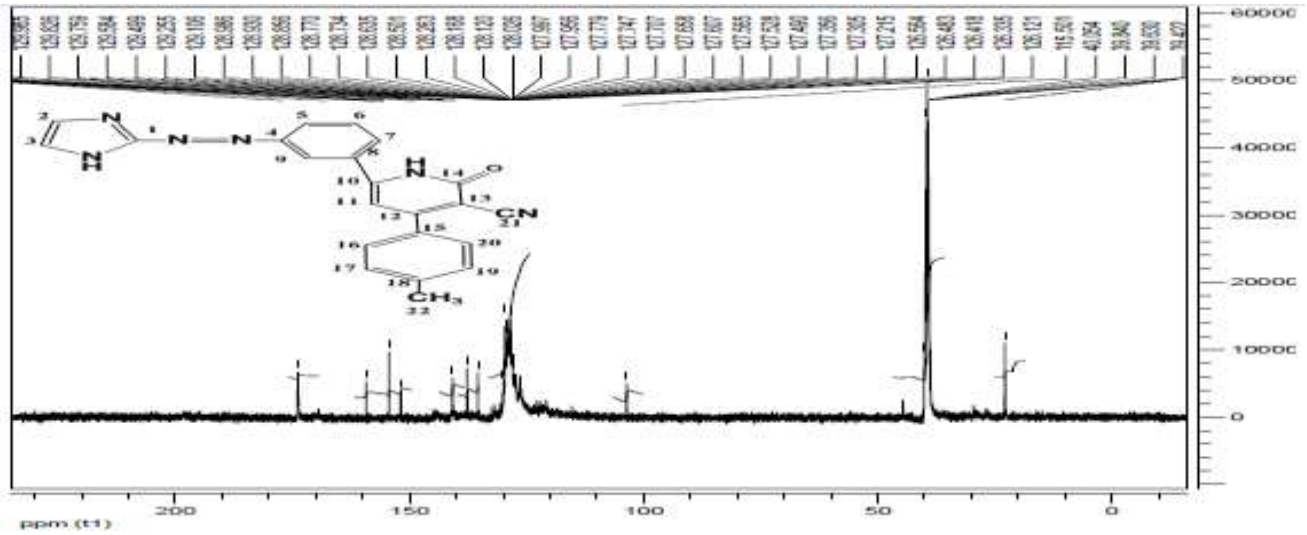

Fig. 46: ^{13}C-NMRspectrum of compound (16)

Compound (17):6-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-4-(4-(dimethylamino) phenyl)-2-oxo-1, 2-dihydropyridine-3-carbonitrile

The infrared spectrum data of compound (17) showed band at 1735 cm^{-1} for (C=O), 3031 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (N-H)of pyridine that show at 3425cm^{-1}, 1650 cm^{-1} for (C=N) inside imidazole ring, 2916 cm^{-1} for (C-H) for (CH_3), 1434 cm^{-1} for (N=N) , 1573 cm^{-1} due to aromatic (C=C) and 2214 cm^{-1} (C≡N) .The ^{1}H NMR (DMSO) spectrum data of compound (17) show δ:6.7-8.3 (m ,8H,Ar-H), 3(S,6H,CH3),13(S,1H,NH imidazol ring),8.4(S, 2H, CH imidazol ring),6.6(S,1H,CH pyridine ring),11(S,1H,NH pyridine ring)..The C^{13}-NMR (DMSO) spectrum data of compound (17) show δ: 26.9($C_{21,22}$), 183 (C_{14}), 162(C_{10}), 158 (C_{12}),152(C_{18}),111 (C_{11}),111.7(C23),121-131 (Chromatic).

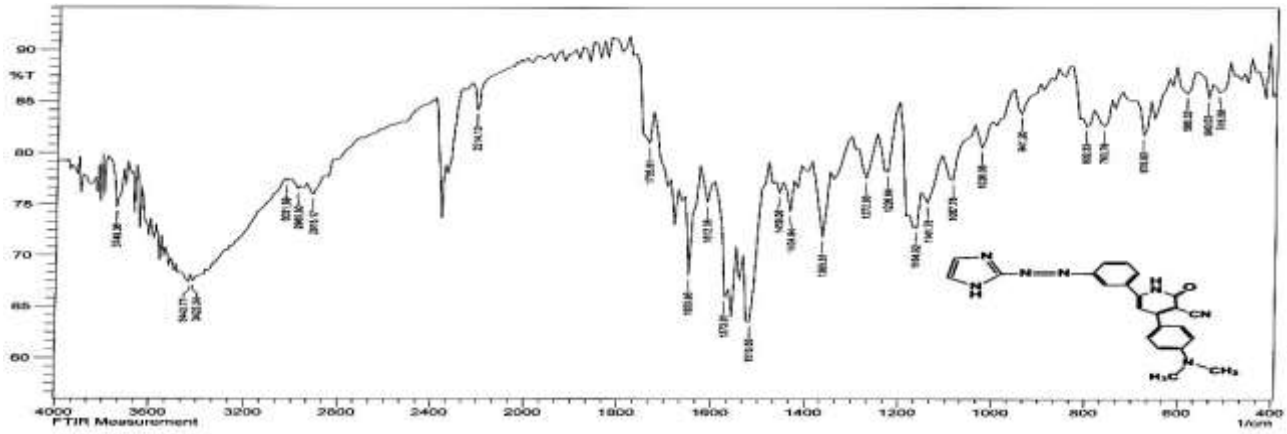

Fig 47: .FT-IRspectra of compound [17]

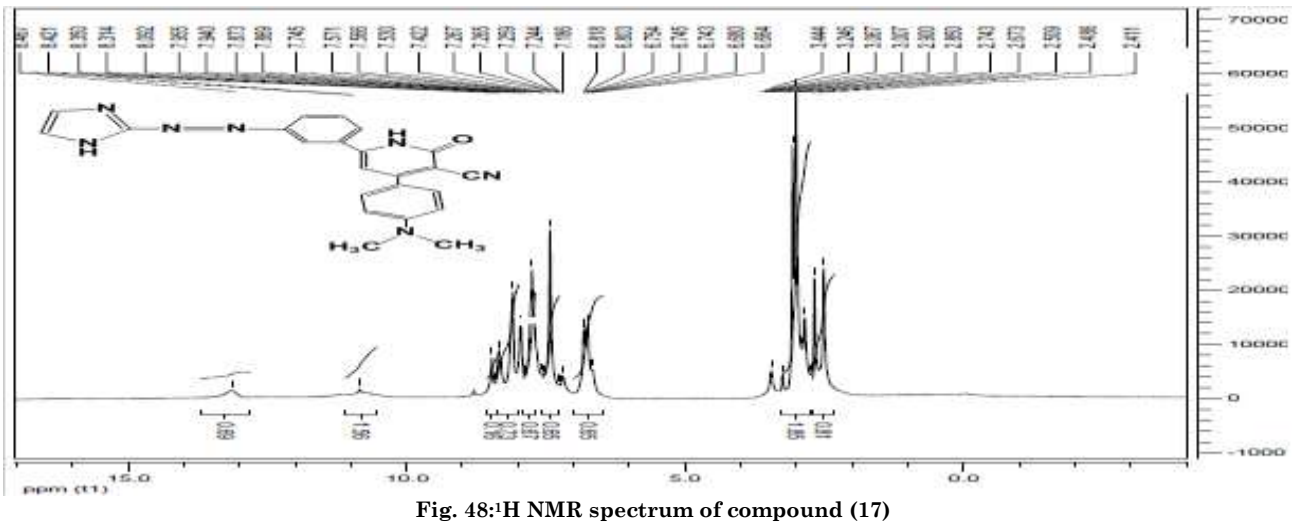

Fig. 48:^{1}H NMR spectrum of compound (17)

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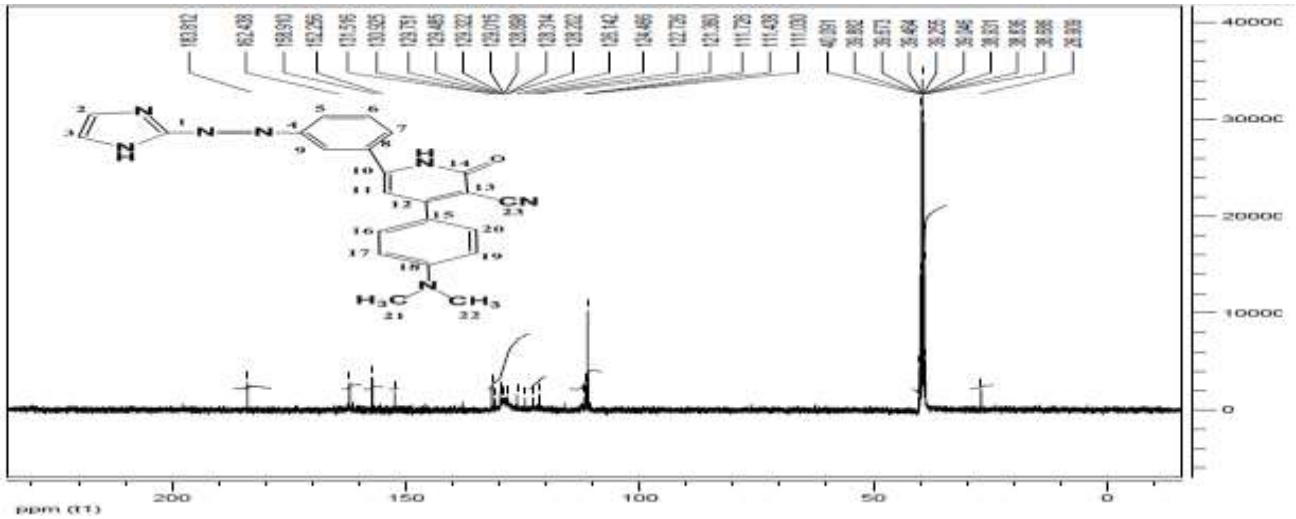

Fig. 49:^{13}C-NMRspectrum of compound (17)

***Compound (18)*: 6-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-2-amino-4-(p-tolyl) nicotinonitrile**

The infrared spectrum data of compound (18) showed band at 1654 $cm^{-1}$for (C=N) pyridine ,3028 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (NH_2)of pyridine that show at 3406cm^{-1}, 1566 cm^{-1} for (C=N) inside imidazole ring, 2920 cm^{-1} for (C-H) for (CH_3), 1404 cm^{-1} for (N=N) , 1515 cm^{-1} (C=C) aromatic ring and 2198 cm^{-1} for(C≡N) .The ^{1}H NMR (DMSO) spectrum data of compound (18) show δ:7.1-7.9 (m ,9H,Ar-H), 1.9(S,3H,CH3),13 (S,1H,NH imidazol ring), 7.9(S, 2H, CH imidazol ring),5.5 (S,2H,NH_2pyridine ring) The C^{13}-NMR (DMSO) spectrum data of compound (18) show δ: 138 (C_8), 157 (C_{10}), 188(C_{11}), 82 (C_{12}),152 (C_{13}) 131 (C_{15}), 130(C_{18}), 21 (C_{21}), 115 (C_{22}),120 -144 (C aromatic).

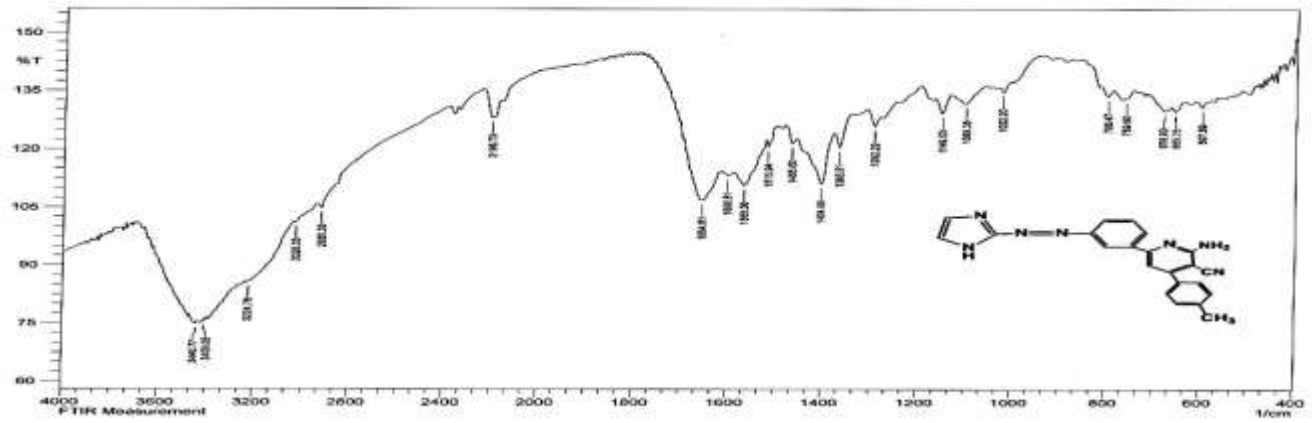

Fig 50:FT-IRspectra of compound [18]

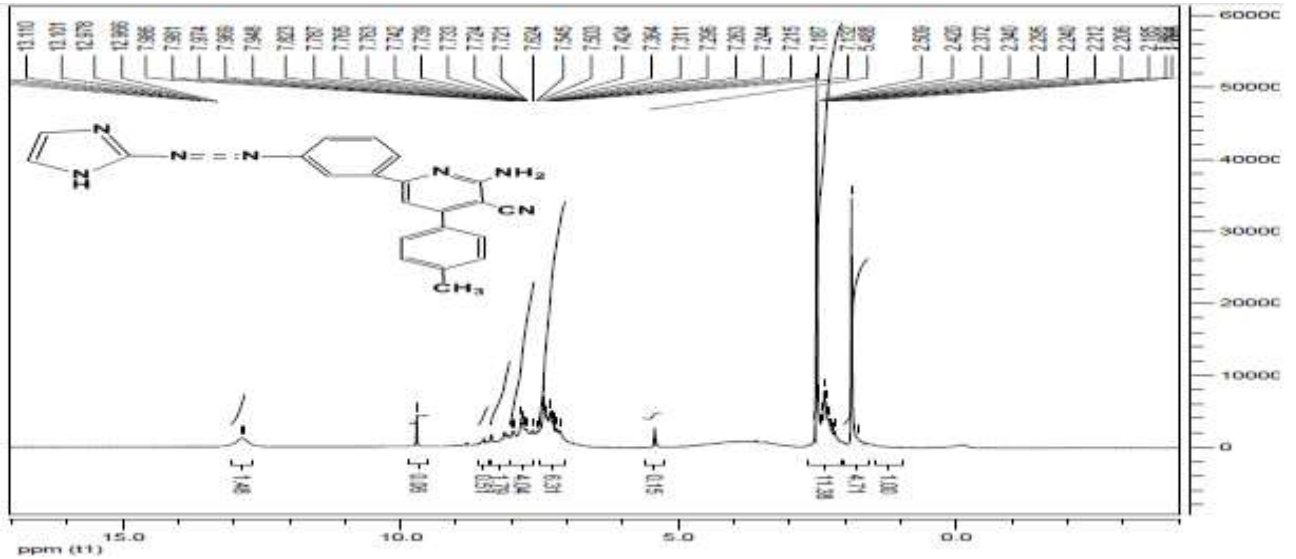

Fig. 51:^{1}H NMR spectrum of compound (18)

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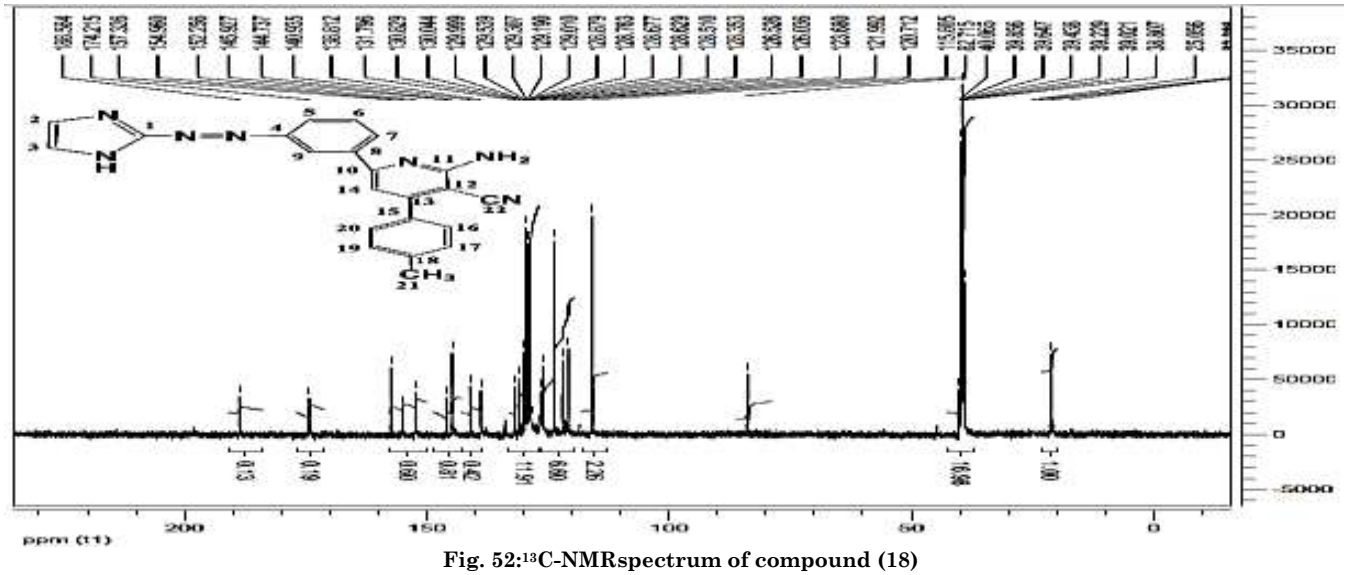

Fig. 52:^{13}C-NMRspectrum of compound (18)

Compound *(19):*6-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-2-amino-4-(4-(dimethylamino) phenyl) nicotinonitrile

The infrared spectrum data of compound (19) showed band at (1650) cm^{-1} for (C=N), 3008 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (NH_2)of pyridine that show at 3263cm^{-1}, 1635 cm^{-1} for (C=N) inside imidazole ring, 2923 cm^{-1} for (C-H) for (CH_3), 1442 cm^{-1} for (N=N) , 1558cm^{-1} due to aromatic (C=C) and 2214 cm^{-1} (C≡N) .The ^{1}H NMR (DMSO) spectrum data of compound (19) show δ:6.7-8.4(m ,9H,Ar-H), 3(S,6H,CH3),13 (S,1H,NH imidazol ring), 8.3(S, 2H, CH imidazol ring),5.4 (S,2H,NH_2pyridine ring) The C^{13}-NMR (DMSO) spectrum data of compound (19) show δ: 154 (C_{11}), 153(C_{18}) , 152 (C_{10}), 151 (C_{13}) , 138 (C_1), 139 (C_8), 116 (C_{14}), 44 (C_{22}, C_{23}),112 (C_{21}), 126-130 (C aromatic).

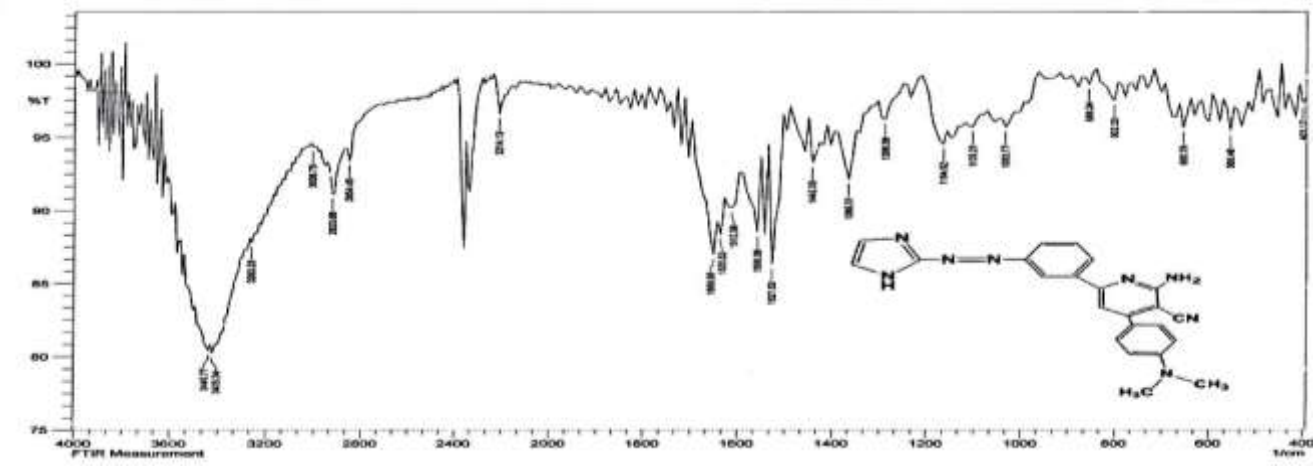

Fig 53: FT-IRspectra of compound [19]

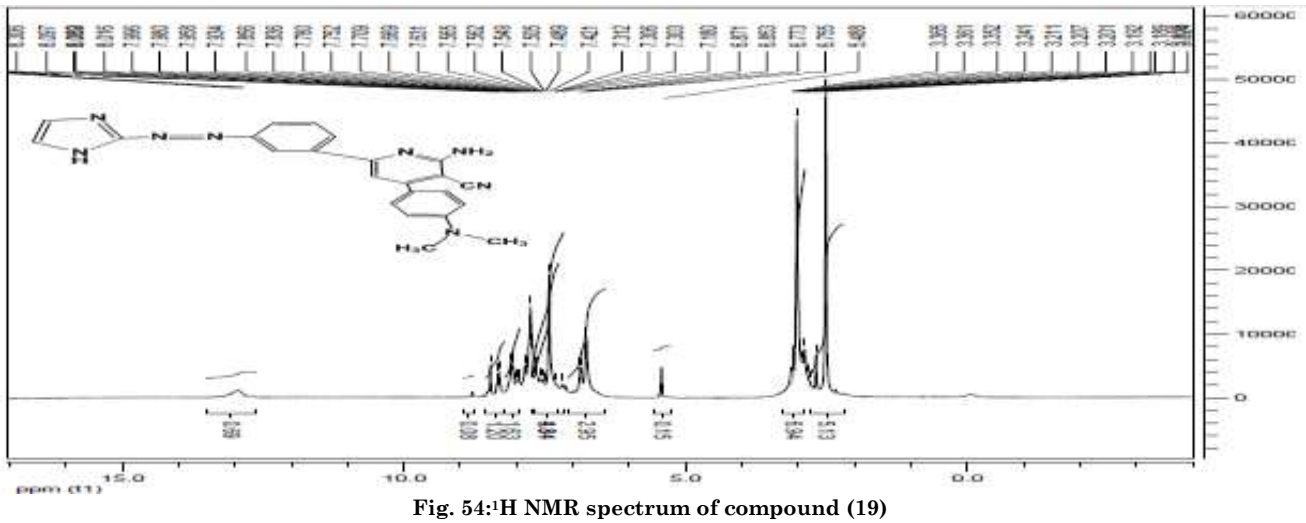

Fig. 54:^{1}H NMR spectrum of compound (19)

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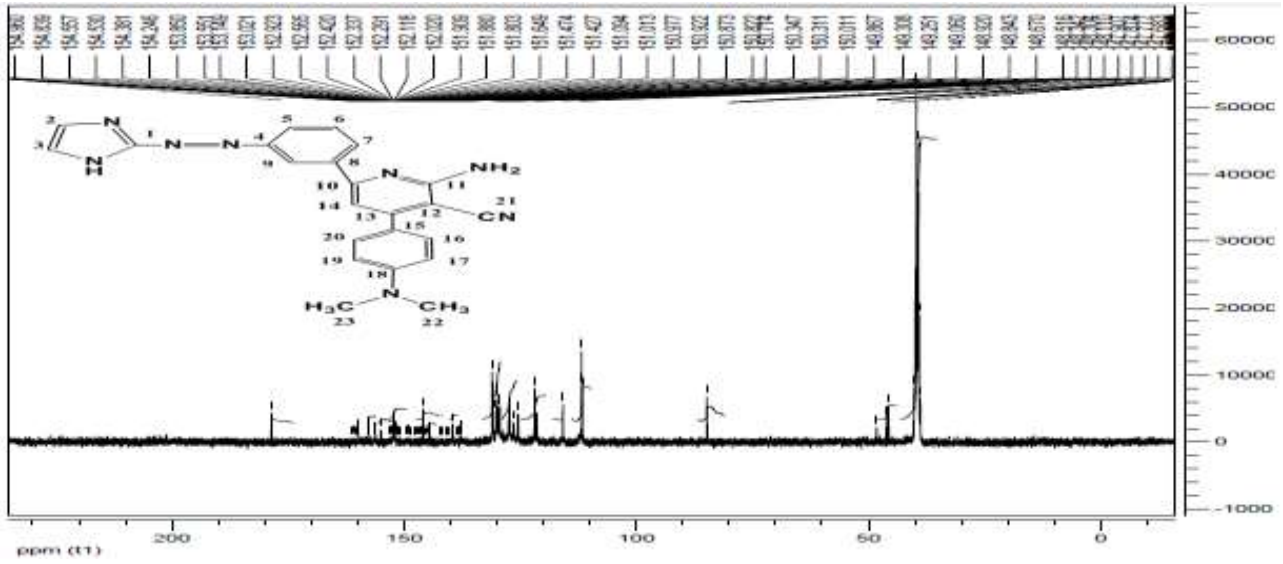

Fig. 55:^{13}C-NMRspectrum of compound (19)

Compound (20):4-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-6-(p-tolyl)-1, 6-dihydropyrimidin-2-amine

The infrared spectrum data of compound (20) showed band at 1666 cm^{-1}for (C=N) pyrimidine, 3085 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (NH_2)of pyrimidine that show at 3355cm^{-1},1596 cm^{-1} for (C=N) inside imidazole ring, 2839 cm^{-1} for (C-H) for (CH_3),1411 cm^{-1} for (N=N) and 1542 cm^{-1} due to aromatic (C=C) .The ^{1}H NMR (DMSO) spectrum data of compound (20) show δ:6.6-8.4(m ,9H,Ar-H), 2.13 (S,3H,CH3), 13 (S,1H,NH imidazol ring), 8.4(S, 2H, CH imidazol ring) , 5 (S,2H,NH_2pyrimidinering)The C^{13}-NMR (DMSO) spectrum data of compound (20) show δ: 175 (C_{13}), 158(C_{10}) , 144 (C_1), 140 (C_8) , 24 (C_{20}), 162 (C_{12}), 120-138 (C aromatic).

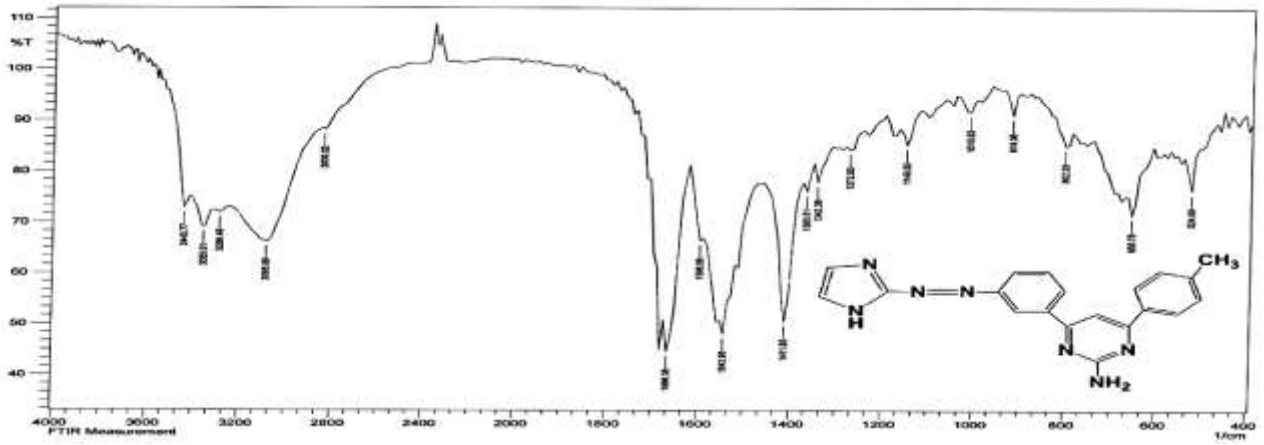

Fig 56: FT-IRspectra of compound [20]

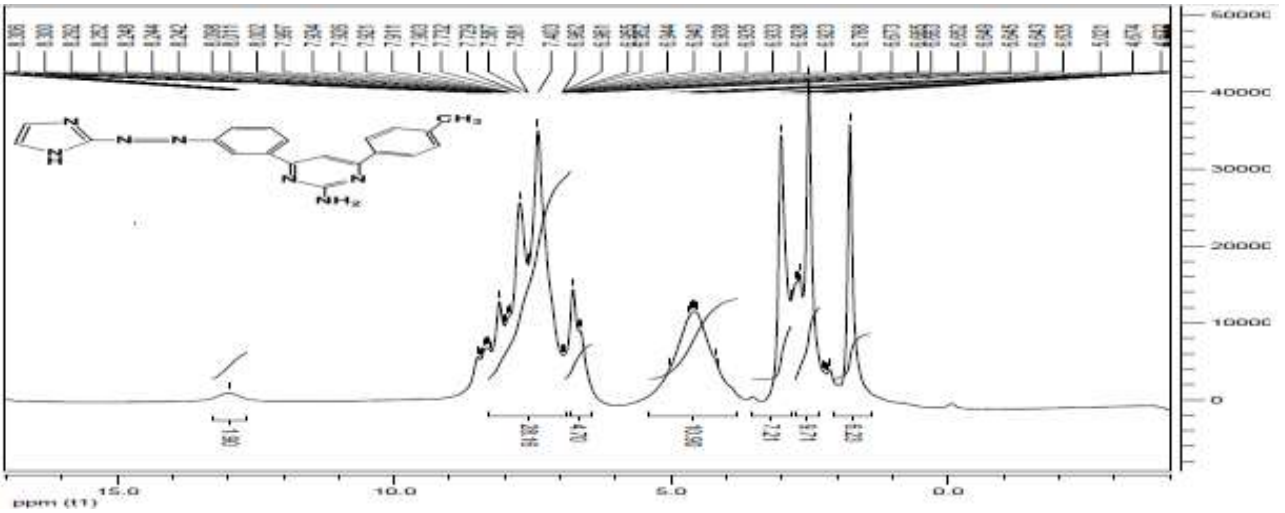

Fig. 57:^{1}H NMR spectrum of compound (20)

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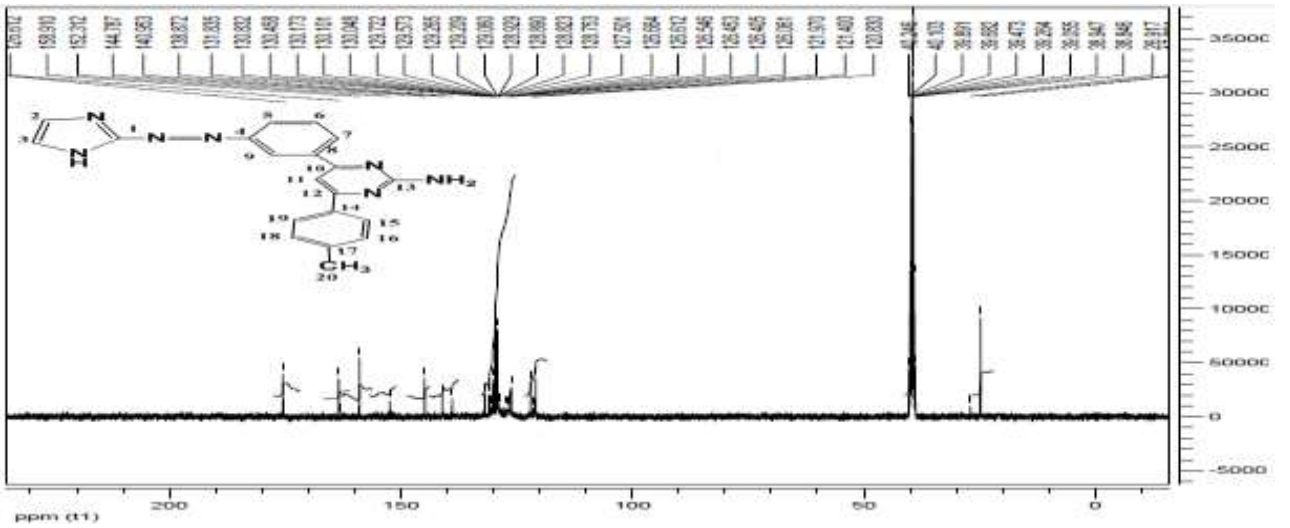

Fig. 58:^{13}C-NMRspectrum of compound (20)

Compound (21):4-(3-((1H-imidazol-2-yl) diazenyl) phenyl)-6-(4-(dimethylamino) phenyl)-1, 6-dihydropyrimidin-2-amine

The infrared spectrum data of compound (21) showed band at 1650 cm^{-1}for (C=N) pyrimidine, 3008 cm^{-1} for (Ar-H), 3440 cm^{-1} for (N-H) imidazole with band for (NH_2)of pyridine that show at 3425cm^{-1}, 1596 cm^{-1} for (C=N) inside imidazole ring, 2923 cm^{-1} for (C-H) for (CH_3), 1419 cm^{-1} for (N=N) ,and 1558 cm^{-1} due to aromatic (C=C).The ^{1}H NMR (DMSO) spectrum data of compound (21) show δ:7.4 -8.4(m ,9H,Ar-H), 3(S,6H,CH3),13 (S,1H,NH imidazol ring), 8.4 (S, 2H, CH imidazol ring),6.7(S,2H,NH_2pyrimidine ring) .The C^{13}-NMR (DMSO) spectrum data of compound (21) show δ:155 (C_{17}),175(C_{13}),158 (C_{12}), 154 (C_{10}),145 (C_1), 35 ($C_{20,21}$), 111-131 (Caromatic).

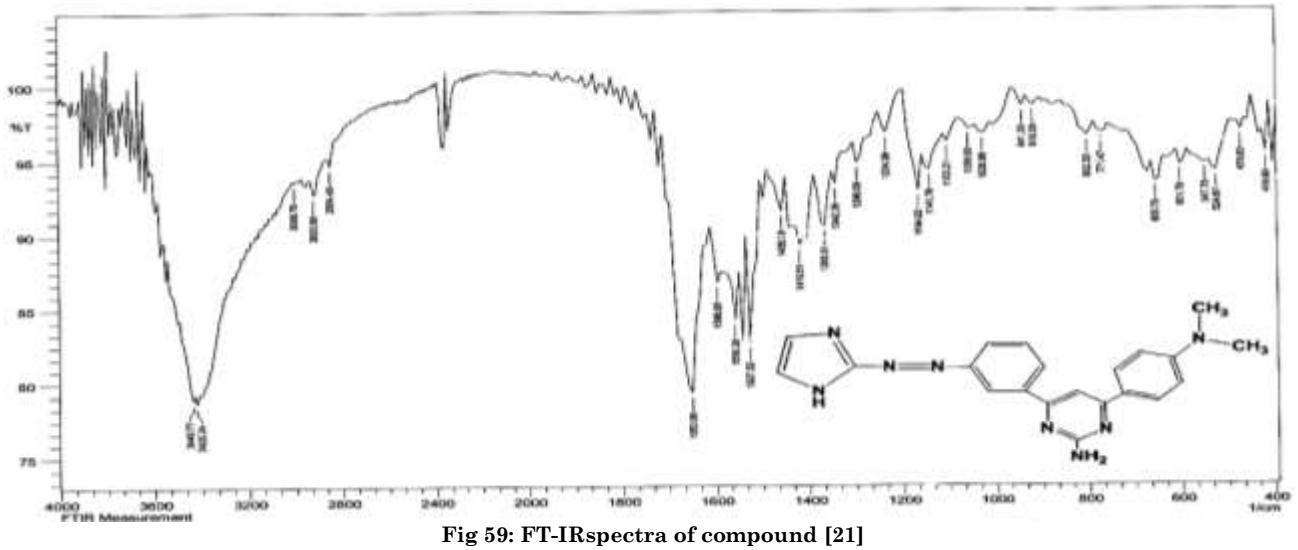

Fig 59: FT-IRspectra of compound [21]

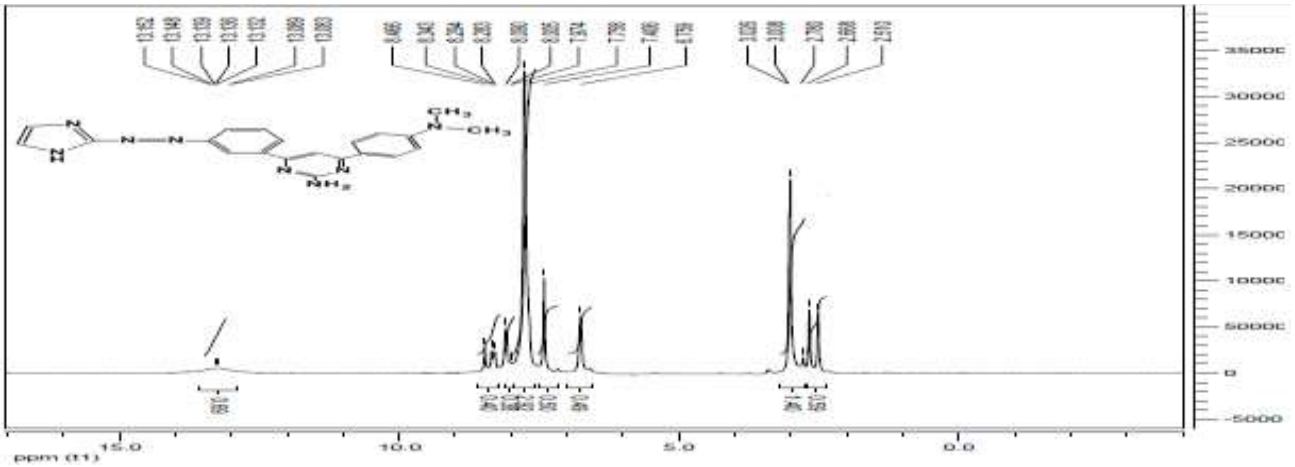

Fig. 60:^{1}H NMR spectrum of compound (21)

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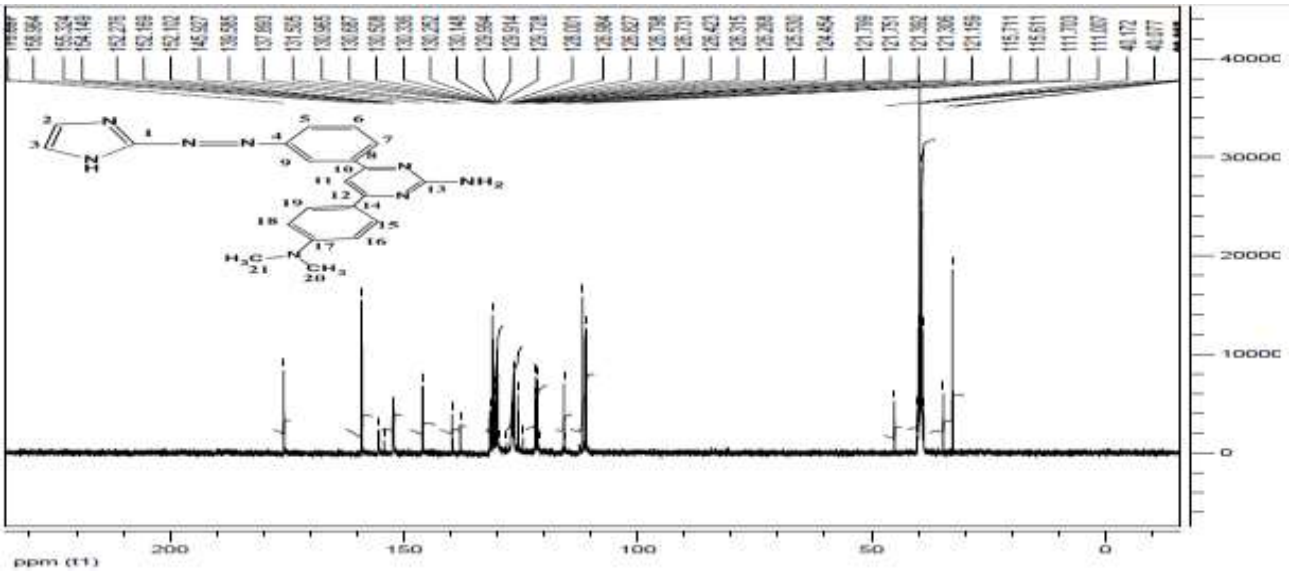

Fig. 61:^{13}C-NMRspectrum of compound (21)

Conclusion

From the above studies it can be concluded that the synthesized compounds exhibit significant antibacterial activityagainst bacteria staphylococcus aurous and Escherichia coli, the compounds that appeared good activity are (1,2,5,6,7,8,12,17,21,22,23,27) against (staphylococcus aurous) on other hand, compounds (1,3,4,6,8,21,22,23,27) show good activity against (Escherichia coli), the results of the antibacterial activity are shown in the Fig. (62,63).

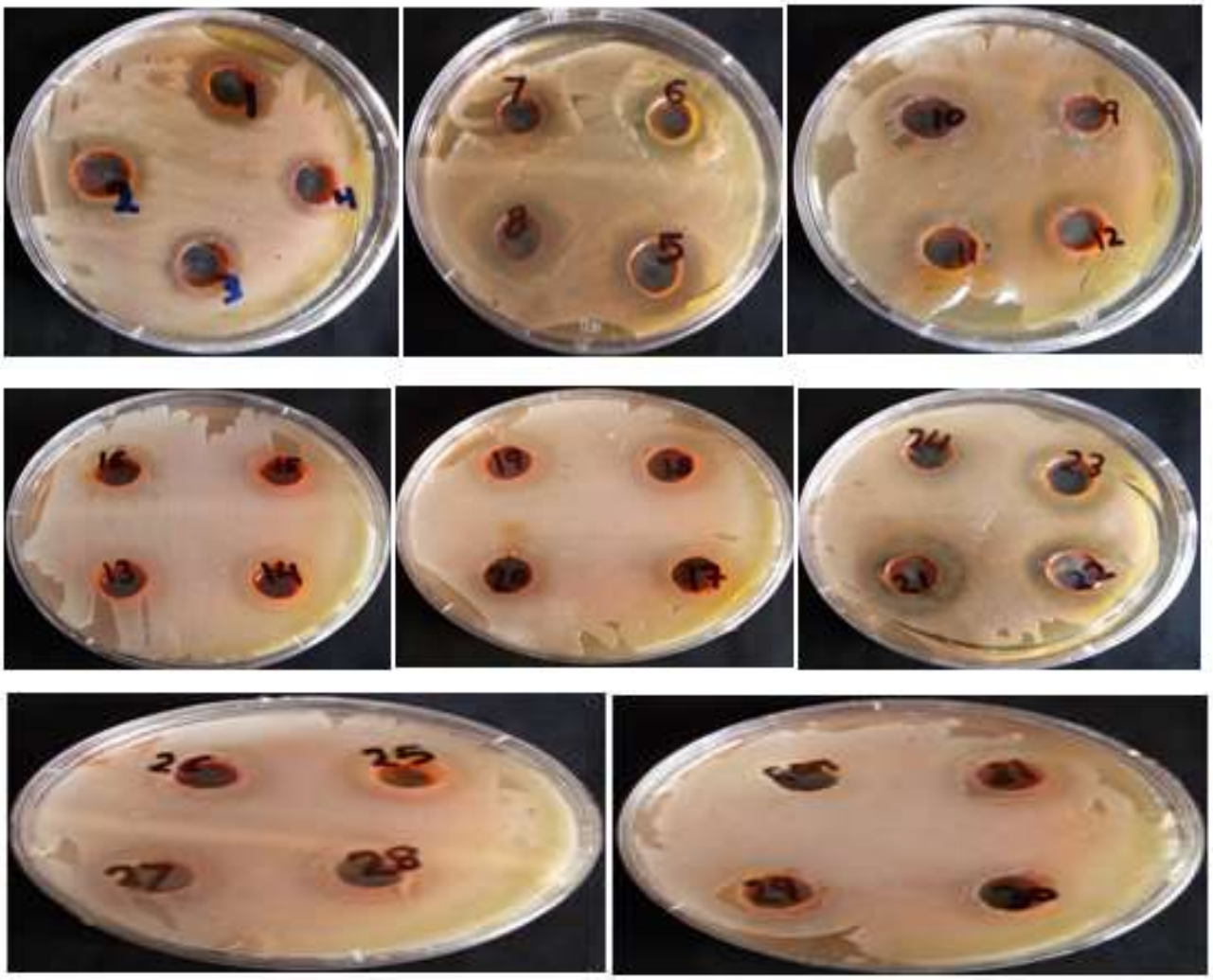

Fig. 62: Biological activity of compounds prepared against *Escherichia coli* bacteria

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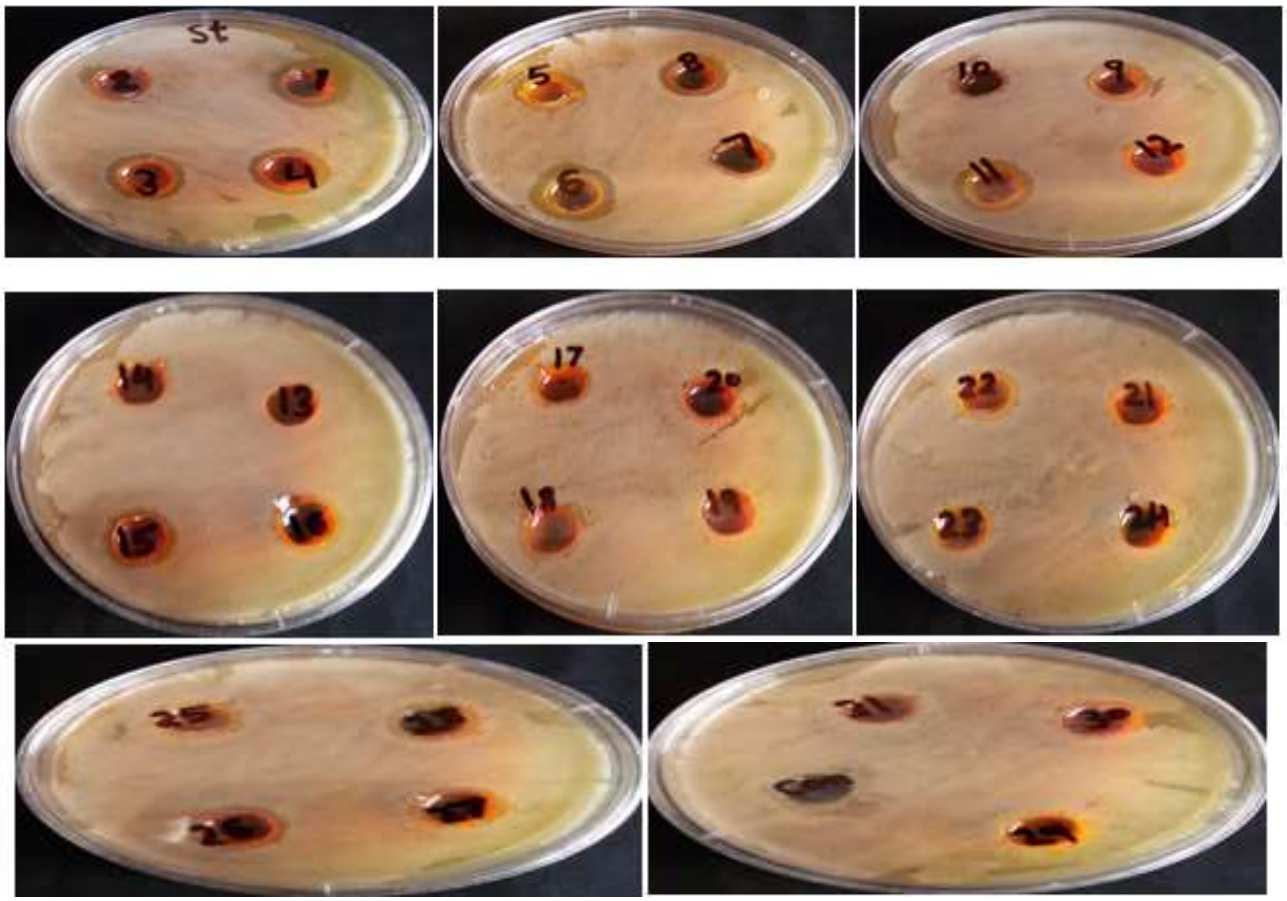

Fig. 63:Biological activity of compounds prepared against Staphylococcusureus bacteria

Table 1: Show Biological activity for compounds (1-21)

Bacterial species		Compounds No.	Bacterial species		Compounds No.
Staph. aureus	E. coli		Staph. aureus	E. coli	
++	+++	12	+++	+++	1
+	+++	13	++	+++	2
+++	+++	14	++	+++	3
+	++	15	+++	++	4
++	++	16	-	+	5
-	++	17	+++	++	6
+	++	18	-	++	7
-	+	19	++	+++	8
++	++	20	++	++	9
-	+++	21	+++	+++	10
			+	++	11

- = No inhibition = inactive, + = (5-10) mm = slightly active, ++ = (11-20) mm = moderately active, +++ = (more than 20) mm = Good active.

Table 2:Physical properties of compounds (1-21)

%	Colour	R.f	M.P (°C)	M. W	M. F	Name of comp.	No.
88	orange	0.3	175-177	214.23	$C_{11}H_{10}N_4O$	1-(3-((1H-imidazol-2-yl)diazenyl)phenyl)ethan-1-one	1
79	Reddish orange	0.35	140-142	316.36	$C_{19}H_{16}N_4O$	*1-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-3-(p-tolyl)prop-2-en-1-one*	**2**
63	Dark orange	0.34	95-97	345.41	$C_{20}H_{19}N_5O$	*1-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-3-(4-(dimethylamino)phenyl)prop-2-en-1-one*	**3**
75	Reddish orange	0.32	103-105	330.40	$C_{19}H_{18}N_6$	3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazole	**4**
85	Reddish orange	0.36	105-107	359.44	$C_{20}H_{21}N_7$	4-(3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-4,5-dihydro-1H-pyrazol-5-yl)-N,N-dimethylaniline	**5**
87	Reddish orange	0.4	75-77	406.49	$C_{25}H_{22}N_6$	3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-1-phenyl-5-(p-tolyl)-4,5-dihydro-1H-pyrazole	**6**
79	Reddish brown	0.3	79-81	435.54	$C_{26}H_{25}N_7$	*4-(3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-5-yl)-N,N-dimethylaniline*	**7**
81	Reddish brown	0.25	98-100	496.49	$C_{25}H_{20}N_8O_4$	*3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-1-(2,4-dinitrophenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazole*	**8**
88	brown	0.37	65-67	525.53	$C_{26}H_{23}N_9O_4$	*4-(3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-1-(2,4-dinitrophenyl)-4,5-dihydro-1H-pyrazol-5-yl)-N,N-dimethylaniline*	**9**
88	Yellowish brown	0.31	130-132	331.38	$C_{19}H_{17}N_5O$	*3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-5-(p-tolyl)-4,5-dihydroisoxazole*	**10**
89	Yellowish brown	0.35	116-118	360.42	$C_{20}H_{20}N_6O$	*4-(3-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-4,5-dihydroisoxazol-5-yl)-N,N-dimethylaniline*	**11**

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71	red	0.37	125-127	358.41	$C_{20}H_{18}N_6O$	*4-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-6-(p-tolyl)-6H-1,3-oxazin-2-amine*	**12**
66	red	0.32	69-71	387.45	$C_{21}H_{21}N_7O$	*4-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-6-(4-(dimethylamino)phenyl)-6H-1,3-oxazin-2-amine*	**13**
78	red	0.4	111-113	374.47	$C_{20}H_{18}N_6S$	*4-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-6-(p-tolyl)-6H-1,3-thiazin-2-amine*	**14**
70	Dark red	0.38	86-88	403.51	$C_{21}H_{21}N_7S$	*4-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-6-(4-(dimethylamino)phenyl)-6H-1,3-thiazin-2-amine*	**15**
67	Reddish brown	0.34	83-85	380.41	$C_{22}H_{16}N_6O$	*6-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-2-oxo-4-(p-tolyl)-1,2-dihydropyridine-3-carbonitrile*	**16**
81	Red brown	0.29	73-75	409.45	$C_{23}H_{19}N_7O$	*6-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-4-(4-(dimethylamino)phenyl)-2-oxo-1,2-dihydropyridine-3-carbonitrile*	**17**
65	brown	0.29	135-137	379.43	$C_{22}H_{17}N_7$	*6-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-2-amino-4-(p-tolyl)nicotinonitrile*	**18**
68	Reddish orange	0.42	106-108	408.47	$C_{23}H_{20}N_8$	*6-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-2-amino-4-(4-(dimethylamino)phenyl)nicotinonitrile*	**19**
87	Reddish brown	0.3	154-156	355.41	$C_{20}H_{17}N_7$	*4-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-6-(p-tolyl)pyrimidin-2-amine*	**20**
78	Yellowish brown	0.35	131-133	384.45	$C_{21}H_{20}N_8$	*4-(3-((1H-imidazol-2-yl)diazenyl)phenyl)-6-(4-(dimethylamino)phenyl)pyrimidin-2-amine*	**21**

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