Synthesis and Characterization of Hetrocyclic Compounds Derived from ethyl-4-aminobenzoate

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Abstract

New series of Schiff Bases were synthesized by many steps starting from treatment of ethyl-4-aminobenzoate with hydrazine hydrate to yield 4-aminobenzohydrazide (1) which was reacted with ethyl acetoacetate in ethanol to form pyrazole derivative (2) and this reacted with salicylaldehyde to yield azo compound (3). The azo compound condensation with appropriate amines (ethyl-4-aminobenzoate and 3-nitroaniline) to give new Schiff bases (4,5). The synthesized compounds were characterized by melting points, FTIR and ^{1}HNMR. [DOI: 10.22401/JNUS.21.2.09]

Keywords**:** acid hydrazide, pyrazole, heterocyclic compounds, Schiff bases.

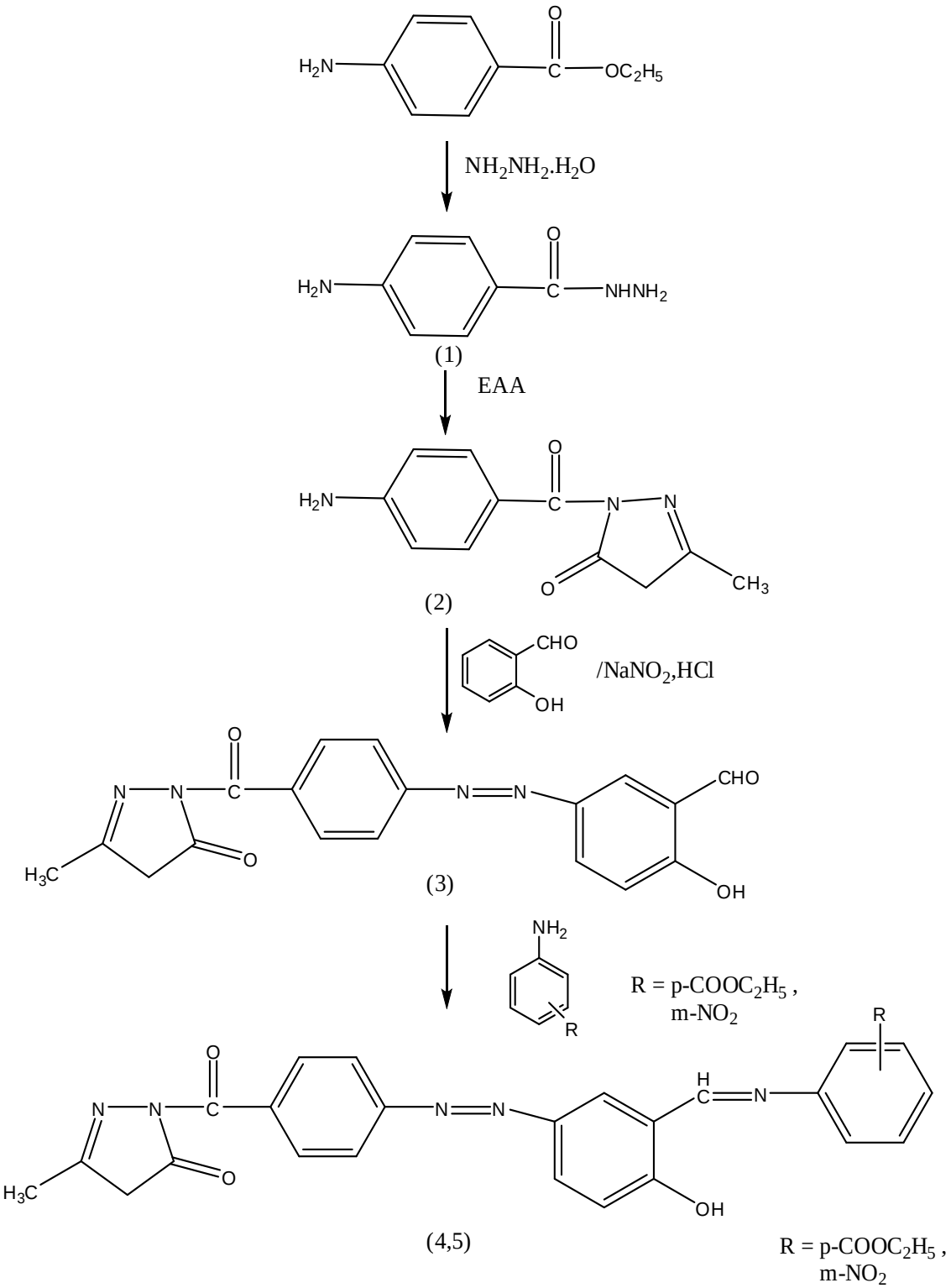
Introduction

Heterocyclic compounds chemistry are a wide and developing area of chemistry because of the clear applications of organic compounds derived by heterocyclic rings by pharmacy and medicine, agriculture and else fields. The organic chemistry of heterocyclic compounds was as pertinent as that of alicyclic and aromatic compounds. Heterocyclic organic compounds applied as pharmaceuticals, agrochemicals and veterinary yields, applied as optical brightening agents, like antioxidants, like corrosion inhibitors and like additives with a variety of else functions [1]. Also, numerous dyestuffs and pigments were heterocyclic structures [2].

Pyrazole is an organic compound with the formula $C_3H_3N_2H$. It is a heterocycle characterized by a 5-membered ring of three carbon atoms and two adjacent nitrogen atoms. Pyrazoles are also a class of compounds that have the ring C_3N_2 with adjacent nitrogen atoms. Notable drugs containing a pyrazole ring are celecoxib (Celebrex) and the anabolic steroid stanozolol.

The pyrazole ring is found within a variety of pesticides as fungicides, insecticides and herbicides, including chlorfenapyr, fenpyroximate, fipronil, tebufenpyrad, tolfenpyrad, and tralopyril [3-5].

Schiff's bases are compounds which contain an isomethine group (N=C), they are named after Schiff who prepared a number of these bases via condensation of aliphatic and aromatic aldehyes and ketones with primary amines [6]. The general formula of these Schiffs bases ($R\text{-}N{=}CR^{I}R^{II}$) and their nomenclature depend on the nature of the groups R, R^{I}, $R.^{II}$. Schiff's bases, which are derived from ketones, are known as ketemines, while those derived from aldehydes known as aldimines [7,8]. Schiff bases form a significant class of the most vastly used organic compounds and was been a vast variety of applications in numerous fields, (biological, inorganic and analytical chemistry). Several of them were the basic units in certain dyes and were also applied as liquid crystals [9]. Schiff base are classes of important compounds in the pharmaceutical field [10]. They show biological activities, including antibacterial, antifungal, and anticancer [11]. This investigation demonstrated synthesis of new Schiff's bases compounds derived from pyrazole with fully characterization, and aiming to further biochemical studies.



Scheme (1): Synthesis scheme of compounds.

Materials and Methods

The melting points were determined in open capillary tubes on a Gallen Kamp melting point apparatus and are uncorrected. The FT.IR Spectra of prepared derivatives were taken on Shimadzu-2N, FTIR-8400S,^{1}H-NMR Spectra of some prepared derivatives were recorded on a Varian-Mercury 300MHZ Spectrometer, d6-DMSO was use as a solvent in^{1}H-NMR Spectra.

Synthesis of 4-aminobenzohydrazide (1) [12]

A solution of 4-aminobenzoate (1.65 g., 0.01 mole) in ethanol (25mL.), hydrazine hydrate (80%) (0.5g.,0.01 mole) was added

drop wise with stirring. The mixture has been refluxed for 12 hrs. After cooling the product formed, filtered off, and recrystallize by ethanol: water (1:1). Melting point:217-219^{0}C, Yields: 90%. The FTIR spectral data showed absorption at (1629cm^{-1} for υC=O), (1562cm^{-1} for υC=C, Ar.), (3034cm^{-1}, for υC-H, Aromatic) and (3429-3234 cm^{-1} for υNHNH$_2$). The ¹HNMR spectrum from compound [1] show the data: (DMSO,): 4.5ppm(s,due to 2H of – NH$_2$), 5.5pmm(s,due to 2H of Ar– NH$_2$), 6.7-7.5 (m, 4H, due to 4H of Benzene ring,), 8.9(S,due to 1H of –NH).

Synthesis of 1-(4-aminobenzoyl)-3-methyl-1H-pyrazol-5(4H)-one (2)

A solution of 4-aminobenzohydrazide (1) (1.5g.,0.01mole) and ethyl acetoacetate (1.3g.,0.015mole) were taken in absolute ethanol (25 ml.). The solution was refluxed for 4 hrs. The solution was cooled to give the precipitate [13] and recrystallized by ethanol. Melting point: 240-242 ^{0}C, Yields: 75%. The FTIR spectral data showed absorption at (3213cm^{-1}, for υ-NH$_2$), (3082cm^{-1}, for υC-H, Ar.), (2962,2920cm^{-1}, for υCH, aliphatic), (1750cm^{-1}, for υC=O, pyrazole), (1697cm^{-1}, for υC=O), (1604cm^{-1}, for υC=N), and (1444cm^{-1}, for υC=C, Ar.). The ^{1}H-NMR spectrum of 1-(4-aminobenzoyl)-3-methyl-1H-pyrazol-5-(4H)-one (2) show the absorotion bands at: 2.00 ppm(s, 3H, CH$_3$ of pyrazole ring), 2.23 ppm (s,2H, CH$_2$ of pyrazole ring), 5 (s,due to 2H of –NH$_2$), and 6.1-7.6 ppm (m,4H, Ar-H) .

Synthesis of 2-hydroxy-5-((4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carbonyl)phenyl)diazenyl)benzaldehyde (3)

Compound (2) (2g.,0.01mole) was dissolved in distilled water (4 mL) and conc. HCl (2.25 ml). The mixture was stirring for 15 min at 0^{0}C. A mixture of NaNO$_2$ (0.69g.,0.01 mole) in water (2.55 mL) was added gradually. After stirring for 15 min., the mixture of diazonium salt has been added gradually to a solution of salicylaldehyde (1.22g., 0.01 mole) in ethanol and 10% NaOH (10mL.) at (0-5)^{0}C and pH=6. The solution is stirring for 20 min. then is left for 1.5 hr. The solid has been filtered off, dry the precipitation and recrystallize by ethanol. Melting point: 231-233^{0}C, Yields: 78%. The FTIR spectral data showed absorption in at (3200cm^{-1}, for υOH), (1726cm^{-1}, for υC=O, pyrazole), (1701cm^{-1}, for υC=O,aldehyde), (1685cm^{-1}, for υC=O), (1604cm^{-1}, for υC=N), and (1577cm^{-1}, for υN=N). The ^{1}H-NMR spectrum of compound (3) showed the following data: 2.00 ppm(s, 3H, CH$_3$ of pyrazole ring), 2.30 ppm (s,2H, CH$_2$ of pyrazole ring), 7.1-8.3 ppm (m,7H, Ar-H), 9.88 ppm (s, 1H,CHO) and 11.40 ppm (s, 1H , for OH).

General procedure to synthesis of Schiff's basses compounds (4,5)

A solution of 2-hydroxy-5-((4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carbonyl) phenyl)diazenyl)benzaldehyde (3) (0.35 g., 0.001mole) in absolute ethanol (10ml), and appropriate aromatic amine (ethyl 4-aminobenzoate and 3-nitroaniline) (0.001mole) was refluxed for 4-6 hrs. in the presence of few drops of glacial acetic acid. After cooling the product, a solid formed, filtered off, dried and purified by recrystallization from ethanol.

Synthesis of 1-(4-((4-hydroxy-3-((4-propionylphenylimino)methyl)phenyl) diazenyl)benzoyl)-3-methyl-1H-pyrazol-5(4H)-one (4)

Melting point: 198-200^{0}C, Yields: 82%. The FTIR spectral data showed absorption at (2923,2845cm^{-1}, for υCH, aliphatic), (1732cm^{-1}, for υC=O pyrazole), (1712cm^{-1}, for υC=O, ester), (1698cm^{-1}, for υC=O, amide), (1616cm^{-1}, for υC=N). The ^{1}H-NMR spectrum of compound (4) showed the following data :1.6 ppm(t, 3H,CH$_3$), 2.00 ppm(s, 3H, CH$_3$ of pyrazole ring), 2.30 ppm (s,2H, CH$_2$ of pyrazole ring), 3.1 ppm (q,2H, -CH$_2$-), 7.2-9 ppm (m,10H, Aromatic-H) ,8.4 ppm (s,1H for N=C-H)) and 11.2 ppm (s,1H for OH).

Synthesis of 1-(4-((4-hydroxy-3-((3-nitrophenylimino)methyl)phenyl) diazenyl)benzoyl)-3-methyl-1H-pyrazol-5(4H)-one (5)

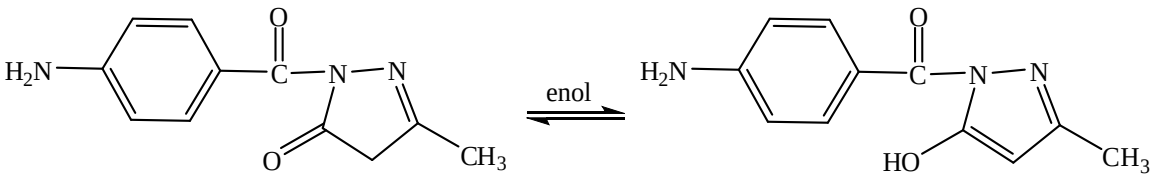
Melting point: 125-127^{0}C, Yields: 80%. The FTIR spectral data showed absorption at (1730cm^{-1}, for υC=O pyrazole), (1707cm^{-1}, for υC=O, amide), (1618cm^{-1}, for υC=N). The ^{1}H-NMR spectrum to 1-(4-((4-hydroxy-3-((3-

nitrophenylimino)methyl)phenyl)diazenyl)ben zoyl)-3-methyl-1H-pyrazol-5(4H)-one (5) show the data in at: 2.3 ppm(s, 3H, CH_3 of pyrazole ring), 2.5 ppm (s,2H, CH_2 of pyrazole ring), 6.1 – 8.9 ppm (m, 10H, Aromatic-H) 8.4 ppm (s,1H for N=C-H) and 10.5 ppm (s,1H , for OH).

Result and Discussion

The 4-aminobenzohydrazide (1) is prepared by substitution reaction between 4-aminobenzoate and hydrazine hydrate (80%) in the presence of ethanol as a solvent. The reaction proceeds by nucleophilic substitution of hydrazine hydrate to the ester carbonyl group in 4-aminobenzoate followed by losing of CH_3CH_2OH molecule. The FTIR spectrum for hydrazide derivative (1) shows the stretching vibration at regions(3419-3200)cm^{-1} for asymmetric and symmetric ($NH-NH_2$), and disappearance band at (1685) cm^{-1} which belong to stretching vibration of carbonyl group of ester. The ¹HNMR spectrum of 4-aminobenzohydrazide (1) show the data: (DMSO,): 4.5 ppm(s,due to 2H of – NH_2), 5.5 ppm (s,due to 2H of Ar– NH_2), 6.7-7.5 ppm (m, 4H, due to 4H of Benzene ring,), 8.9 ppm (s,due to 1H of –NH).

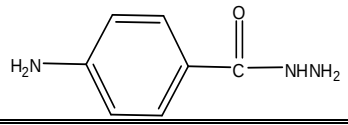
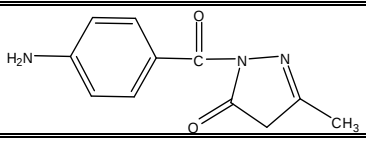
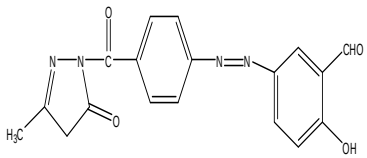
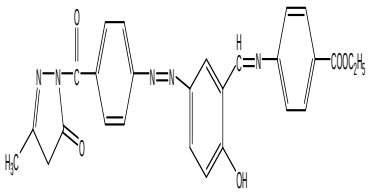
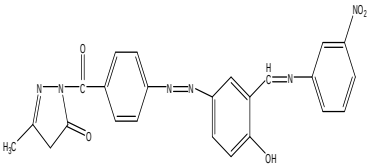
The pyrazole derivative is prepared through the reaction of hydrazide derivative (1) and ethyl acetoacetate to give compound (2). The FTIR spectrum of 1-(4-aminobenzoyl)-3-methyl-1H-pyrazol-5(4H)-one (2) showed new band at (1570) cm^{-1} which belong to stretching absorbtion of C=N of pyrazole, and the disappearance of the bands at (3419-3200) for NH_2 Its worth to mention, that pyrazole (2) has other important bands at (1750) cm^{-1} for carbonyl in pyrazole ring. The ^{1}H-NMR spectrum of 1-(4-aminobenzoyl)-3-methyl-1H-pyrazol-5(4H)-one (2) showed the appearance 2 ppm (s,3H for CH_3).



The synthesis of an azo dye requires two molecules a diazonium salt and a coupling component. The diazonium salt reacts an electrophile reaction for an electron-rich coupling component, such as a phenol derivative over an electrophilic aromatic substitution mechanism. The -OH group like salicylaldehyde direct the aryl diazonium ion to the para position exceot if that position is occupied, in which condition the ion link ortho [14]. The FTIR spectrum 2-hydroxy-5-((4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carbonyl)phenyl)diazenyl) benzaldehyde (3) showed an absorption band at (3200 cm^{-1}) because of stretching vibration for hydroxyl group, band at (1685 cm^{-1}) because of stretching vibration at C=O of aldehyde, band at (1510 cm^{-1}) indicating the (N=N).

The Schiff bases (4,5) were synthesized through the condensation of 2-hydroxy-5-((4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carbonyl) phenyl)diazenyl)benzaldehyde (3) for appropriate aromatic amine (ethyl-4-aminobenzoate and 3-nitroaniline) at absolute ethanol like a solvent. The reaction proceeds via nucleophilic attack of the amine on the carbonyl carbon of the aldehyde with the loss of a water molecule. The FTIR spectrum of compound (4) show the new band at (1610) cm^{-1} which could be attributed to C=N, and the disappearance of absorption band at (1685) cm^{-1} for (C=O) of aldehyde.

Table (1)
The physical properties for the yields.

Comp. No.	Nomenclature	Structural formula	Molecular formula	Color
(1)	4-aminobenzohydrazide		$C_9H_{11}NO_2$	White
(2)	1- (4-aminobenzoyl)-3-methyl-1H-pyrazol-5(4H) -one		$C_7H_9N_3O$	White-Milky
(3)	2-hydroxy-5-((4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carbonyl) phenyl) diazenyl) benzaldehyde		$C_{11}H_{11}N_3O_2$	Red
(4)	1-(4-((4-hydroxy-3-((4-propionylphenylimino) methyl)phenyl)diazenyl)benzoyl) -3-methyl-1H-pyrazol-5(4H)-one		$C_{24}H_{18}N_6O_5$	Yellow
(5)	1-(4-((4-hydroxy-3-((3-nitrophenylimino) methyl)phenyl)diazenyl)benzoyl)-3-methyl-1H-pyrazol-5(4H)-one		$C_{24}H_{18}N_6O_5$	Orange

Conclusion

The acid hydrazide (1) derivative can be synthesized through the reaction of 4-aminobenzoate for hydrazine hydrate. The obtained yields of final product when ethanol was used as solvent. In this study synthesized pyrazole derivative using simple and inexpensive method using ethyl acetoacetate to cyclization compound. A series of Schiff bases derivatives were successfully synthesized using glacial acetic acid as catalysts. The newly synthesized compounds were characterized by using melting points and spectroscopic methods (FTIR and ^{1}H NMR).

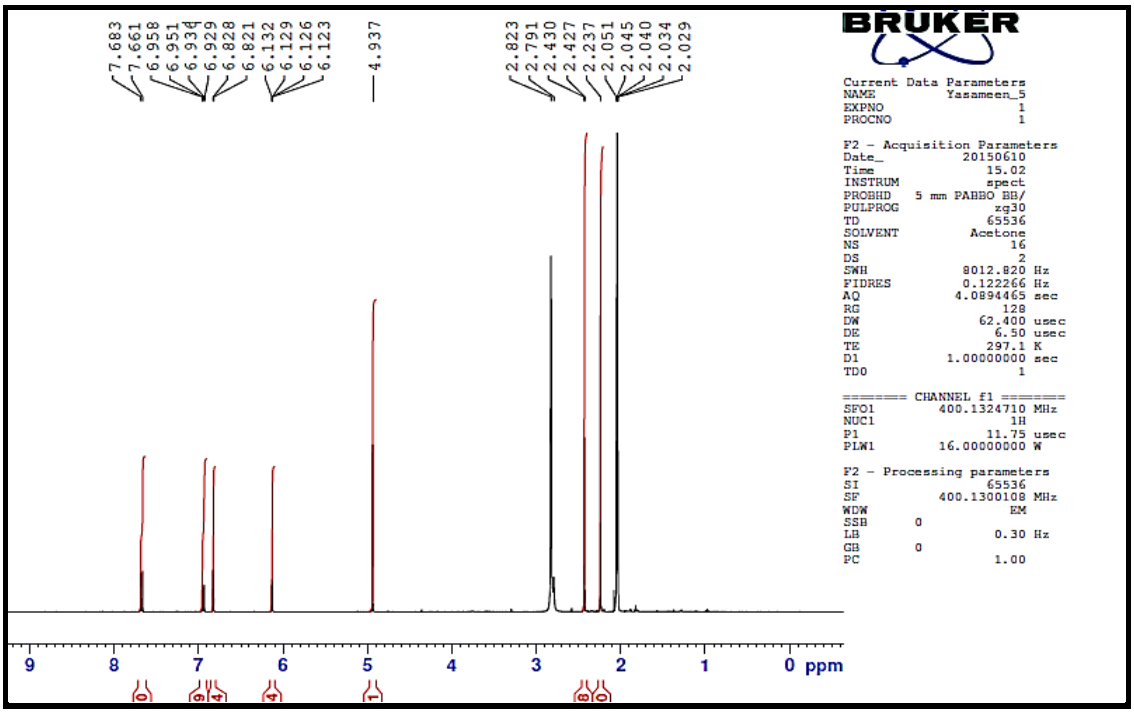


Fig.(1): ^{1}H NMR Spectrum of Compound (2).

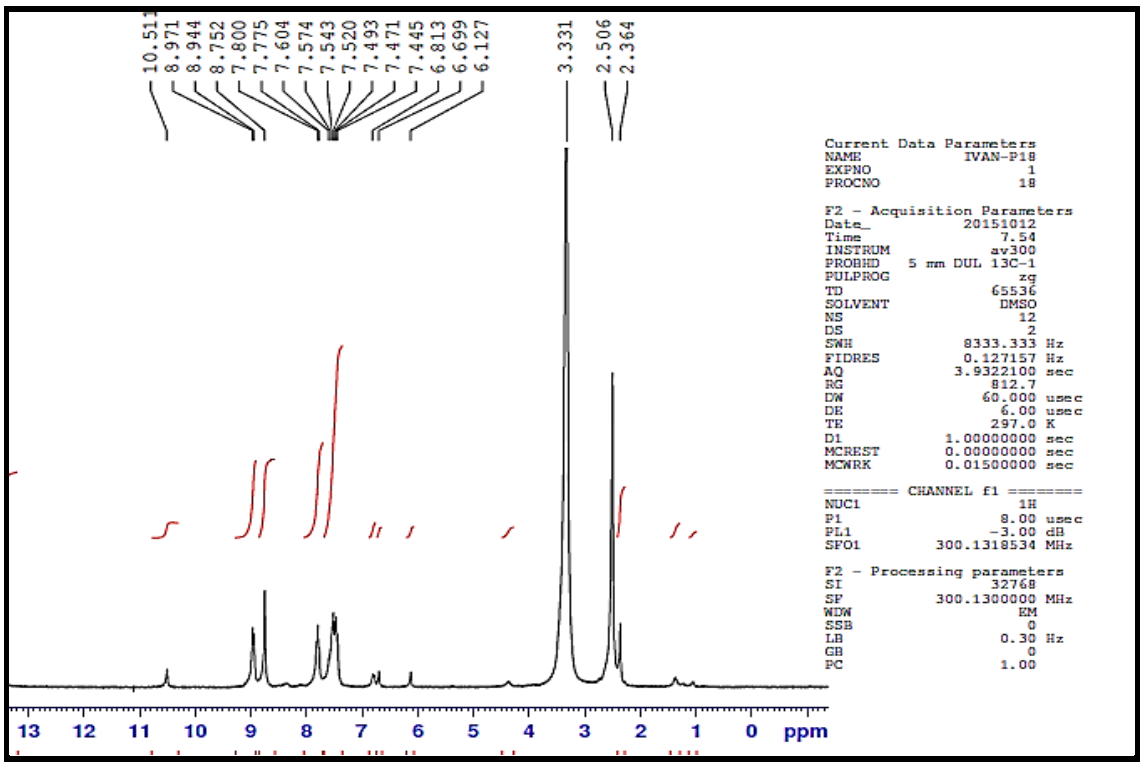


Fig.(2): ^{1}H NMR Spectrum of Compound (5).

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