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Synthesis, Characterization and Biological Activity of Some new 1,3,4-Oxadiazole and β-Lactams from poly Acryloyl chloride

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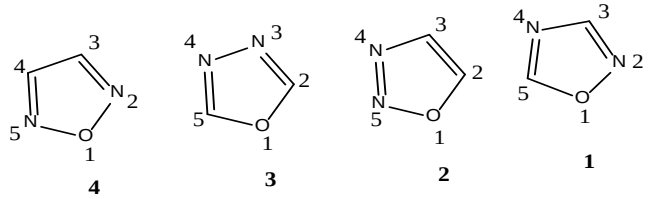
Abstract:
In this work the new poly acryloyl chloride derivatives by reaction with hydrazine hydrate in presence of triethyl amine (Et_3N) and DMSO as a solvent to prepare polymer (1). These derivatives polymers were synthesized by two parts. The first part(I) was included to formation of Schiff base polymers (2-5) by treatment polymer (1) with various aldehydes and ketones in presence DMSO as a solvent and glacial acetic acid. Then treatment the prepared polymers (2-5) with chloroacetyl chloride, triethyl amine and 1,4-dioxane as a solvent to product β- Lactam polymers (6-9). The second part (II) was reaction of polymer (1) with different aromatic carboxylic acid in presence $POCl_3$, triethyl amine and DMSO as a solvent to prepared 1,3,4-oxadiazole polymers (10-12). All the newly prepared polymers were identified by physical properties, FT-IR , softening point, screened antibacterial studies and some of them ^{1}H-NMR.

Key word: poly acryloyl chloride , Schiff base , β-Lactam and 1,3,4-oxadiazole .

INTRODUCTION :

Poly acryloyl chloride can be prepared be reaction poly acrylic acid with thionyl chloride [1]. Also, can be prepared Poly acryloyl chloride by exposure Acryloyl chloride by UV light in quartz tubes to formation linear polymer at room temperature [2-3]. In (1864), Schiff who prepared a new compound called Schiff base or imine, it has been obtained by condensation of aliphatic or aromatic aldehydes or ketones with primary aliphatic or aromatic amine or amino acid [4]. They contain an isomethine group (-N=C-)[5]. Schiff base derivatives have consistently attracted scientific and practical interest because of their widely varying chemical properties, synthetic versatility, and pharmacological activities, such as antitumor, antibacterial, antifungal and herbicidal activities[6].Monocyclic β-lactam (2-azetidinone) is the main feature of the most of the penicillin's , cephalosporins and other antibiotics[7] such as antifungal, antitubercular, antitumor, cholesterol absorption inhibition and enzyme inhibition activity[8]. 1,3,4-Oxadiazole is a heterocyclic compound containing an oxygen atom and two nitrogen atoms in a five-membered ring, it is derived from furan by substitution of two methylene groups (=CH) with two pyridine type nitrogen (-N=)[9] . There are four possible isomers of oxadiazole (1, 2, 3, 4) depending on the position of nitrogen atom in the ring and are numbered as shown in Fig. 1:



4 **3** **2** **1**

Fig.-1-

1,3.4-Oxadiazole has a wide range of variety of biological activities, such as analgesic, anti-inflammatory, anti-bacterial and anti-tubercular activity [10].

EXPERIMENTAL

A) Supplied chemicals:

The chemicals such as Poly acryloyl chloride , DMSO, Phosphoryl chloride , Different aldehydes and ketones , hydrazine etc. were of Merck product, BDH, sigma Aldrich, Fluke, GCC companies.

B) Instruments:

1) Softening points were determined using thermal microscope(kofler-method) . Reichert thermosvar.SP.10/0.25,160.
2) The FT-IR spectra were recorded in KBr pellets using FT-IR shimadzu FTIR-8400 Fourier transform Infrared spectrophotometer .
3) The 1H-NMR Spectra were recorded on Bruker 300M Hzistrument using DMSO-d6 as solvent and TMS as internal reference measurements spectrophotometer and chemical shifts were expressed in ppm.

C) Experimental methods:

First part(I):

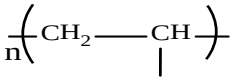
Preparation of Poly [N- acryl hydrazine] (1) [11]:

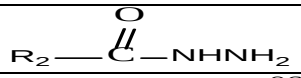
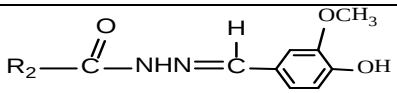
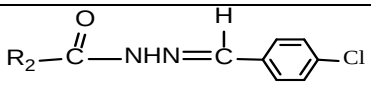
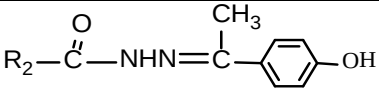
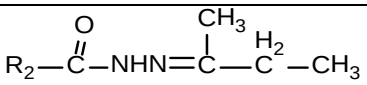
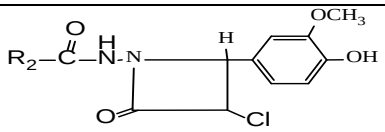
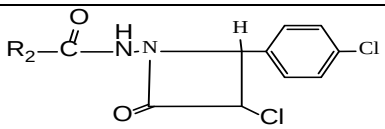
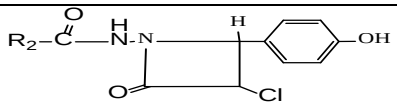
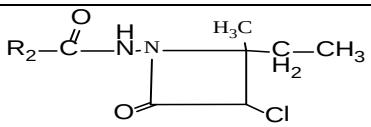
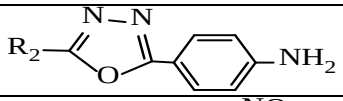
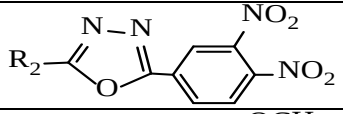
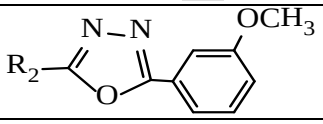
To a mixture of poly (acryloyl chloride) (0.01mole) in Dimethyl sulfoxide (DMSO) (10ml) , hydrazine hydrate (90%) (0.01mole) was added and the reaction mixture was heated under reflux for (7 hrs). The solvent was then evaporated and the product was cooled, filtered and recrystallized by using ethanol. The physical properties of polymer (1) is listed in table (1).

Preparation of Poly[N-(substituted imine) acryl amide] [poly Schiff bases] (2-5)[12]:

To a stirred solution of polymer (1) (0.01mole) in Dimethyl sulfoxide (DMSO) (10ml) was added different aldehydes and ketones (0.01 mole) and glacial acetic acid (1ml). The mixture was refluxed for (6hrs) and cooled. The precipitate was filtered and crystallized from an appropriate solvent. The physical properties of polymers (2-5) is listed in table (1).

Table (1): Physical properties of compounds [1-12].

$R_2 =$ 

Comp .No	Comp. Structure	S. P C^0	Yield %	Color
1		190-198	42	Off white
2		212-220	56	yellow
3		177-186	47	Light brown
4		243-249	52	Light yellow
5		245-251	66	brown
6		oil	55	Dark brown
7		oil	67	orange
8		oil	52	Off white
9		oil	45	brown
10		178-184	63	yellow
11		217-223	67	Dark red
12		237-243	59	Dark brown

Preparation of Poly β-lactams (6-9)[13]:

The polymers (2-5) (0.01mole) ,chloroacetyl chloride (0.01mole), Et_3N and dry1,4-dioxan (30ml) at (10^0C) were stirred for (20hrs) . The reaction mixture was kept aside for 4 days at room temperature. The product was filtered, dried and recrystallized from ethanol. The physical properties of polymers (6-9) is listed in table (1).

Second part(II):

Preparation of Polymer (10-12) [14]:

A mixture of polymer (1) (0.01mole) and different aromatic acid (0.01 mole) in Dimethyl sulfoxide (DMSO)(10ml) as a solvent containing phosphorus oxychloride ($POCl_3$) (0.01mole) as a catalyst was refluxed for (5hrs.) at (110 ^{0}C) . The mixture was cooled and poured into crushed ice and made basic by 10 % KOH. The resulting solid was, filtered, and the separated product was purified by recrystallization from ethanol. The physical properties of polymers (10-12) is listed in table (1).

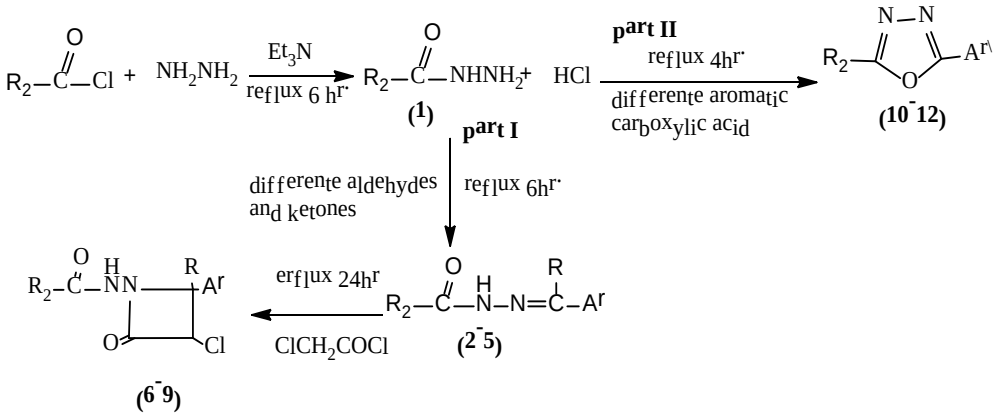
RESULTS AND DISCUSSION:

The general reaction was summarized in Scheme (1):

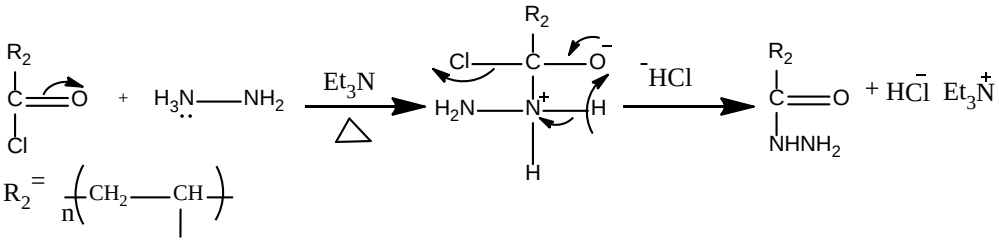
Polymer (1) was prepared via the reaction of the poly acryloyl chloride with acid hydrazide in the presence of Dimethyl sulfoxide (DMSO) as a solvent and triethyl amine (Et_3N) as a catalyst. All physical properties for Poly [N- acryl hydrazine] (1) is listed in tables (1). FT-IR data

of polymer (1) clearly shows a strong bands at 3160cm^{-1} for ν(NH), 3350cm^{-1} for ν(NH2),1620cm^{-1} for ν(C=O) amide, these and other bands shown in table (2). The mechanism of the reaction involves a nucleophilic attack on the carbonyl as shown in scheme-2-[15]:

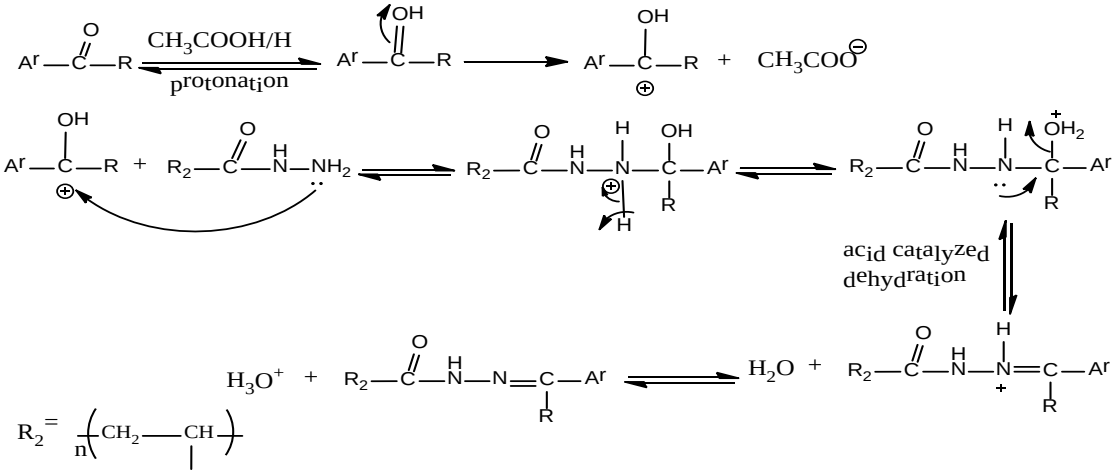
Polymers (2-5) were prepared by refluxing polymer (1) with different aldehydes and ketones in dimethyl sulfoxide (DMSO) as a solvent in presence glacial acetic acid as a catalyst. All physical properties for polymers (2-5) are listed in table (1). FT-IR data of polymer (2-5) clearly shows a strong band at (3217-3288) cm^{-1} for ν(NH), (1657-1685) cm^{-1} for ν(C=O) amide, these and other bands shown in table (2). ^{1}H-NMR spectrum of compound (4) was show bands at δ1.5 for (d,2H, -CH_2), δ2.6 for (t, 1H, -CH) , δ7 for (s,1H ,NH),δ2.3 for (s, 3H,-CH_3) , δ5.3 for (s, 1H,OH) and δ7.8 due to (s,4H, HAr). The mechanism of the reaction involves a nucleophilic attack on the carbonyl as shown in scheme -3- [16]:



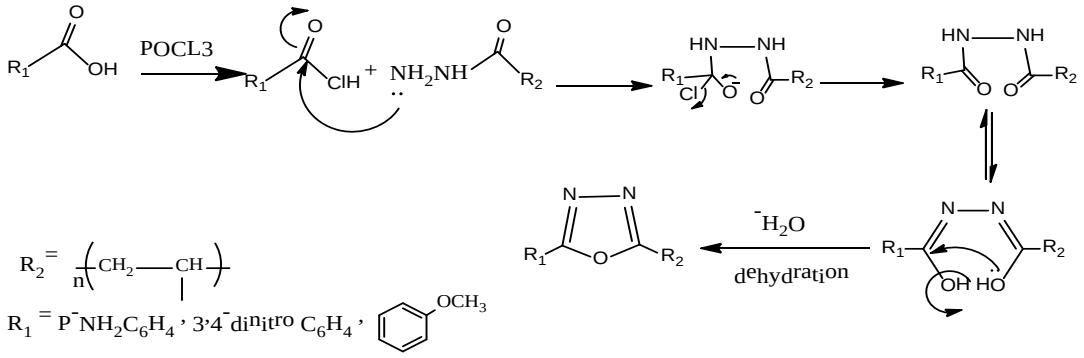
Shceme-1-



Scheme-2-



Scheme-3-



Scheme-4

Polymers (2-5) in 1,4-dioxane were added to well-stirred mixture of chloroacetyl chloride and triethylamine to get polymers (6-9). All physical properties for polymers (6-9) are listed in table (1). FT-IR data of polymer (6-9) clearly shows a strong band at (3210-3290) cm^{-1} for ν(NH), (1629-1682) cm^{-1} for ν(C=O) amide, (1535-1567) cm^{-1} for ν(C=O) cyclic amide, these and other bands shown in table (2). Polymers (10-12) synthesized through acylation of acid hydrazide (polymer 1) by reaction with different carboxylic acid in presence phosphorus oxychloride ($POCl_3$) as a catalyst and using at ($110C^0$) temperature. All physical properties for polymers (10-12) are listed in table (1). FT-IR data of polymer (10-12) clearly shows a strong band at (1410-1435) cm^{-1} for ν(N-N), (1658-1670) cm^{-1} for ν(N=C), these and other bands shown in table (2). ^{1}-H-NMR spectrum of compound (11) was show bands at δ1.3 for (d,2H, -CH2), δ2.9 for (t, 1H, -CH) and δ8.9 due (s,4H ,HAr), ^{1}-H-NMR spectrum of compound (12) was show bands at δ1.3 for (d,2H, -CH_2), δ2.5 for (t, 1H, -CH) , δ3.7 for (s,1H ,-OCH_3) and δ7.6 due (s, 4H,HAr).The mechanism of the reaction involves a nucleophilic attack on the carbonyl as shown in scheme-4- [17]:

Antimicrobial Activity:

The synthesized compounds were subjected to antimicrobial screening by disc diffusion method [18] at concentration using 5mmg filter paper disc and filled with (100,50) mg/ml of compounds. The antibacterial activity was tested against various gram positive [*Staphylococcus aureus and Staphococcus epidermis*] and Gram-negative[*E.Coli*] bacteria and anti-fungal activity against various fungal stains [*A.nigar*] compared with standard drug .The solvent (DMSO) was used as a negative control while ciprofloxacin(10mg/disc)was a used positive control, plates were incubated at $37C^0$ for 24 hr. The results were described in the table (3).

Table [2]: FT-IR Spectral data of compounds [1 - 12] in cm^{-1}

	FT-IR Spectral data cm^{-1}						
Comp. No.	ν (N-H)	ν (C-H) aliphatic	ν (C-H) aromatic	ν (C=O) amide	ν (N-N)	ν (C=C) aromatic	Others band cm^{-1}
1	3160	2998	-	1620	1478	-	ν(NH_2)3350
2	3217	2999	3160	1660	1410	1437	ν(C-OH) phenolic 3500, ν(N=C) 1620, ν(C-O) 1263,ν(C-N) 1313,ν(O-CH3) 2845
3	3288	2970-2999	3190	1685	1487	1525	ν(C=N)1670, ν(C-N) 1334,ν(C-Cl) 779
4	3219	2988-2990	3180	1657	1466	1502	ν(OH)phenolic3346, ν(C=N)1658,ν(C-N) 1323
5	3267	2999-2998	-	1660	1435	-	ν(C=N)1667,ν(C-N) 1313
6	3223	2989-2993	3013	1678	1469	1454	ν(OH)phenolic3516, ν(C-O)1267,ν(C-N) 1320, ν(O-CH3) 2815 ν(C-Cl) 733, ν(C=O) cyclic amide 1535
7	3290	2998-2999	3113	1682	1437	1517	ν(C-N)1343,ν(C-Cl) 756, ν(C=O)cyclic amide 1567
8	3212	2984-2991	3005	1673	1420	1539	ν(OH)phenolic3379, ν(C=O)cyclic amide 1558, ν(C-N)1298, ν(C-Cl)780
9	3310	2999-2994	-	1629	1448	-	ν(C=O)cyclic amide 1540, ν(C-N)1398, ν(C-Cl)771
10	-	2981-2995	3010	-	1433	1587	ν(NH_2)3304, ν(N=C) 1670, ν(C-O)1224
11	-	2914-2956	3003	-	1435	1571	ν(C-NO_2)1546, ν(N=C) 1658, ν(C-O) 1224
12	-	2999-2990	3019	-	1410	1558	ν(N=C) 1669, ν(C-O) 1315, ν(O-CH_3)2825

Table [3]: Antibacterial effect of β-Lactams compounds [6-12]

Comp. No.	Bacteria									Fungi		
	Gram (+)						Gram (-)			*A.nigar*		
	Staphylococcus aureus			*Staphococcus epidermis*			*E.Coli*					
	conc. mg/ml		ciprofloxacin	conc. mg/ml		ciprofloxacin	conc. mg/ml		ciprofloxacin	Conc. mg/ml		ciprofloxacin
	100	50		100	50		100	50		100	50	
6	31	22	23	13	10	17	12	8	22	25	23	23
7	17	12	20	27	14	19	19	10	20	22	20	18
8	23	15	19	31	17	22	27	17	21	23	19	20
9	25	13	22	19	11	23	24	12	16	26	20	22
10	28	17	18	26	12	15	29	16	19	25	19	16
11	23	13	23	20	13	13	25	18	20	24	15	13
12	26	16	24	28	14	14	28	20	30	28	21	19
DMSO	-	-	-	-	-	-	-	-	-	-	-	-

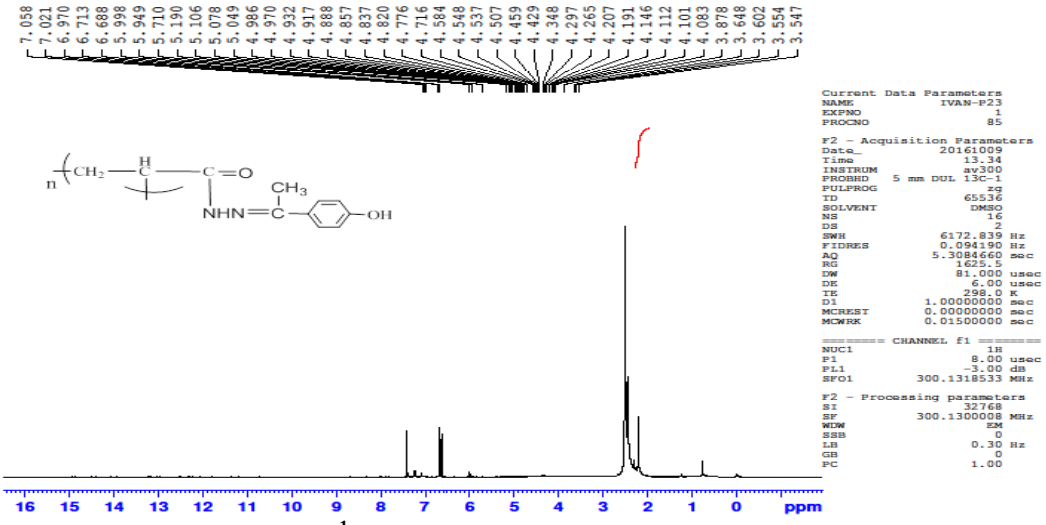


Fig.(3) : ^{1}H-NMR spectrum for compound [4]

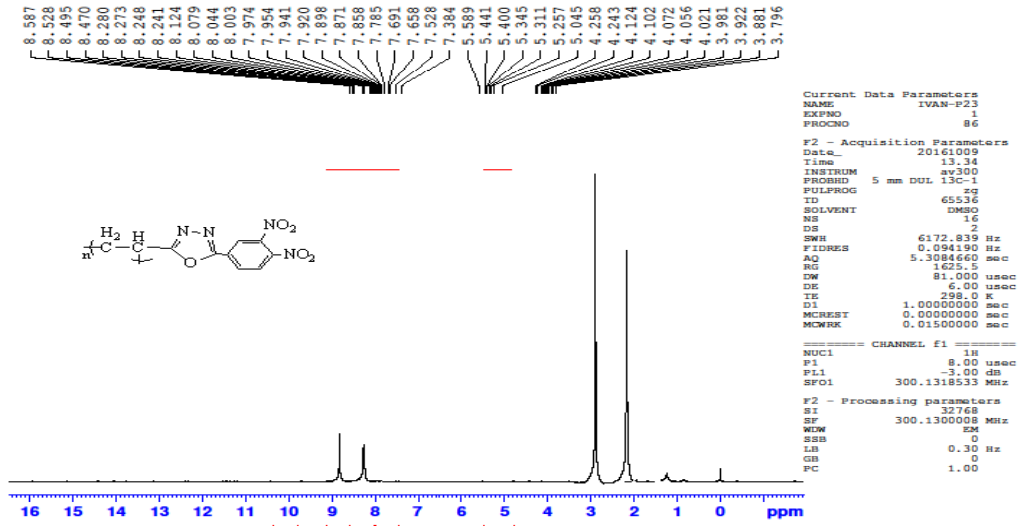


Fig.(4) : 1-H-NMR spectrum for compound [11]

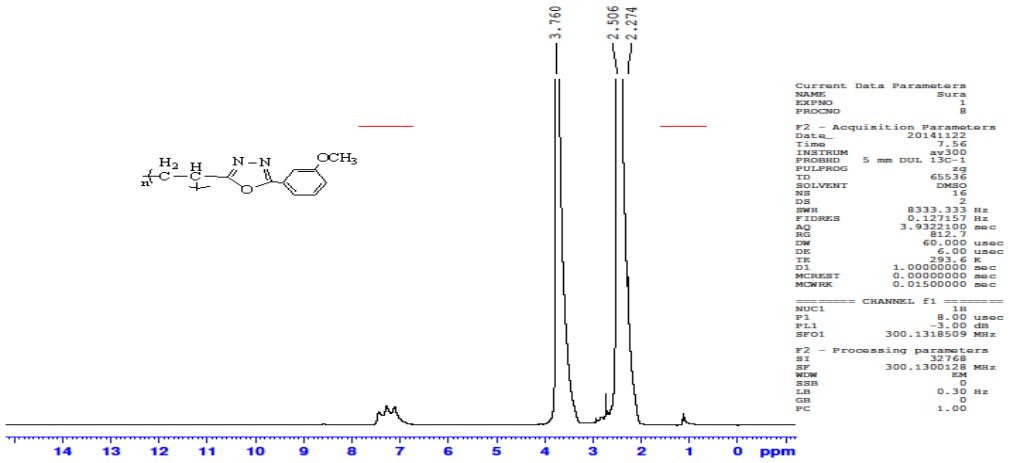


Fig.(5) : 1-H-NMR spectrum for compound [12]

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