Synthesis and Characterization of new 3-(4-acetylphenyl) -2- (4-nitrophenyl) thiazolidin-4-one derivatives

Nisreen Kais Abood , Hanan Ghadban Sha'aban and Nagham majed Abd-Alhassan
Department of Chemistry,College of Science, Al-Mustansiriya University, Baghdad, Iraq.

الخلاصة

البحث الحالي يوصف تحضير مركبات حلقية غير متجانسة جديدة عن طريق تفاعل 4-نايتروبنزالديهايد مع 4-امينو اسيتوفينون ليعطي المركب (1), مركبتوحامض الخليك تفاعل مع المركب (1) بوجود البنزين الجاف اعطى المركب (2), تفاعل المركب (2) مع الالديهايدات الاروماتية المختلفة (4- برموبنزالديهايد و 2-كلورو بنزالديهايد) ليعطي مركبات الجالكون (4,3) . فوعلت هذه المركبات مع الهيدرازين اللامائي و الفنيل هيدرازين فتعطي مركبات البايروزول (8,7,6,5). الثايويوريا وااليوريا تفاعلت مع مركب الجالكون (4,3) اعطت مشتقات جديدة من الثايازين و الاكسازين (12,11,10,9) بالتتابع. تفاعل هيدروكسيل الامين هيدروكلورايد مع مركبات الجالكون(4,3) اعطت مشتقات الازواوكسازول (14.13). شخصت هذه المركبات بالطرائق الطيفية (FT-IR) وElemental Analysis وبعضها شخص بأطياف (^{1}HNMR), وكذلك تم قياس درجات انصهارها.

Abstract

The present research work describes the synthesis of new heterocyclic compounds using 4-nitro benzaldhyde react with 4-amino acetophenone to afford 1(4-(4nitro benzylidene amino)phenyl) ethanon copm.(1). Mercapto acetic acid reacts with comp.(1) in dry benzene afford 3(4-acetyl phenyl)-2-(4-nitro phenyl)thiazolidin 4-one copm.(2), comp.(2)allowed to react with different aldehydes namely :4-bromo benzaldhyde ;2-Chloro benzaldehyde to give the corresponding chalcones (3,4),the latter compounds react with hydrazine hydrate 99% and phenyl hydrazine to give the pyrazole derivatives (5,6,7,8). Thiouurea and urea react with chalcones (3,4) to give the thiazine and oxazine derivatives respectively (9,10,11,12), hydroxylamine hydrochloride react with chalcones(3,4) in ethanol to afford isooxazole derivatives (13,14). All compounds were confirmed by their FT-IR Spectrum ,Elemental analysis ,^{1}H-NMR Spectrum for some them and melting point.

***Key words** : Chalcone , Pyrazole, Thiazine, Oxazine, Isoxazole*

Introduction

The synthesis of the chalcone compounds by claisn-Schmidt condensation of aldehyde and ketone by base catalyzed followed by dehydration to yield chalcones [1],chalcone compounds in corporation with heterocyclic became great important in medicinal chemistry [2]. Chalcone constitute an important group of natural product and serve precursors for the synthesis and their good intermediates for synthesis various heterocyclic compounds like [3,4] pyrazol, thiazine, oxazine and Isoxazole derivatives ,chalcone are highly biological active as anticancer, antileishmanial, antiulsar[5], antifungal and antitumor [6]. Pyrazol belongs to the family of azoles ,five membered heterocyclic [7], pyrazol ring is a prominent structural motif found in numerous pharmaceutically active compound ,pyrazol important biological active such anti-inflammatory, postmenopausal and osteoporosis [8].Varity of thaiazine derivatives have been reported claiming diversified biological profile like antimicrobial and anti-tuberculosis[9]. Oxazines derivatives are prominent class of N,O-heterocyclic compound due to the constitute a part of many fine chemicals and have been assigned as privileged structure in biologically active moreover it has been found that some of them have plasma lipid altering characterize, act as inhibitors of human leukocyte elastase [10,11].

Experimental

The melting point were determined in open capillary tubes on a Gallen Kamp melting point apparatus and were uncorrected .The FT.IR Spectra of some prepared derivatives were taken on Shimadzu-2N,FTIR-8400 S, and use Rotary evaporate. Elemental analysis measured in College of Science, Al-Mustansiriya University ^{1}H-NMR Spectra of some prepared derivatives were recorded on a Varian-Mercury 300MHZ Spectrometer, d6-DMSO use as a solvent in^{1}H-NMR Spectra measured in Jordan ,Al-albayt university.

Synthesis of 1-(4-(4-nitrobenzylideneamino)phenyl)ethanone(1)

A mixture of 4-nitro benzaldehyde (0.01 mol),4-amino acetophenon (0.01 mol) and ethanol (30 ml),then the mixture was refluxed for 8 hrs.,and cooled to room temperature. The precipitat was filtered and recrystallized from ethanol.

Synthesis of 3-(4-acetylphenyl)-2-(4-nitrophenyl) thiazolidin-4-one(2)

Thioglycolic acid (0.01mol) was added dropwise to (0.01 mol) of1-(4-(4-nitrobenzylidene amino) phenyl)ethanone(1) in(15ml) dry benzene with stirring . The reaction mixture was refluxed for 10 hrs., the solvent distilled off and the residue neutralized with sodium bicarbonate ,then was filtered and recrystallized by ethanol .

Synthesis of 3-(4-(3-substitutedphenyl)acryloyl)phenyl)-2-(4-nitrophenyl) thiazo lidine-4-one (3,4).

The solution of compound (2) (0.01 mol) in ethanol (50 ml),substituted benzaleyhyde (0.01 mol) , NaOH were added and refluxed for 10 hrs., the reaction was cold .filtered and neutralized with dil. HCl. The solid residue thus obtained was crystallized by ethanol.

Synthesis of3-(4-(5-(subsisted phenyl)-4H-pyrazol-3-yl)phenyl)-2-(4-nitrophenyl) thiazolidin -4-one (5,6), Synthesis of 3-(4-(5-(substituted phenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)-2-(4-nitrophenyl)thiazolidin-4-one (7,8).

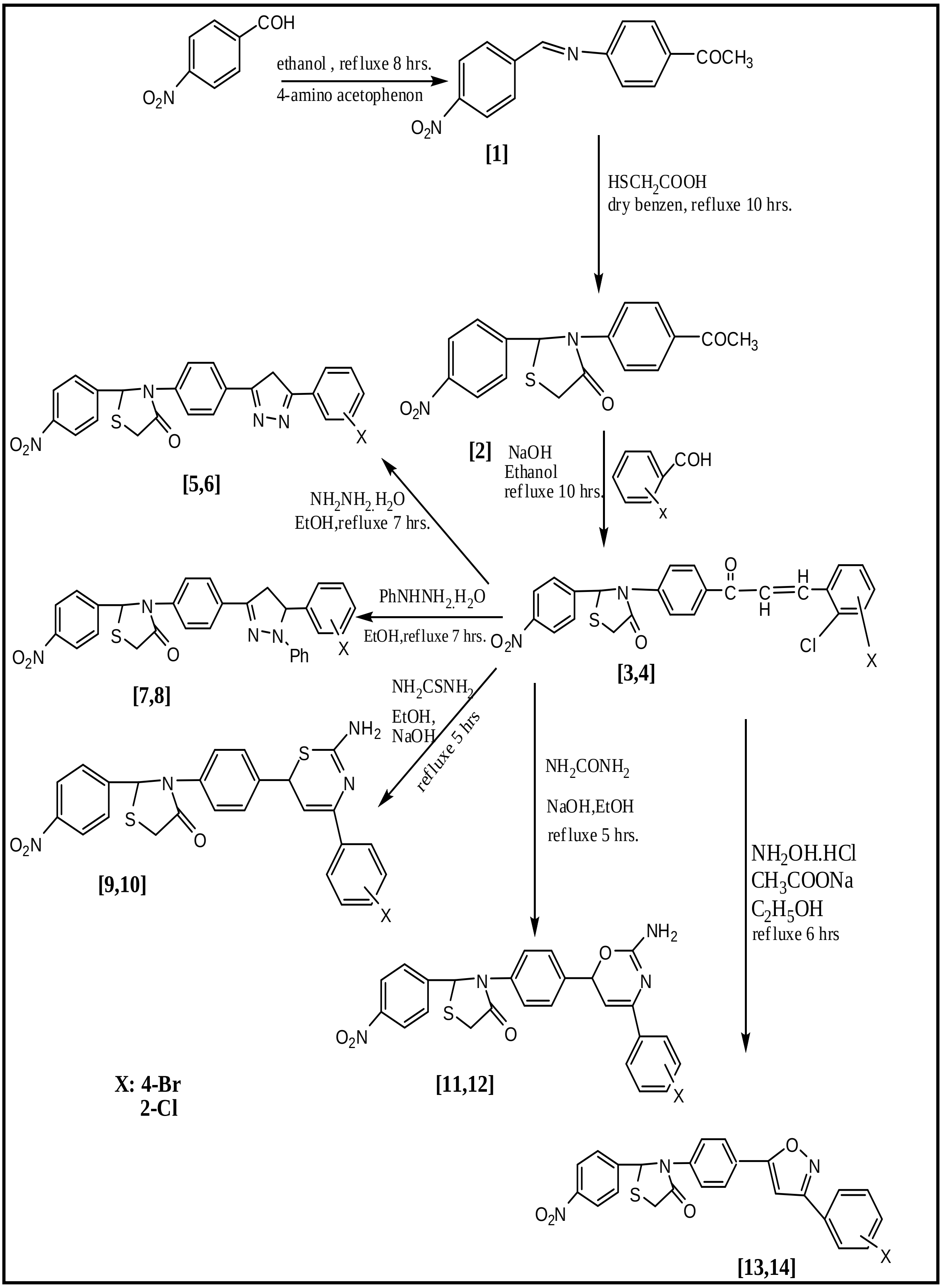
A mixture of chalcones (3,4) (0.01 mol),hydrazine hydrate 99%,phenyl hydrazine (0.01 mol) respectively in ethanol 50 ml refluxed for 7 hrs. Then the mixture was concentrate and allow to cool , the resulting solid was filtered and recrystallized from ethanol.

Synthesis of 3-(4-(2-amino-4-(substituted phenyl)-6H-1,3-thiazin-6-yl)phenyl)-2-(4-nitro phenyl)thiazolidin-4-one (9,10) and 3-(4-(2-amino-4-(substitutedphenyl)-6H-1,3-oxazin-6-yl)phenyl)-2-(4-nitro phenyl)thiazolidin-4-one (11,12).

A mixture of chalcone (3,4) (0.01 mol) ,thiourea, urea (0.01 mol)were dissolved in ethanolic sodium hydroxid (10 ml)was refluxed 5 hrs., then pourd into 400ml cold water with continuous stirring for an hour and then kept in refrigerator for 24 hrs. The precipitate obtained was filtered ,washed and recrystallized by ethanol.

Synthesis of Isoxazole derivatives (13,14).

A mixture of chalcon (3,4) (0.01 mol), hydroxylamine hydrochlorid (0.01 mol) and sodium acetate in ethanol (30ml) was refluxed for 6 hrs. The mixture was concentrated by distilling out the solvent under reduced pressure and poured into ice water , the precipitate obtaind was filtered ,washed and recrystallized by ethanol.



Scheme 1: Synthesis new compounds

Results And Discussion

The derivatives were prepared following the reaction sequences outlined in **scheme I**. all prepared derivatives (1-14) have been characterized by spectroscopic method such as (FT-IR, ^{1}H-NMR) spectra and C.H.N analysis . Reaction 4-nitro benzaldehyde with 4-amino acetophenon to afford compound (1) indicated by appearance the azomethine CH=N stretching at 1640 cm^{-1} and disappearance NH_2 band show **Table 1**. Reaction compound (1) with Thioglycolic acid in dry benzene to form compound (2) ,the IR show disappearance azomethine and appearance the carbonyl of thiazolidion 1735cm^{-1} ,condensation compound (2) with different substituted aldehyde to form the chalcons compounds(3,4) ,show the FT-IR appearance the C=C alkenes at the bands 1608,1610 cm^{-1} respectively **Table 1**, ^{1}HNMR(DMSO_d$_6$) of compound **3** : 6.44(s,1H,C$\underline{H}$), 4.00(s,2H,C$\underline{H}_2$,of thiazolidin-4-one ring) ,8.2 (s,1H,CH=C$\underline{H}$ ethylene) ,7.4 (s1H,C$\underline{H}$ ethylene) 7.7-8.3 proton of heterocyclic **Table 2** The chalcones (3,4) react with hydrazine hydrate 99% and phenyl hydrazine to afford pyrazole derivatives (5,6,7,8) FT-IR show the disappearance C=C alkenes and appearance the pyrazole ring N-N 1284,1288,1290,1298 cm^{-1}respectively and band C=N at 1658,1660,1640,1635 cm^{-1}respectively **Table 1**, ^{1}HNMR(DMSO_d$_6$) of compound **5 ,7** respectively : 6.44(s,1H,C$\underline{H}$ methine), 4.0(s,2H ,C$\underline{H}_2$) ,1.2 (s,2H, C$\underline{H}_2$ methylene),7.3-8.14 proton of heterocyclic **Table 2,** compound **7** : 6.44(s,1H,C$\underline{H}$ methine) ,4.0 (s,2H ,C$\underline{H}_2$ of thiazolidin-4-one ring) ,3.91 (s,2H ,C$\underline{H}_2$ methylene) ,5.19(s,1H,C$\underline{H}$ methine),7.3-8.14 proton of heterocyclic **Table 2**. Chalcon (3,4) condensation with thiourea and urea afford thiazine and oxazine derivatives (9,10,11,12) the FT-IR of compound (9,10) show the appearance SH at the 2250,2330 cm^{-1} and make tutomersim with NH_2 that appearance at band 3210,3110 cm^{-1} respectively **Table 1**,^{1}HNMR(DMSO_d$_6$) of compound **9** : 6.44(s,1H,C$\underline{H}$ methine) ,4.0 (s,2H,C$\underline{H}_2$) ,4.5(s,2H,C$\underline{H}_2$methylene),6.7(s,1H,C$\underline{H}$=),7.5 (s,2H,N$\underline{H}_2$)7.7-8.14 proton of heterocyclic **Table 2** , the compound (11,12) show FT-IR appearance band of OH in both compounds at 3400,3458 cm^{-1}, broad band of NH due to tutomersim between (OH) and C=N(3296 , 3210) cm^{-1}, band of C=N endo cyclic shifted to frequency about (1675-1665) cm^{-1} respectively due to tutomersim witch showed previously ,C=C aromatic (1610,1600)cm^{-1} show **Table 1**. ^{1}HNMR (DMSO_d$_6$) of compound **11** : 6.44(s,1H,C$\underline{H}$ methine) ,4.0 (s,2H,C$\underline{H}_2$ methylene) ,5.19(s,1H,C$\underline{H}$ methine),6.5(s,1H,C$\underline{H}$=),7.6-8.14 proton of heterocyclic **Table 2**. React chalcones (3,4) with hydroxylamine hydrochlorid and sodium acetate afforded compounds (13,14) show the FT-IR appearance the C-O (1223-1234)cm^{-1} , C-N(1099-1190) cm^{-1} respectively show **Table 1**.

Table 1: Physical Properties and Spectral Data of Compounds

NO	*Formula*	*Mp C°*	*Yield %*	*Element analysis calculate /Found*	*FT-IR cm^{-1}*
1	$C_{15}H_{12}N_2O_3$	220-222	70	**C**:67.16/67.13, **H**:4.51/4.50 **N**:10.44/10.40	3040 C-H arom.,2920 C-H aliph., 1676 C=O,1640 CH=N,
2	$C_{17}H_{14}N_2O_4S$	240-242	65	**C**:59.64/59.60, **H**:4.12/4.00 **N**:8.18/8.10	3019 C-H arom.,2099 C-H aliph., 1735 C=O,603 C-S-C,1680 CO CH $_3$
3	$C_{24}H_{17}BrN_2O_4S$	180-182	60	**C**:56.59/56.53, **H**:3.36/3.30 **N**:5.52/5.50	3031 C-H arom.,2990 C-H aliph.,1720 C=O,1608 C=C alkene,1530 C=C.
4	$C_{24}H_{17}ClN_2O_4S$	199-200	55	**C**:62.11/62.00, **H**:3.59/3.54 **N**:6.10/6.00	3091 C-H arom.,2890 C-H aliph.,1730 C=O,1600 C=C alkene,1540 C=C.
5	$C_{24}H_{17}BrN_4O_3S$	233-235	66	**C**:55.29/55.23, **H**:3.29/3.24 **N**:10.75/10.70	3010 C-H arom.,2890 C-H aliph.,1720 C=O,1284 N-N,1658 C=N,1544C=C ,858 C-Br.
6	$C_{24}H_{17}ClN_4O_3S$	244-246	60	C: 60.44/60.40, **H**:3.59/3.54 **N**: 11.75/11.70	3090 C-H arom.,2880 C-H aliph.,1725 C=O,1284 N-N,1658 C=N,1544C=C ,660 C-Cl.
7	$C_{30}H_{23}BrN_4O_3S$	180-182	66	**C**:60.10/60.00, **H**:3.87/3.83 **N**:9.35/9.30	3018 C-H arom.,2990 C-H aliph.,1718 C=O,1290 N-N,1330 C-N,1606C=N ,805 C-Br,606 C-S.
8	$C_{30}H_{23}ClN_4O_3S$	200-202	56	**C**:64.92/60.90, **H**:4.18/4.15 **N**:10.09/10.00	3030 C-H arom.,2980 C-H aliph.,1725 C=O,1298 N-N,1335 C-N,1616C=N ,618 C-Cl,603 C-S.
9	$C_{25}H_{19}BrN_4O_4S$	288-290	70	**C**:54.45/54.40, **H**:3.47/3.41 **N**:10.16/10.10	3010 C-H arom.,2909 C-H ailph.,1718 C=O,1606 C=N , 1504 C=C, 3210 NH$_2$,608 C-S, 2550 SH tutomersim
10	$C_{25}H_{19}ClN_4O_4S$	210-212	65	**C**:59.23/59.20, **H**:3.78/3.71 **N**:11.05/11.00	3090 CH arom.,2980 CH aliph.,1720 C=O,1610 C=N , 1520 C=C, 3245 NH$_2$,610 C-S, 2555 SH tutomersim
11	$C_{25}H_{19}BrN_4O_3S_2$	176-178	60	**C**:59.91/59.88, **H**:3.37/3.32 **N**:9.89/9.82	3090 CH arom.,2980 CH aliph.,1720 C=O,1660 C=N , 1610 C=C, 3285 NH$_2$,610 C-S, 3458 OH tutomersim
12	$C_{25}H_{19}ClN_4O_3S_2$	210-212	55	**C**:57.41/57.38, **H**:3.66/3.61 **N**:10.71/10.66	3080 CH arom.,2990 CH aliph.,1720 C=O,1670 C=N , 1600 C=C, 3296 NH$_2$,612 C-S, 3400 OH tutomersim
13	$C_{24}H_{16}BrN_3O_4S$	198-200	60	**C**:55.18/55.14, **H**:3.09/3.03 **N**:8.09/8.00	3090 C-H arom.,2990 C-H aliph.,1720 C=O,1630 C=N ,1608 C=C,1223 C-O, 1099 C-N.
14	$C_{24}H_{16}ClN_3O_4S$	180-182	65	**C**:60.31/60.29, **H**:3.37/3.30 **N**:8.79/8.70	3099 C-H arom.,2990 C-H aliph.,1720 C=O,1645 C=N , 1600 C=C,1234 C-O, 1190 C-N.

Table 2: Chemical Schiff's ^{1}H-NMR Spectra

No.	*^{1}H-NMR (DMSO_d$_6$)δ ppm*
3	6.44(s,1H,C$\underline{H}$), 4.00(s,2H,C$\underline{H_2}$ thiazolidin-4-one ring) ,8.3 (s,1H,CH=C$\underline{H}$ ethylene),7.4 (s1H,C$\underline{H}$ ethylene) 7.7-8.3 proton of heterocyclic
5	6.44(s,1H,C$\underline{H}$ methine), 4.0(s,2H ,C$\underline{H_2}$ thiazolidin-4-one ring) ,1.2 (s,2H, C$\underline{H_2}$ methylene),7.3-8.14 proton of heterocyclic
7	6.44(s,1H,C$\underline{H}$ methine) ,4.0 (s,2H ,C$\underline{H_2}$ thiazolidin-4-one ring) ,3.91(s,2H ,C$\underline{H_2}$methylene),5.19 (s,1H,C$\underline{H}$ methine),7.3-8.14 proton of heterocyclic
9	6.44(s,1H,C$\underline{H}$ methine),4.0(s,2H,C$\underline{H_2}$ thiazolidin-4-one ring), 4.5(s,2H ,C$\underline{H_2}$ methylene),6.7 (s,1H,C$\underline{H}$=),7.5 (s,2H,N$\underline{H_2}$)7.7-8.14 proton of heterocyclic
11	6.44(s,1H,C$\underline{H}$ methine) ,4.0 (s,2H,C$\underline{H_2}$ thiazolidin-4-one ring) ,5.19(s,1H,C$\underline{H}$ methine) ,6.5(s,1H,C$\underline{H}$=),7.6-8.14 proton of heterocyclic

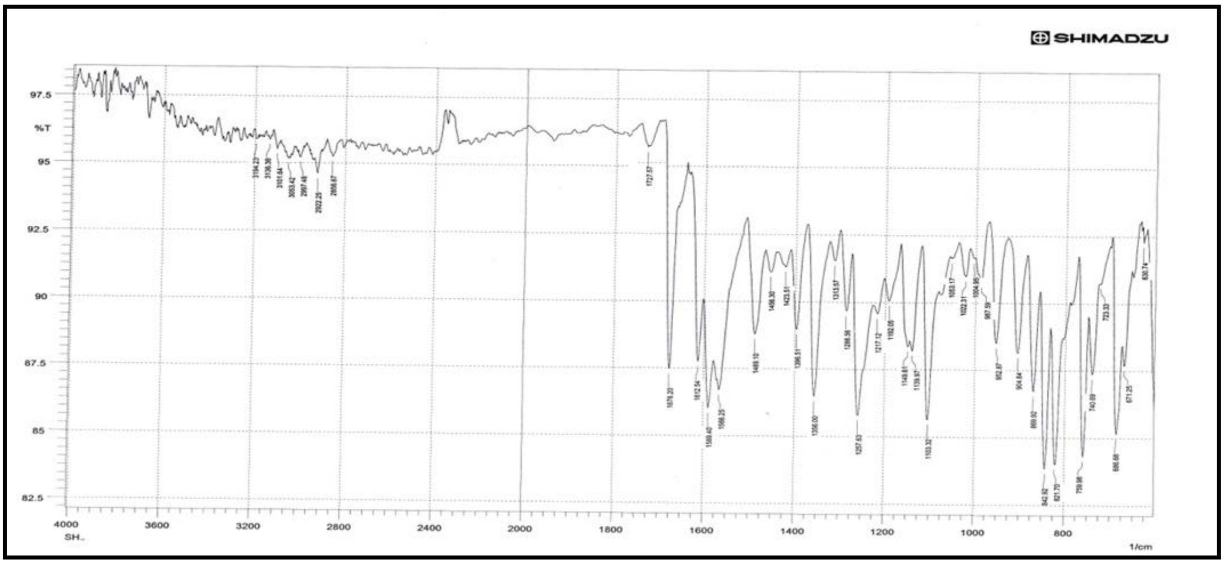
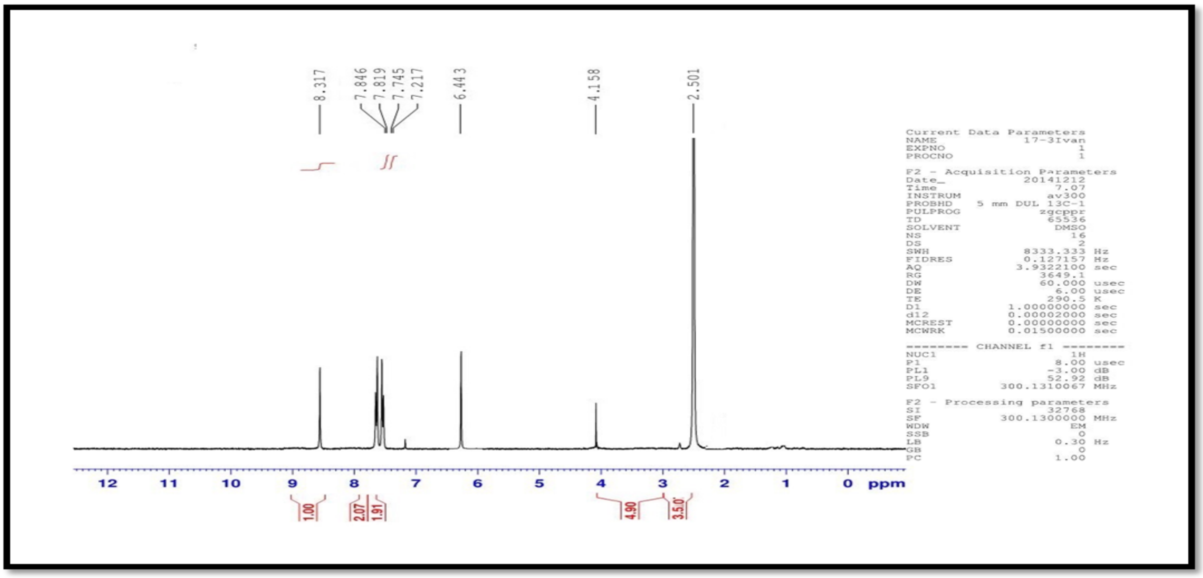


Fig. 1: FT-IR Spectrum of compound 3



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PROCNO                     1

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TD                     65536
SOLVENT                 DMSO
NS                        16
DS                         2
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FIDRES              0.127157 Hz
AQ                 3.9322100 sec
RG                    3649.1
DW                    60.000 usec
DE                      6.00 usec
TE                     290.5 K
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d12               0.00002000 sec
MCREST            0.00000000 sec
MCWRK             0.01500000 sec

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PL1                    -3.00 dB
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PC                      1.00
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Fig. 2: ^{1}H-NMR Spectrum of compound 3

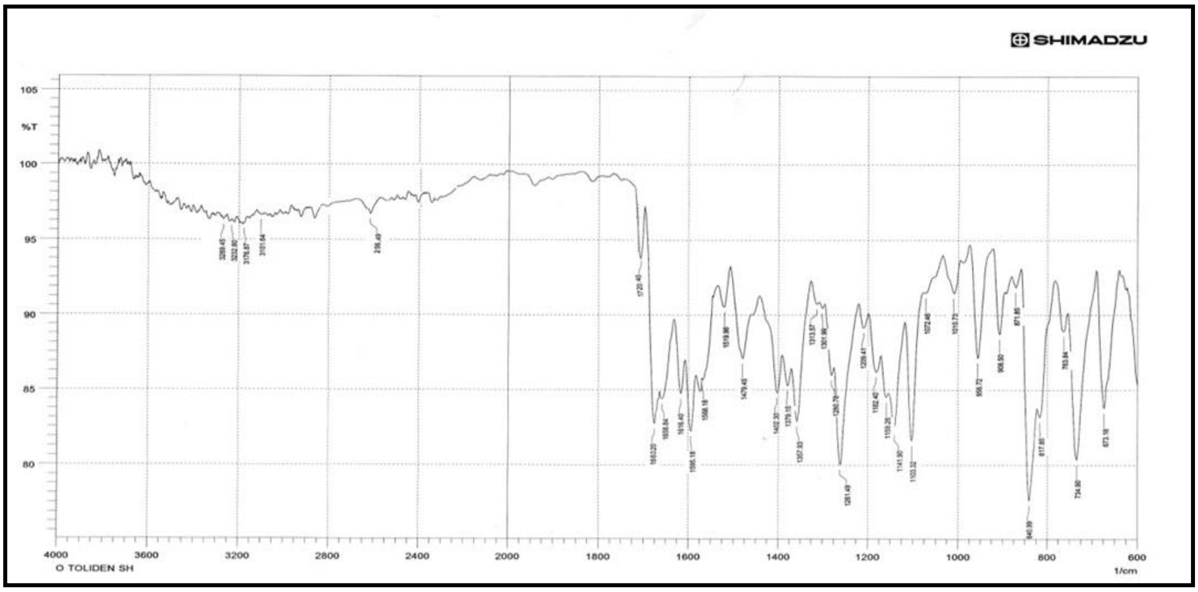
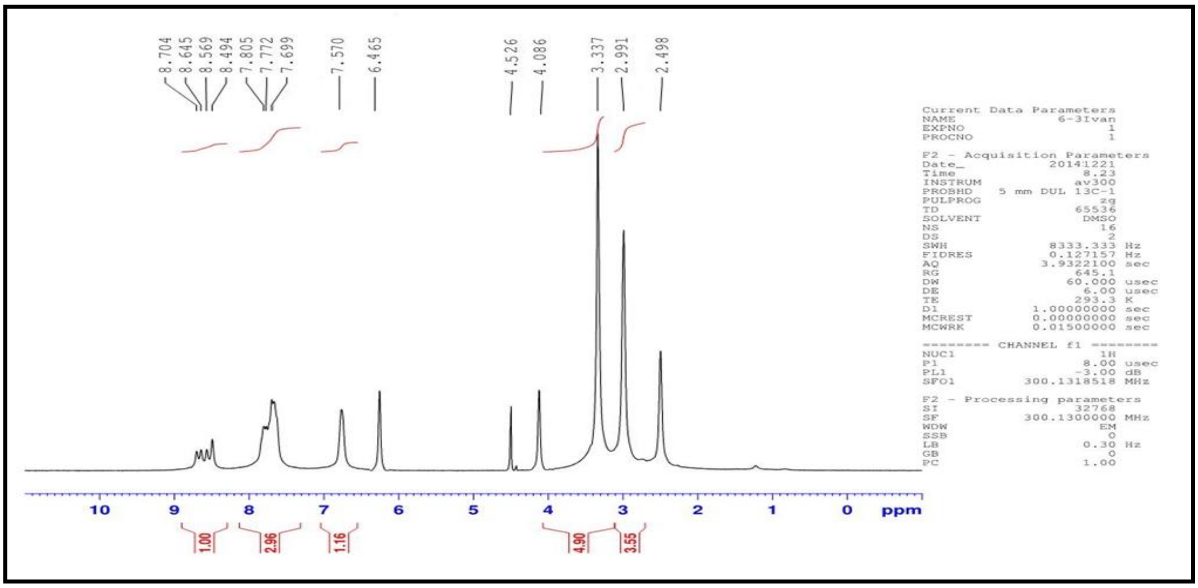


Fig. 3: FT-IR Spectrum of compound 9



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PC                  1.00
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Fig. 4: ^{1}H-NMR Spectrum of compound 9

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