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RESEARCH ARTICLE

Synthesis and Characterization of Some Oxazepine Compounds from 2- Amino Thiazole

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Abstract

A chains of new heterocyclic oxazepin compounds contain thiazole ring were Produced via two steps, the first step comprising condensation of 2- amino thiazol and various aldehydes, (3- hydroxy benzaldhyede, 4- nitro benzaldhyede, 4- chloro benzaldhyede and 4-dimethylamino benzaldhyede), and second step formation oxazepin as sevene membred ring compounds, by cycloreaction of these Schiff bases and (pathalic, malic anhydride) in tolune as solvent. These compounds were established via melting point, FTIR, HNMR, C^{13}NMR spactra.

Keywords: *2 amino thiazol, oxazepin heterocyclic, Schiff base.*

Introduction

Thiazole belongs to a period of heterocyclic compounds .Thiazoles are five membered ring systems with sulfur and nitrogen at 1 and 3 positions respectively [1]. Thiazoles are showing a great potential agricultural fields [2], pharmacological [3] and biological activities [4], such as antifungal, anti-inflammatory, antitumor, anti-tubercular, anti-diabetic, antiviral [5], antimicrobial [6] anticancer [7], prospective antimicrobial and anti-proliferative agents [8], anaesthetic, antidepressant [9], corrosion inhibitors for mild steel protection as will [10] and optical and nonlinear optical properties of thiazole [11].

Schiff bases are chemical compounds hold general group (-HC=N-) called azomethine [12].These compounds intermediates of preparation of diverse compounds and use as antimicrobial [13, 14] and anticancer [15] Oxazepine is seven member ring that covers two heteroatom (Oxygen and Nitrogen).,these compounds formation by cycloaddition reaction between Schiff compounds with different anhydrides [16, 17] Oxazepine and their derivatives have more important biological pharmacological activities [18, 19], like antibacterial [20]. Antifungal [12], hypotic muscal relaxant [22], anti-inflammatory [23], antiepileptic [24].

Experimental

All chemicals secondhand were supplied from, fluka, Merck and BDH chemical company; Melting points were recorded using Electro thermal melting point apparatus, UK. FT-IR spactra were recarod by Shimadzu _8400S. Japan, using KBr disc. H^{1}NMR, C^{13}NMR were recorded by Spectrophotometer Varian 500 MHZ. Thin layer chromatography (TLC) was done an aluminum plates coated , with layer of silica gel.

Synthesis Schiff bases Derivatives (S1_S5)

S1=1-(4-Nitro pheny) – N-(thiazol-2-yl) methanimine

S2= 1-(4-chlorophenyl) – N-(thiazol-2-yl) methanimine

S3= 1-(4-dimethylaminophenyl) – N-(thiazol-2-yl) methanimine

S4= 1-(3-hydroxyphenyl) – N-(thiazol-2-yl) methanimine

S5= 1-(4-methoxyphenyl) – N-(thiazol-2-yl) methanimine

A series of Schiff base were prepared by reaction of 2-amino thiazol (0.5gm, 0.0049mol) with different substituted aromatic aldehyde (4-nitro, 4-chloro, 4-dimethyleamino, 3-hydroxy and 4-methoxybenzaldehyde), (0.75gm, 0.70gm, 0.74gm, 0.60, 0.67gm) respectively, (0.0049mol) in (35 ml) absolute ethanol and (2-3drops) of glacial acetic acid, then this mixture was refluxed for(19-23hour), the end reaction examined by using TLC (methanol: benzene 1.5:3.5),then the precipitate was filtered and recrystallized by ethanol. Physical properties are listed in Table (1).

Preparation of Oxazepine (Z1-Z5)

Z1 = 2-(4-nitrophenyl)-3-(thiazol-2-yl)-2, 3-dihydro-1, 3-oxazepine-4,7dion

Z2 = 2-(4-chlorophenyl)-3-(thiazol-2-yl)-2, 3-dihydro-1, 3-oxazepine-4,7dion

Z3 = 2-(4-dimethylaminophenyl)-3-(thiazol-2-yl)-2, 3-dihydro-1, 3-oxazepine-4,7dion

Z4 = 2-(3-hydroxyphenyl)-3-(thiazol-2-yl)-2, 3-dihydro-1, 3-oxazepine-4,7dion

Z5 =2-(4-methoxyphenyl)-3-(thiazol-2-yl)-2, 3-dihydro-1, 3-oxazepine-4,7dion

A mixture of Schiff bases derivatives (S1_S5), (0.47gm, 0,50gm, 0.41gm, 0.48gm, 0.35gm) with (0.196gm, 0.220gm, 0,166gm, 0.230gm, 0.156gm) malic anhydride in 25 ml of toluene was refluxed at 70C° for (25h, 29h, 20h, 23h, 22h) respectively. The end reaction examined by using TLC (methanol: benzene 1.5:3.5), then recrystallized from ethanol

Preparation of Oxazepine(Z6-Z10)

Z6 = 3-(4-nitro phenyl)-4- (thiazol-2-yl)-3,4dihydrobenzo (e) (1, 3) oxazepine-1, 5-dione

Z7 = 3-(4-chlorophenyl)-4-(thiazol-2-yl)-3,4dihydrobenzo (e) (1, 3) oxazepine-1, 5-dione

Z8 =3-(4-(dimethylamino) phenyl)-4- (thiazol-2-yl)-3,4dihydrobenzo (e) (1, 3) oxazepine-1, 5-dione

Z9 = 3-(3-hydroxyphenyl)-4-(thiazol-2-yl)-3,4dihydrobenzo (e) (1, 3) oxazepine-1, 5-dione

Z10 = 3-(4-methoxyphenyl)-4-(thiazol-2-yl)-3,4dihydrobenzo (e) (1, 3) oxazepine-1, 5-dione

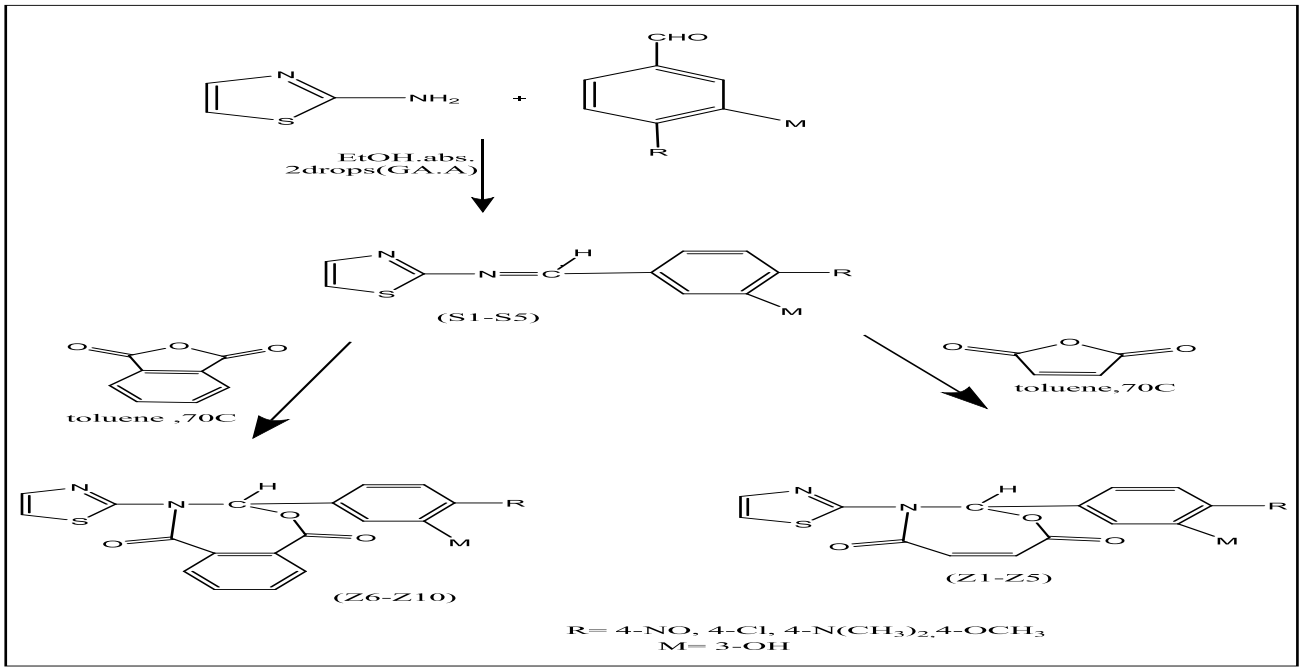
A combination of Schiff bases derivatives (S1_S5) (0.47gm, 0.42gm ,0.41gm, 0.38,0.35gm) with (0.296gm, 0.279gm, 0.251gm, 0.236gm, 0.275gm) phthalic anhydride in 25 ml of toluene was refluxed at 70C° for (20h, 25h, ,31h, 10h, 19h), then recrystallization was done by ethanol. Table-1 shows the physical properties of these compounds, the end reaction examined by using TLC (methanol: benzene 1.5:3.5), then recrystallized from ethanol.

Table 1: Physical topographies of systematized compounds

No.	Molecular formal	Molecular Weight	Melting point C°	yield	Rf
S1	$C_{10}H_7N_3O_2S$	233	170-174	83%	0.73
S2	$C_{10}H_8N_2OS$	204	198-200	73%	0.71
S3	$C_{10}H_7N_2ClS$	222.69	150-153	81%	0.68
S4	$C_{12}H_{13}N_3S$	231	189-192	83%	0.63
S5	$C_{11}H_{10}N_2OS$	218	137-140	66%	0.61
Z1	$C_{14}H_9N_3O_5S$	331.3	212-215	84%	0.74
Z2	$C_{14}H_9Cl\ N_2O_3S$	320.75	156-158	78%	0.64
Z3	$C_{16}H_{15}N_3O_3S$	329.37	189-192	60%	0.58
Z4	$C_{14}H_{10}N_2O_4S$	302.3	211-213	82%	0.74
Z5	$C_{15}H_{12}N_2O_4S$	316.33	241-244	82%	0.64
Z6	$C_{18}H_{11}N_3O_5S$	381.36	264-267	77%	0.87
Z7	$C_{18}H_{11}ClN_2O_3S$	370.81	241-243	73%	0,71
Z8	$C_{20}H_{17}N_3O_3S$	379.34	193-195	66%	0.67
Z9	$C1_8H_{12}N_2O_4S$	352.36	201-203	87%	0.65
Z10	$C_{19}H_{14}N_2O_4S$	366.39	178-182	65%	0.75

Results and Discussion

The synthetic orders for preparation of sequences of Schiff base and oxazapine derivatives are shown in Scheme (1).



Scheme

Schiff bases (S1-S5) were equipped via retort of hetrocyclic compound (2-amino thiazol) thru altered aromatic aldehydes in company of glacial acetic acid; these compounds were inveterate via physical properties recorded in Table (1).

The FT-IR spectrum exposed loss of absorption band for NH_2 group of (2-amino thiazol).

S1= 1670.35(C=N), 3039.81-3113.11 (C-H aromatic), 1593.20 (C=N) thiazol, 1340.53 (aromatic NO_2)

S2= 1680.00(C=N), 3007.18-3163.26 (C-H aromatic), 1591.27(C=N) thiazol, 779.24 (C-Cl)

S3 = 1666.50(C=N), 3080.32-3186.40(C-H aromatic), 1593.20(C=N) thiazol, 1313.52 (-N $(CH_3)_2$)

S4 = 1683.86(C=N), 3055-3190.28 (C-H aromatic), 1595.13(C=N) thiazol, 3282.84 (OH)

S5=1685.79(C=N), 3057.17-3172.92(C-H aromatic), 1062.85(C=N) thiazol

Z1 = 1699.29 (C=O), 3051.39-3109 (C-H aromatic), 1350.17 (C-N), 1151.50(C-O-C)

Z2= 1693.50(C=O), 3072.39-3116 (C-H aromatic), 1303.88(C-N), 1151.50 (C-O-C)

Z3 = 1697.24(C=O), 3070.46 (C-H aromatic), 1303.79(C-N), 1149.50 (C-O-C)

Z4= 1697.24(C=O), 3070.46-3193.90(C-H aromatic), 1296.08(C-N), 1164.92(C-O-C), 3224.76(OH)

Z5 =1718.58(C=O), 3076.48(C-H aromatic), 1261.46(C-N), 1166.93 (C-O-C)

Z6= 1708.93(C=O), 3020.79-3105.39(C-H aromatic), 1350.17(C-N), 1147.65 (C-O-C)

Z7= 1712.79(C=O), 3041.74-3080.32(C-H aromatic), 1305.81(C-N), 1078.21 (C-O-C)

Z8= 1707.00(C=O), 3068.75(C-H aromatic), 1338.60(C-N), 1141.86 (C-O-C)

Z9= 1712.67(C=O), 3031.89-3070.46(C-H aromatic), 1380.94(C-N), 1172.64 (C-O-C)

Z10 =1707.93(C=O), 3034.03(C-H aromatic), 1307.74(C-N), 1163.08 (C-O-C)

The FT-IR spectrums prepared derivatives are painted in Figures (1, 2, 5, 8, 11, 14, 17)

H^1NMR Spectra of Prepared Compounds:

H^1NMR Spectra of Prepared Compounds are presented in Figures (3, 6, 9, 12, 15, 18) using DMSO as solvent:

Z1= singlet 8.477ppm (N-CH), multipleting singal 7.616-8.469ppm (aromatic-H), doublet singnal 6.299-6.616ppm (CH=CH) , 2.5ppm (DMSO).

Z2 = singlet 8.478ppm (N-CH), Multipleting singal 7.195-8.461ppm (Aromatic-H), doublet singnal 6.584-6.586ppm (CH=CH)

Z3= singlet 8.638 ppm (N-CH), multipleting singal 7.131-8.477ppm (Aromatic-H), doublet singnal 6.484-6.581ppm (CH=CH), 2.218ppm (CH3)

Z4 = singlet 8.732 ppm (N-CH), multipleting singal 7.032-8.487ppm (Aromatic-H) singlet 9.911(OH).

Z5 = singlet 8.116 ppm (N-CH), multipleting singal 7.220-8.074ppm (Aromatic-H), singlet 3.798(OCH3).

Z6= singlet 8.415 ppm (N-CH), multipleting singal 7.183-8.411ppm (Aromatic-H), Z7= singlet 8.660ppm (N-CH), multipleting singal 7.181-8.643ppm (Aromatic-H),

Z8= singlet 8.636 ppm (N-CH), multipleting singal 6.750-8.630ppm (Aromatic-H), 1.283ppm (CH_3)

Z9= singlet 8.622ppm (N-CH), multipleting singal 6.467-8.605ppm (Aromatic-H), siglet 9.894ppm (OH).

Z10 = singlet 8.640(N-CH), multipleting singal 6.747-8.623ppm (Aromatic-H), siglet 3.798ppm (OCH_3).

The H^1NMR spectrums prepared derivatives are painted in figures 10, 11, 12, 13, 14, 15.

C^{13}NMR Spectra of Prepared Compounds

C^{13}NMR Spectra of Prepared Compounds are presented in Figures 4, 7, 10, 13, 16, 19 using DMSO as solvent:

Z1= 192.703ppm (lactone), 169.771ppm (lactam), 109.959-166.881ppm (Aromtic- C), 39.520ppm (DMSO)

Z2=190.703ppm (lactone), 169.351ppm (lactam), 109.545-166.464ppm (Aromtic- C), Z3= 190.223ppm (lactone), 170.058ppm (lactam), 114.449-169.844ppm (Aromtic- C),

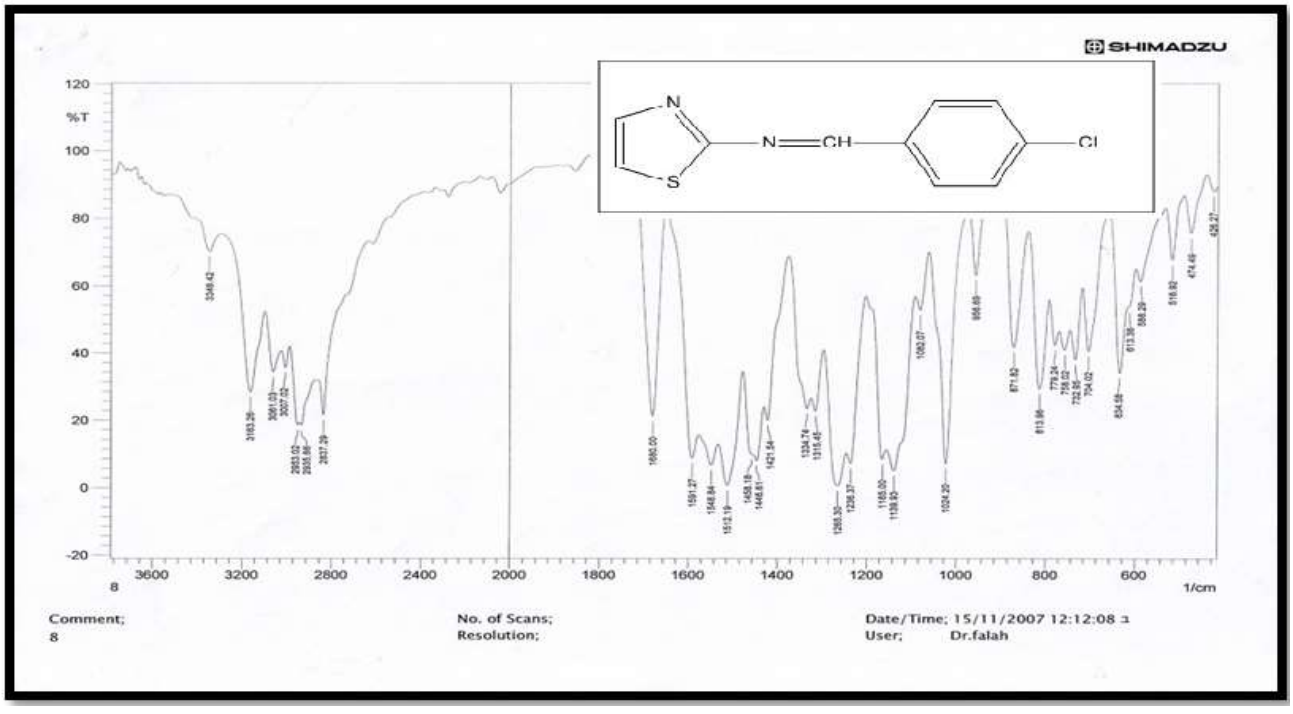
Z4= 193.465ppm (lactone), 115.063-158.384ppm (Aromtic- C),

Z5 = 193.131 ppm (lactone), 113.116-141.262 ppm(Aromtic- C), 55.576-60.645 ppm (OCH3)

Z6= 192.186ppm (lactone), 169.638ppm (lactam), 116.376-168.664ppm (Aromtic- C). Z7= 192.186ppm (lactone), 169.638m (lactam), 116.376-168.664ppm (Aromtic- C).

Z8= 189.681ppm (lactone), 169.473ppm (lactam), 110.911-168.550ppm (Aromtic- C), 13.655ppm 2(CH3).

Z9= 193.382ppm (lactone), 169.027ppm (lactam), 114.986-163.568ppm (Aromtic- C). Z10 =190.301382ppm (lactone), 169.713ppm (lactam), 114.623-167.676ppm (Aromtic- C).



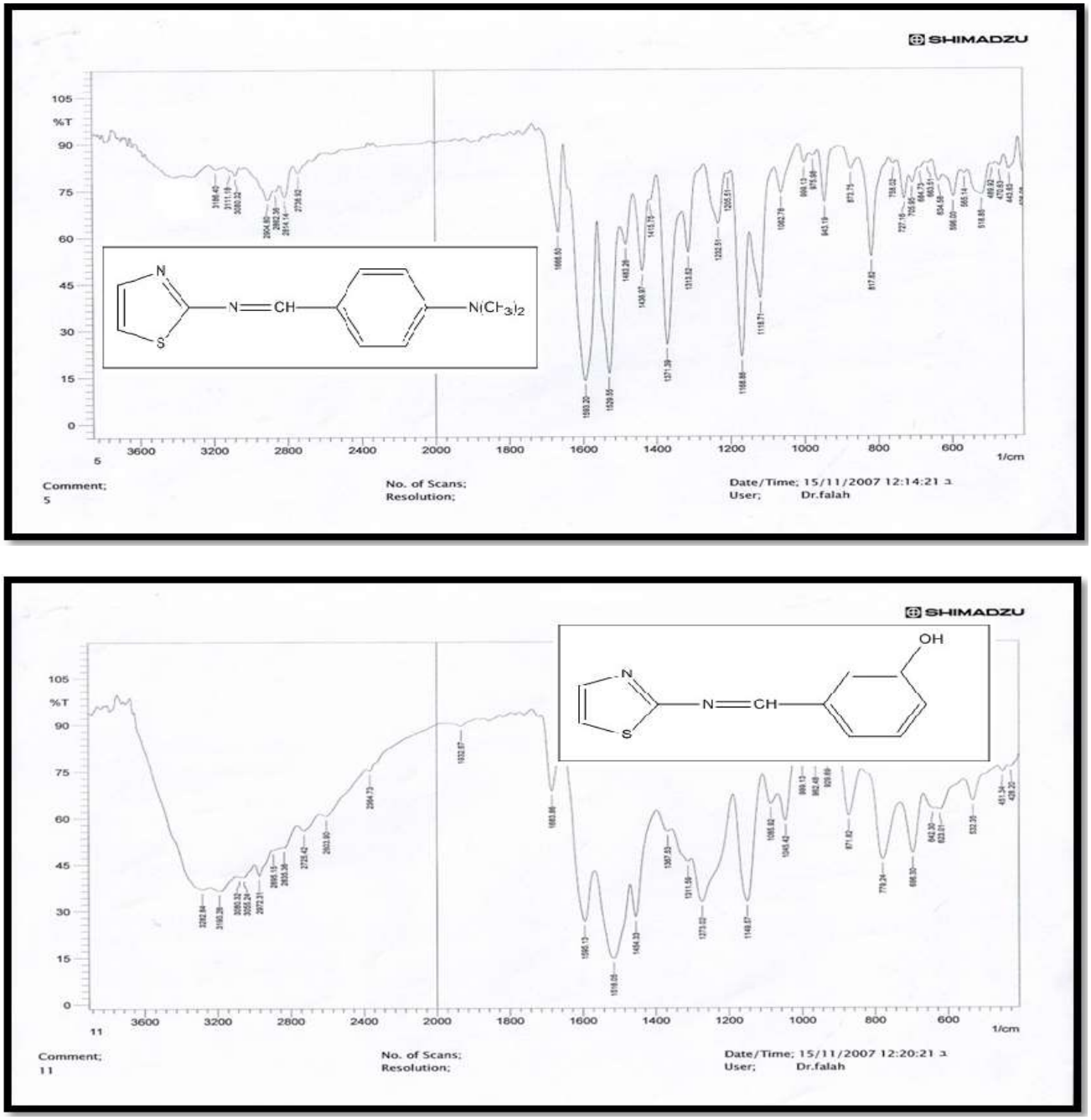


Figure 1: S2=1-(4-chloro pheny) – N-(thiazol-2-yl)methanimineyl)methanimine , S3 = 1-(4-dimethylaminopheny) – N-(thiazol-2-yl)methanimineyl)methanimine , S4 = 1-(3-hydroxypheny) – N-(thiazol-2-yl)methanimineyl)methanimin

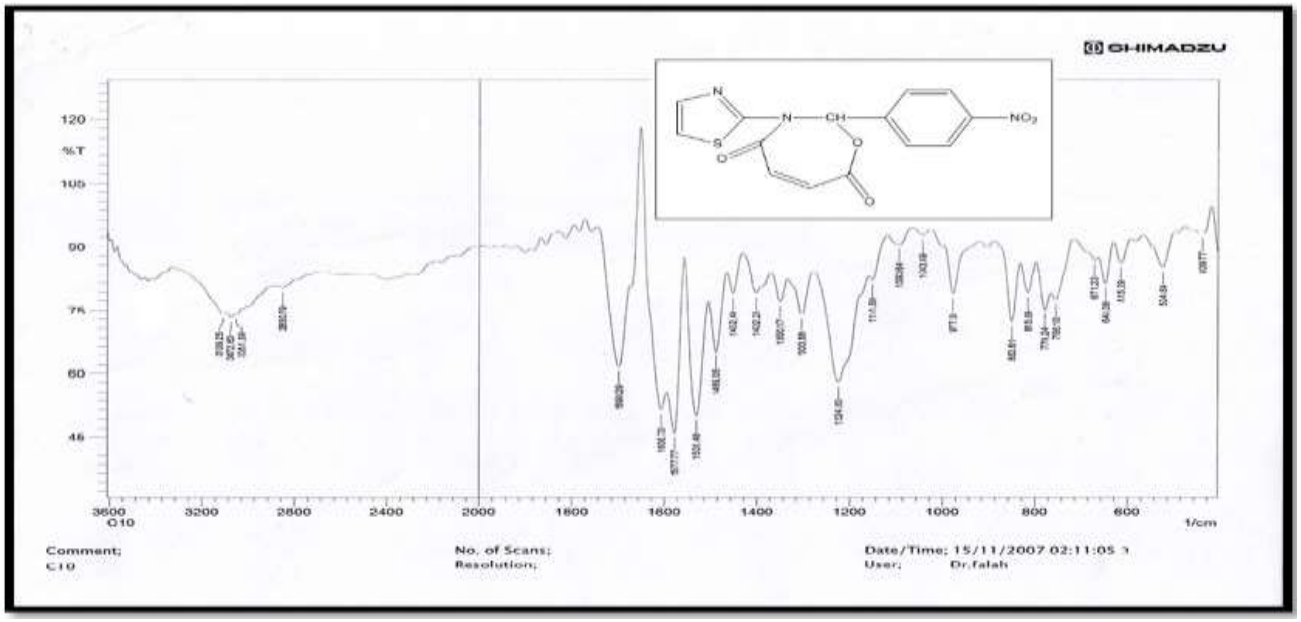


Figure 2: FTIR Spectra of compound (Z1)

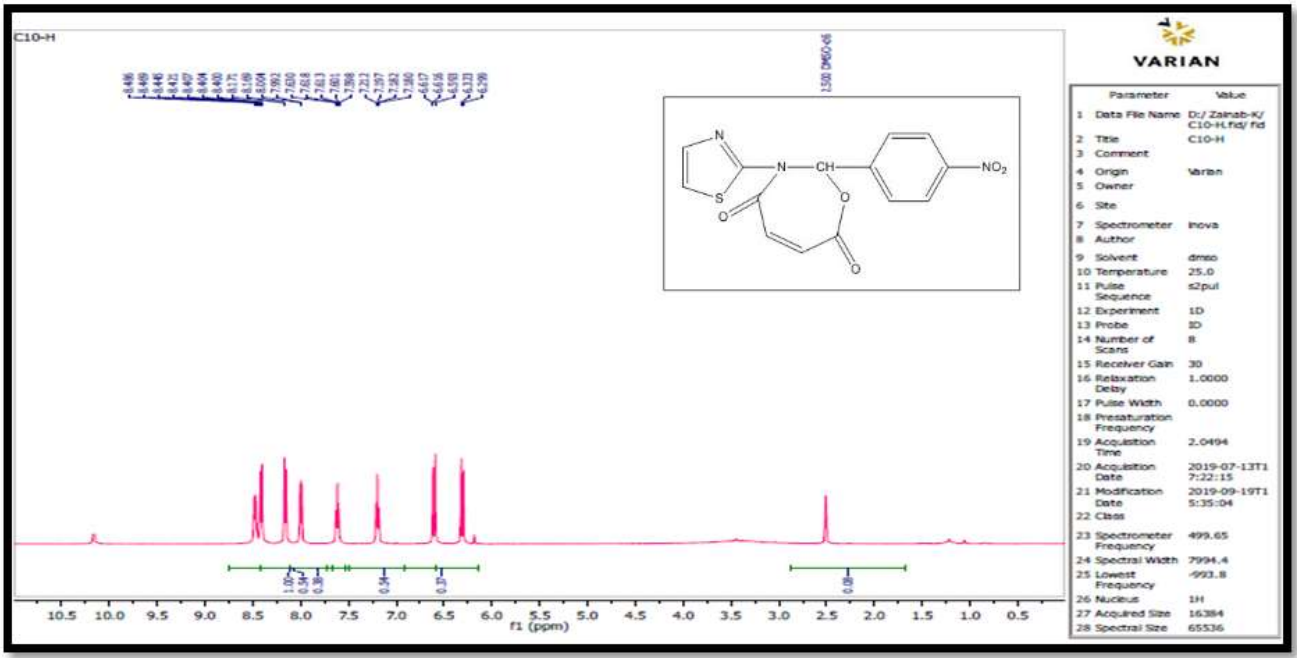


Figure 3 : ^{1}HNMR Spectra of compound (Z1)

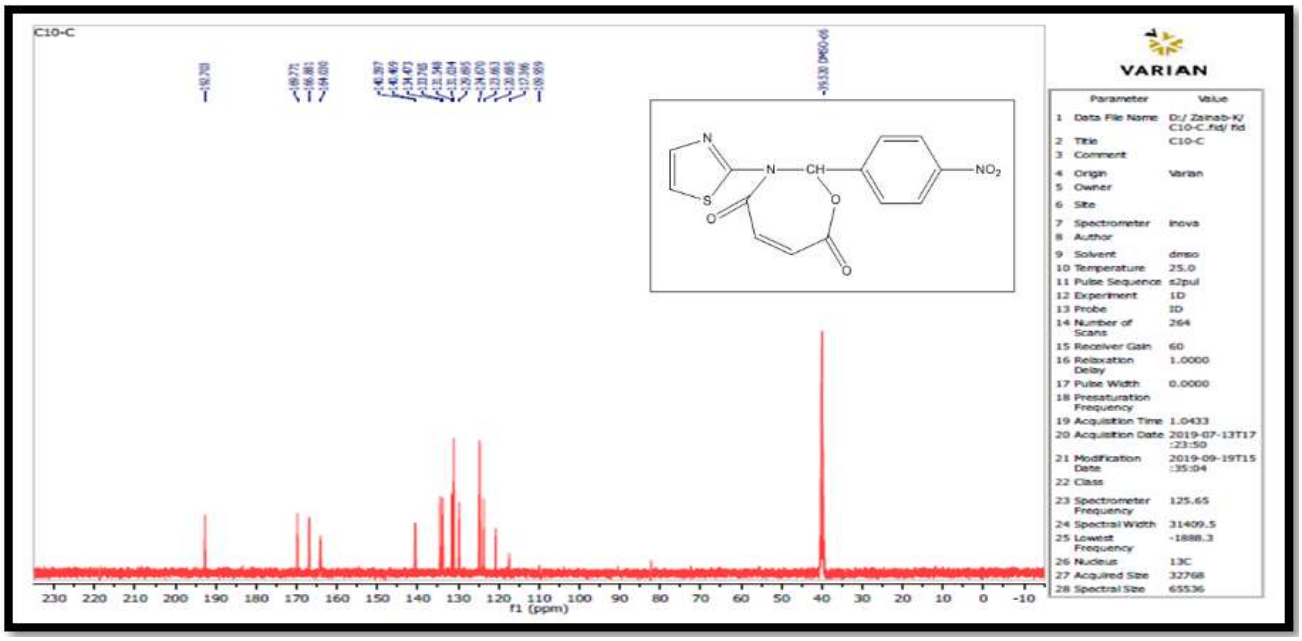


Figure 4: C^{13}NMR Spectra of compound (Z1)

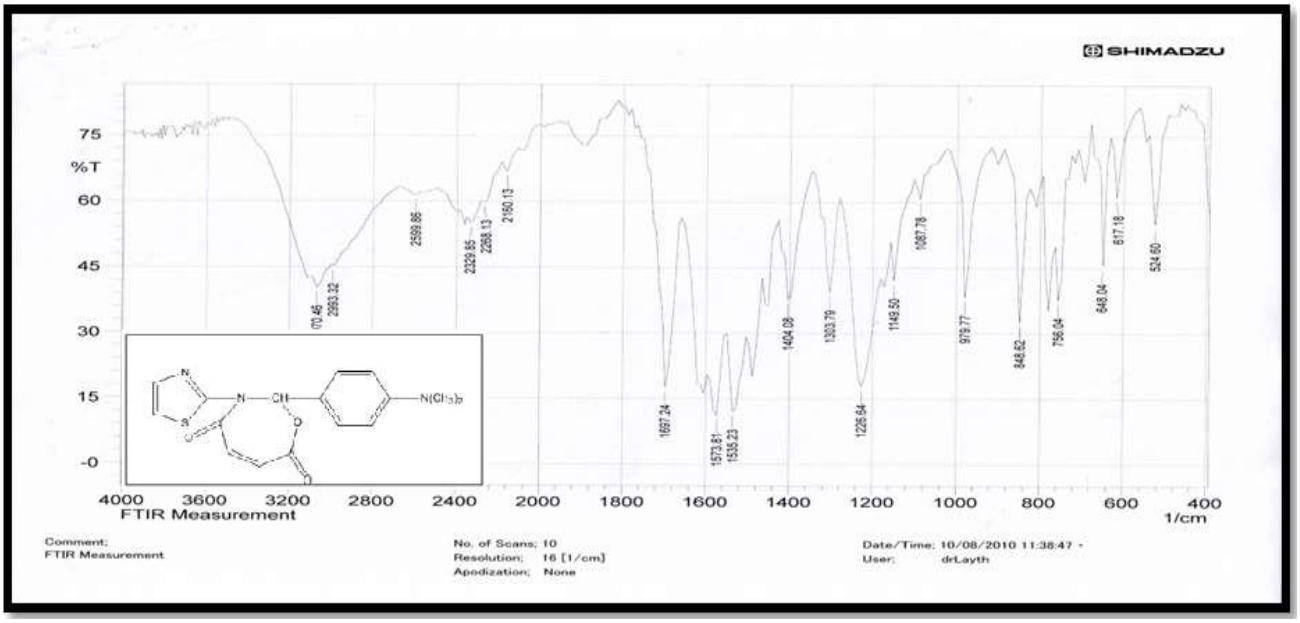


Figure 5: FTIR Spectra of compound (Z3)

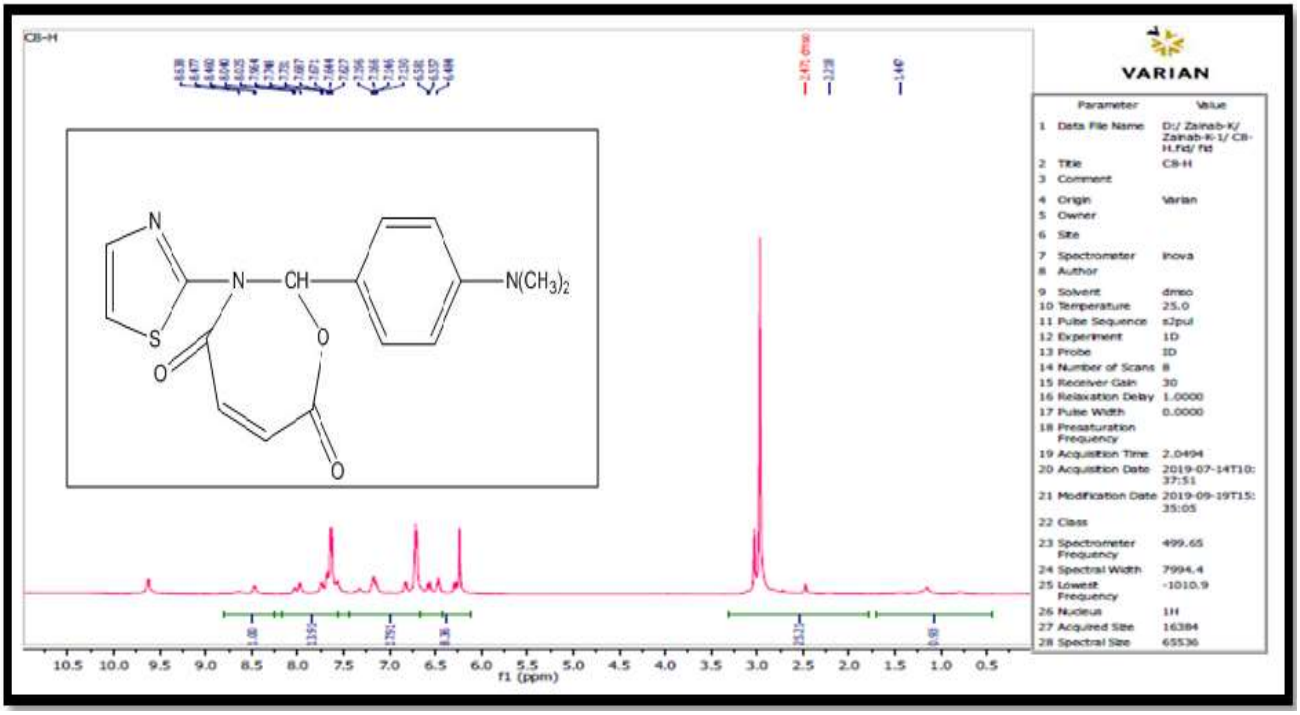


Figure 6 : ^{1}HNMR Spectra of compound (Z3)

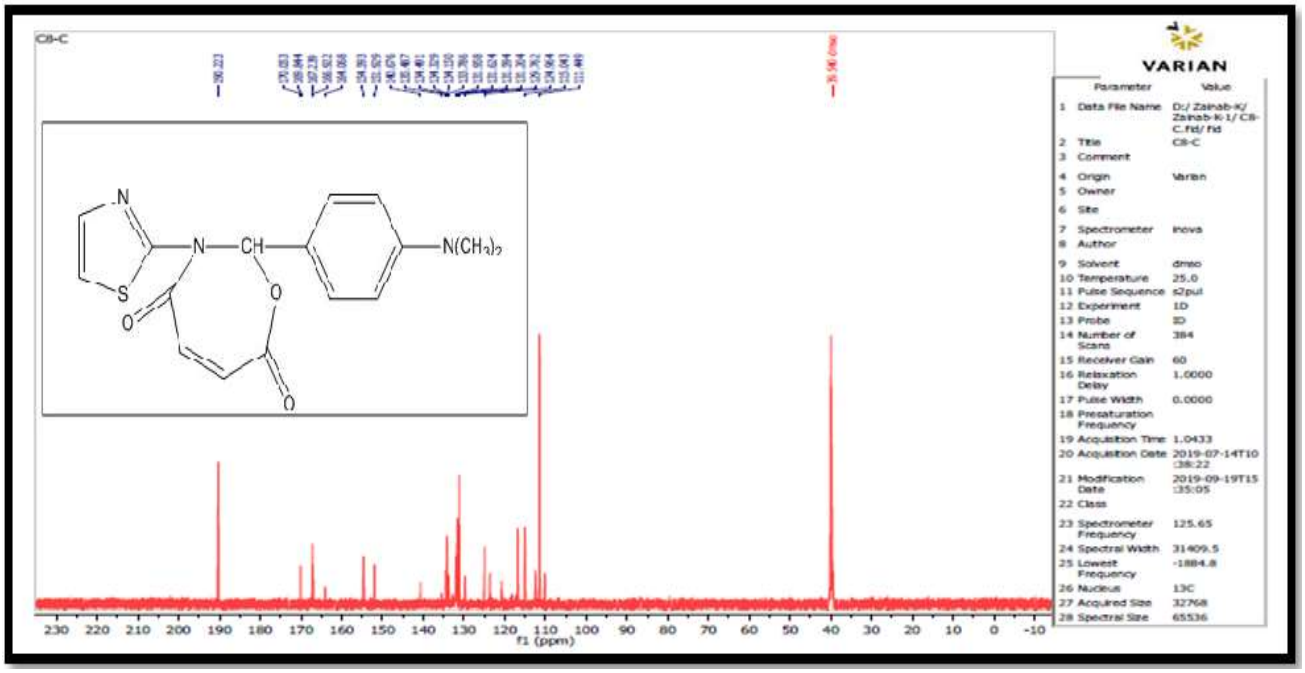


Figure 7 : C^{13}NMR Spectra of compound (Z3)

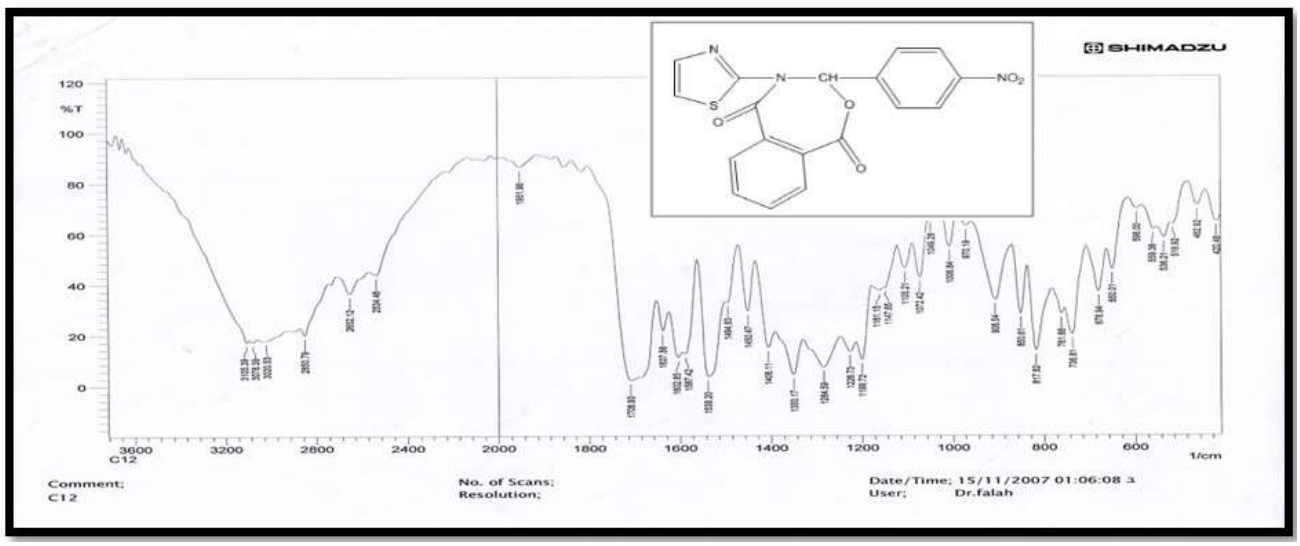


Figure 8: FTIR Spectra of compound (Z6)

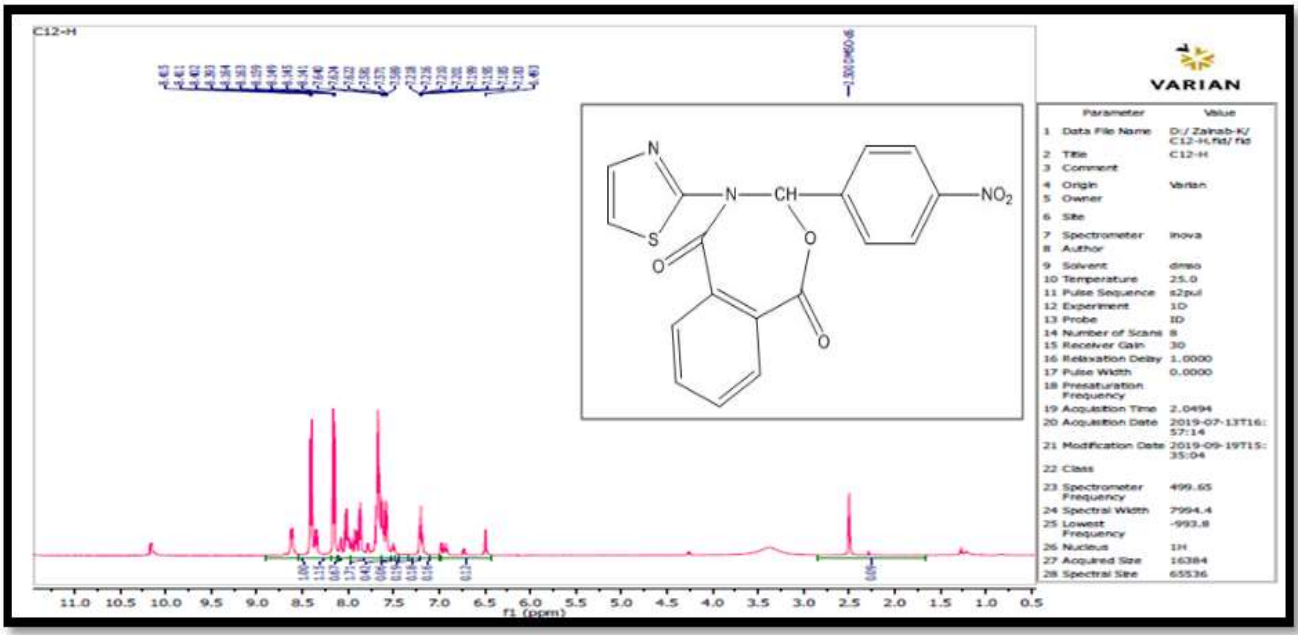


Figure 9: ^{1}HNMR Spectra of compound (Z6)

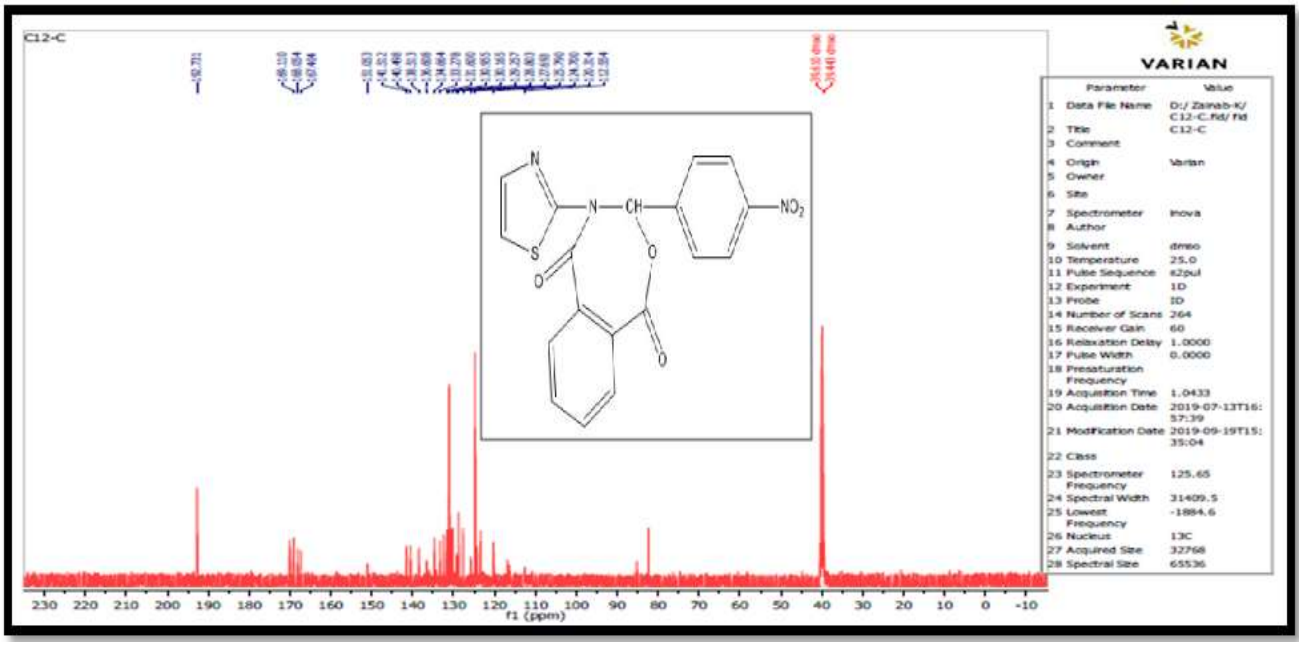


Figure 10: C^{13}NMR Spectra of compound (Z6)

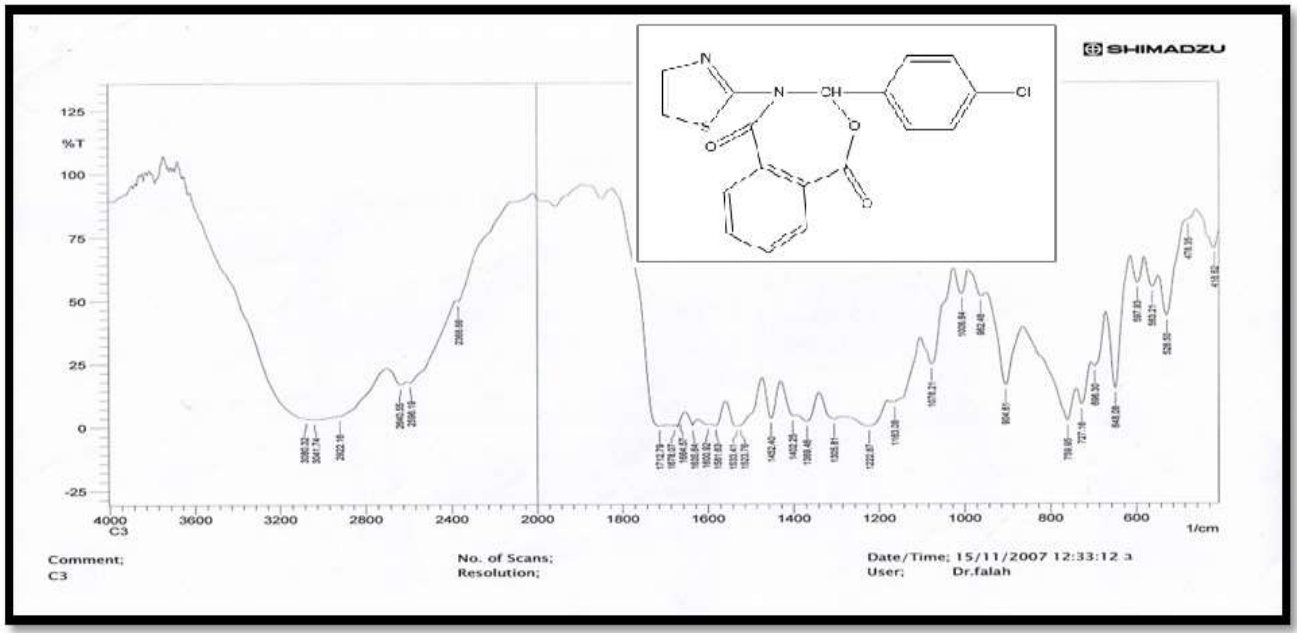


Figure 11: FTIR Spectra of compound (Z7)

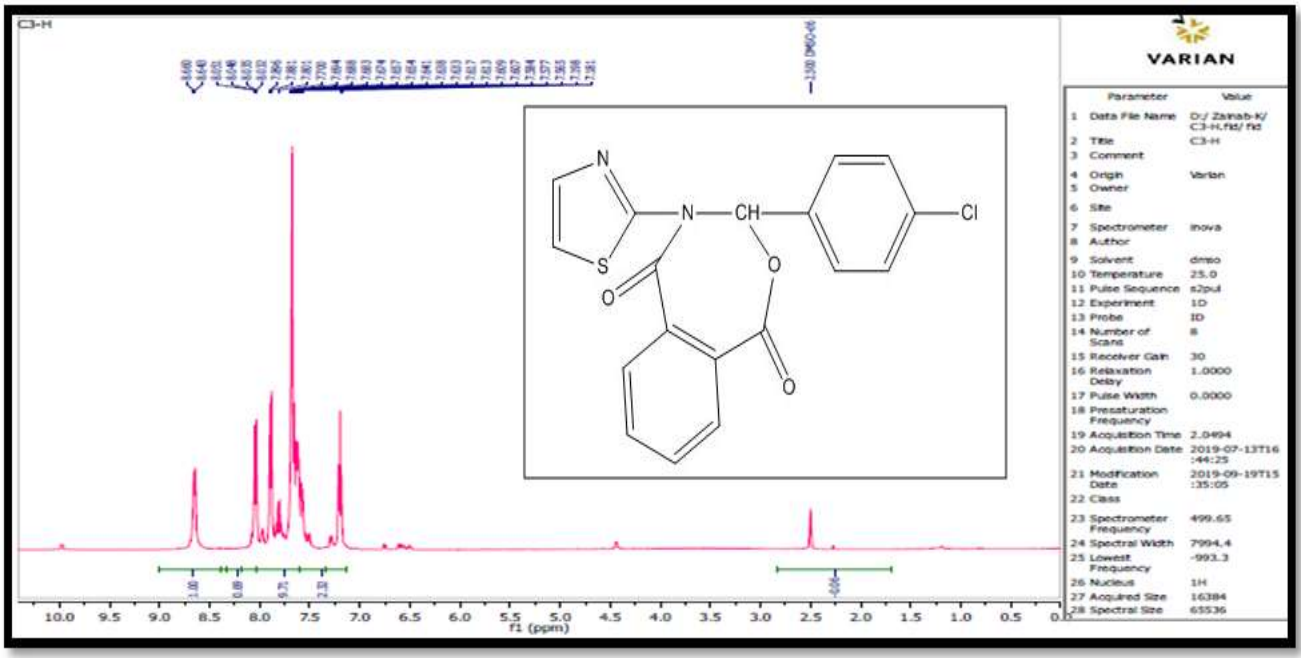


Figure 12: H1NMR spectra of compound (Z7)

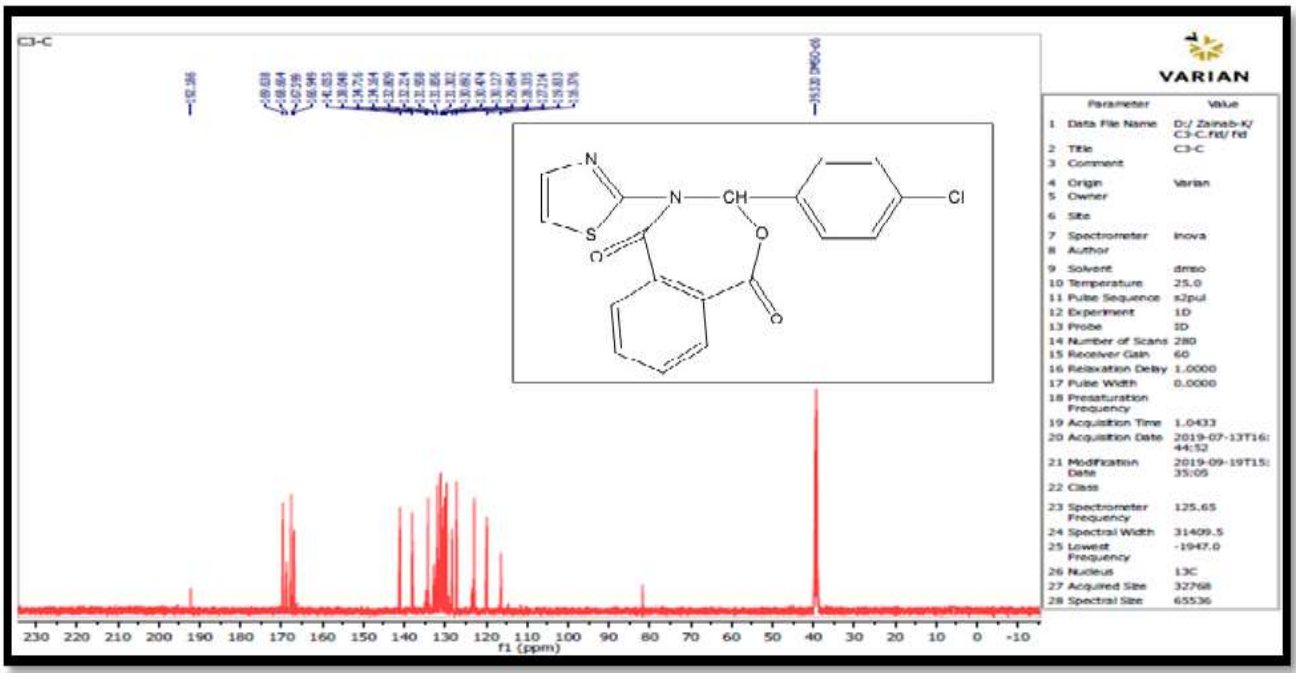


Figure 13: C[13]NMR spectra of compound (Z7)

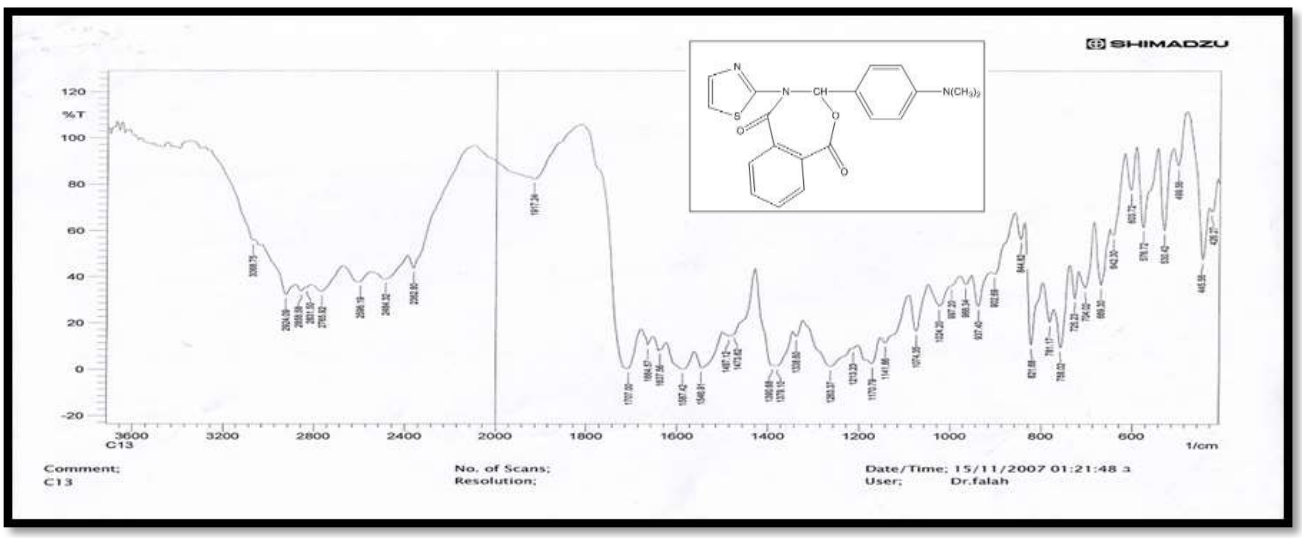


Figure 14 : FTIR spectra of compound (Z8)

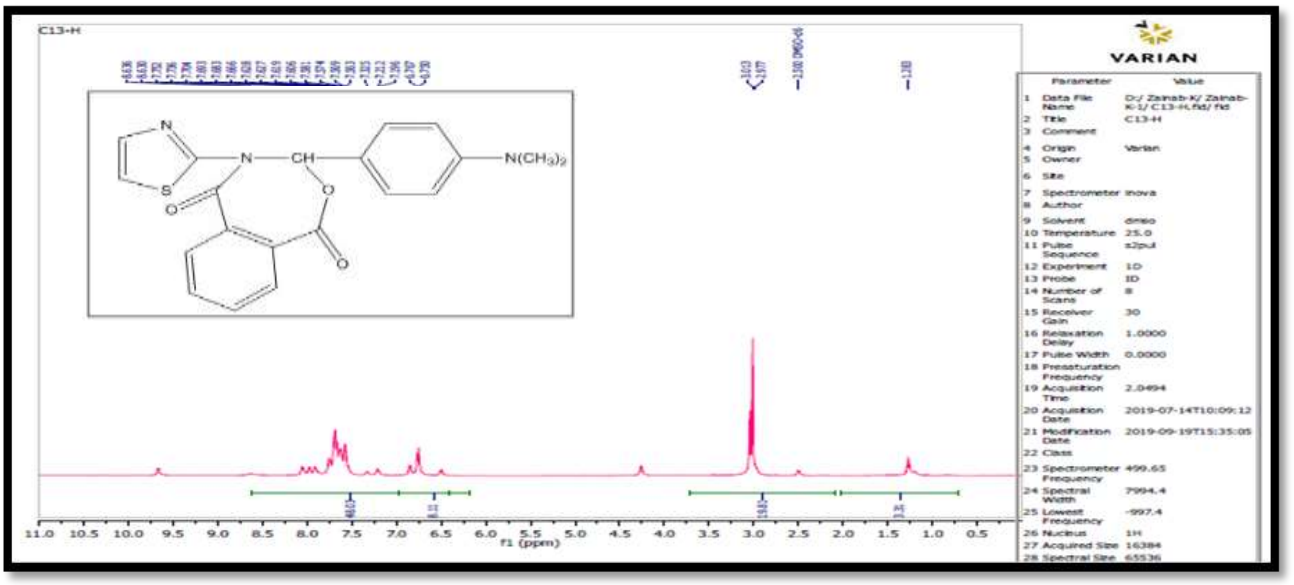


Figure 15: H[1]NMR spectra of compound (Z8)

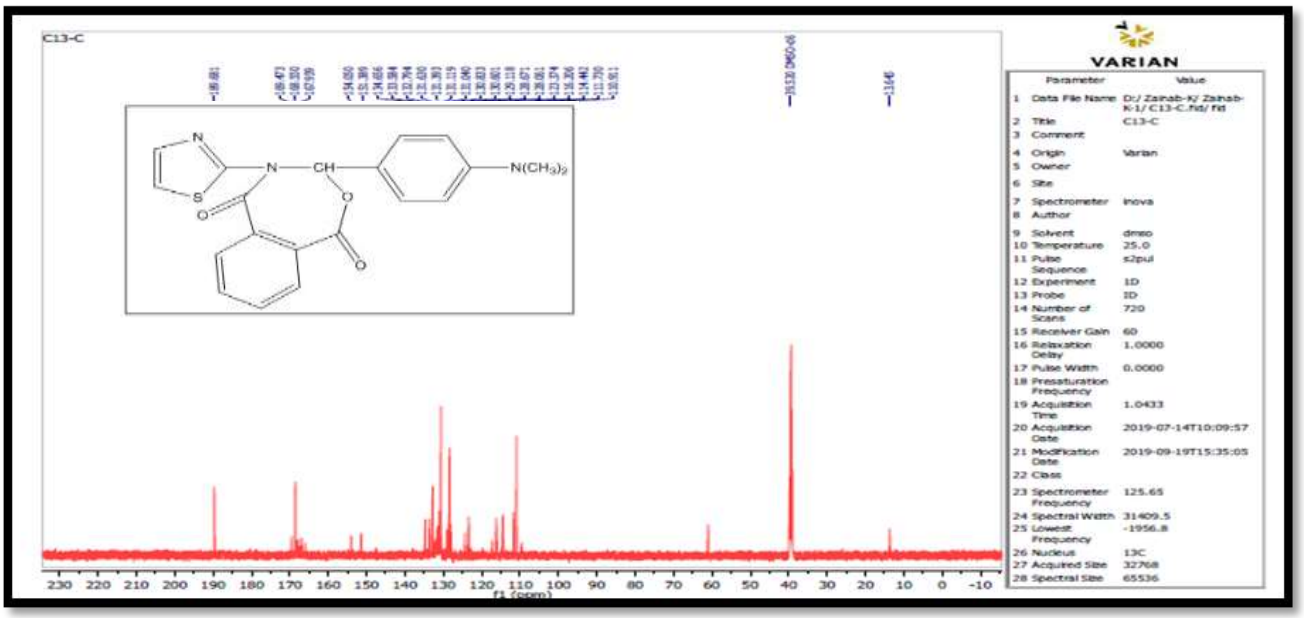


Figure 16: C[13]NMR spectra of compound (Z8)

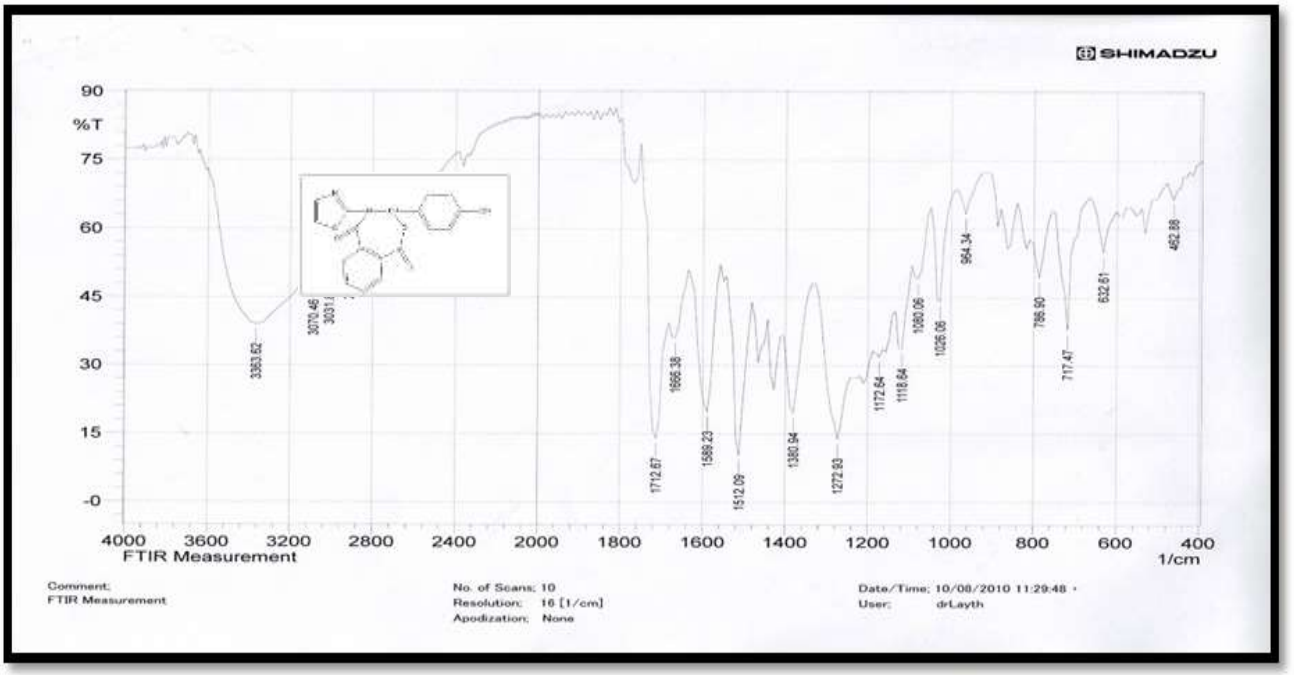


Figure 17 : FTIR spectra of compound of compound (Z9)

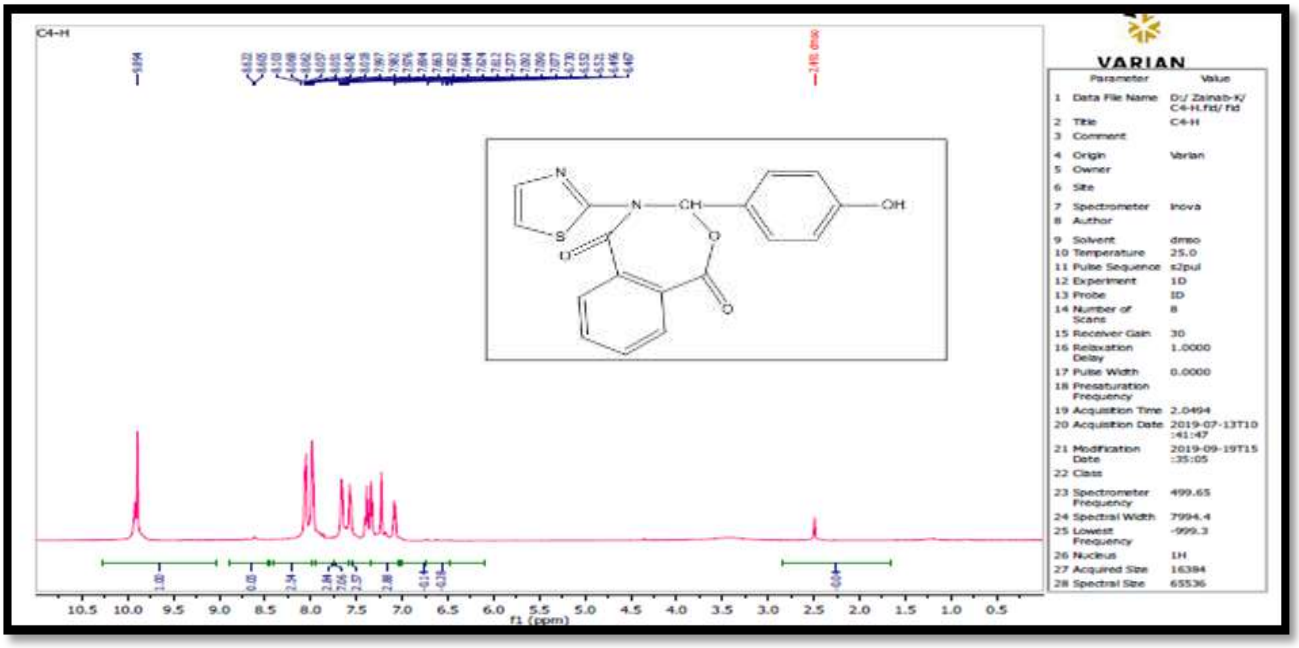


Figure 18 : H[1]NMR spectra of compound of compound (Z9)

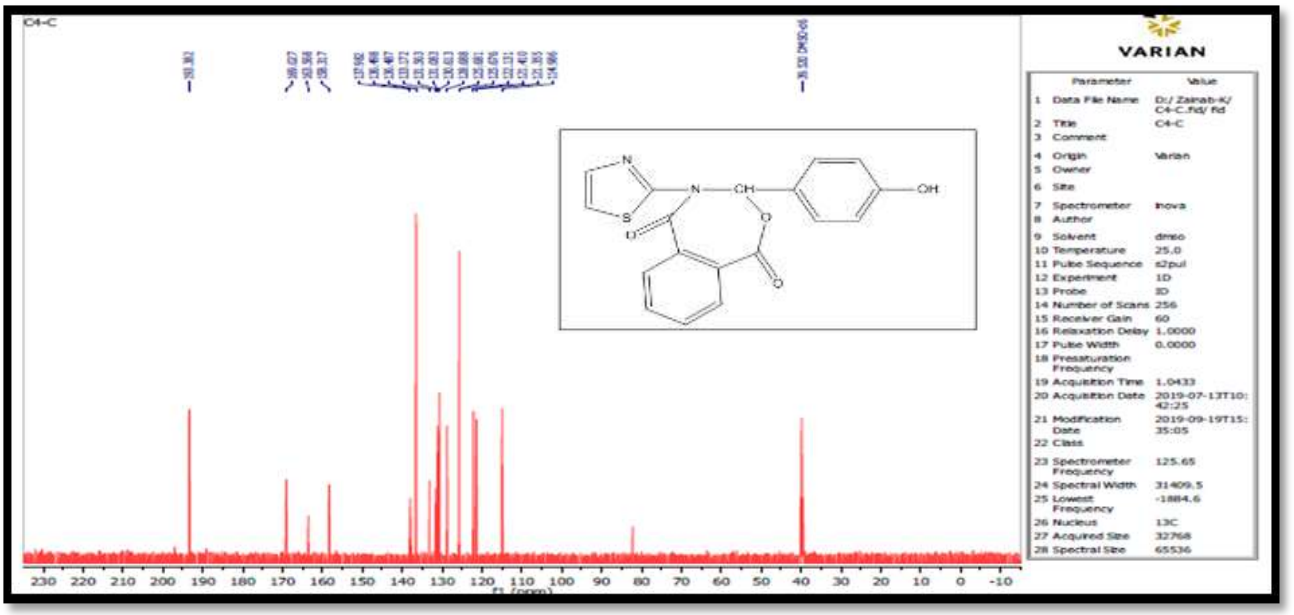


Figure 19: C[13]NMR spectra of compound of compound (Z9)

Conclusions

This paper involves the custom of 2-amino thiazole compound for the synthesis a chains of new heterocyclic oxazepin compounds were produced via two steps, the first step comprising condensation of 2- amino thiazol and various aldehydes ,(4- nitro benzaldhyede, 4- chloro benzaldhyede, 4-dimethylamino benzaldhyede, 3- hydroxy benzaldhyede and, 4-methoxy benzaldhyede), the second step formation oxazepin as sevene membred ring compounds, by cycloreaction of these Schiff bases and (pathalic, malic anhydride) in tolune as solvent .These compounds were distinct by a high stability that can be proved by a high fusion degrees . Also it is been noted that the effect of electron donating group on compounds had a role in decreasing the time of the cycloreaction.

References

1. Neethu V, Jemi J, Mythri M, Nija B (2016) "Synthesis of thiazole derivatives- A review" , World J. of Pharmacy and Pharmaceutical Sciences, 5 (11): 624-636.
2. Mohammed A AL-Omair, Abdelwahed R Sayed, Magdy M Youssef (2018) "Synthesis and Biological Evaluation of Bisthiazoles and polythiazoles", "Molecules", 23: 11-33.

3. Raghav Mishra, Pramod Kumar, Prabhakar K Verma, Prashant K Dhakad (2017) "Biological Potential of Thiazol Derivatives of Synthetic Origin" J. of Hetrocyclic Chemistry", 54: 2103-2116.
4. Konstantinos Liaras, Maria Fesatidou, Athina Geronikaki (2018) "Thiazoles and thiazolidinones as COX-LOX Inhibitors", "Molecules ", 23 (685): 1-21.
5. Preeti Arora, Rakesh Narang Vikramjeet Judge (2016)" 2, 4-Disubstituted thiazoles as multi-targeted bioactive molecules ", Med. Chemistry Research".
6. Dominique S Ngono, Dan C Vodnar, Ovidiu Oniga (2017) "Synthesis of 2-phenylamino- thiazole Derivatives as antimicrobial agents", J. of Saudi Chemical Society", 21: 861-868.
7. Manzoor A Malik, Ovas A Dar, Paveez Gull, Athar A Hashmi (2018) "Hetrocyclic Schiff base transition metal complexes in antimicrobial and anticancer chemotherapy), "Med. Chem. Comm.", 3: 1-5.
8. Deepika Sharma, Sanjiv Kumar, Balasubramanian Narasimhan (2019) "Synthesis, molecular modeling and biological significance of N-(4-(4-bromophenyl) thiazol-2-yl)-2-chloroacetamide Derivatives as prospective antimicrobial and anti-proliferative agents" "BMC Chemistry", 1-14.
9. Bhupender S Rawat, Roopali Tandon, Shrawan K Shukla (2016) "Synthesis and evaluation of some new ortho hydroxyl benzylidines derivatives of hetrocyclic compounds for their biological activates", Int. J. of Engineering and scientific Research", 4 (10): 91-101.
10. Mohamed Ezzat Khalifa (2018) "Recent Developments and Biological Activities of 2-Aminothiazole Derivatives", Acta Chim. Slov.", 65: 1-20.
11. Shabbir M, Santosh K, Joonseok K, Mukesh CH (2018) "Synthesis and characterization, optical and nonlinear optical properties of thiazole and benzothiazole derivatives: dual approach"."Molecular simulation", 1-10.
12. Taha N I," (2017) Synthesis of 1, 3 oxazepine derivatives from 2-(1H-Benzo triazol-1-yl) acetohydrazide by using microwave irradiation", International J. of organic chemistry ", 7: 03.
13. Shipra Baluja, Sumitra Chanda, Kajal Nandha (2019) "Synthesis and antimicrobial screening of some Schiff bases, "MOJ Bioorganic and organic chemistry", 3 (1): 15-20.
14. Ganesh M, Darshana R, K Aruna (2017) "Synthesis, spectroscopic characterization and antimicrobial activity evaluation of tridentate Schiff bases and their Co (Π) complexes", J. of Saudi Chemistry Society", 21: 954-964.
15. Sobhi M Gomha, Mohamad R Abdelaziz, Yahia N Mabkhot (2017) "A facile accesses and evaluation of some novel thiazole and 1, 3, 4-thiazole derivatives incorporating thiazole moiety as potent anticancer agents", "Chemistry Central Journal", 1-8.
16. Muhanned A Mahmoud (2019) "Synthesis and characterization of some newhetrocyclic compounds derived from benzothiazole", "Materials Science and Engineering", 577: 1-5.
17. Hawraa M. Sadiq (2017) "Synthesis and characterization of novle 1, 3-oxazepine derivatives from aminopyrazine", "World J. of Pharmacy and Pharmaceutical Sciences", 6 (5): 186-198.
18. Zainab A Sallal, Hassan Th Ghanem (2018) "Synthesis and Identification of new oxazepine derivatives bearing azo group in their structures", "Iraqi J. of science ", 59 (1A): 1-8.
19. Naeemah AL-Iami, KhawlaJ Salom (2019) "Pharmacological studies on some new 3-cyclic oxazepine-2-aryl imidazo(1,2-A)pyridine derivatives", "J. Pharm. Sci. and Res.", 11 (1): 125-130.
20. Issam A Mohammed, Mahmood Ahmed, Riaz Hussain (2018) 1,3 oxazepine compounds derived from azomethine: Synthesis ,characterization and antibacterial evaluation", Latin American J. of Pharmacy", 37: 3.
21. Kadhim ZJ (2017) "Synthesis and characterization of compounds containing 1, 3 oxazepine ring ", Misan J. of academic studies", 16 (32): 176-186.
22. Mohammad HJ, Alsamarri AS, Mahmood RT (2019) "Synthesis and Identification of 1, 3- oxazepine derivatives by reaction of Schiff bases with anhydride derivatives of

cycloheptatrien:, J. Pharm. Sci. and Res, "11 (3): 1073-1077

23. Jarallah SA, Nief OA, Actia AJK (2019) "Synthesis, characterization of hetrocyclic compounds and preliminary evaluation of their antibacterial activity and antioxidant agents", J. Pharm. Sci. and Res, "11 (3): 1010-1015.
24. Khitam T, A AL-Sultani (2017) "Synthesis, Identification and Evaluation the Biological Activities for Some New Heterocyclic Compounds Derived from Schiff bases, "J. of Pharmacy and Biological Sciences", 12 (2): 39-47.

