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RESEARCH ARTICLE

Synthesis and Characterization of Some New Di-amines Derived from Di-amines Supplemented with Di-heterocyclic Five Membered Rings and Some Aromatic Aldehydes

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Abstract

It has been documented that imines and heterocyclic compounds with five membered rings and their derivatives, have enormous biological activity in various area as medicinal and pharmaceutical. Therefore, supplementing the di imines with five -membered heterocyclic rings, perhaps enhance the biological activity characters of the resulting products. Consequently, the target of present work involve the developing of new imines derived from selected di amines after connecting a five membered heterocyclic rings of the type di thiazole and di oxazole to the parent molecules via the reaction of the previous di amines with chloroacetyl chloride yield the corresponding amides [A_1-A_3] , then subsequent reaction of the later with of thiourea and urea give substantially new di thiazol [th_1-th_3] and di oxazole [Ox_1-Ox_3] respectively .Reaction of these new developed di amines with selected aromatic aldehydes result a pavantly in the formation of the desired bis imines [Sc_1-Sc_{10}]. On the other hand the structures of all the synthesized compounds were confirmed by their physical properties, such as colors and melting points and spectroscopic measurements FT-IR, ^{1}H-NMR and ^{13}C-NMR for selected compounds.

Keywords: *Di imines, Chloroacetyl chloride, Thiazole-2, 4-diamines, oxazole-2, 4-diamines.*

Introduction

Oxazoles the parent compound for a vast class of hetero cyclic aromatic compounds. These are azoles with oxygen and nitrogen separated by one carbon. They are aromatic compounds but less so than the thiazoles [1]. Oxazole is a heterocyclic compound exhibits a wide variety of pharmacological activities such as antidepressants [2], anti-diabetic [3], anti-microbial [4] and diuretics [5]. Thiazole belongs to a class of heterocyclic compounds having a nitrogen atom and sulfur atom as part of the aromatic 5-member ring [6].

It is one of the most intensively studied classes of aromatic five-membered heterocyclic and it was first defined by Hantzsch and Weber in 1887 [7]. The thiazole ring is a constituent of medicinal agents, agrochemicals, and dyes. Thiazole found application in drug development for the treatment of different diseases, for example, allergies [8] hypertension, fungal infections, and schizophrenia [9]. Natural products containing the thiazole nucleus have been previously described as biologically active agents, for example vitamin B1 is an important precursor for the synthesis of acetylcholine, which improves the function of the nervous system [10]. Amides functionalities are inarguably among the most abundant motif having presence in biologically significant molecules, such as proteins [11] natural products, marketed drugs and synthetic intermediates.

Amide bond is progressively important in pharmaceutical chemistry, being present in 25% of available drugs, with amidation reactions being among the most commonly used reactions in medicinal chemistry [12].The amide group is a common functional group in natural compounds. Many commercial pesticide compounds have acyl amino group in the molecule, for example

benzoyl phenyl urea insecticides, urea, amides and carbonates herbicides [13].Schiff bases are a well-known class of compounds with the general structure $R_1R_2C=NR_3$ [14], and they are named in honour to Hugo Schiff, the scientist who first synthesized members of this class of substances in 1864 [15]. Schiff bases are some of the most widely used organic compounds [16]. Schiff bases also exhibit a wide variety of biological activities, including antifungal, antibacterial, antitumor, anti-inflammatory, trypanocidal, anti-HIV, anti-malarial and antimicrobial [17].

Experimental

Materials and Instruments

Chemicals and solvents used in this work are supplied from BDH, Fluka, Merck and Sigma Aldrich companies and used without further purification. Melting points were uncorrected and registered via digital Stuart scientific SMP3 melting point device. FT-IR spectra of the compounds in the (4000-600) cm^{-1} spectral range were recorded on SHIMADZU FT-IR-8400 Fourier transform Infrared spectrophotometer using KBr discs. ^{1}H-NMR, ^{13}C-NMR was recorder on Bruker Ultra Shield, 300MHz, using DMSO-d6 as solvent and TMS as internal standard. Thin-layer chromatography was performed glass plats coated with 0.25 mm layer of silica-gel (Fluka).

General Procedures

Synthesis of Chloroacetyl Substituted Amides (A_1-A_3)

The amides of chloroacetyl chloride were synthesized according to the published procedure with some modification, a solution of chloroacetyl chloride (0.02mol), in dry benzene (250 ml), was added to the solution of diamine (0.01 mol) in dry benzene (100 ml) at 0-5 °C and (3-5) drops of triethyl amine with constant stirring during half an hour. The reaction mixture was refluxed for 4 hour. Then was poured into ice water .The obtained product was filtered and washed with cold water, dried and recrystallized from ethanol [18, 19], Physical properties of the amides products Table (1) .

Synthesis of oxazole -2, 4-diamine Compounds (Ox_1-Ox_3)

A mixture of (0.01 mol) of compounds (A_1-A_3) and (0.02 mol) of urea was dissolved in (40 ml) of ethanol. The mixture was refluxed for (6) hrs. The solid product was filtered and recrystallized from ethanol, The Physical properties of compounds (Ox_1-Ox_3) shown in Table (2).

Synthesis of thiazole-2, 4-diamine Compounds (th_1-th_3)

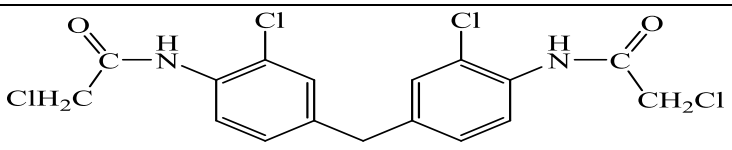
A mixture of (0.01 mol) of compound (A_1-A_3) and (0.02 mol) of thiourea was dissolved in (40 ml) of ethanol. The mixture was refluxed for (4) hrs. The solid product was filtered and recrystallized from ethanol**,** The Physical properties of compounds (th_1-th_3) shown in Table (3).

Reaction of the Previously Prepared Heterocyclic Di amines with Some Selected Aldehyde to Form Di imines or Schiff bases (Sc_1-Sc_{10}).

- Reaction (0.01 mol) of oxazole -2,4-diamine compounds (Ox_1-Ox_3) with (0.02 mol) aromatic aldehyde was dissolved in (30 ml)of ethanol and add 3 drops of glacial acetic acid as a catalyst .The mixture was refluxed for (4) hrs. The solid product was filtered and recrystallized from ethanol (Sc_1-Sc_6).

- Reaction (0.01 mol) of thiazole-2, 4-diamine compounds (th_1-th_3) with (0.02 mol) aromatic aldehyde was dissolved in (40 ml) of ethanol and add 3 drops of glacial acetic acid as a catalyst .The mixture was refluxed for (6) hrs. The solid product was filtered and recrystallized from ethanol (Sc_7-Sc_{10}) [20]. Table (4).

Table 1: Structures, colors, m.p, %yields for the amides compounds (A_1-A_3)

Comp. No.	Physical Properties			
	Structures	M.P°C	Yield%	Color
A_1	 N,N'-(methylenebis(2-chloro-4,1-phenylene))bis(2-chloroacetamide)	180–184	90	Off white

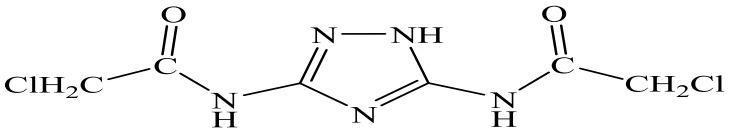
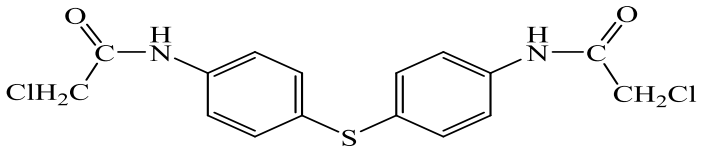
A_2	 N,N'-(1H-1,2,4-triazole-3,5-diyl)bis(2-chloroacetamide)	**78–81**	**79**	**Pink**
A_3	 N,N'-(thiobis(4,1-phenylene))bis(2-chloroacetamide)	**80–82**	**75**	**Brown**

Table 2: Structures, colors, m. p, %yields for the oxazoles compounds (Ox_1-Ox_3)

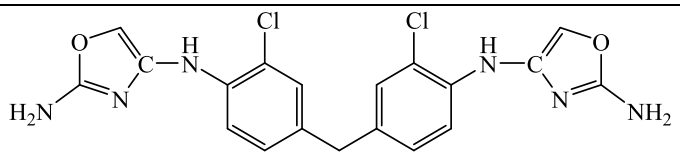
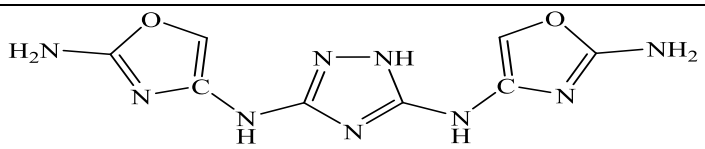
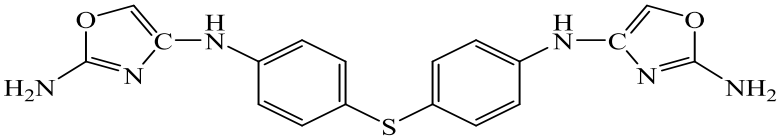
Comp. No.	Physical Properties			
	Structures	**M.P°C**	**Yield%**	**Color**
Ox_1	 N4,N4'-(methylenebis(2-chloro-4,1-phenylene))bis (oxazole-2,4-diamine)	**190–192**	**90**	**Pale Yellow**
Ox_2	 N4,N4'-(1H-1,2,4-triazole-3,5-diyl)bis(oxazole-2,4-diamine)	**60-62**	**79**	**Pink**
Ox_3	 N4,N4'-(thiobis(4,1-phenylene))bis(oxazole-2,4-diamine)	**93–95**	**75**	**Gray**

Table 3.Structures, colors, m. p, %yields for the thiazoles compounds (th_1-th_3)

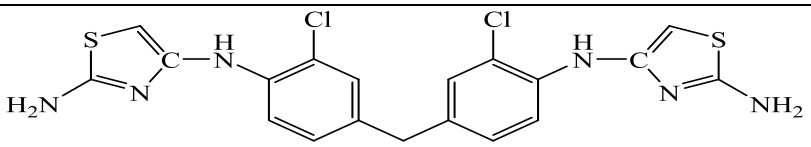
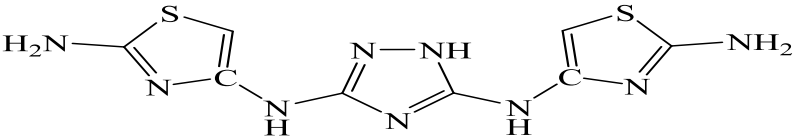
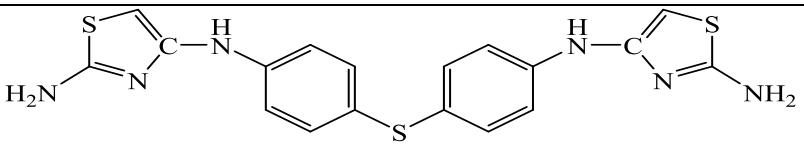
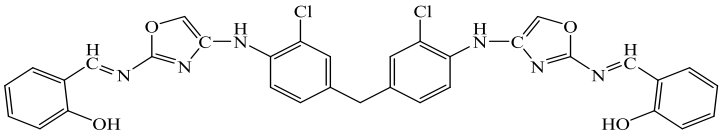
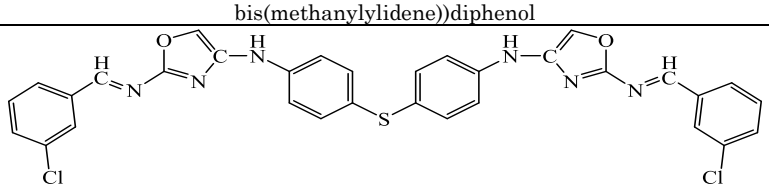
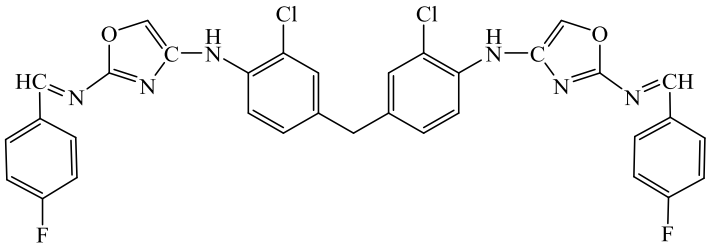
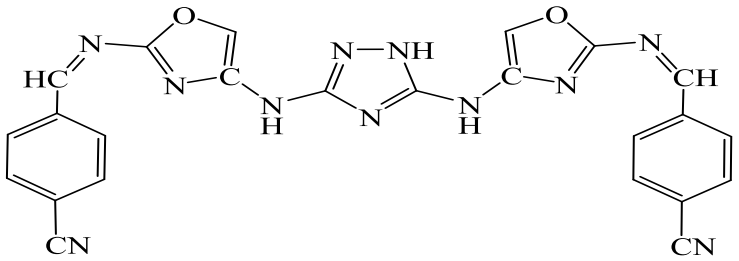
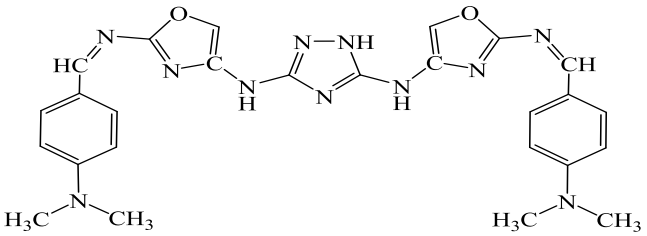
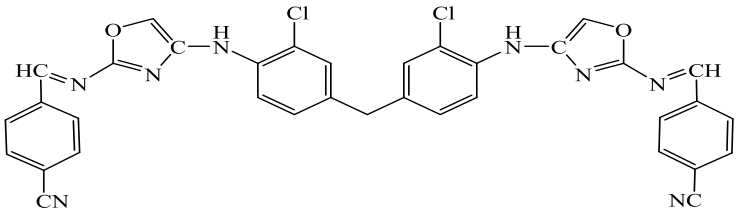
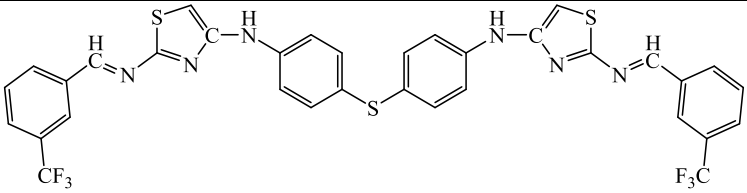
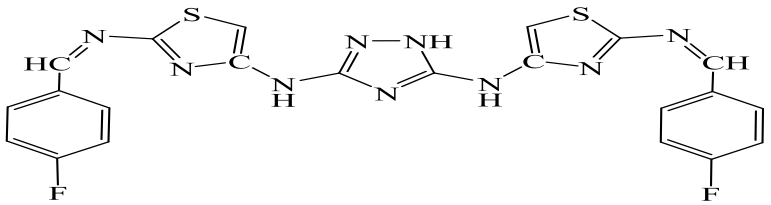
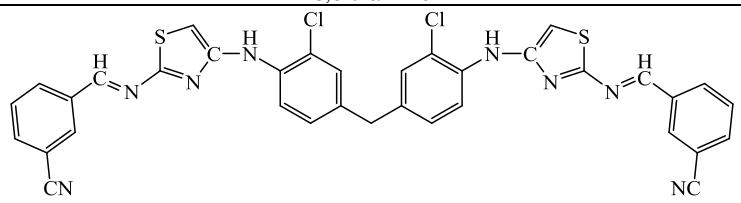
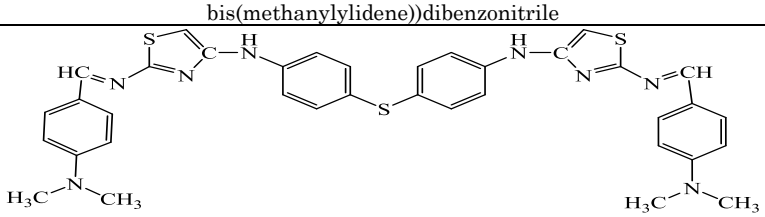
Comp. No.	Physical Properties			
	Structures	**M.P°C**	**Yield%**	**Color**
th_1	 N4,N4'-(methylenebis(2-chloro-4,1-phenylene))bis (thiazole-2,4-diamine)	**98–100**	**77**	**Off White**
th_2	 N4,N4'-(1H-1,2,4-triazole-3,5-diyl)bis(thiazole-2,4-diamine)	**61 –63**	**87**	**Off white**
th_3	 N4,N4'-(thiobis(4,1-phenylene))bis(thiazole-2,4-diamine)	**190–192**	**72**	**Brown**

Table 4: Structures, colors, m. p, %yields for the di iminescompounds (Sc_1-Sc_{10})

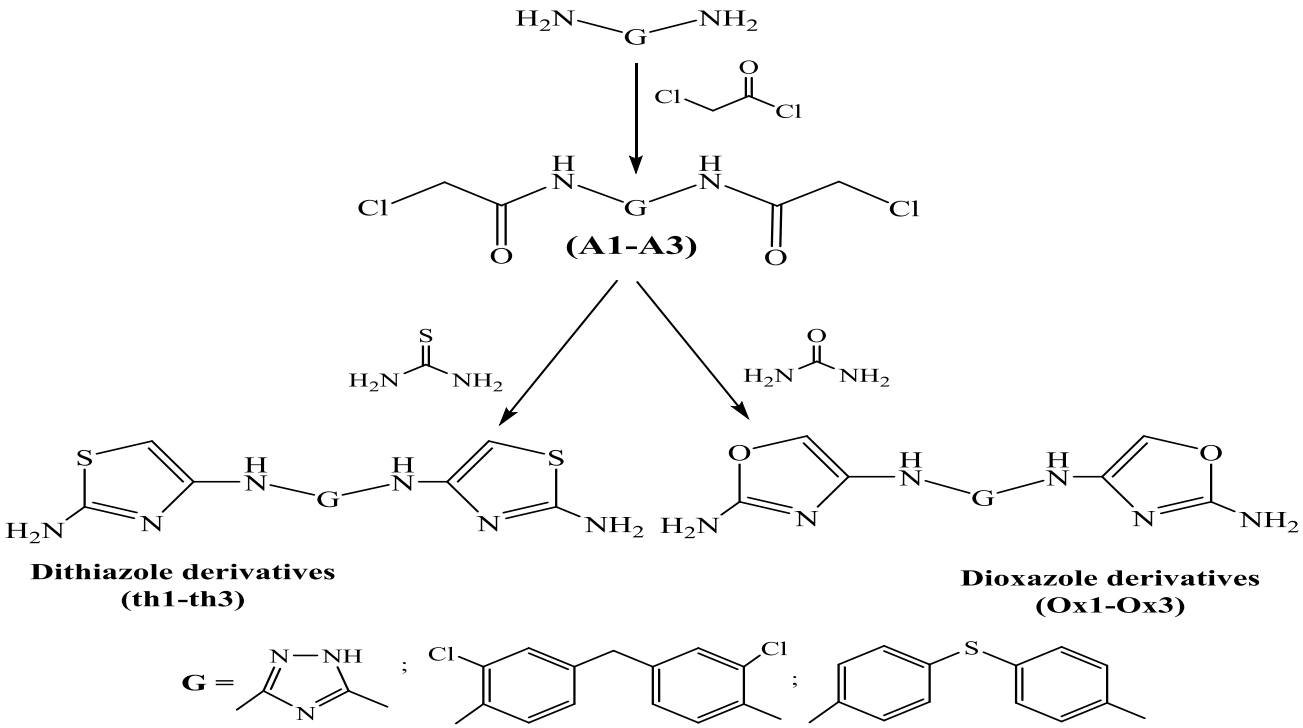
Comp. No.	Physical Properties			
	Structures	**M.P°C**	**Yield%**	**Color**
Sc_1	 2,2'-((1E,1'E)-((((methylenebis(2-chloro-4,1-phenylene)) bis(azanediyl))bis(oxazole-4,2-diyl))bis(azanylylidene)) bis(methanylylidene))diphenol	**186-188**	**80**	**White**
Sc_2	 N,N'-(thiobis(4,1-phenylene))bis(2-(((E)-3-chloro benzylidene) amino)oxazol-4-amine)	**195-197**	**79**	**Yellow**
Sc_3	 N,N'-(methylenebis(2-chloro-4,1-phenylene))bis(2-(((E)-4-fluorobenzylidene) amino)oxazol-4-amine)	**184-185**	**85**	**Pale Yellow**
Sc_4	 4,4'-((1Z,1'Z)-((((1H-1,2,4-triazole-3,5-diyl)bis(azanediyl)) bis(oxazole-4,2-diyl))bis(azanylylidene))bis (methanylylidene))dibenzonitrile	**220-221**	**69**	**Pink**
Sc_5	 N3,N5-bis(2-(((Z)-4-(dimethylamino)benzylidene) amino)oxazol-4-yl)-1H-1,2,4-triazole-3,5-diamine	**60-62**	**84**	**Light yellow**
Sc_6	 4,4'-((1E,1'E)-((((methylenebis(2-chloro-4,1-phenylene))bis (azanediyl))bis(oxazole-4,2-diyl))bis(azanylylidene))bis (methanylylidene))dibenzonitrile	**135-137**	**77**	**Orange**
Sc_7	 N,N'-(thiobis(4,1-phenylene))bis(2-(((E)-3-(trifluoromethyl)benzylidene) amino)thiazol-4-amine)	**184-185**	**78**	**Dark - Yellow**

Sc8	 N3,N5-bis(2-(((E)-4-fluorobenzylidene)amino)thiazol-4-yl)-1H-1,2,4-triazole-3,5-diamine	**270-271**	**84**	**Dark - Yellow**
Sc9	 3,3'-((1E,1'E)-((((methylenebis(2-chloro-4,1-phenylene)) bis(azanediyl))bis(thiazole-4,2-diyl))bis(azanylylidene)) bis(methanylylidene))dibenzonitrile	**210-212**	**90**	**Pale Yellow**
Sc10	 N,N'-(thiobis(4,1-phenylene))bis(2-(((E)-4-(dimethylamino)benzylidene) amino)thiazol-4-amine)	**175-174**	**75**	**Brown**

Results and Discussion

Part one

The synthetic sequences for preparation of series of new hetero cyclic compounds derived from di amines after developing of five membered heterocyclic ring of the thiazole or oxazole to these di amines in the mean time a new diamines groups are formed which are susceptible to enter all characteristic organic reaction according to this new compounds have been prepared as in Scheme -1.



Scheme -1: **Synthesis of chloroacetyl substituted amides**, **oxazole -2, 4-diamine and thiazole-2, 4-diamine**

The FT-IR spectrum of chloroacetyl substituted amides (A_1-A_3) showed the appearance of bands at (3153- 3205) cm^{-1} due to v (NH) and (3214-3374) $cm^{-1}$for vibration of v (C-H)arom . While v(C-H) for aliphatic at (2700- 2898) cm^{-1}.Besides the appearance of bands at (1511-1589) cm^{-1}due to (C=C) aromatic and at (1624-1687) cm^{-1}attributed to v (C=O).Table (5).

The ^{1}H-NMR spectrum of compound (A_1) showed singlet signal at δ= (2.5) ppm due to DMSO, singlet signal at δ= (3.5) ppm due to (-CH_2-) protons, singlet signal at δ= (4.4) ppm due to (Cl-CH_2) protons, multi signals at δ=(6.8- 7.8) ppm due to aromatic rings protons, besides to these a singlet signals appears at δ=(9.9) ppm due to ((C=O)N-H) amide proton. Table (9) and Figure (2).

The FT-IR spectrum of Oxazole -2,4-diamine compounds (Ox_1-Ox_3) showed the appearance of bands at (3265-3376) cm^{-1}due to ν (NH_2, NH) and (3011-3180) $cm^{-1}$for vibration of ν (C-H) arom. while ν(C-H) for aliphatic at (2722- 2877) cm^{-1}. Besides the appearance of bands at (1000- 1128) cm^{-1}attributed to ν (C-O-C). Table (6).

The ^{1}H-NMR spectrum of compound (Ox_3) showed singlet signal at δ= (2.5) ppm due to DMSO, singlet signal at δ= (4.1) ppm due to (C=C-H) protons, singlet signal at δ= (6.3) ppm , (6.5) ppm due to (-NH_2) protons and (-NH) protons, multi signals at δ=(7.6 – 8.1) ppm due to aromatic rings protons. Table (9) and figure (4).

The ^{13}C-NMR spectrum of this compound (Ox_3) figure (5). In ^{13}C NMR (DMSO-d_6) spectrum showed many signals at δ: 177.45 ppm (C_1), 121.84 ppm (C_2) , 129.07 ppm (C_3), 1143.38 ppm (C_4), 151.83 ppm (C_5) and 112.13 ppm (C_6).

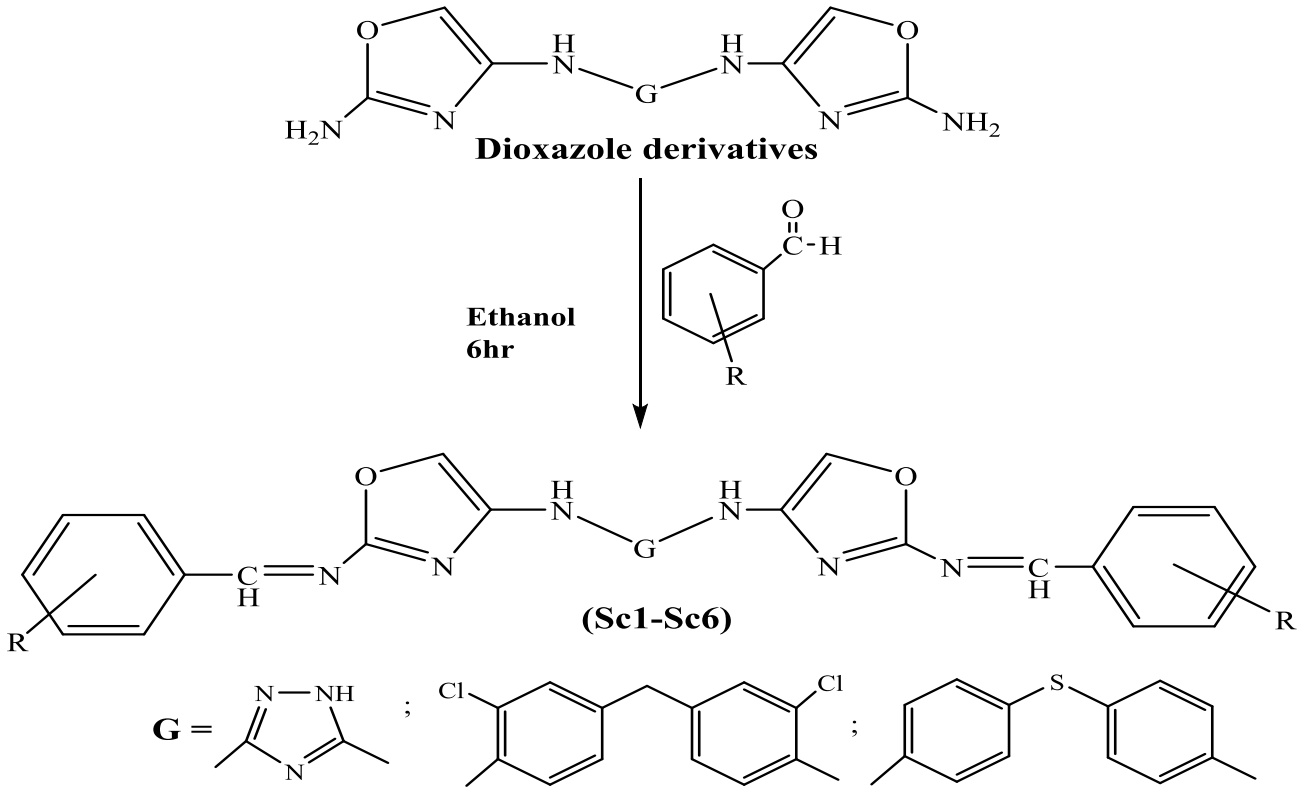
The FT-IR spectrum of Thiazole-2,4-diamine compounds (th_1-th_3) showed the appearance of bands at (3125 - 3380) cm^{-1}due to ν (NH_2 , NH) and (2010 - 3170) $cm^{-1}$for vibration of ν (C-H) arom. While ν (C-H) for aliphatic at (2884) cm^{-1}. Besides the appearance of bands at (700 - 750) cm^{-1}attributed to ν (C-S).Table (7).

The ^{1}H-NMR spectrum of compound (th_2) showed singlet signal at δ= (1.2) ppm due to DMSO, singlet signal at δ= (2.5) ppm due to (C=C-H) protons, singlet signal at δ= (7.3) ppm , (3.4) ppm due to (-NH_2) protons and (-NH) protons, Table (9).Figure (7).

The ^{13}C-NMR spectrum of this compound (th_2) figure (8). In ^{13}C NMR (DMSO-d_6) spectrum showed many signals at δ: 115.01 ppm (C_1), 121.66 ppm (C_2), 148.58 ppm (C_3) and 133.04 ppm (C_4).

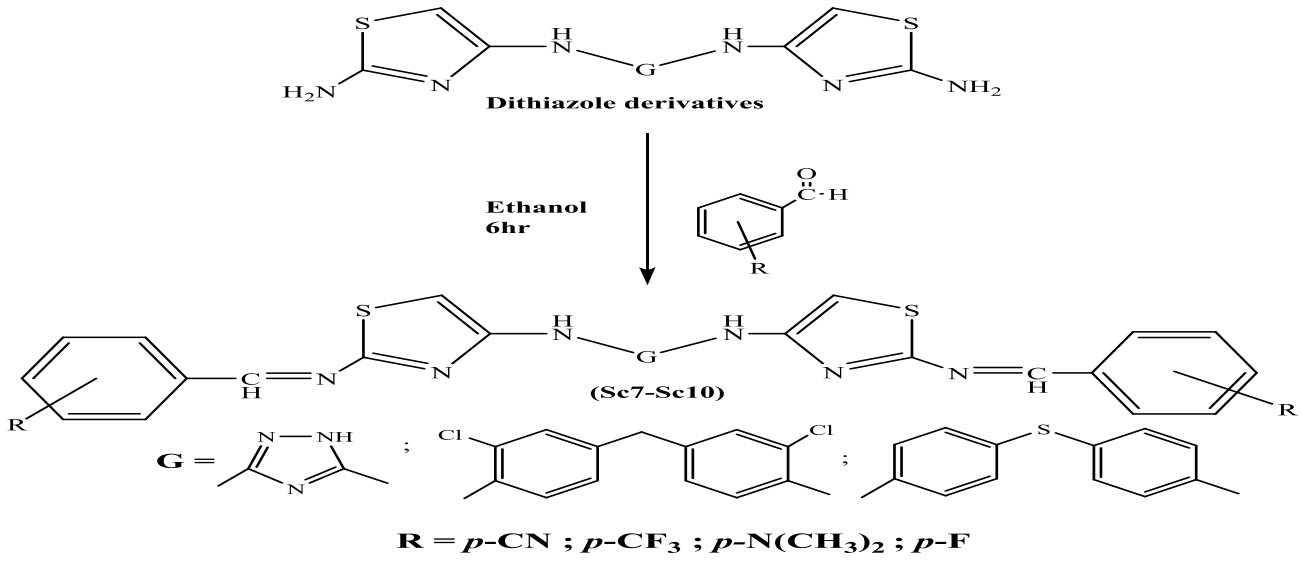
Part Two

Reaction of diamine dioxazol derivatives with aromatic aldehydes as in Scheme -2.



Scheme -2: Synthesis of oxazole -2-imino-4-amine

Reaction of diamine dithiazol derivatives with aromatic aldehydes as in Scheme -3.



Scheme -3: **Synthesis of thiazol -2-imino-4-amine**

The formation of Schiff bases (Sc_1-Sc_{10}) were indicated by the presence in its FTIR-spectra of the azomethine v (CH=N) stretching band at (1604- 1653) cm^{-1} [21] other absorption bands appeared at (3055- 3344), (2810-2925), (2965-3163) and (1533-1604) cm^{-1}due to (NH), v (C-H) aliph., v (C-H) arom. And v (C=C) arom. Respectively [22].All the spectral data show disappearance the absorption of the v (NH_2) stretching band indicating success of formation reaction as shown in table (8).The figure (9,10) belongs to compound (Sc_1,Sc_4) of some them.

Table 5: FTIR spectral data cm^{-1} of the chloroacetyl substituted amides (A_1-A_3)

Com. No.	Major FTIR Absorption cm^{-1}					
	v (C-H) arom.	□(C=C) arom.	v (C=O)	v (C-H) aliph.	v (NH)	Others
A_1	3136	1511	1662	2860	3285	v(C-Cl) 831, v(C-N) 1230
A_2	3153	1535	1687	2898	3214	v (C=N) 1646 , v (C-Cl) 789, v (C-N) 1295
A_3	3205	1589	1624	2700	3331	v(C-S) 733, v(C-Cl) 824, v(C-N) 1171

Table 6: FT-IR spectral data cm^{-1} of the oxazoles compounds (Ox_1-Ox_3)

Comp. No.	Major FTIR Absorption cm^{-1}					
	v (C-H) arom.	□(C=C) arom.	v (C-O-C)	v (C-H) aliph.	v (NH_2, NH)	Others
Ox_1	3011	1581	1056	2877	3376,3360	v(C-N) 1310, v(C-Cl) 811
Ox_2	3135	1575	1128	-	3363,3358	v (C=N) 1644 ,
Ox_3	3180	1531	1000	-	3369,3265	v (C-S) 601 , v (C=N) 1645

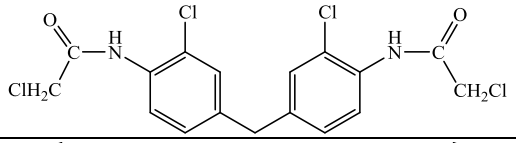
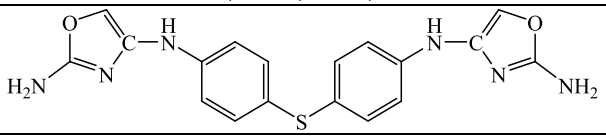
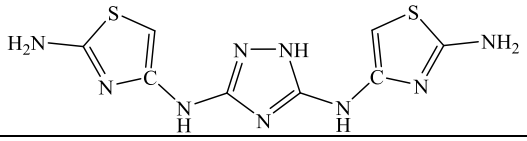
Table 7: FT-IR spectral data cm^{-1} of the thiazoles compounds (th_1-th_3)

Comp. No.	Major FTIR Absorption cm^{-1}					
	v (C-H) arom.	□(C=C) arom.	v (C=N)	v (C-H) aliph.	v (NH_2, NH)	Others
th_1	3010	1504	1646	2884	3293,3125	v(C-N) 1372 , v(C-S) 750
th_2	3170	1473	1609	-	3380,3276	v (C-N) 1174 , v (C-S) 700
th_3	3034	1487	1615	-	3325,3212	v(C-N) 1397, v(C-S) 719

Table 8: FTIR spectral data cm^{-1} of the di imines compounds (Sc_1-Sc_{10})

Comp. No.	Major FTIR Absorption cm^{-1}					
	v(C-H) arom.	v(C=C) arom.	v(C=N)	v (C-H) aliph.	v(NH)	Others
Sc_1	3163	1591	1643	2837	3271	v (C-N) 1240, v (C-Cl) 819, v (C-O-C) 1078, v (OH)3334
Sc_2	3055	1557	1613	2876	3337	v (C-N) 1229, v (C-Cl) 824, v (C-O-C)1071
Sc_3	3078	1570	1638	2850	3344	v (C-N) 1237, v (C-F) 931, v (C-O-C) 1025
Sc_4	2965	1553	1653	2882	3261	v (C-N) 1390 , v (C-O-C)1027 , v (CN)2229
Sc_5	3045	1533	1618	2810	3220	v (C-N) 1323, v (C-O-C)1020
Sc_6	3002	1595	1637	2925	3273	v (C-N) 1230, v (C-O-C)1073, v (CN)2225
Sc_7	3066	1560	1635	2881	3267	v (C-N) 1229, v (C-F) 924, v (C-S)718
Sc_8	3103	1595	1639	2923	3248	v (C-N) 1237, v (C-F) 9011, v (C-S)720
Sc_9	3086	1604	1604	2904	3205	v (C-N) 1266, v (CN)2236 , v (C-S)724
Sc_{10}	3008	1578	1626	2885	3055	v (C-N) 1277, v (C-S)757

Table 9:[1]H-NMR spectral data (δ ppm) for some synthesized compounds

Com. No.	Structures	Chemical Shift (δ ppm)	No. of Protons	Group
A_1		3.5	2	(-CH_2-)
		4.4	2	(Cl-CH_2)
		6.8- 7.8	6	Aro.Protons
		9.9	1	(C=O)N-H)
Ox_3		4.1	1	(C=C-H)
		6.3	2	NH_2
		6.5	1	NH
		7.6- 8.1	8	Aro.Protons
th_2		2.5	1	(C=C-H)
		7.3	2	NH_2
		3.4	1	NH

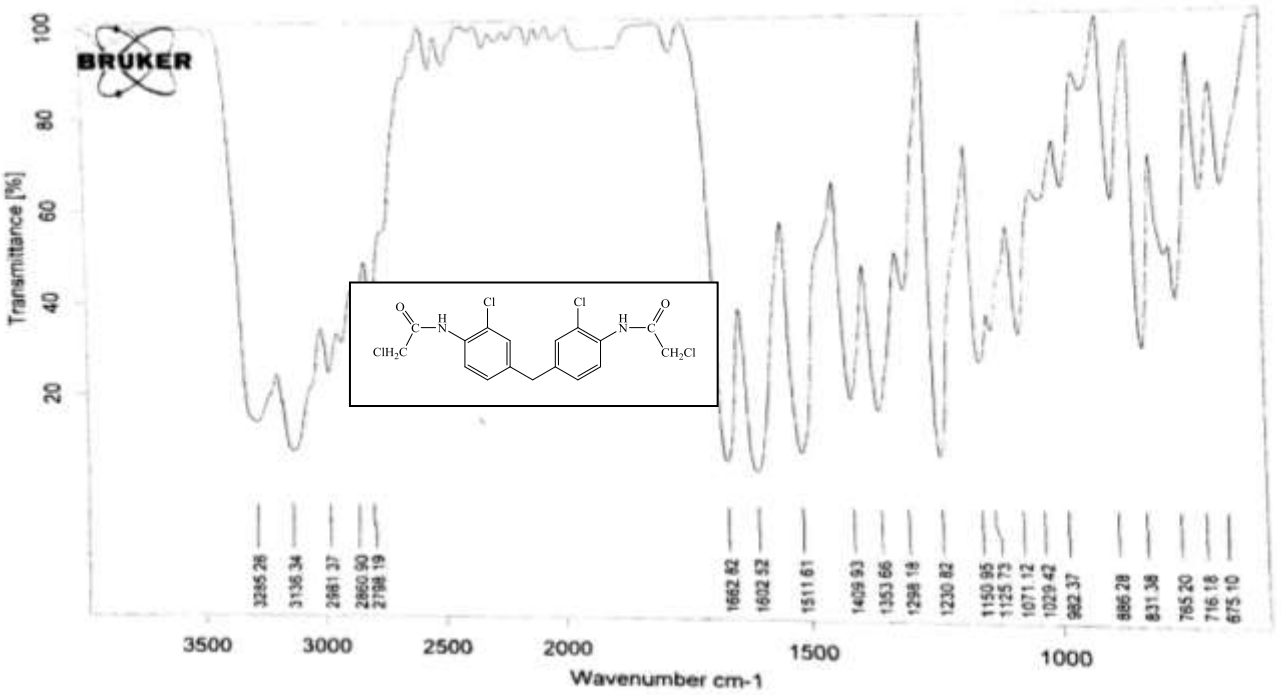


Figure 1: FT-IR spectrum of compound (A_1)

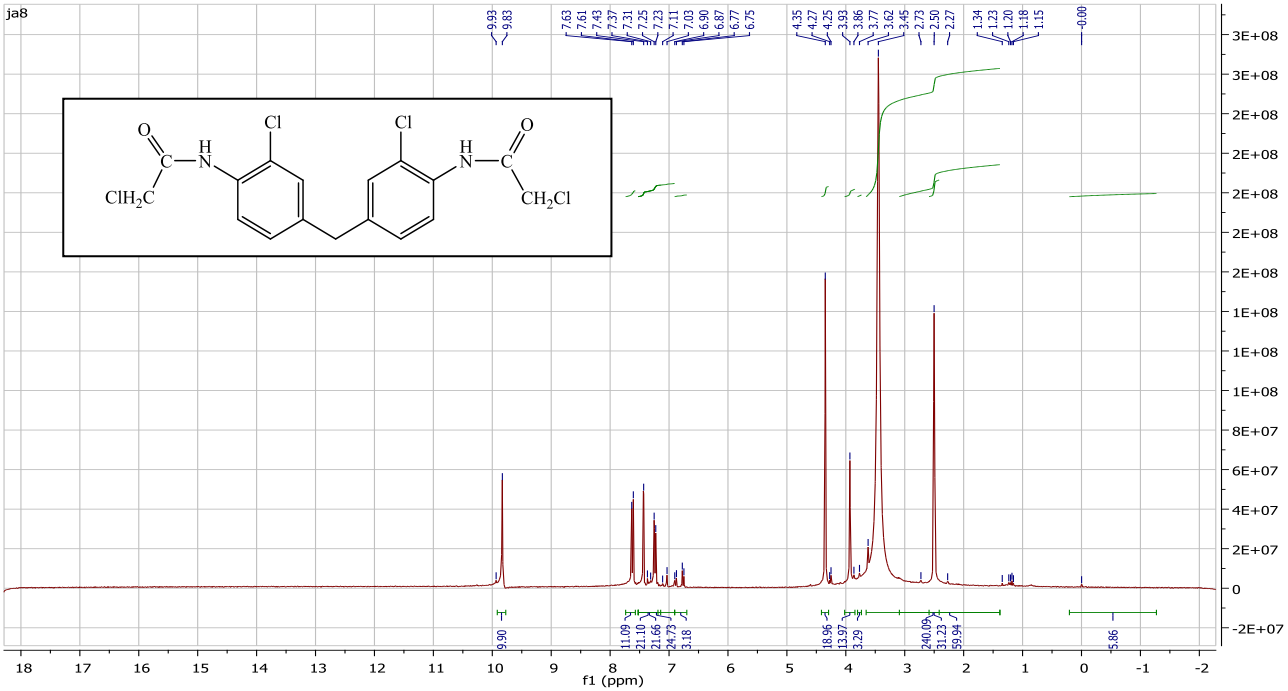


Figure 2: [1]H-NMR spectrum of compound (A1)

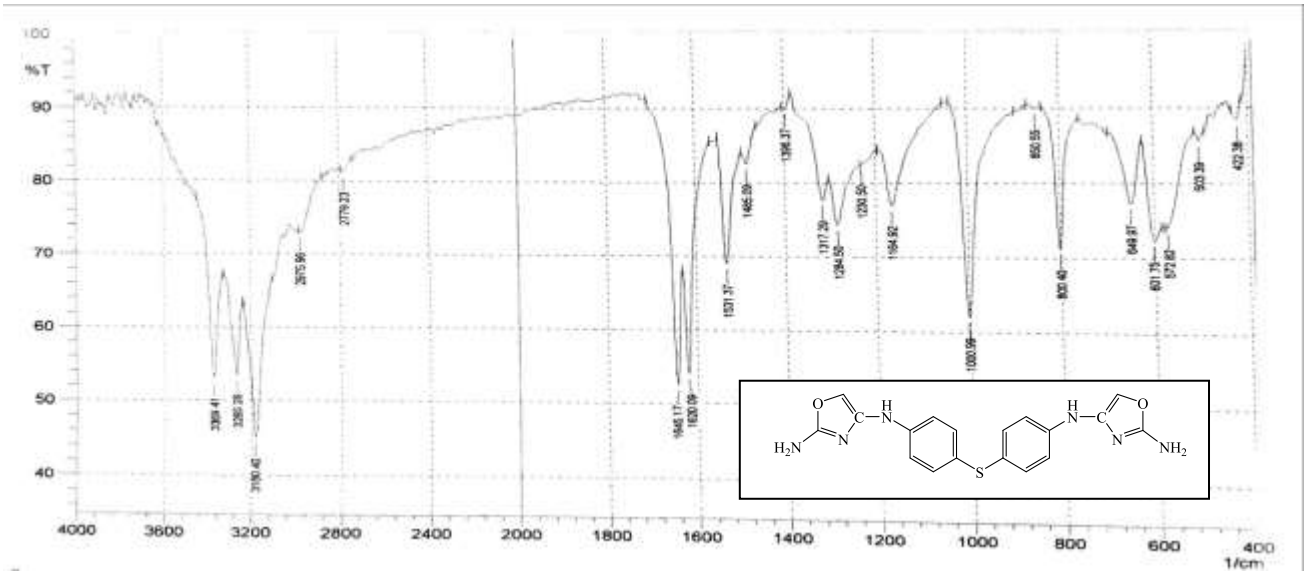


Figure 3: FT-IR spectrum of compound (Ox_3)

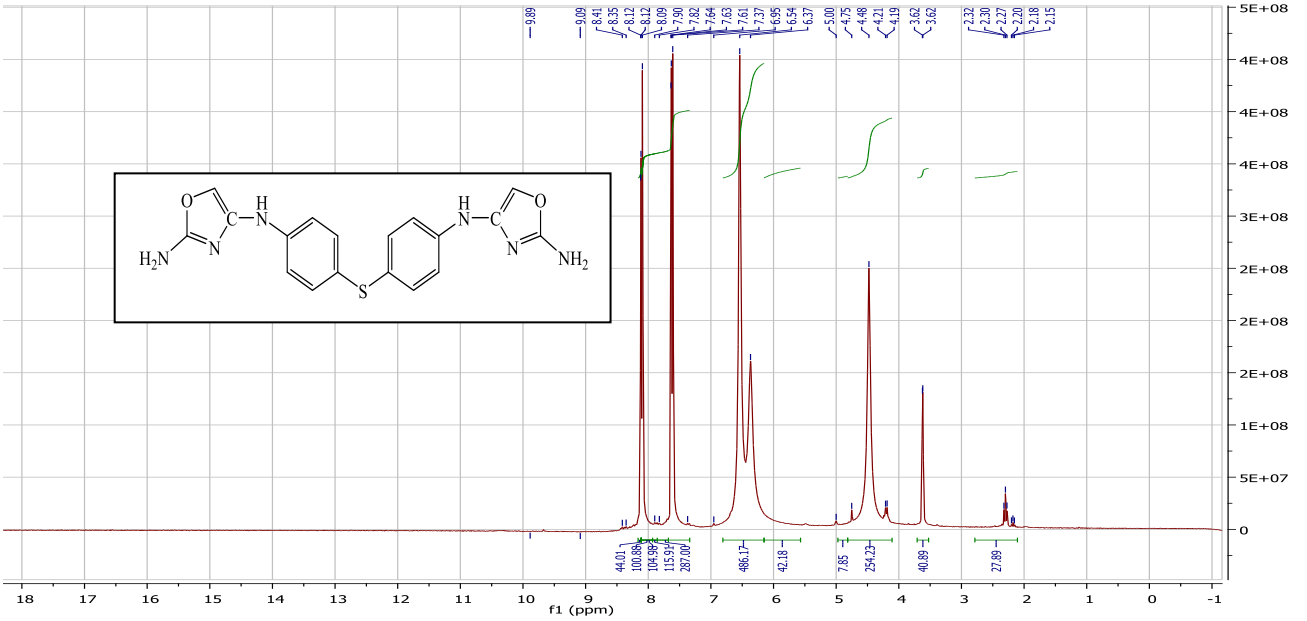


Figure 4:^{1}H-NMR spectrum of compound (Ox_3)

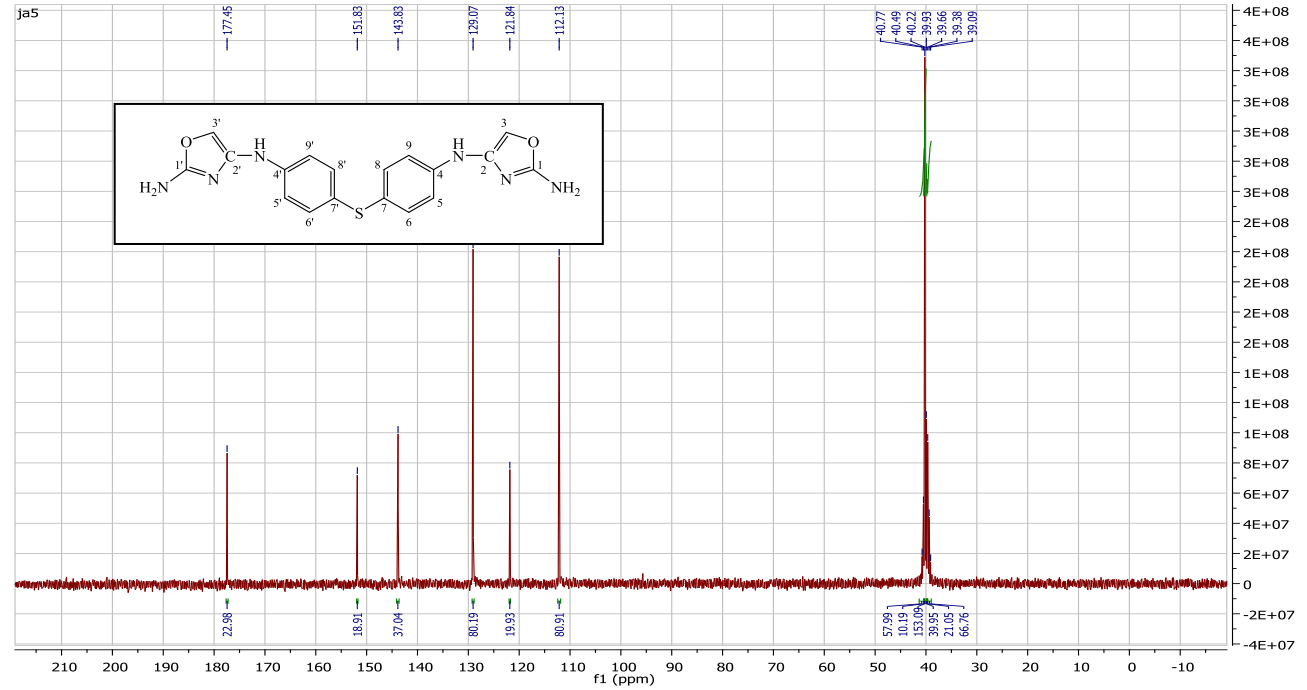


Figure 5:^{13}C-NMR spectrum of compound (Ox_3)

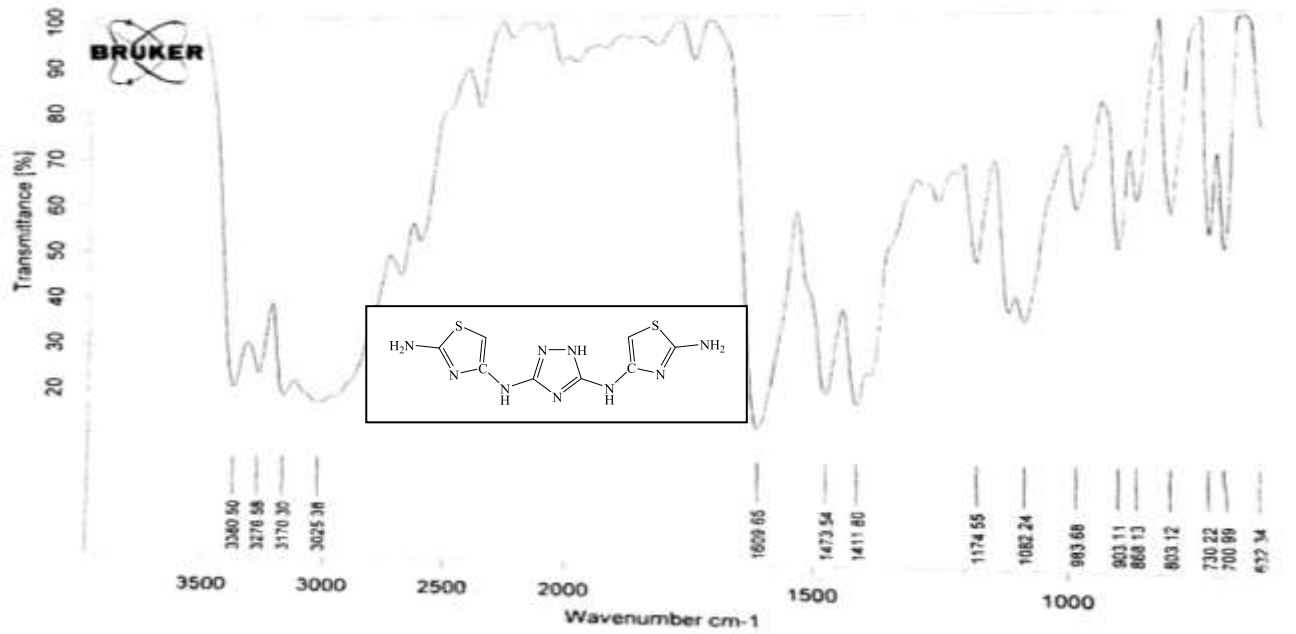


Figure 6: FT-IR spectrum of compound (th_2)

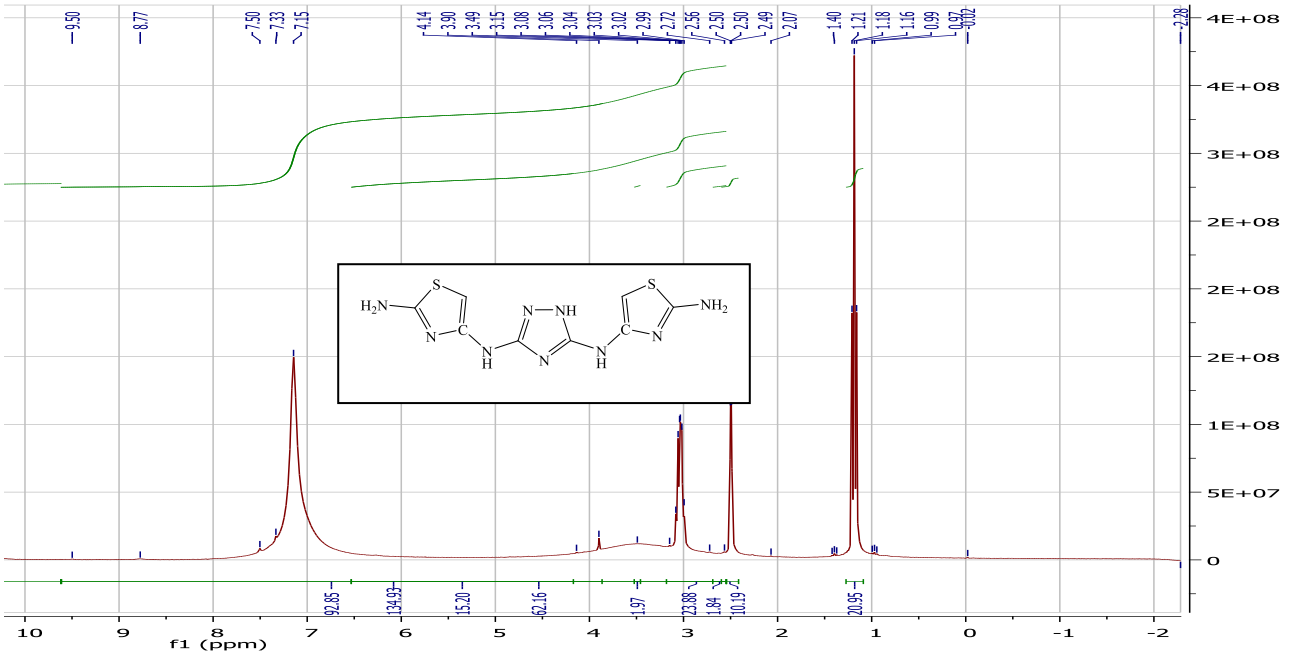


Figure 7:^{1}H-NMR spectrum of compound(th_2)

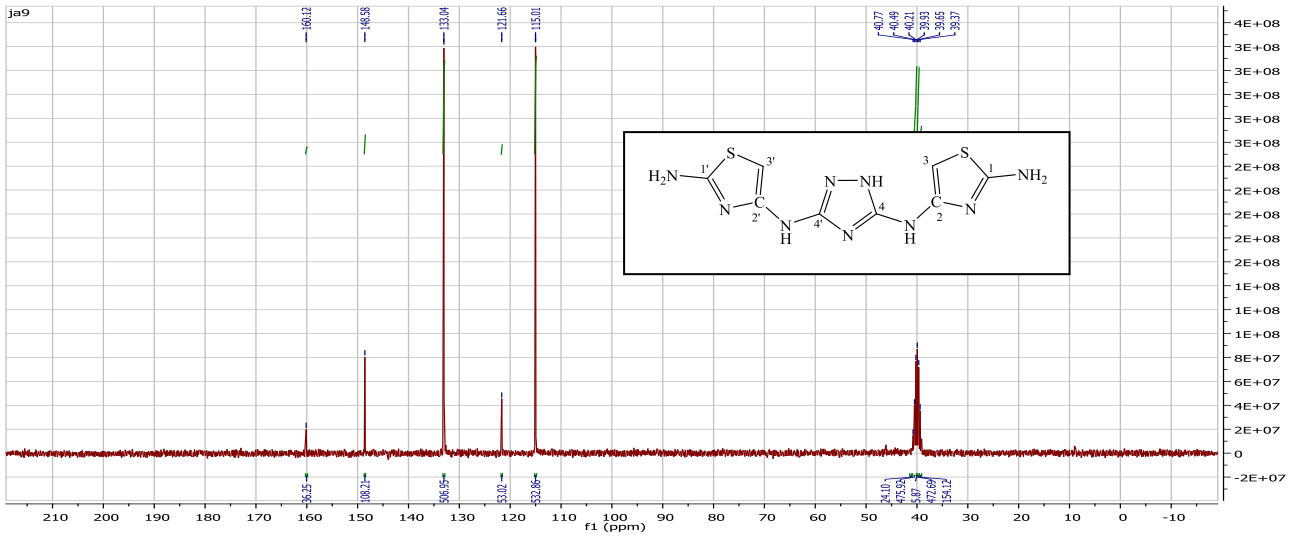


Figure (8):^{13}C-NMR spectrum of compound (th_2)

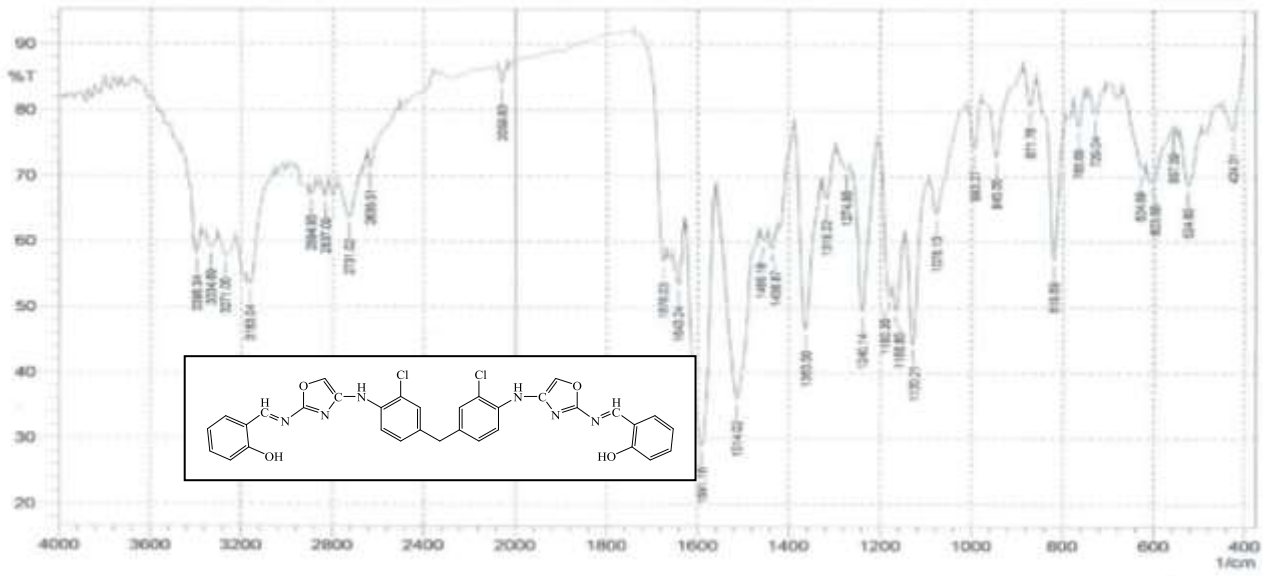


Figure 9: FT-IR spectrum of compound (Sc_1)

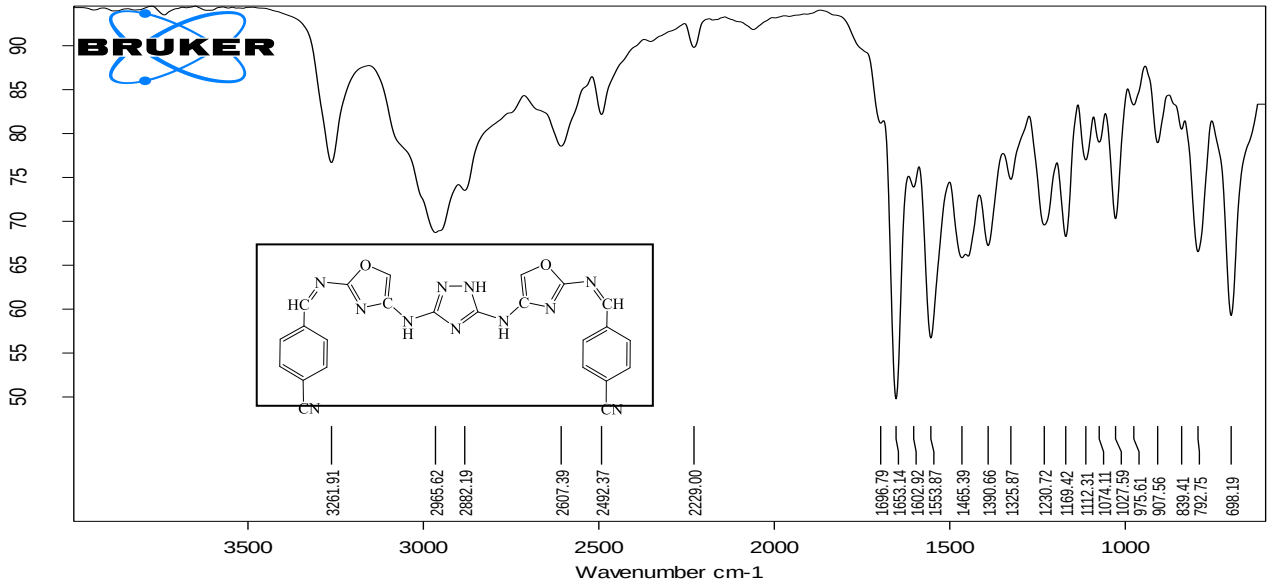


Figure 10: FT-IR spectrum of compound (Sc_4)

Conclusions

It was possible to prepare of new derivatives of di-heterocyclic five membered rings. The different results of FT-IR between the imines compounds and final derivatives showed that the final compounds were the least obstructed in all preparation processes and because of the complete clarity in infrared beams, this is the basis of organic preparation processes. The resonance results of ^{1}H-NMR demonstrated high accuracy in urbanization in terms of the number of protons compatible with the integral area.

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