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Synthesis of some Bis 1 , 3, 4 –Oxadiazole Derivatives and Bis 1,2,4-Triazole Derivatives

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Abstract

Aseries of Bis-1,4.[5(2-thio-ethanoic hydrazide-2N-Arylidene) –1,3,4-Oxadiazole-2-yl] butane derivatives.[6 a-h],and another series at Bis-1,4-[4N-amino Arylidene -5-thiol -1,2,4-triazole –3-yl] butane derivatives [9a-f] were synthesized from diethyl adipate ester .

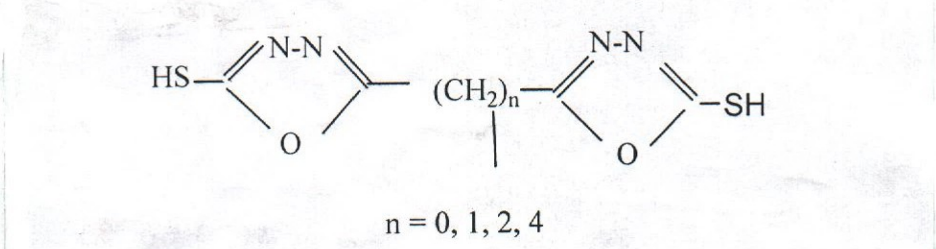
Representive samples of the prepared compound were characterized from their I.R. and mass spectral data .

Introduction

During the course of extensive program directed towards the synthesis of novel heterocycles of potential biological application , avariety of new 1,3,4- oxadiazole, 1,2,4- triazole, mercapto triazoles and fused heterocyclic systems of both were synthesized and screened for biological activities(1-5) substituted 1,3,4- oxadiazoles have received intensive interest due to their biological activities and their wide use in medicine and agriculture (6-9), and heat resistant polymers.(10-11) Accounts concerned with the synthesis of substitute bis 1,3,4-oxadiazole have, comparison, remained rara(12,13). This has stimulated us to synthesized and characterize different substituted bis 1,3,4-oxadiazoles.

1,2,4-triazole nucleus has been recently incorporated into awide variety of the rapeutically interesting drugs(14) . 4-5 Disubstituted-1,2,4-triazoles have remerged as potential drugs and are known to possess a broad pharmacological spectrum(15).

Some bis (5-thiol -1,3,4 –oxadiazole -2-yl) alkanes revealed the antifungal activity (2) also showed that aslight increase in activity takes place as the number of methlene groups increases



The above observations Created futher interteest for the Synthesis of many Compounds Containing 1,3,4- oxadiazole and 1,2,4- triazolering. Table (1-1) Summarizes the structers and biological activity of some of these compounds.

Experimental Work

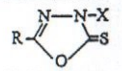
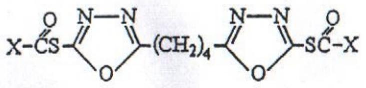
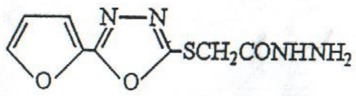
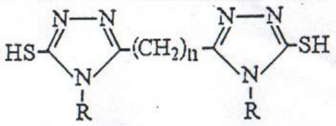
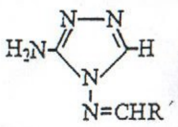
The purity of the resulting compounds was checked by, melting points are un corrected were taken on a "Electrothermal" melting point apparatus (mettle), mass spectra were recorded on shimadzo Qp1000, Gas mass spectrometer (Gc-Ms), using direct insertion system for range of *m/z* 10-1000 and ionization energy (EI), of 20ev.or 70ev by the laboratories of the Iraqi Atomi-Energy commission,Analytical Chemistry Center.

IR Spectra were measured using a perkin-*E/mer* 1310 infrared spectrophotometer on KBr disc by the laboratories of the chemistry Department ,college of Education-Ibn AL-Haitham,Baghdad University.

Adipic dihydrazide [2] General procedure(20)

Diethyl adipate (0.01 mole) and hydrazine hydrate 98% (0.02 mole) were dissolved in ethanol (10 ml) and refluxed for 30 mint. The precipitate ,which separated on cooling, was filtered and washed with absolute ethanol.Yield 100% , m.p 182 C° lit 182 C° (21).

Table (1-1)

Compound Name	Structure	Biological activity	References No.
5-aryl/ aryloxymethyl-1,3,4 – oxadiazol -2- thiones	 $X=H, CH_2OH, ph-\overset{H}{N}-\underset{R}{CH}$ R= different Ar	Antifungal activity against	16
5,5̄ – (1,4-Butane)bis- [Δ^2-1,3,4-oxadiazole -2-thiol substituent]	 $X = C_2H_5$,$MeO-C_6H_4$	Antimicrobial activity	17
α -[5-(2-Furyl)-1,3,4- oxadiazole-2-yl –thiol] acetone hydrazide		Antitubercular activity	18
Bis (4-aryl-5-thio- 1,2,4- triazole-3- yl) –alkane	 n =0, 1, 2, 3 R = P-Anicyl , phenetyl	Fungicidal activity againet	2
3-amino -4-(arylidene amino)-4-H-1,2,4- triazole	 R = ph , substituted ph	Antihypertensive activity	19

IR (KBr) ϒmax of these hydrazide show stretching bands (3300,3160,3060 cm^{-1}) NH_2 and N-H groups, (1630cm^{-1}) C=O amide I,(1540cm^{-1}) C=O amid II.

Bis-1′,4′-[5-thiol -1,3,4-oxadiazole-2-yl] butane[3]

To a mixture of adipic dihydrazide [2] (1.74 g,0.01 mol)in 10 ml of 2N KOH solution , methanol was added until the mixture become clear about (20 ml) .

Carbon disulphide (0.02 mole) was added gradually and the mixture was refluxed for 3 hr, until evolution of H_2S ceases . Excess solvent was removed in vacuo and the residue was mixed with ice and poured onto ic water containing 10% Hcl.

The precipitate was formed filtered, washed with water and recrystallized from ethanol to give white crystals of compound [3], Yield 80% m.p 192C° lit 192 C° (22).

The IR spectrum showed stretching bands at 3100 cm^{-1} (N-H),1600 cm^{-1} (C=N),1050 cm^{-1} (C=S) and1275 cm^{-1} of (C-O-C) stretching vibration combined with (N-N)band of 1,3,4- oxadiazole moiety.

Bis-1′,4′-[5(2′-thio ethyl ethanoate)-1,3,4-oxadiazole-2-yl] butane[4]

Compound [3] (1gm ,0.03 mole) in (10ml) water containing sodium carbonate (0.82g, 0.0077 mole).Reaction mixture was evaporated to dryness and the residue was dissolved in absolute ethanal (15ml) .Then ethyl chloroacetate (0.94g,0.0077mole) was added to the mixture which was then vigorously shaken for 1hr .Finally left over night at room temperature. Reaction mixture was filtered, the filterate evaporated to dryness under reduced pressure and the residue was extracted with ethylacetate (40 ml) the extract was dried over anhydrous magnesium sulphate,filtered and evaporated under reduced pressure to give asolid which was recrystallized from methanol-water (mixture) to give ethyl ester [4] yield 90%,m.p.85C°.The IR spectrum showed the appearance of a sharp strong band of the ester (C=O) stretching at 1740 cm^{-1} ,(-SCH_2) at 1420 cm^{-1} and (OC_2H_5) at 1275 cm^{-1}.

Bis-1́,4́-[5(2-thio ethanoic hydrazide)-1,3,4-oxadiazole-2-yl] butane[5]

To a solution of ester [4] (0.6g,0.0014mole) in absolute ethanol (10ml) was added excess of hydrazine hydrate (1ml). Reaction mixture was heated under reflux for 20-30min, cooled, concentrated and left at 0c°for 2 day.The solid was formed filtered off,dried and recrystallized from water to give the acid hydrazide [5], yield 71% m.p. 183C°.

The IR spectrum showed 1650 cm^{-1} (C=O)amide 1 in the acid hydrazide other bands at 3300,3200 cm^{-1} stretching bands of NH_2 and NH groups.

Bis-1́,4́-[5(2-thio ethanoic hydrazide-2N-Arylidene)-1,3,4-oxadiazole-2-yl]butane [6 a-h].

Acid hydrazide [5] (0.4g,0.001 mole) was dissolved in a mixture of dry DMF (5ml) and absolute ethanol (10ml). Appropriate aromatic aldehyde (0.002mole) was added to reaction mixture refluxed for 90min., cooled, the solid was separated filtered off, washed with hot ethanol and sucked dry.

The physical data for the synthesized compounds are given in table 1.

Bis-1́,4́-[4N-amino-5-thiol-1,2,4-triazole-3-yl]butane [8]

To a solution mixture of potassium hydroxide (1.68g ;0.03mole), and adipic dihydrazide [2] (2.5g ; 0.01mole) in absolute ethanal (15ml). Carbon disulfide (1.8 ml, 0.03 mole) was added . The reaction mixture was diluted with ethanol (15ml) and stirred over night. Then diluted with dry ether (25ml) and a pale yellow precipitate was formed , filtered washed with ether and dried at room temperature to give the potassium salt [7] in quantitative yield (m.p 175 C°). The salt was employed in the next step without further purification.

To a suspension of potassium salt [7] (5g, 0.01mole), hydrazine hydrate (5ml) was added and refluxed with stirring until the evolution of hydrogen sulfide was ceased using (lead acetate paper as indicator); After cooling, the reaction mixture was diluted with water (30ml) and acidified with 10% HCL, awhite solid separate which was filtered washed with (30ml) water and recrystallized from DMF-water to give compound [8], yield 28% m.p 260 C°.

Bis-1,4-[4N- amino arylidene -5-thiol-1,2,4-triazole-3yl]butane [9 a-f].

To a hot stirred solution of triazole [8] (0.286g,0.001 mole)in dry DMF, absolute ethanol mixture (1:1), appropriate aromatic aldehyde (0.02 mole) was added .The reaction mixture was refluxed for 24hr.Solid was separated filtered and dried to yield the desired Schiff - bases derivative[9 a-f] Table (2) lists the physical properties-of the schiff-base derivatives
[9 a-f].

Results and Discussion

The Bis 1,3,4- oxadiazole [3] was prepared from reaction of adipic hydrazide [2] with carbon disulfide in the presence of potassium hydroxide solution.The structure of oxadiazole was characterized by its melting point and IR spectroscopy.
The IR spectram showed stretching bands at 3100cm^{-1}(N-H),1600cm^{-1}(C=N) and 1050cm^{-1}(C=S).

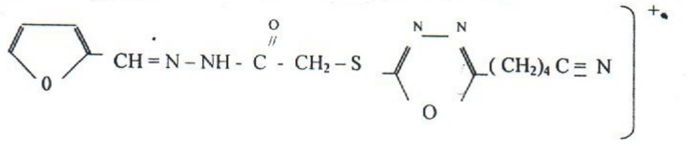
Thio ethanoate ester oxadiazole [4] have been prepared by the reaction of the sodium salt of the bis-1,4-[5-thiol-1,3,4-oxadiazole-2-yl] butane with ethyl chloro acetate in absolute ethanol.Structure of the prepared compounds was confirmed by melting point and by IR spectrum.Which show a sharp strong band of the ester carbonyl stretching at 1740 cm^{-1} is agood evidence for the formation of ester [4], and a new weak band at 1420 cm^{-1} appeared which could be attributed to the new S-CH$_2$. Then thio ethanoic hydrazide oxadiazole [5] was obtain when thio ethanoate [4] was refluxed with hydrazine hydrate 98%. The IR spectrum of compound [5] showed ashift in the carbonyl stretching band from 1740 cm^{-1} in ester [4] to 1650 cm^{-1} (amide 1) of the acid hydrazide[5], other bands at 3300 cm-1,3200 cm^{-1} were also observed which are assigned to the asymmetric and symmetric stretching bands of NH_2 and N-H of hydrazide groups.

Schiff bases derivatives [6a-h] were obtained by reaction of amino group of hydrazide compound [5]with avariety of aromatic aldehyde in DMF as a solvent. Structures of compound [6] were confirmed by infrared spectral data figure (1), show disappearance of the (NH_2) stretching bands at 3300 cm^{-1} ,3200 cm^{-1} as well as appearance of C=N and appearance of NH stretching band at 1570 cm^{-1} , and C=O stretching band at (1650 cm^{-1})(19).

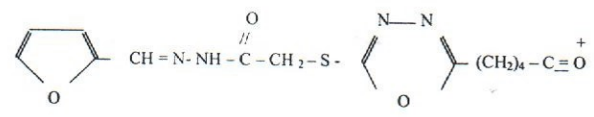
Table (1) show characteristic IR absorption bands of compound [6a-h].

Mass spectral data of compounds [6a-h] showed molecular ions which correspond to the Mol. Masses of the suggested structures fragment assigned to these compounds.

The mass spectram of compound[6f] give the most characteristic Fragments at m/z 335,333 which is good evidence for the presence of two oxadiazole rings.



m / z = 333



m / z = 335

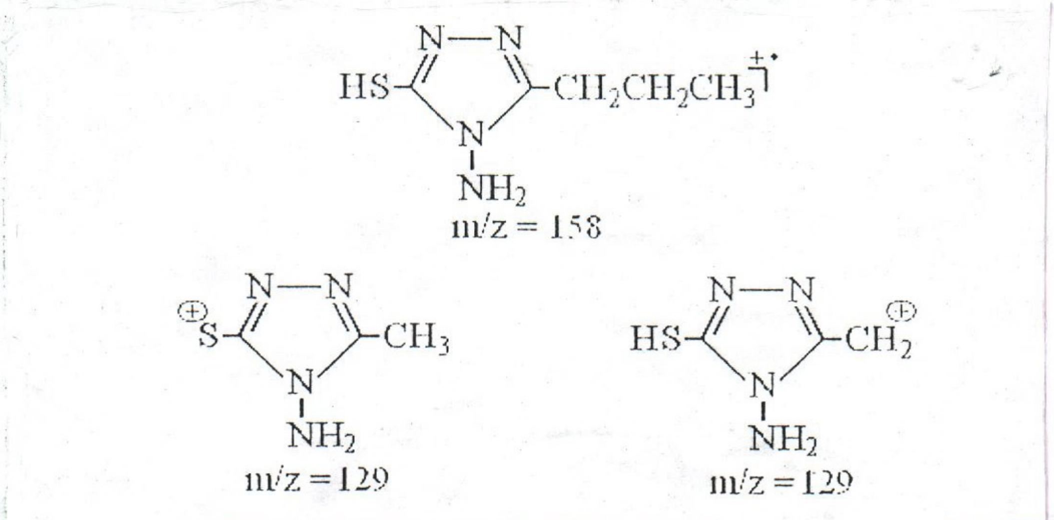
Other fragments were also observed and were assigned as is depicted in (Scheme 2), Figure (2).

The Second series 1,2,4-triazole derivatives have been synthesized as outlined in [scheme1], stirring acid hydrazide[2] with carbon disulfide in ethanoic potassium hydroxide gave the salt [7] in excellent yield . The salt was characterized from solubility and its infrared spectrum, which showed multiple (N-H) stretching bands at (3100-3300) cm^{-1} intense broad band at (1600-1640) cm^{-1} regarded as combination of amide I, amide II and (C=N) stretching vibrations. The spectram also showed absorption at (1050) cm^{-1} and (1210)cm^{-1} attributed to (C=S) and (N-N) stretching vibrations respectively.

Triazole derivative compound [8] was characterized by its infrared and mass spectral data, Figure (3,4) it shows displayed bands at 3230 cm^{-1} and 3100 cm^{-1}, which can be attributed to (NH_2) and (NH) asymmetrical and symmetrical stretching vibration. The IR also showed two distinct peaks, the first at (1040) cm^{-1} which could be attributed to (C=S) stretching while the second one appeared as weak band at (2760)cm^{-1} which could due to S-H stretehing (20).

The bands at (1590) cm^{-1} and (1300) cm^{-1} are indicative of (C=N) and (N-N) stretching vibrations respectively.

In the mass spectrum fig, (3,4) the fragmentation pattern is in agreement with the proposed structure . Upon electron impact this compound give low aboundance of molecular ion at m/z 286 which corresponds to the molecular weight of the structure suggested for this compound . The most informative fragments that gives a strong evidence for the structure assigned to this compound were are observe at m/z 158 (base peak) and 129.



Other fragments were also observed in the mass spectrum of this compound and were assigned structures as is shown in scheme(3).

Schiff base derivatives [9 a-f] were obtained by reaction of amino-triazole [8] with appropriate aromatic aldehyde in DMF, these shiff bases [9a-f] were confirmed by infrared spectral data Table (2) .

The two stretching bands at (3300) cm^{-1} and (3150) cm^{-1} due to NH_2 stretching in compound [8] were replaced by only one at (3080-3110) cm^{-1} due to N-H stretching which could be main observation noticed in the IR spectra of these compounds All suggested bands for (C-H) aromatic, endocyclic (C=N) and exocyclic (C=N) stretching vibration in addition to out of plane bending of substituted benzene ring . On the other band it showed in [Table2] lists the most informative bands in the IR spectra of the compounds [9a-f].

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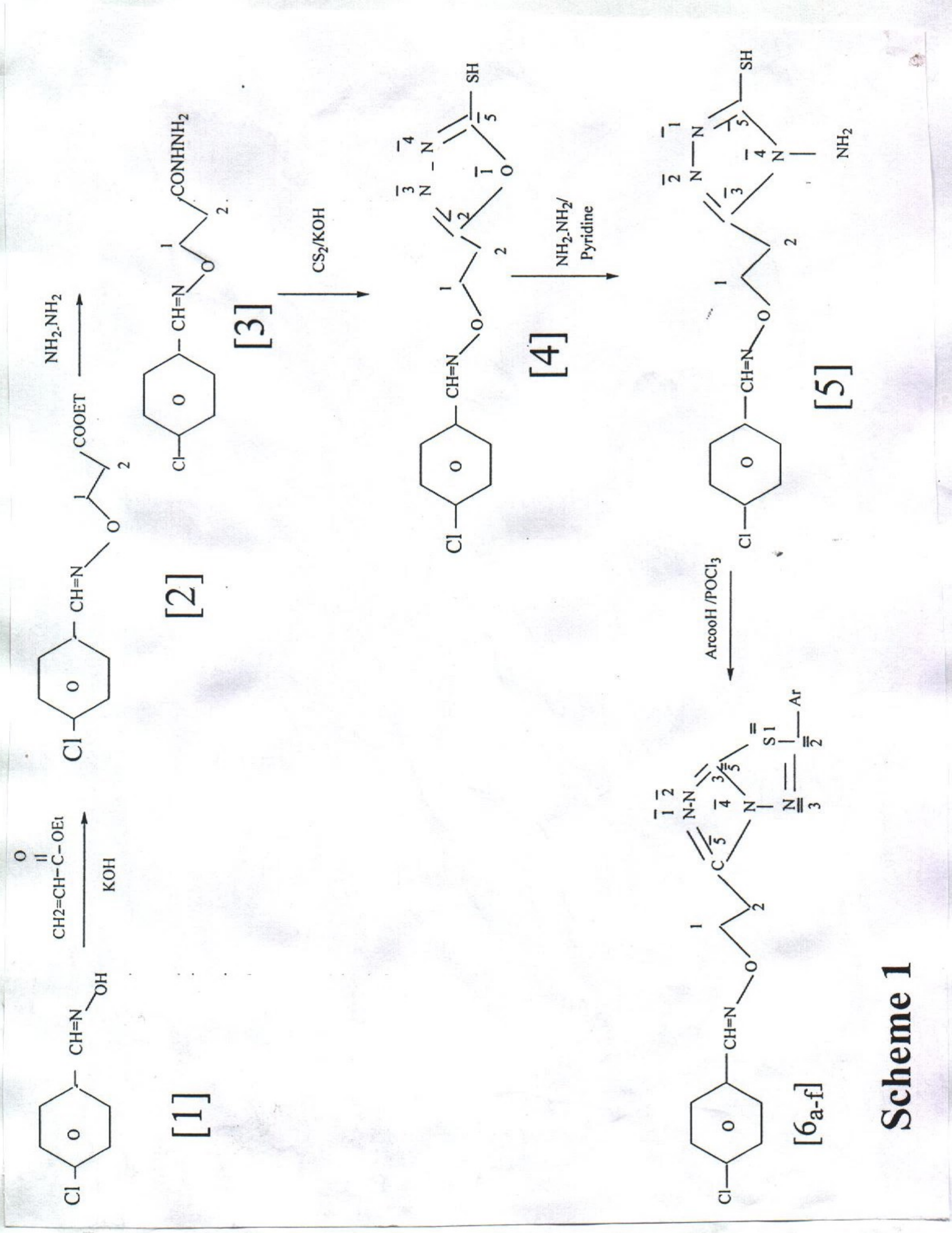
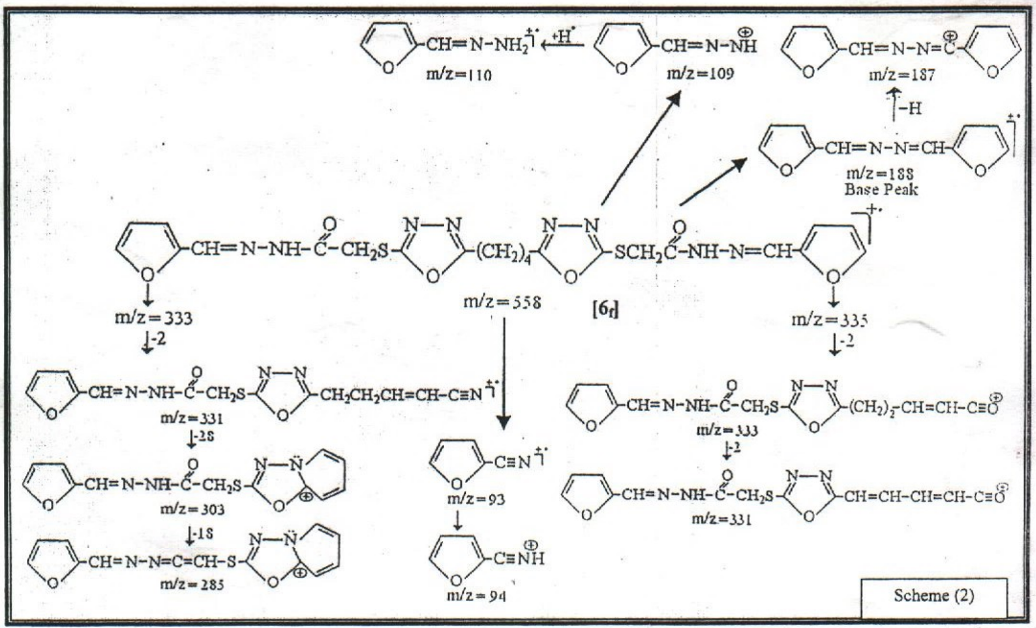
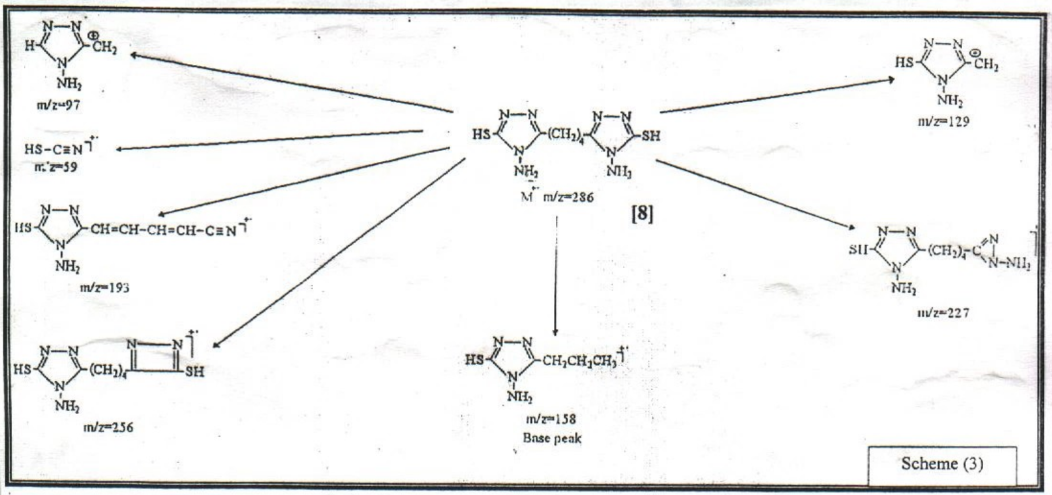

[1]
CH2=CH−C(=O)−OEt
KOH
[2]
NH2.NH2
[3]
CS2/KOH
[4]
NH2.NH2/ Pyridine
[5]
ArcooH /POCl3
[6a-f]
Ar
SH
NH2
COOET
CONHNH2

Scheme 1



Scheme (2)



Scheme (3)

Table(1) The physical properties of the Schiff base derivatives [6 a-h]

Comp. [6]	Ar	Molecular weight	Yield%	m.p.c°	(N-H) νcm^{-1}	ν (C-H)cm^{-1} arom.	ν(CH)cm^{-1} aliph	ν(C=H)cm^{-1}	$\nu(\overset{O}{\overset{\|}{C}}-NH)$ cm^{-1}
a	4-NO_2-C_6H_4-	668	70	198-200	3200	3100	2950	1570	1670
b	4-$MeOC_6H_4$.	638	73	202-205	3220	3050	2940	1590	1640
c	4-HOC_6H_4.	610	33	236-240	3000 -	3280	2900	1600	1660
d	$C_6H_5CH=CH$-	630	76	221-225	3240	3050	2900	1575	1650
e	piperongl	666	78	209-211	3240	3040	2900	1580	1650
f	2-Furyl	558	79	212	3200	3055	2900	1570	1650
g	4-ClC_6H_4.	646	69	222-224	3250	3050	2900	1580	1665
h	3,4$(Meo)_2C_6H_3$-	698	78	200-201	3200	3025	2900	1560	1675

Table(2) The physical data of the Schiff - base derivatives [9 a-F]

Comp. [9]	RC_6H_4	Molecular weight	Yield%	m.p.c°	ν (NH) cm-1	ν (C-H) cm-1	ν (C=N) cm-1 exocyclic	ν (C=N) cm-1 endocyclic	Other bands
a	4-HOC6H4-	488	36	270	3000	3300	1650	1560	(O-H)combined with (N-H) and (CH) arom
b	4-MeOC6H4 -	522	32	225	3080	3020	1650	1580	-
c	4-ClC6H4-	530	54	240	3100	3040	1660	1560	-
d	4-MeC6H4 -	490	41	285	3080	3040	1610	1575	-
e	4- O2NC6H4-	552	63	289	3100	3050	1650	1575	(N=O) at 1520 (N=O) at 1340
f	3-O2N-C6H4-	552	95	286	3080	3030	1650	1575	(N=O) at 1530 (N=O) at 1340

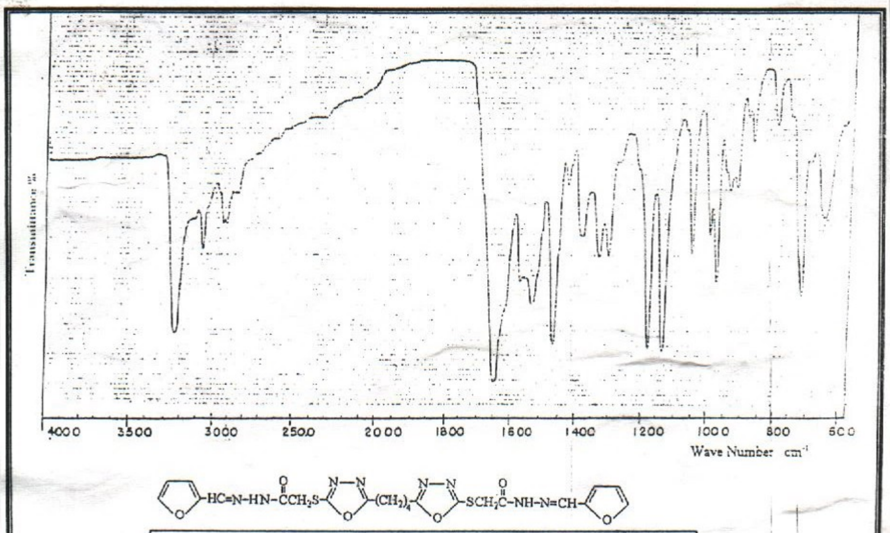


Figure (1) IR Spectrum of compound [6_f]

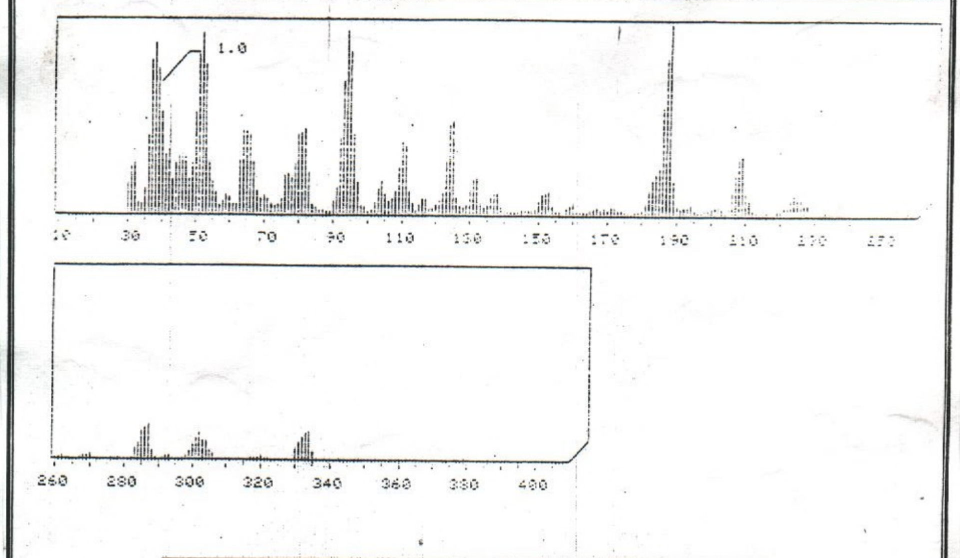


Figure (2) Mass Spectrum of compound [6_f]

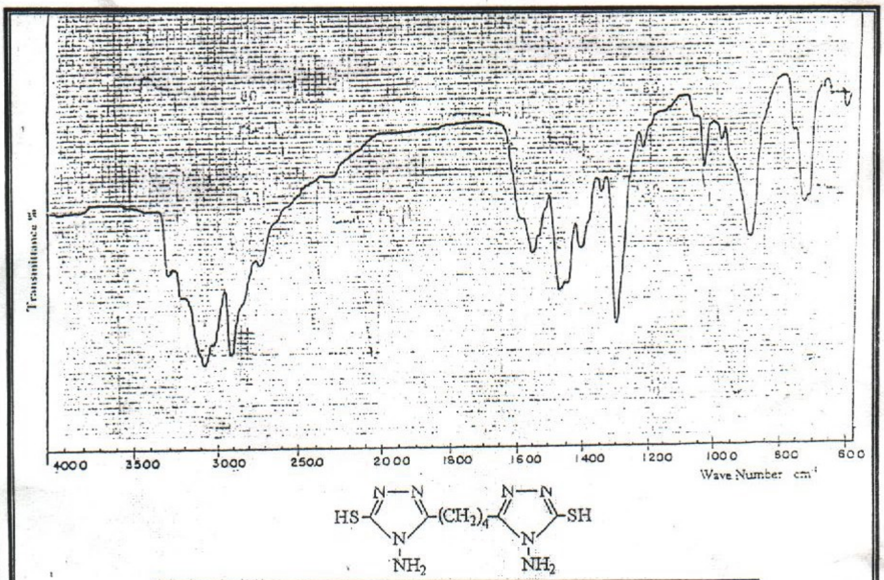


Figure (3) IR Spectrum of compound [8]

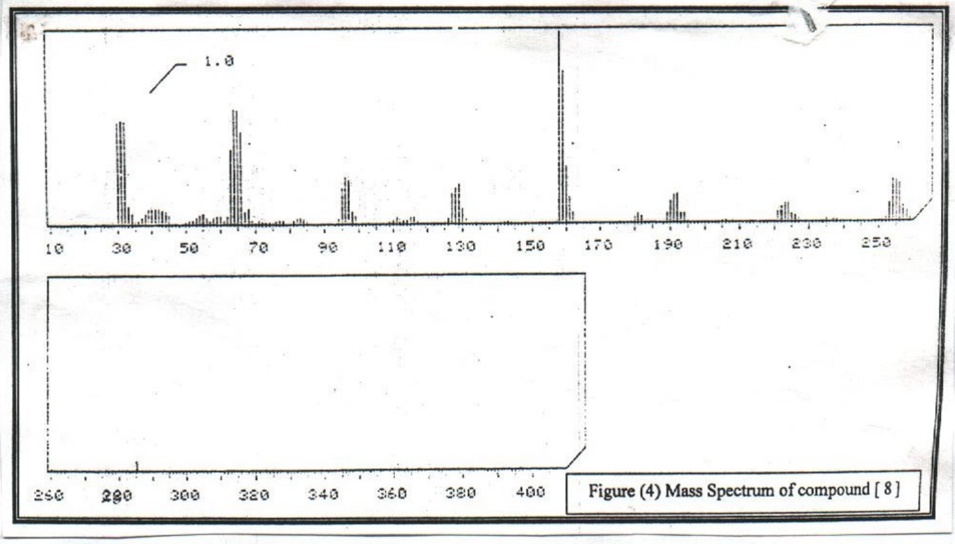


Figure (4) Mass Spectrum of compound [8]

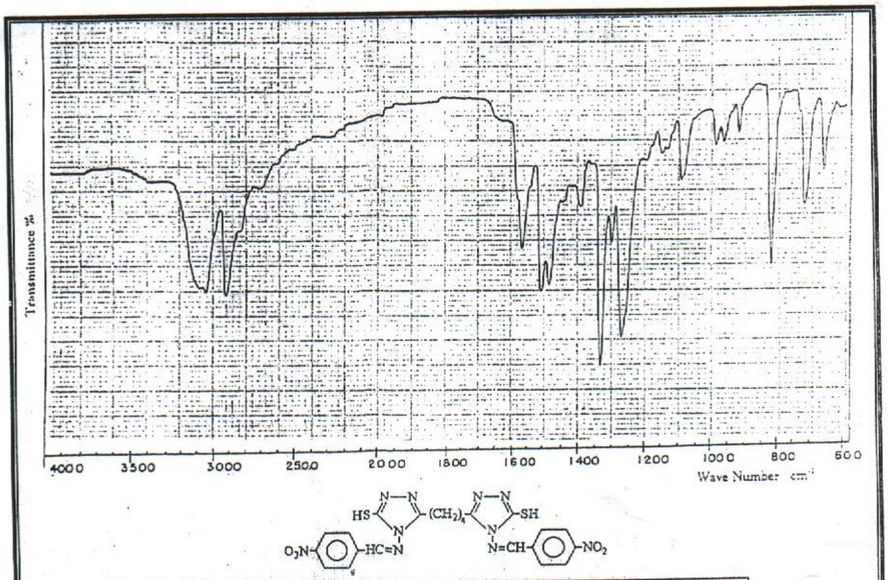


Figure (5) IR Spectrum of compound [9_e]

مجلة ابن الهيثم للعلوم الصرفة والتطبيقية   المجلد20 (2) 2007

تحضير بعض مشتقات بس 4,3,1- اوكسادايزول ومشتقات بس 4,2,1-ترايازول

حسين عليوي السعدي

قسم الكيمياء، كلية التربية – ابن الهيثم ، جامعة بغداد

الخلاصة

تم تحضير سلسلة من مشتقات بس 1′،4′ [5 (2″– ثايوايثانوك هيدرازايد–N2–
اريليدين–3،1 ،4 – اوكسادايزول–2″–يل) بيوتان [6a –h] ، وتم تحضير سلسلة اخرى من
مشتقات بس 1′،4′ – [N4– امينو اريليدين –5–ثايول – 4,2,1 ترايازول –3– يل] بيوتان
[9 a-f] من ثنائي اثيل اديبيت استر .

وقد تم تشخيص هذه المركبات بأستخدام اطياف الاشعة تحت الحمراء واطياف الكتلة .