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Synthesis of 1,2,3 –Trisubstituted- 1,2,3- Trihydro-1,3-Diazepine-4,7-Diones (part3)

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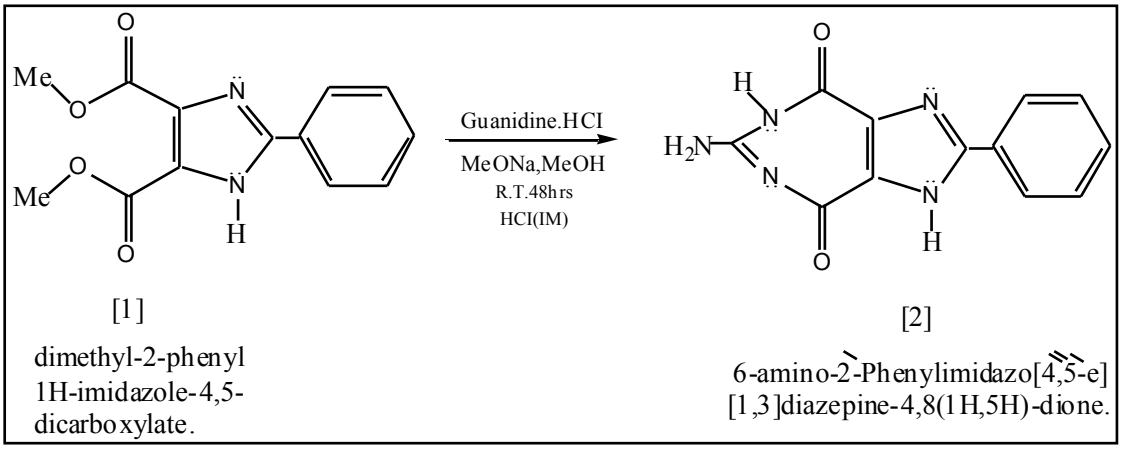
Abstract

1,3- Oxazepines, benz [1,2-e] [1,3]-oxazepines, and 3- nitrobenz [1,2-e] [1,3] -oxazepines were reacted with ammonia derivatives, $H2\ddot{N}$-Z to give 1,3 – diazepine -4,7-dione, benzodiazepine - 4,7- dione, and 3 – nitrobenzo -1,3- diazepine - 4,7- dione, respectively.

Introduction

The starting imidazole diester [1] reacts with guanidine hydrochloride to yield 1,3-diazepine derivatives [2] (1):



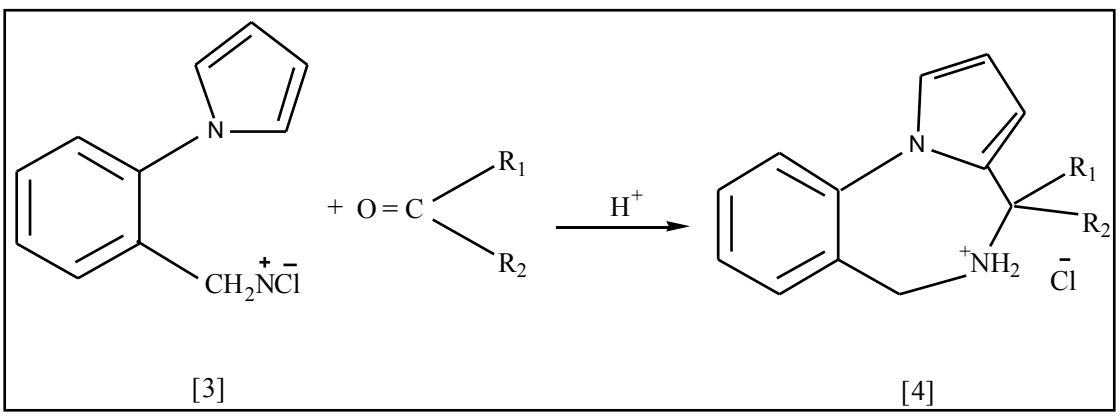
[1]

dimethyl-2-phenyl 1H-imidazole-4,5-dicarboxylate.

[2]

6-amino-2-Phenylimidazo[4,5-e] [1,3]diazepine-4,8(1H,5H)-dione.

The reaction of 1- (2-aminomethylphenyl) pyrrole hydrochloride [3] with carbonyl compounds gives diazepines [4] in a ring closure reaction(2)

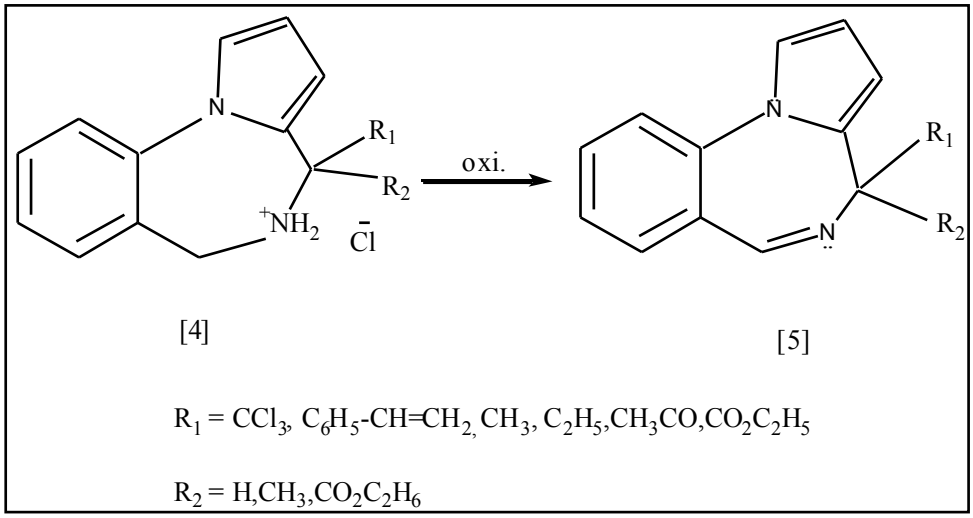


[3]

[4]

Compound[4] was oxidized by manganes dioxide in toluene to give 4H-pyrrolobenzodiazepine [5] (2).

Many of the diazepines show interesting sedatives, muscle relaxant, and anticonvulsant properties in animals (2).



[4] [5]

R_1 = CCl_3, C_6H_5-CH=CH_2, CH_3, C_2H_5, CH_3CO, $CO_2C_2H_5$

R_2 = H, CH_3, $CO_2C_2H_6$

Several clinical useful drugs were found which contain a hetrocyclic moity fused onto the seven membered ring, like pyrrolobenzodiazepines which are now accessible by several routes (2).

Aim of the work

Synthesis new diazepines derivatives which are expected to have a biological activity in the medical field.

Experimental Part

Material and Solvents:

1. 1,3-Oxazepine -4,7- diones (II),(III) and (IV) prepared as part 1 (3).
2. Ammonia derivatives H_2N-Z.
3. Dry benzene (Merck 99).
4. Ethanol (Merck 99.7-100).
5. Dioxane.

The instruments:

1. Melting points were determined with: Strut Melting point Apparatus and were uncorrected.
2. IR. Spectra were recorded with: PYE UNICAM SP3-300 Infrared Spectrophotometer (KBr disc) in the range (4000-200)cm^{-1}.
3. FTIR Spectra, Were recorded with: SHIMADZU FTIR-8400S Infrared Spectrophotometer (KBr disc).
4. Elemental Analysis (C.H.N.) was carried with: Perkin Elmer B-240 Elemental Analyzer.

Experimental:

Synthesis of :2- styryl -3- aryl -1,2,3-trihydro [1,3]- diazepine - 4,7- dione -1- thiocarbamide (VIIIf) , 2 – styryl – 3 – aryl - 1,2,3, - trihydrobenzo [1,2-e] [1,3] –diazepine - 4,7- dione -1- thiocarbamide (1Xf), 1- Hydroxy - 2- styryl-3-(p-nitrophenyl) - 1,2.3 – trihydrobenzo [1,2-e] [1,3] – diazepine - 4,7- dione (1Xb) ,1-amino -2- styryl -3- (p-methylphenyl) - 1,2,3 - trihydrobenzo [1,2-e] [1,3] - diazepine 4,7-dione (1Xd), 2 – styryl -3-

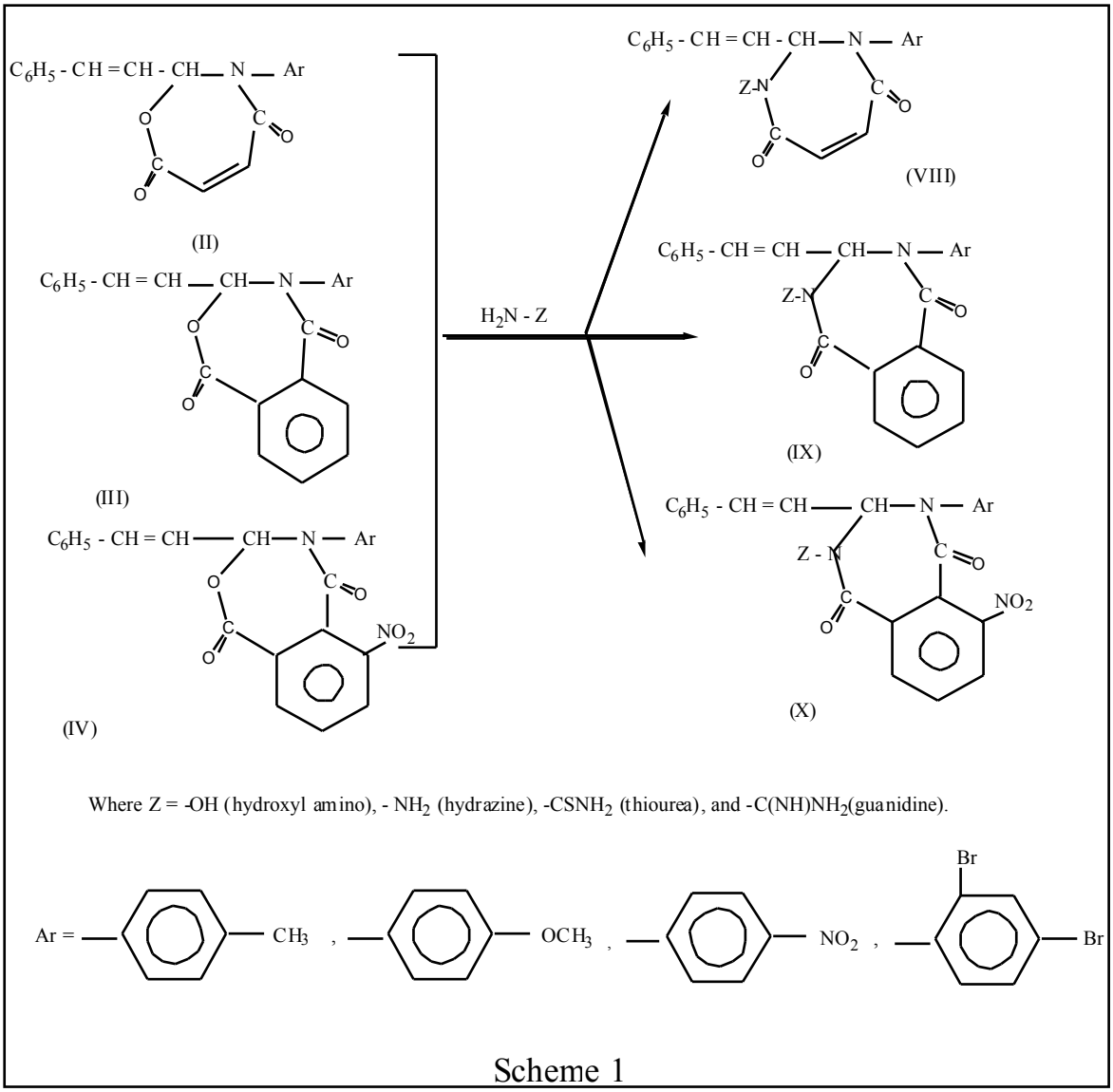
(2,4-dibromophenyl) - 1,2,3 – trihydrobenzo -[1,2-e] [1,3] – diazepine - 4,7 – dione - 1- thiocarbamide (1Xf), 1- hydroxy -2- styryl -3- (p-methylphenyl) - 1,2,3-trihydro -3- nitrobenzo [1,2-e] [1,3] – diazepine - 4,7-dione (Xd) ,1- formamidino-2- styryl -3- (p-methoxyphenyl) - 1,2,3 – trihydro -3- nitrobenzo [1,2-e][1,3]- diazepine-4,7-dione (Xe), 2-styryl -3- (2,4-dibromophenyl)-1,2,3- trihydro -3- nitrobenzo [1,2-e][1,3]-diazepine -4,7-dione -1- thiocarbamide (Xf).

A mixture of (0.0015 mole) of 2-styryl -3- aryl -2,3- dihydro [1,3]-oxazepine -4, 7-dione (II) and (0.0015 mole) of thiourea (or guanidine hydrochloride + Na_2CO_3) suspended in (20 mL) of dry benzene (or absolute ethanol) was heated and refluxed in water bath for 3hrs, the solvent was evaporated leaving light yellow crystals of 2-styryl -3- aryl-1,2,3-trihydro [1,3]-diazepine -4,7- dione-1-thiocarbamide (VIII) filtered and recrystallized from dioxane. This experiment was repeated by using other 1,3-oxazepines with ammonia derivatives in order to obtain different diazepine derivatives (IX) and (X).

Discussion

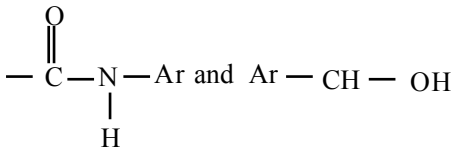
In a previous paper (3) synthesis of 1,3 - oxazepine - 4, 7- dione (II) benzo [1,2-e][1,3]- oxazepine -4,7- dione (III) and 3- nitrobenzo [1,2-e][1,3] oxazepine-4,7- dione (IV) was described.

These oxazepines were found to be good starting compounds for the synthesis of another class of heterocylic compounds (4) by the reaction with ammonia derivatives H_2N-Z as shown below(4,5,6):



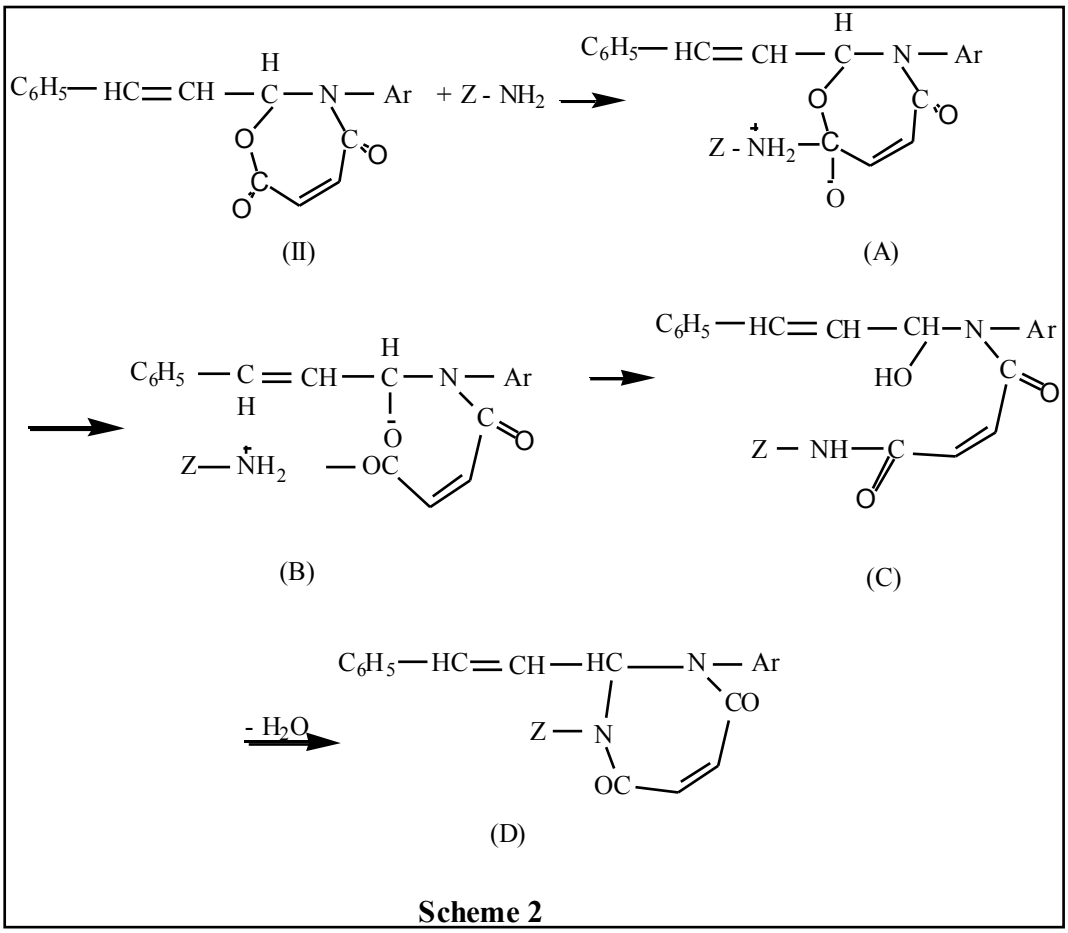
Scheme 1

The mechanism (7) involves the addition of the amine to the carbonyl group of the lactone forming the dipolar intermediate (A) which undergoes cleavge to give another dipolar intermediate (B). Intermediate (B) undergoes hydrogen transfer from nitrogen to oxygen to give the open chain hydroxyl amide (C) in which both



and

maintain their configuration throughout the course of the reaction that permits the elimination of H_2O and the reclosure of the structure to give 1,3-diazepine-4, 7-dione (D).



Scheme 2

The resulting diazepines VIII, IX and X are identified by their m.ps,elemental analysis (tables 1,3,6,8,11) and IR, FTIR spectra (tables 2,4,5,7,9,10,12).

It is noticeable that the IR spectra of the expected products show the appearance of (NH, OH) absorption bands at (3580,3320)cm^{-1}, respectively (8). This value indicates that the alcoholic part of the lactam (c) maintains its configuration throughout the course of the reaction of the 1,3-oxazepine-4,7-diones with ammonia derivatives, Scheme 2.

References

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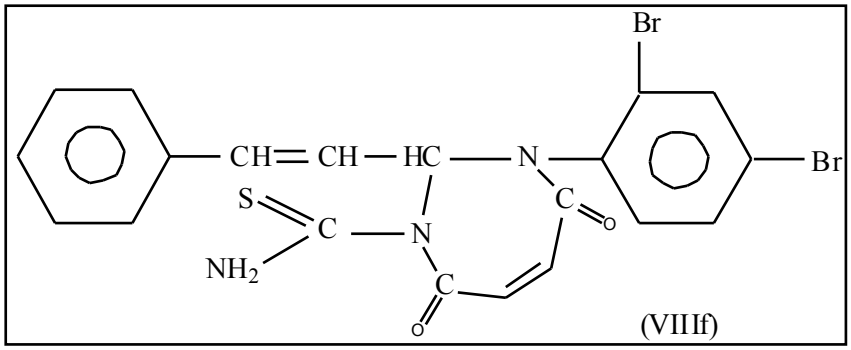
Table :(1) M.F., M.Ps, Yields %, and Elemental Analysis of 2-styryl-3-(2,4-dibromophenyl)-1,2,3-trihydro [1,3]-diazepine-4, 7-dione -1- thiocarbamide (VIIIf).



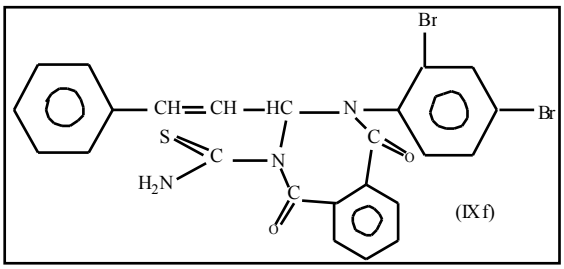
(VIIIf)

Comp.	M.F.	Color	m.p(c°)	Yield (%)	Calc.			Found		
					C%	H%	N%	C%	H%	N%
VIIIf	$C_{20}H_{15}O_2N_3SBr_2$	Light yellow	192-193	68	45.96	2.87	8.04	45.47	2.97	8.41

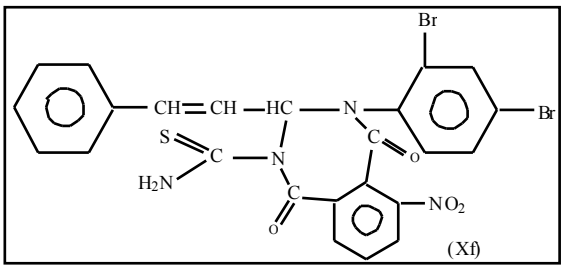
Table: (2) IR absorption bands (cm^{-1}) of 2-styryl -3- (2,4- dibromophenyl)- 1,2,3-trihydro [1,3]-diazepine -4, 7-dione-1-thiocarbamide (VIIIf).

Comp.	NH str.	C-H str. Allylic	= CH str. Vinylic	C-H str. Aromatic	C=O str. lactam	C=S str.	C=C str. Vinylic	C=C str. Aromatic	C-N str.	N-H bend.	C-H bend. Allylic	= CH bend.	C-Br
VIIIf	3470Asym. 3345 Sym.	3195	3120	3040	1690	1260	1495	1625	1145	1590	1280	830	575

Table:(3) M.F., m.ps, yields %, and Elemental Analysis of 2-styryl-3-(2,4-dibromophenyl)-1,2,3-trihydrobenzo [1,2-e][1,3]-diazepine-4,7-dione-1-thiocarbamide (IXf).&2-styryl-3-(2,4-dibromophenyl)-1,2,3-trihydro-3-nitrobenzo[1,2,e][1,3]-diazepine-4,7-dione-1-thiocarbamide(Xf).



(IXf)



(Xf)

Comp.	M.F.	Color	m.p(c°)	Yield (%)	Calc.			Found		
					C%	H%	N%	C%	H%	N%
IXf	$C_{24}H_{17}O_2N_3SBr_2$	Light brown	170-171	58	50.349	2.97	7.342	50.11	3.11	7.66
Xf	$C_{24}H_{16}O_4N_4SBr_2$	Dark yellow	158-159	62	46.67	2.59	9.07	46.59	2.26	9.54

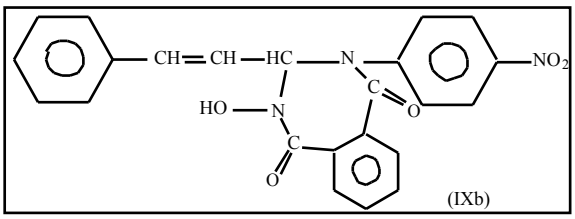
Table:(4)IR absorption bands (cm^{-1}) of 2-styryl -3-(2,4-dibromophenyl)-1,2,3-trihydrobenzo [1,2-e][1,3]-diazepine-4,7-dione-1-thiocarbamide(IXf). & 2-Styryl-3-(2-4-dibromophenyl)-1,2,3-trihydro-3-nitrobenzo[1,2-e][1,3]-diazepine-4,7-dione-1-thiocarbamide(Xf).

Comp.	N-H str.	C-H str. Allylic	= C H str. Vinylic	C-H str. Aromatic	C=O str. lactam	C=S str.	C=C str. Vinylic	C=C str. Aromatic	C-N str.	C-NO_2 Aromatic	N-H bend.	C-H bend. Allylic	Cis-CH bend. Vinylic	C-Br
IXf	3580 Asym. 3480 Sym.	3195	3120	3040	1710	1260	1510	1585	1170	-	1590	1280	830	575
Xf	3585 Asym. 3440 Sym.	3195	3120	3040	1735	1260	1490	1625	1170	1560 ,1360	1630	1280	835	570

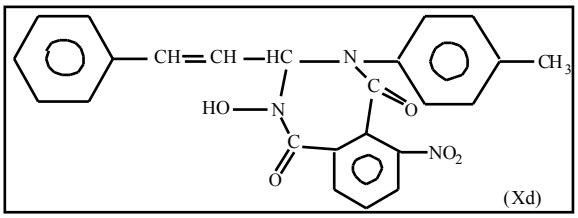
Table:(5) FTIR absorption bands (cm^{-1}) of 2-Styryl -3-(2,4-dibromophenyl)-1,2,3-trihydro-3-nitrobenzo [1,2,e][1,3]-diazepine-4,7-dione-1-thiocarbamide(Xf)

Comp.	N-H str.	C-H str. Allylic	= C H str. Vinylic	C-H str. Aromatic	C=O str. lactam	C=S str.	C=C str. Vinylic	C=C str. Aromatic	C-N str.	C-NO_2 Aromatic	N-H bend.	C-H bend. Aromatic.	= C H bend.	C-H bend. Allylic	C-Br Allylic
Xf	3479 Asym. 3372 Sym.	3168	3145	3112	1733	1255	1493	1559	1153	1537, 1355	1620	830, 790	840	1320	541

Table:(6) M.F., m.ps, Yields%, Elemental Analysis of 1-Hydroxy-2-styryl-3-(p-nitrophenyl)-1,2,3-trihydrobenzo[1,2-e][1,3]diazepine-4,7-dione(IXb). & 1-Hydroxy-2-styryl-3-(p-methylphenyl)-1,2,3-trihydro-3-nitrobenzo[1,2-e][1,3]diazepine-4,7-dione(Xd).



(IXb)



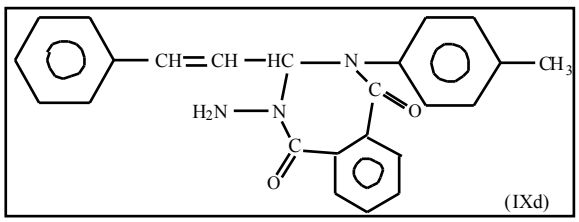
(Xd)

Comp.	M.F.	Color	m.p(c°)	Yield (%)	Calc.			Found		
					C%	H%	N%	C%	H%	N%
IXb	$C_{23}H_{17}O_5N_3$	Dark yellow	Over 270	64	66.50	4.09	10.12	66.62	3.96	9.74
Xd	$C_{24}H_{19}O_5N_3$	Brown	Over 270	61	67.13	4.42	9.79	67.31	4.17	9.57

Table:(7) IR absorption bands (cm^{-1}) of 1-Hydroxy -2-styrl-3-(p-nitrophenyl)-1,2,3-trihydrobenzo [1,2-e][1,3]-diazepine-4,7-dione(IXb).
& 1-Hydroxy-2-styrl-3-(p-methylphenyl)-1,2,3-trihydro-3-nitrobenzo [1,2-e][1,3]diazepine-4,7-dione(Xd)

Comp.	O-H str.	C-H str. Allylic	= CH str. Vinylic	C-H str. Aromatic	C=H str. aliphatic	C=O str. Lactam	C=C str. Vinylic	C=C str. Aromatic	C-N str.	$C-NO_2$ Aromatic	C-H bend. Aromatic	C-H bend. Allylic	= CH bend. vinylic
IXb	3570	3195	3120	3040	-	1680	1510	1650	1170	1570, 1350	-	1280	830
Xd	3570	3195	3120	3045	2875	1645	1525	1640	1165	1570, 1340	820, 780	1265	830

Table:(8) M.F., m.ps, Yields% and Elemental Analysis of 1-Amino-2-styryl-3- (p-methylphenyl)-1,2,3-trihydrobenzo[1,2-e][1,3]-diazepine-4,7-dione(IXd).



(IXd)

Comp.	M.F.	Color	m.p(C°)	Yield (%)	Calc.			Found		
					C%	H%	N%	C%	H%	N%
IXd	$C_{24}H_{21}O_2N_3$	Light brown	Over 270	59	75.19	5.48	10.96	75.26	5.83	10.6

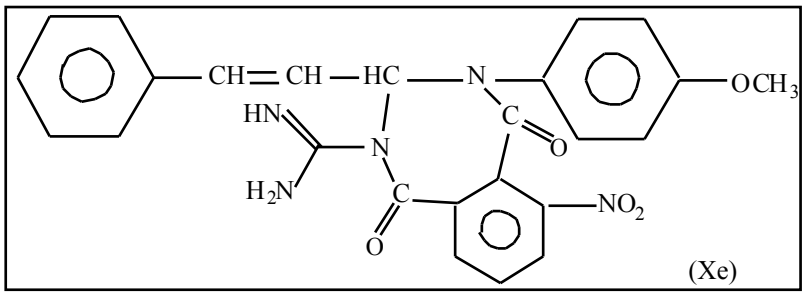
Table:(9) IR absorption bands (cm^{-1}) of 1-Amino-2-styryl -3-(p-methylphenyl)-1,2,3-trihydrobenzo[1,2-e][1,3]-diazepine-4,7-dione(IXd)

Comp.	N-H str.	C-H str. Allylic	= CH str. Vinylic	C-H str. Aromatic	C-H str.	C=O str. Lactam	C=C str. Vinylic	C=C str. Aromatic	C-N str.	N-H bend.	C-H bend. Aromatic	C-H bend. Allylic	= CH bend. vinylic
IXd	3530 Asym. 3420 Sym.	3245	3165	3060	2830	1670	1475	1530	1140	1550	840,750	1345	840

Table :(10) FTIR absorption bands (cm^{-1}) of 1-Amino -2-styryl-3-(p-methylphenyl)-1,2,3-trihydrobenzo-[1,2-e][1,3]-diazepine-4,7-dione(IXd)

Comp.	N-H str.	C-H str. Allylic	= CH str. Vinylic	C-H str. Aromatic	C-H str.	C=O str. Lactam	C=C str. Vinylic	C=C str. Aromatic	C-N str.	N-H bend.	C-H bend. Aromatic	C-H bend. Allylic	= CH bend. vinylic
IXd	3527 Asym. 3398 Sym.	3255	3178	3064	2825	1676	1488	1552	1147	1565	849, 761	1363	835

Table:(11) M.F., m.ps, yields% and Elemental Analysis of 1-Formamidino -2-styryl-3-(p-methoxyphenyl)-1,2,3-trihydro-3-nitrobezno[1,2-e][1,3]-diazepine-4,7-dione(Xe)



(Xe)

Comp.	M.F.	m.p(C°)	Yield (%)	Calc.			Found		
				C%	H %	N%	C%	H %	N%
Xe	$C_{25}H_{21}O_5N_5$	Over 270	62	63.69	4.45	14.86	63.75	4.38	15.24

Table: (12) IR absorption bands (cm^{-1}) of 1-Formamidino -2-styryl-3- (p-methoxyphenyl)-1,2,3- trihydro-3-nitrobenzo [1,2-e][1,3] –diazepine -4,7-dione(Xe).

Comp.	N-H str.	C-H str. Allylic	=CH str. Vinylic	C-H str. Aromati	C-H str. Aliphati	C=O str. Lactam	C=C str. Vinylic	C=C str. Aromati	C-O str. Ether	C-N str.	C-NO_2	N-H bend.	C-H bend.	C-H bend.	C is C-H bend. Vinylic
Xe	3540 ,3400	3175	3150	3050	2880	1720	1480	1630	1135	1150	1570 , 1360	1580	825	1280	835

مجلة ابن الهيثم للعلوم الصرفة والتطبيقية المجلد23 (2) 2010

تحضير 1، 2، 3- ثلاثي التعويض – 1، 2، 3- ثلاثي هيدرو -1، 3- دايازيبين - 4، 7- دايونات (الجزء الثالث).

فهد علي حسين ، مهند جميل محمود، ميسون طارق توفيق
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الخلاصة

تم مفاعلة 3,1- اوكسازيبين ، بنز [e-2,1][3,1] – اوكسازيبين و 3- نتروبنز [e-2,1] [3,1] اوكسازيبين مع مشتقات الامونيا $H2\dot{N}$-Z فأعطت 1، 3- دايازيبين 4,7-دايون ، بنزودايازيبين -7,4- دايون و 3- نتروبنزو -3,1- دايازيبين -7,4- دايون على التوالي.