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Synthesis Of Some New Hydrazones And 1,3-Oxazepine Derivatives Containing Benzimidazole.

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ABSTRACT

Ethyl benimidazole acetate (1) reacted with hydrazine hydrate to give hydrazide (2) . Hydrazones (3-13) were prepared by reaction of hydrazide (2) with a number of various substituted benzaldehyde. 1, 3-Oxazepine (14-24) were prepared by reaction of hydrazones with maleic anhydride .

Keywords: Benzimidazole,1,3-Oxazepine , Hydrazones, Schiff base ,Heterocyclic compounds

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INTRODUCTION

Most of the potent and biologically active medicinal agents contain heterocyclic ring with nitrogen and oxygen as the special element . The present work involves the synthesis of eleven hydrazones and eleven 1,3-oxazepine-4,7-dione from the above hydrazones . The chemical structures of the oxazepinedione derivatives were studied. The newly synthesized compounds 1,3-oxazepine-4,7,dione contains oxazepine as the core nucleus , which is a seven membered heterocyclic compound which contain oxygen and nitrogen as the hetero atom in 1st and 3rd position , were two ketone moiety attached to the4th and 7th position of the ring[1,2] . The intermediate (schiff base) used in this reaction hydrazones which is synthesized by the usual condensation reaction in which an substituted aldehyde with a hydrazide forms an imine , mechanism involve nucleophilic addition to the carbonyl group and elimination of a water molecule . The overall reaction results in replacement of C=O by C=N. Schiff base compounds have been used as fine chemicals and medical substrates. Compared to other derivatives of oxazepine much less studies are so far conducted for oxazepinediones. It includes antimicrobial studies[3] , antitumor activity[4] , anticorrosive studies[5]and anticonvulsant studies[6].

MATERIALS AND METHODS

The melting point were determined in open capillary tubes and are uncorrected . The FT-IR Spectra of some prepared derivatives were taken on a Sidco Biotech FT-IR 600 spectrometer , ^{1}H-NMR and ^{13}C-NMR Spectra of some prepared derivatives were recorded on a Bruker advance 400 MHz spectrometer using tetra methyl silane as internal standard in DMSO-d_6 . Purity of the compounds was checked on TLC using iodinevapor as visualizing agent. some compounds were analyzed for elemental analysis and the percentage of elements were found tobe very near that of the calculated values. The UV-Visible spectra were recorded on Shimadzu UV-210 Double Beam Spectrophotometer .

Synthesis of Ethyl benzimidazole acetate[7](1)

The solution of Benzimidazole (0.06 mole) in acetone (40 ml) was mixed with ethyl chloroacetate (0.07 mole) and potassium carbonate (0.12 mole) and refluxed for (6 hr) , completion of the reaction was monitored by (TLC), The reaction mixture was filtered , from the clear filtrate , excess acetone was removed by distillation and then was added to water . The solid product separated was collected by filtration and dried . further purification was done by crystallization from ethyl acetate . M.P. 88-90 °C , Yield 86% , Colour white . as well as identification of the ester (1) by using chemical detectors , the detection test known as (Ferric hydroxamate) give positive result , which denote's the existence of ester[8] .

Synthesis of Benzimidazole acetic acid hydrazide[7](2)

The solution of ethyl benzimidazole acetate (1) (0.04 mole) in ethanol (25 ml) was mixed with hydrazine hydrate (99%) (0.04 mole) and refluxed for (4 hr) , completion of the reaction was monitored by (TLC) , The excess of solvent was removed by distillation and the contents were added to excess of water . The crude product was purified by recrystallization from ethanol . M.P. 180-181 °C , Yield 90% , colour Grey .

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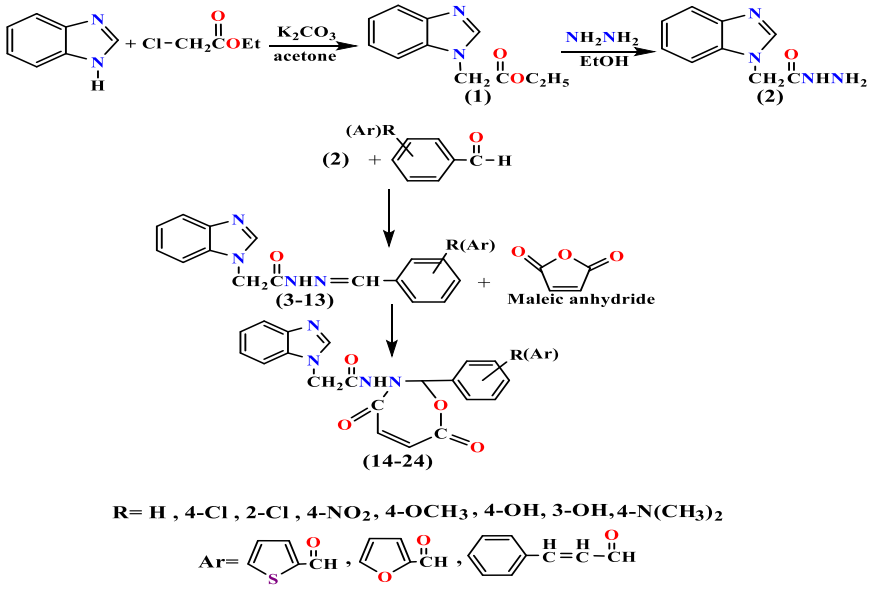
Reaction Scheme I



Synthesis of Hydrazones[9](3-13)

A mixture of hydrazide (2) (1.9 gm , 0.01 mole) in (50ml) ethanol , and substituted aldehyde (0.01 mole) in (25ml) ethanol was added . the reaction mixture was heated under reflux for (2) hours . the reaction was followed by thin layer chromatography (TLC) , the reaction mixture was allowed to cool . The precipitate was filtered and recrystallized from ethanol , to give the hydrazones (3-10) . Some physical and spectral data indicated in tables (1,3).

Synthesis of 1,3-oxazepine-4,7-dione[10](14-24)

A mixture of hydrazone derivatives (0.002 mole) in (30ml) ethanol and maleic anhydride (0.01 mole) , were refluxed for (4) hours, there action was followed by thin layer chromatography (TLC) , the solvent was evaporated , The solid obtained was washed with cold methanol , and precipitate was recrystallized from dioxane, giving the required products . The physical and spectral data were listed intable (2,4).

Anal. Calcd. for(23)$C_{24}H_{18}N_4O_5$:C,59.02;H,3.85;N, 15.29. Found: C, 58.88;H,3.92;N,15.34% .

RESULTS AND DISCUSSION

The hydrazides (2) were obtained from refluxing ester (1) with 99% hydrazine hydrate in absolute ethanol . These hydrazide was identified by IR which exhibits characteristic peak at(1650 cm^{-1}) (C=O amide) , this is the frequency at hydrazide it is falling at lower frequency [11] , because of existence the resonas in the hydrazide , accordingly minimize the constant power shows absorption bands at (3392cm^{-1}) (NH) , (3015cm^{-1}) (C-H aromatic) , (1586cm^{-1}) (C=N) . The ultraviolet spectrum gave the highest absorption at (nm 322)λ_{max} .

Hydrazones (3-10) were prepared by reaction of the Benzimidazole acetic acid hydrazide (2) and different substituted aldehyde . The structure of hydrazones were elucidated from spectra evidence , peak at (1652-1685cm^{-1}) for the carbonyl group, also the peak at (1585-1644 cm^{-1}) for C=N.In addition to that the stretching banding at (3305-3412 cm^{-1}) is assigned for N-H. The spectral data shows at table (3).

Refluxing hydrazones (3-10) with maleic anhydride will produce oxazepine-4,7-dione derivatives (14-24) and their structure was confirmed by spectroscopic data . IR shows the carbonyl (O-C=O) at (1681-1726cm^{-1}) and carbonyl (N-C=O) at (1655-1688cm^{-1}) and carbonyl amide at (1640-1662cm^{-1}) other absorption bands shows in table (4) . The ^{1}HNMR and ^{13}C-NMR spectrum for compound (23) showed results that confirm our expectation as mention in table (5) .

ISSN: 0975-8585

Mechanism for compounds (14-24)

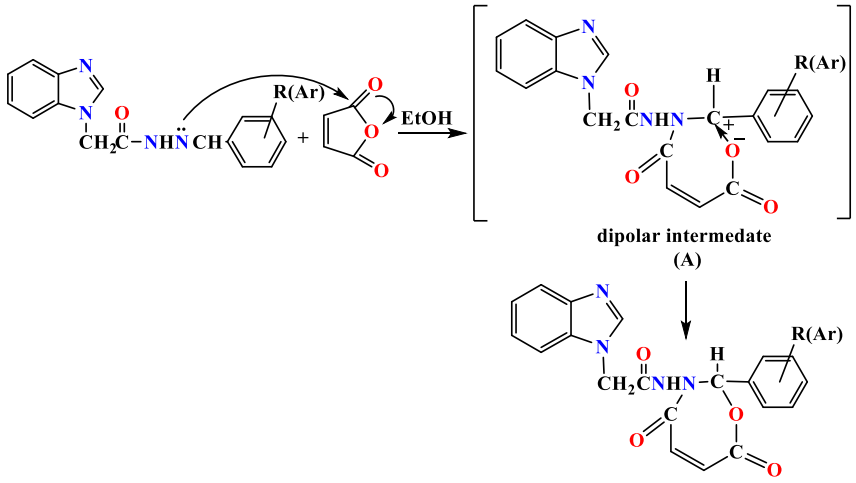


Table (1): Some physical constant for compounds (3-13)

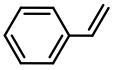
Comp. No.	R(Ar)	Molecular formula	m.p. (°C)	Yield (%)	Colour
3	H	$C_{16}H_{14}N_4O$	190-192	75	Gray
4	4-Cl	$C_{16}H_{13}ClN_4O$	114-115	66	Purple
5	2-Cl	$C_{16}H_{13}ClN_4O$	139-140	54	Brouwn
6	4-NO_2	$C_{16}H_{13}N_5O_3$	127-128	87	Yellow
7	4-OCH_3	$C_{17}H_{16}N_4O_2$	173-174	60	White
8	4-OH	$C_{16}H_{15}N_5O_2$	158-160	81	Gray
9	3-OH	$C_{16}H_{14}N_4O_2$	160-161	89	Gray
10	4-$N(CH_3)_2$	$C_{18}H_{19}N_5O$	105-107	85	Orange
11		$C_{14}H_{12}N_4OS$	144-145	70	Brouwn
12		$C_{14}H_{12}N_4O_2$	159	76	Brouwn
13		$C_{18}H_{16}N_4O$	87-88	62	Yellow

Table (2): Some physical constant for compound (14-24)

Comp. No.	R(Ar)	Molecular formula	m.p. (°C)	Yield (%)	Colour
14	H	$C_{20}H_{16}N_4O_4$	275-276	70	White
15	4-Cl	$C_{20}H_{15}ClN_4O_4$	255-258	72	Yellow
16	2-Cl	$C_{20}H_{15}ClN_4O_4$	168-170	69	Yellow
17	4-NO_2	$C_{20}H_{15}N_5O_6$	90-92	78	Pale Yellow
18	4-OCH_3	$C_{21}H_{18}N_4O_5$	225-226	81	White
19	4-OH	$C_{20}H_{16}N_4O_5$	181-182	86	Purple
20	3-OH	$C_{20}H_{16}N_4O_5$	229-231	63	Purple
21	4-$N(CH_3)_2$	$C_{22}H_{21}N_5O_4$	147-149	58	Yellow
22		$C_{24}H_{18}N_4O_4S$	280-282	55	Yellow

ISSN: 0975-8585

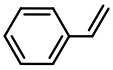
23		$C_{24}H_{18}N_4O_5$	269-270	61	Yellow
24		$C_{21}H_{18}N_4O_4$	110-112	73	White

Table (3): Spectral data for hydrazones (3-13)

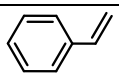
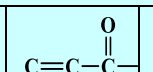
Comp. No.	R(Ar)	IR ? cm^{-1} (KBr)				UV (EtOH) ?max (nm)
		N-H	C=O	C=N	Others	
3	H	3412	1661	1585	-	315
4	4-Cl	3310	1672	1615	749 (C-Cl)	320
5	2-Cl	3365	1684	1617	744 (C-Cl)	323
6	4-NO_2	3305	1675	1593	as. 1340 (C-NO_2) sy. 1108 (C-NO_2)	344
7	4-OCH_3	3351	1666	1608	as. 1265(C-O-C) sy.1104(C-O-C)	314
8	4-OH	3311	1652	1620	3196 (OH)	319
9	3-OH	3401	1660	1605	3187 (OH)	320
10	4-$N(CH_3)_2$	3395	1671	1610	-	340
11		3299	1685	1601	741 (C-S-C)	346
12		3401	1682	1599	as. 1275(C-O-C) sy.1132(C-O-C)	342
13		3372	1677	1644	-	356

Table (4): Spectral data for1,3-oxazepine-4,7-dione (14-24)

Comp. No.	R(Ar)	IR ? cm^{-1} (KBr)								UV (EtOH) ?max (nm)
				C=O amide	C-N	C-O-C		Ar C⋯C	Others	
14	H	1681	1665	1641	1270	Sy 1151 As 1250	1519	1475	-	305
15	4-Cl	1710	1674	1662	1278	Sy 1164 As 1216	1590	1445	771 (C-Cl)	315
16	2-Cl	1690	1655	1645	1261	Sy 1143 As 1286	1561	1459	748 (C-Cl)	313
17	4-NO_2	1726	1668	1642	1228	Sy 1175 As 1269	1522	1456	1391Sy(C-NO_2) 1504As(C-NO_2)	296
18	4-OCH_3	1701	1688	1658	1275	Sy 1144 As 1224	1535	1450	-	316

ISSN: 0975-8585

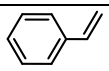
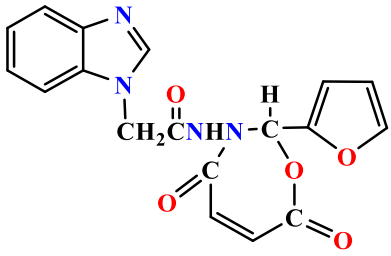
19	4-OH	1698	1674	1649	1265	Sy 1139 As 1277	1541	1465	3319 (OH)	294
20	3-OH	1691	1670	1648	1268	Sy 1185 As 1239	1555	1436	3364 (OH)	299
21	4-N(CH_3)$_2$	1688	1668	1650	1272	Sy 1145 As 1299	1569	1430	-	310
22		1704	1686	1646	1231	Sy 1191 As 1264	1571	1441	667 (C-S-C)	319
23		1696	1677	1652	1244	Sy 1122 As 1274	1575	1462	-	314
24		1699	1682	1640	1261	Sy 1180 As 1215	1556	1429	-	304

Table (5): ^{1}H-NMR and^{13}C-NMR spectrum data for compound(23)

Comp. No.	Structure compound	^{1}H-NMR (ppm)	^{13}C-NMR (ppm)
23		2.49 (DMSO) 3.78 (N-C**H**$_2$) 6.66-7.07 (**H**, Benzimidazole) 6.51-6.55 (C**H**=C**H**) for Oxazepine 10.52 (N**H**) 8.00 (N-C**H**)	39.54 (DMSO) 58.13 (**C**H$_2$) 99.72 (N-**C**H) 156.22 (O-**C**=O) 153.16 (N-**C**=O) 125.89-125.95 (**C**H=**C**H) 152.74,152.68,126.14, 108.86(4**C**-Furane) 128.41-144.52 (**C**-Benzimidazole)

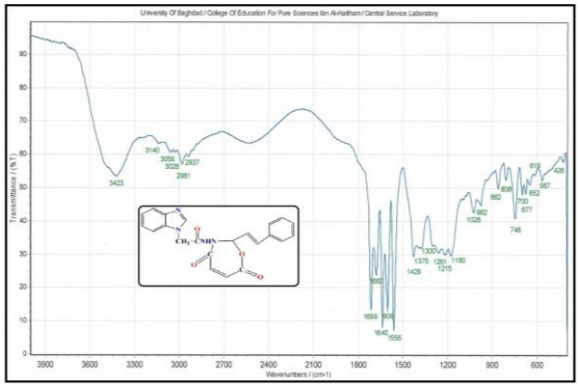
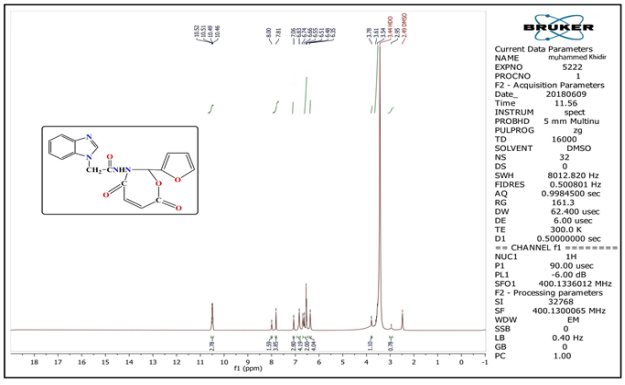


Fig 1: IR spectrum of compound (24)



ISSN: 0975-8585

Fig 2: ^{1}HNMR spectrum of compound (23)

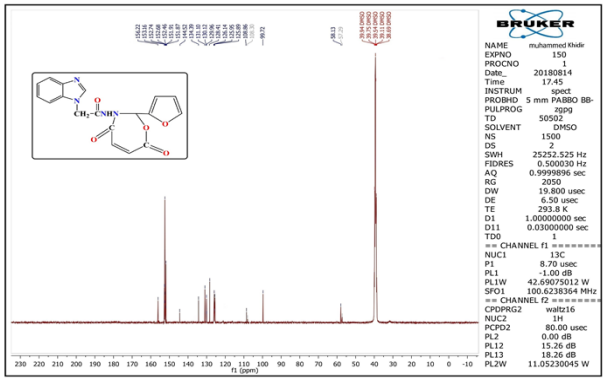


Fig 3: ^{13}CNMR spectrum of compound (23)

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