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SYNTHESIS AND CHARACTERIZATION OF NOVEL 1,3-OXAZEPANE DERIVATIVES VIA REACTION OF PHENYI SUCCINIC ANHYDRIDE WITH SCHHIF'S BASES

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ABSTRACT

Novel 1,3-oxazepane-4,7-dione derivatives were synthesized by the reaction of phenyl succinic anhydride with Schiff‘s bases in anhydrous benzen with high yields. Schiff's bases were synthesized by the reaction of heteroaromatic aldehydes or ketones with primary heterocyclic amines. The resulting products were identified by their melting point and their molecular structures were confirmed by FT-IR , UV-Vis. and ^{1}HNMR spectroscopy.

Introduction

Schiff's bases are used as substrates in the preparation of a large of bioactive and industrial compounds via ring closure,cyclo addition and replacement reactions . In addition , Schiff bases are well known to have biological activities (1-3) . "Oxazepine" refers to any seven-membered ring Containing an oxygen and nitrogen atom . The 1,3-Oxazepine is a branch of many types of the heterocyclic oxazepine (4–10). The core structure of 1,3-Oxazepane-4,7diones consists of a seven-membered ring along with two carbonyl group. Over the years, the syntheses of oxazepine derivatives have been investigated and documented (11-16). Oxazepines is used as antibiotics ,enzyme inhibitors pharmacological interst,it has much chemical and biological studied (17-19).

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Experimental:-

All solvents were distilled and dried on anhydrous $CaCl_2$ immediately prior to use, and all non-aqueous Reaction were conducted in dried glass ware , the Reflux condenser was equipped with anhydrous $CaCl_2$ guard tube. Schiff's bases and phenyl succinic anhydride were purified before use. Melting points were recorded on Electro thermal Melting Point (Stuart) mode l samp 30 . All FT-IR spectra were recorded at room temperature from 4000cm^{-1} to 400cm^{-1} with KBr disce on Shimadzu FT-IR 84005 spectrophotometer and UV-Vis. spectra were recorded at room temperature from 200 nm to 400 nm in absolute ethanol on Shimadzu Double-Beam Spectrophotometer UV-210A . The^{1}H-NMR spectra were recorded on Bruker 500 MHz -Avance III spectrometer in DMSO-d6 as a solvent using δ(ppm) for chemical shift relative to tetra methyl saline (TMS) as an internal standard.

General procedure for synthesis of Schiff's bases (A_{1-10}).

A mixture of 4-Aminoantipyrine (0.001mol) and4-Chlorobenzaldehyde (0.001mol) and trace of glacial acetic acid in absolute ethanol (50ml) was

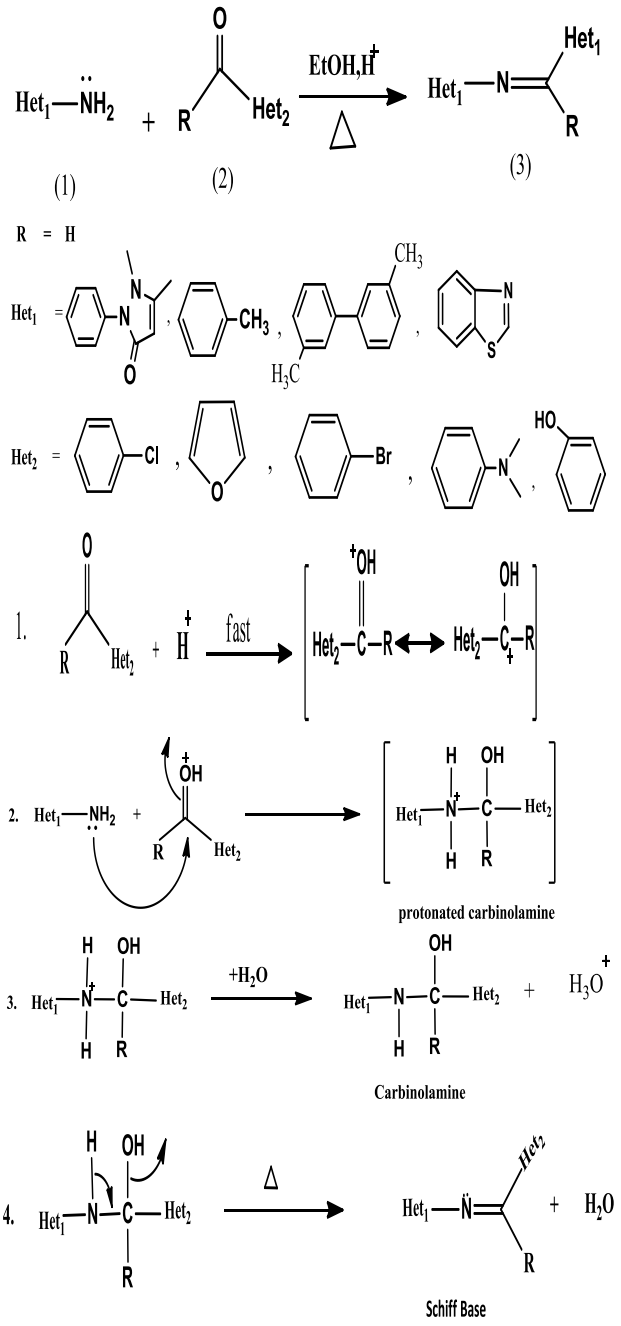
placed in a(100ml) round-bottom flask equipped with condenser and stir bar. The mixture was allowed to react at reflux temperature for 4hr, then allowed to cool down to room temperature , where by a crystalline solid of Schiff's base (A_1) separated Out . The solid product was recrystallized twice from ethanol . Other Schiff's bases(A_{2-10}) were synthesized by following the same Procedure .The structural formulas, names, melting points ,colures ,and percentage yields for the synthesized Schiff's bases are given in (table6).

General procedure for synthesis of 1,3-Oxazepane- 4,7-dione (B_1-B_{10}).

In well dried 100-ml round-bottom flask equipped with condenser and anhydrous calcium chloride tube guard a mixture of Schiff's base s (0.002mol) and phenyl succinic anhydride (0.002mol) dissolved in (30ml) of anhydrous benzene ,the reaction mixture was refluxed for (5hr) and left to stand for (24hr) , then solid product of (B_1) precipitated. The solid product was filtered off and recrystallized form ethanol . Other derivatives (B_{2-10}) were synthesized following the same procedure . The structural formulas , names , melting points, colures, and percentage yields for the synthesized1,3-Oxazepane- 4,7-dione are given in (table7) .

Results and Discussion

In this work the synthesis of novel 1,3-Oxazepane - 4,7- dione by direct reaction of Schiff's bases with phenyl succinic anhydride in anhydrous benzene is reported . Schiff's bases were synthesized from the condensation reaction of commercially available heterocyclic aldehydes or ketones with primary heterocyclic amines of very well known mechanism (20).

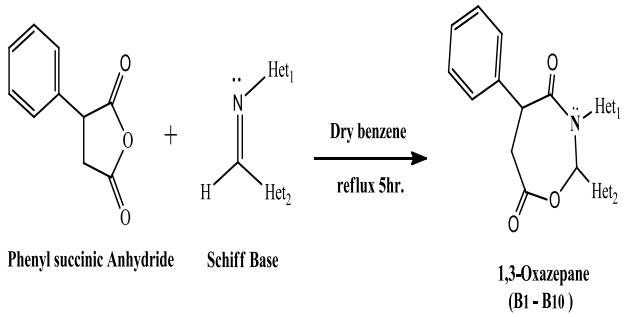


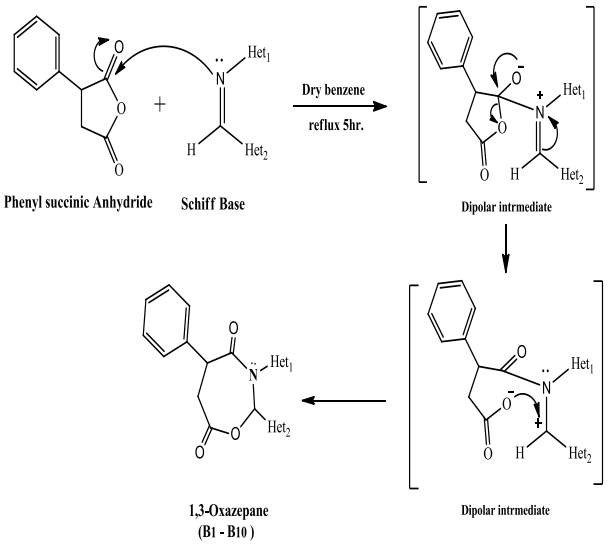
They were identified by their melting points and their molecular structures were confirmed by FT-IR , UV-Vis. spectroscopy, tables,(1), (3) &(6).

Formation of the Schiff's bases products were followed up by the disappearance of both (C=O) absorption bands at (1660-1700)cm^{-1} and (-NH_2) absorption bands at (3340-3420cm^{-1}) in the FT-IR spectra of the carbonyl compounds and the primary amines respectively, and the appearance of the absorption frequency of azomethene group (C=N) at

(1630-1680) cm^{-1} in the FT-IR spectra of the resulting imines. The UV-Vis. Spectra of these imines show absorption maxima at (202- 430 nm) owing to the electronic transfer $\pi \rightarrow \pi*$ and $n \rightarrow \pi*$ characteristic of the structures of the synthesized Schiff's bases.

The synthesis of novel 1,3-Oxazepane-4,7-dione were achieved by the polar cycloaddition reaction of imines to phenyl succinic anhydride fairly anhydrous benzene at reflux condition.





It may be concluded that the reaction takes place via concerted dipolar cycloaddition mechanism as in the following reaction scheme:

In the slow step of this mechanism ,the nucleophilic azomethine group attacks the electrophilic carbon atom of the carbonyl group of the anhydride associated to give dipolar reactive intermediate. Collapse of the reactive intermediate in an intramolcular cycloaddition in a fast step gives the target molecule.

The resulting products were identified by their melting points and their molecular structures were confirmed by FT-IR, UV-Vis. and ^{1}HNMR spectroscopy, tables,(2),(4),(5) &(7).

The FT-IR spectra of the products show characteristic absorption band at (1608-1724cm^{-1}) indicative of C=O group formation of (lactam/lactone) beside the characteristic bands of the residual groups in the structure, table,(4).

The UV-Vis. spectra show absorption maxima at (212-445nm) owing to the electronic transfers $\pi \rightarrow \pi*$ and $n \rightarrow \pi*$ characteristic of the structure of the synthesized1,3-Oxazepane-4,7-dione, table,(2).

Table(1):The UV-Visible absorption λ max(nm) in ethanol of Schiff's bases(A_{1-10})

Comp.	λ max (nm)			
A_1	222	250	352	__
A_2	223	260	382	__
A_3	220	264	340	__
A_4	227	256	308	__
A_5	205	252	342	430
A_6	215	248	322	___
A_7	215	252	__	__
A_8	228	260	310	405
A_9	220	265	307	__
A_{10}	202	260	305	335

Table 2:The UV-Visible absorption of λ max in ethanol of 1,3-Oxazepane- 4,7- dione (B1-10).

Comp.	λ max (nm)			
B_1	235	250	340	__
B_2	220	274	370	__

B_3	**225**	**265**	**330**	**__**
B_4	**230**	**258**	**300**	**__**
B_5	**215**	**250**	**334**	**445**
B_6	**213**	**240**	**314**	**___**
B_7	**220**	**255**	**__**	**__**
B_8	**222**	**270**	**305**	**415**
B_9	**230**	**265**	**310**	**375**
B_{10}	**212**	**265**	**300**	**__**

Table 3:The major FT-IR absorptions (cm-1) of the prepared Imines(A1-10).

Comp.Code	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10
N-C-H	3110	3159	3098	3124	3181	3105	3088	3170	3135	3110
υs C-H Aromatic	3055	3071	3076	3073	3087	3091	3035	3043	3095	3086
υ_s C-H Aliphatic	2920	2937	2916	2896	-	2953	2922	2925	2943	2975
υ_s C=O Lactam	1647	---	-	1655	-	-	-	1647	-	-
υ_s C=N Imine	1593	1598	1587	1632	1652	1577	1578	1598	1651	1581
υ_s C=C Aromatic	1485	1496	1475	1567	1573	1485	1499	1485	1476	1542
υ_s C-N	1168	1210	1229	1178	1123	1178	1182	1211	1262	1180
δ C-H bending in-plane	1342	1342	1345	1326	1340	1326	1335	1320	1327	1315
δ C-H out of-plane	874	854	822	881	943	836	839	935	833	814
Others	C-CI 779	C-CI 741	C-O 1212	C-O 1190	C-Br 598 C-S 1202	C-Br 575	-----	C-Br 572	O-H 3326	C-CI 766

Table 4:The majer FT-IR absorptions (cm^{-1}) of the prepared 1,3-Oxazepane- 4,7-dione (B_{1-10})

Comp. Code	B_1	B_2	B_3	B_4	B_5	B_6	B_7	B_8	B_9	B_{10}
υs C-H Aromatic	3059	3055	3112	3047	3032	3062	3032	3045	3059	3045
υ_s C-H Aliphatic	2989	2920	2991	2958	2982	2975	2916	2933	2974	2934
υ_s C=O Lactone	1724	1724	1712	1716	1707	1713	1712	1681	1712	1716
υ_s C=O Lactam	1647	1651	1608	1647	1677	1683	1654	1612	1647	1625
υ_s C=C Aromatic	1593	1570	1589	1546	1560	1504	1512	1516	1540	1552
υ_s C-N	1165	1166	1284	1265	1255	1280	1269	1253	1211	1217
δ_w C-O	1215	1211	1273	1207	1232	1215	1234	1192	1168	1147
δ C-H bending in-plane	1300	1342	1303	1330	1355	1351	1330	1300	1303	1327
δ C-H out of-plane	875	875	879	829	879	813	887	894	875	1002
Others	C-CI 767	C-CI 748	---	---	C-S 1207 C-Br 578	C-Br 568	---_	C-Br 563	O-H 3425	C-CI 769

Table5.The1HNMR spectra of compounds (B1-10) in DMSO-d6 relative to TMS.

Comp.	Chemical Shift δ ppm
B_1	**3.01(3H,N-CH_3), 2.23 (3H,=C-CH_3), 2.51(2H, CH_2-CO), 3.58(1H, Ring-CH) , 7.38-7.85(14H,Ar.).**
B_2	**2.47 (3H,=C-CH_3), 3.32(2H, CH_2-CO), 3.58(1H, Ring-CH) ,7.37-7.78(13H,Ar.).**
B_3	**2.15 (6H, C-CH_3), 7.23-8.12(18H,Arom,), 6.41(4H,=CH) 2.52(4H,CH_2-CO) ,3.78(2H, Ring-CH),7.42(2H,CH. Het.),**
B_4	**3.21(3H,N-CH_3), 2.63(3H,=C-CH_3),2.81(2H, CH_2-CO), ,3.87(1H, Ring-CH) 6.52-7.92(13H,Ar.).**
B_5	**7.12-8.63 (13H,Ar.), 2.61(2H, CH_2-**

	CO),3.28(1H, Ring-CH)
B_6	**3.11(2H, CH_2-CO) , 3.92(1H, Ring-CH),6.98-7.82 (14H,Ar.).**
B_7	**2.43(3H,C-CH_3),3.11(6H,N-CH_3), 3.93 (1H, Ring-CH), 2.61(2H, CH_2-CO),6.62-7.81 (13H,Ar.)**
B_8	**3.21(3H,N-CH_3), 2.33 (3H,=C-CH_3), 2.84(2H, CH_2-CO), 3.65(1H, Ring-CH) , 6.78-7.82(14H,Ar.).**
B_9	**6.72-7.68 (13H,Arom.), 2.22(3H,C-CH_3), 2.94(2H, CH_2-CO), 3.55(1H, Ring-CH) , 5.49 (1H, -OH),**
B_{10}	**2.25 (6H, C-CH_3),3.24 (4H, CH_2-CO),3.85(1H, Ring-CH), 7.13-7.65 (24H,Arom.).**

Table 6 .Structural formulas ,names ,melting points, coloures ,and % yields of Schiff's bases (A1-10).

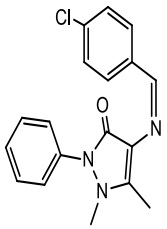
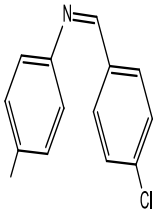
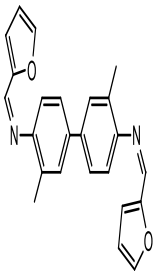
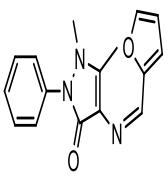
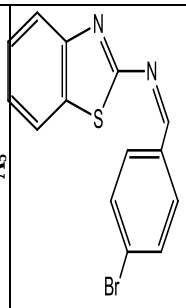
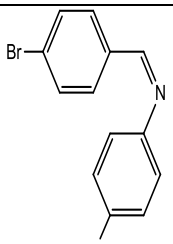
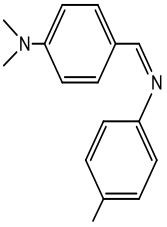
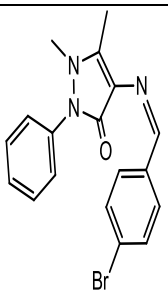
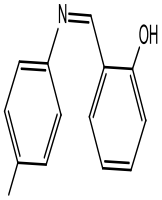
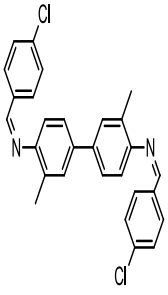
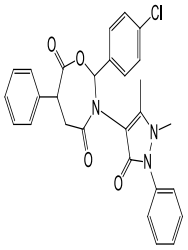
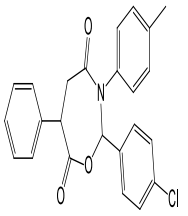
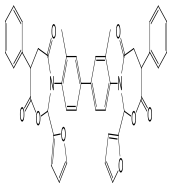
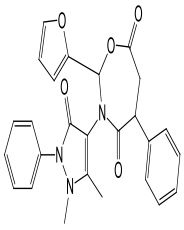
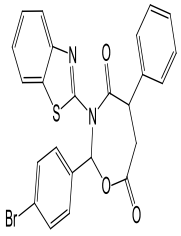
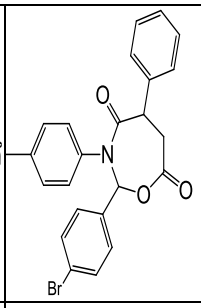
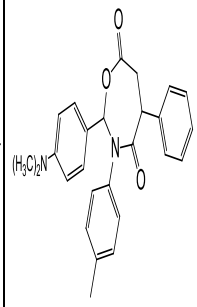
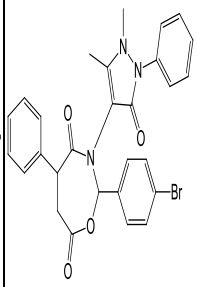
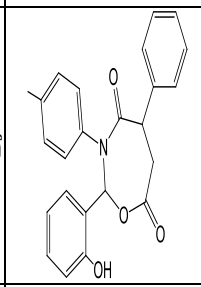
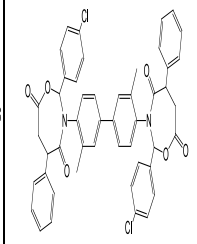
Comp. No.	Structural formula	Name	Yield %	m.p. °C	Colour
A_1		**4-(4-chlorobenzylidene amino)-1,5-dimethyl-2-phenyl-1*H* -pyrazol-3(2*H*)-one**	**82**	**250-253**	**Pale yellow**
A_2		***N*-(4-chlorobenzylidene)-4-methylaniline**	**93**	**124-127**	**White**
A_3		**(N^4E)-N^4,$N^{4'}$ -bis(furan-2-ylmethylene)-3,3'-dimethylbiphenyl-4,4'-diamine**	**66**	**187 -189**	**Green Light**
A_4		**4-(furan-2-ylmethylene amino)-1,5-dimethyl-2-phenyl-1*H* -pyrazol-3(2*H*)- one**	**91**	**212 -213**	**yellow**
A_5		***N*-(4-bromo benzylidene)benzo[*d*] thiazol-2-amine**	**88**	**111 -113**	**White Light**
A_6		***N*-(4-bromo benzylidene)-4-methyl aniline**	**92**	**140 -142**	**Pale yellow**
A_7		***N*,*N*-dimethyl-4-((*p*-tolylimino) methyl) aniline**	**85**	**96 -98**	**Pale Yellow**
A_8		**4-(4-bromobenzylidene amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one**	**85**	**253 -254**	**yellow**
A_9		**2-((*p*-tolylimino)methyl) phenol**	**87**	**95 -96**	**Dark yellow**
A_{10}		**(N^4E)-N^4,$N^{4'}$-bis(4-chlorobenzylidene)-3,3'-dimethylbiphenyl-4,4'-diamine**	**91**	**157 -159**	**Green**

Table7.Structural formulas ,names ,melting points ,colures ,and % yields of 1,3-Oxazepane-4,7-dione (B1-10).

Comp No.	Structural formula	Name	Yield%	m.p.°C	Color
B_1		2-(4chlorophenyl)-3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-6-phenyl-1,3-oxazepane-4,7-dione	70	245-247	White
B_2		2-(4-chlorophenyl)-6-phenyl-3-(p-tolyl)-1,3-oxazepane-4,7-dione	45	250 -252	Pale yellow
B_3		3,3' - (3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(2-(furan-2-yl)-6-phenyl-1,3-oxazepane-4,7-dione)	55	240 -241	Brown
B_4		3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-(furan-2-yl)-5-phenyl-1,3-oxazepane-4,7-dione	49	187 - 190	Brown
B_5		3-(benzo[d]thiazol-2-yl)-2-(4-bromophenyl)-5-phenyl-1,3-oxazepane-4,7-dione	65	190 - 193	White

Comp No.	Structural formula	Name	Yield%	m.p.°C	Color
B_6		2-(4-bromophenyl)-5-phenyl-3-(p-tolyl)-1,3-oxazepane-4,7-dione	72	277 - 280	White
B_7		2-(4-(dimethylamino)phenyl)-5-phenyl-3-(p-tolyl)-1,3-oxazepane-4,7-dione	80	231 - 233	Orange
B_8		2-(4-bromophenyl)-3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-5-phenyl-1,3-oxazepane-4,7-dione	77	245 -248	Yellow
B_9		2-(2-hydroxyphenyl)-5-phenyl-3-(p-tolyl)-1,3-oxazepane-4,7-dione	72	89 -91	Yellow
B_{10}		3,3'-(3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(2-(4-chlorophenyl) -5-phenyl-1,3-oxazepane-4,7-dione)	65	117 - 120	Light Green

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تحضير وتشخيص مشتقات 3,1–أوكسازبان جديدة من تفاعل فنيل سكسنيك انهدريد مع قواعد شف.

عبيد حسن عبد ا.ف. نصار

الخلاصة:

حُضرت مشتقات 3,1–اوكسازبان جديدة من تفاعل فنيل سكسنيك انهدريد مع قواعد شف في البنزين الجاف بمنتوج عالي. حُضرت قواعد شف من تفاعل الديهيدات او كيتونات حلقية غير متجانسة مع امينات اولية حلقية غير متجانسة.FT.IR. و V-Vis و, H1NMR. شخصت النواتج بواسطة درجات الانصهار واثبتت ذلك أطياف.