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RESEARCH ARTICLE

Preparation and Characterization of Novel disubstituted 1,3- Oxazepine-tetra-one from Schiff bases reaction with 3-methylfuran-2,5-dione and 3-Phenyldihydrofuran-2,5-dione

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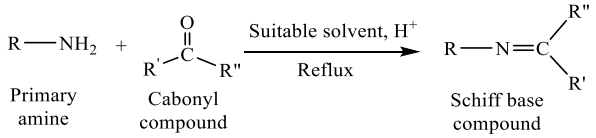
ABSTRACT:
This research includes synthesis of new heterocyclic derivatives of novel disubstituted 1,3- oxazepine-tetra-one from Schiff bases reaction with 3-methylfuran-2,5-dione and 3-phenyldihydrofuran-2,5-dione. Schiff bases [A_1-A_5] were synthesized by the reaction of aromatic aldehydes with primary aromatic amines, in the presence of glacial acetic acid as catalyst in absolute ethanol. The novel derivatives[A_6-A_{10}] were obtained from treatment of Schiff bases with anhydrides. The synthesized compounds were identified by TLC and via spectral methods, their (FT-IR, ^{1}H-NMR and ^{13}C-NMR) and measurements of some of its physical properties.

KEYWORDS: ^{1}H-NMR, ^{13}C-NMR, TLC, Schiff bases, oxazepine-tetra-one.

INTRODUCTION:
Schiff basesare class of the compounds which contain the group (-HC=N-) (**Scheme 1**), Schiff bases are synthesizing by the reaction between primary aromatic amine with aromatic aldehyde[1-3]. These compoundswere classified as a class of organic compounds and these compounds contain a group known as imine(azomethine) of the formula (R-C=N),[2-6] see (scheme 1).



Scheme 1. Structure of Schiff bases

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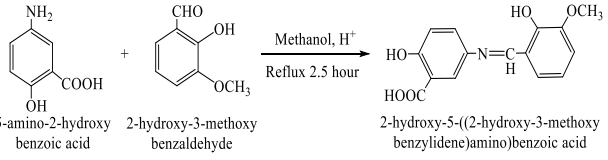
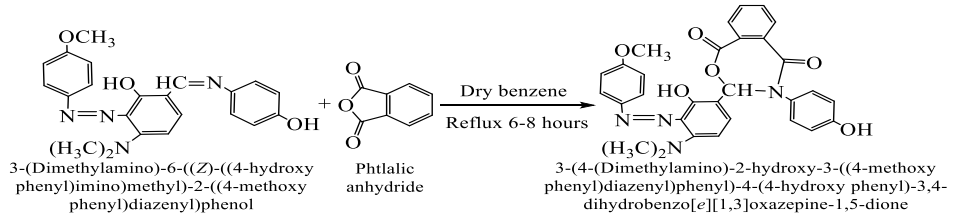
The compound 5-aminosalicylic acid was dissolved in methanol with 2-hydroxy-3-methoxybenzaldehyde the two refluxed to prepared the 2-hydroxy-5-((2-hydroxy-3-methoxybenzylidene) amino) benzoic acid[7,8], see (**Scheme 2**).



Scheme 2. Uses of methanolin Schiff base formation:

Oxazepine is unsaturated seven membered heterocycle containing oxygen in position 1 and nitrogenin position 3 in addition to the five carbon atoms. It is prepared by the pericycliccyclo addition of schiff bases with maleic, phthalic, nitrophthalic and succinic anhydrides[9,10]. The reaction of 3-(dimethylamino)-6-((Z)-((4-hydroxyphenyl) imino) methyl)-2-((4-methoxy phenyl) diazenyl) phenol with Phthalic anhydride (**Scheme 3**) produces the following oxazepine derivative[11].



Scheme 3. Using dry benzene to prepare the oxazepine derivative

MATERIALS AND METHODS:

General procedure for synthesis of Schiff bases[12-14]:

Equimolar mixtures 0.01mole aromatic amines and 0.01 mole aromatic aldehydes presence trace of glacial acetic acid dissolved in 25 ml absolute ethanol was placed in a 100-ml round-bottom flask equipped with condenser and stirrer bar. The mixture was allowed to react at reflux temperature for 4hours, then allowed to cool down to the room temperature, the progress of the reaction and the purity of the compounds were monitored with TLC technique, whereby a crystalline solid was separated out. The solid product was recrystallized twice from ethanol. The structural formulae, names, melting points, colors, and percentage of yields for the synthesized Schiff bases are recorded in table1.

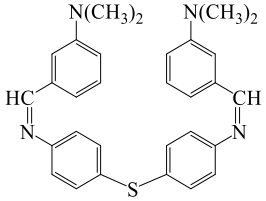
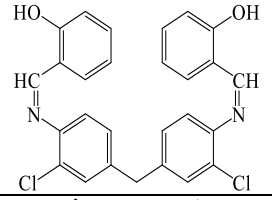
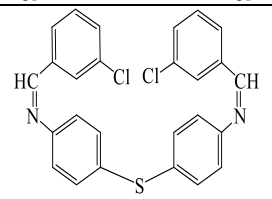
General procedure for synthesis of disubstituted 1,3-oxazepine-tetra-one derivatives[15-17]:

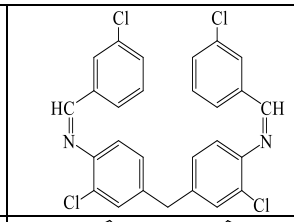
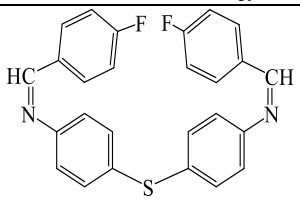
A mixture of synthesized Schiff base 0.001 mole with 0.002 mole of anhydride respectively in 25 ml of dry benzene, was refluxed for 3 hours, the progress of the reaction and the purity of the compounds were monitored with TLC technique[18,19], then, recrystallization was done with absolute ethanol. Table 2 shows the physical properties of the prepared compounds.

RESULTS AND DISCUSSION:

Tables 1 and 2 exhibited structural formula, nomenclature, the percentage of yield, melting point and the color of all prepared compounds. The best yield of the synthesized Schiff bases was for compound $A_1$85%, while the lower yield was for compound A_3 73% and the best yield of the synthesized disubstituted1,3- oxazepine-tetra-one derivatives was for $A_7$90% while the lower yield was for A_{10}75%. The higher melting point for azomethine compounds was for compound A_1 (220-222^{O}C), the lower melting point was for compound A_3 (99-100^{O}C), while the higher melting point of the synthesized disubstituted 1,3- oxazepine-tetra-one derivatives was for compound A_7 (205-207 ^{O}C), the lower melting point was for compound A_9 (79-80 ^{O}C). The different colors, melting points and the number with distance of spots in the TLC technique to the products comparisonwith the raw material are initial evidence of interaction.

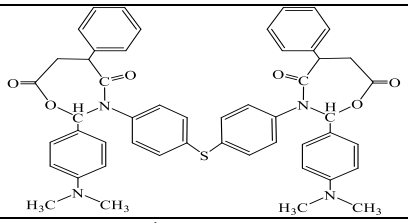
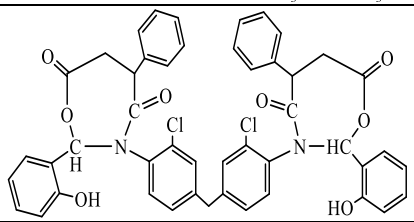
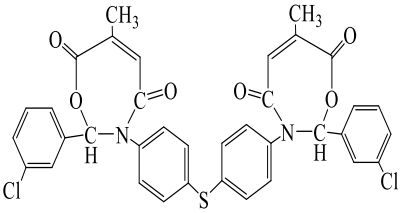
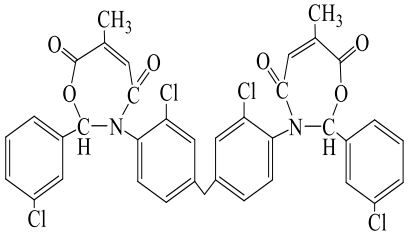
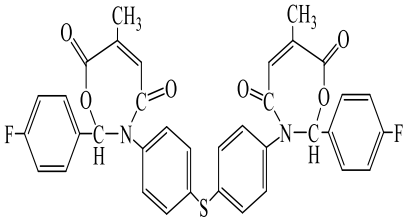
Table 1. Structural formulae, nomenclature, melting points, colors and percentages of yield of synthesized Schiff bases

Comp. Code	Structural formula	Nomenclature	Yield %	m. p.[a] °C	Color
A_1		4,4'-(((thiobis(4,1-phenylene) bis (azanylylidene) bis (methanylylidene) bis (N,N-dimethylaniline)	85	220-222	Dark Yellow
A_2		2,2'-((1Z,1'Z)-((methylenebis(2-chloro-4,1-phenyl ene))bis (azanylylidene)) bis(methanylylidene))diphenol	78	200-202	Yellow
A_3		N,N'-(thiobis(4,1-phenyle ne))bis(1-(3-chlorophenyl) methanimine)	73	99-100	Pale green

A_4		(1Z,1'Z)-N, N'-(methylene bis(2-chloro-4,1-phenyle ne))bis(1-(3-chlorophenyl) methanimine)	77	110-112	Dark Yellow
A_5		N,N'-(thiobis(4,1-phenyle ne))bis(1-(4-fluorophenyl) methanimine)	82	186-188	Silver

[a]Melting point (Celsius).

Table 2. Structural formulae, nomenclature, melting points, colors and percentages of yield of disubstituted 1,3- oxazepine-tetra-one derivatives

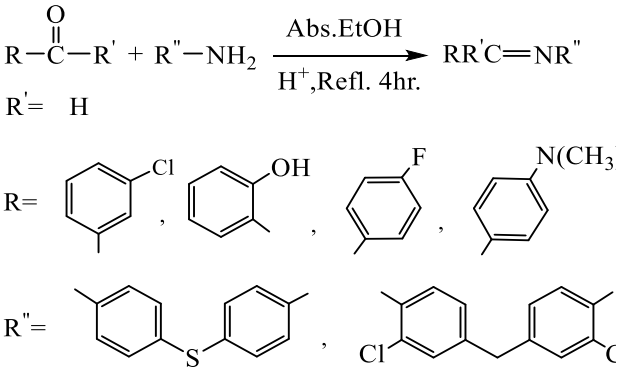
Comp. Code	Structural formula	Nomenclature	Yield %	m. p.[a] °C	Color
A_6		3,3'-(thiobis(4,1-phenylene))bis(2-(4-(dimethylamino)phenyl)-5-phenyl-1,3-oxazepane-4,7-dione)	85	120-122	Yellow
A_7		3,3'-(methylenebis(2-chloro-4,1-phenylene))bis(2-(2-hydroxyphenyl)-5-phenyl-1,3-oxazepane-4,7-dione)	90	205-207	Light Yellow
A_8		3,3'-(thiobis(4,1-phenylene))bis(2-(3-chlorophenyl)-6-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione)	88	132-133	Orange
A_9		3,3'-(methylenebis(2-chloro-4,1-phenylene))bis(2-(3-chlorophenyl)-6-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione)	80	79-80	Off White
A_{10}		3,3'-(thiobis(4,1-phenylene))bis(2-(4-fluorophenyl)-6-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione)	75	143-145	White

[a]Melting point (Celsius)

Synthesized Schiff bases:

Schiff bases were synthesized from commercially available aromatic aldehydes and primary aromatic amines. Thin layer chromatography were used to follow the chemical reaction[20], the synthesized azomethine identified by their melting points and Fourer transfer infra red spectra FT-IR.

The FT-IR spectra showed the appearance of the stretching absorption bands of azomethine group C=N at (1697-1664)cm^{-1} indicative of the formation of the resulting azomethine compounds and the stretching absorption bands of C-N group at(1193-1160) cm^{-1}, C-S group at (700-680) cm^{-1}, C-Cl group at (700-680cm^{-1} beside the characteristic bands of the residual groups in the structure[21], See table 3, figure 1 and figure 2.



Scheme 4. Structure of the synthesized Schiff bases

Table 3. FT-IR of synthesized Schiff bases

FT-IR[a], ν(cm^{-1})[b]						
Compound	**C=N**	**C=C Aromatic**	**C-H Aromatic**	**C-H Ali.**		**Others**
				Asymmetric	**symmetric**	
A_1	1690	1525	3054	2887	2854	C-S 734
A_2	1697	1566	3049	2929	2860	C-Cl1051
A_3	1693	1560	3058	--	2927	C-S 686. C-Cl 1006
A_4	1685	1564	3085	2908	2862	C-Cl1051
A_5	1664	1569	3074	--	2875	C-S 844. C-F 1240

[a]Fourer Transform - Infra Red.[b]The wavenumber (centimeter unit)$^{-1}$. Dash means no stretching; N.A.: Not applicable.

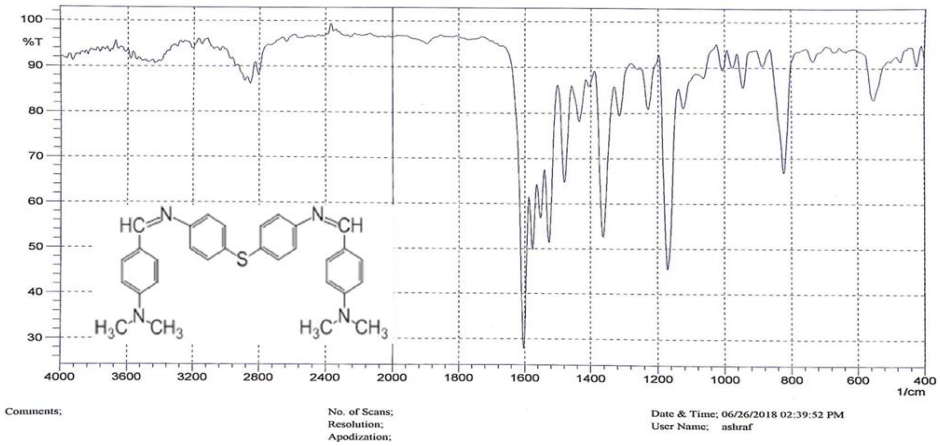


Figure 1. FT-IR spectra of A_1

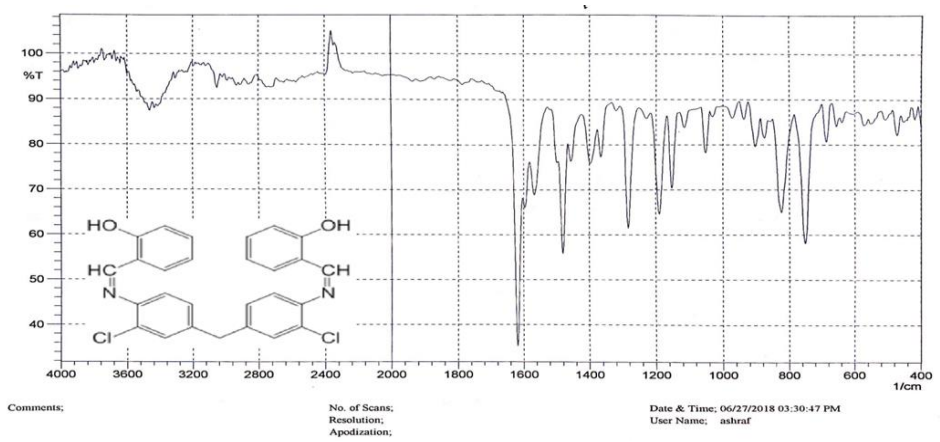
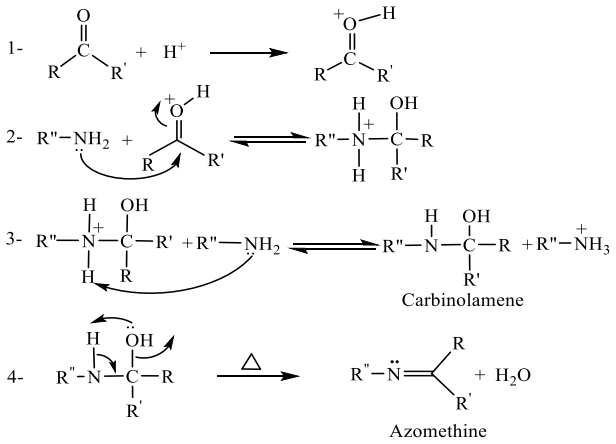


Figure 2. FT-IR spectra ofA_2

The mechanism of Schiff bases formation was established by literature as given by scheme 6, the reaction involves a nucleophile attack of the double-electronic of the amino group (NH_2) of aromatic amine on the carbonyl group (C=O) of aromatic aldehydes to form a hemiaminal N-substituted medium that loses a water molecule to give the stable compound (Schiff base). The reaction is believed to occur in the following mechanism[22], see scheme 5.



Scheme 5. Mechanism of Schiff bases formation

Synthesized disubstituted 1,3-oxazepine-tetra-one derivatives:

The FT-IR spectra of disubstituted 1,3-oxazepine-tetra-one derivatives showed the disappearance of the stretching absorption bands of the group (C=N) of the azomethine compounds and the stretching absorption bands of two anhydride compounds and showed the appearance of the stretching absorption bands at (1683-1627) cm^{-1} indicative of C=O lactam bonds, stretching absorption bands at (1712-1619) cm^{-1} indicative of C=O lacton bonds, stretching absorption bands at (1398-1284) cm^{-1} indicative of C-O bonds, stretching absorption bands at (1193-1160) cm^{-1} indicative of C-N bonds, stretching absorption bands at (664-588) cm^{-1} indicative of C-S bonds, beside the characteristic bands of the residual groups in the structure[21,23], see the table 4 and example figures 3 and 4.

Table 4. FT-IR of disubstituted 1,3- oxazepine-tetra-one derivatives

FT-IR[a], ν(cm^{-1})[b]									
Compound	**C=C** Aromatic	**C-O**	**C-H** Aromatic	**C-N**	**C=O** Lactam	**C=O** Lacton	**C-H** Aliphatic		**Others**
							Asymmetric	**Symmetric**	
A_6	1529	1361	3197	1170	1683	1654	3089	2988	C-S 700
A_7	1599	1284	3055	1160	1566	1619	2929	2892	C-Cl 1051
A_8	1568	1398	3197	1178	1627	1708	2923	2918	C-S 690 C-Cl 1008
A_9	1525	1305	3055	1193	1627	1712	2925	2852	C-Cl 1058
A_{10}	1527	1321	3055	1186	1627	1712	2989	2862	C-S 680 C-F 1242

[a]Fourer Transform - Infra Red. [b]The wavenumber (centimeter unit)$^{-1}$.
Dash means no stretching; N.A.: Not applicable.

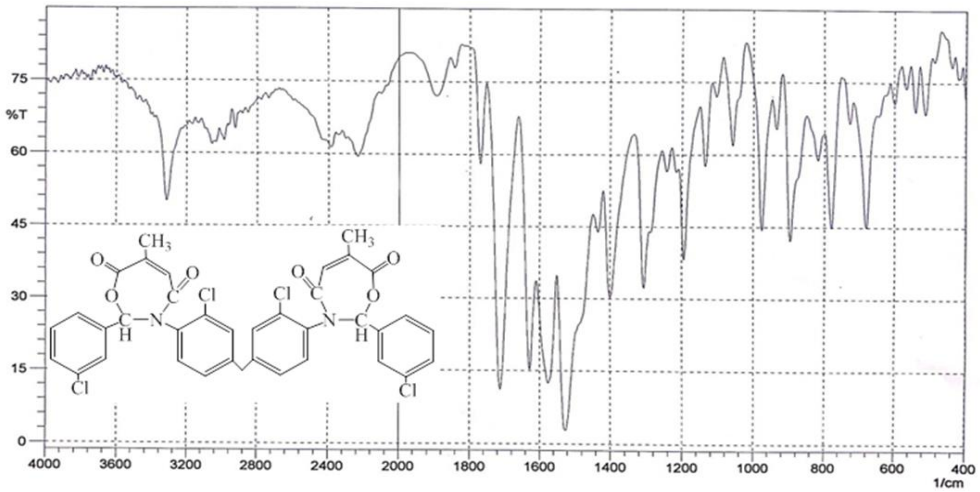


Figure 3. FT-IR spectra of A_9

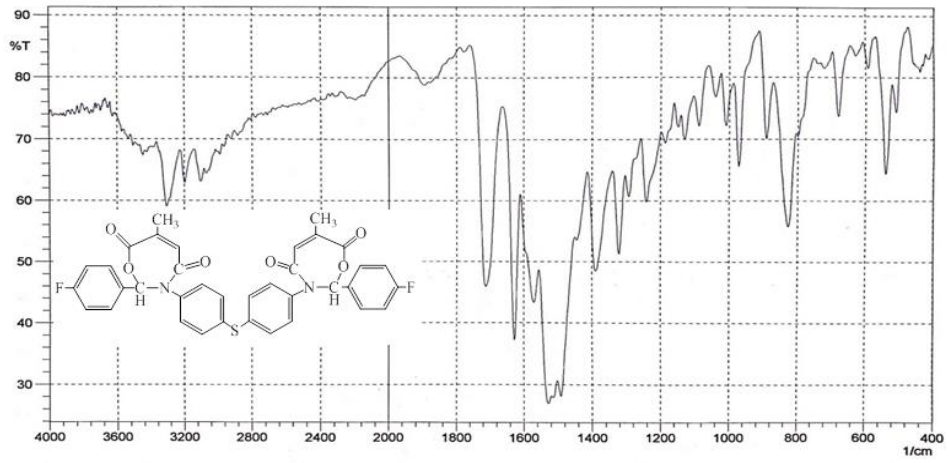


Figure 4. FT-IR spectra of A_{10}

The ^{1}H-NMR spectrum of compound A_6 in DMSO solvent (figure 5) showed chemical shifts, δ(ppm), Singlet in 1.43 for (12H, 4 N-C<u>H</u>$_3$), doublet in 3.09 for (4H, C<u>H</u>$_2$-CH), triplet in 3.57 for (2H, CH$_2$-<u>CH</u>), singlet in 9.74 for (2H, 2 N-<u>CH</u>), multiplet in 6.70-7.75 for (26H, aromatic protons).. Spectrum of compound A_{10} (figure 6) showed chemical shifts, δ(ppm) at: Singlet in 2.21 for (6H, 2 =C-C<u>H</u>$_3$), singlet in 5.53 for (2H, 2 =C<u>H</u>), singlet in 9.98 for (2H, 2 N-C<u>H</u>), multiplet in 6.49-7.93 for (16H, aromatic protons)[24]. Other chemical shifts of A_7, A_8 and A_9, δ(ppm) are presented in table 5.

Table 5. The ^{1}H-NMR Spectra of disubstituted 1,3- oxazepine-tetra-one derivatives in DMSO

Comp. Code	Chemical Shift δ ppm[a]
A_6	Singlet in 1.43(12H, 4 N-C<u>H</u>$_3$), doublet in3.09 (4H, C<u>H</u>$_2$-CH), triplet in 3.57 (2H, CH$_2$-<u>CH</u>), singlet in 9.74 (2H, 2 N-<u>CH</u>), multiplet in 6.70-7.75 (26H, aromatic protons).
A_7	Doublet in 3.50 (4H, C<u>H</u>$_2$-CH), triplet in 3.99 (2H, CH$_2$-<u>CH</u>), singlet in 4.10 (2H, Ph-C<u>H</u>$_2$-Ph), singlet in 8.64 (2H, 2 N-<u>CH</u>), singlet in 13.22 (2H, 2 -O<u>H</u>), multiplet in 6.94-7.42 (24H, aromatic protons),
A_8	Singlet in 1.87 (6H, 2=C-C<u>H</u>$_3$), singlet in 6.50(2H, 2 =C<u>H</u>), singlet in 9.99 (2H, 2 N-C<u>H</u>), multiplet in 7.16-7.87 (16H, aromatic protons).
A_9	Singlet in 2.20 (6H, 2 =C-C<u>H</u>$_3$), 3.49 (2H, Ph-C<u>H</u>$_2$-Ph), singlet in 6.51 (2H, 2 =C<u>H</u>), singlet in 9.98 (2H, 2 N-C<u>H</u>), multiplet in 6.72-7.87 (14H, aromatic protons).
A_{10}	Singlet in 2.21 (6H, 2 =C-C<u>H</u>$_3$), singlet in 5.53 (2H, 2 =C<u>H</u>), singlet in 9.98 (2H, 2 N-C<u>H</u>), multiplet in 6.49-7.93 (16H, aromatic protons).

[a] The references point (the chemical shift of tetramethylsilane $(CH_3)_4Si$)

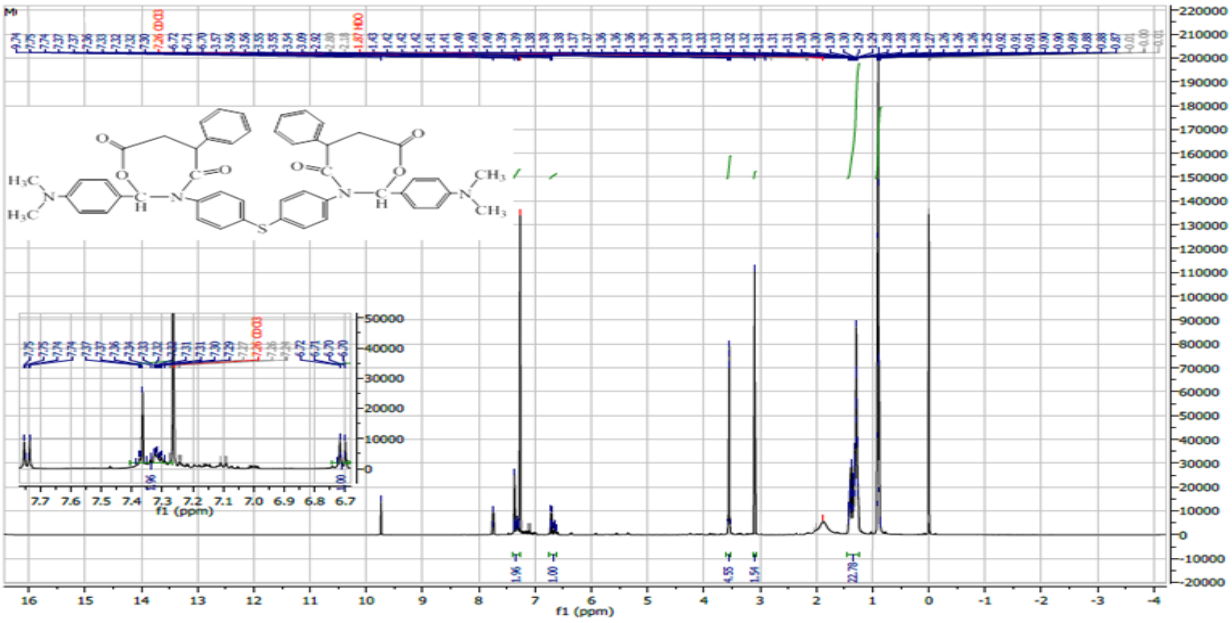


Figure 5.^{1}H-NMR Spectra of A_6

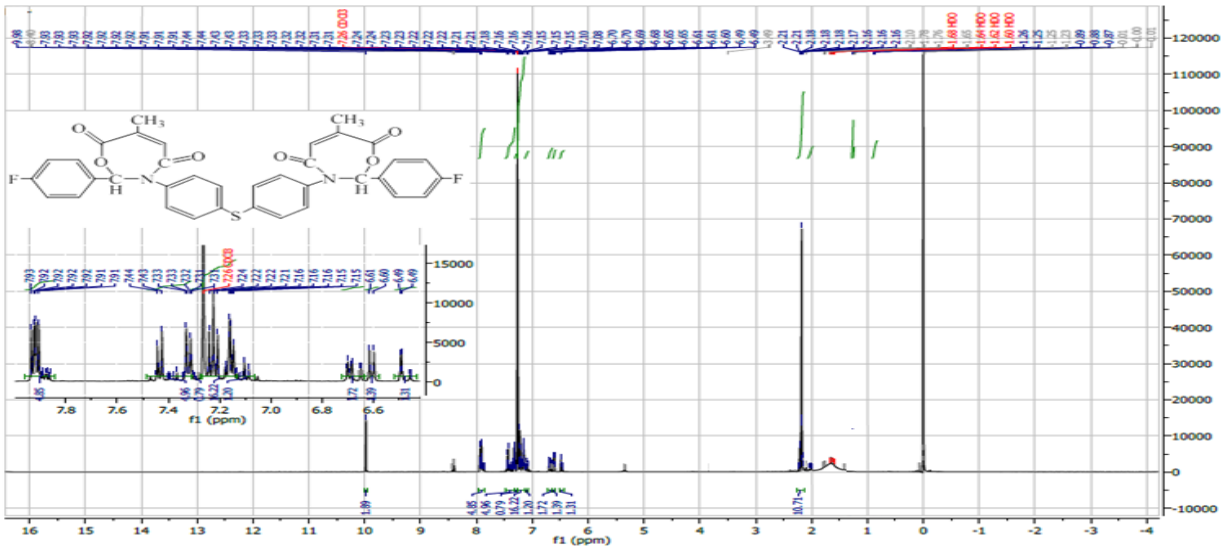


Figure 6.^{1}H-NMR Spectra ofA_{10}

The ^{13}C-NMR spectrum of compound A_7 in DMSO solvent (figure 7) showed chemical shifts, δ(ppm), 38.98 for (Ph-$\underline{C}H_2$-Ph), 70.10 for ($\underline{C}H_2$-CH), 116.17 for (CH_2-$\underline{C}$H), 142.65 for (2 N-$\underline{C}$H), 180.03 for (2 N-$\underline{C}$=O), 164.14 for (2 O-$\underline{C}$=O), 119-129 for (aromatic carbon).. While spectrum of compound A_9 (figure 8) exhibited chemical shifts, δ(ppm), 40.63 for (Ph-$\underline{C}H_2$-Ph), 77.28 for (2 =C-$\underline{C}H_3$), 116.05 for (2 =$\underline{C}$H), 119.17 for (2 =$\underline{C}$-CH_3), 141.03 for (2 N-$\underline{C}$H), 149.23 for (2 N-$\underline{C}$=O), 193.83 for (2 O-$\underline{C}$=O), 128-137 for (aromatic carbon)[25].Other chemical Shifts of A_6, A_8, A_{10}, δ(ppm) are displayed in table 6.

Table 6. The ^{13}C-NMR spectra of disubstituted 1,3- oxazepine-tetra-one derivatives in DMSO

Comp. code	Chemical Shift δ ppm
A_6	40.43 (4 N-$\underline{C}H_3$), 70.98 ($\underline{C}H_2$-CH), 112.80 (CH_2-$\underline{C}$H), 145.02 (2 N-$\underline{C}$H),172.34 (2 N-$\underline{C}$=O), 174.46 (2 O-$\underline{C}$=O),115.16-127.53 (aromatic carbon).
A_7	38.98 (Ph-$\underline{C}H_2$-Ph), 70.10 ($\underline{C}H_2$-CH), 116.17 (CH_2-$\underline{C}$H), 142.65 for (2 N-$\underline{C}$H),180.03 (2 N-$\underline{C}$=O), 164.14 (2 O-$\underline{C}$=O), 119-129 (aromatic carbon).
A_8	79.11 (2 =C-$\underline{C}H_3$), 113.67(2 =$\underline{C}$H), 115.49 (2 =$\underline{C}$-CH_3), 131.08 (2 N-$\underline{C}$H), 169.05 (2 N-$\underline{C}$=O), 173.22 (2 O-$\underline{C}$=O), 118-126 (aromatic carbon).
A_9	40.63 (Ph-$\underline{C}H_2$-Ph), 77.28 (2 =C-$\underline{C}H_3$), 116.05 (2 =$\underline{C}$H), 119.17 (2 =$\underline{C}$-CH_3), 141.03 (2 N-$\underline{C}$H), 149.23 (2 N-$\underline{C}$=O), 193.83 (2 O-$\underline{C}$=O), 128-137 (aromatic carbon).
A_{10}	77.31 (2 =C-$\underline{C}H_3$), 116.26(2 =$\underline{C}$H), 116.47 (2 =$\underline{C}$-CH_3), 132.29 (2 N-$\underline{C}$H), 160.03 (2 N-$\underline{C}$=O), 190.51 (2 O-$\underline{C}$=O), 126-131 (aromatic carbon).

[a] The references point (the chemical shift of tetramethylsilane $(CH_3)_4Si$).

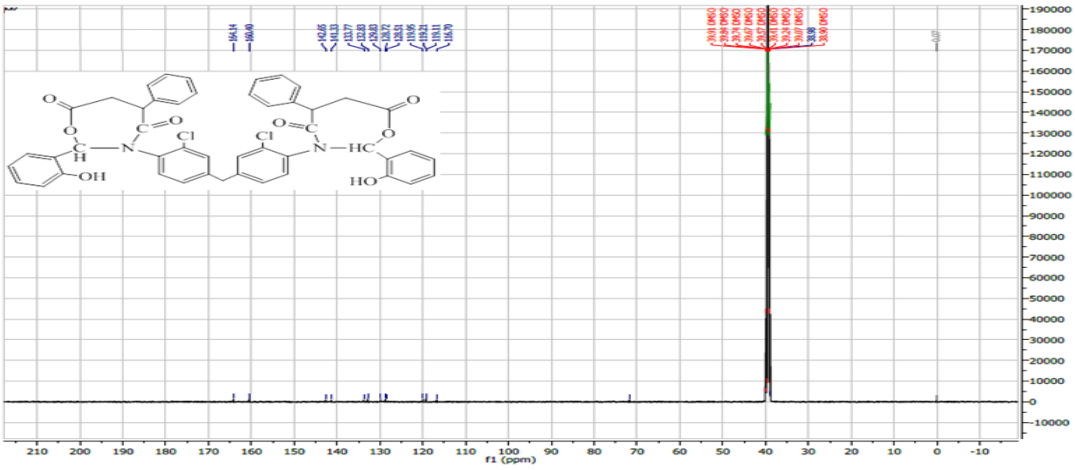


Figure 7.^{13}C-NMR Spectra ofA_7

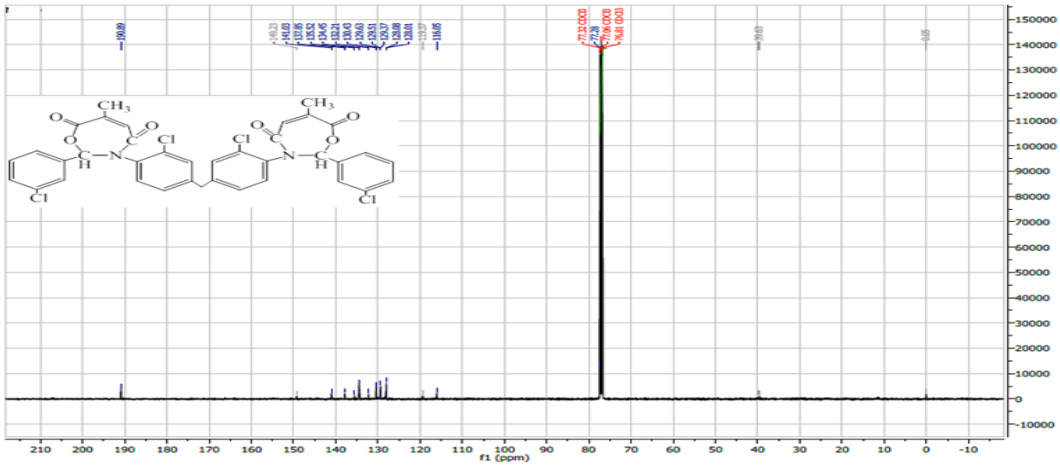
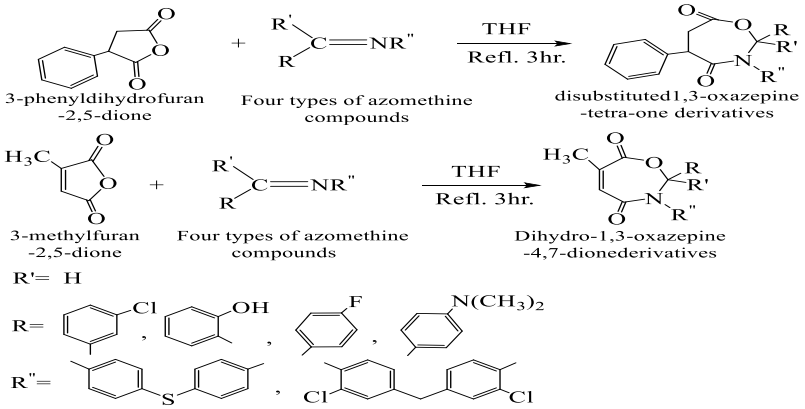
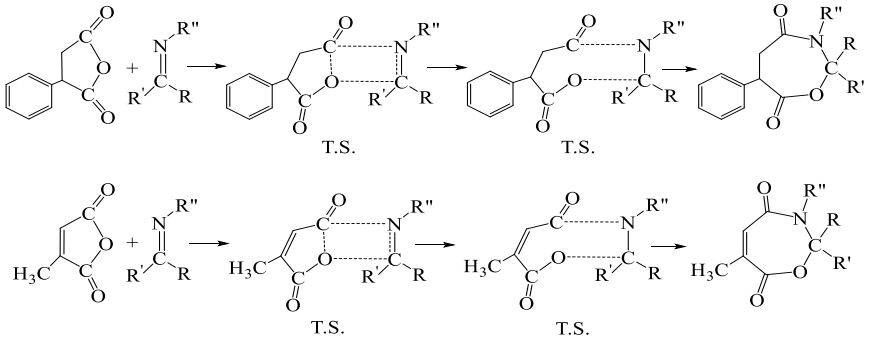


Figure 8.^{13}C-NMR Spectra ofA_9



Scheme 7. Structure of the synthesized disubstituted 1,3- oxazepine-tetra-one derivatives from two types of anhydrides



Scheme 8. Mechanism of disubstituted 1,3- oxazepine-tetra-one derivatives formation for two types of anhydrides

The both reactions of the synthesized Schiff bases with two anhydridesare given by the following equation[26,27], see scheme 7.

It may be concluded that the both reactions takes places via interaction between HOMO orbital of anhydrides with LUMO orbital of (C=N) group by concerted dipolar cycloaddition mechanism[28] as represented in the flowing reaction[29], see scheme 8.

The mechanism involves the addition of one σ-carbonyl to π-bond (N=C) to give 4- membered cyclic and 5-membered cyclic ring of anhydride in the same transition state [T.S.], which opens into 3-methylfuran-2,5-dione and 3-phenyldihydrofuran-2,5-dione anhydrides to give 7- membered cyclic ring disubstituted 1,3-oxazepine-tetra-one derivatives[30,31-33].

CONCLUSION:

It was possible to prepare derivatives of disubstituted 1,3- oxazepine-tetra-one derivatives. The results of FT-IR, ^{13}C-NMR and ^{1}H-NMR showed that the seven-ringed compounds were the least obstructed in all preparation processes. Because of the complete clarity in infrared beams and clear signals separated from each another by the resonance spectrum nuclear magnetic of hydrogen and carbon, this is the basis of organic preparation processes.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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