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Synthesis and characterization Some of heterocyclic compounds from Nitrogen derivative

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ABSTRACT

This paper involves the synthesis of new oxazepine derivatives by multi-reaction steps. The first step synthesis azo derivative from 2-naphthol with 3-aminoacetophenone. The second step was the condensation reaction between ketone group of the azo compound and different primary aromatic amines (4-amino phenol, 3-nitro aniline and 4-methyl aniline) to yiled new azo Schiff base compounds (S1-S3) respectively. In the final step, Oxazepine compounds (L1-L3)and (L4-L6)were prepared from reaction imine compounds (S1-S3) with maleic and phthalic anhydride in toluene as solvent. All these derivatives were characterized by melting point, FTIR, HNMR and 13CNMR.

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INTRODUCTION

The chemistry of heterocyclic compounds has been an interesting field of study (Verma *et al.*, 2015) for a long time due its more application in several fields such as medicinal, pharmaceutical and selective drugs (Mohammad *et al.*, 2017) Oxazepine stands for unsaturated non-homologous seven associated heterocycle having Oxygen in position 1 and nitrogen in position 3 along with five carbon atoms (Abid and Ramadan, 2018). Oxazepine has three isomers bases on the location of oxygen and nitrogen atoms in the seventh ring (Abid *et al.*, 2017).

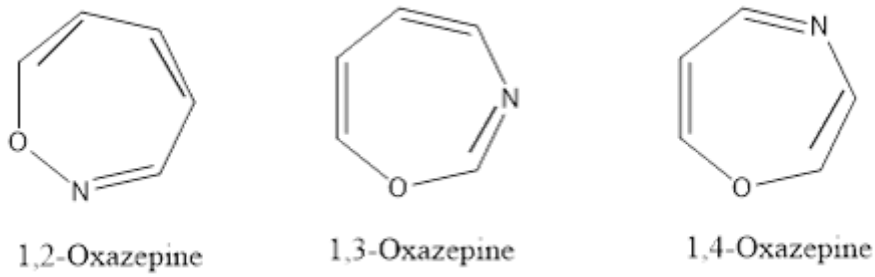
It is organized through the Pericycliccyclo addition of Schiff bases with maleic and phthalic anhydrides (Ali and Ghanim, 2016). Oxazepine derivatives have a huge diversity of biological activities like antifungal (Taha, 2017), hypotic muscle relaxant (Kadhim, 2017), antibacterial (Choudhary *et al.*, 2018) telomerase inhibitors (Mohammed *et al.*, 2017), anti-inflammatory (Mohammad *et al.*, 2019) and antiepileptic (Jarallah *et al.*, 2019) (1,4)Oxazepine was taken up to designing potent progesterone receptor antagonists (Al-Lami and Salom, 2019). (1,4) Oxazepine is found to be a dynamic moiety in numerous psychoactive pharmaceuticals (Majeed *et al.*, 2018).

PREPARATION METHODS

The methods of chemical preparations are as below in details. Table 1 shows the physical features of organized compounds.

(1) Synthesis1-(3-((2-hydroxy naphthalene-1-yl)diazenyl)acetophenone

3-aminoacetophenone (0.03 mol, 4.05 gm) was dissolved in (3ml)of concentrated hydrochloric acid and (20 ml) of distilled water. The solution was cold at (0 c^o) in an ice-water bath. The sodium nitrite (0.03 mol, 2.07 gm)was dissolved in (10 ml) of distilled water and added dropwise to the solution with stirring .2- naphthol (0.03 mol, 4.32 gm) was dissolved in (20 ml) of ethanol and (10 ml) of sodium hydroxide 10% and cooled to (0C^o), added to the diazonium solution is dropwise and stirring at (0C^o)for (2h) for obtaining the coupling agent. The result of the orang gold compound was precipitated,



Scheme 1: Oxazepine with three isomers bases

filtered and washed with water.

(2)Synthesis of azo Schiff bases derivatives (S_1–S_3)

Ethanolic mixture (30 ml) containing 1 drop of concentrated hydrochloric acid to azo acetophenone derivative (A) of (0.003 mol, 1.0 gm)then adding (0.37gm, 0.47gm, 0.36 gm) of primary aromatic amines (4-amino phenol, 3-nitro aniline and 4-methyl aniline). The reaction mixture was refluxed with stirring for (10-35) hours at (78) C^o, the reaction was completed and examined by using TLC (Methanol: dry benzene 1:4)recrystallized from ethanol.

(3)Synthesis of (L_1-L_3) Oxazepine and (L_4-L_6) Oxazepine

A mixture of azo-Schiff bases derivatives (S_1-S_3) (0.5gm, 0.3gm,0.3 gm) with (0.16 gm , 0.1 gm , 0.1gm) maleic anhydreid (0.25gm ,0.14gm ,0.11gm) phthalic anhydride respectively in (30 ml) of Tolouene , was refluxed for (19h, 6h ,33h) hours for compounds (L_1-L_3) and (19h,4h,32h) hours for compounds (L_4-L_6).

RESULTS AND DISCUSSION

The coupling reaction (Hamdan *et al.*, 2018) between diazonium salt with 2-naphthol to produce 1-(3((2-hydroxynaphthalen-1-yl)diazenyl) acetophenone. Azo-Schiff bases (S_1-S_3) were synthesized by condensation of the equimolar quantity of primary aromatic amines (4-amino phenol, 3-nitro aniline, 4-methal aniline) with azo acetophenone derivative (A). Apericyclic reaction (Nief, 2018) is one that occurs by a concerted process through a cyclic transition state. The word concerted means that all bonding changes occure simultaneously; no intermediates are involved (Khidir *et al.*, 2018). Pericyclic reaction represents an imperative type of concerted (solitary step) processes including π-systems (Sallal and Ghanem, 2018) A concerted rearrangement of the electrons that causes δ and π-bonds break and from to simultaneously (Taha, 2017). Apericyclic reaction between imine groups of azo-Schiff bases (S_1-S_3) as two membered compounds and cyclic acid oanhydride (maleic, phthalic anhydride)as five-membered compounds in Tluene were syntheized compounds (L_1-L_3) and (L_4-L_6) respectively (Choudhary *et al.*, 2018). Scheme 2 depicts the mechanism of synthesis of 1,3-Oxazepine.

The structures of all synthesis compounds were depicted in Scheme 3.

Spectral Characterization

Our derivative identified with variety spectral methods like (FT.IR, H.NMR, C^{13}.NMR) spectra with microbial assay

FT.IR Spectra of Derivatives

The FT.IR Spectrums of derivatives are depicted in Figures 1, 2, 3, 4, 5 and 6.

A\ 1498 (N=N), 3421.72(OH) , 3062.96-3014.74(C-H , aromatic) , 1618.28 (C=C), 1224.16-1203.58 (C-O), 1147.65 (C-N).

S_1\max 1683.86 (C=N), 1502.55 (N=N) , 3061.03 -3030.17 (-CH,aromatic), 3414.00-3406.29(OH), 1618.28 (C=C) , 1355.96(CH3).

S_2\ max 1683.86 (C=N), 1500.62 (N=N) , 3066.82 -32972.31 (-CH,aromatic), 3458.37-3437.15 (OH), 1620.21 (C=C) , 1357.89 (CH3).

S_3\ max 1689.64 (C=N), 1581.63 (N=N), 3099.61 -3062.96 (-CH,aromatic), 3439.08-3360.00(OH), 1641.42 (C=C), 1355.96 (CH3).

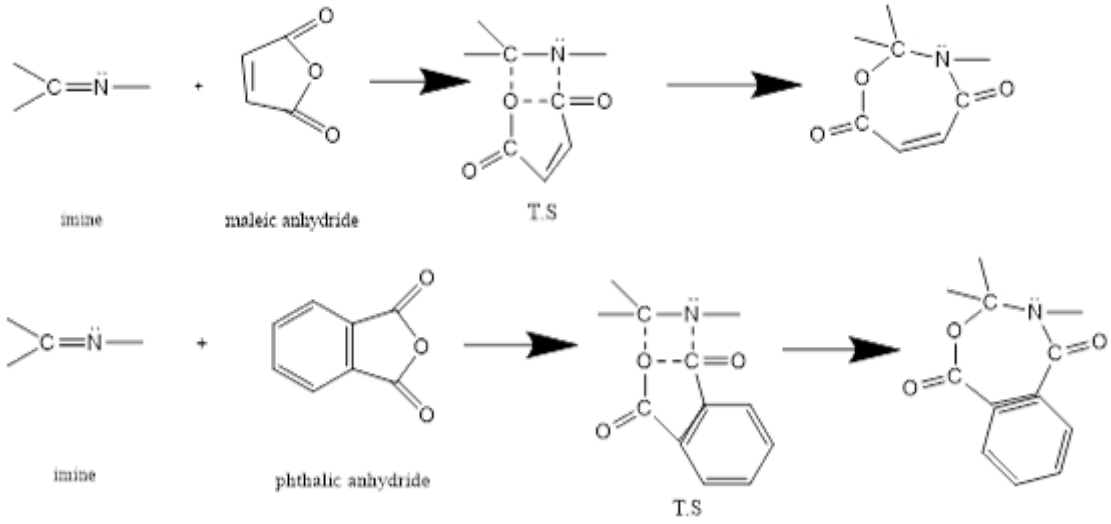
L_1\ max 1712.79 (Lactone C=O), 1685.79-1658.78 (C=O ester and amide), 3061.03 to 2922. 16 (C-H,aromatic), 1600.92-1581.63 (C=C,aromatic),1398.39 and 1361.74 (O-C-O and –N-C-), 1168.86 (C-O).

L_2\max 1718.58(Lactone C=O),1681.93 and 1624.06 (C=O ester and amide),3088.03 to 2922.16(C-H, aromatic), 1593.20-1519.91(C=C,aromatic).

L_3\ max 1712.79(Lactone C=O),1681.93 and 1618.28 (C=O ester and amide),3059.10

Table 1: Physical features of organized compounds

Yiled %	R.F	m.p co	M.wt g\mol	m.f	Compound No.
91	—	156-158	290.32	$C_{18}H_{14}N_2O_2$	A
87	0.9	162-164	381.44	$C_{24}H_{19}N_3O_2$	S1
81	0.9	160-162	410.43	$C_{24}H_{18}N_4O_3$	S2
87	0.7	174-176	379.46	$C_{25}H_{21}N_3O_1$	S3
70	0.9	108-110	481.51	$C_{28}H_{23}N_3O_5$	L1
93	0.8	136-138	510.51	$C_{28}H_{22}N_4O_6$	L2
90	0.9	105-106	479.54	$C_{29}H_{25}N_3O_4$	L3
63	0.9	116-118	529.55	$C_{32}H_{23}N_3O_5$	L4
79	0.8	130-132	558.55	$C_{32}H_{22}N_4O_6$	L5
88	0.9	111-113	527.58	$C_{33}H_{25}N_3O_4$	L6



Scheme 2: Mechanism of synthesis 1,3-Oxazepine

to 3028.24(C-H, aromatic), 1587.42-1556.55(C=C,aromatic).

L_4\ max 1712.79(Lactone C=O),1639.49 and 1616.35 (C=O ester and amide),3064.89 to 2987.74(C-H, aromatic), 1589.34(C=C,aromatic).

L_5\ max 1681(Lactone C=O),1618.28 (C=O ester and amide),3062.96 to 3018.60(C-H, aromatic), 1568.13-1552.70(C=C,aromatic).

L_6\ max 1720.50(Lactone C=O),1681.93 and 1618.28 (C=O ester and amide),3064.89 to 3014.74(C-H, aromatic), 1589.34-1568.13(C=C,aromatic.

^{1} HNMR- Spectra of derivatives

Using DMSO as a solvent, ^{1}HNMR- Spectra of derivatives are shown in Figures 7, 8, 9, 10 and 11.

A\Singlet 2.101 ppm(CH3),singlet 2.5 ppm (Dmso), multipleting singal at 6.996-7.377 ppm (phenol ring), singlet 11.01ppm(OH).

S_1\Singlet 2.077ppm(CH3), 2.512 ppm(Dmso), multipleting singal at 6.998-7.643 ppm (phenal ring), 10.743-11-381 ppm (OH).

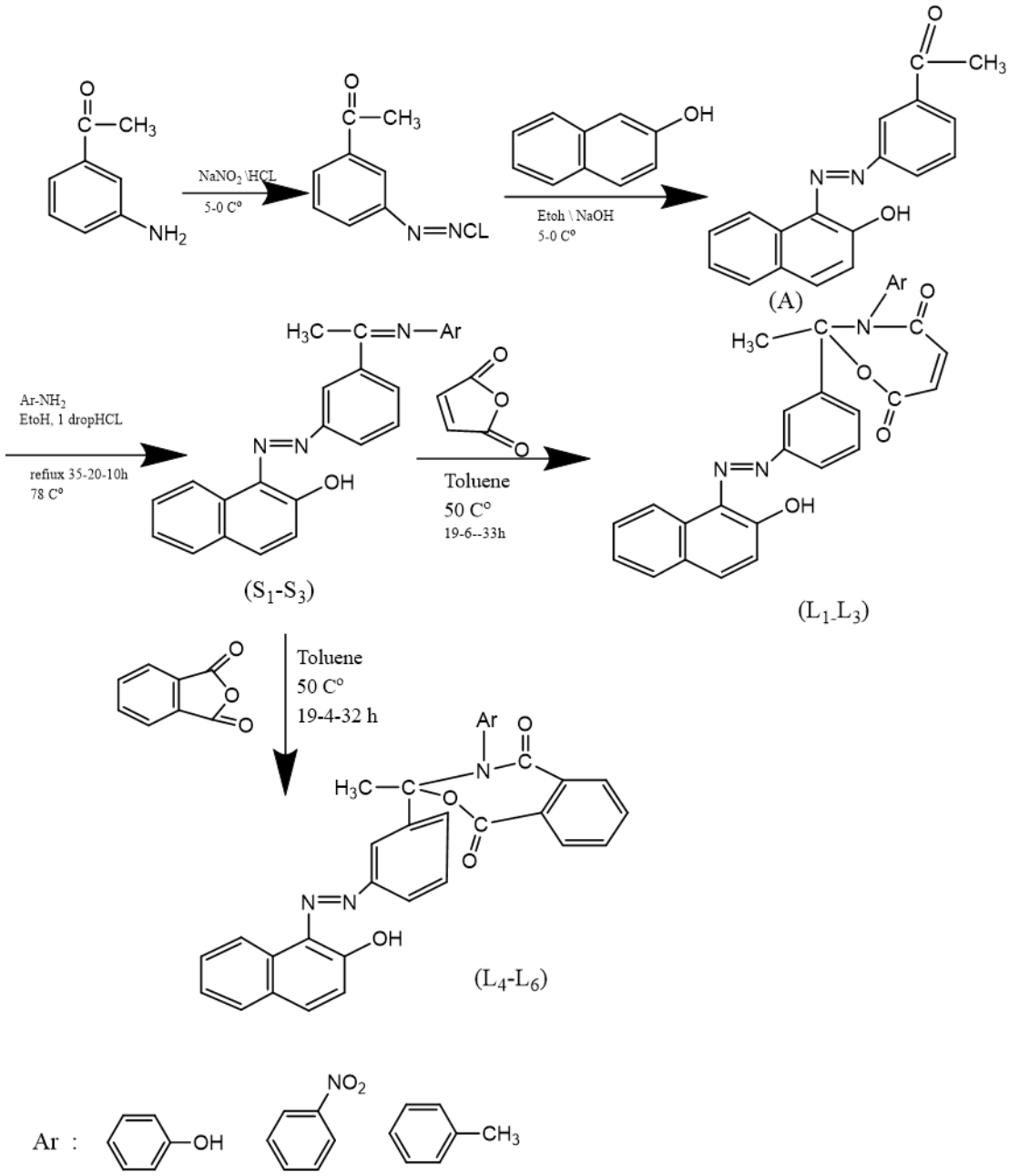
S_2\Singlet 2.064ppm(CH3), singlet 2.515ppm (Dmso), multipleting singal at 7.038-7.980 ppm (phenal ring),11.814 ppm (OH).

S_3\Singlet 1.718ppm-2.088ppm (CH3) , singlet 2.518ppm (Dmso) , multipleting singal at 7.401-8.498 ppm (phenal ring) , single 11.518ppm (OH).

L_1\Singlet 2.018ppm (CH3), singlet 2.524 ppm (Dmso),doublet singnal at 6.849-6. 23ppm (CH=CH), multipleting signal at 7.536-8.392ppm(phenal ring) , singlet 10.818-11.497ppm(OH).

L_2\ Singlet 2.097ppm (CH3),singlet 2.523 ppm (Dmso),doublet singnal at 6.6-6.8ppm (CH=CH),multipleting signal at 7.717-8.159ppm(phenal ring), singlet 11.797ppm(OH).

L_3\ Singlet 1.813-2.113ppm (CH3),singlet



Scheme 3: Structures of each synthesized compounds

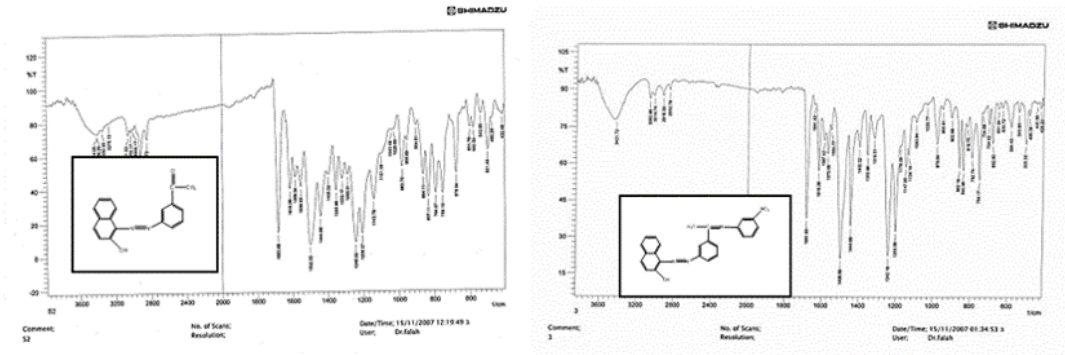


Figure 1: 1-(3-((2- hydroxynaphthalen-1-yl)diazenyl)acetophenone (A) and 1-((3-(1-((3 nitrophenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol (S2)

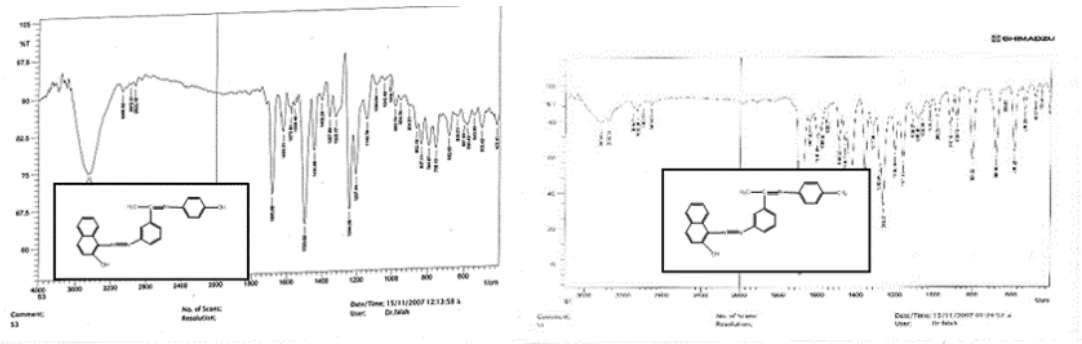


Figure 2: 1-((3-(1-((4-hydroxyphenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol(S1) and 1-((3-(1-(p-tolylimino)ethyl)phenyl)diazenyl)naphthalen-2-ol (S3)

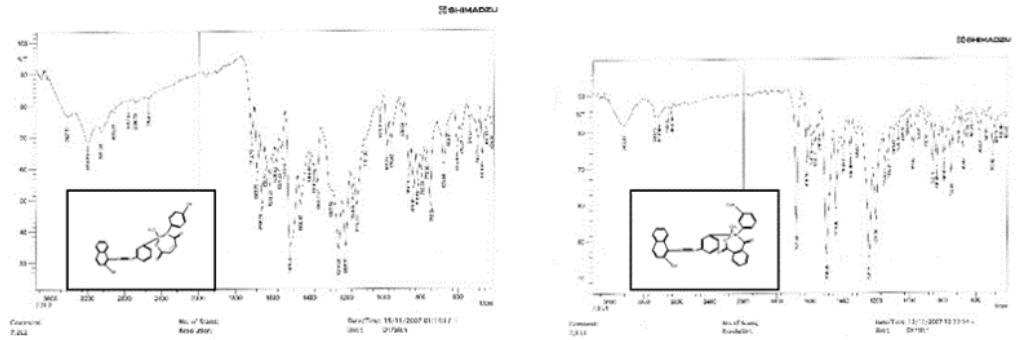


Figure 3: 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-(4-hydroxyphenyl)-2-methyl-1,3-oxazepane-4,7-dione(L1)
and3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-methyl-4-(3-nitrophenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione
(L5)

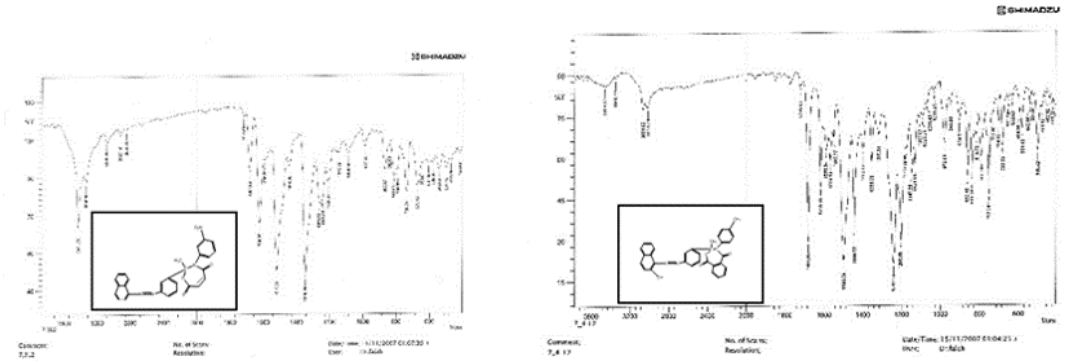


Figure 4: 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(3-nitrophenyl)-1,3-oxazepane-4,7-dione(L2)
and3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-methyl-4-(p-tolyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione(L6)

2.522 ppm (Dmso),doublet singnal at 6.483-6.493ppm (CH=CH),multipleting signal at 7.152 – 7.376ppm(phenal ring), singlet 11.028ppm(OH).

L_4\Singlet 2.019ppm(CH3), singlet 2.520 ppm (Dmso), multipleting signal 6.8 – 7.8ppm(phenal ring), 10.135- 11.435ppm(OH).

L_5\ Singlet 2.053ppm(CH3), singlet 2.520 ppm (Dmso), multipleting signal 7.036 – 7.932 ppm(phenal ring), 11.728 ppm(OH).

L_6\ Singlet 1.534 - 2.084ppm(CH3, singlet 2.523 ppm (Dmso), multipleting signal 7.6-8.2 ppm(phenal ring), 11.584 ppm(OH).

The C^{13}.NMR Spectral of derivatives

Using DMSO as a Solvent, the C^{13}.NMR Spectrums of derivatives are shown in Figures 12, 13, 14, 15, 16 and 17.

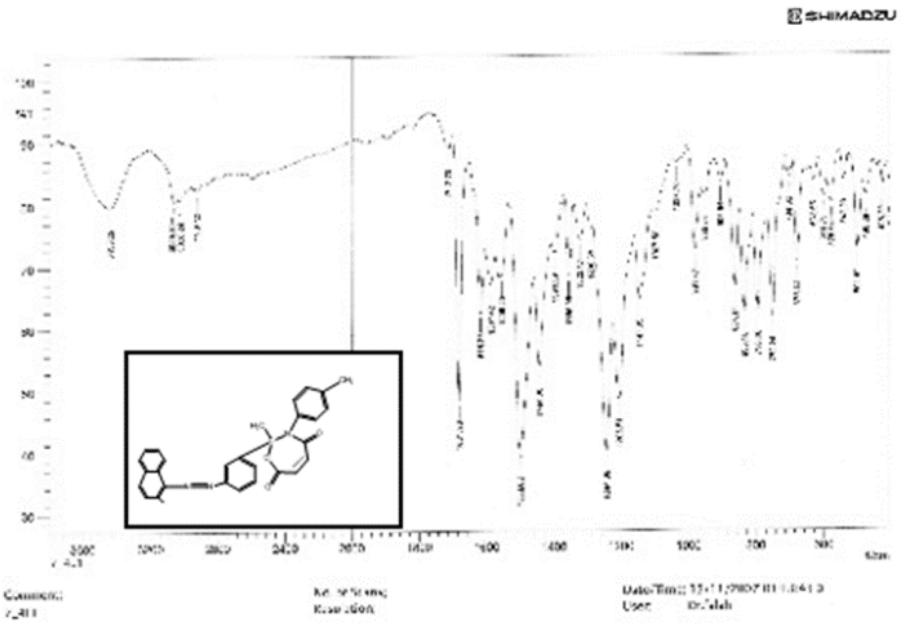


Figure 5:
2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(p-tolyl)-1,3-oxazepane-4,7-dione (L3)

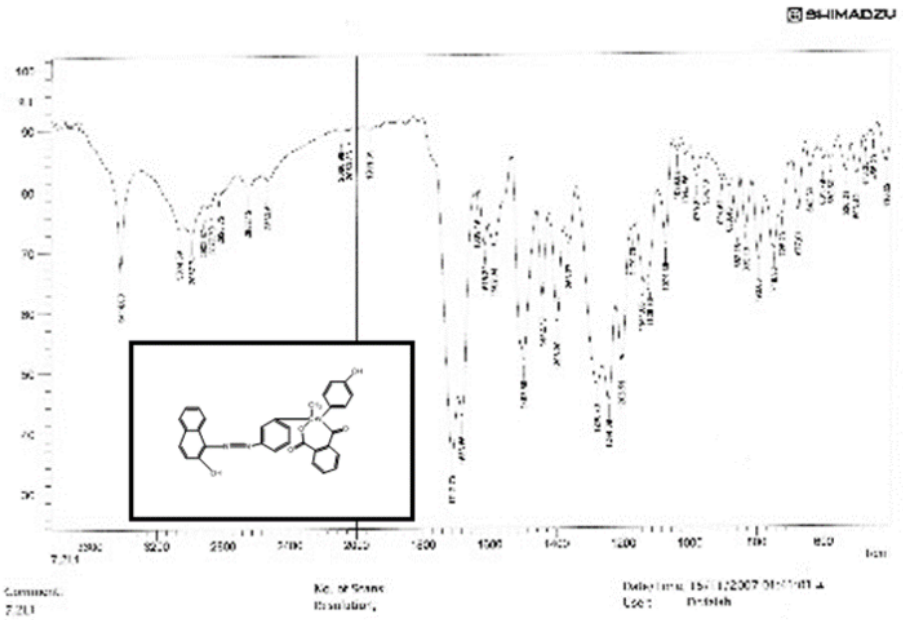


Figure 6: 3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-4-(4-hydroxyphenyl)-3-methyl-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione
(L4)

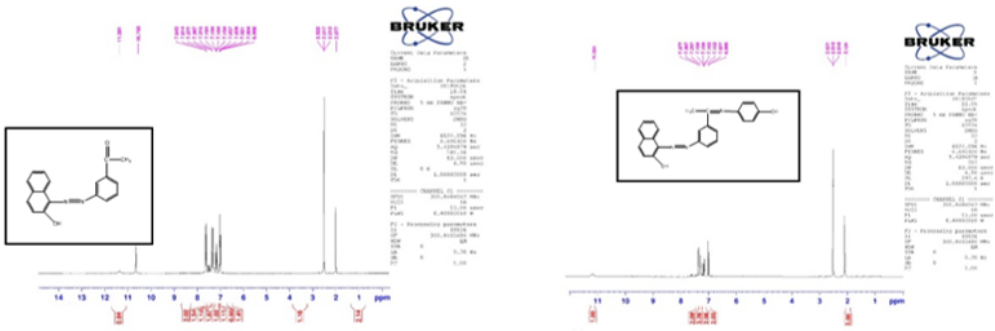


Figure 7: 1-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl) ethan-1-one (A) and 1-((3-(1-((4-hydroxyphenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol(S1)

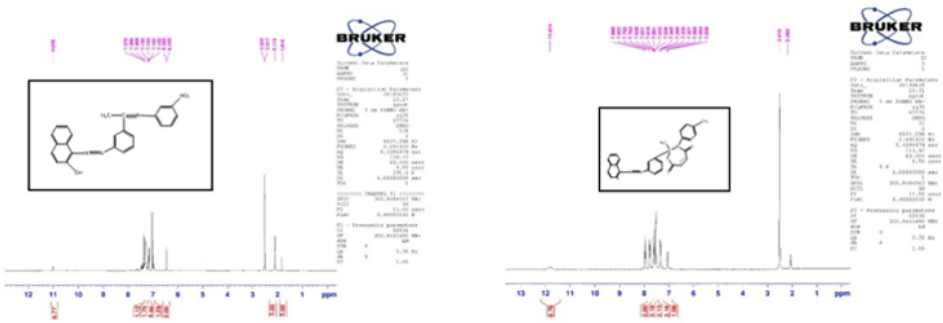


Figure 8: 1-((3-(1-((3-nitrophenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol(S2) and 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(p-tolyl)-1,3-oxazepane-4,7-dione(L3)

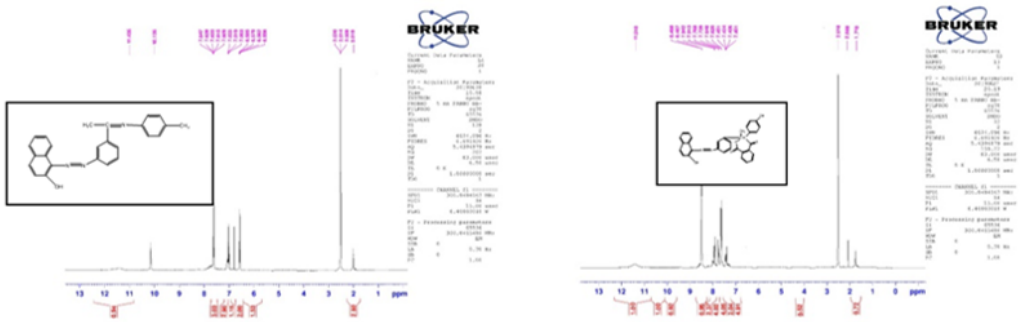


Figure 9: 1-((3-(1-(p-tolylimino)ethyl)phenyl)diazenyl)naphthalen-2-ol(S3) and 3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-4-(4-hydroxyphenyl)-3-methyl-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione (L4)

A\Singlet 26.36 ppm(CH3),197.52ppm(C=O), multipleting singal at 111.1-149.148 ppm (phenol ring), singlet 155. 1ppm(OH).

S_1\Singlet273ppm(CH3), 159PPM (C=N),153-154 ppm (OH).

S_2\Singlet 26.411(CH3), 159.054PPM(C=N),154 ppm (OH).

S_3\Singlet 21.605-25605 (CH3), 159.432PPM, single153.442PPM (OH).

L_1\Singlet 27.57PPM (CH3),160.7PPM (O-C-N), 172.57 – 174.4 PPM (C=O), 163.7 PPM (HC=CH), 153.6-154.8ppm(OH).

L_2\ Singlet 25.63PPM (CH3),161.12PPM (O-C-N),172.77-173.56ppm(C=O) ,164.12PPM(HC=CH), 155.057ppm(OH).

L\ Singlet 24.827-27.116PPM (CH3),160.449PPM(O-C-N),173-175.2PPM(C=O),163.827PPM (CH=CH), singlet 154.474 PPM(OH)

L_4\Singlet26.46ppm(CH3),160.2PPM(O-C-N),174.6-175.1PPM(C=O),153.1-154.1ppm(OH).

L_5\Singlet 26.5ppm(CH3),160.7PPM(O-C-N),172.4-173.9PPM(C=O),154.6ppm(OH).

L_6\Singlet26.6-22.2ppm(CH3),163PPM(O-C-

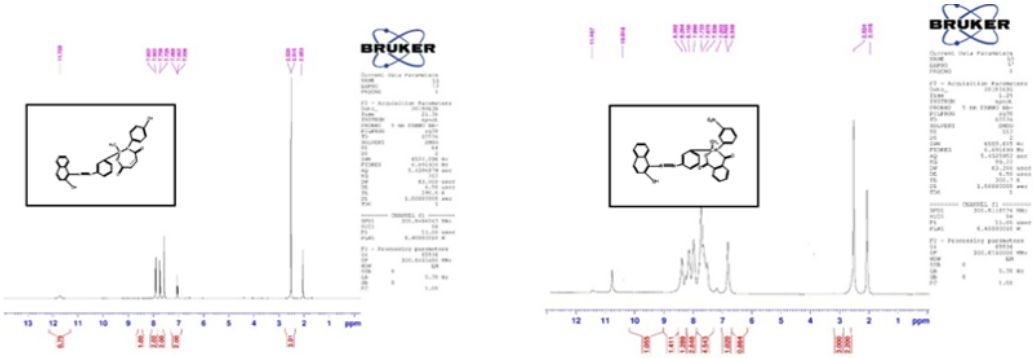


Figure 10: 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-(4-hydroxyphenyl)-2-methyl-1,3-oxazepane-4,7-dione(L1) and 3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-methyl-4-(3-nitrophenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione (L5)

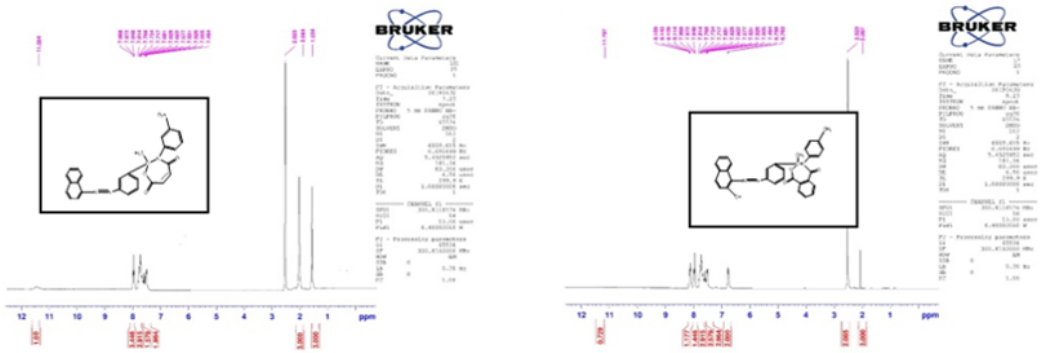


Figure 11: 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(3-nitrophenyl)-1,3-oxazepane-4,7-dione(L2) and3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-methyl-4-(p-tolyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione(L6)

Figure 12: 1-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl) ethan-1-one (A) and 1-((3-(1-((4-hydroxyphenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol(S1)

Figure 13: 1-((3-(1-((3-nitrophenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol(S2) and 1-((3-(1-(p-tolylimino)ethyl)phenyl)diazenyl)naphthalen-2-ol (S3)

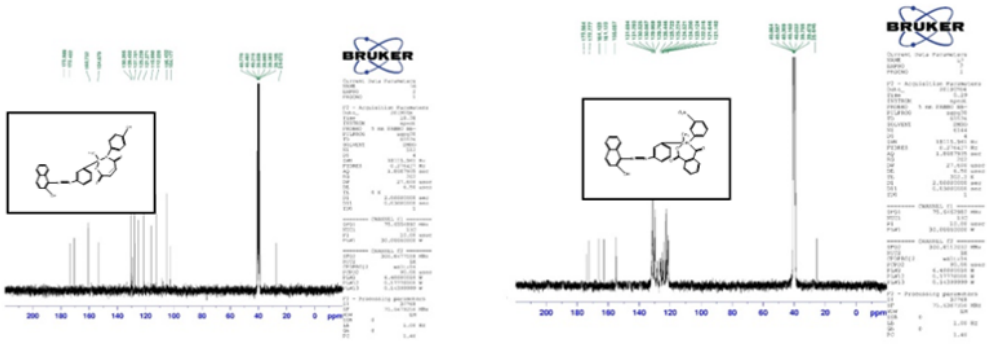


Figure 14: 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-(4-hydroxyphenyl)-2-methyl-1,3-oxazepane-4,7-dione(L1)
and3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-methyl-4-(3-nitrophenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione
(L5)

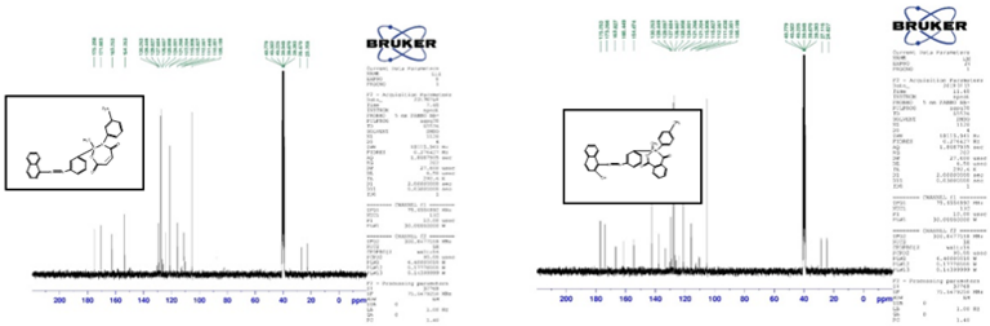


Figure 15: 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(3-nitrophenyl)-1,3-oxazepane-4,7-dione(L2)
and3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-methyl-4-(p-tolyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione(L6)

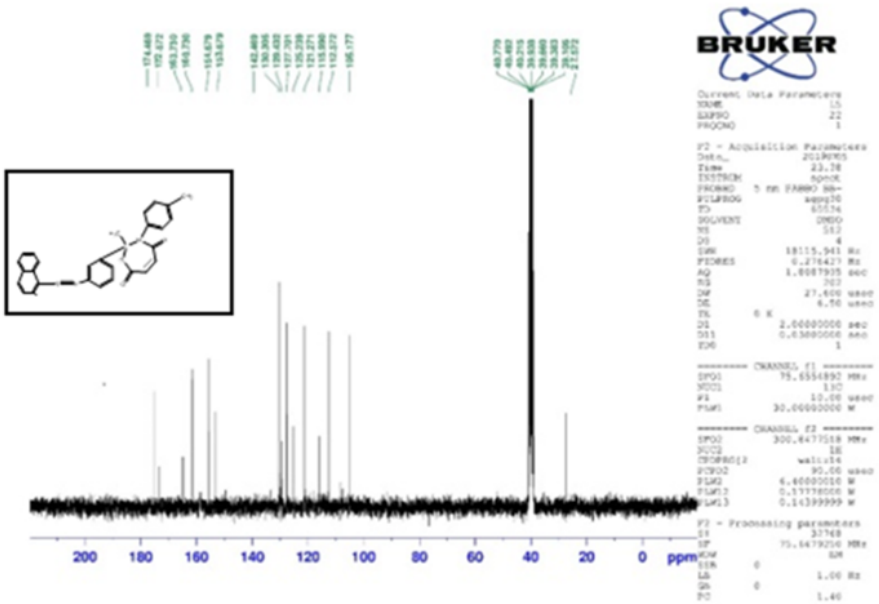


Figure 16: 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(p-tolyl)-1,3-oxazepane-4,7-dione(L3)

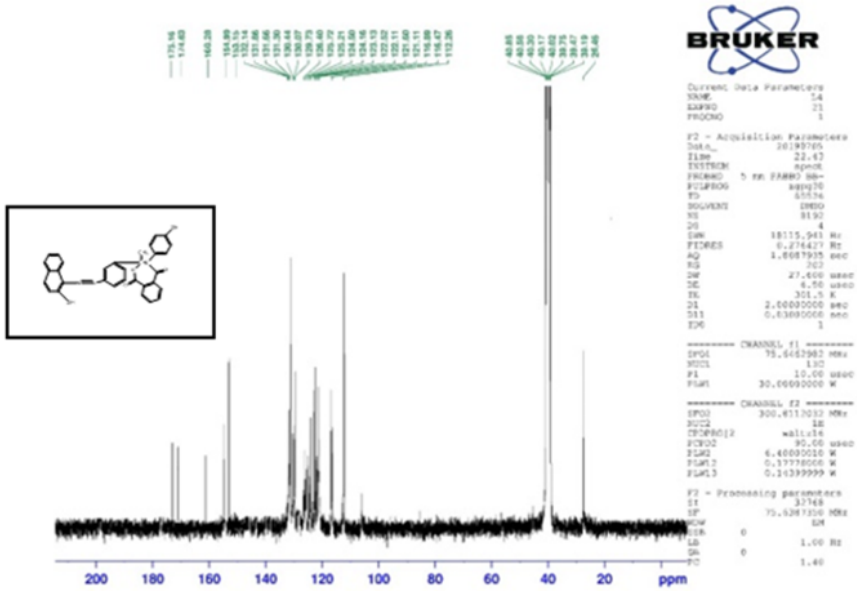


Figure 17: 3-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-4-(4-hydroxyphenyl)-3-methyl-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione
(L4)

N),171-175PPM(C=O),154.2ppm(OH).

CONCLUSION

This study presents a synthesis of innovative oxazepine derivatives by multi-reaction steps. The initial step synthesis azo derivative from 2-naphthol with 3-aminoacetophenone. The second step has been the condensation reacting between ketone group of the azo compound and diverse primary aromatic amines (4-amino phenol, 3-nitro aniline and 4-methyl aniline) to yiled new azo Schiff base compounds (S_1–S_3) respectively. In the last step, Oxazepine compounds (L_1–L_3)and (L_4–L_6) have been organized by reacting imine compounds (S_1–S_3) with maleic and phthalic anhydride in toluene as solvent. All these derivatives have categorized by melting point, FTIR, HNMR and ^{13}CNMR.

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