ISSN: 0067-2904

Synthesis and Identification of New Oxazepine Derivatives bearing Azo group in their structures

Zainab Amer Sallal[*1], Hasan Thamer Ghanem[2]
[1]Department of Chemistry, College of Science, University of Baghdad, Baghdad, Iraq.
[2]Department of Chemistry, College of Education, University of Kufa, Al-Najif, Iraq.

Abstract

In this contribution new oxazepine compounds containing azo group were preppared. In the firststep,4-(dimethylamino)-3-((4-methoxy phenyl) diazenyl) benzaldehyde [Z] was synthesised by using 4-methoxyaniline. The second step was the condensation reaction between aldehyde group of the azo compound [Z] and different primary aromatic amines [4-hydroxyaniline, 4-chloroaniline and 4-amino-N-(pyrimidin-2-yl) benzenesulfonamide] to yield new azo Schiff bases compounds [A_1-A_3] respectively. In the final step, oxazepine compounds [B_1-B_3] and [B_4-B_6] were prepared from reaction imines compounds [A_1-A_3] with maleic anhydride and phathalic anhydride in dry benzene respectively. All these derivatives were characterized by melting points and FTIR spectroscopy, some of them were characterized by ^{1}H-NMR spectroscopy.

Keywords: Azo compound, Schiff base, oxazpines.

تحضير وتشخيص مشتقات جديدة للاوكسازيبين تحتوي على مجموعة الازو في تركيبها

زينب عامر صلال[*1]، حسن ثامر غانم[2]
[1] قسم الكيمياء ، كلية العلوم ، جامعة بغداد، بغداد، العراق.
[2] قسم الكيمياء ، كلية التربية للبنات ، جامعة الكوفة، النجف ، العراق.

الخلاصة

تم من خلال هذا العمل تحضير مشتقات جديدة للاوكسازيبين تحتوي على مجموعة أزو. تم في الخطوة الاولى تحضير 4-(داي مثيل أمينو)-3-((4-ميثوكسي فنيل)) داي ازو) بنزلديهايد [Z] من (4-ميثوكسي أنلين). وتم في الخطوة الثانية تكثيف بين مجموعة ألديهايد مركب الأزو [Z] وأمينات أورماتية أولية مختلفة (4-هيدروكسي إنلين و 4- كلورو أنلين و 4-إمينو-N-(بيرمدين-2-ايل) بنزين سلفونأمايد) بوجود الأيثانول المطلق بغرض الحصول على مشتقات ازو لقواعد شف الجديدة [A_3-A_1] على التوالي. أما الخطوة الأخيرة فتتضمن تحضير المركبات [B_3-B_1] و [B_6-B_4] من تفاعل المركبات الامينية [A_3-A_1] مع إنهدريد المالك وإنهدريد الفثاليك في البنزين الجاف على التوالي. وتم تشخيص جميع المركبات المحضرة بوساطة درجات الأنصهار ومطيافية الأشعة تحت الحمراء والبعض منها تم تشخيصه بوساطة مطيافية الرنين النووي المغناطيسي ألبروتوني.

*Email: zainabamer34@yahoo.com

Introduction

Aliphatic azo compound, like azobisisobutylonitrile (AIBN), can be used as radical initiators in polymerization of alkenes to make plastics [1]. Aromatic azo compounds are used as acid-base indicators such as methyl red, methyl orange and Congo red [2]. Mkpenie et al. [3] have prepared 1-(4-methylphenylazo)-2-naphtol and study its inhibition like *E.coli* and *S.aureus*. Schiff bases are important intermediates for synthesis of some bioactive compounds [4]. Furthermore , they are reported to show a variety of interesting biological actions, including antibacterial[5, 6], antifungal [7] anticonvulsant [8], anti-inflammatory [9] and antitubercular [10].

Oxazepine is non-homologous seven member ring that contains two heteroatom (Oxygen and Nitrogen). Oxazepine and their derivatives have some important biological pharmacological activities [11] such as enzyme inhibitors [12], analgesic [13], antidepressant [14], and psychoactive drugs [15]. Amoxapine is a group of drugs called tricyclic antidepressants. It is used to treat symptoms of depression, anxiety and agitation [16].

Experimental

1. All using materials supplied from merck and BDH chemical company.
2. Melting points used electrothermal melting point apparatus, UK.
3. FTIR spectra used on SHIMADZU FT.IR-8400S infrared, Kufa University.
4. ^{1}H-NMR spectroscopy, operate at 300 MH_Z with tetramethylsilane as internal standard, measurements were made on chemistry department, AL-Al-Bayt University, Jordan.

Preparation Methods

1- Synthesis of 4-(dimethylamino)-3-((4-methoxyphenyl)diazenyl) benzaldehyde [Z] .

4-Methoxyaniline (1.28 gm , 0.01 mole) was dissolved in (2 ml) of concentrated hydrochloric acid and (20 ml) of distilled water. The solution was cold at (0 ^{0}C) in ice-water bath. The sodium nitrite (0.69 gm, 0.01 mole) was dissolved in (10 ml) of distilled water and added drop wise to the solution with stirring. 4-N,N-dimethylaminobenzaldehyde (1.49 gm, 0.01 mole) was dissolved in (20 ml) of ethanol and (5 ml) of (10 %) sodium hydroxide and cooled to (0 ^{0}C), added to the diazonium solution in drope wise and stirring at (0 ^{0}C) for 2 hours for obtaining the coupling agent. The result of the orange compound was precipitated, filtered and washed well with ethanol. The m.p.=69 ^{0}C and R_F=0.72 by using two solvent (benzene: methanol, 3 : 2).

2- Synthesis of azo Schiff bases derivatives [A_1-A_3]

A mixture of ethanol (20 ml) containing two drops of glacial acetic acid was added to azo benzaldehyde derivative [Z] of (1.42 gm, 0.005 mole) then adding (0.005 mole) of a primary aromatics amines (4-hydroxyaniline, 4- chloroaniline and 4-amino-N-(pyrimidin-2-yl) benzenesulfonamide). The reaction mixture was refluxed with stirring for (3-4) hours, then, the reaction was complete and monitered by using TLC (ethyl acetate: toluene, 1 : 1). The mixture allowing to cool at room temperature and recrystallized from ethanol.

3- Synthesis of 2-(4-(dimethylamino)-3-((4-methoxyphenyl)diazenyl) phenyl)-3-(aryl)-2-hydro-1,3-oxazepine-4,7-dione [B_1-B_3] and Synthesis of 2-(4-(dimethylamino)-3-((4-methoxyphenyl)diazenyl)phenyl)-3-(aryl)-2-hydrobenzo[e]-1,3-oxazepine-4,7-dione[B_4-B_6]:

A mixture of azo Schiff bases derivatives [A_1-A_3] (0.001 mole) with (0.001 mole) of malic anhydride and phthalic anhydride respectively in (20 ml) of dry benzene, was refluxed for (5-7) hours for compounds [B_1-B_3] and (6-8) hours for compounds [B_4-B_6], then, recrystallization was done with dry 1,4-dioxan. Table-1 shows the physical properties of the prepared compounds.

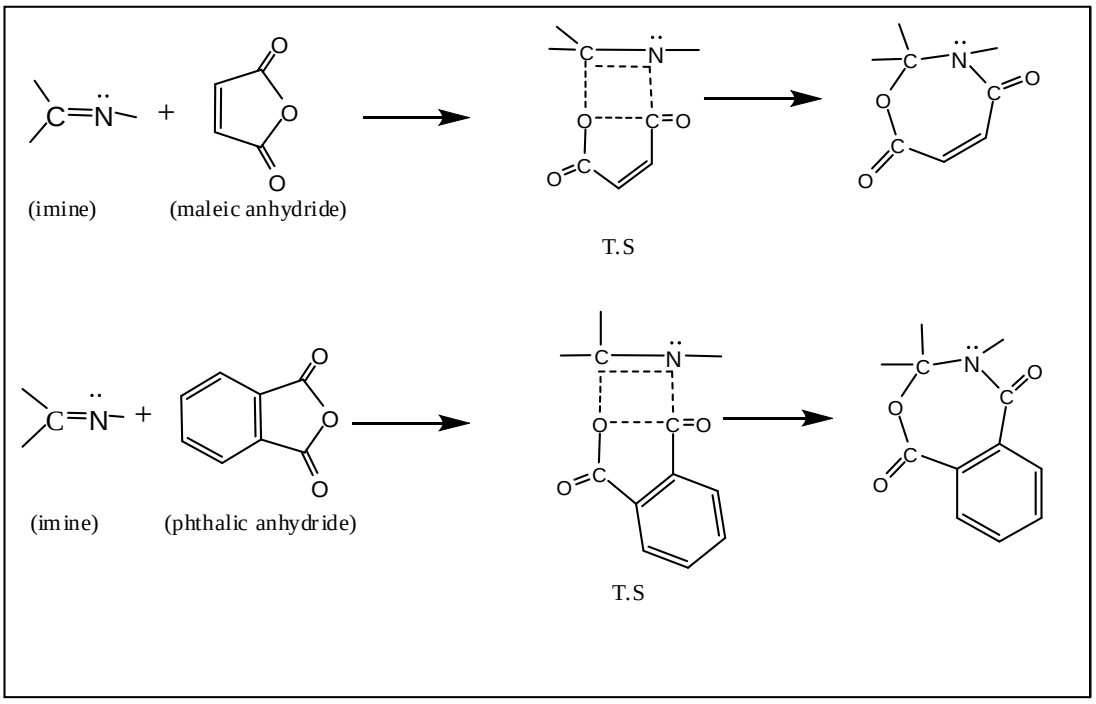
Table 1- the physical properties of the compounds [A_1-A_3] and [B_1-B_6]

Comp. no.	Molecular formula	M.Wt g/mole	M.P. ^{0}C	Yield %	R_F
A_1	$C_{22}H_{22}N_4O_2$	374	236	71	0.78
A_2	$C_{22}H_{21}N_4OCl$	392.5	137	65	0.71
A_3	$C_{26}H_{25}N_7O_3S$	515	221	54	0.82

B_1	$C_{26}H_{24}N_4O_5$	472	165	41	0.83
B_2	$C_{26}H_{23}N_4O_4Cl$	490.5	208	52	0.59
B_3	$C_{30}H_{27}N_7O_6S$	613	197	55	0.75
B_4	$C_{30}H_{26}N_4O_5$	522	108	85	0.71
B_5	$C_{30}H_{25}N_4O_4Cl$	540.5	214	48	0.54
B_6	$C_{34}H_{29}N_7O_6S$	663	188	46	0.84

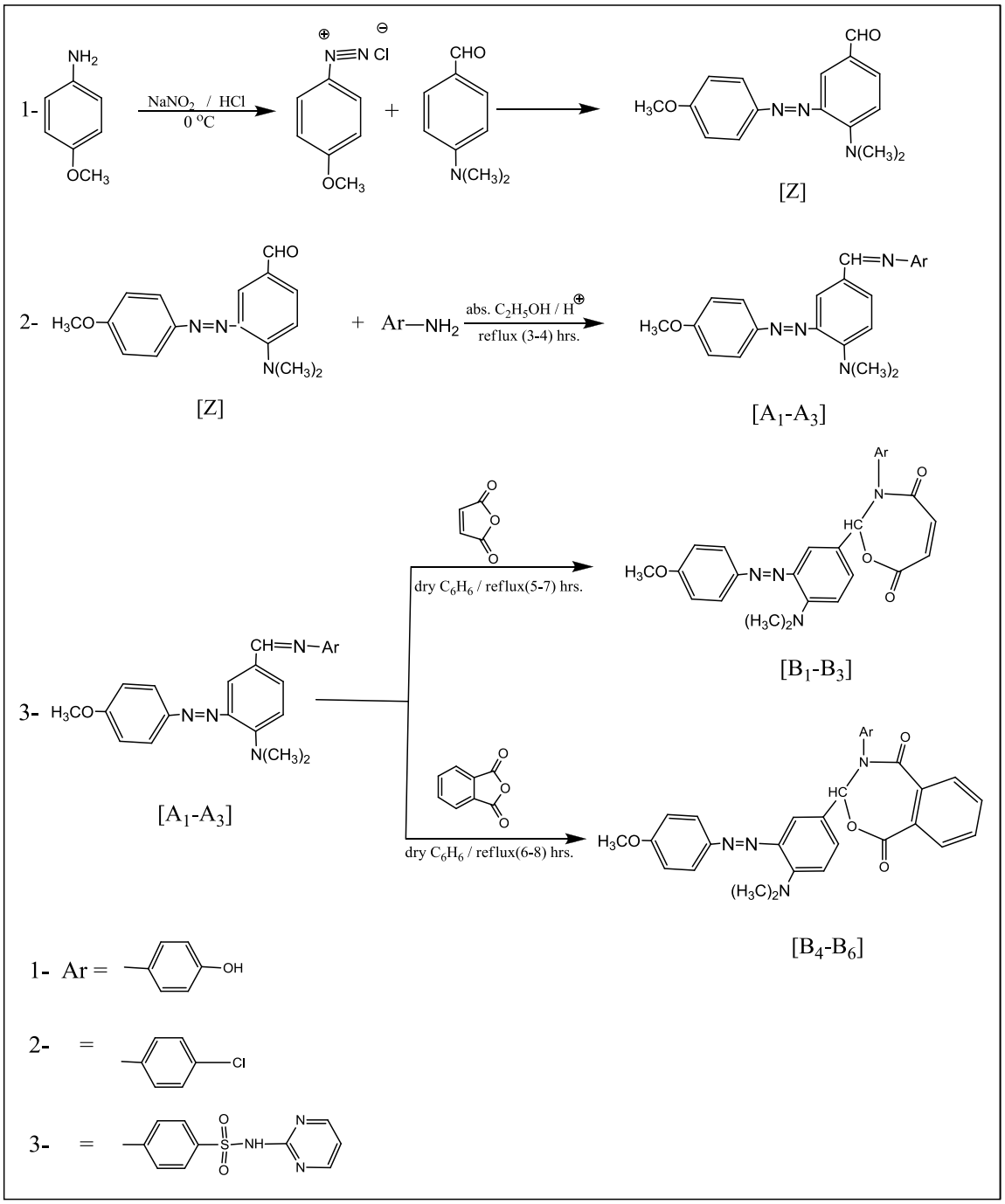
Result and Discussion

The coupling reaction [17] between diazonium salt with 4-N,N-dimethylamino benzaldehyde to produce 4-(dimethylamino)-3-((4-methoxy phenyl)diazenyl) benzaldehyde [Z]. Azo Schiff bases [A_1-A_3] were synthesized by condensation of equimolar quantity of aromatic primary amines (4-hydroxyaniline, 4- chloroaniline and 4-amino-N-(pyrimidin-2-yl) benzenesulfonamide) with azo benazldehyde derivative [Z]. Apericyclic reaction [18] is one that occurs by a concerted process through a cyclic transitionstate. The word concerted means that all bonding changes occur simultaneously; no intermediates are involved. Pericyclic reaction represents an important class of concerted (single step) processes involving Π-systems, a concerted rearrangement of the electrons takes place that causes σ and Л-bonds break and form to simultaneously. A pericyclic reactions, between imine groups of azo Schiff bases [A_1-A_3] as two-membered components and cyclic acid anhydride [maleic anhydride and phthalic anhydride] as five-membered components in dry benzene, were synthesis compounds [A_4-A_6] and [A_7-A_9] [19] respectively.



Scheme 1 - Mechanism of synthesis 1, 3-oxazepine.

The structures of all synthesis compounds were shown in scheme [2].



Scheme 2

The FTIR spectra of compound Z showed a disappearance of two absorption bands at (3423, 3348) cm^{-1} respectively belonging to the stretching vibrations of ($-NH_2$) of 4-methoxyaniline with in appearance of strong and sharp absorption band at 1660 cm^{-1} owing to (C=O) of aldehyde group [20], 3000 cm^{-1} for (C-H) aromatic stretching, 2910 cm^{-1} for (C-H) aliphatic stretching and weak bands at (2821, 2732) cm^{-1} attributed to (C-H) aldehyde group, showed 1548 cm^{-1} for (N=N) group, absorption band at 1232 cm^{-1} owing to (C-O) asymmetric stretching vibration of ether, 1600 cm^{-1} belonging to (C=C) stretching vibration of aromatic rings, absorption bands at (813, 727) cm^{-1} owing to the (C-H) aromatic out of plane and 1371 cm^{-1} attributed to the ($-N(CH_3)_2$) stretching of aromatic group [21].

The FTIR spectra of compounds [A_1-A_3] showed disappearance of two bands at (3425, 3340) cm^{-1} belong to the symmetric and asymmetric stretching vibrations of ($-NH_2$) groups of aromatic amines,

disappearance of the strong band at 1660 cm^{-1} for (C=O) of aldehyde group, appearance of the stretching vibration between (1600-1608) cm^{-1} for (C=N) of imine group[22], (1363-1367) cm^{-1} vibration of the ($-N(CH_3)_2$) aromatic group and (1228-1270) cm^{-1} belong to stretching vibration of (C-O) ether group.

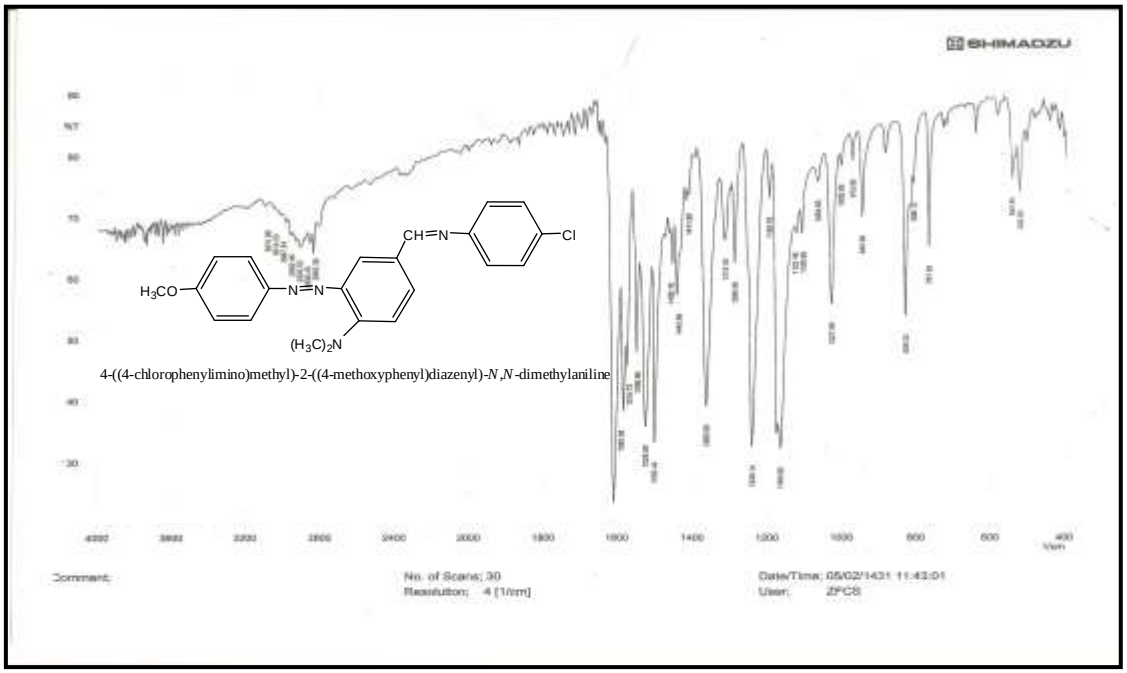


Figure1- FTIR spectra of compound [A_2].

The FTIR spectra of the compounds [B_1-B_3] and [B_4-B_6] showed a disappearance of absorption band at (1600-1608) cm^{-1} of (C=N) imine group, appearance of a strong band at (1695-1718) cm^{-1} for (C=O) lactone group [21], appearance of a strong band at (1633-1660) cm^{-1} for stretching vibration of the (C=O) lactam group [21]. It was noticeable that the absorption band of the stretching vibration of the (C-H) benzylic was rather high. This shift toward higher frequency explained for linking the benzylic carbon to the three electron-withdrawing groups (phenyl, oxygen and nitrogen) [23].

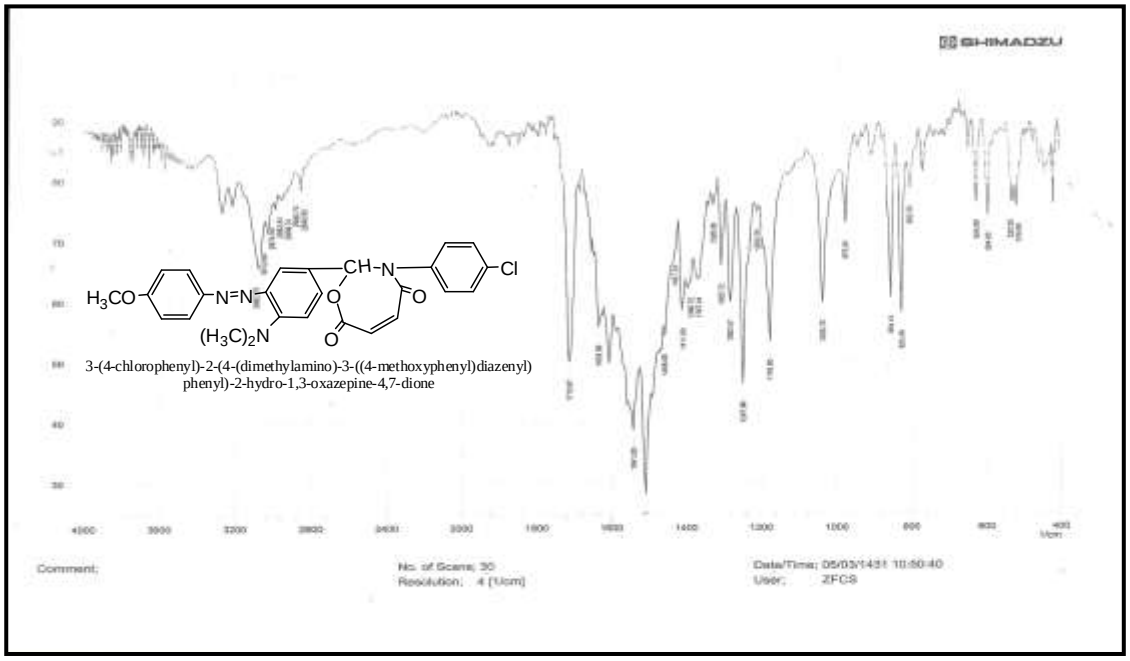


Figure 2- FTIR spectra of compound [B_2].

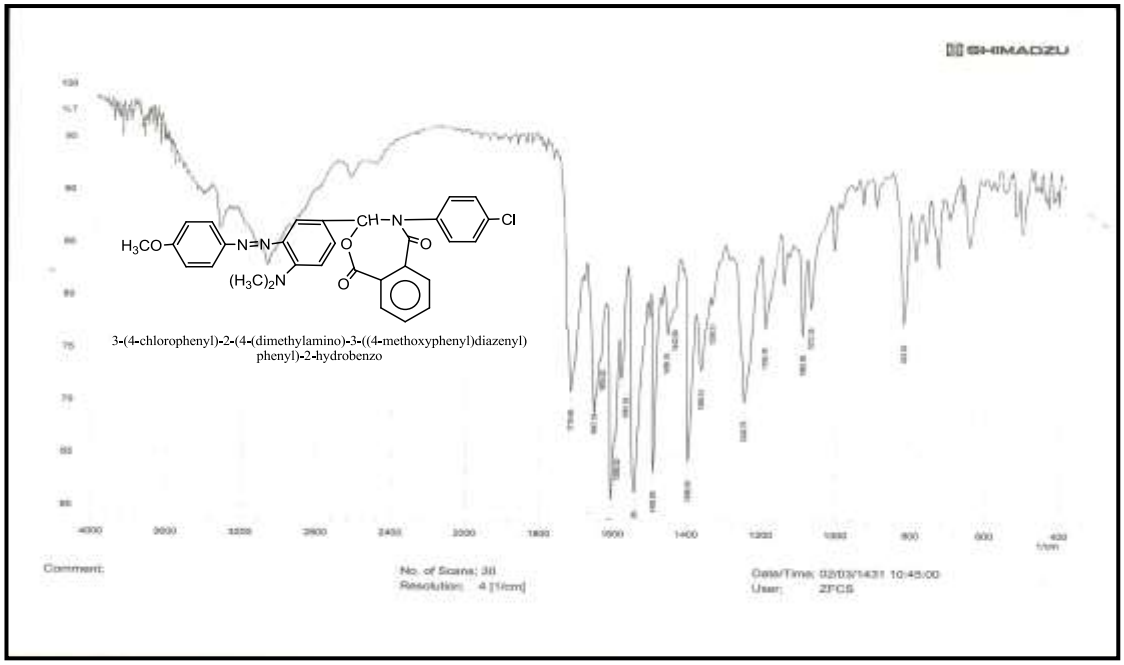


Figure 3-FTIR spectra of compound [B_5].

Figure-4 showed the ^{1}H-NMR spectra, of compound [B_2] using (C_6D_6 as a solvent): singlet signal at δ(1.81 ppm) attributed to the methyl protons of (-N(CH_3)$_2$) group, singlet signal at δ(3.83 ppm) attributed to the methyl protons of (O-CH_3) group while the multiplet signal at δ(6.8-7.2)ppm attributed to the aromatic protons of the three phenyl rings and the doublet signal at δ(7.7-7.79)ppm attributed to protons of seven membered ring of oxazepine (CH=CH). Finally the singlet signal at δ(9.7 ppm) attributed to the proton of oxazepine (O-CH-N) group[24].

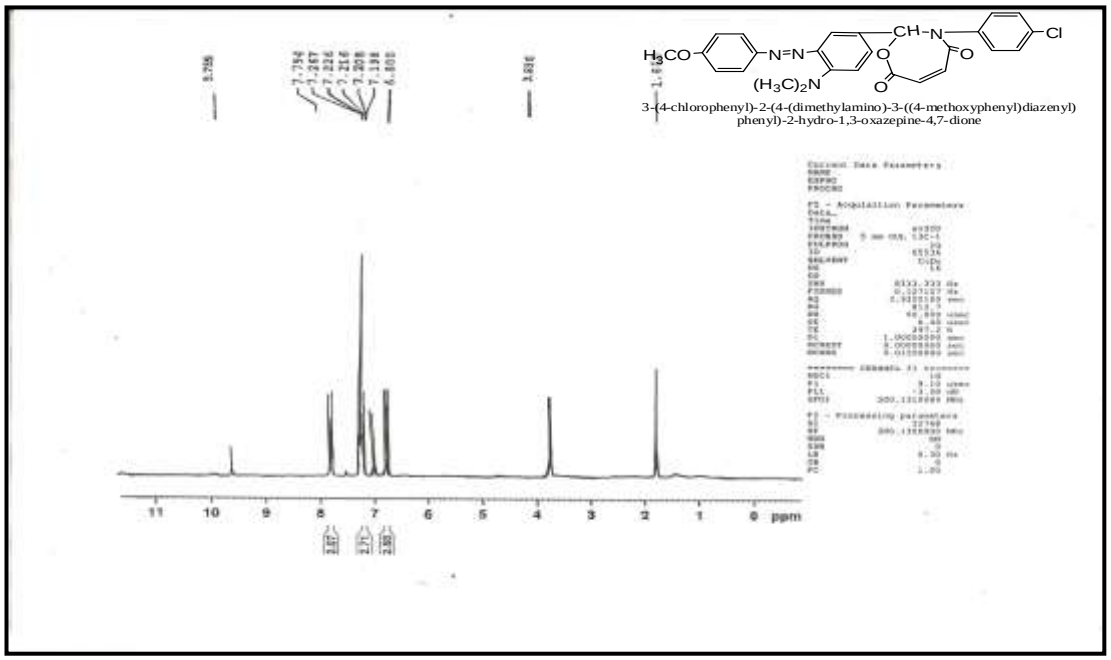


Figure 4-^{1}H-NMR spectra of compound [B_2].

The ^{1}H-NMR spectra, of compound [B_5] Figure-5 showed the following characteristic chemical shifts using (C_6D_6 as a solvent): singlet signal at δ(1.83 ppm) attributed to the methyl protons of (-N(CH_3)$_2$) group, singlet signal at δ(3.93 ppm) attributed to the methyl protons of (O-CH_3) group,

multiplet signal at δ(6.87-7.21)ppm attributed to aromatic protons of the four phenyl rings and the singlet signal at δ(9.71 ppm) attributed to the proton of oxazepine (O-CH-N) group.

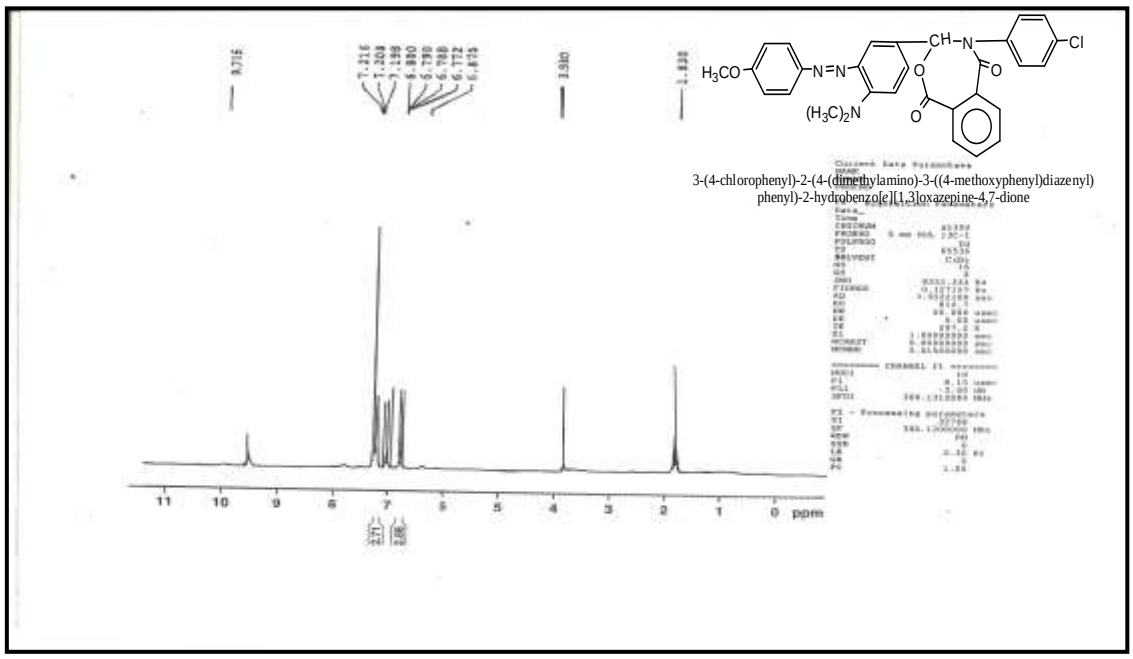


Figure 5-^{1}H-NMR spectra of compound [B_5].

Table 2 - The FTIR spectral data for compounds [A_1-A_3] and [B_1-B_6] (cm^{-1}).

Comp. no.	υ (C-H) Str. Benzylic	υ (C-H) Str. Aromatic	υ (C-H) Str. Aliphatic	υ (C=N) Str. Imine	υ (C=O) Str. Lactone	υ (C=O) Str. Lactam	υ (C=C) Str. Aromatic	υ (C-O) Str. Lacone	4-N(CH_3)$_2$ Str. Aromatic	Others
A_1	-	3006	2891	1600	-	-	1591	-	1373	υ (O-H) Str. : 3398
A_2	-	3031	2933	1608	-	-	1585	-	1363	υ (C-Cl) Str. : 767
A_3	-	3099	2912	1602	-	-	1600	-	1361	υ(N-H) Str. : 3282
B_1	3240	3010	2906	-	1712	1652	1600	1251	1367	υ (O-H) Str. : 3429
B_2	3258	3062	2840	-	1712	1633	1596	1247	1367	υ (C-Cl) Str. : 825
B_3	3260	3031	2839	-	1695	1660	1600	1247	1303	υ(N-H) Str. : 3282
B_4	3244	3130	2968	-	1718	1652	1600	1247	1369	υ (O-H) Str. : 3319
B_5	3235	3067	2910	-	1718	1647	1600	1249	1365	υ (C-Cl) Str. : 810
B_6	3246	3072	2906	-	1706	1654	1602	1249	1369	υ(N-H) Str. : 3280

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