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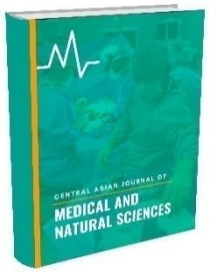

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Synthesis and Characterization of the 1,3- Oxazepine Derivatives

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Abstract: The Study Included The synthesis of some new heterocyclic compounds such as 1,3-Oxazepines from reaction between malic anhydride with Schiff bases in the precence of some drops of glacial acetic acid. Schiff-base (c1-c2) were prepared from the raction of aromatic aldehyde with aromatic amines and then reacted with maleic anhydride and phthalic Anhydride to produce new compounds 1,3- oxazepine derivatives The synthesized compounds have been characterization by the determination physical properties as such as m.p.c and the spectroscopy methods such as FlT-IR, 1H-NMR, 13C-NMR.

Key words: 1,3- Oxazepine, Schiff-bases, DMF, Maleic anhydride and phthalic anhydride.

INTRODUCTION

Heterocyclic chemistry is today recognized as a distinct branch of chemistry with a lengthy history, a current social context, and promising future developments. The most hetero atoms that are now understood are those of nitrogen, oxygen, and sulfur(1). Due to their use in pharmaceuticals and industrial studies, heterocyclic compounds are regarded as one of the most significant types of organic molecules.(2). Schiff bases are formed by the condensation of primary (aromatic) amines with aldehydes or ketones that contain the azomethine (imine) moiety (-CR=N-) They are regarded as versatile pharmacophores for a variety of pharmacological activities(3). in which the azomethine group has been shown to be critical to bioactivity(4). Oxazepine has a seven-member unsaturated non-homologous ring containing two heteroatoms, oxygen and nitrogen, and five carbon atoms One sort of pericyclic reaction used to make 1,3- oxazepine was the cycloaddition process (5) Oxazepine and their derivatives have some important biological pharmacological activities (6) such as enzyme inhibitors [7], anticancer, antiviral, analgesic, anticonvuls antanalgesic [8],antifungal, antidepr-essant [9] and psychoactive drug [10].

MATERIALS AND METHODS

The chemicals were 4-methoxyaniline, 4-bromobenzaldehyde, 4-nitrobenzaldehyde, maleic anhydride, phthalic anhydride were purchased from Hyperchem and Merck. Frigidaire Company purchased the microwave that was used in the experiments. All melting points were determined using Stuart SMP3 in an open capillary tube and are uncorrected. The silica Gel used for TLC was purchased from Merk. TLC spots were visualized using iodine. FT-IR spectra for the synthesized compounds

were recorded on KBr disc in the region (600-4000) cm-1by using "Perkin Elmer, tensor 27 (Bruker)" in the Labs of chemistry department , Science College, Thi- Qar University. Proton Nuclear magnetic spectra ^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker by College of Education for Pure Sciences at Basrah University.

General Procedure for the preparation of imines c1-c2

Preparation of imines c1-c2

In general, imines c1-c2 were prepared by refluxing 0.001 mol amine, 0.001 mol aldehyde and 5 drops of acetic acid in ethanol (20 mL) at 70 ℃ for 2-5h with stirring. The progress of the reaction was followed by TLC. After completion of the reaction, the solvent evaporated and the product was recrystallized from a suitable solvent[11-12]. The physical data of imines c1-c2 and the reactants are given below table 1.

(E)-1-(4-bromophenyl)-N-(4-methoxyphenyl)methanimine (c1)

Compound (c1) was prepared by the reaction of 4-methoxyaniline (1g, 0.008 mole) with 4-bromobenzaldehyde (1.47 g, 0.008 mole). yield = 89%, m.p =133-134 ^{o}C IR (KBr disk): 1621 cm-1 (C=N). crystalline white solid.

(E)-N-(4-methoxyphenyl)-1-(4-nitrophenyl)methanimine (c2)

Compound (c2) was prepared by the reaction of 4-nitrobenzaldehyde (1 g, 0.006 mole) with 4-Methoxybenzaldehyde (0.8g, 0.006mole). yield = 87%, m.p =122-123^{0}C IR (KBr disk): 1623 cm-1 (C=N).,crystalline white solid.

Table 1: Physical Properties of Imine(a_1-a_4).

Imines(a1-b4)	M.P °C	Yield %	Color
C1	133-134	89	white
C2	122-123	87	orange

General Procedure for the preparation of imines (d1-d3)

Preparation of 1,3- oxazepine compounds(d1-d3)

In general, 1,3- oxazepine compounds (d1-d3) were prepared by microwave 0.01 mol Schiff bases(a1-a4), 0.01 mol maleic anhydride and phthalic anhydride and 3 drops of acetic acid in DMF (10mL) at 50W for (30-50min) The progress of the reaction was followed by TLC. After completion of the reaction, the solvent evaporated and the product was recrystallized from a suitable solvent. The physical data of1,3- oxazepine(d1-d3) and the reactants are given below table2.

3-(4-methoxyphenyl)-2-(4-nitrophenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione (d1)

Compound (d1) was prepared by the reaction of (E)-N-(4-methoxyphenyl)-1-(4-nitrophenyl)methanimine (0.7g, 0.0029 mole) with maleic anhydride(0.28g, 0.0029 mole). yield =60%, m.p =105-106^{o}C, crystalline orange solid.FTIR (νmax. cm−1,KBr): 3031 (Ar-H), 2937 (C- H), 1709 (C=O lactone), 1598(C=O amide), , 1248 (C-N), 1252 (C-O-C) ,1514(C=C aromatic) . 1 H-NMR: 3.81 (s,3H, OCH_3) (7. 06- 8. 42ppm) (8H aromatic protones), 8.82 (s,1H, ,O-CH-N, oxazepine ring),7.06-7.03 (2H, CH=CH, oxazepine ring). ^{13}C-NMR: (114.5,159.2 ,123.7 ,131.1,156.4, 148.4 , 129.7,129.2) (Aromatic C),159.3 (N-C=O),167.7 (O-C=O),95.8 (N-C-O),123.4,135 (aliphatic C),55.8 (-OCH_3).

3-(4-bromophenyl)-4-(4-methoxyphenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione (d2)

Compound (d2)was prepared by the reaction of (E)-1-(4-bromophenyl)-N-(4-

methoxyphenyl)methanimine (1g , 0.0034 mole) with phthalic Anhydride (0.5g, 0.0034 mole). yield =71%, m.p =126-127^{o}C, crystalline Pale green solid .

FTIR (vmax. cm−1,KBr): 3136 (Ar-H), 2986 (C- H), 1715 (C=O lactone), 1598(C=O amide), , 1248 (C-N), 1177 (C-O-C) ,1512 (C=C aromatic) . 1 H-NMR: 3.81 (s,3H, OCH_3) (6.96- 7.92 ppm) (12H aromatic protones), 8.62 (s,1H, ,O-CH-N, oxazepine ring). ^{13}C-NMR: 128.8,124,135,135.9, 114.5,158.6 ,123.7, 132, 144.1,130.6,123,132.2 (aromatic carbon),159.3 (N-C=O),167.7 (O-C=O),95.8 (N-C-O),123.4,135 (aliphatic C),55.8 (-OCH_3).

4-(4-methoxyphenyl)-3-(4-nitrophenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5 dione(d3)

Compound (d3) was prepared by the reaction of (E)-N-(4-methoxyphenyl)-1-(4-nitrophenyl)methanimine (0.6g,0.0027 mole) with phthalic Anhydride (0.34 g, 0.0027 mole). yield =65%, m.p =139-140^{o}C, crystalline orange solid . FTIR (vmax. cm−1,KBr): 2981(Ar-H), 2941 (C- H), 1714 (C=O lactone), 1600 (C=O amide), , 1303 (C-N), 1251 (C-O-C) ,1514 (C=C aromatic) . 1 H-NMR: 3.81 (s,3H, OCH_3) (7.01-8.35 ppm) (12H aromatic protones), 8.83 (s,1H, ,O-CH-N, oxazepine ring). ^{13}C-NMR: 114.5,114.8 ,123, ,123.7 , 124.8,129.2 , 129.3,130.4, 132,134.7 ,135,1157.4 (aromatic carbon),159.3 (N-C=O),167.7 (O-C=O),95.8 (N-C-O),123.4,135 (aliphatic C),55.8 (-OCH_3).

Table2: Physical Properties of 1,3- oxazepine (d1-d3).

Oxazepin(d1-d3)	M.P °C	Yield %	Color
d1	105-106	60	orange
d2	126-127	71	Pale green
d3	139-140	65	orange

RESULTS AND DISCUSSIONS.

In the present study four derivatives of 1,3- oxazepine derivatives were synthesized through the Schiff-base reaction with maleic anhydride and phthalic anhydride in the presence of glacial acetic acid as catalyst in DMF.

The IR spectra of the imines(c1-c2) in KBr disc showed absorption bond at 1621-1623 cm^{-1} corresponding to the azomethine group of imine compounds. The IR spectra of1,3- oxazepine derivatives (d1-d3) are characterized by the seven bands corresponding to the stretching vibration of the aromatic C- H(2981-3136), aliphatic C-H(2937- 2986) carbonyl lactone group (1709-1714), carbonyl amide group(1598-1600) [13-14], aromatic C=C(1512-1514),C-N(1248-1303),C-O(1177-1252) cm^{-1}. as shown in Fig(1,4 ,7)

Table (3): FT-IR spectra of 1,3- oxazepine derivatives.

Com. No.	Aromatic C-H stretching cm-1	Aliphatic C-H stretching cm-1	υ C=O cm-1 Lactone	υ C=O cm-1 amide	Aromatic C=C stretching cm-1	υ C-N cm-1	υ C-O cm-1
d1	3031	2937	1709	1598	1512	1248	1252
d2	3136	2986	1715	1598	1512	1248	1177
d3	2981	2941	1714	1600	1514	1303	1251

^{1}H-NMR spectral analysis. Some representative ^{1}H NMR spectrum of the 1,3- oxazepine derivatives (d1-d3).[15-16] The ^{1}H-NMR spectrum of compound (d1) showed double signal at δ (7. 06– 8. 42ppm) (dd,8 H ,J=8,aromatic protones) also showed double signal at δ(7.01 -7.03ppm) (dd,2H, HC=CH) for tow protone in oxazepine ring, and showed singlet signal at δ(8.82 ppm) (s,1H,) for one protone of

carbon present in the oxazepine ring (N-CH-O), and showed singlet signal at δ(3.81 ppm)(s,3 H,) (-OCH_3). . as shown in Fig(2)

The 1H-NMR spectrum of (d2), showed double signal at δ (6.98-7.83 ppm) (d,4H,J =8, aromatic protones),δ(7.85-7.92ppm) (m,4H,aromatic protones), and showed singlet signal at δ(8.62ppm) (s,1H,) for one protone of carbon present in the oxazepine ring (N-CH-O), and showed singlet signal at δ(3.81 ppm)(s,3 H,) (-OCH_3). as shown in Fig(5)

The 1H-NMR spectrum of (d3), showed double signal at δ (7.01–7.96ppm) (d,4H,J=8, aromatic protones), δ (8.16–8.35ppm) (m,4H,aromatic protones), and showed singlet signal at δ(8.83 ppm) (s,1H,) for one protone of carbon present in the oxazepine ring (N-CH-O), and showed singlet signal at δ(3.81 ppm)(s,3H,) (-OCH_3). as shown in Fig(8)

The ^{13}C-NMR spectral data of the 1,3- oxazepine derivatives described along with syntheses of these compounds in the experimental section. The compound (d1-d3).

The 13C-NMR of compound(d1). showed chemical shifts δ(159.3 ppm) for (N-C=O), δ(167.7 ppm) for (O-C=O), δ(95.8ppm) for (O-C-N) , δ(114.5,159.2 ,123.7 ,131.1,156.4, 148.4 , 129.7,129.2 ppm)for aromatic carbon, δ(123.4,135 ppm) for alipfatic carbon, δ(55.8 ppm) for (-OCH_3).[17] as shown in Fig (3)

The 13C-NMR of compound (d2). showed chemical shifts δ(159.3 ppm) for (N-C=O), δ(167.7 ppm) for(O-C=O), δ(95.8ppm) for (O-C-N) , δ(128.8,124,135,135.9, 114.5,158.6 ,123.7, 132, 144.1,130.6,123,132.2 ppm) for aromatic carbon , δ(55.8 ppm) for (-OCH_3). as shown in Fig(6)

The 13C-NMR of compound (d3). showed chemical shifts δ(159.3 ppm) for (N-C=O), δ(167.7ppm)for(O-C=O),δ(95.8ppm)for(O-C-N) ,δ(128.9,123.7,132,135,131.1,114.5,123.4,159.2,142.5,148.6,129.2,124.8 ppm)for aromatic carbon, δ(55.8 ppm) for (-OCH_3). as shown in Fig(9)

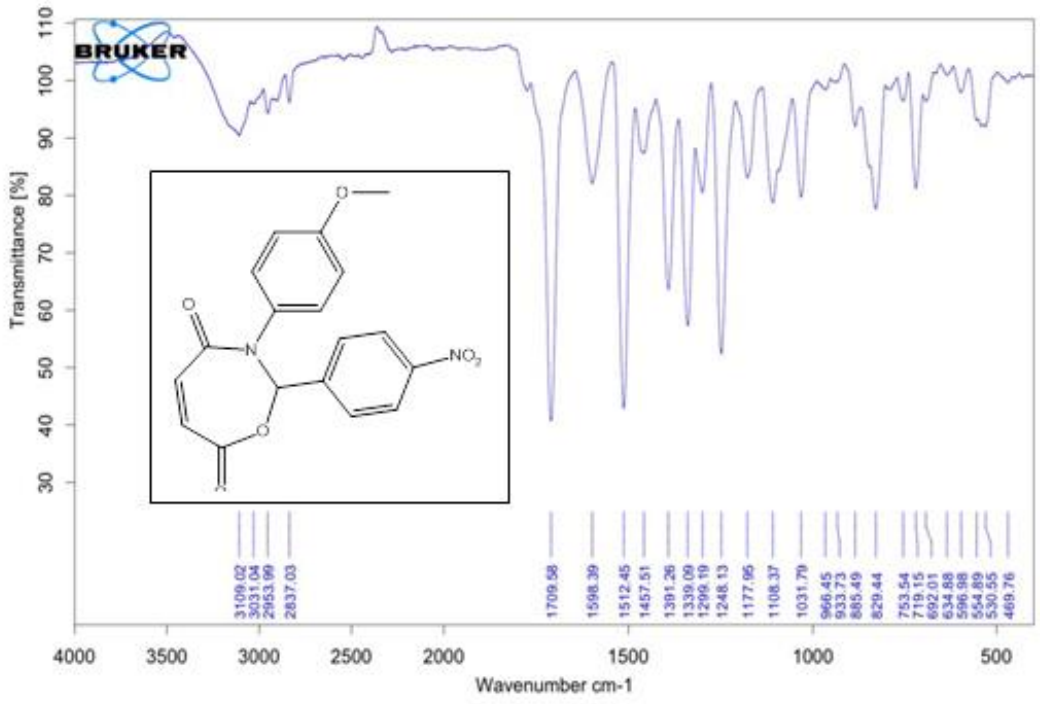
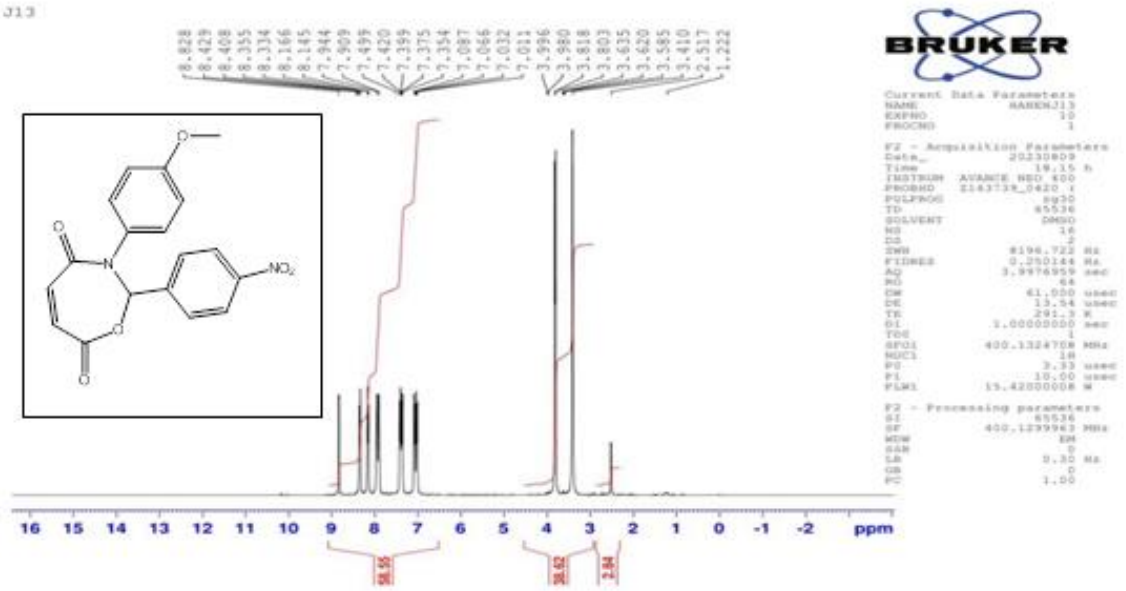
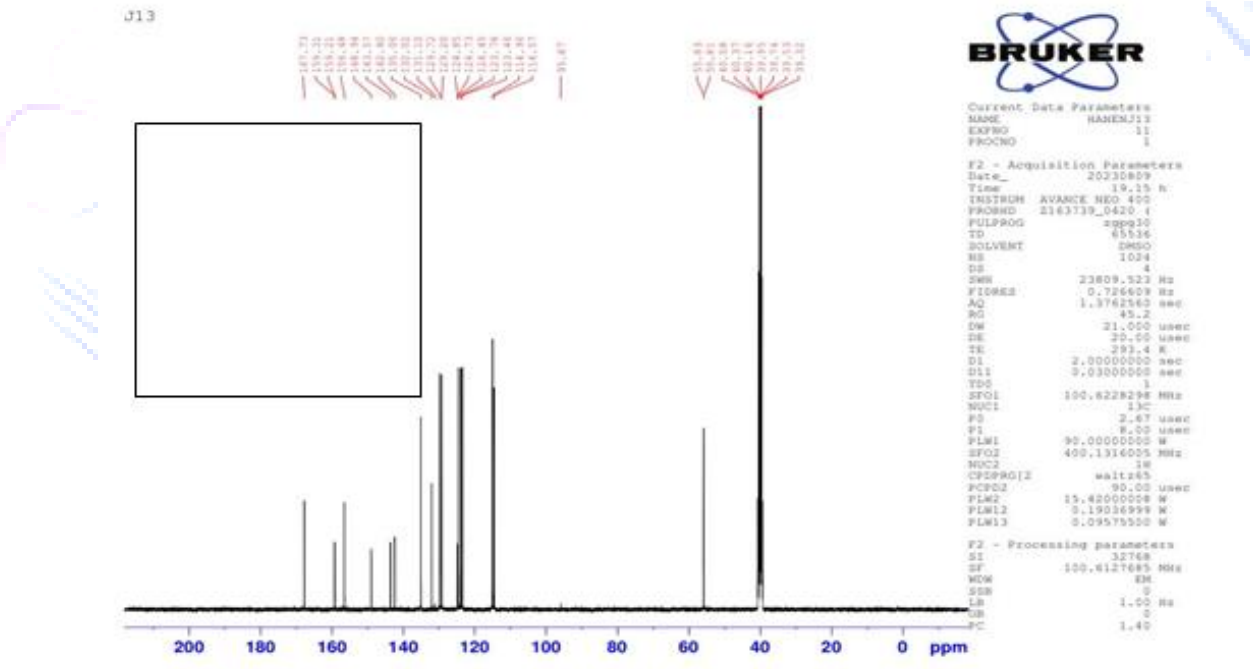


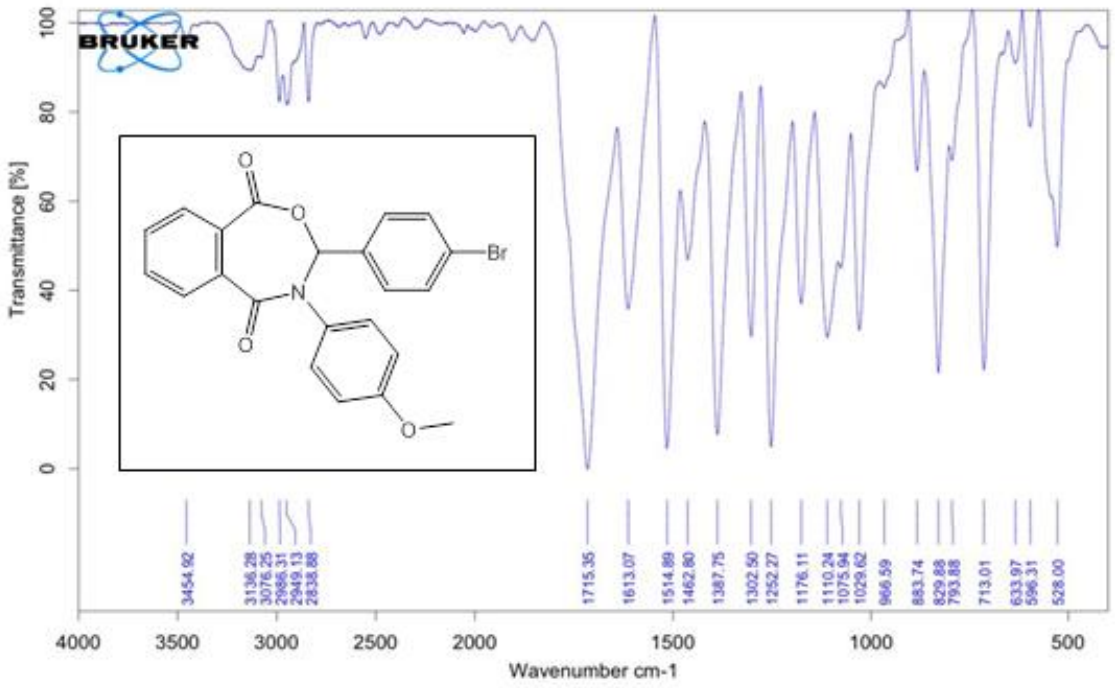
Fig (1): FT-IR spectrum of 3-(4-methoxyphenyl)-2-(4-nitrophenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione (d1)



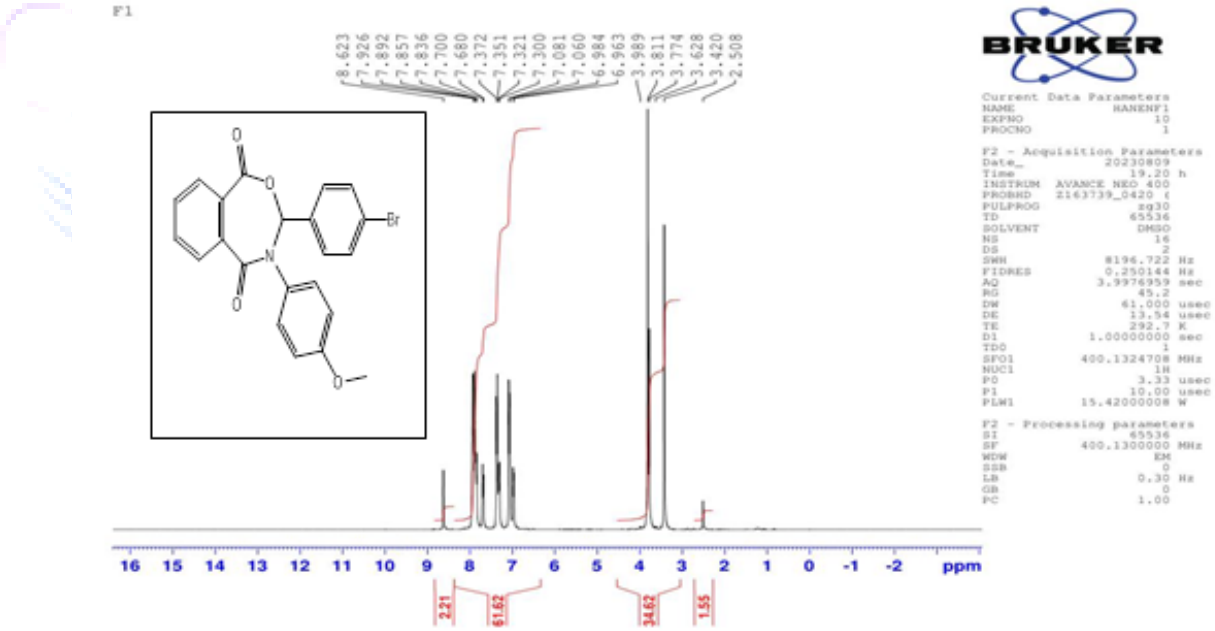
Fig(2): [1] H-NMR spectrum of 3-(4-methoxyphenyl)-2-(4-nitrophenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione (d1)



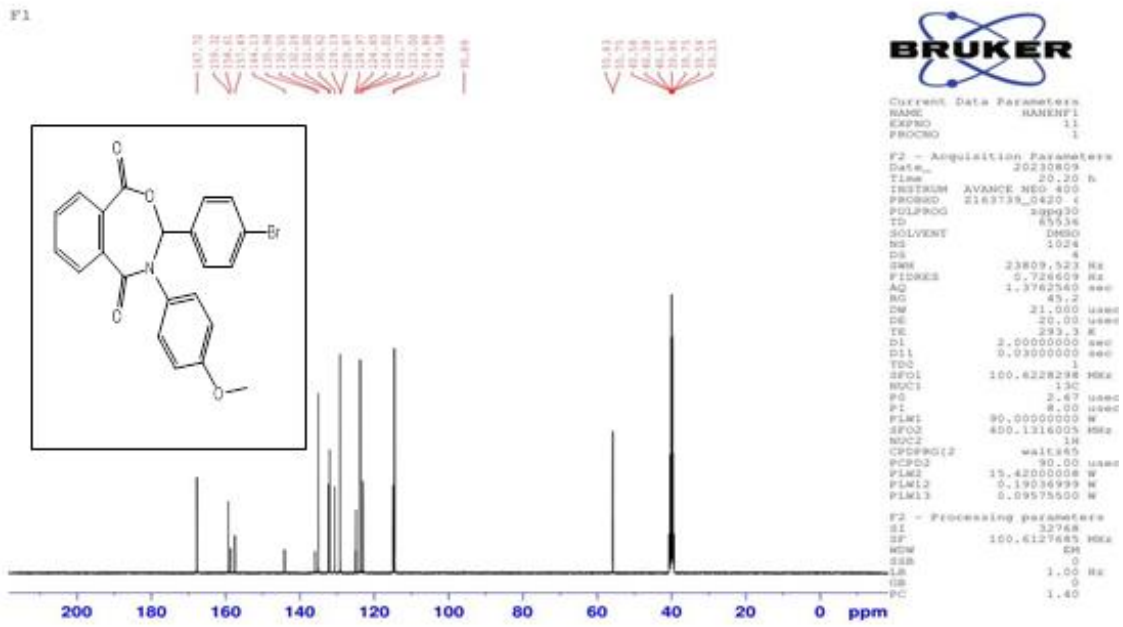
Fig(3):[13] C-NMR spectrum of 3-(4-methoxyphenyl)-2-(4-nitrophenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione (d1)



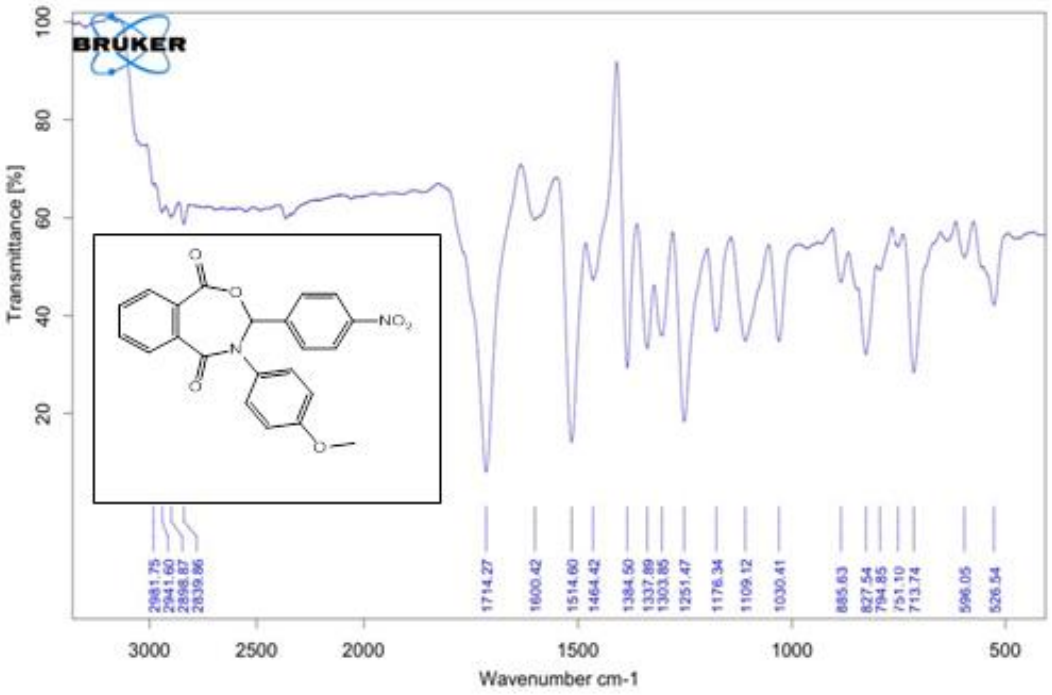
Fig(4): FT-IR spectrum of 3-(4-bromophenyl)-4-(4-methoxyphenyl)-3,4-dihydrobenzo [e][1,3]oxazepine-1,5-dione (d2)



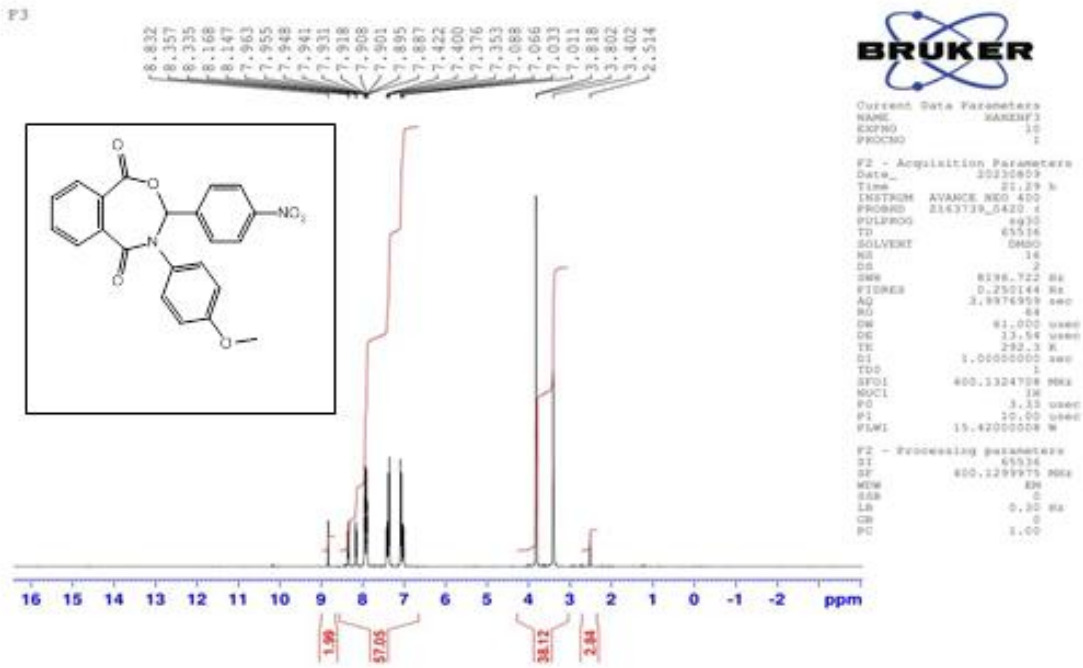
Fig(5): ^{1} H-NMR spectrum of 3-(4-bromophenyl)-4-(4-methoxyphenyl)-3,4-dihydrobenzo [e][1,3]oxazepine-1,5-dione (d2)



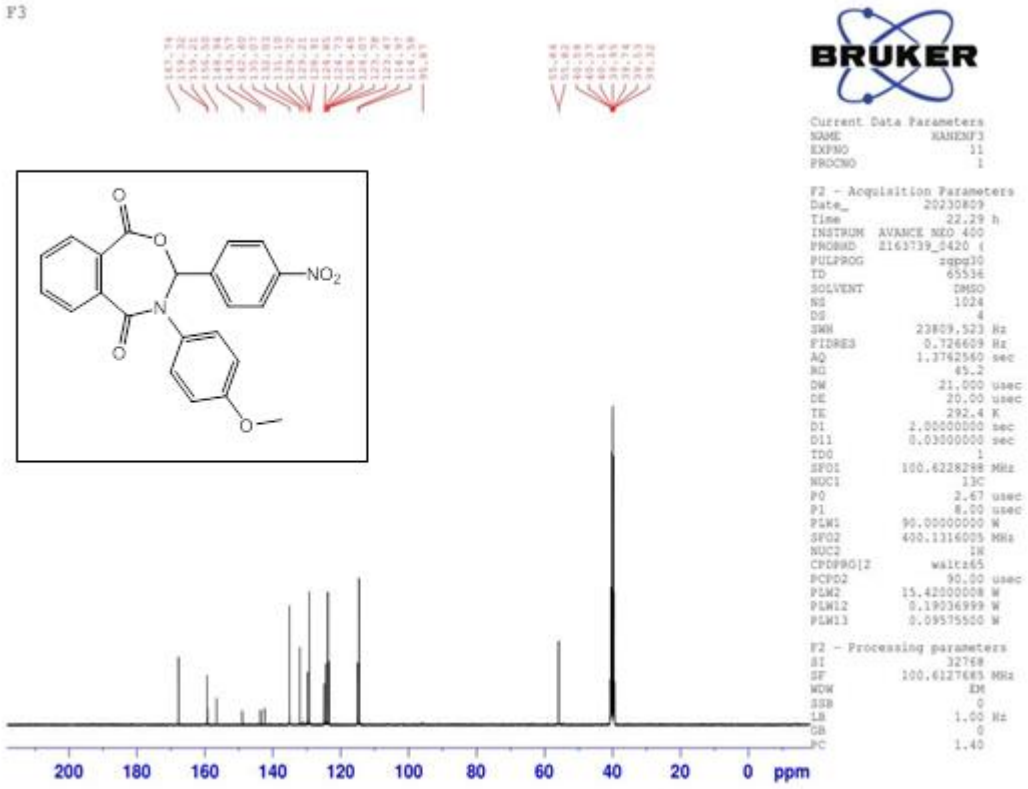
Fig(6):[13] C-NMR spectrum of 3-(4-bromophenyl)-4-(4-methoxyphenyl)-3,4-dihydrobenzo [e][1,3]oxazepine-1,5-dione (d2)



Fig(7): FT-IR spectrum of 4-(4-methoxyphenyl)-3-(4-nitrophenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione(d3)



Fig(8): [1] H-NMR spectrum of 4-(4-methoxyphenyl)-3-(4-nitrophenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione(d3)



Fig(9):[13] C-NMR spectrum of 4-(4-methoxyphenyl)-3-(4-nitrophenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione(d3)

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