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Structural Investigation of Novel Heterocyclic 1,3-oxazepine by 2DNMR

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Abstract: The complete ^{1}H and ^{13}C signals of three series novel heterocyclic 1,3-oxazepinediones analogues were achieved using two dimensional experiments (COSY, NOESY, ^{1}H-^{13}C HMQC and HMBC spectra).

Key words: 2DNMR, 1,3-oxazepinediones, COSY, NOESY, HMQC, HMBC.

INTRODUCTION

[1,3]oxazepine-diones is a seven-membered ring containing nitrogen, oxygen and two carbonyl group. Many researchers have investigated the molecular properties of the 1, 4-, 4, 1-, and 1, 5-benzoxazepines they constitute an important class of heterocyclic compounds which have many biological uses (Aiello *et al*, 2004; Audouze *et al*, 2004; Dols *et al*, 2008; Franzen *et al*, 2000; Ichikawa *et a*l, 1995; Kaneko *et al*, 2002; Liao *et al*, 1999; Ott *et al*, 2004; Serrano *et al*, 2002 and Smith *et al*, 2006). A considerable number of methods towards the formation of oxazepine ring have been reported in recent years (Bajaja *et al*, 2004 and Kamal *et al* 2008). However, convenient and efficient way to form the oxazepine rings is still preferred owing to its importance as pharmaceutical drugs and active substances in biological systems. Our interesting to modification of oxazepine core as liquid-crystalline compounds has been reported in earlier publication (Yeap *et al*, 2010). The incorporation of the heteroatoms (S, O and N) can result in significant change upon liquid-crystalline phase as the atoms thus introduced are claimed to be more polarizable than carbon (Grunanger 1991; Cristiano *et al*; 2005; Merio *et al* 2000; Demus *et al*, 1998; Haino 2004 and Zuniga *et al*, 2001).

Experimental:

The experimental part for the synthesized of three series of 1,3-oxazepin-diones and recording of all proton and carbon NMR have been reported elsewhere (Yeap *et al*, accepted). The types of compounds were shown in (Scheme 1). The ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO (for **1a-7b, 1b-7b** and **1c-7c**) at 298 K on a Bruker 400 MHz Ultrashied^{TM} FT-NMR spectrometer equipped with a 5 mm BBI inverse gradient probe. Chemicals shift were referenced to internal TMS. The concentration of solute molecules was 50 mg in 1.0 ml DMSO. Standard Bruker pulse programs (Bruker program) were used throughout the entire experiment. The spectroscopic details of NMR are summarized in Table 1.

RESULTS AND DISCUSSION

The data of the ^{1}H and ^{13}C NMR chemical shifts for title compounds in DMSO solution are listed in respective Tables 2a, 2b and 4. A complete assignment for the title compounds can be described by based on respective compounds shown in **scheme 1** in which three types of compounds have been differentiated by **a**, **b** and **c**.

The complete ^{1}H assignment of molecules of title compounds were achieved by means of proton-proton correlation methods COSY and NOESY Table 3. The COSY experiments confirm the ^{1}H-^{1}H coupling interaction in molecules. From 2D COSY spectra of title compounds all the connections between the hydrogen atoms are clearly observed. The correlations between the doublet at $\delta = 6.21$-6.26 ppm which assigned to H9 in heterocyclic ring of compounds **1a-7a** correlated with the proton H10 in the same ring which can be observed as doublet at $\delta = 6.39$-6.41 ppm. The 2D COSY spectra of compounds **1b-7b** enabled us to assign the proton triplet at $\delta = 2.25$-2.28 ppm which could be assigned to H9 in heterocyclic ring correlated with triplet at $\delta = 2.40$-2.42 ppm for proton H10. The correlation by COSY also reveals that the NMR doublet signal of aromatic protons at $\delta = 7.35$-7.88 ppm in respective compounds **1a-7a, 1b-7b** and **1c-7c**, have been

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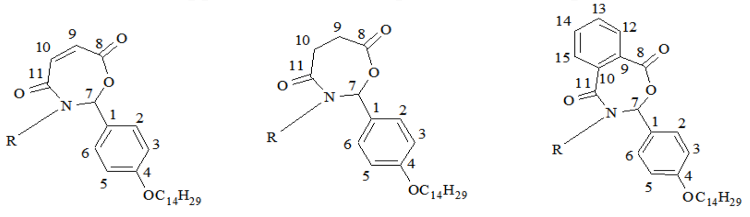
correlated with NMR doublet signal of aromatic ring protons at δ =7.10-7.43 ppm. Moreover, the aromatic ring protons adjacent with heterocyclic ring of respective compounds **1c-7c** have been confirmed by the correlation between the doublet at δ = 7.84-7.88 ppm which has been assigned to aromatic proton H12 with the triplet at δ = 7.50-7.53 ppm for aromatic ring proton H13. Similarly, the correlation between the triplet for aromatic proton H14 at δ = 7.47-7.49 ppm with the doublet at δ = 7.73-7.75 ppm was observed. This can be attributed to aromatic proton H15. In the same way, at lowerfield we can assign the proton triplet at δ = 4.03-4.09 ppm O-CH_2 of the ether linking groups which found to be correlated with the signal assigned in the region δ = 1.70-1.76 ppm for (O-$CH_2(CH_2)$). The triplet at δ = 3.00-3.17 ppm attributed to N-CH_2 has found to be correlated with signal at δ = 1.70-1.76 ppm. The COSY spectrum of compound **7a** was shown in Fig 1.



1a-7a **1b-7b** **1c-7c**

R= C_6H_{13}, C_8H_{17}, $C_{10}H_{21}$, $C_{12}H_{25}$, $C_{14}H_{29}$, $C_{16}H_{33}$, $C_{18}H_{37}$

Scheme 1: Structures of the three types of heterocyclic 1,3-oxazepindiones

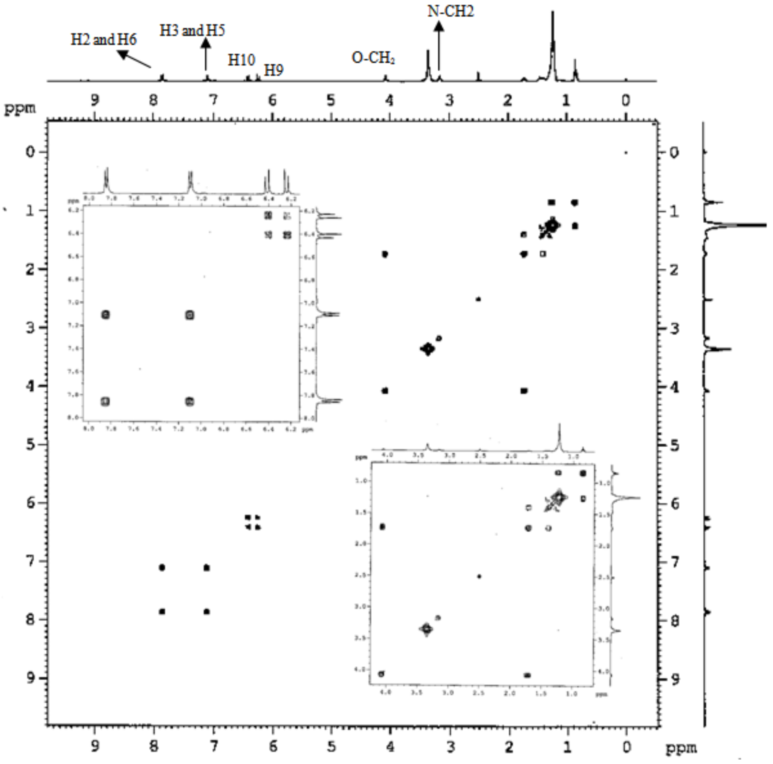


Fig. 1: ^1H-^1H connectiveiteis in the COSY spectra for compound **7a.**

The NOESY spectra of all investigated compounds allow us to assign the correlation between the aromatic ring protons at δ = 7.09-7.43 ppm with the proton triplet at δ = 4.03-4.09 ppm which can be assigned for proton C_4-OCH_2 and with doublet at δ = 7.35-7.88 ppm which can be assigned for aromatic protons H2 or (H6). In the same experiment we can observed the correlation between the triplets at δ = 3.00-3.17 ppm and δ = 4.03-4.09 ppm with multiplets at δ = 1.21-1.76 ppm. The triplet proton at δ = 0.85-0.88 ppm was also correlated with the same multiplet. The NOESY spectra of compounds **1a-7a** showed a clear correlation between the proton doublet of heterocyclic ring at δ = 6.21-6.26 ppm with proton doublet at δ = 6.39-6.41 ppm in the same ring. On the other hand, the NOESY spectra of compounds **1b-7b** assigned the correlation between the proton triplet at δ = 2.25-2.28 ppm with the proton triplet at δ = 2.40-2.42 ppm. Moreover, the NOESY spectra enabled us to assign the protons of aromatic ring adjacent to heterocyclic ring in compounds **1c-7c.** Through this technique we can observe the correlation between the doublet at δ = 7.84-7.88 ppm with the two triplets at δ = 7.50-7.53 ppm and δ = 7.47-7.49 ppm. These protons can be assigned for protons H12, H13 and H14, respectively. A doublet which located in the same aromatic ring in the region of about δ = 7.73-7.75 ppm have been correlated with the respective protons H13 and H15. Select relationship for compound **7a** in the COSY and NOESY spectrums shown in Fig 2.

The structures of the title compounds are further substantiated by the ^{13}C NMR and DEPT135 data (Table 4).

Table 1: Acquisition parameter used in the NMR measurements

Parameters	Experiment					
	^{1}H NMR	^{13}C NMR	2D COSY	2D NOESY	2D HMQC	2D HMBC
SF	400.1 MHz	100.6 MHz	400.1 MHz	400.1 MHz	F_1 =100.6 MHz F_2 =400.1 MHz	F_1 =100.61MHz F_2 =400.1 MHz
SW	10ppm	180 ppm	10 ppm	10 ppm	F_1 = 180 ppm F_2 = 10 ppm	F_1 =180 ppm F_2 =10 ppm
PW	8.3 μs (30^0 flip angle)	20.0 μs (90^0 flip angle)	8.3 μs (90^0 flip angle)	8.3 μs (90^0 flip angle)	8.3 μs (90^0 flip angle)	8.3 μs (90^0 flip angle)
AQ	4.0 s	1.3 s	0.3 s	0.3 s	0.09 s	0.4 s
D1	1.0 s	2.0 s	2.0 s	2.0 s	1.0 s	1.0 s
NS	16	20 000	16	32	88	92
TD	66 k	66 k	F_1 = 256 F_2 = 2048	F_1 = 256 F_2 = 2048	F_1 = 512 F_2 = 1024	F_1 = 512 F_2 = 4096

- Abbreviations: F_1, ^{13}C Channel (except 2D COSY where F_1 and F_2 are ^{1}H channel); SF. spectrometer frequency; SW, spectral width; AQ , acquisition time; DI, relaxation delay; NS, number ; TD, number of data point .

Table 2(a): ^{1}H NMR chemical shift (ppm) of compounds **1a-7a** and **1b-7b**.

Compounds	n	H2 and H6	H3 and H5	H7	H9	H10	C_4-OCH_2	N-CH_2	OCH_2-$(CH_2)_2$-$(CH_2)_{13}$* NCH_2- $(CH_2$-$CH_n)^+$	CH_3
1a	3	7.83 (d, J=8.12 Hz)	7.11 (d, J=8.36 Hz)	9.85 s	6.22 (d, J=12.48 Hz)	6.41 (d, J=12.60 Hz)	4.05 t	3.15 t	1.75-1.24 m	0.87 t
2a	5	7.82 (d, J=8.17 Hz)	7.10 (d, J=8.34 Hz)	9.85 s	6.23 (d, J=12.51 Hz)	6.40 (d, J=12.56 Hz)	4.04 t	3.15 t	1.74-1.23 m	0.86 t
3a	7	7.85 (d, J=8.20 Hz)	7.12 (d, J=8.39 Hz)	9.87 s	6.26 (d, J=12.55 Hz)	6.40 (d, J=12.54 Hz)	4.06 t	3.16 t	1.76-1.23 m	0.86 t
4a	9	7.82 (d, J=8.15 Hz)	7.11 (d, J=8.34 Hz)	9.85 s	6.21 (d, J=12.42 Hz)	6.42 (d, J=12.59 Hz)	4.03 t	3.14 t	1.75-1.22 m	0.85 t
5a	11	7.81 (d, J=8.14 Hz)	7.12 (d, J=8.40 Hz)	9.84 s	6.20 (d, J=12.39 Hz)	6.39 (d, J=12.50 Hz)	4.04 t	3.15 t	1.73-1.22 m	0.86 t
6a	13	7.80 (d, J=8.11 Hz)	7.10 (d, J=8.36 Hz)	9.85 s	6.23 (d, J=12.48 Hz)	6.40 (d, J=12.52 Hz)	4.05 t	3.15 t	1.72-1.22 m	0.85 t
7a	15	7.85 (d, J=8.18 Hz)	7.43 (d, J=8.55 Hz)	9.85 s	6.24 (d, J=12.52 Hz)	6.41 (d, J=12.57 Hz)	4.05 t	3.16 t	1.71-1.21 m	0.85 t
1b	3	7.86 (d, J=8.64 Hz)	7.12 (d, J=8.69 Hz)	9.85 s	2.27 (t, J=7.09 Hz)	2.41 (t, J=7.18 Hz)	4.06 t	3.01 t	1.70-1.21 m	0.86 t
2b	5	7.87 (d, J=8.66 Hz)	7.13 (d, J=8.69 Hz)	9.86 s	2.27 (t, J=7.09 Hz)	2.40 (t, J=7.16 Hz)	4.07 t	3.01 t	1.71-1.22 m	0.87 t
3b	7	7.86 (d, J=8.64 Hz)	7.11 (d, J=8.68 Hz)	9.86 s	2.28 (t, J=7.08 Hz)	2.40 (t, J=7.16 Hz)	4.07 t	3.02 t	1.71-1.23 m	0.86 t
4b	9	7.88 (d, J=8.65 Hz)	7.12 (d, J=8.69 Hz)	9.85 s	2.27 (t, J=7.07 Hz)	2.41 (t, J=7.17 Hz)	4.06 t	3.01 t	1.72-1.22 m	0.86 t
5b	11	7.85 (d, J=8.64 Hz)	7.10 (d, J=8.66 Hz)	9.84 s	2.26 (t, J=7.07 Hz)	2.42 (t, J=7.19 Hz)	4.06 t	3.02 t	1.71-1.22 m	0.86 t
6b	13	7.86 (d, J=8.64 Hz)	7.11 (d, J=8.68 Hz)	9.85 s	2.25 (t, J=7.06 Hz)	2.41 (t, J=7.17 Hz)	4.05 t	3.00 t	1.72-1.23 m	0.86 t
7b	15	7.88 (d, J=8.66 Hz)	7.13 (d, J=8.69 Hz)	9.86 s	2.26 (t, J=7.07 Hz)	2.41(t, J=7.16 Hz)	4.06 t	3.01 t	1.71-1.22 m	0.85 t

* OCH_2-$((CH_2)_2$-$(CH_2)_{13})$ = the number of carbon atom in ether chain.

$^+$ NCH_2- $(CH_2$-$CH_n)$ = the number of carbon atom in aliphatic chain which adjacent with (N) in heterocyclic ring.

Table 2(b): ^{1}H NMR chemical shift (ppm) of compounds **1c-7c**

Compounds	n	H2 and H6	H3 and H5	H7	H12	H13	H14	H15	C_4-OCH_2	N-CH_2	OCH_2- $(CH_2)_2$-$(CH_2)_{13}$* NCH_2- $(CH_2$-$CH_n)^+$	CH_3
1c	3	7.35 (d, J=8.35 Hz)	7.09 (d, J=8.21 Hz)	9.84 s	7.84 (d, J=7.58 Hz)	7.51 (t, J=7.25 Hz)	7.47 (t, J=7.46 Hz)	7.74 (d, J=7.71 Hz)	4.06 t	3.14 t	1.74-1.22 m	0.85 t
2c	5	7.36 (d, J=8.38 Hz)	7.10 (d, J=8.20 Hz)	9.85 s	7.85 (d, J=7.58 Hz)	7.50 (t, J=7.24 Hz)	7.48 (t, J=7.46 Hz)	7.74 (d, J=7.71 Hz)	4.06 t	3.15 t	1.74-1.21 m	0.86 t
3c	7	7.39 (d, J=8.39 Hz)	7.11 (d, J=8.21 Hz)	9.86 s	7.86 (d, J=7.60 Hz)	7.52 (t, J=7.25 Hz)	7.49 (t, J=7.44 Hz)	7.75 (d, J=7.74 Hz)	4.07 t	3.15 t	1.73-1.23 m	0.85 t
4c	9	7.39 (d, J=8.39 Hz)	7.11 (d, J=8.21 Hz)	9.85 s	7.85 (d, J=7.59 Hz)	7.52 (t, J=7.25 Hz)	7.48 (t, J=7.46 Hz)	7.74 (d, J=7.71 Hz)	4.08 t	3.15 t	1.72-1.22 m	0.87 t
5c	11	7.40 (d, J=8.48 Hz)	7.14 (d, J=8.23 Hz)	9.86 s	7.88 (d, J=7.60 Hz)	7.52 (t, J=7.25 Hz)	7.49 (t, J=7.44 Hz)	7.74 (d, J=7.71 Hz)	4.09 t	3.17 t	1.74-1.23 m	0.88 t
6c	13	7.38 (d, J=8.39 Hz)	7.11 (d, J=8.20 Hz)	9.86 s	7.86 (d, J=7.61 Hz)	7.53 (t, J=7.26 Hz)	7.48 (t, J=7.46 Hz)	7.73 (d, J=7.70 Hz)	4.08 t	3.16 t	1.73-1.23 m	0.86 t
7c	15	7.40 (d, J=8.39 Hz)	7.15 (d, J=8.22 Hz)	9.85 s	7.87 (d, J=7.59 Hz)	7.50 (t, J=7.22 Hz)	7.49 (t, J=7.44 Hz)	7.75 (d, J=7.74 Hz)	4.08 t	3.16 t	1.73-1.24 m	0.87 t

Table 3: ^{1}H-^{1}H correlation from 2D COSY and NOESY for **1a-7a, 1b-7b** and **1c-7c**

Compounds	Atom H	COSY	NOESY
1a-7a	H2 or H6	H3 or H5	H3 or H5
	H3 or H5	H2 or H5	H2 or H6, O-CH_2
	H9	H10	H10
	H10	H9	H9
	O-CH_2	O-$CH_2(CH_2)$	O-$CH_2(CH_2)$, H3 or H5
	N-CH_2	N-$CH_2(CH_2)$	N-$CH_2(CH_2)$

Table 3: Continue

1b-7b	H2 and H6	H3 or H5	H3 or H5
	H3 and H5	H2 or H5	H2 or H6 O-CH_2
	H9	H10	H10
	H10	H9	H9
	O-CH_2	O-$CH_2(CH_2)$	O-$CH_2(CH_2)$, H3 or H5
	N-CH_2	N-$CH_2(CH_2)$	N-$CH_2(CH_2)$
1c-7c	H2 or H6	H3 or H5	H3 or H5
	H3 or H5	H2 or H5	H2 or H6, O-CH_2
	H12	H13	H13, H14
	H14	H15	H15
	O-CH_2	O-$CH_2(CH_2)$	O-$CH_2(CH_2)$, H2 or H6
	N-CH_2	N-$CH_2(CH_2)$	N-$CH_2(CH_2)$

Table 4: ^{13}C NMR chemical shift (ppm) of compounds **1a-7a, 1b-7b** and **1c-7c**

Compounds	C1	C2, C6	C4	C3, C5	C7	C8	C9	C10	C11	C_4-OCH_2	N-CH_2	$(CH_2)_2$-$(CH_2)_{13}$* NCH_2- $(CH_2$-$CH_n)^+$	CH_3
1a	130.35	132.57	164.41	115.80	90.06	166.05	132.62	130.87	166.29	68.89	39.70	22.98-32.11	14.66
2a	130.35	132.56	164.37	115.79	90.12	166.04	132.62	130.90	166.24	68.90	39.70	22.99-32.17	14.61
3a	130.36	132.59	164.50	115.71	90.06	166.06	132.64	130.88	166.22	68.88	39.74	22.96-32.16	14.62
4a	130.36	132.57	164.32	115.90	90.05	166.05	132.64	130.89	166.25	68.89	39.73	22.97-32.12	14.59
5a	130.35	132.55	164.61	116.05	90.00	166.09	132.65	130.88	166.23	68.90	39.73	22.99-32.18	14.65
6a	130.34	132.56	164.41	116.09	90.05	166.10	132.66	130.90	166.24	68.92	39.74	23.07-32.16	14.68
7a	130.33	132.57	164.61	115.84	90.06	166.11	132.64	130.89	166.25	68.90	39.73	23.07-32.19	14.68
1b	130.05	132.76	164.32	115.72	90.10	171.12	29.33	27.81	174.52	68.88	39.35	22.91-32.31	14.70
2b	130.06	132.77	164.33	115.71	90.11	171.11	29.32	27.82	174.50	68.89	39.33	22.90-32.33	14.72
3b	130.00	132.75	164.34	115.70	90.10	171.12	29.32	27.80	174.52	68.90	39.36	22.92-32.34	14.73
4b	130.06	132.77	164.32	115.72	90.12	171.11	29.31	27.82	174.51	68.91	39.33	22.91-32.35	14.73
5b	130.06	132.76	164.33	115.71	90.11	171.13	29.33	27.82	174.50	68.92	39.37	22.98-32.39	14.75
6b	130.07	132.76	164.34	115.72	90.12	171.12	29.33	27.80	174.52	68.90	39.36	22.97-32.38	14.78
7b	130.10	132.77	164.34	115.72	90.12	171.11	29.34	27.81	174.52	68.90	39.36	22.98-32.38	14.79

Compounds	C1	C2, C6	C4	C3, C5	C7	C8	C9	C10	C11	C12	C13	C14	C15	C_4-OCH_2	N-CH_2	$(CH_2)_2$-$(CH_2)_{13}$* NCH_2- $(CH_2$-$CH_n)^+$	CH_3
1c	139.65	125.45	163.14	115.00	89.98	167.45	130.35	132.44	168.84	129.97	128.41	135.22	122.35	68.03	39.03	22.95-32.16	14.56
2c	139.66	125.44	163.12	115.01	89.97	167.44	130.36	132.45	168.85	129.97	128.40	135.23	122.34	68.05	39.05	22.94-32.17	14.55
3c	139.64	125.46	163.22	115.04	89.98	167.45	130.34	132.44	168.85	129.98	128.44	135.22	122.32	68.05	39.04	22.94-32.16	14.55
4c	139.66	125.45	163.13	115.03	89.99	167.43	130.35	132.45	168.84	129.99	128.43	135.24	122.36	68.08	39.04	22.95-32.17	14.56
5c	139.65	125.44	163.12	115.07	90.08	167.44	130.32	132.44	168.84	129.98	128.44	135.23	122.36	68.08	39.05	22.94-32.18	14.57
6c	139.66	125.46	163.11	115.07	90.08	167.45	130.33	132.45	168.95	129.98	128.45	135.22	123.37	68.06	39.08	22.96-32.18	14.56
7c	139.65	125.45	163.12	115.08	90.07	167.44	130.36	132.46	169.16	129.97	128.45	135.24	123.37	68.07	39.11	22.97-32.19	14.57

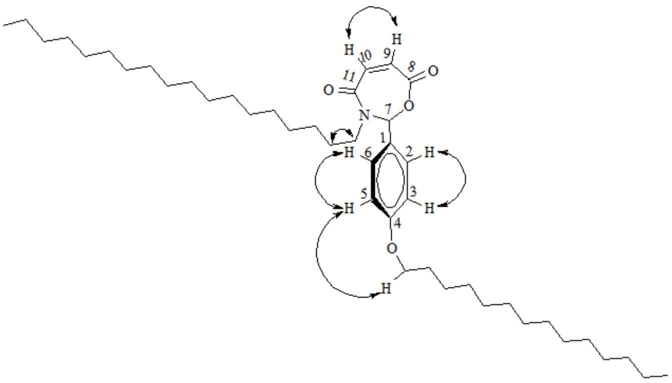


Fig. 2: Select relationship for compound **7a** in the COSY and NOESY spectrum.

All aromatic and aliphatic carbons were identified by HMQC and HMBC Table 5. The HMQC experiment provides information regarding the interaction between the protons and the carbon atoms to which they are directly attached. In the present compounds **1a-7a, 1b-7b** and **1c-7c** the carbon signals observed at δ = 125.44-132.77 ppm, δ = 115.00-116.09 ppm have correlation with respective aromatic protons at δ =7.35-7.88 ppm and δ = 7.10-7.43 ppm. Furthermore, the carbon signal located at the region δ = 89.97-90.12 ppm in the spectra was correlated with the proton resonances at δ = 9.84-9.87 ppm which observed to H7 in heterocyclic ring. The HMQC spectra of compounds **1a-7a** showed the correlation of proton signals at δ = 6.21-6.26 ppm and δ = 6.39-6.41 ppm with respective carbon signals at δ = 132.62-132.66 ppm and δ = 130.87-130.90 ppm, which led to the assignment of these signals to the C9 and C10 in heterocyclic ring. Similarly, the proton signals at δ = 2.25-2.28 ppm and δ = 2.40-2.42 ppm in respective, compounds **1b-7b** were observed the correlation with carbon signals at δ = 29.31-29.34 ppm and δ = 27.80-27.82 ppm. In the same way the carbon signals in compounds **1c-7c** at δ = 129.97-129.99 ppm, δ = 128.40-128.45 ppm, δ = 135.22-135.24 ppm and δ = 122.32-123.37 ppm showed correlation with respective proton chemical shift at δ = 7.84.7.88 ppm, δ = 7.50-7.53 ppm, δ = 7.47-7.49 ppm and δ = 7.73-7.75 ppm. The HMQC of title compounds were able to assign the proton triplet at δ = 4.03-4.09 ppm which correlated with the carbon signal at δ = 68.03-68.92 ppm, also revealed the correlation between carbon signal at δ = 39.03-39.74 ppm with chemical shift at δ = 3.00-3.17 ppm.

Table 5: 2D ^{1}H-^{13}C HMQC and HMBC correlation for **1a-7a, 1b-7b** and **1c-7c**

Compounds	Atom	HMQC	HMBC [J(C,H)]		
		^1J	^2J	^3J	^4J
1a-7a	H2 or H6	C2 or C6	C1, C3orC5	C4, C7	-
	H3 or H5	C3 or C5	C2orC6, C4	-	-
	H7	C7	C1	C2orC6	-
	H9	C9	C8, C10	C11	-
	H10	C10	C9, C11	C8	-
	O-CH_2	O-C	OC1-(C2)	OC1-C2-(C3), C4	OC1-C2-C3(C4)
	N-CH_2	N-C	NC-(Cn)	NC-(Cn), C11	NC-(Cn)
1b-7b	H2 or H6	C2 or C6	C1, C3orC5	C4, C7	-
	H3 or H5	C3 or C5	C2orC6, C4	-	
	H7	C7	C1	C2orC6	-
	H9	C9	C8, C10	C11	-
	H10	C10	C9, C11	C8	-
	O-CH_2	O-C	OC1-(C2)	OC1-C2-(C3), C4	OC1-C2-C3(C4)
	N-CH_2	N-C	N-C	NC-(Cn)	NC-(Cn), C11
1c-7c	H2 or H6	C2 or C6	C1, C3orC5	C4	-
	H3 or H5	C3 or C5	C2orC6, C4	-	-
	H7	C7	C1	C2orC6	C15
	H12	C12	C13	C8	C15
	H13	C13	C12	C15	C8
	H14	C14	C15	C12	C11
	H15	C15	C14	C11	-
	O-CH_2	O-C	OC1-(C2)	OC1-C2-(C3), C4	OC1-C2-C3(C4)
	N-CH_2	N-C	N-C	NC-(Cn)	NC-(Cn), C11

The assignment for the carbon nuclei can also be supported by long range connectivities. The HMBC spectra of title compounds help to observe the correlation of aromatic quaternary carbon and its neighboring proton. In addition the HMBC experiment allowed us to assign the aromatic non-protonated and protonated carbons. The spectra of compounds **1a-7a** and **1b-7b** showed that the doublet at δ = 7.80-7.85 ppm and δ = 7.85-7.88 ppm which has been assigned to the aromatic proton H2 or (H6) was correlated with C1 and C3 or (C5) which located at the respective ^{13}C NMR signal δ =130.00-130.36 ppm and δ = 115.70-116.09 ppm through the long-range cross peak ^{2}J also with the carbon signal at δ = 164.32-164.61 ppm and δ = 90.00-90.12 ppm through the long-range cross peak ^{3}J. In addition, the protons doublet located at the region δ = 7.10-7.43 ppm and δ = 7.10-7.13 ppm in the respective spectra of compounds **1a-7a** and **1b-7b**, was correlated with the carbon signal at δ = 132.55-132.77 ppm and δ = 164.32-164.61 ppm through the long-range cross peak ^{2}J. Moreover, the emergence of the cross peaks associated with the correlation of proton doublets at δ = 6.21-6.26 ppm and δ = 6.39-6.41 ppm assigned to respective protons H9 and H10 in compounds **1a-7a** with respective carbon signals at δ = 166.04-166.10 ppm, δ = 130.87-130.90 ppm and δ = 132.62-132.66 ppm, δ = 166.22-166.29 through the long-range cross peak ^{2}J, and with carbon signal at δ = 166.22-166.29 ppm and δ = 166.04-166.10 ppm as ^{3}J has confirmed that these carbon nuclei (C8, C9, C10 and C11) from heterocyclic ring. The proton triplets H9 and H10 in compounds **1b-7b**, located at the chemical shift δ = 2.25-2.28 ppm and δ = 2.40-2.42, respectively, was correlated through the long-range cross peak ^{2}J with respective carbons at δ = 171.11-171.13 ppm, δ = 27.80-27.82 ppm and δ = 29.31-29.34 ppm, δ = 174.50-174.52 ppm also with ^{3}J with carbons at δ = 174.50-174.52 ppm and δ = 171.11-171.13 ppm, respectively. This information suggests that these carbon nuclei (C8, C9, C10 and C11) from heterocyclic ring. In addition, the proton singlet H7 at δ = 9.84-9.87 ppm in both series of compounds **1a-7a** and **1b-7b**, was correlated through ^{2}J and ^{3}J with C1 and C2 or (C6), respectively, which is located at the chemical shifts δ = 130.00-130.36 ppm and δ = 132.55-132.77 ppm. The HMBC of compound **1a-7a** showed that doublet of aromatic protons H2 or (H6) at the chemical shifts δ = 7.35-7.40 ppm was correlated with through the ^{2}J with the carbons C1 and C3 or (C5) which assigned at the chemical shifts δ = 139.64-139.66 ppm and δ = 115.00-115.08 ppm, respectively, and through the ^{3}J with C4 at δ = 163.11-163.22 ppm. While the doublet at δ = 7.09-7.15 ppm attributed to aromatic protons H3 or (H5) was correlated through ^{2}J with the carbons at δ = 125.44-125.46 ppm and δ = 163.11-163.22 ppm. The chemical shift of proton H7 δ = 9.84-9.86 ppm was correlated through ^{2}J, ^{3}J and ^{4}J with carbons at δ = 139.64-139.66 ppm, δ = 125.44-125.46 ppm and δ = 122.32-123.37 ppm. The HMBC spectra of compound **5c** was shown in Fig 3. While the Select intramolecular interaction Long range ^{1}H- ^{13}C correlation HMBC was shown in Fig. 4.

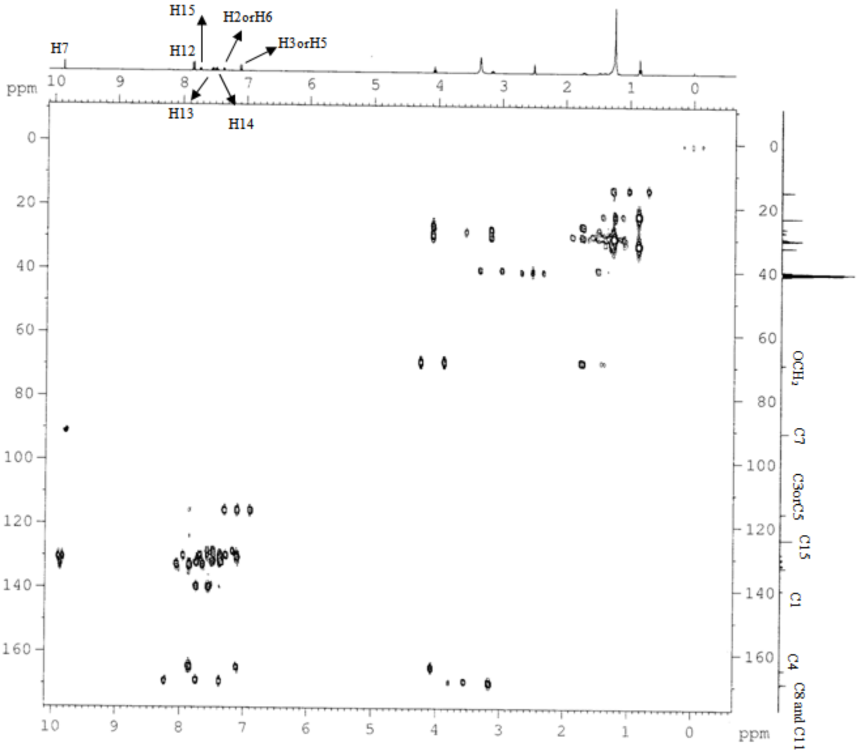


Fig. 3: ^{1}H-^{13}C connectiveities in the HMBC spectra for compound **5c.**

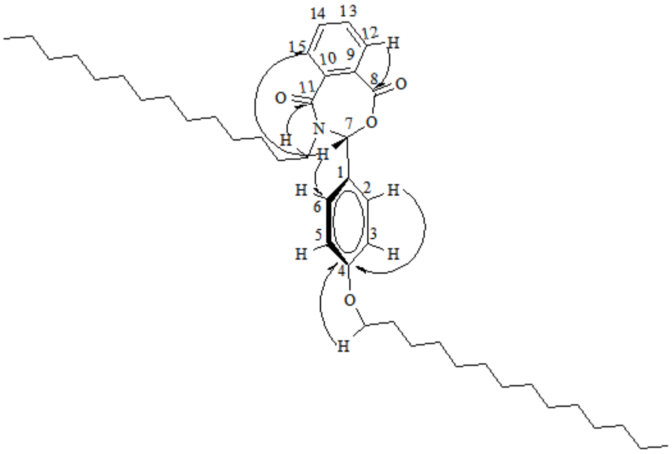


Fig. 4: Select intramolecular interaction Long range ^{1}H- ^{13}C correlation HMBC connectiveities in spectra for compound **5c.**

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