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Research Article

1,3-Oxazepane-4,7-Diones Compounds: ^{1}H and ^{13}C NMR High-Resolution Spectroscopy (1D and 2D)

AbdulKarim-Talaq Mohammad, Hasnah Osman, and Guan-Yeow Yeap

School of Chemical Sciences, Universiti Sains Malaysia, Minden 11800, Penang, Malaysia

Correspondence should be addressed to Hasnah Osman, ohasnah@usm.my

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The complete ^{1}H and ^{13}C NMR assignment of new 1,3-oxazepane-4,7-dione compounds has been obtained using one- and two-dimensional NMR techniques including COSY, HMQC, and HMBC experiments. The data deduced from this study show that the alkyl chain and the phenyl ring are in different planes compared to the oxazepine ring.

1. Introduction

"Oxazepine" refers to any seven-membered ring containing an oxygen and nitrogen atom. The 1,3-oxazepine is a branch of many types of the heterocyclic oxazepine [1–7]. The core structure of 1,3-oxazepane-4,7diones consists of a seven-memebred ring along with two carbonyl group. Over the years, the syntheses of oxazepine derivatives have been investigated and documented. The result is important of heterocyclic compounds having significant biological uses [8–13]. Recently, we prepared a variety of 1,3-oxazepinediones in order to study the spectroscopic and liquid crystal properties [14]. In this paper, we present the structural elucidation by 1D and 2D NMR experiments of 3-alkyl-2-(3-hydroxyphenyl)-1,3-oxazepane-4,7-diones with general formula$(HOC_6H_4)CONC_nH_{2n+1}CH\text{-}CH(CO)_2$ (where n = 2, 4, 6, 8, 10, 12, 14, 16, and 18). Here, the hydroxyphenyl and the terminal alkyl chain are attached to the oxazepane ring.

2. Experimental

2.1. Material. The experimental part for the synthesized of 1,3-oxazepane-4,7-dione compounds and recording of CHN, FT-IR, and all proton and carbon NMR spectra have been reported elsewhere [15].

2.2. Physical Measurements. Melting points were recorded by GALLENKAMP digital melting point apparatus. The elemental microanalyses (CHN) were performed using a Perkin Elmer 2400 LS Series CHNS/O analyzer. The NMR spectra were recorded in deuterated methyl sulphoxide (DMSO-d_6) at 298 K on a Bruker 400 MHz Ultrashied FT-NMR spectrometer equipped with a 5 mm BBI inverse gradient probe. Chemical shifts were referenced to internal tetramethylsilane (TMS). The concentration of solute molecules was 50 mg in 1.0 mL of (DMSO-d_6). Standard Bruker pulse programs [16] were used throughout the entire experiment. The spectroscopic details of NMR are summarized in Table 1.

3. 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 2 and 3.

3.1. 1D and 2D ^{1}H NMR Spectral Assignment. A complete assignment for the title compounds can be given based on the representative compound **18oxa** (Figure 1). The ^{1}H NMR spectra of **2oxa–18oxa** shows three different regions of chemical shift. The signals of the aromatic proton, which appear as a doublet in the region of δ = 7.05–7.14 ppm is assigned to the H4 proton, while a doublet in the range of

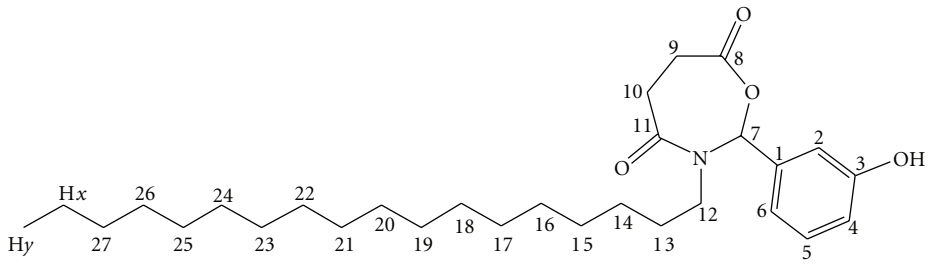

Figure 1: Molecular structure with numbering scheme for compound **18oxa**.

Table 1: Acquisition parameter used in the NMR measurements.

Parameters	Experiment				
	^{1}H NMR	^{13}C NMR	2D COSY	2D HMQC	2D HMBC
SF	400.1 MHz	100.6 MHz	400.1 MHz	F_1 = 100.6 MHz	F_1 = 100.61 MHz
				F_2 = 400.1 MHz	F_2 = 400.1 MHz
SW	10 ppm	180 ppm	10 ppm	F_1 = 180 ppm	F_1 = 180 ppm
				F_2 = 10 ppm	F_2 = 10 ppm
PW	8.3 μs (30° flip angle)	20.0 μs (90° flip angle)	8.3 μs (90° flip angle)	8.3 μs (90° flip angle)	8.3 μs (90° flip angle)
AQ	4.0 s	1.3 s	0.3 s	0.09 s	0.4 s
D1	1.0 s	2.0 s	2.0 s	1.0 s	1.0 s
NS	16	20 000	16	88	92
TD	66 k	66 k	F_1 = 256	F_1 = 512	F_1 = 512
			F_2 = 2048	F_2 = 1024	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: ^{1}H NMR chemical shifts (ppm) of compounds **2oxa–18oxa**.

Atom	Chemical shift (ppm)								
	2oxa	**4oxa**	**6oxa**	**8oxa**	**10oxa**	**12oxa**	**14oxa**	**16oxa**	**18ox**
H2	7.15	7.21	7.12	7.14	7.14	7.15	7.10	7.24	7.21
H4	7.10	7.13	7.14	7.11	7.09	7.05	7.10	7.11	7.08
H5	7.41	7.45	7.38	7.38	7.39	7.25	7.24	7.36	7.38
H6	6.67	6.64	6.68	6.74	6.70	6.82	6.81	6.92	6.94
H7	7.56	7.60	7.62	7.64	7.93	7.89	7.93	7.92	7.91
OH	9.50	9.46	9.23	9.19	9.81	9.92	9.91	9.92	9.94
H9	2.21	2.35	2.27	2.25	2.26	2.30	2.28	2.29	2.28
H10	2.40	2.42	2.41	2.43	2.45	2.48	2.40	2.42	2.41
H12	3.12	3.22	3.10	3.13	3.21	3.01	3.03	3.01	3.05
H13	1.74	1.73	1.71	1.70	1.76	1.76	1.73	1.71	1.75
H14-H15-27		—	1.30	1.25	1.24	1.25	1.24	1.23	1.23
Hx		1.28	1.32	1.31	1.27	1.29	1.29	1.30	1.28
Hy		0.94	0.86	0.87	0.88	0.85	0.85	0.85	0.86

δ = 6.64–6.94 ppm attributed to H6. The singlet in the region of δ = 7.10–7.24 ppm is due to the H2 proton. The triplet in the region δ = 7.24–7.45 ppm can be ascribed to the H5 proton. The protons (H2, H4, H5, and H6) are found to be nonequivalent. The hydroxyl proton appears as a singlet at δ = 9.19–9.94 ppm. ^{1}H NMR spectra of all these compounds show two two-proton triplets in the high field region of about δ = 2.21–2.35 ppm and 2.40–2.48 ppm due to the heterocyclic ring protons H9 and H10, respectively. The chemical shift of the H7 proton is a singlet in the range of δ = 7.56–7.93 ppm. The alkyl group shows four signals and a quintet in the range of δ = 1.71–1.76 ppm. This quintet is attributed to the H13.

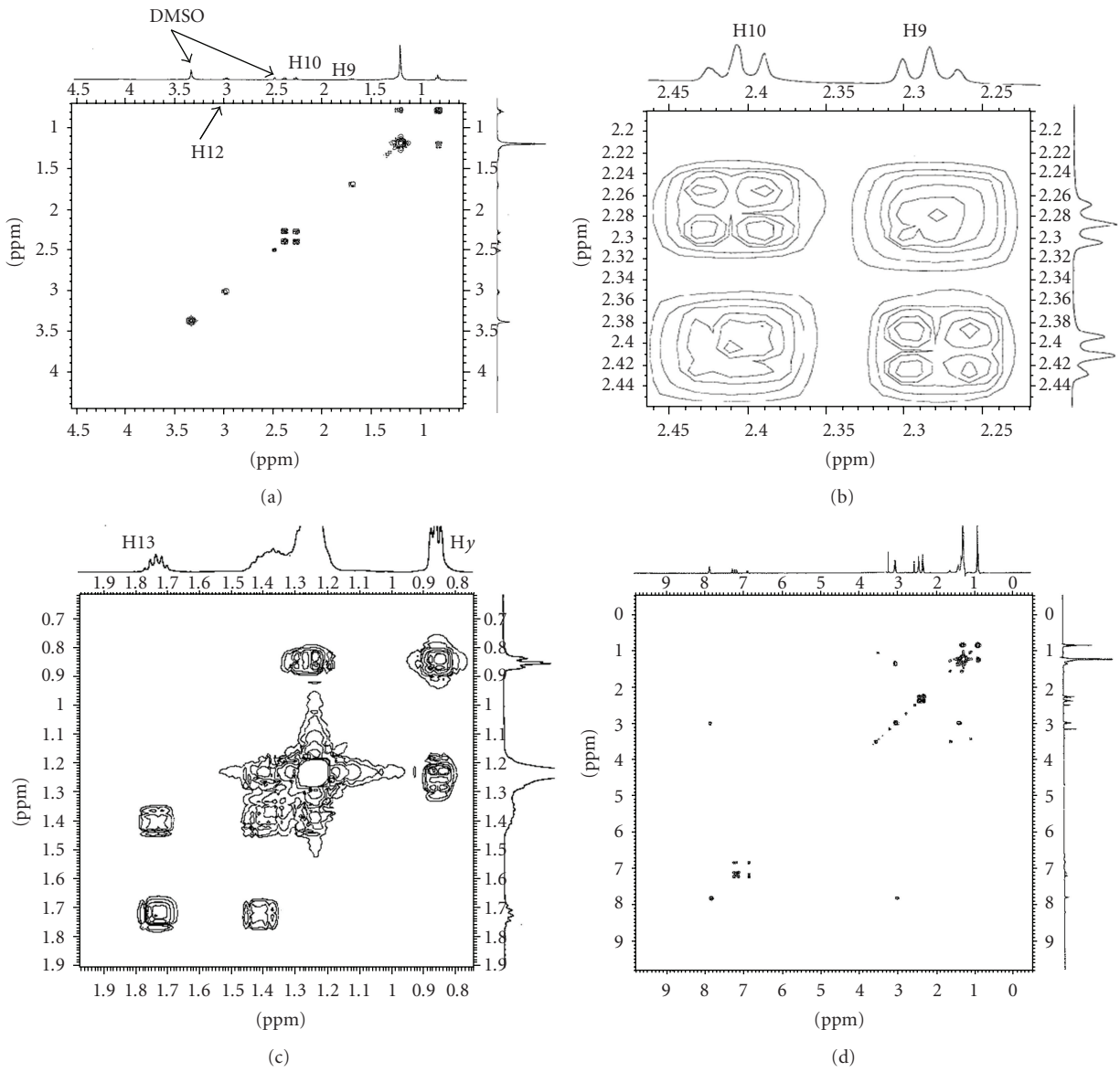

Figure 2: ^{1}H-^{1}H connectiveities in the COSY spectra with select relationship for compound **6oxa.** (a) Expansion of aliphatic and hetero cyclic proton spectrum. (b) Expansion of heterocyclic proton spectrum. (c) Expansion of aliphatic proton region. (d) full ^{1}H-^{1}H COSY spectrum.

The two triplets in the range of δ = 0.85–0.94 ppm and δ = 3.01–3.22 ppm can be assigned to the methyl protons (Hy) and the methylene protons (H12), respectively. The signals of the alkyl protons from H14 to H27 are confirmed by multiplets in the range of δ = 1.23–1.30 ppm.

The assignments of the ^{1}H NMR spectra of these compounds were aided by 2D COSY experiments. The COSY experiments further substantiated the correlation between the equivalent proton pairs with the adjacent protons, wherein the cross peak resulting from these correlations appear at the same region. A typical COSY spectrum of the ^{1}H-^{1}H connectivities in **6oxa** is shown in Figure 2. At the upper field, H9 in heterocyclic ring correlated with the proton H10 in the same ring observed as triplets at δ = 2.27 and 2.41 ppm, respectively. The quintet at δ = 1.71 ppm is assigned to H13 proton which correlated with the multiplets at δ = 1.30 ppm. A similar phenomenon can also be found for Hx at δ = 1.32 ppm which correlated with Hy at δ = 0.86 ppm. However, the H14 to H27 protons for compounds (**8oxa** to **18oxa**) exhibit complexity which cannot be resolved using homonuclear decoupling. The COSY correlation also reveals that the NMR signal of proton H5 at δ = 7.38 ppm had correlated with the NMR signal of aromatic protons H4 (δ = 7.14) and H6 (δ = 6.68) ppm, respectively. In the same way, the aromatic proton (H2) in the region of δ = 7.12 ppm was found to be not correlated with any other aromatic protons. However, COSY data also reveals that the (OH) proton at δ = 9.23 ppm was found to be correlated with the signal assigned to the singlet in the region of δ = 7.12 ppm but not with doublet assigned at δ = 7.14 ppm (H4). This result

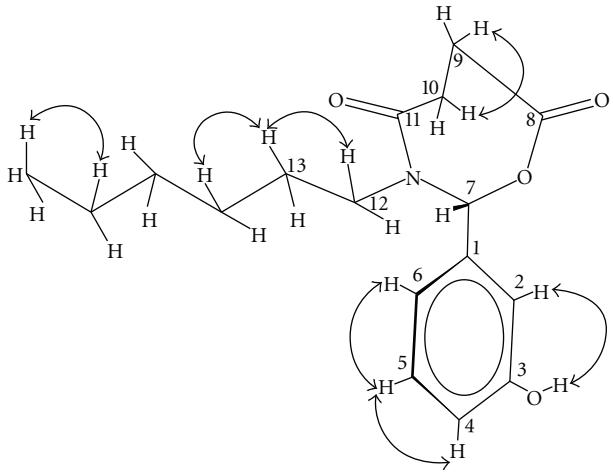

Figure 3: ^{1}H-^{1}H connectiveities in the COSY, select relationship for compound **6oxa**.

helps to show the hydrogen atom of the hydroxyl group is not coplanar with the phenyl ring. Select relationship for compound **6oxa** was shown in Figure 3.

3.2. ^{13}C NMR and 2D Spectral Assignment. Compounds **2oxa–18oxa** were also characterized by ^{13}C NMR and DEPT135 for the protonated carbons which are governed by the additive rules and substitution effect. The ^{13}C NMR spectra of these compounds were all similar. Two downfield signals observed at δ = 171.54–172.35 ppm and δ = 174.64–176.70 ppm are attributed to the carbonyl carbons (C8 and C11) of the seven-membered ring. However, the highfield signal in the region of δ = 13.80–15.03 ppm is assigned for C*y* of the methyl in the alkyl chain. The signals in the range of δ = 39.36–40.15 ppm, 29.60–30.85 ppm, 26.40–34.93 ppm, and 22.50–23.12 ppm are attributed to the respective C12, C13, C14 to C25, and C*x* in the aliphatic chain. In addition to the aliphatic carbons, the signal for C9 and C10 of the seven-membered ring appear in the range of δ = 27.20–28.80 ppm and δ = 29.50–29.98 ppm, respectively. The signal in the region of δ = 67.56–70.58 ppm is attributed to C7. The resonance due to the aromatic carbon at δ = 137.16–138.74, 114.10–115.80, 119.42–122.49, 130.18–132.66, and 121.12–123.05 ppm are assigned to C1, C2, C4, C5, and C6. The ^{13}C NMR signal for C3 (δ = 158.43–161.06 ppm) showed comparatively downfield shift as compared to the other phenyl carbons in all the title compounds due to adjacent to hydroxyl group. The only difference observed was the increase in the number of aliphatic carbon signals by two each time when compound **2oxa** to **18oxa** was analyzed.

The HMQC spectra of all the compounds were recorded, and the chemical shifts are assigned. The HMQC spectra provide information regarding the through bond connection between the protons and the carbon atoms to which they are directly attached. The data of compound **18oxa** are discussed as an example. The HMQC experiment enabled the assignment of the one-bond connectivity in the proton singlet at δ = 7.21 ppm, which correlated with carbon signal at δ = 115.54 ppm, a doublet at δ = 7.08 ppm with the methine at δ = 121.91 ppm, the triplet at δ = 7.38 ppm with the signal at δ = 131.13 ppm, and the doublet at δ = 6.94 ppm shows the correlation with the signal at δ = 122.65. The signals were observed at δ = 27.23 ppm and 29.51 ppm which are assigned to carbon atoms in the heterocyclic ring (C9 and C10) due to its interaction with proton resonances at δ = 2.28 ppm and 2.41 ppm. The proton singlet for H7 at δ = 7.91 ppm is correlated with the carbon signal δ = 69.21 ppm. At upper field, we were able to assign the three proton triplet at δ = 0.86 ppm which correlated with the carbon signal at δ = 14.89 ppm, and also a signal at δ = 1.28 ppm correlated with the carbon signal at δ = 22.90 ppm. In the same way, the multiplets of the aliphatic proton signal at δ = 1.23 ppm is correlated with the carbon signals at δ = 27.80 ppm to 33.87 ppm.

As for the HMBC spectra, the assignment for the carbon nuclei can also be supported by long-range connectivities. The HMBC spectra of compounds help to observe the correlation of aromatic quaternary carbon and its neighboring proton. In addition, the HMBC experiment allowed the assignment of the aromatic nonprotonated and protonated carbons. For example, in **16oxa** Figure 4, the proton singlet at δ = 7.24 ppm correlated through ^{2}J bond with the aromatic carbons at δ = 137.16 and 158.82 ppm, respectively, and with the aromatic carbon at δ = 122.95 ppm via ^{3}J, while it also correlated with the aromatic carbon at δ = 132.66 ppm through ^{4}J. Finally, the long-range connectivities through intramolecular interaction ($^{\text{intra}}$J) of this proton correlate with the carbon at δ = 39.90 ppm. Likewise, the doublet at δ = 7.11 ppm which was assigned to the H4 proton is correlated through ^{2}J, ^{3}J, and ^{4}J with the respective aromatic carbons at δ = 132.66 ppm, 122.95 ppm, and 137.16 ppm. The one proton doublet at δ = 6.92 ppm was also shown to be correlated with the carbons at δ = 132.66 ppm, 120.49 ppm, 69.86 ppm, and 158.82 ppm through the long-range connectivities via ^{2}J, ^{3}J, and ^{4}J, respectively. The aromatic proton, observed as a triplet at δ = 7.36 ppm was correlated with the aromatic carbons at δ = 120.49, 122.95 ppm, 137.16 ppm, and 115.49 ppm through the respective long-range connectivities of ^{2}J, ^{3}J, and ^{4}J. The spectrum also allowed the assignment of the protons of the heterocyclic ring which was observed as a triplet at δ = 2.29 ppm which correlated with the carbonyl carbon at δ = 171.56 ppm and with the carbon at δ = 29.56 ppm through the long-range connectivity ^{2}J. It also correlated with the carbon signal at δ = 174.71 through the long range connectivity ^{3}J. In the same way the triplet of the seven-membered ring at δ = 2.42 ppm, is correlated with the carbon at δ = 27.25 ppm and the carbonyl carbon at δ = 174.71 ppm through ^{2}J. Furthermore, the singlet at δ = 7.92 ppm which was assigned for proton H7 was observed to correlate with the aromatic carbon at δ = 137.16 ppm through ^{2}J, with the carbons at δ = 171.56 ppm and 39.90 ppm through ^{3}J, and finally with the carbon at δ = 29.96 ppm through the long-range connectivity ^{4}J.

The aliphatic chain protons is assigned from the triplet at δ = 3.01 ppm which correlated with carbon at δ = 29.96 through ^{2}J, with carbons at δ = 69.86 and 27.44 ppm through ^{3}J, and with the aromatic carbon at δ = 137.16 ppm

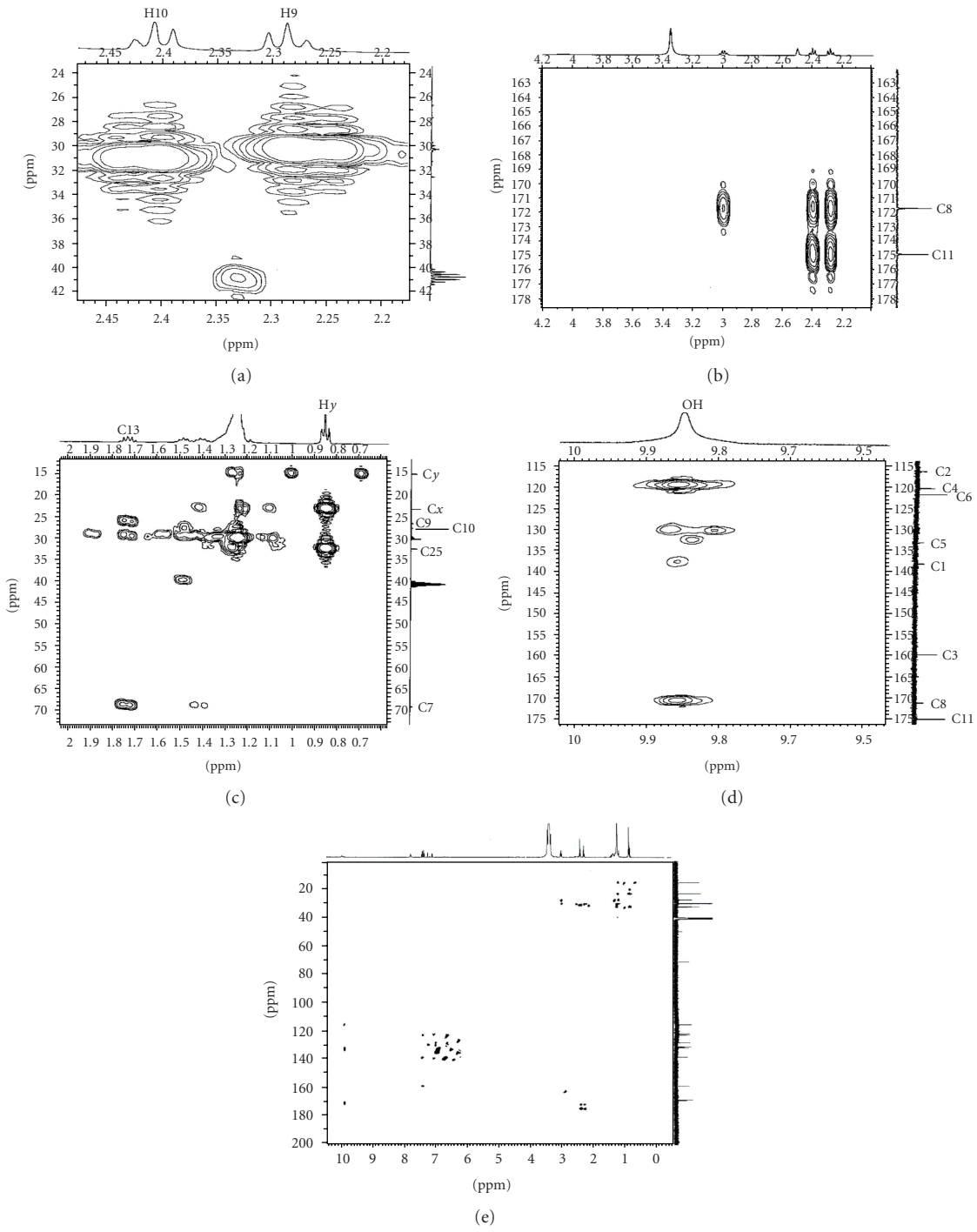

Figure 4: Long range C-H correlations in the HMBC spectra of compound **16oxa**. From (a) to (d) Expansion of aliphatic and hetero cyclic proton spectra. (e) HMBC spectrum of **16oxa**.

through ^{4}J. It also correlated with the aromatic carbon at δ = 122.95 ppm and the carbonyl carbon which was located at δ = 171.56 ppm through long-range connectivities ($^{\text{intra}}$J). Additional correlation for the aliphatic protons were detected from the observed triplet at δ = 0.85 ppm which was assigned to the Hy protons with the carbon at δ = 22.95 ppm, with the carbon at δ = 33.57 ppm, and with carbon at δ = 31.19 ppm in the respective, long-range connectivities ^{2}J, ^{3}J, and ^{4}J. These data help to confirm the correlation between the proton signal at δ = 1.30 ppm with the carbon signals at δ = 14.76 ppm and 33.57 ppm, 31.19 ppm and 31.30 ppm through the long-range connectivities ^{2}J, ^{3}J, and ^{4}J, respectively.

Selected intramolecular through bond connectivities from HMBC spectrum for compound **16oxa** is shown in Figure 5.

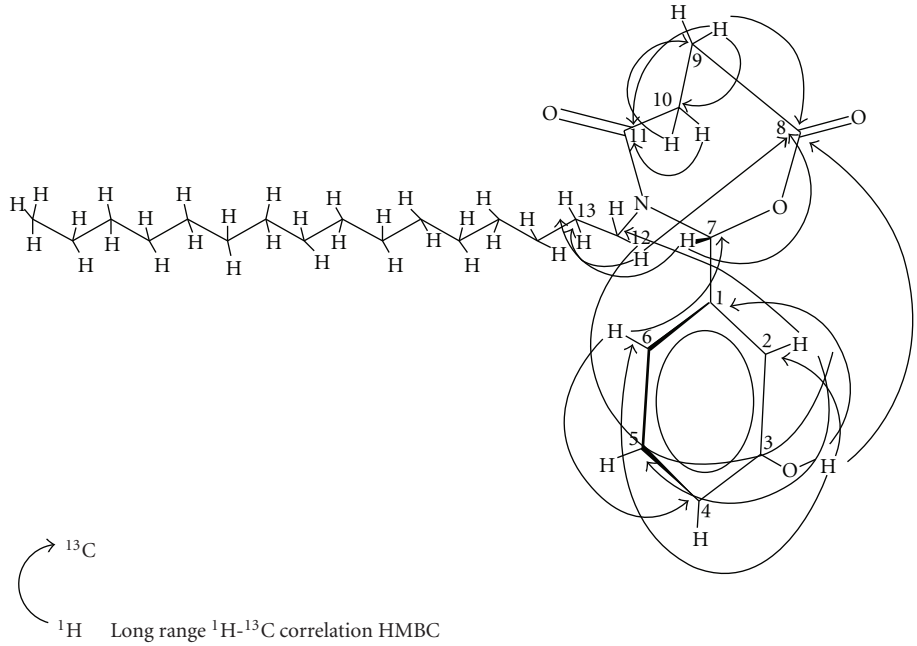

Figure 5: ^{1}H-^{13}C correlation HMBC, select intramolecular interaction for **16oxa.**

Table 3: ^{13}C NMR and DEPT135 chemical shifts (ppm) of compounds **2oxa–18oxa**.

Carbon no.	Chemical shift (ppm)								
	2oxa	**4oxa**	**6oxa**	**8oxa**	**10oxa**	**12oxa**	**14oxa**	**16oxa**	**18ox**
1	137.22	138.10	138.10	138.50	138.65	138.49	138.74	137.16	138.13
2	114.10	114.95	115.80	115.50	115.01	114.48	115.08	115.49	115.54
3	158.43	158.72	161.06	158.85	158.65	158.83	158.88	158.82	158.83
4	119.42	120.43	122.40	121.90	121.01	122.49	121.18	120.49	121.91
5	130.45	131.53	130.40	132.36	130.18	130.42	131.18	132.66	131.13
6	121.23	121.35	122.60	122.63	121.12	123.05	122.62	122.95	122.65
7	70.58	70.50	70.03	67.56	67.92	68.34	68.62	69.86	69.21
8	172.35	172.05	172.12	171.54	172.05	171.58	171.92	171.56	171.57
9	28.58	28.80	27.20	28.08	27.70	27.62	27.27	27.25	27.23
10	29.50	29.50	29.70	29.98	29.81	29.52	29.53	29.56	29.51
11	175.64	176.32	176.70	174.71	175.54	174.73	174.64	174.71	174.64
12	40.15	40.15	40.03	40.06	39.80	39.36	39.83	39.90	39.85
13	30.41	30.51	30.30	30.85	30.03	29.67	29.60	29.96	29.95
14			27.12	27.77	27.65	27.80	26.40	27.44	27.80
15			34.40	29.60	29.48	29.89	29.90	29.88	30.62
16				31.37	29.56	29.78	29.83	29.76	29.57
17				34.93	31.70	29.60	29.70	29.70	29.50
18					31.10	29.58	29.63	29.64	29.47
19					34.70	31.40	29.59	29.57	29.42
20						31.10	29.50	29.50	29.38
21						34.60	31.46	31.48	29.30
22							31.12	31.40	29.29
23							32.50	31.30	29.15
24								31.19	29.07
25								33.57	28.78
26									31.17
27									33.87
X		22.50	22.80	23.12	22.94	22.53	22.91	22.95	22.90
y		13.80	14.04	15.01	15.03	15.00	14.82	14.76	14.89

4. Conclusions

In this paper, we present some new heterocyclic compounds with 1,3-oxazepane cores. The detail NMR assignments of these compounds have been discussed by ^{1}H, ^{13}C NMR, and DEPT135 spectra along with two-dimensional COSY, ^{1}H-^{13}C HMQC, and HMBC spectra. Synthesis results of this work could be useful for other chemists working on the field of heterocyclic oxazepine.

Acknowledgments

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References

[1] A. Al-Harrasi and H. U. Reissig, "Ring enlargement of enantiopure 1,2-oxazines to 1,2-oxazepine derivatives and their palladium-catalyzed couplings," *Synlett*, no. 15, pp. 2376–2378, 2005.

[2] E. S. Kumar and D. N. Dhar, "A simple route for the synthesis of oxazepine-2-one systems using chlorosulfonyl isocyanate," *Synthetic Communications*, vol. 25, no. 13, pp. 1939–1945, 1995.

[3] J. P. Praly, C. D. Stèfano, and L. A. Somsák, "Photolysis of glycopyranosyl azides C-1 substituted by cyano-, amido-, or tetrazolyl-groups," *Tetrahedron Asymmetry*, vol. 11, no. 2, pp. 533–537, 2000.

[4] J. P. Wolfe, R. A. Rennels, and S. L. Buchwald, "Intramolecular palladium-catalyzed aryl amination and aryl amidation," *Tetrahedron*, vol. 52, no. 21, pp. 7525–7546, 1996.

[5] C. Ma, S. J. Liu, L. Xin, J. R. Falck, and D. S. Shin, "Novel formation of 1,3-oxazepine heterocycles via palladium-catalyzed intramolecular coupling reaction," *Tetrahedron*, vol. 62, no. 38, pp. 9002–9009, 2006.

[6] A. A. Abdel-Hafez and B. A. Abdel-Wahab, "5-(4-chlorophenyl)-5,6-dihydro-1,3-oxazepin-7(4H)-one derivatives as lipophilic cyclic analogues of baclofen: design, synthesis, and neuropharmacological evaluation," *Bioorganic and Medicinal Chemistry*, vol. 16, no. 17, pp. 7983–7991, 2008.

[7] Y. Tang, J. C. Fettinger, and J. T. Shaw, "One-step synthesis of complex nitrogen heterocycles from lmines and alkyl-substituted maleic anhydrides," *Organic Letters*, vol. 11, no. 17, pp. 3802–3805, 2009.

[8] C. L. Allaway, M. Daly, M. Nieuwenhuyzen, and G. C. Saunders, "Synthesis of polyfluorodibenz[*b*, *f*][1,4]oxazepines by the cyclization of 2-[(polyfluorobenzylidene)amino]phenols," *Journal of Fluorine Chemistry*, vol. 115, no. 1, pp. 91–99, 2002.

[9] B. Doherty, M. Nieuwenhuyzen, G. C. Saunders, and M. S. Sloan, "Functionalized fluorinated arylethers by ring-opening of 1,2,3,4-tetrafluorodibenz[*b*, *f*][1,4]oxazepine," *Journal of Fluorine Chemistry*, vol. 119, no. 1, pp. 15–19, 2003.

[10] A. Kamal, V. Tekumalla, P. Raju, V. G. M. Naidu, P. V. Diwan, and R. Sistla, "Pyrrolo[2,1-c][1,4]benzodiazepine-*β*-glucuronide prodrugs with a potential for selective therapy of solid tumors by PMT and ADEPT strategies," *Bioorganic and Medicinal Chemistry Letters*, vol. 18, no. 13, pp. 3769–3773, 2008.

[11] K. Bajaj, Archana, and A. Kumar, "Synthesis and pharmacological evaluation of newer substituted benzoxazepine derivatives as potent anticonvulsant agents," *European Journal of Medicinal Chemistry*, vol. 39, no. 4, pp. 369–376, 2004.

[12] M. T. Crimmins and A. L. Choy, "An asymmetric aldol-ring-closing metathesis strategy for the enantioselective construction of oxygen heterocycles: an efficient approach to the enantioselective synthesis of (+)-laurencin," *Journal of the American Chemical Society*, vol. 121, no. 24, pp. 5653–5660, 1999.

[13] J. Taunton, J. L. Collins, and S. L. Schreiber, "Synthesis of natural and modified trapoxins, useful reagents for exploring histone deacetylase function," *Journal of the American Chemical Society*, vol. 118, no. 43, pp. 10412–10422, 1996.

[14] G. Y. Yeap, A. T. Mohammad, and H. Osman, "Synthesis, spectroscopic and mesomorphic studies on heterocyclic liquid crystals with 1,3-oxazepine-4,7-dione, 1,3-oxazepane-4,7-dione and 1,3-oxazepine-1,5-dione cores," *Journal of Molecular Structure*, vol. 982, no. 1–3, pp. 33–44, 2010.

[15] A. T. Mohammad, H. Osman, and G. Y. Yeap, "Synthesis of new 1,3-oxazepane-4,7diones," submitted to *Journal of Synthetic Communications*.

[16] Bruker program 1D WIN-NMR (release 6.0) and 2D WIN-NMR (release 6.1).