Synthesis and Characterization of New 3-(3-Hydroxyphenyl)-4-alkyl-3,4-dihydrobenzo[*e*][1,3]oxazepine-1,5-dione Compounds

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A series of 3-(3-hydroxyphenyl)-4-alkyl-3,4-dihydrobenzo[*e*][1,3]oxazepine-1,5-dione compounds with general formula $C_nH_{2n+1}CNO(CO)_2C_6H_4(C_6H_4OH)$ in which *n* are even parity numbers from 2 to 18. The structure determinations on these compounds were performed by FT-IR spectroscopy which indicated that the terminal alkyl chain attached to the oxazepine ring was fully extended. Conformational analysis in DMSO at ambient temperature was carried out for the first time via high resolution ^{1}H NMR and ^{13}C NMR spectroscopy.

Keywords 3,4-dihydrobenzo[*e*][1,3]oxazepine-1,5-diones, synthetic method, structure elucidication

Introduction

1,3-Oxazepinediones are a seven-membered ring that contains nitrogen, oxygen, and two carbonyl groups. The molecular properties of 1,4-benzoxazepine, 4,1-benzoxazepines, and 1,5-benzoxazepines have been extensively studied due to their biological activity[1-10] and their great importance in organic and medicinal chemistry.[11-16] There are no general procedures for the synthesis of these compounds. However, benzoxazepines with appropriate side chains must be synthesized for drug research. The nitrogen heteroatom is a convenient site for a side chain attachment to benzoxazepine. This usually takes place via acylation.[17,18] The *N*-alkylation of 2,3-dihydro-1,5-benzoxazepin-4(5*H*)-one type compounds had been reported.[19-21] Our interest in [1,3]oxazepine-4,7-dione molecules arise from our earlier observation of other heterocyclic molecules which have liquid crystalline properties.[22] This has encouraged us to build a new seven-membered ring from easily acquired starting materials. The major purpose of this paper is to report on new 3-(3-hydroxyphenyl)-4-alkyl-3,4-dihydrobenzo[*e*][1,3]-oxazepine-1,5-dione compounds, **2ozpn—18ozpn**. The N atoms of the heterocyclic ring next to 1,3-oxazepine fragments were linked by an alkyl chain. To the best of our knowledge, the synthesis and spectral data of these molecules have not yet been reported.

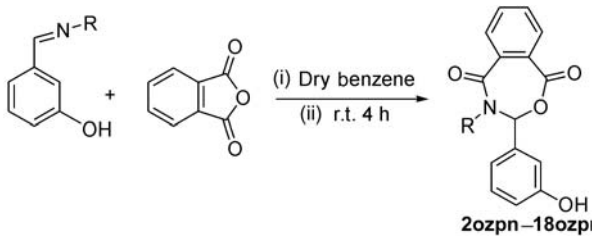
Experimental

Material

The 3-((alkylimino)methyl)phenol derivatives were prepared in our laboratory. Phthalic anhydride was purchased from Aldrich and was used without further purification. Thin-layer chromatography (TLC) was performed on silica-gel plates. Benzene and THF were dried by standard method.

Synthesis of 3,4-dihydrobenzo[*e*][1,3]oxazepine-1,5-diones derivatives

All Compounds were prepared by the same method. The synthetic route used to prepare the series of 3-(3-hydroxyphenyl)-4-alkyl-3,4-dihydrobenzo[*e*][1,3]-oxazepine-1,5-diones compounds is shown in Figure 1.



2ozpn–18ozpn

2ozpn	R=C_2H_5	**4ozpn**	R=C_4H_9
6ozpn	R=C_6H_{13}	**8ozpn**	R=C_8H_{17}
10ozpn	R=$C_{10}H_{21}$	**12ozpn**	R=$C_{12}H_{25}$
14ozpn	R=$C_{14}H_{29}$	**16ozpn**	R=$C_{16}H_{33}$
18ozpn	R=$C_{18}H_{37}$		

Figure 1 General procedure for the synthesis of **2ozpn—18ozpn**.

A solution of phthalic anhydride (0.01 mol) in dry benzene (10 mL) was added dropwise to a hot dry benzene solution (20 mL) of 3-((ethylimino)alkyl)phenol (0.01 mol), in a round bottom flask equipped with a double surface condenser fitted with calcium chloride guard tube. The reaction mixture was refluxed for 4 h. The reaction was monitored by TLC and the solvent

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was distilled off *in vacuo*. The solid product obtained was filtered and washed with cold distilled water. The resulting solid was recrystallized twice from 1,4-dioxane. The analytical data for the series of compounds from **2ozpn** to **18ozpn** are summarized as follows.

2ozpn: Yield 66%. m.p. 90—92 ℃. ^{1}H NMR (DMSO) δ: 9.53 (s, OH), 8.25 (d, J=8.1 Hz, H-12), 8.05 (s, H-7), 7.85 (t, J=8.6 Hz, H-14), 7.78 (t, J=7.8 Hz, H-13), 7.69 (d, J=7.2 Hz, H-15), 7.16 (t, J=8.6 Hz, H-5), 7.09 (s, H-2), 6.89 (d, J=7.9 Hz, H-6), 6.72 (d, J=8.1 Hz, H-4), 3.22 (q, H-1'), 1.28 (t, H-2'); ^{13}C NMR (DMSO) δ: 114.76—138.32 (Ar-C), 158.20 (Ar-C-O), 86.65 (C-7), 169.32 (C-8), 131.59 (C-9), 132.25 (C-10), 168.10 (C-11), 128.31 (C-12), 130.21(C-13), 138.42 (C-14), 123.74 (C-15), 33.86 (C-x), 13.83 (C-y); IR (KBr) v: 3410, 3214, 3017, 2945, 2932, 2862, 2789, 2728, 1751, 1554, 1539, 1451, 1310, 1068, 860, 751, 714 cm^{-1}. Anal. calcd for $C_{17}H_{15}NO_4$: C 68.68, H 5.09, N 4.71; found C 68.76, H 5.18, N 4.64.

4ozpn: Yield 70%. m.p. 98—100 ℃. ^{1}H NMR (DMSO) δ: 9.68 (s, OH), 8.21 (d, J=8.3 Hz, H-12), 8.03 (s, H-7), 7.81 (t, J=8.2 Hz, H-14), 7.63 (t, J=7.0 Hz, H-13), 7.51 (d, J=7.0 Hz, H-15), 7.19 (t, J=8.4 Hz, H-5), 7.10 (s, H-2), 6.97 (d, J=7.4 Hz, H-6), 6.81 (d, J=8.9 Hz, H-4), 3.17 (t, H-1'), 1.73 (q, H-2'); ^{13}C NMR (DMSO) δ: 115.74—139.83 (Ar-C), 158.89 (Ar-C-O), 86.85 (C-7), 169.74 (C-8), 131.63 (C-9), 132.59 (C-10), 168.92 (C-11), 128.43 (C-12), 130.47 (C-13), 138.66 (C-14), 123.46 (C-15), 40.99 (C-1'), 31.96 (C-2'), 21.13 (C-x), 14.23 (C-y); IR (KBr) v: 3444, 3011, 2958, 2938, 2870, 2782, 1728, 1560, 1541, 1082, 1448, 1312, 3222, 2734, 820, 751, 719 cm^{-1}. Anal. calcd for $C_{19}H_{19}NO_4$: C 70.14, H 5.89, N 4.31; found C 70.10, H 5.83, N 4.38.

6ozpn: Yield 60%. m.p. 94—96 ℃. ^{1}H NMR (DMSO) δ: 9.96 (s, OH), 8.24 (d, J=8.7 Hz, H-12), 8.14 (s, H-7), 7.76 (t, J=8.3 Hz, H-14), 7.61 (t, J=7.1 Hz, H-13), 7.43 (d, J=6.90 Hz, H-15), 7.24 (t, J=8.2 Hz, H-5), 7.14 (s, H-2), 7.13 (d, J=7.5 Hz, H-6), 6.95 (d, J=8.6 Hz, H-4), 3.15 (t, H-1'), 1.72, (q, H-2'); ^{13}C NMR (DMSO) δ: 115.36—139.62 (Ar-C), 158.60 (Ar-C-O), 86.95 (C-7), 169.64 (C-8), 131.42 (C-9), 132.83 (C-10), 168.73 (C-11), 128.57 (C-12), 130.36 (C-13), 138.54 (C-14), 122.82 (C-15), 40.84 (C-1'), 32.25 (C-2'), 29.53—33.10 (C-3'—C-4'), 22.86 (C-x), 15.22 (C-y); IR (KBr) v: 3440, 3015, 2949, 2929, 2861, 2855, 1740, 1590, 1466, 1050, 1452, 1314, 3225, 2727, 872, 824, 783 cm^{-1}. Anal. calcd for $C_{21}H_{23}NO_4$: C 71.37, H 6.56, N 3.96; found C 71.27, H 6.61, N 3.94.

8ozpn: Yield 59%. m.p. 102—104 ℃. ^{1}H NMR (DMSO) δ: 9.98 (s, OH), 8.23 (d, J=8.3 Hz, H-12), 8.21 (s, H-7), 7.74 (t, J=8.0 Hz, H-14), 7.59 (t, J=7.0 Hz, H-13), 7.38 (d, J=7.0 Hz, H-15), 7.26 (t, J=8.4 Hz, H-5), 7.19 (s, H-2), 7.12 (d, J=7.7 Hz, H-6), 6.97 (d, J=8.9 Hz, H-4), 3.12 (t, H-1'), 1.71, (q, H-2'), 1.35 (H-x), 1.32 (m, H-3'—H-6'), 0.88 (H-y); ^{13}C NMR (DMSO) δ: 115.01—139.85 (Ar-C), 158.82 (Ar-C-O), 86.87 (C-7), 169.24 (C-8), 131.58 (C-9), 132.43 (C-10), 168.83 (C-11), 128.91 (C-12), 130.87 (C-13), 138.49 (C-14), 123.45 (C-15), 40.91 (C-1'), 32.16 (C-2'), 29.66—33.16 (C-3'—C-6'), 22.96 (C-x), 15.37 (C-y); IR (KBr) v: 3428, 3045, 2954, 2928, 2870, 2858, 1731, 1596, 1585, 1079, 1457, 1315, 3240, 2729, 871, 776, 722 cm^{-1}. Anal. calcd for $C_{23}H_{27}NO_4$: C 72.42, H 7.13, N 3.67; found C 72.39, H 7.08, N 3.72.

10ozpn: Yield 61%. m.p. 99—101 ℃. ^{1}H NMR (DMSO) δ: 9.98 (s, OH), 8.32 (d, J=8.5 Hz, H-12), 8.10 (s, H-7), 7.72 (t, J=8.3 Hz, H-14), 7.56 (t, J=7.4 Hz, H-13), 7.36 (d, J=7.5 Hz, H-15), 7.23 (t, J=8.7 Hz, H-5), 7.16 (s, H-2), 7.14 (d, J=7.8 Hz, H-6), 6.95 (d, J=8.7 Hz, H-4), 3.13 (t, H-1'), 1.77, (q, H-2'), 1.34 (H-x), 1.31 (m, H-3'—H-8'), 0.89 (H-y); ^{13}C NMR (DMSO) δ: 115.62—139.64 (Ar-C), 158.75 (Ar-C-O), 86.27 (C-7), 169.23 (C-8), 131.20 (C-9), 132.06 (C-10), 168.81 (C-11), 128.40 (C-12), 131.62 (C-13), 138.39 (C-14), 122.50 (C-15), 40.56 (C-1'), 32.18 (C-2'), 27.44—32.24 (C3'—C8'), 22.95 (C-x), 14.83 (C-y); IR (KBr) v: 3411, 3012, 2952, 2918, 2857, 2828, 1726, 1577, 1523, 1080, 1431, 1312, 3213, 2760, 833, 770, 719. Anal. calcd for $C_{25}H_{31}NO_4$: C 73.32, H 7.63, N 3.42; found C 73.40, H 7.51, N 3.49.

12ozpn: Yield 59%. m.p. 97—99 ℃. ^{1}H NMR (DMSO) δ: 9.91 (s, OH), 8.35 (d, J=8.6 Hz, H-12), 8.23 (s, H-7), 7.76 (t, J=8.2 Hz, H-14), 7.51 (t, J=7.3 Hz, H-13), 7.39 (d, J=7.1 Hz, H-15), 7.21 (t, J=8.9 Hz, H-5), 7.17 (s, H-2), 6.92 (d, J=7.9 Hz, H-6), 6.81 (d, J=8.6 Hz, H-4), 3.18 (t, H-1'), 1.73 (q, H-2'), 1.34 (H-x), 1.31 (m, H-3'—H-10'), 0.87 (H-y); ^{13}C NMR (DMSO) δ: 115.50—138.50 (Ar-C), 158.40 (Ar-C-O), 86.38 (C-7), 169.19 (C-8), 131.27 (C-9), 131.73 (C-10), 168.92 (C-11), 128.94 (C-12), 131.73 (C-13), 138.41 (C-14), 123.84 (C-15), 40.45 (C-1'), 32.15 (C-2'), 27.60—32.48 (C-3'—C-10') 23.01 (C-x), 15.21 (C-y); IR (KBr) v: 3437, 3017, 2962, 2921, 2862, 2854, 1750, 1597, 1573, 1081, 1453, 1315, 3218, 2725, 872, 824, 785 cm^{-1}. Anal. calcd for $C_{27}H_{35}NO_4$: C 74.11, H 8.06, N 3.20; found C 74.19, H 8.17, N 3.28.

14ozpn: Yield 63%. m.p. 122—124 ℃. ^{1}H NMR (DMSO) δ: 9.93 (s, OH), 8.25 (d, J=8.3 Hz, H-12), 8.11 (s, H-7), 7.75 (t, J=8.4 Hz, H-14), 7.56 (t, J=7.1 Hz, H-13), 7.38 (d, J=7.0 Hz, H-15), 7.28 (d, J=7.6 Hz, H-6), 7.25 (t, J=8.7 Hz, H-5), 7.20 (s, H-2), 7.18 (d, J=8.8 Hz, H-4), 3.19 (t, H-1'), 1.71, (q, H-2'), 1.38 (H-x), 1.35 (m, H-3'—H-12'), 0.88 (H-y); ^{13}C NMR (DMSO) δ: 115.51—139.61 (Ar-C), 158.84 (Ar-C-O), 86.21 (C-7), 169.18 (C-8), 131.15 (C-9), 131.94 (C-10), 168.84 (C-11), 128.97 (C-12), 130.45 (C-13), 138.52 (C-14), 122.84 (C-15), 40.78 (C-1'), 32.16 (C-2'), 27.62—32.67 (C-3'—C-12') 23.03 (C-x), 14.95 (C-y); IR (KBr) v: 3437, 3059, 2958, 2920, 2861, 2850, 1690, 1597, 1561, 1081, 1463, 1316, 3211, 2723, 824, 785, 720. Anal. calcd for $C_{29}H_{39}NO_4$: C 74.81, H 8.44, N 3.01; found C 74.88, H 8.39, N 3.01.

16ozpn: Yield 60%. m.p. 116—118 ℃. ^{1}H NMR (DMSO) δ: 10.02 (s, OH), 8.29 (d, J=8.2 Hz, H-12),

8.17 (s, H-7), 7.73 (t, J=8.6 Hz, H-14), 7.58 (t, J=7.1 Hz, H-13), 7.39 (d, J=6.8 Hz, H-15), 7.24 (t, J=8.9 Hz, H-5), 7.2 (s, H-2), 7.19 (d, J=7.3 Hz, H-6), 6.99 (d, J=8.7 Hz, H-4), 3.15 (t, H-1'), 1.78 (q, H-2'), 1.39 (H-*x*), 1.36 (m, H-3'—H-14'), 0.86 (H-*y*); ^{13}C NMR (DMSO) δ: 115.49—139.54 (Ar-C), 158.82 (Ar-C-O), 86.34 (C-7), 169.22 (C-8), 131.17 (C-9), 131.93 (C-10), 168.88 (C-11), 128.97 (C-12), 131.64 (C-13), 138.50 (C-14), 122.67 (C-15), 40.92 (C-1'), 32.14 (C-2'), 27.84—32.78 (C-3'—C-14') 22.74 (C-*x*), 14.94 (C-*y*); IR (KBr) ν: 3308, 3015, 2949, 2916, 2849, 2835, 1680, 1610, 1594, 1050, 1404, 1341, 3239, 2698, 837, 824, 784. Anal. calcd for $C_{31}H_{43}NO_4$: C 75.42, H 8.78, N 2.84; found C 75.54, H 8.81, N 2.90.

18ozpn: Yield 62%. m.p. 108—110 ℃. ^{1}H NMR (DMSO) δ: 10.02 (s, OH), 8.25 (d, J=8.3 Hz, H-12), 8.12 (s, H-7), 7.74 (t, J=8.4 Hz, H-14), 7.54 (t, J=7.2 Hz, H-13), 7.37 (d, J=7.1 Hz, H-15), 7.25 (t, J=8.7 Hz, H-5), 7.23 (s, H-2), 7.09 (d, J=7.6 Hz, H-6), 6.84 (d, J=8.9 Hz, H-4), 3.13 (t, H-1'), 1.72, (q, H-2'), 1.37 (H-*x*), 1.34 (m, H-3'—H-16'), 0.89 (H-*y*); ^{13}C NMR (DMSO) δ: 115.73—139.85 (Ar-C), 158.90 (Ar-C-O), 86.26 (C-7), 169.83 (C-8), 131.27 (C-9), 131.84 (C-10), 168.64 (C-11), 128.83 (C-12), 131.59 (C-13), 138.49 (C-14), 122.71 (C-15), 40.96 (C-1'), 32.13 (C-2'), 27.71—32.63 (C-3'—C-14') 22.84 (C-*x*), 14.71 (C-*y*); IR (KBr) ν: 3307, 3094, 2953, 2918, 2867, 2850, 1675, 1594, 1581, 1051, 1469, 1313, 3246, 2725, 842, 796, 784. Anal. calcd for $C_{33}H_{47}NO_4$: C 75.97, H 9.08, N 2.68; found C 75.88, H 9.05, N 2.62.

Physical measurements

The elemental microanalyses (CHN) were performed using a Perkin Elmer 2400 LS Series CHNS/O analyzer. Melting points were recoded with a Gallenkamp digital melting point apparatus.

Characterization

The FT-IR spectra of all the title compounds **2ozpn—18ozpn** were recorded by using a Perkin Elmer 2000-FT-IR spectrophotometer in the frequency range 4000—400 cm^{-1}. The measurement was carried out with the samples in KBr discs.

NMR spectra were recorded in DMSO at 298 K on a Bruker 400 MHz Ultrashied^{TM} FT-NMR spectrometer equipped with a 5 mm BBI inverse gradient probe. Chemical shifts were referenced to internal TMS. The concentration of solute molecules was 50 mg in 1.0 mL DMSO. Standard Bruker pulse programs[23] were used throughout the entire experiment. The spectroscopic details (^{1}H NMR and ^{13}C NMR assignment) are summarized in Table 1 for the diagnostic peaks. The NMR assignments with respect to different nuclei in the title compounds are accomplished based on the atomic-numbering represented by compound **14ozpn** (Figure 2).

Table 1 Acquisition parameter used in the NMR measurements[a]

Parameter	^{1}H NMR	^{13}C NMR	2D COSY
SF/MHz	400.1	100.6	400.1
SW/10^{-6}	10	180	10
PW/μs	8.3 (30° flip angle)	20.0 (90° flip angle)	8.3 (90° flip angle)
AQ/s	4.0	1.3	0.3
D1/s	1.0	2.0	2.0
NS	16	20000	16
TD	66 k	66 k	F_1=256
			F_2=2048

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

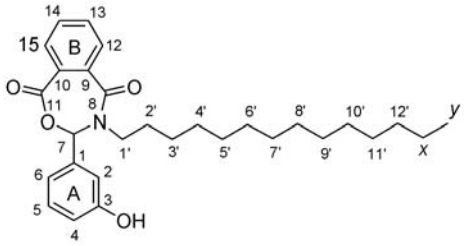

Figure 2 Molecular structure with numbering scheme for compound **14ozpn**.

Results and discussion

The condensation for the entire series of 3-[(alkylimino)methyl]phenol derivatives with phthalic anhydride produced the 3-(3-hydroxyphenyl)-4-alkyl-3,4-dihydrobenzo[*e*][1,3]oxazepine-1,5-dione compounds with a general formula $C_nH_{2n+1}CNO(CO)_2C_6H_4(C_6H_4OH)$, in which n is an even parity number from 2 to 18. The synthesized compounds have two carbonyl groups in a heterocyclic ring adjacent to the aromatic ring. To the best of our knowledge, majority of these compounds has not been reported in the literature. All title compounds are stable solids with a sharp melting point. The molecular structure of the title compounds were investigated by using FTIR analysis and further studied by advanced NMR techniques.

Characterization by FT-IR spectroscopy

Compounds **2ozpn—18ozpn** were analyzed by FT-IR, which show some important features with respect to the nature of the functional groups. The stretching frequencies of the lactone and lactam carbonyl groups $\upsilon_{C=O}$, gave rise to one intense band in the range 1675—1751 cm^{-1}. However, as observed in our earlier study, a band in the range of 1310—1344 cm^{-1} was assigned to the bending of lactone υ_{C-O}.[22] A medium intense band at the 3307—3444 cm^{-1} region is attributed to the stretching of the O—H group. The bands at 1554—1610 and 1466—1594 cm^{-1} are attrib-

uted to the stretching of the phenyl ring[24] while bands at 3011—3094 cm^{-1} are attributed to the aromatic C—H stretching υ_{CPh-H}. Peaks in the range of 820—872, 751—824, and 714—785 cm^{-1} are ascribed to the out-of-plane (γ_{C-H}) bending.[22,25] The titled compounds gave a medium band at 1050—1081 cm^{-1} due to υ_{C-N}. A stretching band from the benzene group appeared at 3211—3246 cm^{-1}. The characteristic absorption bands of the alkyl group (long chain) can be assigned by symmetric, υ_{CH_3s} and asymmetric, υ_{CH_3} as stretching which appear within the range of 2949—2962 and 2916—2938 cm^{-1}. The absorption bands for υ_{CH_3s} and υ_{CH_2} as appear in the range of 2849—2870 and 2782—2858 cm^{-1} respectively.[22,26] The band observed in the range of 1404—1469 cm^{-1} is ascribed to the stretching of υ_{C-H}[27] and a very weak band at 2760—2698 cm^{-1} is assigned to υ_{C-H}.

Characterization by NMR spectra

The ^1H NMR, ^{13}C NMR spectroscopy were used to further substantiate the molecular structure of the title compounds in DMSO at ambient temperature.

^1H spectral assignment

A complete assignment for the title compounds can be made based on the representative compound, **14ozpn** (Figure 2). Two aromatic rings are differentiated by A and B. The ^1H NMR spectra for **2ozpn**—**18ozpn** can be separated into two different regions of chemical shift. Signals of the aromatic proton A due to the H-2 proton appears as a singlet at δ 7.09—7.28 whereas the H-4 proton appears as a doublet in the range of δ 6.72—7.18. The occurrence of a doublet in the range of δ 6.89—7.28 is attributed to the H-6 proton. A triplet at δ 7.16—7.26 is assigned to the H-5 proton. The singlet in the region of δ 9.53—10.02 corresponds to the hydroxyl group (OH). In the same way, the chemical shift of the aromatic ring B protons appears as a doublet in the range of δ 8.21—8.35, which is assigned to the H-12 proton. Furthermore, two triplets exist at δ 7.51—7.78 and δ 7.72—7.85 which can be attributed to H-13 and H-14, respectively. The signal for the H-15 proton appears as a doublet at δ 7.36—7.69. A singlet in the most downfield region (δ 8.03—8.23) is assigned to H-7 from the heterocyclic ring. The alkyl chain has four signals that can be observed in the highfield region. There is also a quintet at δ 1.28—1.78, which is attributed to the H-2' proton. Two triplets assigned to the methyl proton H-*y* and the methylene proton H-1' are observed at δ 0.86—0.93 and δ 3.12—3.22, respectively. The alkyl protons from H-3' to H-4'—H-16' atoms were confirmed by multiplets in the range of δ 1.31—1.36.

The assignments of ^1H NMR spectra of these compounds were subsequently confirmed with the aid of 2D COSY experiments. The COSY experiments further confirmed the correlation between the equivalent proton pairs with adjacent protons. Cross peaks resulting from these correlations appear in the same region (Table 2). The downfield region of the spectrum is assigned to the aromatic proton ring (A and B). Thus, a proton triplet at δ 7.23 correlates with the doublet at δ 6.84 and 7.09. These protons are assigned to the respective aromatic ring proton (A) H-5, H-4, and H-6. Likewise, the aromatic ring proton (B) was observed through the correlation between the signal that appears as a doublet at δ 8.25 with the triplet at δ 7.54. The doublet at δ 7.37 correlates with the triplet at δ 7.74. However, COSY data also reveals that the (OH) proton at δ 10.02 is correlated with the signal which is assigned to a singlet in the region of δ 7.23 but not with the doublet at δ 6.84. A proton at C-7 in the seven membered-ring shows a singlet at δ 8.12 and does not show any correlation in this spectrum. Long chain protons are established through the correlation between the chain's hydrogen, which is exemplified by the correlation of H-1' located at δ 3.13 with H-2' located at δ 1.72. In addition, the alkyl protons exhibit complexity that can not be resolved using homonuclear decoupling. This phenomenon was observed in our earlier publications.[22]

Table 2 ^1H-^1H correlation from 2D COSY for **2ozpn**—**18ozpn**

Compound	Atom H	COSY
2ozpn—**18ozpn**	H-2	OH
	H-4	H-5
	H-5	H-4, H-6
	H-6	H-5
	O-H	H-2
	H-7	—
	H-12	H-13
	H-13	H-12
	H-14	H-15
	H-15	H-14
	H-1'	H-2'
	H-2'	H-1'

Characterization by ^{13}C NMR spectroscopy

The structures of the compounds were further confirmed by ^{13}C NMR and DEPT135 spectroscopy for the protonated carbons. The ^{13}C NMR spectra provide direct information about the carbon skeleton of the molecule. Detailed assignments of different resonance peaks to their respective carbon atoms are based on the representative compound **10ozpn**. The ^{13}C NMR spectra of this series of compounds show similarities. Two signals observed downfield at δ 169.188—169.832 and δ 168.102—168.923 are attributed to the carbonyl carbon (C-8, C-11) of the seven-membered ring. In addition, the signal of the hydroxyl carbon (C-3) appears at δ 158.203—158.901. A signal at δ 13.832—15.371 is due to the aliphatic carbon (C-*y*) of the methyl group. Signals at δ 40.454—40.992, 31.967—32.258, 27.446—32.785, and δ 21.132—33.867 are attributed to C-1', C-2', C-3'

to C-4'—C-16', and C-*x* in the alkyl group, respectively. The only difference is the increase in the number of signals by two between **2ozpn—18ozpn**. The C-7 signal, which is located in the heterocyclic ring, appears at δ 86.213—86.953. The resonances due to the aromatic ring A and B are located at δ 138.321—139.852, 114.765 — 115.734, 121.968 — 122.871, 129.114 — 129.848, 130.077 — 130.457, 131.127 — 131.632, 131.735 — 132.830, 128.318 — 128.978, 130.213 — 131.735, 138.396—138.663, and 122.503—123.843, which are ascribed to C-1, C-2, C-4, C-5, C-6, C-9, C-10, C-12, C-13, C-14, and C-15, respectively.

Aromatic quaternary carbons for all compounds were established through the connectivities between carbon and its neighboring proton by using a long-range correlation HMBC experiment (Table 3). The spectra of the compounds have similar correlations.

Table 3 2D ^{1}H-^{13}C HMBC correlation for compounds **2ozpn—18ozpn**

Compound	Atom	HMBC [*J*(C,H)]			
		^{2}J	^{3}J	^{4}J	$^{intra}J$
2oznp—18ozpn	H-2	C-3	C-4	C-6	—
	H-4	C-5	C-2, C-6	C-1	—
	H-5	C-4, C-6	C-1	C-2	—
	H-6	C-5	C-4	C-3	C-15
	OH	C-4	C-1	C-6	C-15
	H-7	—	—	—	—
	H-12	C-9, C-13	C-10, C-14	C-15	—
	H-13	C-12, C-14	C-9, C-15	C-8, C-10	C-2
	H-14	C-13, C-15	C-10, C-12	C-9, C-11	—
	H-15	C-10, C-14	C-13	C-12	C-5
	H-1'	C-2'	C-3'	—	—
	H-2'	C-1', C-3'	C-4'	—	—

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