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Short Report

NMR Study of 1,4-Dihydropyridine Derivatives Endowed with Long Alkyl and Functionalized Chains

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Neste trabalho, realizou-se um estudo por ressonância magnética nuclear de ^{1}H, ^{13}C e ^{15}N de derivados de 1,4-dihidropiridinas que contêm, nos grupos ésteres das posições C-3 e C-5, longas cadeias alquílicas ou funcionalizadas. Atribuíram-se inequivocamente os sinais dos espectros utilizando experimentos 1D e 2D (DEPT, nOe, HMQC, HMBC, COSY).

The ^{1}H , ^{13}C and ^{15}N NMR spectroscopic data for 1,4-dihydropyridine endowed with long alkyl and functionalized chain on C-3 and C-5, have been fully assigned by combination of one- and two dimensional experiments (DEPT, HMBC, HMQC, COSY, nOe).

Keywords: ^{1}H NMR, ^{13}C NMR, ^{15}N NMR, 1,4-dihydropyridines

Introduction

Throughout the recent years the synthesis and structural characterization of novel analogues of 1,4-dihydropyridines (1,4-DHPs) derivatives has received particular attention due to the interesting pharmacological and biological properties that they display.[1,2] It is well known that the 1,4-DHP nucleus serves as scaffold for important cardiovascular drugs, and that the calcium modulating activity is determined by structural requirements.[3] It has been proved that 1,4-DHP-calcium antagonists with a high degree of lipophilicity display a slow onset action after administration as vasodilator and hypertensive medications.[4,5]

In order to gain a better understanding of the effect of the substitution pattern of the 1,4-DHPs on biological activity, we have prepared several new 1,4-DHPs endowed with long alkyl and functionalised chains.[6] In addition we have reported the study of the ESI mass spectra and sequential product ion fragmentation of 1,4-DHP derivatives endowed with long alkyl chains.[7]

In connection with our studies of the NMR behaviour of 1,4-dihydropyridine derivatives, in this paper reports the ^{1}H and ^{13}C assignments of a series of differently substituted 1,4-dihydropyridines endowed with long and functionalized chains, **1a**-**d**, **2a**-**b**, **3a**-**e**, **4a**-**c** and **5a**-**b** (see Figure 1). Also we describe the ^{15}N NMR spectra of some chosen compounds. These data are of interest to determine the effect that this substitution pattern has on the chemical shifts of the 1,4-DHPs ring and to complete the reference data on the previously reported related systems.[8,11]

Results and Discussion

The 1,4-DHPs derivatives here studied were prepared by a Hantzsch-like synthesis, and obtained as stable crystalline solids with good yields.

In order to assign unequivocally all NMR signals, we used 1D and 2D techniques such as DEPT(135), HMQC and HMBC.

The ^{1}H NMR spectra at 300 MHz of 1,4-DHPs (Table 1) show a singlet corresponding to the NH proton at 9.19-8.76 ppm when the spectra were registered in DMSO-d_6 or at 6.55-7.97 when they were registered in $CDCl_3$. Also at 4.75-5.02 ppm appears another singlet corresponding to the H4 proton.

The methyl groups on C-2 and C-6 of the 1,4-DHP ring appear as singlets at δ *ca.* 2.2 ppm, and cannot be

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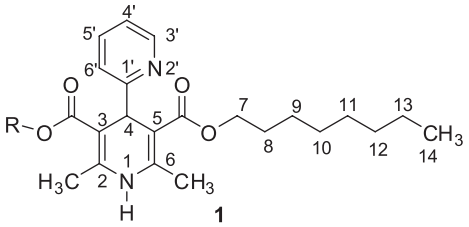


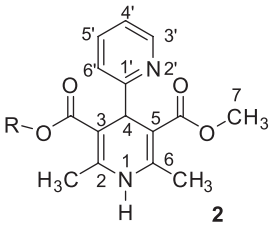
1

1a R = $^{15}CH_3$

1b R = $^{15}CH_2$-$^{16}CH_3$

1c R = $^{15}CH_2$-$^{16}CH_2$-^{17}CN

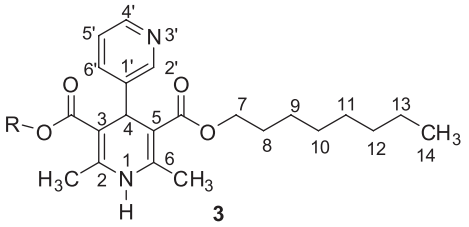
1d R = $^{7}CH_2$-$^{8}CH_2$-$^{9}CH_2$-$^{10}CH_2$-$^{11}CH_2$-$^{12}CH_2$-$^{13}CH_2$-$^{14}CH_3$



2

2a R = $^{8}CH_2$-$^{9}CH_2$-^{10}CN

2b R = $^{8}CH_2$-$^{9}CH_2$-$^{10}CH_2$-$^{11}CH_2$-$^{12}CH_2$-$^{13}CH_2$-$^{14}CH_2$-$^{15}CH_2$-$^{16}CH_2$-$^{17}CH_2$-$^{18}CH_2$-$^{19}CH_3$



3

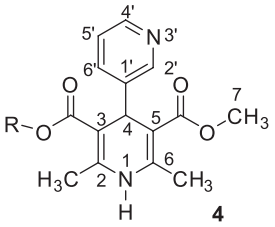
3a R = $^{15}CH_3$

3b R = $^{15}CH_2$-$^{16}CH_3$

3c R = $^{15}CH_2$-$^{16}CH_2$-^{17}CN

3d R = $^{7}CH_2$-$^{8}CH_2$-$^{9}CH_2$-$^{10}CH_2$-$^{11}CH_2$-$^{12}CH_2$-$^{13}CH_2$-$^{14}CH_3$

3e R = $^{15}CH_2$-$^{16}CH_2$-$^{17}CH_2$-$^{18}CH_2$-$^{19}CH_2$-$^{20}CH_2$-$^{21}CH_2$-$^{22}CH_2$-$^{23}CH_2$-$^{24}CH_3$

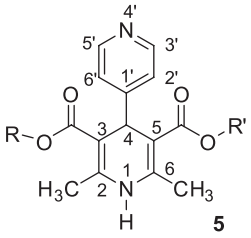


4

4a R = $^{8}CH_2$-$^{9}CH_2$-^{10}CN

4b R = $^{8}CH_2$-$^{9}CH_2$-$^{10}CH_2$-$^{11}CH_2$-$^{12}CH_2$-$^{13}CH_2$-$^{14}CH_2$-$^{15}CH_2$-$^{16}CH_2$-$^{17}CH_3$

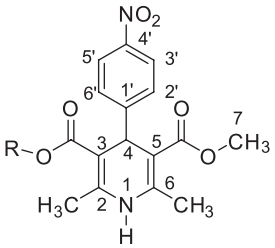
4c R = $^{8}CH_2$-$^{9}CH_2$-^{10}O-$^{11}CH_2$-$^{12}CH_2$-$^{13}CH_2$-$^{14}CH_3$



5

5a R = $^{7}CH_2$-$^{8}CH_2$-^{9}CN R' = $^{10}CH_3$

5b R = R' = $^{7}CH_2$-$^{8}CH_2$-$^{9}CH_2$-$^{10}CH_2$-$^{11}CH_2$-$^{12}CH_2$-$^{13}CH_2$-$^{14}CH_3$



6

6a R = $^{8}CH_2$-$^{9}CH_2$-^{10}CN

6b R = $^{8}CH_2$-$^{9}CH_2$-$^{10}CH_2$-$^{11}CH_2$-$^{12}CH_2$-$^{13}CH_2$-$^{14}CH_2$-$^{15}CH_3$

Figure 1. Chemical structures for 1,4-dihydropyridine derivatives.

distinguished in compounds **1d**, **3d** and **3e**, because of the similarity of the substituents on C-3 and C-5. The ^{1}H NMR spectra of compounds **1**, **2**, **3**, **4** and **5**, also show signals between 7.0-8.5 ppm corresponding to the protons of the pyridine ring on C-4, showing the characteristic multiplicity depending on the position of the nitrogen atom in the pyridine ring. In compounds **6a** and **6b** endowed with a *p*-nitrophenyl ring, the aromatic protons appear at 8.1 and 7.4 ppm as an AA'BB' system.

The alkoxycarbonyl group shows a number of signals which depends of the size of the chain. In these cases, the methylene group joint to the oxygen atom of the alkoxycarbonyl chain (–O–CH_2–R) on C-3 and C-5, appears at *ca.* 3.9 ppm as a multiplet due to the presence of a stereogenic center on C-4. The rest of the aliphatic protons appear as a broad multiplet at *ca.* 1.2 ppm and terminal methyl group as a triplet at δ 0.8 ppm. The protons of the α-methylene group corresponding to the

cyanoethyl group in compounds **1c**, **2a**, **3c**, **4a**, **5a** and **6a** appear as a multiplet at δ 2.8 ppm while the β-protons resonate at 4.1 ppm forming a triplet.

The ^{13}C NMR spectra of these compounds exhibit signals in the carbonyl, aromatic and aliphatic regions. In order to assign unequivocally the signals corresponding to the heterocyclic ring, we used 1D and 2D techniques: DEPT(135), HMQC and HMBC.

For the 1,4-DHP ring, the spectra showed four quaternary carbon signals (C-2, C-3, C-5, and C-6) and one tertiary carbon signal (C-4). As can be seen in Table 2, the signals corresponding to the 1,4-DHP carbons ring are relatively insensitive to the nature of the substituents on C-3, C-4, and C-5. The ^{13}C NMR spectra of these compounds show the signal for C-3 and C-5 at lower δ values (*ca.*100 ppm) than those expected for typical olefinic carbons atoms, while C-2 and C-6 signals appear at higher δ values (*ca.*146 ppm) and C-4 appears between 36.8 and 41.3 ppm. These findings have been accounted for by the strong push-pull effect of the groups linked to the olefinic double bonds, similar to that previously observed in other related molecules.[8-11] The alkoxycarbonyl sp^2-carbon (COOR or COOR^1) on C-3 and C-5 appears at 166-167 ppm. In compounds **1c**, **2a**, **3c**, **4a**, **5a** and **6a** the cyano group appears at *ca.*119 ppm.

As we can see in Table 2, some carbons of the alkoxy chain do not present remarkable difficulties to be resolved and all nuclei were assigned on the basis of coupling constant and cross peaks on the 2D spectra. The rest of the signals are in agreement with the nature of aromatic or aliphatic carbon atoms. All the compounds showed a similar trend in the chemical shifts of the common moiety of the molecular backbone.

Also the ^{15}N NMR spectrum of the compounds **2a**, **4a**, **4c** and **5a** were recorded in order to ensure the structure. The ^{15}N HMQC, using two different values

Table 1. ^{1}H NMR data for compounds **1a-d**, **2a-b**, **3a-e**, **5a-b**, **6a-b** (δ, ppm; *J*, Hz)

Comp.	N-H	H-4	CH_3-C-2	CH_3-C-5	H-7	H-8	H-9	H-10	H-11	H-12	H-13	H-14	H-15	H-16
1a	8.78, s	5.01, s	2.23, s	2.22, s	3.94, m	1.48, m			1.24, br s			0.85, t, (*J* 6.8)	3.53, s	-
1b	8.76, s	5.00, s	2.23, s	2.21, s	3.90, m	1.47, m			1.20, br s			0.84, t, (*J* 6.8)	3.90, m	1.12, t, (*J* 7.4)
1c	8.99, s	5.02, s	2.24, s	2.23, s	3.93, m	1.48, m			1.20, br. s			0.85, t, (*J* 6.7)	4.13, t, (*J* 5.8)	2.83, m
1d	8.77, s	5.02, s	2.22, s		3.91, m	1.48, m			1.21, br s			0.85, t, (*J* 6.4)		
2a	8.90, s	5.01, s	2.25, s	2.24, s	3.53, s	4.14, t, (*J* 6.0)	2.83, m	-	-	-	-	-	-	-
2b	8.79, s	5.01, s	2.23, s	2.21, s	3.53, s	3.91, m	1.47, m				1.23, br s			
3a	8.97, s	4.89, s	2.28, s	2.26, s	3.90, m	1.48, m			1.21, br s			0.85, t, (*J* 6.6)	3.54, s	-
3b[a]	6.61, s	4.98, s	2.34, s	2.32, s	4.05, m	1.58, m			1.20, br s			0.88, t, (*J* 6.7)	4.05, m	1.19, t, (*J* 7.1)
3c	9.05, s	4.86, s	2.28, s	2.27, s	4.16, m	1.48, m			1.20 br s			0.85, t, (*J* 6.9)	4.13, m	2.84, m
3d[a]	7.97, s	4.75, s	2.10, s		3.36 t, (*J* 6.5)	1.35, m			1.02, m			0.64, t, (*J* 6.5)	-	-
3e[a]	6.55, s	5.03, s	2.36, s		4.02, m	1.58, m			1.25, m			0.88, t, (*J* 6.4)	4.02, m	1.58, m
4a	9.08, s	4.86, s	2.29, s	2.28, s	3.54, s	4.15, t, (*J* 5.9)	2.84, m	-	-	-	-	-	-	-
4b	8.98, s	4.85, s	2.27, s	2.25, s	3.54, s	3.92, m	1.47, m				1.22, br. s			
4c	9.00, s	4.86, s	2.26, s	2.21, s	3.52, s	4.06, m	3.49, m	-	3.35, m	1.45, m	1.30, m	0.86, t, (*J* 6.91)	-	-
5a	9.11, s	4.88, s	2.29, s	2.28, s	4.16, t, (*J* 5.95)	2.84, m	-	3.55, s	-	-	-	-	-	-
5b	8.99, s	4.88, s	2.27, s	2.29, s	3.94,m	1.49, m			1.21, m			0.85, t, (*J* 6.46)		
6a	9.19, s	4.98, s	2.29, s	2.28, s	3.53, s	4.14, t, (*J* 5.3)	2.83, m	-	-	-	-	-	-	-
6b	9.03, s	4.97, s	2.29, s	2.25, s	3.54, s	3.97, m		1.44, m			1.08, br s		0.83, t, (*J* 7.0)	-

Table 1. Continuation

Comp.	H-17	H-18	H-19	H-20	H-21	H-22	H-23	H-24	Aromatics
1a	-	-	-	-	-	-	-	-	8.38 (1H, d, *J* 4.7, H3'), 7.58 (1H, td, *J* 7.7, *J* 1.8, H5'), 7.11 (2H, m, H4', H6')
1b	-	-	-	-	-	-	-	-	8.38 (1H, br d, *J* 4.5, H3'), 7.58 (1H, td, *J* 7.6, *J* 1.9, H5'), 7.12 (1H, d, H6', overlaping with 7.09), 7.09 (1H, d, H4', overlaping with 7.12)
1c	-	-	-	-	-	-	-	-	8.39 (1H, br. d, *J* 4.8, H3'), 7.56 (1H, td, *J* 7.8, *J* 1.6, H5'), 7.19 (1H, d, *J* 7.8, H6'), 7.09 (1H, dd, *J* 7.8, *J* 4.8, H4')
1d	-	-	-	-	-	-	-	-	8.38 (1H, d, *J* 4.0, H3'), 7.55 (1H, td, *J* 7.6, *J* 1.8, H5'), 7.10 (2H, m, H4', H6')
2a	-	-	-	-	-	-	-		8.40 (1H, d, *J* 4.7, H3'), 7.58 (1H, td, *J* 7.7, *J* 1.8, H5'), 7.18 (1H, d, *J* 7.7, H6'), 7.11 (1H, dd, *J* 7.7, *J* 4.7, H4')
2b	1.23, m		0.85, t, (*J* 6.4)	-	-	-	-	-	8.38 (1H, d, *J* 4.0, H3'), 7.59 (1H, td, *J* 7.6, *J* 1.8, H5'), 7.09 (2H, m, H4', H6')
3a	-	-	-	-	-	-	-	-	8.35 (1H, d, *J* 1.6, H2'), 8.31 (1H, dd, *J* 4.7, *J* 1.6, H4'), 7.47 (1H, dt, *J* 7.8, *J* 1.6, H6'), 7.23 (1H, dd, *J* 7.8, *J* 4.7, H5')
3b[a]	-	-	-	-	-	-	-	-	8.52 (1H, d, *J* 1.6, H2'), 8.36 (1H, dd, *J* 4.8, *J* 1.6, H4'), 7.61 (1H, dt, *J* 7.8, *J* 1.6, H6'), 7.15 (1H, dd, *J* 7.8, *J* 4.8, H5')
3c	-	-	-	-	-	-	-	-	8.39 (1H, d, *J* 1.6, H2'), 8.30 (1H, dd, *J* 4.7, *J* 1.6, H4'), 7.53 (1H, dt, *J* 7.8, *J* 1.6, H6'), 7.23 (1H, dd, *J* 7.8, *J* 4.7, H5')
3d[a]				1.02, m				0.85, t, (*J* 6. 9)	8.26 (1H, d, *J* 1.8, H2'), 8.10 (1H, dd, *J* 5.0, *J* 1.8, H4') 7.43 (1H, dt, *J* 7.0, *J* 1.8, H6'), 6.98 (1H, dd, *J* 7.0, *J* 5.0, H5')
3e[a]	-	-	-	-	-	-	-	-	8.51 (1H, d, *J* 1.8, H2'), 8.38 (1H, dd, *J* 5.0, *J* 1.8, H4') 7.83 (1H, dt, *J* 7.8, *J* 1.8, H6'), 7.30 (1H, dd, *J* 7.8, *J* 5.0, H5')
4a	-	-	-	-	-	-	-	-	8.38 (1H, d, *J* 1.7, H2'), 8.32 (1H, dd, *J* 4.7, *J* 1.7, H4'), 7.52 (1H, dt, *J* 7.7, *J* 1.7, H6'), 7.24 (1H, dd, *J* 7.7, *J* 4.7, H5')
4b	0.85, t, (*J* 6.4)	-	-	-	-	-	-	-	8.35 (1H, d, *J* 1.6, H2'), 8.30 (1H, dd, *J* 4.7, *J* 1.6, H4'), 7.48 (1H, dt, *J* 7.9, *J* 1.6, H6'), 7.24 (1H, dd, *J* 7.9, *J* 4.7, H5')
4c	-	-	-	-	-	-	-	-	8.38 (1H, d, *J* 1.7, H2'), 8.31 (1H, dd, *J* 4.7, *J* 1.7, H4'), 7.50 (1H, dt, *J* 7.9, *J* 1.7, H6'), 7.23 (1H, dd, *J* 7.9, *J* 4.7, H5')
5a	-	-	-	-	-	-	-	-	8.40 (2H, d, *J* 5.9, H3', H5'), 7.14 (2H, d, *J* 5.95, H2', H6')
5b	-	-	-	-	-	-	-	-	8.38 (2H, d, *J* 5.95, H3', H5'), 7.10 (2H, d, *J* 5.9, H2', H6')
6a	-	-	-	-	-	-	-	-	8.09 (2H, d, *J* 8.7, H3', H5'), 7.44 (2H, d, *J* 8.7, H2', H6')
6b	-	-	-	-	-	-	-	-	8.10 (2H, d, *J* 8.7, H3', H5'), 7.40 (2H, d, *J* 8.7, H2', H6')

[a]Registred in $CDCl_3$.

of the N,H coupling constants, allow us to determine the chemical shift of the nitrogen atoms present in the molecule. In the HMQC, using a value of ^1J(N,H) 80 Hz, the hydrogen signal correlates with the N-1 atom at *ca.* −239 ppm. However in the HMQC using values of ^nJ(N,H) 5 Hz the hydrogen signals showing correlation were those bonded through more than one bond. This confirms the position of N-1 and allows us to assign the position of the pyridine nitrogen at *ca.* −66 ppm, which is in agreement with values reported in the literature[12] (see Table 3).

Experimental

Material

Compounds **1**, **2**, **3**, **4**, **5** and **6** were prepared according to the synthetic method described previously.[6] The 1,4-DHPs derivatives were purified by recrystallization. Compatible IR and mass spectra and combustion analyses were taken for each compound.

Spectra

All NMR experiments were performed at 298 K for a solution of 30 mg of compound dissolved in 0.7 mL of DMSO-d_6 on a Bruker AVANCE-300 instrument with a 5-mm QNP probe head equipped with shielded Z-gradient coil. ^{1}H NMR spectra were recorded at a proton frequency of 300.13 MHz with a spectral width of 4.5 kHz and a 2.15 μs (30°) pulse. The acquisition time was 1.8 s and relaxation delay 1 s; 16 scans with 16k data points each were used. The ^{13}C NMR were obtained using a spectral width of 20 kHz, a 1.9 μs (30°) pulse, and a 1.7 s acquisition time; 512 scans with 64k data points each were used. Exponential multiplication was applied before Fourier transformation in both cases. The chemical shifts were referenced to DMSO-d_6. The one-bond heteronuclear correlation (HMQC) spectra were obtained using the inv4gs program in the Bruker software. The spectra resulted from a 256 × 2048 data matrix with 8 scans *per* t_1 increment. Spectral widths of 3.5 kHz in f_2 and 16.0 kHz in f_1 were used. The acquisition time was 0.30 s, the delay was set to

3.45 ms, (corresponding to an average ^1J(C,H) of 145 Hz), and the recycle time was 1.44 s. Fourier transformation was done on a 2k × 1k data matrix. The long-range ^{1}H-^{13}C correlation (HMBC) spectra were obtained using the inv4gslplrnd program in the Bruker software. The spectra resulted from a 256 × 2048 data matrix with 16 scans *per* t_1 increment. A spectral width of 3.5 kHz in f_2 and 16.7 kHz in f1 were used. The acquisition time was 0.30 s, the delays were set to 3.45 ms ($1/2J_{C,H}$) and 65 ms (corresponding to an average $1/^nJ_{C,H}$ of 7.7Hz), and the recycle time was 1.44 s. Fourier transformation was done on a 2k × 1k data matrix.

^{15}N NMR spectra were recorded at 50.687 MHz on a Bruker Avance-500 instrument. The chemical shifts were referenced to CH_3NO_2 at 0.00 ppm. The one-bond heteronuclear correlation (HMQC) was obtained using the inv4gpqf program in the Bruker software. The spectra resulted from a 128 × 1024 data matrix with 32 scans *per* t_1 increment. Spectral widths of 6.5 kHz in f_2 and 20.5 kHz in f_1 were used. The acquisition time was 0.1 s and delay was set to 6 ms (corresponding to ^1J(N,H) of 80 Hz) and 100 ms for ^nJ (N,H) of 5 Hz using a recycle time of 2s.

Table 2. ^{13}C NMR data for compounds **1a-d, 2a-b, 3a-e, 5a-b, 6a-b** (δ, ppm)

	Aromatics	(C-5-C=O)	(C-3-C=O)	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
1a	164.9 (C1'), 149.1 (C3'); 135.6 (C5'), 121.4, 121.3 (C4', C6')	167.5	166.9	146.1[b] 146.0[b]	100.3	41.2	100.2	146.1[b] 146.0[b]	62.9	28.3	25.5
1b	165.1 (C1'), 135.4 (C5'), 121.7 (C6'), 121.3 (C4'), 149.1 (C3')	166.9	166.9	146.2[b] 145.9[b]	100.4[b] 100.3[b]	41.3	100.4[b] 100.3[b]	146.2[b] 145.9[b]	62.9	28.3	25.6
1c	164.8 (C1'), 149.1 (C3'), 135.5 (C5'), 121.8 (C6'), 121.4 (C4')	166.9	166.5	147.1[b] 146.0[b]	100.7	41.1	99.5	147.1[b] 146.0[b]	63.0	28.2	25.5
1d	165.1 (C1'), 149.1 (C3'), 121.6, 121.3 (C4', C6'), 135.3 (C5')	166.9		146.1	100.3	41.2	100.3	146.1	62.9	28.3	25.6
2a	164.7 (C1'), 149.1 (C3'), 121.4 (C4'), 135.8 (C5')	167.4	166.5	147.2[b] 146.1[b]	99.5	41.0	100.5	147.2[b] 146.1[b]	50.6	58.4	17.5
2b	164.9 (C1'), 149.1 (C3'), 135.5 (C5'), 121.4, 121.2 (C4', C6')	167.4	166.9	146.1[b] 146.0[b]	100.3	41.1	100.2	146.1[b] 146.0[b]	50.0	62.9	28.2
3a	148.5 (C2'), 147.2 (C4'), 143.2 (C1'), 134.6 (C6'), 123.5 (C5')	167.1	166.6	146.3	100.9[b] 100.8[b]	36.8	100.9[b] 100.8[b]	146.3	63.2	28.2	25.5
3b[a]	149.4 (C2'), 147.1 (C4'), 143.5 (C1'), 135.6 (C6'), 123.0 (C5')	167.3[b] 167.2[b]	167.3[b] 167.2[b]	145.0[b] 144.9[b]	103.1	37.7	103.1	145.0[b] 144.9[b]	64.0	28.6	26.0
3c	148.6 (C2'), 147.2 (C4'), 143.1 (C1'), 123.4 (C5'), 134.8 (C6')	166.1	166.5	147.2[b] 146.1[b]	101.4[b] 100.3[b]	36.8	101.4[b] 100.3[b]	147.2[b] 146.1	63.2	28.2	25.5
3d[a]	147.7 (C2'), 145.3 (C4'), 143.7 (C1'), 135.9 (C6'), 122.8 (C5')	166.8	166.8	145.8	101.3	37.2	101.3	145.8	63.2	28.0	25.4
3e[a]	144.7, 144.6 (C4', C1'), 147.3 (C2'), 138.1 (C6'), 123.8 (C5')	167.6	167.6	145. 5	103.2	38.0	103.2	145.5	64.5	28.6	26.0
4a	148.5 (C2'), 147.3 (C4'), 142.9 (C1'), 134.7 (C6'), 123.5 (C5')	166.9	166.1	146.3[b] 146.2[b]	100.2	36.7	101.2	146.3[b] 146.2[b]	50.8	58.6	17.4
4b	148.5 (C2'), 147.1 (C4'), 143.1 (C1'), 134.6 (C6'), 123.5 (C5')	167.1	166.5	146.3[b] 146.2[b]	100.8	37.2	100.9	146.3[b] 146.2[b]	50.7	63.1	28.3
4c	148.8 (C2'), 147.3 (C4'), 143.0 (C1'), 134.9 (C6'), 123.7 (C5')	166.5	167.0	147.7	101.2	36.9	101.0	147.7	50.8	68.3	62.8
5a	155.8 (C1'), 149.8 (C3', C5'), 122.7 (C2', C6')	167.4	166.5	147.1[b] 146.9[b]	100.9	38.6	100.5	147.1[b] 146.9[b]	58.9	17.7	-
5b	157.0 (C1'), 149.5 (C3', C5'), 122.5 (C2', C6')	167.5	167.5	147.6	101.3	38.6	101.3	147.6	63.5	28.6	25.4
6a	155.2 (C4'), 147.7 (C1'), 128.8 (C2', C6'), 123.8 (C3', C5')	167.0	166.2	146.5[b] 146.0[b]	100.1	39.8	100.1	146.5[b] 146.0[b]	51.2	58.9	17.7
6b	155.7 (C4'), 145.7 (C1'), 128.7 (C2', C6'), 123.7 (C3', C5')	167.0	166.5	146.6[b] 146.4[b]	100.7[b] 100.6[b]	39.6	100.7[b] 100.6[b]	146.6[b] 146.4[b]	51.2	63.6	28.2

Table 2. Continuation

	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18	C-19	C-20	C-21	C-22	C-23	C-24	CH_3-C-6	CH_3-C-2	CN
1a	31.2	28.6	28.6	22.1	13.9	50.6	-	-	-	-	-	-	-	-	-		18.3		-
1b	31.2	28.6	28.6	22.1	13.9	58.9	14.2	-		-	-	-	-	-	-		18.2		-
1c	31.2	28.6	28.6	22.1	13.9	58.4	17.5	-	-	-	-	-	-	-	-	18.3		18.6	118.8
1d	31.2	28.6	28.6	22.1	13.9	62.9	28.3	25.6	31.2	28.6	28.6	22.1	13.9	-	-	18.3		18.6	-
2a	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	18.3		18.6	118.8
2b	31.3	29.0	29.0	28.9	28.7	28.6	28.6	25.5	22.1	13.9	-	-	-	-	-		18.3		-
3a	31.1	28.6	28.6	22.1	13.9	50.8	-	-	-	-	-	-	-	-	-	18.2		18.1	-
3b[a]	31.7	29.2	29.2	22.6	14.1	59.8		-	-	-	-	-	-	-	-		19.3		-
3c	31.2,	28.6	28.6	22.1	13.9	58.6	17.4	-	-	-	-	-	-	-	-	18.1		18.4	118.6
3d[a]	31.1	28.6,	28.5	21.9	13.5	-	-	-	-	-	-	-	-	-	-		18.2		-
3e[a]	31.9	29.5	29.3	22.7	14.4	64.5	28.6	26.0	29.5	23.3	29.2	29.3	31.8	22.6	14.2	19.5		19.5	-
4a	-	-	-	-	-	-	-	-	-	-	-	-				18.2		18.5	118.7
4b	25.9	31.6	29.2	29.2	29.0	28.9	22.5	13.0	-	-		-	-	-	-	18.1		18.2	-
4c	-	70.1	31.5	19.4	14.1	-	-	-	-	-	-	-	-	-	-		18.5		-
5a	51.2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	18.6		18.5	119.9
5b	31.6	28.9	28.9	22.4	14.1												18.2		-
6a	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	18.6		18.8	119.9
6b	25.5	31.5	28.7	28.6	22.1	13.9										18.3		18.2	-

[a]Registred in $CDCl_3$; [b]Interchangeable.

Table 3. ^{15}N HMQC data for 1,4-dihydropyridine derivatives (ppm)

Compound	N-1	N-2'	N-3'	N-4'
2a	−238.28	−65.15	-	-
4a	−239.44	-	−63.22	-
4c	−240.17	-	−62.53	-
5a	−238.88	-	-	−67.01

Conclusions

We have recorded the ^1H and ^{13}C NMR spectra of several substituted 1,4-dihydropyridines (1,4-DHPs) endowed with long and functionalized chains in order to assign unequivocally all the chemical shifts. These spectral data are of interest to report the effect of the substitution pattern on the chemical shifts and to complete reference data previously reported. The 1,4-DHPs carbons ring are practically insensitive to the nature of substituents. Also, we present the ^{15}N NMR spectroscopic data of the reported molecules.

References

1. Goldmann, S.; Stoltefuss, J.; *Angew. Chem., Int. Ed.* **1991**, *30*, 1559; Richter, M.; Molnar, J.; Hilgeroth, A.; *J. Med. Chem.* **2006**, *49*, 2838.
2. Jain, P.; Narang, G.; Jindal, D. P.; Bansal, R.; Calle, C.; Carron, R.; Pemberton, K.; Harvey, A. L.; *Pharmazie* **2006**, *61*, 400; Evdokimov, N. M.; Magedov , I. V.; Kireev, A. S.; Kornienko, A.; *Org. Lett.* **2006**, *8*, 899.
3. Triggle, D. J.; *Mini-Rev. Med. Chem.* **2003**, *3*, 215; Triggle, D.; *J. Cell. Moll. Neurobiol.* **2003**, *23*, 293.
4. Boschi, D.; Caron, G.; Visentin, S.; Di Stilo, A.; Rolando, B.; Fruttero, R.; Gasco, A.; *Pharm. Res.* **2001**, *18*, 987.
5. Minsane, I.; Klusa, V.; Dambrova, M.; Germane, S.; Duburs, G.; Bisennieks, E.; Roimondini, R.; Ogren, S. O.; *Eur. Neuropsychopharmacol.* **1998**, *8*, 329.
6. Suárez, M.; de Armas, M.; Ramírez, O.; Alvarez, A.; Martinez, R.; Molero, D.; Seoane, C.; Liz, R.; Novoa, H.; Blaton, N.; Peeters, O.; Martín, N.; *New J. Chem.* **2005**, *12*, 1567.
7. Suárez, M.; de Armas, M.; Ramírez, O.; Álvarez, A.; Martínez-Álvarez, R.; Kayali, N.; Seoane, C.; Martin, N.; *Rapid Commun. Mass Spectrom.* **2005**, *19*, 1906.
8. Suárez, M.; Molero, D.; Salfrán, E.; Martín, N.; Verdecia, Y.; Martinez, R.; Ochoa, E.; Alba, L.; Quinteiro, M.; Seoane, C.; *Magn. Reson. Chem.* **2001**, *39*, 105.
9. Suárez, M.; Martín, N.; Martínez, R.; Verdecia, Y.; Molero, D.; Alba, L.; Seoane, C.; Ochoa, E.; *Magn. Reson. Chem.* **2002**, *40*, 303.
10. Molero, D.; Suárez, M.; Martínez-Álvarez, R.; Verdecia, Y.; Martín, N.; Seoane, C.; Ochoa, E.; *Magn. Reson. Chem.* **2004**, *42*, 704.
11. Salfrán, E.; Suárez, M.; Molero, D.; Martínez-Álvarez, R.; Verdecia, Y.; Ochoa, E.; Álvarez, A.; Seoane, C.; Herrera, A.; Martín, N.; *Magn. Reson. Chem.* **2006**, *44*, 637.
12. Berger, S.; Braun, S.; Kalinowski, H. O.; *NMR Spectroscopy of the Non-Metallic Elements*, John Wiley & Sons: Chichester, 1997 (ISBN 0 471 96763 7).

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