

Spectral Assignments and Reference Data

¹H and ¹³C chemical shifts for 2-aryl and 2-N-arylamino benzothiazole derivatives

S. Billeau, F. Chatel, M. Robin,* R. Faure and J.-P. Galy

Laboratoire de Valorisation de la Chimie Fine, UMR CNRS 6178 Symbio, Faculté des Sciences et Techniques de Saint-Jérôme, Université Paul Cézanne, Av. Escadrille Normandie-Niemen, 13397 Marseille Cedex 20, France

Received 25 May 2005; accepted 25 July 2005

The ¹H and ¹³C NMR resonances for forty-three 2-aryl and 2-N-arylamino benzothiazole derivatives were completely assigned using a concerted application of one- and two-dimensional experiments (DEPT, gs-COSY, gs-HMQC and gs-HMBC). Copyright © 2005 John Wiley & Sons, Ltd.

KEYWORDS: NMR; ¹H NMR; ¹³C NMR; COSY; HMQC; HMBC; 2-aryl benzothiazoles; 2-N-arylamino benzothiazoles

INTRODUCTION

During the last decade, a large number of 2-aryl benzothiazoles (Scheme 1) and 2-N-arylamino benzothiazoles (Scheme 3) have been prepared because of their wide pharmacological potency. In fact, this important class of compounds has interesting anti-inflammatory,¹ antimicrobial,^{2–4} antitumor^{5,6} and neuroprotective properties.⁷ Recently, these compounds were also used as precursors for *in vivo* imaging of β -amyloid plaques,⁸ and for nonlinear optical application.⁹ As a part of our program aimed at developing new heterocyclics bearing a thiazole ring,^{10–13} we report in this paper the complete ¹H and ¹³C NMR chemical shift assignments using one- and two-dimensional NMR techniques, including DEPT, gs-COSY, gs-HMQC and gs-HMBC, for 2-N-arylamino benzothiazole and 2-aryl benzothiazole derivatives.

EXPERIMENTAL

Materials:

General procedures for benzothiazoles formation

For 2-aryl benzothiazoles (**1–26**),¹⁴ typically, the corresponding substituted benzoic acid (10 mmol), 2-amino thiophenol (11 mmol) and PPA (10 g) were heated at 140 °C for 24 h. The resulting mixture was poured into water. The precipitate was collected by filtration, dried and recrystallized from CH₂Cl₂ (yield 80–90%).

For 2-N-(aryl)-6-nitro benzothiazoles (**27, 29–32, 34, 36, 38–40, 42**),³ a mixture of 2-chloro-6-nitrobenzothiazole (10 mmol) and phenol (3 g) was heated at 100 °C under nitrogen. When the chloro compound was dissolved in phenol, the corresponding substituted anilines (11 mmol) were introduced into the reaction mixture. The mixture was stirred at 80 °C for 4 h, cooled to room temperature and poured into water. The precipitate was then filtered and recrystallized from ethanol (yield 50–70%).

2-N-(aryl)-6-aminobenzothiazoles (**28, 33, 35, 37, 41, 43**) were prepared and purified as described previously (yield 50–70%),³ using catalytic hydrogenation with H₂, Pd/C, and an ethanol system.

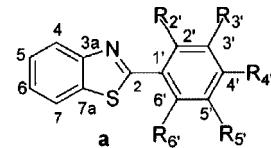
NMR techniques

NMR spectra were recorded in DMSO-*d*₆ solutions at 300 K using a Brüker Avance DRX 500 spectrometer equipped with a Brüker CryoPlatform and a 5 mm cryo TXI probe. The temperature of the probe and preamplifier was 30 K. Chemical shifts were referenced

to DMSO-*d*₆: δ_H = 2.50 ppm, δ_C = 39.6 ppm.¹⁵ Resonance multiplicities for ¹³C signals were established via the acquisition of DEPT spectra. For two-dimensional experiments, Brüker microprograms using gradient selection (gs) were applied. The gs-COSY spectra¹⁶ were obtained with an *F*₂ spectral width of 10 ppm and 2 K data points and an *F*₁ spectral width of 256 *t*₁ increments with sine-bell windows in both dimensions. The gs-HMQC spectra¹⁷ resulted from a 256 × 1024 data matrix size with 2–16 scans per *t*₁ depending on the sample concentration, an interpulse delay of 3.2 ms and a 5:3:4 gradient combination. The gs-HMBC spectra¹⁸ were measured using a pulse sequence optimized for 10 Hz (interpulse delay for the evolution of long-range couplings, 50 ms) and the same gradient ratios.

RESULTS AND DISCUSSION

In Schemes 1–3, the structures and numbering of substituted benzothiazoles **1–43** are presented. Their ¹H and ¹³C NMR chemical shifts are given in Tables 1 and 2 respectively. Routine ¹³C NMR are insufficient to obtain unambiguous determination of chemical shifts since strict additivity using SCS values of all substituents¹⁹ does not apply for polysubstituted aromatic compounds.^{20–22} Therefore, we employed a sequence of NMR techniques as follows: (i) DEPT experiments to determine the multiplicities of the ¹³C signals; (ii) gs-COSY diagrams to determine the connectivity of protons; (iii) HMQC spectra to determine the ¹³C resonances of the protonated carbons; (iv) gs-HMBC sequences to assign the signals of quaternary and protonated carbons via two- and three-bond interactions.

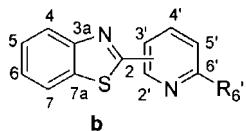


No	R ₂	R _{3'}	R _{4'}	R _{5'}	R _{6'}
1	H	H	H	H	H
2	H	H	N(CH ₃) ₂	H	H
3	H	H	OH	H	H
4	H	H	OCH ₃	H	H
5	H	H	Br	H	H
6	H	H	NH ₂	H	H
7	H	H	NHCOC ₆ H ₅	H	H
8	H	H	CH(CH ₃) ₂	H	H
9	Cl	H	H	H	H
10	OH	H	H	H	H
11	NH ₂	H	H	H	H
12	H	NHCOC ₆ H ₅	H	H	H
13	OH	H	NH ₂	H	H
14	Cl	H	Cl	H	H
15	Cl	H	F	H	H
16	Cl	H	NH ₂	H	H
17	Cl	H	H	NO ₂	H
18	Br	H	H	OCH ₃	H
19	Cl	H	H	H	F
20	H	NH ₂	OCH ₃	H	H
21	H	OCH ₃	NO ₂	H	H
22	H	CO ₂ CH ₃	H	NO ₂	H

Scheme 1. Structures of 2-aryl-benzothiazoles derivatives **1–22** (the numbering of the atoms is arbitrary).

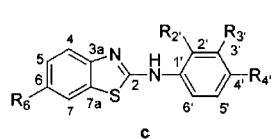
*Correspondence to: M. Robin, Laboratoire de Valorisation de la Chimie Fine, Université Paul Cézanne, Av. Escadrille Normandie-Niemen, 13397 Marseille Cedex 20, France. E-mail: maxime.robin@univ-3-mrs.fr

Spectral Assignments and Reference Data



No	Link	R _{6'}
23	ortho	H
24	meta	H
25	para	H
26	meta	OH

Scheme 2. Structures of 2-pyridinyl-benzothiazoles derivatives **23–26**.



No	R ₆	R ₂	R ₃	R ₄	R ₅	R ₆
27	NO ₂	H	H	CH ₃	H	H
28	NH ₂	H	H	CH ₃	H	H
29	NO ₂	H	H	NH ₂	H	H
30	NO ₂	H	H	CO ₂ H	H	H
31	NO ₂	H	H	CH ₂ CO ₂ H	H	H
32	NO ₂	H	H	Cl	H	H
33	NH ₂	H	H	Cl	H	H
34	NO ₂	Cl	H	CH ₃	H	H
35	NH ₂	Cl	H	CH ₃	H	H
36	NO ₂	H	Cl	CH ₃	H	H
37	NH ₂	H	Cl	CH ₃	H	H
38	NO ₂	CH ₃	H	Cl	H	H
39	NO ₂	H	OCH ₃	CO ₂ CH ₃	H	H
40	NO ₂	OCH ₃	H	H	CO ₂ H	H
41	NH ₂	H	CO ₂ H	H	H	H
42	NO ₂	OH	H	NO ₂	H	H
43	NH ₂	NH ₂	H	CH ₃	H	H

Scheme 3. Structures of 2-N(aryl)-benzothiazoles derivatives **27–43**.

Benzothiazole ring resonances

The ¹H 500 MHz spectra for benzothiazoles **1–26** showed the expected four-spin system where complete ¹H assignment cannot be achieved solely by the analysis of the COSY connectivities. For the compounds **27–43**, the protons would constitute a well-resolved AMX spin system for which ¹H signals were assigned with certainty on the basis of appearance of the multiplet patterns and the magnitude of the splittings. Also, for these derivatives, the NH proton appears as a singlet at ~11 ppm. For all the compounds, H-4 and H-7 displayed long-range correlations (³J coupling) with, respectively, C-7a and C-3a; assignment of both these carbons was straightforward based on their chemical shifts.²³ Additionally, C-2 exhibits three-bond cross peaks with H-2' and (or) H-6' (compounds **1–26**) or with NH (compounds **27–43**). In the case of **19**, C-2 was easily assigned on the basis of ³J C, F coupling. All these data are in agreement with the previously reported results on benzothiazole derivatives.^{23–27}

Phenyl and pyridyl rings resonances

The assignment of ¹H and ¹³C chemical shifts for benzothiazoles **1–8** and **27–33** was trivial based on signal intensities and chemical shifts. Spectral data for **15** and **17** were determined from the magnitude of ⁿJ H, F and ⁿJ C, F coupling constants. Finally, the complete ¹H and ¹³C assignment of these rings followed from HMBC correlation peaks observed for methyl protons (²J and ³J couplings) and aromatic signals (³J couplings).

Table 1. ¹H chemical shifts of benzothiazole derivatives **1–43**^a

Atom	1a	2a ^b	3a	4a ^c	5a	6a	7a ^d
H-4	8.06	7.93	8.03	8.01	7.84	7.88	8.04
H-5	7.53	7.46	7.53	7.51	7.47	7.43	7.54
H-6	7.44	7.35	7.44	7.42	7.36	7.32	7.45
H-7	8.10	8.03	8.12	8.10	8.04	7.98	8.13
H-2'	8.07	7.89	8.08	8.03	7.89	7.76	8.11
H-3'	7.55	6.82	7.35	7.12	7.56	6.68	8.05
H-4'	7.55	—	—	—	—	—	—
H-5'	7.55	6.82	7.35	7.12	7.56	6.68	8.05
H-6'	8.07	7.89	8.08	8.03	7.89	7.76	8.11
NH-2	—	—	—	—	—	—	—
Atom	8a ^e	9a	10a	11a	12a ^f	13a	14a
H-4	8.04	8.10	8.10	8.01	8.10	7.85	8.15
H-5	7.51	7.63	7.56	7.50	7.58	7.43	7.62
H-6	7.42	7.55	7.47	7.41	7.50	7.30	7.54
H-7	8.07	8.14	8.16	8.07	8.19	7.95	8.23
H-2'	7.97	—	—	—	8.69	—	—
H-3'	7.37	7.62	7.66	6.89	—	6.19	7.92
H-4'	—	7.53	7.57	7.21	8.04	—	—
H-5'	7.37	7.47	7.34	6.65	7.58	6.26	7.67
H-6'	7.97	8.18	8.45	7.63	7.84	7.57	8.28
NH-2	—	—	—	—	—	—	—
Atom	15a	16a	17a	18a ^g	19a	20a ^h	21a ⁱ
H-4	8.11	7.96	8.23	8.11	7.99	7.96	8.10
H-5	7.58	7.47	7.64	7.53	7.58	7.48	7.57
H-6	7.51	7.36	7.58	7.48	7.49	7.37	7.49
H-7	8.19	8.03	8.26	8.15	8.23	8.03	8.13
H-2'	—	—	—	—	—	7.47	7.91
H-3'	7.71	6.77	8.02	7.68	7.37	—	—
H-4'	—	—	8.38	7.05	7.40	—	—
H-5'	7.45	6.69	—	—	7.17	6.90	8.02
H-6'	8.26	8.03	9.06	7.55	—	7.26	7.73
NH-2	—	—	—	—	—	—	—
Atom	22a ^j	23b	24b	25b	26b	27c ^k	28c ^l
H-4	8.11	8.09	8.09	8.09	7.94	7.62	7.25
H-5	7.58	7.54	7.55	7.56	7.48	8.13	6.58
H-6	7.50	7.47	7.47	7.48	7.38	—	—
H-7	8.14	8.14	8.16	8.14	8.05	8.76	6.89
H-2'	8.80	—	9.24	8.74	8.14	7.18	7.11
H-3'	—	8.31	—	7.94	—	7.62	7.59
H-4'	8.89	8.01	8.41	—	8.05	—	—
H-5'	—	7.58	7.58	7.94	6.50	7.62	7.59
H-6'	8.66	8.71	8.73	8.74	—	7.18	7.11
NH-2	—	—	—	—	—	10.87	9.95
Atom	29c	30c	31c ⁿ	32c	33c	34c ^o	35c ^p
H-4	7.49	7.68	7.65	7.66	7.30	7.55	7.26
H-5	8.09	8.12	8.15	8.14	6.61	8.11	6.62
H-6	—	—	—	—	—	—	—
H-7	8.68	8.77	8.79	8.79	6.92	8.75	6.95
H-2'	7.32	7.84	7.28	7.42	7.35	—	—
H-3'	6.62	7.94	7.70	7.79	7.76	7.35	7.28
H-4'	—	—	—	—	—	—	—

(continued overleaf)

Spectral Assignments and Reference Data

Table 1. (Continued)

H-5'	6.62	7.94	7.70	7.79	7.76	7.19	7.14
H-6'	7.32	7.84	7.28	7.42	7.35	7.88	8.12
NH-2	10.53	m	11.00	11.06	10.23	10.49	10.11
Atom	36c ^q	37c ^r	38c ^s	39c ^t	40c ^u	41c	42c
H-4	7.75	7.32	7.60	7.60	7.64	7.30	7.68
H-5	8.20	6.62	8.16	8.07	8.15	6.61	8.11
H-6	—	—	—	—	—	—	—
H-7	8.87	6.93	8.82	8.71	8.81	6.92	8.79
H-2'	8.02	7.97	—	7.62	—	8.29	—
H-3'	—	—	7.41	—	7.18	—	7.66
H-4'	—	—	—	—	7.74	7.61	—
H-5'	7.37	7.26	7.34	7.68	—	7.34	7.77
H-6'	7.54	7.44	7.90	7.25	8.97	8.00	8.75
NH-2	11.09	10.18	10.23	11.15	10.63	10.40	10.80

^a In ppm from TMS. DMSO-d₆ as solvent.

^b δNCH₃ = 3.01 ppm.

^c δOCH₃ = 3.85 ppm.

^d δNH-7 = 10.58 ppm; δH-10' = 7.96; 8.02 ppm; δH-11' = 7.51; 7.56 ppm; δH-12' = 7.63 ppm.

^e δCH = 2.91 ppm; δCH₃ = 1.19 ppm.

^f δNH-7 = 10.55 ppm; δH-10' = 8.03 ppm; δH-11' = 7.58 ppm; δH-12' = 7.63 ppm.

^g δOCH₃ = 3.81 ppm.

^h δOCH₃ = 3.83 ppm.

ⁱ δOCH₃ = 4.05 ppm.

^j δCO₂CH₃ = 3.98 ppm.

^k δCH₃ = 2.27 ppm.

^l δCH₃ = 2.24 ppm.

^m Signal not observed.

ⁿ δCH₂ = 3.54 ppm.

^o δCH₃ = 2.29 ppm.

^p δCH₃ = 2.25 ppm.

^q δCH₃ = 2.31 ppm.

^r δCH₃ = 2.26 ppm.

^s δCH₃ = 2.31 ppm.

^t δOCH₃ = 3.84 ppm; δOCH₃ = 3.73 ppm.

^u δOCH₃ = 4.01 ppm.

^v δCH₃ = 2.28 ppm.

Table 2. ¹³C chemical shifts of benzothiazole derivatives 1–43^a

Atom	1a	2a ^b	3a	4a ^c	5a	6a	7a ^e	8a ^f
C-2	167.47	168.01	166.81	167.22	166.56	168.15	167.13	167.42
C-3a	153.77	154.09	153.80	153.87	153.96	153.96	153.77	153.79
C-4	123.09	122.04	122.96	122.64	123.22	121.92 ^d	122.72	122.87
C-5	126.80	126.47	126.86	126.67	126.40	126.38	126.71	126.65
C-6	125.69	124.64	125.64	125.25	125.35	124.52	125.40	125.44
C-7	122.47	122.31	122.54	122.33	122.56	122.04 ^d	122.39	122.32
C-7a	134.67	133.98	134.68	134.43	134.93	133.86	134.45	134.51
C-1'	133.06	120.33	121.10	125.71	132.41	120.94	128.05	130.78
C-2'	127.36	128.65	128.94	129.04	128.78	128.89	127.98	127.38
C-3'	129.53	112.00	121.04	114.90	132.10	114.38	120.57	127.38
C-4'	131.54	152.40	154.20	161.95	125.35	151.22	142.48	152.20
C-5'	129.53	112.00	121.04	114.90	132.10	114.38	120.57	127.38
C-6'	127.36	128.65	128.94	129.04	128.78	128.89	127.98	127.38

Table 2. (Continued)

Atom	9a	10a	11a	12a ^g	13a	14a	15a	16a
C-2	163.39	161.51	169.04	167.36	168.38	162.29	162.65	164.49
C-3a	152.14	151.13	153.42	153.67	153.96	152.00	152.11	152.28
C-4	123.41	122.19	121.91	123.02	122.06	123.41	123.29	122.41
C-5	126.74	125.89	126.59	126.85	126.77	126.89	126.95	126.59
C-6	125.86	124.78	125.28	125.74	124.58	126.17	126.06	125.01
C-7	122.16	121.37	122.23	122.53	121.09	122.41	122.37	121.96
C-7a	135.56	135.14	132.57	134.57	132.56	135.53	135.50	134.99
C-1'	131.49	123.51	116.72	134.75	107.57	130.40	118.39	118.24
C-2'	131.65	149.26	147.86	118.67	159.05	132.35	132.88	132.78
C-3'	130.97	119.74	113.33	140.27	99.78	130.61	118.37	114.35
C-4'	131.70	131.42	131.54	123.02	151.99	135.89	162.98	152.36
C-5'	127.84	123.65	115.81	129.92	106.56	128.27	115.67	113.40
C-6'	132.06	128.56	130.10	122.53	130.27	133.00	133.69	132.88
Atom	17a	18a ^h	19a	20a ⁱ	21a ^j	22a ^k	23b	24b
C-2	161.20	164.88	158.92	167.76	165.18	163.36	169.16	164.73
C-3a	151.74	152.30	153.44	153.98	153.52	153.01	153.90	153.57
C-4	123.49	123.37	124.31	122.45	123.58	123.18	123.44	123.30
C-5	127.15	126.78	126.74	126.80	127.23	126.77	126.73	127.07
C-6	126.44	125.96	126.22	125.36	126.44	126.07	126.08	126.12
C-7	122.29	122.27	121.97	122.72	122.75	122.19	122.67	122.70
C-7a	135.69	135.69	136.73	134.56	135.23	134.71	135.57	134.76
C-1'	135.24	134.54	122.50	119.99	138.01	132.23	—	—
C-2'	137.84	111.68	135.42	111.60	112.04	132.16	150.50	152.11
C-3'	132.71	135.04	126.27	133.89	152.62	132.23	126.23	129.09
C-4'	125.97	118.46	132.23	151.01	135.23	124.85 ^c	137.95	134.88
C-5'	148.62	158.75	115.01	115.06	119.63	148.50	120.49	124.61
C-6'	125.85	116.94	161.25	126.04	126.44	124.80 ^c	150.07	147.95
Atom	25b	26b	27c ^l	28c ^m	29c	30c ⁿ	31c ^o	32c
C-2	165.06	164.17	166.93	157.58	168.66	166.17	166.91	166.41
C-3a	153.48	153.47	157.81	143.36	158.46	157.19	157.73	157.39
C-4	123.62	122.23	118.51	119.64	117.83 ^c	119.28	118.68	118.92
C-5	127.14	126.72	122.20	113.59	122.30	122.17	122.25	122.18
C-6	126.50	125.22	141.79	144.75	141.19	142.32	141.92	142.11
C-7	122.75	122.23	118.00	105.03	117.72 ^c	118.18	118.10	118.12
C-7a	134.94	134.00	130.99	131.23	130.83	131.21	131.04	131.06
C-1'	—	—	137.48	138.92	128.94	143.72	138.53	138.85
C-2'	150.99	138.73	118.97	117.40	122.16	117.83	118.90	120.15
C-3'	121.02	112.49	129.62	129.44	114.42	130.92	130.30	129.12
C-4'	139.62	136.56	132.59	130.21	146.13	124.96	130.23	126.80
C-5'	121.02	120.64	129.62	129.44	114.42	130.92	130.30	129.12
C-6'	150.99	162.34	118.97	118.97	122.16	117.83	118.90	120.15
Atom	33c	34c ^p	35c ^q	36c ^r	37c ^s	38c ^t	39c ^u	40c ^v
C-2	157.09	169.13	159.25	166.44	157.24	169.25	165.48	167.24
C-3a	143.05	157.18	143.11	157.36	143.26	157.50	157.05	157.18
C-4	119.96	118.40	119.68	118.98	120.02	118.41	119.40	119.01
C-5	113.74	122.16	114.13	122.02	113.92	122.18	122.13	122.27
C-6	145.10	141.79	143.87	142.09	144.73	141.69	142.35	141.94
C-7	104.96	118.16	105.69	118.18	105.22	118.14	118.19	118.16
C-7a	131.35	131.41	131.96	130.97	131.34	131.33	131.10	131.60

Spectral Assignments and Reference Data

Table 2. (Continued)

C-1'	140.23	136.94	135.33	138.95	140.44	136.89	144.69	119.59
C-2'	118.72	126.54	123.83	118.54	117.12	133.59	102.09	152.92
C-3'	128.89	130.27	129.94	133.49	133.44	130.48	160.01	111.01
C-4'	124.68	133.98	133.93	129.92	127.71	129.33	113.38	126.48
C-5'	128.99	128.76	128.45	131.67	131.46	126.61	132.73	121.97
C-6'	118.72	125.68	122.95	117.30	116.08	125.41	109.68	128.48
Atom	41c ^w	42c	43c ^x	—	—	—	—	—
C-2	157.81	166.44	161.78	—	—	—	—	—
C-3a	143.45	156.49	143.60	—	—	—	—	—
C-4	119.95	119.42	119.01	—	—	—	—	—
C-5	113.89	121.92	113.54	—	—	—	—	—
C-6	144.97	141.85	144.16	—	—	—	—	—
C-7	105.28	118.08	105.41	—	—	—	—	—
C-7a	131.62	131.97	131.57	—	—	—	—	—
C-1'	141.25	129.55	123.99	—	—	—	—	—
C-2'	118.79	146.48	141.84	—	—	—	—	—
C-3'	136.47	108.99	116.35	—	—	—	—	—
C-4'	120.03	142.43	134.83	—	—	—	—	—
C-5'	128.67	115.80	117.47	—	—	—	—	—
C-6'	122.83	118.44	124.52	—	—	—	—	—

^a In ppm from TMS. DMSO-*d*₆ as solvent.

^b δNCH₃ = 39.90 ppm.

^c δOCH₃ = 55.85 ppm.

^d May be reversed.

^e δC-8' = 167.43; 166.01 ppm; δC-9' = 130.88; 128.56 ppm; δC-10' = 129.39; 127.95 ppm; δC-11' = 128.68; 128.56 ppm; δC-12' = 132.97; 131.96 ppm.

^f δCH = 33.52 ppm; δCH₃ = 23.63 ppm.

^g δC-8' = 165.93 ppm; δC-9' = 133.35 ppm; δC-10' = 127.87 ppm; δC-11' = 128.58 ppm; δC-12' = 131.93 ppm.

^h δOCH₃ = 55.85 ppm.

ⁱ δOCH₃ = 56.14 ppm.

^j δOCH₃ = 57.10 ppm.

^k δCO₂CH₃ = 163.58 ppm; δCO₂CH₃ = 52.67 ppm.

^l δCH₃ = 20.63 ppm.

^m δCH₃ = 20.57 ppm.

ⁿ δCO₂H = 167.14 ppm.

^o δCH₂ = 40.32 ppm; δCO₂H = 173.00 ppm.

^p δCH₃ = 20.37 ppm.

^q δCH₃ = 20.24 ppm.

^r δCH₃ = 19.08 ppm.

^s δCH₃ = 19.04 ppm.

^t δCH₃ = 17.81 ppm.

^u δOCH₃ = 55.80 ppm; δCO₂CH₃ = 166.12 ppm; δCO₂CH₃ = 51.72 ppm.

^v δOCH₃ = 56.33 ppm; δCO₂H = 167.45 ppm.

^w δCO₂H = 167.54 ppm.

^x δCH₃ = 21.04 ppm.

REFERENCES

1. Sakai H, Suzuki T, Murota M, Oketani K, Uchiumi T, Murakami M, Takeuchi N. *Br. J. Pharmacol.* 2002; **136**: 383.
2. Mahran MA, El-Nassry SM, Allam SR, El-Zawawy LA. *Pharmazie* 2003; **58**: 527.
3. Hout S, Azas N, Darque A, Robin M, Di Giorgio C, Gasquet M, Galy JP, Timon-David P. *Parasitology* 2004; **129**: 525.
4. Delmas F, Avellaneda A, Di Giorgio C, Robin M, De Clercq E, Timon-David P, Galy JP. *Eur. J. Med. Chem.* 2004; **39**: 685.
5. Brantley E, Patel V, Stinson SF, Trapani V, Hose CD, Ciolino HP, Yeh GC, Gutkind JS, Sausville EA, Loaiza-Perez AI. *Anti-Cancer Drugs* 2005; **16**: 137.
6. Leong CO, Suggitt M, Swaine DJ, Bibby MC, Stevens MF, Bradshaw TD. *Mol. Cancer Ther.* 2004; **3**: 1565.
7. Heiser V, Engemann S, Bröcker W, Dunkel I, Boeddrich A, Waelter S, Nordhoff E, Lurz R, Schugardt N, Rautenberg S, Herhaus C, Barnickel G, Böttcher H, Lehrach H, Wanker EE. *PNAS* 2002; **99**: 16 400.
8. Alagille D, Baldwin RM, Tamagnan GD. *Tetrahedron Lett.* 2005; **46**: 1349.
9. Hrobárik P, Sigmundova I. *Synthesis* 2005; **4**: 600.
10. Robin M, Faure R, Perichaud A, Galy JP. *Heterocycles* 2000; **53**: 387.
11. Robin M, Galy JP, Faure R. *Magn. Reson. Chem.* 2001; **39**: 225.
12. Robin M, Mialhe S, Pique V, Faure R, Galy JP. *J. Heterocyclic Chem.* 2002; **39**: 295.
13. Avellaneda A, Robin M, Faure R, Perichaud A, Galy JP. *Magn. Reson. Chem.* 2002; **40**: 545.
14. Mathis CA, Wang Y, Holt DP, Huang GF, Debnath ML, Klunk WE. *J. Med. Chem.* 2003; **46**: 2740.
15. Günther H. *La spectroscopie de RMN*. Masson: Paris, 1994; 60.
16. Hurd RE. *J. Magn. Reson.* 1990; **87**: 422.
17. Hurd RE, John BK. *J. Magn. Reson.* 1991; **91**: 648.
18. Wilker W, Leibfritz D, Kerssebaum R, Bermel W. *Magn. Reson. Chem.* 1993; **31**: 287.
19. Ewing DF. *Org. Magn. Reson.* 1979; **12**: 499.
20. Bromilow J, Brownlee RTC, Craik DJ, Sadek M, Taft RW. *J. Org. Chem.* 1980; **45**: 2429.
21. Sudmeijer O, Wilson AE, Hays GR. *Org. Magn. Reson.* 1984; **22**: 459.
22. Bromilow J, Brownlee RTC, Craik DJ, Sadek M. *Magn. Reson. Chem.* 1986; **24**: 862.
23. Faure R, Elguero J, Vincent EJ, Lazaro R. *Org. Magn. Reson.* 1978; **11**: 617.
24. Sawhney SN, Boykin DW. *J. Org. Chem.* 1979; **44**: 1136.
25. Abdelhamid AO, Parkanyi C, Khaledur Rashid SM, Loyd D. *J. Heterocycl. Chem.* 1988; **25**: 403.
26. Babudri F, Florio S, Ingrosso G, Turco AM. *Heterocycles* 1986; **24**: 2215.
27. Solcaniova E, Culak I. *Magn. Reson. Chem.* 1989; **27**: 663.