# **Spectral Assignments and Reference Data**

## Complete assignment of <sup>1</sup>H and <sup>13</sup>C NMR spectra of some α-arylthio and α-arylsulfonyl substituted N-methoxy-N-methyl propionamides

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Received 3 August 2006; revised 5 September 2006; accepted 29 September 2006

The complete assignments of the <sup>1</sup>H and <sup>13</sup>C NMR spectra of the some  $\alpha$ -arylthio and  $\alpha$ -arylsulfonyl substituted *N*-methoxy-*N*-methyl propionamides, bearing methoxy, methyl, chloro, and nitro as substituents at the phenyl ring are reported. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: NMR; <sup>1</sup>H NMR; <sup>13</sup>C NMR; *N*-methyl propionamides

## INTRODUCTION

*N*-methoxy-*N*-methylamides<sup>1</sup> (commonly named *Weinreb amides*) are important carboxylic acid derivatives that have been widely used for the preparation of ketones, whose synthetic utility has been extensively demonstrated.<sup>2–4</sup> The efficiency of the reaction involving these compounds has been attributed to the formation of an intermediate stable tetrahedral lithium chelate,<sup>5</sup> which precludes the second nucleophilic addition to the carbonyl group. This important characteristic of the chelate allowed us to synthesize some ketone derivatives of  $\beta$ -lactams in good yields, which had not been possible through traditional methods employing other carboxylic acid derivatives.<sup>6</sup>

The aim of this work was to prepare some 4'-substituted *N*-methoxy-*N*-methyl-2-phenylthio- and 4'-substituted *N*-methoxy-*N*-methyl-2-phenylsulfonyl-propionamides (Scheme 1) and to characterize them through their <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra.

#### **EXPERIMENTAL**

#### Compounds

The mild acylating agents 4'-substituted *N*-methoxy-*N*-methyl-2phenylthio-propionamides are easy to prepare and are very stable for a long time.

Initially, the 4'-substituted 2-phenylthiopropionic acids were obtained from the reaction of 2-bromopropionic acid with an aqueous solution of 4-substituted thiophenols and two equivalents of sodium hydroxide.<sup>7</sup> These acids were converted to the corresponding acyl chlorides, which led to the 4'-substituted *N*-methoxy-*N*-methyl-2-phenylthiopropionamides by their reaction with *N*,*O*-dimethylhydroxylamine hydrochloride.

The obtained amides were oxidized to the corresponding sulfones using oxone [potassium peroxymonosulfate (2KHSO<sub>5</sub>. KHSO<sub>4</sub>.K<sub>2</sub>SO<sub>4</sub>)] in acetone solution and five equivalents of sodium



Scheme 1. Structures and numbering for compounds 1-10.

bicarbonate. These compounds were obtained in 85–97% yield. Elemental analyses were carried out on a Perkin-Elmer 2400 CHN-standard analyzer (Table 1).

#### Spectra

<sup>1</sup>Ĥ NMR and <sup>13</sup>C NMR spectra were recorded on a Varian Inova 300 spectrometer (10% in CDCl<sub>3</sub> solutions) operating at 299.947 MHz and 75.423 MHz, respectively. Data processing was carried out on a Solaris workstation.

 $^{1}\mathrm{H}$  NMR parameters were as follows: spectral width, 4000 Hz; data points, 32K, zero-filled to 64K; pulse width 45°, acquisition time, 4.10 s; digital resolution, 0.25 Hz.  $^{13}\mathrm{C}$  NMR parameters were as follows: spectral width, 18860 Hz; data points, 64K, zero-filled to 128 K; pulse width 90°; acquisition time, 1.76 s; digital resolution, 0.57 Hz, with a delay of 2.05 s between transients.

<sup>1</sup>H and <sup>13</sup>C chemical shifts are given on the  $\delta$  scale (ppm) and were referenced to TMS, and coupling constants *J* are reported in Hz. The following abbreviations were used: s, d, q and m, for singlet, doublet, quartet and multiplet, respectively.

#### **RESULTS AND DISCUSSION**

As a first step, the <sup>1</sup>H NMR spectra of compounds **3** and **8** (Y = H) were fully assigned and are in agreement with literature data.<sup>8</sup> The remaining compounds were then assigned by analogy. For compounds **1–10**, the doublet signal at  $\delta \sim 1.4-1.6$  ppm corresponds to the H-3 methyl group, attached to the chiral carbon (C-5), with a coupling constant of ~7.0 Hz. (Table 2). The singlets at  $\delta \sim 3.2$  ppm and  $\delta \sim 3.6-3.8$  ppm correspond to H-1 and H-2 methyl groups, respectively, and the quartet at  $\delta \sim 4.1-4.8$  ppm to the H-5 methine group, which has the chiral carbon (C-5). The low-frequency multiplet signals at  $\delta 6.8-9.0$  ppm were identified as the aromatic protons chemical shifts.

The <sup>13</sup>C NMR chemical shifts are presented in Table 3. The signals at  $\delta \sim 32$  ppm and at  $\delta \sim 61$  ppm, for the whole series, correspond to C-1 and C-2, respectively. The deshielding for the chiral carbon C-5 ( $\delta \cong 60$  ppm) in compounds **6–10**, in relation to **1–5** ( $\delta \cong 41$  ppm), may be ascribed to the larger inductive effect of the arylsulfonyl group ( $\sigma_I = +0.56$ ),<sup>9</sup> in comparison to the arylthio group ( $\sigma_I = +0.31$ ).<sup>9</sup> The inverse effect was observed for the C-3 methyl carbon attached to the chiral carbon and for the C-4 carbonyl carbon, where the corresponding shifts are deshielded in compounds **1–5** ( $\delta \cong 17$  ppm and  $\delta \cong 173$  ppm, respectively). in relation to **6–10** ( $\delta \cong 13$  ppm and  $\delta \cong 166$  ppm, respectively).

The C-6 and C-9 aromatic carbons at  $\delta \sim 120-140$  and  $\delta \sim 130-160$  ppm, respectively, were largely dependent on the substituent in the aryl group, as expected, while less pronounced effects were observed for C-7/C-11 and C-8/C-10 chemical shifts, which are in agreement with reported values.<sup>10</sup>



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Compound						1	Analysis (%	%)	
	Y	m.p./b.p. (°C/mmHg)	Molecular formula	FW		С	Н	N	
1	MeO	a	C <sub>12</sub> H <sub>17</sub> NO <sub>3</sub> S	255.3	Calc.	56.45	6.71	5.49	
					Found	56.46	6.51	5.73	
2	Me	а	$C_{12}H_{17}NO_2S$	239.3	Calc.	60.22	7.16	5.85	
					Found	60.43	7.14	6.14	
3	Н	113/0.07	$C_{11}H_{15}NO_2S$	225.3	Calc.	58.64	6.71	6.22	
					Found	58.68	6.65	6.52	
4	Cl	а	$C_{11}H_{14}ClNO_2S$	259.7	Calc.	50.86	5.43	5.39	
					Found	51.11	5.36	5.56	
5	NO <sub>2</sub>	а	$C_{11}H_{14}N_2O_4S$	270.3	Calc.	48.88	5.22	10.36	
					Found	48.90	5.25	10.15	
6	MeO	113.5-116.8	$C_{12}H_{17}NO_5S$	287.3	Calc.	50.16	5.96	4.87	
					Found	49.79	5.85	4.69	
7	Me	64.2-67.4	$C_{12}H_{17}NO_4S$	271.3	Calc.	53.12	6.32	5.16	
					Found	52.82	6.20	4.83	
8	Н	92-93	$C_{11}H_{15}NO_4S$	257.3	Calc.	51.35	5.88	5.44	
					Found	51.50	5.88	5.78	
9	Cl	81.1-84.5	C <sub>11</sub> H <sub>14</sub> ClNO <sub>4</sub> S	291.7	Calc.	45.28	4.84	4.80	
					Found	45.26	4.83	5.20	
10	NO <sub>2</sub>	105.7-107.8	$C_{11}H_{14}N_2O_6S$	302.3	Calc.	43.70	4.67	9.27	
					Found	44.01	4.73	9.59	

 Table 1. Physical data for compounds 1–10

<sup>a</sup> As an oil/b.p. not measurable.

Table 2. <sup>1</sup> H NMR chemical shifts (ppm), coupling constants (Hz) and multiplicities for compount	nds <b>1–10</b>
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Compound	Y	$H_1$	H <sub>2</sub>	H <sub>3</sub>	$H_5$	${\rm H_{7}/H_{11}}$	${\rm H_{8}/H_{10}}$	H <sub>12</sub>
1	MeO	3.17 s	3.64 s	1.38 d ( $J = 6.9$ ) <sup>a</sup>	4.11  q (J = 6.9)	7.43 m	6.83 m	3.79 s
2	Me	3.19 s	3.66 s	1.41 d ( $J = 7.0$ )	4.27  q (J = 7.0)	7.37 m	7.11 m	2.33 s
3	Н	3.19 s	3.64 s	1.43 d (J = 6.9)	4.25  q (J = 6.9)	7.30 m	7.50 m	7.30 m
4	Cl	3.19 s	3.67 s	1.42 d (J = 6.7)	4.24  q (J = 6.7)	7.27 m	7.41 m	-
5	NO <sub>2</sub>	3.23 s	3.77 s	1.58 d (J = 6.7)	4.50  q (J = 6.7)	7.49 m	8.14 m	-
6	MeO	3.19 s	3.81 s	1.44 d (J = 6.9)	4.72  q (J = 6.9)	7.80 m	7.00 m	3.88 s
7	Me	3.19 s	3.80 s	1.44 d (J = 7.0)	4.73  q (J = 7.0)	7.77 m	7.38 m	2.44 s
8	Н	3.18 s	3.80 s	1.46 d (J = 6.9)	4.75  q (J = 6.9)	7.57 m	7.90 m	7.66 s
9	Cl	3.19 s	3.82 s	1.45 d ( <i>J</i> = 7.2)	4.75  q (J = 7.2)	7.53 m	7.81 m	-
10	NO <sub>2</sub>	3.20 s	3.84 s	1.48 d ( <i>J</i> = 6.9)	4.81 q ( <i>J</i> = 6.9)	8.08 m	8.39 m	-

 ${}^{a}J = {}^{3}J_{H_3,H_5}$ 

Table 3.	<sup>13</sup> C NMR c	hemical	shifts	(ppm)	for	compounds	1-10	)
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Compound	Y	C <sub>1</sub>	C <sub>2</sub>	C <sub>3</sub>	C4	C <sub>5</sub>	C <sub>6</sub>	$C_7/C_{11}$	C <sub>8</sub> /C <sub>10</sub>	C9	C <sub>12</sub>
1	MeO	32.53	61.45	17.43	173.36	41.90	122.89	136.89	114.36	160.22	55.28
2	Me	32.54	61.43	17.68	173.17	41.74	129.22	134.24	129.60	138.28	21.14
3	Н	32.53	61.42	17.81	172.98	41.68	133.26	133.42	128.83	127.94	_
4	Cl	32.42	61.37	17.46	172.64	41.32	128.81	134.91	131.24	134.17	-
5	NO <sub>2</sub>	32.68	61.75	17.81	172.10	40.71	144.51	129.53	123.91	146.11	-
6	MeO	32.31	61.78	13.33	166.81	60.24	132.31	127.72	113.92	164.10	55.66
7	Me	32.30	61.75	13.27	166.59	60.18	133.31	130.07	129.35	145.11	21.70
8	Н	32.24	61.69	13.09	166.43	60.22	136.44	129.97	128.64	133.99	_
9	Cl	32.26	61.77	13.26	166.35	60.37	134.70	131.59	128.97	140.92	_
10	NO <sub>2</sub>	32.31	61.93	13.42	165.96	60.74	141.83	131.79	123.69	151.02	

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### Acknowledgements

The authors thank the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) for financial support of this research and for a fellowship (to A.K.C.A.R.), and the Conselho Nacional de Desenvolvimento e Tecnológico (CNPq) for fellowships (to N.L.C.D, P.R.O. and R.R).

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