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Reference Data

^{13}C NMR of thia- or aza-substituted butyric acid derivatives

Johannes Fröhlich,[1] Fritz Sauter[1] and Viktor Milata[2]*

[1] Institute for Organic Chemistry, Technical University Wien, Getreidemarkt 9, A-1110 Vienna, Austria
[2] Department of Organic Chemistry, Faculty of Chemical Technology, Slovak Technical University, Radlinského 9, SK-812 37 Bratislava, Slovak Republic

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Eight thia- or aza-substituted butyric acid derivatives were prepared and the influence of these substituents on aromatic ^{13}C NMR shifts was studied. Copyright © 2001 John Wiley & Sons, Ltd.

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INTRODUCTION

For the synthesis of derivatives of (iso)thiochromanone and isoquinolone, it was necessary to prepare appropriately substituted phenylthia- and phenylazabutyric acids **1a–h** (Scheme 1).

We report here the ^{13}C NMR chemical shifts of these compounds.

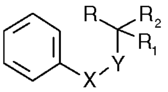
EXPERIMENTAL

The synthesis of thiabutyric acid derivatives has been described.[1–3] In the case of 3-azabutyronitrile derivatives we applied the modified Strecker method[4] for the synthesis of the corresponding 2,2-tetramethylene analogs according to Ref. 5

NMR spectra were determined with a Bruker AC 200 FT-NMR spectrometer. Chemical shifts were assigned from HETCOR spectra and are expressed in ppm downfield from tetramethylsilane. The sweep width was kHz, the digital resolution was 0.1 ppm and the concentration of the samples was 30 mg of the compound in 0.5 ml of the appropriate solvent.

4-Phenyl-3-aza-2,2-tetramethylene acid derivatives I

Into a mixture of 20 mmol of *N*-(un)substituted benzylamine, 20 mmol of hydrochloric acid, 40 ml of of 25% ethanol, 20 mmol of cyclopentanone and 20 ml of ethanol was dropped a solution of 30 mmol of potassium cyanide in 10 ml of water with magnetic stirring. After 4 days the precipitate (**1e**) was filtered off or the reaction mixture (**1g**) was extracted with diethyl ether, dried with



1a-h

	X	Y	R_1	R_2	R		X	Y	R_1	R_2	R
1a	CH_2	S	H	H	COOH	**1e**	CH_2	NH	$-(CH_2)_4-$		CN
1b	S	CH_2	H	H	COOH	**1f**	CH_2	NH	$-(CH_2)_4-$		COOH
1c	CH_2	S	H	H	COOMe	**1g**	CH_2	NMe	$-(CH_2)_4-$		CN
1d	S	CH_2	H	H	COOMe	**1h**	CH_2	NMe	$-(CH_2)_4-$		COOH

Scheme 1

Table 1. ^{13}C chemical shifts [δ (ppm) rel. to TMS] for 4-phenyl-3-(or 4-)thia(or aza)butyric acid derivatives[a]

—X—Y—CR_1R_2R	C_{ipso}	C_{ortho}	C_{meta}	C_{para}	Other signals
—CH_2—S—CH_2—COOH, **1a**	136.8	129.2	128.6	127.4	176.8 (COOH), 36.3 ($PhCH_2$—), 31.9 (—CH_2COOH)
—S—CH_2CH_2—COOH, **1b**	135.0	130.1	129.0	126.6	177.1 (COOH), 34.4 (CH_2COOH), 30.9 (—SCH_2—)
—CH_2—S—CH_2-COOMe, **1c**	137.0	128.9	128.3	127.0	170.5 (COOMe), 52.0 (O*Me*), 36.1 ($PhCH_2$—), 31.8 (—CH_2COOMe)
—S—CH_2CH_2—COOMe, **1d**	135.0	129.8	128.8	126.3	171.8 (COOMe), 51.5 (O*Me*), 33.9 (CH_2COOMe), 28.7 (—SCH_2—)
—CH_2—NH—$C(CH_2)_4CN$, **1e**	139.2	128.5	128.3	127.3	122.9 (CN), 61.2 (N—C), 50.2 ($PhCH_2$—), 39.0 [$C(CH_2CH_2)_2$], 23.5 [$C(CH_2CH_2)_2$]

(*continued overleaf*)

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*Correspondence to: V. Milata, Department of Organic Chemistry, Faculty of Chemical Technology, Slovak Technical University, Radlinského 9, SK-812 37 Bratislava, Slovak Republic.

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Table 1. (***continued***)

—X—Y—CR$_1$R$_2$R	C$_{ipso}$	C$_{ortho}$	C$_{meta}$	C$_{para}$	Other signals
—CH$_2$—NH—C(CH$_2$)$_4$COOH, **1f**	140.0	128.4	127.7	127.0	179.5 (COOH), 70.0 (N—*C*), 48.4 (PhCH$_2$—), 35.8 [C(CH$_2$CH$_2$)$_2$], 24.2 [C(CH$_2$CH$_2$)$_2$]
—CH$_2$—NMe—C(CH$_2$)$_4$CN, **1g**	138.3	128.5	128.2	126.8	120.2 (CN), 68.8(N—*C*), 58.4 (PhCH$_2$), 38.5 (N*Me*), 37.9 (C(CH$_2$CH$_2$)$_2$), 23.2 [C(CH$_2$CH$_2$)$_2$]
—CH$_2$—NMe—C(CH$_2$)$_4$COOH, **1h**[b]	140.0	128.3	128.2	126.7	176.6 (COOH), 74.7 (N—*C*), 56.7 (PhCH$_2$), 36.0 (N*Me*), 32.1 (C(CH$_2$CH$_2$)$_2$), 24.8 [C(CH$_2$CH$_2$)$_2$]

[a] $\delta_{\text{Chloroform}} = 77.0$ ppm.

[b] In DMSO-d_6, $\delta_{\text{DMSO}} = 39.5$ ppm.

sodium sulfate and evaporated. Hydrolysis of the nitriles to the corresponding acids was achieved with concentrated sulfuric acid at 20–100 °C for 12 h, followed by work-up after neutralization and filtration or extraction, drying and evaporation. **1e**, 62%, 42–43 °C; **1g**, 76%, 130–140 °C/0.45 Torr.

RESULTS

The ^{13}C chemical shifts of the eight substituted 4-phenyl-3-(or 4-) thia(or aza)butyric acids **1a–h** are collected in Table 1.

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