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## Influence of Some Thia or Azasubstituted Butyric Acid Derivatives on Chemical Shift of Carbon Atom of Benzene Ring

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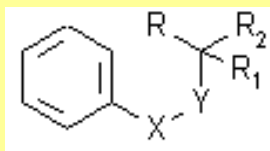
Eight thia- or azasubstituted butyric acid derivatives was prepared and influence of this substituent onto carbon atoms of benzene ring was studied.

**KEY WORDS** - 4-phenyl-3-thiabutyric acid derivatives / 4-phenyl-4-thiabutyric acid derivatives / 4-phenyl-3-azabutyric acid derivatives / substituent chemical shifts

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## INTRODUCTION

For the synthesis of the derivatives of (iso)thiochromanon and isoquinolone was necessary to prepare 8 appropriate substituted 4-phenyl-3-(or 4-)thia(or aza)butyric acid and its derivatives **1**:



**1a-h**

	X	Y	R <sub>1</sub>	R <sub>2</sub>	R		X	Y	R <sub>1</sub>	R <sub>2</sub>	R
<b>1a</b>	CH <sub>2</sub>	S	H	H	COOH		<b>1e</b>	CH <sub>2</sub>	NH	-(CH <sub>2</sub> ) <sub>4</sub> -	CN
<b>1b</b>	S	CH <sub>2</sub>	H	H	COOH		<b>1f</b>	CH <sub>2</sub>	NH	-(CH <sub>2</sub> ) <sub>4</sub> -	COOH
<b>1c</b>	CH <sub>2</sub>	S	H	H	COOMe		<b>1g</b>	CH <sub>2</sub>	NMe	-(CH <sub>2</sub> ) <sub>4</sub> -	CN
<b>1d</b>	S	CH <sub>2</sub>	H	H	COOMe		<b>1h</b>	CH <sub>2</sub>	NMe	-(CH <sub>2</sub> ) <sub>4</sub> -	COOH

## EXPERIMENTAL SECTION

The synthesis of thiabutyric acid derivatives was long ago described [1-3] but their  $^{13}\text{C}$  NMR spectra were till now not published. In the case of 3-azabutyronitrile derivatives was applied the modified Strecker's method [4] for the synthesis the corresponding 2,2-tetramethylene analogs according lit. [5]. NMR spectra were determined with a Bruker AC 200 FT-NMR spectrometer and are expressed in ppm downfield to tetramethylsilane (internal standard).

### 4-Phenyl-3-aza-2,2-tetramethylene acid derivatives **1**

To a mixture of 20 mmol N-(un)substituted benzylamine, 20 mmol hydrochloric acid, 40 ml of 25 % ethanol, 20 mmol cyclopentanone and 20 ml of ethanol was dropped a solution of 30 mmol kalium cyanide in 10 ml of water under magnetic stirring. After 4 days was the precipitate (**1e**) filtered off or was the reaction mixture (**1g**) extracted with ether, dried with sodium sulfate and evaporated. Hydrolysis of the nitriles to corresponding acids was occurred with concentrated sulfuric acid by 20-100°C during 12 hours and than worked-up after neutralisation and filtration or extraction, drying and evaporation. **1e**: 62 %, 42-3 °C; **1g**: 76 %, 130-140 °C / 0.45 Torr.

## RESULTS AND DISCUSSION

Chemical shifts of all of the studied compounds were established on the basis of comparison of the experimental values of the chemical shifts acquired from recorded spectra and calculated ones using the following programs: ACD / CNMR ver. 1.1 [6], CS Chem Draw Pro, ver. 4.5 [7] and ChemWindow3, ver. 3.0.0 with C13-module [8], respectively. We obtained a good accordance of the measured and calculated values of the chemical shifts obtained using all three programs.

Chemical shifts (CS) and a substituent chemical shift (SCS) of all of the compounds with heteroatom in b-position are in the same range for all compounds. The compounds with heteroatom in a-position (**1b,d**) have the ipso-carbon not so much shifted like the analogues having heteroatom in b-position (**1a,1c,1e-1h**). Substituent chemical shifts of meta-carbon atoms of the benzene ring of compounds **1a, 1b** and **1d** have positive value unlike the all others compounds **1c, 1e-1h**.

Influence of the studied substituents on chemical shifts of carbon atoms of the benzene ring is possible to compare for example with  $\text{CH}_2\text{SMe}$  (**1a, 1c**),  $\text{SMe}$  (**1b, 1d**) or  $\text{CH}_2\text{NHCHMe}_2$ ,  $\text{CH}_2\text{NMeCH}_2\text{Ph}$  substituents [9] with good agreement with model compounds. Perhaps SCS for  $\text{C}_{\text{ipso}}$  are slight reduced for all compounds for about 2 ppm and **1b, 1d** have positive values for  $\text{C}_{\text{ortho}}$  in comparison with  $\text{SMe}$  substituent, but this is also depending from solvents used [9]..

### Chemical shifts (CS, in $\delta$ ppm) and substituent chemical shifts (SCS) of carbon atom of benzene ring of 4-phenyl-3-(or 4-thia(or aza)butyric acid derivatives

- X - Y - CR <sup>1</sup> R <sup>2</sup> R <sup>*</sup>		C <sub>ipso</sub>	C <sub>ortho</sub>	C <sub>meta</sub>	C <sub>para</sub>	Other signals
- CH <sub>2</sub> -S-CH <sub>2</sub> -COOH, <b>1a</b>	CS	136.8	129.2	128.6	127.4	176.8, 36.3, 31.9
	SCS	+8.3	+0.7	+0.1	-1.1	
-S-CH <sub>2</sub> CH <sub>2</sub> -COOH, <b>1b</b>	CS	135.0	130.1	129.0	126.6	177.1, 34.4, 30.9
	SCS	+6.5	+1.6	+0.5	-1.9	
-CH <sub>2</sub> -S-CH <sub>2</sub> -COOMe, <b>1c</b>	CS	137.0	128.9	128.3	127.0	170.5, 52.0, 36.1, 31.8
	SCS	+8.5	+0.4	-0.2	-1.5	
-S-CH <sub>2</sub> CH <sub>2</sub> -COOMe, <b>1d</b>	CS	135.0	129.8	128.8	126.3	171.8, 51.5, 33.9, 28.7
	SCS	+6.5	+1.3	+0.3	-2.2	
-CH <sub>2</sub> -NH-C(CH <sub>2</sub> ) <sub>4</sub> CN, <b>1e</b>	CS	139.2	128.5	128.3	127.3	122.9, 61.2, 50.2, 39.0, 23.5
	SCS	+10.7	0	-0.2	-1.2	
-CH <sub>2</sub> -NH-C(CH <sub>2</sub> ) <sub>4</sub> COOH, <b>1f</b>	CS	140.0	128.4	127.7	127.0	179.5, 70.0, 48.4, 35.8, 24.2
	SCS	+11.5	-0.1	-0.8	-1.5	

-CH <sub>2</sub> -NMe-C(CH <sub>2</sub> ) <sub>4</sub> CN, <b>1g</b>	CS	138.3	128.5	128.2	126.8	120.2, 68.8, 58.4, 38.5, 37.9, 23.2
	SCS	+9.8	0	-0.3	-1.7	
-CH <sub>2</sub> -NMe-C(CH <sub>2</sub> ) <sub>4</sub> COOH, <b>1h</b> <sup>a</sup>	CS	140.0	128.3	128.2	126.7	176.6, 74.7, 56.7, 36.0, 32.1, 24.8
	SCS	+11.5	-0.2	-0.3	-1.8	

\*d (Benzene) = 128.5 ppm, d (Chloroform) = 77.0 ppm, <sup>a</sup>in DMSO-d<sub>6</sub>, d (DMSO) = 39.0 ppm

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