Isothiocyanates. XXXI. Synthesis, Ultraviolet and Infrared Spectra of 3-Substituted 2-Thiohydantoins and N-Substituted Ethyl Thiocarbamoylmercaptoacetates

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Received December 18, 1970

The preparation, ultraviolet and infrared spectra of 3-aryl- and aralkyl-2--thiohydantoins as well as N-aryl- and N-aralkylthiocarbamoylmercaptoacetic acids and their ethyl esters are described. Both types of the above-mentioned substances are synthetic producers of the corresponding aryl or aralkyl iso-thiocyanates. N-Substituted ethyl thiocarbamoylmercaptoacetates are new, hitherto not described substances.

3-Substituted 2-thiohydantoins described in this paper were prepared on the basis of previous studies of the kinetics of nucleophilic addition reaction of glycine to isothiocyanates and their cyclization in acid medium [1] to give the corresponding thiocarbamoyl derivatives.

N-Substituted ethyl thiocarbamoylmercaptoacetates (IX - XIII) were prepared by condensation of N-substituted dithiocarbamates with ethyl chloroacetate by method used for preparation of ethyl N-phenylthiocarbamoylmercaptoacetate [2]. These substances could be prepared also by the nucleophilic addition of ethyl thioglycolate to isothiocyanates under analogous conditions as when investigating kinetics of isothiocyanate with thioglycolate [3]. In this case, however, the reaction products are N-substituted thiocarbamoylmercaptoacetic acids, the isolation of which is rather difficult because of their ability to cyclize and furnish the corresponding 3-substituted rhodanines, or decompose to yield isothiocyanates [4, 5]. Addition products resulting from the reaction of relatively less reactive isothiocyanates are more stable; this fact accounts for the preparation of two derivatives with free carboxyl group: N-benzyl- and N-(p-bromobenzyl)thiocarbamoylmercaptoacetic acids.

3-Substituted 2-thiohydantoins as well as N-substituted ethyl thiocarbamoylmercaptoacetates could be considered synthetic producers of isothiocyanates, *i.e.* substances, which liberate isothiocyanates. This paper deals with their preparation and also with their ultraviolet and infrared spectra.

Experimental

Infrared absorption spectra of the synthesized substances were measured in 0.05 m chloroform solutions with a double-beam UR-10 (Zeiss, Jena) spectrophotometer in the

700-3600 cm⁻¹ range. LiF prism and NaCl cells 0.147 mm in width were used. Ultraviolet absorption spectra were taken with a VSU-1 (Zeiss, Jena) spectrophotometer in the 220-360 nm range. Methanolic solutions (2.5×10^{-5} M to 5×10^{-5} M) were measured in 10-mm cells.

3-Substituted 2-thiohydantoins

The title compounds were prepared by a modified method reported by *Pujari* [6]. The appropriate isothiocyanate (0.13 mole) was dissolved in ethanol (50 ml) and added to a mixture of glycine (0.14 mole) and NaOH (9 g in 20 ml of water). After 1 hour of refluxing, during which a yellow substance was separated, the excess of ethanol was distilled off, the distillation residue dissolved in concentrated hydrochloric acid and evaporated to dryness. The solid was washed with water and crystallized from a suitable solvent. Physicochemical constants of 3-substituted 2-thiohydantoins prepared according to this process are listed in Table 1.

Table 1

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No.	R	Formula	M		Calculated/ /found		M.p.
				% N	% S	[%]	[°C]
I	phenyl-	$C_9H_8N_2OS$	192.23		-	60.5	245 - 247
II	p-bromophenyl-	$C_9H_7BrN_2OS$	271.13	-	_	54.3	238
III	p-tolyl-	$\mathbf{C_{10}H_{10}N_2OS}$	206.26		_	62.1	235 - 236
IV	p-nitrophenyl-	$\mathrm{C_9H_7N_3O_3S}$	237.23	_	-	49.5	170 - 172
V	p-methoxyphenyl-	${\rm C_{10}H_{10}N_{2}O_{2}S}$	222.26	_	_	58.5	212 - 214
VI	p-dimethylaminophenyl-	$\mathrm{C_{11}H_{13}N_3OS}$	235.30	$17.85 \\ 17.35$	$13.60 \\ 13.20$	56.3	172 - 174
VII	p-acetylphenyl-	$C_{11}H_{10}N_2O_2S$	234.27	11.95 11.71	13.68 13.20	50.1	274 - 275
V 111	benzyl-	$\mathbf{C_{10}H_{10}N_2OS}$	206.26	$11.71 \\ 13.58 \\ 13.48$	15.20 15.54 15.70	49.2	173 — 174.5ª

a) In [7] the m.p. is reported to be 128°C.

N-Substituted thiocarbam oylmercaptoacetic acids and their esters

The title compounds were synthesized by a modified method described by *von Braun* [2].

Ethyl monochloroacetate (0.1 mole, 12.4 g) was gradually added, whilst vigorously stirred and cooled with ice, to an N-substituted ammonium dithiocarbamate (0.1 mole). Stirring was continued for 1 to 2 hours during which a pasty material was formed. The solid was washed several times with cold water and crystallized from ether.

Besides the above-mentioned esters also N-benzyl- and N-(p-bromobenzyl)thiocarbamoylmercaptoacetic acids were prepared similarly using free monochloroacetic acid.

·····		Formula	·	Calculated/ /found		Yield : [%]	М.р. [°С]
No.	R		M				
			-	% N	% S		
IX	benzyl-	C ₁₂ H ₁₅ NO ₂ S ₂	269.38	5.19	23.81	48.5	80- 81
	-			5.38	24.20		
X	p-tolyl-	$C_{12}H_{15}NO_2S_2$	269.38	5.19	23.81	38.0	75- 77
				5.28	24.24		
XI	p-bromophenyl-	$C_{11}H_{12}BrNO_2S_2$	334.25	4.19	19.18	42.1	80 - 82
				4.33	19.16		
XII	p-dimethylaminophenyl-	$C_{13}H_{18}N_2O_2S_2$	298.42	9.38	21.48	33.1	105 - 106
				9.40	21.85		
XIII	p-methoxyphenyl-	$C_{12}H_{15}NO_3S_2$	285.38	4.20	22.47	45.2	104 - 105
				4.32	22.81		
XIV	benzyl-	$C_{10}H_{11}NO_2S_2$	241.33	-		54.5	88- 90
XV	p-bromobenzyl-	$C_{10}H_{10}BrNO_2S_2$	320.10	4.37	20.02	48.5	119 - 120
				4.52	20.30		

Table 2 N-Substituted thiocarbamoylmercaptoacetic acids (XIV, XV) and ethyl N-R-thiocarbamoylmercaptoacetates (IX - XIII)

Table 3

Characteristic u.v. and i.r. spectral data of 3-substituted 2-thiohydantoins

No.	R	λ _{max I} [nm]	$\log \epsilon$	$\widetilde{\nu}(C=O)$ [cm ⁻¹]
I	phenyl-	264	4.29	1768
II	<i>p</i> -bromophenyl-	264	4.15	1771
III	p-tolyl-	266	4.29	1758
IV	p-nitrophenyl-	236	4.10	1642
V	p-methoxyphenyl-	264	4.28	1769
VI	p-dimethylaminophenyl-	262	4.42	1751
VII	<i>p</i> -acetylphenyl-	246	4.34	1690
				1756
VIII	benzyl-	264	4.23	1760

 $\lambda_{\text{max II}}$ of derivative IV - 334 nm (log $\varepsilon 4.29$).

Table 4

 $\label{eq:characteristic u.v. and i.r. spectral data of N-substituted thiocarbamoylmercaptoacetic acids and their esters$

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No.	R	λ _{max 1} [nm]	log ε	λ _{max II} [nm]	log ε	$\widetilde{v}(C=0)$ [cm ⁻¹]
IX	benzyl-	250	4.02	270	3.93	1744
\boldsymbol{X}	p-tolyl-	276	4.19		<u> </u>	1734
XI	<i>p</i> -bromophenyl-	276	4.29	305 sh	4.21	1735
XII	p-dimethylaminophenyl-	264	4.24	300 sh	4.12	1732 - 1740
XIII	p-methoxyphenyl-	290	4.10		-	1735 - 1748
XIV	benzyl-	252	4.03	276	4.02	1735
XV	p-bromobenzyl-	250	4.09	276	4.01	1738

Derivatives XIV and XV are N-substituted thiocarbamoylmercaptoacetic acids. sh — shoulder. Physicochemical properties of N-substituted thiocarbamoylmercaptoacetic acids and their esters are shown in Table 2.

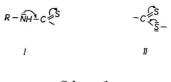
 λ_{\max} and log ϵ values as well as characteristic $\tilde{\nu}(C=O)$ vibrations of 3-substituted 2-thiohydantoins and N-substituted thiocarbamoylmercaptoacetic acids and their ethyl esters are given in Tables 3 and 4.

Results and Discussion

N-Substituted thiocarbamoylmercaptoacetic acid is formed by nucleophilic addition reaction of glycine to the proper isothiocyanate. Cyclization of the addition product afforded 3-substituted 2-thiohydantoins. All prepared 2-thiohydantoins are substances of high melting points. The m.p. of 3-benzyl-2-thiohydantoin differs from that reported in [7]. Ethanol has been found to be the most convenient solvent for crystallization.

All N-substituted ethyl thiocarbamoylmercaptoacetates are new, as yet not reported substances. The synthesis of these compounds had to be carried out under intensive cooling because isothiocyanate would be liberated during the reaction at higher temperature. Free, N-substituted thiocarbamoylmercaptoacetic acids have to be isolated at pH about 5, since at lower pH a rapid cyclization occurs to yield the corresponding rhodanine.

As seen in Table 4, N-aralkyl substituted thiocarbamoylmercaptoacetic acids, either free or esterified, exhibit two absorption bands similarly as do other substances of this type (dithiocarbamates, rhodanines, *etc.*), whereas N-aryl substituted derivatives reveal only one absorption band of multiplet structure. It seems likely, that due to conjugation I in conjunction with the conjugation of an aromatic ring and that of II (Scheme 1)



Scheme 1

a shift of electrons, resulting in a strong absorption band of relatively high $\log \varepsilon$ value (above 4.0), takes place. 3-Substituted 2-thiohydantoins having no dithiocarbamate grouping show only one absorption band at 260 nm associated with the so-called "N" conjugation ("thioamide" band) [5].

The character of the 3-(p-nitrophenyl)-2-thiohydantoin absorption differs from that of other derivatives as could be seen in Table 3. It exhibits two intensive absorption bands the second of which absorbs at 334 nm and could be regarded as "K" band of the conjugated system, whereas that at 236 nm is associated with the modified benzene ring. In the infrared spectrum 2-thiohydantoins (with the exception of the derivative IV; Table 3) display absorption bands of the C=O stretching vibrations in the 1756-1771 cm⁻¹, whereas esterified and free N-substituted thiocarbamoylmercaptoacetic acids in the 1732-1745 and 1735-1738 cm⁻¹ regions.

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Translated by Z. Votický