TRANSFORMATIONS OF SOME SUBSTITUTED 5-BENZYL-1,2,4-

TRIAZOLINE-3-THIONES

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UDC 547.792.7:542.951.1

The acylation of some substituted 5-benzyl-1,2,4-triazoline-3-thiones both in the presence of triethylamine and in alkaline media gives N-substituted derivatives. N-Substituted derivatives were obtained by cyanoethylation, whereas S-substituted derivatives were obtained by alkylation. Bromination of the acyl derivatives gives disulfides.

It is known that compounds with amide and thioamide groups, which have dual reactivities, may undergo reaction with transfer of the reaction center [1, 2]. The cyanoethylation of 4-R-1,2,4-triazoline-3-thiones occurs at the N-thioamide group [3], whereas S-substituted derivatives are obtained by alkylation [3, 4]. An N-phenyl substituent plays a substantial role in the thione-thiol tautomerism of triazoline thiones.

N-Substituted derivatives IIa-d were obtained by acylation of 4-phenyl (allyl)-5-benzyl-1,2,4-triazoline-3-thiones (Ia, b) with acid chlorides (benzoyl and cinnamoyl chlorides) in the presence of triethylamine. The action of alcoholic sodium hydroxide on Ia, b gives sodium salts I', which also form only N-substituted derivatives IIa-d with acid chlorides (benzoyl and cinnamoyl chloride) in benzene at room temperature.



In contrast to 5-phenyltriazolines [7], we were unable to isolate S-substituted derivatives under these conditions. The UV spectra of N-acyl derivatives II obtained by acylation of Ia, b and of their sodium derivatives (I') are similar.

Bromination of IIa, b in chloroform gives disulfide IVa, which was also obtained by alternative synthesis by bromination of sodium salt I'a. The UV spectra of the products of bromination in both cases are identical. Hydrobromide Vb was obtained by the action of bromine on 4-allyl-5-benzyl-1,2,4-triazoline-3-thione. The UV spectrum of Vb is similar to the UV spectra of the S-alkyl derivatives.

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Uzhgorod State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 844-846, June, 1975. Original article submitted March 4, 1974.

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TABLE	1.	Characteristics	of	the	Compounds	Obtai	ned
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Com- pound	R	RI	mp , ° C	Emp iric al formula	found N.	calc. %	$\lambda_{max'}$ nm	1g e	Yield % (method)
IIa	C ₆ H ₅	COC_6H_5	172—173	$\mathrm{C}_{22}\mathrm{H}_{17}\mathrm{N}_3\mathrm{OS}$	11,3	11,3	240 270	4,89 4,10	73(A) 52(B)
ПÞ	C_6H_5	COCH=CH	174—175	$C_{24}H_{19}N_3\mathrm{OS}$	10,6	10,6	260 310	4,20 4,20 3,50	79(A) 56(B)
IIc	CH ₂ CH=CH ₂	COC ₆ H ₅	110—110,5	$C_{19}H_{17}N_3OS$	12,4	12,2	265 300 310	4,10 4,20 4,17	76 (A) 64 (B)
ILd	CH ₂ CH=CH ₂	COCH=CH- C ₆ H ₅	95—96	$C_{21}H_{19}N_3OS$	11,6	11,6	260 310	4,20 3,59	74(A) 62(B)
IIe IIf IIIa IIIc IIIb IIIb IIId	$\begin{array}{c} C_6H_5\\ CH_2CH=CH_2\\ C_6H_5\\ CH_2CH=CH_2\\ C_6H_5\\ CH_2CH=CH_2\\ CH_2CH=CH_2 \end{array}$	CH ₂ CH ₂ CN CH ₂ CH ₂ CN CH ₂ COOH CH ₂ COOH CH ₂ COOH CH ₂ CH ₂ COOH CH ₂ CH ₂ COOH	$\begin{array}{r} 82 \\ - 83 \\ 76,5 \\ - 77 \\ 167 \\ - 168 \\ 129 \\ - 130 \\ 152 \\ - 153 \\ 150,5 \\ - 151 \end{array}$	$\begin{array}{c} C_{18}H_{16}N_4S\\ C_{15}H_{16}N_4S\\ C_{17}H_{15}N_3S\\ C_{14}H_{15}N_3O_2S\\ C_{18}H_{17}N_3O_2S\\ C_{15}H_{17}N_3O_2S \end{array}$	17,7 19,8 12,9 14,6 12,2 13,9	17,5 19,7 12,9 14,5 12,4 13,9	260 260 240 240 240 240 240	4,06 4,10 3,63 3,51 3,52 3,50	88 66 68 69 47 56

Cyanoethylation of Ia, b gives N-cyanoethyl derivatives IIe, f, whereas the corresponding S-acids IIIa-d are obtained by alkylation with β -bromopropionic and monochloro-acetic acids in alkaline media. Hydrolysis of IIe gave N-acid IIg, the melting point of which differs from that of S-acid IIIb. Only amide IIh was obtained by hydrolysis of IIf, inasmuch as we were unable to isolate the acid in pure form.

The UV spectra of the N-derivatives of the acids are similar to one another and to those of the starting materials but differ from the UV spectra of the S-derivatives of the acids.

EXPERIMENTAL METHOD

The UV spectra of ethanol solutions of the compounds were recorded with an SF-4 spectrophotometer. Compounds Ia, b were obtained by the method in [8].

Sodium Salt of 4-Phenyl-5-benzyl-1,2,4-triazoline-3-thione (I'a). A 2-g (7.5 mmole) sample of Ia was added to an aqueous alcohol solution of 0.3 g (7.5 mmole) of sodium hydroxide, after which the mixture was heated for 5 min. It was then cooled, and ether was added to precipitate a crystalline substance, which was removed by filtration to give 2.38 g (quantitative yield) of product.

Sodium Salt of 4-Ally1-5-benzy1-1,2,4-triazoline-3-thione (I'b). This compound was obtained in 87% yield from Ib by the method used to prepare I'a.

<u>2-Benzoyl-4-allyl-5-benzyl-1,2,4-triazoline-3-thione (IIc)</u>. A) A mixture of 1.15 g (0.05 mole) of Ib, 0.7 g (0.05 mole) of benzoyl chloride, and 1 g of triethylamine in benzene was refluxed for 30 min, after which it was cooled, and the precipitated crystals were removed by filtration and washed with ether. Compounds IIa, b, d were similarly obtained (see Table 1).

B) A suspension of 0.66 g (2.6 mmole) of Ib and 0.36 g (2.6 mmole) of benzoyl chloride in benzene was stirred for 30 min at room temperature. The resulting precipitate was removed by filtration and from the ether filtrate was produced a crystalline substance. Compounds IIa, b, d were obtained similarly (see Table 1).

No melting-point depression was observed for a mixture of the compounds obtained by methods A and B.

Bis(4-phenyl-5-benzyl-1,2,4-triazol-3-yl) Disulfide (IVa). A solution of 0.15 g (1.9 mmole) of bromine in chloroform was added dropwise with cooling and stirring to 1.1 g (3.8 mmole) of I'a in chloroform, and the resulting precipitate was removed by filtration and washed with ether to give 0.62 g (63%) of a product with mp 217-218° (from alcohol). UV spectrum: λ_{max} 265 nm (log ϵ 4.5). Found: N 15.6%. C₃₀H₂₄N₆S₂. Calculated: N 15.8%.

Compound IVa was similarly obtained by bromination of IIa, b. No melting-point depression was observed for a mixture of the products obtained by bromination of the various starting compounds.

<u>2-Bromomethyl-5-benzyl-2,3-dihydro-1,3,4-thiazolo[2,1-b]triazolidine Hydrobromide (Vb)</u>. A solution of 0.32 g (2 mmole) of bromine in chloroform was added dropwise with cooling and stirring to 0.4 g (2 mmole) of Ib, and the resulting precipitate was removed by filtration and washed with ether to give 0.62 g (79%) of a product with mp 178-179P (from alcohol). Found: Br 20.4; N 10.8%; Equiv. wt. 387. $C_{12}H_{13}Br_2N_3S$ ·HBr. Calculated: Br 20.5; N 10.7%; Equiv. wt. 391.

 $\frac{4-\text{Allyl-5-benzyl-3-(}\beta-\text{carboxyethyl)}\text{thio-1,2,4-triazole (IIId).} A 1.15-g (5 mmole)}{\text{sample of Ib was dissolved in an aqueous alcohol solution of 0.4 g} (10 mmole) of sodium hydroxide, and 0.76 g (6 mmole) of <math>\beta$ -bromopropionic acid was added. The mixture was refluxed for 1 h, after which it was acidified with hydrochloric acid, and the resulting precipitate was removed by filtration. Compounds IIIa-c were similarly obtained.

 $\frac{4-\text{Allyl-5-benzyl-2-(}\beta-\text{cyanoethyl)-1,}2,}{\text{g (0.01 mole) of Ib, 5.2 g (0.01 mole) of acrylonitrile, and 4 g of triethylamine}}$ was refluxed in ethanol for 20 min, after which the precipitated crystals were removed by filtration and washed with alcohol and ether. Compound IIe was similarly obtained.

 $\frac{4-\text{Allyl-5-benzyl-2-(2-aminocarbonyl)ethyl-1,2,4-triazoline-3-thione (IIh).}{4 g (1.4 mmole) of IIf and 10 ml of hydrochloric acid was allowed to stand at room temperature for 2 days. The resulting precipitate was removed by filtration and washed with ether to give 0.2 g (47%) of a product with mp 107-107.5° (from alcohol). Found: N 18.4%. C15H18N4OS. Calculated: N 18.5%.$

 $\frac{4-\text{Phenyl-5-benzyl-2-}(\beta-\text{carboxyethyl})-1,2,4-\text{triazoline-3-thione (IIg).} A \text{ mixture of } 0.8 \text{ g (2.5 mmole) of IIe and 20 ml of hydrochloric acid was heated for 30 min, and the resulting precipitate was removed by filtration to give 0.34 g (40%) of a product with mp 71° (from aqueous alcohol). Found: N 12.3%. C18H17N302S. Calculated: N 12.4%.$

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