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REACTION OF AMINO THIOLS WITH CHLOROACETIC ACID AND ITS ESTERS

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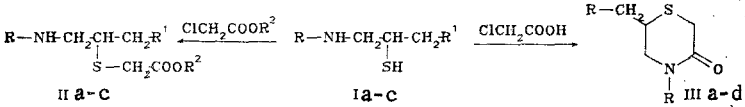
UDC 547.869.2'466.318'26'269.1.07:543.422

The reaction of amino thiols with chloroacetic acid esters leads to the formation of amino mercapto esters, whereas 6-alkyl(alkoxy)-N-aryltetrahydro-1,4-thiazine-3-ones are formed in the reaction with chloroacetic acid.

Tetrahydro-1,4-thiazine-3-ones or thiomorpholones are biologically active compounds [1-3]. Their synthesis is realized by the reaction of ethyleneimine with thioglycolic acid esters [4] or by the reaction of aminoethanethiol with haloacetic acid esters [5-8].

In the present research we set out to study the reaction between various amino thiols (I) and chloroacetic acid or its esters and to synthesize a number of new analogs of tetrahydro-1,4-thiazin-3-one. In contrast to [1, 8], we established that 1-anilino-2-propanethiol, 1-benzylamino-2-propanethiol, and other amino thiols react with chloroacetic acid esters to give amino mercapto esters and that the corresponding thiazinones are not formed.



II a-c Ia-c III a-d

I—III a R=Ph, R^1=H, R^2=Et; b R=CH_2Ph, R^1=H, R^2=Et; c R=Ph, R^1=BuO, R^2=Et(Bu); d R=CH_2Ph, R^1=BuO

In addition to this, as we have previously reported [9], thiazinones are formed in the reaction of the corresponding amino thiols with chloroacetic acid in the presence of sodium

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0009-3122/84/2003-0261$08.50

TABLE 1. Spectral Characteristics of Amino Mercapto Esters II and Thiazinones III

Compound	IR spectrum, cm^{-1}	PMR spectrum, ppm							
		C_6H_5	$ArCH_2$	H	CH_2CH	CH_2CO	OCH_2	$(CH_2)_2$	CH_3
IIa	3370, 1725	6,35 6,75	—	3,72	3,10	3,95	3,02	—	1,32
IIb	3375, 1720	7,08	3,51	3,65	3,05	4,25	3,15	—	1,15
IIc	3350, 1715	6,48 6,80	—	3,70	3,00	4,20	3,14	1,40	0,92
[illegible]	3370, 1720	6,35 6,70	—	3,56	3,12	4,30	3,15	1,55	0,90
IIIa	[illegible]15	6,72	—	—	2,95	3,45	—	—	1,15
IIIb	1650	6,80	3,45	—	2,85	4,20	—	—	1,20
IIIc	1675	7,15	—	—	3,20	4,10	3,35	1,55	1,00
IIId	1660	6,93	3,30	—	2,95	4,15	3,24	1,35	0,95

hydroxide at 30-40°C for 1 h. It should be noted that benzyl-containing amino thiols do not react with chloroacetic acid in the presence of sodium hydroxide under the conditions mentioned above; for the synthesis of thiazinones IIIb, d we therefore obtained the sodium mercaptides of the corresponding amino thiols in toluene solution by the reaction of sodium metal with amino thiols and then treated them with chloroacetic acid.

The vibration of an ester carbonyl group at 1715-1735 cm^{-1} and absorption bands at 3350-3375 cm^{-1}, which correspond to the absorption of associated and nonassociated NH groups, appear in the IR spectra of amino mercapto esters II (Table 1). In contrast to the spectra of amino mercapto esters II, an absorption band of an NH group is absent in the IR spectra of thiazinones III, but absorption of an amide carbonyl group at 1645-1675 cm^{-1} is observed.

The position of the signal of the proton of the NH group in the PMR spectrum of amino mercapto ester IIa (Table 1) was established on the basis of the change in the multiplet of signals of the CH_2CO protons when D_2O was added. The PMR spectra of thiazinones III differ regularly from the spectra of the corresponding amino mercapto esters II. The assignment of the signals of all of the synthesized compounds was confirmed by the integral curve.

EXPERIMENTAL

The PMR spectra were recorded with a Varian T-60 spectrometer with tetramethylsilane as the internal standard. The IR spectra of liquid films or suspensions in mineral oil were recorded with a UR-20 spectrometer.

The starting amino thiols were obtained by the methods in [10-12].

1-Anilino-2-ethoxycarbonylmethylmercaptopropane (IIa). A mixture of 0.1 mole of 1-anilino-2-propanethiol and 0.1 mole of sodium hydroxide in 30 ml of water was stirred vigorously, 0.1 mole of ethyl monochloroacetate was added dropwise, and the mixture was heated at 30-40°C for 1 h. The organic layer was extracted with ether, and the extract was washed three times with water, dried over calcined sodium sulfate, and distilled *in vacuo*.

The other amino mercapto esters II were similarly obtained (Table 2).

6-Methyl-N-phenyltetrahydro-1,4-thiazin-3-one (IIIa). A mixture of 0.1 mole of the sodium salt of 1-anilino-2-propanethiol and sodium chloroacetate was heated at 30-40°C for 1 h, after which it was acidified with 20% HCl and extracted with ether. The extract was dried over calcined sodium sulfate and distilled *in vacuo*.

6-Butoxymethyl-N-phenyltetrahydro-1,4-thiazin-3-one (IIIc) was similarly synthesized.

6-Methyl-N-benzyltetrahydro-1,4-thiazin-3-one (IIIb). A mixture of 0.1 mole of 1-benzylamino-2-propanethiol and 0.1 mole of sodium metal in 30 ml of anhydrous toluene was stirred with heating until all of the sodium has vanished, after which 0.1 mole of sodium monochloroacetate was added, and the mixture was heated at 80-90°C for 2 h. It was then acidified with 20% HCl and extracted with ether. The extract was dried over calcined sodium sulfate and distilled *in vacuo*.

TABLE 2. Characteristics of the Synthesized Compounds

Compound	bp, °C (mm)	n_D^{20}	d_4^{20}	Found, %				Empirical formula	Calc., %				Yield, %
				C	H	N	S		C	H	N	S	
IIa	148—150 (0,25)	1,5569	1,1096	61,4	7,8	5,8	12,7	$C_{13}H_{19}NO_2S$	61,6	7,6	5,5	12,6	80
IIb	141—142 (0,3)	1,5740	1,1706	62,6	8,1	5,5	11,7	$C_{14}H_{21}NO_2S$	62,9	7,9	5,2	12,0	35
IIc	164—165 (0,18)	1,5379	1,0703	62,5	8,1	4,6	10,0	$C_{17}H_{27}NO_3S$	62,7	8,4	4,3	9,8	32
IIc'	172—173 (0,25)	1,5121	1,0648	64,3	8,7	4,1	9,3	$C_{19}H_{31}NO_3S$	64,6	8,8	4,0	9,1	30
IIIa	154 (0,1), 34—35*	—	—	63,6	6,5	6,5	15,2	$C_{11}H_{13}NOS$	63,7	6,3	6,8	15,5	55
IIIb	106 (0,05)	1,5670	—	65,5	6,8	6,2	14,0	$C_{12}H_{15}NOS$	65,1	6,8	6,3	14,5	50
IIIc	161—162 (0,1), 45*	1,5531	—	64,7	7,7	4,8	11,2	$C_{15}H_{21}NO_2S$	64,5	7,6	5,0	11,5	52
IIId	164—165 (0,1)	1,5365	—	65,7	7,7	4,9	10,6	$C_{16}H_{23}NO_2S$	65,5	7,9	4,8	10,9	45

*Melting point.

Compound IIId was similarly synthesized.

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RESEARCH IN THE CHEMISTRY OF HETEROCYCLIC QUINONEIMINES.

3.* OXIDATIVE CYCLIZATION OF 2,5-DIARYLAMINO-SUBSTITUTED 1,4-BENZOQUINONE-4-PHENYLIMINES — SIMPLE METHOD FOR THE PREPARATION OF 2-ARYLAMINO-5-ARYL-3-PHENAZINONES

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UDC 547.864.6'86.5.7'867.6'869.2'567.5.07:542.943:543.422

2,5-Diarylamino-1,4-benzoquinone-4-phenylimines, which are formed in the reaction of 1,4-benzoquinone-4-phenylimine with aromatic amines, are converted under oxidative conditions to products of intramolecular oxidative cyclization, viz., 2-arylamino-5-aryl-3-phenazinones.

In a series of studies devoted to the chemistry of 3-phenoxazinones, 3-phenothiazinones, and 3-phenazinones it was established that in the reaction of these compounds with various O-, S-, and N-nucleophiles substitution of hydrogen may occur in both the quinoneimine and aryl parts of the molecules [1-4].

*See [4] for Communication 2.

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 330-333, March, 1984. Original article submitted July 22, 1983.