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A number of 2-benzothiazolylmethylaminocarboxylic acids and their derivatives (esters, amides, hydrazides, and alcohols) were synthesized. It is shown that the condensation of isatoic anhydride with o-aminothiophenol and o-phenylenediamine leads to the formation of o-aminophenyl-2-benzothiazole and o-aminophenyl-2-benzimidazole, respectively.

2-Benzothiazolylcarboxylic acids are of interest as intermediates for the synthesis of new heterocycles, cyanin dye photosensitizers, physiologically active substances, and other compounds.

A method for the synthesis of 2-benzothiazolylalkylcarboxylic acids is described in [1], but acids I were not obtained.

$$\begin{array}{c}
 S \\
 N \\
 -CH_2 - X - CH_2 - COOH \\
 Ia X = NR \\
 Ib X = Se
 Ib X = Se$$

The aim of this investigation was to study the condensation of o-aminothiophenol with dicarboxylic acid anhydrides (III) [2] and with the anhydrides of selenodiglycolic and isatoic acids. The condensation proceeds via the following scheme:



IIa X = SH; IIb X = NH₂; III, IVa R' = R" = R" = H; b R' = R" = H, R" = CH₃; c R^e = OCH₃, R" = R" = H; d R' = R" = H, R" = OCH₃; e R'=R" = H, R" = OCH₃;

IV are colorless, crystalline substances (Table 1).

Several derivatives of acids IV (esters, amides, hydrazides, and alcohols) were also obtained (Table 2).



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TABLE 1. 2-Benzothiazolylmethylaminocarboxylic Acids

Com-		R²	R³	Mp*		S,		
pound	R١				Empirical formula	found	cale.	Yield, %
IVa	Н	н	Н	143	$C_{16}H_{14}N_2O_2S$	10,6 9.6 †	10,7 9.4 †	81,0
IVb	Н	CH3	H	158	$C_{17}H_{16}N_2O_2S$	10,3	10,3	65,9
IVC	UCH3	OCH.		170	$C_{17}H_{16}N_2O_3S$	9,5	9,8	05 4
IVe	H	H	OCH ₃	166	C17H16142O35	9.5	9.8	90.0
ĪVf	ОН	H	H	146	C ₁₆ H ₁₄ N ₂ O ₃ S	10,4	10,2	39,8

*IV a and c were crystallized from alcohol-water (2:1), while the remaining compounds were crystallized from alcohol.

†N, %.

TABLE 2. Derivatives of 2-Benzothiazolylmethylaminocarboxylic Acids

CH ₂ R										
Com- pound	R1	R ²	R3	R	Mp*	Empirical	S, %			
						formula	found	calc.	Yield, %	
Va Vb Vc VIa VIb VIIa VIIb VIII	H H H H H H H	H H H H H H H	H H OCH ₃ H OCH ₃ H OCH ₃ H	COOCH ₃ COOC ₂ H ₅ COOCH ₃ CONH ₂ CONH ₂ CONHNH ₂ CONHNH ₂ CONHNH ₂ CONHNH ₂	$ \begin{array}{r} 108 \\ 63 \\ 132 \\ 165 \\ 184 \\ 146 \\ 188 \\ 87 \\ \end{array} $	$\begin{array}{c} C_{17}H_{16}N_2O_2S\\ C_{18}H_{18}N_2O_2S\\ C_{18}H_{18}N_2O_8S\\ C_{16}H_{15}N_3OS\\ C_{16}H_{15}N_3OS\\ C_{17}H_{17}N_3O_2S\\ C_{16}H_{18}N_4OS\\ C_{17}H_{18}N_4O_2S\\ C_{16}H_{16}N_2OS \end{array}$	10,2 9,9 9,6 14,2 13,0 18,0 16,3 11,1	10,3 9,8 9,4 14,2 12,9 17,9 16,4 11,2	76,1 50,6 54,7 92,1 91,0 44,2 49,0 69,7	

 $\begin{array}{c} S \\ S \\ C \\ H_2 \\ - N \\ - N$

*Va and VIa were crystallized from methanol, Vc was recrystallized from butanol, VIII was recrystallized from CCl_4 -petroleum ether, and the remaining compounds were crystallized from alcohol.

†N, %.

VIII was identified from the IR spectrum ($\nu_{OH} = 3290 \text{ cm}^{-1}$, $\delta_{OH} = 1050 \text{ cm}^{-1}$).

The formation of compounds with structures IX and X is possible during the preparation of several acids of the benzothiazole and benzimidazole series by condensation of isatoic anhydride with o-aminothio-phenol and o-phenylenediamine, respectively:



However, on the basis of the data of elementary analysis, IR spectroscopy, and the chemical properties of the compounds (they are insoluble in sodium carbonate and alkali and are capable of undergoing diazotization and coupling with amines and phenols to give azo dyes), it can be assumed that decarboxylation occurs during the reaction to form compounds which have primary amine structure XI:



Reactions of the synthesized 2-benzothiazolylmethylaminocarboxylic acids were carried out with solutions of heavy metal salts [2]. A change in the color of the solutions or the formation of precipitates were observed. The copper salt of 2-benzothiazolylmethylselenoacetic acid was properly isolated. Investigations in this direction are continuing.

EXPERIMENTAL

2-Benzothiazolylmethylphenylaminoacetic Acid (IVa). An equimolar amount of o-aminothiophenol in benzene was added to 11 g (0.056 mole) of anilinediacetic anhydride [3] in benzene. After the solution became clear, it was allowed to stand for 30 min. Removal of the solvent by distillation and crystallization of the results gave 13.9 g of product.

<u>2-Benzothiazolylmethyl-(m-tolyl)-aminoacetic Acid (IVb)</u>. An equimolar amount of o-aminothiophenol was added to a toluene solution of 18 g (0.088 mole) of m-toluidineacetic anhydride [2]. The mixture was refluxed for 0.5-1 h, the solvent was removed by distillation, and the residue was crystallized to give 18.1 g of product.

IVc-f were similarly obtained (see Table 1).

2-Benzothiazolylmethylselenoacetic Acid (Ib). This was synthesized in 39.6% yield from selenodiglycolic anhydride [2] and had mp 200 deg. Found %: Se 27.2. $C_{10}H_9NO_2SSe$. Calc. %: Se 27.6.

Copper Salt of Ib. Ib [0.57 g (0.002 mole)] was dissolved in dimethylformamide, and an excess of a hot, saturated aqueous solution of copper sulfate was added. The resulting precipitate of light-green powdery salt was crystallized from dimethylformamide-water to give 0.59 g (93%) of product. Found %: N 4.3; Se 24.0. $C_{20}H_{18}CuN_2O_4S_2Se_2$. Calc. %: N 4.4; Se 24.9.

Esters V (a-c) were obtained by esterification of acids IV with alcohols in the presence of hydrogen chloride; amides VIa and b were obtained by ammonia saturation of methanol solutions of the esters of the corresponding acids; hydrazides VII a and b were obtained by heating V with hydrazine hydrate (see Table 2).

<u>2-Benzothiazolylmethylphenylaminoethanol (VIII)</u>. A solution of 27.7 g (0.085 mole) of Vb in 400 ml of absolute ether was added dropwise to a stirred solution of 7.2 g (0.18 mole) of lithium aluminum hydride in 250 ml of absolute ether cooled to -60 deg. Wet ether (200 ml) was added dropwise to this mixture (warmed to -25 deg) to decompose the unchanged lithium aluminum hydride. A solution of 12 g of NaOH in 70 ml of water was added to the mixture at -15 deg to decompose the precipitated alkoxide, after which the reaction mass was allowed to warm to room temperature. The solution was filtered, the ether filtrate was dried with magnesium sulfate, and the ether was removed by distillation. The residue was recrystallized to give 16.8 g of product.

o-Aminophenyl-2-benzothiazole (XIa). A solution of 27 g (0.16 mole) of isatoic anhydride [4] and 27 ml of dimethylformamide was refluxed for 18-20 h with 20.6 g (0.16 mole) of o-aminothiophenol and then diluted twice with hot water. The resulting solid precipitate was crystallized from alcohol to give 26.1 g (59%) of a product with mp 125 deg. Found %: S 14.1. $C_{13}H_{10}N_2S$. Calc. %: S 14.2.

o-Aminophenyl-2-benzimidazole (XIb). This was similarly obtained in 62% yield from equimolar amounts of isatoic anhydride and o-phenylenediamine and had mp 266 deg. Found %: N 20.0. $C_{13}H_{11}N_3$. Calc. %: N 20.1.

<u>2-Hydroxynaphthylene-1-azo[2'-(2"-benzothiazolyl)benzene]</u>. A solution of sodium nitrite [0.69 g (0.03 mole) of NaNO₂ in 4 ml of water] was added to a suspension of 2.27 g (0.01 mole) of XIa in 6-7 ml of HCl (1:1) with stirring at 2-5 deg. After this, the reaction mixture was stirred for another 15-30 min. The diazotized amine was added dropwise to a cooled solution of socium β -naphthoxide [1.44 g (0.01 mole) of β -naphthol, 0.8 g (0.025 mole) of NaOH, 10 ml of water]. The precipitated dye was crystallized from dimethylformamide to give 3.48 g (91.3%) of a product with mp >350 deg. Found %: S 8.34. C₂₃H₁₅N₃OS. Calc. %; S 8.4.

The IR spectrum of VIII in KBr pellets (190 mg of KBr and 2 mg of compound) were obtained with a UR-10 spectrometer, while the spectra of the remaining compounds were obtained with a UR-20 spectrometer with KBr, LiF, and NaCl prisms. The following bands were detected: for IVd and f 2500-3000 cm⁻¹ ($\nu_{\rm C}$ = 0); for Vc 1735 cm⁻¹ ($\nu_{\rm C}$ = 0); for Vlb 1690 cm⁻¹ ($\nu_{\rm C}$ = 0 "amide I" band); for XIa 3470 cm⁻¹ ($\nu_{\rm NH_2}$) and 1620 cm⁻¹ ($\delta_{\rm NH_2}$).

System symbol	Solvents	Ratio
A B C D E F G	Isobutanol - formic acid -water Dichloroethane - methanol Dichloroethane - methanol 90 % ethanol-25 % ammonia - water Benzene - Dioxane - acetic acid Benzene - methanol - acetic acid Dichloroethane - methanol	7:2:19:195:5100:12:1690:25:445:8:47:3

TABLE 4. R_f Values in Various Solvent Systems

Com- pound	R _f in systems								
	A	В	с	Ď	E	F			
IVa IVb IVc IVd IVe IVf IVb	0,76 0,76 0,76 0,76 0,74 0,76 0,76	0,06 0,07 0,06 0,06 0,03 0,76 0,02	0,78 0,80 0,78 0,79 0,79 0,79 0,78 0,72	0,38 0,38 0,61 0,36 0,48 0,58 0,16	0,76 0,78 0,73 0,82 0,19 0,35	0,33 0,33 0,32 0,31 0,28 0,28 0,28			

TABLE 5. R_f Values in System C

Com- pound	Vb	Vc	VIb	VIIa	VIIb	VIII	XIa	XIb
R_f	0,66	0,63	0,23	0,17	0,13	0,41	0,69	0,51

The compounds we obtained were chromatographed on plates in a thin-layer of Merck G silica gel with the various solvent systems (Table 3). The chromatograms were developed in iodine vapor. The calculated R_f values are presented in Tables 4 and 5.

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