BENZOSELENAZOL-2-YLALKYLCARBOXYLIC AND BENZOSELENAZOL-2-YLARYLCARBOXYLIC ACIDS AND THEIR DERIVATIVES

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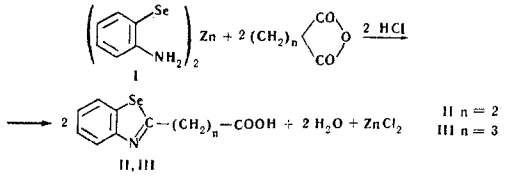
A preparative method for the synthesis of the previously unknown benzoselenazol-2-ylalkylcarboxylic and benzoselenazol-2-ylarylcarboxylic acids consisting in the condensation of zinc o-aminoselenophenoxide with dicarboxylic anhydrides in the presence of hydrochloric acid is proposed.

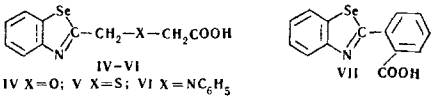
A simple preparative method for the synthesis of benzothiazol-2-ylalkylcarboxylic and benzothiazol-2-ylarylcarboxylic acids has been described previously which consists of the condensation of o-aminophenol with anhydrides of dibasic carboxylic acids [1]. The acids obtained have proved to be convenient starting materials for obtaining new types of benzothiazole derivatives [2–4].

In development of these investigations, in the present work we have studied the reaction of o-aminoselenophenol with dicarboxylic acid anhydrides. o-Aminoselenophenol has not hitherto been obtained in the free state because of its ready oxidizability to the diselenide. Zinc o-aminoselenophenoxide (I) is usually used for the synthesis of benzoselenazole derivatives [5]. The condensation of this compound with monocarboxylic acid chlorides gives 2-alkyl- and 2-arylbenzoselenazoles while dicarboxylic acid chlorides give α,ω-(dibenzoselenazolyl)hydrocarbons [5].

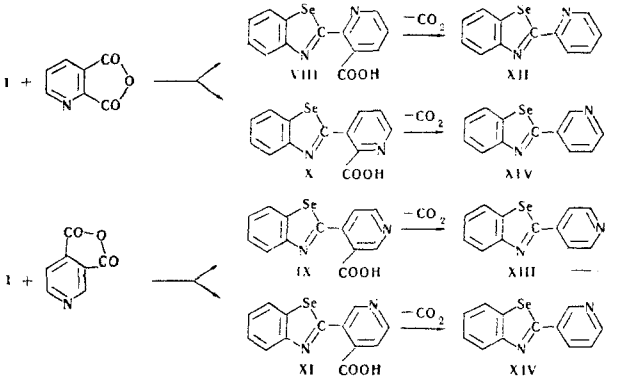
The reaction of dicarboxylic acid anhydrides with o-aminoselenophenol has not previously been studied. It was found that in the presence of small amounts of hydrochloric acid (necessary to convert the zinc salt into the free o-aminoselenophenols [6]), I condenses extremely readily with the anhydrides of dibasic acids to form benzoselenazol-2-ylalkylcarboxylic or benzoselenazol-2-ylarylcarboxylic acids:



Compound I reacts with dicarboxylic anhydrides even in the absence of hydrochloric acid, but in this case the reaction products are not the acids II and III but amorphous products which have not been studied further. If the condensation of I with the anhydride is carried out in ethanol in the presence of hydrochloric acid, it is not the free acids II and III that are obtained but their ethyl esters. The condensation can be performed in various inert solvents—ether, benzene, chloroform—but the highest yields are obtained in dimethylformamide. In addition to succinic and glutaric anhydrides, the reaction has been carried out with the anhydrides of diglycolic, thiodiglycolic, and N-phenyliminodiacetic acids, giving the acids IV–VI, while phthalic anhydride gives the acid VII.



In the reaction of o-aminoselenophenol with anhydrides of unsymmetrical dicarboxylic acids, as in the case of o-aminothiophenol [7], the formation of two isomeric acids is theoretically possible according to which carbonyl group of the anhydride takes part in this reaction. Thus, for example, in the reaction with quinolinic anhydride the formation of the acids VIII and X and with cinchomeronic anhydride the acids IX and XI is possible:



In fact, we succeeded in isolating only one compound in each case. Quinolinic anhydride gives the acid VIII and cinchomeronic anhydride the acid IX. The structures of the acids VIII and IX were determined accurately by their decarboxylation into the corresponding pyridylbenzoselenazoles. On decarboxylation, the product of condensation with quinolinic anhydride was converted into 2-(pyridy-2'-yl)benzoselenazole. XII and the acid formed from cinchomeronic anhydride gave 2-(pyrid-4'-yl)benzoselenazole (XIII). On decarboxylation, the isomeric acids X and XI would give 2-(pyrid-3'-yl)benzoselenazole (XIV). Since the 2-pyridylbenzoselenazoles have not been described in the literature previously, we prepared them by independent synthesis, condensing I with the chlorides of the corresponding pyridinecarboxylic acids. 2-Pyridylbenzothiazoles have been obtained previously by the analogous method [8]. Compound XII is formed from picolinoyl chloride, XIII from isonicotinoyl chloride, and XIV from nictoinoyl chloride.

Table 1 gives data on the new acids, Table 2 on their esters, and Table 3 on their amides.

Table 1

Benzoselenazol-2-ylalkylcarboxylic and Benzoselenazol-2-ylarylcarboxylic Acids

Compound	Name of the acid	Initial anhydride	Mp, °C	Solvent for crystallization	Empirical formula	Found, %		Calculated, %		Yield, %
						Se	N	Se	N	
II	β-(Benzoselenazol-2-yl)propionic	Succinic	98	Ethanol + water	$C_{10}H_9NO_2Se$	31.24 31.28	5.70 5.64	31.10	5.55	69
III	γ-(Benzoselenazol-2-yl)butyric	Glutaric	131	Ethanol + water	$C_{11}H_{11}NO_2Se$	29.89 29.74	5.20 5.26	29.47	5.22	44
IV	Benzoselenazol-2-ylmethoxyacetic	Diglycolic [9]	155	Water	$C_{10}H_9NO_3Se$	29.56 29.38	5.28 5.49	29.25	5.18	41
V	Benzoselenazol-2-ylmethylthioacetic	Thiodiglycolic [10]	128	Ethanol	$C_{10}H_9NO_2SSe$	27.72 27.68	4.82 4.78	27.62	4.89	46
VI	N-(Benzoselenazol-2-ylmethyl)-N-phenylaminoacetic	N-Phenyliminodiacetic [11]	167	Toluene	$C_{16}H_{14}N_2O_2Se$	—	8.30 8.21	—	8.11	53
VII	2-(Benzoselenazol-2′-yl)benzoic	Phthalic	188	Ethanol + water	$C_{14}H_9NO_2Se$	26.46 26.33	4.47 4.61	26.15	4.63	67.5
VIII	2-(Benzoselenazol-2′-yl)pyridine-3-carboxylic	Quinolinic [12]	203	Ethanol	$C_{13}H_8N_2O_2Se$	—	9.26 9.32	—	9.24	44
IX	4-(Benzoselenazol-2′-yl)pyridine-3-carboxylic	Cinchomeronic [13, 14]	239	Ethanol	$C_{13}H_8N_2O_2Se$	—	9.12 9.09	—	9.24	39

Table 2

Esters of Benzoselenazol-2-ylalkylcarboxylic and Benzoselenazol-2-ylarylcarboxylic Acids

Initial acid	Method of preparation	Mp of the methyl esters, °C	Solvent for crystallization	Empirical formula	Found, %		Calculated, %		Yield, %
					N	Se	N	Se	
II	a	56*	Mixture of ethanol and water	$C_{12}H_{13}NO_2Se$	5.12 5.29	28.42 28.37	4.96	28.01	42.8
III**	a	—	—	$C_{13}H_{15}NO_2Se$	5.02 5.09	28.46 28.32	4.73	28.01	49
IV	b	57	Ethanol + water	$C_{11}H_{11}NO_3Se$	5.12 5.20	27.98 27.97	4.93	27.81	69.6
VI	a	101—102	Ethanol	$C_{17}H_{16}N_2O_2Se$	8.00 7.96	—	7.79	—	54.6
VII	a	88	Methanol	$C_{15}H_{11}NO_2Se$	4.47 4.61	25.08 25.10	4.43	25.0	76.5
VIII	b	117	Methanol	$C_{14}H_{10}N_2O_2Se$	9.13 8.98	—	8.83	—	72.9
IX	b	117	Ethanol	$C_{14}H_{10}N_2O_2Se$	9.06 8.93	—	8.83	—	71.0

*Ethyl ester.
**Bp 184–185° C (1 mm).

Table 3

Amides of Benzoselenazol-2-ylalkylcarboxylic and Benzoselenazol-2-ylarylcarboxylic Acids

Initial acid	Mp of the amide, °C	Solvent for crystallization	Empirical formula	N, %		Yield of amide, %
				found	calculated	
II	140	Benzene	$C_{10}H_{10}N_2OSe$	11.33 11.27	11.06	51.6
III	133	Methanol	$C_{11}H_{12}N_2OSe$	10.36 10.60	10.48	55.3
IV	148	Benzene	$C_{10}H_{10}N_2O_2Se$	10.63 10.51	10.40	64
V	155	Methanol	$C_{10}H_{10}N_2OSSe$	9.63 9.81	9.82	60
VI	170	Methanol	$C_{16}H_{15}N_3OSe$	12.00 12.21	12.20	52
VIII	117	Methanol	$C_{13}H_9N_3OSe$	13.84 14.06	13.90	50

EXPERIMENTAL

Zinc o-aminoselenophenoxide (I) was obtained as described by Develotte [5].

Benzoselenazol-2-ylalkylcarboxylic and -arylcarboxylic acids. A mixture of 0.01 mole of I, 0.01 mole of a dibasic acid anhydride, and 2 ml of conc. HCl in 3-5 ml of dimethylformamide was heated for 15 min, whereupon the zinc salt dissolved completely. After this, 10-15 ml of water was added to the reaction mixture, and the acid that deposited was separated off, washed with water, and recrystallized from a suitable solvent (with the use of activated carbon).

The esters of the benzoselenazol-2-ylalkylcarboxylic and -arylcarboxylic acids were obtained by esterifying the acids with ethanol in the presence of hydrogen chloride (a), by methylating the acids with diazomethane (b), and also directly by carrying out the condensation of I with the dicarboxylic anhydrides in ethanol in the presence of hydrochloric acid (c).

a) A solution of 10.62 g (0.035 mole) of the acid VII in 170 ml of methanol was saturated with dry hydrogen chloride with cooling, and then the reaction mixture was boiled for 2 hr. The methanol was distilled off and, with cooling, the residue was treated with a solution of sodium carbonate to give an alkaline reaction. The methyl ester of the acid VII that deposited was filtered off, washed with water, and recrystallized from ethanol. The esters of the acids II, III, VI, and VII were obtained similarly.

b) An ethereal solution of diazomethane was added to a suspension of 0.47 g (~1.5 mM) of the acid VIII in ether until the acid had dissolved completely and the evolution of bubbles of nitrogen had ceased. Then the ether was distilled off and the residue was recrystallized. The esters of the acids IV, VIII, and IX were obtained by this method.

c) A mixture of 21 g (0.05 mole) of I, 10 g (0.1 mole) of succinic anhydride, 170 ml of ethanol, and 12.6 ml of conc. HCl was boiled for 30 min. Then the solution was filtered and was treated with 70 ml of hot water, and, after cooling, the crystals of the ester were filtered off and washed with water. Yield 16.8 g (58%), mp 56° C (from a mixture of ethanol and water). The product was identical with the ethyl β-(benzoselenazol-2-yl)propionate obtained by method (a).

Amides of the benzoselenazol-2-ylalkylcarboxylic and -arylcarboxylic acids. A solution of 5 mM of an ester of one of these acids in 10 ml of methanol was saturated with dry ammonia with cooling, and the resulting solution was left at room temperature for 3-5 days. If the amide had not then precipitated, the methanol was partially distilled off. The amide was filtered off, washed with methanol, and recrystallized.

Picrate of the ethyl ester of the acid III, mp 102° C (from ethanol). Found, %: N 10.92, 10.81. Calculated for $C_{13}H_{15}NO_2Se \cdot C_6H_2(NO_2)_3OH$, %: N 10.66.

Picrate of the methyl ester of the acid IV, mp 110° C (from ethanol). Found, %: N 10.72, 10.66. Calculated for $C_{11}H_{11}NO_3Se \cdot C_6H_2(NO_2)_3OH$, %: N 10.91.

Picrate of the methyl ester of the acid VII, mp 136° C (from ethanol). Found, %: N 10.63, 10.56. Calculated for $C_{15}H_{11}NO_2Se \cdot C_6H_2(NO_2)_3OH$, %: N 10.27.

Decarboxylation of 2-(benzoselenazol-2'-yl)pyridine-3-carboxylic acid (VIII). The acid (0.2 g) was heated at 225° C for 30 min, and after cooling the product was triturated with sodium carbonate solution, filtered off, and washed with water. The yield of 2-(pyrid-2'-yl)benzoselenazole (XII) was 0.14 g (65%) in the form of colorless needles, mp 149° C (from ethanol). Found, %: N 10.73, 10.86. Calculated for $C_{12}H_8N_2Se$, %: N 10.81.

Decarboxylation of 4-(benzoselenazol-2'-yl)pyridine-3-carboxylic acid (IX). The acid (0.15 g) was heated at 235° C for 7 min, and the product was washed with ammonia and water. The yield of 2-(pyrid-4'-yl)benzoselenazole (XIII) was 0.12 g (83%), mp 156° C (from ethanol). Found, %: N 11.03, 10.80. Calculated for $C_{12}H_8N_2Se$, %: N 10.81.

2-(Pyrid-2'-yl)benzoselenazole (XII). A solution of 2.21 g (~0.015 mole) of picolinoyl chloride in 50 ml of dry benzene was added to a suspension of 4 g (0.01 mole) of I in 4 ml of dry pyridine. On mixing there was a vigorous evolution of heat, and the mixture was then boiled until the zinc salt had dissolved completely (15 min). The resulting solution was cooled and poured into water acidified with hydrochloric acid. After the elimination of the benzene, the product was filtered off and carefully washed with water. Yield of XII, 4.51 g (88.7%), mp 149° C (from a mixture of dimethylformamide with ethanol). The material was identical with the product of the decarboxylation of the acid VIII.

2-(Pyrid-4'-yl)benzoselenazole (XIII) was obtained in a similar manner to the preceding compound from I and isonicotinoyl chloride, yield almost quantitative, mp 156° C (from a mixture of dimethylformamide and ethanol). The substance was identical with the product of the decarboxylation of the acid IX.

2-(Pyrid-3'-yl)benzoselenazole (XIV). A solution of 4.5 g (0.03 mole) of nicotinoyl chloride in 8 ml of chloroform was added in small portions to 8.1 g (0.02 mole) of compound I in 8 ml of pyridine. The reaction mixture was boiled for 7 min and, after cooling, dilute hydrochloric acid was added to it; the compound XIV was filtered off and carefully washed with water. Yield almost quantitative, mp 216° C (from a mixture of dimethylformamide and ethanol). Found, %: N 10.56, 10.70. Calculated for $C_{12}H_8N_2Se$, %: 10.81.

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