SYNTHESIS OF 2-AMINO-3-CARBETHOXY-4,5,6,7-TETRAHYDROBENZO[b]SELENOPHENE AND SOME TRANSFORMATIONS BASED ON IT

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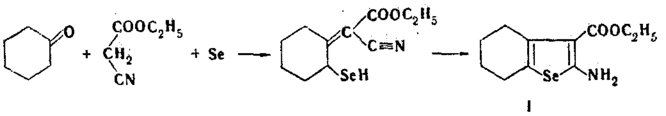
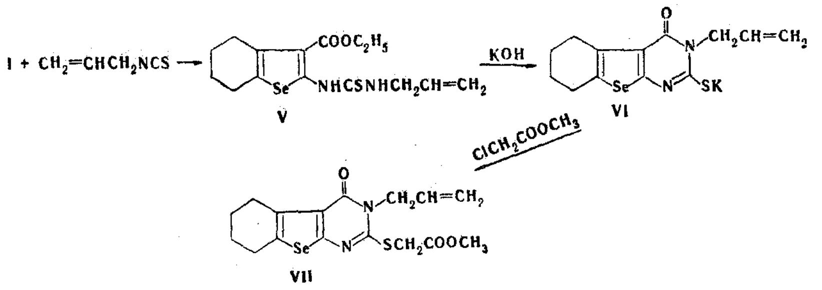
A new method for the synthesis of 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene was developed. The reaction of the latter with allyl isothiocyanate gave 2-(N'-allylthioureido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene, which is cyclized to the potassium salt of 3-allyl-4-oxo-2-thio-3,4,5,6,7,8-hexahydrobenzo[b]selenopheno[2,3-d]pyrimidine on treatment with potassium hydroxide.

Up until now, the most convenient method for the preparation of benzo[b]selenophene has been a multistep synthesis from anthranilic acid and sodium diselenide [1]. Methods for the preparation of 2-aminoselenophene derivatives on the basis of the reaction of elemental selenium with cyanoacetic ester and ketones, which is a method similar to that used to obtain 2-aminothiophene derivatives [2], are not presently known. Cyanoacetic ester and ketones do not react with selenium in ethanol and in higher-boiling solvents [dimethyl sulfoxide (DMSO) and dimethylformamide (DMF)] in the presence of diethylamine. 2-Amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (I) could be obtained only on prolonged heating with dimethylacetamide as the solvent.



The amino group of I readily reacts with maleic and succinic anhydrides and 2,4-dinitrobenzaldehyde to give, respectively, the monoamides of maleic (II) and succinic (III) acids and azomethine derivative (IV).

In order to obtain a condensed system from selenophene and pyrimidine rings, we synthesized 2-(N'-allylthioureido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (V) and obtained the potassium salt of 3-allyl-4-oxo-2-thio-3,4,5,6,7,8-hexahydrobenzo[b]selenopheno[2,3-d]pyrimidine (VI) by the action of potassium hydroxide on it. The salt readily reacts with methyl chloroacetate to give 3-allyl-2-(carbomethoxymethylthio)-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]selenopheno[2,3-d]pyrimidine (VII).



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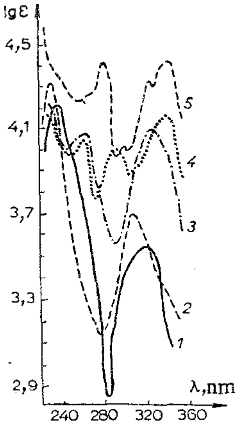

Fig. 1. UV spectra: 1) 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (I) 2) 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophene (VIII); 3) 3-allyl-2-(carbomethoxymethylthio)-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]selenopheno-[2,3-d]pyrimidine (VII); 4) potassium salt of 3-allyl-4-oxo-2-thio-3,4,5,6,7,8-hexahydrobenzo[b]selenopheno[2,3-d]pyimidine (VI), 5) potassium salt of 3-allyl-4-oxo-2-thio-3,4,5,6,7,8-hexahydrobenzo[b]-thieno[2,3-d]pyrimidine (IX).

The UV spectra of I and VI are similar to the spectra of the corresponding sulfur-containing derivatives – 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophene (VIII) [3] and the potassium salt of 3-allyl-4-oxo-2-thio-3,4,5,6,7,8-hexahydrobenzo-[b]thieno[2,3-d]pyrimidine (IX) (see Fig. 1).

The absorption maxima of selenium-containing compounds I and VI are shifted as compared with the maxima of the corresponding sulfur-containing analogs (VIII and IX) and have lower extinctions; this is probably explained by the fact that the electron pair of selenium in the selenium compounds participates to a lesser extent in conjugation of the sextet of electrons of the selenophene ring than the electron pair of sulfur in the thiophene ring of VIII and IX.

EXPERIMENTAL

The UV spectra of 10^{-5} M solutions of the compounds in ethanol (d 1 cm) were recorded with an SF-4A spectrometer. The IR spectrum of I was recorded with a UR-10 spectrophotometer.

2-Amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (I). A 7.89-g (0.1 g-atom) sample of selenium, 2.94 g (0.3 mole) of cyclohexanone, 33.9 g (0.3 mole) of ethyl cyanoacetate, 5 ml of diethylamine, and 50 ml of dimethylacetamide were refluxed for 25 h, after which the hot solution was filtered, and 2 volumes of water were added to the filtrate. The resulting oily liquid began to crystallize in the cold after 24 h to give 2.2 g (8%) of a product with mp 137-138° (from ethanol). λ_{max}, nm (log ε): 235 (4.21), 320 (3.55). IR spectrum (KBr pellet): 3400, 3290 cm^{-1} (ν_{NH}), 1640, 1580 cm^{-1} (δ_{NH_2}), 1300, 1050 cm^{-1} (ν_{COC}). Found: C 48.6; 48.6; N 5.3; 5.2; Se 29.2; 29.3%. $C_{11}H_{15}NO_2Se$. Calculated: C 48.5; N 5.2; Se 29.0%.

2-(3-Carboxyacryloylamino)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (II). A thoroughly ground mixture of 0.27 g (0.001 mole) of I and 0.098 g (0.001 mole) of maleic anhydride was fused at 100°. The mixture melted and immediately began to solidify to give 0.36 g (98%) of a product with mp 172-173° (from ethanol). λ_{max}, nm (log ε): 285 (3.98), 340 (4.02). Found: C 48.8; 48.6; N 3.9; 4.0; Se 21.6; 21.7%. $C_{15}H_{17}NO_5Se$. Calculated: C 48.6; N 3.8; Se 21.3%.

2-(3-Carboxypropionamido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (III). A mixture of 0.27 g (0.001 mole) of I and 0.1 g (0.001 mole) of succinic anhydride was heated in dry benzene for 1 h, after which it was cooled to precipitate 0.34 g (92%) of a product with mp 160-162° (from methanol). λ_{max}, nm (log ε): 275 (3.70), 282 (3.55), 315 (3.76), 325 (3.80). Found: C 48.6; 48.4; N 3.8; 3.8%. $C_{15}H_{19}NO_5Se$. Calculated: C 48.4; N 3.8%.

2-(2,4-Dinitrobenzylideneamino)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (IV). A mixture of 0.14 g (0.0005 mole) of I and 0.098 g (0.0005 mole) of 2,4-dinitrobenzaldehyde was pulverized thoroughly and fused at 100°. The melt began to solidify on cooling to give 0.21 g (95%) of a product with mp 59-61° (from ethanol). λ_{max}, nm (log ε): 240 (4.59), 305 (3.76). Found: C 48.1; 48.2; N 9.4; 9.4%. $C_{18}H_{17}N_3O_6Se$. Calculated: C 48.0; N 9.3%.

2-(N'-Allylthioureido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]selenophene (V). A mixture of 0.95 g (0.0035 mole) of I and 0.35 g (0.0035 mole) of allyl isothiocyanate was heated in 7 ml of ethanol for 7 h on a boiling-water bath, after which it was cooled to give 1.3 g (90%) of V with mp 131-133° (from methanol). λ_{max}, nm (log ε): 235 (3.56), 242 (3.50), 285 (3.47), 295 (3.53), 318 (3.42), 340 (3.70). Found: C 48.5; 48.6; N 7.4; 7.6%. $C_{15}H_{20}N_2O_2SSe$. Calculated: C 48.5; N 7.6%.

Potassium Salt of 3-Allyl-4-oxo-2-thio-3,4,5,6,7,8-hexahydrobenzo[b]selenopheno[2,3-d]pyrimidine (VI). A solution of 0.37 g (0.001 mole) of V in 5 ml of ethanol and 2 ml of a 2 N alcohol solution of potassium hydroxide was heated on a boiling-water bath for 30 min, after which it was cooled to give 0.28 g

(77%) of VI with mp 280° (dec.). λ_{max}, nm (log ε): 260 (4.05), 295 (4.00), 340 (4.18). Found: C 43.0; 42.8; N 7.8; 7.7%. $C_{13}H_{13}KN_2OSSe$. Calculated: C 43.0; N 7.7%.

3-Allyl-2-(carbomethoxymethylthio)-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]selenopheno[2,3-d]pyrimidine (VII). A mixture of 0.36 g (0.001 mole) of VI and 0.11 g (0.001 mole) of methyl chloroacetate in 5 ml of methanol was heated at 100° for 2 h, after which it was cooled to give a flocculent precipitate, which was removed by filtration and washed with water to give 0.36 g (91%) of a product with mp 103-105° (from ethanol). λ_{max}, nm (log ε): 265 (4.07), 330 (4.10). Found: C 48.4; 48.4; N 7.0; 7.0%. $C_{16}H_{18}N_2O_3SSe$. Calculated: C 48.4; N 7.1%.

2-Amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophene (VIII) [3]. λ_{max}, nm (log ε): 230 (4.31), 308 (3.70).

Potassium Salt of 3-Allyl-4-oxo-2-thio-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidine (IX) [4]. λ_{max}, nm (log ε): 285 (4.42), 305 (4.02), 330 (4.32), 350 (4.41).

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