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SYNTHESIS OF 2-SELENOTHIENO[2,3-d]PYRIMIDINE DERIVATIVES

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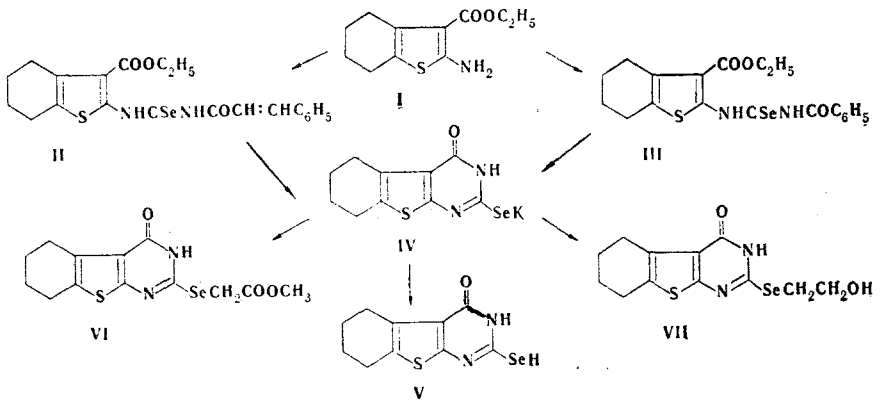
Intramolecular cyclization of 2-(N-acylselenoureido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophenes in alkaline media leads to the formation of the potassium salt (I) of 2-seleno-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidine, acidification of which yielded the corresponding base in free form. Some pyrimidine compounds containing a selenium atom in the side chain were obtained by reaction of potassium salt I with halo derivatives ($ClCH_2CH_2COOCH_3$ and $ClCH_2CH_2OH$).

A convenient method for the synthesis of thiouracil derivatives is intramolecular cyclization of compounds containing a carboxyl or ester group in the α position relative to the acylthioureido group [1, 2]. Up until now, the cyclization of similarly constructed acylselenoureides has not been studied.

2-N-Acylselenoureido derivatives of 3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophene (AST) undergo cyclization with splitting out of acyl groups to give the condensed 2-selenothieno[2,3-d]pyrimidine system. The AST were obtained by reaction of 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophene (I) [3] with cinnamoyl and benzoyl isoselenocyanates (II and III).



Heating II and III in an alkali solution gave potassium salt IV, which readily forms base V when it is acidified. Selenium-containing pyrimidine derivatives VI and VII were obtained by reaction of potassium salt IV with halo derivatives.

The AST undergo cyclization on treatment with a twofold excess of alkali. The same compounds (IV and V) are formed in the case of cyclization in the presence of an equimolar amount of alkali, but the yields are approximately halved.

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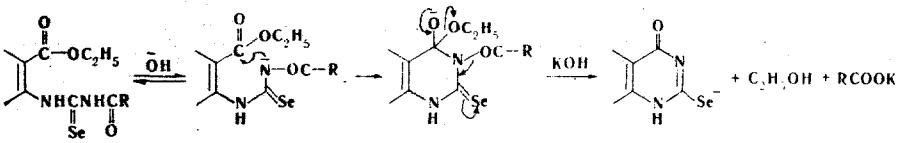
The ease of intramolecular cyclization of the AST is evidently due to the fact that under the influence of two electron-withdrawing substituents in the acylselenoureido group, a hydrogen of the imino group acquires acidic properties, and a potassium salt of the imino group is readily formed under the influence of alkali, during which the nucleophilicity of the nitrogen atom is increased. Intramolecular nucleophilic substitution at the unsaturated carbon atom of the carbethoxy group subsequently leads to ring formation:



When AST II and III are refluxed in alkali solution for more than 20 and 60 min, respectively, they undergo decomposition with the production of selenium metal.

Characteristic bands for the thiophene ring are observed at 1400 and 780 cm^{-1} in the IR spectra of all of the compounds obtained. An absorption band of a carbonyl group at 1600 cm^{-1} is characteristic for thieno[2,3-d]pyrimidine derivatives IV-VII. The band at 1580 cm^{-1} in the spectra of AST II and III, which is due to the presence of a benzene ring conjugated with an unsaturated grouping, vanishes in connection with its elimination during cyclization of the AST I to IV.

EXPERIMENTAL

The IR absorption spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer.

2-(N-Cinnamoylselenoureido)-3-carbethoxy-4,5,6,7,tetrahydrobenzo[b]thiophene (II). A mixture of 20 ml of ethanol, 2.25 g (0.01 mole) of I, and 2.4 g (0.01 mole) of cinnamoyl isoselenocyanate was refluxed on a water bath for 6 h, after which it was cooled, and the precipitate was removed by filtration to give 2.5 g (54.3%) with 165-167° (from ethanol). Found: N 6.18; S 6.95%. $C_{21}H_{22}N_2O_3SSe$. Calculated: N 6.07; S 6.94%.

2-(N-Benzoylisoselenoureido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophene (III). This compound, with mp 160-161° (from ethanol), was obtained in 46% yield from equimolar amounts of I and benzoyl isoselenocyanate by the method used to prepare II. Found: N 6.4; S 7.7%. $C_{19}H_{20}N_2O_3SSe$. Calculated: N 6.5; S 7.4%.

2-Seleno-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidine Potassium Salt (IV). Compound II or III was heated on a boiling-water bath for 15 or 50 min, respectively, with a twofold excess of potassium hydroxide in aqueous alcohol solution, after which the mixture was cooled and the precipitated crystals were separated by filtration to give IV, with mp 325° (dec., from ethanol), in 37 and 50% yields, respectively. Found: N 8.7; S 10.0%. $C_{10}H_9KN_2OSSe$. Calculated: N 8.7; S 9.9%

2 Seleno-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidine (V). A mixture of 1.1 g (3.4 mmole) of IV, 0.4 g (6.8 mmole) of acetic acid, and 10 ml of ethanol was refluxed on a water bath for 2 h, after which the precipitate was removed by filtration to give 0.7 g (72%) of a product with mp 192-194° (from ethanol). Found: N 10.2%; S 10.9%. $C_{10}H_{10}N_2OSSe$. Calculated: N 9.8%; S 11.2%.

2-Methylcarboxymethylseleno-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidine (VI). This compound, with mp 178-179° (from ethanol), was obtained in 68% yield by heating equimolar amounts of IV and methyl chloroacetate in ethanol solution for 2 h on a boiling-water bath. Found: N 7.9%. $C_{13}N_{14}N_2O_3SSe$. Calculated: N 7.8%.

2-(β-Hydroxyethylseleno)-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d pyrimidine] (VII). This compound, with mp 168-170° (from methanol), was obtained in 70% yield from equimolar amounts of IV and ethylene chlorohydrin by the method used to prepare IV. Found: N 8.4%. $C_{12}H_{14}N_2O_2SSe$. Calculated: N 8.5%.

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