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Acid-Base Initiated Cyclization and Retrocyclization Reactions of Ethyl 2-(3-Acylselenoureido)benzoates, -thiophene-3-carboxylates and the Corresponding 2-(3-Acylisoselenoureido) Derivatives

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Dedicated to Prof. Milan Kratochvíl on the occasion of his 75th birthday

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Abstract: Acid and base initiated cyclization and retrocyclization reactions of the selenoureas **1-6** and isoselenoureas **7-12** to fused 4*H*-1,3-selenazine and 1,2,3,4-tetrahydropyrimidine-4-one skeletons are reported. Fused 2-acylamino-4*H*-1,3-selenazine-4-ones **13-18** were formed by the action of concentrated sulfuric acid on acylselenoureas **1-6** or on 2,2-dimethylpropanoylisoselenoureas **10-12** at room temperature. On the other hand, benzoylisoselenoureas **7-9** were not obtained in this cyclocondensation under the same conditions. The reaction of potassium ethoxide on selenazines **13-18** in the ethanol solution evoked retrocyclization to the starting acylselenoureas **1-6**. Both types of the title compounds, *i.e.* selenoureas **1-6** and isoselenoureas **7-12,** were deprotonated in a methanol solution of potassium hydroxide used in an equimolar amount, giving rise to potassium salts **19-24**, which were isolated only for the thiophene series. By heating the separated potassium salts **20, 21, 23** and **24** in the methanol solution provided, deacylation and isoselenoureas **26, 27** were formed. The *in situ* prepared salts **19, 22** cyclized under the same conditions with deacylation to 4-selanyl-3,4-dihydroquinazoline-4-one **28**. The title compounds **1-6**, **7-12** and products of their deacylation **26, 27** on boiling in methanolic potassium hydroxide cy-

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clized to the corresponding fused 2-selenoxo-1,2,3,4-tetrahydropyrimidine-4-one potassium salts. These compounds provided pyrimidine-4-ones **28**-**30** on acidification. Acid initiated retrocyclization **28**-**30** to the corresponding 2-amino-4H-1,3-selenazine-4-ones was unsuccessful. C, H, N, Se elemental analyses, FTIR, 1H-NMR, and 13C-NMR spectroscopies supported the structure of synthesized compounds.A short review on cardiotonic steroids and their analogues is presented. The natural, semisynthetic and synthetic derivatives, as well as their mechanism of action and structure-activity relationships are shown, with a special reference to aminoguanidine derivatives.

Keywords: Selenoureas, isoselenoureas, fused 1,3-selenazines, fused 2-selenoxo-1,2,3,4-tetrahydropyrimidine-4-ones, acid-base initiated cyclocondensations.

Introduction

We reported the title compounds **1**-**12** in this journal [1] for the first time. We described the preparation of acylselenoureas **1**-**6** and their isomerization to acylisoselenoureas **7**-**12** evoked by light, by controlled heating in the solid state and in the case of benzoyl derivatives **1**-**3** also by action of acetic acid. On the other hand, we found that retroisomerization of 2,2-dimethylpropanoylisoselenoureas **10**-**12** to 2,2-dimethylpropanoylselenoureas **4**-**6** proceeded when treated with acetic acid (Scheme 1). We elucidated the structure of both types of the title compounds by FTIR and NMR, experiments in paper [1]. Detailed structure was confirmed by X-ray analysis and by *ab initio* methods of molecular modeling.

We found that the flexibility of acylselenoureas **1**-**6** is limited, due to the existence of two types of hydrogen bonds - first between H-N6 and C=O of the ethoxycarbonyl group, second between the same hydrogen atom and C=O of the acyl group. The molecular flexibility of compounds **7**-**12** is fixed *via* two other H-bond types - between H-N6 and C=O of the ethoxycarbonyl group, this interaction is more stable than that in acylselenoureas **1**-**6**, and between Se-H and C=O of the acyl group. Other reactions of the title compounds were not described.

Now we would like to report our results obtained during studies of acid-base initiated transformations of the title compounds **1**-**12**.

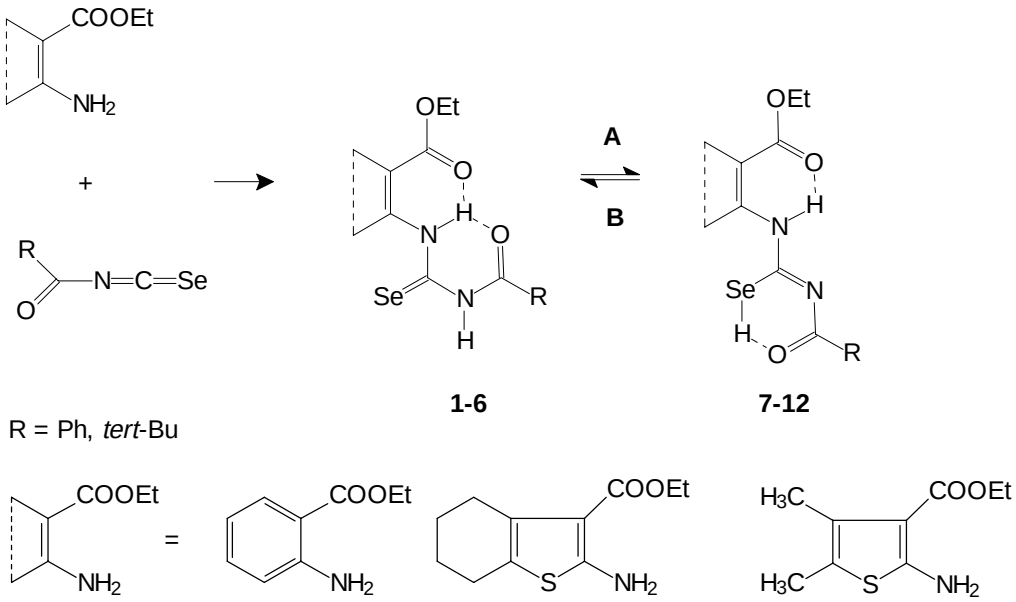
Results and Discussion

Starting with acylselenoureido **1**-**6** and acylisoselenoureido **7**-**12**, derivatives were prepared as mentioned in ref. [1] (Scheme 1).

Sulfur analogues of the title compounds were cyclized in acid medium to 4*H*-1,3-thiazine skeleton formation as mentioned in the introduction. This cyclization proceeded by attack of sulfur on the carbon atom of the alkoxycarbonyl group. Fused 2-acylamino-4*H*-1,3-thiazine-4-ones were formed after

neutralization of the reaction mixture also in the cases of the benzene and thiophene skeleton. The products of deacylation, *i.e.* the corresponding 2-amino compounds were formed at 100°C [2-5].

We prepared the corresponding 1,3-selenazine compounds with the aim of comparing the properties and reactivity of the 1,3-thiazine and 1,3-selenazine skeletons. Acylselenourea **1-6** or acylisoselenourea **7-12** underwent reaction in 94-96% sulfuric acid at room temperature (Scheme 2). Fused 2-acylamino-4*H*-1,3-selenazine-4-ones **13-18** were isolated after mixing with ice as free bases. We attempted deacylation of **13-18** by increasing the temperature of the reaction mixture but oxidative destruction gave elimination of elementary selenium. We also attempted to deacylation of compounds **13-18** by treating with hydrogen chloride in refluxing methanolic solution. Destruction of these compounds was also observed during this operation. Selane was eliminated and oxidized by oxygen in the air to the red modification of selenium. Selane was identified in the vapors over the reaction mixture by a saturated solution of silver nitrate. The conversion of starting compounds **1-12** to **13-18** occurred considerably quickly in comparison to sulfur analogues.



A R=Ph, *tert*-Bu: 1. irradiation by sunlight or filament lamp, $CHCl_3$ solution or solid sample on TL(
2. controlled heating (80-100 deg.C)
3. boiling AcOH for R=Ph
B boiling AcOH for R=*tert*-Bu

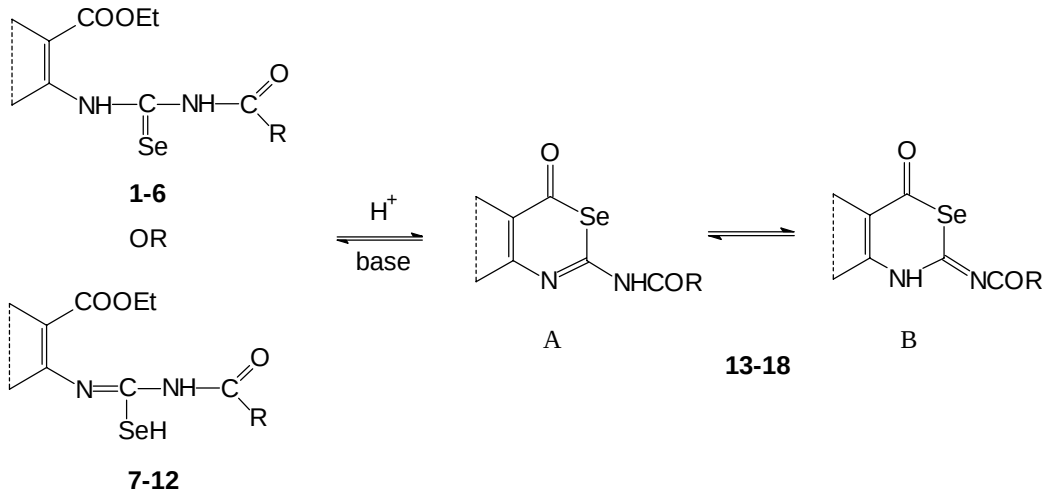
Scheme 1.

Identification of 1,3-selenazine-4-ones **13-18** was supported by C, H, N, Se elemental analysis, FTIR, ^{1}H- and ^{13}C-NMR spectra and by comparison of data with simulated values and with data of sulfur analogues.

FTIR and NMR spectra of compounds **13-18** showed that they may exist in two tautomeric forms

(A and B). This was also observed for sulfur analogues: 2-acylamino-4*H*-1,3-selenazine-4-ones (A) and 2-acylimino-1*H*,4*H*-selenazine-4-ones (B) (Scheme 2). The tautomeric form B is favored in the case of benzoyl derivatives. The tautomeric form of **14** is in the ratio 1:5 in favor (B) and **17** are in the ratio 7:1 in favor (A). The ratio of tautomers was measured on the basis of NMR experiments. This form is stabilized probably by a hydrogen bond between the hydrogen atom of N1 and the oxygen atom of the benzoyl group. A similar case occurs acylselenoureas **1-6**.

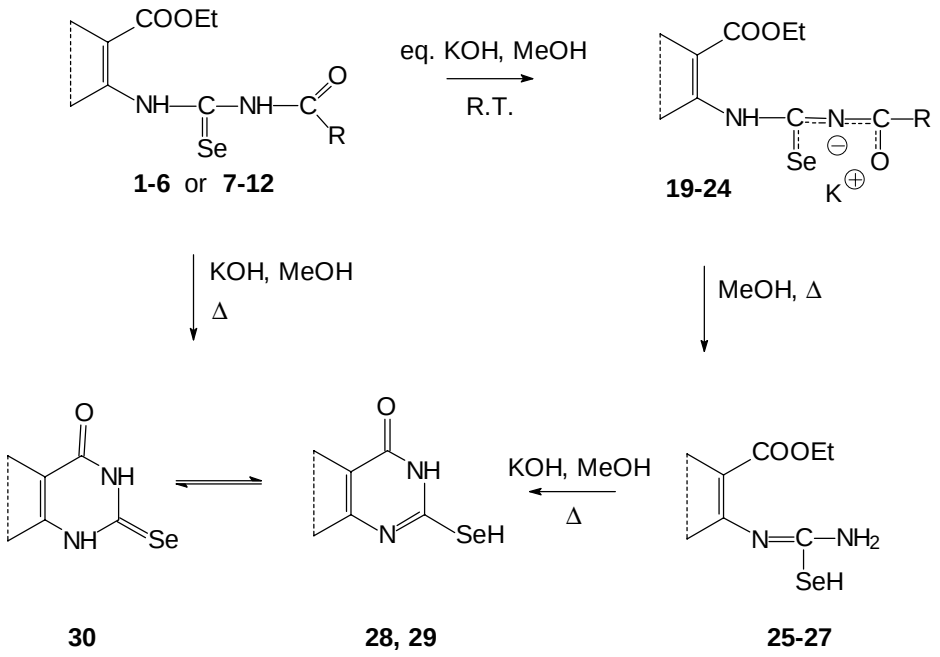
Our attention was also concentrated on the cyclization of both types of the title compounds, *i.e.* selenoureas **1-6** and isoselenoureas **7-12** in the presence of base. Cyclization of acylthioureas similar to selenoureas **1-6** occurred by an attack of the nitrogen atom of a functionalized carboxyl group on the pyrimidine skeleton, provided by the action of a base (ammonium, sodium or potassium carbonate, hydroxide in water or water-alcoholic solution)[4, 6-8]. Cyclization proceeded in independently of either pH or reaction temperature either with deacylation or without elimination of the acyl group.



Scheme 2.

Application of the mentioned methods for the cyclization of acylselenoureas **1-6** and acylisoselenoureas **7-12** was not successful because the conditions evoked their destruction and selenium elimination. The destruction proceeded also in the atmosphere of an inert gas at -20^{o}C.

Deprotonation of the compounds **1-12**, treated with anhydrous methanolic potassium hydroxide evoked formation of their potassium salts (Scheme 3). We have assumed that deprotonation is predominately on the nitrogen atom of the acylamino group. The created anion may be thermodynamically more stable than in the case of deprotonation of the amino group in the vicinity of an aryl skeleton. This is in consequence of delocalization of the negative charge in the $[C(Se)NC(O)]^-$ fragment. A similar situation occurs for example on deprotonation of the 1,3-dioxo compounds.



Scheme 3.

If the deprotonations were accomplished with an equivalent of potassium hydroxide at room temperature, potassium salts **20**, **21**, **23**, **24** were isolated in the thiophene series in comparison to the sulfur analogues because their solubility is lower.

Potassium salts **19** and **22** were not obtained in crystalline form nor eliminated from solution by addition of solvents such as benzene, dichlormethane, and their mixtures with petroleum ether, respectively. The products **19** and **22** were obtained after precipitation as a tar substance.

Identification of potassium salts **20**, **21**, **23**, **24** was confirmed by C, H, N, Se elemental analysis, FTIR, ^{1}H- and ^{13}C-NMR (in the case of **20** and **23**) spectroscopies. The ^{13}C-NMR of salts **21** and **24** were not measured because of their low solubility and stability in hexadeuterodimethyl sulfoxide. The corresponding vibration bands of NHCO or NHCSe groups were not found in the FTIR spectra of potassium salts. On the other hand two very intense bands were observed at the wave number 1460 and 1340 cm^{-1}. We have assumed that these are vibration bands of the deprotoned [C(Se)NC(O)]$^{-}$ group.

If the reaction mixture containing salts **20**, **21**, **23** and **24** in a methanolic suspension or salts **19**, **22** prepared *in situ* in methanolic solution were refluxed in the presence of an excess of potassium hydroxide, cyclization and deacylation proceeded to the corresponding pyrimidine-4-ones. After acidification of the reaction mixture, they crystallized as free bases (fused 2-selanyl-pyrimidine-4-one **28**, **29** and 2-selenoxo compounds **30**) (Scheme 3).

Cyclization of salts **19**, **22** (prepared *in situ*) proceeded in methanolic solution with an equivalent of potassium hydroxide. 2-Selanyl-3,4-dihydroquinazoline-4-one **28** was formed by standing of the reaction mixture at room temperature or by short reflux. Compound **28** was obtained directly as free base. We assume deacylation is the first process. Then the formed 2-selenoureidobenzoate **25** thermally and spontaneously cyclizes. Similar results were observed by the addition of ammonia to 2-

isoselenocyanatobenzonitrile [9] or its sulfur analogue[10]. The adducts formed *in situ* already cyclized below 0^oC. The corresponding selenoureas or thioureas were not observed.

Isolated potassium salts **20**, **21**, **23**, and **24** did not cyclize because of their lower reactivity under the same conditions. The lower reactivity of thiophene *vs.* benzoderivatives was also found during cyclocondensation of thioureas[11]. The deacylated isoselenoureas **26** and **27** were isolated as the finished products. Their cyclizations were by base action only. The lower reactivity of cyclization in the thiophene series in comparison with the benzene series may be explained by a more favorable distribution of electron density on the reaction centers of benzo derivatives. Another explanation may be by due to the higher internal strain of the thienopyrimidine skeleton as a consequence of the higher external bond angles of the thiophene ring compared to the benzoanalogue [11].

Our results indicate a different course of base initiated cyclization in the comparison with acylselenoureas and their sulfur analogues. In the case of the latter, reaction courses were preparative [7] and by kinetic methods[12] confirmed that deacylation proceeded after pyrimidine skeleton formation. The title compounds were converted in the reverse order during this process.

The identity of synthesized isoselenoureas **26**, **27** was supported by elemental analysis, FTIR, ^{1}H- and ^{13}C-NMR spectroscopy. In FTIR spectra there were observed intensive C=N vibration, but vibration bands of selenoamide group I, III were not found. The chemical shift of ^{13}C(Se) signal with a lower value than 160 ppm and value of coupling ^{13}C-^{77}Se showed that this carbon is bonded to the selenium atom by a single bond as was observed in acylisoselenoureas[1]. This fact shows that the compounds **26** and **27** exist mainly in the tautomeric 3-isoselenoureido form, as was confirmed by ^{1}H-NMR spectra in which two different protons were not observed. Existence of the tautomeric 1-isoselenourea form was not found. The proton signal of the imino group would be at a higher value of the chemical shift than was found, in implication of magnetic anisotropy of C=N bond.

The structure of fused 4-pyrimidinones **28-30** were supported by elemental analysis, FTIR, ^{1}H- and ^{13}C- NMR spectroscopy. FTIR and ^{13}C- NMR spectra of products showed that compound **28** and **29** were stable under the experimental conditions in tautomeric form as fused 2-selanylpyrimidine-4-one but **30** as selenoxo compounds. NMR spectra of **28**-**30** compounds was measured in deuterotrifluoroacetic acid solution because of their low solubility in other solvents.

Experimental

General

Chemicals and reagents were purchased from Fluka Chemie Co. and used without further purification. The title selenoureas derivatives were prepared according to paper [1]. Melting points of prepared the compounds were measured on Boetius Rapido PHMK 79/2106 (Wägetechnik) instruments and were not corrected. Purity of all compounds was determined by C, H, N elemental analyses on an instrument 1102 (Erba) and by determinations of selenium on spectrometer ICP AES 7500 (Unicam). TLC was carried out on Silufol UV 254 plates (Kavalier, Votice) and the detection with Fluotes Universal (Quartzlampen, Hanau) and with iodine vapors, respectively. Chloroform, diethyl ether or ace-

tonitrile was used as eluent in a container saturated with vapors of the used solvent. FTIR spectra were taken on a spectrometer Genesis (Unicam) in potassium bromide pellets or in chloroform solution.NMR spectra were measured in deuterochloroform, hexadeuterodimethyl sulfoxide or in deuterotrifluoroacetic acid on a Bruker Avance DRX-500 spectrometer. The ^{13}C- and ^{1}H-NMR spectra were referenced to tetramethylsilane as internal standard or to the solvent signals of $CDCl_3$ and of residual $CHCl_3$ at 77.00 ppm (^{13}C) and 7.27 ppm (^{1}H), respectively. Spectral width : 9000 Hz for ^{1}H, 27500 Hz for ^{13}C. The measured ^{13}C - and ^{1}H-NMR spectra were correlated with those obtained by on-line simulation (Advanced Chemistry Development, INC., Toronto, Canada).

Fused 2-acylamino-4H-1,3-selenazine-4-ones **13-18**

Acylselenourea **1-6** or acylisoselenourea **10-12** (10 mmol) was suspended under stirring in concentrated sulfuric acid (ca 96%, 50 ml) at a temperature of under 20^{o}C. The formed reaction solution was stirred at room temperature for 2-3 h, and subsequently mixed with 100 g crushed ice. The suspension of products (**13-18**) was separated by suction. Crystals were washed with cold water, methanol and diethyl ether. Drying was *in vacuo* at room temperature.

2-Benzoylimino-1H,4H-benzo[d][3,1]selenazine-4-one **13B**

M.w. 329.22.
$C_{15}H_{10}N_2O_2Se$
M.p. 188-189^{o}C.
Elemental analysis (%calc./%found.) C 54.73/54.55, H 3.06/3.08 N5.51/8.49, Se 23.98/23.99.
Yield (from **1**) 3.2 g (96%), (from **7**) 3.0 g (91%).
FTIR (KBr pellets) cm^{-1}: 3195 (NH), 1670 (Se-C=O), 1689, 1560 (NHCO), 1634 (C=N).
^{1}H NMR ($CDCl_3$, B) δ: 7.26-8.15 (m, 9H, C_6H_4 and C_6H_5), 12.75 (s, 1H, NH).
^{13}C NMR ($CDCl_3$, B) δ: 120.93 (CH), 124.35 (CH), 124.22 (CH), 127.28 (CH), 127.52 (CH), 127.99 (CH), 133.22 (CH), 135.33 (C), 142.41 (C), 142.39 (C), 143.41 (N-C-Se), 175.97 (C=O, COC_6H_5), 191.88 (Se-C=O).

2-Benzoylamino-5,6,7,8-tetrahydro-4H-benzo[1]thieno[2,3-d][1,3]selenazine-4-one **14A** and
2-Benzoylimino-5,6,7,8-tetrahydro-4H-benzo[1]thieno[2,3-d][1,3]selenazine-4-one **14B** (in ratio 1:5)

M.w. 389.33.
$C_{17}H_{14}N_2O_2SSe$
M.p. 204-205^{o}C.
Elemental analysis (%calcd/%found) C 52.54/52.42, H 3.62/3.63, N 7.20/7.12, Se 20.49/20.53.
Yield (from **2**) 3.8 g (98%), (from **8**) 3.7 g (95%).
FTIR (KBr pellets) cm^{-1}: 3190 (NH), 1670 (Se-C=O), 1695, 1540 (NHCO), 1620 (C=N).

^{1}H NMR ($CDCl_3$, A) δ: 1.82-1.84 (m, 4H, 5-CH_2 and 6-CH_2), 2.74-2.76 (m, 2H, 4-CH_2), 2.94-2.96 (m, 2H, 7-CH_2), 7.55-8.07 (m, 5H, C_6H_5CO), 9.30 (s, 1H, NHCO).

^{1}H NMR ($CDCl_3$, B) δ: 1.44-1.45 (m, 4H, 5-CH_2 and 6-CH_2), 2.68-2.70 (m, 2H, 4-CH_2), 2.77-2.79 (m, 2H, 7-CH_2), 7.65-7.94 (m, 5H, C_6H_5CO), 13.28 (s, 1H, NH).

^{13}C NMR ($CDCl_3$, A) δ: 22.24 (CH_2), 22.68 (CH_2), 24.81 (CH_2), 26.46 (CH_2), 128.23 (CH), 127.45 (C), 129.16 (C), 131.31 (C), 133.36 (CH), 133.48 (CH), 140.95 (C), 163.07 (N-C-Se), 167.01 (C=O, COC_6H_5), 183.54 (Se-C=O).

^{13}C NMR ($CDCl_3$, B) δ: 22.24 (CH_2), 22.68 (CH_2), 24.81 (CH_2), 26.46 (CH_2), 128.23 (CH), 127.45 (C), 129.16 (C), 131.31 (C), 133.36 (CH), 133.48 (CH), 140.95 (C), 157.52 (N-C-Se), 165.64 (C=O, COC_6H_5), 183.54 (Se-C=O).

2-Benzoylimino -5,6-dimethyl-4H-thieno[2,3-d][1,3]selenazine-4-one **15B**

M.w. 363.29.

$C_{15}H_{12}N_2O_2SSe$

M.p. 217-220°C.

Elemental analysis (%calcd/%found) C 49.59/49.12, H 3.33/3.17, N 7.71/7.26, Se 21.96/21.34.

Yield (from **3**) 3.5 g (96%), (from **9**) 3.5 g (96%).

FTIR (KBr pellets) cm^{-1}: 3300, 3190 (NH), 1680 (Se-C=O), 1662, 1534 (NHCO), 1624 (C=N).

^{1}H NMR ($CDCl_3$, B) δ: 2.37 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 7.52-8.04 (m, 5H, C_6H_5CO), 11.92 (s, 1H, NH).

^{13}C NMR ($CDCl_3$, B) δ: 12.63 (CH_3), 14.24(CH_3), 120.56 (C), 127.42 (C), 128.22 (CH), 128.38 (C), 129.15 (C), 129.24 (CH), 131.69 (CH), 133.49 (C), 157.21 (N-C-Se), 165.65 (C=O, COC_6H_5), 183.45 (Se-C=O).

2-(2,2-dimethylpropanoyl)amino-4H-[3,1]-benzoselenazine-4-one **16A**

M.w. 309.23.

$C_{13}H_{14}N_2O_2Se$

M.p. 118.120°C.

Elemental analysis (%calcd/%found) C 50.49/50.42, H 4.56/4.48, N 9.06/8.98, Se 25.78/25.69.

Yield (from **4**) 2.8 g (91%), (from **10**) 2.6 g (84%).

FTIR (KBr pellets) cm^{-1}: 3190 (NH), 1677 (Se-C=O), 1651, 1630 (NHCO), 1620 (C=N).

^{1}H NMR ($CDCl_3$, A) δ: 1.21 (s, 9H, $(CH_3)_3CO$), 8.22-8.87 (m, 4H, C_6H_4), 9.24 (s, 1H, NHCO).

^{13}C NMR ($CDCl_3$, A) δ: 27.61 (CH_3, (CH_3)C), 42.15 (C), 128.65 (C), 134.25 (C), 142.83 (C), 145.87 (C), 157.26 (N-C-Se), 163.15 (C=O, COC_6H_5), 186.32 (Se-C=O).

2-(2,2-dimethylpropanoyl)amino-5,6,7,8-tetrahydro-4H-benzo[1]thieno[2,3-d][1,3]selenazine-4-one **17A**
and
2-(2,2-dimethylpropanoyl)imino-5,6,7,8-tetrahydro-4H-benzo[1]thieno[2,3-d][1,3]selenazine-4-one **17B**

(in ratio 7:1)
M.w. 369.34.
$C_{15}H_{18}N_2O_2SSe$
M.p. 158-161°C.
Elemental analysis (%calcd/%found) C 48.78/48.63, H 4.91/4.94, N 7.58/7.64, Se 21.60/21.62.
Yield (from **5**) 3.6 g (97%), (from **11**) 3.4 g (92%).
FTIR (KBr pellets) cm^{-1}: 3280 (NH), 1685 (Se-C=O), 1650, 1540 (NHCO), 1630 (C=N).
^{1}H NMR ($CDCl_3$, A) δ: 1.37 (s, 9H, $(CH_3)_3CO$), 1.51-1.64 (m, 4H, 5-CH_2 and 6-CH_2), 2.72-2.79 (m, 2H, 4-CH_2), 2.92-2.97 (m, 2H, 7-CH_2), 8.72 (s, 1H, NH).
^{1}H NMR ($CDCl_3$, B) δ: 1.81 (s, 9H, $(CH_3)_3CO$), 1.59-1.78 (m, 4H, 5-CH_2 and 6-CH_2), 2.69-2.73 (m, 2H, 4-CH_2), 2.91-2.96 (m, 2H, 7-CH_2), 11.95 (s, 1H, NH).
^{13}C NMR ($CDCl_3$) δ: 23.22 (CH_2), 25.15 (CH_2), 26.48 (CH_2), 27.85 (CH_3, $(CH_3)_3C$), 28.65 (CH_2), 42.32 (C), 131.15 (C), 131.52 (C), 134.25 (C), 142.67 (C), 157.22 (N-C-Se), 164.12 (C=O, COC_6H_5), 186.34 (Se-C=O).

5,6-dimethyl-2-(2,2-dimethylpropanoyl)amino-4H-thieno[2,3-d][1,3]selenazine-4-one **18A**

M.w. 343.30.
$C_{13}H_{16}N_2O_2SSe$
M.p. 207-208°C.
Elemental analysis (%calcd/%found) C 45.48/45.59, H 4.70/4.67, N 8.16/8.19, Se 23.23/23.25.
Yield (from **6**) 3.2 g (93%), (from **12**) 3.0 g (87%).
FTIR (KBr pellets) cm^{-1}: 3257 (NH), 1674 (Se-C=O), 1721, 1546 (NHCO), 1616 (C=N).
^{1}H NMR ($CDCl_3$, A) δ: 1.37 (s, 9H, $(CH_3)_3CO$), 2.65 (s, 3H, CH_3), 2.92 (s, 3H, CH_3), 8.64 (s, 1H, NH).
^{13}C NMR ($CDCl_3$, A) δ: 13.51 (CH_3), 15.51(CH_3), 27.45 (CH_3, $(CH_3)_3C$), 42.11 (C), 126.05 (C), 126.55 (C), 130.05 (C), 138.40 (C), 154.21 (N-C-Se), 163.25 (C=O, COC_6H_5), 184.19(Se-C=O).

Retrocyclizations of fused 2-acylamino-4*H*-1,3-selenazine-4-ones **13**-**18**

Compound **13**-**18** was dissolved under stirring in an argon atmosphere in potassium ethoxide solution, prepared by reaction of potassium *tert.*butoxid (1.12 g, 10 mmol) with 25 ml of dry ethanol - dried by azeotropic distillation with benzene and after by distillation with magnesium. The reaction

mixture was stirred at room temperature for 50 - 90 min, the conversion of the reaction was monitored by TLC after acidification of the reaction mixture with acetic acid. With the reactions of thiophene derivatives **14, 15, 16** and **17** potassium salts of the title acylselenoureas **20, 21, 23, 24** were formed, in the case of benzoderivatives **13, 16**, corresponding salts **19, 22** were dissolved in the reaction mixtures. The produts **1-6** were obtained after acidification of the reaction mixture by acetic acid (ca 1 ml) at 5-10^{o}C, removing of the solvent on an evaporator at 25-30^{o}C. The evaporated residue was suspended in chloroform (50 ml) and filtered with charcoal. The filtrate was concentrated to 1/5 original volume and mixed with an equivalent volume of petroleum ether. The precipitated crystals were filtered, washed with petroleum ether and cold methanol (5-10^{o}C). The pure products **1**-**6**, dried *in vacuo*, were identical to standard **1**-**6** by TLC, m. p. and FTIR [1].

Potassium salts of title acylselenoureas **20**, **21**, **23**, **24**

Retrocyclization of compounds **14, 15, 16** *and* **17** (a)

Suspensions of salts **20, 21, 23, 24**, were prepared as mentioned above and were filtered by suction. The precipitate was washed with methanol, diethyl ether and dried in *vacuo* at room temperature.

Deprotonation of compounds **2, 3, 5** *and* ***6*** *or* **8, 9, 11** *and* **12** *by action of potassium hydroxide in equivalent (b)*

Acylselenourea **2, 3, 5** and **6** or corresponding acylisoselenourea **8, 9, 11** and **12** (5 mmol) was dissolved under stirring in argon atmosphere in 50 ml methanol containing potassium hydroxide (340 mg, 6 mmol). After 30 min product was formed separated by suction, washed with methanol, diethyl ether and dried *in vacuo* at room temperature.

Ethyl 2-(3-benzoylselenoureido)-4,5,6,7-tetrahydrobenzo[1]thiophene-3-carboxylate potassium salt **20**

M.w. 473.49.

$C_{19}H_{19}N_2O_3SSeK$

M.p. 292-293^{o}C (decomp.).

Elemental analysis (%calcd/%found) C 48.20/47.86, H 4.04/3.95, N 5.92/5.86, Se 16.68/16.68.

Yield (a) 3.7 g (78%), (b) 2.0 g (86%).

FTIR (KBr pellets) cm^{-1}: 3363, 3158 (NH), 1677 (O-C=O), 1467, 1365 (C(Se)N^{-}C(O)).

^{1}H NMR (d^{6}-DMSO) δ: 1.38 (t, 3H, CH_2CH_3, J = 7.0 Hz), 1.78-1.83 (m, 4H, 5-CH_2 and 6-CH_2), 2.79-2.81 (m, 2H, 4-CH_2), 2.82-2.86 (m, 2H, 7-CH_2), 4.29 (q, 2H, CH_2CH_3, J = 7.0 Hz), 7.23-7.96 (m, 5H, C_6H_5), 8.46 (s, 1H, NH).

^{13}C NMR (d^{6}-DMSO) δ: 14.71 (CH_2CH_3), 22.45 (C-5), 24.21 (C-6), 25.62 (C-4), 26.47 (C-7), 59.22 (CH_2CH_3), 104.30 (C-3), 111.60 (C-4, thiophene), 126.83 (C-2'and C-6', C_6H_5), 128.78 (C-

3'and C-5', C_6H_5), 132.27 (C-5, thiophene), 134.18 (C-1', C_6H_5), 136.43 (C-4', C_6H_5), 157.64 (C-2, thiophene), 164.43 (C=O, *C*OOCH$_2$CH$_3$), 173.10 (C=O, *C*OC_6H_5), 193.10 (C=Se, $^1J_{C, Se}$ = 200 Hz).

Ethyl 2-(3-benzoylselenoureido)-4,5-dimethylthiophene-3-carboxylate - potassium salt **21**

M.w. 447.45

$C_{17}H_{17}N_2O_3SSeK$

M.p. 188-189°C (decomp.)

Elemental analysis (%calcd/%found) C 45.63/45.16, H 3.83/3.75, N 6.26/6.14, Se 17.65/17.69.

Yield (a) 3.3 g (74%), (b) 1.8 g (82%).

FTIR (KBr pellets) cm^{-1}: 3265, 3134 (NH), 1664 (O-C=O), 1414, 1359 (C(Se)N$^-$C(O)).

^{1}H NMR (d^6-DMSO) δ: 1.28 (t, 3H, CH$_2$*CH$_3$*, J = 7.1 Hz), 2.15 (s, 3H, CH$_3$, C-4 thiophene), 2.24 (s, 3H, CH$_3$, C-5 thiophene), 4.34 (q, 2H, *CH$_2$*CH$_3$, J = 7.1 Hz), 7.32-7.95 (m, 5H, C_6H_5), 8.39 (s, 1H, NH).

Ethyl 2-[3-(2,2-dimethylpropanoyl)selenoureido]-4,5,6,7-tetrahydrobenzo[1]thiophene-3-carboxylate potassium salt **23**

M.w. 453.50.

$C_{17}H_{23}N_2O_3SSeK$

M.p. 265-267°C (decomp.)

Elemental analysis (%calcd/%found) C 45.02/44.91, H 5.11/ 5.03, N 6.18/6.17, Se 17.41/17.46.

Yield (a) 3.7 g (82%), (b) 2.1 g (92%).

FTIR (KBr pellets) cm^{-1}: 3347, 3133 (NH), 1682 (O-C=O), 1458, 1361 (C(Se)N$^-$C(O)).

^{1}H NMR (d^6-DMSO) δ: 1.12 (s, 9H, CH$_3$, C(*CH$_3$)$_3$*),) 1.23 (t, 3H, CH$_2$*CH$_3$*, J = 7.0 Hz), 1.76-1.79 (m, 4H, 5-CH$_2$ and 6-CH$_2$), 2.74-2.78 (m, 2H, 4-CH$_2$), 2.96-3.01 (m, 2H, 7-CH$_2$), 4.35 (q, 2H, *CH$_2$*CH$_3$, J = 7.1 Hz), 8.96 (s, 1H, NH).

^{13}C NMR (d^6-DMSO) δ: 14.65 (CH$_2$*CH$_3$*), 22.48 (C-5), 24.26 (C-6), 25.59 (C-4), 26.52 (C-7), 27.81 (CH$_3$, C(CH$_3$)$_3$), 52.83 (CH$_2$, C(CH$_3$)$_3$), 59.28 (*CH$_2$*CH$_3$), 104.36 (C-3), 111.57 (C-4, thiophene), 133.24(C-5, thiophene), 157.62 (C-2, thiophene), 166.01(C=O, *C*OOCH$_2$CH$_3$), 173.56 (C=O, *C*OC(CH$_3$)$_3$), 181.94 (C=Se, $^1J_{C, Se}$ = 200 Hz).

Ethyl 2-[3-(2,2-dimethylpropanoyl)selenoureido]-4,5-dimethylthiophene-3-carboxylate potassium salt **24**

M.w. 427.46.

$C_{15}H_{21}N_2O_3SSeK$

M.p. 184-185°C (decomp.)

Elemental analysis (%calcd/%found) C 42.15/41.38, H 4.95/4.87, N 6.55/6.54, Se 18.47/18.59.

Yield (a) 3.3 g (77%), (b) 1.8 g (84%).

FTIR (KBr pellets) cm^{-1}: 3324, 3166 (NH), 1669 (O-C=O), 1443, 1371 (C(Se)N-C(O)).

^{1}H NMR (d^6-DMSO) δ: 1.20 (t, 3H, CH_2CH_3, J 7.1 Hz), 1.26 (s, 9H, CH_3, $(CH_3)_3C$), 2.04 (s, 3H, CH_3, C-4 thiophene), 2.18 (s, 3H, CH_3, C-5 thiophene), 4.31 (q, 2H, CH_2CH_3, J 7.1 Hz), 7.99 (s, 1H, NH).

Isoselenoureas **26**, **27**

Potassium salts **20, 21, 23** and **24** (2.5 mmol) were suspended in methanol (30 ml) and heated for 10 min on a steam bath under reflux. The product **26, 27,** which was crystallized from the reaction solution by holding overnight in a freezing box, was separated by suction and recrystallized from methanol.

Ethyl 2-(3-isoselenoureido)-4,5,6,7-tetrahydrobenzo[1]thiophene-3-carboxylate **26**

M.w. 331.23

$C_{12}H_{16}N_2O_2SSe$

M.p. 218-222°C

Elemental analysis (%calcd/%found) C 43.51/42.16, H 4.87/4.73, N8.46/8.46, Se 23.82/23.94.

Yield (from **20**) 0.7 g (85%), (from **23**) 0.7 g (85%).

FTIR (KBr pellets) cm^{-1}: 3248, 3188 (NH), 1746 (C=O), 1650 (C=N).

^{1}H NMR ($CDCl_3$) δ: 1.27 (t, 3H, CH_3, J = 7.1 Hz), 1.54 (s, 1H, SeH), 1.76-1.84 1.56 (m, 4H, 5-CH_2 and 6-CH_2), 3.05-3.13 (m, 4H, 4-CH_2 and 7-CH_2), 4.33 (q, 2H, CH_2, J = 7.1 Hz), 6.45 (s, 2H, NH_2).

^{13}C NMR ($CDCl_3$) δ: 13.85 (CH_3), 21.15 (C-6), 24.24 (C-5), 26.64 (C-7), 26.98 (C-4), 60.02(CH_2), 98.12 (C-3), 128.24 (C-5 thiophene), 132.08 (C-4 thiophene), 159.12 (C-2), 163.28 (N=C-Se, $^1J_{C,\ Se}$ 134 Hz), 169.45 (C=O).

Ethyl 2-(3-isoselenoureido)-4,5-dimethylthiophene-3-carboxylate **27**

M.w. 305.19

$C_{10}H_{14}N_2O_2SSe$

M.p. 195-196°C

Elemental analysis (%calcd/%found) C 39.36/39.12 , H 4.62/4.61, N9.18/9.03, Se 25.85/25.79.

Yield (from **21**) 0.7 g (92%), (from **24**) 0.6 g (77%).

FTIR (KBr pellets) cm^{-1}: 3249, 3197 (NH), 1736 (C=O), 1652 (C=N).

^{1}H NMR ($CDCl_3$) δ: 1.29 (t, 3H, CH_3, J = 7.1 Hz), 1.44 (s, 1H, SeH), 2.41(s, 3H, CH_3, C-4 thiophene), 2.45 (s, 3H, CH_3, C-5 thiophene), 4.24 (q, 2H, CH_2, J = 7.1 Hz), 6.14 (s, 2H, NH_2).

^{13}C NMR ($CDCl_3$) δ: 12.26 (CH_3, C-4 thiophene), 13.84 (CH_3), 14.87 (CH_3, C-5 thiophene), 59.85

(CH_3), 111.10 (C-3, thiophene), 127.35 (C-5, thiophene), 132.74 (C-4, thiophene), 152.68 (C-2, thiophene), 159.56 (N=C-Se, $^1J_{C, Se}$ 138 Hz). 168.32 (C=O).

Fused 3,4-dihydropyrimidinones **28**-**30**

A: Acylselenourea **1**-**6** (5 mmol) was suspended in a 50 ml 5% methanolic solution of potassium hydroxide and refluxed until a colorless solution (5-10 min) was obtained. The solution was filtered with charcoal. After cooling to 5-10^{o}C it was neutralized by glacial acetic acid. The precipitated product **28**-**30** was filtered by suction, washed with methanol and dried *in vacuo*.

B: Isoselenoureas **26, 27** (2 mmol) were suspended in a 20 ml 5% methanolic solution of potassium hydroxide and refluxed until a colorless solution (5-10 min) was obtained. Then the solution was treated by method A.

2-Selanyl-3,4-dihydroquinazoline-4-one **28**

M.w. 225.05

$C_8H_6N_2OSe$

M.p. 282-284^{o}C

Elemental analysis (%calcd/%found) C 42.70/ 42.48, H 2.69/2.62, N12.45/12.48, Se 35.06/35.50.

Yield (A, from **1**) 0.9 g (80%), (A, from **4**) 0.9 g (80%).

FTIR (KBr pellets) cm^{-1}: 1682 (C=O).

^{1}H NMR (d-TFA) δ: 7.48-7.79 (m, 4H, C_6H_4).

^{13}C NMR (d-TFA) δ: 122.07 (C-5, pyrimidine), 126.18 (C-6), 127.98 (C-8), 128.17 (C-5), 137.42 (C-7), 143.64 (C-6, pyrimidine), 151.46 (C-2), 158.26 (C-4).

2-Selanyl-1,2,5,6,7,8-hexahydrobenzo[1]thieno[2,3-d]pyrimidine-4-one **29**

M.w. 285.16

$C_{10}H_{10}N_2OSSe$

M.p. 310-313^{o}C

Elemental analysis (%calcd/%found) C 42.12/41.83, H 3.53/3.51, N 9.82/9.74, Se 27.67/27.63.

Yield (A, from **2**) 1.30 g (91%), (A, from **5**) 1.20 g (84%), (B, from **26**) 0.40 g (70%).

FTIR (KBr pellets) cm^{-1}: 1655 (C=O).

^{1}H NMR (d-TFA) δ: 1.63-1.82 (m, 4H, 6-CH_2 and 7-CH_2), 2.79-2.85 (m, 4H, 5-CH_2 and 8-CH_2).

^{13}C NMR (d-TFA) δ: 22.76 (C-7), 23.49 (C-6), 24.15 (C-8), 29.47 (C-5), 113.85 (C-5, pyrimidine), 116.85 (C-10, cyclohexane), 129.74 (C-9, cyclohexane), 139.01(C-6, pyrimidine), 153.49 (C-4).

5,6-Dimethyl-2-selenoxo-1,2-dihydrothieno[2,3-d]pyrimidine-4-one **30**

M.w. 259.12
$C_8H_8N_2OSSe$
M.p. 315-318^oC
Elemental analysis (%calcd/%found) C 37.07/36.79 , H 3.50/3.49, N16.22/16.16, Se 30.56/30.42.
Yield (A, from **3**) 1.10 g (85%), (A, from **6**) 1.10 g (85%), (B, from **27**) 0.35 g (67%).
FTIR (KBr pellets) cm^{-1}: 3440, 3293 (NH), 1622 (C=N), 1527, 954 (NHCSe, selenoamide III, I).
^1H NMR (d-TFA) δ: 2.82 (s, 3H, CH_3), 2.83 (s, 3H, CH_3).
^{13}C NMR (d-TFA) δ: 11.12 (CH_3, C-5), 11.80 (CH_3, C-6), 126.51 (C-5), 132.91 (C-6), 152.48 (C-5, pyrimidine), 155.16 (C-4), 169.71 (C-6, pyrimidine), 181.29 (C=Se, $^1J_{C, Se}$ = 220 Hz).

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Sample availability: samples are available from the authors.

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