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Synthesis of dihydrothiazoles and thiazoles based on monothiooxamides

Vladimir N. Yarovenko[a]*, Anna V. Polushina[a], Igor V. Zavarzin[a], Michail M. Krayushkin[a], Svetlana K. Kotovskaya[b] and Valeriy N. Charushin[c]

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This paper is dedicated to Professor Juzo Nakayama on the occasion of his 65th birthday and retirement.

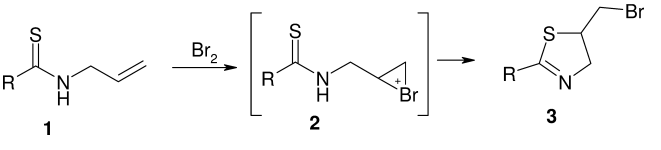
Dihydrothiazoles and thiazoles were synthesized by the reaction of monothiooxamides containing allylamine and propargylamine fragments with halogens in ionic liquids.

Keywords: thiazoles; dihydrothiazoles; chloroacetamides; monothiooxamides; ionic liquids

1. Introduction

The thiazole and dihydrothiazole rings are parts of many natural products; they are widely used in the development of bioactive compounds, drugs, and industrial products (*1–3*). This stimulates researchers to look for the methods of synthesis of previously inaccessible compounds of this series.

A known reaction is the bromine-induced heterocyclization of thioamides **1** having an allylamine fragment to give dihydrothiazole ring **3** (*4*) (Scheme 1).



Scheme 1. Interaction of thioamides having an allylamine fragment with bromine.

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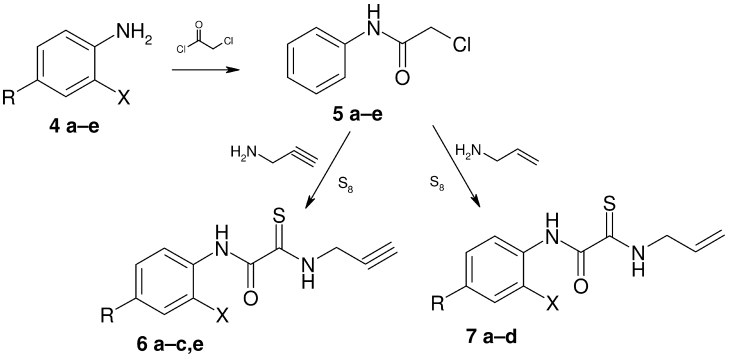
Previously, we developed a convenient method for the preparation of monothiooxamides comprising the reaction of α-chloroacetamides with a solution of sulfur in amines prepared beforehand, and demonstrated the possibility of converting them into various heterocyclic compounds (*5*).

This communication describes studies of the reactions of halogens with monothiooxamides containing allylamine and propargylamine fragments aimed at the synthesis of dihydrothiazoles and thiazoles.

2. Results and discussion

The key intermediates of dihydrothiazole and thiazole syntheses, namely, monothiooxamides **6** and **7**, were obtained by S-functionalization of chloroacetamides **5a–e** in the presence of allylamine or propargylamine (Scheme 2). Chloroacetamides were synthesized by the reaction of chloroacetyl chloride with aminonitrobenzenes **4a–e** in dimethylformamide.



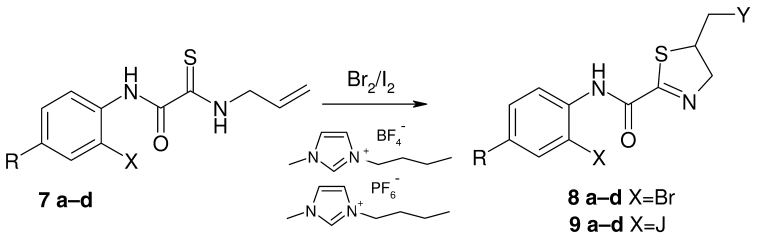
Scheme 2. Synthesis of monothiooxamides having an allylamine or propargylamine fragment. **4–7**: X = NO_2, R = H (**a**); *X* = NO_2, R = Cl (**b**); X = NO_2, R = Me (**c**); X = R = H (**d**); X = H, R = NO_2(**e**).

The effects of halogen and solvents on the course of the reaction between monothiooxamides and halogens were studied. The reaction of thioamides **7a–d** induced by bromine in CH_2Cl_2 was found to proceed within 1.5 h with cooling, resulting in dihydrothiazoles **8a–d** in up to 70% yields. A similar reaction in the presence of iodine required a 5 h refluxing in the same solvent in the presence of Na_2CO_3, and product yields did not exceed 60%. The reaction of monothiooxamides with bromine or iodine in ionic liquids (1-butyl-3-methylimidazolium hexafluorophosphate and 1-butyl-3-methylimidazolium tetrafluoroborate) proceeded very easily (within 2–5 min at room temperature) to give products in high yields (80–88%) (Scheme 3).

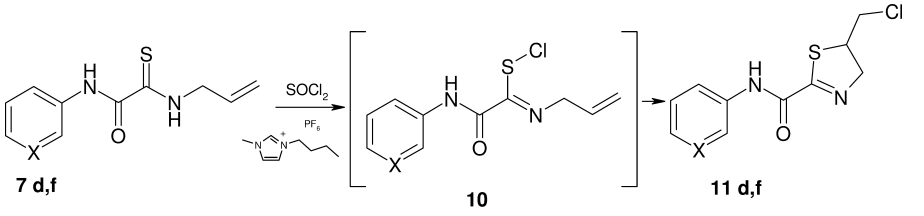
Unfortunately, we were unable to carry out a similar reaction with chlorine under these conditions, as these reactions gave multicomponent mixtures. We suggested that the thiocarbonyl group of monothiooxamides may react with thionyl chloride to give sulfonyl chloride derivatives **10**, which would cyclize to give dihydrothiazoles containing a chloromethyl group. Indeed, we found that monothiooxamides react with thionyl chloride in 1-butyl-3-methylimidazolium hexafluorophosphate at room temperature for 4 min, furnishing dihydrothiazoles **11** in 60–65% yields (Scheme 4).

The halomethyl groups in dihydrothiazole **8d** can be easily modified, yielding derivatives **12** and **13** (Scheme 5).

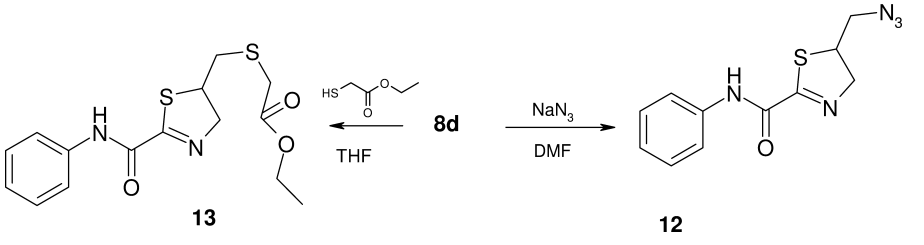
In this work, we report the first study of reactions of monothiooxamides containing a propargylamine fragment with bromine. The process was found to depend appreciably on the solvent



Scheme 3. Synthesis of dihydrothiazoles by the reaction with bromine or iodine. **8**: X = NO_2, R = H, Y = Br (**a**); X = NO_2, R = Cl, Y = Br (**b**); X = NO_2, R = Me, Y = Br (**c**); X = R = H, Y = Br (**d**). **9**: X = NO_2, R = H, Y = J (**a**); X = NO_2, R = Cl, Y = J (**b**); X = NO_2, R = Me, Y = J (**c**); X = R = H, Y = J (**d**).



Scheme 4. Synthesis of dihydrothiazoles by the reaction with thionyl chloride. **7**, **11**: X = CH (**d**), N (**f**).

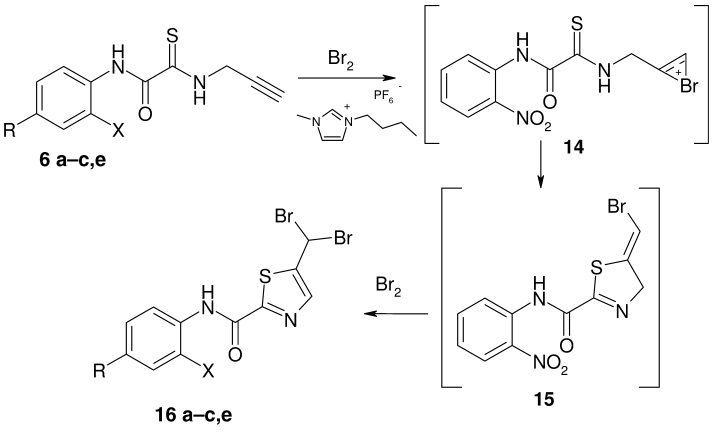


Scheme 5. Modification of dihydrothiazoles.

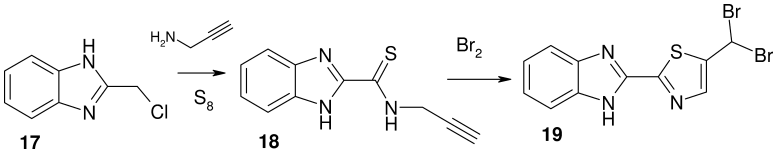
nature. Thus, the reaction of thioamides **6a–c,e** with bromine in dichloromethane afforded thiazoles **16a–c,e** in 50–55% yields. Under the same conditions in methanol, the yields did not exceed 30–35%. In the case of dichloroethane or acetonitrile as solvent, only the initial monothiooxamide was recovered, whereas in acetic acid (with or without sodium acetate), dioxane, DMF, or nitromethane multicomponent mixtures were formed.

As in the case of allyl derivatives, the situation became much better when the reactions were carried out in ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate. The reactions took place at room temperature within 3–5 min, giving products in 80–85% yields. It is known that for alkylacetylenes, the formation of cyclic bromirenium ion is the rate-determining step for the whole process (*6*). Apparently, in our case, this ion reacts with the thiocarbonyl group to give the dihydrothiazole ring **15**, which is then transformed under the action of bromine atoms into thiazole **16** containing a dibromomethyl fragment (Scheme 6).

The developed approach to dibromomethyl-containing thiazoles is general for other readily accessible products having an *N*-propargylthioamide fragment. An example of this approach is presented below. Thiolation of the chloromethyl group of accessible product **17** occurs smoothly under the action of propargylamine and sulfur; this allows the subsequent preparation of thiazole **19** under these conditions in good yields (Scheme 7).



Scheme 6. Synthesis of thiazoles. **16**: X = NO_2, R = H (**a**); X = NO_2, R = Cl (**b**); X = NO_2, R = Me (**c**); X = H, R = NO_2 (**e**).



Scheme 7. Synthesis of thiazoles from the chloromethyl group.

In conclusion, we proposed approaches to the synthesis of dihydrothiazoles and thiazoles containing halomethyl groups convenient for subsequent modification.

3. Experimental

3.1. *General procedures*

^{1}H NMR spectra were recorded on Bruker AC-200 (200 MHz) and WM-250 (250 MHz) instruments in DMSO-d_6. Mass spectra were recorded on a Varian MAT CH-6 with direct sample injection into the ion source, ionization energy 70 eV, and control voltage 1.75 kV. The melting points were measured on a Boetius hot stage and were not corrected. All reaction mixtures were analyzed and the product purity was checked using TLC on Merck silica gel 60 F254 UV-254 plates.

3.2. *Chloroacetamides (5a–e)*

Chloroacetamides **5a–e** were prepared by a previously described method (*7*). The synthesis of 2-(chloromethyl)-1H-benzimidazole **17** was reported in the literature (*8*).

3.2.1. *N-(2-nitrophenyl)-2-chloroacetamide (**5a**)*

Yield 98%, m.p. 109–111 °C (lit. m.p. 108–110 °C (*9*)). ^{1}H NMR, δ, ppm: 4.33 s (2H, CH_2), 7.60 m (2H, $2H_{arom.}$), 7.78 m (1H, $1H_{arom.}$), 8.80 m (1H, $1H_{arom.}$), 11.60 s (1H, NH). MS, m/z: 214 $[M]^+$. Found, %: C 44.67; H 3.35; N 13.10; Cl 16.58. $C_8H_7N_2O_3Cl$. Calcd, %: C 44.77; H 3.29; N 13.05; Cl 16.52.

3.2.2. *N-(2-nitro-4-chlorophenyl)-2-chloroacetamide (**5b**)*

Yield 97%, m.p. 140–141 °C (lit. m.p. 140 °C (*10*)). ^{1}H NMR, δ, ppm: 4.30 s (2H, CH_2), 7.30 m (1H, $1H_{arom.}$), 8.35 m (1H, $1H_{arom.}$), 8.60 m (1H, $1H_{arom.}$), 11.35 s (1H, NH). MS, m/z: 249 $[M]^+$. Found, %: C 38.62; H 2.50; N 11.16; Cl 28.50. $C_8H_6N_2O_3Cl_2$. Calcd, %: C 38.58; H 2.43; N 11.25; Cl 28.47.

3.2.3. *N-(4-methyl-2-nitrophenyl)-2-chloroacetamide (**5c**)*

Yield 96%, m.p. 199–121 °C (lit. m.p. 198–199 °C (*11*)). ^{1}H NMR, δ, ppm: 2.40 s (3H, CH_3), 4.35 s (2H, CH_2), 7.55 d (1H, $1H_{arom.}$, $J = 8.3$ Hz), 7.65 d (1H, $1H_{arom.}$, $J = 8.3$ Hz), 7.85 s (1H, $1H_{arom.}$), 10.55 s (1H, NH). MS, m/z: 229 $[M]^+$. Found, %: C 47.34; H 3.82; N 12.20; Cl 15.48. $C_9H_9N_2O_3Cl$. Calcd, %: C 47.28; H 3.97; N 12.25; Cl 15.51.

3.2.4. *2-Chloro-N-phenylacetamide (**5d**)*

Yield 96%, m.p. 137 °C (lit. m.p. 136–137 °C (*12*)). MS, m/z: 169 $[M]^+$.

3.2.5. *2-Chloro-N-(4-nitrophenyl)acetamide (**5e**)*

Yield 96%, m.p. 185–186 °C (lit. m.p. 185 °C (*12*)). MS, m/z: 214 $[M]^+$.

3.3. *General procedure for the preparation of monothiooxamides (6a–c,e, 7a–d, 18)*

Chloroacetanilide (**5a–e**) (0.47 mmol) was added to a mixture of sulfur (1.4 mmol, 0.045 g), allylamine or propargylamine (0.94 mmol), and triethylamine (0.94 mmol) in DMF (1 ml), which had been kept preliminarily for 30 min. The reaction mixture was stirred for 7 h at room temperature and allowed to stand for 10 h. Then the mixture was poured in water and the precipitate formed was filtered off and dried. To remove unreacted sulfur, the product was dissolved in acetone, the acetone solution was separated, the solvent was evaporated *in vacuo*, and the product was chromatographed on a silica gel-packed column with an ethyl acetate–petroleum ether mixture (1:5) as the eluent.

3.3.1. *N-(2-nitrophenyl)-2-(prop-2-yn-1-ylamino)-2-thioxoacetamide (**6a**)*

Yield 63%, m.p. 169–171 °C. ^{1}H NMR, δ, ppm: 2.15 s (1H, CH), 4.30 m (2H, CH), 7.30 m (1H, $1H_{arom.}$), 7.50 m (2H, $2H_{arom.}$), 7.85 m (1H, $1H_{arom.}$), 11.70 s (1H, NH), 12.50 s (1H, NH). MS: m/z 263 $[M]^+$. Found, %: C 50.14; H 3.37; N 15.88; S 12.23. $C_{11}H_9N_3O_3S$. Calculated, %: C 50.18; H 3.45; N 15.96; S 12.18.

3.3.2. *N-(4-Chloro-2-nitrophenyl)-2-(prop-2-yn-1-ylamino)-2-thioxoacetamide (**6b**)*

Yield 67%, m.p. 123–125 °C. ^{1}H NMR, δ, ppm: 2.10 s (1H, CH), 4.40 s (2H, CH2), 7.90 m (1H, $1H_{arom.}$), 8.25 m (1H, $1H_{arom.}$), 8.45 m (1H, $1H_{arom.}$), 11.40 s (1H, NH), 12.10 s (1H, NH). MS: m/z 297.5 $[M]^+$. Found, %: C 44.31; H 2.62; Cl 11.99; N 14.02; S 10.87. $C_{11}H_8ClN_3O_3S$. Calcd, %: C 44.38; H 2.71; Cl 11.91; N 14.11; S 10.77.

3.3.3. *N-(4-methyl-2-nitrophenyl)-2-(prop-2-yn-1-ylamino)-2-thioxoacetamide (**6c**)*

Yield 69%, m.p. 200–202 °C. ^{1}H NMR, δ, ppm: 2.10 s (1H, CH), 2.30 s (3H, CH_3), 4.40 s (2H, CH), 7.70 m (1H, $1H_{arom.}$), 7.90 m (1H, $1H_{arom.}$), 8.20 m (1H, $1H_{arom.}$), 11.40 s (1H, NH), 11.90 s (1H, NH). MS: m/z 277 $[M]^+$. Found, %: C 51.91; H 3.87; N 15.26; S 11.64. $C_{12}H_{11}N_3O_3S$. Calcd, %: C 51.98; H 4.00; N 15.15; S 11.56.

3.3.4. *N-(4-nitrophenyl)-2-(prop-2-yn-1-ylamino)-2-thioxoacetamide (**6e**)*

Yield 73%, m.p. 234–235°C. ^{1}H NMR, δ, ppm: 2.15 s (1H, CH), 4.35 s (2H, CH), 7.85 d (2H, $2H_{arom.}$, $J = 9.2$ Hz), 8.25 d (2H, $2H_{arom.}$, $J = 9.2$ Hz), 10.90 s (1H, NH), 11.70 s (1H, NH). MS: m/z 263 $[M]^+$. Found, %: C 50.03; H 3.31; N 15.90; S 12.26. $C_{11}H_9N_3O_3S$. Calcd, %: C 50.18; H 3.45; N 15.96; S 12.18.

3.3.5. *2-(Allylamino)-N-(2-nitrophenyl)-2-thioxoacetamide (**7a**)*

Yield 57%, m.p. 217–219 °C. ^{1}H NMR, δ, ppm: 4.10 s (2H, CH_2); 4.95 s (2H, CH_2); 5.40 s (1H, CH); 7.20 m ($1H_{arom.}$); 7.60 m ($2H_{arom.}$); 8.20 m ($1H_{arom.}$); 11.50 s (1H, NH); 12.10 s (1H, NH). MS: m/z 265 $[M]^+$. Found, %: C 49.69; H 4.23; N 15.79; S 12.20. $C_{11}H_{11}N_3O_3S$. Calcd, %: C 49.80; H 4.18; N 15.84; S 12.09.

3.3.6. *2-(Allylamino)-N-(4-chloro-2-nitrophenyl)-2-thioxoacetamide (**7b**)*

Yield 60%, m.p. 229–231 °C. ^{1}H NMR, δ, ppm: 4.10 s (2H, CH_2); 4.40 s (1H, CH); 4.60 (2H, CH_2); 7.90 s ($1H_{arom.}$); 8.20 ($1H_{arom.}$); 8.45 m ($1H_{arom.}$); 11.30 s (1H, NH); 12.0 s (1H, NH). MS: m/z 299 $[M]^+$. Found, %: C 44.20; H 3.41; Cl 11.81; N 14.18; S 10.59. $C_{11}H_{10}ClN_3O_3S$. Calcd, %: C 44.08; H 3.36; Cl 11.83; N 14.02; S 10.70.

3.3.7. *2-(Allylamino)-N-(4-methyl-2-nitrophenyl)-2-thioxoacetamide (**7c**)*

Yield 62%, m.p. 241–243 °C. ^{1}H NMR, δ, ppm: 2.35 s (3H, CH_3); 4.10 s (2H, CH_2); 4.70 s (1H, CH); 5.0 s (2H, CH_2); 7.60 m ($1H_{arom.}$); 7.80 m ($1H_{arom.}$); 8.10 m ($1H_{arom.}$); 11.30 s (1H, NH); 12.0 s (1H, NH). MS: m/z 279 $[M]^+$. Found, %: C 51.51; H 4.74; N 15.17; S 11.31. $C_{12}H_{13}N_3O_3S$. Calcd, %: C 51.60; H 4.69; N 15.04; S 11.48.

3.3.8. *2-(Allylamino)-N-phenyl-2-thioxoacetamide (**7d**)*

Yield 59%, m.p. 266–268°C. ^{1}H NMR, δ, ppm: 4.30 s (2H, CH_2); 5.20 s (2H, CH_2); 5.90 s (1H, CH); 7.15 t ($1H_{arom.}$, $J = 7.3$ Hz); 7.40 t ($2H_{arom.}$, $J = 7.8$ Hz); 7.75 d ($2H_{arom.}$, $J = 8.1$ Hz); 10.30 s (1H, NH); 11.00 s (1H, NH). MS: m/z 220 $[M]^+$. Found, %: C 59.81; H 5.40; N 12.82; S 14.61. $C_{11}H_{12}N_2OS$. Calcd, %: C 59.97; H 5.49; N 12.72; S 14.56.

3.3.9. *N-prop-2-yne-1H-benzimidazole-2-carbothioamide (**18**)*

Yield 60%, m.p. 123–125°C. ^{1}H NMR, δ, ppm: 2.10 s (1H, CH), 4.50 s (2H, CH), 7.40 m (2H, $2H_{arom.}$), 7.60 m (2H, $2H_{arom.}$), 10.10 s (1H, NH), 11.30 s (1H, NH). MS: m/z 215$[M]^+$. Found, %: C 61.21; H 4.39; N 19.69; S 14.71. $C_{11}H_9N_3S$. Calcd, %: C 61,37; H 4,21; N 19,52; S 14,90.

3.4. *General procedure for the preparation of 5-bromomethyl-4,5-dihydro-1,3-thiazole-2-carboxamides (8a–d)*

Method A. Monothiooxamide (**7a–d**) (0.1 mmol) was dissolved in dichloromethane (5 ml). The solution was cooled to 0–5 °C, and bromine (0.25 mmol) was added in small portions with vigorous stirring. The mixture was kept for 30 min at +5 °C and for 1 h at room temperature. The precipitate was filtered off, washed with water, and recrystallized from ethanol.

Method B. Monothiooxamide (**7a–d**) (0.1 mmol) was dissolved in a minimum amount of ionic liquid (1-butyl-3-methylimidazolium hexafluorophosphate), and bromine (0.25 mmol) was added. After 2–3 min, the mixture was extracted with benzene or ether, and the organic layer was washed with water. The solvent was removed *in vacuo* and the product did not require additional purification.

3.4.1. *5-(Bromomethyl)-N-(2-nitrophenyl)-4,5-dihydro-1,3-thiazole-2-carboxamide (**8a**)*

Yield 80% (according to Method B, in 1-butyl-3-methylimidazolium hexafluorophosphate), m.p. 120–122°C. ^{1}H NMR, δ, ppm: 4.10–4.60 m (5H, CH), 7.35 m (1H, 1H$_{arom.}$), 7.65 m (2H, 2H$_{arom.}$), 7.90 m (1H, 1H$_{arom.}$), 11.90 s (1H, NH). MS: m/z 344 $[M]^+$. Found, %: C 38.22; H 3.02; Br 23.17; N 12.30; S 9.40. $C_{11}H_{10}BrN_3O_3S$. Calcd, %: C 38.39; H 2.93; Br 23.22; N 12.21; S 9.32.

3.4.2. *5-(Bromomethyl)-N-(4-chloro-2-nitrophenyl)-4,5-dihydro-1,3-thiazole-2-carboxamide (**8b**)*

Yield 80% (by Method B, in 1-butyl-3-methylimidazolium hexafluorophosphate), m.p. 169–171 °C. ^{1}H NMR, δ, ppm: 4.10–4.50 m (5H, CH), 7.90 m (1H, 1H$_{arom.}$), 8.20 m (1H, 1H$_{arom.}$), 8.50 m (1H, 1H$_{arom.}$), 11.40 s (1H, NH). MS: m/z 379 $[M]^+$. Found, %: C 34.81; H 2.38; Br 21.19; Cl 9.44; N 11.17; S 8.30. $C_{11}H_9BrClN_3O_3S$. Calcd, %: C 34.89; H 2.40; Br 21.10; Cl 9.36; N 11.10; S 8.47.

3.4.3. *5-(Bromomethyl)-N-(4-methyl-2-nitrophenyl)-4,5-dihydro-1,3-thiazole-2-carboxamide (**8c**)*

Yield 79% (according to Method B, in 1-butyl-3-methylimidazolium hexafluorophosphate), m.p.155–157°C. ^{1}H NMR, δ, ppm: 2.30 s (3H, CH$_3$), 4.20–4.60 m (5H, CH), 7.60 m (1H, 1H$_{arom.}$), 7.80 m (1H, 1H$_{arom.}$), 8.15 m (1H, 1H$_{arom.}$), 11.30 s (1H, NH). MS: m/z 358 $[M]^+$. Found, %: C 40.17; H 3.49; Br 22.24; N 11.82; S 8.99. $C_{12}H_{12}BrN_3O_3S$. Calcd, %: C 40.24; H 3.38; Br 22.31; N 11.73; S 8.95.

3.4.4. *5-(Bromomethyl)-N-phenyl-4,5-dihydro-1,3-thiazole-2-carboxamide (**8d**)*

Yield 70% by Method A and 93% or 88% by Method B (in 1-butyl-3-methylimidazolium tetrafluoroborate or 1-butyl-3-methylimidazolium hexafluorophosphate, respectively), m.p. 140–142°C. ^{1}H NMR, δ, ppm: 4.20–4.40 m (5H, CH), 7.15 m (1H, 1H$_{arom.}$), 7.35 m (2H, 2H$_{arom.}$), 7.70 m (2H, 2H$_{arom.}$), 10.45 s (1H, NH). MS: m/z 299 $[M]^+$. Found, %: C 44.10; H 3.81; Br 26.62; N 9.21; S 10.89. $C_{11}H_{11}BrN_2OS$. Calcd, %: C 44.16; H 3.71; Br 26.71; N 9.36; S 10.72.

3.5. *General procedure for the preparation of 5-iodomethyl-4,5-dihydro-1,3-thiazole-2-carboxamides (9a–d)*

Method A. Monothiooxamide (**7a–d**) (0.1 mmol) and Na_2CO_3 (0.2 mmol) were stirred in dichloromethane (6 ml). Iodine (0.15 mmol) was added. The mixture was refluxed for 4–5 h (TLC monitoring), cooled, and washed with a solution of Na_2SO_3 until it became colorless. The organic layer was washed with water (3 × 30 ml) and dried with $MgSO_4$, and the solvent was evaporated *in vacuo*.

Method B. Monothiooxamide (**7a–d**) (0.1 mmol) was dissolved in a minimum amount of ionic liquid (1-butyl-3-methyimidazolium hexafluorophosphate) and iodine (0.15 mmol) was added. After 4–5 min, the mixture was extracted with benzene or ether and the organic layer was washed with water. The solvent was removed *in vacuo*.

3.5.1. *5-(Iodomethyl)-N-(2-nitrophenyl)-4,5-dihydro-1,3-thiazole-2-carboxamide (**9a**)*

Yield 72% (by Method B, in 1-butyl-3-methylimidazolium hexafluorophosphate), m.p. 166–168 °C. ^{1}H NMR, δ, ppm: 4.10–4.40 m (5H, CH), 7.30 m (1H, $1H_{arom.}$), 7.65 m (2H, $2H_{arom.}$), 7.85 m (1H, $1H_{arom.}$), 11.85 s (1H, NH). MS: m/z 391 $[M]^+$. Found, %: C 33.62; H 2.69; I 32.30; N 10.59; S 8.34. $C_{11}H_{10}IN_3O_3S$. Calcd, %: C 33.77; H 2.58; I 32.44; N 10.74; S 8.20.

3.5.2. *5-(Iodomethyl)-N-(4-chloro-2-nitrophenyl)-4,5-dihydro-1,3-thiazole-2-carboxamide (**9b**)*

Yield 75% (by Method B, in 1-butyl-3-methylimidazolium hexafluorophosphate), m.p. 110–112 °C. ^{1}H NMR, δ, ppm: 4.20–4.50 m (5H, CH), 7.90 m (1H, $1H_{arom.}$), 8.20 m (1H, $1H_{arom.}$), 8.50 m (1H, $1H_{arom.}$), 11.30 s (1H, NH). MS: m/z 426 $[M]^+$. Found, %: C 31.19; H 2.24; I 29.84; Cl 8.49; N 9.74; S 7.67. $C_{11}H_9ICIN_3O_3S$. Calcd, %: C 31.04; H 2.13; I 29.82; Cl 8.33; N 9.87; S 7.53.

3.5.3. *5-(Iodomethyl)-N-(4-methyl-2-nitrophenyl)-4,5-dihydro-1,3-thiazole-2-carboxamide (**9c**)*

Yield 70% (by Method B, in 1-butyl-3-methylimidazolium hexafluorophosphate), m.p. 198–200 °C. ^{1}H NMR, δ, ppm: 2.30 s (3H, CH_3), 4.15–4.60 m (5H, CH), 7.60 m (1H,$1H_{arom.}$), 7.80 m (1H, $1H_{arom.}$), 8.15 m (1H, $1H_{arom.}$), 11.25 s (1H, NH). MS: m/z 405 $[M]^+$. Found, %: C 35.44; H 2.91; I 31.29; N 10.24; S 8.06. $C_{12}H_{12}IN_3O_3S$. Calcd, %: C 35.57; H 2.98; Br 31.32; N 10.37; S 7.91.

3.5.4. *5-(Iodomethyl)-N-phenyl-4,5-dihydro-1,3-thiazole-2-carboxamide (**9d**)*

Yield 60% by Method A and 71% or 88% by Method B (in 1-butyl-3-methylimidazolium tetrafluoroborate or 1-butyl-3-methylimidazolium hexafluorophosphate, respectively), m.p. 144–146°C. ^{1}H NMR, δ, ppm: 4.10–4.40 m (5H, CH), 7.10 m (1H, $1H_{arom.}$), 7.40 m (2H, $2H_{arom.}$), 7.70 m (2H, $2H_{arom.}$), 10.40 s (1H, NH). MS: m/z 346 $[M]^+$. Found, %: C 38.05; H 3.28; I 36.52; N 8.20; S 9.20. $C_{11}H_{11}IN_2OS$. Calcd, %: C 38.16; H 3.20; I 36.66; N 8.09; S 9.26.

3.6. *Preparation procedure of 5-chlormethyldihydrothiazoles (11d,f)*

Thioamide (0.1 mmol) was dissolved in a minimum amount of ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate, and thionyl chloride (0.15 mmol) was added. After 2–4 min, the mixture was extracted with benzene or ether (3 × 5 ml), the organic layer was washed with water, and the solvent was evaporated *in vacuo*. The product was purified by TLC (petroleum ether:ethyl acetate, 3:1, as the eluent).

3.6.1. *5-(Chloromethyl)-N-phenyl-4,5-dihydro-1,3-thiazole-2-carboxamide (**11d**)*

Yield 60% m.p.133–135 °C. ^{1}H NMR, δ, ppm: 4.20–4.45 m (5H, CH), 7.20 m (1H, 1H$_{arom.}$), 7.45 m (2H, 2H$_{arom.}$), 7.80 m (2H, 2H$_{arom.}$), 10.50 s (1H, NH). MS: m/z 255 $[M]^+$. Found, %: C 51.92; H 4.49; Cl 13.79; N 11.12; S 12.67. $C_{11}H_{11}ClN_2OS$. Calcd, %: C 51.86; H 4.35; Cl 13.92; N 11.00; S 12.59.

3.6.2. *5-(Chloromethyl)-N-pyridino-4,5-dihydro-1,3-thiazole-2-carboxamide (**11f**)*

Yield 65% m.p.165–167 °C. ^{1}H NMR, δ, ppm: 4.10–4.45 m (5H, CH), 7,90 m (1H, 1H$_{pyridine}$), 8.30 m (1H, 1H$_{pyridine}$), 8.40 m (1H, 1H$_{pyridine}$), 9.00 m (1H, 1H$_{pyridine}$), 11.50 s (1H, NH). MS: m/z 256 $[M]^+$. Found, %: C 47.04; H 3.83; Cl 13.92; N 16.50; S 12.41. $C_{10}H_{10}ClN_3OS$. Calcd, %: C 46.97; H 3.94; Cl 13.86; N 16.43; S 12.54.

3.7. *Preparation of (5-azidomethyl)-N-phenyl-4,5-dihydro-1,3-thiazole-2-carboxamide (12)*

Sodium azide NaN_3 (0.14 mmol) was added to 5-(bromomethyl)-*N*-phenyl-4,5-dihydro-1,3-thiazole-2-carboxamide (**8e**) (0.1 mmol) in DMF (3 ml). The reaction mixture was stirred at 30–40 °C. After 3.5 h, it was poured in water and the precipitate was filtered off and washed with water.

Yield 63%, m.p. 123–125 °C. ^{1}H NMR, δ, ppm: 4.20 s (2H, CH), 4.50 m (3H, CH), 7.10 t (1H, 1H$_{arom.}$, J = 7.3 Hz), 7.40 t (2H, 2H$_{arom.}$, J = 7.0 Hz), 7.75 d (2H, 2H$_{arom.}$, J = 7.8 Hz), 10.50 s (1H, NH). MS: m/z 261 $[M]^+$. IR, υ/cm^{-1}: 2108 (–N_3), 1660 (C=O). Found, %: C 50.62; H 4.31; N 26.94. $C_{11}H_{11}N_5OS$. Calcd, %: C 50.56; H 4.24; N 26.80.

3.8. *Preparation of S-{[2-(anilinocarbonyl)-4,5-dihydro-1,3-thiazol-5-yl]methyl}O-ethyl thiocarbonate (13)*

Ethyl thioglycolate (0.13 mmol) was added to 5-(bromomethyl)-*N*-phenyl-4,5-dihydro-1,3-thiazole-2-carboxamide (**8e**) (0.1 mmol) in THF (1 ml). The reaction mixture was stirred for 1.5 h at room temperature at 25 °C. During the reaction, a precipitate formed. The precipitate was filtered off and washed with water.

Yield 80%, m.p.187–189 °C. ^{1}H NMR, δ, ppm: 2.30 s (4H, CH), 2.60 s (1H, CH), 2.60 s (1H, CH), 3.80–4.20 m (5H, CH), 7.15 t (1H, 1H$_{arom.}$, J = 7.2 Hz), 7.40 t (2H, 2H$_{arom.}$, J = 7.2 Hz), 7.80 d (2H, 2H$_{arom.}$, J = 7.7 Hz), 10.65 s (1H, NH). MS: m/z 324 $[M]^+$. Found, %: C 51.94; H 5.06; N 8.74. $C_{14}H_{16}N_2O_3S_2$. Calcd, %: C 51.83; H 4.97; N 8.63.

3.9. *General procedure for the preparation of 1,3-thiazolecarboxamides (16a–c,e, 19).*

Monothiooxamide (0.1 mmol) was dissolved in a minimum amount of ionic liquid (1-butyl-3-methylimidazolium hexafluorophosphate), and bromine (0.23 mmol) was added. The mixture

was stirred at room temperature and, after 2–3 min, extracted with benzene or ether (3 × 5 ml), the organic layer was washed with water, and the solvent was evaporated *in vacuo*.

3.9.1. *5-(Dibromomethyl)-N-(2-nitrophenyl)-1,3-thiazole-2-carboxamide (**16a**)*

Yield 83%, m.p. 245–247 °C. ^{1}H NMR, δ, ppm: 2.10 s (1H, CH), 7.35 m (1H, $1H_{arom.}$), 7.60 m (2H, $2H_{arom.}$), 7.80 m (1H, $1H_{arom.}$), 8.20 m (1H, CH), 11.70 s (1H, NH). MS: m/z 421 $[M]^+$. Found, %: C 31.27; H 1.61; Br 38.04; N 9.88; S 7.64. $C_{11}H_7Br_2N_3O_3S$. Calcd, %: C 31.38; H 1.68; Br 37.95; N 9.98; S 7.62.

3.9.2. *5-(Dibromomethyl)-N-(4-chloro-2-nitrophenyl)-1,3-thiazole-2-carboxamide (**16b**)*

Yield 86%, m.p. 229–231 °C. ^{1}H NMR, δ, ppm: 2.10 s (1H, CH), 7.85 m (1H, $1H_{arom.}$), 8.30 m (1H, $1H_{arom.}$), 8.55 m (1H, $1H_{arom.}$), 8.70 s (1H, CH),11.70 s (1H, NH). MS: m/z 455 $[M]^+$. Found, %: C 29.11; H 1.41; Br 35.17; Cl 7.69; N 9.20; S 7.14. $C_{11}H_6Br_2ClN_3O_3S$. Calcd, %: C 29.00; H 1.33; Br 35.08; Cl 7.78; N 9.22; S 7.04.

3.9.3. *5-(Dibromomethyl)-N-(4-methyl-2-nitrophenyl)-1,3-thiazole-2-carboxamide (**16c**)*

Yield 87%, m.p. 203–205 °C. ^{1}H NMR, δ, ppm: 2.10 s (1H, CH), 2.35 s (3H, CH_3), 7.65 m (1H, $1H_{arom.}$), 7.85 m (1H, $1H_{arom.}$), 8.10 m (1H, $1H_{arom.}$), 8.35 s (1H, CH),11.60 s (1H, NH). MS: m/z 435 $[M]^+$. Found, %: C 33.27; H 2.14; Br 36.61; N 9.72; S 7.27. $C_{12}H_9Br_2N_3O_3S$. Calcd, %: C 33.13; H 2.08; Br 36.73; N 9.66; S 7.37.

3.9.4. *5-(Dibromomethyl)-N-(4- nitrophenyl)-1,3-thiazole-2-carboxamide (**16e**)*

Yield 85%, m.p. 176–178 °C. ^{1}H NMR, δ, ppm: 2.15 s (1H, CH), 7.80 d (2H, $2H_{arom.}$, $J = 9.2$ Hz), 8.20 d (2H, $2H_{arom.}$, $J = 9.2$ Hz), 8.40 s (1H, CH),11.00 s (1H, NH). MS: m/z 421 $[M]^+$. Found, %: C 31.21; H 1.74; Br 37.83; N 9.91; S 7.50. $C_{11}H_7Br_2N_3O_3S$. Calcd, %: C 31.38; H 1.68; Br 37.95; N 9.98; S 7.62.

3.9.5. *2-**[**5-(Dibromomethyl)-1,3-thiazol-2-yl**]**-1H-benzimidazole (**19**)*

Yield 78%, m.p. 150–152 °C. ^{1}H NMR, δ, ppm: 2.10 s (1H, CH), 7.45 m (2H, $2H_{arom.}$), 7.70 m (2H, $2H_{arom.}$), 8.10 s (1H, CH),10.60 s (1H, NH). MS: m/z 373 $[M]^+$. Found, %: C 35.34; H 1.97; Br 42.74; N 11.22; S 8.73. $C_{11}H_7Br_2N_3S$. Calcd, %: C 35.41; H 1.89; Br 42.84; N 11.26; S 8.60.

References

(1) Nora de Souza, M.V. *J. Sulfur Chem*. **2005,** *26*, 4–5, 429–449.
(2) Sasmal, P.K.; Sridhar, S.; Idbal, J. *Tetrahedron Lett*. **2006,** *47*, 8661–8665.
(3) Figueira, V.B.C.; Prabhakar, S.; Lobo, A.M. *ARKIVOC* **2005,** *xiv*, 14–19.
(4) Singh, A.P.; Sandhu, A.S. *Indian J. Chem. Section B*. **1979,** *17*, 7–12.
(5) Yarovenko, V.N.; Polushina, A.V.; Levchenko, K.S.; Zavarzin, I.V.; Krayushkin, M.M.; Kotovskaya, S.K.; Charushin, V.N. *Russ. J. Org. Chem.*, **2007,** *43*, 1391–1396.
(6) Selina, A.A.; Karlov, S.S.; Zaitseva, G.S. *Vestn. Mosk. Univ. Ser. 2. Khim.* **2004,** *45*, 147–149.

(7) Zavarzin, I.V.; Yarovenko, V.N.; Shirokov, A.V.; Smirnova, N.G.; Es'kov, A.A.; Krauyshkin, M.M. *ARKIVOC* **2003,** *13,* 205–223.
(8) Fuerst, H. *J. Prak. Chem. Ge*. **1962,** *17,* 299–313.
(9) Tumer, H. *J. Chem. Soc*. **1948,** *7,* 1909–1912.
(10) Frerichts, B. *Arch. Pharm*. **1915,** *253,* 246–251.
(11) Bauer, L.; Welsh, T.L. *J. Org. Chem.* **1962,** *27,* 4382–4385.
(12) Boudreau, W. *J. Chem. Soc. Perkin Trans. II*. **1977,** 2028–2030.