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Heterocyclic Syntheses on the Basis of Arylation Products of Unsaturated Compounds: X.* 3-Aryl-2-chloropropanals as Reagents for the Synthesis of 2-Amino-1,3-thiazole Derivatives

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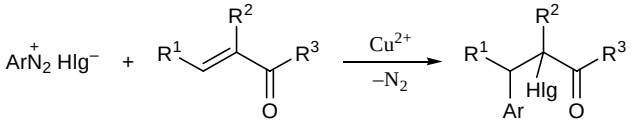
Abstract—Meerwein reaction of arenediazonium chlorides with acrolein gave 3-aryl-2-chloropropanals which were brought into cyclocondensation with thiourea. The resulting 2-amino-5-benzyl-1,3-thiazoles were acylated with carboxylic acid chlorides and phthalic anhydride to afford, respectively, 2-acylamino-5-benzyl-1,3-thiazoles and *N*-(5-benzyl-1,3-thiazol-2-yl)phthalimides.

Arylation of unsaturated compounds with arenediazonium salts according to Meerwein provides a convenient method for the synthesis of polyfunctional compounds [2–8]. Numerous examples of purposeful utilization in organic synthesis of products obtained by these reactions have been reported [8, 9]. In the preceding communications of this series we demonstrated the potential of such compounds for the synthesis of heterocycles.

Scheme 1.



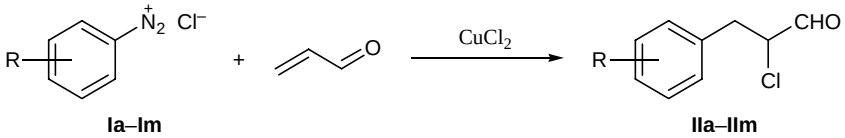
R^1, R^2, R^3 = Alk, Ar.

Classical reagents for cyclizations are α-halocarbonyl compounds. Unlike α-halo ketones, the series of α-halo aldehydes available for the synthesis of heterocycles is strongly limited [10, 11] due to difficulties in their preparation. From the synthetic viewpoint, an attractive procedure for the preparation of α-halo aldehydes may be that involving the Meerwein reaction according to Scheme 1. However, α,β-unsaturated carbonyl compounds can react with arenediazonium salt along different pathways, and arylation products are often formed instead of the desired haloarylation products [4–8]; also, the available data are insufficient to draw some conclusions and practical recommendations. A procedure for the preparation of 2-chloro(bromo)-3-phenylpropanals was reported in [12, 13], but it received no further development in later studies [8]. An attempt was made to extend the scope of this reaction; however, 3-aryl-2-chloropropanals were obtained in poor yields [14]. Therefore, elaboration of a preparative procedure for chloroarylation of acrolein seems to be important, for it would open a simple synthetic route to α-chloro-substituted aldehydes as reagents for heterocyclizations.

In the present work we examined the reaction of arenediazonium salts with acrolein and found conditions for the preparation of α-chloro aldehydes **IIa**–**IIm** in moderate yields (Scheme 2; see table), which may be regarded as a good result for such reactions [4–8]. The first results were reported in [15]. The reactions of arenediazonium chlorides **Ia**–**Im** with acrolein were carried out in aqueous acetone in the presence of $CuCl_2$ as catalyst. The yields of the products strongly depend on the acidity of the medium. The best yields of aldehydes **IIa**–**IId** from toluene- and methoxybenzenediazonium chlorides **Ia**–**Id** were obtained in a nearly neutral medium. Diazonium salts having electron-acceptor substituents in the aromatic ring successfully react with acrolein in acidic medium. Here, contrary to published data [14], the yields of

* For communication IX, see [1].

Scheme 2.



Ia–Im **IIa–IIm**

I, **II**, R = 3-Me (**a**), 4-Me (**b**), 4-MeO (**c**), 3-Me-4-Cl (**d**), 4-F (**e**), 4-Cl (**f**), 4-Br (**g**), 3-CF_3 (**h**), 2,3-Cl_2 (**i**), 2,4-Cl_2 (**j**), 2,5-Cl_2 (**k**), 3,4-Cl_2 (**l**), 4-FCH_2S (**m**).

compounds **IIe**–**IIm** were not lower. However, it is advisable to perform the synthesis in a two-phase system (rather than in aqueous acetone) using an aqueous solution of diazonium salt **I** and $CuCl_2$–acrolein or a solution of acrolein in benzene. Addition of acetone reduces the yield of aldehydes **IIe**–**III** and favors formation of tarry products, presumably via side aldol condensation processes. The latter were likely to be responsible for the poor yields of 3-aryl-2-chloropropanals in [14]. Our attempts to avoid tarring by reacting acrolein with diazonium salts having electron-acceptor substituents in neutral medium were unsuccessful: as a result, the contribution of side transformations of diazonium salts increased. When the reactions were carried out in a two-phase system, the fraction of tarry product was considerably reduced, and the procedure for isolation of compounds **IIe**–**IIm** was more facile.

Thus we have shown that chloroarylation of acrolein is a general reaction for different diazonium salts. The proposed procedure is much more advantageous than the other methods for the preparation of α-chloro aldehydes: it utilizes accessible initial reactants and is simple to perform.

Aldehydes **IIa**–**IIm** were subjected to heterocyclization with thiourea on heating in alcohol (Scheme 3). The reaction was not accompanied by elimination of HCl with formation of substituted cinnamaldehydes, and the corresponding 2-amino-5-benzyl-1,3-thiazoles **IIIa**–**IIIm** were obtained in high yields. The cyclization can also be effected in other solvents. Compounds **IIIa**–**IIIm** were isolated by treatment of aqueous solutions of the respective hydrochlorides with bases. Thiazoles **IIIa**–**IIIm** are readily soluble in DMF, DMSO, alcohol, and dioxane, and some products, in benzene and toluene.

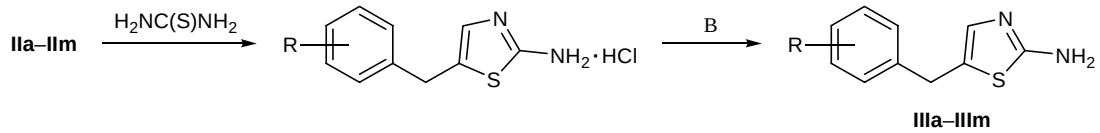
Aldehydes **IIa**–**IIm** were also brought into reaction with acylthioureas **IV**. However, these reactions resulted in formation of mixtures of products, and products **Va**–**Vo** were difficult to isolate. Therefore,

Yields, boiling points, refractive indices, C=O stretching vibration frequencies, and elemental analyses of 3-aryl-2-chloropropanals **IIa**–**IIm**

Comp. no.	Yield, %	bp, °C (3 mm)	n_D^{20}	IR spectrum, ν(C=O), cm^{-1}	Found Cl, %	Formula	Calculated Cl, %
IIa	42	105	1.5370	1706	19.28	$C_{10}H_{11}ClO$	19.41
IIb	39	106	1.5382	1706	19.20	$C_{10}H_{11}ClO$	19.41
IIc	30	110	1.5469	1705	17.66	$C_{10}H_{11}ClO_2$	17.85
IId	44	119	1.5378	1707	32.30	$C_{10}H_{10}Cl_2O$	32.66
IIe	42	100	1.5320	1709	19.04	C_9H_8ClFO	19.00
IIf	43	115	1.5518	1705	35.01	$C_9H_8Cl_2O$	34.92
IIg	41	172	1.5801	1706	46.30[a]	C_9H_8BrClO	46.61[a]
IIh	49	110	1.5622	1717	15.10	$C_{10}H_8ClF_3O$	14.98
IIi	49	165	1.5722	1711	44.45	$C_9H_7Cl_3O$	44.78
IIj	45	169	1.5752	1710	44.69	$C_9H_7Cl_3O$	44.78
IIk	46	170	1.5790	1708	44.57	$C_9H_7Cl_3O$	44.78
IIl	56	178	1.5779	1709	44.50	$C_9H_7Cl_3O$	44.78
IIm	42	190	1.6120	1710	14.03	$C_{10}H_9ClF_2OS$	14.14

[a] Cl + Br.

Scheme 3.



this procedure for the synthesis of 2-acylamino-5-benzyl-1,3-thiazoles **V** (method *b*) cannot be regarded as preparative (Scheme 4). An alternative route involves acylation of aminothiazoles **III** (method *a*). The latter were treated with aliphatic and aromatic acid chlorides and substituted cinnamoyl chlorides. In all cases, the acylation occurred at a high rate and with high selectivity at the exocyclic nitrogen atom. Aminothiazoles **III** were also acylated with phthalic anhydride. As a result, N-substituted phthalimides **VIa**–**VIg** were isolated in high yields. This reaction was also performed with aminothiazoles **IIIn** (R = 2-Cl) and **IIIo** (R = 3-NO_2) which were described by us previously [15].

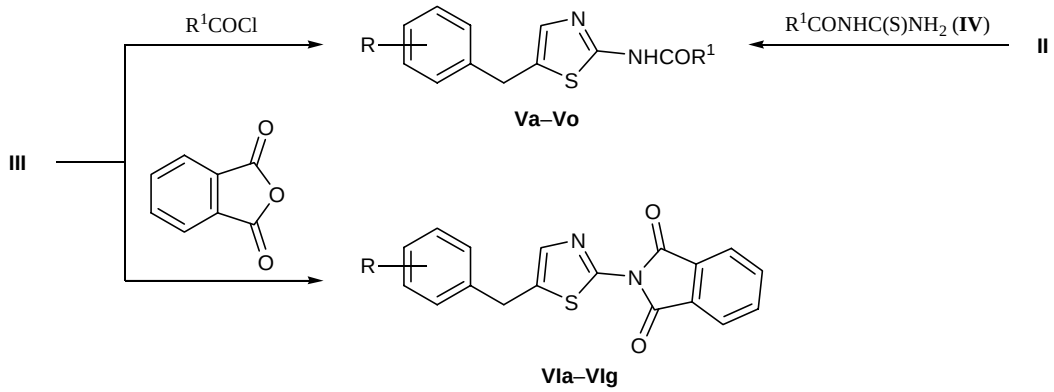
Thus, the results of our study made 3-aryl-2-chloropropanal accessible. These compounds were used to synthesize poorly studied [16] 2-amino-5-benzyl-1,3-thiazoles which attract interest as reagents for organic synthesis.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded from solutions in DMSO-d_6 on Bruker instruments operating at 400 (**IIId**, **IIIm**, **VIb**–**VIf**), 300 (**IIIa**–**IIIc**, **IIIe**–**IIIl**, **Va**–**Vg**, **Vi**–**Vo**), and 200 MHz (**Vh**, **VIa**, **VIg**). The chemical shifts were measured relative to the solvent signal (DMSO, δ 2.50 ppm). The IR spectra were obtained on a Specord 75IR spectrometer.

3-Aryl-2-chloropropanals IIa–IIm (*general procedure***).** A three-necked flask equipped with a stirrer, a dropping funnel, and a gas-outlet tube (attached to a bubble counter) was charged with 0.2 mol (13.5 ml) of acrolein, 10 g of $CuCl_2 \cdot 2H_2O$, and 50 ml of acetone (in the synthesis of **IIa**–**IId**) or 50 ml of benzene (in the synthesis of **IIe**–**IIm**). A cold aqueous solution of arenediazonium chloride **Ia**–**Im** (prepared by diazotization of 0.2 mol of the corresponding aromatic amine) was added dropwise under vigorous stirring. In the synthesis of aldehydes **IIa**–**IId**, the diazonium salt was preliminarily neutralized with $NaHCO_3$ to pH 6–7, and 2 g of MgO was added to the mixture. The temperature was maintained within 10–30°C. When the reaction was complete, the organic layer was separated, and the aqueous layer was extracted with chloroform. The extract was combined with the organic phase, dried over $MgSO_4$, and evaporated, and the residue was distilled under reduced pressure. The yields, boiling points, refractive indices, C=O stretching vibration frequencies, and elemental analyses of 3-aryl-2-chloropropenals **IIa**–**IIm** are given in table.

Scheme 4.



V, R = 4-F, R^1 = Me (**a**); R = 2,5-Cl_2, R^1 = Me (**b**); R = 2,3-Cl_2, R^1 = $CH_3(CH_2)_3$ (**c**); R = 2,5-Cl_2, R^1 = $(CH_3)_2CHCH_2$ (**d**); R = 4-MeO, R^1 = $CH_3(CH_2)_5$ (**e**); R = 4-F, R^1 = 2-tetrahydrofuryl (**f**); R = 3-CF_3, R^1 = 4-ClC_6H_4 (**g**); R = 4-Cl, R^1 = 2-furyl (**h**); R = 4-MeO, R^1 = 2-thienyl (**i**); R = 3-Me, R^1 = 2-MeC_6H_4CH=CH (**j**); R = 4-Me, R^1 = 4-$EtOC_6H_4CH$=CH (**k**); R = 4-MeO, R^1 = 3-$CF_3C_6H_4CH$=CH (**l**); R = Cl, R^1 = 3-$CF_3C_6H_4CH$=CH (**m**); R = 4-F, R^1 = 4-ClC_6H_4CH=CH (**n**); R = 4-Cl, R^1 = 2-(2-furyl)-ethenyl (**o**); **VI**, R = 2-Cl (**a**), 4-Cl (**b**), 4-Br (**c**), 3-NO_2 (**d**), 2,3-Cl_2 (**e**), 2,5-Cl_2 (**f**), 3-CF_3 (**g**).

2-Amino-5-benzyl-1,3-thiazoles IIIa–IIIm (*general procedure*). A mixture of 0.8 g of thiourea and 0.01 mol of aldehyde **IIa**–**IIm** in 10 ml of ethanol was heated for 1.5–2 h under reflux. The mixture was cooled, diluted with 100 ml of water, and made alkaline by adding aqueous ammonia. The precipitate was filtered off and recrystallized from CCl_4 or $CHCl_3$–CCl_4.

2-Amino-5-(3-methylbenzyl)-1,3-thiazole (IIIa). Yield 72%, mp 101–102°C. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, Me), 3.83 s (2H, CH_2), 6.56 s (2H, NH_2), 6.62 s (1H, 4-H, thiazole), 6.93–7.02 m (3H, C_6H_4), 7.14 t (1H, C_6H_4, J = 7.5 Hz). Found, %: C 64.32; H 5.90; N 13.78. $C_{11}H_{12}N_2S$. Calculated, %: C 64.67; H 5.92; N 13.71.

2-Amino-5-(4-methylbenzyl)-1,3-thiazole (IIIb). Yield 69%, mp 142–143°C. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, Me), 3.82 s (2H, CH_2), 6.55 s (2H, NH_2), 6.60 s (1H, 4-H, thiazole), 7.06 s (4H, C_6H_4). Found, %: C 64.48; H 5.75; N 13.67. $C_{11}H_{12}N_2S$. Calculated, %: C 64.67; H 5.92; N 13.71.

2-Amino-5-(4-methoxybenzyl)-1,3-thiazole (IIIc). Yield 78%, mp 133–134°C. ^{1}H NMR spectrum, δ, ppm: 3.72 s (3H, MeO), 3.80 s (2H, CH_2), 6.54 s (2H, NH_2), 6.59 s (1H, 4-H, thiazole), 6.80 d (2H, C_6H_4), 7.09 d (2H, C_6H_4, J = 8.4 Hz). Found, %: C 60.05; H 5.36; N 12.58. $C_{11}H_{12}N_2OS$. Calculated, %: C 59.98; H 5.49; N 12.72.

2-Amino-5-(4-chloro-3-methylbenzyl)-1,3-thiazole (IIId). Yield 82%, mp 125–127°C. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, Me), 3.87 s (2H, CH_2), 6.72 s (1H, 4-H, thiazole), 6.75 s (2H, NH_2), 7.08 d (1H, C_6H_3, J = 8.0 Hz), 7.24 s (1H, C_6H_3), 7,26 d (1H, C_6H_3). Found, %: C 55.39; H 4.50; N 11.54. $C_{11}H_{11}ClN_2S$. Calculated, %: C 55.34; H 4.64; N 11.73.

2-Amino-5-(4-fluorobenzyl)-1,3-thiazole (IIIe). Yield 85%, mp 135–136°C. ^{1}H NMR spectrum, δ, ppm: 3.87 s (2H, CH_2), 6.62 s (2H, NH_2), 6.63 s (1H, 4-H, thiazole), 7.03 t (2H, C_6H_4, J = 8.4 Hz), 7.21 d.d (2H, C_6H_4, J = 5.7 Hz). Found, %: C 57.67; H 4.17; N 13.16. $C_{10}H_9FN_2S$. Calculated, %: C 57.67; H 4.36; N 13.45.

2-Amino-5-(4-chlorobenzyl)-1,3-thiazole (IIIf). Yield 88%, mp 122–124°C. ^{1}H NMR spectrum, δ, ppm: 3.88 s (2H, CH_2), 6.62 s (2H, NH_2), 6.64 s (1H, 4-H, thiazole), 7.21 d (2H, C_6H_4), 7.27 d (2H, C_6H_4, J = 7.2 Hz). Found, %: C 53.33; H 3.97; N 12.50. $C_{10}H_9ClN_2S$. Calculated, %: C 53.45; H 4.04; N 12.47.

2-Amino-5-(4-bromobenzyl)-1,3-thiazole (IIIg). Yield 84%, mp 123–125°C. ^{1}H NMR spectrum, δ, ppm: 3.86 s (2H, CH_2), 6.61 s (2H, NH_2), 6.64 s (1H, 4-H, thiazole), 7.15 d (2H, C_6H_4), 7.42 d (2H, C_6H_4, J = 8.1 Hz). Found, %: C 44.38; H 3.38; N 10.26. $C_{10}H_9BrN_2S$. Calculated, %: C 44.62; H 3.37; N 10.41.

2-Amino-5-(3-trifluoromethylbenzyl)-1,3-thiazole (IIIh). Yield 77%, mp 121–123°C. ^{1}H NMR spectrum, δ, ppm: 3.97 s (2H, CH_2), 6.45 s (2H, NH_2), 6.60 s (1H, 4-H, thiazole), 7.40–7.50 m (4H, C_6H_4). Found, %: C 51.10; H 3.56; N 10.62. $C_{11}H_9F_3N_2S$. Calculated, %: C 51.16; H 3.51; N 10.85.

2-Amino-5-(2,3-dichlorobenzyl)-1,3-thiazole (IIIi). Yield 79%, mp 126–128°C. ^{1}H NMR spectrum, δ, ppm: 4.01 s (2H, CH_2), 6.68 s (1H, 4-H, thiazole), 6.73 s (2H, NH_2), 7.26–7.36 m (2H, C_6H_3), 7.47 d.d (1H, C_6H_3, ^4J = 1.2, ^3J = 7.8 Hz). Found, %: C 46.09; H 3.05; N 10.80. $C_{10}H_8Cl_2N_2S$. Calculated, %: C 46.35; N 3.11; N 10.81.

2-Amino-5-(2,4-dichlorobenzyl)-1,3-thiazole (IIIj). Yield 91%, mp 112–113°C. ^{1}H NMR spectrum, δ, ppm: 3.99 s (2H, CH_2), 6.70 s (1H, 4-H, thiazole), 6.79 s (2H, NH_2), 7.38 m (2H, C_6H_3), 7.60 d (1H, C_6H_3). Found, %: C 46.51; H 3.14; N 10.55. $C_{10}H_8Cl_2N_2S$. Calculated, %: C 46.35; H 3.11; N 10.81.

2-Amino-5-(2,5-dichlorobenzyl)-1,3-thiazole (IIIk). Yield 85%, mp 124–125°C. ^{1}H NMR spectrum, δ, ppm: 3.98 s (2H, CH_2), 6.67 s (1H, 4-H, thiazole), 6.69 s (2H, NH_2), 7.26 d.d (1H, C_6H_3, ^4J = 2.4, ^3J = 8.7 Hz), 7.34 d (1H, C_6H_3, J = 2.4 Hz), 7.40 d (1H, C_6H_3, J = 8.7 Hz). Found, %: C 46.27; H 2.97; N 10.58. $C_{10}H_8Cl_2N_2S$. Calculated, %: C 46.35; H 3.11; N 10.81.

2-Amino-5-(3,4-dichlorobenzyl)-1,3-thiazole (IIIl). Yield 83%, mp 92–94°C. ^{1}H NMR spectrum, δ, ppm: 3.90 s (2H, CH_2), 6.67 s (3H, 4-H, thiazole, NH_2), 7.17 d.d (1H, C_6H_3, ^4J = 1.8, ^3J = 8.4 Hz), 7.40 d (1H, C_6H_3), 7.47 d (1H, J = 8.4 Hz). Found, %: C 46.08; H 3.05; N 10.97. $C_{10}H_8Cl_2N_2S$. Calculated, %: C 46.35; H 3.11; N 10.81.

2-Amino-5-(4-difluoromethylsulfanylbenzyl)-1,3-thiazole (IIIm). Yield 74%, mp 78–80°C. ^{1}H NMR spectrum, δ, ppm: 3.94 s (2H, CH_2), 6.74 s (1H, 4-H, thiazole), 6.78 s (2H, NH_2), 7.44 t (1H, $SCHF_2$, J_{FH} = 56 Hz), 7.31 d (2H, C_6H_4), 7.51 d (2H, C_6H_4, J = 8.0 Hz). Found, %: C 48.18; H 3.69; N 10.25. $C_{11}H_{10}F_2N_2S_2$. Calculated, %: C 48.51; H 3.70; N 10.29.

2-Acylamino-5-benzyl-1,3-thiazoles Va–Vo (*general procedure*). *a.* To a solution of 0.01 mol of 2-aminothiazole **III** and 1 ml of triethylamine in 30 ml

of anhydrous dioxane we added under stirring 0.01 mol of the corresponding acid chloride. The mixture was left to stand for 0.5 h and diluted with water, and the precipitate was filtered off, washed with water, and recrystallized from alcohol, DMF, or their mixture.

b. A mixture of 0.01 mol of acylthiourea **IV** and 0.01 mol of aldehyde **II** in 20 ml of ethanol was heated for 1.5–2 h under reflux. The mixture was cooled, diluted with 100 ml of water, and made alkaline by adding aqueous ammonia. The oily residue was repeatedly treated with water and alcohol, and the precipitate was filtered off and recrystallized.

***N*-[5-(4-Fluorobenzyl)-1,3-thiazol-2-yl]acetamide (Va).** Yield 86%, mp 184–185°C. ^{1}H NMR spectrum, δ, ppm: 2.11 s (3H, Me), 4.05 s (2H, CH_2), 7.10 s (1H, 4-H, thiazole), 7.05 t (2H, C_6H_4), 7.21–7.30 m (2H, C_6H_4), 11.82 br.s (1H, NH). Found, %: N 10.95; S 12.78. $C_{12}H_{11}FN_2OS$. Calculated, %: N 11.19; S 12.81.

***N*-[5-(2,5-Dichlorobenzyl)-1,3-thiazol-2-yl]acetamide (Vb).** Yield 77%, mp 186–187°C. ^{1}H NMR spectrum, δ, ppm: 2.11 s (3H, Me), 4,16 s (2H, CH_2), 7.15 s (1H, 4-H, thiazole), 7.28 d.d (1H, C_6H_3), 7.39–7.46 m (2H, C_6H_3), 11.88 br.s (1H, NH). Found, %: N 9.19; S 10.53. $C_{12}H_{10}Cl_2N_2OS$. Calculated, %: N 9.30; S 10.65.

***N*-[5-(2,3-Dichlorobenzyl)-1,3-thiazol-2-yl]pentanamide (Vc).** Yield 75%, mp 141–142°C. ^{1}H NMR spectrum, δ, ppm: 0.93 t (3H, Me), 1.37 sext (2H, CH_2), 1.61 quint (2H, CH_2), 2.39 t (2H, CH_2CO), 4.23 s (2H, CH_2), 7.11 s (1H, 4-H, thiazole), 7.22–7.35 m (2H, C_6H_3), 7.43 d (1H, C_6H_3), 11.68 br.s (1H, NH). Found, %: N 8.03; S 9.27. $C_{15}H_{16}Cl_2N_2OS$. Calculated, %: N 8.16; S 9.34.

***N*-[5-(2,5-Dichlorobenzyl)-1,3-thiazol-2-yl]-4-methylbutanamide (Vd).** Yield 56%, mp 134–136°C. ^{1}H NMR spectrum, δ, ppm: 0.96 d (6H, Me), 2.11 m (1H, CH), 2.28 d (2H, CH_2CO), 4.17 s (2H, CH_2), 7.12 s (1H, 4-H, thiazole), 7.26 m (1H, C_6H_3), 7.35–7.44 m (2H, C_6H_3), 11.69 br.s (1H, NH). Found, %: N 7.99; S 9.40. $C_{15}H_{16}Cl_2N_2OS$. Calculated, %: N 8.16; S 9.34.

***N*-[5-(4-Methoxybenzyl)-1,3-thiazol-2-yl]heptanamide (Ve).** Yield 59%, mp 135–136°C. ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, Me), 1.32 br.s (6H, CH_2), 1.61 m (2H, CH_2), 2.36 t (2H, CH_2SO), 3.77 s (3H, MeO), 3.99 s (2H, CH_2), 7.05 s (1H, 4-H, thiazole), 6.81 d (2H, C_6H_4), 7.15 d (2H, C_6H_4), 11.63 br.s (1H, NH). Found, %: N 8.38; S 9.50. $C_{18}H_{24}N_2O_2S$. Calculated, %: N 8.43; S 9.64.

***N*-[5-(4-Fluorobenzyl)-1,3-thiazol-2-yl]tetrahydrofuran-2-carboxamide (Vf).** Yield 65%, mp 127–128°C. ^{1}H NMR spectrum, δ, ppm: 1.80–1.98 m (3H), 2.17 m (1H), 3.80 m (1H), 3.95 m (1H), 4.49 m (1H, tetrahydrofuran), 4.08 s (2H, CH_2), 7.22 s (1H, 4-H, thiazole), 7.10 t (2H, C_6H_4), 7.30 d.d (2H, C_6H_4), 11.57 br.s (1H, NH). Found, %: N 8.97; S 10.39. $C_{15}H_{15}FN_2O_2S$. Calculated, %: N 9.14; S 10.47.

***N*-[5-(3-Trifluoromethylbenzyl)-1,3-thiazol-2-yl]-4-chlorobenzamide (Vg).** Yield 86%, mp 165–166°C. ^{1}H NMR spectrum, δ, ppm: 4.23 s (2H, CH_2), 7.24 s (1H, 4-H, thiazole), 7.47–7.63 m (4H, 3-$CF_3C_6H_4$), 7.51 d (2H, C_6H_4), 8.12 d (2H, C_6H_4), 12.32 br.s (1H, NH). Found, %: N 6.93; S 8.05. $C_{18}H_{12}ClF_3N_2OS$. Calculated, %: N 7.06; S 8.08.

***N*-[5-(4-Chlorobenzyl)-1,3-thiazol-2-yl]furan-2-carboxamide (Vh).** Yield 75%, mp 135–137°C. ^{1}H NMR spectrum, δ, ppm: 4.09 s (2H, CH_2), 7.15–7.48 m (5H, 4-H, thiazole, C_6H_4), 6.70 m (1H, 4-H, furan), 7.55 d (1H, 3-H, furan), 7.97 br.s (1H, 5-H, furan), 12.46 br.s (1H, NH). Found, %: N 8.71; S 10.08. $C_{15}H_{11}ClN_2O_2S$. Calculated, %: N 8.79; S 10.06.

***N*-[5-(4-Methoxybenzyl)-1,3-thiazol-2-yl]thiophene-2-carboxamide (Vi).** Yield 89%, mp 193–194°C. ^{1}H NMR spectrum, δ, ppm: 3.73 s (3H, MeO), 4.03 s (2H, CH_2), 6.88 d (2H, C_6H_4), 7.20 d (2H, C_6H_4), 7.22 m (1H, 4-H, thiophene), 7.27 s (1H, 4-H, thiazole), 7.91 d (1H, 3-H, thiophene), 8.16 d (1H, 5-H, thiophene), 12.48 br.s (1H, NH). Found, %: N 8.28; S 19.31. $C_{16}H_{14}N_2O_2S_2$. Calculated, %: N 8.48; S 19.41.

***N*-[5-(3-Methylbenzyl)-1,3-thiazol-2-yl]-3-(2-methylphenyl)acrylamide (Vj).** Yield 80%, mp 196–198°C. ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, Me), 2.47 s (3H, Me), 4.05 s (2H, CH_2), 6.76 d (1H, CH=), 7.18 s (1H, 4-H, thiazole), 7.03 d (1H), 7.12–7.28 m (6H), 7.58 d (1H, C_6H_4), 7.90 d (1H, CH=), 11.98 br.s (1H, NH). Found, %: N 7.97; S 9.15. $C_{21}H_{20}N_2OS$. Calculated, %: N 8.04; S 9.20.

***N*-[5-(4-Methylbenzyl)-1,3-thiazol-2-yl]-3-(4-ethoxyphenyl)acrylamide (Vk).** Yield 76%, mp 215–217°C. ^{1}H NMR spectrum, δ, ppm: 1.40 t (3H, Me), 2.31 s (3H, Me), 4.02 s (2H, CH_2), 4.10 q (2H, CH_2O), 6.70 d (1H, CH=), 7.12 s (1H, 4-H, thiazole), 7.10 d (2H, 4-MeC_6H_4), 7.15 d (2H, 4-MeC_6H_4), 7.59 d (1H, CH=), 6.90 d (2H, C_6H_4), 7.50 d (2H, C_6H_4), 11.84 br.s (1H, NH). Found, %: N 7.41; S 8.29. $C_{22}H_{22}N_2O_2S$. Calculated, %: N 7.40; S 8.47.

***N*-[5-(4-Methoxybenzyl)-1,3-thiazol-2-yl]-3-(3-trifluoromethylphenyl)acrylamide (Vl).** Yield 81%,

mp 227–228°C. ^{1}H NMR spectrum, δ, ppm: 3.78 s (3H, MeO), 4.04 s (2H, CH_2), 6.99 d (1H, CH=), 7.15 s (1H, 4-H, thiazole), 6.84 d (2H, 4-$MeOC_6H_4$), 7.17 d (2H, 4-$MeOC_6H_4$), 7.72 d (1H, CH=), 7.60–7.69 m (2H, C_6H_4), 7.87 m (2H, C_6H_4), 11.96 br.s (1H, NH). Found, %: N 6.89; S 8.01. $C_{21}H_{17}F_3N_2O_2S$. Calculated, %: N 6.69; S 7.66.

***N*-[5-(4-Chlorobenzyl)-1,3-thiazol-2-yl]-3-(3-trifluoromethylphenyl)acrylamide (Vm).** Yield 75%, mp 228–229°C. ^{1}H NMR spectrum, δ, ppm: 4.10 s (2H, CH_2), 6.99 d (1H, CH=), 7.19 s (1H, 4-H, thiazole), 7.73 d (1H, CH=), 7.24–7.35 m (4H), 7.60–7.69 m (2H), 7.86 m (2H, C_6H_4), 11.97 br.s (1H, NH). Found, %: N 6.39; S 7.50. $C_{20}H_{14}ClF_3N_2OS$. Calculated, %: N 6.62; S 7.58.

***N*-[5-(4-Fluorobenzyl)-1,3-thiazol-2-yl]-3-(4-chlorophenyl)acrylamide (Vn).** Yield 89%, mp 245–246°C. ^{1}H NMR spectrum, δ, ppm: 4.09 s (2H, CH_2), 6.86 d (1H, CH=), 7.16 s (1H, 4-H, thiazole), 7.05 t (2H, 4-FC_6H_4), 7.23–7.33 m (2H, 4-FC_6H_4), 7.42 d (2H, C_6H_4), 7.60 d (2H, C_6H_4), 7.62 d (1H, CH=), 11.94 br.s (1H, NH). Found, %: N 7.25; S 8.56. $C_{19}H_{14}ClFN_2OS$. Calculated, %: N 7.51; S 8.60.

***N*-[5-(4-Chlorobenzyl)-1,3-thiazol-2-yl]-3-(2-furyl)acrylamide (Vo).** Yield 85%, mp 252–253°C. ^{1}H NMR spectrum, δ, ppm: 4.09 s (2H, CH_2), 6.54 m (1H, 4-H, furan), 6.77 d (1H, 3-H, furan), 6.68 d (1H, CH=), 7.16 s (1H, 4-H, thiazole), 7.27 d (2H, C_6H_4), 7.31 d (2H, C_6H_4), 7.45 d (1H, CH=), 7.68 br.s (1H, 5-H, furan), 11,92 br.s (1H, NH). Found, %: N 7.96; S 9.22. $C_{17}H_{13}ClN_2O_2S$. Calculated, %: N 8.12; S 9.30.

***N*-(5-Benzyl-1,3-thiazol-2-yl)phthalimides VIa–VIg**. 2-Aminothiazole **III**, 0.01 mol, was fused with 0.01 mol of phthalic anhydride until water no longer liberated. The melt was ground with alcohol, and the product was recrystallized from DMF.

***N*-[5-(2-Chlorobenzyl)-1,3-thiazol-2-yl]phthalimide (VIa).** Yield 87%, mp 190–192°C. ^{1}H NMR spectrum, δ, ppm: 4.34 s (2H, CH_2), 7.60 s (1H, 4-H, thiazole), 7.27–7.56 m (4H, 2-ClC_6H_4), 7.87–8.03 m (4H, C_6H_4). Found, %: C 60.90; H 3.05. $C_{18}H_{11}ClN_2O_2S$. Calculated, %: C 60.93; H 3.12.

***N*-[5-(4-Chlorobenzyl)-1,3-thiazol-2-yl]phthalimide (VIb).** Yield 82%, mp 177–178°C. ^{1}H NMR spectrum, δ, ppm: 4.24 s (2H, CH_2), 7.36 d (2H, 4-ClC_6H_4), 7.41 d (2H, 4-ClC_6H_4, J = 8.4 Hz), 7.63 s (1H, 4-H, thiazole), 7.91–7.95 m (2H, C_6H_4), 7.97–8.01 m (2H, C_6H_4). Found, %: C 60.74; H 3.16. $C_{18}H_{11}ClN_2O_2S$. Calculated, %: C 60.93; H 3.12.

***N*-[5-(4-Bromobenzyl)-1,3-thiazol-2-yl]phthalimide (VIc).** Yield 86%, mp 193–194°C. ^{1}H NMR spectrum, δ, ppm: 4.22 s (2H, CH_2), 7.30 d (2H, 4-BrC_6H_4), 7.54 d (2H, 4-BrC_6H_4, J = 8.4 Hz), 7.63 s (1H, 4-H, thiazole), 7.91–7.95 m (2H, C_6H_4), 7.96–8.01 m (2H, C_6H_4). Found, %: C 53.85; H 2.71. $C_{18}H_{11}BrN_2O_2S$. Calculated, %: C 54.15; H 2.78.

***N*-[5-(3-Nitrobenzyl)-1,3-thiazol-2-yl]phthalimide (VId).** Yield 79%, mp 222–223°C. ^{1}H NMR spectrum, δ, ppm: 4.43 s (2H, CH_2), 7.70 s (1H, 4-H, thiazole), 7.90–7.95 m (2H, C_6H_4), 7.96–8.01 m (2H, C_6H_4), 7.65 t (1H, 3-$NO_2C_6H_4$, J = 7.6 Hz), 7.83 d (1H, 3-$NO_2C_6H_4$, J = 7.6 Hz), 8.13 d.d (1H, 3-$NO_2C_6H_4$, ^4J = 2.4, ^3J = 8.0 Hz), 8.25 br.s (1H, 3-$NO_2C_6H_4$). Found, %: C 58.88; H 2.97. $C_{18}H_{11}N_3O_4S$. Calculated, %: C 59.17; H 3.03.

***N*-[5-(2,3-Dichlorobenzyl)-1,3-thiazol-2-yl]-phthalimide (VIe).** Yield 80%, mp 142–144°C. ^{1}H NMR spectrum, δ, ppm: 4.40 s (2H, CH_2), 7.38 t (1H, C_6H_3, J = 8.0 Hz), 7.50 d (1H, C_6H_3, J = 7.6 Hz), 7.58 d (1H, C_6H_3, J = 8.0 Hz), 7.63 s (1H, 4-H, thiazole), 7.90–7.94 m (2H, C_6H_4), 7.96–8.01 m (2H, C_6H_4). Found, %: C 55.36; H 2.53. $C_{18}H_{10}Cl_2N_2O_2S$. Calculated, %: C 55.54; H 2.59.

***N*-[5-(2,5-Dichlorobenzyl)-1,3-thiazol-2-yl]-phthalimide (VIf)**. Yield 82%, mp 199–200°C. ^{1}H NMR spectrum, δ, ppm: 4.33 s (2H, CH_2), 7.39 d.d (1H, C_6H_3, ^4J = 2.4, ^3J = 8.0 Hz), 7.52 d (1H, C_6H_3, J = 8.0 Hz), 7.64 d (1H, C_6H_3, J = 2.4 Hz), 7.63 s (1H, 4-H, thiazole), 7.90–7.94 m (2H, C_6H_4), 7.96–8.01 m (2H, C_6H_4). Found, %: C 55.51; H 2.39. $C_{18}H_{10}Cl_2N_2O_2S$. Calculated, %: C 55.54; H 2.59.

***N*-[5-(3-Trifluoromethylbenzyl)-1,3-thiazol-2-yl]-phthalimide (VIg)**. Yield 84%, mp 154–155°C. ^{1}H NMR spectrum, δ, ppm: 4.40 s (2H, CH_2), 7.64 s (1H, 4-H, thiazole), 7.53–7.76 m (4H, 3-$CF_3C_6H_4$), 7.91–7.95 m (2H, C_6H_4), 7.96–8.01 m (2H, C_6H_4). Found, %: C 58.81; H 2.76. $C_{19}H_{11}F_3N_2O_2S$. Calculated, %: C 58.76; H 2.85.

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