Preparation and Root Growth-Inhibitory Activity of *N*-Substituted 2-(2-Chloroacetamido)-3-(furan-2-yl)propanamides

Tokujiro KITAGAWA* and Makoto ASADA

Faculty of Pharmaceutical Sciences and High Technology Research Center, Kobe Gakuin University; Ikawadani, Nishi-ku, Kobe 651–2180, Japan. Received March 10, 2005; accepted May 23, 2005

A series of *N*-substituted 2-(2-chloroacetamido)-3-(furan-2-yl)propanamides (16—18) was prepared through the reaction of chloroacetyl chloride with *N*-substituted 2-amino-3-(furan-2-yl)propanamides (15), which were obtained *via* condensation of 2-(*tert*-butoxycarbonylamido)-3-(furan-2-yl)propanoic acid (Boc-furylalanine) (8) with amines (9, 11, 13), followed by hydrolysis of the resultant *N*-substituted Boc-furylalanine acid amides (10, 12, 14) in the presence of HCl/dioxane. The biological activity of the prepared 16, 17 and 18 as root growth inhibitors was examined by germination assay using rape seed. At the concentration of 5.0×10^{-5} M, the most active compound, 2-(2-chloroacetamido)-*N*-(2,6-diethylphenyl)-3-(furan-2-yl)propanamide (16n), showed potent root growth-inhibitory activity of 76% towards rape seedlings.

Key words furylalanine; chloroacetamide; herbicidal activity; propanoic acid; plant growth regulator

The application of herbicides or plant growth regulators to crop production is considered essential for the efficiency of the agricultural economy.[1] For example, chloroacetamide herbicides, such as acetochlor (**1**), alachlor (**2**), and dimethenamide-P (**3**), are widely used for weed management in corn production to promote sustainable agriculture.[2] S-Metolachlor (**4**), which is the S-isomer of metolachlor, shows growth inhibition of seedling-shoots and root tissues soon after germination.[3]

Agrochemical-related furan derivatives, 3-(furan-2-yl)-propanamides (**5a**) and 3-(furan-2-yl)propanoates (**5b**), have been synthesized and found to have moderate phytogrowth-inhibitory activity.[4] It has been suggested that the asymmetric carbon at the 2-position of 2-substituted propionic acids such as 2-(2,4-dichlorophenoxy)propanoic acid (2,4-DP, **6b**) plays a key role in the root-withering of perennial weeds, because of its significance in translocation of herbicides within plants.[5]

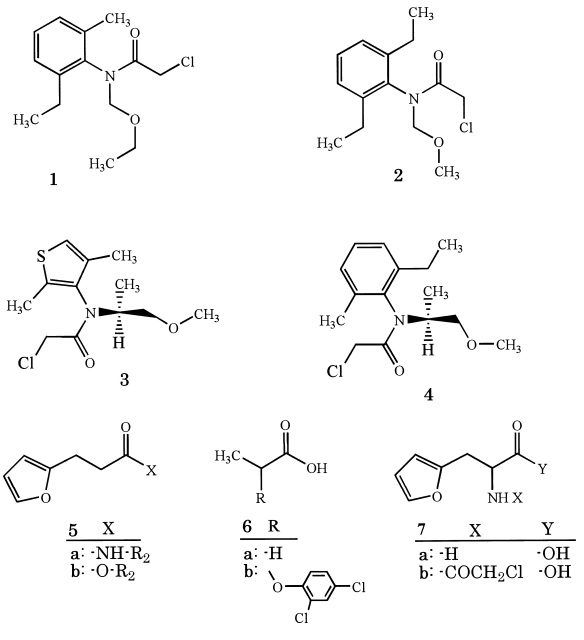


Chart 1

Recently, we developed an improved preparation of racemic 2-amino-3-(furan-2-yl)propanoic acid (furylalanine) (**7a**),[6] and we used the same approach for synthesis of 2-(chloroacetamido)-3-(furan-2-yl)propanoic acid [*N*-(chloroacetyl)furylalanine] (**7b**) for the evaluation of plant growth-inhibitory activity. We found that **7b** inhibited the root growth of rape seedlings by about 51% at the concentration of 1.0×10^{-4} M.[7] As a continuation of that work, we have investigated the biological activity of various *N*-substituted 2-(2-chloroacetamido)-3-(furan-2-yl)propanamides (**16**—**18**).

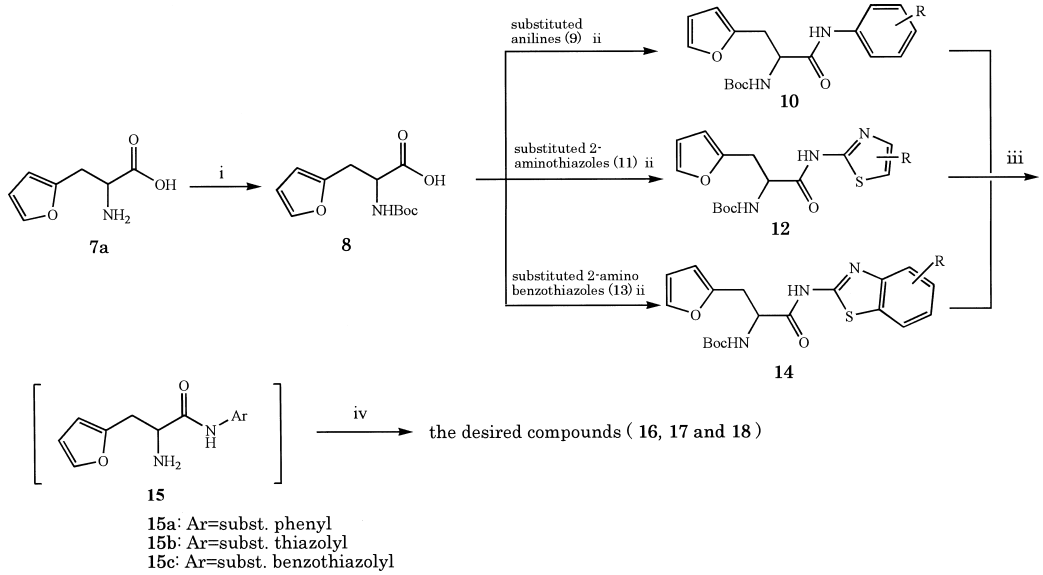
Here, we report the preparation of the acid amides **16**, **17** and **18**, and the results of examination of their root growth-inhibitory activity in rape seedlings.

Preparation of *N*-Substituted 2-(2-Chloroacetamido)-3-(furan-2-yl)propanamides (16—18) The key intermediate in this work was racemic 2-amino-3-(furan-2-yl)propanoic acid (furylalanine) (**7a**), which was synthesized in 77% yield by the reduction of 3-(furan-2-yl)-2-(hydroxyimino)propanoic acid with zinc dust and formic acid in the presence of a catalytic amount of iron dust at 60 °C for 2 h.[6] Protection of the amino nitrogen of the furylalanine (**7a**) with *tert*-butoxycarbonyl (Boc) using di-*tert*-butyl dicarbonate [$(Boc)_2O$], and activation of the carboxylic acid of **7a** using 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide·hydrochloride (EDCI·HCl), followed by condensation with amines (**9**, **11**, **13**), provided the corresponding acid amides (**16**—**18**), as shown in Table 1.

The reaction of 3- or 4-halogen-substituted anilines with 2-(*tert*-butoxycarbonylamido)-3-(furan-2-yl)propanoic acid (Boc-furylalanine) (**8**)[8] give the corresponding *N*-substituted Boc-furylalanine acid amides (**10a**, **c**—**d**, **f**—**g**, **i**—**p**) in 37—98% yield. However, when 2-fluoro- (**9b**), 2-chloro- (**9e**) or 2-bromoanilines (**9h**) were used as the amine component, the desired Boc-furylalanine acid amides (**10b**, **e**, **h**) were not obtained owing to the weaker nucleophilicity of the amines. On the other hand, alkyl substituted anilines such as 2-ethylaniline (**9k**), 2,6-diethylaniline (**9n**), 2-ethyl-6-methylaniline (**9o**) or 2,6-dimethylaniline (**9p**) reacted smoothly with Boc-furylalanine (**8**) to afford the corresponding Boc-furylalanine acid amides (**10k**, **n**—**p**).

We also selected 2-aminothiazoles (**11**) and 2-aminoben-

* To whom correspondence should be addressed. e-mail: kitagawa@pharm.kobegakuin.ac.jp



Reagents and conditions: (i) $(Boc)_2O$, 5 °C, 10 min, and then r.t., 1 h, (ii) EDCI·HCl, r.t., overnight, (iii) 4 N HCl/dioxane, r.t., 4 h, (iv) $ClCH_2COCl$, r.t., overnight.

Chart 2. Preparation of *N*-Substituted 2-(2-Chloroacetamido)-3-(furan-2-yl)propanamides (**16**—**18**)

zothiazoles (**13**) as heteroaromatic amines to prepare the corresponding Boc-furylalanine acid amides (**12**, **14**), because we have suggested that the thiazole nucleus is a "magic radical"[9] for high root growth-inhibitory activity, based on the fact pointed out by Yamabe[9] that the thiazole ring is found as a partial substructure of drugs such as bleomycins,[10] used as anticancer agents, and ceftazidime,[11] a third-generation cephalosporin antibiotic, as well as in herbicides such as thiazopyr[12] and methabenzthiazuron[13] used as pre- and post-emergence herbicides for crops.

Removal of the Boc group of the Boc-furylalanine acid amides (**10**, **12**, **14**) with dioxane/HCl, followed by condensation of chloroacetyl chloride in the presence of triethylamine gave the desired *N*-substituted 2-(chloroacetamido)-3-(furan-2-yl)propanamides (**16**—**18**).

Root Growth-Inhibitory Activity This activity was assayed according to the reported procedure[14] using seeds of rape, *Brassica campestris* L. (Brassicaceae), as a dicotyledon. The root length (in millimeters) of the seedlings was measured and averaged for each group. The herbicide 2,4-dichlorophenoxyacetic acid (2,4-D, **19**) was used as a positive control. The results are summarized in Table 1.

At the concentration of 5.0×10^{-5} M, the chlorine-substituted test compounds, namely *N*-(3-chlorophenyl)- (**16f**) and *N*-(4-chlorophenyl)propanamide (**16g**), showed inhibition percentages of 30% and 19%, respectively, but contrary to our expectation, these values were lower than the value of 52% of the unchlorinated *N*-phenylpropanamide (**16a**). The fluorinated anilides (**16c**—**d**) and brominated anilides (**16i**—**j**) were also less active than **16a**. Thus, introduction of halogens on the phenyl ring of **16a** does not enhance the inhibitory activity.

Next, we examined the effect of alkyl groups, which function as an electron-donating substituents, on the phenyl ring of the *N*-phenylpropanamide (**16a**). The 2-ethyl- (**16k**), 3-ethyl- (**16l**) and *N*-(4-ethylphenyl)propanamide (**16m**) showed 20%, 35% and 41% inhibitory activity, again being less potent than the unsubstituted phenyl compound (**16a**). In the series of 2,6-dialkylated phenyl derivatives with methyl–methyl, ethyl–methyl, and ethyl–ethyl substitution, the 2,6-diethylphenyl derivative (**16n**) showed 76% inhibitory activity, which is close to that of 2,4-D (**19**) used as a positive control. The inhibitory activity of the 2,6-disubstituted *N*-phenylpropanamides (**16n**—**p**) was in the following order; 2,6-diethyl- (**16n**)>2-ethyl-6-methyl- (**16o**)>2,6-dimethyl- (**16p**). Thus, ethyl substitution at the 2 and 6 positions of the phenyl ring of the *N*-(phenyl)propanamide (**16a**) seems to be prerequisite for high root growth-inhibitory activity in rape seedlings. It is noteworthy that **16n** is structurally similar to herbicides such as acetochlor (**1**) and alachlor (**2**), as shown in Chart 1.

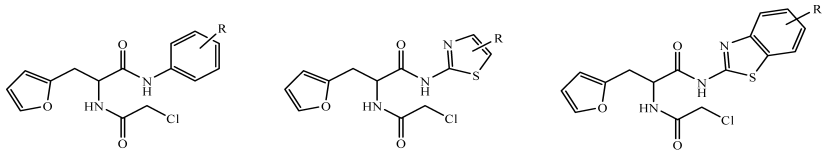
Among the thiazole derivatives (**17a**—**g**), the *N*-(thiazol-2-yl)propanamide (**17a**) showed 57% inhibitory activity, being slightly greater active than the corresponding *N*-phenylpropanamide (**16a**). Among the other substituted thiazole compounds (**17b**—**g**), *N*-(5-bromothiazol-2-yl)propanamide (**17b**) showed 69% inhibitory activity. *N*-(5-Nitrothiazol-2-yl)propanamide (**17c**), *N*-(4-methylthiazol-2-yl)propanamide (**17d**) and the corresponding 5-methylthiazole derivative (**17e**) showed 20—56% inhibitory activity. Thus, nitro and methyl groups did not enhance the inhibitory activity in comparison with the *N*-(thiazol-2-yl)propanamide (**17a**).

Finally, the *N*-(benzthiazol-2-yl)propanamides (**18a**—**c**) showed 34—58% inhibitory activity, *i.e.*, almost same potency as the *N*-(phenyl)propanamide (**16a**) and the *N*-(thiazole-2-yl)propanamide (**17a**).

In conclusion, application of traditional amidation methodology to the *C*-terminal and *N*-terminal of racemic 2-amino-3-(furan-2-yl)propanoic acid (**7a**) smoothly gave the desired *N*-substituted 2-(chloroacetamido)-3-(furan-2-yl)propanamides (**16**—**18**) as shown in Chart 2. Preliminary examination of the root growth-inhibitory activity revealed that 2-(2-chloroacetamido)-*N*-(2,6-diethylphenyl)-3-(furan-2-yl)propanamide (**16n**) inhibited the root growth of rape seedlings by about 76% at the concentration of 5.0×10^{-5} M. The two ethyl substituents at the 2 and 6 positions of the

Table 1. Root Growth-Inhibitory Activities of *N*-Substituted 2-(Chloroacetamido)-3-(furan-2-yl)propanamides (**16**—**18**) and Related Compounds (2,4-D: **19**)

Dicotyledoneae, Rape; *Brassica campestris* L.
Growth (mm)[a)]



16 **17** **18**

No.	R	Phenyl series			No.	R	Thiazole series		
		Control	5.0×10^{-5} M	Inhibition (%)[c)]			Control	5.0×10^{-5} M	Inhibition (%)[c)]
16a	H	40±11.1	19±5.4**	52	**17a**	H	40±10.6	17±7.8**	57
16c	3-F	42±13.1	28±12.9**	33	**17b**	5-Br	46±18.1	14±9.8**	69
16d	4-F	45±10.3	28±16.2**	37	**17c**	5-NO_2	40±18.4	25±14.9**	37
16f	3-Cl	43±21.2	30±9.9*	30	**17d**	4-Me	41±13.3	18±10.2**	56
16g	4-Cl	42±15.9	34±7.6*	19	**17e**	5-Me	43±13.0	34±11.2*	20
16i	3-Br	42±16.1	24±13.6**	42	**17f**	4,5-Me	44±14.4	33±12.7*	25
16j	4-Br	41±12.9	29±10.0**	29	**17g**	4-(4-Cl-Ph)	42±15.1	20±14.9**	52
16k	2-Et	40±13.8	32±11.7**	20			Benzothiazole series		
16l	3-Et	40±13.6	26±13.7**	35	**18a**	H	41±18.4	17±9.3**	58
16m	4-Et	39±10.2	23±10.1**	41	**18b**	4-Cl	42±18.6	24±17.3**	42
16n	2,6-diEt	46±16.6	11±2.8**	76	**18c**	6-EtO	41±14.1	27±9.7**	34
16o	2-Et-6-Me	40±17.7	13±7.0**	67			Positive control		
16p	2,6-diMe	40±12.7	15±11.7**	62	**19**	2,4-D[b)]	41±19.0	1±0.7**	97

a) The values represent mean±S.D. of 20 seeds after 7 d. Significant differences from the corresponding control level are shown: * and ** indicate $p<0.05$ and $p<0.01$, respectively. Light intensity: 127 μmol·m^{-2}·s^{-1}. Temperature 25 °C. Relative humidity 60%. Experimental size: 10 seeds/group, 2 groups. *b*) 2,4-Dichlorophenoxyacetic acid (2,4-D; **19**) was used as a positive control. *c*) % inhibition=[(mean value of control−mean value at the concentration (M) of 1.0×10^{-4})/mean value of control]×100.

phenyl ring of **16n** seem to be prerequisite for potent root growth-inhibitory activity towards rape seedlings.

Experimental

$(Boc)_2O$, EDCI·HCl, amines (**9**, **11**, **13**), 1-hydroxybenzotriazole, chloroacetyl chloride, and triethylamine were purchased from commercial sources and used as received. 2-Amino-3-(2-furyl)propanoic acid (**7a**) was prepared as previously described.[6)] Melting points were taken on a Yanagimoto melting point apparatus. All melting points are uncorrected. IR spectra were measured on an Avata model 320 FT-IR spectrometer. ^{1}H-NMR spectra were measured on a Bruker DPX-400 spectrometer (400 MHz) using tetramethylsilane as an internal reference, and chemical shifts were recorded as delta-values.

2-(*tert*-Butoxycarbonylamido)-3-(furan-2-yl)propanoic Acid (8)[8)] The procedure of Bladon[15)] was employed with some modifications. Racemic furylalanine (**7a**, 15.5 g, 0.1 mol) was suspended in dioxane and water (2 : 1, 300 ml), then cooled to *ca.* 5 °C, and 1 M sodium hydroxide (100 ml) was further added. $(Boc)_2O$ (24 g, 0.11 mol) was added and the resultant mixture was stirred at 5 °C for 10 min and then at room temperature for 1 h. The solvent was evaporated, and the residue was taken up in water and acidified to between pH 2 and 3 with 5% sodium hydrogen sulfate. The solution was extracted with ethyl acetate (3×100 ml) and the combined organic phases were washed with water, dried sodium sulfate and evaporated to yield the Boc-furylalanine (**8**) (23 g, 92%), which was purified by recrystallization from a mixture of AcOEt–cyclohexane; mp 82—84 °C (mp 78.5—80 °C).[8)] IR (single bounce ART): 1728 (acid CO) and 1686 (amide CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.35 (s, 9H, –Boc), 2.89—2.95 (dd, 1H, J=15.23, 9.64 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=15.15, 4.79 Hz, one proton of furan–$\underline{CH_2}$–), 4.14—4.20 (td, 1H, J=8.96, 4.91 Hz, –$CH_2\underline{CH}$–), 6.13—6.14 (d, 1H, J=2.97 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.00, 1.89 Hz, furan-4H), 7.06—7.08 (d, 1H, J=8.27 Hz, –$\underline{NH}$Boc), 7.52 (d, 1H, J=1.05 Hz, furan-5H) and 12.66 (br s, 1H, –COOH).

General Procedure for *tert*-Butyl 1-(Phenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10a) The procedure of Bladon[15)] was employed with some modifications. To a solution of the Boc-furylalanine (**8**, 2.6 g, 10 mmol), 1-hydroxybenzotriazole (1.4 g, 10 mmol) and aniline (**9a**, 0.93 g, 10 mmol) in methylene chloride (180 ml) was added EDCI·HCl (2.7 g, 14 mmol) for the mixture was stirred overnight at room temperature, then the solvent was removed *in vacuo*, and the residue was poured onto ice and extracted with ethyl acetate. Washing of the ethyl acetate extract with 10% citric acid, 4% sodium hydroxide and brine, followed by drying with sodium sulfate and evaporation of the solvent left 1.6 g (48%) of the crude product (**10a**). Recrystallization from a mixture of toluene and cyclohexane gave **10a** of mp 120—122 °C. IR (single bounce ART): 3303 (NH), 1683 and 1666 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.91—2.97 (dd, 1H, J=9.14, 15.10 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=5.30, 14.94 Hz, one proton of furan–$\underline{CH_2}$–), 4.38—4.43 (m, 1H, –$CH_2\underline{CH}$–), 6.16—6.17 (bd, 1H, J=2.84 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=2.88, 1.95 Hz, furan-4H), 7.03—7.07 (t, 1H, J=7.39 Hz, benzene-4H), 7.09 (bd, 1H, –$\underline{NH}$Boc), 7.28—7.32 (t, 2H, J=7.96 Hz, benzene-3,5H), 7.52 (bd, 1H, furan-5H), 7.57—7.60 (dd, 2H, J=8.60, 1.09 Hz, benzene-2,6H), 10.03 (s, 1H, –CONH–). *Anal.* Calcd for $C_{18}H_{22}N_2O_4$: C, 65.43; H, 6.71; N, 8.48. Found: C, 65.29; H, 6.50; N, 8.52.

***tert*-Butyl 1-(3-Fluorophenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10c)** 90% yield, mp 141—143 °C. IR (single bounce ART): 3259 (NH), 1674 and 1659 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.91—2.97 (dd, 1H, J=15.07, 9.16 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=15.06, 5.32 Hz, one proton of furan–$\underline{CH_2}$–), 4.36—4.42 (td, 1H, J=8.51, 5.63 Hz, –$CH_2\underline{CH}$–), 6.17 (bd, 1H, furan-3H), 6.35 (bd, 1H, furan-4H), 6.86—6.90 (m, 1H, benzene-4H), 7.14—7.16 (d, 1H, J=7.93 Hz, –$\underline{NH}$Boc), 7.30—7.37 (m, 2H, benzene-2,5H), 7.53 (bd, 1H, furan-5H), 7.57—7.60 (m, 1H, benzene-6H), 10.27 (s, 1H, –CONH–). *Anal.* Calcd for: $C_{18}H_{21}FN_2O_4$: C, 62.06; H, 6.08; N, 8.04, Found: C, 61.96; H, 5.96; N, 8.03.

***tert*-Butyl 1-(4-Fluorophenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10d)** 97% yield, mp 120—121 °C. IR (single bounce ART): 3310 (NH), 1683 and 1666 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.90—2.96 (dd, 1H, J=15.14, 9.26 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=14.96, 5.45 Hz, one proton of furan–$\underline{CH_2}$–), 4.37—4.38 (m, 1H, –$CH_2\underline{CH}$–), 6.17 (bd, 1H, furan-3H), 6.34—6.35 (dd, 1H, J=2.89, 2.01 Hz, furan-4H), 7.12—7.16 (t, 2H, J=8.93 Hz, benzene-3,5H), 7.52 (bd, 1H, furan-5H), 7.58—7.62 (m, 2H, benzene-2,6H), 10.09 (s, 1H, –CONH–). *Anal.* Calcd for $C_{18}H_{21}FN_2O_4$: C, 62.06; H, 6.08; N, 8.04. Found: C, 61.98; H, 6.04; N, 8.05.

***tert*-Butyl 1-(3-Chlorophenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10f)** 37% yield, mp 114—116 °C, IR (single bounce ART): 3271 (NH), 1666 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.91—2.97

(dd, 1H, J=15.06, 9.00 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=15.01, 5.35 Hz, one proton of furan–$\underline{CH_2}$–), 4.37—4.39 (m, 1H, –$CH_2\underline{CH}$–), 6.17 (bd, 1H, furan-3H), 6.34 (bd, 1H, furan-4H), 7.10—7.13 (dt, 1H, J=7.91, 1.05 Hz, benzene-4H), 7.14—7.16 (d, 1H, J=8.10 Hz, –$\underline{NH}$Boc), 7.31—7.36 (t, 1H, J=8.08 Hz, benzene-5H), 7.45—7.47 (bd, 1H, J=8.25 Hz, benzene-6H), 7.53 (bd, 1H, furan-5H), 7.81 (t, 1H, J=1.85 Hz, benzene-2H), 10.25 (s, 1H, –CONH–). *Anal.* Calcd for $C_{18}H_{21}ClN_2O_4$: C, 59.26; H, 5.80; N, 7.68. Found: C, 59.08; H, 5.88; N, 7.65.

***tert*-Butyl 1-(4-Chlorophenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10g)** 80% yield, mp 171—172 °C, IR (single bounce ART): 3303 (NH), 1683 and 1666 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.91—2.96 (dd, 1H, J=15.09, 9.08 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=15.05, 5.26 Hz, one proton of furan–$\underline{CH_2}$–), 4.36—4.41 (m, 1H, –$CH_2\underline{CH}$–), 6.16—6.17 (bd, 1H, J=2.83 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=2.90, 1.94 Hz, furan-4H), 7.11—7.13 (d, 1H, J=8.06 Hz, –$\underline{NH}$Boc), 7.35—7.37 (d, 2H, J=8.93 Hz, benzene-3,5H), 7.52 (bd, 1H, furan-5H), 7.61—7.63 (d, 2H, J=8.98 Hz, benzene-2,6H), 10.18 (s, 1H, –CONH–). *Anal.* Calcd for $C_{18}H_{21}ClN_2O_4$: C, 59.26; H, 5.80; N, 7.68. Found: C, 59.52; H, 5.84; N, 7.72.

***tert*-Butyl 1-(3-Bromophenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10i)** 91% yield, mp 126—127 °C, IR (single bounce ART): 3304 (NH), 1670 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.90—2.96 (dd, 1H, J=15.13, 9.04 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=15.08, 5.52 Hz, one proton of furan–$\underline{CH_2}$–), 4.36—4.38 (m, 1H, –$CH_2\underline{CH}$–), 6.17 (bd, 1H, furan-3H), 6.34 (bd, 1H, furan-4H), 7.14—7.16 (d, 1H, J=7.78 Hz, –$\underline{NH}$Boc), 7.23—7.29 (m, 2H, benzene-4,5H), 7.49—7.51 (m, 1H, benzene-6H), 7.53 (bd, 1H, furan-5H), 7.94 (s, 1H, benzene-2H), 10.23 (s, 1H, –CONH–). *Anal.* Calcd for $C_{18}H_{21}BrN_2O_4$: C, 52.82; H, 5.17; N, 6.85. Found: C, 52.92; H, 5.14; N, 6.91.

***tert*-Butyl 1-(4-Bromophenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10j)** 79% yield, mp 188—189 °C, IR (single bounce ART): 3304 (NH), 1683 and 1666 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.90—2.96 (dd, 1H, J=15.08, 9.07 Hz, one proton of furan–$\underline{CH_2}$–), 3.00—3.05 (dd, 1H, J=15.07, 5.44 Hz, one proton of furan–$\underline{CH_2}$–), 4.37—4.39 (m, 1H, –CH_2CH–), 6.16 (bd, 1H, J=2.65 Hz, furan-3H), 6.33—6.35 (dd, 1H, J=2.97, 1.86 Hz, furan-4H), 7.11—7.13 (d, 1H, J=8.15 Hz, –$\underline{NH}$Boc), 7.47—7.50 (d, 2H, J=8.95 Hz, benzene-3,5H), 7.52 (bd, 1H, furan-5H), 7.56—7.58 (d, 2H, J=8.99 Hz, benzene-2,6H), 10.18 (s, 1H, –CONH–). *Anal.* Calcd for $C_{18}H_{21}BrN_2O_4$: C, 52.82; H, 5.17; N, 6.85. Found: C, 52.66; H, 5.09; N, 6.89.

***tert*-Butyl 1-(2-Ethylphenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10k)** 76% yield, mp 131—133 °C, IR (single bounce ART): 3299 (NH), 1686 and 1664 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.07—1.11 (t, 3H, J=7.53 Hz, –$CH_2\underline{CH_3}$), 1.30 (s, 9H, –Boc), 2.51—2.56 (q, 2H, J=7.48 Hz, –$\underline{CH_2}CH_3$), 2.94—3.00 (dd, 1H, J=15.10, 8.73 Hz, one proton of furan–$\underline{CH_2}$–), 3.07—3.12 (dd, 1H, J=15.27, 5.70 Hz, one proton of furan–$\underline{CH_2}$–), 4.44—4.45 (m, 1H, –$CH_2\underline{CH}$–), 6.20 (bd, 1H, furan-3H), 6.37—6.38 (bd, 1H, furan-4H), 7.11—7.18 (m, 3H, benzene-4,5H and –$\underline{NH}$Boc), 7.21—7.23 (dd, 1H, J=6.49, 2.35 Hz, benzene-3H), 7.28—7.31 (dd, 1H, J=7.02, 2.06 Hz, benzene-6H), 7.55 (bd, 1H, furan-5H), 9.34 (s, 1H, –CONH–). *Anal.* Calcd for $C_{20}H_{26}N_2O_4$: C, 67.01; H, 7.31; N, 7.82. Found: C, 67.14; H, 7.28; N, 7.77.

***tert*-Butyl 1-(3-Ethylphenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10l)** 98% yield, mp 123—124 °C, IR (single bounce ART): 3310 (NH), 1680 and 1663 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.16—1.19 (t, 3H, J=7.59 Hz, –$CH_2\underline{CH_3}$), 1.37 (s, 9H, –Boc), 2.55—2.61 (q, 2H, J=7.58 Hz, –$\underline{CH_2}CH_3$), 2.90—2.97 (dd, 1H, J=15.07, 9.18 Hz, one proton of furan–$\underline{CH_2}$–), 3.01—3.06 (dd, 1H, J=15.04, 5.40 Hz, one proton of furan–$\underline{CH_2}$–), 4.37—4.43 (td, 1H, J=8.65, 5.26 Hz, –$CH_2\underline{CH}$–), 6.17—6.18 (d, 1H, J=2.71 Hz, furan-3H), 6.35—6.36 (dd, 1H, J=2.92, 1.89 Hz, furan-4H), 6.90—6.92 (bd, 1H, J=8.13 Hz, benzene-4H), 7.06—7.08 (d, 1H, J=8.21 Hz, –$\underline{NH}$Boc), 7.19—7.23 (t, 1H, J=7.80 Hz, benzene-5H), 7.41—7.43 (d, 1H, J=8.01 Hz, benzene-6H), 7.45 (bd, 1H, furan-5H), 7.53 (s, 1H, benzene-2H), 10.00 (s, 1H, –CONH–). *Anal.* Calcd for $C_{20}H_{26}N_2O_4$: C, 67.01; H, 7.31; N, 7.82. Found: C, 66.88; H, 7.24; N, 7.79.

***tert*-Butyl 1-(4-Ethylphenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10m)** 69% yield, mp 165—166 °C, IR (single bounce ART): 3299 (NH), 1682 and 1663 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.13—1.17 (t, 3H, J=7.57 Hz, –$CH_2\underline{CH_3}$), 1.36 (s, 9H, –Boc), 2.52—2.58 (q, 2H, J=7.56 Hz, –$\underline{CH_2}CH_3$), 2.90—2.96 (dd, 1H, J=14.88, 9.30 Hz, one proton of furan–$\underline{CH_2}$–), 3.00—3.05 (dd, 1H, J=15.00, 5.32 Hz, one proton of furan–$\underline{CH_2}$–), 4.38—4.40 (m, 1H, –CH_2CH–), 6.16 (bd, 1H, furan-3H), 6.34—6.35 (bd, 1H, J=1.87 Hz, furan-4H), 7.04—7.06 (d, 1H, J=8.31 Hz, –$\underline{NH}$Boc), 7.12—7.14 (d, 2H, J=8.47 Hz, benzene-3,5H), 7.47—7.49 (d, 2H, J=8.48 Hz, benzene-2,6H), 7.52 (bd, 1H, furan-5H), 9.94 (s, 1H, –CONH–). *Anal.* Calcd for $C_{20}H_{26}N_2O_4$: C, 67.01; H, 7.31; N, 7.82. Found: C, 66.94; H, 7.34; N, 7.77.

***tert*-Butyl 1-(2,6-Diethylphenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10n)** 83% yield, mp 195—196 °C, IR (single bounce ART): 3297 (NH), 1683 and 1661 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.02—1.06 (t, 6H, J=7.55 Hz, –CH_3×2), 1.39 (s, 9H, –Boc), 2.39—2.44 (q, 4H, J=7.49 Hz, –$\underline{CH_2}CH_3$×2), 2.93—2.99 (dd, 1H, J=15.11, 9.18 Hz, one proton of furan–$\underline{CH_2}$–), 3.06—3.11 (dd, 1H, J=15.04, 5.92 Hz, one proton of furan–$\underline{CH_2}$–), 4.44—4.50 (td, 1H, J=8.73, 5.80 Hz, –$CH_2\underline{CH}$–), 6.22 (bd, 1H, J=2.72 Hz, furan-3H), 6.37—6.39 (dd, 1H, J=3.04, 1.92 Hz, furan-4H), 7.05—7.07 (d, 1H, J=7.55 Hz, –$\underline{NH}$Boc), 7.07 (m, 1H, benzene-4H), 7.12—7.18 (m, 2H, benzene-3,5H), 7.55—7.56 (d, 1H, J=1.03 Hz, furan-5H), 9.35 (s, 1H, –CONH–). *Anal.* Calcd for $C_{22}H_{30}N_2O_4$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.29; H, 7.92; N, 7.32.

***tert*-Butyl 1-(2-Ethyl-6-methylphenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10o)** 41% yield, mp 179—180 °C, IR (single bounce ART): 3291 and 3221 (NH), 1683 and 1661 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.02—1.06 (t, 3H, J=7.53 Hz, –$CH_2\underline{CH_3}$), 1.38 (s, 9H, –Boc),2.06 (s, 3H, –CH_3), 2.41—2.46 (q, 2H, J=7.45 Hz, –$\underline{CH_2}CH_3$), 2.94—3.00 (dd, 1H, J=15.10, 9.08 Hz, one proton of furan–$\underline{CH_2}$–), 3.07—3.13 (dd, 1H, J=15.16, 5.85 Hz, one proton of furan–$\underline{CH_2}$–), 4.43—4.48 (td, 1H, J=8.65, 5.86 Hz, –$CH_2\underline{CH}$–), 6.21—6.22 (bd, 1H, J=3.09 Hz, furan-3H), 6.37—6.38 (dd, 1H, J=2.98, 1.90 Hz, furan-4H), 7.04—7.14 (m, 4H, benzene-3,4,5H and –$\underline{NH}$Boc), 7.55 (bd, 1H, J=0.94 Hz, furan-5H), 9.36 (s, 1H, –CONH–). *Anal.* Calcd for: $C_{21}H_{28}N_2O_4$: C, 67.72; H, 7.58; N, 7.52. Found: C, 67.74; H, 7.32; N, 7.65.

***tert*-Butyl 1-(2,6-Dimethylphenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (10p)** 85% yield, mp 160—162 °C, IR (single bounce ART): 3297 and 3246, 1685 and 1657 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.31 (s, 9H, –Boc), 2.07 (s, 6H, –CH_3×2), 2.94—3.00 (dd, 1H, J=15.12, 9.00 Hz, one proton of furan–$\underline{CH_2}$–), 3.08—3.13 (dd, 1H, J=15.15, 5.88 Hz, one proton of furan–$\underline{CH_2}$–), 4.40—4.46 (td, 1H, J=8.62, 5.86 Hz, –$CH_2\underline{CH}$–), 6.21—6.22 (bd, 1H, J=3.13 Hz, furan-3H), 6.36—6.38 (dd, 1H, J=2.86, 2.50 Hz, furan-4H), 7.03—7.05 (m, 3H, benzene-3,4,5H), 7.11—7.13 (d, 1H, J=8.24 Hz, –$\underline{NH}$Boc), 7.55 (bd, 1H, furan-5H), 9.36 (s, 1H, –CONH–). *Anal.* Calcd for $C_{20}H_{26}N_2O_4$: C, 67.01; H, 7.31; N, 7.82. Found: C, 66.99; H, 7.18; N, 7.73.

***tert*-Butyl 1-(Thiazol-2-ylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (12a)** 91% yield, mp 199—201 °C, IR (single bounce ART): 3316 (NH), 1715 and 1685 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc) 2.93—2.99 (dd, 1H, J=9.19, 15.01 Hz, one proton of furan–CH_2–), 3.02—3.07 (dd, 1H, J=5.39, 15.07 Hz, one proton of furan–$\underline{CH_2}$–), 4.53—4.54 (m, 1H, –$CH_2\underline{CH}$–), 6.17 (bd, 1H, furan-3H), 6.34—6.35 (dd, 1H, furan-4H), 7.20 (d, 1H, J=3.55 Hz, thiazol-5H), 7.5 (d, 1H, J=3.55 Hz, thiazol-4H), 7.52 (bd, 1H, furan-5H). *Anal.* Calcd for $C_{15}H_{19}N_3O_4S$: C, 53.39; H, 5.68; N, 12.46. Found: C, 53.27; H, 5.67; N, 12.25.

***tert*-Butyl 1-(5-Bromothiazol-2-ylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (12b)** 75% yield, mp 130—132 °C, IR (single bounce ART): 3341 (NH), 1690 and 1665 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.35 (s, 9H, –Boc), 2.92—2.98 (dd, 1H, J=14.95, 8.81 Hz, one proton of furan–$\underline{CH_2}$–), 3.03—3.08 (dd, 1H, J=15.28, 5.32 Hz, one proton of furan–$\underline{CH_2}$–), 4.44—4.45 (m, 1H, –$CH_2\underline{CH}$–), 6.14 (bd, 1H, furan-3H), 6.33 (bd, 1H, furan-4H), 7.11—7.12 (d, 1H, J=7.53 Hz, –CONH–), 7.50 (s, 1H, thiazol-4H), 7.50 (bd, 1H, furan-5H). *Anal.* Calcd for $C_{15}H_{18}BrN_3O_4S$: C, 43.27; H, 4.36; N, 10.10. Found: C, 43.26; H, 4.30; N, 9.91.

***tert*-Butyl 1-(5-Nitrothiazol-2-ylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (12c)** 85% yield, mp 170—172 °C, IR (single bounce ART): 3265 (NH), 1686 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.95—3.02 (dd, 1H, J=15.12, 9.35 Hz, one proton of furan–$\underline{CH_2}$–), 3.06—3.11 (dd, 1H, J=15.36, 5.52 Hz, one proton of furan–$\underline{CH_2}$–), 4.54—5.46 (m, 1H, –$CH_2\underline{CH}$–), 5.62 (bd, 1H, furan-3H), 6.34—6.36 (dd, 1H, J=3.03, 1.78 Hz, furan-4H) 7.52 (bd, 1H, furan-5H), 8.63 (s, 1H, thiazol-4H), 8.79 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{18}N_4O_6S$: C, 47.11; H, 4.74; N, 14.65. Found: C, 47.02; H, 4.69; N, 14.84.

***tert*-Butyl 1-(4-Methylthiazol-2-ylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (12d)** 60% yield, mp 90—92 °C, IR (single bounce ART): 3291 3284 (NH), 1690 and 1664 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.35 (s, 9H, –Boc), 2.26 (d, 3H, J=0.81 Hz, –CH_3), 2.95—3.02 (m, 2H, one proton of furan–$\underline{CH_2}$–), 4.51 (m, 1H, –$CH_2\underline{CH}$–), 6.17 (bd, 1H, furan-3H), 6.34—6.35 (dd, 1H, J=2.96, 1.87 Hz, furan-4H), 6.76 (d, 1H, J=1.01 Hz, thiazol-5H), 7.52 (bd, 1H, furan-5H). *Anal.* Calcd for $C_{16}H_{21}N_3O_4S$: C, 54.68; H, 6.02; N,

11.96. Found: C, 54.59; H, 5.99; N, 11.75.

***tert*-Butyl 1-(5-Methylthiazol-2-ylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (12e)** 87% yield, mp 143—144 °C, IR (single bounce ART): 3338 (NH), 1714 and 1682 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.35 (s, 9H, –Boc), 2.34 (d, 3H, J=1.27 Hz, $-CH_3$), 2.91—2.97 (dd, 1H, J=14.83, 9.19 Hz, one proton of furan–$\underline{CH_2}$–), 3.00—3.05 (dd, 1H, J=15.06, 5.39 Hz, one proton of furan–$\underline{CH_2}$–) 4.49—4.51 (m, 1H, –$CH_2\underline{CH}$–), 6.16 (bd, 1H, furan-3H), 6.33—6.35 (dd, 1H, J=3.03, 1.88 Hz, furan-4H), 7.13 (d, 1H, J=1.29 Hz, thiazol-4H), 7.18—7.20 (d, 1H, J=7.94 Hz, –CONH–). *Anal.* Calcd for $C_{16}H_{21}N_3O_4S$: C, 54.68; H, 6.02; N, 11.96. Found: C, 54.48; H, 5.83; N, 11.85.

***tert*-Butyl 1-(4,5-Dimethylthiazol-2-ylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (12f)** 85% yield, mp 149—151 °C, IR (single bounce ART): 3225 (NH), 1710 and 1662 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.35 (s, 9H, –Boc), 2.15 (d, 3H, J=0.76 Hz, $-CH_3$), 2.23 (d, 3H, J=0.76 Hz, $-CH_3$), 2.90—2.96 (dd, 1H, J=14.92, 8.87 Hz, one proton of furan–$\underline{CH_2}$–), 2.99—3.05 (dd, 1H, J=14.88, 5.44 Hz, one proton of furan–$\underline{CH_2}$–), 4.47—4.48 (m, 1H, –$CH_2\underline{CH}$–), 6.15 (bd, 1H, furan-3H), 6.33—6.34 (bd, 1H, furan-4H), 7.14—7.16 (d, 1H, J=7.97 Hz, –CONH–), 7.52 (bd, 1H, furan-5H). *Anal.* Calcd for $C_{17}H_{23}N_3O_4S$: C, 55.87; H, 6.34; N, 11.50. Found: C, 55.67; H, 6.27; N, 11.51.

***tert*-Butyl 1-(4-(4-Chlorophenyl)thiazol-2-ylcarbamoyl)-2-(furan-2-yl)-ethylcarbamate (12g)** 77% yield, mp 217—219 °C, IR (single bounce ART): 3316 (NH), 1670 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 2.95—3.09 (m, 2H, furan–$\underline{CH_2}$–), 4.55 (m, 1H, –$CH_2\underline{CH}$–), 6.19 (bd, 1H, furan-3H), 6.35—6.36 (dd, 1H, J=2.89, 1.92 Hz, furan-4H), 7.49—7.51 (dd, 2H, J=6.69, 1.93 Hz, benzene-2,6H), 7.53 (bd, 1H, furan-5H), 7.70 (s, 1H, thiazol-5H), 7.91—7.93 (dd, 2H, J=6.68, 1.93 Hz, benzene-3,5H). *Anal.* Calcd for $C_{21}H_{22}ClN_3O_4S$: C, 56.30; H, 4.95; N, 9.38. Found: C, 56.21; H, 4.95; N, 9.32.

***tert*-Butyl 1-(Benzo[*d*]thiazol-2-ylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (14a)** 95% yield, mp 203—205 °C, IR (single bounce ART): 3299 (NH), 1670 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.37 (s, 9H, –Boc), 2.98—3.04 (dd, 1H, J=9.02, 15.14 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.14 (dd, 1H, J=5.4, 15.11 Hz, one proton of furan–$\underline{CH_2}$–), 4.55—4.56 (m, 1H, –$CH_2\underline{CH}$–), 6.18 (bd, 1H, furan-3H), 6.34—6.35 (bd, 1H, furan-4H), 7.27—7.45 (m, 2H, benzothiazole-5,6H), 7.52 (bd, 1H, furan-5H), 7.72—7.74 (d, 1H, J=7.7 Hz, benzothiazole-7H), 7.95—8.00 (d, 1H, J=7.77 Hz, benzothiazole-4H). *Anal.* Calcd for $C_{19}H_{21}N_3O_4S$: C, 58.89; H, 5.46; N, 10.85. Found: C, 58.81; H, 5.57; N, 10.71.

***tert*-Butyl 1-(4-Chlorobenzo[d]thiazol-2-ylcarbamoyl)-2-(furan-2-yl)-ethylcarbamate (14b)** 79% yield, mp 172—174 °C, IR (single bounce ART): 3327 (NH), 1659 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.36 (s, 9H, –Boc), 3.01—3.09 (m, 2H, one proton of furan–$\underline{CH_2}$–), 4.55 (m, 1H, –$CH_2\underline{CH}$–), 6.20 (bd, 1H, furan-3H), 6.34—6.36 (dd, 1H, J=3.09, 1.88 Hz, furan-4H), 7.29—7.33 (t, 1H, J=7.89 Hz, benzothiazole-6H), 7.53 (bd, 1H, furan-5H), 7.53—7.55 (dd, 1H, J=7.84, 1.06 Hz, benzothiazole-5H), 7.61—7.64 (dd, 1H, J=7.81, 1.12 Hz, benzothiazole-7H), 7.97—7.99 (d, 1H, J=7.03 Hz, –CONH–). *Anal.* Calcd for $C_{19}H_{20}ClN_3O_4S$: C, 54.09; H, 4.78; N, 9.96. Found: C, 54.21; H, 4.64; N, 9.76.

***tert*-Butyl 1-(6-Ethoxybenzo[*d*]thiazol-2-ylcarbamoyl)-2-(furan-2-yl)-ethylcarbamate (14c)** 98% yield, mp 199—201 °C, IR (single bounce ART): 3303 (NH), 1671 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.18 (t, 3H, J=6.78 Hz, $-CH_2\underline{CH_3}$), 1.36 (s, 9H, –Boc), 2.95—3.07 (m, 2H, furan–$\underline{CH_2}$–), 4.04—4.10 (q, 2H, J=6.97 Hz, $-\underline{CH_2}CH_3$), 4.55 (m, 1H, –$CH_2\underline{CH}$–), 6.19 (bd, 1H, furan-3H), 6.34—6.35 (dd, 1H, J=3.01, 1.93 Hz, furan-4H), 7.01—7.03 (dd, 1H, J=8.84, 2.58 Hz, benzothiazole-5H), 7.53 (bd, 1H, furan-5H), 7.55—7.56 (d, 1H, J=2.53 Hz, benzothiazole-7H), 7.62—7.64 (d, 1H, J=8.84 Hz, benzothiazole-4H). *Anal.* Calcd for $C_{21}H_{25}N_3O_5S$: C, 58.45; H, 5.84; N, 9.74. Found: C, 58.01; H, 5.87; N, 9.51.

General Procedure for 2-(2-Chloroacetamido)-3-(furan-2-yl)-*N*-phenylpropanamide (16a) The procedure of Sheehan[16] was employed with some modifications. To 4 N hydrochloric acid/dioxane (25 ml) was added *tert*-butyl 1-(phenylcarbamoyl)-2-(furan-2-yl)ethylcarbamate (**10a**, 1.65 g, 5 mmol) in a single portion with vigorous stirring. The mixture was stirred for 4 h at room temperature, and the solvent was removed *in vacuo* to give an oily residue. To a mixture of the oily residue and chloroacetyl chloride (0.5 g, 5 mmol) suspended in ethylene chloride (5 ml) at 0—5 °C was added slowly a solution of triethylamine (1.3 ml) in ethylene chloride (5 ml). After the addition was completed, the resultant mixture was brought rapidly to the boiling point and then allowed to stand overnight. The solvent was removed *in vacuo*, and the residue was poured onto ice and extracted with ethyl acetate. Washing of the ethyl acetate extract with 2% hydrochloric acid and brine, followed by drying under sodium sulfate and evaporation of the solvent left 0.6 g (40%) of the crude product (**8a**). Recrystallization from a mixture of ether and ethyl acetate gave **16a** of mp 150—152 °C. IR (single bounce ART): 3265 (NH), 1650 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.97—3.03 (dd, 1H, J=8.32, 15.21 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.16 (dd, 1H, J=15.24, 5.97 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, $-CH_2Cl$), 4.73—4.78 (td, 1H, J=8.10, 5.92 Hz, –$CH_2\underline{CH}$–), 6.17—6.18 (d, 1H, J=3.14 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.11, 1.88 Hz, furan-4H), 7.05—7.09 (t, 1H, J=7.39 Hz, benzene-4H), 7.29—7.33 (t, 2H, J=7.91 Hz, benzene-3,5H), 7.52 (bd, 1H, J=1.80 Hz, furan-5H), 7.57—7.59 (d, 2H, J=7.59 Hz, benzene-2,6H), 8.61—8.63 (d, 1H, J=8.07 Hz, –$\underline{NH}COCH_2Cl$), 10.19 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{15}ClN_2O_3$: C, 58.73; H, 4.93; N, 9.13. Found: C, 58.76; H, 4.79; N, 9.13.

2-(2-Chloroacetamido)-*N*-(3-fluorophenyl)-3-(furan-2-yl)propanamide (16c) 64% yield, mp 150—153 °C, IR (single bounce ART): 3284 (NH), 1690 and 1649 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.97—3.03 (dd, 1H, J=15.24, 8.39 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.15 (dd, 1H, J=15.13, 5.90 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, $-CH_2Cl$), 4.70—4.76 (td, 1H, J=8.23, 5.83 Hz, –$CH_2\underline{CH}$–), 6.17—6.18 (d, 1H, J=3.14 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.05, 1.94 Hz, furan-4H), 6.88—6.92 (m, 1H, benzene-4H), 7.30—7.38 (m, 2H, benzene-2,5H), 7.52—7.53 (bd, 1H, furan-5H), 7.56—7.59 (m, 1H, benzene-6H), 8.65—8.67 (d, 1H, J=7.88 Hz, –$\underline{NH}COCH_2Cl$), 10.42 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{14}ClFN_2O_3$: C, 55.48; H, 4.35; N, 8.63. Found: C, 55.39; H, 4.28; N, 8.68.

2-(2-Chloroacetamido)-*N*-(4-fluorophenyl)-3-(furan-2-yl)propanamide (16d) 42% yield, mp 160—161 °C, IR (single bounce ART): 3265 (NH), 1652 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.97—3.03 (dd, 1H, J=15.21, 8.32 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.14 (dd, 1H, J=15.24, 6.01 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (d, 2H, J=0.57 Hz, $-CH_2Cl$), 4.70—4.75 (td, 1H, J=8.14, 5.93 Hz, –$CH_2\underline{CH}$–), 6.17 (dd, 1H, J=3.17, 0.71 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.17, 1.87 Hz, furan-4H), 7.13—7.18 (t, 2H, J=8.94 Hz, benzene-3,5H), 7.52 (bd, 1H, furan-5H), 7.58—7.61 (m, 2H, benzene-2,6H), 8.62—8.64 (d, 1H, J=7.97 Hz, –$\underline{NH}COCH_2Cl$), 10.24 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{14}ClFN_2O_3$: C, 55.48; H, 4.35; N, 8.63. Found: C, 55.27; H, 4.37; N, 8.80.

2-(2-Chloroacetamido)-*N*-(3-chlorophenyl)-3-(furan-2-yl)propanamide (16f) 68% yield, mp 155—157 °C, IR (single bounce ART): 3278 (NH), 1651 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.97—3.03 (dd, 1H, J=15.18, 8.33 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.15 (dd, 1H, J=15.11, 5.94 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, $-CH_2Cl$), 4.69—4.75 (td, 1H, J=8.08, 5.96 Hz, –$CH_2\underline{CH}$–), 6.17—6.18 (bd, 1H, furan-3H), 6.34—6.35 (dd, 1H, J=3.13, 1.86 Hz, furan-4H), 7.12—7.15 (m, 1H, benzene-4H), 7.33—7.37 (t, 1H, J=8.09 Hz, benzene-5H), 7.44—7.47 (m, 1H, benzene-6H), 7.53 (bd, 1H, furan-5H), 7.78—7.79 (t, 1H, J=1.99 Hz, benzene-2H), 8.65—8.66 (d, 1H, J=7.83 Hz, –$\underline{NH}COCH_2Cl$), 10.37 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{14}Cl_2N_2O_3$: C, 52.80; H, 4.14; N, 8.21. Found: C, 52.68; H, 4.17; N, 8.22.

2-(2-Chloroacetamido)-*N*-(4-chlorophenyl)-3-(furan-2-yl)propanamide (16g) 73% yield, mp 170—171 °C, IR (single bounce ART): 3276 (NH), 1653 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.97—3.03 (dd, 1H, J=15.29, 8.34 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.14 (dd, 1H, J=15.15, 5.88 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, $-CH_2Cl$), 4.70—4.76 (td, 1H, J=8.08, 5.88 Hz, –$CH_2\underline{CH}$–), 6.16—6.17 (dd, 1H, J=3.19, 0.76 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.18, 1.87 Hz, furan-4H), 7.36—7.38 (d, 2H, J=8.96 Hz, benzene-3,5H), 7.52 (dd, 1H, J=1.87, 0.86 Hz, furan-5H), 7.60—7.62 (d, 2H, J=8.98 Hz, benzene-2,6H), 8.64—8.66 (d, 1H, J=7.95 Hz, –$\underline{NH}COCH_2Cl$), 10.33 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{14}Cl_2N_2O_3$: C, 52.80; H, 4.14; N, 8.21. Found: C, 52.73; H, 4.11; N, 8.27.

***N*-(3-Bromophenyl)-2-(2-chloroacetamido)-3-(furan-2-yl)propanamide (16i)** 56% yield, mp 151—153 °C, IR (single bounce ART): 3278 (NH), 1651 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.97—3.03 (dd, 1H, J=15.19, 8.36 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.15 (dd, 1H, J=15.14, 5.85 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, $-CH_2Cl$), 4.68—4.74 (td, 1H, J=8.12, 5.87 Hz, –$CH_2\underline{CH}$–), 6.17—6.18 (d, 1H, J=3.17 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.10, 1.84 Hz, furan-4H), 7.27—7.29 (m, 2H, benzene-4,5H), 7.48—7.51 (m, 1H, benzene-6H), 7.52—7.53 (bd, 1H, furan-5H), 7.92—7.93 (bd, 1H, benzene-2H), 8.64—8.66 (d, 1H, J=7.82 Hz, –$\underline{NH}COCH_2Cl$), 10.36 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{14}BrClN_2O_3$: C, 46.71; H, 3.66; N, 7.27. Found: C, 46.51; H, 3.71; N, 7.21,

***N*-(4-Bromophenyl)-2-(2-chloroacetamido)-3-(furan-2-yl)propanamide (16j)** 52% yield, mp 190—192 °C, IR (single bounce ART): 3276

(NH), 1652 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.97—3.03 (dd, 1H, J=15.25, 8.34 Hz, one proton of furan–$\underline{CH_2}$–), 3.07—3.14 (dd, 1H, J=15.11, 5.76 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, –CH_2Cl), 4.70—4.76 (td, 1H, J=8.10, 5.92 Hz, –$CH_2\underline{CH}$–), 6.16—6.17 (dd, 1H, J=3.17, 0.72 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.17, 1.87 Hz, furan-4H), 7.49—7.50 (d, 2H, J=9.03 Hz, benzene-3,5H), 7.51—7.52 (dd, 1H, J=1.86, 0.86 Hz, furan-5H), 7.55—7.58 (d, 2H, J=9.04 Hz, benzene-2,6H), 8.64—8.66 (d, 1H, J=7.95 Hz, –$\underline{NH}$COCH_2Cl), 10.33 (s, 1H, –CONH–). *Anal.* Calcd for $C_{15}H_{14}BrClN_2O_3$: C, 46.71; H, 3.66; N, 7.27. Found: C, 46.57; H, 3.57; N, 7.21.

2-(2-Chloroacetamido)-*N*-(2-ethylphenyl)-3-(furan-2-yl)propanamide (16k) 59% yield, mp 169—171 °C, IR (single bounce ART): 3265 (NH), 1648 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.06—1.10 (t, 3H, J=7.53 Hz, –$CH_2\underline{CH_3}$), 2.48—2.54 (q, 2H, J=7.49 Hz, –$\underline{CH_2}CH_3$), 3.00—3.06 (dd, 1H, J=15.24, 8.10 Hz, one proton of furan–$\underline{CH_2}$–), 3.12—3.18 (dd, 1H, J=15.22, 6.05 Hz, one proton of furan–$\underline{CH_2}$–), 4.13 (s, 2H, –CH_2Cl), 4.79—4.85 (td, 1H, J=8.03, 6.03 Hz, –$CH_2\underline{CH}$–), 6.20—6.21 (bd, 1H, J=2.93 Hz, furan-3H), 6.37—6.38 (dd, 1H, J=3.11, 1.89 Hz, furan-4H), 7.15—7.27 (m, 4H, benzene-3,4,5,6H), 7.55 (bd, 1H, furan-5H), 8.59—8.61 (d, 1H, J=8.10 Hz, –$\underline{NH}$COCH_2Cl), 9.55 (s, 1H, –CONH–). *Anal.* Calcd for $C_{17}H_{19}ClN_2O_3$: C, 60.98; H, 5.72; N, 8.37. Found: C, 60.79; H, 5.74; N, 8.41.

2-(2-Chloroacetamido)-*N*-(3-ethylphenyl)-3-(furan-2-yl)propanamide (16l) 60% yield, mp 132—133 °C, IR (single bounce ART): 3282 (NH), 1691 and 1649 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.15—1.19 (t, 3H, J=7.59 Hz, –$CH_2\underline{CH_3}$), 2.54—2.60 (q, 2H, J=7.57 Hz, –$\underline{CH_2}CH_3$), 2.96—3.02 (dd, 1H, J=15.24, 8.39 Hz, one proton of furan–$\underline{CH_2}$–), 3.09—3.14 (dd, 1H, J=15.24, 5.74 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (d, 2H, J=0.43 Hz, –CH_2Cl), 4.71—4,76 (td, 1H, J=8.13, 5.82 Hz, –$CH_2\underline{CH}$–), 6.17—6.18 (dd, 1H, J=3.17, 0.70 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.17, 1.87 Hz, furan-4H), 6.91—6.93 (bd, 1H, benzene-4H), 7.19—7.23 (t, 1H, J=7.80 Hz, benzene-5H), 7.39—7.41 (m, 1H, benzene-6H), 7.44 (s, 1H, benzene-2H), 7.52—7.53 (dd, 1H, J=1.85, 0.83 Hz, furan-5H), 8.59—8.60 (d, 1H, J=7.99 Hz, –$\underline{NH}$COCH_2Cl), 10.12 (s, 1H, –CONH–). *Anal.* Calcd for $C_{17}H_{19}N_2O_3$: C, 60.98; H, 5.72; N, 8.37. Found: C, 60.96; H, 5.74; N, 8.45.

2-(2-Chloroacetamido)-*N*-(4-ethylphenyl)-3-(furan-2-yl)propanamide (16m) 74% yield, mp 177—178 °C, IR (single bounce ART): 3278 (NH), 1650 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.13—1.17 (t, 3H, J=7.57 Hz, –$CH_2\underline{CH_3}$), 2.52—2.58 (q, 2H, J=7.56 Hz, –$\underline{CH_2}CH_3$), 2.96—3.02 (dd, 1H, J=15.10, 8.28 Hz, one proton of furan–$\underline{CH_2}$–), 3.08—3.13 (dd, 1H, J=15.29, 5.95 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, –CH_2Cl), 4.71—4.76 (td, 1H, J=8.08, 6.00 Hz, –$CH_2\underline{CH}$–), 6.16—6.17 (d, 1H, J=3.12 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.06, 1.87 Hz, furan-4H), 7.13—7.15 (d, 2H, J=8.42 Hz, benzene-3,5H), 7.47—7.49 (d, 2H, J=8.44 Hz, benzene-2.6H), 7.52 (bd, 1H, furan-5H), 8.59—8.61 (d, 1H, J=8.16 Hz, –$\underline{NH}$COCH_2Cl), 10.10 (s, 1H, –CONH–). *Anal.* Calcd for $C_{17}H_{19}ClN_2O_3$: C, 60.98; H, 5.72; N, 8.37. Found: C, 60.88; H, 5.73; N, 8.42.

2-(2-Chloroacetamido)-*N*-(2,6-diethylphenyl)-3-(furan-2-yl)propanamide (16n) 57% yield, mp 184—185 °C, IR (single bounce ART): 3259 (NH), 1645 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.02—1.06 (t, 6H, J=7.52 Hz, –CH_3×2), 2.40—2.42 (dq, 4H, –$\underline{CH_2}CH_3$×2), 2.98—3.04 (dd, 1H, J=15.09, 8.30 Hz, one proton of furan–$\underline{CH_2}$–), 3.16—3.22 (dd, 1H, J=15.17, 6.11 Hz, one proton of furan–$\underline{CH_2}$–), 4.11 (s, 2H, –CH_2Cl), 4.81—4.86 (td, 1H, J=8.24, 6.11 Hz, –$CH_2\underline{CH}$–), 6.23—6.24 (bd, 1H, J=2.90 Hz, furan-3H), 6.38—6.39 (dd, 1H, J=3.09, 1.89 Hz, furan-4H), 7.06—7.19 (m, 3H, benzene-3,4,5H), 7.56 (bd, 1H, furan-5H), 8.67—8.69 (d, 1H, J=8.29 Hz, –$\underline{NH}$COCH_2Cl), 9.54 (s, 1H, –CONH–), furan-5H), 9.54 (s, 1H, –CONH–). *Anal.* Calcd for $C_{19}H_{23}ClN_2O_3$: C, 62.89; H, 6.39; N, 7.72. Found: C, 62.72; H, 6.24; N, 7.80.

2-(2-Chloroacetamido)-*N*-(2-ethyl-6-methylphenyl)-3-(furan-2-yl)-propanamide (16o) 46% yield, mp 175—178 °C, IR (single bounce ART): 3265 (NH), 1647 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.02—1.06 (t, 3H, J=7.54 Hz, –$CH_2\underline{CH_3}$), 2.05 (s, 3H, –CH_3), 2.39—2.45 (q, 2H, J=7.46 Hz, –$\underline{CH_2}CH_3$), 2.99—3.05 (dd, 1H, J=15.25, 5.96 Hz, one proton of furan–$\underline{CH_2}$–), 3.16—3.22 (dd, 1H, J=15.25, 5.96 Hz, one proton of furan–$\underline{CH_2}$–), 4.11 (s, 2H, –CH_2Cl), 4.79—4.84 (td, 1H, J=8.21, 6.04 Hz, –$CH_2\underline{CH}$–), 6.22—6.23 (bd, 1H, J=3.06 Hz, furan-3H), 6.38—6.39 (dd, 1H, J=3.07, 1.90 Hz, furan-4H), 7.05—7.14 (m, 3H, benzene-3,4,5H), 7.55 (bd, 1H, J=1.47 Hz, furan-5H), 8.63—8.65 (d, 1H, J=8.16 Hz, –$\underline{NH}$COCH_2Cl), 9.52 (s, 1H, –CONH–). *Anal.* Calcd for $C_{18}H_{21}ClN_2O_3$: C, 61.98; H, 6.07; N, 8.03. Found: C, 61.94; H, 5.97; N, 8.02.

2-(2-Chloroacetamido)-3-(furan-2-yl)-*N*-(2,6-dimethylphenyl)propanamide (16p) 55% yield, mp 181—183 °C, IR (single bounce ART): 3265 (NH), 1649 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.06 (s, 6H, –CH_3×2), 2.99—3.05 (dd, 1H, J=15.13, 8.50 Hz, one proton of furan–$\underline{CH_2}$–), 3.16—3.22 (dd, 1H, J=15.23, 5.95 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, –CH_2Cl), 4.76—4.82 (td, 1H, J=7.42, 5.99 Hz, –$CH_2\underline{CH}$–), 6.22 (d, 1H, J=3.02 Hz, furan-3H), 6.37—6.38 (dd, 1H, J=3.09, 1.89 Hz, furan-4H), 7.05—7.07 (m, 3H, benzene-3,4,5H), 7.55 (bd, 1H, J=1.09 Hz, furan-5H), 8.62—8.64 (d, 1H, J=7.92 Hz, –$\underline{NH}$COCH_2Cl), 9.53 (s, 1H, –CONH–). *Anal.* Calcd for $C_{17}H_{19}ClN_2O_3$: C, 60.98; H, 5.72; N, 8.37. Found: C, 61.18; H, 5.66; N, 8.42.

2-(2-Chloroacetamido)-3-(furan-2-yl)-*N*-(thiazol-2-yl)propanamide (17a) 60% yield, mp 145—148 °C, IR (single bounce ART): 3361 (NH), 1669 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.02—3.08 (dd, 1H, J=8.47, 15.33 Hz, one proton of furan–$\underline{CH_2}$–), 3.13—3.18 (dd, 1H, J=5.63, 15.24 Hz, one proton of furan–$\underline{CH_2}$–), 4.13 (s, 2H, –CH_2Cl), 4.81—4.87 (td, 1H, J=5.54, 8.0 Hz, –$CH_2\underline{CH}$–), 6.17—6.18 (bd, 1H, J=3.15 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=1.88, 3.15 Hz, furan-4H), 7.24—7.25 (d, 1H, J=3.56 Hz, thiazol-5H), 7.49 (d, 1H, J=3.56 Hz, thiazol-4H), 7.52 (dd, 1H, J=0.79, 1.83 Hz, furan-5H), 8.66—8.68 (d, 1H, J=7.67 Hz, –CONH–). *Anal.* Calcd for $C_{12}H_{12}ClN_3O_3S$: C, 45.93; H, 3.86; N, 13.40. Found: C, 45.71; H, 3.87; N, 13.29.

2-(2-Chloroacetamido)-*N*-(5-bromothiazol-2-yl)-3-(furan-2-yl)-propanamide (17b) 64% yield, mp 182—184 °C, IR (single bounce ART): 3246 (NH), 1662 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.02—3.08 (dd, 1H, J=15.30, 8.35 Hz, one proton of furan–$\underline{CH_2}$–), 3.12—3.17 (dd, 1H, J=15.32, 5.66 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, –CH_2Cl), 4.78—4.84 (td, 1H, J=7.89, 5.54 Hz, –$CH_2\underline{CH}$–), 6.16—6.17 (dd, 1H, J=3.20, 0.77 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.18, 1.87 Hz, furan-4H), 7.51—7.52 (dd, 1H, J=1.87, 0.85 Hz, furan-5H), 7.59 (s, 1H, thiazol-4H), 8.69—8.71 (d, 1H, J=7.56 Hz, –CONH–). *Anal.* Calcd for $C_{12}H_{11}BrClN_3O_3S$: C, 36.70; H, 2.82; N, 10.70. Found: C, 36.90; H, 2.83; N, 10.58.

2-(2-Chloroacetamido)-3-(furan-2-yl)-*N*-(5-nitrothiazol-2-yl)-propanamide (17c) 53% yield, mp 181—183 °C, IR (single bounce ART): 3208 (NH), 1666 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.05—3.11 (dd, 1H, J=15.36, 8.47 Hz, one proton of furan–$\underline{CH_2}$–), 3.16—3.21 (dd, 1H, J=15.31, 5.54 Hz, one proton of furan–$\underline{CH_2}$–), 4.13 (s, 2H, –CH_2Cl), 4.80—4.86 (m, 1H, –$CH_2\underline{CH}$–), 6.18—6.19 (bd, 1H, J=3.18 Hz, furan-3H), 6.35—6.36 (dd, 1H, J=3.17, 1.87 Hz, furan-4H), 7.52—7.53 (dd, 1H, J=1.86, 0.85 Hz, furan-5H), 8.64 (s, 1H, thiazol-4H), 8.78—8.80 (d, 1H, J=7.16 Hz, –CONH–). *Anal.* Calcd for $C_{12}H_{11}ClN_4O_5S$: C, 40.17; H, 3.09; N, 15.62. Found: C, 40.33; H, 3.26; N, 15.75.

2-(2-Chloroacetamido)-3-(furan-2-yl)-*N*-(4-methylthiazol-2-yl)-propanamide (17d) 65% yield, mp 116—118 °C, IR (single bounce ART): 3197 and 3067 (NH), 1685 and 1659 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.26 (d, 3H, J=0.98 Hz, –CH_3), 3.01—3.07 (dd, 1H, J=15.31, 8.37 Hz, one proton of furan–$\underline{CH_2}$–), 3.11—3.17 (dd, 1H, J=15.30, 5.54 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, –CH_2Cl), 4.77—4.82 (td, 1H, J=7.98, 5.61 Hz, –$CH_2\underline{CH}$–), 6.16—6.17 (bd, 1H, J=2.70 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.17, 1.88 Hz, furan-4H), 6.78 (d, 1H, J=1.07 Hz, thiazol-5H), 7.52 (dd, 1H, J=1.85, 0.80 Hz, furan-5H), 8.62—8.64 (d, 1H, J=7.57 Hz, –CONH–). *Anal.* Calcd for $C_{13}H_{14}ClN_3O_3S$: C, 47.63; H, 4.31; N, 12.82. Found: C, 47.36; H, 4.10; N, 12.66.

2-(2-Chloroacetamido)-3-(furan-2-yl)-*N*-(5-methylthiazol-2-yl)-propanamide (17e) 78% yield, mp 185—187 °C, IR (single bounce ART): 3231 (NH), 1657 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.34 (d, 3H, J=1.20 Hz, –CH_3), 3.00—3.06 (dd, 1H, J=15.23, 8.30 Hz, one proton of furan–$\underline{CH_2}$–), 3.10—3.16 (dd, 1H, J=15.29, 5.74 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, –CH_2Cl), 4.79—4.84 (td, 1H, J=7.97, 5.66 Hz, –$CH_2\underline{CH}$–), 6.16 (bd, 1H, J=3.13 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.16, 1.87 Hz, furan-4H), 7.15 (d, 1H, J=1.28 Hz, thiazol-4H), 7.51—7.52 (dd, 1H, J=1.82, 0.78 Hz, furan-5H), 8.64—8.66 (d, 1H, J=7.69 Hz, –CONH–). *Anal.* Calcd for $C_{13}H_{14}ClN_3O_3S$: C, 47.63; H, 4.31; N, 12.82. Found: C, 47.83; H, 4.33; N, 12.71.

2-(2-Chloroacetamido)-3-(furan-2-yl)-*N*-(4,5-dimethylthiazol-2-yl)-propanamide (17f) 60% yield, mp 128—130 °C, IR (single bounce ART): 3180 (NH), 1697 and 1654 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.15 (s, 3H, –CH_3), 2.23 (s, 3H, –CH_3), 2.99—3.05 (dd, 1H, J=15.31, 8.22 Hz, one proton of furan–$\underline{CH_2}$–), 3.10—3.15 (dd, 1H, J=15.26, 5.33 Hz, one proton of furan–$\underline{CH_2}$–), 4.12 (s, 2H, –CH_2Cl), 4.75—4.81 (td, 1H, J=7.94, 5.73 Hz, –$CH_2\underline{CH}$–), 6.14—6.15 (bd, 1H, J=2.69 Hz, furan-3H), 6.33—6.35 (dd, 1H, J=3.16, 1.87 Hz, furan-4H), 7.51—7.52 (dd, 1H, J=1.85, 0.80 Hz, furan-5H), 8.61—8.63 (d, 1H, J=7.74 Hz, –CONH–). *Anal.* Calcd for $C_{14}H_{16}ClN_3O_3S$: C, 49.19; H, 4.72; N, 12.30. Found: C, 49.27; H, 4.61; N, 12.21.

2-(2-Chloroacetamido)-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-(furan-2-yl)propanamide (17g) 69% yield, mp 191—193 °C, IR (single bounce ART): 3310 (NH), 1645 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.04—3.10 (dd, 1H, J=15.14, 8.65 Hz, furan–$\underline{CH_2}$–), 3.16—3.21 (dd, 1H, J=15.51, 5.51 Hz, furan–$\underline{CH_2}$–), 4.14 (s, 2H, –CH_2Cl), 4.82—4.88 (m, 1H, –$CH_2\underline{CH}$–), 6.19 (bd, 1H, J=3.27 Hz, furan-3H), 6.35—6.36 (dd, 1H, J=3.11, 1.88 Hz, furan-4H), 7.49—7.51 (d, 2H, J=8.65 Hz, benzene-3,5H), 7.53 (bd, 1H, furan-5H), 7.72 (s, 1H, thiazol-5H), 7.91—7.93 (d, 2H, J=8.65 Hz, benzene-2,6H), 8.67—8.69 (d, 1H, J=7.57 Hz, –CONH–). *Anal.* Calcd for $C_{18}H_{15}Cl_2N_3O_3S$: C, 50.95; H, 3.56; N, 9.91. Found: C, 50.93; H, 3.56; N, 9.90.

2-(2-Chloroacetamido)-*N*-(benzo[*d*]thiazol-2-yl)-3-(furan-2-yl)propanamide (18a) 43% yield, mp 168—171 °C, IR (single bounce ART): 3265 (NH), 1656 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.07—3.13 (dd, 1H, J=15.26, 8.31 Hz, one proton of furan–CH_2–), 3.18—3.23 (dd, 1H, J=15.20, 5.60 Hz, one proton of furan–CH_2–), 4.16 (s, 2H, –CH_2Cl), 4.86—4.91 (td, 1H, J=7.94, 5.52 Hz, –$CH_2\underline{CH}$–), 6.19—6.20 (dd, 1H, J=3.18, 0.72 Hz, furan-3H), 6.35—6.36 (dd, 1H, J=3.18, 3.27 Hz, furan-4H), 7.31—7.35 (m, 1H, benzothiazole-6H), 7.44—7.48 (m, 1H, benzothiazole-5H), 7.53 (dd, 1H, J=1.85, 0.85 Hz, furan-5H), 7.76—7.78 (bd, 1H, J=7.65 Hz, benzothiazole-7H), 7.98—8.01 (ddd, 1H, J=7.92, 1.23, 0.60 Hz, benzothiazole-4H), 8.73—8.75 (d, 1H, J=7.57 Hz, –CONH–). *Anal.* Calcd for $C_{16}H_{14}ClN_3O_3S$: C, 52.82; H, 3.88; N, 11.55. Found: C, 52.80; H, 3.85; N, 11.46.

2-(2-Chloroacetamido)-*N*-(4-chlorobenzo[d]thiazol-2-yl)-3-(furan-2-yl)propanamide (18b) 66% yield, mp 181—183 °C, IR (single bounce ART): 3297 (NH), 1701 and 1665 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.08—3.14 (dd, 1H, J=15.27, 8.21 Hz, one proton of furan–$\underline{CH_2}$–), 3.18—3.28 (dd, 1H, J=15.21, 5.58 Hz, one proton of furan–$\underline{CH_2}$–), 4.15 (s, 2H, –CH_2Cl), 4.82—4.88 (m, 1H, –$CH_2\underline{CH}$–), 6.19—6.20 (bd, 1H, J=3.10 Hz, furan-3H), 6.35—6.36 (dd, 1H, J=3.17, 1.87 Hz, furan-4H), 7.30—7.34 (t, 1H, J=7.89 Hz, benzene-5H), 7.52—7.53 (dd, 1H, J=1.85, 0.82 Hz, furan-5H), 7.54—7.56 (dd, 1H, J=7.84, 1.06 Hz, benzothiazole-5H), 7.98—8.00 (dd, 1H, J=7.97, 1.05 Hz, benzothiazole-7H), 8.71—8.73 (d, 1H, J=7.54 Hz, –CONH–). *Anal.* Calcd for $C_{16}H_{13}Cl_2N_3O_3S$: C, 48.25; H, 3.29; N, 10.55. Found: C, 48.27; H, 3.27; N, 10.70.

2-(2-Chloroacetamido)-*N*-(6-ethoxybenzo[*d*]thiazol-2-yl)-3-(furan-2-yl)propanamide (18c) 81% yield, mp 172—174 °C, IR (single bounce ART): 3278 (NH), 1652 (CO) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.33—1.37 (t, 3H, J=6.95 Hz, –$CH_2\underline{CH_3}$), 3.05—3.11 (dd, 1H, J=15.50, 8.45 Hz, one proton of furan–$\underline{CH_2}$–), 3.15—3.21 (dd, 1H, J=15.36, 5.69 Hz, one proton of furan–$\underline{CH_2}$–), 4.05—4.10 (q, 2H, J=6.96 Hz, –$\underline{CH_2}CH_3$), 4.14 (s, 2H, –CH_2Cl), 4.83—4.88 (m, 1H, –$CH_2\underline{CH}$–), 6.18—6.19 (bd, 1H, J=3.15 Hz, furan-3H), 6.34—6.35 (dd, 1H, J=3.14, 1.86 Hz, furan-4H), 7.01—7.04 (dd, 1H, J=8.85, 2.57 Hz, benzothiazole-5H), 7.52—7.53 (dd, 1H, J=1.81, 0.80 Hz, furan-5H), 7.56 (d, 1H, J=2.53 Hz, benzothiazole-7H), 7.63—7.65 (d, 1H, J=8.81 Hz, benzothiazole-4H), 8.70—8.72 (d, 1H, J=7.57 Hz, –CONH–). *Anal.* Calcd for $C_{18}H_{18}ClN_3O_4S$: C, 53.00; H, 4.45; N, 10.30. Found: C, 52.98; H, 4.58; N, 10.21.

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