

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

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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 phyto-growth-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⁾

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-ethyl-aniline (**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-

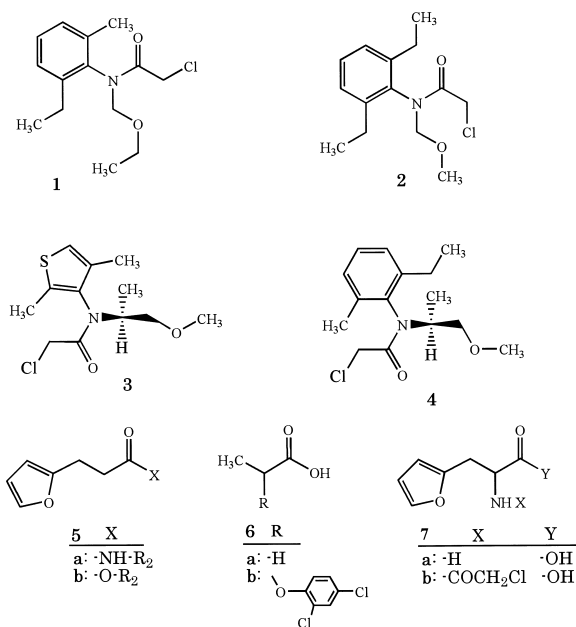
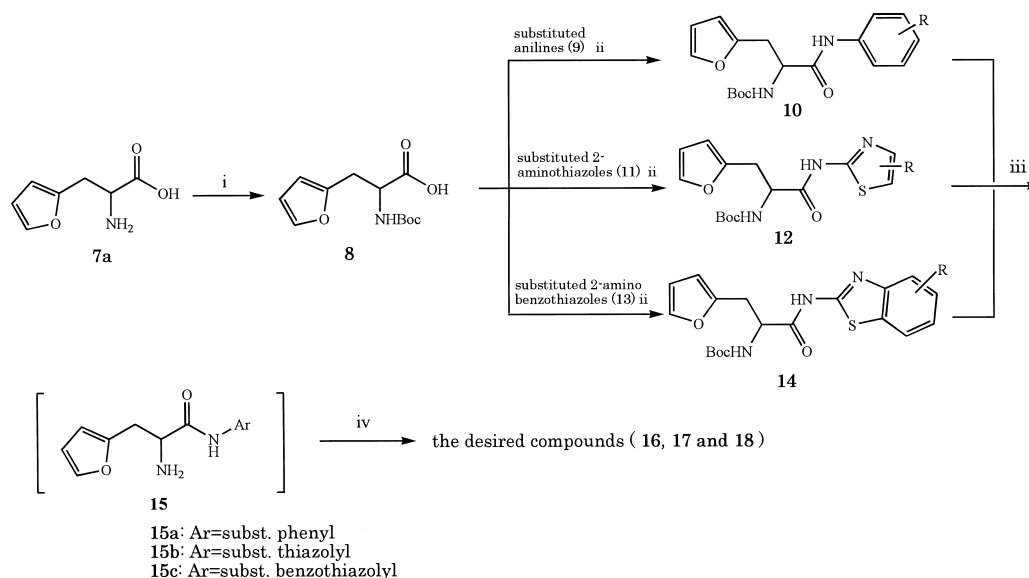


Chart 1

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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) ClCH₂COCl, 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 Yamabe⁹⁾ 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 thiazopyr¹²⁾ and methabenzthiazuron¹³⁾ 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 procedure¹⁴⁾ 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

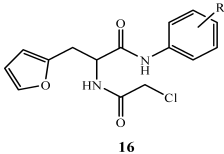
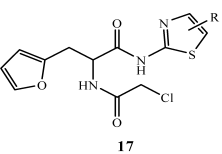
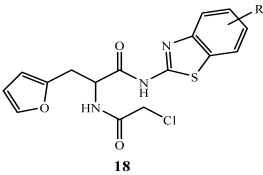
the series of 2,6-dialkylated phenyl derivatives with methyl-methyl, ethyl-methyl, and ethyl-ethyl substitution, the 2,6-diethylphenyl derivative (16n) showed 76% inhibitory activity, which is close to that of 2,4-D (19) used as a positive control. The inhibitory activity of the 2,6-disubstituted *N*-phenylpropanamides (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; <i>Brassica campestris</i> L. Growth (mm) ^{a)}									
									
									
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: $127 \mu\text{mol} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$. 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. ¹H-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 Bladon¹⁵⁾ 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. ¹H-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–CH₂–), 3.01–3.06 (dd, 1H, *J*=15.15, 4.79 Hz, one proton of furan–CH₂–), 4.14–4.20 (td, 1H, *J*=8.96, 4.91 Hz, –CH₂CH–), 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, –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 Bladon¹⁵⁾ 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. ¹H-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–CH₂–), 3.01–3.06 (dd, 1H, *J*=5.30, 14.94 Hz, one proton of furan–CH₂–), 4.38–4.43 (m, 1H, –CH₂CH–), 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, –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 C₁₈H₂₂N₂O₄: 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. ¹H-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–CH₂–), 3.01–3.06 (dd, 1H, *J*=15.06, 5.32 Hz, one proton of furan–CH₂–), 4.36–4.42 (td, 1H, *J*=8.51, 5.63 Hz, –CH₂CH–), 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, –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: C₁₈H₂₁FN₂O₄: 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. ¹H-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–CH₂–), 3.01–3.06 (dd, 1H, *J*=14.96, 5.45 Hz, one proton of furan–CH₂–), 4.37–4.38 (m, 1H, –CH₂CH–), 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 C₁₈H₂₁FN₂O₄: 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. ¹H-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-CH₂-), 3.01—3.06 (dd, 1H, $J=15.01$, 5.35 Hz, one proton of furan-CH₂-), 4.37—4.39 (m, 1H, -CH₂CH-), 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, -NHBoc), 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 C₁₈H₂₁ClN₂O₄: 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. ¹H-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-CH₂-), 3.01—3.06 (dd, 1H, $J=15.05$, 5.26 Hz, one proton of furan-CH₂-), 4.36—4.41 (m, 1H, -CH₂CH-), 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, -NHBoc), 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 C₁₈H₂₁ClN₂O₄: 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. ¹H-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-CH₂-), 3.01—3.06 (dd, 1H, $J=15.08$, 5.52 Hz, one proton of furan-CH₂-), 4.36—4.38 (m, 1H, -CH₂CH-), 6.17 (bd, 1H, furan-3H), 6.34 (bd, 1H, furan-4H), 7.14—7.16 (d, 1H, $J=7.78$ Hz, -NHBoc), 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 C₁₈H₂₁BrN₂O₄: 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. ¹H-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-CH₂-), 3.00—3.05 (dd, 1H, $J=15.07$, 5.44 Hz, one proton of furan-CH₂-), 4.37—4.39 (m, 1H, -CH₂CH-), 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, -NHBoc), 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 C₁₈H₂₁BrN₂O₄: 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. ¹H-NMR (DMSO-*d*₆) δ : 1.07—1.11 (t, 3H, $J=7.53$ Hz, -CH₂CH₃), 1.30 (s, 9H, -Boc), 2.51—2.56 (q, 2H, $J=7.48$ Hz, -CH₂CH₃), 2.94—3.00 (dd, 1H, $J=15.10$, 8.73 Hz, one proton of furan-CH₂-), 3.07—3.12 (dd, 1H, $J=15.27$, 5.70 Hz, one proton of furan-CH₂-), 4.44—4.45 (m, 1H, -CH₂CH-), 6.20 (bd, 1H, furan-3H), 6.37—6.38 (bd, 1H, furan-4H), 7.11—7.18 (m, 3H, benzene-4,5H and -NHBoc), 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 C₂₀H₂₆N₂O₄: 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. ¹H-NMR (DMSO-*d*₆) δ : 1.16—1.19 (t, 3H, $J=7.59$ Hz, -CH₂CH₃), 1.37 (s, 9H, -Boc), 2.55—2.61 (q, 2H, $J=7.58$ Hz, -CH₂CH₃), 2.90—2.97 (dd, 1H, $J=15.07$, 9.18 Hz, one proton of furan-CH₂-), 3.01—3.06 (dd, 1H, $J=15.04$, 5.40 Hz, one proton of furan-CH₂-), 4.37—4.43 (td, 1H, $J=8.65$, 5.26 Hz, -CH₂CH-), 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, -NHBoc), 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 C₂₀H₂₆N₂O₄: 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. ¹H-NMR (DMSO-*d*₆) δ : 1.13—1.17 (t, 3H, $J=7.57$ Hz, -CH₂CH₃), 1.36 (s, 9H, -Boc), 2.52—2.58 (q, 2H, $J=7.56$ Hz, -CH₂CH₃), 2.90—2.96 (dd, 1H, $J=14.88$, 9.30 Hz, one proton of furan-CH₂-), 3.00—3.05 (dd, 1H, $J=15.00$, 5.32 Hz, one proton of furan-CH₂-), 4.38—4.40 (m, 1H, -CH₂CH-), 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,

-NHBoc), 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 C₂₀H₂₆N₂O₄: 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. ¹H-NMR (DMSO-*d*₆) δ : 1.02—1.06 (t, 6H, $J=7.55$ Hz, -CH₃×2), 1.39 (s, 9H, -Boc), 2.39—2.44 (q, 4H, $J=7.49$ Hz, -CH₂CH₃×2), 2.93—2.99 (dd, 1H, $J=15.11$, 9.18 Hz, one proton of furan-CH₂-), 3.06—3.11 (dd, 1H, $J=15.04$, 5.92 Hz, one proton of furan-CH₂-), 4.44—4.50 (td, 1H, $J=8.73$, 5.80 Hz, -CH₂CH-), 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, -NHBoc), 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 C₂₂H₃₀N₂O₄: 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. ¹H-NMR (DMSO-*d*₆) δ : 1.02—1.06 (t, 3H, $J=7.53$ Hz, -CH₂CH₃), 1.38 (s, 9H, -Boc), 2.06 (s, 3H, -CH₃), 2.41—2.46 (q, 2H, $J=7.45$ Hz, -CH₂CH₃), 2.94—3.00 (dd, 1H, $J=15.10$, 9.08 Hz, one proton of furan-CH₂-), 3.07—3.13 (dd, 1H, $J=15.16$, 5.85 Hz, one proton of furan-CH₂-), 4.43—4.48 (td, 1H, $J=8.65$, 5.86 Hz, -CH₂CH-), 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 -NHBoc), 7.55 (bd, 1H, $J=0.94$ Hz, furan-5H), 9.36 (s, 1H, -CONH-). *Anal.* Calcd for C₂₁H₂₈N₂O₄: 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. ¹H-NMR (DMSO-*d*₆) δ : 1.31 (s, 9H, -Boc), 2.07 (s, 6H, -CH₃×2), 2.94—3.00 (dd, 1H, $J=15.12$, 9.00 Hz, one proton of furan-CH₂-), 3.08—3.13 (dd, 1H, $J=15.15$, 5.88 Hz, one proton of furan-CH₂-), 4.40—4.46 (td, 1H, $J=8.62$, 5.86 Hz, -CH₂CH-), 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, -NHBoc), 7.55 (bd, 1H, furan-5H), 9.36 (s, 1H, -CONH-). *Anal.* Calcd for C₂₀H₂₆N₂O₄: 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. ¹H-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-CH₂-), 3.02—3.07 (dd, 1H, $J=5.39$, 15.07 Hz, one proton of furan-CH₂-), 4.53—4.54 (m, 1H, -CH₂CH-), 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 C₁₅H₁₉N₃O₄S: 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. ¹H-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-CH₂-), 3.03—3.08 (dd, 1H, $J=15.28$, 5.32 Hz, one proton of furan-CH₂-), 4.44—4.45 (m, 1H, -CH₂CH-), 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 C₁₅H₁₈BrN₃O₄S: 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. ¹H-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-CH₂-), 3.06—3.11 (dd, 1H, $J=15.36$, 5.52 Hz, one proton of furan-CH₂-), 4.54—4.56 (m, 1H, -CH₂CH-), 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 C₁₅H₁₈N₄O₆S: 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. ¹H-NMR (DMSO-*d*₆) δ : 1.35 (s, 9H, -Boc), 2.26 (d, 3H, $J=0.81$ Hz, -CH₃), 2.95—3.02 (m, 2H, one proton of furan-CH₂-), 4.51 (m, 1H, -CH₂CH-), 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 C₁₆H₂₁N₃O₄S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.35 (s, 9H, -Boc), 2.34 (d, 3H, $J=1.27$ Hz, -CH₃), 2.91–2.97 (dd, 1H, $J=14.83$, 9.19 Hz, one proton of furan-CH₂-), 3.00–3.05 (dd, 1H, $J=15.06$, 5.39 Hz, one proton of furan-CH₂-), 4.49–4.51 (m, 1H, -CH₂CH-), 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 C₁₆H₂₁N₃O₄S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.35 (s, 9H, -Boc), 2.15 (d, 3H, $J=0.76$ Hz, -CH₃), 2.23 (d, 3H, $J=0.76$ Hz, -CH₃), 2.90–2.96 (dd, 1H, $J=14.92$, 8.87 Hz, one proton of furan-CH₂-), 2.99–3.05 (dd, 1H, $J=14.88$, 5.44 Hz, one proton of furan-CH₂-), 4.47–4.48 (m, 1H, -CH₂CH-), 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 C₁₇H₂₃N₃O₄S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.36 (s, 9H, -Boc), 2.95–3.09 (m, 2H, furan-CH₂-), 4.55 (m, 1H, -CH₂CH-), 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 C₂₁H₂₂ClN₃O₄S: 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} . $^1\text{H-NMR}$ (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-CH₂-), 3.09–3.14 (dd, 1H, $J=5.4$, 15.11 Hz, one proton of furan-CH₂-), 4.55–4.56 (m, 1H, -CH₂CH-), 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 C₁₉H₂₁N₃O₄S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.36 (s, 9H, -Boc), 3.01–3.09 (m, 2H, one proton of furan-CH₂-), 4.55 (m, 1H, -CH₂CH-), 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 C₁₉H₂₀ClN₃O₄S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.18 (t, 3H, $J=6.78$ Hz, -CH₂CH₃), 1.36 (s, 9H, -Boc), 2.95–3.07 (m, 2H, furan-CH₂-), 4.04–4.10 (q, 2H, $J=6.97$ Hz, -CH₂CH₃), 4.55 (m, 1H, -CH₂CH-), 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 C₂₁H₂₅N₃O₅S: 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 Sheehan¹⁶⁾ 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.97–3.03 (dd, 1H, $J=8.32$, 15.21 Hz, one proton of furan-CH₂-), 3.09–3.16 (dd, 1H, $J=15.24$, 5.97 Hz, one proton of furan-CH₂-), 4.12 (s, 2H, -CH₂Cl), 4.73–4.78 (td, 1H, $J=8.10$, 5.92 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.19 (s, 1H, -CONH-). *Anal.* Calcd for C₁₅H₁₅ClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.97–3.03 (dd, 1H, $J=15.24$, 8.39 Hz, one proton of furan-CH₂-), 3.09–3.15 (dd, 1H, $J=15.13$, 5.90 Hz, one proton of furan-CH₂-), 4.12 (s, 2H, -CH₂Cl), 4.70–4.76 (td, 1H, $J=8.23$, 5.83 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.42 (s, 1H, -CONH-). *Anal.* Calcd for C₁₅H₁₄ClF₂N₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.97–3.03 (dd, 1H, $J=15.21$, 8.32 Hz, one proton of furan-CH₂-), 3.09–3.14 (dd, 1H, $J=15.24$, 6.01 Hz, one proton of furan-CH₂-), 4.12 (d, 2H, $J=0.57$ Hz, -CH₂Cl), 4.70–4.75 (td, 1H, $J=8.14$, 5.93 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.24 (s, 1H, -CONH-). *Anal.* Calcd for C₁₅H₁₄ClF₂N₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.97–3.03 (dd, 1H, $J=15.18$, 8.33 Hz, one proton of furan-CH₂-), 3.09–3.15 (dd, 1H, $J=15.11$, 5.94 Hz, one proton of furan-CH₂-), 4.12 (s, 2H, -CH₂Cl), 4.69–4.75 (td, 1H, $J=8.08$, 5.96 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.37 (s, 1H, -CONH-). *Anal.* Calcd for C₁₅H₁₄Cl₂N₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.97–3.03 (dd, 1H, $J=15.29$, 8.34 Hz, one proton of furan-CH₂-), 3.09–3.14 (dd, 1H, $J=15.15$, 5.88 Hz, one proton of furan-CH₂-), 4.12 (s, 2H, -CH₂Cl), 4.70–4.76 (td, 1H, $J=8.08$, 5.88 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.33 (s, 1H, -CONH-). *Anal.* Calcd for C₁₅H₁₄Cl₂N₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.97–3.03 (dd, 1H, $J=15.19$, 8.36 Hz, one proton of furan-CH₂-), 3.09–3.15 (dd, 1H, $J=15.14$, 5.85 Hz, one proton of furan-CH₂-), 4.12 (s, 2H, -CH₂Cl), 4.68–4.74 (td, 1H, $J=8.12$, 5.87 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.36 (s, 1H, -CONH-). *Anal.* Calcd for C₁₅H₁₄BrClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.97–3.03 (dd, 1H, $J=15.25$, 8.34 Hz, one proton of furan-CH₂), 3.07–3.14 (dd, 1H, $J=15.11$, 5.76 Hz, one proton of furan-CH₂), 4.12 (s, 2H, -CH₂Cl), 4.70–4.76 (td, 1H, $J=8.10$, 5.92 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.33 (s, 1H, -CONH-). *Anal.* Calcd for C₁₅H₁₄BrClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.06–1.10 (t, 3H, $J=7.53$ Hz, -CH₂CH₃), 2.48–2.54 (q, 2H, $J=7.49$ Hz, -CH₂CH₃), 3.00–3.06 (dd, 1H, $J=15.24$, 8.10 Hz, one proton of furan-CH₂), 3.12–3.18 (dd, 1H, $J=15.22$, 6.05 Hz, one proton of furan-CH₂), 4.13 (s, 2H, -CH₂Cl), 4.79–4.85 (td, 1H, $J=8.03$, 6.03 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 9.55 (s, 1H, -CONH-). *Anal.* Calcd for C₁₇H₁₉ClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.15–1.19 (t, 3H, $J=7.59$ Hz, -CH₂CH₃), 2.54–2.60 (q, 2H, $J=7.57$ Hz, -CH₂CH₃), 2.96–3.02 (dd, 1H, $J=15.24$, 8.39 Hz, one proton of furan-CH₂), 3.09–3.14 (dd, 1H, $J=15.24$, 5.74 Hz, one proton of furan-CH₂), 4.12 (d, 2H, $J=0.43$ Hz, -CH₂Cl), 4.71–4.76 (td, 1H, $J=8.13$, 5.82 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.12 (s, 1H, -CONH-). *Anal.* Calcd for C₁₇H₁₉N₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.13–1.17 (t, 3H, $J=7.57$ Hz, -CH₂CH₃), 2.52–2.58 (q, 2H, $J=7.56$ Hz, -CH₂CH₃), 2.96–3.02 (dd, 1H, $J=15.10$, 8.28 Hz, one proton of furan-CH₂), 3.08–3.13 (dd, 1H, $J=15.29$, 5.95 Hz, one proton of furan-CH₂), 4.12 (s, 2H, -CH₂Cl), 4.71–4.76 (td, 1H, $J=8.08$, 6.00 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 10.10 (s, 1H, -CONH-). *Anal.* Calcd for C₁₇H₁₉ClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.02–1.06 (t, 6H, $J=7.52$ Hz, -CH₃×2), 2.40–2.42 (dq, 4H, -CH₂CH₃×2), 2.98–3.04 (dd, 1H, $J=15.09$, 8.30 Hz, one proton of furan-CH₂), 3.16–3.22 (dd, 1H, $J=15.17$, 6.11 Hz, one proton of furan-CH₂), 4.11 (s, 2H, -CH₂Cl), 4.81–4.86 (td, 1H, $J=8.24$, 6.11 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 9.54 (s, 1H, -CONH-), furan-5H, 9.54 (s, 1H, -CONH-). *Anal.* Calcd for C₁₉H₂₃ClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.02–1.06 (t, 3H, $J=7.54$ Hz, -CH₂CH₃), 2.05 (s, 3H, -CH₃), 2.39–2.45 (q, 2H, $J=7.46$ Hz, -CH₂CH₃), 2.99–3.05 (dd, 1H, $J=15.25$, 5.96 Hz, one proton of furan-CH₂), 3.16–3.22 (dd, 1H, $J=15.25$, 5.96 Hz, one proton of furan-CH₂), 4.11 (s, 2H, -CH₂Cl), 4.79–4.84 (td, 1H, $J=8.21$, 6.04 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 9.52 (s, 1H, -CONH-). *Anal.* Calcd for C₁₈H₂₁ClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.06 (s, 6H, -CH₃×2), 2.99–3.05 (dd, 1H, $J=15.13$, 8.50 Hz, one proton of furan-CH₂), 3.16–3.22 (dd, 1H, $J=15.23$, 5.95 Hz, one proton of furan-CH₂), 4.12 (s, 2H, -CH₂Cl), 4.76–4.82 (td, 1H, $J=7.42$, 5.99 Hz, -CH₂CH-), 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, -NHCOCH₂Cl), 9.53 (s, 1H, -CONH-). *Anal.* Calcd for C₁₇H₁₉ClN₂O₃: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 3.02–3.08 (dd, 1H, $J=8.47$, 15.33 Hz, one proton of furan-CH₂), 3.13–3.18 (dd, 1H, $J=5.63$, 15.24 Hz, one proton of furan-CH₂), 4.13 (s, 2H, -CH₂Cl), 4.81–4.87 (td, 1H, $J=5.54$, 8.0 Hz, -CH₂CH-), 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 C₁₇H₁₅ClN₃O₃S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 3.02–3.08 (dd, 1H, $J=15.30$, 8.35 Hz, one proton of furan-CH₂), 3.12–3.17 (dd, 1H, $J=15.32$, 5.66 Hz, one proton of furan-CH₂), 4.12 (s, 2H, -CH₂Cl), 4.78–4.84 (td, 1H, $J=7.89$, 5.54 Hz, -CH₂CH-), 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 C₁₂H₁₁BrClN₃O₃S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 3.05–3.11 (dd, 1H, $J=15.36$, 8.47 Hz, one proton of furan-CH₂), 3.16–3.21 (dd, 1H, $J=15.31$, 5.54 Hz, one proton of furan-CH₂), 4.13 (s, 2H, -CH₂Cl), 4.80–4.86 (m, 1H, -CH₂CH-), 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 C₁₂H₁₁ClN₄O₅S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.26 (d, 3H, $J=0.98$ Hz, -CH₃), 3.01–3.07 (dd, 1H, $J=15.31$, 8.37 Hz, one proton of furan-CH₂), 3.11–3.17 (dd, 1H, $J=15.30$, 5.54 Hz, one proton of furan-CH₂), 4.12 (s, 2H, -CH₂Cl), 4.77–4.82 (td, 1H, $J=7.98$, 5.61 Hz, -CH₂CH-), 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 C₁₃H₁₄ClN₃O₃S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.34 (d, 3H, $J=1.20$ Hz, -CH₃), 3.00–3.06 (dd, 1H, $J=15.23$, 8.30 Hz, one proton of furan-CH₂), 3.10–3.16 (dd, 1H, $J=15.29$, 5.74 Hz, one proton of furan-CH₂), 4.12 (s, 2H, -CH₂Cl), 4.79–4.84 (td, 1H, $J=7.97$, 5.66 Hz, -CH₂CH-), 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 C₁₃H₁₄ClN₃O₃S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 2.15 (s, 3H, -CH₃), 2.23 (s, 3H, -CH₃), 2.99–3.05 (dd, 1H, $J=15.31$, 8.22 Hz, one proton of furan-CH₂), 3.10–3.15 (dd, 1H, $J=15.26$, 5.33 Hz, one proton of furan-CH₂), 4.12 (s, 2H, -CH₂Cl), 4.75–4.81 (td, 1H, $J=7.94$, 5.73 Hz, -CH₂CH-), 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 C₁₄H₁₆ClN₃O₃S: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 3.04–3.10 (dd, 1H, $J=15.14$, 8.65 Hz, furan-CH $_2$ -), 3.16–3.21 (dd, 1H, $J=15.51$, 5.51 Hz, furan-CH $_2$ -), 4.14 (s, 2H, -CH $_2$ Cl), 4.82–4.88 (m, 1H, -CH $_2$ 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 $\text{C}_{18}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_3\text{S}$: 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} . $^1\text{H-NMR}$ (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 $_2$ Cl), 4.86–4.91 (td, 1H, $J=7.94$, 5.52 Hz, -CH $_2$ 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 $\text{C}_{16}\text{H}_{14}\text{ClN}_3\text{O}_3\text{S}$: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 3.08–3.14 (dd, 1H, $J=15.27$, 8.21 Hz, one proton of furan-CH $_2$ -), 3.18–3.28 (dd, 1H, $J=15.21$, 5.58 Hz, one proton of furan-CH $_2$ -), 4.15 (s, 2H, -CH $_2$ Cl), 4.82–4.88 (m, 1H, -CH $_2$ 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 $\text{C}_{16}\text{H}_{13}\text{Cl}_2\text{N}_3\text{O}_3\text{S}$: 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} . $^1\text{H-NMR}$ (DMSO- d_6) δ : 1.33–1.37 (t, 3H, $J=6.95$ Hz, -CH $_2$ CH $_3$), 3.05–3.11 (dd, 1H, $J=15.50$, 8.45 Hz, one proton of furan-CH $_2$ -), 3.15–3.21 (dd, 1H, $J=15.36$, 5.69 Hz, one proton of furan-CH $_2$ -), 4.05–4.10 (q, 2H, $J=6.96$ Hz, -CH $_2$ CH $_3$), 4.14 (s, 2H, -CH $_2$ Cl), 4.83–4.88 (m, 1H, -CH $_2$ 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 $\text{C}_{18}\text{H}_{18}\text{ClN}_3\text{O}_4\text{S}$: C, 53.00; H, 4.45; N, 10.30. Found: C, 52.98; H, 4.58; N, 10.21.

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