Synthesis and Antioxidant Activity of Amido-Linked Benzoxazolyl/Benzothiazolyl/Benzimidazolyl-Pyrazoles and Isoxazoles

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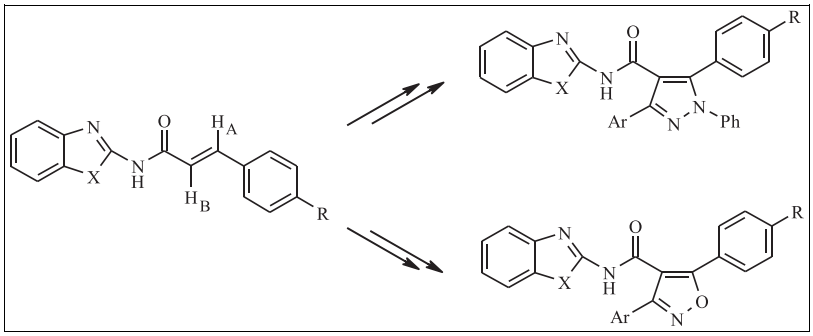

A new class of amido-linked bis heterocycles-benzoxazolyl/benzothiazolyl/benzimidazolyl-pyrazoles and isoxazoles were prepared from benzoxazolyl /benzothiazolyl/benzimidazolyl-cinnamamides and tested for antioxidant activity.

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INTRODUCTION

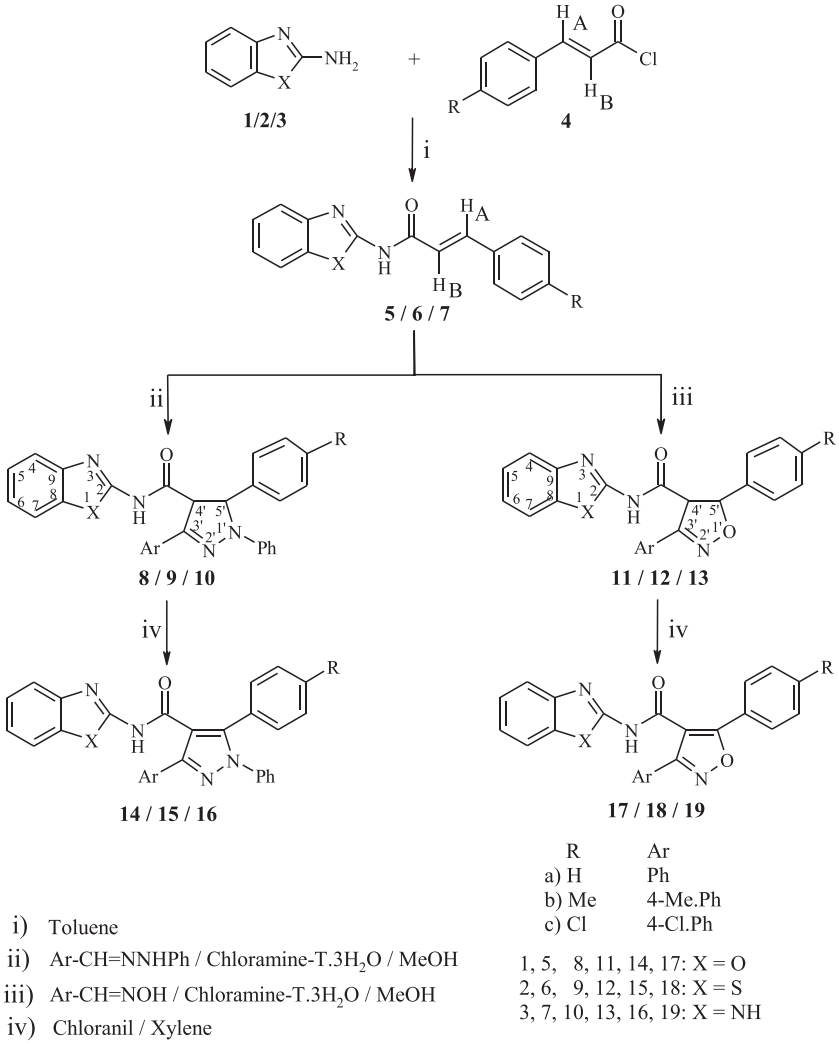
Nitrogen containing five-membered heterocycles has attracted widespread attention in the field of synthetic organic chemistry as well as in medicinal chemistry [1]. Amongst them, the prominent classes of compounds are benzoxazole, benzothiazole, benzimidazole, pyrazole, isoxazole and their derivatives. Benzoxazoles, benzothiazoles and benzimidazoles are important fragments in medicinal chemistry because of their wide range of biological activities [2–7]. Pyrazoles show pronounced pharmacological applications as antianxiety [8], antidiabetic [9], antimicrobial [10,11], herbicidal [12] and anti-inflammatory [13]. Isoxazoles exhibit analgesic [14], anti-inflammatory [14], ulcerogenic [14], antimicrobial [15], antifungal [15], COX-2 inhibitory [16,17] and anticancer [18] activities. Amongst different methods for the preparation of pyrazolines and isoxazolines, the 1,3-dipolar cycloaddition is the most important and versatile one. The dipolar reagents can be generated by the dehydrogenation of araldehyde hydrazones and araldoximes with lead tetraacetate [19], mercury acetate [20], 1-chlorobenzotriazole [21], chloramine-T (CAT) [22–26], etc. In fact, we have reported novel oxo-linked bis heterocycles by 1,3-dipolar cycloaddition of dipolar reagents *viz*., TosMIC, diazomethane, nitrile imines and nitrile oxides to symmetrical and unsymmetrical bischalcones [27,28]. It is well known that the combination of two or more heterocycles in a single molecule could afford a novel entity with increased bioactivities [29,30]. In a continuation quest for the development of a new class of biologically potent bis heterocycles from simple substrates, the present work benzoxazolyl/benzothiazolyl/benzimidazolyl-pyrazoles and isoxazoles has been taken up.

RESULTS AND DISCUSSION

The synthetic scheme involves the synthesis of a new class of amide-linked benzoxazolyl/benzothiazolyl/benzimidazolyl-pyrazoles and isoxazoles from (*E*)-*N*-(benzoxazol-2-yl)cinnamamide (**5**)/(*E*)-*N*-(benzothiazol-2-yl) cinnamamide (**6**)/(*E*)-*N*-(1*H*-benzimidazol-2-yl)cinnamamide (**7**). In fact, the compounds **5**, **6** and **7** were prepared by the condensation of respective heteroaromatic amines-benzoxazol-2-amine (**1**), benzothiazol-2-amine (**2**) and 1*H*-benzimidazol-2-amine (**3**) with cinnamoyl chloride in toluene (Scheme 1). The ^{1}H-NMR spectra of **5a**, **6a** and **7a** showed two doublets at δ 7.84, 7.86, 7.74 and at 6.72, 6.78 6.68 ppm as a result of the olefin protons, H_A and H_B, respectively. The coupling constant values J_{AB} = 16.0 Hz (**5a**), 16.2 Hz (**6a**) and 15.8 Hz (**7a**) indicated that they possess *trans* geometry. Further, a broad singlet was also observed at δ 8.32 in **5a**, at 8.38 in **6a** and at 8.18 in **7a** ppm as a result of NH. In addition to these, the compound **7a** exhibited another broad singlet at δ 12.85 ppm for NH of benzimidazole ring. The signals of highly acidic protons disappeared on deuteration.

The 1,3-dipolar cycloaddition of dipolar reagents to dipolarophiles is one of the facile techniques for the preparation of pyrazoles and isoxazoles. It was reported that the cycloaddition of 1,3-dipolar reagents to α,β-unsaturated systems proceed in such a way that the electron-rich atom

Scheme 1. Synthesis of benzoxazolyl/benzothiazolyl/benzimidazolyl-pyrazoles and isoxazoles.



of 1,3-dipolar species attacks β-carbon of α,β-unsaturated systems followed by isomerization [31]. In fact, the cycloaddition of nitrile imine generated from araldehyde phenylhydrazone and nitrile oxide generated from araldoxime in the presence of CAT to compound **5/6/7** proceeded regioselectively. Thus, *N*-(benzoxazol-2-yl)-4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (**8**), *N*-(benzothiazol-2-yl)-4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (**9**) and *N*-(1*H*-benzimidazol-2-yl)-4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (**10**) were obtained by the cycloaddition of nitrile imine generated from araldehyde phenylhydrazone in the presence of CAT to **5**, **6** and **7** (Scheme 1). The ^{1}H-NMR spectra of **8a**, **9a** and **10a** displayed two doublets at δ 5.10, 5.16, 5.05 and at 5.28, 5.33, 5.25 ppm as a result of C_4′-H and C_5′-H of pyrazoline ring. Moreover, a broad singlet was observed in these compounds at δ 8.37 (**8a**), 8.40 (**9a**) and at 8.32 (**10a**) ppm as a result of NH. Apart from these, compound **10a** exhibited another broad singlet at δ 12.78 ppm that was assigned to NH of benzimidazole ring. The signals as a result of NH disappeared when D_2O was added.

Adopting similar methodology, the cycloaddition of nitrile oxide generated from araldoxime in the presence of CAT to **5**, **6** and **7** yielded *N*-(benzoxazol-2-yl)-4′,5′-dihydro-3′,5′-diarylisoxazole-4′-carboxamide (**11**), *N*-(benzothiazol-2-yl)-4′,5′-dihydro-3′,5′-diarylisoxazole-4′-carboxamide (**12**) and *N*-(1*H*-benzimidazol-2-yl)-4′,5′-dihydro-3′,5′-diarylisoxazole-4′-carboxamide (**13**), respectively (Scheme 1). The ^{1}H-NMR spectra of **11a**, **12a** and **13a** displayed two doublets at δ 5.07, 5.11, 4.98 and at 5.42, 5.49, 5.37 ppm that were attributed to C_4′-H and C_5′-H. Furthermore, a broad singlet was observed at δ 8.39 in **11a**, at 8.42 in **12a** and at 8.37 ppm in **13a** as a result of NH. Apart from these, compound **13a** showed another broad signal at δ 12.82 ppm as a result of NH of benzimidazole ring. The signals of highly acidic protons disappeared on deuteration.

The oxidation of compounds **8–13** with chloranil in xylene produced *N*-(benzoxazol-2-yl)-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (**14**), *N*-(benzothiazol-2-yl)-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (**15**), *N*-(1*H*-benzimidazol-2-yl)-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (**16**), *N*-(benzoxazol-2-yl)-3′,5′-diarylisoxazole-4′-carboxamide (**17**), *N*-(benzothiazol-2-yl)-3′,5′-diarylisoxazole-4′-carboxamide (**18**) and *N*-(1*H*-benzimidazol-2-yl)-3′,5′-diarylisoxazole-4′-carboxamide (**19**) (Scheme 1). The absence of doublets as a result of pyrazoline and isoxazoline ring protons in the ^{1}H-NMR spectra of compounds **14–19** indicated that aromatization took place. In the ^{1}H-NMR spectra of **14a**, **15a**, **16a**, **17a**, **18a** and **19a**, a broad singlet was observed at δ 8.54, 8.56, 8.49, 8.55, 8.60 and 8.52 ppm as a result of NH. Furthermore, compounds **16a** and **19a** exhibited another broad singlet at δ 12.85 and 12.87 ppm as a result of NH of benzimidazole ring. The signals of NH disappeared when D_2O was added. The structures of all the new compounds were further confirmed by IR, ^{13}C-NMR, mass spectra and microanalyses.

ANTIOXIDANT STUDIES

The compounds **8–19** were tested for antioxidant property by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) [32,33], nitric oxide (NO) [34,35] and hydrogen peroxide (H_2O_2) [36] methods at three different concentrations 50, 75 and 100 μg/mL. The Ascorbic acid was used as the standard

Table 1

The *in vitro* antioxidant activity of compounds **8–19** in DPPH method.

	Concentration (μg/mL)		
Compound	50	75	100
8a	30.31 ± 0.41	32.75 ± 0.25	34.07 ± 0.08
8b	33.98 ± 0.67	35.42 ± 0.52	37.58 ± 0.47
8c	—	—	—
9a	28.97 ± 0.82	31.16 ± 0.33	32.21 ± 0.11
9b	32.64 ± 1.17	34.49 ± 0.05	35.54 ± 0.86
9c	—	—	—
10a	—	—	—
10b	25.48 ± 0.28	26.22 ± 0.74	27.69 ± 1.09
10c	—	—	—
11a	34.54 ± 0.05	36.67 ± 0.86	39.82 ± 1.01
11b	37.79 ± 0.10	38.83 ± 0.95	41.91 ± 0.07
11c	—	—	—
12a	31.03 ± 0.49	33.54 ± 0.17	35.42 ± 0.77
12b	35.91 ± 0.32	36.24 ± 0.54	39.04 ± 0.13
12c	—	—	—
13a	—	—	—
13b	27.65 ± 0.28	28.80 ± 0.06	30.10 ± 1.02
13c	—	—	—
14a	70.33 ± 0.11	71.12 ± 0.71	73.94 ± 0.38
14b	77.54 ± 0.85	80.64 ± 0.12	82.25 ± 0.43
14c	62.71 ± 1.09	64.47 ± 0.25	65.12 ± 0.02
15a	58.29 ± 0.33	59.09 ± 0.79	61.57 ± 0.96
15b	64.96 ± 0.52	67.38 ± 0.11	69.45 ± 0.71
15c	51.68 ± 0.41	52.59 ± 0.65	53.09 ± 1.01
16a	40.03 ± 1.17	42.86 ± 0.42	43.39 ± 0.05
16b	44.27 ± 0.32	47.62 ± 0.50	49.97 ± 0.47
16c	35.39 ± 0.63	38.15 ± 0.25	39.84 ± 0.21
17a	72.34 ± 0.11	73.63 ± 0.76	75.39 ± 1.05
17b	80.16 ± 0.69	83.47 ± 0.33	84.72 ± 0.88
17c	63.82 ± 0.04	65.29 ± 0.64	66.58 ± 0.60
18a	60.54 ± 1.07	60.98 ± 0.03	62.30 ± 0.37
18b	66.24 ± 0.75	69.32 ± 0.58	70.06 ± 0.15
18c	54.93 ± 1.09	55.11 ± 0.97	58.81 ± 0.52
19a	52.44 ± 0.46	53.93 ± 0.32	55.32 ± 0.22
19b	59.98 ± 0.54	60.54 ± 0.30	63.29 ± 0.63
19c	47.21 ± 0.19	49.91 ± 0.75	50.57 ± 0.87
Ascorbic acid	74.37 ± 0.15	76.63 ± 0.09	79.21 ± 0.45
Blank	—	—	—

(—) Showed no scavenging activity.
Values were the means of three replicates ± SD.

Table 2

The *in vitro* antioxidant activity of compounds **8–19** in NO method.

	Concentration (μg/mL)		
Compound	50	75	100
8a	33.16 ± 0.84	34.77 ± 0.38	35.62 ± 0.02
8b	36.74 ± 0.17	37.26 ± 1.02	38.53 ± 0.45
8c	—	—	—
9a	32.29 ± 0.52	33.01 ± 0.49	34.04 ± 1.08
9b	35.84 ± 0.33	36.25 ± 0.11	37.79 ± 0.67
9c	—	—	—
10a	—	—	—
10b	30.07 ± 0.65	31.66 ± 0.19	32.35 ± 0.07
10c	—	—	—
11a	35.32 ± 0.28	36.59 ± 0.52	37.81 ± 1.14
11b	39.54 ± 0.79	40.22 ± 0.03	42.57 ± 0.46
11c	—	—	—
12a	34.07 ± 0.12	35.76 ± 0.98	36.74 ± 0.60
12b	37.65 ± 0.95	38.20 ± 0.31	39.25 ± 0.18
12c	—	—	—
13a	—	—	—
13b	31.72 ± 0.41	32.56 ± 1.12	33.07 ± 0.97
13c	—	—	—
14a	73.42 ± 0.29	75.71 ± 0.85	76.01 ± 0.30
14b	81.74 ± 0.06	84.06 ± 0.76	87.54 ± 1.11
14c	64.57 ± 0.54	66.32 ± 0.08	68.09 ± 0.59
15a	60.19 ± 0.71	61.96 ± 0.13	63.37 ± 0.45
15b	66.48 ± 0.04	69.51 ± 0.64	71.42 ± 0.10
15c	52.35 ± 0.50	54.32 ± 0.97	56.55 ± 0.12
16a	42.10 ± 0.82	44.82 ± 0.04	45.75 ± 0.99
16b	47.27 ± 1.15	49.14 ± 0.25	52.04 ± 1.21
16c	39.17 ± 0.66	40.63 ± 0.09	41.20 ± 0.27
17a	75.54 ± 0.63	76.25 ± 1.02	77.97 ± 0.64
17b	83.65 ± 0.12	85.42 ± 0.48	88.06 ± 0.01
17c	65.32 ± 0.91	68.21 ± 0.44	69.29 ± 0.52
18a	60.61 ± 0.56	62.57 ± 0.70	64.63 ± 0.31
18b	68.12 ± 0.09	70.92 ± 0.68	72.14 ± 0.17
18c	56.78 ± 0.70	57.16 ± 0.83	59.84 ± 0.40
19a	53.35 ± 0.56	55.44 ± 0.97	56.05 ± 1.13
19b	62.12 ± 0.08	63.23 ± 0.77	64.11 ± 0.12
19c	50.17 ± 0.21	51.56 ± 0.56	52.86 ± 1.10
Ascorbic acid	77.20 ± 0.09	79.92 ± 022	82.24 ± 0.34
Blank	—	—	—

(—) Showed no scavenging activity.
Values were the means of three replicates ± SD.

Table 3

The *in vitro* antioxidant activity of compounds **8–19** in H_2O_2 method.

Compound	Concentration (μg/mL)		
	50	75	100
8a	31.47 ± 0.41	34.11 ± 0.57	35.46 ± 0.11
8b	34.02 ± 0.33	35.55 ± 1.03	37.27 ± 0.75
8c	—	—	—
9a	30.35 ± 0.65	32.60 ± 0.97	34.62 ± 0.38
9b	33.76 ± 0.74	34.52 ± 0.06	36.15 ± 0.67
9c	—	—	—
10a	—	—	—
10b	25.67 ± 0.30	28.01 ± 0.44	29.32 ± 0.55
10c	—	—	—
11a	33.51 ± 0.97	34.25 ± 1.16	36.74 ± 0.13
11b	38.43 ± 1.06	39.82 ± 0.11	40.10 ± 0.34
11c	—	—	—
12a	32.68 ± 0.68	33.13 ± 0.37	35.09 ± 0.72
12b	35.15 ± 0.30	36.91 ± 0.56	38.52 ± 0.41
12c	—	—	—
13a	—	—	—
13b	27.74 ± 0.05	29.82 ± 0.28	30.76 ± 0.66
13c	—	—	—
14a	71.27 ± 0.49	73.37 ± 0.92	75.12 ± 1.16
14b	79.65 ± 0.68	83.30 ± 0.13	84.99 ± 0.01
14c	63.01 ± 0.44	64.22 ± 0.61	65.34 ± 0.09
15a	59.52 ± 0.65	61.11 ± 1.03	62.07 ± 0.48
15b	65.35 ± 0.31	69.29 ± 0.96	70.56 ± 1.14
15c	52.19 ± 1.21	53.52 ± 0.18	55.79 ± 0.76
16a	41.08 ± 0.86	42.97 ± 0.39	44.23 ± 0.62
16b	47.27 ± 0.18	49.14 ± 0.57	52.04 ± 0.05
16c	38.81 ± 0.66	39.32 ± 0.28	40.51 ± 1.02
17a	72.21 ± 0.39	75.07 ± 0.17	77.54 ± 0.58
17b	81.52 ± 0.42	84.26 ± 0.50	86.75 ± 0.12
17c	63.96 ± 0.17	65.62 ± 0.83	66.05 ± 0.09
18a	60.32 ± 1.18	61.96 ± 0.99	63.32 ± 0.15
18b	67.29 ± 0.26	70.12 ± 0.01	71.17 ± 0.63
18c	55.04 ± 0.69	56.53 ± 0.35	59.20 ± 0.71
19a	52.29 ± 0.26	53.32 ± 0.17	55.54 ± 0.42
19b	61.52 ± 0.50	63.11 ± 0.32	65.92 ± 1.09
19c	49.90 ± 0.01	50.02 ± 0.28	51.93 ± 0.54
Ascorbic acid	76.54 ± 0.32	78.12 ± 0.05	80.67 ± 0.69
Blank	—	—	—

(—) Showed no scavenging activity.
Values were the means of three replicates ± SD.

drug. The perusal of the results (Tables 1–3) revealed that aromatized compounds (**14–19**) exhibited greater activity than the corresponding non-aromatized compounds (**8–13**). In general, amido-linked benzoxazolyl pyrazoles (**14**) and isoxazoles (**17**) displayed higher radical scavenging activity than benzothiazolyl pyrazoles (**15**) and isoxazoles (**18**), benzimidazolyl pyrazoles (**16**) and isoxazoles (**19**). Further, it was observed that the compounds with benzothiazolyl moiety (**15**, **18**) exhibited greater activity than those with benzimidazolyl moiety (**16**, **19**). It was also observed that compounds having methyl substituent on the phenyl ring displayed significant activity than unsubstituted and chloro-substituted ones. This may be because of electron-donating effect of the alkyl substituent. In fact, compounds **14b** and **17b** showed higher radical scavenging activity in all the three methods when compared with the standard drug ascorbic acid. The compounds **14a**, **14c**, **15b**, **17a**, **17c**, **18a** and **18b** exhibited good activity whereas the compounds **15a**, **15c**, **18c**, **19a** and **19b** displayed moderate activity. On the other hand, the compounds **8a**, **8b**, **9a**, **9b**, **10b**, **11a**, **11b**, **12a**, **12b**, **13b**, **16a**, **16b**, **16c** and **19c** exhibited low activity. However, the other compounds showed no activity. The free radical-scavenging activity of the compounds **14a**, **14b**, **17a** and **17b** was measured at different concentrations, monitored by the change in absorbance at 10, 20 and 30 min in the DPPH method (Table 4). It was observed that at these 10 min time intervals, the values are very close and the results exemplify that the antioxidant activity is independent of time.

Table 4

Antioxidant activities of compounds **14a**, **14b**, **17a** and **17b** at 10 min time intervals determined by the DPPH radical-scavenging method.

Compound	10 min	20 min	30 min
14a	71.95	72.02	72.08
14b	75.01	75.15	75.92
17a	73.50	73.80	73.98
17b	79.12	79.28	79.55

CONCLUSION

A new class of amido-linked bis heterocycles-benzoxazolyl/benzothiazolyl/benzimidazolyl-pyrazoles and benzoxazolyl/benzothiazolyl/benzimidazolyl-isoxazoles were prepared adopting 1,3-dipolar cycloaddition methodology from the easily accessible building blocks benzoxazol-2-amine, benzothiazol-2-amine, 1*H*-benzimidazol-2-amine and cinnamoyl chloride. All the new compounds were assayed for antioxidant activity. It was observed that benzoxazolyl/benzothiazolyl/benzimidazolyl-pyrazoles and isoxazoles exhibited comparatively greater activity than the benzoxazolyl/benzothiazolyl/benzimidazolyl-pyrazolines and isoxazolines. The compounds **14b** and **17b** showed greater radical scavenging activity when compared with the standard drug ascorbic acid.

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The progress of reaction was monitored by TLC (silica gel H, BDH, hexane/ethyl acetate, 3:1). The IR spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets, and the wave numbers were given in cm^{-1}. The ^{1}H-NMR spectra were recorded in $CDCl_3$ /DMSO-d_6 on a Jeol JNM λ 400 MHz. The ^{13}C-NMR spectra were recorded in $CDCl_3$ /DMSO-d_6 on a Jeol JNM spectrometer operating at λ 100 MHz. The mass spectra were recorded on Jeol JMS-D 300 and Finnigan Mat 1210 B at 70 eV with an emission current of 100 μA. All chemical shifts are reported

in ppm using TMS as an internal standard. The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer. The compounds benzoxazol-2-amine (**1**)/benzothiazol-2-amine (**2**)/1*H*-benzimidazol-2-amine (**3**) and cinnamoyl chloride (**4**) were prepared as per the literature precedent [37–39].

(*E*)-*N*-(Benzoxazol-2-yl)cinnamamide (5)/(*E*)-*N*-(benzothiazol-2-yl)cinnamamide (6)/(*E*)-*N*-(1*H*-benzimidazol-2-yl)cinnamamide (7). General procedure. A mixture of **1/2/3** (1 mmol), cinnamoyl chloride (**4**) (1.1 mmol) and toluene (10 mL) was heated to reflux for 15–18 h. After completion of the reaction, the contents were cooled to room temperature. The separated solid was collected and purified by column chromatography (silica gel, ethyl acetate/hexane, 1.5:3).

(E)-N-(Benzoxazol-2-yl)cinnamamide (5a). White solid (0.17 g, 68%); m.p. 202–204°C; IR (KBr): 1597 (C=N), 1618 (C=C), 1654 (C=O), 3309 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.72 (d, 1H, H_B, J = 16.0 Hz), 7.13–7.35 (m, 9H, Ar–H), 7.84 (d, 1H, H_A, J = 16.0 Hz), 8.32 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 117.8 (C-H_B), 143.2 (C-H_A), 163.1 (C-2), 168.0 (CO), 117.3, 120.4, 123.5, 124.5, 127.3, 128.1, 128.8, 133.4, 142.5, 150.2 (aromatic carbons) ppm; MS (*m/z*): 264.28 [M^+]; *Anal.* Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.70; H, 4.59; N, 10.81; Found: C, 72.64; H, 4.62; N, 10.71%.

(E)-N-(Benzoxazol-2-yl)-3-(4-methylphenyl)acrylamide (5b). White solid (0.18 g, 65%); m.p. 195–197°C; IR (KBr): 1595 (C=N), 1615 (C=C), 1651 (C=O), 3302 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H, Ar–CH_3), 6.70 (d, 1H, H_B, J = 15.9 Hz), 7.11–7.31 (m, 8H, Ar–H), 7.79 (d, 1H, H_A, J = 15.9 Hz), 8.29 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.6 (Ar–CH_3), 117.5 (C-H_B), 142.8 (C-H_A), 162.7 (C-2), 167.1 (CO), 117.1, 119.4, 123.4, 125.2, 126.8, 128.3, 133.5, 137.4, 142.4, 149.8 (aromatic carbons) ppm; MS (*m/z*): 278.31 [M^+]; *Anal.* Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.34; H, 5.18; N, 10.35; Found: C, 73.21; H, 5.13; N, 10.15%.

(E)-N-(Benzoxazol-2-yl)-3-(4-chlorophenyl)acrylamide (5c). White solid (0.21 g, 72%); m.p. 212–214°C; IR (KBr): 1600 (C=N), 1620 (C=C), 1658 (C=O), 3311 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.75 (d, 1H, H_B, J = 16.1 Hz), 7.15–7.39 (m, 8H, Ar–H), 7.87 (d, 1H, H_A, J = 16.1 Hz), 8.34 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 118.2 (C-H_B), 143.5 (C-H_A), 163.5 (C-2), 167.9 (CO), 117.8, 120.3, 123.8, 124.7, 127.4, 128.6, 134.2, 134.8, 140.3, 151.3 (aromatic carbons) ppm; MS (*m/z*): 298.73 [M^+]; *Anal.* Calcd. for $C_{16}H_{11}ClN_2O_2$: C, 64.62; H, 3.85; N, 9.73; Found: C, 64.47; H, 3.77; N, 9.46%.

(E)-N-(Benzothiazol-2-yl)cinnamamide (6a). White solid (0.21 g, 75%); m.p. 148–150°C; IR (KBr): 1601 (C=N), 1623 (C=C), 1659 (C=O), 3318 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.78 (d, 1H, H_B, J = 16.2 Hz), 7.18–8.20 (m, 9H, Ar–H), 7.86 (d, 1H, H_A, J = 16.2 Hz), 8.38 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 118.4 (C-H_B), 144.8 (C-H_A), 166.8 (C-2), 169.2 (CO), 121.3, 121.9, 125.3, 126.0, 126.3, 127.2, 128.7, 129.4, 136.5, 147.3 (aromatic carbons) ppm; MS (*m/z*): 280.35 [M^+]; *Anal.* Calcd. for $C_{16}H_{12}N_2OS$: C, 68.74; H, 4.24; N, 10.17; Found: C, 68.67; H, 4.25; N, 10.08%.

(E)-N-(Benzothiazol-2-yl)-3-(4-methylphenyl)acrylamide (6b). White solid (0.20 g, 71%); m.p. 137–139°C; IR (KBr): 1585 (C=N), 1619 (C=C), 1657 (C=O), 3315 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H, Ar–CH_3), 6.74 (d, 1H, H_B, J = 16.0 Hz), 7.16–8.15 (m, 8H, Ar–H), 7.81 (d, 1H, H_A, J = 16.0 Hz), 8.26 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.8 (Ar–CH_3), 117.9 (C-H_B), 144.5 (C-H_A), 167.6 (C-2), 168.8 (CO), 120.4, 121.1, 124.5, 125.4, 125.8, 126.2, 128.3, 132.4, 136.4, 146.3 (aromatic carbons) ppm; MS (*m/z*): 294.38 [M^+]. *Anal.* Calcd. for $C_{17}H_{14}N_2OS$: C, 69.18; H, 4.69; N, 9.61; Found: C, 69.22; H, 4.67; N, 9.47%.

(E)-N-(Benzothiazol-2-yl)-3-(4-chlorophenyl)acrylamide (6c). White solid (0.24 g, 78%); m.p. 161–163°C; IR (KBr): 1605 (C=N), 1625 (C=C), 1660 (C=O), 3331 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.85 (d, 1H, H_B, J = 16.3 Hz), 7.20–8.23 (m, 8H, Ar–H), 7.89 (d, 1H, H_A, J = 16.3 Hz), 8.40 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 118.7 (C-H_B), 145.2 (C-H_A), 168.6 (C-2), 169.4 (CO), 121.8, 122.1, 124.6, 125.5, 125.9, 127.3, 128.4, 133.0, 133.8, 148.4 (aromatic carbons) ppm; MS (*m/z*): 314.80 [M^+]; *Anal.* Calcd. for $C_{16}H_{11}ClN_2OS$: C, 61.03; H, 3.63; N, 9.17; Found: C, 60.94; H, 3.59; N, 8.99%.

(E)-N-(1H-Benzimidazol-2-yl)cinnamamide (7a). Brown solid (0.22 g, 86%); m.p. 255–257°C; IR (KBr): 1590 (C=N), 1616 (C=C), 1653 (C=O), 3302 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.68 (d, 1H, H_B, J = 15.8 Hz), 7.10–7.64 (m, 9H, Ar–H), 7.74 (d, 1H, H_A, J = 15.8 Hz), 8.18 (bs, 1H, NH), 12.85 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 117.4 (C-H_B), 141.9 (C-H_A), 150.4 (C-2), 167.4 (CO), 119.2, 123.5, 126.4, 128.3, 128.9, 134.3, 138.4 (aromatic carbons) ppm; MS (*m/z*): 263.30 [M^+]; *Anal.* Calcd. for $C_{16}H_{13}N_3O$: C, 73.21; H, 5.07; N, 15.97; Found: C, 73.15; H, 5.05; N, 15.84%.

(E)-N-(1H-Benzimidazol-2-yl)-3-(4-methylphenyl)acrylamide (7b). Brown solid (0.22 g, 80%); m.p. 238–240°C; IR (KBr): 1587 (C=N), 1613 (C=C), 1650 (C=O), 3297 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H, Ar–CH_3) 6.65 (d, 1H, H_B, J = 15.7 Hz), 7.06–7.62 (m, 8H, Ar–H), 7.70 (d, 1H, H_A, J = 15.7 Hz), 8.14 (bs, 1H, NH), 12.82 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.1 (Ar–CH_3), 117.2 (C-H_B), 141.5 (C-H_A), 150.3 (C-2), 166.6 (CO), 119.0, 123.1, 126.3, 128.2, 128.8, 137.4, 138.1 (aromatic carbons) ppm; MS (*m/z*): 277.33 [M^+]; *Anal.* Calcd. for $C_{17}H_{15}N_3O$: C, 73.59; H, 5.56; N, 15.18; Found: C, 73.50; H, 5.52; N, 15.02%.

(E)-N-(1H-Benzimidazol-2-yl)-3-(4-chlorophenyl)acrylamide (7c). White solid (0.26 g, 88%); m.p. 272–275°C; IR (KBr): 1598 (C=N), 1617 (C=C), 1655 (C=O), 3305 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.70 (d, 1H, H_B, J = 15.9 Hz), 7.12–7.69 (m, 8H, Ar–H), 7.79 (d, 1H, H_A, J = 15.9 Hz), 8.20 (bs, 1H, NH), 12.90 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 117.7 (C-H_B), 142.0 (C-H_A), 150.7 (C-2), 167.2 (CO), 119.4, 123.9, 126.6, 128.7, 129.1, 134.5, 138.9 (aromatic carbons) ppm; MS (*m/z*): 297.74 [M^+]; *Anal.* Calcd. for $C_{16}H_{12}ClN_3O$: C, 64.57; H, 4.06; N, 14.38; Found: C, 64.44; H, 4.00; N, 14.21%.

***N*-(Benzoxazol-2-yl)-4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (8)/*N*-(benzothiazol-2-yl)-4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (9)/*N*-(1*H*-benzimidazol-2-yl)-4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (10).** General procedure. The compound **5/6/7** (1.0 mmol), araldehyde phenylhydrazone (1.2 mmol), CAT (0.33 g, 1.2 mmol) and methanol (20 mL) were refluxed for 23–25 h. The precipitated inorganic salts were filtered off. The filtrate was concentrated, and the residue was extracted with dichloromethane. The organic layer was washed with water, brine and dried (an. Na_2SO_4). Evaporation of the solvent under reduced pressure yielded a solid that was purified by column chromatography (silica gel, 60–120 mesh) using hexane/ethyl acetate (4:1) as eluent.

N-(Benzoxazol-2-yl)-4′,5′-dihydro-1′,3′,5′-triphenyl-1′H-pyrazole-4′-carboxamide (8a). White solid (0.33 g, 74%); m.p. 218–220°C; IR (KBr): 1567 (C=N), 1658 (C=O), 3274 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.10 (d, 1H, C_4'-H, J = 7.12 Hz), 5.28 (d, 1H, C_5'-H, J = 7.2 Hz), 6.50–7.60 (m, 19H, Ar–H), 8.37 (bs, 1H,

NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 62.3 (C-4′), 82.5 (C-5′), 151.9 (C-3′), 162.5 (C-2), 168.2 (CO), 110.5, 113.4, 117.6, 119.3, 123.6, 124.5, 126.4, 127.7, 128.4, 128.8, 129.6, 129.9, 131.3, 134.4, 141.6, 143.5, 144.3, 150.3 (aromatic carbons) ppm; MS (*m/z*): 458.52 [M$^+$]; *Anal.* Calcd. for $C_{29}H_{22}N_4O_2$: C, 76.05; H, 4.82; N, 12.33; Found: C, 75.97; H, 4.84; N, 12.22%.

***N*-(Benzoxazol-2-yl)-3′,5′-bis(4-methylphenyl)-4′,5′-dihydro-1′-phenyl-1′*H*-pyrazole-4′-carboxamide (8b).** White solid (0.32 g, 67%); m.p. 206–208°C; IR (KBr): 1561 (C=N), 1651 (C=O), 3262 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.34 and 2.37 (s, 6H, Ar–CH_3), 5.04 (d, 1H, C_4′-H, *J* = 6.9 Hz), 5.24 (d, 1H, C_5′-H, *J* = 6.9 Hz), 6.44–7.53 (m, 17H, Ar–H), 8.34 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 23.5 and 24.2 (Ar–CH_3), 62.1 (C-4′), 81.9 (C-5′), 151.2 (C-3′), 162.1 (C-2), 168.0 (CO), 110.1, 113.2, 117.4, 119.1, 123.4, 124.1, 126.0, 127.2, 128.1, 128.5, 129.1, 129.5, 131.0, 134.2, 141.3, 143.2, 144.1, 149.8 (aromatic carbons) ppm; MS (*m/z*): 486.58 [M$^+$]; Anal. Calcd. for $C_{31}H_{26}N_4O_2$: C, 76.47; H, 5.39; N, 11.59; Found: C, 76.52; H, 5.38; N, 11.52%.

***N*-(Benzoxazol-2-yl)-3′,5′-bis(4-chlorophenyl)-4′,5′-dihydro-1′-phenyl-1′*H*-pyrazole-4′-carboxamide (8c).** White solid (0.40 g, 77%); m.p. 229–230°C; IR (KBr): 1575 (C=N), 1667 (C=O), 3283 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.12 (d, 1H, C_4′-H, *J* = 7.3 Hz), 5.32 (d, 1H, C_5′-H, *J* = 7.3 Hz), 6.54–7.67 (m, 17H, Ar–H), 8.39 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 62.5 (C-4′), 82.7 (C-5′), 152.4 (C-3′), 162.8 (C-2), 168.5 (CO), 110.4, 113.6, 117.7, 119.5, 123.8, 124.7, 126.6, 128.3, 128.5, 128.9, 129.8, 130.2, 131.5, 134.7, 141.8, 143.6, 144.9, 150.7 (aromatic carbons) ppm; MS (*m/z*): 527.48 [M$^+$]; *Anal.* Calcd. for $C_{29}H_{20}Cl_2N_4O_2$: C, 66.12; H, 3.85; N, 10.75; Found: C, 66.03; H, 3.82; N, 10.62%.

***N*-(Benzothiazol-2-yl)-4′,5′-dihydro-1′,3′,5′-triphenyl-1′*H*-pyrazole-4′-carboxamide (9a).** White solid (0.38 g, 81%); m.p. 262–264°C; IR (KBr): 1579 (C=N), 1663 (C=O), 3289 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.16 (d, 1H, C_4′-H, *J* = 7.4 Hz), 5.33 (d, 1H, C_5′-H, *J* = 7.4 Hz), 6.61–7.94 (m, 19H, Ar–H), 8.40 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 63.5 (C-4′), 83.5 (C-5′), 152.6 (C-3′), 168.7 (CO), 169.3 (C-2), 113.5, 117.5, 121.1, 121.8, 124.6, 125.2, 125.7, 126.2, 127.5, 128.4, 128.7, 129.3, 129.8, 131.5, 134.2, 143.2, 143.8, 149.2 (aromatic carbons) ppm; MS (*m/z*): 474.59 [M$^+$]; *Anal.* Calcd. for $C_{29}H_{22}N_4OS$: C, 73.46; H, 4.69; N, 11.97; Found: C, 73.39; H, 4.67; N, 11.81%.

***N*-(Benzothiazol-2-yl)-3′,5′-bis(4-methylphenyl)-4′,5′-dihydro-1′-phenyl-1′*H*-pyrazole-4′-carboxamide (9b).** White solid (0.39 g, 79%); m.p. 245–247°C; IR (KBr): 1571 (C=N), 1657 (C=O), 3275 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.36 and 2.39 (s, 6H, Ar–CH_3), 5.13 (d, 1H, C_4′-H, *J* = 7.2 Hz), 5.30 (d, 1H, C_5′-H, *J* = 7.2 Hz), 6.52–7.90 (m, 17H, Ar–H), 8.38 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 23.8 and 24.3 (Ar–CH_3), 63.0 (C-4′), 83.1 (C-5′), 152.3 (C-3′), 168.2 (CO), 169.1 (C-2), 113.2, 117.3, 120.6, 121.7, 124.3, 125.1, 125.6, 126.1, 127.3, 128.1, 128.4, 129.2, 129.7, 131.2, 134.3, 143.1, 143.5, 148.7 (aromatic carbons) ppm; MS (*m/z*): 502.65 [M$^+$]; *Anal.* Calcd. for $C_{31}H_{26}N_4OS$: C, 74.14; H, 5.21; N, 11.27; Found: C, 74.08; H, 5.22; N, 11.15%.

***N*-(Benzothiazol-2-yl)-3′,5′-bis(4-chlorophenyl)-4′,5′-dihydro-1′-phenyl-1′*H*-pyrazole-4′-carboxamide (9c).** White solid (0.45 g, 83%); m.p. 288–290°C; IR (KBr): 1585 (C=N), 1668 (C=O), 3307 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.19 (d, 1H, C_4′-H, *J* = 7.6 Hz), 5.35 (d, 1H, C_5′-H, *J* = 7.6 Hz), 6.67–8.13 (m, 17H, Ar–H), 8.43 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 64.1 (C-4′), 83.9 (C-5′), 152.8 (C-3′), 168.9 (CO), 169.7 (C-2), 113.7, 117.8, 121.4, 121.9, 124.7, 125.3, 125.9, 126.7, 127.8, 128.6, 128.8, 129.4, 129.9, 131.9, 134.5, 143.5, 143.9, 149.5 (aromatic carbons) ppm; MS (*m/z*): 543.49 [M$^+$]; *Anal.* Calcd. for $C_{29}H_{20}Cl_2N_4OS$: C, 64.21; H, 3.70; N, 10.46; Found: C, 64.09; H, 3.71; N, 10.31%.

***N*-(1H-Benzimidazol-2-yl)-4′,5′-dihydro-1′,3′,5′-triphenyl-1′*H*-pyrazole-4′-carboxamide (10a).** Brown solid (0.31 g, 69%); m.p. 275–277°C; IR (KBr): 1564 (C=N), 1650 (C=O), 3264 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.05 (d, 1H, C_4′-H, *J* = 6.8 Hz), 5.25 (d, 1H, C_5′-H, *J* = 6.8 Hz), 6.55–7.71 (m, 19H, Ar–H), 8.32 (bs, 1H, NH), 12.78 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 61.7 (C-4′), 81.9 (C-5′), 150.8 (C-3′), 153.9 (C-2), 167.5 (CO), 113.6, 115.5, 117.6, 123.5, 126.5, 127.4, 128.2, 129.4, 130.3, 131.5, 132.7, 134.5, 138.6, 143.5, 144.4 (aromatic carbons) ppm; MS (*m/z*): 457.53 [M$^+$]; *Anal.* Calcd. for $C_{29}H_{23}N_5O$: C, 76.23; H, 5.11; N, 15.50; Found: C, 76.13; H, 5.07; N, 15.31%.

***N*-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-methylphenyl)-4′,5′-dihydro-1′-phenyl-1′*H*-pyrazole-4′-carboxamide (10b).** Brown solid (0.32 g, 66%); m.p. 261–263°C; IR (KBr): 1560 (C=N), 1645 (C=O), 3255 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.31 and 2.35 (s, 6H, Ar–CH_3), 5.01 (d, 1H, C_4′-H, *J* = 6.7 Hz), 5.17 (d, 1H, C_5′-H, *J* = 6.7 Hz), 6.51–7.66 (m, 17H, Ar–H), 8.28 (bs, 1H, NH), 12.74 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 23.2 and 24.1 (Ar–CH_3), 61.1 (C-4′), 81.4 (C-5′), 150.1 (C-3′), 152.7 (C-2), 167.5 (CO), 113.5, 115.3, 117.1, 123.0, 126.2, 127.3, 128.0, 129.3, 130.2, 131.4, 132.1, 134.3, 138.2, 143.1, 144.0 (aromatic carbons) ppm; MS (*m/z*): 485.58 [M$^+$]; *Anal.* Calcd. for $C_{31}H_{27}N_5O$: C, 76.81; H, 5.62; N, 14.59; Found: C, 76.68; H, 5.60; N, 14.42%.

***N*-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-chlorophenyl)-4′,5′-dihydro-1′-phenyl-1′*H*-pyrazole-4′-carboxamide (10c).** Brown solid (0.39 g, 76%); m.p. 283–285°C; IR (KBr): 1568 (C=N), 1658 (C=O), 3273 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.08 (d, 1H, C_4′-H, *J* = 7.0 Hz), 5.28 (d, 1H, C_5′-H, *J* = 7.0 Hz), 6.58–7.75 (m, 17H, Ar–H), 8.35 (bs, 1H, NH), 12.79 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 61.9 (C-4′), 82.2 (C-5′), 151.3 (C-3′), 154.3 (C-2), 168.2 (CO), 113.8, 115.7, 117.7, 123.8, 126.9, 127.8, 128.9, 129.5, 130.6, 131.7, 132.9, 134.8, 138.8, 143.8, 144.7 (aromatic carbons) ppm; MS (*m/z*): 526.43 [M$^+$]; *Anal.* Calcd. for $C_{29}H_{21}Cl_2N_5O$: C, 66.28; H, 4.07; N, 13.44; Found: C, 66.17; H, 4.02; N, 13.30%.

***N*-(Benzoxazol-2-yl)-4′,5′-dihydro-3′,5′-diarylisoxazole-4′-carboxamide (11)/*N*-(benzothiazol-2-yl)-4′,5′-dihydro-3′,5′-diarylisoxazole-4′-carboxamide (12)/*N*-(1*H*-benzimidazol-2-yl)-4′,5′-dihydro-3′,5′-diarylisoxazole-4′-carboxamide (13).** General procedure. A mixture of **5/6/7** (1.0 mmol), araldoxime (1.2 mmol), CAT (0.33 g, 1.2 mmol) and methanol (20 mL) was refluxed for 17–20 h. The precipitated inorganic salts were filtered off. The filtrate was concentrated, and the residue was extracted with dichloromethane. The organic layer was washed with water, brine and dried (an. Na_2SO_4). The solvent was removed under vacuum. The resultant residue was purified by column chromatography (silica gel, 60–120 mesh) using hexane/ethyl acetate (4:1) as eluent.

***N*-(Benzoxazol-2-yl)-4′,5′-dihydro-3′,5′-diphenylisoxazole-4′-carboxamide (11a).** White solid (0.27 g, 72%); m.p. 209–211°C; IR (KBr): 1570 (C=N), 1660 (C=O), 3278 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.07 (d, 1H, C_4′-H, *J* = 6.9 Hz), 5.42 (d, 1H, C_5′-H, *J* = 7.4 Hz), 7.01–7.65 (m, 14H, Ar–H), 8.39 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 61.5 (C-4′), 83.6 (C-5′), 153.1 (C-3′), 163.4 (C-2), 168.5 (CO), 110.5, 119.4,

123.6, 124.5, 127.2, 127.8, 128.4, 129.5, 129.8, 131.5, 134.5, 140.5, 141.3, 150.8 (aromatic carbons) ppm; MS (*m/z*): 383.40 [M^+]; *Anal.* Calcd. for $C_{23}H_{17}N_3O_3$: C, 72.01; H, 4.49; N, 11.08; Found: C, 72.05; H, 4.47; N, 10.96%.

N-(Benzoxazol-2-yl)-3′,5′-bis(4-methylphenyl)-4′,5′-dihydroisoxazole-4′-carboxamide (11b). White solid (0.27 g, 67%); m.p. 194–195°C; IR (KBr): 1565 (C=N), 1654 (C=O), 3265 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.30 and 2.33 (s, 6H, Ar–CH_3), 5.03 (d, 1H, C_4'-H, J = 6.8 Hz), 5.39 (d, 1H, C_5'-H, J = 6.8 Hz), 6.94–7.60 (m, 12H, Ar–H), 8.35 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 24.3 and 25.1 (Ar–CH_3), 61.1 (C-4′), 83.4 (C-5′), 152.4 (C-3′), 162.9 (C-2), 168.3 (CO), 110.2, 119.3, 123.1, 124.2, 127.1, 127.6, 128.0, 129.3, 129.4, 131.2, 134.3, 140.1, 141.2, 150.5 (aromatic carbons) ppm; MS (*m/z*): 411.47 [M^+]; *Anal.* Calcd. for $C_{25}H_{21}N_3O_3$: C, 73.04; H, 5.15; N, 10.31; Found: C, 72.98; H, 5.14; N, 10.21%.

N-(Benzoxazol-2-yl)-3′,5′-bis(4-chlorophenyl)-4′,5′-dihydroisoxazole-4′-carboxamide (11c). White solid (0.33 g, 75%); m.p. 216–218°C; IR (KBr): 1580 (C=N), 1666 (C=O), 3289 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.09 (d, 1H, C_4'-H, J = 7.1 Hz), 5.46 (d, 1H, C_5'-H, J = 7.1 Hz), 7.06–7.71 (m, 12H, Ar–H), 8.41 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 62.2 (C-4′), 83.8 (C-5′), 153.6 (C-3′), 163.7 (C-2), 168.8 (CO), 110.7, 119.6, 123.8, 124.7, 127.5, 127.9, 129.1, 129.6, 129.9, 131.8, 134.7, 140.9, 141.6, 151.1 (aromatic carbons) ppm; MS (*m/z*): 452.30 [M^+]; *Anal.* Calcd. for $C_{23}H_{15}Cl_2N_3O_3$: C, 61.21; H, 3.31; N, 9.49; Found: C, 61.08; H, 3.34; N, 9.29%.

N-(Benzothiazol-2-yl)-4′,5′-dihydro-3′,5′-diphenylisoxazole-4′-carboxamide (12a). White solid (0.30 g, 77%); m.p. 238–240°C; IR (KBr): 1583 (C=N), 1665 (C=O), 3295 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.11 (d, 1H, C_4'-H, J = 7.2 Hz), 5.49 (d, 1H, C_5'-H, J = 7.2 Hz), 6.85–8.10 (m, 14H, Ar–H), 8.42 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 62.9 (C-4′), 83.9 (C-5′), 154.2 (C-3′), 168.9 (CO), 169.6 (C-2), 121.1, 121.6, 124.3, 125.2, 125.7, 126.3, 127.8, 128.5, 129.2, 129.7, 131.5, 134.6, 140.3, 149.3 (aromatic carbons) ppm; MS (*m/z*): 399.47 [M^+]; *Anal.* Calcd. for $C_{23}H_{17}N_3O_2S$: C, 69.30; H, 4.34; N, 10.79; Found: C, 69.15; H, 4.29; N, 10.52%.

N-(Benzothiazol-2-yl)-3′,5′-bis(4-methylphenyl)-4′,5′-dihydroisoxazole-4′-carboxamide (12b). White solid (0.29 g, 70%); m.p. 226–228°C; IR (KBr): 1575 (C=N), 1661 (C=O), 3286 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.32 and 2.37 (s, 6H, Ar–CH_3), 5.06 (d, 1H, C_4'-H, J = 6.9 Hz), 5.44 (d, 1H, C_5'-H, J = 6.9 Hz), 6.81–8.05 (m, 12H, Ar–H), 8.40 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 24.5 and 25.8 (Ar–CH_3), 62.4 (C-4′), 83.5 (C-5′), 153.7 (C-3′), 168.4 (CO), 169.2 (C-2), 121.0, 121.4, 124.1, 125.1, 125.4, 126.1, 127.5, 128.2, 129.1, 129.4, 131.2, 134.3, 140.2, 148.7 (aromatic carbons) ppm; MS (*m/z*): 427.54 [M^+]; *Anal.* Calcd. for $C_{25}H_{21}N_3O_2S$: C, 70.30; H, 5.03; N, 9.74; Found: C, 70.23; H, 4.95; N, 9.83%.

N-(Benzothiazol-2-yl)-3′,5′-bis(4-chlorophenyl)-4′,5′-dihydroisoxazole-4′-carboxamide (12c). White solid (0.37 g, 81%); m.p. 257–259°C; IR (KBr): 1585 (C=N), 1670 (C=O), 3310 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.15 (d, 1H, C_4'-H, J = 7.4 Hz), 5.52 (d, 1H, C_5'-H, J = 7.4 Hz), 6.90–8.24 (m, 12H, Ar–H), 8.45 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 63.3 (C-4′), 84.1 (C-5′), 154.6 (C-3′), 169.1 (CO), 169.9 (C-2), 121.5, 121.9, 124.6, 125.5, 125.9, 126.7, 127.9, 128.8, 129.4, 129.9, 132.5, 134.8, 140.5, 149.7 (aromatic carbons) ppm; MS (*m/z*): 468.37 [M^+]; *Anal.* Calcd. for $C_{23}H_{15}Cl_2N_3O_2S$: C, 58.94; H, 3.22; N, 9.11; Found: C, 58.98; H, 3.23; N, 8.97%.

N-(1H-Benzimidazol-2-yl)-4′,5′-dihydro-3′,5′-diphenylisoxazole-4′-carboxamide (13a). Brown solid (0.29 g, 78%); m.p. 268–270°C; IR (KBr): 1568 (C=N), 1655 (C=O), 3261 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.98 (d, 1H, C_4'-H, J = 6.5 Hz), 5.37 (d, 1H, C_5'-H, J = 6.5 Hz), 7.19–7.72 (m, 14H, Ar–H), 8.37 (bs, 1H, NH), 12.82 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 60.4 (C-4′), 83.1 (C-5′), 152.5 (C-3′), 153.9 (C-2), 168.0 (CO), 115.4, 123.8, 127.1, 127.7, 128.6, 129.2, 129.7, 131.7, 134.5, 138.7, 140.8 (aromatic carbons) ppm; MS (*m/z*): 382.42 [M^+]; *Anal.* Calcd. for $C_{23}H_{18}N_4O_2$: C, 72.33; H, 4.76; N, 14.83; Found: C, 72.24; H, 4.74; N, 14.65%.

N-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-methylphenyl)-4′,5′-dihydroisoxazole-4′-carboxamide (13b). White solid (0.31 g, 76%); m.p. 255–257°C; IR (KBr): 1563 (C=N), 1650 (C=O), 3254 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.28 and 2.31 (s, 6H, Ar–CH_3), 4.95 (d, 1H, C_4'–H, J = 6.3 Hz), 5.31 (d, 1H, C_5'-H, J = 6.3 Hz), 7.15–7.64 (m, 12H, Ar–H), 8.32 (bs, 1H, NH), 12.78 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 24.1 and 25.0 (Ar–CH_3), 60.1 (C-4′), 82.9 (C-5′), 152.1 (C-3′), 153.2 (C-2), 167.6 (CO), 115.1, 123.2, 126.5, 127.4, 128.4, 129.0, 129.5, 131.2, 134.3, 138.2, 140.3 (aromatic carbons) ppm; MS (*m/z*): 410.48 [M^+]; *Anal.* Calcd. for $C_{25}H_{22}N_4O_2$: C, 73.21; H, 5.44; N, 13.78; Found: C, 73.15; H, 5.40; N, 13.65%.

N-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-chlorophenyl)-4′,5′-dihydroisoxazole-4′-carboxamide (13c). Brown solid (0.37 g, 84%); m.p. 277–279°C; IR (KBr): 1578 (C=N), 1659 (C=O), 3275 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.02 (d, 1H, C_4'-H, J = 6.7 Hz), 5.40 (d, 1H, C_5'-H, J = 6.7 Hz), 7.21–7.75 (m, 12H, Ar–H), 8.38 (bs, 1H, NH), 12.84 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 61.3 (C-4′), 83.4 (C-5′), 152.7 (C-3′), 154.3 (C-2), 168.3 (CO), 115.7, 123.9, 127.2, 127.9, 128.8, 129.3, 129.8, 131.8, 134.9, 138.8, 141.1 (aromatic carbons) ppm; MS (*m/z*): 451.32 [M^+]; *Anal.* Calcd. for $C_{23}H_{16}Cl_2N_4O_2$: C, 61.30; H, 3.59; N, 12.56; Found: C, 61.21; H, 3.57; N, 12.41%.

***N*-(Benzoxazol-2-yl)-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (14)/*N*-(benzothiazol-2-yl)-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (15)/*N*-(1*H*-benzimidazol-2-yl)-1′-phenyl-3′,5′-diaryl-1′*H*-pyrazole-4′-carboxamide (16)/*N*-(benzoxazol-2-yl)-3′,5′-diarylisoxazole-4′-carboxamide (17)/*N*-(benzothiazol-2-yl)-3′,5′-diarylisoxazole-4′-carboxamide (18)/*N*-(1*H*-benzimidazol-2-yl)-3′,5′-diarylisoxazole-4′-carboxamide (19).** General procedure: A solution of **8/9/10/11/12/13** (1 mmol) in xylene (10 mL) and chloranil (1.2 mmol) were refluxed for 24–28 h. Then, it was treated with 5% NaOH solution. The organic layer was separated and repeatedly washed with water and dried (an. Na_2SO_4). The solvent was removed *in vacuo*. The solid obtained was purified by recrystallization from 2-propanol.

N-(Benzoxazol-2-yl)-1′,3′,5′-triphenyl-1′H-pyrazole-4′-carboxamide (14a). White solid (0.31 g, 68%); m.p. 210–212°C; IR (KBr): 1570 (C=N), 1617 (C=C), 1662 (C=O), 3283 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 6.92–7.51 (m, 19H, Ar–H), 8.54 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 137.3 (C-4′), 147.5 (C-5′), 154.6 (C-3′), 163.9 (C-2), 167.6 (CO), 110.5, 119.4, 120.5, 123.8, 124.7, 126.5, 127.3, 127.8, 128.1, 128.6, 129.4, 129.7, 130.2, 133.4, 133.8, 139.6, 141.7, 150.3 (aromatic carbons) ppm; MS (*m/z*): 456.51 [M^+]; *Anal.* Calcd. for $C_{29}H_{20}N_4O_2$: C, 76.43; H, 4.46; N, 12.38; Found: C, 76.30; H, 4.42; N, 12.27%.

N-(Benzoxazol-2-yl)-3′,5′-bis(4-methylphenyl)-1′-phenyl-1′H-pyrazole-4′-carboxamide (14b). White solid (0.31 g, 65%); m.p. 197–199°C; IR (KBr): 1567 (C=N), 1611 (C=C), 1657 (C=O), 3279 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.36 and 2.39 (s, 6H, Ar–CH_3), 6.90–7.48 (m, 17H, Ar–H), 8.51 (bs, 1H,

NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 22.5 and 22.6 (Ar–CH_3), 137.0 (C-4′), 147.1 (C-5′), 154.3 (C-3′), 163.4 (C-2), 167.1 (CO), 110.3, 119.2, 120.4, 123.5, 124.4, 126.2, 127.2, 127.5, 128.0, 128.5, 129.2, 129.5, 130.1, 133.0, 133.7, 139.1, 141.3, 149.7 (aromatic carbons) ppm; MS (*m/z*): 484.56 [M^+]; *Anal.* Calcd. for $C_{31}H_{24}N_4O_2$: C, 76.94; H, 5.05; N, 11.74; Found: C, 76.84; H, 4.99; N, 11.56%.

N-(Benzoxazol-2-yl)-3′,5′-bis(4-chlorophenyl)-1′-phenyl-1′H-pyrazole-4′-carboxamide (14c). White solid (0.37 g, 71%); m.p. 223–225°C; IR (KBr): 1582 (C=N), 1619 (C=C), 1669 (C=O), 3291 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 6.96–7.55 (m, 17H, Ar–H), 8.58 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 137.7 (C-4′), 147.9 (C-5′), 154.9 (C-3′), 164.2 (C-2), 167.8 (CO), 110.8, 119.7, 120.7, 123.9, 124.8, 126.7, 127.4, 127.9, 128.3, 129.1, 129.6, 129.8, 130.7, 133.8, 134.2, 139.9, 142.1, 150.8 (aromatic carbons) ppm; MS (*m/z*): 525.40 [M^+]; *Anal.* Calcd. for $C_{29}H_{18}Cl_2N_4O_2$: C, 66.42; H, 3.47; N, 10.86; Found: C, 66.30; H, 3.45; N, 10.66%.

N-(Benzothiazol-2-yl)-1′,3′,5′-triphenyl-1′H-pyrazole-4′-carboxamide (15a). White solid (0.36 g, 77%); m.p. 258–260°C; IR (KBr): 1581 (C=N), 1623 (C=C), 1677 (C=O), 3305 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.25–8.19 (m, 19H, Ar–H), 8.56 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 137.9 (C-4′), 148.7 (C-5′), 155.5 (C-3′), 168.2 (CO), 169.0 (C-2), 120.5, 121.4, 121.9, 124.8, 125.4, 125.8, 126.5, 127.2, 127.7, 128.2, 128.5, 129.3, 129.4, 130.5, 133.2, 133.6, 139.5, 149.3 (aromatic carbons) ppm; MS (*m/z*): 472.58 [M^+]; *Anal.* Calcd. for $C_{29}H_{20}N_4OS$: C, 73.78; H, 4.30; N, 11.99; Found: C, 73.71; H, 4.27; N, 11.86%.

N-(Benzothiazol-2-yl)-3′,5′-bis(4-methylphenyl)-1′-phenyl-1′H-pyrazole-4′-carboxamide (15b). White solid (0.36 g, 73%); m.p. 236–238°C; IR (KBr): 1572 (C=N), 1618 (C=C), 1673 (C=O), 3298 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.39 and 2.41 (s, 6H, Ar–CH_3), 7.21–8.16 (m, 17H, Ar–H), 8.54 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 22.7 and 22.9 (Ar–CH_3), 137.4 (C-4′), 148.2 (C-5′), 155.1 (C-3′), 167.1 (CO), 168.7 (C-2), 120.2, 121.1, 121.7, 124.3, 125.3, 125.6, 126.1, 127.0, 127.3, 128.1, 128.3, 129.1, 129.3, 129.8, 133.0, 133.4, 139.5, 149.1 (aromatic carbons) ppm; MS (*m/z*): 500.63 [M^+]; *Anal.* Calcd. for $C_{31}H_{24}N_4OS$: C, 74.52; H, 4.84; N, 11.47; Found: C, 74.38; H, 4.83; 11.19%.

N-(Benzothiazol-2-yl)-3′,5′-bis(4-chlorophenyl)-1′-phenyl-1′H-pyrazole-4′-carboxamide (15c). White solid (0.42 g, 79%); m.p. 280–282°C; IR (KBr): 1584 (C=N), 1627 (C=C), 1681 (C=O), 3314 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.28–8.22 (m, 17H, Ar–H), 8.62 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 138.3 (C-4′), 149.3 (C-5′), 156.1 (C-3′), 168.4 (CO), 169.5 (C-2), 120.6, 121.6, 122.2, 124.9, 125.7, 125.9, 126.7, 127.4, 127.9, 128.4, 128.8, 129.5, 129.9, 130.7, 133.5, 133.8, 139.7, 149.9 (aromatic carbons) ppm; MS (*m/z*): 541.47 [M^+]; *Anal.* Calcd. for $C_{29}H_{18}Cl_2N_4OS$: C, 64.49; H, 3.30; N, 10.60; Found: C, 64.33; H, 3.35; N, 10.35%.

N-(1H-Benzimidazol-2-yl)-1′,3′,5′-triphenyl-1′H-pyrazole-4′-carboxamide (16a). Brown solid (0.30 g, 66%); m.p. 271–273°C; IR (KBr): 1573 (C=N), 1607 (C=C), 1656 (C=O), 3261 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.10–7.72 (m, 19H, Ar–H), 8.49 (bs, 1H, NH), 12.85 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 136.5 (C-4′), 146.4 (C-5′), 154.2 (C-3′), 154.9 (C-2), 167.1 (CO), 115.5, 120.5, 123.3, 126.3, 127.1, 127.8, 128.2, 128.7, 129.2, 129.5, 130.1, 133.3, 134.2, 138.7, 139.5 (aromatic carbons) ppm; MS (*m/z*): 455.52 [M^+]. *Anal.* Calcd. for $C_{29}H_{21}N_5O$: C, 76.41; H, 4.72; N, 15.48; Found: C, 76.47; H, 4.65; N, 15.37%.

N-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-methylphenyl)-1′-phenyl-1′H-pyrazole-4′-carboxamide (16b). Brown solid (0.30 g, 64%); m.p. 258–260°C; IR (KBr): 1564 (C=N), 1602 (C=C), 1649 (C=O), 3252 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.35 and 2.37 (s, 6H, Ar–CH_3), 7.07–7.67 (m, 17H, Ar–H), 8.45 (bs, 1H, NH), 12.80 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 22.1 and 22.4 (Ar–CH_3), 136.2 (C-4′), 145.2 (C-5′), 153.8 (C-3′), 154.4 (C-2), 166.9 (CO), 115.1, 120.3, 123.2, 126.1, 127.0, 127.5, 128.1, 128.5, 129.1, 129.4, 129.7, 133.1, 133.9, 138.4, 139.1 (aromatic carbons) ppm; MS (*m/z*): 483.57 [M^+]; *Anal.* Calcd. for $C_{31}H_{25}N_5O$: C, 77.09; H, 5.23; N, 14.65; Found: C, 77.00; H, 5.21; N, 14.48%.

N-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-chlorophenyl)-1′-phenyl-1′H-pyrazole-4′-carboxamide (16c). Brown solid (0.36 g, 69%); m.p. 286–288°C; IR (KBr): 1579 (C=N), 1612 (C=C), 1663 (C=O), 3275 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.16–7.73 (m, 17H, Ar–H), 8.52 (bs, 1H, NH), 12.88 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 136.9 (C-4′), 146.8 (C-5′), 154.7 (C-3′), 155.7 (C-2), 167.6 (CO), 115.8, 120.7, 123.6, 126.7, 127.4, 127.9, 128.4, 128.8, 129.3, 129.8, 130.5, 133.4, 134.5, 138.8, 139.9 (aromatic carbons) ppm; MS (*m/z*): 524.41 [M^+]; *Anal.* Calcd. for $C_{29}H_{19}Cl_2N_5O$: C, 66.53; H, 3.69; N, 13.54; Found: C, 66.42; H, 3.65; N, 13.35%.

N-(Benzoxazol-2-yl)-3′,5′-diphenylisoxazole-4′-carboxamide (17a). White solid (0.27 g, 71%); m.p. 202–204°C; IR (KBr): 1580 (C=N), 1620 (C=C), 1668 (C=O), 3285 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.14–7.66 (m, 14H, Ar–H), 8.55 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 137.1 (C-4′), 151.2 (C-5′), 156.1 (C-3′), 163.8 (C-2), 168.1 (CO), 110.5, 119.6, 123.4, 124.7, 127.2, 127.8, 128.4, 128.7, 129.3, 129.7, 130.7, 133.3, 141.6, 150.4 (aromatic carbons) ppm; MS (*m/z*): 381.39 [M^+]; *Anal.* Calcd. for $C_{23}H_{15}N_3O_3$: C, 72.49; H, 4.01; N, 11.15; Found: C, 72.43; H, 3.96; N, 11.02%.

N-(Benzoxazol-2-yl)-3′,5′-bis(4-methylphenyl)isoxazole-4′-carboxamide (17b). White solid (0.26 g, 65%); m.p. 188–190°C; IR (KBr): 1572 (C=N), 1615 (C=C), 1665 (C=O), 3277 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.30 and 2.32 (s, 6H, Ar–CH_3), 7.08–7.60 (m, 12H, Ar–H), 8.53 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 22.4 and 23.6 (Ar–CH_3), 136.4 (C-4′), 150.8 (C-5′), 155.6 (C-3′), 163.4 (C-2), 167.2 (CO), 110.2, 119.4, 123.1, 124.3, 127.1, 127.6, 128.0, 128.5, 129.1, 129.5, 130.2, 133.1, 141.3, 150.1 (aromatic carbons) ppm; MS (*m/z*): 409.45 [M^+]; *Anal.* Calcd. for $C_{25}H_{19}N_3O_3$: C, 73.26; H, 4.66; N, 10.10; Found: C, 73.34; H, 4.68; N, 10.26%.

N-(Benzoxazol-2-yl)-3′,5′-bis(4-chlorophenyl)isoxazole-4′-carboxamide (17c). White solid (0.31 g, 70%); m.p. 215–217°C; IR (KBr): 1583 (C=N), 1625 (C=C), 1670 (C=O), 3298 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.18–7.71 (m, 12H, Ar–H), 8.59 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 137.5 (C-4′), 151.8 (C-5′), 156.8 (C-3′), 164.1 (C-2), 168.4 (CO), 110.6, 119.9, 123.5, 124.8, 127.3, 127.9, 128.6, 128.9, 129.4, 129.5, 130.8, 133.9, 141.7, 150.7 (aromatic carbons) ppm; MS (*m/z*): 450.28 [M^+]; *Anal.* Calcd. for $C_{23}H_{13}Cl_2N_3O_3$: C, 61.45; H, 2.94; N, 9.47; Found: C, 61.35; H, 2.91; N, 9.33%.

N-(Benzothiazol-2-yl)-3′,5′-diphenylisoxazole-4′-carboxamide (18a). White solid (0.32 g, 82%); m.p. 242–244°C; IR (KBr): 1578 (C=N), 1622 (C=C), 1680 (C=O), 3311 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.25–8.05 (m, 14H, Ar–H), 8.60 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 137.3 (C-4′), 152.5 (C-5′), 156.7 (C-3′), 168.5 (CO), 169.5 (C-2), 121.3, 121.7, 124.3, 125.2, 125.6, 127.3, 127.8, 128.2, 128.8, 129.1, 129.4, 130.5, 133.4, 149.3 (aromatic carbons) ppm; MS

(*m/z*): 397.46 [M$^+$]; *Anal.* Calcd. for $C_{23}H_{15}N_3O_2S$: C, 69.57; H, 3.84; N, 10.75; Found: C, 69.50; H, 3.80; N, 10.57%.

N-(Benzothiazol-2-yl)-3′,5′-bis(4-methylphenyl)isoxazole-4′-carboxamide (18b). White solid (0.34 g, 80%); m.p. 221–223°C; IR (KBr): 1576 (C=N), 1617 (C=C), 1675 (C=O), 3304 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.35 and 2.39 (s, 6H, Ar–CH_3), 7.18–8.03 (m, 12H, Ar–H), 8.54 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 22.7 and 23.8 (Ar–CH_3), 136.7 (C-4′), 151.9 (C-5′), 156.2 (C-3′), 168.3 (CO), 169.3 (C-2), 121.2, 121.6, 124.1, 125.0, 125.5, 127.1, 127.4, 128.1, 128.6, 129.0, 129.3, 130.3, 133.2, 149.0 (aromatic carbons) ppm; MS (*m/z*): 425.52 [M$^+$]; *Anal.* Calcd. for $C_{25}H_{19}N_3O_2S$: C, 70.70; H, 4.52; N, 10.11; Found: C, 70.57; H, 4.50; N, 9.87%.

N-(Benzothiazol-2-yl)-3′,5′-bis(4-chlorophenyl)isoxazole-4′-carboxamide (18c). White solid (0.39 g, 85%); m.p. 250–252°C; IR (KBr): 1584 (C=N), 1628 (C=C), 1687 (C=O), 3328 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.26–8.20 (m, 12H, Ar–H), 8.63 (bs, 1H, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 137.9 (C-4′), 152.7 (C-5′), 157.1 (C-3′), 168.9 (CO), 169.8 (C-2), 121.5, 121.9, 124.7, 125.4, 125.8, 127.6, 127.9, 128.3, 128.9, 129.5, 129.9, 130.9, 133.6, 149.7 (aromatic carbons) ppm; MS (*m/z*): 466.35 [M$^+$]; *Anal.* Calcd. for $C_{23}H_{13}Cl_2N_3O_2S$: C, 59.28; H, 2.82; N, 9.08; Found: C, 59.24; H, 2.81; N, 9.01%.

N-(1H-Benzimidazol-2-yl)-3′,5′-diphenylisoxazole-4′-carboxamide (19a). Brown solid (0.29 g, 78%); m.p. 203–205°C; IR (KBr): 1575 (C=N), 1610 (C=C), 1664 (C=O), 3263 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.25–7.77 (m, 14H, Ar–H), 8.52 (bs, 1H, NH), 12.87 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 136.1 (C-4′), 149.5 (C-5′), 155.2 (C-3′), 156.7 (C-2), 167.3 (CO), 115.7, 123.6, 126.5, 127.3, 128.2, 128.8, 129.5, 129.7, 130.4, 133.5, 138.5 (aromatic carbons) ppm; MS (*m/z*): 380.41 [M$^+$]; *Anal.* Calcd. for $C_{23}H_{16}N_4O_2$: C, 72.74; H, 4.30; N, 14.92; Found: C, 72.62; H, 4.24; N, 14.73%.

N-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-methylphenyl)isoxazole-4′-carboxamide (19b). Brown solid (0.30 g, 75%); m.p. 197–198°C; IR (KBr): 1569 (C=N), 1605 (C=C), 1651 (C=O), 3254 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.24 and 2.28 (s, 6H, Ar–CH_3), 7.20–7.71 (m, 12H, Ar–H), 8.47 (bs, 1H, NH), 12.84 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 22.1 and 23.2 (Ar–CH_3), 135.8 (C-4′), 149.3 (C-5′), 154.8 (C-3′), 156.2 (C-2), 167.0 (CO), 115.5, 123.3, 126.2, 127.1, 128.1, 128.5, 129.0, 129.4, 130.1, 133.2, 138.3 (aromatic carbons) ppm; MS (*m/z*): 408.47 [M$^+$]; *Anal.* Calcd. for $C_{25}H_{20}N_4O_2$: C, 73.46; H, 4.97; N, 13.81; Found: C, 73.51; H, 4.94; N, 13.72%.

N-(1H-Benzimidazol-2-yl)-3′,5′-bis(4-chlorophenyl)isoxazole-4′-carboxamide (19c). White solid (0.36 g, 81%); m.p. 232–234°C; IR (KBr): 1582 (C=N), 1614 (C=C), 1668 (C=O), 3276 (NH) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.29–7.80 (m, 12H, Ar–H), 8.56 (bs, 1H, NH), 12.89 (bs, 1H, imidazole-NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 136.3 (C-4′), 150.1 (C-5′), 155.5 (C-3′), 156.9 (C-2), 168.4 (CO), 115.9, 123.7, 126.9, 127.7, 128.4, 128.9, 129.6, 129.8, 130.5, 133.7, 138.9 (aromatic carbons) ppm; MS (*m/z*): 449.30 [M$^+$]; *Anal*. Calcd. for $C_{23}H_{14}Cl_2N_4O_2$: C, 61.64; H, 3.21; N, 12.75; Found: C, 61.48; H, 3.14; N, 12.47%.

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REFERENCES AND NOTES

[1] Elguero, J.; Goya, P.; Jagerovic, N.; Silva, A. M. S. Targets Heterocycl Syst 2002, 6, 52.

[2] Sheng, C.; Xu, H.; Wang, W.; Cao, Y.; Dong, G.; Wang, S.; Che, X.; Ji, H.; Miao, Z.; Yao, J.; Zhang, W. Eur J Med Chem 2010, 45, 3531.

[3] Satyendra, R. V.; Vishnumurthy, K. A.; Vagdevi, H. M.; Rajesh, K. P.; Manjunatha, H.; Shruthi, A. Eur J Med Chem 2011, 46, 3078.

[4] Eicher, T.; Hauptmann, S. The Chemistry of Heterocycles, Wiley-VCH GmbH & Co. KGaA: Weinheim, 2003.

[5] Shi, D. Q.; Rong, S. F.; Dou, G. L. Synth Commun 2010, 40, 2302.

[6] Tong, Y. S.; Bouska, J. J.; Ellis, P. A.; Johnson, E. F.; Leverson, J.; Liu, X. S.; Marcotte, P. A.; Olson, A. M.; Osterling, D. J.; Przytulinska, M.; Rodriguez, L. E.; Shi, Y.; Soni, N.; Stavropoulos, J.; Thomas, S.; Donawho, C. K.; Frost, D. J.; Luo, Y.; Giranda, V. L.; Penning, T. D. J Med Chem 2009, 52, 6803.

[7] Kalai, T.; Balog, M.; Szabo, A.; Gulyas, G.; Jeko, J.; Sumegi, B.; Hideg, K. J Med Chem 2009, 52, 1619.

[8] Wustrow, D. J.; Capiris, T.; Rubin, R.; Knobelsdorf, J. A.; Akunne, H.; Davis, M. D.; MacKenzie, R.; Pugsley, T. A.; Zoski, K. T.; Heffner, T. G.; Wise, L. D. Bioorg Med Chem Lett 1998, 8, 2067.

[9] Kees, K. L.; Fitzgerald, J. J.; Steiner, K. E. Jr.; Mattes, J. F.; Mihan, B.; Tosi, T.; Mondoro, D.; McCaleb, M. L. J Med Chem 1996, 39, 3920.

[10] Chen, H. S.; Li, Z. M.; Han, Y. F. J Agric Food Chem 2000, 48, 5312.

[11] Tanitame, A.; Oyamada, Y.; Ofuji, K.; Terauchi, H.; Kawasaki, M.; Wachi, M.; Yamagishi, J. Bioorg Med Chem Lett 2005, 15, 4299.

[12] Meazz G.; Bettarini F.; La Porta P.; Piccardi P.; Signorini, E.; Portoso, D.; Fornara L. Pest Manag Sci 2004, 60, 1178.

[13] Penning, T. D.; Talley, J. J.; Bertenshaw, S. R.; Carter, J. S.; Collins, P. W.; Docter, S.; Graneto, M. J.; Lee, L. F.; Malecha, J. W.; Miyashiro, J. M.; Rogers, R. S.; Rogier, D. J.; Yu, S. S.; Anderson, G. D.; Burton, E. G.; Cogburn, J. N.; Gregory, S. A.; Koboldt, C. M.; Perkins, W. E.; Seibert, K.; Veenhuizen, A. W.; Zhang, Y. Y.; Isakson, P. C. J Med Chem 1997, 40, 1347.

[14] Daidone, G.; Raffa, D.; Maggio, B.; Plescia, F.; Cutuli, V. M. C.; Mangano, N. G.; Caruso, A. Arch Pharm Pharm Med Chem 1999, 332, 50.

[15] Tomita, K.; Takahi, Y.; Ishizuka, R.; Kamamura, S.; Nakagawa, M.; Ando, M.; Nakanishi, T.; Nakamura, T.; Udaira, H. Ann Sankyo Res Lab 1973, 1, 25; Chem Abstr 1974, 80, 120808.

[16] Talley, J. J. Prog Med Chem 1999, 13, 201.

[17] Talley, J. J.; Brown, D. L.; Carter, J. S.; Graneto, M. J.; Koboldt, C. M.; Masferrer, J. L.; Perkins, W. E.; Rogers, R. S.; Shaffer, A. F.; Zhang, Y. Y.; Zweifel, B. S.; Seibert, K. J Med Chem 2000, 43, 775.

[18] Li, W.-T.; Hwang, D.-R.; Chen, C.-P.; Shen, C.-W.; Huang, C.-L.; Chen, T.-W.; Lin, C.-H.; Chang, Y.-L.; Chang, Y.-Y.; Lo, Y.-K.; Tseng, H.-Y.; Lin, C.-C.; Song, J.-S.; Chen, H.-C.; Chen, S.-J.; Wu, S.-H.; Chen, C.-T. J Med Chem 2003, 46, 1706.

[19] Just, G.; Dhal, K. Tetrahedron 1968, 24, 5251.

[20] Lokanath Rai, K. M.; Linganna, N.; Hassner, A.; Murthy, C. A. Org Prep Proc Intl 1992, 24, 91.

[21] Kim, J. N.; Ryu, E. K. Synth Commun 1990, 20, 1373.

[22] Lokanath Rai, K. M.; Hassner, A. Synth Commun 1989, 19, 2799.

[23] Lokanath Rai, K. M.; Hassner, A. Synth Commun 1997, 27, 467.

[24] Hassner, A.; Lokanath Rai, K. M. Synthesis 1989, 57.

[25] Padmavathi, V.; Sumathi, R. P.; Chandrasekhar Babu, N.; Bhaskar Reddy, D. J Chem Res (S), 1999, 610.

[26] Padmavathi, V.; Sumathi, R. P.; Venugopal Reddy, K.; Somasekhar Reddy, A.; Bhaskar Reddy, D. Synth Commun 2000, 30, 4007.

[27] Padmavathi, V.; Jagan Mohan Reddy, B.; Venkata Subbaiah, D. R. C. New J Chem 2004, 28, 1479.

[28] Padmavathi, V.; Jagan Mohan Reddy, B.; Chandra Obula Reddy, B.; Padmaja, A. Tetrahedron 2005, 61, 2407.
[29] Zhou, C. H.; Wang Y. Curr Med Chem 2012, 19, 239.
[30] Wang, Y.; Zhou, C. H. Sci Sin Chim 2011, 41, 1429 (in Chinese).
[31] Simovic, D.; Di, M.; Marks, V.; Chatfield, D. C.; Rein, K. S. J Org Chem 2007, 72, 650.
[32] Burits, M.; Bucar, F. Phytother Res 2000, 14, 323.
[33] Cuendet, M.; Hostettmann, K.; Potterat, O. Helv Chim Acta 1997, 80, 1144.
[34] Green, L. C.; Wagner, D. A.; Glogowski, J.; Skipper, P. L.; Wishnok, J. K. S. R. Anal Biochem 1982, 126, 131.
[35] Marcocci, L.; Maguire, J. J.; Droy-Lefaix, M. T.; Packer, L. Biochem Biophys Res Commun 1994, 201, 748.
[36] Ruch, R. J.; Cheng, S. J.; Klaunig, J. E. Carcinogenesis 1989, 10, 1003.
[37] Saritha, G.; Sarangapani, M.; Prasad, G.; Swathi, C. Der Pharmacia Let 2011, 3, 427.
[38] Robert, W. H. III; Samuel, R.; Catherine, S. R.; Cynthia, B.; Steven, A. R.; Andrew, T. S.; Christian, M. Bioorg Med Chem 2010, 18, 663.
[39] Vogel's, A. I. Text Book of Practical Organic Chemistry 5th edn. Longman Group UK Ltd.: London 1989.