A Novel and Efficient One Pot Synthesis of 2,4-Disubstituted Thiazoles and Oxazoles Using Phenyltrimethylammoniumtribromide in Ionic Liquid

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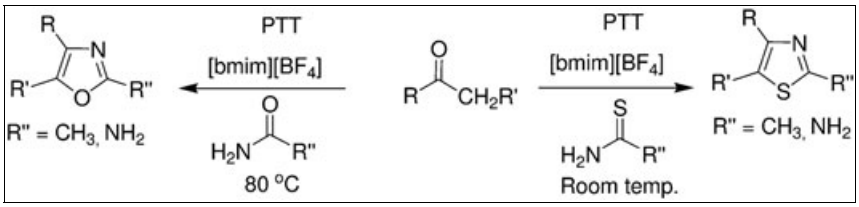

A novel and efficient one-pot procedure has been described for synthesis of 2,4-disubstituted thiazoles and oxazoles from substituted ketones using phenyltrimethylammoniumtribromide as *in situ* brominating agent followed by reaction with thioamide/thiourea and amides/ureas, respectively in [bmim][BF_4] ionicliquid. The advantages of the procedure include avoiding the handling of lacrymetric compounds, hazardous and toxic organic solvents along with good to excellent yield of the products.

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INTRODUCTION

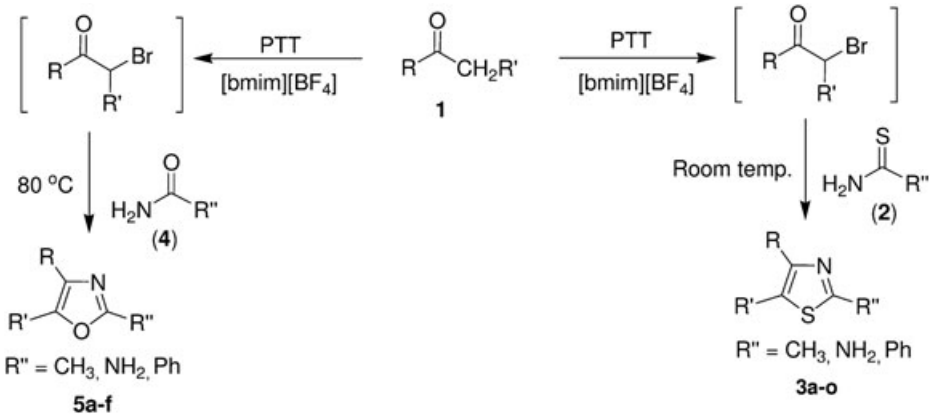
Thiazoles and oxazoles are common structural motif found in both natural products and pharmaceuticals with broad spectrum of biological activities [1]. These molecules are also synthetic intermediates for the synthesis of large number of pharmaceutical compounds. Compounds containing these motifs display antifungal [2], antibacterial [2,3], anti-HIV [4], antiinflammatory [5], antitubercular [6], histone deacetylase inhibition [7], and are ligands for estrogen-receptors (ER) [8]. Occurrence of these motifs in natural products and their diverse biological activities has inspired significant interest in their synthesis [1b,9]. The well known method for synthesis of thiazole and oxazole skeleton is Hantzsch's method, which involves condensation of α-haloketones with thioamide/thiourea and amides/ureas, respectively. Many other methods have been reported for the synthesis of 2,4-disubstituted thiazoles and oxazoles using β-cyclodextrin in water [10], alkynyl(aryl)iodonium reagents [11], ammonium-12-molybdophosphate [12], oxodiphosphonium salt [13], and microwave irradiation [14]. Owing to stress on development on green synthetic methodologies, recently synthesis of thiazoles was also achieved in alternative solvents such as water [15], ionic liquid [16], and PEG [17]. However, many of these methods suffer from one or more drawbacks that include use of reactive or unsafe starting materials such as α-haloketones, use of expensive and corrosive catalysts, use of volatile organic solvents, tedious reaction work-up, long reaction times, low yields, and harsh reaction conditions. Furthermore, most of these procedure are for the synthesis of 2,4-disubstituted thiazoles, there have been far fewer methods that describe the synthesis of oxazoles starting directly from ketones. Thus, there is a need for an economical, environmentally safe and practical method for the synthesis of thiazoles and oxazoles.

Ionic liquids have currently received much attention as alternative reaction media for various chemical and biochemical reactions [18]. In continuation of our research work towards development of eco-friendly reaction methodologies [19] and our interest in thiazoles and oxazoles, herein we report a greener one-pot synthesis of 2,4-disubstituted thiazoles and oxazoles from ketones using phenyltrimethylammoniumtribromide (PTT) as *in-situ* brominating agent in [bmim][BF_4] ionic liquid (Scheme 1). To the best of our knowledge this is the first report on the synthesis of oxazoles in ionic liquid using PTT as *in-situ* brominating agent.

RESULT AND DISCUSSION

Initially, we tried reaction of *p*-chloroacetophenone and thiourea in the presence of NBS or Br_2 to yield 4-(4′-chlorophenyl)thiazol-2-amine (**3b**). The yield of **3b** was very low (<20%) with both NBS and Br_2. With our earlier experience with PTT as *in situ* brominating agent in ionic liquid [19d], we replaced NBS or Br_2 with PTT in the above reaction and to our delight the yield of **3b** increased to 90%. The added advantage with PTT is that it does not require any acidic conditions or radical initiator like NBS and handling of PTT is very easy as compare to other brominating agents. With PTT *in-situ* bromination of *p*-chloroacetophenone was completed

Scheme 1. Outline for synthesis of thiazoles and oxazoles.



within 2 h. After bromination, the condensation of *insitu* generated α-bromo-*p*-chloroacetophenone with thiourea was carried out in the same reaction media to give 4-(4′-chlorophenyl)thiazol-2-amine (**3b**).

To understand the role of solvent the model reaction was carried out in different solvents such as [bmim][BF_4], [bmim][PF_6], methanol, THF, DMF, DCM, toluene, and water. In DMF and toluene, no appreciable yield of product was obtained whereas in other organic solvents such as DCM, THF and methanol the yield of **3b** was between 65 and 80% (Table 1). Among two ionic liquids screened, [bmim][BF_4] was found to give the best yield (90%) of **3b** (Table 1). The results are in agreement with previous report on the synthesis of thiazoles from α-bromoketones in ionic liquid where [bmim][BF_4] was found to be better medium over [bmim][PF_6] and other ionic liquids [16]. The ionic liquid [bmim][BF_4] was selected as solvent of choice keeping in view of its non volatile and environmentally benign nature. The role of ionic liquid to enhance the rate of reaction may be in terms of some Lewis/ Brønsted acidity of the imidazolium cation leading to increased electropositive character of carbonyl group of *in situ* generated α-bromoketone as proposed earlier [16,19c]. The [bmim][BF4] also enhances the rate of *in-situ* bromination of ketones by PTT as reported earlier [19d]. The structure of **3b** was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, and HRMS data. In HRMS spectrum a peak appeared at *m/z* 210.9817 corresponding to $[M+H]^+$ ion for $C_9H_8ClN_2S$. In ^{1}H-NMR characteristic peak at δ 6.72 appeared for C_5-proton of the thiazole ring and in ^{13}C-NMR characteristic peak appeared at δ 165.28 and 102.21 ppm for C_2-carbon and C_4-carbon of the thiazole ring, respectively. The IR spectrum showed two peaks at 3446 and 3216 cm^{-1} corresponding to the NH_2 group.

After obtaining optimum reaction conditions, to study the scope of the reaction different substituted ketones (**1**) and thioamides/thiourea (**2**) were allowed to react to give corresponding thiazoles (**3a–o**). The results for these thiazoles are summarized in Table 2. The yields of the thiazoles are excellent (75–92%) and the synthetic strategy allows synthesis of diverse thiazoles. As per the yields of thiazoles (Table 2) it can be observed that acetophenones containing both electron withdrawing and electron releasing substituents were tolerated as good substrate for this reaction under these conditions.

To explore the generality and increase the utility of the protocol we extended it for the synthesis of 2,4-disubstituted oxazoles (**5a–f**) from ketones. Initially, we failed to achieve the desired 2-methyl-4-phenyloxazole (**5f**) from the reaction of acetophenone and acetamide using PTT in [bmim][BF_4] at room temperature. After exploring different reaction conditions the best yield of **5f** was obtained when the reaction mixture was heated at 80°C in [bmim][BF_4]. The lower reactivity at room temperature can be attributed to the lower nucleophilicity of oxygen in acetamide as compared to sulfur in thioamides. The structure of oxazole **5f** was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR, and HRMS data. In HRMS, a peak at *m/z* 160.0431 was observed for $[M+H]^+$ ion. In

Table 1

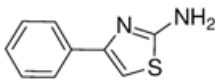
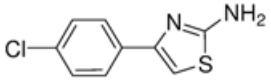
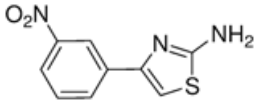
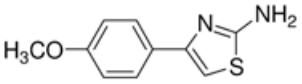
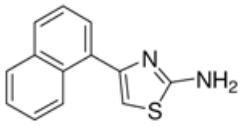
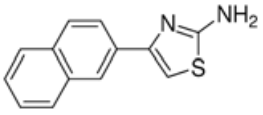
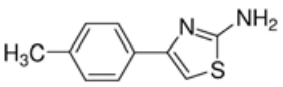
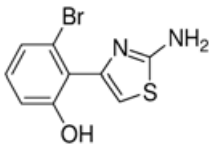
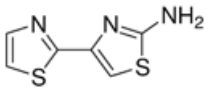
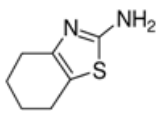
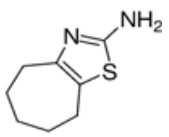
Solvent effect on the yield of 4-(4′-chlorophenyl)thiazol-2-amine (**3b**).

Sr. No.	Solvent	Time (h)	Yield (%)
1	[bmim][BF_4]	4	90
2	[bmim][PF_6]	6	65
3	DCM	4	82
4	Methanol	6	70
5	THF	6	75
6	DMF	24	<10
7	Toluene	24	–
8	Water	24	–

[a]Isolated yields.
[b]No product observed on TLC.

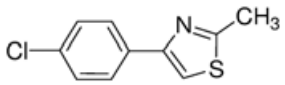
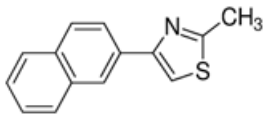
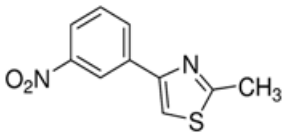
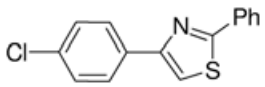
Table 2

Synthesis of 2,4-disubstituted thiazoles in [bmim][BF_4].

Sr. No.	R	R′	R″	Product		Time (h)	Yield (%)	Mp °C (Lit. Mp)
1	Ph	H	NH_2		**3a**	4	92	148–150 (150) [15]
2	4-ClPh	H	NH_2		**3b**	4	90	163–165 (163–164) [16]
3	3-NO_2Ph	H	NH_2		**3c**	4	86	187–189 (188–190) [15]
4	4-OCH_3Ph	H	NH_2		**3d**	4	87	204–207 (204–205) [15]
5	1-Naphthyl	H	NH_2		**3e**	4	80	157–158
6	2-Naphthyl	H	NH_2		**3f**	4	80	152–154 (152–153) [15]
7	4-CH_3Ph	H	NH_2		**3g**	4	85	130 (125–126) [16]
8	6-OH, 2-BrPh	H	NH_2		**3h**	4	85	209–212
9	2-Thiazolyl	H	NH_2		**3i**	4	87	186–189
10	-$CH_2(CH_2)_2CH_2$-		NH_2		**3j**	4	83	87–90 (88–90) [20]
11	-$CH_2(CH_2)_3CH_2$-		NH_2		**3k**	4	81	63–66

(*Continues*)

Table 2
(Continued)

Sr. No.	R	R′	R″	Product		Time (h)	Yield (%)	Mp °C (Lit. Mp)
12	4-ClPh	H	CH_3		**3l**	5	81	112–115 (111–112) [16]
13	2-Naphthyl	H	CH_3		**3m**	5	78	88–89
14	3-NO_2Ph	H	CH_3		**3n**	5	80	87–89
15	4-ClPh	H	Ph		**3o**	6	75	130–132

[a]All the products gave satisfactory ^{1}H-NMR, ^{13}C-NMR, and mass data.
[b]Isolated yield.

similarity with **3b**, a characteristic peak for C_3-proton of oxazole ring was observed at δ 8.36 ppm whereas a peak appeared at δ 2.40 for C_2-methyl protons in ^{1}H-NMR spectrum. Two peaks appeared at δ 167.73 and 125.42 ppm for C_2-carbon and C_4-carbon, respectively in ^{13}C-NMR spectrum. After obtaining the optimum reaction conditions, the scope of protocol was examined for the synthesis of diversified oxazoles by the reaction of different substituted ketones and amides/ureas in the presence of PTT in [bmim][BF_4]. The results for different oxazoles are summarized in Table 3. It was observed that yields were lower for oxazoles (68–76%) and reaction required longer time and high temperature as compared to thiazoles. Like thiazoles, in the synthesis of oxazole as well acetophenones containing both electron withdrawing and electron releasing substituents were tolerated as good substrate for this reaction under these conditions.

CONCLUSIONS

In conclusion, we have demonstrated a novel, highly efficient one-pot procedure for synthesis of 2,4-disubstituted thiazoles and oxazoles from the reaction of ketones with thioamides/thiourea and amides/urea using PTT as *in-situ* brominating agent in ionic liquid [bmim][BF_4]. The main advantages of this procedure are avoiding the handling of lacrymetric compounds, hazardous organic solvents, and toxic catalysts. Further studies for the synthesis of 1,3-imidazoles using this method is in progress in our laboratory.

EXPERIMENTAL

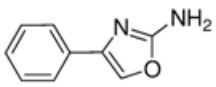
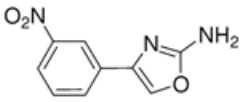
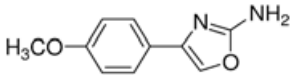
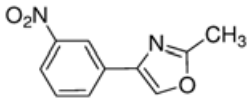
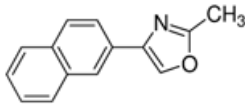
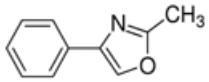
1-Methylimidazole, *n*-butyl bromide, $NaBF_4$, and KPF_6 were purchased from Sigma-Aldrich. All other reagents and solvents were purchased from S. D. Fine, India and used without further purification unless otherwise specified. Column chromatography was carried out over silica gel (60–120 mesh, S. D. Fine, India). NMR spectra were recorded on a Brucker Heaven Avance 11 400 spectrophotometer using $CDCl_3$ and DMSO-d_6 as solvent and the chemical shifts were expressed in ppm. Mass spectra were recorded on a QSTAR® ELITE LX/MS/MS mass spectrometer from applied biosystem. The purity of the products was determined on silica-coated aluminium plates (Merck). The ionic liquid, [bmim][BF_4] and [bmim][PF_6] were prepared from 1-methylimidazole by minor modification of literature procedure [23].

General procedure for synthesis of 2,4-disubstitutedthiazoles. PTT (655 mg, 1.1 mmol) was added to a mixture of ketone (1.0 mmol) in [bmim][BF_4] (2.0 mL) and reaction mixture was stirred vigorously at room temperature for 2 h then thioamide/thiourea (1.2 mmol) was added to this reaction mixture and stirred for additional 1 h at room temperature. Progress of the reaction was monitored by thin layer chromatography (TLC), after completion of reaction aqueous sodium bicarbonate wash was given to reaction mixture and pH ∼9 was maintained. The precipitation occurred, which was filtered and washed with diethyl ether. The residue obtained after diethyl wash was percolated through a band of silica gel (60–120 mesh) using hexane/ethyl acetate (9: 1 *v/v*) as an eluent to afford corresponding compounds in 75–92% yield.

Spectral data for selected thiazoles. ***4-(Napthalen-1-yl) thiazol-2-amine (3e).*** ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 6.75 (s, 1H), 7.09 (s, 2H, NH_2), 7.50 (d, *J* = 6.5 Hz, 3H), 7.62 (d, *J* = 7.1 Hz, 1H), 7.97–7.82 (m, 2H), 8.44 (d, *J* = 8.0 Hz,

Table 3

Synthesis of 2,4-disubstituted oxazoles in [bmim][BF_4].

Sr. No.	R	R′	R″	Product		Time (h)	Yield (%)	Mp (°C) (Lit. Mp)
1	Ph	H	NH_2		**5a**	8	76	150–152 (151–152) [21]
2	3-NO_2Ph	H	NH_2		**5b**	8	75	149–153
3	4-CH_3OPh	H	NH_2		**5c**	8	74	179–181 (179–180) [21]
4	3-NO_2Ph	H	CH_3		**5d**	9	70	113–115
5	2-Naphthyl	H	CH_3		**5e**	10	68	70–72
6	Ph	H	CH_3		**5f**	10	71	45 (45) [22]

[a]All the products gave satisfactory ^{1}H-NMR, ^{13}C-NMR, and mass data.
[b]Isolated yield.

1H). ^{13}C-NMR (126 MHz, DMSO-d_6): δ = 168.41, 150.49, 133.94, 133.91, 131.17, 128.56, 128.35, 127.01, 126.67, 126.31, 126.21, 125.85, and 105.41; HRMS: *m/z* calcd. for $C_{13}H_{10}N_2S$ 226.0565, found: 227.0343 $[M+H]^+$.

4-(Naphthalene-2yl)thiazol-2-amine (3f). ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 7.09 (s, 2H), 7.15 (s, 1H), 7.50–7.42 (m, 2H), 7.95–7.83 (m, 4H), 8.30 (s, 1H); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 168.68, 150.20, 133.63, 132.76, 132.72, 128.50, 128.32, 127.96, 126.77, 126.24, 124.47, 124.44, and 102.85; HRMS: *m/z* calcd. for $C_{13}H_{10}N_2S$ 226.0565, found 227.0341 $[M+H]^+$.

4-p-Tolylthiazol-2-amine (3g). ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 7.70 (d, *J* = 7.9 Hz, 2H, ArH), 7.14 (d, *J* = 7.8 Hz, 2H, ArH), 6.99 (brs, 2H, NH_2), 6.89 (s, 1H), 2.27 (s, 3H, CH_3); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 168.52, 150.30, 136.80, 132.70, 129.45, 125.91, 100.99, and 21.22; HRMS: *m/z* calcd. for $C_{10}H_{10}N_2S$ 190.0565, found 191.0347 $[M+H]^+$.

2-(2-Aminothiazol-4-yl)-3-bromophenol (3h). ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 11.93 (s, 1H, OH), 7.92–7.90 (m, 1H, ArH), 7.45–7.39 (m, 2H, ArH), 7.24 (brs, 2H, NH_2), 7.16 (s, 1H); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 168.62, 155.10, 145.95, 131.51, 129.14, 121.23, 119.46, 110.60, and 103.09; HRMS: *m/z* calcd. for $C_9H_7BrN_2OS$ 269.9462, found 270.9342 $[M+H]^+$.

4-(Thiazol-2-yl)thiazol-2-amine (3i). ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 7.83–7.74 (m, 1H), 7.68–7.58 (m, 1H), 7.28 (brs, 2H, amine), 7.16 (s, 1H); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 169.16, 163.21, 144.51, 143.95, 120.15, and 104.50; MS (ESI) *m/z* calcd. for $C_6H_5N_3S_2$ 182.9925, found 183.8932 $[M+H]^+$.

4,5,6,7-Tetrahydrobenzo(d)thiazol-2-amine (3j). ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 5.06 (brs, 2H), 3.01–2.43 (m, 4H), 2.00–1.53 (m, 4H); ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 165.21, 145.23, 118.07, 26.50, 23.54, 23.17, and 22.95; MS (ESI) *m/z* calcd. for $C_7H_{10}N_2S$ 154.0565, found 155.0235 $[M+H]^+$.

5,6,7,8-Tetrahydro-4H-cyclohepta(d)thiazol-2-amine (3k). ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 4.88 (brs, 2H, NH_2), 2.63–2.56 (m, 4H), 1.78–1.55 (m, 6H); ^{13}C-NMR (101 MHz, DMSO-d_6) δ = 163.18, 149.71, 121.12, 31.58, 31.29, 28.25, 26.60, and 26.02; MS (ESI) *m/z* calcd. for $C_8H_{12}N_2S$ 168.0721, found 169.0452 $[M+H]^+$.

4-(4′-Chlorophenyl)-2-methylthiazole (3l). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.82–7.79 (d, *J* = 8.4 Hz, 2H), 7.39–7.29 (m, 2H), 7.26 (s, 1H), 2.76 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 169.32, 150.36, 138.06, 133.03, 128.88, 127.57, 112.61, and 19.33; HRMS: *m/z* calcd. for $C_{10}H_8ClNS$ 209.0066, found 209.9316 $[M+H]^+$.

2-Methyl-4-(naphthalene-2′-yl)thiazole (3m). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.41 (s, 1H), 7.94–7.81 (m, 4H), 7.47–7.42 (m, 3H), 2.80 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.76, 152.80, 131.37, 130.80, 129.52, 126.14, 126.10,

125.39, 124.04, 123.78, 123.00, 121.98, 110.4, and 17.12; HRMS: *m/z* calcd. for $C_{14}H_{11}NS$ 225.0612, found 226.0389 $[M+H]^+$.

2-Methyl-(4′-nitrophenyl)thiazole (3n). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.72 (s, 1H), 8.23–8.15 (m, 2H), 7.61–7.55 (t, *J* = 8.1 Hz, 1H), 7.48 (s, 1H), 2.79 (s, 3H); ^{13}C-NMR (75MHz, $CDCl_3$) δ = 166.71, 152.59, 148.72, 136.14, 132.08, 129.68, 122.52, 121.14, 114.43, and 19.33; HRMS: *m/z* calcd. for $C_{10}H_8N_2O_2S$ 220.0306, found 221.0278 $[M+H]^+$.

4-(4′-Chlorophenyl)-2-phenylthiazole (3o). ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 8.24 (s, 1H), 8.12–8.05 (m, 3H), 8.05–7.96 (m, 2H), 7.62–7.45 (m, 4H); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 167.73, 154.32, 133.30, 133.27, 133.17, 130.94, 129.75, 129.31, 128.30, 126.69, and 115.84; HRMS: *m/z* calcd. for $C_{15}H_{10}ClNS$ 271.0222, found 272.0103 $[M+H]^+$.

General procedure for synthesis of 2,4-disubstituted oxazoles. PTT (655 mg, 1.1 mmol) was added portion wise to a mixture of ketone (1.0 mmol) in [bmim][BF_4] (2.0 mL) and the reaction was stirred vigorously at room temperature for 2 h then acetamide/urea (1.2 mmol) was added to the reaction mixture and stirred it for additional 7–10 h at 80°C. Progress of the reaction was monitored by TLC. After completion of reaction aqueous sodium bicarbonate wash was given to the reaction mixture to maintain pH ~9. The compound was extracted using ethyl acetate (3 × 3 mL). The combined organic layer was dried with anhydrous sodium sulphate and concentrated under reduced pressure. The crude product obtained was purified by column chromatography on silica gel (60–120 mesh) using hexane/ethyl acetate (9: 1 *v/v*) as eluent to afford corresponding compounds in 71–85% yield.

Spectral data for selected oxazoles. ***4-Phenyloxazol-2-amine (5a).*** ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 7.29–7.24 (m, 1H, ArH), 7.40–7.33 (m, 2H, ArH), 7.70 (d, *J* = 8.2 Hz, 2H, ArH), 8.36 (s, 1H); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 161.99, 139.43, 132.49, 128.91, 127.66, 127.57, and 125.10; HRMS: *m/z* calcd. for $C_9H_8N_2O$ 160.0637, found 161.0345 $[M+H]^+$.

4-(3′-Nitrophenyl)oxazol-2-amine (5b). ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 8.34 (s, 1H), 8.03–7.96 (m, 3H), 7.57 (s, 1H), 6.79 (br, 2H, NH_2); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 164.45, 150.85, 139.81, 136.45, 133.45, 132.76, 131.71, 124.30, and 121.55; HRMS: *m/z* calcd. for $C_9H_7N_3O_3$ 205.0487, found 206.0038 $[M+H]^+$.

2-Methyl-4-(3′-nitrophenyl)oxazole (5d). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.54 (s, 1H), 8.16–8.13 (d, *J* = 8.4 Hz, 1H), 8.05–8.03 (d, *J* = 7.5 Hz, 1H), 8.02–7.94 (m, 1H), 7.57–7.54 (d, *J* = 8.1 Hz, 1H), 2.55 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 162.46, 151.03, 146.32, 138.87, 134.42, 131.14, 129.73, 122.50, 120.27, and 13.95; HRMS: *m/z* calcd. for $C_{10}H_8N_2O$ 204.0535, found 205.0437 $[M+H]^+$.

2-Methyl-(napthalen-2′-yl)oxazole (5e). ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.26 (s, 1H), 7.91–7.88 (m, 2H), 7.83–7.81 (m, 2H), 7.74–7.71 (m, 1H), 7.50–7.43 (m, 2H), 2.56 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.0, 153.22, 141.70, 134.55, 134.01, 129.37, 129.18, 128.67, 127.37, 126.98, 125.11, 124.37, 118.31, and 15.01; HRMS: *m/z* calcd. for $C_{14}H_{11}NO$ 209.0841, found 210.0734 $[M+H]^+$.

2-Methyl-4-phenyloxazole (5f). ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 2.40 (s, 3H, CH_3), 7.27 (s, 1H), 7.46–7.35 (m, 3H, ArH), 7.70 (d, *J* = 8.2 Hz, 2H, ArH), 8.36 (s, 1H, ArH); ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 162.10, 139.99, 134.96, 131.28, 129.20, 128.24, 125.42, and 13.86; HRMS: *m/z* calcd. for $C_{10}H_9NO$ 159.0684, found 160.0431 $[M+H]^+$.

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REFERENCES AND NOTES

[1] (a) Yeh, V. S. C. Tetrahedron 2004, 60, 11995; (b) Jin, Z. Nat Prod Rep 2006, 23, 464; (c) Lewis, J. R. Nat Prod Rep 1999, 16, 389.

[2] George, C.; Martin, N.; Ray, R. J Med Chem 1973, 16, 1402.

[3] Kaspady, M.; Narayanaswamy, V. K.; Raju, M.; Rao, G. K. Lett Drug Des Discov 2009, 6, 21.

[4] Bell, F. W.; Cantrell, A. S.; Hoegberg, M.; Jaskunas, S. R.; Johansson, N. G.; Jordan, C. L.; Kinnick, M. D.; Lind, P.; Morin, J. M. J Med Chem 1995, 38, 4929.

[5] (a) George, C.; Michael, J. F. J Med Chem 1971, 14, 1075; (b) Venugopala, K. N.; Jayashree, B. S. Indian J Heterocycl Chem 2003, 12, 307.

[6] (a) Wang, W.; Nan, F. J Org Chem 2003, 68, 1636; (b) Andreani, A.; Burnelli, S.; Granaiola, M.; Leoni, A.; Locatelli, A.; Morigi, R.; Rambaldi, M.; Varoli, L.; Calonghi, N.; Cappadone, C.; Farruggia, G.; Zini, M.; Stefanelli, C.; Masotti, L.; Radin, N. S.; Shoemaker, R. H. J Med Chem 2008, 51, 809.

[7] Anandan, S. K.; Ward, J. S.; Brokx, R. D.; Denny, T.; Bray, M. R.; Patel, D. V.; Xiao, X. Y. Bioorg Med Chem Lett 2007, 17, 5995.

[8] Fink, B. E.; Mortensen, D. S.; Stauffer, S. R.; Aron, Z. D.; Katzenellenbogen, J. A. Chem Biol 1999, 6, 205.

[9] Wipf, P. Chem Rev (Washington, DC, US) 1995, 95, 2115.

[10] Narender, M.; Reddy, M. S.; Sridhar, R.; Nageswar, Y. V. D.; Rao, K. R. Tetrahedron Lett 2005, 46, 5953.

[11] Wipf, P.; Venkatraman, S. J Org Chem 1996, 61, 8004.

[12] Das, B.; Reddy, V. S.; Ramu, R. J Mol Catal A: Chem 2006, 252, 235.

[13] You, S.-L.; Kelly, J. W. J Org Chem 2003, 68, 9506.

[14] (a) Kabalka, G. W.; Mereddy, A. R. Tetrahedron Lett 2006, 47, 5171; (b) Lee, J. C.; Choi, H. J.; Lee, Y. C. Tetrahedron Lett 2003, 44, 123.

[15] Potewar, T. M.; Ingale, S. A.; Srinivasan, K. V. Tetrahedron 2008, 64, 5019.

[16] Potewar, T. M.; Ingale, S. A.; Srinivasan, K. V. Tetrahedron 2007, 63, 11066.

[17] Jawale, D. V.; Lingampalle, D. L.; Pratap, U. R.; Mane, R. A. Chin Chem Lett 2010, 21, 412.

[18] Jain, N.; Kumar, A.; Chauhan, S.; Chauhan, S. M. S. Tetrahedron 2005, 61, 1015.

[19] (a) Kumar, A.; Rao, M. S.; Rao, V. K. Aust J Chem 2010, 63, 1538; (b) Kumar, A.; Rao, M. S.; Rao, V. K. Aust J Chem 2010, 63, 135; (c) Kumar, D.; Patel, G.; Kumar, A.; Roy, R. K. J Heterocycl Chem 2009, 46, 791; (d) Kumar, A.; Ahmed, I.; Rao, M. S.; Patel, G.; Kumar, D. Indian J Chem 2009, 48B, 416; (e) Rao, M. S.; Ahmad, I.; Khungar, B.; Kumar, A. Can J Chem 2009, 87, 714; (f) Kumar, A.; Ahmad, I.; Rao, M. S. J Sulfur Chem 2009, 30, 570.

[20] Gasteiger, J.; Herzig, C. Tetrahedron 1981, 37, 2607.

[21] Nath, J. P.; Dash, M.; Satrusallya, S. C.; Mahapatra, G. N. Indian J Chem 1981, 20B, 606.

[22] Ang, K. H.; Prager, R. H.; Smith, J. A.; Weber, B.; Williams, C. M. Tetrahedron Lett 1996, 37, 675.

[23] (a) Chauhan, S. M. S.; Kumar, A.; Srinivas, K. A. Chem Commun (Cambridge, UK) 2003, 2348; (b) Srinivas, K. A.; Kumar, A.; Chauhan, S. M. S. Chem Commun (Cambridge, UK) 2002, 2456.