Synthesis of 2-Arylquinazolin-4(3*H*)-ones by *N*-Aryl Benzamidines with Aromatic Carbonates

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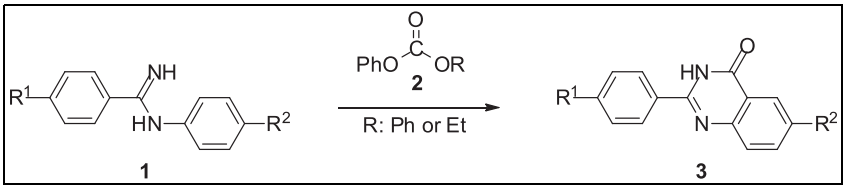

The reaction of *N*-aryl benzamidines **1a–n** with diphenyl carbonate **2a** or ethyl phenyl carbonate **2b** synthesized 2-arylquinazolin-4(3*H*)-ones **3a–n** in simple and safe process with good yields (71–90%). It was suggested that different electron-donating substituent in *N*-aryl benzamidines **1a–n** afforded similar effect to the yields of 2-arylquinazolin-4(3*H*)-ones **3a–n**. In these reactions, *N*-aryl benzamidines **1a–n** built up intermediate compounds by nucleophilic addition to carbonates **2** to give annulation products **3a–n**, following to cyclization involving the elimination of ethanol/phenol.

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INTRODUCTION

In 1946, M. M. Endicott et al. [1] first described a synthesis of quinazolin-4(3*H*)-ones from anthranilic acid with formamide. Quinazolin-4(3*H*)-ones, one of the heterocycles, are applied to intermediate compounds to synthesize antibacterial and anticancer agents [2], of which synthetic processes have been developed by many researchers. Y. Kabri et al. and X. Zhang et al. reported the green chemical success to provide quinazolin-4(*3H*)-ones with good yields by microwave-assisted synthetic process [3]. Additionally, recent studies of quinazolin-4(*3H*)-ones developed the novel catalysts to be achieved with mild reaction and one-pot and/or solvent-free reaction process [4].

Our earlier studies have certified the reaction to obtain heterocycles from pyrimidine or oxazine derivatives with some electrophilic reagents and their reaction mechanism [5]. Herein, we report the easy and safe one-pot process synthesizing 2-arylquinazolin-4(3*H*)-ones **3** by the reaction of *N*-aryl benzamidines **1** and aromatic carbonates **2**, diphenyl carbonate or ethyl phenyl carbonate, without catalyst, as shown in Scheme 1.

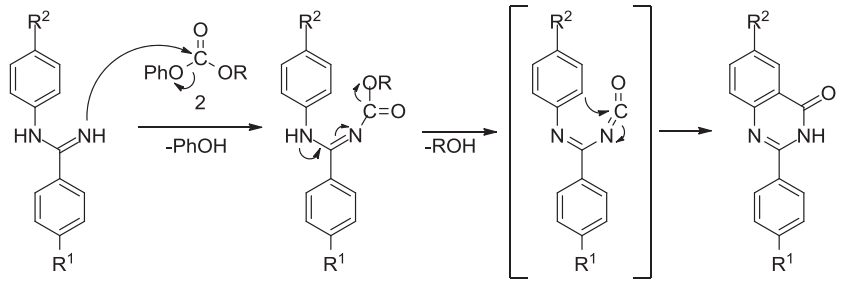
RESULTS AND DISCUSSION

N-aryl benzamidines **1a–n** were synthesized and characterized with ^{1}H NMR analysis and measurement of melting point [6]. The reactions of *N*-aryl benzamidines **1a–n** with diphenyl carbonate **2a** at 180°C for 5 h afforded 2-arylquinazolin-4(3*H*)-ones **3a–n** in good yields (71–90%). It was found that the yields of 2-arylquinazolin-4(3*H*)-ones **3a–n** were remarkably independent on different species of electron-donating group replaced on *N*-aryl benzamidines **1**. On the other hand, the yields of the products obtained by *N*-aryl benzamidines **1** with ethyl phenyl carbonate **2b** were similar in comparison with those yields as shown in Table 1. The compounds **3a–n** produced in both of the reaction were characterized by ^{1}H NMR spectral and elemental analysis data. Also, products formed isoindolin-1-one ring were not found in these reactions [7].

In addition, *N*-aryl benzamidines **1a, 1c**, and **1d** unreacted with diethyl carbonate as dialkyl carbonate under the same or stronger reaction conditions. It seems reasonable to suppose that this reaction was related to the elimination of alcohol by means of nucleophilic attack of *N*-aryl benzamidines **1** to carbonate. In fact, *N*-ethoxycarbonyl-*N*′-(4-methylphenyl)-4-methylbenzamidine **4e** as an intermediate compound was isolated with the reaction of *N*-(4-methylphenyl)-4-methylbenzamidine **1e** and ethyl phenyl carbonate **2b** at 70°C for 72 h with 80.7% yield and then provided 6-methyl-2-*p*-tolylquinazolin-4(3*H*)-one **3e** with 88.0% yield calculated on the basis of its carbamate derivative **4e** by heating at 180°C for 5 h in tetraglyme. These results did not only provide a relationship between their yields and elimination of alcohol from carbonate **2** but also a definitive evidence of mechanism passing through intermediate compound **4** for these reactions [7].

It was concluded that their *N*-aryl benzamidines **1** reacted with aromatic carbonates **2** to give 2-arylquinazolin-4-ones **3** within good yield in easy and safe process.

Scheme 1



1 **4** **4'** **3**

	R^1	R^2		R^1	R^2
a	H	H	h	OMe	Me
b	H	Me	i	OMe	OMe
c	H	Me	j	H	Br
d	Me	H	k	H	Cl
e	Me	Me	l	Me	Cl
f	Me	OMe	m	Cl	Me
g	OMe	H	n	Cl	H

Table 1

Yield of 2-arylquinazoline-4(3*H*)-ones **3** obtained by the reaction of *N*-aryl benzamidines **1a–n** with aryl carbonates **2**.

3	R^1	R^2	Diphenyl carbonate **2a** %	Ethyl phenyl carbonate **2b** %
a	H	H	81.2	77.5
b	H	Me	84.2	85.3
c	H	OMe	81.7	82.1
d	Me	H	83.2	73.0
e	Me	Me	89.8	84.1
f	Me	OMe	70.4	78.5
g	OME	H	83.7	85.7
h	OME	Me	85.6	85.1
i	OMe	OMe	82.6	84.7
j	H	Br	84.2	73.5
k	H	CI	71.3	59.8
l	Me	CI	80.0	63.2
m	CI	Me	89.0	85.5
n	CI	H	81.5	83.2

EXPERIMENTAL

All melting points were provided with uncorrected measurement. ^{1}H NMR data were obtained using a JEOL JNM-ECX500M (500 MHz) spectrometer in $CDCl_3$ or DMSO-d_6 with tetramethylsilane (0.03%) as an internal standard. Elemental analyses of 2-arylquinazolin-4(3*H*)-ones **3** and the intermediate compound **4e** were performed using a Perkin-Elmer 2400 II CHN analyzer.

General procedure for the synthesis of *N*-aryl benzamidines 1. *N*-Aryl benzamidines **1a–n** were prepared by modifying the literature procedure [6]. A mixture of corresponding 4-substituted benzonitriles with 4-substituted anilines was heated at 180–200°C (oil bath) with a mechanical stirring in the presence of $AlCl_3$ as catalyst. After 20 min, the mixture was recovered by treatment of diluted HCl solution, neutralized with diluted NaOH aqueous solution, and then extracted with sufficient ether. Organic layer was dried with an excess of Na_2SO_4 overnight and then evaporated with a rotary evaporator. *N*-aryl benzamidines were recystallized from a solution mixed benzene and *n*-hexane and dried *in vacuo*.

***N*-Phenyl benzamidine (1a) [6].** The product was collected as colorless powder, synthesized by the reaction of benzonitrile (50 mmol), aniline (50 mmol), and $AlCl_3$ (50 mmol); 72.8% yield; mp 117–118°C; ^{1}H NMR δ 4.83 (2H, brs, NH × 2), 7.00 (2H, d, J = 8.3 Hz, Ar-H), 7.07 (1H, t, J = 7.6 Hz, Ar-H), 7.35 (2H, d, J = 7.6 Hz, Ar-H), 7.43–7.49 (3H, m, Ar-H), 7.89 (2H, d, J = 8.3 Hz, Ar-H).

***N*-(4-Methylphenyl) benzamidine (1b).** The product was collected as colorless powder, synthesized by the reaction of benzonitrile (30 mmol), *p*-toluidine (24 mmol), and $AlCl_3$ (23 mmol); 77.3% yield; mp 99–101°C; ^{1}H NMR δ 2.33 (3H, s, CH_3), 4.83 (2H, brs, NH × 2), 6.89 (2H, d, J = 8.3 Hz, Ar-H), 7.16 (1H, d, J = 7.6 Hz, Ar-H), 7.42–7.49 (3H, m, Ar-H), 7.88 (2H, d, J = 8.3 Hz, Ar-H).

***N*-(4-Methoxylphenyl) benzamidine (1c).** The product was collected as pale pink powder, synthesized by the reaction of benzonitrile (21 mmol), *p*-anisidine (21 mmol), and $AlCl_3$ (20 mmol); 30.7% yield; mp 112–113°C; ^{1}H NMR δ 3.80 (3H, s, OCH_3), 4.85 (2H, brs, NH × 2), 6.91 (4H, brs, Ar-H), 7.42–7.49 (3H, m, Ar-H), 7.87 (2H, d, J = 6.9 Hz, Ar-H).

N-Phenyl 4-methylbenzamidine (1d). The product was collected as colorless powder, synthesized by the reaction of *p*-tolylnitrile (20 mmol), aniline (20 mmol), and $AlCl_3$ (20 mmol); 48.0% yield; mp 151–153°C; ^{1}H NMR δ 3.80 (3H, s, OCH_3), 4.85 (2H, brs, NH × 2), 6.91 (4H, brs, Ar-H), 7.42–7.49 (3H, m, Ar-H), 7.87 (2H, d, *J* = 6.9 Hz, Ar-H).

N-(4-Methylphenyl) 4-methylbenzamidine (1e). The product was collected as light gray powder, synthesized by the reaction of *p*-tolylnitrile (20 mmol), *p*-toluidine (20 mmol), and $AlCl_3$ (20 mmol); 45.0% yield; mp 116–117°C; ^{1}H NMR δ 2.33 (3H, s, CH_3), 2.40 (3H, s, CH_3), 4.79 (2H, brs, NH × 2), 6.88 (2H, d, *J* = 8.0 Hz, Ar-H), 7.16 (2H, d, *J* = 8.0 Hz, Ar-H), 7.23 (2H, d, *J* = 8.0 Hz, Ar-H), 7.76 (2H, d, *J* = 8.0 Hz, Ar-H).

N-(4-Methoxyphenyl) 4-methylbenzamidine (1f). The product was collected as pink powder, synthesized by the reaction of *p*-tolylnitrile (30 mmol), *p*-anisidine (30 mmol), and $AlCl_3$ (30 mmol); 15.7% yield; mp 139–140°C; ^{1}H NMR δ 2.40 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 4.81 (2H, brs, NH × 2), 6.92 (4H, brs, Ar-H), 7.24 (2H, d, *J* = 8.0 Hz, Ar-H), 7.77 (2H, d, *J* = 8.0 Hz, Ar-H).

N-Phenyl 4-methoxybenzamidine (1g). The product was collected as pale pink powder, synthesized by the reaction of *p*-anisonitrile (19 mmol), aniline (19 mmol), and $AlCl_3$ (19 mmol); 23.0% yield; mp 146–148°C; ^{1}H NMR δ 3.89 (3H, s, OCH_3), 4.76 (2H, brs, NH × 2), 6.95 (2H, d, *J* = 8.9 Hz, Ar-H), 6.98 (2H, d, *J* = 7.4 Hz, Ar-H), 7.05 (1H, t, *J* = 7.4 Hz, Ar-H), 7.35 (2H, t, *J* = 7.4 Hz, Ar-H), 7.84 (2H, d, *J* = 8.9 Hz, Ar-H).

N-(4-Methylphenyl) 4-methoxybenzamidine (1h). The product was collected as pink powder, synthesized by the reaction of *p*-anisonitrile (20 mmol), *p*-toluidine (20 mmol), and $AlCl_3$ (20 mmol); 12.6% yield; mp 125–127°C; ^{1}H NMR δ 2.33 (3H, s, CH_3), 3.86 (3H, s, OCH_3), 4.76 (2H, brs, NH × 2), 6.88 (2H, d, *J* = 8.0 Hz, Ar-H), 6.95 (2H, d, *J* = 8.5 Hz, Ar-H), 7.16 (2H, d, *J* = 8.0 Hz, Ar-H), 7.84 (2H, d, *J* = 8.5 Hz, Ar-H).

N-(4-Methoxyphenyl) 4-methoxybenzamidine (1i). The product was collected as pink powder, synthesized by the reaction of *p*-anisonitrile (20 mmol), *p*-anisidine (20 mmol), and $AlCl_3$ (20 mmol); 9.7% yield; mp 151–153°C; ^{1}H NMR δ 3.81 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 4.77 (2H, brs, NH × 2), 6.92 (4H, brs, Ar-H), 6.95 (2H, d, *J* = 8.6 Hz, Ar-H), 7.83 (2H, d, *J* = 8.6 Hz, Ar-H).

N-Phenyl 4-bromobenzamidine (1j). The product was collected as pale purple powder, synthesized by the reaction of benzonitrile (14 mmol), 4-bromobenzenamine (14 mmol), and $AlCl_3$ (14 mmol); 70.5% yield; mp 122–124°C; ^{1}H NMR δ 4.84 (2H, brs, NH × 2), 6.88 (2H, d, *J* = 8.6 Hz, Ar-H), 7.43–7.51 (5H, m, Ar-H), 7.86 (2H, d, *J* = 8.4 Hz, Ar-H).

N-Phenyl 4-chlorobenzamidine (1k). The product was collected as colorless powder, synthesized by the reaction of benzonitrile (30 mmol), 4-chlorobenzenamine (30 mmol), and $AlCl_3$ (30 mmol); 71.7% yield; mp 118–120°C; ^{1}H NMR δ 4.84 (2H, brs, NH × 2), 6.93 (2H, d, *J* = 8.6 Hz, Ar-H), 7.32 (2H, d, *J* = 8.6 Hz, Ar-H), 7.44–7.51 (3H, m, Ar-H), 7.86 (2H, d, *J* = 8.3 Hz, Ar-H).

N-(4-Chlorophenyl) 4-methylbenzamidine (1l). The product was collected as colorless powder, synthesized by the reaction of *p*-tolylnitrile (20 mmol), 4-chlorobenzenamine (20 mmol), and $AlCl_3$ (20 mmol); 90.6% yield; mp 142–144°C; ^{1}H NMR δ 2.41 (3H, s, CH_3), 4.81 (2H, brs, NH × 2), 6.92 (2H, d, *J* = 8.6 Hz, Ar-H), 7.25 (2H, d, *J* = 8.3 Hz, Ar-H), 7.31 (2H, d, *J* = 8.6 Hz, Ar-H), 7.75 (2H, d, *J* = 8.3 Hz, Ar-H).

N-(4-Methylphenyl) 4-chlorobenzamidine (1m). The product was collected as colorless powder, synthesized by the reaction of 4-chlorobenzonitrile (18 mmol), *p*-toluidine (18 mmol), and $AlCl_3$ (18 mmol); 63.1% yield; mp 140–142°C; ^{1}H NMR δ 2.33 (3H, s, CH_3), 4.81 (2H, brs, NH × 2), 6.87 (2H, d, *J* = 8.0 Hz, Ar-H), 7.17 (2H, d, *J* = 8.0 Hz, Ar-H), 7.41 (2H, d, *J* = 8.6 Hz, Ar-H), 7.82 (2H, d, *J* = 8.6 Hz, Ar-H).

N-(4-Chlorophenyl) benzamidine (1n). The product was collected as light brown powder, synthesized by the reaction of 4-chlorobenzonitrile (40 mmol), aniline (40 mmol), and $AlCl_3$ (40 mmol); 49.6% yield; mp 143–144°C; ^{1}H NMR δ 4.81 (2H, brs, NH × 2), 6.97 (2H, d, *J* = 7.5 Hz, Ar-H), 7.07 (1H, t, *J* = 7.5 Hz, Ar-H), 7.36 (2H, t, *J* = 7.5 Hz, Ar-H), 7.42 (2H, d, *J* = 8.5 Hz, Ar-H), 7.83 (2H, d, *J* = 8.5 Hz, Ar-H).

Ethyl phenyl carbonate (2b). Ethyl phenyl carbonate was prepared by modifying the literature procedure [8]. Toluene solution containing phenol (0.39 mol) and pyridine (0.26 mol) was added into ethyl chloroformate (0.26 mol) and dissolved with toluene at room temperature. After heating at 100°C for 1 h, a reaction mixture was washed with benzene and diluted HCl aqueous solution, neutralized with diluted NaOH aqueous solution, and washed with plenty of ion-exchanged water twice. Organic layer was dried with Na_2SO_4 overnight, and then evaporated. The residue was purified by distilling under reduced pressure to afford the product as colorless liquid; 65.2% yield; bp 125°C/10 mmHg; ^{1}H NMR δ 1.39 (3H, t, *J* = 7.0 Hz, CH_3), 4.32 (2H, q, *J* = 7.0 Hz, CH_2), 7.18 (2H, d, *J* = 8.0 Hz, Ar-H), 7.24 (1H, t, *J* = 8.0 Hz, Ar-H), 7.38 (2H, t, *J* = 8.0 Hz, Ar-H).

General procedure for the synthesis of 2-arylquinazolin-4(3*H*)-ones 3 by reaction of *N*-aryl benzamidines 1 and diphenyl carbonate 2a. A mixture of *N*-aryl benzamidines **1** and diphenyl carbonate **2a** in triglyme was heated at 180°C for 5 h with stirring. After the reaction mixture was cooled to room temperature, the precipitated material was collected by filtration, washed with mixed solution of benzene and *n*-hexane, and dried in high vacuum. Samples for analysis were recrystallized from ethyl acetate.

2-Phenylquinazolin-4(3H)-one (3a) [7]. The product was obtained as colorless powder, synthesized by the reaction of *N*-phenyl benzamidine **1a** (20 mmol) and diphenyl carbonate **2** (20 mmol) in triglyme (40 mL); 81.2% yield; mp 236–237°C; ^{1}H NMR: δ 7.51–7.62 (4H, m, Ar-H), 7.75 (1H, d, *J* = 7.9 Hz, Ar-H), 7.85 (1H, t, *J* = 7.9 Hz, Ar-H), 8.16 (1H, d, *J* = 7.9 Hz, Ar-H), 8.19 (2H, d, *J* = 7.9 Hz, Ar-H), 12.5 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.65; H, 4.63; N, 12.64.

6-Methyl-2-phenylquinazolin-4(3H)-one (3b). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-methylphenyl) benzamidine **1b** (20 mmol) and diphenyl carbonate **2** (20 mmol) in triglyme (40 mL); 84.2% yield; mp 255–256°C; ^{1}H NMR: δ 2.46 (3H, s, CH_3), 7.53–7.60 (3H, m, Ar-H), 7.65 (1H, d, *J* = 8.6 Hz, Ar-H), 7.67 (1H, dd, *J* = 8.6 Hz, 2.0 Hz, Ar-H), 7.96 (1H, d, *J* = 2.0 Hz, Ar-H), 8.17 (2H, d, *J* = 7.7 Hz, Ar-H), 12.5 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.01; H, 4.86; N, 11.80.

6-Methoxy-2-phenylquinazolin-4(3H)-one (3c). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-methoxylphenyl) benzamidine **1c** (15 mmol) and diphenyl carbonate **2a** (15 mmol) in triglyme (30 mL); 81.7% yield; mp 260–261°C; ^{1}H NMR: δ 3.90 (3H, s, OCH_3), 7.52–7.59 (4H, m, Ar-H), 7.45 (1H, dd, *J* = 8.9 Hz, 3.2 Hz, Ar-H), 7.70 (1H, d, *J* = 8.9 Hz, Ar-H), 8.16 (2H, d, *J* = 7.7 Hz, Ar-H), 12.5 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79 N, 11.10. Found: C, 71.70; H, 4.86; N, 11.14.

2-p-Tolylquinazolin-4(3H)-one (3d) [7]. The product was obtained as pale yellow powder, synthesized by the reaction of *N*-phenyl-4-methylbenzamidine **1d** (20 mmol) and diphenyl

carbonate **2a** (20 mmol) in triglyme (40 mL); 83.2% yield; mp 236–237°C; ^{1}H NMR: δ 2.50 (3H, s, CH_3), 7.36 (2H, d, J = 8.3 Hz, Ar-H), 7.50 (1H, t, J = 7.7 Hz, Ar-H), 7.73 (1H, d, J = 7.7 Hz, Ar-H), 7.83 (1H, t, J = 7.7 Hz, Ar-H), 8.10 (2H, d, J = 8.3 Hz, Ar-H), 8.14 (1H, d, J = 7.7 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.48; H, 5.23; N, 11.80.

6-Methyl-2-p-tolylquinazolin-4(3H)-one (3e) [7]. The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methylphenyl)-4-methylbenzamidine **1e** (20 mmol) and diphenyl carbonate **2a** (20 mmol) in triglyme (40 mL); 89.8% yield; mp 272–273°C; ^{1}H NMR: δ 2.39 (3H, s, CH_3), 2.46 (3H, s, CH_3), 7.35 (2H, d, J = 8.3 Hz, Ar-H), 7.63 (1H, d, J = 8.3 Hz, Ar-H), 7.65 (1H, dd, J = 8.3 Hz, J = 2.0 Hz, Ar-H), 7.94 (1H, d, J = 2.0 Hz, Ar-H), 8.08 (2H, d, J = 8.3 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.86; H, 5.69; N, 11.29.

6-Methoxy-2-p-tolylquinazolin-4(3H)-one (3f). The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methoxyphenyl)-4-methylbenzamidine **1f** (20 mmol) and diphenyl carbonate **2a** (20 mmol) in triglyme (40 mL); 70.4% yield; mp 231–233°C; ^{1}H NMR: δ 2.45 (3H, s, CH_3), 3.89 (3H, s, OCH_3), 7.34 (2H, d, J = 8.3 Hz, Ar-H), 7.44 (1H, dd, J = 8.9 Hz, 3.2 Hz, Ar-H), 7.54 (1H, d, J = 3.2 Hz, Ar-H), 7.68 (1H, d, J = 8.9 Hz, Ar-H), 8.08 (2H, d, J = 8.3 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.35; H, 5.22; N, 10.46.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (3g) [8,9]. The product was obtained as colorless powder, synthesized by the reaction of *N*-phenyl-4-methoxybenzamidine **1g** (10 mmol) and diphenyl carbonate **2a** (10 mmol) in triglyme (20 mL); 83.7% yield; mp 240–242°C; ^{1}H NMR: δ 3.85 (3H, s, OCH_3), 7.09 (2H, d, J = 8.9 Hz, Ar-H), 7.48 (1H, t, J = 7.6 Hz, Ar-H), 7.70 (1H, d, J = 7.6 Hz, Ar-H), 7.81 (1H, t, J = 7.6 Hz, Ar-H), 8.13 (1H, d, J = 7.6 Hz, Ar-H), 8.19 (2H, d, J = 8.9 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.64; H, 5.01; N, 11.25.

2-(4-Methoxyphenyl)-6-methylquinazolin-4(3H)-one (3h) [7]. The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methylphenyl)-4-methoxybenzamidine **1h** (10 mmol) and diphenyl carbonate **2a** (10 mmol) in triglyme (20 mL); 85.6% yield; mp 256–257°C; ^{1}H NMR: δ 2.37 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 7.08 (2H, d, J = 8.9 Hz, Ar-H), 7.61 (1H, d, J = 8.3 Hz, Ar-H), 7.64 (1H, dd, J = 8.3 Hz, 2.1 Hz, Ar-H), 7.93 (1H, d, J = 2.1 Hz, Ar-H), 8.18 (2H, d, J = 8.9 Hz, Ar-H), 12.3 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.44; H, 5.55; N, 10.66.

6-Methoxy-2-(4-methoxyphenyl)quinazolin-4(3H)-one (3i). The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methoxyphenyl)-4-methoxybenzamidine **1i** (10 mmol) and diphenyl carbonate **2a** (10 mmol) in triglyme (20 mL); 82.6% yield; mp 264–266°C; ^{1}H NMR: δ 3.85 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 7.09 (2H, d, J = 8.9 Hz, Ar-H), 7.43 (1H, dd, J = 8.9 Hz, 2.9 Hz, Ar-H), 7.53 (1H, d, J = 2.9 Hz, Ar-H), 7.67 (1H, d, J = 8.9 Hz, Ar-H), 8.17 (2H, d, J = 8.9 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 68.23; H, 5.23; N, 9.98.

6-Bromo-2-phenylquinazolin-4(3H)-one (3j). The product was obtained as colorless powder, synthesized by the reaction of *N*-phenyl-4-bromobenzamidine **1j** (20 mmol) and diphenyl carbonate **2a** (20 mmol) in triglyme (40 mL); 84.2% yield; mp 296–297°C; ^{1}H NMR: δ 7.56 (2H, t, J = 7.5 Hz, Ar-H), 7.61 (1H, t, J = 7.5 Hz, Ar-H), 7.70 (1H, d, J = 8.6 Hz, Ar-H), 7.99 (1H, dd, J = 8.6 Hz, 2.3 Hz, Ar-H), 8.18 (2H, d, J = 7.5 Hz, Ar-H), 8.24 (1H, d, J = 2.3 Hz, Ar-H), 12.7 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_9BrN_2O$: C, 55.84; H, 3.01; N, 9.30. Found: C, 55.83; H, 2.88; N, 9.34.

6-Chloro-2-phenylquinazolin-4(3H)-one (3k). The product was obtained as colorless powder, synthesized by the reaction of *N*-phenyl-4-chlorobenzamidine **1k** (20 mmol) and diphenyl carbonate **2a** (20 mmol) in triglyme (40 mL); 71.3% yield; mp 290–291°C; ^{1}H NMR: δ 7.56 (2H, t, J = 7.4 Hz, Ar-H), 7.61 (1H, t, J = 7.4 Hz, Ar-H), 7.77 (1H, d, J = 8.6 Hz, Ar-H), 7.87 (1H, dd, J = 8.6 Hz, 2.3 Hz, Ar-H), 8.10 (1H, d, J = 2.3 Hz, Ar-H), 8.18 (2H, d, J = 7.4 Hz, Ar-H), 12.7 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.51; H, 3.50; N, 10.89.

6-Chloro-2-p-tolylquinazolin-4(3H)-one (3l) [7]. The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-chlorophenyl)-4-methylbenzamidine **1l** (20 mmol) and diphenyl carbonate **2a** (20 mmol) in triglyme (40 mL); 80.0% yield; mp 292–293°C; ^{1}H NMR: δ 2.40 (3H, s, CH_3), 7.36 (2H, d, J = 8.3 Hz, Ar-H), 7.75 (1H, d, J = 8.5 Hz, Ar-H), 7.85 (1H, dd, J = 8.5 Hz, 2.6 Hz, Ar-H), 8.08 (1H, d, J = 2.6 Hz, Ar-H), 8.09 (2H, d, J = 8.3 Hz, Ar-H), 12.5 (1H, brs, NH); $C_{15}H_{11}ClN_2O$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.61; H, 3.85; N, 10.41.

2-(4-Chlorophenyl)-6-methylquinazolin-4(3H)-one (3m). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-methylphenyl)-4-chlorobenzamidine **1m** (20 mmol) and diphenyl carbonate **2a** (20 mmol) in triglyme (40 mL); 89.0% yield; mp 306–307°C; ^{1}H NMR: δ 2.47 (3H, s, CH_3), 7.62 (2H, d, J = 8.6 Hz, Ar-H), 7.65 (1H, d, J = 8.3 Hz, Ar-H), 7.67 (1H, dd, J = 8.3 Hz, 2.0 Hz, Ar-H), 7.96 (1H, d, J = 2.0 Hz, Ar-H), 8.19 (2H, d, J = 8.6 Hz, Ar-H), 12.6 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.85; H, 4.01; N, 10.21.

2-(4-Chlorophenyl)quinazolin-4(3H)-one (3n). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-chlorophenyl) benzamidine **1n** (20 mmol) and diphenyl carbonate **2a** (20 mmol) in triglyme (40 mL); 81.5% yield; mp 305–306°C; ^{1}H NMR: δ 7.63 (2H, d, J = 8.6 Hz, Ar-H), 7.54 (1H, t, J = 7.5 Hz, Ar-H), 7.75 (1H, d, J = 7.5 Hz, Ar-H), 7.85 (1H, t, J = 7.5 Hz, Ar-H), 8.16 (1H, d, J = 7.5 Hz, Ar-H), 8.21 (2H, d, J = 8.6 Hz, Ar-H), 12.6 (1H, brs, NH); *Anal.* Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.50; H, 3.50; N, 10.86.

General procedure for the synthesis of 2-arylquinazolin-4(3*H*)-ones 3 by reaction of *N*-aryl benzamidines 1 and ethyl phenyl carbonate 2b. A mixture of *N*-aryl benzamidines **1** and ethyl phenyl carbonate **2b** in tetraglyme was heated at 180°C for 5 h with stirring. After the reaction mixture was cooled to room temperature, the precipitated material was collected by filtration and washed with ethyl acetate. Samples for analysis were recrystallized from ethyl acetate.

2-Phenylquinazolin-4(3H)-one (3a) [7]. The product was obtained as colorless powder, synthesized by the reaction of *N*-phenyl benzamidine **1a** (20 mmol) and ethyl phenyl carbonate **2b** (25 mmol) in tetraglyme (25 mL); 77.5% yield; mp 236–237°C; ^{1}H NMR: δ 7.51–7.62 (4H, m, Ar-H), 7.75 (1H, d, J = 7.9 Hz, Ar-H), 7.85 (1H, t, J = 7.9 Hz, Ar-H), 8.16 (1H, d, J = 7.9 Hz, Ar-H), 8.19 (2H, d, J = 7.9 Hz, Ar-H), 12.5 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.76; H, 4.80; N, 12.78.

6-Methyl-2-phenylquinazolin-4(3H)-one (3b). The product was obtained as colorless powder, synthesized by the reaction of *N*-

(4-methylphenyl) benzamidine **1b** (20 mmol) and ethyl phenyl carbonate **2b** (26 mmol) in tetraglyme (40 mL); 85.3% yield; mp 255–256°C; ^{1}H NMR: δ 2.46 (3H, s, CH_3), 7.53–7.60 (3H, m, Ar-H), 7.65 (1H, d, J = 8.6 Hz, Ar-H), 7.67 (1H, dd, J = 8.6 Hz, 2.0 Hz, Ar-H), 7.96 (1H, d, J = 2.0 Hz, Ar-H), 8.17 (2H, d, J = 7.7 Hz, Ar-H), 12.5 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.10; H, 5.35; N, 11.93.

6-Methoxy-2-phenylquinazolin-4(3H)-one (3c). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-methoxylphenyl) benzamidine **1c** (20 mmol) and ethyl phenyl carbonate **2b** (27 mmol) in tetraglyme (40 mL); 82.1% yield; mp 260–261°C; ^{1}H NMR: δ 3.90 (3H, s, OCH_3), 7.52–7.59 (4H, m, Ar-H), 7.45 (1H, dd, J = 8.9 Hz, 3.2 Hz, Ar-H), 7.70 (1H, d, J = 8.9 Hz, Ar-H), 8.16 (2H, d, J = 7.7 Hz, Ar-H), 12.5 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79 N, 11.10. Found: C, 71.60; H, 5.06; N, 11.01.

2-p-Tolylquinazolin-4(3H)-one (3d) [7]. The product was obtained as pale yellow powder, synthesized by the reaction of *N*-phenyl-4-methylbenzamidine **1d** (20 mmol) and ethyl phenyl carbonate **2b** (25 mmol) in tetraglyme (40 mL); 73.0% yield; mp 236–237°C; ^{1}H NMR: δ 2.50 (3H, s, CH_3), 7.36 (2H, d, J = 8.3 Hz, Ar-H), 7.50 (1H, t, J = 7.7 Hz, Ar-H), 7.73 (1H, d, J = 7.7 Hz, Ar-H), 7.83 (1H, t, J = 7.7 Hz, Ar-H), 8.10 (2H, d, J = 8.3 Hz, Ar-H), 8.14 (1H, d, J = 7.7 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.46; H, 5.34; N, 11.88.

6-Methyl-2-p-tolylquinazolin-4(3H)-one (3e) [7]. The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methylphenyl)-4-methylbenzamidine **1e** (20 mmol) and ethyl phenyl carbonate **2b** (25 mmol) in tetraglyme (40 mL); 84.1% yield; mp 272–273°C; ^{1}H NMR: δ 2.39 (3H, s, CH_3), 2.46 (3H, s, CH_3), 7.35 (2H, d, J = 8.3 Hz, Ar-H), 7.63 (1H, d, J = 8.3 Hz, Ar-H), 7.65 (1H, dd, J = 8.3 Hz, J = 2.0 Hz, Ar-H), 7.94 (1H, d, J = 2.0 Hz, Ar-H), 8.08 (2H, d, J = 8.3 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.83; H, 5.92; N, 11.32.

6-Methoxy-2-p-tolylquinazolin-4(3H)-one (3f). The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methoxyphenyl)-4-methylbenzamidine **1f** (20 mmol) and ethyl phenyl carbonate **2b** (25 mmol) in tetraglyme (40 mL); 78.5% yield; mp 231–233°C; ^{1}H NMR: δ 2.45 (3H, s, CH_3), 3.89 (3H, s, OCH_3), 7.34 (2H, d, J = 8.3 Hz, Ar-H), 7.44 (1H, dd, J = 8.9 Hz, 3.2 Hz, Ar-H), 7.54 (1H, d, J = 3.2 Hz, Ar-H), 7.68 (1H, d, J = 8.9 Hz, Ar-H), 8.08 (2H, d, J = 8.3 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.29; H, 5.17; N, 10.44.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (3g) [8,9]. The product was obtained as colorless powder, synthesized by the reaction of *N*-phenyl-4-methoxybenzamidine **1g** (10 mmol) and ethyl phenyl carbonate **2b** (13 mmol) in tetraglyme (20 mL); 85.7% yield; mp 240–242°C; ^{1}H NMR: δ 3.85 (3H, s, OCH_3), 7.09 (2H, d, J = 8.9 Hz, Ar-H), 7.48 (1H, t, J = 7.6 Hz, Ar-H), 7.70 (1H, d, J = 7.6 Hz, Ar-H), 7.81 (1H, t, J = 7.6 Hz, Ar-H), 8.13 (1H, d, J = 7.6 Hz, Ar-H), 8.19 (2H, d, J = 8.9 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.44; H, 5.17; N, 11.29.

2-(4-Methoxyphenyl)-6-methylquinazolin-4(3H)-one (3h) [7]. The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methylphenyl)-4-methoxybenzamidine **1h** (20 mmol) and ethyl phenyl carbonate **2** (25 mmol) in tetraglyme (40 mL); 85.1% yield; mp 256–257°C; ^{1}H NMR: δ 2.37 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 7.08 (2H, d, J = 8.9 Hz, Ar-H), 7.61 (1H, d, J = 8.3 Hz, Ar-H), 7.64 (1H, dd, J = 8.3 Hz, 2.1 Hz, Ar-H), 7.93 (1H, d, J = 2.1 Hz, Ar-H), 8.18 (2H, d, J = 8.9 Hz, Ar-H), 12.3 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.92; H, 5.55; N, 10.58.

6-Methoxy-2-(4-methoxyphenyl)quinazolin-4(3H)-one (3i). The product was obtained as pale yellow powder, synthesized by the reaction of *N*-(4-methoxyphenyl)-4-methoxybenzamidine **1i** (10 mmol) and ethyl phenyl carbonate **2b** (13 mmol) in tetraglyme (20 mL); 84.7% yield; mp 264–266°C; ^{1}H NMR: δ 3.85 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 7.09 (2H, d, J = 8.9 Hz, Ar-H), 7.43 (1H, dd, J = 8.9 Hz, 2.9 Hz, Ar-H), 7.53 (1H, d, J = 2.9 Hz, Ar-H), 7.67 (1H, d, J = 8.9 Hz, Ar-H), 8.17 (2H, d, J = 8.9 Hz, Ar-H), 12.4 (1H, brs, NH); *Anal*. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 68.17; H, 5.28; N, 10.06.

6-Bromo-2-phenylquinazolin-4(3H)-one (3j). The product was obtained as pale yellow powder, synthesized by the reaction of *N*-phenyl-4-bromobenzamidine **1j** (15 mmol) and ethyl phenyl carbonate **2b** (20 mmol) in tetraglyme (30 mL); 73.5% yield; mp 296–297°C; ^{1}H NMR: δ 7.56 (2H, t, J = 7.5 Hz, Ar-H), 7.61 (1H, t, J = 7.5 Hz, Ar-H), 7.70 (1H, d, J = 8.6 Hz, Ar-H), 7.99 (1H, dd, J = 8.6 Hz, 2.3 Hz, Ar-H), 8.18 (2H, d, J = 7.5 Hz, Ar-H), 8.24 (1H, d, J = 2.3 Hz, Ar-H), 12.7 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_9BrN_2O$: C, 55.84; H, 3.01; N, 9.30. Found: C, 55.86; H, 3.15; N, 9.15.

6-Chloro-2-phenylquinazolin-4(3H)-one (3k). The product was obtained as colorless powder, synthesized by the reaction of *N*-phenyl-4-chlorobenzamidine **1k** (20 mmol) and ethyl phenyl carbonate **2b** (26 mmol) in tetraglyme (40 mL); 59.8% yield; mp 290–291°C; ^{1}H NMR: δ 7.56 (2H, t, J = 7.4 Hz, Ar-H), 7.61 (1H, t, J = 7.4 Hz, Ar-H), 7.77 (1H, d, J = 8.6 Hz, Ar-H), 7.87 (1H, dd, J = 8.6 Hz, 2.3 Hz, Ar-H), 8.10 (1H, d, J = 2.3 Hz, Ar-H), 8.18 (2H, d, J = 7.4 Hz, Ar-H), 12.7 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.41; H, 3.51; N, 10.84.

6-Chloro-2-p-tolylquinazolin-4(3H)-one (3l) [7]. The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-chlorophenyl)-4-methylbenzamidine **1l** (20 mmol) and ethyl phenyl carbonate **2b** (27 mmol) in tetraglyme (40 mL); 63.2% yield; mp 292–293°C; ^{1}H NMR: δ 2.40 (3H, s, CH_3), 7.36 (2H, d, J = 8.3 Hz, Ar-H), 7.75 (1H, d, J = 8.5 Hz, Ar-H), 7.85 (1H, dd, J = 8.5 Hz, 2.6 Hz, Ar-H), 8.08 (1H, d, J = 2.6 Hz, Ar-H), 8.09 (2H, d, J = 8.3 Hz, Ar-H), 12.5 (1H, brs, NH); $C_{15}H_{11}ClN_2O$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.68; H, 4.21; N, 10.35.

2-(4-Chlorophenyl)-6-methylquinazolin-4(3H)-one (3m). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-methylphenyl)-4-chlorobenzamidine **1m** (20 mmol) and ethyl phenyl carbonate **2b** (27 mmol) in tetraglyme (40 mL); 85.5% yield; mp 306–307°C; ^{1}H NMR: δ 2.47 (3H, s CH_3), 7.62 (2H, d, J = 8.6 Hz, Ar-H), 7.65 (1H, d, J = 8.3 Hz, Ar-H), 7.67 (1H, dd, J = 8.3 Hz, 2.0 Hz, Ar-H), 7.96 (1H, d, J = 2.0 Hz, Ar-H), 8.19 (2H, d, J = 8.6 Hz, Ar-H), 12.6 (1H, brs, NH); *Anal*. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.35; H, 4.19; N, 10.32.

2-(4-Chlorophenyl)quinazolin-4(3H)-one (3n). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-chlorophenyl) benzamidine **1n** (20 mmol) and ethyl phenyl carbonate **2b** (26 mmol) in tetraglyme (40 mL); 83.2% yield; mp 305–306°C; ^{1}H NMR: δ 7.63 (2H, d, J = 8.6 Hz, Ar-H), 7.54 (1H, t, J = 7.5 Hz, Ar-H), 7.75 (1H, d, J = 7.5 Hz, Ar-H), 7.85 (1H, t, J = 7.5 Hz, Ar-H), 8.16 (1H, d, J = 7.5 Hz, Ar-H), 8.21 (2H, d, J = 8.6 Hz, Ar-H), 12.6 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.66; H, 3.62; N, 10.87.

Intermediate compound 4

N-Ethoxycarbonyl-N′-(4-methylphenyl)-4-methylbenzamidine (4e). The product was obtained as colorless powder, synthesized by the reaction of *N*-(4-methylphenyl)-4-methylbenzamidine **1e** (10 mmol) and ethyl phenyl carbonate **2b** (10 mmol) at 70°C for 72 h in diglyme (20 mL); 80.7% yield; ^{1}H NMR: δ 0.99 (3H, t, J = 7.2 Hz, CH_3), 2.27 (3H, s, CH_3), 2.36 (3H, s, CH_3), 3.85 (2H, q, J = 7.2 Hz, CH_2), 7.13 (2H, d, J = 8.0 Hz, Ar-H), 7.29 (2H, d, J = 8.0 Hz, Ar-H), 7.37 (2H, d, J = 8.0 Hz, Ar-H), 7.55 (2H, d, J = 8.0 Hz, Ar-H), 9.69 (1H, brs, NH); *Anal*. Calcd for $C_{14}H_9ClN_2O$: C, 72.95; H, 6.80; N, 9.45. Found: C, 73.15; H, 7.08; N, 9.49.

REFERENCES AND NOTES

[1] Endicott, M. M.; Wick, E.; Mercury, L. M.; Sherrill, L. M. J Am Chem Soc 1946, 68, 1299.

[2] Chandrinka, L. M.; Yakaiah, T.; Narsaiah, B.; Sridhar, V.; Venugopal, G.; Rao, J. V.; Kumar, K. P.; Murthy, S. N. U.; Rao, A. R. R. Indian J Chem 2009, 48B, 840.

[3] a) Kabri, Y.; Gellis, A.; Vanelle, P. Green Chem 2009, 11, 201; b) Zhang, X.; Ye, D.; Sun, H.; Guo, D.; Wang, J.; Huang, H.; Zhang, X.; Jiang, H.; Liu, H. Green Chem 2009, 11, 1881.

[4] a) Raid, J. A.-J.; Wolfgang, V.; Muhammad, S. Tetrahedron Lett 2004, 45, 3475; b) Liu, X.; Fu, H.; Jiang, Y.; Zhao, Y. Angew Chem Int 2009, 48, 348; c) Roopan, S. M.; Maiyalagan, T.; Khan, F. N. Can J Chem 2008, 86, 1019; d) Adib, M.; Ansari, S.; Mohammadi, A.; Bijanzadeh, R. H. Tetrahedron Lett 2010, 51, 30.

[5] a) Ihara, S.; Soma, T.; Yano, D.; Aikawa, S.; Yoshida, Y. Synth Commun 2011, 41, 3600; b) Ihara, S.; Soma, T.; Yano, D.; Aikawa, S.; Yoshida, Y., J Heterocyclic Chem 2011, 48, 577.

[6] Cooper, C. F.; Partridge, W. M. Org Synth 1956, 36, 64.

[7] Dean, D. W.; Papadopoulos, P. E. J Heterocyclic Chem 1982, 19, 171.

[8] Nassar, N. M.; Agha, J. B.; Digenis, A. G. Journal of Labelled compounds and radiopharmanceuticals 1986, XXIII, 667.

[9] Chatterjee, A.; Raychauhuri, R. J Indian Chem Soc 1969, 46, 103.