

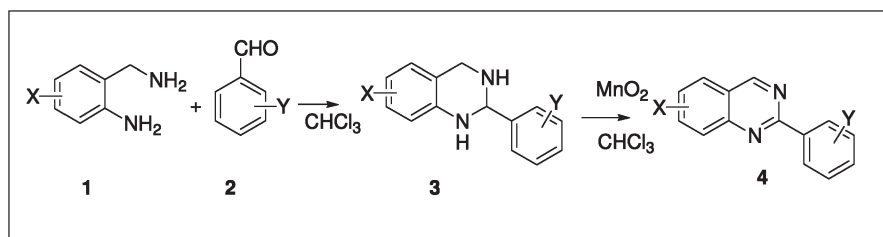
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A variety of 2-aryl quinazolines were synthesized from the condensation of 2-aminobenzylamines and aryl aldehydes to form 2-aryl-1,2,3,4-tetrahydroquinazolines and subsequent oxidation of the intermediates with MnO<sub>2</sub>.

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## INTRODUCTION

The quinazoline ring is a frequently encountered moiety in organic syntheses as well as in medicinal chemistry [1–10]. Many alkaloids containing a quinazoline skeleton in the molecule exhibit anticonvulsant, antibacterial, antidiabetic, and anticancer activities [6,11–14]. A number of methods for the synthesis of quinazolines are known [15–19]. We found five basic types of synthetic strategies for the synthesis of 2-substituted quinazolines: (1) three-step reaction from aryl azides to form 2-alkylquinazolines [20], (2) reaction of amidines with cyano- or nitro-activated *o*-fluorobenzaldehydes [21], (3) condensation of *o*-phenyl oxime of 2-aminoacetophenone with aldehydes or ketones by irradiation with microwaves to form 4-methylquinazolines [22], (4) reaction of 2-aminobenzaldehyde with an acyl halide and by heating the obtained amide in a sealed tube with saturated alcoholic ammonia [19,23–26], and then dehydrogenation with mercuric EDTA complex or aromatization with alkaline potassium ferricyanide [27,28], (5) condensation of 1,3-diamines **1** with aromatic aldehydes **2** to form 2-aryl-1,2,3,4-tetrahydroquinazolines **3**, and then oxidation of **3** to form the 2-aryl substituted quinazolines **4** (Scheme 1).

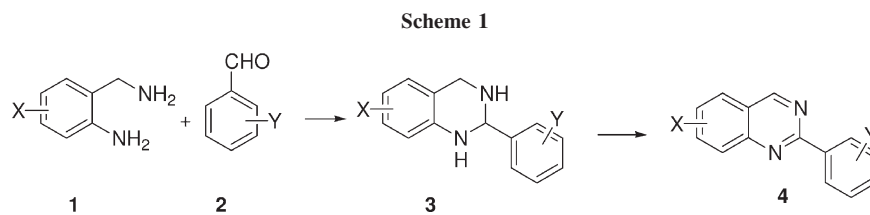
The fifth synthetic strategy involves two steps: condensation and oxidation. The condensation products, 2-aryl-1,2,3,4-tetrahydroquinazolines, have been prepared in solvent-free [29] and a number of solvents, including benzene or xylene, methanol or ethanol/acetic acid mix-

tures [30,31], alkali media [32,33], H<sub>2</sub>O [34], and ionic liquids [35]. Vandeneysde et al. reported alternative methods where aldehydes were converted, *in situ*, to *N*-(1-chloroalkyl)pyridinium, which reacted with 2-aminobenzylamine to yield tetrahydroquinazoline hydrochloride salts **3·HCl** [36]. Two oxidation reagents were used to oxidize 2-aryl-tetrahydroquinazolines to the corresponding quinazolines **4**. One is 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) and the other tetrachloro-1,4-benzoquinone (TCQ) [36]. More recently, Coskun reported a reaction where the *in situ* formed 2-substituted-1,2,3,4-tetrahydroquinazolines were oxidized to quinazolin-1-oxides [37].

No one-pot reaction to synthesize 2-arylquinazolines was reported. The methods described above to synthesize the 2-arylquinazolines either require multistep preparations of special reagents/reactants, or suffer severe limitations such as tedious experimental procedure and poor yields. Here we report the first one-pot synthesis of 2-aryl substituted quinazolines, from condensation of 1,3-diamines **1** with aryl aldehydes **2** to form 2-aryl-1,2,3,4-tetrahydroquinazolines **3**, and oxidation of **3** to form the 2-aryl substituted quinazolines **4**, using MnO<sub>2</sub> as the oxidant.

## RESULTS AND DISCUSSION

The condensation of 2-aminobenzylamine and benzaldehyde was selected as the model reaction. Among the

**Table 1**

The solvent effect on the condensation reaction.

Entry	Solvent	Time (h)	Yield <sup>a</sup> (%)
1	H <sub>2</sub> O	4	85
2	CHCl <sub>3</sub>	10	84
3	THF	16	66
4	CH <sub>3</sub> OH	17	73
5	CH <sub>3</sub> CN	16	74
6	CH <sub>2</sub> Cl <sub>2</sub>	18	63

<sup>a</sup> Isolated yield based on 2-aminobenzylamine.

solvents we screened, we found CHCl<sub>3</sub> or H<sub>2</sub>O was the best solvent to give the product in high yield (Table 1, entries 1 and 2). Other solvents such as THF, CH<sub>3</sub>OH, CH<sub>3</sub>CN, and CH<sub>2</sub>Cl<sub>2</sub> gave lower yields (entries 3–6). This is consistent with the findings of Gawinecki et al. [38].

Several oxidants were evaluated for the transformation of tetrahydroquinazoline **3** to quinazoline **4** in CHCl<sub>3</sub> (Table 2). Among the oxidants we used, only DDQ and MnO<sub>2</sub> were effective for the transformation from the tetrahydroquinazoline to the quinazoline (Table 2, entries 4–5).

We then evaluated the solvent effects on the oxidation of the tetrahydroquinazoline to the quinazoline. The reaction did not proceed in water or in CH<sub>3</sub>COOH (Table 3, Entries 1 and 2). Moderate yields were obtained in CH<sub>3</sub>OH, C<sub>2</sub>H<sub>5</sub>OH, CH<sub>2</sub>Cl<sub>2</sub>, CH<sub>3</sub>CN, Dioxane, DMF, and THF (Entries 3–9). The best yield was obtained in CHCl<sub>3</sub> (Entry 10). Because both condensation and oxidation reactions proceed well in CHCl<sub>3</sub>, we envisioned

**Table 2**

The effect of oxidants on the oxidation of 2-phenyltetrahydroquinazoline to quinazoline.

Entry	Oxidant	Time (h)	Yield <sup>a</sup> (%)
1	NBS	36	0
2	Br <sub>2</sub>	36	0
3	Pb(OAc) <sub>4</sub>	36	0
4	DDQ	36	65
5	MnO <sub>2</sub>	36	70

<sup>a</sup> Isolated yield.

that the synthesis of quinazolines might proceed in one pot.

We then investigated the one-pot reactions of 2-aminobenzylamines and benzaldehydes to synthesize 2-arylquinazolines without isolating the tetrahydroquinazoline intermediate. First, the reaction of 2-aminobenzylamine with benzaldehyde gave tetrahydroquinazoline in CHCl<sub>3</sub> at room temperature. After TLC indicated the reaction was completed, we added 4.0 mol equivalents of MnO<sub>2</sub>. After refluxing for 12 h, the corresponding quinazoline was isolated in 70% yield. To explore the generality and scope of this one-pot reaction, we synthesized 2-arylquinazolines from a variety of 2-aminobenzylamines and aryl aldehydes (Table 4).

A variety of substituents are tolerated on both 2-aminobenzylamines and benzaldehydes. For the 2-aminobenzylamines, ortho F or CF<sub>3</sub> substituents slowed the reaction, probably due to the electronic and steric effect in the first step (entries 15–18). For benzaldehydes, the electron-withdrawing substituents speeded the reaction. Overall the reaction gave 2-arylquinazolines in yields from 26 to 75%.

## CONCLUSION

In summary, We have developed an one-pot method to synthesize a variety of 2-arylquinazoline derivatives, from the condensation of 1,3-diamines and aryl aldehydes to form 2-aryl-1,2,3,4-tetrahydroquinazolines and subsequent oxidation of tetrahydroquinazolines with

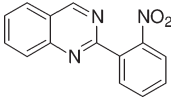
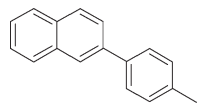
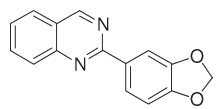
**Table 3**

The solvent effect on the oxidation of 2-phenyltetrahydroquinazolin.

Entry	Solvent	Time <sub>1</sub> (h)	Time <sub>2</sub> (h)	Yield <sup>a</sup> (%)
1	H <sub>2</sub> O	5	24	–
2	CH <sub>3</sub> COOH	4	12	–
3	CH <sub>3</sub> OH	24	12	37
4	C <sub>2</sub> H <sub>5</sub> OH	24	12	35
5	CH <sub>2</sub> Cl <sub>2</sub>	36	12	30
6	CH <sub>3</sub> CN	16	12	51
7	Dioxane	15	12	54
8	DMF	16	8	54
9	THF	16	12	68
10	CHCl <sub>3</sub>	10	12	70

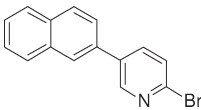
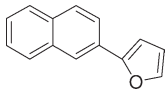
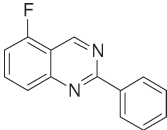
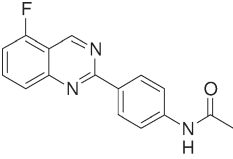
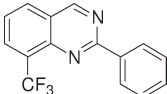
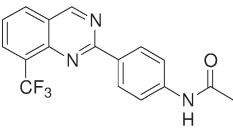
<sup>a</sup> Isolated yield.

**Table 4**  
One-pot synthesis of 2-arylquinazolines.

Entry	Product	Time <sub>1</sub> (h)	Time <sub>2</sub> (h)	Yield <sup>a</sup> (%)
1		10	12	70
2		6	12	72
3		5	12	62
4		5	12	52
5		5	12	66
6		5	12	75
7		7	12	50
8		8	12	66
9		10	12	56
10		10	12	48
11		9	12	40
12		10	12	30

(Continued)

**Table 4**  
(Continued)

Entry	Product	Time <sub>1</sub> (h)	Time <sub>2</sub> (h)	Yield <sup>a</sup> (%)
13		10	12	50
14		4	13	48
15		20	14	42
16		20	14	40
17		20	12	48
18		20	20	26

<sup>a</sup> Isolated yield based on 2-aminobenzylamines.

MnO<sub>2</sub> in moderate to high yield. This method provided quick access to different quinazolines.

### EXPERIMENTAL

Melting points were determined on an Electrothermal 9100 capillary melting point apparatus. <sup>1</sup>H NMR spectra were recorded on a Bruker AV400 (400 MHz) spectrometer, and chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. <sup>13</sup>C NMR spectra were recorded on a Bruker AV400 spectrometer, and chemical shifts are reported in parts per million relative to solvent resonance as the internal standard (CDCl<sub>3</sub>, δ 77.16). IR spectra were recorded as solid in pellets on a Perkin-Elmer FTIR 683 spectrometer. Mass spectra were obtained with a TRIO 2 (electronic ionization 70 eV) spectrometer and a Perkin-Elmer Claruss 500 mass spectrometer (electronic ionization 20 eV).

**General procedure for the synthesis of 2-aryl-tetrahydroquinazolines.** A mixture of 2-aminobenzylamine (1.1 mmol), aryl aldehyde (1.0 mmol), and 10 mL of solvent were stirred at room temperature. The reaction was followed by TLC. When the reaction was completed, 4 mmol of active

MnO<sub>2</sub> was added and refluxed. After the reaction was completed, the organic material was extracted with ethyl acetate. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, and the solvents were removed. The residue was purified by flash chromatography on silica gel column, using petroleum/ethyl acetate as eluate to give products.

**2-Phenylquinazoline.**<sup>37</sup> This compound was obtained as yellow solid, mp 91–92°C; <sup>1</sup>H NMR (dimethyl sulfoxide *d*<sub>6</sub>): δ 7.53–7.56 (m, 3H, Ar–H), 7.69–7.73 (m, 1H, Ar–H), 8.00–8.04 (m, 2H, Ar–H), 8.13 (d, *J* = 8.0 Hz, 1H), 8.54–8.56 (m, 2H, Ar–H), 9.67 (s, 1H); <sup>13</sup>C NMR (deuteriochloroform): δ 123.6, 127.1, 127.3, 128.6, 128.7, 130.6, 134.1, 138.0, 150.8, 160.5, 161.1.

**2-(4-Nitro-phenyl)quinazoline.**<sup>33</sup> This compound was obtained as yellow solid, mp 197–198°C; <sup>1</sup>H NMR (deuteriochloroform): δ 7.70 (t, 1H, *J* = 7.2 Hz), 7.89–7.96 (m, 1H), 8.38 (d, 2H, *J* = 8.8 Hz), 8.83 (d, 2H, *J* = 8.8 Hz), 9.50 (s, 1H); <sup>13</sup>C NMR (deuteriochloroform): δ 123.8, 123.9, 127.2, 128.3, 128.9, 129.4, 134.6, 143.8, 149.2, 150.6, 158.8, 160.7.

**2-(3-Nitro-phenyl)quinazoline.**<sup>33</sup> This compound was obtained as yellow solid, mp 194–195°C; <sup>1</sup>H NMR (deuteriochloroform): δ 7.68–7.73 (m, 2H), 7.98 (t, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.98 (d, *J*

= 7.6 Hz, 1H), 9.51 (s, 2H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  123.6, 123.9, 125.1, 127.3, 128.1, 128.8, 129.6, 134.2, 134.6, 139.9, 150.6, 158.7, 160.8.

**2-(2-Nitro-phenyl)quinazoline.**<sup>37</sup> This compound was obtained as yellow solid, mp 91–92°C;  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  7.68–7.73 (m, 2H), 7.98 (t,  $J = 8.0$  Hz, 2H), 8.14 (d,  $J = 8.0$  Hz, 1H), 8.34 (d,  $J = 8.0$  Hz, 1H), 8.98 (d,  $J = 7.6$  Hz, 1H), 9.51 (s, 2H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  123.6, 124.0, 125.1, 127.2, 128.1, 128.8, 129.6, 134.2, 134.6, 139.8, 148.9, 150.6, 158.7, 160.8.

**2-(4-Chloro-phenyl)quinazoline.**<sup>33</sup> This compound was obtained as yellow solid, mp 116–117°C;  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  7.49 (d,  $J = 7.6$  Hz, 2H), 7.62–7.65 (m, 1H, Ar–H), 7.90–7.95 (m, 2H, Ar–H), 8.07 (d,  $J = 8.4$  Hz, 1H), 8.58 (d,  $J = 8.8$  Hz, 2H, Ar–H), 9.46 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  123.6, 127.2, 127.5, 128.6, 128.9, 129.9, 134.3, 136.5, 136.9, 150.7, 160.1, 160.6.

**2-(4-Bromo-phenyl)-quinazoline.** This compound was obtained as yellow solid, mp 131–132°C; IR (potassium bromide): 2925, 1693, 1618, 1582, 1546, 1405, 1369, 1067  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  7.62–7.68 (m, 3H, Ar–H), 7.91–7.95 (m, 2H), 8.08 (d, 1H,  $J = 8.4$  Hz), 8.51 (d, 2H,  $J = 8.4$  Hz), 9.46 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  123.7, 125.5, 127.2, 127.6, 128.6, 130.2, 131.8, 134.4, 136.9, 150.7, 160.1, 160.6. HRMS calcd. for  $\text{C}_{14}\text{H}_9\text{BrN}_2$ : 283.9949, found: 283.9951.

**2-(4-Trifluoromethyl-phenyl)quinazoline.** This compound was obtained as brown-yellow solid, mp 120–122°C; IR (potassium bromide): 2925, 2854, 1621, 1553, 1326, 1163, 1116  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  7.68 (t,  $J = 7.6$  Hz, 1H), 7.78 (d,  $J = 8.4$  Hz, 2H), 7.94–7.98 (m, 2H, Ar–H), 8.12 (d,  $J = 8.4$  Hz, 1H), 8.75 (d,  $J = 8.4$  Hz, 2H), 9.51 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  122.7 (q,  $J = 262.0$  Hz), 123.7, 123.9, 127.2, 128.3, 128.9, 129.4, 134.6, 143.8, 149.2, 150.6, 158.8, 160.7. HRMS calcd. for  $\text{C}_{15}\text{H}_9\text{F}_3\text{N}_2$ : 274.0718, found: 274.0720.

**2-(4-Acetamido-phenyl)quinazoline.** This compound was obtained as brown-yellow solid, mp 136–139°C; IR (potassium bromide): 3445, 3259, 2925, 1697, 1602, 1532, 1408, 1312, 799  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  2.23 (s, 3H), 7.39 (br s, 1H), 7.60 (t,  $J = 7.6$  Hz, 1H), 7.68 (d,  $J = 8.4$  Hz, 2H), 7.88–7.93 (m, 2H), 8.06 (d,  $J = 8.4$  Hz, 1H), 8.59 (d,  $J = 8.4$  Hz, 2H), 9.44 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  24.8, 119.4, 123.5, 127.1, 128.5, 129.5, 131.1, 133.9, 134.1, 140.2, 150.8, 160.5, 168.4. HRMS calcd. for  $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}$ : 263.1059, found: 263.1057.

**2-(4-Methyl-phenyl)quinazoline.**<sup>36</sup> This compound was obtained as yellow solid, mp 99–101°C; IR (potassium bromide): 3027, 2922, 2854, 1620, 1610, 1589, 1552, 1402, 1380, 797, 726  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  2.44 (s, 3H), 7.33 (d,  $J = 7.2$  Hz, 2H), 7.57–7.60 (m, 1H), 7.87–7.91 (m, 2H), 8.05 (d,  $J = 8.8$  Hz, 1H), 8.50 (d,  $J = 7.2$  Hz), 9.44 (d,  $J = 0.8$  Hz);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  21.5, 123.5, 127.1, 128.6, 129.4, 134.1, 135.3, 140.9, 150.8, 160.5.

**2-(4-Methoxy-phenyl)quinazoline.**<sup>36</sup> This compound was obtained as yellow solid, mp 85–86°C;  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  3.89 (s, 3H), 7.03 (d,  $J = 8.8$  Hz, 2H), 7.56 (t,  $J = 7.6$  Hz, 1H), 7.82–7.89 (m, 2H, Ar–H), 8.02 (d,  $J = 8.4$  Hz, 1H), 8.56 (d,  $J = 8.8$  Hz, 2H), 9.41 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  55.4, 113.9, 123.3, 126.8, 127.1, 128.4, 130.2, 130.7, 134.0, 150.8, 160.4, 160.8, 161.8.

**2-(Benzo[1,3]dioxol-5-yl)quinazoline.** This compound was obtained as yellow solid, mp 123–125°C; IR (potassium bromide): 2921, 2850, 1618, 1584, 1568, 1502, 1460, 1256, 1099, 1039, 793  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  6.06 (s, 2H,  $\text{OCH}_2\text{O}$ ), 6.97 (d, 1H,  $J = 8.4$  Hz, Ar–H), 7.59 (s, 1H, Ar–H), 7.91–7.89 (m, 2H, Ar–H), 8.04–8.03 (m, 1H, Ar–H), 8.20 (s, 1H, Ar–H), 8.23 (d, 1H,  $J = 7.0$  Hz, Ar–H), 9.41 (s, 1H, Ar–H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  29.7, 46.5, 69.4, 101.2, 107.1, 108.3, 115.0, 118.2, 120.1, 121.3, 126.2, 127.3, 135.8, 143.7, 147.7. HRMS calcd. for  $\text{C}_{15}\text{H}_{10}\text{N}_2\text{O}_2$ : 250.0742, found: 250.0740.

**2-(4-Hydroxyl-phenyl)quinazoline.** This compound was obtained as yellow solid, mp 210–212°C; IR (potassium bromide): 3168, 1670, 1606, 1555, 1457, 1405, 1385, 1240, 1165, 799  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  6.92 (d,  $J = 8.4$  Hz, 3H), 7.64–7.69 (m, 1H), 7.97 (d,  $J = 3.2$  Hz, 2H), 8.09 (d,  $J = 8.0$  Hz, 1H), 8.41 (d,  $J = 8.8$  Hz, 2H), 9.61 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  115.9, 116.3, 123.4, 127.4, 128.1, 128.2, 128.9, 130.4, 135.1, 150.4, 160.5, 161.5. HRMS calcd. for  $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}$ : 222.0793, found: 222.0795.

**2-(6-Bromo-pyridin-3-yl)quinazoline.** This compound was obtained as black solid, mp 158–160°C; IR (potassium bromide): 3061, 2924, 1619, 1572, 1448, 1404, 1088, 734  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  7.61–7.69 (m, 2H, Ar–H), 7.92–7.96 (m, 2H), 8.07 (d,  $J = 8.8$  Hz, 1H), 8.73 (dd, 1H,  $J = 1.6, 8.4$  Hz), 9.45 (s, 1H), 9.55 (d,  $J = 1.6$  Hz, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  123.9, 127.2, 127.9, 128.0, 128.7, 133.0, 134.6, 138.2, 144.2, 150.6, 150.7, 158.3, 160.7. HRMS calcd. for  $\text{C}_{13}\text{H}_8\text{BrN}_3$ : 284.9902, found: 284.9905.

**2-(2-Furyl)quinazoline.**<sup>37</sup> This compound was obtained as black solid, mp 131–132°C;  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  6.63 (dd,  $J = 2.0, 3.6$  Hz, 1H), 7.46 (d,  $J = 3.2$  Hz, 1H), 7.59–7.63 (m, 1H), 7.70 (d,  $J = 0.8$  Hz, 1H), 7.89–7.93 (m, 2H), 8.09 (d,  $J = 9.2$  Hz, 1H), 9.39 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  112.4, 114.1, 123.4, 127.3, 128.4, 134.6, 145.4, 150.4, 152.5, 154.1, 160.8.

**2-Phenyl-5-flouroquinazoline.** This compound was obtained as yellow solid, mp 111–113°C; IR (potassium bromide): 3058, 2925, 1635, 1582, 1555, 1465, 1398, 1240, 790, 699  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (deuteriochloroform):  $\delta$  7.22 (t, 1H,  $J = 8.4$  Hz), 7.53–7.56 (m, 3H, Ar–H), 7.83–7.90 (m, 2H, Ar–H), 8.62–8.63 (m, 2H, Ar–H), 9.74 (s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  110.9 (d,  $J = 19.0$  Hz), 114.1, 124.6 (d,  $J = 4.0$  Hz), 128.7 (d,  $J = 6.0$  Hz), 131.0, 134.1 (d,  $J = 10.0$  Hz), 137.6, 152.0, 154.9 (d,  $J = 3.0$  Hz), 157.0 (d,  $J = 257.0$  Hz), 161.2. HRMS calcd. for  $\text{C}_{14}\text{H}_9\text{FN}_2$ : 224.0750, found: 224.0752.

**2-(4-Acetamido-phenyl)-5-flouroquinazoline.** This compound was obtained as yellow solid, mp 207–208°C; IR (potassium bromide): 3536, 3283, 3126, 2926, 1633, 1656, 1580, 1556, 1463, 1397, 1376, 1347, 1237, 1089, 822.  $^1\text{H}$  NMR (dimethyl sulfoxide  $d_6$ ):  $\delta$  2.10 (s, 3H), 7.49 (t,  $J = 8.8$  Hz, 1H), 7.77 (d,  $J = 8.4$  Hz, 2H), 7.85 (d,  $J = 8.4$  Hz, 1H), 7.97–8.03 (m, 1H), 8.48 (d,  $J = 8.8$  Hz, 2H), 9.78 (s, 1H), 10.23 (br s, 1H);  $^{13}\text{C}$  NMR (deuteriochloroform):  $\delta$  24.5, 111.7 (d,  $J = 18.0$  Hz), 113.9 (d,  $J = 16.0$  Hz), 119.1 (d,  $J = 8.0$  Hz), 124.6 (d,  $J = 4.0$  Hz), 129.6, 131.9, 135.7 (d,  $J = 10.0$  Hz), 142.6, 151.2, 155.6, 156.8 (d,  $J = 246$  Hz), 160.7, 169.2. HRMS calcd. for  $\text{C}_{16}\text{H}_{12}\text{FN}_3\text{O}$ : 281.0964, found: 281.0967.

**2-Phenyl-8-trifluoromethylquinazoline.** This compound was obtained as yellow solid, mp 94–96°C; IR (potassium

bromide): 3070, 1621, 1590, 1568, 1468, 1475, 1410, 1343, 1281, 1159, 1078, 773 cm<sup>-1</sup>. <sup>1</sup>H NMR (dimethyl sulfoxide *d*<sub>6</sub>): δ 7.54 (d, *J* = 4.0 Hz, 3H), 7.66 (t, *J* = 7.6 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 8.23 (d, *J* = 7.2 Hz, 1H), 8.68 (d, *J* = 4.0 Hz, 2H), 9.52 (s, 1H); <sup>13</sup>C NMR (dimethyl sulfoxide *d*<sub>6</sub>): δ 123.7(q, *J* = 242.2 Hz), 125.8, 128.7, 129.0, 131.3, 131.4, 132.1, 132.2, 137.4, 147.7, 160.7, 161.4. HRMS calcd. for C<sub>15</sub>H<sub>9</sub>F<sub>3</sub>N<sub>2</sub>: 274.0718, found: 274.0721.

**2-(4-Acetamido-phenyl)-8-trifluoromethylquinazoline.** This compound was obtained as yellow solid, mp 166–168°C; IR (potassium bromide): 3265, 3121, 2926, 2853, 1675, 1601, 1596, 1471, 1327, 1286, 1139, 833, 775 cm<sup>-1</sup>. <sup>1</sup>H NMR (dimethyl sulfoxide *d*<sub>6</sub>): δ 2.23 (s, 3H), 7.56–7.72 (m, 3H), 7.84 (d, *J* = 7.6 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 6.8 Hz, 1H), 8.64 (d, *J* = 8.0 Hz, 1H), 9.49 (s, 1H). <sup>13</sup>C NMR (dimethyl sulfoxide *d*<sub>6</sub>): δ 24.3, 113.0, 113.2, 116.3, 121.7 (q, *J* = 248.3), 124.9, 127.1, 129.1, 129.8, 131.1, 131.8, 136.7, 138.5, 144.3, 169.5. HRMS calcd. for C<sub>17</sub>H<sub>12</sub>F<sub>3</sub>N<sub>3</sub>O: 331.09325, found: 331.09367.

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