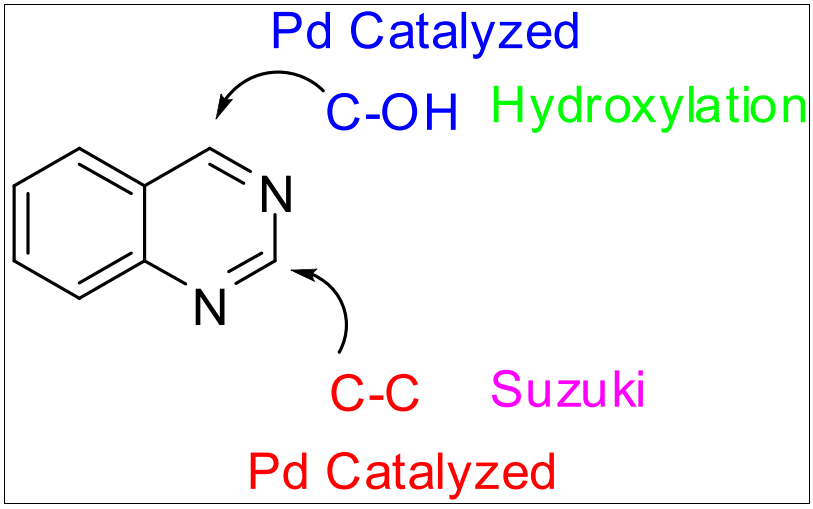
Csp^2–O and C–C Bond Formation via Pd-Catalyzed Coupling Reaction of 2,4-Dichloroquinazoline

Alka Sharma, Vijay Luxami, and Kamaldeep Paul*

School of Chemistry and Biochemistry, Thapar University, Patiala 147004, India
*E-mail: kpaul@thapar.edu

Additional Supporting Information may be found in the online version of this article.
Received May 8, 2014
DOI 10.1002/jhet.2330
Published online 23 March 2015 in Wiley Online Library (wileyonlinelibrary.com).



An efficient palladium-catalyzed C–O and subsequent C–C bond formation of 2,4-dichloroquinazoline have been described. The designed strategy results in the synthesis of novel 2-arylated quinazolin-4-ones framework with various aryl/heteroaryl boronic acids in moderate to good yields along with 2,4-diarylated quinazolines. This methodology offers a direct transformation of aryl halides to aryl alcohols/ketone as well as the straight forward application to generate a wide variety of monoaryl and diaryl quinazoline.

J. Heterocyclic Chem., **53**, 241 (2016).

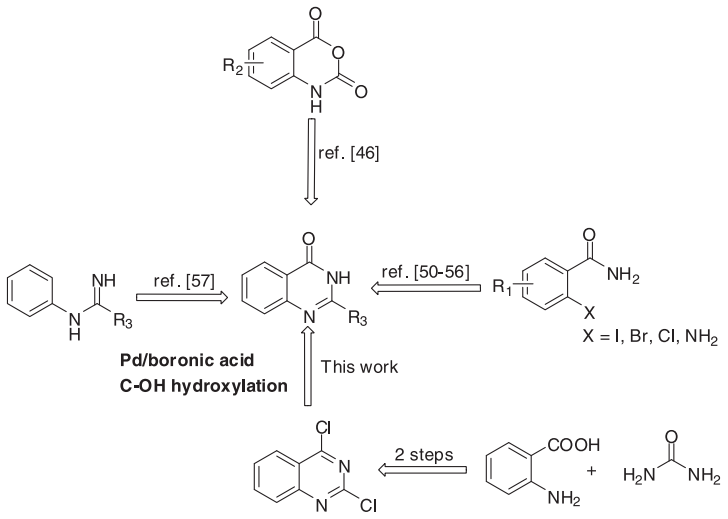
INTRODUCTION

The formation of C–O bonds, e.g. hydroxylation and alkoxylation, is one of the fundamental transformations in organic synthesis. Recently, several research groups reported palladium-catalyzed and copper catalyzed hydroxylation of aryl halides under relatively mild conditions [1–5], but many such reactions are limited to the couplings of aromatic iodides and bromides because much higher energy is required for the oxidative insertion of palladium catalysts into the C–Cl bond of aryl chlorides [6–13]. The different functionalizations of halogenated heteroaromatics in such reactions has been extensively studied [14], for example, Suzuki, Heck, Negishi reactions in the presence of palladium catalysts including imidazopyridines [15], pyridines [16,17], pyrazines [18–20], triazines [21,22], quinazolines [23,24], cinnolines [25], α-carbolines [26], imidazopyridazines [27–29], pyrazolopyrimidines [30–33], triazolopyrimidines [34], pyrrolopyrimidines [35], purines [36], and uridines [37].

Quinazoline scaffold is present in a number of biologically active drugs including potent kinase inhibitors [38,39], anti-inflammatory [40], antiviral [41], anticancer [42,43], antitubercular agents [44], and also components of several approved drugs, such as erlotinib, gefitinib, canertinib, vandetanib, and lapatinib [45]. Hence, the functionalization of 2,4-dichloroquinazoline provides an interesting challenge in medicinal/organic chemistry [46–49].

The most widely used method is probably with 2-aminobenzamide or their derivatives under acidic or basic conditions or in the presence of copper catalyst (Scheme 1) [50,51]. Recently, Fu and coauthors developed novel cascade methods starting from 2-halobenzoic acids or 2-halobenzamides [52–56]. Zhu and coauthors reported alternative approaches via intramolecular C(sp^2)-H carboxamidation reaction of *N*-arylamidines involving palladium catalyst [57]. Herein, we have reported the palladium-catalyzed synthesis of 2-arylated-3*H*-quinazolin-4-one and subsequently 2,4-diarylation quinazoline from cheap and easily available starting material. This synthetic strategy delivers palladium-catalyzed single-step oxidation of 2,4-dichloroquinazoline at C4 position and arylation at C2 position with aryl boronic acids **(1a)** along with diarylation at C2 and C4 positions **(1b)** in the presence of water and mild base.

Scheme 1. Major approaches to quinazolin-4(3*H*)-ones.



RESULTS AND DISCUSSION

A variety of conditions and combinations of catalyst systems, bases, and solvents were screened for optimal reaction conditions for 2,4-dichloroquinazoline (derived from anthranillic acids and urea followed by chlorination with $POCl_3$ [58]) with phenyl boronic acid (Table 1). Interestingly, under most of the reaction conditions, C4 hydroxylated/C2 arylated was the major product, with varying amounts of C2 and C4 diarylation product resulting from different aryl/heteroaryl boronic acid. Csp^2–O and C–C coupling reactions between 2,4-dichloroquinazoline and phenylboronic acid with palladium-based catalysts like $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$, and $Pd_2(dba)_3$; $Pd(PPh_3)_4$ proved as an effective catalyst for monoarylation (hydroxylated) and diarylation (Table 1, entries 1–3). Among the variation of bases such as K_2CO_3, Na_2CO_3, NaO^tBu, and Cs_2CO_3, with $Pd(PPh_3)_4$ catalyst (Table 1, entries 3–6), revealed that K_2CO_3 turned out to be the most effective base to give desired products (Table 1, entry 3). Further, catalytic reactions using $Pd(PPh_3)_2Cl_2$, better yields were obtained with Na_2CO_3 (Table 1, entry 7) than K_2CO_3, Cs_2CO_3, or NaO^tBu (Table 1, entries 1, 8–9), but with $Pd_2(dba)_3$ and different bases viz., K_2CO_3, Na_2CO_3, NaO^tBu, or Cs_2CO_3, a significant decrease in yields were observed (Table 1, entries 2, 10–12). The effect of different solvents like toluene, acetonitrile, dioxane, and THF along with water as a cosolvent were also studied, and toluene:H_2O (9:1) proved to be the best solvent system for the reactions (Table 1, entries 3, 13–15). The arylation and hydroxylation failed completely when the reaction was carried out in the absence of palladium catalyst or base (Table 1, entries 16–17).

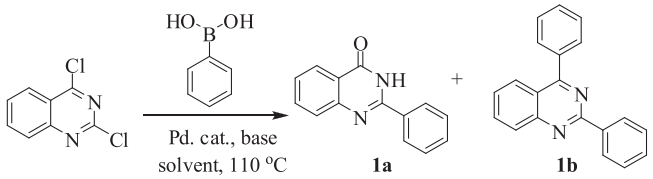
Having optimized the reaction conditions, we performed a palladium-catalyzed reaction of 2,4-dichloroquinazoline with 2.0 equivalent of phenylboronic acid, 10 mol% Pd $(PPh_3)_4$, 2.0 equivalents of K_2CO_3 in 9:1 mixture of toluene and water (Table 1, entry 3) in a sealed tube at 110°C for 12 h to give 2-phenyl-3*H*-quinazolin-4-one (**1a**) and 2,4-diphenylquinazoline (**1b**) in 75 and 16% yields respectively. The ^1H NMR spectrum of the 2-phenyl-3*H*-quinazolin-4-one (**1a**) revealed the characteristic broad 1H singlet of NH proton (exchangeable with D_2O) at downfield region of δ 11.20 ppm. Moreover, aromatic region showed three triplet signals of six protons, one doublet of one proton, and one multiplet of two protons. Absence of NH singlet and appearance of 14 protons in the aromatic region confirmed the formation of 2, 4-diphenylquinazoline (**1b**).

Thus, number of 2-aryl-3*H*-quinazolin-4-one and 2, 4-diarylquinazolines was prepared via coupling of 2, 4-dichloroquinazoline with variety of aryl boronic acids under the optimized reaction conditions as shown in Table 2. Both monosubstitution at C2 along with hydroxylation at C4 and disubstitution at C2 and C4 positions of quinazoline participated well in C–O and C–C bond forming reaction to afford the desired products.

We also examined the reactions of activated and nonactivated substituted hetero (aryl) boronic acids including electron-withdrawing and electron-donating groups. Phenyl boronic acids with electron withdrawing para-substituent such as fluoro, chloro, and bromo produced the corresponding hydroxylated monoaryl (major) and diaryl (minor) products (Table 2, entries 2–4). Compared with reaction of 4-bromophenyl boronic acids, the yields in the case of corresponding 4-fluorophenyl and 4-chlorophenyl boronic acids were lower indicating that electron-withdrawing halogen substitution on the phenyl boronic acid ring has major role for the reactivity. 4-Methoxyphenyl boronic acids with an electron donating-methoxy group underwent smooth conversion for monoarylation and diarylation of quinazoline to obtain

Table 1

Optimization of Pd-catalyzed hydroxylation and arylation of 2,4-dichloroquinazoline.



Entry	Catalyst	Base	Solvent	Time	Yield (%)[a] 1a	1b
1	$Pd(PPh_3)_2Cl_2$	K_2CO_3	Toluene:H_2O	10	42	10
2	$Pd_2(dba)_3$	K_2CO_3	Toluene:H_2O	14	40	11
3	$Pd(PPh_3)_4$	K_2CO_3	Toluene:H_2O	12	75	16
4	$Pd(PPh_3)_4$	Na_2CO_3	Toluene:H_2O	8	60	12
5	$Pd(PPh_3)_4$	Cs_2CO_3	Toluene:H_2O	8	65	10
6	$Pd(PPh_3)_4$	NaO^tBu	Toluene:H_2O	8	62	10
7	$Pd(PPh_3)_2Cl_2$	Na_2CO_3	Toluene:H_2O	10	44	11
8	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	Toluene:H_2O	10	42	9
9	$Pd(PPh_3)_2Cl_2$	NaO^tBu	Toluene:H_2O	10	40	5
10	$Pd_2(dba)_3$	Na_2CO_3	Toluene:H_2O	14	40	10
11	$Pd_2(dba)_3$	Cs_2CO_3	Toluene:H_2O	14	35	5
12	$Pd_2(dba)_3$	NaO^tBu	Toluene:H_2O	14	38	8
13	$Pd(PPh_3)_4$	K_2CO_3	CH_3CN: H_2O	8	68	13
14	$Pd(PPh_3)_4$	K_2CO_3	THF:H_2O	10	65	15
15	$Pd(PPh_3)_4$	K_2CO_3	Dioxane:H_2O	10	68	10
16	—	K_2CO_3	Toluene:H_2O	9	-	-
17	$Pd(PPh_3)_4$	-	Toluene:H_2O	14	-	-

[a]Isolated yields, — indicates <5%.

75 and 20% yields respectively (Table 2, entry 5). Selective hydroxylation/monoarylation products were obtained with 3-methylphenyl boronic acids, thiophen-2-boronic acids, and furan-2-boronic acids with 60–65% yields (Table 2, entries 6–8). Finally, naphthalene-1-boronic acids, hydroxylated/monosubstituted product was predominant with 55% yield, and only 17% of disubstituted product was obtained (Table 2, entry 9 and Fig. 1). The, ^{1}H and ^{13}C-NMR as well as mass spectroscopic data are in accordance with the proposed structures that were confirmed also by elemental analyses (C, H, N).

The catalytic cycle of the palladium-catalyzed arylation of quinazoline for C–C bond is thought to proceed via Suzuki–Miyaura cross-coupling reactions. The process begins with the oxidative addition of an aryl halide to Pd(0) complex to form an aryl palladium(II)halide intermediate. The transmetalation with a boronic acid and the reductive elimination complete the catalytic cycle to form C2 monoarylation and C2/C4 diarylation products of quinazoline. The cosolvent H_2O has subsequently participated for the oxidation at C4 position for hydroxylation product. Base is involved in the coordination sphere of the palladium, and the formation of Ar–Pd–OH from Ar–Pd–X has accelerated the transmetalation step for hydroxylation (Scheme 2).

CONCLUSION

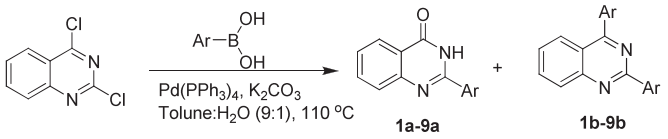
We have developed an efficient, economical, and practical method for the synthesis of palladium-catalyzed cross coupling and subsequent hydroxylation of 2,4-dichloroquinazoline. A variety of diarylated quinazoline have also been prepared from activated and nonactivated heteroaryl substrates. Key to the success is the use of water and boronic acids for unique simultaneous C–O and C–C bond formation in the presence of palladium catalyst. Future work will be directed at further optimization of this process and on the development of related coupling reactions.

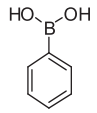
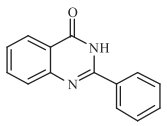
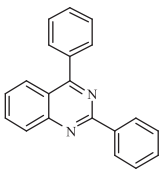
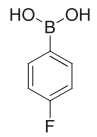
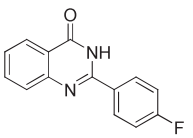
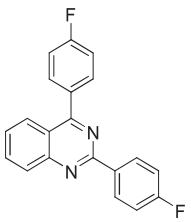
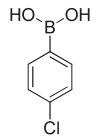
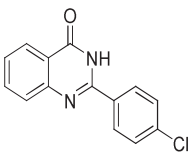
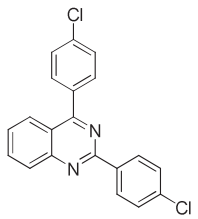
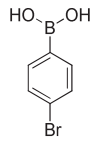
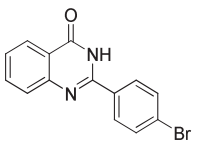
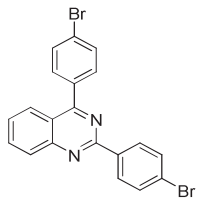
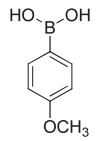
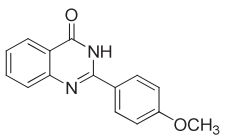
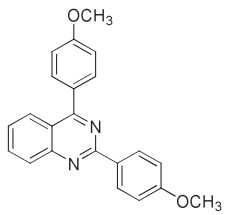
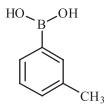
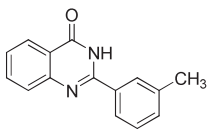
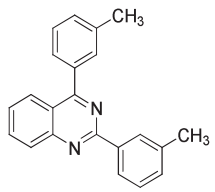
EXPERIMENTAL SECTION

General information. All commercially available compounds were used without purification. Unless otherwise noted, reactions were performed in oven-dried glassware. All reactions were run under argon or nitrogen atmosphere. The reactions were carried out in an oil bath using Microwave Vials (10–15 ml). Melting points were determined in open capillaries and were uncorrected. ^{1}H

Table 2

Hydroxylation/monoarylation and diarylation products with different arylboronic acids[a].

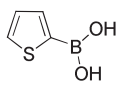
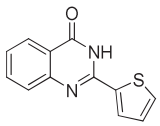
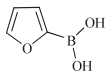
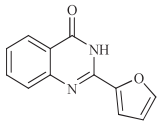
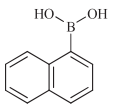
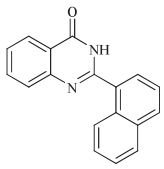


Entry	Ar	Products		Time	Products (%)	
1				12	**1a** (75)	**1b** (16)
2				8	**2a** (64)	**2b** (25)
3				8	**3a** (68)	**3b** (19)
4				8	**4a** (70)	**4b** (trace)
5				8	**5a** (75)	**5b** (20)
6				8	**6a** (65)	**6b** (trace)

(*Continued*)

Table 2

(*Continued*)

Entry	Ar	Products	Time	Products (%)	
7			8	**7a** (60)	**7b** (trace)
8			7	**8a** (60)	**8b** (trace)
9			8	**9a** (55)	**9b** (17)

[a]Conditions: 2.0 mmol boronic acid, 10 mol% catalyst, 2.0 mmol base, solvent: cosolvent (9:1), reflux, 110°C, 8–12 h.

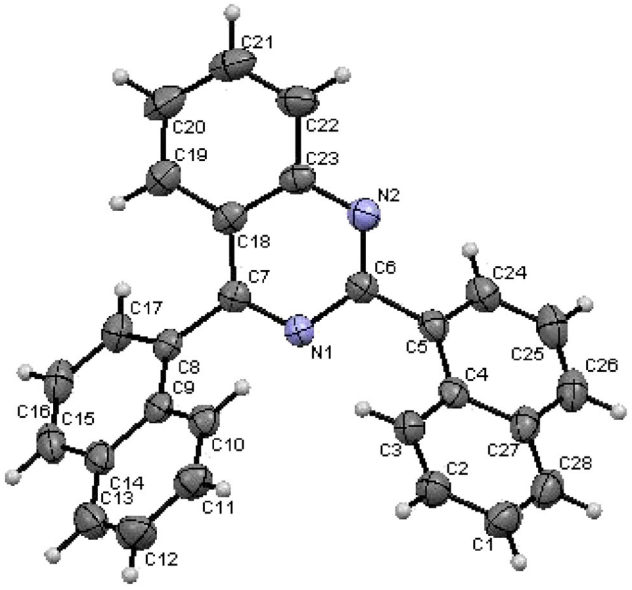


Figure 1. X-ray structure of compound **9b** (CCDC No. 974588) [59]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

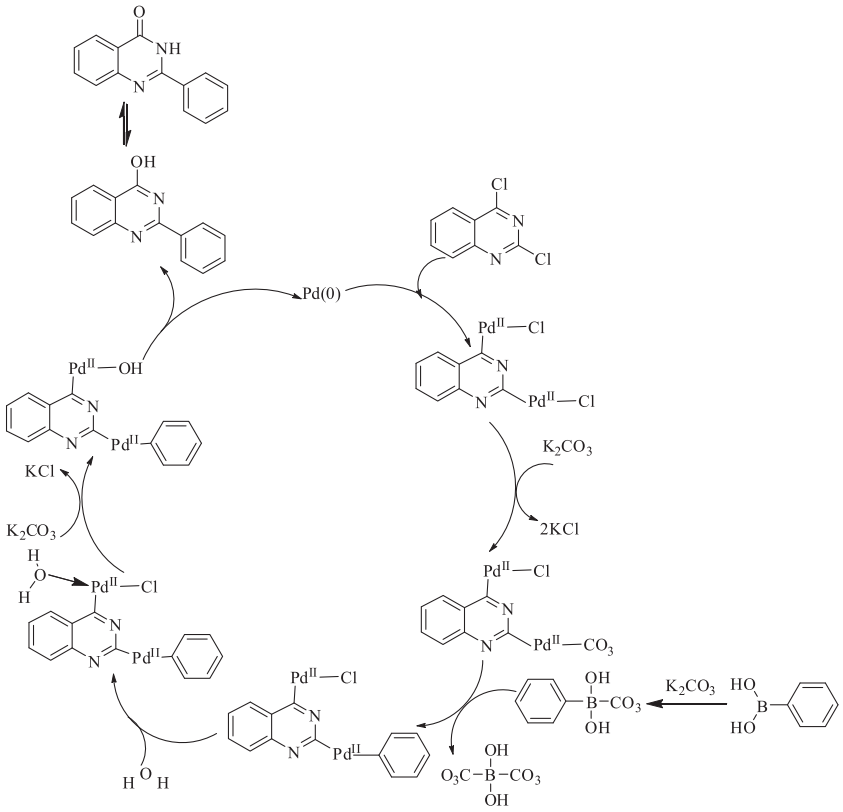
NMR and ^{13}C NMR spectra were recorded on Jeol ECS-400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometer (Tokyo, Japan) at ambient temperature, using $CDCl_3$ and DMSO-d_6 as solvents. Chemical shifts are reported in parts per million (ppm) with TMS as internal reference, and *J* values are given in hertz. Mass spectra of the synthesized compounds were recorded at Waters Micromass Q-Tof Micro (Milford, MA). The crystal structure was collected on Bruker AXS KAPPA APEX II CCD diffractometer (Billerica, Massachusttes). Reactions were monitored by thin layer chromatography (TLC) with silica plate coated with silica gel HF-254, and column chromatography was performed with silica gel 60–120/100–200 mesh. Chloroform/methanol was adopted solvent systems.

General procedure. A vial equipped with stirring bar was charged with 2,4-dichloroquinazoline (0.2 g, 1.0 mmol), K_2CO_3 (0.28 g, 2.0 mmol), and boronic acids (2.0 mmol), dissolved in toluene:H_2O (9:1) at 110°C under inert atmosphere. Then, 10 mol% of $Pd(PPh_3)_4$ was added, and vial was capped. The reaction mixture was refluxed for 8–12 h. After the completion of the reaction (monitored by TLC), the reaction mixture was cooled and then extract with water and chloroform. Organic layer was dried over sodium sulfate, filtered, and concentrated under *vacuo* to get crude product. The residue was purified by silica gel (60–120 mesh) column chromatography using hexane: ethyl acetate (3:2) as eluents to give pure solid.

2-Phenyl-3H-quinazolin-4-one (1a). This compound was obtained as light yellow-colored solid (ethanol); mp 238–240°C (Lit. [56] mp 235–237°C); 167 mg, 75% yield; IR (KBr, cm^{-1}) ν: 3359, 3060, 1658, 1334, 1289; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.20 (1H, s, NH), 8.33–8.31 (1H, d, J = 7.8 Hz), 8.21–8.19 (2H, t, J = 6.0 Hz), 7.88–7.78 (2H, m), 7.59–7.57 (3H, t, J = 2.28 Hz), 7.52–7.48 (1H, t, J = 6.64 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 151.7, 149.5, 135.0, 132.9, 131.8, 129.2, 128.1, 127.4, 126.9, 126.5, 120.8; MS-ESI, *m/z*: 223.1 $(M+1)^+$.

2,4-Diphenyl-quinazoline (1b). This compound was obtained as white-colored solid (ethanol); mp 118–119°C (Lit. [60] mp 116–117°C); 45 mg, 16% yield; IR (KBr, cm^{-1}) ν: 3061, 1336, 1289; ^{1}H

Scheme 2. Plausible reaction mechanism for hydroxylated monoarylation.



NMR (400 MHz, $CDCl_3$): δ 8.70–8.68 (2H, d, J = 7.76 Hz), 8.17–8.12 (2H, t, J = 8.72 Hz), 7.90–7.89 (3H, t, J = 4.60 Hz), 7.60–7.51 (7H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 160.3, 152.1, 138.3, 137.8, 133.7, 130.6, 130.3, 130.0, 129.3, 128.8, 128.7, 127.1, 121.8; MS-ESI, *m/z*: 283.1 $(M+1)^+$.

2-(4-Fluoro-phenyl)-3H-quinazolin-4-one (2a). This compound was obtained as light yellow-colored solid (ethanol); mp 238–240°C (Lit. [61] mp 251–253°C); 154 mg, 64% yield; IR (KBr, cm^{-1}) ν: 3350, 3044, 1660, 1286, 1164; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.62 (1H, s, NH), 8.33–8.31 (1H, d, J = 7.76 Hz), 8.20–8.16 (2H, m), 7.83–7.82 (2H, d, J = 3.28 Hz), 7.54–7.50 (1H, m), 7.27–7.26 (2H, d, J = 5.04 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 162.4, 150.5, 149.4, 135.1, 131.8, 129.5, 129.4, 128.1, 127.1, 126.5, 126.3, 120.8, 116.5, 116.3; MS-ESI, *m/z*: 241.1 $(M+1)^+$.

2,4-bis(4-Fluoro-phenyl)-quinazoline (2b). This compound was obtained as white-colored solid (ethanol); mp 170–172°C; 79 mg, 25% yield; IR (KBr, cm^{-1}) ν: 3047, 1336, 1219, 1146; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70–8.67 (2H, dd, ^2J = 5.48 Hz, ^3J = 3.10 Hz), 8.15–8.08 (2H, dd, ^2J = 8.28 Hz, ^3J = 3.01 Hz), 7.91–7.87 (3H, m), 7.59–7.55 (1H, t, J = 7.32 Hz), 7.32–7.27 (2H, t, J = 10.08 Hz), 7.22–7.18 (2H, t, J = 8.72 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 161.2, 160.5, 158.7, 158.1, 154.6, 147.3, 129.6, 129.1, 129.0, 127.5, 127.4, 126.1, 126.0, 124.5, 122.5, 122.1, 116.8, 111.2, 110.9, 110.7; MS-ESI, *m/z*: 319.1 $(M+1)^+$; *Anal.* Calcd for $C_{20}H_{12}F_2N_2$: C, 75.46; H, 3.80; N, 8.80. Found: C, 75.30; H, 3.49; N, 9.03.

2-(4-Chloro-phenyl)-3H-quinazolin-4-one (3a). This compound was obtained as light yellow-colored solid (ethanol); mp 298–300°C (Lit. [51] mp 299–300°C); 175 mg, 68% yield; IR (KBr, cm^{-1}) ν: 3341, 3046, 1671, 1342, 1281, 938; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.55 (1H, s, NH), 8.17–8.15 (2H, d, J = 8.24 Hz), 8.11–8.09 (1H, d, J = 7.80 Hz), 7.79–7.75 (1H, t, J = 7.56 Hz), 7.69–7.67 (1H, d, J = 8.28 Hz), 7.54–7.52(2H, d, J = 8.24 Hz), 7.48–7.44 (1H, t, J = 7.32 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8, 151.7, 149.1, 136.9, 134.9, 132.0, 130.0, 129.1, 127.9, 127.0, 126.3, 121.5; MS-ESI, *m/z*: 257.5 $(M+1)^+$.

2,4-bis(4-Chloro-phenyl)-quinazoline (3b). This compound was obtained as white-colored solid (ethanol); mp 198–200°C; 67 mg, 19% yield; IR (KBr, cm^{-1}) ν: 3048, 1336, 1219, 1014; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.57–8.55 (2H, d, J = 8.68 Hz), 8.19 (1H, s), 8.09–8.04 (2H, q, J = 8.28 Hz), 8.00–7.96 (1H, t, J = 7.80 Hz), 7.87–7.85 (2H, d, J = 8.72 Hz), 7.67–7.63 (2H, t, J = 8.72 Hz), 7.55–7.53 (2H, d, J = 8.72 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.4, 158.6, 151.7, 136.7, 136.4, 136.1, 135.8, 134.9, 132.2, 130.3, 129.2, 128.6, 127.1, 121.5; MS-ESI, *m/z*: 352.1 $(M+1)^+$; *Anal.* Calcd for $C_{20}H_{12}Cl_2N_2$: C, 68.39; H, 3.44; N, 7.98. Found: C, 68.32; H, 3.81; N, 8.28.

2-(4-Bromo-phenyl)-3H-quinazolin-4-one (4a). This compound was obtained as gray-colored solid (ethanol); mp 291–294°C (Lit. [51] mp 295–296°C); 212 mg, 70% yield; IR (KBr, cm^{-1}) ν: 3375, 3034, 1656, 1384, 1340, 504; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.18 (1H, s, NH), 7.93–7.89 (2H, t, J = 8.24 Hz), 7.86 (1H, s), 7.73–7.71 (2H, dd, ^2J = 6.88 Hz, ^3J = 1.84 Hz), 7.60 (2H, s), 7.57–7.56 (1H, d, J = 4.60 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.9, 161.8, 160.7, 135.8, 134.6, 134.5, 131.5, 131.4, 128.3, 128.2, 127.0, 126.8, 125.3, 120.9; MS-ESI, *m/z*: 302.1 $(M+1)^+$.

2-(4-Methoxy-phenyl)-3H-quinazolin-4-one (5a). This compound was obtained as light yellow-colored solid (ethanol); mp 245–247°C (Lit. [51] mp 247–248°C); 190 mg, 75% yield;

IR (KBr, cm^{-1}) ν: 3350, 3061, 1672, 1298, 1242, 1026; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.02 (1H, s, NH), 8.32–8.31 (1H, d, J = 6.88 Hz), 8.19–8.16 (2H, t, J = 6.88 Hz), 7.80–7.79 (2H, t, J = 3.24 Hz), 7.50–7.48 (1H, m), 7.13–7.07(2H, m), 3.92 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2, 162.5, 151.1, 149.6, 134.8, 131.8, 130.2, 128.8, 127.8, 126.4, 126.4, 125.0, 114.5, 113.9, 113.8, 55.5; GC-MS: 252.2 $(M)^+$

2,4-bis(4-Methoxy-phenyl)-quinazoline (5b). This compound was obtained as white-colored solid (ethanol) [60]; mp 115–117°C; 68 mg, 20% yield; IR (KBr, cm^{-1}) ν: 3100, 1291, 1254, 1137; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17–8.15 (1H, d, J = 8.24 Hz), 8.02–8.00 (2H, d, J = 8.28 Hz), 7.92–7.83 (2H, m), 7.80–7.77 (2H, d, J = 8.68 Hz), 7.61–7.58 (2H, t, J = 7.32 Hz), 7.11–7.06 (3H, t, J = 8.20 Hz), 3.90 (6H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 161.9, 157.1, 153.1, 134.8, 132.1, 128.4, 128.1, 127.9, 127.6, 121.6, 114.3, 55.6; MS-ESI, m/z: 343.2 $(M + 1)^+$.

2-m-Tolyl-3H-quinazolin-4-one (6a). This compound was obtained as light yellow-colored solid (ethanol); mp 210–212°C (Lit.[51] mp 210–211°C); 154 mg, 65% yield; IR (KBr, cm^{-1}) ν: 3290, 3044, 1675, 1305, 1248; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.96 (1H, s, NH), 8.34–8.32 (1H, d, J = 7.32 Hz), 8.03 (1H, s), 7.97–7.95 (1H, d, J = 7.80 Hz), 7.84–7.81 (2H, m), 7.53–7.39 (3H, m), 2.51 (1H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 151.7, 149.4, 138.8, 134.7, 132.6, 132.4, 128.9, 127.8, 126.6, 126.2, 124.2, 120.7, 21.4; MS-ESI, m/z: 237.3 $(M + 1)^+$.

2-(Thiophen-2-yl)-3H-quinazolin-4-one (7a). This compound was obtained as yellow-colored solid (ethanol); mp 277–280°C (Lit. [56] mp 275–276°C); 137 mg, 60% yield; IR (KBr, cm^{-1}) ν: 3365, 2991, 1681, 1375, 1252, 1057; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.96 (1H, s, NH), 7.71–7.70 (2H, dd, ^2J = 7.36 Hz, ^3J = 2.76 Hz), 7.56–7.38 (3H, m), 7.09–7.01 (2H, m); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.9, 150.4, 140.7, 134.3, 131.4, 131.3, 128.3, 128.2, 126.7, 126.7, 121.9, 115.2, 114.3; MS-ESI, m/z: 229.2 $(M + 1)^+$.

2-Furan-2-yl-3H-quinazolin-4-one (8a). This compound was obtained as light-yellow colored solid (ethanol); mp 217–219°C (Lit. [50] mp 219–220°C); 127 mg, 60% yield; IR (KBr, cm^{-1}) ν: 3325, 3116, 1609, 1337, 1280, 1106; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.43 (1H, s, NH), 8.95 (1H, d, J = 8.68 Hz), 7.99–7.90 (2H, m), 7.83 (1H, s), 7.69 (2H, d, J = 3.68 Hz), 6.72–6.70 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$); δ 157.8, 157.0, 153.8, 152.5, 147.0, 139.4, 134.9, 128.3, 128.2, 127.2, 119.5, 118.3, 114.2, 112.9; GC-MS: 212.3 $(M)^+$.

2-Naphthalen-1-yl-3H-quinazolin-4-one (9a). This compound was obtained as light yellow-colored solid (ethanol); mp 291–293°C (Lit. [52] mp 289–292°C); 150 mg, 55% yield; IR (KBr, cm^{-1}) ν: 3433, 2981, 1669, 1284, 1252; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.59 (1H, s, NH), 8.27–8.21 (2H, m), 8.06–8.04 (1H, d, J = 8.24 Hz), 7.98–7.90 (2H, dd, ^2J = 5.48 Hz, ^3J = 1.84 Hz), 7.83–7.74 (1H, m), 7.64–7.55 (4H, m); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.5, 154.1, 149.2, 134.8, 133.6, 132.2, 130.8, 130.8, 128.7, 128.1, 127.9, 127.4, 127.1, 126.7, 126.3, 125.7, 125.4, 121.8; MS-ESI, m/z: 273.1 $(M + 1)^+$.

2,4-Di-naphthalen-1-yl-quinazoline (9b). This compound was obtained as white-colored solid (ethanol) [60]; mp 160–163°C; 65 mg, 17% yield; IR (KBr, cm^{-1}) ν: 2977, 1335, 1249; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84–8.82 (1H, d, J = 8.24 Hz), 8.28–8.23 (2H, dd, ^2J = 7.32 Hz, ^3J = 2.80 Hz), 8.05–8.03 (1H, d, J = 8.24 Hz), 7.98–7.90 (4H, m), 7.71–7.49 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 163.0, 151.3, 134.8, 134.3, 133.8, 131.7, 131.4, 130.4, 130.0, 129.9, 129.1, 128.6, 128.0, 127.6, 127.5, 126.9, 126.9, 126.4, 126.1, 125.9, 125.8, 125.4, 125.2, 123.0; MS-ESI, m/z: 383.2 $(M + 1)^+$.

Acknowledgment. We wish to thank UGC, New Delhi (41-322/2012, SR) for providing funds. We wish to thank IISER, Mohali and Punjab University, Chandigarh for carrying out crystallographic and mass analysis respectively.

REFERENCES AND NOTES

[1] Yu, C. W.; Chen, G. S.; Huang, C. W.; Chern, J. W. Org Lett 2012, 14, 3688.
[2] Xiao, Y.; Xu, Y.; Cheon, H. S.; Chae, J. J Org Chem 2013, 78, 5804.
[3] (a) Sergeev, A. G.; Schulz, T.; Torborg, C.; Spannenberg, A.; Neumann, H.; Beller, M. Angew Chem Int Ed 2009, 48, 7595; (b) Schulz, T.; Torborg, C.; Schaffner, B.; Huang, J.; Zapf, A.; Kadyrov, R.; Borner, A.; Beller, M. Angew Chem Int Ed 2009, 48, 918.
[4] Lavery, C. B.; Rotta-Loria, N. L.; McDonald, R.; Stradiotto, M. Adv Synth Catal 2013, 355, 981.
[5] Chen, G.; Chan, A. S. C.; Kwong, F. Y. Tetrahedron Lett 2007, 48, 473.
[6] Khanapure, S. P.; Garvey, D. S. Tetrahedron Lett 2004, 45, 5283.
[7] Miyaura, N.; Suzuki, A. Chem Rev 1995, 95, 2457.
[8] Ohta, H.; Tokunaga, M.; Obora, Y.; Iwai, T.; Iwasawa, T.; Fujihara, T.; Tsuji, Y. Org Lett 2007, 9, 89.
[9] Han, F. S. Chem Soc Rev 2013, 42, 5270.
[10] Kotha, S.; Lahiri, K.; Kashinath, D. Tetrahedron 2002, 58, 9633.
[11] Alonso, F.; Beletskaya, I. P.; Yus, M. Tetrahedron 2008, 64, 3047.
[12] Littke, A. F.; Fu, G. C. Angew Chem Int Ed 2002, 41, 4176.
[13] Roy, D.; Mom, S.; Beauperin, M.; Doucet, H.; Hierso, J. C. Angew Chem Int Ed 2010, 49, 6650.
[14] Schroter, S.; Stock, C.; Bach, T. Tetrahedron 2005, 61, 2245.
[15] Ducray, R.; Boutron, P.; Didelot, M.; Germain, H.; Lach, F.; Lamorlette, M.; Legriffon, A.; Maudet, M.; Ménard, M.; Pasquet, G.; Renaud, F.; Simpson, I.; Young, G. L. Tetrahedron Lett 2010, 51, 4755.
[16] Guram, A. S.; Wang, X.; Bunel, E. E.; Faul, M. M.; Larsen, R. D.; Martinelli, M. J. J Org Chem 2007, 72, 5104.
[17] Bianchini, C.; Giambastiani, G.; Luconi, L.; Meli, A. Coordin Chem Rev 2010, 254, 431.
[18] Fauber, B. P.; Dragovich, P. S.; Chen, J.; Corson, L. B.; Ding, C. Z.; Eigenbrot, C.; Giannetti, A. M.; Hunsaker, T.; Labadie, S.; Liu, Y.; Liu, Y.; Malek, S.; Peterson, D.; Pitts, K.; Sideris, S.; Ultsch, M.; Vander Porten, E.; Wang, J.; Wei, B.; Yen, I.; Yue, Q. Bioorg Med Chem Lett 2013, 23, 5533.
[19] Mishra, N. M.; Vachhani, D. D.; Modha, S. G.; Van der Eycken, E. V. Eur J Org Chem 2013, 693.
[20] Nikishkin, N. I.; Huskens, J.; Verboom, W. Org Biomol Chem 2013, 11, 3583.
[21] Courme, C.; Gresh, N.; Vidal, M.; Lenoir, C.; Garbay, C.; Florent, J. C.; Bertounesque, E. Eur J Med Chem 2010, 45, 244.
[22] Wagner, D.; Hoffmann, S. T.; Heinemeyer, U.; Munster, I; Kohler, A.; Strohriegl, P. Chem Mater 2013, 25, 3758.
[23] Bursavich, M. G.; Dastrup, D.; Shenderovich, M.; Yager, K. M.; Cimbora, D. M.; Williams, B.; Kumar, D. V. Bioorg Med Chem Lett 2013, 23, 6829.
[24] Parhi, A. K.; Zhang, Y.; Saionz, K. W.; Pradhan, P.; Kaul, M.; Trivedi, K.; Pilch, D. S.; LaVoie, E. J Bioorg Med Chem Lett 2013, 23, 4968.
[25] Scott, D. A.; Dakin, L. A.; Daly, K.; Del Valle, D. J.; Diebold, R. B.; Drew, L.; Ezhuthachan, J.; Gero, T. W.; Ogoe, C. A.; Omer, C. A.; Redmond, S. P.; Repik, G.; Thakur, K.; Ye, Q.; Zheng, X. Bioorg Med Chem Lett 2013, 23, 4591.
[26] Schneider, C.; Gueyrard, D.; Joseph, B.; Goekjian, P. G. Tetrahedron 2009, 65, 5427.
[27] Chapman, T. M.; Osborne, S. A.; Bouloc, N.; Large, J. M.; Wallace, C.; Birchall, K.; Ansell, K. H.; Jones, H. M.; Taylor, D.; Clough, B.; Green, J. L.; Holder, A. A. Bioorg Med Chem Lett 2013, 23, 3064.
[28] Enguehard-Gueiffier, C.; Musiu, S.; Henry, N.; Véron, J. B.; Mavel, S.; Neyts, J.; Leyssen, P.; Paeshuyse, J.; Gueiffier, A. Eur J Med Chem 2013, 64, 448.

[29] Akkaoui, A. E.; Berteina-Raboin, S.; Mouaddib, A.; Guillaumet, G. Eur J Org Chem 2010, 862.

[30] Dwyer, M. P.; Paruch, K.; Labroli, M.; Alvarez, C.; Keertikar, K. M.; Poker, C.; Rossman, R.; Fischmann, T. O.; Duca, J. S.; Madison, V.; Parry, D.; Davis, N.; Seghezzi, W.; Wiswell, D.; Guzi, T. J Bioorg Med Chem Lett 2011, 21, 467.

[31] Engers, D. W.; Frist, A. Y.; Lindsley, C. W.; Hong, C. C.; Hopkins, C. R. Bioorg Med Chem Lett 2013, 23, 3248.

[32] Lee, W.; Ortwine, D. F.; Bergeron, P.; Lau, K.; Lin, L.; Malek, S.; Nonomiya, J.; Pei, Z.; Robarge, K. D.; Schmidt, S.; Sideris, S.; Lyssikatos, J. P. Bioorg Med Chem Lett 2013, 23, 5097.

[33] Kumar, P. M.; Kumar, K. S.; Meda, C. L. T.; Reddy, G. R.; Mohakhud, P. K.; Mukkanti, K.; Krishna, G. R.; Reddy, C. M.; Rambabu, D.; Kumar, K. S.; Priya, K. K.; Chennubhotla, K. S.; Banote, R. K.; Kulkarni, P.; Parsa, K. V. L.; Pal, M. Med Chem Commun 2012, 3, 667.

[34] Gillespie, R. J.; Bamford, S. J.; Botting, R.; Comer, M.; Denny, S.; Gaur, S.; Griffin, M.; Jordan, A. M.; Knight, A. R.; Lerpiniere, J.; Leonardi, S.; Lightowler, S.; McAteer, S.; Merrett, A.; Misra, A.; Padfield, A.; Reece, M.; Saadi, M.; Selwood, D. L.; Stratton, G. C.; Surry, D.; Todd, R.; Tong, X.; Ruston, V.; Upton, R.; Weiss, S. M. J Med Chem 2009, 52, 33.

[35] Tumkevicius, S.; Dodonova, J. Chem Heterocyc Compd 2012, 48, 258.

[36] Manvar, A.; Shah, A. Tetrahedron 2013, 69, 8105.

[37] Gallagher-Duval, S.; Herve, G.; Sartori, G.; Enderlin, G.; Len, C. New J Chem 2013, 37, 1989.

[38] Bebbington, D.; Binch, H.; Charrier, J.-D.; Everitt, S.; Fraysse, D.; Golec, J.; Kay, D.; Knegtel, R.; Mak, C.; Mazzei, F.; Miller, A.; Mortimore, M.; O'Donnell, M.; Patel, S.; Pierard, F.; Pinder, J.; Pollard, J.; Ramaya, S.; Robinson, D.; Rutherford, A.; Studley, J.; Westcott, J. Bioorg Med Chem Lett 2009, 19, 3586.

[39] Jung, F. H.; Pasquet, G.; Lambert-van der Brempt, C. A.; Heron, N.; Wilkinson, R. W.; Wedge, S. R.; Heaton, S. P.; Odedra, R.; Keen, N. J.; Green, S.; Brown, E.; Thompson, K.; Brightwell, S. J Med Chem 2006, 49, 955.

[40] Smits, R. A.; Adami, M.; Istyastono, E. P.; Zuiderveld, O. P.; van Dam, C. M. E.; de Kanter, F. J. J.; Jongejan, A.; Coruzzi, G.; Leurs, R.; de Esch, I. J. P. J Med Chem 2010, 53, 2390.

[41] Herget, T.; Freitag, M.; Morbitzer, M.; Kupfer, R.; Stamminger, T.; Marschall, M. Antimicrob Agents Chemother 2004, 48, 4154.

[42] Sharma, A.; Luxami, V.; Paul, K. Bioorg Med Chem Lett 2013, 23, 3288.

[43] Paul, K.; Sharma, A.; Luxami, V. Bioorg Med Chem Lett 2014, 24, 624.

[44] Waisser, K.; Gregor, J.; Dostal, H.; Kunes, J.; Kubicova, L.; Klimesova, V.; Kaustova, J. Farmaco 2001, 56, 803.

[45] Bikker, J. A.; Brooijmans, N.; Wisser, A.; Mansour, T. S. J Med Chem 2009, 52, 1493.

[46] Chen, J.; Wu, D.; He, F.; Liu, M.; Wu, H.; Ding, J.; Su, W. Tetrahedron Lett 2008, 49, 3814.

[47] Connolly, D. J.; Cusack, D.; O'Sullivan, T. P.; Guiry, P. J. Tetrahedron 2005, 61, 10153.

[48] Zhang, X. D.; Ye, D. J.; Sun, H. F.; Guo, D. L.; Wang, J.; Huang, H.; Zhang, X.; Jiang, H. L.; Liu, H. Green Chem 2009, 11, 1881.

[49] Gupta, S.; Agarwal, P. K.; Kundu, K. B. Tetrahedron Lett 2010, 51, 1887.

[50] Ge, W.; Zhu, X.; Wei, Y. RSC Adv 2013, 3, 10817.

[51] Zhou, J.; Fang, J. J Org Chem 2011, 76, 7730.

[52] Xu, W.; Jin, Y.; Liu, H.; Jiang, H.; Fu, H. Org Lett 2011, 13, 1274.

[53] Yang, D.; Fu, H.; Hu, L.; Jiang, Y.; Zhao, Y. J Comb Chem 2009, 11, 653.

[54] Liu, X.; Fu, H.; Jiang, Y.; Zhao, Y. Angew Chem Int Ed 2009, 48, 348.

[55] Huang, C.; Fu, H.; Jiang, Y.; Zhao, Y. Chem Commun 2008, 47, 6333.

[56] Xu, W.; Fu, H. J Org Chem 2011, 76, 3846.

[57] Ma, B.; Wang, Y.; Peng, J.; Zhu, Q. J Org Chem 2011, 76, 6362.

[58] Sun, Z.; Wang, H.; Wen, K.; Li, Y.; Fan, E. J Org Chem 2011, 76, 4149.

[59] Crystallographic data for the structural analysis have been deposited at the Cambridge Crystallographic Data Centre. (E-mail: deposit@ccdc.cam.ac.uk).

[60] Panja, S. S.; Saha, S. RSC Adv 2013, 3, 14495.

[61] Montazeri, N.; Pourshamsian, K.; Yosefiyan, S.; Samaneh Momeni, S. J Chem Sci 2012, 124, 883.