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Efficient access to 2,6,8-trisubstituted 4-aminoquinazolines via microwave-assisted one-pot chemoselective tri-Suzuki-Miyaura or S_NAr/bis-Suzuki-Miyaura reactions in water

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Abstract: An efficient sequential one-pot strategy for synthesizing polyfunctionalized quinazoline derivatives is presented. After selective amination of **4** at C-4 position, 2,6,8-trisubstituted 4-aminoquinazoline derivatives are prepared through one-pot chemoselective sequential tri-Suzuki-Miyaura or S_NAr/bis-Suzuki-Miyaura reactions under microwave irradiation in an aqueous medium. This approach used with a variety of boronic acids affords the polysubstituted quinazoline derivatives in good to excellent yields in only a few steps and in environmentally benign solvent water.

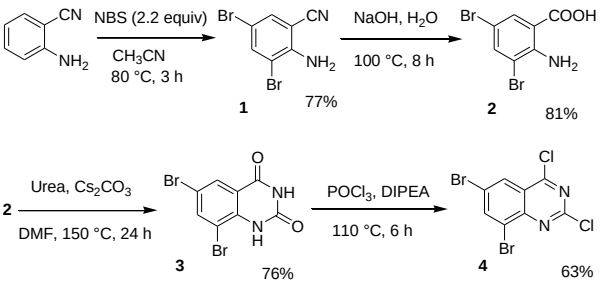
Introduction

The Suzuki-Miyaura coupling reaction has proven to be one of the most reliable routes for C-C bond construction since its discovery in 1979.[1] It has been applied widely in the synthesis of bioactive complex molecules thanks to its mild reaction conditions and its compatibility with a broad range of functional groups such as ester, nitrile and amide.[2] In recent years, organic reactions using water[3] as a cheap, non-toxic, non-volatile solvent, together with multistep sequences carried out in a single flask, such as tandem, cascade or sequential reactions, have received considerable attention in organic chemistry.[4] In this context and in connection with our research program on the design and synthesis of original molecules with pharmacological properties,[5] the S_NAr reaction was combined with the Suzuki-Miyaura cross-coupling reaction to perform one-pot sequential polyfunctionalization of the quinazoline ring.

The quinazoline ring is a privileged motif present in a wide range of natural products and bioactive molecules. As a result, this versatile scaffold has been widely exploited in medicinal chemistry, affording many highly-substituted quinazolines with a broad spectrum of biological properties, including antibacterial,[6] antiviral,[7] antitubercular[8] and anticancer[9] agents. Additionally, 4-aminoquinazoline derivatives such as gefitinib (Iressa)[10] and erlotinib (Tarceva)[11] are known to act as selective inhibitors of the tyrosine-kinase activity of the epidermal growth factor receptor (EGFR). Taking our previous study of sequential polyfunctionalization of 6,8-dibromo-2,4-dichloroquinazoline **4**,[12] a step further, we selectively introduced an amino group at the C-4 position of **4**, keeping chloride at C-2 and bromide at C-6 and C-8 as supplementary reactive centers for further study. Herein we report efficient access to 2,6,8-trisubstituted 4-aminoquinazolines *via* microwave-assisted consecutive one-pot chemoselective tri-Suzuki-Miyaura or S_NAr/bis-Suzuki-Miyaura cross-coupling reactions in water.

Results and Discussion

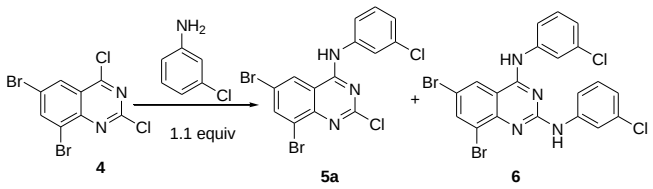
As described in our previous work,[12] the synthesis of 6,8-dibromo-2,4-dichloroquinazoline **4** was achieved in 30% overall yield in four steps using 2-aminobenzonitrile as starting material as shown in Scheme 1. Bromination of 2-aminobenzonitrile with *N*-bromosuccinimide (NBS) led to 2-amino-3,5-dibromobenzonitrile **1** in 77% yield. Then, using an aqueous solution of NaOH, the nitrile group was hydrolyzed into an acid group, leading to compound **2** in 81% yield. Anthranilic acid **2** was converted into 6,8-dibromoquinazolin-2,4-(1*H*,3*H*)-dione **3** in good yield (76%) using urea and cesium carbonate in DMF. In the last step, the intermediate **3** was chlorinated in presence of phosphorus oxychloride and diisopropylethylamine, leading to the substrate **4** in 63% yield.



Scheme 1. Synthesis of 6,8-dibromo-2,4-dichloroquinazoline **4**

Our study began with the S_NAr regio- and chemoselective reaction between **4** and 3-chloroaniline (1.1 equiv) in a mixture of CH_2Cl_2/EtOH (2/1) at room temperature (Table 1, entry 1). These conditions were previously found to be effective in the S_NAr reaction with 4-chloroquinazoline derivatives.[13] Complete conversion of the reaction (monitoring by LC-MS) was achieved within 1 h, and the expected 4-aminoquinazoline derivative **5a** was isolated in 70% yield. In addition to the desired compound, the disubstituted quinazoline

derivative **6** was obtained in 20% yield (Scheme 2). Decreasing temperature to 0 °C limited the formation of **6** (entry 2, Table 1); however, using potassium acetate (1.3 equiv) in a mixture of THF/H_2O (2/1) at room temperature[14] gave compound **5a** in excellent yield and complete selectivity for the C-4 position (Table 1, entry 3). The same result was obtained with diethylamine but the reaction took longer (entry 4, Table 1).



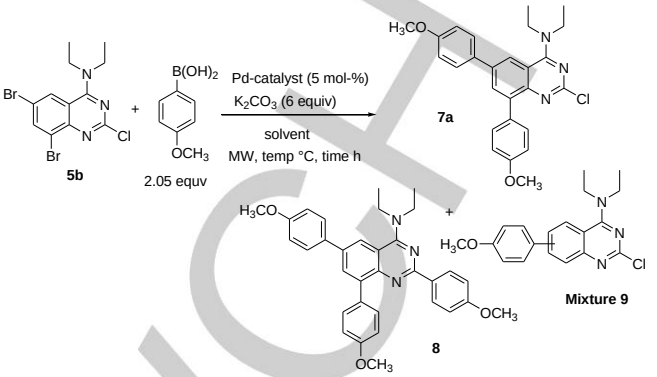
Scheme 2. S_NAr regio- and chemoselective reaction at 4-position of **4**

Table 1. Study of S_NAr region-and chemoselective reaction at 4-position of **4**

Entry	Condition	Amine	Yield **5**	Yield **6**
1	CH_2Cl_2/EtOH (2/1), r.t., 1 h	3-Chloroaniline	**5a**/70%	20%
2	CH_2Cl_2/EtOH (2/1), 0 °C, 8 h	3-Chloroaniline	**5a**/82%	10%
3	THF/H_2O(2/1), CH_3COOK (1.3 equiv), r.t., 4 h	3-Chloroaniline	**5a**/93%	0%
4	THF/H_2O(2/1), CH_3COOK (1.3 equiv), r.t., 24 h	Diethylamine	**5b**/91%	0%

To overcome the problem of solubility, we decided to use **5b** as starting material for our study. Our investigation began with the bis-Suzuki-Miyaura chemoselective reaction at the C-6 and C-8 positions between **5b** and 4-methoxyphenylboronic acid under similar experimental conditions to those recently described.[12] When the reaction was performed in the presence of 4-methoxyphenyl boronic acid (2.05 equiv), K_2CO_3, $PdCl_2(PPh_3)_2$ in a DME/EtOH mixture (9/1) at 100 °C under microwave irradiation (Table 2, entry 1), we obtained a 61% yield of dicoupled product **7a**, a 10% yield of tricoupled product **8** and a 19% yield of mixture **9**, as a result both of the mono cross-coupling Suzuki-Miyaura reaction and palladium-catalyzed reduction of aromatic bromide (analyzed by LC-MS). This result revealed that the reactivity of C-6-Br and C-8-Br bonds toward Suzuki-Miyaura is similar and superior to that of the C-2-Cl bond. Decreasing the temperature to 90 °C allowed **7a** to be obtained in somewhat higher yield (77%) and limited the formation of **8** and **9** (Table 1, entry 2). Varying the solvent, for instance using dioxane/EtOH (9/1) and DMF/EtOH (9/1) did not improve product yield **7a** (Table 2, entries 3-4). Interestingly, the use of an H_2O/EtOH mixture (9/1) as solvent in the presence of tetra-*N*-butylammonium bromide (TBAB) as phase-transfer reagent at 90 °C for 1 h 30 afforded **7a** in 82% isolated yield and no traces of mixture **9**. Trials with different catalysts revealed that bis(triphenylphosphine) palladium(II) dichloride performed best in our reaction conditions (entries 6-11, Table 2). Note that, with $Pd(OAc)_2$/PPh_3 and $Pd(dba)_2$, the reaction was not complete and starting material was observed (entries 10 and 11); there was no reaction with $Pd(PPh_3)_4$ in water, and only starting material was recovered (entry 7).

Table 2. Optimization of bis-Suzuki-Miyaura chemoselective reaction of **5b** with 4-methoxyphenylboronic acid.

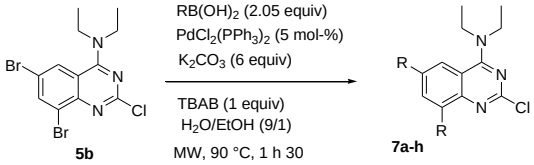


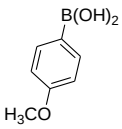
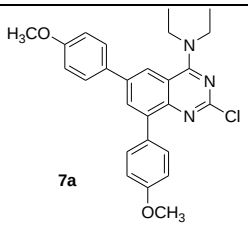
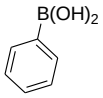
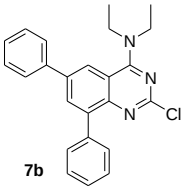
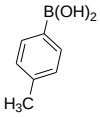
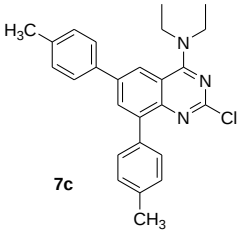
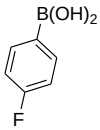
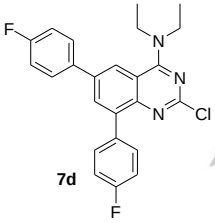
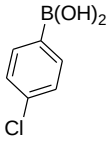
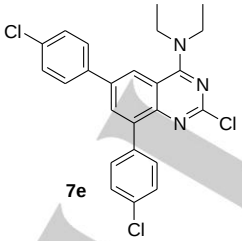
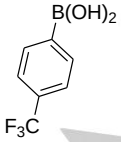
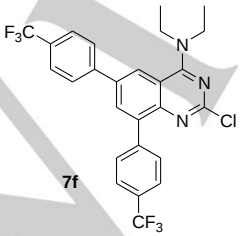
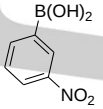
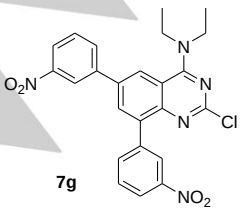
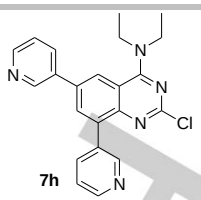
Entry	Catalyst	Solvent V (9/1)	Temp (°C)	Time	Yield **7a/8/9**
1	$PdCl_2(PPh_3)_2$	DME/EtOH	100	1 h	61/10/19
2	$PdCl_2(PPh_3)_2$	DME/EtOH	90	1 h	77/5/10
3	$PdCl_2(PPh_3)_2$	Dioxane/EtOH	90	1 h	68/10/15
4	$PdCl_2(PPh_3)_2$	DMF/EtOH	100	1 h	49/5/36
5	$PdCl_2(PPh_3)_2$	H_2O/EtOH TBAB	100	1 h	71/19/0
6	$PdCl_2(PPh_3)_2$	H_2O/EtOH TBAB (1 equiv)	90	1 h 30	82/5/0
7	$Pd(PPh_3)_4$	H_2O/EtOH TBAB (1 equiv)	100	1 h	0/0/0
8	$Pd(PPh_3)_4$	DME/EtOH	100	1 h	63/12/10
9	$PdCl_2(dppf)_2$	H_2O/EtOH TBAB (1 equiv)	100	1 h	70/10/0
10	$Pd(OAc)_2$, PPh_3	H_2O/EtOH TBAB (1 equiv)	100	1 h	20/0/0
11	$Pd(dba)_2$	H_2O/EtOH TBAB (1 equiv)	100	1 h	55/trace/ trace

The scope and limitations of this bis-Suzuki-Miyaura chemoselective reaction were then investigated using the optimized procedure; namely $PdCl_2(PPh_3)_2$ (5 mol-%), TBAB (1 equiv), K_2CO_3 (6 equiv) in H_2O/EtOH (9/1) under microwave irradiation at 90 °C for 1 h 30 using (hetero)arylboronic acids (Table 3).

As first observations, good to high yields of 6,8-disubstituted 4-aminoquinazoline derivatives were obtained with a wide range of aryl and heteroarylboronic acids bearing an electron-donating or-withdrawing group (entries 1-8, Table 3). However, with heteroarylboronic acid and boronic acids bearing an electron-withdrawing group, the reactions were achieved respectively after 1 h 30 at 105 °C (entry 8, Table 3) and 2 h at 95 °C (entries 6 and 7, Table 3).

Table 3. Scope of bis-Suzuki-Miyaura chemoselective reaction of **5b** with various boronic acids.

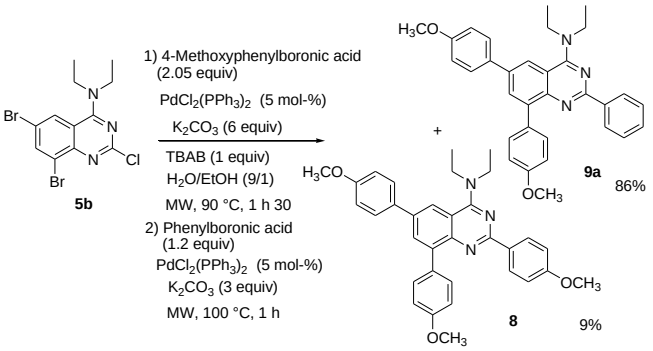


Entry	Boronic acid	Product	Yield
1		 **7a**	82%
2		 **7b**	80%
3		 **7c**	76%
4		 **7d**	81%
5		 **7e**	77%
6[a]		 **7f**	65%
7[a]		 **7g**	61%
8[b]		 **7h**	64%

Reaction conditions: boronic acids (2.05 equiv), $PdCl_2(PPh_3)_2$ (5 mol-%), K_2CO_3 (6 equiv), TBAB (1 equiv), H_2O/EtOH (9/1), MW, 90 °C, 1 h 30. [a] MW, 95 °C, 2 h, [b] MW, 105 °C, 1 h 30.

Next, after optimization of the bis-Suzuki-Miyaura chemoselective reaction, we investigated the one-pot chemoselective tri-Suzuki-Miyaura reaction of 6,8-dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine **5b**. One-pot multistep processes are economically advantageous in terms of the outlay for catalyst, solvent, purification materials and time.

The sequential one-pot two-step tri-Suzuki-Miyaura reactions of compound **5b** were studied using 4-methoxyphenylboronic acid and phenylboronic acid under microwave irradiation, allowing the synthesis of 2,6,8-trisubstituted 4-aminoquinazoline derivatives. First, 4-methoxyphenylboronic acid can be expected to react selectively at the C-6 and C-8 positions, with the subsequent addition of phenylboronic acid leading to reaction at the C-2 position of compound **5b** (Scheme 3). In the first step, we treated the 6,8-dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine **5b** according to our typical bis-Suzuki-Miyaura conditions: 4-methoxyphenylboronic acid (2.05 equiv), $PdCl_2(PPh_3)_2$ (5 mol-%), TBAB (1 equiv), K_2CO_3 (6 equiv) in H_2O/EtOH (9/1) under microwave irradiation at 90 °C for 1 h 30. In the second step, phenylboronic acid (1.2 equiv), $PdCl_2(PPh_3)_2$ (5 mol-%) and K_2CO_3 (3 equiv) were added and the mixture was heated again under microwave irradiation for 1 h at 100 °C to give the isolated trisubstituted 4-aminoquinazoline derivative **9a** in good yield (86%) and the tricoupled compound **8** in 9% yield. Note that, without adding fresh Pd and base, the conversion of the intermediate **7a** to compound **9a** is not complete (monitoring by LC-MS). Microwave heating the mixture at 90 °C for 1 h 30 in this second step resulted in incomplete conversion of the intermediate from the first step to compound **9a**, according to LC-MS analysis.



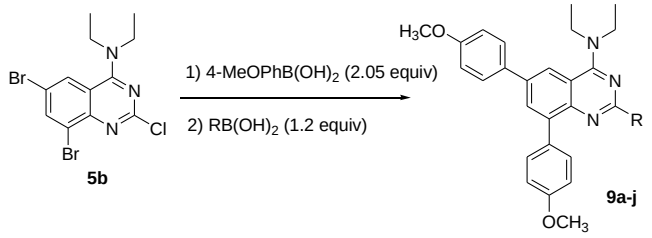
Scheme 3. One-pot chemoselective tri-Suzuki-Miyaura reaction

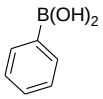
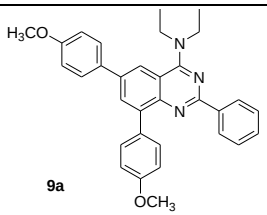
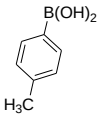
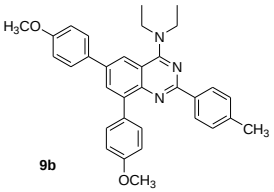
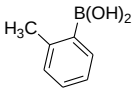
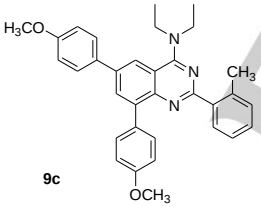
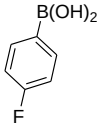
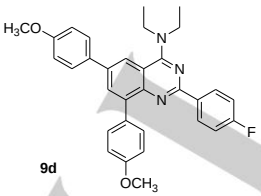
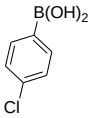
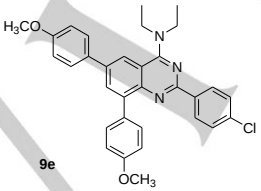
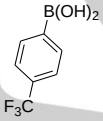
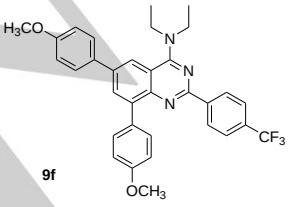
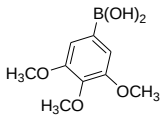
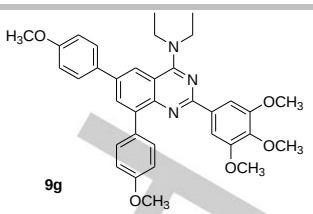
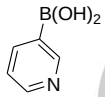
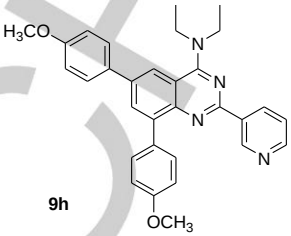
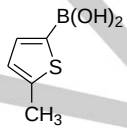
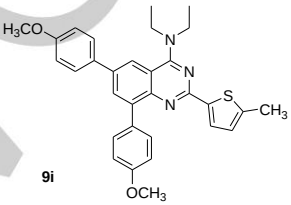
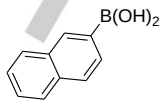
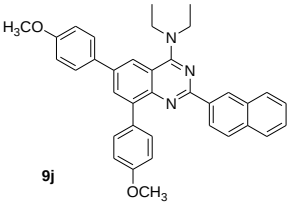
The scope and generality of this one-pot chemoselective tri-Suzuki-Miyaura reaction was next assessed using various boronic acids. We chose 4-methoxyphenyboronic acid for the first step and different boronic acids for the second step (Table 4).

High yields of 2,6,8-trisubstituted 4-aminoquinazoline derivatives **9a-j** were obtained under the reaction conditions previously described

with a broad range of (hetero)arylboronic acids bearing an electron-donating or withdrawing group (Table 4, entries 1-10).

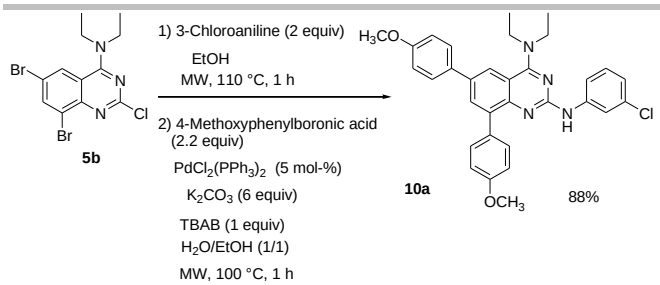
Table 4. Scope of the one-pot chemoselective tri-Suzuki-Miyaura reaction of **5b** with various boronic acids.



Entry	Boronic acid	Product	Yield
1		 **9a**	86%
2		 **9b**	90%
3		 **9c**	66%
4		 **9d**	85%
5		 **9e**	71%
6		 **9f**	82%
7		 **9g**	84%
8		 **9h**	71%
9		 **9i**	69%
10		 **9j**	89%

Reaction conditions: Step 1: 4-methoxyphenylboronic acid (2.05 equiv), $PdCl_2(PPh_3)_2$ (5 mol-%), K_2CO_3 (6 equiv), TBAB (1 equiv), H_2O/EtOH (9/1), MW, 90 °C, 1 h 30. Step 2: boronic acid (1.2 equiv), $PdCl_2(PPh_3)_2$ (5 mol-%), K_2CO_3 (3 equiv), MW, 100 °C, 1 h.

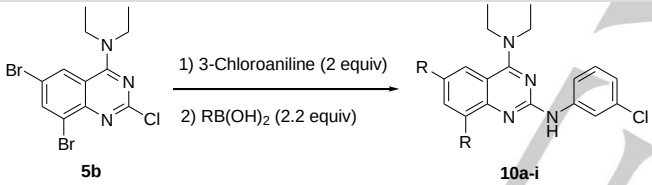
Finally, we turned our attention to the sequential one-pot chemoselective S_NAr/bis-Suzuki-Miyaura reaction of 6,8-dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine **5b**. As in our previous study,[12] the chemoselective reaction of an excess of 3-chloroaniline with 6,8-dibromo-2,4-dichloroquinazoline **4** led to the 2,4-disubstituted quinazoline derivative, and no reactivity of C-6-Br and C-8-Br bonds toward S_NAr was observed. With the optimized reaction conditions in hand, we performed the sequential one-pot synthesis of 2,6,8-trisubstituted 4-aminoquiazoline derivative **10a** from 3-chloroaniline and 4-methoxyphenylboronic acid (Scheme 4). In the first step, we reacted the 3-chloroaniline (2 equiv) with **5b** in EtOH (2.5 mL) under microwave irradiation at 110 °C for 1 h. After cooling to room temperature, 4-methoxyphenylboronic acid (2.2 equiv), $PdCl_2(PPh_3)_2$ (5 mol-%), TBAB (1 equiv), K_2CO_3 (6 equiv) and H_2O (2.5 mL) were added and the mixture was heated under microwave irradiation at 100 °C for 1 h. S_NAr reaction occurred exclusively at C-2 position and bis-Suzuki-Miyaura at C-6 and C-8 positions, and the corresponding product **10a** was isolated in high yield (88%). When the reaction mixture was heated at 100 °C for 1 h in the first step, a mixture of the starting material and the aminated product in C-2 position was observed by LC-MS analysis. For the second step, in order to decrease the reaction time and guided by the results of the previous bis-Suzuki-Miyaura chemoselective study, the reaction was carried out at 100 °C.

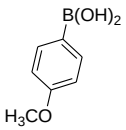
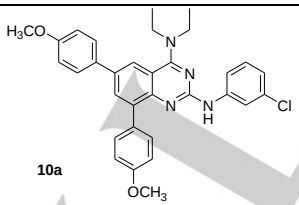
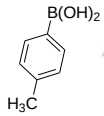
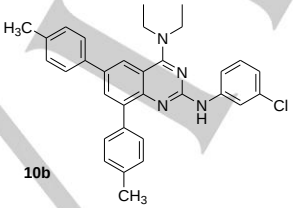
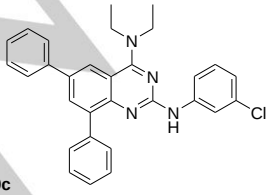
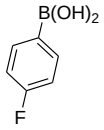
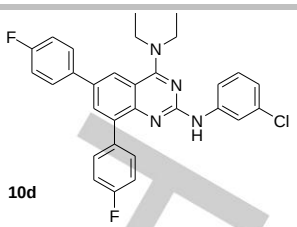
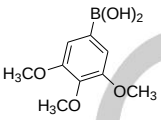
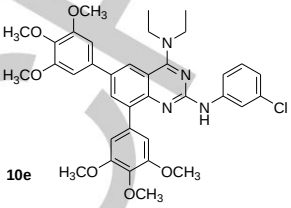
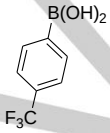
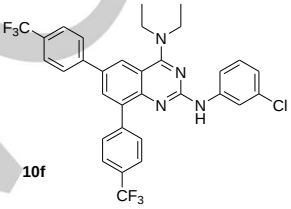
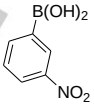
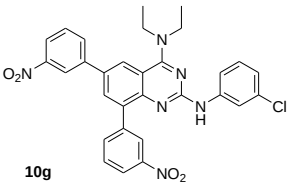
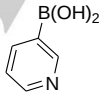
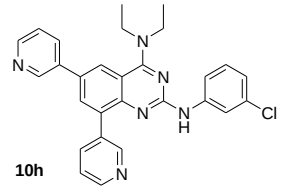
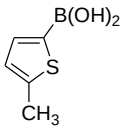
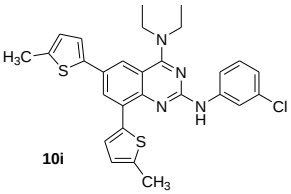


Scheme 4. One-pot chemoselective S_NAr/bis-Suzuki-Miyaura reaction

To ascertain the scope of the one-pot chemoselective S_NAr/bis-Suzuki-Miyaura reaction, we prepared a new series of 2,6,8-trisubstituted 4-aminoquinazoline derivatives using our optimized reaction conditions. In the first step, we used 3-chloroaniline and in the second step various boronic acids (Table 5). The reaction conditions showed a broad tolerance for the presence of a wide range of (hetero)arylboronic acids bearing an electron-donating or withdrawing group. Good to excellent yields of 2,6,8-trisubstituted 4-aminoquinazoline derivatives were obtained (Table 5, entries 1-9).

Table 5. Scope of the one-pot chemoselective S_NAr/bis-Suzuki-Miyaura reaction of **5b** with 3-chloroaniline and various boronic acids.



Entry	Boronic acid	Product	Yield
1		 **10a**	88%
2		 **10b**	85%
3		 **10c**	83%
4		 **10d**	92%
5		 **10e**	89%
6		 **10f**	83%
7		 **10g**	90%
8		 **10h**	83%
9		 **10i**	69%

Reaction conditions: Step 1: 3-chloroaniline (2 equiv), EtOH, MW, 110 °C, 1 h. Step 2: boronic acid (2.2 equiv), $PdCl_2(PPh_3)_2$ (5 mol-%), K_2CO_3 (6 equiv), TBAB (1 equiv), H_2O/EtOH (1/1), MW, 100 °C, 1 h.

Conclusions

In summary, an original one-pot chemoselective tri-Suzuki-Miyaura reaction and one-pot chemoselective S_NAr/bis-Suzuki-Miyaura reaction were developed using 6,8-dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine **5b**, allowing the chemoselective functionalization of C-2, C-6 and C-8 positions of this quinazoline scaffold. This sequential one-pot approach affords easy access to 2,6,8-trisubstituted 4-aminoquinazoline derivatives in good to excellent yields in water under microwave irradiation. In addition, this environmentally friendly procedure tolerates a wide range of boronic acids and represents a promising green route for the synthesis of these important pharmaceutical heterocyclic compounds.

Experimental Section

Melting points were determined on Büchi B-540 and are uncorrected. Elemental analyses and HRMS were carried out at the Spectropole, Faculté des Sciences et Techniques de Saint-Jérôme, Marseille. 200 or 250 MHz ^{1}H NMR spectra (reference $CDCl_3$ δ = 7.26, [D_6]DMSO δ = 2.50) and 50 or 62.5 MHz ^{13}C NMR spectra (reference $CDCl_3$ δ = 77.0, [D_6]DMSO δ = 39.7) were recorded on a Bruker ARX 200 spectometer in $CDCl_3$ and [D_6]DMSO solvents at the Faculté de Pharmacie de Marseille. Solvents were dried by conventional methods. The following adsorbent was used for column chromatography: silica gel 60 (Merck, particle size 0.063-0.200 mm, 70-230 mesh ASTM). TLC was performed on 5 cm x 10 cm aluminium plates coated with silica gel 60F-254 (Merck) in an appropriate eluent. HRMS spectra were recorded on a QStar Elite (Applied Biosystems SCIEX) spectrometer. PEG was a matrix for HRMS.

Microwave reactions were performed with a Biotage® Initiator Microwave oven using 2-5 mL sealed vials; temperatures were measured with an IR-sensor and reaction times are given as hold times.

LC/MS analyses were performed at the Faculté de Pharmacie de Marseille on an Accela High System® chain U-HPLC coupled with a Thermo MSQ Plus® simple quadripole. A Thermo Hypersil Gold® 50 x 2.1 mm chromatographic column was used (SiO_2 C18) with 1.9 µm diameter particles. Analysis is 8 min running, with an MeOH/H_2O eluent gradient from 50/50 to 95/05.

2-Amino-3,5-dibromobenzonitrile (1):

A mixture of 2-aminobenzonitrile (5 g, 42.3 mmol) and NBS (16.57 g, 93.1 mmol, 2.2 equiv) was refluxed in MeCN (80 mL) for 3 h. After cooling, a precipitate appeared and was filtered, washed with water (3 x 60 mL) and dried in a vacuum drying oven (desiccator cabinet). Recrystallization from propan-2-ol gave 8.90 g (77%) of 1 as brown solid; Mp 158 °C (Lit.[15] 156 °C). 1H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 4.91 (s, 2 H, NH_2), 7.47 (d, $^4J_{H\text{-}H}$ = 2.1 Hz, 1 H, Ar-H), 7.71 (d, $^4J_{H\text{-}H}$ = 2.1 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 97.9 (C_{CN}), 108.2 (C_{Ar}), 109.7 (C_{Ar}), 115.6 (C_{Ar}), 133.6 (CH_{Ar}), 139.4 (CH_{Ar}), 146.2 (C_{Ar}) ppm.

2-Amino-3,5-dibromobenzoic acid (2):

To a solution of 2-amino-3,5-dibromobenzonitrile **1** (8 g, 29.0 mmol) in water (100 mL), NaOH (1.16 g, 1 equiv) was added. The reaction mixture was heated at 100 °C for 8 h. After cooling, a precipitate appeared and was filtered, washed with water (3 x 60 mL) and dried in a vacuum drying oven (desiccator cabinet). Recrystallization from propan-2-ol gave 6.58 g (81%) of **2** as yellow solid; Mp 223 °C (Lit.[16] 226-228 °C). ^{1}H NMR ([D_6]DMSO, 200 MHz, 24 °C): δ = 6.80 (s, 2 H, NH_2), 7.72 (d, $^4J_{H\text{-}H}$ = 1.9 Hz, 1 H, Ar-H), 7.78 (d, $^4J_{H\text{-}H}$ = 1.9 Hz, 1 H, Ar-H), 8.05 (s, 1 H, COOH) ppm. ^{13}C NMR ([D_6]DMSO, 50 MHz, 24 °C): δ = 105.1 (C_{Ar}), 110.6 (C_{Ar}), 117.0 (C_{Ar}), 130.9 (CH_{Ar}), 136.8 (CH_{Ar}), 146.2 (C_{Ar}), 169.4 (C_{COOH}) ppm.

6,8-Dibromoquinazoline-2,4-(1*H*,3*H*)-dione (3):

A mixture of 2-amino-3,5-dibromobenzoic acid **2** (5 g, 16.95 mmol), urea (5.09 g, 84.75 mmol, 5 equiv) and Cs_2CO_3 (0.55 g, 1.69 mmol, 0.1 equiv) was refluxed in DMF (80 mL) for 24 h. After cooling, a precipitate appeared and was filtered, washed with water (3 x 60 mL) and dried in a vacuum drying oven (desiccator cabinet). Recrystallization from propan-2-ol gave 4.14 g (76%) of **3** as brown solid; Mp 289 °C (Lit.[17] 291-292 °C). ^{1}H NMR ([D_6]DMSO, 200 MHz, 24 °C): δ = 7.84 (d, $^4J_{H\text{-}H}$ = 2.2 Hz, 1 H, Ar-H), 7.94 (d, $^4J_{H\text{-}H}$ = 2.2 Hz, 1 H, Ar-H), 10.76 (s, 2 H, 2 NH) ppm. ^{13}C NMR ([D_6]DMSO, 50 MHz, 24 °C): δ = 110.4 (C_{Ar}), 114.0 (C_{Ar}), 118.0 (C_{Ar}), 128.5 (CH_{Ar}), 138.8 (CH_{Ar}), 145.1 (C_{Ar}), 153.4 (C_{CO}), 162.7 (C_{CO}) ppm.

6,8-Dibromo-2,4-dichloroquinazoline (4):

A solution of 6,8-dibromoquinazoline-2,4-(1*H*,3*H*)-dione **3** (4 g, 12.5 mmol), $POCl_3$ (11.4 mL, 10 equiv), diisopropyl ethylamine (4.4 mL, 25.0 mmol, 2 equiv) was heated at reflux for 6 h. Following this, the reaction mixture was poured with care over crushed ice and stirred vigorously. This aqueous mixture was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure. Flash chromatography (silica gel, CH_2Cl_2/petroleum ether, 2/1) provided after recrystallization from propan-2-ol 2.81 g (63%) of **4** as yellow solid; Mp 145 °C (Lit.[18] 148-149 °C). ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 8.37 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H), 8.39 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 122.7 (C_{Ar}), 124.1 (C_{Ar}), 124.2 (C_{Ar}), 127.7 (CH_{Ar}), 142.3 (CH_{Ar}), 149.0 (C_{Ar}), 156.3 (C_{Ar}), 163.3 (C_{Ar}) ppm.

6,8-Dibromo-2-chloro-*N*-(3-chlorophenyl)quinazolin-4-amine (5a):

To a solution of 6,8-dibromo-2,4-dichloroquinazoline **4** (1 g, 2.23 mmol) in a THF/H_2O mixture (2/1, 12 mL) were added 3-chloroaniline (0.3 mL, 1.1 equiv, 2.45 mmol) and potassium acetate (0.36 g, 1.3 equiv, 2.9 mmol). The reaction mixture was stirred at room temperature for 4 h. At the end of this time, a precipitate appeared and was filtered, washed with water (3 x 10 mL) and dried in a vacuum drying oven (desiccator cabinet). Recrystallization from propan-2-ol gave 1.15 g (92%) of **5a** as yellow solid; Mp 235 °C. ^{1}H NMR ([D_6]DMSO, 200 MHz , 24 °C): δ = 7.26-7.46 (m, 2 H, 2 Ar-H), 7.76-7.93 (m, 2 H, 2 Ar-H), 8.38 (s, 1 H, Ar-H), 8.83 (s, 1 H, Ar-H), 10.32 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 50 MHz, 24 °C): δ = 116.4 (C_{Ar}), 119.0 (C_{Ar}), 121.2 (CH_{Ar}), 122.3 (CH_{Ar}), 123.0 (C_{Ar}), 124.8 (CH_{Ar}), 125.8 (CH_{Ar}), 130.5 (CH_{Ar}), 133.0 (C_{Ar}), 139.5 (C_{Ar}), 139.5 (CH_{Ar}), 147.6 (C_{Ar}), 157.4 (C_{Ar}), 158.7 (C_{Ar}) ppm. $C_{14}H_7Br_2Cl_2N_3$ (447.94): calcd. C 37.54, H 1.58, N 9.38; found C 37.42, H 1.49, N 9.22.

6,8-Dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine (5b):

To a solution of 6,8-dibromo-2,4-dichloroquinazoline **4** (1 g, 2.23 mmol) in a THF/H_2O mixture (2/1, 12 mL) were added diethyamine (0.23 mL, 1.1 equiv, 2.45 mmol) and potassium acetate (0.36 g, 1.3 equiv, 2.9 mmol). The reaction mixture was stirred at room temperature for 24 h. At the end of this time, water was added (10 mL) and solution was extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. Flash chromatography (silica gel, CH_2Cl_2/petroleum ether, 1/1) provided after recrystallization from propan-2-ol 1.00 g (91%) of **5b** as yellow solid; Mp 128 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.40 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.73 (q, $^3J_{H\text{-}H}$ = 7.0 Hz, 4 H, 2 CH_2), 7.95 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H), 8.07 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 12.7 (2 CH_3), 45.7 (2 CH_2), 116.2 (C_{Ar}), 116.7 (C_{Ar}), 123.6 (C_{Ar}), 126.8 (CH_{Ar}), 138.8 (CH_{Ar}), 150.0 (C_{Ar}), 157.7 (C_{Ar}), 162.4 (C_{Ar}) ppm. $C_{12}H_{12}Br_2ClN_3$ (393.50): calcd. C 36.63, H 3.07, N 10.68; found C 36.86, H 2.95, N 10.72.

6,8-Dibromo-N^2,N^4-bis(3-chlorophenyl)quinazoline-2,4-diamine (6):

To a solution of 6,8-dibromo-2,4-dichloroquinazoline **4** (1 g, 2.23 mmol) in a CH_2Cl_2/EtOH mixture (2/1, 12 mL) was added 3-chloroaniline (0.3 mL, 1.1 equiv, 2.45 mmol). The reaction mixture was stirred at room temperature for 1 h. At the end of this time, a precipitate appeared and was filtered, washed with water (3 x 10 mL) and

dried in a vacuum drying oven (desiccator cabinet). Flash chromatography (silica gel, CH_2Cl_2/petroleum ether, 1/2) provided after recrystallization from propan-2-ol 0.23 g (20%) of **6** as yellow solid; Mp 222 °C. ^{1}H NMR ([D$_6$]DMSO, 200 MHz , 24 °C): δ = 7.01 (d, $^3J_{H\text{-}H}$ = 6.3 Hz, 1 H, Ar-H), 7.19-7.34 (m, 2 H, 2 Ar-H), 7.43 (t, $^3J_{H\text{-}H}$ = 7.7 Hz, 1 H, Ar-H), 7.81 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 1 H, Ar-H), 7.93 (s, 1 H, Ar-H), 8.02 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 1 H, Ar-H), 8.23 (s, 1 H, Ar-H), 8.48 (s, 1 H, Ar-H), 8.75 (s, 1 H, Ar-H), 9.81 (s, 1 H, NH), 9.93 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 50 MHz, 24 °C): δ = 114.1 (C_{Ar}), 114.4 (C_{Ar}), 117.7 (CH_{Ar}), 118.9 (CH_{Ar}), 121.0 (CH_{Ar}), 121.3 (CH_{Ar}), 121.9 (CH_{Ar}), 124.0 (CH_{Ar}), 125.6 (CH_{Ar}), 130.1 (CH_{Ar}), 130.4 (CH_{Ar}), 133.1 (C_{Ar}), 133.3 (2 C_{Ar}), 138.5 (CH_{Ar}), 140.5 (C_{Ar}), 142.0 (C_{Ar}), 147.4 (C_{Ar}), 156.1 (C_{Ar}), 157.7 (C_{Ar}) ppm. HRMS (ESI): m/z [M+H]$^+$ Calcd for $C_{20}H_{12}Br_2Cl_2N_4$: 538.8857; found: 538.8858.

General procedure for the one-pot chemoselective bis-Suzuki-Miyaura coupling reaction: A solution of 6,8-dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine **5b** (0.15 g, 0.38 mmol), boronic acid (0.78 mmol, 2.05 equiv), $PdCl_2(PPh_3)_2$ (13 mg, 0.019 mmol, 0.05 equiv), K_2CO_3 (0.32 g, 2.29 mmol, 6 equiv), TBAB (0.12 g, 1 equiv, 0.38 mmol) in a H_2O/EtOH mixture (9/1, 5 mL) was heated at 90 °C under microwave irradiation for 1 h 30. After cooling, 80 mL of water were added and the solution was extracted with dichloromethane (3 x 60 mL). The organic layer was washed with water (3 x 100 mL), dried over Na_2SO_4 and evaporated. The crude product was purified by column chromatography [silica gel, petroleum ether/ethyl acetate (5%), (15% for **7g**), (100% for **7h**)] and recrystallized from propan-2-ol.

2-Chloro-*N*,*N*-diethyl-6,8-bis(4-methoxyphenyl)quinazolin-4-amine (7a): Yield 82% (140 mg); yellow solid; Mp 173 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.45 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.80 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 4 H, 2 CH_2), 3.88 (s, 6 H, 2 OCH_3), 7.03 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 4 H, 4 Ar-H), 7.58 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.68 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.93 (d, $^4J_{H\text{-}H}$ = 1.7 Hz, 1 H, Ar-H), 7.98 (d, $^4J_{H\text{-}H}$ = 1.7 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.1 (2 CH_3), 45.5 (2 CH_2), 55.3 (OCH_3), 55.4 (OCH_3), 113.6 (2 CH_{Ar}), 114.6 (2 CH_{Ar}), 115.5 (C_{Ar}), 121.0 (CH_{Ar}), 128.1 (2 CH_{Ar}), 131.0 (C_{Ar}), 131.7 (2 CH_{Ar}), 132.3 (CH_{Ar}), 132.8 (C_{Ar}), 136.6 (C_{Ar}), 139.1 (C_{Ar}), 150.0 (C_{Ar}), 155.8 (C_{Ar}), 159.3 (C_{Ar}), 159.5 (C_{Ar}), 164.5 (C_{Ar}) ppm. $C_{26}H_{26}ClN_3O_2$ (447.96): calcd. C 69.71, H 5.85, N 9.38; found C 69.54, H 5.88, N 9.58.

2-Chloro-*N*,*N*-diethyl-6,8-diphenylquinazolin-4-amine (7b): Yield 80% (118 mg); yellow solid; Mp 150 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.47 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.81 (q, $^3J_{H\text{-}H}$ = 7.0 Hz, 4 H, 2 CH_2), 7.37-7.55 (m, 6 H, 6 Ar-H), 7.65-7.76 (m, 4 H, 4 Ar-H), 8.01 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H), 8.08 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.0 (2 CH_3), 45.5 (2 CH_2), 115.4 (C_{Ar}), 122.2 (CH_{Ar}), 127.0 (2 CH_{Ar}), 127.6 (CH_{Ar}), 127.8 (CH_{Ar}), 128.0 (2 CH_{Ar}), 129.2 (2 CH_{Ar}), 130.6 (2 CH_{Ar}), 132.9 (CH_{Ar}), 136.8 (C_{Ar}), 138.5 (C_{Ar}), 139.6 (C_{Ar}), 140.2 (C_{Ar}), 150.4 (C_{Ar}), 156.2 (C_{Ar}), 164.4 (C_{Ar}) ppm. $C_{24}H_{22}ClN_3$ (387.90): calcd. C 74.31, H 5.72, N 10.83; found C 74.41, H 5.74, N 10.78.

2-Chloro-*N*,*N*-diethyl-6,8-di*p*-tolylquinazolin-4-amine (7c): Yield 76% (95 mg); yellow solid; Mp 213 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 C°): δ = 1.45 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 2.43 (s, 6 H, 2 CH_3), 3.80 (q, $^3J_{H\text{-}H}$ = 6.8 Hz, 4 H, 2 CH_2), 7.27-7.32 (m, 4 H, 4 Ar-H), 7.55 (d, $^3J_{H\text{-}H}$ = 7.9 Hz, 2 H, 2 Ar-H), 7.62 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 2 H, 2 Ar-H), 7.98 (d, $^4J_{H\text{-}H}$ = 1.3 Hz, 1 H, Ar-H), 8.03 (d, $^4J_{H\text{-}H}$ = 1.3 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.1 (2 CH_3), 21.1 (CH_3), 21.3 (CH_3), 45.5 (2 CH_2), 115.4 (C_{Ar}), 121.6 (CH_{Ar}), 126.9 (2 CH_{Ar}), 128.8 (2 CH_{Ar}), 129.9 (2 CH_{Ar}), 130.4 (2 CH_{Ar}), 132.6 (CH_{Ar}), 135.6 (C_{Ar}), 136.8 (C_{Ar}), 137.3 (C_{Ar}), 137.4 (C_{Ar}), 137.7 (C_{Ar}), 139.6 (C_{Ar}), 150.3 (C_{Ar}), 156.0 (C_{Ar}), 164.5 (C_{Ar}) ppm. HRMS: calcd. for $C_{26}H_{26}ClN_3$ [M + H+] 416.1888; found 416.1888.

2-Chloro-*N*,*N*-diethyl-6,8-bis(4-fluorophenyl)quinazolin-4-amine (7d): Yield 81% (131 mg); yellow solid; Mp 186 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.46 (t, $^3J_{H\text{-}H}$ = 7.1 Hz, 6 H, 2 CH_3), 3.81 (q, $^3J_{H\text{-}H}$ = 6.6 Hz, 4 H, 2 CH_2), 7.13-7.23 (m, 4 H, 4 Ar-H), 7.57-7.63 (m, 2 H, 2 Ar-H), 7.66-7.71 (m, 2 H, 2 Ar-H), 7.90 (s, 1 H, Ar-H), 8.01 (s, 1H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.0 (2 CH_3), 45.6 (2 CH_2), 115.0 (d, $^3J_{C\text{-}F}$ = 21.6 Hz, 2 CH_{Ar}), 115.4 (C_{Ar}), 116.1 (d, $^3J_{C\text{-}F}$ = 21.6 Hz, 2 CH_{Ar}), 122.2 (CH_{Ar}), 128.6 (d, $^4J_{C\text{-}F}$ = 8.3 Hz, 2 CH_{Ar}), 132.2 (d, $^4J_{C\text{-}F}$ = 8.3 Hz, 2 CH_{Ar}), 132.5 (CH_{Ar}), 134.3 (d, $^5J_{C\text{-}F}$ = 2.8 Hz, C_{Ar}), 135.9 (C_{Ar}), 136.2 (d, $^5J_{C\text{-}F}$ = 3.7 Hz, C_{Ar}), 138.7 (C_{Ar}), 150.3 (C_{Ar}), 156.3 (C_{Ar}), 162.6 (d, $^2J_{C\text{-}F}$ = 246.8 Hz, C_{Ar}), 162.7 (d, $^2J_{C\text{-}F}$ = 247.7 Hz, C_{Ar}), 164.3 (C_{Ar}) ppm. $C_{24}H_{20}ClF_2N_3$ (423.89): calcd. C 68.00, H 4.76, N 9.91; found C 68.19, H 4.54, N 10.52.

2-Chloro-6,8-bis(4-chlorophenyl)-*N*,*N*-diethylquinazolin-4-amine (7e): Yield 77% (134 mg); yellow solid; Mp 208 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.46 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.81 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 4 H, 2 CH_2), 7.42-7.49 (m, 4 H, 4 Ar-H), 7.56 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.65 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 2 H, 2 Ar-H), 7.89 (d, $^4J_{H\text{-}H}$ = 1.9 Hz, 1 H, Ar-H), 8.02 (d, $^4J_{H\text{-}H}$ = 1.9 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.0 (2 CH_3), 45.6 (2 CH_2), 115.3 (C_{Ar}), 122.5 (CH_{Ar}), 128.2 (2 CH_{Ar}), 128.3 (2 CH_{Ar}), 129.4 (2 CH_{Ar}), 131.8 (2 CH_{Ar}), 132.3 (CH_{Ar}), 133.8 (C_{Ar}), 134.1 (C_{Ar}), 135.7 (C_{Ar}), 136.7 (C_{Ar}), 138.5 (C_{Ar}), 138.6 (C_{Ar}), 150.4 (C_{Ar}), 156.5 (C_{Ar}), 164.2 (C_{Ar}) ppm. $C_{24}H_{20}Cl_3N_3$ (456.79): calcd. C 63.10, H 4.41, N 9.20; found C 63.19, H 4.33, N 9.19.

2-Chloro-*N*,*N*-diethyl-6,8-bis[4-(trifluoromethyl)phenyl]-quinazolin-4-amine (7f): Yield 65% (129 mg); yellow solid; Mp 215 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.48 (t, $^3J_{H\text{-}H}$ = 6.9 Hz, 6 H, 2 CH_3), 3.82 (q, $^3J_{H\text{-}H}$ = 7.0 Hz, 4 H, 2 CH_2), 7.72-7.76 (m, 6 H, 6 Ar-H), 7.82 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 2 H, 2 Ar-H), 7.96 (s, 1 H, Ar-H), 8.13 (s, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.1 (2 CH_3), 45.7 (2 CH_2), 115.4 (C_{Ar}), 123.6 (CH_{Ar}), 124.0 (q, $^2J_{C\text{-}F}$ = 272.6 Hz, CF_3), 124.3 (q, $^2J_{C\text{-}F}$ = 272.6 Hz, CF_3), 125.0 (q, $^4J_{C\text{-}F}$ = 3.7 Hz, 2 CH_{Ar}), 126.2 (q, $^4J_{C\text{-}F}$ = 3.7 Hz, 2 CH_{Ar}), 127.4 (2 CH_{Ar}), 129.7 (q, $^3J_{C\text{-}F}$ = 32.2 Hz, C_{Ar}), 130.1 (q, $^3J_{C\text{-}F}$ = 32.6 Hz, C_{Ar}), 130.9 (2 CH_{Ar}), 132.7 (CH_{Ar}), 135.4 (C_{Ar}), 138.6 (C_{Ar}), 141.9 (C_{Ar}), 143.5 (C_{Ar}), 150.8 (C_{Ar}), 157.0 (C_{Ar}), 164.1 (C_{Ar}) ppm. $C_{26}H_{20}ClF_6N_3$ (523.90): calcd. C 59.61, H 3.85, N 8.02; found C 59.70, H 3.35, N 8.21.

2-Chloro-*N*,*N*-diethyl-6,8-bis(3-nitrophenyl)quinazolin-4-amine (7g): Yield 61% (111 mg); yellow solid; Mp 221 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.50 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.85 (q, $^3J_{H\text{-}H}$ = 7.0 Hz, 4 H, 2 CH_2), 7.66 (t, $^3J_{H\text{-}H}$ = 8.1 Hz, 1 H, Ar-H), 7.71 (t, $^3J_{H\text{-}H}$ = 81 Hz, 1 H, Ar-H), 7.99 (d, $^3J_{H\text{-}H}$ = 8.1 Hz, 1 H, Ar-H), 8.01 (s, 1 H, Ar-H), 8.08 (d, $^3J_{H\text{-}H}$ = 7.4 Hz, 1 H, Ar-H), 8.18 (s, 1 H, Ar-H), 8.28 (d, $^3J_{H\text{-}H}$ = 8.1 Hz, 2 H, 2 Ar-H), 8.51 (s, 1 H, Ar-H), 8.55 (s, 1 H, Ar-H) ppm. NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.0 (2 CH_3), 45.7 (2 CH_2), 115.3 (C_{Ar}), 121.8 (CH_{Ar}), 122.7 (2 CH_{Ar}), 123.9 (CH_{Ar}), 125.3 (CH_{Ar}), 128.9 (CH_{Ar}), 130.3 (CH_{Ar}), 132.2 (CH_{Ar}), 132.8 (CH_{Ar}), 134.2 (C_{Ar}), 136.9 (CH_{Ar}), 137.7 (C_{Ar}), 139.6 (C_{Ar}), 141.4 (C_{Ar}), 148.2 (C_{Ar}), 149.0 (C_{Ar}), 150.9 (C_{Ar}), 157.3 (C_{Ar}), 163.9 (C_{Ar}) ppm. HRMS: calcd. for $C_{24}H_{20}ClN_5O_4$ [M + H+] 478.1277; found 478.1277.

2-Chloro-*N*,*N*-diethyl-6,8-di(pyridin-3-yl)quinazolin-4-amine (7h): Yield 64% (95 mg); yellow solid; Mp 176 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.47 (t, $^3J_{H\text{-}H}$ = 6.8 Hz, 6 H, 2 CH_3), 3.82 (q, $^3J_{H\text{-}H}$ = 7.0 Hz, 4 H, 2 CH_2), 7.41-7.47 (m, 2 H, 2 Ar-H), 7.95 (s, 2 H, 2 Ar-H), 8.12 (s, 2 H, 2 Ar-H), 8.66 (t, $^3J_{H\text{-}H}$ = 4.4 Hz, 2 H, 2 Ar-H), 8.90-8.91 (m, 2 H, 2 Ar-H) ppm. NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.0 (2 CH_3), 45.6 (2 CH_2), 115.4 (C_{Ar}), 122.9 (CH_{Ar}), 123.3 (CH_{Ar}), 123.9 (CH_{Ar}), 132.3 (CH_{Ar}), 133.5 (C_{Ar}), 134.0 (C_{Ar}), 134.3 (CH_{Ar}), 135.5 (C_{Ar}), 136.6 (C_{Ar}), 138.3 (CH_{Ar}), 148.1 (CH_{Ar}), 148.7 (CH_{Ar}), 149.1 (CH_{Ar}), 150.4 (CH_{Ar}), 150.8 (C_{Ar}), 157.0 (C_{Ar}), 163.9 (C_{Ar}) ppm. HRMS: calcd. for $C_{22}H_{20}ClN_5$ [M + H+] 390.1480; found 390.1484.

***N*,*N*-Diethyl-2,6,8-tris(4-methoxyphenyl)quinazolin-4-amine (8):** Yield 19% (37 mg); yellow solid; Mp 173 °C. ^{1}H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.48 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.83 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 4 H, 2 CH_2), 3.87 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 6.96 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 2 H, 2 Ar-H), 7.04 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 2 H, 2 Ar-H), 7.08 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.63 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 2 H, 2 Ar-H), 7.84 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 2 H, 2 Ar-H), 7.96 (d, $^4J_{H\text{-}H}$ = 1.9 Hz, 1 H, Ar-H), 8.02 (d, $^4J_{H\text{-}H}$ = 1.9 Hz, 1 H, Ar-H), 8.45 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 2 H, 2 Ar-H) ppm. NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.3 (2 CH_2), 55.3 (OCH_3), 55,4 (2 OCH_3), 113.2 (2 CH_{Ar}), 113.5 (2 CH_{Ar}), 114.5 (2 CH_{Ar}), 115.9 (C_{Ar}), 121.0 (CH_{Ar}), 128.1 (2 CH_{Ar}), 129.9 (2 CH_{Ar}), 131.2 (CH_{Ar}), 132.0 (C_{Ar}), 132.1 (2 CH_{Ar}), 133.4 (C_{Ar}), 135.5 (C_{Ar}), 139.5 (C_{Ar}), 143.5 (C_{Ar}), 149.5 (C_{Ar}), 157.9 (C_{Ar}), 158.9 (C_{Ar}), 159.2 (C_{Ar}), 161.1 (C_{Ar}), 164.0 (C_{Ar}) ppm. HRMS: calcd. for $C_{33}H_{33}N_3O_3$ [M + H+] 520.2595; found 520.2594.

General procedure for the one-pot chemoselective tri-Suzuki-Miyaura coupling reaction: A solution of 6,8-dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine **5b** (0.2 g, 0.508 mmol), 4-methoxyphenylboronic acid (0.16 g, 1.04 mmol, 2.05 equiv), $PdCl_2(PPh_3)_2$ (18 mg, 0.025 mmol, 0.05 equiv), K_2CO_3 (0.42 g, 3.05 mmol, 6 equiv), TBAB (0.16 g, 1 equiv, 0.508 mmol) in a H_2O/EtOH mixture (9/1, 5 mL) under argon was heated at 90 °C under microwave irradiation for 1 h 30. After cooling, boronic acid (0.70 mmol, 1.2 equiv), $PdCl_2(PPh_3)_2$ (18 mg, 0.025 mmol, 0.05 equiv), K_2CO_3 (0.21 g, 1.525 mmol, 3 equiv) were introduced under argon. The mixture was heated at 100 °C for 1 h under microwave irradiation. After cooling, 80 mL of water were added and the solution was extracted with dichloromethane (3 x 60 mL). The organic layer was washed with water (3 x 100 mL), dried over Na_2SO_4 and evaporated. The crude product was purified by column chromatography [silica gel, petroleum ether/ethyl acetate (5%), (10% for **9g**), (30% for **9h**)] and recrystallized from propan-2-ol.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-phenylquinazolin-4-amine (9a):** Yield 86% (214 mg); yellow solid; Mp 170 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.50 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.85 (q, $^3J_{H\text{-}H}$ = 7.2 Hz, 4 H, 2 CH_2), 3.89 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 7.05 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.10 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.40-7.49 (m, 3 H, 3 Ar-H), 7.64 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.86 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.99 (d, $^4J_{H\text{-}H}$ = 1.7 Hz, 1 H, Ar-H), 8.05 (d, $^4J_{H\text{-}H}$ = 1.8 Hz, 1 H, Ar-H), 8.51-8.53 (m, 2 H, 2 Ar-H) ppm. NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.3 (2 CH_2), 55.3 (OCH_3), 55,4 (OCH_3), 113.3 (2 CH_{Ar}), 114.5 (2 CH_{Ar}), 116.0 (C_{Ar}), 121.0 (CH_{Ar}), 128.1 (2 CH_{Ar}), 128.2 (2 CH_{Ar}), 128.4 (2 CH_{Ar}), 129.8 (CH_{Ar}), 131.4 (CH_{Ar}), 131.7 (C_{Ar}), 132.0 (2 CH_{Ar}), 133.2 (C_{Ar}), 136.0 (C_{Ar}), 138.8 (C_{Ar}) 138.9 (C_{Ar}), 139.6 (C_{Ar}), 157.8 (C_{Ar}), 159.1 (C_{Ar}), 159.3 (C_{Ar}), 164.0 (C_{Ar}) ppm. $C_{32}H_{31}N_3O_2$ (489.91): calcd. C 78.50, H 6.38, N 8.58; found C 78.25, H 6.37, N 8.69.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-*p*-tolylquinazolin-4-amine (9b):** Yield 90% (230 mg); yellow solid; Mp 167 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.49 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 6 H, 2 CH_3), 2.41 (s, 3 H, CH_3), 3.85 (q, $^3J_{H\text{-}H}$ = 7.2 Hz, 4 H, 2 CH_2), 3.88 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 7.05 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 2 H, 2 Ar-H), 7.09 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 2 H, 2 Ar-H), 7.25 (d, $^3J_{H\text{-}H}$ = 8.0 Hz, 2 H, 2 Ar-H), 7.64 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.85 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.97 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H), 8.03 (d, $^4J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H), 8.39 (d, $^3J_{H\text{-}H}$ = 8.0 Hz, 2 H, 2 Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.2 (2 CH_3), 21.5 (CH_3), 45.4 (2 CH_2), 55.3 (OCH_3), 55.4 (OCH_3), 113.3 (2 CH_{Ar}), 114.5 (2 CH_{Ar}), 115.9 (C_{Ar}), 121.0 (CH_{Ar}), 128.1 (2 CH_{Ar}), 128.4 (2 CH_{Ar}), 129.0 (2 CH_{Ar}), 131.5 (CH_{Ar}), 131.5 (C_{Ar}), 132.0 (2 CH_{Ar}), 133.2 (C_{Ar}), 136.0 (C_{Ar}), 139.3 (C_{Ar}), 140.1 (C_{Ar}), 140.2 (C_{Ar}), 157.7 (C_{Ar}), 157.9 (C_{Ar}), 159.1 (C_{Ar}), 159.3 (C_{Ar}), 163.9 (C_{Ar}) ppm. $C_{33}H_{33}N_3O_2$ (503.63): calcd. C 78.70, H 6.60, N 8.34; found C 79.02, H 6.71, N 8.66.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-*o*-tolylquinazolin-4-amine (9c):** Yield 66% (169 mg); yellow solid; Mp 151 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.46 (t, $^3J_{H\text{-}H}$ = 6.9 Hz, 6 H, 2 CH_3), 2.62 (s, 3 H, CH_3), 3.83 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 4 H, 2 CH_2), 3.89 (s, 6 H, 2 OCH_3), 7.03 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.05 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.20-7.30 (m, 3 H, 3 Ar-H), 7.66 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.75 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.98 (d, $^3J_{H\text{-}H}$ = 2.0 Hz, 1 H, Ar-H), 8.04-8.10 (m, 2 H, 2 Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.4 (2 CH_3), 22.2 (CH_3), 45.5 (2 CH_2), 55.3 (OCH_3), 55,4 (OCH_3), 113.5 (2 CH_{Ar}), 114.6 (2 CH_{Ar}), 115.2 (C_{Ar}), 121.1 (CH_{Ar}), 125.6 (CH_{Ar}), 128.1 (2 CH_{Ar}), 129.0 (CH_{Ar}), 130.9 (CH_{Ar}), 131.3 (CH_{Ar}), 131.8 (3 CH_{Ar}), 133.0 (C_{Ar}), 136.5 (C_{Ar}), 137.9 (2 C_{Ar}), 138.3 (C_{Ar}), 139.3 (C_{Ar}), 159.2 (C_{Ar}), 159.5 (2 C_{Ar}), 160.5 (C_{Ar}), 163.8 (C_{Ar}) ppm. $C_{33}H_{33}N_3O_2$ (503.63): calcd. C 78.70, H 6.60, N 8.34; found C 78.44, H 6.60, N 8.25.

***N*,*N*-Diethyl-2-(4-fluerophenyl)-6,8-bis(4-methoxyphenyl)-quinazolin-4-amine (9d):** Yield 85% (219 mg); yellow solid; Mp 128 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.49 (t, $^3J_{H\text{-}H}$ = 6.9 Hz, 6 H, 2 CH_3), 3.85 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 4 H, 2 CH_2), 3.89 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 7.05 (d, $^3J_{H\text{-}H}$ = 9.5 Hz, 2 H, 2 Ar-H), 7.10 (d, $^3J_{H\text{-}H}$ = 9.3 Hz, 2 H, 2 Ar-H), 7.15 (d, $^3J_{H\text{-}H}$ = 9.2 Hz, 2 H, 2 Ar-H), 7.64 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.83 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.98 (d, $^4J_{H\text{-}H}$ = 1.8 Hz, 1 H, Ar-H), 8.03 (d, $^4J_{H\text{-}H}$ = 1.8 Hz, 1 H, Ar-H), 8.46-8.53 (m, 2 H, 2 Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.3 (2 CH_2), 55.3 (OCH_3), 55,4 (OCH_3), 113.3 (2 CH_{Ar}), 114.5 (2 CH_{Ar}), 115.0 (d, $^3J_{C\text{-}F}$ = 21.2 Hz, 2 CH_{Ar}), 115.9 (C_{Ar}), 121.0 (CH_{Ar}), 128.1 (2 CH_{Ar}), 130.3 (d, $^4J_{C\text{-}F}$ = 8.4 Hz, 2 CH_{Ar}), 131.5 (C_{Ar}), 131.7 (CH_{Ar}), 132.0 (2 CH_{Ar}), 133.1 (C_{Ar}), 135.1 (C_{Ar}), 136.0 (C_{Ar}), 139.6 (C_{Ar}), 149.0 (d, $^5J_{C\text{-}F}$ = 4.0 Hz, C_{Ar}), 157.0 (C_{Ar}), 159.1 (C_{Ar}), 159.4 (C_{Ar}), 163.9 (C_{Ar}), 164.2 (d, $^2J_{C\text{-}F}$ = 248.5 Hz, C_{Ar}) ppm. $C_{32}H_{30}FN_3O_2$ (507.60): calcd. C 75.72, H 5.96, N 8.28; found C 75.86, H 5.71, N 8.33.

2-(4-Chlorophenyl)-*N*,*N*-diethyl-6,8-bis(4-methoxyphenyl)quinazolin-4-amine (9e): Yield 71% (190 mg); yellow solid; Mp 158 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.49 (t, $^3J_{H\text{-}H}$ = 6.9 Hz, 6 H, 2 CH_3), 3.84 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 4 H, 2 CH_2), 3.88 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 7.04 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.09 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.40 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 2 H, 2 Ar-H), 7.63 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.82 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.98 (d, $^3J_{H\text{-}H}$ = 1.8 Hz, 1 H, Ar-H), 8.03 (d, $^3J_{H\text{-}H}$ = 1.8 Hz, 1 H, Ar-H), 8.43 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 2 H, 2 Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.4 (2 CH_2), 55.3 (OCH_3), 55,4 (OCH_3), 113.3 (2 CH_{Ar}), 114.5 (2 CH_{Ar}), 116.0 (C_{Ar}), 121.0 (CH_{Ar}), 128.1 (2 CH_{Ar}), 128.3 (2 CH_{Ar}), 129.7 (2 CH_{Ar}), 131.5 (CH_{Ar}), 131.6 (C_{Ar}), 132.0 (2 CH_{Ar}), 133.1 (C_{Ar}), 135.9 (C_{Ar}), 136.3 (C_{Ar}), 137.4 (C_{Ar}), 137.5 (C_{Ar}), 139.6 (C_{Ar}), 156.9 (C_{Ar}), 159.1 (C_{Ar}), 159.4 (C_{Ar}), 163.9 (C_{Ar}). $C_{32}H_{30}ClN_3O_2$ (524.05): calcd. C 73.34, H 5.77, N 8.02; found C 73.17, H 5.68, N 8.01.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-[4-(trifluoromethyl)-phenyl]quinazolin-4-amine (9f):** Yield 82% (232 mg); yellow solid; Mp 143 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.50 (t, $^3J_{H\text{-}H}$ = 6.9 Hz, 6 H, 2 CH_3), 3.87 (q, $^3J_{H\text{-}H}$ = 6.8 Hz, 4 H, 2 CH_2), 3.89 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 7.05 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 2 H, 2 Ar-H), 7.09 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 2 H, 2 Ar-H), 7.64 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 2 H, 2 Ar-H), 7.70 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 2 H, 2 Ar-H), 7.82 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 2 H, 2 Ar-H), 8.00 (d, $^4J_{H\text{-}H}$ = 1.8 Hz, 1 H, Ar-H), 8.05 (d, $^4J_{H\text{-}H}$ = 1.8 Hz, 1 H, Ar-H), 8.57 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, 2 H, 2 Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.5 (2 CH_2), 55.3 (OCH_3), 55.4 (OCH_3), 113.4 (2 CH_{Ar}), 114.6 (2 CH_{Ar}), 116.0 (C_{Ar}), 121.0 (CH_{Ar}), 124.3 (q, $^2J_{C\text{-}F}$ = 272.3 Hz, CF_3), 125.1 (q, $^4J_{C\text{-}F}$ = 4.0 Hz, 2 CH_{Ar}), 128.2 (2 CH_{Ar}), 128.7 (2 CH_{Ar}), 131.3 (q, $^3J_{C\text{-}F}$ = 31.8 Hz, C_{Ar}), 131.4 (C_{Ar}), 131.8 (CH_{Ar}), 132.0 (2 CH_{Ar}), 133.0 (C_{Ar}), 136.8 (C_{Ar}), 139.7 (C_{Ar}), 142.1 (C_{Ar}), 148.5 (C_{Ar}), 156.5 (C_{Ar}), 159.3 (C_{Ar}), 159.6 (C_{Ar}), 163.9 (C_{Ar}) ppm. HRMS: calcd. for $C_{33}H_{30}F_3N_3O_2$ [M + H+] 558.2363; found 558.2366.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)-quinazolin-4-amine (9g):** Yield 84% (247 mg); yellow solid; Mp 189 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.50 (t, $^{3}J_{H-H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.86 (q, $^{3}J_{H-H}$ = 7.0 Hz, 4 H, 2 CH_2), 3.88 (s, 6 H, 2 OCH_3), 3.91 (s, 3 H, OCH_3), 3.96 (s, 6 H, 2 OCH_3), 7.04 (d, $^{3}J_{H-H}$ = 8.7 Hz, 4 H, 4 Ar-H), 7.63 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.86 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.87 (s, 2 H, 2 Ar-H), 7.99 (d, $^{4}J_{H-H}$ = 1.8 Hz, 1 H, Ar-H), 8.03 (d, $^{4}J_{H-H}$ = 1.8 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.1 (2 CH_3), 45.4 (2 CH_2), 55.3 (OCH_3), 55,4 (OCH_3), 55,9 (2 OCH_3), 60.9 (OCH_3), 105.5 (CH_{Ar}), 113.1 (2 CH_{Ar}), 114.5 (3 CH_{Ar}), 115.7 (C_{Ar}), 121.0 (CH_{Ar}), 128.1 (3 CH_{Ar}), 131.4 (C_{Ar}), 131.5 (C_{Ar}), 132.1 (2 CH_{Ar}), 133.1 (C_{Ar}), 136.2 (C_{Ar}), 139.2 (C_{Ar}), 139.9 (C_{Ar}), 152.9 (3 C_{Ar}), 157.0 (C_{Ar}), 159.2 (C_{Ar}), 159.4 (C_{Ar}), 163.8 (C_{Ar}) ppm. $C_{35}H_{37}N_3O_5$ (579.69): calcd. C 72.52, H 6.43, N 7.25; found C 72.02, H 6.33, N 7.21.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-(pyridin-3-yl)-quinazolin-4-amine (9h):** Yield 71% (177 mg); yellow solid; Mp 204 °C. 1H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.49 (t, $^{3}J_{H-H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.86 (q, $^{3}J_{H-H}$ = 7.0 Hz, 4 H, 2 CH_2), 3.88 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 7.04 (d, $^{3}J_{H-H}$ = 8.9 Hz, 2 H, 2 Ar-H), 7.08 (d, $^{3}J_{H-H}$ = 8.9 Hz, 2 H, 2 Ar-H), 7.39-7.46 (m, 1 H, Ar-H), 7.63 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.79 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.99 (d, $^{4}J_{H-H}$ = 2.0 Hz, 1 H, Ar-H), 8.04 (d, $^{4}J_{H-H}$ = 2.0 Hz, 1 H, Ar-H), 8.63-8.65 (m, 1 H, Ar-H), 8.75-8.79 (m, 1 H, Ar-H), 9.68 (s, 1H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.3 (2 CH_2), 55.3 (OCH_3), 55,4 (OCH_3), 113.3 (2 CH_{Ar}), 114.6 (2 CH_{Ar}), 116.2 (C_{Ar}), 121.0 (CH_{Ar}), 123.5 (CH_{Ar}), 128.1 (2 CH_{Ar}), 131.6 (2 CH_{Ar}), 132.0 (2 CH_{Ar}), 133.0 (C_{Ar}), 135.3 (C_{Ar}), 136.6 (C_{Ar}), 136.7 (CH_{Ar}), 140.0 (C_{Ar}), 148.8 (C_{Ar}), 148.9 (CH_{Ar}), 149.2 (C_{Ar}), 155.6 (C_{Ar}), 159.1 (C_{Ar}), 159.5 (C_{Ar}), 163.8 (C_{Ar}) ppm. HRMS: calcd. for $C_{31}H_{30}N_4O_2$ [M + H+] 491.2442; found 491.2441.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-(5-methylthiophen-2-yl)-quinazolin-4-amine (9i):** Yield 69% (179 mg); yellow solid; Mp 139 °C. 1H NMR ($CDCl_3$, 200 MHz, 24 °C): δ =1.47 (t, $^{3}J_{H-H}$ = 6.9 Hz, 6 H, 2 CH_3), 2.53 (s, 3 H, CH_3), 3.80 (q, $^{3}J_{H-H}$ = 6.9 Hz, 4 H, 2 CH_2), 3.88 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 6.76 (d, $^{4}J_{H-H}$ = 2.9 Hz, 1 H, Ar-H), 7.03 (d, $^{3}J_{H-H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.07 (d, $^{3}J_{H-H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.60 (d, $^{3}J_{H-H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.74 (d, $^{3}J_{H-H}$ = 3.5 Hz, 1 H, Ar-H), 7.83 (d, $^{3}J_{H-H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.94 (d, $^{4}J_{H-H}$ = 1.8 Hz, 1 H, Ar-H), 7.98 (d, $^{4}J_{H-H}$ = 1.8 Hz, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.2 (2 CH_3), 15.9 (CH_3), 45.4 (2 CH_2), 55.3 (OCH_3), 55,4 (OCH_3), 113.3 (2 CH_{Ar}), 114.6 (2 CH_{Ar}), 115.7 (C_{Ar}), 121.0 (CH_{Ar}), 126.4 (CH_{Ar}), 128.0 (2 CH_{Ar}), 128.5 (CH_{Ar}), 128.6 (C_{Ar}), 131.4 (C_{Ar}), 131.7 (CH_{Ar}), 132.1 (2 CH_{Ar}), 133.2 (C_{Ar}), 135.7 (C_{Ar}), 138.8 (C_{Ar}), 142.4 (C_{Ar}), 144.2 (C_{Ar}), 154.9 (C_{Ar}), 159.2 (C_{Ar}), 159.4 (C_{Ar}), 163.7 (C_{Ar}) ppm. $C_{31}H_{31}N_3O_2S$ (509.66): calcd. C 73.05, H 6.13, N 8.24; found C 73.09, H 6.26, N 8.26.

***N*,*N*-Diethyl-6,8-bis(4-methoxyphenyl)-2-(naphtalen-2-yl)-quinazolin-4-amine (9j):** Yield 89% (244 mg); yellow solid; Mp 178 °C. ^{1}H NMR ($CDCl_3$, 200 MHz, 24 °C): δ = 1.53 (t, $^{3}J_{H-H}$ = 6.9 Hz, 6 H, 2 CH_3), 3.90 (q, $^{3}J_{H-H}$ = 7.0 Hz, 4 H, 2 CH_2), 3.89 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 7.05 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.14 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.46-7.52 (m, 2 H, 2 Ar-H), 7.66 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.85-7.99 (m, 5 H, 5 Ar-H), 8.01 (d, $^{4}J_{H-H}$ = 1.9 Hz, 1 H, Ar-H), 8.06 (d, $^{4}J_{H-H}$ = 1.9 Hz, 1 H, Ar-H), 8.63 (dd, $^{3}J_{H-H}$ = 8.6, $^{4}J_{H-H}$ = 1.3 Hz, 1 H, Ar-H), 9.04 (s, 1 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 24 °C): δ = 13.3 (2 CH_3), 45.4 (2 CH_2), 55.4 (2 OCH_3), 113.3 (2 CH_{Ar}), 114.5 (2 CH_{Ar}), 116.1 (C_{Ar}), 121.1 (CH_{Ar}), 125.7 (CH_{Ar}), 125.8 (CH_{Ar}), 126,5 (CH_{Ar}), 127.6 (CH_{Ar}), 127.8 (CH_{Ar}), 128.1 (2 CH_{Ar}), 128.4 (CH_{Ar}), 129.2 (CH_{Ar}), 131.5 (CH_{Ar}), 131.7 (C_{Ar}), 132.1 (2 CH_{Ar}), 133.2 (C_{Ar}), 133.3 (C_{Ar}), 134.4 (C_{Ar}), 136.1 (C_{Ar}), 136.4 (C_{Ar}), 139.6 (C_{Ar}), 148.9 (C_{Ar}), 157.8 (C_{Ar}), 159.2 (C_{Ar}), 159.4 (C_{Ar}), 164.0 (C_{Ar}) ppm. $C_{36}H_{33}N_3O_2$ (539.67): calcd. C 80.12, H 6.16, N 7.79; found C 79.36, H 6.12, N 7.70.

General procedure for the one-pot chemoselective S_NAr/bis-Suzuki-Miyaura coupling reaction: A solution of 6,8-dibromo-2-chloro-*N*,*N*-diethylquinazolin-4-amine **5b** (0.1 g, 0.25 mmol), 3-chloroaniline (0.05 mL, 0.51 mmol, 2 equiv) in EtOH (2.5 mL) was heated at 110 °C under microwave irradiation for 1 h. After cooling, boronic acid (0.56 mmol, 2.2 equiv), $PdCl_2(PPh_3)_2$ (9 mg, 0.013 mmol, 0.05 equiv), K_2CO_3 (0.21 g, 1.53 mmol, 6 equiv), TBAB (0.08 g, 1 equiv, 0.25 mmol) and water (2.5 mL) were added under argon. The mixture was heated at 100 °C for 1 h under microwave irradiation. After cooling, 80 mL of water were added and the solution was extracted with dichloromethane (3 x 60 mL). The organic layer was washed with water (3 x 100 mL), dried over Na_2SO_4 and evaporated. The crude product was purified by column chromatography [silica gel, petroleum ether/ethyl acetate (10%), (30% for **10e**), (50% for **10h**)] and recrystallized from propan-2-ol.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-bis(4-methoxyphenyl)-quinazoline-2,4-diamine (10a):** Yield 88% (120 mg); yellow solid; Mp 167 °C. 1H NMR ($CDCl_3$, 250 MHz, 24 °C): δ = 1.44 (t, $^{3}J_{H-H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.75 (q, $^{3}J_{H-H}$ = 7.0 Hz, 4 H, 2 CH_2), 3.88 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 6.88 (d, $^{3}J_{H-H}$ = 7.9 Hz, 1 H, Ar-H), 7.01-7.14 (m, 6 H, 6 Ar-H), 7.27 (d, $^{3}J_{H-H}$ = 7.9 Hz, 1 H, Ar-H), 7.60 (d, $^{3}J_{H-H}$ = 8.7 Hz, 2 H, 2 Ar-H), 7.71 (d, $^{3}J_{H-H}$ = 8.6 Hz, 2 H, 2 Ar-H), 7.86 (d, $^{4}J_{H-H}$ = 2.0 Hz, 1 H, Ar-H), 7.95 (d, $^{4}J_{H-H}$ = 2.0 Hz, 1 H, Ar-H), 8.03 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.3 (2 CH_2), 55.3 (OCH_3), 55.4 (OCH_3), 113.6 (2 CH_{Ar}), 114.1 (C_{Ar}), 114.5 (2 CH_{Ar}), 116.1 (CH_{Ar}), 117.9 (CH_{Ar}), 120.9 (CH_{Ar}), 121.5 (CH_{Ar}), 127.8 (2 CH_{Ar}), 129.3 (CH_{Ar}), 131.4 (2 CH_{Ar}), 131.7 (CH_{Ar}), 132.2 (C_{Ar}), 133.3 (C_{Ar}), 133.4 (C_{Ar}), 134.4 (C_{Ar}), 138.2 (C_{Ar}), 141.8 (C_{Ar}), 150.6 (C_{Ar}), 155.0 (C_{Ar}), 158.9 (C_{Ar}), 159.1 (C_{Ar}), 164.8 (C_{Ar}) ppm. $C_{32}H_{31}ClN_4O_2$ (536.07): calcd. C 71.30, H 5.80, N 10.39; found C 71.18, H 5.64, N 10.28.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-di*p*-tolylphenyl-quinazoline-2,4-diamine (10b):** Yield 85% (110 mg); yellow solid; Mp 149 °C. 1H NMR ([D_6]DMSO, 250 MHz, 24 °C): δ = 1.38 (t, $^{3}J_{H-H}$ = 6.6 Hz, 6 H, 2 CH_3), 2.35 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 3.73 (q, $^{3}J_{H-H}$ = 6.5 Hz, 4 H, 2 CH_2), 6.84 (d, $^{3}J_{H-H}$ = 7.1 Hz, 1 H, Ar-H), 7.12 (t, $^{3}J_{H-H}$ = 7.7 Hz, 1 H, Ar-H), 7.29 (d, $^{3}J_{H-H}$ = 7.9 Hz, 4 H, 4 Ar-H), 7.58 (d, $^{3}J_{H-H}$ = 7.9 Hz, 2 H, 2 Ar-H), 7.66 (d, $^{3}J_{H-H}$ = 8.1 Hz, 3 H, 3 Ar-H), 7.85 (s, 1 H, Ar-H), 7.96 (s, 1 H, Ar-H), 8.08 (s, 1 H, Ar-H), 9.23 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 20.8 (CH_3), 21.1 (CH_3), 44.9 (2 CH_2), 113.5 (C_{Ar}), 117.0 (CH_{Ar}), 117.5 (C_{Ar}), 120.2 (CH_{Ar}), 121.8 (CH_{Ar}), 126.6 (3 CH_{Ar}), 128.8 (CH_{Ar}), 129.7 (C_{Ar}), 129.9 (4 CH_{Ar}), 130.1 (2 CH_{Ar}), 131.3 (CH_{Ar}), 132.7 (C_{Ar}), 133.2 (C_{Ar}), 136.2 (C_{Ar}), 136.7 (C_{Ar}), 137.2 (C_{Ar}), 138.1 (C_{Ar}), 142.9 (C_{Ar}), 155.2 (C_{Ar}), 163.9 (C_{Ar}) ppm. $C_{32}H_{31}ClN_4$ (507.07): calcd. C 75.80, H 6.16, N 11.05; found C 75.93, H 6.14, N 10.86.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-diphenylquinazoline-2,4-diamine (10c):** Yield 83% (101 mg); yellow solid; Mp 153 °C. 1H NMR ([D_6]DMSO, 250 MHz, 24 °C): δ = 1.40 (bs, 6 H, 2 CH_3), 3.75-3.77 (bs, 4 H, 2 CH_2), 6.84 (d, $^{3}J_{H-H}$ = 7.4 Hz, 1 H, Ar-H), 7.11 (t, $^{3}J_{H-H}$ = 7.4 Hz, 1 H, Ar-H), 7.38-7.50 (m, 6 H, 6 Ar-H), 7.64-7.78 (m, 5 H, 5 Ar-H), 7.91 (s, 1 H, Ar-H), 8.03 (s, 2 H, 2 Ar-H), 9.26 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.0 (2 CH_2), 113.5 (C_{Ar}), 117.0 (CH_{Ar}), 117.6 (CH_{Ar}), 120.2 (CH_{Ar}), 122.4 (CH_{Ar}), 126.8 (2 CH_{Ar}), 127.1 (CH_{Ar}), 127.4 (CH_{Ar}), 128.2 (2 CH_{Ar}), 129.3 (2 CH_{Ar}), 129.7 (CH_{Ar}), 130.3 (2 CH_{Ar}), 131.8 (CH_{Ar}), 132.7 (C_{Ar}), 133.1 (C_{Ar}), 138.1 (C_{Ar}), 139.8 (C_{Ar}), 140.0 (C_{Ar}), 142.9 (C_{Ar}), 150.6 (C_{Ar}), 155.4 (C_{Ar}), 163.9 (C_{Ar}) ppm. $C_{30}H_{27}ClN_4$ (479.02): calcd. C 75.22, H 5.68, N 11.70; found C 75.19, H 5.59, N 11.34.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-bis(4-fluorophenyl)-quinazoline-2,4-diamine (10d):** Yield 92% (120 mg); yellow solid; Mp 157 °C. 1H NMR ([D_6]DMSO, 250 MHz, 24 °C): δ = 1.38 (t, $^{3}J_{H-H}$ = 6.8 Hz, 6 H, 2 CH_3), 3.75 (q, $^{3}J_{H-H}$ = 6.8 Hz, 4 H, 2 CH_2), 6.86 (d,

$^3J_{H-H}$ = 7.9 Hz, 1 H, Ar-H), 7.13 (t, $^3J_{H-H}$ = 8.2 Hz, 1 H, Ar-H), 7.26-7.35 (m, 4 H, 4 Ar-H), 7.55 (d, $^3J_{H-H}$ = 8.2 Hz, 1 H, Ar-H), 7.73 (d, $^3J_{H-H}$ = 8.5 Hz, 1 H, Ar-H), 7.76 (d, $^3J_{H-H}$ = 8.7 Hz, 1 H, Ar-H), 7.81 (d, $^3J_{H-H}$ = 8.7 Hz, 1 H, Ar-H), 7.83 (d, $^3J_{H-H}$ = 8.5 Hz, 1 H, Ar-H), 7.88 (d, $^4J_{H-H}$ = 1.7 Hz, 1 H, Ar-H), 7.98 (d, $^4J_{H-H}$ = 1.7 Hz, 1 H, Ar-H), 8.08 (s, 1 H, Ar-H), 9.28 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 44.9 (2 CH_2), 113.5 (C_{Ar}), 115.0 (d, $^3J_{C-F}$ = 21.1 Hz, 2 CH_{Ar}), 116.1 (d, $^3J_{C-F}$ = 21.1 Hz, 2 CH_{Ar}), 117.0 (CH_{Ar}), 117.5 (CH_{Ar}), 120.3 (CH_{Ar}), 122.5 (CH_{Ar}), 128.8 (d, $^4J_{C-F}$ = 8.3 Hz, 2 CH_{Ar}), 129.7 (CH_{Ar}), 131.6 (C_{Ar}), 131.7 (CH_{Ar}), 132.1 (d, $^4J_{C-F}$ = 8.3 Hz, 2 CH_{Ar}), 133.1 (C_{Ar}), 136.0 (d, $^5J_{C-F}$ = 3.2 Hz, C_{Ar}), 136.5 (d, $^5J_{C-F}$ = 3.2 Hz, C_{Ar}), 137.0 (C_{Ar}), 142.8 (C_{Ar}), 150.5 (C_{Ar}), 155.37 (C_{Ar}), 161.8 (d, $^2J_{C-F}$ = 243.6 Hz, C_{Ar}), 162.0 (d, $^2J_{C-F}$ = 244.5 Hz, C_{Ar}), 163.5 (C_{Ar}) ppm. $C_{30}H_{25}ClF_2N_4$ (515.00): calcd. C 69.97, H 4.89, N 10.88; found C 69.98, H 4.49, N 10.58.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-bis(3,4,5-trimethoxyphenyl)quinazoline-2,4-diamine (10e):** Yield 89% (149 mg); yellow solid; Mp 198 °C. 1H NMR ([D$_6$]DMSO, 250 MHz, 24 °C): δ = 1.43 (t, $^3J_{H-H}$ = 6.8 Hz, 6 H, 2 CH_3), 3.71 (s, 3 H, OCH_3), 3.73 (q, $^3J_{H-H}$ = 6.5 Hz, 4 H, 2 CH_2), 3.75 (s, 3 H, OCH_3), 3.78 (s, 6 H, 2 OCH_3), 3.89 (s, 6 H, 2 OCH_3), 6.86 (d, $^3J_{H-H}$ = 7.9 Hz, 1 H, Ar-H), 6.99 (s, 2 H, 2 Ar-H), 7.02 (s, 2 H, 2 Ar-H), 7.10 (t, $^3J_{H-H}$ = 8.2 Hz, 1 H, Ar-H), 7.72 (d, $^3J_{H-H}$ = 8.4 Hz, 1 H, Ar-H), 7.99 (s, 1 H, Ar-H), 8.00 (s, 1 H, Ar-H), 8.16 (s, 1 H, Ar-H), 9.29 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 44.9 (2 CH_2), 55.9 (2 OCH_3), 56.2 (2 OCH_3), 60.1 (OCH_3), 60.3 (OCH_3), 104.3 (2 CH_{Ar}), 107.8 (2 CH_{Ar}), 113.3 (C_{Ar}), 116.8 (CH_{Ar}), 117.6 (CH_{Ar}), 120.1 (CH_{Ar}), 122.3 (CH_{Ar}), 129.6 (CH_{Ar}), 131.8 (CH_{Ar}), 132.8 (C_{Ar}), 133.2 (C_{Ar}), 135.5 (C_{Ar}), 135.9 (C_{Ar}), 136.8 (C_{Ar}), 137.2 (C_{Ar}), 138.1 (C_{Ar}), 142.9 (C_{Ar}), 150.4 (C_{Ar}), 152.6 (2 C_{Ar}), 153.6 (2 C_{Ar}), 155.3 (C_{Ar}), 163.9 (C_{Ar}) ppm. $C_{36}H_{39}ClN_4O_6$ (659.17): calcd. C 65.60, H 5.96, N 8.50; found C 65.71, H 5.85, N 8.34.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-bis[4-(trifluoromethyl)-phenyl]quinazoline-2,4-diamine (10f):** Yield 83% (130 mg); yellow solid; Mp 161 °C. 1H NMR ([D$_6$]DMSO, 250 MHz, 24 °C): δ = 1.39 (t, $^3J_{H-H}$ = 6.5 Hz, 6 H, 2 CH_3), 3.76 (d, $^3J_{H-H}$ = 6.8 Hz, 4 H, 2 CH_2), 6.84 (d, $^3J_{H-H}$ = 8.1 Hz, 1 H, Ar-H), 7.10 (t, $^3J_{H-H}$ = 7.9 Hz, 1 H, Ar-H), 7.46 (d, $^3J_{H-H}$ = 7.7 Hz, 1 H, Ar-H), 7.82 (d, $^3J_{H-H}$ = 8.7 Hz, 4 H, 4 Ar-H), 7.93 (d, $^3J_{H-H}$ = 8.4 Hz, 2 H, 2 Ar-H), 8.00 (d, $^3J_{H-H}$ = 7.5 Hz, 3 H, 3 Ar-H), 8.11 (s, 2 H, 2 Ar-H), 9.36 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.0 (2 CH_2), 113.5 (C_{Ar}), 117.0 (CH_{Ar}), 117.6 (CH_{Ar}), 120.5 (CH_{Ar}), 124.0 (CH_{Ar}), 124.6 (q, $^2J_{C-F}$ = 272.1 Hz, CF_3), 124.8 (q, $^2J_{C-F}$ = 272.1 Hz, CF_3), 125.1 (q, $^4J_{C-F}$ = 3.2 Hz, 2 CH_{Ar}), 126.1 (q, $^4J_{C-F}$ = 3.2 Hz, 2 CH_{Ar}), 127.6 (2 CH_{Ar}), 128.7 (q, $^3J_{C-F}$ = 30.1 Hz, C_{Ar}), 128.8 (q, $^3J_{C-F}$ = 32.7 Hz, C_{Ar}), 129.7 (CH_{Ar}), 130.9 (C_{Ar}), 131.0 (2 CH_{Ar}), 131.8 (C_{Ar}), 131.9 (CH_{Ar}), 133.2 (C_{Ar}), 136.7 (C_{Ar}), 142.6 (C_{Ar}), 143.9 (C_{Ar}), 151.1 (C_{Ar}), 155.8 (C_{Ar}), 163.5 (C_{Ar}) ppm. $C_{32}H_{25}ClF_6N_4$ (615.01): calcd. C 62.49, H 4.10, N 9.11; found C 62.33, H 3.93, N 8.91.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-bis(3-nitrophenyl)-quinazoline-2,4-diamine (10g):** Yield 90% (130 mg); yellow solid; Mp 192 °C. 1H NMR ([D$_6$]DMSO, 250 MHz, 24 °C): δ = 1.41 (t, $^3J_{H-H}$ = 6.3 Hz, 6 H, 2 CH_3), 3.77 (q, $^3J_{H-H}$ = 6.7 Hz, 4 H, 2 CH_2), 6.82 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, Ar-H), 7.08 (t, $^3J_{H-H}$ = 7.9 Hz, 1 H, Ar-H), 7.46 (d, $^3J_{H-H}$ = 8.1 Hz, 1 H, Ar-H), 7.73-7.83 (m, 2 H, 2 Ar-H), 8.05 (s, 1 H, Ar-H), 8.12 (s, 2 H, 2 Ar-H), 8.19 (d, $^3J_{H-H}$ = 7.7 Hz, 2 H, 2 Ar-H), 8.28 (t, $^3J_{H-H}$ = 7.7 Hz, 2 H, 2 Ar-H), 8.56 (s, 1 H, Ar-H), 8.63 (s, 1 H, Ar-H), 9.38 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.5 MHz, 24 °C): δ = 13.1 (2 CH_3), 45.0 (2 CH_2), 113.5 (C_{Ar}), 117.1 (CH_{Ar}), 117.5 (CH_{Ar}), 120.5 (CH_{Ar}), 121.2 (CH_{Ar}), 122.1 (CH_{Ar}), 122.2 (CH_{Ar}), 124.2 (CH_{Ar}), 125.4 (CH_{Ar}), 129.6 (CH_{Ar}), 129.9 (CH_{Ar}), 130.1 (C_{Ar}), 130.7 (CH_{Ar}), 131.8 (CH_{Ar}), 133.1 (C_{Ar}), 133.3 (CH_{Ar}), 135.5 (C_{Ar}), 136.9 (CH_{Ar}), 141.0 (C_{Ar}), 141.3 (C_{Ar}), 142.5 (C_{Ar}), 147.7 (C_{Ar}), 148.7 (C_{Ar}), 151.0 (C_{Ar}), 155.8 (C_{Ar}), 163.5 (C_{Ar}) ppm. $C_{30}H_{25}ClN_6O_4$ (569.01): calcd. C 63.32, H 4.43, N 14.77; found C 62.79, H 4.29, N 14.34.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-di(pyridin-3-yl)-quinazoline-2,4-diamine (10h):** Yield 83% (101 mg); yellow solid; Mp 183 °C. 1H NMR ([D$_6$]DMSO, 250 MHz, 24 °C): δ = 1.40 (t, $^3J_{H-H}$ = 7.0 Hz, 6 H, 2 CH_3), 3.78 (q, $^3J_{H-H}$ = 7.1 Hz, 4 H, 2 CH_2), 6.86 (dd, $^3J_{H-H}$ = 7.7, $^4J_{H-H}$ = 1.1 Hz, 1 H, Ar-H), 7.13 (t, $^3J_{H-H}$ = 8.1 Hz, 1 H, Ar-H), 7.50-7.60 (m, 3 H, 3 Ar-H), 7.98 (s, 1 H, Ar-H), 8.08 (dd, $^3J_{H-H}$ = 9.3, $^4J_{H-H}$ = 1.7 Hz, 2 H, 2 Ar-H), 8.16-8.24 (m, 2 H, 2 Ar-H), 8.58-8.62 (m, 2 H, 2 Ar-H), 8.90 (s, 1 H, Ar-H), 9.04 (s, 1 H, Ar-H), 9.33 (s, 1 H, NH) ppm. ^{13}C NMR (DMSO-d_6, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 45.0 (2 CH_2), 113.4 (C_{Ar}), 117.1 (C_{Ar}), 117.7 (C_{Ar}), 120.4 (C_{Ar}), 123.2 (CH_{Ar}),123.6 (CH_{Ar}), 124.2 (CH_{Ar}), 129.5 (CH_{Ar}), 129.8 (CH_{Ar}), 131.8 (CH_{Ar}), 133.1 (C_{Ar}), 134.3 (CH_{Ar}), 134.8 (C_{Ar}), 135.2 (C_{Ar}), 135.4 (CH_{Ar}), 137.8 (CH_{Ar}), 142.7 (CH_{Ar}), 147.9 (CH_{Ar}), 148.2 (CH_{Ar}), 148.5 (CH_{Ar}), 150.5 (C_{Ar}), 151.1 (CH_{Ar}), 155.7 (C_{Ar}), 163.5 (C_{Ar}) ppm. $C_{28}H_{25}ClN_6$ (480.99): calcd. C 69.92, H 5.24, N 17.47; found C 69.60, H 5.16, N 17.20.

***N*^{2}-(3-Chlorophenyl)-*N*^{4},*N*^{4}-diethyl-6,8-bis(5-methylthiophen-2-yl)-quinazoline-2,4-diamine (10i):** Yield 69% (91 mg); yellow solid; Mp 168 °C. 1H NMR ([D$_6$]DMSO, 250 MHz, 24 °C): δ = 1.40 (t, $^3J_{H-H}$ = 6.8 Hz, 6 H, 2 CH_3), 2.48 (s, 3 H, CH_3), 2.49 (s, 3 H, CH_3), 3.69 (q, $^3J_{H-H}$ = 7.0 Hz, 4 H, 2 CH_2), 6.84-6.86 (m, 2 H, 2 Ar-H), 6.95 (dd, $^3J_{H-H}$ = 7.9, $^4J_{H-H}$ = 1.3 Hz, 1 H, Ar-H), 7.25 (t, $^3J_{H-H}$ = 8.1 Hz, 1 H, Ar-H), 7.39 (d, $^3J_{H-H}$ = 3.5 Hz, 1 H, Ar-H), 7.57 (d, $^3J_{H-H}$ = 8.2 Hz, 1 H, Ar-H), 7.63 (d, $^3J_{H-H}$ = 3.5 Hz, 1 H, Ar-H), 7.79 (d, $^4J_{H-H}$ = 1.5 Hz, 1 H, Ar-H), 8.12 (d, $^4J_{H-H}$ = 1.5 Hz, 1 H, Ar-H), 8.35 (s, 1 H, Ar-H), 9.30 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 62.5 MHz, 24 °C): δ = 13.2 (2 CH_3), 15.2 (CH_3), 15.3 (CH_3), 45.0 (2 CH_2), 113.3 (C_{Ar}), 117.7 (CH_{Ar}), 118.6 (CH_{Ar}), 119.8 (CH_{Ar}), 120.7 (CH_{Ar}), 123.7 (CH_{Ar}), 125.3 (CH_{Ar}), 126.6 (CH_{Ar}), 126.7 (C_{Ar}), 127.2 (CH_{Ar}), 127.3 (CH_{Ar}), 129.9 (CH_{Ar}), 130.4 (C_{Ar}), 133.2 (C_{Ar}), 137.0 (C_{Ar}), 139.1 (C_{Ar}), 140.8 (C_{Ar}), 141.3 (C_{Ar}), 142.4 (C_{Ar}), 149.1 (C_{Ar}), 155.2 (C_{Ar}), 163.6 (C_{Ar}) ppm. HRMS: calcd. for $C_{28}H_{27}ClN_4S_2$ [M + H+] 519.1438; found 519.1437.

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