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One-pot chemoselective synthesis of 2,4,6,8-tetrasubstituted quinazolines *via* microwave-assisted consecutive bis-S_NAr/bis-Suzuki-Miyaura cross-coupling reactions

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Abstract: A practical and efficient synthesis of 2,4,6,8-tetrasubstituted quinazolines through one-pot chemoselective sequential bis-S_NAr/bis-Suzuki-Miyaura reactions under microwave irradiation is presented. The bis-S_NAr occurs selectively at C-2 and C-4 positions of 6,8-dibromo-2,4-dichloroquinazoline **4** and the bis-Suzuki-Miyaura cross-coupling at C-6 and C-8 positions of **4**. This procedure affords convergent synthesis of polysubstituted quinazoline derivatives in high yields in a very few steps and tolerates a wide range of boronic acids and amines.

Key words: quinazoline, Suzuki-Miyaura, chemoselectivity, microwave irradiation, palladium.

The palladium catalyzed Suzuki-Miyaura reaction is one of the most highly regarded processes in synthetic chemistry and a widely studied cross-coupling reaction for carbon-carbon bond formation.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 The recent development of multistep sequences in a single flask, such as tandem, cascade or sequential reactions is making this reaction a hot topic in organic chemistry.³ In this context and in connection with our research program on the design and synthesis of original molecules with pharmacological properties,⁴ the S_NAr reaction was combined with the Suzuki-Miyaura cross-coupling reaction to perform one-pot sequential polyfunctionalization of the quinazoline ring.

Quinazoline and its derivatives are important compounds widely found in natural products and synthetic pharmaceuticals. They are valued for their biological and physiological activities, such as antibacterial,⁵ antiviral,⁶ antitubercular⁷ and anticancer⁸ activities. Several procedures for S_NAr⁹ and palladium-catalyzed¹⁰ functionalization of 4-chloroquinazoline have been reported, but the polyhalogenated quinazoline series has to date been little explored.¹¹ Herein, we report an efficient procedure for the sequential polyfunctionalization of 6,8-dibromo-2,4-dichloroquinazoline **4** through a one-pot chemoselective sequential bis-S_NAr/bis-Suzuki-Miyaura cross-coupling reactions.

6,8-Dibromo-2,4-dichloroquinazoline **4** was obtained in four steps using 2-aminobenzonitrile as starting

material in 30% overall yield 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, led 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%) due to the use of urea and cesium carbonate in DMF. In the last step, the intermediate **3** was chlorinated in presence of phosphorus oxychloride and diisopropylethylamine, which leading to our key substrate **4** in 63% yield.

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

When 3-chloroaniline (4 equiv) was added to **4** in DME/EtOH (9/1) under microwave irradiation at 100 °C (Scheme 2), the corresponding chemoselective substitution product **5** was isolated in high yield (96%) and the structure confirmed by HRMS analysis. This result indicated the high reactivity of C-2-Cl and C-4-Cl bonds toward S_NAr and no reactivity was observed with C-6-Br and C-8-Br bonds with a complete conversion into **5** occurred for a short time (1 h). However, when the reaction was performed at 80 °C, a mixture of the mono and disubstituted quinazoline derivatives was observed. The DME/EtOH mixture was chosen as solvent for the subsequent one-pot chemoselective bis-S_NAr and bis-Suzuki-Miyaura reactions. In previous studies, we showed the DME/EtOH mixture to be very useful for Suzuki-Miyaura cross-coupling reactions.¹²

Scheme 2 Bis- S_NAr chemoselective reaction of 3-chloroaniline on **4** at C-2 and C-4 positions

The versatility of one-pot chemoselective synthesis of 2,4,6,8-tetrasubstituted quinazoline was then assessed. One-pot multistep processes are economically advantageous in terms of the outlay for catalyst, solvent, purification materials and time. Having established the protocol to produce the bis- S_NAr adduct at C-2 and C-4 positions of **4**, we focused our attention on the one-pot chemoselective bis- S_NAr and bis-Suzuki-Miyaura reactions of 6,8-dibromo-2,4-dichloroquinazoline **4**.

Scheme 3 One-pot chemoselective bis- S_NAr /bis-Suzuki-Miyaura reactions

The one-pot two-step bis- S_NAr /bis-Suzuki-Miyaura reactions of compound **4** were studied using 3-chloroaniline and 4-methoxyphenylboronic acid under microwave irradiation (Scheme 3). Here, we began by treating compound **4** with 3-chloroaniline (4 equiv), expected to react selectively at the C-2, 4 positions, in a mixture of DME/EtOH (9/1) for 1 h at 100 °C under MW irradiation. After cooling to room temperature, 4-methoxyphenylboronic acid (2.2 equiv), $PdCl_2(PPh_3)_2$ (0.05 equiv), K_2CO_3 (6 equiv) and H_2O (0.5 mL) were added and the reaction mixture was irradiated again for 1 h at 110 °C. These sequences afforded the desired polysubstituted quinazoline **6a** in an overall yield of 84% (entry 1, Table 1). In addition to compound **6a**, we observed by LC-MS analysis the presence of the product of a palladium-catalyzed reduction of aromatic halides, as previously observed in the literature.¹³ When the reaction was performed with $Pd(PPh_3)_4$ as catalyst, compound **6a** was obtained in somewhat lower yield (71%, entry 2). However, the desired compound **6a** was isolated in good yield when the temperature of the second step was decreased to 100 °C (entry 3, 90%). In these conditions, only traces of reduced product were observed. The use of DMF as solvent instead of DME,

gave a low yield of compound **6a** (79%, entry 5, Table 1) and the complete diamination reaction of the first step took longer to achieve (2 h).

Table 1 Optimization of step 2 of the one-pot chemoselective bis- S_NAr and bis-Suzuki-Miyaura reactions

Entry	Catalyst	Solvent	Temp (step 2)	Yield 6a
1	$PdCl_2(PPh_3)_2$ (5%)	DME/EtOH	110 °C	84%
2	$Pd(PPh_3)_4$ (5%)	DME/EtOH	110 °C	71%
3	$PdCl_2(PPh_3)_2$ (5%)	DME/EtOH	100 °C	90%
4	$Pd(PPh_3)_4$ (5%)	DME/EtOH	100 °C	76%
5	$PdCl_2(PPh_3)_2$ (5%)	DMF/EtOH	100 °C	79%

Once the optimized conditions were established, the scope of this one-pot bis- S_NAr /bis-Suzuki-Miyaura sequence was explored by using 3-chloroaniline for the first step and a wide variety of aryl or heteroarylboronic acids for the second step (Table 2).

Table 2 One-pot chemoselective reaction of **4** with 3-chloroaniline and various boronic acids

Entry	Boronic acid	Product	Yield (%)
1			90
2			94
3			89

Reaction conditions: Step 1; 3-chloroaniline (4 equiv), DME/EtOH (9/1), MW, 100 °C, 1 h. Step 2; boronic acids (2.2 equiv), PdCl₂(PPh₃)₂ (0.05 equiv), K₂CO₃ (6 equiv), H₂O, MW, 100 °C, 1 h.

Good to excellent yields of tetrasubstituted quinazolines **6a-k** were obtained with a wide range of arylboronic acids bearing electron-donating, electron-withdrawing and sterically bulky groups (entries 1-7, 10, 11, Table 2). The same good results were observed with heteroarylboronic acids (entries 8-9, Table 2).

Under the same microwave conditions, the scope of the one-pot reaction was investigated using various amines for the first step and 4-fluorophenylboronic acid for the second step (Table 3). Various aromatic and aliphatic amines were used for the preparation of a new series of compound **6** derivatives, including anilines, primary and secondary amines. The use of aniline derivatives with no steric hindrance gave in good to excellent yields of the corresponding products under the optimal conditions (Table 3, entries 1, 2 and 5). However, slightly low reactivity was observed with aniline derivatives with steric hindrance toward the bis-S_NAr under these experimental conditions. By increasing the reaction temperature of the first step from 100 °C (Table 3, entry 3, 4 and 6) to 110 °C and finally to 130 °C and increasing the reaction time to 2 h, complete conversion (bis-S_NAr/bis-Suzuki-Miyaura cross-coupling) of the compound **4** was achieved (as monitored by LC-MS) affording the desired products in good yields. With primary and secondary amines, the complete conversion of compound **4** into the bis-S_NAr adduct during the first step was achieved after 2 h at 130 °C. Then, after 1 h under the cross-coupling reaction conditions, the corresponding products **6r-t** were isolated in very good yields (entries 7-9, Table 3).

Table 3 One-pot chemoselective reaction of **4** with various amines and 4-fluorophenylboronic acid

Entry	Amine	Product	Yield (%)
1			71

In summary, we report here the synthesis of 6,8-dibromo-2,4-dichloroquinazoline **4** and its controlled chemoselectivity diversification through various

combinations of S_NAr and cross-coupling Suzuki-Miyaura reactions. This approach allows rapid and efficient access to 2,4,6,8-tetrasubstituted quinazoline derivatives with high yields using a one-pot chemoselective methodology *via* consecutive bis-S_NAr/bis-Suzuki-Miyaura reactions under microwave irradiation. In addition, this strategy tolerates a wide range of boronic acids and amines and could rapidly produce numerous and varied analogues of polysubstituted quinazoline derivatives potentially bioactive heterocyclic compounds.

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 MHz ¹H NMR (reference CDCl₃ δ = 7.26, DMSO-*d*₆ δ = 2.50) and 50 MHz ¹³C NMR spectra (reference CDCl₃ δ = 77.0, DMSO-*d*₆ δ = 39.7) were recorded on a Bruker ARX 200 spectrometer in CDCl₃ and DMSO-*d*₆ 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 QStar Elite (Applied Biosystems SCIEX) spectrometer. PEG was the 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 quadrupole. A Thermo Hypersil Gold® 50 x 2.1 mm chromatographic column was used (SiO₂ C18) with 1.9 μm diameter particles. The analysis is 8 min running, with a MeOH/H₂O gradient eluent from 50/50 to 95/05.

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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 **1** as brown solid; yield 77% (8.9 g); mp 158 °C (Lit.¹⁴ 156 °C).

¹H NMR (200 MHz, CDCl₃): δ = 4.91 (s, 2 H, NH₂), 7.47 (d, *J* = 2.1 Hz, 1 H, H-4), 7.71 (d, *J* = 2.1 Hz, 1 H, H-6).

¹³C NMR (50 MHz, CDCl₃): δ = 97.9, 108.2, 109.7, 115.6, 133.6, 139.4, 146.2.

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 **2** as yellow solid; yield 81% (6.58 g); mp 223 °C (Lit.¹⁵ 226-228 °C).

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.80 (s, 2 H, NH₂), 7.72 (d, *J* = 1.9 Hz, 1 H, H-4), 7.78 (d, *J* = 1.9 Hz, 1 H, H-6), 8.05 (s, 1 H, COOH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 105.1, 110.6, 117.0, 130.9, 136.8, 146.2, 169.4.

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 Cs₂CO₃ (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 **3** as brown solid; yield 76% (4.14 g); mp 289 °C (Lit.¹⁶ 291-292 °C).

¹H NMR (200 MHz, DMSO-*d*₆): δ = 7.84 (d, *J* = 2.2 Hz, 1 H, H-6), 7.94 (d, *J* = 2.2 Hz, 1 H, H-8), 10.76 (s, 2 H, 2 NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 110.4, 114.0, 118.0, 128.5, 138.8, 145.1, 153.4, 162.7.

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), POCl₃ (11.4 mL, 10 equiv), diisopropyl ethylamine (4.4 mL, 25.0 mmol, 2 equiv) was heated at reflux for 6 h. After this time, the reaction mixture was poured with care over crushed ice and stirred vigorously. This aqueous mixture was extracted with CH₂Cl₂, and the combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated under reduced pressure. Flash chromatography (silica gel, CH₂Cl₂/petroleum ether, 2/1) provided after recrystallization from propan-2-ol **4** as yellow solid; yield 63% (2.81 g); mp 145 °C (Lit.¹⁷ 148-149 °C).

¹H NMR (200 MHz, CDCl₃): δ = 8.37 (d, *J* = 2.0 Hz, 1 H, H-6), 8.39 (d, *J* = 2.0 Hz, 1 H, H-8).

¹³C NMR (50 MHz, CDCl₃): δ = 122.7, 124.1, 124.2, 127.7, 142.3, 149.0, 156.3, 163.3.

6,8-Dibromo-*N*²,*N*⁴-bis(3-chlorophenyl)-quinazoline-2,4-diamine (**5**)

A solution of 6,8-dibromo-2,4-dichloroquinazoline **4** (0.2 g, 0.56 mmol), 3-chloroaniline (0.24 mL, 2.24 mmol, 4 equiv) in a DME/EtOH mixture (9/1, 5 mL) was heated at 100 °C under microwave irradiation for 1 h. After cooling, 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 **5** as yellow solid; yield 96% (0.29 g); mp 222 °C.

¹H NMR (200 MHz, DMSO-*d*₆): δ = 7.01 (d, *J* = 6.3 Hz, 1 H), 7.19-7.34 (m, 2 H), 7.43 (t, *J* = 7.7 Hz, 1 H), 7.81 (d, *J* = 8.2 Hz, 1 H), 7.93 (s, 1 H), 8.02 (d, *J* = 8.2 Hz, 1 H), 8.23 (s, 1 H), 8.48 (s, 1 H), 8.75 (s, 1 H), 9.81 (s, 1 H, NH), 9.93 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 114.1, 114.4, 117.7, 118.9, 121.0, 121.3, 121.9, 124.0, 125.6, 130.1, 130.4, 133.1, 133.3, 138.5, 140.5, 142.0, 147.6, 156.1, 157.7.

HRMS (ESI): *m/z* [M+H]⁺ Calcd for C₂₀H₁₂Br₂Cl₂N₄: 538.8857; found: 538.8858.

General procedure of the one-pot chemoselective bis-S_NAr and bis-Suzuki-Miyaura reactions

Synthesis of compounds 6a-k

A solution of 6,8-dibromo-2,4-dichloroquinazoline **4** (0.1 g, 0.28 mmol), 3-chloroaniline (0.12 mL, 1.12 mmol, 4 equiv) in a DME/EtOH mixture (9/1, 5 mL) was heated at 100 °C under microwave irradiation for 1 h. After cooling, boronic acid (0.62 mmol, 2.2 equiv), PdCl₂(PPh₃)₂ (10 mg, 14 μmol, 0.05 equiv), K₂CO₃ (0.23 g, 1.68 mmol, 6 equiv) and water (0.5 mL) 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 Na₂SO₄ and evaporated. The crude product was purified by column chromatography (silica gel, petroleum ether/ethyl acetate (9/1), (8/2 for **6d**), ethyl acetate for **6i**)) and recrystallized from acetonitrile.

*N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-bis(4-methoxyphenyl)quinazoline-2,4-diamine (**6a**)

Yellow powder; yield 90% (0.15 g); mp 156 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 3.83 (s, 6 H, 2 OCH₃), 6.89-7.31 (m, 7 H), 7.45 (s, 1 H), 7.70-8.08 (m, 9 H), 8.61 (s, 1 H), 9.38 (s, 1 H, NH), 9.83 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 55.3 (OCH₃), 55.4 (OCH₃), 112.9, 113.7, 114.5, 117.2, 117.8, 118.9, 120.5, 120.7, 121.6, 123.3, 128.2, 129.8, 130.4, 131.4, 131.7, 132.0, 132.1, 133.1, 133.2, 134.0, 137.5, 141.3, 142.6, 148.3, 155.2, 158.7, 159.1.

HRMS (ESI): *m/z* [M+H]⁺ Calcd for C₃₄H₂₆Cl₂N₄O₂: 593.1506; found: 593.1506.

*N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-bis(4-fluorophenyl)quinazoline-2,4-diamine (**6b**)

Yellow powder; yield 94% (0.15 g); mp 178 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.89 (d, *J* = 8.4 Hz, 1 H), 7.12–7.22 (m, 2 H), 7.28–7.49 (m, 5 H), 7.62 (d, *J* = 8.4 Hz, 1 H), 7.74–7.81 (m, 2 H), 7.91–7.98 (m, 4 H), 8.06–8.13 (m, 2 H), 8.68 (s, 1 H), 9.44 (s, 1 H, NH), 9.86 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 112.8, 115.0 (d, *J* = 21.2 Hz), 115.9 (d, *J* = 21.6 Hz), 117.3, 117.9, 120.3, 120.7, 120.8, 121.7, 123.4, 129.1 (d, *J* = 8.1 Hz), 129.8, 130.4, 132.2 (d, *J* = 8.1 Hz), 132.4, 133.1, 133.2, 135.6 (d, *J* = 2.9 Hz), 136.1 (d, *J* = 2.9 Hz), 136.9, 141.1, 142.5, 148.7, 155.5, 158.7, 161.8 (d, *J* = 243.7 Hz), 162.1 (d, *J* = 244.4 Hz).

Anal. Calcd for C₃₂H₂₀Cl₂F₂N₄: C, 67.50; H, 3.54; N, 9.84. Found: C, 67.56; H, 3.21; N, 10.23.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-dip-tolyl-quinazoline-2,4-diamine (6c)**

Yellow powder; yield 89% (0.14 g); mp 177 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 2.37 (s, 3 H, CH₃), 2.40 (s, 3 H, CH₃), 6.88 (d, *J* = 7.9 Hz, 1 H), 7.10–7.22 (m, 2 H), 7.33 (d, *J* = 7.5 Hz, 4 H), 7.45 (t, *J* = 8.2 Hz, 1 H), 7.63 (d, *J* = 7.8 Hz, 2 H), 7.70 (s, 1 H), 7.80 (d, *J* = 7.8 Hz, 2 H), 7.95–7.98 (m, 2 H), 8.07–8.14 (m, 2 H), 8.67 (s, 1 H), 9.40 (s, 1 H, NH), 9.85 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 20.9 (CH₃), 21.1 (CH₃), 112.8, 117.2, 117.8, 119.5, 120.6, 120.8, 121.7, 123.3, 126.9, 128.9, 129.7, 130.1, 130.4, 132.1, 133.1, 133.2, 134.2, 136.3, 136.5, 136.8, 136.9, 137.9, 141.2, 142.6, 148.6, 155.3, 158.7.

Anal. Calcd for C₃₄H₂₆Cl₂N₄: C, 72.73; H, 4.67; N, 9.98. Found: C, 72.34; H, 4.64; N, 9.82.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-bis(3,4,5-trimethoxyphenyl)quinazoline-2,4-diamine (6d)**

Yellow powder; yield 91% (0.18 g); mp 269 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 3.73 (s, 3 H, OCH₃), 3.76 (s, 3 H, OCH₃), 3.79 (s, 6 H, 2 OCH₃), 3.93 (s, 6 H, 2 OCH₃), 6.89 (d, *J* = 2.6 Hz, 1 H), 7.01 (s, 2 H), 7.11 (s, 2 H), 7.16–7.22 (m, 2 H), 7.47 (t, *J* = 8.0 Hz, 1 H), 7.82 (d, *J* = 7.6 Hz, 1 H), 8.03 (d, *J* = 6.8 Hz, 2 H), 8.11–8.15 (m, 2 H), 8.62 (s, 1 H), 9.47 (s, 1 H, NH), 9.82 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 55.8 (2 OCH₃), 56.4 (2 OCH₃), 60.1 (OCH₃), 60.4 (OCH₃), 105.1, 107.8, 112.7, 117.0, 117.8, 120.4, 120.5, 120.8, 121.7, 123.4, 129.7, 130.5, 132.9, 133.1, 133.3, 134.7, 135.1, 135.8, 136.9, 137.5, 138.0, 141.2, 142.6, 148.6, 152.6, 153.5, 155.4, 158.7.

Anal. Calcd for C₃₈H₃₄Cl₂N₄O₆: C, 63.96; H, 4.80; N, 7.85. Found: C, 63.83; H, 4.82; N, 7.74.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-diphenyl-quinazoline-2,4-diamine (6e)**

Yellow powder; yield 81% (0.12 g); mp 168 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.88 (d, *J* = 7.0 Hz, 1 H), 7.11–7.22 (m, 2 H), 7.46–7.53 (m, 7 H), 7.74

(bs, 3 H), 7.90–8.14 (m, 6 H), 8.73 (s, 1 H), 9.43 (s, 1 H, NH), 9.89 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 112.9, 117.3, 117.9, 120.3, 120.6, 120.8, 121.7, 123.4, 127.1, 127.2, 127.6, 128.2, 129.1, 129.8, 130.4, 132.6, 133.1, 134.3, 137.9, 139.5, 139.7, 141.2, 142.5, 148.8, 155.5, 158.8.

Anal. Calcd for C₃₂H₂₂Cl₂N₄: C, 72.05; H, 4.16; N, 10.50. Found: C, 71.92; H, 4.13; N, 10.42.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-bis(4-chlorophenyl)-quinazoline-2,4-diamine (6f)**

Yellow powder; yield 77% (0.13 g); mp 261 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.90 (d, *J* = 7.0 Hz, 1 H), 7.11–7.22 (m, 2 H), 7.43 (d, *J* = 8.0 Hz, 1 H), 7.50–7.58 (m, 5 H), 7.74 (d, *J* = 8.1 Hz, 2 H), 7.91–7.97 (m, 4 H), 8.09 (s, 2 H), 8.71 (s, 1 H), 9.46 (s, 1 H, NH), 9.87 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 112.8, 117.3, 117.9, 120.6, 120.8, 121.7, 123.4, 128.3, 128.8, 129.0, 129.7, 130.4, 132.0, 132.2, 132.5, 132.7, 133.1, 133.2, 136.6, 138.1, 138.3, 141.1, 142.4, 148.8, 155.6, 158.6.

Anal. Calcd for C₃₂H₂₀Cl₄N₄: C, 63.81; H, 3.35; N, 9.30. Found: C, 63.35; H, 3.43; N, 9.09.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-di(naphthalen-2-yl)-quinazoline-2,4-diamine (6g)**

Yellow powder; yield 85% (0.15 g); mp 137 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.80 (d, *J* = 7.0 Hz, 1 H), 6.98 (t, *J* = 7.7 Hz, 1 H), 7.22 (d, *J* = 7.4 Hz, 1 H), 7.44–7.57 (m, 5 H), 7.74 (d, *J* = 7.4 Hz, 1 H), 7.96–8.02 (m, 8 H), 8.11–8.15 (m, 3 H), 8.26 (s, 1 H), 8.33 (s, 1 H), 8.49 (s, 1 H), 8.93 (s, 1 H), 9.47 (s, 1 H, NH), 9.99 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 113.0, 117.2, 117.9, 120.6, 120.7, 121.0, 121.9, 123.5, 125.5, 126.1, 126.2, 126.4, 126.7, 127.4, 127.7, 127.8, 128.4, 128.7, 128.8, 129.0, 129.7, 130.4, 132.4, 132.5, 133.0, 133.1, 133.3, 133.6, 134.1, 136.9, 137.4, 138.0, 141.2, 142.4, 149.2, 155.6, 158.8.

HRMS (ESI): *m/z* [M+H]⁺ Calcd for C₄₀H₂₆Cl₂N₄: 633.1607; found: 633.1606.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-bis(5-methylthiophen-2-yl)quinazoline-2,4-diamine (6h)**

Yellow powder; yield 76% (0.12 g); mp 147 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 2.50 (s, 6 H, 2 CH₃), 6.87 (s, 2 H), 6.97 (d, *J* = 8.6 Hz, 1 H), 7.18–7.28 (m, 2 H), 7.40–7.48 (m, 2 H), 7.59–7.63 (m, 2 H), 7.92 (s, 1 H), 8.00 (d, *J* = 8.2 Hz, 1 H), 8.10 (s, 1 H), 8.24 (s, 1 H), 8.45 (s, 1 H), 9.38 (s, 1 H, NH), 9.82 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 15.2 (CH₃), 15.3 (CH₃), 113.0, 117.7, 118.2, 119.2, 121.2, 121.3, 122.1, 123.6, 124.2, 125.4, 127.0, 128.3, 128.6, 129.9, 130.4, 133.1, 133.2, 136.7, 139.4, 140.5, 141.0, 141.4, 142.0, 147.3, 155.5, 158.7.

Anal. Calcd for C₃₀H₂₂Cl₂N₄S₂: C, 62.82; H, 3.87; N, 9.77. Found: C, 62.70; H, 3.79; N, 9.86.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-di(pyridin-3-yl)-quinazoline-2,4-diamine (6i)**

Yellow powder; yield 80% (0.12 g); mp 247 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.90 (d, *J* = 7.8 Hz, 1 H), 7.11-7.23 (m, 2 H), 7.42-7.58 (m, 3 H), 7.66 (d, *J* = 7.8 Hz, 1 H), 7.95 (d, *J* = 8.9 Hz, 2 H), 8.08-8.23 (m, 3 H), 8.34 (d, *J* = 7.2 Hz, 1 H), 8.63 (bs, 2 H), 8.84 (s, 1 H), 8.91 (s, 1 H), 9.19 (s, 1 H), 9.50 (s, 1 H, NH), 9.90 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 112.9, 117.5, 118.1, 120.9, 121.4, 121.8, 123.2, 123.6, 124.0, 129.9, 130.5, 131.0, 132.5, 133.2, 134.4, 134.7, 134.8, 134.9, 137.9, 141.0, 142.3, 148.1, 148.4, 148.7, 149.3, 150.4, 155.9, 158.7.

HRMS (ESI): *m/z* [M+H]⁺ Calcd for C₃₀H₂₀Cl₂N₆: 535.1199; found: 535.1202.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-bis(3-nitrophenyl)-quinazoline-2,4-diamine (6j)**

Yellow powder; yield 71% (0.12 g); mp 245 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.86 (d, *J* = 7.2 Hz, 1 H), 7.10 (t, *J* = 7.6 Hz, 1 H), 7.22 (d, *J* = 7.2 Hz, 1 H), 7.43-7.54 (m, 2 H), 7.82 (t, *J* = 7.2 Hz, 2 H), 7.96 (s, 1 H), 8.05-8.11 (m, 2 H), 8.22-8.42 (m, 5 H), 8.66 (s, 1 H), 8.74 (s, 1 H), 8.85 (s, 1 H), 9.54 (s, 1 H, NH), 9.96 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 113.0, 117.4, 117.8, 120.9, 121.1, 121.4, 122.0, 122.3, 122.4, 123.7, 125.4, 129.7, 129.9, 130.5, 130.6, 131.7, 132.8, 133.1, 133.7, 135.4, 137.0, 140.7, 140.9, 141.1, 142.2, 147.7, 148.8, 149.2, 156.1, 158.7.

Anal. Calcd for C₃₃H₂₀Cl₂N₆O₄: C, 61.65; H, 3.23; N, 13.48. Found: C, 61.14; H, 3.35; N, 13.39.

***N*²,*N*⁴-Bis(3-chlorophenyl)-6,8-bis[3-(trifluoromethyl)phenyl]quinazoline-2,4-diamine (6k)**

Yellow powder; yield 75% (0.14 g); mp 141 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.89 (d, *J* = 7.5 Hz, 1 H), 7.10 (d, *J* = 8.1 Hz, 1 H), 7.16-7.23 (m, 1 H), 7.43 (d, *J* = 8.1 Hz, 1 H), 7.51 (d, *J* = 9.0 Hz, 1 H), 7.81-7.88 (m, 4 H), 7.93-7.95 (m, 3 H), 8.10-8.15 (m, 5 H), 8.82 (s, 1 H), 9.50 (s, 1 H, NH), 9.90 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 112.9, 117.4, 118.0, 120.9, 121.8, 123.6, 124.7 (q, *J* = 271.9 Hz), 124.8 (q, *J* = 270.5 Hz), 125.2 (q, *J* = 3.7 Hz), 126.0 (q, *J* = 3.7 Hz), 127.8, 127.9 (q, *J* = 31.5 Hz), 128.0 (q, *J* = 32.0 Hz), 129.7, 130.5, 131.1, 132.4, 132.6, 133.2, 133.3, 136.5, 141.0, 142.3, 143.4 (q, *J* = 1.1 Hz), 143.6 (q, *J* = 1.1 Hz), 149.3, 156.0, 158.7.

Anal. Calcd for C₃₄H₂₀Cl₂F₆N₄: C, 61.00; H, 3.01; N, 8.37. Found: C, 61.33; H, 3.03; N, 8.23.

Synthesis of compounds 6l-t

A solution of 6,8-dibromo-2,4-dichloroquinazoline **4** (0.1 g, 0.28 mmol), amine (1.12 mmol, 4 equiv) in a DME/EtOH mixture (9/1, 5 mL) was heated under microwave irradiation (cf temperature in Table 3).

After cooling, 4-fluorophenylboronic acid (86 mg, 0.62 mmol, 2.2 equiv), PdCl₂(PPh₃)₂ (10 mg, 14 μmol, 0.05 equiv), K₂CO₃ (0.23 g, 1.68 mmol, 6 equiv) and water (0.5 mL) were introduced under argon. The mixture was heated at 100 °C under microwave irradiation for 1 h. 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 Na₂SO₄ and evaporated. The crude product was purified by column chromatography (silica gel, petroleum ether/ethyl acetate (9/1), (8/2 for **6r** and **6s**)) and recrystallized from acetonitrile.

6,8-Bis(4-fluorophenyl)-*N*²,*N*⁴-diphenyl-quinazoline-2,4-diamine (6l)

Brown powder; yield 71% (0.1 g); mp 114 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.88 (t, *J* = 6.7 Hz, 1 H), 7.10-7.16 (m, 3 H), 7.35-7.48 (m, 6 H), 7.82-7.97 (m, 9 H), 8.70 (s, 1 H), 9.15 (s, 1 H, NH), 9.77 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 112.8, 114.6 (d, *J* = 20.9 Hz), 115.9 (d, *J* = 21.2 Hz), 119.0, 120.4, 121.0, 122.6, 123.7, 128.3, 128.7, 129.0 (d, *J* = 8.1 Hz), 132.0, 132.6 (d, *J* = 7.3 Hz), 135.8 (d, *J* = 3.3 Hz), 136.2 (d, *J* = 3.3 Hz), 136.4, 139.7, 141.1, 148.9, 156.0, 158.8, 161.8 (d, *J* = 243.7 Hz), 162.0 (d, *J* = 244.8 Hz).

HRMS (ESI): *m/z* [M+H]⁺ Calcd for C₃₂H₂₂F₂N₄: 501.1885; found: 501.1884.

***N*²,*N*⁴,6,8-Tetrakis(4-fluorophenyl)quinazoline-2,4-diamine (6m)**

Brown powder; yield 93% (0.14 g); mp 230 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 6.96 (t, *J* = 8.8 Hz, 2 H), 7.22-7.39 (m, 6 H), 7.77-7.83 (m, 4 H), 7.93-7.96 (m, 5 H), 8.67 (s, 1 H), 9.18 (s, 1 H, NH), 9.80 (s, 1 H, NH).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 112.7, 114.6 (d, *J* = 21.2 Hz), 115.3 (d, *J* = 22.0 Hz), 115.9 (d, *J* = 21.2 Hz), 120.3, 120.5 (d, *J* = 7.3 Hz), 124.7 (d, *J* = 7.7 Hz), 129.0 (d, *J* = 8.1 Hz), 132.1, 132.5, 132.6 (d, *J* = 7.7 Hz), 135.7 (d, *J* = 3.3 Hz), 135.9 (d, *J* = 1.8 Hz), 136.2 (d, *J* = 3.3 Hz), 136.4, 137.4 (d, *J* = 1.8 Hz), 148.8, 155.9, 157.1 (d, *J* = 245.5 Hz), 158.9, 161.8 (d, *J* = 243.7 Hz), 162.0 (d, *J* = 244.4 Hz), 163.5 (d, *J* = 243.0 Hz).

HRMS (ESI): *m/z* [M+H]⁺ Calcd for C₃₂H₂₀F₄N₄: 537.1697; found: 537.1698.

***N*²,*N*⁴-Bis(2,5-dimethoxyphenyl)-6,8-bis(4-fluorophenyl)quinazoline-2,4-diamine (6n)**

Yellow powder; yield 76% (0.13 g); mp 184 °C

¹H NMR (200 MHz, DMSO-*d*₆): δ = 3.45 (s, 3 H, OCH₃), 3.76 (s, 9 H, 3 OCH₃), 6.39 (dd, *J* = 2.3 Hz, *J* = 8.6 Hz, 1 H), 6.81-6.87 (m, 2 H), 7.09 (d, *J* = 8.6 Hz, 1 H), 7.23-7.39 (m, 6 H), 7.76-7.83 (m, 2 H), 7.93-8.00 (m, 4 H), 8.66 (s, 1 H, NH), 9.57 (s, 1 H, NH).

^{13}C NMR (50 MHz, DMSO- d_6): δ = 55.3 (OCH₃), 55.6 (OCH₃), 56.2 (OCH₃), 56.3 (OCH₃), 104.6, 106.1, 110.6, 111.5, 112.9, 113.1, 113.6, 115.0 (d, J = 21.6 Hz), 115.9 (d, J = 21.2 Hz), 120.4, 128.0, 128.9 (d, J = 8.1 Hz), 129.9, 132.2, 132.3 (d, J = 8.4 Hz), 132.8, 135.6 (d, J = 3.3 Hz), 136.0 (d, J = 2.9 Hz), 136.6, 141.8, 148.0, 148.5, 153.2, 153.6, 155.7, 159.9, 161.7 (d, J = 244.8 Hz), 162.1 (d, J = 244.8 Hz).

Anal. Calcd for C₃₆H₃₀F₂N₄O₄: C, 69.67; H, 4.87; N, 9.03. Found: C, 69.96; H, 4.81; N, 8.88.

6,8-Bis(4-fluorophenyl)-*N*²,*N*⁴-dimesityl-quinazoline-2,4-diamine (6o)

Yellow powder; yield 87% (0.14 g); mp 205 °C

^1H NMR (200 MHz, DMSO- d_6): δ = 2.01 (s, 6 H, 2 CH₃), 2.19 (s, 6 H, 2 CH₃), 2.25 (s, 3 H, CH₃), 2.28 (s, 3 H, CH₃), 6.80 (s, 2 H), 6.90-6.96 (m, 4 H), 7.28-7.35 (m, 2 H), 7.71 (bs, 2 H), 7.90 (bs, 4 H), 8.62 (s, 1 H, NH), 9.28 (s, 1 H, NH).

^{13}C NMR (50 MHz, DMSO- d_6): δ = 18.3 (2 CH₃), 18.4 (2 CH₃), 20.7 (CH₃), 20.8 (CH₃), 112.0, 113.8 (d, J = 20.5 Hz), 115.8 (d, J = 20.5 Hz), 120.5, 128.1, 128.6 (d, J = 7.3 Hz), 128.7, 131.1, 132.2 (d, J = 7.7 Hz), 133.9, 134.1, 134.3, 135.0 (d, J = 2.6 Hz), 135.2, 135.6, 135.8, 136.5 (d, J = 2.9 Hz), 149.1, 158.7, 160.3, 161.2 (d, J = 243.7 Hz), 161.8 (d, J = 243.4 Hz).

Anal. Calcd for C₃₈H₃₄F₂N₄: C, 78.06; H, 5.86; N, 9.58. Found: C, 78.02; H, 5.72; N, 9.32.

***N*²,*N*⁴-Bis(3-fluorophenyl)-6,8-bis(4-fluorophenyl)-quinazoline-2,4-diamine (6p)**

Yellow powder; yield 86% (0.13 g); mp 125 °C

^1H NMR (200 MHz, DMSO- d_6): δ = 6.68-6.71 (m, 1 H), 6.98-7.01 (m, 1 H), 7.19 (t, J = 6.9 Hz, 1 H), 7.32-7.42 (m, 6 H), 7.79 (bs, 3 H), 7.97-8.00 (m, 5 H), 8.72 (s, 1 H), 9.53 (s, 1 H, NH), 9.92 (s, 1 H, NH).

^{13}C NMR (50 MHz, DMSO- d_6): δ = 112.7, 114.9 (d, J = 22.0 Hz), 115.9 (d, J = 21.2 Hz), 117.9, 120.4, 129.2 (d, J = 8.1 Hz), 129.6 (d, J = 9.2 Hz), 130.1 (d, J = 9.5 Hz), 132.4 (d, J = 8.1 Hz), 133.3, 135.5, 136.0, 136.7, 141.4, 142.7, 148.6, 155.4, 158.7, 161.9 (d, J = 244.1 Hz), 162.1 (d, J = 244.4 Hz), 162.4 (d, J = 241.1 Hz), 162.5 (d, J = 240.1 Hz).

Anal. Calcd for C₃₂H₂₀F₄N₄: C, 71.64; H, 3.76; N, 10.44. Found: C, 71.55; H, 3.65; N, 10.30.

***N*²,*N*⁴-Bis(3,4-dichlorophenyl)-6,8-bis(4-fluorophenyl)quinazoline-2,4-diamine (6q)**

Yellow powder; yield 73% (0.13 g); mp 231 °C

^1H NMR (200 MHz, DMSO- d_6): δ = 7.30-7.38 (m, 5 H), 7.57-7.67 (m, 2 H), 7.72-7.78 (m, 2 H), 7.91-7.99 (m, 3 H), 8.09 (d, J = 7.9 Hz, 1 H), 8.18 (s, 1 H), 8.24 (s, 1 H), 8.66 (s, 1 H), 9.57 (s, 1 H, NH), 9.96 (s, 1 H, NH).

^{13}C NMR (50 MHz, DMSO- d_6): δ = 112.7, 115.3 (d, J = 21.6 Hz), 115.9 (d, J = 21.6 Hz), 119.1, 119.8,

120.4, 122.7, 123.8, 124.0, 125.6, 129.1 (d, J = 8.1 Hz), 129.6, 130.1, 130.5, 131.0, 131.1, 131.4, 132.2 (d, J = 8.1 Hz), 132.8 (d, J = 3.3 Hz), 133.6, 135.0, 135.8 (d, J = 2.6 Hz), 139.4, 140.6, 154.8, 158.8, 162.0 (d, J = 244.1 Hz), 162.2 (d, J = 244.8 Hz).

HRMS (ESI): m/z [M+H]⁺ Calcd for C₃₂H₁₈Cl₄F₂N₄: 639.0302; found: 639.0302.

***N*²,*N*⁴-Dicyclopentyl-6,8-bis(4-fluorophenyl)-quinazoline-2,4-diamine (6r)**

Yellow powder; yield 95% (0.13 g); mp 242 °C

^1H NMR (200 MHz, CDCl₃): δ = 1.65-1.85 (m, 10 H, 5 CH₂), 2.02-2.14 (m, 6 H, 3 CH₂), 4.30-4.37 (m, 1 H, CH), 4.60-4.69 (m, 1 H, CH), 6.90 (bs, 3 H), 7.17-7.23 (m, 2 H), 7.48-7.61 (m, 3 H), 8.74 (s, 1 H), 9.00 (s, 1 H), 9.24 (s, 1 H, NH), 10.58 (s, 1 H, NH).

^{13}C NMR (50 MHz, CDCl₃): δ = 23.9 (2 CH₂), 24.3 (2 CH₂), 32.1 (2 CH₂), 32.8 (2 CH₂), 53.5 (CH), 54.7 (CH), 111.0, 115.4 (d, J = 21.6 Hz), 116.3 (d, J = 22.0 Hz), 122.8, 128.9 (d, J = 8.1 Hz), 129.3, 131.0 (d, J = 2.2 Hz), 131.3 (d, J = 8.1 Hz), 134.3, 134.6 (d, J = 2.6 Hz), 135.3, 152.7, 159.5, 162.4 (d, J = 247.4 Hz), 162.7 (d, J = 248.5 Hz).

HRMS (ESI): m/z [M+H]⁺ Calcd for C₃₀H₃₀F₂N₄: 485.2511; found: 485.2511.

***N*²,*N*⁴-Dibenzyl-6,8-bis(4-fluorophenyl)-quinazoline-2,4-diamine (6s)**

Yellow powder; yield 88% (0.13 g); mp 165 °C

^1H NMR (200 MHz, CDCl₃): δ = 4.60 (s, 2 H, CH₂), 4.81 (d, J = 4.6 Hz, 2 H, CH₂), 7.00-7.07 (m, 5 H), 7.26-7.38 (m, 10 H), 7.52-7.59 (m, 5 H), 7.72 (s, 2 H).

^{13}C NMR (50 MHz, CDCl₃): δ = 45.2 (CH₂), 45.3 (CH₂), 111.6, 114.5 (d, J = 21.2 Hz), 115.7 (d, J = 21.6 Hz), 118.3, 126.8, 127.5, 127.8 (d, J = 21.9 Hz), 128.0, 128.3, 128.5 (d, J = 8.4 Hz), 128.6, 132.0 (d, J = 7.8 Hz), 132.5 (d, J = 9.2 Hz), 134.9, 136.1 (d, J = 2.6 Hz), 136.6, 138.4, 138.5, 140.1, 160.3, 160.4, 162.2 (d, J = 245.9 Hz), 162.3 (d, J = 246.6 Hz).

HRMS (ESI): m/z [M+H]⁺ Calcd for C₃₄H₂₆F₂N₄: 529.2198; found: 529.2197.

***N*²,*N*²,*N*⁴,*N*⁴-Tetraethyl-6,8-bis(4-fluorophenyl)-quinazoline-2,4-diamine (6t)**

Yellow oil; yield 85% (0.11 g).

^1H NMR (200 MHz, CDCl₃): δ = 1.17 (t, J = 7.0 Hz, 6 H, 2 CH₃), 1.39 (t, J = 7.0 Hz, 6 H, 2 CH₃), 3.61 (q, J = 6.7 Hz, 4 H, 2 CH₂), 3.68 (q, J = 6.9 Hz, 4 H, 2 CH₂), 7.07-7.19 (m, 4 H), 7.55-7.62 (m, 2 H), 7.74-7.81 (m, 3 H), 7.87 (d, J = 2.1 Hz, 1 H).

^{13}C NMR (50 MHz, CDCl₃): δ = 13.2 (2 CH₃), 13.6 (2 CH₃), 41.8 (2 CH₂), 45.2 (2 CH₂), 112.3, 114.1 (d, J = 22.3 Hz), 115.6 (d, J = 21.2 Hz), 122.6, 128.1 (d, J = 7.7 Hz), 130.1, 131.2, 132.0 (d, J = 7.7 Hz), 135.9 (d, J = 3.2 Hz), 136.0, 137.4 (d, J = 2.6 Hz), 151.8, 157.3, 161.9 (d, J = 245.2 Hz), 162.4 (d, J = 242.6 Hz).

HRMS (ESI): m/z $[M+H]^+$ Calcd for $C_{28}H_{30}F_2N_4$: 461.2511; found: 461.2511.

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