SUPPORTING INFORMATION

Characterizing the Antimicrobial Activity of N^2,N^4-Disubstituted Quinazoline-2,4-Diamines Towards Multidrug Resistant *Acinetobacter baumannii*

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Materials and Methods. All commercially available chemical reagents, except for the boronic acids, and anhydrous solvents were purchased from either Sigma Aldrich, Oakwood Products, Inc. or TCI America and used without any further purification. Boronic acids used were purchased through Frontier Scientific. NMR spectra were recorded at ambient temperature on a 400 MHz or 500 MHz Varian NMR spectrometer in the solvent indicated. Data for ^{1}H NMR are reported as follows: chemicals shift (δ ppm), multiplicity (s

= singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), integration and coupling constant (Hz) whereas ^{13}C NMR analyses were reported in terms of chemical shift (δ ppm). NMR data was analyzed by using MestReNova Software version 10.0.1-14719. The purity of the final compounds was determined to be ≥95% by high-performance liquid chromatography (HPLC) using an Agilent 1100 LC/MSD-VL with electrospray ionization. Low-resolution mass spectra were performed on an Agilent 1100 LC/MSD-VL with electrospray ionization. High resolution mass spectra (HRMS) were performed on an Agilent LC/MSD TOF system G3250AA. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 precoated plates (0.25 mm) from EMD Chemical Inc., and components were visualized by ultraviolet light (254 nm). EMD silica gel 230-400 (particle size 40-63 μm) mesh was used for all flash column chromatography.

Synthetic Protocols and Compound Characterization: See Supplemental Figure S1.

Procedure A: Suzuki-Miyaura Cross Coupling with N^2-benzyl-6-bromo-N^4-methylquinazolin-2,4-diamine to yield 6-alkenyl-N^2-benzyl-N^4-methylquinazolin-2,4-diamine and 6-aryl-N^2-benzyl-N^4-methylquinazoline-2,4-diamine.[22] One equivalent of N^2-benzyl-6-bromo-N^4-methylquinazolin-2,4-diamine (0.23 mmol), 1.5 equivalents of the boronic acid (0.35 mmol), 5 mol-% of tetrakis-palliadium, a saturated solution of sodium bicarbonate (1.23 mL), and anhydrous dimethoxyethane (1.87 mL) were combined in a sealed microwave tube, under argon, and heated in the microwave to 150 ºC. The reaction was monitored by TLC and LCMS until no starting material was observed. The reaction was cooled to room temperature, diluted with dichloromethane. The organic layer was separated and washed with equal volume of water three times, then dried over sodium sulfate. Purification of final product was completed by column chromatography using dichloromethane and methanol.

Procedure B: Hydrogenation of 6-alkenyl-N^2-benzyl-N^4-methylquinazolin-2,4-diamine to Yield 6-alkanyl-N^2-benzyl-N^4-methylquinazoline-2,4-diamine

One equivalent of 6-alkenyl-N^2-benzyl-N^4-methylquinazolin-2,4-diamine was combined with 5 mol% of palladium on carbon in methanol to afford a 2mg/mL solution and fixed with a hydrogen balloon. The reaction was monitored by LC-MS until no starting material was present. The reaction was filtered over celite and rinsed with three equal volumes of methanol. Purification by column chromatography using dichloromethane and methanol was used to obtain the pure product.

Procedure C: Cyclization of Anthranilic Acids to the Corresponding Quinazoline-2,4-diones

One equivalent of the commercially available anthranilic acid and three equivalents of urea were ground in a mortar and pestle until a homogenous mixture was obtained. This powder was then transferred to a round bottom flask and heated to 200 ºC uncovered. After 3 hours the mixture was cooled, triturated with 10 mL of water, the solid filtered and subsequently washed with 40 mL of water. Crude product was dried and no further purification was completed.

Procedure D: Chlorination of Quinazoline-2,4-diones to the Corresponding 2,4-Dichloroquinazoline

One equivalent of quinazoline-2,4-dione and one equivalent of *N,N*-dimethylaniline were combined in a round bottom flask, 12 equivalents of phosphorus oxychloride was then added. The mixture was refluxed under argon until the presence of starting material was no longer seen by TLC or by LC-MS (6-24 hours). Upon completion the reaction mixture was cooled and slowly added to ice equaled to ten times that of the reaction volume. Upon precipitation the reaction was filtered and washed with water to afford the crude 2,4-dichloroquinazoline which was purified by column chromatography using hexanes and ethyl acetate.

Procedure E: Amine Substitution of 2,4-Dichloroquinzaolines to Yield 4-Amino-substituted-2-chloroquinazoline

One equivalent of the crude 2,4-dichloroquinazoline, 1.1 equivalents of sodium acetate, and 1.1 equivalents were combined in a round bottom flask and mixed with a three to one solution of tetrahydrofuran and water to afford a 0.1 M solution. The reaction was heated to 65 ºC and monitored until no starting material was

seen by TLC or LC-MS. The reaction was diluted with ethyl acetate and the organic layer separated. This organic layer was washed three times with equal amounts of water and then dried over sodium sulfate. The crude 4-amino-substituted-2-chloroquinazoline was then purified by column chromatography using hexane and ethyl acetate.

Procedure F: Amine Substitution of 4-Aminosubstutited-2-chloroquinazolines to Yield 2,4-Diamino-substituted Quinazolines

One equivalent of 4-aminosubstituted-2-chloroquinazoline and 1.5 equivalents of amine were combined with ethanol to create a 0.2 M solution which was heated to 150 ºC in a sealed tube. The reaction was monitored by TLC and LC-MS for the absence of starting material (8-18 hours). The reaction was purified by either method F^1 or F^2.

Purification Method F^1: Compound crystallized out of the cool solution, was filtered, and rinsed with cold ethanol.

Purification Method F^2: Solvent was evaporated and crude product was purified via column chromatography using dichloromethane and methanol.

Compound **8** has been reported previously.[7]

2,6-Dichloro-*N*-methylquinazolin-4-amine: 0.13 g (0.54 mmol) of 2,4,6-trichloroquinazoline was reacted with methylamine and purified according to general procedure C to furnish 0.11 g of the title compound in 92 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 9.1 Hz, 1H), 7.37 (dd, J = 9.1, 2.6 Hz, 1H), 6.97 (d, J = 2.7 Hz, 1H), 3.86 (s, 3H), 3.22 (d, J = 4.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2, 158.9, 151.5, 139.6, 126.9, 123.5, 122.2, 111.7, 28.6. R_f = 0.82 (DCM/MeOH 10:1).

***N^2*-Benzyl-6-chloro-*N^4*-methylquinazoline-2,4-diamine (1):** 0.10 g (0.44 mmol) of 2,6-dichloro-*N*-methylquinazolin-4-amine was reacted with benzylamine and purified according to general procedure D to furnish 87.0 mg of the title compound as a white crystalline solid in 45 % yield. ^{1}H NMR (400 MHz,

CD_3OD) δ 7.80 (d, *J* = 2.3 Hz, 1H), 7.41 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.34 (dd, *J* = 7.9, 0.9 Hz, 2H), 7.29 – 7.22 (m, 3H), 7.20 – 7.13 (m, 1H), 4.63 (s, 2H), 2.98 (s, 3H). HRMS: m/z calculated for $C_{16}H_{16}ClN_4$ $[M+H]^+$ 299.1058; found 299.1061. R_f = 0.33 (DCM/MeOH 10:1).

2,7-Dichloro-*N*-methylquinazolin-4-amine: 0.20 g (0.86 mmol) of 2,4,7-trichloroquinazoline was reacted with methylamine and purified according to general procedure C to furnish 0.17 g of the title compound in 72 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 2.0 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.39 (dd, *J* = 8.7, 2.0 Hz, 1H), 3.22 (d, *J* = 4.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2, 158.9, 151.5, 139.6, 126.9, 122.2, 123.5, 111.7, 28.6. R_f = 0.80 (DCM/MeOH 10:1).

***N*^{2}-Benzyl-7-chloro-*N*^{4}-methylquinazoline-2,4-diamine (2):** 0.15 g (0.66 mmol) of 2,7-dichloro-*N*-methylquinazolin-4-amine was reacted with benzylamine and purified according to general procedure D to furnish 66.0 mg of the title compound as a white crystalline solid in 68 % yield. ^{1}H NMR (500 MHz, DMSO) δ 8.21 – 8.11 (m, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.35 (q, *J* = 7.5, 6.3 Hz, 2H), 7.18 (d, *J* = 8.6 Hz, 1H), 4.70 (d, *J* = 6.4 Hz, 2H), 3.53 (s, 1H), 3.09 (d, *J* = 4.5 Hz, 3H). HRMS: m/z calculated for $C_{16}H_{16}ClN_4$ $[M+H]^+$ 299.1058; found 299.1059. R_f = 0.38 (DCM/MeOH 10:1).

2-Chloro-6-methoxy-*N*-methylquinazolin-4-amine: 0.10 g (0.44 mmol) of 2,4-dichloro-6-methoxyquinazoline was reacted with methylamine and purified according to general procedure C to furnish 81 mg of the title compound in 83 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.5 Hz, 1H), 7.56 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.78 (d, *J* = 1.4 Hz, 1H), 3.87 (s, 2H), 2.91 (s, 2H), 2.30 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.7, 158.5, 154.2, 148.7, 127.3, 121.8, 110.5, 109.0, 55.8, 28.3. R_f = 0.48 (DCM/MeOH 10:1).

***N*^{2}-Benzyl-6-methoxy-*N*^{4}-methylquinazoline-2,4-diamine (3):** 70.0 mg (0.24 mmol) of 2-chloro-6-methoxy-*N*-methylquinazolin-4-amine was reacted with benzylamine and purified according to general procedure D to furnish 30.0 mg of the title compound as a white crystalline solid in 45 % yield. ^{1}H NMR

(500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 9.1 Hz, 1H), 7.41 (d, *J* = 7.1 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.21 (m, 2H), 6.87 (d, *J* = 2.7 Hz, 1H), 4.73 (d, *J* = 5.7 Hz, 2H), 3.83 (s, 3H), 3.11 (d, *J* = 4.7 Hz, 3H). HRMS: m/z calculated for $C_{17}H_{19}N_4$ $[M+H]^+$ 295.1553; found 295.1556. R_f = 0.26 (DCM/MeOH 10:1).

6-Bromo-2,4-dichloroquinazoline: 3.0 g (13.89 mmol) of commercially available 2-amino-5-bromobenzoic acid was reacted according to general procedure C to give crude 6-bromoquinazoline-2,4(1*H*,3*H*)-dione. Without further purification, 3.4g (14.12 mmol) of crude 6-bromoquinazoline-2,4(1*H*,3*H*)-dione was reacted and purified according to general procedure D to give 1.18 g of the title compound as a beige solid in 30% yield.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, *J* = 2.1 Hz, 1H), 8.05 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.77, 155.44, 151.02, 139.71, 129.62, 128.21, 123.35, 123.21. R_f = 0.88 (DCM/MeOH 10:1).

6-Bromo-2-chloro-*N*-methylquinazolin-4-amine: 100 mg (0.36 mmol) of 6-bromo-2,4-dichloroquinazoline was reacted with methylamine and purified according to procedure E to furnish 89 mg of the title compound in 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 1.9 Hz, 1H), 7.79 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 5.98 (s, 1H), 3.22 (d, *J* = 4.9 Hz, 3H). ^{13}C NMR (126 MHz, CDCl) δ 160.48, 158.07, 149.43, 136.75, 129.62, 123.44, 119.29, 114.59, 28.67. R_f = 0.54 (DCM/MeOH 10:1).

***N*^{2}-Benzyl-6-bromo-*N*^{4}-methylquinazoline-2,4-diamine (4):** 80 mg (0.29 mmol) of 6-bromo-2-chloro-*N*-methylquinazolin-4-amine was reacted with benzylamine and purified according to method F[2] to furnish 78 mg of the title compound as a white crystalline solid in 78% yield. ^{1}H NMR (500 MHz, DMSO) δ 8.27 (s, 1H), 8.10 (s, 1H), 7.64 (d, *J* = 8.9 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.27 (dd, *J* = 14.6, 7.7 Hz, 2H), 4.64 (d, *J* = 6.3 Hz, 2H), 3.47 (d, *J* = 4.2 Hz, 1H), 3.02 (d, *J* = 3.1 Hz, 3H). HRMS: m/z calculated for $C_{16}H_{16}BrN_4$ $[M+H]^+$ 343.0553; found 343.0544. R_f = 0.51 (DCM/MeOH 10:1).

2,4-Dichloro-6-methylquinazoline: 1.5 g (9.93 mmol) of commercially available 2-Amino-5-methylbenzoic acid was reacted according to general procedure C to give crude 6-methylquinazoline-

2,4(1*H*,3*H*)-dione. Without further purification, 1.6 g (9.52 mmol) of crude 6-methylquinazoline-2,4(1*H*,3*H*)-dione was reacted and purified according to general procedure D to give 465 mg of the title compound as a beige solid in 23% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 2H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.81 (dd, *J* = 8.6, 1.8 Hz, 2H), 2.60 (s, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.07, 154.19, 150.96, 139.97, 138.37, 127.64, 124.66, 122.24, 21.88.

2-Chloro-*N*,6-dimethylquinazolin-4-amine: 150 mg (0.70 mmol) of 2,4-dichloro-6-methylquinazoline was reacted with methylamine and purified according to procedure E to furnish 95 mg of the title compound in 66% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.5 Hz, 1H), 7.53 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.45 (s, 1H), 6.13 (s, 1H), 3.20 (d, *J* = 4.9 Hz, 3H), 2.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.24, 156.96, 148.85, 136.28, 135.23, 127.42, 120.03, 113.20, 28.51, 21.61. R_f = 0.44 (DCM/MeOH 10:1).

***N*^{2}-Benzyl-*N*^{4},6-dimethylquinazoline-2,4-diamine (5):** 80 mg (0.38 mmol) of 2-chloro-*N*,6-dimethylquinazolin-4-amine was reacted with benzylamine and purified according to method F[1] to furnish 47 mg of the title compound as a beige crystalline solid in 57% yield.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.23 (m, 8H), 5.85 (s, 1H), 5.41 (s, 1H), 4.75 (d, *J* = 5.4 Hz, 2H), 3.10 (d, *J* = 4.8 Hz, 3H), 2.39 (s, 3H). HRMS: m/z calculated for $C_{17}H_{19}N_4$ $[M+H]^+$ 279.1604; found 279.1607. R_f = 0.55 (DCM/MeOH 10:1).

7-Bromo-2,4-dichloroquinazoline: 5.0 g (23.2 mmol) of commercially available 2-amino-6-bromobenzoic acid was reacted according to general procedure C to give crude 7-bromoquinazoline-2,4(1*H*,3*H*)-dione. Without further purification, 5.2 g (21.6 mmol) of crude 7-bromoquinazoline-2,4(1*H*,3*H*)-dione was reacted and purified according to general procedure D to give 2.82 g of the title compound as a beige solid in 47% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 1.6 Hz, 1H), 8.12 (d, *J* = 8.9 Hz, 1H), 7.83 (dd, *J* = 8.9, 1.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.02, 156.23, 152.76, 133.01, 131.61, 130.47, 127.20, 121.10. R_f = 0.90 (DCM/MeOH 10:1).

7-Bromo-2-chloro-*N*-methylquinazolin-4-amine: 100 mg (0.36 mmol) of 7-bromo-2,4-dichloroquinazoline was reacted with methylamine and purified according to procedure E to furnish 95 mg

of the title compound in 97% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 1.7 Hz, 2H), 7.53 (dt, *J* = 18.2, 5.3 Hz, 5H), 5.97 (s, 2H), 3.22 (d, *J* = 4.9 Hz, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.31, 158.76, 151.61, 130.40, 129.59, 127.99, 121.95, 112.01, 28.64. R_f = 0.35 (DCM/MeOH 10:1).

***N*^{2}-Benzyl-7-bromo-*N*^{4}-methylquinazoline-2,4-diamine (6):** 90 mg (0.33 mmol) of 7-bromo-2-chloro-*N*-methylquinazolin-4-amine was reacted with benzylamine and purified according to method F^2 to furnish 58 mg of the title compound as a white crystalline solid in 51% yield. ^{1}H NMR (500 MHz, methanol-d_4) δ 7.69 (d, *J* = 8.7 Hz, 1H), 7.49 (s, 1H), 7.39 – 7.36 (m, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.23 – 7.20 (m, 1H), 7.19 (dd, *J* = 8.7, 2.0 Hz, 1H), 4.66 (s, 2H), 3.02 (s, 3H). HRMS: m/z calculated for $C_{16}H_{16}BrN_4$ $[M+H]^+$ 343.0553; found 343.0548. R_f = 0.59 (DCM/MeOH 10:1).

2,4-Dichloro-7-methylquinazoline: 2.38 g (15.8 mmol) of commercially available 2-amino-6-methylbenzoic acid was reacted according to general procedure C to give crude 7-methylquinazoline-2,4(1*H*,3*H*)-dione. Without further purification, 2.8 g (16.4 mmol) of crude 7-methylquinazoline-2,4(1*H*,3*H*)-dione was reacted and purified according to general procedure D to give 1.2 g of the title compound as a beige solid in 34% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H), 7.26 – 7.22 (m, 1H), 6.20 (s, 1H), 3.19 (d, *J* = 4.9 Hz, 3H), 2.47 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.47, 157.79, 150.81, 144.35, 128.04, 126.97, 120.59, 111.22, 28.46, 21.85.

2-Chloro-*N*,7-dimethylquinazolin-4-amine: 150 mg (0.70 mmol) of 2,4-dichloro-7-methylquinazoline was reacted with methylamine and purified according to procedure E to furnish 125 mg of the title compound in 86% yield ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.6 Hz, 2H), 7.75 (s, 2H), 7.55 (dd, *J* = 8.6, 1.3 Hz, 2H), 2.61 (s, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.40, 155.13, 152.64, 147.95, 131.44, 126.93, 125.65, 120.46, 22.32. R_f = 0.38 (DCM/MeOH 10:1).

***N*^{2}-Benzyl-*N*^{4},7-dimethylquinazoline-2,4-diamine (7):** 110 mg (0.53 mmol) of 2-chloro-*N*,7-dimethylquinazolin-4-amine was reacted with benzylamine and purified according to method F^1 to furnish 129 mg of the title compound as a beige crystalline solid in 88% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60

(d, J = 8.4 Hz, 1H), 7.51 (s, 1H), 7.25 (dd, J = 8.4, 1.7 Hz, 1H), 4.80 (s, 2H), 3.20 (d, J = 4.8 Hz, 3H), 2.48 (s, 3H). HRMS: m/z calculated for $C_{17}H_{19}N_4$ $[M+H]^+$ 279.1604; found 279.1598. R_f = 0.49 (DCM/MeOH 10:1).

***N*^{4}-Benzyl-6-chloro-*N*^{2}-methylquinazoline-2,4-diamine (9):** 80.0 mg (0.26 mmol) of *N*-benzyl-2,6-dichloroquinazolin-4-amine was reacted with methylamine and purified according to general procedure F to furnish 72.0 mg of the title compound as a beige crystalline solid in 67 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.36 (m, 7H), 7.34 (dd, J = 5.8, 2.7 Hz, 1H), 4.79 (s, 2H), 3.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.3, 159.0, 150.8, 138.3, 133.1, 129.0, 128.8, 128.0, 127.7, 127.3, 125.7, 120.2, 45.2, 28.4. HRMS: m/z calculated for $C_{16}H_{16}ClN_4$ $[M+H]^+$ 299.1058; found 299.1058. R_f = 0.28 (DCM/MeOH 10:1).

***N*-Benzyl-6-bromo-2-chloroquinazolin-4-amine:** 0.10 g (0.36 mmol) of 6-bromo-2,4-dichloroquinazoline was reacted with benzylamine and purified according to general procedure E to furnish 0.13 g of the title compound in 99 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 2H), 7.67 (d, J = 8.8 Hz, 1H), 7.44 – 7.36 (m, 5H), 6.01 (s, br, 1H), 4.86 (d, J = 5.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 158.0, 149.7, 138.3, 136.9, 129.7, 129.0, 128.4, 128.3, 123.4, 119.4, 114.4, 46.0. R_f = 0.60 (DCM/MeOH 10:1).

***N*^{4}-Benzyl-6-bromo-*N*^{2}-methylquinazoline-2,4-diamine (10):** 0.12 g (0.34 mmol) *N*-benzyl-6-bromo-2-chloroquinazolin-4-amine was reacted with methylamine and purified according to general procedure F to furnish 92.0 mg of the title compound as a beige crystalline solid in 88 % yield. ^{1}H NMR (500 MHz, DMSO) δ 8.65 (s, br, 1H), 8.48 (s, 1H), 7.75 (d, J = 8.9, 1H), 7.55 - 7.40 (m, 5H), 6.81 (s, br, 1H), 4.88 (d, J = 5.8 Hz, 2H), 2.98 (t, J = 3.6 Hz, 3H). HRMS: m/z calculated for $C_{16}H_{16}BrN_4$ $[M+H]^+$ 343.0553; found 343.0549. R_f = 0.52 (DCM/MeOH 10:1).

***N*-Benzyl-2-chloro-6-methylquinazolin-4-amine:** 0.10 g (0.47 mmol) of 2,4-dichloro-6-methylquinazoline was reacted with benzylamine and purified according to general procedure E to furnish

0.13 g of the title compound in 86 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.45 – 7.32 (m, 6H), 6.05 (s, br, 1H), 4.86 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.3, 156.9, 149.2, 137.4, 136.39, 135.4, 131.8, 128.9, 128.4, 127.6, 119.9, 113.0, 45.7, 21.6. R_f = 0.61 (DCM/MeOH 10:1).

***N*^{4}-Benzyl-*N*^{2},6-dimethylquinazoline-2,4-diamine (11):** 0.11 g (0.41 mmol) *N*-benzyl-2-chloro-6-methylquinazolin-4-amine was reacted with methylamine and purified according to general procedure F to furnish 92.0 mg of the title compound as a beige crystalline solid in 81 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 8H), 4.81 (d, *J* = 5.4 Hz, 2H), 3.05 (d, *J* = 5.1 Hz, 3H), 2.37 (s, 3H). HRMS: m/z calculated for $C_{17}H_{19}N_4$ $[M+H]^+$ 279.1604; found 279.1595. R_f = 0.55 (DCM/MeOH 10:1).

***N*-Benzyl-2-chloro-6-methoxyquinazolin-4-amine:** 0.10 g (0.51 mmol) of 2,4-dichloro-6-methoxyquinazoline was reacted with benzylamine and purified according to general procedure E to furnish 0.12 g of the title compound in 93 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 9.1 Hz, 1H), 7.38 (m, 6H), 6.95 (d, J 2.4 Hz, 1H), 6.16 (s, br, 1H), 4.86 (d, *J* = 5.2 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 157.7, 155.5, 146.1, 137.5, 129.3, 128.9, 128.4, 128.0, 124.4, 113.6, 100.5, 55.8, 45.8. R_f = 0.63 (DCM/MeOH 10:1).

***N*^{4}-Benzyl-6-methoxy-*N*^{2}-methylquinazoline-2,4-diamine (12):** 0.10 g (0.33 mmol) *N*-benzyl-2-chloro-6-methoxyquinazolin-4-amine was reacted with methylamine and purified according to general procedure F to furnish 85.0 mg of the title compound as a beige crystalline solid in 78 % yield. ^{1}H NMR (500 MHz, DMSO) δ 8.74 (s, br, 1H), 7.82 (s, 1H), 7.61 (d, *J* = 6.7 Hz, 2H), 7.57 – 7.38 (m, 5H), 6.66 (s, 1H), 4.96 (s, 2H), 4.02 (s, 3H), 3.02 (s, 3H). HRMS: m/z calculated for $C_{17}H_{19}N_4O$ $[M+H]^+$ 295.1553; found 295.1543. R_f = 0.29 (DCM/MeOH 10:1).

***N*-Benzyl-2,7-dichloroquinazolin-4-amine:** 0.20 g (0.86 mmol) of 2,4,7-trichloroquinazoline was reacted with benzylamine and purified according to general procedure E to furnish 0.26 g of the title compound in 98 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.42 – 7.32 (m, 6H), 6.18

(s, br, 1H), 4.85 (d, J = 5.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 158.8, 151.7, 139.8, 137.0, 129.0, 128.4, 128.2, 127.1, 127.0, 122.2, 111.5, 45.9. R_f = 0.66 (DCM/MeOH 10:1).

***N*^{4}-Benzyl-7-chloro-*N*^{2}-methylquinazoline-2,4-diamine (13):** 0.25 g (0.82 mmol) *N*-benzyl-2,7-dichloroquinazolin-4-amine was reacted with methylamine and purified according to general procedure F to furnish 77.0 mg of the title compound as a beige crystalline solid in 48/ % yield. ^{1}H NMR (500 MHz, CD_3OD) δ 7.85 (d, J = 8.7 Hz, 1H), 7.42 – 7.28 (m, 5H), 7.21 (d, J = 10.6, 1H), 7.03 (d, J = 8.7, 1H), 4.78 (s, 2H), 2.93 (s, 3H). HRMS: m/z calculated for $C_{16}H_{16}ClN_4$ $[M+H]^+$ 299.1058; found 299.1046. R_f = 0.38 (DCM/MeOH 10:1).

***N*-Benzyl-7-bromo-2-chloroquinazolin-4-amine:** 0.10 g (0.36 mmol) of 7-bromo-2,4-dichloroquinazoline was reacted with benzylamine and purified according to general procedure E to furnish 0.12 g of the title compound in 97 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.53 (s, 2H), 7.43 – 7.33 (m, 5H), 6.1 (s, br, 1H) 4.85 (d, J = 5.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 158.0, 149.7, 138.3, 136.9, 129.7, 129.0, 128.4, 128.3, 123.4, 119.4, 114.4, 45.9. R_f = 0.71 (DCM/MeOH 10:1).

***N*^{4}-Benzyl-7-bromo-*N*^{2}-methylquinazoline-2,4-diamine (14):** 0.11 g (0.33 mmol) *N*-benzyl-7-bromo-2-chloroquinazolin-4-amine was reacted with methylamine and purified according to general procedure F to furnish 90.0 mg of the title compound as a beige crystalline solid in 79 % yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.70 (s, 1H), 8.20 (d, J = 9.0 Hz, 1H), 7.56 (dd, J = 27.3, 7.7 Hz, 5H), 7.41 (dd, J = 29.9, 7.6 Hz, 2H), 6.91 (s, 1H), 4.92 (s, 2H), 3.71 (s, 1H), 3.01 (s, 3H). HRMS: m/z calculated for $C_{16}H_{16}BrN_4$ $[M+H]^+$ 343.0553; found 343.0543. R_f = 0.58 (DCM/MeOH 10:1).

***N*-Benzyl-2-chloro-7-methylquinazolin:** 0.10 g (0.47 mmol) of 2,4-dichloro-7-methylquinazoline was reacted with benzylamine and purified according to general procedure E to furnish 0.12 g of the title compound in 96 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 8.4 Hz, 1H), 7.54 (s, 1H), 7.42 – 7.31 (m, 5H), 7.27 – 7.24 (m, 1H), 4.85 (d, J = 5.3 Hz, 2H), 2.49 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6,

157.7, 151.1, 144.5, 137.4, 128.9, 128.3, 128.1, 127.2, 120.6, 111.0, 45.7, 28.4, 21.9. R_f = 0.68 (DCM/MeOH 10:1).

N^4-Benzyl-N^2,7-dimethylquinazoline-2,4-diamine (15): 0.10 g (0.35 mmol) *N*-benzyl-2-chloro-7-methylquinazolin was reacted with methylamine and purified according to general procedure F to furnish 77.0 mg of the title compound as a beige crystalline solid in 76 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 5H), 7.31 (d, *J* = 6.9 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 1H), 4.80 (d, *J* = 5.4 Hz, 2H), 3.06 (d, *J* = 5.0 Hz, 3H), 2.41 (s, 3H). HRMS: m/z calculated for $C_{17}H_{19}N_4$ $[M+H]^+$ 279.1604; found 279.1597. R_f = 0.47 (DCM/MeOH 10:1).

N^4-Methyl-N^2-phenethylquinazoline-2,4-diamine (16): 0.10 g (0.52 mmol) of 2-chloro-*N*-methylquinazolin-4-amine was reacted with phenethylamine and purified according to general procedure F to furnish 55.0 mg of the title compound as a beige crystalline solid in 55 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.29 (q, *J* = 6.4, 5.1 Hz, 2H), 7.27 – 7.18 (m, 3H), 7.03 (td, *J* = 7.1, 6.1, 1.7 Hz, 1H), 6.46 (s, 1H), 5.36 (s, 1H), 3.79 (t, *J* = 7.4 Hz, 2H), 3.09 (s, 3H), 2.95 (t, *J* = 7.3 Hz, 2H). HRMS: m/z calculated for $C_{17}H_{19}N_4$ $[M+H]^+$ 279.1604; found 279.1602. R_f = 0.40 (DCM/MeOH 10:1).

6-Chloro-N^4-methyl-N^2-phenethylquinazoline-2,4-diamine (17): 90.0 mg (0.39 mmol) 2,6-dichloro-*N*-methylquinazolin-4-amine was reacted with phenethylamine and purified according to general procedure F to furnish 55.0 mg of the title compound as a beige crystalline solid in 48 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.40 (m, 2H), 7.35 (d, *J* = 9.4 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.23 – 7.17 (m, 1H), 5.53 (s, 1H), 5.08 (s, 1H), 3.75, (q, *J* = 6.8 Hz, 2 Hz), 3.08 (d, *J* = 4.8 Hz, 3H), 2.93 (t, *J* = 7.2 Hz, 2H). HRMS: m/z calculated for $C_{17}H_{18}ClN_4$ $[M+H]^+$ 312.8073; found 312.7996. R_f = 0.38 (DCM/MeOH 10:1).

6-Methoxy-N^4-methyl-N^2-phenethylquinazoline-2,4-diamine (18): 60.0 mg (0.20 mmol) 2,4-dichloro-6-methoxyquinazoline was reacted with phenethylamine and purified according to general procedure F to furnish 17.0 mg of the title compound as a beige crystalline solid in 23 % yield. ^{1}H NMR (500 MHz, $CDCl_3$)

δ 7.43 (d, *J* = 9.1 Hz, 1H), 7.34 – 7.25 (m, 4H), 7.25 – 7.18 (m, 2H), 6.88 (d, *J* = 2.7 Hz, 1H), 5.75 (s, 1H), 5.06 (s, 1H), 3.81 (s, 3H), 3.80 – 3.75 (m, 2H), 3.14 (d, *J* = 4.7 Hz, 3H), 2.96 (t, *J* = 7.2 Hz, 2H). R_f = 0.29 (DCM/MeOH 10:1).

6-Bromo-*N*^{4}-methyl-*N*^{2}-phenethylquinazoline-2,4-diamine (19): 65.0 mg (0.24 mmol) 6-bromo-2-chloro-*N*-methylquinazolin-4-amine was reacted with phenethylamine and purified according to general procedure F to furnish 31.0 mg of the title compound as a beige crystalline solid in 37 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 2.2 Hz, 1H), 7.57 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 3H), 7.29 – 7.25 (m, 2H), 7.25 – 7.21 (m, 1H), 5.72 (s, 1H), 5.28 (s, 1H), 3.77 (q, *J* = 7.0 Hz, 2H), 3.11 (d, *J* = 4.6 Hz, 3H), 2.96 (t, *J* = 7.2 Hz, 2H). HRMS: m/z calculated for $C_{17}H_{18}BrN_4$ $[M+H]^+$ 357.0709; found 357.0714. R_f = 0.59 (DCM/MeOH 10:1).

***N*^{4},6-Dimethyl-*N*^{2}-phenethylquinazoline-2,4-diamine (20):** 75.0 mg (0.36 mmol) 2-chloro-*N*,6-dimethylquinazolin-4-amine was reacted with phenethylamine and purified according to general procedure F to furnish 49.0 mg of the title compound as a beige crystalline solid in 46 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.3 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.26 (d, *J* = 7.4 Hz, 2H), 7.21 (d, *J* = 6.5 Hz, 2H), 6.28 (s, 1H), 5.37 (s, 1H), 3.78 (t, *J* = 6.5 Hz 2H), 3.09 (s, 3H), 2.96 (t, *J* = 6.5 Hz, 2H), 2.34 (s, 3H). HRMS: m/z calculated for $C_{18}H_{21}N_4O$ $[M+H]^+$ 293.1761; found 293.1764. R_f = 0.34 (DCM/MeOH 10:1).

***N*^{2}-Benzyl-*N*^{4}-methyl-6-vinylquinazoline-2,4-diamine (22):** 50 mg (0.14 mmol) of *N*^{2}-benzyl-6-bromo-*N*^{4}-methylquinazoline-2,4-diamine was reacted with commercially available vinyl boronic acid dibutyl ester and purified according to procedure A to furnish 13 mg of the title compound as a yellow solid in 31% yield. ^{1}H NMR (500 MHz, methanol-d_4) δ 7.84 (d, *J* = 1.9 Hz, 1H), 7.68 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.38 (d, *J* = 6.9 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 3H), 7.21 (t, *J* = 7.3 Hz, 1H), 6.75 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.78 (d, *J* = 17.6 Hz, 1H), 5.21 (d, *J* = 11.0 Hz, 1H), 4.67 (s, 2H), 3.04 (s, 3H). HRMS: m/z calculated for $C_{18}H_{19}N_4$ $[M+H]^+$ 291.1604; found 291.1633. R_f = 0.33 (DCM/MeOH 10:1).

N^2-Benzyl-6-ethyl-N^4-methylquinazoline-2,4-diamine (23): 10 mg (0.03 mmol) of N^2-benzyl-N^4-methyl-6-vinylquinazoline-2,4-diamine was reacted with palladium on carbon in a 10 mL round bottom flask affixed with a hydrogen balloon and purified according to procedure B to furnish 7 mg of the title compound as a yellow solid in 70% yield.^{1}H NMR (500 MHz, DMSO-d_6) δ 7.67 (d, J = 8.6 Hz, 1H), 7.62 (s, 1H), 7.52 (d, J = 7.38 Hz, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.33 (d, J = 8.6 Hz, 1H), 7.25 (t, J = 7.4 Hz, 1H), 4.64 (d, J = 5.9 Hz, 2H), 2.98 (d, J = 5.2 Hz, 3H), 2.65 (q, J = 7.3 Hz, 2H), 1.31 (t, J = 7.3 Hz, 3H). HRMS: m/z calculated for $C_{18}H_{21}N_4$ $[M+H]^+$ 293.1761; found 293.1768. R_f = 0.31 (DCM/MeOH 9:1).

N^2-Benzyl-N^4-methyl-6-(prop-1-en-2-yl)quinazoline-2,4-diamine (24): 80 mg (0.23 mmol) of N^2-benzyl-6-bromo-N^4-methylquinazoline-2,4-diamine was reacted with commercially available isopentyl pinacol boronic ester and purified according to procedure A to furnish 22 mg of the title compound as a yellow solid in 31% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.05 – 7.90 (m, 3H), 7.52 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.25 (t, J = 7.4 Hz, 1H), 5.68 (s, 1H), 5.32 (s, 1H), 4.64 (d, J = 5.9 Hz, 2H), 2.99 (d, J = 5.2 Hz, 3H), 2.32 (s, 3H). HRMS: m/z calculated for $C_{19}H_{21}N_4$ $[M+H]^+$ 305.1761; found 305.1766. R_f = 0.31 (DCM/MeOH 9:1).

N^2-Benzyl-6-isopropyl-N^4-methylquinazoline-2,4-diamine (25): 10 mg (0.03 mmol) of N^2-benzyl-N^4-methyl-6-(prop-1-en-2-yl)quinazoline-2,4-diamine was reacted with palladium on carbon in a 10 mL round bottom flask affixed with a hydrogen balloon and purified according to procedure B to furnish 5 mg of the title compound as a yellow solid in 50% yield.^{1}H NMR (500 MHz, DMSO-d_6) δ 7.69 (s, 1 H), 7.57 – 7.48 (m, 4H), 7.36 (t, J = 7.4 Hz, 2H), 7.25 (t, J = 7.4 Hz, 1H), 4.64 (d, J = 5.9 Hz, 2H), 3.14 (sept, J = 6.9 Hz, 1H), 2.99 (d, J = 5.2 Hz, 3H), 1.32 (d, J = 6.9 Hz, 6H). HRMS: m/z calculated for $C_{19}H_{23}N_4$ $[M+H]^+$ 307.1917; found 307.1643. R_f = 0.28 (DCM/MeOH 9:1).

(*E*)-N^2-Benzyl-N^4-methyl-6-(pent-1-en-1-yl)quinazoline-2,4-diamine (26): 80 mg (0.23 mmol) of N^2-benzyl-6-bromo-N^4-methylquinazoline-2,4-diamine was reacted with commercially available (*E*)-1-Pentenyl pinacol boronic ester and purified according to procedure A to furnish 24 mg of the title compound

as a yellow solid in 31% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (s, 1 H), 7.65 – 7.56 (m, 2H), 7.52 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.25 (t, J = 7.4 Hz, 1H), 6.93 – 6.78 (m, 2H), 4.64 (d, J = 5.9 Hz, 2H), 2.99 (d, J = 5.2 Hz, 3H), 2.17 (td, J = 7.4, 6.7 Hz, 2H), 1.48 (sext, J=7.4 Hz, 2H), 0.95 (t, J = 7.2 Hz, 3H). HRMS: m/z calculated for $C_{21}H_{25}N_4$ $[M+H]^+$ 333.2074; found 333.2064. R_f = 0.33 (DCM/MeOH 9:1).

***N*^{2}-Benzyl-*N*^{4}-methyl-6-pentylquinazoline-2,4-diamine (27):** 11 mg (0.03 mmol) of (*E*)-*N*^{2}-benzyl-*N*^{4}-methyl-6-(pent-1-en-1-yl)quinazoline-2,4-diamine was reacted with palladium on carbon and purified according to procedure B to furnish 7 mg of the title compound as a yellow solid in 70% yield. ^{1}H NMR (500 MHz, methanol-d_4) δ 7.66 (d, J = 1.8 Hz, 1H), 7.42 (dd, J = 8.5, 1.9 Hz, 1H), 7.38 (d, J = 7.2 Hz, 2H), 7.29 (td, J = 8.5, 8.0, 2.5 Hz, 3H), 7.21 (t, J = 7.3 Hz, 1H), 4.67 (s, 2H), 3.05 (s, 3H), 2.66 (t, J = 7.7 Hz, 2H), 1.65 (p, J = 7.5 Hz, 2H), 1.41 – 1.25 (m, 4H), 0.91 (t, J = 6.9 Hz, 3H). HRMS: m/z calculated for $C_{21}H_{27}N_4$ $[M+H]^+$ 335.2230; found 335.2083.

***N*^{2}-Benzyl-6-(cyclopent-1-en-1-yl)-*N*^{4}-methylquinazoline-2,4-diamine (28):** 80 mg (0.23 mmol) of *N*^{2}-benzyl-6-bromo-*N*^{4}-methylquinazoline-2,4-diamine was reacted with commercially available 1-cyclopentenylboronic acid pinacol ester and purified according to procedure A to furnish 8 mg of the title compound as a yellow solid in 10% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, J = 8.7, 2.0 Hz, 1H), 7.49 – 7.36 (m, 7H), 7.32 (t, J = 7.4 Hz, 2H), 7.29 – 7.22 (m, 2H), 6.18 (p, J = 2.1 Hz, 1H), 5.83 (s, 1H), 4.74 (d, J = 4.9 Hz, 2H), 3.12 (d, J = 4.6 Hz, 3H), 2.74 (dp, J = 7.7, 2.4 Hz, 2H), 2.56 (tq, J = 7.5, 2.5 Hz, 2H), 2.05 (p, J = 7.5 Hz, 2H). HRMS: m/z calculated for $C_{21}H_{23}N_4$ $[M+H]^+$ 331.1917; found 331.1995. R_f = 0.33 (DCM/MeOH 9:1).

***N*^{2}-Benzyl-6-(cyclohex-1-en-1-yl)-*N*^{4}-methylquinazoline-2,4-diamine (29):** 80 mg (0.14 mmol) of *N*^{2}-benzyl-6-bromo-*N*^{4}-methylquinazoline-2,4-diamine was reacted with commercially available cyclohexenyl boronic acid and purified according to procedure A to furnish 11 mg of the title compound as a yellow solid in 14% yield. ^{1}H NMR (500 MHz, methanol-d_4) δ 7.84 (d, J = 2.0 Hz, 1H), 7.67 (dd, J = 8.7, 2.1 Hz, 1H),

7.38 (d, *J* = 7.2 Hz, 2H), 7.30 (dt, *J* = 9.9, 7.7 Hz, 3H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.18 (tt, *J* = 4.1, 1.7 Hz, 1H), 4.68 (s, 2H), 3.06 (s, 3H), 2.45 (tq, *J* = 6.4, 2.2 Hz, 2H), 2.23 (ddt, *J* = 8.4, 6.4, 3.3 Hz, 2H), 1.85 – 1.78 (m, 2H), 1.71 – 1.64 (m, 2H). HRMS: m/z calculated for $C_{22}H_{25}N_4$ $[M+H]^+$ 345.2074; found 345.2077. R_f = 0.33 (DCM/MeOH 9:1).

***N*^{2}-Benzyl-6-cyclohexyl-*N*^{4}-methylquinazoline-2,4-diamine (30):** 10 mg (0.03 mmol) of *N*^{2}-benzyl-6-(cyclohex-1-en-1-yl)-*N*^{4}-methylquinazoline-2,4-diamine was reacted with palladium on carbon and purified according to procedure B to furnish 8 mg of the title compound as a yellow solid in 80% yield. ^{1}H NMR (500 MHz, methanol-d_4) δ 7.69 (d, *J* = 1.9 Hz, 1H), 7.45 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.38 (d, *J* = 7.0 Hz, 2H), 7.29 (td, *J* = 8.3, 7.8, 2.1 Hz, 3H), 7.21 (t, *J* = 7.4 Hz, 1H), 4.67 (s, 2H), 3.05 (s, 3H), 2.56 (tt, *J* = 11.7, 3.2 Hz, 1H), 1.91 – 1.82 (m, 5H), 1.81 – 1.74 (m, 1H), 1.53 (dd, *J* = 12.4, 2.9 Hz, 1H), 1.50 – 1.45 (m, 2H), 1.43 (t, *J* = 3.3 Hz, 1H). HRMS: m/z calculated for $C_{22}H_{27}N_4$ $[M+H]^+$ 347.2230; found 347.2231. R_f = 0.32 (DCM/MeOH 9:1).

***N*^{2}-Benzyl-*N*^{4}-methyl-6-phenylquinazoline-2,4-diamine (31):** 50 mg (0.14 mmol) of *N*^{2}-benzyl-6-bromo-*N*^{4}-methylquinazoline-2,4-diamine was reacted with commercially available phenyl boronic acid and purified according to procedure A to furnish 11 mg of the title compound as a yellow solid in 22% yield. ^{1}H NMR (500 MHz, methanol-d_4) δ 8.17 (s, 1H), 7.91 – 7.85 (m, 1H), 7.68 (d, *J* = 7.7 Hz, 2H), 7.48 – 7.38 (m, 5H), 7.33 (q, *J* = 7.6 Hz, 3H), 7.24 (t, *J* = 7.5 Hz, 1H), 4.71 (s, 2H), 3.08 (s, 3H). HRMS: m/z calculated for $C_{22}H_{21}N_4$ $[M+H]^+$ 341.1761; found 341.1763. R_f = 0.36 (DCM/MeOH 10:1.

***N*^{2}-Benzyl-6-(furan-2-yl)-*N*^{4}-methylquinazoline-2,4-diamine (32):** 50 mg (0.14 mmol) of *N*^{2}-benzyl-6-bromo-*N*^{4}-methylquinazoline-2,4-diamine was reacted with commercially available 2-furyl boronic acid and purified according to procedure A to furnish 6 mg of the title compound as a yellow solid in 13% yield. ^{1}H NMR (500 MHz, methanol-d_4) δ 8.19 (d, *J* = 1.8 Hz, 1H), 7.87 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.55 (d, *J* = 1.8 Hz, 1H), 7.39 (d, *J* = 7.3 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.31 (dd, *J* = 8.5, 6.8 Hz, 2H), 7.22 (t, *J* =

7.3 Hz, 1H), 6.75 (d, J = 3.3 Hz, 1H), 6.52 (dd, J = 3.4, 1.8 Hz, 1H), 4.68 (s, 2H), 3.06 (s, 3H). HRMS: m/z calculated for $C_{20}H_{19}N_4O$ $[M+H]^+$ 331.1553; found 331.1549. R_f = 0.43 (DCM/MeOH 10:1).

Table S1. *A. baumannii* strains used in this study. Strains used in this study are listed below along with their resistance profiles and provenance. The stains were chosen based on creating a screening panel of isolates with broad spectrum of resistance and clonal diversity.

Strain ID	Identifying features	Provenance	References
1403	R=Ampicillin, Ciprofloaxacin, Gentamycin, PolymyxinB, Sulfamethoxazole, Trimethoprim, Sulfamethoxazole S= Rifampin, Chloramphenicol, Tetracycline, Imepenem	Moffitt Cancer Center	Fleeman et al. (2015)(1)
1646	R= Sulfamethoxazole, Ciprofloaxacin, Ampicillin, Trimethoprim S= Meropenem, Imipenem, Amikacin, Aztreonam, Amp-Sulbactam, Gentamycin, Piperacillin, Polymyxin B, Rifampin, Chloramphenicol, Cefepime, Cefotaxime, Ceftazidime, Ceftriaxone, Tetracycline, Tobramycin,	ATCC (1951)	Jacobs et al. (2010)(2)
1649	R= Ampicillin, Aztreonam, Cefotaxime, Sulfamethoxazole, Ceftriaxone, Tetracycline, Trimethoprim S= Amikacin, Amp-Sulbactam, Cefepime, Gentamycin, Piperacillin, Timentin, Tobramycin, Levofloxacin, Polymyxin B, Rifampin, Ciprofloxacin, Chloramphenicol	CDC (TX, 1998)	Jacobs et al. (2010)(2)
1650	R= Ampicillin, Aztreonam, Sulfamethoxazole, Tetracycline, Chloramphenicol, Trimethoprim S= Amikacin, Amp-Sulbactam, Cefepime, Gentamycin, Piperacillin, Timentin, Tobramycin, Levofloxacin, Polymyxin B, Rifampin, Ciprofloxacin, Cefotaxime, Ceftriaxone	CDC (TX, 1998)	Jacobs et al. (2010)(2)
1651	R= Ampicillin, Aztreonam, Sulfamethoxazole, Chloramphenicol, Trimethoprim S= Amikacin, Amp-Sulbactam, Cefepime, Gentamycin, Piperacillin, Timentin, Tobramycin, Levofloxacin, Polymyxin B, Rifampin, Ciprofloxacin, Cefotaxime, Ceftriaxone, Tetracycline	CDC (TX, 1998)	Jacobs et al. (2010)(2)
1652	R= Ampicillin, Aztreonam, Chloramphenicol, Sulfamethoxazole, Trimethoprim S= Imipenem, meropenem, amikacin, Amp-Sulbactam, Levofloxacin, Cefepime, Cefotaxime, Ceftazidime, Ceftriaxone, Ciprofloxacin, Gentamicin, Piperacillin, Timentin, Tobramycin	CDC (TX, 1998)	Jacobs et al. (2010)(2)

Table S2. In vitro antibacterial assessment of front runner quinazoline compounds against a library of *A. baumannii* strains. Lead quinazolines were screened for MIC, MBC_{90}, and $MBEC_{90}$ against six *A. baumannii* strains (1403, 1646, 1649, 1650, 1651 and 1652). All data is in μM.

	4	**5**	**26**	**29**	**27**	**30**	**SMX***	**TMP***
MIC								
1403	25	10	10	3	15	20	138	103
1646	0.5	1	1	2	1	2	118	34
1649	11	21	10	8	10	15	118	517
1650	12	35	25	10	10	20	118	120
1651	5	7	2	2	10	20	118	103
1652	20	20	30	30	20	20	118	103
MBC_{90}								
1403	22	30	40	22	20	32	152	103
1646	0.81	0.77	1.8	1.5	1.1	1.1	120	45
1649	4.7	9.3	10	9.1	43	33	134	>517
1650	15	27	16	16	20	22	138	157
1651	2.1	1.5	5.7	4.0	4.1	28	150	166
1652	9.7	12	23	11	23	17	124	136
$MBEC_{90}$								
1403	26	13	24	20	12	21	189	>200
1646	3.3	2.8	8.9	8.9	12	41	167	100
1649	44.33	34	63	58	62	68	175	>200
1650	9.61	21	50	48	49	46	180	>200
1651	37.34	11	24	21	18	33	192	>200
1652	> 100	68	97	77	64	>100	145	>200

*SMX, sulfamethoxazole; TMP, trimethoprim

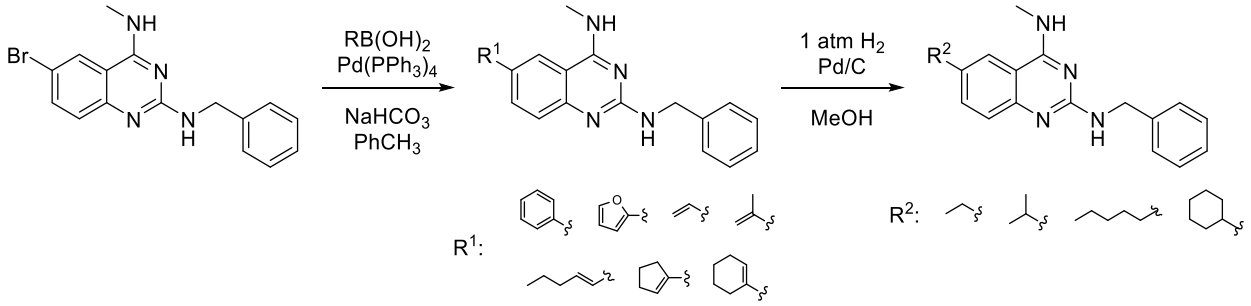

Figure S1. Synthesis of 6-aryl/vinyl/alkyl-N^2-benzyl-N^4-methylquinazolin-2,4-diamines from N^2-benzyl-6-bromo- N^4-methylquinazolin-2,4-diamine

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