Supplementary Information

Structure-Activity Relationship Studies of Isomeric 2,4-Diaminoquinazolines on β-Amyloid Aggregation Kinetics

Tarek Mohamed [a, b], Arash Shakeri [a], Gary Tin [a] and Praveen P. N. Rao [a,*]

[a] *School of Pharmacy, Health Sciences Campus, University of Waterloo, 200 University Ave. West., Waterloo, Ontario, Canada, N2L 3G1*

[b] *Department of Chemistry, University of Waterloo, 200 University Ave. West., Waterloo, Ontario, Canada, N2L 3G1*

*Corresponding author contact information: praopera@uwaterloo.ca

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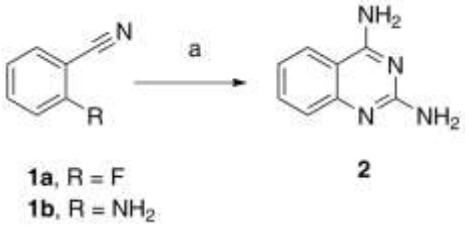
1. General information

All chemicals and reagents utilized in the synthesis were purchased from commercial sources (Sigma Aldrich and Alfa Aesar, USA) and used without further purification. Melting points were determined using a Fisher-Johns melting point apparatus and are uncorrected. ^{1}H NMR (300 MHz) and ^{13}C NMR spectra (100 MHz) were recorded on a Bruker Avance NMR spectrometer in DMSO-d_6. Coupling constants (J values) were recorded in hertz (Hz) and the following abbreviations were used to represent multiplets of NMR signals: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. Carbon multiplicities (C, CH, CH_2 and CH_3) were assigned by DEPT 90/135 experiments. High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific Q ExactiveTM mass spectrometer with an ESI source, Department of Chemistry, University of Waterloo. Compound purity was assessed (~ 95% purity) using an Agilent 6100 series single quad LCMS equipped with an Agilent 1.8 μm Zorbax Eclipse Plus C18 (2.1 x 50 mm) running 50:50 Water/ACN with 0.1% FA at a flow rate of 0.5 mL/min with detection at 254 nm by UV.

2. General procedure for synthesis of quinazoline-2,4-diamine (2)[1, 2]

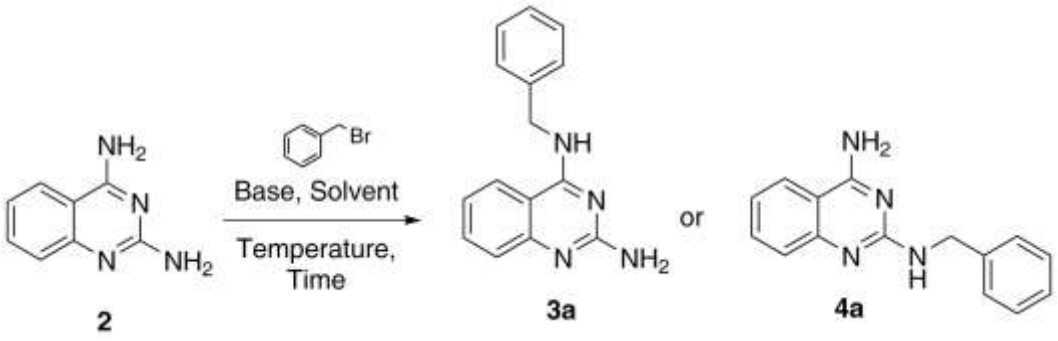


Scheme S1: Reagents and conditions: (a) DMA, guanidine carbonate, 140 °C (pressure vial), 24 h.

In a 250 mL round-bottom pressure flask, 2-fluorobenzonitrile (4.6 mL, 42.32 mmol) or 2-aminobenzonitrile (5 g, 42.32 mmol) was combined with guanidine carbonate (11.43 g, 126.96 mmol) and diluted in 30 mL dimethylacetaminde (DMA). Contents were heated in an oil bath at 150 °C overnight (~14 h) then was diluted with 50 mL of water before extracting thrice with EtOAc (50 mL x 3) and washing with brine (2 x 20 mL). Combined organic layer was dried with

$MgSO_4$ and concentrated in vacuo before purifying with silica gel column chromatography using 5:1 EtOAc/MeOH to afford an off-white solid (80% yield). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.91 (d, J = 8.1 Hz, 1H), δ 7.47 – 7.41 (m, 1H), δ 7.21 (br s, 2H), δ 7.15 (d, J = 8.1 Hz, 1H), δ 7.00 – 6.95 (m, 1H), δ 5.91 (br s, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 162.45, δ 160.75, δ 152.52, δ 132.30, δ 124.22, δ 123.52, δ 119.73, δ 110.34.

3. Table S1. The reaction conditions used for selective alkylation



Condition	Base (1 eq.)	Time	Temp.	Solvent	Yield
1	No base	24 h or 5 h	R.T or 85 °C	Methanol or DMA	20–25%
2	Pyridine				<10%
3	Methylmorpholine				<15%
4	DMAP				<15%
5	DIPEA				20–25%
6	Piperidine				N. R
7	DBU				10–15%
8	NaH	14 h	R.T	DMSO	25–31%

N. R- No reaction

4. General procedure for synthesis of N^4-substituted-quinazoline-2,4-diamines (3a-q)

In a 50 mL round-bottom flask, 2,4-diaminoquinazoline (**2**, 1 g, 6.24 mmol) was dissolved in 3 mL DMSO. With stirring and periodic cooling over ice-water, NaH (60%, 0.25 g, 6.24 mmol) was added over a 10-15 min. period. After complete addition of NaH, flask was stirred at room temperature with slow, dropwise addition of the appropriate alkyl/aryl halide (6.24 mmol) dissolved in 3 mL DMSO. Contents were allowed to stir at r.t. overnight (~14 h) before diluting with 20 mL of water and was stirred at r. t for 15 min. The mixture is extracted thrice with diethyl ether (40 mL x 3). The combined organic layers were washed twice with brine (20 mL x 2). Combined organic layer was dried with $MgSO_4$ and concentrated in vacuo before purifying with silica gel column chromatography using 5:1 EtOAc/MeOH to afford beige to off-white solid (20-31% yield). Analytical data for compounds **3a-q** are provided below:

***N^4*-Benzylquinazoline-2,4-diamine (3a)[3].** Yield: 0.48 g, 31%; Mp: 178-180 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.38 (br s, 1H), δ 8.21 (d, J = 8.2 Hz, 1H), δ 7.63 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), δ 7.39 – 7.27 (m, 5H), δ 7.25 – 7.19 (m, 2H), δ 7.14 (br s, 2H), δ 4.75 (d, J = 5.7 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.24, δ 156.96, δ 144.18, δ 138.66, δ 133.85, δ 128.27, δ 127.56, δ 126.91, δ 123.68, δ 122.46, δ 119.81, δ 110.17, δ 43.61. HRMS (ESI) m/z calcd for $C_{15}H_{15}N_4$ $[M + H]^+$ 251.1297, found 251.1289. Purity: 97.3%

***N^4*-(3-Methylbenzyl)quinazoline-2,4-diamine (3b).** Yield: 0.39 g, 24%; Mp: 117-119 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.80 (br s, 1H), δ 8.09 (d, J = 8.2 Hz, 1H), δ 7.53 (ddd, J = 8.3, 7.0, 1.3 Hz, 1H), δ 7.25 (dd, J = 8.4, 1.1 Hz, 1H), δ 7.21 – 7.05 (m, 4H), δ 7.04 – 7.01 (m, 1H), δ 6.56 (br s, 2H), δ 4.69 (d, J = 5.7 Hz, 2H), δ 2.25 (s, 3H). HRMS (ESI) m/z calcd for $C_{16}H_{17}N_4$ $[M + H]^+$ 265.1453, found 265.1446. Purity: 100%

***N*^{4}-(4-Methylbenzyl)quinazoline-2,4-diamine (3c).** Yield: 0.35 g, 21%; Mp: 113-115 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.95 (br s, 1H), δ 8.11 (d, *J* = 8.0 Hz, 1H), δ 7.56 (ddd, *J* = 8.4, 7.0, 1.3 Hz, 1H), δ 7.28 – 7.23 (m, 3H), δ 7.17 – 7.08 (m, 3H), δ 6.74 (br s, 2H), δ 4.68 (d, *J* = 5.8 Hz, 2H), δ 2.24 (s, 3H). HRMS (ESI) m/z calcd for $C_{16}H_{17}N_4$ $[M + H]^+$ m/z 265.1453, found 265.1453. Purity: 98.6%

***N*^{4}-(3-Methoxybenzyl)quinazoline-2,4-diamine (3d).** Yield: 0.35 g, 20%; Mp: 132-134 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.89 (br s, 1H), δ 8.11 (d, *J* = 8.2 Hz, 1H), δ 7.55 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), δ 7.31 – 7.06 (m, 3H), δ 6.97 – 6.87 (m, 2H), δ 6.80 – 6.77 (m, 1H), δ 6.64 (br s, 2H), δ 4.70 (d, *J* = 5.6 Hz, 2H), δ 3.69 (s, 3H). HRMS m/z calcd for $C_{16}H_{17}N_4O$ $[M + H]^+$ 281.1402, found 281.1396. Purity: 96.3%

***N*^{4}-(4-Methoxybenzyl)quinazoline-2,4-diamine (3e).** Yield: 0.44 g, 25%; Mp: 140-142 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.77 (br s, 1H), δ 8.29 (d, *J* = 8.2 Hz, 1H), δ 7.69 – 7.62 (m, 2H), δ 7.39 – 7.30 (m, 5H), δ 6.86 (d, *J* = 8.3 Hz, 2H), δ 4.68 (d, *J* = 5.7 Hz, 2H), 3.69 (s, 3H). HRMS m/z calcd for $C_{16}H_{17}N_4O$ $[M + H]^+$ 281.1402, found 281.1396. Purity: 97.3%

***N*^{4}-(3-(Trifluoromethyl)benzyl)quinazoline-2,4-diamine (3f).** Yield: 0.37 g, 19%; Mp: 104-106 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.00 (br s, 1H), δ 8.10 (d, *J* = 8.1 Hz, 1H), δ 7.75 – 7.64 (m, 2H), δ 7.61 – 7.49 (m, 3H), δ 7.27 (d, *J* = 8.2 Hz, 1H), δ 7.14 (t, *J* = 7.9 Hz, 1H), δ 6.69 (br s, 2H), δ 4.80 (d, *J* = 5.6 Hz, 2H). HRMS (ESI) m/z calcd for $C_{16}H_{14}F_3N_4$ $[M + H]^+$ 319.1171, found 319.1163. Purity: 99.5%

***N*^{4}-(4-(Trifluoromethyl)benzyl)quinazoline-2,4-diamine (3g).** Yield: 0.40 g, 20%; Mp: 110-112 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.51 (br s, 1H), δ 8.00 (d, *J* = 8.1 Hz, 1H), δ 7.65 (d, *J* = 8.1 Hz, 2H), δ 7.59 – 7.40 (m, 3H), δ 7.19 (d, *J* = 8.0 Hz, 1H), δ 7.03 (t, *J* = 7.9 Hz, 1H), δ

6.07 (br s, 2H), δ 4.77 (d, *J* = 5.9 Hz, 2H). HRMS (ESI) m/z calcd for $C_{16}H_{14}F_3N_4$ $[M + H]^+$ m/z 319.1171, found 319.1164. Purity: 99.4%

***N*^{4}-(3-Chlorobenzyl)quinazoline-2,4-diamine (3h).** Yield: 0.41 g, 23%; Mp: 117-119 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 9.12 (br s, 1H), δ 8.14 (dd, *J* = 8.3, 1.3 Hz, 1H), δ 7.59 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), δ 7.44 – 7.40 (m, 1H), δ 7.35 – 7.28 (m, 4H), δ 7.23 – 7.11 (m, 1H), δ 6.86 (br s, 2H), δ 4.73 (d, *J* = 5.4 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}ClN_4$ $[M + H]^+$ 285.0907, found 285.0900. Purity: 98.5%

***N*^{4}-(4-Chlorobenzyl)quinazoline-2,4-diamine (3i).** Yield: 0.46 g, 26%; Mp: 132-134 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 9.11 (br s, 1H), δ 8.13 (dd, *J* = 8.3, 1.3 Hz, 1H), δ 7.58 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), δ 7.44 – 7.31 (m, 4H), δ 7.28 (d, *J* = 8.3 Hz, 1H), δ 7.24 – 7.10 (m, 1H), δ 6.81 (br s, 2H), δ 4.70 (d, *J* = 5.5 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}ClN_4$ $[M + H]^+$ m/z 285.0907, found 285.0900. Purity: 96.9%

***N*^{4}-(3-Bromobenzyl)quinazoline-2,4-diamine (3j).** Yield: 0.49 g, 24%; Mp: 127-129 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 8.99 (br s, 1H), δ 8.10 (dd, *J* = 8.2, 1.4 Hz, 1H), δ 7.60 – 7.51 (m, 2H), δ 7.44 – 7.33 (m, 2H), δ 7.27 (d, *J* = 7.9 Hz, 2H), δ 7.18 – 7.10 (m, 1H), δ 6.72 (br s, 2H), δ 4.71 (d, *J* = 5.7 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}BrN_4$ $[M + H]^+$ 329.0402, found 329.0396. Purity: 97.4%

***N*^{4}-(4-Bromobenzyl)quinazoline-2,4-diamine (3k).** Yield: 0.60 g, 29%; Mp: 116-118 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 9.15 (br s, *J* = 8.1 Hz, 1H), δ 8.19 (d, *J* = 8.2 Hz, 1H), δ 7.68 – 7.62 (m, 1H), δ 7.68 – 7.62 (m, 2H), 7.35 – 7.22 (m, 4H), δ 7.02 (br s, 1H), δ 4.54 (d, *J* = 6.3 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}BrN_4$ $[M + H]^+$ 329.0402, found 329.0396. Purity: 94.6%

***N*^{4}-(3-Fluorobenzyl)quinazoline-2,4-diamine (3l).** Yield: 0.40 g, 24%; Mp: 118-120 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 8.92 (br s, 1H), δ 8.10 (dd, *J* = 8.3, 1.3 Hz, 1H), δ 7.55 (ddd, *J* =

8.3, 6.9, 1.3 Hz, 1H), δ 7.40 – 6.97 (m, 6H), δ 6.62 (br s, 2H), δ 4.72 (d, *J* = 5.6 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}FN_4$ $[M + H]^+$ 269.1202, found 269.1195. Purity: 98.7%

***N*^{4}-(4-Fluorobenzyl)quinazoline-2,4-diamine (3m).** Yield: 0.47 g, 28%; Mp: 123-125 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 9.08 (br s, 1H), δ 8.12 (d, *J* = 8.1 Hz, 1H), δ 7.58 (t, *J* = 7.6 Hz, 1H), δ 7.45 – 7.37 (m, 2H), δ 7.28 (d, *J* = 8.3 Hz, 1H), δ 7.17 – 7.08 (m, 3H), δ 6.85 (br s, 2H), δ 4.70 (d, *J* = 5.7 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}FN_4$ $[M + H]^+$ 269.1202, found 269.1195. Purity: 97.9%

***N*^{4}-Phenethylquinazoline-2,4-diamine (3n)[3].** Yield: 0.35 g, 21%; Mp: 168-170 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 9.18 (br s, 1H), δ 8.18 (d, *J* = 8.1 Hz, 1H), δ 7.70 – 7.60 (m, 1H), δ 7.36 (d, *J* = 8.3 Hz, 1H), δ 7.30 – 7.27 (m, 3H), δ 7.24 – 7.16 (m, 2H), δ 3.76 – 3.69 (m, 2H), δ 2.97 – 2.91 (m, 2H). HRMS (ESI) m/z calcd for $C_{16}H_{17}N_4$ $[M + H]^+$ 265.1453, found 265.1447. Purity: 98.8%

***N*^{4}-Propylquinazoline-2,4-diamine (3o).** Yield: 0.25 g, 20%; Mp: 121-123 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 8.09 – 7.95 (m, 2H), δ 7.47 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), δ 7.19 (dd, *J* = 8.4, 1.2 Hz, 1H), δ 7.03 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), δ 6.28 (br s, 2H), δ 3.43 – 3.36 (m, 2H), δ 1.67 – 1.55 (m, 2H), δ 0.89 (t, *J* = 7.4 Hz, 3H). HRMS (ESI) m/z calcd for $C_{11}H_{15}N_4$ $[M + H]^+$ 203.1297, found 203.1291. Purity: 100%

***N*^{4}-Isopropylquinazoline-2,4-diamine (3p).** Yield: 0.24 g, 19%; Mp: 131-133 °C; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 8.25 – 8.02 (m, 2H), δ 7.54 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), δ 7.24 (dd, *J* = 8.4, 1.1 Hz, 1H), δ 7.12 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), δ 6.72 (br s, 2H), δ 4.53 – 4.42 (m, 1H), δ 1.22 (d, *J* = 6.6 Hz, 6H). HRMS (ESI) m/z calcd for $C_{11}H_{15}N_4$ $[M + H]^+$ 203.1297, found 203.1290. Purity: 100%

***N*^{4}-(Cyclohexylmethyl)quinazoline-2,4-diamine (3q).** Yield: 0.32 g, 20%; Mp: 108-110 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.48 (br s, 1H), δ 8.12 (d, *J* = 8.2 Hz, 1H), δ 7.57 (t, *J* = 7.7 Hz, 1H), δ 7.27 (d, *J* = 8.3 Hz, 1H), δ 7.15 (t, *J* = 7.6 Hz, 1H), δ 6.82 (br s, 2H), δ 1.74 – 1.60 (m, 7H), δ 1.19 – 1.09 (m, 4H), δ 1.00 – 0.94 (m, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{21}N_4$ $[M + H]^+$ 257.1766, found 257.1758. Purity: 98.5%

5. General procedure for synthesis of *N*^{2}-substituted-quinazoline-2,4-diamines (4a-q)

In a 50 mL round-bottom flask, 2,4-diaminoquinazoline (**2**, 1 g, 6.24 mmol) was dissolved in 20 mL DMA followed by the addition of potassium carbonate (0.85 g, 6.24 mmol) and the appropriate alkyl/aryl halide (6.24 mmol) at r.t. Contents were refluxed at 85 °C for 5 h before diluting with 30 mL of water and stirring at r.t for 15 min. The mixture was extracted thrice with EtOAc (50 mL x 3). The combined organic layers were washed twice with brine (20 mL x 2). Combined organic layer was dried with $MgSO_4$ and concentrated in vacuo before purifying with silica gel column chromatography using 5:1 EtOAc/MeOH to afford beige to off-white solids (14-26% yield). Analytical data for compounds **4a-q** are provided below:

***N*^{2}-Benzylquinazoline-2,4-diamine (4a).** Yield: 0.41 g, 26%; Mp: 159-161 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.95 (d, *J* = 7.9 Hz, 1H), δ 7.47 (t, *J* = 7.5 Hz, 2H), δ 7.32 – 7.11 (m, 7H), δ 7.04 – 6.99 (t, *J* = 7.5 Hz, 1H), δ 6.78 (br s, 1H), δ 4.53 (d, *J* = 6.3 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.75, δ 159.39, δ 141.41, δ 133.22, δ 128.54, δ 127.86, δ 127.56, δ 126.82, δ 124.68, δ 124.23, δ 120.87, δ 111.07, δ 44.23. HRMS (ESI) m/z calcd for $C_{15}H_{15}N_4$ $[M + H]^+$ 251.1297, found 251.1290. Purity: 97.8%

***N*^{2}-(3-Methylbenzyl)quinazoline-2,4-diamine (4b).** Yield: 0.30 g, 18%; Mp: 104-106 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.05 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.50 (m, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.19 – 7.08 (m, 5H), 7.01 (d, *J* = 7.3 Hz, 2H), δ 6.84 (br s, 1H), 4.55 (d, *J* = 6.2 Hz,

2H), 2.24 (s, 3H). HRMS (ESI) m/z calcd for $C_{16}H_{17}N_4$ $[M + H]^+$ 265.1447, found 265.1453. Purity: 99.4%

***N*^{2}-(4-Methylbenzyl)quinazoline-2,4-diamine (4c).** Yield: 0.33 g, 20%; Mp: 109-111 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.96 (d, J = 8.1 Hz, 1H), δ 7.48 (t, J = 7.7 Hz, 2H), δ 7.24 – 7.15 (m, 4H), δ 7.10 – 6.97 (m, 4H), δ 4.49 (d, J = 6.2 Hz, 2H), δ 2.22 (s, 3H). HRMS (ESI) m/z calcd for $C_{16}H_{17}N_4$ $[M + H]^+$ 265.1453, found 265.1446. Purity: 96.6%

***N*^{2}-(3-Methoxybenzyl)quinazoline-2,4-diamine (4d).** Yield: 0.29 g , 17%; Mp: 147-149 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.98 (d, J = 8.1 Hz, 1H), δ 7.53 (t, J = 7.8 Hz, 1H), δ 7.25 – 7.18 (m, 3H), δ 7.07 (t, J = 7.5 Hz, 2H), δ 6.90 – 6.87 (m, 2H), δ 6.75 – 6.71 (m, 2H), δ 4.53 (d, J = 6.3 Hz, 2H), δ 3.70 (s, 3H). HRMS (ESI) m/z calcd for $C_{16}H_{17}N_4O$ $[M + H]^+$ 281.1402, found 281.1396. Purity: 97.0%

***N*^{2}-(4-Methoxybenzyl)quinazoline-2,4-diamine (4e).** Yield: 0.36 g, 21%; Mp: 139-141 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.03 (d, J = 8.1 Hz, 1H), δ 7.54 – 7.10 (m, 8H), δ 6.85 – 6.81 (m, 2H), δ 4.48 (d, J = 6.0 Hz, 2H), δ 3.68 (d, J = 1.3 Hz, 3H). HRMS (ESI) m/z calcd for $C_{16}H_{17}N_4O$ $[M + H]^+$ 281.1402, found 281.1396. Purity: 95.6%

***N*^{2}-(3-(Trifluoromethyl)benzyl)quinazoline-2,4-diamine (4f).** Yield: 0.30 g, 15%; Mp: 118-120 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.00 (d, J = 8.1 Hz, 1H), δ 7.69 – 7.62 (m, 3H), δ 7.55 – 7.47 (m, 5H), δ 7.24 (d, J = 8.3 Hz, 1H), δ 7.08 (d, J = 7.1 Hz, 1H), δ 4.63 (d, J = 6.2 Hz, 2H). HRMS (ESI) m/z calcd for $C_{16}H_{14}F_3N_4$ $[M + H]^+$ 319.1171, found 319.1163. Purity: 99.0%

***N*^{2}-(4-(Trifluoromethyl)benzyl)quinazoline-2,4-diamine (4g).** Yield: 0.32 g, 16%; Mp: 124-126 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.98 (d, J = 8.2 Hz, 1H), δ 7.63 (d, J = 8.1 Hz, 3H), δ 7.53 (d, J = 8.2 Hz, 4H), δ 7.24 (d, J = 8.3 Hz, 2H), δ 7.08 (d, J = 8.2 Hz, 1H), δ 4.62 (d, J = 6.2

Hz, 2H). HRMS (ESI) m/z calcd for $C_{16}H_{14}F_3N_4$ $[M + H]^+$ 319.1171, found 319.1164. Purity: 93.7%

***N*^{2}-(3-Chlorobenzyl)quinazoline-2,4-diamine (4h).** Yield: 0.28 g, 16%; Mp: 121-123 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.95 (d, J = 7.9 Hz, 1H), δ 7.46 (t, J = 7.9 Hz, 1H), δ 7.36 (s, 1H), δ 7.32 – 7.21 (m, 6H), δ 7.01 (t, J = 7.9 Hz, 2H), δ 4.52 (d, J = 6.2 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}ClN_4$ $[M + H]^+$ 285.0907, found 285.0900. Purity: 99.3%

***N*^{2}-(4-Chlorobenzyl)quinazoline-2,4-diamine (4i).** Yield: 0.34 g, 19%; Mp: 128-130 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.95 (d, J = 9.0 Hz, 1H), δ 7.47 (t, J = 7.9 Hz, 1H), δ 7.36 – 7.21 (m, 7H), δ 7.02 (t, J = 7.9 Hz, 2H), δ 4.51 (d, J = 6.3 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}ClN_4$ [M + H]+ 285.0907, found 285.0900. Purity: 96.7%

***N*^{2}-(3-Bromobenzyl)quinazoline-2,4-diamine (4j).** Yield: 0.43 g, 21%; Mp: 108-110 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.94 (d, J = 9.0 Hz, 1H), δ 7.51– 7.45 (m, 2H), δ 7.38 – 7.31 (m, 3H), δ 7.25 – 7.19 (m, 3H), δ 7.00 (t, J = 7.9 Hz, 2H), δ 4.51 (d, J = 6.4 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}BrN_4$ $[M + H]^+$ 329.0402, found 329.0395. Purity: 96.7%

***N*^{2}-(4-Bromobenzyl)quinazoline-2,4-diamine (4k).** Yield: 0.46 g, 22%; Mp: 119-121 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.98 (d, J = 8.2 Hz, 1H), δ 7.51 – 7.44 (m, 4H), δ 7.29 – 7.22 (m, 4H), δ 7.14 – 7.00 (m, 2H), δ 4.50 (d, J = 6.3 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}BrN_4$ $[M + H]^+$ 329.0396, found 329.0402. Purity: 97.3%

***N*^{2}-(3-Fluorobenzyl)quinazoline-2,4-diamine (4l).** Yield: 0.33 g, 20%; Mp: 138-140 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.95 (d, J = 7.9 Hz, 1H), δ 7.46 (t, J = 7.9 Hz, 1H), δ 7.34 – 7.27 (m, 2H), 7.23 – 6.95 (m, 7H), δ 4.54 (d, J = 6.3 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}FN_4$ $[M + H]^+$ 269.1202, found 269.1195. Purity: 97.1%

***N*^{2}-(4-Fluorobenzyl)quinazoline-2,4-diamine (4m).** Yield: 0.34 g, 20%; Mp: 144-146 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.97 (d, *J* = 8.1 Hz, 1H), δ 7.47 (t, *J* = 7.7 Hz, 2H), δ 7. 38 – 7.33 (m, 3H), δ 7.22 (d, *J* = 8.4 Hz, 1H), δ 7.11 – 7.02 (m, 4H), δ 4.51 (d, *J* = 6.1 Hz, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{14}FN_4$ $[M + H]^+$ 269.1202, found 269.1195. Purity: 97.5%

***N*^{2}-Phenethylquinazoline-2,4-diamine (4n).** Yield: 0.31 g, 19%; Mp: 151-153 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.90 (d, *J* = 8.1 Hz, 1H), δ 7.42 (t, *J* = 7.1 Hz, 1H), δ 7.37 – 7.17 (m, 8H), δ 6.97 (*t* = 7.1 Hz, 1H), δ 6.35 (br s, 1H), δ 3.63 – 3.56 (m, 2H), δ 2.88 (t, *J* = 7.4 Hz, 2H). HRMS (ESI) m/z calcd for $C_{16}H_{16}N_4$ $[M + H]^+$ 265.1447, found 265.1446. Purity: 97.3%

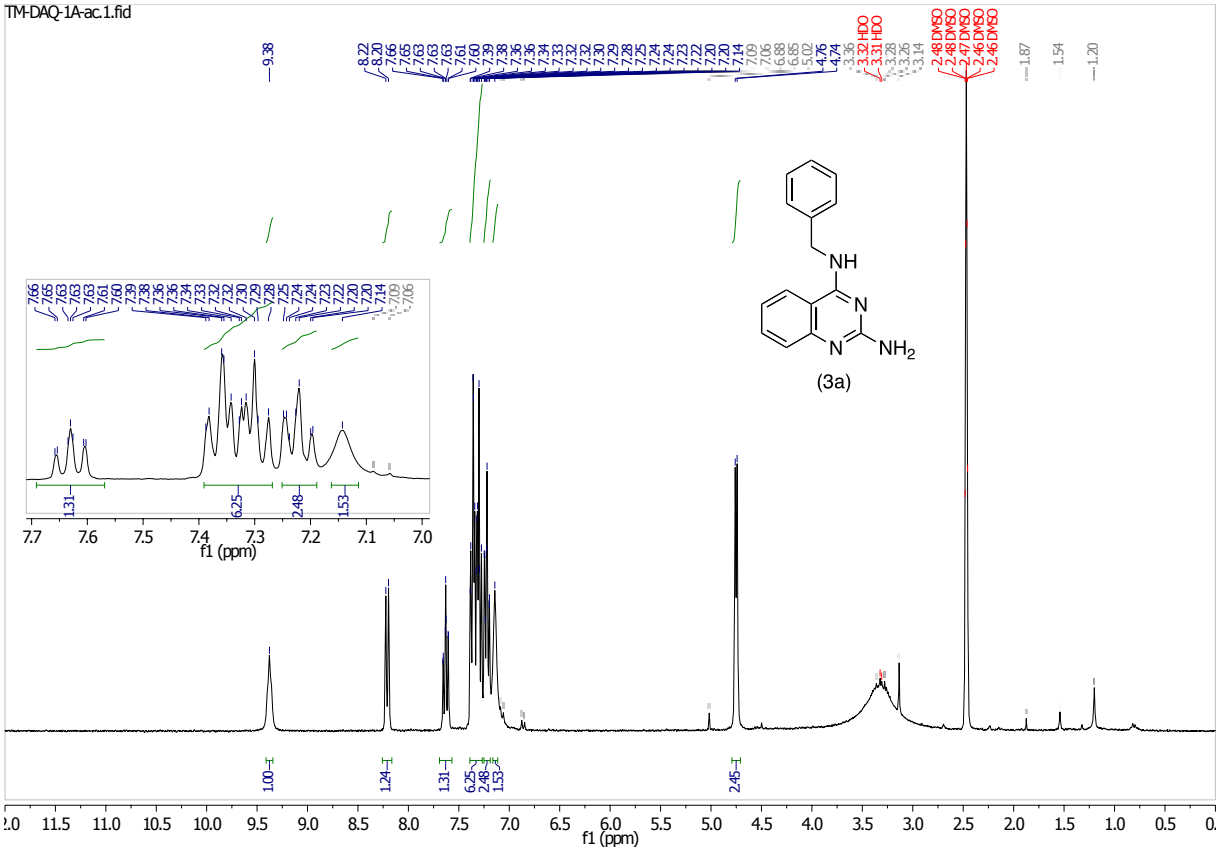
***N*^{2}-Propylquinazoline-2,4-diamine (4o).** Yield: 0.20 g, 16%; Mp: 159-161 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.04 (d, *J* = 8.2 Hz, 1H), δ 7.57 (d, *J* = 7.1 Hz, 2H), δ 7.33 (d, *J* = 8.4 Hz, 2H), δ 7.16 – 7.12 (m, 2H), δ 3.32 – 3.26 (m, 2H), δ 1.59 – 1.47 (m, 2H), δ 0.85 (t, *J* = 7.4 Hz, 3H). HRMS (ESI) m/z calcd for $C_{11}H_{15}N_4$ $[M + H]^+$ 203.1297, found 203.1291. Purity: 97.8%

***N*^{2}-Isopropylquinazoline-2,4-diamine (4p).** Yield: 0.18 g, 14%; Mp: 127-129 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.05 (d, *J* = 8.1 Hz, 1H), δ 7.58 (t, *J* = 7.7 Hz, 2H), δ 7.33 (d, *J* = 8.4 Hz, 2H), δ 7.14 (t, *J* = 7.7 Hz, 2H), δ 4.22 – 4.10 (m, 1H), δ 1.15 (d, *J* = 6.5 Hz, 6H). HRMS (ESI) m/z calcd for $C_{11}H_{15}N_4$ $[M + H]^+$ 203.1297, found 203.1291. Purity: 98.3%

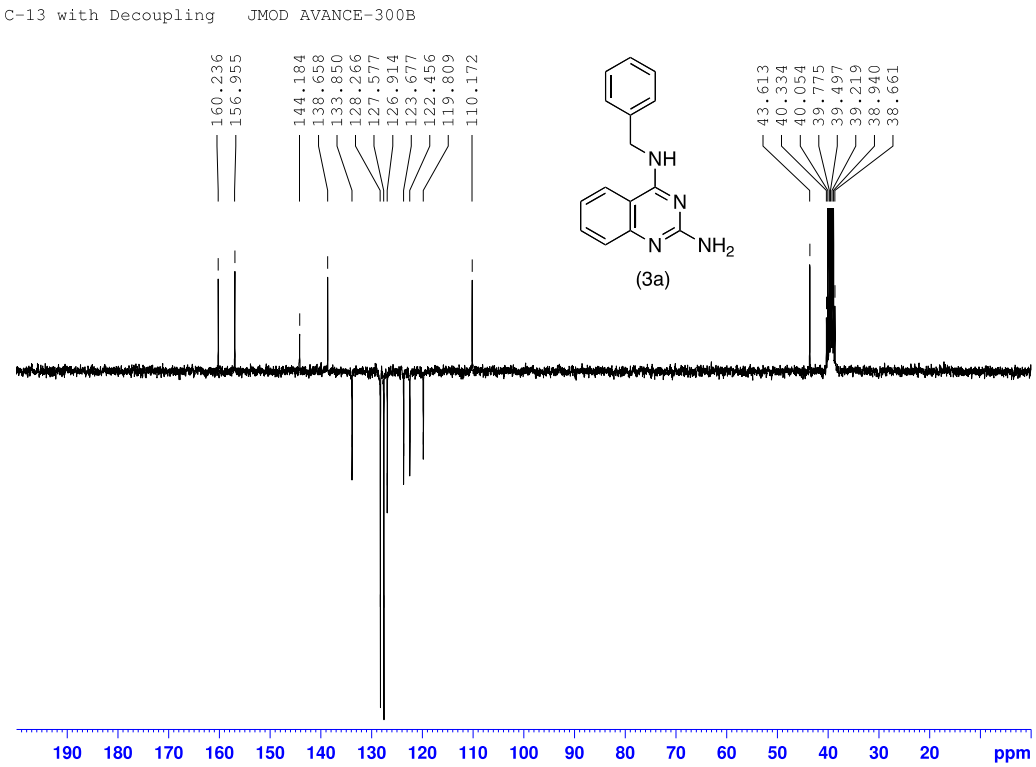
***N*^{2}-(Cyclohexylmethyl)quinazoline-2,4-diamine (4q).** Yield: 0.40 g, 25%; Mp: 193-195 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.05 – 8.94 (m, 1H), δ 8.17 (d, *J* = 8.1 Hz, 2H), δ 7.74 (t, *J* = 7.7 Hz, 2H), δ 7.34 (t, *J* = 7.7 Hz, 2H), δ 1.69 – 1.50 (m, 6H), δ 1.20 – 1.08 (m, 5H), δ 0.98 – 0.87 (m, 2H). HRMS (ESI) m/z calcd for $C_{15}H_{21}N_4$ $[M + H]^+$ 257.1766, found 257.1759 Purity: 97.4%

6. NMR spectra for compounds **3a-q**

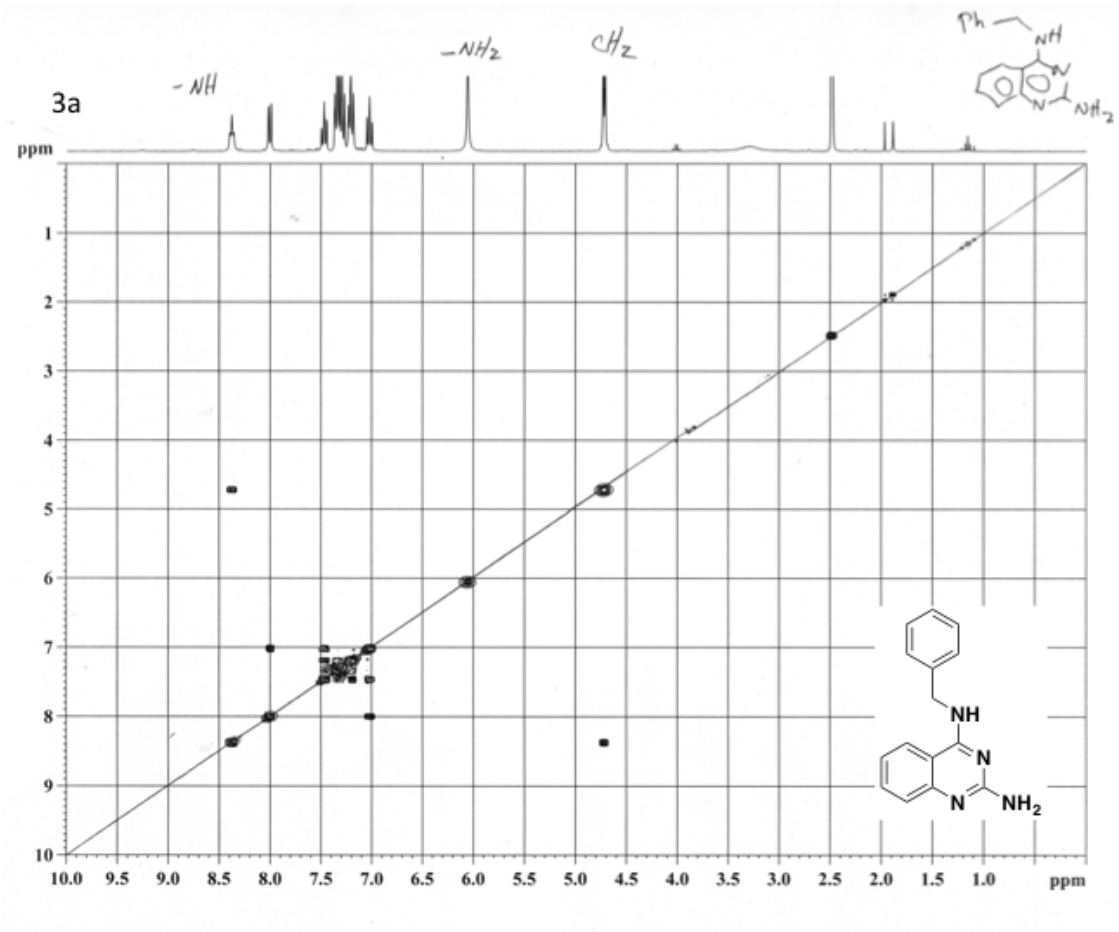
N^4-benzylquinazoline-2,4-diamine (3a)



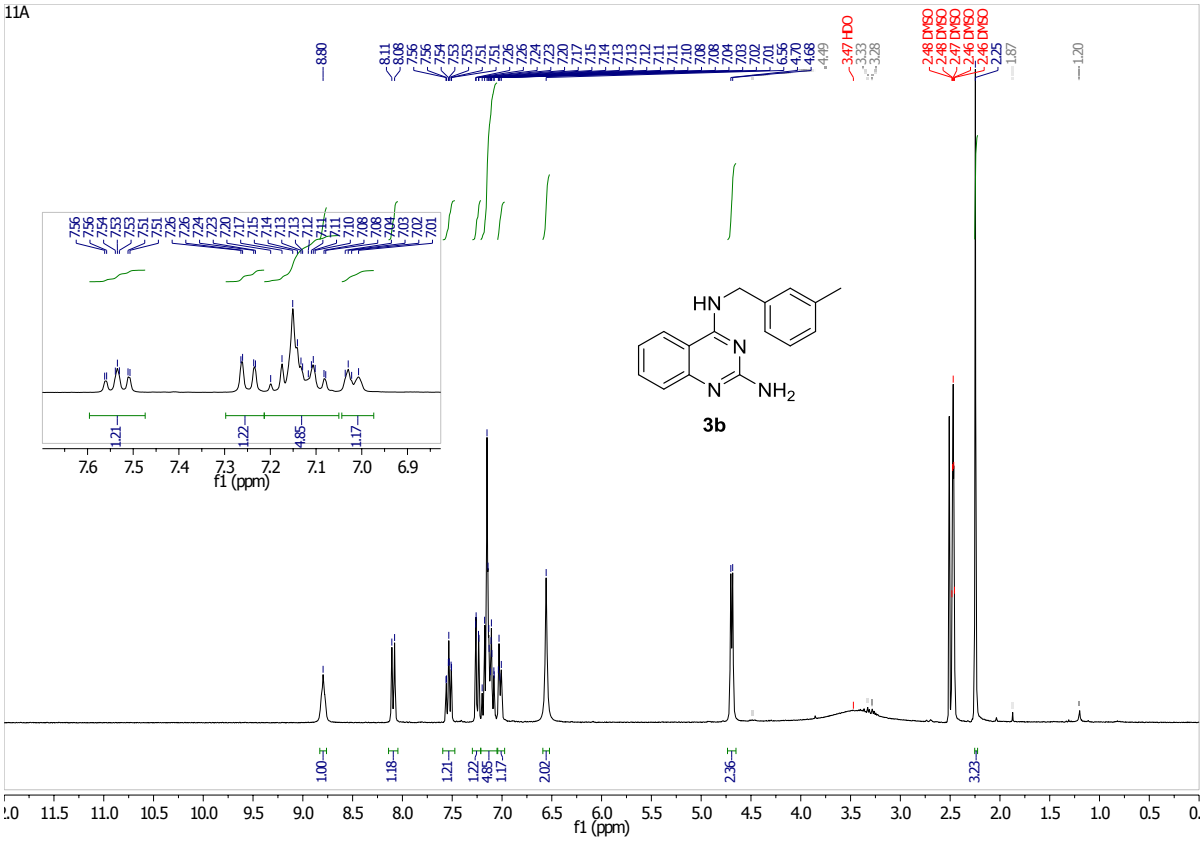
N^4-benzylquinazoline-2,4-diamine (3a)



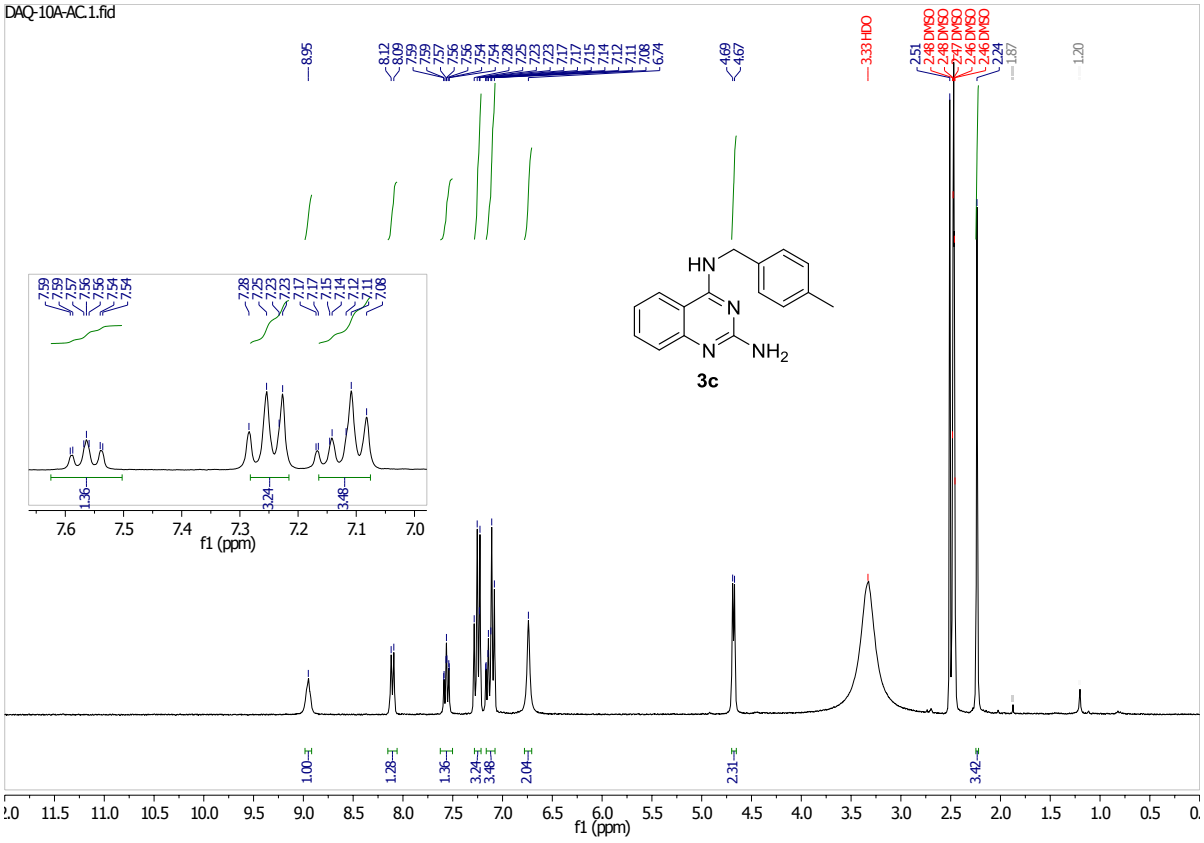
COSY spectra: N^4-benzylquinazoline-2,4-diamine (3a)



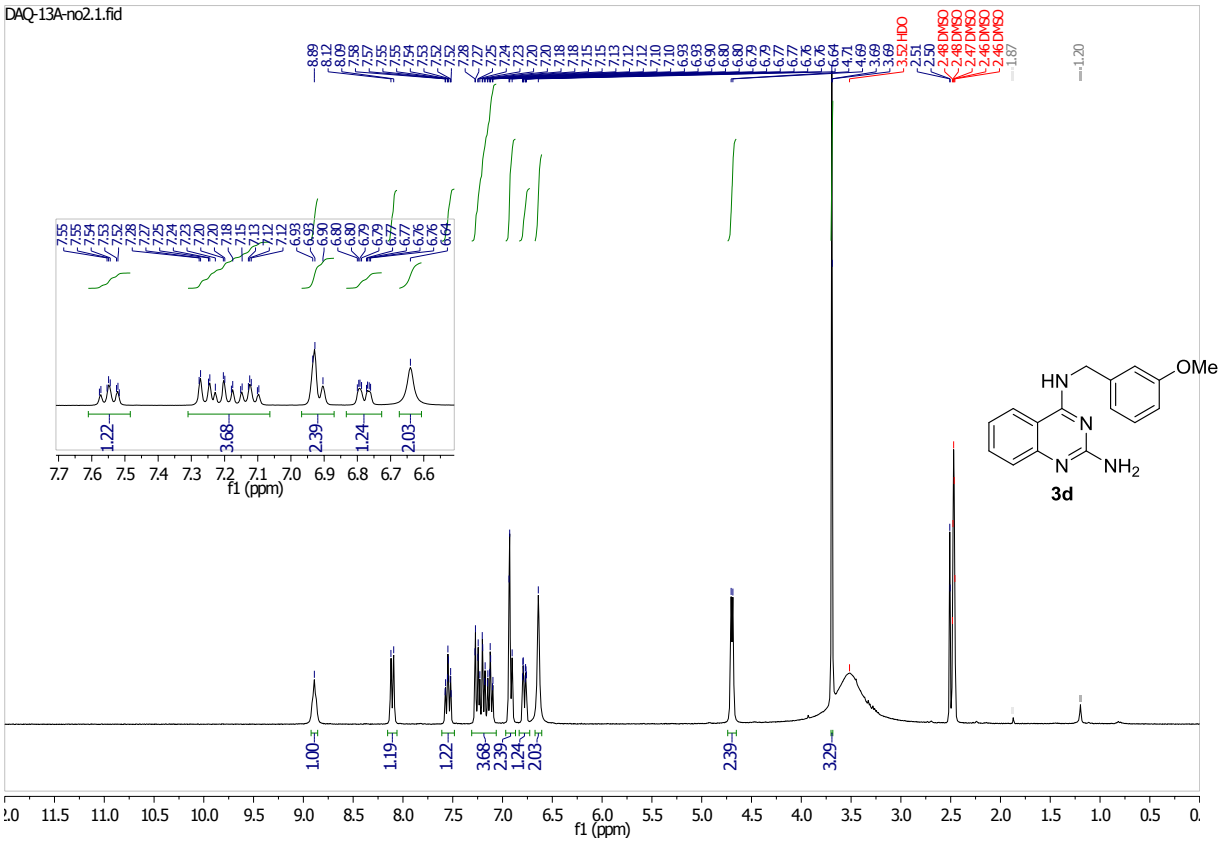
N^4-(3-methylbenzyl)quinazoline-2,4-diamine (3b)



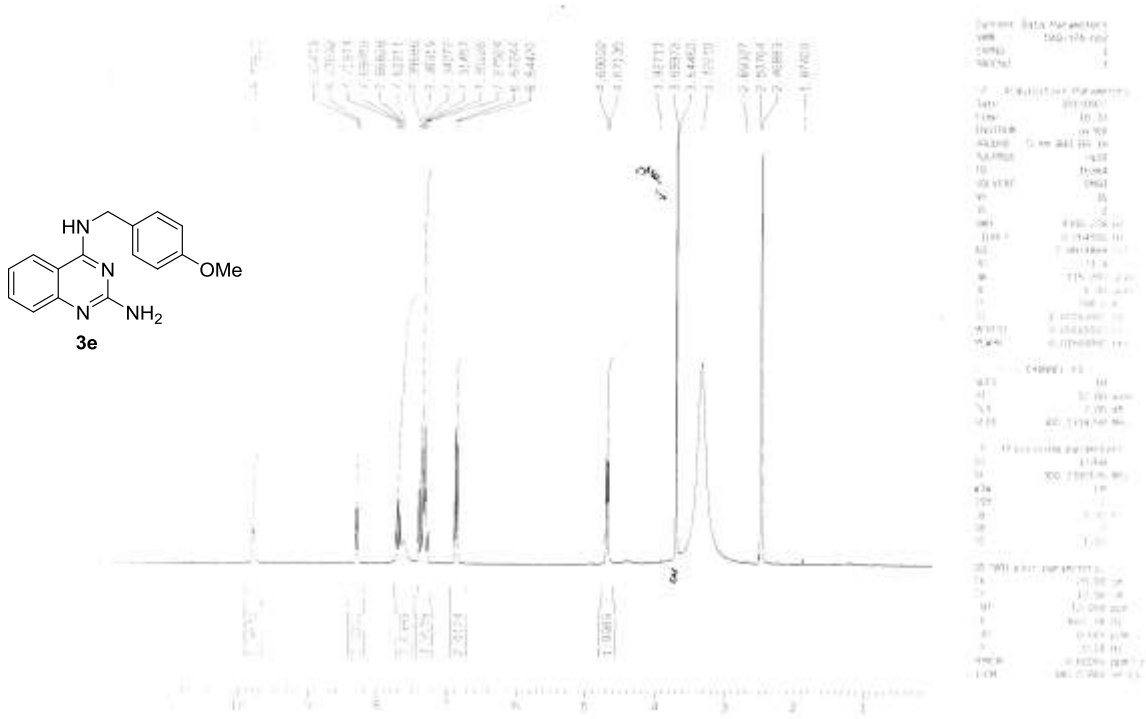
N^4-(4-methylbenzyl)quinazoline-2,4-diamine (3c)



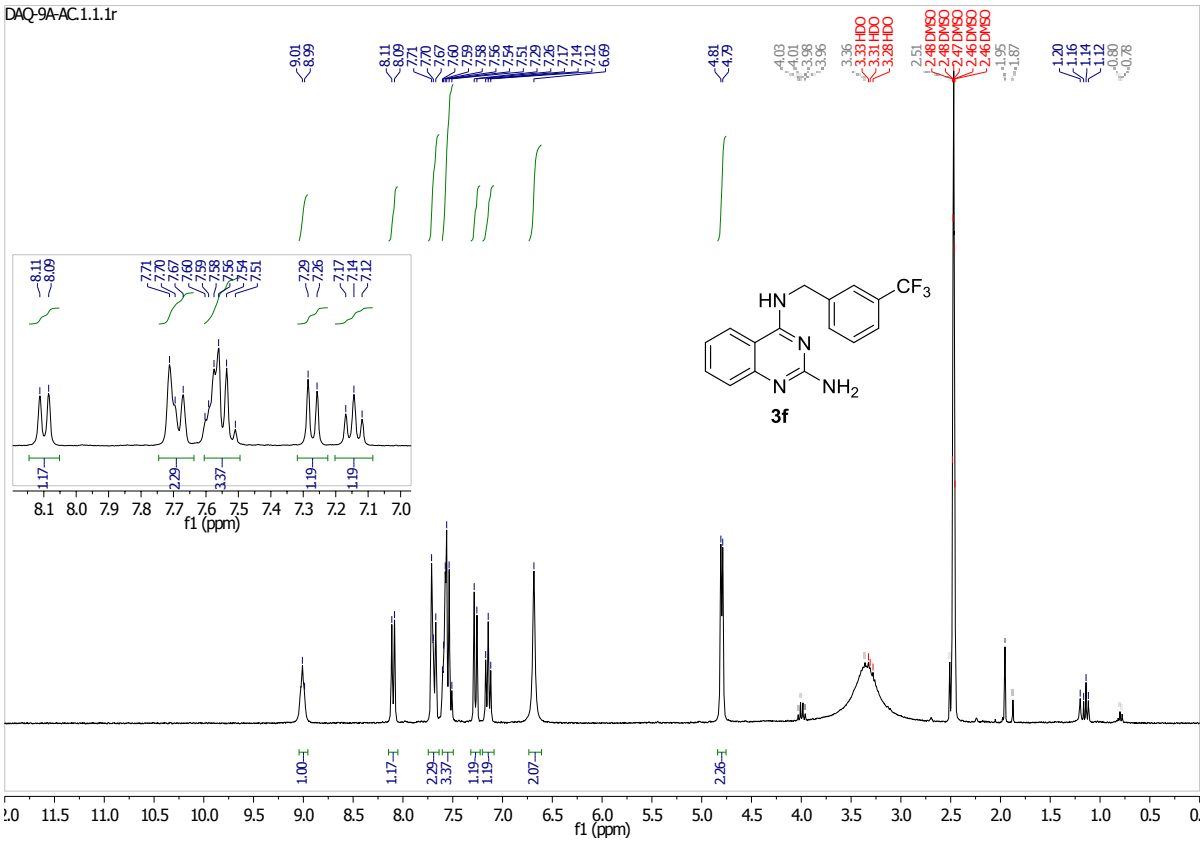
N^4-(3-methoxylbenzyl)quinazoline-2,4-diamine (3d)



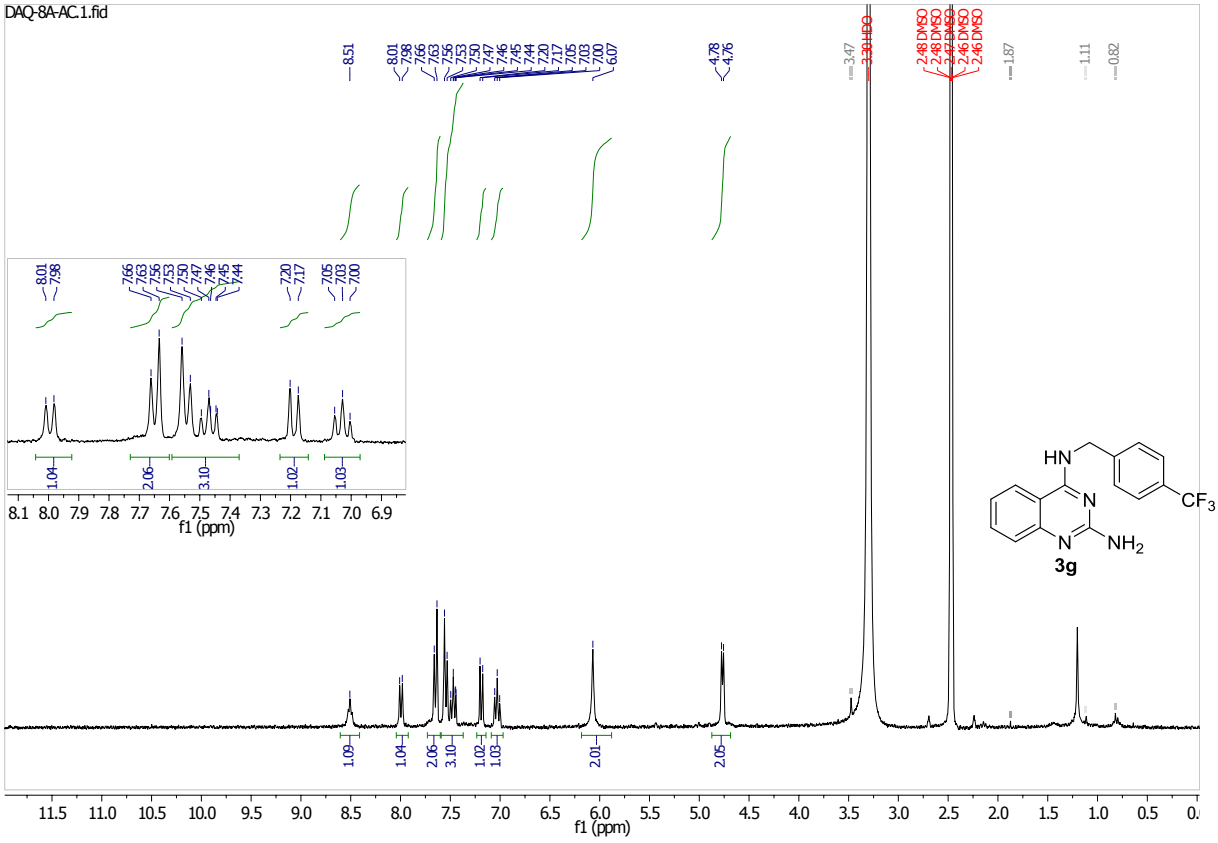
N^4-(4-methoxylbenzyl)quinazoline-2,4-diamine (3e)



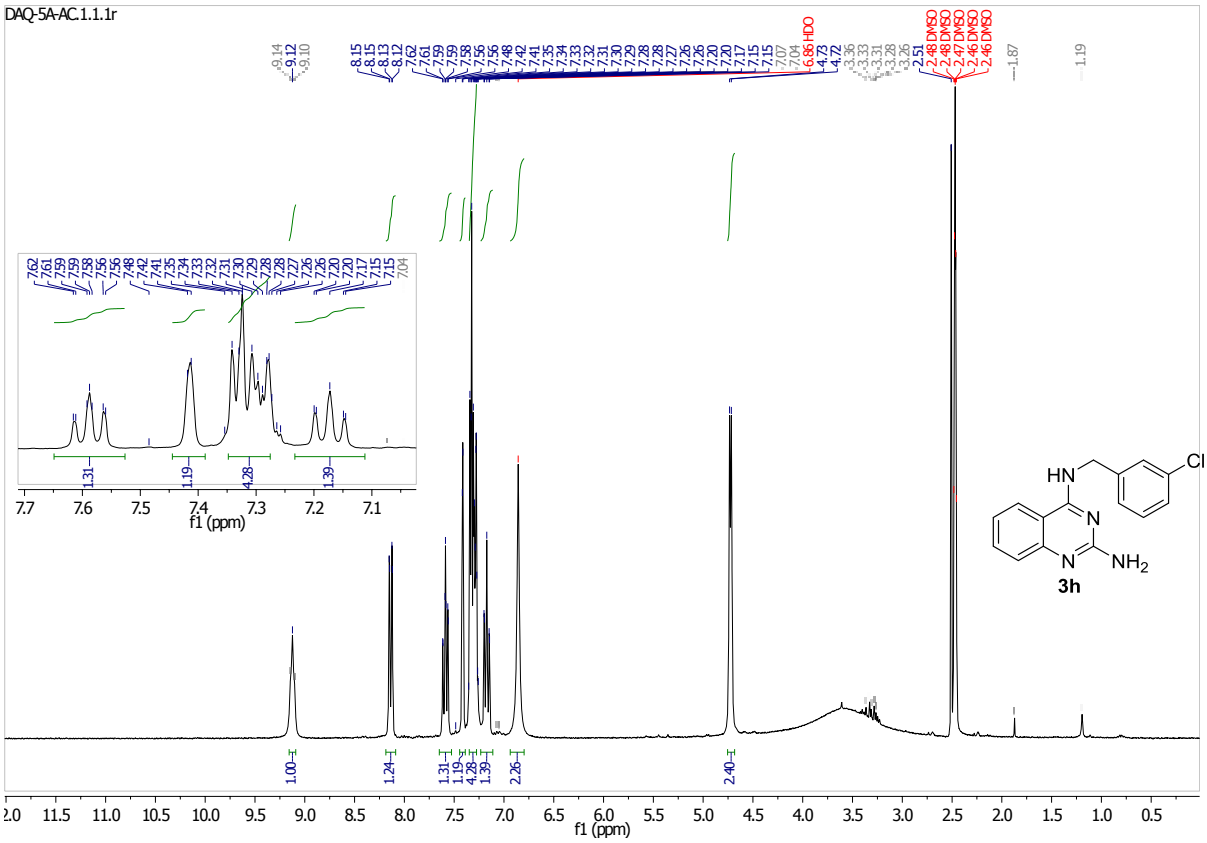
N^4-(3-trifluoromethylbenzyl)quinazoline-2,4-diamine (3f)



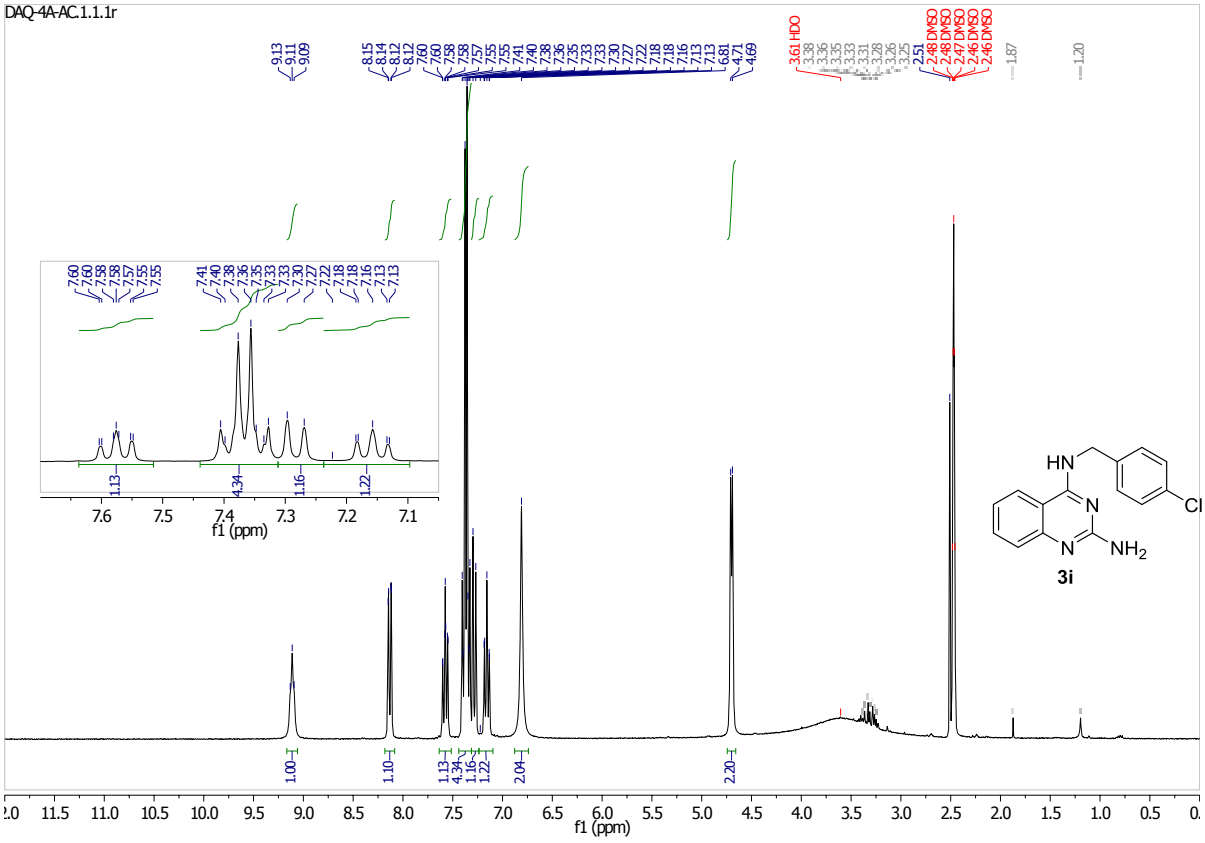
N^4-(4-trifluoromethylbenzyl)quinazoline-2,4-diamine (3g)



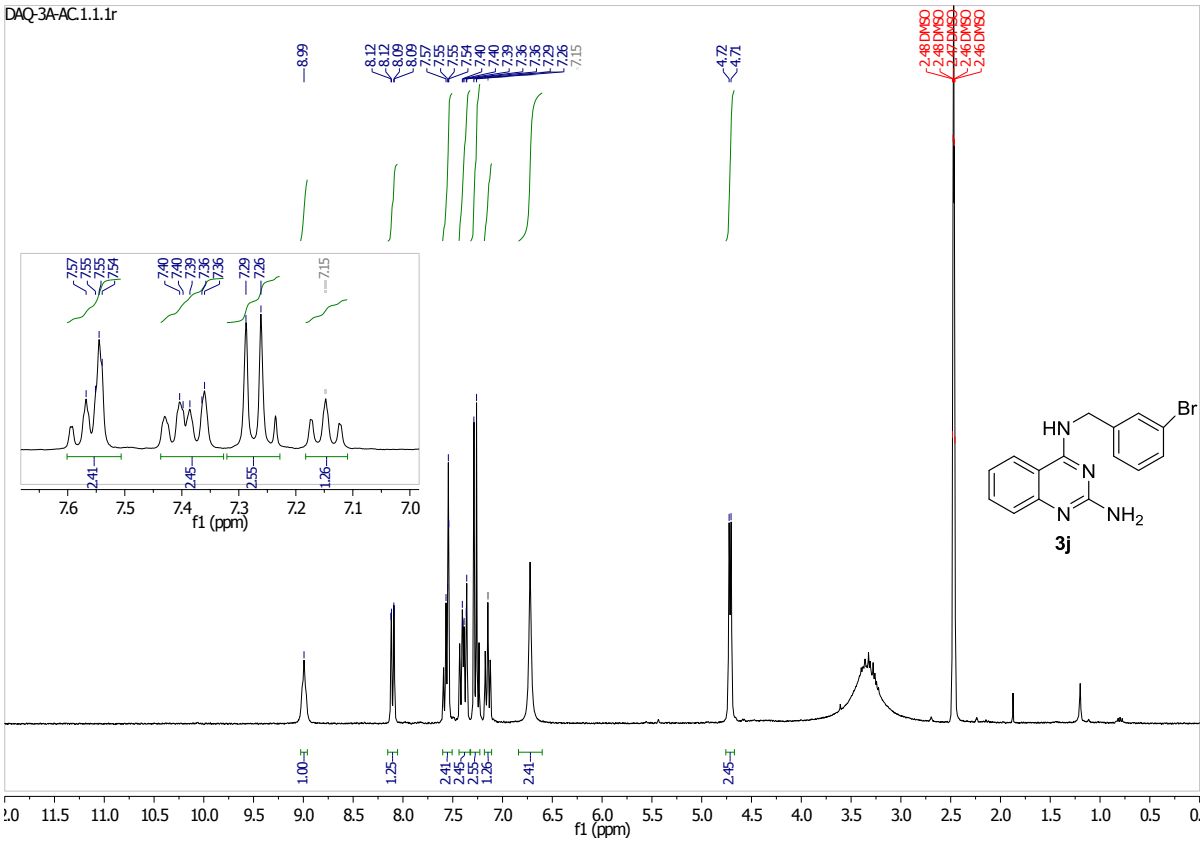
N^4-(3-chlorobenzyl)quinazoline-2,4-diamine (3h)



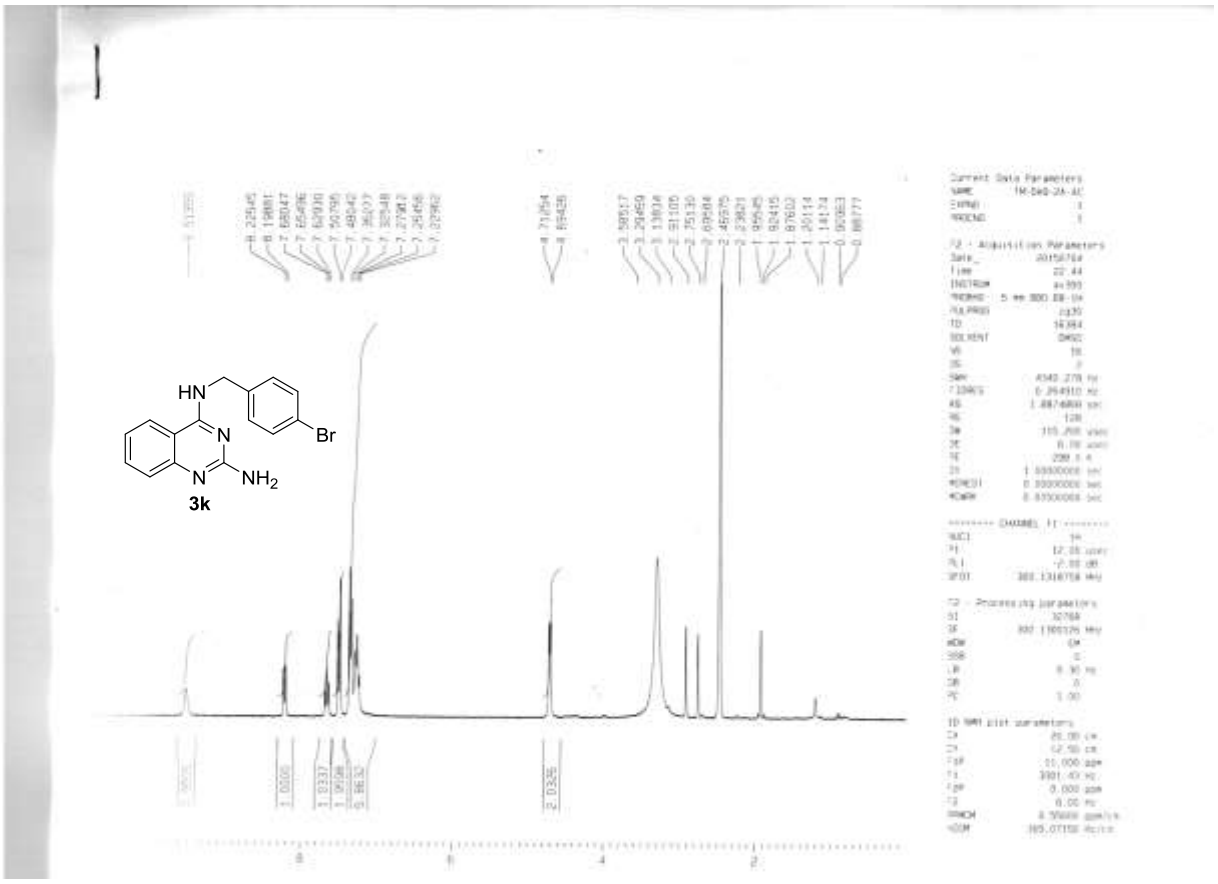
N^4-(4-chlorobenzyl)quinazoline-2,4-diamine (3i)



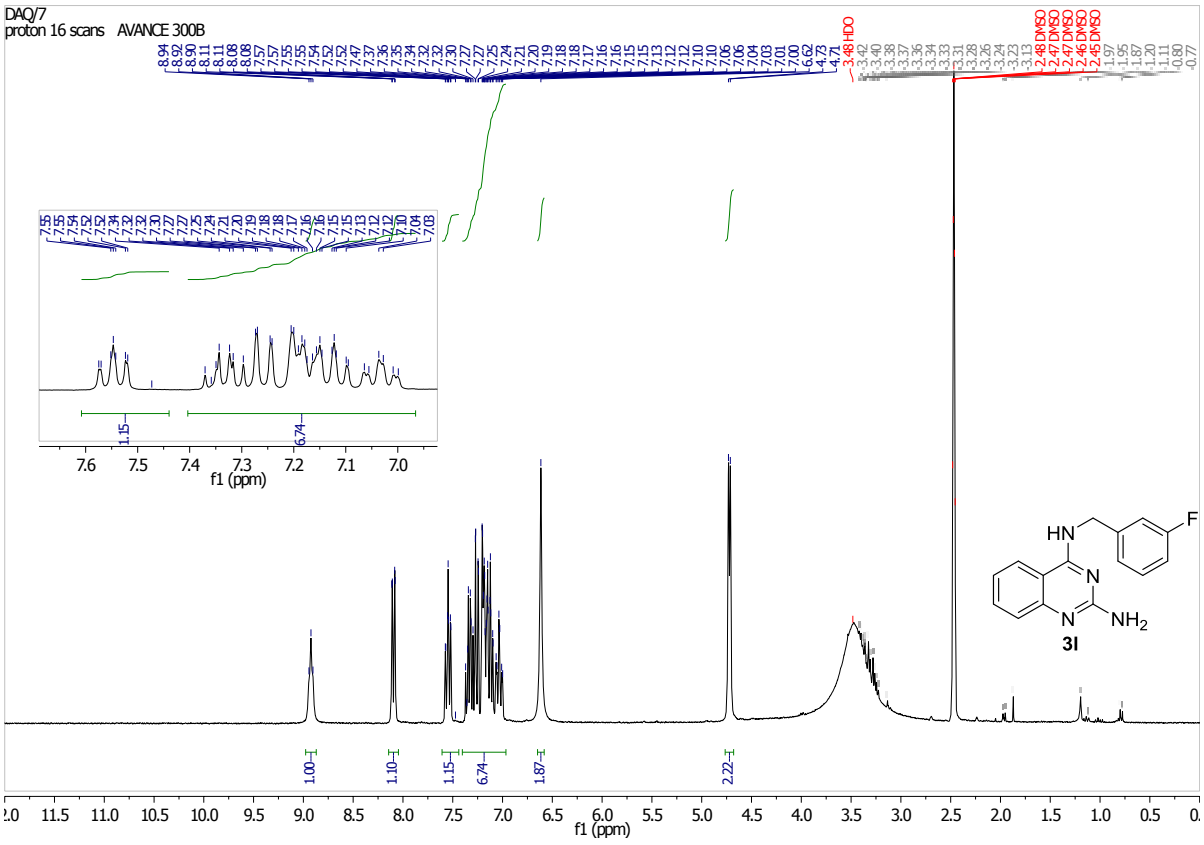
N^4-(3-bromobenzyl)quinazoline-2,4-diamine (3j)



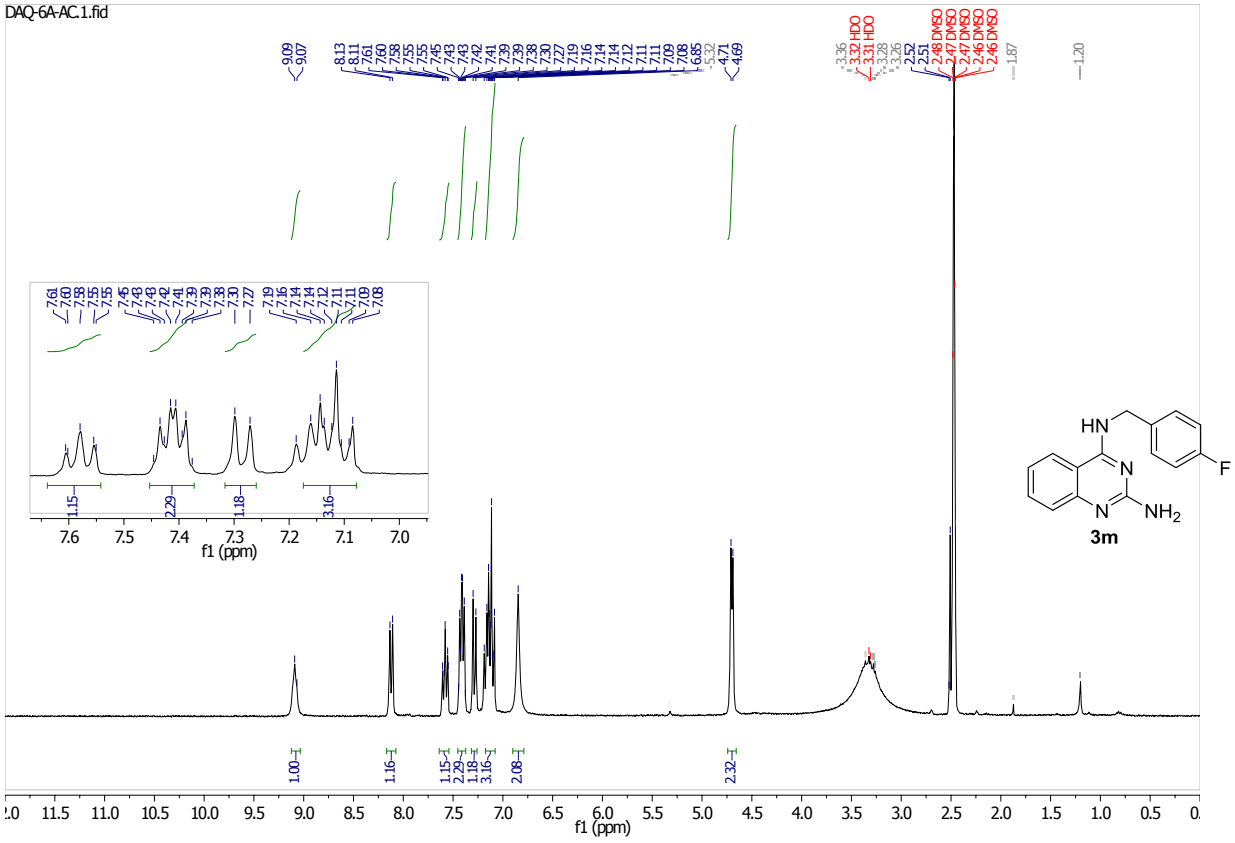
N^4-(4-bromobenzyl)quinazoline-2,4-diamine (3k)



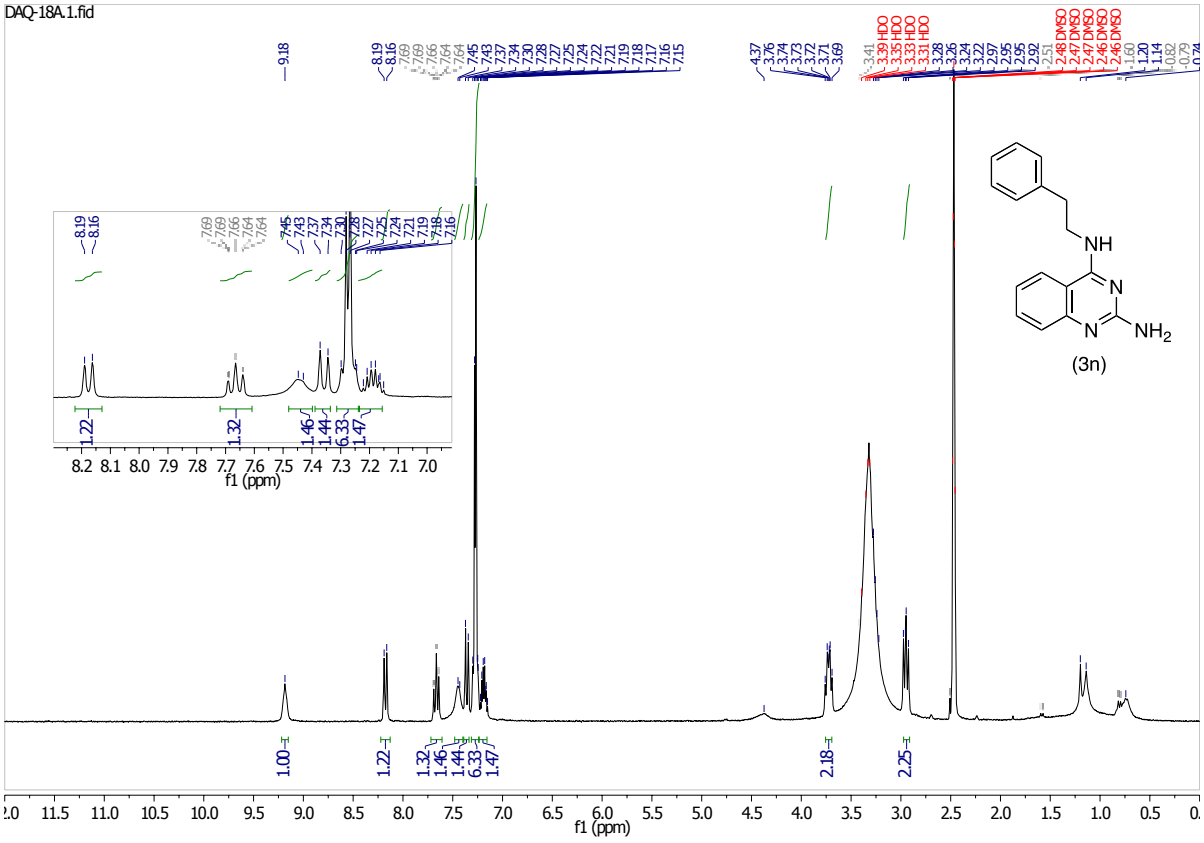
N^4-(3-fluorobenzyl)quinazoline-2,4-diamine (3l)



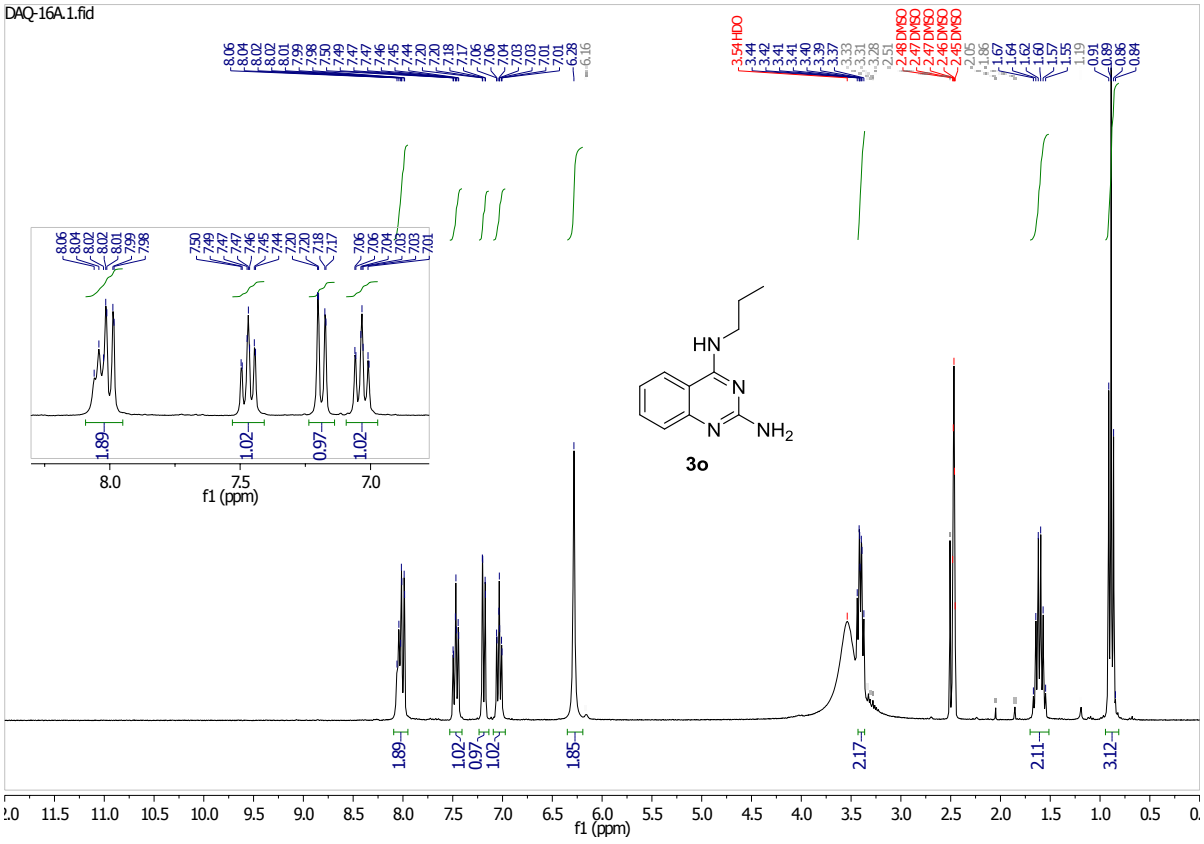
N^4-(4-fluorobenzyl)quinazoline-2,4-diamine (3m)



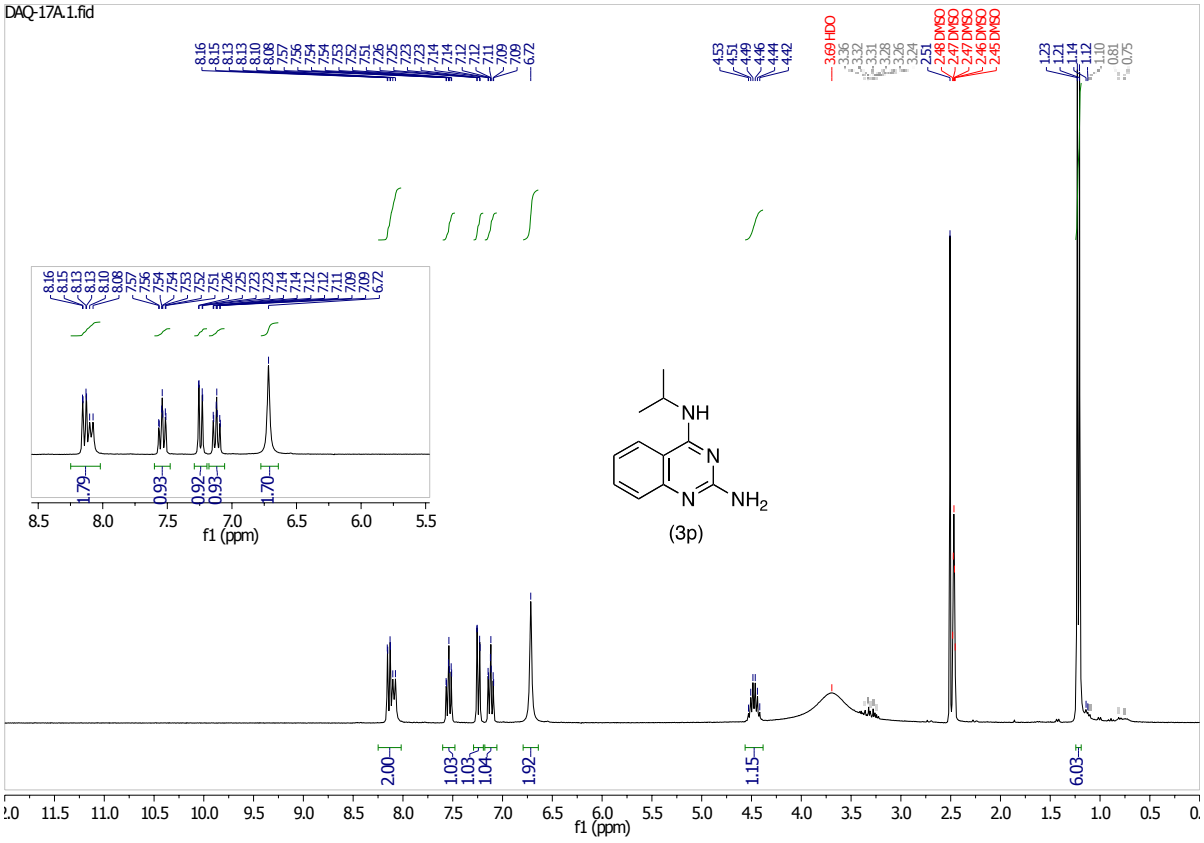
N^4-phenethylquinazoline-2,4-diamine (3n)



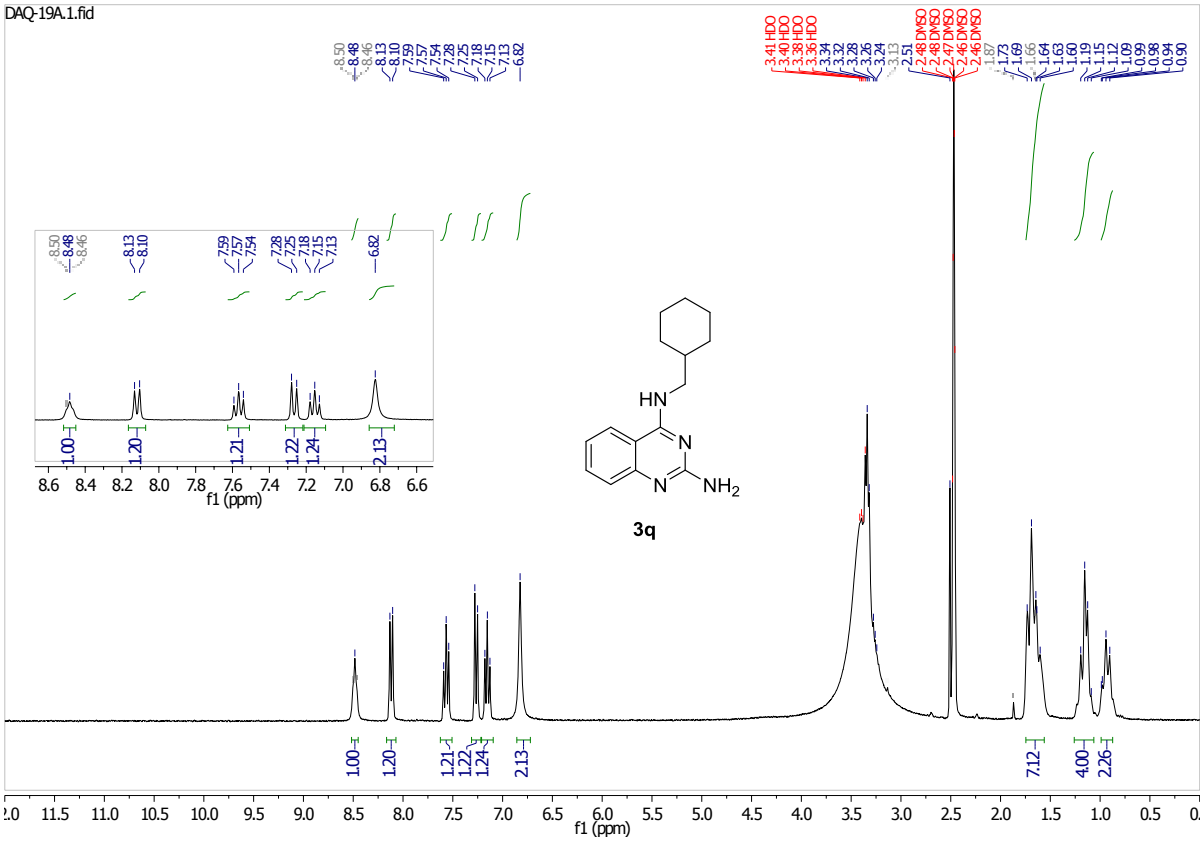
N^4-propylquinazoline-2,4-diamine (3o)



N^4-isopropylquinazoline-2,4-diamine (3p)

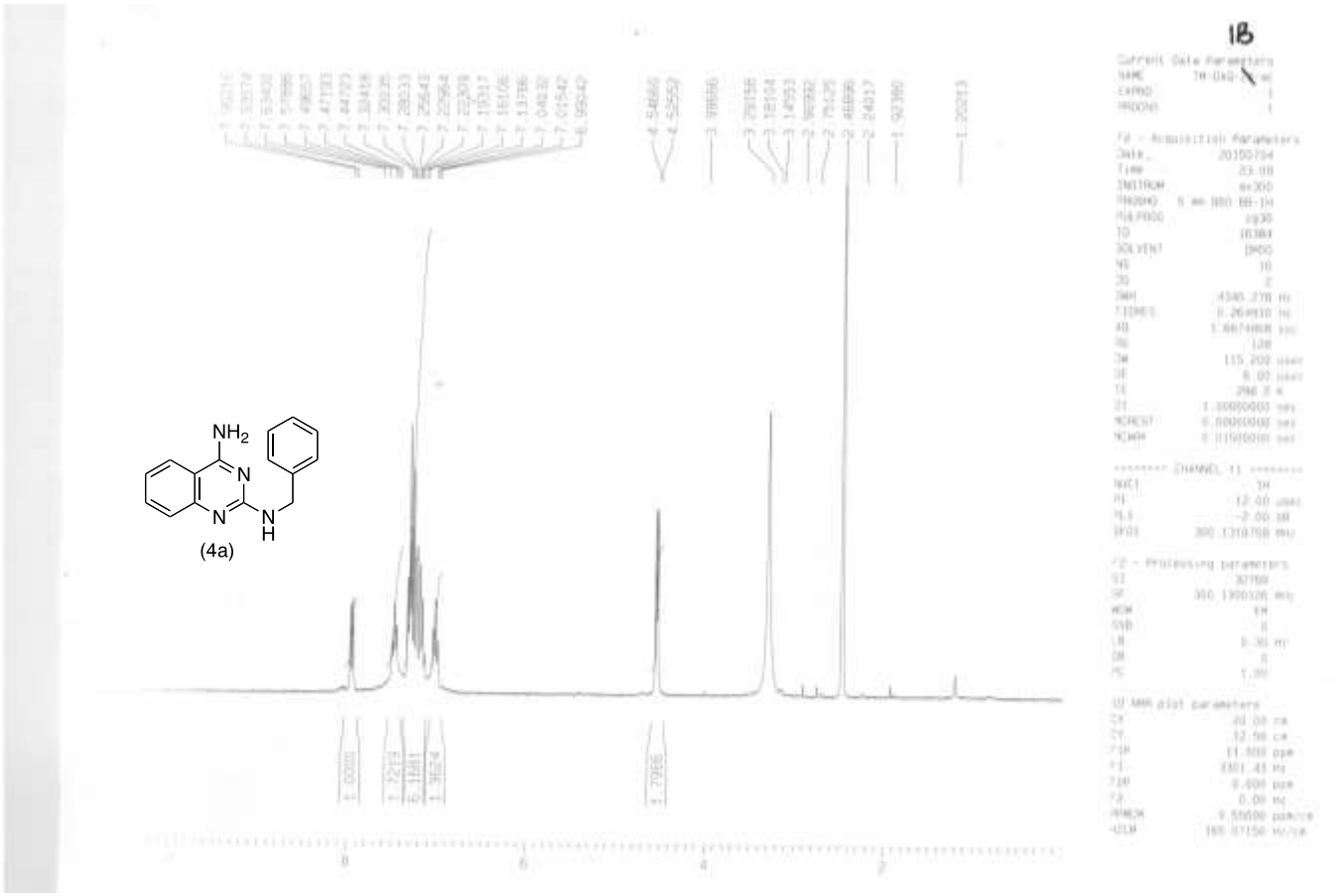


N^4-(cyclohexylmethyl) quinazoline-2,4-diamine (3q)

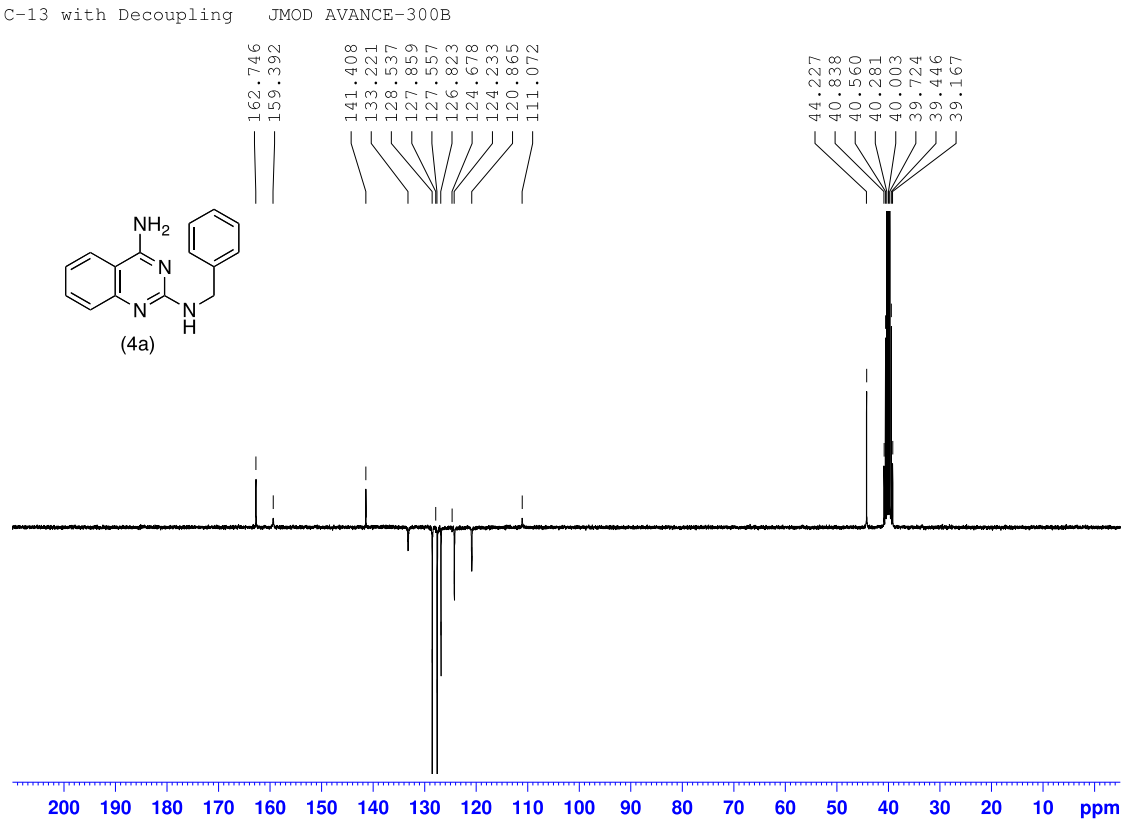


7. NMR spectra for compounds **4a-q**

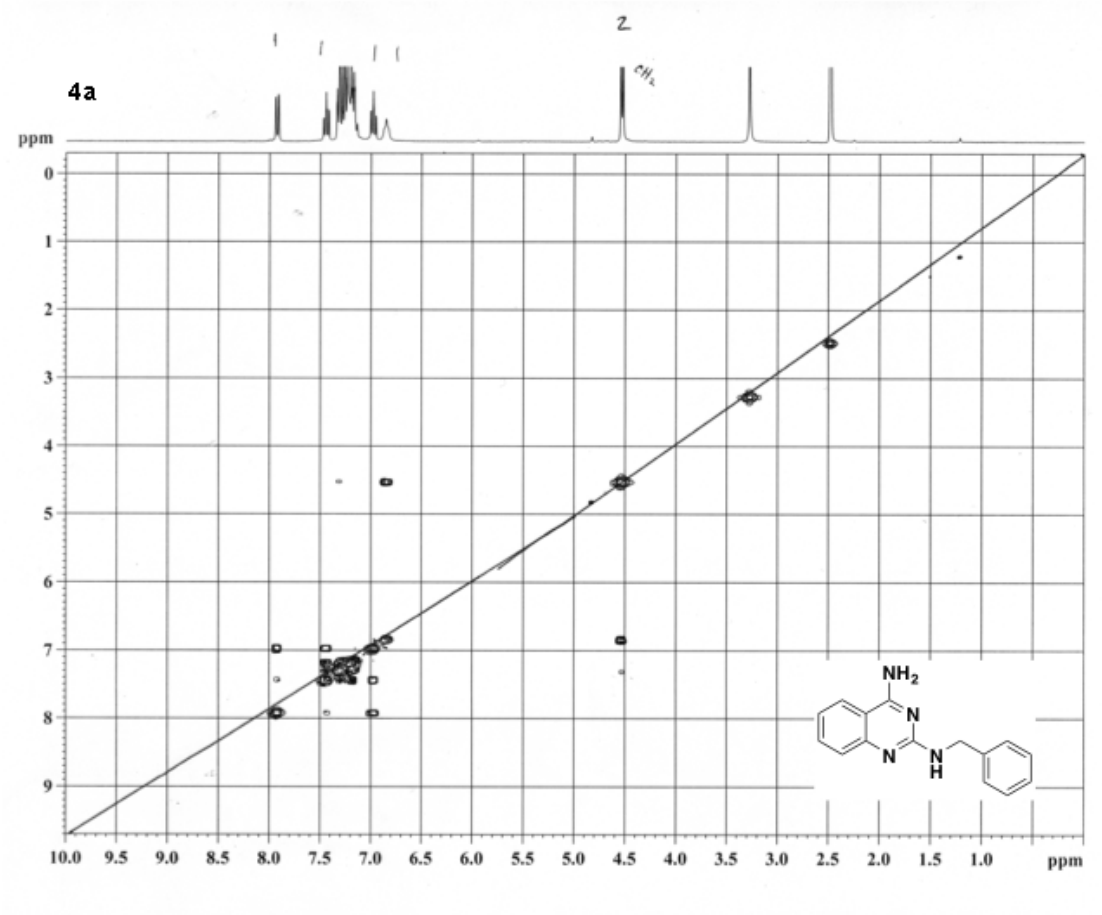
***N*^{2}-benzylquinazoline-2,4-diamine** (**4a**)



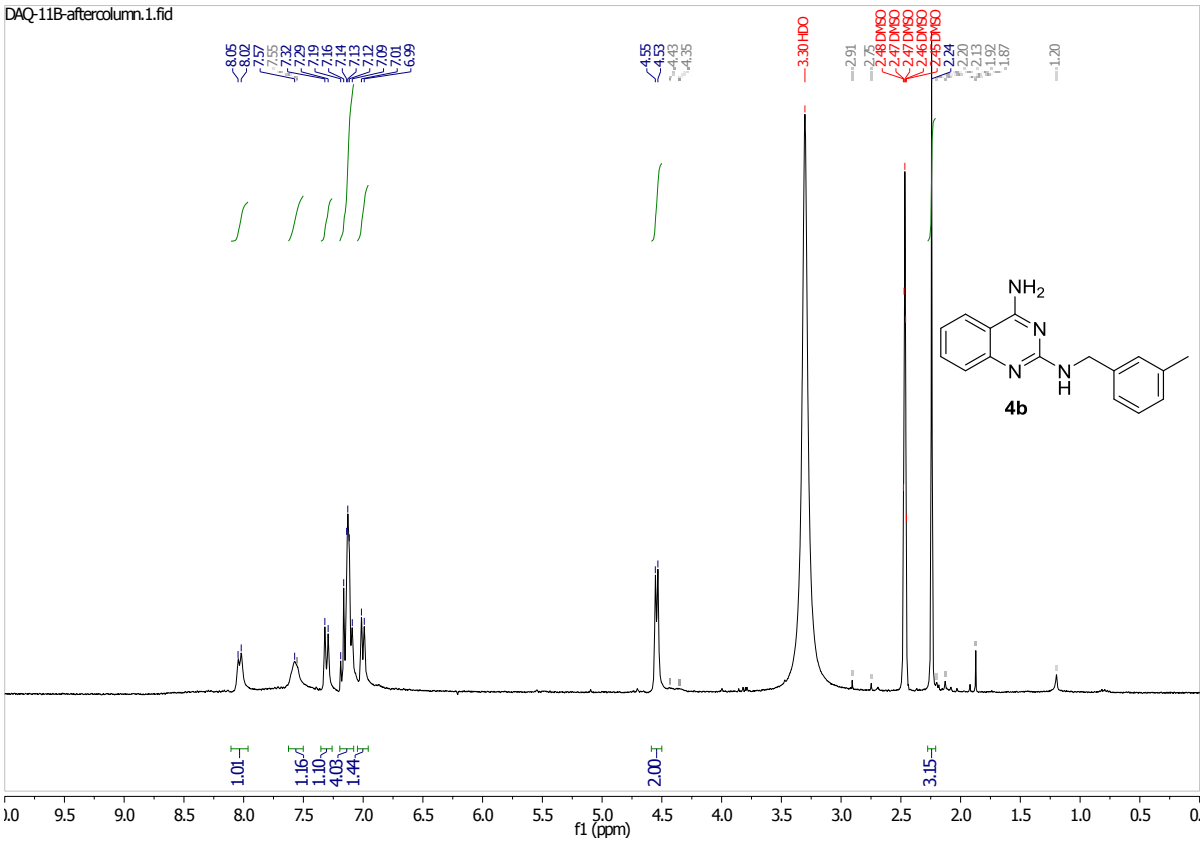
N^2-benzylquinazoline-2,4-diamine (4a)



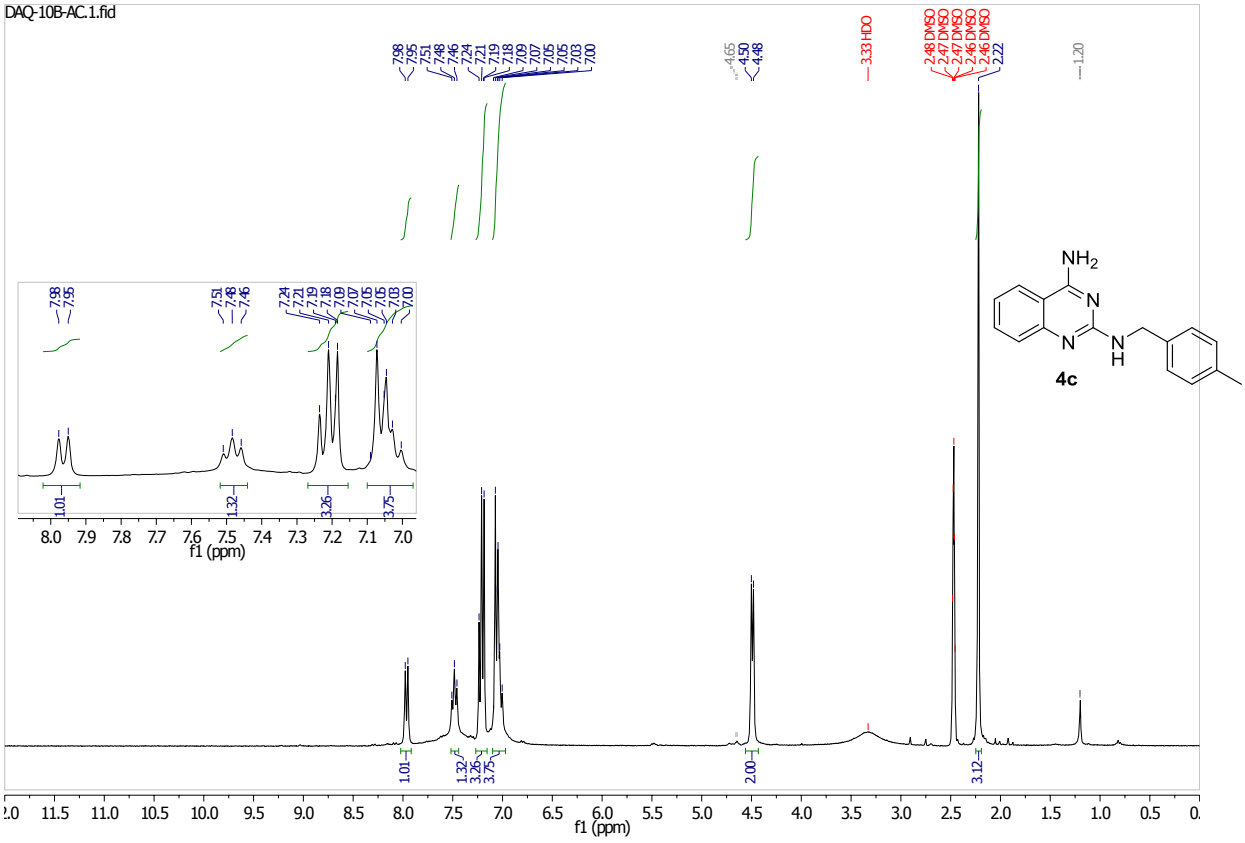
COSY Spectra: N^2-benzylquinazoline-2,4-diamine (4a)



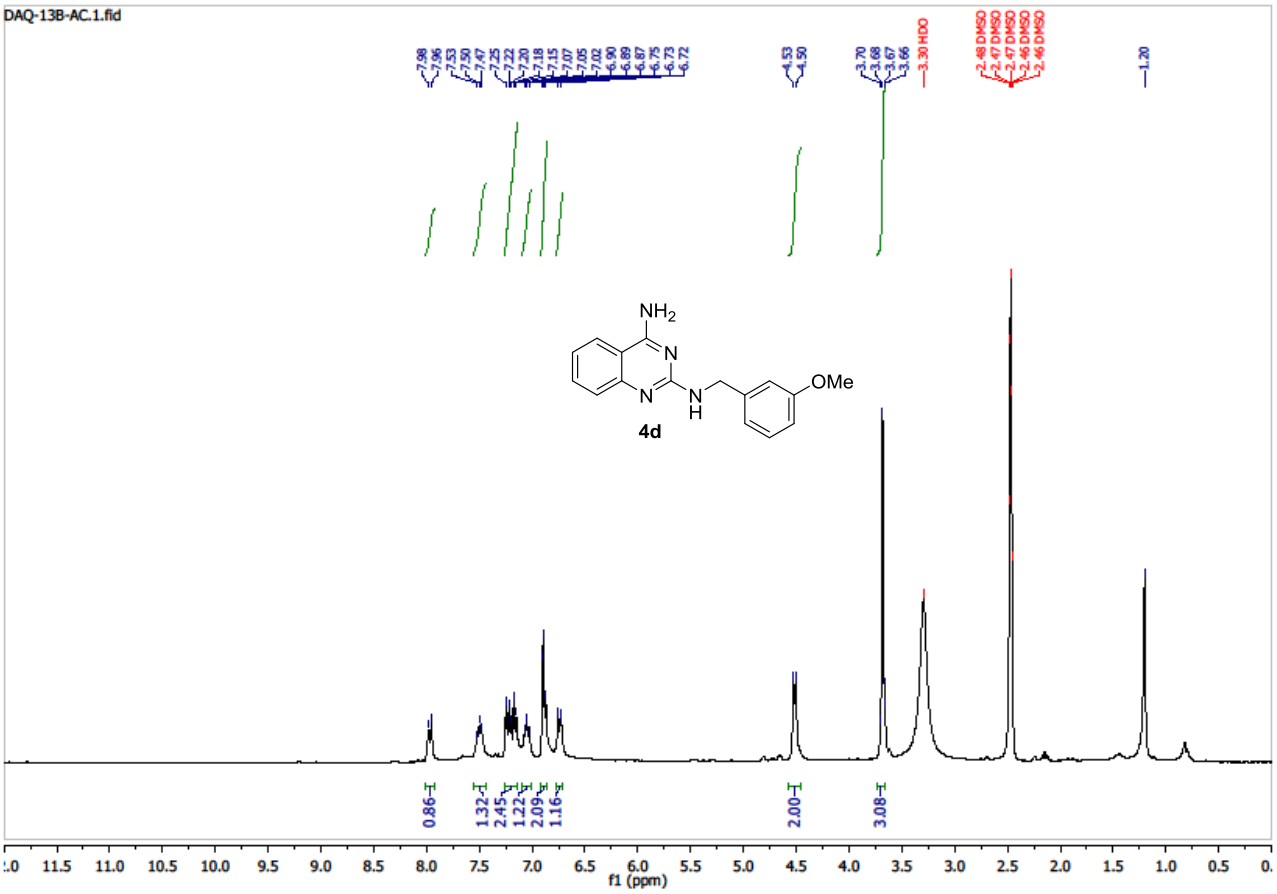
N^2-(3-methylbenzyl)quinazoline-2,4-diamine (4b)



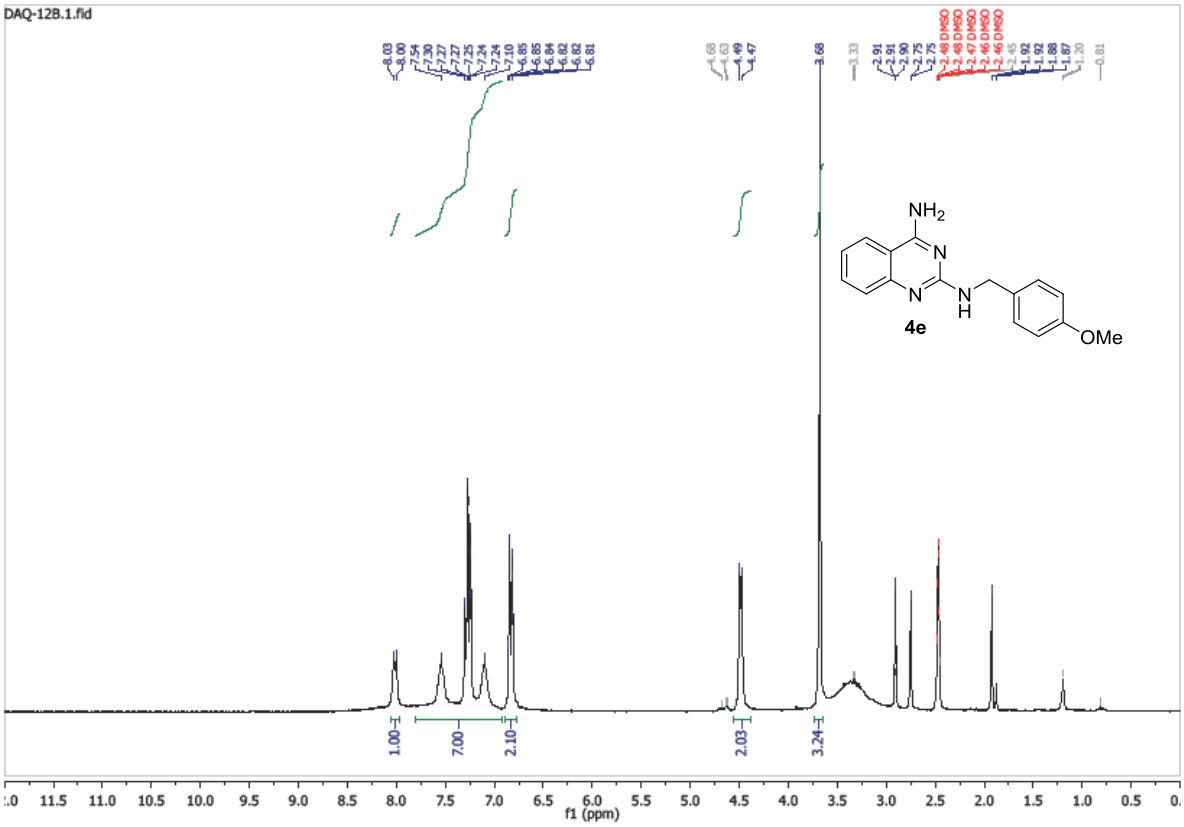
N^2-(4-methylbenzyl)quinazoline-2,4-diamine (4c)



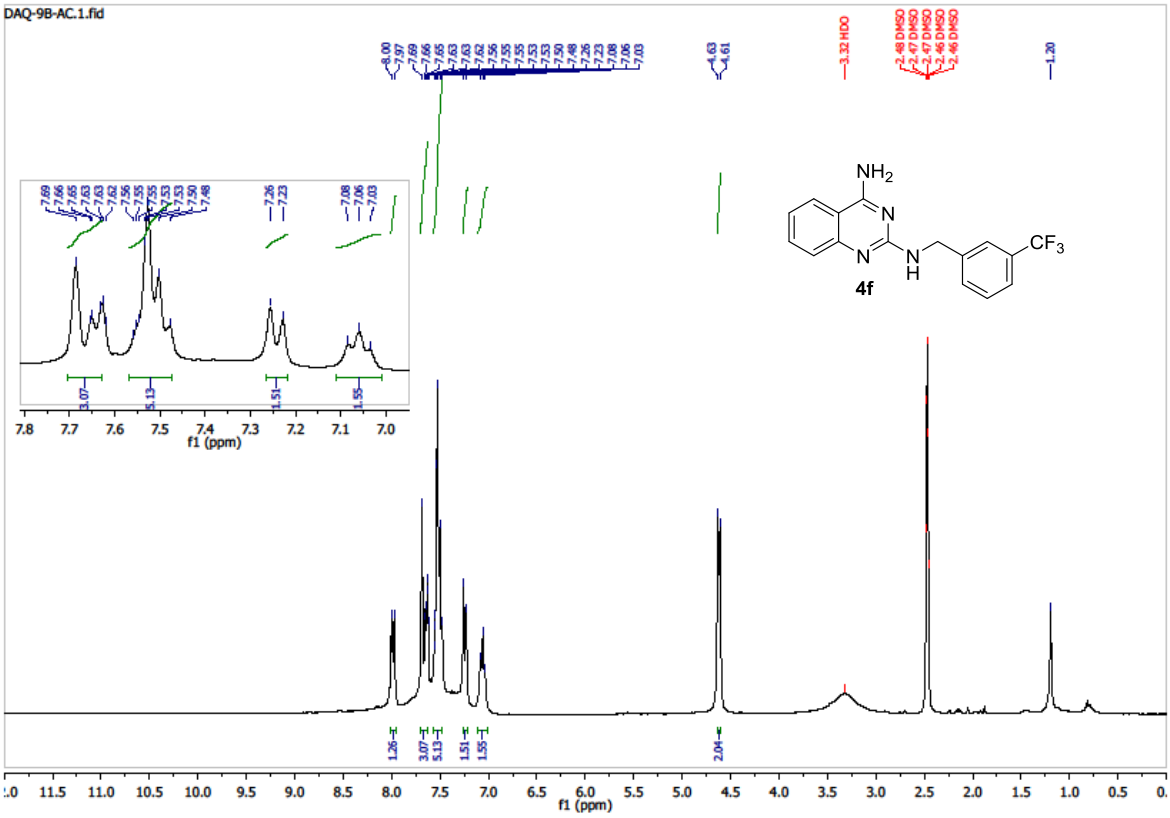
N^2-(3-methoxylbenzyl)quinazoline-2,4-diamine (4d)



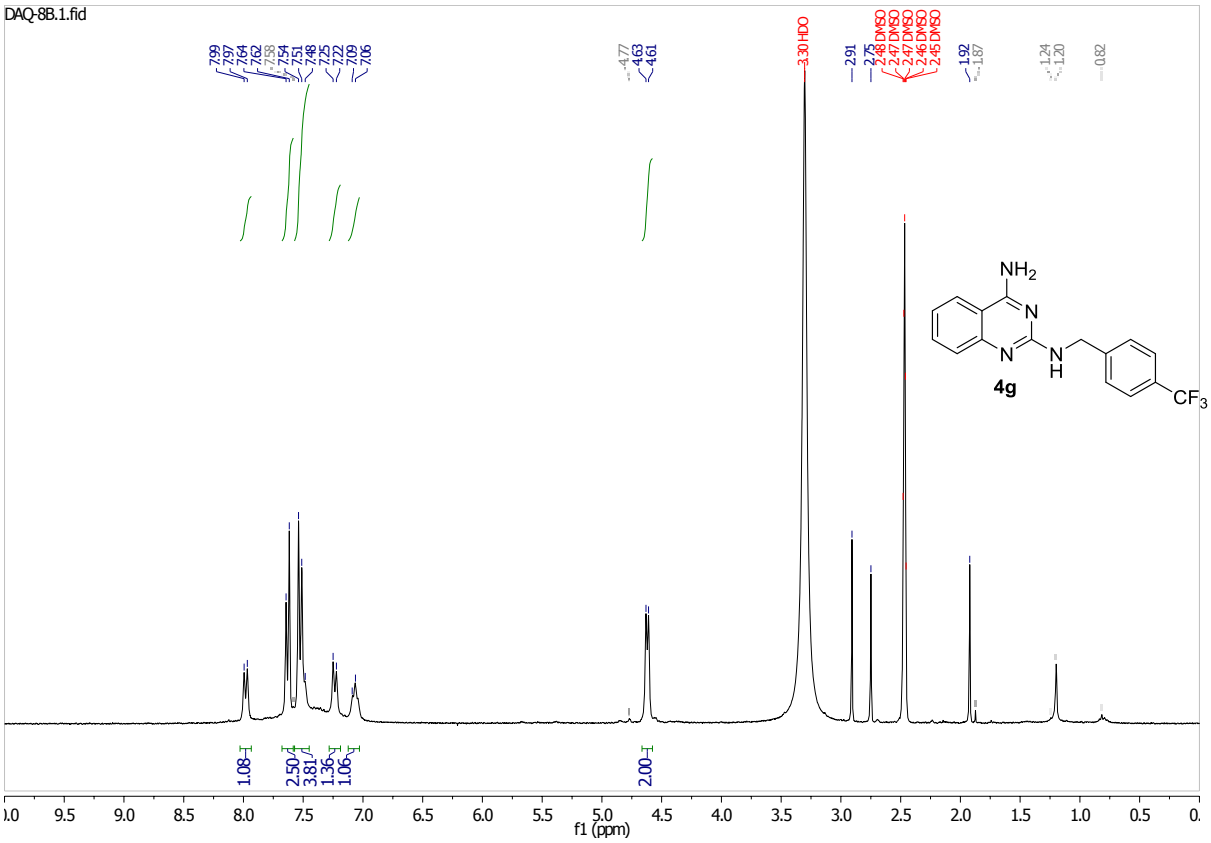
N^2-(4-methoxylbenzyl)quinazoline-2,4-diamine (4e)



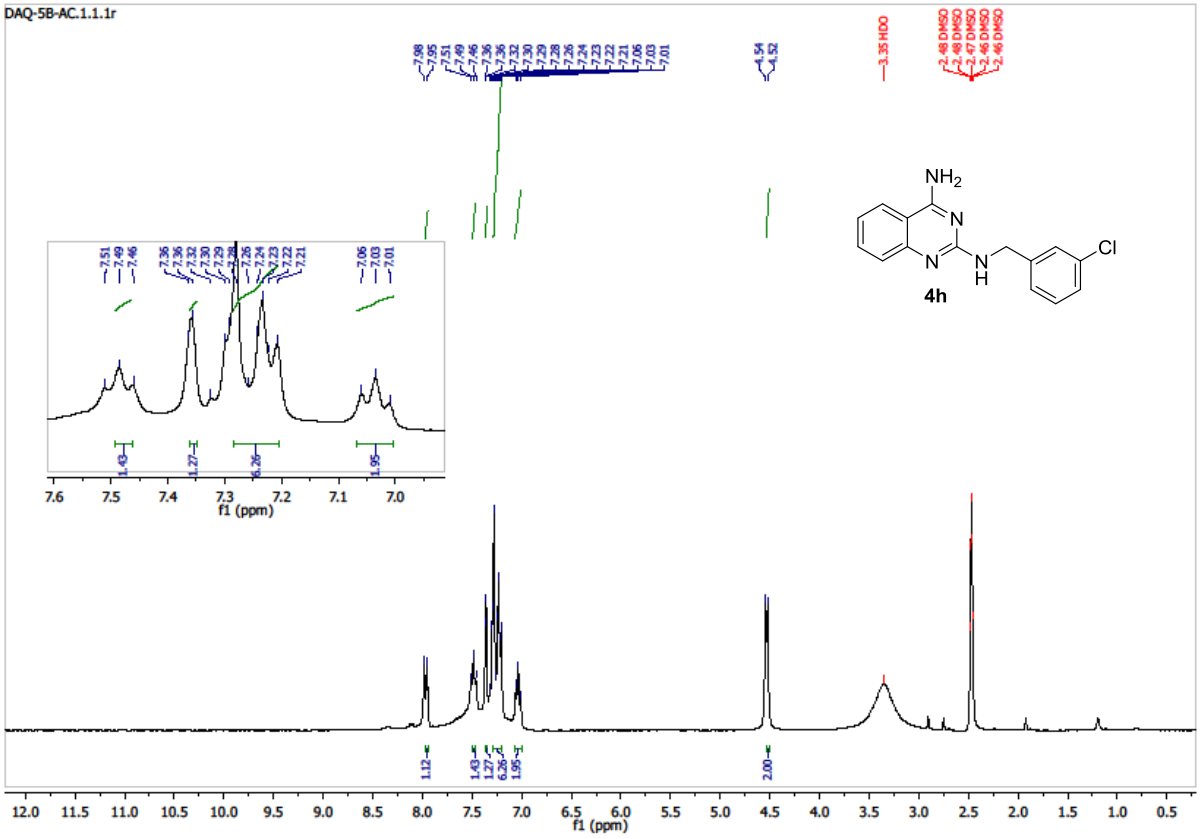
N^2-(3-trifluoromethylbenzyl)quinazoline-2,4-diamine (4f)



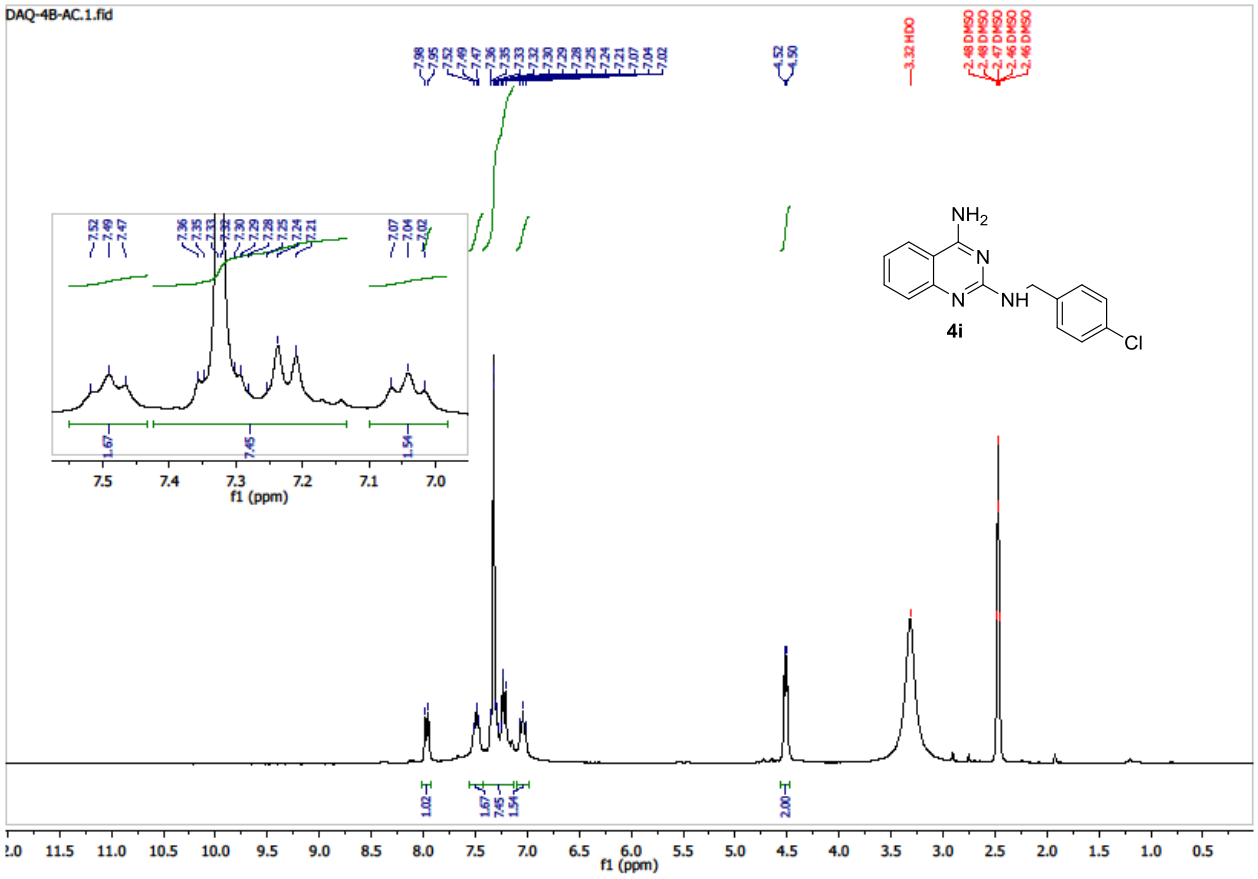
N^2-(4-trifluoromethylbenzyl)quinazoline-2,4-diamine (4g)



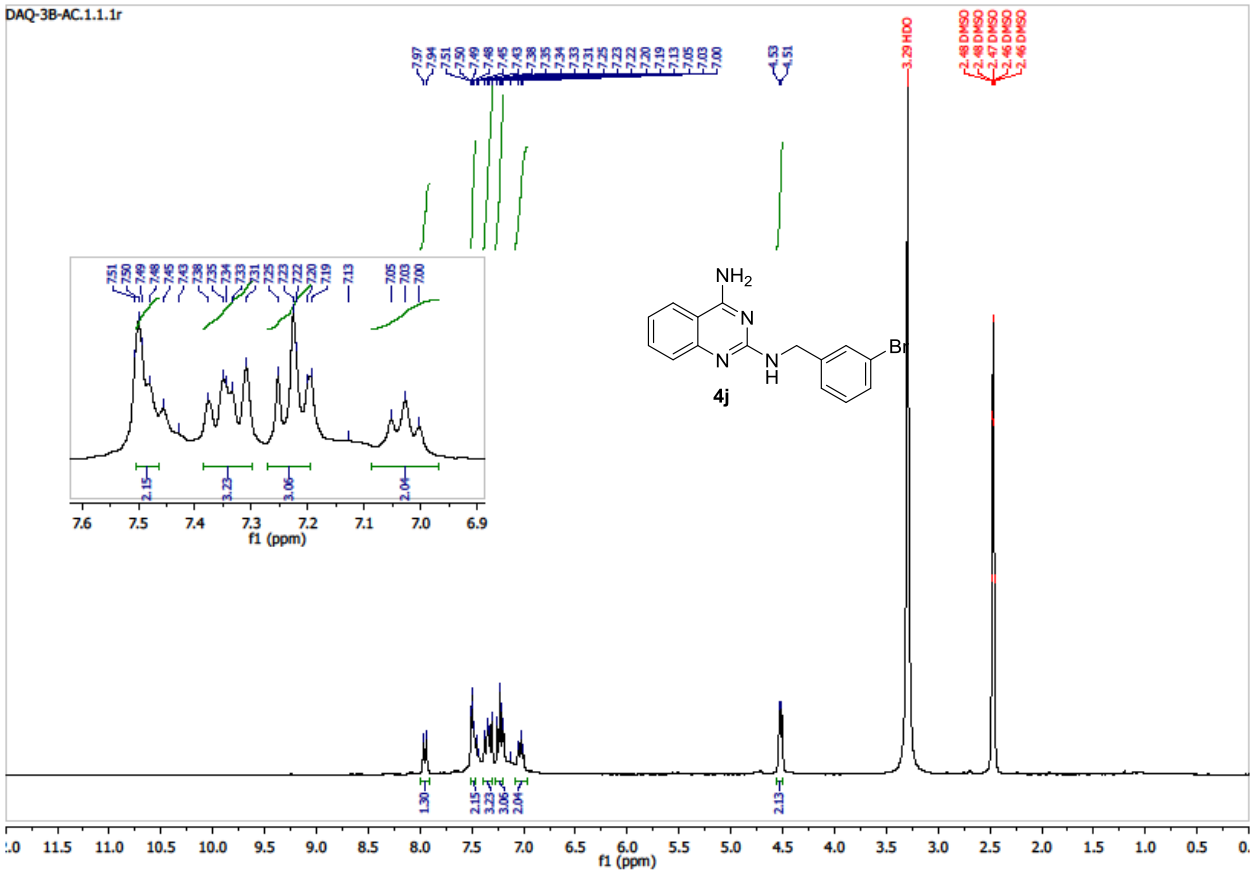
N^2-(3-chlorobenzyl)quinazoline-2,4-diamine (4h)



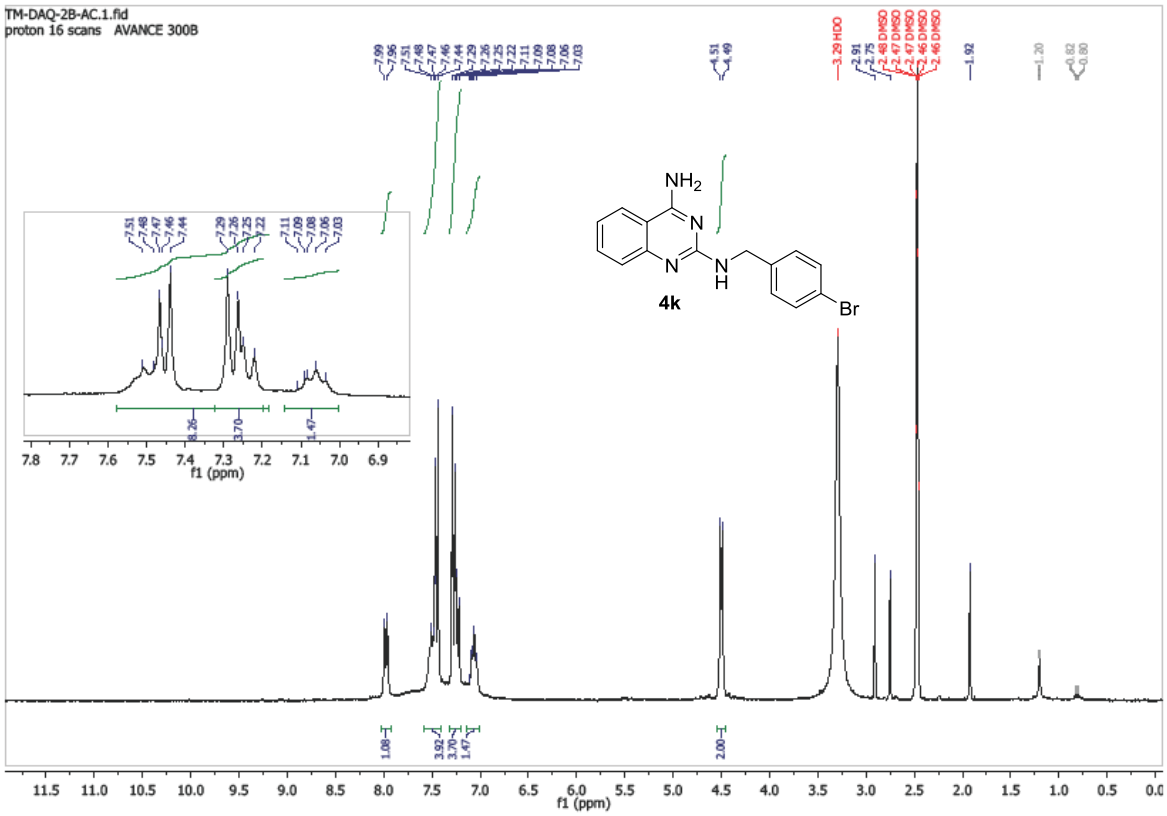
N^2-(4-chlorobenzyl)quinazoline-2,4-diamine (4i)



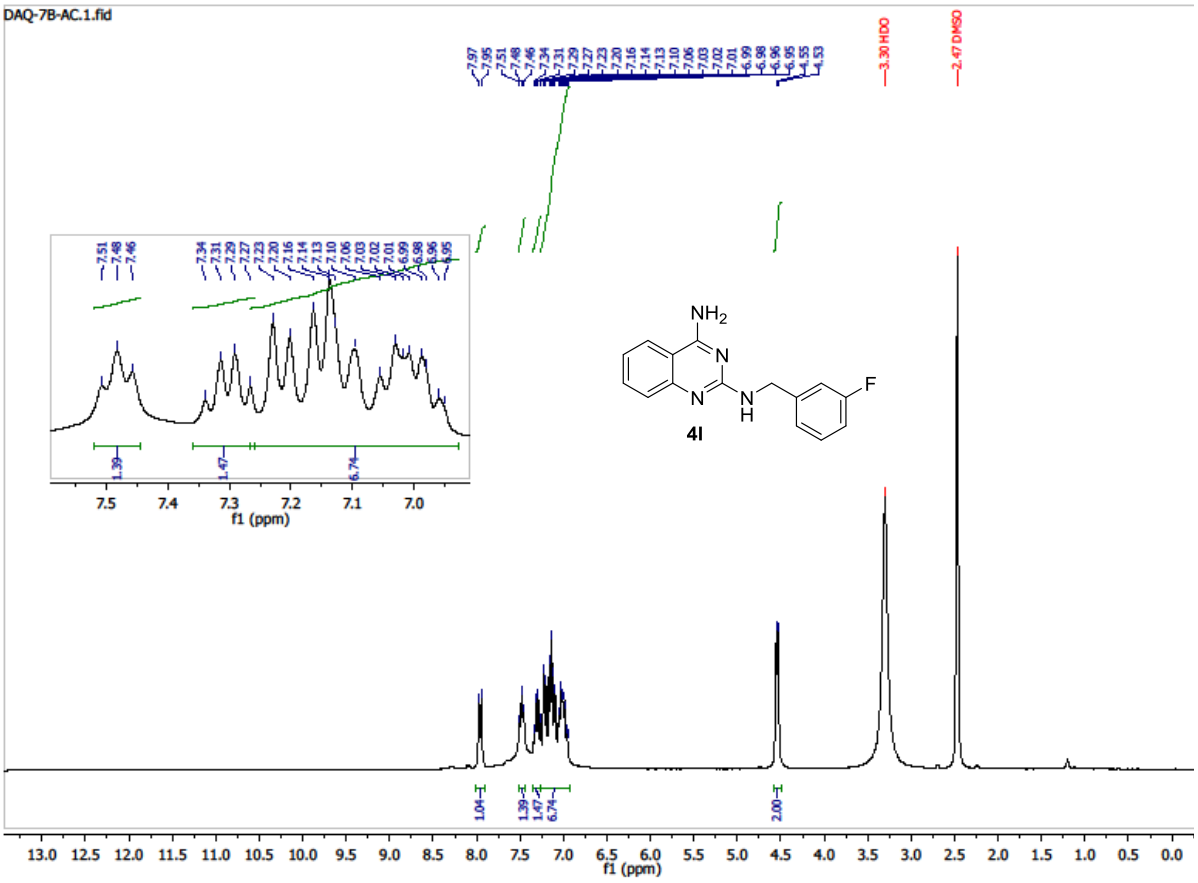
N^2-(3-bromobenzyl)quinazoline-2,4-diamine (4j)



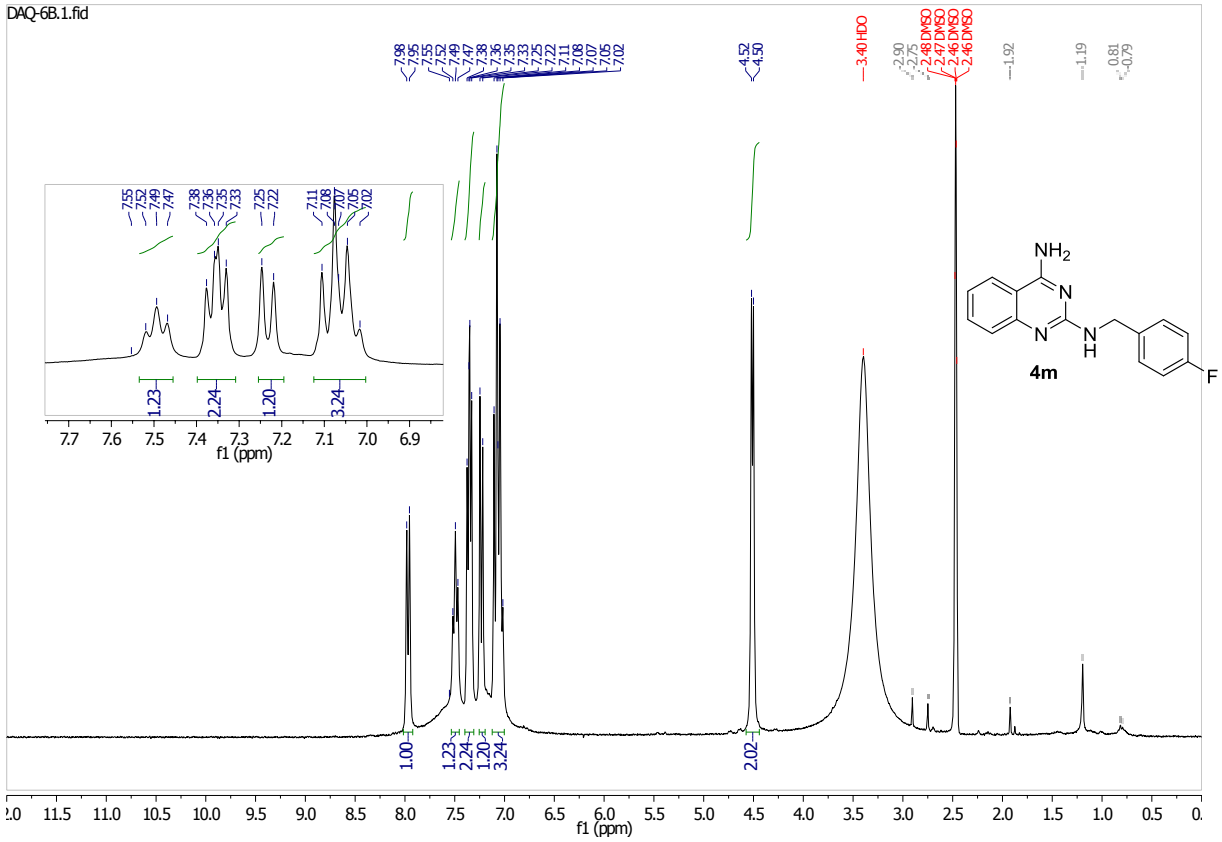
N^2-(4-bromobenzyl)quinazoline-2,4-diamine (4k)



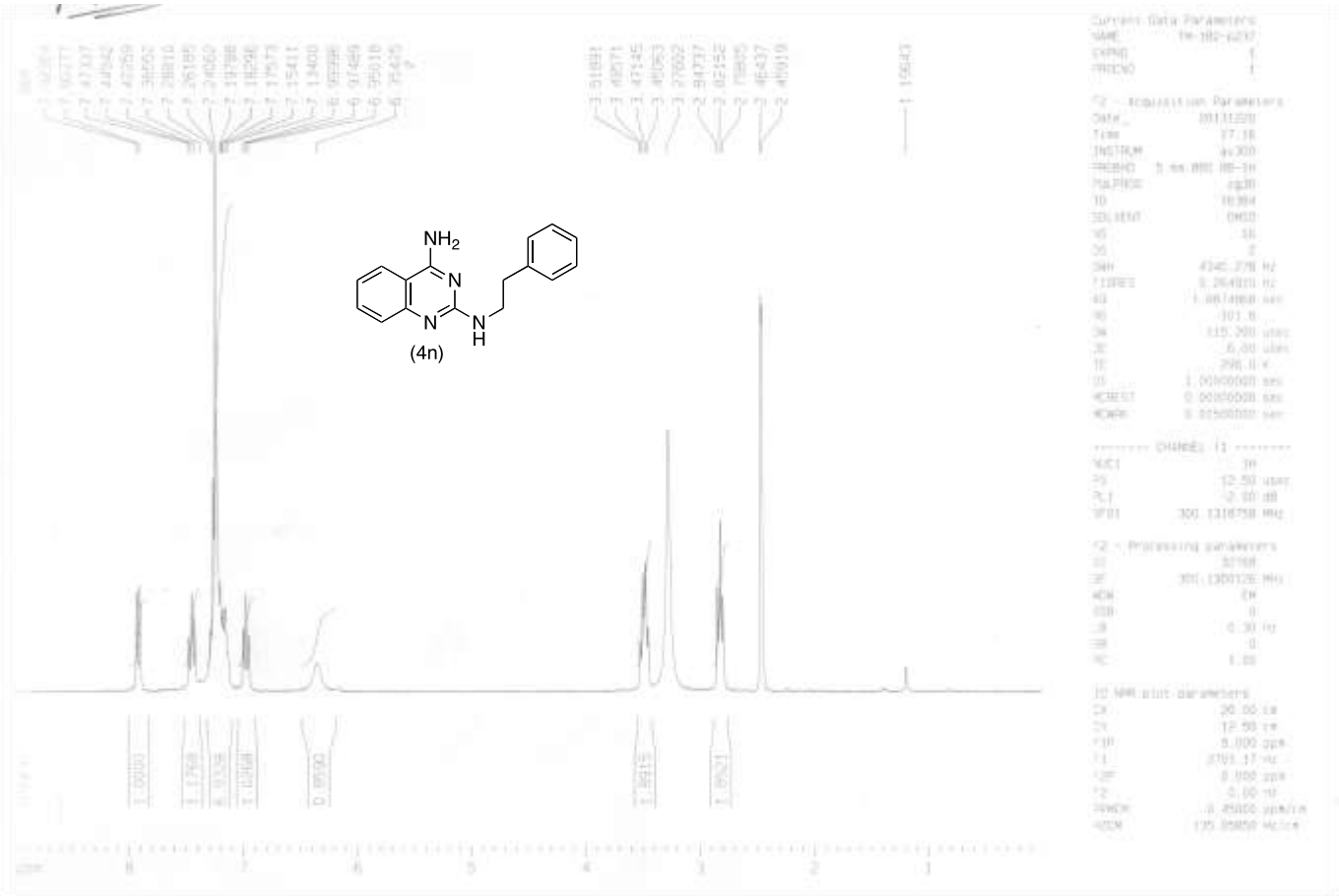
N^2-(3-fluorobenzyl)quinazoline-2,4-diamine (4l)



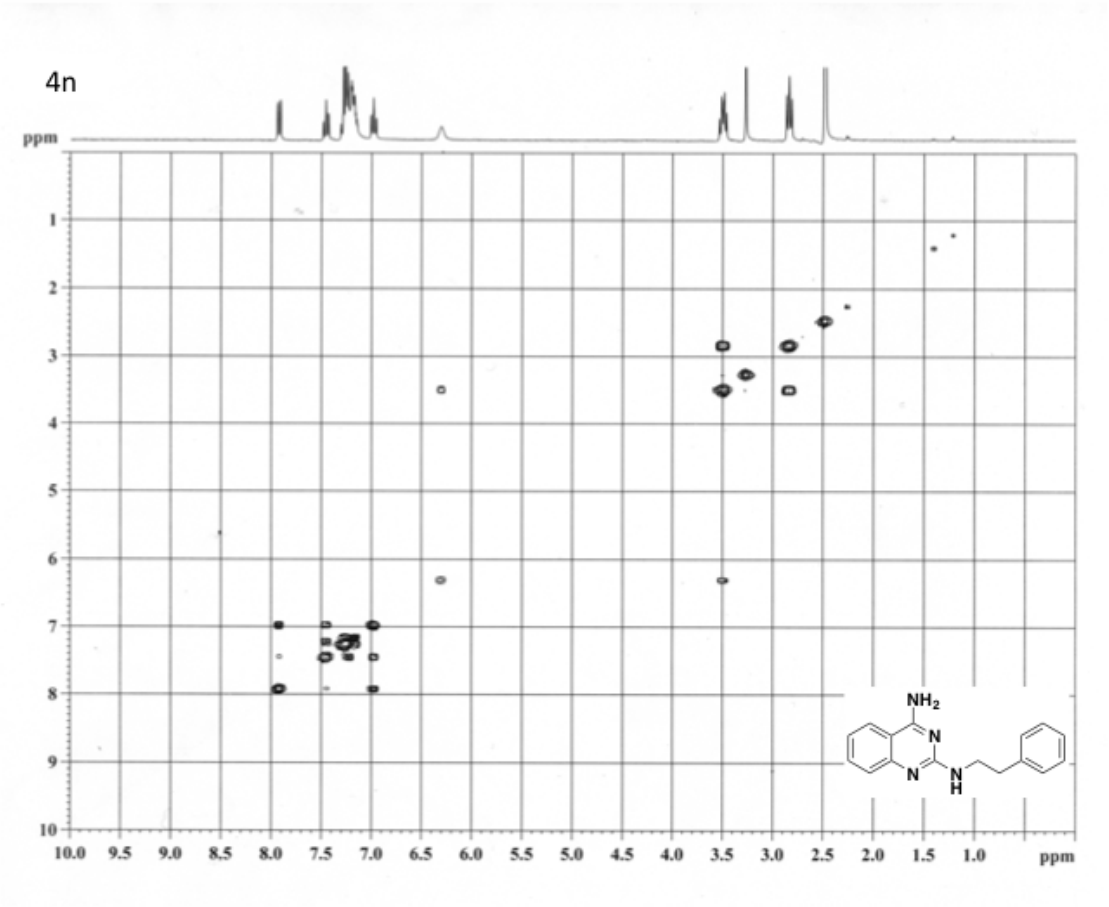
N^2-(4-fluorobenzyl)quinazoline-2,4-diamine (4m)



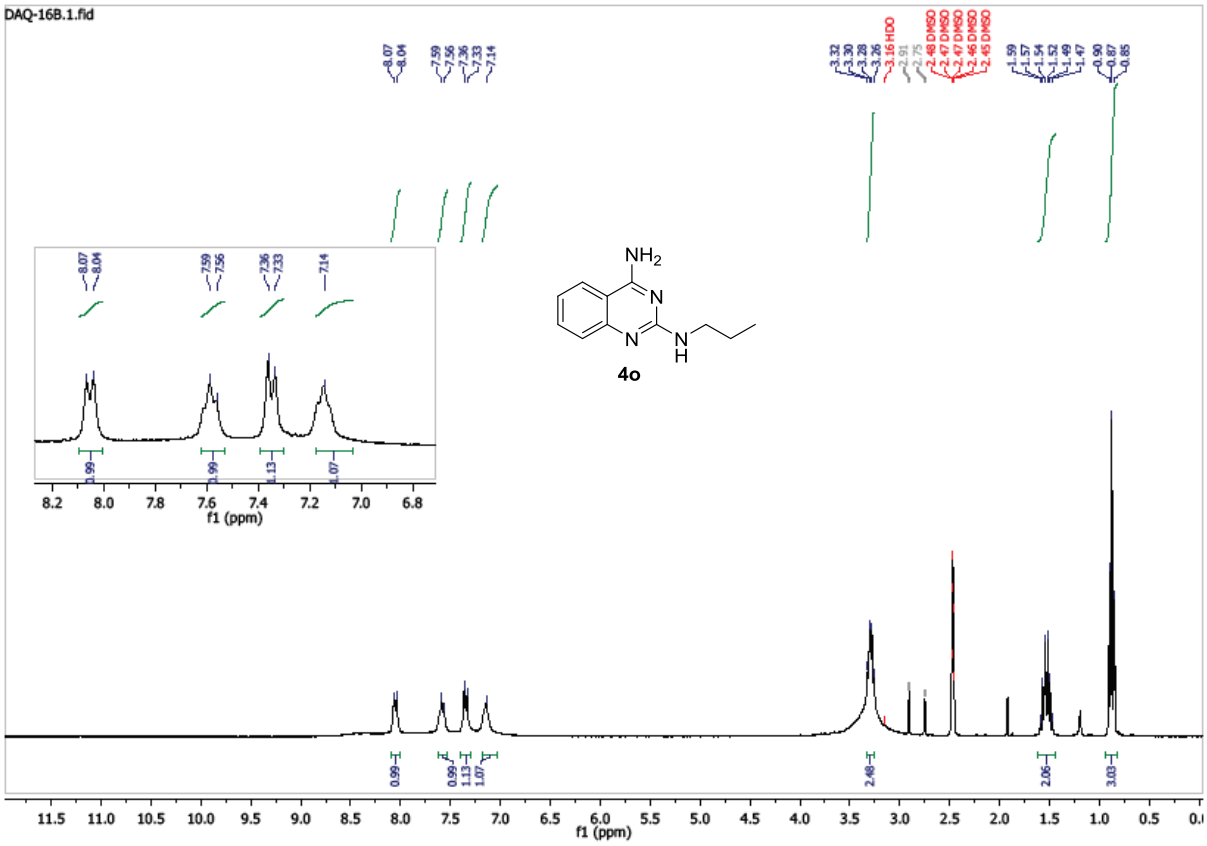
N^2-phenethylquinazoline-2,4-diamine (4n)



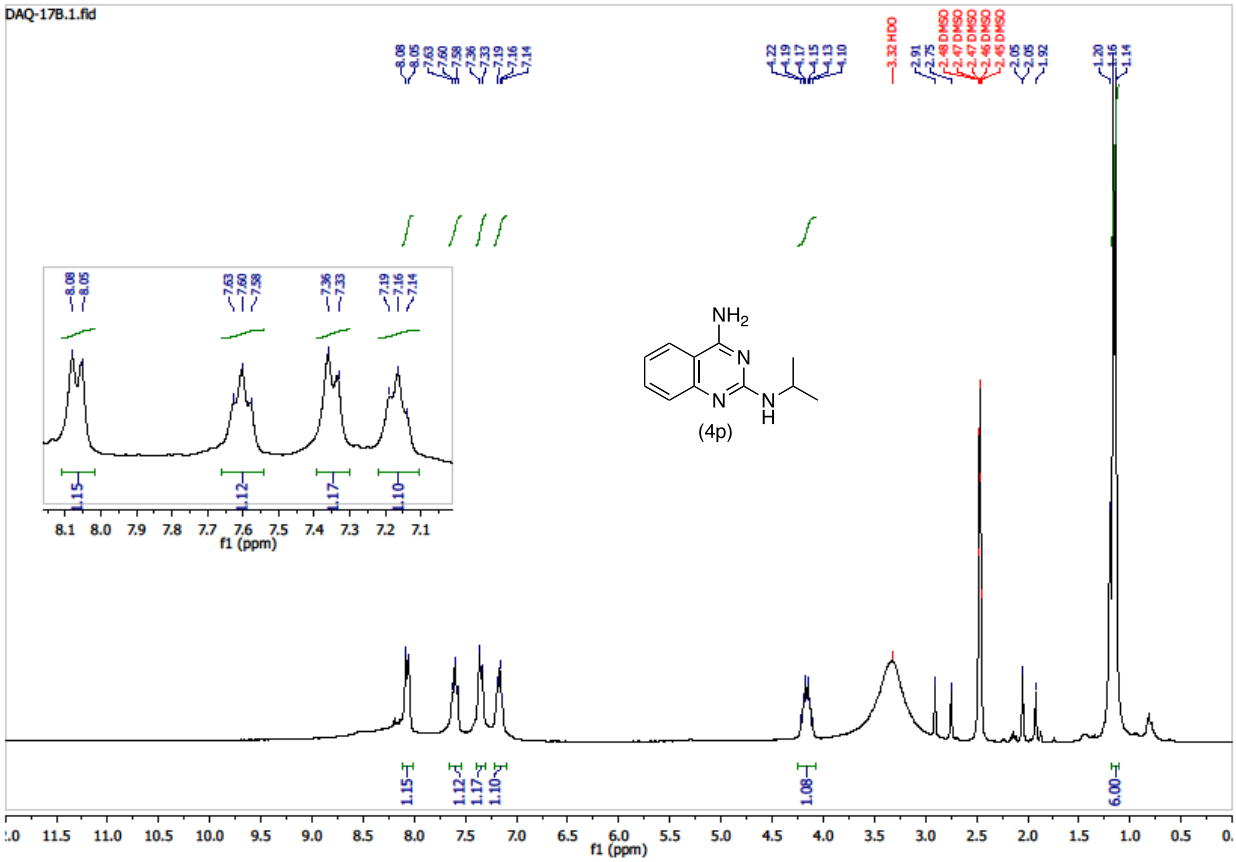
COSY Spectra: N^2-phenethylquinazoline-2,4-diamine (4n)



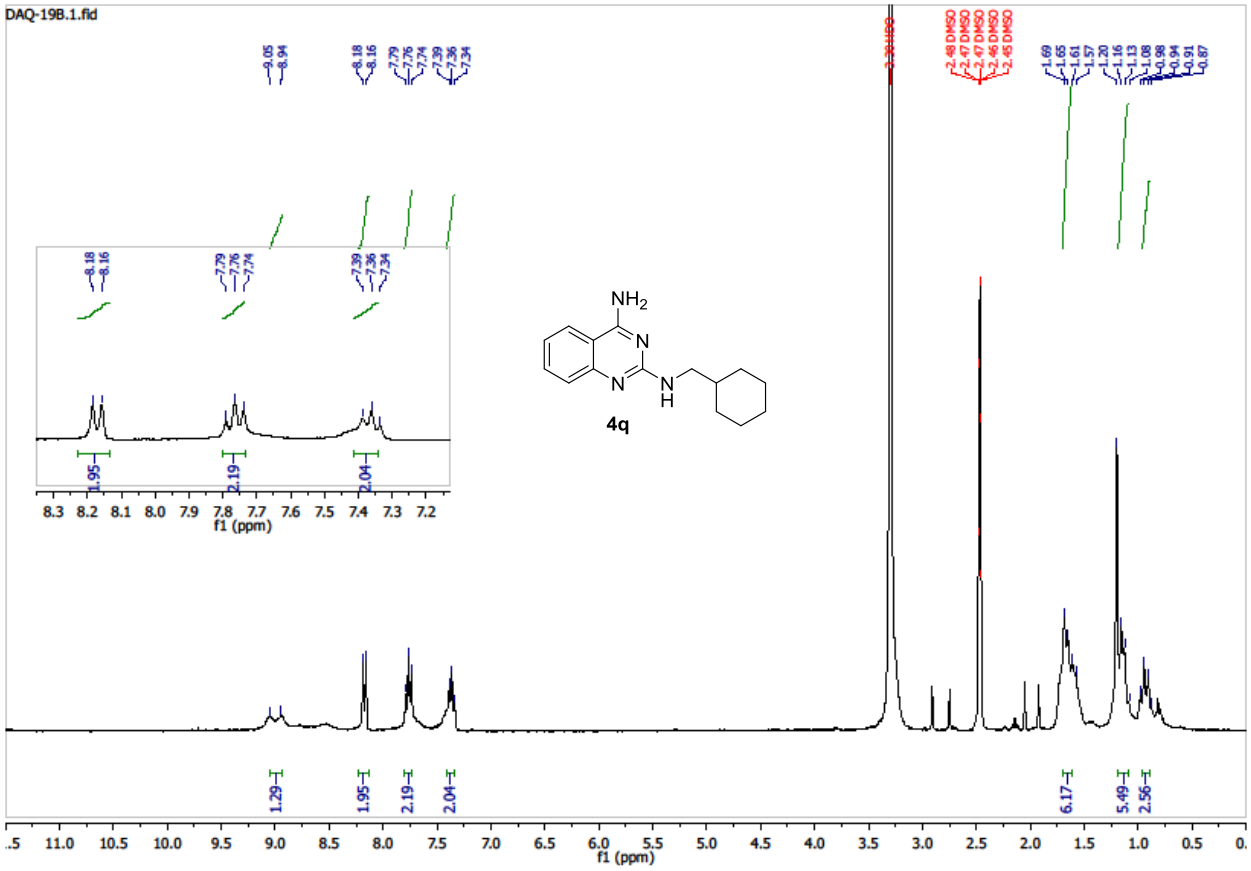
N^2-propylquinazoline-2,4-diamine (4o)



N^2-isopropylquinazoline-2,4-diamine (4p)

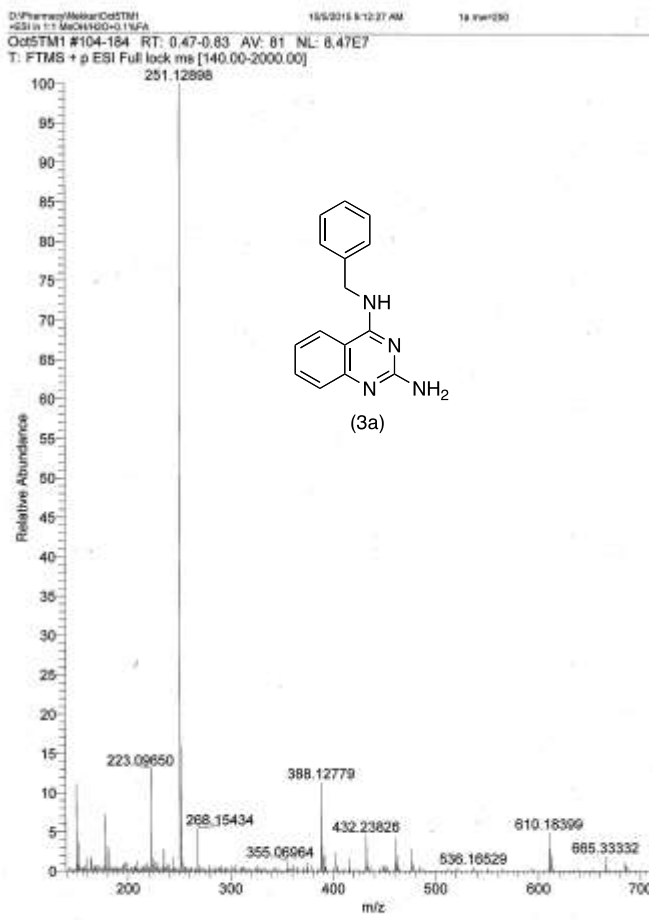


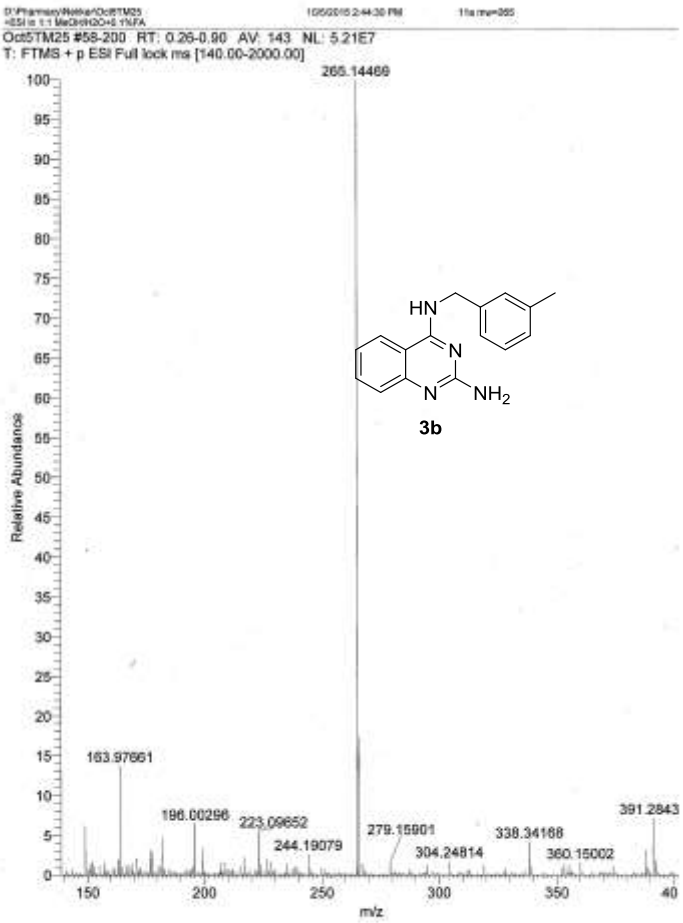
N^2-(cyclohexylmethyl)quinazoline-2,4-diamine (4q)



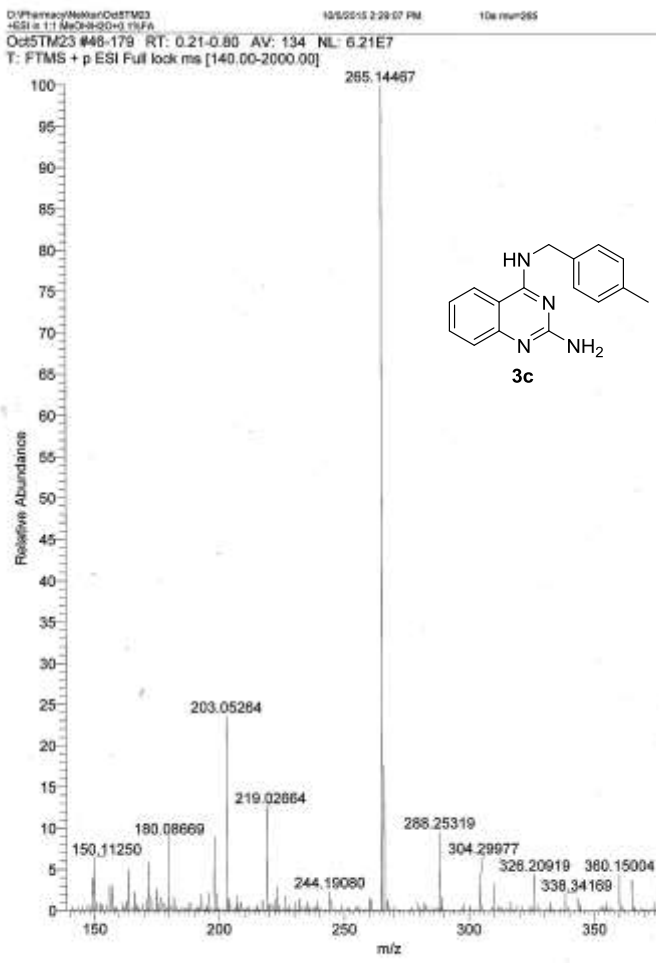
8. HRMS data for compounds **3a-q**

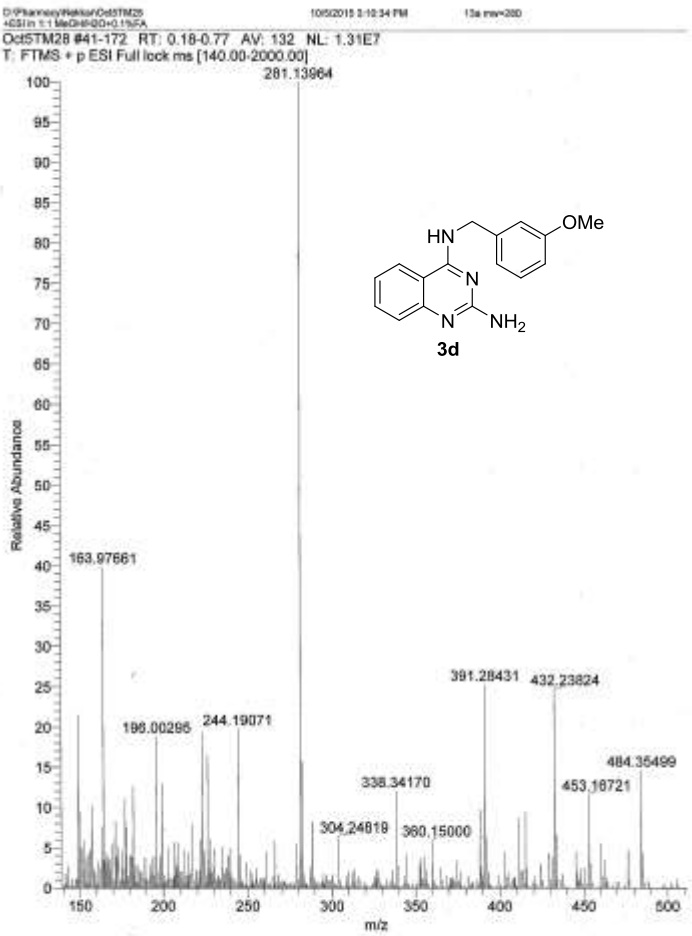
***N*^{4}-benzylquinazoline-2,4-diamine** (**3a**) and ***N*^{4}-(3-methylbenzyl)quinazoline-2,4-diamine** (**3b**)



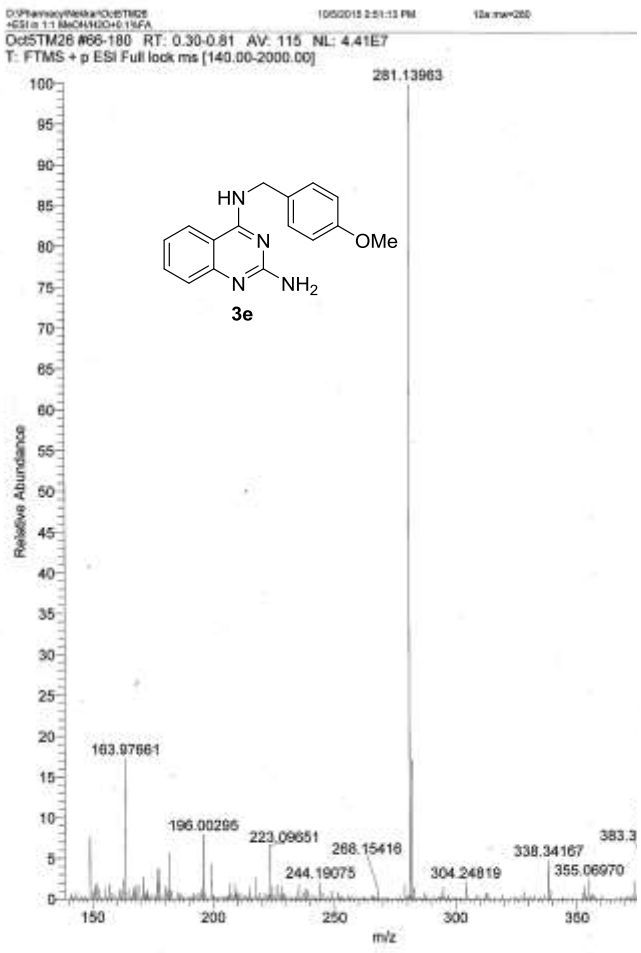


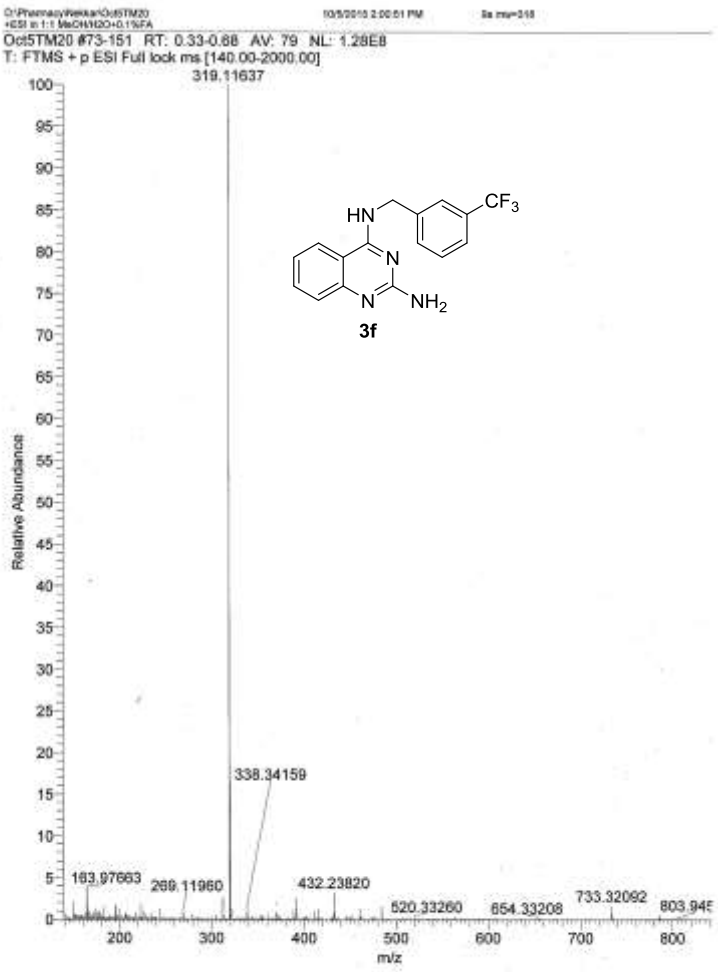
N^4-(4-methylbenzyl)quinazoline-2,4-diamine (**3c**) and **N^4-(3-methoxybenzyl)quinazoline-2,4-diamine** (**3d**)



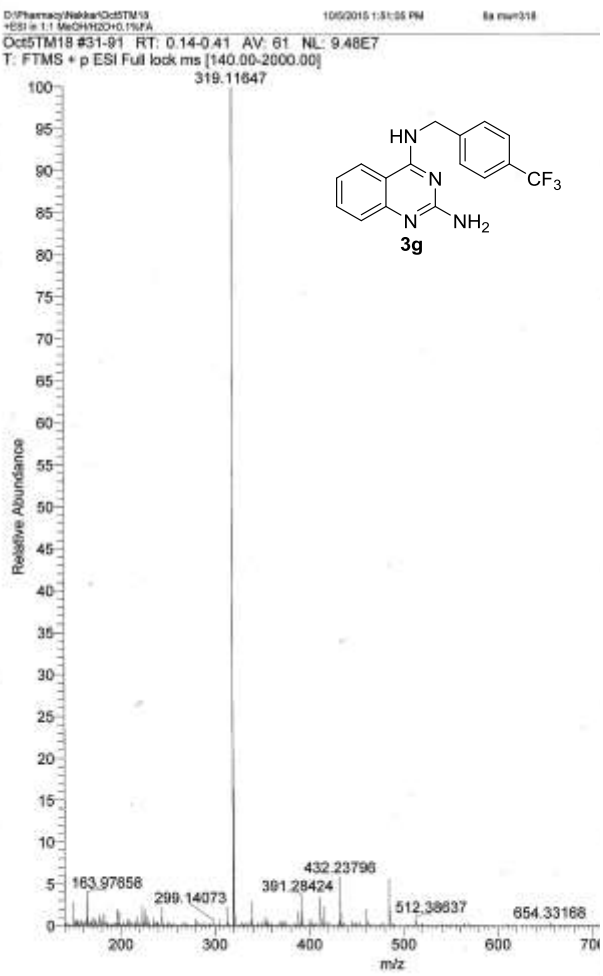


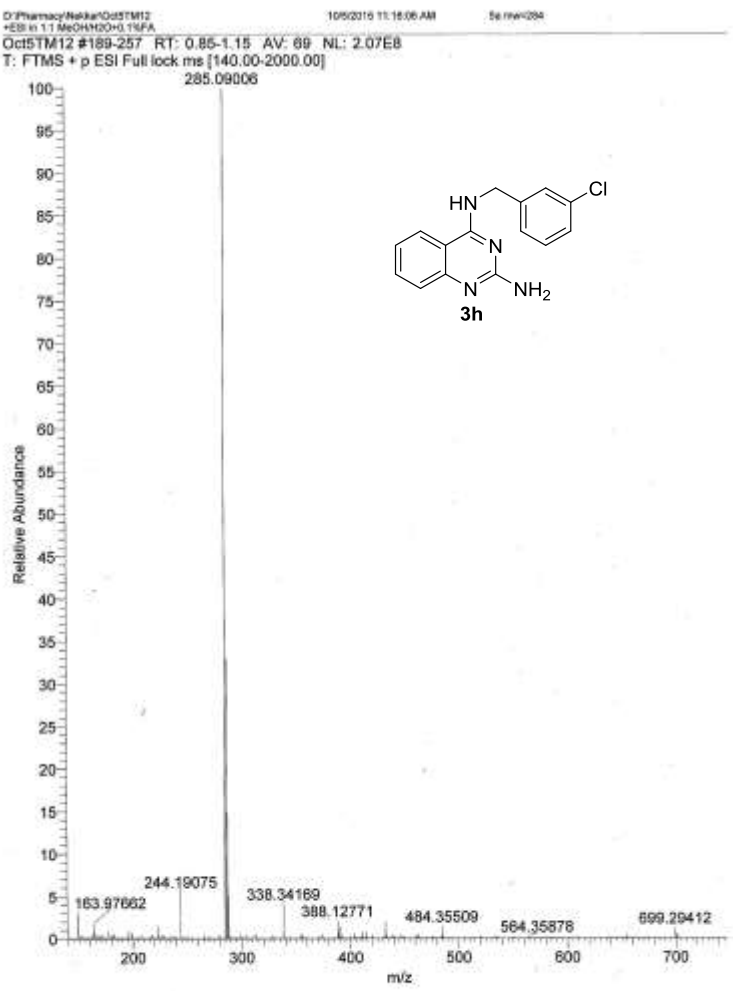
N^4-(4-methoxybenzyl)quinazoline-2,4-diamine (**3e**) and **N^4-(3-trifluoromethylbenzyl)quinazoline-2,4-diamine** (**3f**)



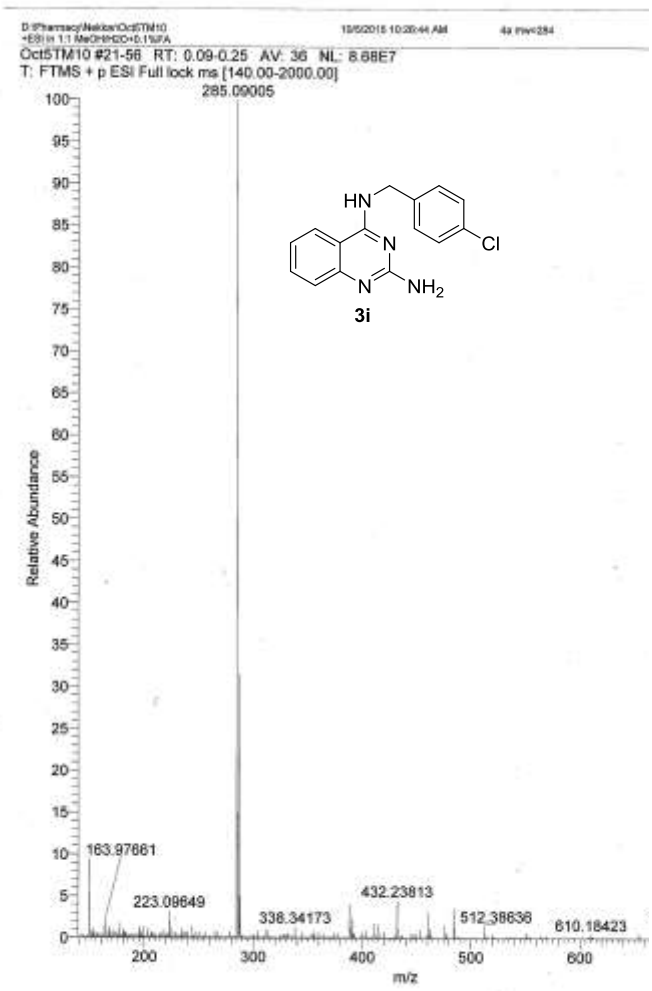


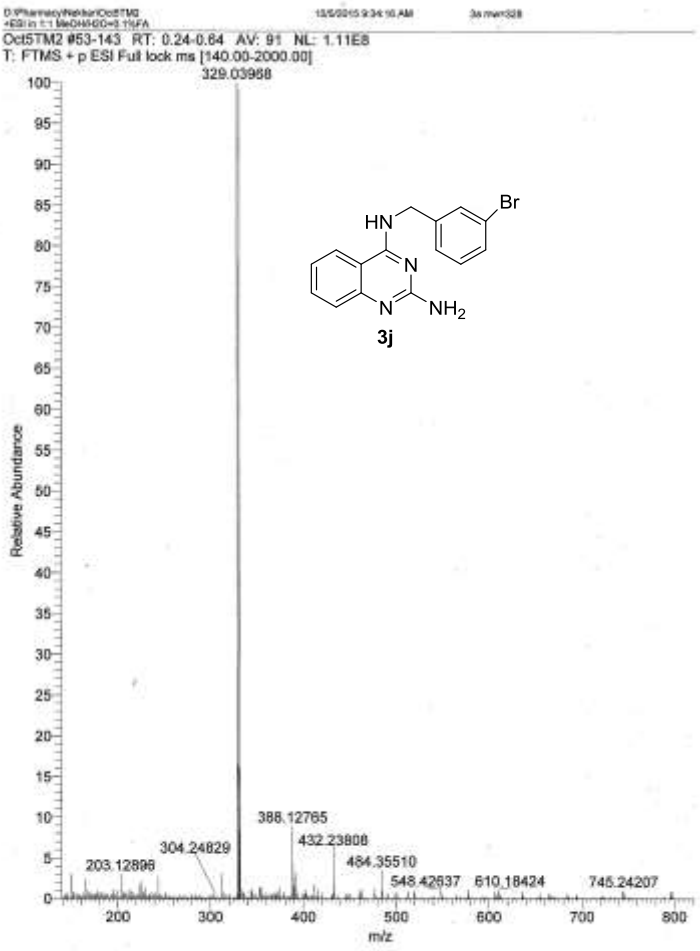
N^4-(4-trifluoromethylbenzyl)quinazoline-2,4-diamine (3g) and N^4-(3-chlorobenzyl)quinazoline-2,4-diamine (3h)



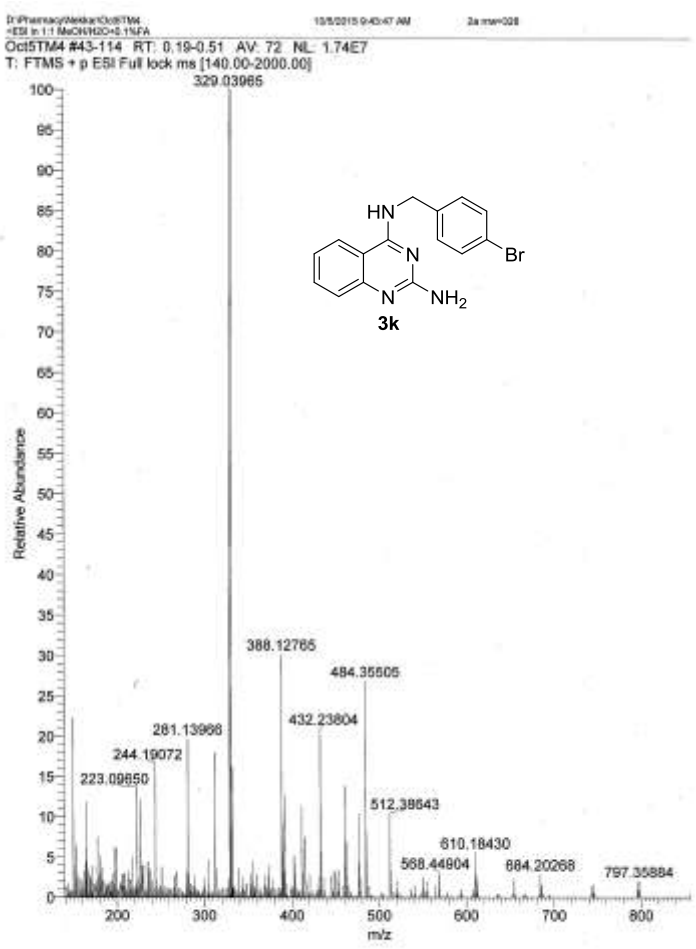


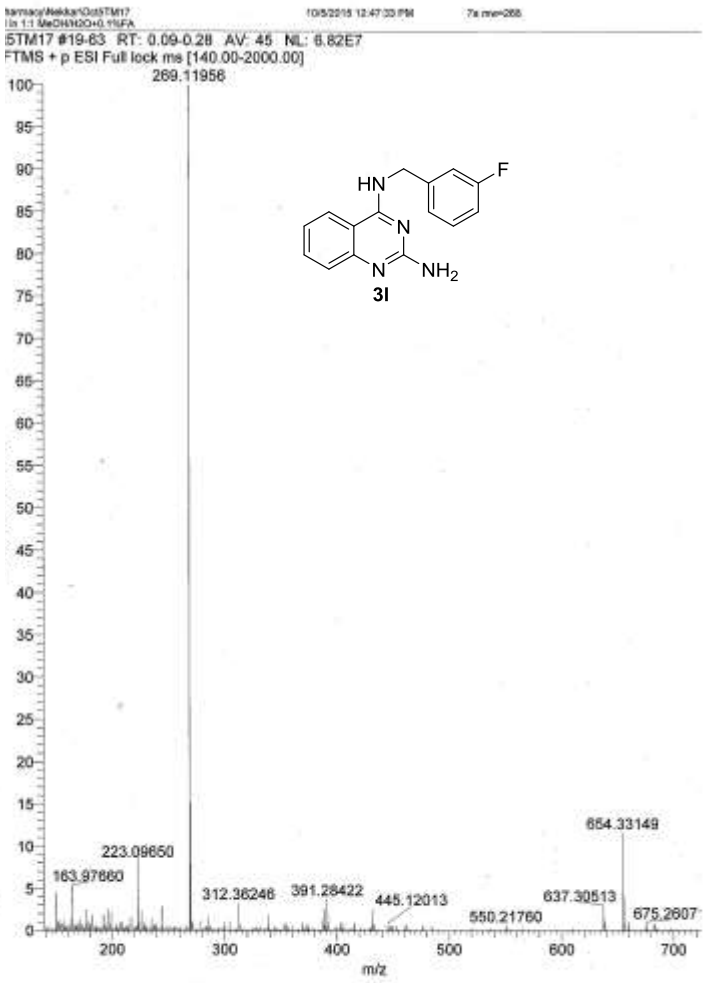
N^4-(4-chlorobenzyl)quinazoline-2,4-diamine (**3i**) and **N^4-(3-bromobenzyl)quinazoline-2,4-diamine** (**3j**)



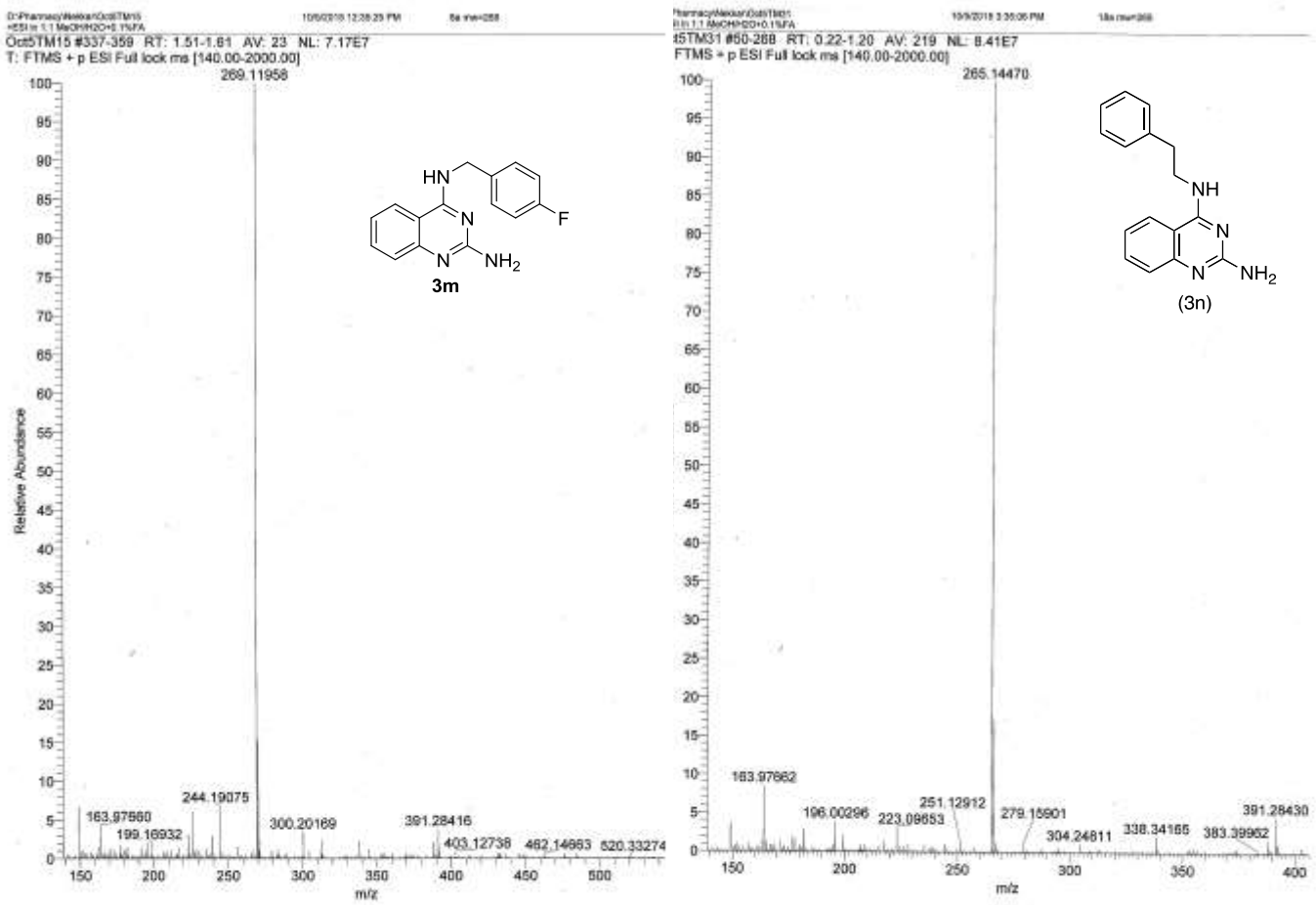


N^4-(4-bromobenzyl)quinazoline-2,4-diamine (**3k**) and **N^4-(3-fluorobenzyl)quinazoline-2,4-diamine** (**3l**)

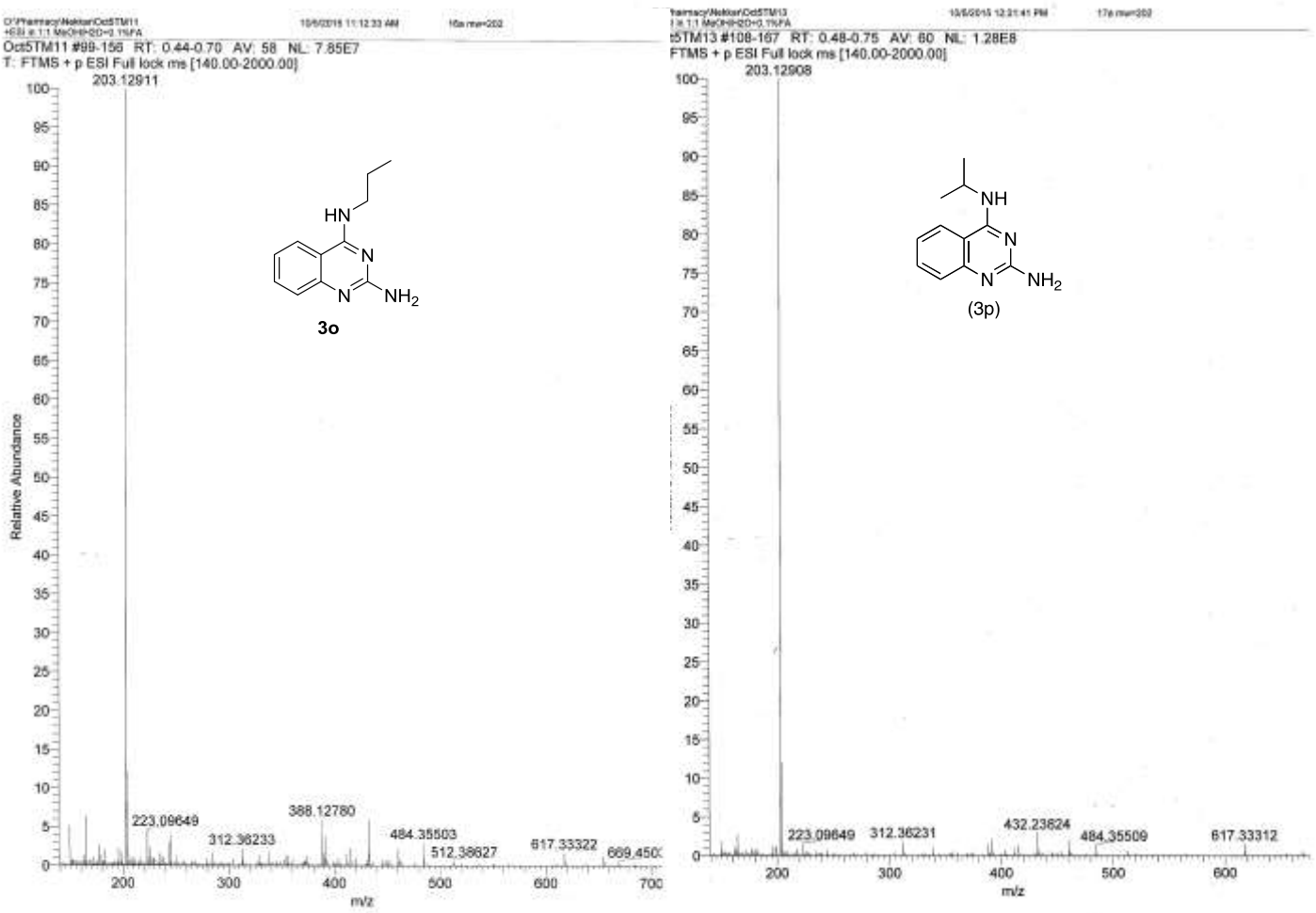




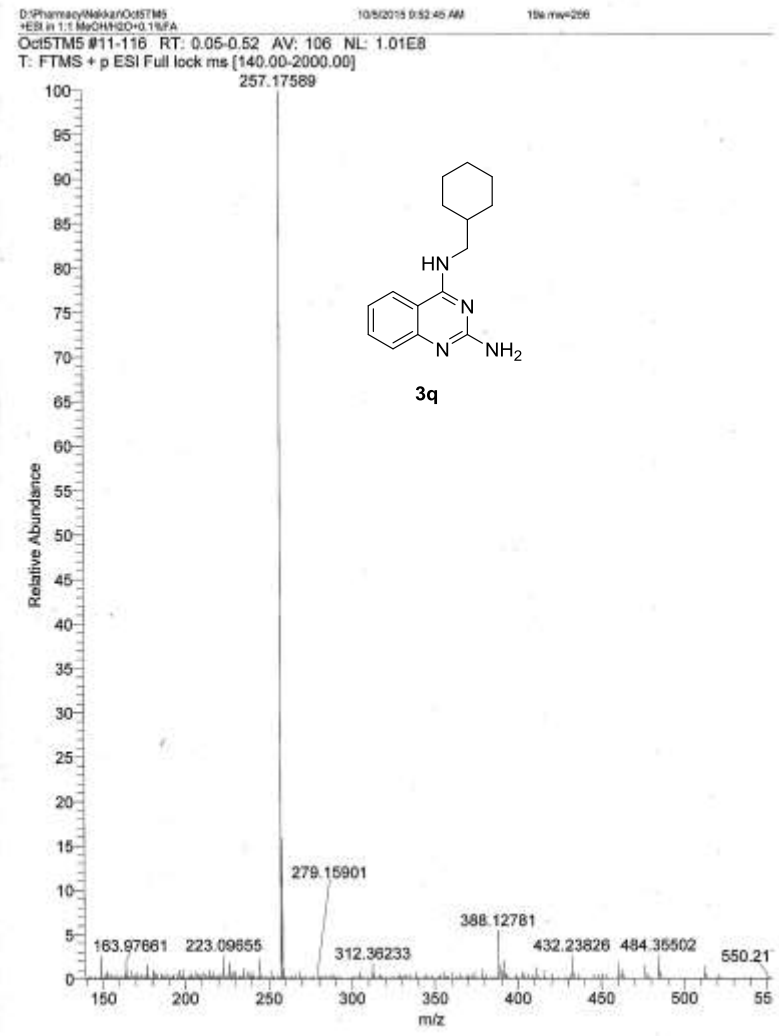
***N*^{4}-(4-fluorobenzyl)quinazoline-2,4-diamine** (**3m**) and ***N*^{4}-phenethylquinazoline-2,4-diamine** (**3n**)



N^4-propylquinazoline-2,4-diamine (**3o**) and **N^4-isopropylquinazoline-2,4-diamine** (**3p**)

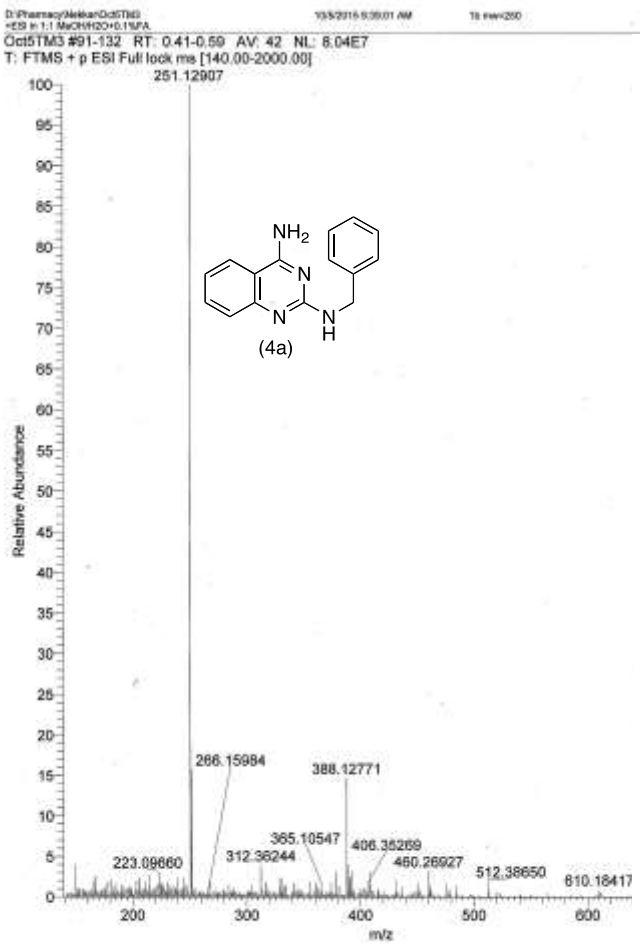


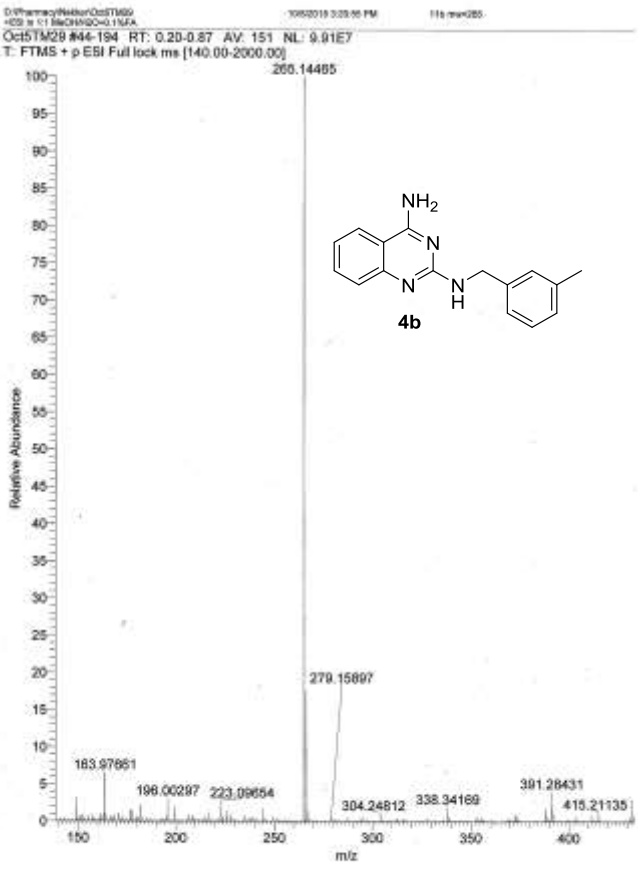
N^4-(cyclohexylmethyl)quinazoline-2,4-diamine (3q)



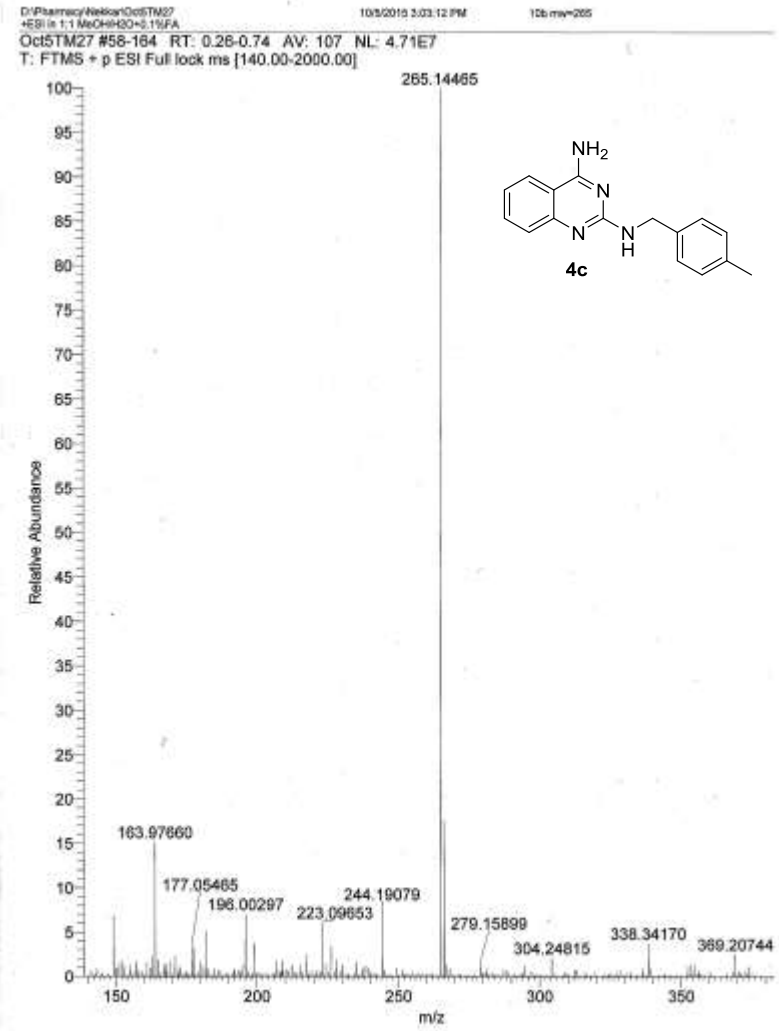
9. HRMS data for compounds **4a-q**

***N*^{2}-benzylquinazoline-2,4-diamine** (**4a**) and ***N*^{2}-(3-methylbenzyl)quinazoline-2,4-diamine** (**4b**)

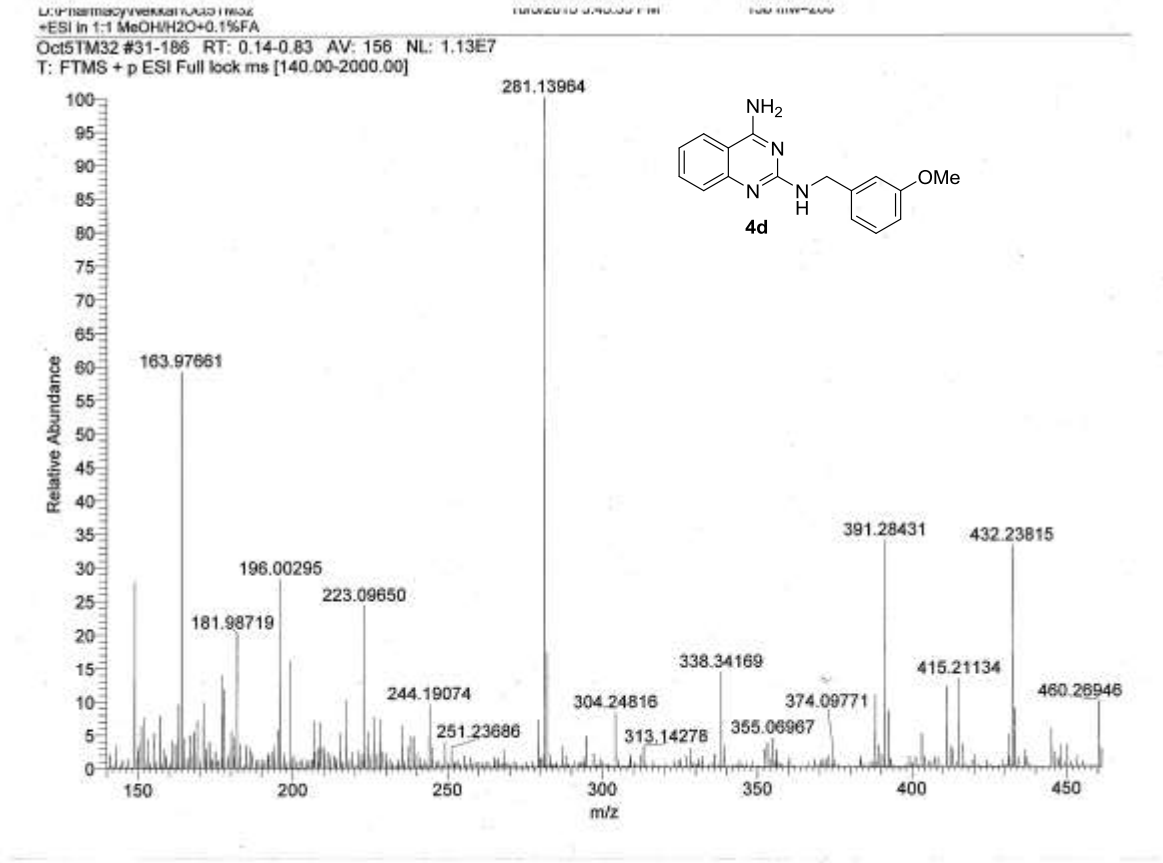




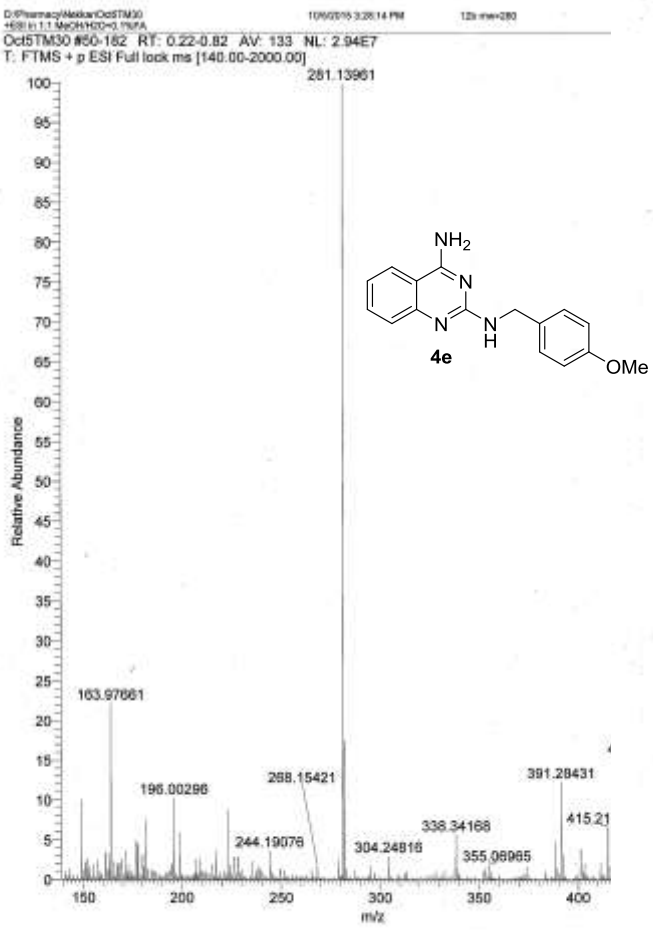
N^2-(4-methylbenzyl)quinazoline-2,4-diamine (4c)

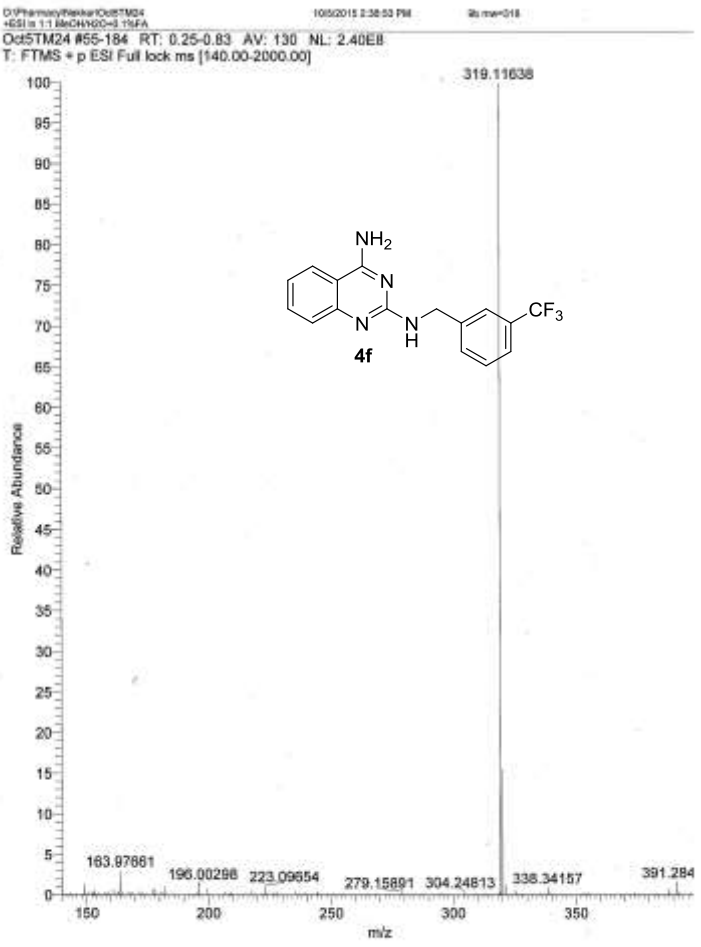


N^2-(3-methoxybenzyl)quinazoline-2,4-diamine (**4d**)

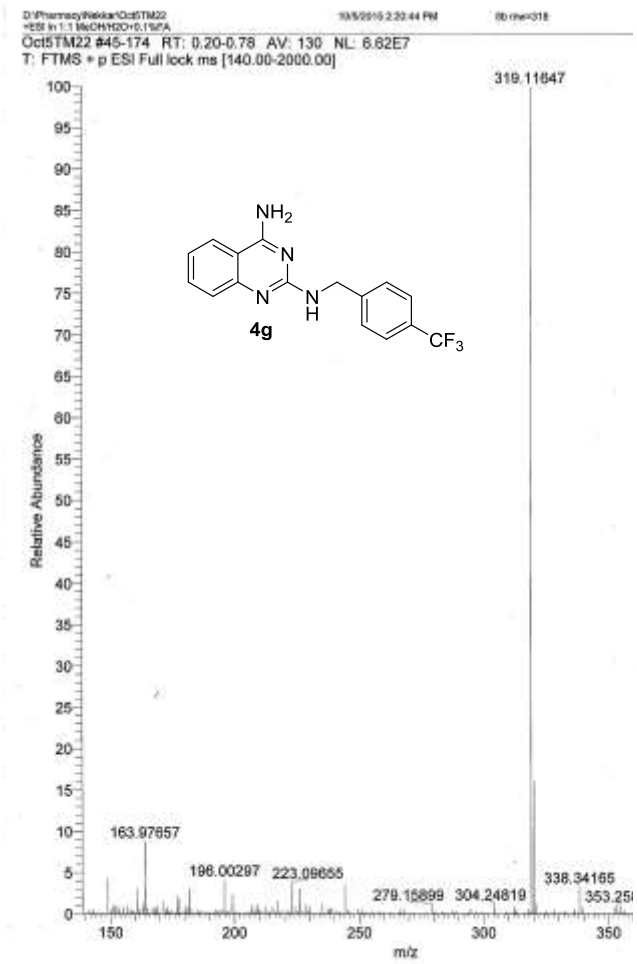


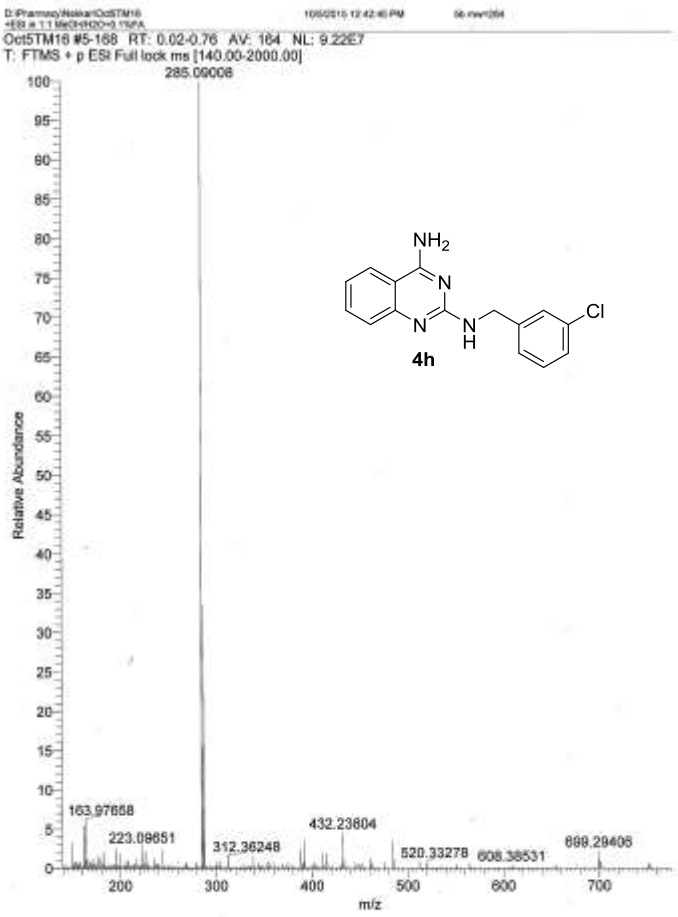
N^2-(4-methoxybenzyl)quinazoline-2,4-diamine (**4e**) and **N^2-(3-trifluoromethylbenzyl)quinazoline-2,4-diamine** (**4f**)



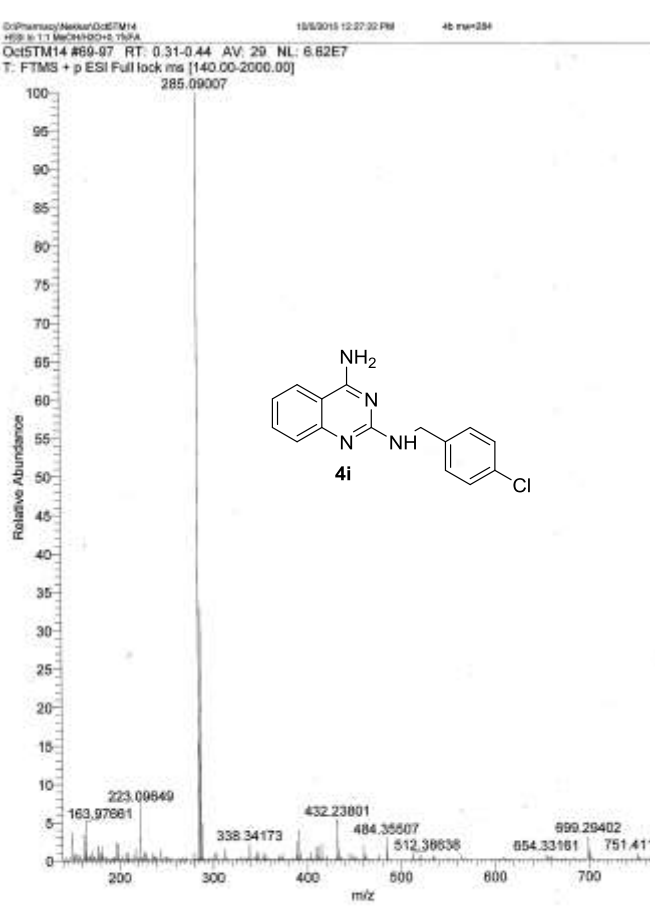


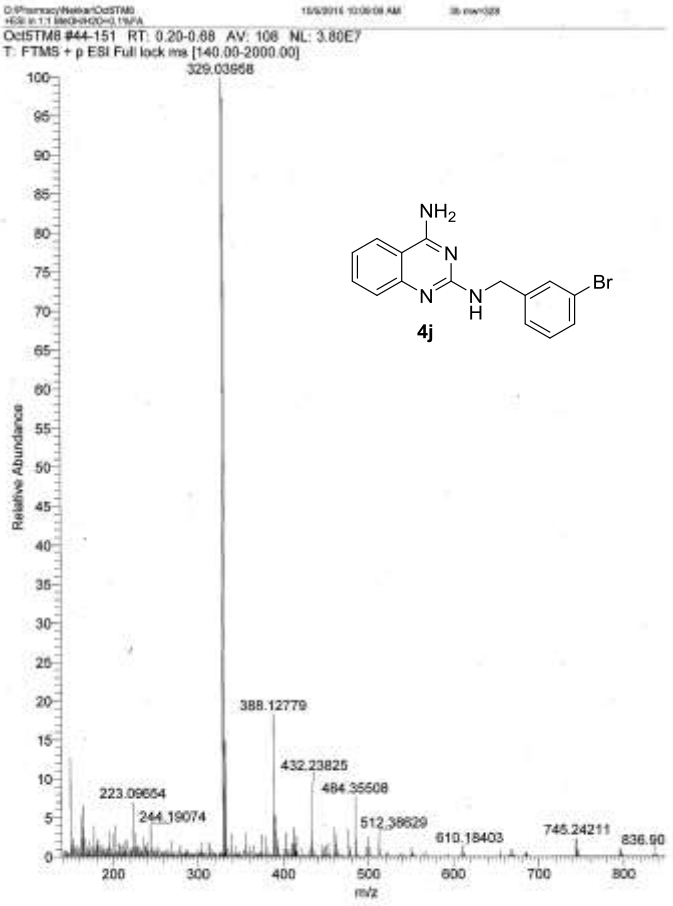
N^2-(4-trifluoromethylbenzyl)quinazoline-2,4-diamine (4g) and N^2-(3-chlorobenzyl)quinazoline-2,4-diamine (4h)



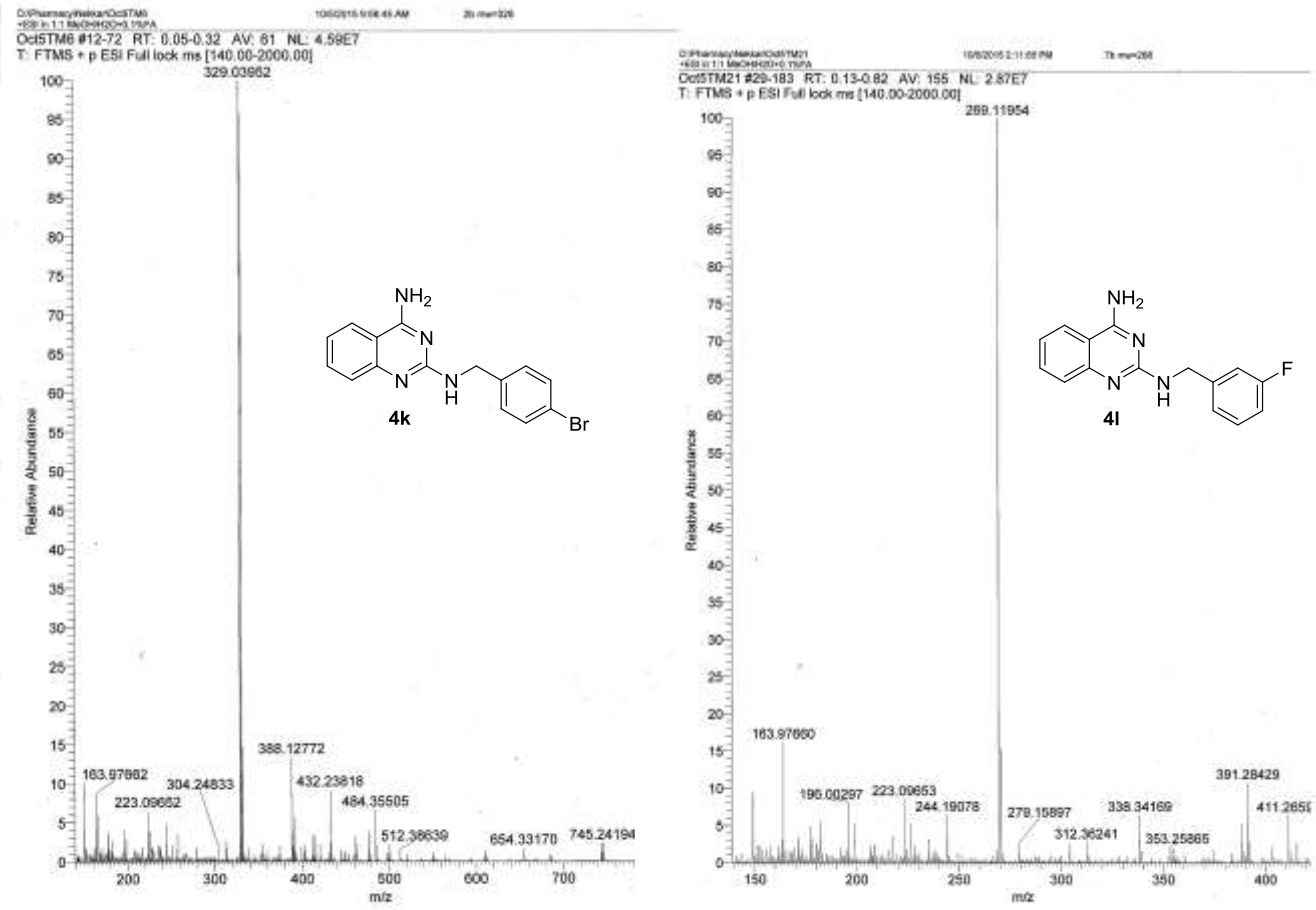


N^2-(4-chlorobenzyl)quinazoline-2,4-diamine (**4i**) and **N^2-(3-bromobenzyl)quinazoline-2,4-diamine** (**4j**)

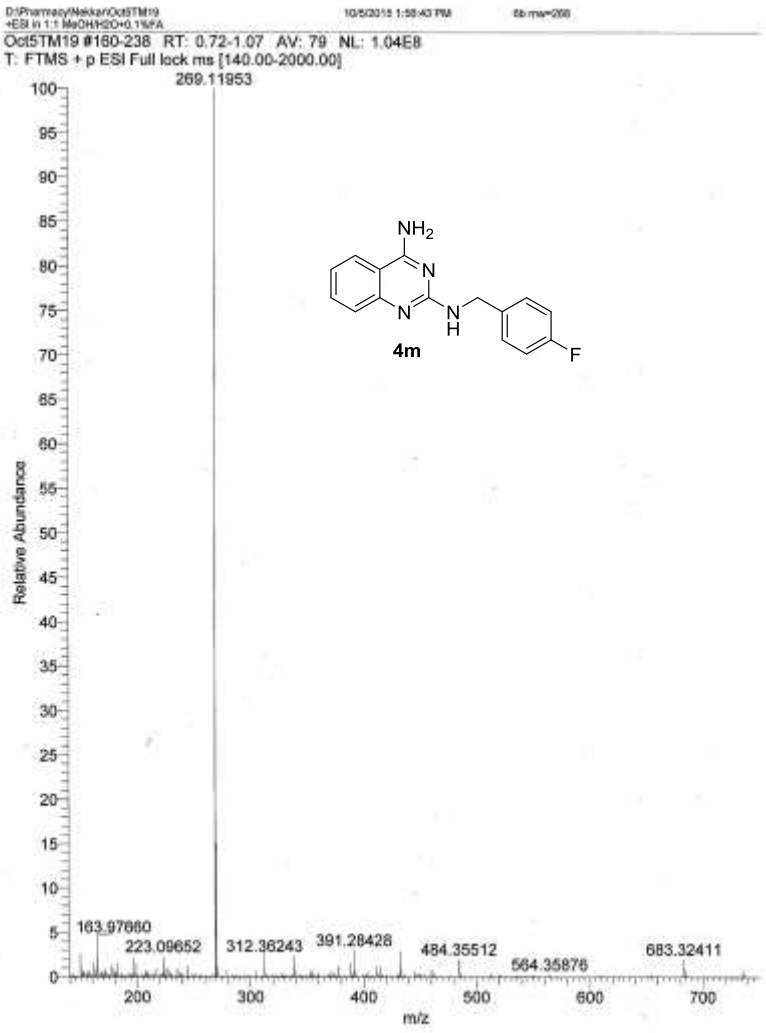




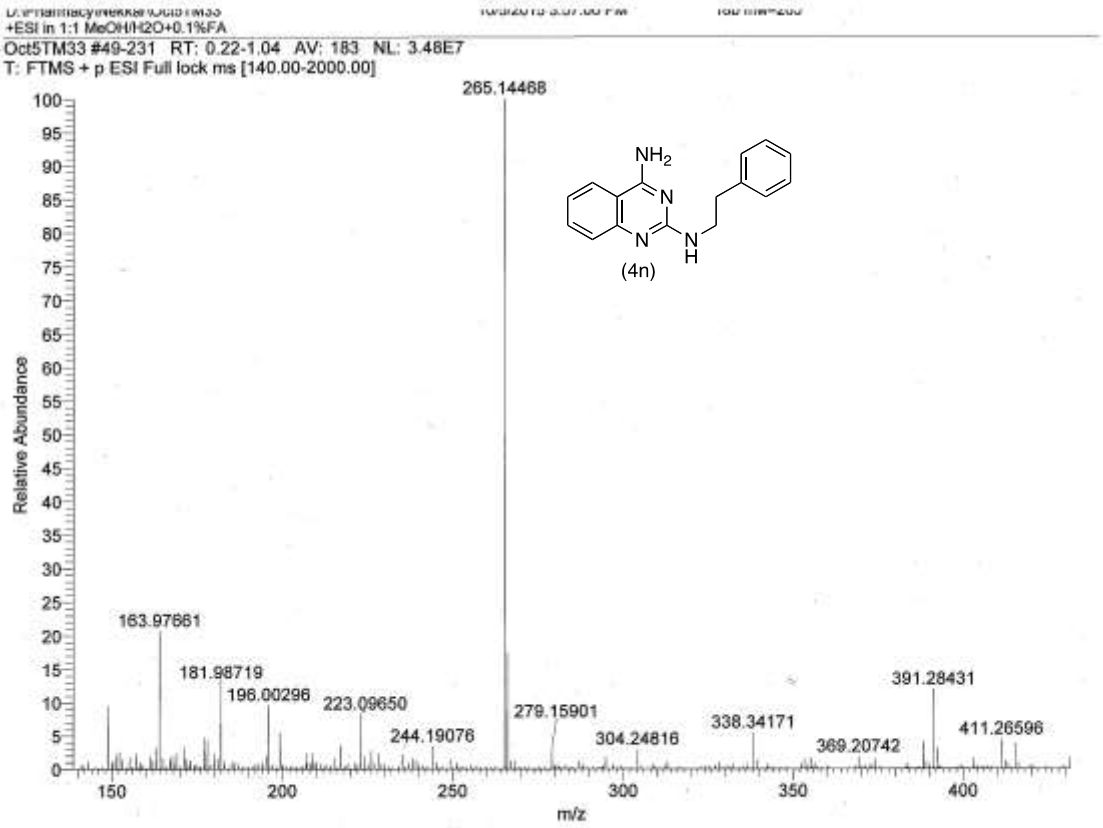
N^2-(4-bromobenzyl)quinazoline-2,4-diamine (**4k**) and **N^2-(3-fluorobenzyl)quinazoline-2,4-diamine** (**4l**)



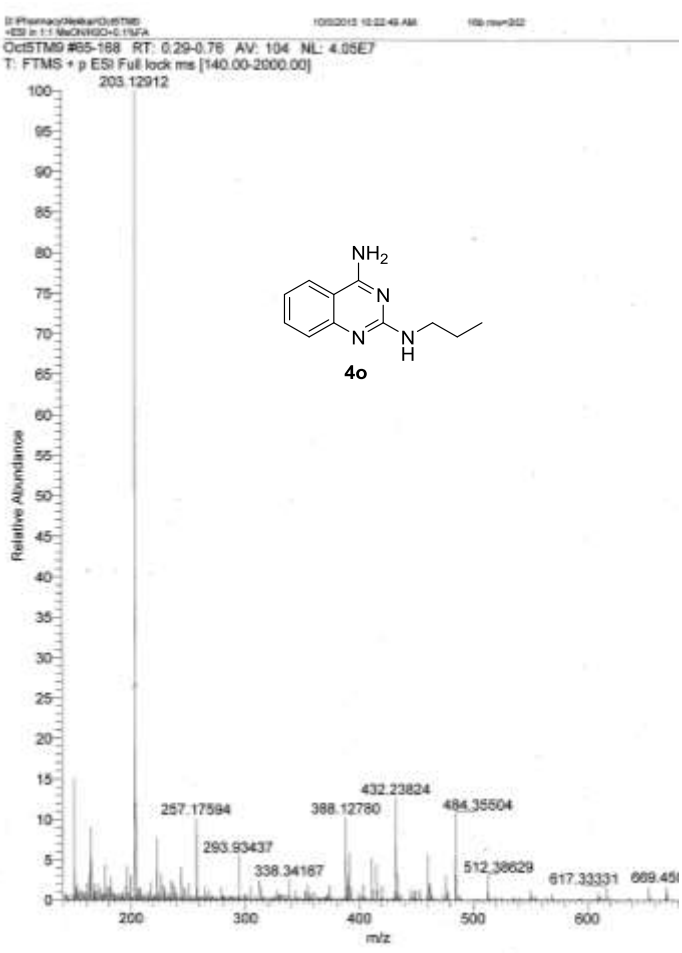
N^2-(4-fluorobenzyl)quinazoline-2,4-diamine (4m)

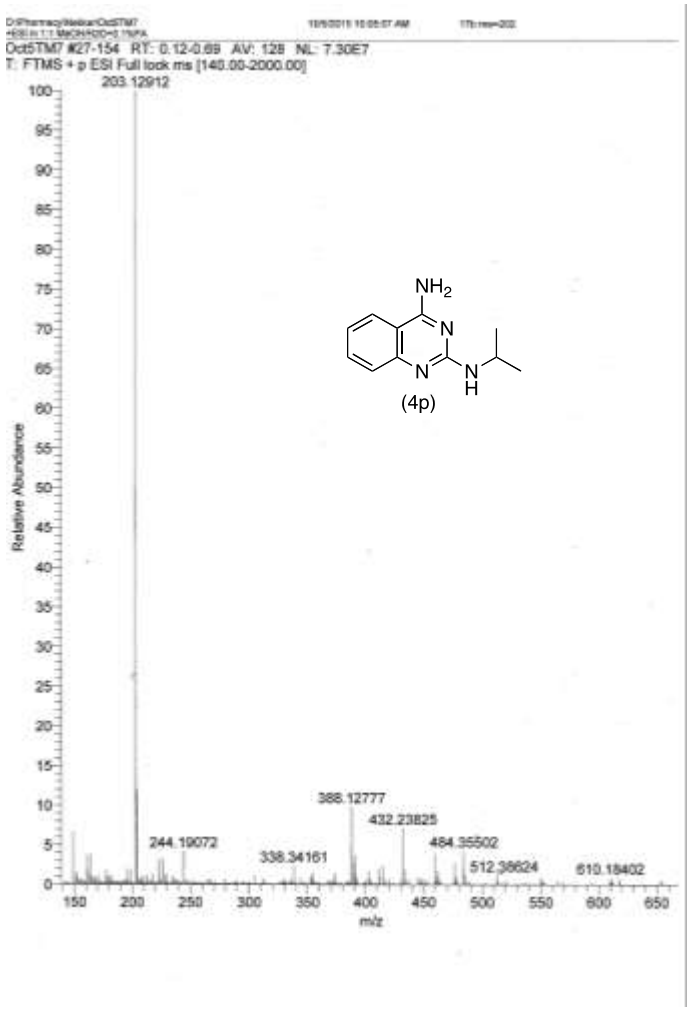


N^2-phenethylquinazoline-2,4-diamine (4n)

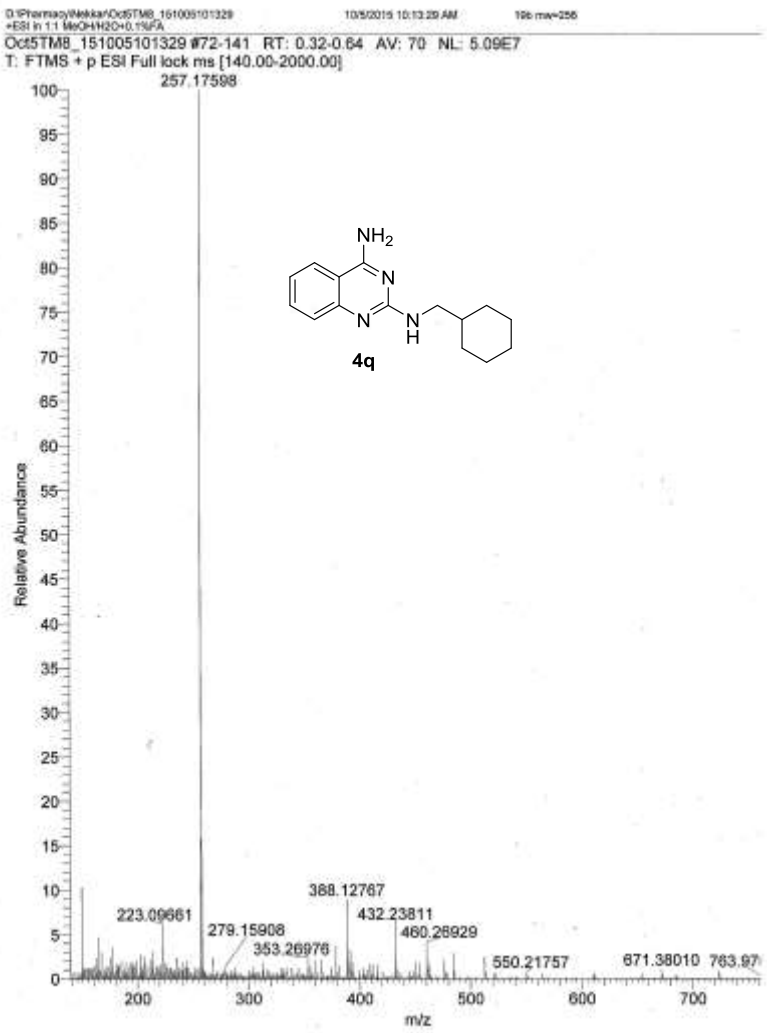


***N*^{2}-propylquinazoline-2,4-diamine** (**4o**) and ***N*^{2}-isopropylquinazoline-2,4-diamine** (**4p**)



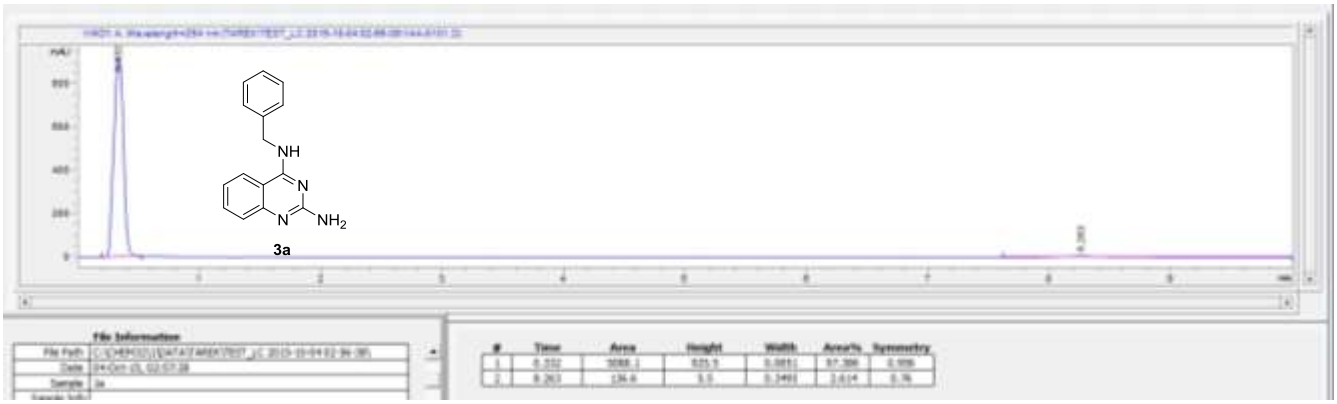


N^2-(cyclohexylmethyl)quinazoline-2,4-diamine (4q)

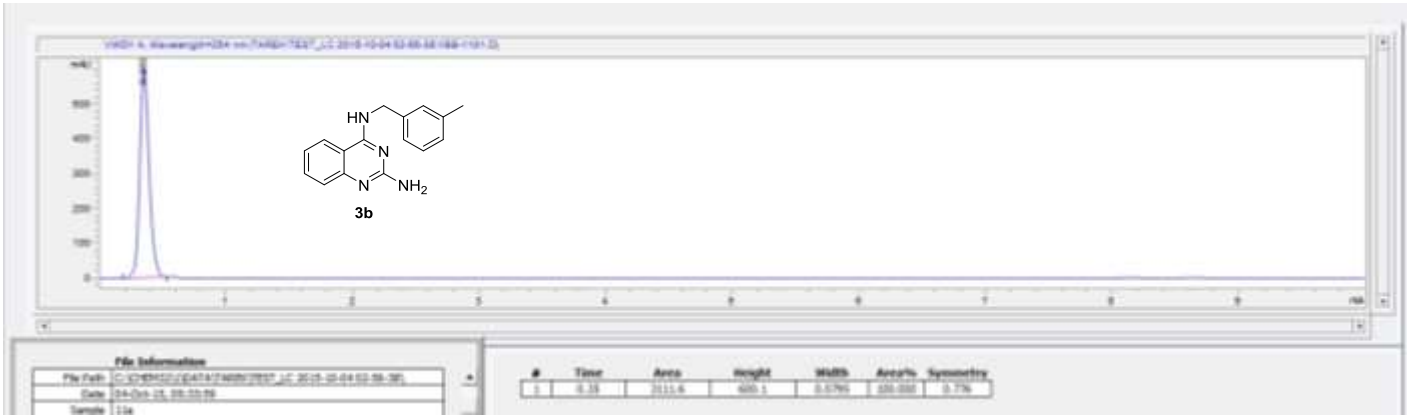


10. HPLC trace for compounds 3a-q

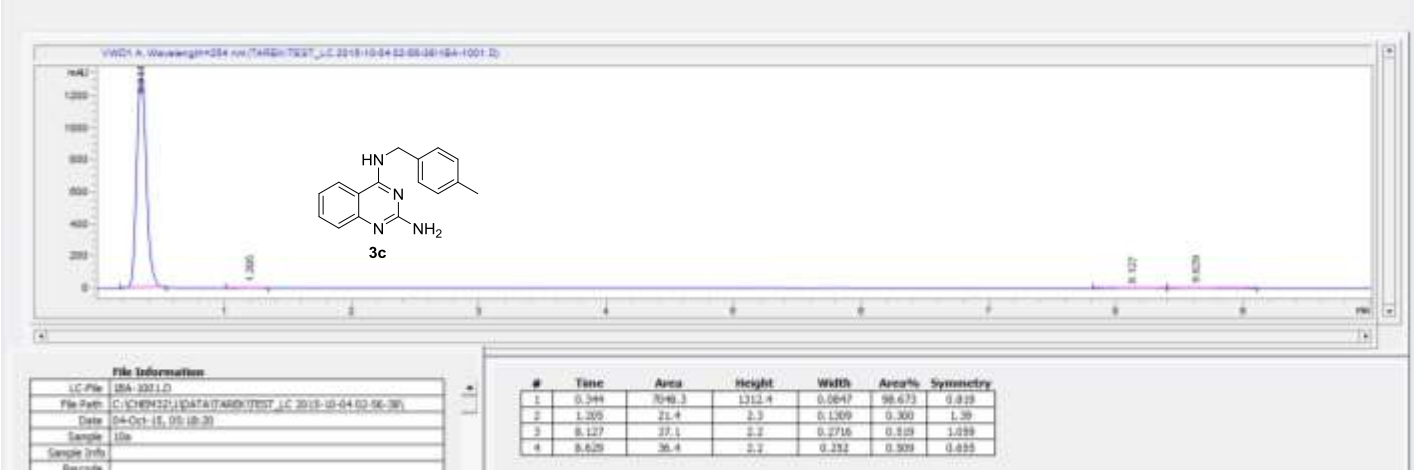
N^4-benzylquinazoline-2,4-diamine (3a)



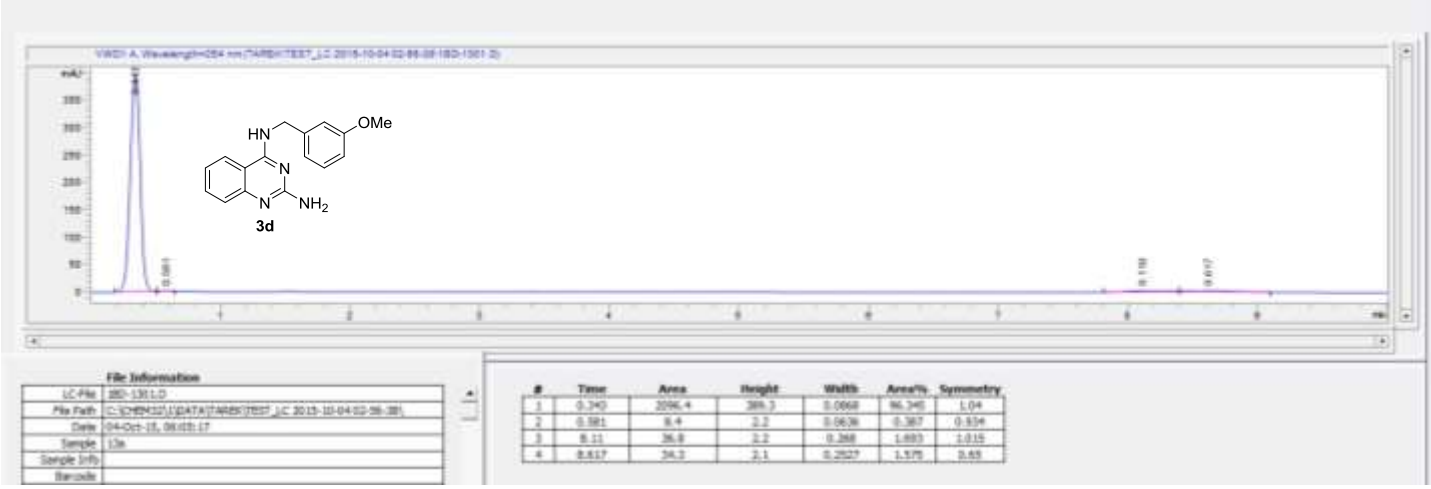
N^4-(3-methylbenzyl)quinazoline-2,4-diamine (3b)



N^4-(4-methylbenzyl)quinazoline-2,4-diamine (3c)

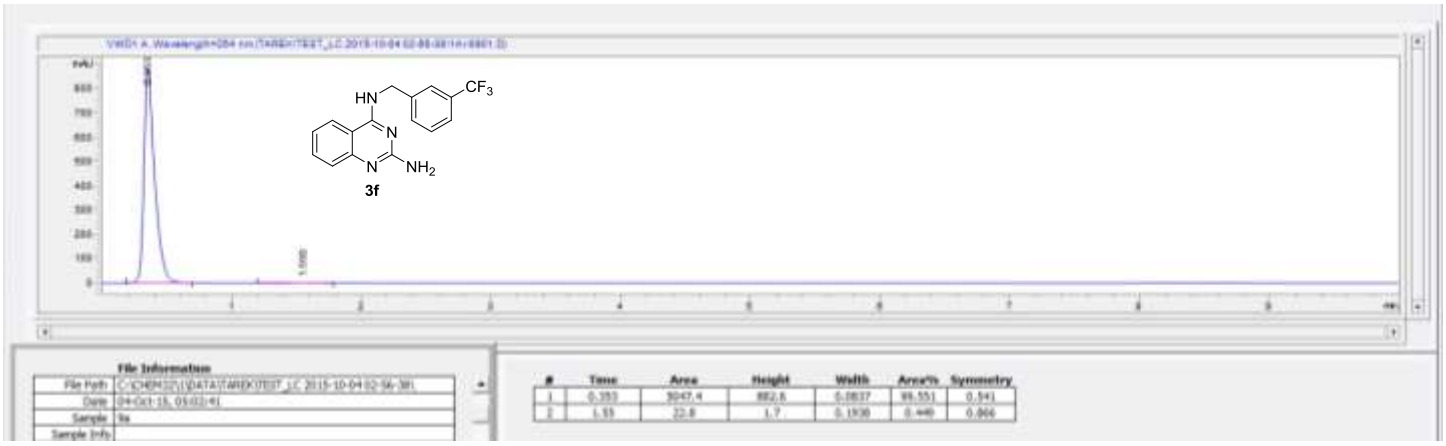


N^4-(3-methoxybenzyl)quinazoline-2,4-diamine (3d)

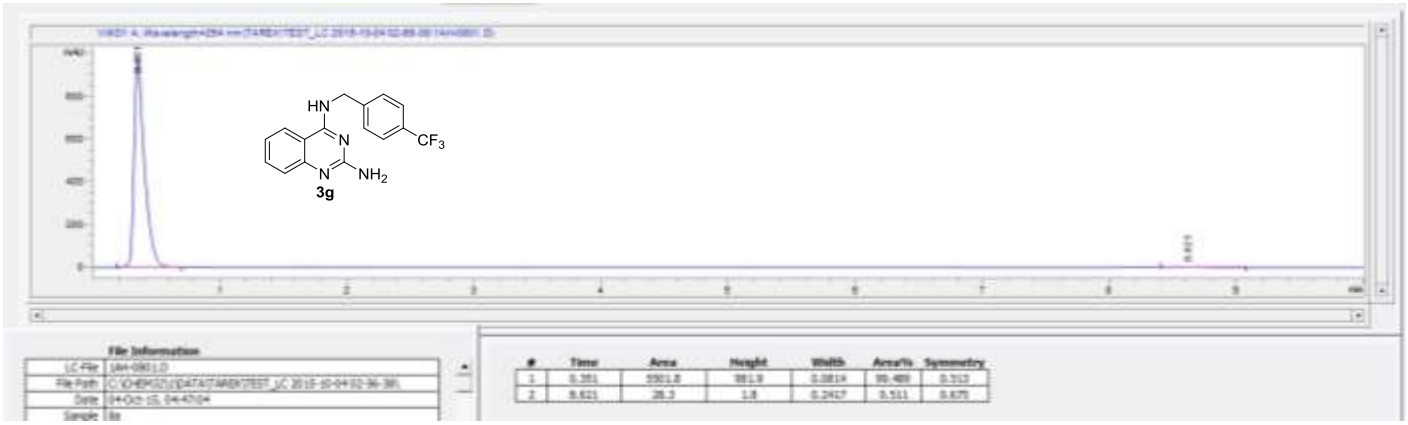


N^4-(4-methoxybenzyl)quinazoline-2,4-diamine (3e)

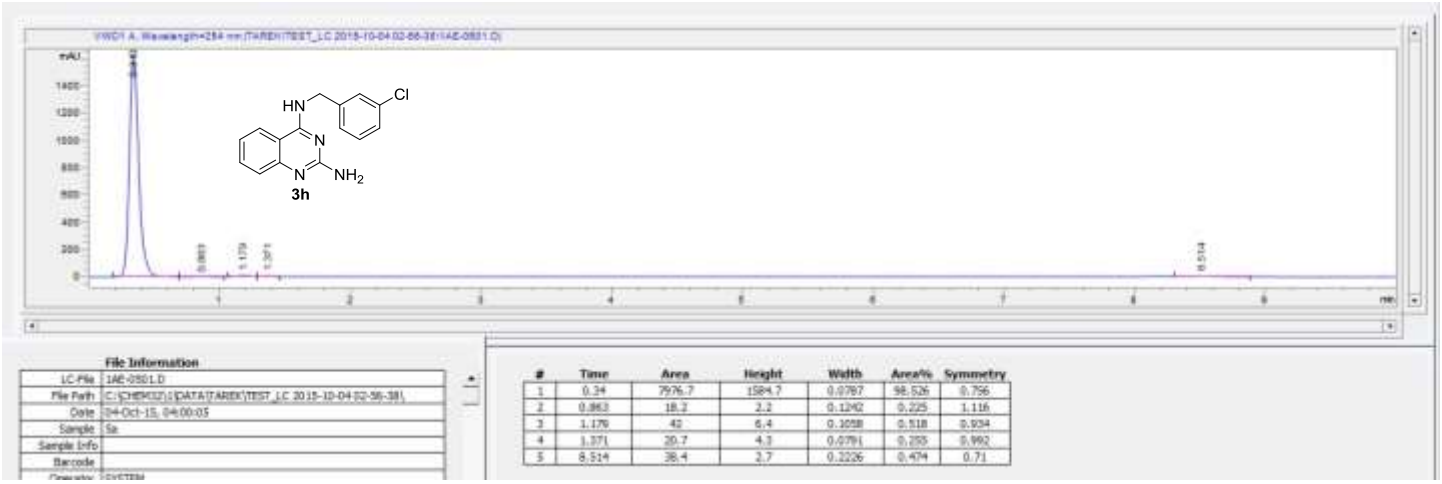
N^4-(3-trifluoromethylbenzyl)quinazoline-2,4-diamine (3f)



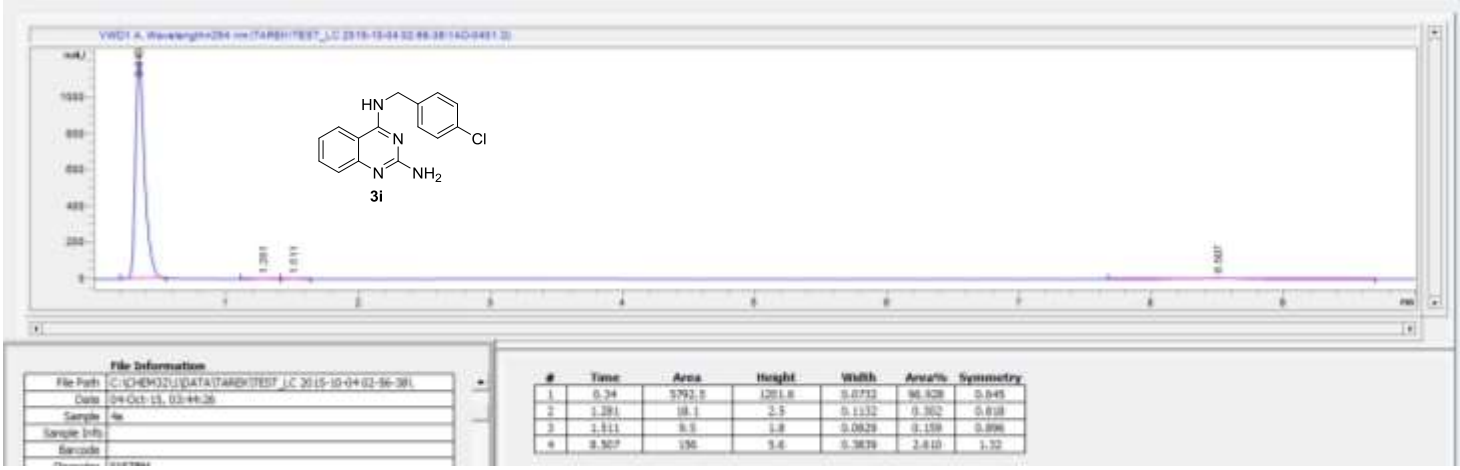
N^4-(4-trifluoromethylbenzyl)quinazoline-2,4-diamine (3g)



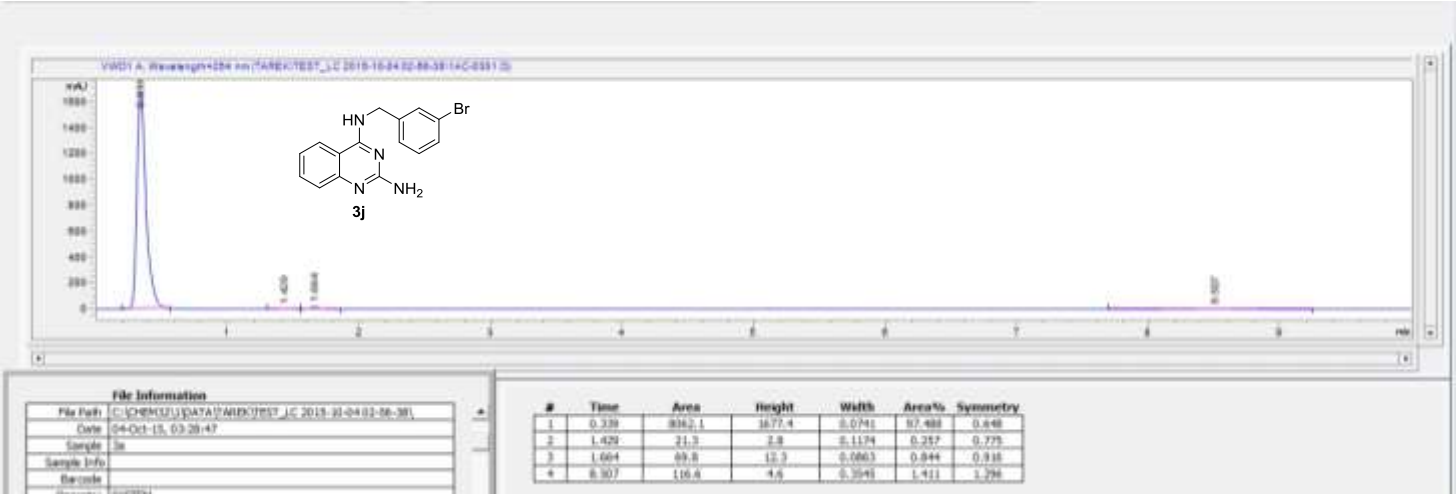
N^4-(3-chlorobenzyl)quinazoline-2,4-diamine (3h)



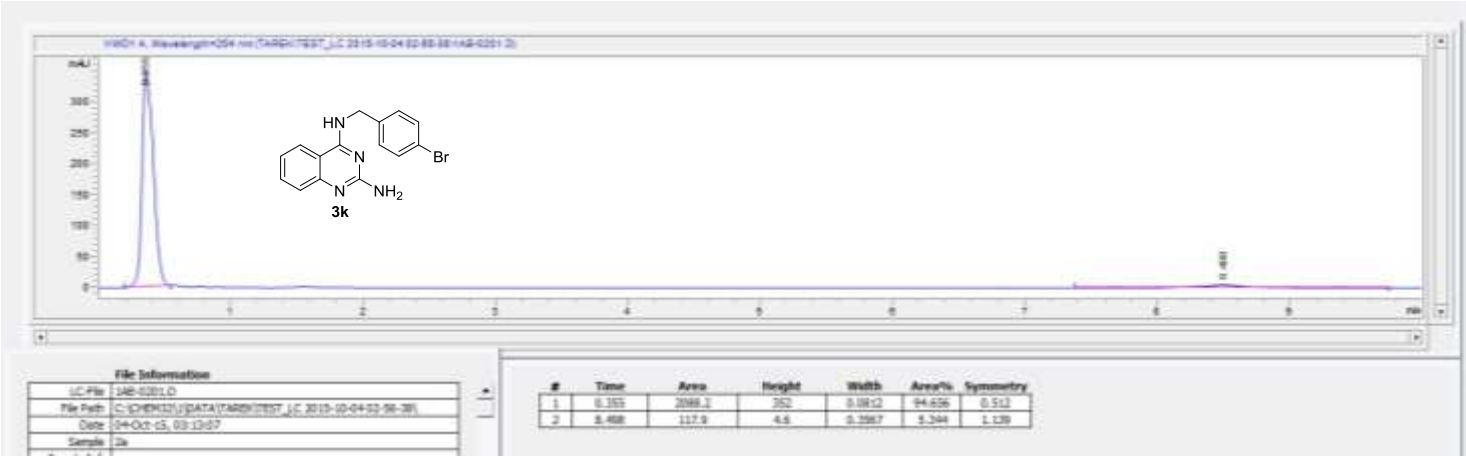
N^4-(4-chlorobenzyl)quinazoline-2,4-diamine (3i)



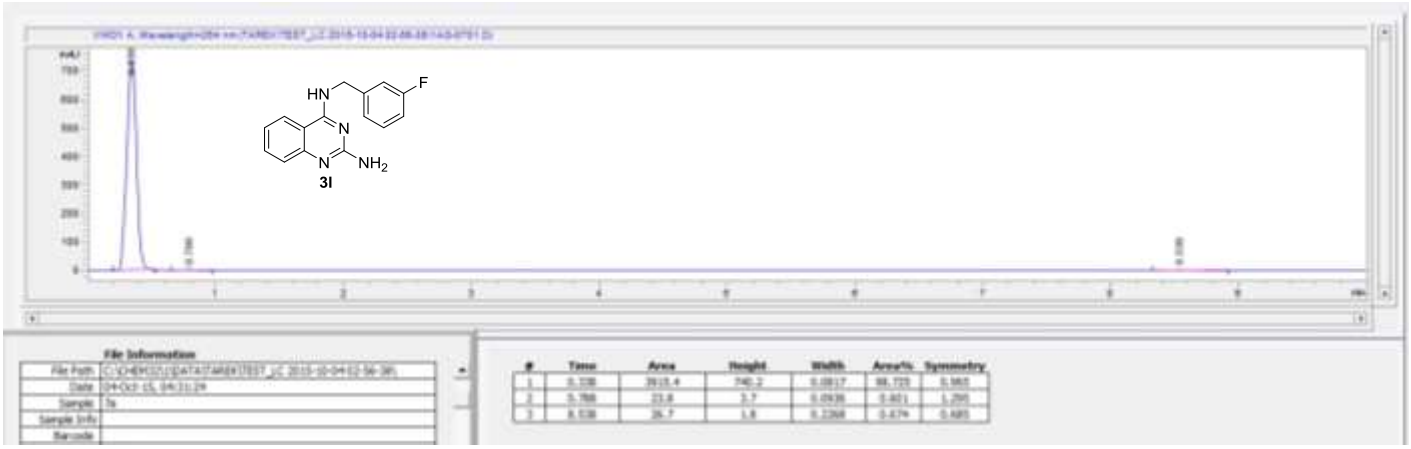
N^4-(3-bromobenzyl)quinazoline-2,4-diamine (3j)



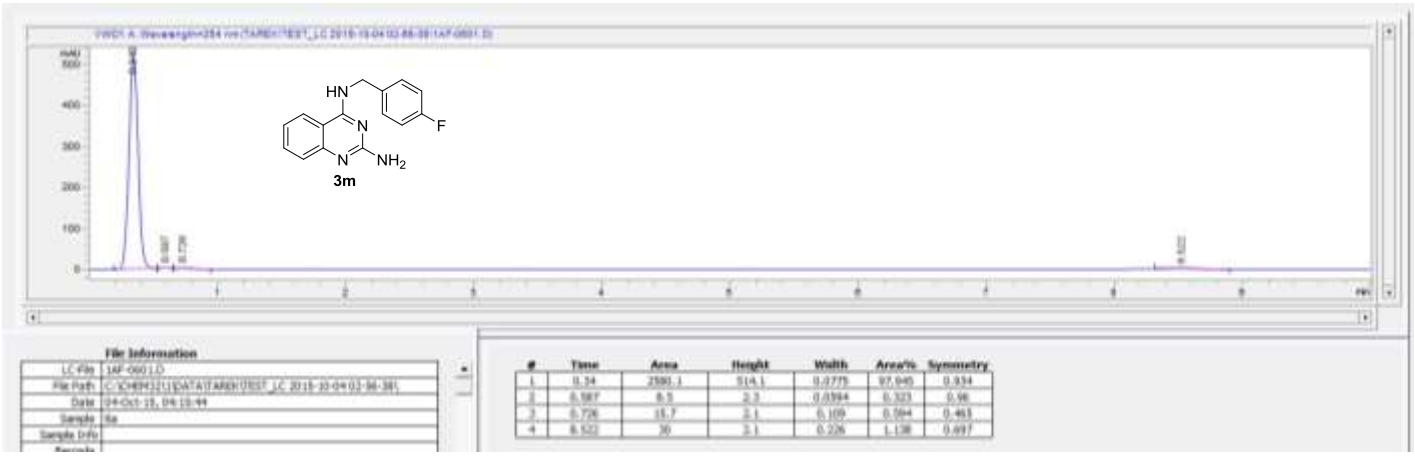
N^4-(4-bromobenzyl)quinazoline-2,4-diamine (3k)



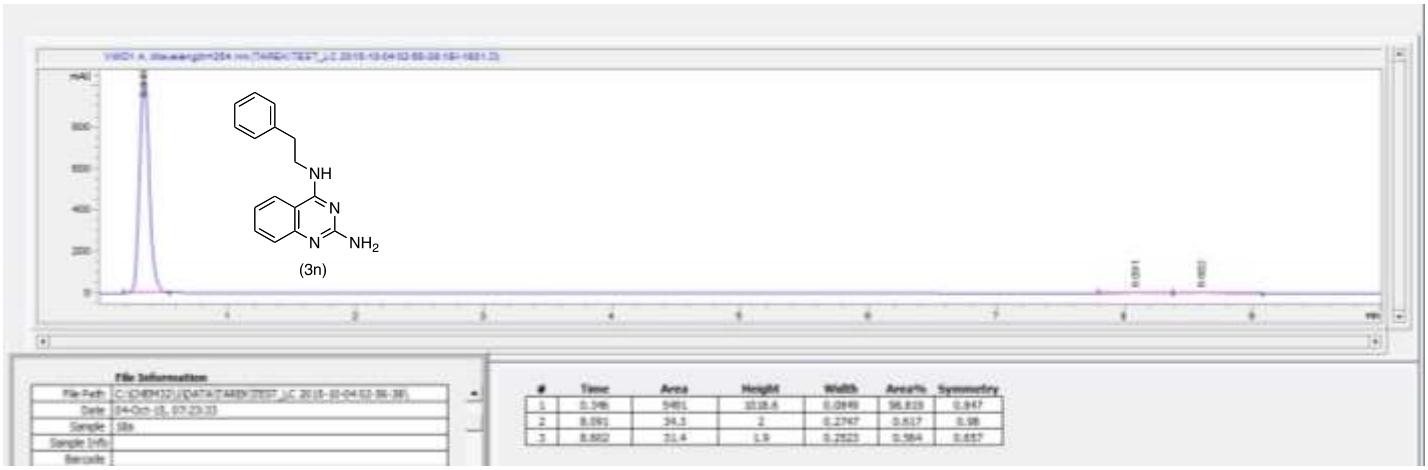
N^4-(3-fluorobenzyl)quinazoline-2,4-diamine (3l)



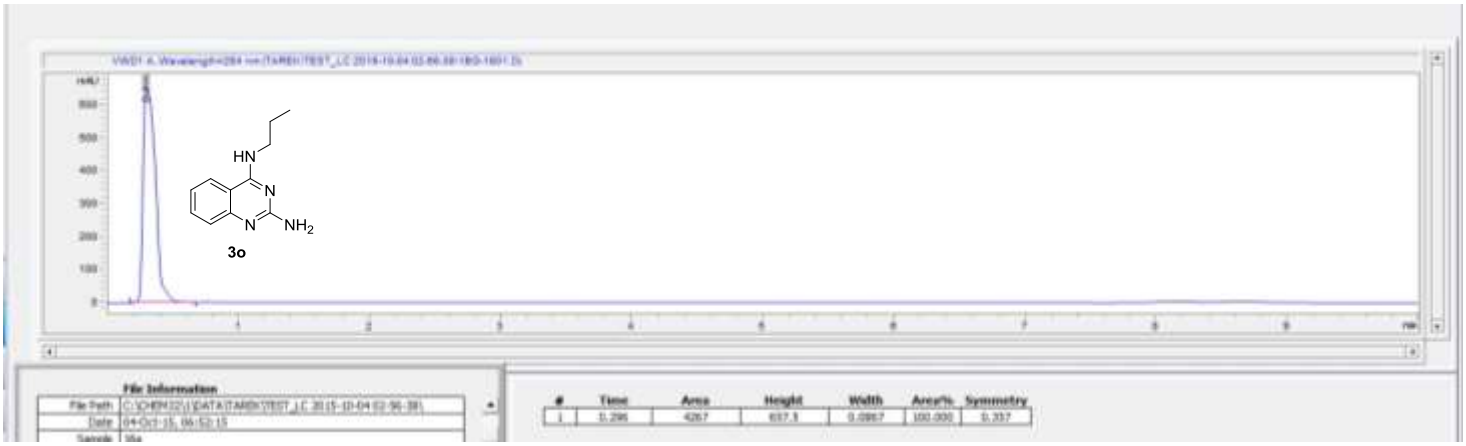
N^4-(4-fluorobenzyl)quinazoline-2,4-diamine (3m)



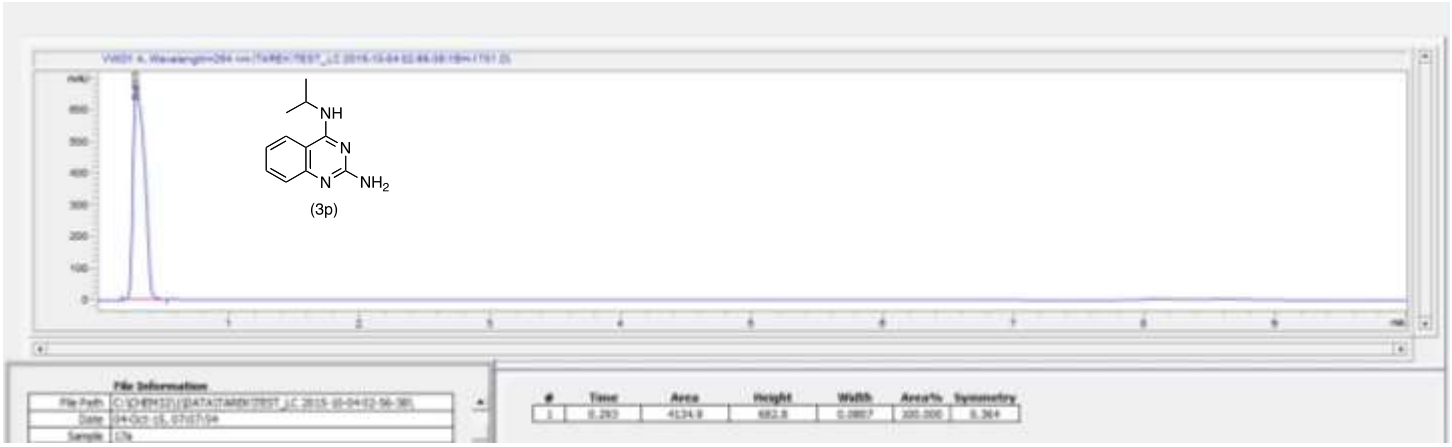
N^4-phenethylquinazoline-2,4-diamine (3n)



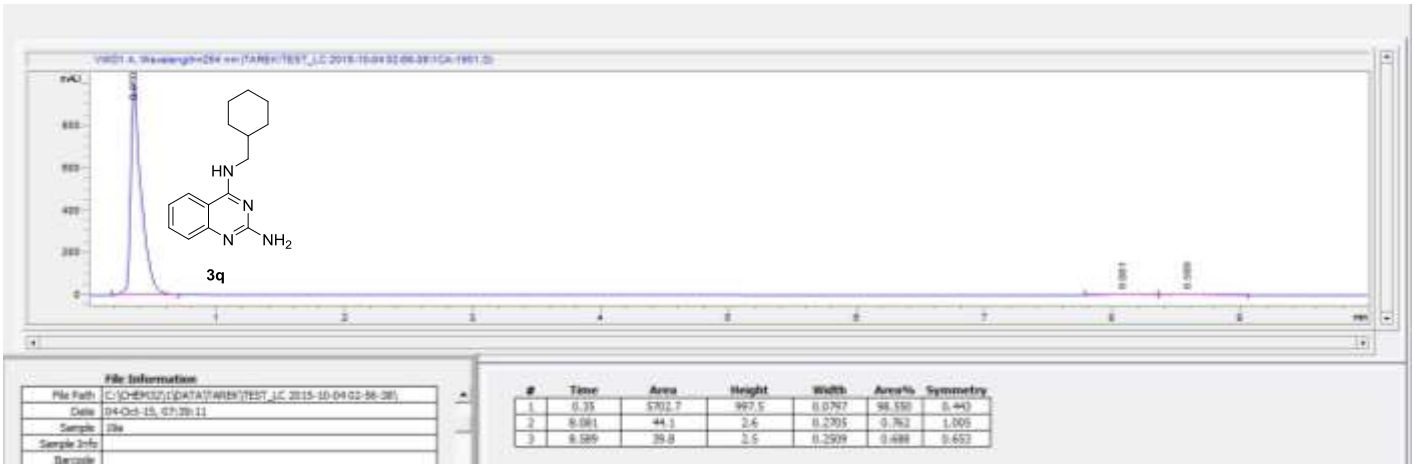
N^4-propylquinazoline-2,4-diamine (3o)



N^4-isopropylquinazoline-2,4-diamine (3p)

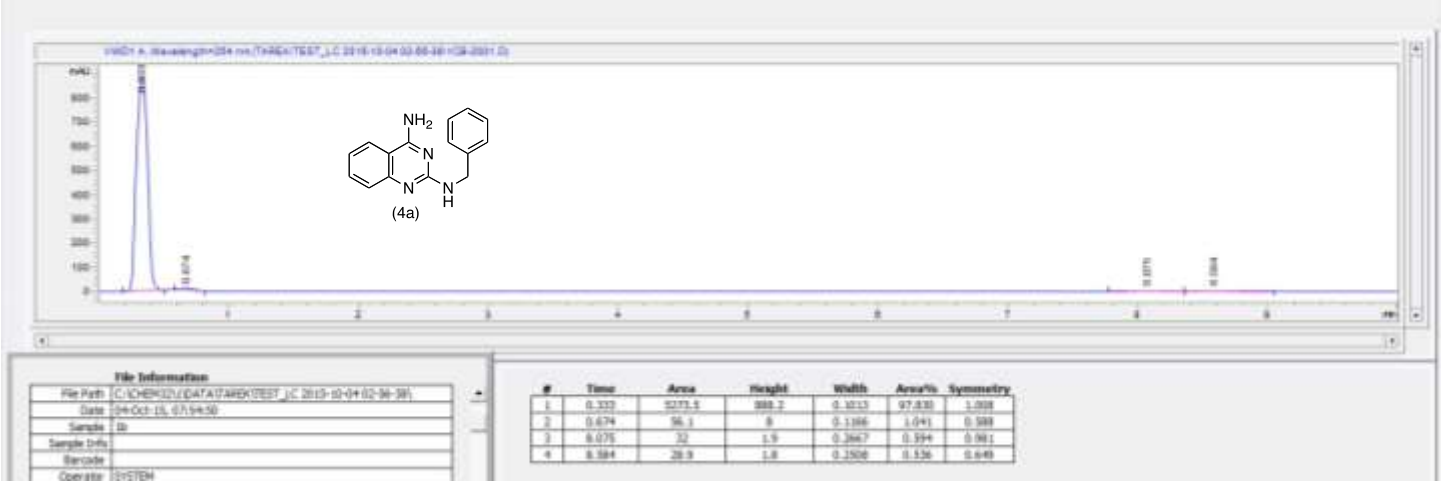


N^4-(cyclohexylmethyl)quinazoline-2,4-diamine (3q)

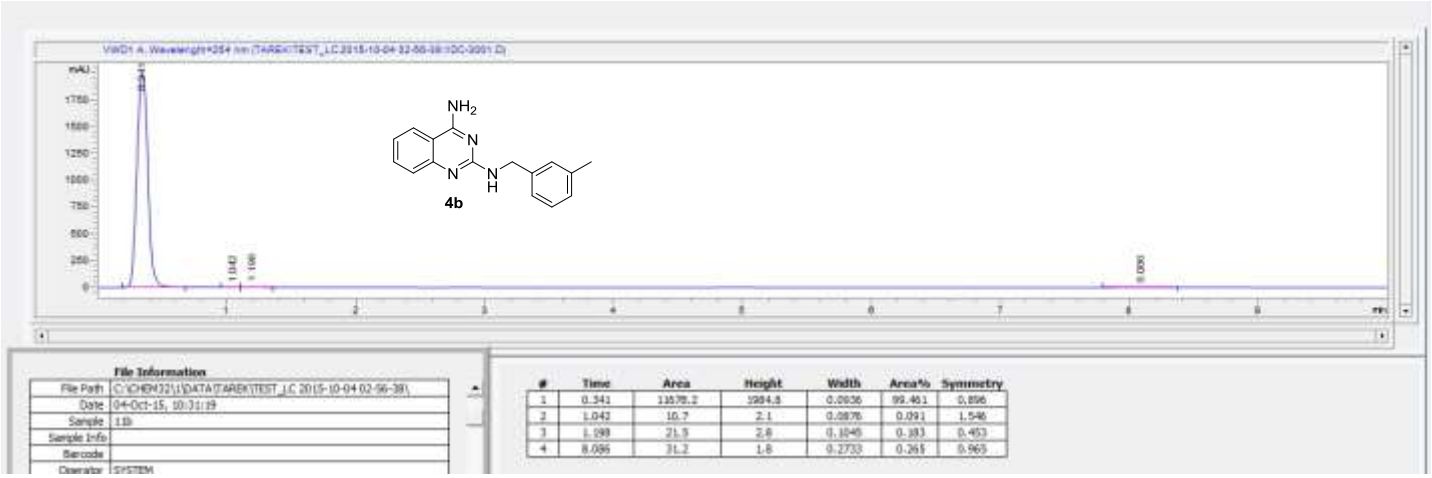


11. HPLC trace for compounds 4a-q

N^2-benzylquinazoline-2,4-diamine (4a)



N^2-(3-methylbenzyl)quinazoline-2,4-diamine (4b)



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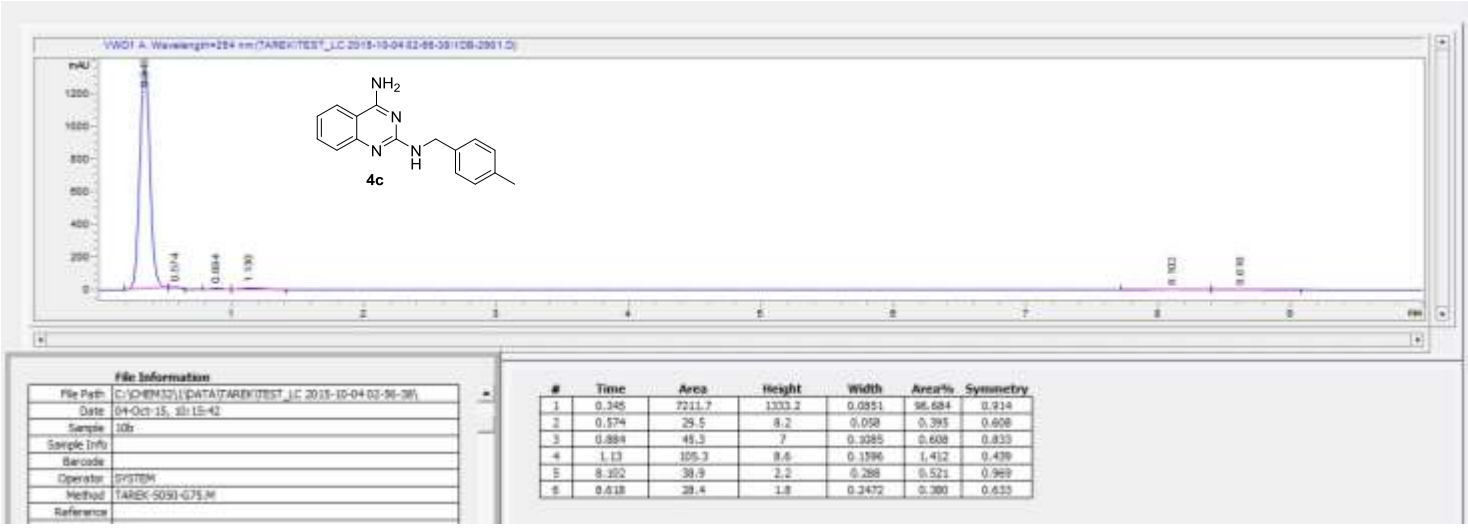

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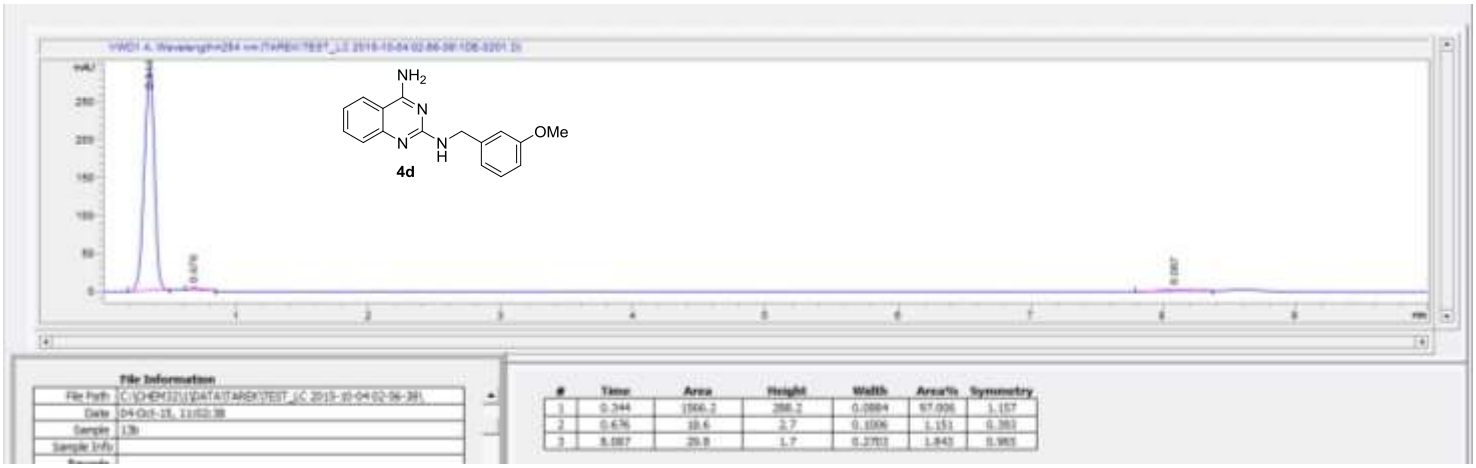

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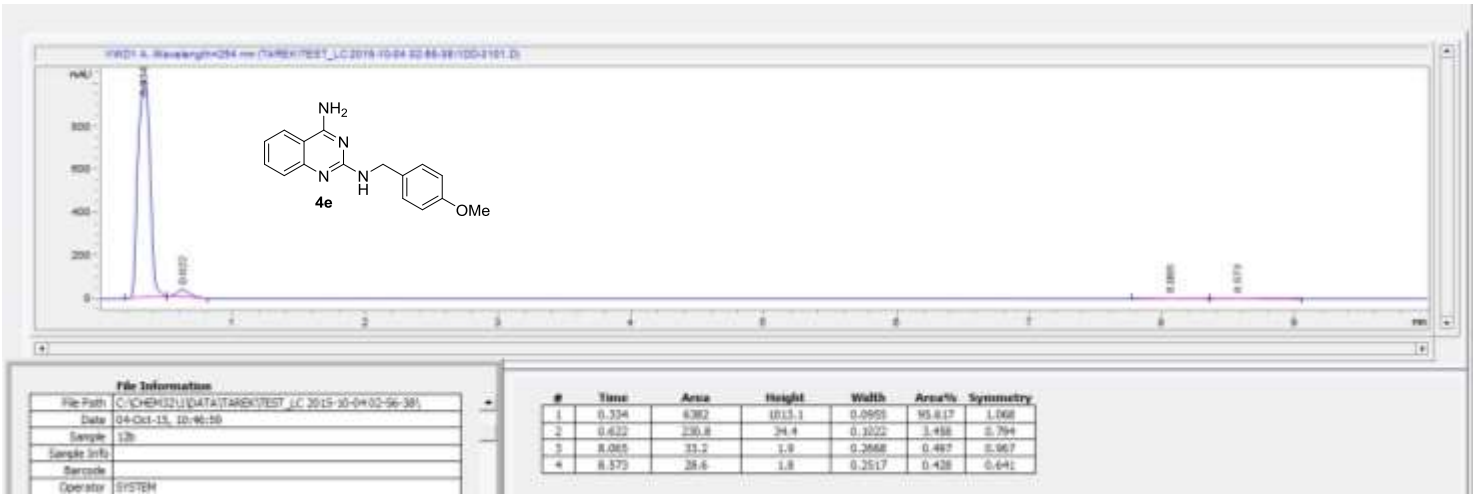
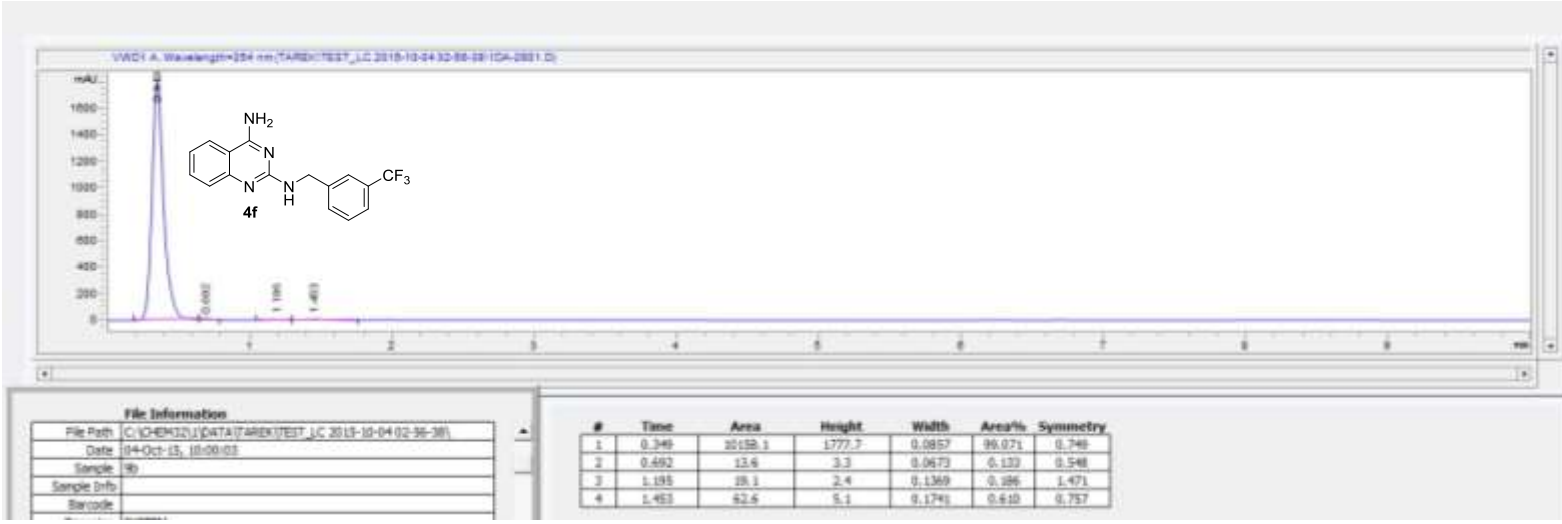


***N*^{2}-(3-trifluoromethylbenzyl)quinazoline-2,4-diamine (4f)**



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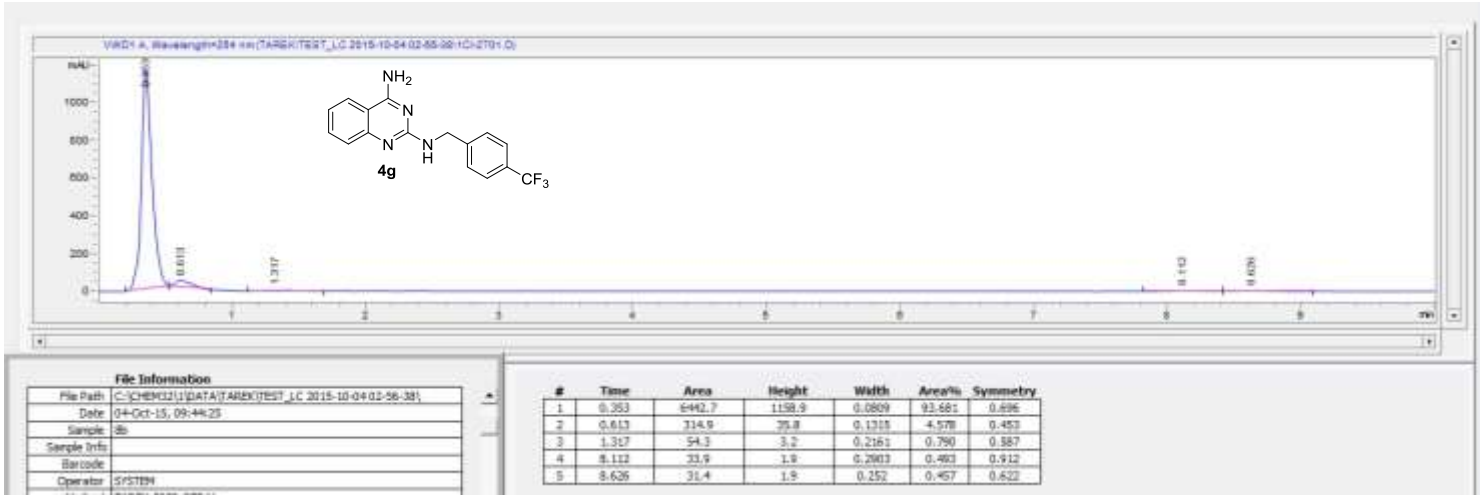

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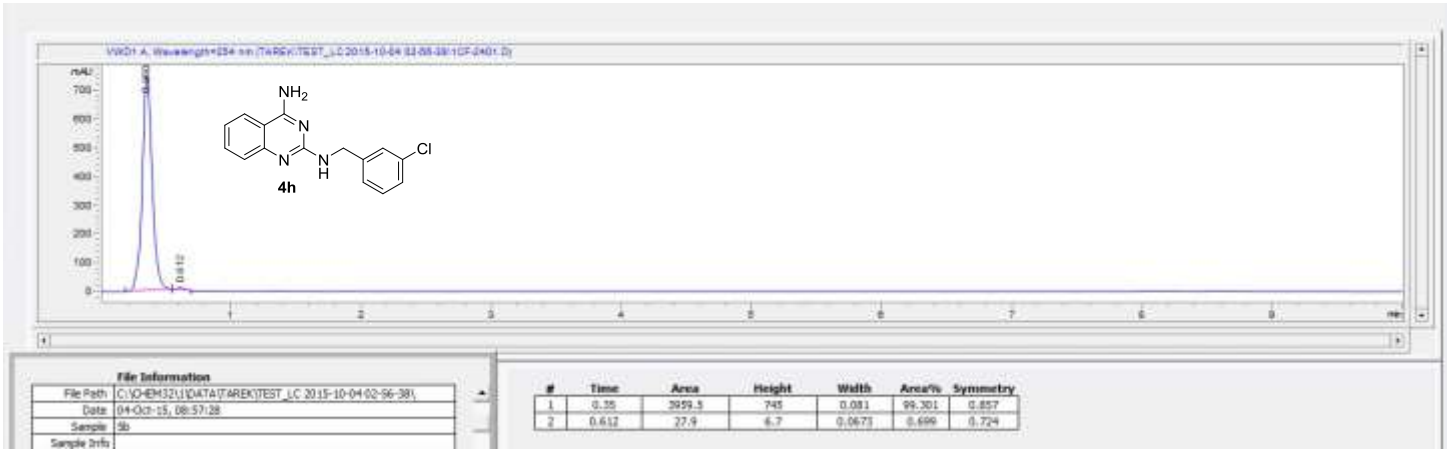
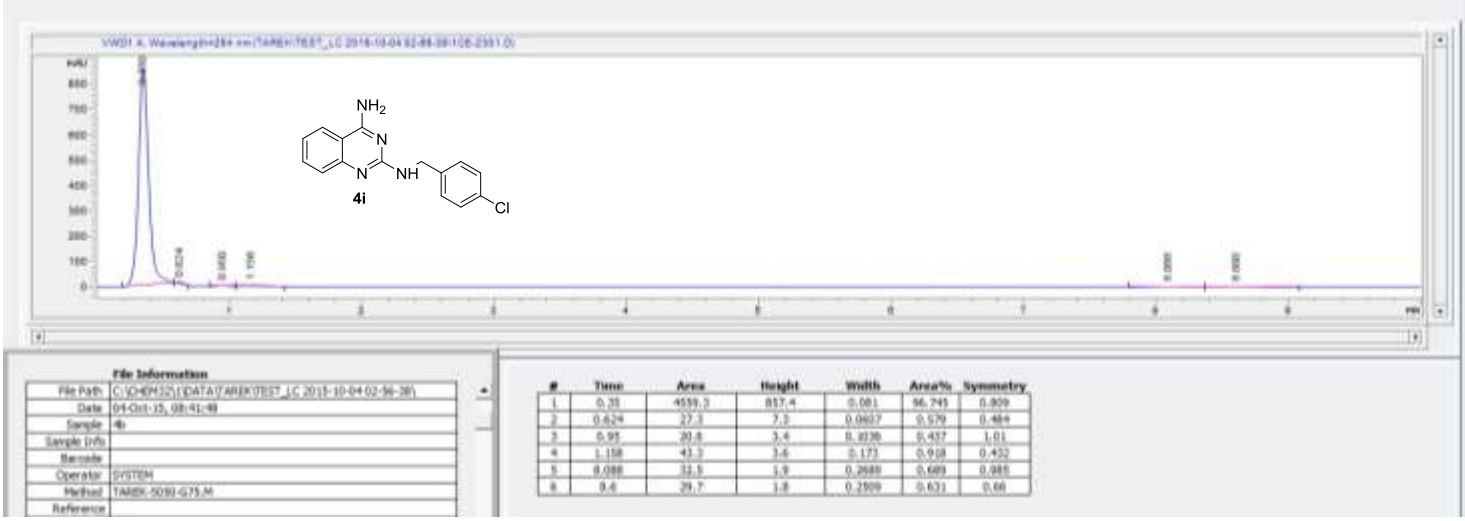
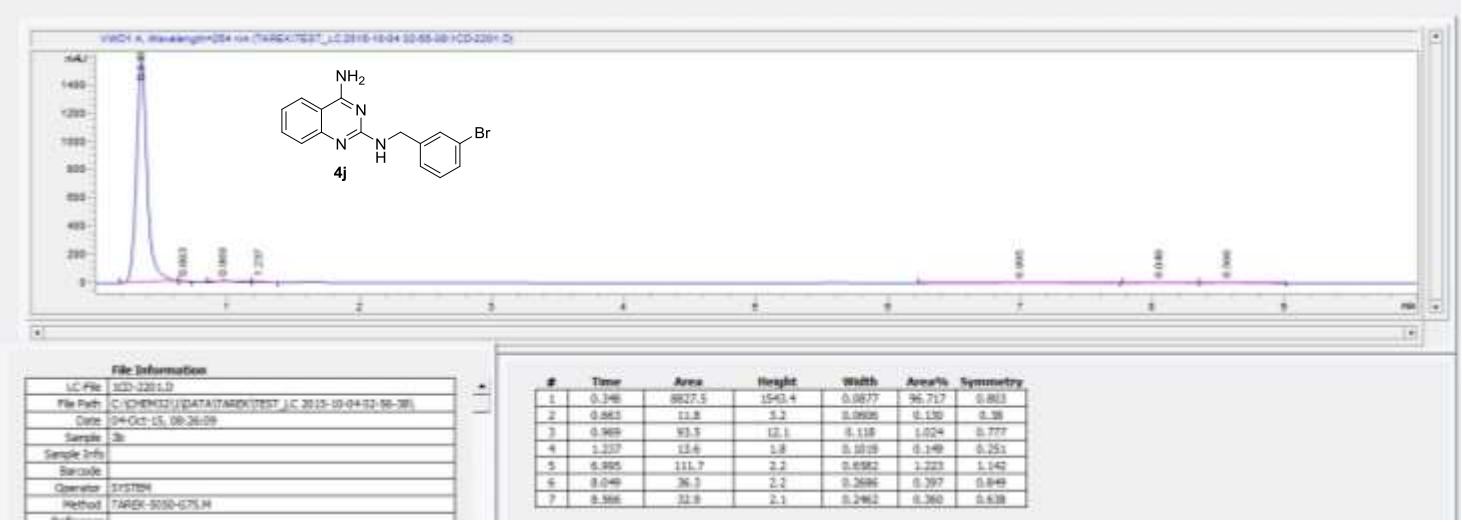


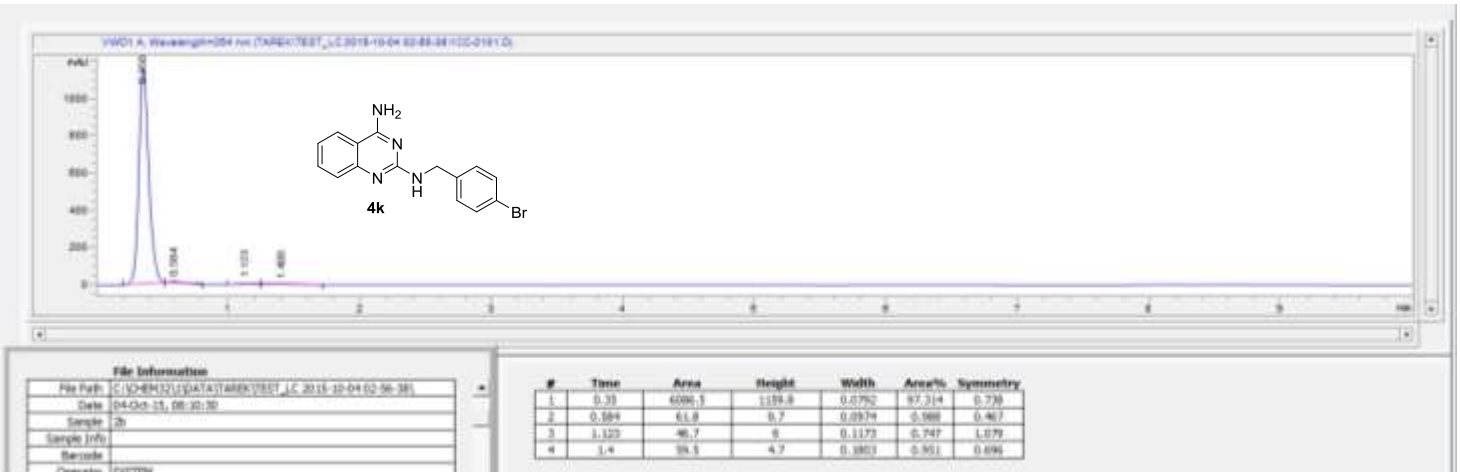
N^2-(4-chlorobenzyl)quinazoline-2,4-diamine (4i)



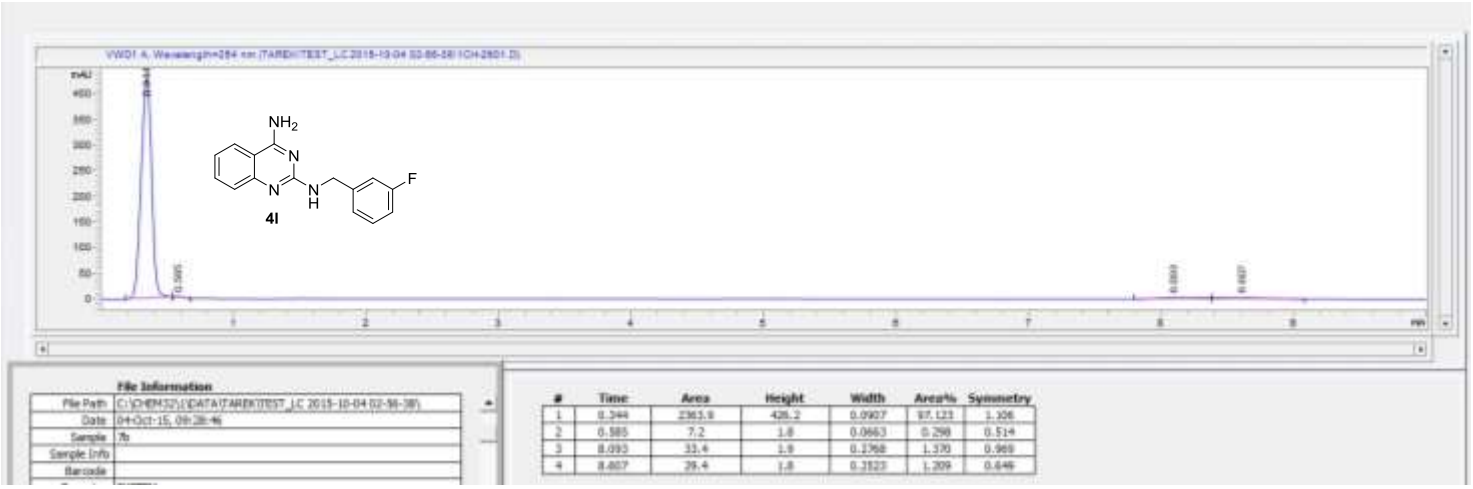
N^2-(3-bromobenzyl)quinazoline-2,4-diamine (4j)



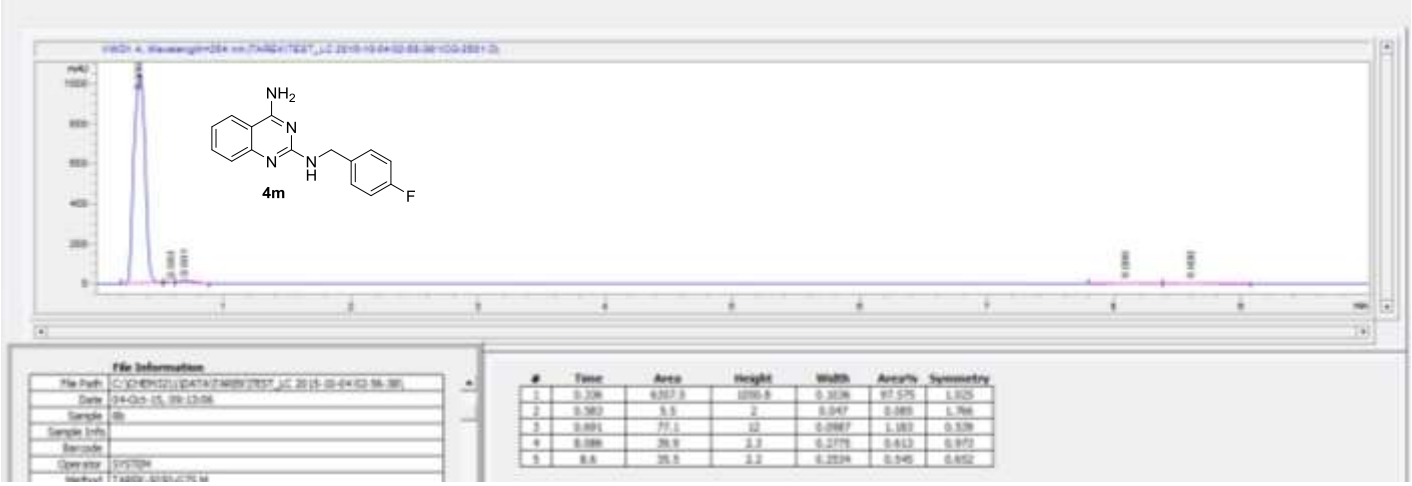
N^2-(4-bromobenzyl)quinazoline-2,4-diamine (4k)



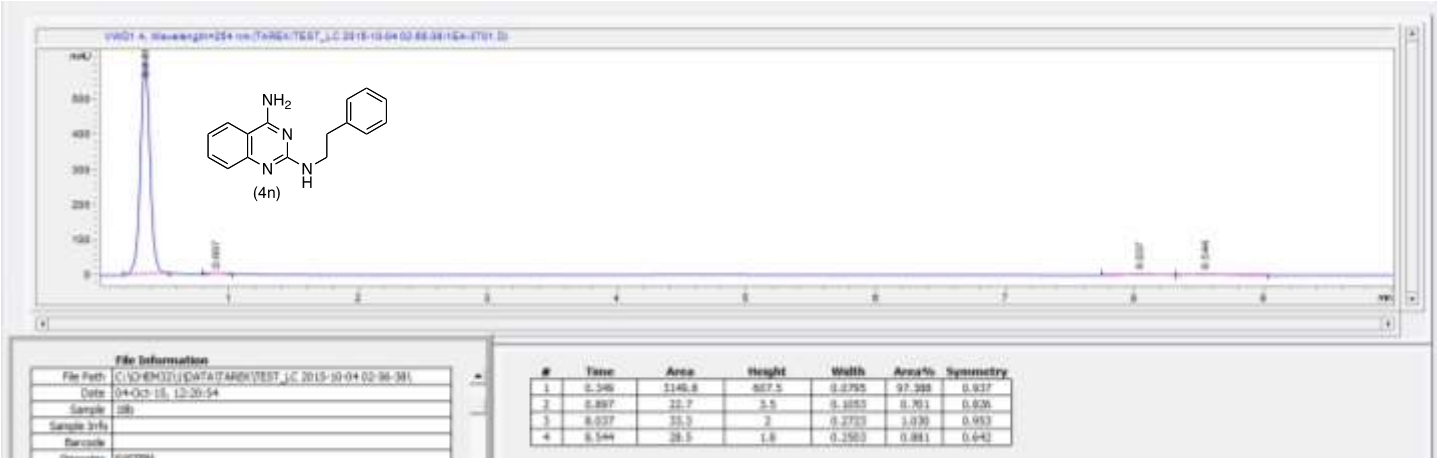
N^2-(3-fluorobenzyl)quinazoline-2,4-diamine (4l)



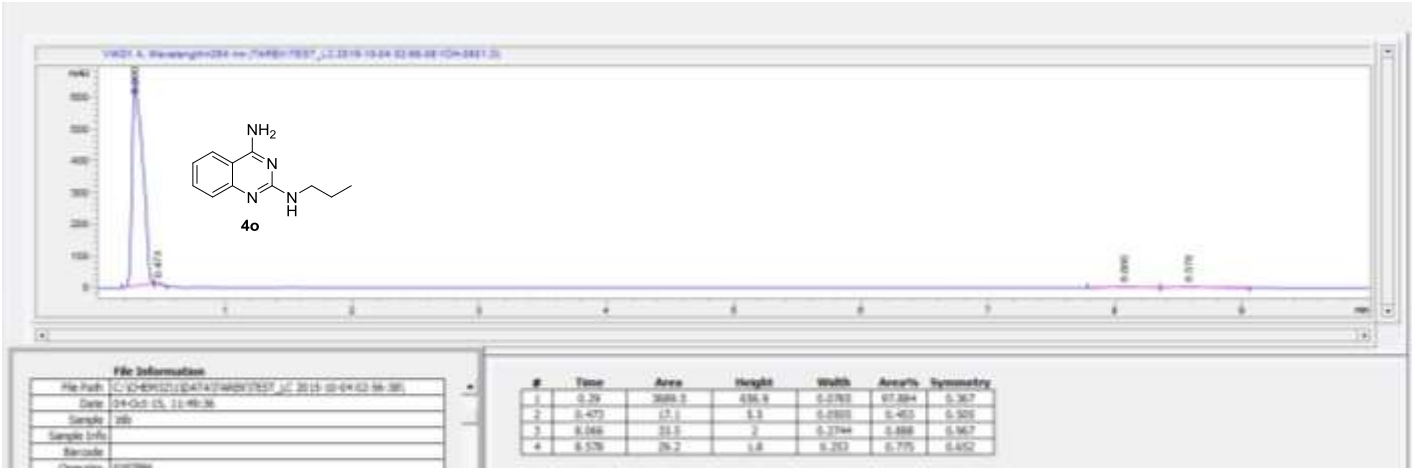
N^2-(4-fluorobenzyl)quinazoline-2,4-diamine (4m)



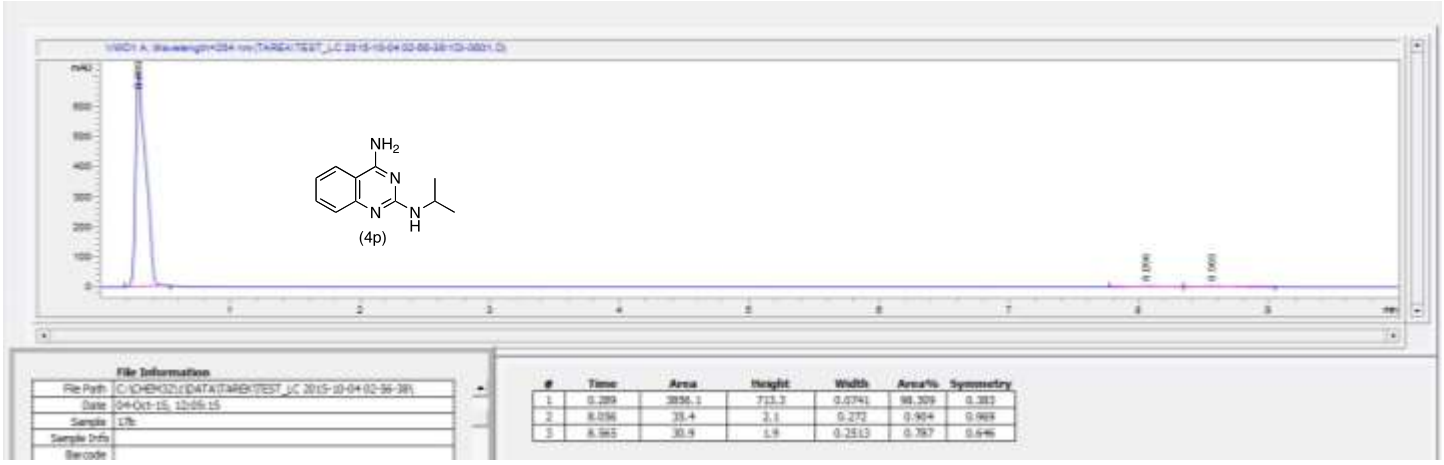
N^2-phenethylquinazoline-2,4-diamine (4n)



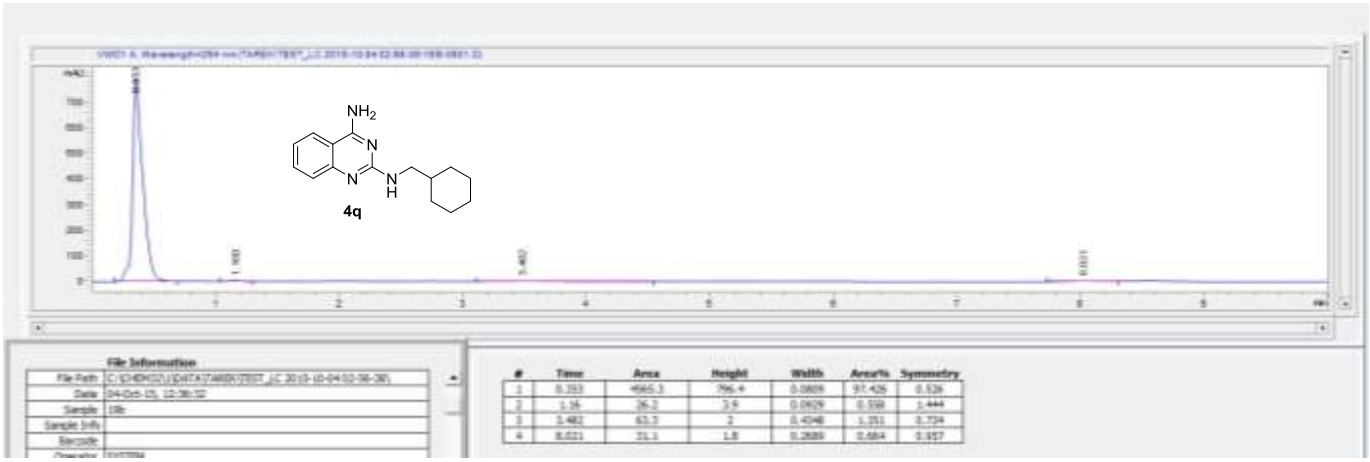
N^2-propylquinazoline-2,4-diamine (4o)



N^2-isopropylquinazoline-2,4-diamine (4p)



N^2-(cyclohexylmethyl)quinazoline-2,4-diamine (4q)



12. Thioflavin-T monitoring of Aβ aggregation kinetics[4]

The ability of isomeric 2,4-diaminoquinazolines to inhibit and/or modulate Aβ aggregation kinetics was determined using a thioflavin T (ThT)-based fluorescence assay. These assays were conducted in Costar, black, clear-bottom 384-well plates with frequent shaking (30 sec. of linear shaking at 730 cpm every 5 minutes) and constant heating at 37 °C for 24 h. The ThT excitation/emission was measured at 440 nm/490 nm and readings were taken every 5 minutes using a BioTek Synergy H1 microplate reader. Compounds were prepared in DMSO and diluted to 10 x in 215mM phosphate buffer at pH 7.4. The Aβ.HFIP samples (either Aβ40 or Aβ42, rPeptide, Bogart, USA) were re-dissolved in 1% ammonium hydroxide, sonicated at room temperature for 5 minutes then diluted to 50 μM in 215mM phosphate buffer (pH 7.4). A 15 μM ThT stock solution was prepared with 50 mM glycine and adjusted to pH 7.4. Plating sequence was as follows: 44 μL ThT, 20-35μL buffer, 1 μL DMSO (for background and controls only), followed by 8 μL of 10x compound dilutions (concentration range tested: 1-25 μM). An end point reading was measured to evaluate for ThT-interference before finally adding 8 uL of Aβ40 or Aβ42 stock solutions (5 μM final). Plates were sealed with a transparent plate film before initiating the assay.

The relative fluorescence intensity units (RFU) were corrected for ThT-interference before calculating end point IC_{50} values and processing the aggregation kinetic plots. Data presented was mean of triplicate readings (3-4 independent experiments).

13. Aggregation kinetics plot for compounds **4j**, **4k** and **3j**, **3k** with either Aβ40 or Aβ42

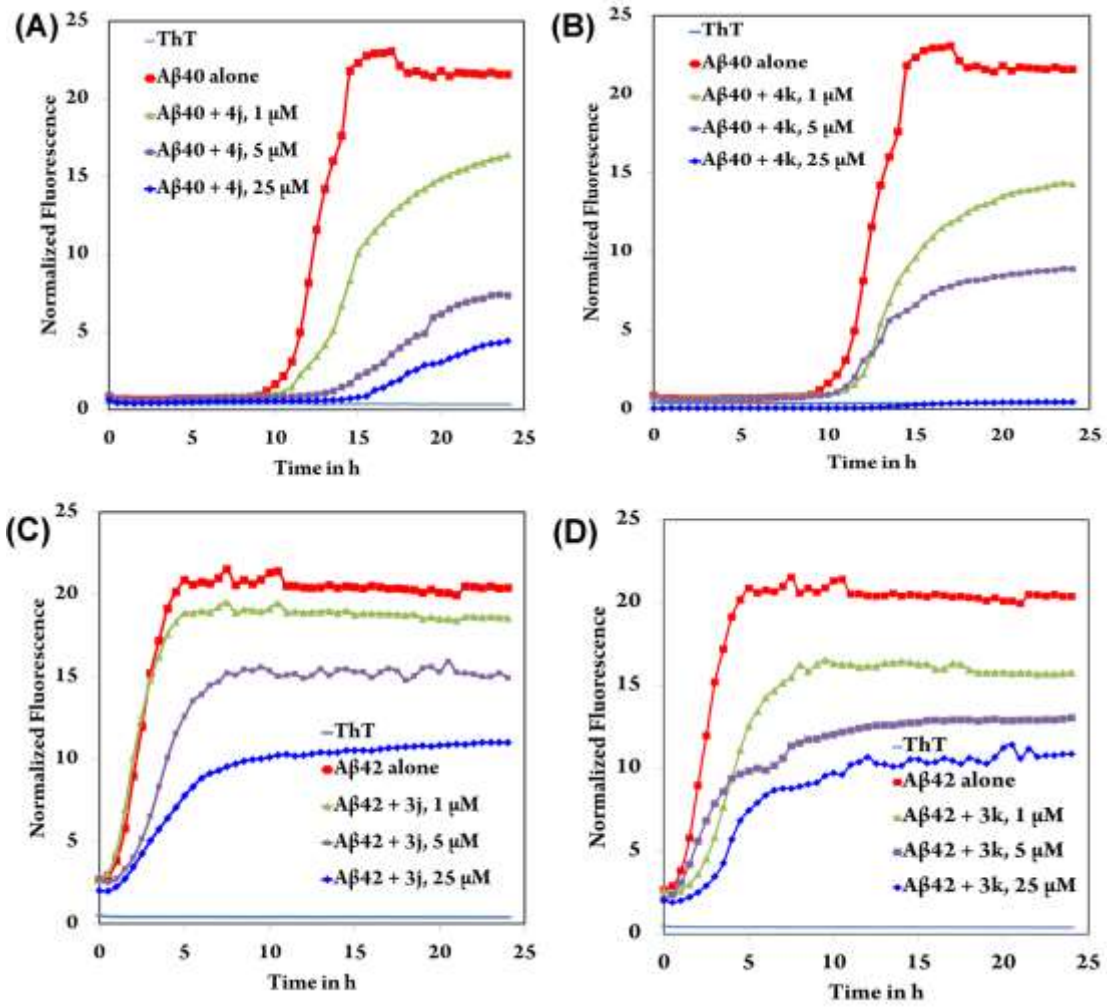


Figure S1: Amyloid aggregation kinetics study. Panels A and B: 5 μM Aβ40 with varying concentrations (1, 5 or 25 μM) of DAQ derivatives **4j** and **4k** respectively. Panels C and D: 5 μM Aβ42 with varying concentrations (1, 5 or 25 μM) of DAQ derivatives **3j** and **3k** respectively. Aggregation kinetics were monitored by ThT-fluorescence spectroscopy (excitation = 440 nm, emission = 490 nm) for 24 h at 37 °C in phosphate buffer at pH 7.4. Results are based on three independent experiments in triplicate measurements.

14. Transmission electron microscopy[5]

In Costar 96-well, round-bottom plates, 80 μL of 215 mM phosphate buffer, 20 μL of 10x test compound dilutions (250 μM – prepared in the same way as for the ThT assay) and 100 μL of 50 μM Aβ40 or 42 were combined. For the control wells, 2 μL of DMSO and 18 μL of phosphate buffer was added. Final Aβ: test compound ratio was 1:1 (25 μM:25 μM). Plates were incubated on a Fisher plate incubator set to 37 °C and the contents were shaken at 730 cpm for 24 h. To prepare the TEM grids, ~ 20 μL droplet was added using a disposable Pasteur pipette over the formvar-coated copper grids (400 mesh). Grids were air-dried for about 3 h before adding two droplets (~ 40 μL, using a disposable Pasteur pipette) of ultra-pure water and using small pieces of filter paper to wash out precipitated buffer salts. After air-drying for ~ 15-20 min, the grids were negatively stained by adding a droplet (~ 20 μL, using a disposable Pasteur pipette) of 2% phosphotungstic acid (PTA) and immediately after the grids were dried using small pieces of filter paper. Grids were further air-dried overnight. The scanning was carried out using a Philips CM 10 transmission electron microscope at 60 kV (Department of Biology, University of Waterloo) and micrographs were obtained using a 14-megapixel AMT camera.

15. TEM images for compounds 3j and 4j in presence of Aβ40 or Aβ42

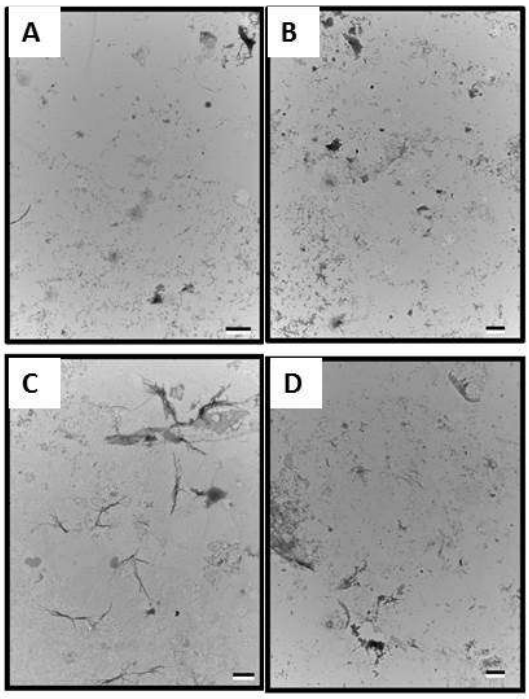


Figure S2: Amyloid morphology analysis using transmission electron microscopy (TEM) after 24 h incubation at 37 °C in phosphate buffer at pH 7.4. Panels A and B: 25 μM Aβ40 with 25 μM of DAQ derivatives **3j** or **4j**; respectively. Panels C and D: 25 μM Aβ42 with 25 μM of DAQ derivatives **3j**, or **4j**; respectively. Scale: black/white bars represent 500 nm.

16. TEM images for resveratrol in presence of Aβ40 or Aβ42

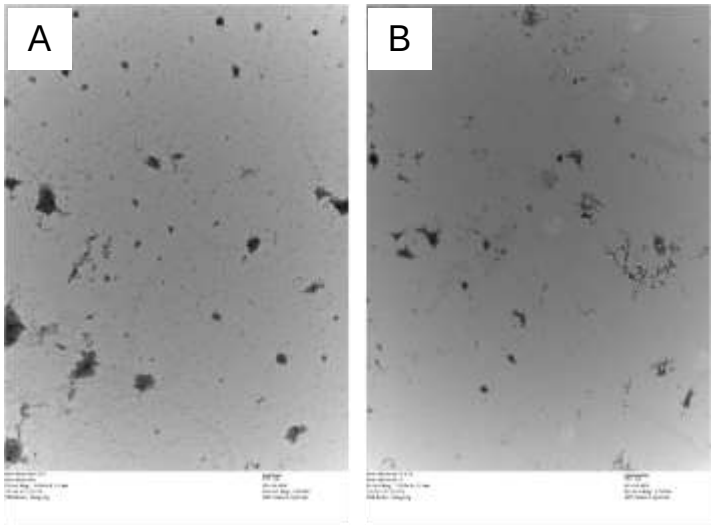


Figure S3: Panel A: 25 μM of Aβ40 and 25 μM of resveratrol at 37 °C for 24 h; Panel B: 25 μM of Aβ40 and 25 μM of resveratrol at 37 °C for 24 h.

17. Computational modeling[6]

The molecular docking experiments were conducted using the computational software Discovery Studio (DS), *Structure-Based-Design* program (version 4.0) from BIOVIA Inc. San Diego, USA. The DAQ compounds **3j**, **3k**, **4j** and **4k** were built using the *small molecules* module in DS. The NMR solution structure of both Aβ dimer and fibrils were obtained from protein data bank (pdb id: 2LMN) and were prepared for docking study using the *macromolecules* module in DS. Ligand binding site was defined by selecting a 15 Å radius sphere for both Aβ dimer and fibrils assembly. Then molecular docking was performed using the *receptor-ligand interactions* module in DS. The CDOCKER alogorithm was used to find the most appropriate binding modes of DAQ derivatives using CHARMm force field. The docked poses obtained were ranked based on the CDOCKER energies and CDOCKER interactions energies in kcal/mol.

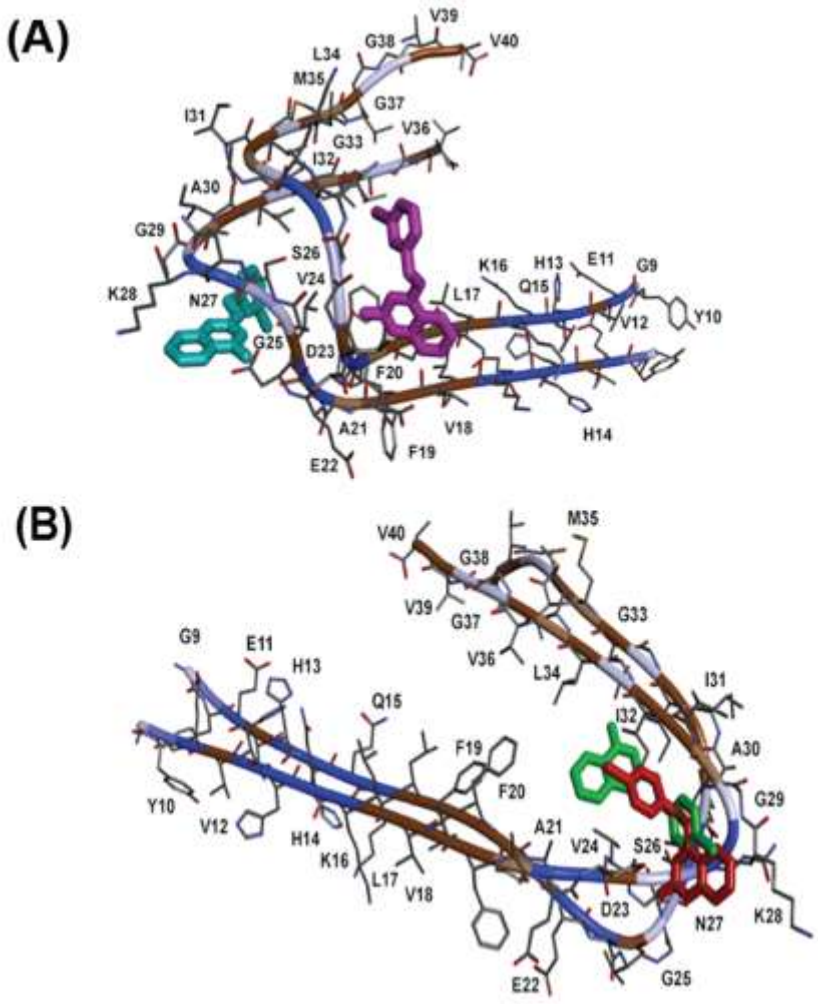


Figure S4. Binding modes of DAQ derivatives in Aβ-dimer (Panels A and B). Hydrogen atoms are not shown to increase clarity. Derivative **3j** = purple, **3k** = red, **4j** = turquoise and **4k** = green.

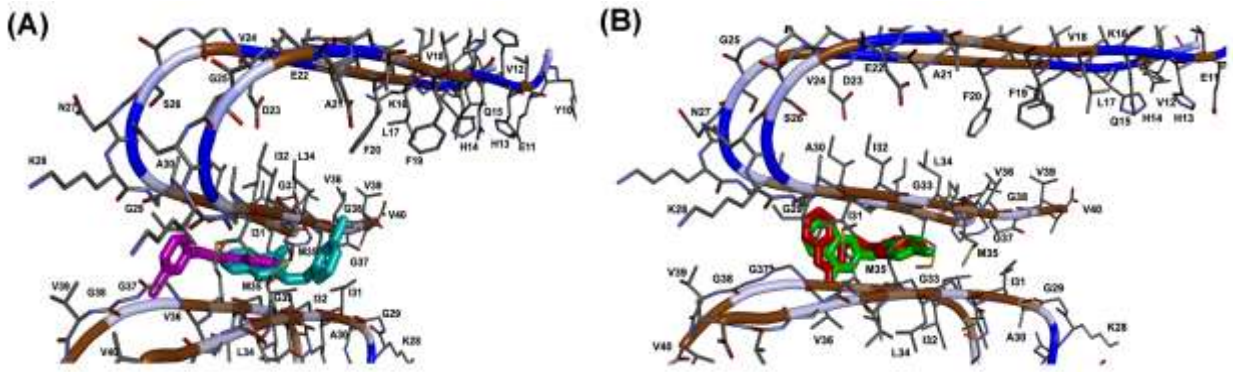


Figure S5: Binding modes of DAQ derivatives in the Aβ-fibril models (Panels A and B). Hydrogen atoms are not shown to increase clarity. Derivative **3j** = purple, **3k** = red, **4j** = turquoise and **4k** = green.

18. References

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