

Chemoselective One-pot Synthesis of Functionalized Amino-azaheterocycles Enabled by COware

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1 General Experimental

All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise stated. Purification was carried out according to standard laboratory methods.¹

1.1 Solvents and Reagents

Solvents and reagents were purchased from commercial suppliers and used as received unless otherwise stated. K_3PO_4 , K_2CO_3 , and Cs_2CO_3 were dried in a Heraeus VacuTherm oven at 40 °C under vacuum for a minimum of 24 hours before use.

1.2 Chromatography

Reactions were monitored by thin layer chromatography (TLC) or liquid chromatography-mass spectrometry (LCMS). Thin layer chromatography (TLC) was carried out using POLYGRAM[®]-backed 50 precoated silica plates (particle size 0.2 mm). Spots were visualised by ultraviolet (UV) light (λ_{max} = 254 nm or 365 nm) and then stained with potassium permanganate solution followed by gentle heating. Flash column chromatography was carried out using the Teledyne ISCO CombiFlash[®] Rf+ apparatus with RediSep[®] or Biotage[®] SNAP KP-NH cartridges.

1.3 Experimental Details

Reactions were carried out using conventional glassware (preparation of intermediates) or in capped 20 mL COware vessels (for all one pot hydrogenation experiments). COware vessels were purchased from Sigma Aldrich (COware, screwable two-chamber glass system, catalogue number 744077). Magnetic stirrer bars were stirred vigorously using stirrer hot plates. Magnetic stirrer bars were used as supplied in the 2–5 mL Biotage Microwave Reaction Kit (2–5 mL Biotage Microwave Reaction Kit, catalogue number 351521). Unless otherwise stated, all reactions were carried out under an atmosphere of nitrogen using anhydrous solvent. The glassware was purged with N_2 before use. Purging refers to a vacuum/nitrogen-refilling procedure. Ambient temperature was generally 23 °C. Reactions carried out at elevated temperatures were heated in a sand bath using a temperature-regulated hotplate/stirrer. Temperature quoted is a measurement of the sand bath heating block. Temperature-regulated hotplate/stirrers employed over the course of this study were either of the following: an IKA[®] RCT basic or a Radleys Carousel Tech Stirring Hotplate.

1.4 Liquid Chromatography Mass Spectrometry (LCMS)

LCMS analysis was carried out on a Waters Acquity ultra performance liquid chromatography instrument equipped with an ethylene bridged hybrid column (50 mm x 2.1 mm, 1.7 μ m packing diameter) and Waters micromass ZQ mass spectrometer using alternate-scan positive and negative electrospray. Analytes were detected as a summed UV wavelength of 210–350 nm. Two liquid phase methods were used:

Method A - Formic – 40 °C, 1 mL/min flow rate. Gradient elution with the mobile phases as (A) H₂O containing 0.1% volume/volume (v/v) formic acid and (B) acetonitrile containing 0.1% v/v formic acid. Gradient conditions were initially 1% B, increasing linearly to 97% B over 1.5 min, remaining at 97% B for 0.4 min then increasing to 100% B over 0.1 min.

Method B - High pH – 40 °C, 1 mL/min flow rate. Gradient elution with the mobile phases as (A) 10 mM aqueous ammonium bicarbonate solution, adjusted to pH 10 with 0.88 M aqueous ammonia and (B) acetonitrile. Gradient conditions were initially 1% B, increasing linearly to 97% B over 1.5 min, remaining at 97% B for 0.4 min then increasing to 100% B over 0.1 min.

1.5 Nuclear Magnetic Resonance (NMR) Spectroscopy

Proton (¹H), carbon (¹³C), and fluorine (¹⁹F) spectra were recorded in deuterated solvents at ambient temperature (unless otherwise stated) using standard pulse methods on any of the following spectrometers and signal frequencies: Bruker AV-400 (¹H = 400 MHz, ¹³C = 101 MHz, ¹⁹F = 376 MHz) and Bruker AV-500 (¹H = 500 MHz, ¹³C = 126 MHz). Chemical shifts are reported in ppm and are referenced to tetramethylsilane for the following solvent signals: CDCl₃ (¹H = 7.26 ppm, ¹³C = 77.16 ppm), *d*₆-Acetone (¹H = 2.05 ppm, ¹³C = 206.7, 29.9 ppm), *d*₆-DMSO (¹H = 2.50 ppm, ¹³C = 39.5 ppm), and MeOD (¹H = 3.31 ppm, ¹³C = 49.0 ppm). Peak assignments were made on the basis of chemical shifts, integrations, and coupling constants, using COSY, DEPT, HMBC, HSQC, and NOESY where appropriate. Coupling constants are quoted to the nearest 0.1 Hz and multiplicities are described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sxt), septet (sept), broad (br.), and multiplet (m).

1.6 Infrared (IR) Spectroscopy

Infrared spectra were recorded using a Perkin Elmer Spectrum 1 Fourier transform infrared spectrometer. Absorption maxima (ν_{\max}) are reported in wavenumbers (cm⁻¹).

1.7 High-resolution Mass Spectrometry (HRMS)

High-resolution mass spectra were recorded on a Micromass Q-ToF Ultima hybrid quadrupole time-of-flight mass spectrometer, with analytes separated on an Agilent 1100 Liquid Chromatography equipped with a Phenomenex Luna C18 (2) reversed phase column (100 mm x 2.1 mm, 3 μm packing diameter). Liquid chromatography conditions were 0.5 mL/min flow rate, 35 °C, and injection volume 2–5 μL. Gradient elution with (A) H₂O containing 0.1% v/v formic acid and (B) acetonitrile containing 0.1% v/v formic acid. Gradient conditions were initially 5% B, increasing linearly to 100% B over 6 min, remaining at 100% B for 2.5 min then decreasing linearly to 5% B over 1 min followed by an equilibration period of 2.5 min prior to the next injection. Mass to charge ratios (*m/z*) are reported in Daltons.

1.8 Melting Points

Melting points were recorded on either Stuart SMP10 or Gallenkamp melting point apparatus.

1.9 Mass Directed Automatic Purification (MDAP)

Mass-directed automatic purification was carried out using a Waters ZQ mass spectrometer using alternate-scan positive and negative electrospray and a summed UV wavelength of 210–350 nm. Two liquid phase methods were used:

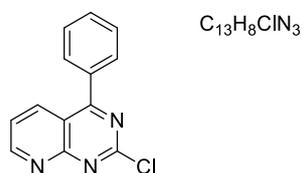
Formic – XSelect CSH C18 column (100 mm x 19 mm, 5 μ m packing diameter, 20 mL/min flow rate) or XSelect CSH C18 column (150 mm x 30 mm, 5 μ m packing diameter, 40 mL/min flow rate). Gradient elution at ambient temperature with the mobile phases as (A) H₂O containing 0.1% v/v formic acid and (B) acetonitrile containing 0.1% v/v formic acid.

High pH – XSelect CSH C18 column (100 mm x 19 mm, 5 μ m packing diameter, 20 mL/min flow rate) or XSelect CSH C18 column (150 mm x 30 mm, 5 μ m packing diameter, 40 mL/min flow rate). Gradient elution at ambient temperature with the mobile phases as (A) 10 mM aqueous ammonium bicarbonate solution, adjusted to pH 10 with 0.88 M aqueous ammonia and (B) acetonitrile.

2 General Experimental Procedures

General procedure A: Suzuki-Miyaura reaction of 2,4-dichloropyrido[2,3-*d*]pyrimidine

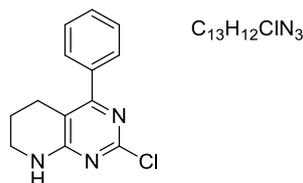
For example, synthesis of 2-chloro-4-phenylpyrido[2,3-*d*]pyrimidine, **2a**²



A microwave vial was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.080 g, 0.375 mmol, 3 equiv), phenylboronic acid (0.023 g, 0.188 mmol, 1.5 equiv), and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%). The reaction vessel was then sealed and purged with nitrogen after which water (0.011 mL, 0.625 mmol, 5 equiv) and THF (0.5 mL, 0.25 M) were added. The vial was sealed, heated to 80 °C, and was allowed to stir for 1 h. After cooling to ambient temperature, conversion to product was determined by HPLC against an internal standard (caffeine) indicating cross-coupling at the 4-position (52% conversion).

General Procedure B: COWare hydrogenation of 2-chloro-4-phenylpyrido[2,3-*d*]pyrimidine

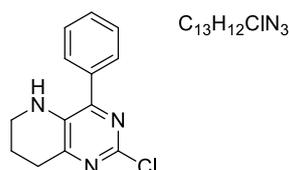
For example, synthesis of 2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4a**



Chamber A of a two chamber COware apparatus was charged with 2-chloro-4-phenylpyrido[2,3-*d*]pyrimidine (0.020 g, 0.083 mmol, 1 equiv), platinum(IV) oxide (0.002 g, 0.008 mmol, 10 mol%), and THF (2 mL, 0.042 M). Zinc (0.229 g, 3.50 mmol, 42.3 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 178 equiv, as a 7.4 M aqueous solution) were then added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 16 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 20–60% TBME/cyclohexane, afforded the *title compound* as a colorless solid (0.008 g, 39%).

Representative General Procedure for Sequential Cross-coupling/Hydrogenation on 1 mmol Scale

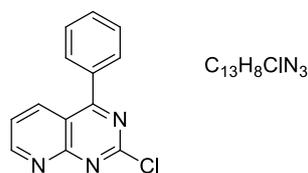
2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[3,2-*d*]pyrimidine, **6f**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[3,2-*d*]pyrimidine (0.204 g, 1.00 mmol, 1 equiv), tripotassium phosphate (0.425 g, 2.00 mmol, 2 equiv), phenylboronic acid (0.128 g, 1.05 mmol, 1.05 equiv), platinum(IV) oxide (0.023 g, 0.10 mmol, 10 mol%) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.029 g, 0.040 mmol, 4 mol%). The reaction vessel was then sealed and purged with nitrogen after which water (0.090 mL, 5.00 mmol, 5 equiv) and CPME (4 mL, 0.25 M) were added. The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.785 g, 12.00 mmol, 12 equiv) and hydrochloric acid (8.00 mL, 59.20 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 8 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (30 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (40 g), eluting with 0–50% TBME/cyclohexane (+1% Et₃N), afforded the *title compound* as a white solid (0.133 g, 54%).

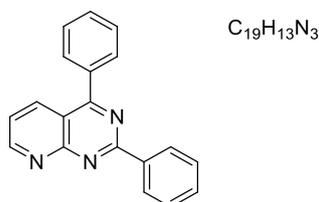
3 Intermediate Compound Characterization

2-Chloro-4-phenylpyrido[2,3-*d*]pyrimidine, **2a**²



A microwave vial was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), potassium carbonate (0.052 g, 0.376 mmol, 1.5 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.05 equiv), and tetrakis(triphenylphosphine)palladium(0) (0.015 g, 0.013 mmol, 5 mol%). The reaction vessel was then sealed and purged with nitrogen before addition of toluene (3 mL, 0.083 M). The vial was heated to 110 °C, and was allowed to stir for 2 h. After cooling, the reaction mixture was filtered through a Celite[®] pad, washing with EtOAc (10 mL) and the filtrate was concentrated under reduced pressure. Purification by MDAP afforded the *title compound* as a colorless solid (0.014 g, 23%). m.p. 147–149 °C (lit. 143–144 °C);² LCMS (Method B, UV, ESI) $R_t = 0.92$ min, $[M+H]^+ = 242$, 92% purity; ¹H NMR (400 MHz, CDCl₃) δ 9.28 (dd, $J = 4.0, 1.8$ Hz, 1 H), 8.52 (dd, $J = 8.3, 1.8$ Hz, 1 H), 7.83–7.76 (m, 1 H), 7.72–7.52 (m, 4 H), 7.50–7.43 (m, 1 H); ¹³C NMR (101 MHz, CDCl₃) δ 173.1, 160.3, 160.2, 158.5, 137.0, 134.9, 131.3, 130.2, 129.0, 125.4, 116.5; ν_{max} (solid)/cm⁻¹ 3089, 3050, 1597, 1556, 1529, 1466, 1115, 895, 796, 770, 712, 694; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₃H₉ClN₃ 242.0480; found ³⁵Cl 242.0475 and ³⁷Cl 244.0444.

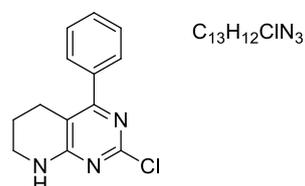
2,4-Diphenylpyrido[2,3-*d*]pyrimidine, **3a**



A vessel was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.500 g, 2.500 mmol, 1 equiv), tripotassium phosphate (2.412 g, 11.360 mmol, 4.5 equiv), phenylboronic acid (0.667 g, 5.470 mmol, 2.2 equiv), and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.186 g, 0.227 mmol, 9 mol%). The vessel was sealed and purged with nitrogen after which water (0.205 mL, 11.36 mmol, 4.5 equiv) and THF (9.5 mL, 0.263 M) were added, the reaction was warmed to 60 °C, and was allowed to stir for 18 h. After cooling, the reaction was filtered through a Celite[®] pad, washing with EtOAc (25 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (80 g), eluting with 0–75% EtOAc/cyclohexane, afforded the *title compound* as an off-colorless solid (0.521 g, 74%). m.p. 174–176 °C; LCMS (Method B, UV, ESI) $R_t = 1.23$ min, $[M+H]^+ = 284$, 99% purity; ¹H NMR (400 MHz, CDCl₃) δ 9.27 (dd, $J = 4.2, 2.0$ Hz, 1 H), 8.87–8.81 (m, 2 H), 8.51 (dd, $J = 8.3, 2.0$ Hz, 1 H), 7.92–7.86 (m, 2 H), 7.67–7.62 (m, 3 H), 7.59–7.49 (m, 4 H); ¹³C NMR

(101 MHz, CDCl₃) δ 170.1, 163.5, 159.9, 157.6, 137.4, 136.7, 136.4, 131.3, 130.5, 130.2, 129.3, 128.8, 128.5, 122.4, 116.4; ν_{\max} (solid)/cm⁻¹ 3058, 1592, 1558, 1539, 1469, 1372, 1344, 1168, 1026, 971, 853, 780, 717, 684; HRMS (ESI-Orbitrap) m/z : [M+H]⁺ calcd for C₁₉H₁₄N₃ 284.1182; found 284.1177.

2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4a**



Chamber A of a two chamber COware apparatus was charged with 2-chloro-4-phenylpyrido[2,3-*d*]pyrimidine (0.050 g, 0.207 mmol, 1 equiv), platinum(IV) oxide (0.005 g, 0.022 mmol, 10 mol%), and CPME (2 mL, 0.104 M). Zinc (0.188 g, 2.880 mmol, 13.9 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 71.5 equiv, as a 7.4 M aqueous solution) were then added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 16 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% TBME/cyclohexane, afforded the *title compound* as a colorless solid (0.049 g, 96%). m.p. 248–250 °C; LCMS (Method B, UV, ESI) R_t = 0.99 min, [M+H]⁺ = 246, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.58–7.52 (m, 2 H), 7.47–7.40 (m, 3 H), 6.87 (br. s, 1 H), 3.56–3.50 (m, 2 H), 2.75 (t, J = 6.1 Hz, 2 H), 1.87 (quin, J = 5.9 Hz, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 163.2, 162.3, 157.5, 137.2, 129.1, 128.8, 128.2, 108.5, 41.2, 24.2, 20.6; ν_{\max} (solid)/cm⁻¹ 3228, 3119, 2962, 2936, 2861, 1593, 1565, 1399, 1329, 1275, 1096, 1018, 846, 760, 694, 626; HRMS (ESI-Orbitrap) m/z : [M+H]⁺ calcd for C₁₃H₁₃ClN₃ 246.0793; found ³⁵Cl 246.0781 and ³⁷Cl 248.0759.

4 Reaction Optimization Data

4.1 HPLC Retention Times and Conversion Factors of Products

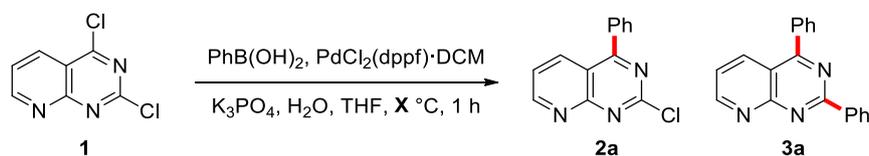
compound	structure	retention time (min)	conversion factor
1		1.76	4.13
2a		2.35	2.57
3a		2.95	1.21



4.2 Suzuki-Miyaura Optimization

4.2.1 Temperature Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.080 g, 0.375 mmol, 3 equiv), phenylboronic acid (0.023 g, 0.188 mmol, 1.5 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to X °C, and was allowed to stir for 1 h. Conversion to product was determined by HPLC against an internal standard (caffeine).



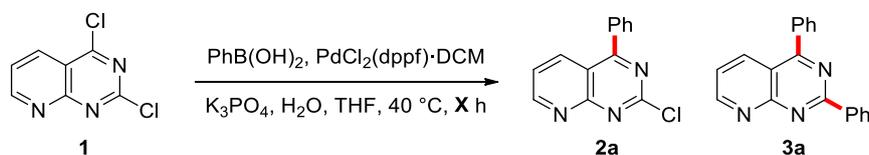
entry	temperature (°C)	conversion (1:2a:3a) ^a
1	23	53:47:0
2	30	1:79:20
3	40	1:74:25
4	50	0:73:27
5	60	1:93:6
6	70	0:54:46
7	80	0:52:48

^aDetermined by HPLC analysis using an internal standard.

4.2.2 Time Study at set Temperature

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.080 g, 0.375 mmol, 3 equiv), phenylboronic acid (0.023 g, 0.188 mmol, 1.5 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane

(0.004 g, 0.005 mmol, 4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for **X** h. Conversion to product was determined by HPLC against an internal standard (caffeine).

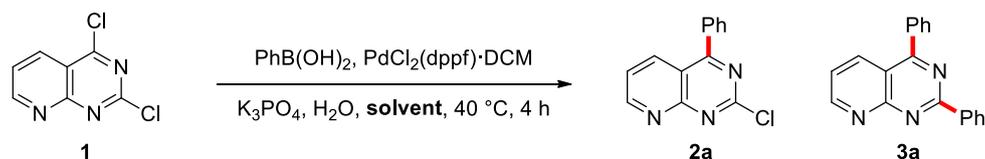


entry	time (h)	conversion (1:2a:3a) ^a
1	1	36:60:4
2	2	15:79:6
3	4	1:86:13
4	6	1:81:15
5	8	1:83:15
6	16	0:78:22
7	24	0:52:48

^aDetermined by HPLC analysis using an internal standard.

4.2.3 Solvent Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.053 g, 0.250 mmol, 2 equiv), phenylboronic acid (0.016 g, 0.131 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and **solvent** (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).



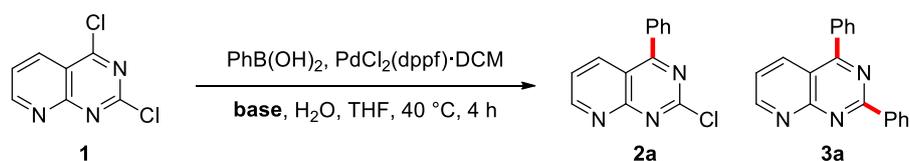
entry	solvent	conversion (1:2a:3a) ^a
1	THF	1:86:13

2	^t BuOH	18:79:3
3	IPA	1:68:10
4	EtOH	7:0:24
5	MeOH	17:0:8
6	EtOAc	1:82:10
7	1,4-Dioxane	1:55:30
8	CPME	2:75:15
9	2-MeTHF	1:76:14
10	TBME	2:65:17

^aDetermined by HPLC analysis using an internal standard.

4.2.4 Base Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), **base** (0.250 mmol, 2 equiv), phenylboronic acid (0.016 g, 0.131 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).

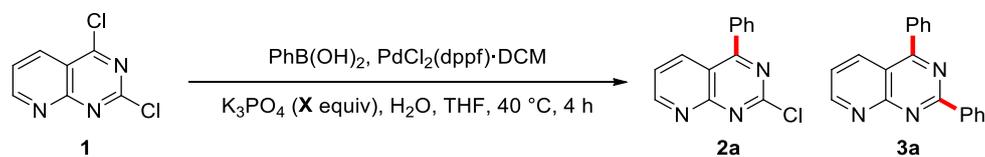


entry	base	conversion (1:2a:3a) ^a
1	K ₃ PO ₄ (0.053 g)	1:86:13
2	2- <i>tert</i> -butyl-1,1,3,3-tetramethylguanidine (0.029 mL)	0:0:10
3	KOAc (0.025 g)	0:23:1
4	Na ₂ CO ₃ (0.027 g)	67:14:0
5	K ₂ CO ₃ (0.035 g)	62:4:23

^aDetermined by HPLC analysis using an internal standard.

4.2.5 Base Equivalents Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (**X** equiv), phenylboronic acid (0.016 g, 0.131 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).

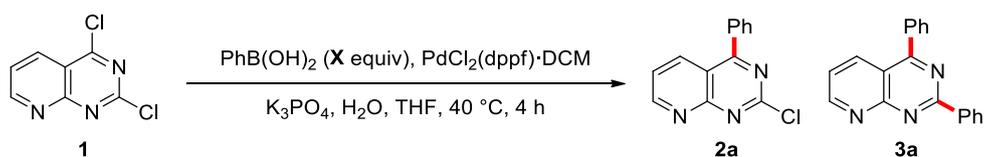


entry	base equivalents	conversion (1:2a:3a) ^a
1	0 (0.000 g)	100:0:0
2	0.5 (0.013 g)	50:50:0
3	1 (0.027 g)	23:76:1
4	1.5 (0.040 g)	19:77:3
5	2 (0.053 g)	1:86:13
6	2.5 (0.066 g)	2:76:22
7	3 (0.080 g)	1:86:13

^aDetermined by HPLC analysis using an internal standard.

4.2.6 Boronic Acid Equivalents Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.053 g, 0.250 mmol, 2 equiv), phenylboronic acid (**X** equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).

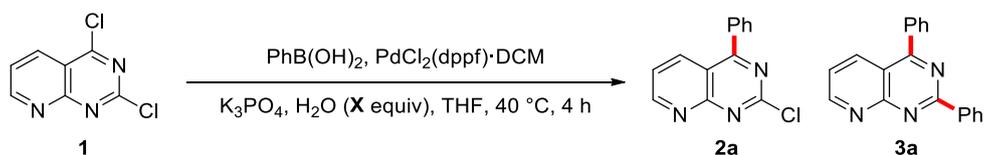


entry	boronic acid equivalents	conversion (1:2a:3a) ^a
1	1.05 (0.016 g)	1:86:13
2	1.10 (0.017 g)	0:74:25
3	1.30 (0.020 g)	0:52:46
4	1.50 (0.023 g)	0:44:56

^aDetermined by HPLC analysis using an internal standard.

4.2.7 Water Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.053 g, 0.250 mmol, 2 equiv), phenylboronic acid (0.016 g, 0.131 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%), water (**X** equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).

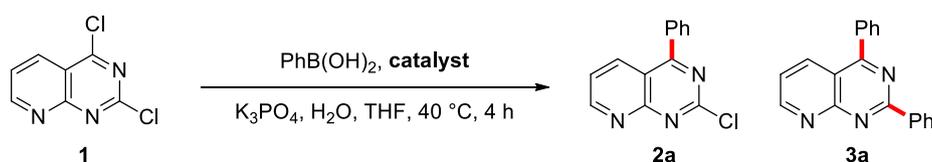


entry	water equivalents	conversion (1:2a:3a) ^a
1	0 (0.000 mL)	33:66:1
2	5 (0.011 mL)	1:86:13
3	10 (0.023 mL)	1:82:16
4	15 (0.034 mL)	0:81:18
5	20 (0.045 mL)	1:85:12

^aDetermined by HPLC analysis using an internal standard.

4.2.8 Catalyst Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.053 g, 0.250 mmol, 2 equiv), phenylboronic acid (0.016 g, 0.131 mmol, 1.05 equiv), **catalyst** (4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).

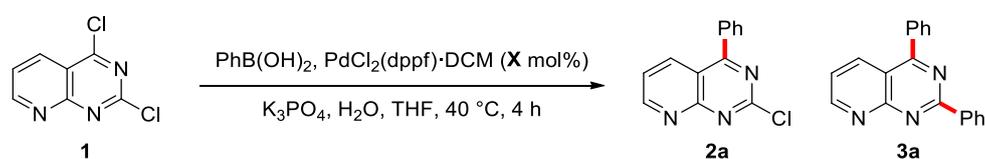


entry	catalyst	conversion (1:2a:3a) ^a
1	PdCl ₂ (dppf)·DCM (0.004 g)	1:86:13
2	[PdCl(allyl)] ₂ (0.002 g)	14:26:7
3	Pd(OAc) ₂ (0.001 g)	1:3:16 ^b
4	PdCl ₂ (0.001 g)	98:0:2
5	PdCl ₂ (CH ₃ CN) ₂ (0.001 g)	100:0:0
6	PEPPSI TM -IPr (0.004 g)	0:98:2

^aDetermined by HPLC analysis using an internal standard. ^bMass balance not 100% due to presence of multiple unidentified products.

4.2.9 Catalyst Equivalents Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.053 g, 0.250 mmol, 2 equiv), phenylboronic acid (0.016 g, 0.131 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (**X** mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (0.5 mL, 0.25 M). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).

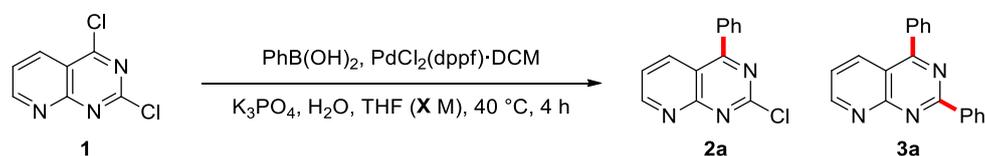


entry	catalyst equivalents (mol%)	conversion (1:2a:3a) ^a
1	1 (0.001 g)	35:65:0
2	2.5 (0.003 g)	1:80:15
3	4 (0.004 g)	1:86:13
4	5 (0.005 g)	0:90:9
5	7.5 (0.008 g)	0:88:11

^aDetermined by HPLC analysis using an internal standard.

4.2.10 Concentration Study

Reaction was carried out according to General Procedure A using 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.025 g, 0.125 mmol, 1 equiv), tripotassium phosphate (0.053 g, 0.250 mmol, 2 equiv), phenylboronic acid (0.016 g, 0.131 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.004 g, 0.005 mmol, 4 mol%), water (0.011 mL, 0.625 mmol, 5 equiv), and THF (**X** mL). The vial was sealed, heated to 40 °C, and was allowed to stir for 4 h. Conversion to product was determined by HPLC against an internal standard (caffeine).

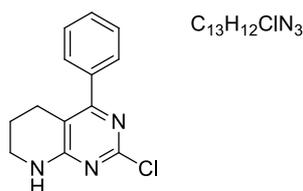


entry	concentration	conversion (1:2a:3a) ^a
1	0.02 (6.25 mL)	99:1:0
2	0.10 (1.25 mL)	1:97:2
3	0.50 (0.25 mL)	0:92:8

^aDetermined by HPLC analysis using an internal standard.

4.3 COWare Hydrogenation Development (Table 1, entries 4-7)

2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4a**



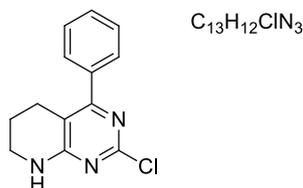
Reaction was carried out according to General Procedure B using with 2-chloro-4-phenylpyrido[2,3-*d*]pyrimidine (0.020 g, 0.083 mmol, 1 equiv), **catalyst** (4 mol%), and **solvent** (0.5 mL, 0.166 M). The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL). The solvent was then removed under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane, afforded the *title compound* as a colourless solid.

entry	reaction conditions ^a	conversion ^b (%)	yield (%) ^c
1	H ₂ , Pd/Al ₂ O ₃ , THF	0	0
2	H ₂ , Pd/Al ₂ O ₃ , CPME	36	34
3	H ₂ , Pt/C, CPME	52	18
4	H ₂ , PtO ₂ , THF	51	39
5	H ₂ , PtO ₂ , CPME	89	95

^a5 mol% of catalyst and 1 mL of solvent were used in COware. Zinc and aqueous hydrochloric acid were used to generate hydrogen. ^bDetermined by LCMS analysis. ^cIsolated yields.

5 Compound Characterization Data for the One-pot Suzuki-Miyaura/hydrogenation Procedure

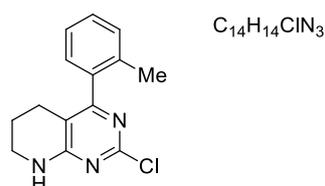
2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4a**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.047 g, 0.235 mmol, 1 equiv), tripotassium phosphate (0.100 g, 0.470 mmol, 2 equiv), phenylboronic acid (0.030 g, 0.246 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.021 mL, 1.175

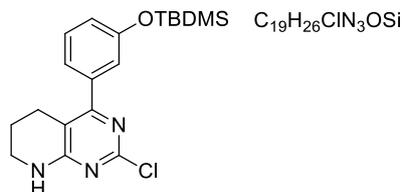
mmol, 5 equiv), and CPME (1 mL, 0.235 M). The reaction vessel was sealed, warmed to 40 °C, and was allowed to stir for 18 h. After cooling, zinc (0.213 g, 3.260 mmol, 13.9 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 63.0 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was then sealed and was allowed to stir at ambient temperature for 8 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colourless solid (0.045 g, 78%). m.p. 248–250 °C; LCMS (Method B, UV, ESI) $R_t = 0.99$ min, $[M+H]^+ = 246$, 95% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.59–7.53 (m, 2 H), 7.47–7.40 (m, 3 H), 6.42 (br. s, 1 H), 3.55–3.49 (m, 2 H), 2.75 (t, $J = 6.1$ Hz, 2 H), 1.87 (quin, $J = 5.9$ Hz, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 163.2, 162.3, 157.5, 137.2, 129.1, 128.8, 128.2, 108.5, 41.2, 24.2, 20.6; ν_{\max} (solid)/cm⁻¹ 3231, 3118, 2965, 2941, 2863, 1590, 1563, 1399, 1328, 1274, 1188, 1092, 1017, 760, 692, 626; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₃H₁₃ClN₃ 246.0793; found ³⁵Cl 246.0781 and ³⁷Cl 248.0757.

2-Chloro-4-(*o*-tolyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4b**



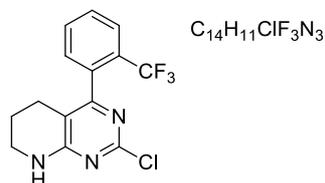
Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.049 g, 0.245 mmol, 1 equiv), tripotassium phosphate (0.104 g, 0.490 mmol, 2 equiv), *o*-tolylboronic acid (0.035 g, 0.257 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.008 g, 0.011 mmol, 5 mol%), water (0.022 mL, 1.225 mmol, 5 equiv), and CPME (1 mL, 0.245 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.451 g, 6.900 mmol, 28.2 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 60.4 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 8 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.047 g, 74%). m.p. 215–217 °C; LCMS (Method B, UV, ESI) $R_t = 1.02$ min, $[M+H]^+ = 260$, 94% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.32–7.20 (m, 3 H), 7.16–7.12 (m, 1 H), 6.82 (br. s, 1 H), 3.51 (td, $J = 5.6, 2.7$ Hz, 2 H), 2.40 (t, $J = 6.0$ Hz, 2 H), 2.20 (s, 3 H), 1.90–1.82 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 164.7, 162.1, 157.3, 136.8, 135.3, 130.3, 128.7, 128.0, 125.7, 109.5, 41.2, 23.0, 20.4, 19.4; ν_{\max} (solid)/cm⁻¹ 3247, 3121, 2959, 2933, 2847, 1590, 1564, 1326, 1292, 1191, 1015, 853, 765; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₄H₁₅ClN₃ 260.0949; found ³⁵Cl 260.0947 and ³⁷Cl 262.0923.

4-(3-((*tert*-Butyldimethylsilyloxy)phenyl)-2-chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4c**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.048 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.480 mmol, 2 equiv), (4-(((*tert*-butyldimethylsilyloxy)methyl)phenyl)boronic acid (0.064 g, 0.254 mmol, 1.06 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.022 mL, 1.200 mmol, 5 equiv), and CPME (2 mL, 0.12 M). The reaction was warmed to 40 °C and allowed to stir for 20 h. After cooling, zinc (0.222 g, 3.400 mmol, 14 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.7 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 40 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–20% TBME/cyclohexane, afforded the *title compound* as a yellow oil (0.074 g, 82%). LCMS (Method B, UV, ESI) $R_t = 1.55$ min, $[M+H]^+ = 376$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.30 (t, $J = 7.8$ Hz, 1 H), 7.13 (dt, $J = 7.8, 1.3$ Hz, 1 H), 7.00–6.97 (m, 1 H), 6.89 (ddd, $J = 8.1, 2.3, 0.9$ Hz, 1 H), 6.55 (br. s, 1 H), 3.54–3.49 (m, 2 H), 2.72 (t, $J = 6.3$ Hz, 2 H), 1.90–1.82 (m, 2 H), 1.00 (s, 9 H), 0.22 (s, 6 H); ¹³C NMR (101 MHz, CDCl₃) δ 163.1, 162.2, 157.5, 155.4, 138.5, 129.3, 121.9, 120.8, 120.5, 108.5, 41.2, 25.7, 24.2, 20.7, 18.2, –4.4; ν_{\max} (thin film)/cm⁻¹ 3250, 3127, 2930, 2858, 1594, 1563, 1327, 1299, 1270, 1254, 948, 853, 840, 779; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₉H₂₇ClN₃OSi 376.1606; found ³⁵Cl 376.1595 and ³⁷Cl 378.1573.

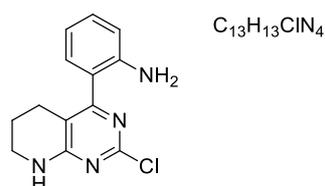
2-Chloro-4-(2-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4d**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), (2-(trifluoromethyl)phenyl)boronic acid (0.050 g, 0.263 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (1 mL, 0.25 M). The reaction was warmed to 40 °C and allowed to stir for 4 h. After cooling, zinc

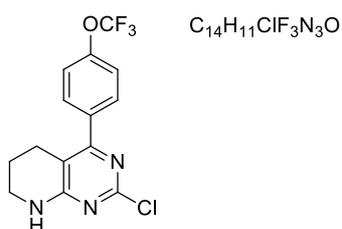
(0.422 g, 6.450 mmol, 25.8 equiv) and hydrochloric acid (4.00 mL, 8.00 mmol, 32 equiv, as a 2 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 16 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–30% MeOH/DCM, afforded the *title compound* as a colourless solid (0.057 g, 73%). m.p. 204–206 °C; LCMS (Method B, UV, ESI) $R_t = 1.06$ min, $[M+H]^+ = 314$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, $J = 7.8$ Hz, 1 H), 7.61 (t, $J = 7.6$ Hz, 1 H), 7.53 (t, $J = 7.6$ Hz, 1 H), 7.30 (d, $J = 7.3$ Hz, 1 H), 6.92 (br. s, 1 H), 3.59–3.44 (m, 2 H), 2.41–2.26 (m, 2 H), 1.94–1.76 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 162.2, 161.8, 156.9, 135.9 (q, $^4J_{C-F} = 1.5$ Hz), 131.9, 129.8, 128.8, 128.1 (q, $^2J_{C-F} = 31.5$ Hz), 126.5 (q, $^3J_{C-F} = 5.1$ Hz), 123.8 (q, $^1J_{C-F} = 274$ Hz), 110.0, 44.2, 23.0, 20.0; ¹⁹F NMR (376 MHz, CDCl₃) δ -59.1; ν_{\max} (solid)/cm⁻¹ 3240, 3121, 2963, 2864, 1595, 1567, 1327, 1289, 1271, 1170, 1108, 1097, 1033, 1016, 771, 654; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₄H₁₂ClF₃N₃ 314.0666; found ³⁵Cl 314.0666 and ³⁷Cl 316.0642.

2-(2-Chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl)aniline, **4e**



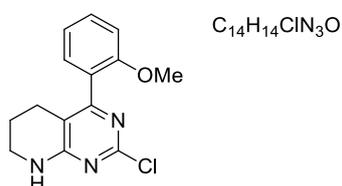
Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.048 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.480 mmol, 2 equiv), (2-aminophenyl)boronic acid (0.035 g, 0.256 mmol, 1.07 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.022 mL, 1.200 mmol, 5 equiv), and CPME (1 mL, 0.24 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.423 g, 6.470 mmol, 27 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.7 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 4 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.048 g, 77%). m.p. 194–196 °C; LCMS (Method B, UV, ESI) $R_t = 1.03$ min, $[M+H]^+ = 261$, 96% purity; ¹H NMR (400 MHz, *d*₆-DMSO) δ 8.17 (s, 1 H), 7.52 (dd, $J = 8.6$, 1.0 Hz, 2 H), 7.31–7.24 (m, 3 H), 7.02–6.96 (m, 1 H), 3.23 (dt, $J = 6.8$, 3.3 Hz, 2 H), 2.50 (t, $J = 6.4$ Hz, 2 H), 1.85–1.77 (m, 2 H); ¹³C NMR (101 MHz, *d*₆-acetone) δ 162.2, 159.1, 157.6, 153.1, 141.3, 129.3, 123.3, 121.9, 121.8, 91.5, 41.1, 21.6, 20.8; ν_{\max} (solid)/cm⁻¹ 3242, 3121, 2847, 1607, 1569, 1495, 1436, 1400, 1333, 766, 744, 683; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₃H₁₄ClN₄ 261.0902; found ³⁵Cl 261.0896 and ³⁷Cl 263.0864.

2-Chloro-4-(4-(trifluoromethoxy)phenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4f**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), (4-(trifluoromethoxy)phenyl)boronic acid (0.054 g, 0.262 mmol, 1.05 equiv), platinum (IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (2 mL, 0.125 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.237 g, 3.620 mmol, 14.5 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.055 g, 67%). m.p. 300 °C (decomposition); LCMS (Method B, UV, ESI) *R*_t = 1.20 min, [M+H]⁺ = 330, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.63–7.58 (m, 2 H), 7.31–7.28 (m, 2 H), 5.68 (br. s, 1 H), 3.53–3.47 (m, 2 H), 2.74 (t, *J* = 6.2 Hz, 2 H), 1.92–1.87 (m, 2 H); ¹³C NMR (126 MHz, CDCl₃) δ 169.9, 162.0, 158.0, 149.8, 135.7, 130.5, 120.7, 118.4 (q, ¹*J*_{C-F} = 259 Hz), 108.5, 41.2, 24.1, 20.6; ¹⁹F NMR (376 MHz, CDCl₃) δ -57.8; *ν*_{max} (solid)/cm⁻¹ 3242, 3128, 2967, 2859, 1597, 1567, 1326, 1251, 1194, 1161, 1097, 1017, 780; HRMS (ESI-Orbitrap) *m/z*: [M+H]⁺ calcd for C₁₄H₁₂ClF₃N₃O 330.0616; found ³⁵Cl 330.0611 and ³⁷Cl 332.0586.

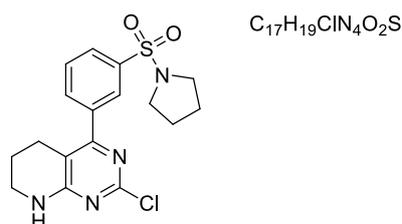
2-Chloro-4-(2-methoxyphenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4g**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), (2-methoxyphenyl)boronic acid (0.040 g, 0.263 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (1 mL, 0.25 M). The reaction was warmed to 40 °C and allowed to stir for 20 h. After cooling, zinc

(0.423 g, 6.470 mmol, 25.9 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 8 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.055 g, 80%). m.p. 258–260 °C; LCMS (Method B, UV, ESI) $R_t = 0.95$ min, $[M+H]^+ = 276$, 100% purity; ¹H NMR (400 MHz, *d*₆-acetone) δ 7.41 (ddd, $J = 8.4, 7.4, 1.8$ Hz, 1 H), 7.24 (dd, $J = 7.3, 1.7$ Hz, 1 H), 7.09 (d, $J = 8.3$ Hz, 1 H), 7.03 (td, $J = 7.5, 1.0$ Hz, 1 H), 6.93 (br. s, 1 H), 3.81 (s, 3 H), 3.47–3.41 (m, 2 H), 2.83–2.74 (m, 2 H), 1.86–1.73 (m, 2 H); ¹³C NMR (101 MHz, *d*₆-acetone) δ 162.8, 162.5, 158.3, 157.5, 131.1, 131.0, 128.0, 121.3, 112.0, 111.5, 55.9, 41.7, 23.9, 21.1; ν_{\max} (solid)/cm⁻¹ 3268, 2974, 2943, 1592, 1560, 1404, 1325, 1282, 1238, 1184, 1012, 745; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₄H₁₅ClN₃O 276.0898; found ³⁵Cl 276.0898 and ³⁷Cl 278.0865.

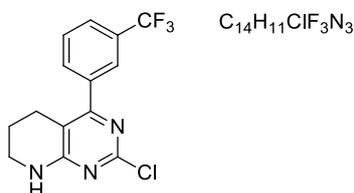
2-Chloro-4-(3-(pyrrolidin-1-ylsulfonyl)phenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4h**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), (3-(pyrrolidin-1-ylsulfonyl)phenyl)boronic acid (0.067 g, 0.262 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (1 mL, 0.25 M). The reaction was warmed to 40 °C and allowed to stir for 20 h. After cooling, zinc (0.188 g, 2.880 mmol, 11.5 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane, afforded the *title compound* as a colorless solid (0.050 g, 53%). m.p. 228–230 °C; LCMS (Method B, UV, ESI) $R_t = 1.01$ min, $[M+H]^+ = 379$, 91% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (t, $J = 1.6$ Hz, 1 H), 7.89 (dt, $J = 7.8, 1.5$ Hz, 1 H), 7.84 (dt, $J = 7.9, 1.3$ Hz, 1 H), 7.67–7.61 (m, 1 H), 6.02 (br. s, 1 H), 3.54–3.49 (m, 2 H), 3.29–3.24 (m, 4 H), 2.73 (t, $J = 6.2$ Hz, 2 H), 1.89 (quin, $J = 5.9$ Hz, 2 H), 1.82–1.76 (m, 4 H); ¹³C NMR (101 MHz, CDCl₃) δ 162.2, 161.5, 158.0, 138.2, 137.1, 133.1, 129.4, 128.0, 127.6, 108.9, 48.0, 41.2, 25.2, 23.9, 20.6; ν_{\max} (solid)/cm⁻¹ 3239, 3123, 2956, 2845, 1591, 1560,

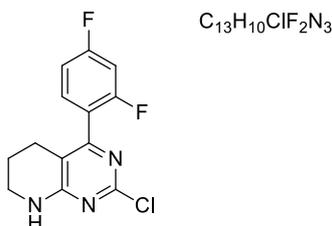
1340, 1327, 1300, 1158, 1102, 1088, 1011, 774, 676, 628, 605; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for $C_{17}H_{20}ClN_4O_2S$ 379.0990; found ^{35}Cl 379.0987 and ^{37}Cl 381.0956.

2-Chloro-4-(3-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4i**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.048 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.480 mmol, 2 equiv), (3-(trifluoromethyl)phenyl)boronic acid (0.500 g, 0.263 mmol, 1.10 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.022 mL, 1.200 mmol, 5 equiv), and CPME (2 mL, 0.12 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.210 g, 3.210 mmol, 13.4 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.7 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.053 g, 70%). m.p. 203–205 °C; LCMS (Method B, UV, ESI) R_t = 1.17 min, $[M+H]^+$ = 314, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.83–7.80 (m, 1 H), 7.77–7.67 (m, 2 H), 7.61–7.55 (m, 1 H), 6.67 (br. s, 1 H), 3.57–3.52 (m, 2 H), 2.73 (t, J = 6.2 Hz, 2 H), 1.89 (quin, J = 5.9 Hz, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 162.3, 161.6, 157.8, 137.9, 132.2, 130.8 (d, ² J_{C-F} = 32.3 Hz), 128.8, 125.9 (q, ³ J_{C-F} = 3.7 Hz), 125.7 (q, ³ J_{C-F} = 3.9 Hz), 121.4 (d, ¹ J_{C-F} = 224.3 Hz), 108.8, 41.2, 24.0, 20.6; ¹⁹F NMR (376 MHz, CDCl₃) δ –62.6; ν_{max} (solid)/cm⁻¹ 3250, 3125, 2969, 1599, 1572, 1326, 1317, 1162, 1118, 1099, 1073, 811, 711, 686; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for $C_{14}H_{12}ClF_3N_3$ 314.0666; found ^{35}Cl 314.0654 and ^{37}Cl 316.0624.

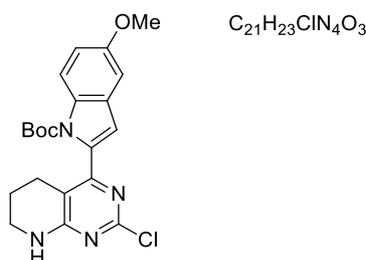
2-Chloro-4-(2,4-difluorophenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4j**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), (2,4-difluorophenyl)boronic acid (0.041 g, 0.260 mmol, 1.04 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-

bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (1 mL, 0.25 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.233 g, 3.560 mmol, 14.3 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.057 g, 81%). m.p. 241–243 °C; LCMS (Method B, UV, ESI) $R_t = 1.02$ min, $[M+H]^+ = 282$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.52–7.44 (m, 1 H), 7.03–6.96 (m, 1 H), 6.92–6.85 (m, 1 H), 6.46 (br. s, 1 H), 3.55–3.49 (m, 2 H), 2.54 (t, $J = 6.4$ Hz, 2 H), 1.88 (quin, $J = 5.8$ Hz, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 163.5 (d, ¹ $J_{C-F} = 253.1$ Hz), 161.8, 159.7 (d, ¹ $J_{C-F} = 263.4$ Hz), 157.9, 157.6, 132.2 (dd, ³ $J_{C-F} = 10.3$ Hz, ³ $J_{C-F} = 5.1$ Hz), 121.4 (dd, ² $J_{C-F} = 15.4$ Hz, ⁴ $J_{C-F} = 3.7$ Hz), 111.9 (dd, ² $J_{C-F} = 21.3$ Hz, ⁴ $J_{C-F} = 3.7$ Hz), 110.8, 104.0 (t, ² $J_{C-F} = 25.7$ Hz), 41.2, 22.9, 20.2; ¹⁹F NMR (376 MHz, CDCl₃) δ -107.9 (d, $J = 10.4$ Hz, 1 F), -109.2 (d, $J = 10.4$ Hz, 1 F); ν_{\max} (solid)/cm⁻¹ 3249, 3125, 2960, 2868, 1598, 1565, 1505, 1416, 1287, 1269, 1253, 1189, 1105, 840, 783; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₃H₁₁ClF₂N₃ 282.0604; found ³⁵Cl 282.0602 and ³⁷Cl 284.0570.

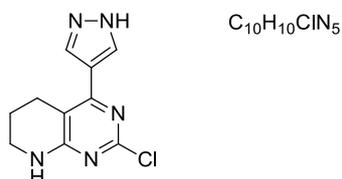
tert-Butyl 2-(2-chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl)-5-methoxy-1*H*-indole-1-carboxylate, **4k**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.048 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.480 mmol, 2 equiv), (1-(*tert*-butoxycarbonyl)-5-methoxy-1*H*-indol-2-yl)boronic acid (0.073 g, 0.252 mmol, 1.05 equiv), platinum(IV) oxide (0.006 mg, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.022 mL, 1.200 mmol, 5 equiv), and CPME (1 mL, 0.24 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.451 g, 6.900 mmol, 28.7 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.7 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 4 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–25% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a yellow solid (0.072 g, 72%). m.p. 208–210 °C; LCMS (Method B, UV, ESI) $R_t = 1.27$ min, $[M+H]^+ = 415$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, $J = 9.0$ Hz, 1 H), 7.03–6.96 (m, 2 H), 6.59 (s, 1 H), 6.32 (br. s, 1 H), 3.86 (s, 3 H), 3.53–3.48 (m, 2 H), 2.66 (t, $J = 6.2$ Hz, 2 H), 1.93–1.86 (m, 2 H), 1.44 (s, 9 H); ¹³C NMR (101 MHz, CDCl₃) δ 161.8, 157.9, 157.1, 156.1,

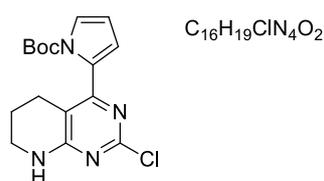
149.3, 134.6, 131.8, 129.4, 116.2, 114.2, 111.1, 110.1, 103.3, 83.6, 55.7, 41.2, 27.7, 23.3, 20.4; ν_{\max} (solid)/ cm^{-1} 3247, 3121, 2969, 2938, 2837, 1730, 1581, 1478, 1354, 1326, 1160, 1121, 1085, 1068, 1016, 807; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{24}\text{ClN}_4\text{O}_3$ 415.1531; found ^{35}Cl 415.1537 and ^{37}Cl 417.1508.

2-Chloro-4-(1*H*-pyrazol-4-yl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4l**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole-1-carboxylate (0.077 g, 0.262 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.090 mL, 5.000 mmol, 20 equiv), and CPME (1 mL, 0.25 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.223 g, 3.410 mmol, 13.7 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B and hydrochloric acid (as a 3 M solution in CPME) (0.100 mL, 0.300 mmol, 1.2 equiv) was added to chamber A. The reaction vessel was sealed and was allowed to stir at ambient temperature for 4 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–100% EtOAc/cyclohexane followed by 0–20% MeOH/EtOAc (+1% Et₃N), afforded the *title compound* as a colorless solid (0.047 g, 80%). m.p. 300 °C (decomposition); LCMS (Method B, UV, ESI) R_t = 0.62 min, $[\text{M}+\text{H}]^+$ = 236, 100% purity; ¹H NMR (400 MHz, *d*₆-DMSO) δ 8.05 (s, 2 H), 7.85 (s, 1 H), 3.30–3.25 (m, 2 H), 2.78–2.71 (m, 2 H), 1.85–1.78 (m, 2 H), one exchangeable proton not observed; ¹³C NMR (101 MHz, *d*₆-DMSO) δ 162.0, 156.7, 155.1, 151.3, 130.5, 118.6, 106.1, 39.6, 23.3, 20.2; ν_{\max} (solid)/ cm^{-1} 3243, 3146, 3120, 3002, 2960, 2852, 1577, 1331, 1117, 1025, 996, 928, 816, 774, 701; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{10}\text{H}_{11}\text{ClN}_5$ 236.0698; found ^{35}Cl 236.0696 and ^{37}Cl 238.0664.

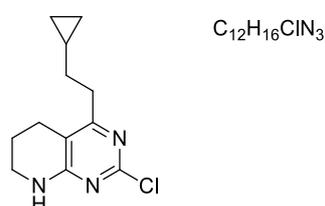
tert-Butyl 2-(2-chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl)-1*H*-pyrrole-1-carboxylate, **4m**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.048 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.480 mmol, 2

equiv), (1-(*tert*-butoxycarbonyl)-1*H*-pyrrol-2-yl)boronic acid (0.055 g, 0.261 mmol, 1.09 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.022 mL, 1.20 mmol, 5 equiv), and CPME (1 mL, 0.24 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.208 g, 3.180 mmol, 13.3 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.7 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 4 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% TBME/cyclohexane, afforded the *title compound* as a colorless solid (0.048 g, 60%). m.p. 160–162 °C; LCMS (Method B, UV, ESI) $R_t = 1.11$ min, $[M+H]^+ = 335$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.35 (dd, $J = 2.9, 1.5$ Hz, 1 H), 6.72 (br. s, 1 H), 6.32 (dd, $J = 3.1, 1.3$ Hz, 1 H), 6.23 (t, $J = 3.3$ Hz, 1 H), 3.52–3.47 (m, 2 H), 2.60 (t, $J = 6.2$ Hz, 2 H), 1.92–1.84 (m, 2 H), 1.43 (s, 9 H); ¹³C NMR (101 MHz, CDCl₃) δ 161.9, 157.4, 156.7, 148.7, 128.7, 123.1, 115.8, 110.5, 110.1, 84.0, 41.1, 27.6, 23.3, 20.4; ν_{\max} (solid)/cm⁻¹ 3251, 3126, 2973, 2868, 1591, 1558, 1411, 1372, 1325, 1310, 1287, 1251, 1129, 1092, 733; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₆H₂₀ClN₄O₂ 335.1269; found ³⁵Cl 335.1265 and ³⁷Cl 337.1241.

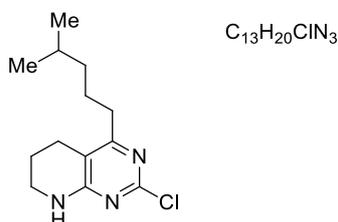
2-Chloro-4-(2-cyclopropylethyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4n**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.048 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.480 mmol, 2 equiv), (*E*)-2-(2-cyclopropylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.055 g, 0.283 mmol, 1.2 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.090 mL, 5.000 mmol, 21 equiv), and CPME (1 mL, 0.24 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.216 g, 3.300 mmol, 14 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.7 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 8 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.027 g, 47%). m.p. 137–139 °C; LCMS (Method B, UV, ESI) $R_t = 1.03$ min, $[M+H]^+ = 238$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 6.18 (br. s, 1 H), 3.48–3.41 (m, 2 H), 2.71–2.62 (m, 4 H), 1.98–1.90 (m, 2 H), 1.59–1.52 (m, 2 H), 0.77–0.66 (m, 1 H), 0.46–0.40 (m, 2 H), 0.09–0.04 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 161.6, 157.3, 108.4,

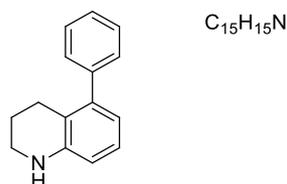
40.9, 33.8, 33.3, 22.0, 20.6, 10.8, 4.5; ν_{\max} (solid)/ cm^{-1} 3249, 3124, 2963, 2852, 1593, 1568, 1537, 1408, 1329, 1292, 1268, 1133, 1014, 992, 923, 893, 690; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{ClN}_3$ 238.1106; found ^{35}Cl 238.1098 and ^{37}Cl 240.1065.

2-Chloro-4-(4-methylpentyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4o**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.048 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.480 mmol, 2 equiv), (*E*)-(4-methylpent-1-en-1-yl)boronic acid (0.032 g, 0.252 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), palladium(II) acetate (0.002 g, 0.009 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphane (0.009 g, 0.019 mmol, 8 mol%), water (0.022 mL, 1.20 mmol, 5 equiv), and CPME (2 mL, 0.12 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.223 g, 3.410 mmol, 14.2 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.7 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% EtOAc/cyclohexane (+1% Et₃N), afforded the title compound as a colorless solid (0.031 g, 51%). m.p. 112–114 °C; LCMS (Method B, UV, ESI) R_t = 1.22 min, $[\text{M}+\text{H}]^+$ = 254, 100% purity; ^1H NMR (400 MHz, CDCl_3) δ 6.37 (br. s, 1 H), 3.48–3.42 (m, 2 H), 2.64 (t, J = 6.4 Hz, 2 H), 2.54–2.48 (m, 2 H), 1.97–1.90 (m, 2 H), 1.67–1.51 (m, 3 H), 1.28–1.20 (m, 2 H), 0.88 (d, J = 6.6 Hz, 6 H); ^{13}C NMR (101 MHz, CDCl_3) δ 167.2, 161.7, 157.3, 108.2, 40.9, 38.9, 34.2, 27.9, 26.2, 22.6, 22.0, 20.6; ν_{\max} (solid)/ cm^{-1} 3242, 3125, 2955, 2865, 1593, 1574, 1408, 1326, 1272, 1155, 1132, 916; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{21}\text{ClN}_3$ 254.1419; found ^{35}Cl 254.1409 and ^{37}Cl 256.1376.

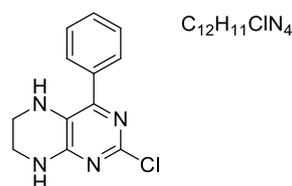
5-Phenyl-1,2,3,4-tetrahydroquinoline, **6a**



Chamber A of a two chamber COware apparatus was charged with 5-bromoquinoline (0.050 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.481 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.09 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), palladium(II) acetate (0.002 g, 0.009 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (0.009 g, 0.019 mmol, 8 mol%), water (0.022 mL,

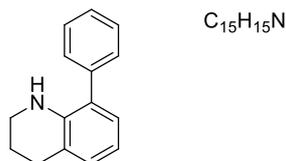
1.202 mmol, 5 equiv), and CPME (1 mL, 0.24 M). The reaction was warmed to 40 °C and allowed to stir for 24 h. After cooling, zinc (0.189 g, 2.890 mmol, 12 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.6 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–20% TBME/cyclohexane, afforded the *title compound* as a colourless oil (0.042 g, 84%). LCMS (Method B, UV, ESI) $R_t = 1.28$ min, $[M+H]^+ = 210$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.44–7.38 (m, 2 H), 7.36–7.30 (m, 3 H), 7.04 (t, $J = 7.8$ Hz, 1 H), 6.59 (dd, $J = 7.3, 1.2$ Hz, 1 H), 6.52 (dd, $J = 7.9, 1.1$ Hz, 1 H), 3.36–3.31 (m, 2 H), 2.63 (t, $J = 6.4$ Hz, 2 H), 1.90–1.82 (m, 2 H), one exchangeable proton not observed; ¹³C NMR (101 MHz, CDCl₃) δ 144.6, 142.6, 142.0, 129.1, 127.9, 126.6, 126.4, 118.9, 118.8, 113.4, 41.8, 25.8, 22.2; ν_{\max} (thin film)/cm⁻¹ 3408, 3054, 2925, 2839, 1586, 1487, 1462, 1346, 1301, 1244, 757, 722, 701; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₅H₁₆N 210.1277; found 210.1270.

2-Chloro-4-phenyl-5,6,7,8-tetrahydropteridine, **6b**



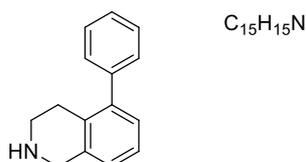
Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropteridine (0.050 g, 0.249 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.497 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.06 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.022 mL, 1.244 mmol, 5 equiv), and CPME (1 mL, 0.249 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.207 g, 3.170 mmol, 12.7 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.5 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 2 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% TBME/cyclohexane (+1% Et₃N) afforded the *title compound* as a colorless solid (0.033 g, 54%). m.p. 264–266 °C; LCMS (Method B, UV, ESI) $R_t = 0.82$ min, $[M+H]^+ = 247$, 100% purity; ¹H NMR (400 MHz, *d*₆-acetone) δ 7.73–7.68 (m, 2 H), 7.48–7.42 (m, 2 H), 7.41–7.37 (m, 1 H), 6.88 (br. s, 1 H), 5.08 (br. s, 1 H), 3.63–3.57 (m, 2 H), 3.35–3.31 (m, 2 H); ¹³C NMR (101 MHz, *d*₆-acetone) δ 155.5, 149.4, 145.1, 137.5, 129.5, 129.4, 129.2, 123.7, 41.6, 40.2; ν_{\max} (solid)/cm⁻¹ 3338, 3227, 3125, 2964, 2857, 2376, 1590, 1568, 1532, 1455, 1358, 1338, 1273, 1226, 1204, 1096, 851, 760, 704, 624; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₂H₁₂ClN₄ 247.0745; found ³⁵Cl 247.0738 and ³⁷Cl 249.0705.

8-Phenyl-1,2,3,4-tetrahydroquinoline, **6c**³



Chamber A of a two chamber COware apparatus was charged with 8-bromoquinoline (0.031 mL, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.481 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.09 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), palladium(II) acetate (0.002 g, 0.009 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (0.009 g, 0.019 mmol, 8 mol%), water (0.022 mL, 1.202 mmol, 5 equiv), and CPME (1 mL, 0.24 M). The reaction was warmed to 40 °C and allowed to stir for 20 h. After cooling, zinc (0.212 g, 3.240 mmol, 13.5 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.6 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 20 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–20% TBME/cyclohexane, afforded the title compound as a colorless gum (0.035 g, 70%). LCMS (Method B, UV, ESI) $R_t = 1.37$ min, $[M+H]^+ = 210$, 100% purity; 1H NMR (400 MHz, $CDCl_3$) δ 7.47–7.43 (m, 4 H), 7.39–7.33 (m, 1 H), 7.01–6.93 (m, 2 H), 6.69 (t, $J = 7.5$ Hz, 1 H), 4.08 (br. s, 1 H), 3.30–3.25 (m, 2 H), 2.87 (t, $J = 6.5$ Hz, 2 H), 2.02–1.94 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 139.6, 129.4, 128.8, 128.8, 128.0, 127.0, 126.6, 121.2, 116.2, 42.0, 27.5, 22.0; ν_{max} (thin film)/ cm^{-1} 3422, 3052, 2926, 2837, 1594, 1497, 1486, 1461, 1421, 1290, 1267, 754, 739, 701; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for $C_{15}H_{16}N$ 210.1277; found 210.1279.

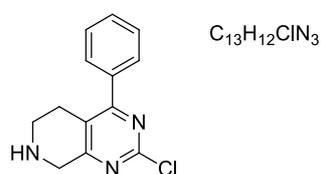
5-Phenyl-1,2,3,4-tetrahydroisoquinoline, **6d**⁴



Chamber A of a two chamber COware apparatus was charged with 5-bromoisoquinoline (0.050 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.481 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.09 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), palladium(II) acetate (0.002 g, 0.009 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (0.009 g, 0.019 mmol, 8 mol%), water (0.022 mL, 1.202 mmol, 5 equiv), and CPME (1 mL, 0.24 M). The reaction was warmed to 40 °C and allowed to stir for 40 h. After cooling, zinc (0.231 g, 3.530 mmol, 14.7 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.6 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 28 h. The reaction mixture was filtered through a Celite[®] pad, washing with

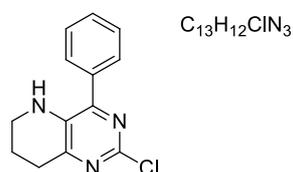
MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–100% TBME/cyclohexane followed by 0–20% MeOH/TBME (+1% Et₃N), afforded the title compound as a colorless gum (0.031 g, 62%). LCMS (Method B, UV, ESI) $R_t = 1.09$ min, $[M+H]^+ = 210$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.45–7.39 (m, 2 H), 7.38–7.29 (m, 3 H), 7.21 (d, $J = 7.6$ Hz, 1 H), 7.10 (d, $J = 7.1$ Hz, 1 H), 7.05 (d, $J = 7.6$ Hz, 1 H), 4.12 (s, 2 H), 3.07 (t, $J = 5.9$ Hz, 2 H), 2.66 (t, $J = 5.9$ Hz, 2 H), 2.06 (br. s, 1 H); ¹³C NMR (101 MHz, CDCl₃) δ 142.3, 141.3, 135.9, 132.4, 129.1, 128.0, 127.5, 126.8, 125.5, 125.5, 48.7, 44.1, 28.3; ν_{\max} (thin film)/cm⁻¹ 3057, 3022, 2924, 2807, 1586, 1496, 1457, 1436, 1131, 953, 757, 700; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₅H₁₆N 210.1277; found 210.1270.

2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[3,4-*d*]pyrimidine, **6e**



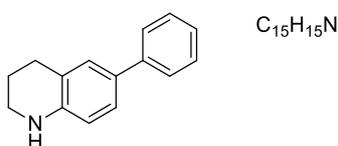
Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[3,4-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (1 mL, 0.25 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.222 g, 3.400 mmol, 13.6 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 20 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–100% EtOAc/cyclohexane followed by 0–20% MeOH/EtOAc (+1% Et₃N), afforded the *title compound* as a colorless solid (0.045 g, 73%). m.p. 300 °C (decomposition); LCMS (Method B, UV, ESI) $R_t = 0.85$ min, $[M+H]^+ = 246$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 8.35–8.17 (m, 1 H), 7.73–7.48 (m, 4 H), 4.06–3.94 (m, 2 H), 3.03–2.90 (m, 2 H), 2.80–2.70 (m, 2 H), one exchangeable proton not observed; ¹³C NMR (101 MHz, *d*₆-DMSO) δ 169.6, 167.3, 165.6, 135.9, 129.9, 128.8, 128.4, 125.7, 50.0, 42.3, 26.6; ν_{\max} (solid)/cm⁻¹ 3327, 2926, 2847, 1533, 1435, 1332, 1262, 1025, 797, 758, 698, 627; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₃H₁₃ClN₃ 246.0793; found ³⁵Cl 246.0791 and ³⁷Cl 248.0777.

2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[3,2-*d*]pyrimidine, **6f**



Chamber A of a two chamber COware apparatus was charged with 2,4-dichloropyrido[3,2-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (1 mL, 0.25 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.202 g, 3.090 mmol, 12.4 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% TBME/cyclohexane (+1% Et₃N), afforded the *title compound* as a colorless solid (0.040 g, 65%). m.p. 87–89 °C; LCMS (Method B, UV, ESI) $R_t = 1.04$ min, $[M+H]^+ = 246$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.71–7.67 (m, 2 H), 7.53–7.43 (m, 3 H), 4.33 (br. s, 1 H), 3.33–3.28 (m, 2 H), 2.97 (t, $J = 6.6$ Hz, 2 H), 2.10–2.02 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 153.6, 151.1, 147.7, 135.5, 135.1, 129.7, 129.1, 128.2, 41.3, 30.1, 20.7; ν_{\max} (solid)/cm⁻¹ 3329, 2966, 2940, 2852, 1557, 1466, 1405, 1380, 1342, 1279, 1205, 1086, 902, 862, 698, 624; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₃H₁₃ClN₃ 246.0793; found ³⁵Cl 246.0797 and ³⁷Cl 248.0767.

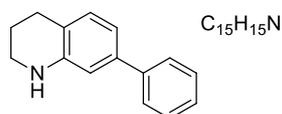
6-Phenyl-1,2,3,4-tetrahydroquinoline, **6g**⁵



Chamber A of a two chamber COware apparatus was charged with 6-bromoquinoline (0.033 mL, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.481 mmol, 2 equiv), phenylboronic acid (0.044 g, 0.360 mmol, 1.5 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), palladium(II) acetate (0.002 g, 0.009 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (0.009 g, 0.019 mmol, 8 mol%), water (0.022 mL, 1.202 mmol, 5 equiv), and CPME (2 mL, 0.12 M). The reaction was warmed to 40 °C and allowed to stir for 24 h. After cooling, zinc (0.212 g, 3.240 mmol, 13.5 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.6 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–20% TBME/cyclohexane, afforded the *title compound* as a yellow oil (0.035 g, 70%). LCMS (Method B, UV, ESI) $R_t = 1.30$ min, $[M+H]^+ = 210$, 99% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.55–7.51 (m, 2 H), 7.41–7.35 (m, 2 H), 7.27–7.22 (m, 4 H), 6.58–6.54 (m, 1 H), 3.38–3.33 (m, 2 H), 2.85 (t, $J = 6.4$ Hz, 2 H), 2.03–1.95 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 144.2, 141.5, 130.0, 128.6, 128.2, 126.3, 125.9, 125.5, 121.6, 114.5, 42.0, 27.1, 22.2; ν_{\max} (thin

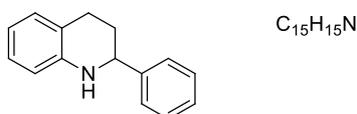
film)/cm⁻¹ 3408, 3024, 2926, 2837, 1612, 1599, 1519, 1486, 1467, 1229, 815, 762, 696; HRMS (ESI-Orbitrap) *m/z*: [M+H]⁺ calcd for C₁₅H₁₆N 210.1277; found 210.1269.

7-Phenyl-1,2,3,4-tetrahydroquinoline, **6h**⁶



Chamber A of a two chamber COware apparatus was charged with 7-bromoquinoline (0.050 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.481 mmol, 2 equiv), phenylboronic acid (0.031 g, 0.254 mmol, 1.06 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), palladium(II) acetate (0.002 g, 0.009 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (0.009 g, 0.019 mmol, 8 mol%), water (0.022 mL, 1.202 mmol, 5 equiv), and CPME (2 mL, 0.12 M). The reaction was warmed to 40 °C and allowed to stir for 24 h. After cooling, zinc (0.212 g, 3.240 mmol, 13.5 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.6 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 16 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–5% TBME/cyclohexane, afforded the title compound as a colorless oil (0.037 g, 74%). LCMS (Method B, UV, ESI) *R*_t = 1.29 min, [M+H]⁺ = 210, 89% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.58–7.53 (m, 2 H), 7.44–7.38 (m, 2 H), 7.34–7.29 (m, 2 H), 7.03 (d, *J* = 7.6 Hz, 1 H), 6.86 (dd, *J* = 7.7, 1.8 Hz, 1 H), 6.71 (d, *J* = 1.7 Hz, 1 H), 3.39–3.32 (m, 2 H), 2.82 (t, *J* = 6.4 Hz, 2 H), 2.03–1.95 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 145.0, 141.6, 140.0, 129.9, 128.5, 126.9, 126.8, 120.7, 116.0, 112.8, 42.0, 26.7, 22.3; ν_{max} (thin film)/cm⁻¹ 3405, 3025, 2924, 2837, 1612, 1566, 1485, 1467, 1449, 1336, 1312, 1227, 1006, 857, 757, 696; HRMS (ESI-Orbitrap) *m/z*: [M+H]⁺ calcd for C₁₅H₁₆N 210.1277; found 210.1266.

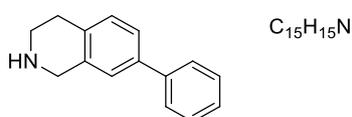
2-Phenyl-1,2,3,4-tetrahydroquinoline, **6i**⁷



Chamber A of a two chamber COware apparatus was charged with 2-chloroquinoline (0.050 g, 0.306 mmol, 1 equiv), tripotassium phosphate (0.130 g, 0.611 mmol, 2 equiv), phenylboronic acid (0.039 g, 0.320 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 9 mol%), palladium(II) acetate (0.003 g, 0.013 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (0.012 g, 0.025 mmol, 8 mol%), water (0.028 mL, 1.528 mmol, 5 equiv), and CPME (2 mL, 0.153 M). The reaction was warmed to 40 °C and allowed to stir for 40 h. After cooling, zinc (0.198 g, 3.030 mmol, 9.9 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 48 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 28 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15

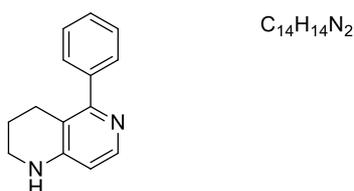
mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–20% TBME/cyclohexane, afforded the title compound as a colorless oil (0.045 g, 70%). LCMS (Method B, UV, ESI) $R_t = 1.33$ min, $[M+H]^+ = 210$, 93% purity; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.43–7.28 (m, 6 H), 7.05–6.99 (m, 2 H), 6.66 (td, $J = 7.3, 1.0$ Hz, 1 H), 6.58–6.53 (m, 1 H), 4.46 (dd, $J = 9.3, 2.9$ Hz, 1 H), 2.99–2.89 (m, 1 H), 2.79–2.71 (m, 1 H), 2.18–2.10 (m, 1 H), 2.07–1.95 (m, 1 H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 144.8, 144.7, 129.3, 128.6, 127.4, 126.9, 126.5, 120.9, 117.2, 114.0, 56.3, 31.0, 26.4; ν_{max} (thin film)/ cm^{-1} 3406, 3058, 3032, 2924, 2845, 1607, 1481, 1310, 1274, 1252, 1110, 747, 700; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{16}\text{N}$ 210.1277; found 210.1269.

7-Phenyl-1,2,3,4-tetrahydroisoquinoline, **6j**



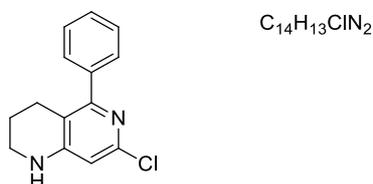
Chamber A of a two chamber COware apparatus was charged with 7-bromoisoquinoline (0.050 g, 0.240 mmol, 1 equiv), tripotassium phosphate (0.102 g, 0.481 mmol, 2 equiv), phenylboronic acid (0.044 g, 0.360 mmol, 1.5 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), palladium(II) acetate (0.002 g, 0.009 mmol, 4 mol%), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (0.009 g, 0.019 mmol, 8 mol%), water (0.022 mL, 1.202 mmol, 5 equiv), and CPME (2 mL, 0.12 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.212 g, 3.240 mmol, 13.5 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 61.6 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–20% TBME/cyclohexane, afforded the title compound as a colorless oil (0.046 g, 91%). LCMS (Method B, UV, ESI) $R_t = 1.09$ min, $[M+H]^+ = 210$, 100% purity; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.46 (br. s, 1 H), 7.57–7.28 (m, 7 H), 7.22 (d, $J = 8.1$ Hz, 1 H), 4.33–4.25 (m, 2 H), 3.42–3.34 (m, 2 H), 3.12–3.03 (m, 2 H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.0, 140.3, 140.0, 131.2, 130.0, 129.5, 128.8, 127.5, 127.0, 126.4, 125.2, 112.0, 44.7, 41.5, 25.8; ν_{max} (thin film)/ cm^{-1} 3032, 2926, 2835, 1674, 1485, 1428, 1231, 1132, 761, 698; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{16}\text{N}$ 210.1277; found 210.1266.

5-Phenyl-5,6,7,8-tetrahydro-1,6-naphthyridine, **6k**⁸



Chamber A of a two chamber COware apparatus was charged with 5-chloro-1,6-naphthyridine (0.050 g, 0.304 mmol, 1 equiv), tripotassium phosphate (0.129 g, 0.608 mmol, 2 equiv), phenylboronic acid (0.039 g, 0.320 mmol, 1.05 equiv), platinum(IV) oxide (0.007 g, 0.031 mmol, 10 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (0.009 g, 0.012 mmol, 4 mol%), water (0.027 mL, 1.519 mmol, 5 equiv), and CPME (2 mL, 0.152 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.218 g, 3.330 mmol, 11 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 49 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–100% TBME/cyclohexane (+1% Et₃N) followed by 0–20% MeOH/TBME (+1% Et₃N), afforded the title compound as a colorless solid (0.043 g, 67%). m.p. 143–145 °C; LCMS (Method B, UV, ESI) $R_t = 0.91$ min, $[M+H]^+ = 211$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (d, $J = 5.5$ Hz, 1 H), 7.52–7.48 (m, 2 H), 7.44–7.32 (m, 3 H), 6.29 (d, $J = 5.5$ Hz, 1 H), 4.50 (br. s, 1 H), 3.37–3.32 (m, 2 H), 2.68 (t, $J = 6.2$ Hz, 2 H), 1.88–1.80 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 158.1, 150.6, 146.9, 140.8, 128.9, 127.9, 127.5, 113.5, 107.3, 41.2, 25.1, 21.4; ν_{\max} (solid)/cm⁻¹ 3227, 3054, 2931, 2852, 1585, 1511, 1432, 1351, 1315, 1185, 1147, 1010, 810, 750, 699; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₁₄H₁₅N₂ 211.1230; found 211.1226.

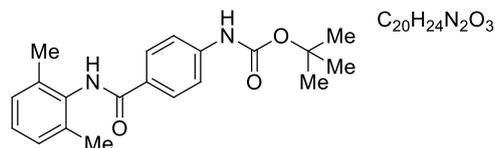
7-Chloro-5-phenyl-1,2,3,4-tetrahydro-1,6-naphthyridine, **6l**



Chamber A of a two chamber COware apparatus was charged with 5,7-dichloro-1,6-naphthyridine (0.050 g, 0.251 mmol, 1 equiv), tripotassium phosphate (0.107 g, 0.502 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.05 equiv), platinum(IV) oxide (0.006 g, 0.026 mmol, 11 mol%), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.256 mmol, 5 equiv), and CPME (2 mL, 0.126 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, zinc (0.197 g, 3.010 mmol, 12 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 58.9 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was sealed and was allowed to stir at ambient temperature for 24 h. The reaction mixture was filtered through a Celite[®] pad, washing with MeOH (15 mL) and the filtrate was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (12 g), eluting with 0–50% TBME/cyclohexane, afforded the *title compound* as a colorless solid (0.038 g, 62%). m.p. 130–132 °C; LCMS (Method B, UV, ESI) $R_t = 1.10$ min, $[M+H]^+ = 245$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.49–7.45 (m, 2 H), 7.43–7.33 (m, 3 H), 6.32 (s, 1 H), 4.63 (br. s, 1 H), 3.36–3.31 (m, 2 H), 2.65 (t, $J = 6.2$ Hz, 2 H), 1.86–1.76 (m, 2 H); ¹³C NMR (101 MHz, CDCl₃) δ 157.7,

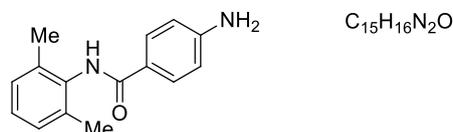
152.6, 148.5, 139.5, 128.9, 128.0, 112.9, 105.6, 41.2, 24.8, 21.2; ν_{\max} (solid)/ cm^{-1} 3310, 3254, 3145, 3068, 2951, 2839, 1574, 1505, 1436, 1348, 1314, 1253, 1197, 1178, 1089, 1072, 1012, 907, 840, 831, 769, 701; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{14}\text{ClN}_2$ 245.0840; found ^{35}Cl 245.0838 and ^{37}Cl 247.0806.

tert-Butyl (4-((2,6-dimethylphenyl)carbamoyl)phenyl)carbamate, **S1**



Oxalyl chloride (0.443 mL, 5.060 mmol, 1.2 equiv), as a solution in THF (5 mL) was added to a stirred solution of 4-((*tert*-butoxycarbonyl)amino)benzoic acid (1.000 g, 4.210 mmol, 1 equiv) and DMF (0.2 mL) in THF (20 mL, 0.167 M) at 0 °C. The reaction mixture was allowed to warm to ambient temperature over 3 h. After cooling to 0 °C, 2,6-dimethylaniline (0.623 mL, 5.060 mmol, 1.2 equiv) and triethylamine (1.175 mL, 8.430 mmol, 2 equiv) were added to the reaction mixture, which was allowed to warm to ambient temperature over 16 h. The solvent was removed under reduced pressure and the reaction mixture was taken up in EtOAc (50 mL) which was then washed with water (20 mL), NaHCO_3 (2 x 20 mL), and brine (20 mL). The organic phase was dried by passing through a hydrophobic frit and was concentrated under reduced pressure. Purification by normal phase column chromatography on Companion silica (80 g), eluting with 0–40% EtOAc/cyclohexane afforded the *title compound* as a colorless solid (0.933 g, 65%). m.p. 230–232 °C; LCMS (Method B, UV, ESI) R_t = 1.15 min, $[\text{M}+\text{H}]^+$ = 341, 100% purity; ^1H NMR (400 MHz, CDCl_3) δ 7.92–7.86 (m, 2 H), 7.54–7.47 (m, 2 H), 7.18–7.10 (m, 3 H), 6.66 (br. s, 1 H), 2.29 (s, 6 H), 1.55 (s, 9 H), one exchangeable proton not observed; ^{13}C NMR (101 MHz, d_6 -DMSO) δ 164.4, 152.6, 142.5, 135.6, 135.5, 128.3, 127.6, 126.5, 117.2, 79.5, 28.1, 18.0; ν_{\max} (solid)/ cm^{-1} 3322, 2976, 2919, 1695, 1646, 1589, 1515, 1487, 1406, 1369, 1316, 1240, 1150, 1056, 773; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_3$ 341.1860; found 341.1844.

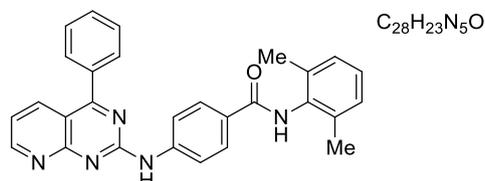
4-Amino-*N*-(2,6-dimethylphenyl)benzamide, **7⁹**



A solution of hydrochloric acid (as a 3 M solution in CPME) (4.406 mL, 13.220 mmol, 5 equiv) and *tert*-butyl (4-((2,6-dimethylphenyl)carbamoyl)phenyl)carbamate (0.900 g, 2.640 mmol, 1 equiv) was stirred at ambient temperature for 2 h. The reaction mixture was taken up in EtOAc (50 mL) which was then washed with water (20 mL), NaHCO_3 (2 x 20 mL), and brine (20 mL). The organic phase was dried by passing through a hydrophobic frit and was concentrated under reduced pressure to afford the *title compound* as a colorless solid (0.612 g, 96%). m.p. 213–215 °C (lit. 210–212 °C),³ LCMS (Method B, UV, ESI) R_t = 0.81 min, $[\text{M}+\text{H}]^+$ = 241, 91% purity; ^1H NMR (400 MHz, d_6 -DMSO) δ 9.24 (br. s, 1 H), 7.74–7.70 (m,

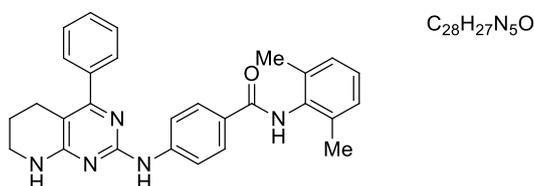
2 H), 7.09–7.07 (m, 3 H), 6.61–6.57 (m, 2 H), 5.65 (br. s, 2 H), 2.15 (s, 6 H); ^{13}C NMR (101 MHz, d_6 -DMSO) δ 164.9, 151.9, 136.0, 135.8, 129.1, 127.5, 126.2, 120.9, 112.6, 18.1; ν_{max} (solid)/ cm^{-1} 3471, 3353, 3218, 3028, 2960, 2919, 1620, 1601, 1567, 1492, 1291, 1175, 837, 770; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}$ 241.1335; found 241.1331.

N-(2,6-Dimethylphenyl)-4-((4-phenylpyrido[2,3-*d*]pyrimidin-2-yl)amino)benzamide, **10**



A microwave vial was charged with 2-chloro-4-phenylpyrido[2,3-*d*]pyrimidine (0.120 g, 0.497 mmol, 1 equiv), *N*-ethyl-*N*-isopropylpropan-2-amine (0.173 mL, 0.993 mmol, 2 equiv), 4-amino-*N*-(2,6-dimethylphenyl)benzamide (0.119 g, 0.497 mmol, 1 equiv), and 1-butanol (10 mL, 0.05 M). The reaction mixture was warmed to 120 °C and was allowed to stir for 61 h. After cooling, the reaction was diluted with EtOAc (20 mL) and was washed with water (20 mL) and brine (20 mL). The organic layer was dried by passing through a hydrophobic frit and concentrated under reduced pressure. Purification by MDAP afforded the title compound as a yellow solid (0.081 g, 37%). m.p. 178–180 °C; LCMS (Method B, UV, ESI) R_t = 1.06 min, $[\text{M}+\text{H}]^+$ = 446, 83% purity; ^1H NMR (400 MHz, CDCl_3) δ 9.10 (d, J = 4.4, 2.0 Hz, 1 H), 8.31 (dd, J = 8.2, 1.8 Hz, 1 H), 8.09 (d, J = 8.6 Hz, 2 H), 7.99 (d, J = 8.6 Hz, 2 H), 7.79–7.75 (m, 3 H), 7.66–7.61 (m, 3 H), 7.32 (dd, J = 8.2, 4.3 Hz, 1 H), 7.17–7.13 (m, 3 H), 2.32 (s, 6 H), one exchangeable proton not observed; ^{13}C NMR (101 MHz, d_6 -DMSO) δ 171.1, 164.5, 159.9, 158.1, 157.5, 143.1, 136.5, 135.7, 135.7, 135.5, 130.3, 129.7, 128.6, 128.2, 127.6, 127.4, 126.5, 120.0, 118.3, 113.0, 18.1; ν_{max} (solid)/ cm^{-1} 3281, 3058, 2966, 1642, 1586, 1567, 1520, 1494, 1464, 1445, 1412, 1366, 1252, 763, 701; HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{24}\text{N}_5\text{O}$ 446.1975; found 446.1991.

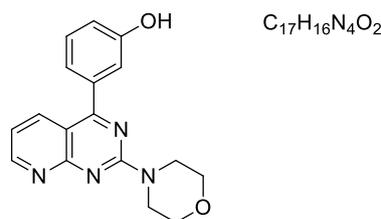
N-(2,6-Dimethylphenyl)-4-((4-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-2-yl)amino)benzamide, **8**



Chamber A of COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), phenylboronic acid (0.032 g, 0.262 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (2 mL, 0.125 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, 4-amino-*N*-(2,6-dimethylphenyl)benzamide (0.072 g, 0.300 mmol, 1.2 equiv), and tripotassium

phosphate (0.080 g, 0.375 mmol, 1.5 equiv) were added to chamber A of COware. The reaction vessel was then sealed, warmed to 40 °C, and was allowed to stir for 24 h. After cooling, palladium on carbon (0.027 g, 0.025 mmol, 10 mol%) was added to chamber A of COware and zinc (0.208 g, 3.180 mmol, 12.7 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was then sealed and then the reaction mixture was allowed to stir for a further 16 h. The reaction mixture was then filtered through Celite[®], washing with MeOH (15 mL). The filtrate was then concatenated under reduced pressure. Purification by MDAP afforded the *title compound* as a colorless solid (0.012 g, 11%). m.p. 250 °C (decomposition); LCMS (Method B, UV, ESI) $R_t = 1.26$ min, $[M+H]^+ = 450$, 100% purity; ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, $J = 8.5$ Hz, 2 H), 7.77 (d, $J = 8.5$ Hz, 2 H), 7.61–7.57 (m, 2 H), 7.50–7.42 (m, 4 H), 7.14–7.11 (m, 3 H), 7.04 (br. s, 1 H), 5.30 (br. s, 1 H), 3.51–3.46 (m, 2 H), 2.72 (t, $J = 6.0$ Hz, 2 H), 2.30 (s, 6 H), 1.92–1.84 (m, 2 H); ¹³C NMR (101 MHz, *d*₆-DMSO) δ 178.8, 170.3, 161.4, 159.7, 151.3, 140.7, 137.8, 136.5, 130.1, 128.9, 128.4, 128.0, 127.6, 126.9, 119.1, 112.3, 104.8, 40.1, 23.8, 20.4, 18.3; ν_{\max} (solid)/cm⁻¹ 3339, 3209, 2957, 1641, 1587, 1566, 1514, 1417, 1384, 1346, 1291, 1249, 1175, 1027, 767, 703; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for C₂₈H₂₈N₅O 450.2288; found 450.2271.

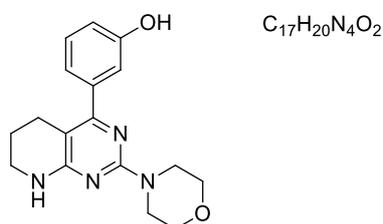
3-(2-Morpholinopyrido[2,3-*d*]pyrimidin-4-yl)phenol, **11**



A microwave vial was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.200 g, 1.000 mmol, 1 equiv), tripotassium phosphate (0.424 g, 2.000 mmol, 2 equiv), (3-((*tert*-butyldimethylsilyloxy)phenyl)boronic acid (0.265 g, 1.050 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.029 g, 0.040 mmol, 4 mol%), water (0.090 mL, 5.000 mmol, 5 equiv), and CPME (10 mL, 0.10 M). The reaction was warmed to 40 °C and allowed to stir for 2 h. After cooling, morpholine (0.130 mL, 1.492 mmol, 1.5 equiv) and *N,N*-diisopropylethylamine (0.350 mL, 3.000 mmol, 2 equiv) were added to the reaction mixture. The reaction vessel was then sealed, warmed to 40 °C, and was allowed to stir for 10 h. After cooling, the reaction mixture was taken up in EtOAc (20 mL) which was then washed with water (20 mL) and brine (20 mL), was dried by passing through a hydrophobic frit, and was concentrated under reduced pressure. Purification by MDAP afforded the *title compound* as a yellow solid (0.172 g, 56%). m.p. 290 °C (decomposition); LCMS (Method B, UV, ESI) $R_t = 0.81$ min, $[M+H]^+ = 309$, 100% purity; ¹H NMR (400 MHz, *d*₆-DMSO) δ 8.91 (dd, $J = 4.3, 1.8$ Hz, 1 H), 8.19 (dd, $J = 8.1, 2.0$ Hz, 1 H), 7.41–7.35 (m, 1 H), 7.26 (dd, $J = 8.2, 4.3$ Hz, 1 H), 7.14–7.09 (m, 2 H), 7.03–6.99 (m, 1 H), 3.92 (t, $J = 4.8$ Hz, 4 H), 3.72 (t, $J = 4.8$ Hz, 4 H), one exchangeable proton not observed; ¹³C NMR (101 MHz, *d*₆-DMSO) δ 170.5, 160.5, 159.7, 157.6, 157.3, 137.4, 136.5, 129.6, 120.3, 118.6, 117.3, 116.3, 111.3, 66.0, 44.1; ν_{\max} (solid)/cm⁻¹ 2978,

2958, 2918, 2871, 2671, 1572, 1548, 1466, 1272 (s), 1254, 1211, 1112, 782, 704; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for $C_{17}H_{17}N_4O_2$ 309.1346; found 309.1332.

3-(2-Morpholino-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl)phenol, **9**

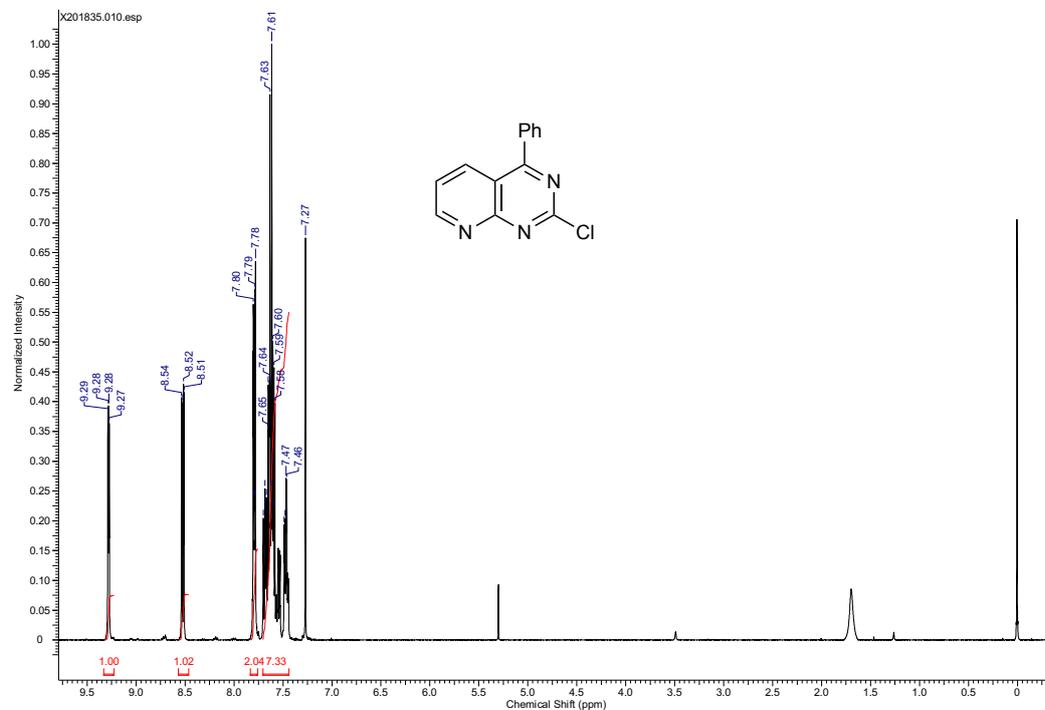


Chamber A of a COware apparatus was charged with 2,4-dichloropyrido[2,3-*d*]pyrimidine (0.050 g, 0.250 mmol, 1 equiv), tripotassium phosphate (0.106 g, 0.500 mmol, 2 equiv), (3-(benzyloxy)phenyl)boronic acid (0.060 g, 0.263 mmol, 1.05 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (0.007 g, 0.010 mmol, 4 mol%), water (0.023 mL, 1.250 mmol, 5 equiv), and CPME (2 mL, 0.125 M). The reaction was warmed to 40 °C and allowed to stir for 16 h. After cooling, morpholine (0.033 mL, 0.375 mmol, 1.5 equiv) and tripotassium phosphate (0.080 g, 0.375 mmol, 1.5 equiv) were added to chamber A. The reaction vessel was then sealed, warmed to 40 °C, and was allowed to stir for 8 h. After cooling, palladium on carbon (0.027 g, 0.025 mmol, 10 mol%) was added to chamber A and zinc (0.206 g, 3.150 mmol, 12.6 equiv) and hydrochloric acid (2.00 mL, 14.80 mmol, 59.2 equiv, as a 7.4 M aqueous solution) were added to chamber B. The reaction vessel was then sealed and the reaction mixture was allowed to stir for a further 64 h. The reaction mixture was then filtered through Celite[®], washing with MeOH (15 mL). The filtrate was then concentrated under reduced pressure. Purification by MDAP afforded the *title compound* as a colorless solid (0.033 g, 42%). m.p. 244–246 °C; LCMS (Method B, UV, ESI) R_t = 0.90 min, $[M+H]^+$ = 313, 100% purity; ¹H NMR (400 MHz, *d*₆-DMSO) δ 8.25 (s, 1 H), 7.19 (t, J = 8.1, 1 H), 6.97 (br. s, 1 H), 6.93–6.89 (m, 2 H), 6.76 (ddd, J = 8.1, 2.3, 1.1 Hz, 1 H), 3.63–3.54 (m, 8 H), 3.26–3.21 (m, 2 H), 2.52 (t, J = 6.1 Hz, 2 H), 1.70–1.63 (m, 2 H); ¹³C NMR (101 MHz, *d*₆-DMSO) δ 160.8, 160.7, 159.6, 156.9, 140.6, 128.6, 119.2, 115.5, 115.0, 99.4, 66.1, 44.1, 40.2, 23.9, 21.4; ν_{\max} (solid)/cm⁻¹ 3073, 2949, 2852, 1574, 1557, 1435, 1352, 1248, 1204, 1112, 993, 890, 785; HRMS (ESI-Orbitrap) m/z : $[M+H]^+$ calcd for $C_{17}H_{21}N_4O_2$ 313.1659; found 313.1647.

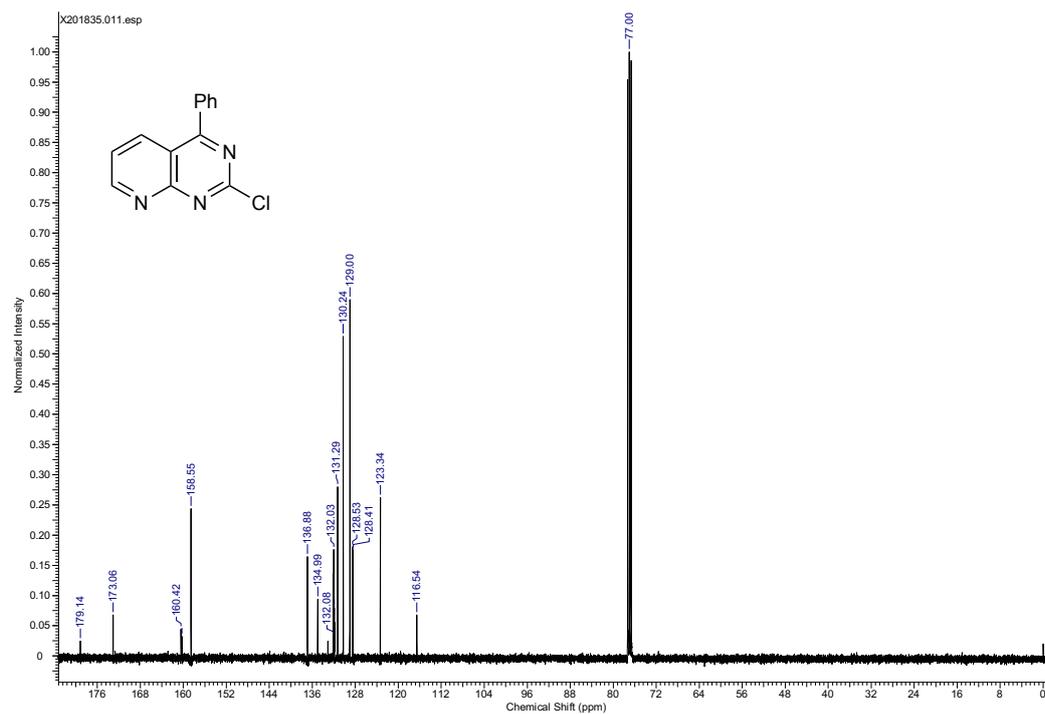
6 ^1H , ^{13}C , and HRMS Spectra

2-Chloro-4-phenylpyrido[2,3-*d*]pyrimidine, **2a**

^1H NMR

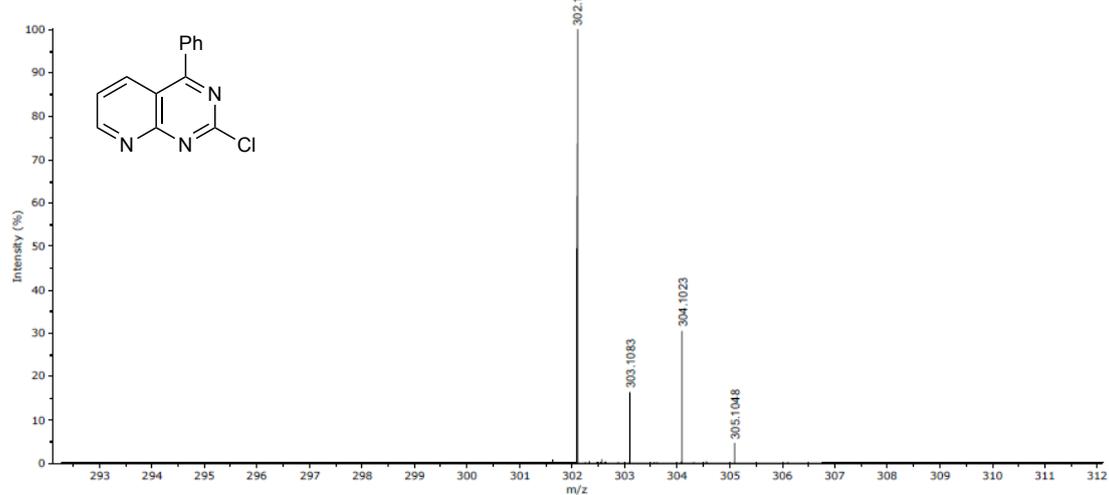


^{13}C NMR



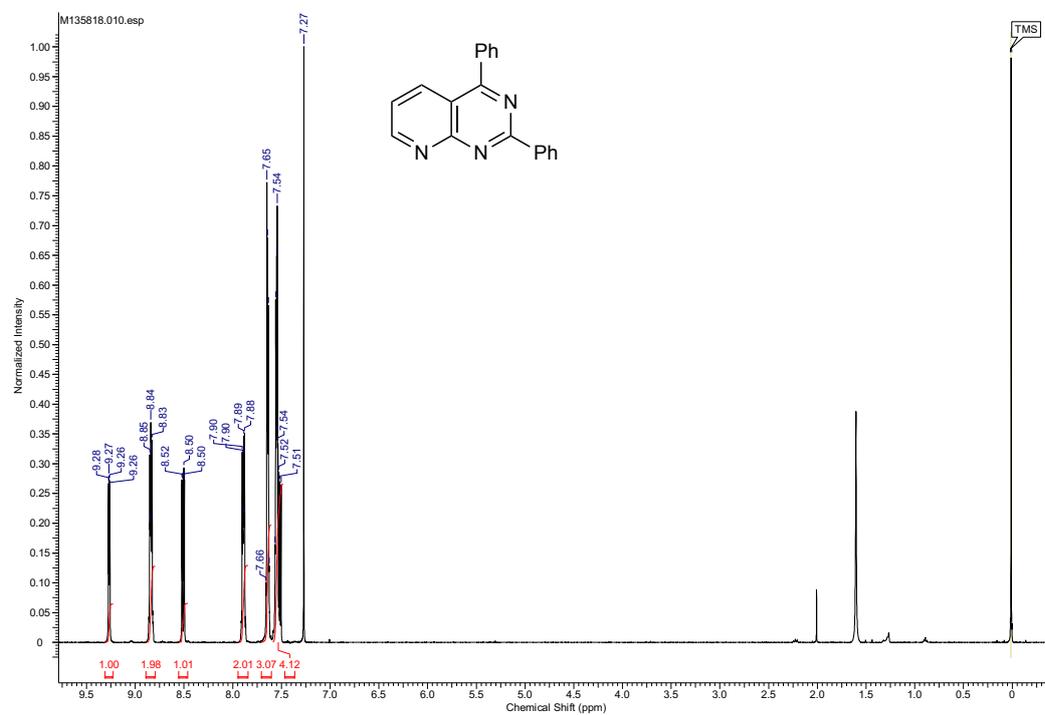
HRMS

Target Mass Spectrum RT 3.20 Peak [1] – Expanded View

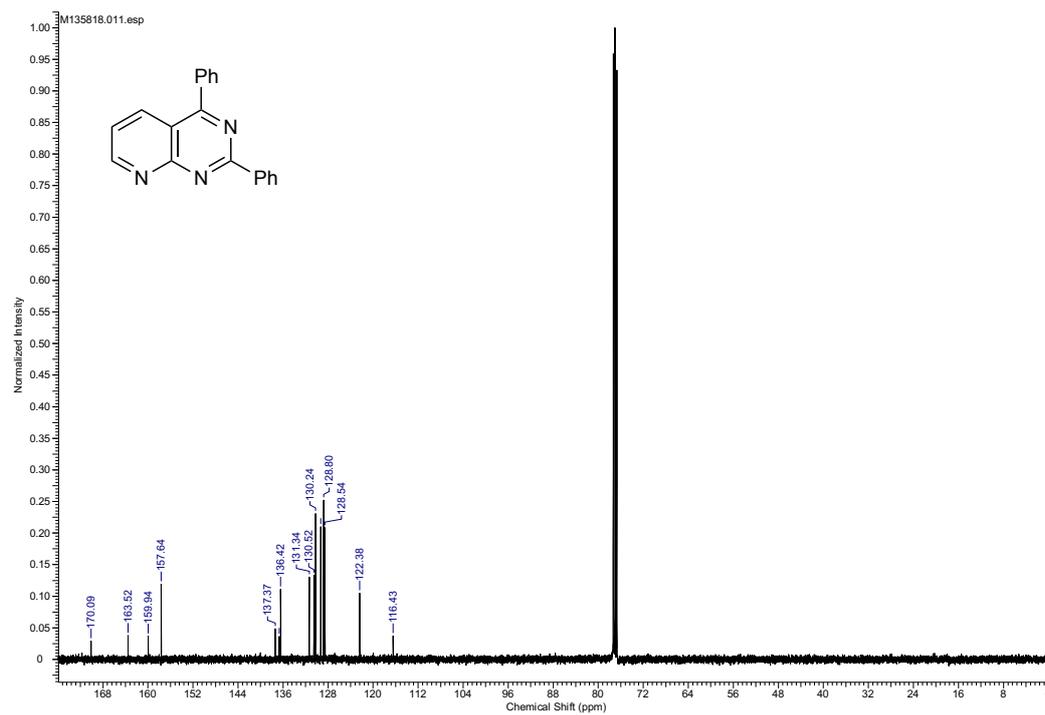


2,4-Diphenylpyrido[2,3-*d*]pyrimidine, **3a**

¹H NMR

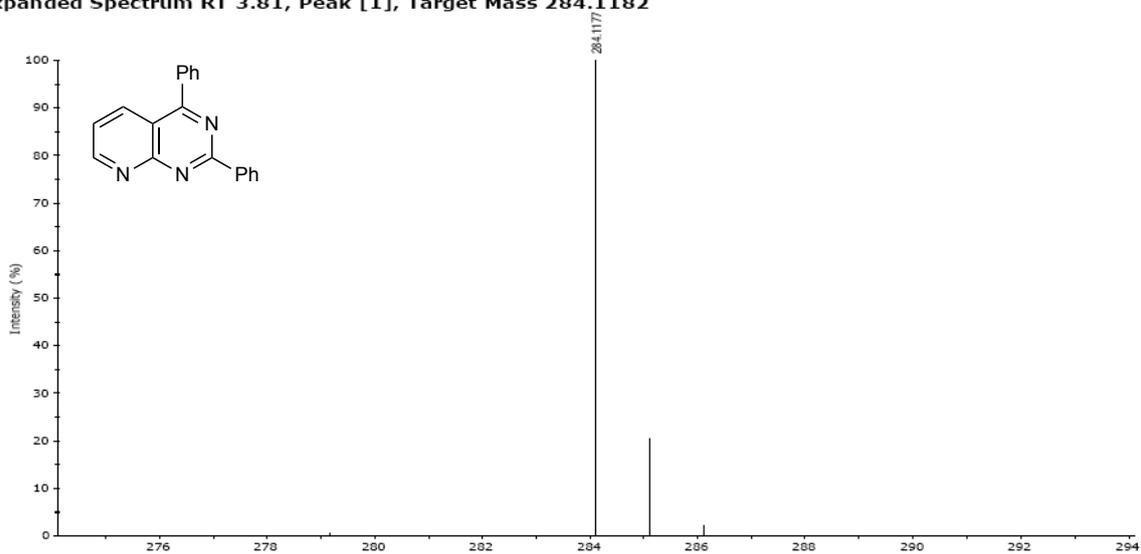


¹³C NMR



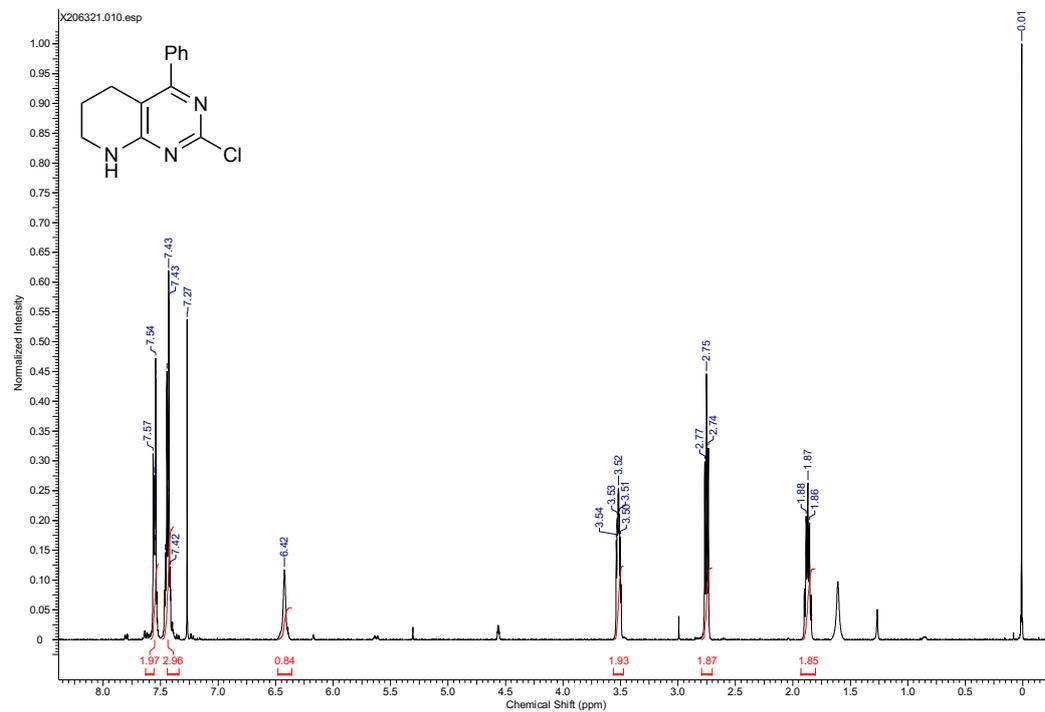
HRMS

Expanded Spectrum RT 3.81, Peak [1], Target Mass 284.1182

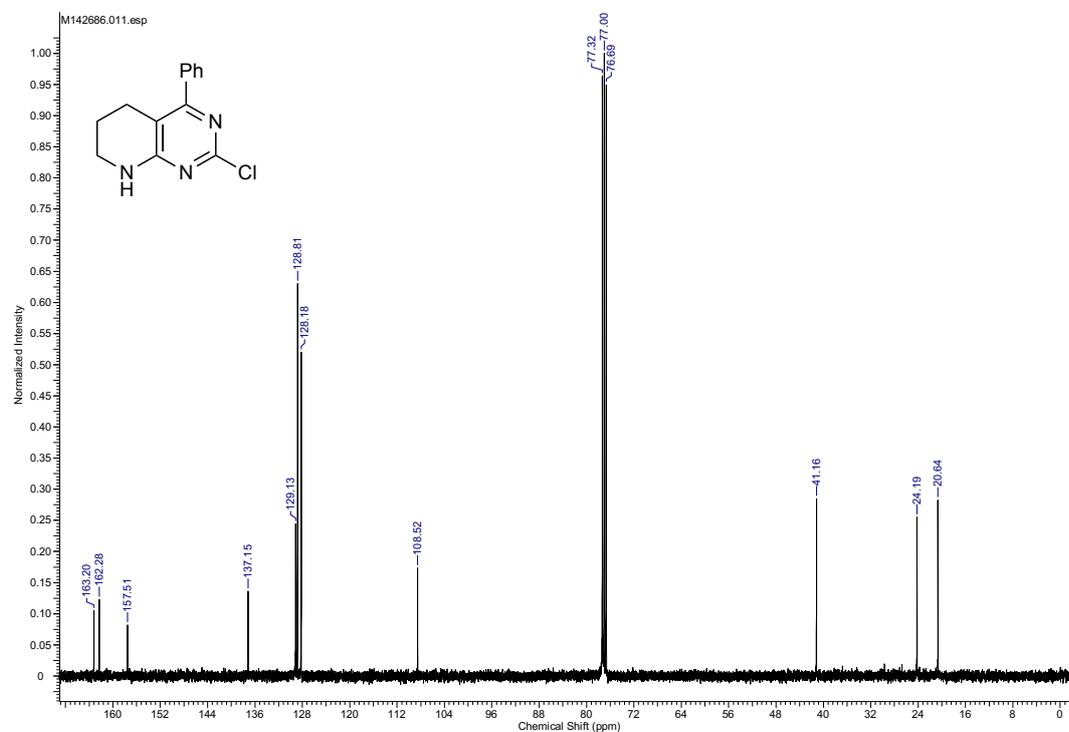


2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4a**

¹H NMR

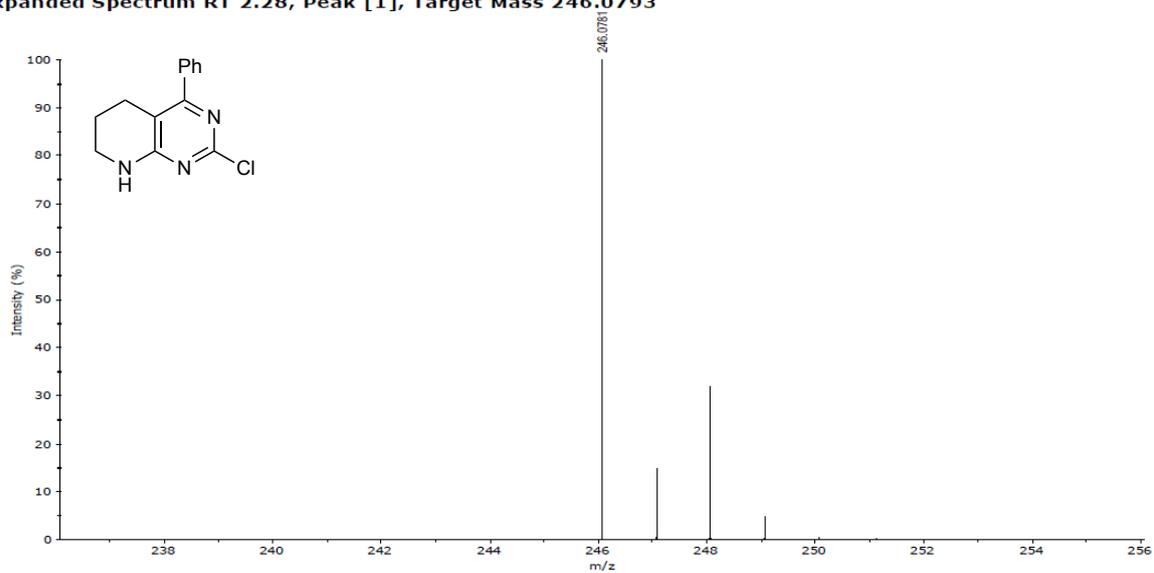


¹³C NMR



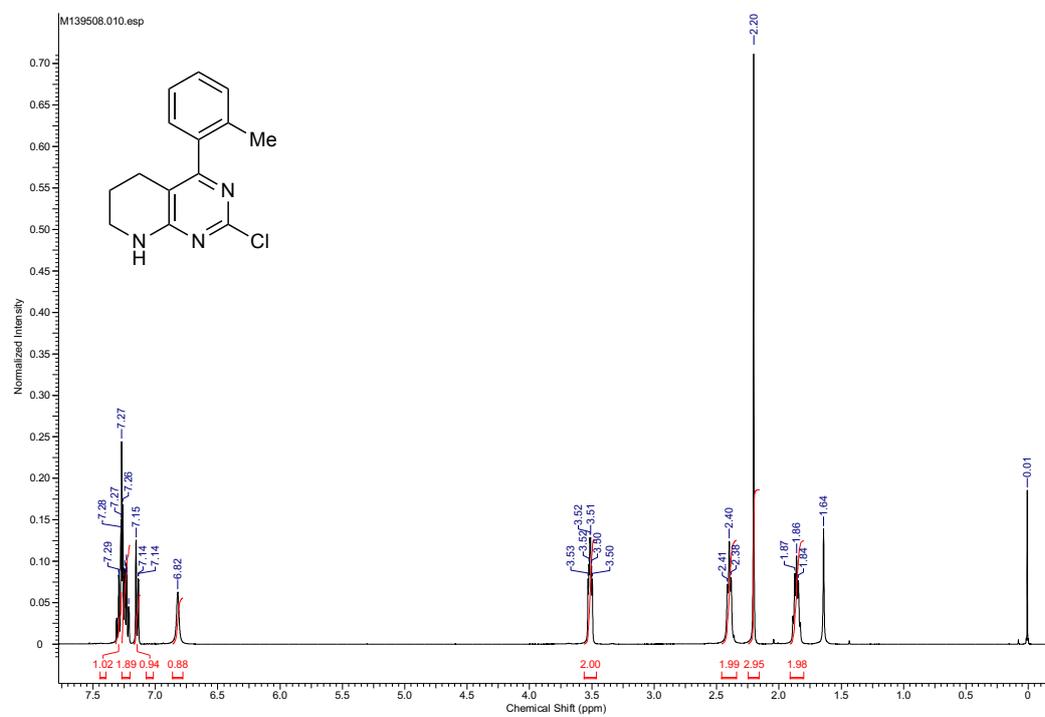
HRMS

Expanded Spectrum RT 2.28, Peak [1], Target Mass 246.0763

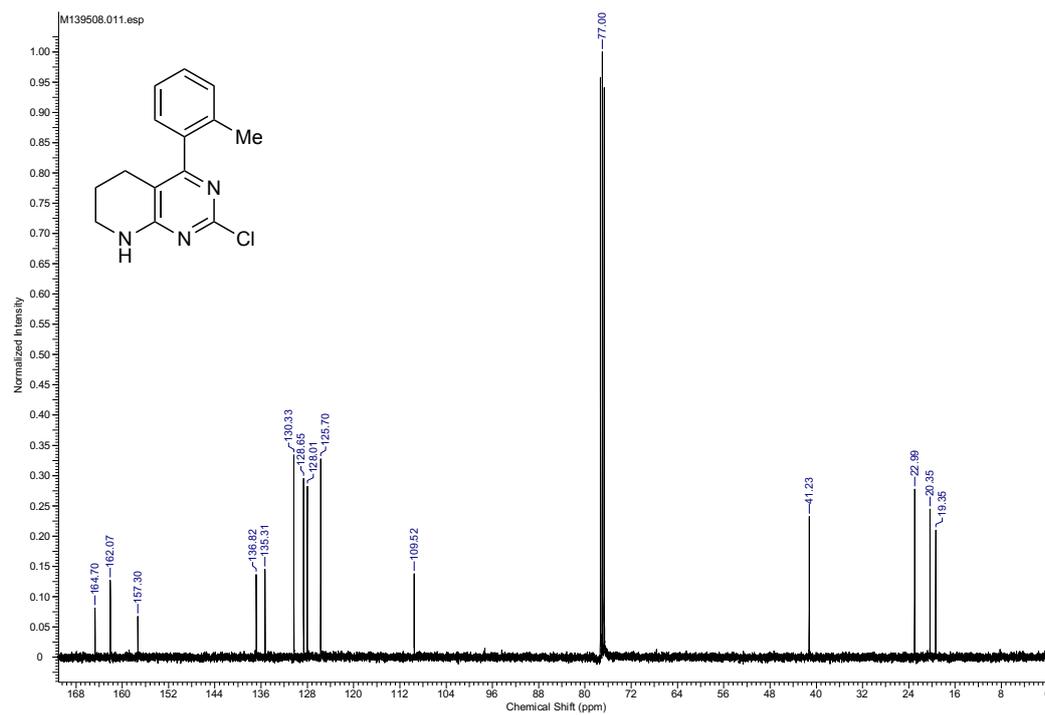


2-Chloro-4-(*o*-tolyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4b**

¹H NMR

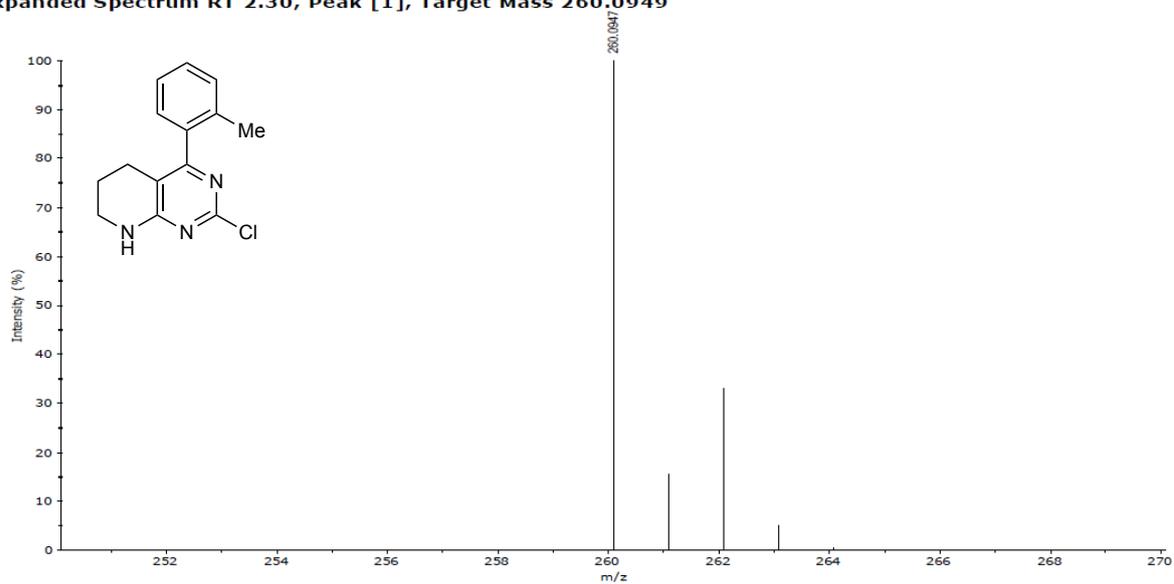


¹³C NMR



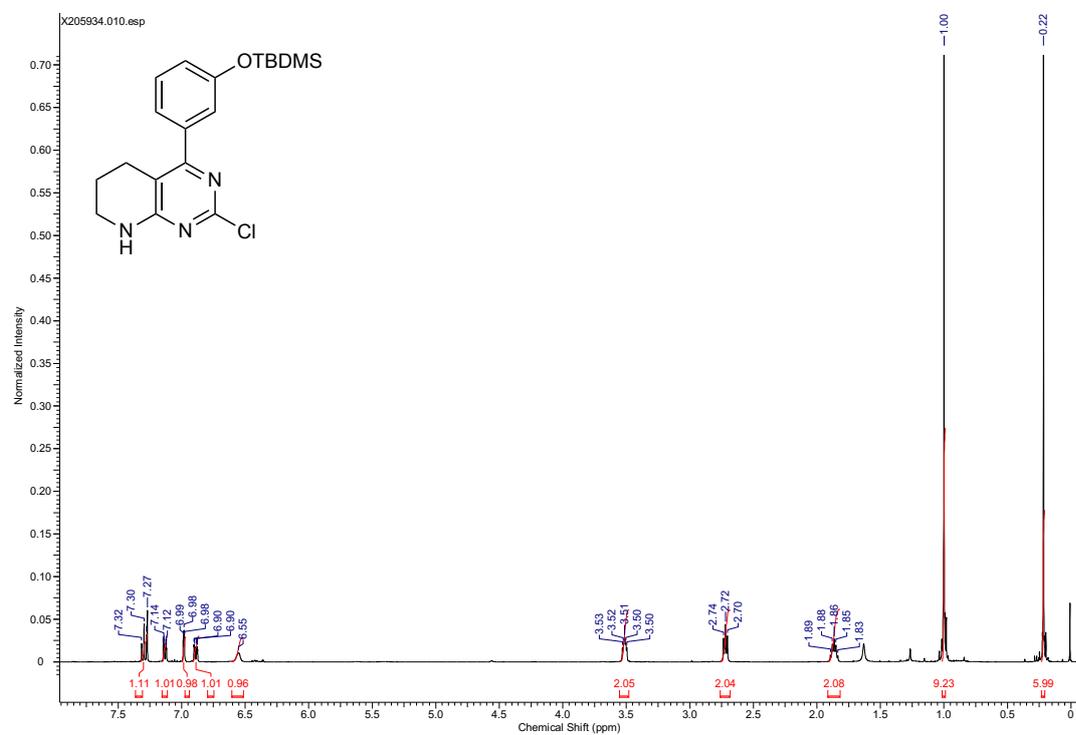
HRMS

Expanded Spectrum RT 2.30, Peak [1], Target Mass 260.0949

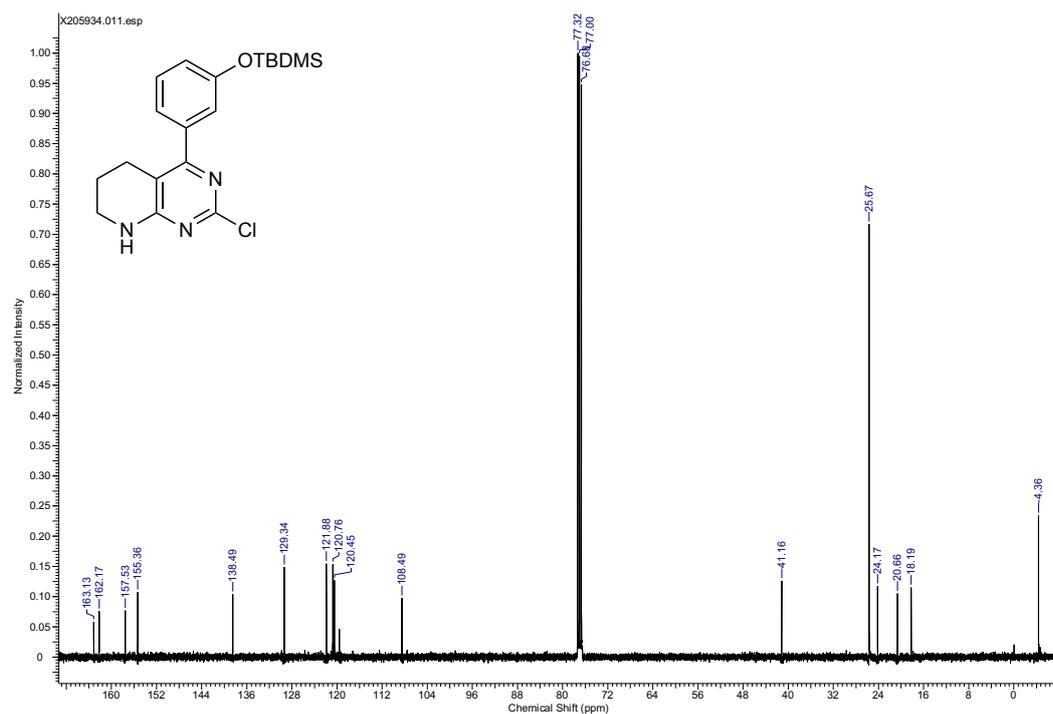


4-(3-((*tert*-Butyldimethylsilyl)oxy)phenyl)-2-chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4c**

¹H NMR

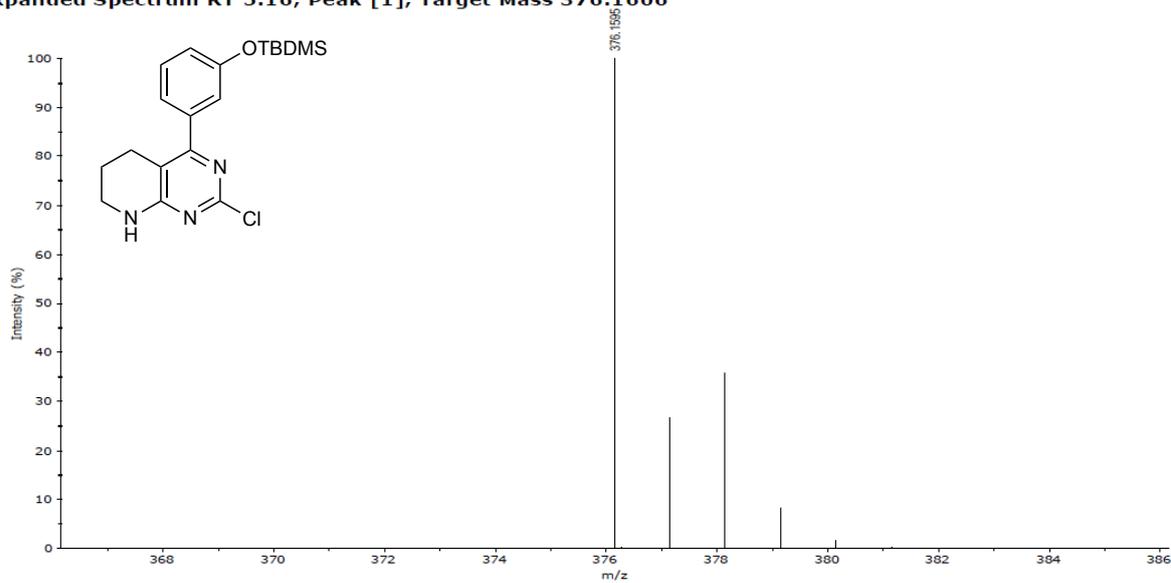


¹³C NMR



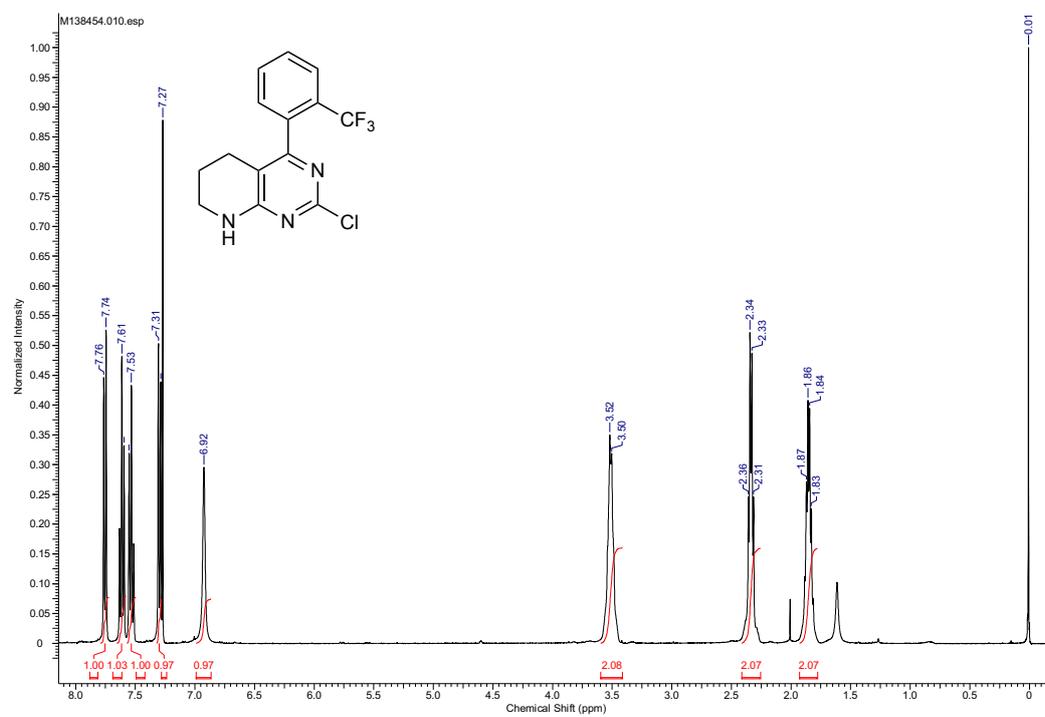
HRMS

Expanded Spectrum RT 5.16, Peak [1], Target Mass 376.1606

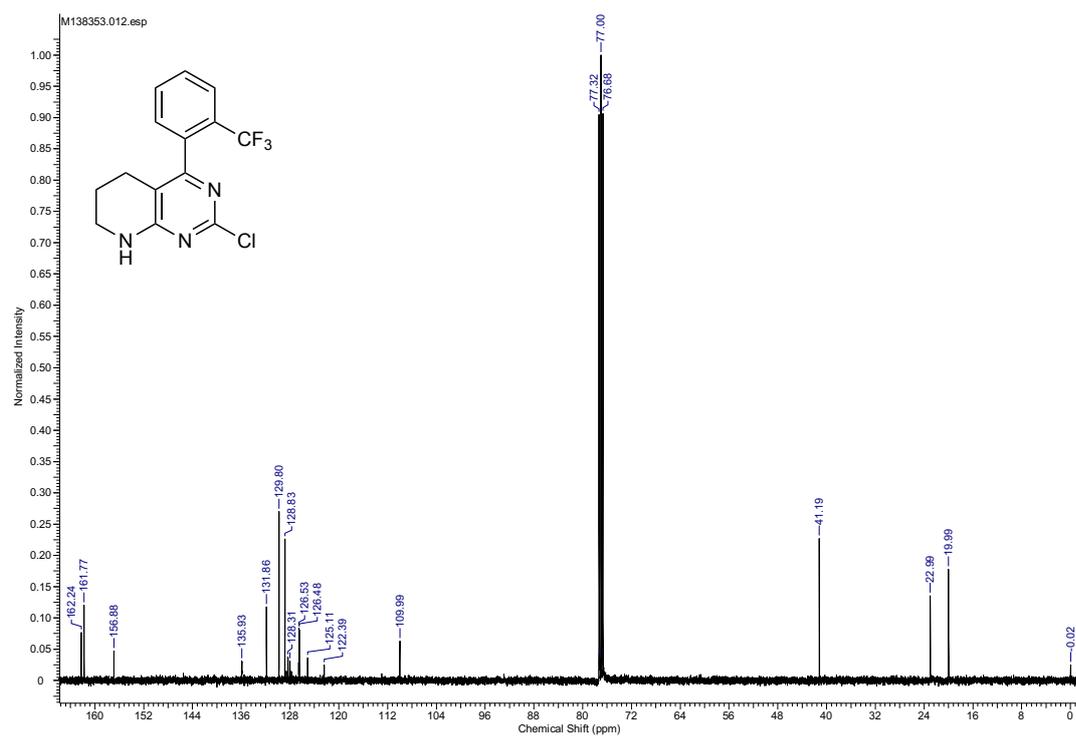


2-Chloro-4-(2-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4d**

¹H NMR

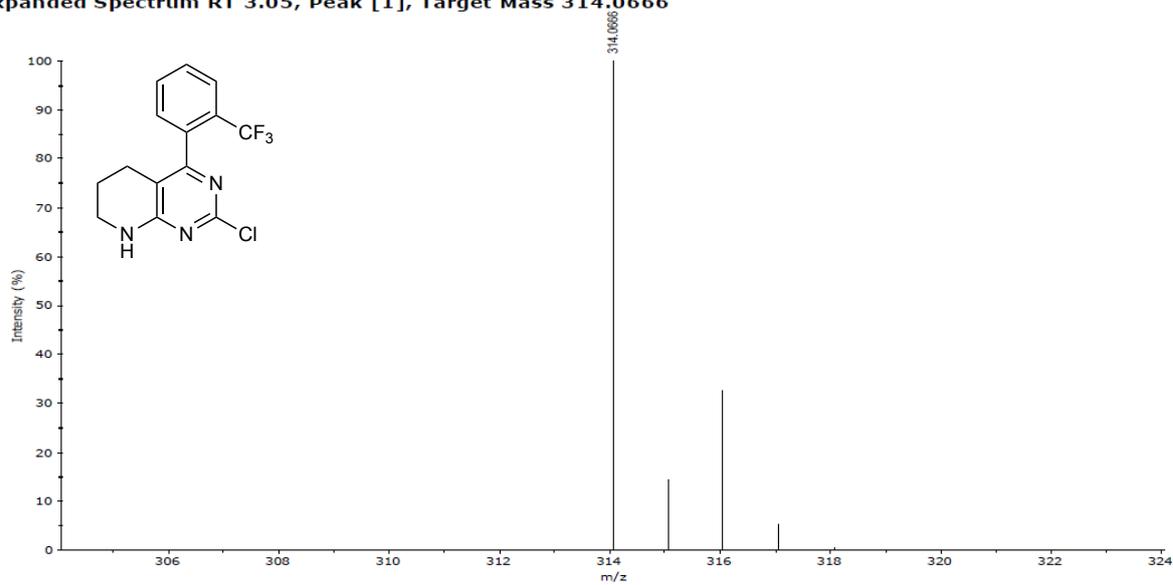


¹³C NMR



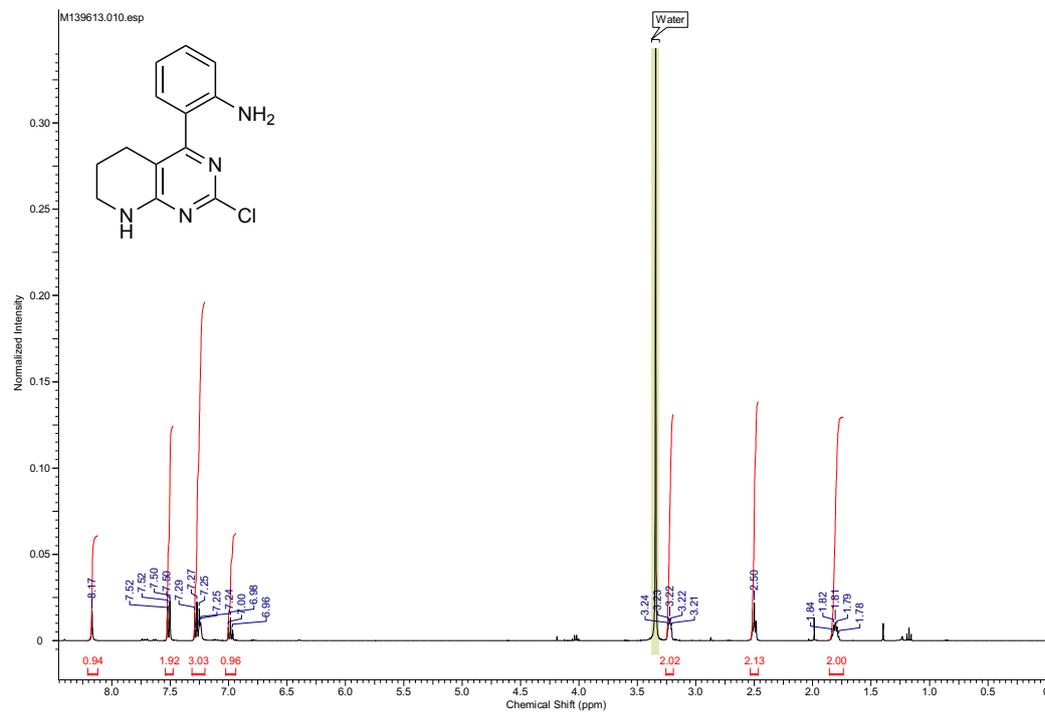
HRMS

Expanded Spectrum RT 3.05, Peak [1], Target Mass 314.0666

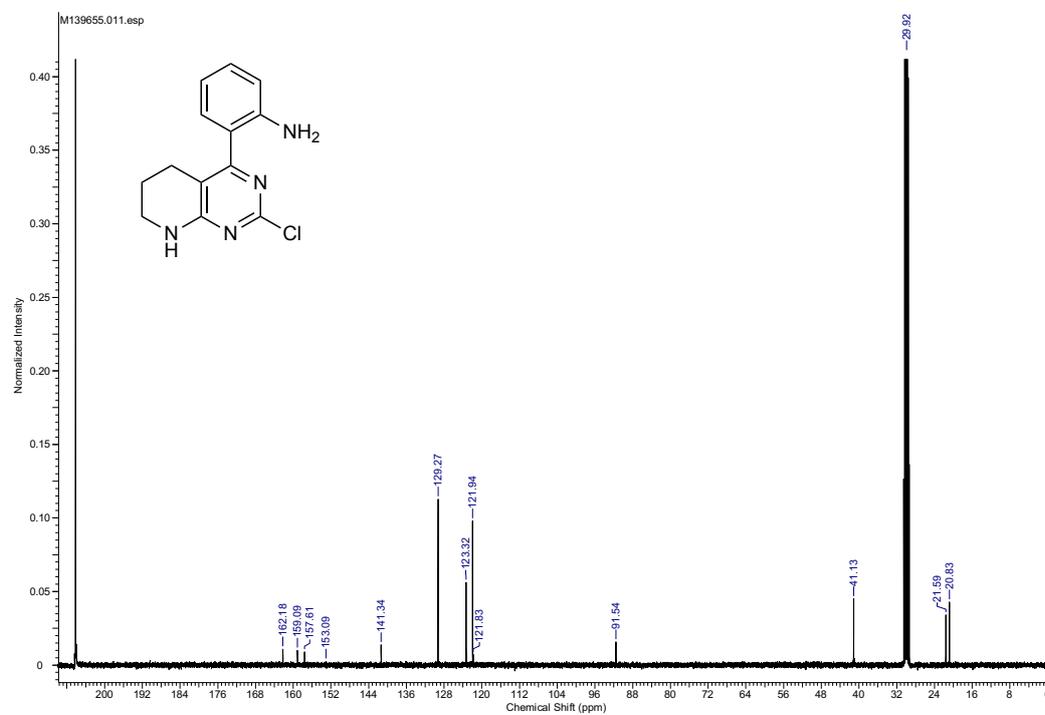


2-(2-Chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl)aniline, **4e**

¹H NMR

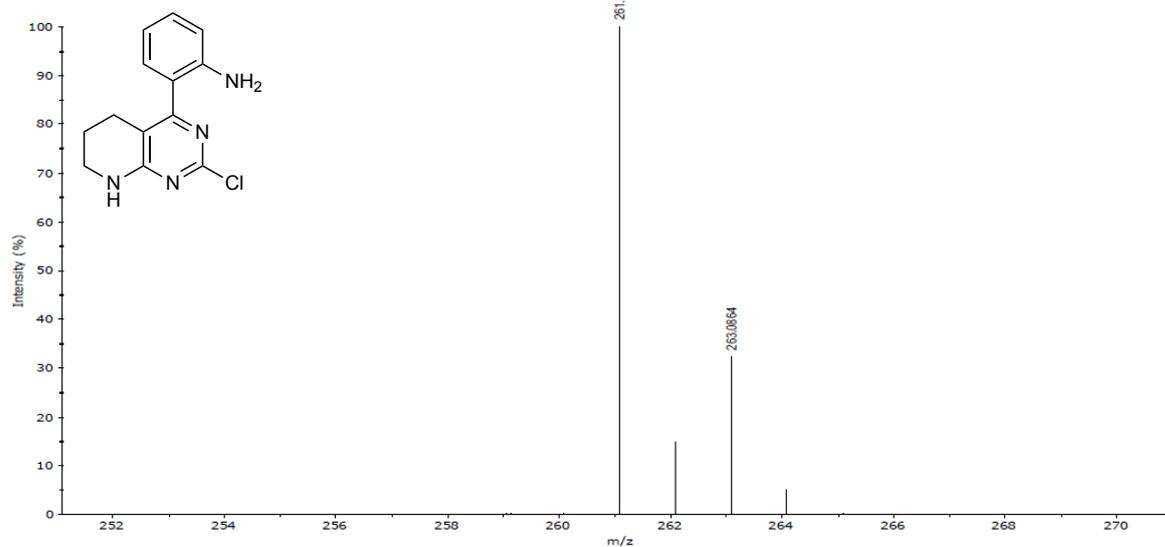


¹³C NMR



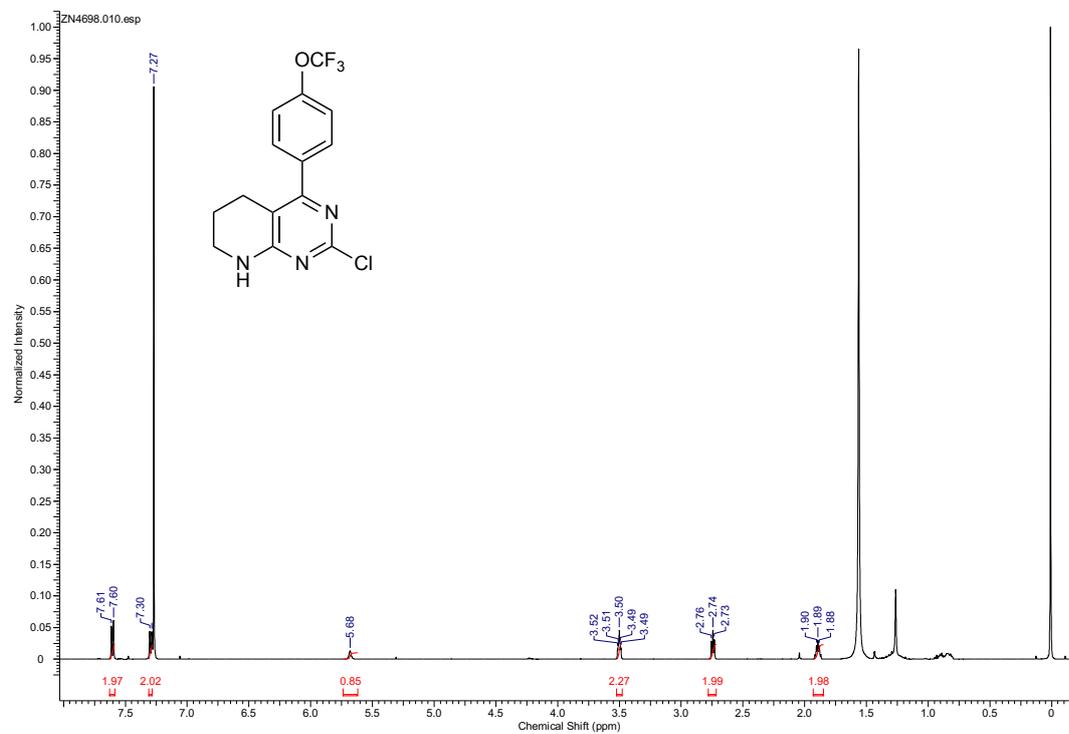
HRMS

Expanded Spectrum RT 2.69, Peak [1], Target Mass 261.0902

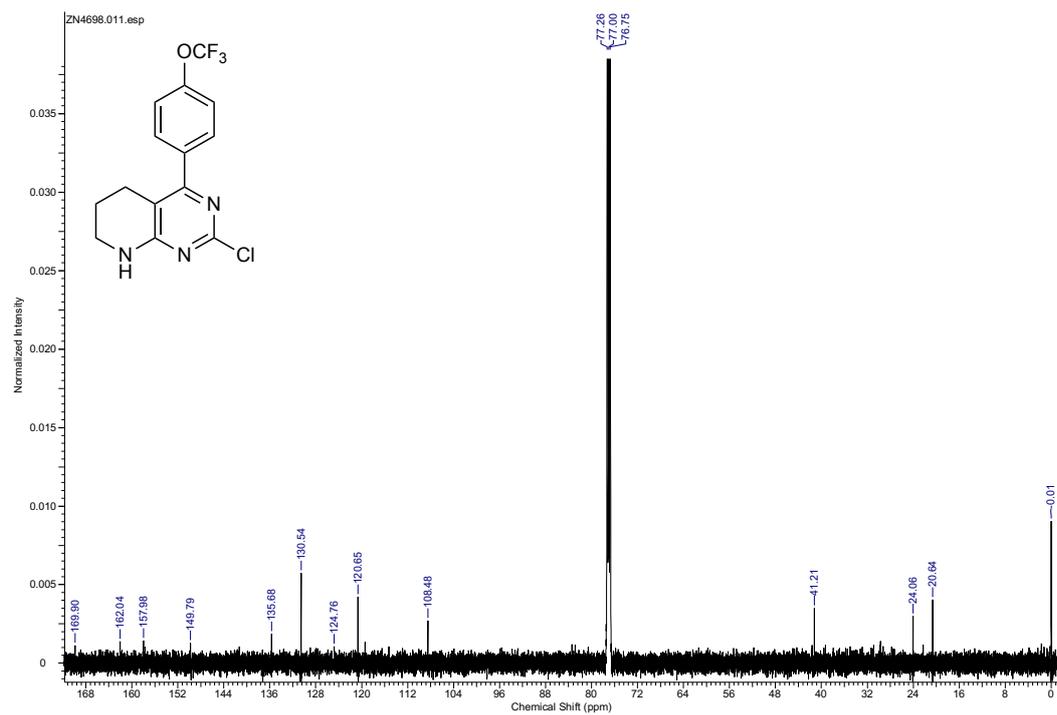


2-Chloro-4-(4-(trifluoromethoxy)phenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4f**

¹H NMR

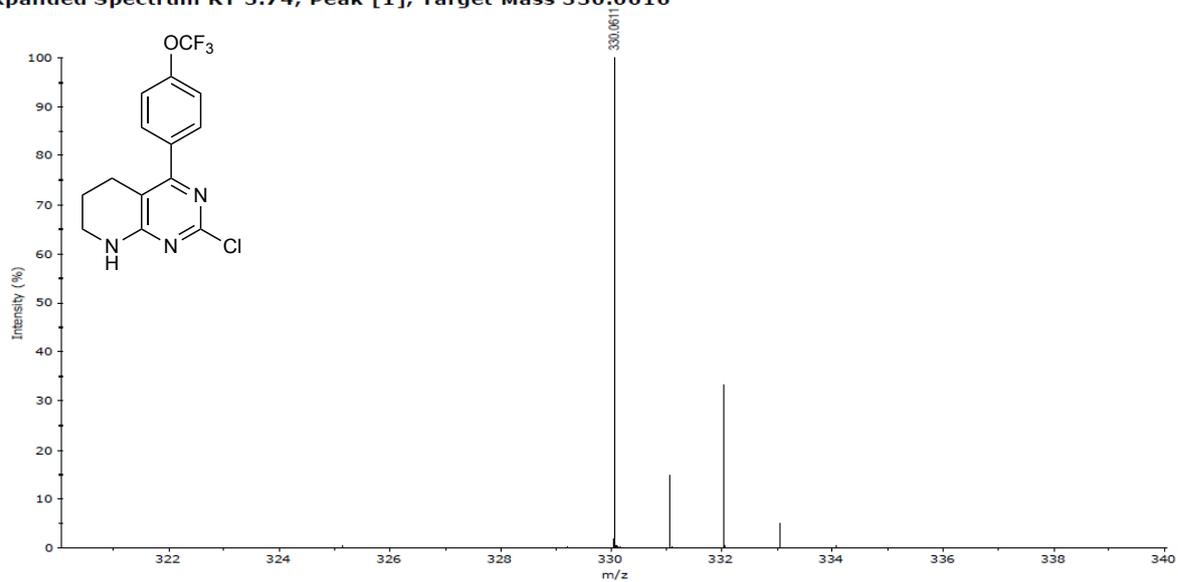


¹³C NMR



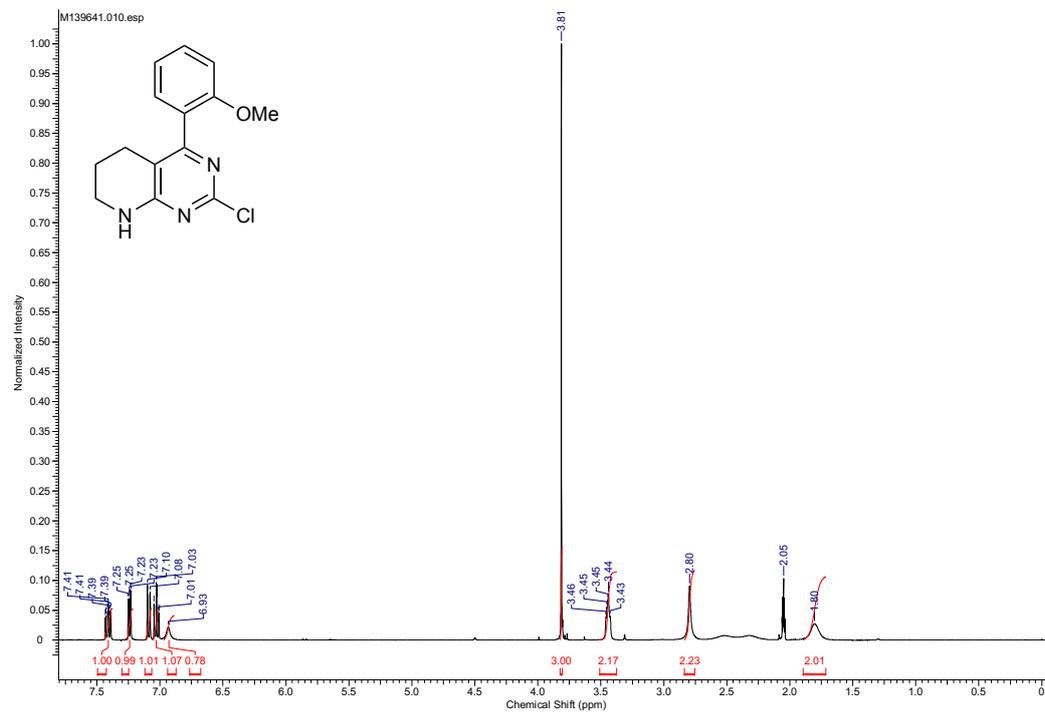
HRMS

Expanded Spectrum RT 3.74, Peak [1], Target Mass 330.0616

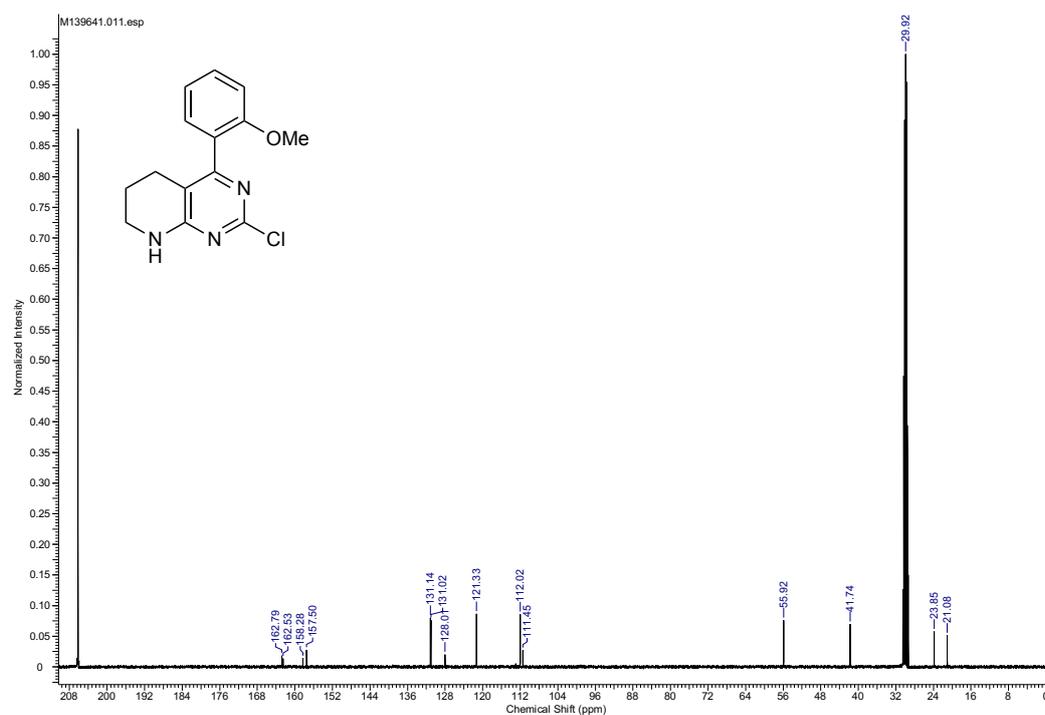


2-Chloro-4-(2-methoxyphenyl)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine, **4g**

¹H NMR

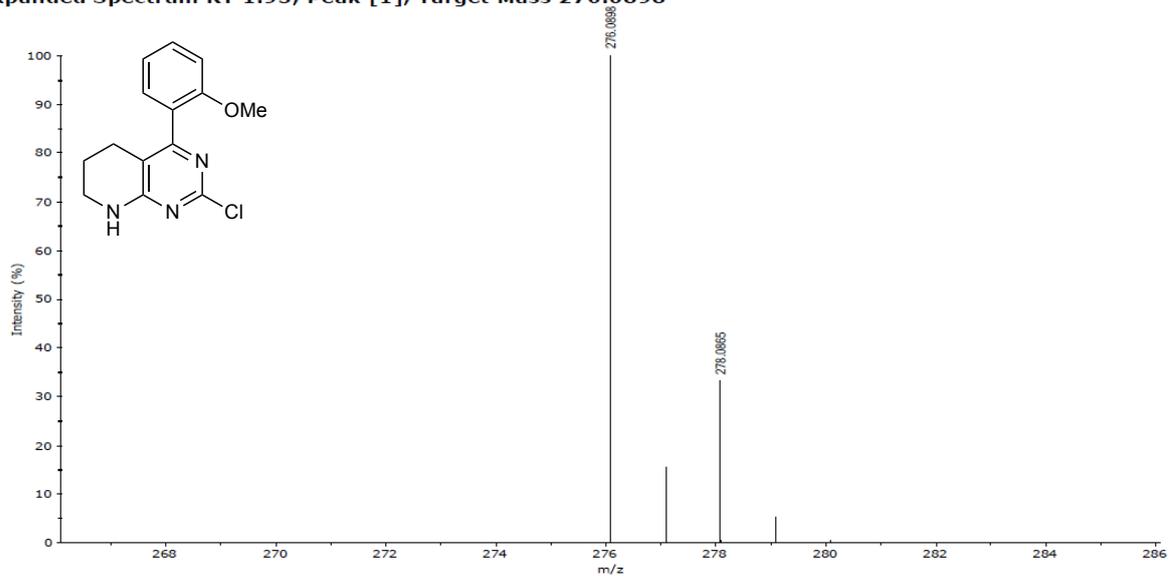


¹³C NMR



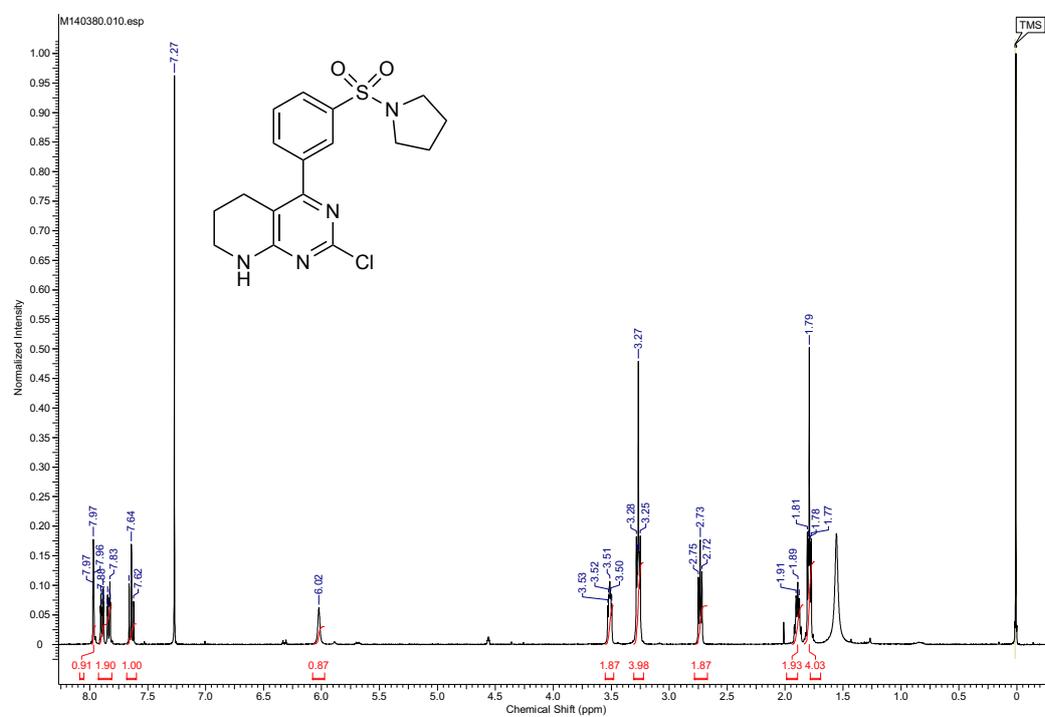
HRMS

Expanded Spectrum RT 1.93, Peak [1], Target Mass 276.0898

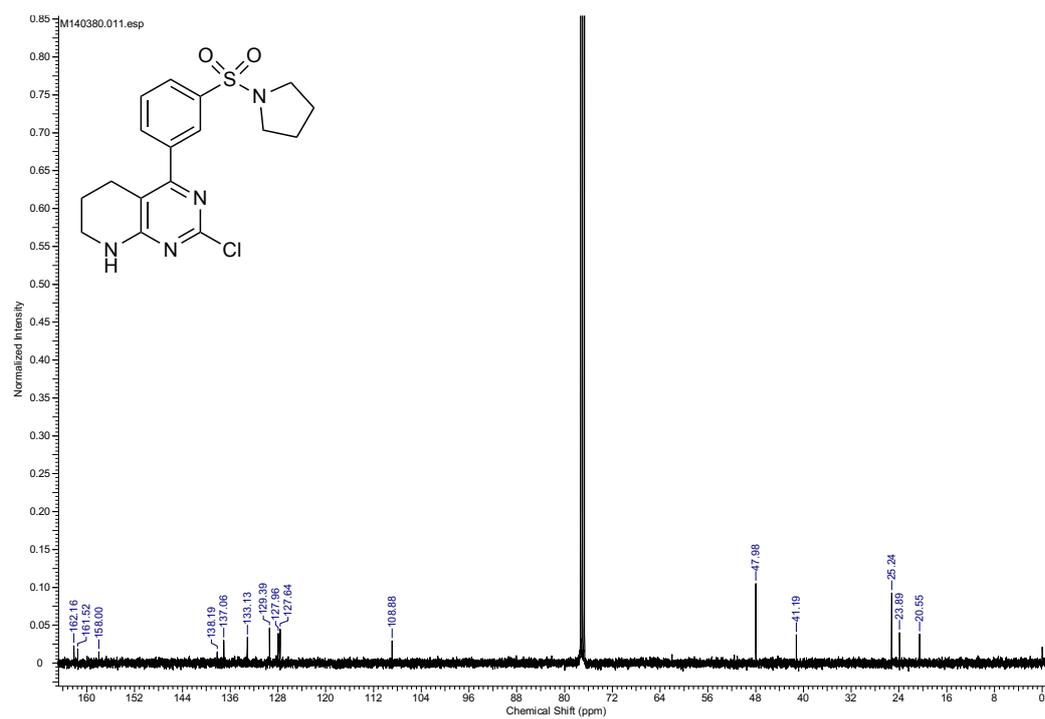


2-Chloro-4-(3-(pyrrolidin-1-ylsulfonyl)phenyl)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine, **4h**

¹H NMR

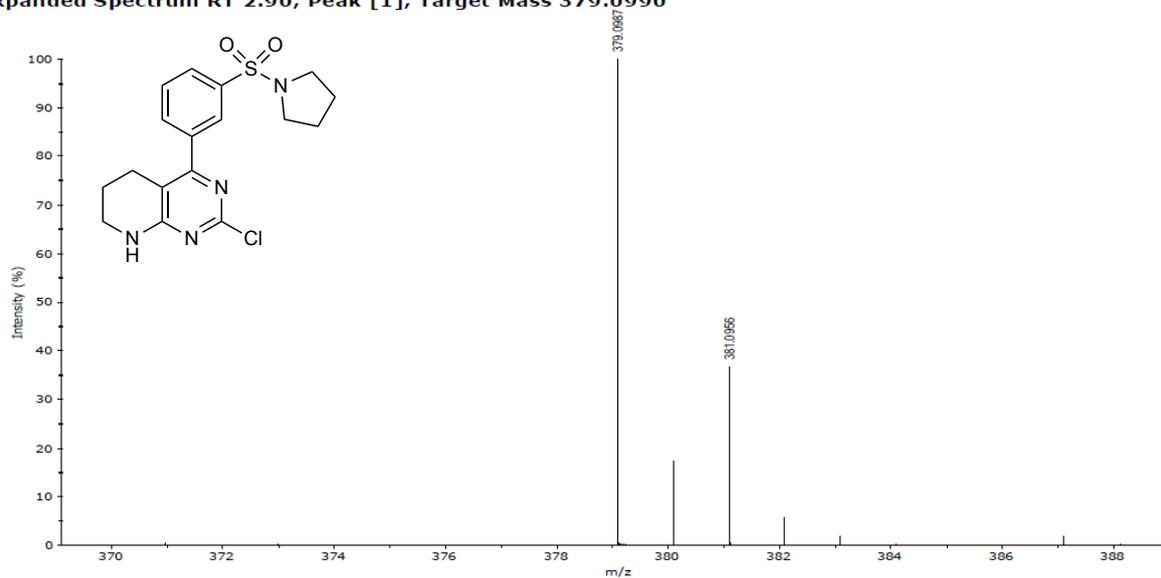


¹³C NMR



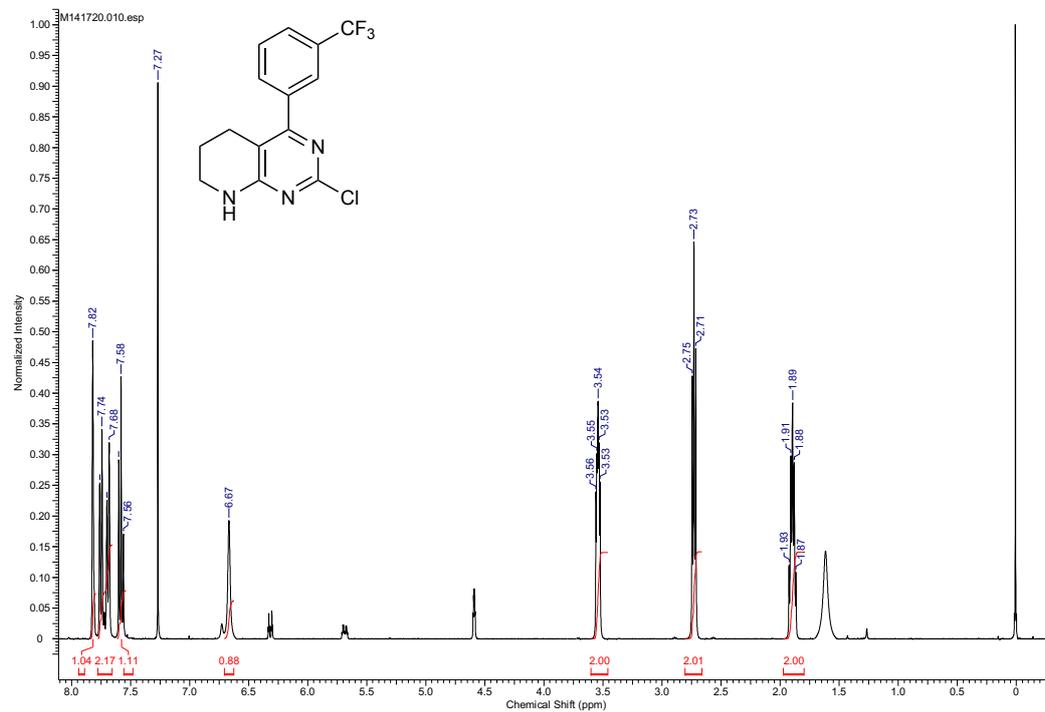
HRMS

Expanded Spectrum RT 2.90, Peak [1], Target Mass 379.0990

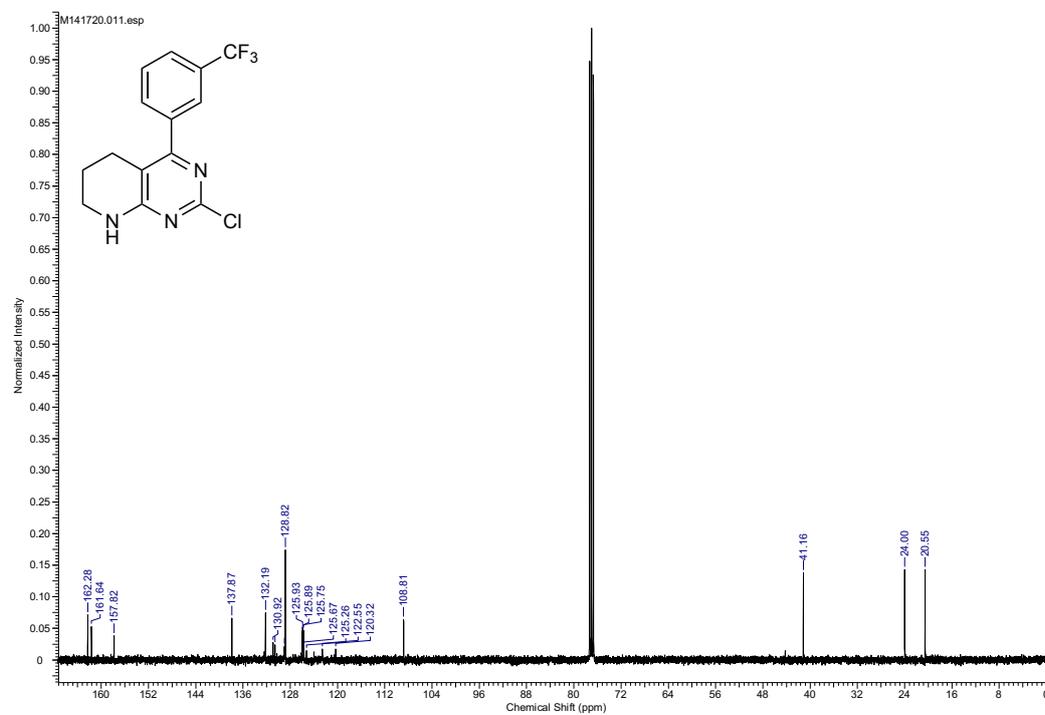


2-Chloro-4-(3-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine, **41**

¹H NMR

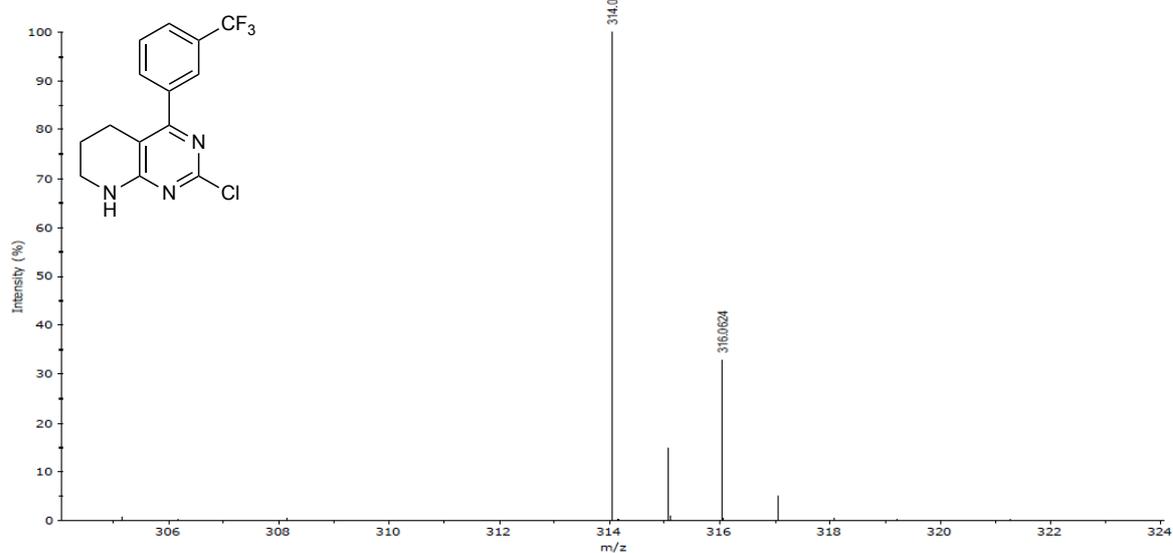


¹³C NMR



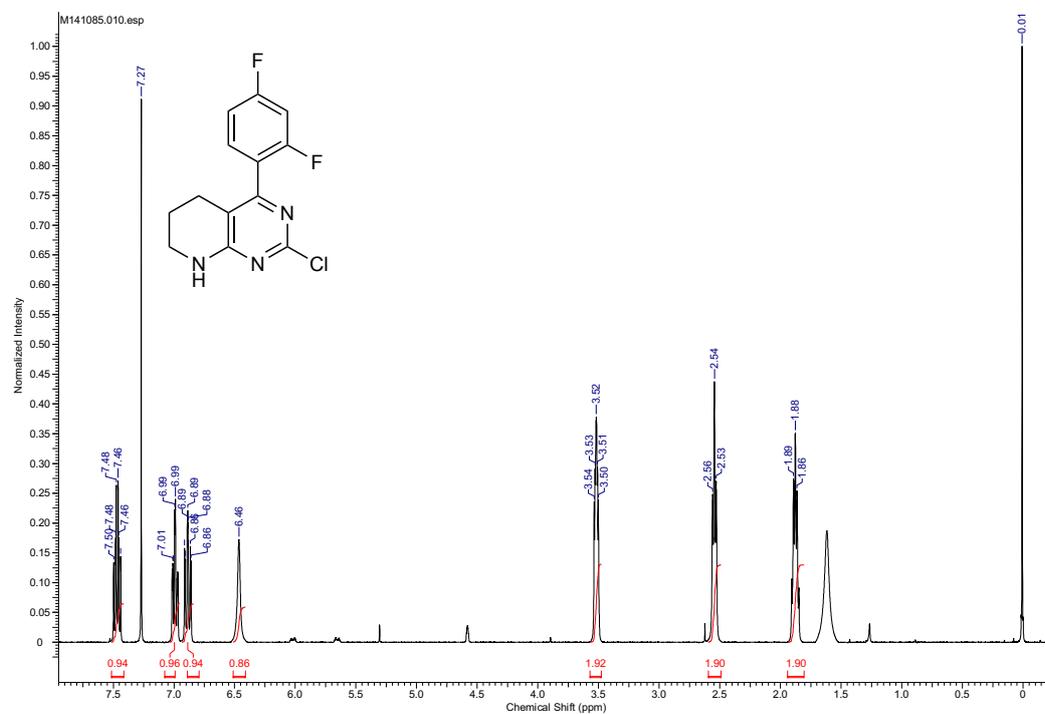
HRMS

Expanded Spectrum RT 3.60, Peak [1], Target Mass 314.0666

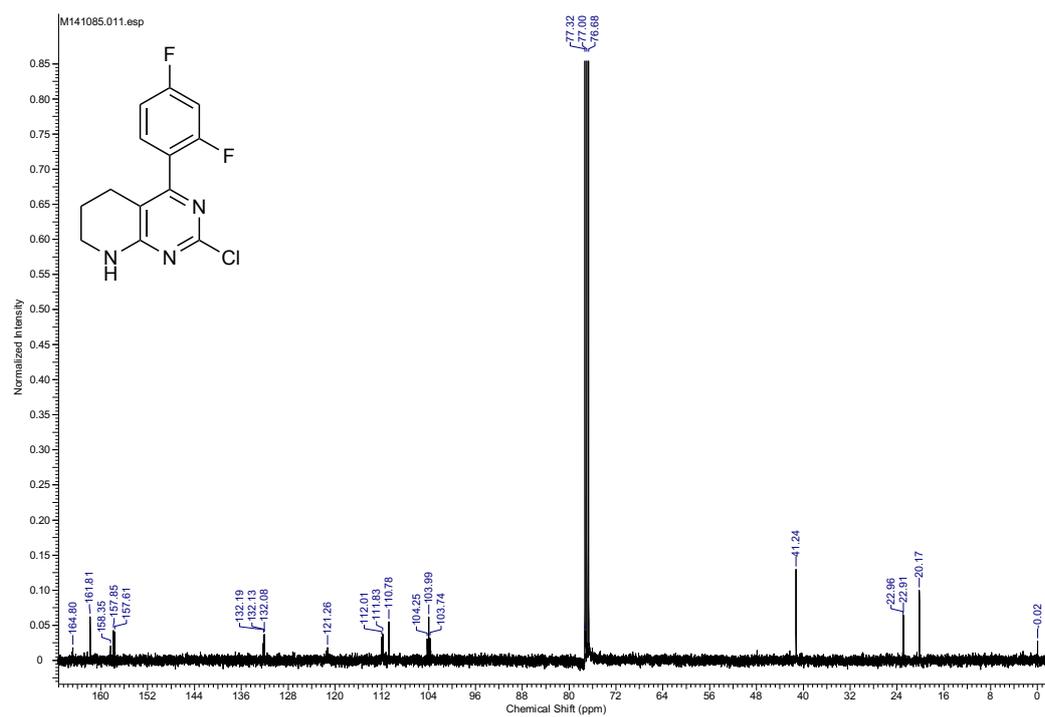


2-Chloro-4-(2,4-difluorophenyl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4j**

¹H NMR

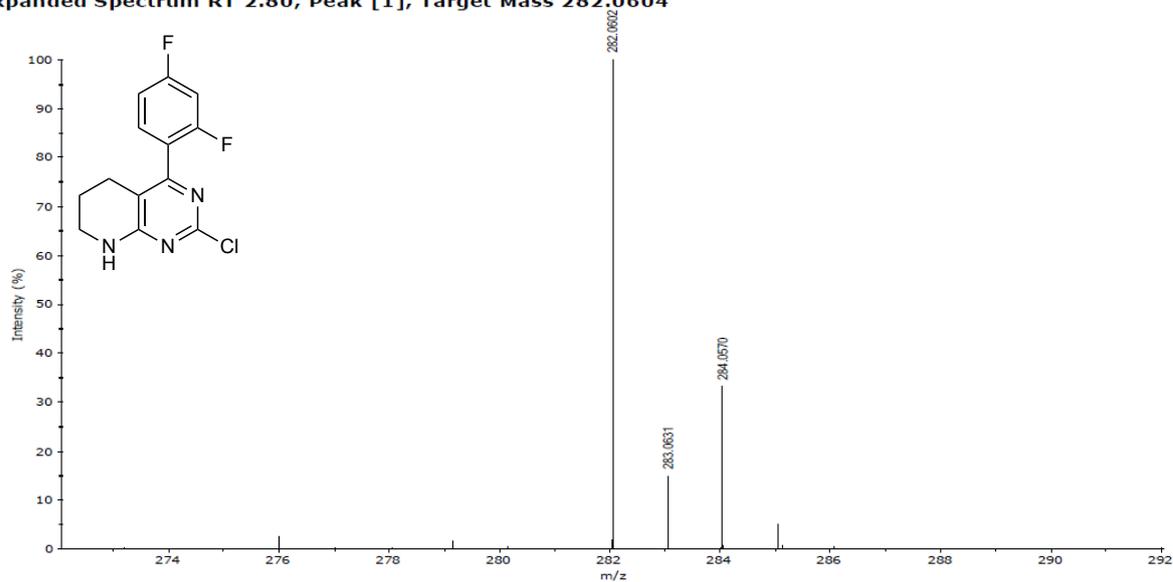


¹³C NMR



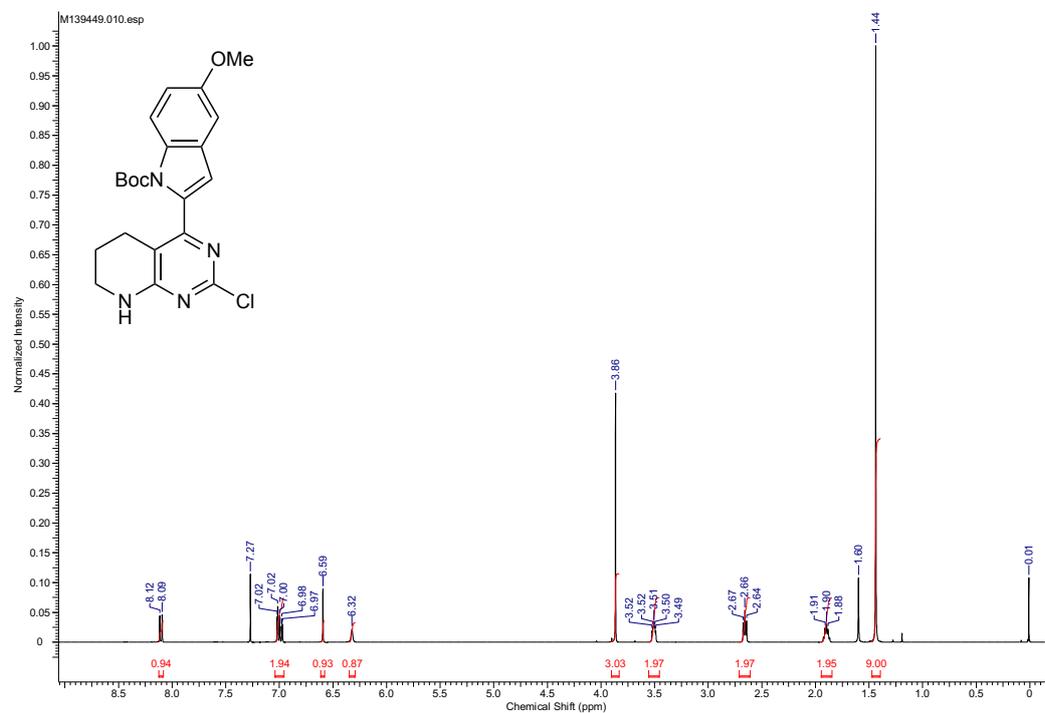
HRMS

Expanded Spectrum RT 2.80, Peak [1], Target Mass 282.0604

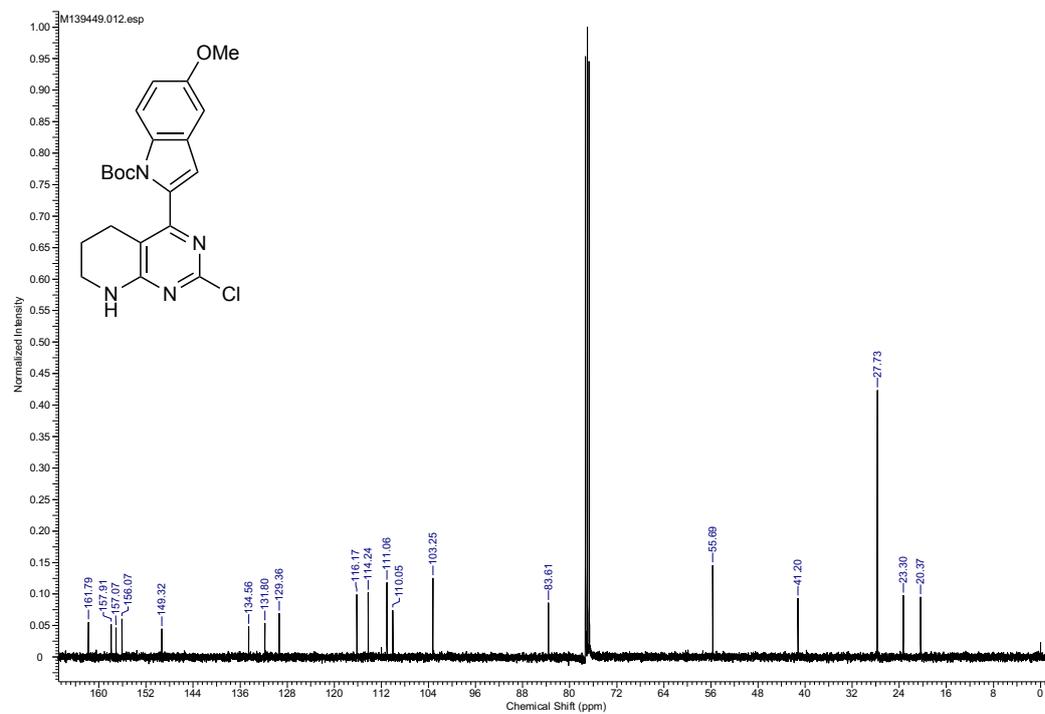


tert-Butyl 2-(2-chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl)-5-methoxy-1*H*-indole-1-carboxylate, **4k**

¹H NMR

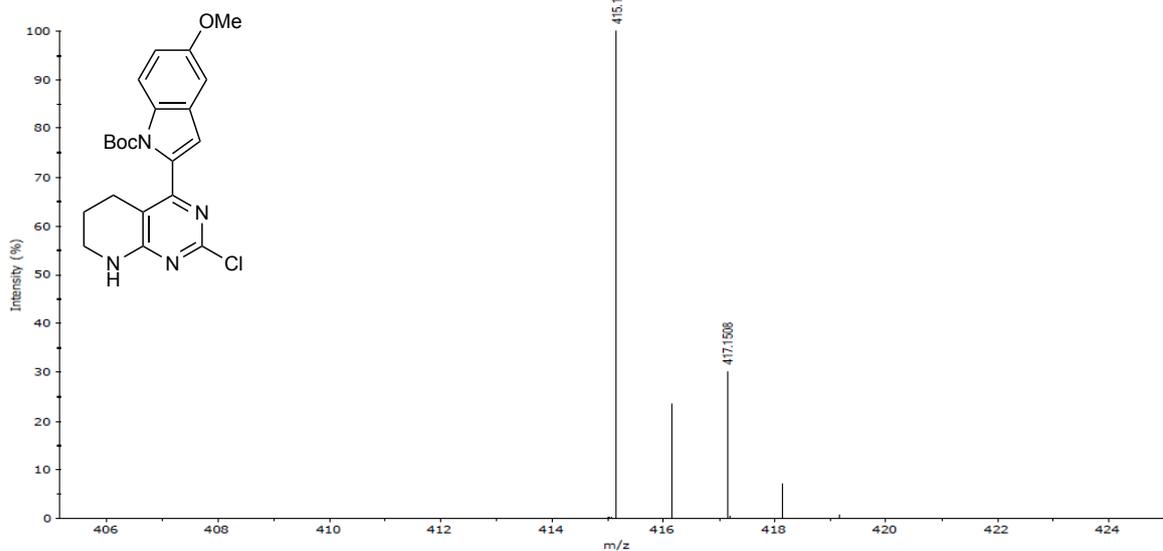


¹³C NMR



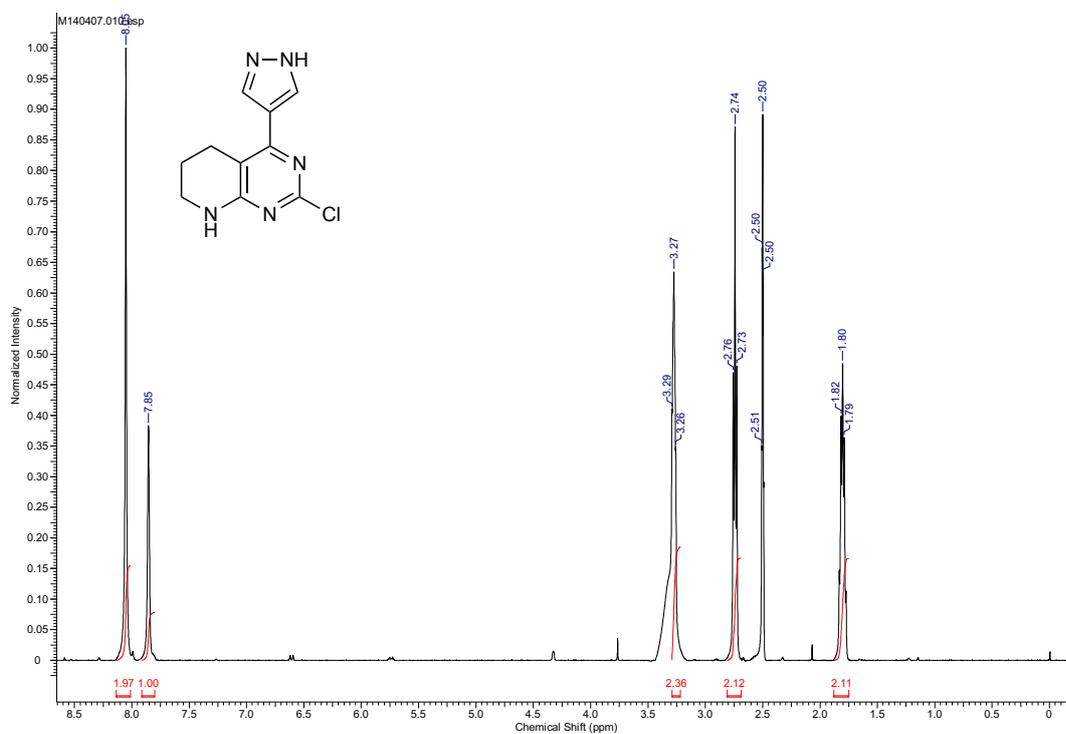
HRMS

Expanded Spectrum RT 4.11, Peak [1], Target Mass 415.1531

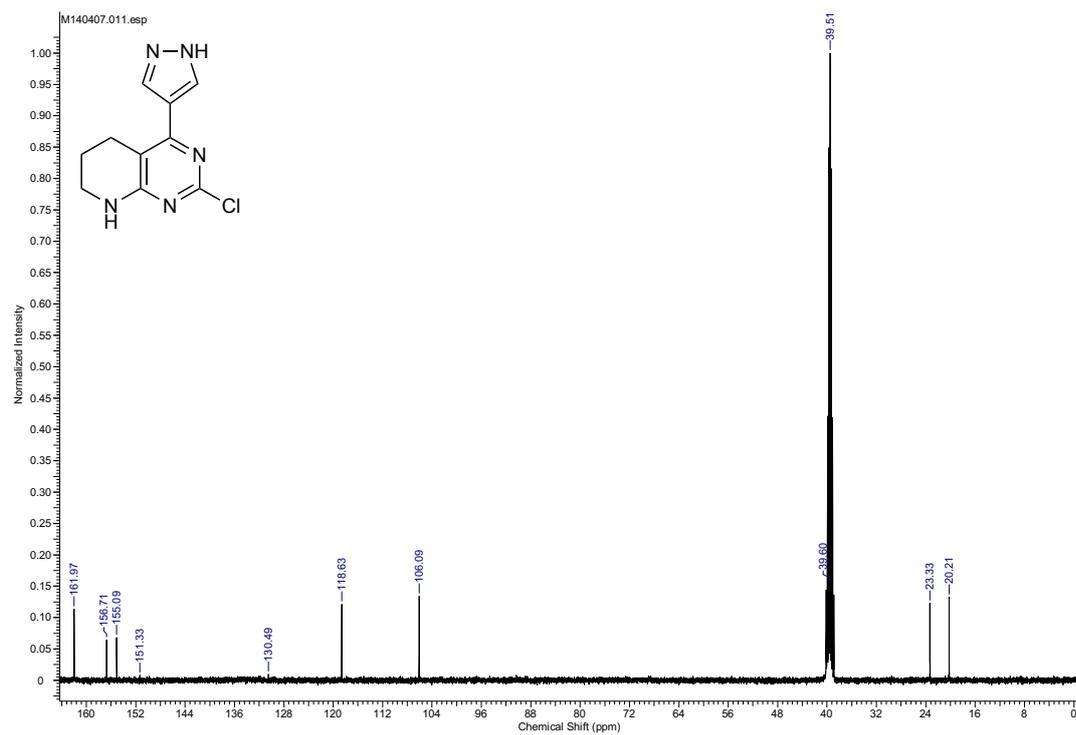


2-Chloro-4-(1*H*-pyrazol-4-yl)-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine, **4I**

¹H NMR

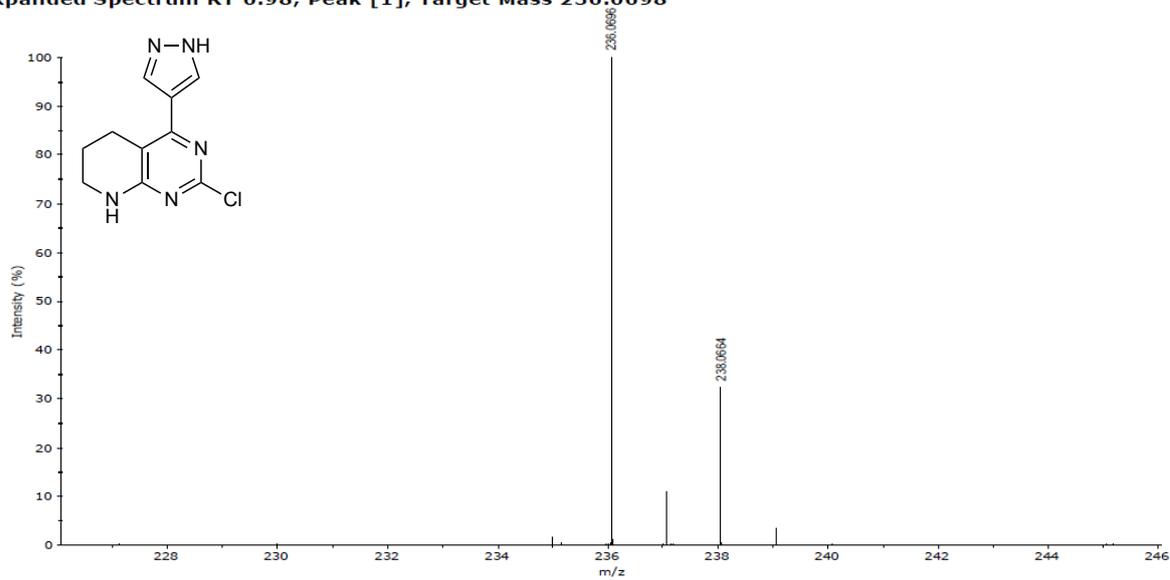


¹³C NMR



HRMS

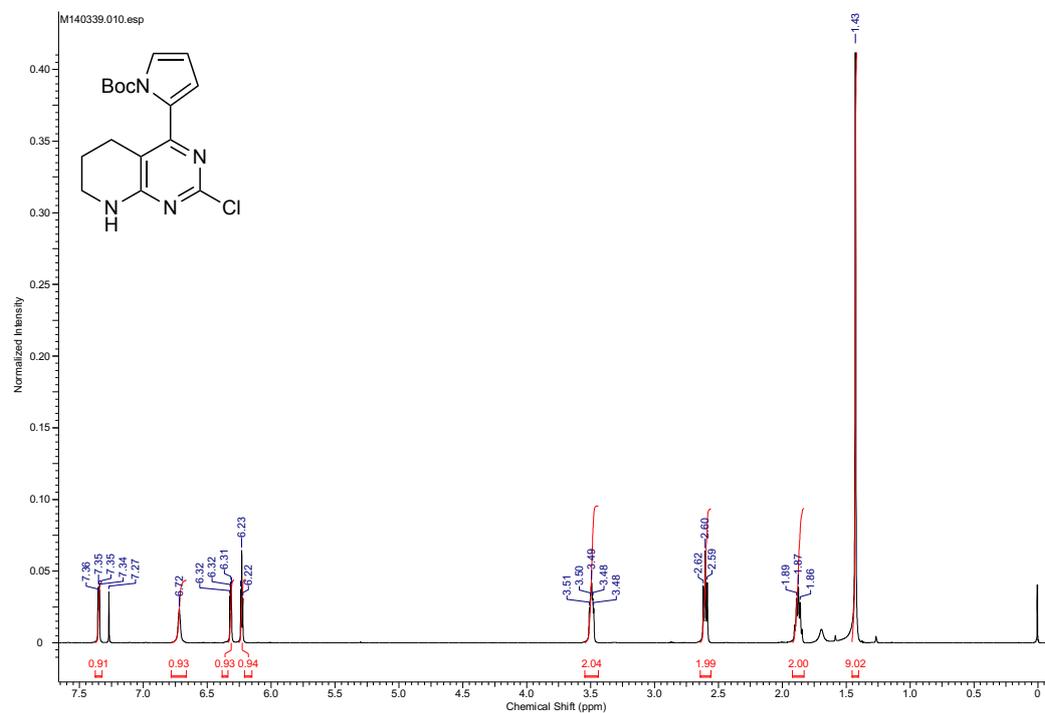
Expanded Spectrum RT 0.98, Peak [1], Target Mass 236.0698



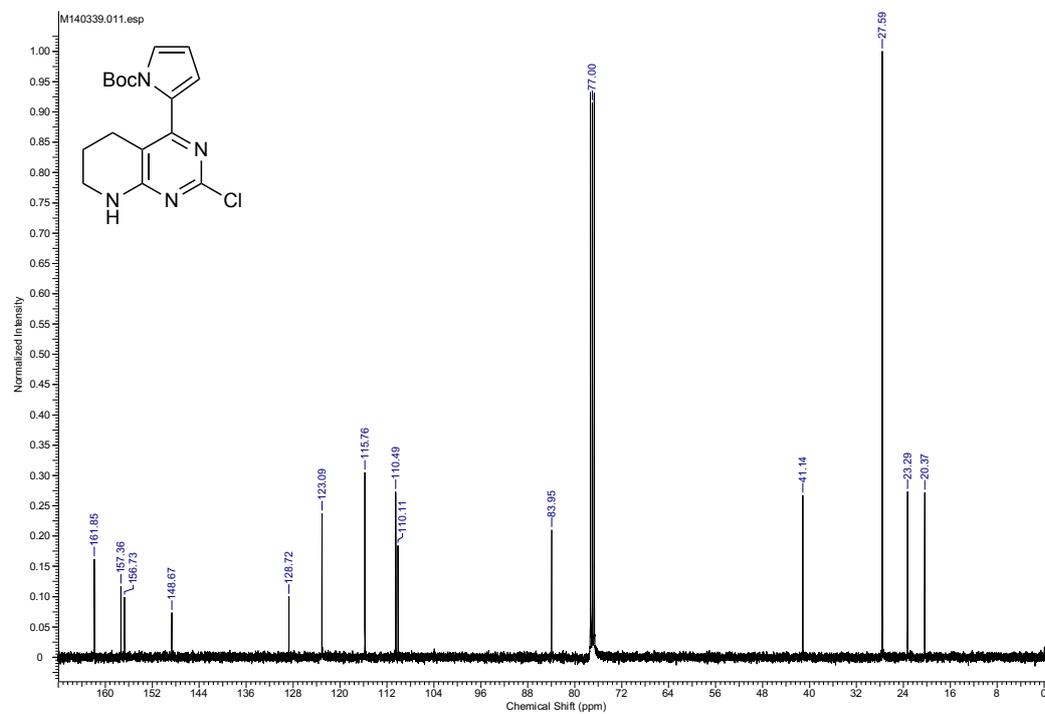
tert-Butyl
carboxylate, **4m**

2-(2-chloro-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl)-1*H*-pyrrole-1

¹H NMR

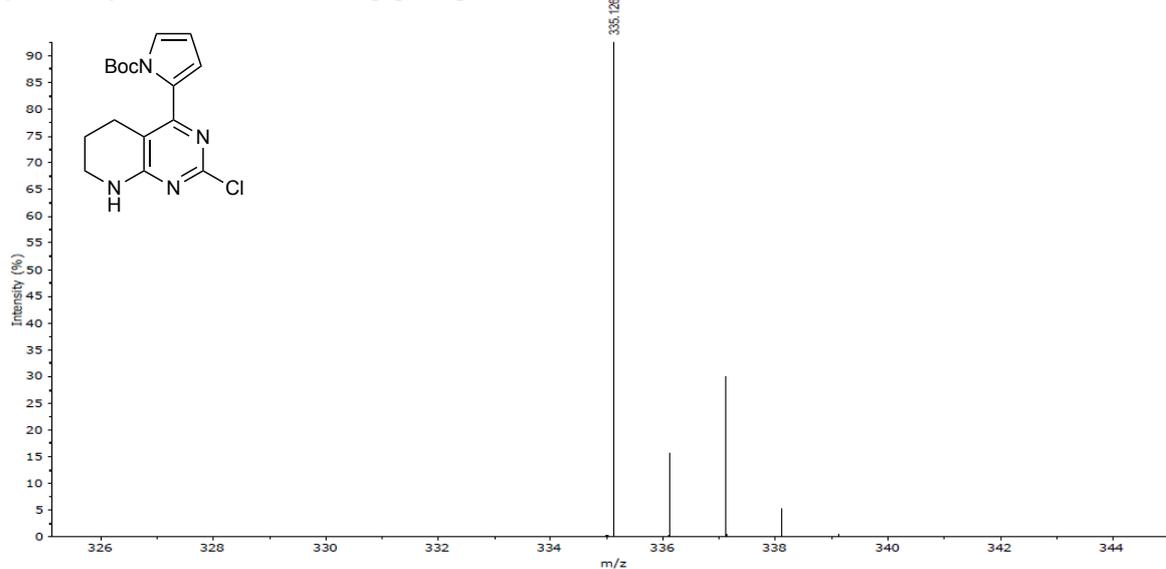


¹³C NMR



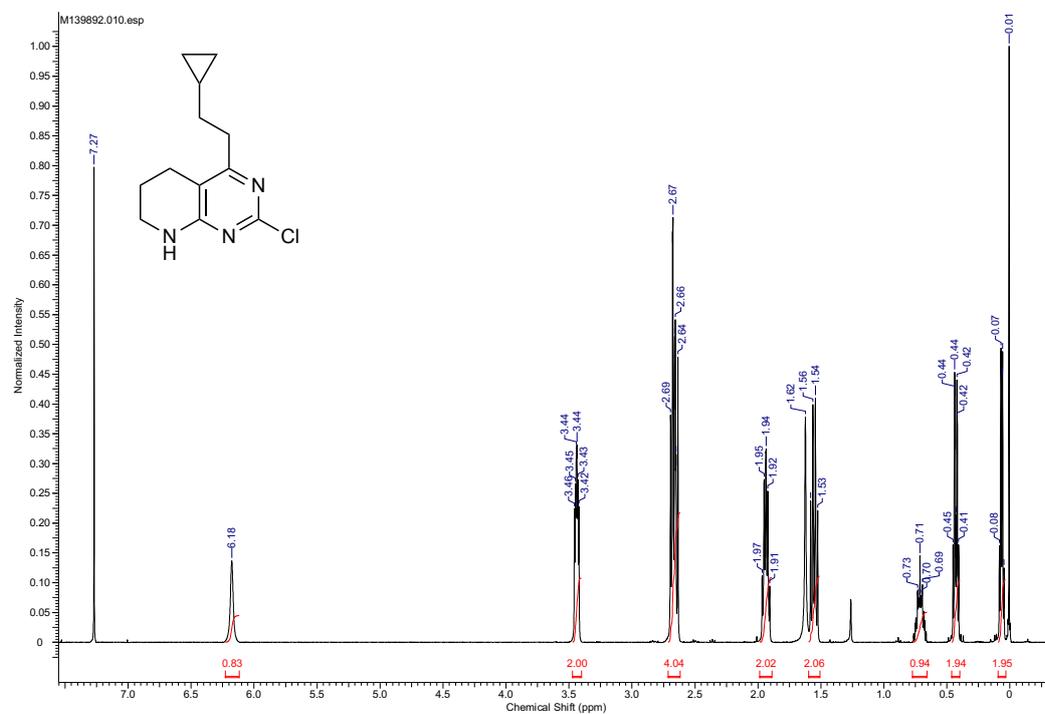
HRMS

Expanded Spectrum RT 3.16, Peak [1], Target Mass 335.1269

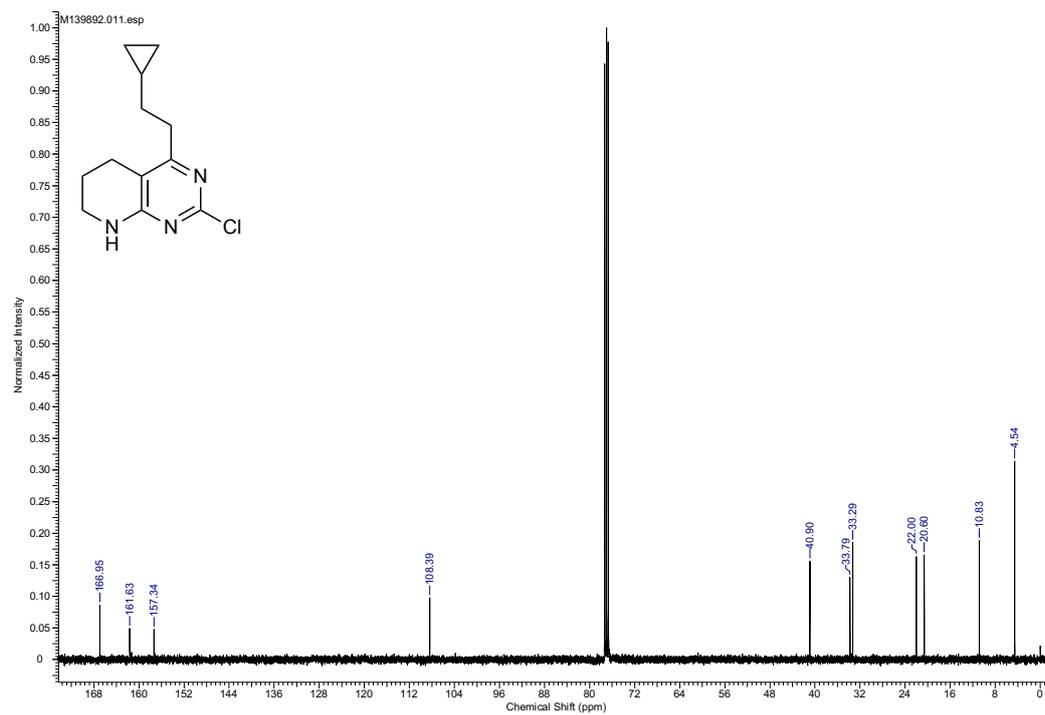


2-Chloro-4-(2-cyclopropylethyl)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine, **4n**

¹H NMR

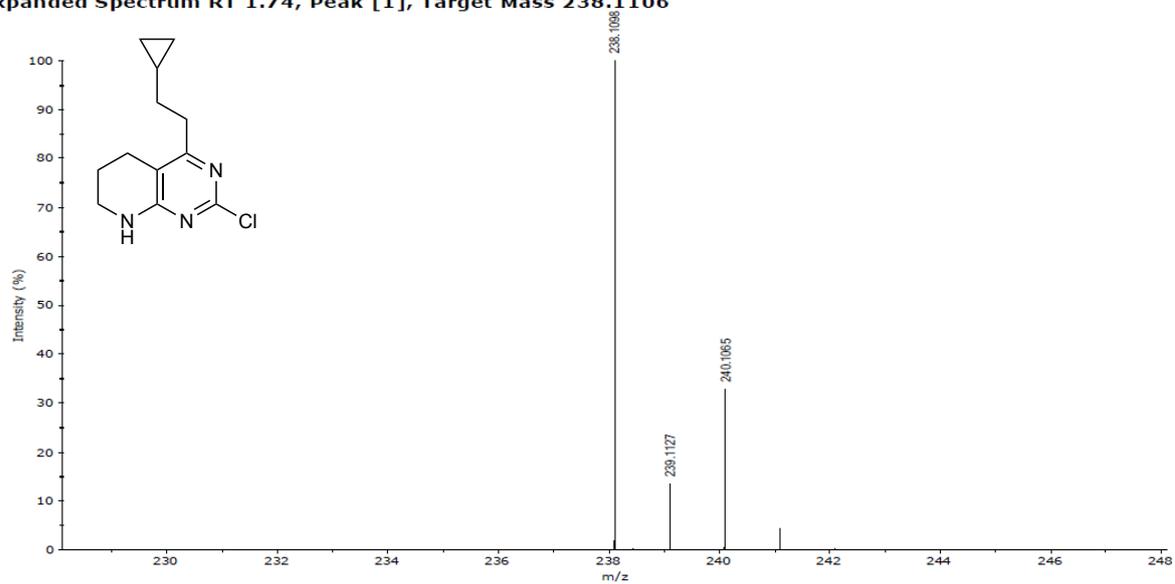


¹³C NMR



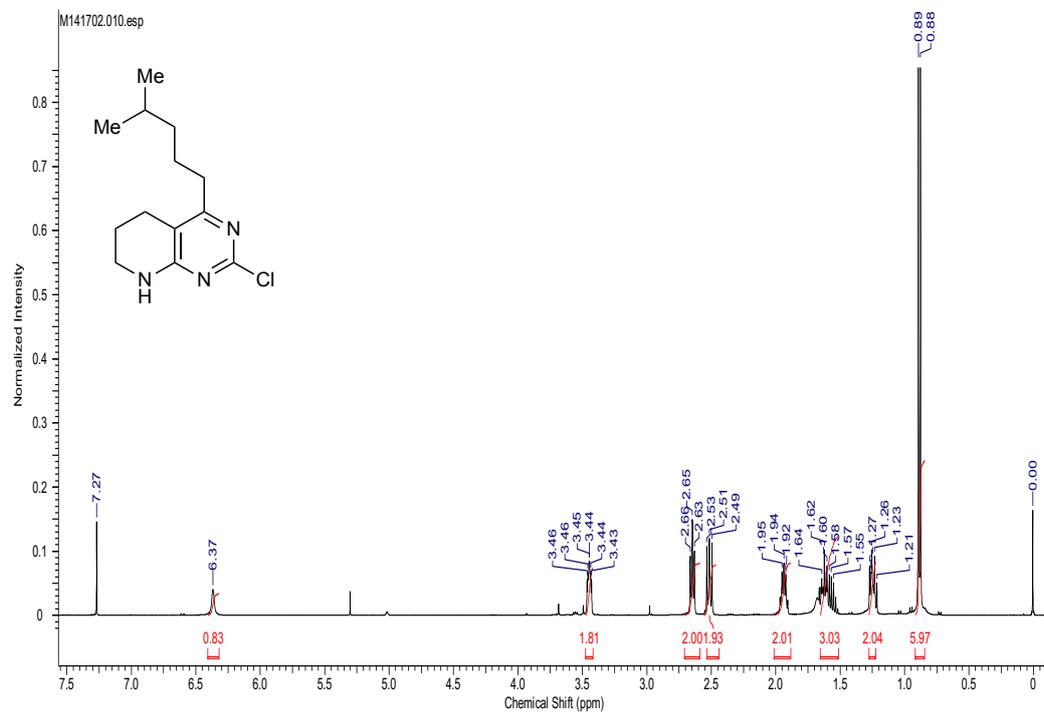
HRMS

Expanded Spectrum RT 1.74, Peak [1], Target Mass 238.1106

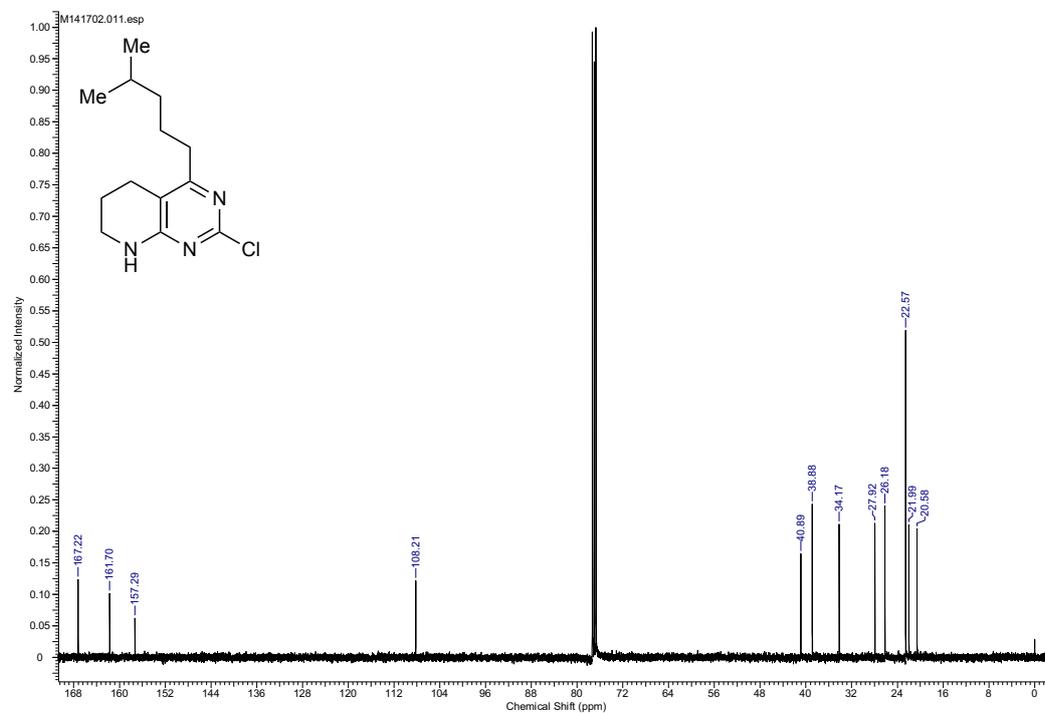


2-Chloro-4-(4-methylpentyl)-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidine, 4o

¹H NMR

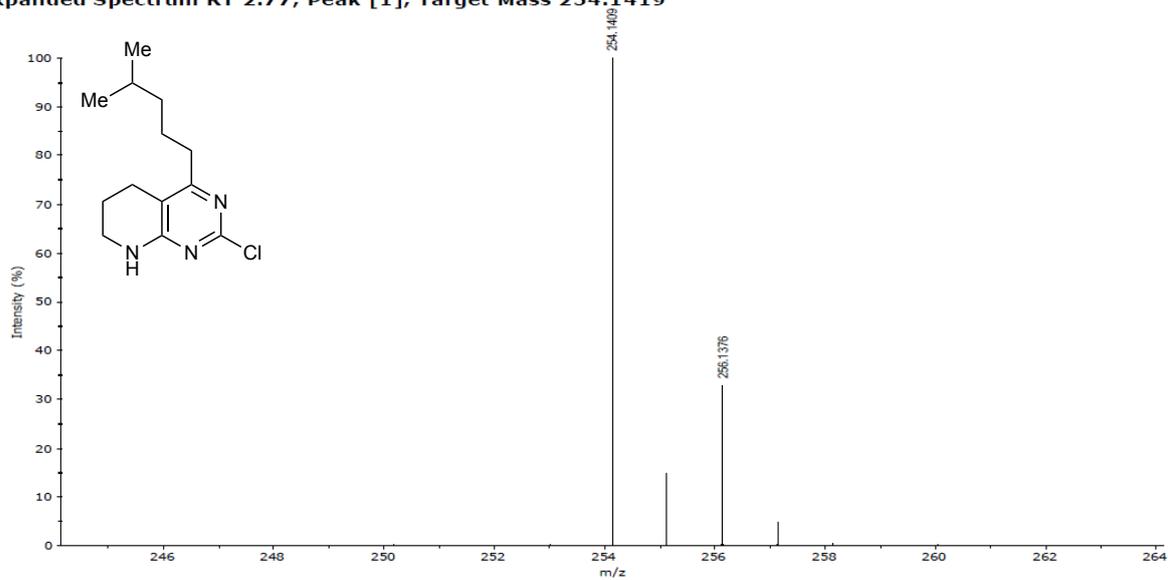


¹³C NMR



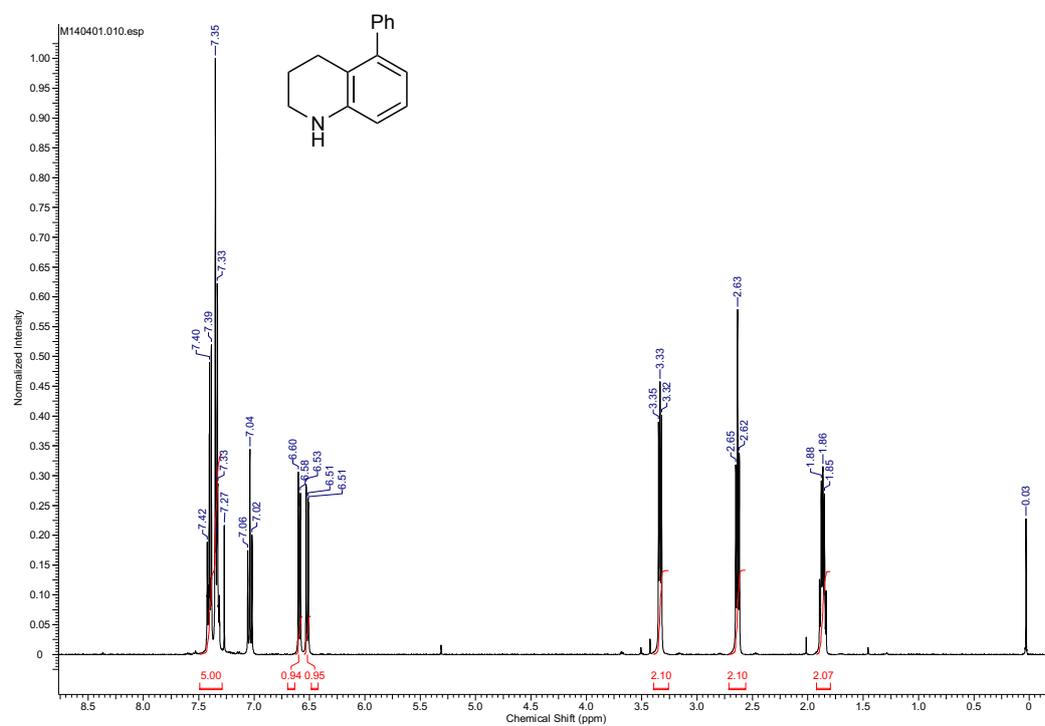
HRMS

Expanded Spectrum RT 2.77, Peak [1], Target Mass 254.1419

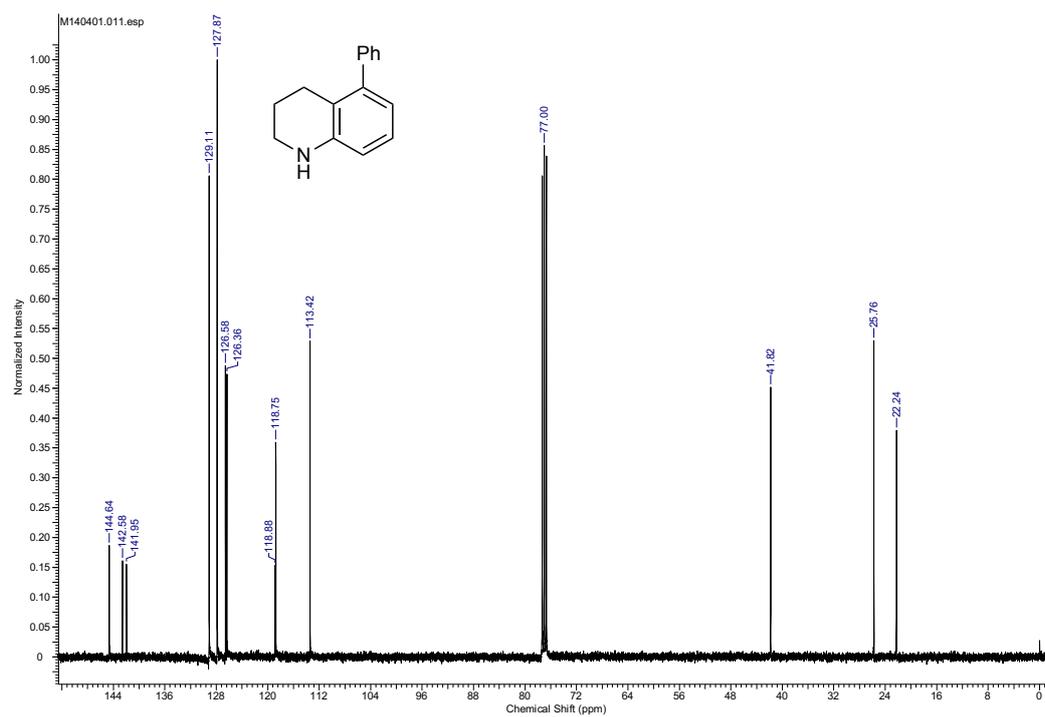


5-Phenyl-1,2,3,4-tetrahydroquinoline, **6a**

¹H NMR

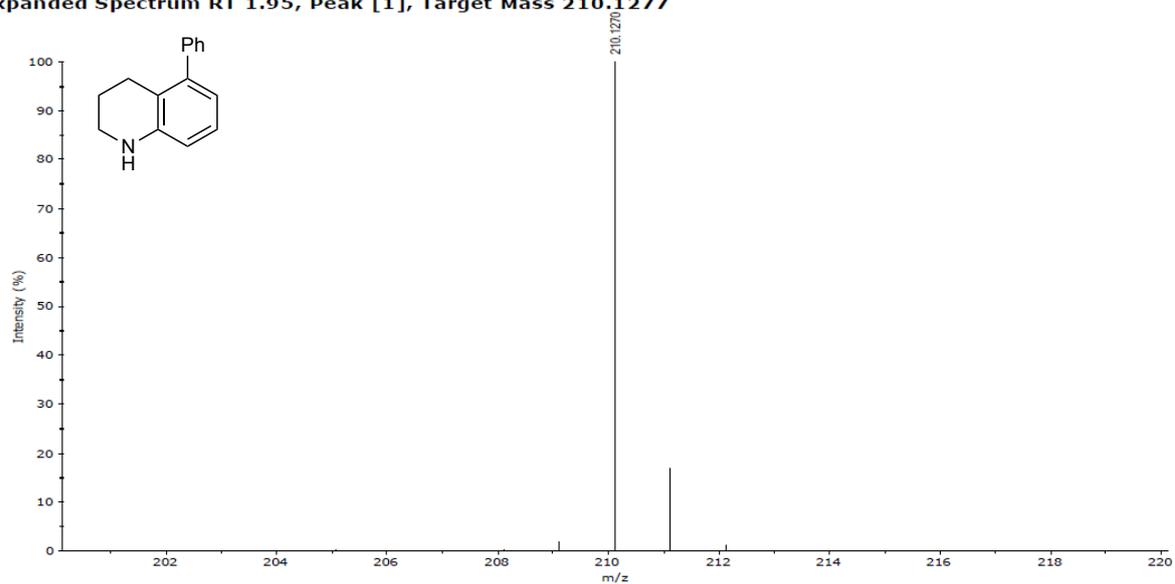


¹³C NMR



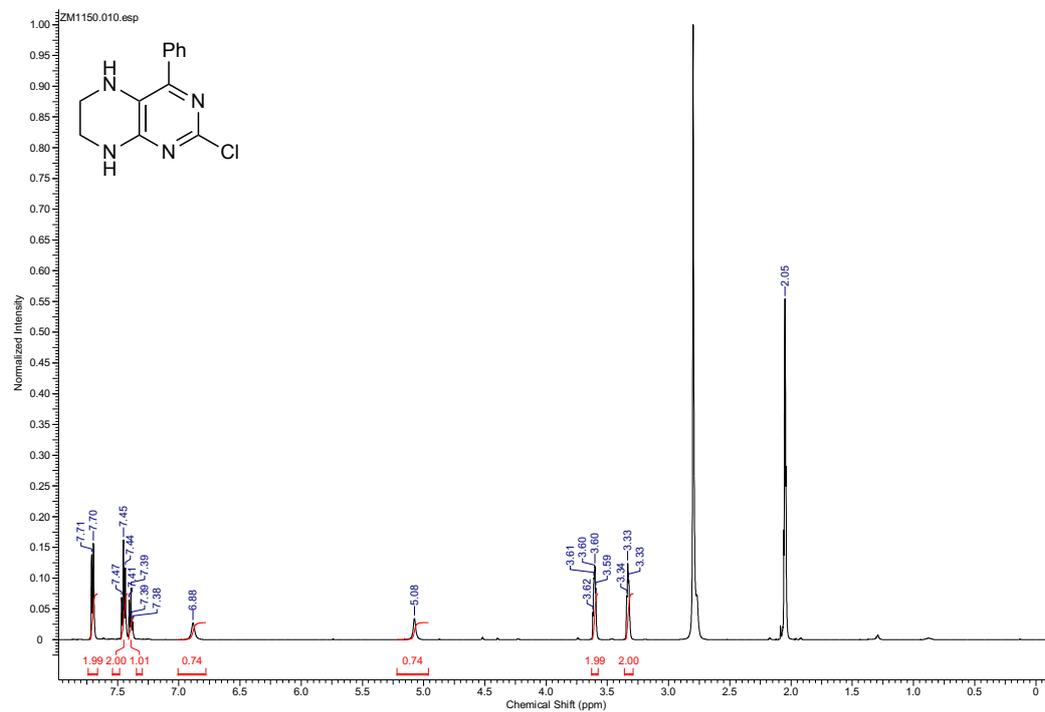
HRMS

Expanded Spectrum RT 1.95, Peak [1], Target Mass 210.1277

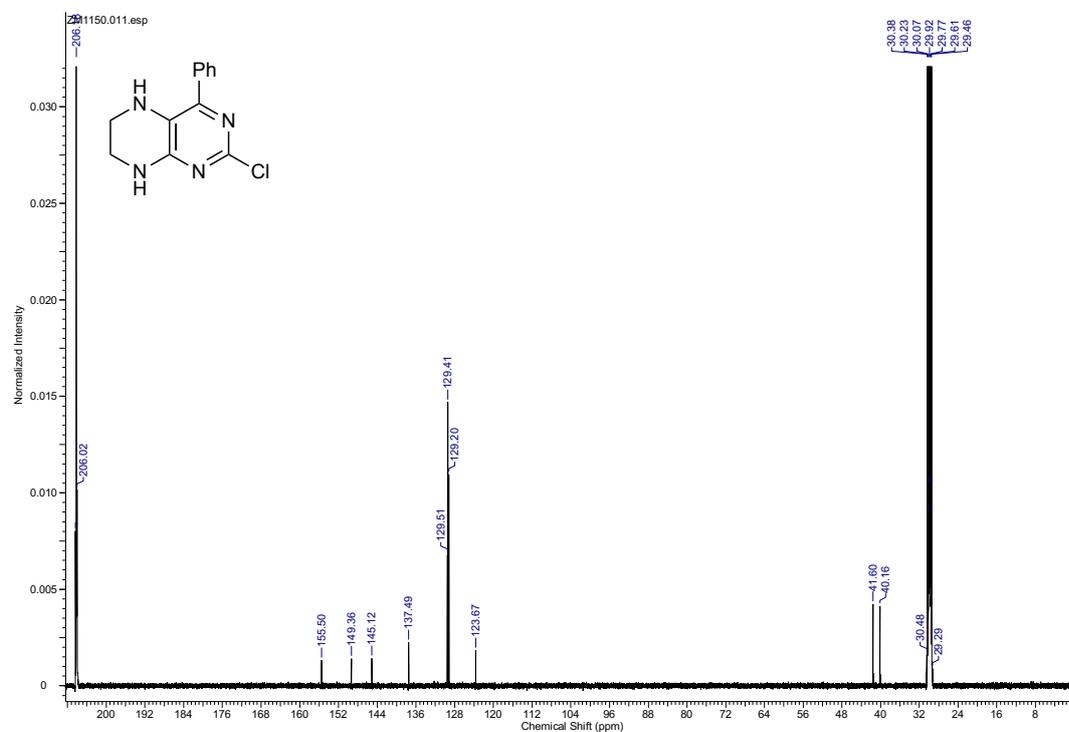


2-Chloro-4-phenyl-5,6,7,8-tetrahydropteridine, **6b**

^1H NMR

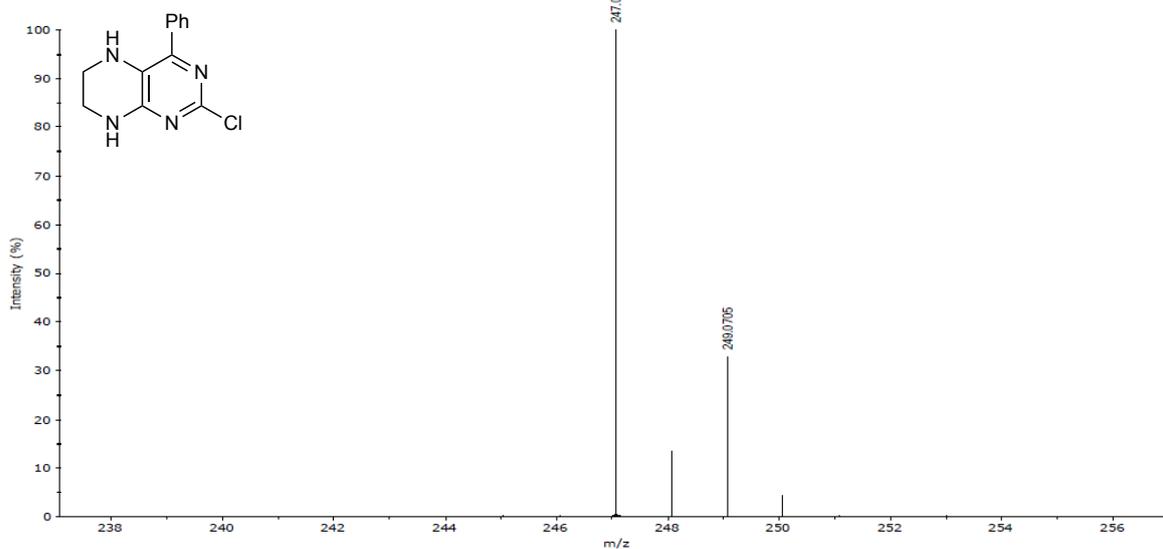


^{13}C NMR



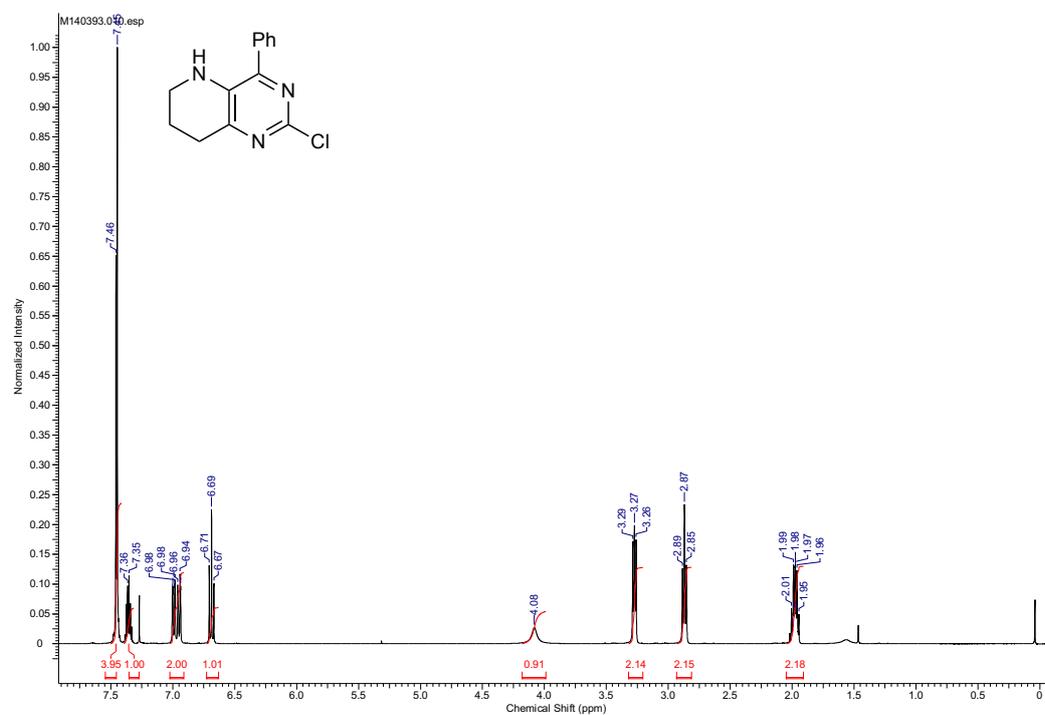
HRMS

Expanded Spectrum RT 1.47, Peak [1], Target Mass 247.0745

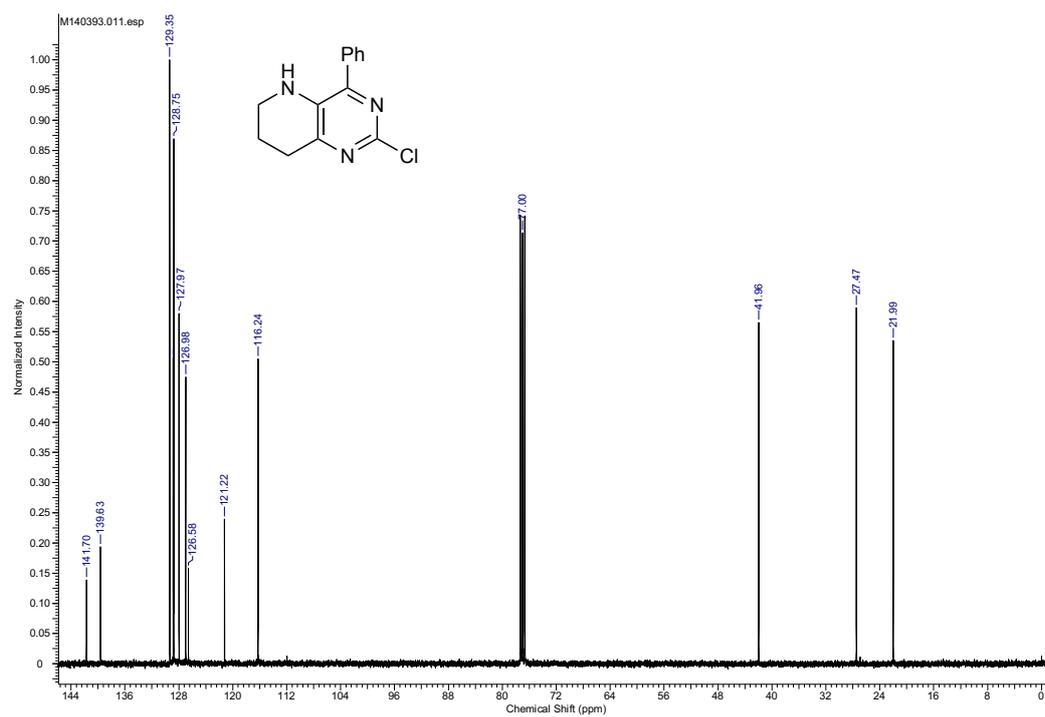


8-Phenyl-1,2,3,4-tetrahydroquinoline, **6c**³

¹H NMR

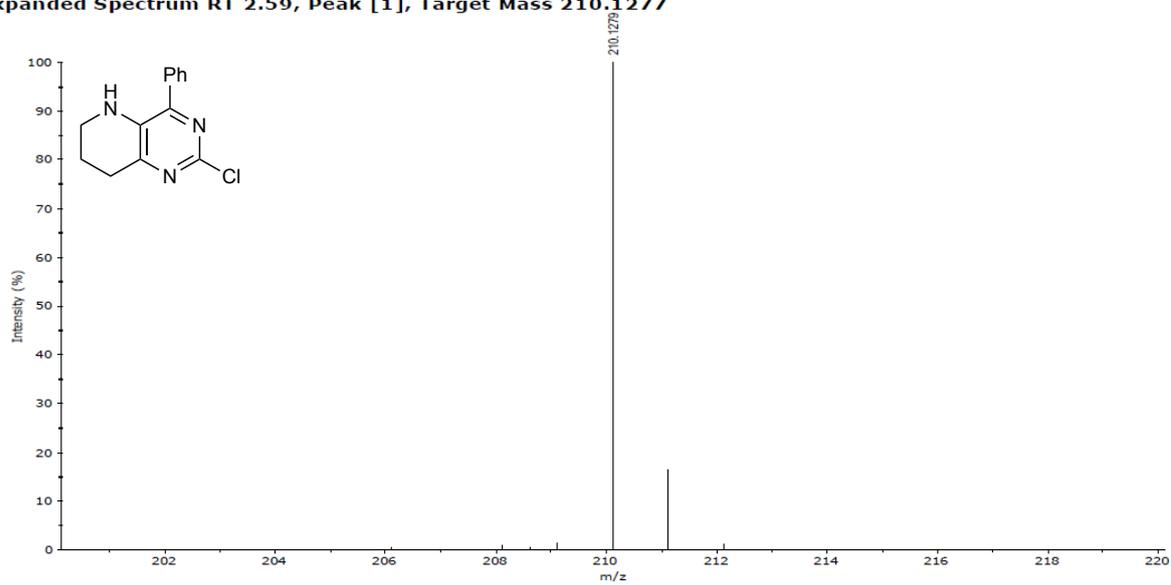


¹³C NMR



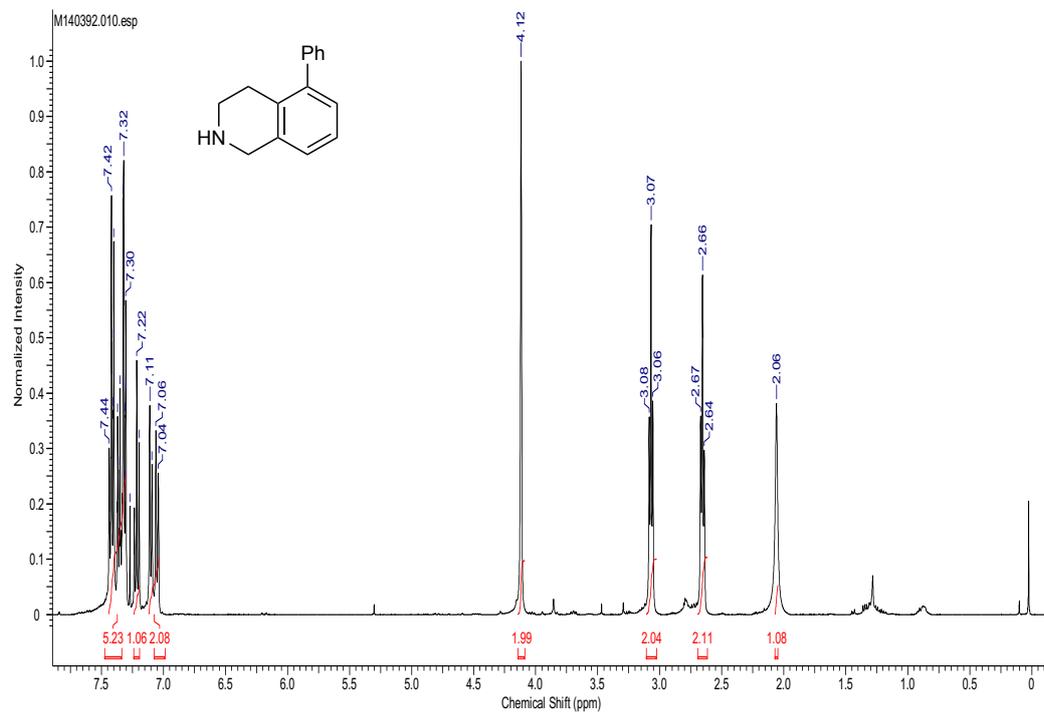
HRMS

Expanded Spectrum RT 2.59, Peak [1], Target Mass 210.1277

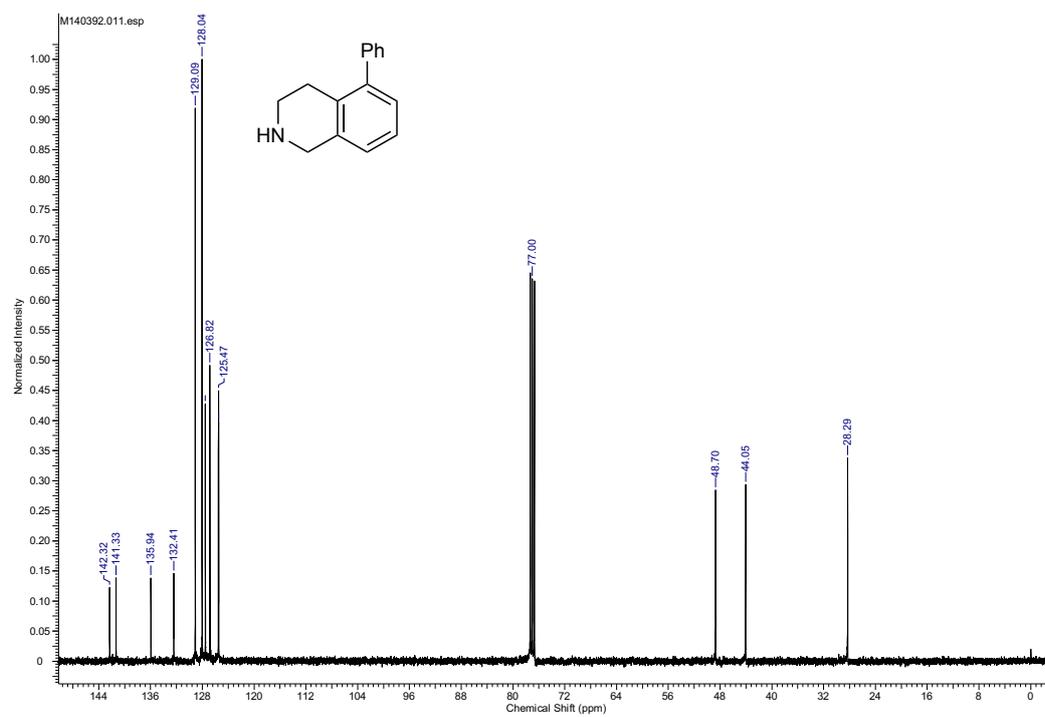


5-Phenyl-1,2,3,4-tetrahydroisoquinoline, **6d**⁴

¹H NMR

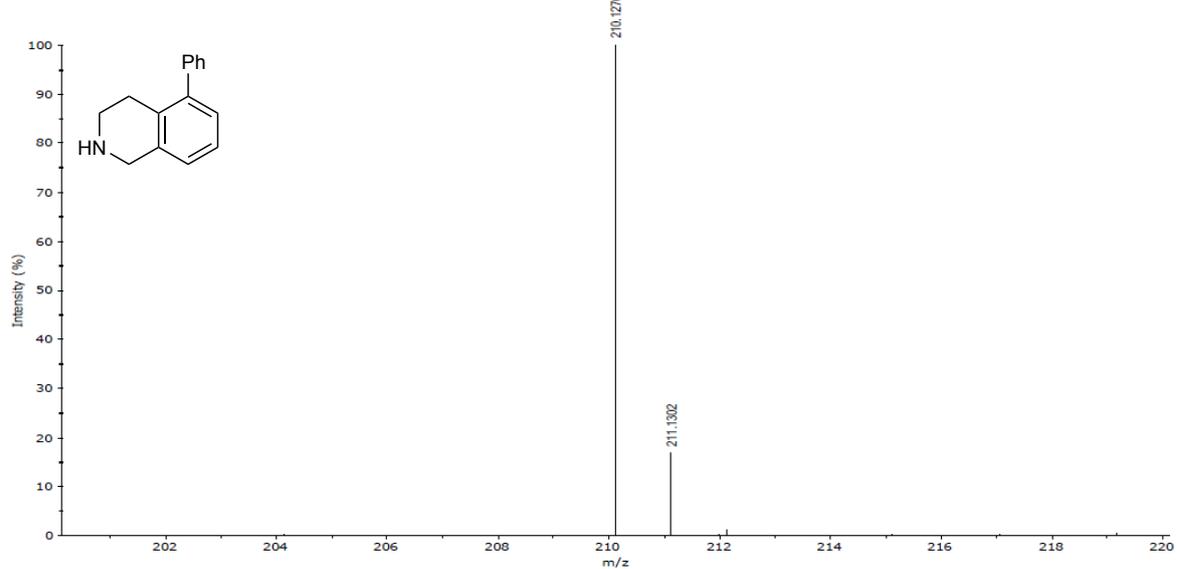


¹³C NMR



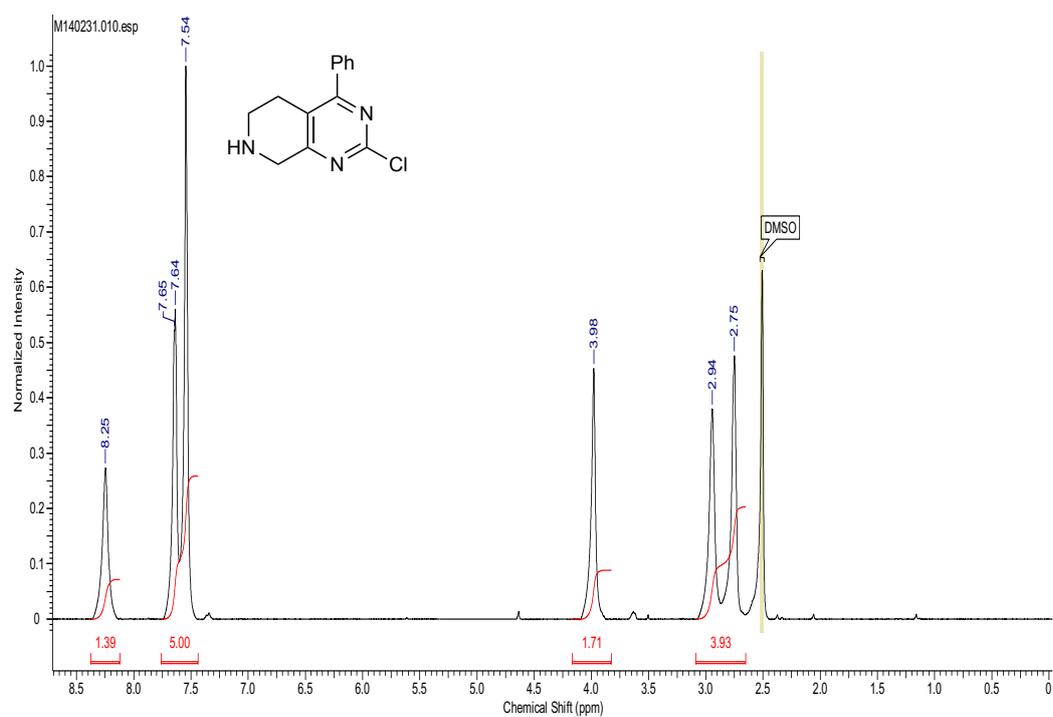
HRMS

Expanded Spectrum RT 1.93, Peak [1], Target Mass 210.1277

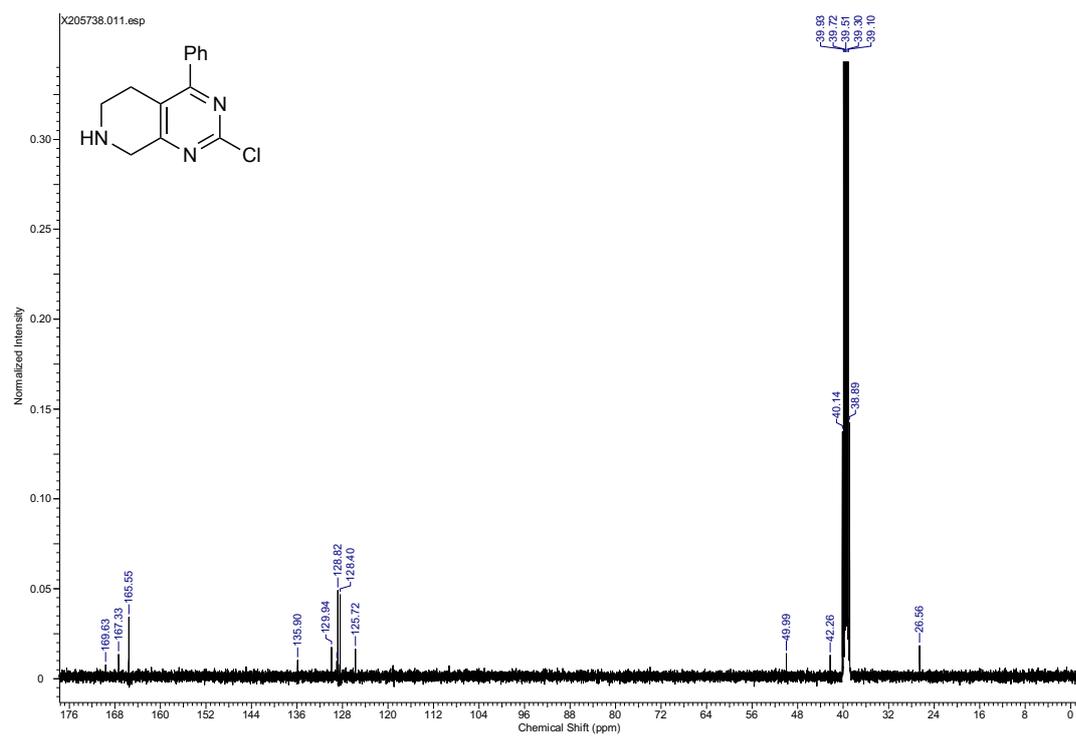


2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[3,4-*d*]pyrimidine, **6e**

¹H NMR

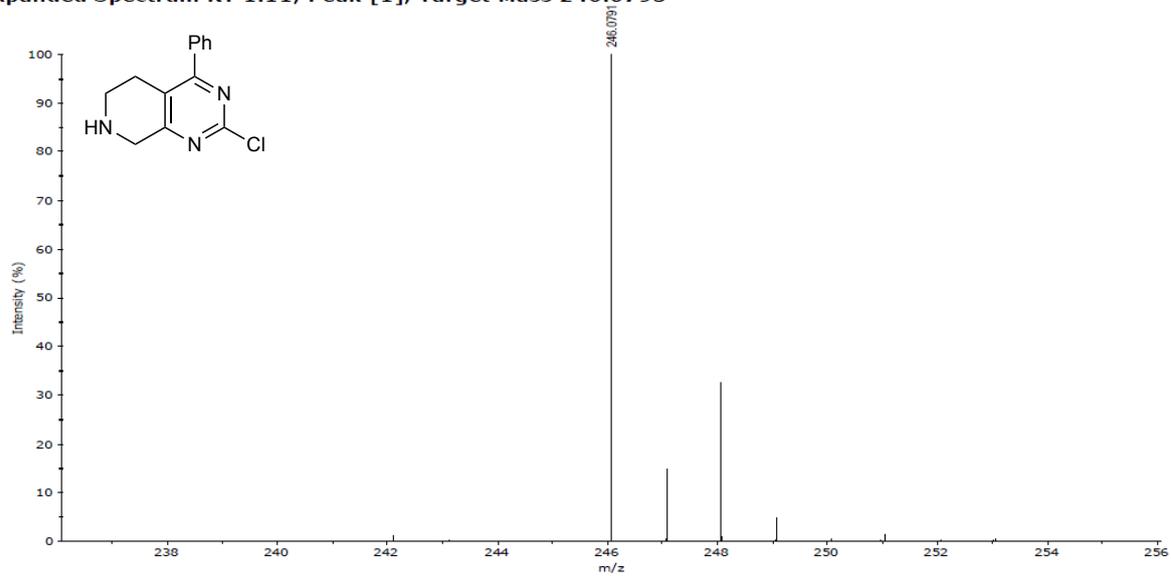


¹³C NMR



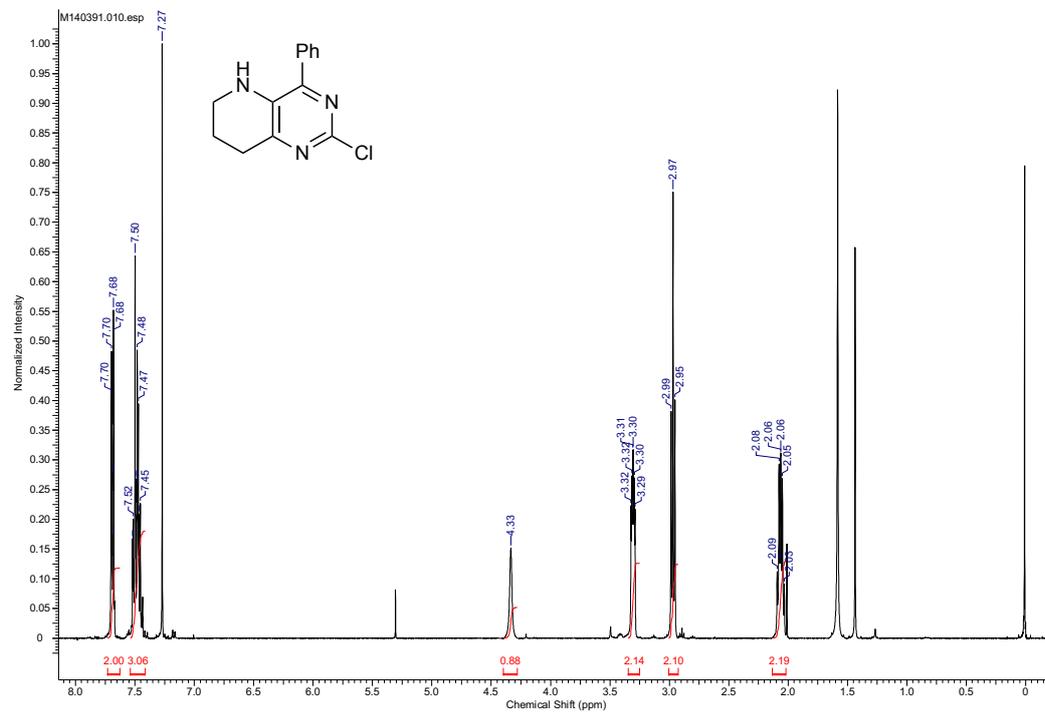
HRMS

Expanded Spectrum RT 1.11, Peak [1], Target Mass 246.0793

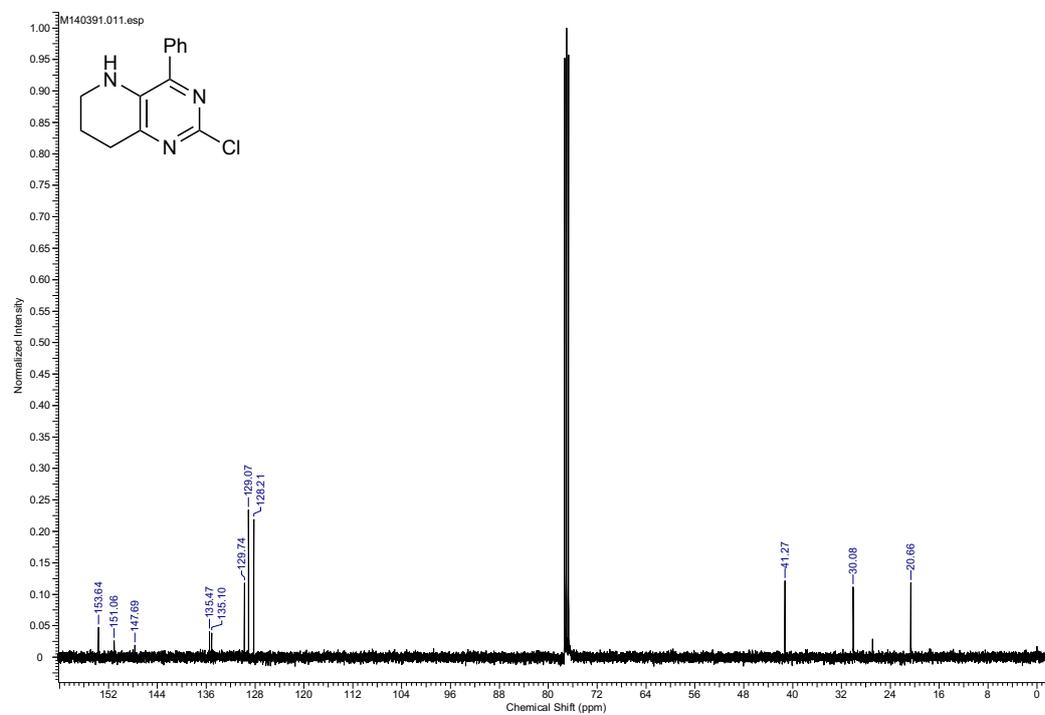


2-Chloro-4-phenyl-5,6,7,8-tetrahydropyrido[3,2-d]pyrimidine, **6f**

¹H NMR

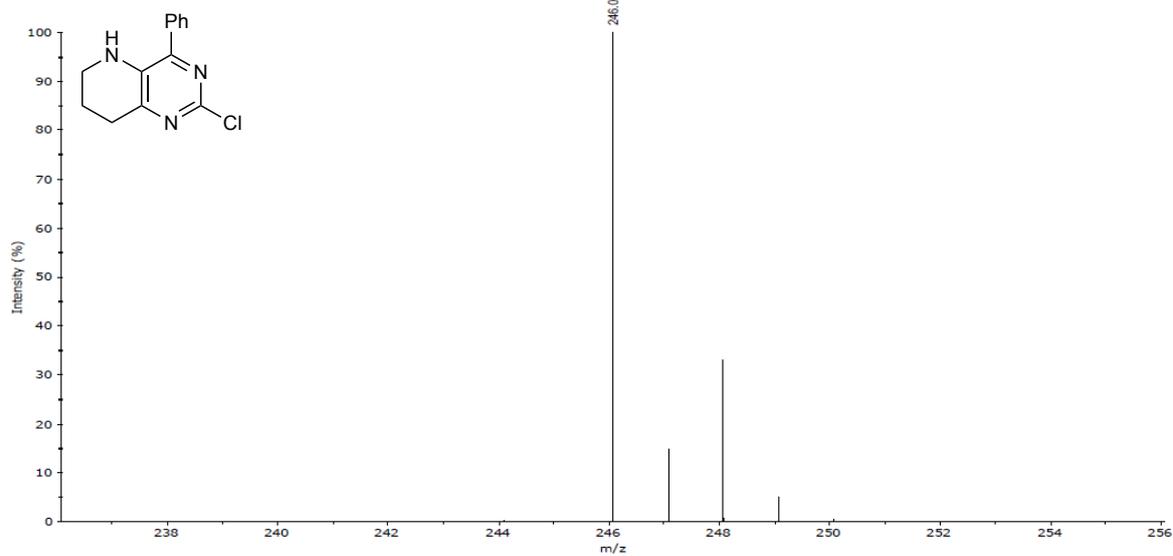


¹³C NMR



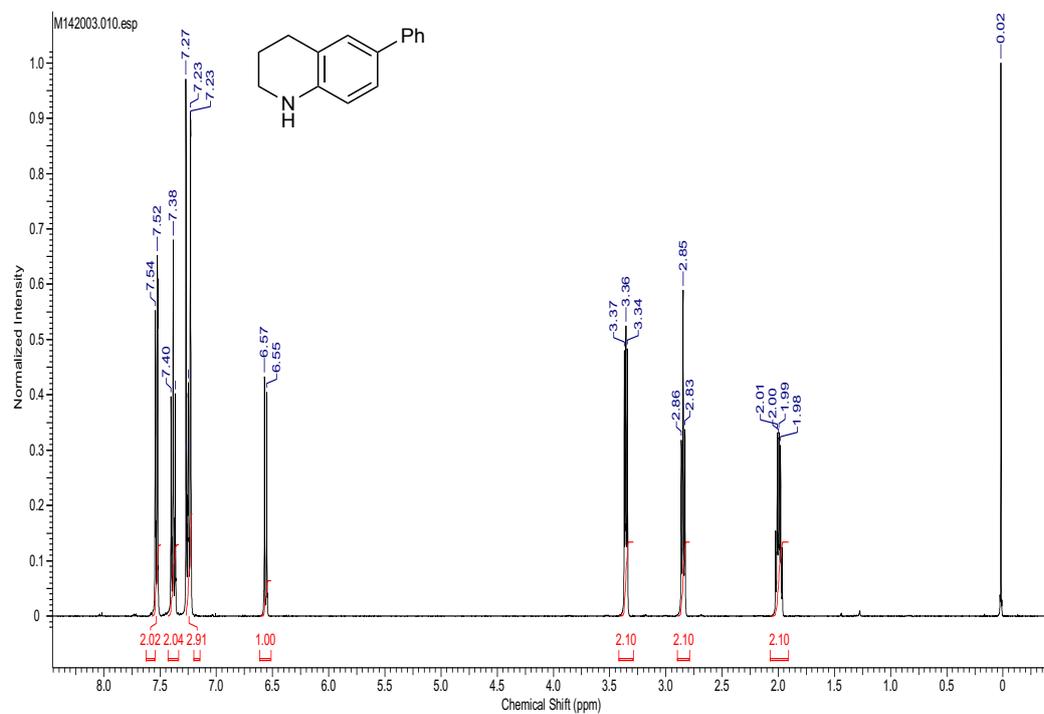
HRMS

Expanded Spectrum RT 2.88, Peak [1], Target Mass 246.0793

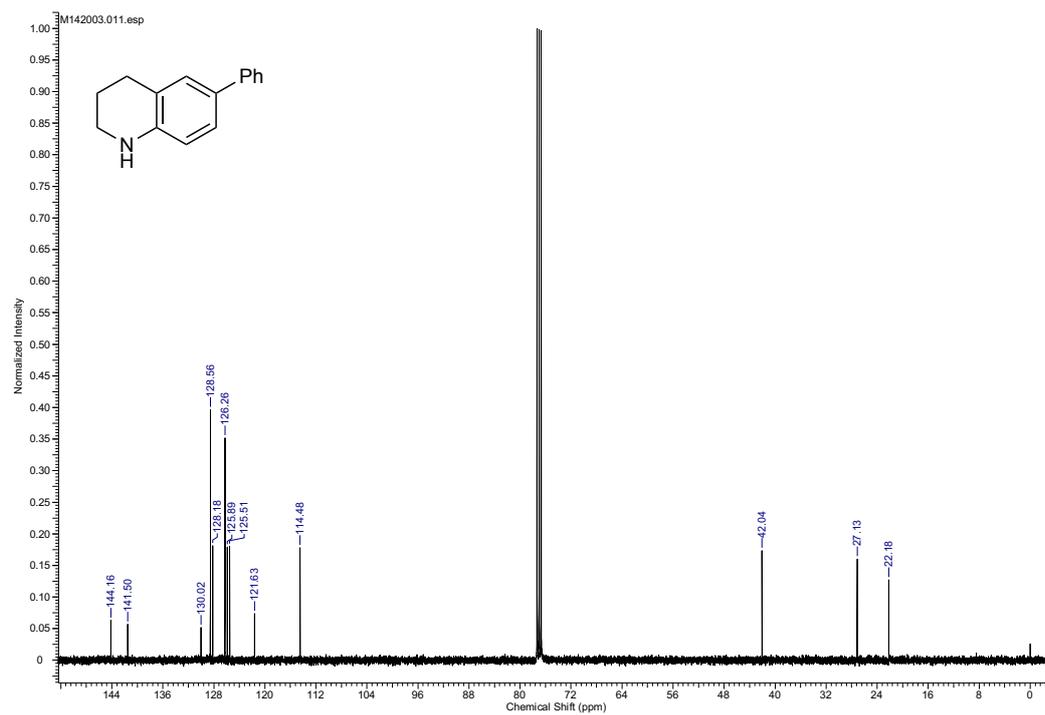


6-Phenyl-1,2,3,4-tetrahydroquinoline, **6g**⁵

¹H NMR

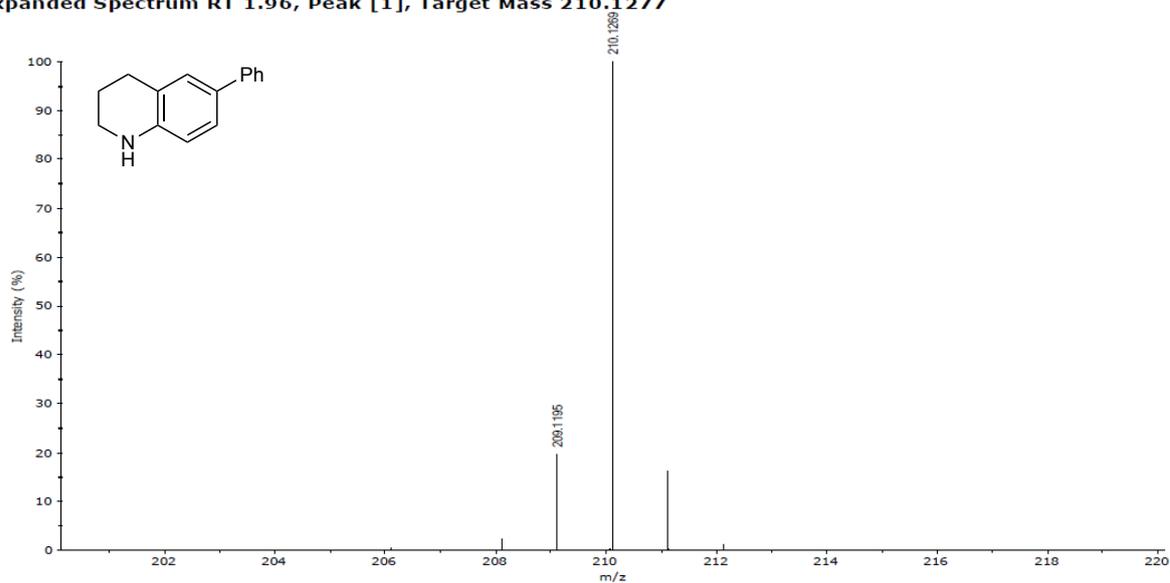


¹³C NMR



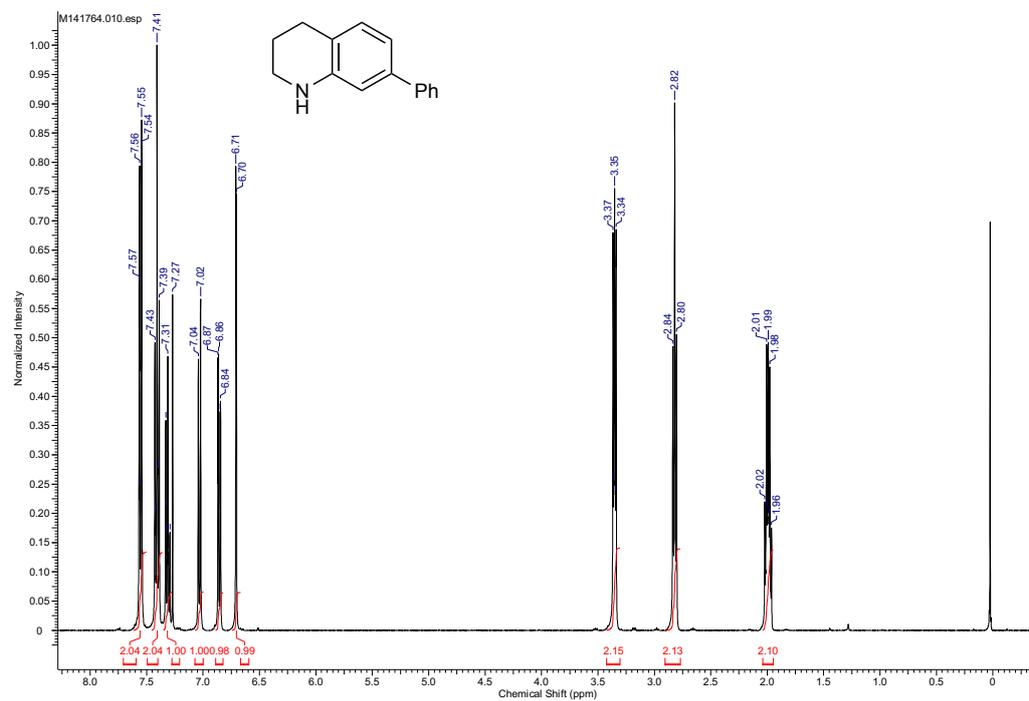
HRMS

Expanded Spectrum RT 1.96, Peak [1], Target Mass 210.1277

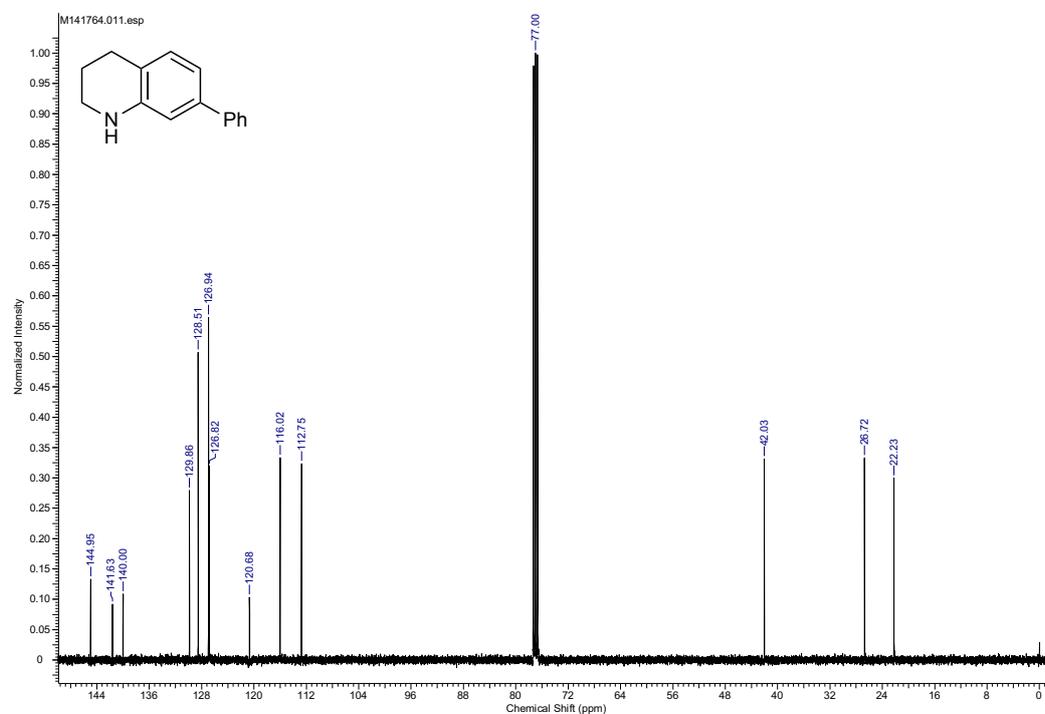


7-Phenyl-1,2,3,4-tetrahydroquinoline, **6h**⁶

¹H NMR

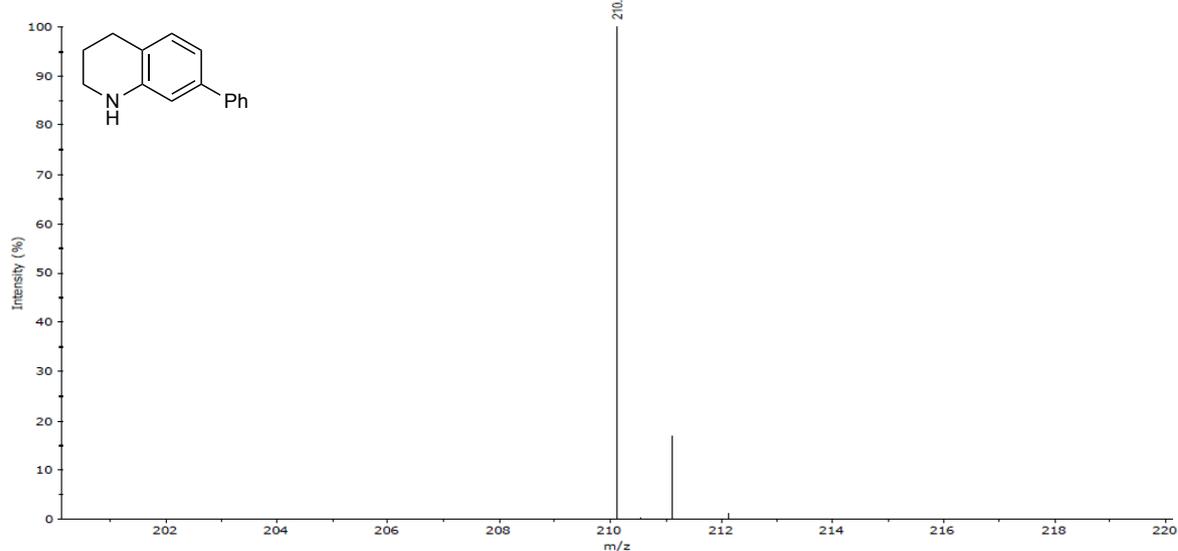


¹³C NMR



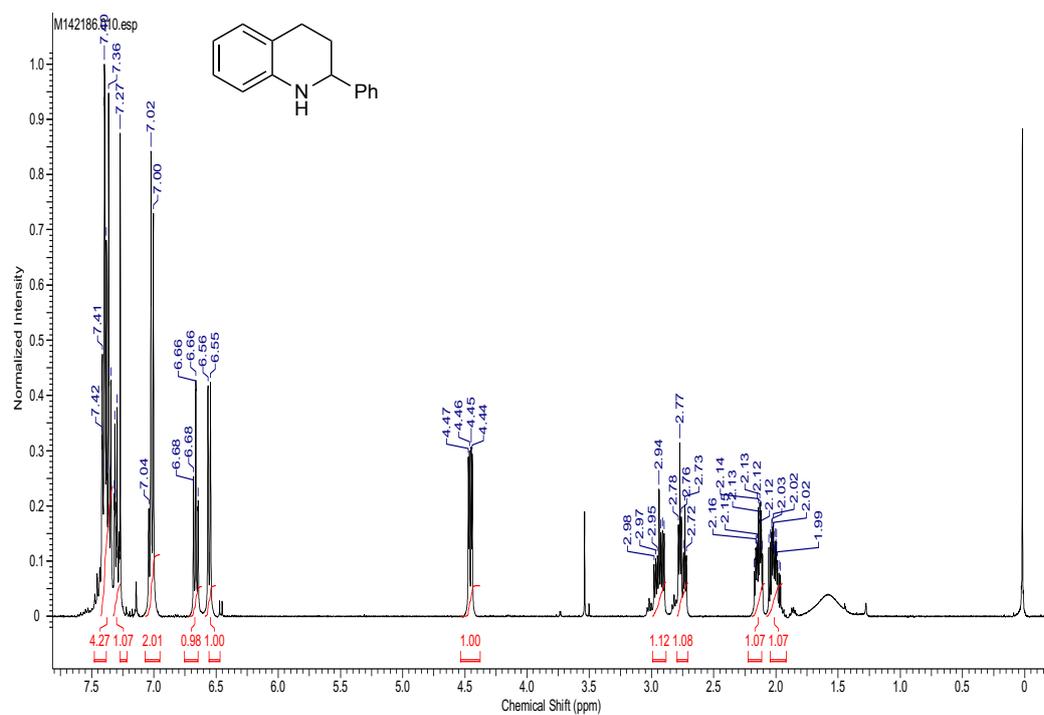
HRMS

Expanded Spectrum RT 1.74, Peak [1], Target Mass 210.1277

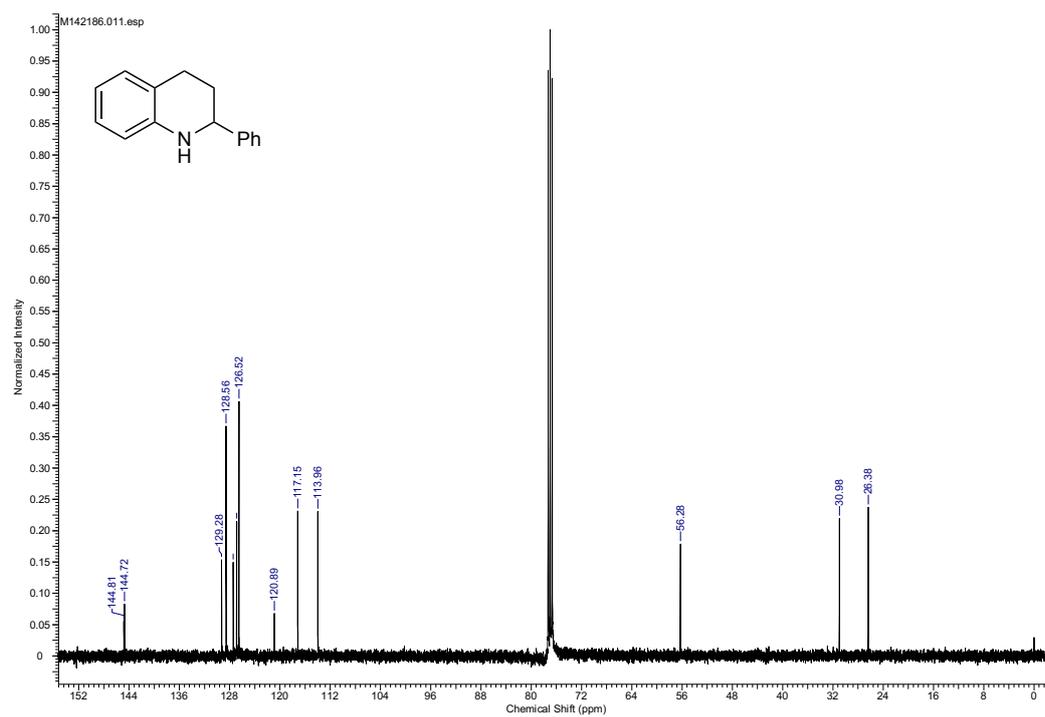


2-Phenyl-1,2,3,4-tetrahydroquinoline, **6i**⁷

¹H NMR

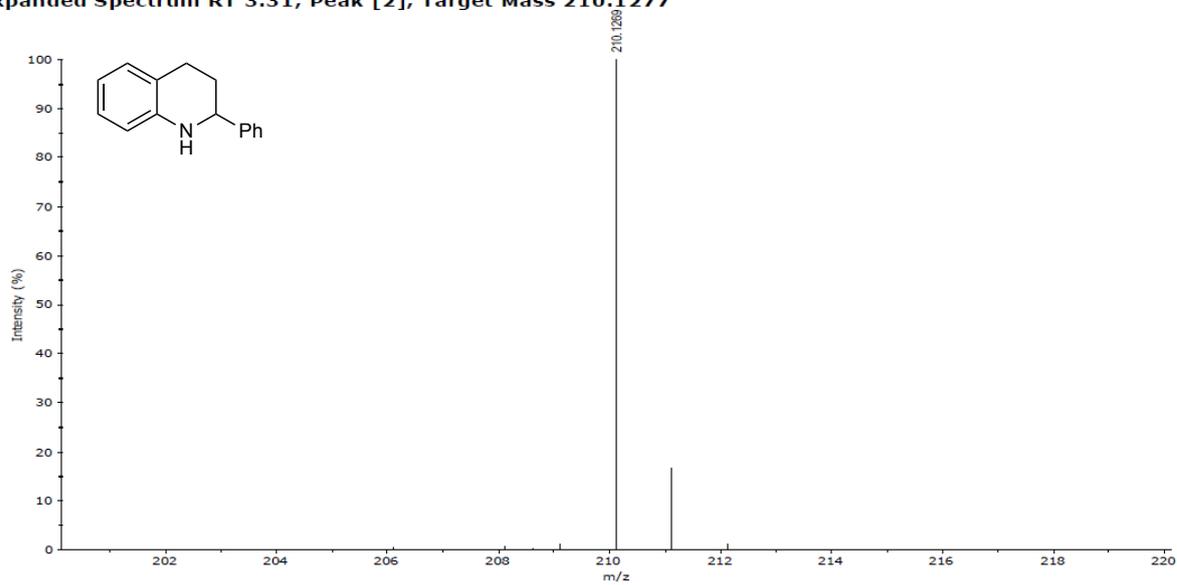


¹³C NMR



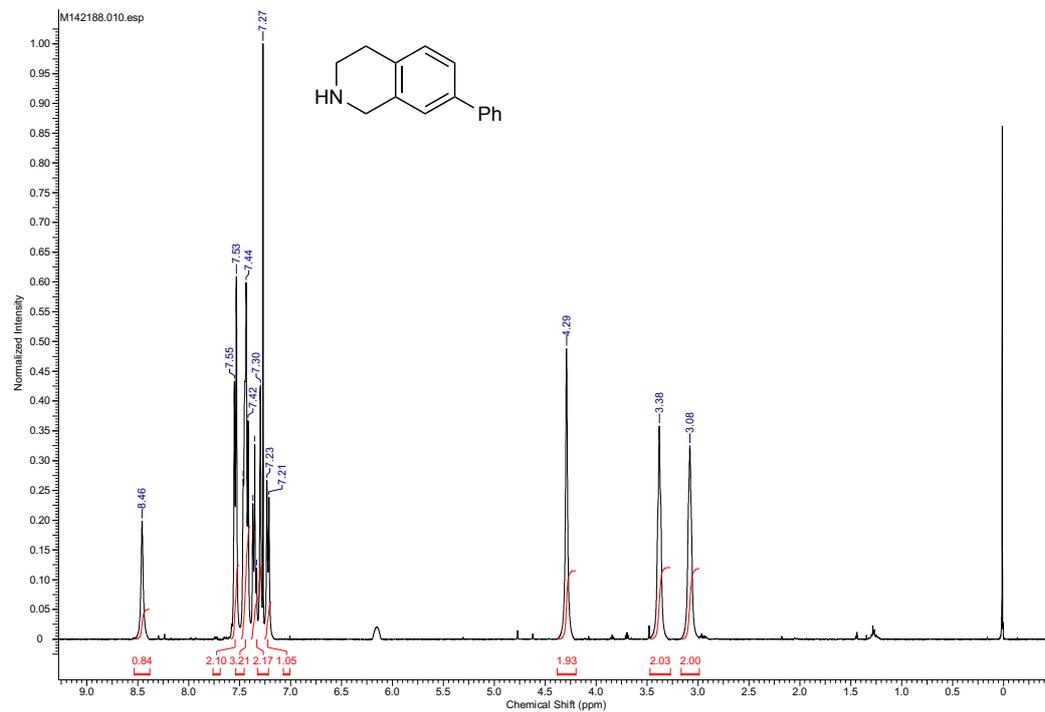
HRMS

Expanded Spectrum RT 3.31, Peak [2], Target Mass 210.1277

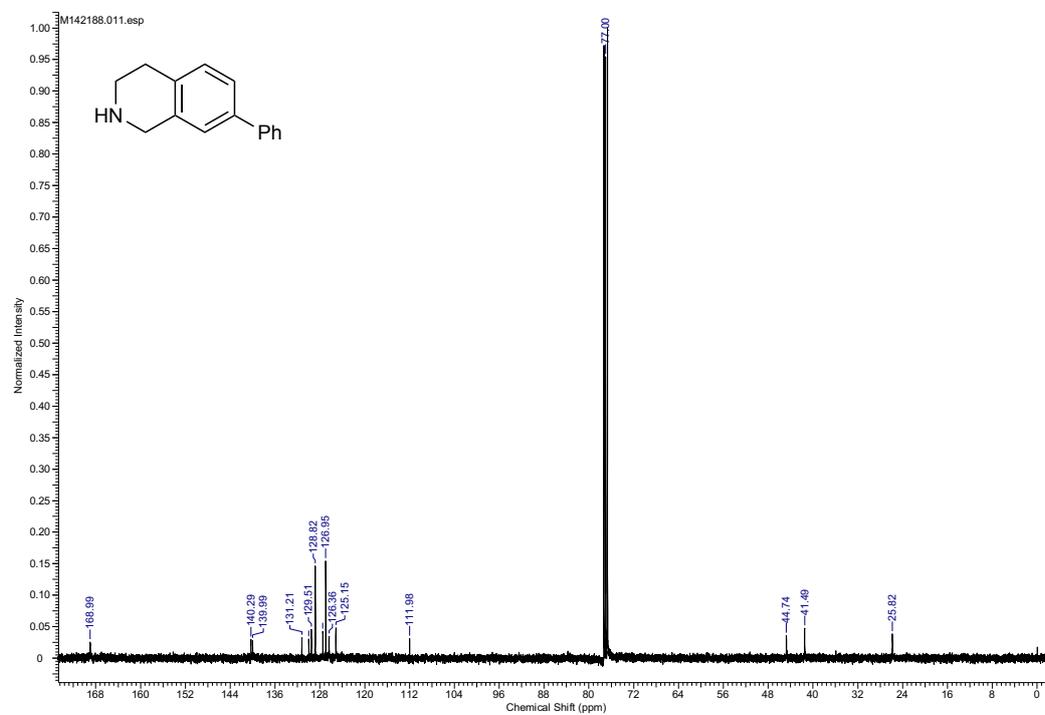


7-Phenyl-1,2,3,4-tetrahydroisoquinoline, **6j**

¹H NMR

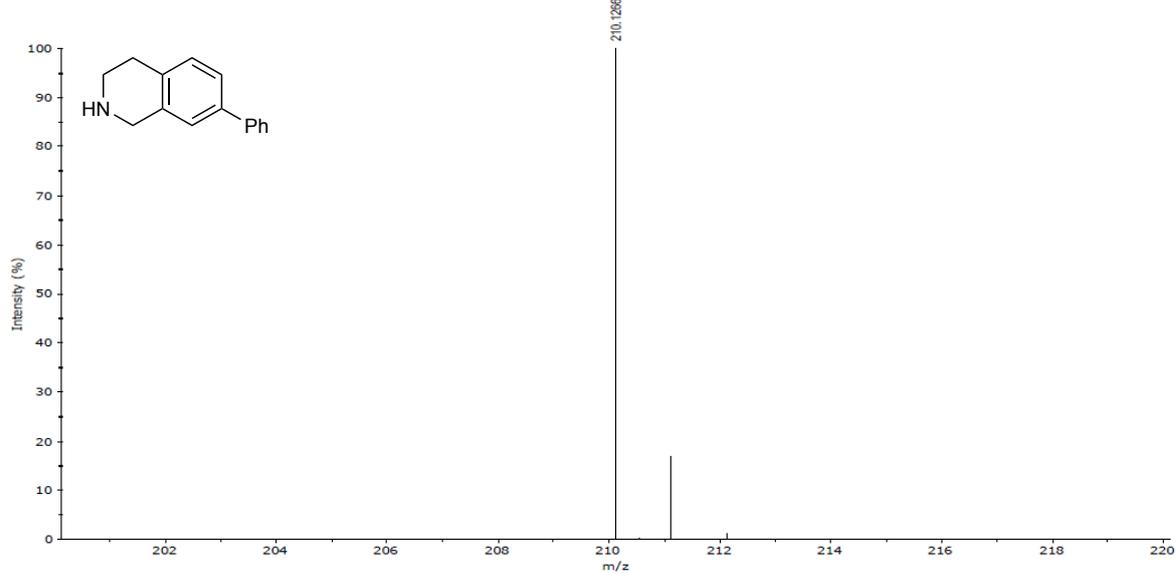


¹³C NMR



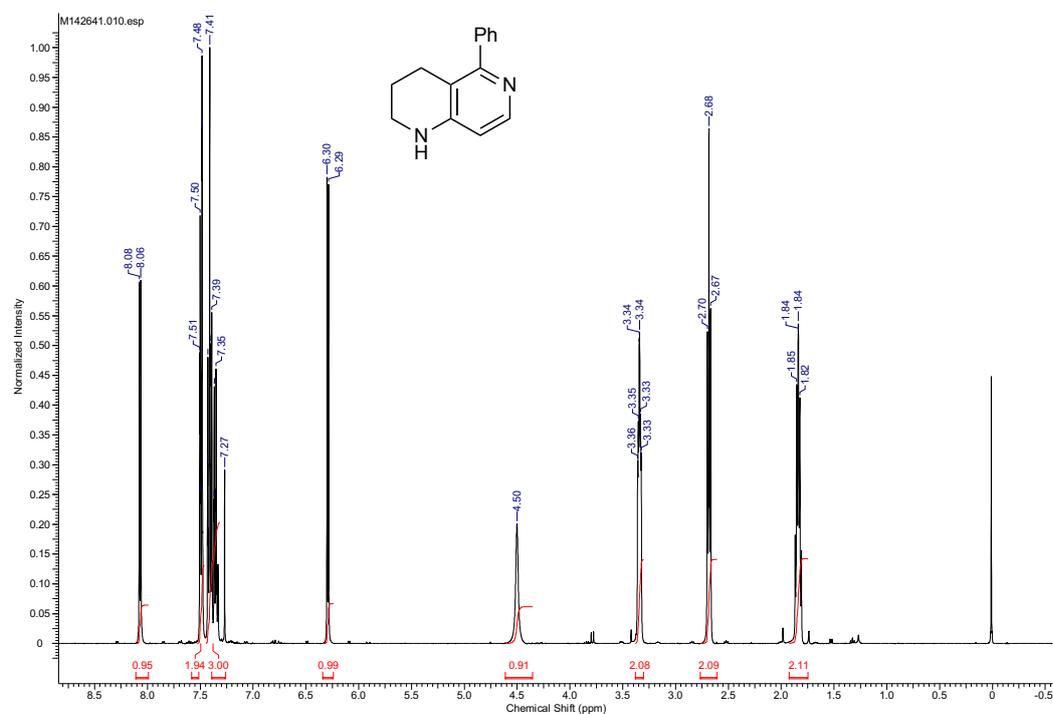
HRMS

Expanded Spectrum RT 1.74, Peak [1], Target Mass 210.1277

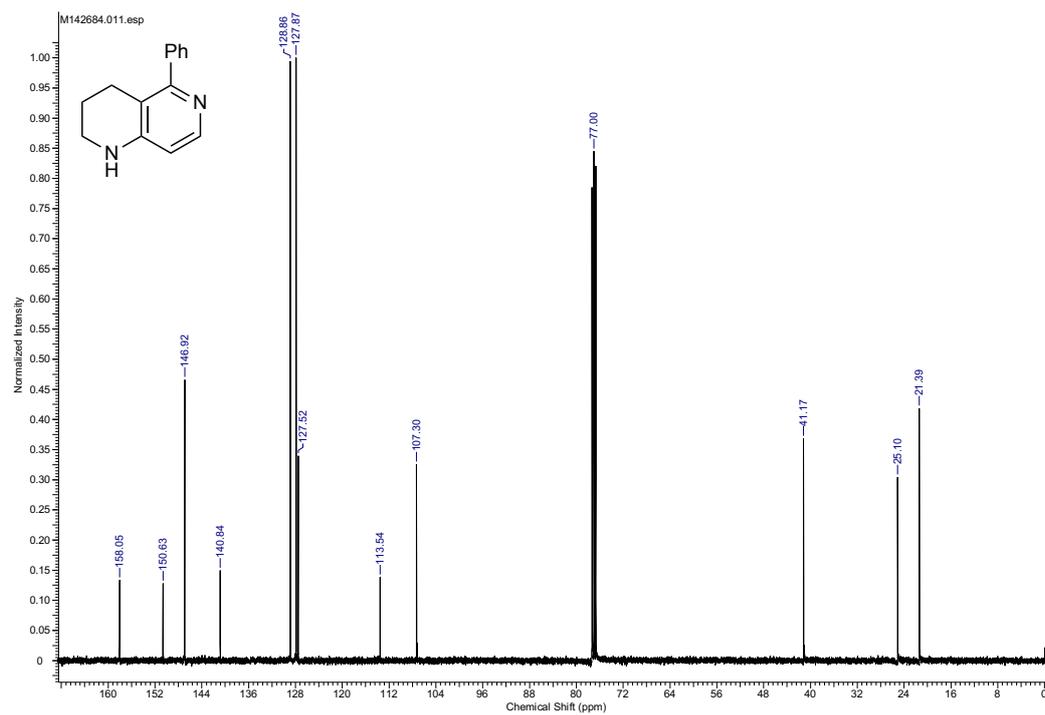


5-Phenyl-5,6,7,8-tetrahydro-1,6-naphthyridine, **6k**

¹H NMR

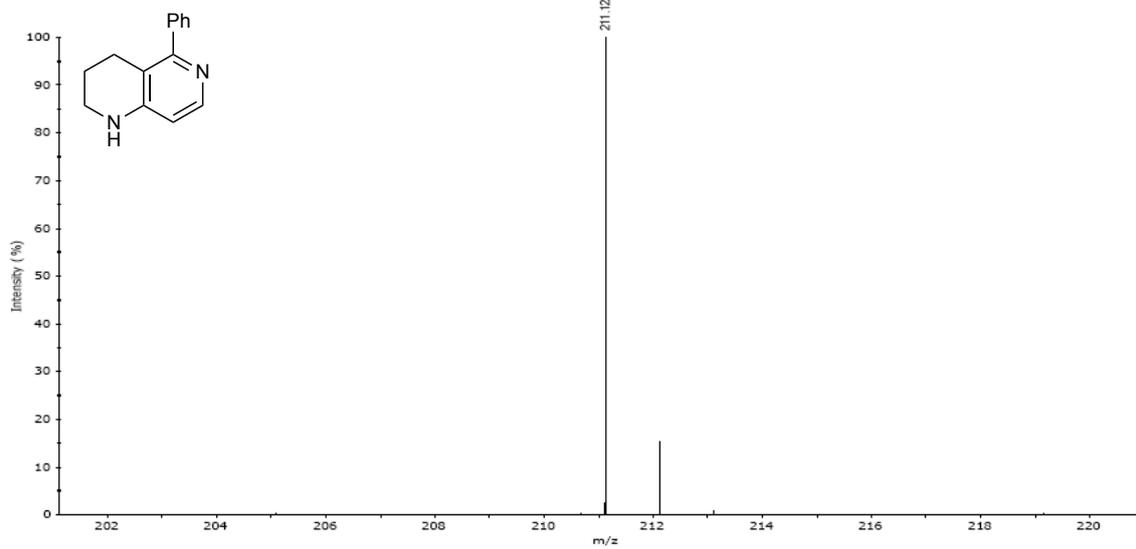


¹³C NMR



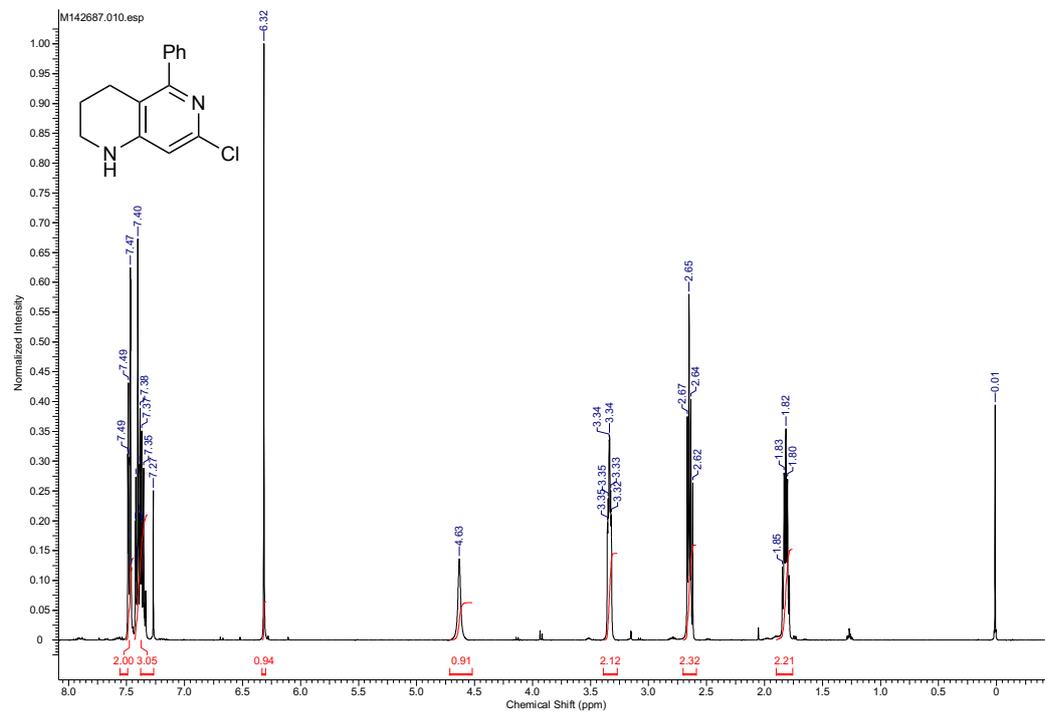
HRMS

Expanded Spectrum RT 1.58, Peak [1], Target Mass 211.1230

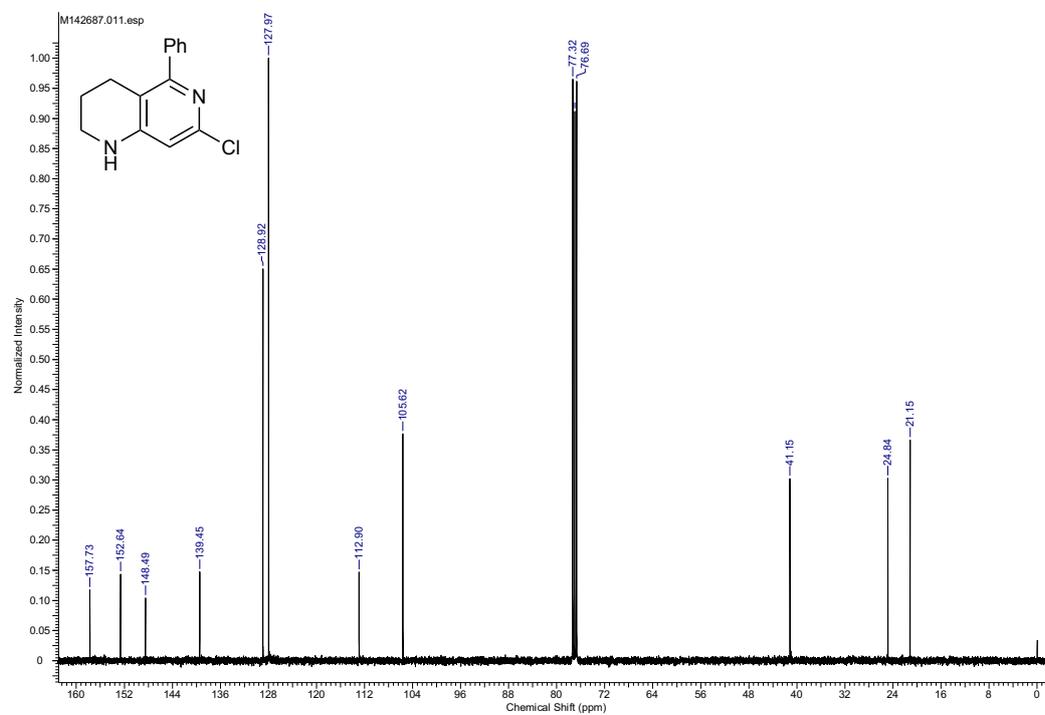


7-Chloro-5-phenyl-1,2,3,4-tetrahydro-1,6-naphthyridine, **6l**

¹H NMR

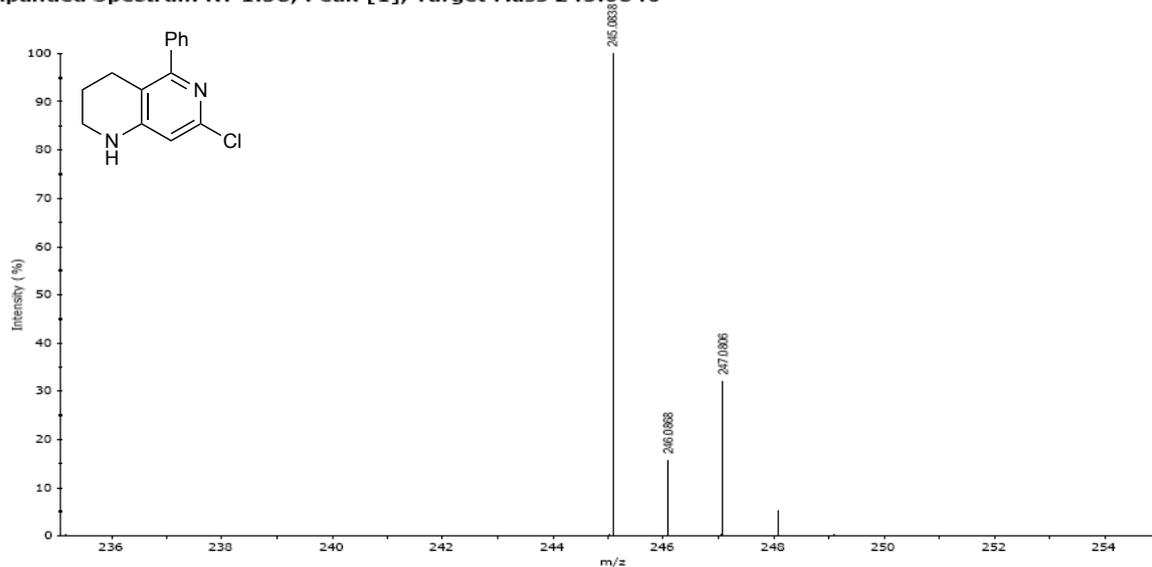


¹³C NMR



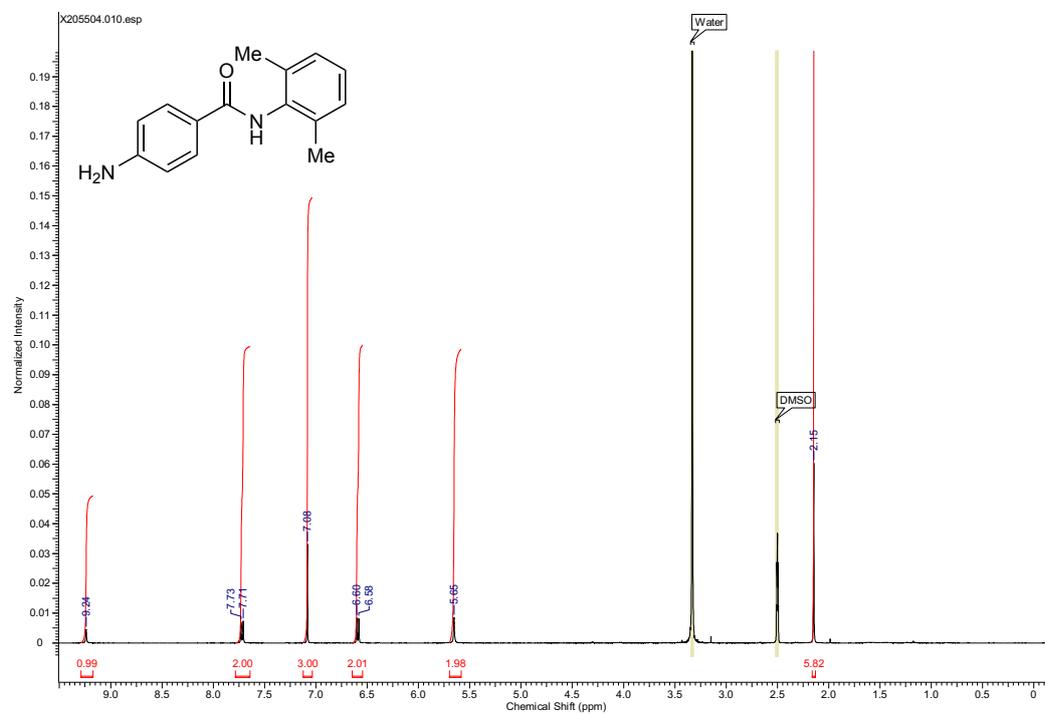
HRMS

Expanded Spectrum RT 1.58, Peak [1], Target Mass 245.0840

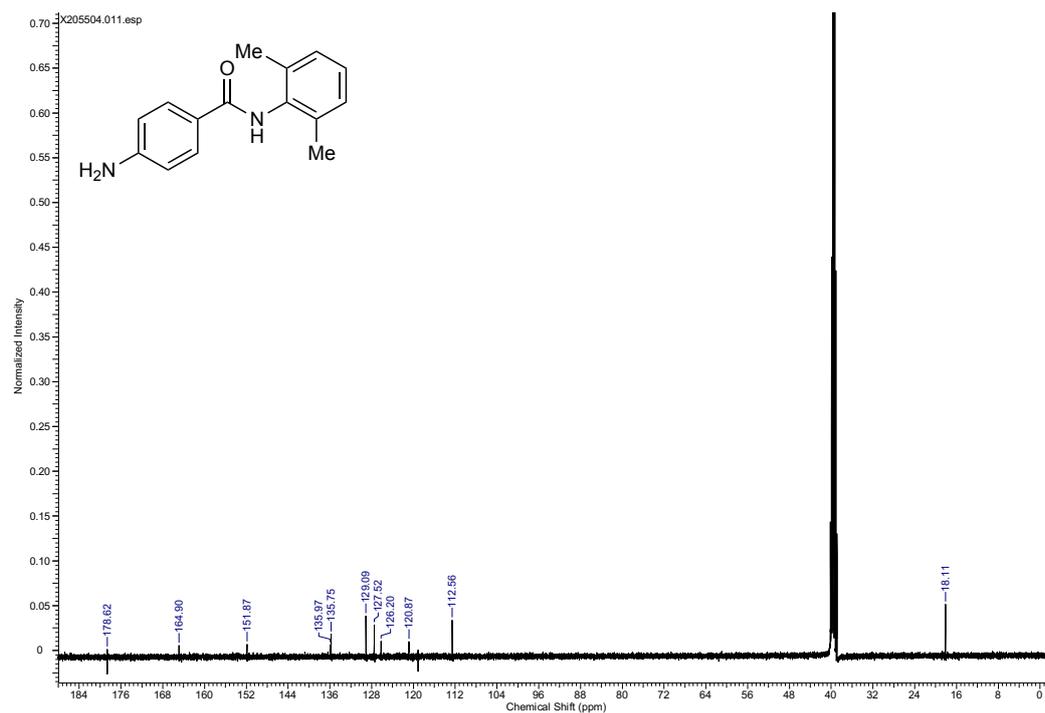


4-Amino-N-(2,6-dimethylphenyl)benzamide, 7

¹H NMR

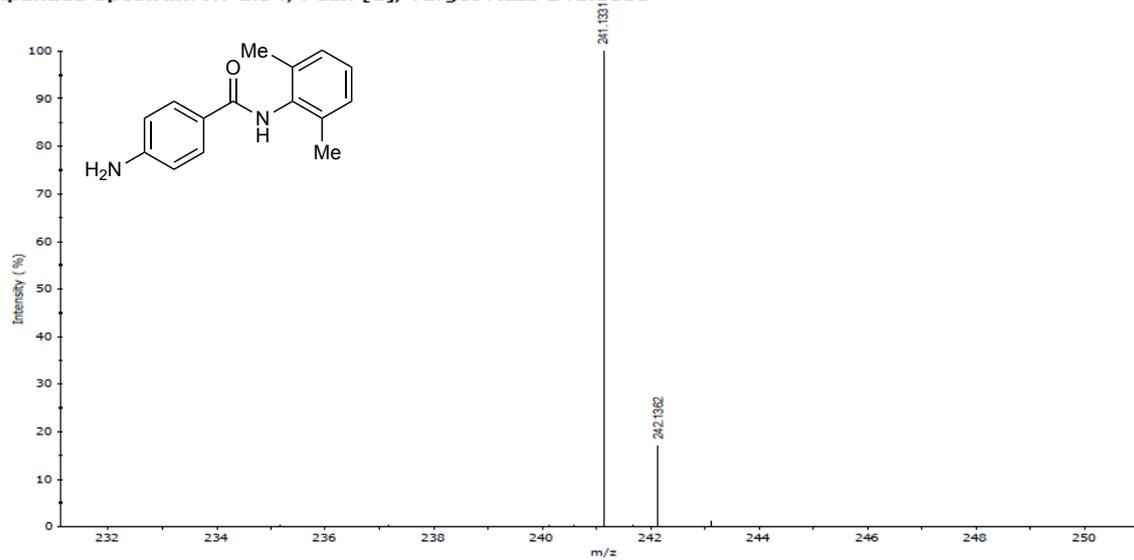


¹³C NMR



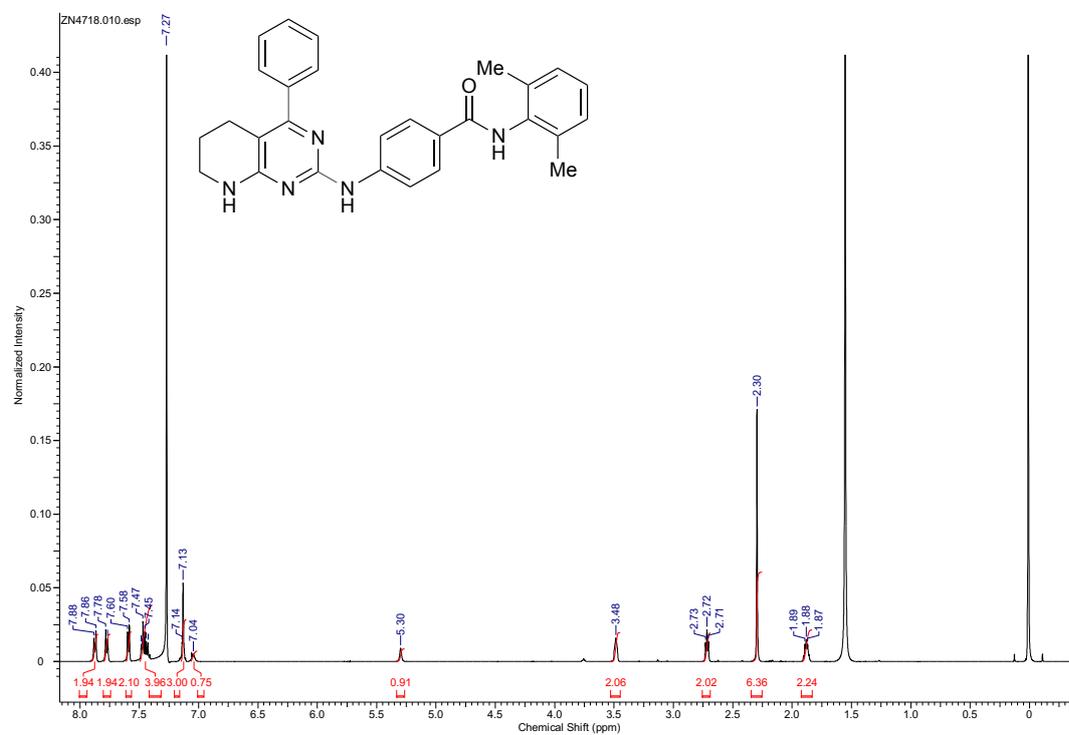
HRMS

Expanded Spectrum RT 1.54, Peak [1], Target Mass 241.1335

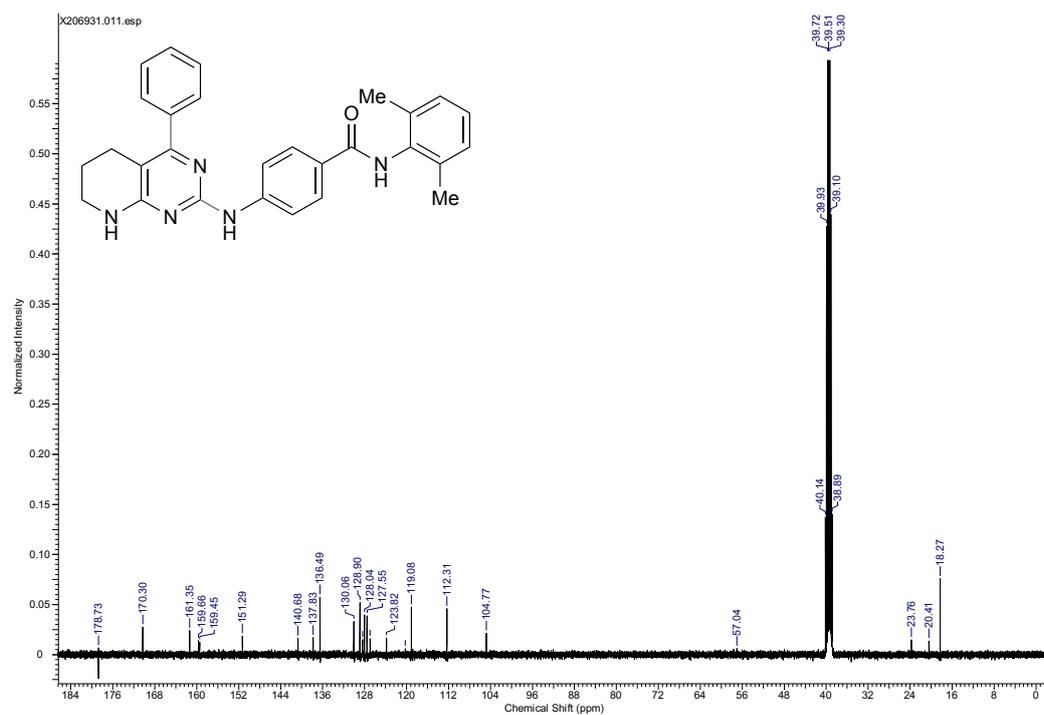


N-(2,6-Dimethylphenyl)-4-((4-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-2-yl)amino)benzamide, **8**

¹H NMR

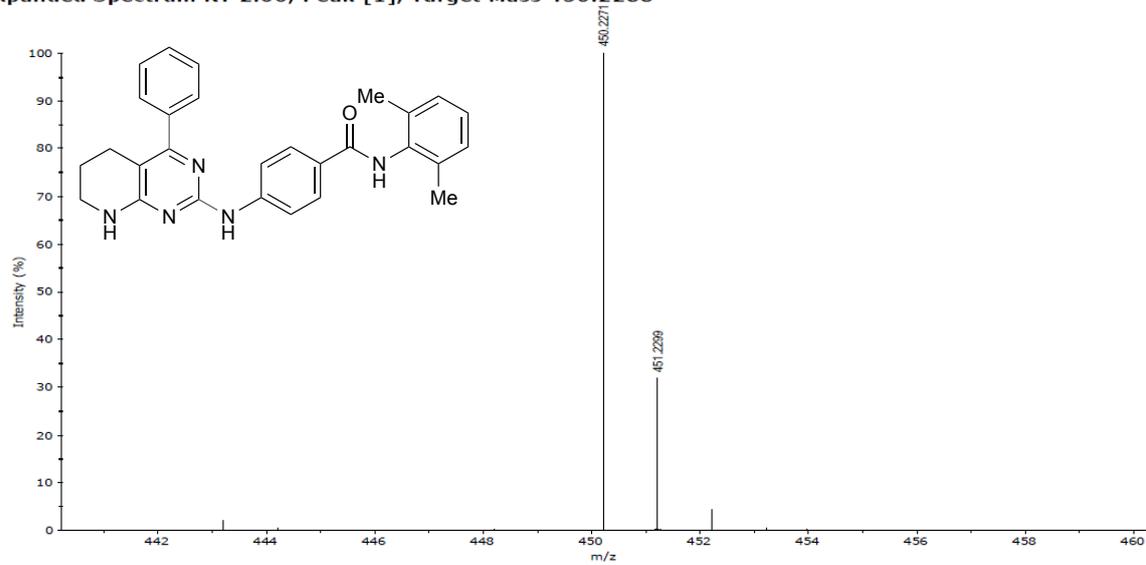


¹³C NMR



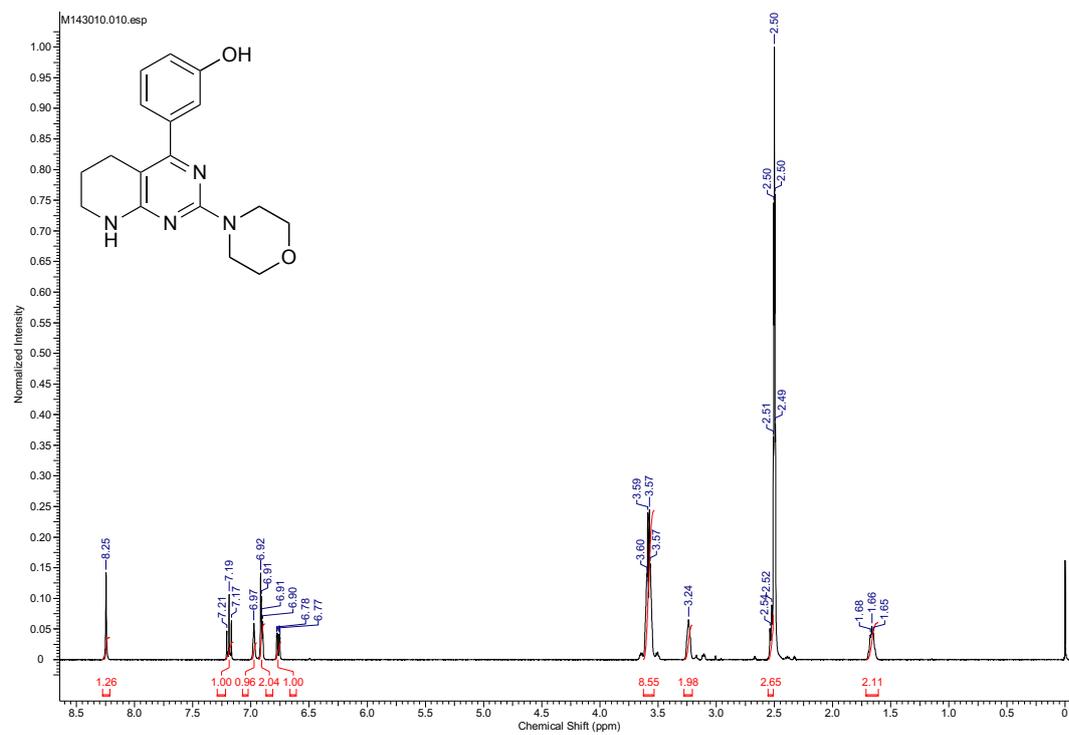
HRMS

Expanded Spectrum RT 2.66, Peak [1], Target Mass 450.2288

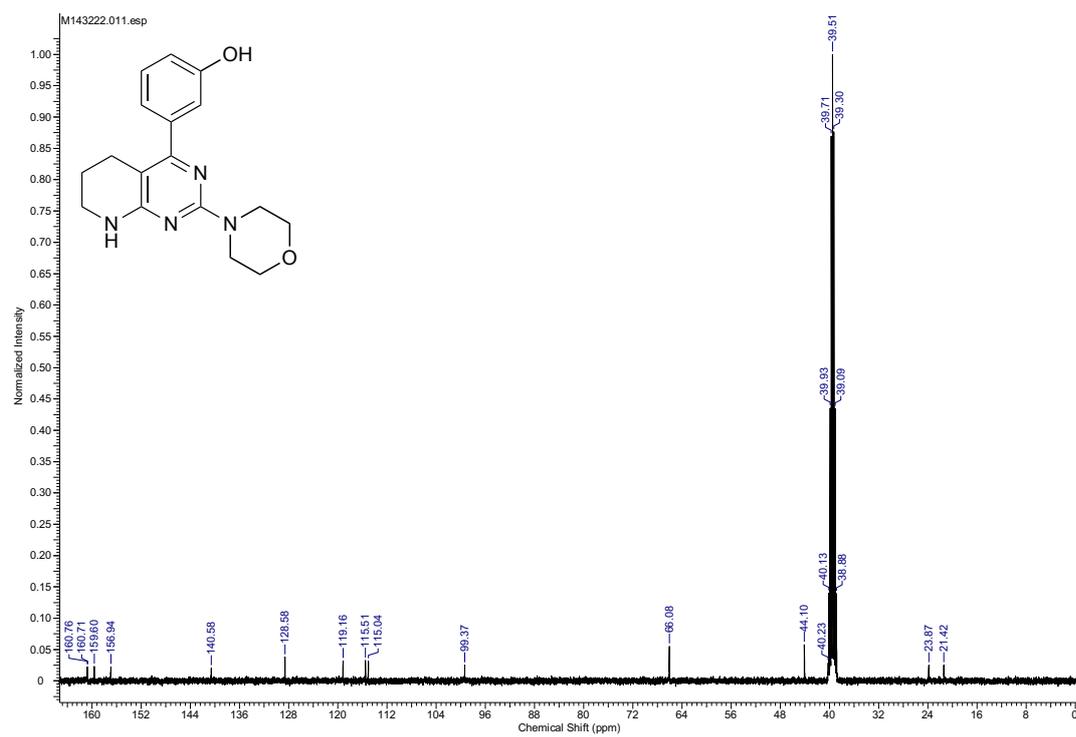


3-(2-Morpholino-5,6,7,8-tetrahydropyrido[3,2-d]pyrimidin-4-yl)phenol, 9

¹H NMR

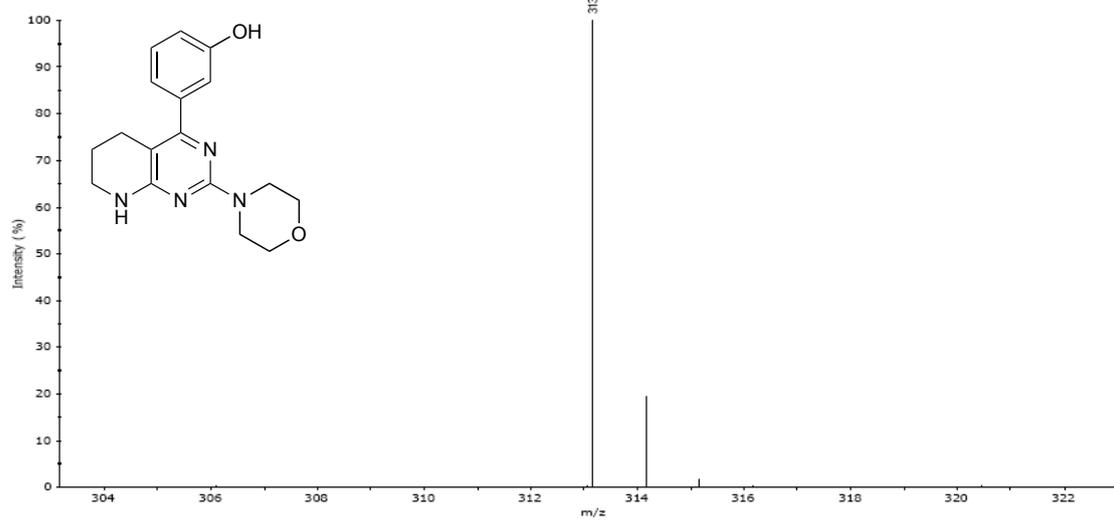


¹³C NMR



HRMS

Expanded Spectrum RT 1.31, Peak [1], Target Mass 313.1659



7 References

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