Electronic Supplementary Material (ESI) for MedChemComm.

Supporting Information

Pyrazolo[3,4-*d*]pyrimidines as Sigma-1 Receptor Ligands. Part 2: Introduction of Cyclic Substituents in Position 4.

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Analytical data: purity, NMR, HRMS

Analytical LC Methods

Method 1: Column Acquity UPLC BEH C18 2.1x50 mm, 1.7 µm; flow rate 0.6 mL/min; A: Ammonium bicarbonate 10mM; B: ACN; Gradient: 0.3 min in 98% A, 98% A to 5% A in 2.52 min, 1.02 min in 5% A.

Method 2: Column XTerra C18 2.1 x 100 mm, 3.5 µm; flow rate 0.3 mL/min; A: ACN:MeOH 1:1, B: water, C: Ammonium acetate 10 mM pH 10 adjusted with NH_4OH; Gradient: 8 min in A:B:C 10:85:5, A:B:C 10:85:5 to A:B:C 95:0:5 in 12 min, 10 min in A:B:C 95:0:5.

Method 3: Column XBridge C18 4.6 x 50 mm, 2.5 µm; flow rate 1.5 mL/min; A: Ammonium bicarbonate 10 mM, B: ACN; Gradient: 0.5 min in 98% A, 98 to 5% A in 4 min, 2 min in 5% A.

Method 4: Column SunFire C18 2.1 x 100 mm, 3.5 µm; flow rate 0.3 mL/min; A: ACN:MeOH 1:1, B: water, C: Ammonium acetate 5 mM pH 7; Gradient 3 min in A:B:C 10:85:5, A:B:C 10:85:5 to A:B:C 95:0:5 in 17 min, 10 min in in A:B:C 95:0:5.

Method 5: Column Acquity UPLC BEH C18 2.1x50 mm, 1.7 µm; flow rate 0.6 mL/min; A: Ammonium bicarbonate 10mM; B: ACN; 0.3 min in 90% A, 90% A to 5% A in 2.7 min, 0.7 min in 5% A.

Method 6: Column SunFire C18 2.1 x 100 mm, 3.5 µm; flow rate 0.3 mL/min; A: ACN:MeOH 1:1, B: water, C: Ammonium acetate 5 mM pH 7; Gradient 3 min in A:B:C 5:90:5, A:B:C 5:90:5 to A:B:C 95:0:5 in 15 min, 10 min in in A:B:C 95:0:5.

Method 7: Column XBridge C18 4.6 x 50 mm, 2.5 µm; flow rate 2 mL/min; A: Ammonium bicarbonate 10 mM, B: ACN; Gradient: 0.5 min in 98% A, 98 to 5% A in 3.7 min, 2 min in 5% A.

comp	PURITY (%)	Rt (min)	Method	FORM	NMR	HRMS $[M+H]^+$ (diff ppm)
9a	99	1.66	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (1H, s), 7.93 (1H, s), 4.79 – 4.49 (2H, m), 4.05 – 3.81 (4H, m), 3.27 – 2.94 (2H, m), 2.84 – 2.49 (4H, m), 1.90 – 1.35 (12H, m).	315.2299 (2.41)
9b	98	1.69	1	Free Base	^{1}H NMR (400 MHz, CDCl3) δ 8.38 (1H, s), 7.94 (1H, s), 4.54 (2H, t, *J*=7.2 Hz), 4.14 – 4.06 (4H, m), 2.85 (2H, t, *J*=7.2 Hz), 2.48 (4H, t, *J*=5.4 Hz), 2.20 – 2.05 (4H, m), 1.59 – 1.48 (4H, m), 1.45 – 1.36 (2H,	351.2108 (1.3)

					m).	
9c	95	3.80	3	Free Base	^{1}H NMR (400 MHz, CD_3OD) δ 8.24 (1H, s), 8.12 (1H, s), 4.59 (2H, t, *J* = 6.6 Hz), 4.02 – 3.79 (2H, m), 3.68 – 3.49 (2H, m), 3.24 – 3.07 (2H, m), 2.92 – 2.69 (4H, m), 2.09 – 1.79 (2H, m), 1.67 (4H, p, *J* = 5.7 Hz), 1.59 – 1.46 (2H, m), 1.30 – 1.14 (6H, m).	329.2456 (2.25)
9d	99	1.56	1	Free Base	^{1}H NMR (400 MHz, CD_3OD) δ 8.24 (1H, s), 8.15 (1H, s), 7.48 – 7.30 (4H, m), 7.25 (1H, t, *J* = 6.9 Hz), 4.58 – 4.45 (2H, m), 4.39 – 3.52 (6H, m), 2.86 (2H, t, *J* = 6.5 Hz), 2.69 – 2.38 (4H, m), 2.39 – 2.11 (1H, m), 1.63 – 1.49 (4H, m), 1.44 (2H, d, *J* = 5.7 Hz).	377.2453 (1.4)
9e	99	0.82	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (1H, s), 7.92 (1H, s), 4.59 (2H, t, *J* = 7.0 Hz), 4.21 – 3.36 (4H, m), 3.11 – 2.91 (2H, m), 2.69 – 2.55 (4H, m), 2.52 (3H, s), 2.40 – 2.01 (1H, m), 1.88 – 1.68 (2H, m), 1.69 – 1.56 (4H, m), 1.53 – 1.27 (2H, m).	330.2404 (1.14)
9f	96	1.45	1	Free Base	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (1H, s), 8.63 (1H, s), 4.63 (2H, t, *J*=7.1 Hz), 4.20 (2H, t, *J*=7.1 Hz), 2.93 (2H, t, *J*=7.1 Hz), 2.75 (2H, t, *J*=8.1 Hz), 2.60 – 2.46 (4H, m), 2.35 – 2.15 (2H, m), 1.66 – 1.48 (4H, m), 1.48 – 1.35 (2H, m).	315.1933 (1.75)
9g	97	1.10	1	Free Base	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (1H, s), 8.65 (1H, dd, *J*=1.3, 0.9 Hz), 8.25 (1H, s), 7.93 (1H, t, *J*=1.5 Hz), 7.31 (1H, dd, *J*=1.6, 0.9 Hz), 4.67 (2H, t, *J*=6.9 Hz), 2.89 (2H, t, *J*=6.9 Hz), 2.47 (4H, t, *J*=5.3 Hz), 1.54 – 1.44 (4H, m), 1.45 – 1.33 (2H, m).	298.1778 (1.25)

9h	100	1.54	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.18 (1H, s), 8.99 (1H, s), 8.74 – 8.55 (2H, m), 7.82 (1H, dd, *J* = 1.8, 6.5 Hz), 7.57 – 7.37 (2H, m), 4.73 (2H, t, *J* = 6.8 Hz), 2.96 (2H, t, *J* = 6.6 Hz), 2.65 – 2.47 (4H, m), 1.66 – 1.49 (4H, m), 1.49 – 1.33 (2H, m).	348.1935 (1.03)
9i	97	1.33	1	Free Base	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (1H, s), 8.29 (1H, br s), 8.18 (1H, s), 6.46 – 6.33 (1H, m), 4.62 (2H, t, *J*=6.8 Hz), 2.96 (2H, t, *J*=6.9 Hz), 2.57 (3H, s), 2.54 (4H, t, *J*=5.3 Hz), 2.29 (3H, s), 1.62 – 1.49 (4H, m), 1.49 – 1.34 (2H, m).	325.2141 (1.9)
10a	99	1.60	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.00 (1H, s), 8.53 (1H, s), 8.32 – 8.16 (2H, m), 7.63 (3H, dq, *J*=5.3, 2.0 Hz), 4.70 (2H, t, *J*=6.8 Hz), 2.94 (2H, t, *J*=6.8 Hz), 2.54 (4H, t, *J*=5.2 Hz), 1.64 – 1.49 (4H, m), 1.49 – 1.37 (2H, m).	308.1786 (1.97)
10b	98	16.96	4	Free Base	^{1}H NMR (250 MHz, $CDCl_3$) δ 9.07 (1H, s), 8.00 (1H, s), 7.53 (1H, d, *J* = 7.1 Hz), 7.51 – 7.29 (3H, m), 4.67 (2H, t, *J* = 7.2 Hz), 2.99 – 2.80 (2H, m), 2.60 – 2.45 (4H, m), 2.43 (3H, s), 1.63 – 1.47 (4H, m), 1.47 – 1.34 (2H, m).	322.2032 (1.81)
10c	95	18.03	4	HCl	^{1}H NMR (250 MHz, $CDCl_3$) δ 12.71 (1H, s), 9.12 (1H, s), 8.44 (1H, s), 8.17 – 7.92 (2H, m), 7.63 – 7.35 (2H, m), 5.43 – 4.98 (2H, m), 3.88 – 3.54 (4H, m), 2.95 – 2.58 (2H, m), 2.50 (3H, s), 2.42 – 2.18 (2H, m), 1.56 – 1.09 (3H, m), 1.09 – 0.64 (1H, m).	322.2030 (1.26)
10d	98	12.54	4	HCl	^{1}H NMR (250 MHz, $CDCl_3$) δ 12.58 (1H, s), 9.25 (1H, s), 8.35 (1H, s), 7.88 (1H, d, *J* = 7.2 Hz), 7.60 (1H, t, *J* = 7.8 Hz), 7.19 (1H, t, *J* = 7.0 Hz),	352.2136 (1.23)

					7.11 (1H, d, *J* = 8.4 Hz), 5.28 – 4.98 (2H, m), 4.21 (2H, q, *J* = 6.6 Hz), 3.83 – 3.52 (4H, m), 2.96 – 2.64 (2H, m), 2.43 – 2.12 (2H, m), 1.35 (3H, t, *J* = 6.8 Hz), 1.48 – 1.21 (3H, m), 0.98 – 0.74 (1H, m).	
10e	95	1.99	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.04 (1H, s), 8.33 (1H, s), 8.23 (2H, dd, *J* = 5.3, 8.9 Hz), 7.28 (2H, t, *J* = 8.6 Hz), 4.74 (2H, t, *J* = 7.0 Hz), 3.13 – 2.87 (2H, m), 2.73 – 2.42 (4H, m), 1.69 – 1.51 (4H, m), 1.51 – 1.31 (2H, m).	326.1781 (0.56)
10f	95	1.91	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (1H, s), 8.35 (1H, s), 8.21 (2H, d, *J* = 8.9 Hz), 7.10 (2H, d, *J* = 8.9 Hz), 4.71 (2H, t, *J* = 7.0 Hz), 3.92 (3H, s), 3.00 (2H, t, *J* = 7.1 Hz), 2.68 – 2.43 (4H, m), 1.67 – 1.51 (4H, m), 1.51 – 1.32 (2H, m).	338.1980 (1.49)
10g	96	1.87	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (1H, s), 8.34 (1H, s), 8.32 (2H, d, *J* = 8.5 Hz), 7.89 (2H, d, *J* = 8.5 Hz), 4.90 – 4.64 (2H, m), 3.15 – 2.89 (2H, m), 2.74 – 2.45 (4H, m), 1.77 – 1.49 (4H, m), 1.50 – 1.33 (2H, m).	333.1828 (1.66)
10h	95	1.95	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.05 (1H, s), 8.13 (1H, s), 7.76 – 7.43 (4H, m), 4.71 (2H, t, *J* = 6.9 Hz), 2.94 (2H, t, *J* = 6.7 Hz), 2.64 – 2.44 (4H, m), 1.63 – 1.49 (4H, m), 1.49 – 1.32 (2H, m).	342.1485 (1.42)
10i	95	2.84	5	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.05 (1H, s), 8.33 (1H, s), 8.16 (2H, d, *J* = 8.6 Hz), 7.58 (2H, d, *J* = 8.6 Hz), 4.78 – 4.71 (2H, m), 3.04 – 2.98 (2H, m), 2.61 – 2.54 (4H, m), 1.77 – 1.49 (4H, m), 1.47 – 1.41 (2H, m).	342.1487 (2.04)

10j	97	6.30	3	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (1H, s), 8.06 (1H, s), 7.44 (1H, d, *J* = 10.4 Hz), 7.43 (1H, s), 7.28 (1H, dd, *J* = 2.2, 10.4 Hz), 4.73 (2H, t, *J* = 6.6 Hz), 3.09 – 2.92 (2H, m), 2.70 – 2.49 (4H, m), 2.41 (3H, s), 1.78 – 1.52 (4H, m), 1.53 – 1.30 (2H, m).	356.1640 (0.92)
10k	95	6.33	3	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.00 (1H, s), 8.10 (1H, s), 7.41 – 7.21 (3H, m), 4.71 (2H, t, *J* = 6.7 Hz), 2.96 (2H, t, *J* = 6.7 Hz), 2.57 (4H, t, *J* = 4.9 Hz), 2.40 (3H, s), 2.31 (3H, s), 1.66 – 1.51 (4H, m), 1.51 – 1.36 (2H, m).	336.2187 (1.21)
10l	95	1.97	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.04 (1H, d, *J* = 1.9 Hz), 8.27 (1H, dd, *J* = 2.0, 3.7 Hz), 8.13 – 7.95 (1H, m), 7.35 – 7.15 (2H, m), 4.71 (2H, t, *J* = 5.7 Hz), 2.95 (2H, t, *J* = 6.7 Hz), 2.73 – 2.41 (4H, m), 1.66 – 1.51 (4H, m), 1.51 – 1.38 (2H, m).	344.1686 (2.19)
10m	99	1.88	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.05 (1H, s), 8.05 (1H, s), 7.81 (1H, dd, *J* = 6.7, 8.5 Hz), 6.95 – 6.71 (2H, m), 4.88 – 4.65 (2H, m), 3.88 (3H, s), 3.22 – 2.89 (2H, m), 2.81 – 2.50 (4H, m), 1.84 – 1.55 (4H, m), 1.55 – 1.32 (2H, m).	356.1886 (1.49)
10n	95	2.03	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.06 (1H, s), 8.00 (1H, s), 7.53 (1H, dd, *J* = 5.8, 8.4 Hz), 7.14 – 7.00 (2H, m), 4.91 – 4.66 (2H, m), 3.24 – 2.88 (2H, m), 2.79 – 2.50 (4H, m), 2.45 (3H, s), 1.79 – 1.52 (4H, m), 1.54 – 1.37 (2H, m).	340.1937 (1.49)

10o	100	2.20	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.05 (1H, s), 8.27 (1H, d, *J* = 4.1 Hz), 7.98 (1H, t, *J* = 8.1 Hz), 7.57 – 7.40 (2H, m), 4.70 (2H, t, *J* = 6.9 Hz), 2.93 (2H, t, *J* = 6.7 Hz), 2.54 (4H, t, *J* = 4.6 Hz), 1.64 – 1.48 (4H, m), 1.48 – 1.35 (2H, m).	360.1389 (1.05)
10p	98	2.11	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (1H, s), 7.92 (1H, s), 7.73 – 7.50 (2H, m), 7.42 (1H, td, *J* = 2.6, 8.4 Hz), 5.07 – 4.64 (2H, m), 3.38 – 2.90 (2H, m), 2.78 – 2.43 (4H, m), 1.87 – 1.54 (4H, m), 1.54 – 1.30 (2H, m).	394.1653 (0.95)
10q	100	2.03	1	Free Base	^{1}H NMR (400 MHz, CD_3OD) δ 9.02 (1H, s), 8.03 (1H, s), 8.00 – 7.92 (1H, m), 7.88 – 7.75 (2H, m), 7.65 (1H, ddt, *J* = 0.7, 1.5, 7.8 Hz), 4.72 (2H, t, *J* = 6.7 Hz), 2.94 (2H, t, *J* = 6.7 Hz), 2.60 – 2.44 (4H, m), 1.53 (4H, p, *J* = 5.5 Hz), 1.48 – 1.36 (2H, m).	376.1748 (1.2)
11a	96	12.56	4	Free Base	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (1H, d, *J* = 1.6 Hz), 9.09 (1H, s), 8.81 (1H, dd, *J* = 1.7, 4.8 Hz), 8.53 (1H, dt, *J* = 2.0, 8.0 Hz), 8.37 (1H, s), 7.54 (1H, ddd, *J* = 0.9, 4.8, 8.0 Hz), 4.69 (2H, t, *J* = 7.0 Hz), 2.92 (2H, t, *J* = 7.0 Hz), 2.50 (4H, t, *J* = 5.2 Hz), 1.52 (4H, p, *J* = 5.5 Hz), 1.46 – 1.34 (2H, m).	309.1828 (1.73)
11b	95	12.55	4	Free Base	^{1}H NMR (250 MHz, $CDCl_3$) δ 9.09 (1H, s), 8.68 (1H, dd, *J* = 1.8, 4.9 Hz), 7.98 (1H, s), 7.85 (1H, dd, *J* = 1.8, 7.7 Hz), 7.33 (1H, dd, *J* = 4.9, 7.8 Hz), 4.68 (2H, t, *J* = 7.1 Hz), 2.91 (2H, t, *J* = 7.1 Hz), 2.65 (3H, s), 2.50 (4H, t, *J* = 5.0 Hz), 1.52 (4H, p, *J* = 5.5 Hz), 1.47 – 1.35 (2H, m).	323.1983 (1.36)

11c	98	12.07	4	HCl	^{1}H NMR (250 MHz, CD_3OD) δ 9.18 (1H, s), 9.10 (1H, s), 8.89 (1H, d, *J* = 7.0 Hz), 8.41 (1H, s), 7.86 (1H, d, *J* = 6.9 Hz), 5.03 (2H, t, *J* = 6.0 Hz), 4.26 (3H, s), 3.90 – 3.70 (4H, m), 3.10 (2H, t, *J* = 12.1 Hz), 2.11 – 1.69 (5H, m), 1.66 – 1.45 (1H, m).	339.1933 (-1.66)
11d	97	12.75	4	HCl	^{1}H NMR (250 MHz, CD_3OD) δ 9.23 (1H, s), 9.14 (1H, s), 8.92 (1H, d, *J* = 6.1 Hz), 8.45 (1H, s), 8.21 (1H, d, *J* = 6.1 Hz), 5.06 (2H, t, *J* = 5.9 Hz), 3.97 – 3.75 (4H, m), 3.10 (2H, t, *J* = 12.0 Hz), 2.78 (3H, s), 2.12 – 1.69 (5H, m), 1.69 – 1.48 (1H, m).	323.1983 (1.46)
11e	97	14.24	4	Free Base	^{1}H NMR (250 MHz, $CDCl_3$) δ 9.21 (1H, d, *J* = 2.2 Hz), 9.08 (1H, s), 8.64 (1H, d, *J* = 2.2 Hz), 8.37 (1H, s), 8.33 (1H, t, *J* = 2.2 Hz), 4.68 (2H, t, *J* = 7.0 Hz), 2.91 (2H, t, *J* = 7.0 Hz), 2.65 – 2.41 (7H, m), 1.52 (4H, p, *J* = 5.0 Hz), 1.47 – 1.32 (2H, m).	323.1985 (2.00)
11f	99	14.41	4	Free Base	^{1}H NMR (250 MHz, $CDCl_3$) δ 9.06 (1H, s), 8.36 (1H, d, *J* = 4.5 Hz), 8.19 (1H, d, *J* = 7.4 Hz), 8.14 (1H, s), 7.11 (1H, dd, *J* = 4.9, 7.5 Hz), 4.66 (2H, t, *J* = 7.2 Hz), 4.04 (3H, s), 2.91 (2H, t, *J* = 7.3 Hz), 2.61 – 2.41 (4H, m), 1.66 – 1.48 (4H, m), 1.48 – 1.33 (2H, m).	339.1934 (1.85)
11g	99	14.92	4	Free Base	^{1}H NMR (250 MHz, $CDCl_3$) δ 9.42 (1H, s), 9.20 (1H, s), 8.90 (1H, s), 8.40 (1H, d, *J* = 8.2 Hz), 8.21 – 8.04 (2H, m), 7.91 – 7.63 (2H, m), 4.72 (2H, t, *J* = 7.1 Hz), 2.95 (2H, t, *J* = 7.1 Hz), 2.53 (4H, t, *J* = 5.2 Hz), 1.63 – 1.47 (4H, m), 1.47 – 1.38 (2H, m).	359.1984 (1.45)

11h	100	19.23	2	Free Base	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (1H, s), 8.95 (1H, s), 8.88 – 8.84 (1H, m), 8.63 (1H, dt, *J* = 1.1, 7.9 Hz), 7.91 (1H, td, *J* = 1.8, 7.7 Hz), 7.46 (1H, ddd, *J* = 1.3, 4.7, 7.5 Hz), 4.68 (2H, t, *J* = 7.1 Hz), 2.92 (2H, t, *J* = 7.0 Hz), 2.50 (4H, t, *J* = 5.3 Hz), 1.51 (4H, p, *J* = 5.5 Hz), 1.46 – 1.31 (2H, m).	309.1829 (2.27)
11i	99	17.37	4	Free Base	^{1}H NMR (250 MHz, $CDCl_3$) δ 9.05 (1H, s), 8.98 (1H, s), 8.41 (1H, d, *J* = 7.9 Hz), 7.79 (1H, t, *J* = 7.8 Hz), 7.31 (1H, d, *J* = 8.1 Hz), 4.67 (2H, t, *J* = 7.0 Hz), 2.90 (6H, t, *J* = 6.7 Hz), 2.72 (3H, s), 2.63 – 2.41 (4H, m), 1.66 – 1.45 (4H, m), 1.45 – 1.31 (2H, m).	323.1984 (1.6)
11j	100	1.47	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.11 (1H, s), 8.83 (2H, d, *J* = 6.2 Hz), 8.65 (1H, s), 8.26 (2H, d, *J* = 6.2 Hz), 4.73 (2H, t, *J* = 6.7 Hz), 2.95 (2H, t, *J* = 6.7 Hz), 2.54 (4H, t, *J* = 5.4 Hz), 1.53 (4H, p, *J* = 5.8 Hz), 1.49 – 1.36 (2H, m).	309.1828 (2.03)
12a	95	1.59	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.52 (1H, s), 9.33 (1H, s), 9.03 (1H, s), 8.34 (1H, s), 4.90 – 4.61 (2H, m), 3.15 – 2.83 (2H, m), 2.73 – 2.37 (4H, m), 1.77 – 1.49 (4H, m), 1.51 – 1.33 (2H, m).	315.1393 (1.96)
12b	99	1.84	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 8.81 (1H, dd, *J* = 0.7, 2.8 Hz), 8.77 (1H, s), 8.68 (1H, s), 7.99 (1H, dd, *J* = 0.7, 1.6 Hz), 6.65 (1H, dd, *J* = 1.6, 2.8 Hz), 4.67 (2H, t, *J* = 6.8 Hz), 2.92 (2H, t, *J* = 6.8 Hz), 2.53 (4H, t, *J* = 5.3 Hz), 1.54 (4H, p, *J* = 5.5 Hz), 1.49 – 1.34 (2H, m).	298.1781 (2.11)

12c	98	1.35	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 8.83 (1H, d, *J* = 1.4 Hz), 8.63 (1H, s), 8.58 (1H, d, *J* = 1.4 Hz), 8.37 (1H, s), 4.65 (2H, t, *J* = 6.9 Hz), 4.03 (3H, s), 2.91 (2H, t, *J* = 6.8 Hz), 2.61 – 2.47 (4H, m), 1.54 (4H, p, *J* = 5.5, 6.0 Hz), 1.48 – 1.35 (2H, m).	312.1936 (1.66)
12d	100	1.62	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 8.82 (1H, s), 8.65 (1H, s), 8.61 (1H, s), 8.40 (1H, s), 4.67 (1H, hept, *J* = 6.8 Hz), 4.66 (2H, t, *J* = 7.0 Hz), 2.92 (2H, t, *J* = 6.8 Hz), 2.53 (4H, t, *J* = 4.8 Hz), 1.59 (6H, d, *J* = 6.7 Hz), 1.57 – 1.49 (4H, m), 1.49 – 1.38 (2H, m).	340.2251 (1.92)
12e	95	13.84	4	HCl	^{1}H NMR (250 MHz, $CDCl_3$) δ 12.71 (1H, br s), 9.10 (1H, s), 8.11 (1H, s), 5.24 – 5.07 (2H, m), 3.86 – 3.51 (4H, m), 2.87 – 2.66 (2H, m), 2.63 (3H, s), 2.47 (3H, s), 2.41 – 2.21 (2H, m), 1.97 – 1.80 (2H, m), 1.50 – 1.26 (2H, m).	327.1936 (2.38)
12f	99	15.20	6	Free Base	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (1H, s), 8.24 (1H, s), 7.64 (1H, d, *J*=2.1 Hz), 7.01 (1H, d, *J*=2.1 Hz), 4.66 (2H, t, *J*=7.0 Hz), 4.38 (3H, s), 2.90 (2H, t, *J*=7.0 Hz), 2.49 (4H, t, *J*=5.2 Hz), 1.57 – 1.46 (4H, m), 1.45 – 1.36 (2H, m).	312.1938 (2.24)
12g	95	2.17	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (1H, s), 8.25 (1H, s), 7.22 (1H, s), 4.73 (2H, t, *J* = 6.4 Hz), 4.42 (3H, s), 3.09 – 2.84 (2H, m), 2.73 – 2.32 (4H, m), 1.71 – 1.49 (4H, m), 1.49 – 1.29 (2H, m).	380.1809 (1.06)
12h	98	1.89	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (1H, s), 8.26 (1H, s), 7.11 (1H, dd, *J* = 1.7, 4.0 Hz), 6.92 (1H, t, *J* = 2.1 Hz), 6.32 (1H, dd, *J* = 2.6, 4.0 Hz), 4.81 – 4.60 (2H, m), 4.16 (3H, s), 3.16 – 2.93 (2H, m), 2.74 – 2.46	311.1986 (2.34)

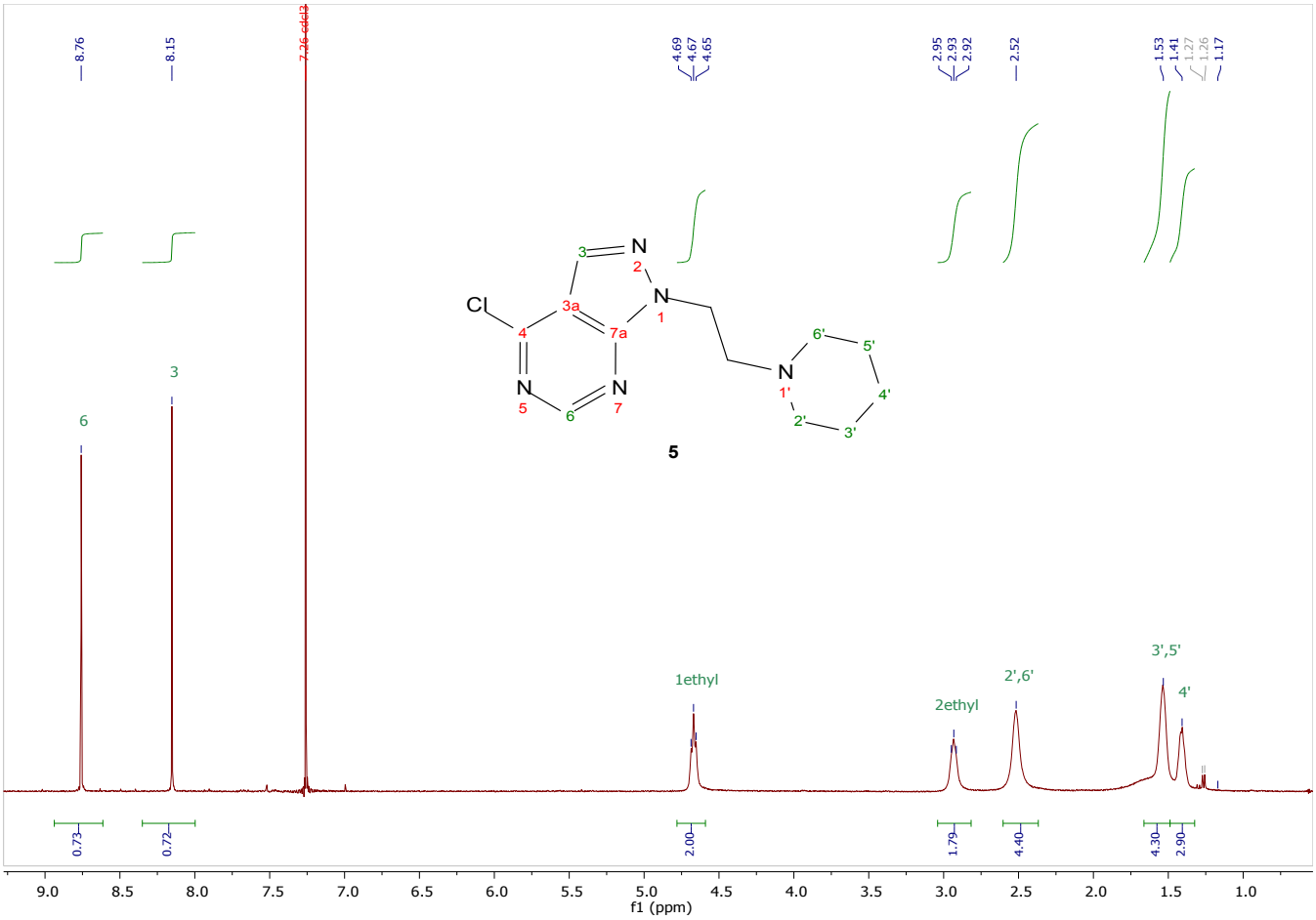
					(4H, m), 1.76 – 1.54 (4H, m), 1.54 – 1.35 (2H, m).	
12i	100	1.40	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 8.95 (1H, s), 8.49 (1H, s), 8.07 (1H, d, *J* = 1.0 Hz), 7.94 (1H, s), 4.67 (2H, t, *J* = 6.8 Hz), 4.19 (3H, s), 2.92 (2H, t, *J* = 6.8 Hz), 2.53 (4H, t, *J* = 5.2 Hz), 1.54 (4H, p, *J* = 5.4, 5.9 Hz), 1.50 – 1.35 (2H, m).	312.1935 (-1.4)
12j	95	1.27	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 8.82 (1H, d, *J* = 1.3 Hz), 8.74 (1H, d, *J* = 1.4 Hz), 8.11 (1H, s), 7.85 (1H, s), 4.65 (2H, t, *J* = 6.8 Hz), 3.86 (3H, d, *J* = 1.3 Hz), 2.94 (2H, t, *J* = 6.8 Hz), 2.65 – 2.44 (4H, m), 1.68 – 1.49 (4H, m), 1.49 – 1.32 (2H, m).	312.1934 (0.82)
12k	99	2.96	5	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 8.82 (1H, d, *J* = 1.3 Hz), 8.61 (1H, d, *J* = 0.9 Hz), 8.10 (1H, dd, *J* = 0.9, 4.3 Hz), 7.20 (1H, dd, *J* = 1.3, 4.2 Hz), 4.66 (2H, t, *J* = 6.7 Hz), 2.92 (2H, t, *J* = 6.7 Hz), 2.53 (4H, t, *J* = 5.3 Hz), 1.53 (4H, p, *J* = 5.4 Hz), 1.48 – 1.29 (2H, m).	348.1049 (1.51)
12l	98	1.46	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (1H, s), 8.71 (1H, s), 8.09 – 7.88 (1H, m), 7.60 – 7.39 (1H, m), 5.06 – 4.68 (2H, m), 3.10 (2H, s), 2.76 – 2.35 (4H, m), 1.86 – 1.52 (4H, m), 1.52 – 1.32 (2H, m).	299.1620 (1.76)
12m	98	1.87	1	Free Base	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.01 (1H, s), 8.82 (1H, s), 8.16 (1H, d, *J* = 3.1 Hz), 7.65 (1H, d, *J* = 3.1 Hz), 4.76 (2H, t, *J* = 6.0 Hz), 3.26 – 2.91 (2H, m), 2.85 – 2.41 (4H, m), 1.84 – 1.52 (4H, m), 1.52 – 1.31 (2H, m).	315.1395 (2.7)

13a	95	1.98	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.05 (1H, d, *J* = 1.5 Hz), 8.13 (1H, d, *J* = 1.5 Hz), 7.76 – 7.47 (4H, m), 4.70 (2H, td, *J* = 1.6, 6.3 Hz), 3.00 (2H, td, *J* = 1.4, 6.2 Hz), 2.66 (4H, t, *J* = 5.7 Hz), 1.83 (4H, tt, *J* = 5.6, 12.9 Hz).	378.1297 (1.54)
13b	95	2.05	1	Free Base	^{1}H NMR (300 MHz, CD_3OD) δ 9.05 (1H, s), 8.16 (1H, s), 7.72 (1H, dd, *J* = 6.0, 8.6 Hz), 7.51 (1H, dd, *J* = 2.5, 8.7 Hz), 7.34 (1H, td, *J* = 2.5, 8.3 Hz), 4.70 (2H, t, *J* = 6.3 Hz), 3.00 (2H, t, *J* = 6.3 Hz), 2.66 (4H, t, *J* = 5.6 Hz), 1.83 (4H, tt, *J* = 5.6, 13.2 Hz).	396.1201 (0.98)

Representative Spectra

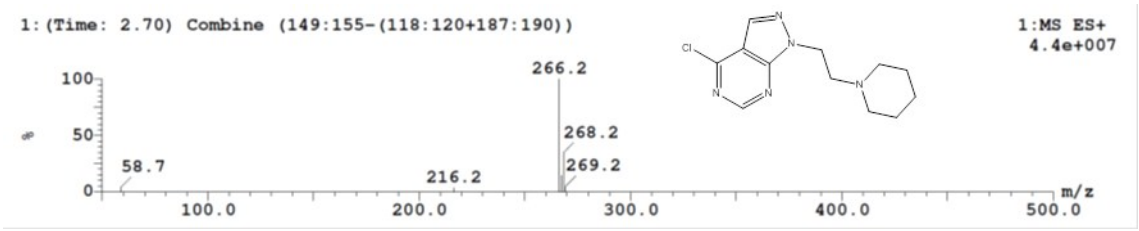
Spectra of Compound 5

^{1}H-NMR spectrum

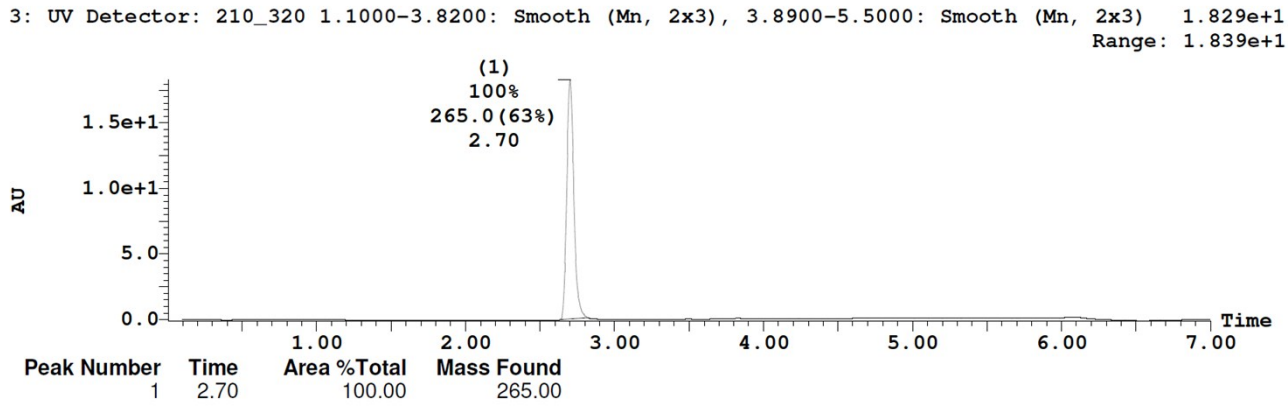


5

MS Spectrum

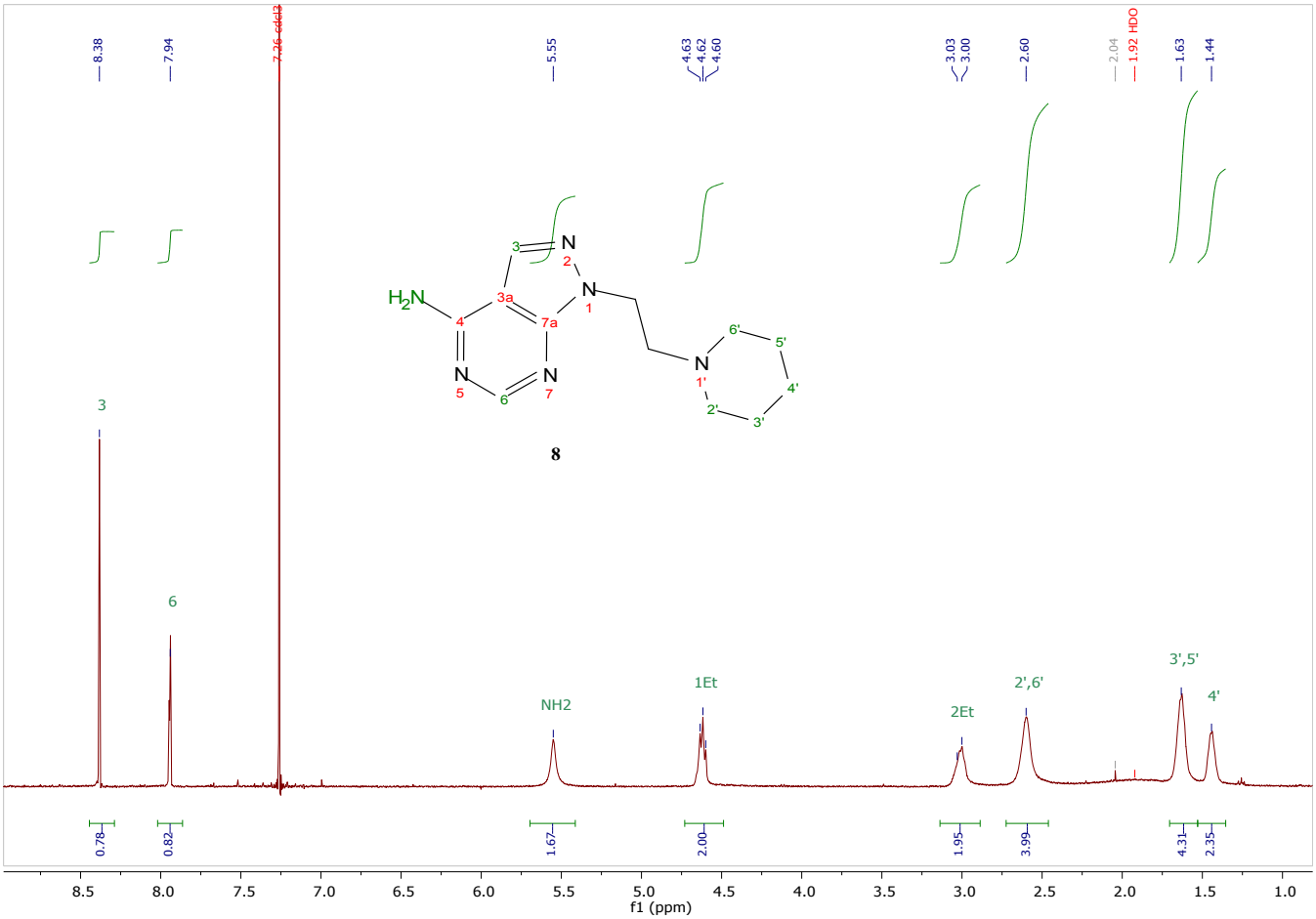


PDA Chromatogram

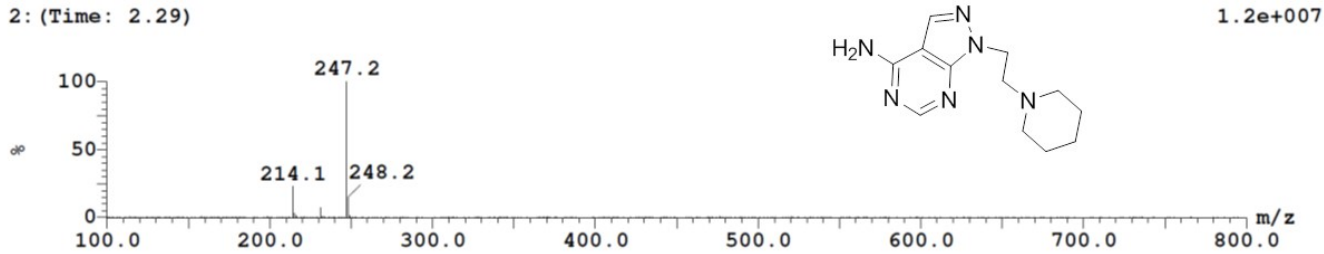


Spectra of Compound 8

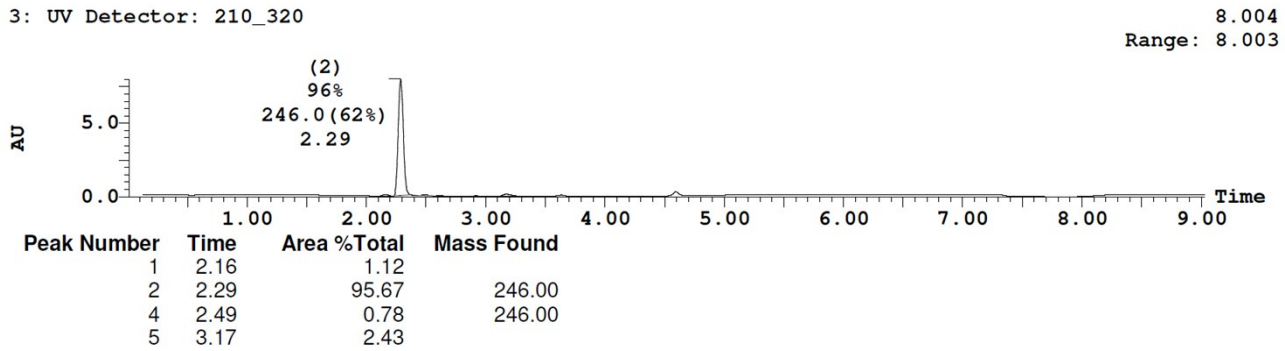
^{1}H-NMR spectrum



MS Spectrum



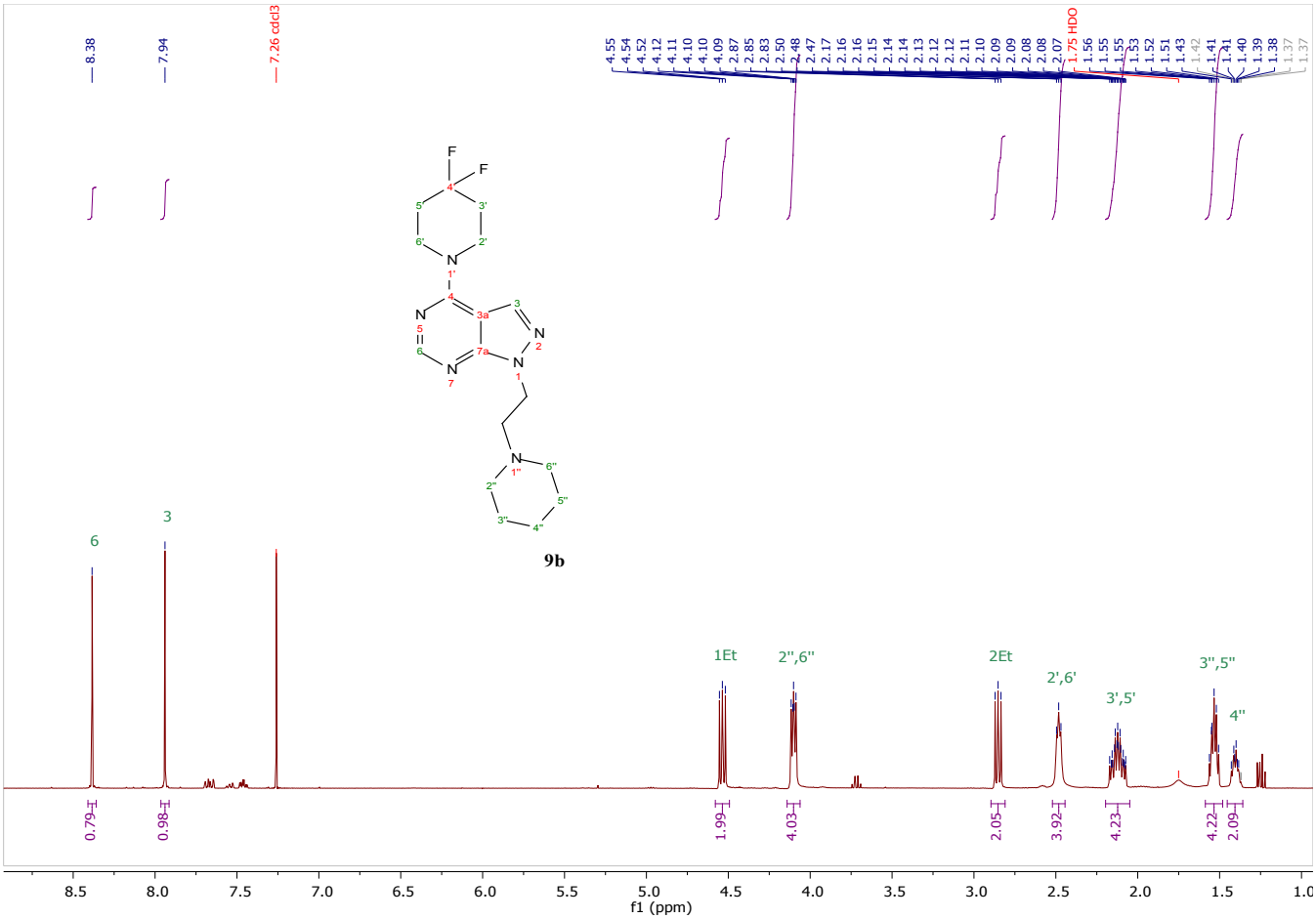
PDA Chromatogram



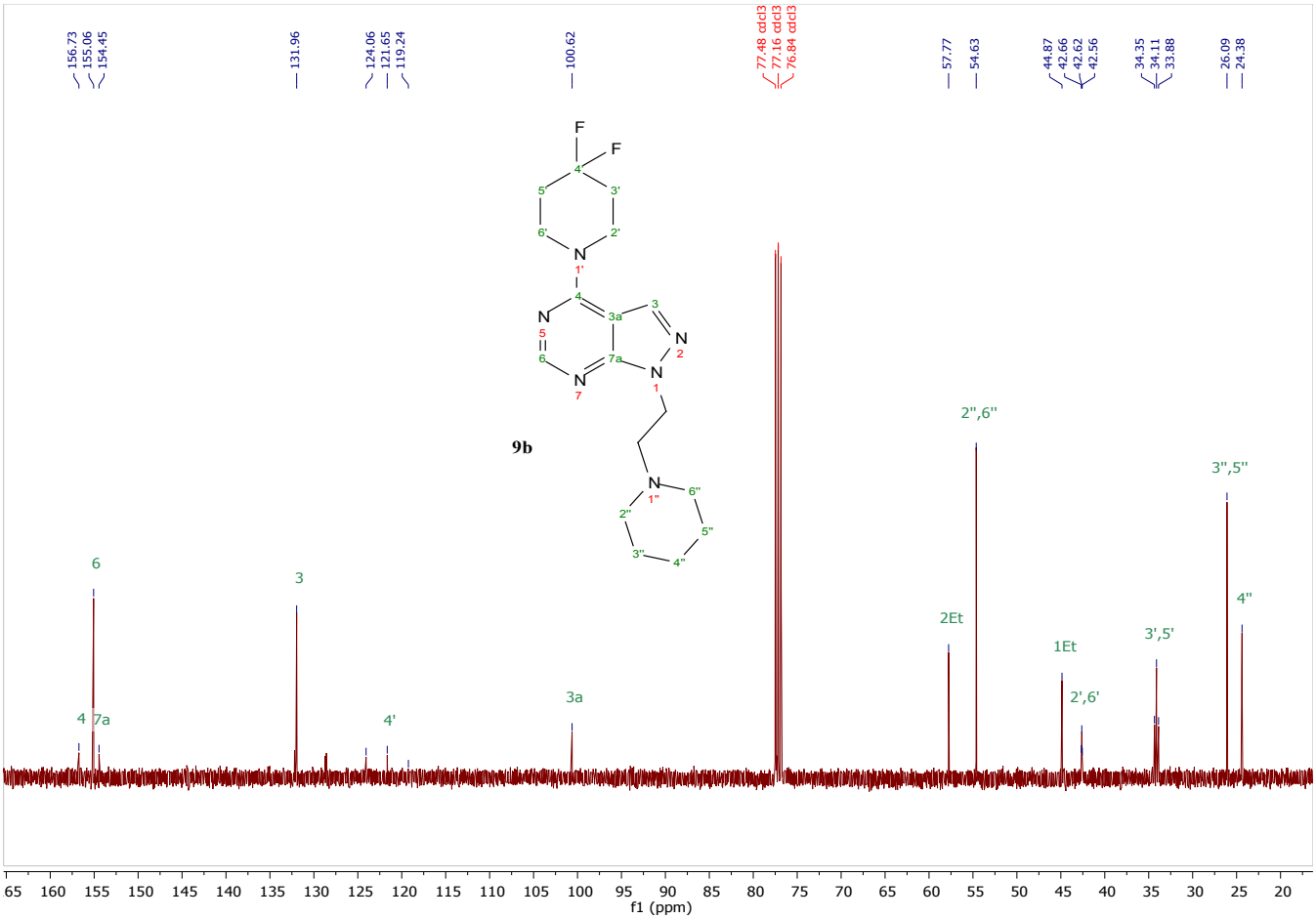
Peak Number	Time	Area %Total	Mass Found
1	2.16	1.12	
2	2.29	95.67	246.00
4	2.49	0.78	246.00
5	3.17	2.43	

Spectra of Compound 9b

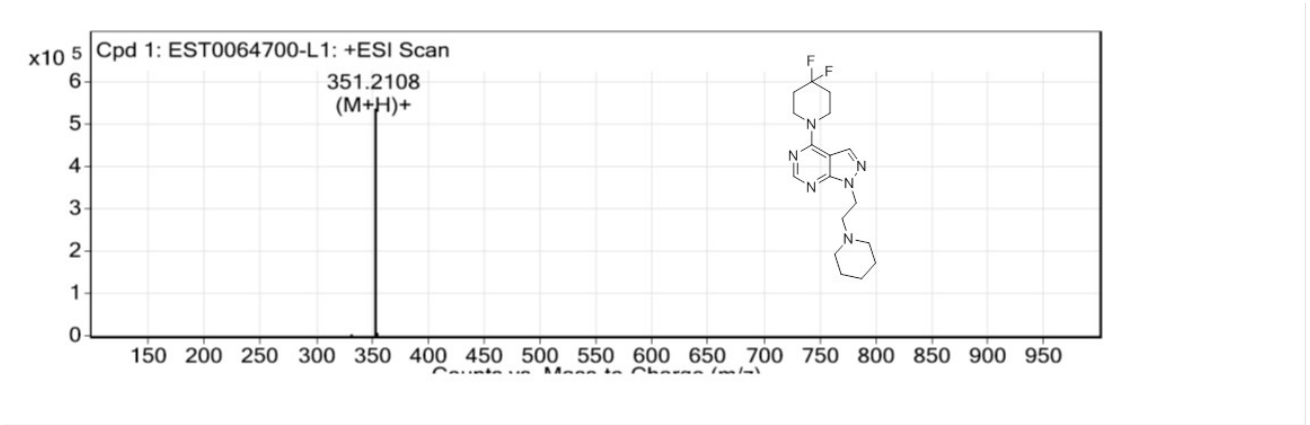
^{1}H-NMR spectrum



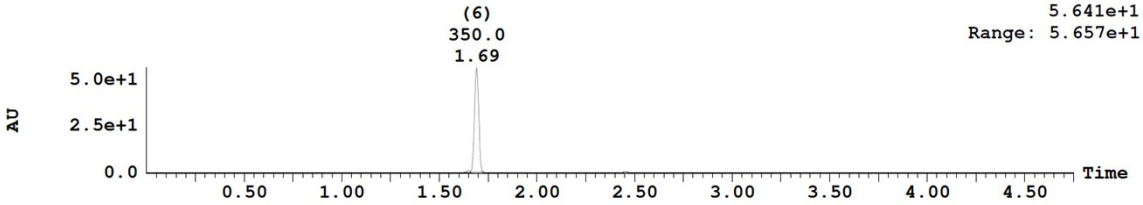
^{13}C-NMR spectrum



HRMS Spectrum



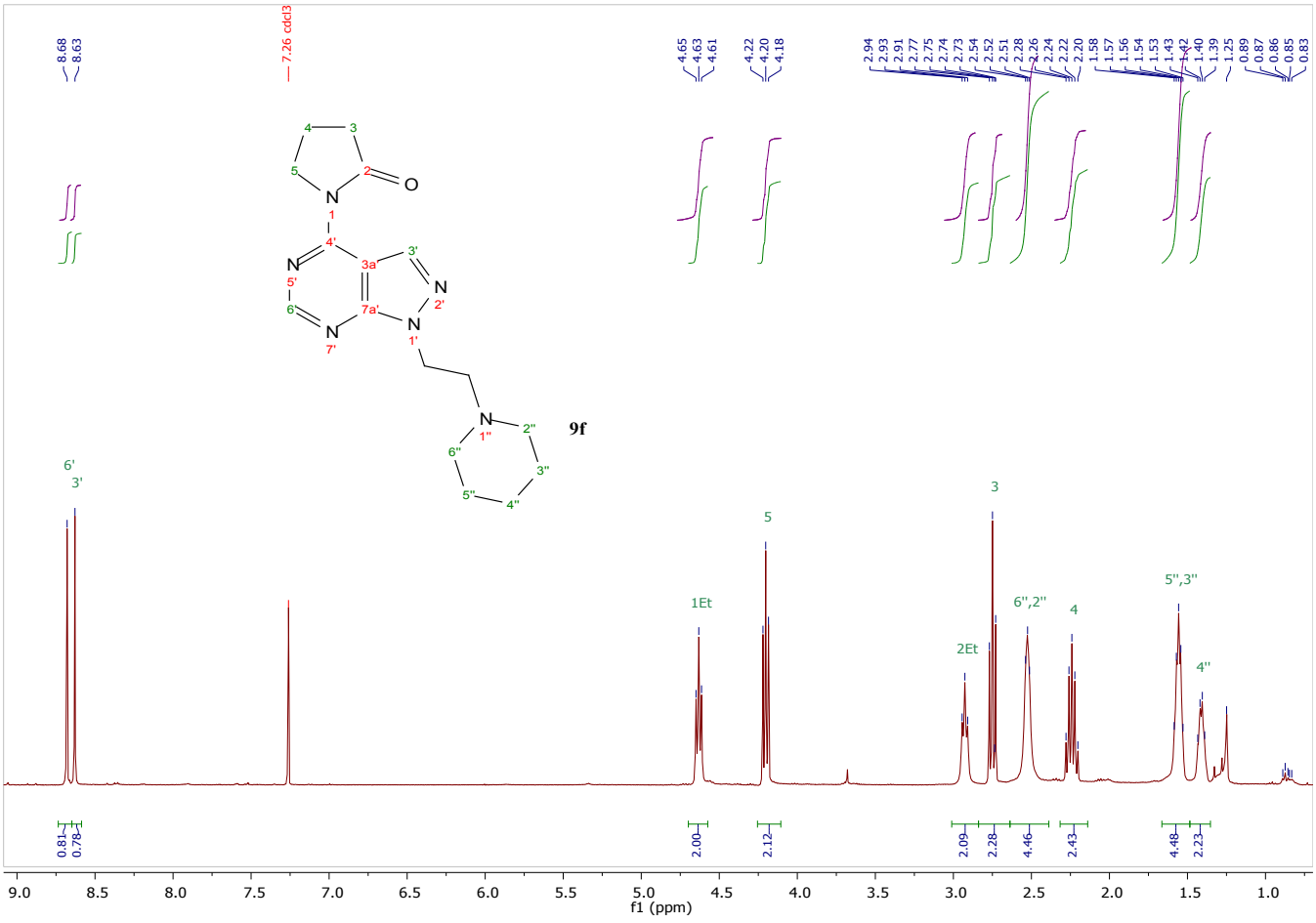
PDA Chromatogram



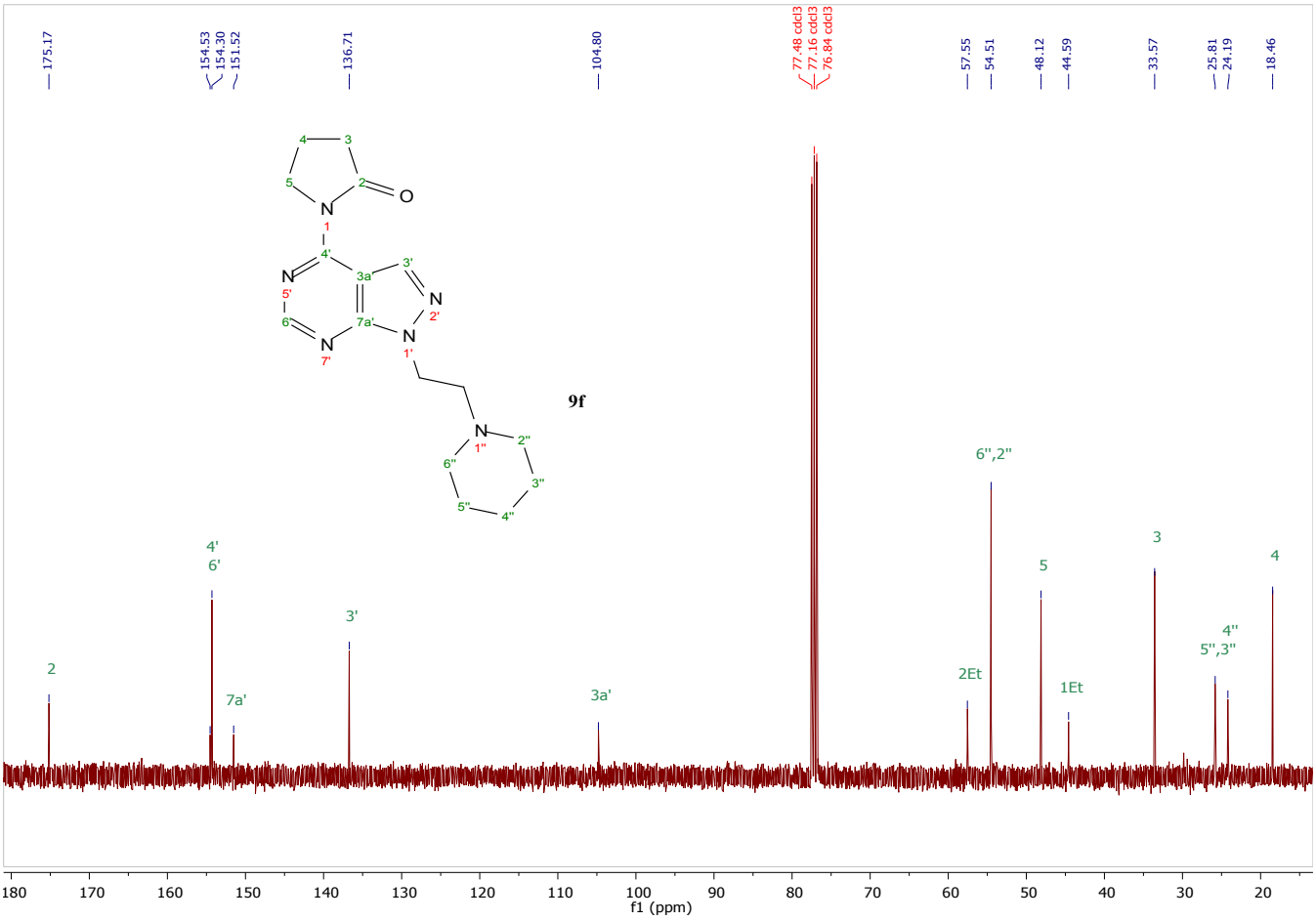
Peak Number	Time	Area %Total	Mass Found
1	1.01	0.30	
2	1.23	0.09	
3	1.65	1.32	350.00
6	1.69	97.57	350.00
7	1.81	0.17	350.00
8	2.00	0.23	
9	2.13	0.33	

Spectra of Compound 9f

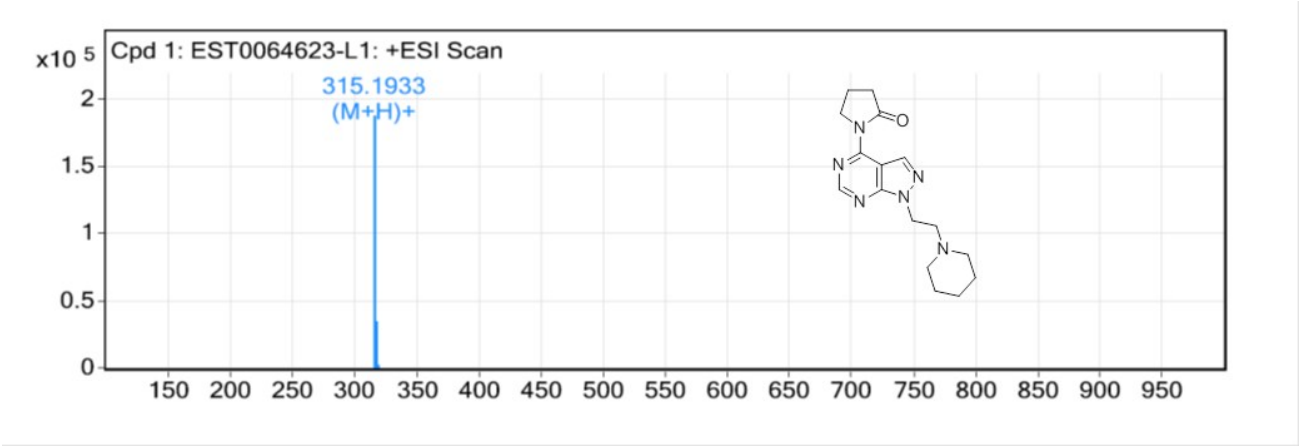
^{1}H-NMR spectrum



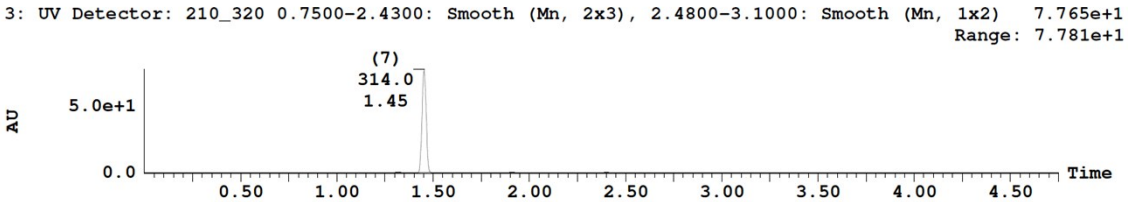
^{13}C-NMR spectrum



HRMS Spectrum



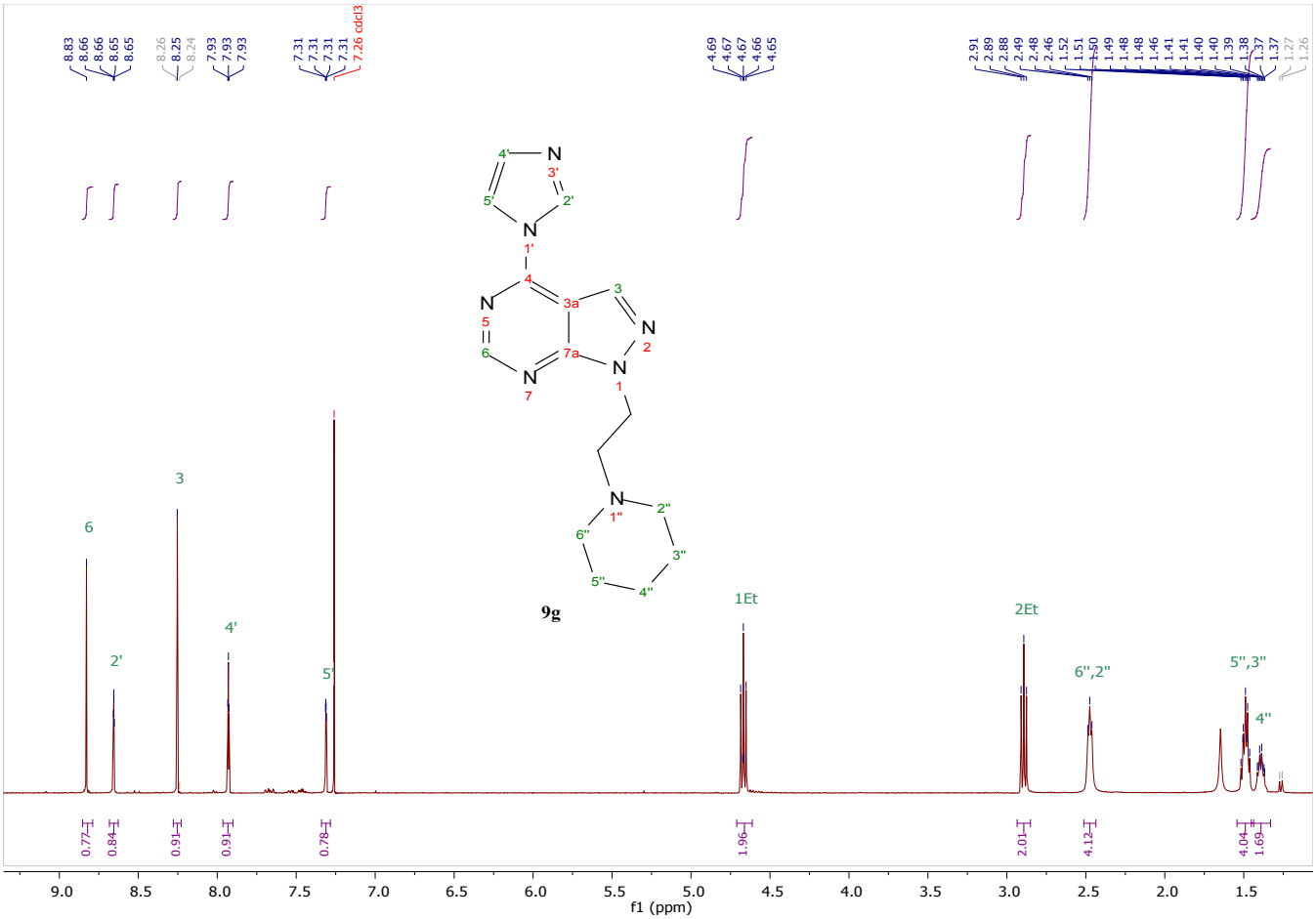
PDA Chromatogram



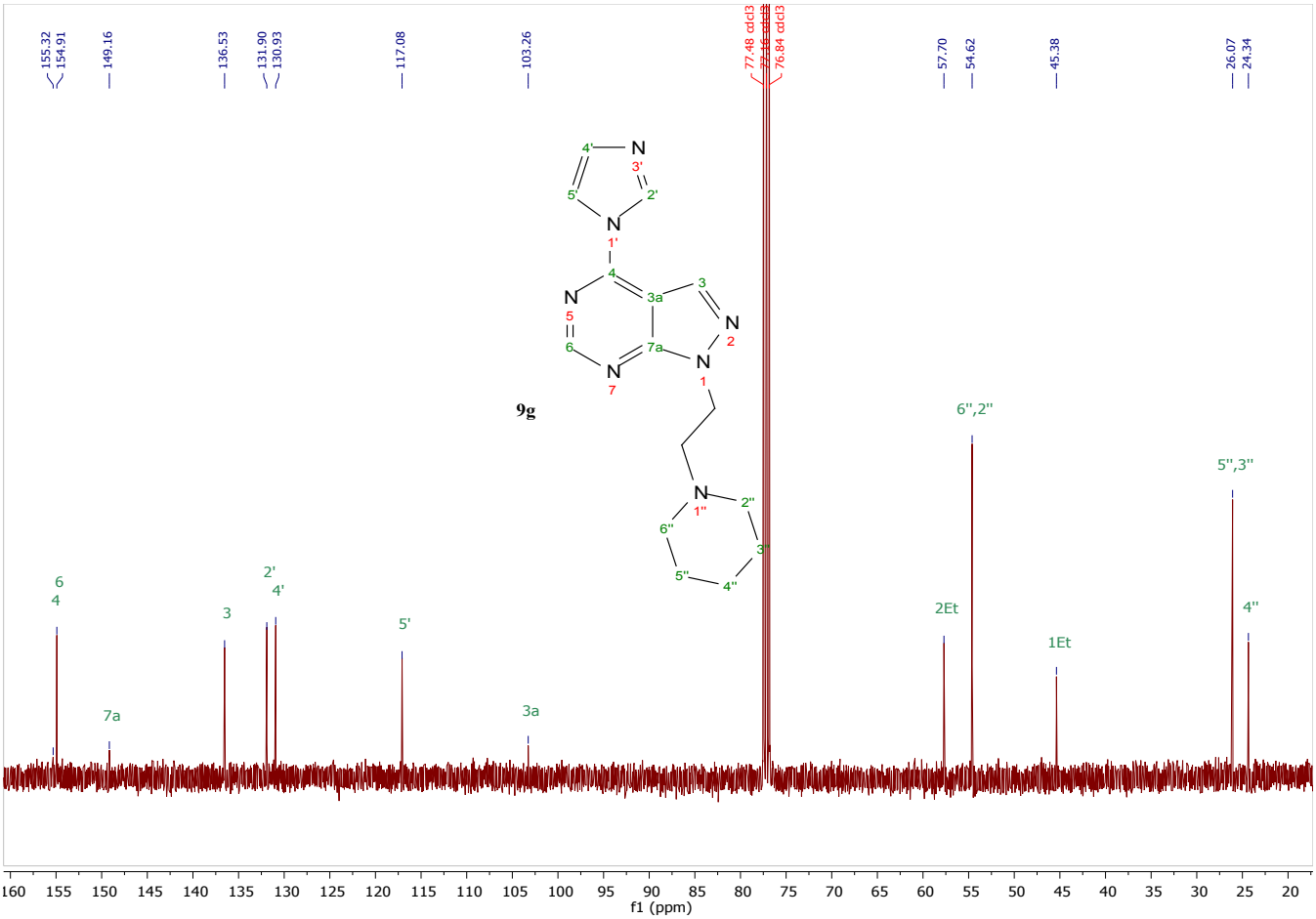
Peak Number	Time	Area %Total	Mass Found
1	0.88	0.13	
2	0.92	0.38	
3	1.03	0.35	
4	1.32	1.11	
7	1.45	96.21	314.00
8	1.56	0.15	314.00
9	1.65	0.09	314.00
10	1.68	0.13	314.00
11	1.91	0.75	
12	2.09	0.12	
13	2.20	0.09	
14	2.40	0.50	

Spectra of Compound 9g

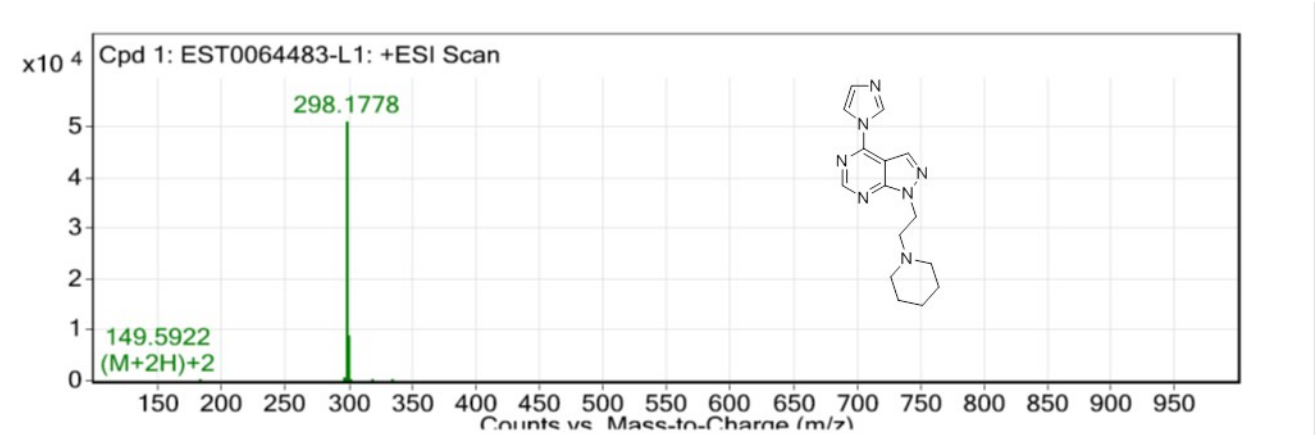
^{1}H-NMR spectrum



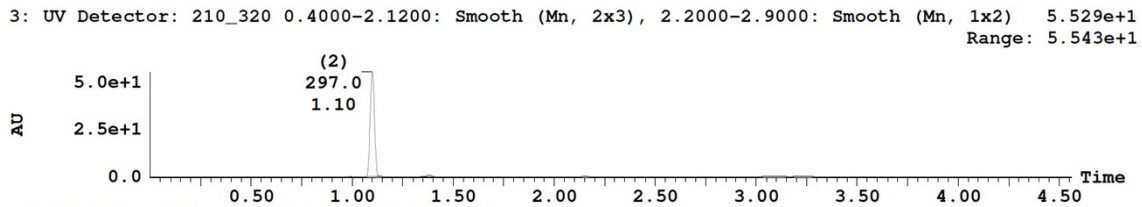
^{13}C-NMR spectrum



HRMS Spectrum



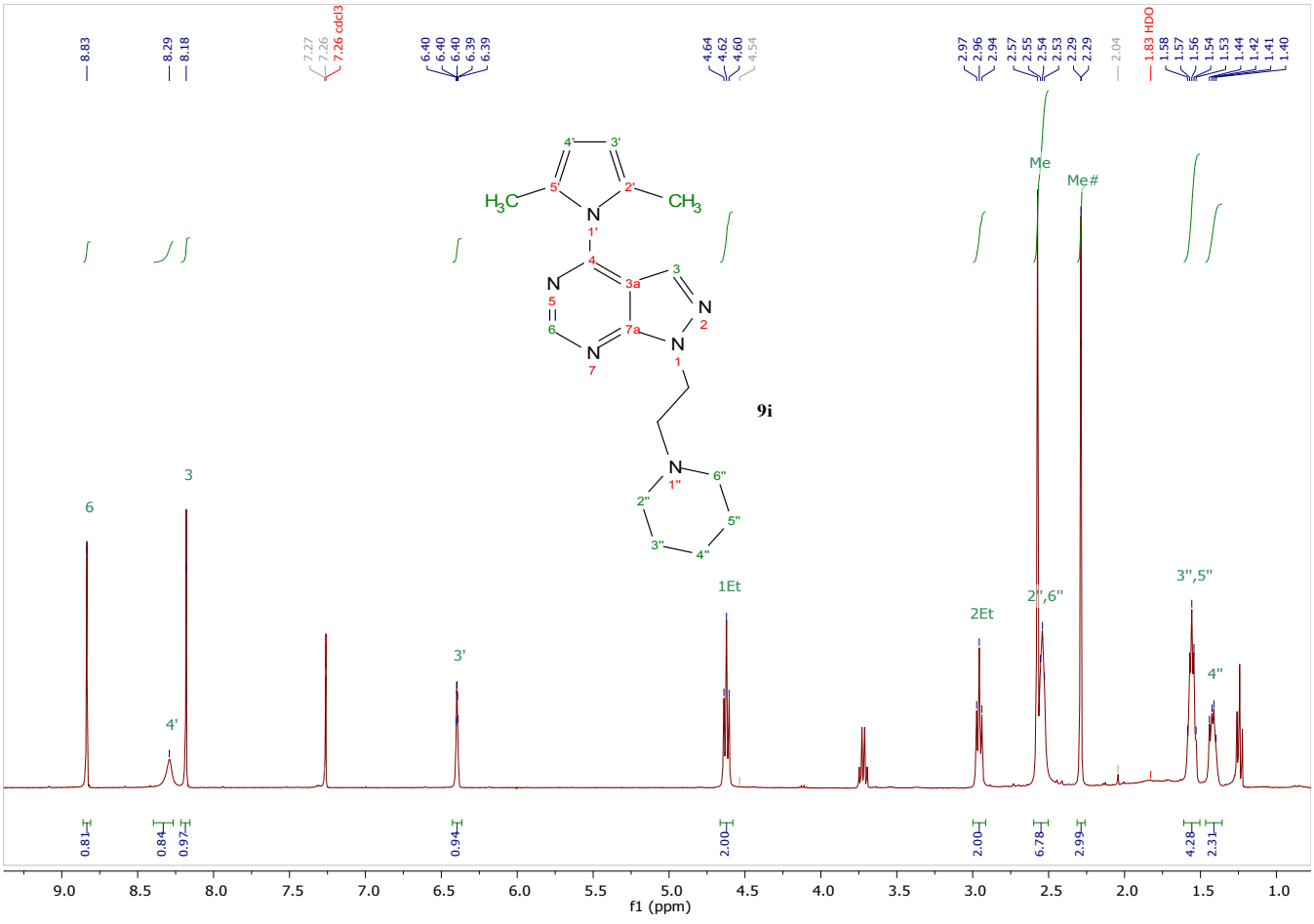
PDA Chromatogram



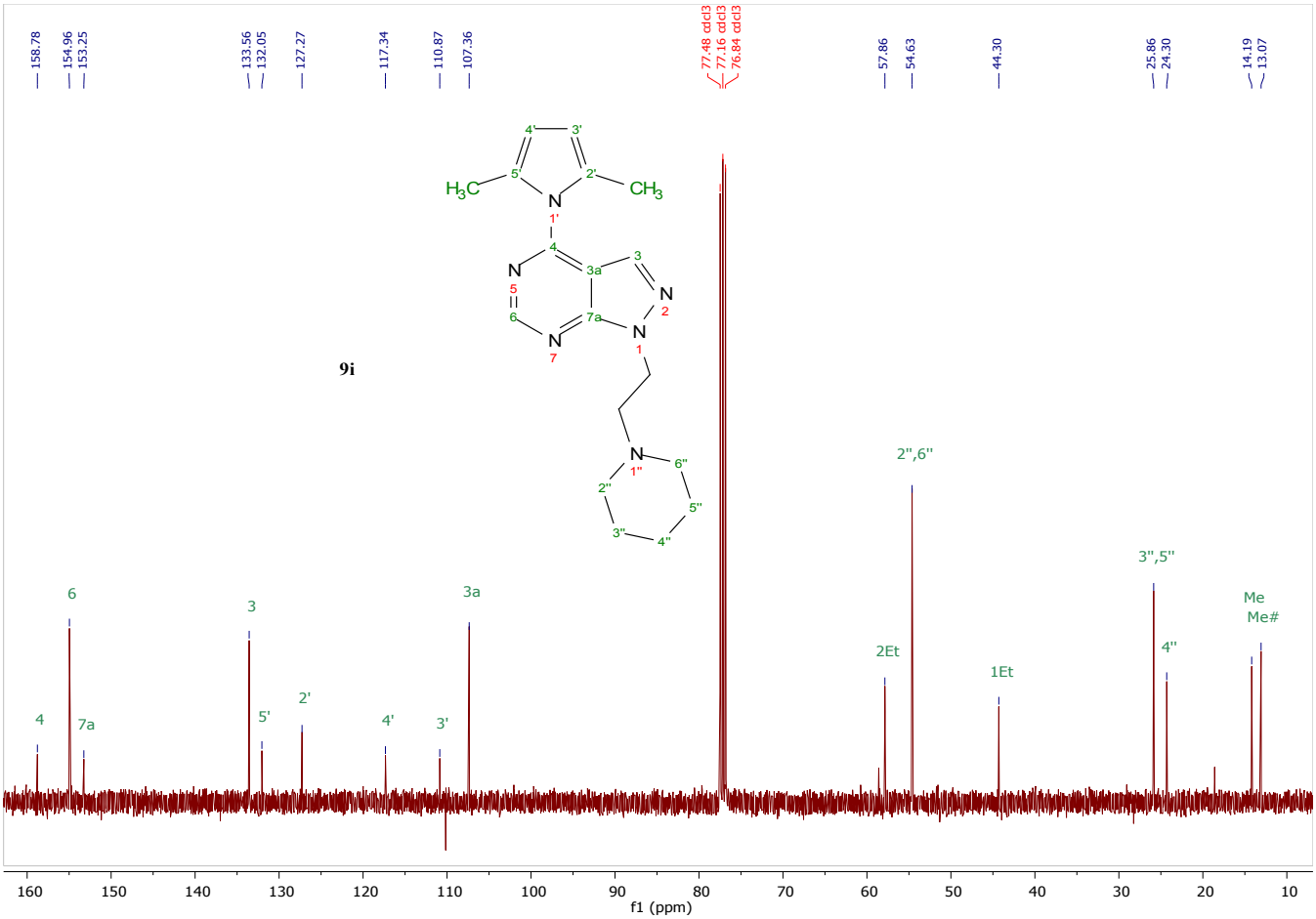
Peak Number	Time	Area %Total	Mass Found
1	0.99	0.25	
2	1.10	97.06	297.00
4	1.38	2.46	
5	1.75	0.09	
6	1.87	0.11	
8	2.51	0.03	

Spectra of Compound 9i

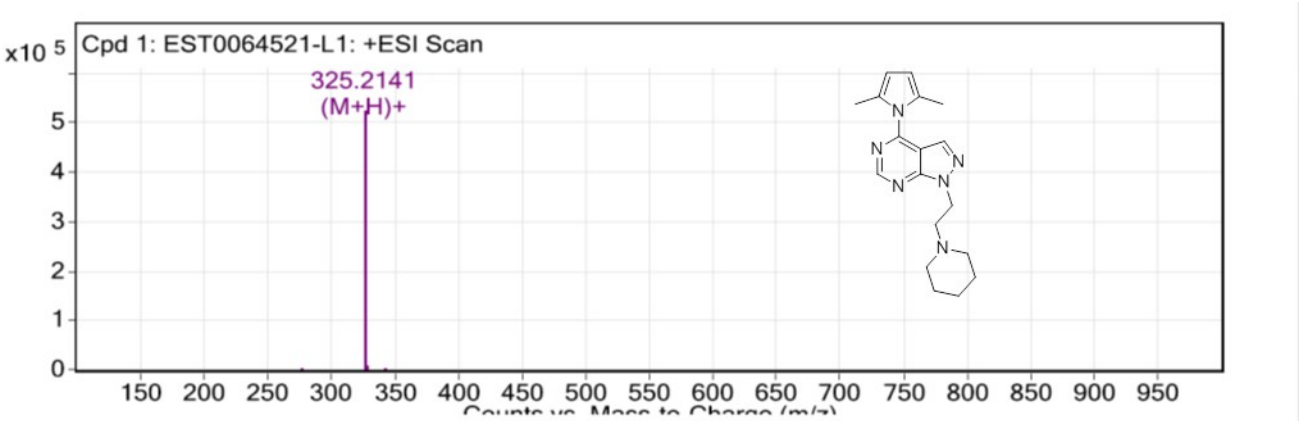
^{1}H-NMR spectrum



^{13}C-NMR spectrum

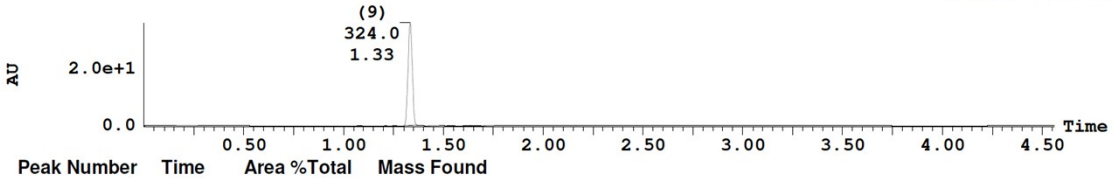


HRMS Spectrum



PDA Chromatogram

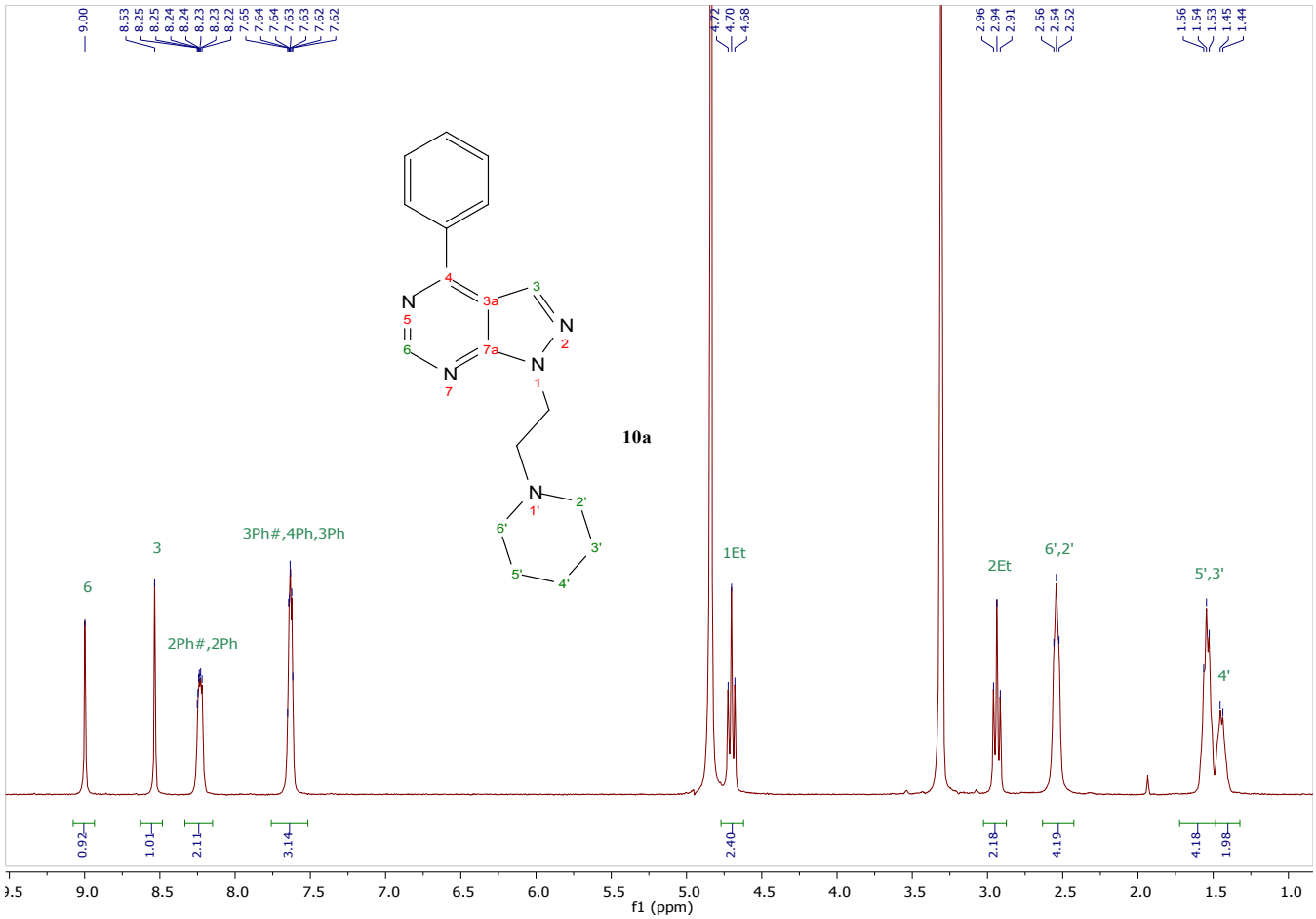
3: UV Detector: 210_320 0.1000-2.1200: Smooth (Mn, 2x3), 2.2000-2.9000: Smooth (Mn, 1x2) 3.614e+1
Range: 3.636e+1



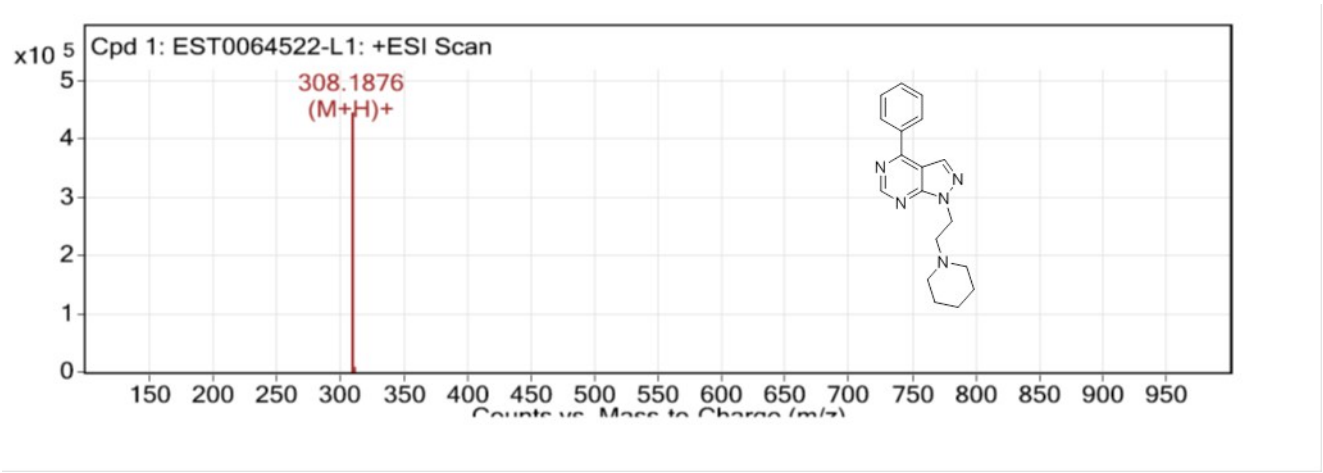
Peak Number	Time	Area %Total	Mass Found
1	0.23	0.49	
2	0.29	0.13	
3	0.72	0.15	
4	1.08	0.28	
5	1.21	0.17	
6	1.26	0.19	
9	1.33	96.82	324.00
10	1.46	0.31	324.00
11	1.54	0.29	
12	1.62	0.12	
13	1.67	0.29	
14	1.73	0.18	
15	1.84	0.21	
16	1.96	0.13	
17	2.03	0.25	

Spectra of Compound 10a

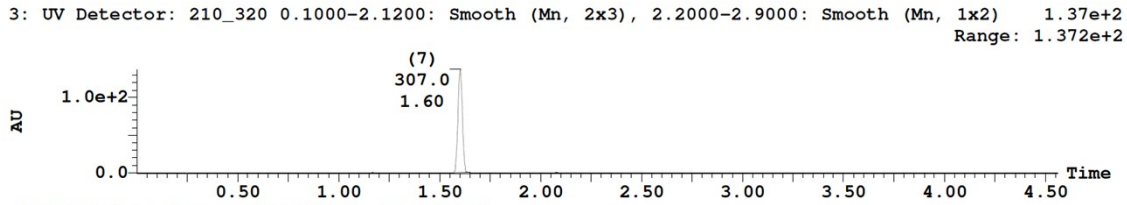
^{1}H-NMR spectrum



HRMS Spectrum



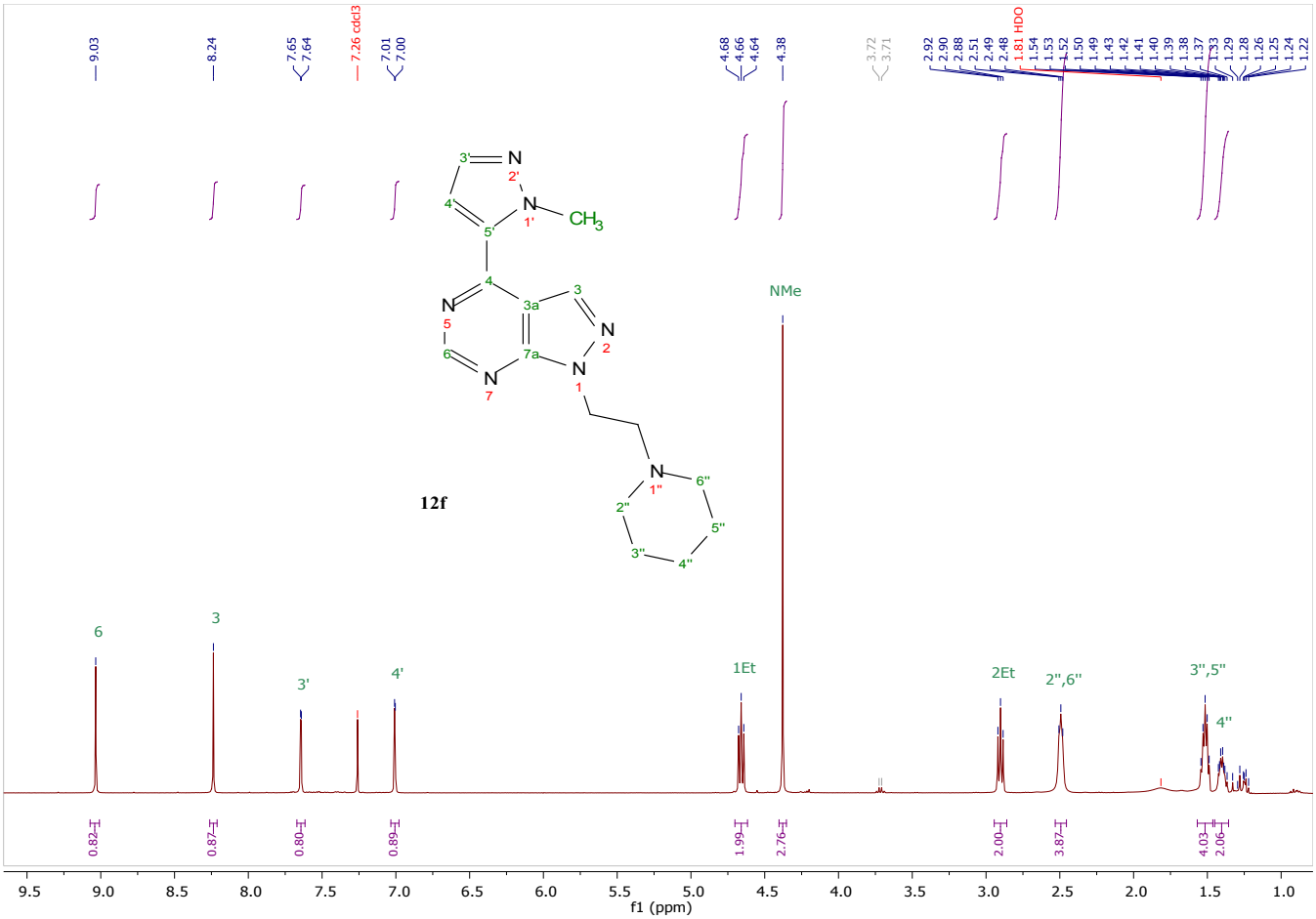
PDA Chromatogram



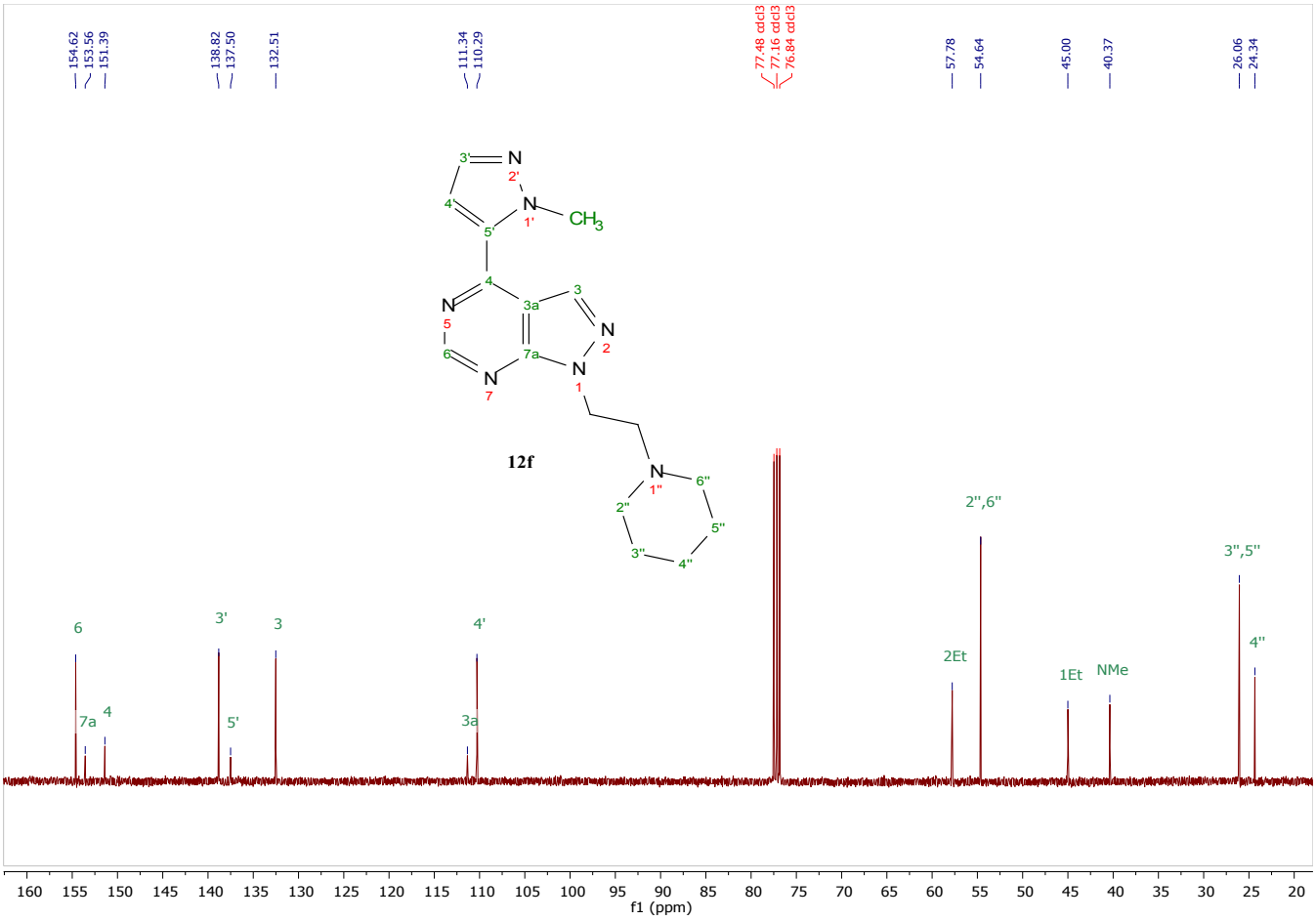
Peak Number	Time	Area %Total	Mass Found
1	0.22	0.13	
2	0.25	0.08	
3	0.29	0.06	
4	1.17	0.29	
5	1.53	0.05	307.00
7	1.60	98.74	307.00
9	1.67	0.06	307.00
10	1.84	0.05	307.00
11	1.95	0.07	
12	2.00	0.09	
13	2.04	0.06	
14	2.08	0.29	
15	2.45	0.04	

Spectra of Compound 12f

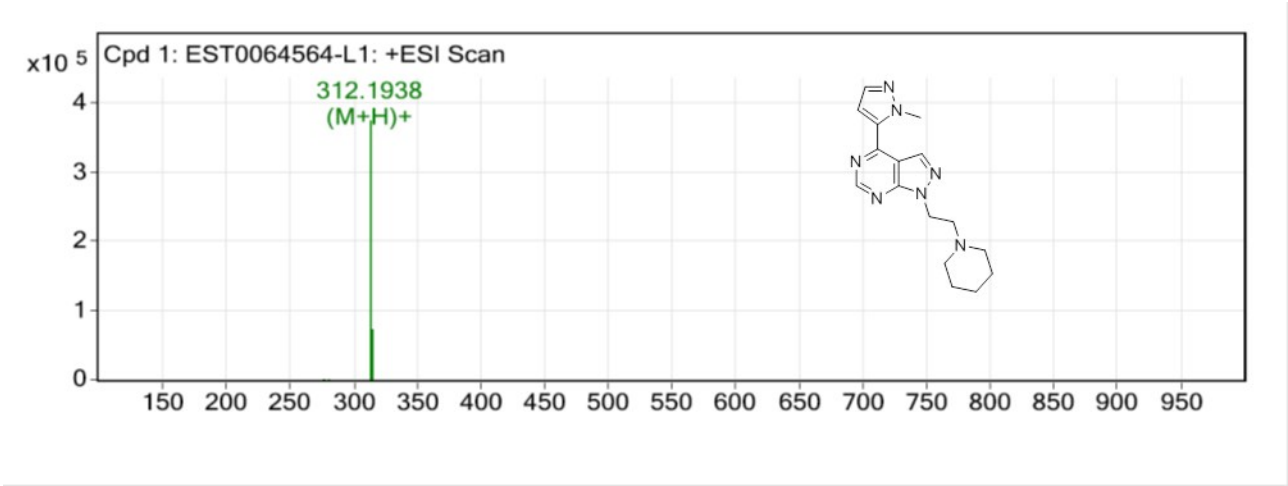
^{1}H-NMR spectrum



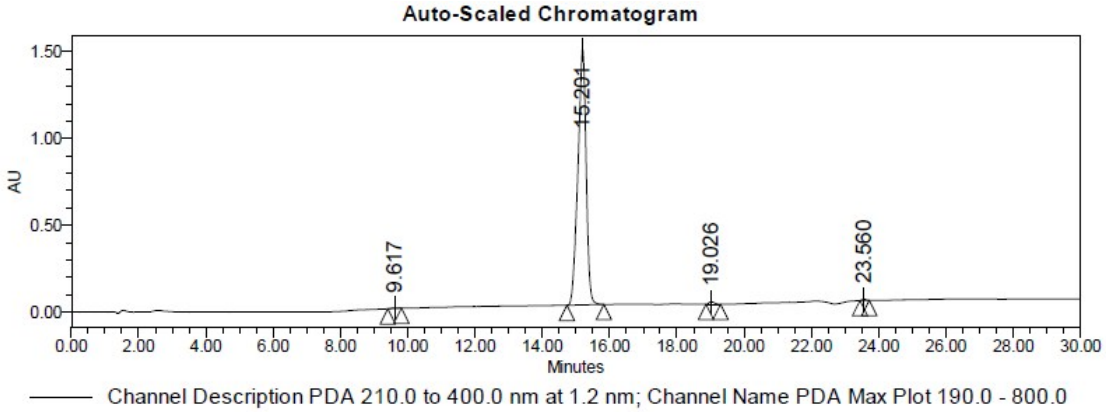
^{13}C-NMR spectrum



HRMS Spectrum



PDA Chromatogram

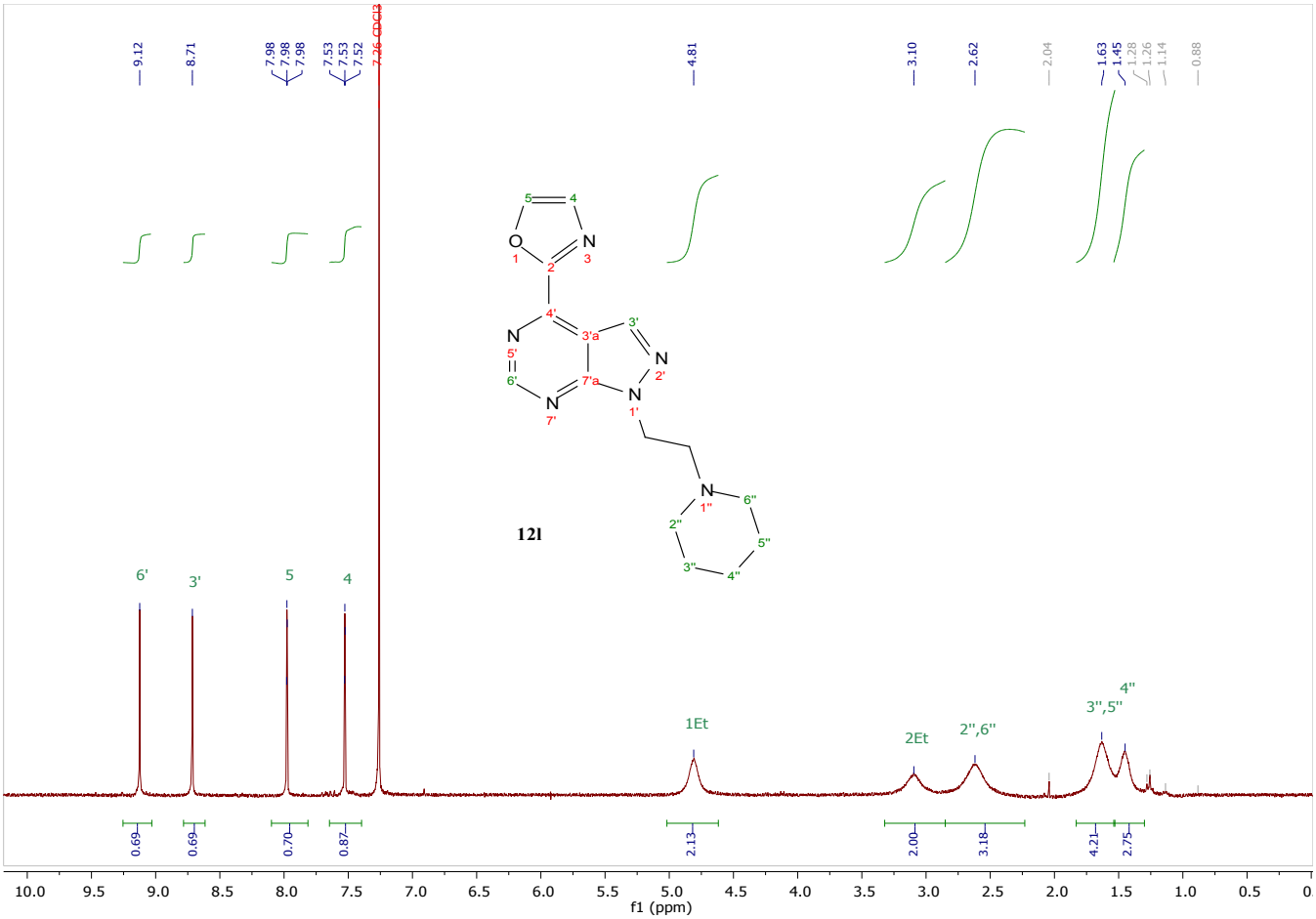


Peak Results

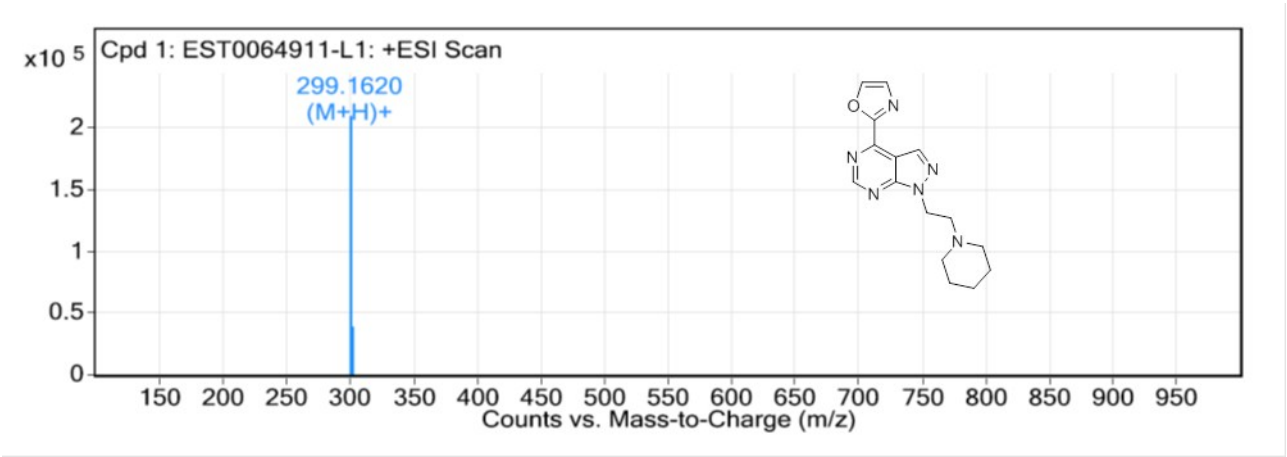
	SampleName	RT	Area	% Area
1	EST64564_ga23904025x	9.617	36167	0.14
2	EST64564_ga23904025x	15.201	24980259	99.02
3	EST64564_ga23904025x	19.026	153697	0.61
4	EST64564_ga23904025x	23.560	57507	0.23

Spectra of Compound 12l

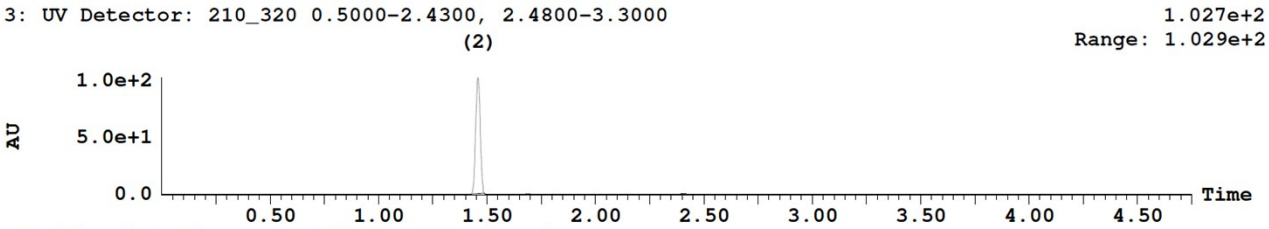
^{1}H-NMR spectrum



HRMS Spectrum



PDA Chromatogram



Peak Number	Time	Area %Total	Mass Found
2	1.46	98.47	298.00
4	1.69	0.79	298.00
5	2.41	0.66	
6	2.56	0.07	
7	2.76	0.01	
8	2.79	0.01	