SUPPORTING INFORMATION

Palladium-Catalyzed Enantioselective 2-(Naphthyl)methylation of Azaarylmethyl Amines

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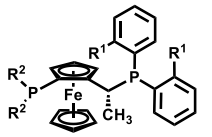
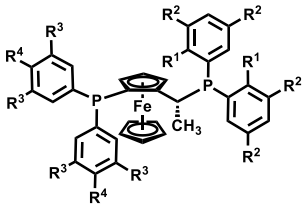
General Information

Anhydrous DME, THF, TBME and *i*-Pr_2O were purchased from Sigma-Aldrich and used as solvents without further purification. Unless otherwise stated, reagents were commercially available and used as purchased without further purification. Chemicals were obtained from Sigma-Aldrich, Acros, Alfa Aesar, TCI China, or Adamas-beta. The progress of reactions was monitored by thin-layer chromatography using TLC plates and visualized by short-wave ultraviolet light. Flash chromatography was performed with Qingdao Haiyang flash silica gel (200–300 mesh). Deactivated silica gel was made by combining 50 g silica gel with 100 mL petroleum ether contain 2% Et_3N. The NMR spectra were obtained using a Brüker 400 MHz Fourier-transform NMR spectrometer. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in hertz. The infrared spectra were obtained with KBr plates by using an IS10 FT-IR Spectrometer (ThermoFisher Corporation). High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (Xevo G2-XS QTof) using electrospray ionization (ESI) in positive or negative mode. Melting points were measured using a SGW X-4 Melt-Temp apparatus and were uncorrected.

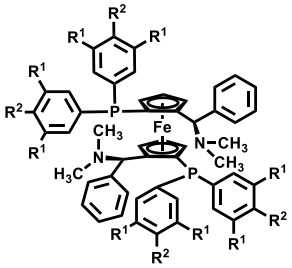
Screening Ligands



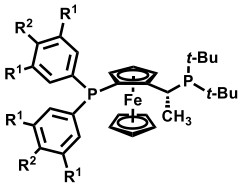
R^1	R^2	Yield(%)	ee(%)
H	t-Bu	52	31
Me	t-Bu	68	47
H	Cy	68	7



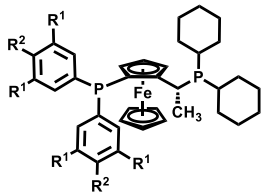
R^1	R^2	R^3	R^4	Yield(%)	ee(%)
H	Me	H	H	56	13
H	Me	Me	MeO	trace	ND
Me	H	Me	MeO	86	27
H	Me	CF_3	H	40	-31



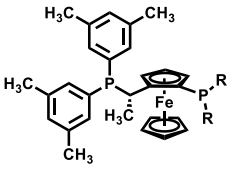
R^1	R^2	Yield(%)	ee(%)
H	H	88	63
CF_3	H	24	-3
Me	H	86	65



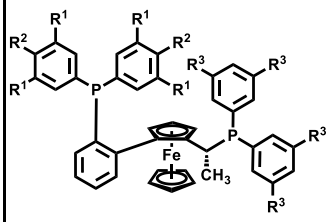
R^1	R^2	Yield(%)	ee(%)
H	H	96	18
Me	MeO	96	37
H	CF_3	86	17



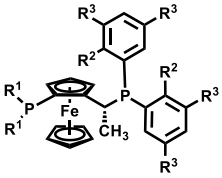
R^1	R^2	Yield(%)	ee(%)
Me	MeO	82	7
H	H	96	41
CF_3	CF_3	36	17



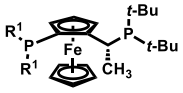
R	Yield(%)	ee(%)
Phenyl	trace	-13
Thienyl	48	5



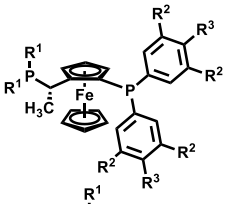
R^1	R^2	R^3	Yield(%)	ee(%)
Me	MeO	CF_3	82	-17
H	H	H	80	-49
H	H	Me	54	-41
Me	H	Me	84	-47



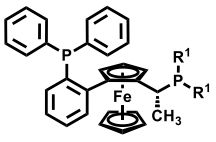
R^1	R^2	R^3	Yield(%)	ee(%)
Thienyl	Me	H	60	21
Naphthyl	H	Me	92	35



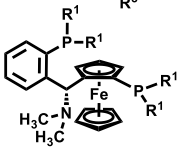
R^1	Yield(%)	ee(%)
Cy	60	33
Thienyl	83	30



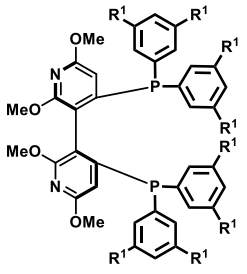
R^1	R^2	R^3	Yield(%)	ee(%)
Cy	H	H	80	15
t-Bu	Me	MeO	90	-24



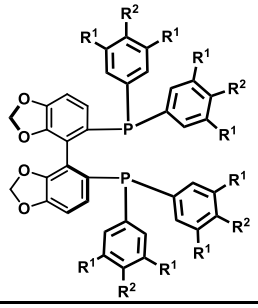
R^1	Yield(%)	ee(%)
Cy	trace	-45
Norbornyl	36	13



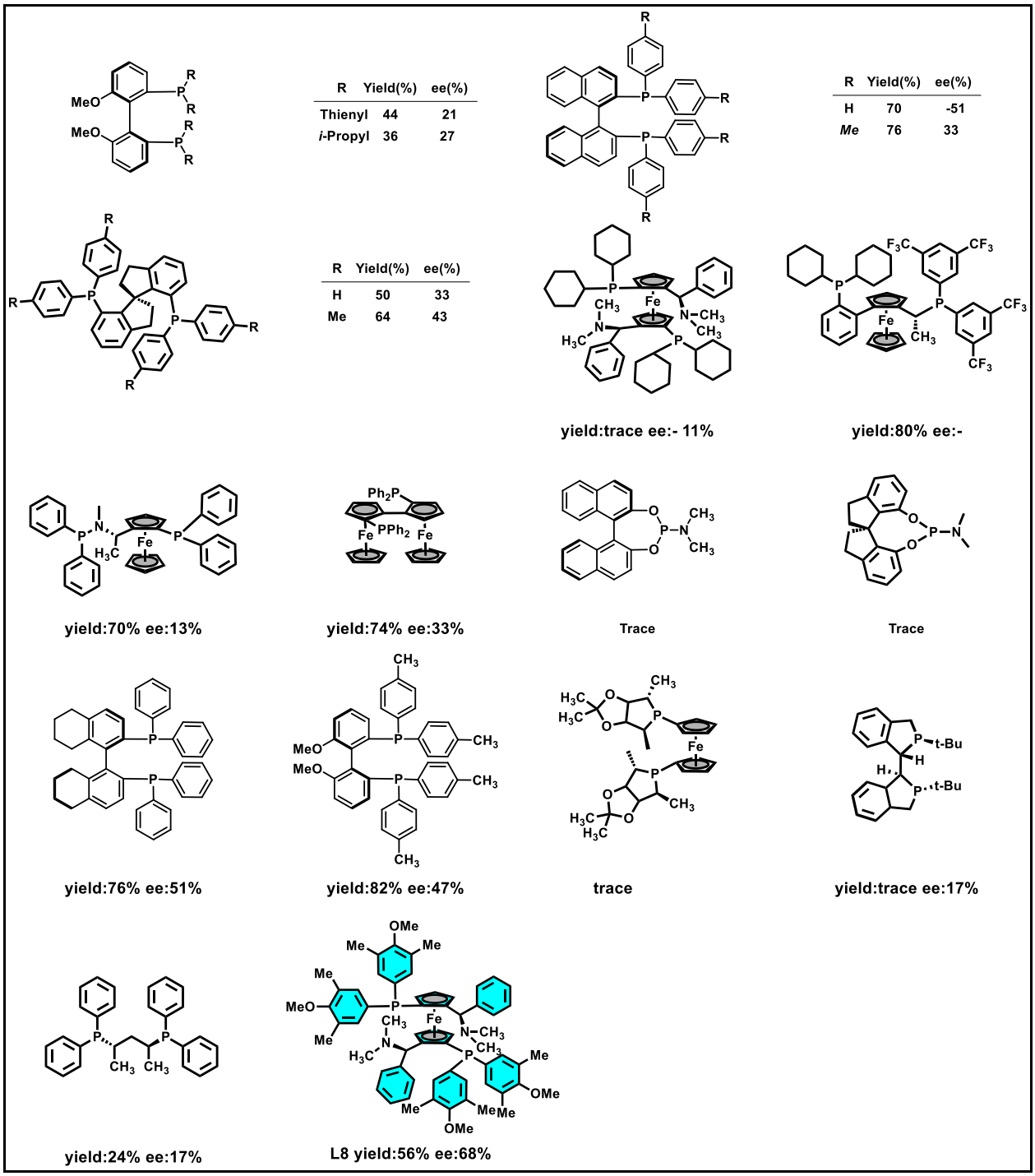
R^1	Yield(%)	ee(%)
Cy	trace	ND
Phenyl	trace	ND



R^1	Yield(%)	ee(%)
H	20	35
Me	56	-39



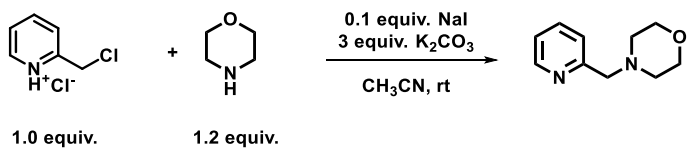
R^1	R^2	Yield(%)	ee(%)
t-Bu	MeO	80	49
H	H	72	35
Me	H	76	55



Synthesis of Azaaryl Amines

Compounds **1a**[1], **1b**[2], **1c**[1], **1d**[1], **1f**[1], **1h**[3], **1i**[1], **1o**[4], **1p**[4], **1q**[4], **1w**[1],**1x**[1],**2b**[5] were prepared according to the literature procedures.

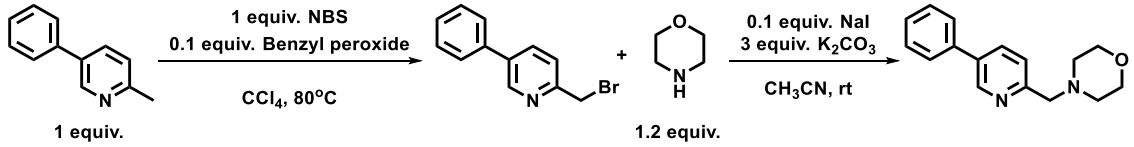
General Procedure A for the Synthesis of Azaaryl Amines



A flame-dried single-neck flask (250 mL) with a stirring bar was charged with 2-(chloromethyl)pyridine hydrochloride (2.0 g, 12.20 mmol, 1.0 equiv.), potassium carbonate (5.1 g, 36.6 mmol, 3 equiv.) and sodium iodide (0.18 g, 1.2 mmol, 0.1

equiv.) in CH_3CN (60 mL, 0.2 M). Morpholine (1.27 g, 14.6 mmol, 1.2 equiv.) was added dropwise to the mixture by syringe under an air atmosphere at room temperature over 10 min. During the addition, the solution changed from colorless to brown. The flask was sealed with a septum and a needle with a balloon attached was pierced through the septum to prevent pressure buildup. The heterogeneous reaction mixture was stirred at room temperature for 12 h followed by removal of the septum and filtration of the solution through filter paper to remove the solids. The resulting brown filtrate was concentrated under reduced pressure, CH_2Cl_2 (100 mL) was added, then the organic solution was transfered to a 500 mL separatory funnel and rinsed with saturated brine (3 × 20 mL). The organic phase was collected, dried over Na_2SO_4 for 1 h, and then filtered. The resulting organic phase was concentrated under reduced pressure and the residue was purified by chromatography.

Synthesis of Azaaryl Amines

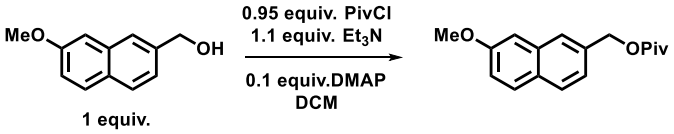


General Procedure B for the Synthesis of Azaaryl Amines

A flame dried single-neck flask (250 mL) with condenser and strring bar was charged with 5-phenyl-2-methylpyridine (2.00 g, 11.83 mmol, 1.0 equiv.) in CCl_4 (50 mL) under an air atmosphere. Then recrystallized white NBS (2.1 g, 11.83 mmol, 1.0 equiv., note that NBS recrystallized from hot water improves the yield) and benzoyl peroxide (0.29 g, 1.2 mmol, 0.1 equiv.) were added to the mixture. The flask was then fitted with a reflux condenser and capped by a stopcock. The stpocock was hooked up to Schlenk line and the reaction system subjected to three cycles of freeze-pump-thaw with backfill using N_2. Next, the mixture was heated to 80 °C in an oil bath and refluxed for 12 h under positive pressure of N_2. After the reaction period, the vessel was cooled to room temperature and the condenser was removed, exposing the contents to air. Next, 10 mL saturated aq. NH_4Cl was added to quench the reaction and 100 mL CH_2Cl_2 was added to flask. The resulting solution was transferred to 250 mL separatory funnel and rinsed with brine (3 × 20 mL). The combined organic phase was dried over Na_2SO_4 for 1 h and filtered. The filtrate was collected and then concentrated *in vacuo* to give a brown oil liquid that was used directly in the next step without further purification. Note that the equivalents of reagents in the next step are the equivalents relative methyl-aza-aromatics

The crude product above was dissolved in CH_3CN (30 mL) and potassium carbonate (4.9 g, 35.5 mmol, 3 equiv.) and sodium iodide (0.18 g, 1.2 mmol, 0.1 equiv.) were added. Morpholine (1.27 g, 14.6 mmol, 1.2 equiv.) was added dropwise to the mixture by syringe under air over 10 min at room temperature to give a brown solution. The flask was sealed with a septum and a needle attached to an empty balloon was pierced through the septum to ensure that the flask did not develop pressure. The heterogeneous reaction mixture was stirred at room temperature for 12 h followed by removal of the septum and filtration of the solution through filter paper to remove the solids. The resulting brown filtrate was concentrated under reduced pressure, CH_2Cl_2 (100 mL) was added, then organic solution was transfered to 250 mL a separatory funnel and rinsed with saturated brine (3 × 20 mL). The organic phase was collected, dried over Na_2SO_4 for 1 h, and filtered. The resulting organic phase was concentrated under reduced pressure and the residue was purified by chromatography.

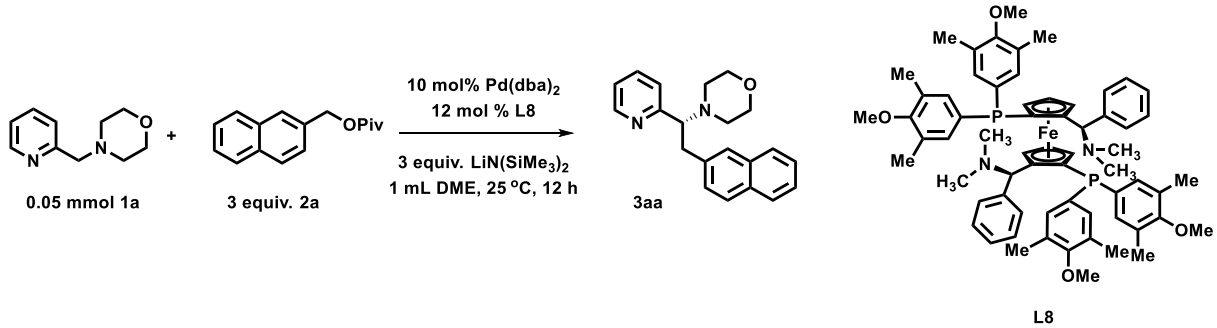
Synthesis of the Naphthalen-2-ylmethyl Pivalates



General Procedure C for Synthesis of Naphthalen-2-ylmethyl Pivalates

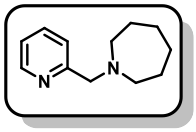
A flame-dried flask (100 mL) with a stirring bar was charged with (7-methoxynaphthalen-2-yl)methanol (1.8 g, 9.57 mmol, 1 equiv.), Et_3N (1.46 mL, 10.53 mmol, 1.1 equiv.) and *N*,*N*-dimethylpyridin-4-amine (0.12 g, 0.96 mmol, 0.1 equiv.) in dry DCM (50 mL) in a glove box under N_2 atmosphere. The flask was sealed with a septum, removed from the glovebox, and a needle with a nitrogen filled balloon was attached by piercing the septum. The reaction mixture was cooled to 0 °C, pivaloyl chloride (0.95 equiv.) was added dropwise over 10 min and the flask was allowed to warm to room temperature. The resulting solution was stirred for 6 h at room temperature. After the reaction period, the solution was cooled to 0° C and quenched with saturated aq. NH_4Cl (2 mL) that was added via a syringe poked through a septum. After the addition, the septum was removed to expose the solution to air, CH_2Cl_2 (20 mL) was added and the organic phase was transferred to a 250 mL separatory funnel where it was rinsed with brine (3 × 20 mL). The combined organic phases were dried over Na_2SO_4 for 1 h and filtered. The filtrate was collected, concentrated under reduced pressure, and the resulting residue was purified by chromatography.

Synthesis of the Benzylation of Azaarylmethyl Amines

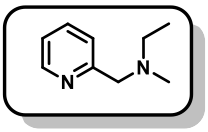


General Procedure D for Benzylation of Azaarylmethyl Amines

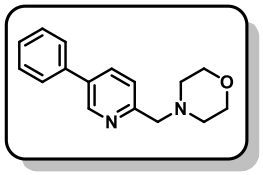
To an oven-dried microwave vial equipped with a stir bar under a nitrogen atmosphere inside a glove box was added $Pd(dba)_2$ (0.005 mmol, 10 mol%), ligand **L8** (0.006 mmol, 12 mol%), $LiN(SiMe_3)_2$ (0.15 mmol, 3 equiv.) and azaarylmethyl amine (0.05 mmol, 1.0 equiv.) and DME (0.5 mL). The microwave vial was sealed with cap containing a septum and removed from the glove box. Then the vial was cooled to 0° C and corresponding naphthalen-2-ylmethyl pivalate (0.15 mmol, 3 equiv.) was added dropwise via 100 *u*L micro-syringe over 5 min. If the pivalate was a solid, it was dissolved in 0.1 mL DME and added dropwise to the reaction mixture via a 250 *u*L micro-syringe. The reaction mixture was stirred at 0 °C for 12 h. After the reaction period, 5 drops of water were added by syringe through the septum in the cap to quench the reaction at 0 °C and then the septum was then removed under air. The reaction mixture was passed through a short pad of silica, washed with ethyl acetate (3 × 2 mL), and the combined solution was concentrated *in vacuo*. The crude material was loaded onto a column of deactivated silica gel and purified using petroleum ether containing 2% Et_3N.



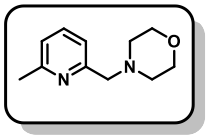
1-(pyridin-2-ylmethyl)azepane (1e): Prepared according to procedure A using 2-(chloromethyl)pyridine hydrochloride (2.0 g, 12.26 mmol, 1.0 equiv.), azepane (1.46 g, 14.71 mmol, 1.2 equiv.), NaI (0.18 g, 1.23 mmol, 0.1 equiv.), CH_3CN (60 mL), 12 h. The crude product was purified by silica gel (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (1.87 g, 80% yield) as a light yellow oil. R_f = 0.30 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.52 (dt, *J* = 5.0, 1.3 Hz, 1H), 7.64 (td, *J* = 7.6, 1.8 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.13 (ddd, *J* = 7.3, 4.8, 1.2 Hz, 1H), 3.79 (s, 2H), 2.63 – 2.71 (m, 4H), 1.72 – 1.56 (m, 8H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 160.5, 149.1, 136.4, 123.0, 121.9, 64.5, 56.0, 28.3, 27.2 ppm. IR (neat): 3063, 2924, 2852, 2813, 1589, 1569, 1471, 1431, 1351, 991, 758 cm^{-1}. HRMS: calcd for $[C_{12}H_{18}N_2 + H]^+$ 191.1548, found 191.1544.



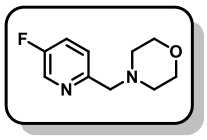
N-methyl-N-(pyridin-2-ylmethyl)ethanamine (1g): Prepared according to procedure A using 2-(chloromethyl)pyridine hydrochloride (2.00 g, 12.26 mmol, 1.0 equiv.), N-methylethyl-2-amine (0.87 g, 14.71 mmol, 1.2 equiv.), NaI (0.18 g, 1.23 mmol, 0.1 equiv.) CH_3CN (60 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (1.41 g, 76% yield) as a light yellow oil. R_f = 0.20 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 – 8.49 (m, 1H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.39 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.15 – 7.09 (m, 1H), 3.62 (s, 2H), 2.65 – 2.48 (q, *J* = 5.5 Hz, 2H), 2.22 (s, 3H), 1.08 (t, *J* = 5.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 149.2, 136.5, 123.2, 122.0, 63.6, 51.7, 42.0, 12.5 ppm. IR (neat): 3065, 2971, 2938, 2840, 1591, 1569, 1471, 1434, 1384, 994, 757 cm^{-1}. HRMS: calcd for $[C_9H_{15}N_2+H]^+$ 151.1235, found 151.1234.



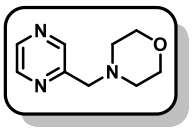
4-((5-phenylpyridin-2-yl)methyl)morpholine (1j): Prepared according to procedure B using 5-phenyl-2-methylpyridine (2.00 g, 11.83 mmol, 1.0 equiv., prepared accroding to leterature[6]), NBS (2.08 g, 11.83 mmol, 1.0 equiv.), benzoyl peroxide (0.29 g, 1.18 mmol, 0.1 equiv.), CCl_4 (60 mL), 12 h. In step 2, morpholine (1.23 g, 14.19 mmol, 1.2 equiv.), NaI (0.18 g, 1.18 mmol, 0.1 equiv.) CH_3CN (20 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.96 g, 32% yield) as a light yellow solid. Mp: 61 – 63 °C, R_f = 0.20 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.77 (m, 1H), 7.84 (ddd, *J* = 7.9, 2.5, 1.1 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.46 (ddd, *J* = 7.8, 4.3, 1.4 Hz, 3H), 7.42 – 7.35 (m, 1H), 3.75 (t, *J* = 4.1 Hz, 4H), 3.69 (s, 2H), 2.54 (t, *J* = 4.5 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 147.9, 137.8, 135.3, 135.0, 129.2, 128.1, 127.2, 123.4, 67.1, 64.8, 53.9. IR (neat): 3058, 2857, 2852, 2812, 1595, 1580, 1557, 1477, 1371, 1157, 867 cm^{-1}. HRMS: calcd for $[C_{16}H_{19}N_2O+H]^+$ 255.1497, found 255.1502.



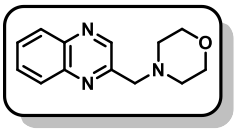
4-((6-methylpyridin-2-yl)methyl)morpholine (1k): Prepared according to procedure A using 2-(bromomethyl)-6-methylpyridine (0.50 g, 2.70 mmol, 1 equiv. prepared according to literature,[7]), morpholine (0.28 g, 3.22 mmol, 1.2 equiv.), NaI (0.04 g, 0.27 mmol, 0.1 equiv.), CH_3CN (15 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.41 g, 78% yield) as a light yellow oil. R_f = 0.20 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (td, *J* = 7.7, 2.2 Hz, 1H), 7.21 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 3.74 – 3.68 (m, 4H), 3.61 (s, 2H), 2.53 (s, 3H), 2.51 – 2.48 (m, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 157.5, 136.7, 121.8, 120.2, 67.1, 65.1, 53.9, 24.6 ppm. IR (neat): 3062, 2957, 2855, 2811, 1593, 1577, 1455, 1397, 1346, 910, 781 cm^{-1}. HRMS: calcd for $[C_{11}H_{16}N_2+H]^+$ 193.1341, found 193.1338.



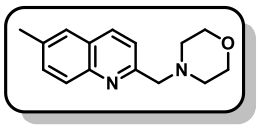
4-((6-methylpyridin-2-yl)methyl)morpholine (1l): Prepared according to procedure B using 5-fluoro-2-methylpyridine (1.0 g, 9.01 mmol, 1 equv.), NBS (1.59 g, 9.01 mmol, 1.0 equiv.), benzoyl peroxide (0.22 g, 0.90 mmol, 0.1 equiv.), CCl_4 (50 mL), 12 h. In the step 2, morpholine (0.94 g, 10.81 mmol, 1.2 equiv.) NaI (0.14 g, 0.90 mmol, 0.1 equiv.), CH_3CN (50 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.61 g, 35% yield) as a light yellow oil. R_f = 0.20 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 2.8 Hz, 1H), 7.43 – 7.31 (m, 2H), 3.70 (t, *J* = 4.7 Hz, 4H), 3.61 (s, 2H), 2.47 (t, *J* = 4.7 Hz, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7 (d, $J_{C\text{-}F}{}^1$ = 254.9 Hz), 154.1 (d, $J_{C\text{-}F}{}^4$ = 3.9 Hz), 137.5 (d, $J_{C\text{-}F}{}^2$ = 23.2 Hz), 124.2 (d, $J_{C\text{-}F}{}^3$ = 4.2 Hz), 123.3 (d, $J_{C\text{-}F}{}^2$ = 18.2 Hz), 67.0, 64.2, 53.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -129.55. IR (neat): 3054, 2959, 2854, 2814, 1635, 1585, 1485, 1455, 1388, 1009, 868 cm^{-1}. HRMS: calcd for $[C_{10}H_{13}N_2FO+H]^+$ 197.1090, found 197.1087.



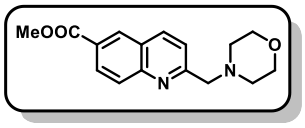
4-(pyrazin-2-ylmethyl)morpholine (1m): Prepared according to procedure A using 2-(bromomethyl)pyrazine (0.50 g, 2.92 mmol, 1 equiv. that was prepared according to literature[8]), morpholine (0.30 g, 3.50 mmol, 1.2 equiv.), NaI (0.04 g, 0.29 mmol, 0.1 equiv.), CH_3CN (15 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.39 g, 75% yield) as a light yellow oil. R_f = 0.10 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.69 (d, *J* = 1.5 Hz, 1H), 8.54 (dd, *J* = 2.6, 1.6 Hz, 1H), 8.48 (d, *J* = 2.6 Hz, 1H), 3.76 (t, *J* = 4.6 Hz, 4H), 3.70 (s, 2H), 2.53 (t, *J* = 4.7 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 153.7, 145.3, 144.2, 143.4, 66.9, 62.5, 53.8. IR (neat): 3044, 2958, 2933, 2854, 1640, 1528, 1478, 1454, 1370, 1116, 868 cm^{-1}. HRMS: calcd for $[C_9H_{13}N_3O+H]^+$ 180.1137, found 180.1133.



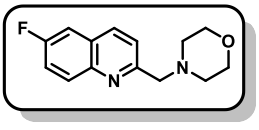
4-(quinoxalin-2-ylmethyl)morpholine (1n): Prepared according to procedure A using 2-(bromomethyl)quinoxaline (0.50 g, 2.26 mmol, 1 equiv. prepared according to literature[9]). morpholine (0.24 g, 2.71 mmol, 1.2 equiv.) NaI (0.03 g, 0.23 mmol, 0.1 equiv.) CH_3CN (15 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.42 g, 81% yield) as a light yellow oil. R_f = 0.10 (petroleum ether : EtOAc : Et_3N = 100 : 50: 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.01 (s, 1H), 8.11 – 8.05 (m, 2H), 7.70 – 7.69 (m, 2H), 3.86 (s, 2H), 3.73 (t, *J* = 4.7 Hz, 4H), 2.56 (t, *J* = 4.6 Hz, 4H) ppm. ^{13}C NMR* (101 MHz, $CDCl_3$) δ: 153.7, 146.1, 141.9, 130.2, 129.7, 129.3, 129.2, 67.0, 63.4, 54.0 ppm with one carbono not observed due to overlapping resonances. IR (neat): 3051, 2953, 2934, 2868, 1652, 1522, 1476, 1452, 1368, 1116, 857 cm^{-1}. HRMS: calcd for $[C_{13}H_{15}N_3O+H]^+$ 230.1293, found 230.1290. Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.



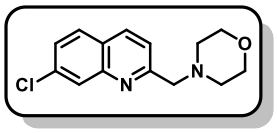
4-((6-methylquinolin-2-yl)methyl)morpholine (1r): Prepared according to procedure A using 2-(chloromethyl)-6-methylquinoline (0.50 g, 2.62 mmol, 1 equiv. prepared according to literature[10]), morpholine (0.27 g, 3.1 mmol, 1.2 equiv.), NaI (0.04 g, 0.26 mmol, 0.1 equiv.), CH_3CN (15 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.48 g, 75 % yield) as a yellow solid. Mp: 56 – 58 ºC, R_f = 0.10 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.56 (s, 1H), 7.53 (dd, *J* = 8.6, 2.0 Hz, 1H), 3.82 (s, 2H), 3.78 – 3.54 (m, 4H), 2.60 – 2.55 (m, 4H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 146.2, 136.0, 135.8, 131.7, 128.7, 127.4, 126.4, 121.1, 67.0, 65.6, 53.9, 21.5. IR (neat): 3015, 2855, 2818, 1600, 1563, 1507, 1451, 1384, 1250, 1017, 960 cm^{-1}. HRMS: calcd for $[C_{15}H_{18}N_2O+H]^+$ 243.1497, found 243.1492.



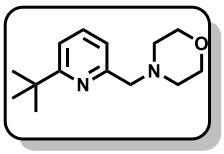
Methyl 2-(morpholinomethyl)quinoline-6-carboxylate (1s) Prepared according to procedure A using methyl 2-(bromomethyl)quinoline-6-carboxylate (0.50 g, 1.78 mmol, 1 equiv. prepared according to literature[11]), morpholine (0.19 g, 2.14 mmol, 1.2 equiv.), NaI (0.03 g, 0.18 mmol, 0.1 equiv.), CH_3CN (10 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.33 g, 65% yield) as a yellow solid. Mp: 103 – 104 ºC, R_f = 0.10 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.27 (dd, *J* = 8.8, 1.8 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.8 Hz, 1H), 7.69 (dd, *J* = 8.5, 1.4 Hz, 1H), 3.98 (s, 3H), 3.84 (s, 2H), 3.73 (t, *J* = 5.2 Hz, 4H), 2.55 (t, *J* = 5.2 Hz, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 161.9, 149.6, 137.8, 130.8, 129.4, 129.1, 127.8, 126.6, 121.9, 67.1, 65.6, 54.0, 52.6 ppm. IR (neat): 2953, 2853, 2856, 2814, 1721, 1624, 1600, 1436, 1271, 1116, 867 cm^{-1}. HRMS: calcd for $[C_{16}H_{18}N_2O_3+H]^+$ 287.1396, found 287.1393.



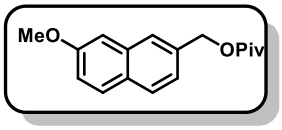
4-((6-fluoroquinolin-2-yl)methyl)morpholine (1t): Prepared according to procedure A using 2-(bromomethyl)-6-fluoroquinoline (0.43 g, 1.80 mmol, 1 equiv. prepared according to literature[12]), morpholine (0.19 g, 2.16 mmol, 1.2 equiv.), NaI (0.03 g, 0.18 mmol, 0.1 equiv.), CH_3CN (10 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.35 g, 78% yield) as a light yellow oil. R_f = 0.2 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 1H), 8.04 (d, *J* = 9.2 Hz,1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.44 (td, *J* = 8.7, 2.8 Hz, 1H), 7.39 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.80 (s, 2H), 3.73 (t, *J* = 4.7 Hz, 4H), 2.54 (t, *J* = 4.7 Hz, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4 (d, $J_{C\text{-}F}{}^1$ = 247.6 Hz), 158.6 (d, $J_{C\text{-}F}{}^5$ = 2.8 Hz), 144.8, 135.9 (d, $J_{C\text{-}F}{}^4$ = 5.3 Hz), 131.6 (d, $J_{C\text{-}F}{}^3$ = 9.1 Hz), 128.1 (d, $J_{C\text{-}F}{}^3$ = 9.8 Hz), 122.0, 119.7 (d, $J_{C\text{-}F}{}^2$ = 25.6 Hz), 110.7 (d, $J_{C\text{-}F}{}^2$ = 21.5 Hz), 67.1, 65.5, 54.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.00. IR (neat): 3062, 2959, 2856, 2815, 1713, 1627, 1608, 1563, 1328, 1116, 869 cm^{-1}. HRMS: calcd for $[C_{14}H_{15}N_2FO+H]^+$ 247.1247, found 247.1246.



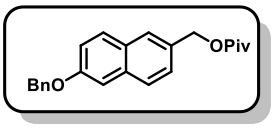
4-((7-chloroquinolin-2-yl)methyl)morpholine (1u): Prepared according to procedure A using 2-(bromomethyl)-7-chloroquinoline (0.45 g, 1.76 mmol, 1 equiv. prepared according to literature[13]), morpholine (0.18 g, 2.12 mmol, 1.2 equiv.), NaI (0.03 g, 0.18 mmol, 0.1 equiv.), CH_3CN (5 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.36 g, 78% yield) as a brown solid. Mp: 66 – 68 ºC, R_f = 0.2 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 2.1 Hz, 1H), 7.72 (d, *J* = 8.6 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.46 (dd, *J* = 8.7, 2.1 Hz, 1H), 3.81 (s, 2H), 3.74 (t, *J* = 4.6 Hz, 4H), 2.55 (t, *J* = 4.6 Hz, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 148.2, 136.3, 135.4, 128.9, 128.3, 127.4, 125.9, 121.5, 67.1, 65.6, 54.0 ppm. IR (neat): 2959, 2854, 2814, 1612, 1583, 1496, 1454, 1386, 1013, 865 cm^{-1}. HRMS: calcd for $[C_{14}H_{15}N_2ClO+H]^+$ 263.0951, found 263.0949.



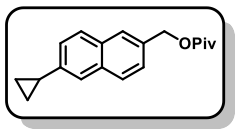
4-((6-(*tert*-butyl)pyridin-2-yl)methyl)morpholine (1v): Prepared according to procedure A using 2-(bromomethyl)-6-(tert-butyl)pyridine (0.41 g, 1.80 mmol, 1 equiv. prepared according to literature[13]), morpholine (0.18 g, 2.16 mmol, 1.2 equiv.), NaI (0.03 g, 0.18 mmol, 0.1 equiv.), CH_3CN (5 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 : 2) to give the target product (0.33 g, 78% yield) as a light yellow oil. R_f = 0.2 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (t, *J* = 7.7 Hz, 1H), 7.18 (td, *J* = 7.5, 0.9 Hz, 2H), 3.75 – 3.70 (m, 4H), 3.67 (s, 2H), 2.72 – 2.39 (m, 4H), 1.34 (s, 9H). ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 156.9, 136.4, 119.8, 117.1, 67.3, 65.2, 53.8, 37.5, 30.3. ppm. IR (neat): 3056, 2858, 2826, 1624, 1566, 1496, 1454, 1378, 1028, 874 cm^{-1}. HRMS: calcd for $[C_{14}H_{22}N_2O+H]^+$ 235.1805, found 235.1801.



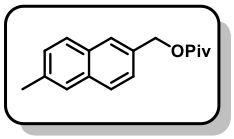
(7-methoxynaphthalen-2-yl)methanol (2c): Prepared according to procedure C using (7-methoxynaphthalen-2-yl)methanol (1.80 g, 9.57 mmol, 1 equiv. prepared according to literature[14]), Et_3N (1.46 mL, 10.53 mmol, 1.1 equiv.), *N*,*N*-dimethylpyridin-4-amine (0.12 g, 0.96 mmol, 0.1 equiv.), pivaloyl chloride (1.10 mL, 9.01 mmoL, 0.95 equiv.), CH_2Cl_2 (50 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc = 50 : 1) to give the target product (1.90 g, 73% yield) as a white solid. Mp: 60 – 62 ºC, R_f = 0.3 (petroleum ether : EtOAc = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.70 (d, *J* = 1.7 Hz, 1H), 7.30 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.18 – 7.11 (m, 2H), 5.25 (s, 2H), 3.93 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 158.1, 134.5, 129.3, 128.6, 128.2, 125.9, 123.5, 119.1, 106.0, 66.4, 55.4, 39.0, 27.4. IR (neat): 3060, 2972, 2873, 1727, 1635, 1610, 1515, 1464, 1150, 838 cm^{-1}. HRMS: calcd for $[C_{17}H_{20}O_3+H]^+$ $[M+H]^+$ 273.1491, found 273.1487.



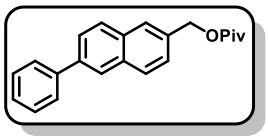
(6-(benzyloxy)naphthalen-2-yl)methyl pivalate (2d): Prepared according to procedure C using (6-(benzyloxy)naphthalen-2-yl)methanol (1.37g, 5.19 mmol, 1 equiv. prepared according to literature[15]), Et_3N (0.79 mL, 5.71 mmol, 1.1 equiv.), *N*,*N*-dimethylpyridin-4-amine (0.06 g, 0.52 mmol, 0.1 equiv.), pivaloyl chloride (0.60 mL, 4.92 mmoL, 0.95 equiv.), CH_2Cl_2 (50 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc = 50 : 1) to give the target product (1.18 g, 65% yield) as a white solid. Mp: 70 – 72 ºC, R_f = 0.3 (petroleum ether : EtOAc = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.69 (m, 3H), 7.50 – 7.46 (m, 2H), 7.46 – 7.38 (m, 3H), 7.37– 7.31 (m, 1H), 7.25 – 7.20 (m, 2H), 5.23 (s, 2H), 5.17 (s, 2H), 1.24 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 157.1, 136.9, 134.3, 131.8, 129.7, 128.9, 128.8, 128.2, 127.7, 127.3, 127.1, 126.5, 119.5, 107.2, 70.2, 66.4, 39.0, 27.3. IR (neat): 3062, 2972, 2934, 2871, 1726, 1635, 1608, 1507, 1480, 1151, 849 cm^{-1}. HRMS: calcd for $[C_{23}H_{24}O_3+H]^+$ 349.1804, found 349.1805.



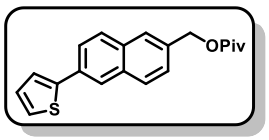
(6-cyclopropylnaphthalen-2-yl)methanol (2e): Prepared according to procedure C using (6-cyclopropylnaphthalen-2-yl)methanol (0.92 g, 4.65 mmol, 1 equiv. prepared according to literature[16]), Et_3N (0.71 mL, 5.12 mmol, 1.1 equiv.), *N*,*N*-dimethylpyridin-4-amine (0.06 g, 0.47 mmol, 0.1 equiv.), pivaloyl chloride (0.54 mL, 4.42 mmoL, 0.95 equiv.), CH_2Cl_2 (20 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc = 50 : 1) to give the target product (1.04 g, 79% yield) as a light yellow solid. Mp: 61 – 63 ºC, R_f = 0.3 (petroleum ether : EtOAc = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.60 (m, 3H), 7.54 – 7.48 (m, 1H), 7.40 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.20 (dd, *J* = 8.5, 1.9 Hz, 1H), 5.23 (s, 2H), 2.11 – 1.96 (m, 1H), 1.23 (s, 9H), 1.11 – 0.97 (m, 2H), 0.90 – 0.76 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 142.1, 133.3, 132.9, 131.7, 128.0, 127.8, 126.9, 126.0, 125.1, 123.7, 66.4, 39.0, 27.3, 15.8, 9.4. IR (neat): 3058, 2988, 2926, 2882, 1734, 1638, 1611, 1523, 14866, 1166, 873 cm^{-1}. HRMS: calcd for $[C_{19}H_{22}O_2+H]^+$ 283.1698, found 283.1691.



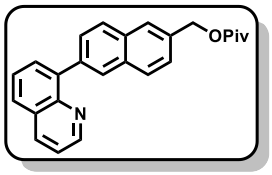
(6-methylnaphthalen-2-yl)methyl pivalate (2f): Prepared according to procedure C using (6-methylnaphthalen-2-yl)methanol (1.30 g, 7.56 mmol, 1 equiv. Prepared according to literature[16]), Et_3N (1.12 mL, 8.32 mmol, 1.1 equiv.), *N*,*N*-dimethylpyridin-4-amine (0.09 g, 0.76 mmol, 0.1 equiv.), pivaloyl chloride (0.88 mL, 7.18 mmoL, 1.1 equiv.), CH_2Cl_2 (20 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc = 50 : 1) to give the target product (1.61 g, 83% yield) as a white solid. Mp: 56 – 58 ºC, R_f = 0.3 (petroleum ether : EtOAc = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.71 (m, 3H), 7.61 (dd, *J* = 1.9, 1.1 Hz, 1H), 7.41 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.33 (dd, *J* = 8.4, 1.7 Hz, 1H), 5.25 (s, 2H), 2.52 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 136.0, 133.4, 133.0, 131.5, 128.7, 127.9, 127.8, 126.82, 126.80, 125.8, 66.4, 39.0, 27.3, 21.8. IR (neat): 3055, 2972, 2934, 2872, 1728, 1606, 1479, 1396, 1281, 1146, 885 cm^{-1}. HRMS: calcd for $[C_{17}H_{20}O_2+H]^+$ 257.1542, found 257.1540.



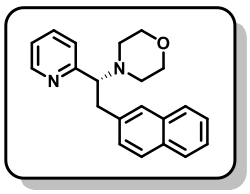
(6-phenylnaphthalen-2-yl)methyl pivalate (2g): Prepared according to procedure C (6-phenylnaphthalen-2-yl)methanol (0.92 g, 3.93 mmol, 1 equiv. prepared according to literature.[17]), Et_3N (0.61 mL, 4.32 mmol, 1.1 equiv.), *N*,*N*-dimethylpyridin-4-amine (0.05 g, 0.39 mmol, 0.1 equiv.), pivaloyl chloride (0.46 mL, 3.73 mmoL, 0.95 equiv.), CH_2Cl_2 (10 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc = 50 : 1) to give the target product (1.08 g, 86% yield) as a white solid. Mp: 88 – 93 ºC, R_f = 0.3 (petroleum ether : EtOAc = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 1.9 Hz, 1H), 7.93 (d, *J* = 5.8 Hz, 1H), 7.91 (d, *J* = 5.6 Hz, 1H), 7.85 – 7.83 (m, 1H), 7.78 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.76 – 7.71 (m, 2H), 7.55 – 7.46 (m, 3H), 7.43 – 7.37 (m, 1H), 5.30 (s, 2H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 141.1, 139.0, 134.1, 133.4, 132.5, 129.0, 128.7, 128.6, 127.6, 127.5, 126.8, 126.2, 126.1, 125.7, 66.3, 39.0, 27.3. IR (neat): 3063, 2969, 2874, 1728, 1635, 1603, 1497, 1454, 1163, 884 cm^{-1}. HRMS: calcd for $[C_{22}H_{22}O_2+H]^+$ $[M+H]^+$ 319.1698, found 319.1703.



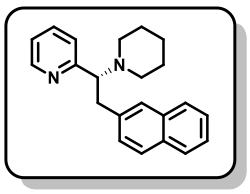
(6-(thiophen-2-yl)naphthalen-2-yl)methyl pivalate (**2h**)**:** Prepared according to procedure C (6-(thiophen-2-yl)naphthalen-2-yl)methanol (1.0 g, 4.16 mmol, 1 equv. Prepared according to literature[17]), Et_3N (0.64 mL, 4.57 mmol, 1.1 equiv.), N,N-dimethylpyridin-4-amine (0.05 g, 0.42 mmol, 0.1 equiv.), pivaloyl chloride (0.48 mL, 3.96 mmoL, 0.95 equiv.), CH_2Cl_2 (10 mL), 12 h. The crude product was purified by silica gel column (eluted with petroleum ether : EtOAc = 50 : 1) to give the target product (1.10 g, 82% yield) as a white solid. Mp: 93 – 98 ºC, R_f = 0.3 (petroleum ether : EtOAc = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 1.7 Hz, 1H), 7.85 (dd, *J* = 8.5, 3.5 Hz, 2H), 7.80 – 7.74 (m, 2H), 7.49 – 7.42 (m, 2H), 7.34 (dt, *J* = 5.1, 1.0 Hz, 1H), 7.14 (ddd, *J* = 5.0, 3.7, 0.9 Hz, 1H), 5.27 (s, 2H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 144.4, 134.1, 133.4, 132.6, 132.2, 128.7, 128.5, 128.3, 126.8, 126.4, 125.3, 125.0, 124.1, 123.7, 66.3, 39.0, 27.3. IR (neat): 2970, 2872, 1729, 1636, 1601, 1478, 1460, 1363, 1280, 1147, 884 cm^{-1}. HRMS: calcd for $[C_{20}H_{20}O_2S+H]^+$ 325.1262, found 325.1267.



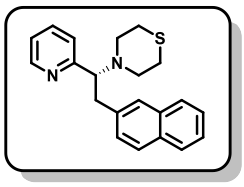
(6-(quinolin-8-yl)naphthalen-2-yl)methyl pivalate (2i): Prepared according to procedure C (6-(quinolin-8-yl)naphthalen-2-yl)methanol (0.31 g, 1.08 mmol, 1 equiv. prepared according to literature[17]), Et_3N (0.17 mL, 1.29 mmol, 1.1 equiv.), *N*,*N*-dimethylpyridin-4-amine (13.42 mg, 0.11 mmol, 0.1 equiv.), pivaloyl chloride (0.13 mL, 1.03 mmoL, 0.95 equiv.), CH_2Cl_2 (10 mL), 12 h. The crude product was purified by silica gel column (eluted with : EtOAc = 10 : 1) to give the target product (0.32 g, 82% yield) as a white solid. Mp: 110–112 ºC, R_f = 0.3 (petroleum ether : EtOAc = 10 : 1). ^{11}H NMR (400 MHz, $CDCl_3$) δ 8.93 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.21 (dd, *J* = 8.3, 1.9 Hz, 1H), 8.12 – 8.04 (m, 1H), 7.99 – 7.73 (m, 6H), 7.62 (dd, *J* = 8.1, 7.1 Hz, 1H), 7.46 – 7.37 (m, 2H), 5.27 (s, 2H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 150.5, 146.3, 140.9, 137.9, 136.5, 134.1, 133.2, 132.7, 130.7, 129.7, 129.1, 128.9, 128.8, 127.9, 127.4, 127.0, 126.5, 126.0, 121.3, 66.5, 39.0, 27.4. IR (neat): 3035, 2904, 2843, 2802, 1718, 1635, 1611, 1502, 1433, 1216, 874 cm^{-1}. HRMS: calcd for $[C_{25}H_{23}O_2+H]^+$ 370.1802, found 370.1807.



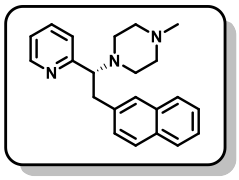
4-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine (3aa): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 ºC, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (11.5 mg, 72% yield) as a yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.81 – 7.68 (m, 1H), 7.67 – 7.63 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.51 – 7.32 (m, 4H), 7.13 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.09 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.98 (dt, *J* = 7.7, 1.1 Hz, 1H), 3.83 (dd, *J* = 8.9, 5.7 Hz, 1H), 3.73 (t, *J* = 4.8 Hz, 4H), 3.55 – 3.27 (m, 2H), 2.73 – 2.60 (m, 2H), 2.57 – 2.52 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 149.3, 136.9, 135.9, 133.4, 132.0, 128.0, 127.9, 127.62, 127.59, 127.55, 125.8, 125.3, 124.4, 122.3, 73.2, 67.4, 51.2, 37.8 ppm. IR (neat): 3051, 2959, 2852, 2815, 1588, 1471, 1433, 1269, 1115, 815 cm^{-1}. HRMS m/z: calcd for $[C_{21}H_{22}N_2O+H]^+$ $[M+H]^+$ 319.1810, found 319.1805. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 90/10/0. 1, 0.6 mL/min, 25 ºC t_R = 23.0 (minor), 25.9 (major) minutes; $[\alpha]_D^{20}$ = -75.3 (c 1.0, MeOH).



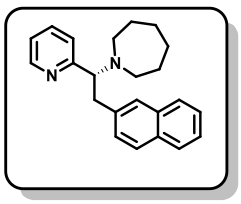
2-(2-(naphthalen-2-yl)-1-(piperidin-1-yl)ethyl)pyridine (3ba): Prepared according to procedure D using 2-(piperidin-1-ylmethyl)pyridine (8.8 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 ºC, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (11.2 mg, 71% yield) as a brown solid. Mp: 52 – 54 ºC, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.73 – 7.71 (m, 1H), 7.66 – 7.64 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.40 – 7.33 (m, 2H), 7.19 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.07 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 3.90 (dd, *J* = 9.4, 5.1 Hz, 1H), 3.51 (dd, *J* = 13.3, 9.4 Hz, 1H), 3.42 (dd, *J* = 13.2, 5.1 Hz, 1H), 2.55 (t, *J* = 5.1 Hz, 4H), 1.62 – 1.55 (m, 4H), 1.41 – 1.36 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 149.0, 137.7, 135.7, 133.5, 132.0, 128.2, 127.8, 127.59, 127.57, 127.50, 125.7, 125.1, 124.4, 122.0, 73.2, 51.6, 37.8, 26.5, 24.8 ppm. IR (neat): 3051, 2930, 2850, 2801, 1588, 1507, 1469, 1270, 1112, 812 cm^{-1}. HRMS m/z: calcd for $[C_{21}H_{24}N_2O+H]^+$ 317.2018, found 317.2018. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 95/05/0. 1, 0.6 mL/min, 25 ºC t_R = 8.9 (minor), 9.4 (major) minutes; $[\alpha]_D^{20}$ = -49.3 (c 1.0, MeOH).



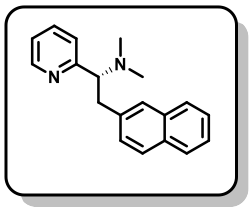
4-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)thiomorpholine (3ca): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)thiomorpholine (9.7 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (13.4 mg, 80% yield) as a brown solid. Mp: 92 – 94 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.62 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.75 – 7.73 (m, 1H), 7.70 – 7.63 (m, 2H), 7.55 – 7.48 (m, 2H), 7.42 – 7.36 (m, 2H), 7.23 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.12 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.04 (dt, *J* = 7.7, 1.0 Hz, 1H), 3.98 (dd, *J* = 8.8, 5.9 Hz, 1H), 3.54 (dd, *J* = 13.4, 8.7 Hz, 1H), 3.38 (dd, *J* = 13.4, 5.8 Hz, 1H), 2.96 (ddd, *J* = 11.9, 6.6, 3.5 Hz, 2H), 2.84 (ddd, *J* = 11.9, 6.6, 3.4 Hz, 2H), 2.71 – 2.56 (m, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.8, 149.1, 137.5, 136.0, 133.5, 132.1 128.1, 127.8, 127.7, 127.61, 127.58, 125.8, 125.3, 124.3, 122.3, 73.2, 52.5, 37.0, 28.5 ppm. IR (neat): 3051, 2950, 2907, 2816, 1599, 1568, 1507, 1432, 1278, 1123, 748 cm^{-1}. HRMS m/z: calcd for $[C_{21}H_{22}N_2S+H]^+$ 335.1582, found 335.1577. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 85/15/0. 1, 0.6 mL/min, 25 °C t_R = 11.2 (minor), 12.2 (major) minutes; $[\alpha]_D^{20}$ = -92.8 (c 1.0, MeOH).



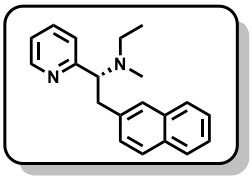
1-methyl-4-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)piperazine (3da): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)thiomorpholine (9.6 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 50 : 50 : 2) to give the target product (11.7 mg, 71% yield) as a light yellow oil. R_f = 0.2 (petroleum ether : EtOAc : Et_3N = 25 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (ddt, *J* = 4.8, 1.5, 0.7 Hz, 1H), 7.76 – 7.67 (m, 1H), 7.67 – 7.53 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.43 – 7.31 (m, 2H), 7.15 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.06 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.03 – 6.94 (m, 1H), 3.89 (dd, *J* = 9.0, 5.6 Hz, 1H), 3.55 – 3.35 (m, 2H), 2.90 – 2.30 (d, *J* = 61.9 Hz, 8H), 2.26 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 149.2, 137.2, 135.8, 133.5, 132.0, 128.1, 127.9, 127.61, 127.58, 127.5, 125.8, 125.2, 124.4, 122.2, 72.6, 55.5, 50.2, 46.1, 37.9 ppm. IR (neat): 3051, 2933, 2878, 2794, 1599, 1587, 1454, 1433, 1283, 1160, 815 cm^{-1}. HRMS m/z: calcd for $[C_{22}H_{25}N_3+H]^+$ 332.2127, found 332.2123. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 95/05/0. 1, 0.5 mL/min, 25 °C t_R = 44.9 (minor), 46.8 (major) minutes; $[\alpha]_D^{20}$ = -66.4 (c 1.0, MeOH).



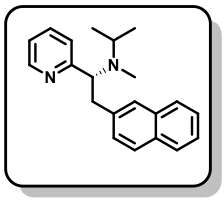
1-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)azepane (3ea): Prepared according to procedure D using 1-(pyridin-2-ylmethyl)azepane (9.5 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (13.8 mg, 84% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (dt, *J* = 5.0, 1.2 Hz, 1H), 7.75 – 7.73 (m, 1H), 7.70 – 7.68 (m, 1H), 7.66 (d, *J* = 8.5 Hz, 1H), 7.56 (s, 1H), 7.53 – 7.48 (m, 1H), 7.42 – 7.35 (m, 2H), 7.28 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.14 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.09 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 4.15 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.52 (dd, *J* = 13.5, 8.4 Hz, 1H), 3.39 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.95 – 2.80 (m, 2H), 2.76 – 2.60 (m, 2H), 1.63 – 1.47 (m, 8H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 148.8, 138.2, 135.7, 133.6, 132.0, 128.3, 127.8, 127.61, 127.57, 127.4, 125.7, 125.1, 124.0, 121.9, 71.9, 52.3, 37.9, 29.4, 27.1 ppm. IR (neat): 3052, 3007, 2922, 2849, 1599, 1568, 1587, 1470, 1432, 1149, 813 cm^{-1}. HRMS m/z: calcd for $[C_{23}H_{26}N_2+H]^+$ 331.2174, found 331.2169. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 95/05/0. 1, 0.6 mL/min, 25 °C t_R = 8.8 (minor), 9.4 (major) minutes; $[\alpha]_D^{20}$ = -77.7 (c 1.0, MeOH).



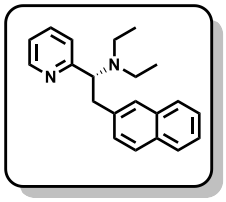
N,N-dimethyl-2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethan-1-amine (3fa): Prepared according to procedure D using N,N-dimethyl-1-(pyridin-2-yl)methanamine (6.8 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (9.8 mg, 71% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.67 – 7.63 (m, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.47 (td, *J* = 7.6, 1.8 Hz, 1H), 7.43 (s, 1H), 7.40 – 7.32 (m, 2H), 7.15 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.08 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.01 (dt, *J* = 7.8, 1.1 Hz, 1H), 3.83 (dd, *J* = 8.8, 5.8 Hz, 1H), 3.44 (dd, *J* = 7.4, 3.9 Hz, 2H), 2.36 (s, 6H). ^{13}C NMR* (101 MHz, $CDCl_3$) δ 159.4, 149.2, 137.1, 135.9, 133.5, 132.0, 128.0, 127.8, 127.61, 127.57, 125.8, 125.2, 124.3, 122.2, 73.0, 42.8, 38.1 with one carbon not observed due to overlapping resonances. IR (neat): 3052, 3006, 2932, 2822, 2778, 1632, 1599, 1588, 1568, 1507, 1472, 1451, 1433, 1366, 1270, 1151, 1043, 817 cm^{-1}. HRMS m/z: calcd for $[C_{19}H_{20}N_2+H]^+$ 277.1705, found 277.1700. HPLC Analysis: Chiralpak ODH ^{n}Hexane/^{i}PrOH = 95/05, 0.5 mL/min, 25 °C t_R = 14.3 (major), 16.1 (minor) minutes; $[\alpha]_D^{20}$ = -123.7 (c 1.0, MeOH). Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.



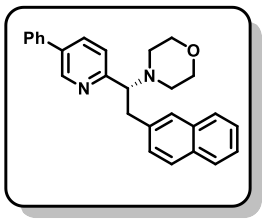
N-ethyl-N-methyl-2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethan-1-amine (3ga): Prepared according to procedure D using N-methyl-N-(pyridin-2-ylmethyl)ethanamine (7.5 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (12.2 mg, 84% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.66 (d, *J* = 2.4 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.51 – 7.43 (m, 2H), 7.41 – 7.32 (m, 2H), 7.18 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.08 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 4.03 (dd, *J* = 9.7, 4.9 Hz, 1H), 3.52 (dd, *J* = 13.2, 9.7 Hz, 1H), 3.38 (dd, *J* = 13.2, 4.8 Hz, 1H), 2.78 – 2.60 (m, 1H), 2.56 – 2.43 (m, 1H), 2.35 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 149.0, 137.6, 135.8, 133.5, 132.0, 128.1, 127.8, 127.60, 127.56, 127.53, 125.7, 125.2, 124.4, 122.0, 70.9, 48.4, 38.2, 37.5, 12.8. IR (neat): 3052, 3006, 2967, 2933, 2844, 2793, 1632, 1599, 1588, 1568, 1507, 1471, 1455, 1382, 1171, 1042, 814, 770 cm^{-1}. HRMS m/z: calcd for $[C_{19}H_{22}N_2+H]^+$ 291.1861, found 291.1857. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 90/10/0.1, 0.6 mL/min, 25 °C t_R = 9.4 (minor), 10.0 (major) minutes; $[\alpha]_D^{20}$ = -157.2 (c 1.0, MeOH).



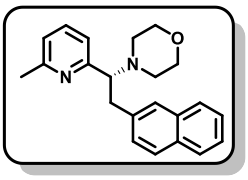
N-methyl-N-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)propan-2-amine (3ha): Prepared according to procedure D using *N*-methyl-*N*-(pyridin-2-ylmethyl)propan-2-amine (8.7 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (13.2 mg, 87% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 – 8.48 (m, 1H), 7.74 – 7.68 (m, 1H), 7.67 – 7.62 (m, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.44 (td, *J* = 7.6, 1.8 Hz, 1H), 7.41 (s, 1H), 7.39 – 7.33 (m, 2H), 7.13 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.09 – 7.02 (m, 2H), 4.10 (dd, *J* = 8.9, 5.7 Hz, 1H), 3.40 (dd, *J* = 7.3, 4.2 Hz, 2H), 3.11 – 2.96 (m, 1H), 2.35 (s, 3H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 149.1, 137.7, 136.0, 133.6, 132.1, 128.3, 127.9, 127.7, 127.7, 127.6, 125.8, 125.3, 124.1, 122.1, 69.7, 50.6, 39.0, 32.5, 19.9, 18.4. IR (neat): 3052, 3007, 2988, 2935, 2846, 2795, 1642, 1600, 1587, 1574, 1501, 1464, 1455, 1385, 1166, 1024, 821, 778 cm^{-1}. HRMS m/z: calcd for $[C_{21}H_{24}N_2+H]^+$ 305.2018, found 305.2015. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 90/10/0. 1, 0.6 mL/min, 25 °C t_R = 8.4 (minor), 8.9 (major) minutes; $[\alpha]_D^{20}$ = -125.8 (c 1.0, MeOH).



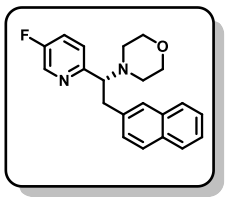
N,N-diethyl-2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethan-1-amine (3ia): Prepared according to procedure D using *N*-ethyl-*N*-(pyridin-2-ylmethyl)ethanamine (8.2 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (9.9 mg, 65% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc :Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (ddd, *J* = 4.7, 1.9, 1.0 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.69 – 7.65 (m, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.42 – 7.33 (m, 2H), 7.21 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.07 (ddd, *J* = 7.5, 5.8, 1.2 Hz, 2H), 4.18 (dd, *J* = 9.2, 5.2 Hz, 1H), 3.50 (dd, *J* = 13.3, 9.2 Hz, 1H), 3.36 (dd, *J* = 13.2, 5.2 Hz, 1H), 2.80 (dq, *J* = 13.1, 7.2 Hz, 2H), 2.54 (dq, *J* = 14.0, 7.0 Hz, 2H), 1.04 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 148.9, 138.0, 135.8, 133.5, 132.0, 128.2, 127.8, 127.62, 127.56, 127.50, 125.7, 125.1, 124.3, 121.9, 67.6, 43.9, 37.5, 13.4. IR (neat): 3053, 3007, 2968, 2929, 2869, 2811, 1632, 1600, 1568, 1507, 1470, 1447, 1432, 1382, 1295, 1198, 995, 652 cm^{-1}. HRMS m/z: calcd for $[C_{21}H_{24}N_2+H]^+$ 305.2018, found 305.2014. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 95/5/0. 1, 0.3 mL/min, 25 °C t_R = 14.7 (minor), 15.6 (major) minutes; $[\alpha]_D^{20}$ = -121.1 (c 1.0, MeOH).



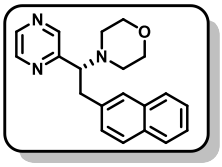
4-(2-(naphthalen-2-yl)-1-(5-phenylpyridin-2-yl)ethyl)morpholine (3ja): Prepared according to procedure D using 4-((5-phenylpyridin-2-yl)methyl)morpholine (12.7 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), Pd(dba)2 (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand L8 (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (17.5 mg, 89% yield) as a yellow solid. Mp: 110 – 112 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 2.4 Hz, 1H), 7.79 – 7.70 (m, 1H), 7.70 – 7.62 (m, 3H), 7.54 (d, *J* = 7.3 Hz, 2H), 7.50 – 7.43 (m, 3H), 7.42 – 7.35 (m, 3H), 7.18 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 3.91 (dd, *J* = 8.3, 6.2 Hz, 1H), 3.75 (t, *J* = 4.7 Hz, 4H), 3.52 – 3.40 (m, 2H), 2.75 – 2.65 (m, 2H), 2.65 – 2.56 (m, 2H) ppm. ^{13}C NMR* (101 MHz, $CDCl_3$) δ 158.0, 147.7, 137.7, 136.9, 135.1, 134.3, 133.5, 132.0, 129.2, 128.1, 128.0, 127.9, 127.7, 127.63, 127.57, 127.2, 125.9, 125.3, 124.3, 72.8, 67.4, 51.2, 37.7 ppm. IR (neat): 3053, 2956, 2852, 2816, 1599, 1507, 1474, 1115, 855 cm^{-1}. HRMS m/z: calcd for $[C_{27}H_{26}N_2O+H]^+$ 395.2123, found 395.2123. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 °C t_R = 19.8 (major), 28.1 (minor) minutes; $[\alpha]_D^{20}$ = -182.1 (c 1.0, MeOH). Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.



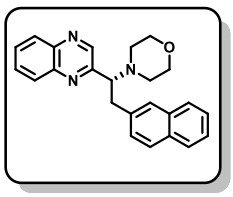
4-(1-(6-methylpyridin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine (3ka): Prepared according to procedure D using 4-((6-methylpyridin-2-yl)methyl)morpholine (9.6 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 ºC, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (11.9 mg, 72% yield) as light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.70 (m, 1H), 7.68 – 7.63 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.49 – 7.43 (m, 1H), 7.42 – 7.32 (m, 3H), 7.14 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.83 (dt, *J* = 7.7, 0.8 Hz, 1H), 3.81 (dd, *J* = 8.0, 6.5 Hz, 1H), 3.72 (ddd, *J* = 5.6, 3.6, 1.9 Hz, 4H), 3.50 – 3.24 (m, 2H), 2.72 – 2.63 (m, 2H), 2.58 – 2.53 (m, 2H), 2.52 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 157.8, 137.2, 136.0, 133.5, 132.0, 128.2, 127.9, 127.6, 127.5, 127.4, 125.7, 125.2, 121.7, 121.1, 73.2, 67.4, 51.2, 37.8, 24.7 ppm. IR (neat): 3055, 2959, 2924, 2852, 1632, 1589, 1452, 1262, 1115, 813 cm^{-1}. HRMS m/z: calcd for $[C_{22}H_{24}N_2O+H]^+$ 333.1967, found 333.1962. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 85/15/0. 1, 0.6 mL/min, 25 ºC t_R = 14.0 (minor), 17.0 (major) minutes; $[\alpha]_D^{20}$ = -88.3 (c 1.0, MeOH).



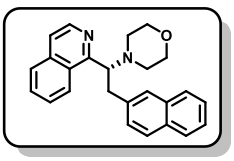
4-(1-(5-fluoropyridin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine (3la): Prepared according to procedure D using 4-((5-fluoropyridin-2-yl)methyl)morpholine (9.8 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 ºC, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (9.9 mg, 59% yield) as a brown solid. Mp: 56 – 60 ºC, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 2.9 Hz, 1H), 7.76 – 7.70 (m, 1H), 7.68 – 7.64 (m, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.46 – 7.33 (m, 3H), 7.17 (td, *J* = 8.4, 3.0 Hz, 1H), 7.11 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.97 (dd, *J* = 8.6, 4.5 Hz, 1H), 3.84 (dd, *J* = 9.6, 5.1 Hz, 1H), 3.73 (t, *J* = 4.7 Hz, 4H), 3.51 – 3.19 (m, 2H), 2.72 – 2.60 (m, 2H), 2.56 – 2.46 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 156.3 (d, $J_{C\text{-}F}^1$ = 203.7 Hz), 137.5 (d, $J_{C\text{-}F}^2$ = 23.1 Hz), 136.7, 133.5, 132.0, 127.89, 127.85, 127.7, 127.6, 127.5, 126.0, 125.4, 125.1 (d, $J_{C\text{-}F}^3$ = 3.9 Hz), 122.7 (d, $J_{C\text{-}F}^2$ = 17.9 Hz), 72.41, 67.32, 51.12, 37.82 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -129.46. IR (neat): 3053, 2957, 2853, 2817, 1600, 1584, 1507, 1480, 1391, 1226, 889 cm^{-1}. HRMS m/z: calcd for $[C_{21}H_{22}FN_2O+H]^+$ 337.1716, found 337.1712. HPLC Analysis: Chiralpak ID (^{n}Hexane/^{i}PrOH = 90/10, 1 mL/min, 25 ºC) t_R = 8.9 (minor), 10.2 (major) minutes, $[\alpha]_D^{20}$ = -78.8 (c 1.0, MeOH).



4-(2-(naphthalen-2-yl)-1-(pyrazin-2-yl)ethyl)morpholine (3ma): Prepared according to procedure D using 4-(pyrazin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 ºC, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (11.9 mg, 75% yield) as a light yellow oil. R_f = 0.1 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ: 8.56 (dd, *J* = 2.6, 1.5 Hz, 1H), 8.37 (d, *J* = 2.6 Hz, 1H), 8.31 (d, *J* = 1.5 Hz, 1H), 7.77 – 7.70 (m, 1H), 7.65 (dd, *J* = 8.9, 5.8 Hz, 2H), 7.44 (d, *J* = 1.7 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.14 (dd, *J* = 8.4, 1.8 Hz, 1H), 3.96 (dd, *J* = 9.5, 5.4 Hz, 1H), 3.73 (t, *J* = 4.7 Hz, 4H), 3.53 – 3.39 (m, 2H), 2.74 – 2.63 (m, 2H), 2.62 – 2.52 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.6, 149.3, 145.6, 135.8, 133.7, 131.8, 128.5, 128.3, 127.6, 126.3, 125.5, 124.5, 115.7, 104.5, 73.5, 67.4, 51.3, 47.9, 37.8, 25.6 ppm. IR (neat): 3050, 2946, 2917, 2844, 1601, 1507, 1451, 1405, 1112, 871 cm^{-1}. HRMS m/z: calcd for $[C_{20}H_{21}N_3O+H]^+$ 320.1763, found 320.1761. HPLC Analysis: Chiralpak ODH ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 ºC t_R = 28.0 (major), 32.4 (minor) minutes; $[\alpha]_D^{20}$ = -64.9 (c 1.0, MeOH).

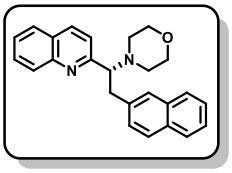


4-(2-(naphthalen-2-yl)-1-(quinoxalin-2-yl)ethyl)morpholine (3na): Prepared according to procedure D using 4-(quinoxalin-2-ylmethyl)morpholine (11.5 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 ºC, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (14.2 mg, 77% yield) as a light yellow oil. R_f = 0.1 (petroleum ether : EtOAc :Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.12 – 8.05 (m, 1H), 8.03 (dd, *J* = 7.5, 2.3 Hz, 1H), 7.79 – 7.67 (m, 3H), 7.62 (dd, *J* = 9.0, 4.8 Hz, 2H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.23 (dd, *J* = 8.5, 1.8 Hz, 1H), 4.22 (dd, *J* = 9.3, 4.9 Hz, 1H), 3.72 (dd, *J* = 5.5, 3.8 Hz, 4H), 3.66 (dd, *J* = 13.4, 9.4 Hz, 1H), 3.53 (dd, *J* = 13.4, 4.9 Hz, 1H), 2.82 – 2.69 (m, 2H), 2.69 – 2.59 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 146.4, 141.8, 141.7, 136.5, 133.5, 132.1, 130.1, 129.7, 129.5, 129.3, 128.03, 127.98, 127.90, 127.7, 127.5, 126.0, 125.5, 71.0, 67.4, 50.8, 35.6 ppm. IR (neat): 3057, 2957, 2852, 2818, 1600, 1507, 1492, 1451, 1384, 1115, 808 cm^{-1}. HRMS m/z: calcd for $[C_{24}H_{23}N_3O+H]^+$ 370.1919, found 370.1916. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 ºC t_R = 22.7 (minor), 32.2 (major) minutes; $[\alpha]_D^{20}$ = -123.1 (c 1.0, MeOH).

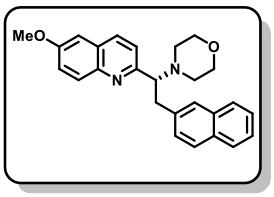


4-(1-(isoquinolin-1-yl)-2-(naphthalen-2-yl)ethyl)morpholine (3oa): Prepared according to procedure D using 4-(isoquinolin-1-ylmethyl)morpholine (11.4 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 ºC, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2)

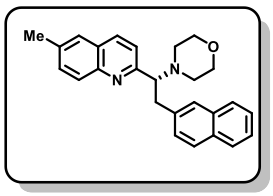
to give the target product (14.9 mg, 81% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 5.6 Hz, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 7.74 (dt, *J* = 8.2, 1.1 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.62 – 7.53 (m, 3H), 7.51 – 7.43 (m, 3H), 7.38 – 7.28 (m, 2H), 7.18 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.79 (dd, *J* = 9.5, 4.6 Hz, 1H), 3.78 (dd, *J* = 13.1, 9.5 Hz, 1H), 3.73 – 3.62 (m, 4H), 3.55 (dd, *J* = 13.2, 4.6 Hz, 1H), 2.92 – 2.72 (m, 2H), 2.70 – 2.54 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 141.3, 137.5, 136.4, 133.4, 131.9, 129.7, 128.2, 128.0, 127.8, 127.53, 127.46, 127.4, 126.9, 125.7, 125.2, 125.1, 120.3, 68.5, 67.44, 50.9, 35.5 ppm. IR (neat): 3051, 2957, 2951, 2817, 1623, 1502, 1450, 1310, 1115, 824 cm^{-1}. HRMS m/z: calcd for $[C_{25}H_{24}N_2O+H]^+$ 369.1967, found 369.1966. HPLC Analysis: Chiralpak ODH ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 °C t_R = 13.1 (major), 16.9 (minor) minutes; $[\alpha]_D^{20}$ = -78.9 (c 1.0, MeOH).



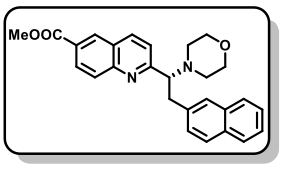
4-(2-(naphthalen-2-yl)-1-(quinolin-2-yl)ethyl)morpholine (3pa): Prepared according to procedure D using 4-(quinolin-2-ylmethyl)morpholine (11.4 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (14.4 mg, 78% yield) as a brown solid. Mp: 98 – 100 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.98 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.72 – 7.65 (m, 2H), 7.65 – 7.60 (m, 1H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.52 – 7.45 (m, 1H), 7.40 – 7.32 (m, 2H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.20 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.09 (dd, *J* = 8.9, 5.2 Hz, 1H), 3.72 (t, *J* = 4.7 Hz, 4H), 3.60 (dd, *J* = 13.5, 8.9 Hz, 1H), 3.51 (dd, *J* = 13.5, 5.2 Hz, 1H), 2.81 – 2.66 (m, 2H), 2.65 – 2.54 (m, 2H) ppm. ^{13}C NMR*(101 MHz, $CDCl_3$) δ: 160.3, 147.7, 137.0, 135.9, 133.4, 132.0, 129.5, 129.4, 128.1, 127.9, 127.58, 127.55, 127.52, 127.4, 126.3, 125.8, 125.2, 122.0, 73.5, 67.4, 51.2, 37.1 ppm with one resonance missing due to overlapping resonances. IR (neat): 3006, 2989, 2921, 1560, 1512, 1436, 1275, 1101, 764 cm^{-1}. HRMS m/z: calcd for $[C_{25}H_{24}N_2O+H]^+$ 369.1967, found 369.1964. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 85/15/0. 1, 0.6 mL/min, 25 °C t_R = 15.5 (minor), 18.5 (major) minutes; $[\alpha]_D^{20}$ = -190.2 (c 1.0, MeOH). Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.



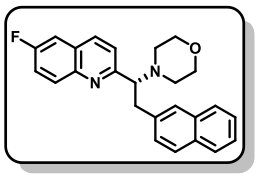
4-(1-(6-methoxyquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine (3qa): Prepared according to procedure D using 4-((6-methoxyquinolin-2-yl)methyl)morpholine (12.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20: 2) to give the target product (18.1 mg, 91% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 9.2 Hz, 1H), 7.86 (d, *J* = 8.5 Hz, 1H), 7.73 – 7.67 (m, 1H), 7.65 – 7.61 (m, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 1.7 Hz, 1H), 7.40 – 7.29 (m, 3H), 7.24 – 7.13 (m, 2H), 6.99 (d, *J* = 2.8 Hz, 1H), 4.12 – 3.98 (m, 1H), 3.89 (s, 3H), 3.73 (t, *J* = 4.7 Hz, 4H), 3.62 – 3.34 (m, 2H), 2.74 (q, *J* = 5.5, 4.6 Hz, 2H), 2.58 (dt, *J* = 11.5, 4.7 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.61, 157.59, 143.7, 137.1, 134.6, 133.4, 131.9, 130.9, 128.3, 128.3, 128.2, 127.9, 127.6, 127.5, 125.7, 125.2, 122.3, 122.0, 105.1, 73.4, 67.4, 55.6, 51.2, 37.3 ppm. IR (neat): 3053, 2957, 2852, 1623, 1599, 1499, 1452, 1380, 1115, 866 cm^{-1}. HRMS m/z: calcd for $[C_{26}H_{26}N_2O_2+H]^+$ 399.2073, found 399.2070. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 °C t_R = 20.3 (minor), 22.5 (major) minutes; $[\alpha]_D^{20}$ = -197.1 (c 1.0, MeOH).



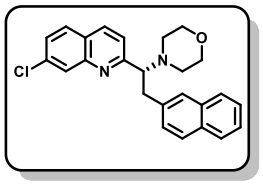
4-(1-(6-methylquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine (3ra): Prepared according to procedure D using 4-((6-methylquinolin-2-yl)methyl)morpholine (12.1 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100: 20 : 2) to give the target product (18.7 mg, 98% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.94 (m, 1H), 7.88 (dd, *J* = 8.5, 0.7 Hz, 1H), 7.74 – 7.66 (m, 1H), 7.65 – 7.60 (m, 1H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.51 (dd, *J* = 9.2, 1.3 Hz, 3H), 7.41 – 7.31 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.05 (dd, *J* = 8.9, 5.3 Hz, 1H), 3.72 (t, *J* = 4.7 Hz, 4H), 3.63 – 3.41 (m, 2H), 2.90 – 2.68 (m, 2H), 2.61– 2.53 (m, 2H), 2.51 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 146.3, 137.1, 136.1, 135.2, 133.4, 132.0, 131.6, 129.2, 128.2, 127.9, 127.56, 127.53, 127.4, 126.4, 125.7, 125.2, 122.0, 73.5, 67.4, 51.3, 37.2, 21.6 ppm with one peak not observed due to overlapping resonances. IR (neat):3053, 2956, 2852, 2816, 1599, 1563, 1497, 1116, 830 cm^{-1}. HRMS m/z: calcd for $[C_{26}H_{26}N_2O+H]^+$ 383.2123, found 383.2122. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 °C t_R = 15.1 (major), 17.6 (minor) minutes; $[\alpha]_D^{20}$ = -141.9 (c 1.0, MeOH).



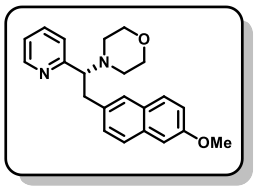
Methyl 2-(1-morpholino-2-(naphthalen-2-yl)ethyl)quinoline-6-carboxylate (3sa): Prepared according to procedure D using methyl 2-(morpholinomethyl)quinoline-6-carboxylate (14.3 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (12.7 mg, 60% yield) as a light yellow oil. R_f = 0.2 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 1.9 Hz, 1H), 8.26 (dd, *J* = 8.8, 2.0 Hz, 1H), 8.15 – 8.02 (m, 2H), 7.77 – 7.64 (m, 1H), 7.63 – 7.56 (m, 2H), 7.51 (s, 1H), 7.43 – 7.31 (m, 3H), 7.19 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.11 (dd, *J* = 8.7, 5.1 Hz, 1H), 3.98 (s, 3H), 3.72 (t, *J* = 4.7 Hz, 4H), 3.64 – 3.43 (m, 2H), 2.83 – 2.66 (m, 2H), 2.65 – 2.54 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 162.9, 149.5, 137.0, 136.7, 133.4, 132.0, 130.7, 129.8, 128.9, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 126.5, 125.9, 125.3, 122.8, 73.5, 67.4, 52.5, 51.2, 36.9 ppm. IR (neat): 2952, 2852, 1720, 1624, 1507, 1269, 1115, 850 cm^{-1}. HRMS m/z: calcd for $[C_{27}H_{26}N_2O_3+H]^+$ 427.2022, found 427.2017. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 °C t_R = 37.9 (minor), 45.0 (major) minutes; $[\alpha]_D^{20}$ = -150.3 (c 1.0, MeOH).



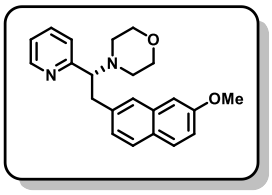
4-(1-(6-fluoroquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine (3ta): Prepared according to procedure D using 4-((6-fluoroquinolin-2-yl)methyl)morpholine (12.3 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 :20 : 2) to give the target product (15.6 mg, 81% yield) as a yellow solid. Mp: 111 – 113 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 9.2, 5.3 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.74 – 7.65 (m, 1H), 7.64 – 7.60 (m, 1H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.50 (s, 1H), 7.44 (td, *J* = 8.8, 2.9 Hz, 1H), 7.36 (m , 3H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.18 (dd, *J* = 8.4, 1.7 Hz, 1H), 4.06 (dd, *J* = 8.9, 5.3 Hz, 1H), 3.73 (t, *J* = 4.6 Hz, 4H), 3.62 – 3.43 (m, 2H), 2.86 – 2.69 (m, 2H), 2.66 – 2.50 (m, 2H) ppm.^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, (d, $J_{C\text{-}F}^1$ = 191.4 Hz), 159.1, 144.7, 136.9, 135.3 (d, *J* = 5.3 Hz), 132.0, 131.9, 128.1, 127.96, 127.92, 127.90, 127.64, 127.59, 127.51, 125.8, 125.3, 122.8, 119.5 (d, $J_{C\text{-}F}^2$ = 25.5 Hz), 110.6 (d, $J_{C\text{-}F}^2$= 21.6 Hz), 73.46, 67.37, 51.22, 37.08 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.08. IR (neat): 3054, 2957, 2852, 2817, 1627, 1604, 1504, 1224, 1115, 871 cm^{-1}. HRMS m/z: calcd for $[C_{25}H_{23}N_2FO+H]^+$ 387.1873, found 387.1868. HPLC Analysis: Chiralpak IC3 ^{n}Hexane/^{i}PrOH/Et_3N = 80/20/0. 1, 0.6 mL/min, 25 °C t_R = 12.7 (minor), 13.7 (major) minutes; $[\alpha]_D^{20}$ = -98.8 (c 1.0, MeOH).



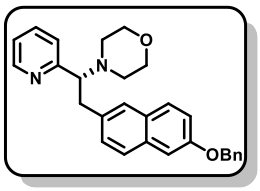
4-(1-(7-chloroquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine (3ua): Prepared according to procedure D using 4-((7-chloroquinolin-2-yl)methyl)morpholine (13.1 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), naphthalen-2-ylmethyl pivalate (36.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (19.3 mg, 96% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 2.0 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.75 – 7.68 (m, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.64 – 7.61 (m, 1H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.51 (s, 1H), 7.44 (ddd, *J* = 8.7, 2.2, 0.9 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.29 – 7.25 (m, 1H), 7.20 (dt, *J* = 8.4, 1.3 Hz, 1H), 4.08 (dd, *J* = 9.2, 5.1 Hz, 1H), 3.72 (t, *J* = 4.7 Hz, 4H), 3.59 (dd, *J* = 13.4, 9.2 Hz, 1H), 3.49 (dd, *J* = 13.4, 5.0 Hz, 1H), 2.87 – 2.71 (m, 2H), 2.62 – 2.51 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 148.0, 136.9, 135.6, 135.2, 133.4, 132.0, 128.8, 128.6, 128.1, 127.9, 127.7, 127.6, 127.5, 127.3, 125.8, 125.7, 125.3, 122.3, 73.4, 67.4, 51.1, 36.8 ppm. IR (neat): 3064, 2957, 2852, 1611, 1598, 1494, 1450, 1415, 1115, 849 cm^{-1}. HRMS m/z: calcd for $[C_{25}H_{23}N_2ClO+H]^+$ 403.1577, found 403.1577. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 85/15/0. 1, 0.6 mL/min, 25 °C t_R = 11.0 (major), 12.0 (minor) minutes; $[\alpha]_D^{20}$ = -117.8 (c 1.0, MeOH).



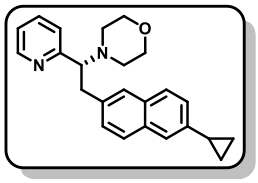
4-(2-(6-methoxynaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine (3ab): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), (6-methoxynaphthalen-2-yl)methyl pivalate (40.8 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (12.3 mg, 71% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 – 8.56 (m, 1H), 7.54 (d, *J* = 8.9 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.44 (td, *J* = 7.6, 1.8 Hz, 1H), 7.33 (s, 1H), 7.06 (td, *J* = 8.9, 4.4 Hz, 3H), 7.02 (d, *J* = 2.5 Hz, 1H), 6.96 (d, *J* = 7.7 Hz, 1H), 3.86 (s, 3H), 3.80 (dd, *J* = 9.2, 5.5 Hz, 1H), 3.73 (t, *J* = 4.8 Hz, 4H), 3.38 (d, *J* = 9.3, 8.6 Hz, 2H), 2.66 (q, *J* = 5.5, 4.7 Hz, 2H), 2.58 – 2.49 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 157.2, 149.3, 135.9, 134.5, 133.3, 129.0, 128.9, 128.5, 127.7, 126.4, 124.4, 122.2, 118.6, 105.6, 73.28, 67.32, 55.33, 51.16, 37.64 ppm. IR (neat):3055, 2962, 2924, 2852, 1634, 1606, 1506, 1434, 1262, 800 cm^{-1}. HRMS m/z: calcd for $[C_{22}H_{24}N_2O_2+H]^+$ 349.1916, found 349.1918. HPLC Analysis: Chiralpak ODH ^{n}Hexane/^{i}PrOH/Et_3N = 90/10/0. 1, 0.6 mL/min, 25 °C t_R = 21.1 (minor), 22.1 (major) minutes; $[\alpha]_D^{20}$ = -165.7 (c 1.0, MeOH).



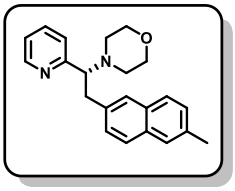
4-(2-(7-methoxynaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine (3ac): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), (7-methoxynaphthalen-2-yl)methyl pivalate (40.8 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (13.2 mg, 76% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 – 8.48 (m, 1H), 7.61 (d, *J* = 8.9 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.46 (td, *J* = 7.7, 1.8 Hz, 1H), 7.33 (s, 1H), 7.11 – 7.07 (m, 1H), 7.04 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.00 – 6.93 (m, 3H), 3.87 (s, 3H), 3.83 (dd, *J* = 9.1, 5.5 Hz, 1H), 3.73 (t, *J* = 4.8 Hz, 4H), 3.52 – 3.26 (m, 2H), 2.75 – 2.61 (m, 2H), 2.60 – 2.39 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 157.7, 149.3, 137.5, 135.9, 134.6, 129.1, 127.5, 127.4, 126.8, 125.7, 124.4, 122.3, 118.0, 105.5, 73.2, 67.3, 55.4, 51.2, 37.9 ppm. IR (neat):3050, 2956, 2852, 1633, 1607, 1514, 1464, 1116, 839 cm^{-1}. HRMS m/z: calcd for $[C_{22}H_{24}N_2O_2+H]^+$ 349.1916, found 349.1911. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 95/5/0. 1, 0.6 mL/min, 25 °C t_R = 29.1 (minor), 31.9 (major) minutes; $[\alpha]_D^{20}$ = -83.3 (c 1.0, MeOH).



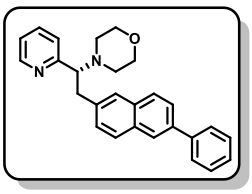
4-(2-(6-(benzyloxy)naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine (3ad)： Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), (6-(benzyloxy)naphthalen-2-yl)methyl pivalate (52.2 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (16.1 mg, 76% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.62 – 8.56 (m, 1H), 7.56 (d, *J* = 8.9 Hz, 1H), 7.52 – 7.43 (m, 4H), 7.42 – 7.30 (m, 4H), 7.18 – 7.05 (m, 4H), 6.97 (dq, *J* = 7.8, 0.9 Hz, 1H), 5.13 (s, 2H), 3.80 (dd, *J* = 9.2, 5.5 z, 1H), 3.73 (t, *J* = 4.7 Hz, 4H), 3.48 – 3.29 (m, 2H), 2.76 – 2.60 (m, 2H), 2.59 – 2.60 (m, 2H) ppm. ^{13}C NMR* (101 MHz, $CDCl_3$) δ 159.3, 156.4, 149.3, 137.0, 135.9, 134.6, 133.0, 129.10, 129.08, 128.7, 128.5, 128.1, 127.7, 126.5, 124.4, 122.3, 119.0, 107.0, 73.3, 70.1, 67.4, 51.2, 37.7 ppm with one resonance missing due to overlapping peaks. IR (neat):3056, 2962, 2925, 2854, 1632, 1604, 1506, 1453, 1261, 799 cm^{-1}. HRMS m/z: calcd for $[C_{28}H_{28}N_2O_2+H]^+$ 425.2229, found 425.2224. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 85/15/0. 1, 0.6 mL/min, 25 °C t_R = 27.7 (minor), 29.7 (major) minutes; $[\alpha]_D^{20}$ = -91.7 (c 1.0, MeOH). Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.



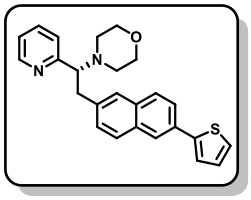
4-(2-(6-cyclopropylnaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine (3ae)： Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), (6-cyclopropylnaphthalen-2-yl)methyl pivalate (42.3 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (12.4 mg, 69% yield) as a yellow solid. Mp: 96 – 98 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.8 Hz, 1H), 7.53 (dd, *J* = 10.3, 8.4 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.35 (s, 1H), 7.14 – 7.05 (m, 3H), 6.95 (d, *J* = 7.8 Hz, 1H), 3.82 (dd, *J* = 9.3, 5.4 Hz, 1H), 3.77 – 3.62 (m, 4H), 3.50 – 3.29 (m, 2H), 2.78 – 2.61 (m, 2H), 2.60 – 2.45 (m, 2H), 2.10 – 1.94 (m, 1H), 1.04 – 0.95 (m, 2H), 0.79 – 0.67 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 149.3, 140.8, 135.9, 135.8, 132.1, 131.9, 128.1, 127.6, 127.5, 126.9, 124.6, 124.4, 123.5, 122.3, 73.2, 67.3, 51.2, 37.8, 15.6, 9.2 ppm. IR (neat):3079, 2960, 2852, 1635, 1606, 1588, 1433, 1116, 814 cm^{-1}. HRMS m/z: calcd for $[C_{24}H_{26}N_2O+H]^+$ 359.2123, found 359.2123. HPLC Analysis: Chiralpak ODH ^{n}Hexane/^{i}PrOH/Et_3N = 96/04/0. 1, 0.6 mL/min, 25 °C t_R = 18.0 (minor), 19.1 (major) minutes; $[\alpha]_D^{20}$ = -123.3 (c 1.0, MeOH).



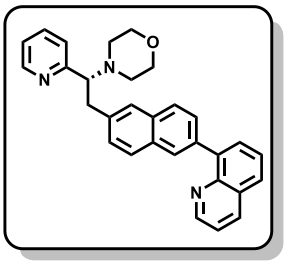
4-(2-(6-methylnaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine (3af)： Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), (6-methylnaphthalen-2-yl)methyl pivalate (38.4 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (14.1 mg, 86% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.57 – 7.48 (m, 4H), 7.44 (td, *J* = 7.6, 1.8 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.22 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.11 – 7.04 (m, 2H), 6.96 (dt, *J* = 7.8, 1.1 Hz, 1H), 3.81 (dd, *J* = 9.3, 5.4 Hz, 1H), 3.73 (t, *J* = 4.7 Hz, 4H), 3.48 – 3.32 (m, 2H), 2.67 (d, *J* = 10.1 Hz, 2H), 2.54 (dt, *J* = 10.7, 4.7 Hz, 2H), 2.45 (d, *J* = 0.9 Hz, 3H) ppm. ^{13}C NMR* (101 MHz, $CDCl_3$) δ 159.3, 149.3, 135.9, 134.9, 132.2, 131.7, 128.10, 128.05, 127.6, 127.4, 126.9, 126.6, 124.4, 122.3, 73.3, 67.4, 51.2, 37.8, 21.8 with one carbon missing due to overlapping resonances. IR (neat):3048, 2961, 2920, 2852, 1637, 1606, 1588, 1433, 1115, 799 cm^{-1}. HRMS m/z: calcd for $[C_{22}H_{24}N_2O+H]^+$ 333.1967, found 333.1967. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 95/05/0. 1, 0.6 mL/min, 25 °C) t_R = 30.1 (minor), 32.5 (major) minutes; $[\alpha]_D^{20}$ = -96.6 (c 1.0, MeOH). Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.



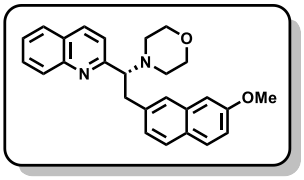
4-(2-(6-phenylnaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine (3ag): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), (6-phenylnaphthalen-2-yl)methyl pivalate (47.7 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 :2) to give the target product (16.9 mg, 86% yield) as a brown solid. Mp: 88 – 90 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.8 Hz, 1H), 7.93 (d, *J* = 1.8 Hz, 1H), 7.76 – 7.55 (m, 5H), 7.52 – 7.39 (m, 4H), 7.41 – 7.32 (m, 1H), 7.19 – 7.14 (m, 1H), 7.10 (dd, *J* = 7.5, 4.9 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 3.86 (dd, *J* = 9.1, 5.5 Hz, 1H), 3.75 (t, *J* = 4.7 Hz, 4H), 3.53 – 3.29 (m, 2H), 2.75 – 2.65 (m, 2H), 2.63 – 2.48 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 149.3, 141.2, 138.0, 137.0, 136.0, 132.6, 132.2, 128.9, 128.5, 128.1, 127.9, 127.6, 127.43, 127.35, 125.58, 125.54, 124.5, 122.3, 73.1, 67.3, 51.1, 37.8 ppm. IR (neat): 3052, 2961, 2923, 2851, 1598, 1588, 1506, 1496, 1261, 802 cm^{-1}. HRMS m/z: calcd for $[C_{27}H_{26}N_2O+H]^+$ 395.2123, found 395.2120. HPLC Analysis: Chiralpak ODH ^{n}Hexane/^{i}PrOH/Et_3N = 95/05/0. 1, 0.6 mL/min, 25 °C) t_R = 23.4 (major), 25.3 (minor) minutes; $[\alpha]_D^{20}$ = -110.7 (c 1.0, MeOH).



4-(1-(pyridin-2-yl)-2-(6-(thiophen-2-yl)naphthalen-2-yl)ethyl)morpholine (3ah): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), ((6-(thiophen-2-yl)naphthalen-2-yl)methyl pivalate (48.6 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 : 2) to give the target product (15.6 mg, 78% yield) as a light yellow oil. R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.93 (s, 1H), 7.72 – 7.57 (m, 3H), 7.50 – 7.42 (m, 1H), 7.38 (dd, *J* = 6.0, 2.3 Hz, 2H), 7.29 (d, *J* = 5.1 Hz, 1H), 7.19 – 7.06 (m, 3H), 6.98 (dd, *J* = 7.7, 1.1 Hz, 1H), 3.82 (dd, *J* = 9.2, 5.5 Hz, 1H), 3.73 (t, *J* = 4.7 Hz, 4H), 3.51 – 3.33 (m, 2H), 2.72 – 2.63 (m, 2H), 2.55 (dt, *J* = 11.3, 4.7 Hz, 2H). ^{13}C NMR* (101 MHz, $CDCl_3$) δ 159.1, 149.3, 144.7, 137.2, 136.0, 132.8, 132.2, 131.3, 128.7, 128.22, 128.19, 127.7, 125.0, 124.5, 124.4, 124.0, 123.4, 122.3, 73.2, 67.4, 51.2, 37.9 with one carbon missing due to overlapping resonances. IR (neat): 3051, 2956, 2852, 2814, 1602, 1588, 1569, 1497, 1471, 1450, 1432, 1115, 1005, 883, 814, 743 cm^{-1}, HRMS m/z: calcd for $[C_{25}H_{24}N_2OS+H]^+$ 401.1683, found 401.1687. HPLC Analysis: Chiralpak ADH ^{n}Hexane/^{i}PrOH/Et_3N = 85/15/0. 1, 0.6 mL/min, 25 °C t_R = 17.2 (major), 18.2 (minor) minutes; $[\alpha]_D^{20}$ = -128.0 (c 1.0, MeOH). Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.



4-(1-(pyridin-2-yl)-2-(6-(quinolin-8-yl)naphthalen-2-yl)ethyl)morpholine (3ai): Prepared according to procedure D using 4-(pyridin-2-ylmethyl)morpholine (8.9 mg, 0.05 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol, 3 equiv.), (6-(quinolin-8-yl)naphthalen-2-yl)methyl pivalate (55.35 mg, 0.15 mmol, 3 equiv.), $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 0.1 equiv.), ligand **L8** (6.3 mg, 0.006 mmoL, 0.12 equiv.), DME (0.5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 50 :2) to give the target product (14.5 mg, 65% yield) as a brown solid. Mp: 95 – 105 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 100 : 50 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.62 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1H), 8.22 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.00 (d, *J* = 1.6 Hz, 1H), 7.84 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.81 – 7.71 (m, 3H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.62 (dd, *J* = 8.1, 7.1 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.16 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.10 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.97 (dt, *J* = 7.8, 1.1 Hz, 1H), 3.85 (dd, *J* = 9.3, 5.4 Hz, 1H), 3.74 (t, *J* = 4.7 Hz, 4H), 3.61 – 3.24 (m, 2H), 2.74 – 2.63 (m, 2H), 2.61 – 2.48 (m, 2H) ppm. ^{13}C NMR* (101 MHz, $CDCl_3$) δ 159.2, 150.4, 149.3, 146.3, 141.1, 137.0, 136.8, 136.4, 136.0, 132.9, 132.1, 130.7, 129.1, 128.9, 128.1, 128.0, 127.69, 127.67, 126.8, 126.4, 124.5, 122.3, 121.2, 73.3, 67.4, 51.3, 38.0 ppm with one carbon missing due to overlapping peaks. IR (neat): 3047, 2962, 2929, 2832, 1603, 1593, 1545, 1513, 1478, 1234, 704 cm^{-1}. HRMS m/z: calcd for $[C_{30}H_{27}N_3O+H]^+$ 446.2277, found 446.2271. HPLC Analysis: Chiralpak IA ^{n}Hexane/^{i}PrOH/Et_3N = 95/05/0. 1, 1 mL/min, 25 °C t_R = 46.1 (minor), 58.7 (major) minutes; $[\alpha]_D^{20}$ = -55.6 (c 0.11, MeOH). Note: In $CDCl_3$, a single resonance is absent from the ^{13}C NMR, apparently due to coincidental overlap.

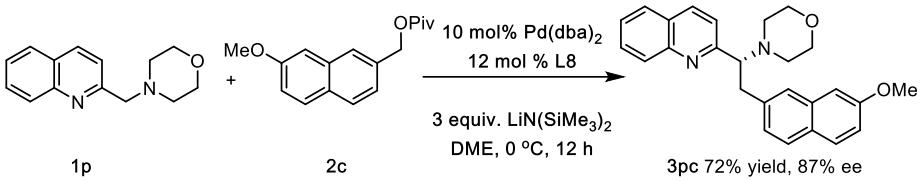


4-(2-(7-methoxynaphthalen-2-yl)-1-(quinolin-2-yl)ethyl)morpholine (3pc): Prepared according to procedure D using 4-(quinolin-2-ylmethyl)morpholine (114 mg, 0.5 mmol, 1 equiv.), $LiN(SiMe_3)_2$ (251 mg, 1.5 mmol, 3 equiv.), (7-methoxynaphthalen-2-yl)methyl pivalate (408 mg, 1.5 mmol, 3 equiv.), $Pd(dba)_2$ (29 mg, 0.05 mmol, 0.1 equiv.), ligand **L8** (63 mg, 0.06 mmoL, 0.12 equiv.), DME (5 mL), 0 °C, 12 h. The crude product was purified by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 :2) to give the target product (147 mg, 74% yield) as a yellow oil and rinsed it with hexane to give a white solid. Mp: 88 – 90 °C, R_f = 0.3 (petroleum ether : EtOAc : Et_3N = 75 : 25 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.98 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.74 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.68 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.59 (d, *J* = 8.9 Hz, 1H), 7.56 – 7.45 (m, 2H), 7.45 – 7.36 (m, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.05 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.02 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.92 (d, *J* = 2.5 Hz, 1H), 4.08 (dd, *J* = 8.9, 5.3 Hz, 1H), 3.85 (s, 3H), 3.72 (t, *J* = 4.7 Hz, 4H), 3.67 – 3.41 (m, 2H), 2.85 – 2.65 (m, 2H), 2.71 – 2.47 (m, 2H). ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 157.6, 147.7, 137.6, 135.9, 134.6, 129.6, 129.3, 129.1, 127.6, 127.5, 127.42, 127.38, 126.9, 126.3, 125.9, 122.0, 118.0, 105.6, 73.6, 67.4, 55.3, 51.3, 37.3. ppm. IR (neat):3033, 2943, 2916, 2878, 1557, 1538, 1503,

1478, 1293, 798 cm^{-1}. HRMS m/z: calcd for $[C_{26}H_{26}N_2O_2+H]^+$ 399.2068, found 399.2062. HPLC Analysis: Chiralpak ADH (Hexane/^{i}PrOH = 95/05, 1 mL/min, 25 ^{o}C) t_R = 14.4 (minor), 16.0 (major) minutes; $[\alpha]_D^{20}$ = -72.08 (c 0.5, MeOH).

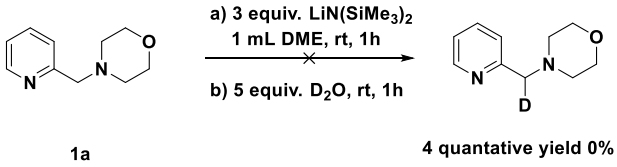
Additional Expeiments

Procedure for scaling up reaction of 1p

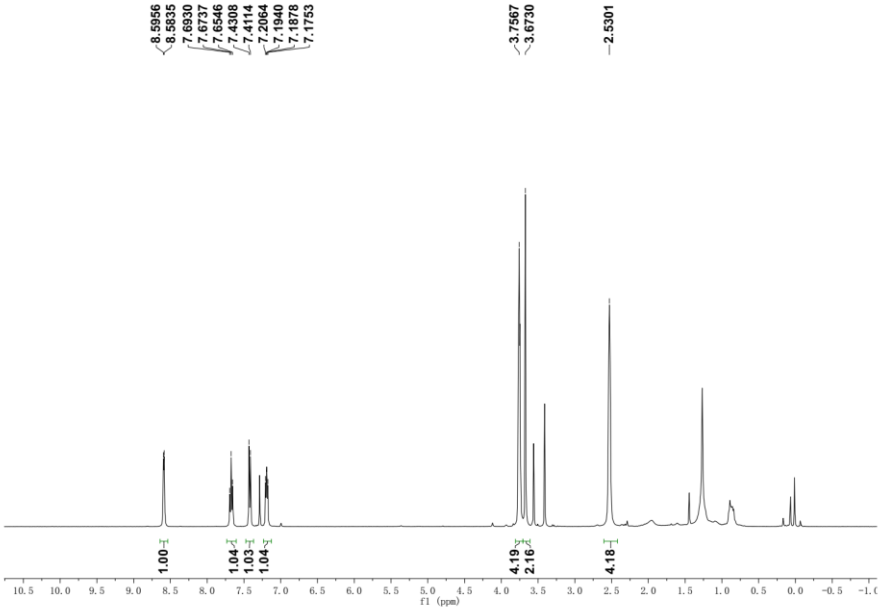


To an 100 mL flamed single-neck flask equipped with a stir bar under a nitrogen atmosphere inside a glove box was added $Pd(dba)_2$ (0.26 g, 13.2 mmol, 10 mol%), ligand **L8** (0.55 g, 13.2 mmol, 12 mol%), $LiN(SiMe_3)_2$ (2.20 g, 13.2 mmol, 3 equiv.) and **1p** (1.05 g, 4.40 mmol, 1.0 equiv.) and DME (50 mL). The flask was sealed with rubber stopper and removed from the glove box. Then the flask was cooled to 0 ^{o}C and corresponding 7-methoxylnaphthalen-2-ylmethyl pivalate (3.59 g, 13.2 mmol, 3 equiv.) 5 mL DME solution was added dropwise over 30 min. The reaction mixture was stirred at 0 ^{o}C for 12 h. After the reaction period, 1 mL water were added by syringe through the rubber stopper to quench the reaction at 0 ^{o}C and then the stopper was then removed under air. After the reaction period, the solution was quenched with saturated aq. NH_4Cl (2 mL) that was added via a syringe poked through the stopper. After the addition, thestopper was removed to expose the solution to air, CH_2Cl_2 (20 mL) was added and the organic phase was transferred to a 250 mL separatory funnel where it was rinsed with brine (3 × 20 mL). The combined organic phases were dried over Na_2SO_4 for 1 h and filtered. The filtrate was collected, concentrated under reduced pressure, and the resulting residue was purified by by silica gel column deactived with petroleum ether containing 2% Et_3N (eluted with petroleum ether : EtOAc : Et_3N = 100 : 20 :2) to give the target product (1.26 g, 72% yield) as a yellow oil and rinsed it with hexane to give a white solid.

Procedure for Deuterated reaction of 1a



To an oven-dried microwave vial equipped with a stir bar under a nitrogen atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.1 mg, 0.3 mmol, 3 equiv.) and azaarylmethyl amine (17.8 mg, 0.1 mmol, 1.0 equiv.) and DME (1 mL). The microwave vial was sealed with cap containing a septum and stirred for 1 hour in glove box, then removed the vial from the glove box. D_2O (9 uL, 0.5 mmol, 5equiv.) (99.9% D) were added by syringe through the septum in the cap to quench the reaction at room temperature and then the septum was then removed under air. The reaction solution was concentrated *in vacuo*. The crude material was transfered to NMR tube with $CDCl_3$ as solvent to take ^{1}H-NMR.



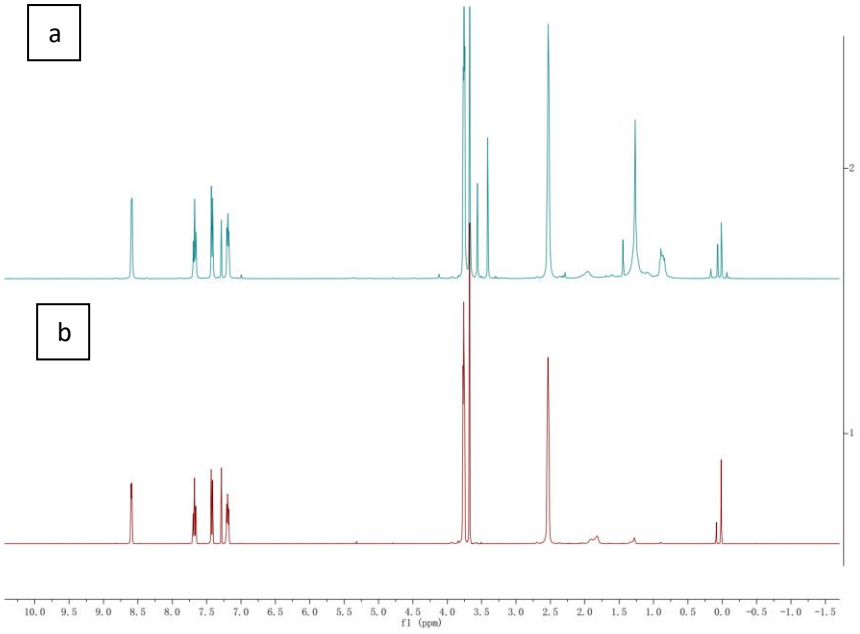
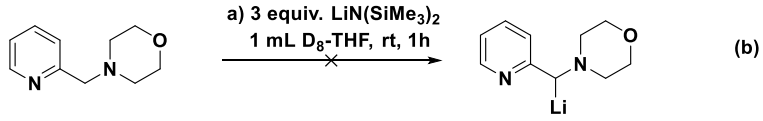
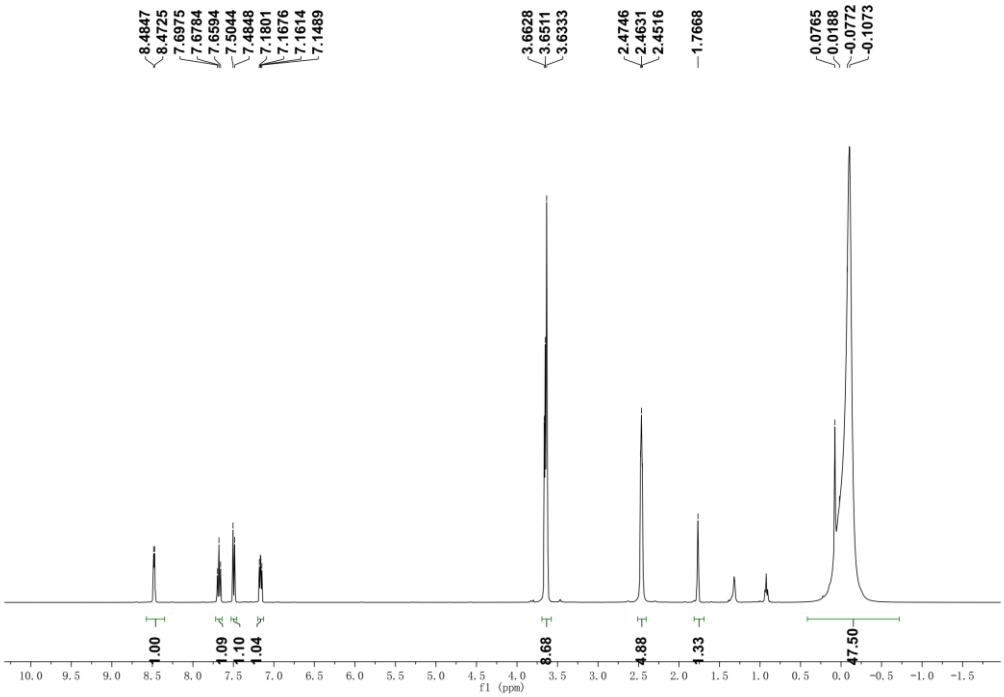


Table S1: Crude ^{1}H-NMR of (a) recycled 1a and (b) compared with pure ^{1}H-NMR of 1a in $CDCl_3$.

Procedure of deprotonating 1a



To an oven-dried microwave vial equipped with a stir bar under a nitrogen atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.1 mg, 0.3 mmol, 3 equiv.) and azaarylmethyl amine (17.8 mg, 0.1 mmol, 1.0 equiv.) and D_8-THF (1 mL, distilled from $LiAlH_4$). The microwave vial was sealed with cap containing a septum and stirred for 1 hour in glove box, Then the mixture was transferred to the J-Yang tube to take the NMR.



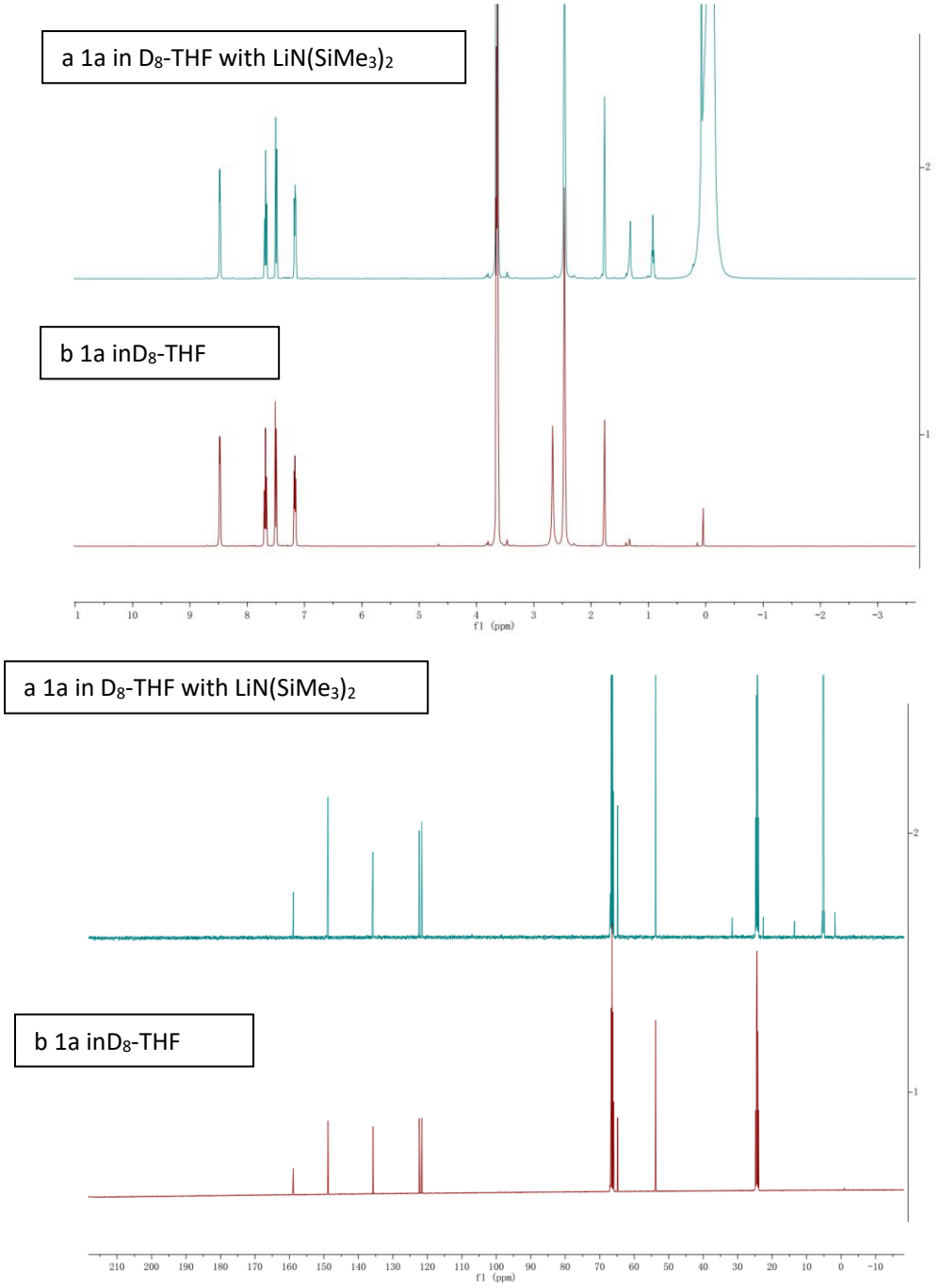


Table S2: Crude ^{1}H-NMR of 1a and compared ^{1}H-NMR and ^{13}C-NMR of 1a with $LiN(SiMe_3)_2$ and 1a in D_8-THF.

Reference：

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NMR Spectra

4-(Pyridin-2-ylmethyl)morpholine

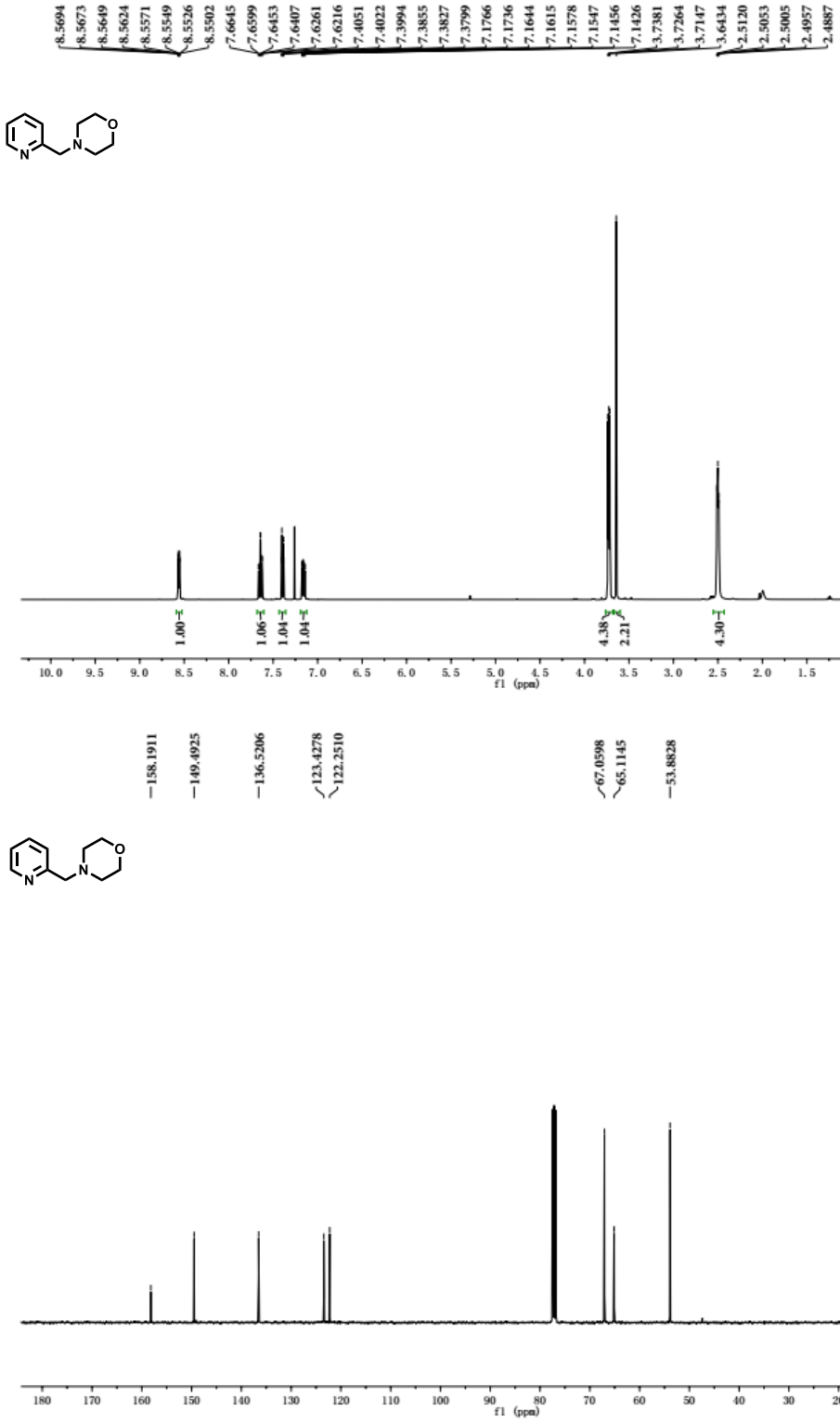


Figure S1. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1a in $CDCl_3$

2-(Piperidin-1-ylmethyl)pyridine

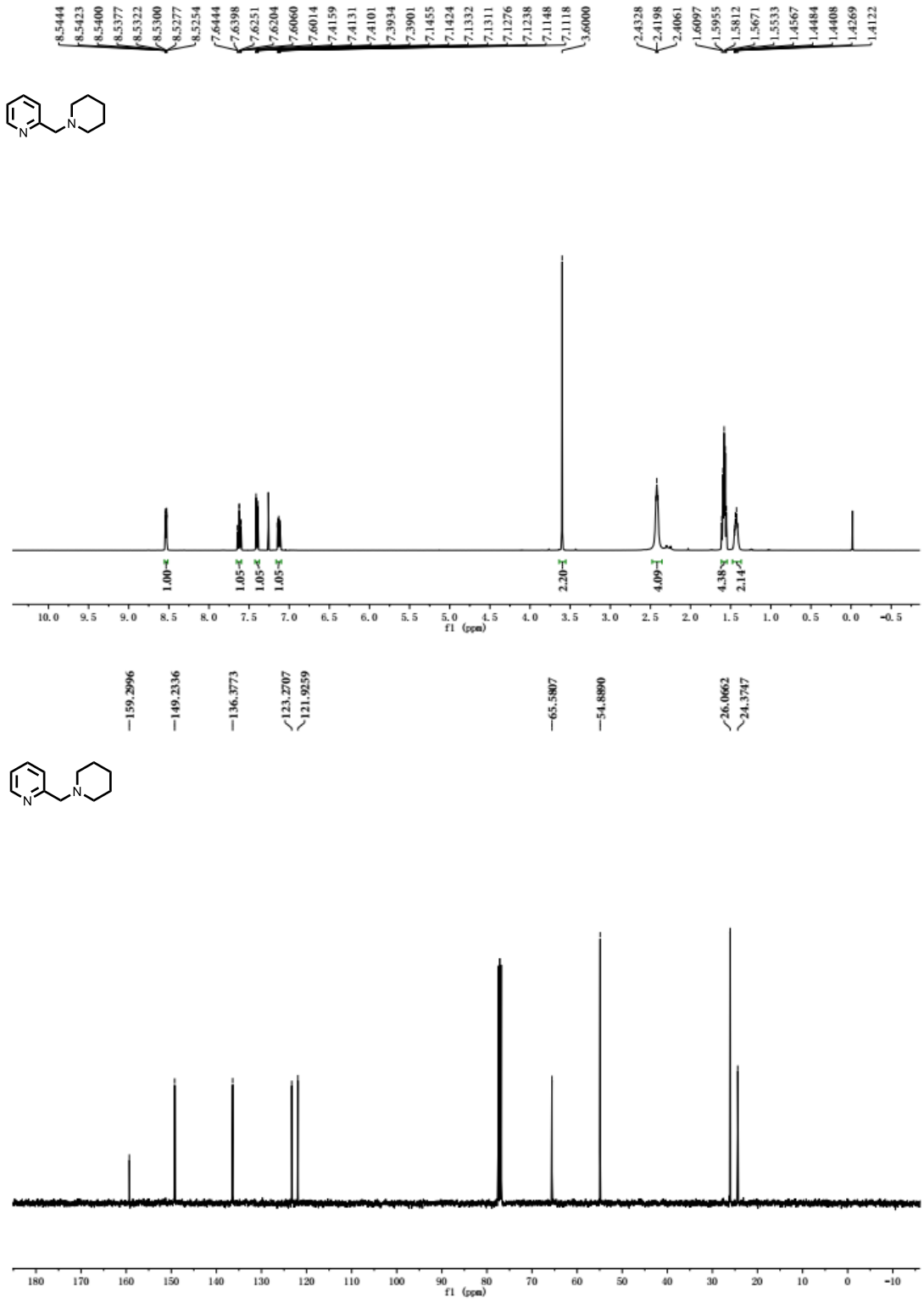


Figure S2. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1b in $CDCl_3$

4-(pyridin-2-ylmethyl)thiomorpholine

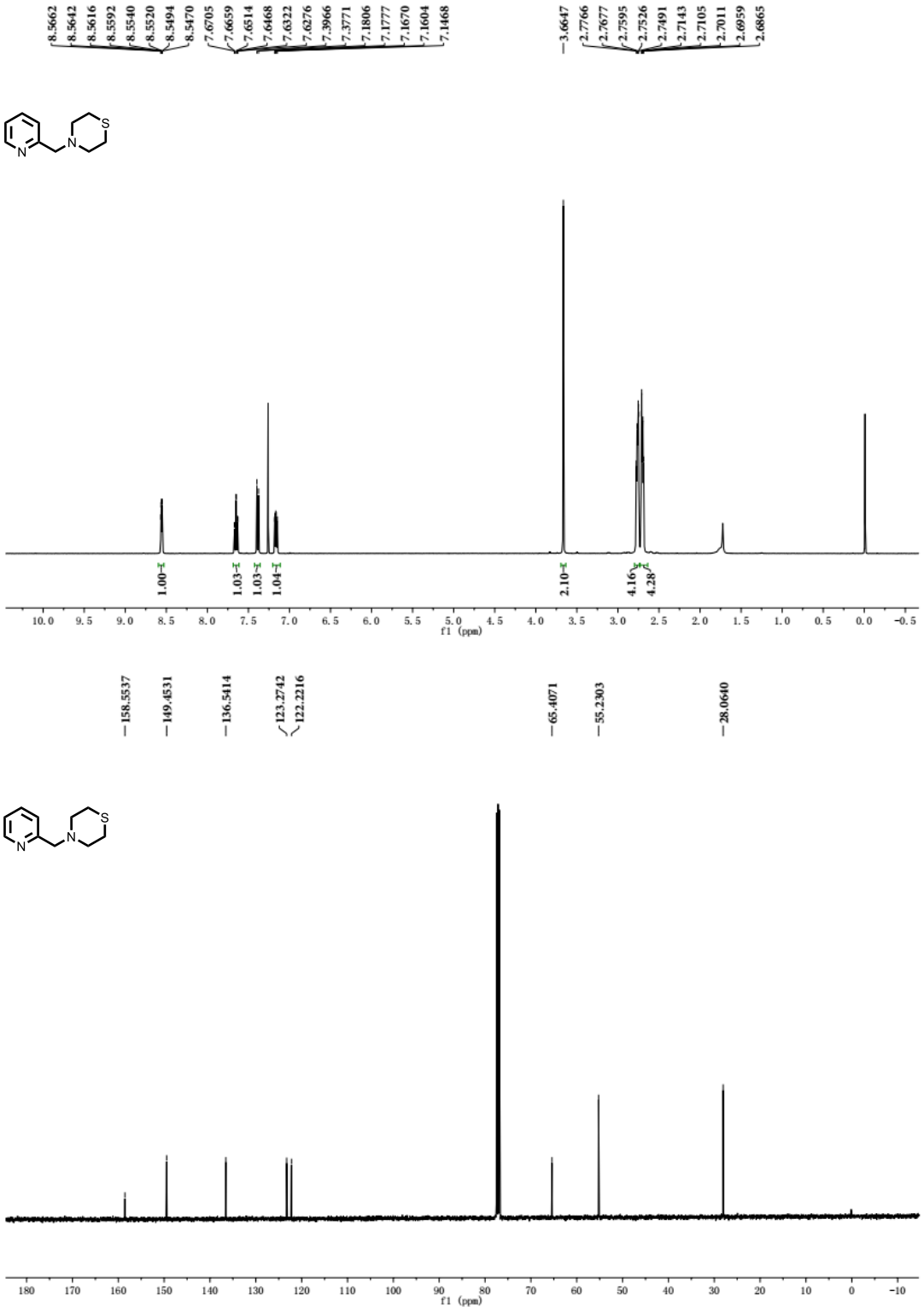


Figure S3. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1c in $CDCl_3$

1-methyl-4-(pyridin-2-ylmethyl)piperazine

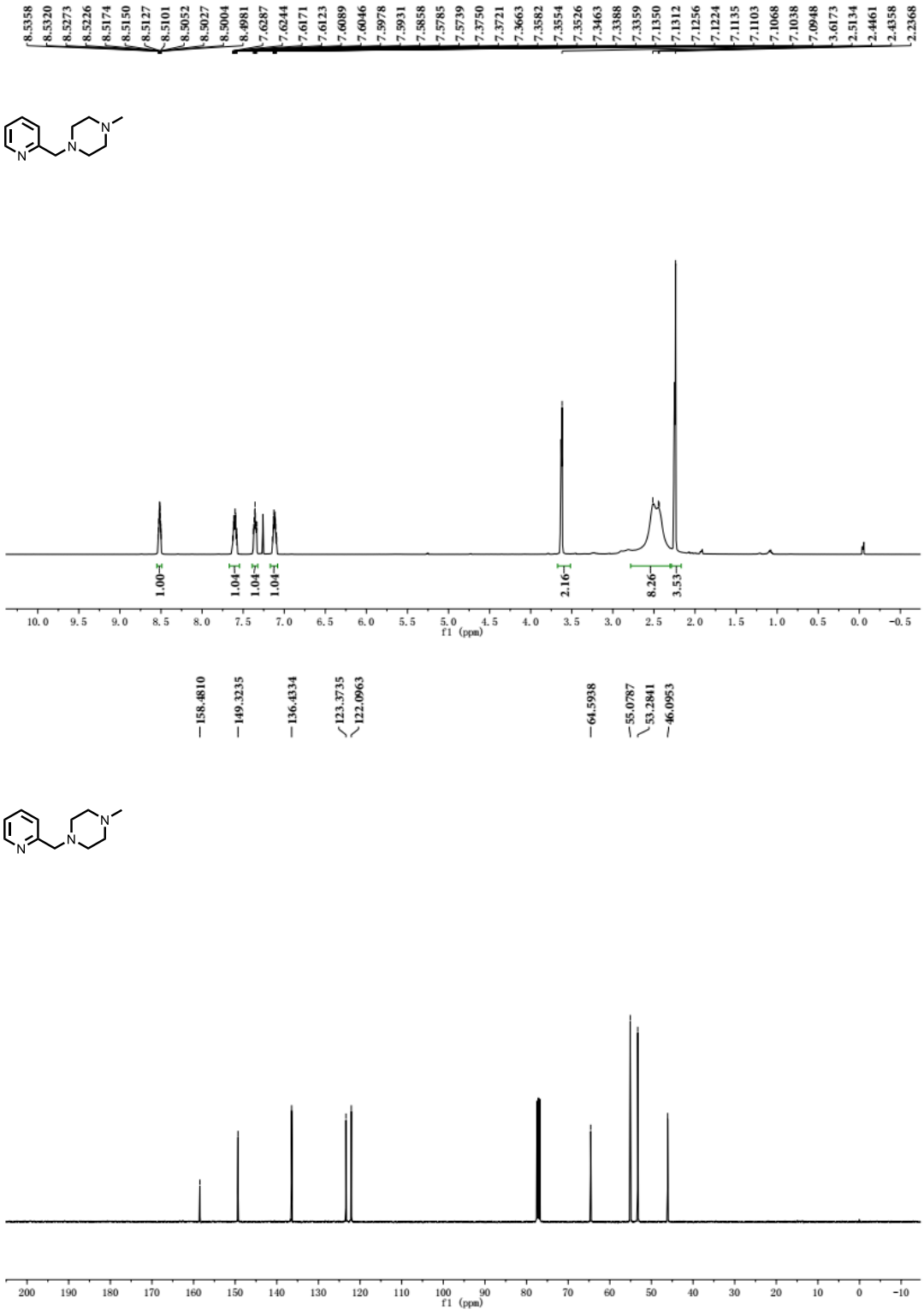


Figure S4. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1d in $CDCl_3$

1-(pyridin-2-ylmethyl)azepane

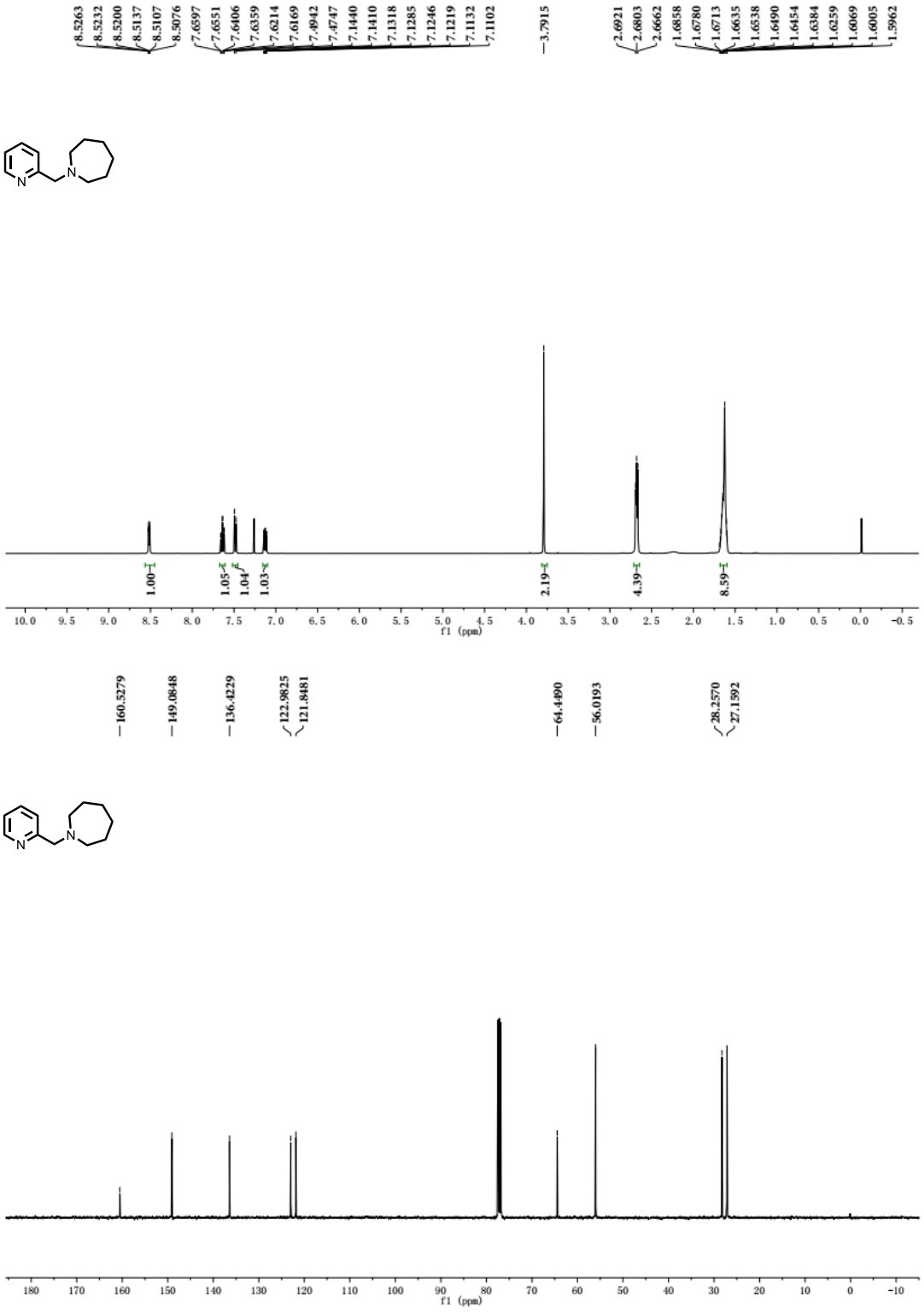


Figure S5. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1e in $CDCl_3$

N,N-dimethyl-1-(pyridin-2-yl)methanamine

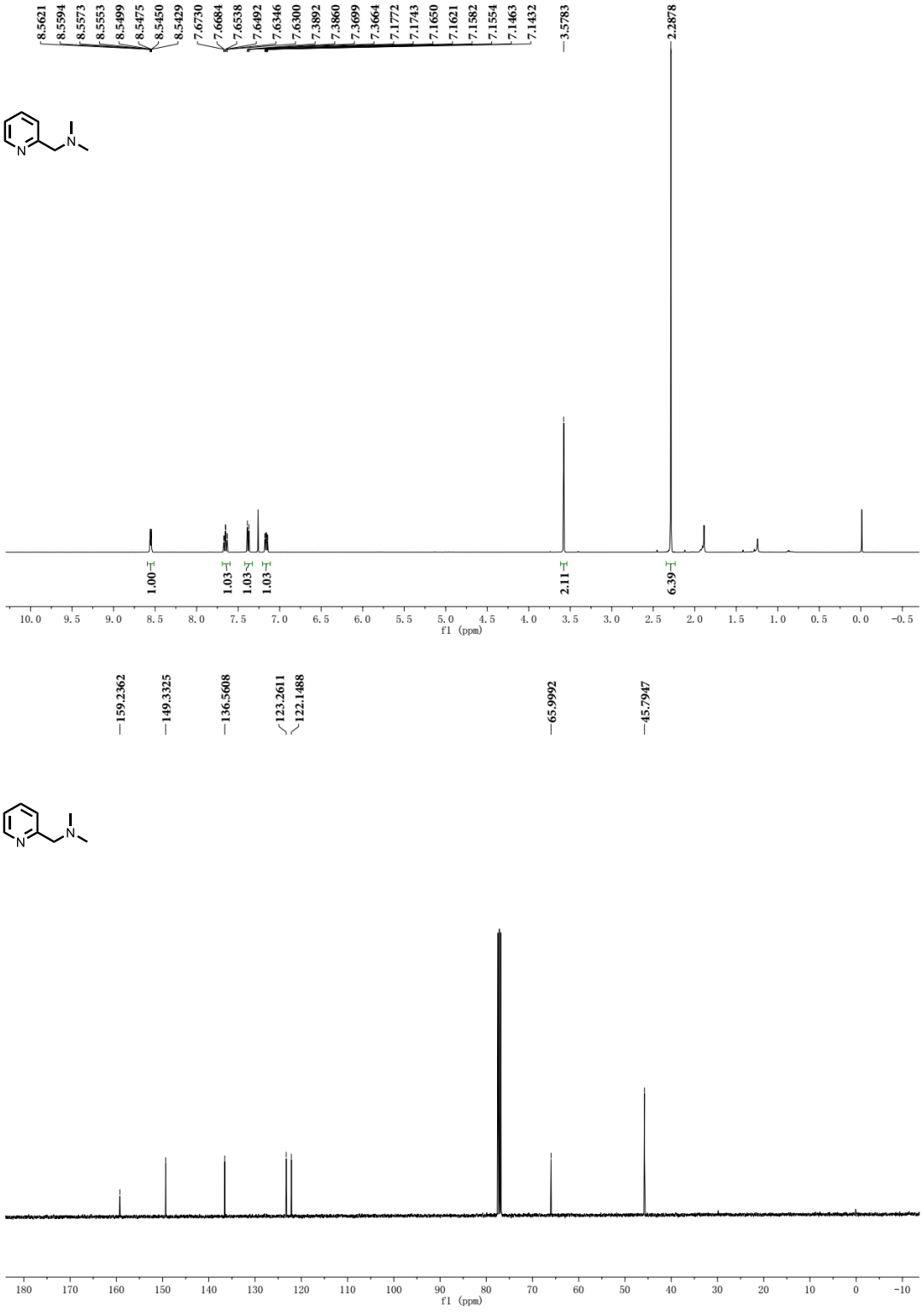


Figure S6. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1f in $CDCl_3$

N-methyl-N-(pyridin-2-ylmethyl)ethanamine

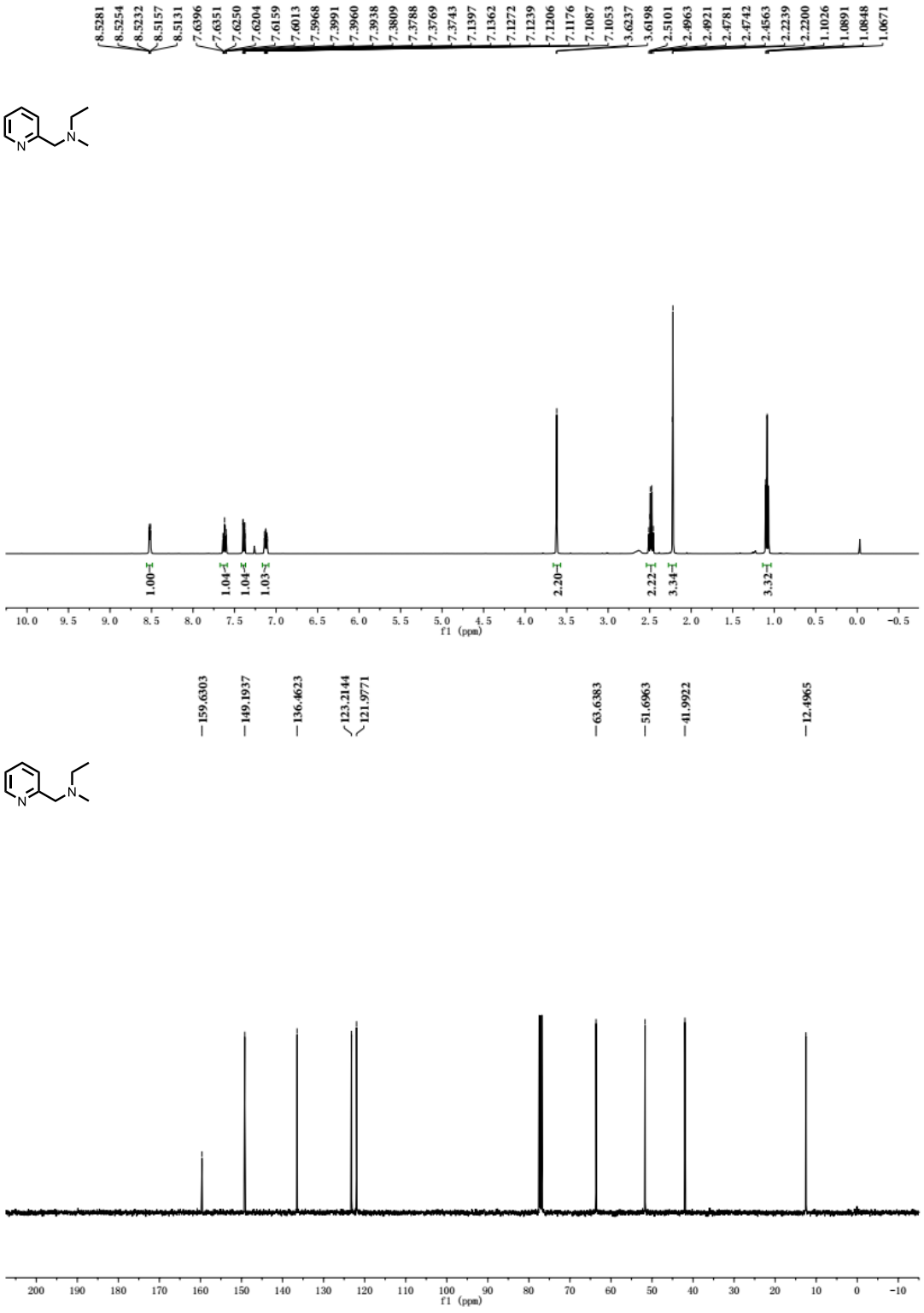


Figure S7. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1g in $CDCl_3$

N-methyl-N-(pyridin-2-ylmethyl)propan-2-amine

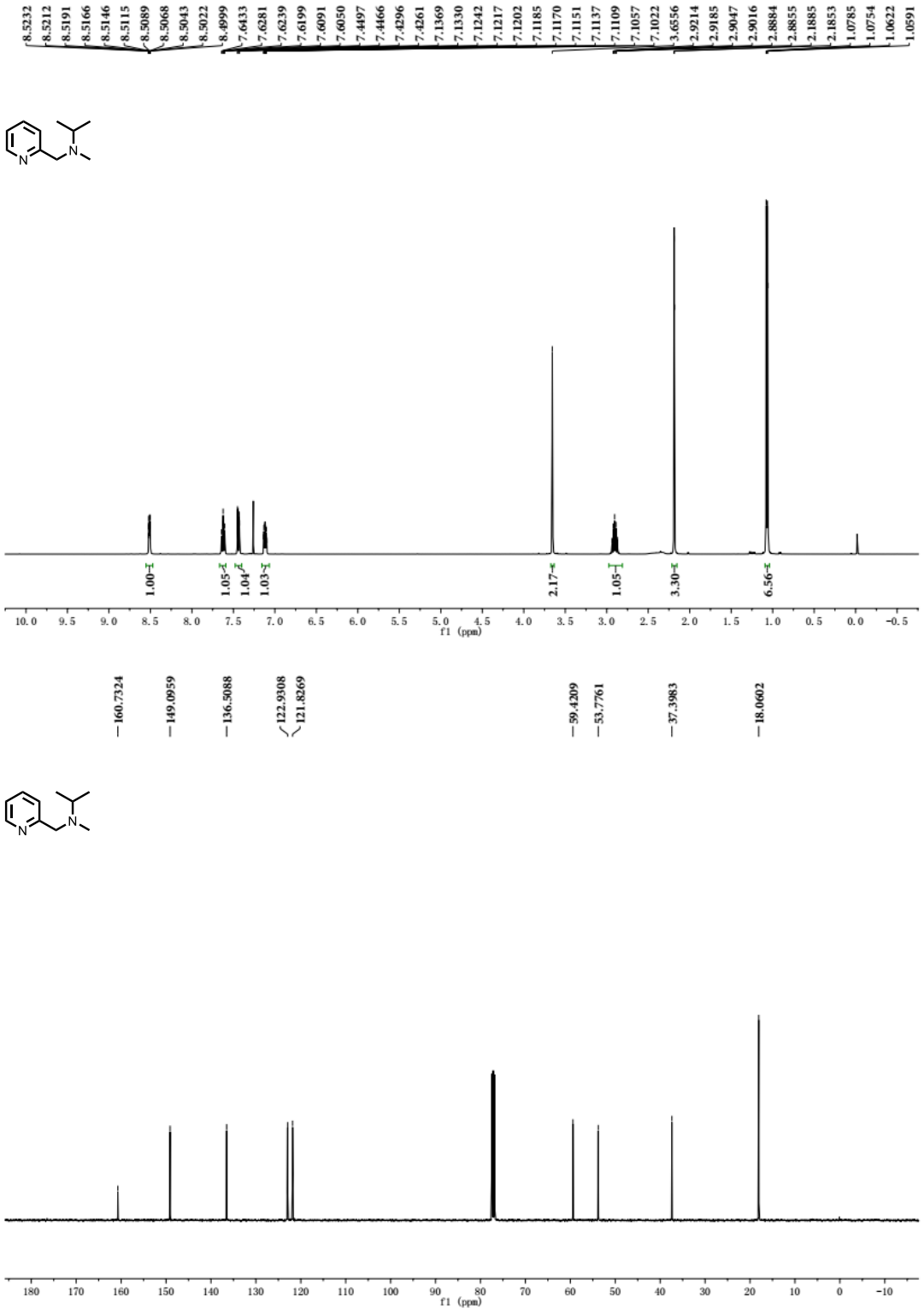


Figure S8. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1h in $CDCl_3$

N-ethyl-N-(pyridin-2-ylmethyl)ethanamine

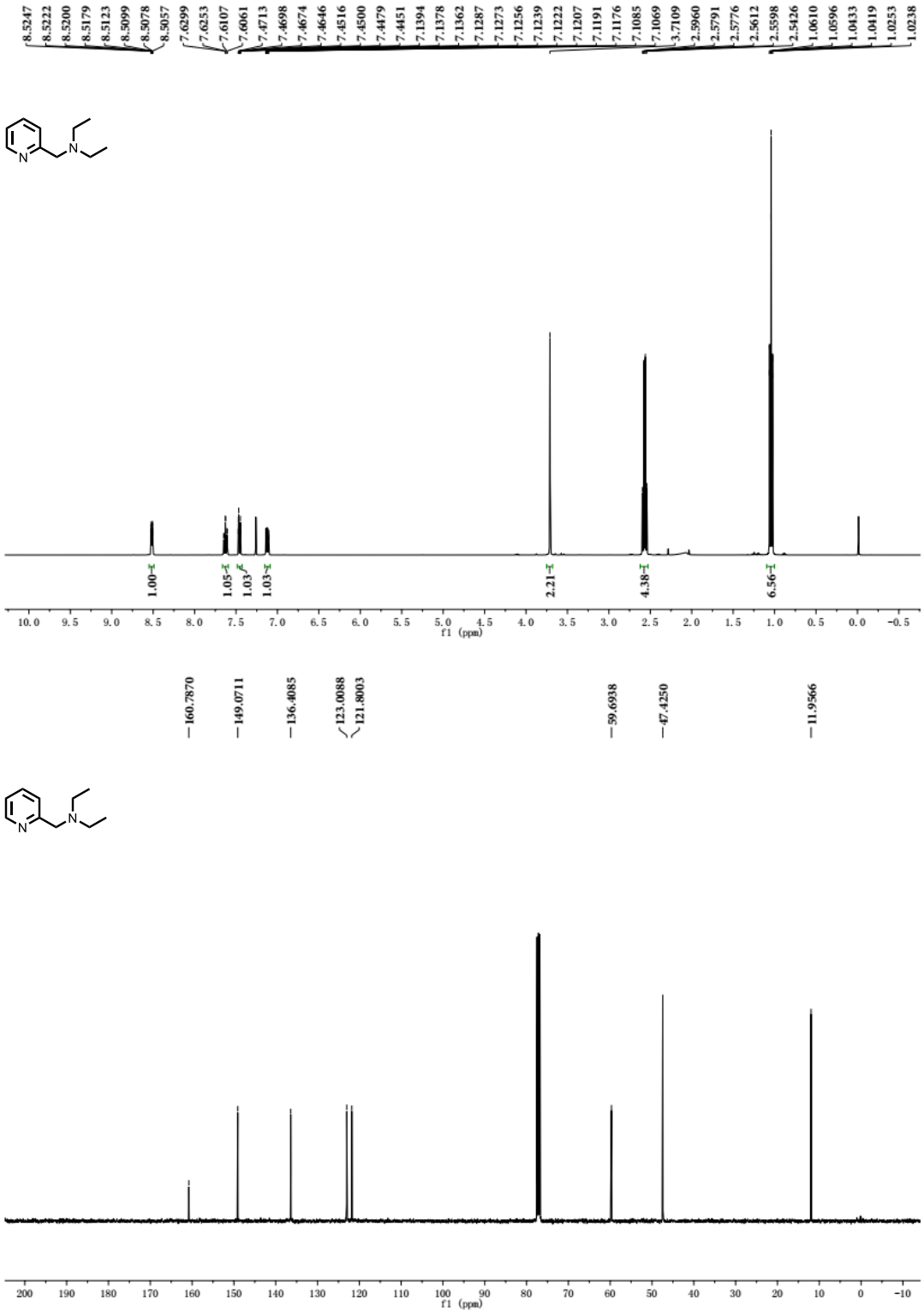


Figure S9. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1i in $CDCl_3$

4-((5-phenylpyridin-2-yl)methyl)morpholine

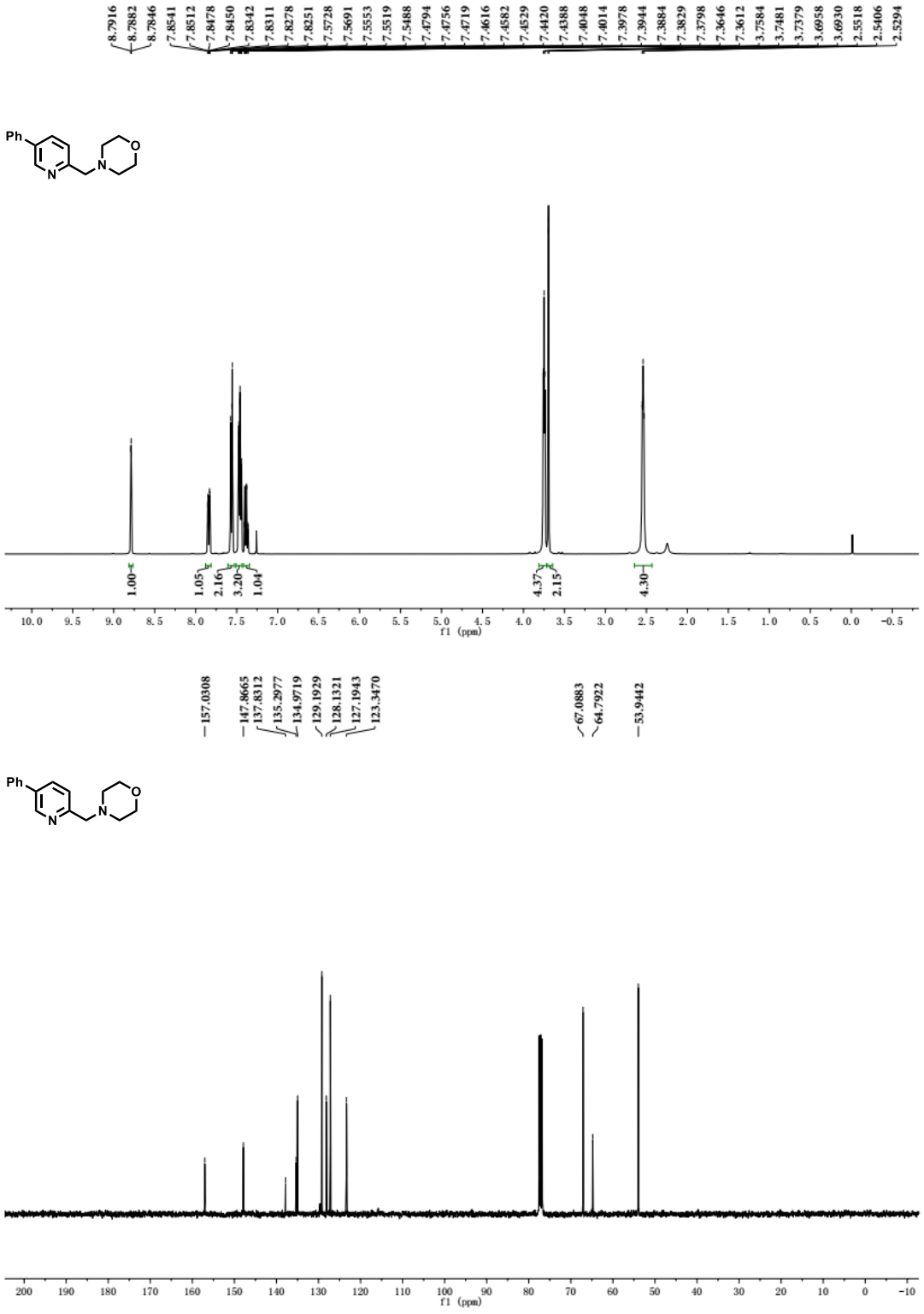


Figure S10. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1j in $CDCl_3$

4-((6-methylpyridin-2-yl)methyl)morpholine

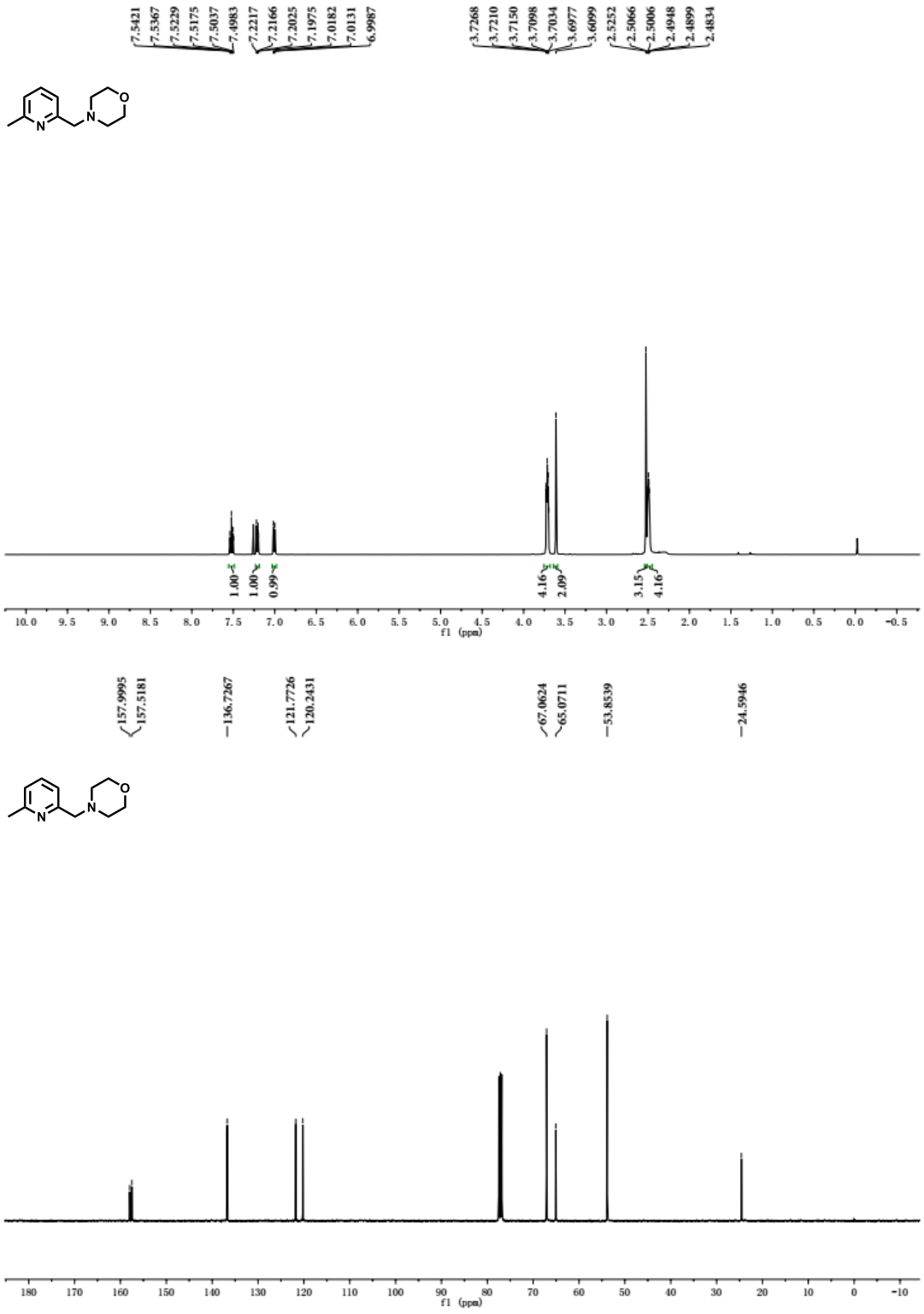
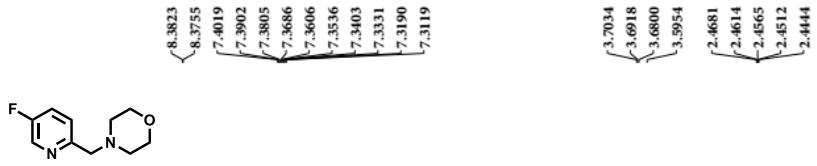
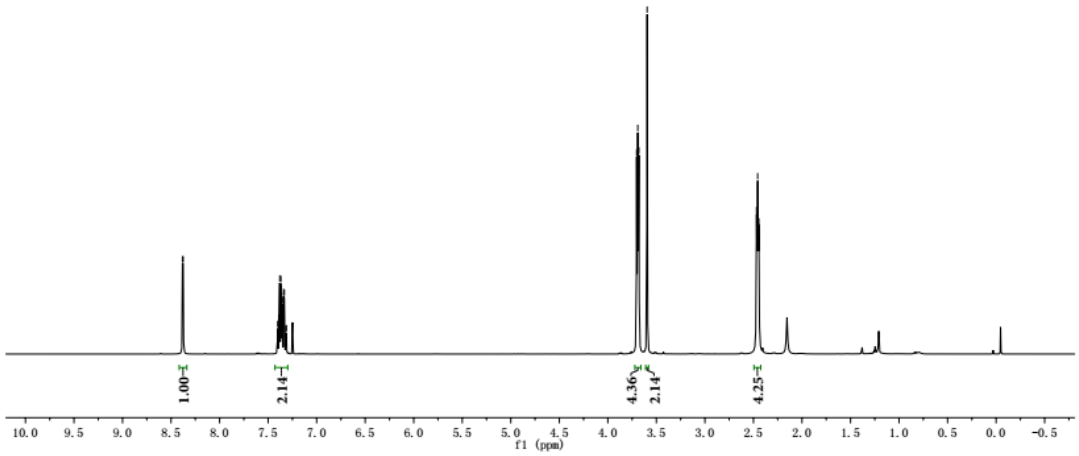
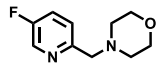


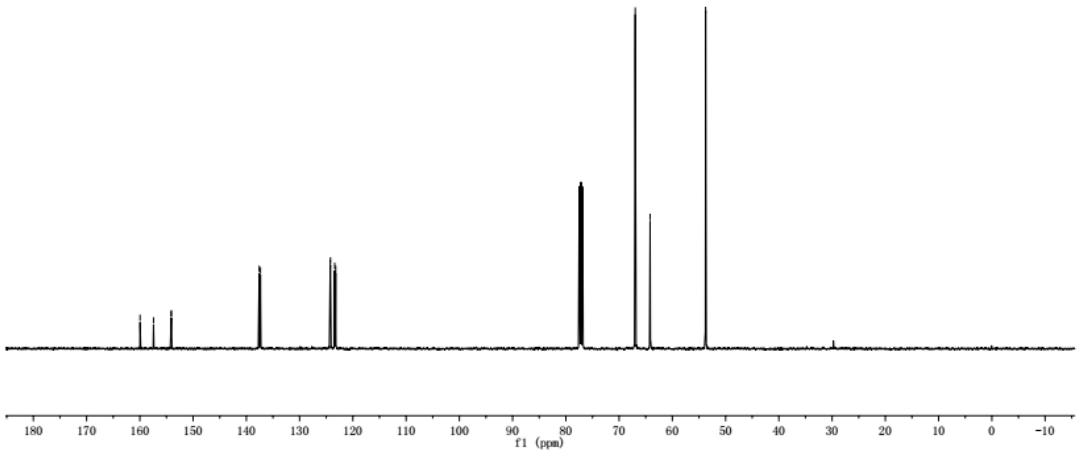
Figure S11. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1k in $CDCl_3$

4-((5-fluoropyridin-2-yl)methyl)morpholine









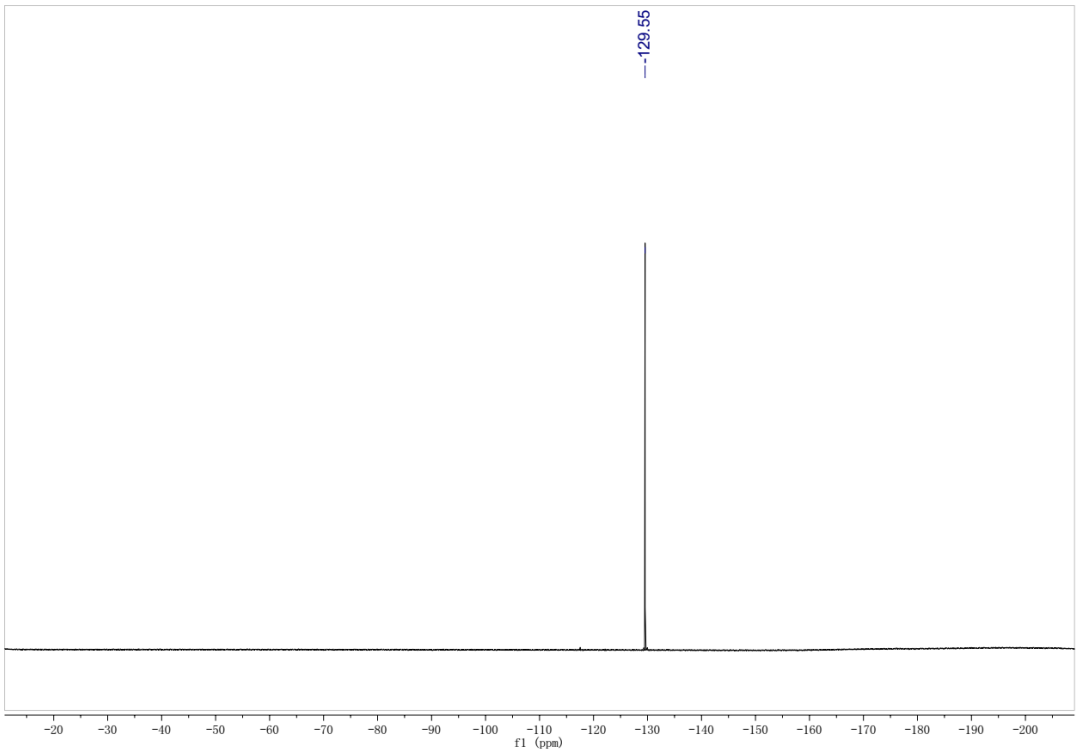
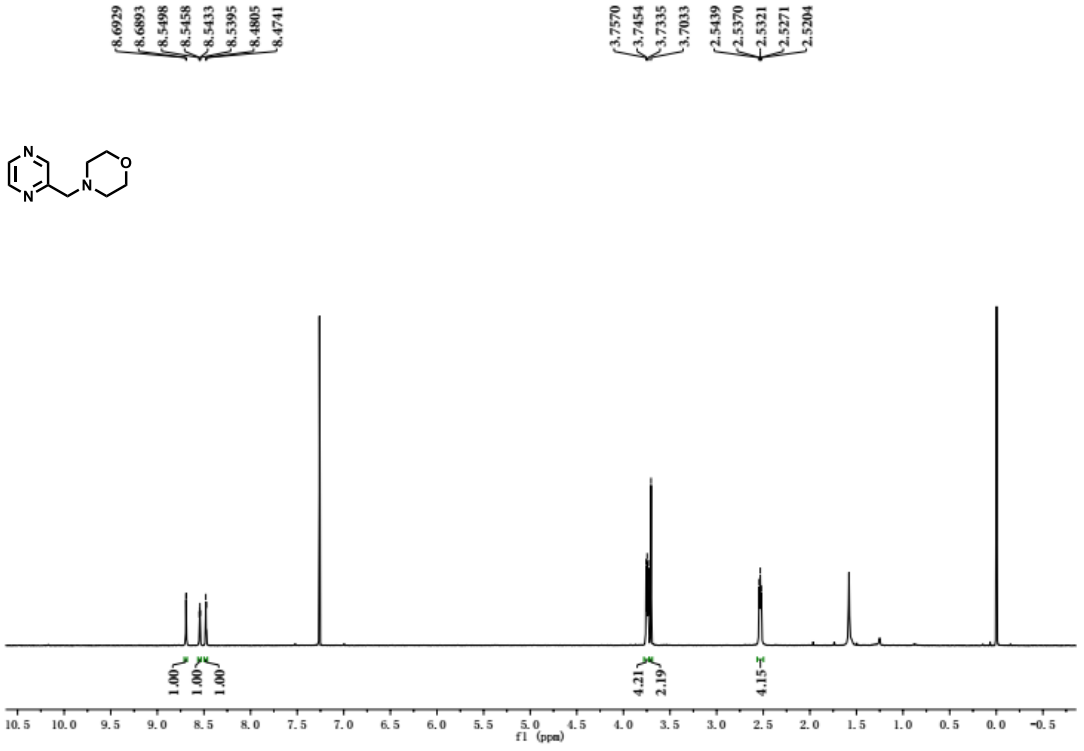


Figure S12. ^{1}H NMR (400 MHZ), ^{13}C {101MHZ} NMR and ^{19}F NMR (376 MHZ) spectra of 1l in $CDCl_3$

4-(pyrazin-2-ylmethyl)morpholine



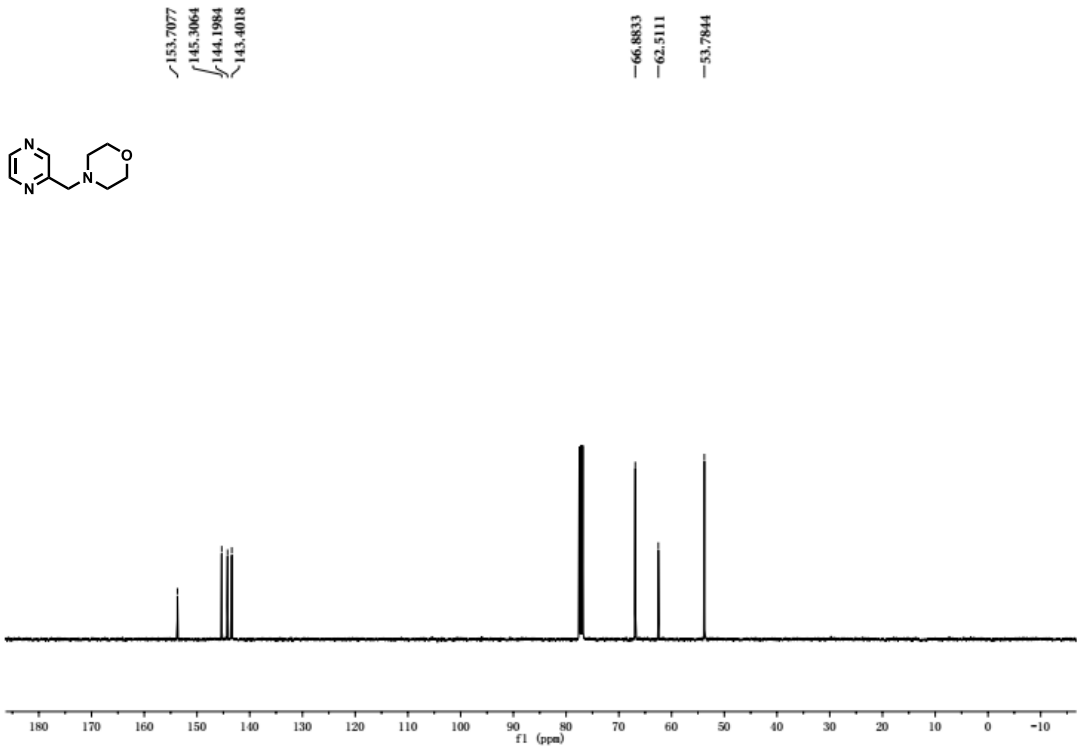
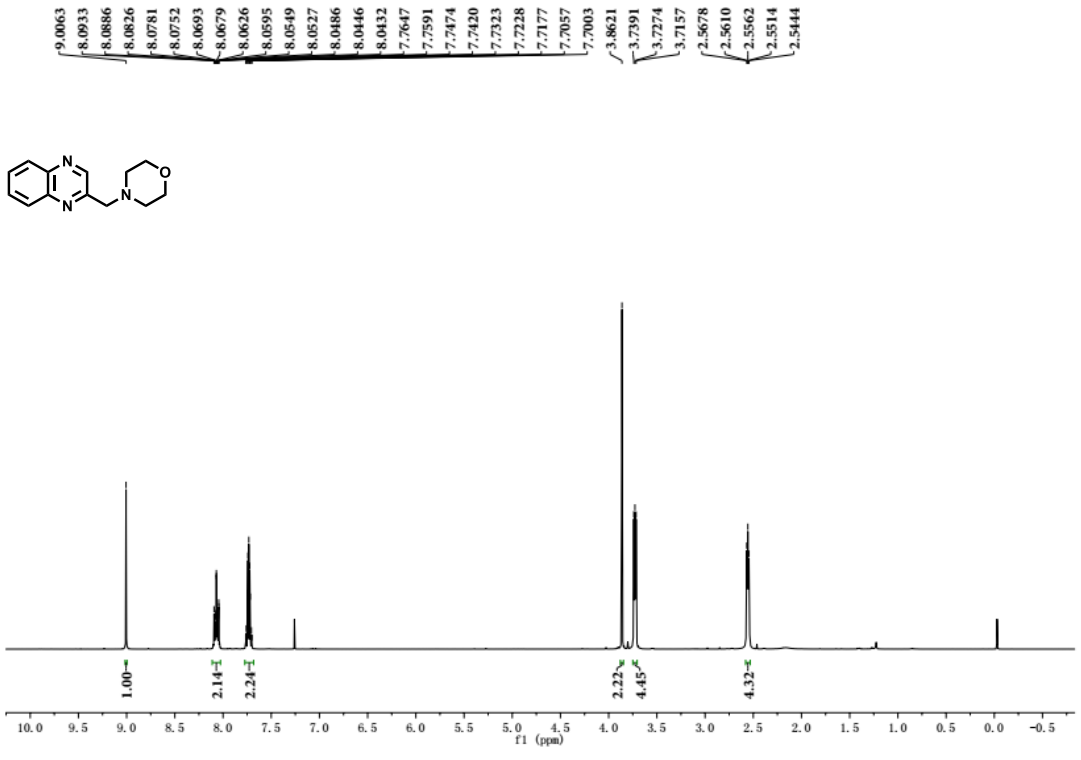


Figure S13. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1m in $CDCl_3$

4-(quinoxalin-2-ylmethyl)morpholine



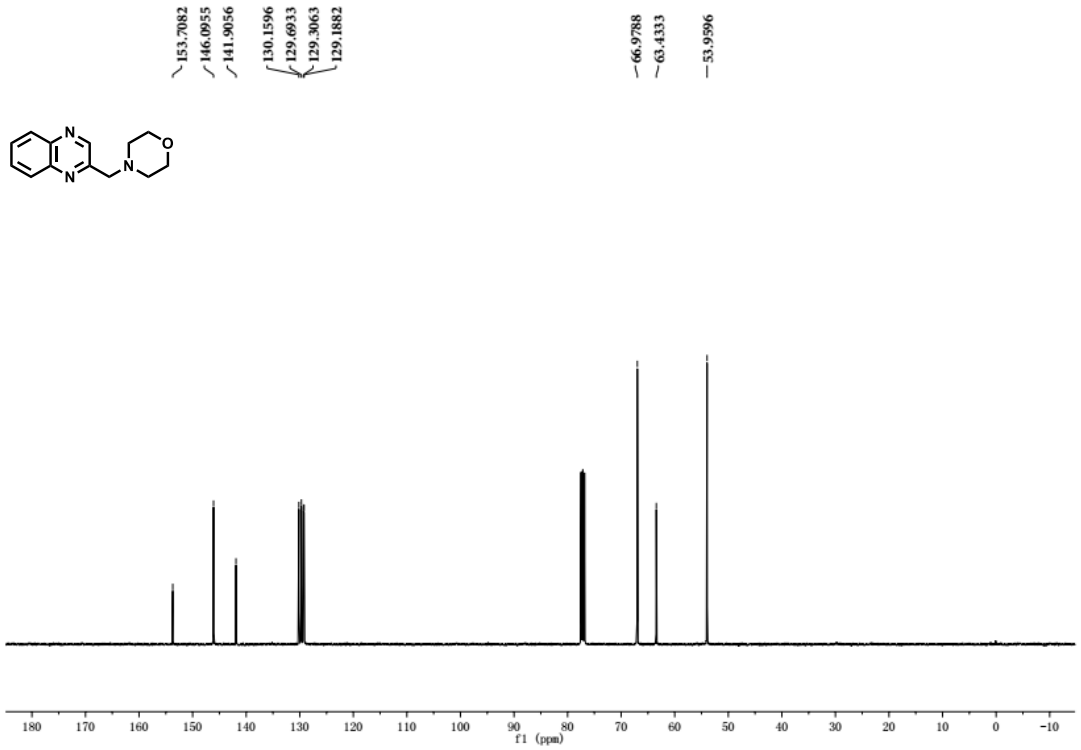
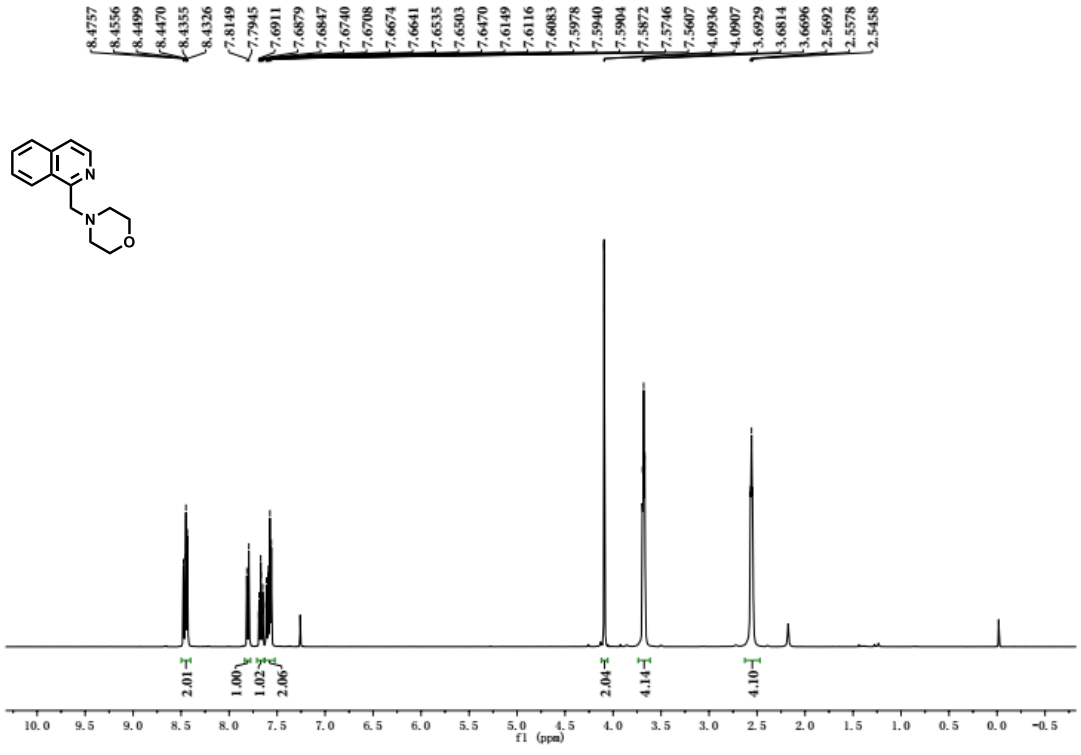


Figure S14. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1n in $CDCl_3$

4-(isoquinolin-1-ylmethyl)morpholine



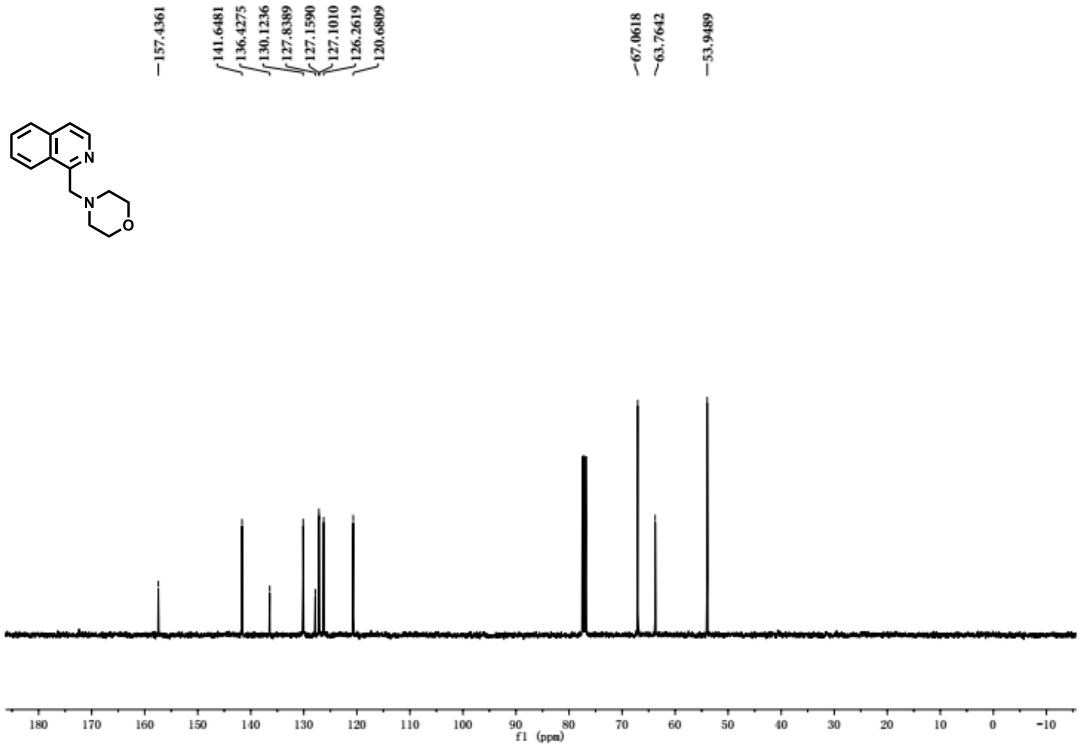
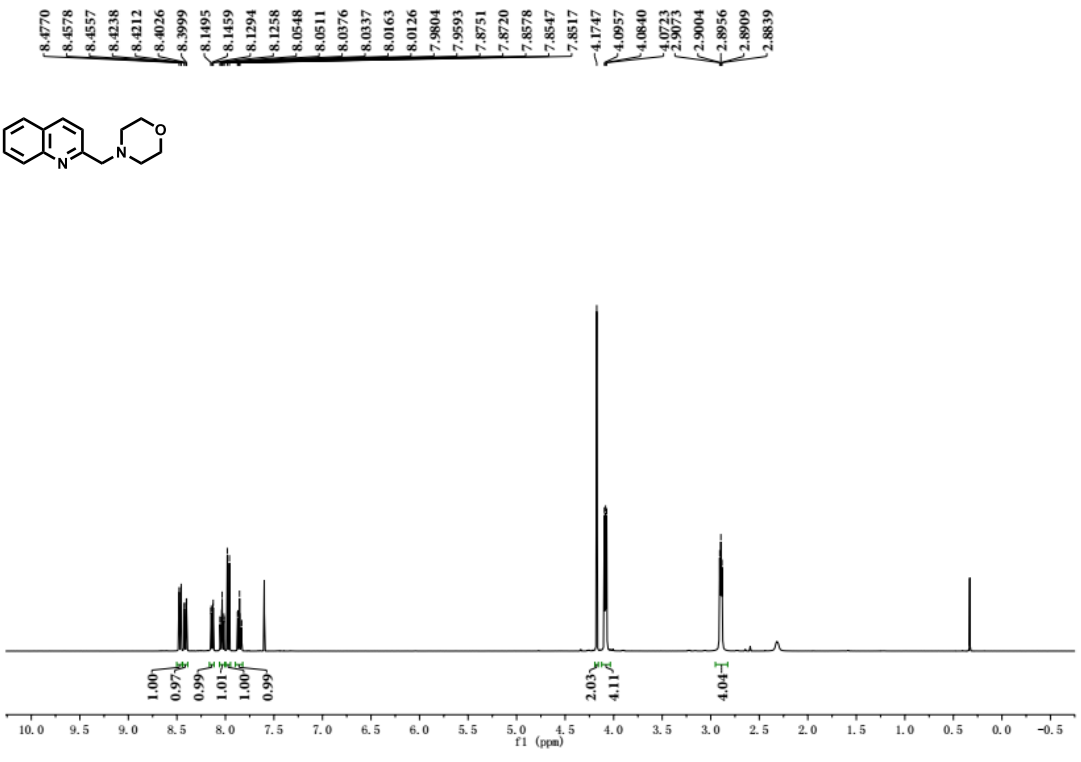


Figure S15. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1o in $CDCl_3$

4-(Quinolin-2-ylmethyl)morpholine



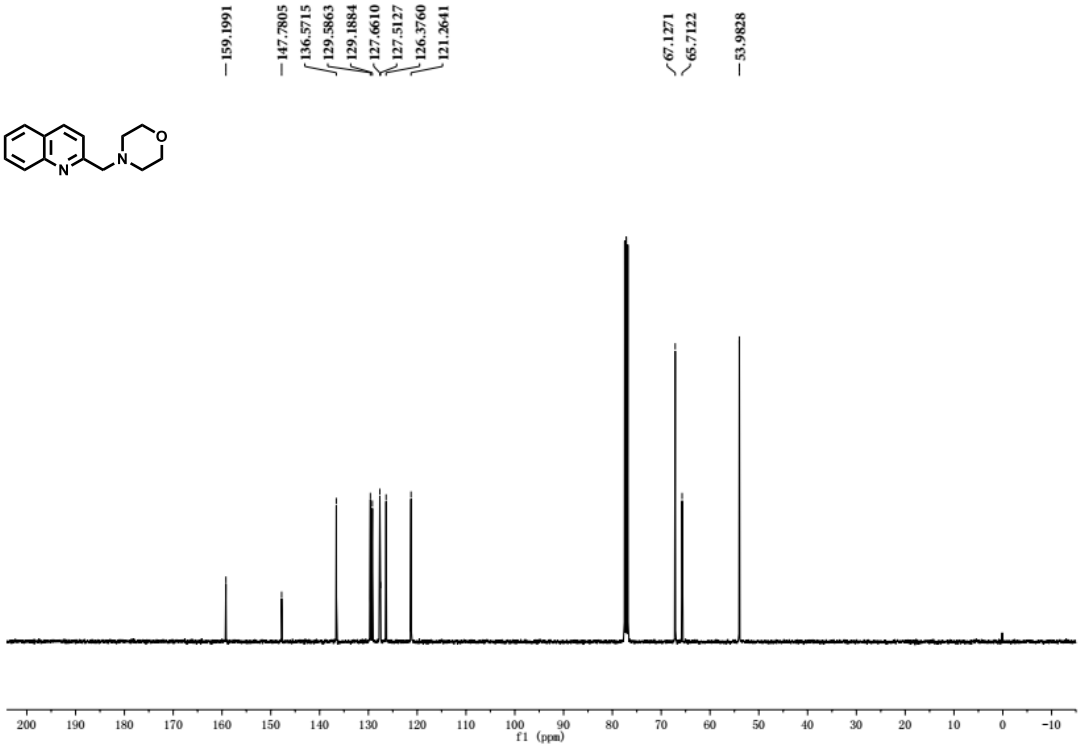
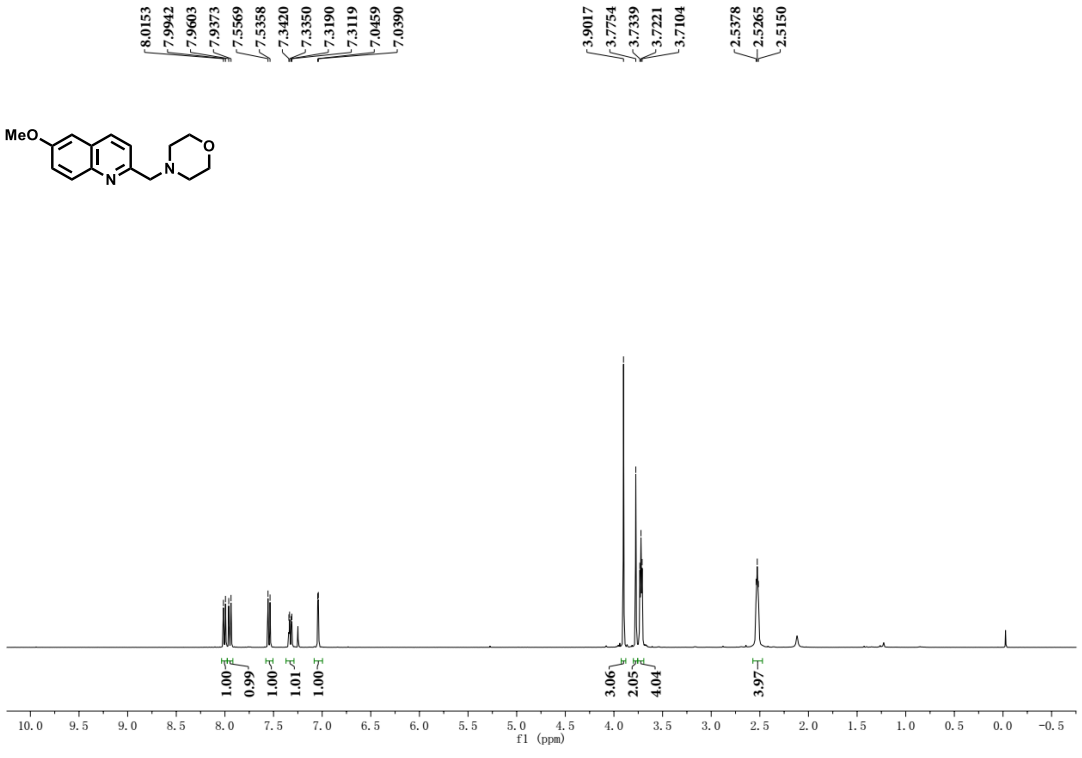


Figure S16. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1p in $CDCl_3$

4-((6-methoxyquinolin-2-yl)methyl)morpholine



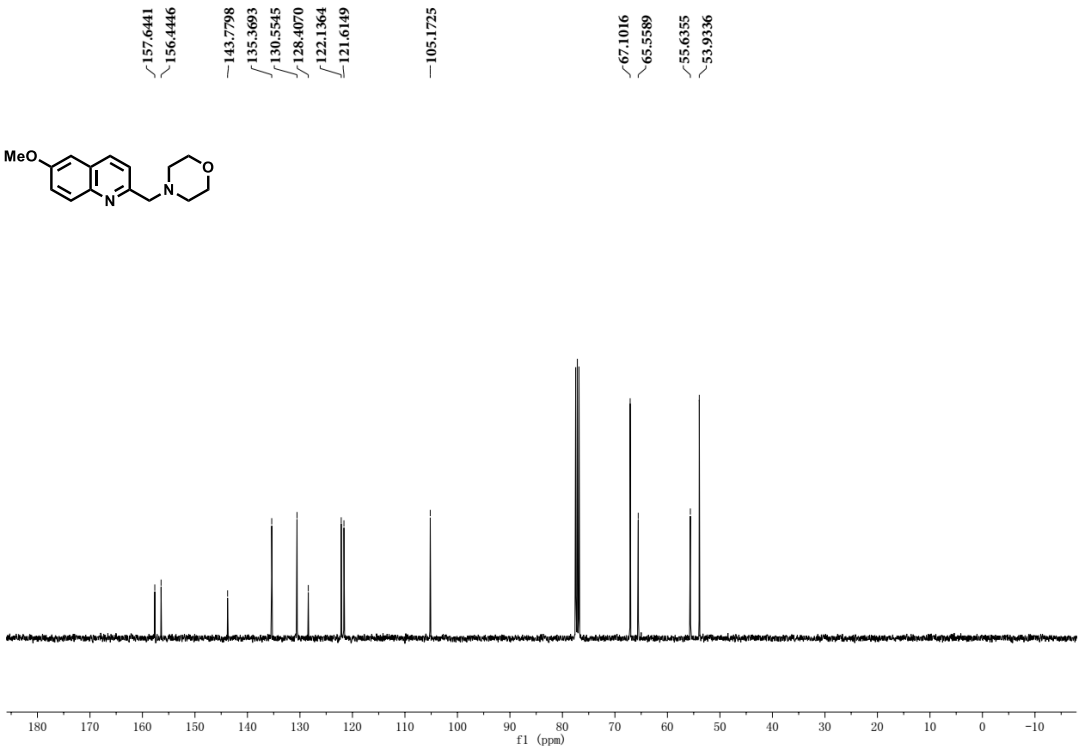
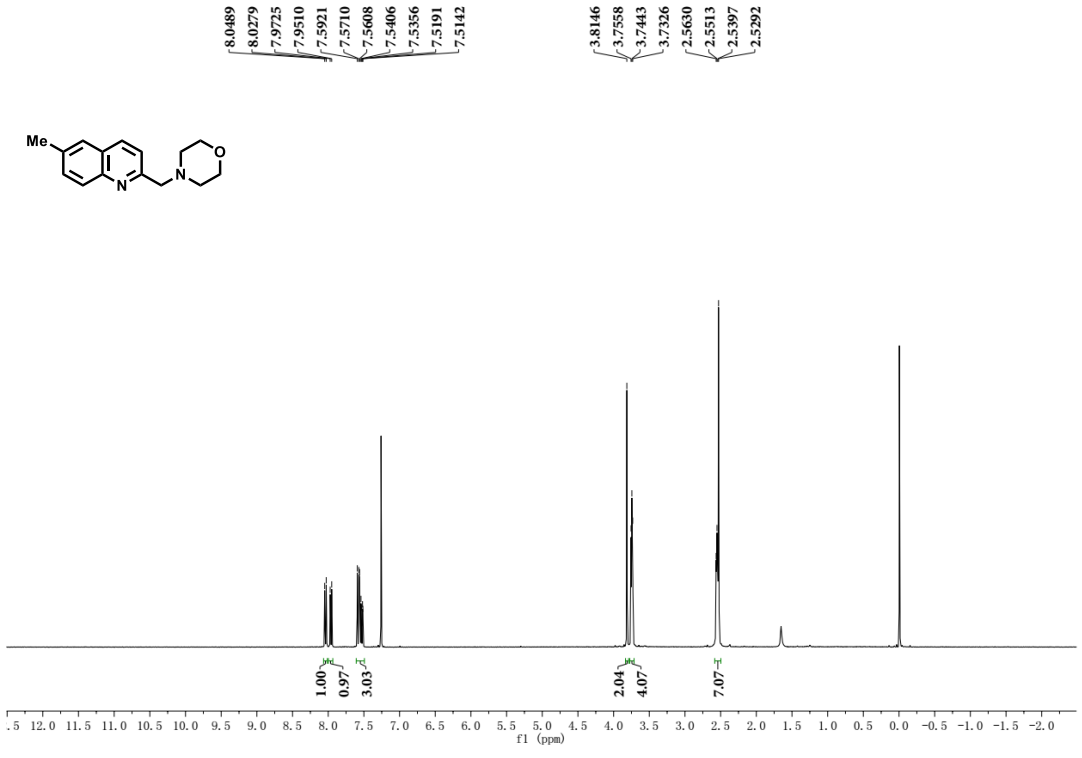


Figure S17. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1q in $CDCl_3$

4-((6-methylquinolin-2-yl)methyl)morpholine



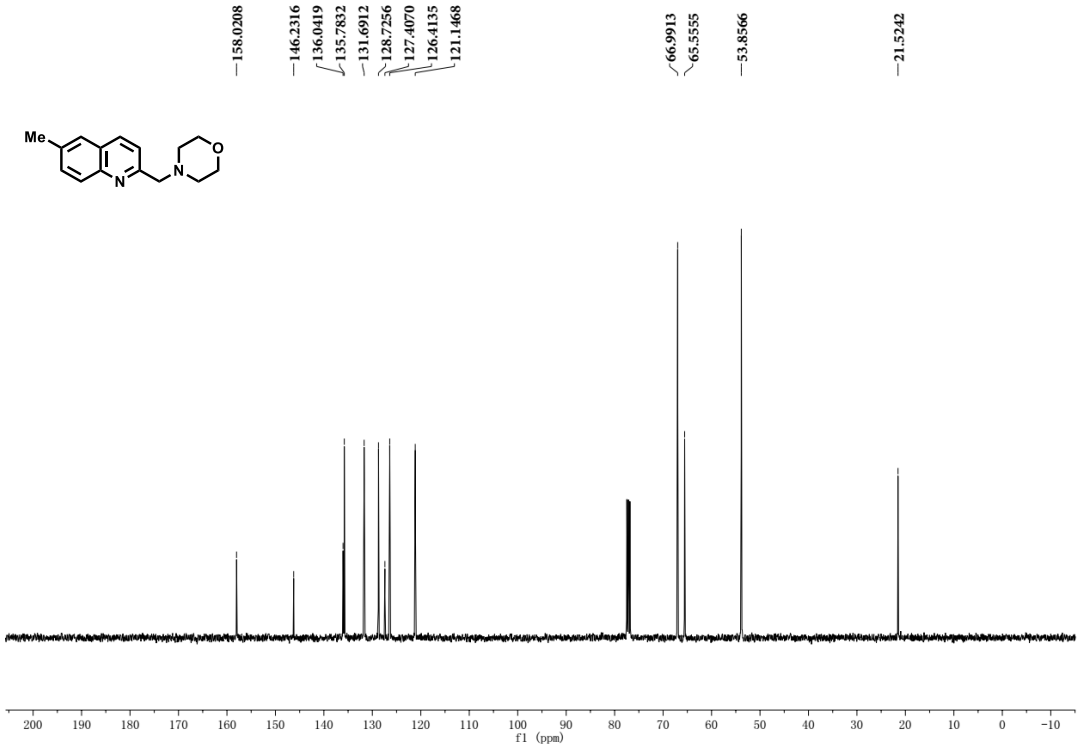
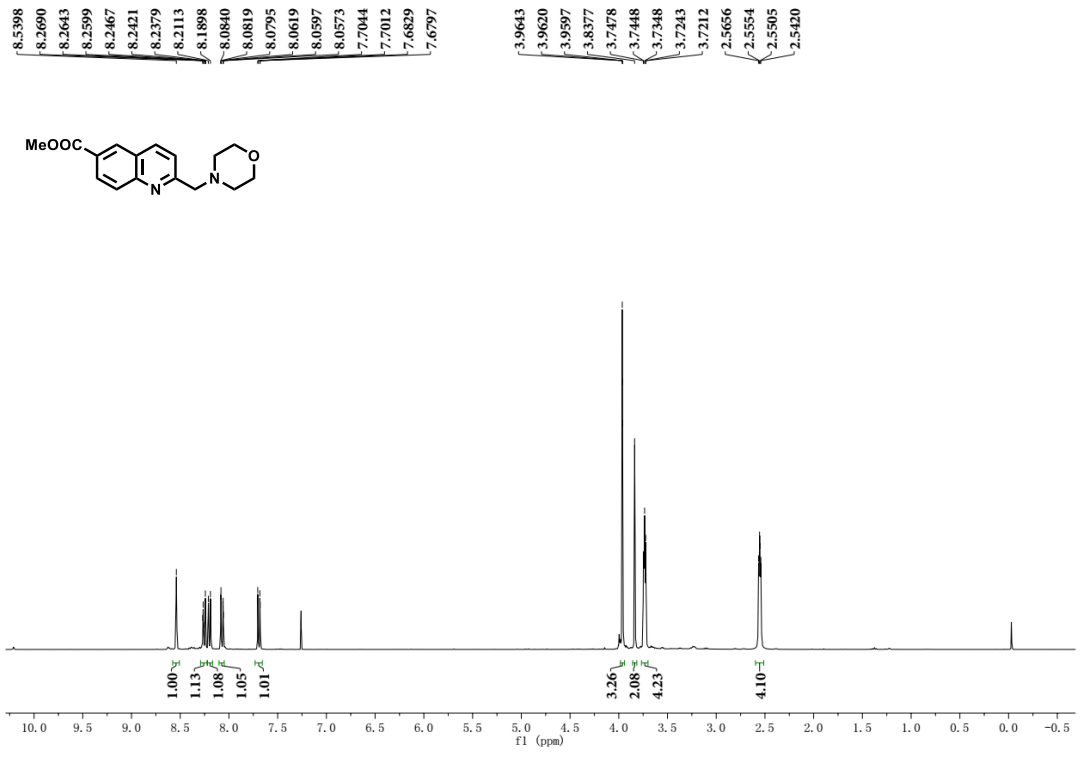


Figure S18. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1r in $CDCl_3$

Methyl 2-(morpholinomethyl)quinoline-6-carboxylate



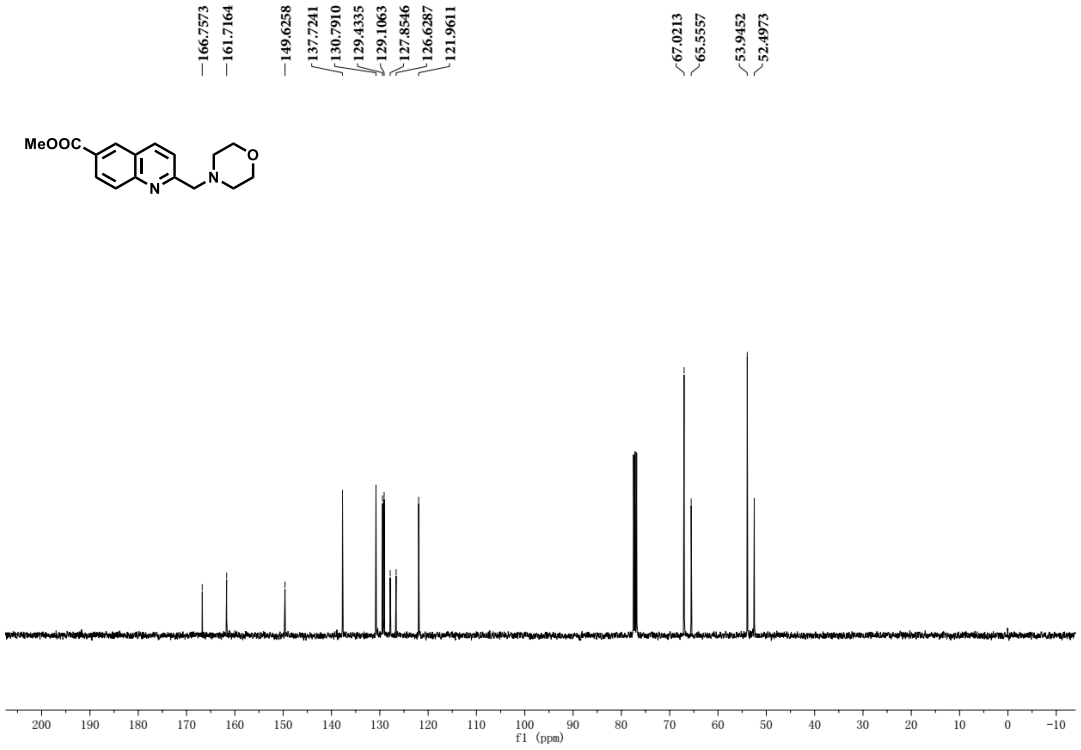
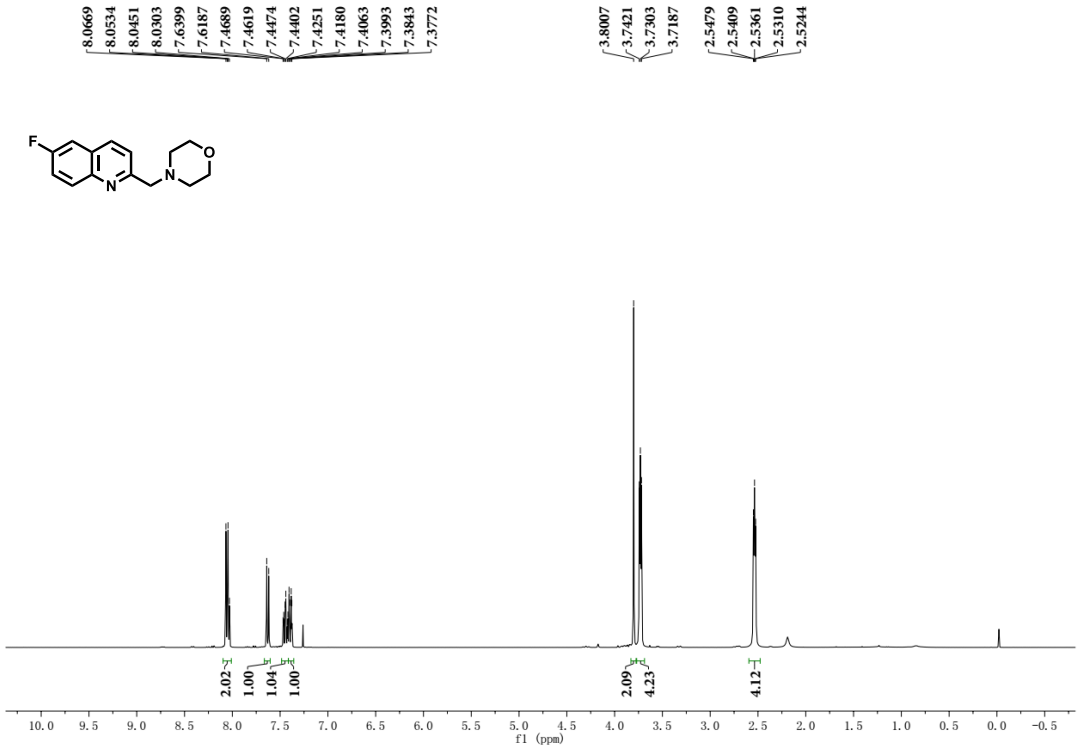


Figure S19. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1s in $CDCl_3$

4-((6-fluoroquinolin-2-yl)methyl)morpholine



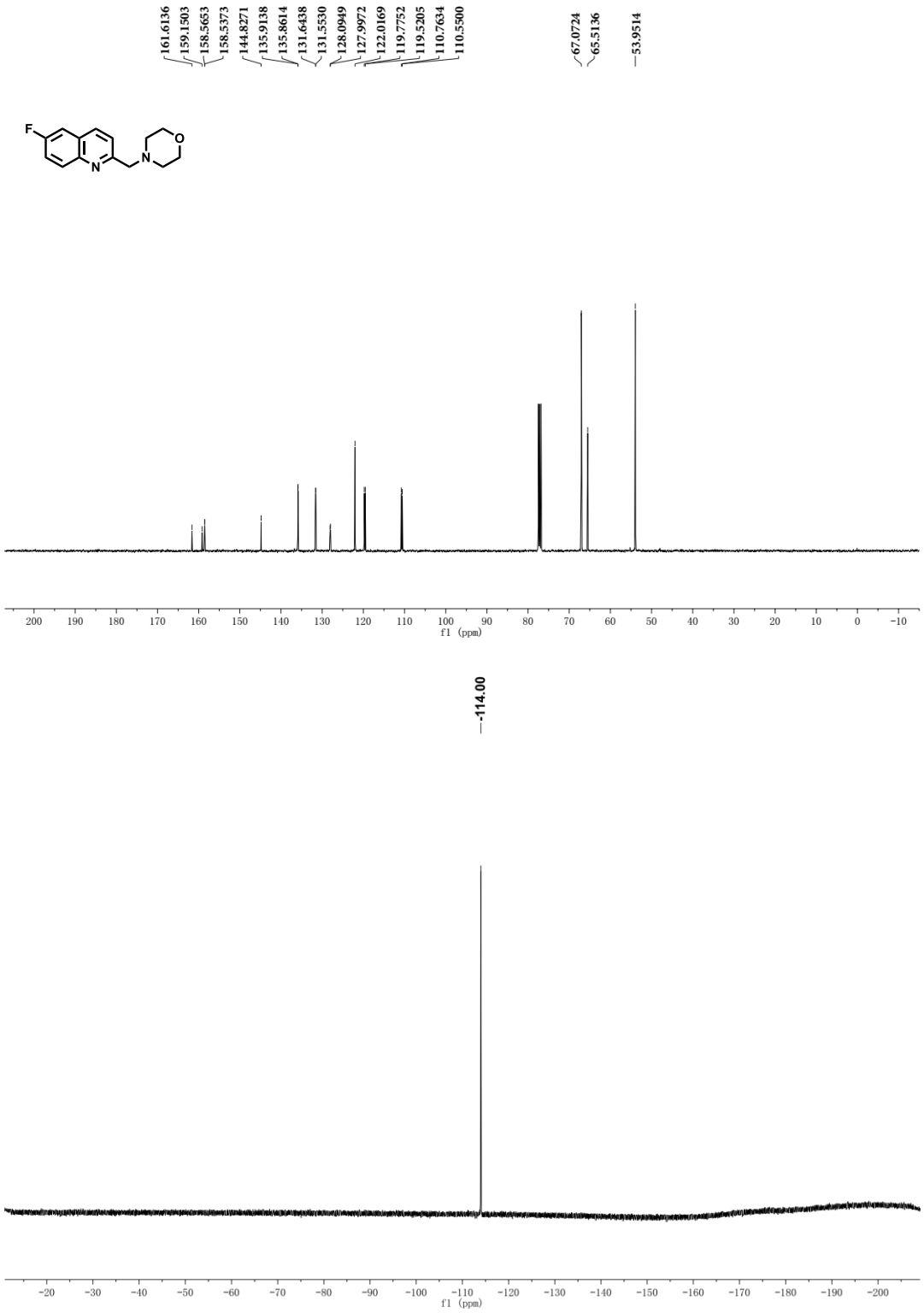


Figure S20. ^{1}H NMR (400 MHZ) , ^{13}C NMR (101MHZ) and ^{19}F (376 MHZ) spectra of 1t in $CDCl_3$

4-((7-chloroquinolin-2-yl)methyl)morpholine

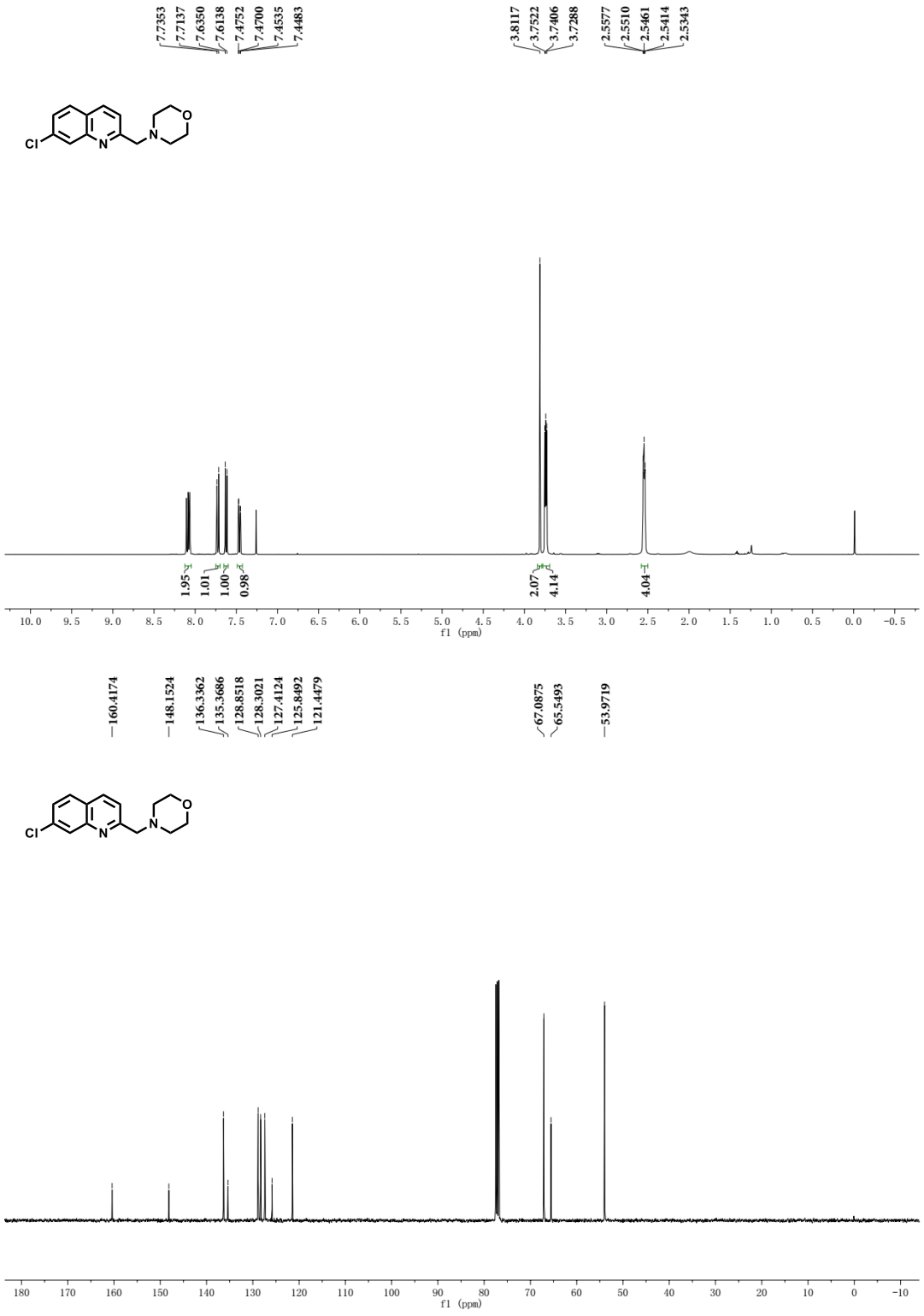


Figure S21. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1u in $CDCl_3$

4-((6-(tert-butyl)pyridin-2-yl)methyl)morpholine

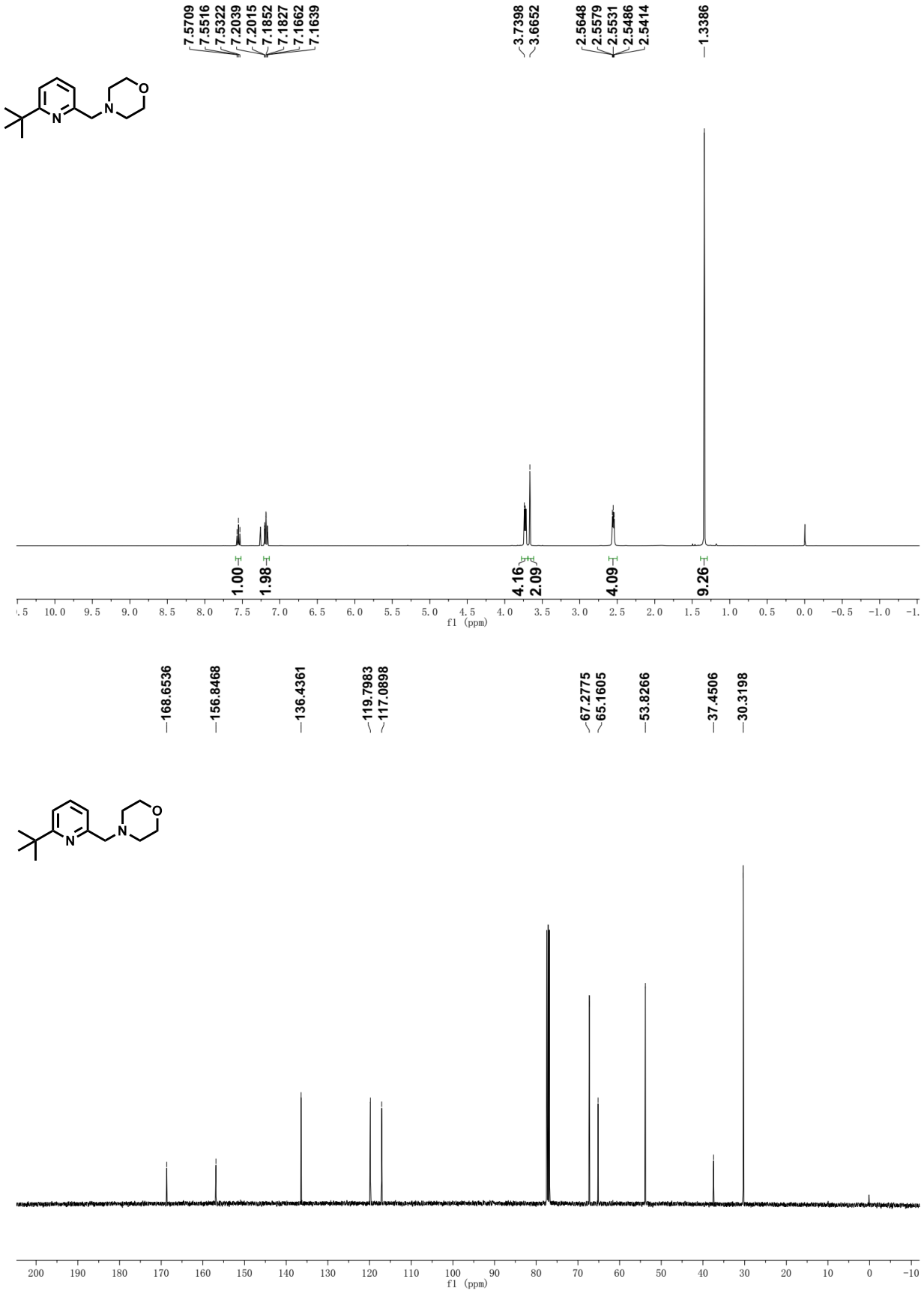


Figure S22. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 1v in $CDCl_3$

(6-methoxynaphthalen-2-yl)methyl pivalate

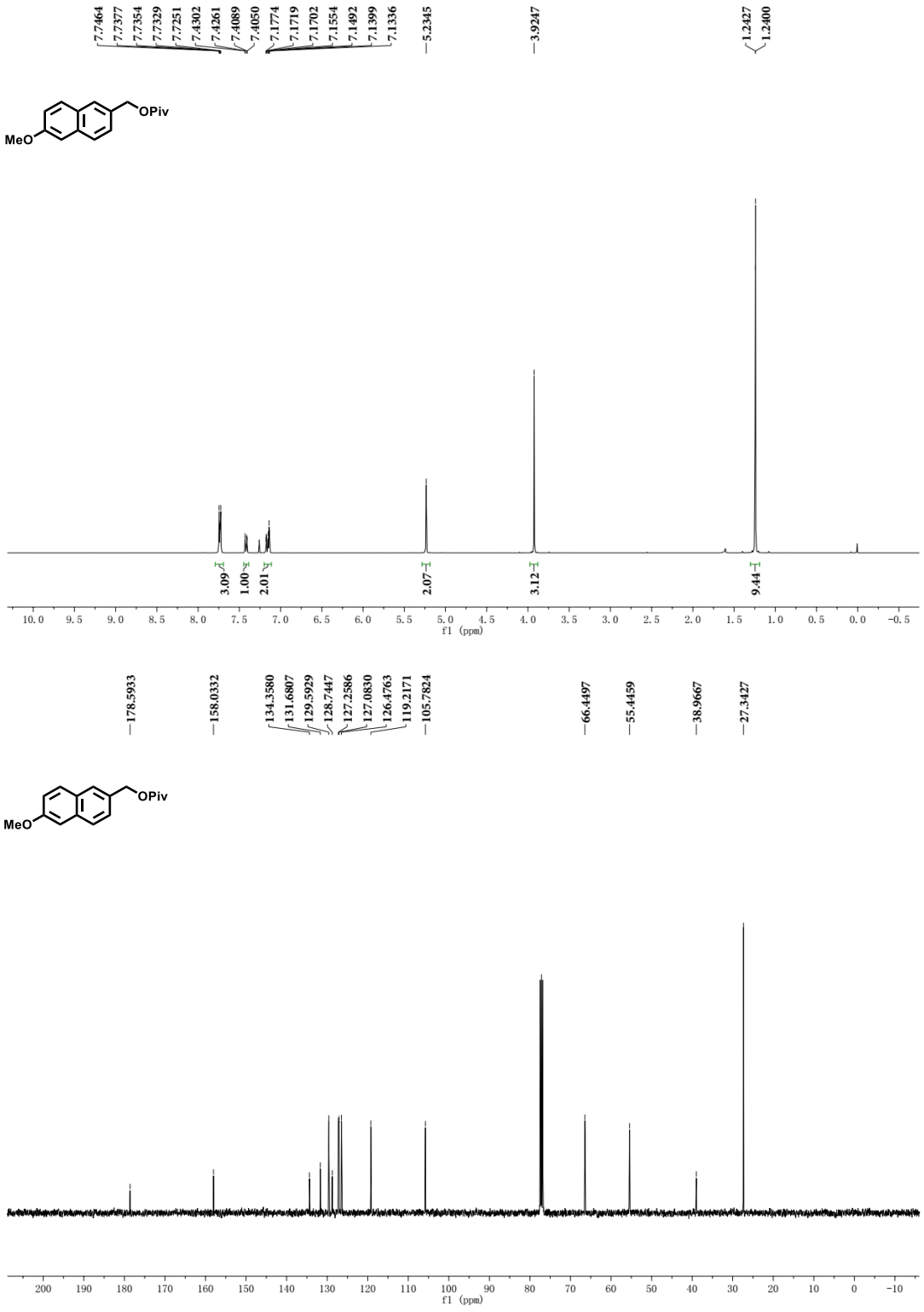


Figure S23. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 2b in $CDCl_3$

(7-methoxynaphthalen-2-yl)methyl pivalate

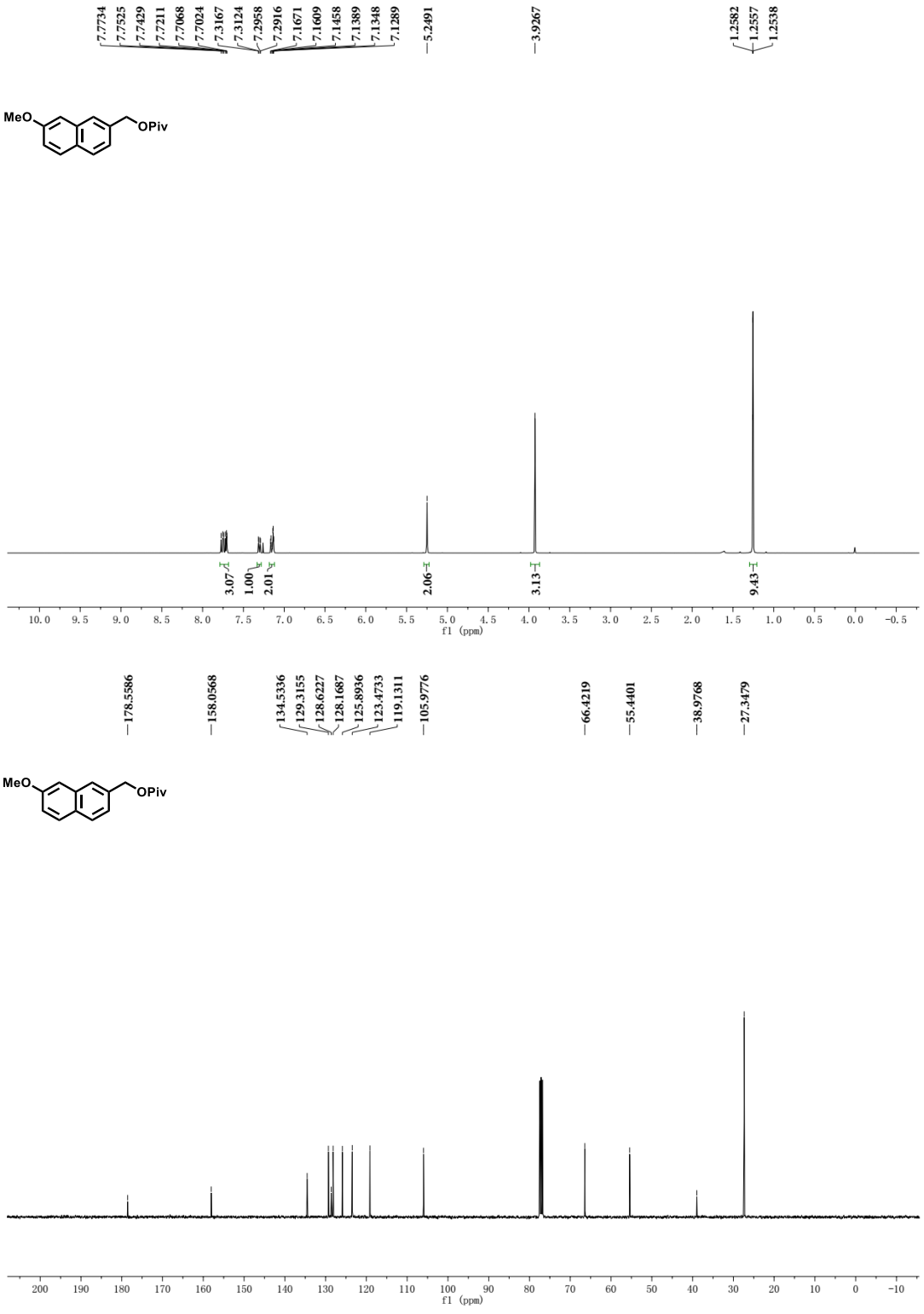


Figure S24. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 2c in $CDCl_3$

(6-(Benzyloxy)naphthalen-2-yl)methyl pivalate

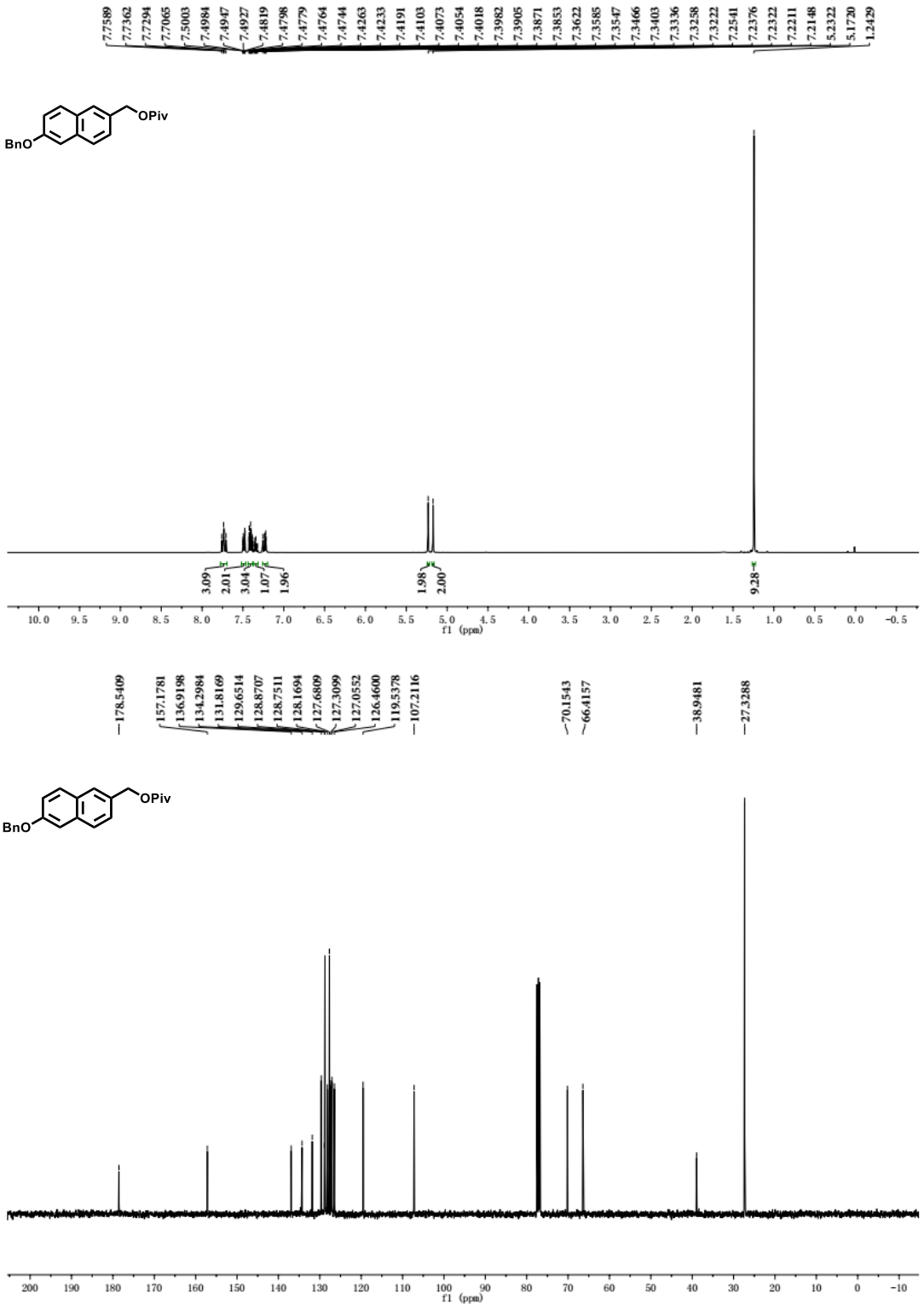


Figure S25. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 2d in $CDCl_3$

(6-cyclopropylnaphthalen-2-yl)methyl pivalate

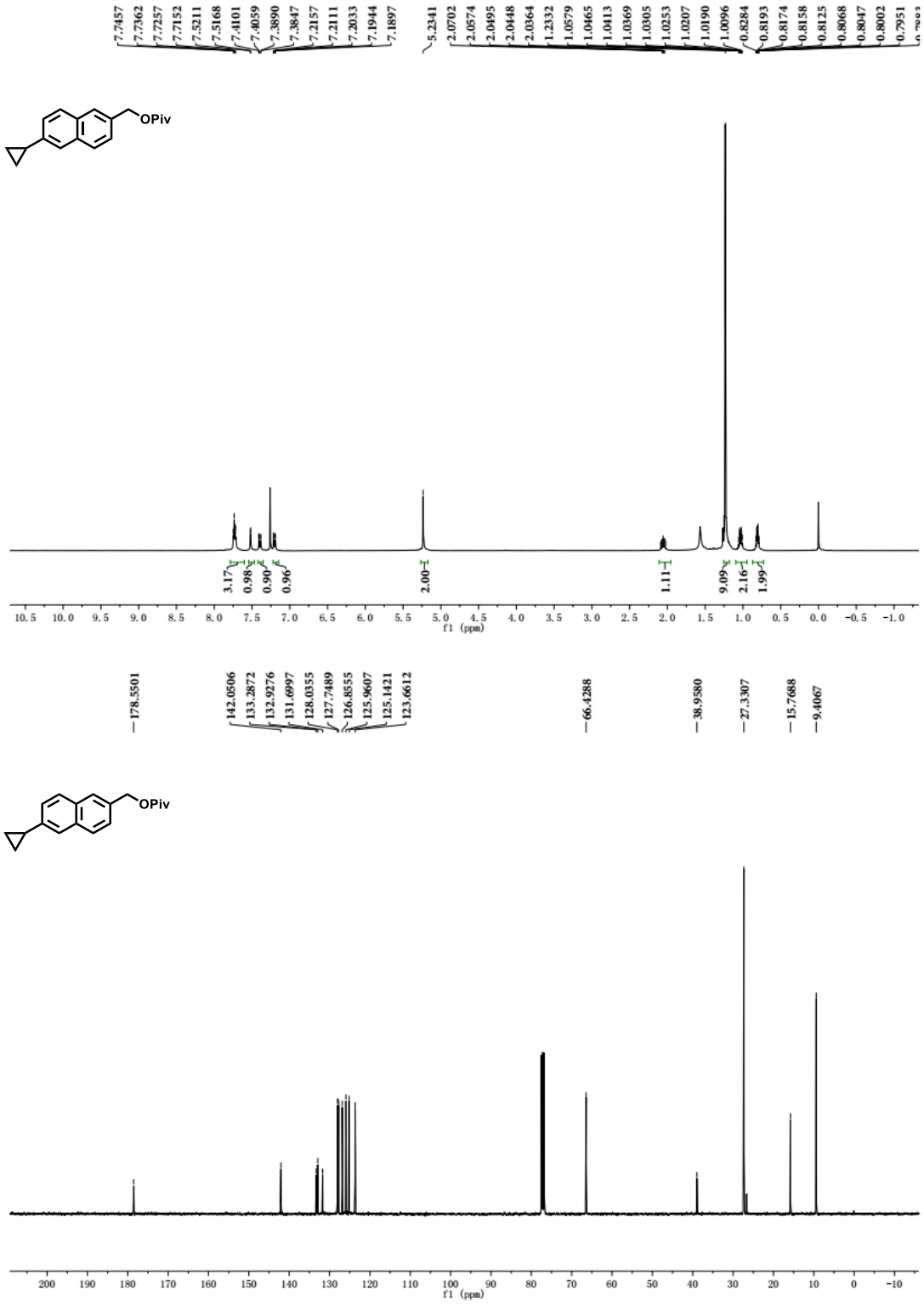


Figure S26. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 2e in $CDCl_3$

(6-methylnaphthalen-2-yl)methyl pivalate

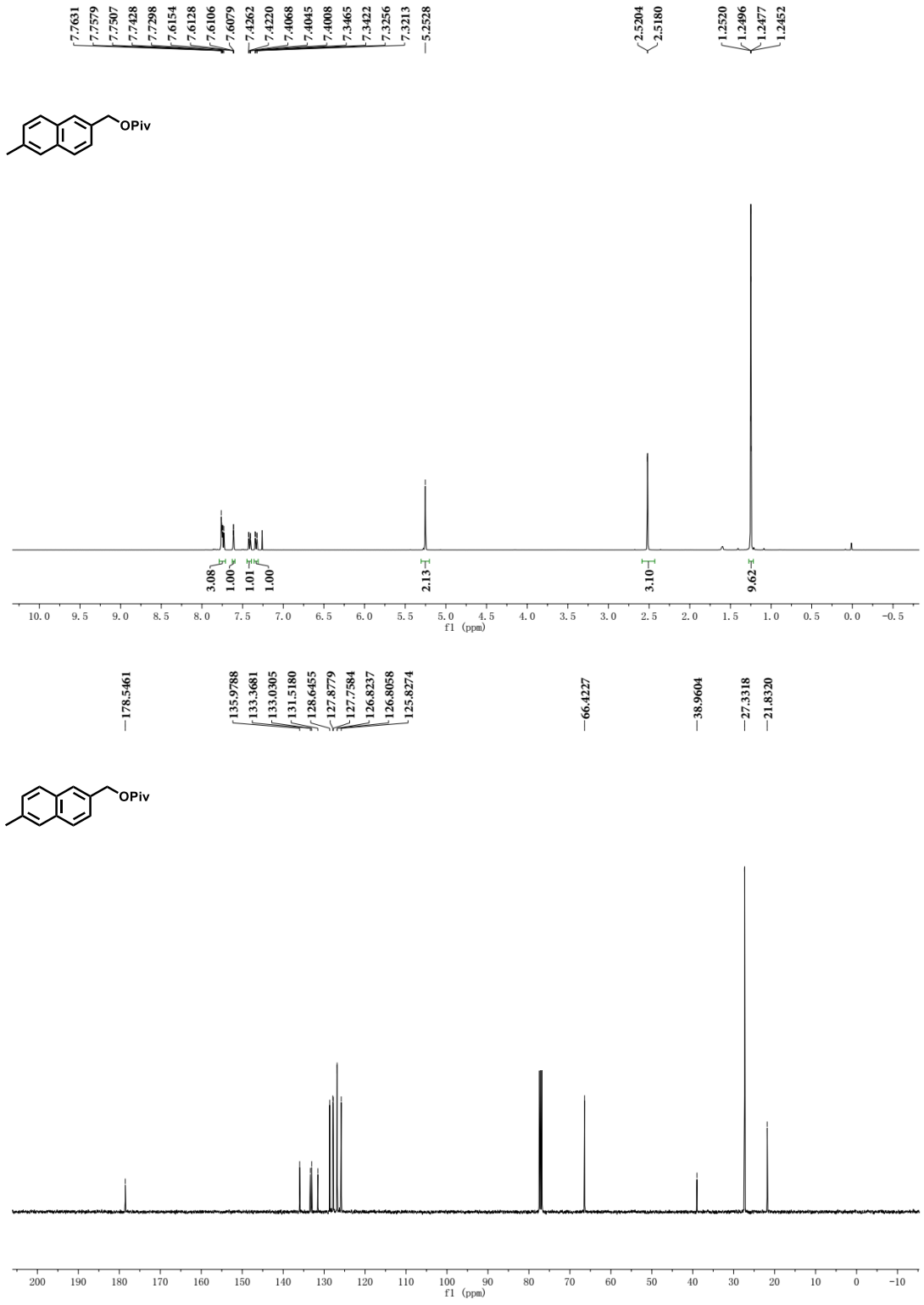


Figure S27. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 2f in $CDCl_3$

(6-phenylnaphthalen-2-yl)methyl pivalate

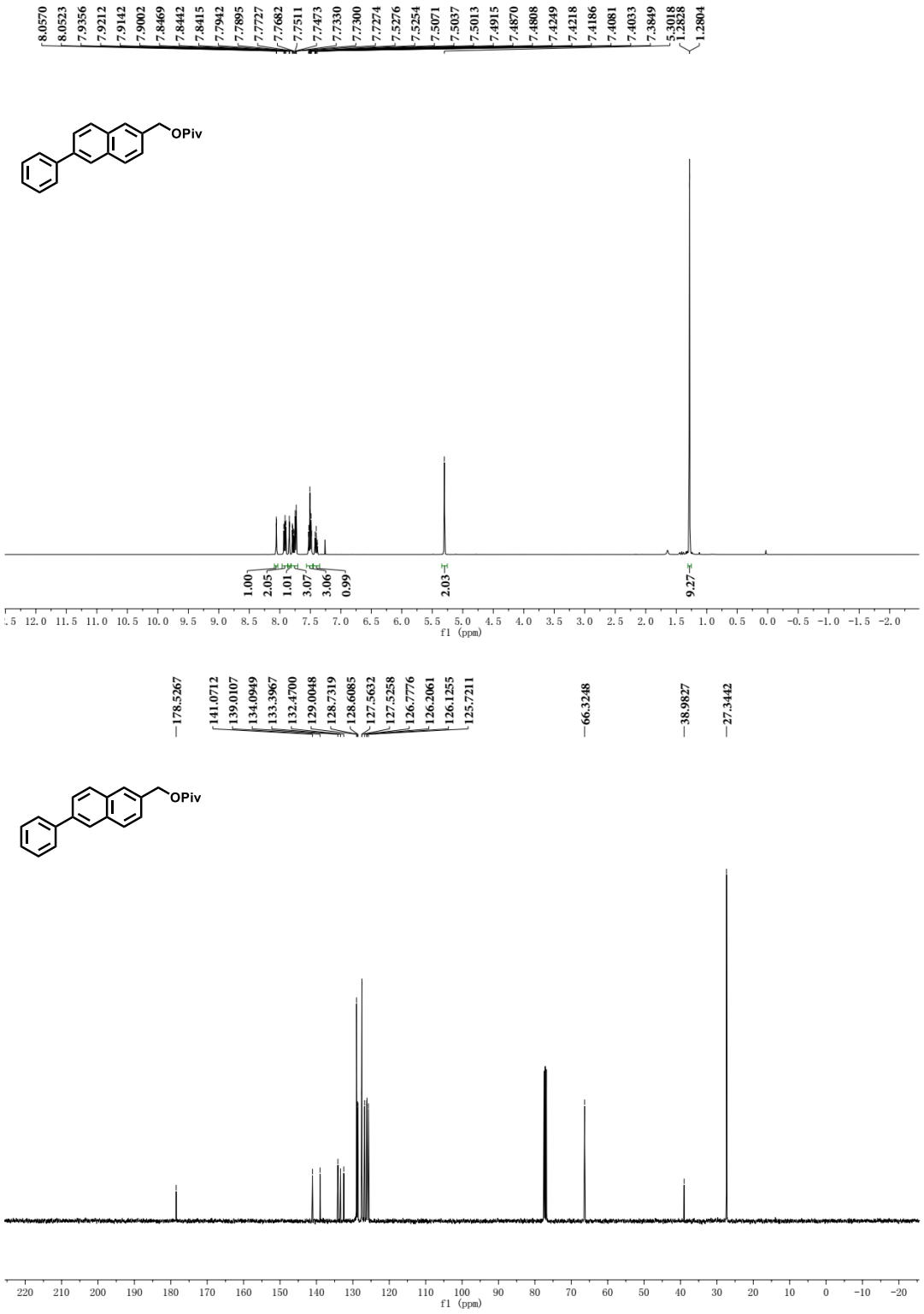


Figure S28. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 2g in $CDCl_3$

(6-(thiophen-2-yl)naphthalen-2-yl)methyl pivalate

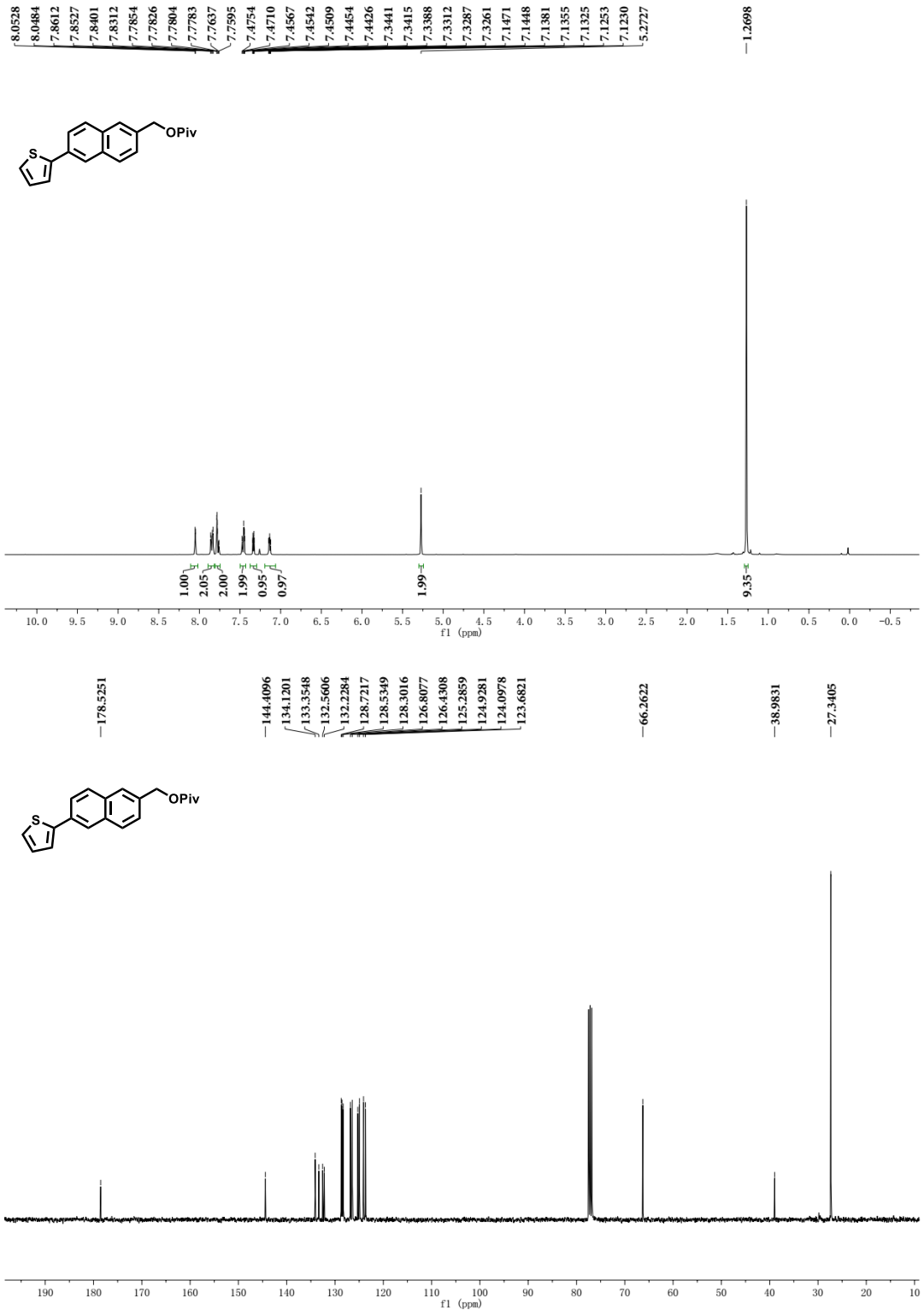


Figure S29. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 2h in $CDCl_3$

(6-(quinolin-8-yl)naphthalen-2-yl)methyl pivalate

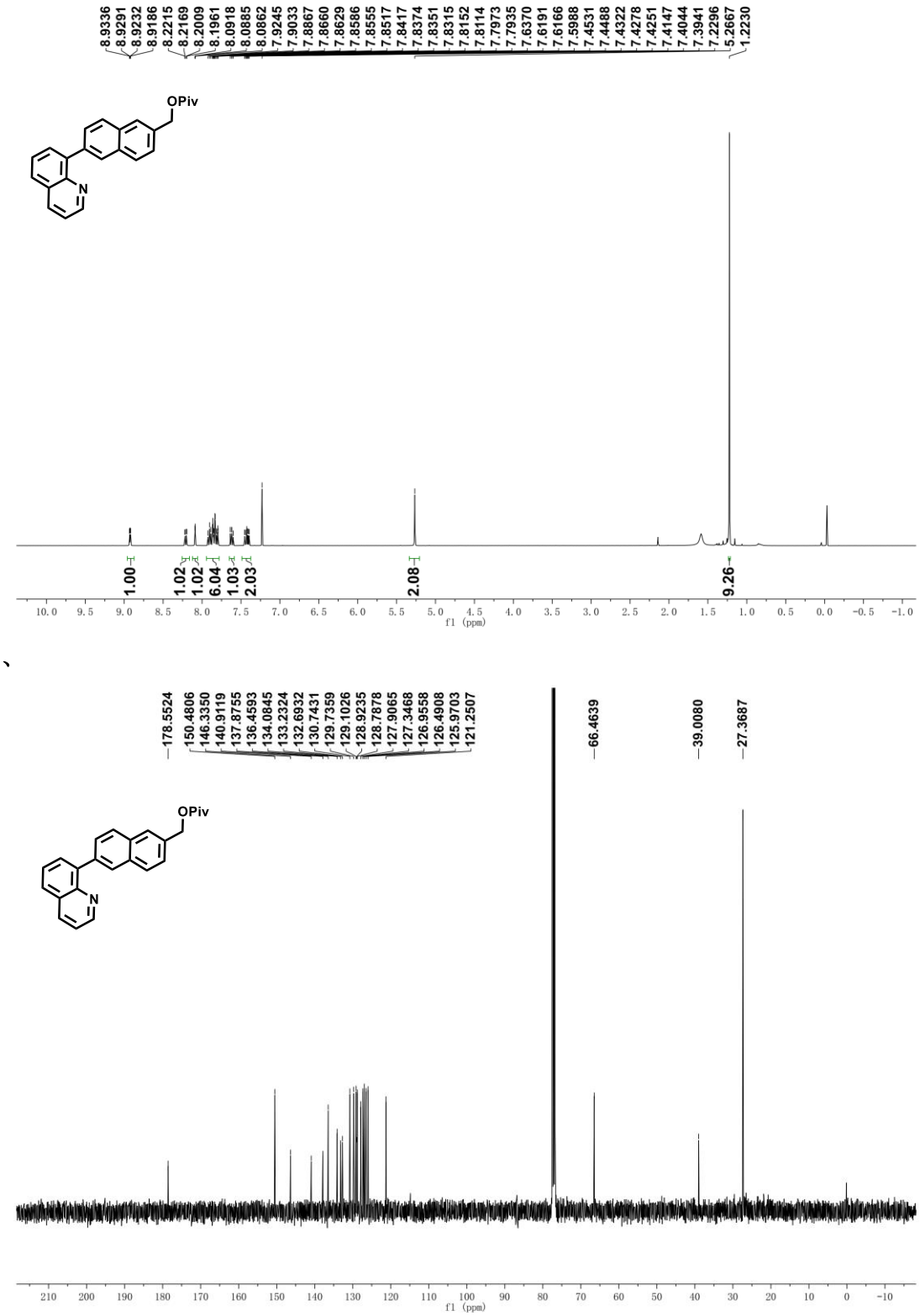


Figure S30. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ}NMR spectra of 2i in $CDCl_3$

4-(2-(naphthalene-2-yl)-1-(pyridine-2-yl)ethyl)morpholine

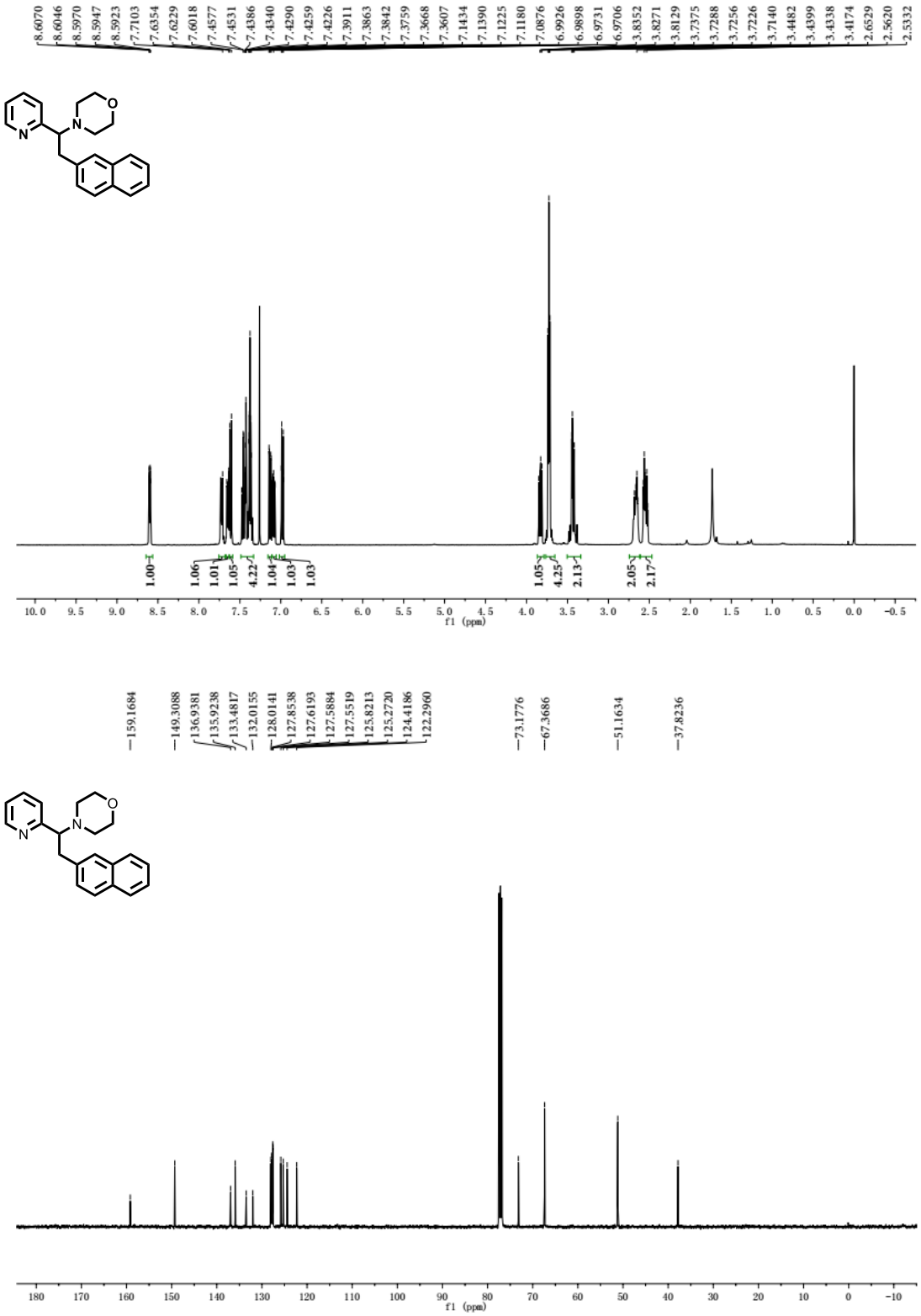


Figure S31. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3aa in $CDCl_3$

4-(2-(Naphthalene-2-yl)-1-(pyridine-2-yl)ethyl)piperidine

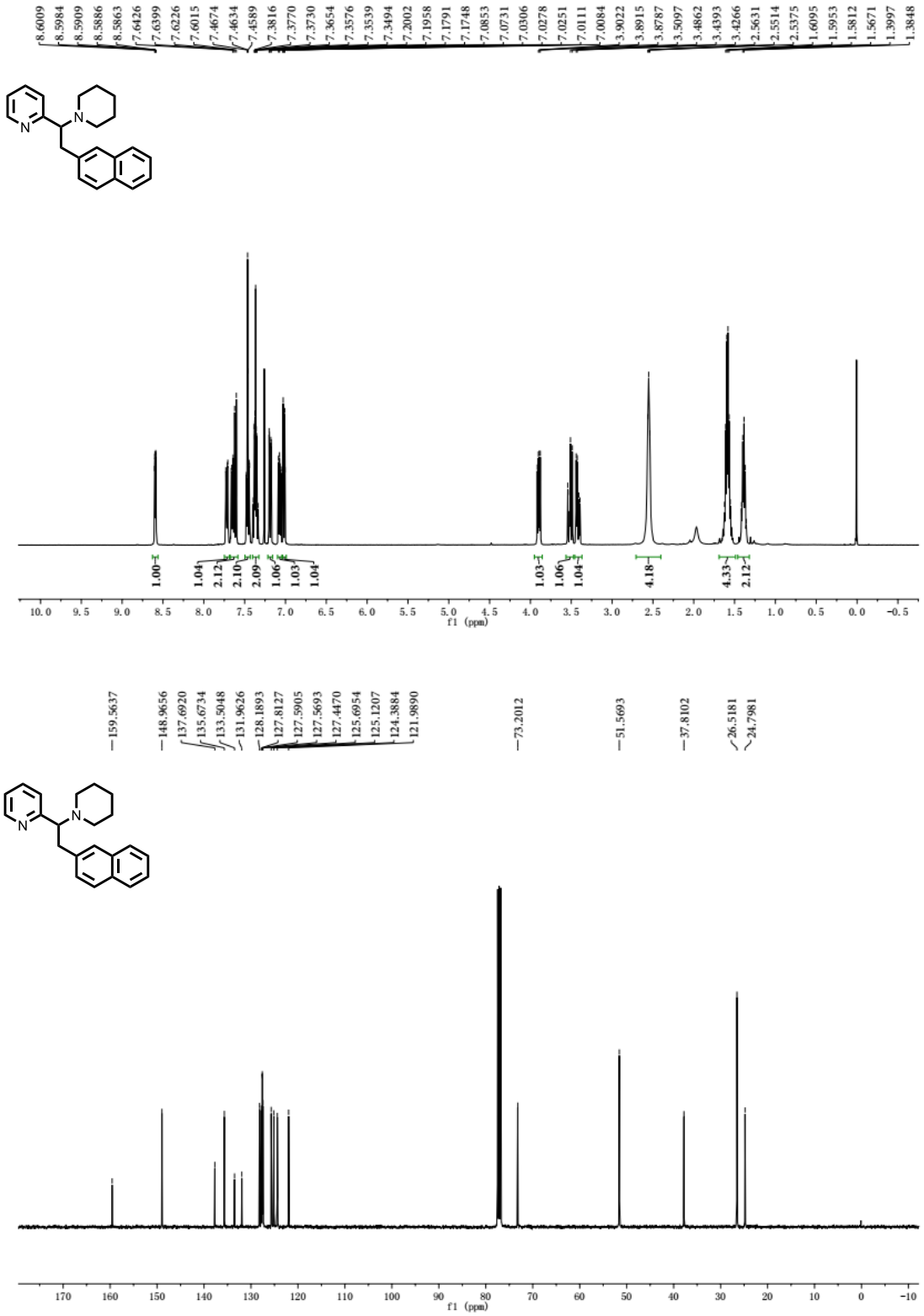


Figure S32. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ba in $CDCl_3$

4-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)thiomorpholine

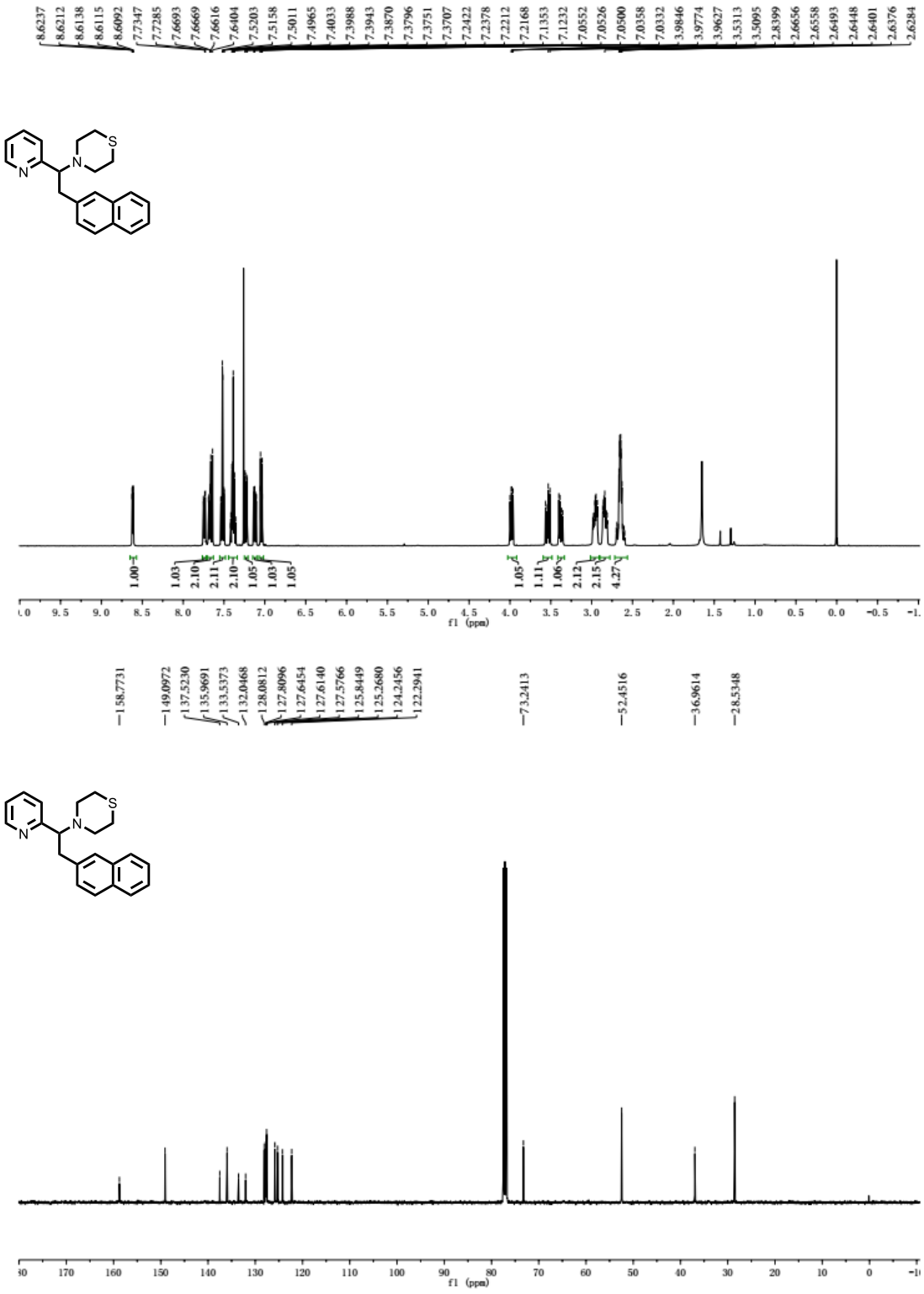


Figure S33. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ca in $CDCl_3$

1-methyl-4-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)piperazine

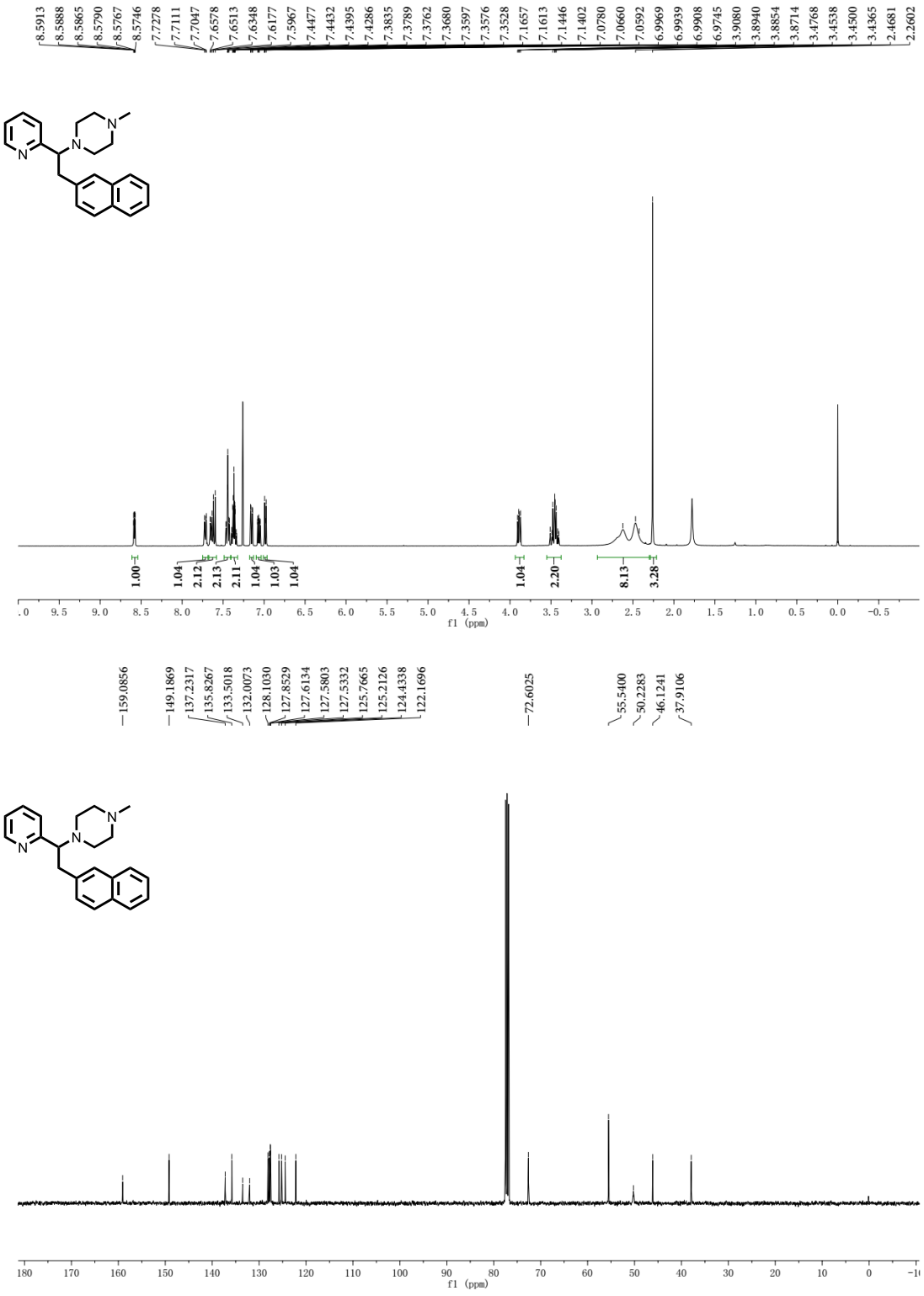


Figure S34. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3da in $CDCl_3$

1-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)azepane

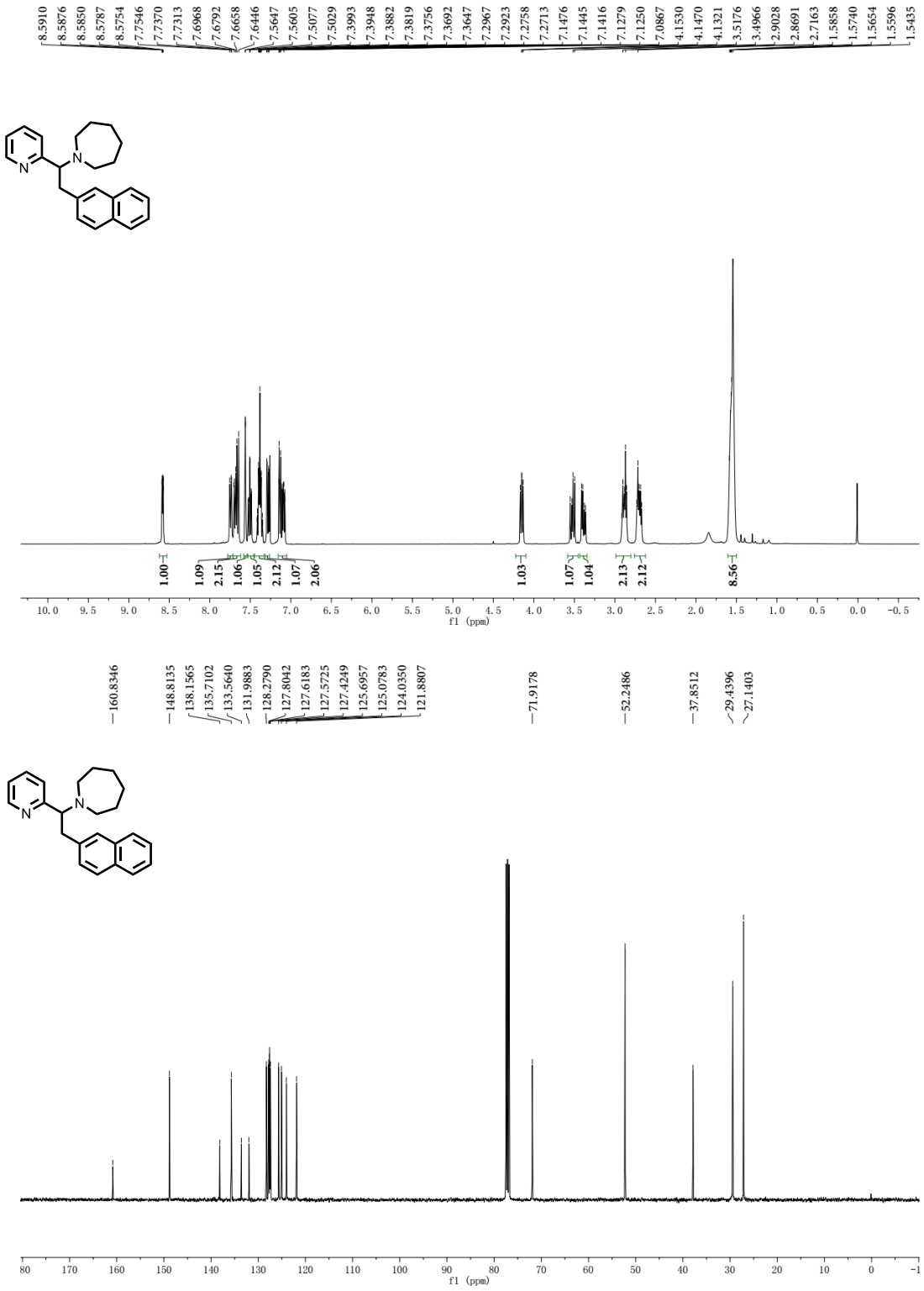


Figure S35. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ea in $CDCl_3$

N,N-dimethyl-2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethan-1-amine

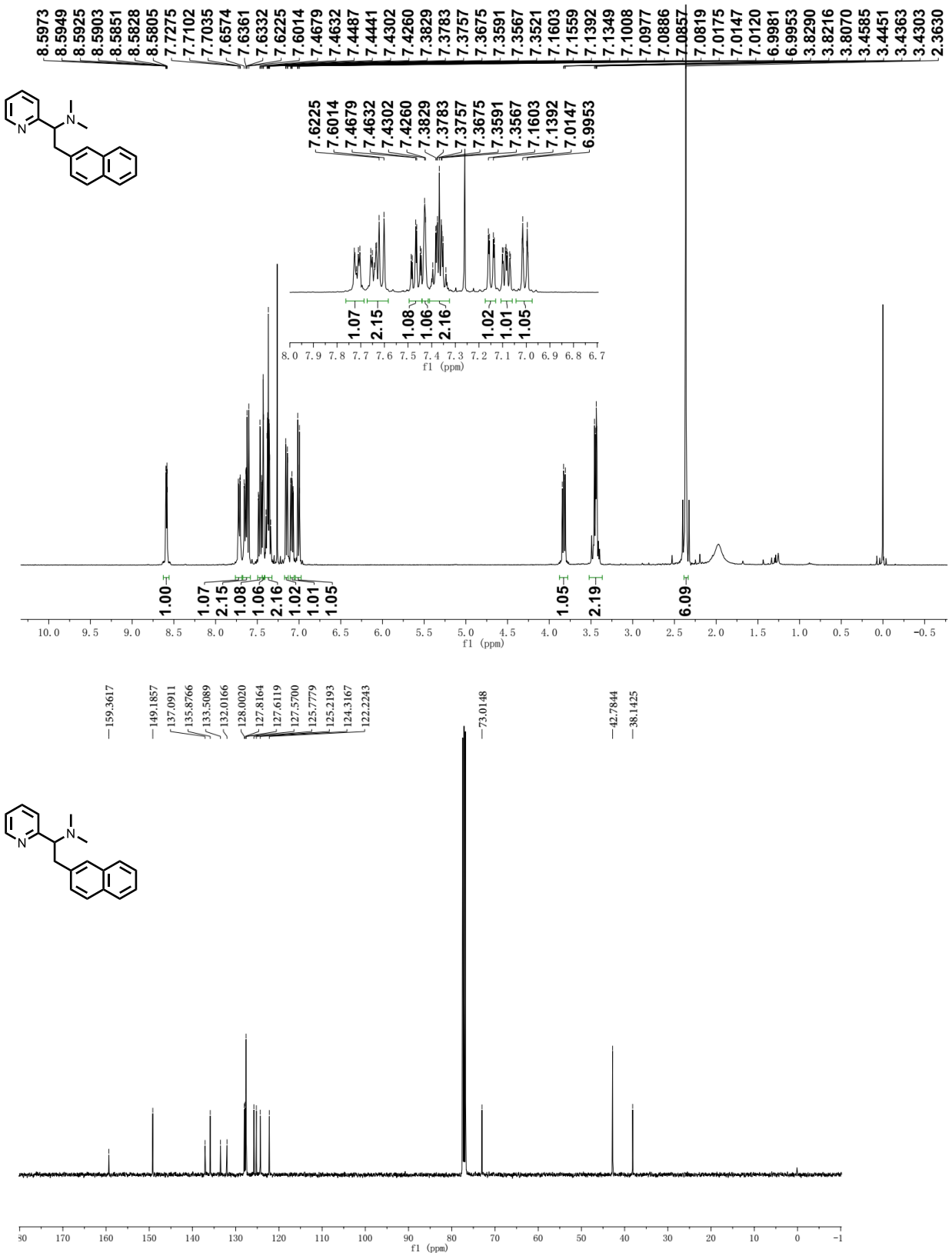


Figure S36. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3fa in $CDCl_3$

N-ethyl-N-methyl-2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethan-1-amine

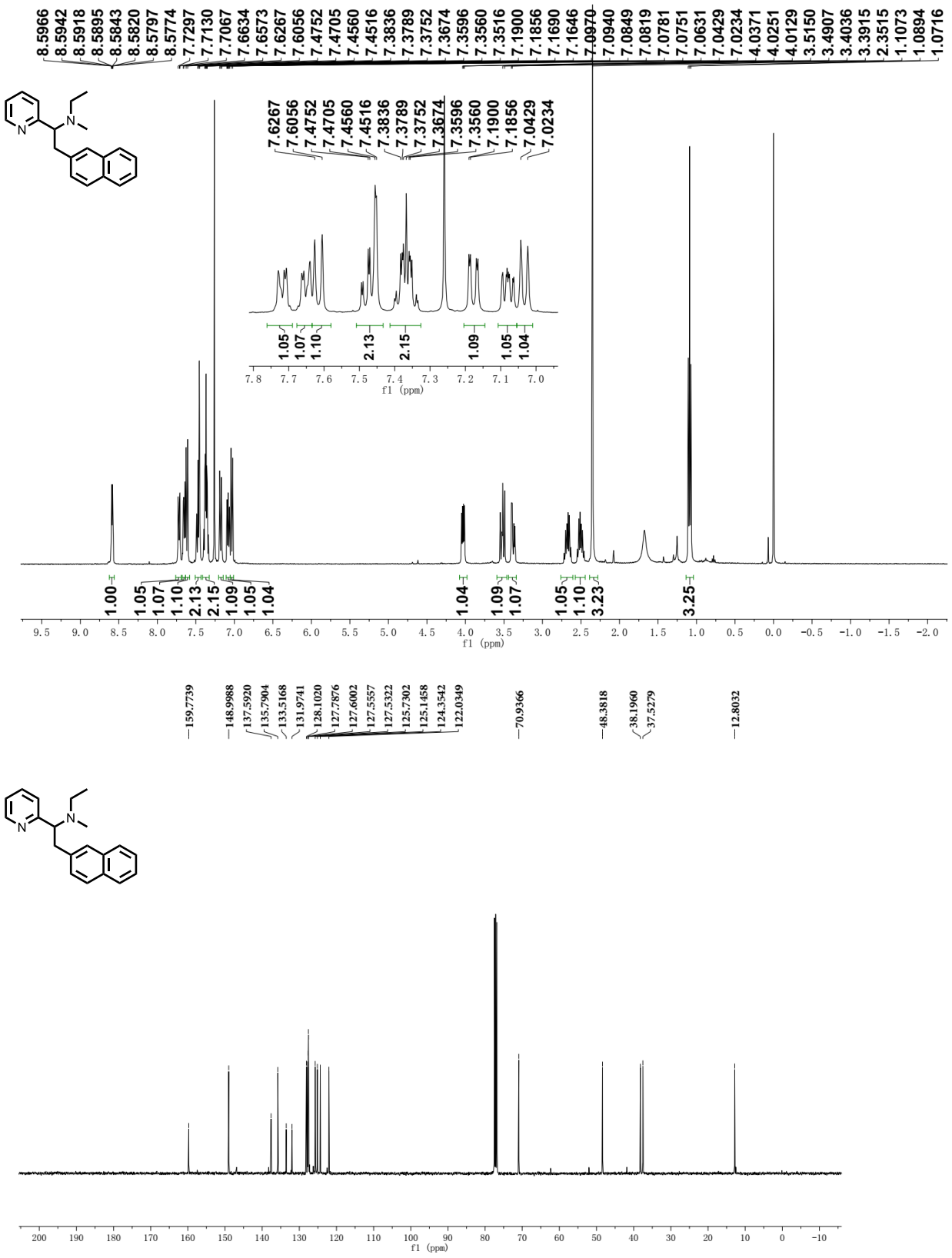


Figure S37. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ga in $CDCl_3$

N-methyl-N-(2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)propan-2-amine

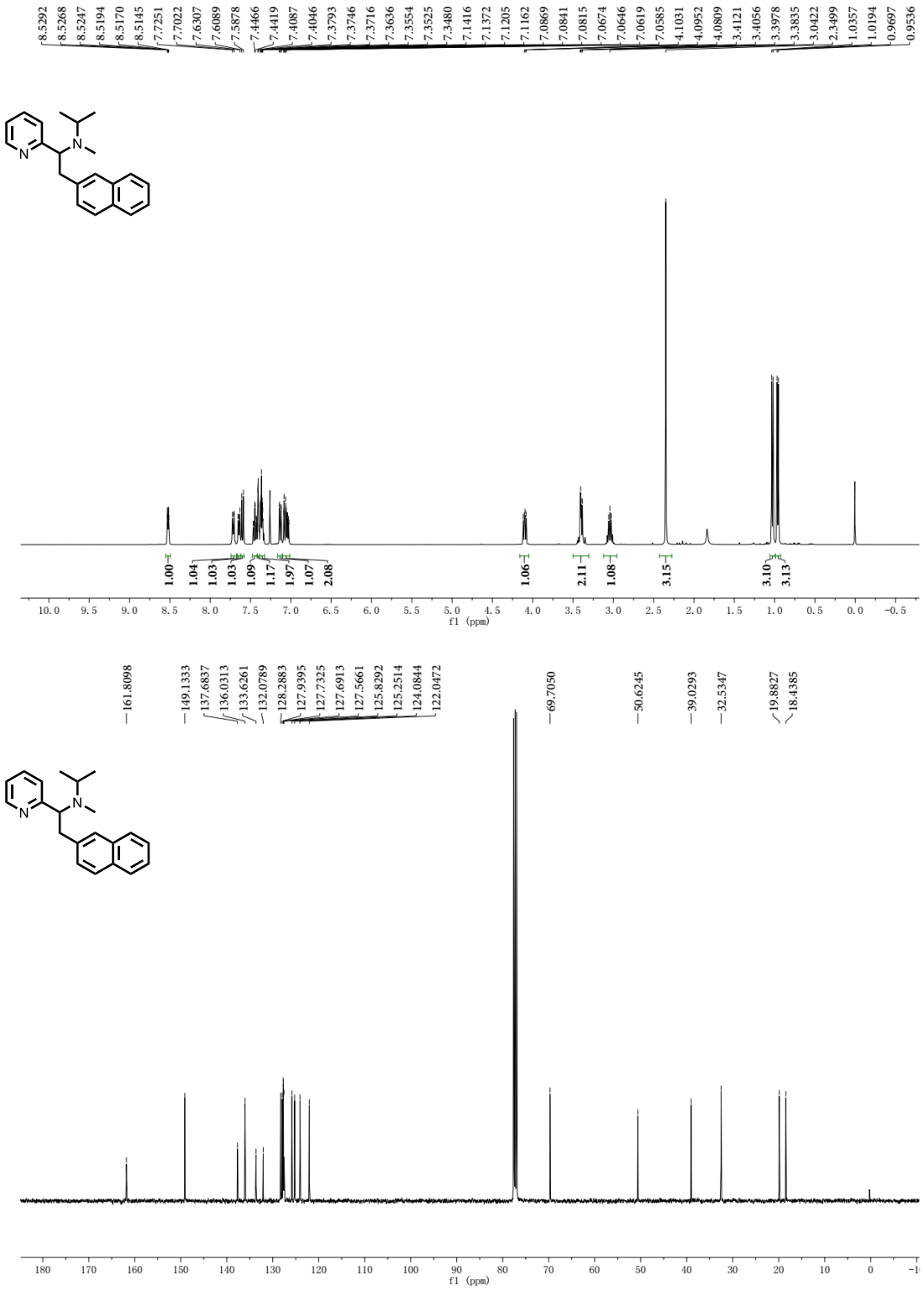


Figure S38. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ha in $CDCl_3$

N,N-diethyl-2-(naphthalen-2-yl)-1-(pyridin-2-yl)ethan-1-amine

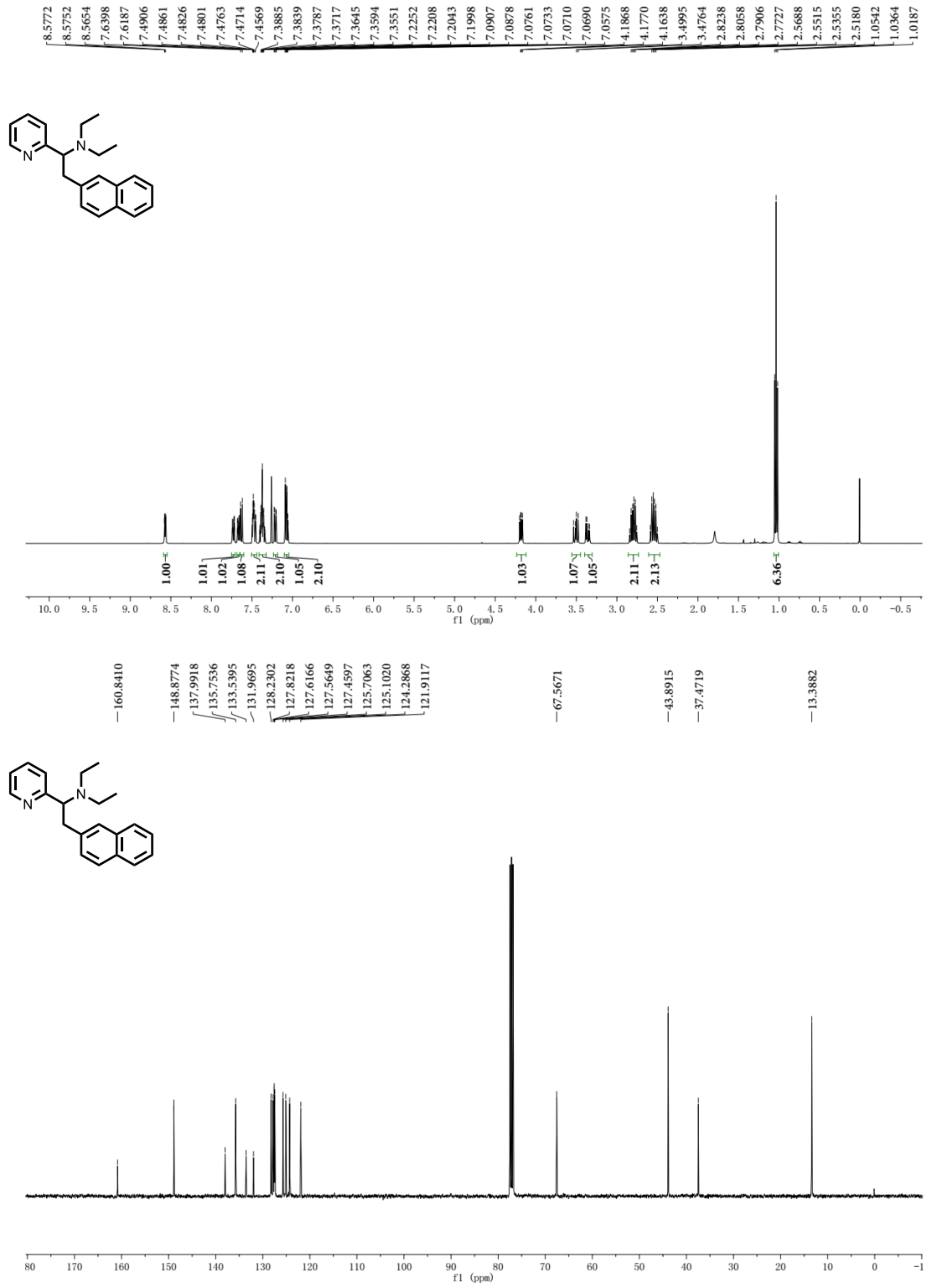


Figure S39. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ia in $CDCl_3$

4-(2-(naphthalen-2-yl)-1-(5-phenylpyridin-2-yl)ethyl)morpholine

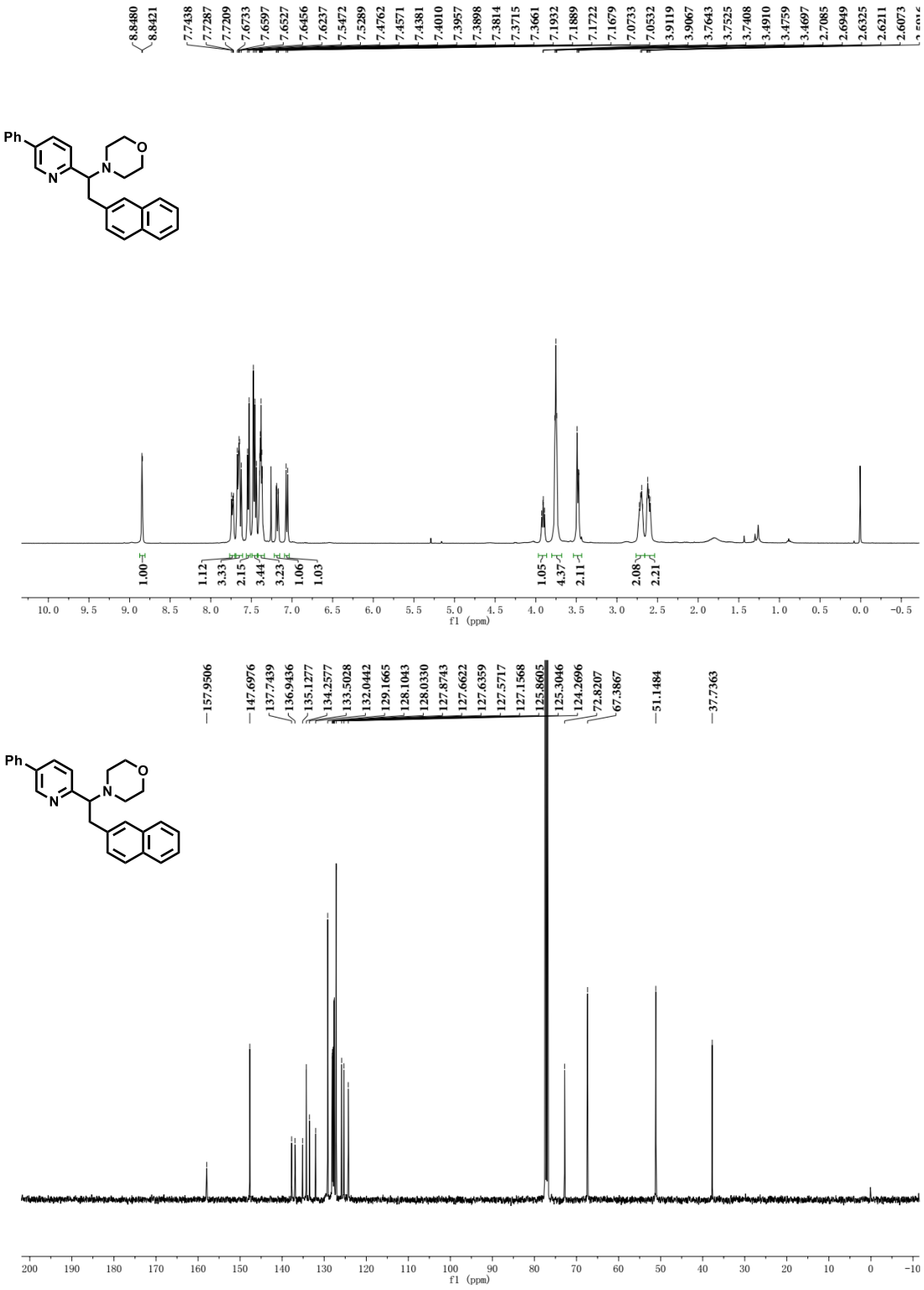


Figure S40. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ja in $CDCl_3$

4-(1-(6-methylpyridin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine

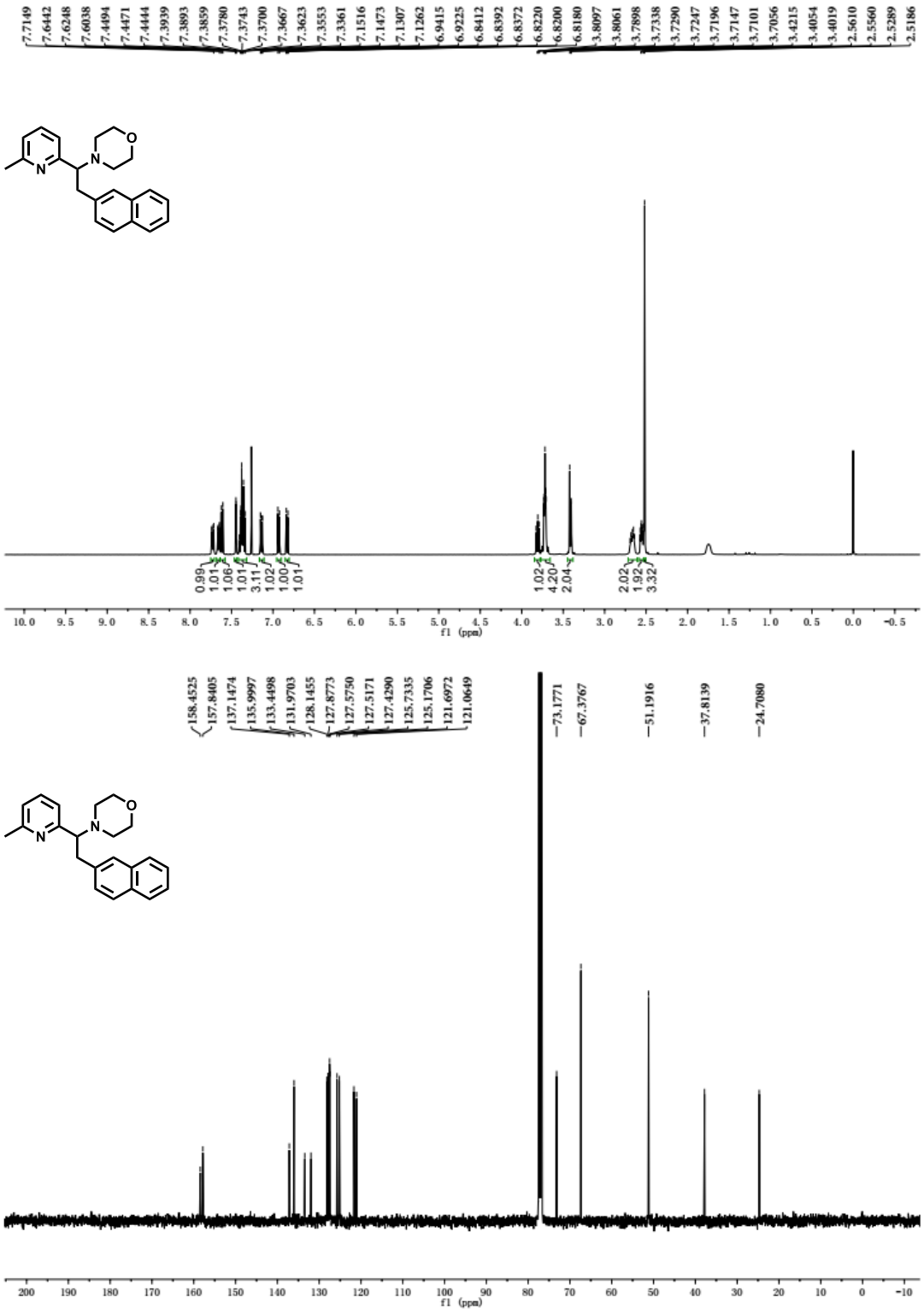
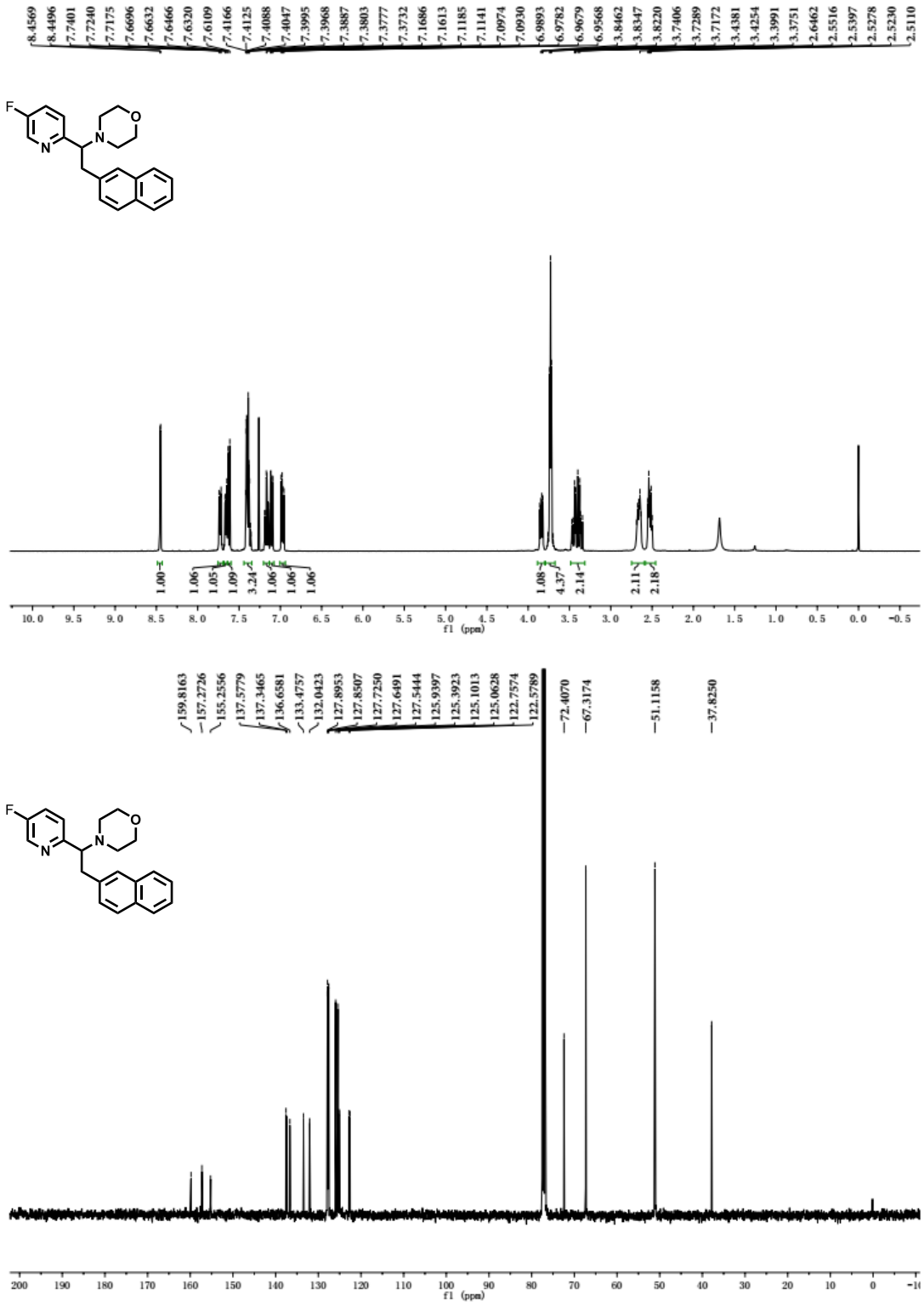


Figure S41. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ka in $CDCl_3$

4-(1-(5-fluoropyridin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine



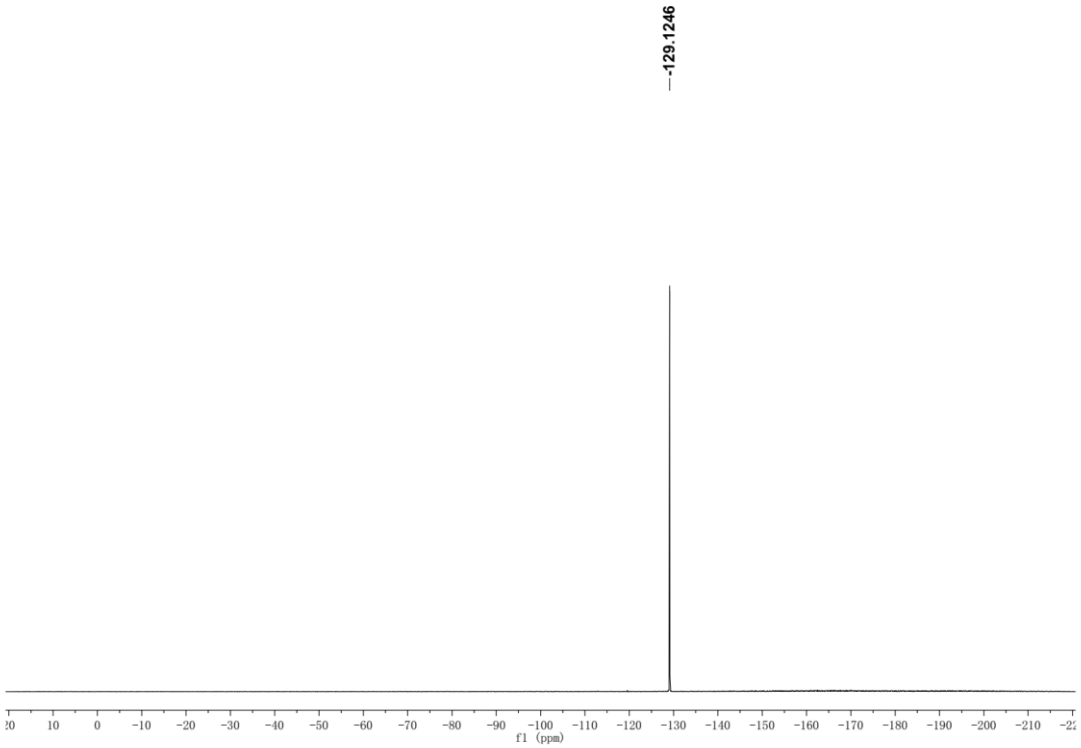
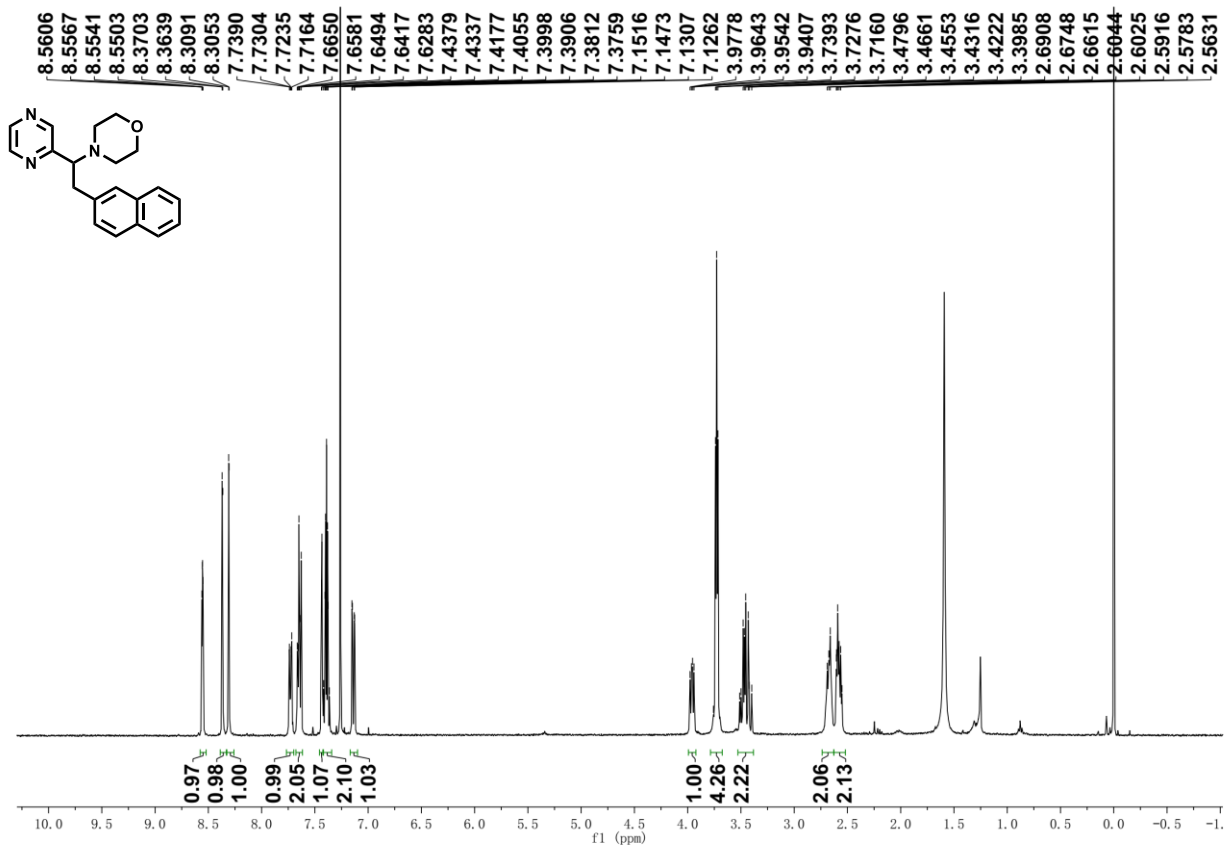


Figure S42. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3la in $CDCl_3$

4-(2-(naphthalen-2-yl)-1-(pyrazin-2-yl)ethyl)morpholine



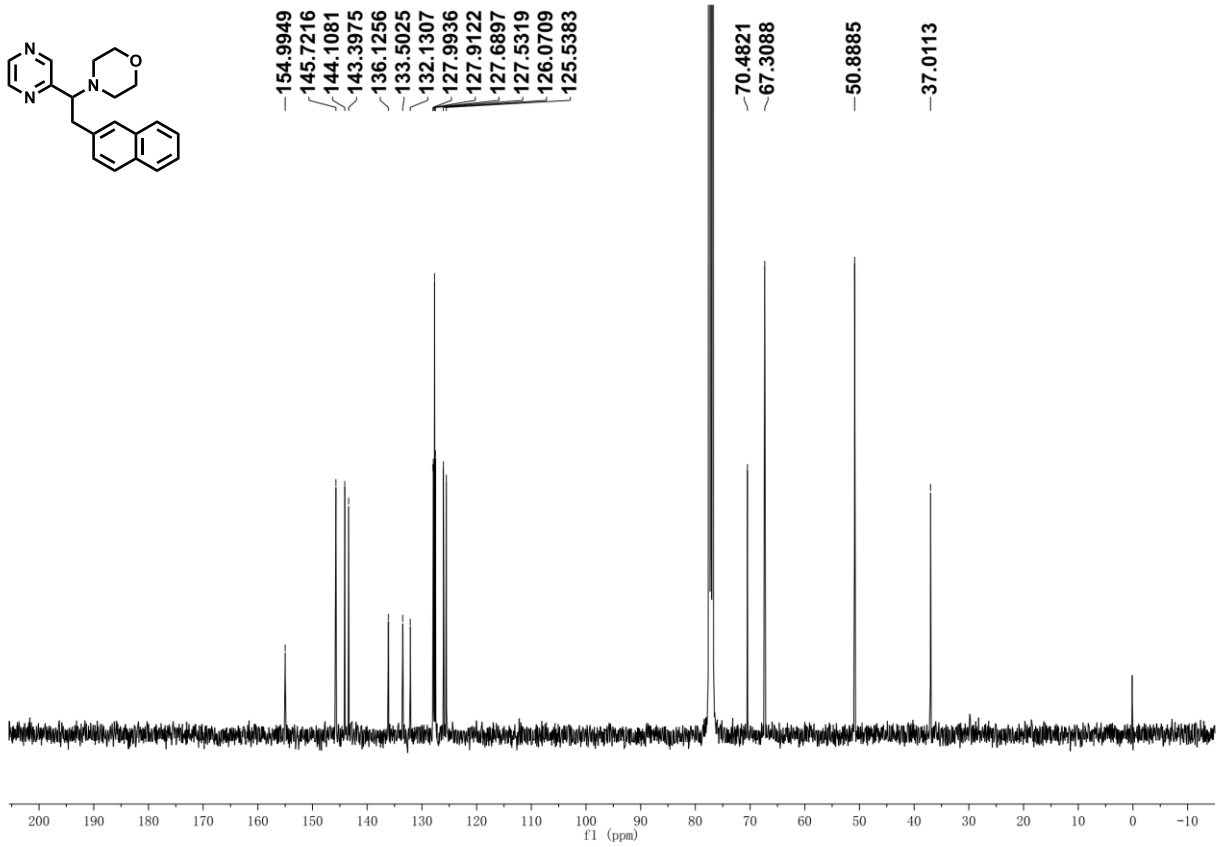
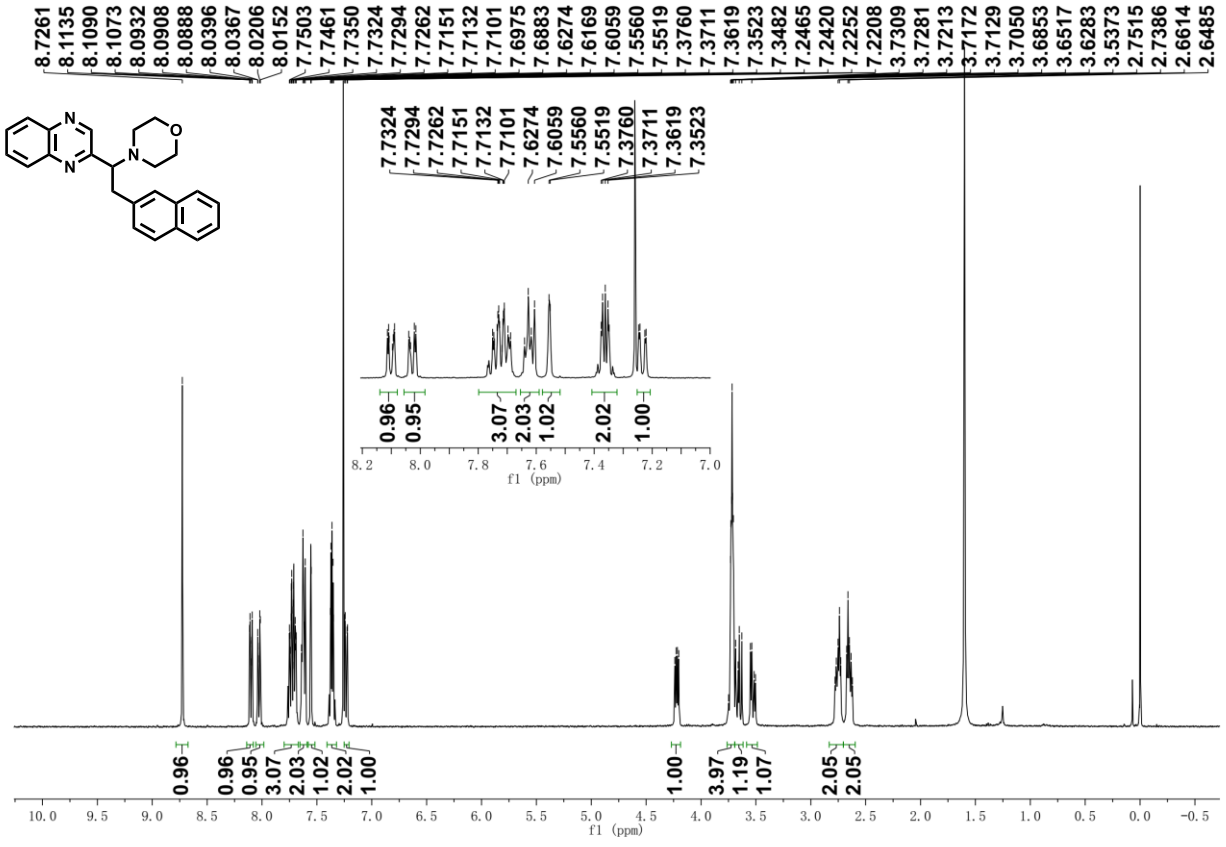


Figure S43. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ma in $CDCl_3$

4-(2-(naphthalen-2-yl)-1-(quinoxalin-2-yl)ethyl)morpholine



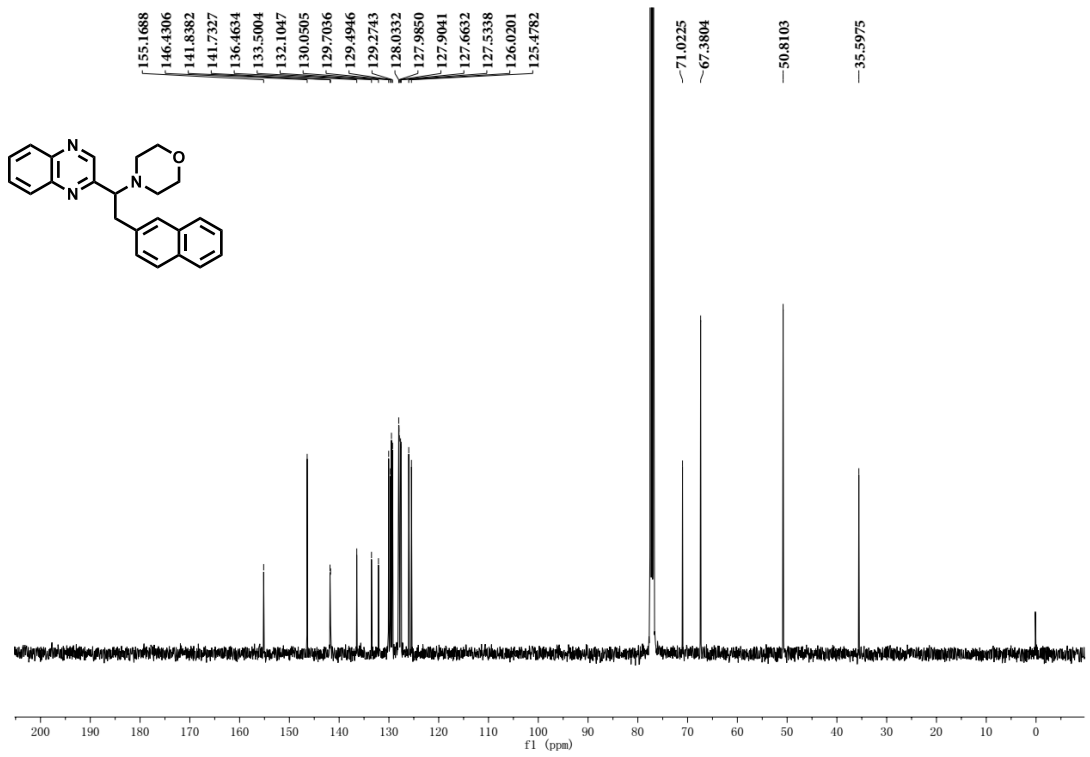
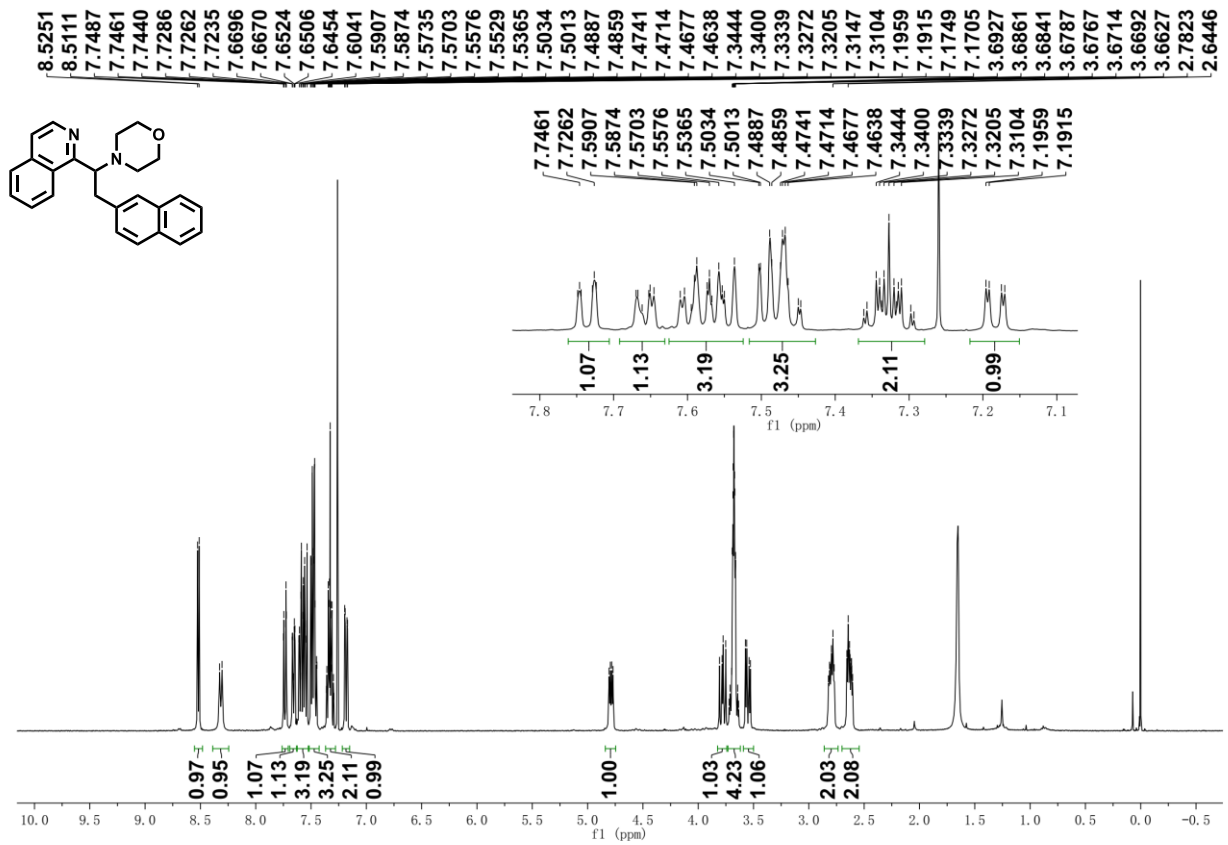


Figure S44. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3na in $CDCl_3$

4-(1-(isoquinolin-1-yl)-2-(naphthalen-2-yl)ethyl)morpholine



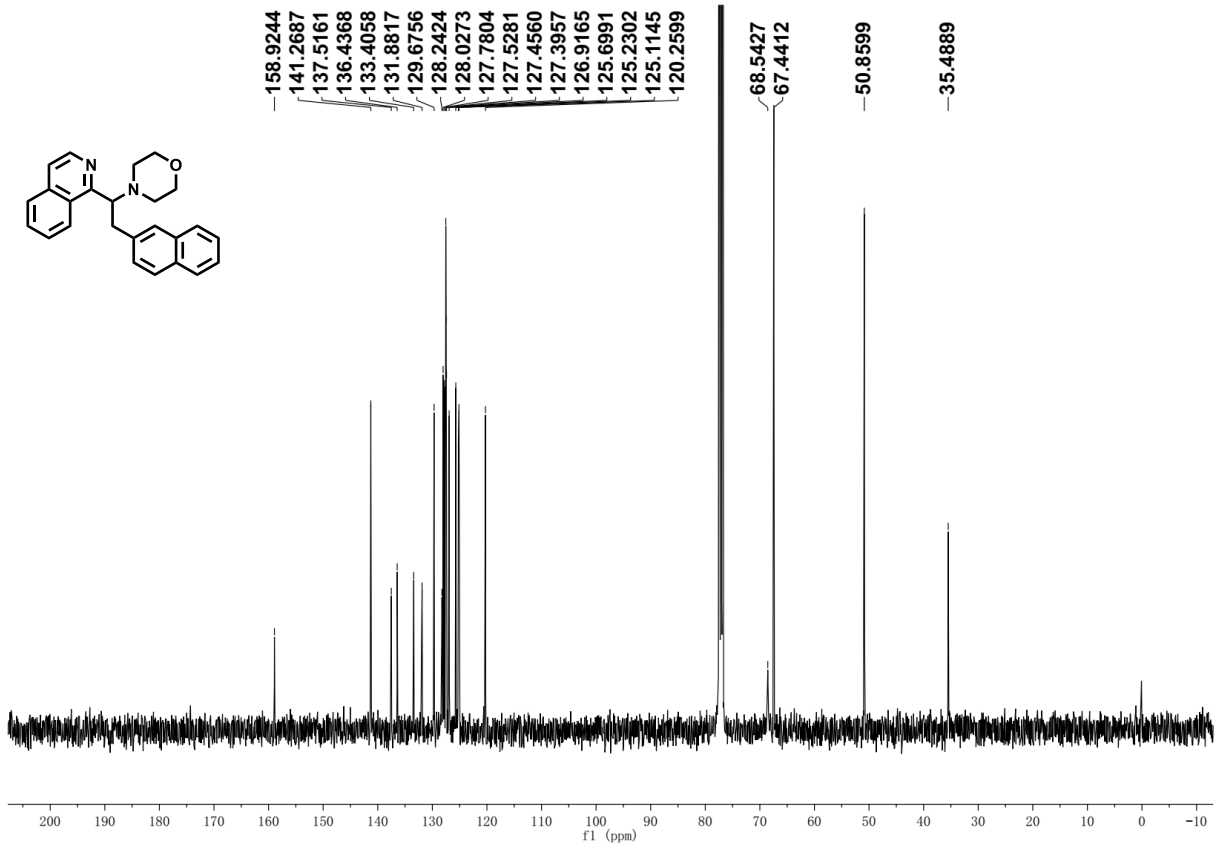
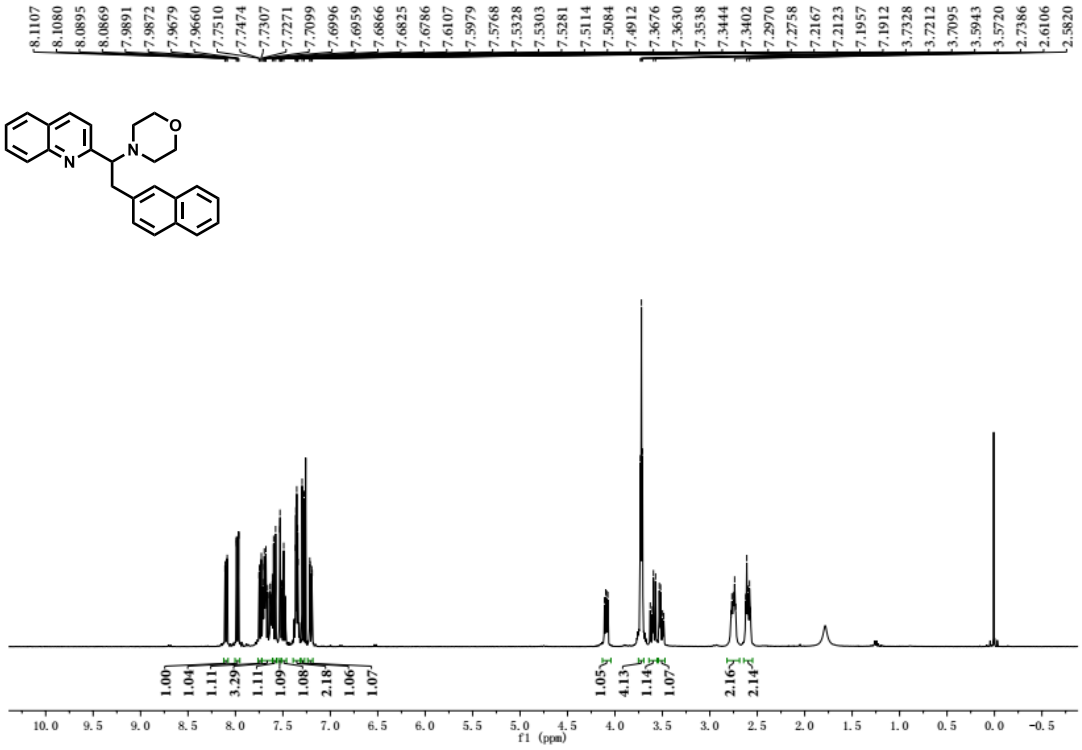


Figure S45. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3oa in $CDCl_3$

4-(2-(naphthalen-2-yl)-1-(quinolin-2-yl)ethyl)morpholine



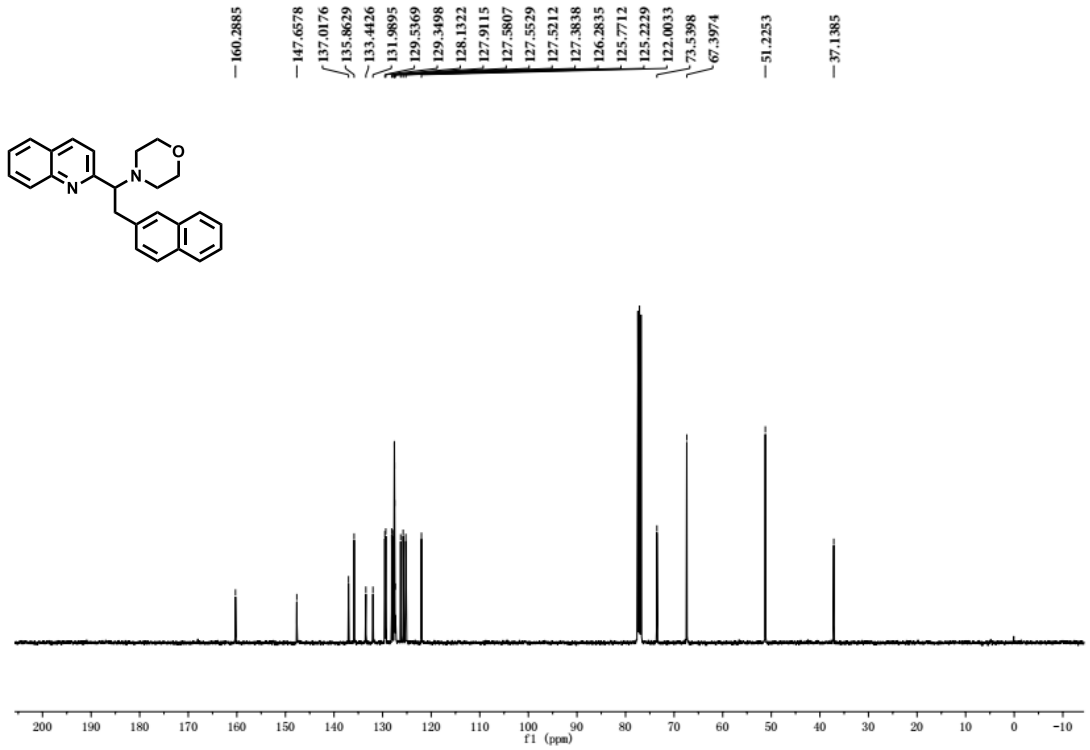
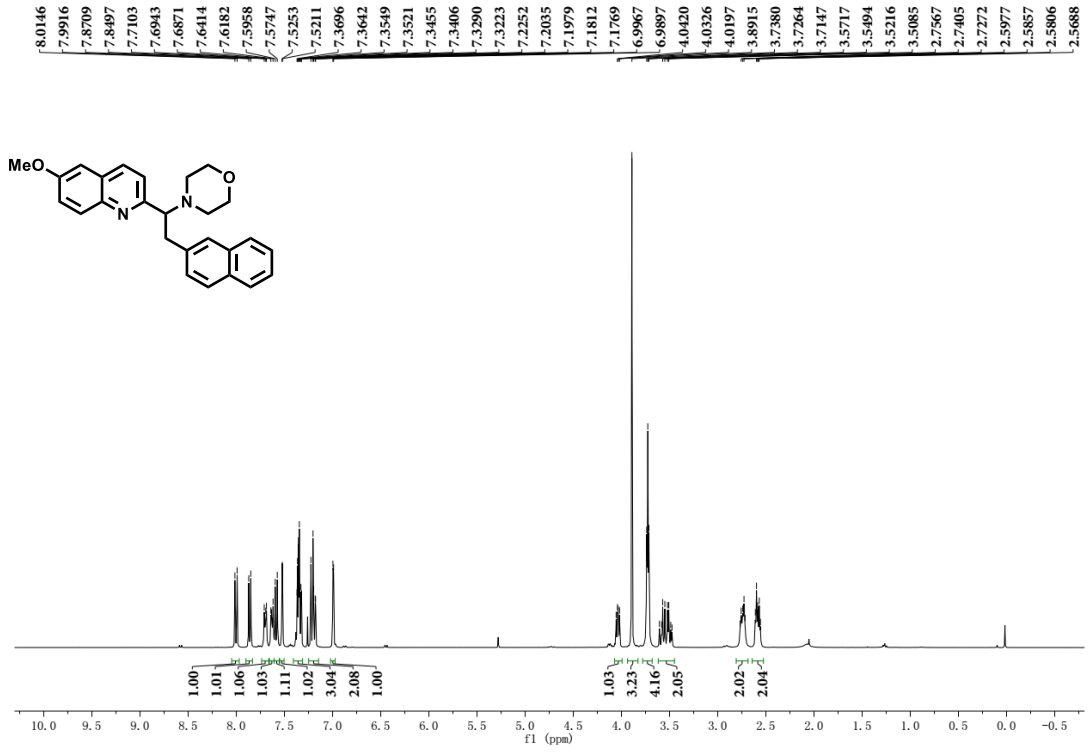


Figure S46. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3pa in $CDCl_3$

4-(1-(6-methoxyquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine



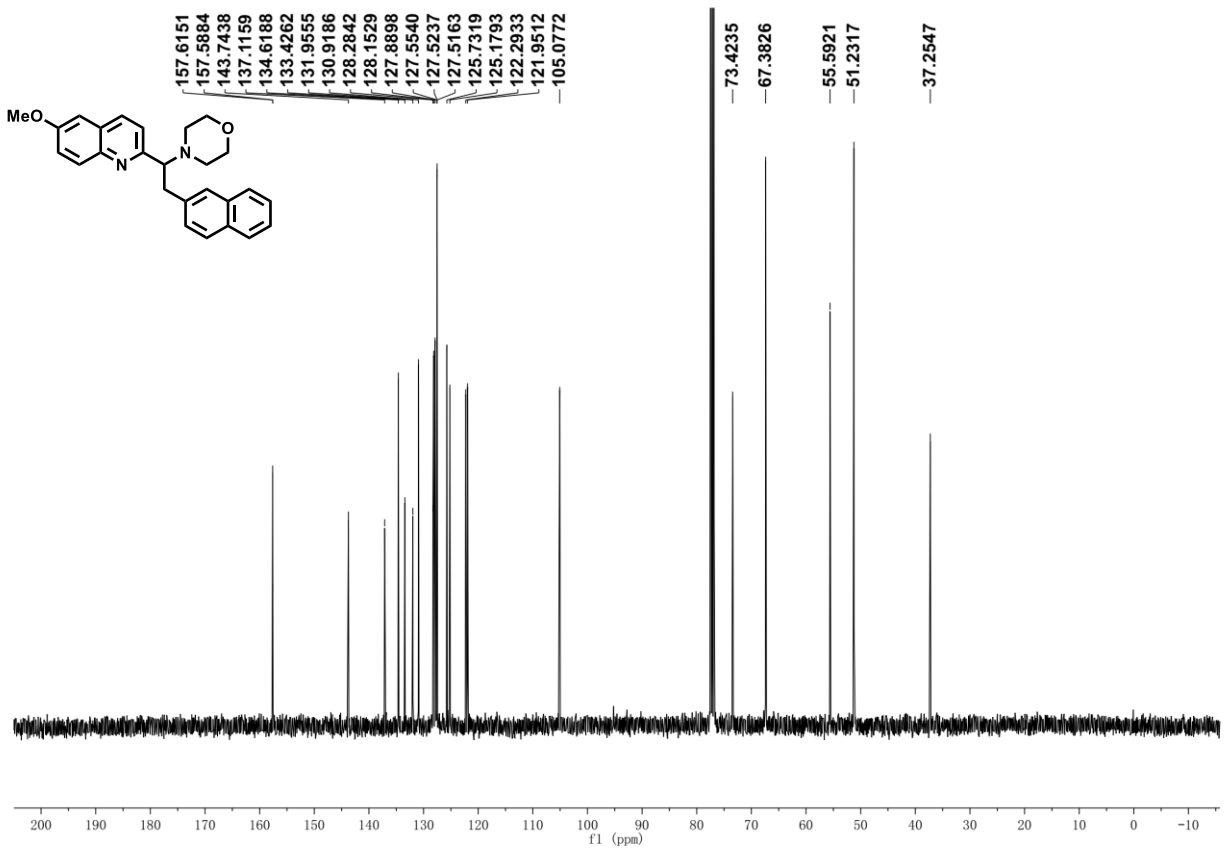
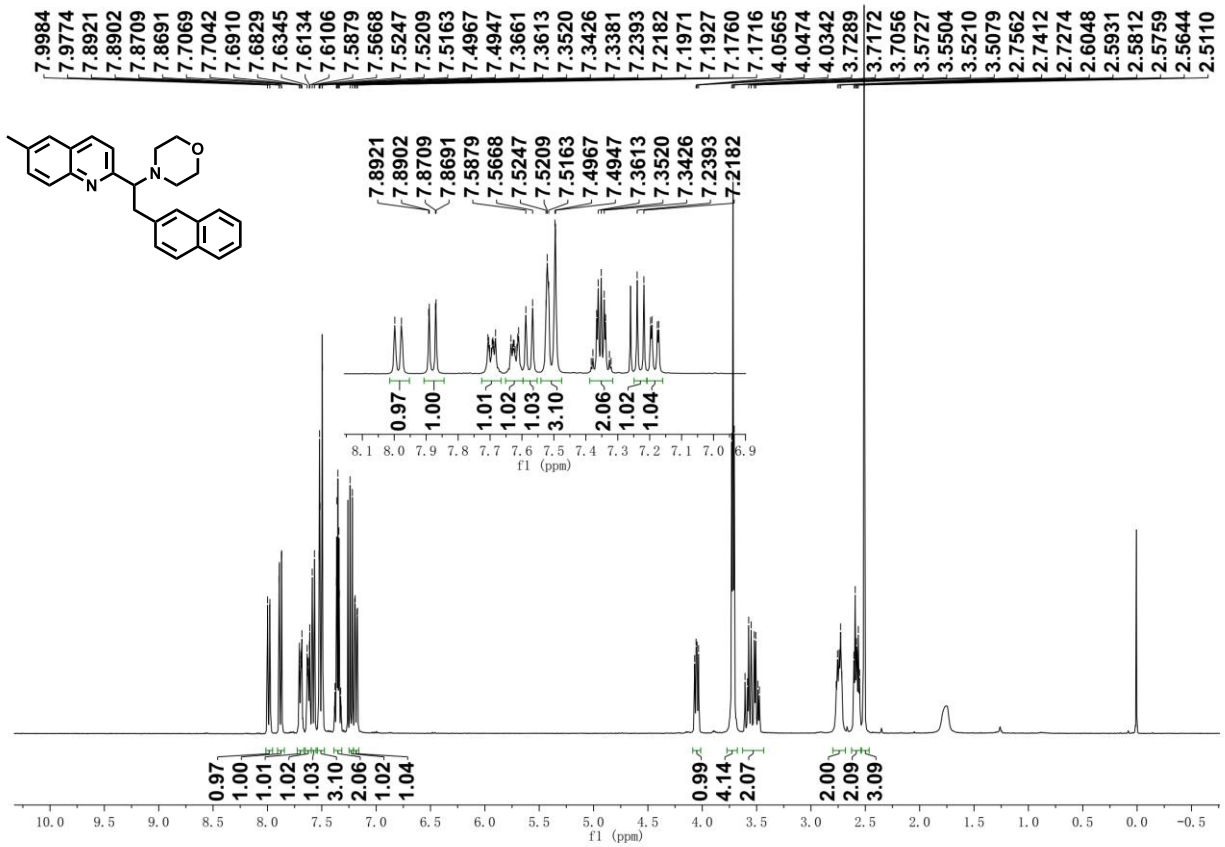


Figure S47. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3qa in $CDCl_3$

4-(1-(6-methylquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine



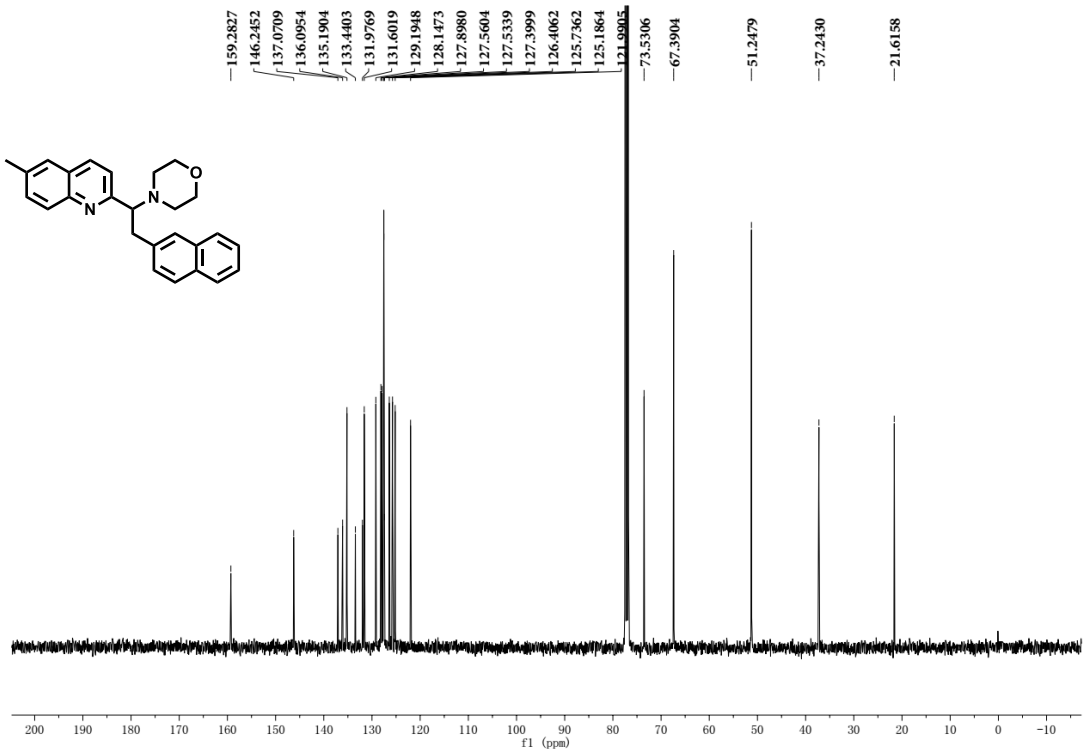
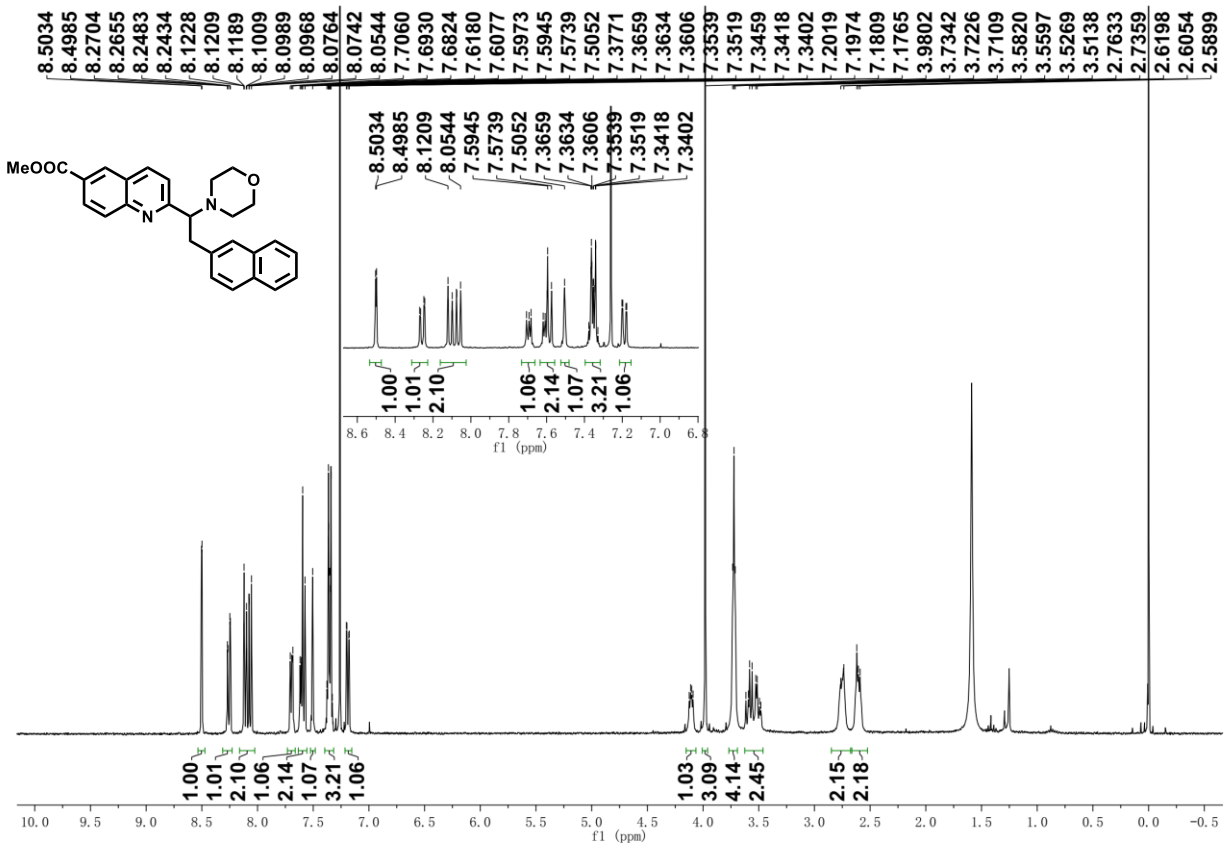


Figure S48. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ra in $CDCl_3$

Methyl 2-(1-morpholino-2-(naphthalen-2-yl)ethyl)quinoline-6-carboxylate



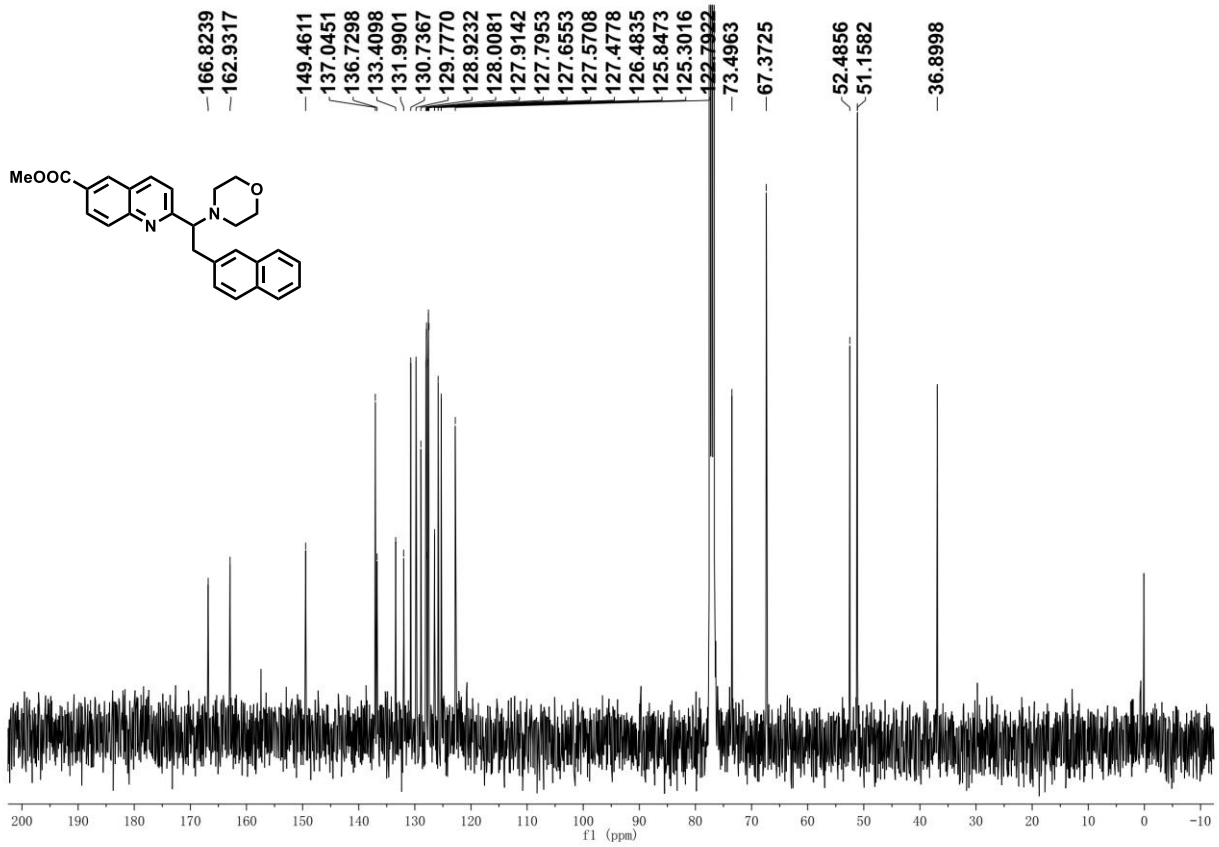
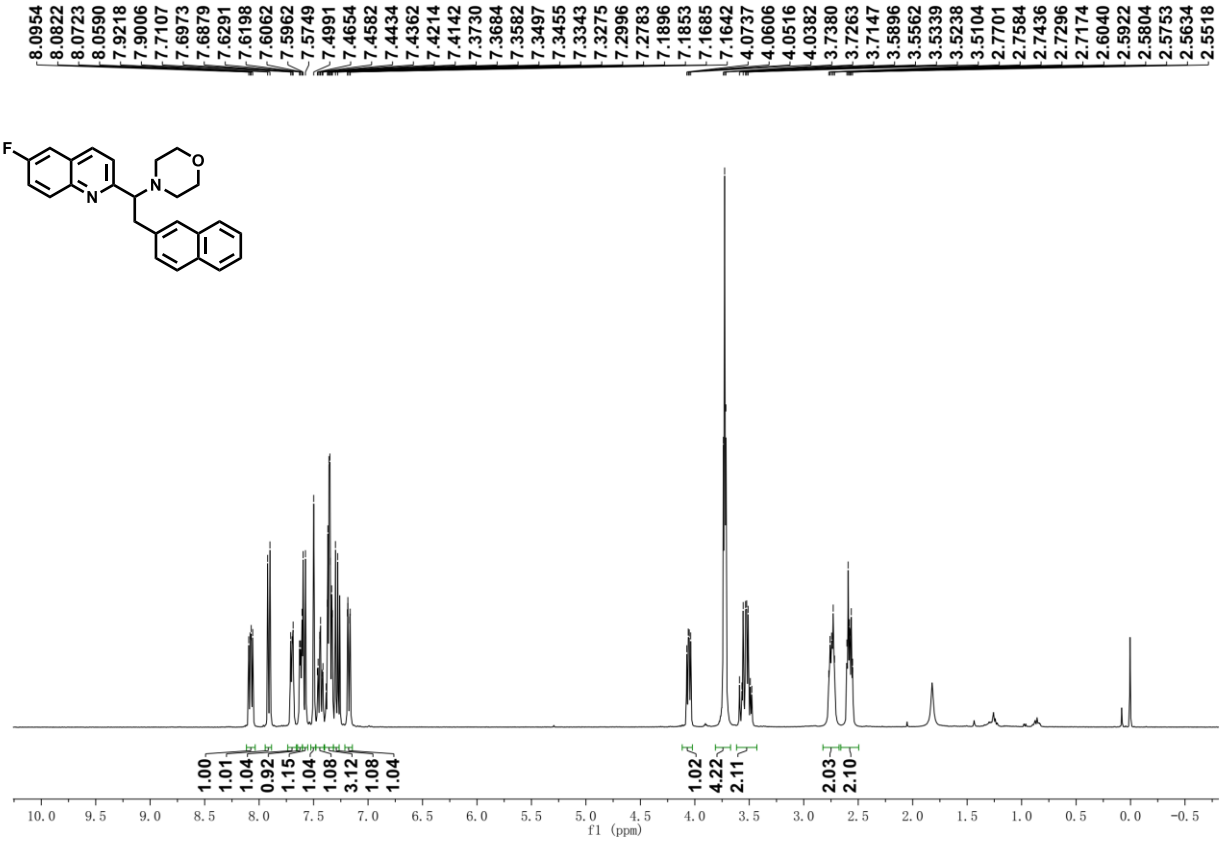


Figure S49. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3sa in $CDCl_3$

4-(1-(6-fluoroquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine



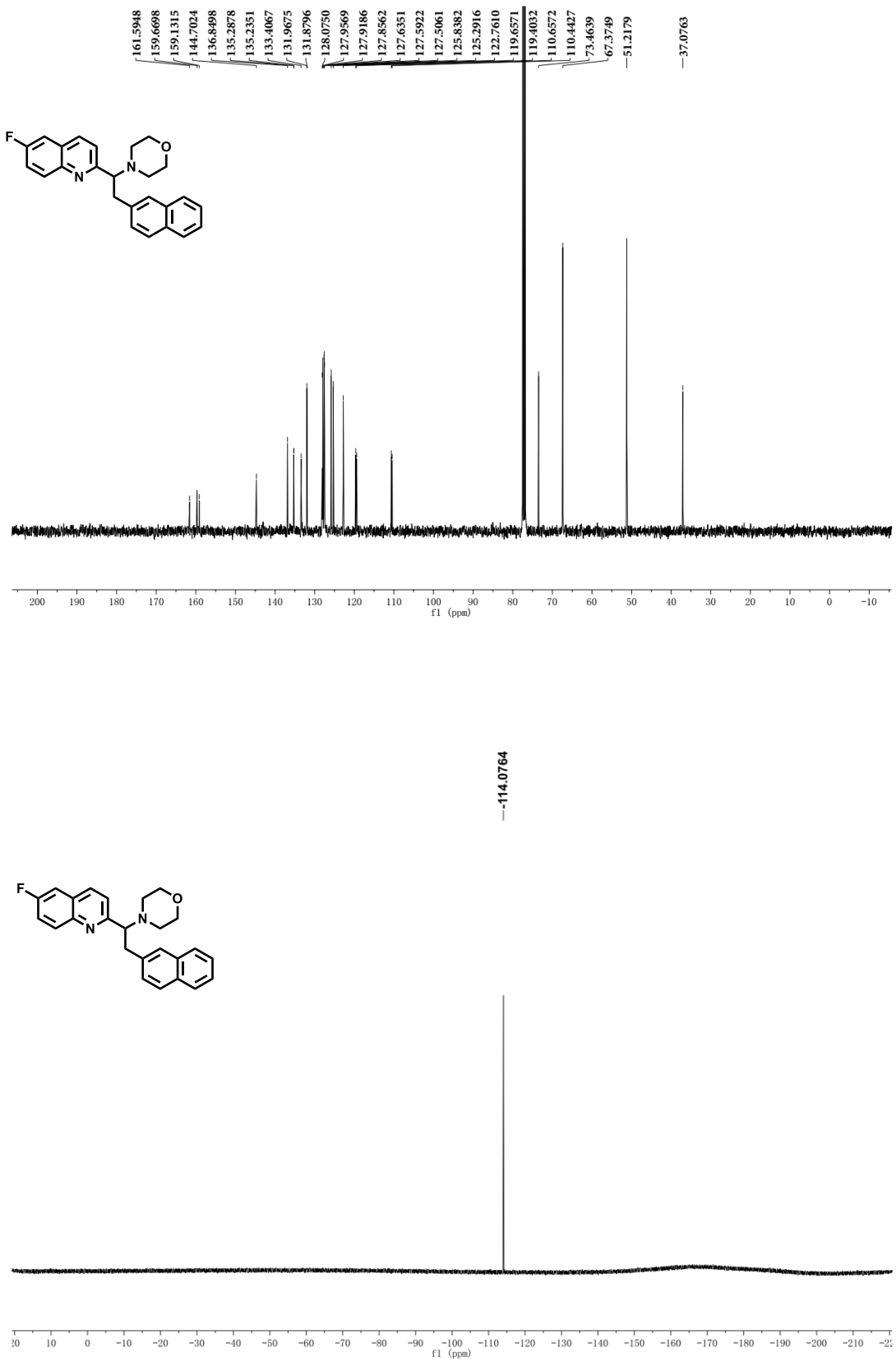


Figure S50. ^{1}H NMR (400 MHZ)，^{13}C {101MHZ} NMR and ^{19}F (376 MHZ) spectra of 3ta in $CDCl_3$

4-(1-(7-chloroquinolin-2-yl)-2-(naphthalen-2-yl)ethyl)morpholine

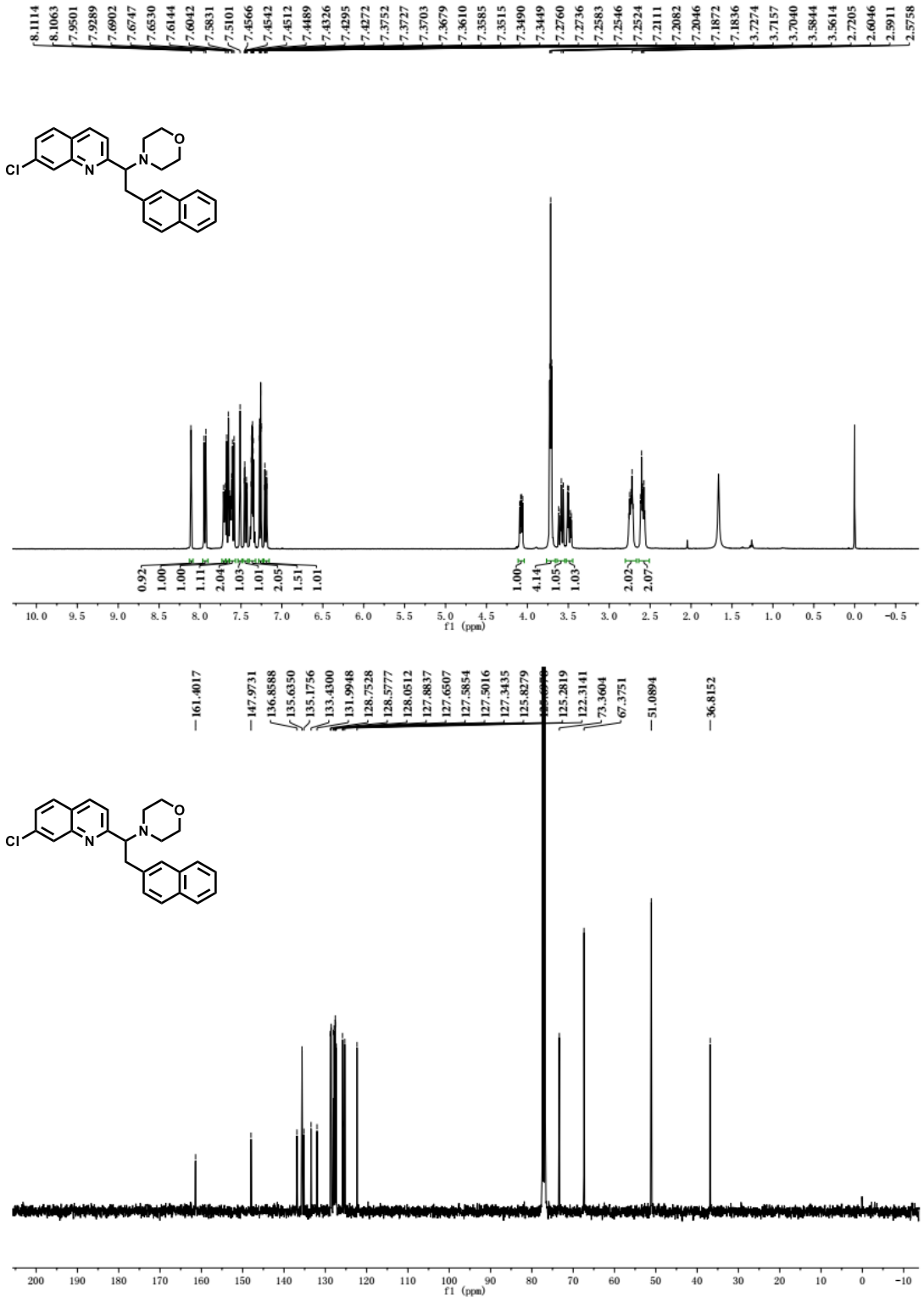


Figure S51. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ua in $CDCl_3$

4-(2-(6-methoxynaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine

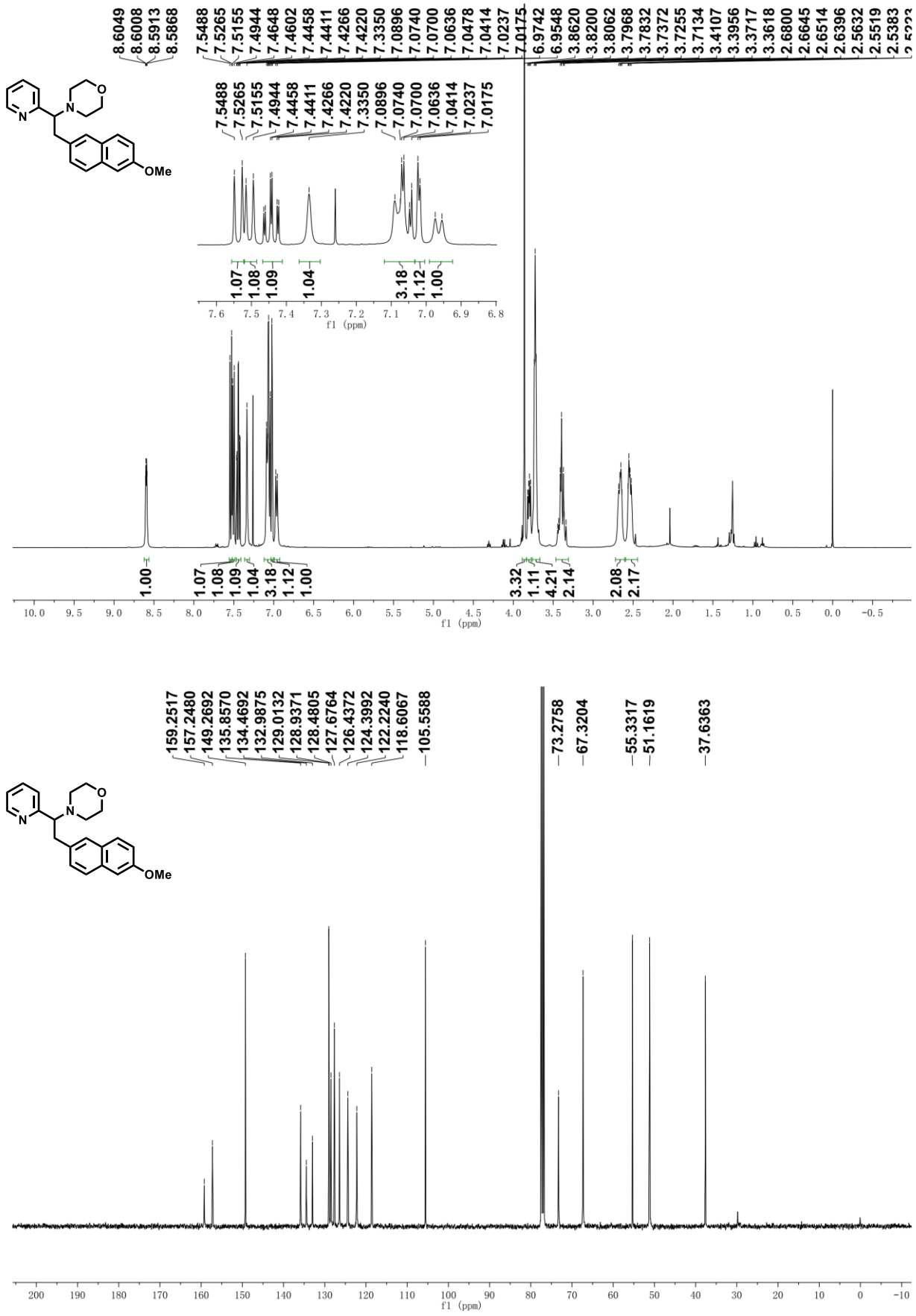


Figure S52. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ab in $CDCl_3$

4-(2-(7-methoxynaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine

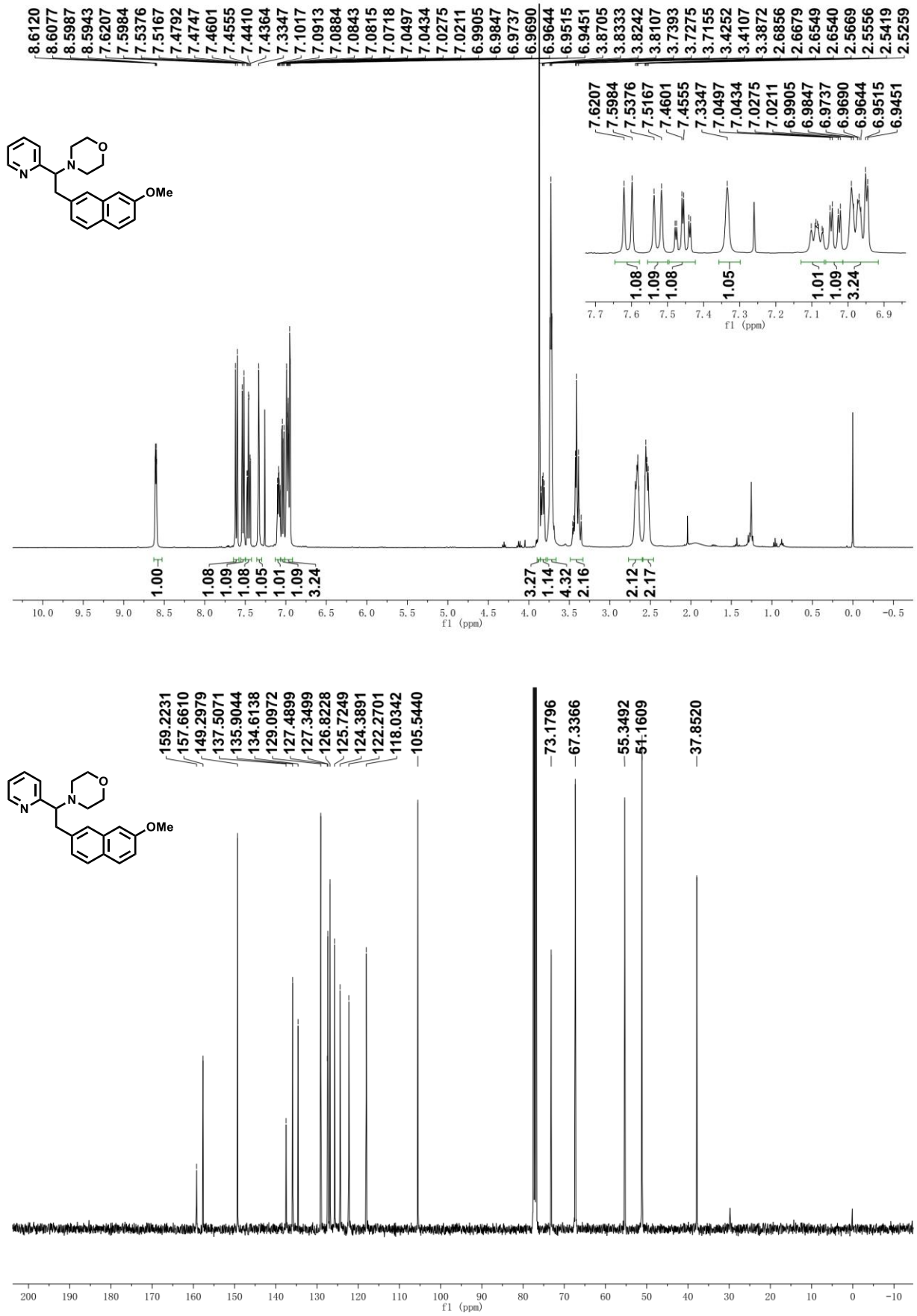


Figure S53. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ac in $CDCl_3$

4-(2-(7-(benzyloxy)naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine

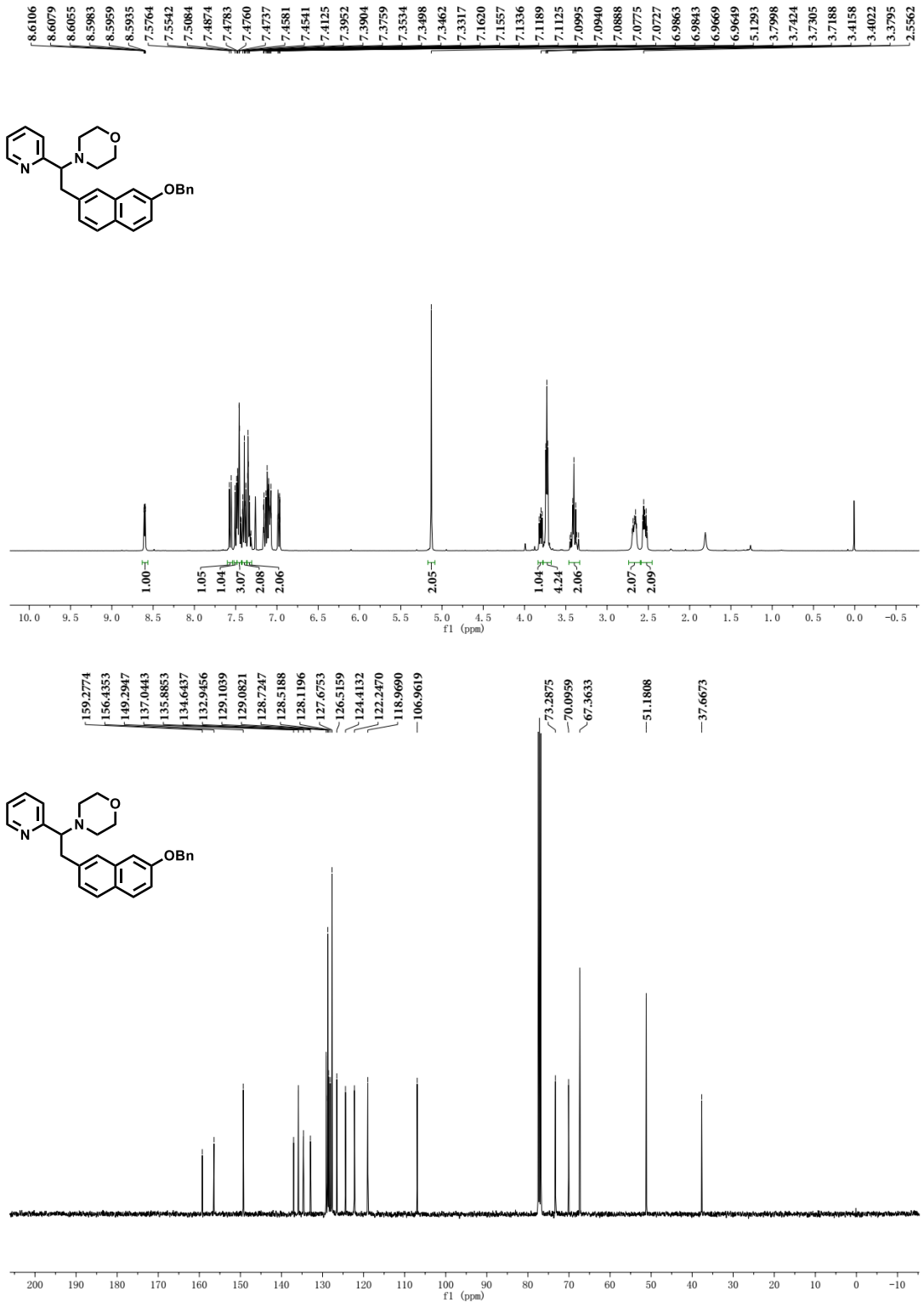


Figure S54. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ad in $CDCl_3$

4-(2-(6-cyclopropylnaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine

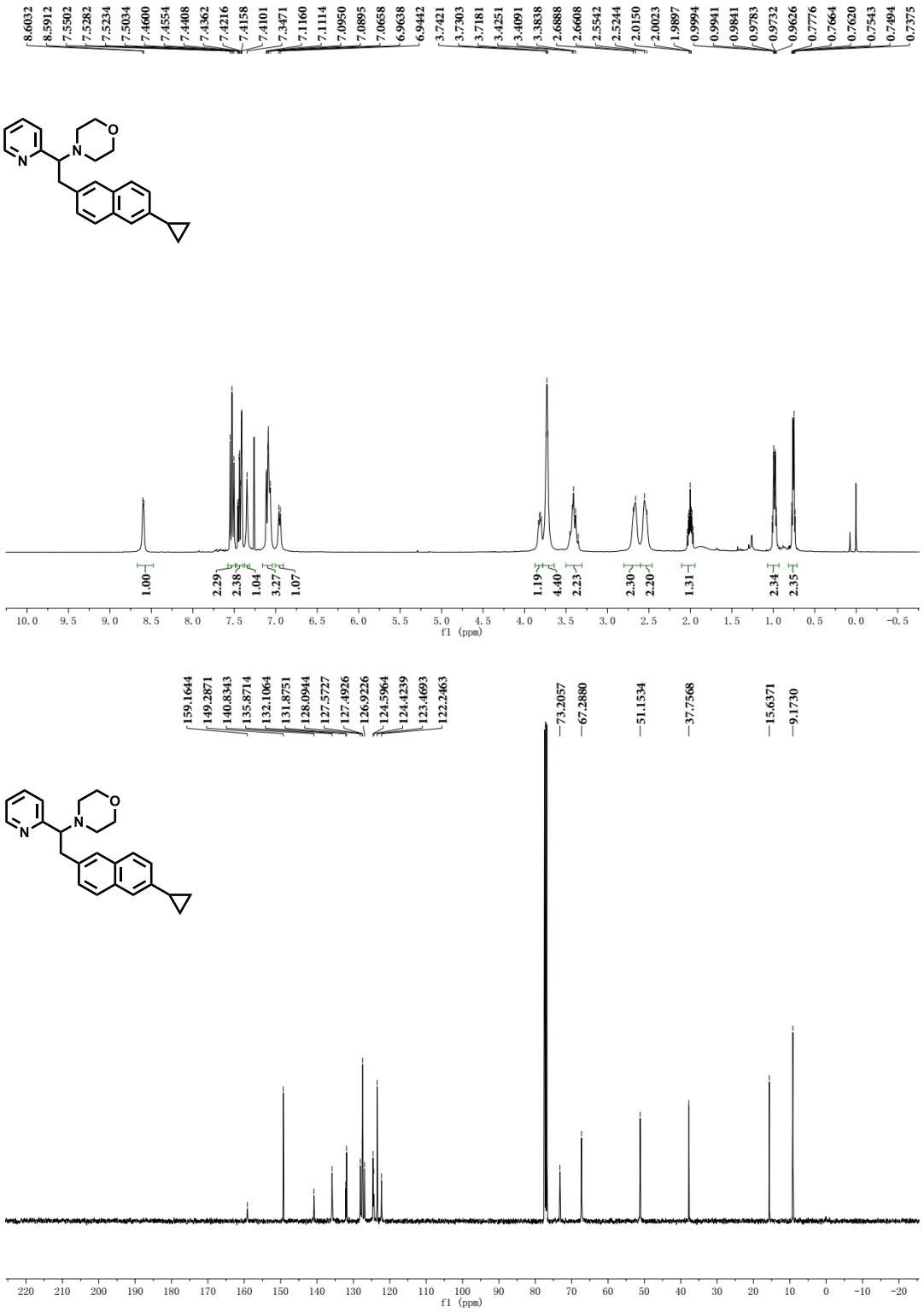


Figure S55. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ae in $CDCl_3$

4-(2-(6-methylnaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine

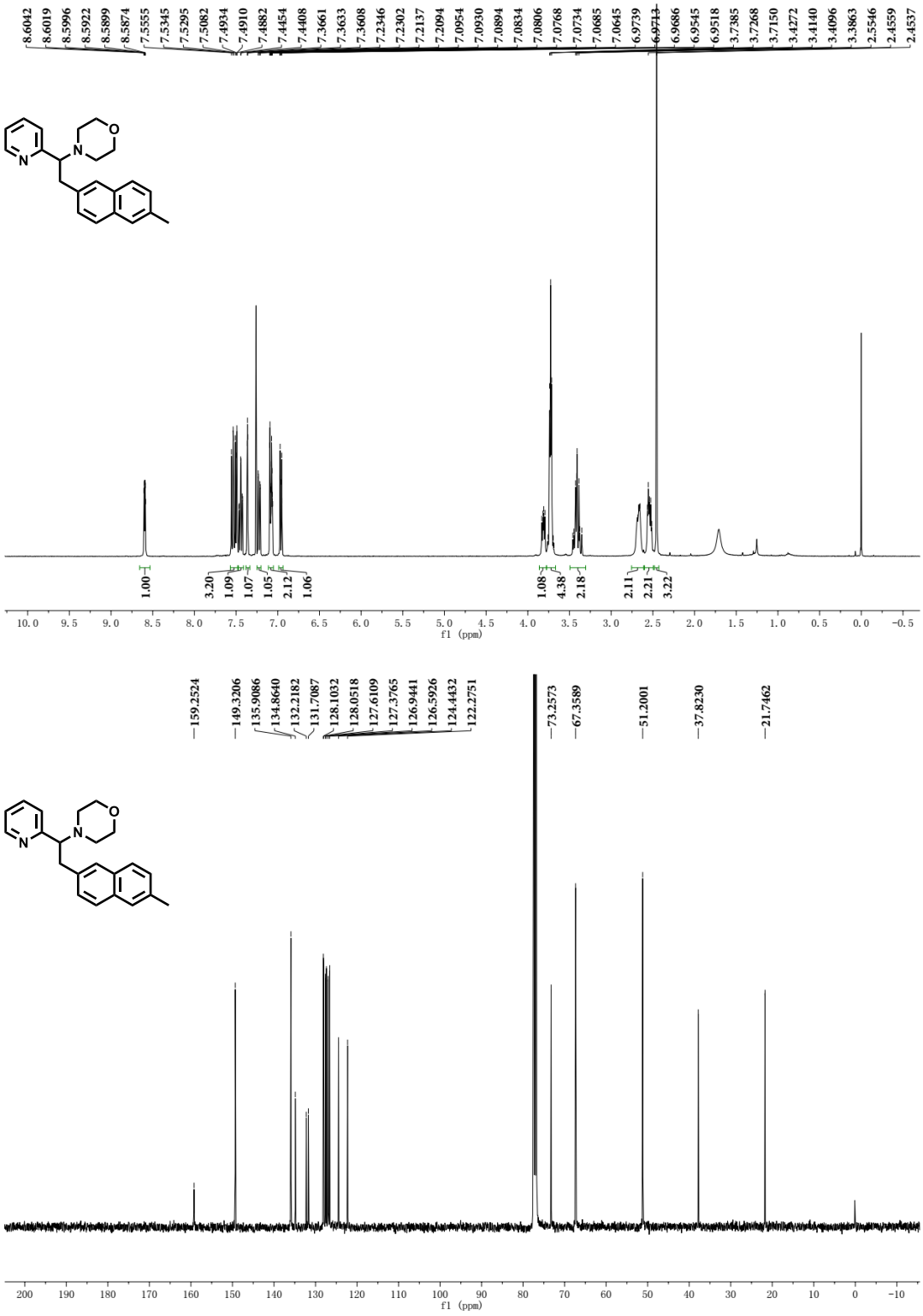


Figure S56. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3af in $CDCl_3$

4-(2-(6-phenylnaphthalen-2-yl)-1-(pyridin-2-yl)ethyl)morpholine

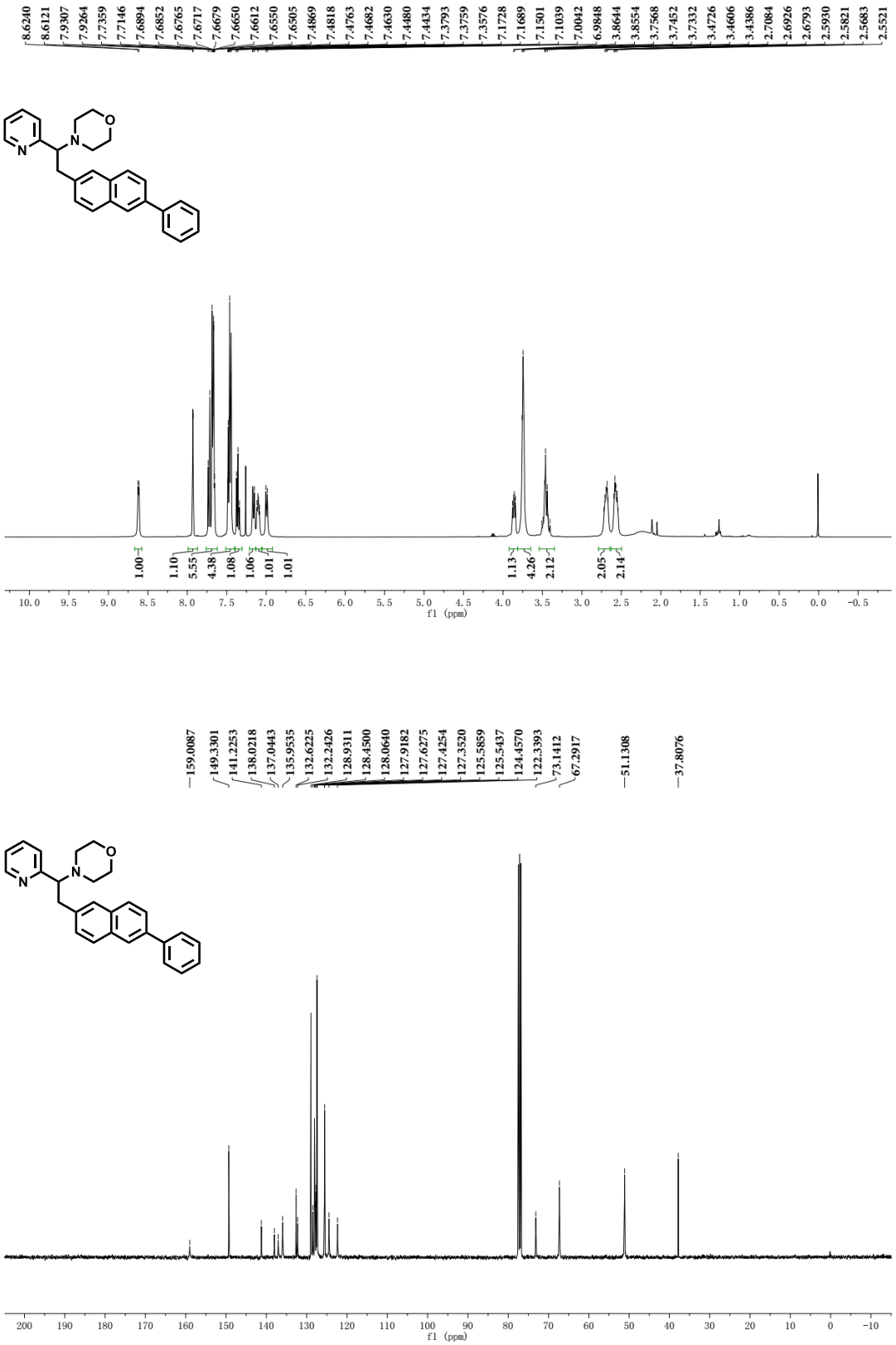


Figure S57. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ag in $CDCl_3$

4-(1-(pyridin-2-yl)-2-(6-(thiophen-2-yl)naphthalen-2-yl)ethyl)morpholine

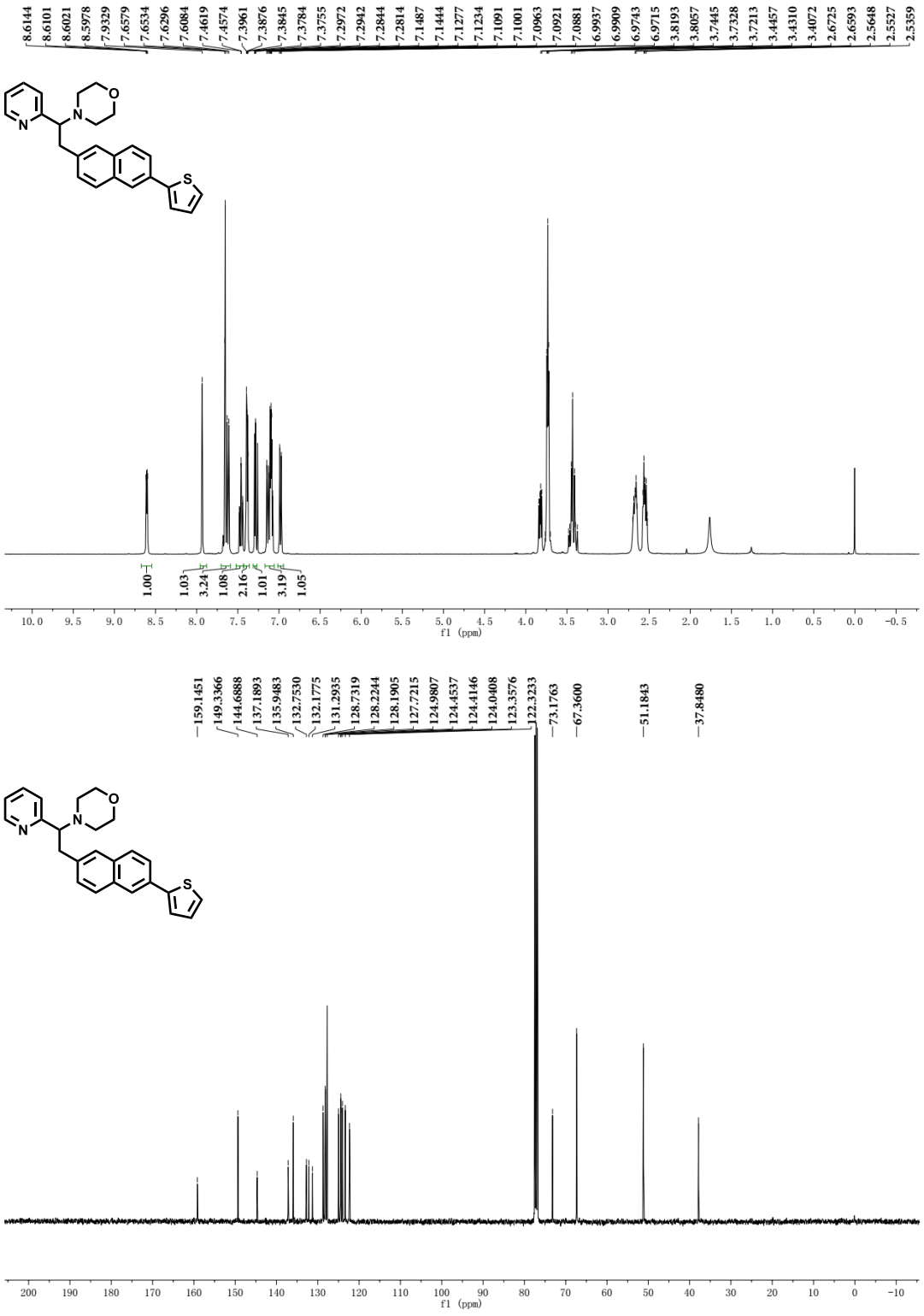


Figure S58. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ah in $CDCl_3$

4-(1-(pyridin-2-yl)-2-(6-(quinolin-8-yl)naphthalen-2-yl)ethyl)morpholine

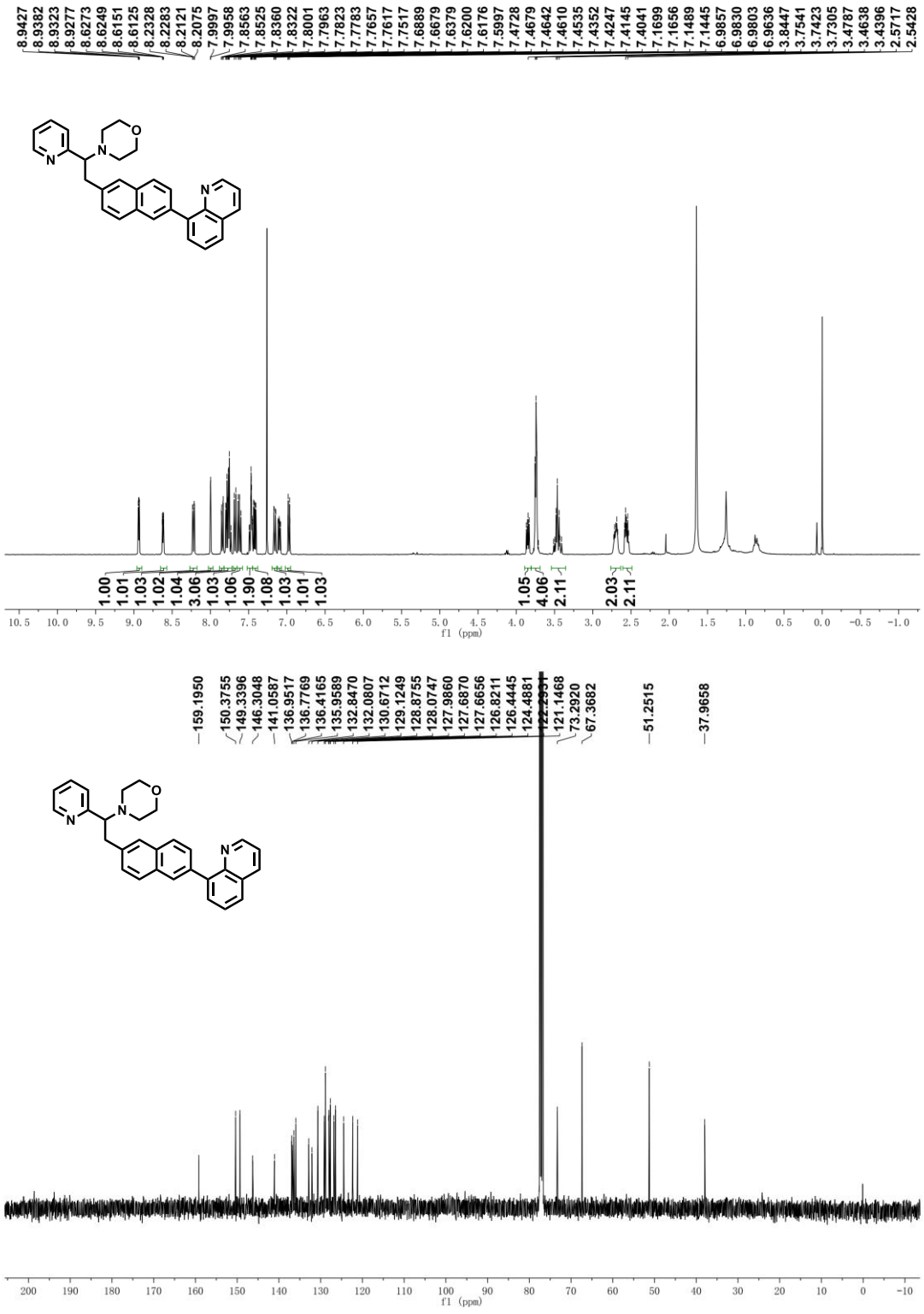
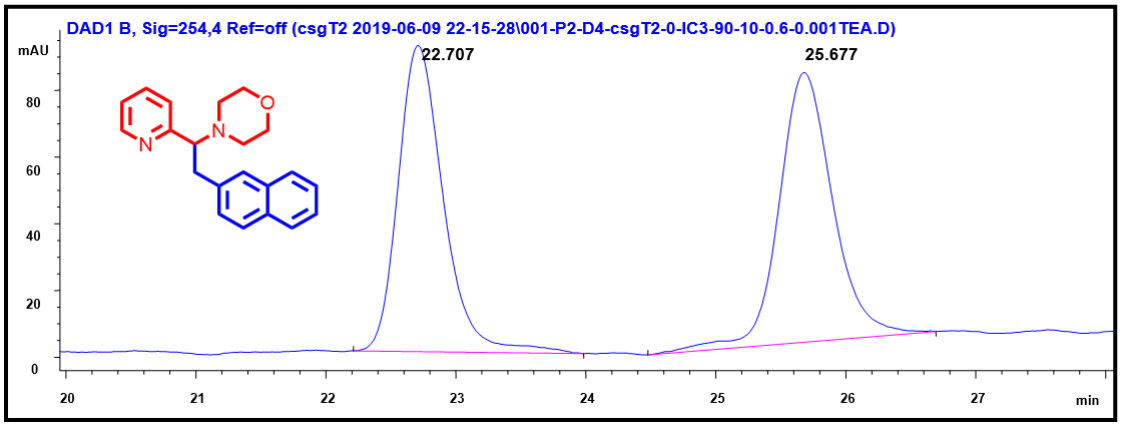


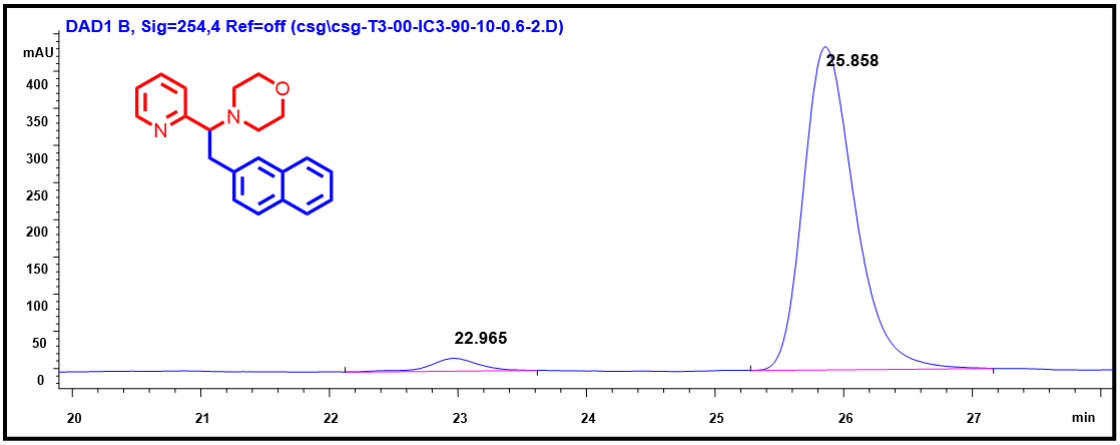
Figure S59. ^{1}H NMR (400 MHZ) and ^{13}C {101MHZ} NMR spectra of 3ai in $CDCl_3$

HPLC Chromatographs



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.707	BB	0.3644	2222.26489	91.79232	48.8207
2	25.677	BB	0.4383	2329.62891	80.81821	51.1793
Totals :				4551.89380	172.61053	



Signal 2: DAD1 B, Sig=254,4 Ref=off

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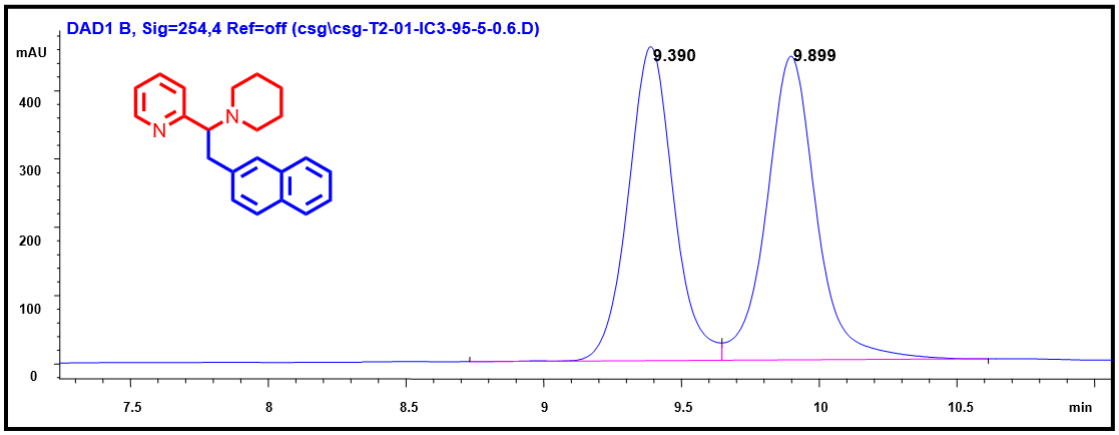
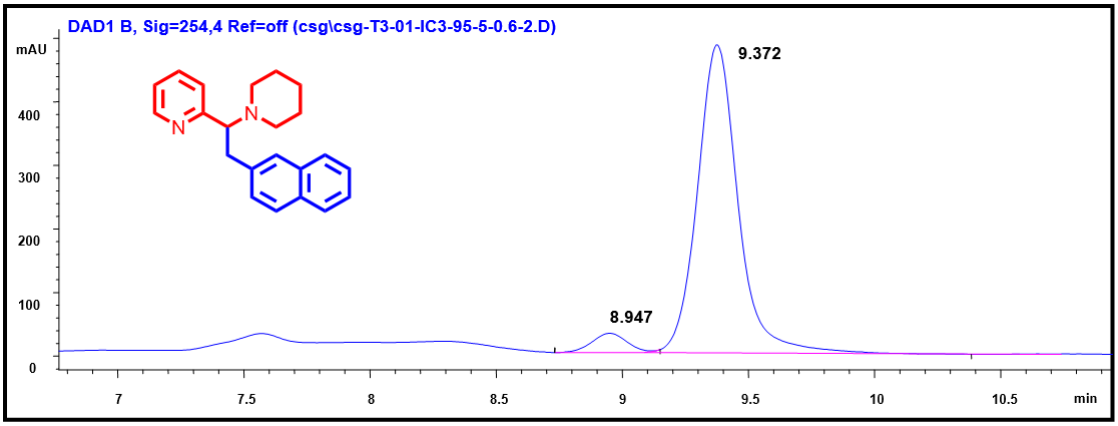
1	22.965	BB	0.3816	456.59448	17.09630	3.6566
2	25.858	BB	0.4230	1.20304e4	434.53262	96.3434
Totals :				1.24870e4	451.62892	



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.390	VV R	0.1737	5272.80518	460.16934	48.5299
2	9.899	VB	0.1886	5592.25537	445.09064	51.4701
Totals :				1.08651e4	905.25998	



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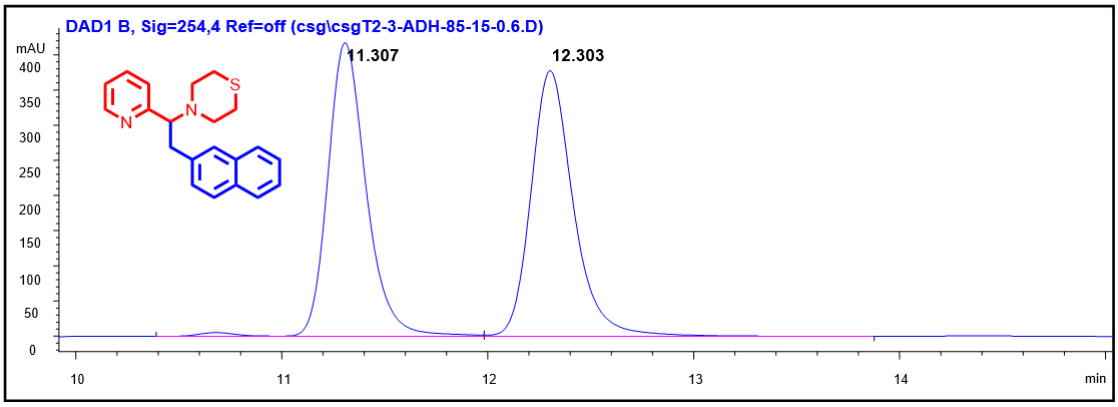
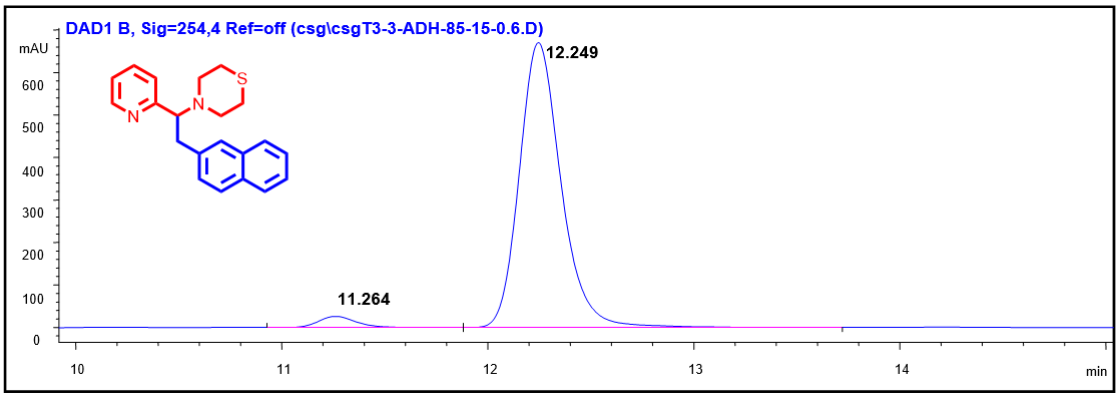
1	8.947	BV E	0.1489	295.47867	30.53528	5.1229
2	9.372	VB R	0.1716	5472.26660	485.31360	94.8771
Totals :				5767.74527	515.84888	



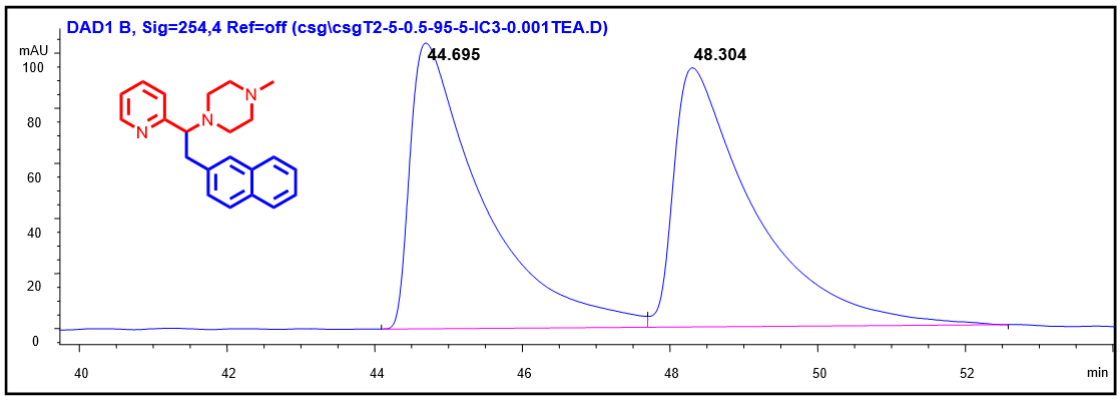
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.307	VV R	0.1964	5456.37598	417.80701	50.1582
2	12.303	VB	0.2193	5421.96484	378.11215	49.8418
Totals :				1.08783e4	795.91916	



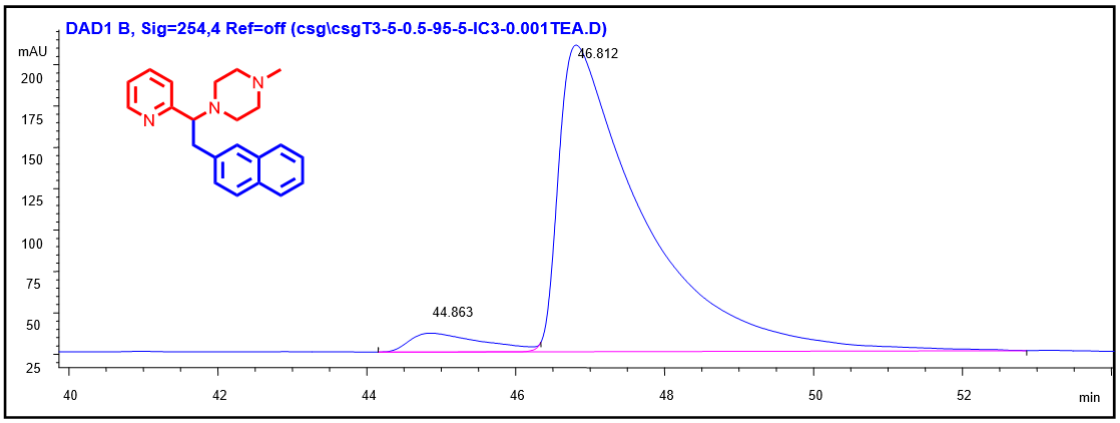
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.264	BB	0.1944	337.27435	26.50817	3.4448
2	12.249	BB	0.2144	9453.56641	670.67737	96.5552
Totals :				9790.84076	697.18554	



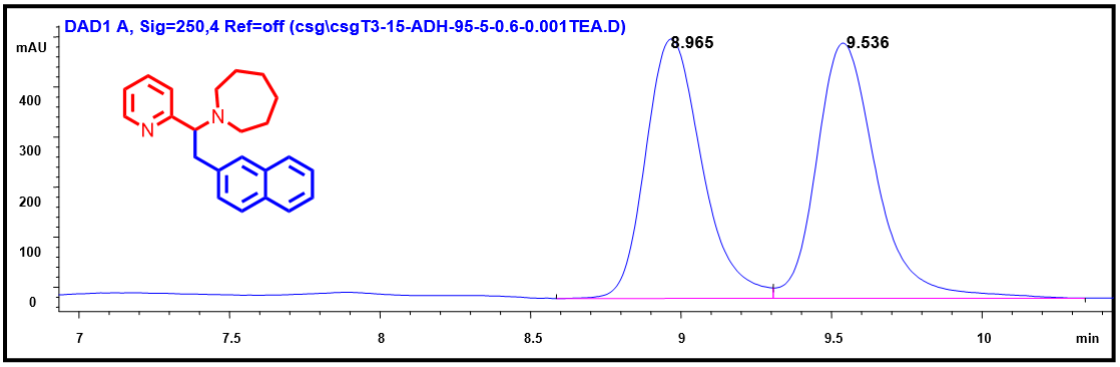
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	44.695	BV	0.9436	7091.25488	103.72829	49.9421
2	48.304	VB	1.0417	7107.69922	94.05173	50.0579
Totals :				1.41990e4	197.78003	



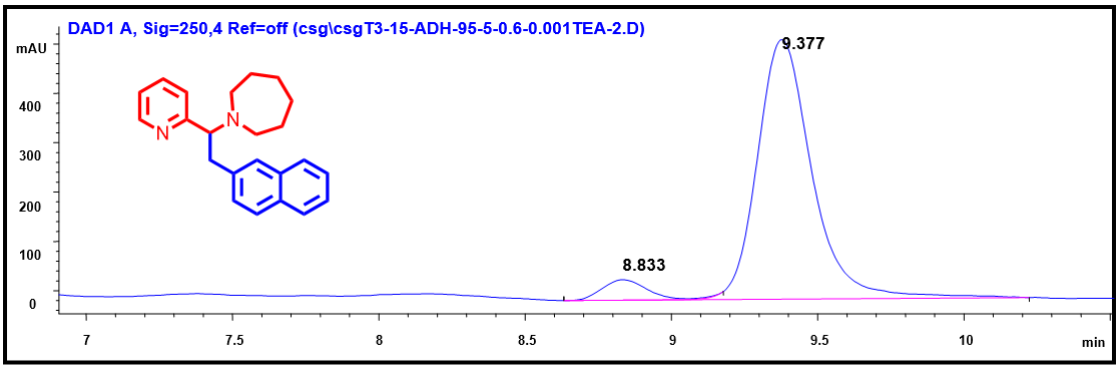
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	44.863	BV E	0.9212	778.51575	11.42139	5.0440
2	46.812	VB R	1.0967	1.46559e4	185.30499	94.9560
Totals :				1.54344e4	196.72639	



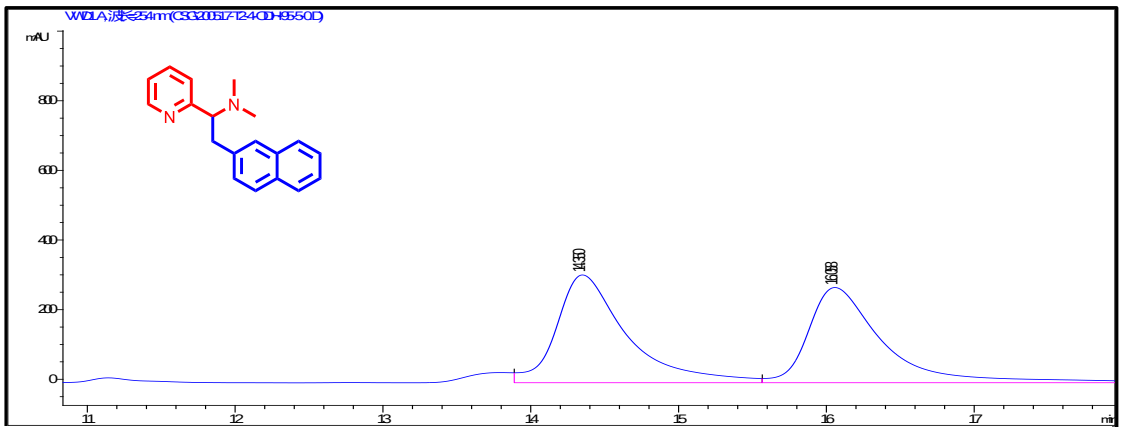
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.965	BV	0.1909	8161.20557	657.28522	48.8478
2	9.536	VB	0.1986	8546.19531	653.17767	51.1522
Totals :				1.67074e4	1310.46289	



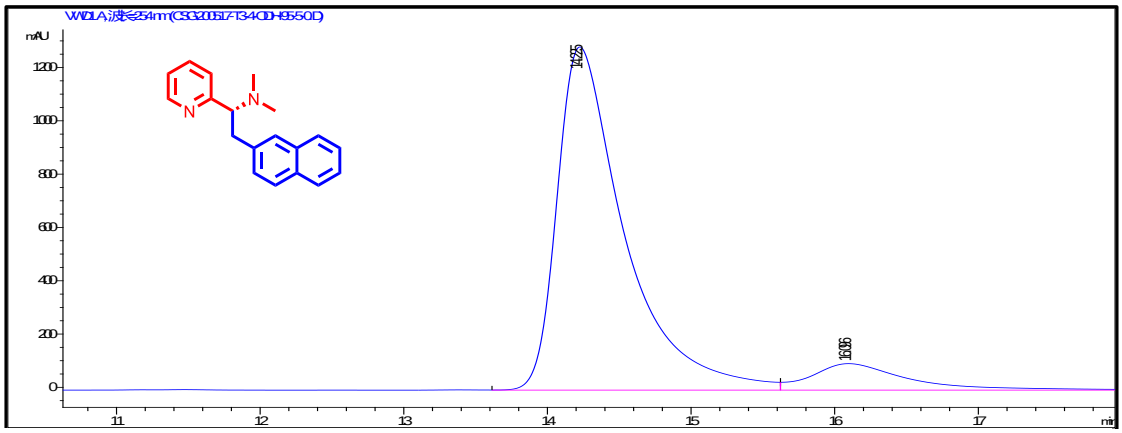
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.835	BV E	0.1866	617.00745	50.49635	7.1080
2	9.377	VV R	0.2026	8063.43750	587.21808	92.8920
Totals :				8680.44495	637.71442	



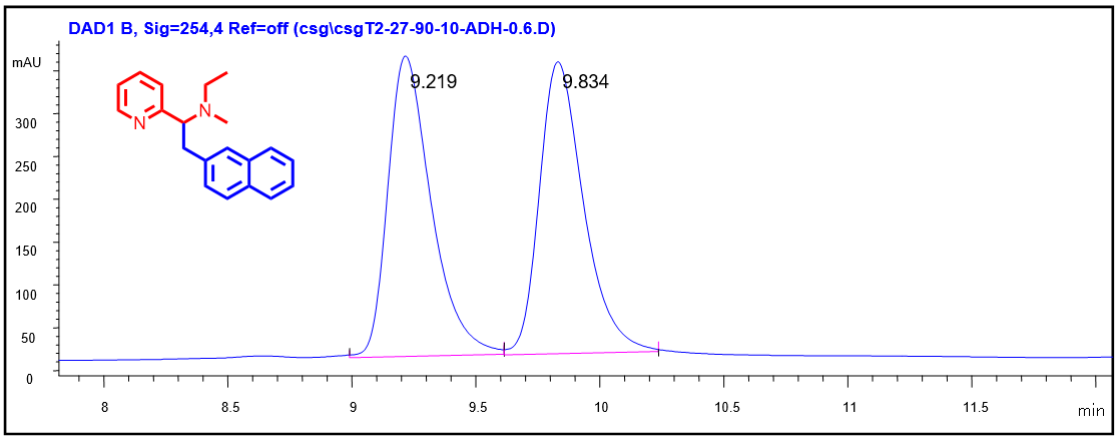
Signal 1: VWD1 A, Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.350	VV	0.4824	1.02979e4	309.82718	51.4447
2	16.058	VBA	0.5206	9719.52539	273.71848	48.5553
Totals :				2.00174e4	583.54565	



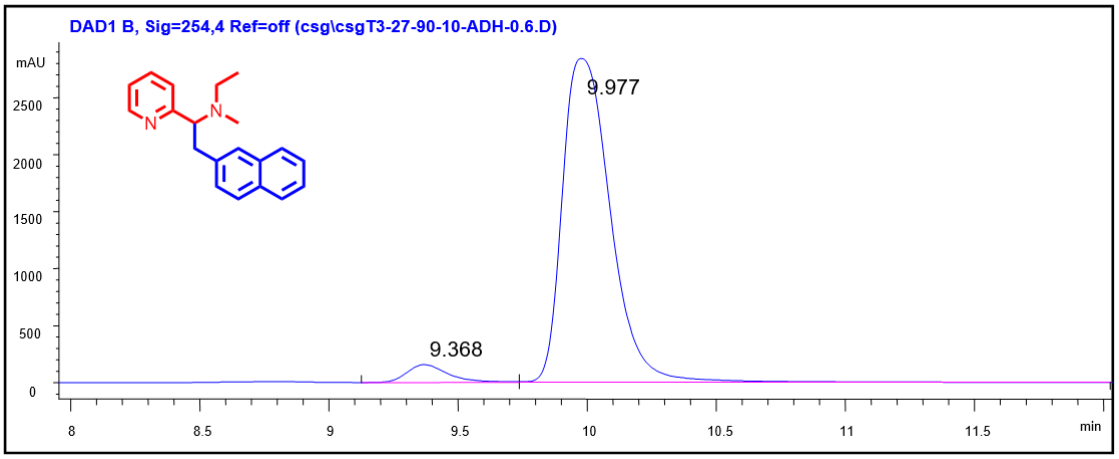
Signal 1: VWD1 A, Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.225	VV	0.4777	4.19568e4	1287.60376	89.9930
2	16.096	VBA	0.6694	4665.48584	99.48910	10.0070
Totals :				4.66223e4	1387.0926	



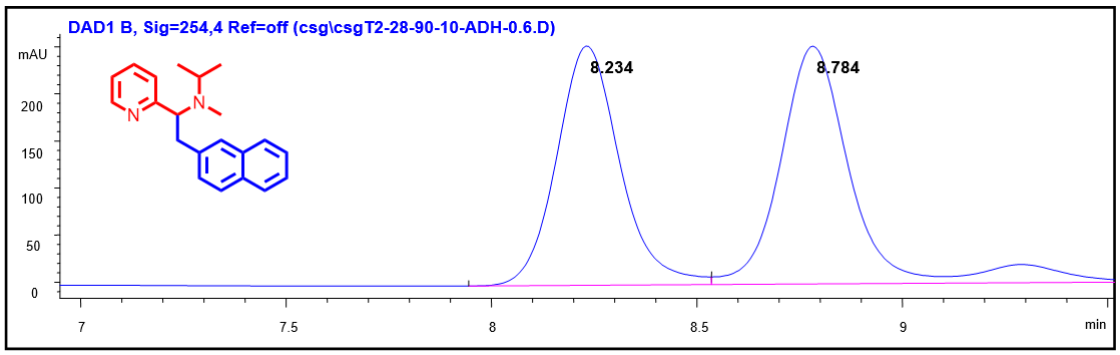
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.219	MM	0.2091	4469.98242	356.27789	49.4927
2	9.834	MM	0.2175	4561.61865	349.59341	50.5073
Totals :				9031.60107	705.87131	



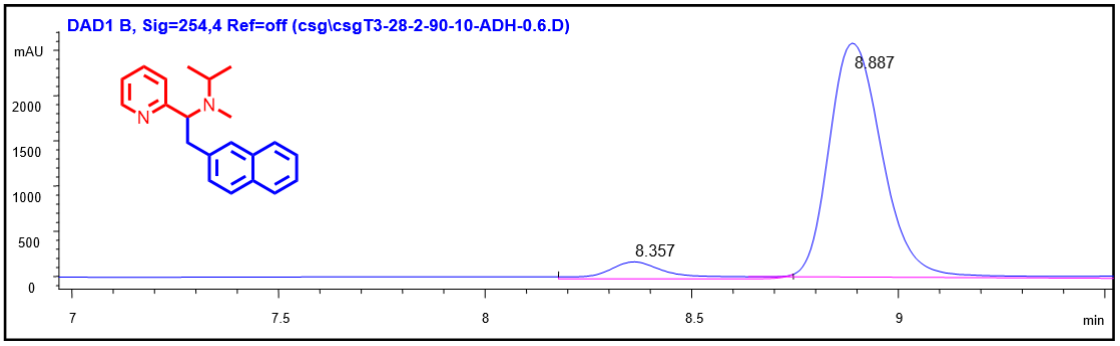
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.368	VV	0.1702	1775.05371	156.65146	4.5815
2	9.977	VB	0.2017	3.69691e4	2842.81763	95.4185
Totals :				3.87442e4	2999.46909	



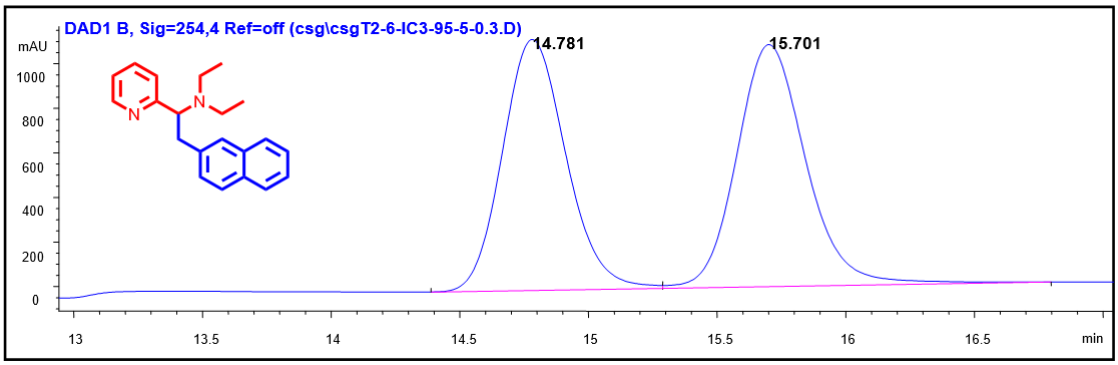
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.234	BV	0.1629	2722.55640	254.37776	46.4907
2	8.784	VV R	0.1705	3133.57446	252.62442	53.5093
Totals :				5856.13086	507.00218	



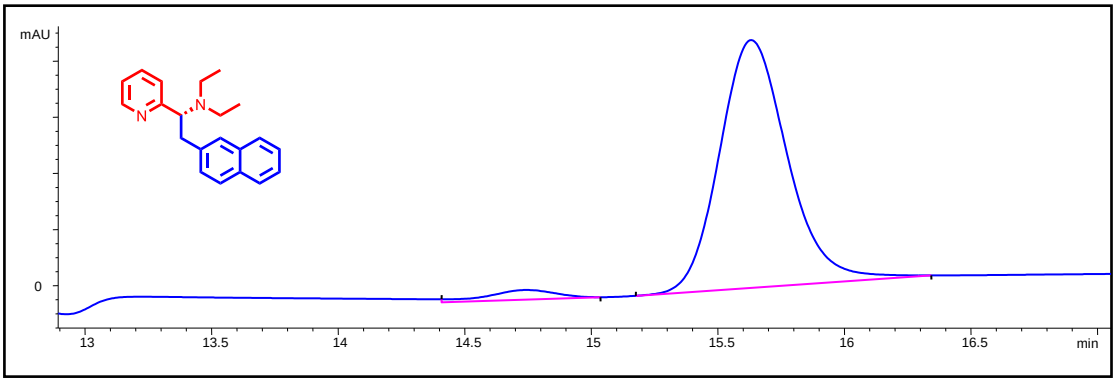
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.357	VV E	0.1540	2043.49072	189.28642	6.7397
2	8.887	VV R	0.1402	2.82767e4	2604.13843	93.2603
Totals :				3.03202e4	2793.42485	



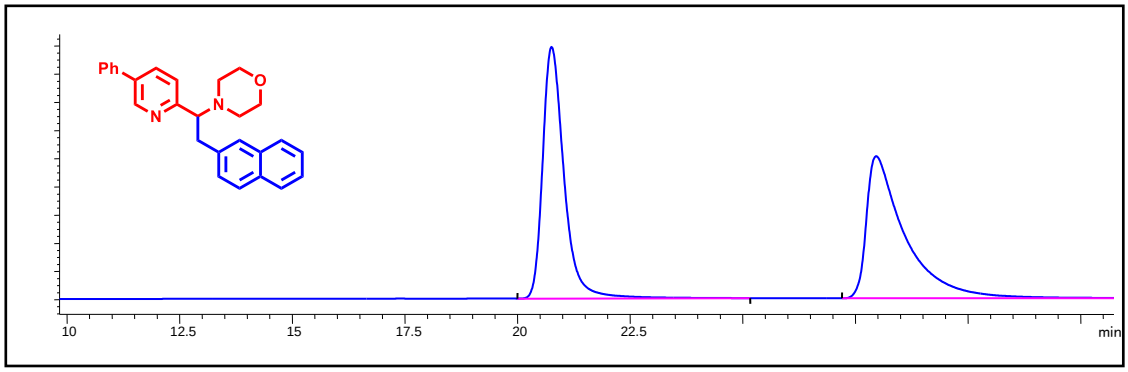
Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.781	BV	0.2643	1.91494e4	1126.69275	48.2856
2	15.701	VB	0.2884	2.05091e4	1095.46863	51.7144
Totals :				3.96585e4	2222.16138	



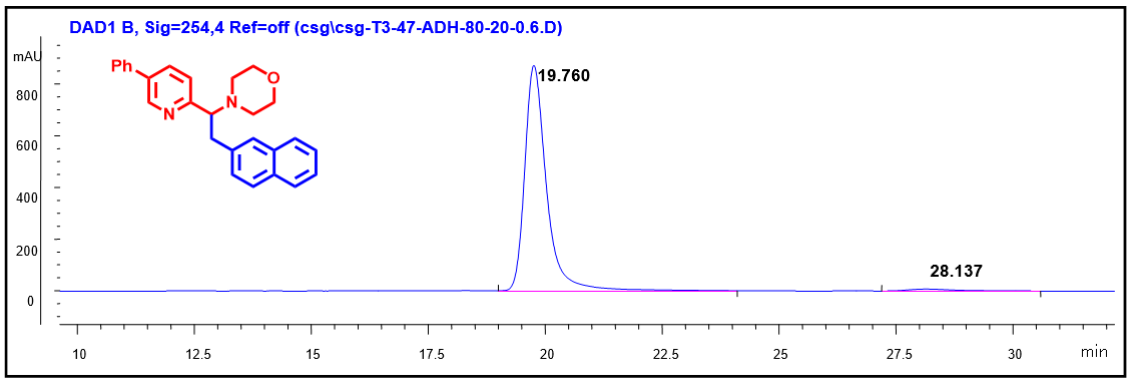
Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.747	VB	0.2861	644.66003	34.17359	3.7600
2	15.635	BB	0.2901	1.65004e4	882.66565	96.2400
Totals :				1.71450e4	916.83924	



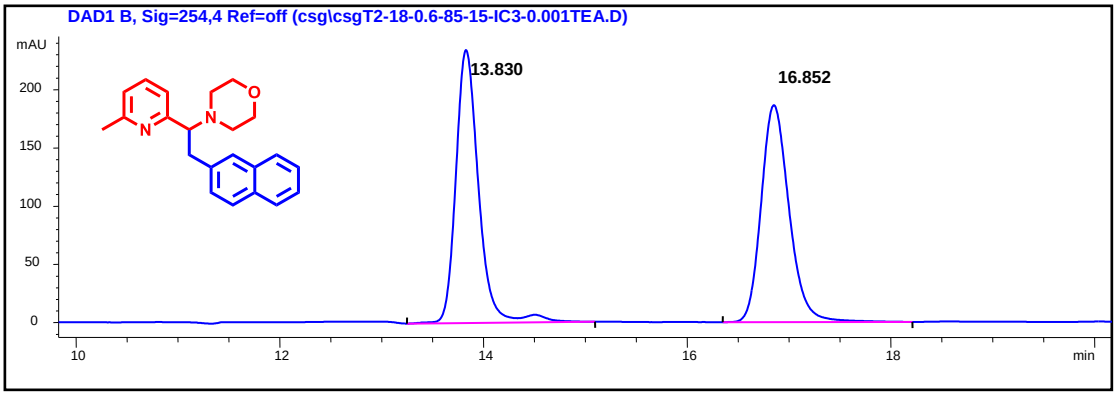
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.753	BB	0.5050	5.92102e4	1784.92493	49.6090
2	27.958	BB	0.8420	6.01437e4	1008.12006	50.3910
Totals :				1.19354e5	2793.04498	



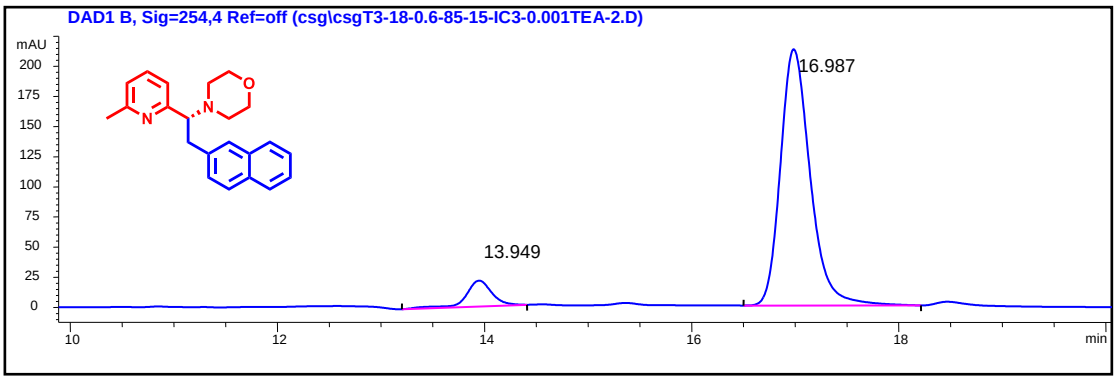
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.760	BB	0.4878	2.82313e4	871.80444	98.2633
2	28.137	BB	0.8280	498.94910	7.34956	1.7367
Totals :				2.87303e4	879.15400	



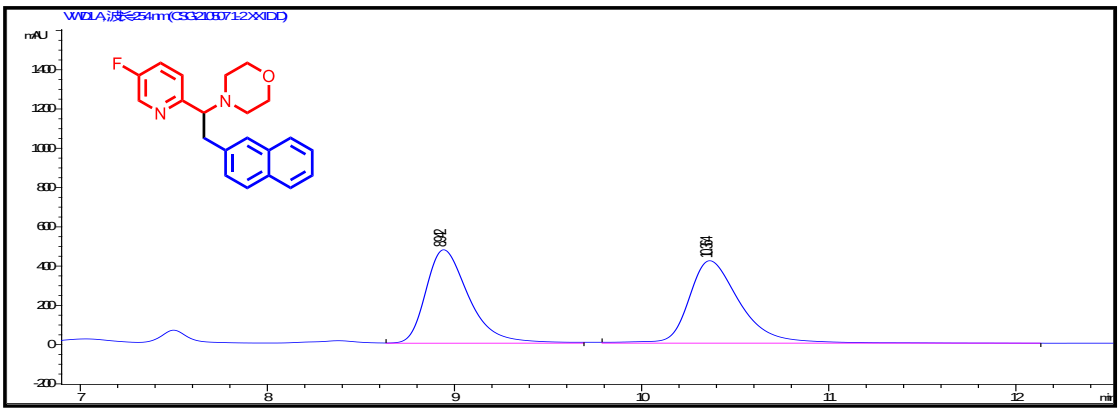
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.830	BV R	0.2315	3657.93457	234.37654	50.6755
2	16.852	BB	0.2951	3560.41235	186.22446	49.3245
Totals :				7218.34692	420.60100	



Signal 2: DAD1 B, Sig=254,4 Ref=off

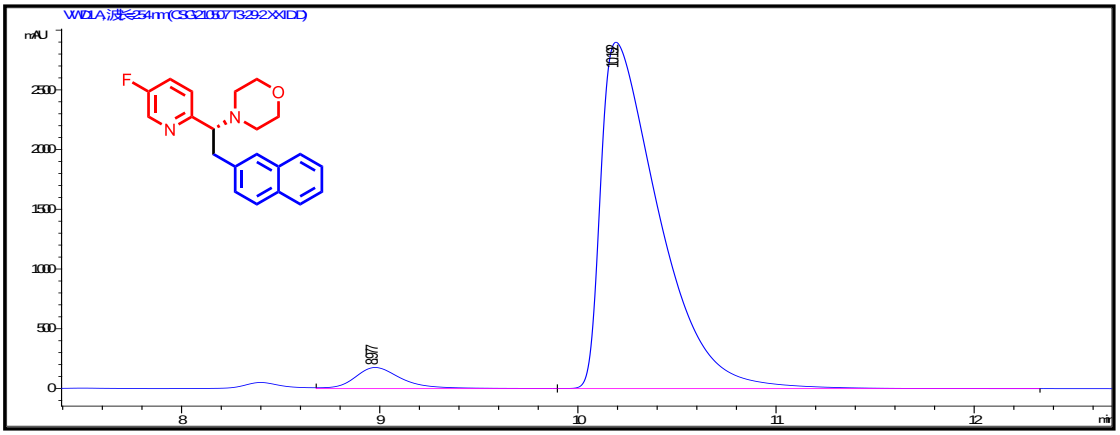
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.955	BB	0.2524	218.66632	12.99039	7.9978
2	16.997	BB	0.2987	2515.40259	129.47586	92.0022
Totals :				2734.06891	142.46625	



Signal 1: VWD1 A, Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.924	VB	0.2446	7602.38477	475.91974	48.6688
2	10.364	BB	0.2882	8018.27979	420.14444	51.3312

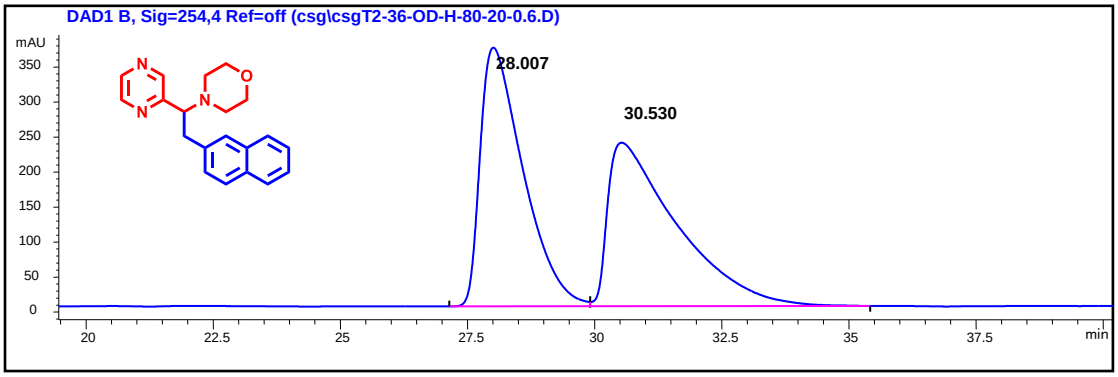
Totals : 1.56207e4 896.06418



Signal 1: VWD1 A, Sig=254 nm

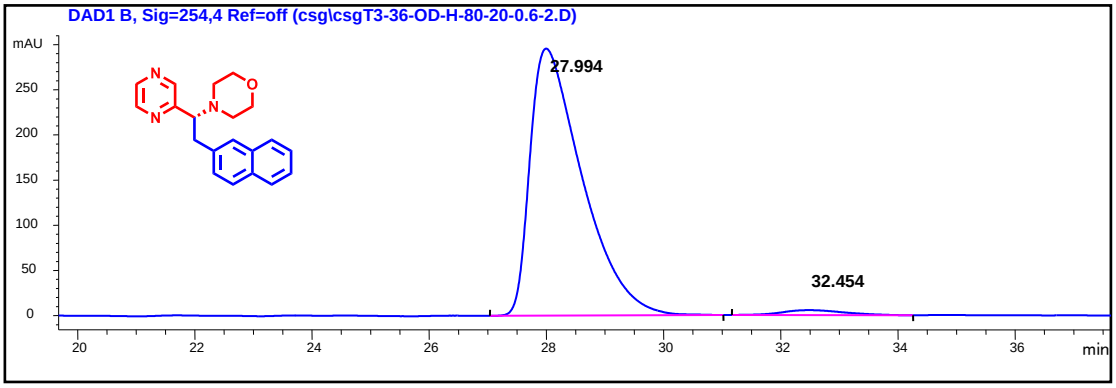
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.977	VB	0.2498	2958.51733	177.44818	4.7671
2	10.192	BB	0.3062	5.91021e4	2900.43457	95.2329

Totals : 6.20606e4 3077.88275



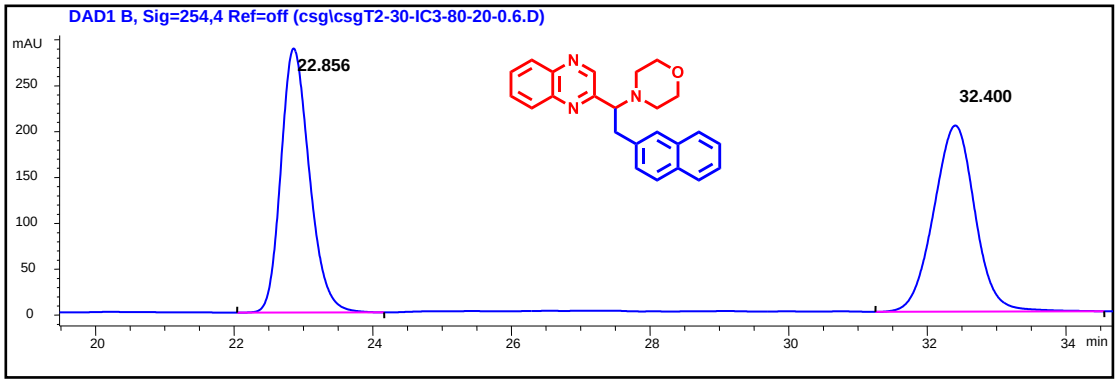
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.007	BV	0.8640	2.17201e4	369.37943	49.6312
2	30.530	VB	1.2753	2.20429e4	233.51183	50.3688
Totals :				4.37630e4	602.89125	



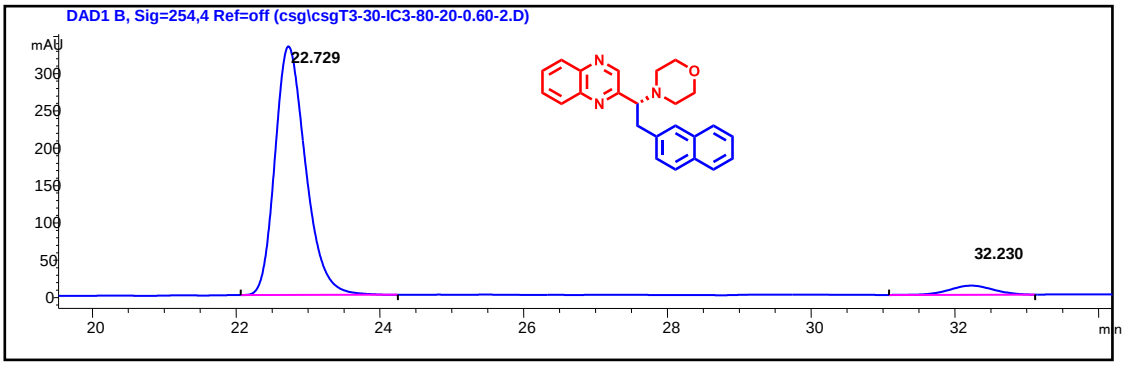
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.994	BB	0.9164	1.82986e4	295.52292	97.7770
2	32.454	BB	0.8985	416.02353	5.47525	2.2230
Totals :				1.87146e4	300.99817	



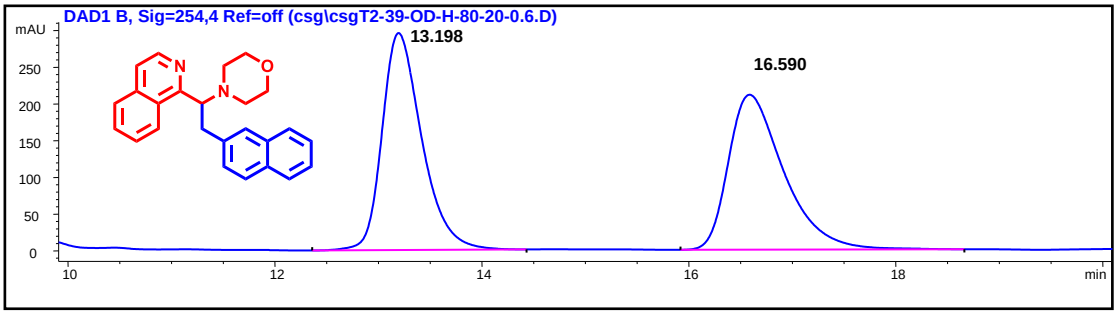
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.856	BB	0.4396	8225.69238	287.67496	49.4211
2	32.401	BB	0.6443	8418.39160	202.80394	50.5789
Totals :				1.66441e4	490.47890	



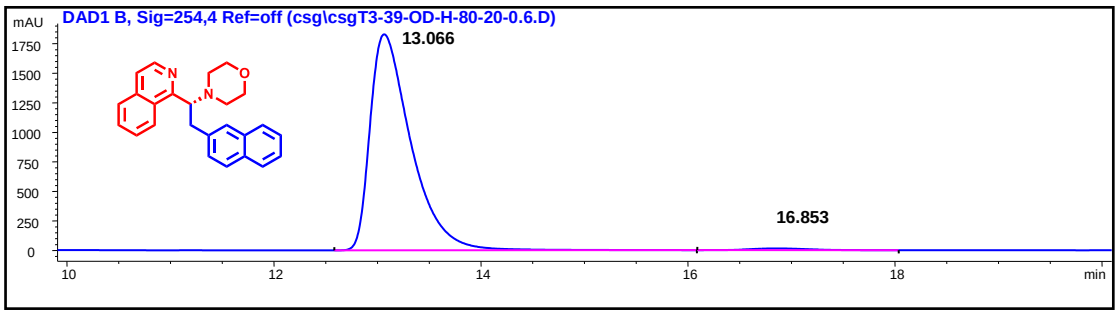
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.729	BB	0.4555	9858.77148	332.94122	94.9823
2	32.230	BB	0.6177	520.81885	12.25815	5.0177
Totals :				1.03796e4	345.19937	



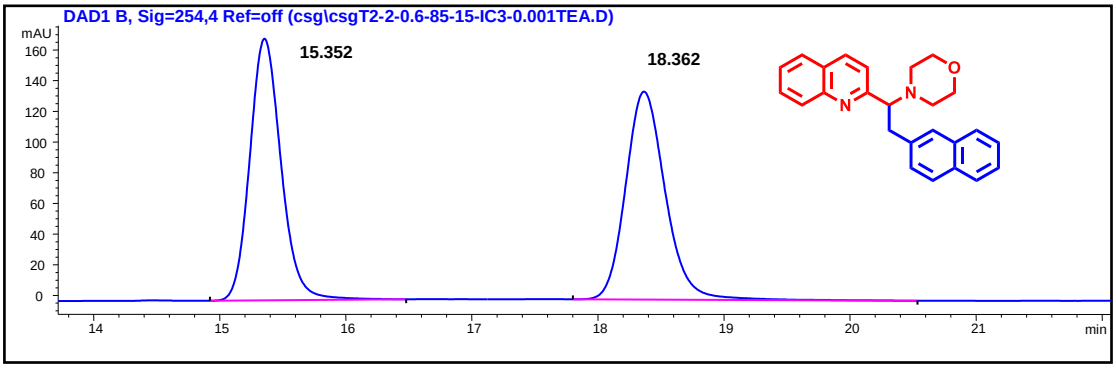
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.198	BB	0.4050	7874.54004	295.40668	50.0520
2	16.590	BB	0.5605	7858.17969	210.98605	49.9480
Totals :				1.57327e4	506.39273	



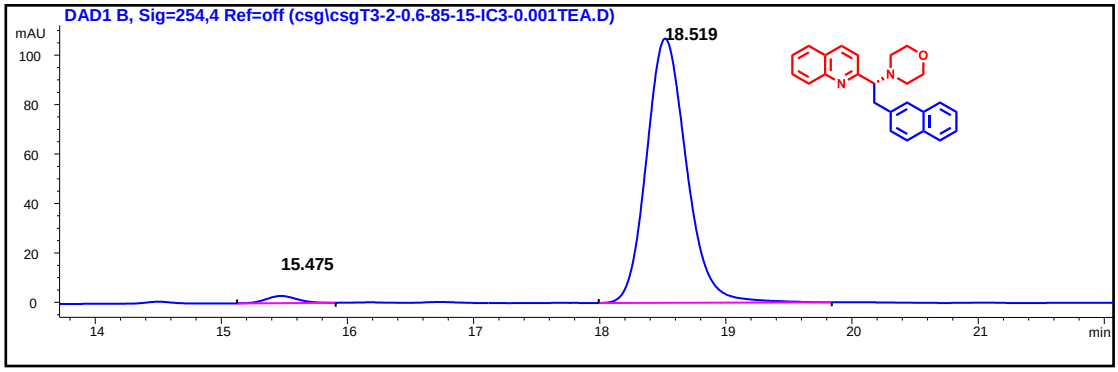
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.066	BB	0.4144	5.02145e4	1828.45203	98.8824
2	16.853	BB	0.5708	567.53217	15.08827	1.1176
Totals :				5.07820e4	1843.54030	



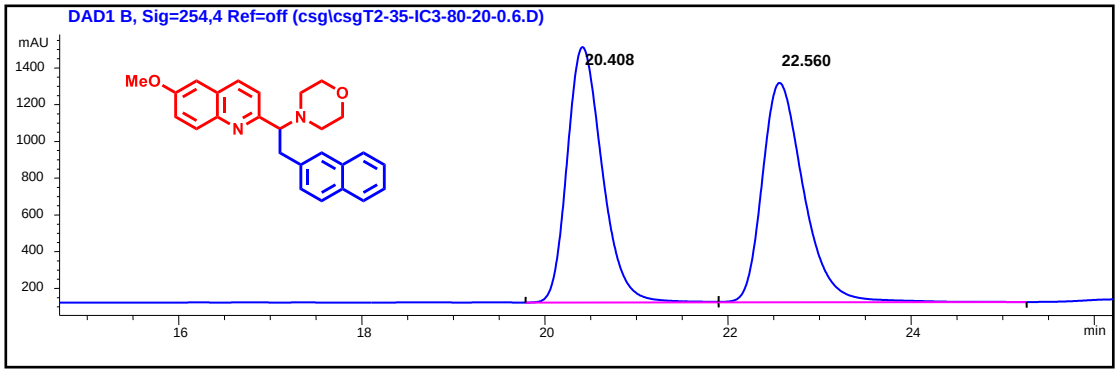
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.352	BB	0.2652	2941.23511	170.56488	49.7591
2	18.362	BB	0.3376	2969.71826	135.57462	50.2409
Totals :				5910.95337	306.13950	



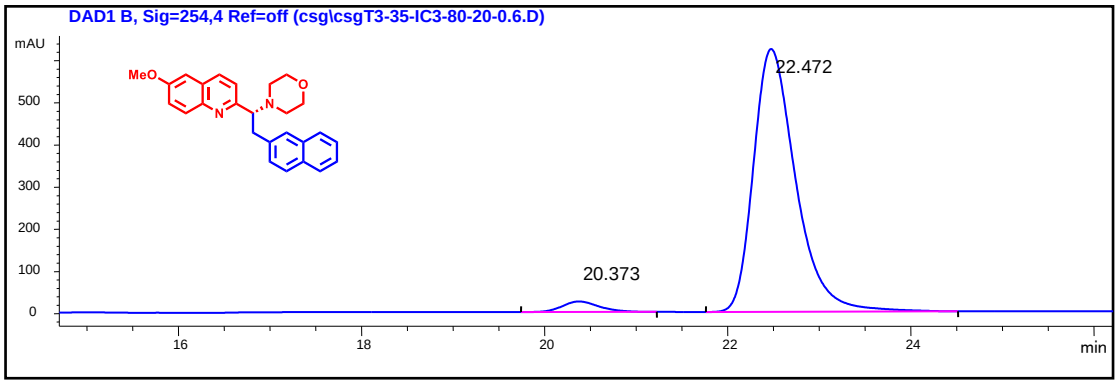
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.475	BB	0.2557	48.66556	2.87254	2.0223
2	18.519	BB	0.3413	2357.75049	106.88648	97.9777
Totals :				2406.41605	109.75903	



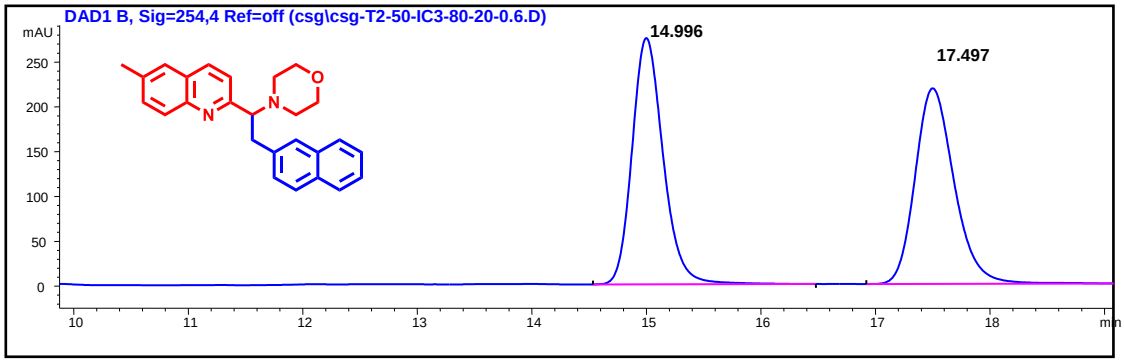
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.408	BV	0.4130	3.70467e4	1389.64636	49.6712
2	22.560	VB	0.4828	3.75371e4	1193.94751	50.3288
Totals :				7.45838e4	2583.59387	



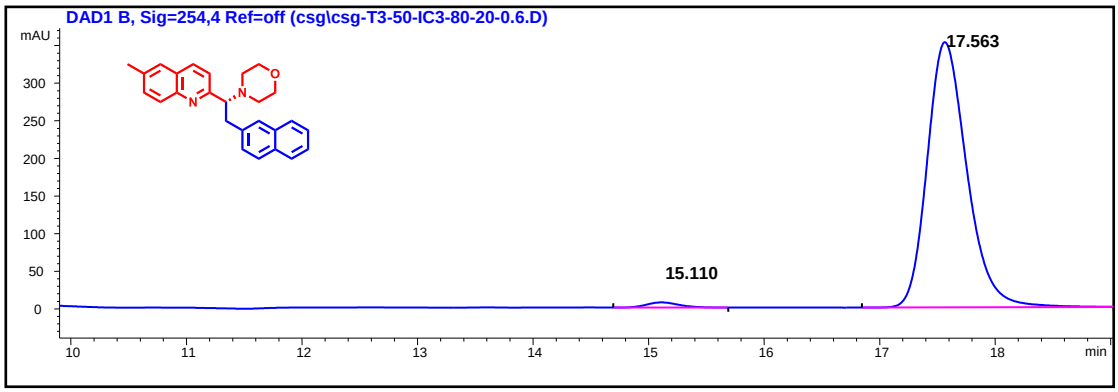
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.373	BB	0.4276	707.41541	25.19656	3.4124
2	22.472	BB	0.4906	2.00233e4	623.56549	96.5876
Totals :				2.07307e4	648.76205	



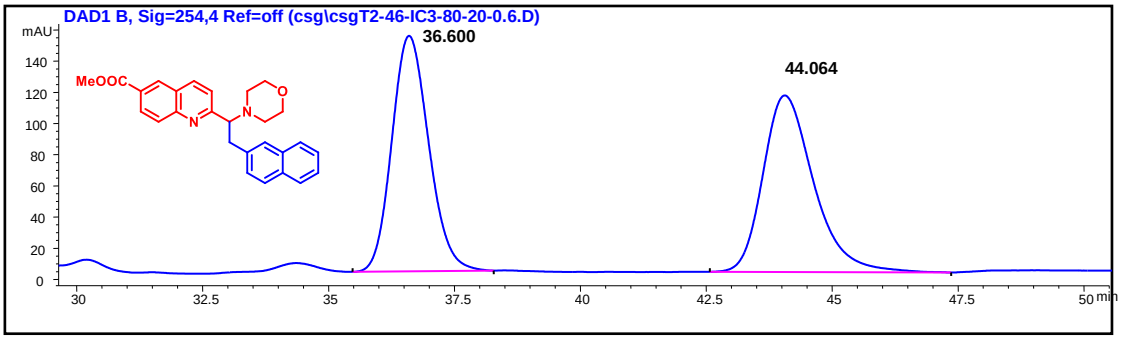
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.996	BB	0.2924	5192.58496	274.85229	50.0529
2	17.497	BBA	0.3649	5181.59912	218.31250	49.9471
Totals :				1.03742e4	493.16479	



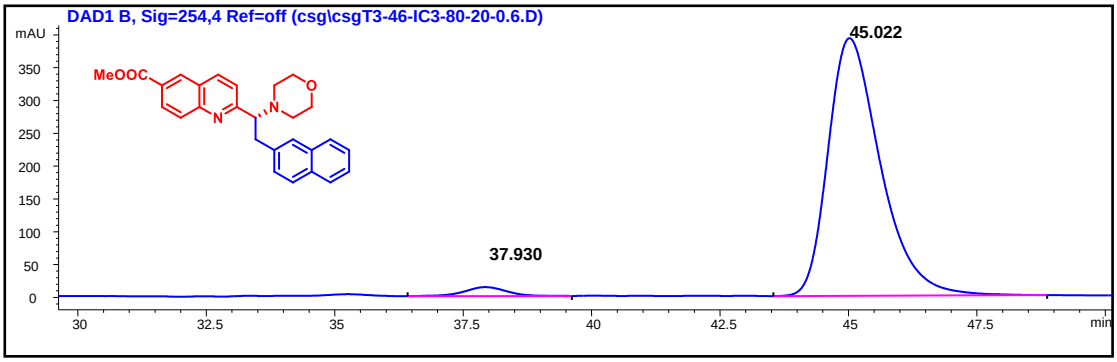
Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.111	BB	0.3073	148.45505	7.48703	1.5974
2	17.563	BBA	0.3674	9145.03223	381.89542	98.4026
Totals :				9293.48727	389.38244	



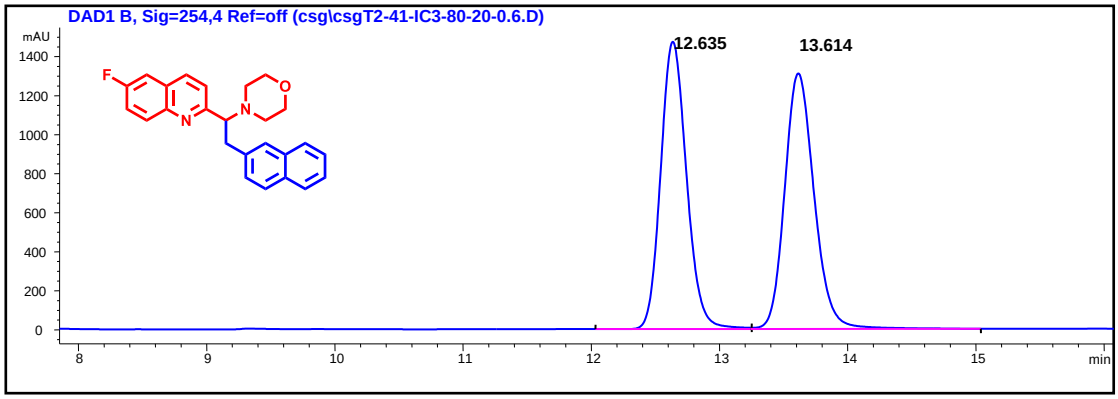
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.600	BB	0.7969	7704.49805	151.08746	49.2457
2	44.064	BB	1.0541	7940.53027	113.24334	50.7543
Totals :				1.56450e4	264.33080	



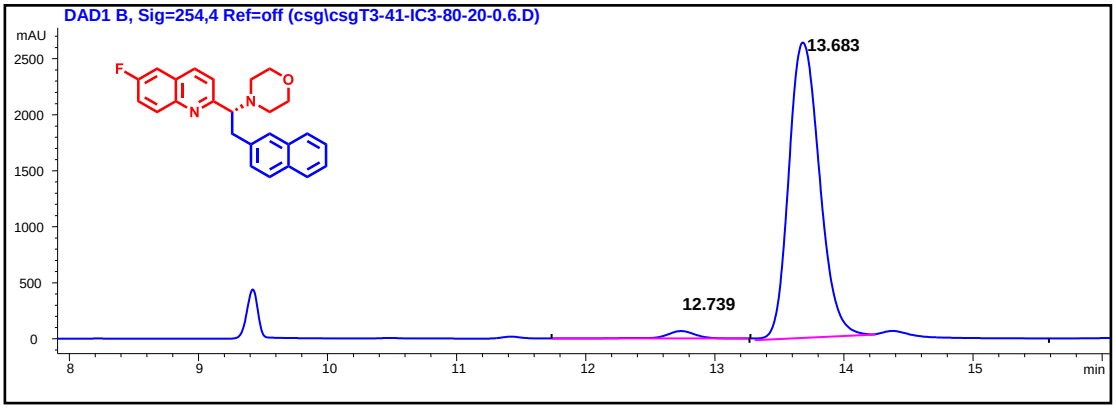
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.930	BB	0.7288	792.75751	13.70533	2.7674
2	45.022	BB	1.0858	2.78535e4	392.54529	97.2326
Totals :				2.86463e4	406.25062	



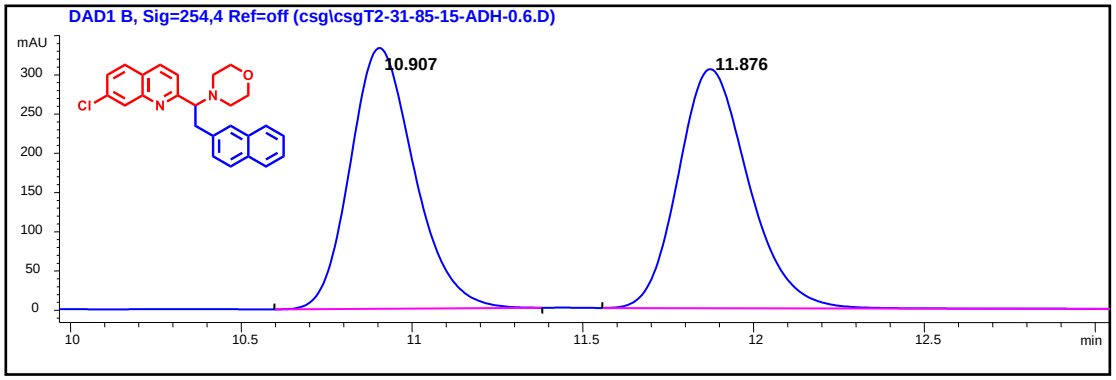
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.635	VV R	0.2196	2.06469e4	1472.50439	49.7079
2	13.614	VB	0.2460	2.08895e4	1309.97827	50.2921
Totals :				4.15364e4	2782.48267	



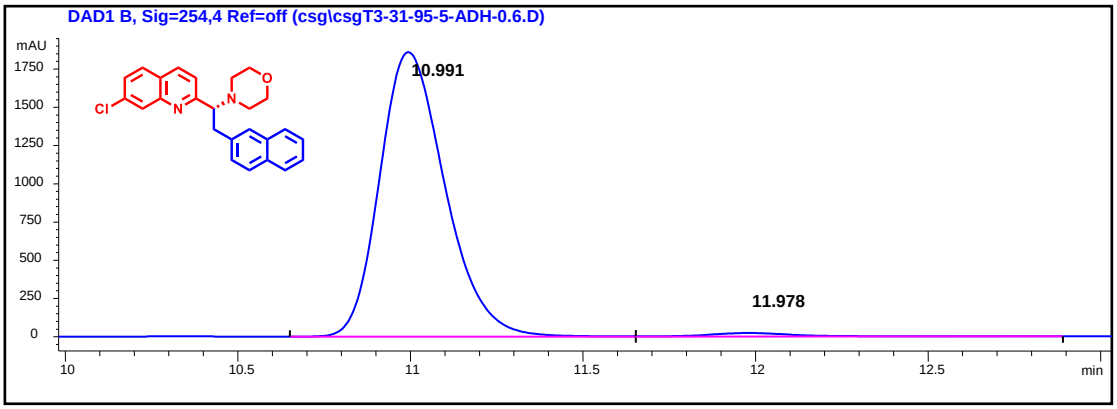
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.739	BB	0.2409	1066.81714	66.59570	2.2890
2	13.683	BV R	0.2604	4.55384e4	2642.94995	97.7110
Totals :				4.66053e4	2709.54565	



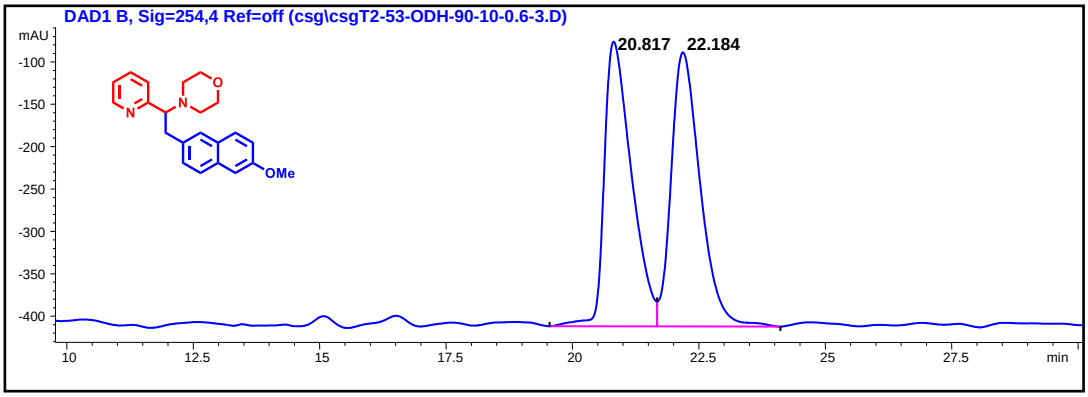
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.907	BB	0.2002	4336.62354	332.36871	49.7648
2	11.876	BB	0.2216	4377.61670	304.76147	50.2352
Totals :				8714.24023	637.13019	



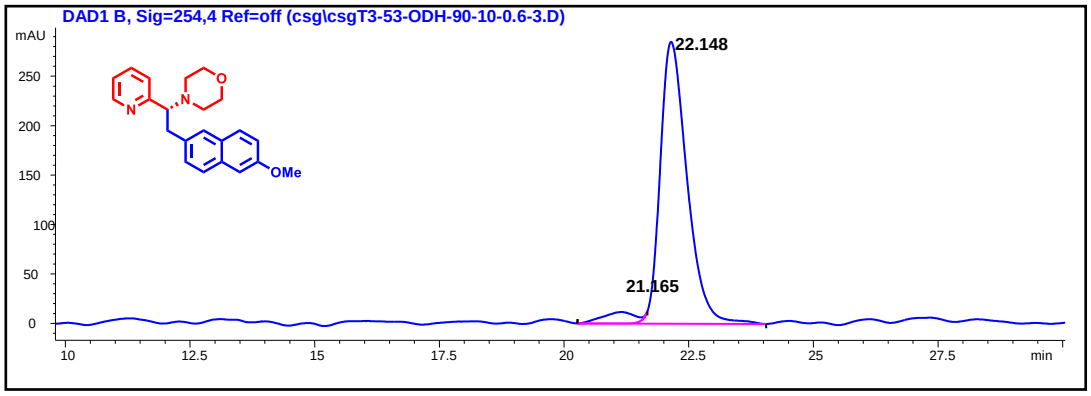
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.991	BV	0.2034	2.44613e4	1860.03503	98.4741
2	11.978	VB	0.2462	379.02768	23.00628	1.5259
Totals :				2.48403e4	1883.04132	



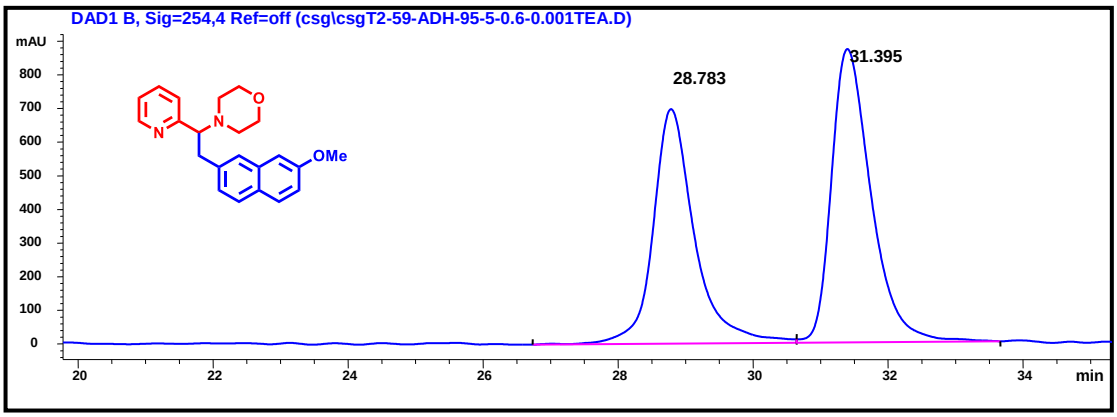
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.817	BV	0.5648	1.26290e4	335.76840	49.4486
2	22.184	VB	0.6060	1.29107e4	323.26077	50.5514
Totals :				2.55397e4	659.02917	



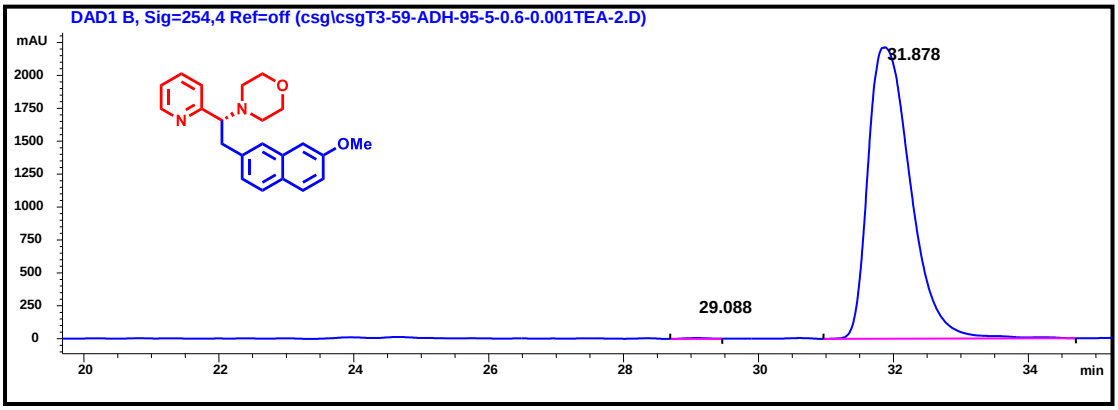
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.165	BV E	0.5366	518.79108	11.62655	4.6228
2	22.148	VB R	0.5798	1.07037e4	285.25458	95.3772
Totals :				1.12225e4	296.88112	



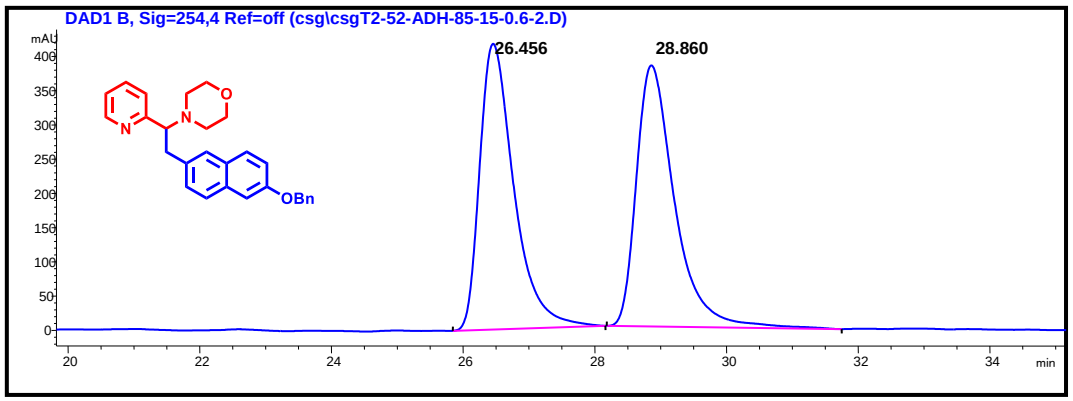
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.783	VV R	0.6361	2.96655e4	696.78918	45.5340
2	31.395	VB	0.6168	3.54848e4	871.93835	54.4660
Totals :				6.51503e4	1568.72754	



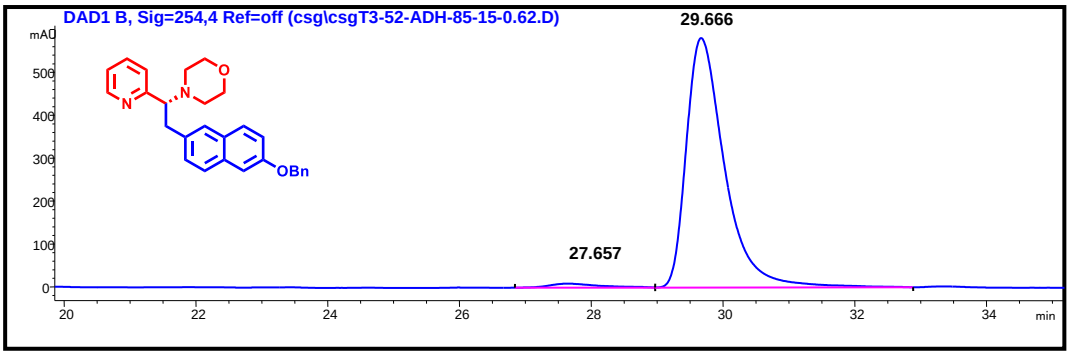
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.088	BV	0.2925	164.72743	6.89947	0.1694
2	31.878	BV R	0.5248	9.70559e4	2213.89429	99.8306
Totals :				9.72207e4	2220.79376	



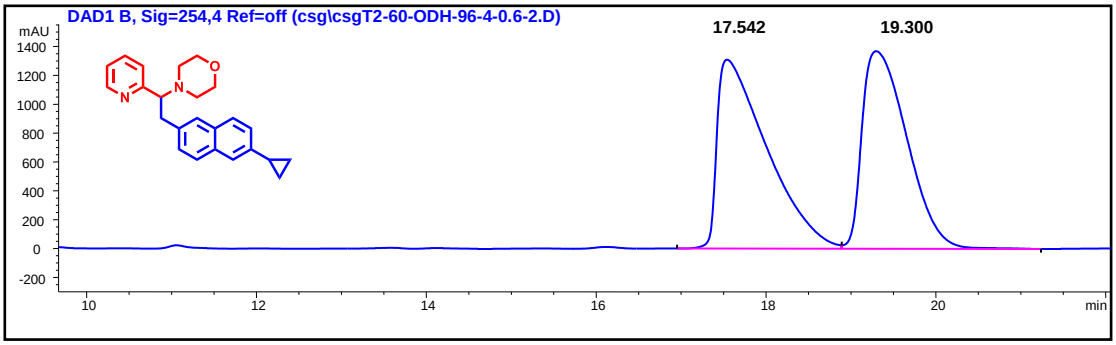
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.456	BB	0.5501	1.51006e4	417.36368	49.4982
2	28.860	BB	0.6133	1.54068e4	381.34698	50.5018
Totals :				3.05075e4	798.71066	



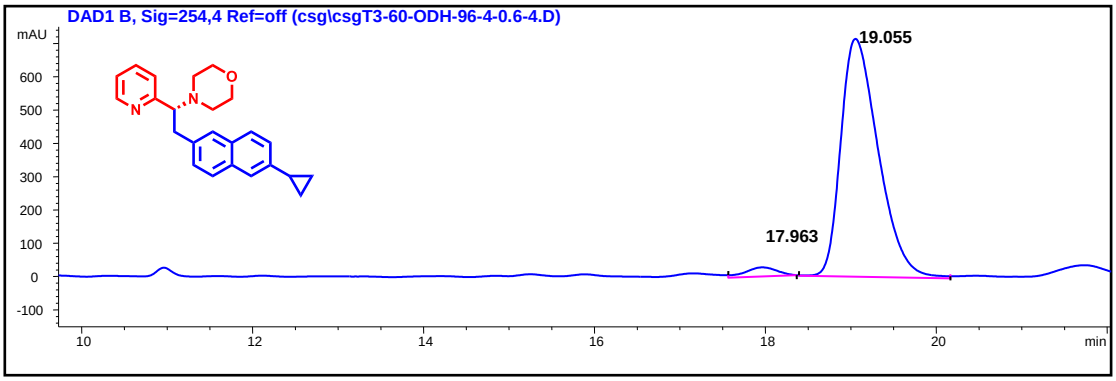
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.657	BV	0.6316	483.05334	9.30580	2.0097
2	29.666	VB	0.6187	2.35525e4	581.24591	97.9903
Totals :				2.40356e4	590.55171	



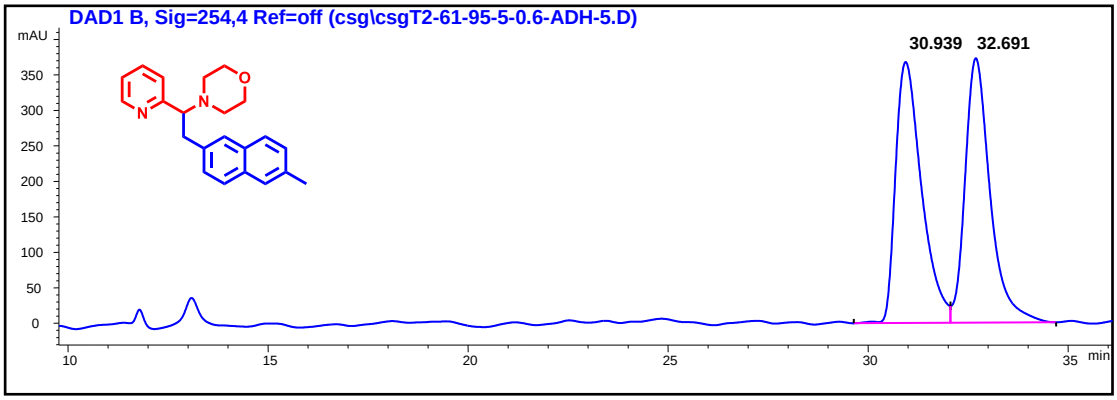
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.542	BV	0.5859	5.33985e4	1308.98523	51.4721
2	19.300	VB	0.5730	5.03441e4	1369.05798	48.5279
Totals :				1.03743e5	2678.04321	



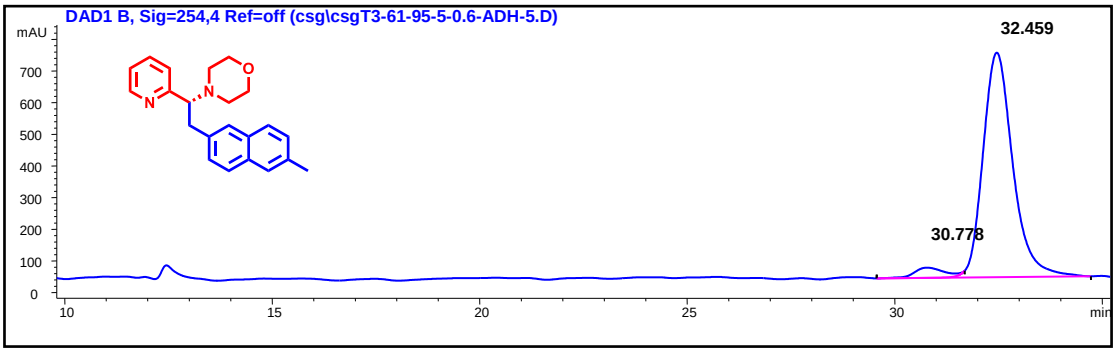
Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.970	BB	0.2809	502.12320	23.16677	2.2425
2	19.054	BV R	0.4666	2.18896e4	713.10663	97.7575
Totals :				2.23917e4	736.27340	



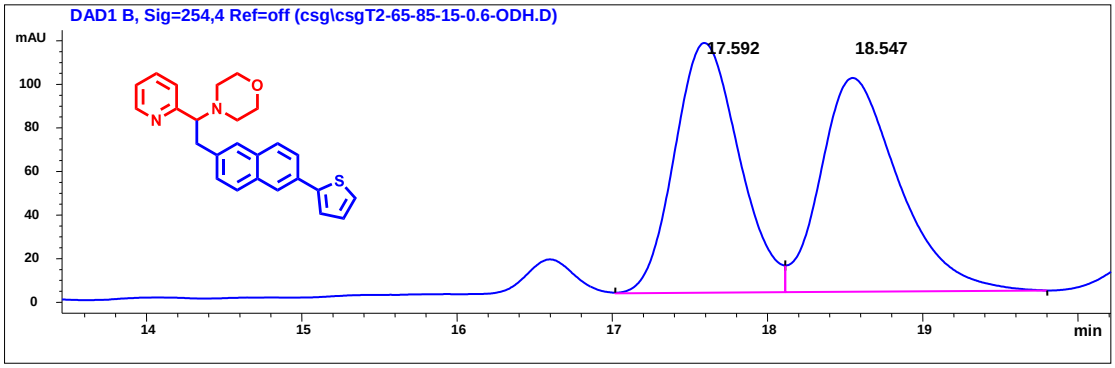
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.939	VV R	0.6904	1.66448e4	367.83392	50.5962
2	32.691	VB	0.6628	1.62526e4	372.65875	49.4038
Totals :				3.28974e4	740.49268	



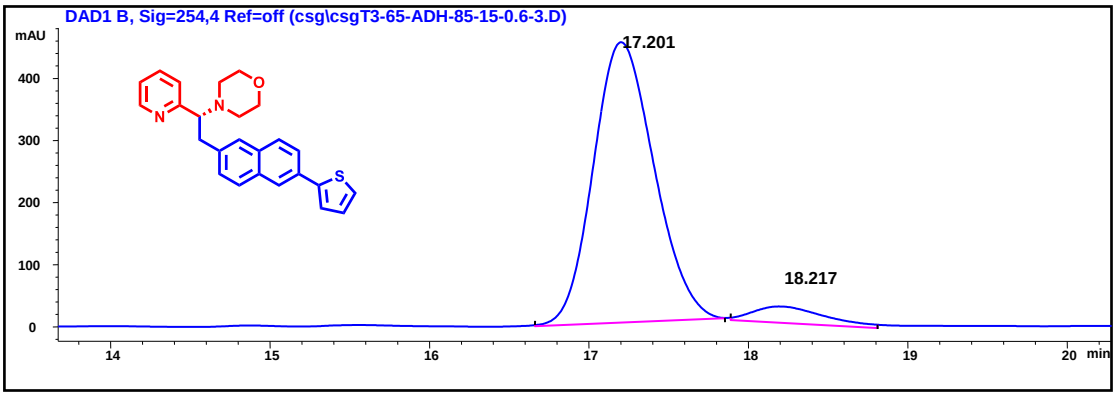
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.778	BV E	0.7290	1632.19287	32.33133	4.3950
2	32.459	VB R	0.7659	3.55054e4	709.38782	95.6050
Totals :				3.71376e4	741.71914	



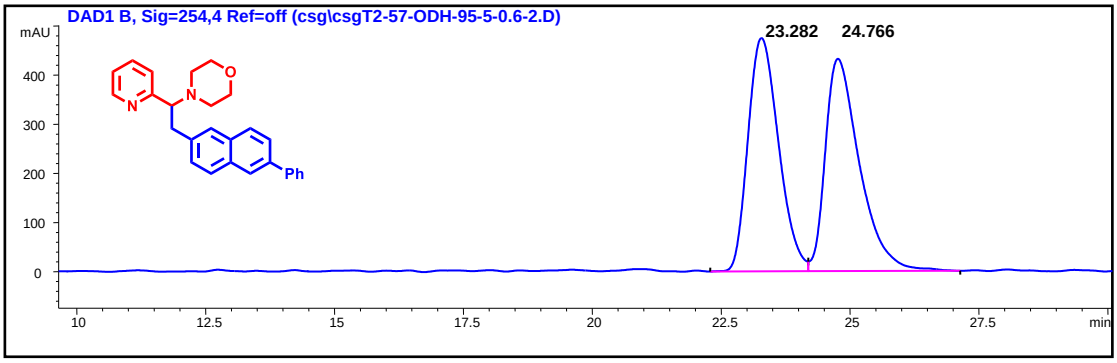
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.592	VV	0.4509	3309.93921	114.63321	49.0680
2	18.547	VB	0.5265	3435.68042	98.11309	50.9320
Totals :				6745.61963	212.74630	



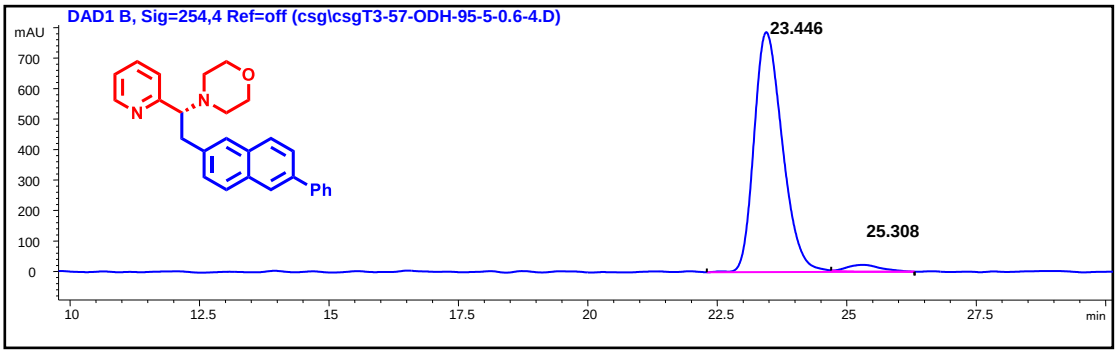
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.201	MM	0.4424	1.19836e4	451.43561	93.4422
2	18.217	MM	0.5298	841.01721	26.45922	6.5578
Totals :				1.28246e4	477.89482	



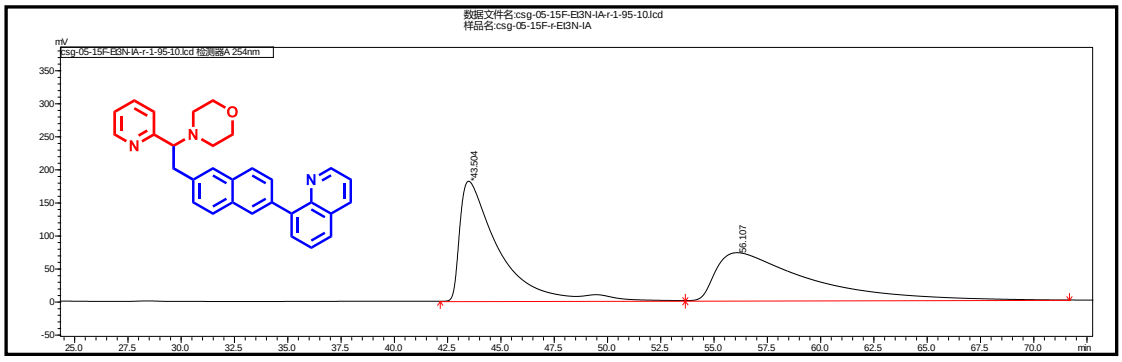
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.282	BV	0.6320	1.96182e4	474.82861	49.5193
2	24.766	VB	0.6879	1.99991e4	432.17130	50.4807
Totals :				3.96174e4	906.99991	



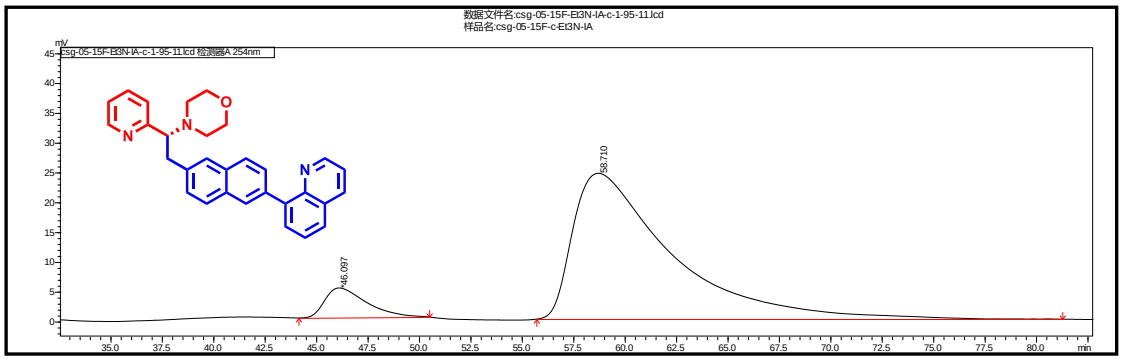
Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.446	VV R	0.5919	2.99793e4	787.00726	96.7273
2	25.308	VB E	0.5627	1014.32208	22.46976	3.2727
Totals :				3.09936e4	809.47702	



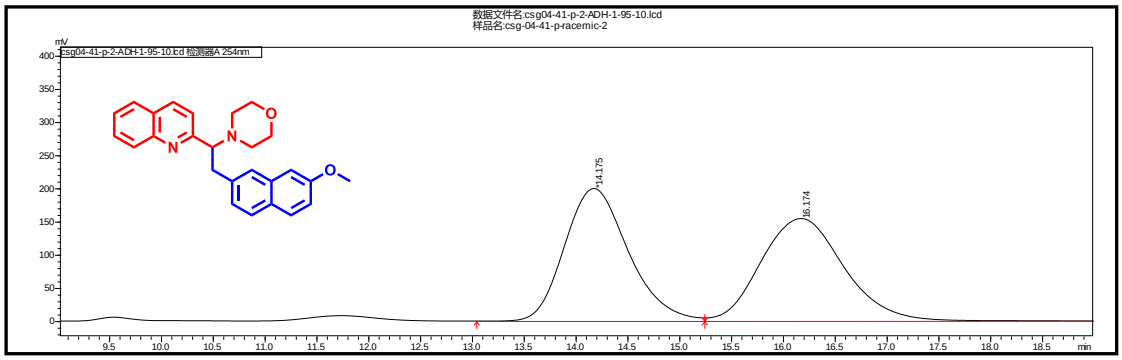
Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	43.504			23137746	181485	51.582
2	56.107			21718542	72611	48.418
Totals :				44856288	254097	



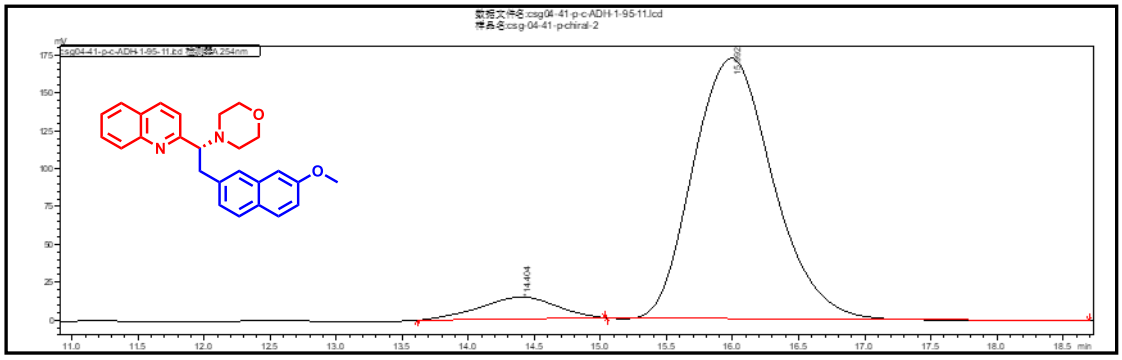
Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.097			700893	4982	7.934
2	58.710			8133217	24471	92.066
Totals :				8834109	29453	



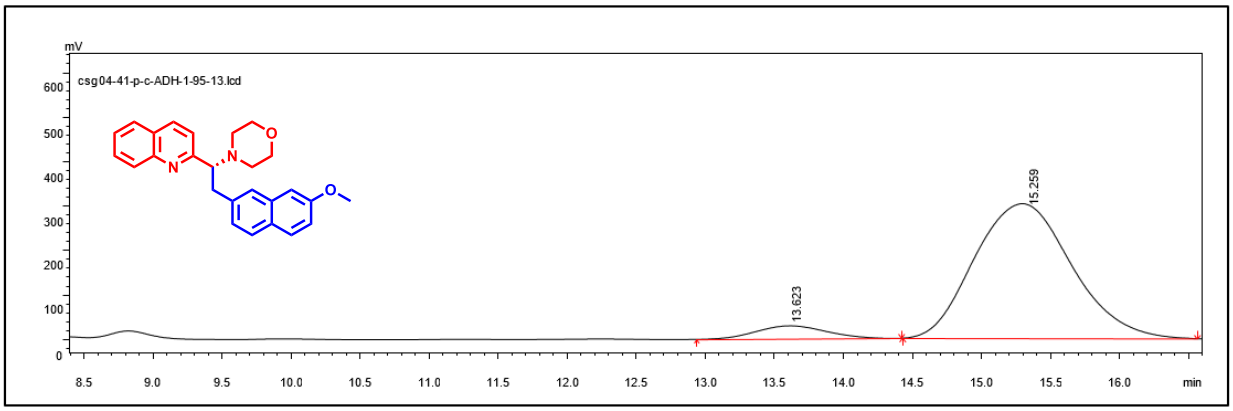
Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.175			8556758	199775	49.935
2	16.174			8578995	154443	50.065
Totals :				17135753	354218	



Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.404			578725	14307	7.445
2	15.992			7194545	171901	92.555
Totals :				7773270	186208	



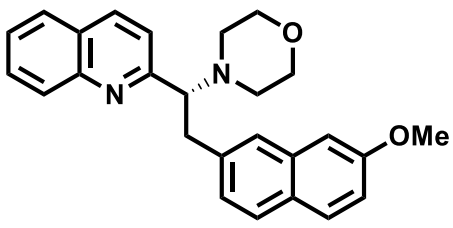
Signal 1: VWD1 A, Sig=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.623			1007518	28975	6.385
2	15.259			14772369	302114	93.615
Totals :				15779887	331089	

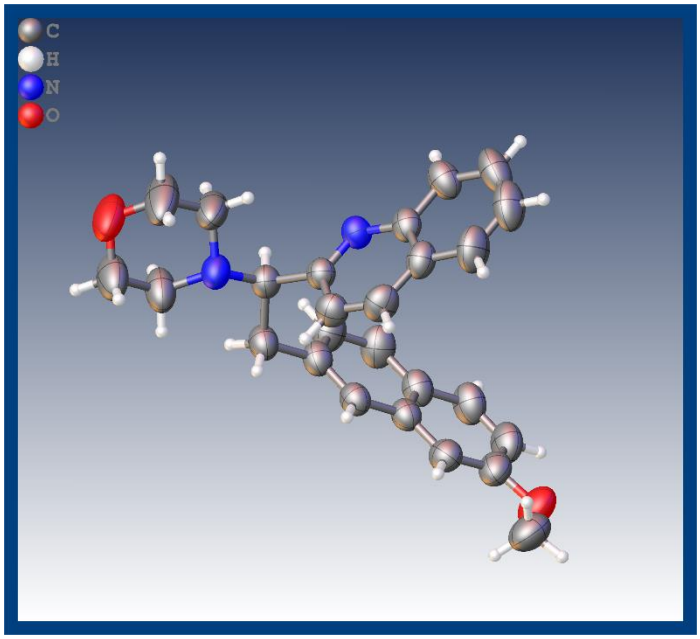
Olex2
Report created with ReportPlus

Crystal datas

3pc CCDC:2107204



Crystal Data and Experimental



Experimental. Single clear light colourless block-shaped crystals of **20210813c** were used as supplied. A suitable crystal with dimensions 0.21 × 0.11 × 0.10 mm^3 was selected and mounted on a Bruker APEX-II CCD diffractometer. The crystal was kept at a steady T = 293.15 K during data collection. The structure was solved with the **ShelXT** 2018/2 (Sheldrick, 2018) solution program using dual methods and by using **Olex2** 1.3 (Dolomanov et al., 2009) as the graphical interface. The model was refined with **ShelXL** 2018/3 (Sheldrick, 2015) using full matrix least squares minimisation on $\boldsymbol{F^2}$.

Crystal Data. $C_{26}H_{26}N_2O_2$, M_r = 398.49, orthorhombic, $P2_12_12_1$ (No. 19), a = 6.1633(4) Å, b = 18.0475(11) Å, c = 19.7364(12) Å, = = = 90°, V = 2195.3(2) Å^3, T = 293.15 K, Z = 4, Z' = 1, (CuK) = 0.603, 69195 reflections measured, 4505 unique (R_{int} = 0.0338) which were used in all calculations. The final wR_2 was 0.1041 (all data) and R_1 was 0.0348 (I≥2 (I)).

Compound	**20210813c**
Formula	$C_{26}H_{26}N_2O_2$
$D_{calc.}$/ g cm^{-3}	1.206
/mm^{-1}	0.603
Formula Weight	398.49
Colour	clear light colourless
Shape	block-shaped
Size/mm^3	0.21×0.11×0.10
T/K	293.15
Crystal System	orthorhombic
Flack Parameter	0.00(5)
Space Group	$P2_12_12_1$
a/Å	6.1633(4)
b/Å	18.0475(11)
c/Å	19.7364(12)
/°	90
/°	90
/°	90
V/Å^3	2195.3(2)
Z	4
Z'	1
Wavelength/Å	1.54178
Radiation type	CuK
$_{min}$/°	3.318
$_{max}$/°	74.741
Measured Refl's.	69195
Indep't Refl's	4505
Refl's I≥2 (I)	4196
R_{int}	0.0338
Parameters	273
Restraints	0
Largest Peak	0.153
Deepest Hole	-0.126
GooF	1.072
wR_2 (all data)	0.1041
wR_2	0.1021
R_1 (all data)	0.0369
R_1	0.0348

Structure Quality Indicators

Reflections:	d min (Cu\a) 2θ=149.5°	0.80	I/σ(I) CIF	76.9	Rint CIF	3.38%	Full 135.4° CIF	100
Refinement:	Shift CIF	0.000	Max Peak CIF	0.2	Min Peak CIF	-0.1	GooF CIF	1.072	Flack CIF	.00(5)

A clear light colourless block-shaped-shaped crystal with dimensions 0.21 × 0.11 × 0.10 mm^3 was mounted. Data were collected using a Bruker APEX-II CCD diffractometer operating at T = 293.15 K.

Data were measured using and scans using CuK radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program SAINT v8.37A (Bruker, 2015). The maximum resolution that was achieved was = 74.741° (0.83 Å).

The unit cell was refined using SAINT v8.37A (Bruker, 2015) on 9931 reflections, 14% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using SAINT v8.37A (Bruker, 2015). The final completeness is 100.00 % out to 74.741° in . SADABS-2016/2 (Bruker, 2016/2) was used for absorption correction. wR_2(int) was 0.1412 before and 0.0522 after correction. The Ratio of minimum to maximum transmission is 0.8890. The /2 correction factor is Not present. The absorption coefficient of this material is 0.603 mm^{-1} at this wavelength (= 1.54178Å) and the minimum and maximum transmissions are 0.670 and 0.754.

The structure was solved and the space group $P2_12_12_1$ (# 19) determined by the ShelXT 2018/2 (Sheldrick, 2018) structure solution program using using dual methods and refined by full matrix least squares minimisation on $\boldsymbol{F^2}$ using version 2018/3 of **ShelXL** 2018/3 (Sheldrick, 2015). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. Hydrogen atom positions were calculated geometrically and refined using the riding model.

_exptl_absorpt_process_details: SADABS-2016/2 (Bruker,2016/2) was used for absorption correction.wR_2(int) was 0.1412 before and 0.0522 after correction.The Ratio of minimum to maximum transmission is 0.8890.The /2 correction factor is Not present.

There is a single molecule in the asymmetric unit, which is represented by the reported sum formula. In other words: Z is 4 and Z' is 1.

The Flack parameter was refined to 0.00(5). Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2 results in None. Note: The Flack parameter is used to determine chirality of the crystal studied, the value should be near 0, a value of 1 means that the stereochemistry is wrong and the model should be inverted. A value of 0.5 means that the crystal consists of a racemic mixture of the two enantiomers.

Citations

O.V. Dolomanov and L.J. Bourhis and R.J. Gildea and J.A.K. Howard and H. Puschmann, Olex2: A complete structure solution, refinement and analysis program, *J. Appl. Cryst.*, (2009), **42**, 339-341.

SADABS, Bruker axs, Madison, WI (?).

SAINT - Software for the Integration of CCD Detector System Bruker Analytical X-ray Systems, Bruker axs, Madison, WI (?).

Sheldrick, G.M., Crystal structure refinement with ShelXL, *Acta Cryst.*, (2015), **C71**, 3-8.

Sheldrick, G.M., ShelXT-Integrated space-group and crystal-structure determination, *Acta Cryst.*, (2015), **A71**, 3-8.