Regioselective Difunctionalization of Pyridines *via* 3,4-Pyridynes

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Supporting Information

Table of Content

General Information

All reactions were carried out under argon or nitrogen atmosphere in glassware dried with a heat gun (650 °C) under high vacuum (<1 mbar). Syringes which were used to transfer anhydrous solvents or reagents were purged thrice with argon or nitrogen prior to use. Indicated yields are isolated yields of compounds estimated to be >95% pure as determined by ^{1}H-NMR (25 °C) and capillary GC analyses. Unless otherwise indicated, all reagents were obtained from commercial sources.

Solvents

Solvents were dried according to standard procedures by distillation over drying agents and stored under argon.

THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen.

Solvents for column chromatography were distilled on a rotary evaporator prior to use.

Reagents

***i*PrMgCl·LiCl:** Magnesium turnings (2.67 g, 110 mmol) and anhydrous LiCl (4.66 g, 100 mmol) were placed in an argon-flushed flask and THF (50 mL) was added. A solution of *i*PrCl (9.13 mL, 100 mmol) in THF (50 mL) was slowly added at 25 °C. The reaction starts within a few minutes. After addition, the reaction mixture was stirred for 12 h at 25 °C. The grey solution of *i*PrMgCl·LiCl was cannulated to another flask under argon and removed in this way from excess of magnesium. A yield of ca. 95-98% of *i*PrMgCl·LiCl is obtained.[1]

Magnesium thiolates: *i*PrMgCl·LiCl (1.05 equiv) was slowly added to a solution of the representative thiol in THF (1 mmol/ mL) at 0 °C and stirred for 30 min.[2]

CuCN·2LiCl solution (1.00 M) was prepared by drying CuCN (80.0 mmol, 7.17 g) and LiCl (160 mmol, 6.77 g) in a Schlenk-flask under vacuum at 140 °C for 5 h. After cooling, dry THF (80 mL) was added and stirring continued until the salts were dissolved.[3]

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[1] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333-3336.
[2] B. Heinz, M. Balkenhohl, P. Knochel, *Synthesis* **2019**, *51*, 4452–4462.
[3] P. Knochel.; M. C. P. Yeh, S. C. Berk, J. J. Talbert, *Org. Chem.* **1988**, *53*, 2390-2392.

$ZnCl_2$ solution (1.00 M) was prepared by drying $ZnCl_2$ (200 mmol, 27.3 g) in a Schlenk-flask under vacuum at 140 °C for 5 h. After cooling, dry THF (200 mL) was added and stirring continued until the salt was dissolved.

Content determination of organometallic reagents

***i*PrMgCl·LiCl** was titrated with I_2 in THF.[4]

Organomagnesium reagents were titrated with I_2 in THF.[4]

Flow reactions

Flow reactions were carried out with solutions of the reactants in dry THF. Flame-dried glassware was used for the reagent solutions and kept under an argon atmosphere during the reactions. Tetradecane was used as internal standard. For all flow reactions a Vapourtec E-series Integrated Flow Chemistry System with 3rd Pump Kit, Organometallic Kit, Collection Valve Kit and Cryogenic Reaction Kit was used. Reactions were performed in coiled tube reactors. Coiled reactors (1.0, 5.0, 10.0 or 20.0 mL) were made from PFA or PTFE Teflon (i.d. = 0.8 mm, o.d. = 1.6 mm). Prior to performing reactions, the system was dried by flushing it with dry THF (blue tubing) or MeOH, followed by hexane (red tubing) (flow rate of all pumps: 1.00 mL·min-1; run-time: 30 min).

Chromatography

Flash column chromatography was performed using silica gel 60 (0.040-0.063 mm) from MERCK.

Thin layer chromatography was performed using SiO_2 pre-coated aluminum plates (Merck 60, F-254). The chromatograms were examined under 254 nm UV irradiation and/or by staining the TLC plate with a $KMnO_4$ solution followed by heating with a heat gun.

HPLC was performed on an Agilent Technologies 1200 Series using a Chromolit® SemiPrep RP-18e 100-10 mm column. The HPLC was run with a gradient of acetonitrile/water.

Analytical Data

[4] P. Knochel, A. Krasovskiy, *Synthesis* **2006**, *2006*, 890-891.

^{1}H-NMR and **^{13}C-NMR** spectra were recorded on VARIAN Mercury 200, BRUKER ARX 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments. Chemical shifts are reported as values in ppm relative to tetramethylsilane. $CDCl_3$ peaks were set to 7.26 ppm in ^{1}H NMR and 77.16 ppm in ^{13}C NMR experiments. The following abbreviations were used to characterize signal multiplicities: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), hept (heptett) as well as m (multiplet).

Mass spectroscopy: High resolution (HRMS) and low resolution (MS) spectra were recorded on a FINNIGAN MAT 95Q instrument. Electron impact ionization (EI) was conducted with an ionization energy of 70 eV. For coupled gas chromatography/mass spectrometry, a HEWLETT-PACKARD HP 6890/MSD 5973 GC/MS system was used. Molecular fragments are reported starting at a relative intensity of 10-20%.

Infrared spectra (IR) were recorded from 4500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument. For detection a SMITHS DETECTION DuraSampl*IR* II Diamond ATR sensor was used. The main absorption peaks are reported in cm^{-1}.

Melting points (m.p.) were determined on a BÜCHI B-540 melting point apparatus and are uncorrected.

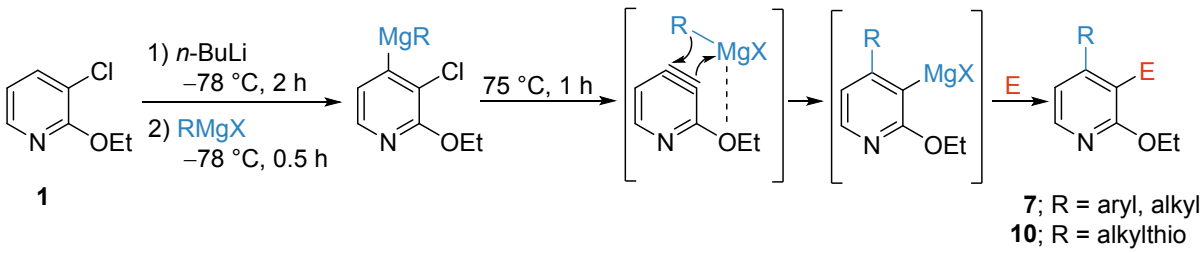
Typical Procedures

Typical Procedure 1: Preparation of organomagnesium reagents of type **3** *via* Mg-insertion.

LiCl (509 mg, 12.0 mmol, 1.2 equiv) was flame dried and cooled to room temperature *in vacuo*. Then, magnesium turnings (288 mg, 12.0 mmol, 1.2 equiv) and THF (10 mL) were added and the reaction mixture was cooled to 0 °C. The organic bromide (10.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred at 0 °C for 1-3 h. Upon complete conversion, the concentration of the organomagnesium reagent **3** was determined by titration against iodine in THF.[5]

Typical Procedure 2: Preparation of 2,3,4-trifunctionalized pyridines of type **7** and **10** *via* 3,4-pyridyne intermediates.

[5] F. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem. Int. Ed*. **2008**, *47*, 6802-6806.



n-Butyllithium (1.1 equiv, 2.6 M) was slowly added to a stirred solution of 3-chloro-2-ethoxypyridine (**1**) (1.0 equiv) in THF (2 mL/mmol of 3-chloro-2-ethoxypyridine) at -78 °C in a sealed tube. After stirring for 2 h, the representative organomagnesium reagent (2.0-5.0 equiv) was slowly added at -78 °C. The solution was allowed to warm to 25 °C after 30 min of stirring at -78 °C. Then, the reaction mixture was heated to 75 °C for 1 h, followed by quenching with the representative electrophile (2.1-2.5 equiv) at 0 °C. The reaction mixture was then stirred at 25 °C until completion. After quenching with *sat. aq.* NH_4Cl, the aqueous phase was extracted with EtOAc and the combined organic phases were dried over Na_2SO_4 and filtrated. After removal of the solvent *in vacuo*, flash column chromatography purification with *iso*hexane (or pentane):EtOAc mixtures afforded the pure products of type **7** and **10**.

Typical Procedure 3: Preparation of 2,3,4-trifunctionalized pyridines of type **12** *via* 3,4-pyridyne intermediates in continuous flow.

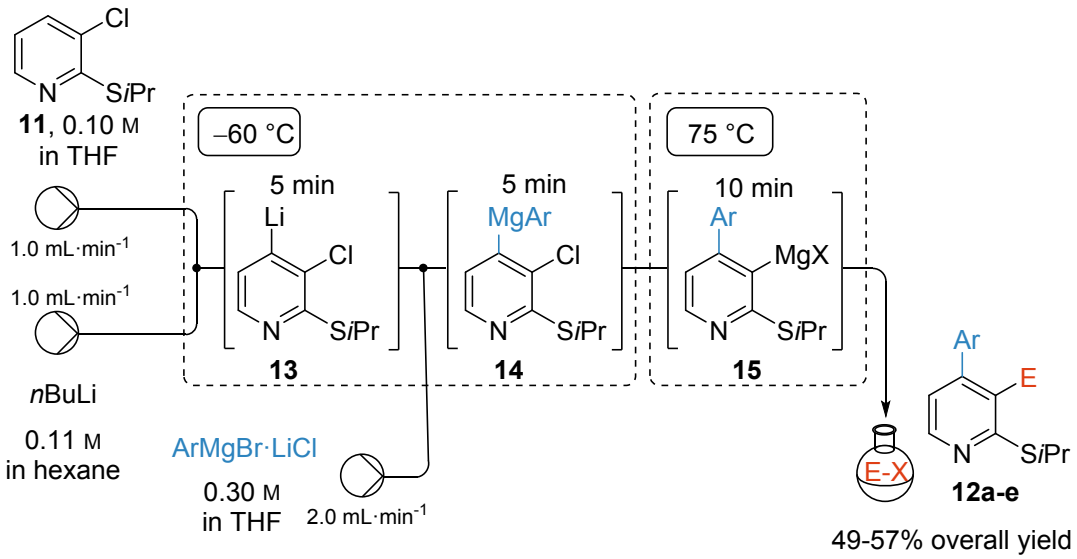


Figure SI1: Flow chemistry set-up for the preparation of of 2,3,4-trifunctionalized pyridines of type **12**.

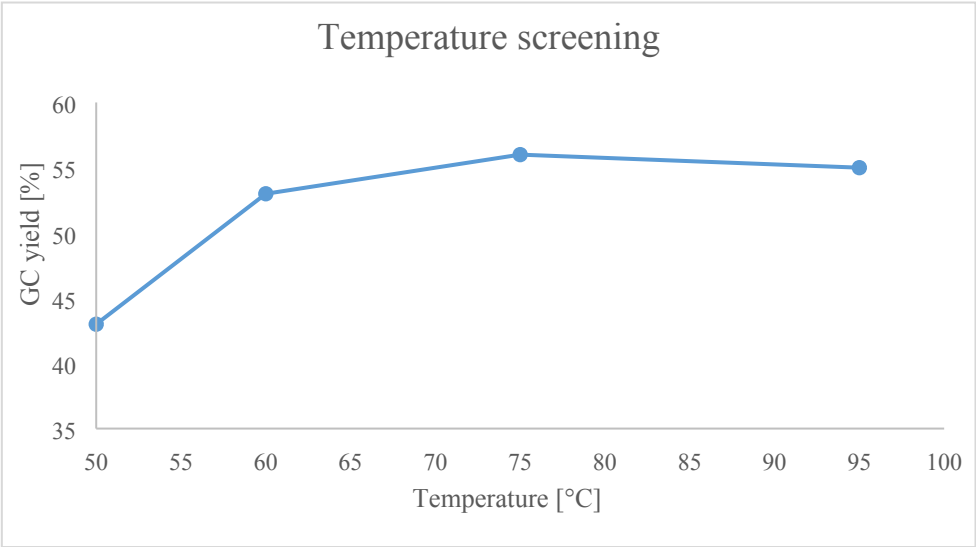
A solution of **11** in THF (0.10 M, 1.0 equiv) and a solution of *n*-BuLi in *n*-hexane (0.11 M, 1.1 equiv) were prepared. The solutions were pumped from their flasks through a suction

needle at flowrate A = 1.0 mL·min^{-1} and flowrate B = flowrate A. After passing a PTFE tubing (Vol_{pre} = 2.0 mL, T = –60 °C, residence time: 2 min) for precooling, the solutions were mixed in a T-mixer (PFA or PTFE, I.D. = 0.5 mm). The combined stream passed a PTFE reactor tube (Vol_{R1} = 10 mL; residence time: t = 5 min, T = –60 °C) and a organomagnesium reagent (0.3 M, 6.0 equiv), prepared *via* **TP1**, was added *via* a third pump (flowrate C = 2.0 mL·min^{-1}, Vol_{pre} = 2.0 mL, T = –60 °C, residence time: 1 min). The combined stream passed a PTFE reactors tube (Vol_{R2} = 20 mL; residence time: t = 5 min, T = –60 °C) and was afterwards heated in another PTFE reactors tube (Vol_{R3} = 40 mL; residence time: t = 10 min, T = 75 °C). The reaction mixture was subsequently injected in a flask at 0 °C, containing an electrophile for quenching (7.0 equiv). The reaction mixture was then stirred at 25 °C until completion. After quenching with *sat. aq.* NH_4Cl, the aqueous phase was extracted with EtOAc and the combined organic phases were dried over Na_2SO_4 and filtrated. After removal of the solvent *in vacuo*, flash column chromatography purification with *iso*hexane (or pentane):EtOAc mixtures afforded the pure product.

Optimization of the Reaction Conditions

The optimizations of the reaction conditions were performed with 3-chloro-2-ethoxypyridine (**1**) and (4-methoxyphenyl)magnesium bromide towards 2-ethoxy-4-(4-methoxyphenyl) pyridine (**7a**) as described in **TP2**.

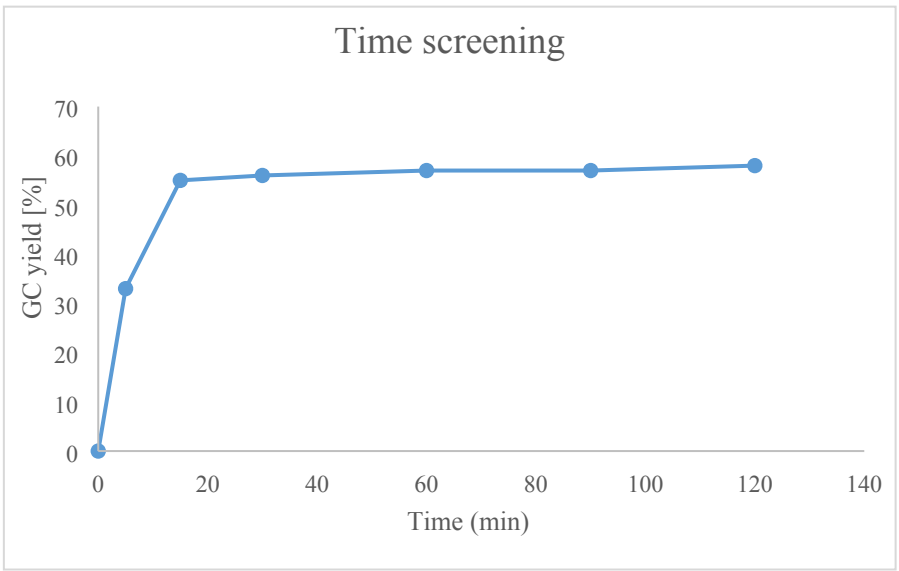
1. Temperature Screening



Entry	Temperature (°C)	Reaction time (h)	RMgBr Equiv.	GC yield (%)[a]
1	50	1	2.0	43
2	60	1	2.0	53
3	**75**	**1**	**2.0**	**56**
4	95	1	2.0	55

[a] Tetradecane ($C_{14}H_{30}$) was used as internal standard.

2. Time Screening

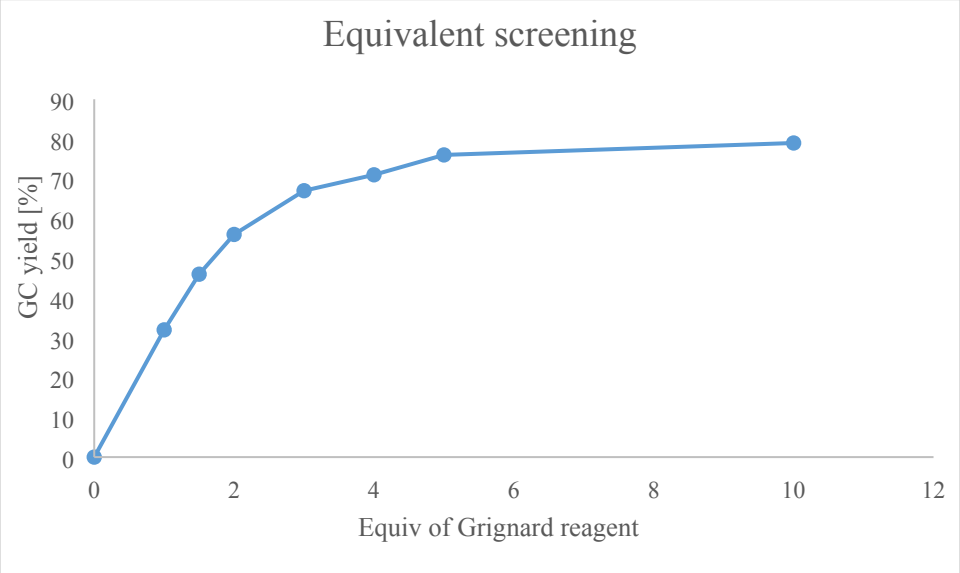


Entry	Temperature (°C)	Reaction time	RMgBr Equiv	GC yield (%)[a]

		(min)		
1	75	5	2.0	33
2	75	15	2.0	55
3	75	30	2.0	56
4	**75**	**60**	**2.0**	**57**
5	75	90	2.0	57
6	75	120	2.0	58

[a] Tetradecane ($C_{14}H_{30}$) was used as internal standard.

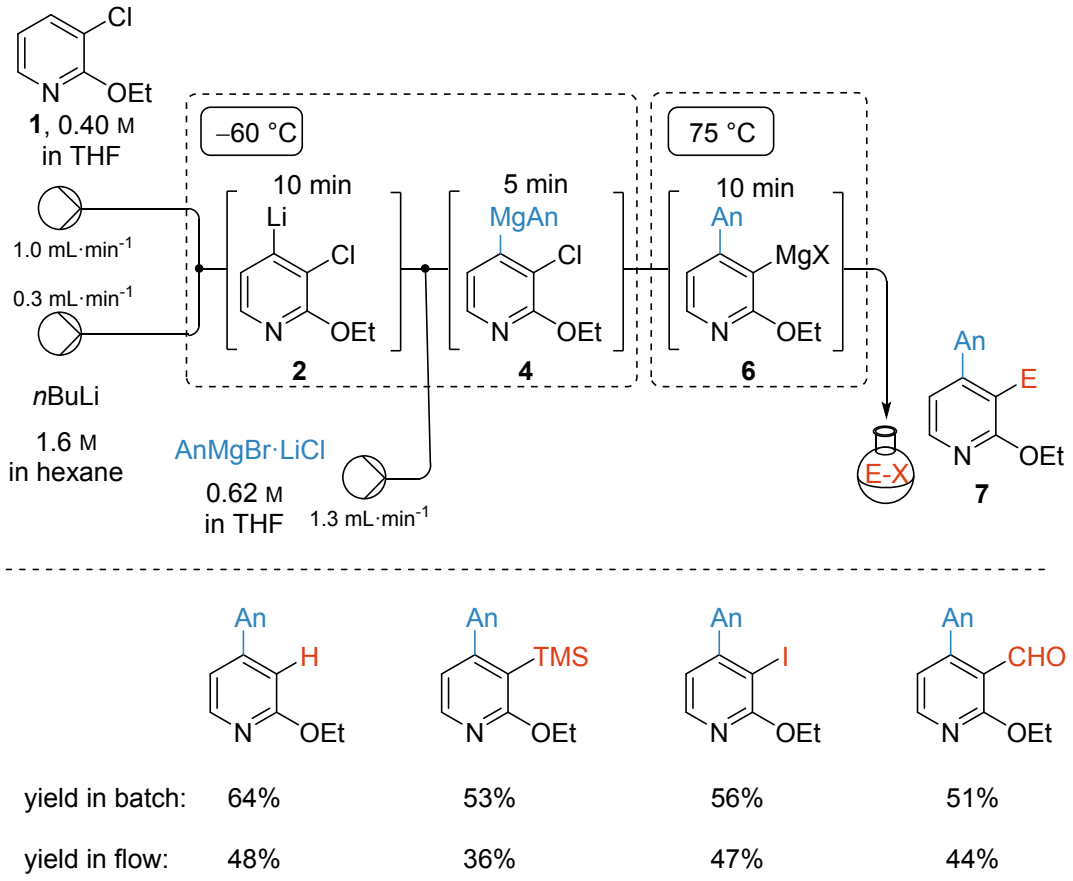
3. Equivalent Screening



Entry	Temperature (°C)	Reaction time (h)	RMgBr Equiv	GC yield (%)[a]
1	75	1	1	32
2	75	1	1.5	46
3	**75**	**1**	**2.0**	**56**
4	75	1	3.0	67
5	75	1	4.0	71
6	75	1	5.0	76
7	75	1	10.0	79

[a] Tetradecane ($C_{14}H_{30}$) was used as internal standard.

Continuous flow/batch comparison starting from 3-chloro-2-ethoxypyridine (1)



yield in batch:	64%	53%	56%	51%
yield in flow:	48%	36%	47%	44%

Figure SI2: Flow chemistry set-up for the preparation of of 2,3,4-trifunctionalized pyridines of type **7**.

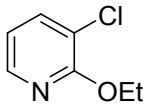
Similar to **TP3**, a solution of **1** in THF (0.10 M, 1.0 equiv) and a solution of *n*-BuLi in *n*-hexane (1.60 M, 1.1 equiv) were prepared. The solutions were pumped from their flasks through a suction needle at flowrate A = 1.0 mL·min^{-1} and flowrate B = 0.3 mL·min^{-1}. After passing a PTFE tubing ($Vol_{pre(A)}$ = 2.0 mL, $Vol_{pre(B)}$ = 0.6 mL, T = –60 °C, residence time: 2 min) for precooling, the solutions were mixed in a T-mixer (PFA or PTFE, I.D. = 0.5 mm). The combined stream passed a PTFE reactor tube (Vol_{R1} = 13 mL; residence time: t = 10 min, T = –60 °C) and a organomagnesium reagent (0.3 M, 6.0 equiv), prepared *via* **TP1**, was added *via* a third pump (flowrate C = 1.3 mL·min^{-1}, Vol_{pre} = 1.3 mL, T = –60 °C, residence time: 1 min). The combined stream passed a PTFE reactors tube (Vol_{R2} = 13 mL; residence time: t = 5 min, T = –60 °C) and was afterwards heated in another PTFE reactors tube (Vol_{R3} = 26 mL; residence time: t = 10 min, T = 75 °C). The reaction mixture was subsequently injected in a flask at 0 °C, containing an electrophile for quenching (3.0 equiv) and the pure products were isolated *via* column chromatography.

Analogously, the same reactions were carried out in batch *via* **TP2**, using the same solutions as used for the continuous flow experiments. The pure products were isolated *via* column chromatography.

This comparison showed, that the continuous flow set-up is not beneficial for the reaction starting from 3-chloro-2-ethoxypyridine (**1**). Even though full metalation was achieved after 10 min residence time at –60 °C (checked *via* in-line iodolysis), the reaction outcome could not compete with the batch procedure. Longer heating time or higher concentrations of organomagnesium reagent might improve the yield but were not achievable due to high pressure and resulting reactor clogging.

Preparation of Products

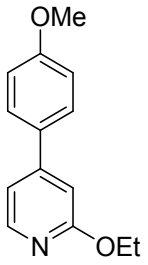
3-Chloro-2-ethoxypyridine (1)



Sodium metal (ca. 6 g) was added to dry ethanol (200 mL) at 0 °C. The resulting suspension was stirred until the sodium was dissolved or the hydrogen liberation ceased. 2,3-Dichloropyridine (14.9 g, 100 mmol) was added and the resulting mixture was refluxed for 12 h. After cooling to 25 °C, the reaction mixture was quenched with *sat. aq.* NH_4Cl. The aqueous phase was extracted with EtOAc and the combined organic phases were dried over Na_2SO_4 and filtrated. After removal of the solvent *in vacuo*, flash column chromatography purification (isohexane:ethyl acetate = 9.7:0.3) afforded the 3-chloro-2-ethoxypyridine (**1**) (13.4 g, 85.0 mmol, 85% yield) as an colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.94 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.52 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.72 (dd, *J* = 7.6, 4.9 Hz, 1H), 4.36 (q, *J* = 7.0 Hz, 2H), 1.35 (t, *J* = 7.0 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 159.2, 144.7, 138.3, 118.3, 117.2, 62.8, 14.6.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2980 (w), 1583 (s), 1472 (m), 1448 (s), 1431 (vs), 1383 (s), 1362 (w), 1352 (m), 1317 (s), 1302 (m), 1281 (w), 1254 (s), 1246 (s), 1129 (m), 1105 (w), 1092 (w), 1072 (s), 1045 (s), 1027 (s), 929 (m), 910 (w), 784 (s), 753 (s), 713 (m), 696 (w).
MS (EI, 70 eV): *m/z* (%) = 144 (33), 142 (100), 130 (14), 129 (42), 113 (19), 103 (15), 101 (46).
HRMS (EI): *m/z* calc. for [C_7H_8ClNO]: 157.0294; found 157.0288.

2-Ethoxy-4-(4-methoxyphenyl)pyridine (7a)

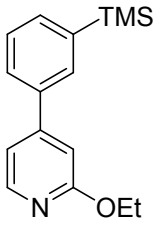


Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat.*

aq. NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give 2-ethoxy-4-(4-methoxyphenyl)pyridine (**7a**) (73.0 mg, 0.32 mmol, 64% yield) as a yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.15 (dd, *J* = 5.4, 0.7 Hz, 1H), 7.60 – 7.54 (m, 2H), 7.05 (dd, *J* = 5.4, 1.6 Hz, 1H), 7.01 – 6.95 (m, 2H), 6.90 (dd, *J* = 1.6, 0.7 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 1.42 (t, *J* = 7.0 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.8, 160.5, 150.7, 147.3, 130.7, 128.2 (2C), 114.9, 114.5 (2C), 107.9, 61.8, 55.5, 14.9.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2977 (w), 1605 (vs), 1582 (m), 1544 (s), 1518 (s), 1473 (m), 1441 (m), 1425 (m), 1405 (w), 1379 (s), 1350 (w), 1327 (s), 1288 (m), 1246 (vs), 1205 (s), 1180 (s), 1056 (m), 1027 (s), 838 (w), 818 (s).
MS (EI, 70 eV): *m/z* (%) = 215 (14), 214 (100), 201 (35), 200 (28), 185 (16), 170 (15), 158 (18).
HRMS (EI): *m/z* calc. for [$C_{14}H_{14}NO_2$]: 228.1019; found 228.1018 [M^+-H].
m.p.: 33.5 – 34.6 °C.

2-Ethoxy-4-(3-(trimethylsilyl)phenyl)pyridine (7b)

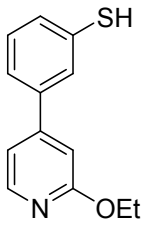


Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-(trimethylsilyl)phenyl)magnesium bromide (1.06 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 2-ethoxy-4-(3-(trimethylsilyl)phenyl)pyridine (**7b**) (76.0 mg, 0.28 mmol, 56% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.20 (dd, *J* = 5.4, 0.7 Hz, 1H), 7.74 (dt, *J* = 1.8, 0.7 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.10 (dd, *J* = 5.4, 1.6 Hz, 1H), 6.95 (dd, *J* = 1.6, 0.7 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 0.31 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.6, 151.9, 147.2, 141.7, 137.7, 134.1, 131.9, 128.5, 127.6, 115.5, 108.9, 62.1, 14.9, -1.0 (3C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (w), 1615 (m), 1603 (s), 1589 (w), 1546 (m), 1470 (m), 1422 (m), 1376 (m), 1348 (m), 1326 (s), 1248 (s), 1206 (s), 1119 (m), 1060 (w), 1039 (s), 990 (w), 951 (w), 862 (s), 836 (vs), 791 (s), 779 (w), 752 (s), 704 (w), 694 (w).
MS (EI, 70 eV): *m/z* (%) = 270 (2), 257 (14), 256 (100), 228 (46).
HRMS (EI): *m/z* calc. for [$C_{16}H_{20}ONSi$]: 270.1308; found 270.1309 [M^+-H].

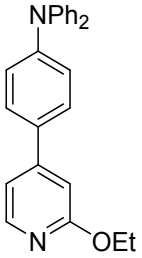
3-(2-Ethoxypyridin-4-yl)benzenethiol (7c)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-(methylthio)phenyl)magnesium bromide (1.00 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 3-(2-ethoxypyridin-4-yl)benzenethiol (**7c**) (60.0 mg, 0.26 mmol, 51% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.92 (d, *J* = 5.6 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.47 – 7.37 (m, 3H), 6.60 (dd, *J* = 5.6, 1.7 Hz, 1H), 6.32 (d, *J* = 1.6 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.9, 145.9, 135.3 (2C), 129.9 (2C), 129.7, 129.4, 114.6, 107.2, 62.2, 14.6.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 1586 (vs), 1580 (vs), 1559 (w), 1542 (s), 1475 (m), 1457 (m), 1440 (m), 1412 (m), 1378 (m), 1347 (m), 1312 (m), 1280 (m), 1221 (w), 1091 (w), 1082 (w), 1043 (s), 1024 (w), 986 (w), 949 (w), 806 (w), 749 (m), 690 (m).
MS (EI, 70 eV): *m/z* (%) = 217 (13), 216 (100), 202 (57), 187 (20), 186 (31).
HRMS (EI): *m/z* calc. for [$C_{13}H_{13}ONS$]: 231.0718; found 231.0714.

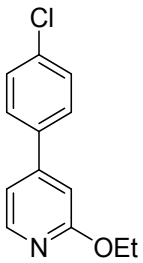
4-(2-Ethoxypyridin-4-yl)-*N,N*-diphenylaniline (7d)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-(diphenylamino)phenyl)magnesium bromide (1.08 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give 4-(2-ethoxypyridin-4-yl)-*N,N*-diphenylaniline (**7d**) (112 mg, 0.31 mmol, 61% yield) as a red oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.18 (dd, *J* = 5.4, 0.7 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.35 – 7.27 (m, 4H), 7.19 – 7.14 (m, 5H), 7.14 – 7.07 (m, 4H), 6.94 (dd, *J* = 1.6, 0.7 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.7, 150.7, 149.0, 147.4 (2C), 147.2, 131.3, 129.5 (4C), 127.7 (2C), 125.1 (4C), 123.6 (2C), 123.0 (2C), 114.7, 107.7, 62.0, 14.9.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 1603 (s), 1589 (vs), 1542 (m), 1515 (s), 1486 (s), 1471 (s), 1451 (w), 1425 (m), 1406 (m), 1380 (m), 1350 (m), 1325 (s), 1274 (s), 1251 (s), 1206 (vs), 1180 (m), 1056 (m), 1035 (m), 942 (w), 840 (w), 815 (s), 754 (s), 732 (m), 696 (vs).
MS (EI, 70 eV): *m/z* (%) = 267 (27), 366 (100), 351 (25), 338 (25).
HRMS (EI): *m/z* calc. for [$C_{25}H_{22}ON_2$]: 366.1732; found 366.1723.

4-(4-Chlorophenyl)-2-ethoxypyridine (7e)

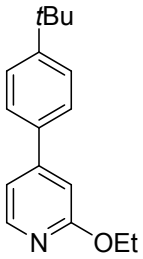


Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-chlorophenyl)magnesium bromide (1.04 mL, 1.00 mmol), prepared *via*

TP1, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 4-(4-chlorophenyl)-2-ethoxypyridine (**7e**) (60.0 mg, 0.26 mmol, 51% yield) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.19 (dd, *J* = 5.4, 0.7 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.46 – 7.40 (m, 2H), 7.04 (dd, *J* = 5.4, 1.6 Hz, 1H), 6.89 (dd, *J* = 1.6, 0.7 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.8, 150.1, 147.5, 136.9, 135.3, 129.3 (2C), 128.4 (2C), 115.0, 108.6, 62.1, 14.8.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2982 (vw), 1608 (w), 1575 (vw), 1545 (w), 1502 (w), 1472 (w), 1423 (w), 1380 (w), 1350 (vw), 1327 (w), 1250 (vw), 1207 (w), 1093 (w), 1057 (w), 1034 (w), 1014 (w), 992 (vw), 904 (s), 874 (w), 838 (w), 814 (m), 725 (vs), 674 (vw).
MS (EI, 70 eV): *m/z* (%) = 220 (32), 219 (12), 218 (100), 205 (31), 204 (21), 189 (28), 177 (23), 154 (22), 115 (15).
HRMS (EI): *m/z* calc. for [$C_{12}H_9ONCl$]: 218.0367; found 218.0367 [M^+-CH_3].
m.p.: 40.4 – 41.2 °C.

4-(4-(*Tert*-butyl)phenyl)-2-ethoxypyridine (7f)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-(*tert*-butyl)phenyl)magnesium bromide (1.11 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 4-(4-(*tert*-butyl)phenyl)-2-ethoxypyridine (**7f**) (55.0 mg, 0.22 mmol, 43% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.18 (dd, *J* = 5.4, 0.7 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.52 – 7.45 (m, 2H), 7.10 (dd, *J* = 5.4, 1.6 Hz, 1H), 6.95 (dd, *J* = 1.6, 0.7 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.0 Hz, 3H), 1.36 (s, 9H).

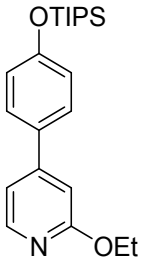
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.7, 152.4, 151.2, 147.2, 135.4, 126.8 (2C), 126.1 (2C), 115.2, 108.4, 62.0, 34.8, 31.4 (3C), 14.9.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2964 (m), 1605 (vs), 1543 (s), 1476 (m), 1421 (s), 1379 (s), 1328 (s), 1208 (s), 1056 (s), 1036 (m), 817 (s).

MS (EI, 70 eV): *m/z* (%) = 241 (18), 240 (100), 227 (11), 212 (41), 211 (11), 184 (13).

HRMS (EI): *m/z* calc. for [$C_{17}H_{20}ON$]: 254.1539; found 254.1538 [M^+-H].

2-Ethoxy-4-(4-((tri*iso*propylsilyl)oxy)phenyl)pyridine (7g)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-((tri*iso*propylsilyl)oxy)phenyl)magnesium bromide (1.04 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 2-ethoxy-4(4((tri*iso*propylsilyl)oxy)phenyl)pyridine (**7g**) (76.0 mg, 0.21 mmol, 41% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.15 (d, *J* = 5.4 Hz, 1H), 7.57 – 7.44 (m, 2H), 7.07 (dd, *J* = 5.5, 1.6 Hz, 1H), 6.97 – 6.93 (m, 2H), 6.91 (d, *J* = 1.6 Hz, 1H), 4.40 (q, *J* = 7.0 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.34 – 1.22 (m, 3H), 1.12 (d, *J* = 7.3 Hz, 18H).

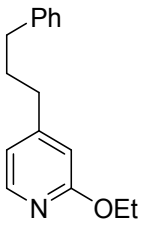
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.5, 157.4, 151.2, 146.8, 130.8, 130.7, 128.2 (2C), 120.5 (2C), 114.9, 107.9, 62.2, 18.0 (6C), 14.9, 12.8 (3C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2943 (m), 2865 (m), 1604 (s), 1543 (m), 1515 (vs), 1471 (s), 1423 (m), 1379 (m), 1326 (m), 1272 (s), 1265 (s), 1249 (s), 1204 (vs), 1174 (m), 1056 (m), 1035 (m), 910 (s), 882 (s), 841 (m), 817 (s), 761 (m), 684 (s).

MS (EI, 70 eV): *m/z* (%) = 371 (9), 328 (43), 300 (38), 290 (26), 273 (15), 272 (100), 258 (35), 228 (10).

HRMS (EI): *m/z* calc. for [$C_{22}H_{33}O_2NSi$]: 371.2281; found 371.2271.

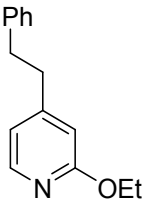
2-Ethoxy-4-(3-phenylpropyl)pyridine (7h)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-phenylpropyl)magnesium bromide (2.55 mL, 2.50 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 2-ethoxy-4-(3-phenylpropyl)pyridine (**7h**) (70.0 mg, 0.29 mmol, 58% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.03 (d, *J* = 5.3 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.22 – 7.15 (m, 3H), 6.69 (dd, *J* = 5.3, 1.5 Hz, 1H), 6.55 (dd, *J* = 1.5, 0.8 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.61 (dt, *J* = 24.8, 7.7 Hz, 4H), 2.00 – 1.82 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.2, 154.5, 146.4, 141.8, 128.5 (2C), 128.5 (2C), 126.1, 117.5, 110.6, 61.9, 35.4, 34.7, 31.7, 14.8.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2934 (m), 1610 (vs), 1558 (s), 1496 (w), 1478 (m), 1453 (m), 1420 (s), 1381 (s), 1351 (w), 1318 (s), 1288 (m), 1158 (m), 1050 (s), 749 (w), 699 (m).
MS (EI, 70 eV): *m/z* (%) = 227 (16), 226 (100), 196 (12), 134 (12), 109 (28).
HRMS (EI): *m/z* calc. for [$C_{16}H_{19}ON$]: 241.1467; found 241.1465.

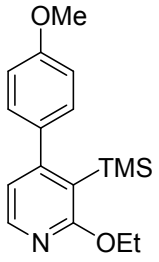
2-Ethoxy-4-phenethylpyridine (7i)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and phenethylmagnesium bromide (2.61 mL, 2.50 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 2-ethoxy-4-phenethylpyridine (**7i**) (64.0 mg, 0.28 mmol, 56% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.07 (dd, *J* = 5.3, 1.1 Hz, 1H), 7.35 – 7.29 (m, 2H), 7.27 – 7.19 (m, 3H), 6.71 (dd, *J* = 5.4, 1.4 Hz, 1H), 6.59 (s, 1H), 4.38 (tdd, *J* = 7.4, 6.9, 1.2 Hz, 2H), 2.98 – 2.87 (m, 4H), 1.52 – 1.37 (m, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.1, 153.1, 146.4, 140.8, 128.3 (2C), 128.2 (2C), 126.0, 117.1, 110.2, 61.3, 36.8, 36.2, 14.5.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2975 (m), 2927 (m), 1609 (vs), 1558 (s), 1496 (m), 1480 (m), 1453 (m), 1440 (w), 1422 (s), 1381 (s), 1319 (s), 1291 (m), 1159 (m), 1050 (s), 814 (w), 698 (m).
MS (EI, 70 eV): *m/z* (%) = 213 (15), 212 (100), 198 (30), 183 (14), 182 (14), 91 (35).
HRMS (EI): *m/z* calc. for [$C_{14}H_{14}ON$]: 212.1070; found 212.1069 [M^+-CH_3].

2-Ethoxy-4-(4-methoxyphenyl)-3-(trimethylsilyl)pyridine (7aa)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 790 mg, 5.00 mmol), *n*-butyllithium (2.10 mL, 5.50 mmol) and (4-methoxyphenyl)magnesium bromide (10.1 mL, 10.0 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with TMSCl (1.59 mL, 12.5 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 2-ethoxy-4-(4-methoxyphenyl)-3-(trimethylsilyl)pyridine (**7aa**) (814 mg, 2.7 mmol, 54% yield) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.06 (d, *J* = 5.2 Hz, 1H), 7.19 – 7.11 (m, 2H), 6.95 – 6.88 (m, 2H), 6.70 (d, *J* = 5.2 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H), -0.01 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.9, 159.9, 159.5, 146.4, 135.3, 129.9 (2C), 119.6, 119.3, 113.4 (2C), 61.8, 55.4, 14.8, 1.1 (3C).

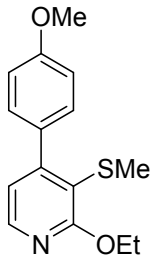
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2953 (w), 1611 (m), 1574 (m), 1528 (m), 1515 (s), 1462 (w), 1448 (m), 1441 (m), 1373 (m), 1331 (s), 1319 (m), 1290 (m), 1269 (m), 1245 (vs), 1174 (m), 1112 (m), 1030 (m), 843 (s), 825 (s), 761 (w), 755 (w).

MS (EI, 70 eV): *m/z* (%) = 301 (26), 300 (12), 283 (20), 256 (15), 242 (22), 241 (100), 239 (11), 225 (26).

HRMS (EI): *m/z* calc. for [$C_{17}H_{23}O_2NSi$]: 301.1498; found 301.1488.

m.p.: 43.1.5 – 45.2 °C.

2-Ethoxy-4-(4-methoxyphenyl)-3-(methylthio)pyridine (7ab)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *S*-methyl-thiomethanesulfonate (158 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.6:0.4) to give 2-ethoxy-4-(4-methoxyphenyl)-3-(methylthio)pyridine (**7ab**) (59.0 mg, 0.22 mmol, 43% yield) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.04 (d, *J* = 5.1 Hz, 1H), 7.33 (d, *J* = 8.7 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 1H), 6.83 (d, *J* = 5.2 Hz, 1H), 4.51 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 2.26 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H).

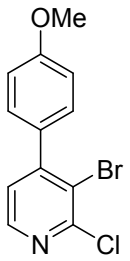
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.8, 160.0, 154.9, 145.1, 132.1, 130.9 (2C), 119.1, 118.2, 113.9 (2C), 63.1, 55.7, 18.4, 15.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 2926 (w), 1609 (m), 1577 (m), 1515 (s), 1453 (m), 1441 (m), 1416 (m), 1402 (w), 1376 (m), 1350 (m), 1337 (s), 1324 (m), 1292 (m), 1273 (m), 1248 (vs), 1177 (m), 1137 (w), 1114 (s), 1028 (s), 1010 (w), 947 (w), 839 (w), 822 (m).

MS (EI, 70 eV): *m/z* (%) = 275 (40), 261 (15), 260 (100), 246 (20), 232 (12), 227 (13), 226 (18), 214 (33), 196 (12).

HRMS (EI): *m/z* calc. for [$C_{15}H_{18}O_2NS$]: 275.0980; found 275.0974.

3-Bromo-2-chloro-4-(4-methoxyphenyl)pyridine (8)



The pyridine **7ac** (308 mg, 1.00 mmol, 1.0 equiv) was dissolved in dry DMF (11.6 mL, 15.0 mmol, 15 equiv). The mixture was cooled to 0 °C, $POCl_3$ (0.28 mL, 3.00 mmol, 3.0 equiv) was added dropwise and the solution was stirred for 1 h at that temperature. After sealing the reaction flask, the reaction mixture was heated to 100 °C and stirred for 4 h. After cooling to 0 °C, it was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give 3-bromo-2-chloro-4-(4-methoxyphenyl)pyridine (**8**) (269 mg, 0.90 mmol, 90% yield) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.24 (d, *J* = 4.8 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.09 (d, *J* = 4.9 Hz, 1H), 6.96 – 6.88 (m, 2H), 3.80 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 160.3, 153.6, 152.4, 147.3, 131.1, 130.2 (2C), 124.6, 120.9, 113.9 (2C), 55.5.

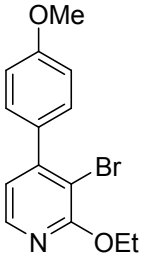
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2362 (s), 2358 (s), 2339 (m), 1608 (m), 1570 (m), 1515 (s), 1506 (m), 1434 (s), 1346 (s), 1297 (m), 1248 (vs), 1180 (s), 1063 (s), 1030 (m), 827 (s), 668 (m).

MS (EI, 70 eV): *m/z* (%) = 300 (24), 299 (100), 297 (77), 175 (21), 140 (39), 113 (23).

HRMS (EI): *m/z* calc. for [$C_{12}H_9ONBrCl$]: 296.9556; found 296.9553.

m.p.: 145.2 – 146.5 °C.

3-Bromo-2-ethoxy-4-(4-methoxyphenyl)pyridine (7ac)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with 1,2-dibromo-tetrachloroethane (407 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 3-bromo-2-ethoxy-4-(4-methoxyphenyl)pyridine (**7ac**) (88.0 mg, 0.29 mmol, 57% yield) as a brown solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.04 (d, *J* = 5.1 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.00 – 6.95 (m, 2H), 6.82 (d, *J* = 5.1 Hz, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 160.6, 159.9, 152.3, 144.7, 131.5, 130.3 (2C), 119.2, 113.7 (2C), 107.5, 63.4, 55.5, 14.7.

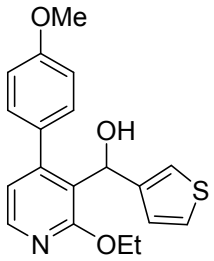
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2928 (m), 2853 (m), 1561 (vs), 1519 (m), 1448 (m), 1358 (m), 1262 (m), 1150 (m), 1087 (m), 809 (m), 792 (s).

MS (EI, 70 eV): *m/z* (%) = 307 (16), 293 (96), 292 (100), 281 (45), 279 (46), 236 (20), 184 (55), 169 (33), 141 (24).

HRMS (EI): *m/z* calc. for [$C_{14}H_{14}O_2NBr$]: 307.0208; found 307.0200.

m.p.: 46.8 – 47.6 °C.

(2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)(thiophen-3-yl)methanol (7ad)



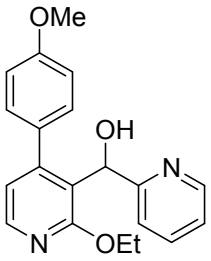
Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via*

TP1, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with freshly purified thiophene-3-carbaldehyde (140 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 8.0:2.0) to give (2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)(thiophen-3-yl)methanol (**7ad**) (102 mg, 0.30 mmol, 60% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.10 (d, *J* = 5.2 Hz, 1H), 7.25 – 7.20 (m, 3H), 6.96 (dt, *J* = 2.9, 1.3 Hz, 1H), 6.94 – 6.90 (m, 3H), 6.86 (d, *J* = 5.2 Hz, 1H), 5.84 (d, *J* = 11.0 Hz, 1H), 4.40 (qd, *J* = 7.0, 2.6 Hz, 2H), 4.15 (d, *J* = 11.9 Hz, 1H), 3.83 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.8, 159.8, 150.6, 145.9, 145.2, 130.6 (2C), 130.0, 126.7, 125.5, 122.6, 120.8, 119.2, 114.1 (2C), 68.5, 62.4, 55.5, 14.6.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3547 (w), 2976 (w), 2835 (w), 1609 (s), 1592 (m), 1578 (w), 1550 (m), 1514 (s), 1463 (m), 1441 (w), 1420 (m), 1405 (m), 1379 (m), 1349 (w), 1324 (m), 1293 (m), 1246 (vs), 1227 (m), 1208 (m), 1178 (s), 1148 (w), 1125 (s), 1110 (w), 1089 (w), 1026 (vs), 953 (w), 841 (m), 826 (m), 788 (m), 738 (w), 729 (w).
MS (EI, 70 eV): *m/z* (%) = 341 (28), 295 (24), 256 (27), 228 (100), 212 (48), 207 (21), 111 (47), 110 (26).
HRMS (EI): *m/z* calc. for [$C_{19}H_{19}O_3NS$]: 341.1086; found 341.1079.

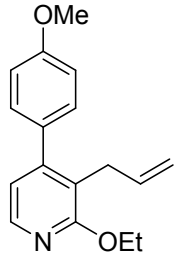
(2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)(pyridin-2-yl)methanol (7ae)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with freshly purified picolinaldehyde (134 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 7.0:3.0) to give (2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)(pyridin-2-yl)methanol (**7ae**) (96.0 mg, 0.29 mmol, 57% yield) as a yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.52 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.08 (d, *J* = 5.3 Hz, 1H), 7.58 (td, *J* = 7.7, 1.7 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.16 – 7.09 (m, 2H), 6.98 – 6.94 (m, 2H), 6.87 (d, *J* = 5.3 Hz, 1H), 5.91 (s, 1H), 5.02 (s, 1H), 3.84 (s, 2H), 0.95 (td, *J* = 7.0, 0.9 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.0, 162.0, 159.8, 152.2, 147.6, 145.7, 136.4, 131.0, 130.5 (2C), 122.3, 121.7, 120.1, 118.9, 114.0 (2C), 69.9, 61.7, 55.5, 14.3.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2364 (s), 2355 (s), 2342 (s), 1609 (s), 1591 (s), 1558 (s), 1539 (m), 1516 (vs), 1506 (s), 1472 (s), 1464 (s), 1456 (s), 1436 (s), 1424 (s), 1419 (s), 1249 (vs), 1030 (s), 668 (s).
MS (EI, 70 eV): *m/z* (%) = 291 (86), 263 (22), 240 (43), 214 (50), 212 (98), 201 (27), 200 (28), 169 (39), 80 (32), 78 (100)
HRMS (EI): *m/z* calc. for [$C_{20}H_{20}O_3N_2$]: 336.1474; found 336.1470.
m.p.: 100.5 – 102.2 °C.

3-Allyl-2-ethoxy-4-(4-methoxyphenyl)pyridine (7af)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with CuCN·2LiCl (0.05 mL, 0.05 mmol) and allyl bromide (0.11 mL, 1.25 mmol) at 0 °C. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.6:0.4) to give 3-allyl-2-ethoxy-4-(4-methoxyphenyl)pyridine (**7af**) (75.0 mg, 0.28 mmol, 56% yield) as a colorless oil.

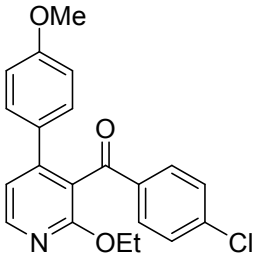
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.04 (d, *J* = 5.2 Hz, 1H), 7.31 – 7.23 (m, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 5.2 Hz, 1H), 5.99 (ddt, *J* = 17.2, 10.1, 6.0 Hz, 1H), 5.01 (dq, *J* = 10.1, 1.6 Hz, 1H), 4.91 (dt, *J* = 17.2, 1.8 Hz, 1H), 4.44 (q, *J* = 7.0 Hz, 2H), 3.88 (s, 3H), 3.32 (dt, *J* = 6.0, 1.7 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.5, 159.4, 151.3, 143.8, 136.8, 131.9, 130.0 (2C), 120.1, 118.6, 115.2, 113.7 (2C), 61.9, 55.4, 31.4, 14.9.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2960 (w), 2927 (w), 2836 (w), 1609 (m), 1588 (s), 1530 (m), 1514 (vs), 1459 (s), 1440 (m), 1417 (w), 1368 (m), 1305 (w), 1290 (m), 1248 (vs), 1180

(s), 1129 (m), 1114 (m), 1097 (m), 1050 (m), 1028 (m), 986 (m), 915 (m), 841 (w), 817 (vs), 770 (m), 696 (w).

MS (EI, 70 eV): *m/z* (%) = 254 (34), 240 (100), 226 (86), 225 (52), 225 (28), 224 (86), 222 (44), 214 (50), 208 (25), 196 (37).

HRMS (EI): *m/z* calc. for [$C_{17}H_{19}O_2N$]: 269.1416; found 269.1410.

(4-Chlorophenyl)(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)methanone (7ag)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with CuCN·2LiCl (0.50 mL, 0.50 mmol) and 4-chlorobenzoyl chloride (219 mg, 1.25 mmol) at 0 °C. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give (4-chlorophenyl)(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)methanone (**7ag**) (107 mg, 0.29 mmol, 58% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.25 (d, *J* = 5.4 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.34 – 7.30 (m, 2H), 7.24 – 7.18 (m, 2H), 6.97 (d, *J* = 5.3 Hz, 1H), 6.82 – 6.75 (m, 2H), 4.35 (q, *J* = 7.0 Hz, 2H), 3.75 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 3H).

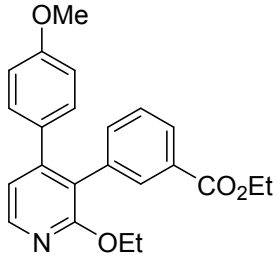
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 194.8, 160.9, 160.1, 150.3, 147.6, 139.8, 135.9, 130.7 (2C), 129.9 (2C), 129.8, 128.9 (2C), 121.1, 117.9, 114.2 (2C), 62.5, 55.3, 14.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 1674 (s), 1609 (m), 1585 (vs), 1547 (m), 1517 (s), 1463 (m), 1420 (m), 1378 (m), 1327 (m), 1298 (m), 1272 (s), 1252 (vs), 1180 (m), 1128 (s), 1091 (m), 1027 (m), 925 (m), 823 (m), 732 (m).

MS (EI, 70 eV): *m/z* (%) = 367 (5), 323 (33), 312 (15), 310 (47), 308 (19), 288 (24), 280 (15), 228 (100), 213 (22), 210 (17), 185 (18), 139 (15).

HRMS (EI): *m/z* calc. for [$C_{21}H_{18}O_3NCl$]: 367.0975; found 367.0971.

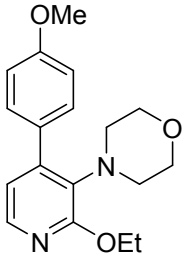
Ethyl 3-(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)benzoate (7ah)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with a solution of $ZnCl_2$ (1.00 mL, 1.00 mmol) in THF at 0 °C. Then, a mixture of ethyl 3-bromobenzoate (286 mg, 1.25 mmol), $Pd(OAc)_2$ (5 mol%) and SPhos (10 mol%) was added. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give ethyl 3-(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)benzoate (**7ah**) (106 mg, 0.28 mmol, 56% yield) as a orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.16 (d, *J* = 5.3 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.30 – 7.21 (m, 3H), 7.01 – 6.94 (m, 3H), 6.74 – 6.68 (m, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.0 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.4, 161.2, 158.8, 150.1, 145.5, 135.7, 135.4, 132.3, 130.9, 130.4 (2C), 129.7, 127.7, 127.5, 121.5, 118.3, 113.3 (2C), 61.8, 60.6, 55.0, 14.4, 14.1.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 1718 (s), 1700 (w), 1609 (m), 1587 (m), 1546 (w), 1515 (s), 1464 (w), 1457 (w), 1441 (w), 1418 (m), 1404 (w), 1378 (m), 1367 (w), 1347 (w), 1323 (w), 1296 (m), 1248 (vs), 1216 (m), 1178 (w), 1132 (m), 1110 (m), 1082 (w), 1031 (m), 823 (m), 754 (w).
MS (EI, 70 eV): *m/z* (%) = 377 (30), 362 (61), 360 (100), 348 (52), 332 (42), 330 (47), 320 (30), 316 (74), 304 (55), 302 (88), 276 (25), 204 (34).
HRMS (EI): *m/z* calc. for [$C_{23}H_{23}O_4N$]: 377.1627; found 377.1624.

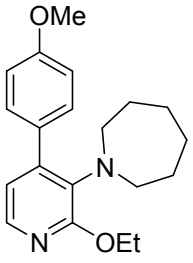
4-(2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)morpholine (7ai)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with a solution of $ZnCl_2$ (0.50 mL, 0.50 mmol) in THF at 0 °C. Then, a solution of *N*-morpholino benzoate (259 mg, 1.25 mmol) was added, followed by a solution of $Cu(OTf)_2$ (10 mol%) in THF. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.3:0.7) to give 4-(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)morpholine (**7ai**) (85.0 mg, 0.27 mmol, 54% yield) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.90 (d, *J* = 5.1 Hz, 1H), 7.42 – 7.35 (m, 2H), 6.97 – 6.92 (m, 2H), 6.79 (d, *J* = 5.2 Hz, 1H), 4.41 (q, *J* = 7.0 Hz, 2H), 3.86 (s, 3H), 3.59 (t, *J* = 4.6 Hz, 4H), 2.97 (t, *J* = 4.2 Hz, 4H), 1.45 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.9, 159.3, 148.1, 141.8, 131.6, 130.8, 130.4 (2C), 118.8, 113.3 (2C), 67.4 (2C), 62.0, 55.3, 50.3 (2C), 14.9.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953 (w), 2849 (w), 1608 (m), 1585 (m), 1513 (s), 1464 (m), 1450 (m), 1440 (m), 1424 (s), 1408 (m), 1380 (s), 1350 (m), 1325 (m), 1290 (m), 1261 (m), 1244 (vs), 1205 (m), 1175 (m), 1127 (s), 1110 (vs), 1028 (s), 952 (w), 925 (m), 844 (m), 820 (s).
MS (EI, 70 eV): *m/z* (%) = 315 (20), 314 (99), 313 (25), 255 (77), 241 (31), 227 (100), 214 (18), 184 (21).
HRMS (EI): *m/z* calc. for [$C_{18}H_{22}O_3N_2$]: 314.1630; found 314.1625.
m.p.: 77.0 – 78.6 °C.

1-(2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)azepane (7aj)

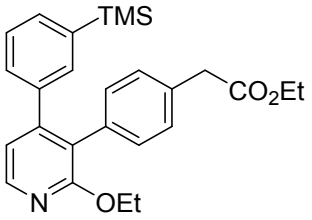


Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (1.02 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with a solution of $ZnCl_2$ (0.50 mL, 0.50 mmol) in THF at 0 °C. Then, a solution of *N*-azepan-1-yl

benzoate (274 mg, 1.25 mmol) was added, followed by a solution of $Cu(OTf)_2$ (10 mol%) in THF. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.3:0.7) to give 1-(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)azepane (**7aj**) (77.0 mg, 0.24 mmol, 47% yield) as an orange solid. *N*-azepan-1-yl benzoate (274 mg, 1.25 mmol)

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.86 (d, *J* = 5.2 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.00 – 6.89 (m, 2H), 6.78 (d, *J* = 5.2 Hz, 1H), 4.42 (q, *J* = 7.0 Hz, 2H), 3.86 (s, 3H), 2.94 (t, *J* = 4.8 Hz, 4H), 1.51 (d, *J* = 1.8 Hz, 8H), 1.44 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.3, 159.2, 147.8, 141.1, 135.1, 131.7, 130.4 (2C), 118.7, 113.4 (2C), 61.8, 55.4, 54.2 (2C), 30.1 (2C), 27.8 (2C), 15.0.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2926 (m), 1609 (m), 1514 (vs), 1464 (m), 1440 (m), 1423 (s), 1379 (m), 1326 (m), 1292 (m), 1246 (vs), 1175 (m), 1128 (s), 1031 (s), 819 (m).
MS (EI, 70 eV): *m/z* (%) = 326 (96), 297 (100), 269 (81), 255 (46), 241 (57), 227 (100), 214 (43).
HRMS (EI): *m/z* calc. for $[C_{20}H_{26}O_2N_2]$: 326.1994; found 326.1990.
m.p.: 81.2 – 82.6 °C.

Ethyl 2-(4-(2-ethoxy-4-(3-(trimethylsilyl)phenyl)pyridin-3-yl)phenyl)acetate (7ba)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-(trimethylsilyl)phenyl)magnesium bromide (1.06 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with a solution of $ZnCl_2$ (1.00 mL, 1.00 mmol) in THF at 0 °C. Then, a mixture of ethyl 2-(4-bromophenyl)acetate (304 mg, 1.25 mmol), $Pd(OAc)_2$ (5 mol%) and SPhos (10 mol%) was added. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give ethyl 2-(4-(2-ethoxy-4-(3-(trimethylsilyl)phenyl)pyridin-3-yl)phenyl)acetate (**7ba**) (119 mg, 0.28 mmol, 55% yield) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm 8.17 (d, *J* = 5.2 Hz, 1H), 7.34 (dt, *J* = 7.2, 1.3 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.20 (dt, *J* = 7.6, 1.7 Hz, 1H), 7.16 – 7.12 (m, 2H), 7.10 – 7.04 (m, 3H), 6.98 (d, *J* = 5.2 Hz, 1H), 4.40 (q, *J* = 7.0 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.54 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.07 (s, 9H).

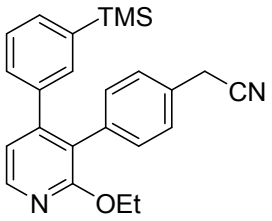
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.6, 161.6, 150.9, 145.5 (2C), 140.0, 138.4, 135.0, 134.3, 132.6, 132.3, 131.4 (2C), 129.6, 128.6 (2C), 127.6, 122.7, 118.6, 62.2, 60.9, 41.3, 14.7, 14.3, -1.3 (3C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2979 (w), 2955 (w), 1736 (s), 1584 (m), 1573 (w), 1547 (m), 1467 (w), 1462 (w), 1419 (m), 1408 (m), 1377 (m), 1346 (m), 1322 (m), 1271 (m), 1262 (m), 1248 (s), 1151 (m), 1138 (s), 1116 (m), 1036 (s), 1002 (m), 863 (m), 838 (vs), 795 (m), 754 (m), 707 (m), 695 (w).

MS (EI, 70 eV): *m/z* (%) = 434 (35), 433 (100), 432 (43), 418 (70), 416 (39), 404 (36), 346 (41), 316 (54), 73 (46).

HRMS (EI): *m/z* calc. for [$C_{26}H_{31}O_3NSi$]: 433. 2073; found 433.2069.

2-(4-(2-Ethoxy-4-(3-(trimethylsilyl)phenyl)pyridin-3-yl)phenyl)acetonitrile (7bb)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-(trimethylsilyl)phenyl)magnesium bromide (1.06 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with a solution of $ZnCl_2$ (1.00 mL, 1.00 mmol) in THF at 0 °C. Then, a mixture of 2-(4-bromophenyl)acetonitrile (245 mg, 1.25 mmol), $Pd(OAc)_2$ (5 mol%) and SPhos (10 mol%) was added. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 2-(4-(2-ethoxy-4-(3-(trimethylsilyl)phenyl)pyridin-3-yl)phenyl)acetonitrile (**7bb**) (102 mg, 0.27 mmol, 53% yield) as an orange solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.25 (d, *J* = 5.2 Hz, 1H), 7.41 (dt, *J* = 7.3, 1.3 Hz, 1H), 7.34 – 7.23 (m, 3H), 7.22 – 7.17 (m, 1H), 7.16 – 7.12 (m, 2H), 7.09 (dd, *J* = 2.0, 1.1 Hz, 1H), 7.05 (d, *J* = 5.2 Hz, 1H), 4.46 (q, *J* = 7.0 Hz, 2H), 3.65 (s, 2H), 1.37 (t, *J* = 7.0 Hz, 3H), 0.13 (d, *J* = 0.6 Hz, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.4, 151.1, 145.9, 140.2, 138.1, 136.7, 134.9, 132.5, 131.1, 130.9, 129.6, 129.3, 128.6, 127.7, 126.3, 122.1, 118.5, 117.8, 62.3, 23.6, 14.7, -1.2 (3C).

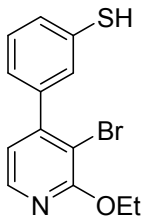
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955 (w), 1584 (m), 1547 (m), 1413 (s), 1378 (s), 1347 (m), 1322 (m), 1276 (m), 1263 (m), 1249 (m), 1138 (m), 1117 (m), 1040 (m), 863 (m), 838 (vs), 794 (m), 754 (m), 708 (m).

MS (EI, 70 eV): *m/z* (%) = 386 (6), 372 (33), 371 (100), 343 (16).

HRMS (EI): *m/z* calc. for [$C_{24}H_{26}ON_2Si$]: 386.1814; found 386.1805.

m.p.: 73.8 – 75.3 °C.

3-(3-Bromo-2-ethoxypyridin-4-yl)benzenethiol (7ca)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-(methylthio)phenyl)magnesium bromide (1.00 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with 1,2-dibromotetrachloroethane (407 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 3-(3-bromo-2-ethoxypyridin-4-yl)benzenethiol (**7ca**) (81.0 mg, 0.26 mmol, 52% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.98 (dq, *J* = 14.3, 8.8, 7.3 Hz, 1H), 7.55 (ddd, *J* = 37.8, 18.9, 8.2 Hz, 2H), 7.32 (td, *J* = 12.0, 5.7 Hz, 1H), 6.64 (p, *J* = 7.9, 7.1 Hz, 1H), 6.43 – 6.32 (m, 1H), 4.34 (dp, *J* = 21.2, 6.9 Hz, 2H), 1.77 (s, 1H), 1.37 (tq, *J* = 9.9, 5.6, 4.2 Hz, 3H).

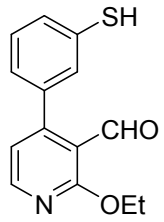
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 164.4, 150.9, 146.8, 137.3, 133.4, 132.6, 132.4, 131.2, 123.4, 115.1, 108.1, 62.0, 14.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2978 (w), 1584 (vs), 1574 (s), 1562 (s), 1542 (s), 1459 (s), 1411 (m), 1378 (s), 1347 (m), 1312 (s), 1280 (m), 1222 (m), 1084 (m), 1070 (w), 1042 (vs), 986 (w), 949 (m), 851 (w), 806 (m), 780 (m), 757 (m), 681 (m).

MS (EI, 70 eV): *m/z* (%) = 310 (62), 308 (64), 282 (100), 280 (99), 201 (86), 154 (81), 127 (82).

HRMS (EI): *m/z* calc. for [$C_{13}H_{12}ONBrS$]: 308.9823; found 308.9818.

2-Ethoxy-4-(3-mercaptophenyl)nicotinaldehyde (7cb)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-(methylthio)phenyl)magnesium bromide (1.00 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with DMF (excess) and heated to 75 °C for 1 h. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give 2-ethoxy-4-(3-mercaptophenyl)nicotinaldehyde (**7cb**) (64.0 mg, 0.25 mmol, 49% yield) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm 10.01 (s, 1H), 8.02 (t, *J* = 1.8 Hz, 1H), 7.95 (d, *J* = 5.5 Hz, 1H), 7.92 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.77 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 6.61 (dd, *J* = 5.5, 1.6 Hz, 1H), 6.34 (d, *J* = 1.6 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H).

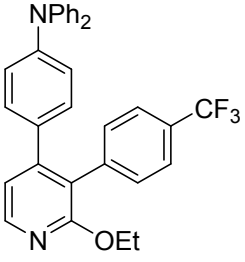
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 191.2, 164.4, 150.6, 146.9, 140.3, 137.8, 135.7, 132.2, 130.6, 130.3, 115.2, 108.3, 62.1, 14.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2979 (w), 1699 (s), 1583 (vs), 1543 (s), 1469 (m), 1460 (m), 1412 (m), 1378 (s), 1348 (m), 1312 (m), 1280 (m), 1222 (m), 1197 (s), 1086 (m), 1042 (s), 986 (w), 950 (w), 865 (w), 795 (m), 731 (w), 684 (m).

MS (EI, 70 eV): *m/z* (%) = 245 (14), 244 (100), 230 (35), 214 (10), 202 (29), 186 (16), 184 (12).

HRMS (EI): *m/z* calc. for [$C_{14}H_{13}O_2NS$]: 259.0667; found 259.0671.

4-(2-Ethoxy-3-(4-(trifluoromethyl)phenyl)pyridin-4-yl)-*N,N*-diphenylaniline (7da)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-(diphenylamino)phenyl)magnesium bromide (1.08 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with a solution of $ZnCl_2$ (1.00 mL, 1.00 mmol) in THF at 0 °C. Then, a mixture of 1-bromo-4-(trifluoromethyl)benzene (245 mg, 1.25 mmol), $Pd(OAc)_2$ (5 mol%) and SPhos (10 mol%) was added. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 4-(2-ethoxy-3-(4-(trifluoromethyl)phenyl)pyridin-4-yl)-*N,N*-diphenylaniline (**7da**) (136 mg, 0.27 mmol, 53% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.18 (d, *J* = 5.3 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.25 (dt, *J* = 8.8, 7.3 Hz, 6H), 7.07 – 6.97 (m, 7H), 6.86 (s, 4H), 4.39 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.0 Hz, 3H).

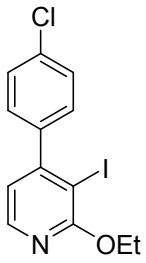
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.3, 150.8, 147.5, 147.4, 146.2, 139.8, 132.2, 131.7, 130.3, 129.4, 124.8, 124.5, 124.2, 123.4, 122.4, 121.5, 118.3, 62.3, 14.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2976 (vw), 2929 (vw), 1588 (m), 1511 (m), 1494 (m), 1487 (m), 1324 (vs), 1292 (w), 1273 (m), 1164 (m), 1126 (m), 1105 (m), 1068 (m), 697 (m).

MS (EI, 70 eV): *m/z* (%) = 367 (28), 366 (100), 352 (23), 351 (87), 339 (16), 338 (62), 337 (22), 167 (16).

HRMS (EI): *m/z* calc. for [$C_{32}H_{25}ON_2F_3$]: 510.1919; found 510. 1915.

4-(4-Chlorophenyl)-2-ethoxy-3-iodopyridine (7ea)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-chlorophenyl)magnesium bromide (1.04 mL, 1.00 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with iodine (318 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 4-(4-chlorophenyl)-2-ethoxy-3-iodopyridine (**7ea**) (90.0 mg, 0.25 mmol, 50% yield) as an orange solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.04 (d, *J* = 5.0 Hz, 1H), 7.49 – 7.35 (m, 2H), 7.32 – 7.17 (m, 2H), 6.76 (d, *J* = 5.0 Hz, 1H), 4.45 (q, *J* = 7.0 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 162.6, 156.2, 146.3, 140.8, 134.7, 130.2 (2C), 128.6 (2C), 118.3, 84.9, 63.7, 14.7.

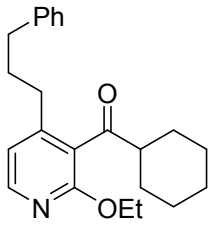
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2980 (w), 1598 (m), 1579 (m), 1522 (m), 1492 (m), 1467 (w), 1450 (m), 1413 (s), 1397 (w), 1377 (s), 1338 (vs), 1321 (m), 1277 (w), 1264 (w), 1131 (w), 1102 (m), 1088 (vs), 1034 (m), 1016 (s), 1005 (s), 948 (w), 817 (s).

MS (EI, 70 eV): *m/z* (%) = 359 (57), 346 (30), 344 (100), 330 (55), 188 (51), 149 (34), 141 (27), 140 (32), 113 (29).

HRMS (EI): *m/z* calc. for [$C_{13}H_{11}ONCII$]: 358.9574; found 358.9572.

m.p.: 76.8 – 78.2 °C.

Cyclohexyl(2-ethoxy-4-(3-phenylpropyl)pyridin-3-yl)methanone (7ha)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (3-phenylpropyl)magnesium bromide (2.55 mL, 2.50 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with CuCN·2LiCl (2.50 mL, 2.50 mmol) and cyclohexanecarbonyl chloride (219 mg, 2.75 mmol) at 0 °C. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give cyclohexyl(2-ethoxy-4-(3-phenylpropyl)pyridine-3-yl) methanone (**7ha**) (97.0 mg, 0.28 mmol, 55% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.02 (d, *J* = 5.3 Hz, 1H), 7.30 – 7.27 (m, 2H), 7.22 – 7.14 (m, 3H), 6.74 (d, *J* = 5.3 Hz, 1H), 4.37 (q, *J* = 7.0 Hz, 2H), 2.83 (tt, *J* = 11.4, 3.4 Hz, 1H), 2.65 (t, *J* = 7.7 Hz, 2H), 2.51 – 2.41 (m, 2H), 1.90 (m, 4H), 1.82 – 1.73 (m, 2H), 1.70 – 1.64 (m, 1H), 1.59 (s, 2H), 1.35 (t, *J* = 7.0 Hz, 3H), 1.26 – 1.17 (m, 3H).

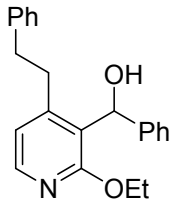
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 209.4, 160.5, 151.3, 146.8, 141.8, 128.5 (4C), 126.0 (4C), 124.4, 117.8, 62.2, 51.4, 35.8, 32.4, 32.3, 28.4, 26.0, 26.0, 14.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2938 (m), 1610 (vs), 1558 (s), 1496 (w), 1478 (w), 1453 (m), 1420 (s), 1381 (s), 1319 (s), 1288 (m), 1159 (m), 1051 (s), 748 (w), 733 (m), 699 (m).

MS (EI, 70 eV): *m/z* (%) = 269 (14), 168 (75), 240 (19), 163 (10), 162 (100), 134 (73), 91 (15).

HRMS (EI): *m/z* calc. for [$C_{23}H_{30}O_2N$]: 352.2271; found 352.2266 [$M+H^+$]

(2-Ethoxy-4-phenethylpyridin-3-yl)(phenyl)methanol (7ia)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and phenethylmagnesium bromide (2.61 mL, 2.50 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with benzaldehyde (0.28 mL mg, 2.75 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.4:0.6) to give (2-ethoxy-4-phenethylpyridin-3-yl)(phenyl)methanol (**7ia**) (82.0 mg, 0.25 mmol, 49% yield) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.01 (d, *J* = 5.2 Hz, 1H), 7.33 – 7.27 (m, 5H), 7.26 – 7.17 (m, 3H), 7.16 – 7.11 (m, 2H), 6.77 (d, *J* = 5.3 Hz, 1H), 6.12 (d, *J* = 10.7 Hz, 1H), 4.40 – 4.25 (m, 2H), 3.99 (d, *J* = 10.9 Hz, 1H), 3.09 – 2.90 (m, 2H), 2.89 – 2.81 (m, 2H), 1.17 (t, *J* = 7.0 Hz, 3H).

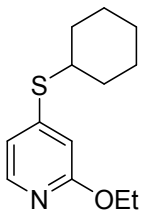
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.5, 145.3, 143.6, 140.8, 128.7 (2C), 128.5 (2C), 128.3 (2C), 127.1, 126.4, 125.8 (2C), 123.5, 119.0, 69.7, 62.5, 36.8, 34.7, 14.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3026 (w), 2978 (w), 1595 (m), 1564 (m), 1416 (m), 1381 (m), 1333 (m), 1316 (m), 1058 (m), 1035 (m), 1024 (m), 904 (m), 727 (s), 698 (vs).

MS (EI, 70 eV): *m/z* (%) = 304 (12), 286 (33), 226 (28), 211 (14), 210 (100), 208 (25), 196 (14), 178 (12), 148 (11), 91 (25).

HRMS (EI): *m/z* calc. for [$C_{22}H_{23}O_2N$]: 333.1729; found 333.1723.

4-(Cyclohexylthio)-2-ethoxypyridine (10a)

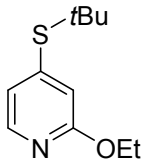


Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium cyclohexanethiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to cyclohexanethiol at 0 °C, were mixed in a sealed tube.

Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.9:0.1) to give 4-(cyclohexylthio)-2-ethoxypyridine (**10a**) (85.0 mg, 0.36 mmol, 72% yield) as an orange oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.19 (dd, *J* = 5.5, 0.7 Hz, 1H), 6.99 (dd, *J* = 1.8, 0.7 Hz, 1H), 6.81 (dd, *J* = 5.4, 1.8 Hz, 1H), 3.31 (tt, *J* = 10.2, 3.7 Hz, 1H), 3.15 (q, *J* = 7.3 Hz, 2H), 2.09 – 1.99 (m, 2H), 1.85 – 1.74 (m, 2H), 1.70 – 1.60 (m, 1H), 1.50 – 1.23 (m, 8H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 159.4, 148.7, 119.4, 118.0, 43.6, 33.0, 26.0, 25.7, 24.7, 14.8.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2928 (m), 2852 (m), 1583 (vs), 1538 (s), 1460 (m), 1449 (m), 1409 (m), 1376 (s), 1346 (m), 1310 (s), 1280 (s), 1263 (m), 1220 (m), 1087 (s), 1042 (vs), 997 (m), 986 (m), 949 (m), 931 (m), 842 (m), 803 (m).
MS (EI, 70 eV): *m/z* (%) = 222 (76), 209 (13), 140 (100), 128 (44), 127 (62), 111 (13), 99 (16).
HRMS (EI): *m/z* calc. for [$C_{13}H_{20}ONS$]: 238.1260; found 238.1259 [$M+H^+$]

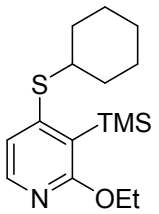
4-(*Tert*-butylthio)-2-ethoxypyridine (10b)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium 2-methylpropane-2-thiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to 2-methylpropane-2-thiol at 0 °C, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.9:0.1) to give 4-(*tert*-butylthio)-2-ethoxypyridine (**10b**) (73.0 mg, 0.35 mmol, 69% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): 8.05 (d, *J* = 5.3 Hz, 1H), 6.93 (dd, *J* = 5.3, 1.5 Hz, 1H), 6.86 (d, *J* = 1.4 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.38 (d, *J* = 9.0 Hz, 12H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.9, 146.2, 122.7, 116.8, 62.2, 47.1, 31.4 (3C), 14.8.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2974 (m), 2963 (m), 1583 (vs), 1540 (vs), 1471 (m), 1461 (m), 1407 (m), 1377 (s), 1364 (m), 1345 (s), 1311 (m), 1273 (m), 1218 (m), 1164 (m), 1043 (s).
MS (EI, 70 eV): *m/z* (%) = 155 (55), 140 (58), 127 (100), 57 (19).
HRMS (EI): *m/z* calc. for [$C_{11}H_{17}ONS$]: 211.2031; found 211.2023.

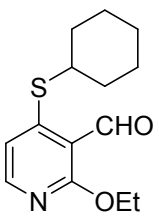
4-(Cyclohexylthio)-2-ethoxy-3-(trimethylsilyl)pyridine (10aa)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium cyclohexanethiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to cyclohexanethiol at 0 °C, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with TMSCl (0.16 mL, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 4-(cyclohexylthio)-2-ethoxy-3-(trimethylsilyl)pyridine (**10aa**) (110 mg, 0.36 mmol, 71% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.93 (d, *J* = 5.5 Hz, 1H), 6.83 – 6.70 (m, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 3.27 (tt, *J* = 10.3, 3.6 Hz, 1H), 2.08 – 1.98 (m, 2H), 1.83 – 1.74 (m, 2H), 1.69 – 1.60 (m, 1H), 1.46 – 1.22 (m, 7H), 0.38 (s, 9H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.5, 157.4, 146.5, 119.3, 115.5, 61.9, 45.2, 33.2, 26.2, 25.9 (2C), 14.7 (2C), 2.5 (3C).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2930 (m), 2900 (w), 2854 (w), 1558 (s), 1524 (s), 1448 (m), 1427 (m), 1372 (m), 1328 (s), 1290 (m), 1262 (m), 1245 (s), 1048 (s), 1035 (s), 997 (w), 953 (w), 842 (vs), 800 (m), 782 (m), 762 (w), 750 (m), 736 (m), 693 (w), 686 (w).
MS (EI, 70 eV): *m/z* (%) = 294 (25), 228 (30), 227 (71), 226 (27), 212 (98), 184 (39), 168 (100), 83 (20), 73 (31), 55 (49), 41 (31).
HRMS (EI): *m/z* calc. for [$C_{16}H_{27}ONSSi$]: 309.1583; found 309.1575.

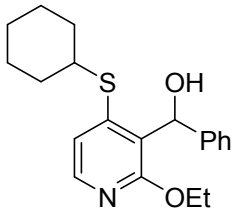
4-(Cyclohexylthio)-2-ethoxynicotinaldehyde (10ab)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium cyclohexanethiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to cyclohexanethiol at 0 °C, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with DMF (excess) and heated to 75 °C for 1 h. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 4-(cyclohexylthio)-2-ethoxynicotinaldehyde (**10ab**) (66.0 mg, 0.25 mmol, 50% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 10.51 (d, *J* = 0.7 Hz, 1H), 8.06 (d, *J* = 5.8 Hz, 1H), 6.87 (d, *J* = 5.8 Hz, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 3.29 (tt, *J* = 10.7, 3.6 Hz, 1H), 2.09 (dd, *J* = 10.4, 4.8 Hz, 2H), 1.84 (dt, *J* = 12.8, 3.7 Hz, 2H), 1.74 – 1.65 (m, 1H), 1.54 – 1.37 (m, 7H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 189.4, 165.7, 157.7, 148.2, 115.0, 113.4, 64.1, 43.0, 32.6, 26.2, 25.7 (2C), 14.7 (2C).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2930 (m), 1670 (s), 1571 (s), 1530 (vs), 1447 (s), 1376 (m), 1339 (m), 1297 (w), 1274 (m), 1038 (s).
MS (EI, 70 eV): *m/z* (%) = 250 (47), 236 (80), 232 (27), 204 (27), 182 (52), 156 (22), 154 (100), 139 (23), 127 (64), 111 (21).
HRMS (EI): *m/z* calc. for [$C_{14}H_{18}O_2NS$]: 264.1053; found 264.1052 [M^+-H]

(4-(Cyclohexylthio)-2-ethoxypyridin-3-yl)(phenyl)methanol (10ac)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium cyclohexanethiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to cyclohexanethiol at 0 °C, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with benzaldehyde (0.13 mL, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give (4-(cyclohexylthio)-2-ethoxypyridin-3-yl)(phenyl)methanol (**10ac**) (121 mg, 0.36 mmol, 71% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.93 (d, *J* = 5.5 Hz, 1H), 7.32 (dq, *J* = 6.6, 1.3 Hz, 2H), 7.29 – 7.23 (m, 2H), 7.22 – 7.16 (m, 1H), 6.88 (d, *J* = 5.6 Hz, 1H), 6.31 (d, *J* = 10.9 Hz, 1H),

4.30 (dtq, *J* = 17.5, 10.4, 7.1 Hz, 3H), 3.28 (tt, *J* = 10.5, 3.7 Hz, 1H), 2.02 (tt, *J* = 11.8, 4.0 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.65 – 1.56 (m, 1H), 1.47 – 1.24 (m, 4H), 1.19 (t, *J* = 7.1 Hz, 3H).

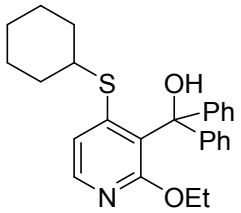
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.2, 147.8, 144.9, 143.3, 128.1 (2C), 126.9, 125.6 (2C), 124.1, 116.7, 70.5, 62.3, 45.5, 33.1, 26.0, 25.7 (2C), 14.5 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2929 (m), 2852 (w), 1575 (s), 1541 (s), 1448 (s), 1406 (m), 1378 (s), 1346 (m), 1331 (w), 1306 (m), 1261 (m), 1221 (s), 1203 (m), 1181 (w), 1168 (w), 1034 (vs), 1023 (s), 997 (m), 958 (m), 941 (w), 909 (m), 863 (m), 815 (w), 802 (m), 732 (s), 696 (s).

MS (EI, 70 eV): *m/z* (%) = 260 (29), 232 (17), 214 (27), 182 (23), 154 (100), 115 (11), 77 (24).

HRMS (EI): *m/z* calc. for [$C_{20}H_{25}O_2NS$]: 343.1606; found 343.1593.

(4-(Cyclohexylthio)-2-ethoxypyridin-3-yl)diphenylmethanol (10ad)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium cyclohexanethiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to cyclohexanethiol at 0 °C, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with benzophenone (228 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.6:0.4) to give (4-(cyclohexylthio)-2-ethoxypyridin-3-yl)diphenylmethanol (**10ad**) (141 mg, 0.34 mmol, 67% yield) as a colorless oil.

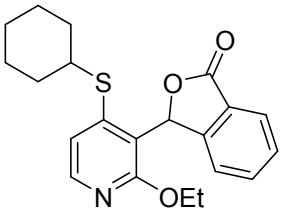
^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.88 (d, *J* = 5.5 Hz, 1H), 7.31 – 7.16 (m, 10H), 6.85 (d, *J* = 5.5 Hz, 1H), 6.07 (s, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 2.94 (dp, *J* = 10.5, 3.8, 2.9 Hz, 1H), 1.77 (dd, *J* = 9.6, 5.2 Hz, 2H), 1.62 (dq, *J* = 10.3, 3.1, 2.6 Hz, 2H), 1.54 – 1.45 (m, 1H), 1.19 – 1.05 (m, 5H), 0.88 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.5, 149.0, 146.3 (2C), 144.1, 129.2, 128.1 (4C), 127.8 (4C), 127.4 (2C), 118.4, 81.9, 62.4, 46.3, 32.6, 25.9, 25.7 (2C), 14.0 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2928 (m), 2852 (w), 1568 (m), 1531 (s), 1492 (w), 1445 (s), 1405 (m), 1377 (m), 1335 (s), 1294 (m), 1271 (w), 1262 (w), 1248 (m), 1034 (s), 1012 (m), 956 (m), 922 (w), 905 (m), 886 (m), 759 (s), 732 (m), 698 (vs), 655 (w).

MS (EI, 70 eV): *m/z* (%) = 290 (100), 242 (88), 214 (75), 202 (43), 198 (31), 165 (55), 91 (31).
HRMS (EI): *m/z* calc. for [$C_{26}H_{27}ONS$]: 401.1802; found 401.1803 [M^+-H_2O]

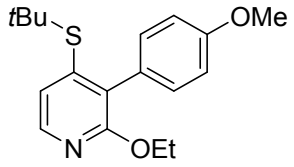
3-(4-Cyclohexylthio)-2-ethoxypyridin-3-yl)isobenzofuran-1(3*H*)-one (10ae)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium cyclohexanethiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to cyclohexanethiol at 0 °C, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with ethyl 2-formylbenzoate (223 mg, 1.25 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.4:0.6) to give 3-(4-cyclohexylthio)-2-ethoxypyridin-3-yl) isobenzofuran-1(3*H*)-one (**10ad**) (131 mg, 0.36 mmol, 71% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = δ 8.00 – 7.97 (m, 1H), 7.95 – 7.90 (m, 1H), 7.58 (tt, *J* = 7.7, 1.5 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.22 (dq, *J* = 7.5, 1.0 Hz, 1H), 7.17 (s, 1H), 6.93 (d, *J* = 5.5 Hz, 1H), 4.15 – 3.91 (m, 2H), 3.42 – 3.22 (m, 1H), 2.04 (t, *J* = 17.3 Hz, 2H), 1.80 (t, *J* = 14.6 Hz, 2H), 1.65 (d, *J* = 11.9 Hz, 1H), 1.57 – 1.25 (m, 5H), 0.90 (d, *J* = 8.6 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 171.4, 162.3, 149.7, 149.5, 146.9, 133.7, 128.8, 127.7, 125.1, 121.7, 117.3, 62.1, 46.6, 33.2, 33.2, 26.0, 25.9 (2C), 25.7, 13.9 (2C).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2929 (m), 2853 (w), 1762 (vs), 1573 (m), 1545 (m), 1465 (m), 1450 (m), 1417 (m), 1381 (m), 1328 (m), 1308 (m), 1284 (m), 1263 (w), 1207 (w), 1091 (w), 1057 (m), 1039 (s), 1013 (m), 997 (m), 964 (m), 816 (w), 744 (m), 723 (w), 687 (w).
MS (EI, 70 eV): *m/z* (%) = 351 (15), 243 (15), 242 (100), 226 (11), 214 (50), 165 (20).
HRMS (EI): *m/z* calc. for [$C_{21}H_{23}O_3NS$]: 369.1399; found 369.1393.

4-(*Tert*-butylthio)-2-ethoxy-3-(4-methoxyphenyl)pyridine (10ba)



Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 79.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and magnesium 2-methylpropane-2-thiolate (1.00 mL, 1.00 mmol), prepared *via* addition of *i*PrMgCl·LiCl (1.05 equiv) to 2-methylpropane-2-thiol at 0 °C, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with a solution of $ZnCl_2$ (1.00 mL, 1.00 mmol) in THF at 0 °C. Then, a mixture of 1-bromo-4-methoxybenzene (234 mg, 1.25 mmol), $Pd(OAc)_2$ (5 mol%) and SPhos (10 mol%) was added. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 4-(*tert*-butylthio)-2-ethoxy-3-(4-methoxyphenyl)pyridine (**10ba**) (106 mg, 0.34 mmol, 67% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm 8.02 (d, *J* = 5.4 Hz, 1H), 7.19 – 7.16 (m, 2H), 7.15 (d, *J* = 5.4 Hz, 1H), 6.94 – 6.91 (m, 2H), 4.34 (q, *J* = 7.0 Hz, 2H), 3.85 (d, *J* = 1.3 Hz, 3H), 1.33 – 1.20 (m, 12H).

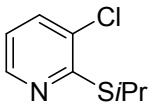
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 161.6, 158.8, 143.9, 132.2 (2C), 127.8, 127.6, 121.9, 113.1 (2C), 62.4, 55.3, 47.8, 31.4 (3C), 14.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2974 (m), 2961 (m), 1611 (m), 1565 (m), 1541 (s), 1511 (m), 1465 (m), 1456 (m), 1441 (m), 1415 (m), 1407 (m), 1377 (s), 1364 (m), 1345 (m), 1291 (m), 1269 (m), 1245 (vs), 1226 (m), 1175 (s), 1161 (m), 1041 (s), 996 (m), 828 (m).

MS (EI, 70 eV): *m/z* (%) = 261 (27), 260 (23), 246 (36), 232 (100), 228 (15), 214 (24).

HRMS (EI): *m/z* calc. for [$C_{18}H_{23}O_2NS$]: 317.1442; found 317.1442.

3-Chloro-2-(isopropylthio)pyridine (11)

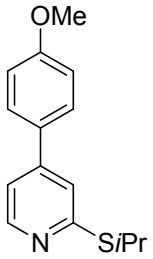


Sodium 2-propanethiolate (3.53 g, 36.0 mmol, 1.2 equiv) was added to a solution of 2,3-dichloropyridine (4.44 g, 30 mmol, 1.0 equiv) in DMF (120 mL) at 0 °C. After stirring the reaction for 12 h at 25 °C, the mixture was quenched with water and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and filtered. After removal of the solvent *in vacuo*, flash column chromatography purification

(isohexane:ethyl acetate = 9.8:0.2) afforded the pure product (5.24 g, 27.9 mmol, 93% yield) as an colorless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.34 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.52 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.93 (dd, *J* = 7.9, 4.7 Hz, 1H), 4.05 (p, *J* = 6.8 Hz, 1H), 1.43 (d, *J* = 6.8 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 158.0, 147.1, 135.9, 129.2, 119.5, 35.2, 23.1 (2C).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2964 (w), 2926 (w), 1566 (m), 1461 (w), 1454 (w), 1432 (w), 1386 (vs), 1365 (w), 1242 (w), 1145 (m), 1126 (m), 1055 (m), 1037 (m), 1028 (m), 785 (m), 762 (m), 729 (m), 656 (m).
MS (EI, 70 eV): *m/z* (%) = 187 (19), 172 (15), 156 (27), 154 (82), 152 (12), 147 (33), 145 (100), 110 (73).
HRMS (EI): *m/z* calc. for [$C_8H_{10}ClNS$]: 187.0222; found 187.0216.

2-(Isopropylthio)-4-(4-methoxyphenyl)pyridine (12a)



Flow procedure: A solution of 3-chloro-2-(isopropylthio)pyridine (**10**) in THF (0.10 M, 1.0 equiv, pump A), *n*-butyllithium in *n*-hexane (0.11 M, 1.1 equiv, pump B) and (4-methoxyphenyl) magnesium bromide in THF (0.3 M, 6.0 equiv, pump C) were prepared. According to **TP3**, the reaction was run in continuous flow (suction-time pump A = 30 min) and afterwards in*J*ected into a flask containing *sat. aq*. NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give 2-(isopropylthio)-4-(4-methoxyphenyl) pyridine (**12a**) (444 mg, 1.71 mmol, 57% yield) as a yellow solid.

Batch procedure: Following **TP2**, 3-chloro-2-(isopropylthio)pyridine (**10**, 94.0 mg, 0.50 mmol), *n*-butyllithium (0.21 mL, 0.55 mmol) and (4-methoxyphenyl)magnesium bromide (3.12 mL, 3.0 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with *sat. aq.* NH_4Cl. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give 2-(isopropylthio)-4-(4-methoxyphenyl)pyridine (**12a**) (73.0 mg, 0.28 mmol, 56% yield) as a yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm 8.45 (dd, *J* = 5.3, 0.8 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.35 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.17 (dd, *J* = 5.3, 1.7 Hz, 1H), 7.01 – 6.96 (m, 2H), 4.06 (p, *J* = 6.8 Hz, 1H), 3.86 (s, 3H), 1.43 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 160.7, 159.9, 149.7, 148.3, 130.2, 128.3 (2C), 120.2, 117.5, 114.7 (2C), 55.5, 35.5, 23.4 (2C).

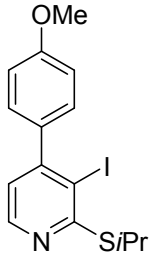
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2962 (w), 2928 (w), 1610 (m), 1590 (vs), 1531 (m), 1516 (vs), 1460 (s), 1441 (m), 1367 (m), 1291 (m), 1251 (vs), 1181 (m), 1130 (m), 1114 (w), 1054 (m), 1029 (w), 820 (s).

MS (EI, 70 eV): *m/z* (%) = 244 (32), 227 (16), 226 (100), 217 (32), 185 (28), 173 (21), 170 (14), 158 (18).

HRMS (EI): *m/z* calc. for [$C_{15}H_{17}ONS$]: 259.1031; found 259.1027.

m.p.: 74.9 – 76.5 °C.

3-Iodo-2-(isopropylthio)-4-(4-methoxyphenyl)pyridine (12b)



A solution of 3-chloro-2-(isopropylthio)pyridine (**10**) in THF (0.10 M, 1.0 equiv, pump A), *n*-butyllithium in *n*-hexane (0.11 M, 1.1 equiv, pump B) and (4-methoxyphenyl)magnesium bromide in THF (0.3 M, 6.0 equiv, pump C) were prepared. According to **TP3**, the reaction was run in continuous flow (suction-time pump A = 5 min) and afterwards in*J*ected into a flask containing iodine (889 mg, 3.5 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 3-iodo-2-(isopropylthio)-4-(4-methoxyphenyl)pyridine (**12b**) (100 mg, 0.27 mmol, 53% yield) as a yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.36 (d, *J* = 4.9 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.01 – 6.96 (m, 2H), 6.88 (d, *J* = 4.8 Hz, 1H), 3.98 (p, *J* = 6.8 Hz, 1H), 3.88 (s, 3H), 1.48 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 163.6, 159.8, 154.7, 148.1, 135.0, 130.1 (2C), 120.3, 113.7 (2C), 99.0, 55.4, 38.4, 22.9 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2961 (w), 2925 (w), 1609 (m), 1562 (m), 1514 (vs), 1462

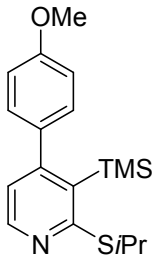
(m), 1428 (s), 1412 (w), 1325 (m), 1304 (m), 1287 (m), 1247 (vs), 1194 (m), 1176 (m), 1156 (m), 1109 (w), 1063 (m), 1054 (m), 1031 (m), 1000 (m), 824 (s), 767 (w).

MS (EI, 70 eV): *m/z* (%) = 344 (11), 259 (18), 258 (100), 216 (14), 184 (19), 173 (15).

HRMS (EI): *m/z* calc. for [$C_{15}H_{16}ONIS$]: 387.9997; found 387.9989.

m.p.: 57.2 – 59.4 °C.

2-(Isopropylthio)-4-(4-methoxyphenyl)-3-(trimethylsilyl)pyridine (12c)



A solution of 3-chloro-2-(isopropylthio)pyridine (**10**) in THF (0.10 M, 1.0 equiv, pump A), *n*-butyllithium in *n*-hexane (0.11 M, 1.1 equiv, pump B) and (4-methoxyphenyl)magnesium bromide in THF (0.3 M, 6.0 equiv, pump C) were prepared. According to **TP3**, the reaction was run in continuous flow (suction-time pump A = 5 min) and afterwards in*J*ected into a flask containing TMSCl (0.44 mL, 3.5 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.7:0.3) to give 2-(isopropylthio)-4-(4-methoxyphenyl)-3-(trimethylsilyl)pyridine (**12c**) (85.0 mg, 0.26 mmol, 51% yield) as a yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm 8.35 (d, *J* = 4.9 Hz, 1H), 7.23 – 7.12 (m, 2H), 6.98 – 6.89 (m, 2H), 6.83 (d, *J* = 4.9 Hz, 1H), 4.21 (p, *J* = 6.8 Hz, 1H), 3.87 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 6H), 0.12 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 165.8, 159.7, 157.8, 147.9, 135.8, 132.3, 130.1 (2C), 121.5, 113.6 (2C), 55.4, 36.8, 23.3 (2C), 2.2 (3C).

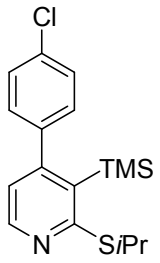
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2961 (w), 1608 (m), 1556 (m), 1512 (s), 1462 (w), 1442 (w), 1422 (m), 1409 (m), 1319 (m), 1304 (w), 1283 (m), 1244 (vs), 1172 (s), 1154 (m), 1107 (w), 1058 (m), 1032 (m), 841 (s), 824 (vs), 783 (m), 772 (m), 758 (m), 752 (m), 734 (m), 693 (w), 684 (w).

MS (EI, 70 eV): *m/z* (%) = 316 (18), 288 (21), 174 (55), 257 (29), 256 (100), 226 (16).

HRMS (EI): *m/z* calc. for [$C_{18}H_{25}NSSi$]: 331.1426; 331.1419.

m.p.: 55.4 – 56.4 °C.

4-(4-Chlorophenyl)-2-(isopropylthio)-3-(trimethylsilyl)pyridine (12d)



A solution of 3-chloro-2-(isopropylthio)pyridine (**10**) in THF (0.10 M, 1.0 equiv, pump A), *n*-butyllithium in *n*-hexane (0.11 M, 1.1 equiv, pump B) and (4-chlorophenyl)magnesium bromide in THF (0.3 M, 6.0 equiv, pump C) were prepared. According to **TP3**, the reaction was run in continuous flow (suction-time pump A = 5 min) and afterwards in*J*ected into a flask containing TMSCl (0.44 mL, 3.5 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 4-(4-chlorophenyl)-2-(isopropylthio)-3-(trimethylsilyl)pyridine (**12d**) (84.0 mg, 0.25 mmol, 50% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.35 (d, *J* = 5.0 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.18 – 7.12 (m, 2H), 6.78 (d, *J* = 5.0 Hz, 1H), 4.21 (p, *J* = 6.9 Hz, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 0.08 (s, 9H).

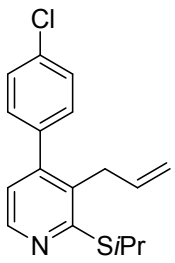
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.2, 156.6, 148.1, 141.6, 134.2, 132.0, 130.2 (2C), 128.4 (2C), 121.1, 36.9, 23.3 (2C), 2.1 (3C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2962 (m), 1597 (m), 1572 (s), 1533 (s), 1492 (s), 1449 (s), 1433 (m), 1362 (vs), 1184 (m), 1164 (m), 1155 (m), 1092 (vs), 1056 (m), 1015 (s), 927 (m), 916 (m), 834 (s), 820 (vs), 792 (vs).

MS (EI, 70 eV): *m/z* (%) = 320 (28), 292 (33), 280 (24), 278 (61), 262 (35), 260 (100), 226 (25).

HRMS (EI): *m/z* calc. for [$C_{17}H_{21}ClNSSi$]: 334.0847; found 334.0847 [M^+-H].

3-Allyl-4-(4-chlorophenyl)-2-(isopropylthio)pyridine (12e)



A solution of 3-chloro-2-(isopropylthio)pyridine (**10**) in THF (0.10 M, 1.0 equiv, pump A), *n*-butyllithium in *n*-hexane (0.11 M, 1.1 equiv, pump B) and (4-chlorophenyl)magnesium bromide in THF (0.3 M, 6.0 equiv, pump C) were prepared. According to **TP3**, the reaction was run in continuous flow (suction-time pump A = 5 min) and afterwards in*J*ected into a flask containing CuCN·2LiCl (0.05 mL, 0.05 mmol) and allyl bromide (0.30 mL, 3.5 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.8:0.2) to give 3-allyl-4-(4-chlorophenyl)-2-(isopropylthio)pyridine (**12e**) (74.0 mg, 0.25 mmol, 49% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.36 (d, *J* = 5.0 Hz, 1H), 7.44 – 7.33 (m, 2H), 7.29 – 7.17 (m, 2H), 6.85 (d, *J* = 5.0 Hz, 1H), 5.88 (ddt, *J* = 17.2, 10.2, 5.6 Hz, 1H), 5.05 (dq, *J* = 10.2, 1.7 Hz, 1H), 4.81 (dq, *J* = 17.2, 1.8 Hz, 1H), 4.14 (p, *J* = 6.8 Hz, 1H), 3.33 (dt, *J* = 5.7, 1.9 Hz, 2H), 1.42 (d, *J* = 6.8 Hz, 6H).

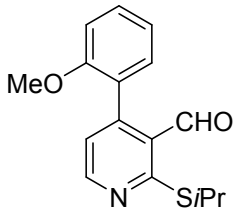
^{13}C-NMR (101 MHz, $CDCl_3$): 159.9, 149.2, 146.5, 137.7, 135.0, 134.4, 130.4, 130.0 (2C), 128.6 (2C), 120.7, 116.6, 35.7, 33.8, 23.3 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2963 (vw), 1555 (vw), 1520 (w), 1486 (vw), 1422 (w), 1318 (vw), 1250 (w), 1174 (w), 1091 (w), 1052 (vw), 1015 (w), 904 (s), 846 (m), 823 (w), 802 (vw), 726 (vs).

MS (EI, 70 eV): *m/z* (%) = 262 (37), 260 (100), 248 (15), 246 (42), 228 (44), 191 (15).

HRMS (EI): *m/z* calc. for [$C_{17}H_{17}ClNS$]: 302.08765; found 302.08764 [M^+-H].

2-(Isopropylthio)-4-(2-methoxyphenyl)nicotinaldehyde (12f)

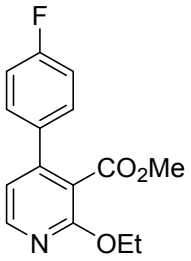


A solution of 3-chloro-2-(isopropylthio)pyridine (**10**) in THF (0.10 M, 1.0 equiv, pump A), *n*-butyllithium in *n*-hexane (0.11 M, 1.1 equiv, pump B) and (2-methoxyphenyl)magnesium bromide in THF (0.3 M, 6.0 equiv, pump C) were prepared. According to **TP3**, the reaction was run in continuous flow (suction-time pump A = 5 min) and afterwards in*J*ected into a flask containing DMF (excess) and heated to 75 °C for 1 h. After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give 2-

(isopropylthio)-4-(2-methoxyphenyl) nicotinaldehyde (**12f**) (73.0 mg, 0.26 mmol, 51% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 9.84 (s, 1H), 8.60 (d, *J* = 5.0 Hz, 1H), 7.44 (ddd, *J* = 8.4, 7.5, 1.8 Hz, 1H), 7.23 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.08 (td, *J* = 7.5, 1.0 Hz, 1H), 6.98 – 6.95 (m, 2H), 4.23 (h, *J* = 6.8 Hz, 1H), 3.74 (s, 3H), 1.44 (d, *J* = 6.9 Hz, 6H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 191.7, 161.8, 156.3, 152.1, 151.9, 131.1, 130.8, 125.8, 125.1, 121.2, 121.1, 110.9, 55.6, 34.2, 23.0 (2C).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2963 (w), 1686 (vs), 1599 (m), 1581 (w), 1558 (s), 1538 (s), 1492 (m), 1462 (m), 1436 (m), 1396 (w), 1359 (m), 1301 (w), 1274 (m), 1242 (s), 1197 (m), 1185 (m), 1124 (m), 1061 (w), 1023 (m), 864 (m), 814 (m), 755 (m), 691 (m).
MS (EI, 70 eV): *m/z* (%) = 256 (81), 229 (67), 226 (100), 217 (57), 214 (34), 201 (41), 184 (40), 154 (43), 143 (30).
HRMS (EI): *m/z* calc. for [$C_{16}H_{17}NO_2S$]: 287.0980; found 287.0977.

Methyl 2-ethoxy-4-(4-fluorophenyl)nicotinate (7ja)

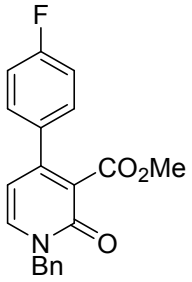


Following **TP2**, 3-chloro-2-ethoxypyridine (**1**, 790 mg, 5.00 mmol), *n*-butyllithium (2.10 mL, 5.50 mmol) and (4-fluorophenyl)magnesium bromide (16.2 mL, 15.0 mmol), prepared *via* **TP1**, were mixed in a sealed tube. Thereafter, the reaction mixture was quenched with methyl cyanoformate (2.00 mL, 25.0 mmol). After workup, the crude product was purified *via* column chromatography (*iso*hexane:ethyl acetate = 9.5:0.5) to give methyl 2-ethoxy-4-(4-fluorophenyl)nicotinate (**7ja**) (73.0 mg, 0.27 mmol, 53% yield) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 8.20 (d, *J* = 5.3 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.17 – 7.06 (m, 2H), 6.87 (d, *J* = 5.3 Hz, 1H), 4.46 (q, *J* = 7.0 Hz, 2H), 3.70 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 167.4, 163.2 (d, *J* = 248.8 Hz), 160.0, 148.99, 147.8, 134.0 (d, *J* = 3.4 Hz), 129.8 (d, *J* = 8.4 Hz), 117.3, 116.7, 115.9 (d, *J* = 21.7 Hz), 62.8, 52.5, 14.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2981 (w), 2951 (w), 1734 (vs), 1607 (m), 1589 (m), 1555 (s), 1514 (s), 1468 (m), 1434 (m), 1421 (s), 1380 (m), 1349 (w), 1328 (s), 1290 (m), 1273 (s), 1227 (s), 1161 (m), 1140 (m), 1117 (s), 1099 (w), 1069 (s), 1032 (m), 824 (m), 733 (m).
MS (EI, 70 eV): *m/z* (%) = 260 (34), 228 (32), 216 (100), 173 (34), 172 (38),133 (20).
HRMS (EI): *m/z* calc. for [$C_{15}H_{14}O_3NF$]: 275.0958; found 275.0947.

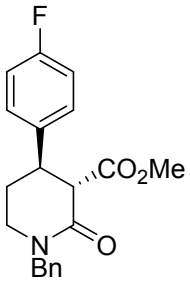
Methyl 1-benzyl-4-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (17)



Methyl 2-ethoxy-4-(4-fluorophenyl)nicotinate (**7ja**, 358 mg, 1.30 mmol) and neat benzylbromide (2.6 mL, ~0.5 M) were added into a sealed tube. The reaction mixture was heated to 120 °C for 30 h in a microwave setup. The crude product was directly purified *via* column chromatography (*iso*hexane:ethyl acetate = 6.0:4.0) to give methyl 1-benzyl-4-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (**17**) (351 mg, 1.04 mmol, 80% yield) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.42 – 7.31 (m, 8H), 7.13 – 7.06 (m, 2H), 6.19 (d, *J* = 7.1 Hz, 1H), 5.17 (s, 2H), 3.72 (s, 3H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 166.9, 163.3 (d, *J* = 249.7 Hz), 159.6, 149.7, 137.5, 135.6, 133.3 (d, *J* = 3.4 Hz), 129.4 (2C, d, *J* = 8.4 Hz), 129.1 (2C), 128.7 (2C), 128.4, 124.1, 115.9 (2C, d, *J* = 21.7 Hz), 107.5.
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2359 (w), 1733 (s), 1647 (vs), 1602 (m), 1599 (m), 1592 (m), 1538 (m), 1533 (m), 1521 (w), 1512 (m), 1456 (w), 1371 (w), 1256 (m), 1239 (w), 1228 (m), 1163 (w), 1127 (m), 1090 (w), 703 (w).
MS (EI, 70 eV): *m/z* (%) = 305 (100), 277 (53), 276 (71), 248 (35), 91 (65).
HRMS (EI): *m/z* calc. for [$C_{20}H_{16}O_3NF$]: 337.1114; found 337.1104.

Methyl 1-benzyl-4-(4-fluorophenyl)-2-oxopiperidine-3-carboxylate (18)



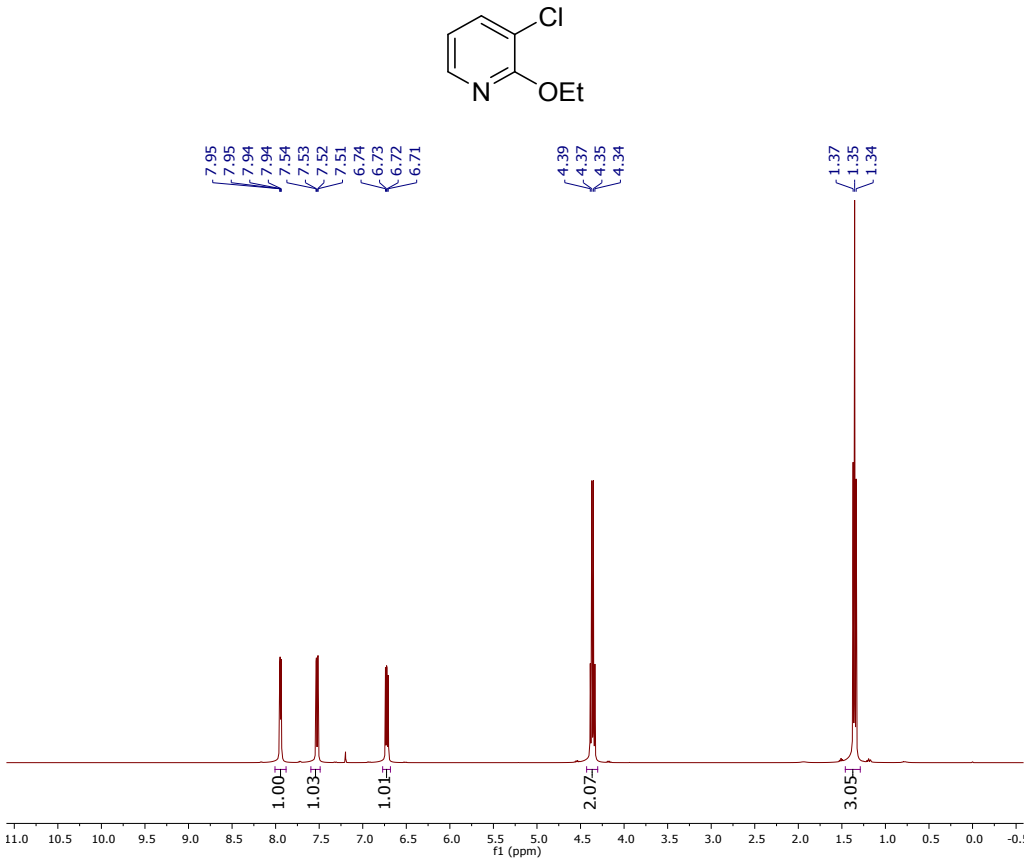
(±)-trans

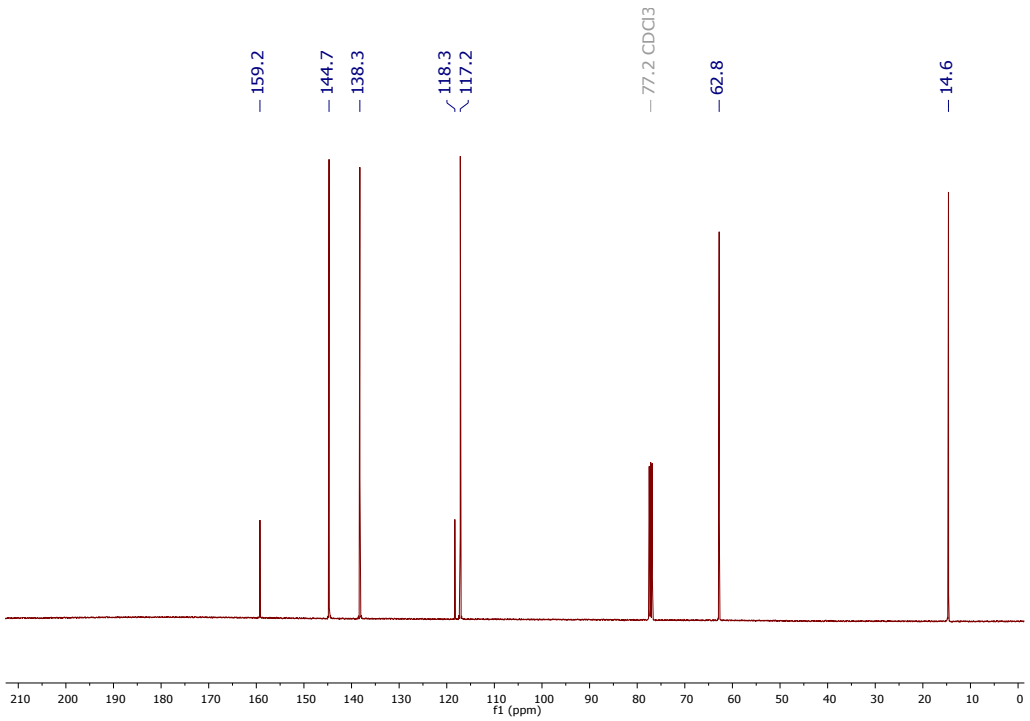
Methyl 1-benzyl-4-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (**17**, 348 mg, 1.00 mmol) and MeOH (30 mL) were added into a flask. Then, 5% Pd/C (2.13 g, 1.0 mmol) was added while stirring and the solution was saturated with hydrogen gas. Under hydrogen-atmosphere (balloon filled with H_2), the reaction mixture was stirred for 16 h at 23 °C. The suspension was filtered and the residue was washed with MeOH several times. After removal of MeOH, the crude product was purified *via* column chromatography (pure ethyl acetate) to give methyl 1-benzyl-4-(4-fluorophenyl)-2-oxopiperidine-3-carboxylate (**18**) (176 mg, 0.50 mmol, 50% yield) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ / ppm = 7.37 – 7.28 (m, 5H), 7.15 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.03 – 6.96 (m, 2H), 4.81 (d, *J* = 14.5 Hz, 1H), 4.47 (d, *J* = 14.5 Hz, 1H), 3.64 (s, 3H), 3.61 – 3.56 (m, 1H), 3.48 – 3.35 (m, 2H), 3.29 (ddd, *J* = 12.3, 5.4, 3.0 Hz, 1H), 2.09 – 1.91 (m, 2H).
^{13}C-NMR (101 MHz, $CDCl_3$): δ / ppm = 170.6, 165.8, 162.1 (d, *J* = 245.8 Hz), 137.2 (d, *J* = 3.3 Hz), 136.7, 128.9 (2C), 128.4 (2C, d, *J* = 8.0 Hz), 128.4 (2C), 127.8, 115.9 (2C, d, *J* = 21.4 Hz), 56.8, 52.5, 50.5, 46.3, 41.9, 29.5 (d, *J* = 0.9 Hz).
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3207 (w), 2952 (w), 1738 (s), 1666 (vs), 1605 (w), 1511 (s), 1491 (m), 1464 (w), 1457 (w), 1435 (w), 1424 (w), 1342 (m), 1304 (w), 1267 (m), 1223 (m), 1210 (m), 1195 (w), 1161 (m), 1121 (w), 1032 (w), 834 (m), 782 (w), 731 (w).
MS (EI, 70 eV): *m/z* (%) = 341 (23), 283 (26), 282 (36), 149 (46), 132 (46), 118 (44), 91 (100).
HRMS (EI): *m/z* calc. for [$C_{20}H_{20}O_3NF$]: 341.1427; found 341.1420.
m.p.: 158.8 – 160.5.

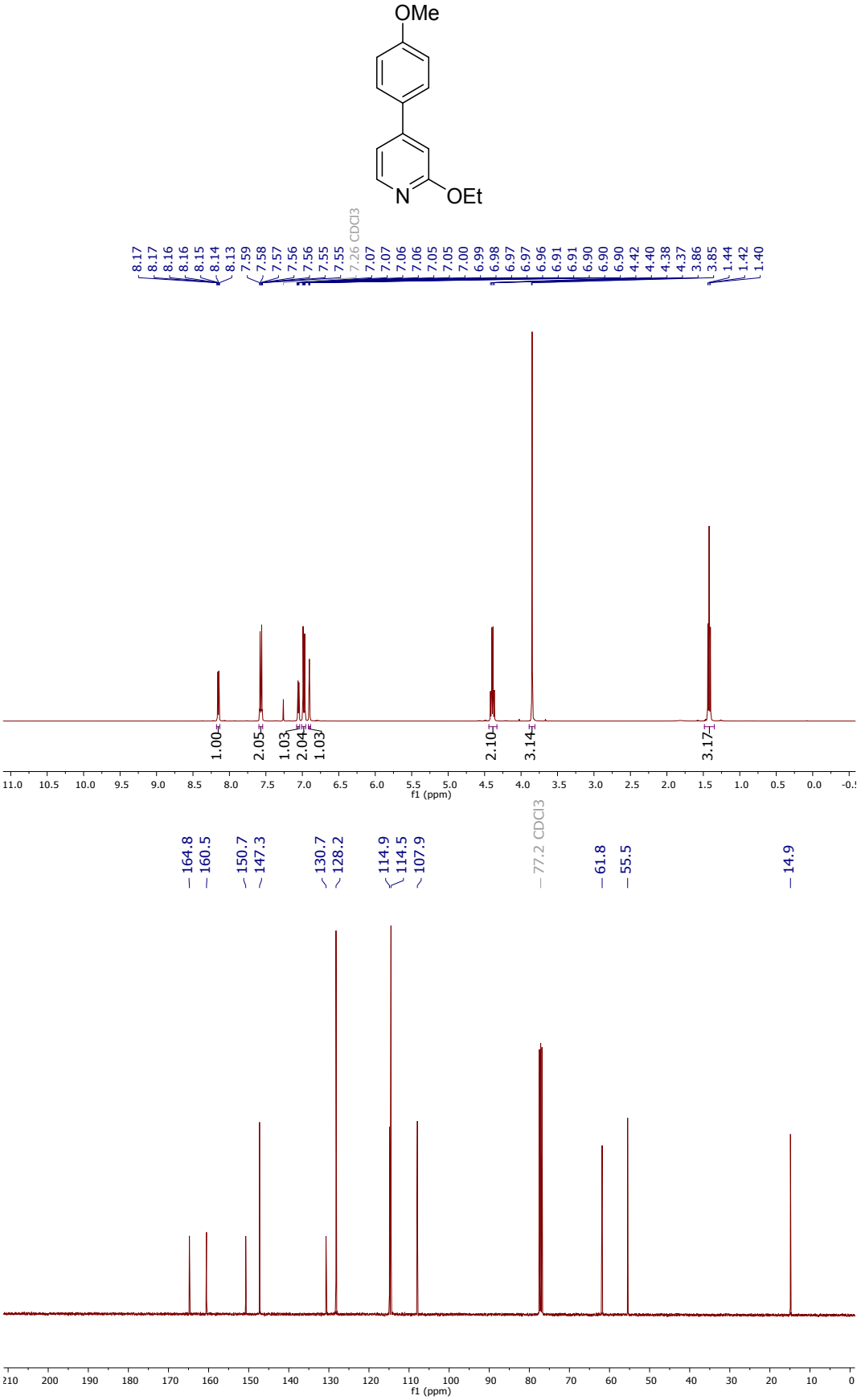
^{1}H-NMR and ^{13}C-NMR Spectra of Products

3-Chloro-2-ethoxypyridine (1)

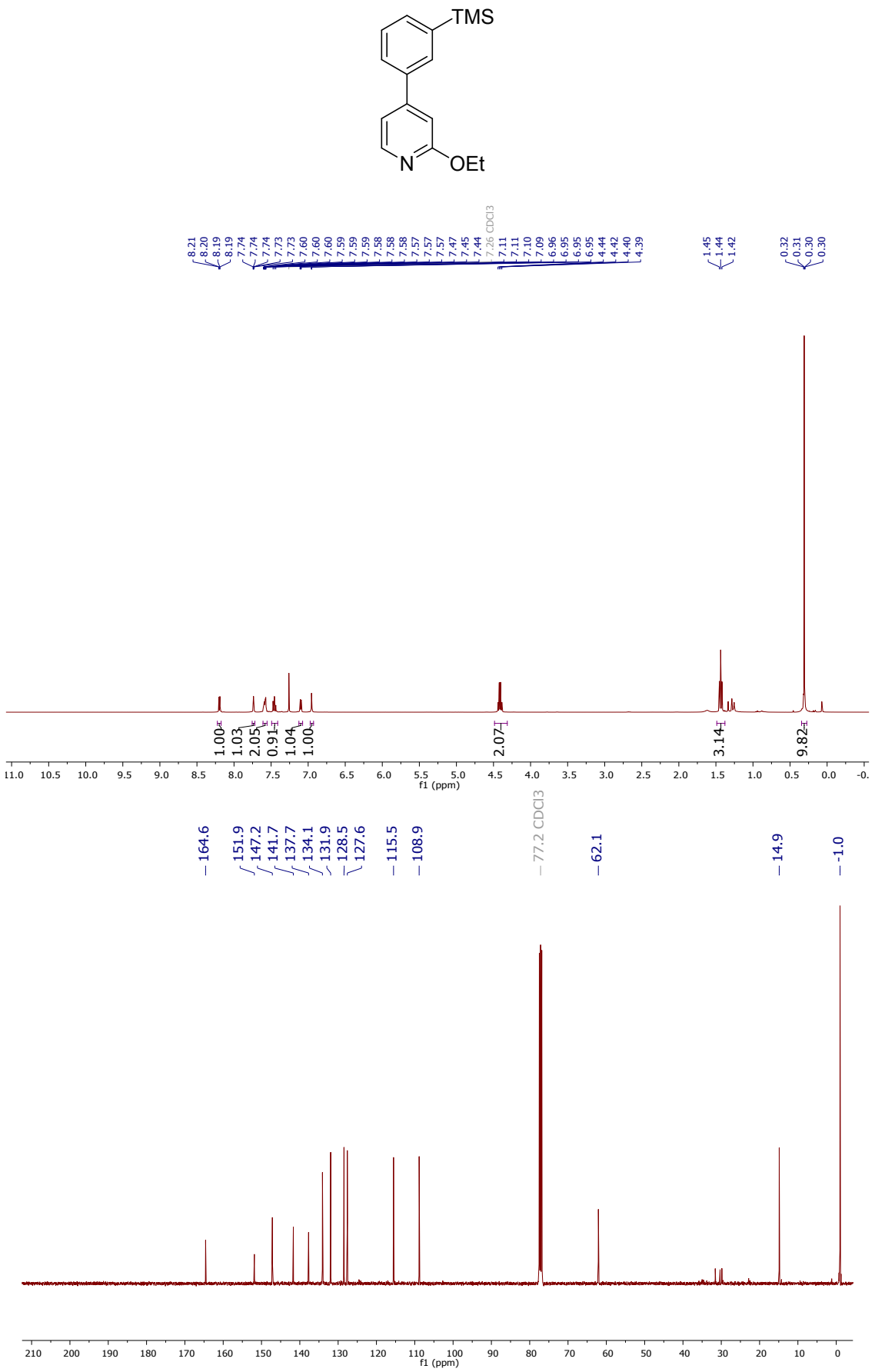




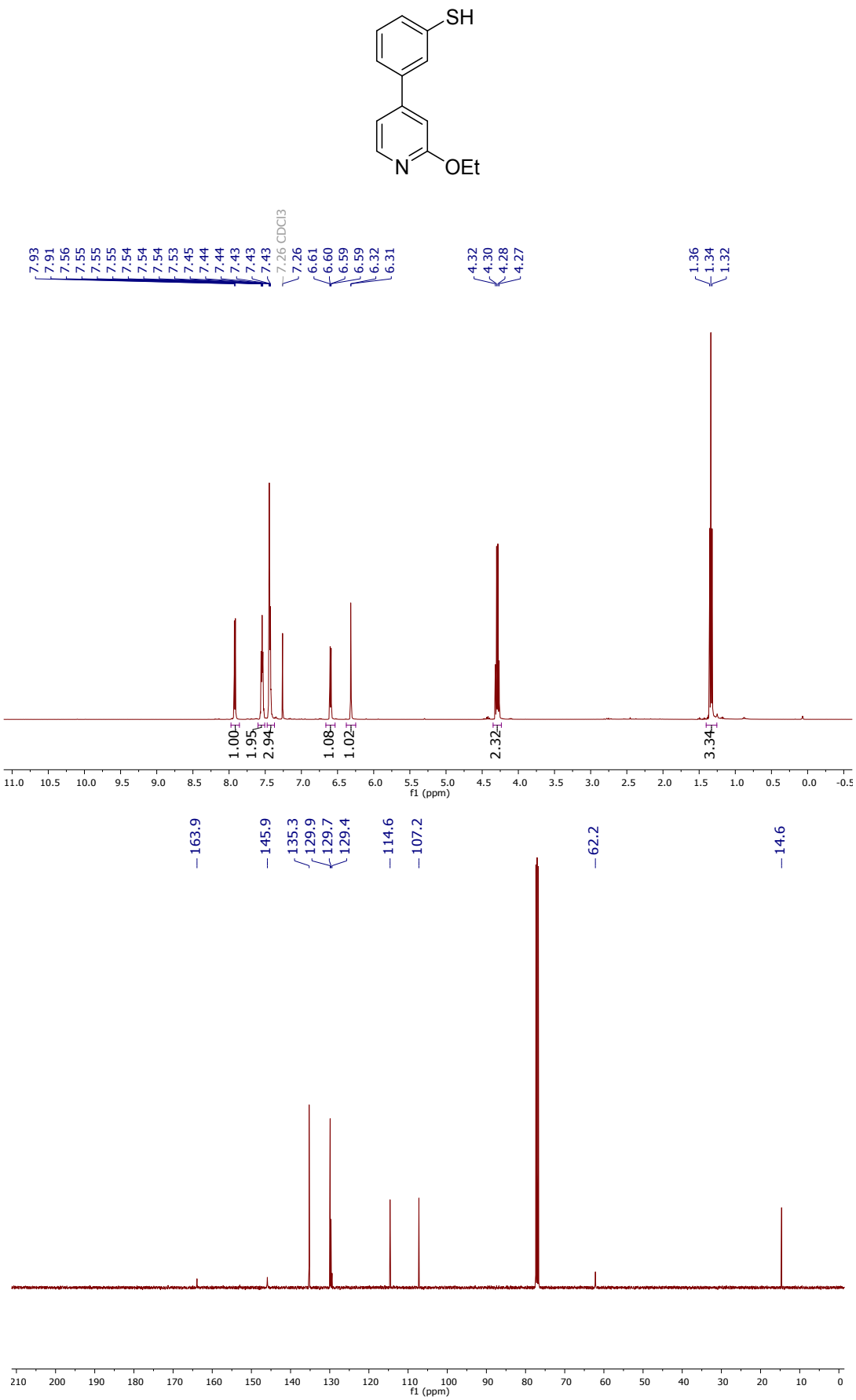
2-Ethoxy-4-(4-methoxyphenyl)pyridine (7a)



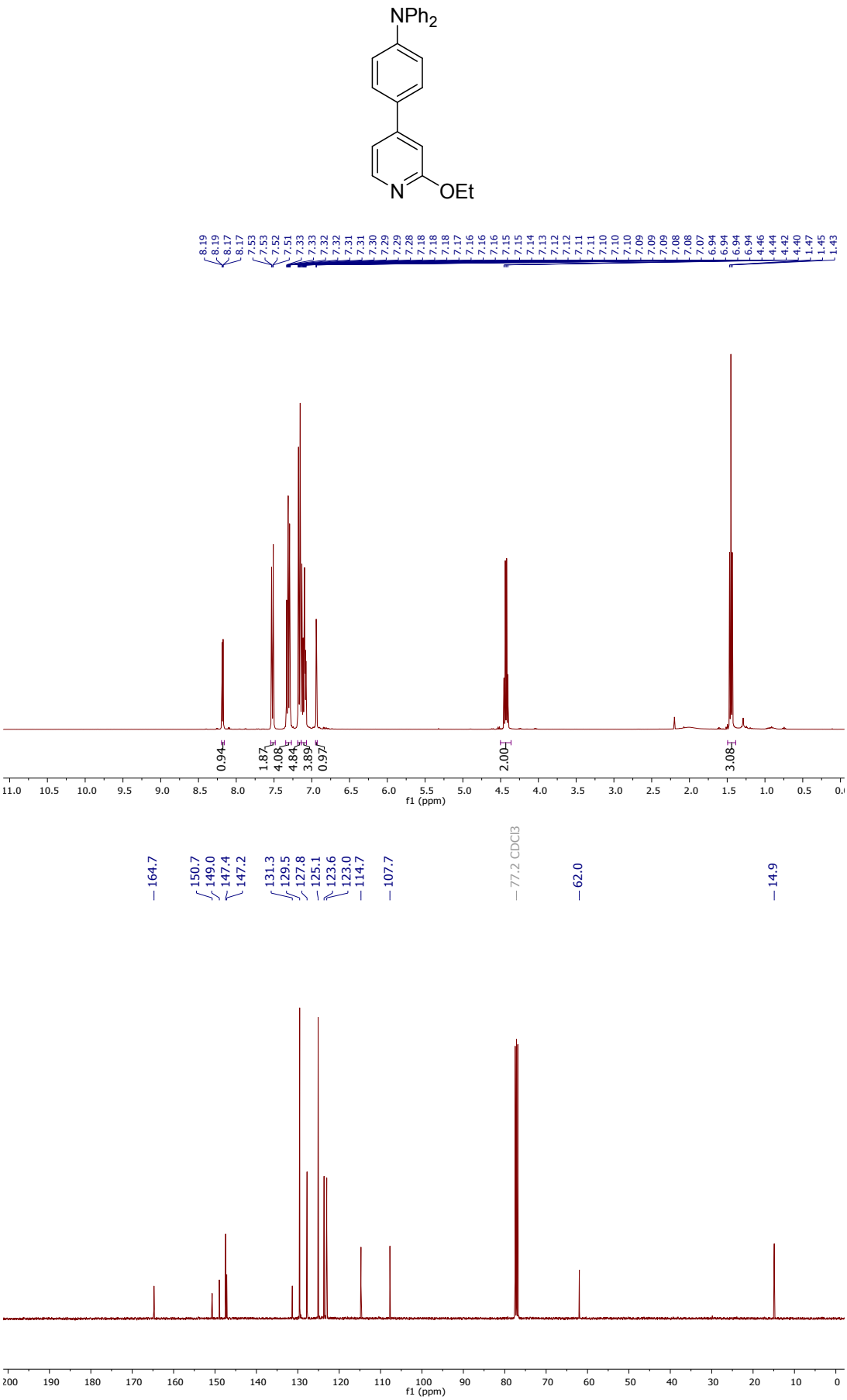
2-Ethoxy-4-(3-(trimethylsilyl)phenyl)pyridine (7b)



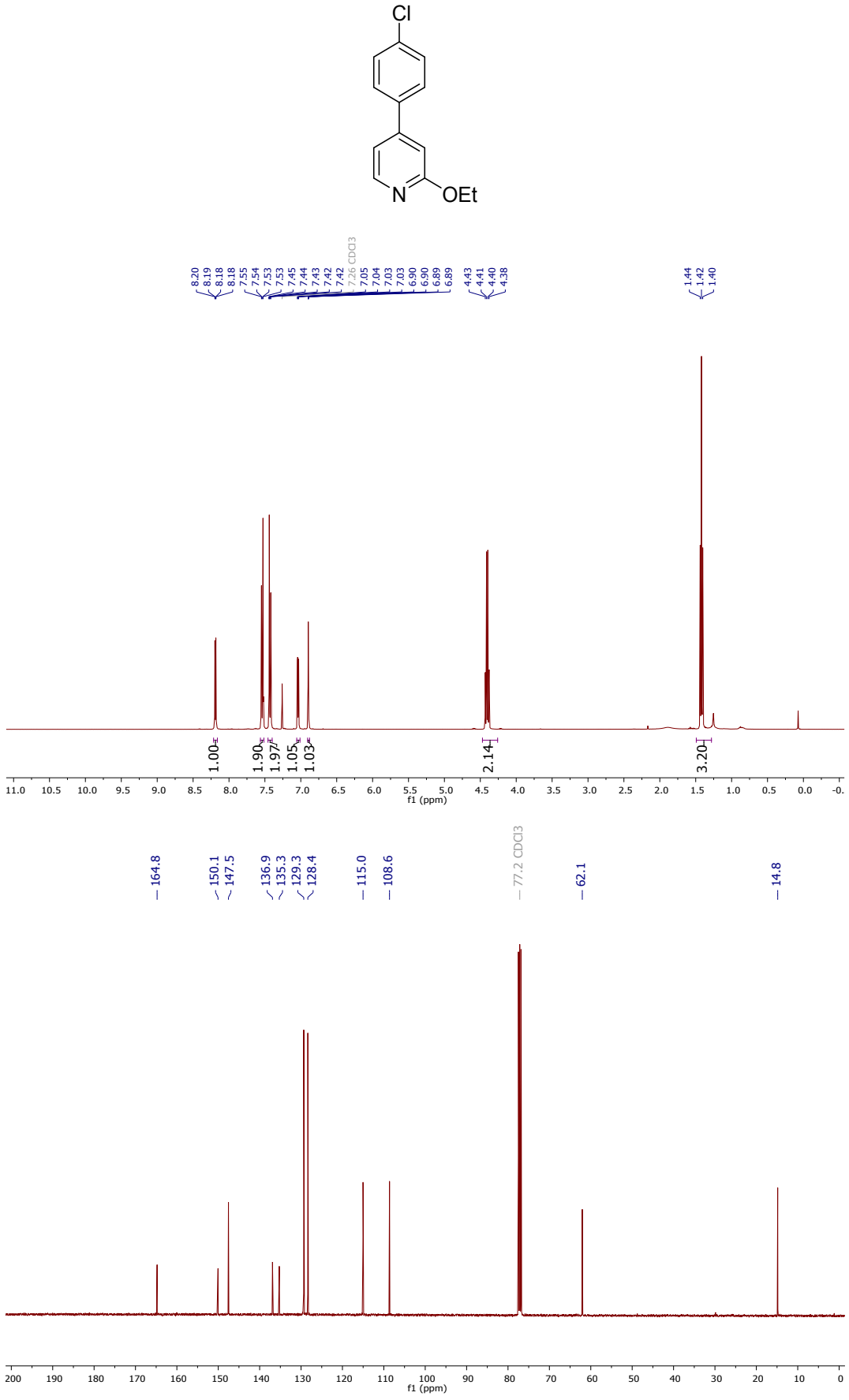
3-(2-Ethoxypyridin-4-yl)benzenethiol (7c)



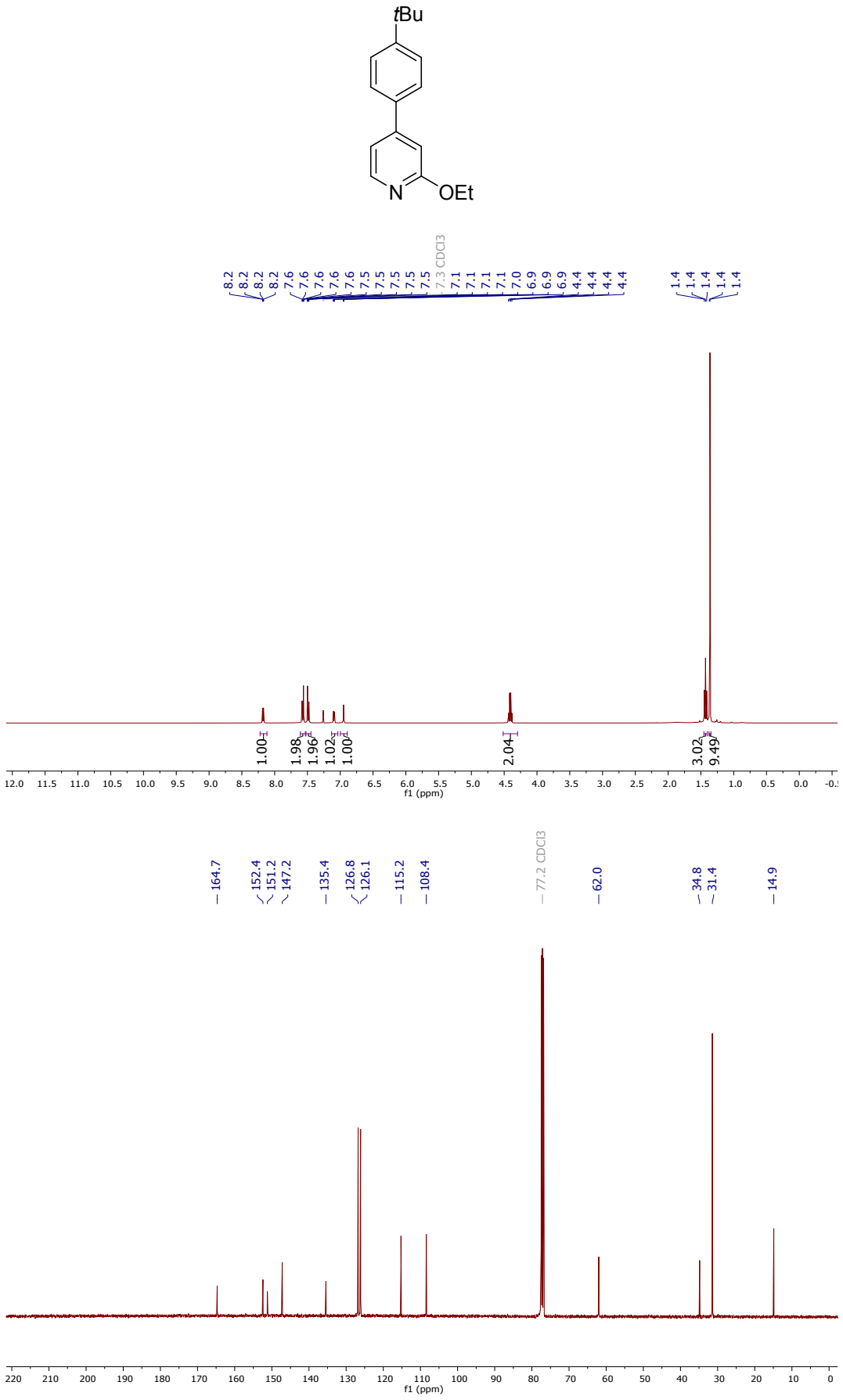
4-(2-Ethoxypyridin-4-yl)-*N,N*-diphenylaniline (7d)



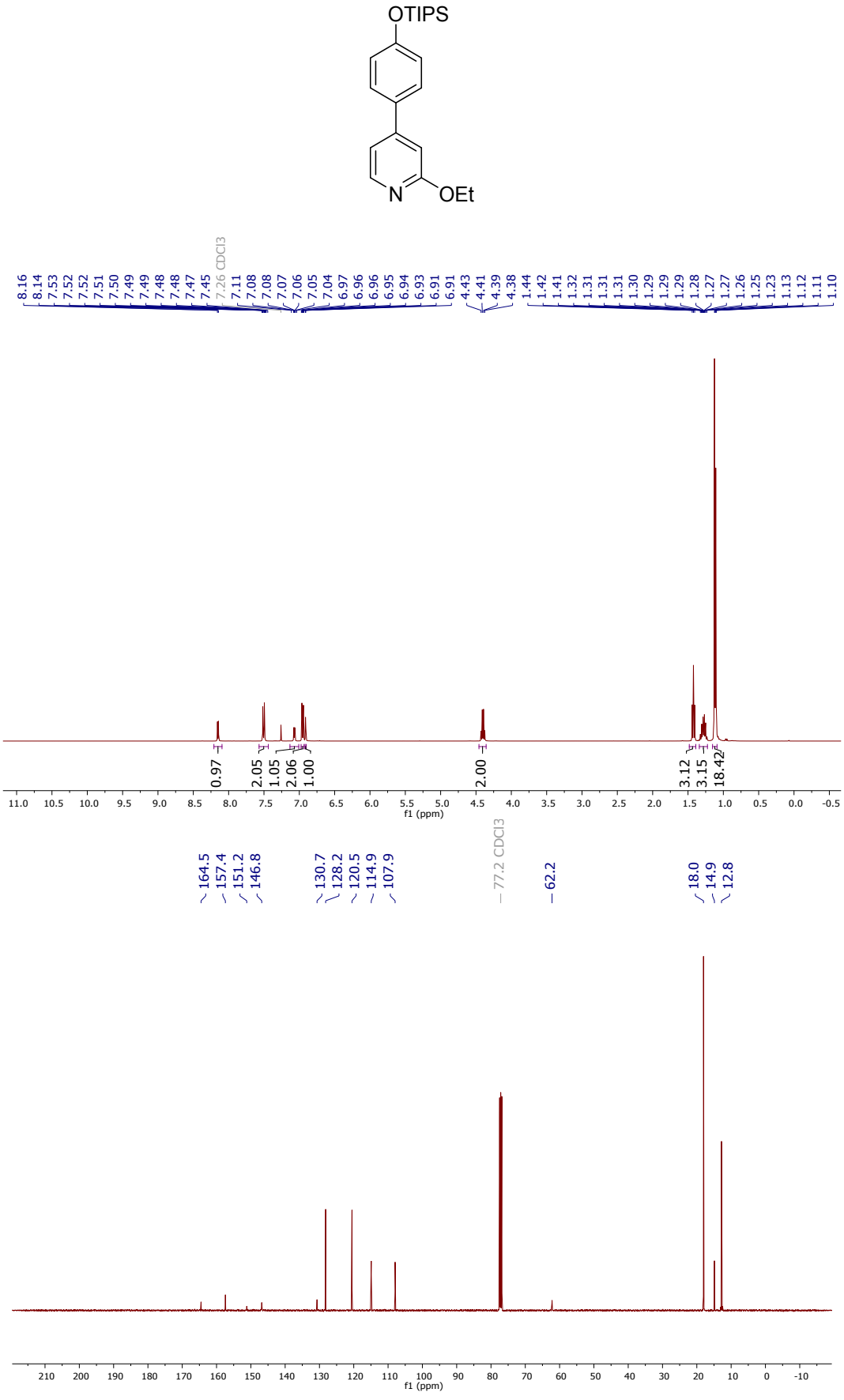
4-(4-Chlorophenyl)-2-ethoxypyridine (7e)



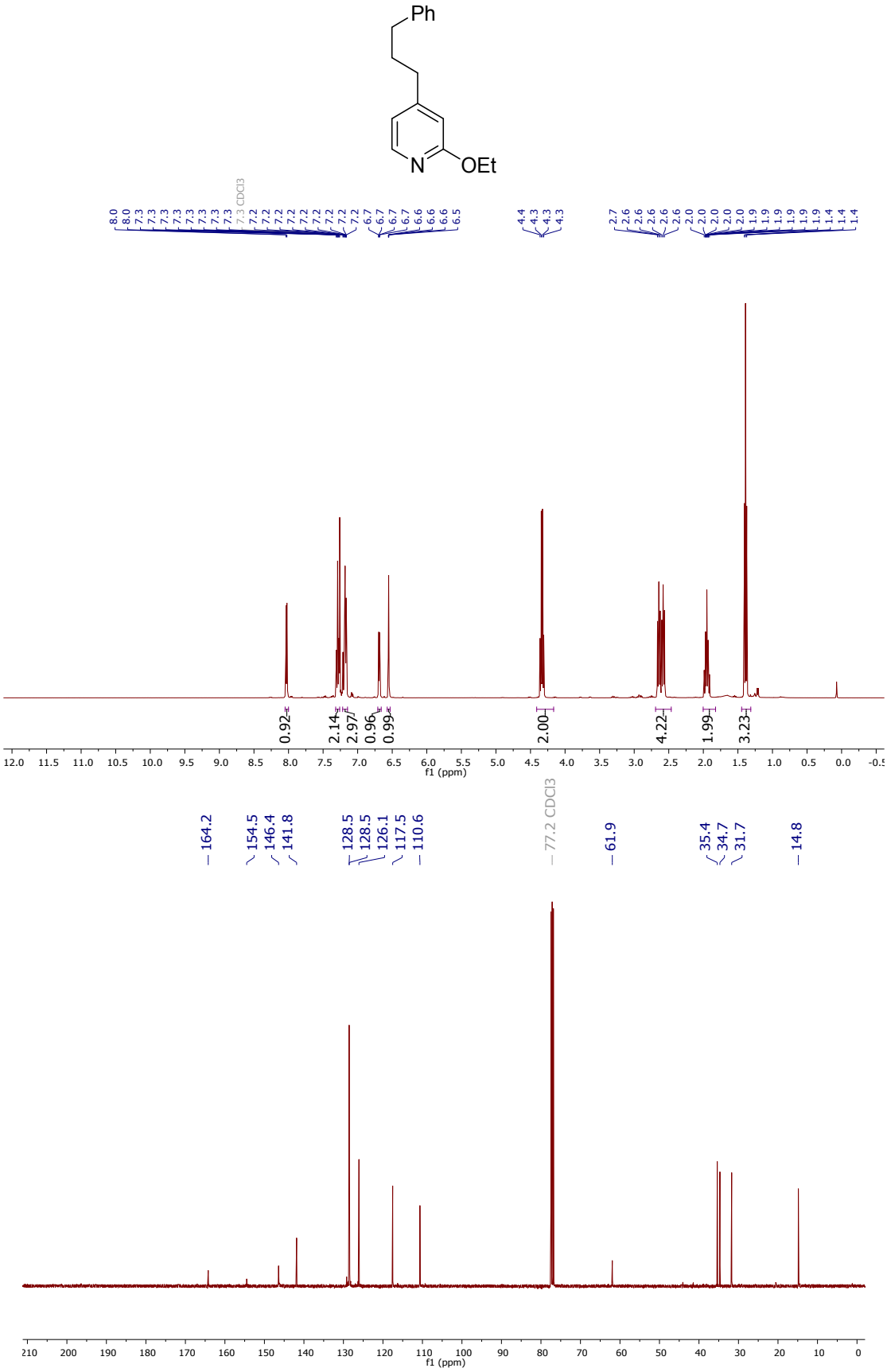
4-(4-(*Tert*-butyl)phenyl)-2-ethoxypyridine (7f)



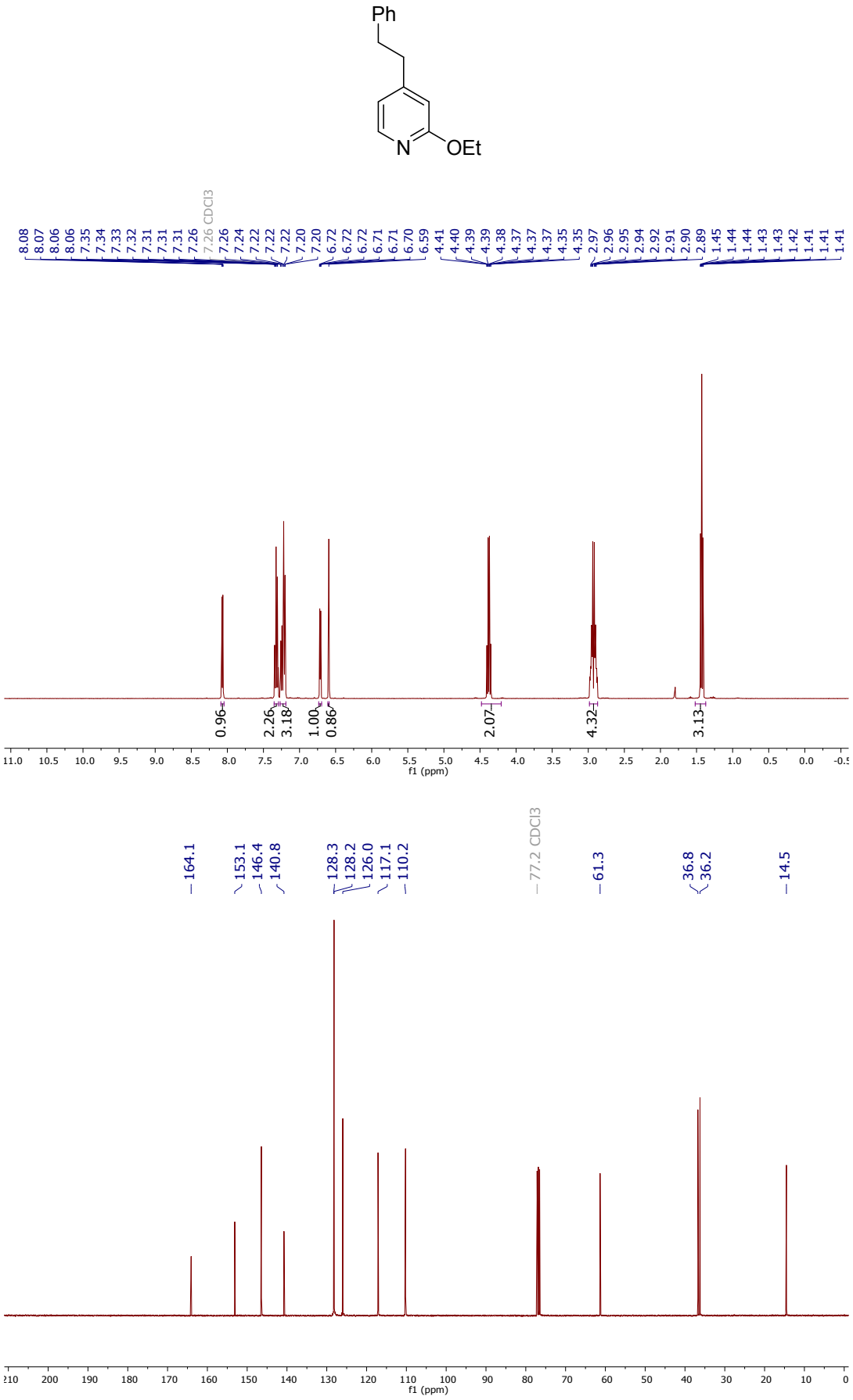
2-Ethoxy-4-(4-((tri*iso*propylsilyl)oxy)phenyl)pyridine (7g)



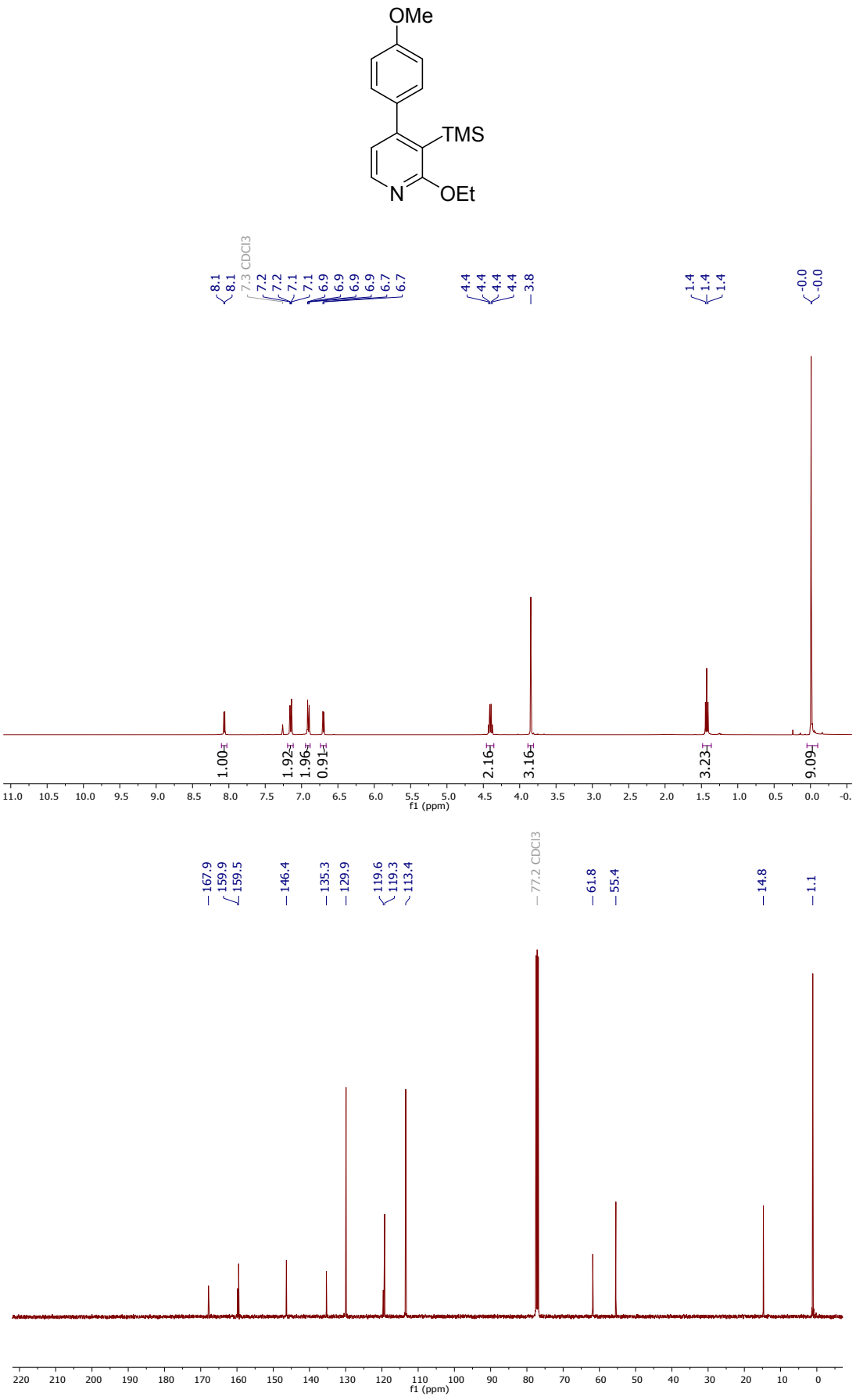
2-Ethoxy-4-(3-phenylpropyl)pyridine (7h)



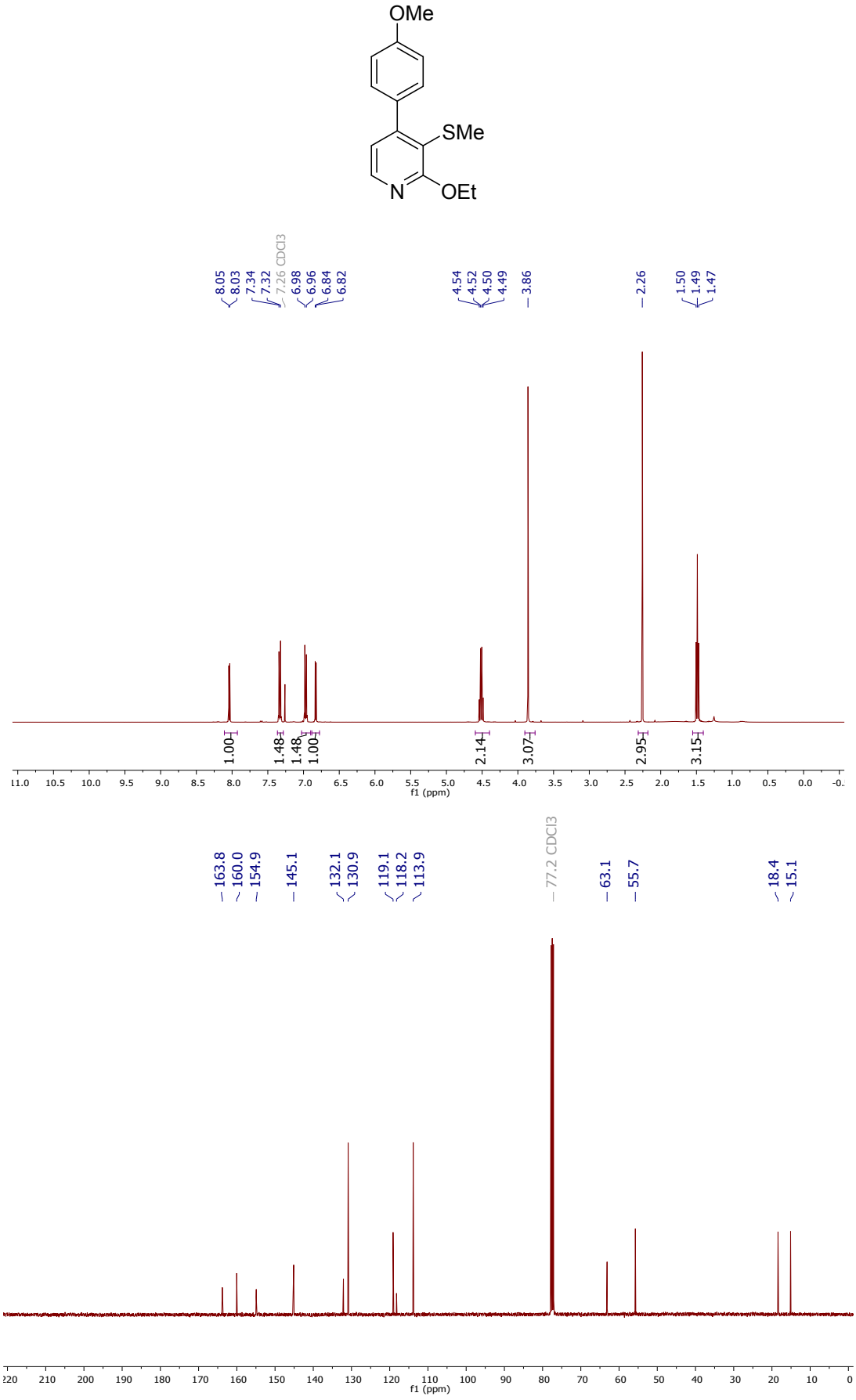
2-Ethoxy-4-phenethylpyridine (7i)



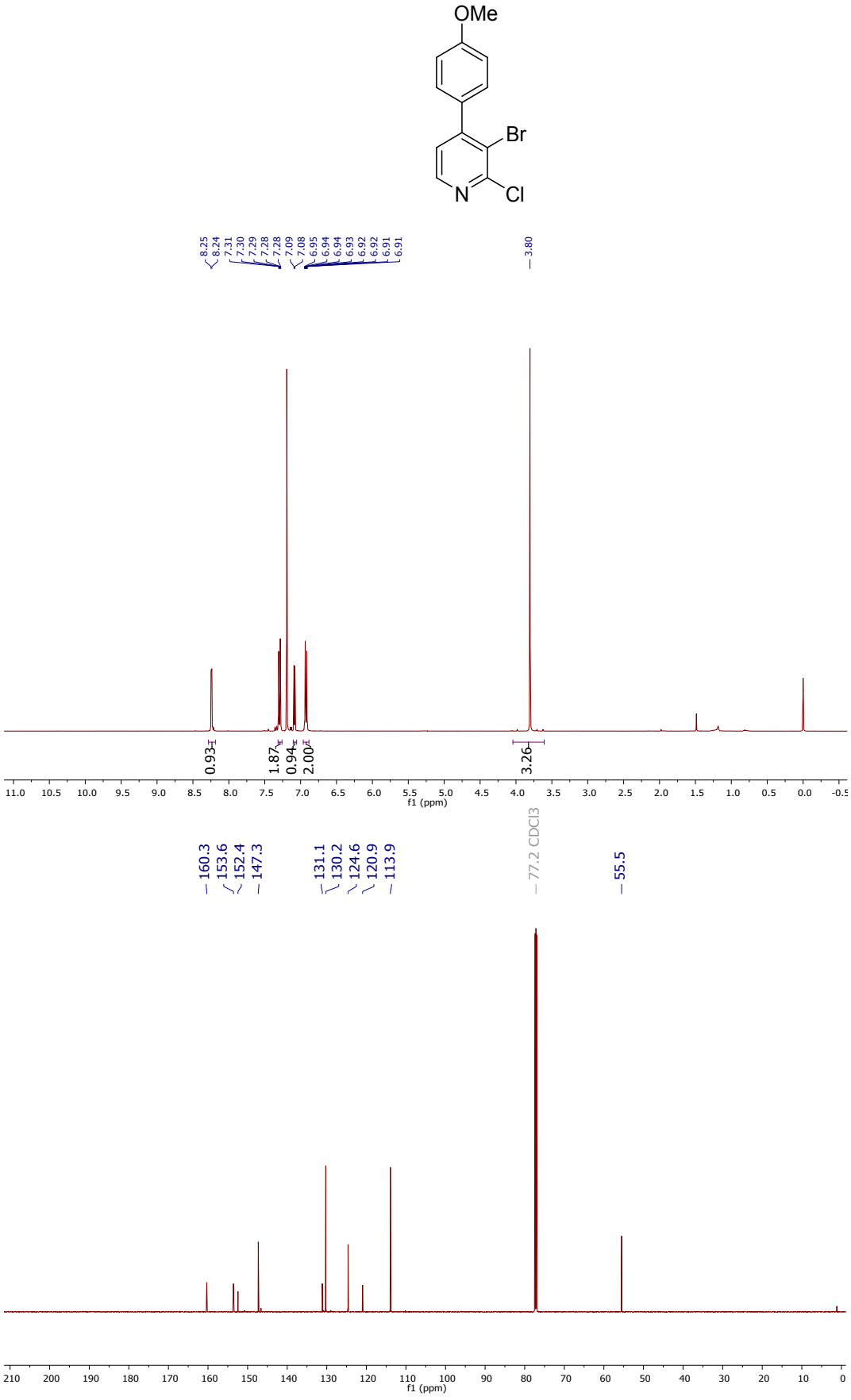
2-Ethoxy-4-(4-methoxyphenyl)-3-(trimethylsilyl)pyridine (7aa)



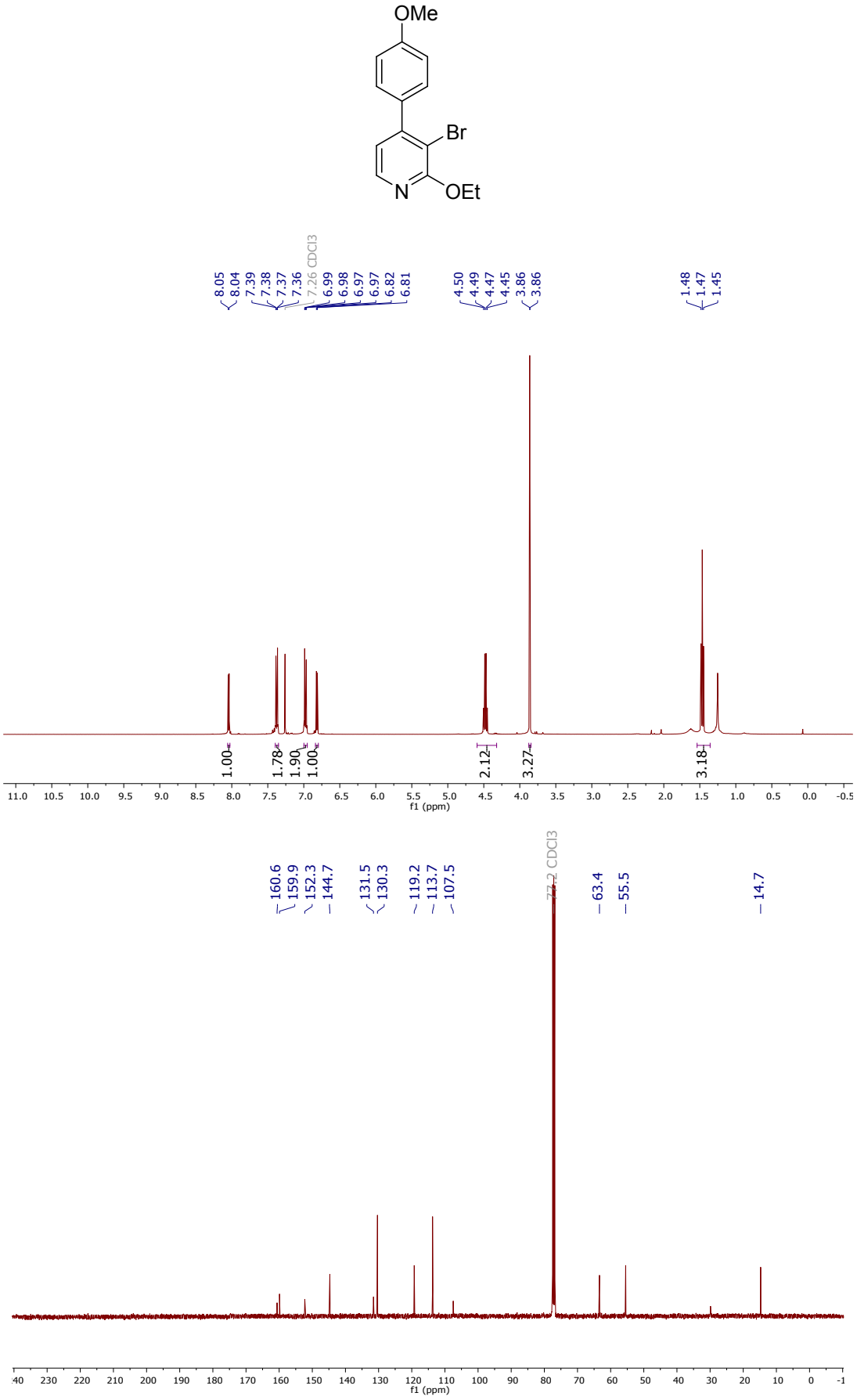
2-Ethoxy-4-(4-methoxyphenyl)-3-(methylthio)pyridine (7ab)



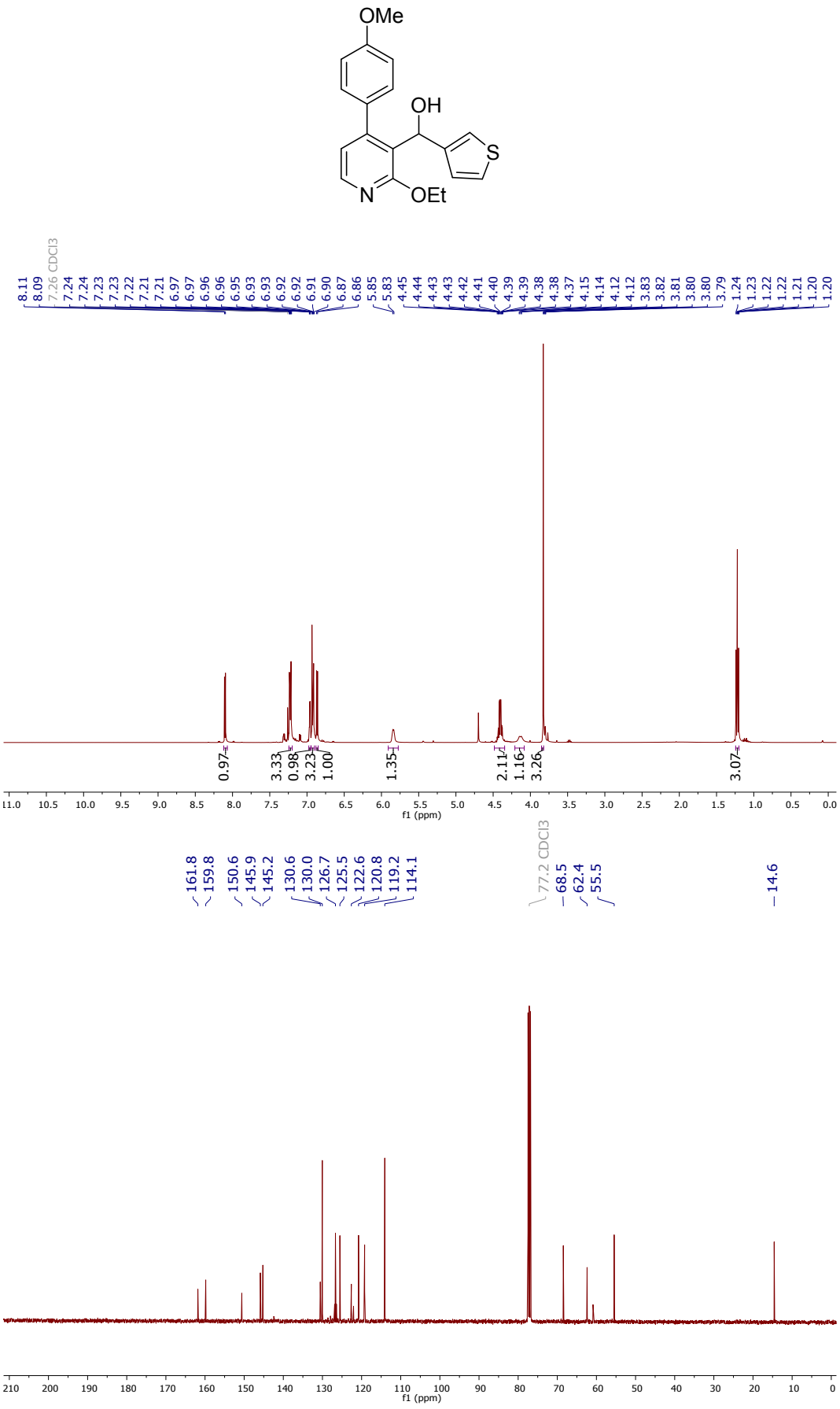
3-Bromo-2-chloro-4-(4-methoxyphenyl)pyridine (8)



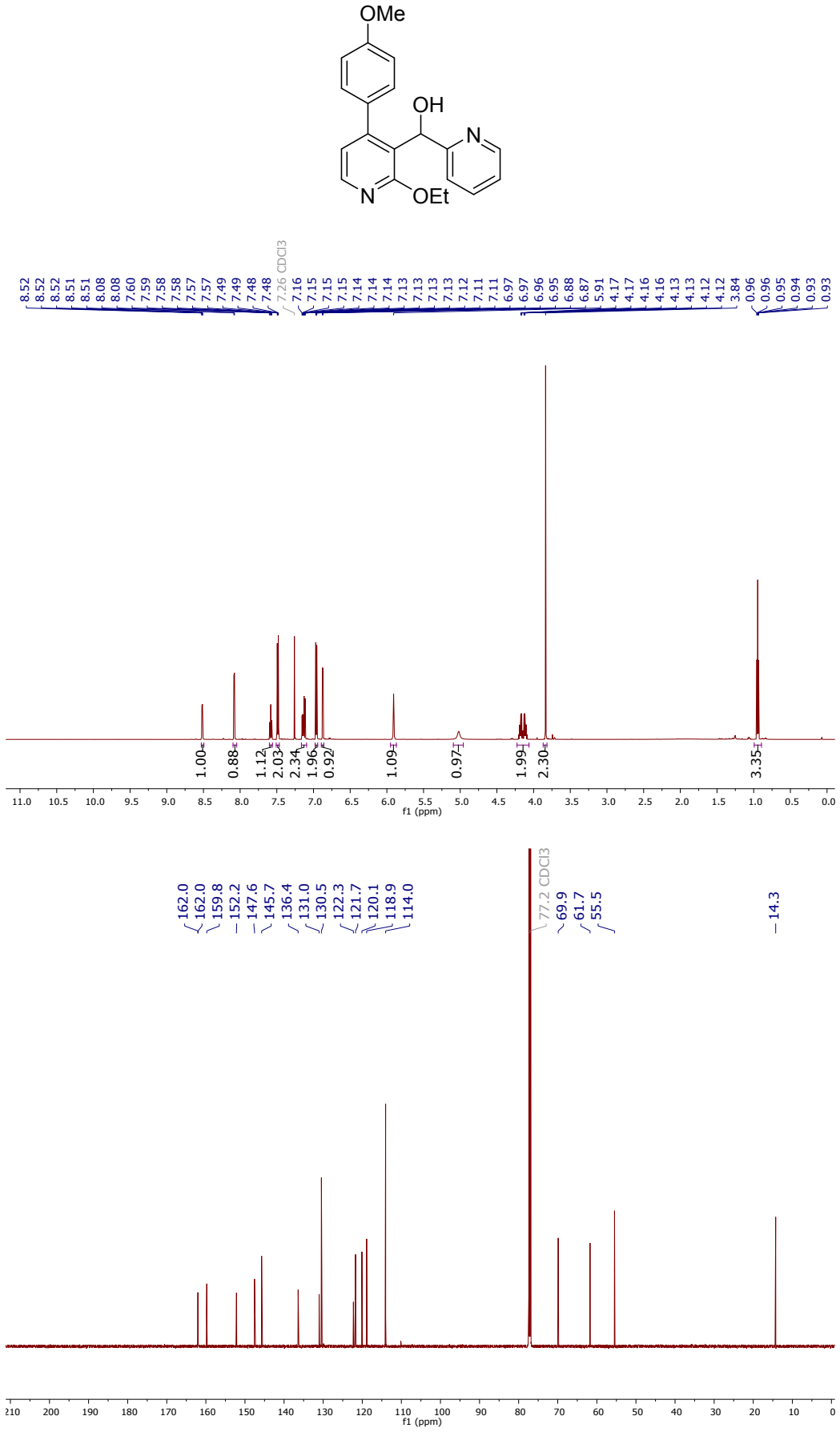
3-Bromo-2-ethoxy-4-(4-methoxyphenyl)pyridine (7ac)



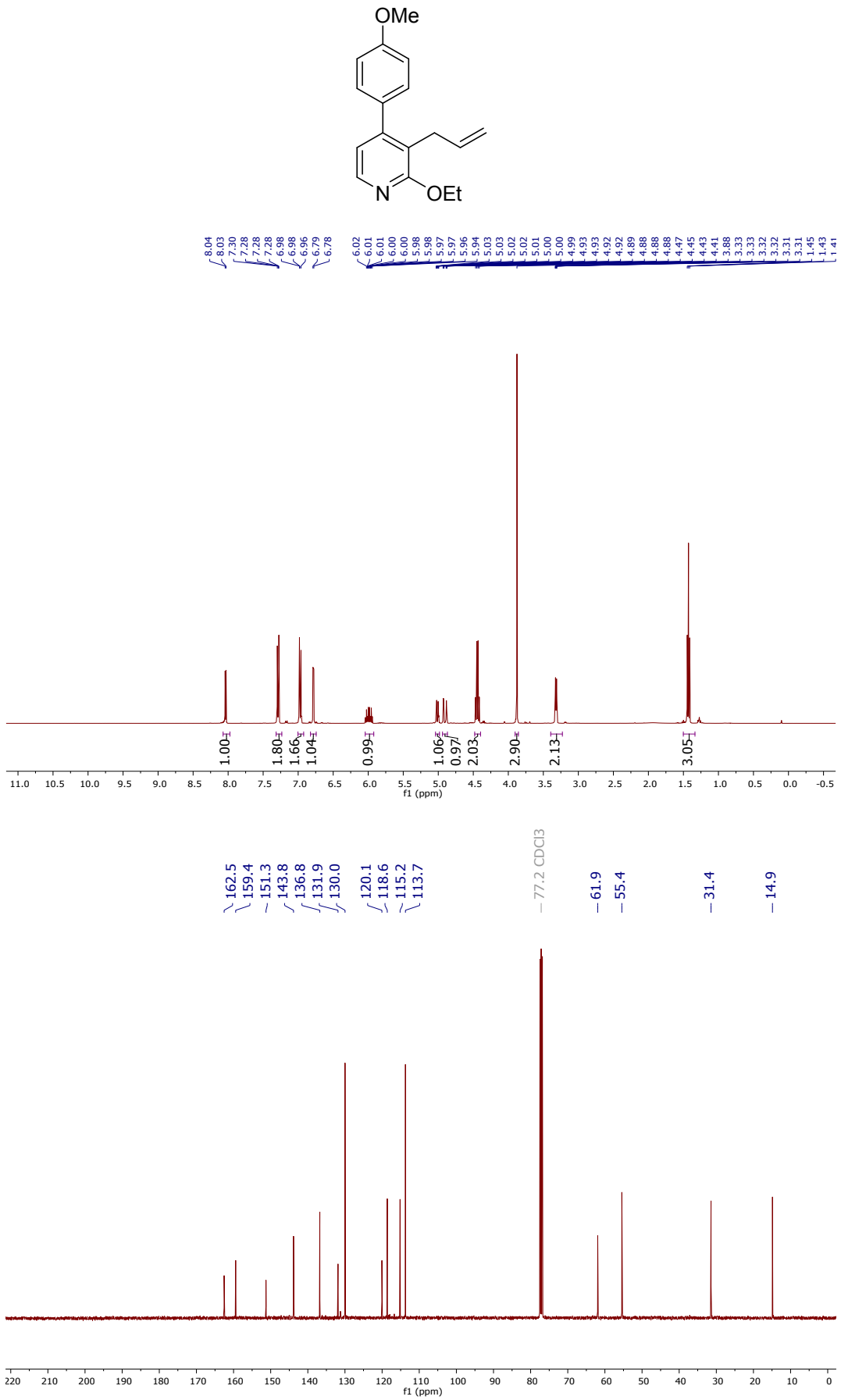
2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)(thiophen-3-yl)methanol (7ad)



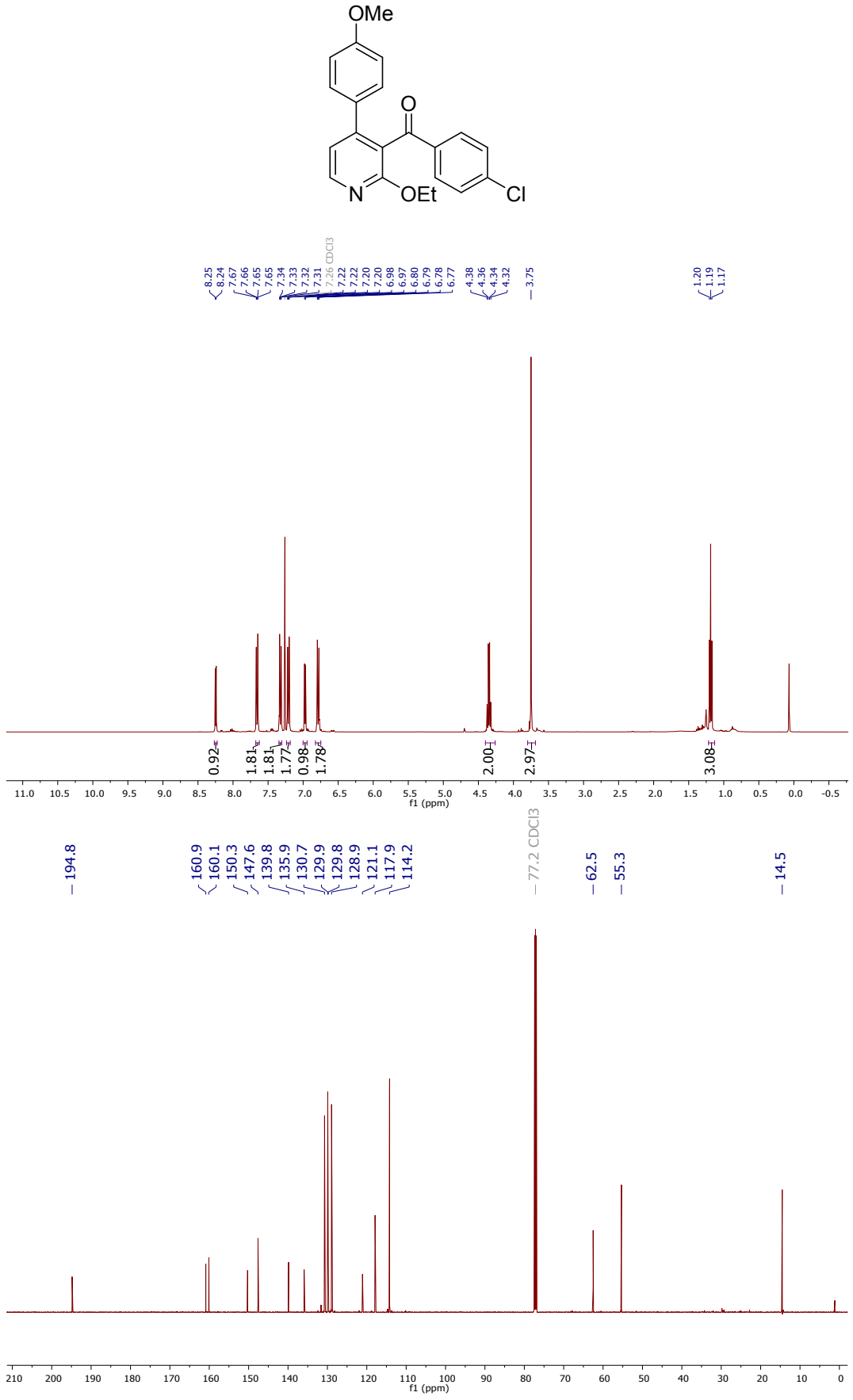
(2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)(pyridin-2-yl)methanol (7ae)



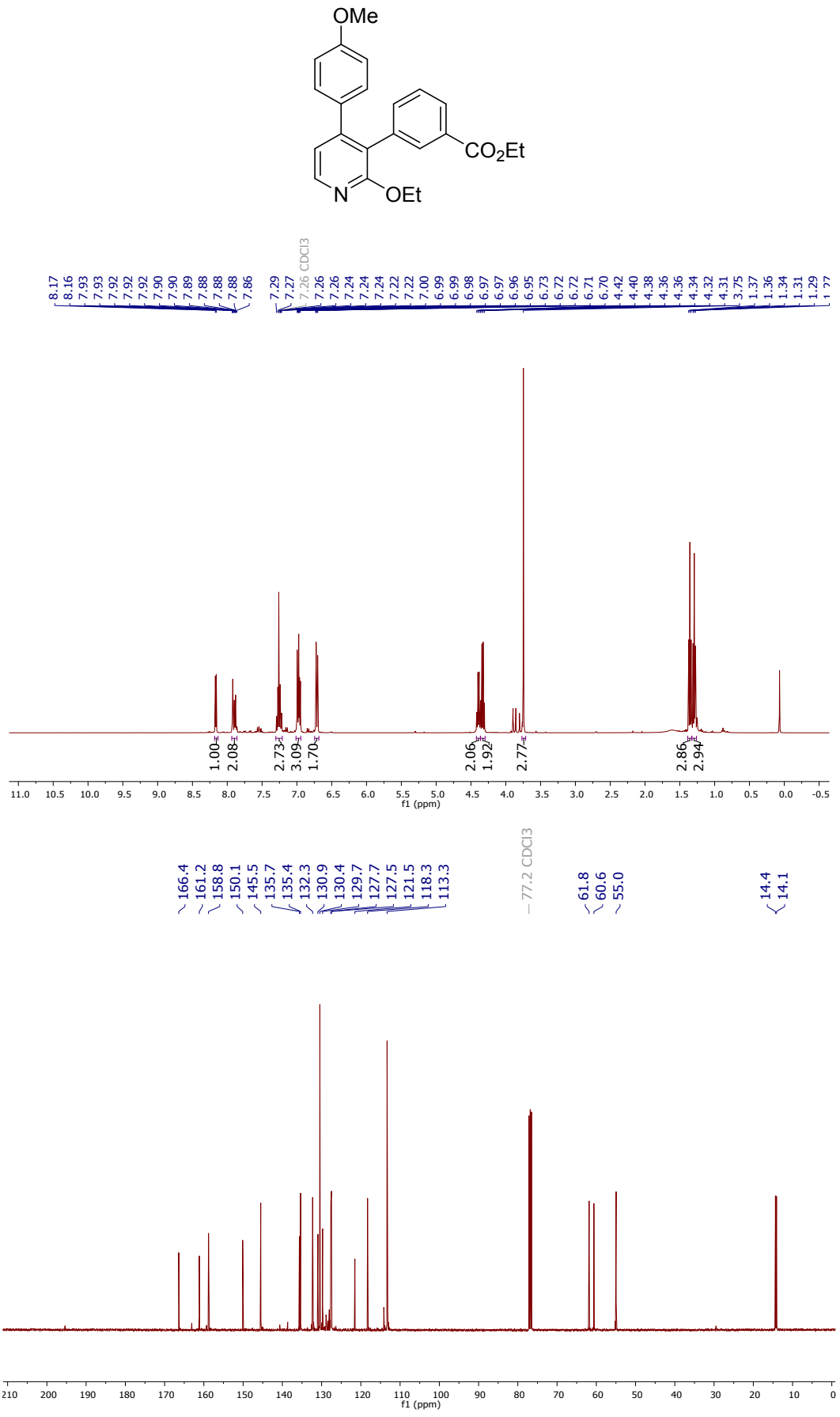
3-Allyl-2-ethoxy-4-(4-methoxyphenyl)pyridine (7af)



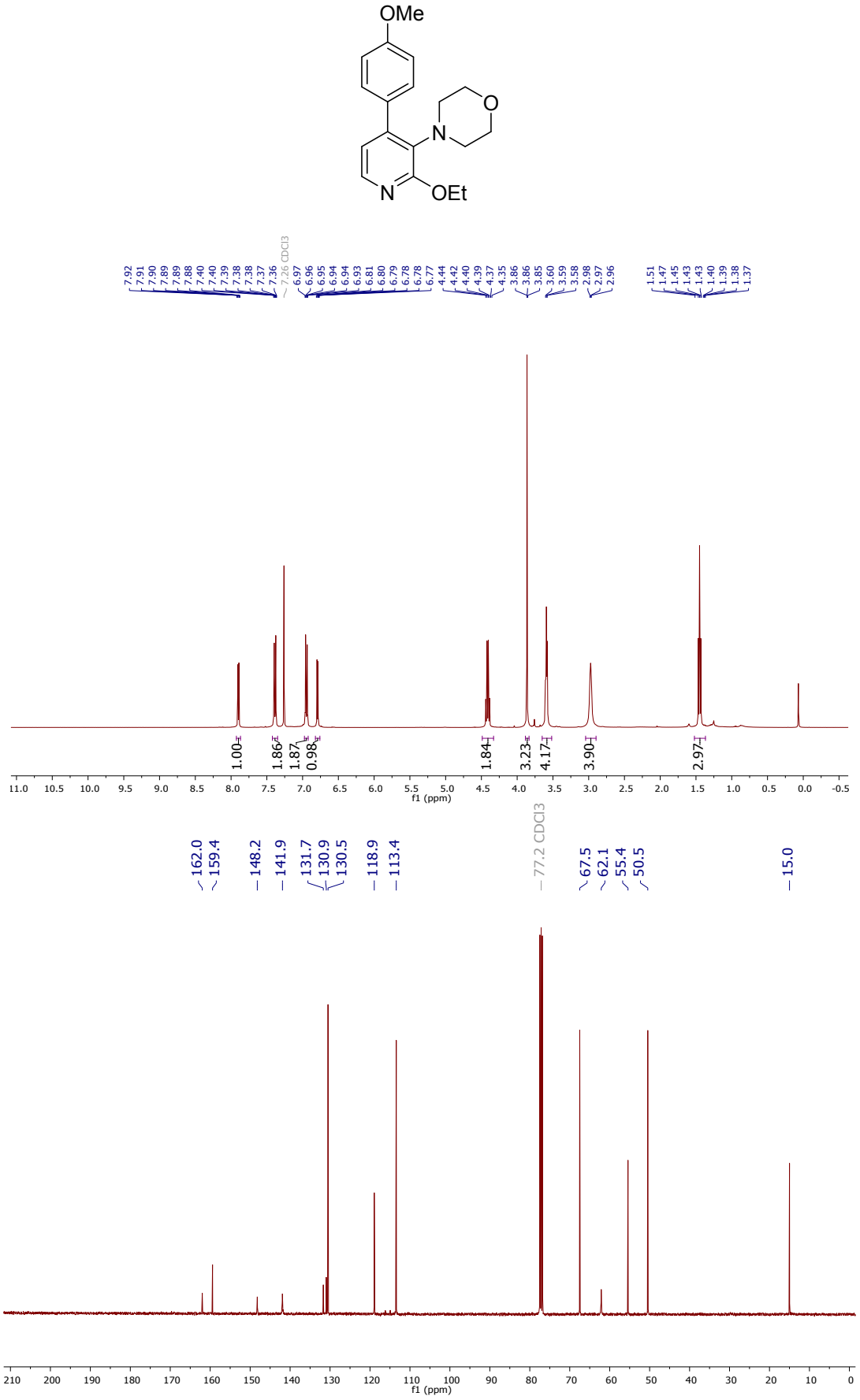
(4-Chlorophenyl)(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)methanone (7ag)



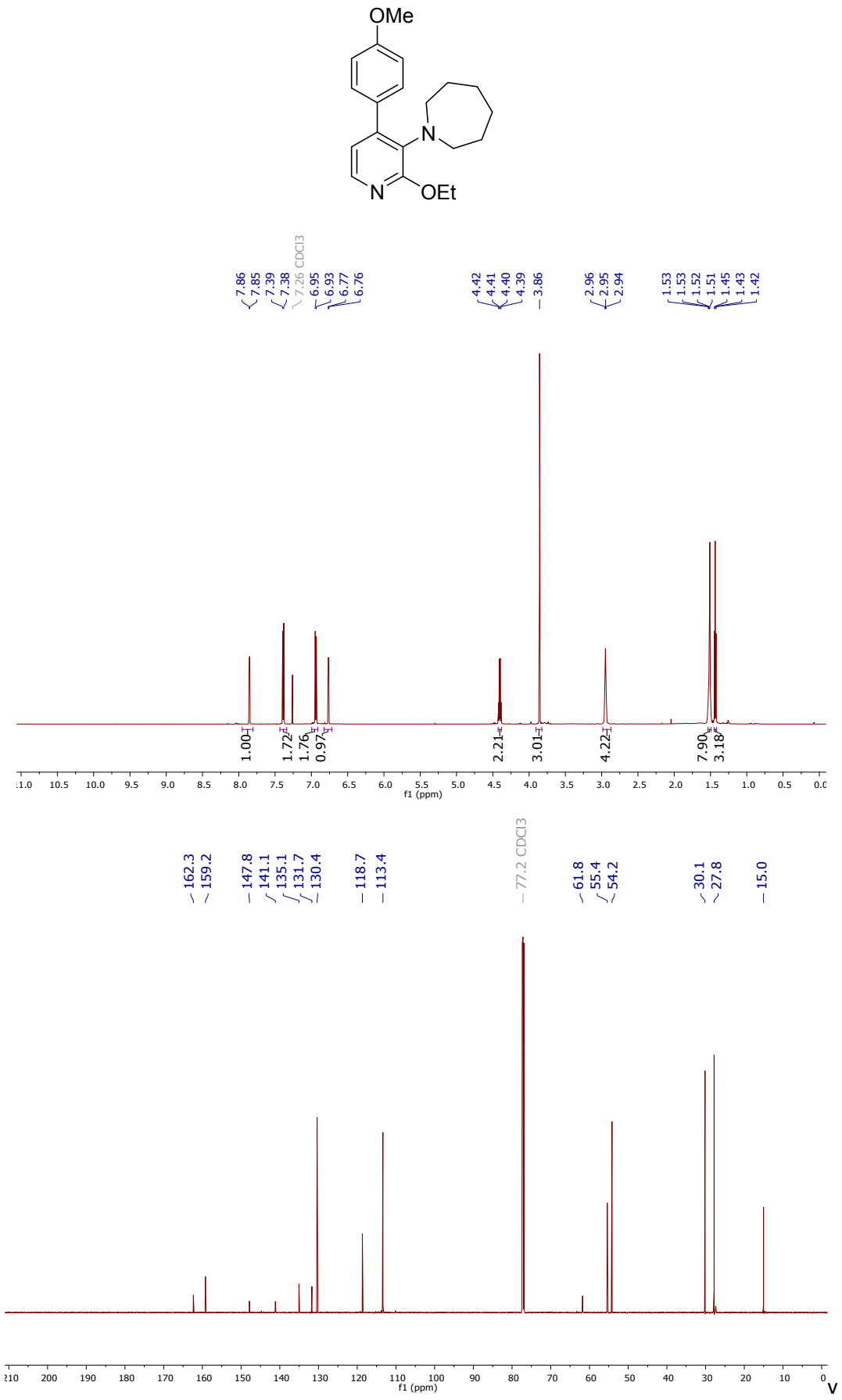
Ethyl 3-(2-ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)benzoate (7ah)



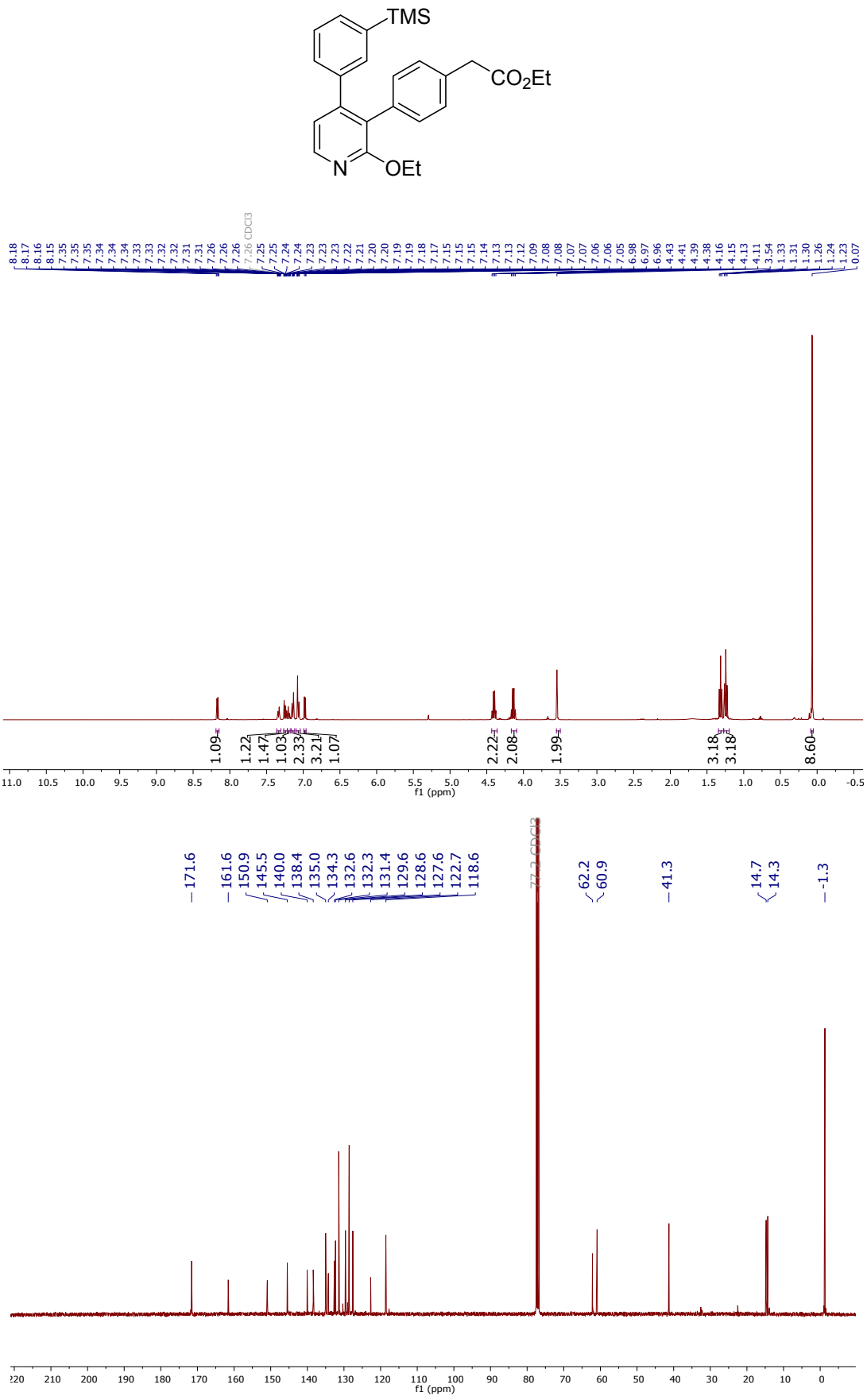
4-(2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)morpholine (7ai)



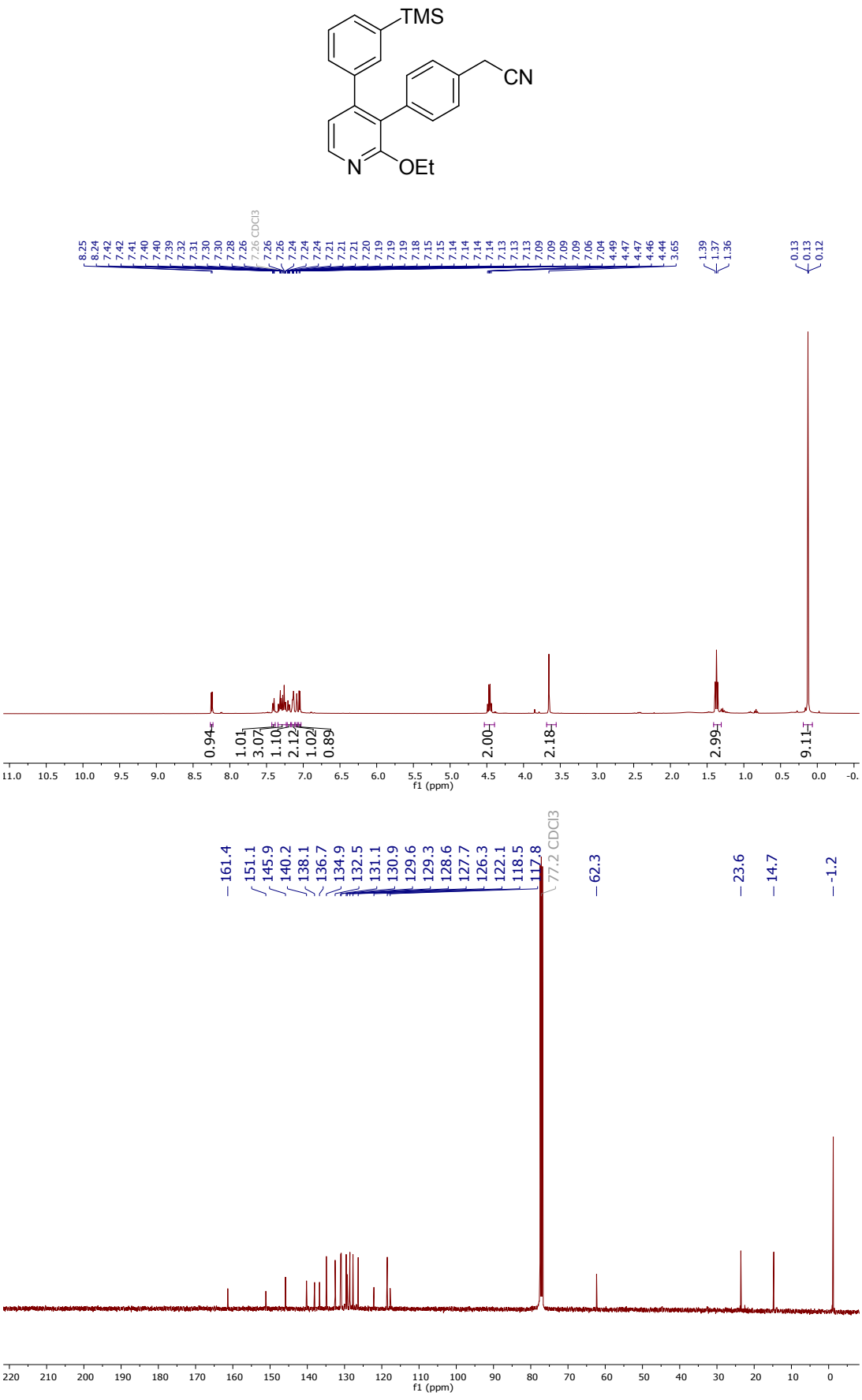
1-(2-Ethoxy-4-(4-methoxyphenyl)pyridin-3-yl)azepane (7aj)



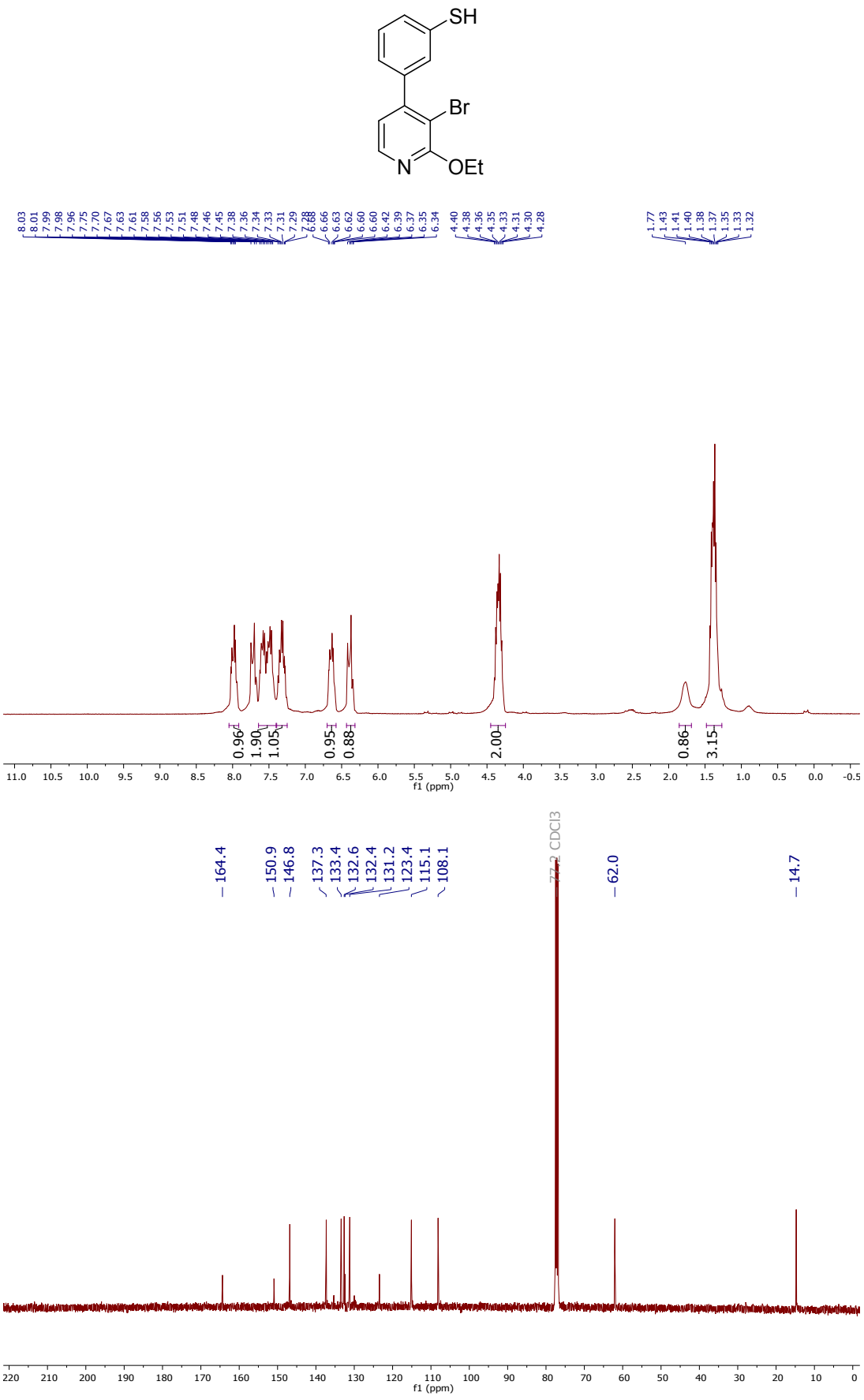
Ethyl 2-(4-(2-ethoxy-4-(3-(trimethylsilyl)phenyl)pyridin-3-yl)phenyl)acetate (7ba)



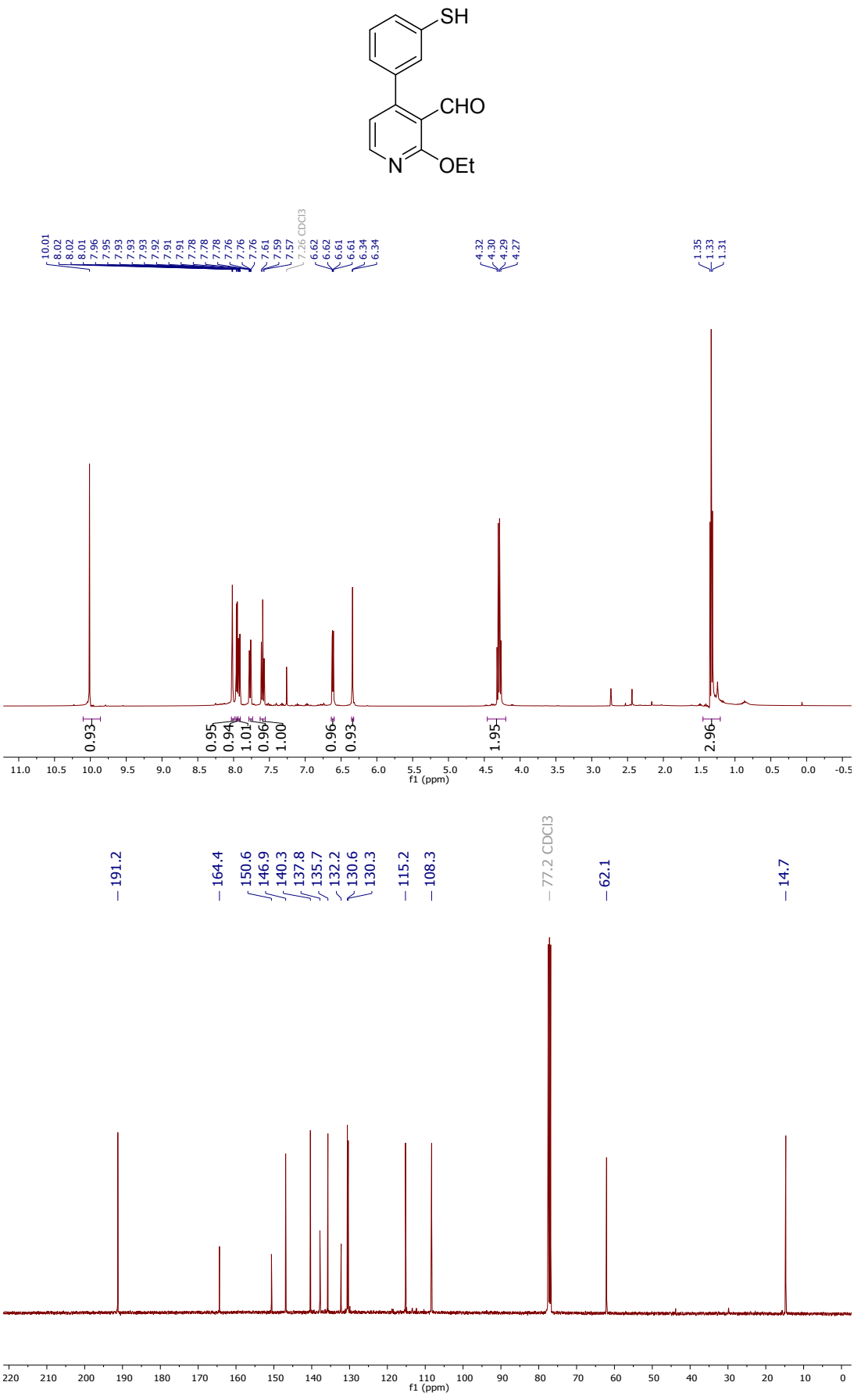
2-(4-(2-Ethoxy-4-(3-(trimethylsilyl)phenyl)pyridin-3-yl)phenyl)acetonitrile (7bb)



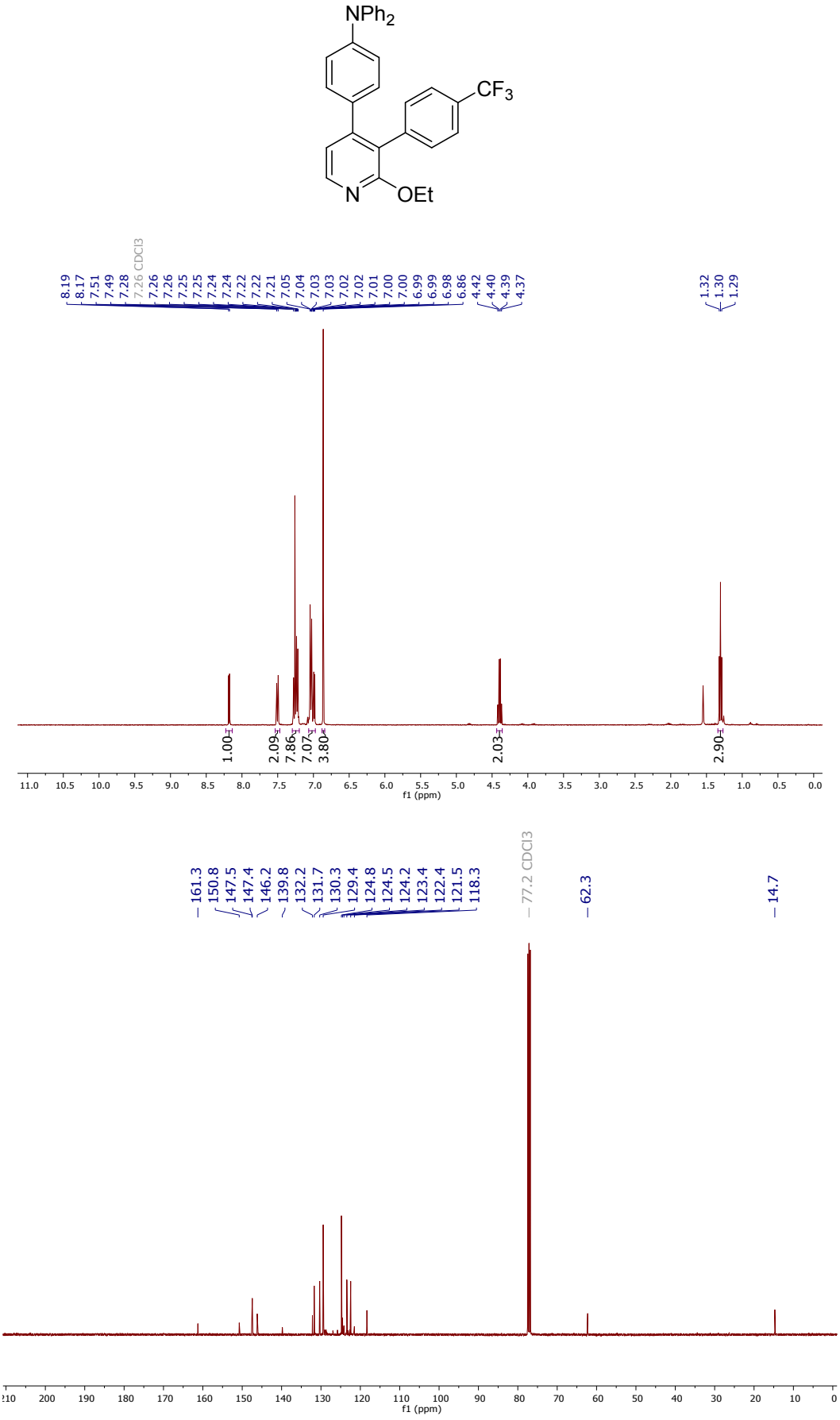
3-(3-Bromo-2-ethoxypyridin-4-yl)benzenethiol (7ca)



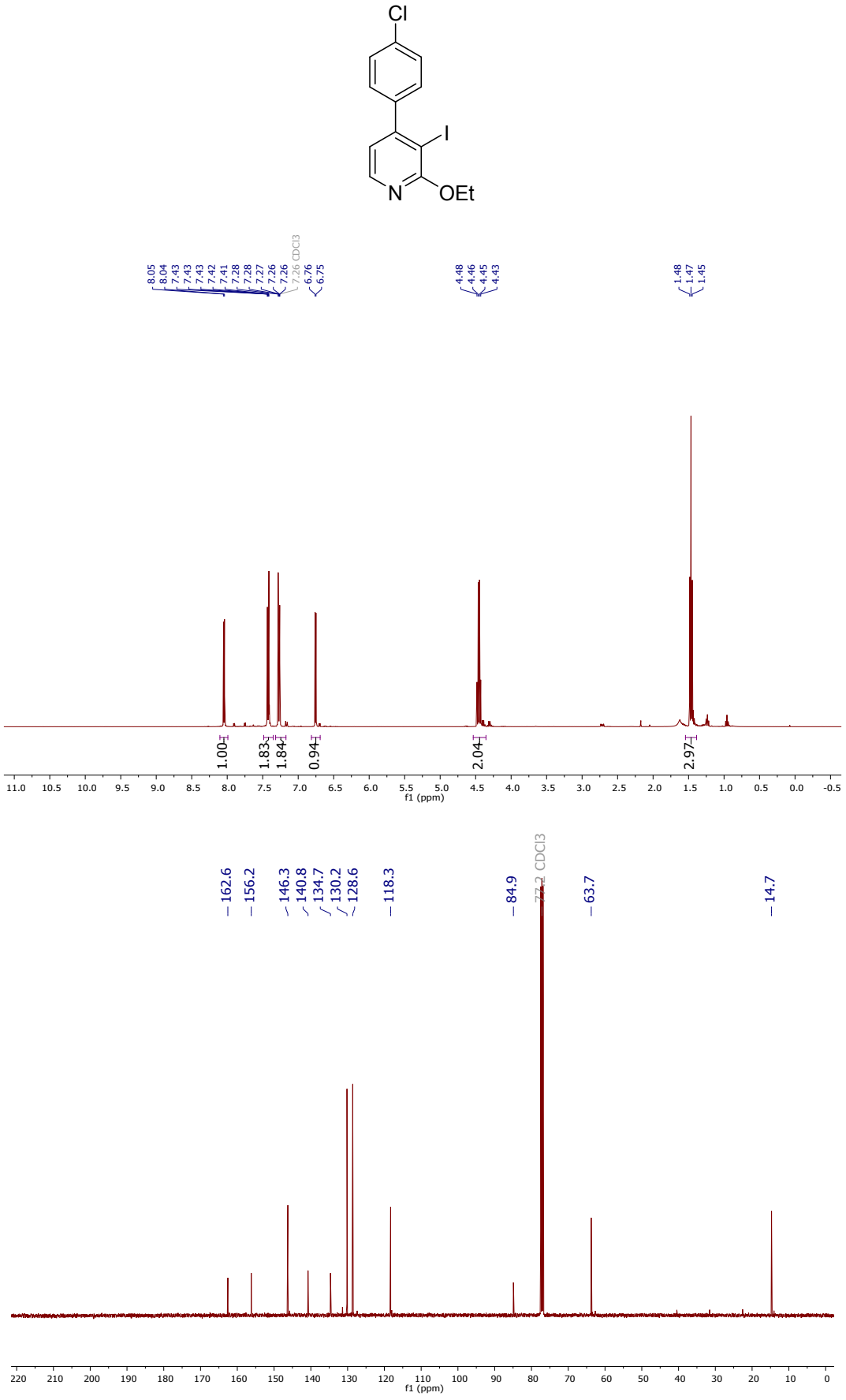
2-Ethoxy-4-(3-mercaptophenyl)nicotinaldehyde (7cb)



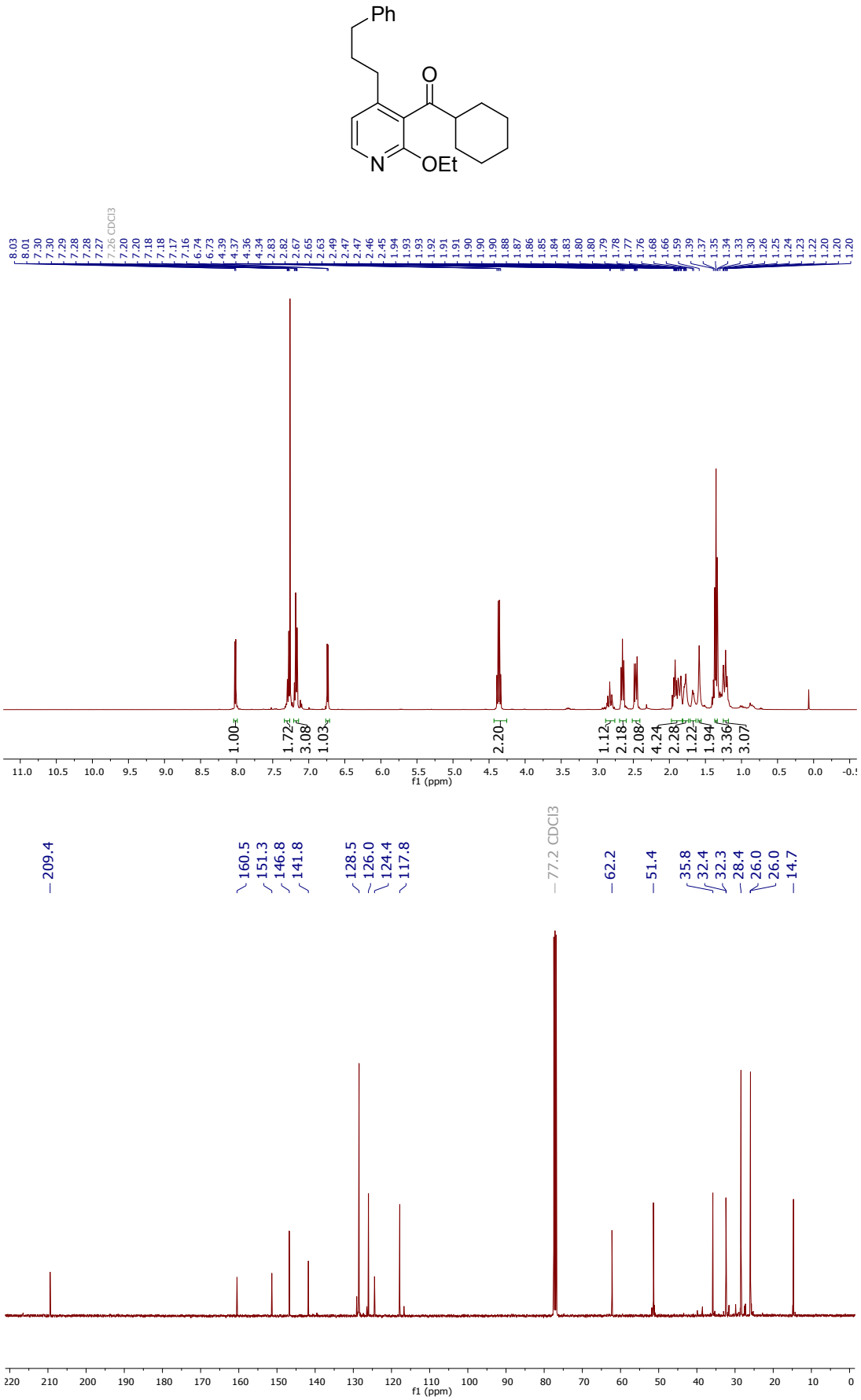
4-(2-Ethoxy-3-(4-(trifluoromethyl)phenyl)pyridin-4-yl)-*N*,*N*-diphenylaniline (7da)



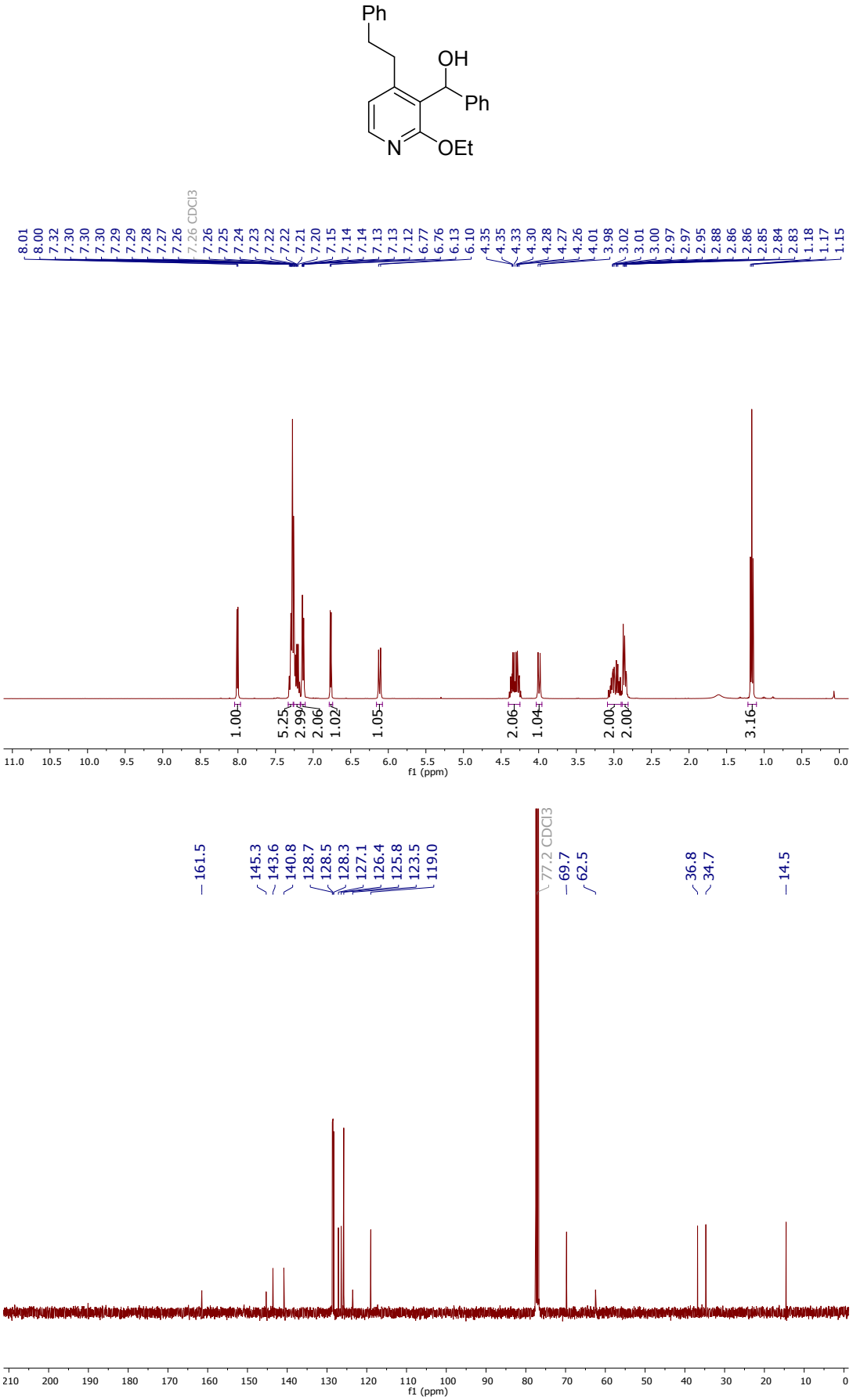
4-(4-Chlorophenyl)-2-ethoxy-3-iodopyridine (7ea)



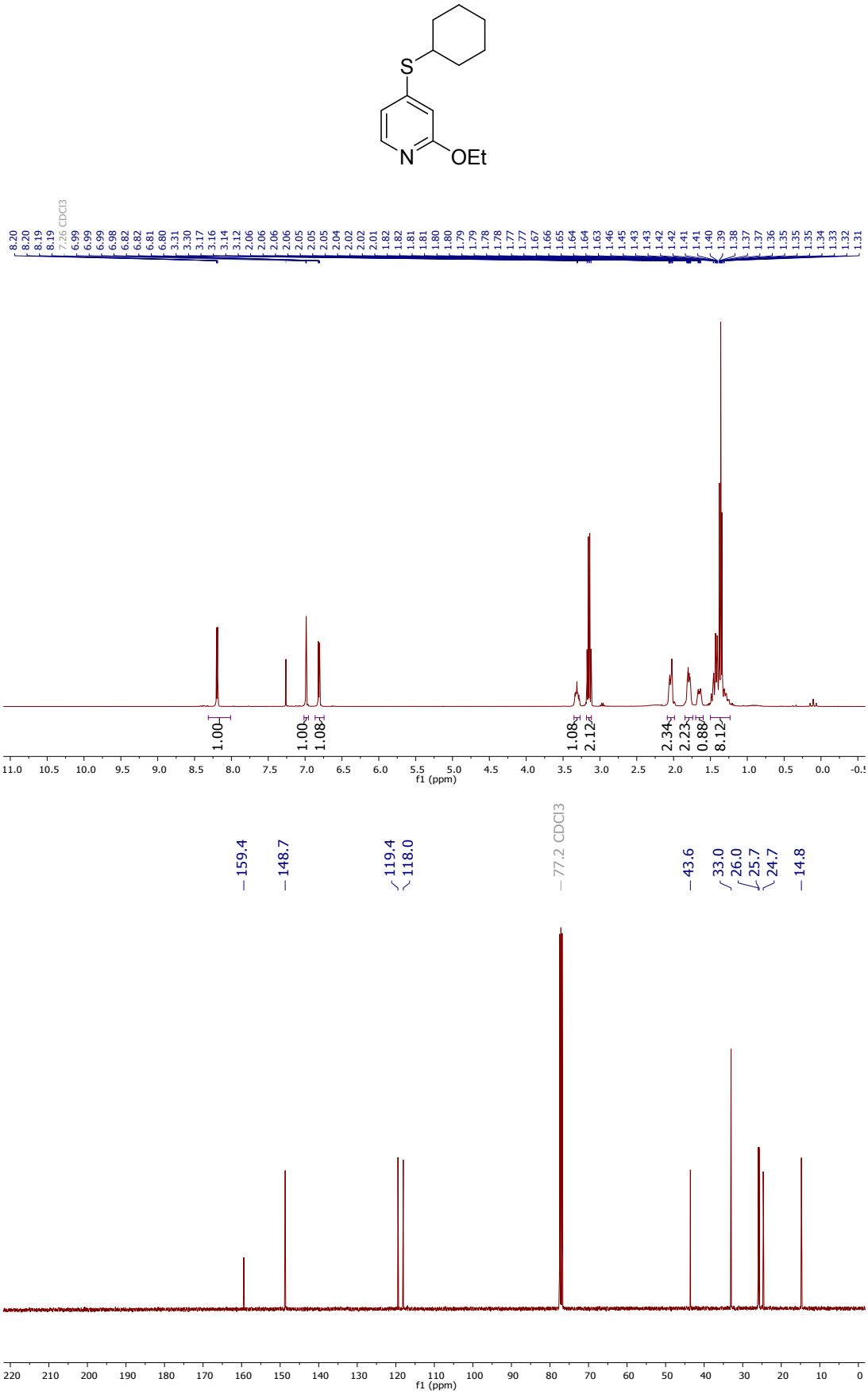
Cyclohexyl(2-ethoxy-4-(3-phenylpropyl)pyridin-3-yl)methanone (7ha)



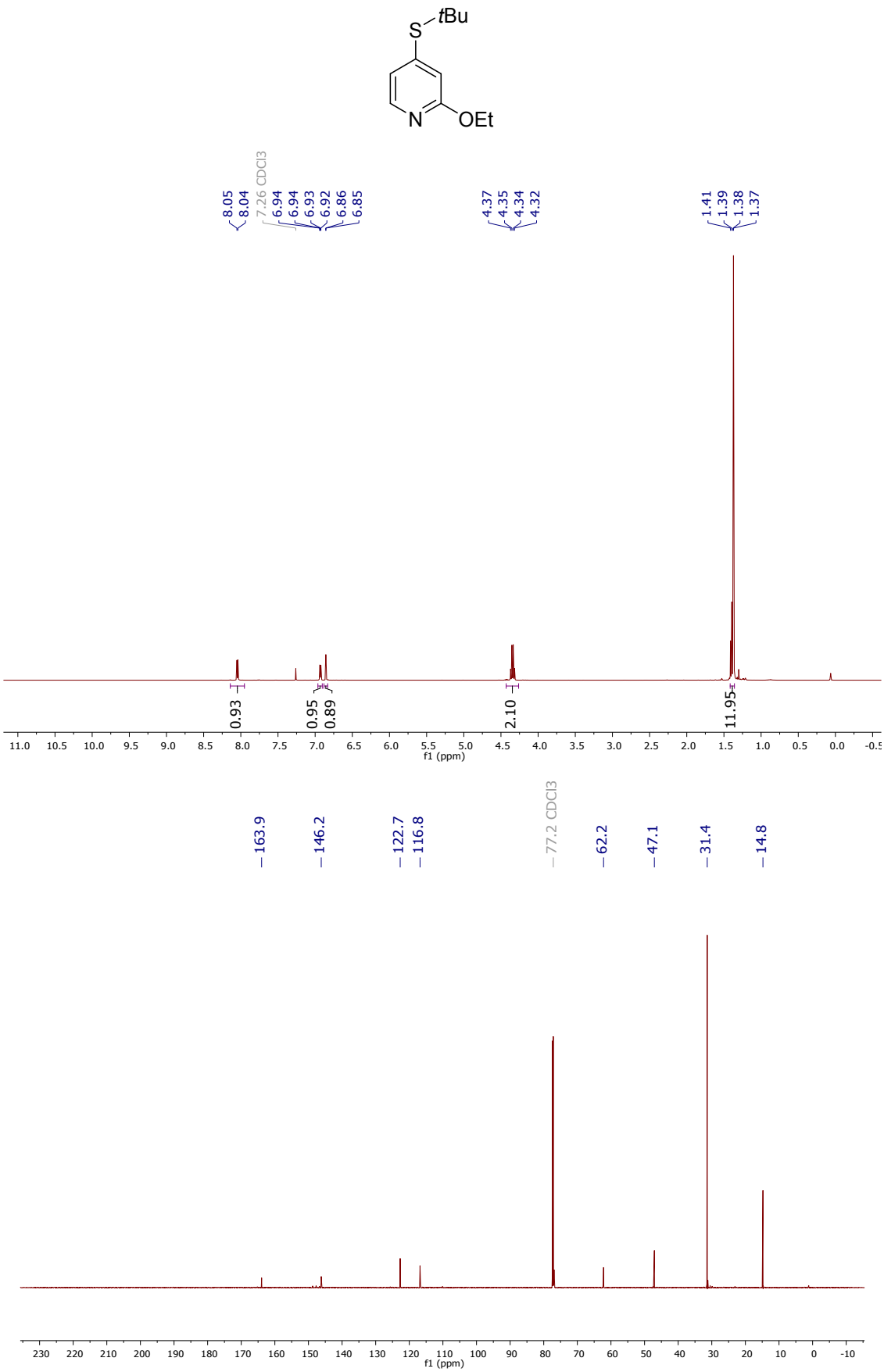
(2-Ethoxy-4-phenethylpyridin-3-yl)(phenyl)methanol (7ia)



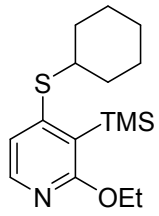
4-(Cyclohexylthio)-2-ethoxypyridine (10a)

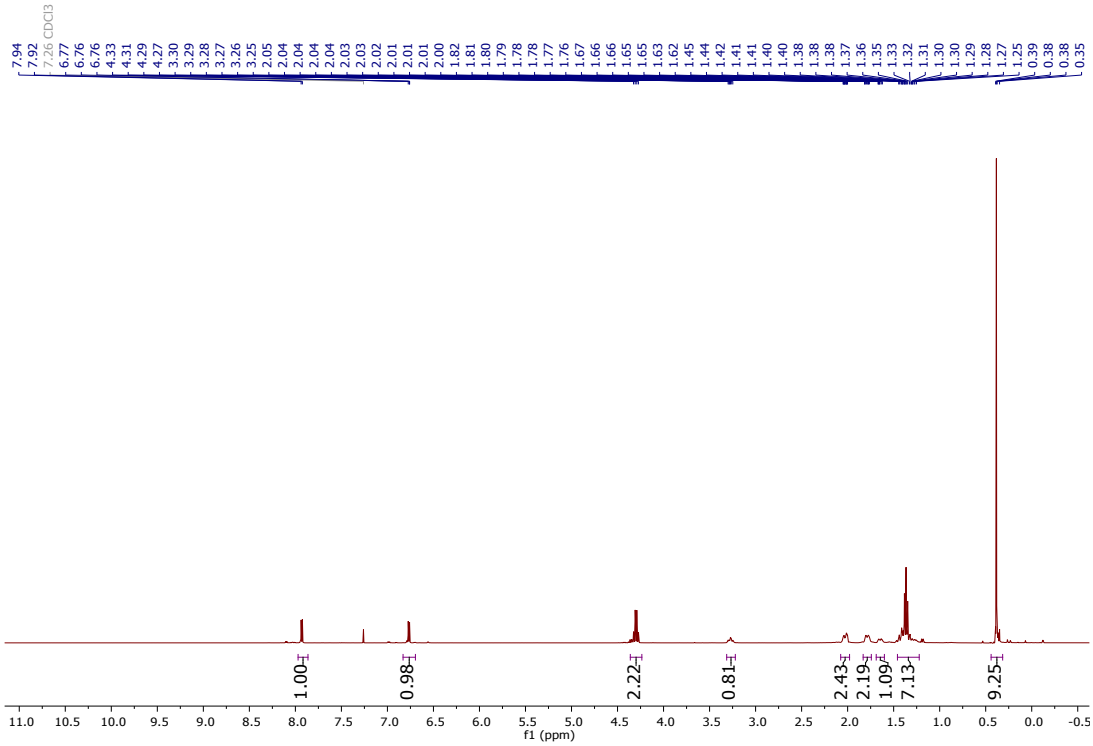


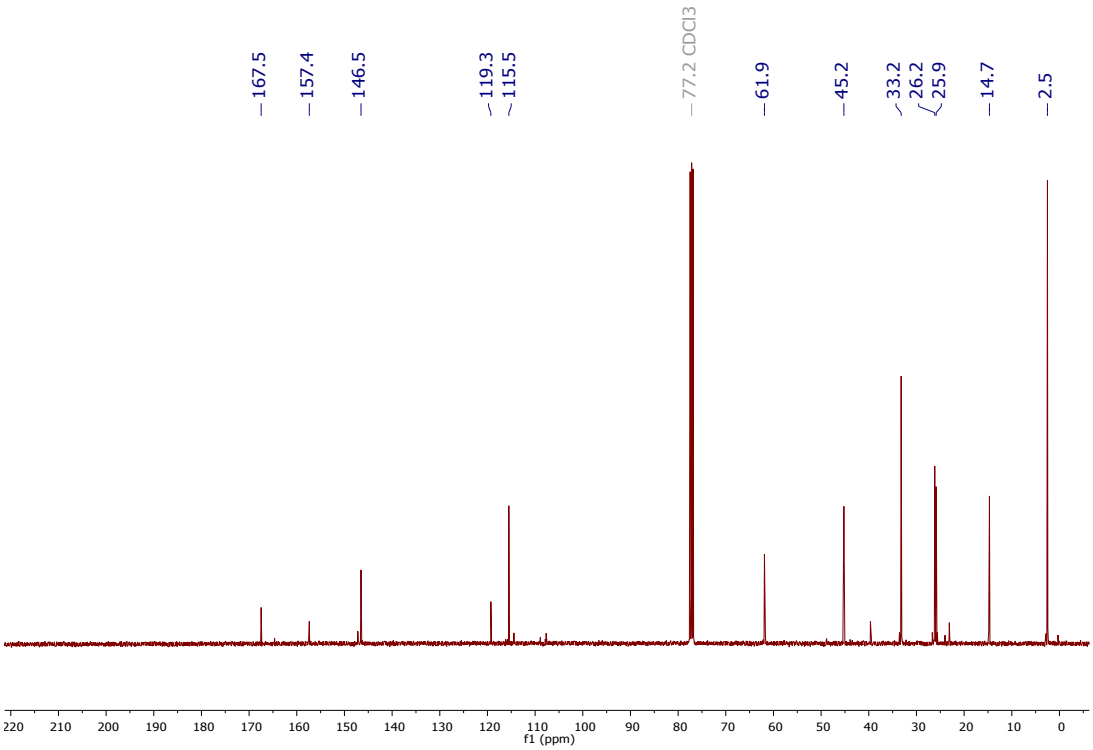
4-(*Tert*-butylthio)-2-ethoxypyridine (10b)



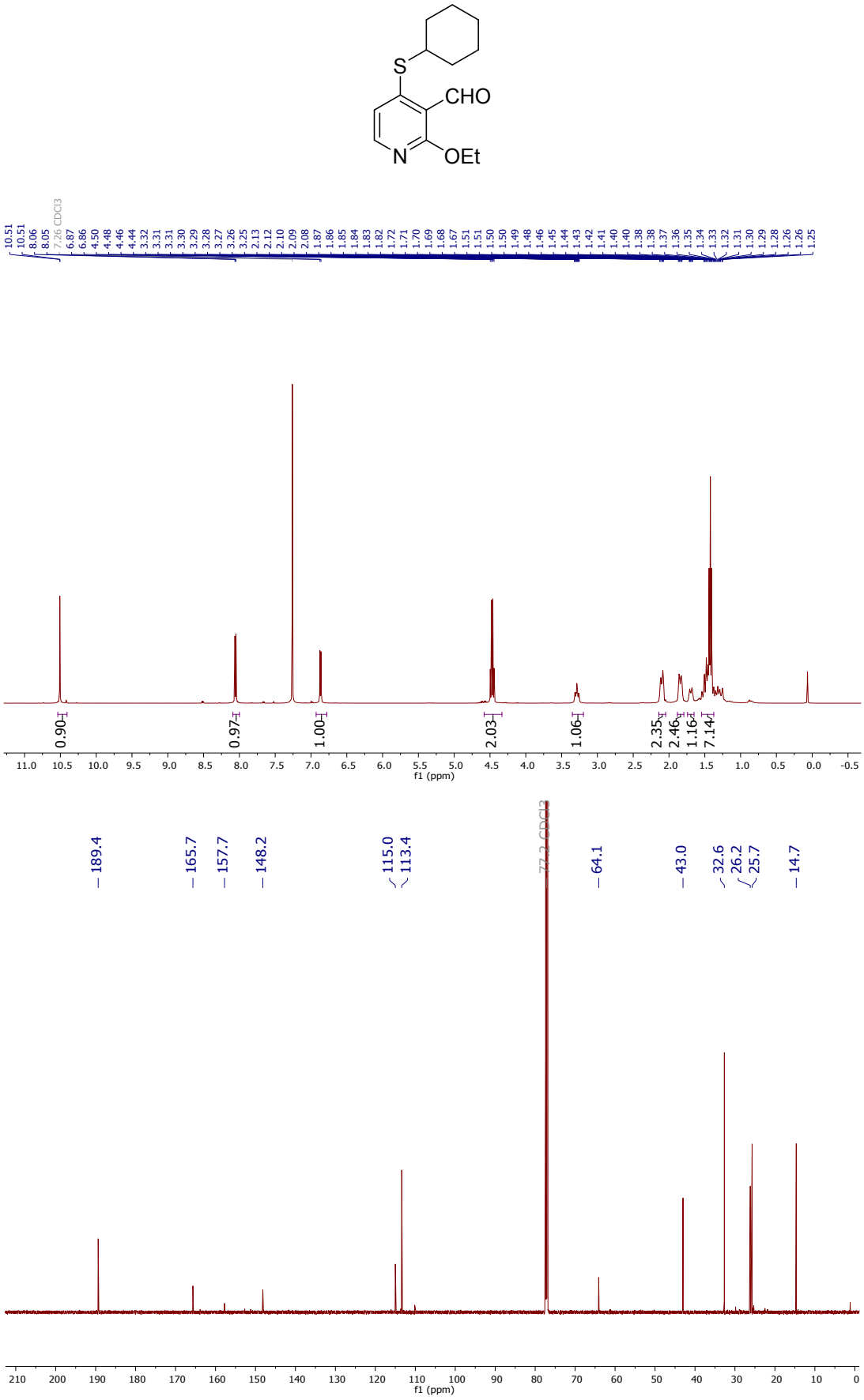
4-(Cyclohexylthio)-2-ethoxy-3-(trimethylsilyl)pyridine (10aa)



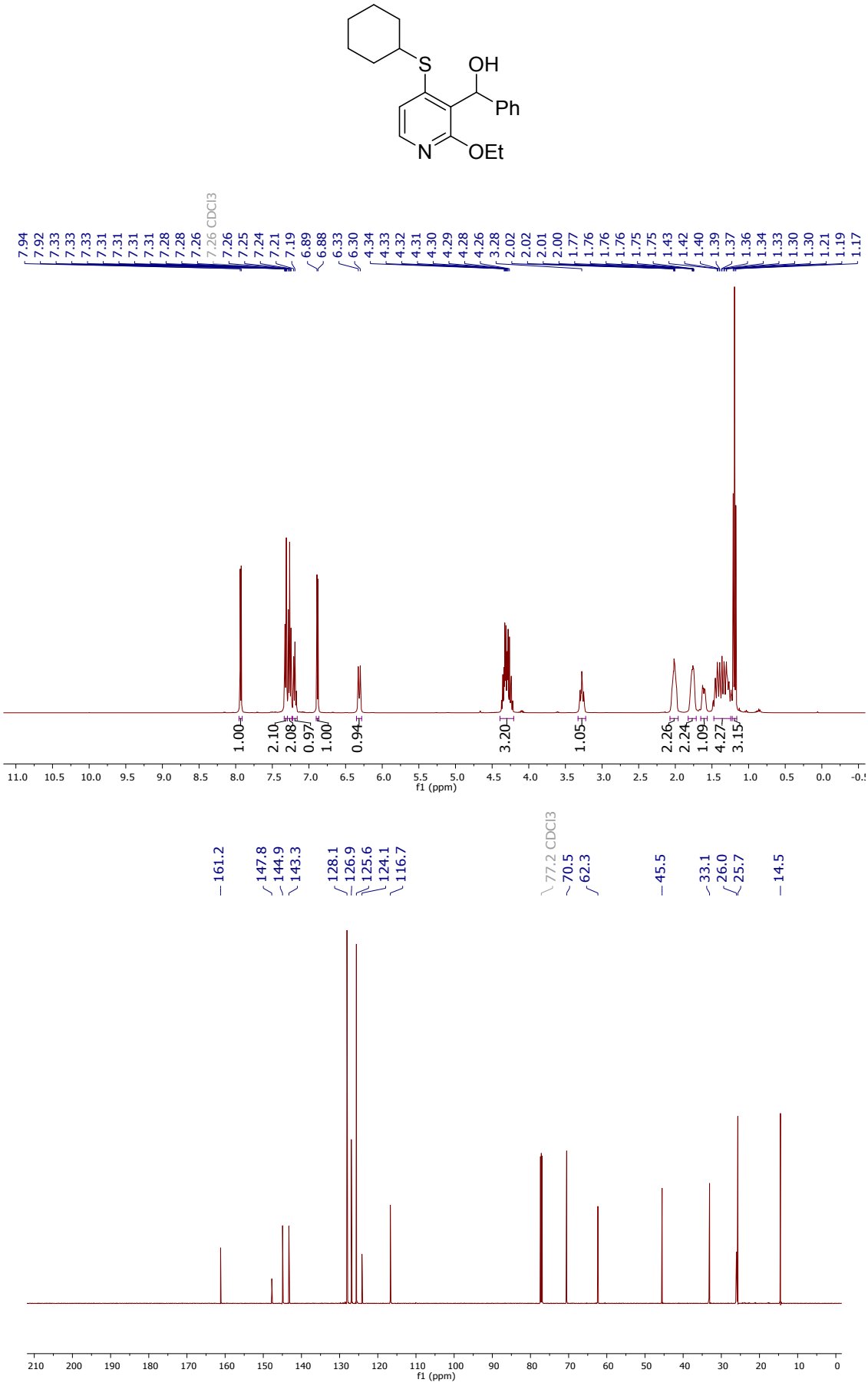




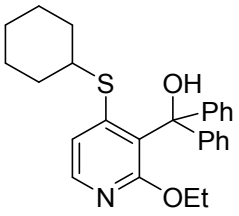
4-(Cyclohexylthio)-2-ethoxynicotinaldehyde (10ab)

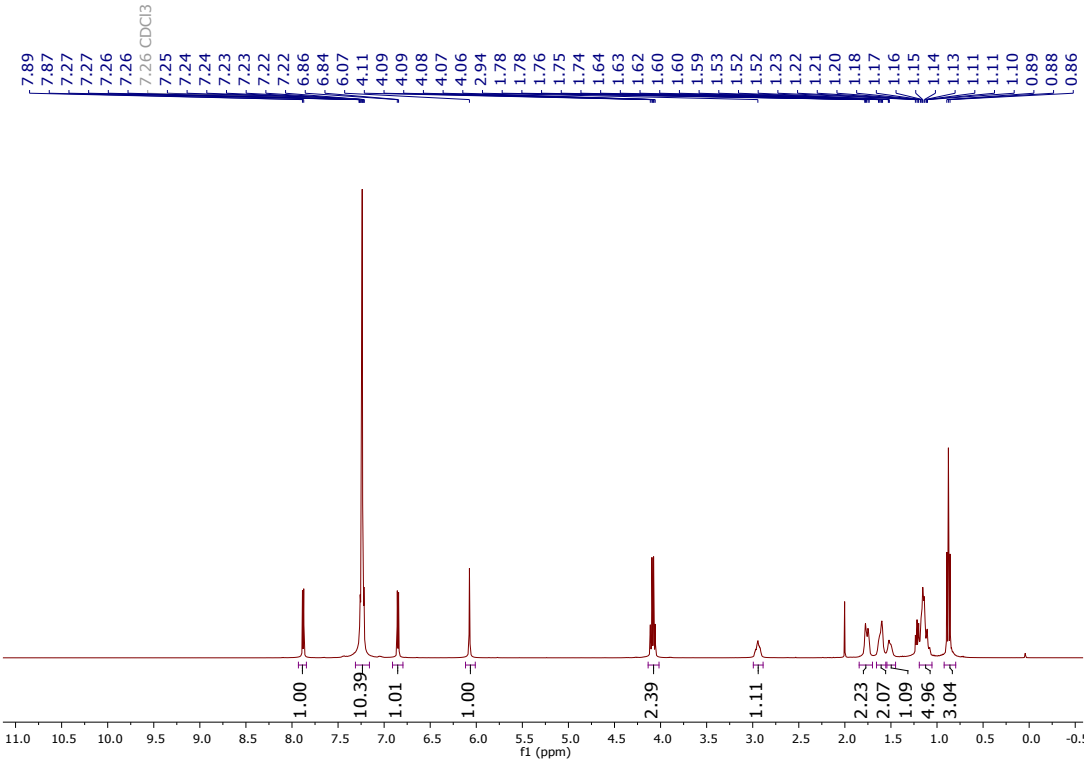


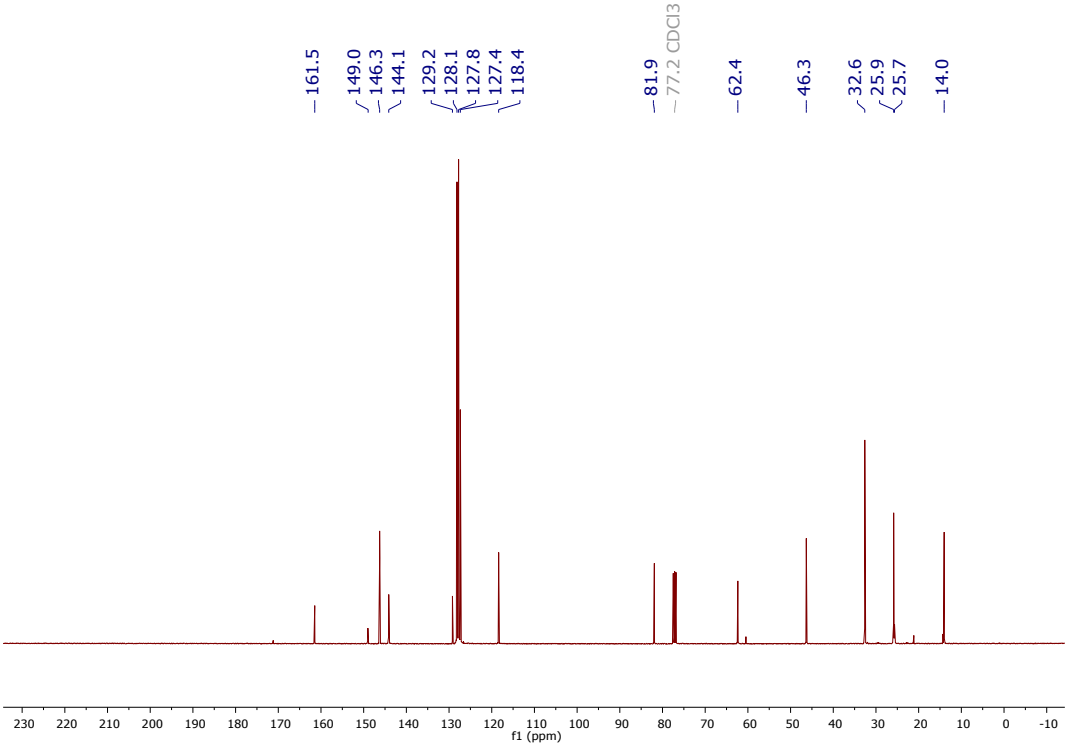
(4-(Cyclohexylthio)-2-ethoxypyridin-3-yl)(phenyl)methanol (10ac)


S
OH
Ph
N
OEt
7.94
7.92
7.33
7.33
7.33
7.31
7.31
7.31
7.31
7.28
7.28
7.26
7.26 CDCl3
7.26
7.25
7.24
7.21
7.19
6.89
6.88
6.33
6.30
4.34
4.33
4.32
4.31
4.30
4.29
4.28
4.26
3.28
2.02
2.02
2.01
2.00
1.77
1.76
1.76
1.76
1.75
1.75
1.43
1.42
1.40
1.39
1.37
1.36
1.34
1.33
1.30
1.30
1.21
1.19
1.17
1.00
2.10
2.08
0.97
1.00
0.94
3.20
1.05
2.26
2.24
1.09
4.27
3.15
f1 (ppm)
161.2
147.8
144.9
143.3
128.1
126.9
125.6
124.1
116.7
77.2 CDCl3
70.5
62.3
45.5
33.1
26.0
25.7
14.5
f1 (ppm)

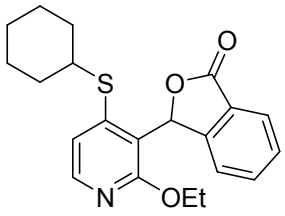
(4-(Cyclohexylthio)-2-ethoxypyridin-3-yl)diphenylmethanol (10ad)

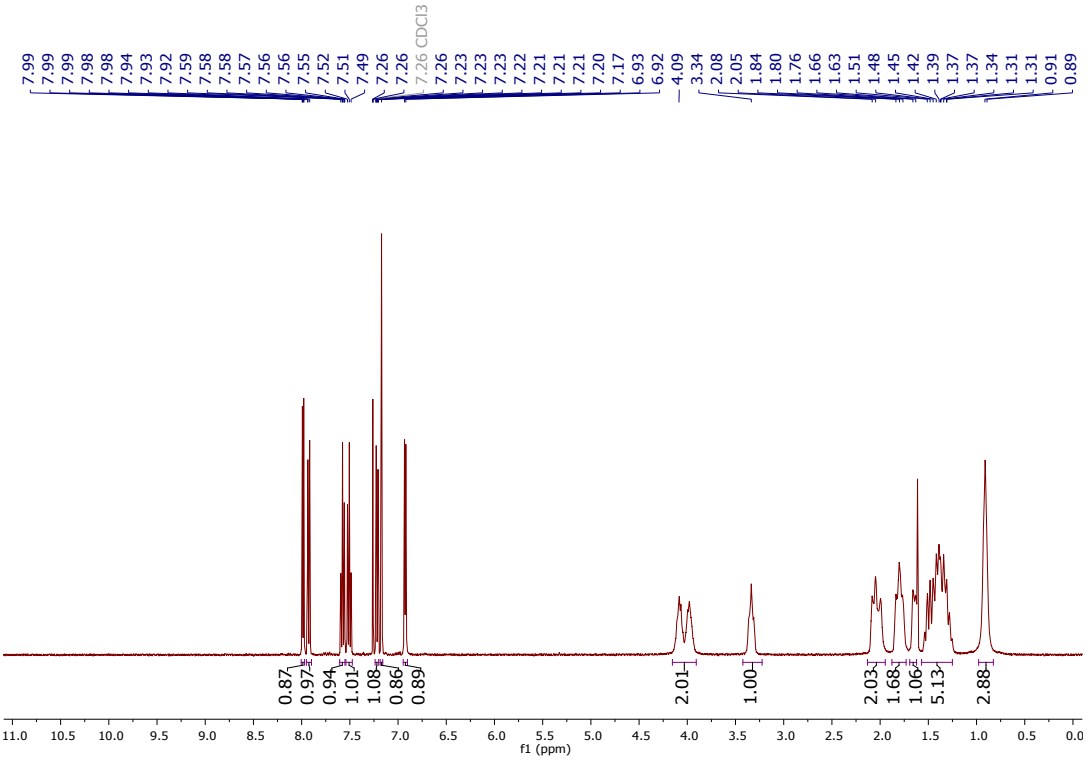


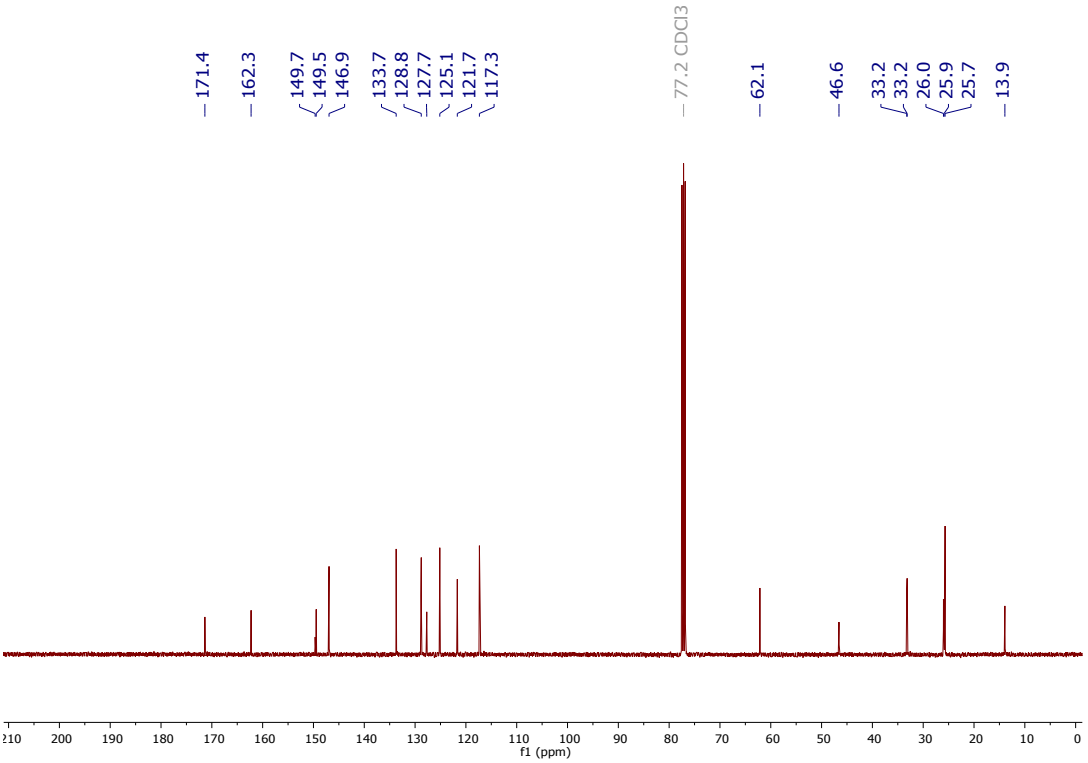




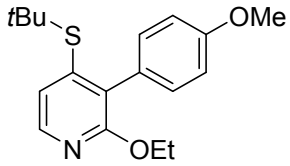
3-(4-Cyclohexylthio)-2-ethoxypyridin-3-yl)isobenzofuran-1(3*H*)-one (10ae)

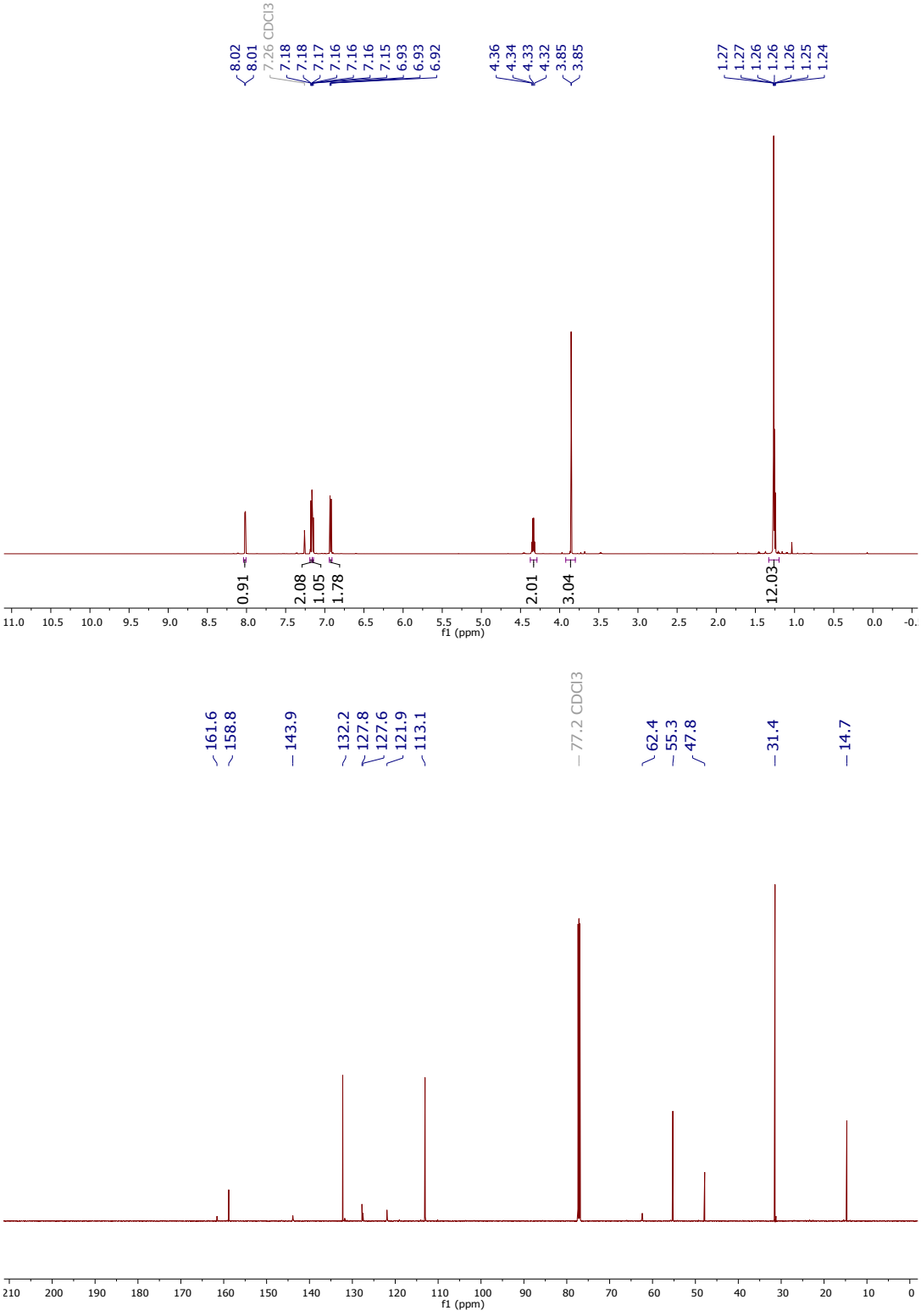




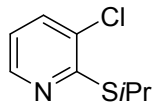


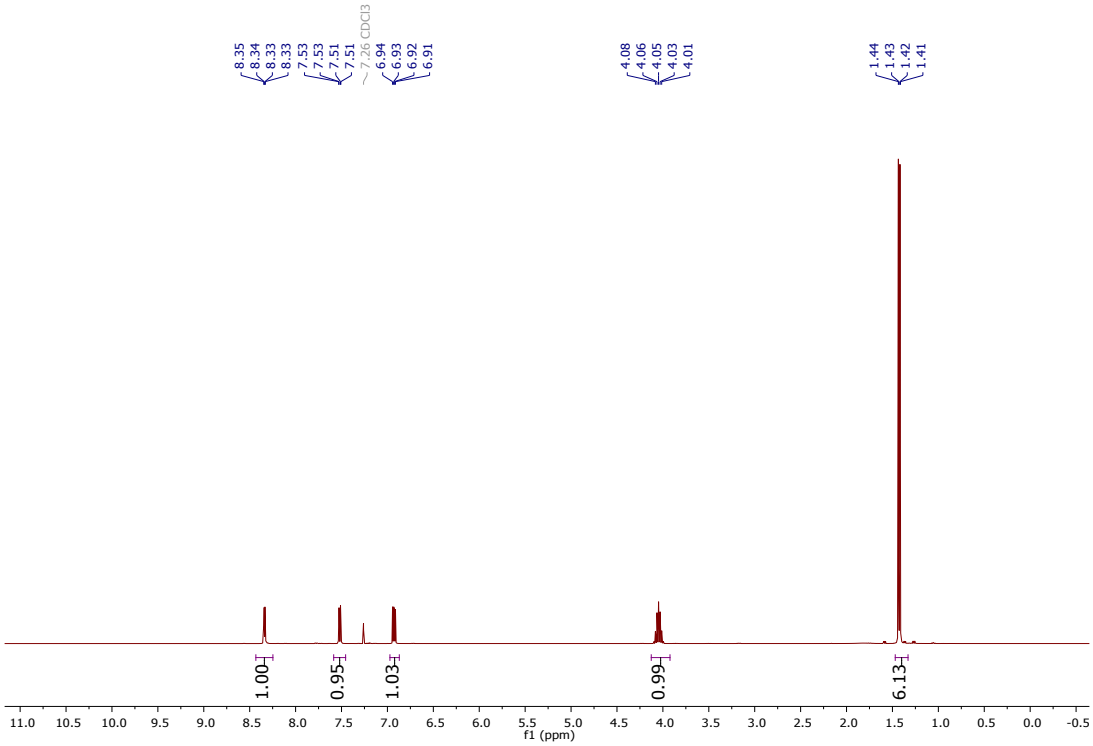
4-(*Tert*-butylthio)-2-ethoxy-3-(4-methoxyphenyl)pyridine (10ba)

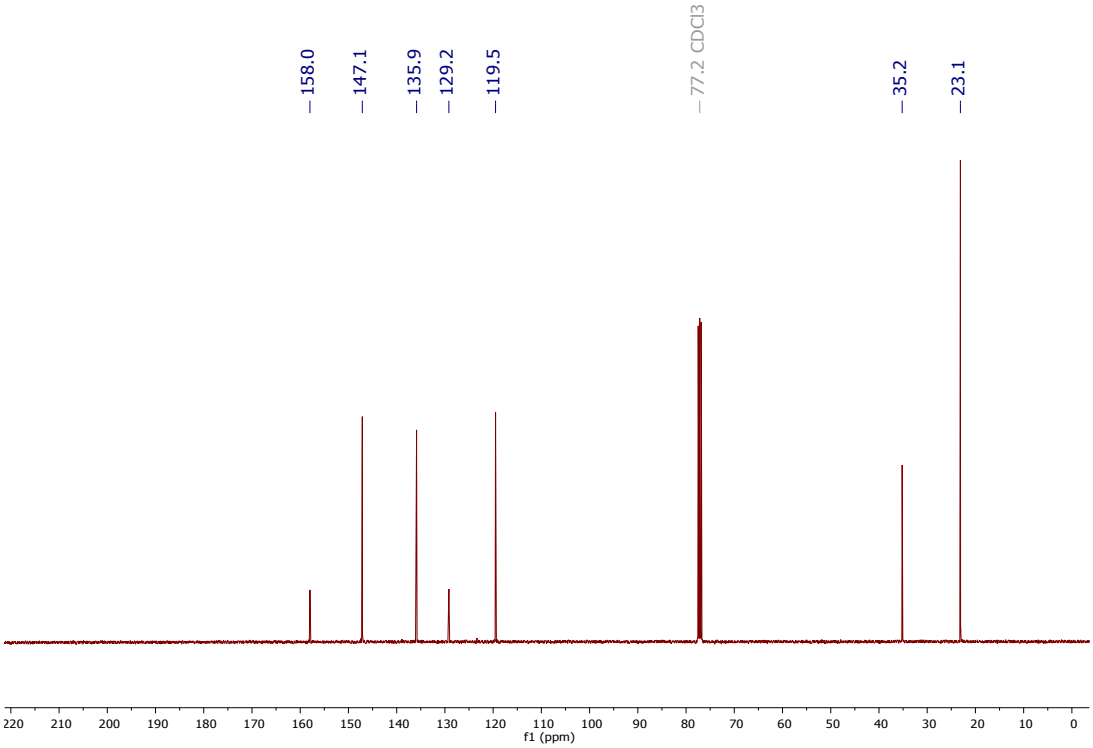




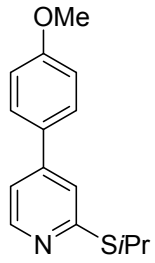
3-Chloro-2-(isopropylthio)pyridine (11)

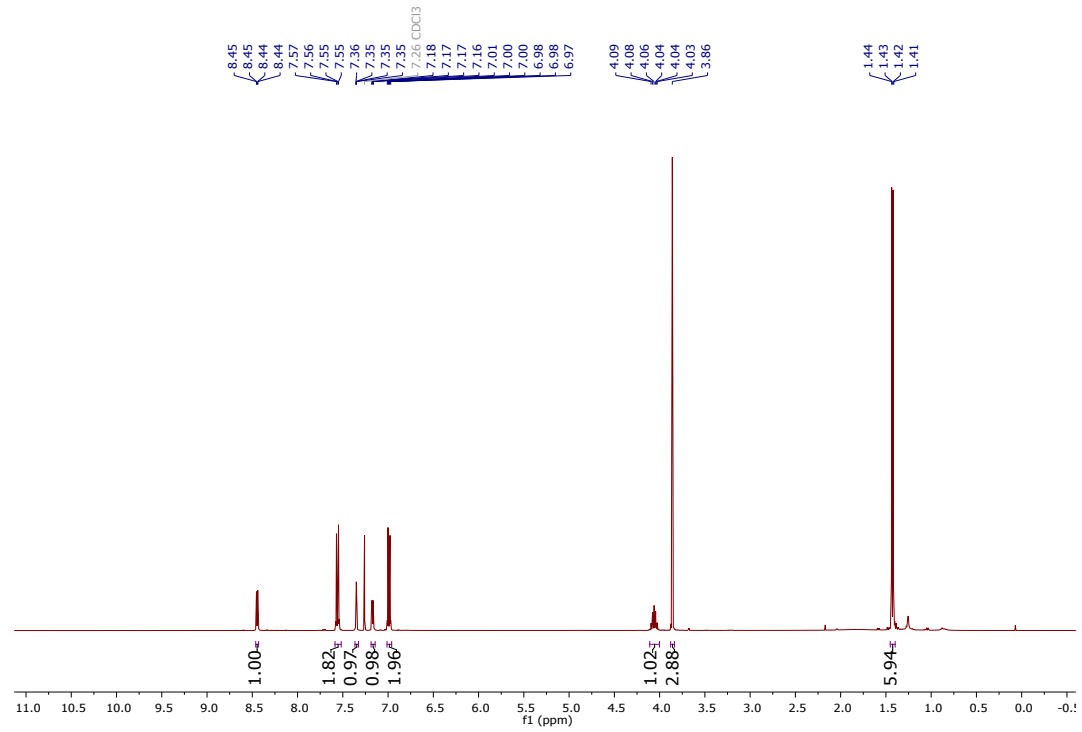


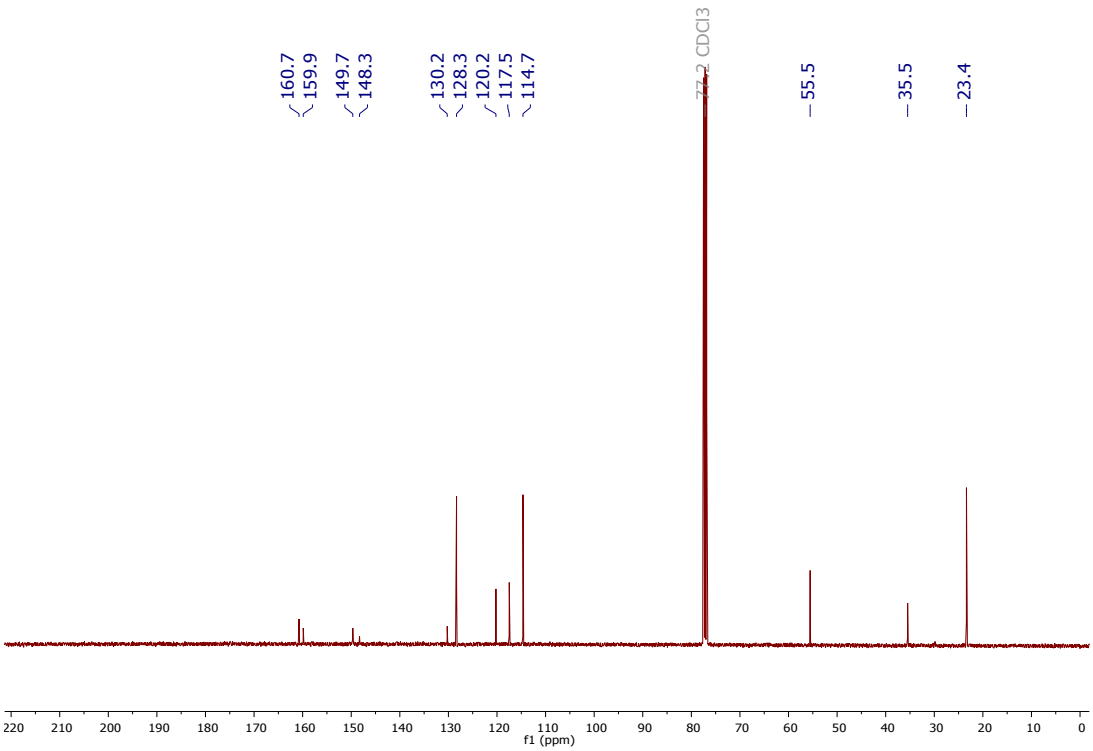




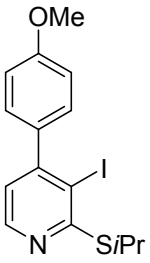
2-(Isopropylthio)-4-(4-methoxyphenyl)pyridine (12a)

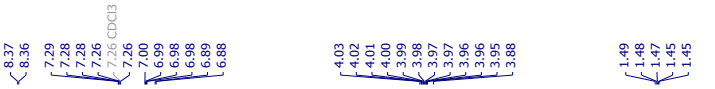


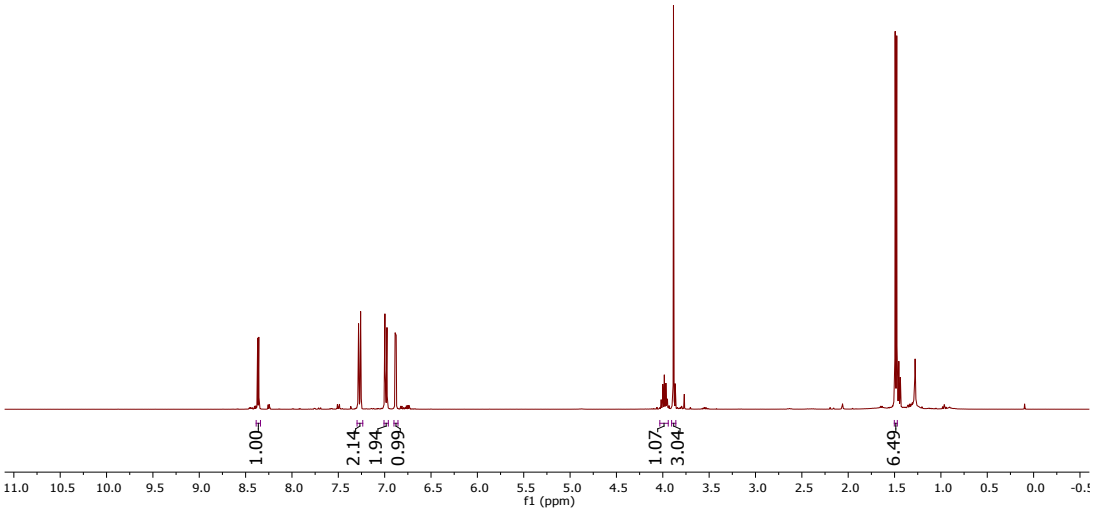


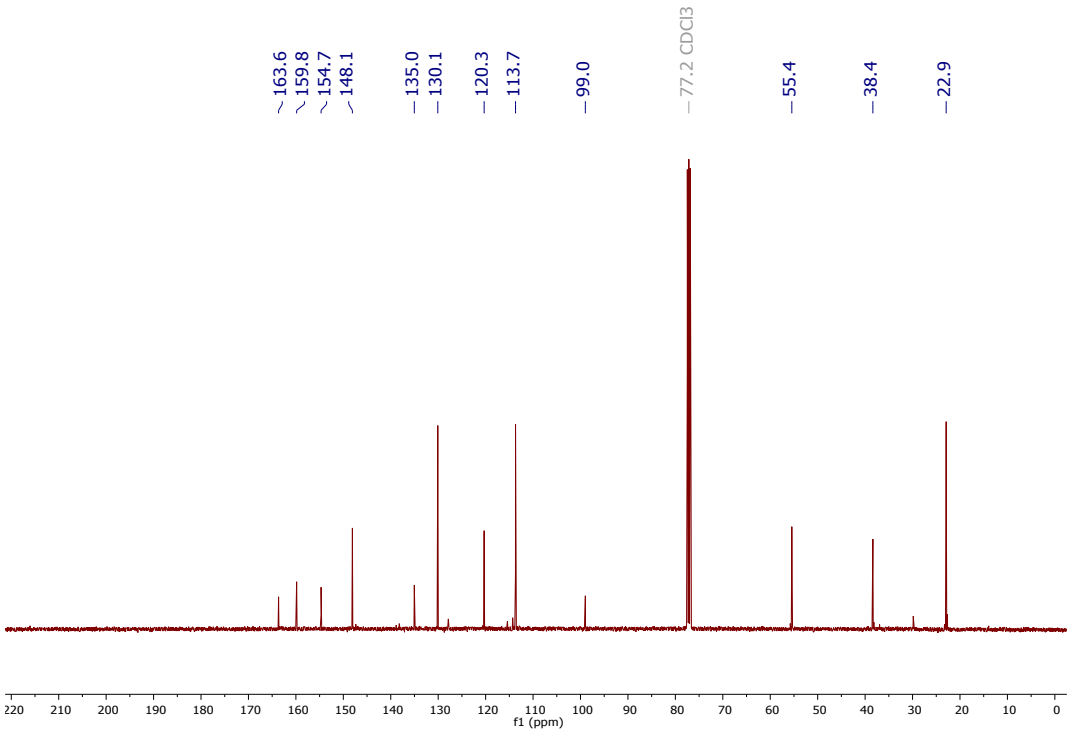


3-Iodo-2-(isopropylthio)-4-(4-methoxyphenyl)pyridine (12b)

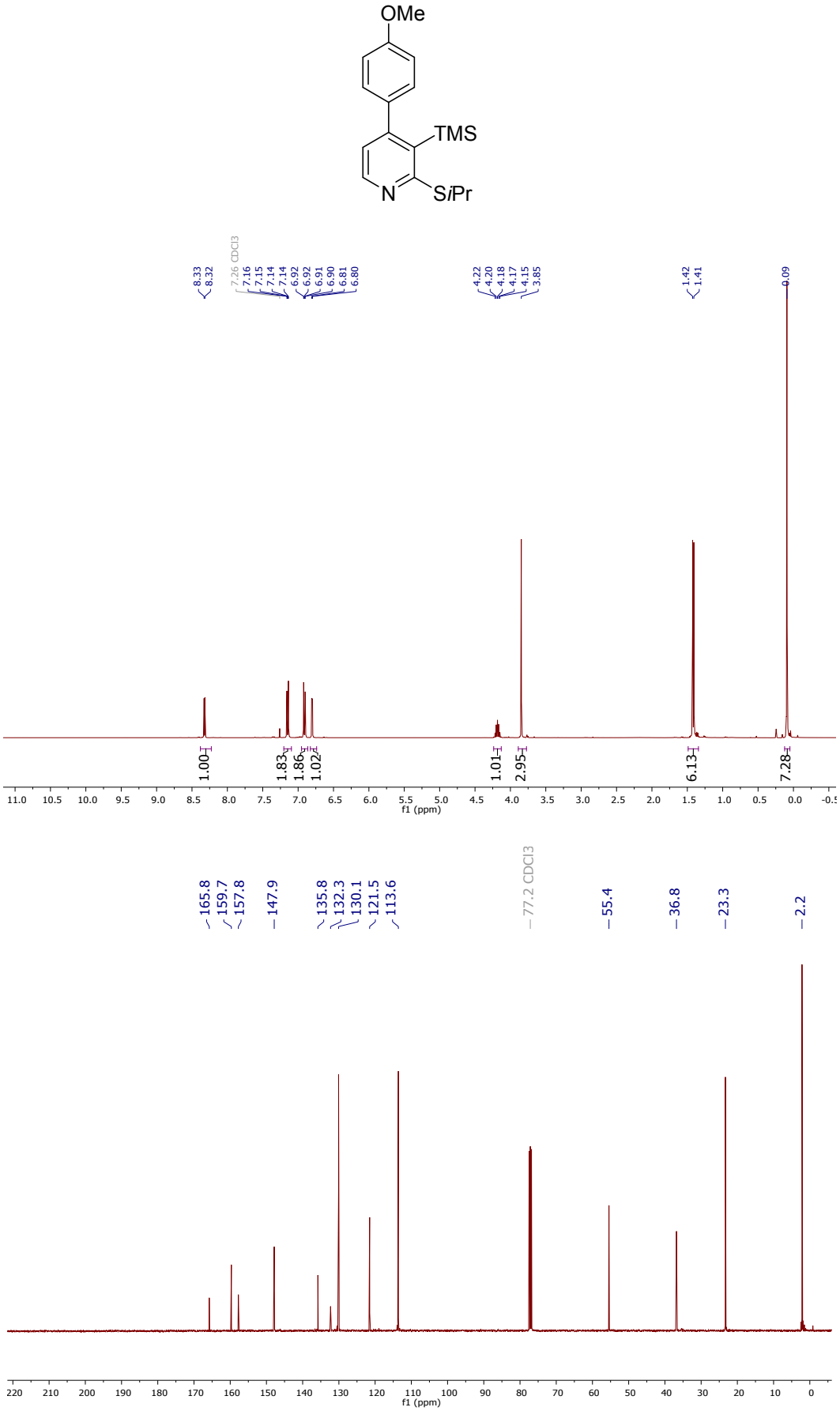




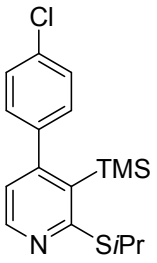


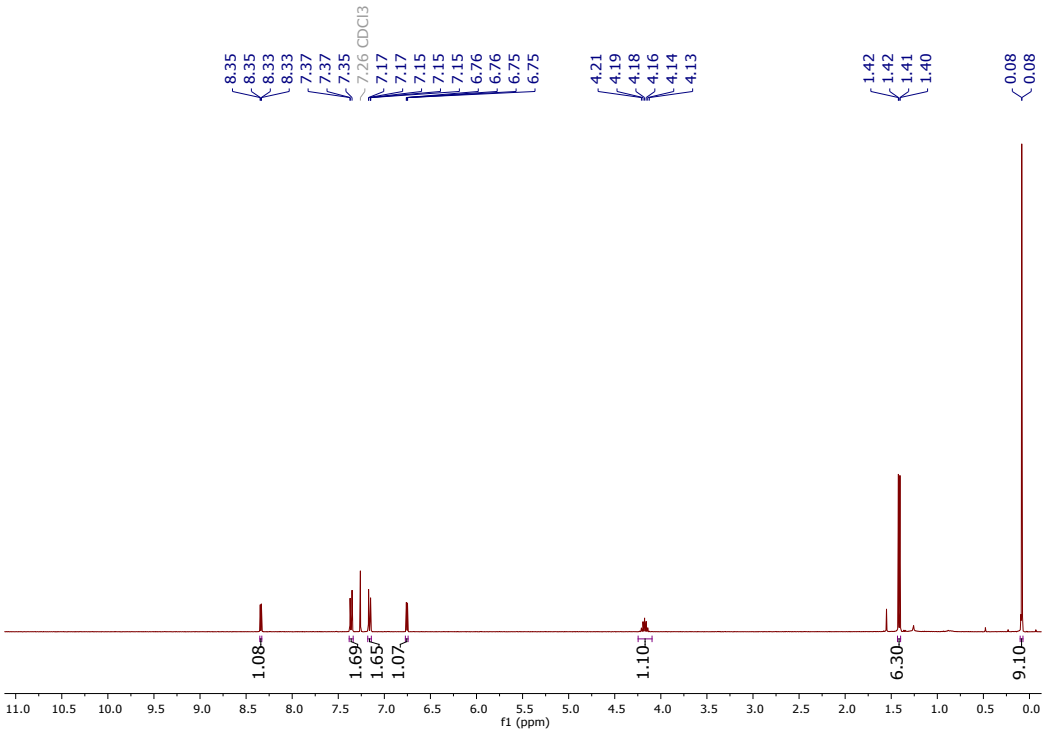


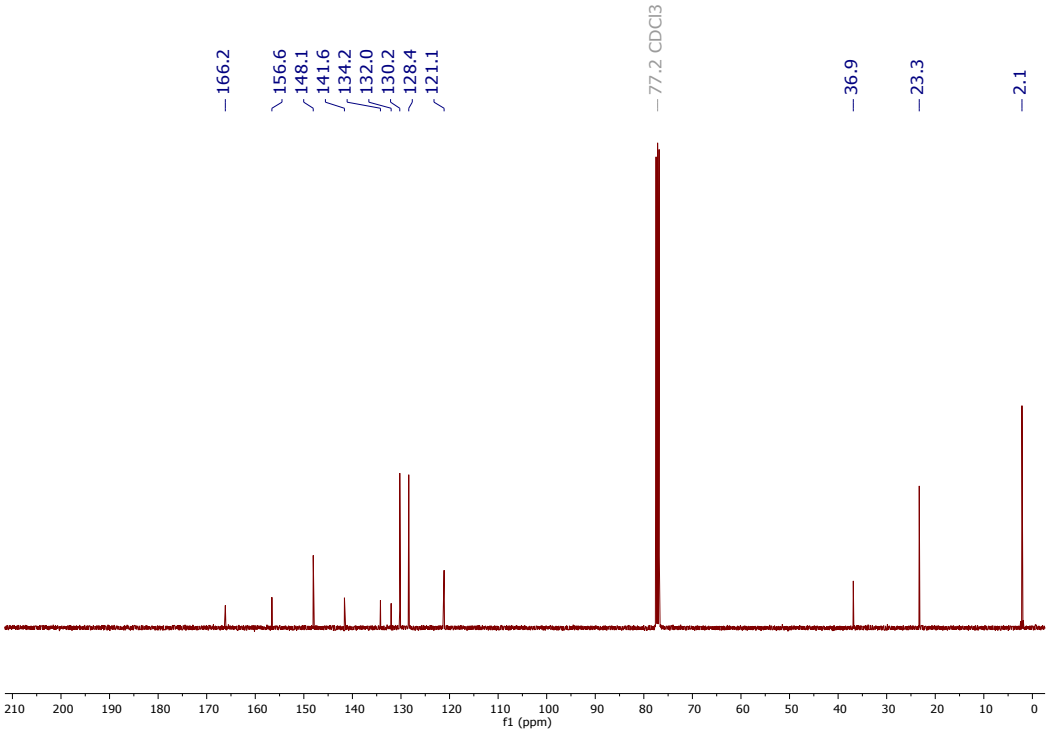
2-(Isopropylthio)-4-(4-methoxyphenyl)-3-(trimethylsilyl)pyridine (12c)



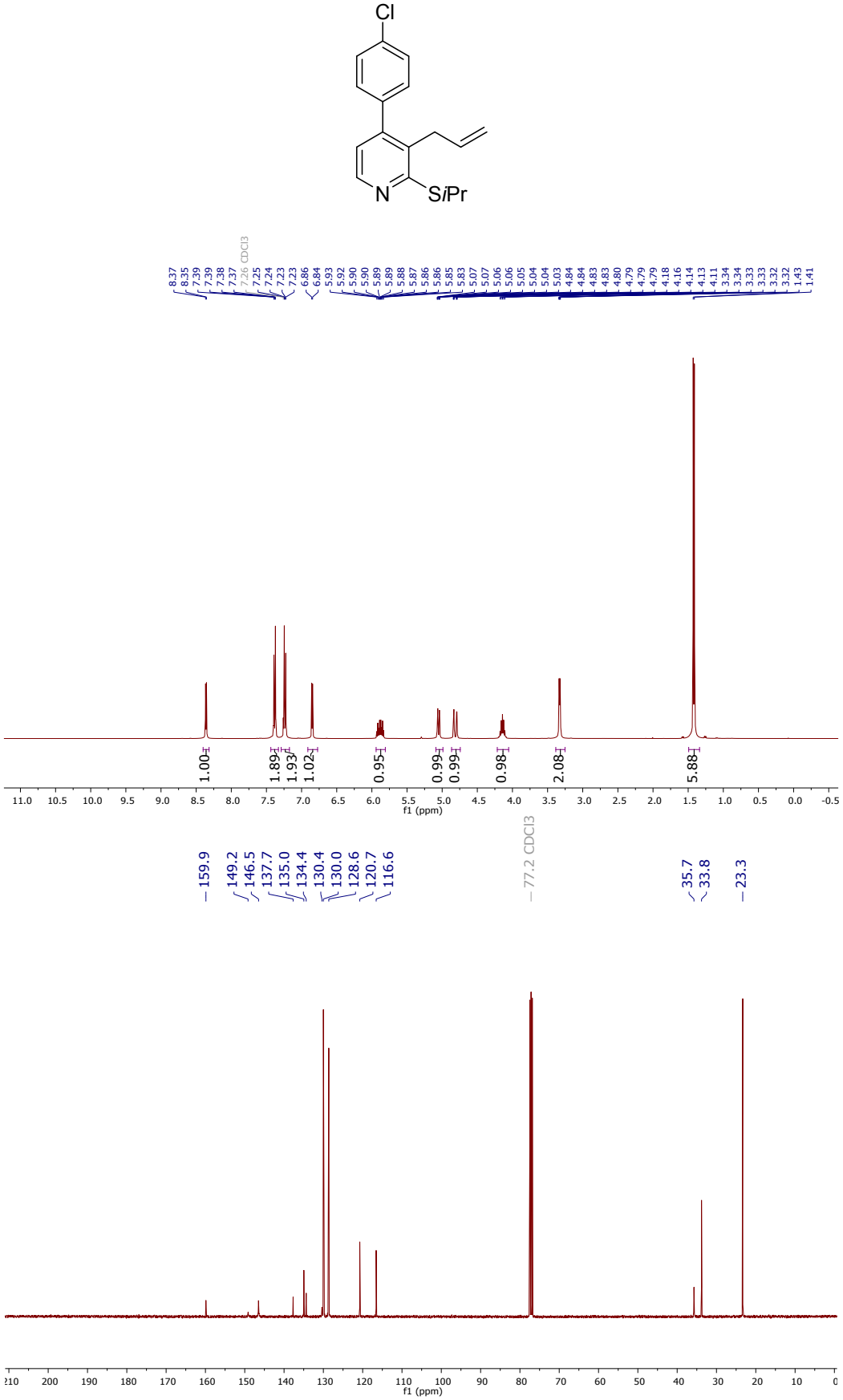
4-(4-Chlorophenyl)-2-(isopropylthio)-3-(trimethylsilyl)pyridine (12d)



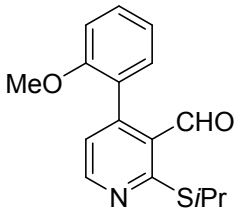


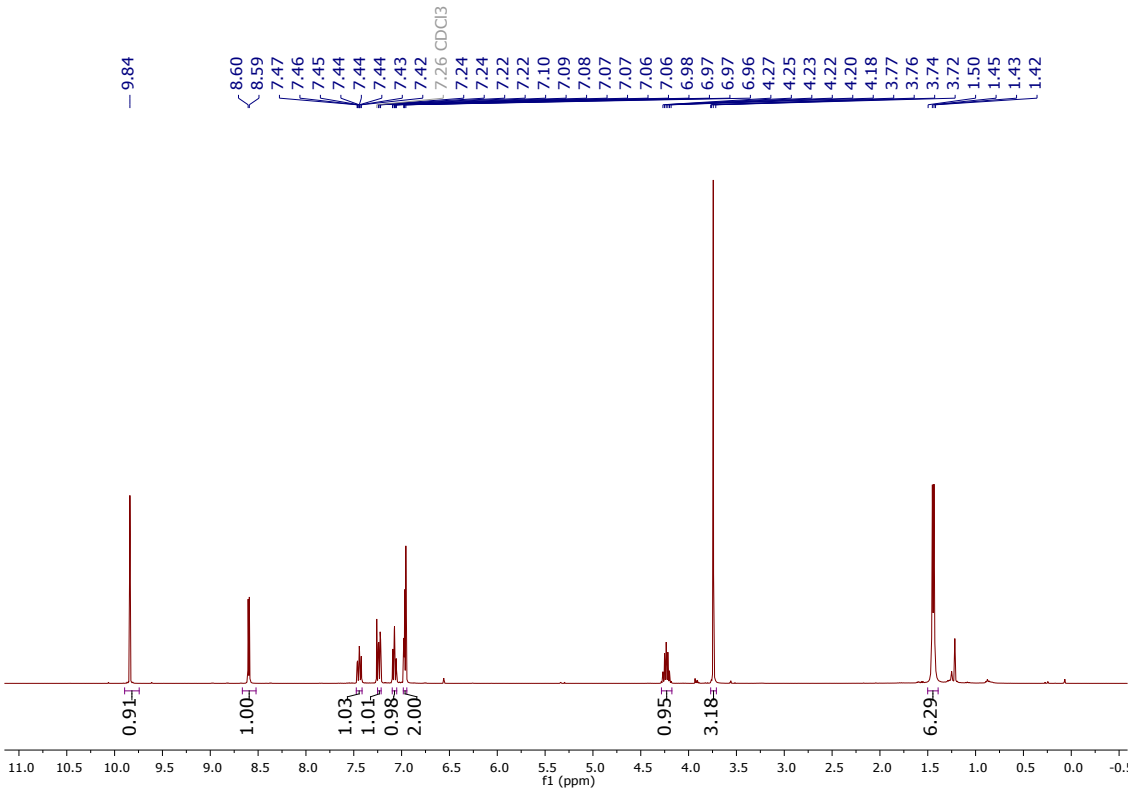


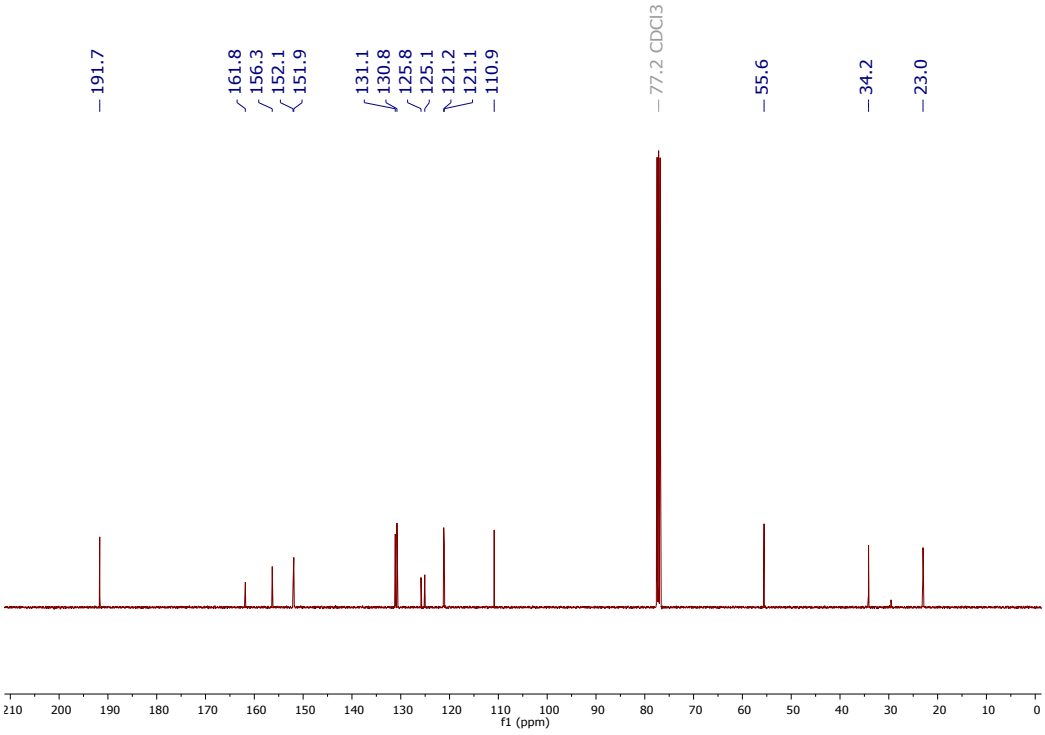
3-Allyl-4-(4-chlorophenyl)-2-(isopropylthio)pyridine (12e)



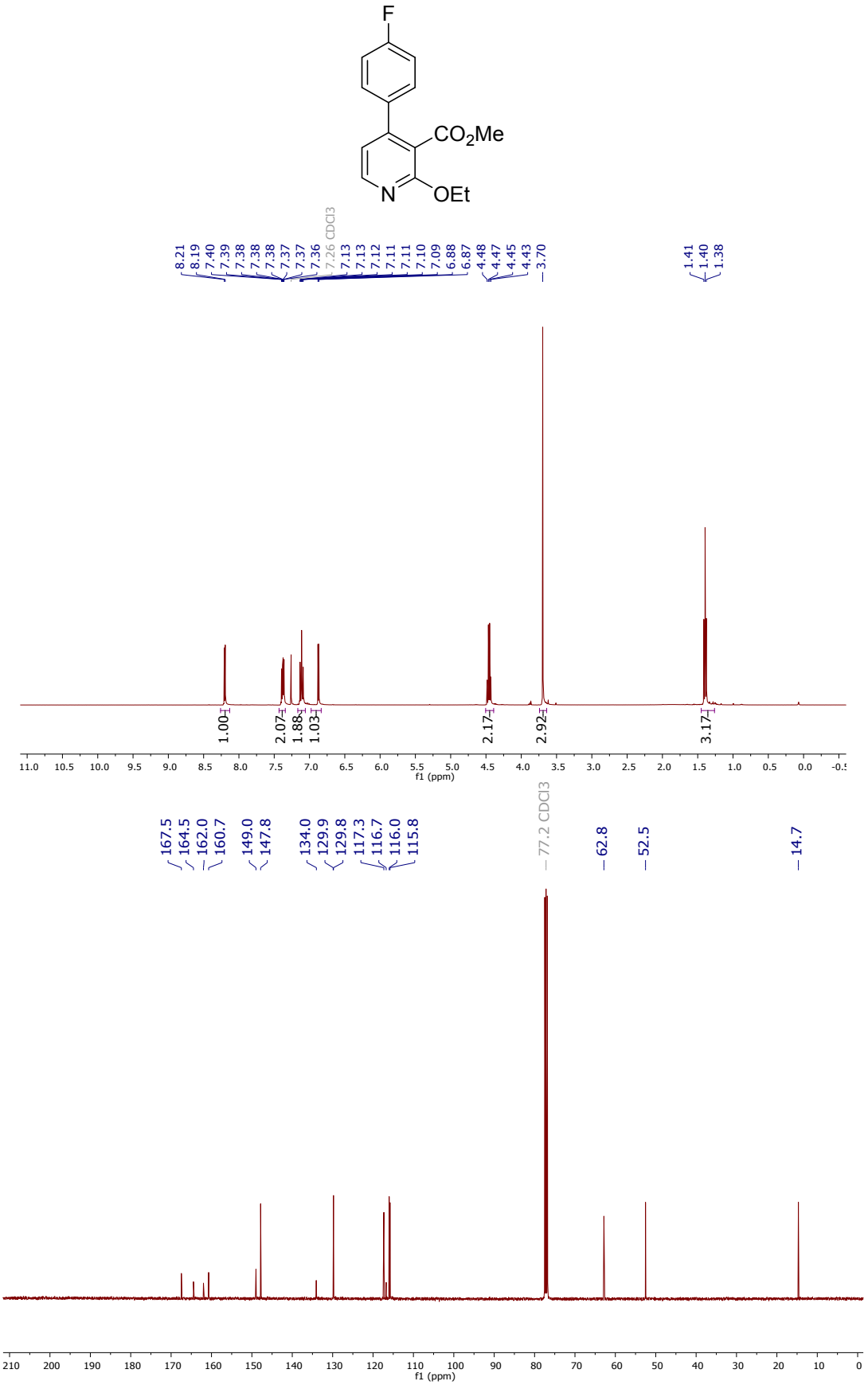
2-(Isopropylthio)-4-(2-methoxyphenyl)nicotinaldehyde (12f)



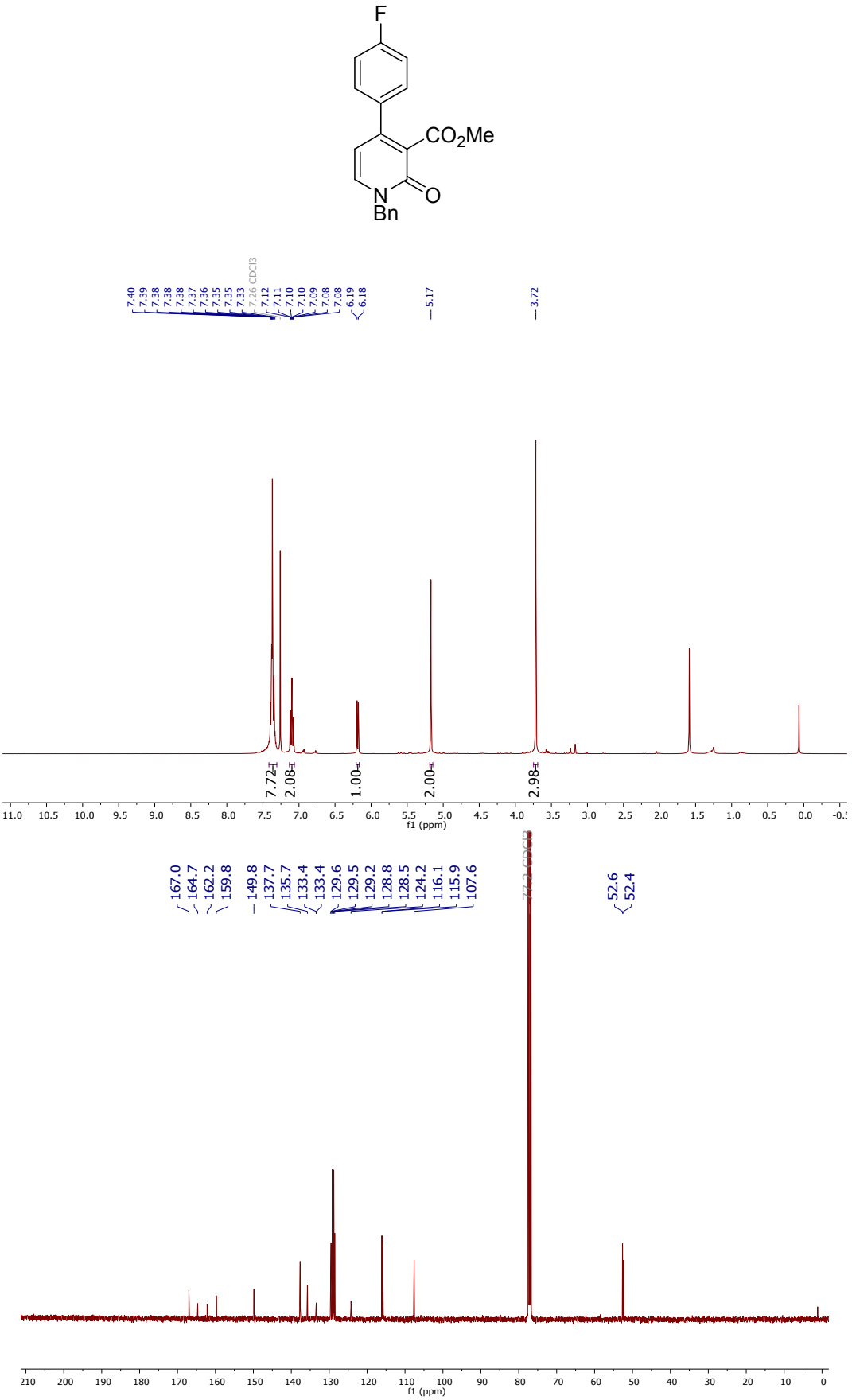




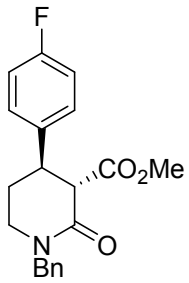
Methyl 2-ethoxy-4-(4-fluorophenyl)nicotinate (7ja)



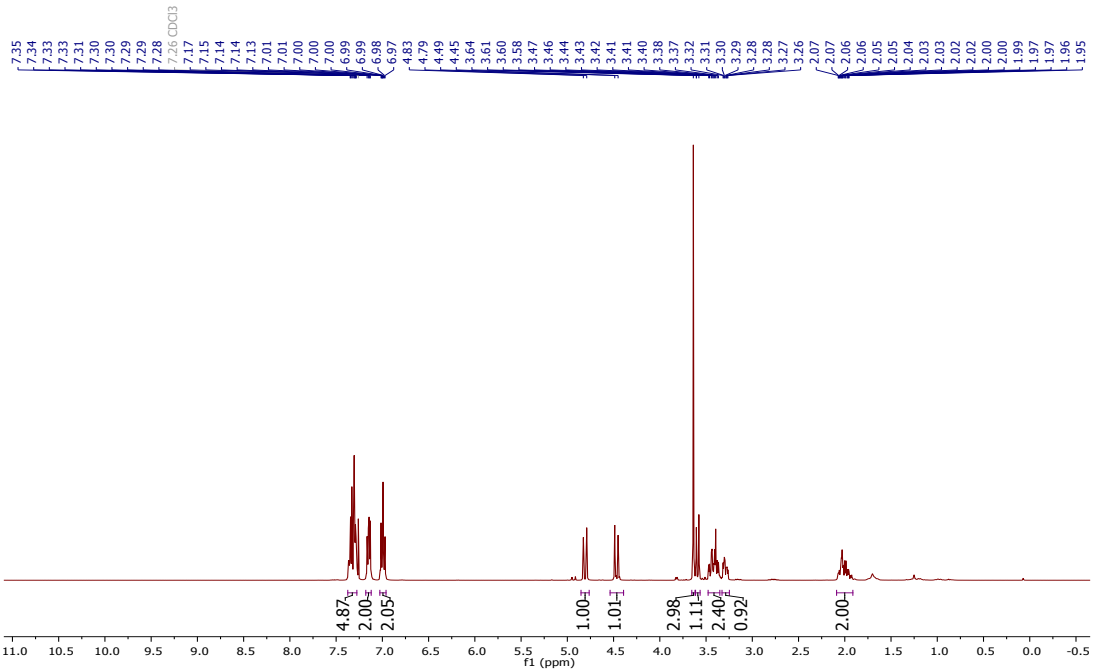
Methyl 1-benzyl-4-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (17)

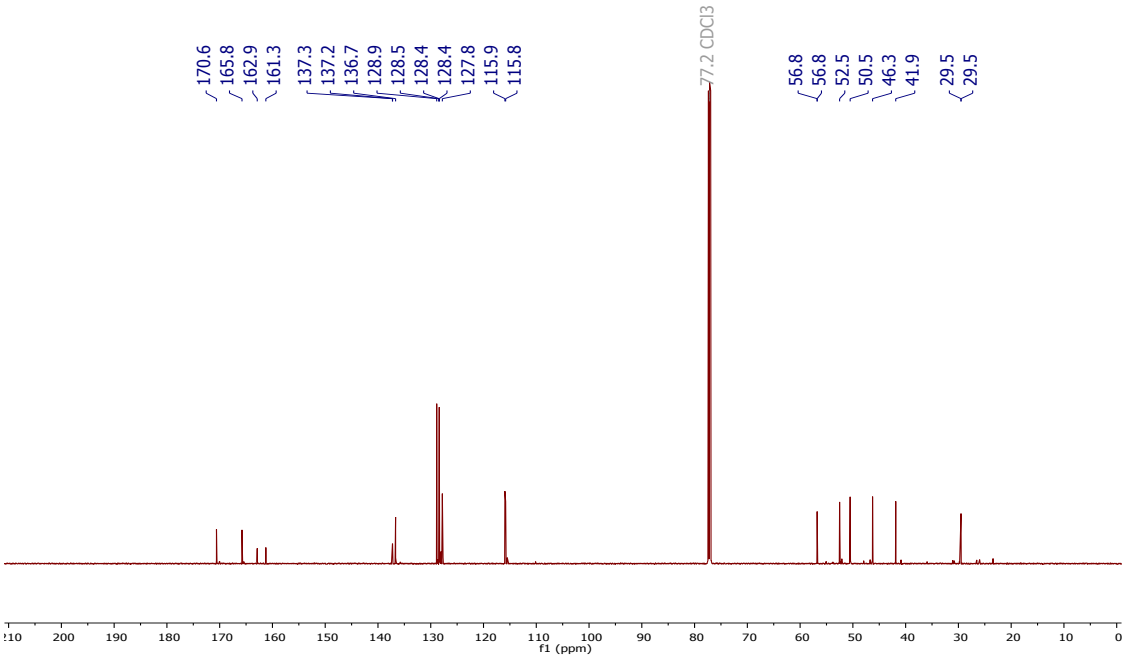


Methyl 1-benzyl-4-(4-fluorophenyl)-2-oxopiperidine-3-carboxylate (18)



(±)-trans





Single crystall X-ray diffraction studies

Single crystals of compound **7aa**, suitable for X-ray diffraction, were obtained by slow evaporation of CH_2Cl_2 solution. The crystals were introduced into perfluorinated oil and a suitable single crystal was carefully mounted on the top of a thin glass wire. Data collection was performed with an Oxford Xcalibur 3 diffractometer equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-K_α radiation (λ = 0.71071 Å).

Data collection and data reduction were performed with the CrysAlisPro software.[6] Absorption correction using the multiscan method[6] was applied. The structures were solved with SHELXS-97,[7] refined with SHELXL-97[8] and finally checked using PLATON.[9] Details for data collection and structure refinement are summarized in Table 1.

CCDC-2057614 contains supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table 1. Details for X-ray data collection and structure refinement for compound **7aa**.

[6] Program package 'CrysAlisPro 1.171.40.81a (Rigaku OD, 2020)'.

[7] Sheldrick, G. M. (1997) SHELXS-97: *Program for Crystal Structure Solution*, University of Goettingen, Germany.

[8] Sheldrick, G. M. (1997) SHELXL-97: *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany.

[9] Spek, A. L. (1999) PLATON: *A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands.

	7aa
Empirical formula	$C_{17}H_{23}NO_2Si$
Formula mass	301.45
T[K]	123(2)
Crystal size [mm]	0.45 × 0.41 × 0.29
Crystal description	colorless block
Crystal system	orthorhombic
Space group	*Pna*21
a [Å]	30.9518(6)
b [Å]	6.9485(2)
c [Å]	15.9226(3)
α [°]	90.0
β [°]	90.0
γ [°]	90.0
V [Å^3]	3424.45(14)
Z	8
$\rho_{calcd.}$ [g cm^{-3}]	1.169
μ [mm^{-1}]	0.141
F(000)	1296
Θ range [°]	2.56 – 25.24
Index ranges	-43 ≤ *h* ≤ 44
	-9 ≤ *k* ≤ 9
	-22 ≤ *l* ≤ 22
Reflns. collected	65322
Reflns. obsd.	8971
Reflns. unique	10423 (R_{int} = 0.0437)
R_1, wR_2 (2σ data)	0.0406, 0.0934
R_1, wR_2 (all data)	0.0513, 0.0995
GOOF on F^2	1.024
Peak/hole [e Å^{-3}]	0.341 / -0.164

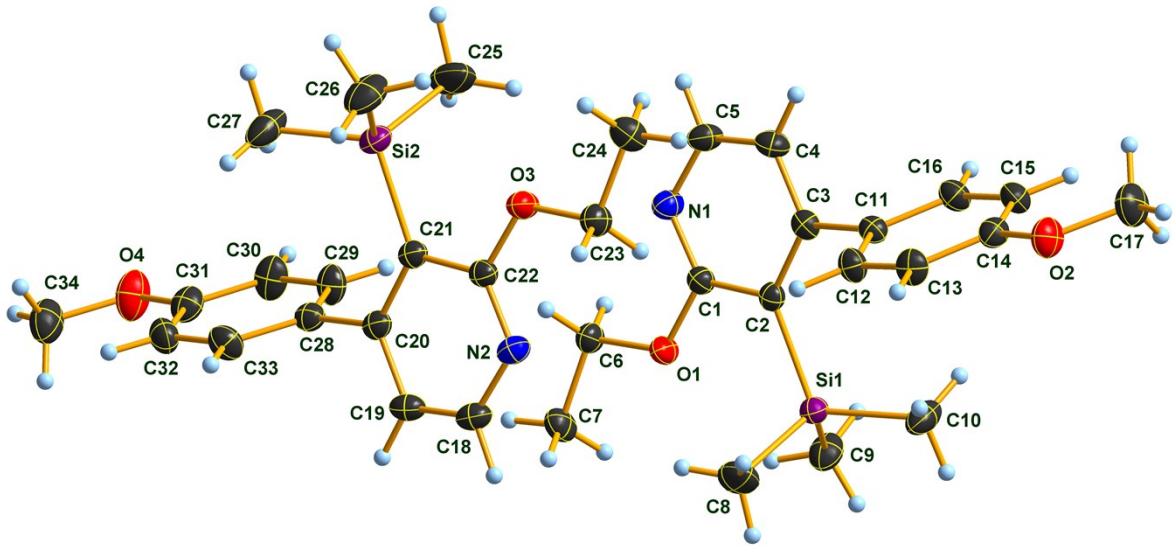


Figure 1. Molecular structure of compound **7aa** in the crystal. DIAMOND[10] representation; thermal ellipsoids are drawn at 50 % probability level.

Table 2. Selected bond lengths (Å) of compound **7aa**.

Si1 – C8	1.865(3)	C32 – C31	1.381(4)
Si1 – C9	1.866(3)	C32 – C33	1.391(4)
Si1 – C10	1.872(3)	C31 – C30	1.396(4)
Si1 – C2	1.903(3)	C28 – C33	1.388(3)
Si2 – C25	1.854(3)	C24 – C23	1.507(3)
Si2 – C26	1.872(3)	O3 – C23	1.443(3)
Si2 – C27	1.872(3)	C22 – C21	1.422(3)
Si2 – C21	1.895(3)	O2 – C17	1.422(3)
O1 – C1	1.353(3)	C2 – C3	1.397(3)
O1 – C6	1.442(3)	C2 – C1	1.420(3)
N1 – C1	1.322(3)	C29 – C30	1.375(4)
N1 – C5	1.340(3)	C29 – C28	1.392(3)
N2 – C22	1.323(3)	C4 – C5	1.378(3)
N2 – C18	1.347(3)	C4 – C3	1.401(4)
C14 – O2	1.364(3)	C3 – C11	1.491(3)
C14 – C15	1.390(4)	C19 – C18	1.370(3)
C14 – C13	1.395(3)	O4 – C31	1.370(3)
C20 – C21	1.397(3)	O4 – C34	1.417(4)
C20 – C19	1.407(4)	C16 – C15	1.390(3)

[10] DIAMOND, Crystal Impact GbR., Version 3.2i.

C20 – C28	1.488(3)	C16 – C11	1.391(3)
C12 – C13	1.384(3)	C7 – C6	1.501(3)
C12 – C11	1.397(3)	O3 – C22	1.351(3)

Table 3. Selected bond angles (°) of compound **7aa**.

C8 – Si1 – C9	111.2(1)	C12 – C13 – C14	120.1(2)
C8 – Si1 – C10	109.0(1)	O1 – C6 – C7	106.7(2)
C9 – Si1 – C10	105.4(1)	C28 – C33 – C32	121.4(2)
C8 – Si1 – C2	109.3(1)	C29 – C30 – C31	119.9(2)
C9 – Si1 – C2	109.1(1)	O3 – C23 – C24	106.5(2)
C10 – Si1 – C2	112.7(1)	N1 – C5 – C4	123.5(2)
C25 – Si2 – C26	111.9(2)	C5 – C4 – C3	119.1(2)
C25 – Si2 – C27	108.7(2)	C2 – C3 – C4	119.5(2)
C26 – Si2 – C27	105.0(1)	C2 – C3 – C11	123.0(2)
C25 – Si2 – C21	108.7(1)	C4 – C3 – C11	117.3(2)
C26 – Si2 – C21	109.7(1)	C18 – C19 – C20	119.3(2)
C27 – Si2 – C21	113.0(1)	N1 – C1 – O1	118.3(2)
C1 – O1 – C6	117.8(2)	N1 – C1 – C2	126.5(2)
C1 – N1 – C5	116.3(2)	O1 – C1 – C2	115.3(2)
C22 – N2 – C18	116.3(2)	C31 – O4 – C34	117.2(2)
O2 – C14 – C15	125.0(2)	C15 – C16 – C11	121.0(2)
O2 – C14 – C13	115.2(2)	C16 – C15 – C14	119.7(2)
C15 – C14 – C13	119.7(2)	N2 – C18 – C19	123.4(2)
C21 – C20 – C19	119.7(2)	C31 – C32 – C33	119.4(2)
C21 – C20 – C28	122.4(2)	C16 – C11 – C12	118.7(2)
C19 – C20 – C28	117.9(2)	C16 – C11 – C3	122.1(2)
C13 – C12 – C11	120.7(2)	C12 – C11 – C3	119.1(2)
C22 – O3 – C23	117.9(2)	O4 – C31 – C32	125.0(2)
N2 – C22 – O3	118.2(2)	O4 – C31 – C30	115.1(2)
N2 – C22 – C21	126.6(2)	C32 – C31 – C30	119.9(2)
O3 – C22 – C21	115.3(2)	C33 – C28 – C29	118.2(2)
C14 – O2 – C17	117.6(2)	C33 – C28 – C20	122.2(2)
C3 – C2 – C1	114.9(2)	C29 – C28 – C20	119.6(2)
C3 – C2 – Si1	127.6(2)	C20 – C21 – C22	114.6(2)
C1 – C2 – Si1	117.4(2)	C20 – C21 – Si2	127.4(2)
C30 – C29 – C28	121.2(2)	C22 – C21 – Si2	118.0(2)

Table 4. Selected torsion angles (°) of compound **7aa**.

C18 – N2 – C22 – O3	-178.3(2)	C11 – C16 – C15 – C14	-1.3(4)
C18 – N2 – C22 – C21	1.0(3)	O2 – C14 – C15 – C16	-179.6(2)
C23 – O3 – C22 – N2	0.9(3)	C13 – C14 – C15 – C16	1.5(4)
C23 – O3 – C22 – C21	-178.5(2)	C22 – N2 – C18 – C19	1.8(3)
C15 – C14 – O2 – C17	-0.2(4)	C20 – C19 – C18 – N2	-1.5(4)
C13 – C14 – O2 – C17	178.8(2)	C15 – C16 – C11 – C12	0.6(3)
C19 – C20 – C21 – C22	4.0(3)	C15 – C16 – C11 – C3	177.2(2)
C28 – C20 – C21 – C22	-172.6(2)	C13 – C12 – C11 – C16	-0.1(3)
C19 – C20 – C21 – Si2	-173.5(2)	C13 – C12 – C11 – C3	-176.8(2)
C28 – C20 – C21 – Si2	9.9(3)	C2 – C3 – C11 – C16	115.5(2)
N2 – C22 – C21 – C20	-3.9(3)	C4 – C3 – C11 – C16	-68.2(3)
O3 – C22 – C21 – C20	175.4(2)	C2 – C3 – C11 – C12	-68.0(3)
N2 – C22 – C21 – Si2	173.8(2)	C4 – C3 – C11 – C12	108.4(2)
O3 – C22 – C21 – Si2	-6.9(3)	C34 – O4 – C31 – C32	-0.6(4)
C25 – Si2 – C21 – C20	-106.9(2)	C34 – O4 – C31 – C30	-179.9(3)
C26 – Si2 – C21 – C20	130.6(2)	C33 – C32 – C31 – O4	179.1(2)
C27 – Si2 – C21 – C20	13.8(2)	C33 – C32 – C31 – C30	-1.6(4)
C25 – Si2 – C21 – C22	75.7(2)	C30 – C29 – C28 – C33	0.3(4)
C26 – Si2 – C21 – C22	-46.8(2)	C30 – C29 – C28 – C20	178.6(2)
C27 – Si2 – C21 – C22	-163.6(2)	C21 – C20 – C28 – C33	-111.0(3)
C1 – C2 – C3 – C4	-3.9(3)	C19 – C20 – C28 – C33	72.3(3)
Si1 – C2 – C3 – C4	171.9(2)	C21 – C20 – C28 – C29	70.8(3)
C1 – C2 – C3 – C11	172.3(2)	C19 – C20 – C28 – C29	-105.9(3)
Si1 – C2 – C3 – C11	-11.8(3)	C11 – C12 – C13 – C14	0.3(4)
C5 – C4 – C3 – C2	2.1(3)	O2 – C14 – C13 – C12	180.0(2)
C5 – C4 – C3 – C11	-174.4(2)	C15 – C14 – C13 – C12	-1.0(4)
C21 – C20 – C19 – C18	-1.7(3)	C1 – O1 – C6 – C7	-177.9(2)
C28 – C20 – C19 – C18	175.1(2)	C29 – C28 – C33 – C32	-0.8(4)
C5 – N1 – C1 – O1	178.4(2)	C20 – C28 – C33 – C32	-179.1(2)
C5 – N1 – C1 – C2	-0.7(3)	C31 – C32 – C33 – C28	1.5(4)
C6 – O1 – C1 – N1	-1.0(3)	C28 – C29 – C30 – C31	-0.5(4)
C6 – O1 – C1 – C2	178.1(2)	O4 – C31 – C30 – C29	-179.5(2)
C3 – C2 – C1 – N1	3.4(3)	C32 – C31 – C30 – C29	1.1(4)
Si1 – C2 – C1 – N1	-172.9(2)	C22 – O3 – C23 – C24	178.0(2)
C3 – C2 – C1 – O1	-175.7(2)	C1 – N1 – C5 – C4	-1.6(4)
Si1 – C2 – C1 – O1	8.0(3)	C3 – C4 – C5 – N1	0.9(4)

Single crystals of compound **12a**, suitable for X-ray diffraction, were obtained by slow evaporation of CH_2Cl_2 solution. The crystals were introduced into perfluorinated oil and a

suitable single crystal was carefully mounted on the top of a thin glass wire. Data collection was performed with an Oxford Xcalibur 3 diffractometer equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-K_α radiation (λ = 0.71071 Å).

Data collection and data reduction were performed with the CrysAlisPro software.[11] Absorption correction using the multiscan method[11] was applied. The structures were solved with SHELXS-97,[12] refined with SHELXL-97[13] and finally checked using PLATON.[14] Details for data collection and structure refinement are summarized in Table 1.

CCDC-2057612 contains supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table 5. Details for X-ray data collection and structure refinement for compound **12a**.

[11] Program package 'CrysAlisPro 1.171.40.81a (Rigaku OD, 2020)'.
[12] Sheldrick, G. M. (1997) SHELXS-97: *Program for Crystal Structure Solution*, University of Goettingen, Germany.
[13] Sheldrick, G. M. (1997) SHELXL-97: *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany.
[14] Spek, A. L. (1999) PLATON: *A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands.

	12a
Empirical formula	$C_{15}H_{17}NOS$
Formula mass	259.35
T[K]	123(2)
Crystal size [mm]	0.40 × 0.20 × 0.02
Crystal description	colorless platelet
Crystal system	monoclinic
Space group	*P*21/*c*
a [Å]	8.8398(4)
b [Å]	22.2474(13)
c [Å]	7.0250(5)
α [°]	90.0
β [°]	105.163(6)
γ [°]	90.0
V [Å^3]	1333.46(14)
Z	4
$\rho_{calcd.}$ [g cm^{-3}]	1.292
μ [mm^{-1}]	0.230
F(000)	552
Θ range [°]	2.39 – 25.24
Index ranges	-11 ≤ *h* ≤ 11
	-29 ≤ *k* ≤ 29
	-9 ≤ *l* ≤ 9
Reflns. collected	23262
Reflns. obsd.	2627
Reflns. unique	3298 (R_{int} = 0.0710)
R_1, wR_2 (2σ data)	0.0513, 0.1161
R_1, wR_2 (all data)	0.0685, 0.1248
GOOF on F^2	1.061
Peak/hole [e Å^{-3}]	0.389 / -0.299

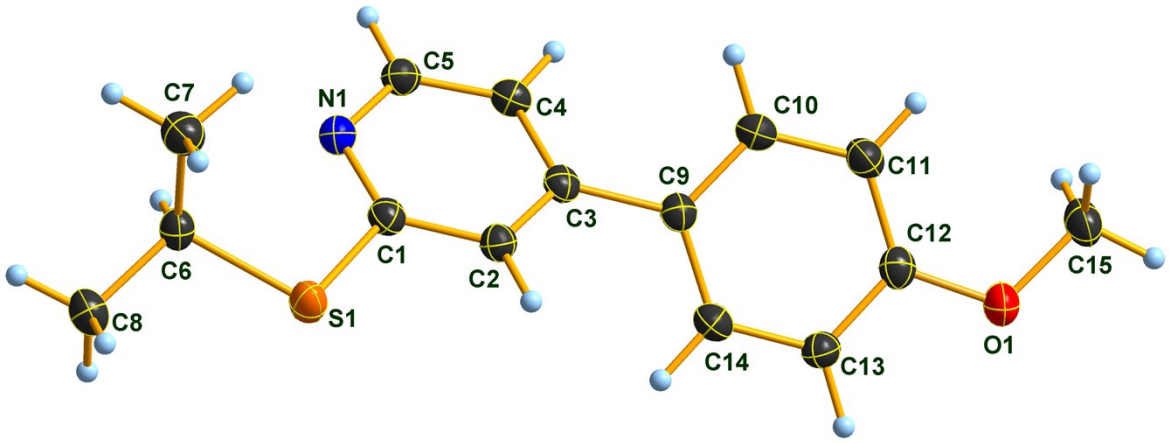


Figure 2. Molecular structure of compound **12a** in the crystal. DIAMOND[15] representation; thermal ellipsoids are drawn at 50 % probability level.

Table 6. Selected bond lengths (Å) of compound **12a**.

S1 – C1	1.771(2)	C14 – C13	1.384(3)
S1 – C6	1.827(2)	C13 – C12	1.398(3)
C5 – N1	1.347(2)	C2 – C1	1.402(3)
C5 – C4	1.383(3)	C12 – O1	1.369(2)
N1 – C1	1.337(2)	C15 – O1	1.430(2)
C6 – C7	1.522(3)	C3 – C2	1.394(3)
C6 – C8	1.525(3)	C3 – C4	1.397(3)
C9 – C10	1.396(2)	C11 – C10	1.385(3)
C9 – C14	1.403(3)	C11 – C12	1.393(3)
C9 – C3	1.485(3)		

[15] DIAMOND, Crystal Impact GbR., Version 3.2i.

Table 7. Selected bond angles (°) of compound **12a**.

C1 – S1 – C6	102.6(1)	C3 – C2 – C1	119.1(2)
N1 – C5 – C4	124.3(2)	O1 – C12 – C11	125.0(2)
C1 – N1 – C5	116.5(2)	O1 – C12 – C13	115.3(2)
C7 – C6 – C8	112.7(2)	C11 – C12 – C13	119.8(2)
C7 – C6 – S1	111.3(1)	N1 – C1 – C2	123.5(2)
C8 – C6 – S1	107.9(1)	N1 – C1 – S1	119.5(1)
C10 – C9 – C14	117.9(2)	C2 – C1 – S1	117.0(1)
C10 – C9 – C3	121.4(2)	C12 – O1 – C15	117.0(2)
C14 – C9 – C3	120.7(2)	C5 – C4 – C3	119.0(2)
C2 – C3 – C4	117.5(2)	C11 – C10 – C9	121.6(2)
C2 – C3 – C9	121.4(2)	C13 – C14 – C9	121.2(2)
C4 – C3 – C9	121.1(2)	C14 – C13 – C12	119.9(2)
C10 – C11 – C12	119.6(2)		

Table 8. Selected torsion angles (°) of compound **12a**.

C4 – C5 – N1 – C1	1.0(3)	C9 – C14 – C13 – C12	0.8(3)
C1 – S1 – C6 – C7	-79.4(2)	C4 – C3 – C2 – C1	2.6(3)
C1 – S1 – C6 – C8	156.5(1)	C9 – C3 – C2 – C1	-176.3(2)
C10 – C9 – C3 – C2	-146.1(2)	C10 – C11 – C12 – O1	178.2(2)
C14 – C9 – C3 – C2	35.2(3)	C10 – C11 – C12 – C13	-1.5(3)
C10 – C9 – C3 – C4	35.0(3)	C14 – C13 – C12 – O1	-179.2(2)
C14 – C9 – C3 – C4	-143.7(2)	C14 – C13 – C12 – C11	0.5(3)
N1 – C5 – C4 – C3	-0.5(3)	C5 – N1 – C1 – C2	0.4(3)
C2 – C3 – C4 – C5	-1.4(3)	C5 – N1 – C1 – S1	-176.5(1)
C9 – C3 – C4 – C5	177.6(2)	C3 – C2 – C1 – N1	-2.2(3)
C12 – C11 – C10 – C9	1.2(3)	C3 – C2 – C1 – S1	174.8(1)
C14 – C9 – C10 – C11	0.1(3)	C6 – S1 – C1 – N1	-10.6(2)
C3 – C9 – C10 – C11	-178.7(2)	C6 – S1 – C1 – C2	172.3(1)
C10 – C9 – C14 – C13	-1.1(3)	C11 – C12 – O1 – C15	2.7(3)
C3 – C9 – C14 – C13	177.7(2)	C13 – C12 – O1 – C15	-177.6(2)

Single crystals of compound **12b**, suitable for X-ray diffraction, were obtained by slow evaporation of CH_2Cl_2 solution. The crystals were introduced into perfluorinated oil and a

suitable single crystal was carefully mounted on the top of a thin glass wire. Data collection was performed with an Oxford Xcalibur 3 diffractometer equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-K_α radiation (λ = 0.71071 Å).

Data collection and data reduction were performed with the CrysAlisPro software.[16] Absorption correction using the multiscan method[16] was applied. The structures were solved with SHELXS-97,[17] refined with SHELXL-97[18] and finally checked using PLATON.[19] Details for data collection and structure refinement are summarized in Table 1.

CCDC-2057613 contains supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table 9. Details for X-ray data collection and structure refinement for compound **12b**.

[16] Program package 'CrysAlisPro 1.171.40.81a (Rigaku OD, 2020)'.
[17] Sheldrick, G. M. (1997) SHELXS-97: *Program for Crystal Structure Solution*, University of Goettingen, Germany.
[18] Sheldrick, G. M. (1997) SHELXL-97: *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany.
[19] Spek, A. L. (1999) PLATON: *A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands.

	12b
Empirical formula	$C_{15}H_{16}INOS$
Formula mass	385.25
T[K]	123(2)
Crystal size [mm]	0.20 × 0.05 × 0.03
Crystal description	colorless rod
Crystal system	monoclinic
Space group	*P*21
a [Å]	8.5870(3)
b [Å]	6.1553(2)
c [Å]	14.6215(5)
α [°]	90.0
β [°]	99.114(3)
γ [°]	90.0
V [Å^3]	763.07(5)
Z	2
$\rho_{calcd.}$ [g cm^{-3}]	1.677
μ [mm^{-1}]	2.227
F(000)	380
Θ range [°]	2.40 – 25.24
Index ranges	-12 ≤ *h* ≤ 12
	-8 ≤ *k* ≤ 8
	-20 ≤ *l* ≤ 20
Reflns. collected	14968
Reflns. obsd.	4430
Reflns. unique	4640 (R_{int} = 0.0254)
R_1, wR_2 (2σ data)	0.0206, 0.0430
R_1, wR_2 (all data)	0.0225, 0.0439
GOOF on F^2	1.029
Peak/hole [e Å^{-3}]	0.819 / -0.251

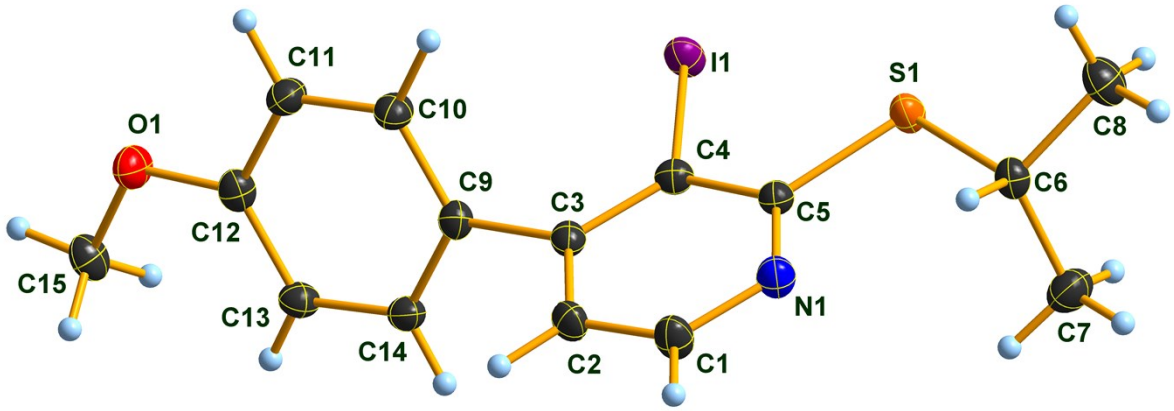


Figure 3. Molecular structure of compound **12b** in the crystal. DIAMOND[20] representation; thermal ellipsoids are drawn at 50 % probability level.

Table 10. Selected bond lengths (Å) of compound **12b**.

I1 – C4	2.107(3)	C12 – C11	1.401(4)
S1 – C5	1.769(3)	N1 – C5	1.336(4)
S1 – C6	1.830(3)	N1 – C1	1.344(4)
C7 – C6	1.520(4)	O1 – C15	1.437(3)
C9 – C14	1.393(4)	C4 – C5	1.409(4)
C9 – C10	1.400(4)	C10 – C11	1.380(4)
C9 – C3	1.486(4)	C6 – C8	1.526(4)
C13 – C14	1.391(4)	C3 – C2	1.401(4)
C13 – C12	1.409(6)	C2 – C1	1.382(5)
C3 – C4	1.395(4)	C12 – O1	1.354(5)

Table 11. Selected bond angles (°) of compound **12b**.

[20] DIAMOND, Crystal Impact GbR., Version 3.2i.

C5 – S1 – C6	102.3(1)	C11 – C10 – C9	120.6(3)
C14 – C9 – C10	118.7(3)	C7 – C6 – C8	112.5(3)
C14 – C9 – C3	120.1(3)	C7 – C6 – S1	110.6(2)
C10 – C9 – C3	121.1(3)	C8 – C6 – S1	107.4(2)
C14 – C13 – C12	119.6(3)	N1 – C5 – C4	122.0(3)
C4 – C3 – C2	116.9(3)	N1 – C5 – S1	118.6(2)
C4 – C3 – C9	123.8(3)	C4 – C5 – S1	119.3(2)
C2 – C3 – C9	119.3(3)	N1 – C1 – C2	123.8(3)
C1 – C2 – C3	119.4(3)	C10 – C11 – C12	120.9(3)
O1 – C12 – C11	116.8(4)	C13 – C14 – C9	121.4(3)
O1 – C12 – C13	124.5(3)	C3 – C4 – C5	120.1(3)
C11 – C12 – C13	118.8(3)	C3 – C4 – I1	120.2(2)
C5 – N1 – C1	117.8(3)	C5 – C4 – I1	119.6(2)
C12 – O1 – C15	116.9(3)		

Table 12. Selected torsion angles (°) of compound **12b**.

C14 – C9 – C3 – C4	117.4(3)	C14 – C9 – C10 – C11	-0.6(5)
C10 – C9 – C3 – C4	-66.2(4)	C3 – C9 – C10 – C11	-177.1(3)
C14 – C9 – C3 – C2	-63.8(4)	C5 – S1 – C6 – C7	83.5(2)
C10 – C9 – C3 – C2	112.7(4)	C5 – S1 – C6 – C8	-153.3(2)
C4 – C3 – C2 – C1	-0.3(6)	C1 – N1 – C5 – C4	-0.3(4)
C9 – C3 – C2 – C1	-179.2(4)	C1 – N1 – C5 – S1	177.7(2)
C14 – C13 – C12 – O1	179.5(3)	C3 – C4 – C5 – N1	0.8(4)
C14 – C13 – C12 – C11	1.0(5)	I1 – C4 – C5 – N1	-176.5(2)
C11 – C12 – O1 – C15	172.7(3)	C3 – C4 – C5 – S1	-177.2(2)
C13 – C12 – O1 – C15	-5.8(4)	I1 – C4 – C5 – S1	5.5(3)
C12 – C13 – C14 – C9	-1.6(5)	C6 – S1 – C5 – N1	4.6(3)
C10 – C9 – C14 – C13	1.4(4)	C6 – S1 – C5 – C4	-177.4(2)
C3 – C9 – C14 – C13	177.9(3)	C5 – N1 – C1 – C2	-0.5(5)
C2 – C3 – C4 – C5	-0.4(4)	C3 – C2 – C1 – N1	0.8(7)
C9 – C3 – C4 – C5	178.4(2)	C9 – C10 – C11 – C12	0.1(5)
C2 – C3 – C4 – I1	176.8(3)	O1 – C12 – C11 – C10	-178.8(3)
C9 – C3 – C4 – I1	-4.3(3)	C13 – C12 – C11 – C10	-0.3(5)