# Nickel-catalyzed cross-electrophile coupling of 2-chloropyridines with alkyl halides

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Supporting Information: Cross-electrophile coupling of 2-chloropyridines with alkyl halides.

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Supporting Information: Cross-electrophile coupling of 2-chloropyridines with alkyl halides.

## 1. Chemicals

$NiBr_2 \bullet 3H_2O$, $NiCl_2$(glyme), Manganese (-325 mesh), Aluminum (powder), lead(II) bromide, DMAc, NMP, NEP, 2,2′-Azobis(2-methylpropionitrile) (AIBN), 2-chloropyridine, 2-chloro-5-(trifluoromethyl)pyridine, ethyl 4-bromobutyrate, 1-bromooctane, cyclohexyl bromide, 1,10-phenanthroline, 4,4'-di-*t*-butyl-2,2'-bipyridine, 4,4'-di-methoxy-butyl-2,2'-bipyridine, 3-bromopyridine, *n*- butyl lithium (2.5 M in hexanes), 2-chloro-5-bromopyridine, tributyltin chloride, and 4-*tert*-butylpyridine were purchased from Aldrich and used as received.

5-Bromo-2-methyl-2-pentene was purchased from Aldrich and filtered through a glass pipette packed with glass wool and 1 inch of basic alumina prior to use.

$NiI_2 \bullet xH_2O$, $NiI_2$, $NiBr_2$, $NiCl_2$, were purchased from Strem Chemicals and used as received.

Zinc (6-9 mm) was purchased from Alfa Aesar and used as received.

DMF and THF were dried and purified by passage though a column of sieves and activated alumina in a Vacuum Atmospheres solvent delivery system.

4-(*tert*-Butyl)-2-chloropyridine,[1] (2-bromoethoxy)(*tert*-butyl)dimethylsilane,[2] 4,4',4''-tri-*tert*-butyl-2,2',:6',2''-terpyridine,[3] and (3-bromopropyl)carbamic acid tert-butyl ester [83948-53-2],[4] were prepared according to literature methods.

## 2. Methods

NMR chemical shifts are reported in ppm and referenced to the residual solvent peak in $CDCl_3$ ($\delta$ = 7.26 ppm $^1H$ or $\delta$ = 77.16 ppm $^{13}C$) as an internal standard or trifluorotoluene ($\delta$ = 0.000 ppm) as an external standard ($^{19}F$). NMR spectra were recorded on Bruker model Avance NMR spectrometer operating at 400.13 MHz or 500.13 MHz proton NMR frequency, and data analysis was performed using the iNMR software package (version 4.0.4).

GC analyses of crude reaction mixtures were performed on an Agilent 7890A GC equipped with dual DB-5 columns (20 m x 180 μm x 0.18 μm), dual FID detectors and using hydrogen as the carrier gas. The analysis method used in all cases was 1 μL injection of sample, injection temp of 300 ºC, 100:1 split ratio, initial inlet pressure was 20.3 psi but varied as the column flow was held constant at 1.8 mL/min for the duration of the run. Initial oven

temperature of 50 ºC was held for 0.46 min followed by a temperature ramp up to 300 ºC at 65 ºC/min and finally the temperature was held at 300 ºC for 0.69 min. Total run time was approx. 5 min. FID temperature was 325 ºC.

GCMS analyses were performed on a Shimadzu GCMS-QP2010 equipped with an RTX-XLB column (30 m x 0.25 mm x 0.28 μm) with a quadrupole mass analyzer using helium as the carrier gas. The analysis method used in all cases was 5 μL injection of sample, injection temp of 225 ºC, 25:1 split ratio, initial inlet pressure was 7.8 psi, but varied as the column flow was held constant at 1.0 mL/min for the duration of the run, the interface temperature was held at 250 ºC, and the ion source (EI, 30 eV) was held at 250 ºC. Initial oven temperature was held at 50 ºC for 3 min with the detector off followed by a temperature ramp, with the detector on, to 280 ºC at 40 ºC/min, and finally the temperature was held at 280 ºC for 3 min. Total run time was 11.75 min.

Chromatography was performed on silica gel (EMD, silica gel 60, particle size 0.040-0.063 mm) using standard flash techniques, or on a Teledyne Isco Combi Flash Rf. Products were visualized by one of the following methods: Dragondorf stain, UV stain, ninhydrin stain, $KMnO_4$ stain, iodine stain, or by GC.

The University of Rochester CENTC Elemental Analysis Facility, Rochester, NY, performed elemental analyses.

**Sampling procedure for analysis of crude reaction mixtures.** A 100 μL gas tight syringe was used to withdraw a 10 μL aliquot of reaction mixture. The aliquot was quenched with water (50 μL), diluted with ether (1 mL), and filtered through a short pad of celite (approx.1/2 in.) in a pipette packed with glass wool.

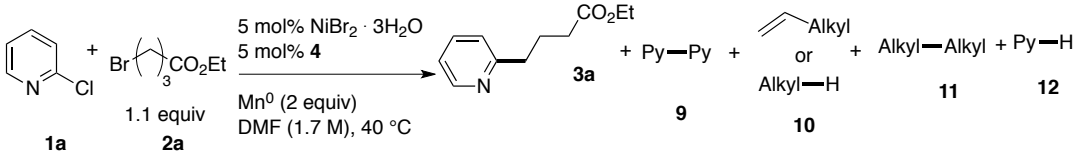
## 3. Optimization and control reactions

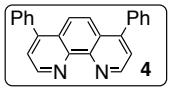
Reactions were set upon the bench-top, in a well-ventilated fume hood, without any precautions to exclude air or moisture. To a 1-dram vial containing a teflon-coated stir-bar was added the required amount of catalyst and ligand(s) followed by DMF (2 mL), and alkyl bomide (0.500-0.600 mmol). The mixtures were then heated to 40, 60, or 80 °C until homogenous. Homogeneity was generally reached within 30 min. The reactions mixtures were allowed to cool to room temperature before adding the halogenated pyridine (0.500-0.600 mmol), $Mn^0$ powder (-325 mesh, 2.00 equiv), and dodecane (10.0 μL internal standard). The reaction vials were capped

with a PTFE-faced silicone septum. The headspace of the vials was purged with argon gas and heated in a reaction block on the bench-top. After 15-41 h reaction time, 10-50 μL aliquots of reaction mixture were removed with a 50 μL gas-tight syringe and quenched with 10-50 μL of water, diluted with ethyl ether or ethyl acetate (1 mL), and filtered through a short celite pad (1.5 cm) in a pipette packed with glass wool. The filtrate was analyzed by gas chromatography and percent yield or percent conversion based on unreacted starting material was calculated.

## 4. Product distribution data for Table 1 in text

**Table S1:** Optimization results and product distribution data for the cross-coupling of 2-chloropyridine (**1a**) with ethyl 4-bromobutyrate (**2a**).[a]



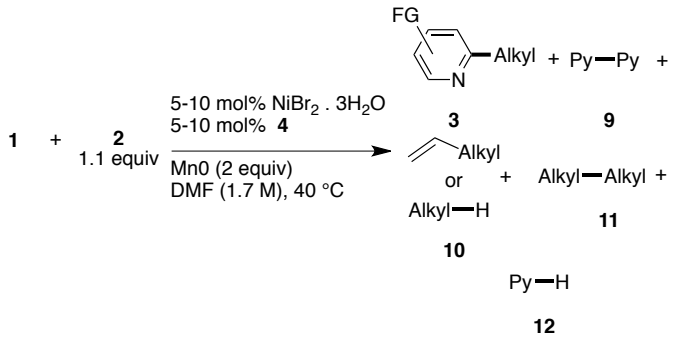




| Entry | Change from above conditions | Yield (%)[b] | **1a**[h] | **2a**[h] | **3a**[h] | **9**[h] | **10**[h] | **11**[h] | **12**[h] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | None | 82 | 0 | 0 | 89 | 0 | 0 | 6 | 0 |
| 2 | 10 mol% $NiBr_2$•$3H_2O$/**4** | 74[c] | 0 | 0 | 83 | 0 | 0 | 16 | 0 |
| 3 | 1 equiv each **1a** and **2a** | 78 | 8 | 0 | 81 | 0 | 1 | 6 | 0 |
| 4 | 1.1 equiv **1a** | 71 | 0 | 0 | 88 | 0 | 1 | 8 | 0 |
| 5 | 1,10-phenanthroline (**5**) in place of **4** | 64 | 0 | 0 | 84 | 0 | 3 | 11 | 0 |
| 6 | 4,4'-di-*t*-butyl-2,2'-bipyridine (**6**) in place of **4** | 66 | 0 | 0 | 81 | 0 | 0.5 | 14 | 0 |
| 7 | 4,4'-di-methoxy-butyl-2,2'-bipyridine (**7**) in place of **4** | 69 | 0 | 0 | 81 | 0 | 0 | 14 | 0 |
| 8 | 4,4',4''-tri-*tert*-butyl-2,2',:6',2''-terpyridine (**8**) in place of **3** | 15 | 23 | 0 | 8 | 0 | 1 | 59 | 6 |
| 9 | $NiCl_2$(glyme) in place of $NiBr_2$•$3H_2O$ | 79 | 0 | 0 | 81 | 0 | 3 | 12 | 0 |
| 10 | $NiI_2$•$xH_2O$ in place of $NiBr_2$•$3H_2O$ | 58 | 4 | 0 | 63 | 0 | 1 | 27 | 3 |
| 11 | $NiI_2$ in place of $NiBr_2$•$3H_2O$ | 47 | 0 | 0 | 57 | 5 | 2 | 33 | 0 |
| 12 | $NiBr_2$ in place of $NiBr_2$•$3H_2O$ | 34 | 0 | 0 | 48 | 9 | 3 | 36 | 0 |
| 13 | $NiCl_2$ in place of $NiBr_2$•$3H_2O$ | 35 | 0 | 0 | 51 | 3 | 4 | 37 | 0 |
| 14 | Reaction run at 20 °C | 55[c] | 0 | 0 | 77 | 0 | 0 | 20 | 0 |
| 15 | Reaction run at 60 °C | 70[c] | 0 | 0 | 86 | 0 | 1 | 7 | 0 |
| 16 | Reaction run at 80 °C | 62[c] | 0 | 0 | 90 | 0 | 2 | 6 | 0 |
| 17 | DMAc in place of DMF | 31[d] | 15 | 13 | 55 | 0 | 10 | 6 | 0 |
| 18 | DMPU in place of DMF | 21[d] | 27 | 26 | 30 | 0 | 8 | 3 | 0 |
| 19 | NMP in place of DMF | 45[d, e] | 8 | 7 | 37 | 34 | 4 | 3 | 1 |
| 20 | NEP in place of DMF | 34[d] | 20 | 24 | 40 | 0 | 7 | 4 | 0 |
| 21 | THF in place of DMF | 4[d] | 37 | 49 | 5 | 0 | 5 | 2 | 0 |
| 22 | 25% DMAc in THF in place of DMF | 15[d] | 25 | 30 | 16 | 0 | 5 | 2 | 2 |
| 23 | $Zn^0$ (<10 μm) in place of $Mn^0$ | 19[f] | 0 | 0 | 37 | 0 | 6 | 54 | 0 |
| 24 | $Al^0$/$PbBr_2$ in place of $Mn^0$ | 2[f,g] | 43 | 6 | 3 | 0 | 10 | 33 | 0 |

[a] Reaction conditions: DMF (1 mL), $NiBr_2$•$3H_2O$ (0.15 mmol), **1a** (3.00 mmol), **2a** (3.30 mmol), ligand (0.15 mmol), and $Mn^0$ (6.00 mmol) were added to a 1 dram vial on the bench top and heated under air for 4-22 h.
[b] GC yield corrected vs. dodecane internal standard.
[c] Isolated yield.
[d] Observed partial conversion of starting material at 24 h.
[e] Major coupled product was the pyridine dimer.
[f] Major coupled product was the alkyl dimer.
[g] No reaction of **2a** was observed.
[h] Area percent determined by GC-FID analysis of crude reaction mixtures. In cases where the A% is 0, a peak of <0.5 A% is present or no peak is observed and the retention time of the compound is known.

## 5. Product distribution data for Table 2 in text

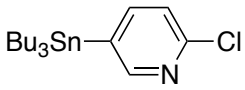
**Table S2:** Product distribution data for the cross-coupling of substituted 2-chloropyridines (**1**) with alkyl bromides (**2**).




| Entry | 3 | 3[a] | 3[b] | 9[b] | 10[b] | 11[b] | 12[b] |
|---|---|---|---|---|---|---|---|
| 1 | **3a** | 72 | 81 | 0 | 1 | 15 | 0 |
| 2 | **3b** | 65 | 76 | 1 | 1 | 21 | 0 |
| 3 | **3b** | 72 | 83 | 0 | 2 | 15 | 0 |
| 4 | **3c** | 60 | 74 | 13 | 0 | 3 | 1 |
| 5 | **3d** | 33 | 31 | 0 | 0 | 43 | 0 |
| 6 | **3e** | 33 | 47 | 5 | 19 | 23 | 6 |
| 7[c] | **3e** | 48 | 30 | 0 | 13 | 46 | 2 |
| 8 | **3f** | 37 | 49 | 0 | 43 | 6 | 0 |
| 9 | **3f** | 45 | 65 | 0 | 33 | 0 | 0 |
| 10 | **3g** | 46 | 71 | 2 | 1 | 12 | 0 |
| 11 | **3h** | 50 | 77 | 5 | 1 | 13 | 0 |
| 12 | **3i** | 27 | 57 | 1 | 4 | 28 | 0 |
| 13[d] | **3i** | 46 | 33 | 4 | 1 | 8 | 0 |

[a] Yield of isolated and purified product.
[b] Area percent determined by GC-FID analysis of crude reaction mixtures. In cases where the A% is 0, no peak or a peak of <0.5 A% is present and the retention time of the compound is known.
[c] The GC trace also contained 7 A% unreacted **2e**.
[d] The GC trace also contained 3 A% unreacted **1d** and 3 A% ethyl 4-chlorobutanoate (**13**).

## 6. Preparation of substrates



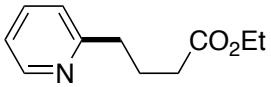

**2-Chloro-5-(tributylstannyl)pyridine (1b) [183545-05-3].** Using standard anhydrous techniques and a known procedure for lithium halogen exchange[5] a solution of 2-chloro-5-bromopyridine (2.0 g, 10.4 mmol) in anhydrous diethyl ether (122 mL) was chilled to -78 °C. Next, *n*-butyl lithium (5.2 mL, 12.5 mmol, 2.5 M in hexanes) was added slowly over the course of 5 min. via syringe. To the resulting red solution tributyltin chloride (4.07 g, 12.5 mmol) was added via syringe and the reaction was allowed to slowly warm to room temperature over 16 h. TLC analysis of the crude reaction mixture confirmed the reaction was complete (TLC: 8: 2

hexanes: ethyl acetate, 2-chloro-5-bromopyridine $R_f$ = 0.73, 2-chloro-5-(tributylstannyl)pyridine $R_f$ = 0.76, visualized by Uv light, $SiO_2$). The reaction was poured in to water (200 mL) and the organics were extracted with diethyl ether (3 x 100 mL). The combined organic extracts were washed with brine (50 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure to give pale yellow oil. The crude material was purified by gradient elution flash column chromatography ($SiO_2$, 0 to 100% ethyl acetate in hexanse) to give colorless oil (2.63 g, 63%). **$^1$H-NMR** (500 MHz; $CDCl_3$): δ 8.36-8.33 (m, 1H), 7.72-7.64 (m, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 1.55-1.46 (m, 6H), 1.35-1.26 (m, 6H), 1.16-1.02 (m, 6H), 0.92 (dd, *J* = 39.9, 10.6 Hz, 9H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 155.9, 151.8, 146.6, 135.4, 124.5, 29.1, 27.4, 13.8, 9.8; **Anal. Calcd.** for $C_{17}H_{30}ClNSn$ requires: C, 50.72; H, 7.51; N, 3.48; **found:** C, 51.60; H, 7.65; N, 3.21. $C_{17}H_{30}ClNSn$ requires: C, 50.72; H, 7.51; N, 3.48%.

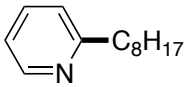
## 7. General procedure for preparative reactions

On the bench top a 15 mL round bottom flask equipped with a Teflon coated magnetic stir bar was charged with $NiBr_2$•$3H_2O$ (40.9 mg, 0.150 mmol, 0.05 equiv), bathophenanthroline (49.9 mg, 0.150 mmol, 0.05 equiv), DMF (2.0 mL), and alkyl bromide (3.3 mmol, 1.1 equiv). The vessel was stoppered with a rubber septum and heated to 40 °C until a green homogenous solution resulted (approx. 20 min). Once homogeneity was achieved the vessel was removed from the heat. The 2-halogenated pyridine (3.00 mmol, 1.00 equiv) and $Mn^0$ (-325 mesh, 330 mg, 6.00 mmol, 2.00 equiv) were added, after which, the vessel was resealed with the septum, purged with argon gas, and heated again to 40 °C for the duration of the reaction. Reaction progress was monitored by GC analysis of aliquots of crude reaction mixture. In general the reactions turn dark brown or black in color when complete. Upon completion the reaction was cooled to room temperature, diluted with ether (10 mL) and filtered through a short pad of celite (approx. 1” x 1” x 1”) that had been wetted with ether (approx. 10 mL) to remove metal salts. The celite pad was washed with additional ether (2 x 10 mL). The filtrate was transferred to a separatory funnel and washed with 1M aqueous $NH_4Cl$ (10 mL). The layers were separated and the aqueous layer was washed with additional ether (3 x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude products were purified by silica gel flash column chromatography.

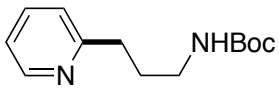
## 8. Compound characterization



**Ethyl 4-(pyridin-2-yl)butanoate [8499-93-9] (3a).**[6] The general procedure was followed with 2-chloropyridine (282 μL, 3.00 mmol) and ethyl 4-bromobutyrate (472 μL, 3.30 mmol). Isolated 420 mg (72%) by flash column chromatography ($SiO_2$, 8: 2 hexanes: ethyl acetate) as faintly yellow oil. **$^1$H-NMR** (400 MHz; $CDCl_3$): δ 8.52 (d, *J* = 4.3 Hz, 1H), 7.59 (t, *J* = 7.1 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.11 (dd, *J* = 6.8, 5.5 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.83 (t, *J* = 7.6 Hz, 2H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.07 (quintet, *J* = 7.5 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 173.3, 161.1, 149.2, 136.3, 122.8, 121.1, 60.2, 37.3, 33.6, 24.8, 14.2; **Anal. Calc.** for $C_{11}H_{15}NO_2$ requires: C, 68.37; H, 7.82; N, 7.25; **found:** C, 67.37; H, 7.91; N, 7.31%.

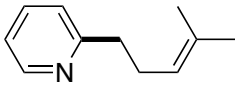


**2-Octylpyridine [33841-61-1] (3b).**[7] The general procedure was followed with 2-chloropyridine (282 μL, 3.00 mmol) and 1-bromooctane (570 μL, 3.30 mmol). Run 1 with 5 mol% catalyst isolated 372 mg (65%) by gradient elution flash chromatography (40 g, $SiO_2$, 0 to 100% ethyl acetate in hexanes) as yellow oil. Run 2 with 10 mol% catalyst isolated 411 mg (72%) by gradient elution flash chromatography (40 g, $SiO_2$, 0 to 100% ethyl acetate in hexanes) as yellow oil. **$^1$H-NMR** (500 MHz; $CDCl_3$): δ 8.49 (d, *J* = 4.3 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.04 (dd, *J* = 6.6, 5.6 Hz, 1H), 2.75 (t, *J* = 7.8 Hz, 2H), 1.69 (quintet, *J* = 7.3 Hz, 2H), 1.33-1.23 (m, 10H), 0.84 (t, *J* = 6.6 Hz, 3H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 213.5, 200.2, 187.1, 173.6, 171.8, 89.5, 82.8, 80.9, 80.45, 80.41, 80.21, 73.6, 65.1; **Anal. Calc.** for $C_{13}H_{21}N$ requires: C, 81.61; H, 11.06; N, 7.32; **found:** C, 80.88; H, 11.09; N, 7.47%.

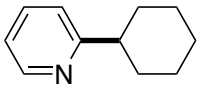


***tert*-Butyl (3-(pyridin-2-yl)propyl)carbamate (3c).** The general procedure was followed with 2-chloropyridine (97 μL, 0.825 mmol) and (3-bromopropyl)carbamic acid tert-butyl ester (185 mg, 0.75 mmol). Isolated 104 mg (60%) by flash column chromatography ($SiO_2$, 85: 15 hexanes: acetone) as brown oil. **$^1$H-NMR** (500 MHz; $CDCl_3$): δ 8.46 (d, *J* = 4.5 Hz, 1H), 7.54 (td, *J* = 7.6,

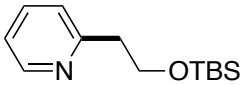
1.5 Hz, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.05 (dd, *J* = 6.8, 5.4 Hz, 1H), 4.89 (s, 1H), 3.13 (q, *J* = 6.4 Hz, 2H), 2.78 (t, *J* = 7.6 Hz, 2H), 1.88 (quintet, *J* = 7.3 Hz, 2H), 1.39 (s, 9H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 161.4, 156.1, 149.2, 136.5, 122.9, 121.2, 79.0, 40.1, 35.5, 29.9, 29.7, 28.5; **Anal. Calc.** for $C_{13}H_{20}N_2O_2$ requires: C, 66.07; H, 8.53; N, 11.85; **Found:** C, 64.873; H, 8.613; N, 10.523%.



**2-(4-Methylpent-3-en-1-yl)pyridine [51082-20-3] (3d).**[8] The general procedure was followed at 10 mol% catalyst loading with 2-chloropyridine (282 mL, 3.00 mmol) and 5-bromo-2-methylpent-2-ene (442 mL, 3.30 mmol). Isolated 160 mg (33%) by gradient elution flash chromatography (40 g, $SiO_2$, 0 to 100% ethyl acetate in hexanes) as yellow oil. **$^{1}$H-NMR** (400 MHz; $CDCl_3$): δ 8.53 (d, *J* = 4.6 Hz, 1H), 7.57 (td, *J* = 7.6, 1.4 Hz, 1H), 7.13-7.07 (m, 2H), 5.18-5.15 (m, 1H), 2.80 (t, *J* = 7.8 Hz, 2H), 2.41 (q, *J* = 7.5 Hz, 2H), 1.67 (s, 3H), 1.55 (s, 3H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 162.0, 149.3, 136.1, 132.4, 123.4, 122.9, 120.9, 38.6, 28.4, 25.7, 17.7; **Anal. Calc.** for $C_{11}H_{15}N$ requires: C, 81.94; H, 9.38; N, 8.69; **found:** C, 81.27; H, 9.51; N, 8.41%.

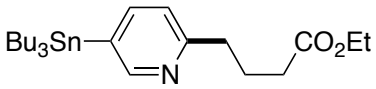


**2-Cyclohexylpyridine [15787-49-2] (3e)**.[9] The general procedure was followed at 10 mol% catalyst loading with 2-chloropyridine (282 mL, 3.00 mmol) and cyclohexyl bromide (406 mL, 3.30 mmol). Isolated 157 mg (33%) by gradient elution flash chromatography (40 g, $SiO_2$, 0 to 100% ethyl acetate in hexanes) as colorless oil. **$^{1}$H-NMR** (500 MHz; $CDCl_3$): δ 8.48 (d, *J* = 4.0 Hz, 1H), 7.54 (td, *J* = 7.7, 1.6 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 7.03 (dd, *J* = 7.2, 5.1 Hz, 1H), 2.65 (tt, *J* = 11.9, 3.4 Hz, 1H), 1.91 (dd, *J* = 13.2, 1.5 Hz, 2H), 1.81 (dt, *J* = 13.0, 3.0 Hz, 2H), 1.73-1.69 (m, 1H), 1.49 (qd, *J* = 12.5, 2.9 Hz, 2H), 1.37 (qt, *J* = 12.8, 3.1 Hz, 2H), 1.24 (qt, *J* = 12.7, 3.5 Hz, 1H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 166.5, 149.1, 136.4, 121.0, 46.6, 26.6; **Anal. Calc.** for $C_{11}H_{15}N$ requires: C, 81.94; H, 9.38; N, 8.69 **found:** C, 81.59; H, 9.51; N, 8.46%.

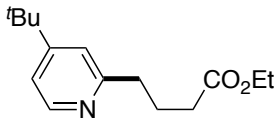


**2-(2-((tert-Butyldimethylsilyl)oxy)ethyl)pyridine [161227-19-6] (3f)**.[10] The general procedure was followed with 2-chloropyridine (282 mL, 3.00 mmol) and (2-bromoethoxy)(*tert*-

butyl)dimethylsilane (790 mg, 3.30 mmol). Run one with 5 mol% catalyst loading isolated 263 mg (37%) by flash column chromatography ($SiO_2$, 9: 1 hexanes: ethyl acetate) as faintly yellow oil. Run two at 10 mol% catalyst loading isolated 322 mg (45%) by gradient elution flash chromatography (40 g, $SiO_2$, 0 to 100% ethyl acetate in hexanes) as yellow oil. Run three at 10 mol% catalyst loading and 4Å molecular sieves (162 mg) to remove water brought in the reaction mixture by the hydrated nickel source isolated 252 mg (35%) by gradient elution flash chromatography (40 g, $SiO_2$, 0 to 100% ethyl acetate in hexanes) as yellow oil. **$^1$H-NMR** (500 MHz; $CDCl_3$): δ 8.53 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.57 (td, *J* = 7.6, 1.8 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 7.11 (ddd, *J* = 7.4, 5.0, 0.9 Hz, 1H), 3.98 (t, *J* = 6.6 Hz, 2H), 2.99 (t, *J* = 6.6 Hz, 2H), 0.83 (s, 9H), -0.05 (s, 6H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 159.6, 149.3, 136.0, 124.2, 121.3, 62.9, 41.9, 25.9, 18.3, -5.4; **Anal. Calc.** for $C_{13}H_{23}NOSi$ requires: C, 65.77; H, 9.76; N, 5.90; **found:** C, 66.09; H, 9.57 N, 6.61%.

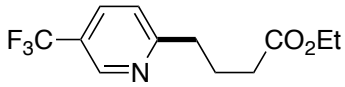



**Ethyl 4-(5-(tributylstannyl)pyridin-2-yl)butanoate** (**3g**). The general procedure was followed at 10 mol% catalyst loading with 2-Chloro-5-(tributylstannyl)pyridine (1.21 g, 3.00 mmol) and ethyl 4-bromobutyrate (472 mL, 3.30 mmol). Isolated 691 mg (48%) by gradient elution flash chromatography (40 g $SiO_2$, 0 to 100% ethyl acetate in hexanes) as yellow oil. **$^1$H-NMR** (500 MHz; $CDCl_3$): δ 8.51-8.48 (m, 1H), 7.67-7.59 (m, 1H), 7.08 (dd, *J* = 7.3, 1.8 Hz, 1H), 4.10 (qd, *J* = 7.0, 3.1 Hz, 2H), 2.77 (t, *J* = 6.6 Hz, 2H), 2.34 (td, *J* = 7.4, 2.3 Hz, 2H), 2.06 (quintet, *J* = 7.1 Hz, 2H), 1.59-1.43 (m, 6H), 1.30 (sextetd, *J* = 7.3, 1.7 Hz, 6H), 1.22 (td, *J* = 7.0, 3.3 Hz, 3H), 1.12-0.99 (m, 6H), 0.86 (td, *J* = 7.2, 2.7 Hz, 9H); **$^{13}$C -NMR** (126 MHz; $CDCl_3$): δ 173.5, 160.5, 155.7, 144.5, 133.5, 123.1, 60.3, 37.5, 33.9, 29.12 (t, *J* = 10.4 Hz), 27.42 (t, *J* = 28.6 Hz), 24.9, 14.3, 13.7, 9.7 (m); **Anal. Calc.** for $C_{23}H_{41}NO_2Sn$ requires: C, 57.28; H, 8.57; N, 2.90; found: C, 57.55; H, 8.62; N, 2.86%.




**Ethyl 4-(4-(tert-butyl)pyridin-2-yl)butanoate** (**3h**). The general procedure was followed at 10 mol% catalyst loading with 4-(*tert*-butyl)-2-chloropyridine (509 mg, 3.00 mmol) and ethyl 4-bromobutyrate (472 mL, 3.30 mmol). Isolated 376 mg (50%) by gradient elution flash

chromatography (40 g $SiO_2$, 0 to 100% ethyl acetate in hexanes) as yellow oil. **$^1$H-NMR** (500 MHz; $CDCl_3$): δ 8.41 (d, *J* = 5.3 Hz, 1H), 7.11-7.08 (m, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.80 (t, *J* = 7.7 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.06 (quintet, *J* = 7.6 Hz, 2H), 1.29 (s, 9H), 1.24 (d, *J* = 14.3 Hz, 3H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 173.6, 161.0, 160.5, 149.2, 119.9, 118.4, 60.4, 37.8, 34.7, 33.9, 30.7, 25.2, 14.4; **Anal. Calc.** for $C_{15}H_{23}NO_2$ requires: C, 72.25; H, 9.30; N, 5.62; found: C, 71.43; H, 9.30; N, 5.74%.




**Ethyl 4-(5-trifluoromethyl)pyridin-2-yl)butanoate [1100766-42-4] (3i).**[11] The general procedure was followed at 10 mol% catalyst loading with 2-chloro-5-trifluoromethylpyridine (272 mg, 1.50 mmol) and ethyl 4-bromobutyrate (236 mL, 1.65 mmol). Run one isolated 108 mg (27%) by flash column chromatography ($SiO_2$, 9: 1 hexanes: ethyl acetate) as yellow oil. Run two at 5 mol% catalyst loading with 10 mol% AIBN and 25 mol% NaI as additives isolated 90 mg (46%) by flash column chromatography ($SiO_2$, 9: 1 hexanes: ethyl acetate) as yellow oil. **$^1$H-NMR** (500 MHz; $CDCl_3$): δ 8.79 (s, 1H), 7.83 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.37 (t, *J* = 7.4 Hz, 2H), 2.10 (quintet, *J* = 7.5 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); **$^{13}$C-NMR** (126 MHz; $CDCl_3$): δ 173.3, 165.4, 146.4 (q, *J* = 4.0 Hz), 133.6 (q, *J* = 3.5 Hz), 124.9, 124.4 (q, *J* = 33.4 Hz), 122.7, 60.5, 37.5, 33.7, 24.6, 14.4; **$^{19}$F-NMR** (376 MHz; $CDCl_3$): δ 0.1; **Anal. Calc.** for $C_{12}H_{14}F_3NO_2$ requires: C, 55.17; H, 5.40; N, 5.36; N; **found:** C, 55.71; H, 5.67; N, 5.46%.

## 9. Spectra

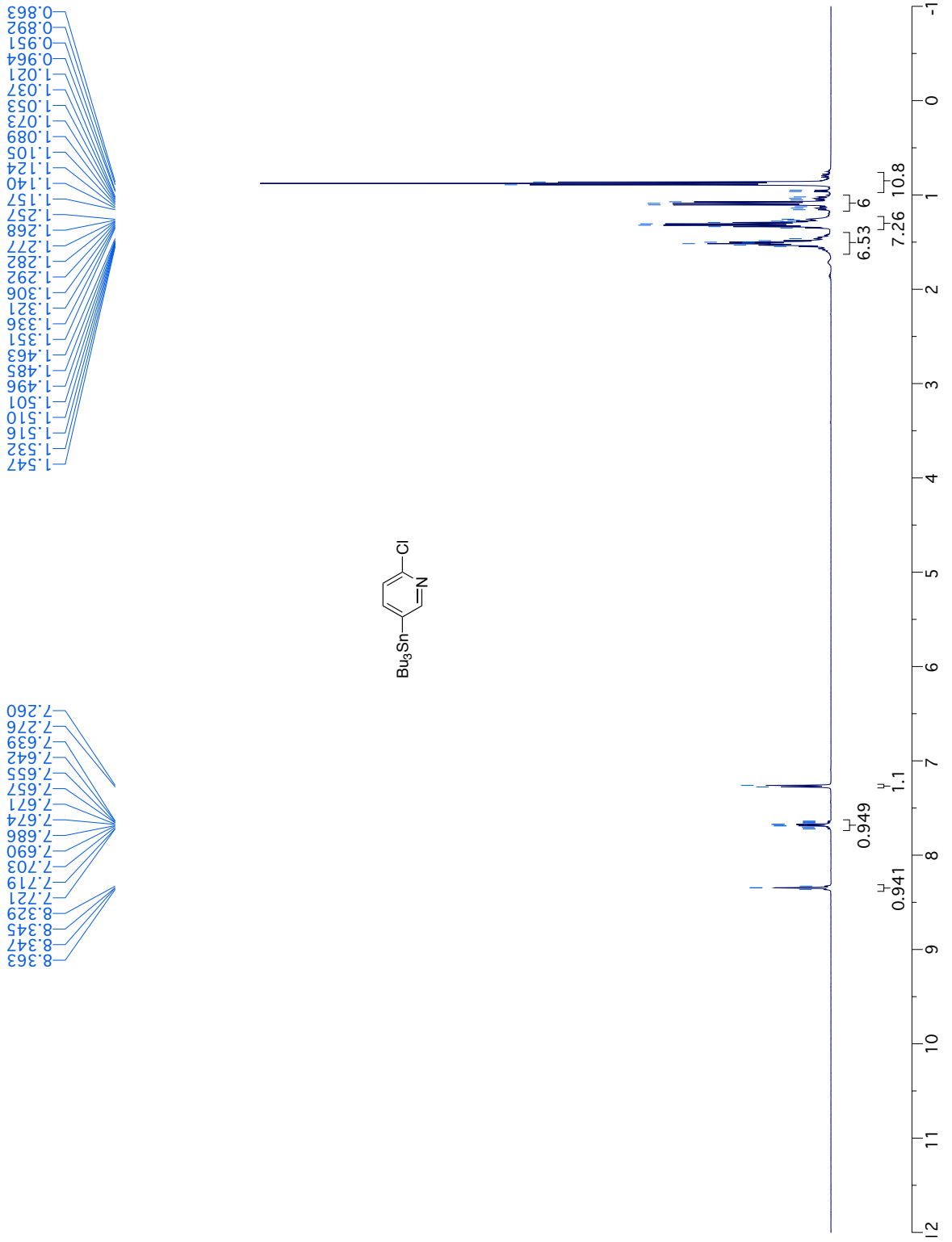



**Figure S1. $^{1}$H-NMR: 2-Chloro-5-(tributylstannyl)pyridine (1b).**

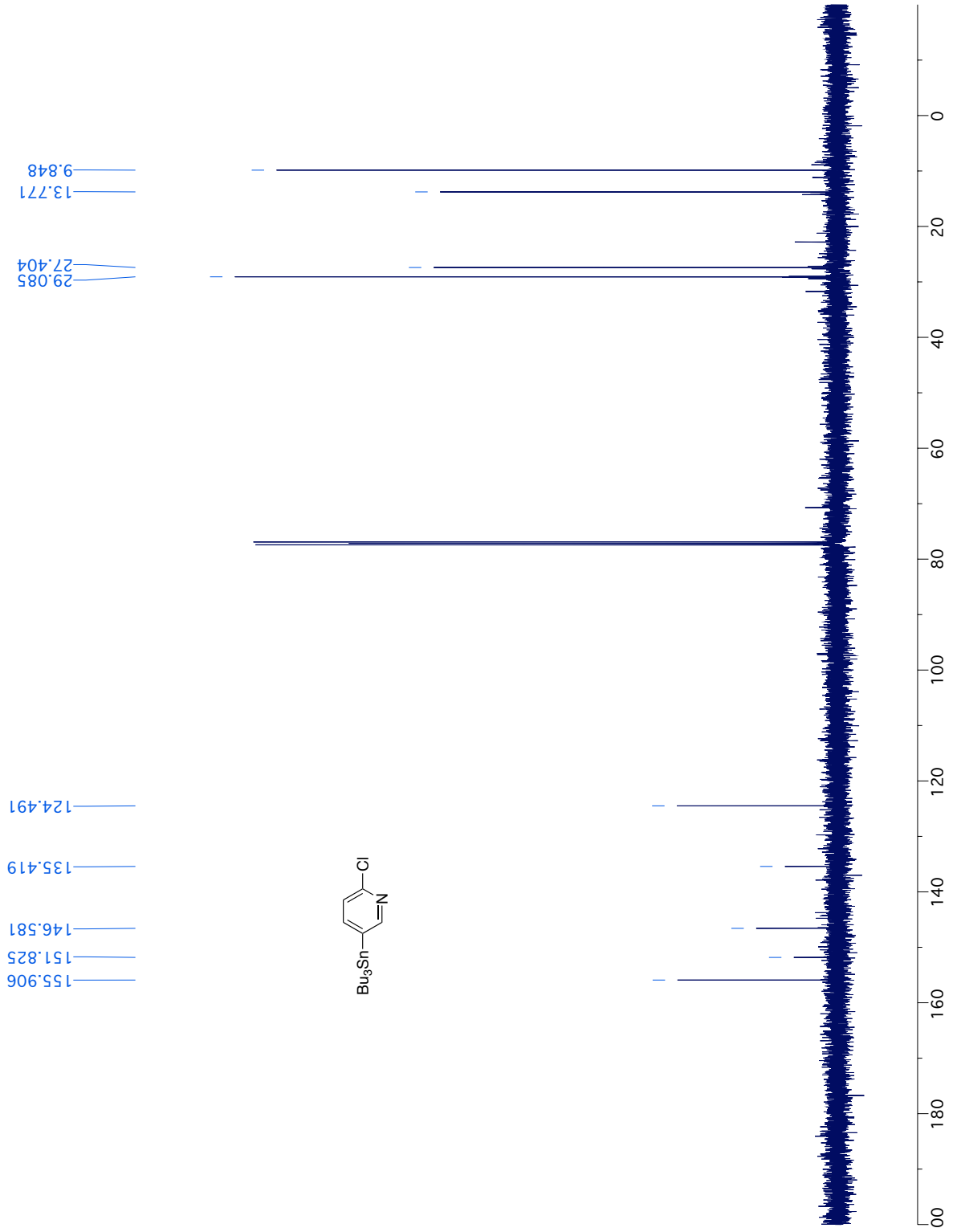



**Figure S2. $^{13}$C-NMR: 2-Chloro-5-(tributylstannyl)pyridine (1b).**

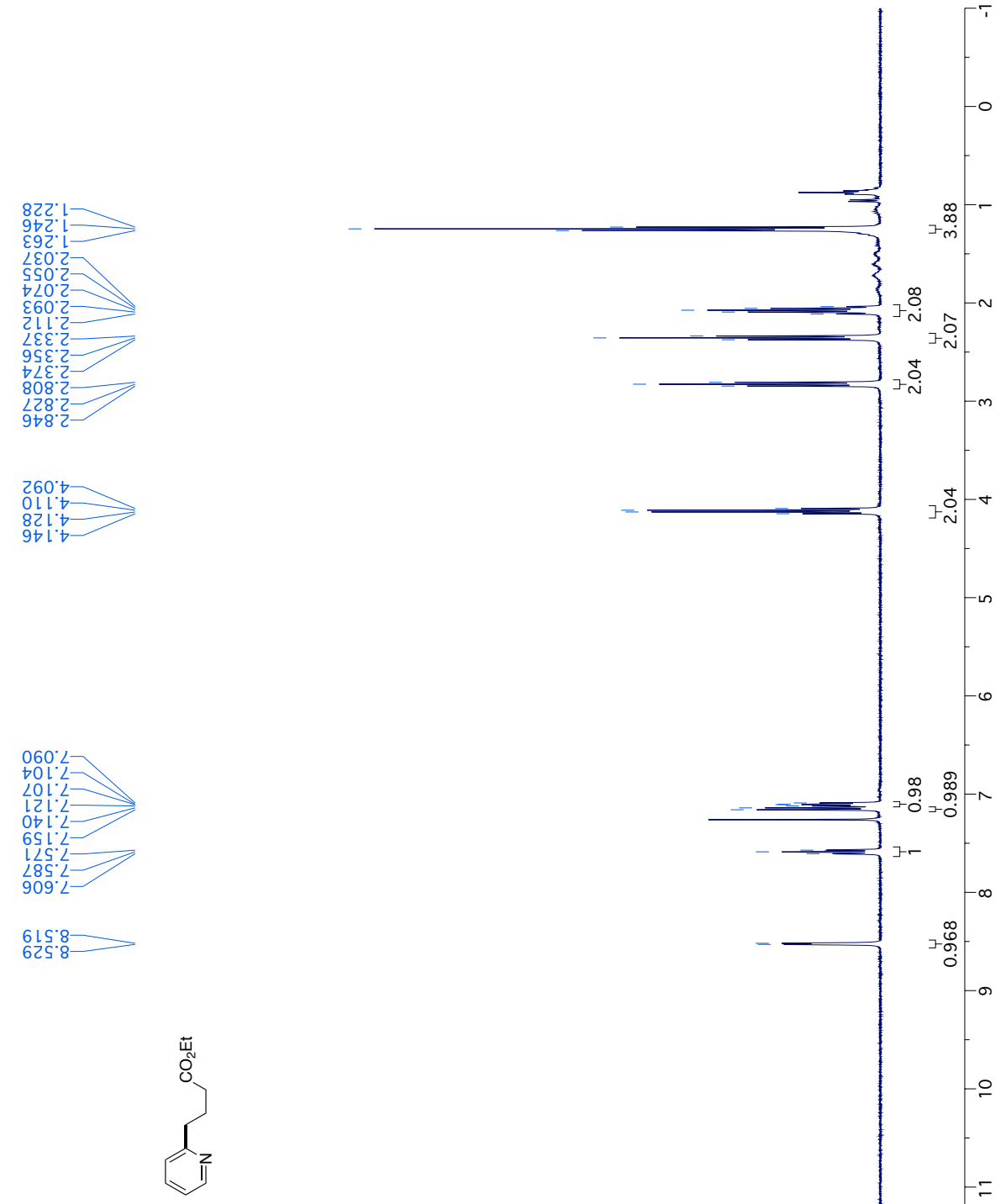



**Figure S3. $^{1}$H-NMR: Ethyl 4-(pyridin-2-yl)butanoate [8499-93-9] (3a).**

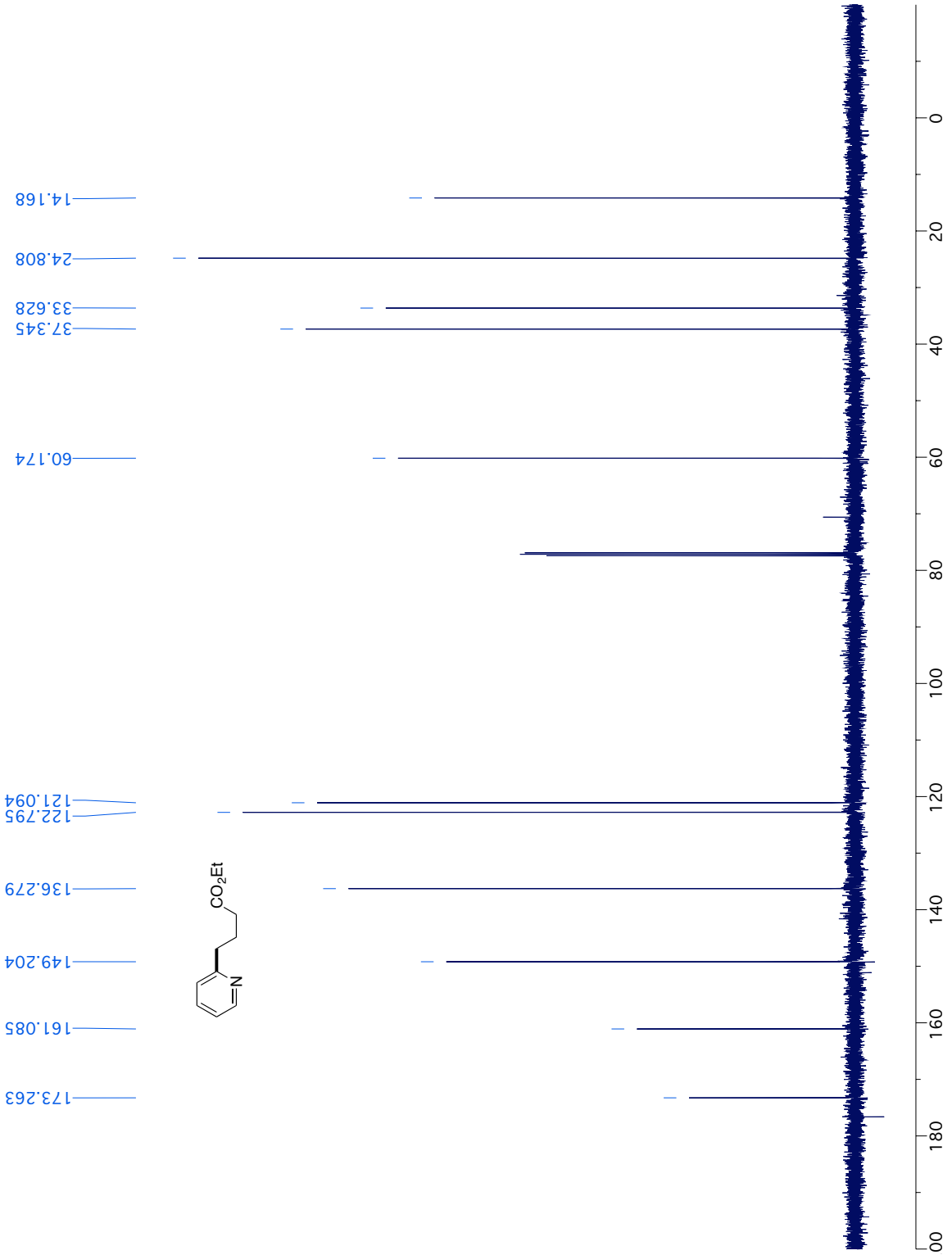



**Figure S4. $^{13}$C-NMR: Ethyl 4-(pyridin-2-yl)butanoate [8499-93-9] (3a).**

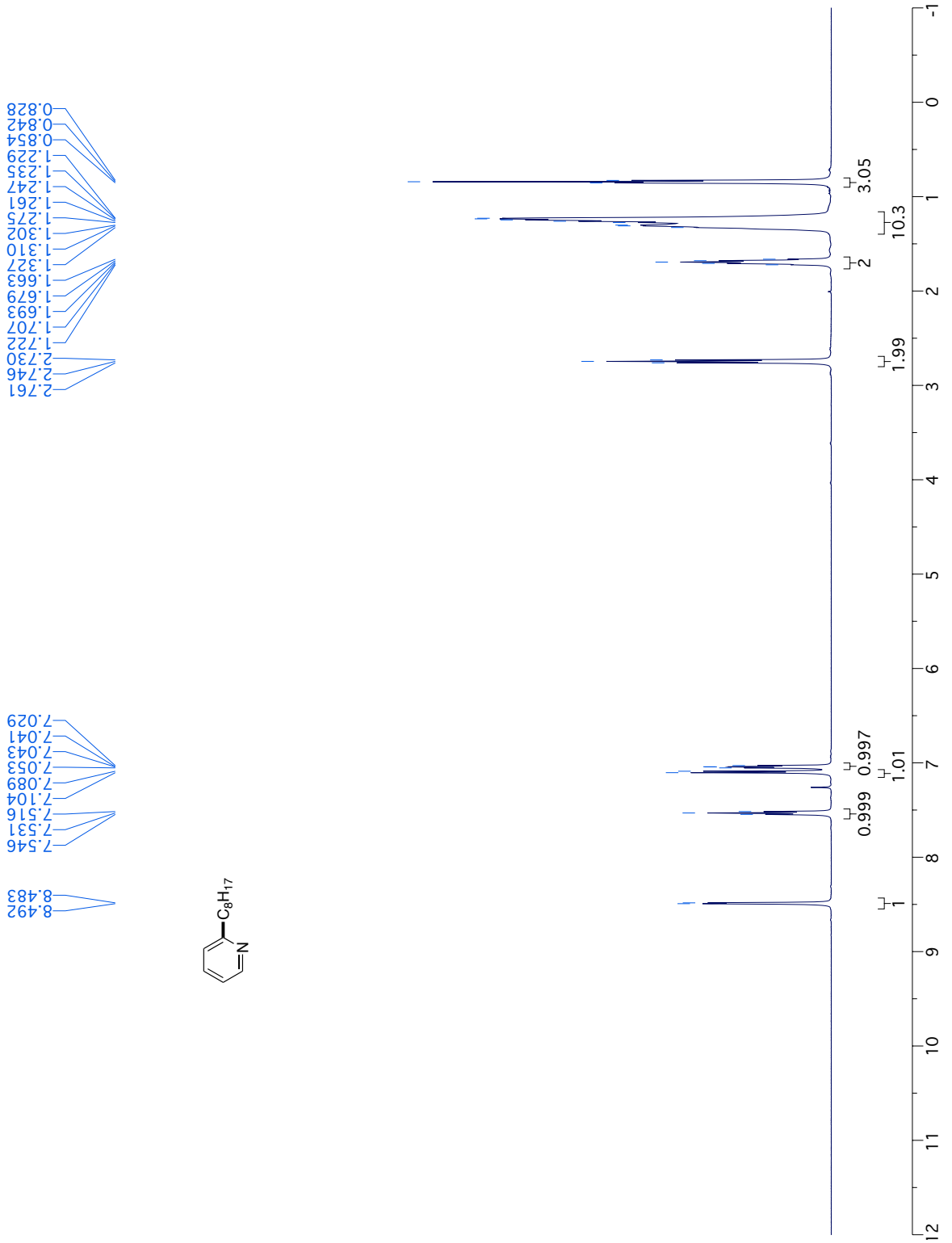



**Figure S5. $^{1}$H-NMR: 2-Octylpyridine [33841-61-1] (3b).**

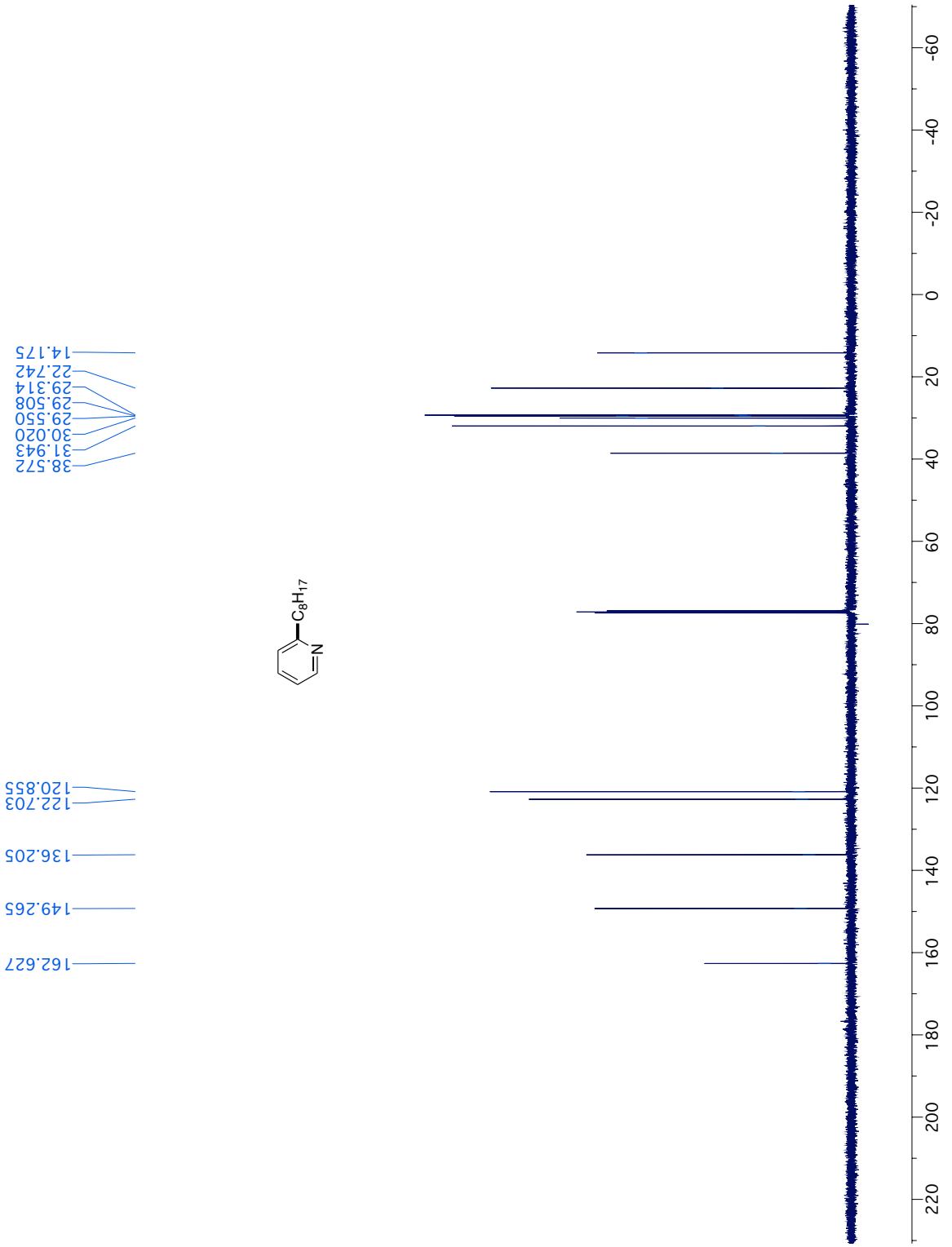



**Figure S6. $^{13}$C-NMR: 2-Octylpyridine [33841-61-1] (3b).**

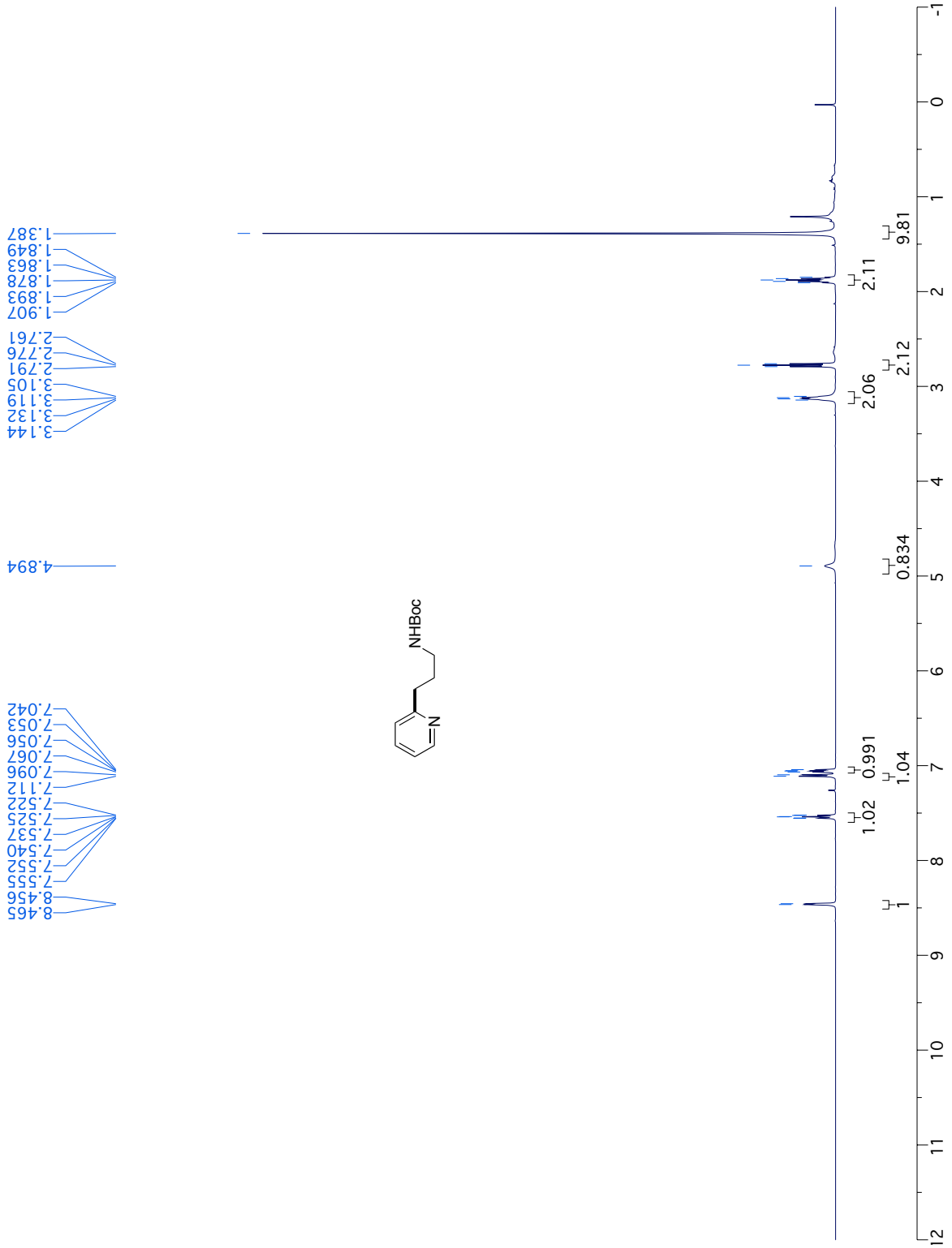



**Figure S7. $^{1}$H-NMR: *tert*-Butyl (3-(pyridin-2-yl)propyl)carbamate (3c).**

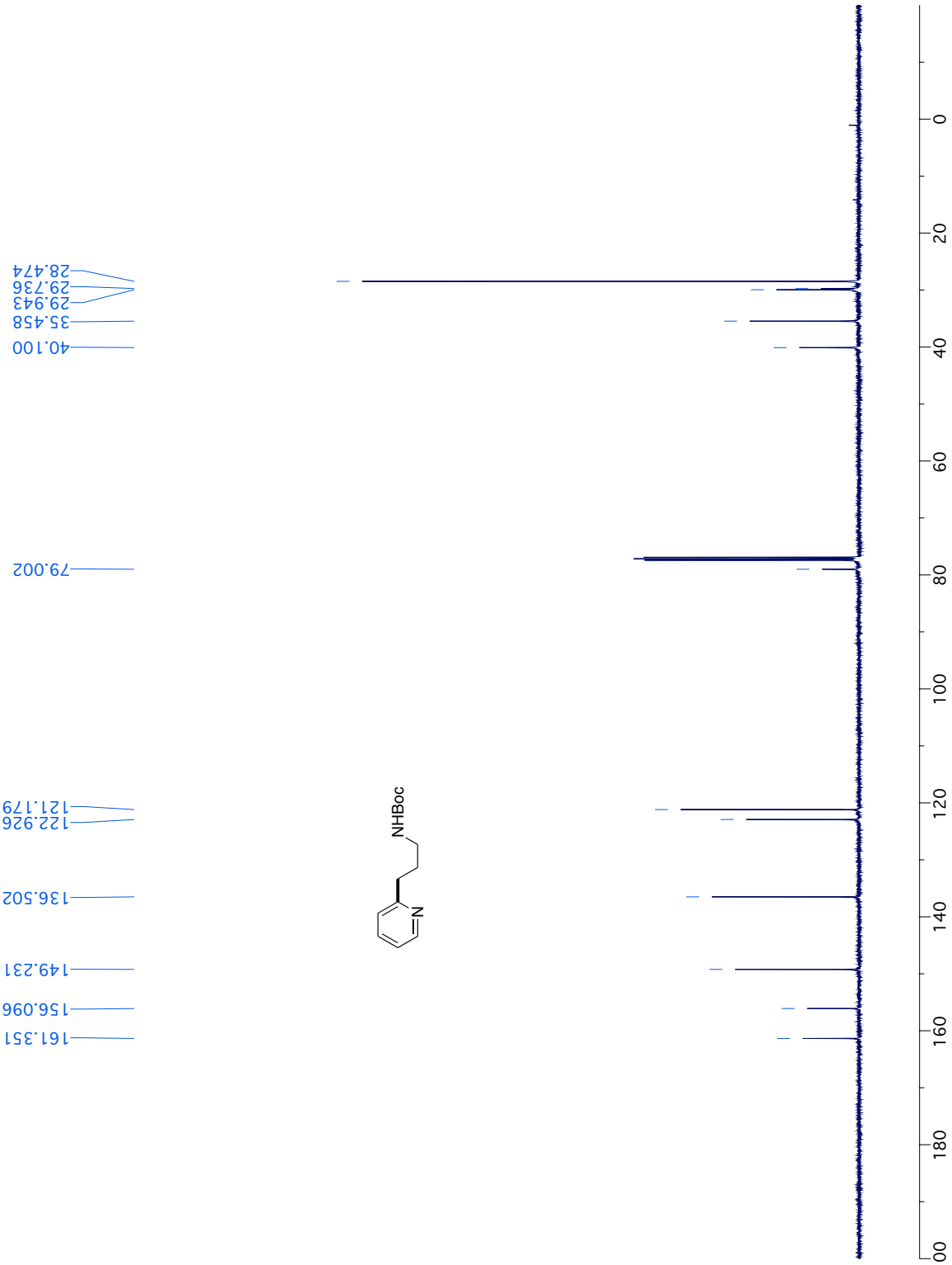



**Figure S8. $^{13}$C-NMR: *tert*-Butyl (3-(pyridin-2-yl)propyl)carbamate (3c).**

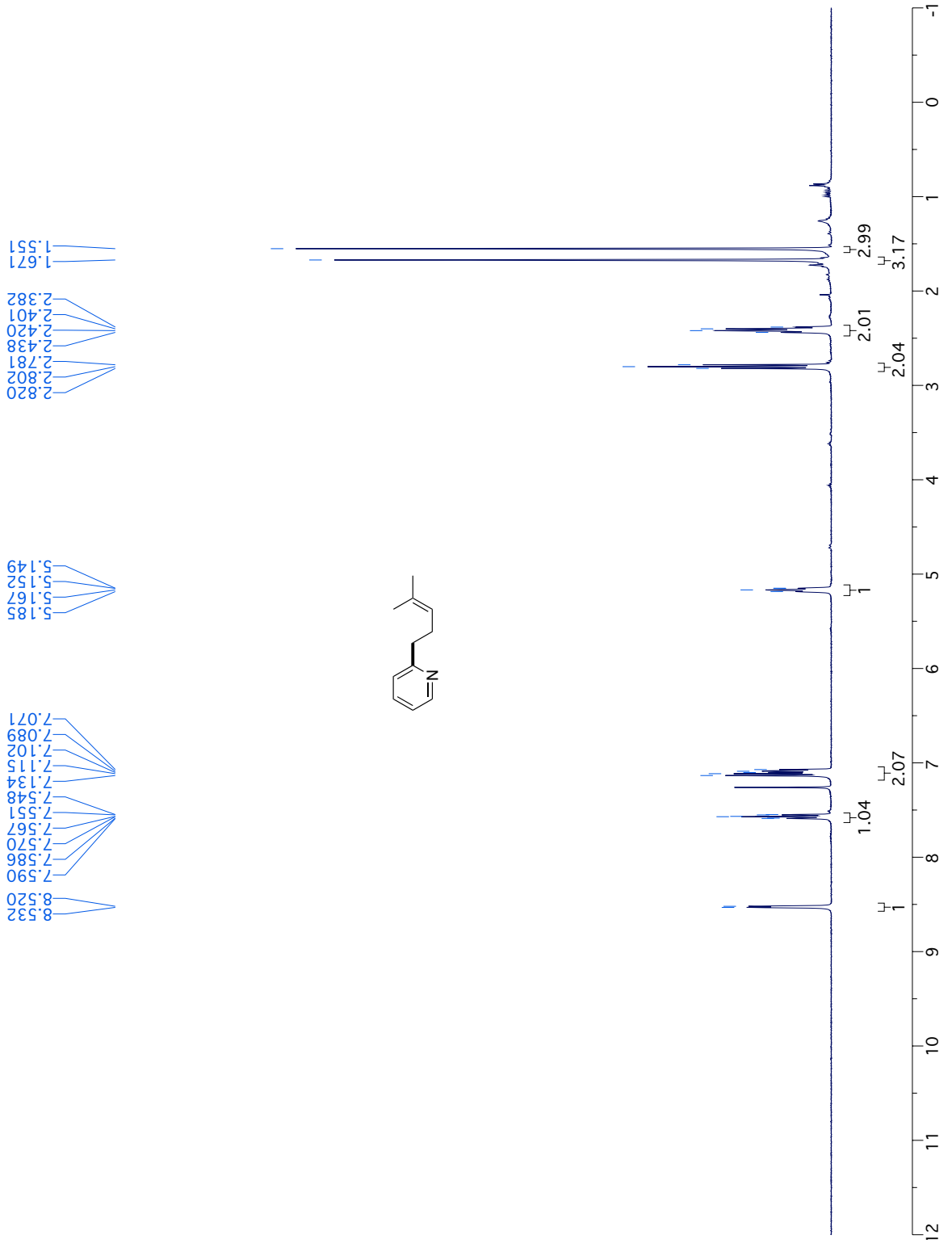



**Figure S9. $^{1}$H-NMR: 2-(4-Methylpent-3-en-1-yl)pyridine [51082-20-3] (3d).**

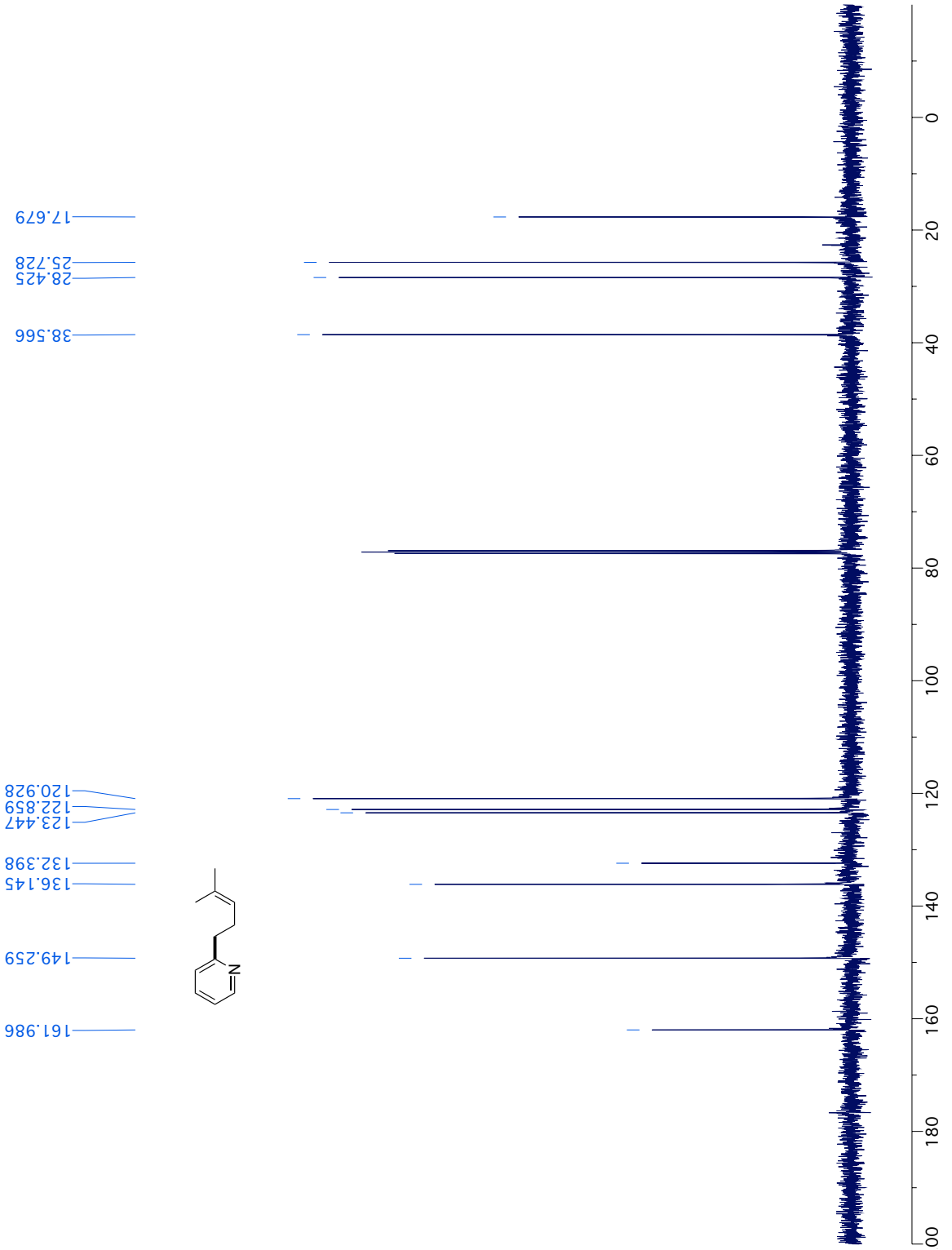



**Figure S10. $^{13}$C-NMR: 2-(4-Methylpent-3-en-1-yl)pyridine [51082-20-3] (3d).**

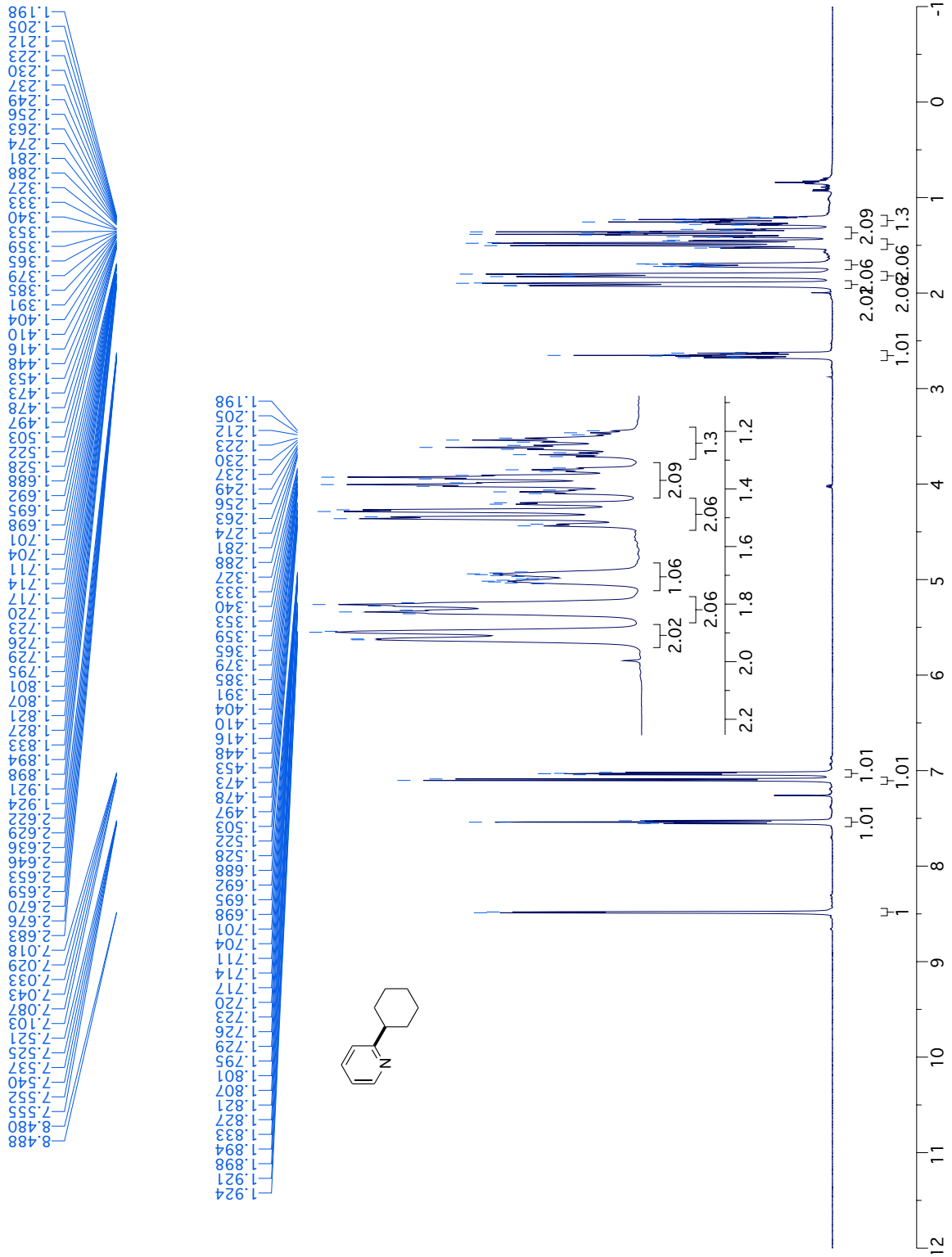


**Figure S11. $^{1}$H-NMR: 2-Cyclohexylpyridine [15787-49-2] (3e).**

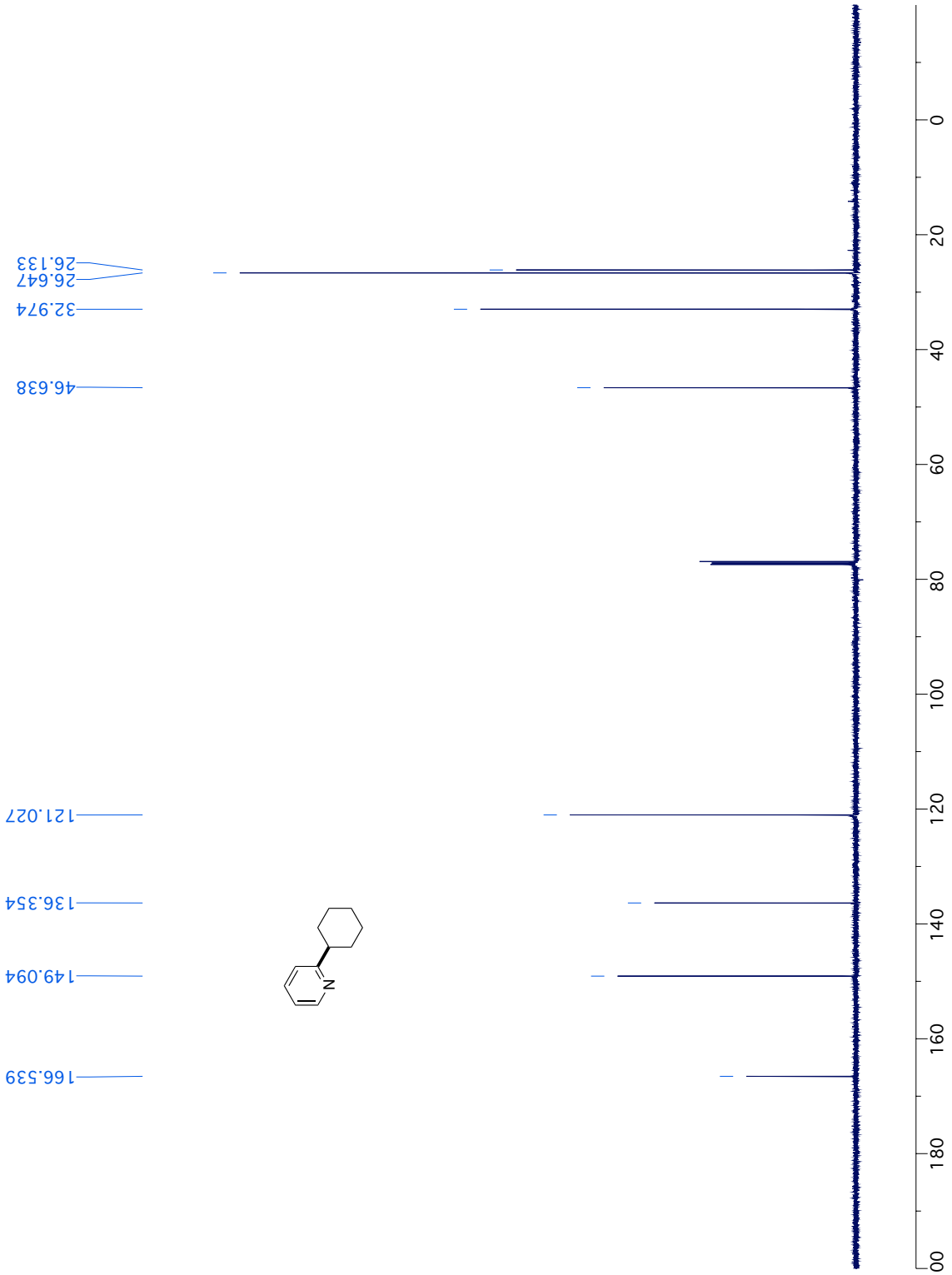



**Figure S12. $^{1}$H-NMR: 2-Cyclohexylpyridine [15787-49-2] (3e).**

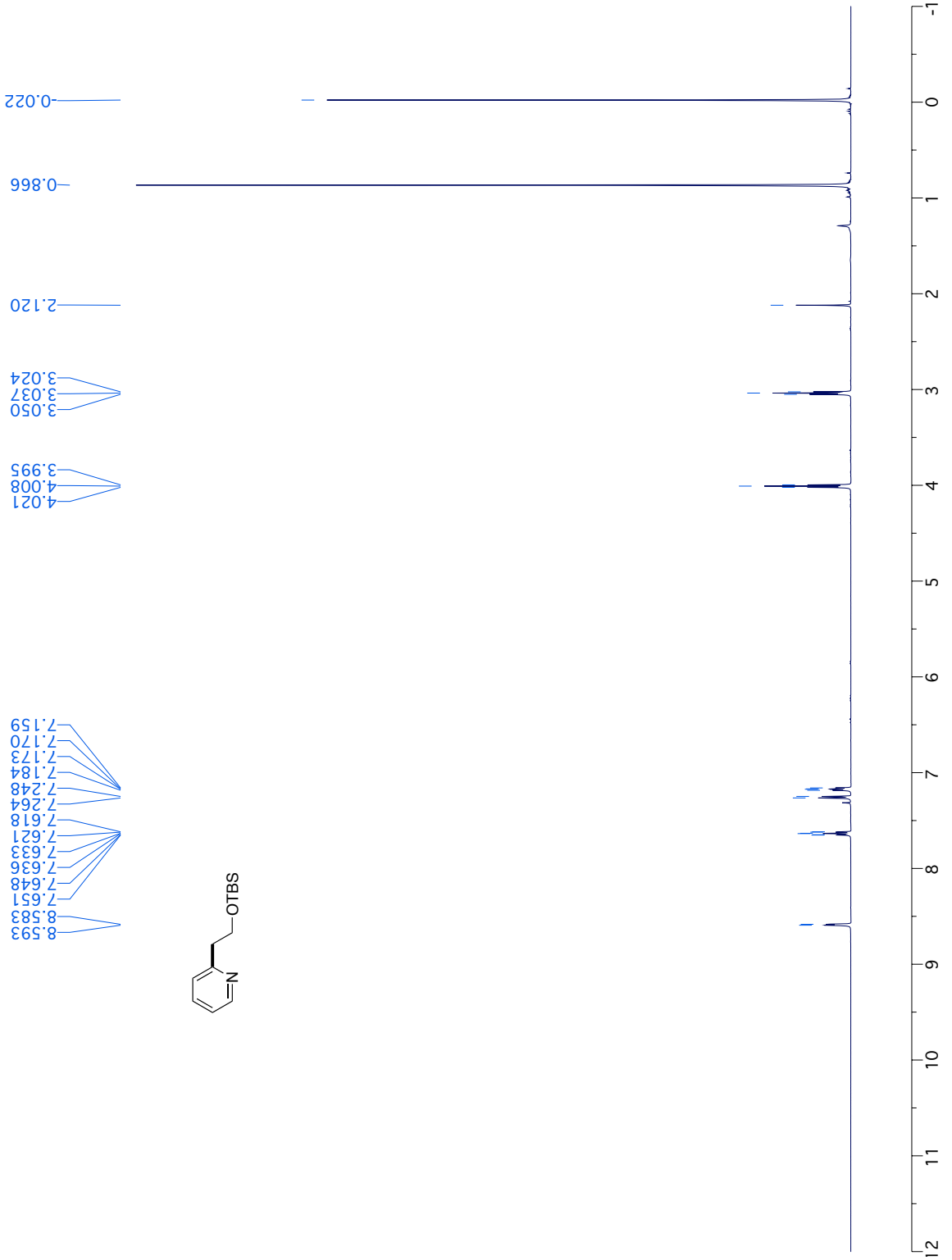



**Figure S13. $^{1}$H-NMR: 2-(2-((tert-Butyldimethylsilyl)oxy)ethyl)pyridine [161227-19-6] (3f).**

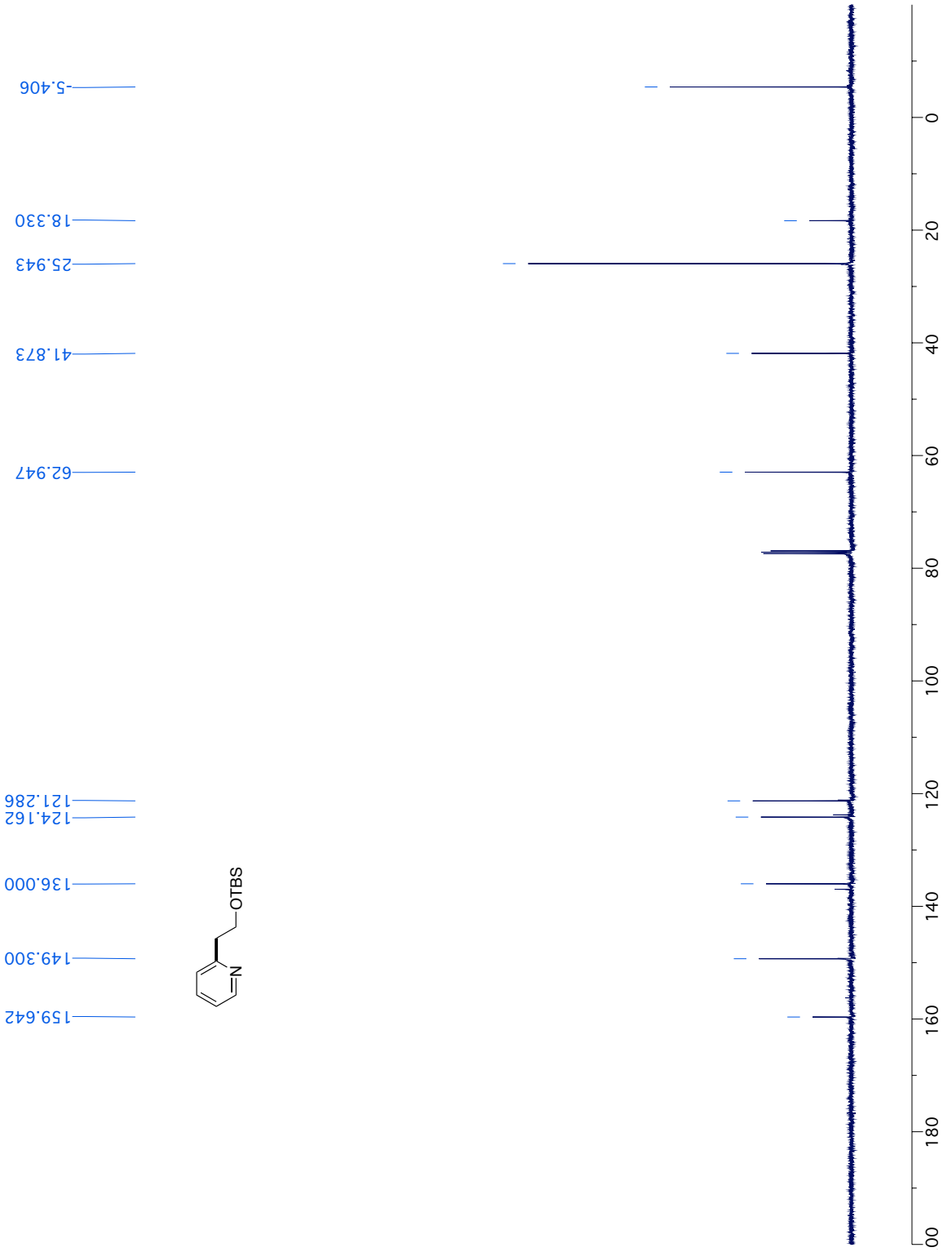



**Figure S14. $^{13}$C-NMR: 2-(2-((tert-Butyldimethylsilyl)oxy)ethyl)pyridine [161227-19-6] (3e).**

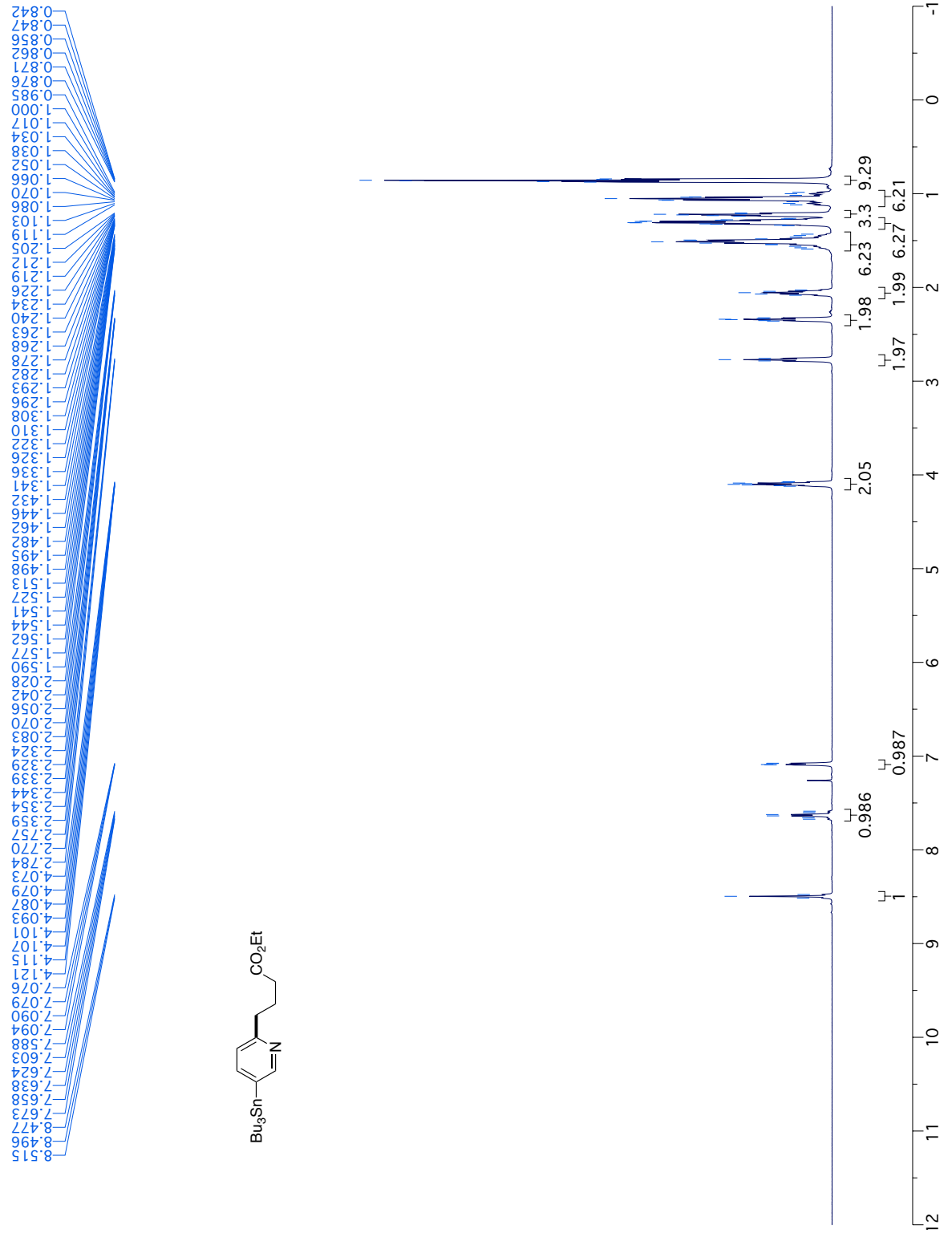



**Figure S15. $^{1}$H-NMR: Ethyl 4-(5-(tributylstannyl)pyridin-2-yl)butanoate (3g).**

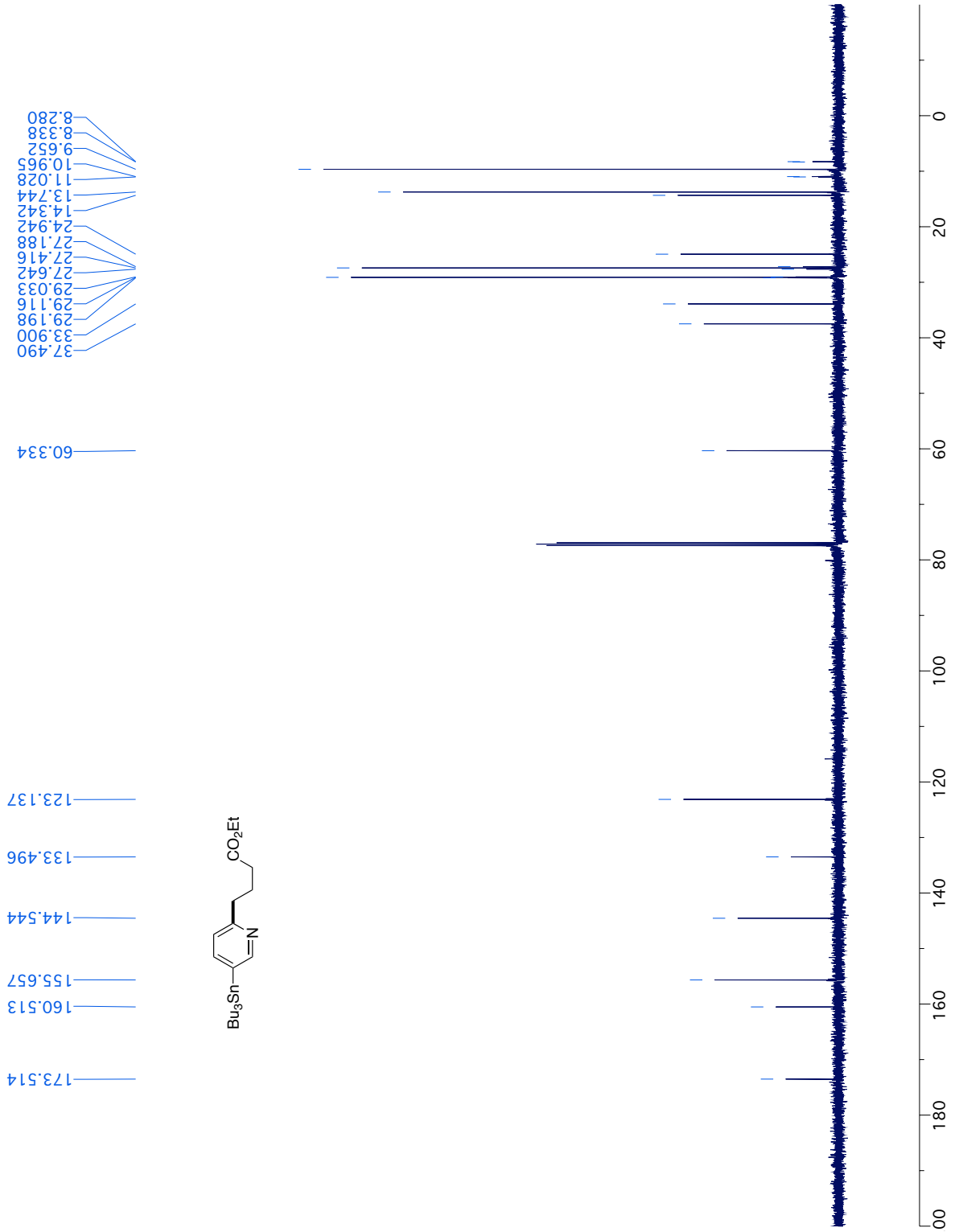



**Figure S16. $^{13}$C-NMR: Ethyl 4-(5-(tributylstannyl)pyridin-2-yl)butanoate (3g).**

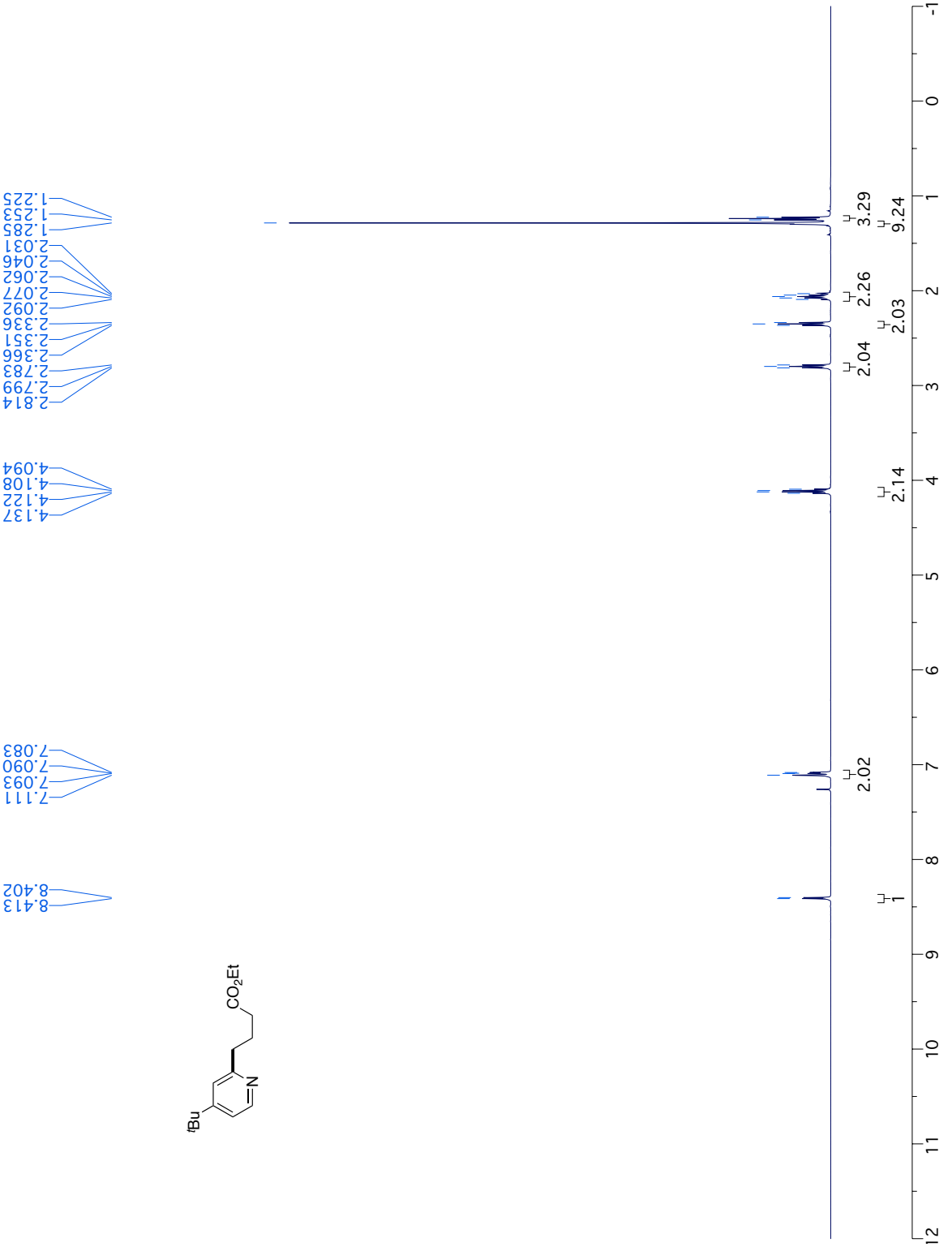



**Figure S17. $^{1}$H-NMR: Ethyl 4-(4-(tert-butyl)pyridin-2-yl)butanoate (3h).**

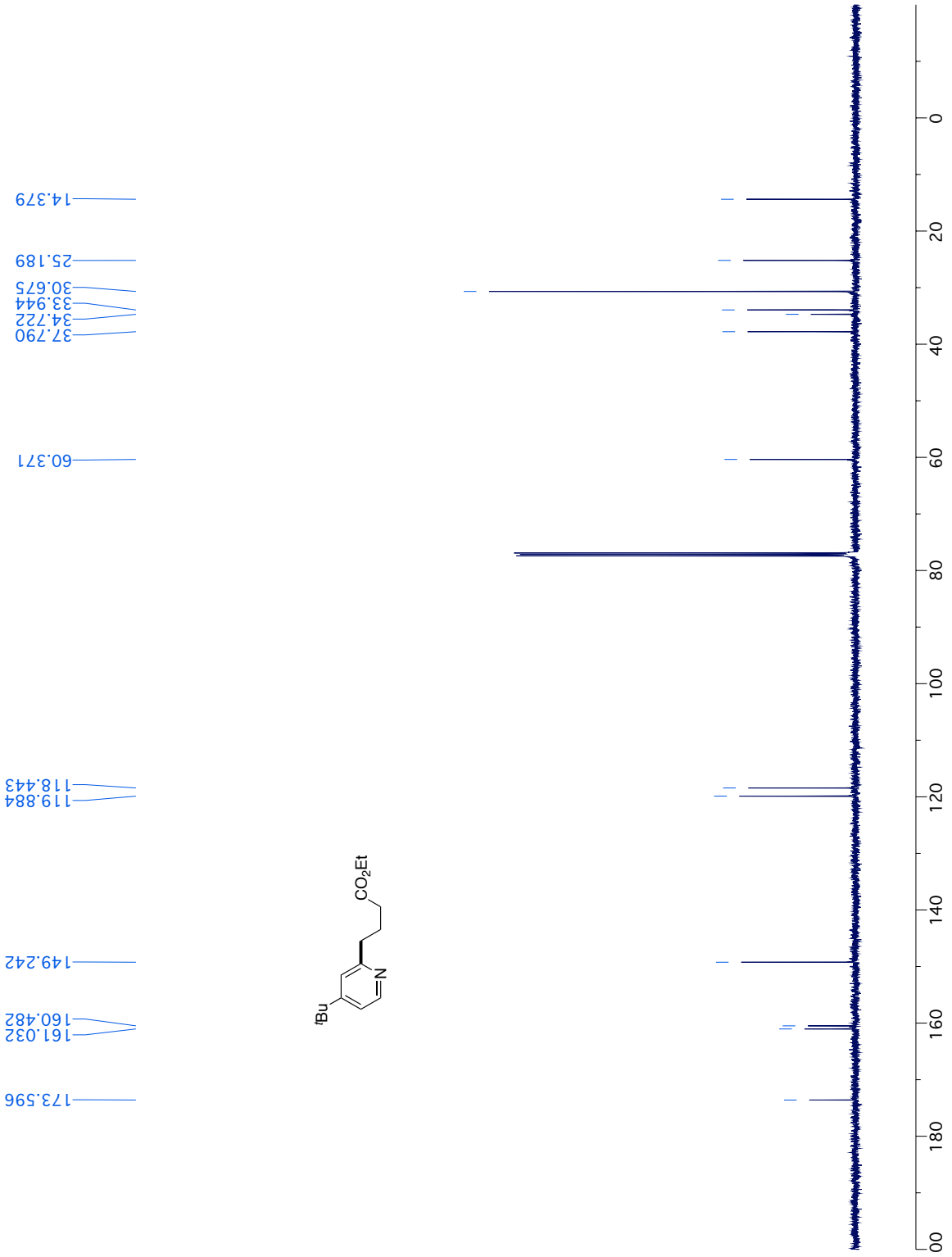



**Figure S18. $^{13}$C-NMR: Ethyl 4-(4-(tert-butyl)pyridin-2-yl)butanoate (3h).**

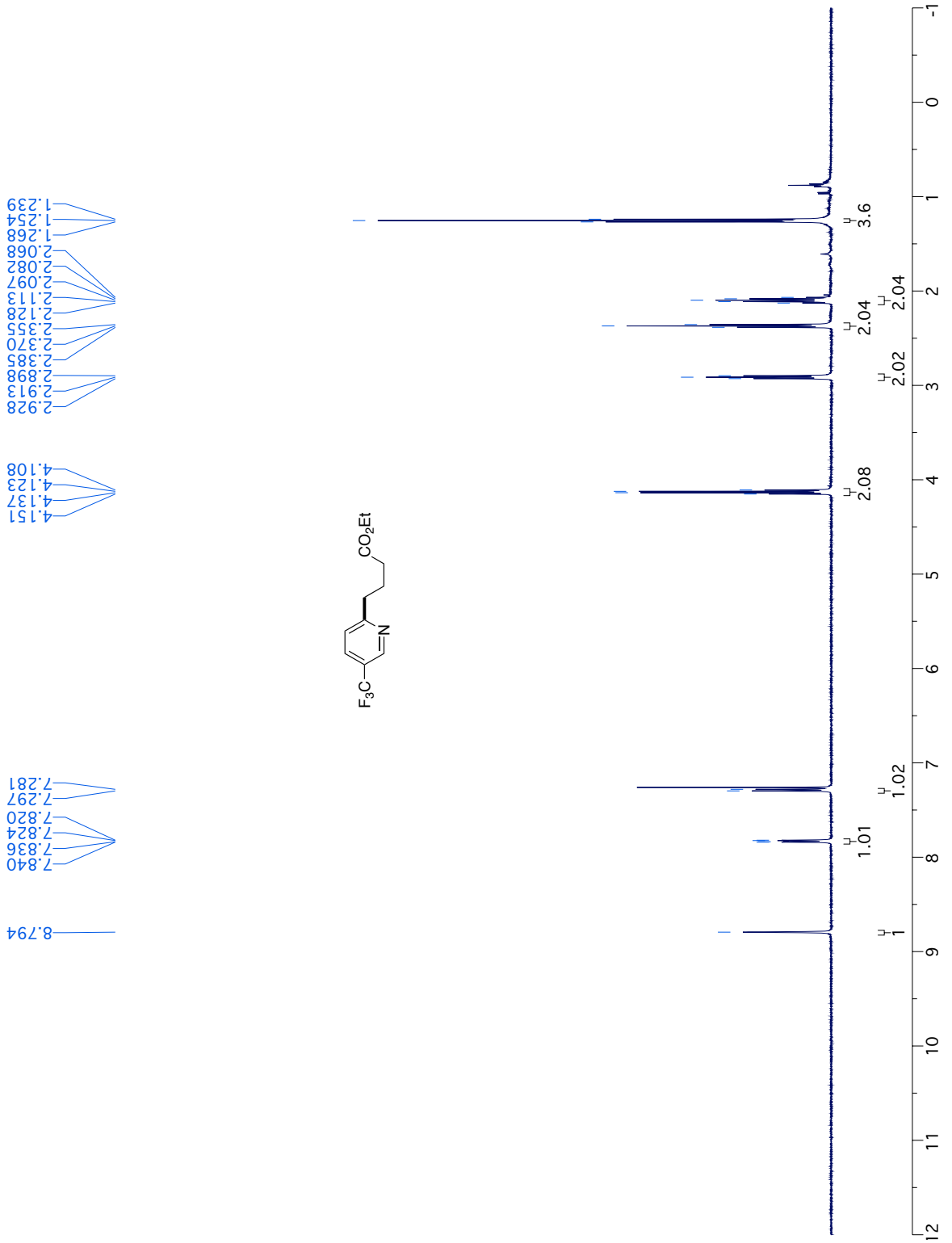



**Figure S19. $^{1}$H-NMR: Ethyl 4-(5-trifluoromethyl)pyridin-2-yl)butanoate [1100766-42-4] (3i).**

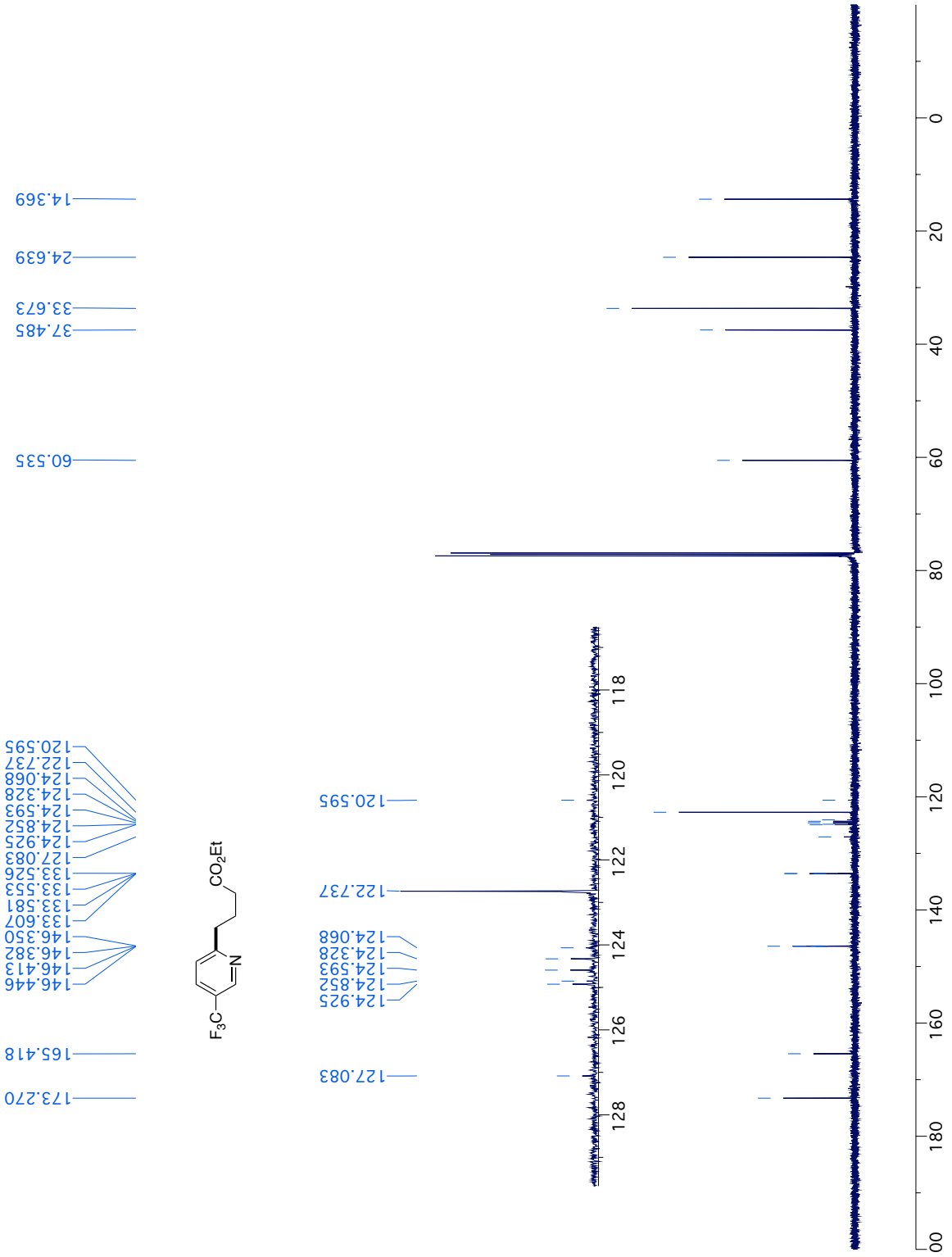



**Figure S20. $^{13}$C-NMR: Ethyl 4-(5-trifluoromethyl)pyridin-2-yl)butanoate [1100766-42-4] (3i).**

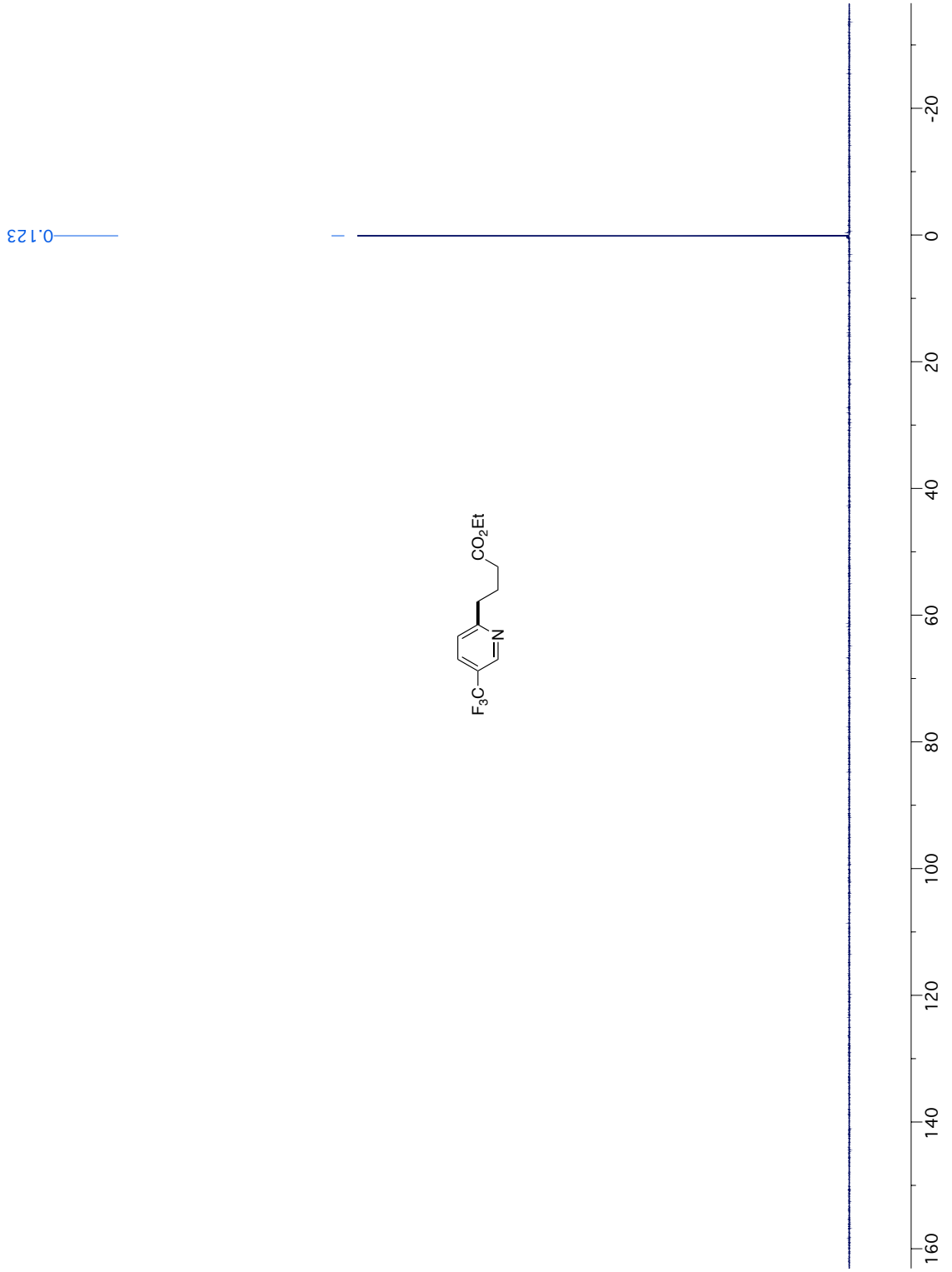



**Figure S21. $^{19}$F-NMR: Ethyl 4-(5-trifluoromethyl)pyridin-2-yl)butanoate [1100766-42-4] (3i).**

## 10. References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