Electronic Supplementary Material (ESI) for ChemComm.

Regioselective oxidative Pd-catalysed coupling of alkylboronic acids with pyridin-2-yl-substituted heterocycles

Electronic Supplementary Information

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General information

All reactions sensitive to air or moisture were carried out in flame-dried glassware under a positive pressure of argon using standard Schlenk techniques. Dry tetrahydrofuran (THF), dichloromethane (CH_2Cl_2) and diethyl ether (Et_2O) were obtained from a MBRAUN MB-SPS 800 solvent purification system. Other dry solvents were obtained from Acros in the highest purity available and used without further purification. Technical solvents used for aqueous workup and for column chromatography [*n*-pentane (pentane), ethyl acetate (EtOAc), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), methanol (MeOH)] were distilled prior to use.

All other chemicals were purchased from Sigma-Aldrich, TCI Europe and Acros Organics and were used without further purification.

Flash Chromatography was performed on silica gel 60 (Merck, 230-240 mesh) with the eluent mixtures given for the corresponding procedures. Thin-layer Chromatography (TLC) was performed on silica-coated glass plates (silica gel 60 F 254). Compounds were detected by UV (λ = 254 nm, 366 nm) and $KMnO_4$ solution. All solvents for chromatography were distilled prior to use.

Infrared spectra (IR) were recorded on a JASCO IR-4100 (ATR), heterocycles were abbreviated as follows: pyridine (Py), thiophene (Thp), pyrrole (Pyrr), furan (Fur). MS and HRMS measurements were performed on a Finnigan MAT 8200 (EI), Finnigan MSD 5973 (HR-EI), Finnigan LCQ classic (ESI), ThermoFinnigan LTQ FT (HRMS-ESI) or a Thermo Sientific LTQ Orbitrap XL (HRMS-ESI). ^{1}H and ^{13}C NMR spectra were recorded at 300 K either on a Bruker AV-360 or a Bruker AV-500 spectrometer. Chemical shifts are reported in parts per million (ppm) relative to residual $CDCl_3$ (δ_H = 7.26 ppm and δ_C = 77.16 ppm). All coupling constants (*J*) are reported in Hertz (Hz). Apparent multiplets that occur as a result of accidental equality of coupling constants those of magnetically non-equivalent protons are marked as virtual (*virt.*). The assignment of all reported signals and the multiplicity of the ^{13}C-NMR signals were determined by two-dimensional NMR experiments (COSY, NOESY, HSQC, HMBC). Analytical gas chromatography (GLC) was performed on an Agilent-HP 6890 with a flame ionisation detector using hydrogen as the carrier gas and a HP-5 column (ø = 0.25 min, l = 30 m). The following temperature program was used for this work (60 °C 3 min, 15 °C/min → 300 °C, 300 °C 5 min). Melting points (mp) and boiling points (bp) are reported uncorrected.

The atom numbering giving in the procedures may vary from the *IUPAC* name of the synthesised compounds. For reader's clarity the numbering on the pyridine, thiophene, furan

and pyrrole atoms are always keep the same throughout the synthesis of a compound disregarding all additional substituents.

General Procedure 1: Esterification via acid chloride

Oxalyl chloride (1.05 eq) was added dropwise to a solution of the carboxylic acid dissolved in dry CH_2Cl_2 (5 mL/mmol), followed by 4 drops of DMF. The resulting solution was stirred for 2 h before adding dry ethanol (4.5 eq) and triethylamine (2.0 eq). After additional 16 h the solution was diluted with CH_2Cl_2 (10 mL/mmol) and water (5 mL/mmol). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL/mmol). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated, yielding the crude product, which was further purified by flash chromatography using a mixture of pentane and Et_2O as eluent.

General Procedure 2: *Negishi* Cross Coupling of 2-bromopyridine

A solution of *n*-butyllithium in hexane (2.5 M, 1.1 eq) was added to a -78 °C cooled solution of 2-bromopyridine (1.1 eq) in dry THF (5 mL/mmol). After 90 min at -78 °C a solution of high-vacuum dried $ZnCl_2$ (1.2 eq) in dry THF (2 mL/mmol) was added dropwise to the lithium species. The resulting solution was allowed to warm up to room temperature over 2 h. Next a solution of the substrate (1.0 eq) and $Pd(PPh_3)_4$ (3 mol%) in dry THF (5 mL/mmol) was added dropwise to the solution. The reaction was completed as indicated by consumption of starting material by TLC. The reaction was diluted with NH_4Cl solution (2.5 mL/mmol) and Et_2O (20 mL/mmol) and water (10 mL/mmol). The aqueous layer was extracted by Et_2O (2 × 20 mL/mmol). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated. The crude product was further purified by flash chromatography using a mixture of pentane and Et_2O as eluent.

General Procedure 3: oxidative C-H activation – preparative reaction

A flame-dried pressure Schlenk-tube was subsequently charged with substrate (400 µmol, 1 eq), alkylboronic acid (3 eq), 2,6-dimethyl-1,4-benzoquinone (**2**) (0.5 eq), Ag_2CO_3 (2 eq) and $Pd(OAc)_2$ (10 mol%). Dry ^{t}AmOH (2 mL) was added, the tube was tightly closed and the resulting suspension was stirred for 5 min at room temperature and at 100 °C for 14 h in a preheated oil bath. The cooled solution was diluted by CH_2Cl_2 (60 mL) and Na_2S solution (10% w/w, 20 mL). The layers were separated and the aqueous layer was further extracted by CH_2Cl_2 (2 × 60 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was completely removed under reduced pressure, yielding a yellow oil. The crude product was further purified by flash chromatography using a mixture of pentane and Et_2O as eluent.

General Procedure 4: oxidative C-H activation – analytical reaction

A 4 mL-HPLC vial with a Teflon-cap was charged with 2-(pyridin-2-yl)thiophene (32.2 mg, 200 µmol, 1eq), *n*-butylboronic acid, 1,4-benzoquinone derivate, silver salt and palladium source under air. Solvent was added the vial was tightly closed. (Reactions carried out under Ar or O_2 atmosphere were performed in a pressure Schlenk-tube and were evacuated and backfilled with the corresponding gas three times after the solvent was added.) The resulting mixture was stirred at room temperature for 5 min and then was submitted to a preheated alumina stirring block for 14 h. The reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (20 mL), and *n*-dodecane (20.0 µL, 88.1 µmol) was added via Hamilton syringe as an internal standard. The solution was washed with aqueous Na_2S solution (10 mL, 10% w/w), dried over Na_2SO_4, filtered and directly submitted to the GLC. Conversions (conv.) and yields were determined by analysing the corresponding peak area. Retention value for internal standard, starting material and product are listed below:

n-Dodecane: t_R = 7.775 min.

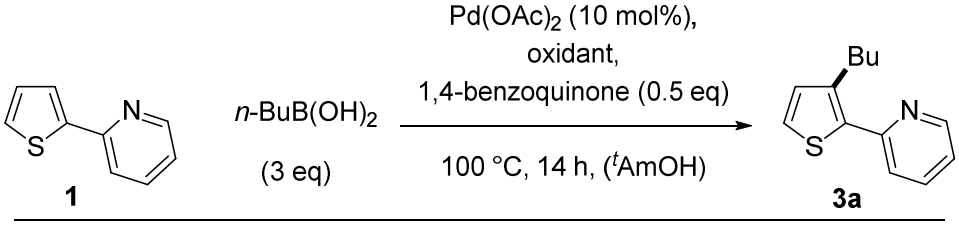
2-(Pyridin-2-yl)thiophene (**1**): t_R = 10.458 min.

3-Butyl-2-(pyridin-2-yl)thiophene (**3a**): t_R = 12.787 min.

Reaction optimisation

The reaction optimisation was carried out according to General Procedure 4, using GLC analysis. The relevant optimisation results are listed in the tables below.

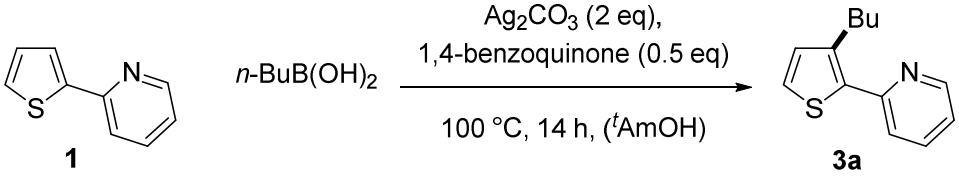
Table 1: Reaction optimisation using different oxidants



entry	oxidant (eq)	conv. (%)[a]	yield (%)[a]
1	Ag_2O (1)	34	30
2	Ag_2O (2)	62	48
3	$Ag(OAc)_2$ (4)	31	21
4	Ag_2CO_3 (2)	90	58
5	O_2 (air)	14	10
6	O_2 (1 atm)	21	14

General Procedure 4: 2-(Pyridin-2-yl)thiophene (200 µmol), *n*-BuB(OH)$_2$ (3 eq), oxidants, Pd(OAc)$_2$ (10 mol%), 1,4-Benzoquinone (0.5 eq), ^{t}AmOH (1 mL), [a] determined by GLC analysis using *n*-dodecane as an internal standard.

Table 2: Reaction optimisation using different equivalents of boronic acid



entry	*n*-BuB(OH)$_2$ (eq)	conv. (%)[a]	yield (%)[a]
1	2.0	86	54
2	2.5	91	55
3	3.0	90	58
4	3.5	82	58
5	4.0	70	55
6	5.0	49	42

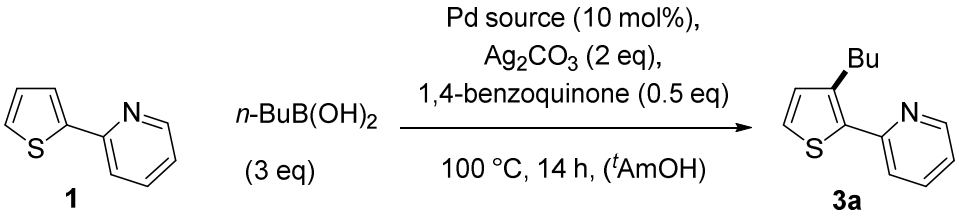
General Procedure 4: 2-(Pyridin-2-yl)thiophene (200 µmol), *n*-BuB(OH)$_2$, Pd(OAc)$_2$ (10 mol%), 1,4-Benzoquinone (0.5 eq), Ag_2CO_3 (2 eq), ^{t}AmOH (1 mL); [a] determined by GLC analysis using *n*-dodecane as an internal standard.

Table 3: Reaction optimisation using different substrate concentrations

entry	conc. (M)	conv. (%)[a]	yield (%)[a]
1	0.10	31	24
2	0.15	44	35
3	0.20	90	58
4	0.25	79	48
5	0.30	78	48
6	0.40	76	51

General Procedure 4: 2-(Pyridin-2-yl)thiophene (200 µmol), *n*-BuB(OH)$_2$ (3 eq), Pd(OAc)$_2$ (10 mol%), 1,4-Benzoquinone (0.5 eq), Ag_2CO_3 (2 eq) , ^{t}AmOH; [a] determined by GLC analysis using n-dodecane as an internal standard.

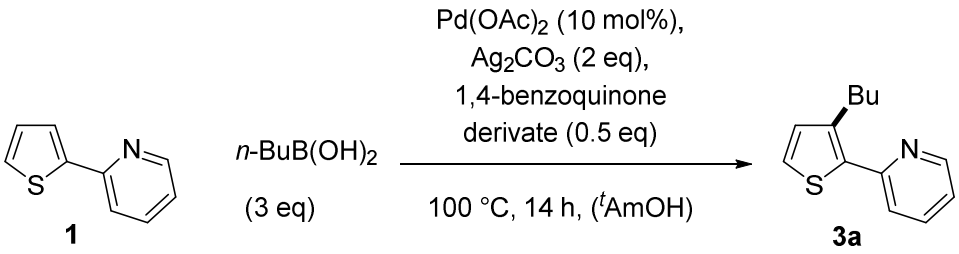
Table 4: Reaction optimisation using different Palladium catalysts



entry	[Pd] (10 mol%)	conv. (%)[a]	yield (%)[a]
1	$PdCl_2$	25	10
2	$Pd(tfa)_2$	32	12
3	$Pd(PPh_3)_2Cl_2$	14	6
4	$Pd(MeCN)_2Cl_2$	8	6
5	$Pd(MeCN)_4(BF_4)_2$	24	19
6	$Pd(OAc)_2$	90	58
7	$Pd(acac)_2$	34	39
8	$Pd(dba)_2$	7	3
9	no Pd	13	0
10	$Pd(piv)_2$	39	37

General Procedure 4: 2-(Pyridin-2-yl)thiophene (200 µmol), *n*-BuB(OH)$_2$ (3 eq), Pd source (10 mol%), 1,4-benzoquinone (0.5 eq), Ag_2CO_3 (2 eq) , ^{t}AmOH (1 mL); [a] determined by GLC analysis using *n*-dodecane as an internal standard.

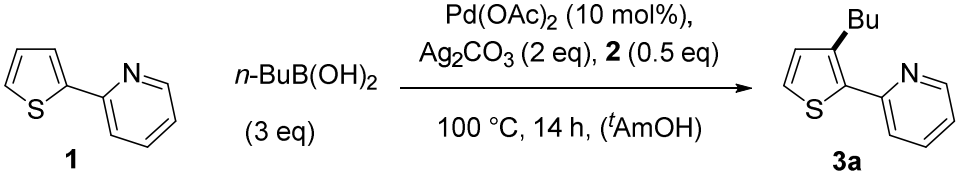
Table 5: Reaction optimisation using different 1,4-benzoquinone derivates



entry	BQ derivate (0.5 eq)	conv. (%)[a]	yield (%)[a]
1	1,4-BQ	90	58
2	Tetrachlor-1,4-BQ	25	14
3	2,5-Di(*tert*-butyl)-1,4-BQ	66	53
4	2,6-Di(*tert*-butyl)-1,4-BQ	56	22
5	2,6-Dimethoxy-1,4-BQ	92	64
6	2,6-Dimethyl-1,4-BQ (**2**)	92	70
7	Tetramethyl-1,4-BQ	97	54
8	2,5-Diphenyl-1,4-BQ	98	50
9	2-Chloro-1,4-BQ	32	25
10	2,3-Methoxy-5-methyl-1,4-BQ	93	61
11	1,4-Napthoquinone	68	51
12	no BQ	37	18

General Procedure 4: 2-(Pyridin-2-yl)thiophen (200 µmol), *n*-BuB(OH)$_2$ (3 eq), Pd(OAc)$_2$ (10 mol%), BQ derivate (0.5 eq), Ag_2CO_3 (2 eq) , ^{t}AmOH (1 mL); [a] determined by GLC analysis using *n*-dodecane as an internal standard.

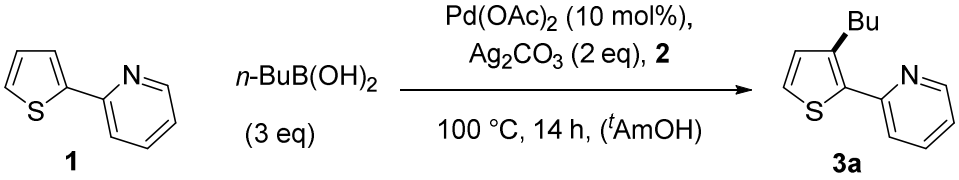
Table 6: Reaction optimisation using different atmospheres



entry	atmosphere	conv. (%)[a]	yield (%)[a]
1	Ar	83	68
2	O_2	84	51
3	air	92	70

General Procedure 4: 2-(Pyridin-2-yl)thiophene (200 µmol), *n*-BuB(OH)$_2$ (3 eq), Pd(OAc)$_2$ (10 mol%), **2** (0.5 eq), Ag_2CO_3 (2 eq), ^{t}AmOH (1 mL); [a] determined by GLC analysis using *n*-dodecane as an internal standard.

Table 7: Reaction optimisation using equivalents of benzoquinone **2**



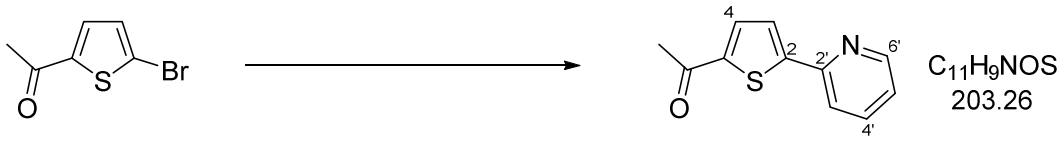
1 **3a**

entry	**2** (eq)	conv. (%)[a]	yield (%)[a]
1	0.25	95	66
2	0.50	92	70
3	1.00	98	62
4	1.50	99	59

General Procedure 4: 2-(Pyridin-2-yl)thiophene (200 µmol), *n*-$BuB(OH)_2$ (3 eq), $Pd(OAc)_2$ (10 mol%), **2**, Ag_2CO_3 (2 eq), ^{t}AmOH (1 mL); [a] determined by GLC analysis using *n*-dodecane as an internal standard.

Synthetic methods and analytical data of new compounds

5-Acetyl-2-(pyridin-2-yl)thiophene



$C_{11}H_9NOS$
203.26

2-Acetyl-5-bromothiophene (2.46 g, 12.0 mmol), 2-bromopyridine (2.09 g, 13.2 mmol, 1.1 eq), *n*-BuLi (5.28 mL, 13.2 mmol, 2.5 M in *n*-hexane 1.1 eq), $ZnCl_2$ (1.96 g, 14.4 mmol, 1.2 eq) and $Pd(PPh_3)_4$ (450 mg, 389 µmol, 3 mol%) in dry THF (65 mL) were reacted according to General Procedure 2.

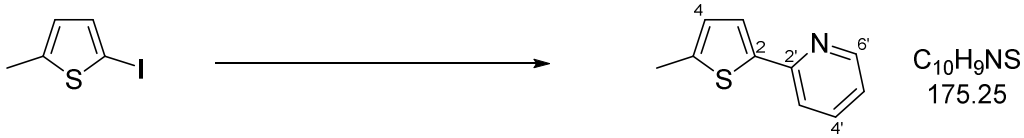
The crude product was purified by flash chromatography (pentane/Et_2O 2:1 → 3:2 → 1:1 → 2:3) yielding 5-acetyl-5-(pyridin-2-yl)thiophene (2.26 g, 11.1 mmol, 93%) as a light-yellow solid.

TLC: R_f = 0.48 (pentane/Et_2O 1:1) [UV].

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.58 (s, 3H, $COCH_3$), 7.24 (ddd, ^3J = 7.2, 4.8 Hz, ^4J = 1.4 Hz, 1H, H-5'), 7.60 (d, ^3J = 4.0 Hz, 1H, H-3), 7.70 (d, ^3J = 4.0 Hz, 1H, H-4), 7.71 (*virt.* dt, ^3J = 7.9 Hz, $^4J \approx {}^5J$ = 1.2 Hz, 1H, H-3'), 7.74 (*virt.* td, $^3J \approx$ 7.9 Hz, ^4J = 1.7 Hz, 1H, H-4'), 8.61 (dd, ^3J = 4.8 Hz, ^4J = 1.7 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 27.1 (q, CO*C*H_3), 119.7 (d, C-3'), 123.4 (d, C-5'), 125.2 (d, C-3), 133.1 (d, C-4), 137.0 (d, C-4'), 144.8 (s, C-5), 150.1 (d, C-6'), 151.7 (s, C-2'), 152.3 (s, C-2), 190.8 (s, *C*OCH_3).
The analytical data obtained matched those reported in the literature.[1]

2-(Pyridin-2-yl)-5-methylthiophene



$C_{10}H_9NS$
175.25

2-Methyl-5-bromothiophene (708 mg, 4.00 mmol, 1.0 eq), 2-bromopyridine (695 mg, 4.40 mmol, 1.1 eq), *n*-BuLi (1.76 mL, 4.40 mmol, 2.5 M in *n*-hexane 1.1 eq), $ZnCl_2$ (654 mg,

4.80 mmol, 1.2 eq) and $Pd(PPh_3)_4$ (139 mg, 120 µmol, 3 mol%) in dry THF (50 mL) were reacted according to General Procedure 2.

The crude product was purified by flash chromatography (pentane/Et_2O 100:5 → 100:7.5 → 10:1 → 8:1 → 6:1) yielding compound 2-(pyridin-2-yl)-5-methylthiophene (422 mg, 2.41 mmol, 60%) as a light yellow solid.

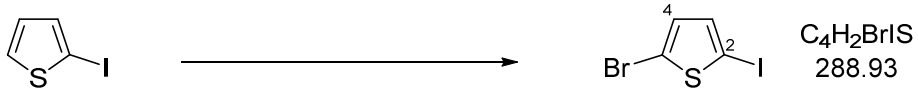
TLC: R_f = 0.45 (pentane/Et_2O 9:1) [UV].

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.52 (s, 3H, CH_3), 6.76 (d, ^3J = 3.5 Hz, 1H, H-4), 7.09 (dd, ^3J = 7.1, 4.9 Hz, 1H, H-5'), 7.38 (d, ^3J = 3.5 Hz, 1H, H-3), 7.57 (d, ^3J = 8.0 Hz, 1H, H-3'), 7.64 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.7 Hz, 1H, H-4'), 8.53 (dd, ^3J = 4.9 Hz, ^4J = 1.7 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.7 (q, CH_3), 118.5 (d, C-3'), 121.5 (d, C-5'), 124.8 (d, C-3), 126.5 (d, C-4), 136.6 (d, C-4'), 142.5 (s, C-2), 142.6 (s, C-5), 149.6 (d, C-6'), 153.0 (s, C-2').

The analytical data obtained matched those reported in the literature.[2]

2-Iodo-5-bromothiophene



C_4H_2BrIS
288.93

2-Iodothiophene (3.15 g, 15.0 mmol, 1 eq) was added to a suspension of *N*-bromosuccinimide (2.67 g, 15.0 mmol, 1 eq) in *n*-hexane. After adding 2 drops of perchloric acid (70% w/w in H_2O) the suspension was vigorously stirred for 17 h. The mixture was neutralised with K_2CO_3 (ca. 20 mg) and filtered to give a clear red solution.

The solvent was removed *in vacuo* and the product was distilled under reduced pressure. The resulting red distillate was diluted with CH_2Cl_2 (60 mL) and washed with sat.-$Na_2S_2O_3$ solution (1 × 10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), the combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to yield 2-iodo-5-bromothiophene (4.00 g, 13.8 mmol, 92%) as a colorless liquid.

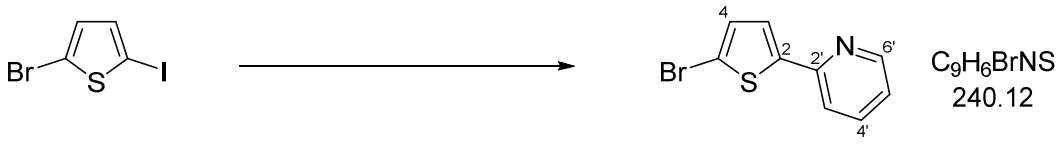
Bp: 70 °C (0.75 Torr).

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 6.75 (d, ^3J = 3.8 Hz, 1H, H-4), 7.04 (d, ^3J = 3.8 Hz, 1H, H-3).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 72.3 (s, C-2), 115.2 (s, C-5), 131.7 (d, C-4), 137.5 (d, C-3).

The analytical data obtained matched those reported in the literature.[3]

2-(pyridin-2-yl)-5-bromothiophene



2-Iodo-5-bromothiophene (3.00 g, 10.4 mmol, 1.0 eq), 2-bromopyridine (1.80 g, 11.4 mmol, 1.1 eq), *n*-BuLi (4.72 mL, 11.4 mmol, 2.4 M in *n*-hexane, 1.1 eq), $ZnCl_2$ (1.56 g, 11.4 mmol, 1.0 eq) and $Pd(PPh_3)_4$ (550 mg, 476 µmol, 5 mol%) in dry THF (67 mL) were reacted according to General Procedure 2.

The crude product was purified by flash chromatography (pentane/Et_2O 99:1 → 9:1) yielding 2-(pyridin-2-yl)-5-bromothiophene (1.94 mg, 8.08 mmol, 78%) as a light yellow solid.

TLC: R_f = 0.42 (pentane/Et_2O 9:1) [UV].

Mp: 87-88 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3079 (w, sp^2-CH), 3049 (w, sp^2-CH), 1584 (m, Py), 1466 (s, Py), 1424 (s, Py), 766 (s, Thp or C-Br).

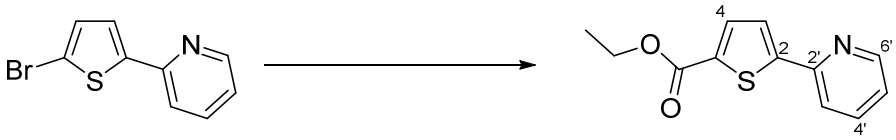
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.06 (d, ^3J = 3.9 Hz, 1H, H-4), 7.15 (ddd, ^3J = 7.5, 4.9 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.30 (d, ^3J = 3.9 Hz, 1H, H-3), 7.57 (*virt.* dt, ^3J = 8.0 Hz, $^4J = {}^5J \approx$ 1.1 Hz, 1H, H-3'), 7.68 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.53 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 115.2 (s, C-5), 118.3 (d, C-3'), 122.3 (d, C-5'), 124.5 (d, C-3), 131.0 (d, C-4), 136.9 (d, C-4'), 146.5 (s, C-2), 149.8 (d, C-6'), 151.9 (s, C-2').

MS (EI): *m/z* (%) = 239/241 (50) $[M]^+$, 160 (100) $[M\text{-}Br]^+$.

HRMS (EI): $C_9H_6N^{79}BrS$ calcd. $[M]^+$: 238.9399 found: 238.9395.
$C_9H_6N^{81}BrS$ calcd. $[M]^+$: 240.9378 found: 240.9378.

Ethyl 2-(pyridin-2-yl)-5-thiophene carboxylate



$C_{12}H_{11}NO_2S$
233.29

2-(Pyridin-2-yl)-5-bromothiophene (300 mg, 1.25 mmol, 1.0 eq) in dry THF (10 mL) was treated with *n*-BuLi (0.62 mL, 1.5 mmol, 2.4 M in *n*-hexane, 1.2 eq) at -78 °C. The corresponding yellow solution was stirred for 1 h at -78 °C, ethyl chloroformate (0.15 mL, 1.9 mmol, 1.5 eq) was added and the solution was stirred for 1.5 h. Next sat.-NH_4Cl solution (5 mL) was added and the solution was warmed up to room temperature and diluted with CH_2Cl_2 (40 mL) and water (10 mL). The aqueous phase was further extracted with CH_2Cl_2 (2 × 30 mL), the combined organic phases were dried over Na_2SO_4, filtered and the solvent was evaporated.

The crude product was purified via flash chromatography (pentane/Et_2O 4:1) yielding ethyl 2-(pyridin-2-yl)-5-thiophene carboxylate (277 mg, 1.19 mmol, 95%) as a white solid.

TLC: R_f = 0.20 (pentane/Et_2O 4:1) [UV].

Mp: 69-70 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3062 (w, sp^2-CH), 2974 (w, sp^3-CH), 2925 (w, sp^3-CH), 1685 (s, COOR), 1434 (s, Py), 1278 (s, COOR), 1110 (s, COOR), 782 (s, Thp).

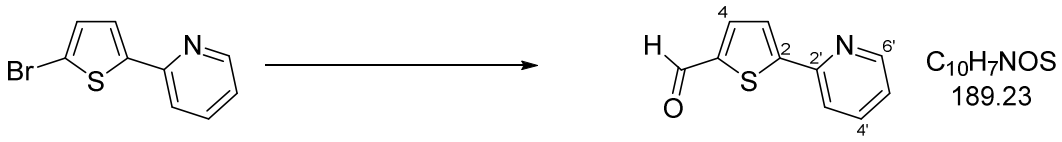
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.38 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 4.36 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 7.21 (ddd, ^3J = 7.2, 4.8 Hz, ^4J = 1.3 Hz, 1H, H-5'), 7.54 (d, ^3J = 4.0 Hz, 1H, H-3), 7.68 (*virt.* dt, ^3J = 8.0 Hz, $^4J = {}^5J \approx$ 1.3 Hz, H-3'), 7.72 (ddd, ^3J = 8.0, 7.2 Hz, ^4J = 1.7 Hz, 1H, H-4'), 7.78 (d, ^3J = 4.0 Hz, 1H, H-4), 8.59 (dd, ^3J = 4.8 Hz, ^4J = 1.7 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.5 (q, CH_2CH_3), 61.4 (t, CH_2CH_3), 119.4 (d, C-3'), 123.2 (d, C-5'), 124.6 (d, C-3), 134.1 (d, C-4), 134.9 (s, C-5), 137.0 (d, C-4'), 150.0 (d, C-6'), 151.1 (s, C-2), 151.8 (s, C-2'), 162.4 (s, COOEt).

MS (EI): *m/z* (%) = 233 (80) $[M]^+$, 205 (30) $[M-C_2H_4]$, 188 (100) $[M-OEt]^+$, 160 (30) $[M-COOEt]^+$.

HRMS (EI) $C_{12}H_{11}NO_2S$: calcd. $[M]^+$: 233.0505 found: 233.0503.

2-(Pyridin-2-yl)-5-thiophene carbaldehyde



$C_{10}H_7NOS$
189.23

2-(Pyridin-2-yl)-5-bromothiophene (400 mg, 1.67 mmol, 1.0 eq) in dry THF (15 mL) was treated with *n*-BuLi (0.67 mL, 1.7 mmol, 2.5 M in *n*-hexane, 1 eq) at -78 °C. The corresponding yellow solution was stirred for 30 min at -78 °C, DMF (0.24 mL, 3.3 mmol, 2 eq) was added and the solution was stirred for 3 h. Next sat.-NH_4Cl solution (3 mL) was added and the solution was warmed up to room temperature and diluted with CH_2Cl_2 (60 mL) and water (10 mL). The water phase was further extracted with CH_2Cl_2 (2 × 60 mL), the combined organic phases were dried over Na_2SO_4, filtered and the solvent was evaporated.

The crude product was purified via flash chromatography (pentane/Et_2O 4:1 → 2:1) yielding 2-(pyridin-2-yl)-5-thiophene carbaldehyde (291 mg, 1.54 mmol, 92%) as a white solid.

TLC: R_f = 0.11 (pentane/Et_2O 4:1) [UV].

Mp: 122-123 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3065 (w, sp^2-C-H), 2927 (w, CHO), 2857 (w, CHO), 1584 (m, CHO), 1482 (s, Py), 1430 (s, Py), 772 (s, Thp).

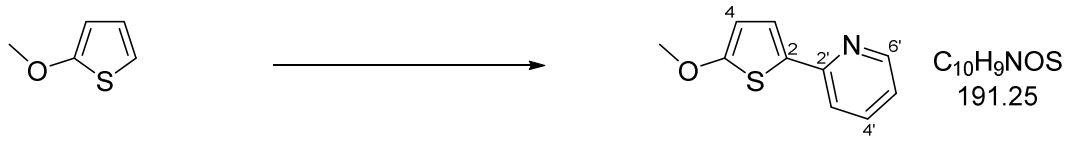
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.27-7.29 (m, 1H, H-5'), 7.68 (d, ^3J = 3.9 Hz, 1H, H-3), 7.71-7.76 (m, 2H, H-4', H-3'), 7.77 (d, ^3J = 3.9 Hz, 1H, H-4), 8.64 (*virt.* dt, ^3J = 4.8 Hz, $^4J = {}^5J \approx$ 1.2 Hz, 1H, H-6'), 9.93 (s, 1H, CHO).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 119.9 (d, C-3'), 123.7 (d, C-5'), 125.2 (d, C-3), 136.8 (d, C-4), 137.1 (d, C-4'), 144.4 (s, C-5), 150.1 (d, C-6'), 151.3 (s, C-2'), 154.0 (s, C-2), 183.2 (d, CHO).

MS (EI): *m/z* (%) = 189 (100) $[M]^+$, 160 (38) $[M\text{-}CHO]^+$.

HRMS (ESI) $C_{10}H_7NOS$: calcd. $[M+H]^+$: 190.0321 found: 190.0319.

2-(Pyridin-2-yl)-5-methoxythiophene



$C_{10}H_9NOS$
191.25

A solution of $MgBr_2 \bullet OEt_2$ (298 mg, 1.16 mmol, 0.33 eq) in dry THF (3 mL) was treated with *n*-BuLi (1.45 mL, 3.50 mmol, 2.4 M in *n*-hexane, 1.0 eq) at -10 °C and stirred for 1 h. Next 2-methoxythiophene (400 mg, 3.50 mmol, 1.0 eq) was added and the corresponding orange solution was stirred at room temperature for 2 h. This solution was added dropwise to a solution of 2-bromopyridine (664 mg, 4.20 mmol, 1.1 eq) and $Pd(dppf)Cl_2$ (76.9 mg, 105 µmol, 3 mol%) in dry THF (5 mL). The solution was refluxed for 19 h, before sat.-NH_4Cl solution (5 mL), water (15 mL) and CH_2Cl_2 (60 mL) were added. The aqueous layer was further extracted with CH_2Cl_2 (2 × 50 mL), the combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated.

The crude product was purified by flash chromatography (pentane/Et_2O 99:1 → 9:1 → 4:1) yielding 2-(pyridin-2-yl)-5-methoxythiophene (522 mg, 2.73 mmol, 78%) as a yellow oil.

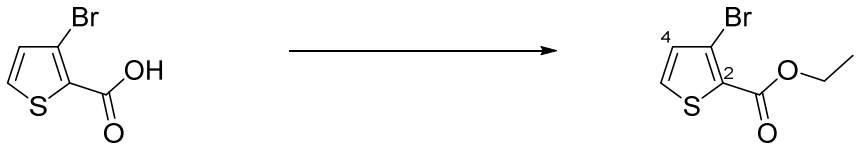
TLC: R_f = 0.36 (pentane/Et_2O 4:1) [UV].

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 3.93 (s, 3H, OCH_3), 6.21 (d, ^3J = 4.1 Hz, 1H, H-4), 7.04 (ddd, ^3J = 7.4, 4.9 Hz, ^4J = 1.0 Hz, 1H, H-5'), 7.23 (d, ^3J = 4.1 Hz, 1H, H-3), 7.52 (*virt.* dt, ^3J = 8.0 Hz, $^4J \approx {}^5J$ = 1.0 Hz, 1H, H-3'), 7.60 (ddd, ^3J = 8.0, 7.4 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.47 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 60.3 (q, OCH_3), 105.2 (d, C-4), 117.5 (d, C-3'), 121.0 (d, C-5'), 122.9 (d, C-3), 130.8 (s, C-2), 136.4 (d, C-4'), 149.4 (d, C-6'), 153.0 (s, C-2'), 168.7 (s, C-5).

The analytical data obtained matched those reported in the literature.[4]

Ethyl 3-bromo-2-thiophene carboxylate



$C_7H_7BrO_2S$
235.10

3-Bromo-2-thiophene carboxylic acid (1.86 g, 9.00 mmol), oxalyl chloride (0.81 mL, 9.5 mmol), DMF (0.05 mL), ethanol (2.40 mL) and triethylamine (2.55 mL) in CH_2Cl_2 (45 mL) were reacted according to General Procedure 1.

The crude product was purified by flash chromatography (pentane/Et_2O 99:1 → 95:5) to yield ethyl 3-bromo-2-thiophene carboxylate (1.90 g, 8.08 mmol, 90%) as a colorless liquid.

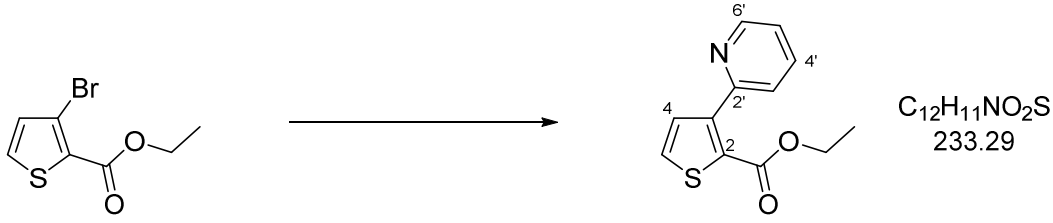
TLC: R_f = 0.68 (pentane/Et_2O 9:1) [UV].

^{1}H-NMR (360 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.38 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 4.37 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 7.09 (d, ^3J = 5.2 Hz, H-4), 7.45 (d, ^3J = 5.2 Hz, 1H, H-5).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.4 (q, CH_2CH_3), 61.6 (t, CH_2CH_3), 117.0 (s, C-3), 128.0 (s, C-2), 131.2 (d, C-4), 133.1 (d, C-5), 160.9 (s, COOEt).

The analytical data obtained matched those reported in the literature.[5]

Ethyl 3-(pyridin-2-yl)thiophen-2-carboxylate



$C_{12}H_{11}NO_2S$
233.29

Ethyl 3-bromo-2-thiophene carboxylate (940 mg, 4.00 mmol), 2-bromopyridine (695 mg, 4.40 mmol, 1.1 eq), *n*-BuLi (1.76 mL, 4.40 mmol, 2.5 M in hexane, 1.1 eq), $ZnCl_2$ (654 mg, 4.80 mmol, 1.2 eq) and $Pd(PPh_3)_4$ (231 mg, 200 µmol, 5 mol%) in dry THF (37 mL) were reacted according to General Procedure 2.

The crude product was purified by flash chromatography (pentane/Et_2O 4:1 → 3:1 → 2:1 → 3:2) yielding ethyl 3-(pyridin-2-yl)-2-thiophene carboxylate (468 mg, 2.01 mmol, 50%) as colorless oil.

TLC: R_f = 0.20 (pentane/Et_2O 2:1) [UV].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3055 (w, sp^2-C-H), 2981 (w, sp^3-C-H), 2935 (w, sp^3-C-H), 1710 (s, COOR), 1589 (m, Py), 1413 (m, Py), 1280 (s, COOR), 1069 (s, COOR), 765 (s, Thp).

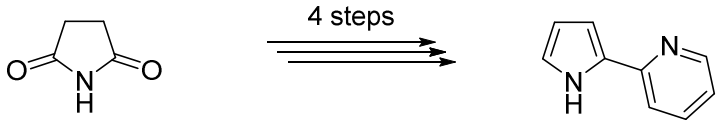
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.25 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 4.25 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 7.27 (ddd, ^3J = 7.5, 4.9 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.33 (d, ^3J = 5.1 Hz, 1H, H-4), 7.52 (d, ^3J = 5.1 Hz, 1H, H-5), 7.64 (*virt.* dt, ^3J = 7.9 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.72 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.66 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.2 (q, CH_2CH_3), 61.3 (t, CH_2CH_3), 122.7 (d, C-5'), 125.2 (d, C-3'), 129.4 (s, C-2), 130.3 (d, C-5), 131.4 (d, C-4), 135.7 (d, C-4'), 147.3 (s, C-3), 149.2 (d, C-6'), 154.2 (s, C-2'), 162.1 (s, COOEt).

MS (EI): *m/z* (%) = 233 (50) $[M]^+$, 204 (40) $[M\text{-}Et]^+$, 188 (100) $[M\text{-}OEt]^+$, 161 (80) $[M\text{-}COOEt]^+$.

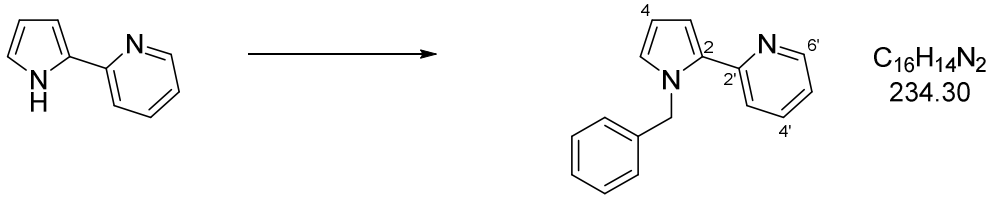
HRMS (ESI) $C_{12}H_{11}NO_2S$: calcd. $[M+H]^+$: 234.0583; found: 234.0582.

2-(Pyrrol-2-yl)pyridine



2-(Pyridin-2-yl)pyrrole was synthesised in 4 steps starting from succinimide following the literature procedure reported by *Savoia* and coworkers.[6]

2-(*N*-Benzylpyrrol-2-yl)pyridine (9)



A solution of 2-(pyridin-2-yl)pyrrole (250 mg, 1.73 mmol, 1 eq) in DMF (0.3 mL) was added dropwise to a suspension of NaH (76.3 mg, 1.91 mmol, 60% w/w in mineral oil, 1.1 eq,) in DMF (1.4 mL) at 0 °C. After stirring for 30 min benzyl bromide (0.21 mL, 1.7 mmol) was added dropwise at 0 °C and the solution was keep at this temperature for 1 h, warmed up to room temperature and further stirred for 48 h. The reaction was stopped by adding H_2O (1 mL). The mixture was diluted with CH_2Cl_2 (60 mL) and H_2O (20 mL). The layers were separated and the aqueous layer was further extracted by CH_2Cl_2 (2 × 60 mL). The

combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*.

The crude product was purified by flash chromatography (pentane/Et_2O 30:1 → 4:1) yielding the benzyl protected pyrrole **10** (276 mg, 1.18 mmol, 68%) as a yellow oil.

TLC: R_f = 0.37 (pentane/Et_2O 9:1) [UV].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3029 (w, sp^2-C-H), 2924 (w, sp^3-C-H), 1586 (s, Py), 1452 (s, Py), 771 (s, Pyrr).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 5.77 (s, 2H, NCH_2Ph), 6.25 (dd, ^3J = 3.7, 2.7 Hz, 1H, H-4), 6.64 (dd, ^3J = 3.7, ^4J = 1.7 Hz, 1H, H-5), 6.81 (*virt.* t, $^3J \approx {}^4J$ = 2.7 Hz, 1H, H-3), 7.00-7.08 (m, 3H, H-5', *o*Ph-H*), 7.14-7.22 (m, 1H, *p*Ph-H), 7.19-7.27 (m, 2H, *m*Ph-H*), 7.50 (*virt.* dt, ^3J = 8.1 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.60 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.9 Hz, 1H, H-4'), 8.51 (dd, ^3J = 4.9 Hz, ^4J = 1.9 Hz, 1H, H-6').

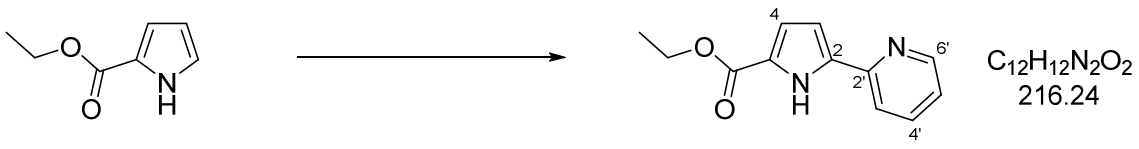
^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 52.0 (t, NCH_2Ph), 108.6 (d, C-4), 111.5 (d, C-5), 120.5 (d, C-5'), 121.7 (d, C-3'), 126.1 (d, C-3), 127.0 (d, *o*PhC*), 127.1 (d, *p*PhC*), 128.5 (d, *m*PhC*), 132.0 (s, C-2), 136.6 (d, C-4'), 139.5 (s, NCH_2C), 148.5 (d, C-6'), 152.5 (s, C-2').

* Signals are interconvertible.

MS (EI): *m/z* (%) = 234 (100) $[M]^+$, 157 (100) $[M\text{-}C_6H_5]^+$, 91 (34) $[C_7H_7]^+$.

HRMS (ESI) $C_{16}H_{14}N_2$: calcd. $[M+H]^+$: 235.1230; found: 235.1223.

Ethyl 2-(pyridin-2-yl)-5-pyrrole carboxylate



$C_{12}H_{12}N_2O_2$
216.24

Following a procedure reported by *Sames* and coworkers[7] ethyl 2-pyrrole carboxylate (125 mg, 900 µmol, 1.0 eq) and Cs_2CO_3 (484 mg, 2.52 mmol, 2.8 eq) in a Schlenk-pressure-tube under Ar atmosphere were treated with 2-bromopyridine (284 mg, 1.80 mmol, 2.0 eq), $Pd(OAc)_2$ (10.1 mg, 45.0 µmol, 5 mol%) and DMA (0.18 mL). The cap was closed and the suspension was heated to 125 °C for six days. The cooled suspension was diluted with CH_2Cl_2 (60 mL) and water (20 mL). The layers were separated and the aqueous layer was

extracted with CH_2Cl_2 (2 × 40 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was evaporated to give a brownish solid.

The crude product was purified by flash chromatography (pentane/Et_2O 100:5 → 100:7.5 → 9:1 → 17:3 → 4:1) to yield ethyl 2-(pyridin-2-yl)-5-pyrrole carboxylate (45.0 mg, 208 µmol, 23%) as light yellow oil with minor impurities, but pure enough for further reactions.

TLC: R_f = 0.16 (pentane/Et_2O 4:1) [UV].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3447 (w, N-H), 2980 (w, sp^3-C-H), 1698 (s, COOR), 1593 (m, Py), 1429 (m, Py), 1264 (s, COOR), 1146 (s, COOR), 777 (m, Pyrr).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.37 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 4.35 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 6.69 (dd, ^3J = 3.9, 2.4 Hz, 1H, H-3*), 6.97 (dd, ^3J = 3.9, 2.4 Hz, 1H, H-4*), 7.13 (ddd, ^3J = 7.4, 4.9 Hz, ^4J = 1.2 Hz, 1H, H-5'), 7.59 (*virt.* dt, ^3J = 8.0 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.67 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.7 Hz, 1H, H-4'), 8.54 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 1H, H-6'), 10.2 (br s, 1H, N-H).

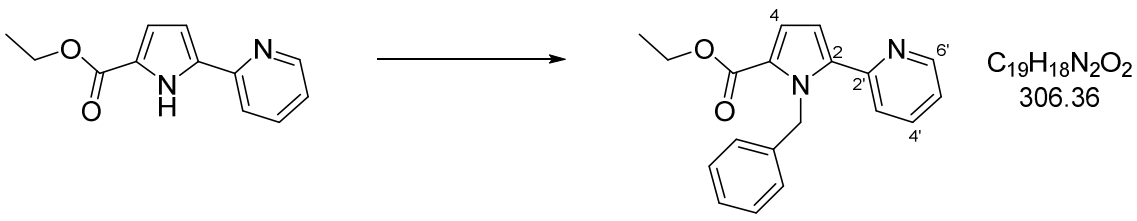
^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.6 (q, CH_2CH_3), 60.6 (t, CH_2CH_3), 108.4 (d, C-3*), 116.8 (d, C-4*), 119.3 (d, C-3'), 122.1 (d, C-5'), 124.2 (s, C-5), 135.5 (s, C-2), 136.8 (d, C-4'), 149.4 (s, C-2'), 149.5 (d, C-5'), 161.0 (s, COOEt).

* Signals are interconvertible.

MS (EI): *m/z* (%) = 216 (100) $[M]^+$, 170 (67) $[M\text{-}EtOH]^+$, 144 (43) $[M\text{-}COOEt]^+$.

HRMS (ESI) $C_{12}H_{12}N_2O_2$: calcd. $[M+H]^+$: 217.0977; found: 217.0970.

Ethyl *N*-benzyl-2-(pyridin-2-yl)-5-pyrrole carboxylate



Ethyl 2-(pyridin-2-yl)-5-pyrrole carboxylate (120 mg, 555 µmol, 1.0 eq) in DMF (2 mL) was added dropwise to a solution of NaH (26.6 mg, 666 µmol, 60% w/w in mineral oil, 1.2 eq) in DMF (2 mL) under Ar atmosphere. After 30 min benzyl bromide (104 mg, 610 µmol, 1.1 eq) was added and the solution was stirred for 16 h at room temperature. The solution was diluted with CH_2Cl_2 (60 mL) and water (20 mL). The layers were separated and the aqueous

layer was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic layers were dried with brine (30 mL) and over Na_2SO_4, filtered and the solvent was removed *in vacuo*. The crude product was coevaporated with toluene (2 × 20 mL).

Purification by flash chromatography (pentane/Et_2O 9:1 → 17:3 → 4:1 → 2:1) yielded pyrrole **11** (151 mg, 492 µmol, 89%) as a light yellow oil.

TLC: R_f = 0.40 (pentane/Et_2O 4:1) [UV].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2979 (w, sp^3-C-H), 1699 (s, COOR), 1586 (m, Py), 1425 (s, Ar), 1263 (s, COOR), 1097 (s, COOR), 754 (s, Pyrr).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.32 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 4.26 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 6.26 (s, 2H, NCH_2Ph), 6.57 (d, ^3J = 4.1 Hz, 1H, H-3*), 6.87-6.93 (m, 2H, *m*Ph-H), 7.10-7.16 (m, 2H, H-5', H-4*), 7.19 (m, 3H, *o*Ph-H, *p*Ph-H), 7.50 (*virt.* dt, ^3J = 8.0 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.68 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.62 (ddd, ^3J = 4.9 Hz, ^3J = 1.8 Hz, ^5J = 0.9 Hz, 1H, H-6').

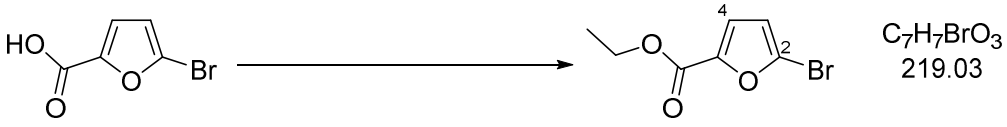
^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.5 (q, CH_2CH_3), 49.1 (t, NCH_2Ph), 60.1 (t, CH_2CH_3), 111.3 (d, C-3*), 118.5 (d, C-4*), 122.1 (d, C-5'), 123.7 (d, C-3'), 125.2 (s, C-5), 126.3 (d, *m*PhC), 126.7 (d, *p*PhC), 128.3 (d, *o*PhC), 136.7 (d, C-4'), 139.2 (s, C-2), 139.9 (s, NCH_2C), 149.2 (d, C-6'), 151.9 (s, C-2'), 161.2 (s, COOEt).

* Signals are interconvertible.

MS (EI): *m/z* (%) = 306 (30) $[M]^+$, 233 (100) $[M\text{-}COOEt]^+$, 91 (39) $[C_7H_7]^+$.

HRMS (ESI) $C_{12}H_{12}N_2O_2$: calcd. $[M+H]^+$: 307.1447; found: 307.1438.

Ethyl 5-bromo-2-furan carboxylate



$C_7H_7BrO_3$
219.03

5-Bromo-2-furan carboxylic acid (5.00 g, 26.2 mmol, 1 eq), oxalyl chloride (2.36 mL, 27.5 mmol, 1.05 eq), DMF (0.1 mL), dry ethanol (6.7 mL) and triethylamine (7.3 mL) in CH_2Cl_2 (100 mL) were reacted according to General Procedure 1.

The crude product was purified using flash chromatography (pentane/EtOAc 19:1) to yield ethyl 5-bromo-2-furan carboxylate (4.82 g, 22.0 mmol, 84%) as a yellow liquid.

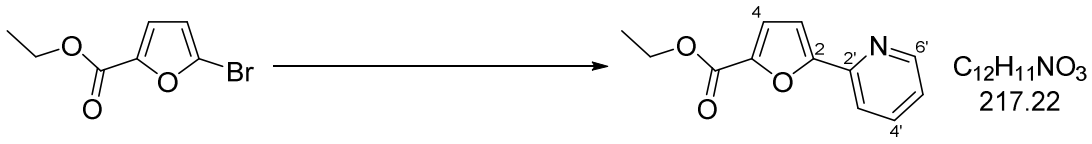
TLC: R_f = 0.82 (pentane/EtOAc 19:1) [UV].

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.37 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 4.36 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 6.44 (d, ^3J = 3.5 Hz, 1H, H-3), 7.11 (d, ^3J = 3.5 Hz, 1H, H-4).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.4 (q, CH_2CH_3), 61.4 (t, CH_2CH_3), 114.0 (d, C-3), 120.1 (d, C-4), 127.5 (s, C-2), 146.7 (s, C-5), 157.9 (s, COOEt).

The analytical data obtained matched those reported in the literature.[8]

Ethyl 2-(pyridine-2-yl)-5-furan carboxylate



$C_{12}H_{11}NO_3$
217.22

Ethyl 5-bromo-2-furan carboxylate (1.75 g, 8.00 mmol, 1 eq), 2-bromopyridin (1.58 g, 10.0 mmol, 1.25 eq), $ZnCl_2$ (1.42 g, 10.4 mmol, 1.3 eq), *n*-BuLi (4.08 mL, 10.0 mmol, 2.45 M in *n*-hexane, 1.25 eq) and $Pd(PPh_3)_4$ (92.5 mg, 80.0 µmol, 1 mol%) in THF (45 mL) were reacted according to General Procedure 2.

The crude product was purified using flash chromatography (pentane/Et_2O 4:1 → 2:1 → 0:1), yielding furan **14** (1.64 g, 7.55 mmol, 94%) as a yellow oil.

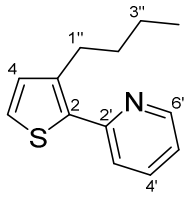
TLC: R_f = 0.55 (pentane/EtOAc 2:1) [UV].

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.40 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 4.39 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 7.15 (d, ^3J = 3.6 Hz, 1H, H-3), 7.23 (ddd, ^3J = 7.6, 4.8 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.27 (d, ^3J = 3.6 Hz, 1H, H-4), 7.76 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 7.90 (d, ^3J = 8.1 Hz, 1H, H-3'), 8.62 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.5 (q, CH_2CH_3), 61.2 (t, CH_2CH_3), 110.1 (d, C-3), 119.8 (d, C-3'), 119.9 (d, C-4), 123.3 (d, C-5'), 136.9 (d, C-4'), 144.9 (s, C-2), 148.4 (s, C-2'), 149.9 (d, C-6'), 156.8 (s, C-5), 158.8 (s, COOEt).

The analytical data obtained matched those reported in the literature.[9]

C-H activation products:



$C_{13}H_{15}NS$
217.33 g/mol

2-(Pyridin-2-yl)thiophene (**1**) (129 mg, 800 µmol), *n*-butylboronic acid (245 mg, 2.40 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2)** (54.5 mg, 400 µmol, 0.5 eq), Ag_2CO_3 (441 mg, 1.60 mmol, 2.0 eq) and $Pd(OAc)_2$ (18.0 mg, 80.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:3 → 100:4 → 9:1 → 4:1) yielding compound **3a** (123 mg, 568 µmol, 71%) as a colorless oil.

TLC: R_f = 0.49 (pentane/Et_2O 9:1) [UV].

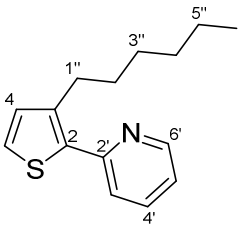
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3052 (w, sp^2-C-H), 2926 (w, sp^3-C-H), 2858 (w, sp^3-C-H), 1582 (s, Py), 1465 (s, Py), 1435 (m, Py), 780 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.92 (t, ^3J = 7.4 Hz, 3H, H-4''), 1.39 (*virt.* sextet, $^3J \approx$ 7.4 Hz, 2H, H-3''), 1.61-1.70 (m, 2H, H-2''), 2.90 (t, ^3J = 7.8 Hz, 2H, H-1''), 6.98 (d, ^3J = 5.1 Hz, 1H, H-4), 7.15 (ddd, ^3J = 7.3, 4.9 Hz, ^4J = 1.0 Hz, 1H, H-5'), 7.29 (d, ^3J = 5.1 Hz, 1H, H-5), 7.52 (*virt.* dt, ^3J = 8.0 Hz, $^4J \approx {}^5J$ = 1.0 Hz, 1H, H-3'), 7.70 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.63 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 22.8 (t, C-3''), 29.4 (t, C-2''), 32.8 (t, C-1''), 121.5 (d, C-3'), 121.9 (d, C-5'), 125.8 (d, C-5), 130.7 (d, C-4), 136.5 (d, C-4'), 137.9 (s, C-2), 140.9 (s, C-3), 149.7 (d, C-6'), 153.7 (s, C-2').

MS (EI): *m/z* (%) = 217 (30) $[M]^+$, 188 (100) $[M\text{-}Et]^+$.

HRMS (EI) $C_{13}H_{15}NS$: calcd. $[M]^+$: 217.0920 found: 217.0921.



$C_{15}H_{19}NS$
245.38 g/mol

2-(Pyridin-2-yl)thiophene (**1**) (64.5 mg, 400 µmol), *n*-hexylboronic acid (156 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:0.5 → 100:1 → 100:1.5 → 100:2 → 100:3 → 100:5) yielding compound **3b** (54.7 mg, 223 µmol, 56%) as a colorless oil.

TLC: R_f = 0.59 (pentane/Et_2O 9:1) [UV].

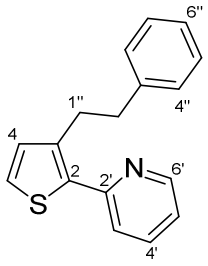
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3055 (w, sp^2-C-H), 2953 (s, sp^3-C-H), 2925 (s, sp^3-C-H), 2854 (s, sp^3-C-H), 1583 (s, Py), 1466 (s, Py), 1435 (m, Py), 780 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.87 (t, ^3J = 6.9 Hz, 3H, H-6''), 1.24-1.33 (m, 4H, H-4'', H-5''), 1.33-1.43 (m, 2H, H-3''), 1.62-1.71 (m, 2H, H-2''), 2.84-2.94 (m, 2H, H-1''), 6.98 (d, ^3J = 6.9 Hz, 1H, H-4), 7.15 (ddd, ^3J = 7.5, 4.9 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.29 (d, ^3J = 5.1 Hz, 1H, H-5), 7.51 (dd, ^3J = 8.0 Hz, ^4J = 1.1 Hz, 1H, H-3'), 7.70 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.9 Hz, 1H, H-4'), 8.63 (dd, ^3J = 4.9 Hz, ^4J = 1.9 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.2 (q, C-6''), 22.7 (t, C-5''), 29.4 (t, C-3''), 29.7 (t, C-1''), 30.6 (t, C-2''), 31.8 (t, C-4''), 121.5 (d, C-3'), 121.9 (d, C-5'), 125.8 (d, C-5), 130.7 (d, C-4), 136.5 (d, C-4'), 137.9 (s, C-2), 141.0 (s, C-3), 150.0 (d, C-6'), 153.8 (s, C-2').

MS (EI): *m/z* (%) = 245 (30) $[M]^+$, 202 (15) $[M\text{-}C_3H_7]^+$, 188 (100) $[M\text{-}C_4H_9]^+$, 173 (40) $[M\text{-}C_5H_{11}]^+$.

HRMS (ESI) $C_{15}H_{19}NS$: calcd. $[M+H]^+$: 246.1311 found: 246.1310.



$C_{17}H_{15}NS$
265.37 g/mol

2-(Pyridin-2-yl)thiophene (**1**) (64.5 mg, 400 µmol), phenethylboronic acid (180 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:0.5 → 100:1 → 100:2 → 100:4 → 100:6 → 100:8) yielding compound **3c** (51.1 mg, 193 µmol, 48%) as a colorless oil.

TLC: R_f = 0.33 (pentane/Et_2O 9:1) [UV].

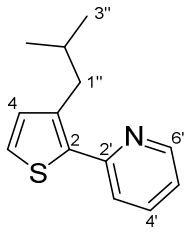
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3024 (w, sp^2-C-H), 2923 (w, sp^3-C-H), 1582 (m, Py), 1468 (m, Ar), 1435 (w, Py), 780 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.96-3.01 (m, 2H, H-2''), 3.22-3.27 (m, 2H, H-1''), 6.98 (d, ^3J = 5.1 Hz, 1H, H-4), 7.16 (ddd, ^3J = 7.6, 4.9 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.16-7.23 (m, 3H, 3xPh-H), 7.26-7.31 (m, 3H, H-5, 2xPh-H), 7.43 (*virt.* dt, ^3J = 8.1 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.67 (*virt.* td, $^3J \approx$ 7.6 Hz, ^4J = 1.9 Hz, 1H, H-4'), 8.65 (ddd, ^3J = 4.9 Hz, ^4J = 1.9 Hz, ^5J = 0.9 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 31.7 (t, C-1''), 36.9 (t, C-2''), 121.5 (d, C-5'), 122.0 (d, C-3'), 125.7 (d, C-6'), 126.1 (d, C-5), 128.5 (d, C-5''), 128.6 (d, C-4''), 130.8 (d, C-4), 136.5 (d, C-4'), 138.1 (s, C-2), 140.0 (s, C-3), 141.9 (s, C-3''), 149.7 (d, C-6'), 153.6 (s, C-2').

MS (EI): *m/z* (%) = 265 (50) $[M]^+$, 174 (60) $[M\text{-}C_7H_7]^+$, 161 (100) $[M\text{-}C_8H_8]^+$.

HRMS (EI) $C_{17}H_{15}NS$: calcd. $[M]^+$: 265.0920 found: 265.0908.



$C_{13}H_{15}NS$
217.33 g/mol

2-(Pyridin-2-yl)thiophene (**1**) (64.5 mg, 400 µmol), 2-methylpropylboronic acid (122 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:0.5 → 100:1 → 100:1.5 → 100:2 → 100:2.5) yielding compound **3d** (37.0 mg, 170 µmol, 43%) as a colorless oil.

TLC: R_f = 0.49 (pentane/Et_2O 9:1) [UV].

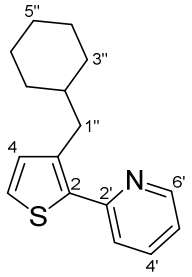
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3055 (w, sp^2-C-H), 2952 (w, sp^3-C-H), 2866 (w, sp^3-C-H), 1582 (m, Py), 1465 (m, Py), 779 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.91 (d, ^3J = 6.7 Hz, 6H, H-3''), 1.96 (*virt.* septet, $^3J \approx$ 6.8 Hz, 1H, H-2''), 2.79 (d, ^3J = 7.2 Hz, 2H, H-1''), 6.94 (d, ^3J = 5.1 Hz, 1H, H-4), 7.14 (dd, ^3J = 7.5, 4.9 Hz, 1H, H-5'), 7.28 (d, ^3J = 5.1 Hz, 1H, H-5), 7.53 (d, ^3J = 8.0 Hz, 1H, H-3'), 7.69 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.60-8.65 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 22.7 (q, C-3''), 29.7 (d, C-2''), 38.6 (t, C-1''), 121.4 (d, C-5'), 122.0 (d, C-3'), 125.5 (d, C-5), 131.4 (d, C-4), 136.4 (d, C-4'), 138.4 (s, C-2), 139.9 (s, C-3), 149.7 (d, C-6'), 153.8 (s, C-2').

MS (EI): *m/z* (%) = 217 (45) $[M]^+$, 202 (100) $[M\text{-}CH_3]^+$.

HRMS (EI) $C_{13}H_{15}NS$: calcd. $[M]^+$: 217.0920 found: 217.0922.



$C_{16}H_{19}NS$
257.39 g/mol

2-(Pyridin-2-yl)thiophene (**1**) (64.5 mg, 400 µmol), cyclohexylmethylboronic acid (170 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:0.5 → 100:1 → 100:2 → 100:4 → 100:5) yielding compound **3e** (44.3 mg, 172 µmol, 43%) as a colorless oil.

TLC: R_f = 0.73 (pentane/Et_2O 9:1) [UV].

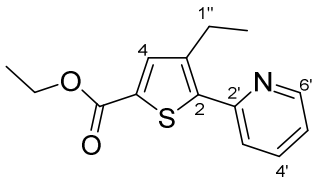
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3056 (w, sp^2-C-H), 2921 (s, sp^3-C-H), 2849 (m, sp^3-C-H), 1583 (s, Py), 1467 (s, Py), 1436 (m, Py), 779 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.88-1.01 (m, 2H, Cy-H), 1.10-1.23 (m, 4H, Cy-H), 1.56-1.76 (m, 5H, Cy-H), 2.79 (d, ^3J = 7.1 Hz, 2H, H-1''), 6.94 (d, ^3J = 5.1 Hz, 1H, H-4), 7.16 (ddd, ^3J = 7.5, 4.8 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.28 (d, ^3J = 5.1 Hz, 1H, H-5), 7.53 (*virt.* dt, ^3J = 7.9 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.70 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.63 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.4 (t, Cy), 26.7 (t, Cy), 33.5 (t, C-3''), 37.2 (d, C-1''), 39.2 (d, C-2''), 121.5 (d, C-5'), 122.1 (d, C-3'), 125.5 (d, C-5), 131.5 (d, C-4), 136.5 (d, C-4'), 138.4 (s, C-2), 139.6 (s, C-3), 149.7 (d, C-6'), 153.8 (s, C-2').

MS (EI): *m/z* (%) = 257 (69) $[M]^+$, 214 (54) $[M\text{-}C_3H_7]^+$, 186 (83) $[M\text{-}C_5H_{11}]^+$, 175 (100) $[M\text{-}C_6H_{12}]^+$.

HRMS (ESI) $C_{16}H_{19}NS$: calcd. $[M+H]^+$: 258.1311 found: 258.1309.



$C_{14}H_{15}NO_2S$
261.34 g/mol

Ethyl 2-(pyridin-2-yl)-5-thiophene carboxylate (93.3 mg, 400 µmol), ethylboronic acid (88.7 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:3 → 100:4 → 20:1 → 100:7.5 → 9:1 → 4:1) yielding compound **5a** (74.7 mg, 286 µmol, 71%) as a colorless solid.

TLC: R_f = 0.33 (pentane/Et_2O 4:1) [UV].

Mp: 55-56 °C.

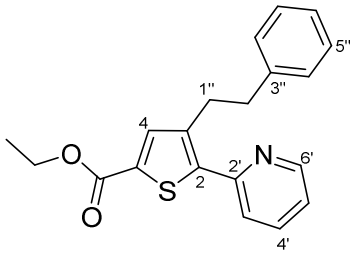
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3062 (w, sp^2-C-H), 2972 (w, sp^3-C-H), 2904 (w, sp^3-C-H), 1678 (s, COOR), 1431 (m, Py), 1285 (s, COOR), 1084 (m, COOR), 791 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.29 (t, ^3J = 7.5 Hz, 3H, H-2''), 1.38 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 2.91 (q, ^3J = 7.5 Hz, 2H, H-1''), 4.35 (q, ^3J = 7.1 Hz, 2H, OCH_2CH_3), 7.22 (ddd, ^3J = 7.6, 4.8 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.56 (dd, ^3J = 8.0 Hz, ^4J = 1.1 Hz, 1H, H-3'), 7.70 (s, 1H, H-4), 7.74 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.65 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.5 (q, OCH_2CH_3), 14.9 (q, C-2''), 23.0 (t, C-1''), 61.3 (t, OCH_2CH_3), 122.3 (d, C-3'), 122.5 (d, C-5'), 132.8 (s, C-5), 135.9 (d, C-4), 136.7 (d, C-4'), 142.6 (s, C-3), 144.3 (s, C-2), 150.0 (d, C-6'), 152.7 (s, C-2'), 162.5 (s, COOEt).

MS (EI): *m/z* (%) = 261 (100) [M]$^+$, 232 (50) [M-Et]$^+$, 188 (20) [M-COOEt]$^+$.

HRMS (EI) $C_{14}H_{15}NO_2S$: calcd. [M]$^+$: 261.0818 found: 261.0808.



$C_{20}H_{19}NO_2S$
337.44

Ethyl 2-(pyridin-2-yl)-5-thiophene carboxylate (93.3 mg, 400 µmol), phenethylboronic acid (180 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:5 → 9:1 → 85:15) yielding compound **5b** (129 mg, 383 µmol, 96%) as a colorless solid.

TLC: R_f = 0.40 (pentane/Et_2O 4:1) [UV].

Mp: 76-77 °C.

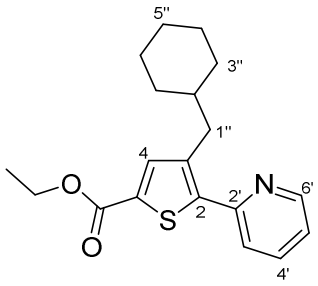
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3065 (w, sp^2-C-H), 3025 (w, sp^2-C-H), 2985 (w, sp^3-C-H), 2953 (w, sp^3-C-H), 2936 (w, sp^3-C-H), 1686 (s, COOR), 1582 (m, Py), 1428 (s, Ar), 1280 (s, COOR), 1078 (s, COOR), 779 (m, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.39 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 2.95-2.99 (m, 2H, H-2''), 3.19-3.23 (m, 2H, H-1''), 4.36 (q, ^3J = 7.1 Hz, 2H, OCH_2CH_3), 7.16-7.21 (m, 3H, H-4'', H-6''), 7.22 (ddd, ^3J = 7.7, 4.9 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.24-7.30 (m, 2H, H-5''), 7.46 (*virt.* dt, ^3J = 8.0 Hz, $^4J \approx {}^5J$ = 1.0 Hz, 1H, H-3'), 7.72-7.68 (m, 2H, H-4, H-4'), 8.66 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.5 (q, OCH_2CH_3), 31.7 (t, C-1''), 36.8 (t, C-2''), 61.3 (t, OCH_2CH_3), 122.4 (d, C-3'), 122.5 (d, C-5'), 126.3 (d, C-6''), 128.5 (d, C-4''), 128.6 (d, C-5''), 132.7 (s, C-5), 136.4 (d, C-4), 136.8 (d, C-4'), 140.5 (s, C-3), 141.5 (s, C-3''), 144.7 (s, C-2), 149.9 (d, C-6'), 152.7 (s, C-2'), 162.5 (s, COOEt).

MS (EI): *m/z* (%) = 337 (34) $[M]^+$, 207 (100) $[C_{15}H_{13}N]^+$.

HRMS (ESI) $C_{16}H_{19}NO_2S$: calcd. $[M+H]^+$: 338.1209; found: 338.1209.



$C_{19}H_{23}NO_2S$
329.46

Ethyl 2-(pyridin-2-yl)-5-thiophene carboxylate (93.3 mg, 400 µmol), cyclohexylmethylboronic acid (170 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:4 → 100:6 → 100:8 → 10:1) yielding compound **5c** (126 mg, 382 µmol, 96%) as a beige solid.

TLC: R_f = 0.41 (pentane/Et_2O 4:1) [UV].

Mp: 79-80 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3059 (w, sp^2-C-H), 2919 (m, sp^3-C-H), 2848 (m, sp^3-C-H), 1698 (s, COOR), 1579 (m, Py), 1427 (s, Py), 1281 (s, COOR), 1080 (s, COOR), 780 (m, Thp).

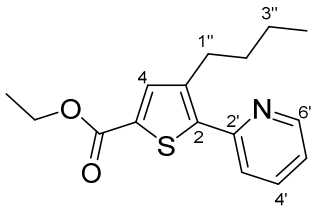
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.88-0.98 (m, 2H, Cy-H), 1.09-1.24 (m, 3H, Cy-H), 1.38 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 1.58-1.73 (m, 6H, Cy-H), 2.78 (d, ^3J = 7.1 Hz, 2H, H-1''), 4.35 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 7.23 (ddd, ^3J = 7.5, 4.8 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.56 (*virt.* dt, ^3J = 7.9 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.62 (s, 1H, H-4), 7.74 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.65 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.5 (q, CH_2CH_3), 26.4 (t, Cy), 26.6 (d, C-2''), 33.4 (t, Cy), 37.2 (t, C-1''), 39.1 (t, Cy), 61.3 (t, CH_2CH_3), 122.4 (d, C-5''*), 122.5 (d, C-3''*), 132.4 (s, C-5), 136.7 (d, C-4'), 137.1 (d, C-4), 140.0 (s, C-3), 145.0 (s, C-2), 149.9 (d, C-6'), 152.9 (s, C-2'), 162.6 (s, COOEt).

* Signals are interconvertible.

MS (EI): *m/z* (%) = 329 (60) [M]$^+$, 247 (100) [M-Cy]$^+$, 173 (31) [M-Cy-COOEt]$^+$.

HRMS (ESI) $C_{19}H_{23}NO_2S$: calcd. [M+H]$^+$: 330.1522 found: 330.1525.



$C_{16}H_{19}NO_2S$
289.39 g/mol

Ethyl 2-(pyridin-2-yl)-5-thiophene carboxylate (140 mg, 600 µmol), *n*-butylboronic acid (183 mg, 1.80 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (40.8 mg, 300 µmol, 0.5 eq), Ag_2CO_3 (331 mg, 1.20 µmol, 2.0 eq) and $Pd(OAc)_2$ (13.5 mg, 60.0 µmol, 10 mol%) in ^{t}AmOH (3.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 20:1 → 9:1 → 4:1) yielding compound **5d** (169 mg, 584 µmol, 97%) as a colorless solid.

TLC: R_f = 0.48 (pentane/Et_2O 4:1) [UV].

Mp: 50-51 °C.

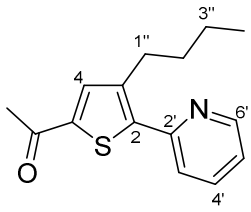
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3060 (w, sp^2-C-H), 2925 (w, sp^3-C-H), 2857 (w, sp^3-C-H), 1700 (s, COOR), 1428 (m, Py), 1378 (m, Thp), 1242 (s, COOR), 1076 (m, COOR), 777 (m, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.92 (t, ^3J = 7.3 Hz, 3H, H-4''), 1.38 (m, 5H, H-3'', OCH_2CH_3), 1.61-1.69 (m, 2H, H-2''), 2.88 (t, ^3J = 7.8 Hz, 2H, OCH_2CH_3), 4.35 (t, ^3J = 7.1 Hz, 2H, H-1''), 7.23 (ddd, ^3J = 7.6, 4.8 Hz, ^4J = 1.0 Hz, 1H, H-5'), 7.56 (*virt.* dt, ^3J = 7.9 Hz, $^4J \approx {}^5J$ = 0.9 Hz, 1H, H-3'), 7.67 (s, 1H, H-4), 7.74 (*virt.* td, $^3J \approx$ 7.7, ^4J = 1.8 Hz, 1H, H-4'), 8.65 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.0 (q, C-4''), 14.5 (q, OCH_2CH_3), 22.7 (t, C-3''), 29.4 (t, C-2''), 32.6 (t, C-1''), 61.3 (t, OCH_2CH_3), 122.3 (d, C-3'), 122.5 (d, C-5'), 132.7 (s, C-5), 136.4 (s, C-4), 136.7 (d, C-4'), 141.3 (s, C-3), 144.5 (s, C-2), 150.0 (d, C-6'), 152.8 (s, C-2'), 162.6 (s, COOEt).

MS (EI): *m/z* (%) = 289 (15) $[M]^+$, 260 (30) $[M\text{-}Et]^+$, 223 (100) $[C_{12}H_{15}O_2S]^+$.

HRMS (EI) $C_{16}H_{19}NO_2S$: calcd. $[M]^+$: 289.1131 found: 289.1129.



$C_{15}H_{17}NOS$
259.37 g/mol

5-Acetyl-2-(pyridin-2-yl)thiophene (81.3 mg, 400 µmol), *n*-butylboronic acid (122 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:5 → 100:7.5 → 9:1 → 7:1 → 4:1) yielding compound **5e** (103 mg, 397 µmol, 99%) as a colorless solid.

TLC: R_f = 0.42 (pentane/Et_2O 4:1) [UV].

Mp: 88-89 °C.

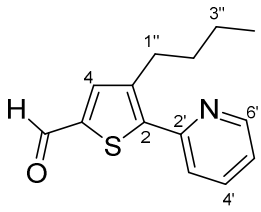
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3068 (w, sp^2-C-H), 2950 (w, sp^3-C-H), 2927 (w, sp^3-C-H), 2868 (w, sp^3-C-H), 1651 (s, C=O), 1578 (m, Py), 1536 (m, Thp) 1421 (s, Py), 788 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.92 (t, ^3J = 7.4 Hz, 3H, H-4''), 1.39 (*virt.* sextet, $^3J \approx$ 7.4 Hz, 2H, H-3''), 1.59-1.70 (m, 2H, H-2''), 2.56 (s, 3H, $COCH_3$), 2.90 (t, ^3J = 7.8 Hz, 2H, H-1''), 7.24 (ddd, ^3J = 7.6, 4.9 Hz, ^4J = 1.0 Hz, 1H, H-5'), 7.57 (dd, ^3J = 8.0 Hz, ^4J = 1.0 Hz, 1H, H-3'), 7.58 (s, 1H, H-4), 7.75 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.66 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.0 (q, C-4''), 22.7 (t, C-3''), 27.1 (q, CO*C*H_3), 29.4 (t, C-1''), 32.7 (t, C-2''), 122.5 (d, C-3'), 122.7 (d, C-5'), 135.4 (d, C-4), 136.8 (d, C-4'), 142.0 (s, C-3), 142.4 (s, C-5), 145.7 (s, C-2), 150.0 (d, C-6'), 152.8 (s, C-2'), 190.8 (s, *C*OCH_3).

MS (EI): *m/z* (%) = 259 (35) $[M]^+$, 230 (100) $[M\text{-}Et]^+$, 173 (15) $[M\text{-}C_3H_7\text{-}Ac]^+$.

HRMS (ESI) $C_{15}H_{17}NOS$: calcd. $[M+H]^+$: 260.1104 found: 260.1102.



$C_{14}H_{15}NOS$
245.34

2-(Pyridin-2-yl)-5-thiophene carbaldehyde (75.7 mg, 400 µmol), *n*-butylboronic acid (122 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:5 → 100:7.5 → 6:1) yielding compound **5f** (70.6 mg, 288 µmol, 72%) as a colorless solid.

TLC: R_f = 0.31 (pentane/Et_2O 4:1) [UV].

Mp: 69-70 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3065 (w, sp^2-C-H), 2951 (w, sp^3-C-H), 2927 (w, sp^3-C-H), 2860 (w, sp^3-C-H), 2801 (w, CHO), 1661 (s, CHO), 1579 (m, Py), 1426 (s, Py), 787 (s, Thp).

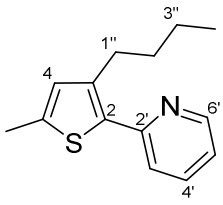
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.93 (t, ^3J = 7.4 Hz, 3H, H-4''), 1.40 (*virt.* sextet, $^3J \approx$ 7.4 Hz, 2H, H-3''), 1.67 (*virt.* pentet, $^3J \approx$ 7.6 Hz, 2H, H-2''), 2.93 (t, ^3J = 7.7 Hz, 2H, H-1''), 7.27 (dd, ^3J = 7.5, 4.9 Hz, 1H, H-5'), 7.59 (d, ^3J = 7.8 Hz, 1H, H-3'), 7.65 (s, 1H, H-4), 7.77 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.68 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, H-6'), 9.89 (s, 1H, CHO).

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 22.7 (t, C-3''), 29.3 (t, C-1''), 32.6 (t, C-2''), 122.7 (d, C-3'), 123.0 (d, C-5'), 136.9 (d, C-4'), 139.2 (d, C-4), 142.0 (s, C-3, C-5*), 147.6 (s, C-2), 150.1 (d, C-6'), 152.4 (s, C-2'*), 183.3 (d, CHO).

* Signals are interconvertible.

MS (EI): *m/z* (%) = 245 (35) $[M]^+$, 216 (100) $[M\text{-}CHO]^+$, 173 (30) $[M\text{-}CHO\text{-}C_3H_7]^+$.

HRMS (ESI) $C_{14}H_{15}NOS$: calcd. $[M+H]^+$: 246.0947; found: 246.0947.



$C_{14}H_{17}NS$
231.36

2-(Pyridin-2-yl)-5-methylthiophene (70.1 mg, 400 µmol), *n*-butylboronic acid (122 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified via flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:3 → 100:4 → 100:5) yielding compound **5g** (91.8 mg, 397 µmol, 99%) as a yellow oil.

TLC: R_f = 0.55 (pentane/Et_2O 9:1) [UV].

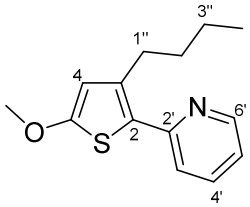
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3048 (w, sp^2-C-H), 2954 (s, sp^3-C-H), 2925 (s, sp^3-C-H), 2857 (m, sp^3-C-H), 1583 (s, Py), 1480 (s, Py), 1432 (m, Py), 779 (m, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.92 (t, ^3J = 7.3 Hz, 3H, H-4''), 1.39 (*virt.* sextet, $^3J \approx$ 7.4 Hz, 2H, H-3''), 1.62 (*virt.* pentet, $^3J \approx$ 7.8 Hz, 2H, H-2''), 2.47 (s, 3H, $ArCH_3$), 2.82 (t, ^3J = 7.8 Hz, 2H, H-1''), 6.65 (s, 1H, H-4), 7.10 (ddd, ^3J = 7.5, 4.9 Hz, ^4J = 1.0 Hz, 1H, H-5'), 7.45 (d, ^3J = 8.0 Hz, 1H, H-3'), 7.66 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.59 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 15.5 (q, Ar*C*H_3), 22.8 (t, C-3''), 29.5 (t, C-1''), 32.8 (t, C-2''), 121.0 (d, C-5'), 121.6 (d, C.3'), 129.4 (d, C-4), 135.2 (s, C-2), 136.6 (d, C-4'), 140.5 (s, C-5), 141.3 (s, C-3), 149.5 (d, C-6'), 153.7 (s, C-2').

MS (EI): *m/z* (%) = 231 (31) $[M]^+$, 202 (100) $[M\text{-}C_2H_5]^+$.

HRMS (ESI) $C_{14}H_{17}NS$: calcd. $[M+H]^+$: 232.1154; found: 232.1153.



$C_{14}H_{17}NOS$
247.36 g/mol

2-(Pyridin-2-yl)-5-methoxythiophene (115 mg, 600 µmol), *n*-butylboronic acid (183 mg, 1.80 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (40.8 mg, 300 µmol, 0.5 eq), Ag_2CO_3

(331 mg, 1.20 µmol, 2.0 eq) and $Pd(OAc)_2$ (13.5 mg, 60.0 µmol, 10 mol%) in ^{t}AmOH (3.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:3 → 100:4 → 20:1 → 9:1) yielding compound **5h** (99.5 mg, 402 µmol, 66%) as a colorless solid.

TLC: R_f = 0.34 (pentane/Et_2O 9:1) [UV].

Mp: 61-62 °C.

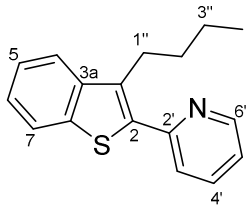
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3066 (w, sp^2-C-H), 2947 (w, sp^3-C-H), 2867 (w, sp^3-C-H), 1482 (s, Py), 1420 (s, Py), 1192 (m, OCH_3), 777 (s, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.94 (t, ^3J = 7.4 Hz, 3H, H-4''), 1.41 (*virt.* sextet, $^3J \approx$ 7.4 Hz, 2H, H-3''), 1.57-1.70 (m, 2H, H-2''), 2.79 (t, ^3J = 7.9 Hz, 2H, H-1''), 3.91 (s, 3H, OCH_3), 6.11 (s, 1H, H-4), 7.05 (ddd, ^3J = 7.1, 4.9 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.42 (dd, ^3J = 8.1 Hz, ^4J = 1.1 Hz, 1H, H-3'), 7.63 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.54 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 22.8 (t, C-3''), 30.2 (t, C-2''), 32.5 (t, C-1''), 60.0 (q, OCH_3), 108.1 (d, C-4), 120.5 (d, C-5'), 120.8 (d, C-3'), 124.4 (s, C-2), 136.3 (d, C-4'), 139.6 (s, C-3), 149.5 (d, C-6'), 153.7 (s, C-2'), 166.7 (s, C-5).

MS (EI): *m/z* (%) = 247 (75) $[M]^+$, 218 (100) $[M–Et]^+$.

HRMS (EI) $C_{14}H_{17}NOS$: calcd.: 247.1025 found: 247.1028.



$C_{17}H_{17}NS$
267.39 g/mol

2-(Pyridin-2-yl)benzothiophene (127 mg, 600 µmol), *n*-butylboronic acid (183 mg, 1.80 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (40.8 mg, 300 µmol, 0.5 eq), Ag_2CO_3 (331 mg, 1.20 mmol, 2.0 eq) and $Pd(OAc)_2$ (13.5 mg, 60.0 µmol, 10 mol%) in ^{t}AmOH (3 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 99.5:0.5 → 99:1 → 98:2 → 9:1 → 4:1) yielding compound **5i** (112 mg, 419 µmol, 70%) as a yellow solid.

TLC: R_f = 0.56 (pentane/Et_2O 9:1) [UV].

Mp: 89-90 °C.

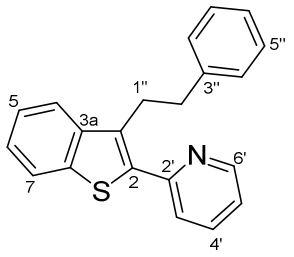
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3059 (w, sp^2-C-H), 2959 (w, sp^3-C-H), 2925 (w, sp^3-C-H), 2851 (w, sp^3-C-H), 1580 (m, Py), 1455 (m, Ar), 762 (s, Ar), 730 (s, Ar).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.97 (t, ^3J = 7.3 Hz, 3H, H-4''), 1.48 (*virt.* sextet, $^3J \approx$ 7.4 Hz, 2H, H-3''), 1.69-1.77 (m, 2H, H-2''), 3.16 (t, ^3J = 8.0 Hz, 2H, H-1''), 7.23 (ddd, ^3J = 7.5, 4.9 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.36 (*virt.* td, $^3J \approx$ 7.4 Hz, ^4J = 1.4 Hz, 1H, H-6), 7.39 (*virt.* td, $^3J \approx$ 7.4 Hz, ^4J = 1.3 Hz, 1H, H-5), 7.65 (dd, ^3J = 8.0 Hz, ^4J = 1.0 Hz, 1H, H-3'), 7.76 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 7.78-7.80 (m, 1H, H-4), 7.86 (dd, ^3J = 8.0 Hz, ^4J = 1.3 Hz, 1H, H-7), 8.71 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 23.2 (t, C-3''), 27.2 (t, C-2''), 32.2 (t, C-1''), 122.1 (d, C-5'), 122.5 (d, C-7), 122.7 (d, C-4), 122.8 (d, C-3'), 124.1 (d, C-5), 125.0 (d, C-5), 135.2 (s, C-3), 136.6 (d, C-4'), 138.1 (s, C-2), 139.9 (s, C-3a), 141.2 (s, C-7a), 149.9 (d, C-6'), 153.7 (s, C-2').

MS (EI): *m/z* (%) = 267 (45) $[M]^+$, 238 (100) $[M\text{-}Et]^+$, 223 (55) $[M\text{-}C_3H_7]^+$.

HRMS (EI) $C_{17}H_{17}NS$: calcd. $[M]^+$: 267.1076 found: 267.1070.



$C_{21}H_{17}NS$
315.43

2-(Pyridin-2-yl)benzothiophene (127 mg, 600 µmol), phenethylboronic acid (270 mg, 1.80 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (40.8 mg, 300 µmol, 0.5 eq), Ag_2CO_3 (331 mg, 1.20 mmol, 2.0 eq) and $Pd(OAc)_2$ (13.5 mg, 60.0 µmol, 10 mol%) in ^{t}AmOH (3 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:5 → 10:1) yielding compound **5j** (134 mg, 425 µmol, 71%) as a yellow solid.

TLC: R_f = 0.31 (pentane/Et_2O 9:1) [UV].

Mp: 87-88 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3059 (w, sp^2-C-H), 2927 (w, sp^3-C-H), 1528 (m, Ar), 1458 (m, Ar), 1431 (s, Py), 699 (s, Ar).

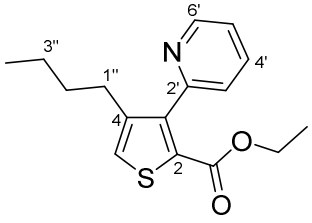
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 3.01-3.09 (m, 2H, H-1''), 3.46-3.53 (m, 2H, H-2''), 7.18-7.25 (m, 4H, H-5', 3xPh), 7.27-7.31 (m, 2H, 2xPh), 7.36-7.44 (m, 2H, H-5, H-6), 7.55 (dd, ^3J = 8.0 Hz, ^4J = 1.3 Hz, 1H, H-3'), 7.72 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 7.83 (d, ^3J = 7.7 Hz, 1H, H-4*), 7.88 (d, ^3J = 8.0 Hz, 1H, H-7*), 8.72 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 29.5 (t, C-1''), 36.1 (t, C-2''), 122.2 (d, C-5'), 122.5 (d, C-4*), 122.6 (d, C-7*), 123.0 (d, C-3'), 124.4 (d, C-5**), 125.1 (d, C-6**), 126.2 (d, C-6''), 128.5 (d, C-4'), 128.6 (d, C-5'), 134.3 (s, C-3), 136.6 (d, C-4'), 138.3 (s, C-2), 139.7 (s, C-3a***), 140.9 (s, C-7a***), 141.9 (s, C-3''), 149.8 (d, C-6'), 153.6 (s, C-2').

* /** /*** Signals are interconvertible.

MS (EI): *m/z* (%) = 315 (35) $[M]^+$, 224 (100) $[M\text{-}C_7H_7]^+$.

HRMS (EI) $C_{21}H_{17}NS$: calcd. $[M]^+$: 315.1076 found: 315.1079.



$C_{16}H_{19}NO_2S$
289.39

Ethyl 3-(pyridin-2-yl)-2-thiophene carboxylate (**8**) (93.3 mg, 400 µmol), *n*-butylboronic acid (122 mg, 1.20 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:5 → 10:1 → 17:1 → 4:1 → 3:1) yielding thiophene **9** (60.5 mg, 209 µmol, 52%) as a yellow oil.

TLC: R_f = 0.28 (pentane/Et_2O 2:1) [UV].

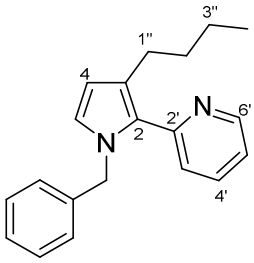
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2956 (w, sp^3-C-H), 2928 (w, sp^3-C-H), 1714 (s, COOR), 1698 (s, COOR), 1589 (m, Py), 1274 (s, COOR), 1096 (s, COOR), 777 (m, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.78 (t, ^3J = 7.4 Hz, 3H, H-4''), 1.11 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 1.16-1.26 (m, 2H, H-3''), 1.40 (tt, ^3J = 7.8, 6.5 Hz, 2H, H-2''), 2.40 (t, ^3J = 7.8 Hz, 2H, H-1''), 4.12 (q, ^3J = 7.1 Hz, 2H, OCH_2CH_3), 7.20 (s, 1H, H-5), 7.28 (ddd, ^3J = 7.6, 4.9 Hz, ^4J = 1.2 Hz, 1H, H-5'), 7.31 (*virt.* dt, ^3J = 7.8 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 1H, H-3'), 7.73 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.68 (ddd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, ^5J = 1.0 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 13.9 (q, C-4''), 14.1 (q, OCH_2CH_2), 22.3 (t, C-3''), 28.8 (t, C-1''), 31.9 (t, C-2''), 60.9 (t, OCH_2CH_3), 122.3 (d, C-5'), 125.1 (d, C-3'), 126.4 (d, C-5), 130.6 (s, C-2), 135.8 (d, C-4'), 144.4 (s, C-4), 146.8 (s, C-3), 149.3 (d, C-6'), 155.5 (s, C-2'), 162.1 (s, COOEt).

MS (EI): *m/z* (%) = 289 (29) $[M]^+$, 260 (84) $[M\text{-}C_2H_5]^+$, 214 (100) $[C_{13}H_{12}NO_2]^+$.

HRMS (ESI) $C_{16}H_{19}NO_2S$: calcd. $[M+H]^+$: 290.1209 found: 290.1209.



$C_{20}H_{22}N_2$
290.41

N-Benzyl-2-(pyridin-2-yl)pyrrole (**10**) (93.7 mg, 400 µmol), *n*-butylboronic acid (122 mg, 1.20 µmol, 3.0 eq), 2,6-dimethylbenzoquinone (27.2 mg, 200 µmol, 0.5 eq), Ag_2CO_3 (221 mg, 800 µmol, 2.0 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) in ^{t}AmOH (2.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:0.5 → 100:1 → 100:1.5 → 100:2 → 100:5 → 10:1 → 5:1) yielding pyrrole **12** (67.5 mg, 232 µmol, 58%) as a colorless oil.

TLC: R_f = 0.20 (pentane/Et_2O 9:1) [UV].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3031 (w, sp^2-C-H), 2954 (w, sp^3-C-H), 2926 (w, sp^3-C-H), 1508 (s, Pyrr), 1470 (s, Py), 790 (m, Pyrr), 725 (s, Pyrr).

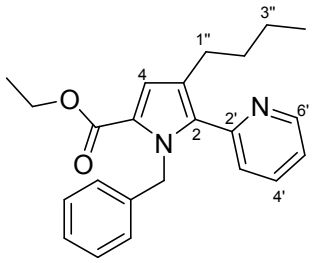
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.89 (t, ^3J = 7.4 Hz, 3H, H-4''), 1.34 (*virt.* q, $^3J \approx$ 7.5 Hz, 2H, H-3''), 1.57 (*virt.* pentet, $^3J \approx$ 7.6 Hz, 2H, H-2''), 2.57 (t, ^3J = 7.8 Hz, 2H, H-1''), 5.37 (s, 2H, NCH_2Ph), 6.16 (d, ^3J = 2.6 Hz, 1H, H-4), 6.74 (d, ^3J = 2.6 Hz, 1H, H-5), 6.94 (d, ^3J = 7.3 Hz, 2H, *o*Ph-H*), 7.09-7.14 (m, 1H, H-5'), 7.19 (dt, ^3J = 13.7, 6.9 Hz, 3H, *m*Ph-H*, *p*Ph-H), 7.28 (d, ^3J = 2.1 Hz, 1H, H-3'), 7.64 (td, ^3J = 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.66 (d, ^3J = 3.9 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 22.7 (t, C-3''), 26.5 (t, C-1''), 33.6 (t, C-2''), 51.3 (t, NCH_2Ph), 108.6 (d, C-4), 120.9 (d, C-5'), 123.3 (d, C-5), 124.9 (d, C-3'), 125.3 (s, C-3), 126.9 (d, *o*PhC*), 127.1 (d, *p*PhC), 128.4 (d, *m*PhC*), 129.3 (s, C-2), 136.2 (d, C-4'), 139.3 (s, NCH_2C), 149.3 (d, C-6'), 152.3 (s, C-2').

* Signals are interconvertible.

MS (EI): *m/z* (%) = 290 (46) $[M]^+$, 91 (100) $[C_7H_7]^+$.

HRMS (EI): $C_{20}H_{22}N_2$ calcd. $[M]^+$: 290.1778; found: 290.1780.



$C_{23}H_{26}N_2O_2$
362.47 g/mol

Ethyl *N*-Benzyl-2-(pyridin-2-yl)-5-pyrrole carboxylate (**11**) (61.3 mg, 200 µmol), *n*-butylboronic acid (61.2 mg, 600 µmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) (13.6 mg, 100 µmol, 0.5 eq), Ag_2CO_3 (110 mg, 400 µmol, 2.0 eq) and $Pd(OAc)_2$ (4.49 mg, 20.0 µmol, 10 mol%) in ^{t}AmOH (1.0 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:1 → 100:2 → 100:5 → 10:1 → 85:15 → 4:1 → 2:1) yielding pyrrole **13** (65.4 mg, 180 µmol, 90%) as a colorless oil.

TLC: R_f = 0.34 (pentane/Et_2O 4:1) [UV].

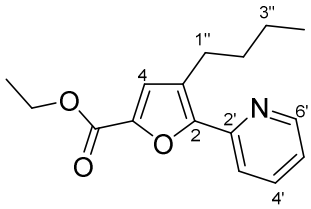
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2956 (m, sp^3-C-H), 2931 (m, sp^3-C-H), 2857 (m, sp^3-C-H), 1699 (s, COOR), 1586 (m, Py), 1434 (m, Ar), 1417 (m, Ar), 1250 (s, COOR), 1186 (s, COOR), 1087 (s, COOR), 727 (s, Pyrr).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.84 (t, ^3J = 7.4 Hz, 3H, H-4''), 1.28 (*virt.* sextet, $^3J \approx$ 7.3 Hz, 2H, H-3''), 1.29 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 1.46-1.57 (m, 2H, H-2''), 2.46 (t, ^3J = 7.7 Hz, 2H, H-1''), 4.23 (q, ^3J = 7.1 Hz, 2H, OCH_2CH_3), 5.80 (s, 2H, NCH_2Ph), 6.75-6.79 (m, 2H, Ph-H), 7.00 (s, 1H, H-4), 7.07-7.10 (m, 1H, Ph-H), 7.11-7.15 (m, 2H, Ph-H), 7.20 (ddd, ^3J = 7.6, 4.8 Hz, ^4J = 1.1 Hz, 1H, H-5'), 7.20-7.23 (m, 1H, H-3'), 7.63 (*virt.* td, $^3J \approx$ 7.7 Hz, ^4J = 1.8 Hz, 1H, H-4'), 8.69 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.0 (q, C-4''), 14.5 (q, OCH_2CH_3), 22.5 (t, C-3''), 25.8 (t, C-2''), 33.2 (t, C-2''), 48.7 (t, NCH_2Ph), 59.9 (t, OCH_2CH_3), 118.2 (d, C-4), 122.3 (d, C-5'), 122.7 (s, C-2), 124.8 (s, C-3), 125.9 (d, C-3'), 126.2 (d, *o*PhC), 126.7 (d, *p*PhC), 128.3 (d, *m*PhC), 136.3 (d, C-4'), 136.8 (s, C-5), 139.6 (s, NCH_2C), 149.8 (d, C-6'), 151.4 (s, C-2'), 161.3 (s, COOEt).

MS (EI): *m/z* (%) = 362 (30) $[M]^+$, 289 (50) $[M\text{-}COOEt]^+$, 271 (30) $[M\text{-}C_7H_7]^+$, 225 (100) [M-Bn -OEt]$^+$.

HRMS (ESI) $C_{23}H_{26}N_2O_2$: calcd. $[M+H]^+$: 363.2067 found: 363.2071.



$C_{16}H_{19}NO_3$
273.33

Ethyl 2-(pyridin-2-yl)-5-furan carboxylate (**14**) (133 mg, 613 µmol), *n*-butylboronic acid (187 mg, 1.84 mmol, 3.0 eq), 2,6-dimethylbenzoquinone (**2**) ((41.7 mg, 306 µmol, 0.5 eq), Ag_2CO_3 (338 mg, 1.23 mmol, 2.0 eq) and $Pd(OAc)_2$ (13.8 mg, 61.3 µmol, 10 mol%) in ^{t}AmOH (3.1 mL) were reacted according to General Procedure 3.

The crude product was purified by flash chromatography (pentane/Et_2O 100:0.5 → 100:1 → 100:2 → 100:3 → 100:5 → 10:1 → 4:1 → 0:1) yielding furan **15** (60.1 mg, 220 µmol, 36%) as a colorless oil.

TLC: R_f = 0.56 (pentane/Et_2O 4:1) [UV].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3055 (w, sp^2-C-H), 2957 (m, sp^3-C-H), 2929 (m, sp^3-C-H), 2871 (m, sp^3-C-H), 1712 (s, COOR), 1603 (m, Py), 1563 (m, Fur), 1423 (m, Py), 1308 (s, COOR), 1185 (s, COOR), 788 (m, Fur).

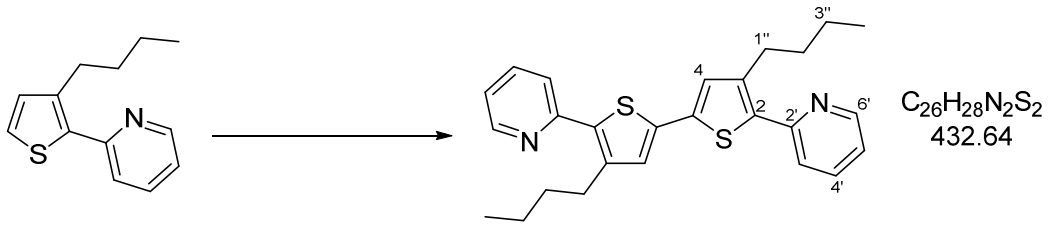
^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.93 (t, ^3J = 7.3 Hz, 3H, H-4''), 1.37-1.43 (m, 5H, H-3'', OCH_3CH_3), 1.57-1.68 (m, 2H, H-2''), 3.02 (t, ^3J = 7.7 Hz, 2H, H-1''), 4.38 (q,

^3J = 7.1 Hz, 2H, OCH_2CH$_3$), 7.15-7.20 (m, 2H, H-4, H-5'), 7.73 (*virt.* td, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 1H, H-4'), 7.86 (*virt.* dt, ^3J = 8.2 Hz, $^4J \approx {}^5J$ = 1.0 Hz, 1H, H-3'), 8.62 (dd, ^3J = 4.9 Hz, ^4J = 1.8 Hz, 1H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 14.5 (q, OCH$_2$*C*H$_3$), 22.5 (t, C-3''), 25.4 (t, C-1''), 32.1 (t, C-2''), 61.1 (t, O*C*H$_2$CH$_3$), 120.8 (d, C-3'), 121.8 (d, C-3), 122.3 (d, C-5'), 128.0 (d, C-4), 136.5 (d, C-4'), 143.0 (s, C-2), 149.4 (d, C-6'), 150.5 (s, C-2'), 150.9 (s, C-5), 159.1 (s, COOEt).

MS (EI): *m/z* (%) = 273 (100) $[M]^+$, 244 (100) $[M\text{-}Et]^+$, 216 (27) $[M\text{-}C_4H_9]^+$.

HRMS (EI) $C_{16}H_{19}NO_3$: calcd. $[M]^+$: 273.1359; found: 273.1360.



$C_{26}H_{28}N_2S_2$
432.64

Thiophene **3a** (86.9 mg, 400 µmol, 1 eq), *n*-butylboronic acid (122 mg, 1.20 mmol, 3 eq), Ag_2CO_3 (221 mg, 800 µmol, 2 eq), 2,6-dimethylbenzoquinone (**2**) (27.2 mg, 200 µmol, 0.5 eq) and $Pd(OAc)_2$ (8.98 mg, 40.0 µmol, 10 mol%) were charged into a flame-dried pressure Schlenk-tube under air. Dry ^{t}AmOH (2 mL) was added and the resulting suspension was stirred at room temperature for 5 min and was then submitted to a preheated oil bath at 100 °C for 14 h. The cooled black solution was diluted with CH_2Cl_2 (60 mL) and Na_2S solution (20 mL, 10% w/w). The layers were separated and the aqueous layer was further extracted by CH_2Cl_2 (2 × 60 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was completely removed under reduced pressure, yielding a yellow oil.

The crude product was further purified by flash chromatography (pentane/Et_2O 100:5 → 100:7.5 → 10:1 → 20:3 → 4:1 → 3:1 → 2:1) yielding the 5,5'-dithiophene **4** (51.0 mg, 118 µmol, 59%) as a bright yellow solid.

TLC: R_f = 0.42 (pentane/Et_2O 4:1) [UV].

Mp: 113-114 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3060 (w, sp^2-C-H), 2953 (w, sp^3-C-H), 2924 (m, sp^3-C-H), 2857 (w, sp^3-C-H), 1578 (m, Py), 1460 (s, Py), 1426 (m, Py), 823 (w, Thp).

^{1}H-NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.95 (t, ^3J = 7.3 Hz, 6H, H-4''), 1.43 (*virt.* sextet, $^3J \approx$ 7.4 Hz, 4H, H-3''), 1.68 (tt, ^3J = 7.7, 6.5 Hz, 4H, H-2''), 2.88 (t, ^3J = 7.7 Hz, 4H, H-1''), 7.12 (s, 2H, H-4), 7.14 (ddd, ^3J = 7.5, 4.8 Hz, ^4J = 1.1 Hz, 2H, H-5'), 7.53 (*virt.* dt, ^3J = 7.9 Hz, $^4J \approx {}^5J$ = 1.1 Hz, 2H, H-3'), 7.70 (*virt.* dt, $^3J \approx$ 7.8 Hz, ^4J = 1.8 Hz, 2H, H-4'), 8.62 (dd, ^3J = 4.8 Hz, ^4J = 1.8 Hz, 2H, H-6').

^{13}C-NMR (91 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 (q, C-4''), 22.8 (t, C-3''), 29.7 (t, C-1''), 32.5 (t, C-2''), 121.4 (d, C-3'), 121.5 (d, C-5'), 127.6 (d, C-4), 136.6 (d, C-4'), 137.0 (s, C-5), 137.3 (s, C-2), 141.8 (s, C-3), 149.7 (d, C-6'), 153.2 (s, C-2').

HRMS (ESI) $C_{26}H_{28}N_2S_2$: calcd. $[M+H]^+$: 433.1767 found: 433.1765.

References for the Supporting Information

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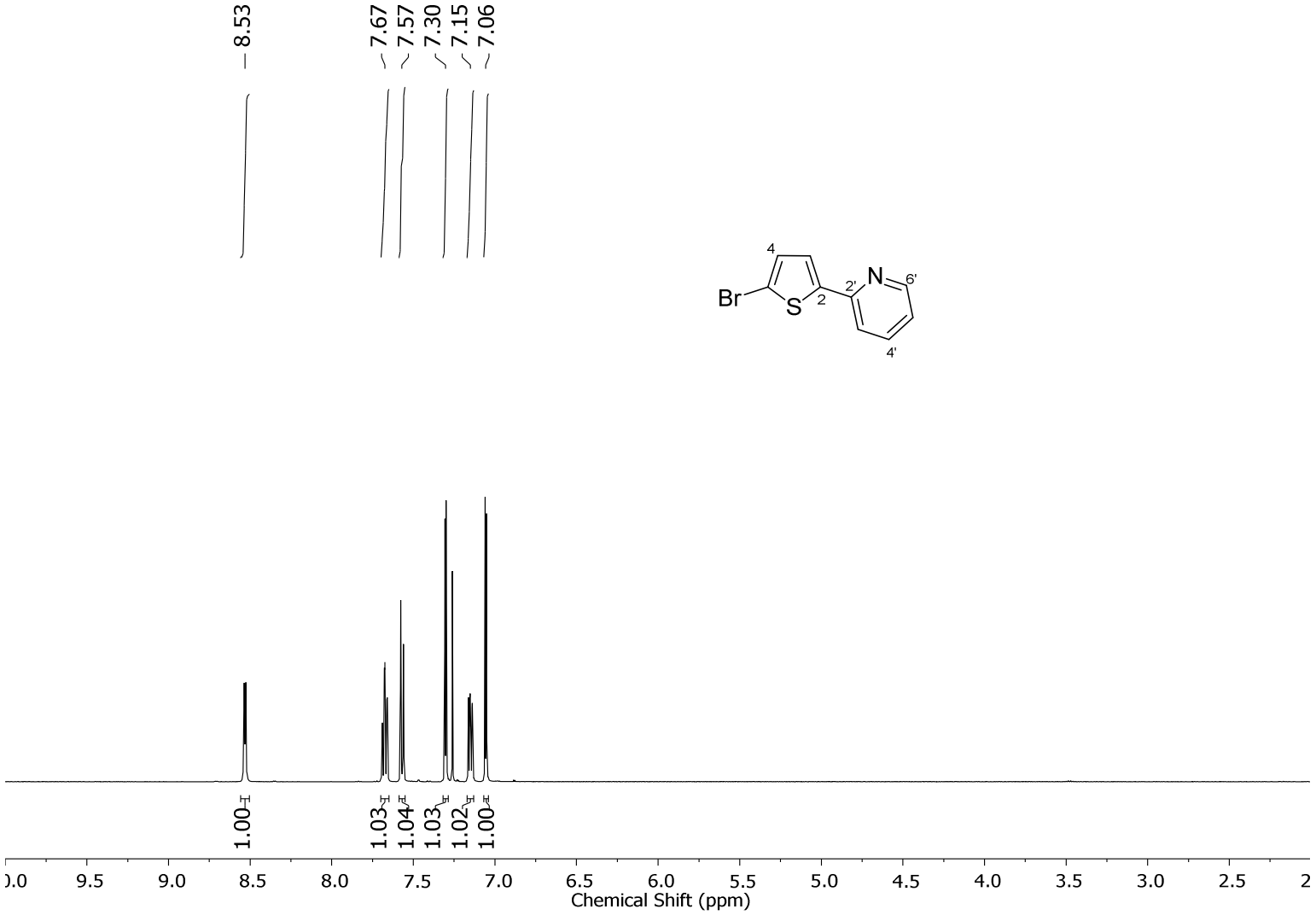
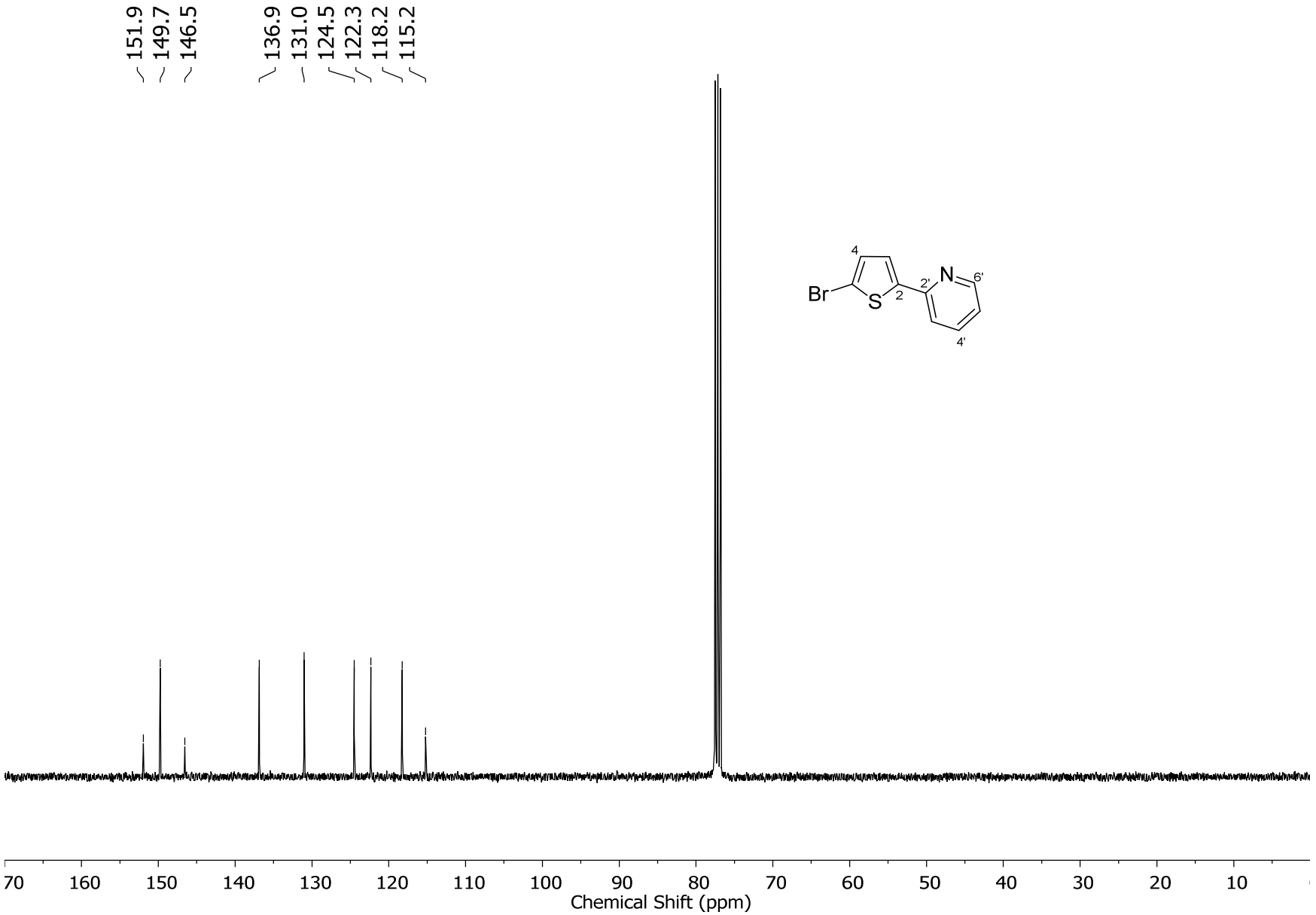
NMR Spectra of new compounds

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2'
4
4'
6'
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50
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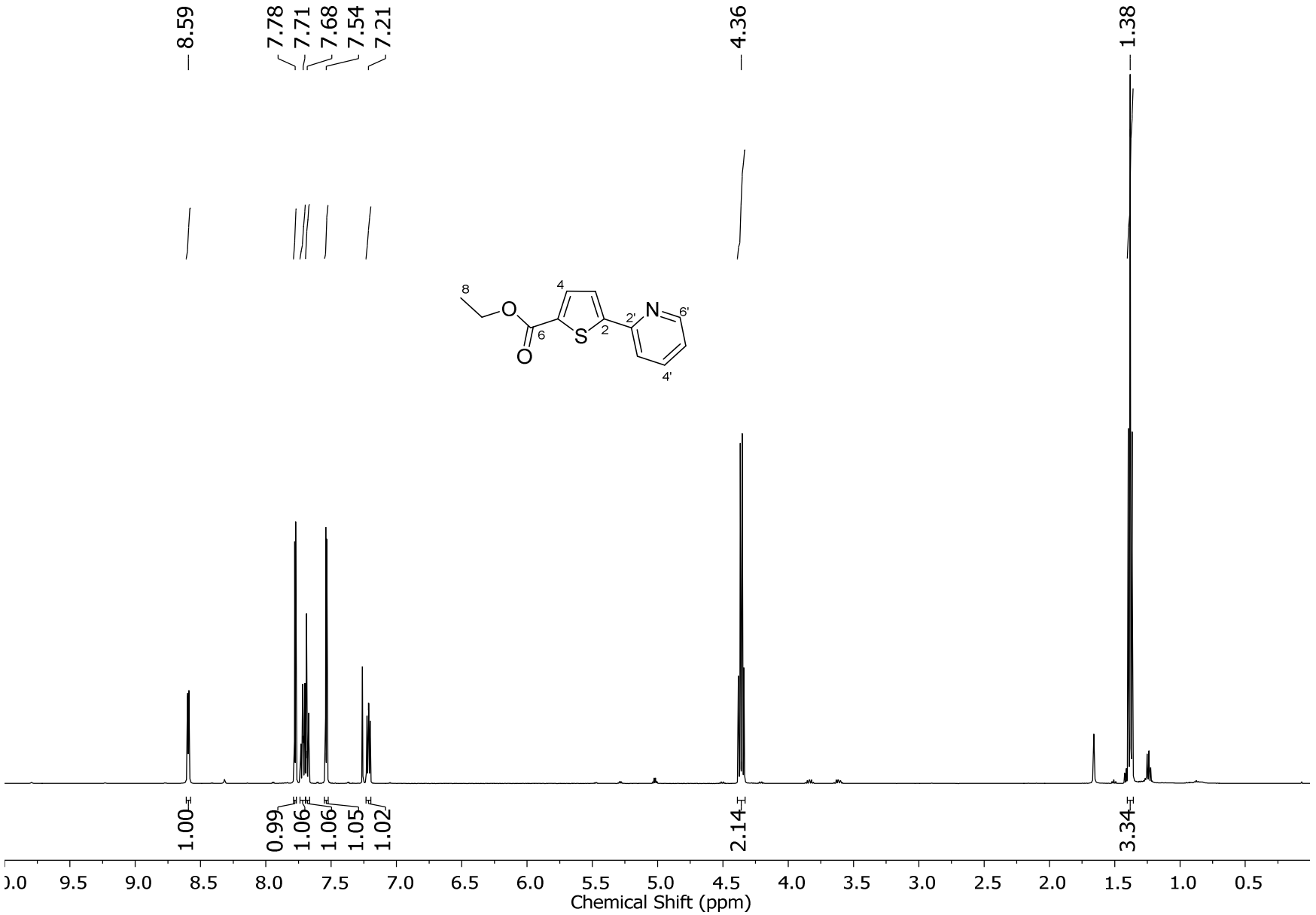
30
20
10
Chemical Shift (ppm)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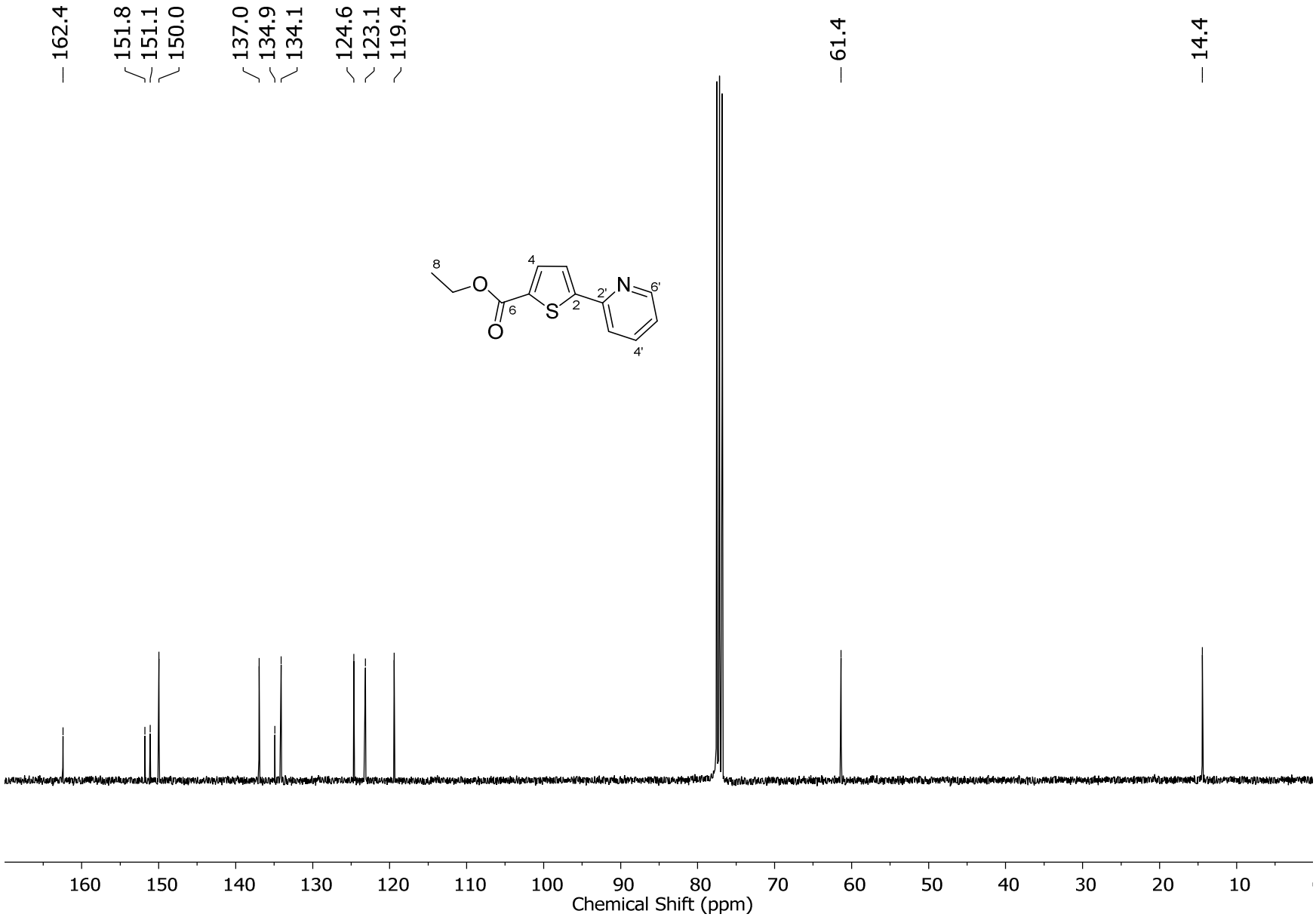
Chemical Shift (ppm)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2
2'
N
6'
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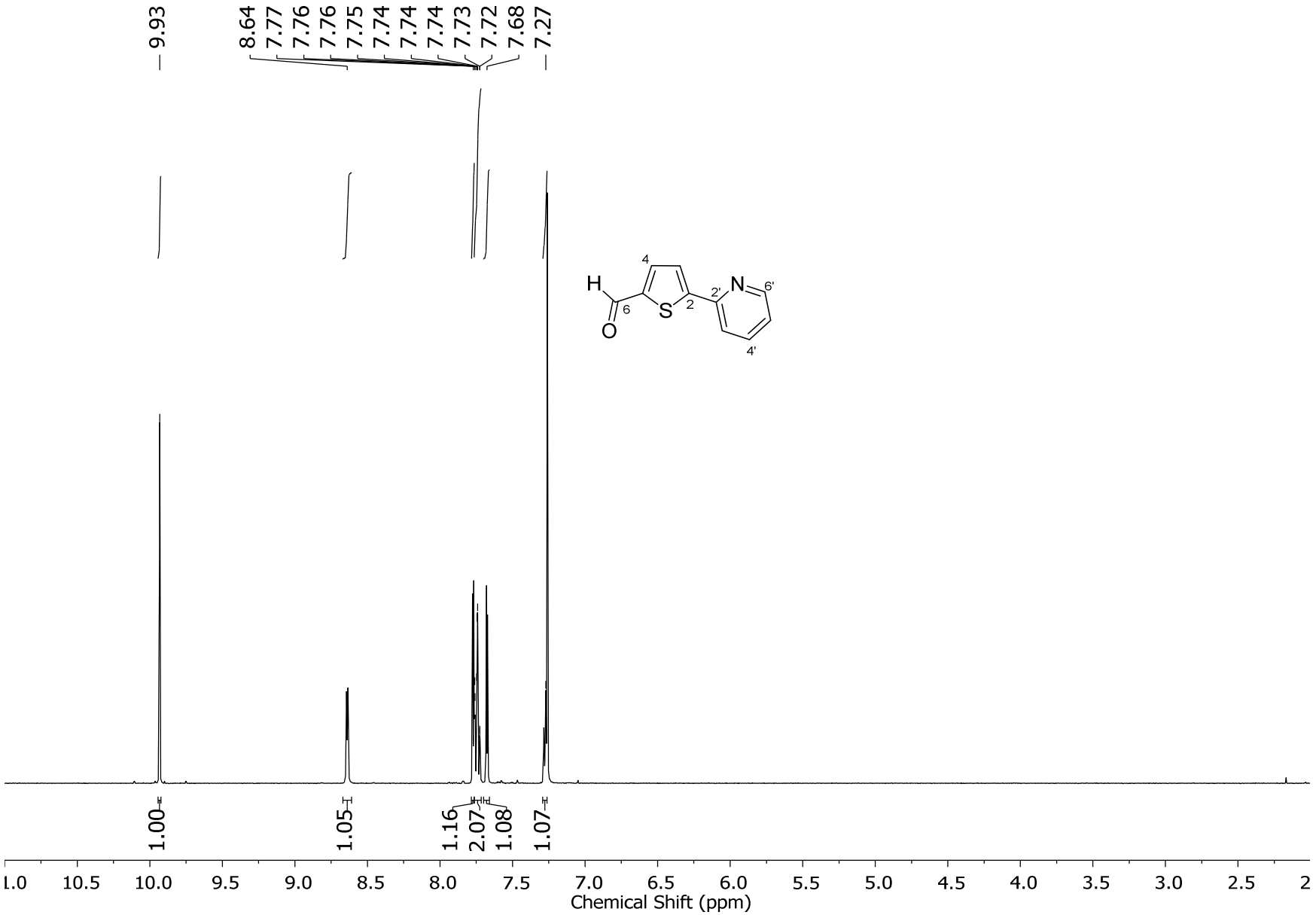
Chemical Shift (ppm)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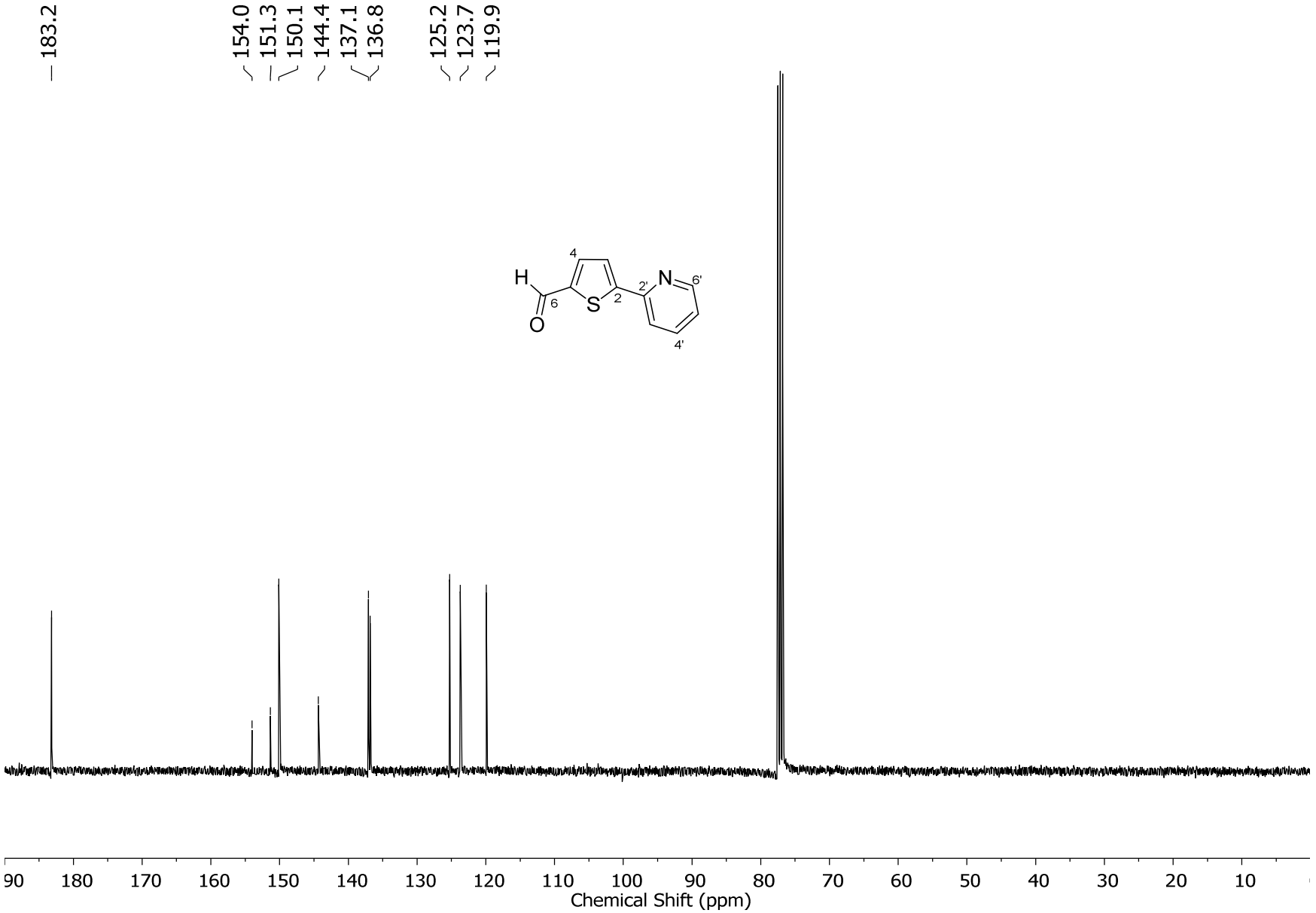
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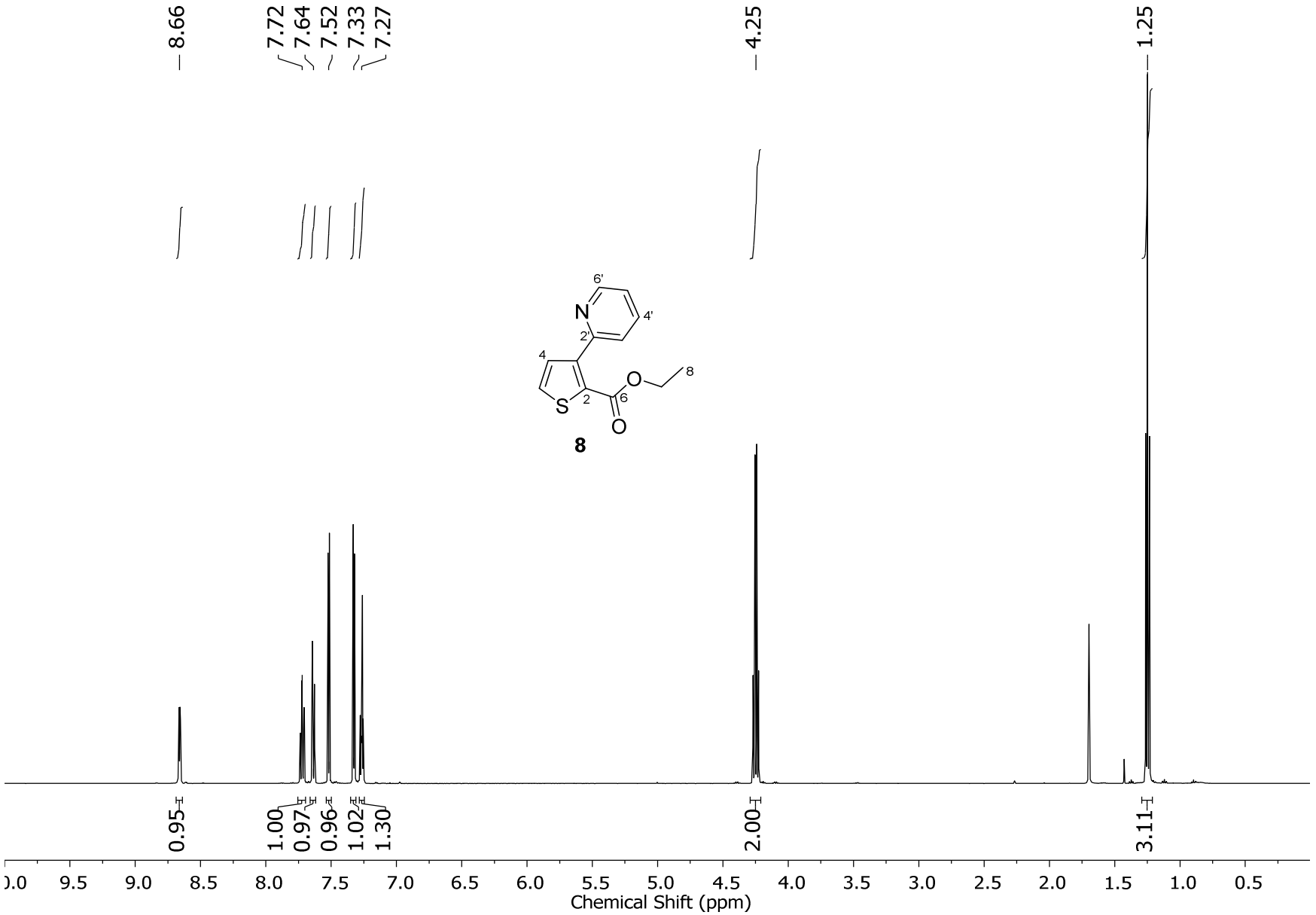
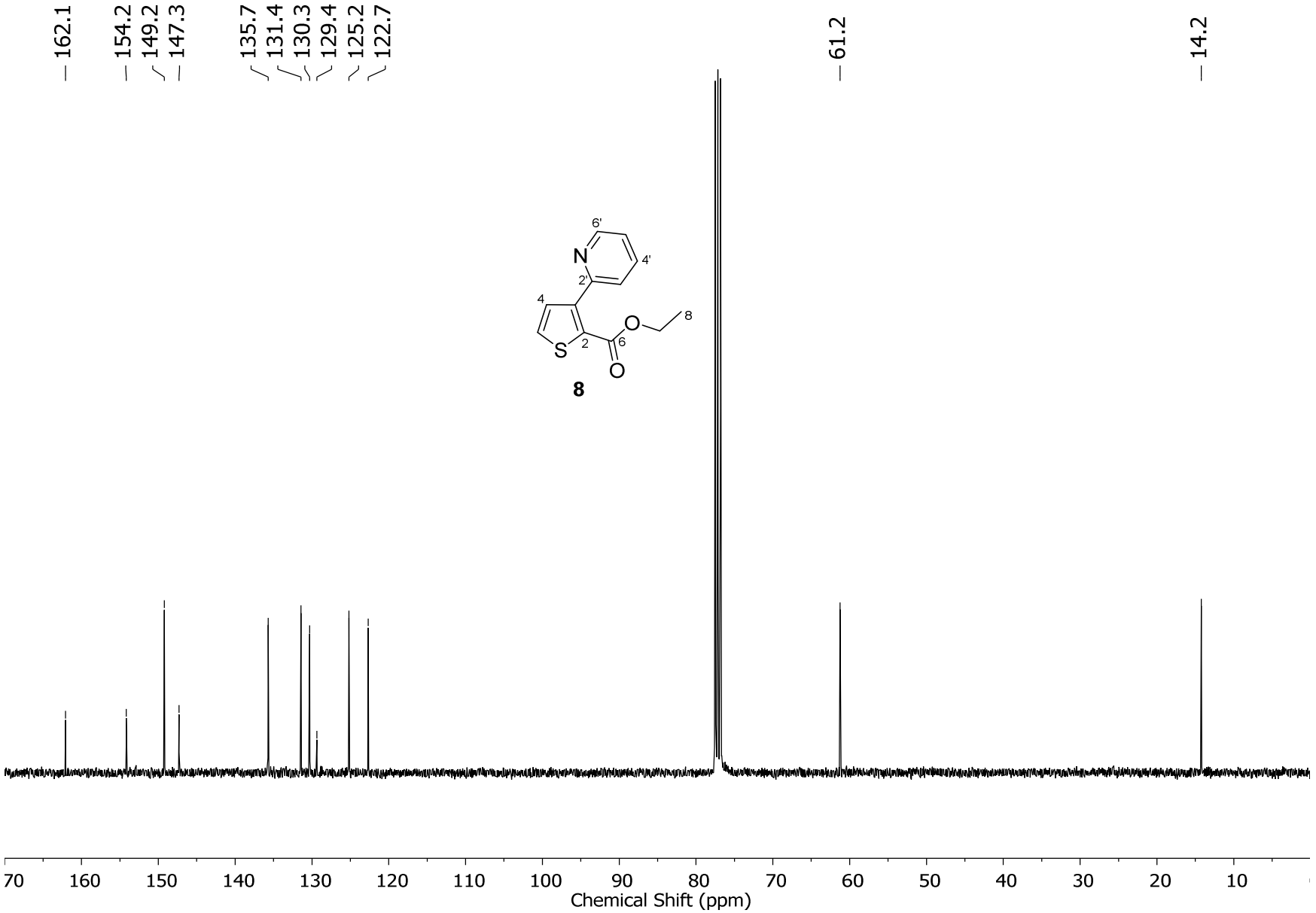
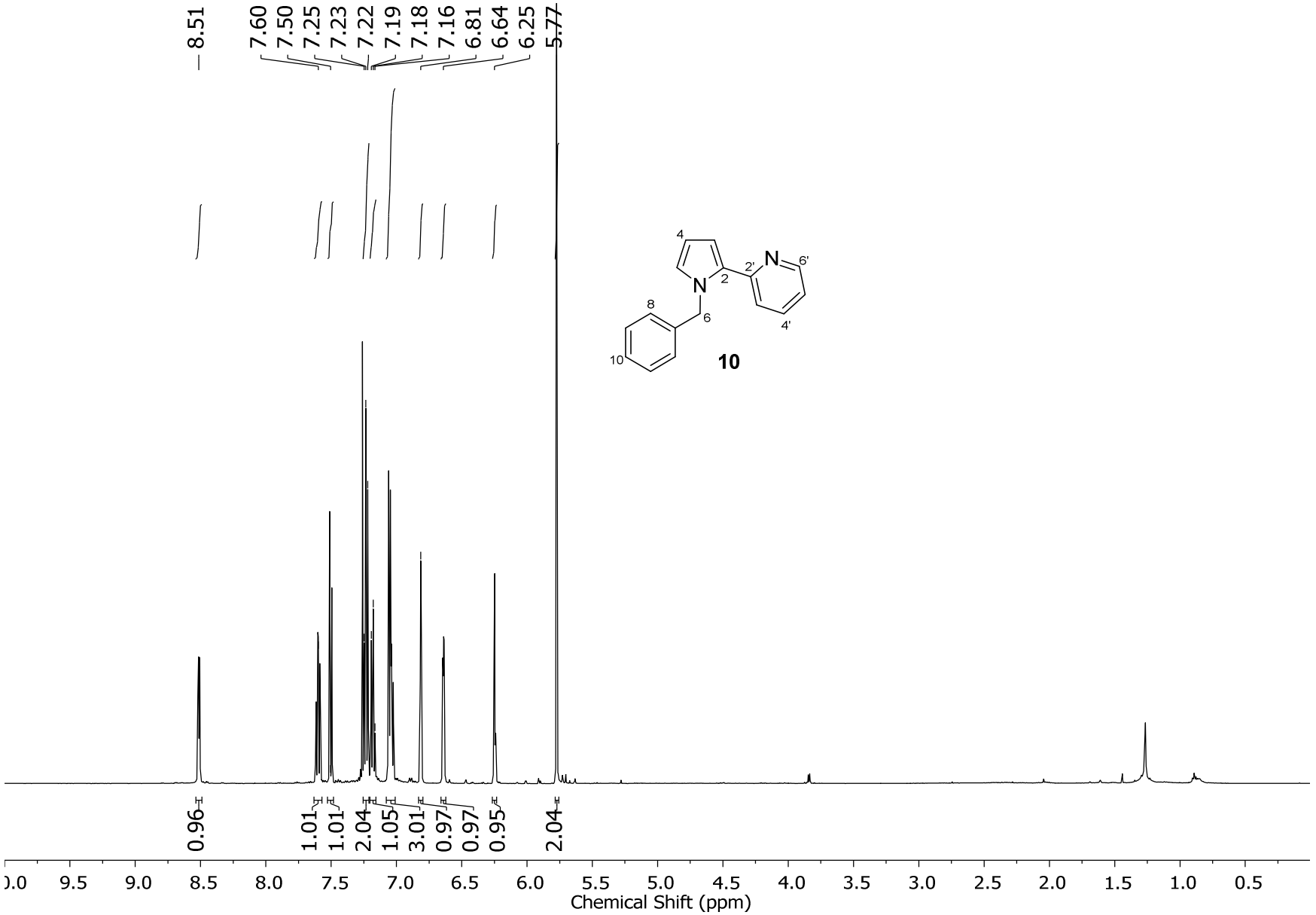
6
2
2'
6'
4'
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)


8.66
7.72
7.64
7.52
7.33
7.27
4.25
1.25
6'
N
4'
2'
4
8
O
S
2
6
O
0.95
1.00
0.97
0.96
1.02
1.30
2.00
3.11
Chemical Shift (ppm)

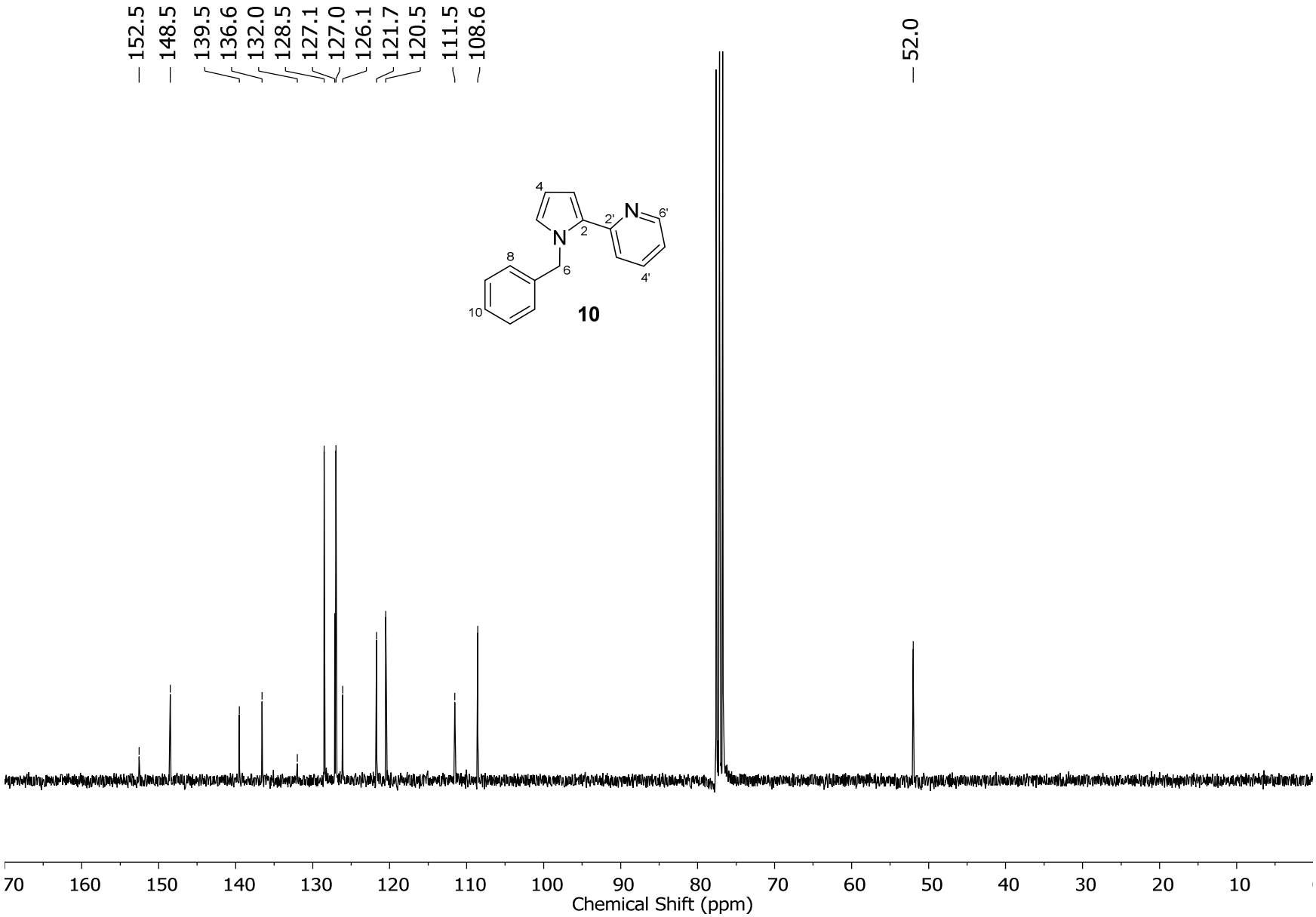
8

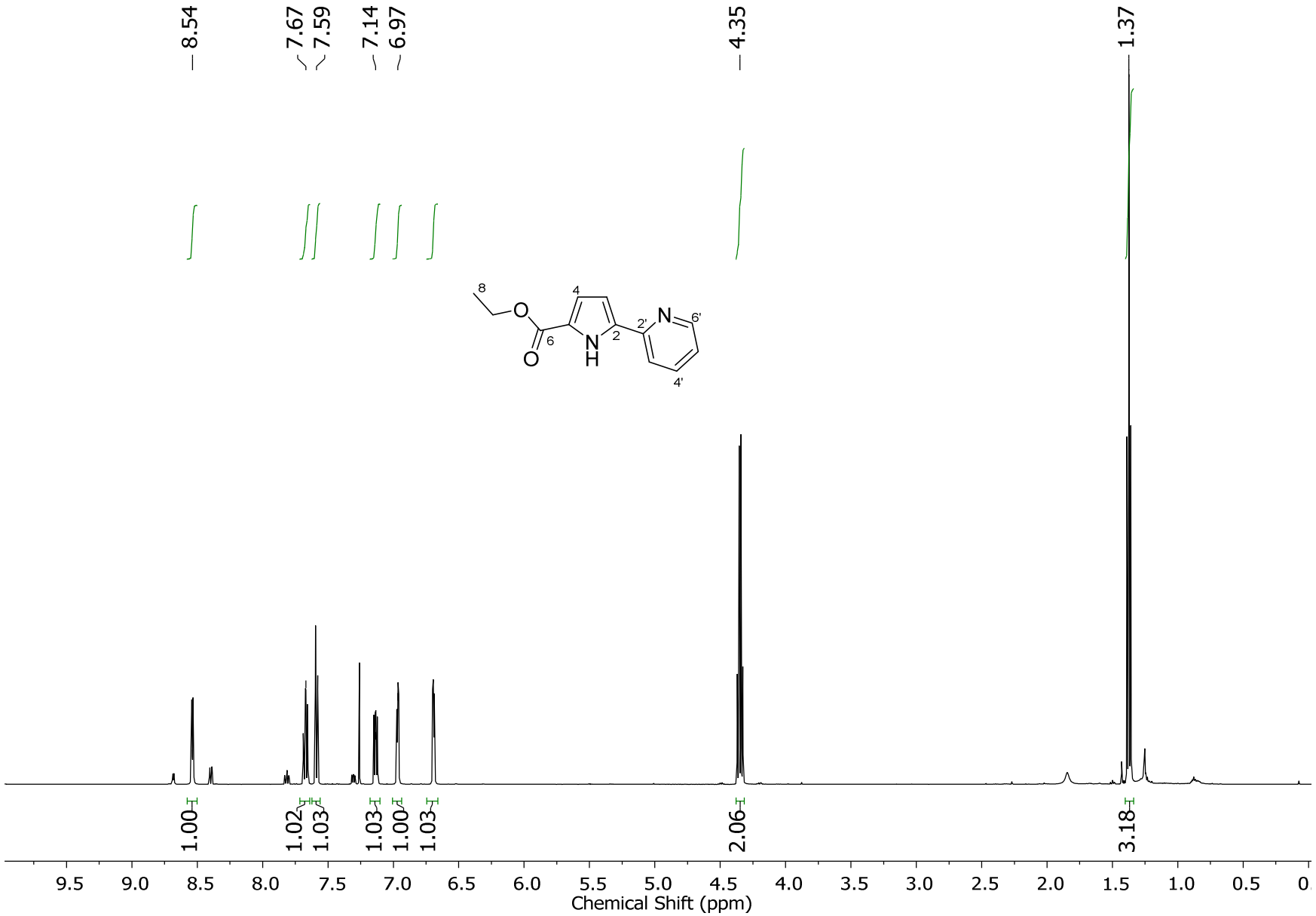

162.1
154.2
149.2
147.3
135.7
131.4
130.3
129.4
125.2
122.7
61.2
14.2
6'
N
4'
2'
4
O
8
2
S
6
O
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

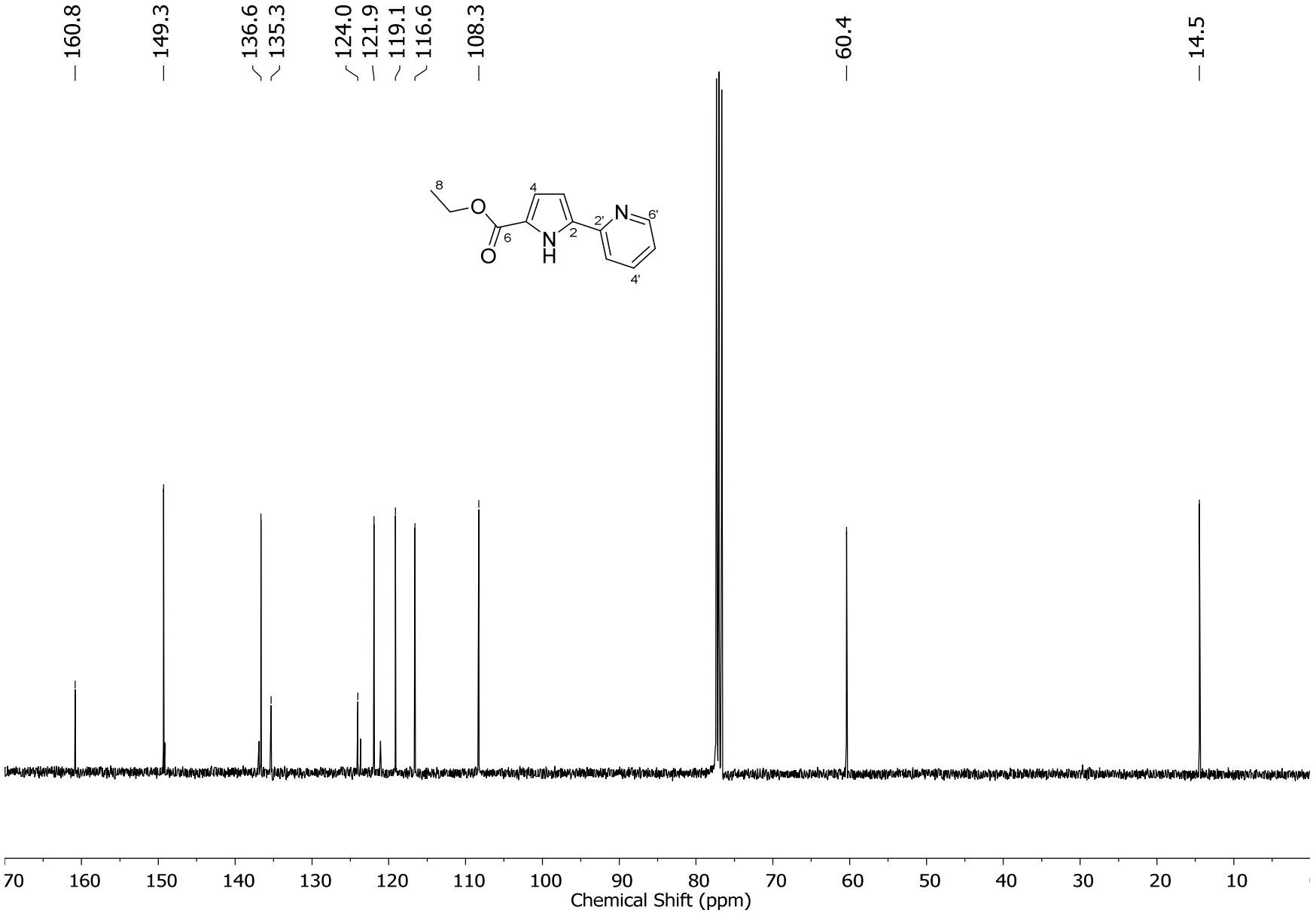
8

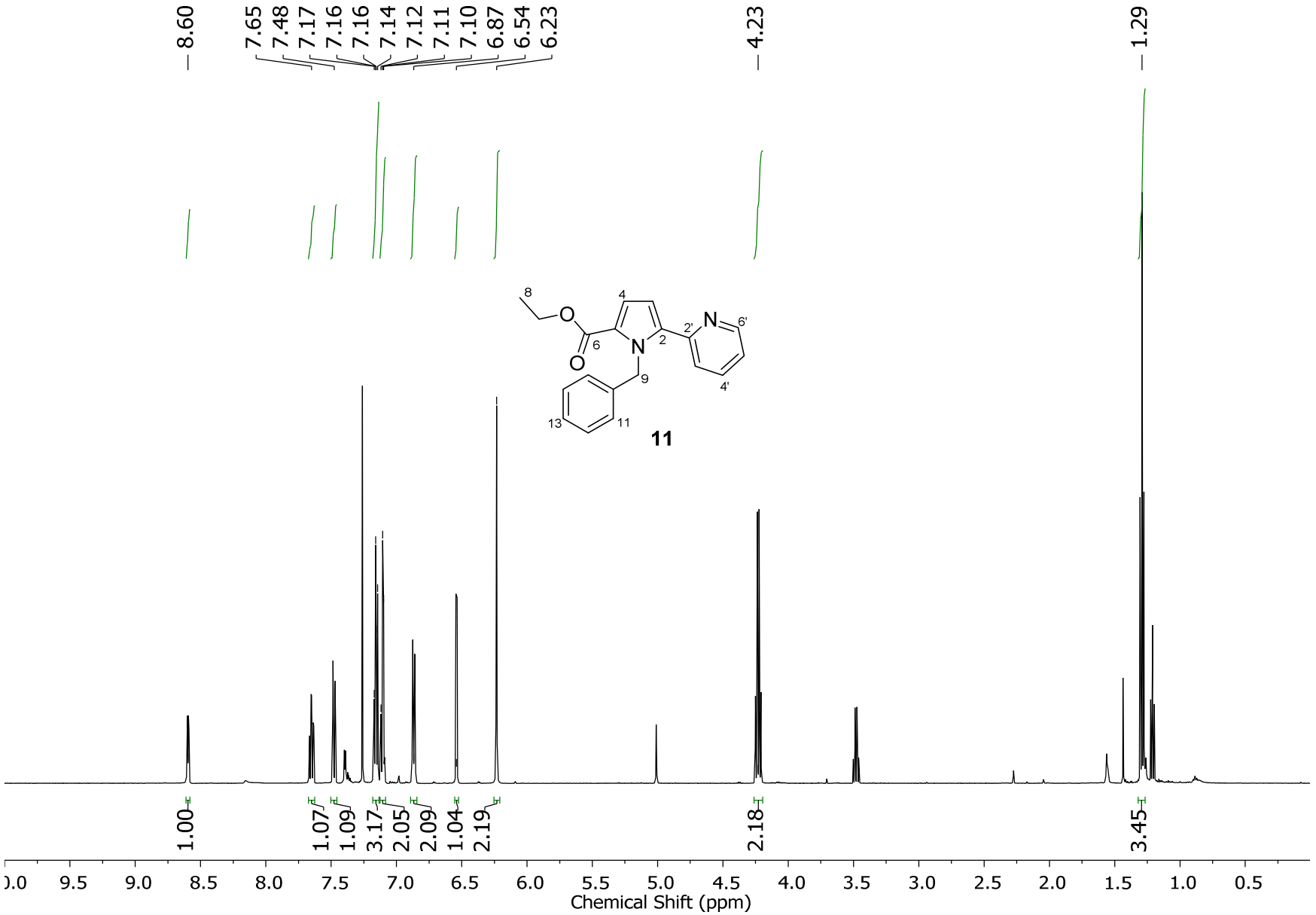

8.51
7.60
7.50
7.25
7.23
7.22
7.19
7.18
7.16
6.81
6.64
6.25
5.77
0.96
1.01
1.01
2.04
1.05
3.01
0.97
0.97
0.95
2.04
Chemical Shift (ppm)

10

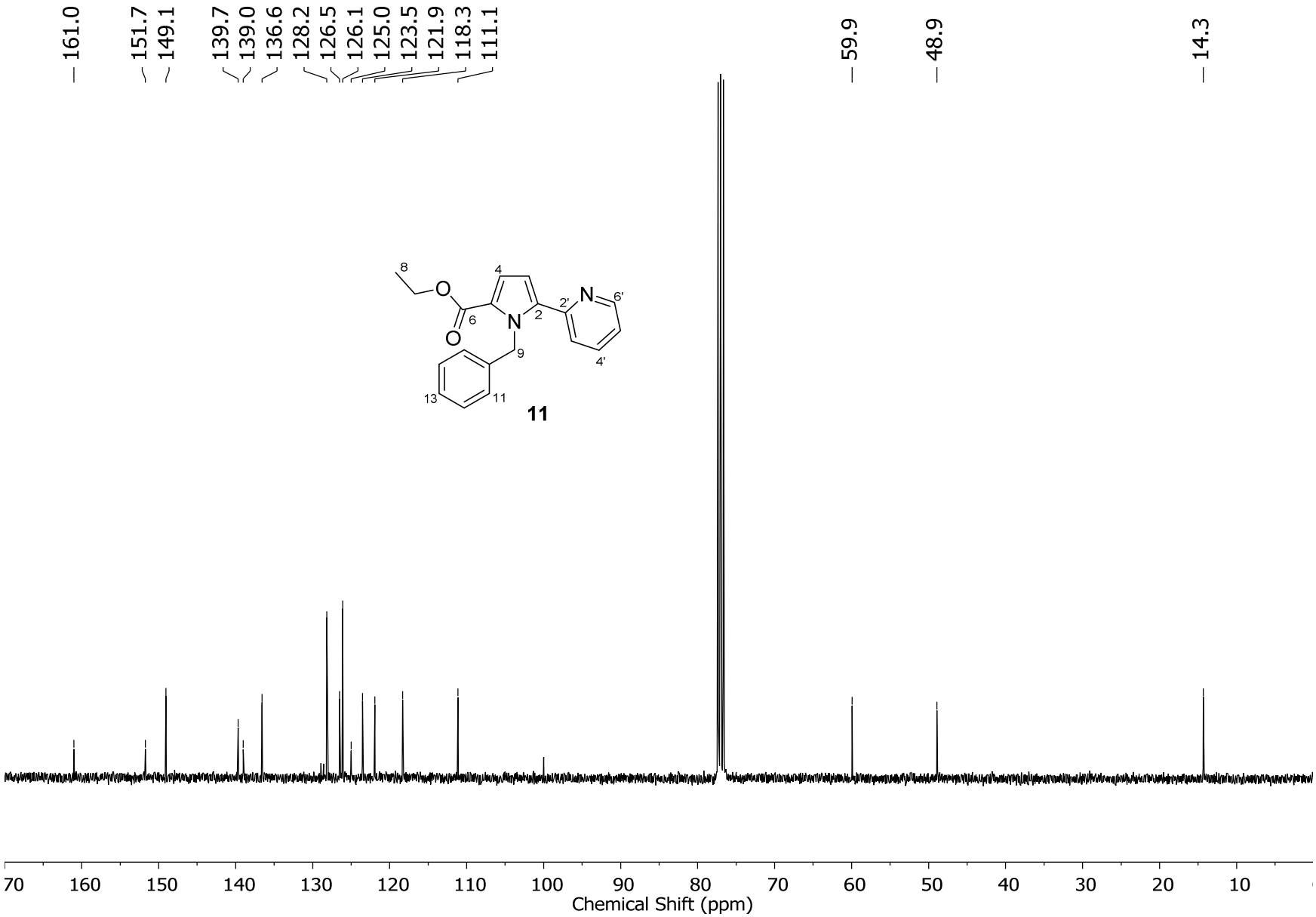

152.5
148.5
139.5
136.6
132.0
128.5
127.1
127.0
126.1
121.7
120.5
111.5
108.6
52.0
4
N
6'
2'
2
N
8
6
4'
10
10
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

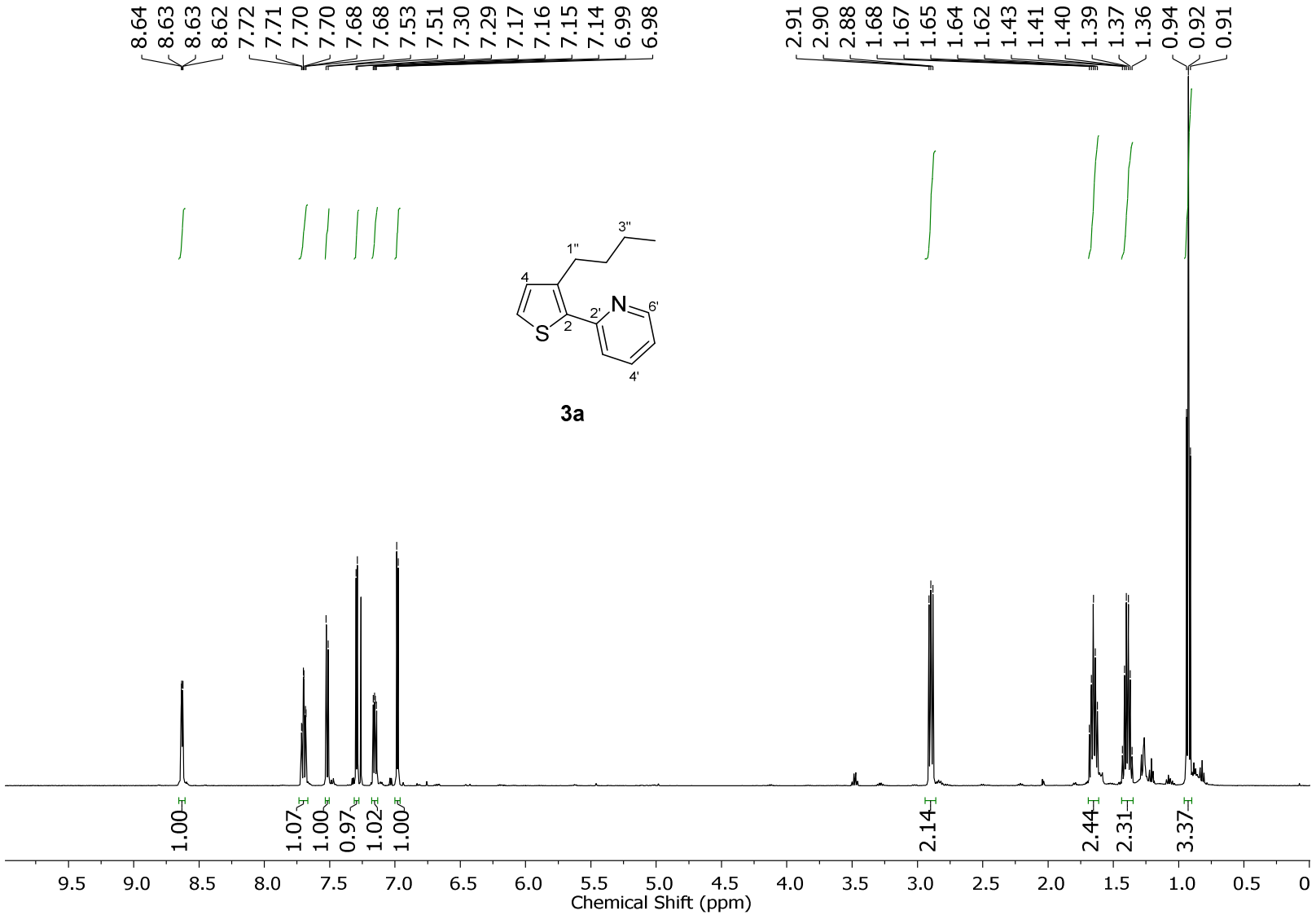

8.54
7.67
7.59
7.14
6.97
4.35
1.37
1.00
1.02
1.03
1.03
1.00
1.03
2.06
3.18
Chemical Shift (ppm)

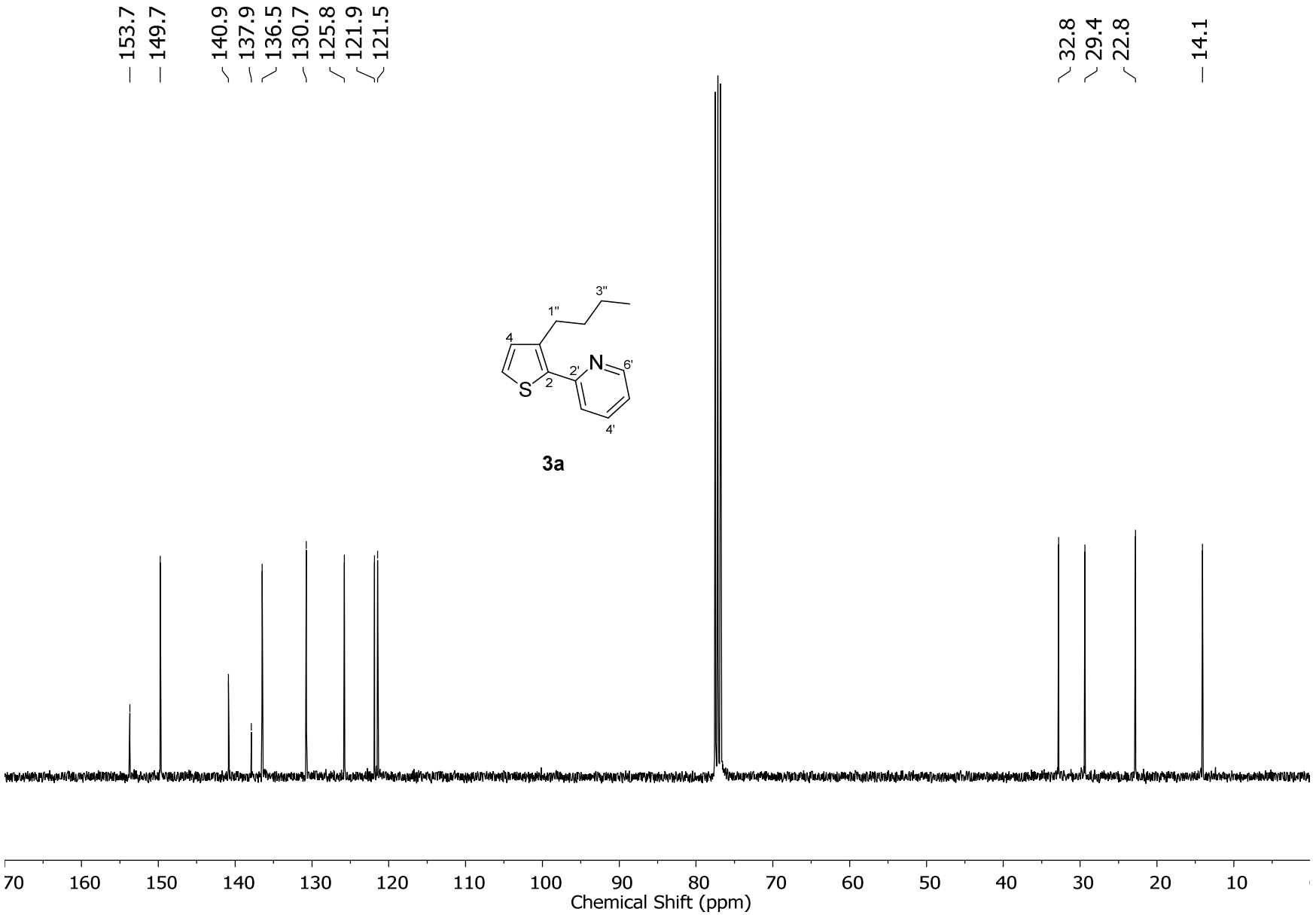

160.8
149.3
136.6
135.3
124.0
121.9
119.1
116.6
108.3
60.4
14.5
8
O
4
6
O
N
H
2
2'
N
6'
4'
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

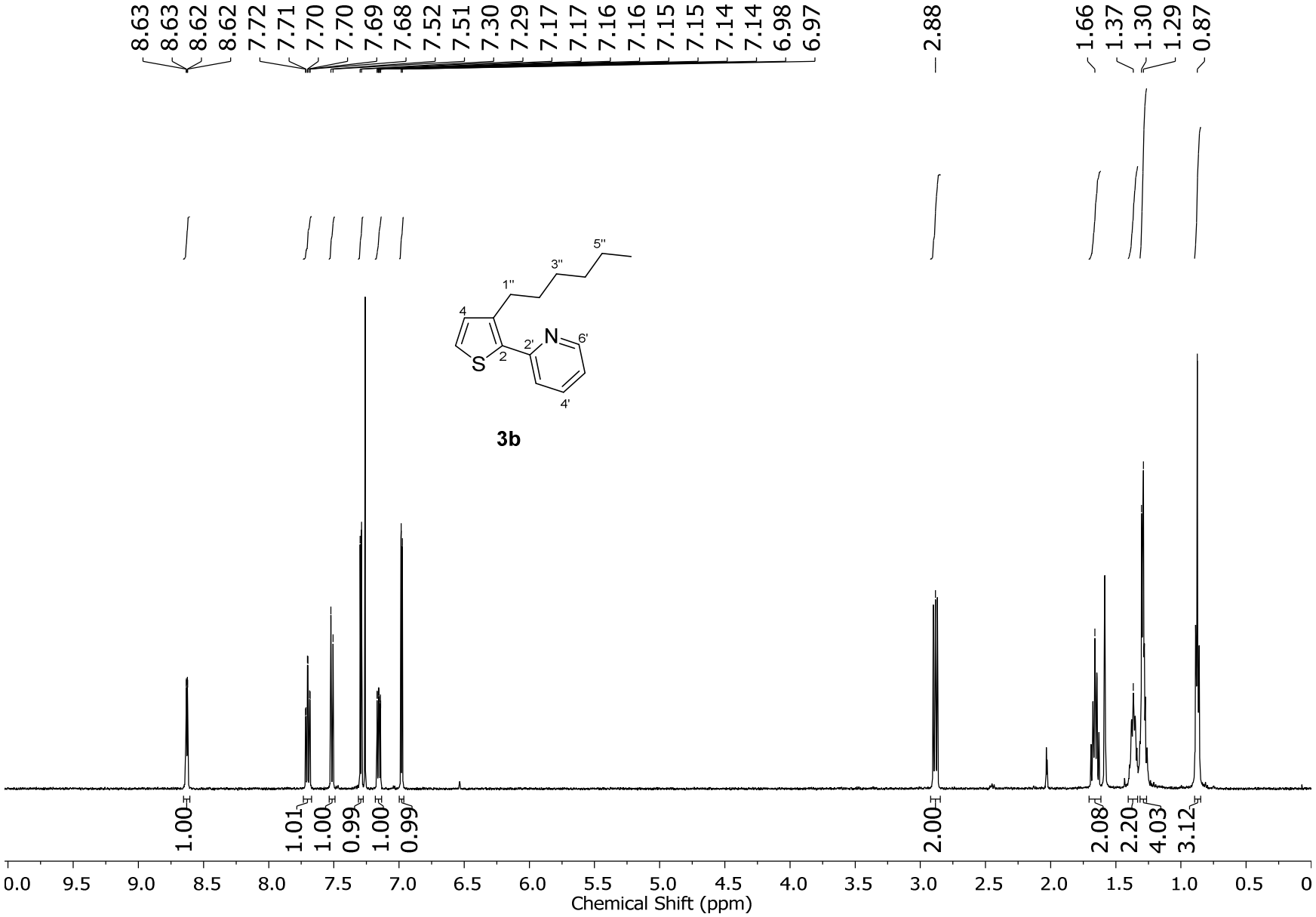

8.60
7.65
7.48
7.17
7.16
7.16
7.14
7.12
7.11
7.10
6.87
6.54
6.23
4.23
1.29
1.00
1.07
1.09
3.17
2.05
2.09
1.04
2.19
2.18
3.45
Chemical Shift (ppm)

11

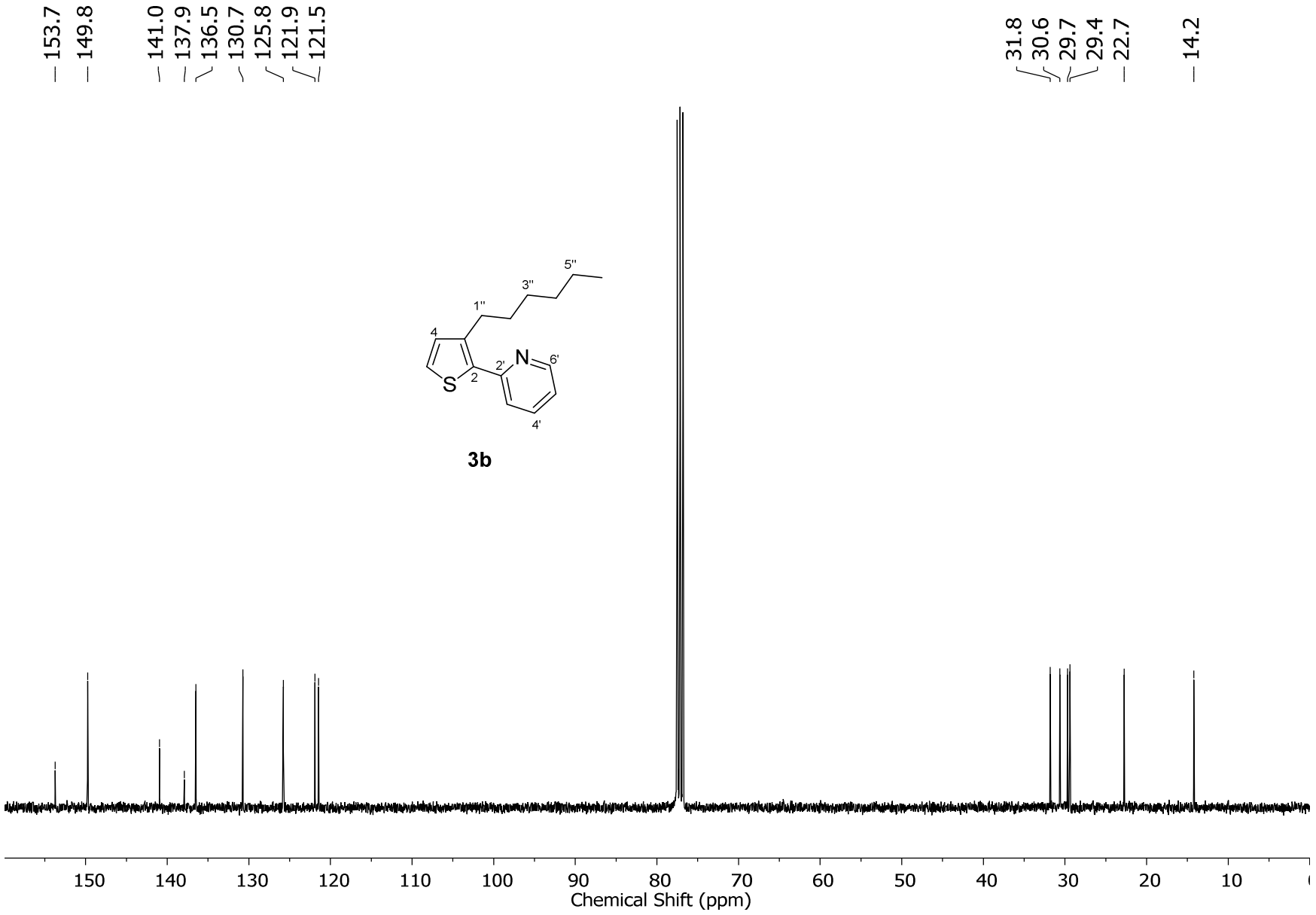

161.0
151.7
149.1
139.7
139.0
136.6
128.2
126.5
126.1
125.0
123.5
121.9
118.3
111.1
59.9
48.9
14.3
8
O
6
O
4
N
2
2'
N
6'
4'
9
13
11
11
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

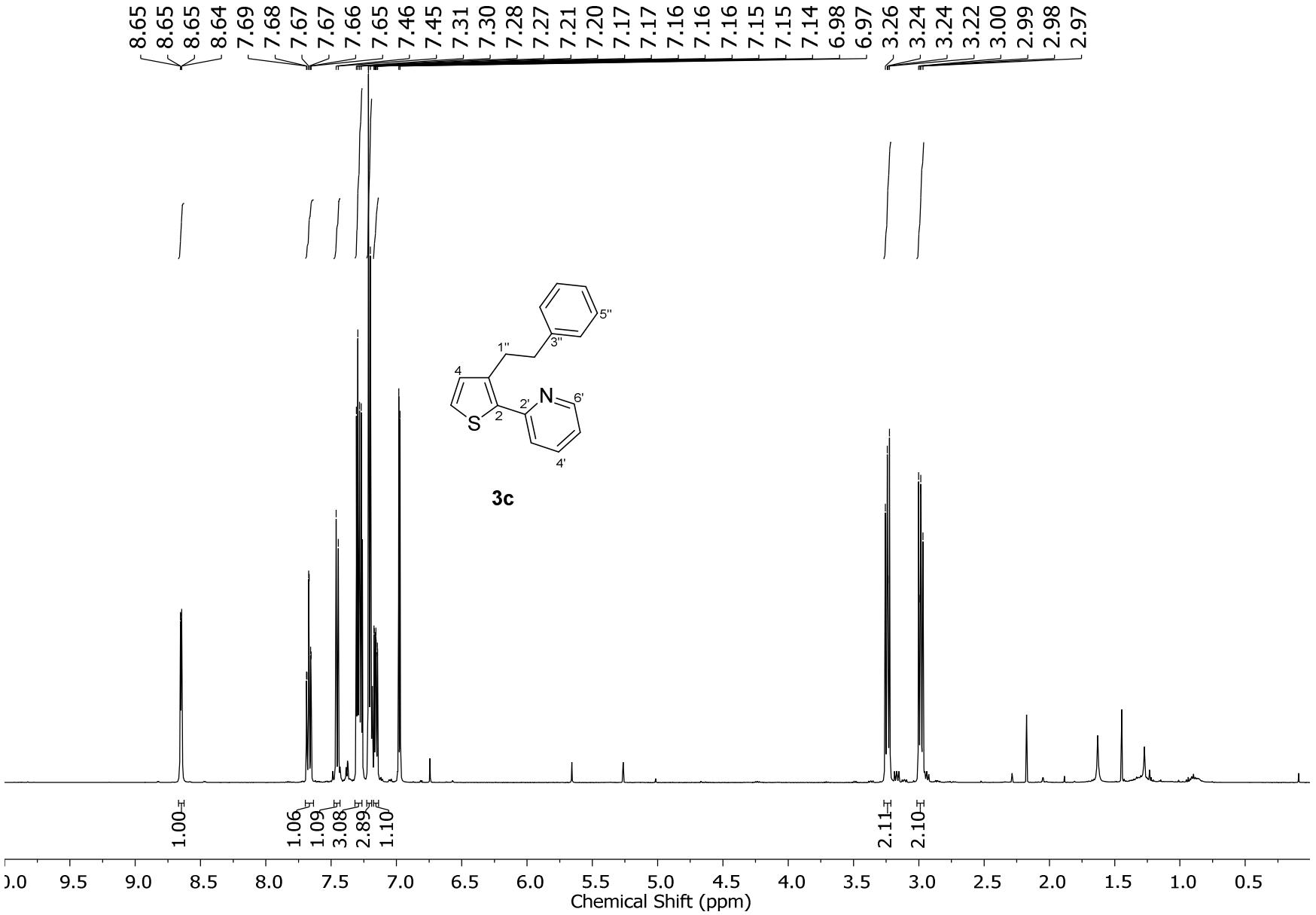

8.64
8.63
8.63
8.62
7.72
7.71
7.70
7.70
7.68
7.68
7.53
7.51
7.30
7.29
7.17
7.16
7.15
7.14
6.99
6.98
2.91
2.90
2.88
1.68
1.67
1.65
1.64
1.62
1.43
1.41
1.40
1.39
1.37
1.36
0.94
0.92
0.91
3"
1"
4
2
S
2'
N
6'
4'
3a
1.00
1.07
1.00
0.97
1.02
1.00
2.14
2.44
2.31
3.37
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

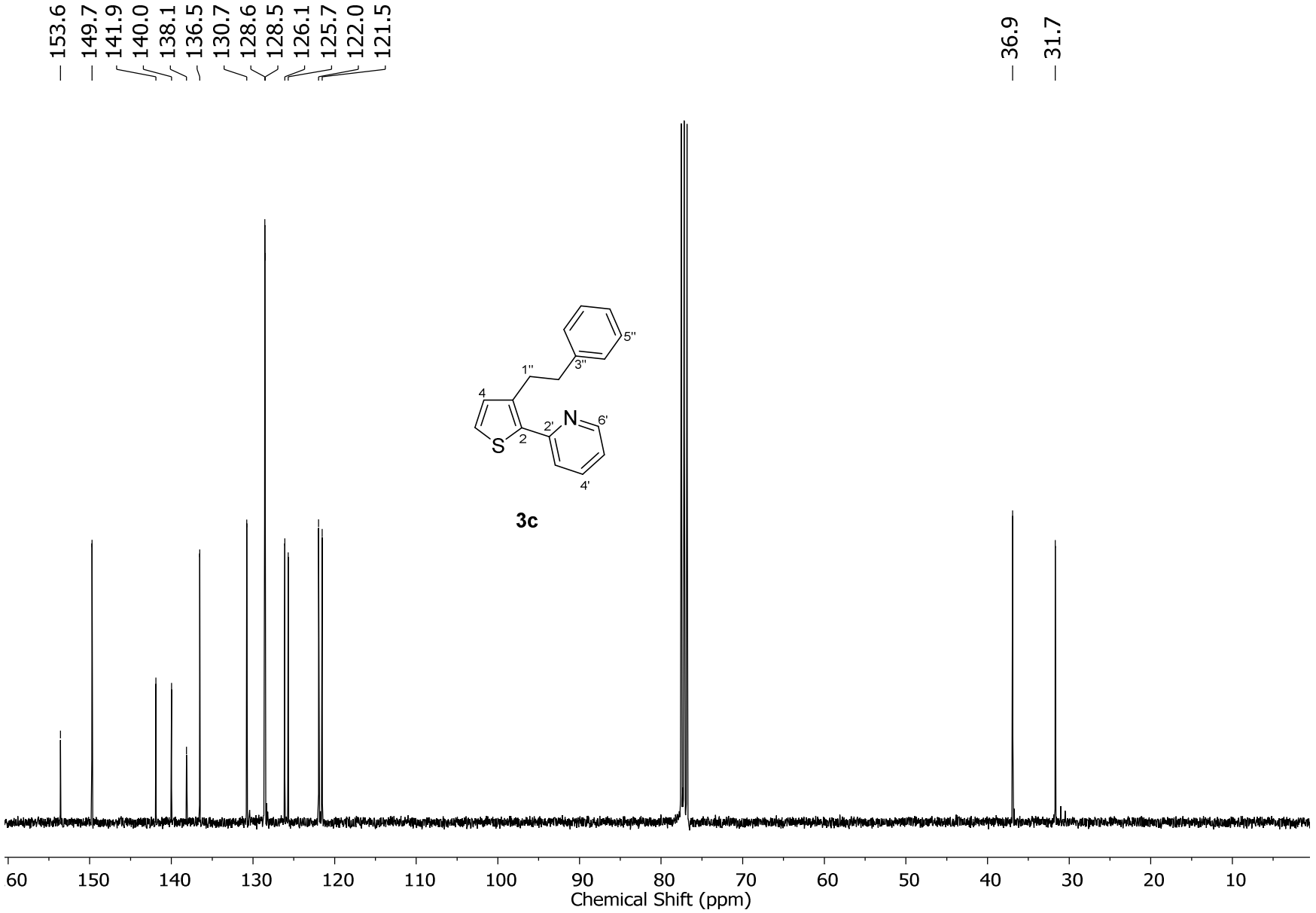

153.7
149.7
140.9
137.9
136.5
130.7
125.8
121.9
121.5
32.8
29.4
22.8
14.1
3"
1"
4
2
S
2'
N
6'
4'
3a
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

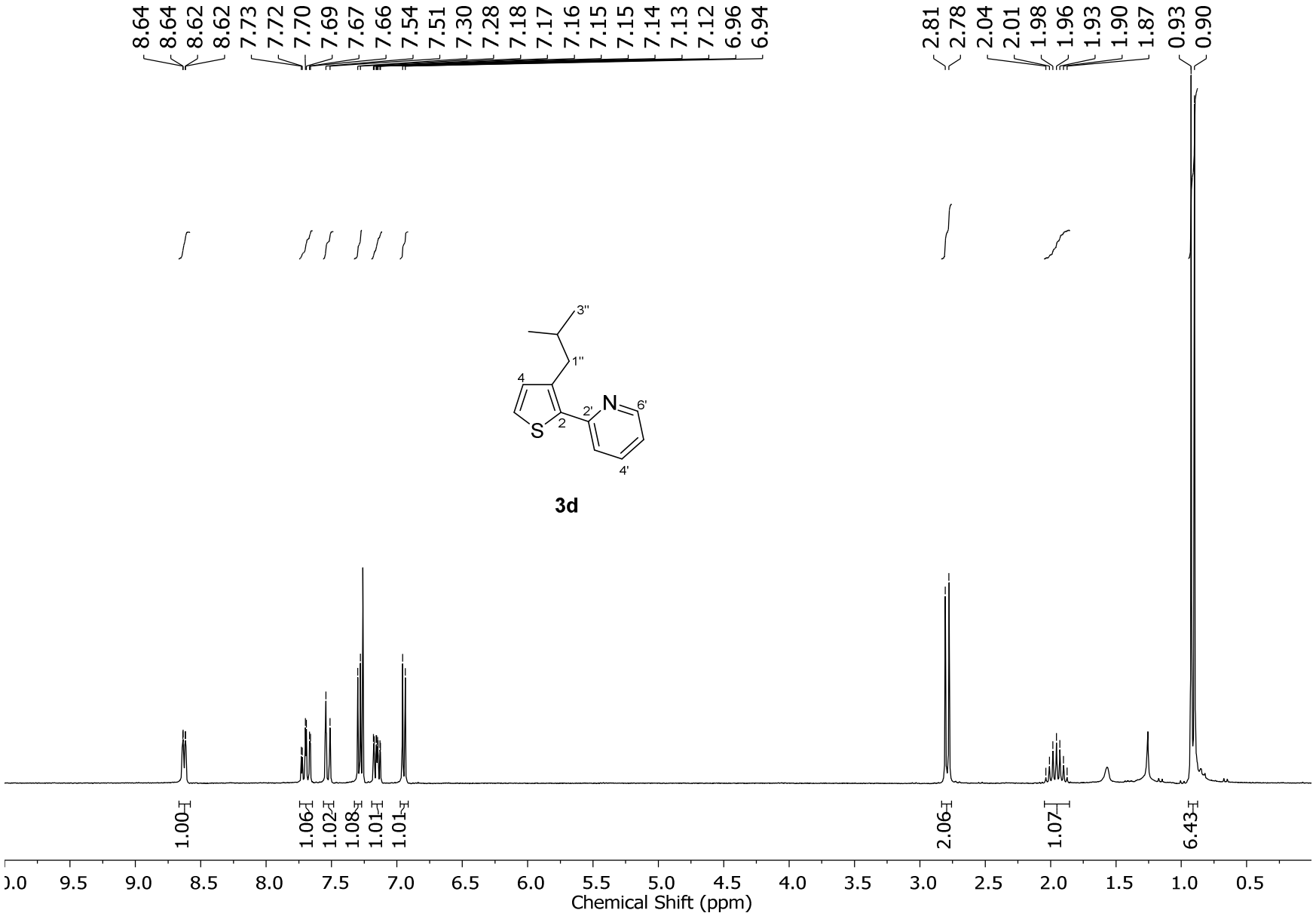

8.63
8.63
8.62
8.62
7.72
7.71
7.70
7.70
7.69
7.68
7.52
7.51
7.30
7.29
7.17
7.17
7.16
7.16
7.15
7.15
7.14
7.14
6.98
6.97
2.88
1.66
1.37
1.30
1.29
0.87
5''
3''
1''
4
2'
N
6'
S
2
4'
1.00
1.01
1.00
0.99
1.00
0.99
2.00
2.08
2.20
4.03
3.12
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

3b

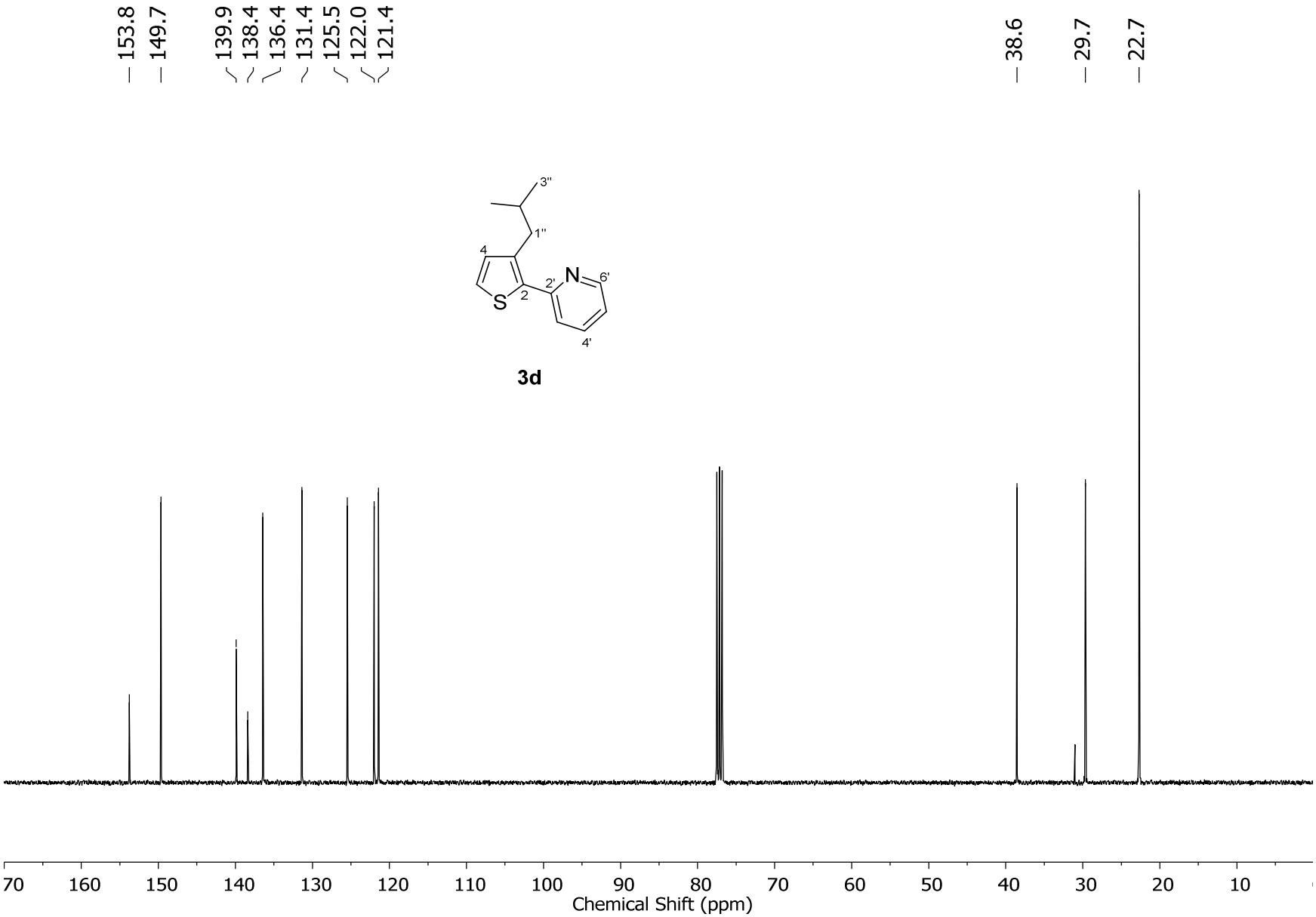

153.7
149.8
141.0
137.9
136.5
130.7
125.8
121.9
121.5
31.8
30.6
29.7
29.4
22.7
14.2
5''
3''
1''
4
2
S
2'
N
6'
4'
3b
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

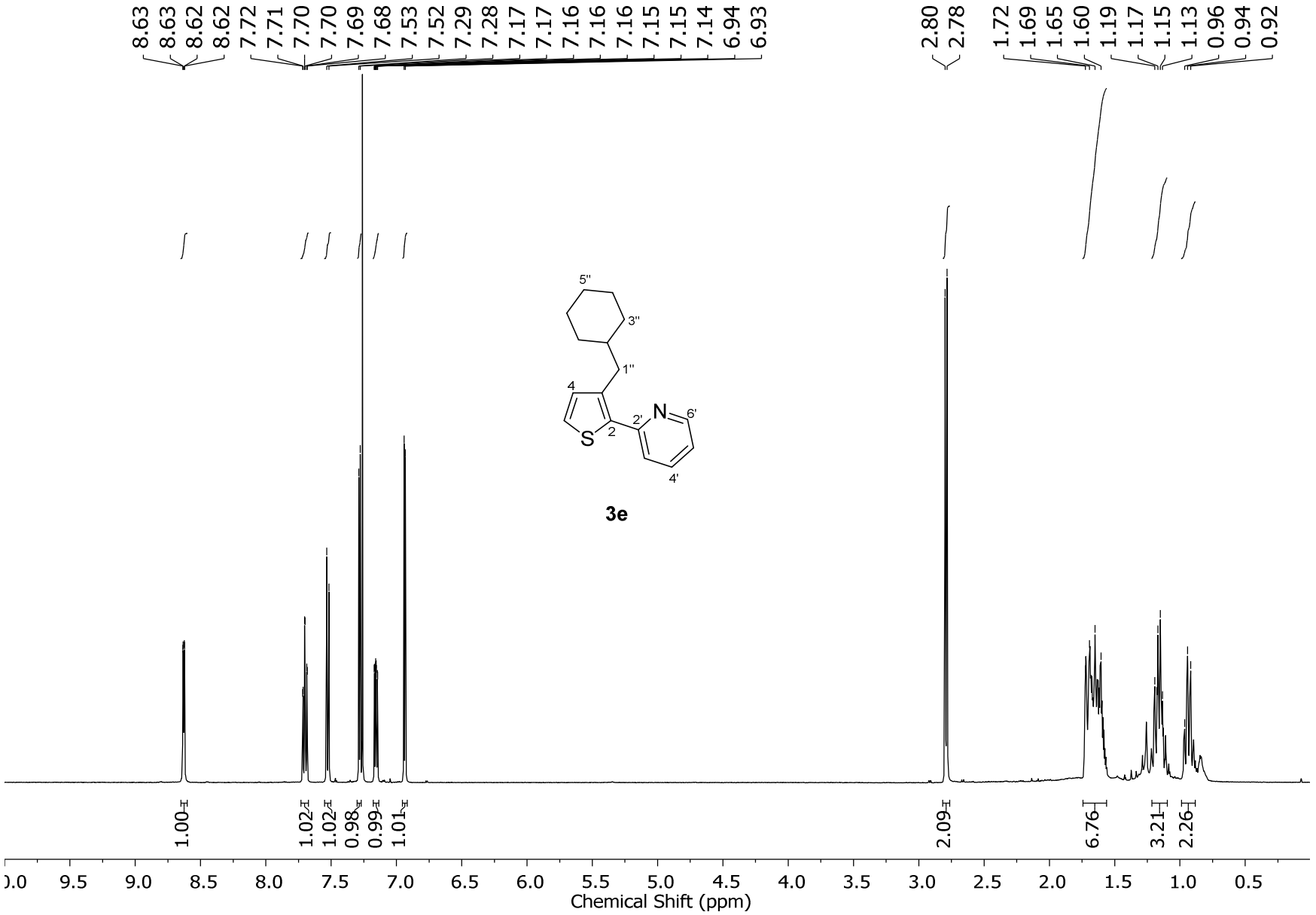

8.65
8.65
8.65
8.64
7.69
7.68
7.67
7.67
7.66
7.65
7.46
7.45
7.31
7.30
7.28
7.27
7.21
7.20
7.17
7.17
7.16
7.16
7.16
7.15
7.15
7.14
6.98
6.97
3.26
3.24
3.24
3.22
3.00
2.99
2.98
2.97
5''
3''
1''
4
2'
N
6'
S
2
4'
3c
1.00
1.06
1.09
3.08
2.89
1.10
2.11
2.10
Chemical Shift (ppm)

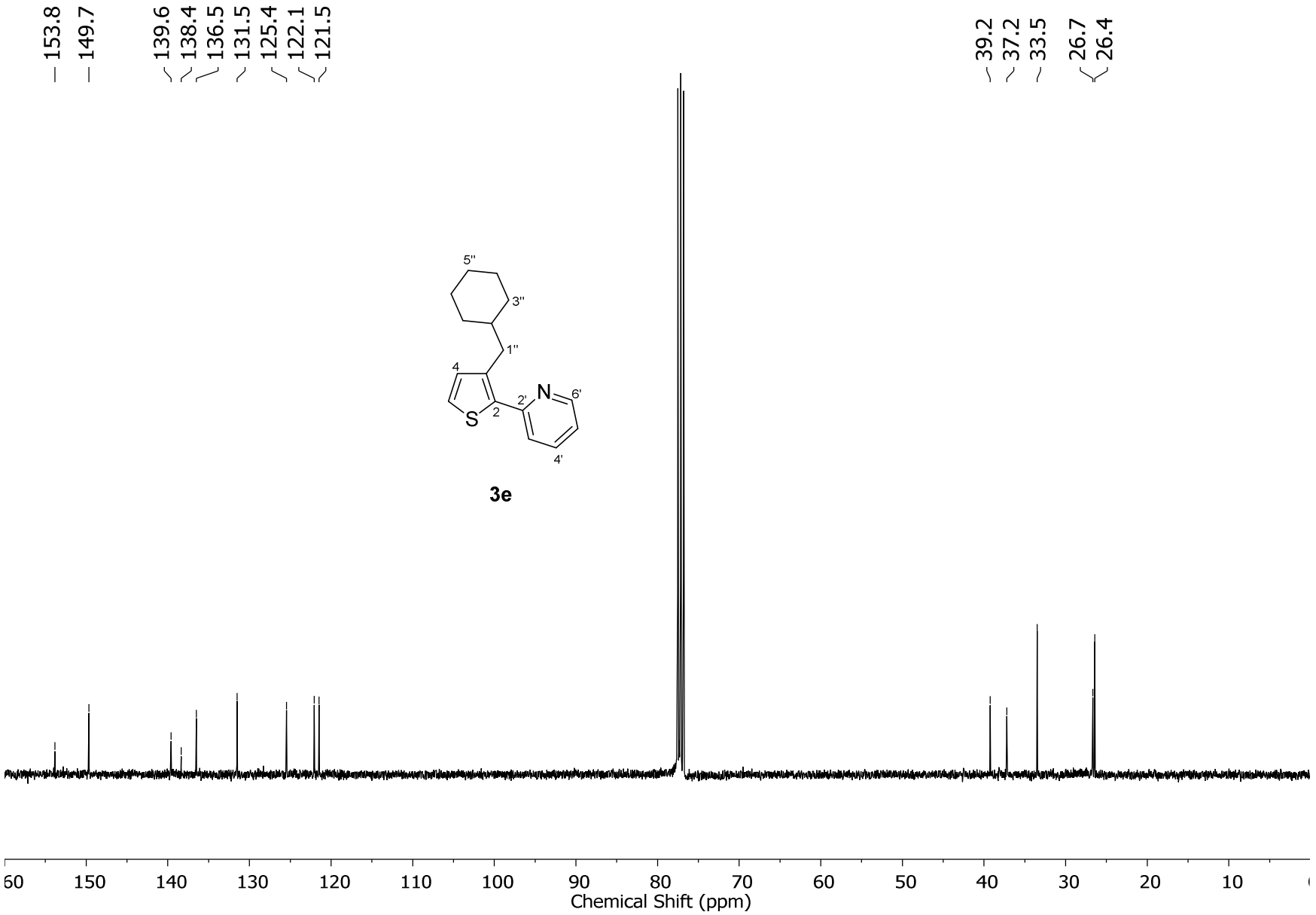

153.6
149.7
141.9
140.0
138.1
136.5
130.7
128.6
128.5
126.1
125.7
122.0
121.5
36.9
31.7
5''
3''
1''
4
2'
N
6'
S
2
4'
3c
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

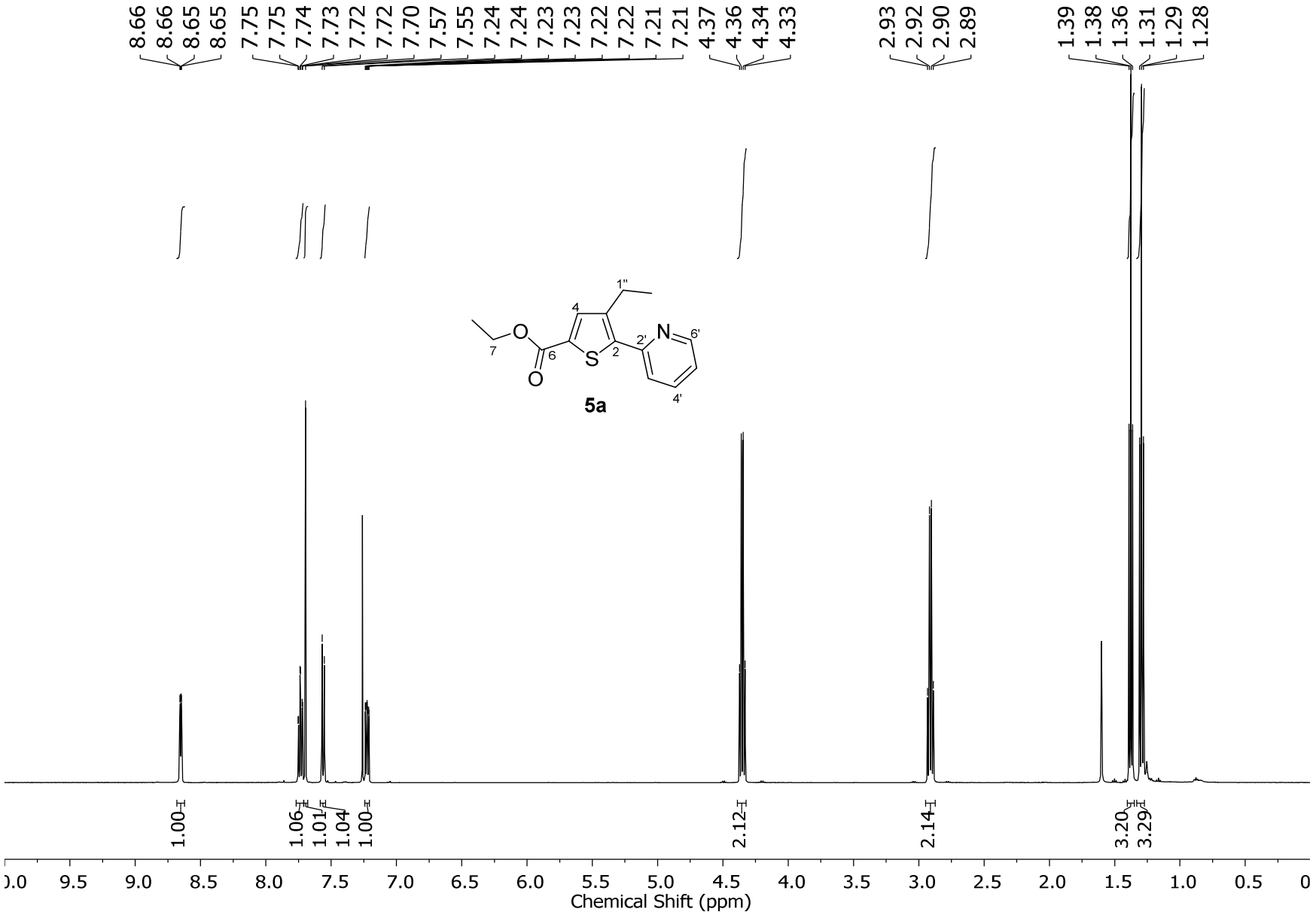

8.64
8.64
8.62
8.62
7.73
7.72
7.70
7.69
7.67
7.66
7.54
7.51
7.30
7.28
7.18
7.17
7.16
7.15
7.15
7.14
7.13
7.12
6.96
6.94
2.81
2.78
2.04
2.01
1.98
1.96
1.93
1.90
1.87
0.93
0.90
3''
1''
4
2
S
2'
N
6'
4'
1.00
1.06
1.02
1.08
1.01
1.01
2.06
1.07
6.43
Chemical Shift (ppm)

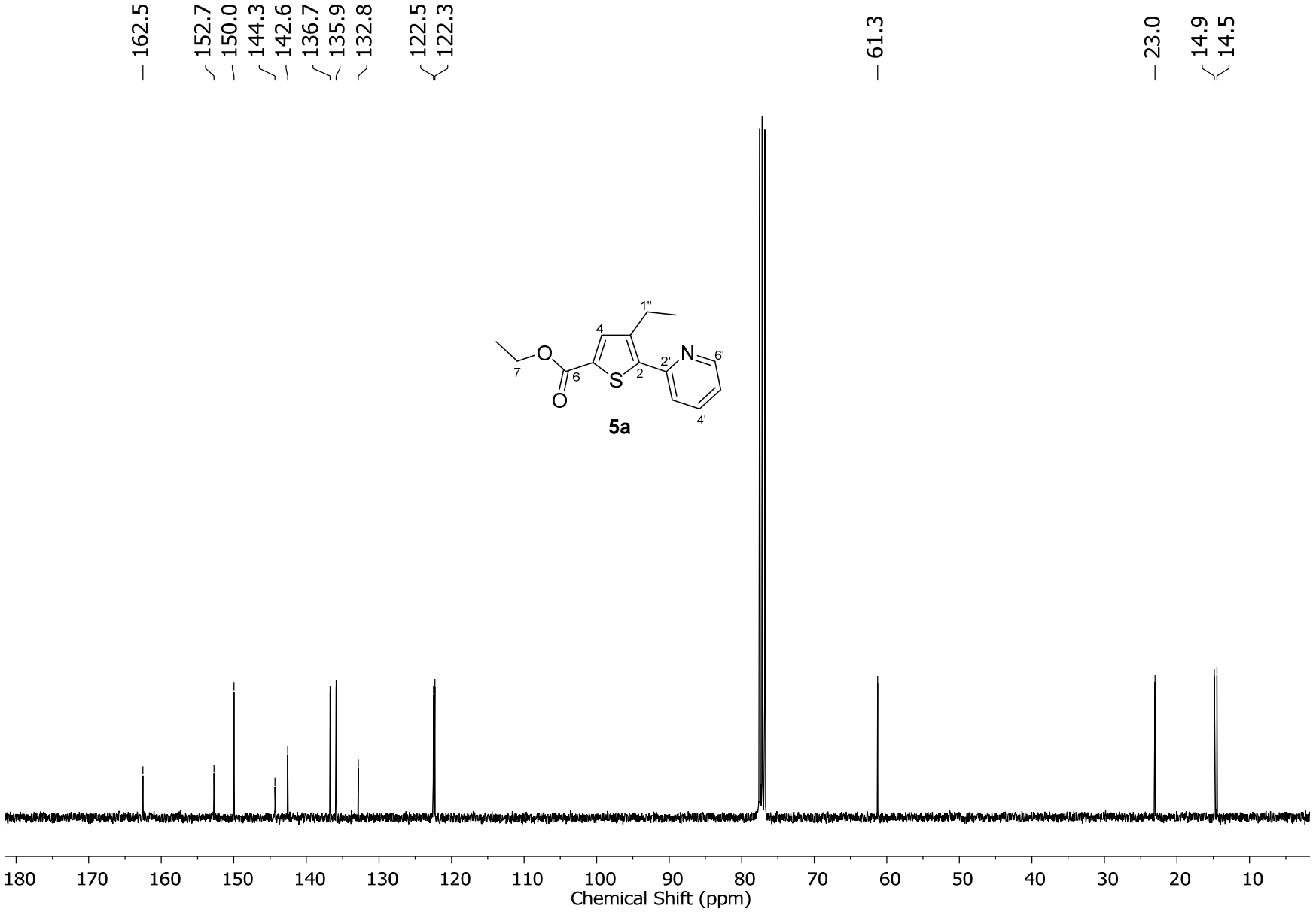
3d

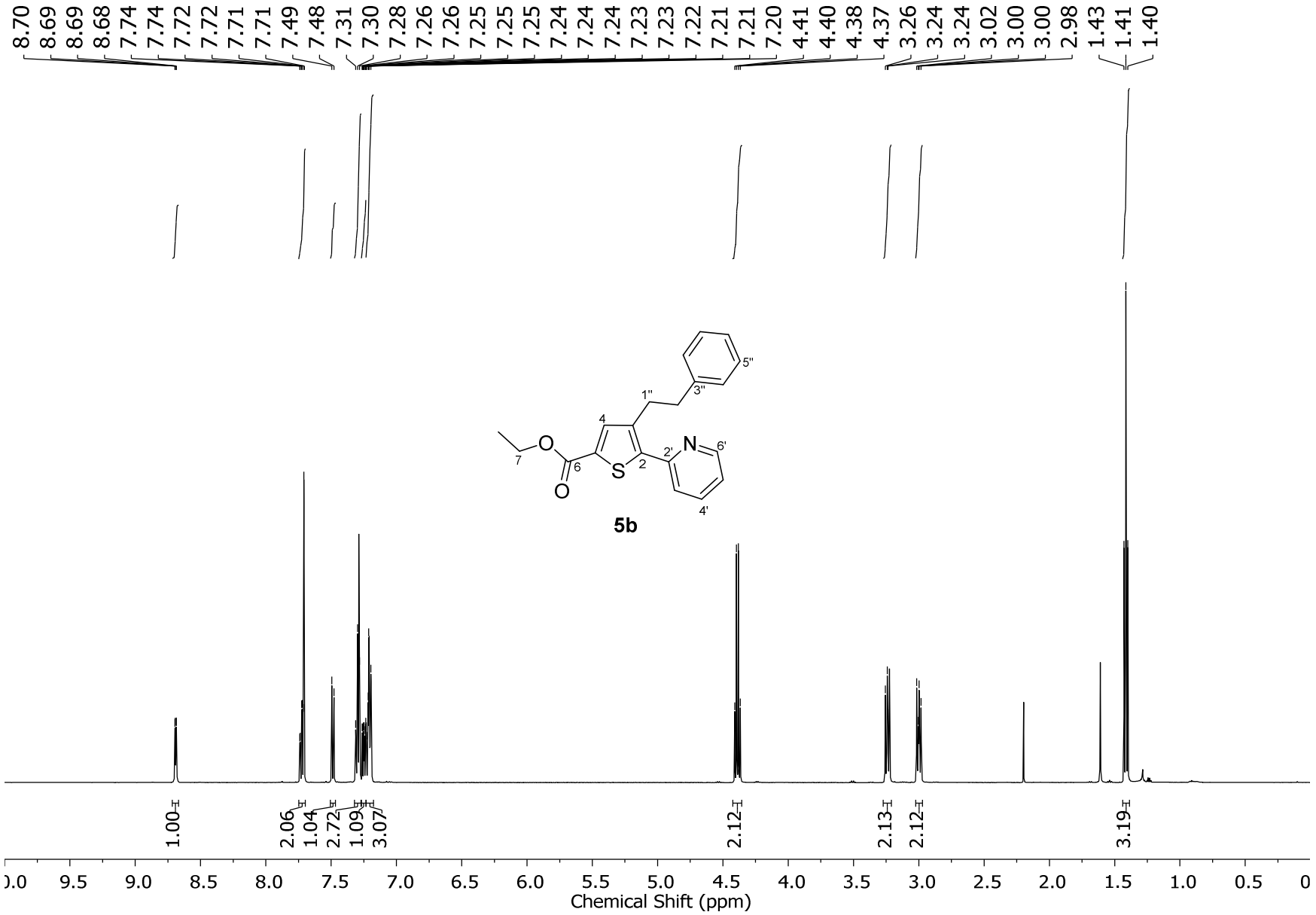

153.8
149.7
139.9
138.4
136.4
131.4
125.5
122.0
121.4
38.6
29.7
22.7
3''
1''
4
2
S
2'
N
6'
4'
3d
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

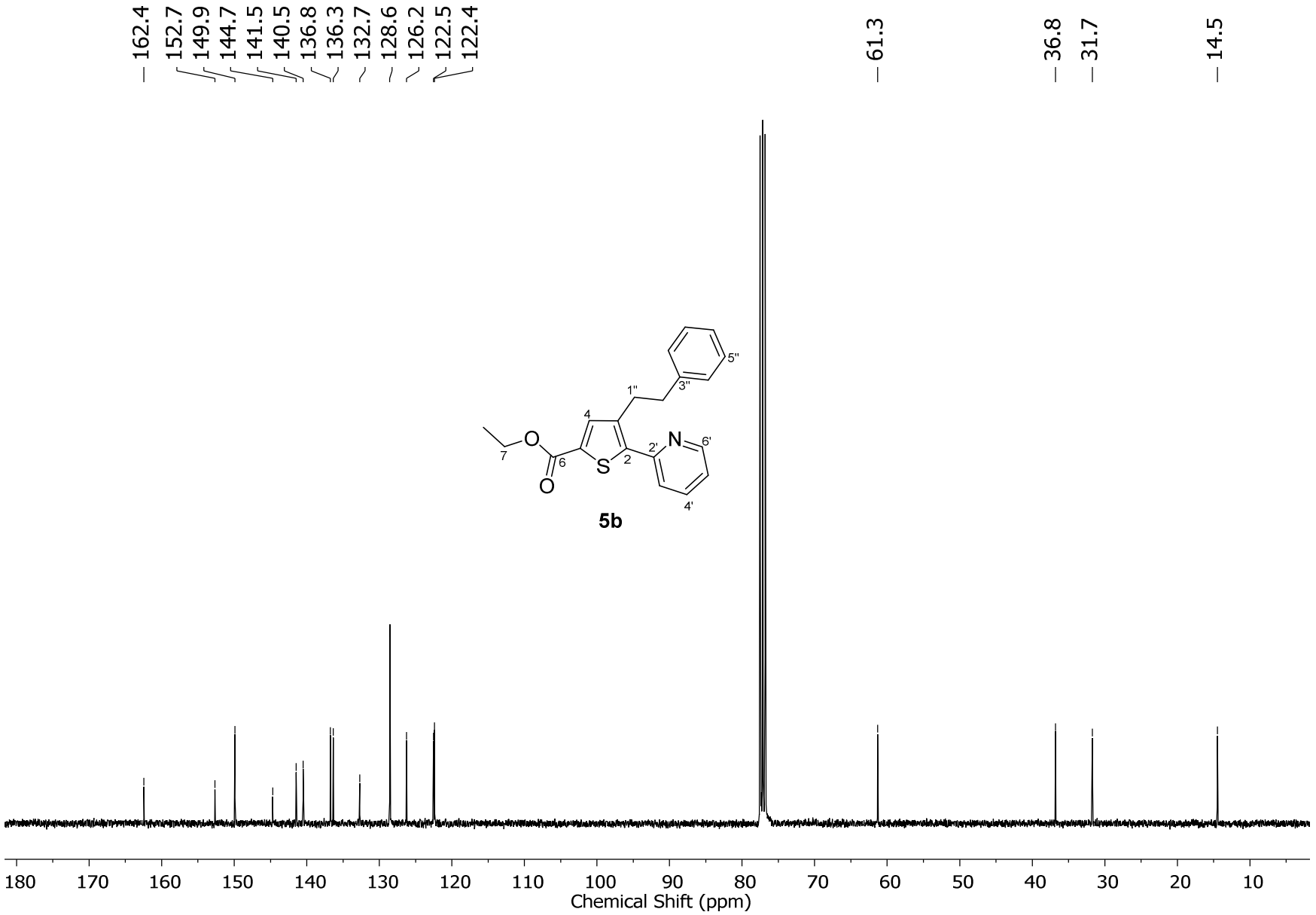

8.63
8.63
8.62
8.62
7.72
7.71
7.70
7.70
7.69
7.68
7.53
7.52
7.29
7.28
7.17
7.17
7.16
7.16
7.16
7.15
7.15
7.14
6.94
6.93
2.80
2.78
1.72
1.69
1.65
1.60
1.19
1.17
1.15
1.13
0.96
0.94
0.92
5''
3''
1''
4
2'
N
6'
S
2
4'
3e
1.00
1.02
1.02
0.98
0.99
1.01
2.09
6.76
3.21
2.26
Chemical Shift (ppm)

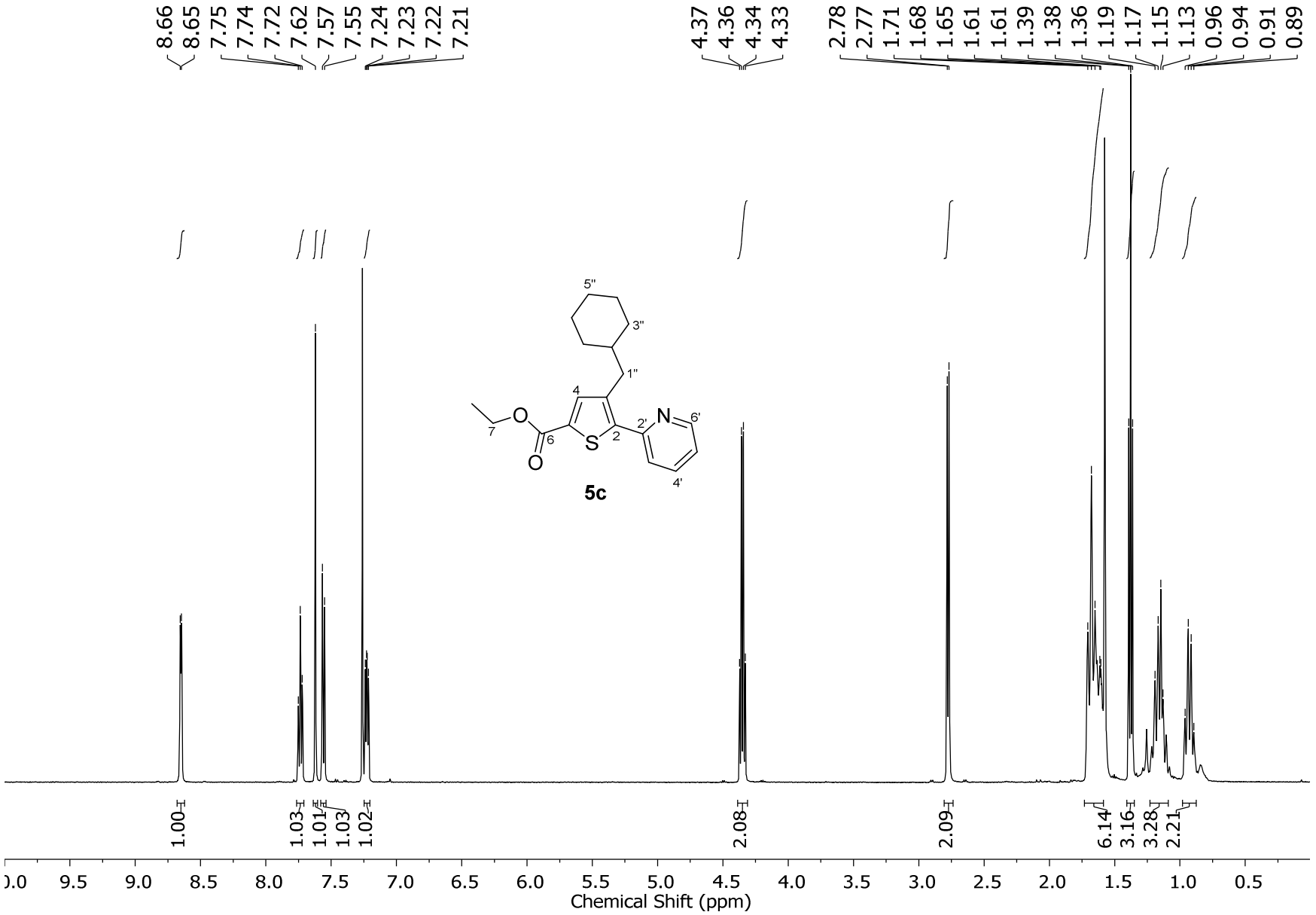

153.8
149.7
139.6
138.4
136.5
131.5
125.4
122.1
121.5
39.2
37.2
33.5
26.7
26.4
5''
3''
1''
4
2
S
2'
N
6'
4'
3e
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

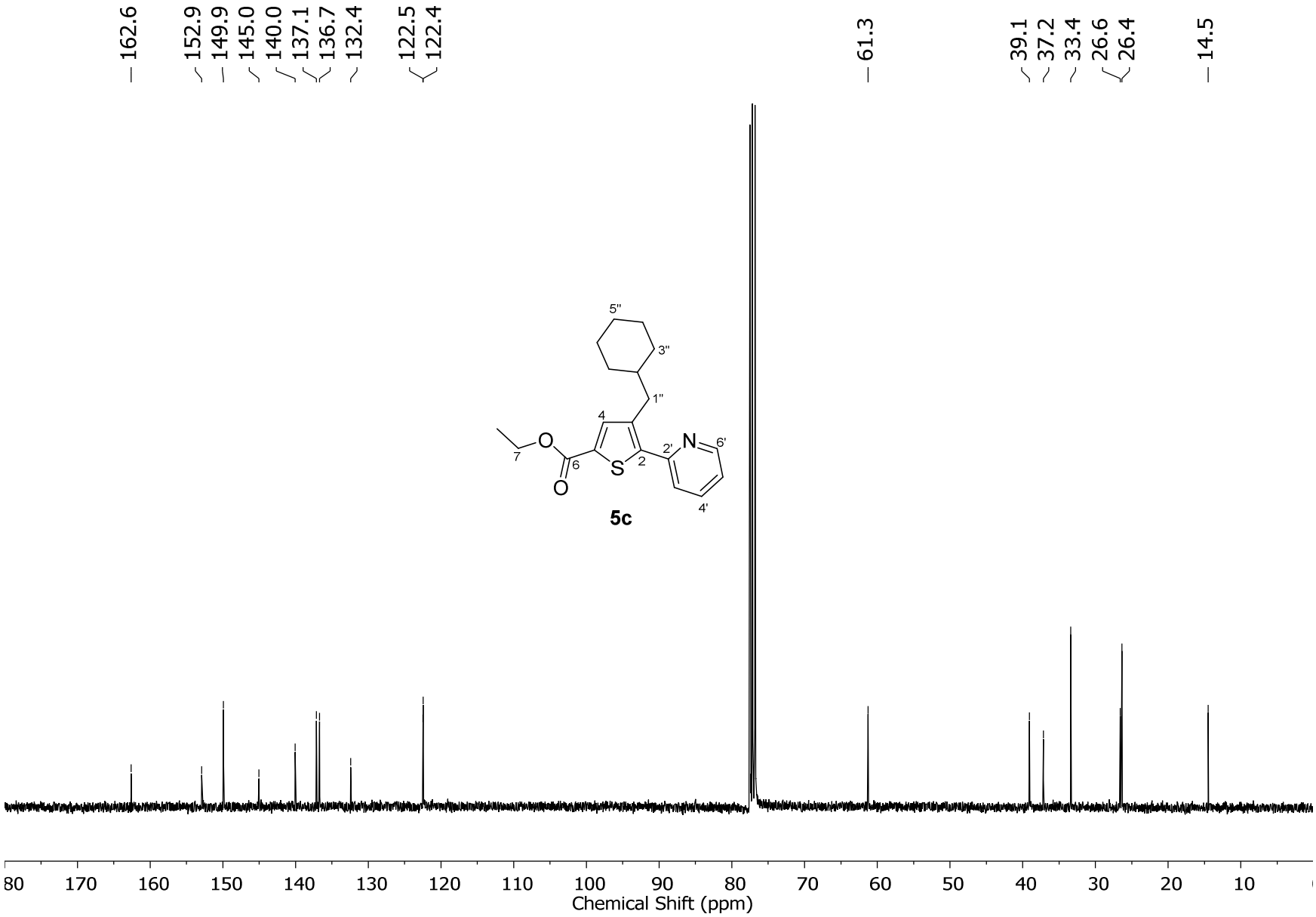

8.66
8.66
8.65
8.65
7.75
7.75
7.74
7.73
7.72
7.72
7.70
7.57
7.55
7.24
7.24
7.23
7.23
7.22
7.22
7.21
7.21
4.37
4.36
4.34
4.33
2.93
2.92
2.90
2.89
1.39
1.38
1.36
1.31
1.29
1.28
1"
4
O
7
6
S
2
2'
N
6'
O
4'
5a
1.00
1.06
1.01
1.04
1.00
2.12
2.14
3.20
3.29
Chemical Shift (ppm)

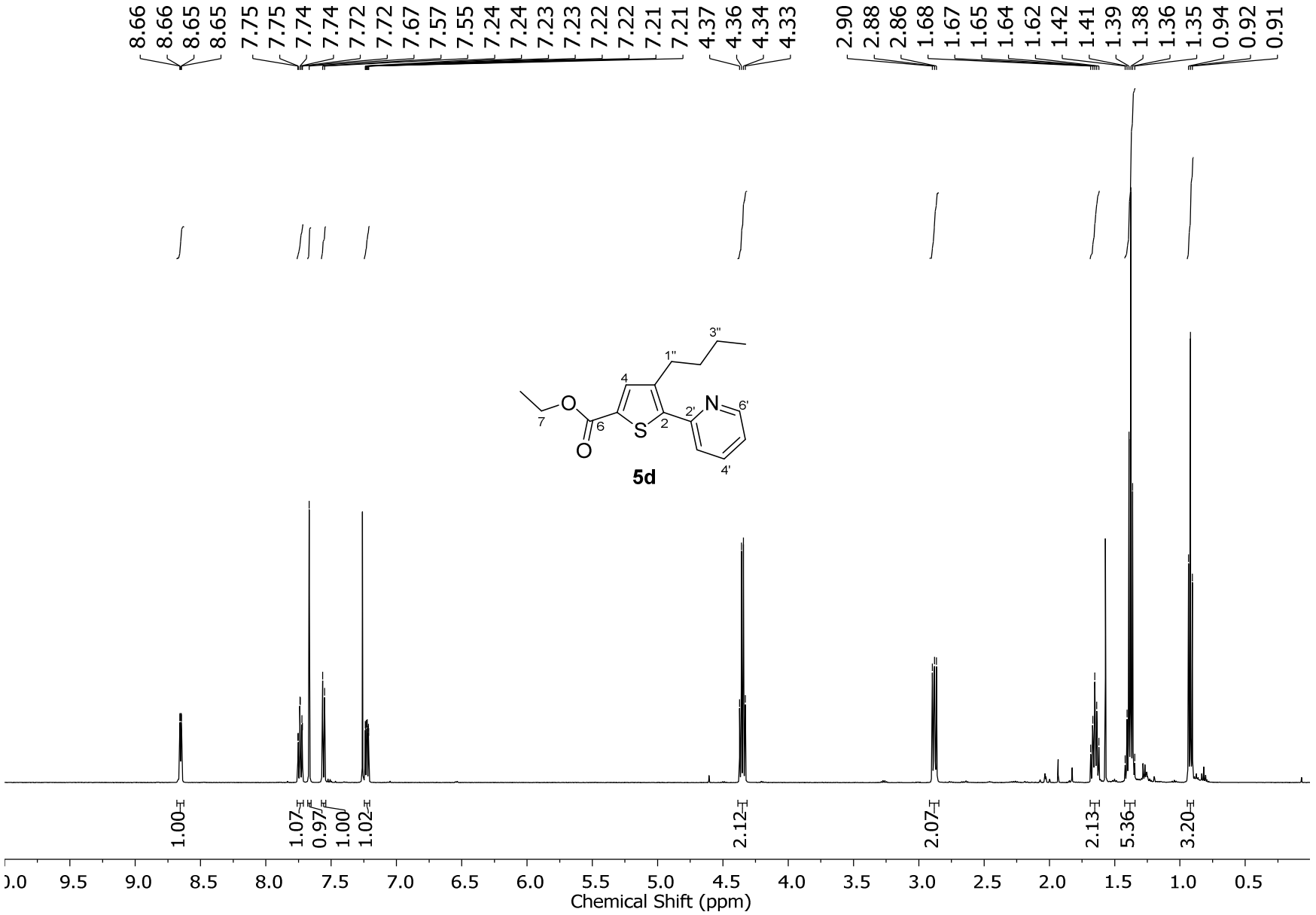

162.5
152.7
150.0
144.3
142.6
136.7
135.9
132.8
122.5
122.3
61.3
23.0
14.9
14.5
1"
4
O
7
6
O
S
2
2'
N
6'
4'
5a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)


8.70
8.69
8.69
8.68
7.74
7.74
7.72
7.72
7.71
7.71
7.49
7.48
7.31
7.30
7.28
7.26
7.26
7.25
7.25
7.25
7.24
7.24
7.24
7.23
7.23
7.22
7.21
7.21
7.20
4.41
4.40
4.38
4.37
3.26
3.24
3.24
3.02
3.00
3.00
2.98
1.43
1.41
1.40
5"
3"
1"
4
2'
N
6'
7
O
6
S
2
O
4'
5b
1.00
2.06
1.04
2.72
1.09
3.07
2.12
2.13
2.12
3.19
Chemical Shift (ppm)


162.4
152.7
149.9
144.7
141.5
140.5
136.8
136.3
132.7
128.6
126.2
122.5
122.4
61.3
36.8
31.7
14.5
5"
3"
1"
4
2'
N
6'
7
O
6
S
2
O
4'
5b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)


8.66
8.65
7.75
7.74
7.72
7.62
7.57
7.55
7.24
7.23
7.22
7.21
4.37
4.36
4.34
4.33
2.78
2.77
1.71
1.68
1.65
1.61
1.61
1.39
1.38
1.36
1.19
1.17
1.15
1.13
0.96
0.94
0.91
0.89
5"
3"
1"
4
O
7
6
O
S
2
2'
N
6'
4'
5c
1.00
1.03
1.01
1.03
1.02
2.08
2.09
6.14
3.16
3.28
2.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


162.6
152.9
149.9
145.0
140.0
137.1
136.7
132.4
122.5
122.4
61.3
39.1
37.2
33.4
26.6
26.4
14.5
5"
3"
1"
4
O
7
6
O
S
2
2'
N
6'
4'
5c
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)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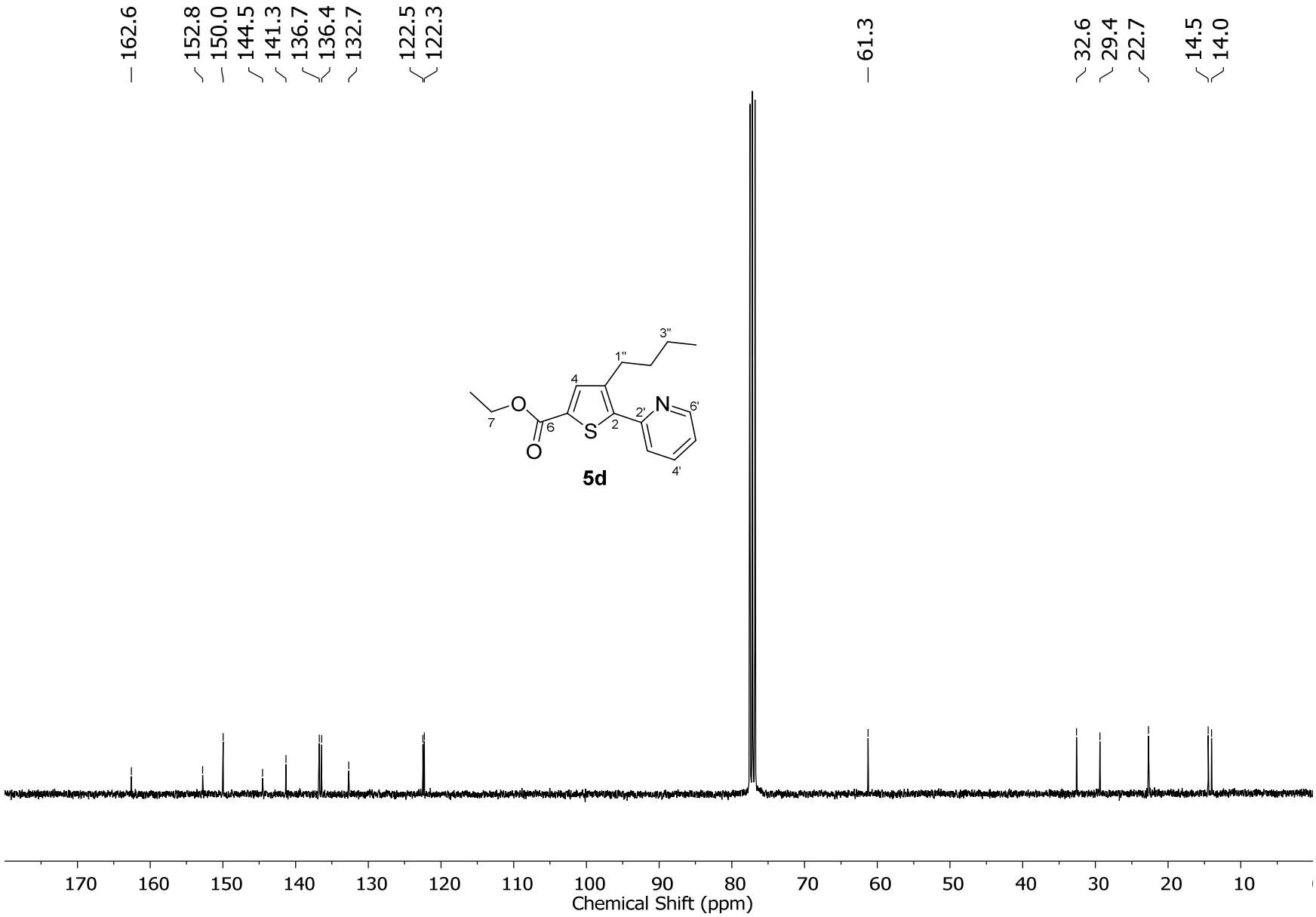
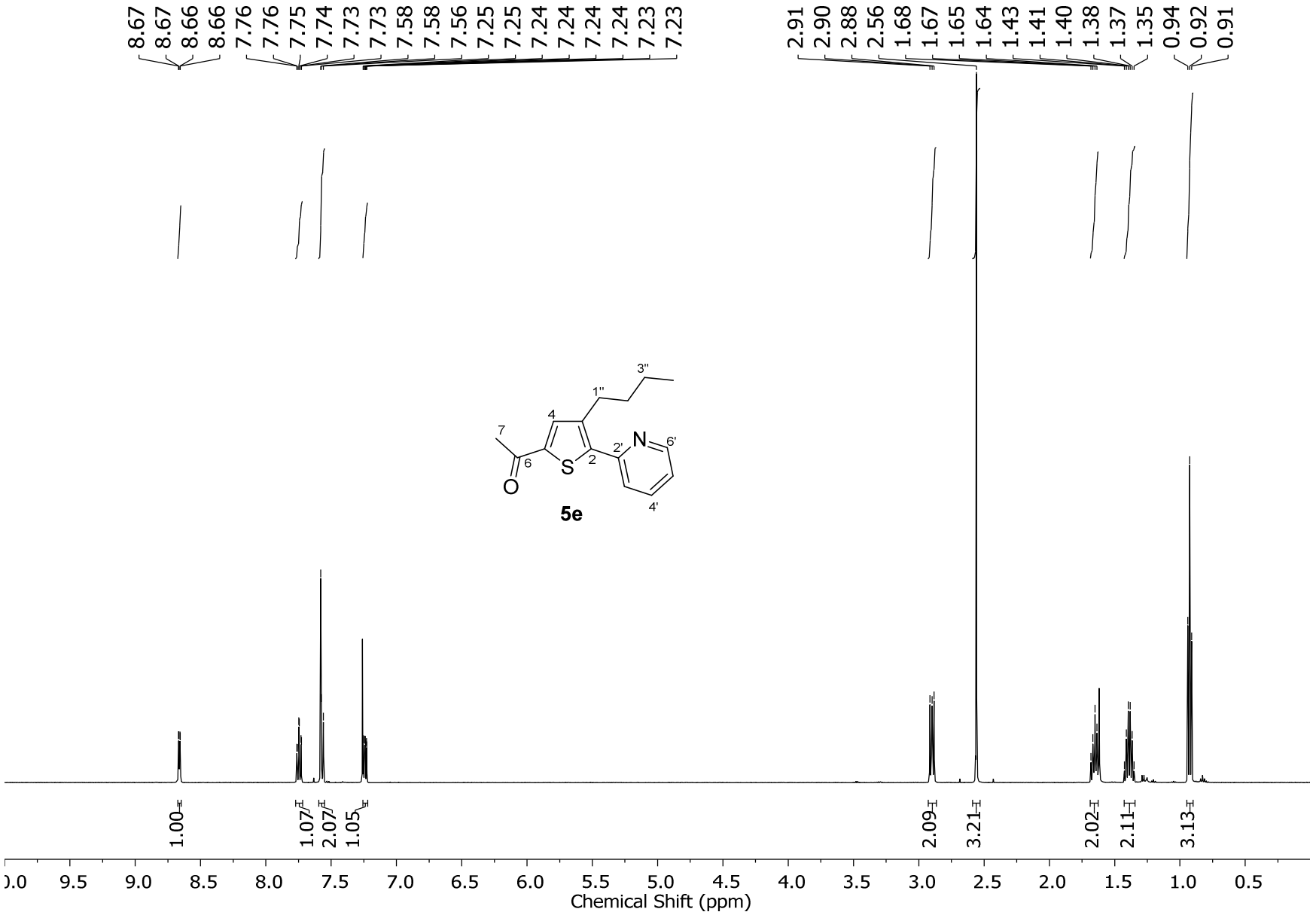
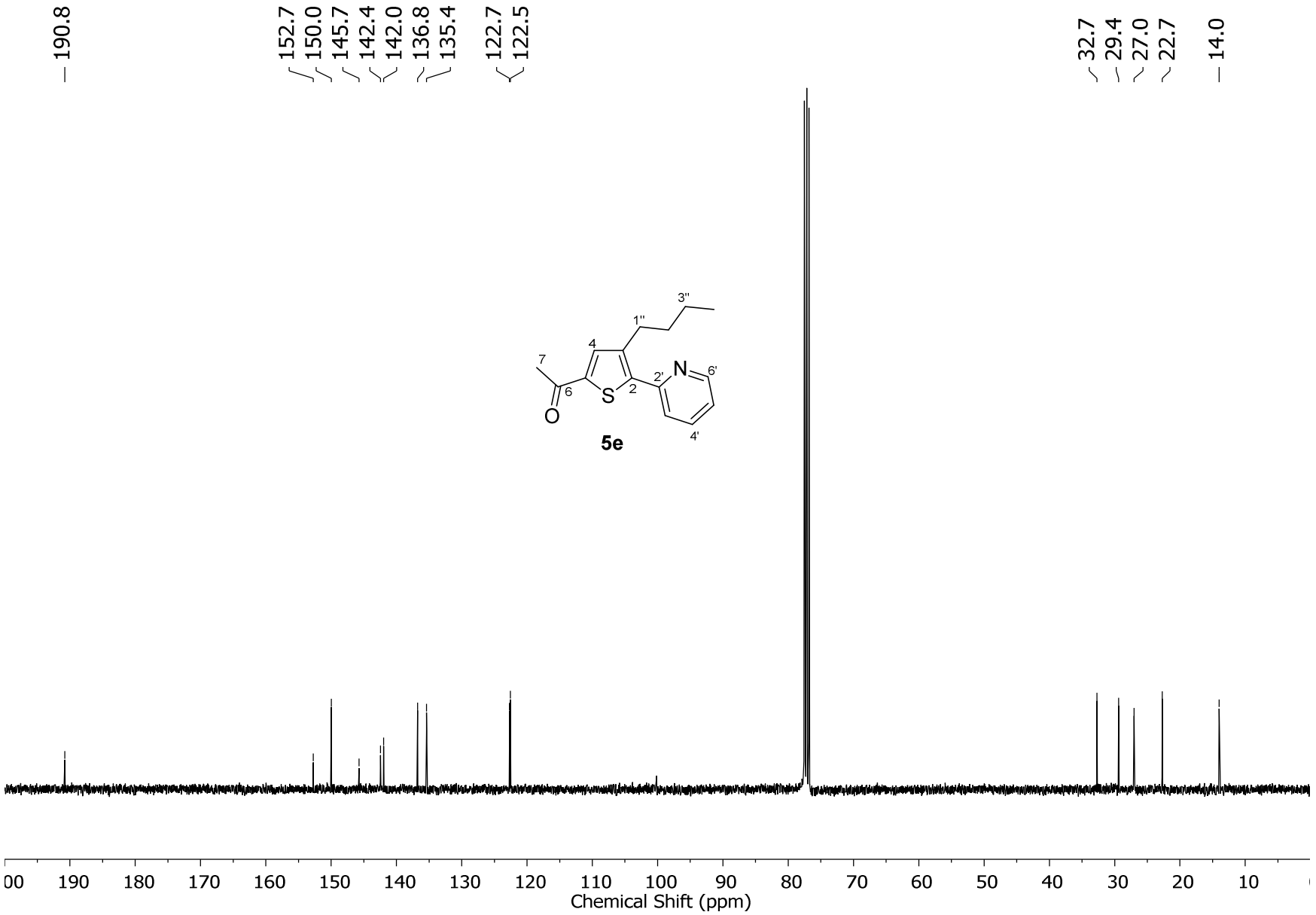
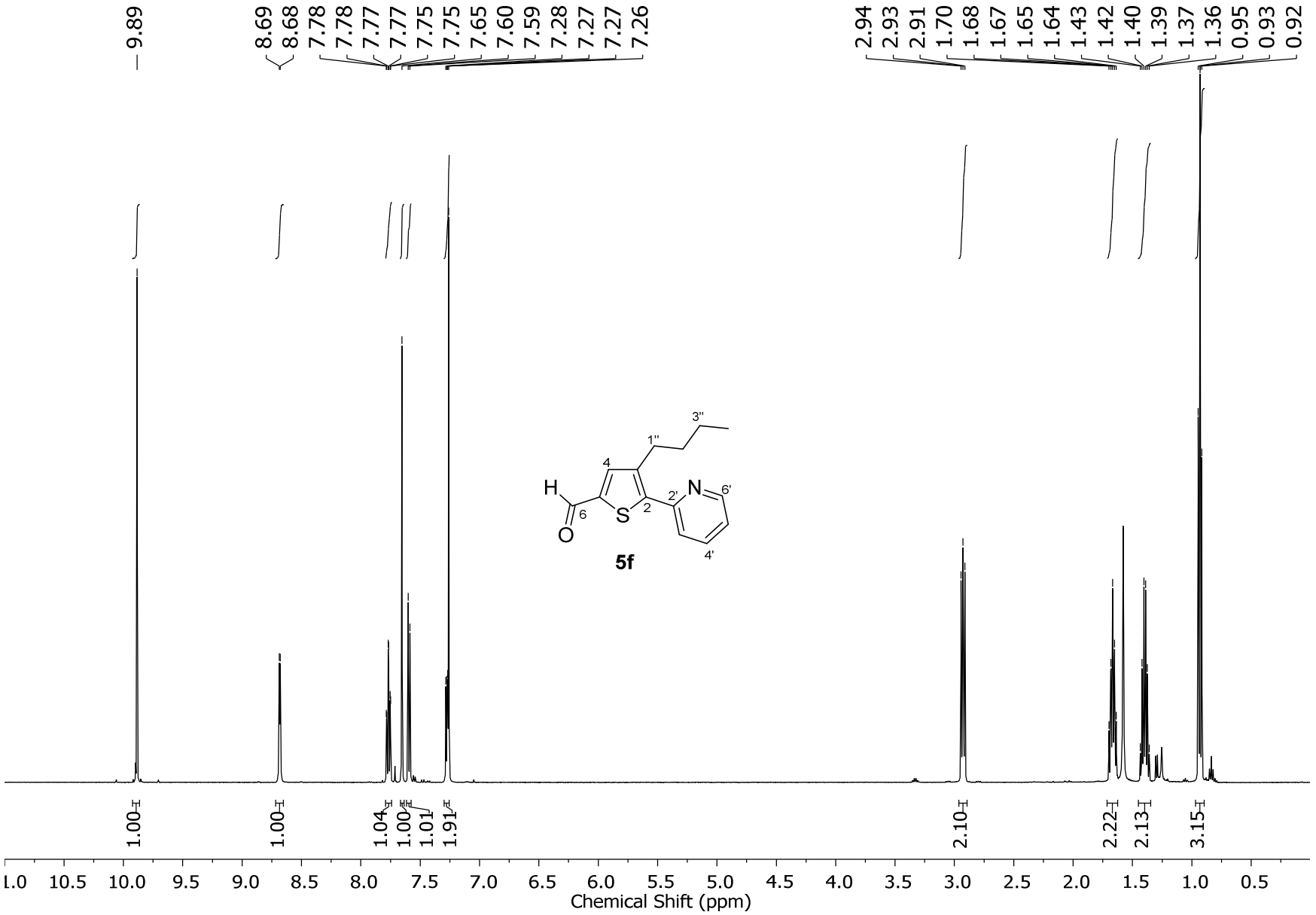
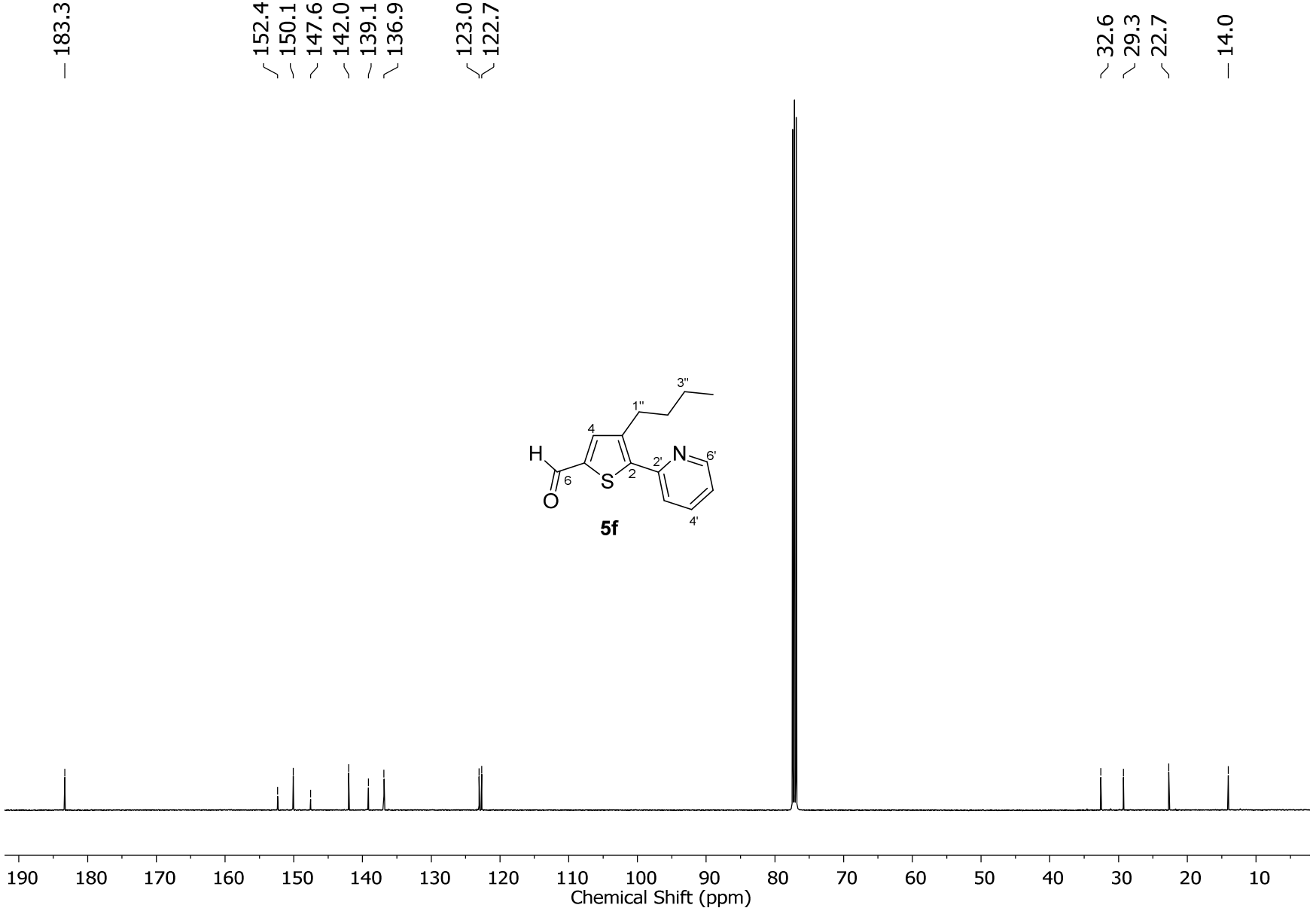
8.66
8.65
8.65
7.75
7.75
7.74
7.74
7.72
7.72
7.67
7.57
7.55
7.24
7.24
7.23
7.23
7.22
7.22
7.21
7.21
4.37
4.36
4.34
4.33
2.90
2.88
2.86
1.68
1.67
1.65
1.64
1.62
1.42
1.41
1.39
1.38
1.36
1.35
0.94
0.92
0.91
3"
1"
4
O
7
6
O
S
2
2'
N
6'
4'
5d
1.00
1.07
0.97
1.00
1.02
2.12
2.07
2.13
5.36
3.20
Chemical Shift (ppm)

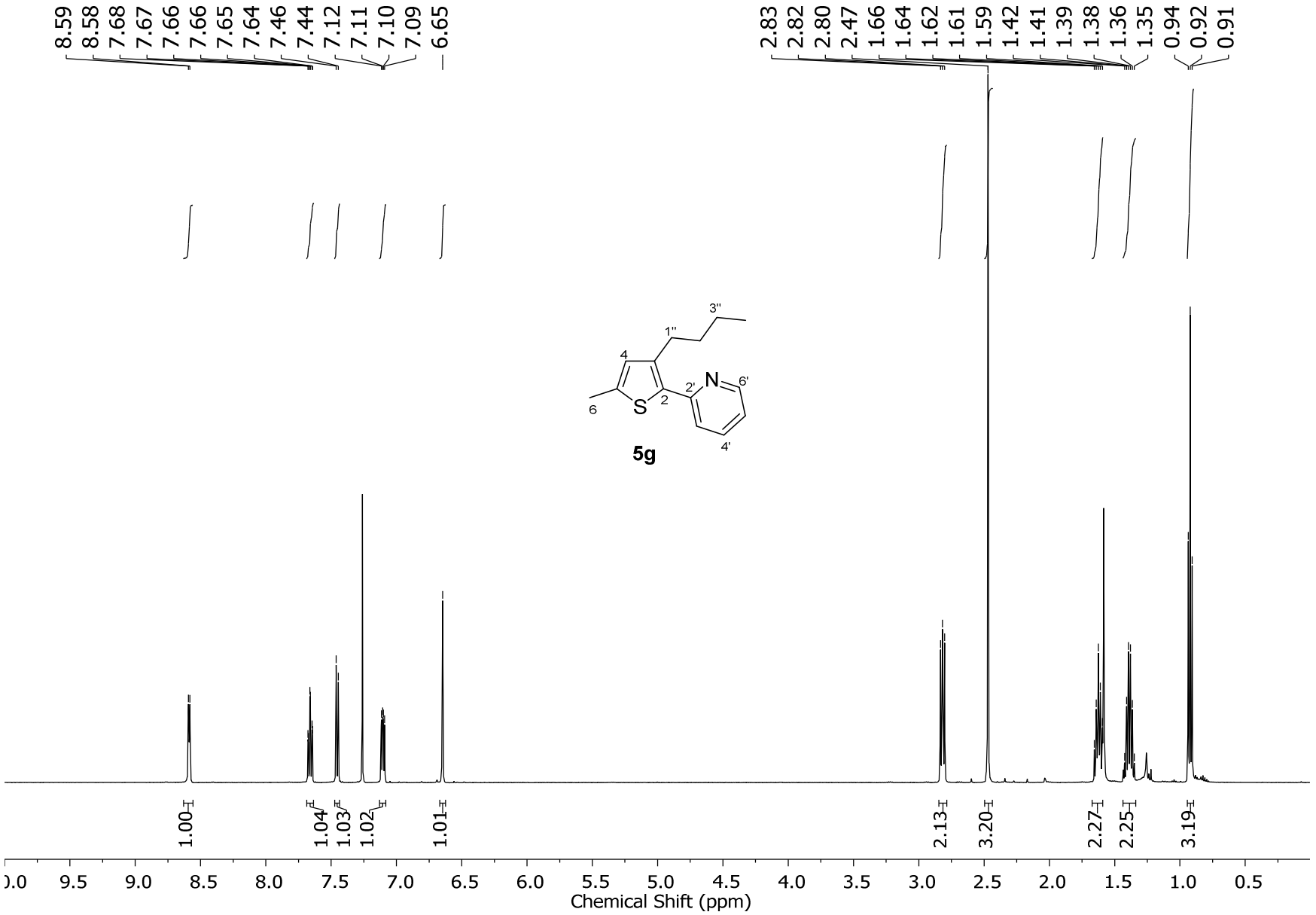

162.6
152.8
150.0
144.5
141.3
136.7
136.4
132.7
122.5
122.3
61.3
32.6
29.4
22.7
14.5
14.0
3''
1''
4
O
7
6
O
S
2
2'
N
6'
4'
5d
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)


8.67
8.67
8.66
8.66
7.76
7.76
7.75
7.74
7.73
7.73
7.58
7.58
7.56
7.25
7.25
7.24
7.24
7.24
7.24
7.23
7.23
2.91
2.90
2.88
2.56
1.68
1.67
1.65
1.64
1.43
1.41
1.40
1.38
1.37
1.35
0.94
0.92
0.91
3''
1''
4
7
2'
N
6'
6
S
2
O
4'
5e
1.00
1.07
2.07
1.05
2.09
3.21
2.02
2.11
3.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

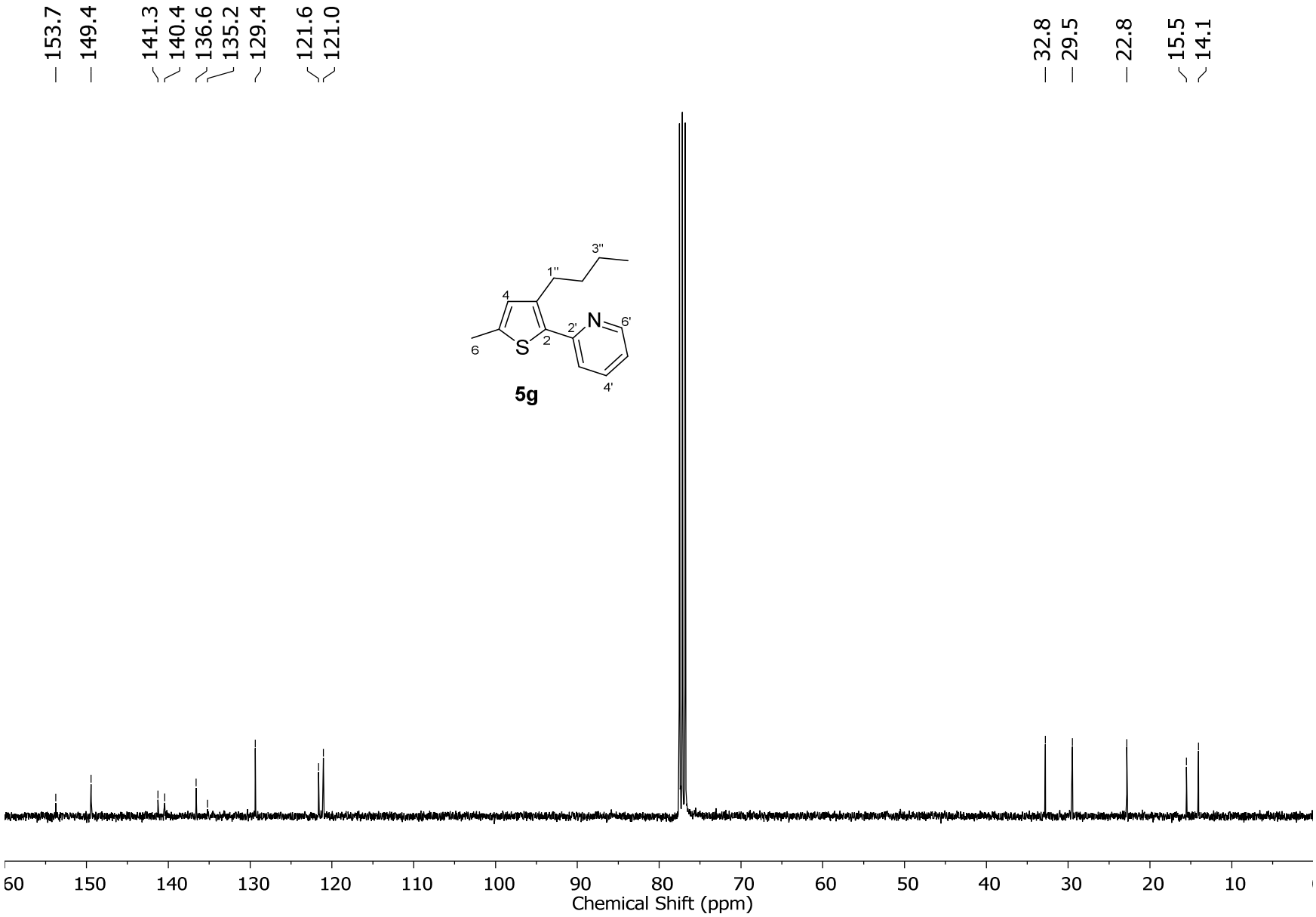

190.8
152.7
150.0
145.7
142.4
142.0
136.8
135.4
122.7
122.5
32.7
29.4
27.0
22.7
14.0
3''
1''
4
7
6
S
2
2'
N
6'
O
4'
5e
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

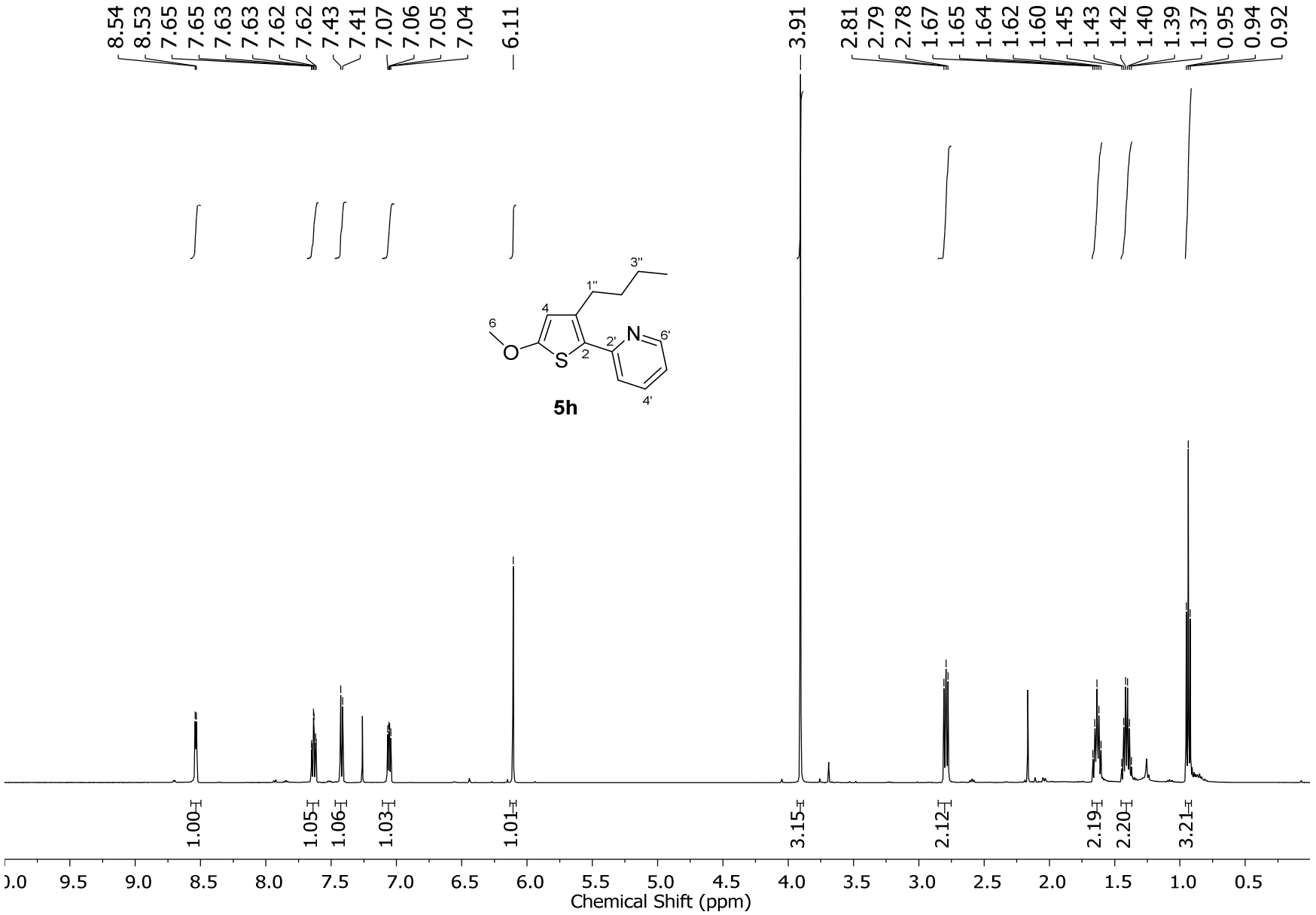

9.89
8.69
8.68
7.78
7.78
7.77
7.77
7.75
7.75
7.65
7.60
7.59
7.28
7.27
7.27
7.26
2.94
2.93
2.91
1.70
1.68
1.67
1.65
1.64
1.43
1.42
1.40
1.39
1.37
1.36
0.95
0.93
0.92
3"
1"
4
H
6
O
S
2
2'
N
6'
4'
5f
1.00
1.00
1.04
1.00
1.01
1.91
2.10
2.22
2.13
3.15
Chemical Shift (ppm)

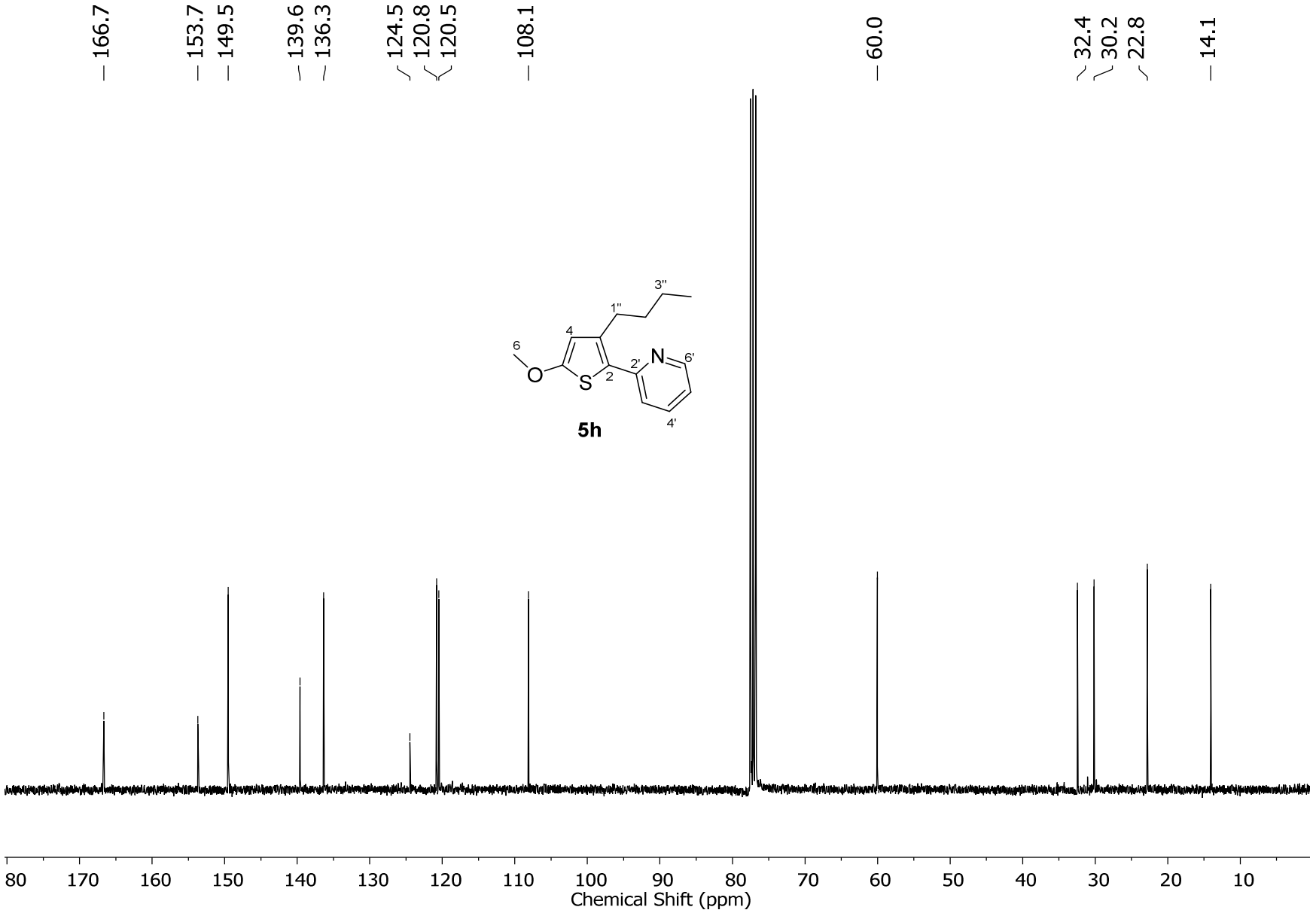

183.3
152.4
150.1
147.6
142.0
139.1
136.9
123.0
122.7
32.6
29.3
22.7
14.0
H
O
S
N
1''
2''
3''
4
2
2'
4'
6
6'
5f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

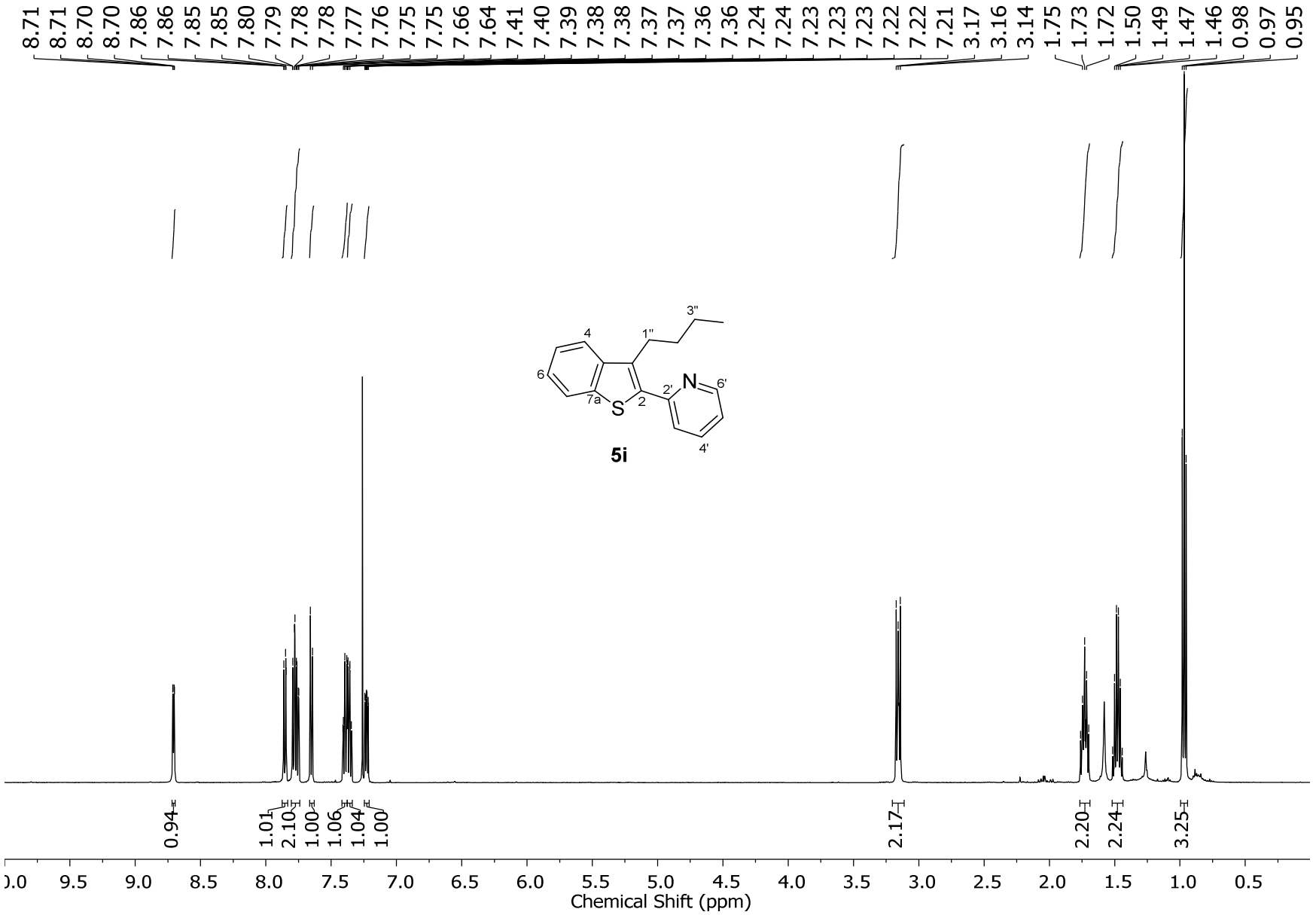

8.59
8.58
7.68
7.67
7.66
7.66
7.65
7.64
7.46
7.44
7.12
7.11
7.10
7.09
6.65
2.83
2.82
2.80
2.47
1.66
1.64
1.62
1.61
1.59
1.42
1.41
1.39
1.38
1.36
1.35
0.94
0.92
0.91
3"
1"
4
2'
N
6'
6
S
2
4'
1.00
1.04
1.03
1.02
1.01
2.13
3.20
2.27
2.25
3.19
Chemical Shift (ppm)

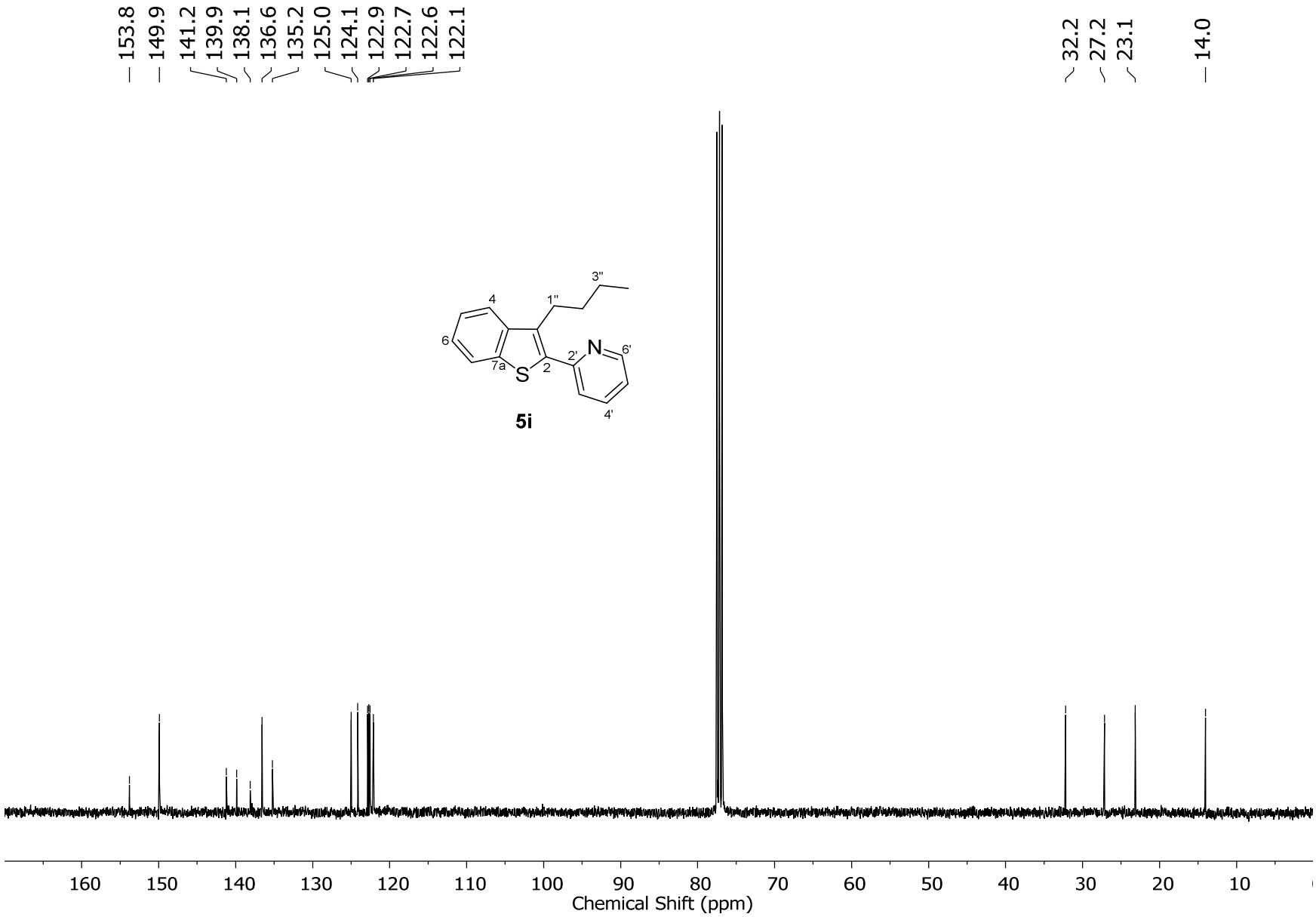
5g

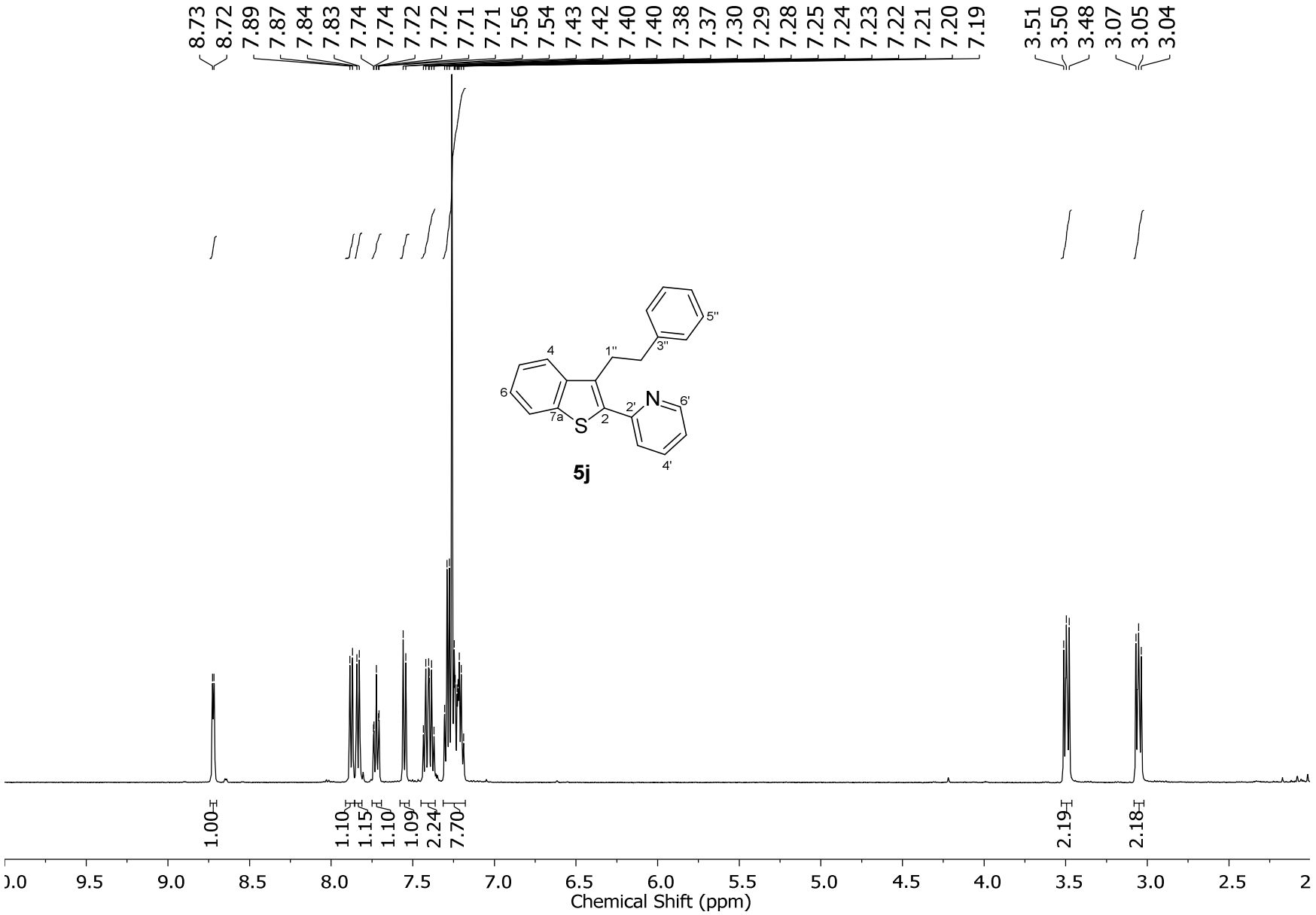

153.7
149.4
141.3
140.4
136.6
135.2
129.4
121.6
121.0
32.8
29.5
22.8
15.5
14.1
3''
1''
4
2'
N
6'
6
S
2
4'
5g
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

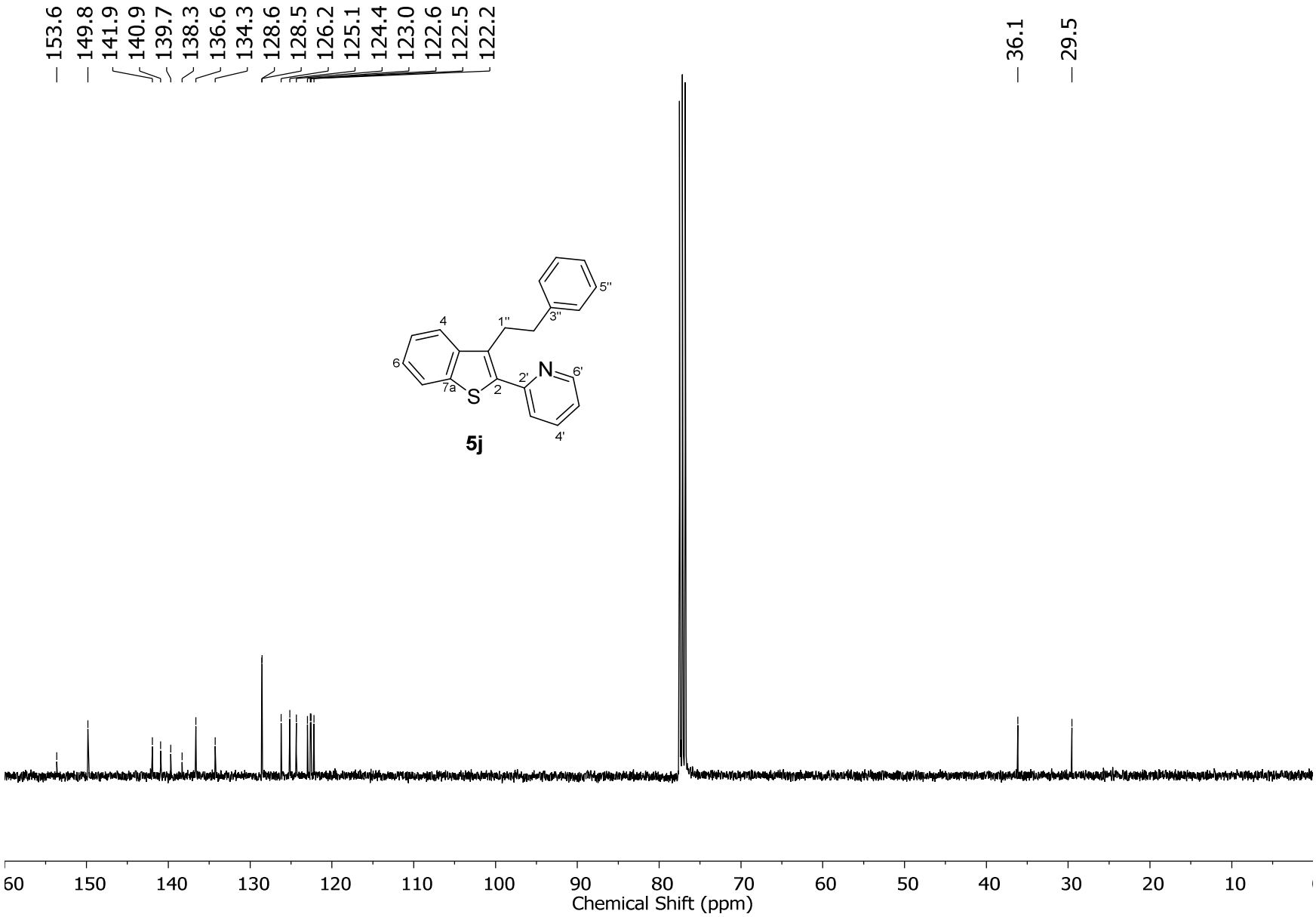

8.54
8.53
7.65
7.65
7.63
7.63
7.62
7.62
7.43
7.41
7.07
7.06
7.05
7.04
6.11
3.91
2.81
2.79
2.78
1.67
1.65
1.64
1.62
1.60
1.45
1.43
1.42
1.40
1.39
1.37
0.95
0.94
0.92
3''
1''
4
6
2'
N
6'
O
S
2
4'
5h
1.00
1.05
1.06
1.03
1.01
3.15
2.12
2.19
2.20
3.21
Chemical Shift (ppm)

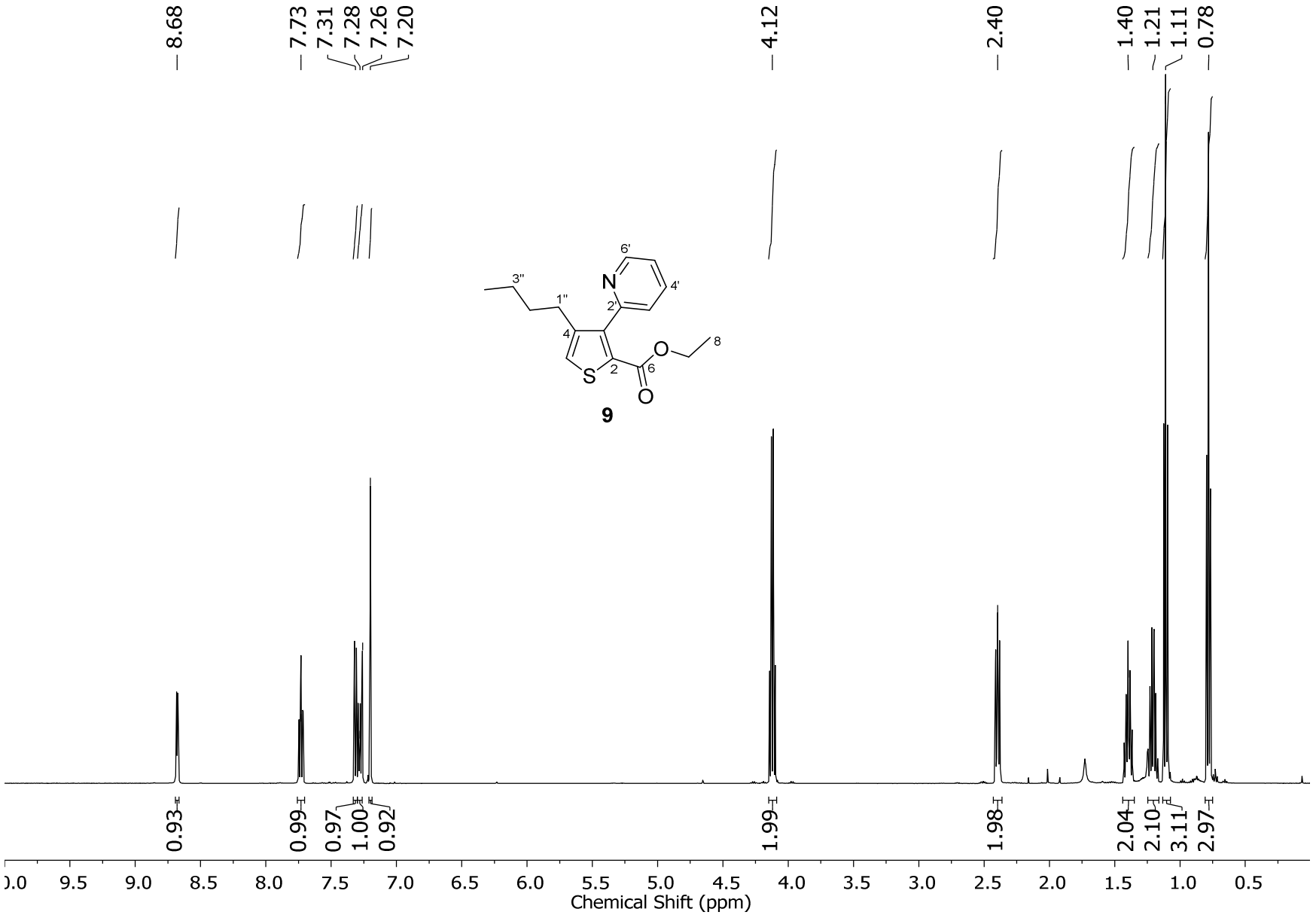

166.7
153.7
149.5
139.6
136.3
124.5
120.8
120.5
108.1
60.0
32.4
30.2
22.8
14.1
3''
1''
4
6
O
S
2
2'
N
6'
4'
5h
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)


8.71 8.71 8.70 8.70 7.86 7.86 7.85 7.85 7.80 7.79 7.78 7.78 7.77 7.76 7.75 7.75 7.66 7.64 7.41 7.40 7.39 7.38 7.38 7.37 7.37 7.36 7.36 7.24 7.24 7.23 7.23 7.23 7.22 7.22 7.21 3.17 3.16 3.14 1.75 1.73 1.72 1.50 1.49 1.47 1.46 0.98 0.97 0.95
3"
1"
4
6
7a
S
2
2'
N
6'
4'
5i
0.94
1.01
2.10
1.00
1.06
1.04
1.00
2.17
2.20
2.24
3.25
Chemical Shift (ppm)

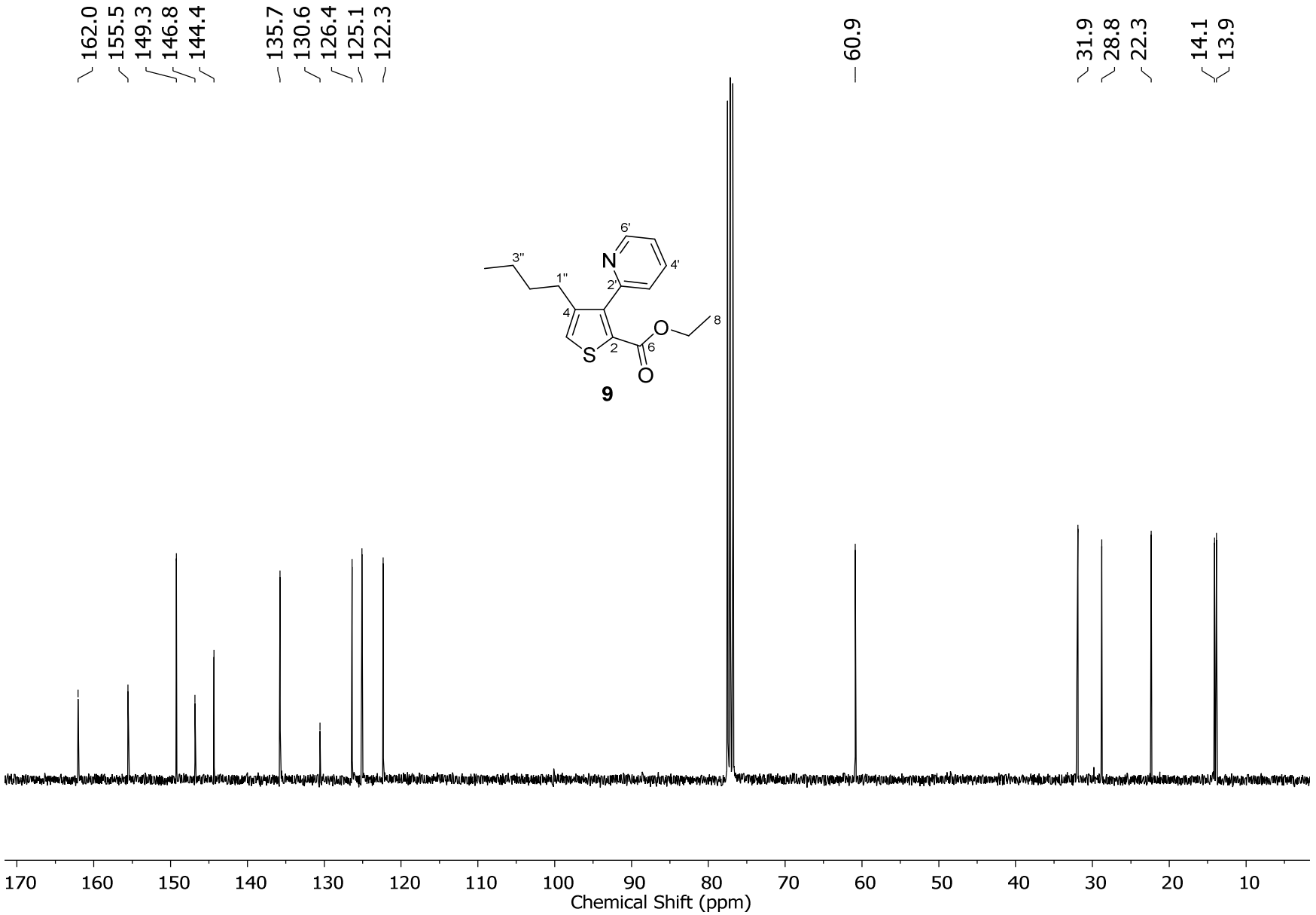

153.8
149.9
141.2
139.9
138.1
136.6
135.2
125.0
124.1
122.9
122.7
122.6
122.1
32.2
27.2
23.1
14.0
3"
1"
4
6
7a
S
2
2'
N
6'
4'
5i
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

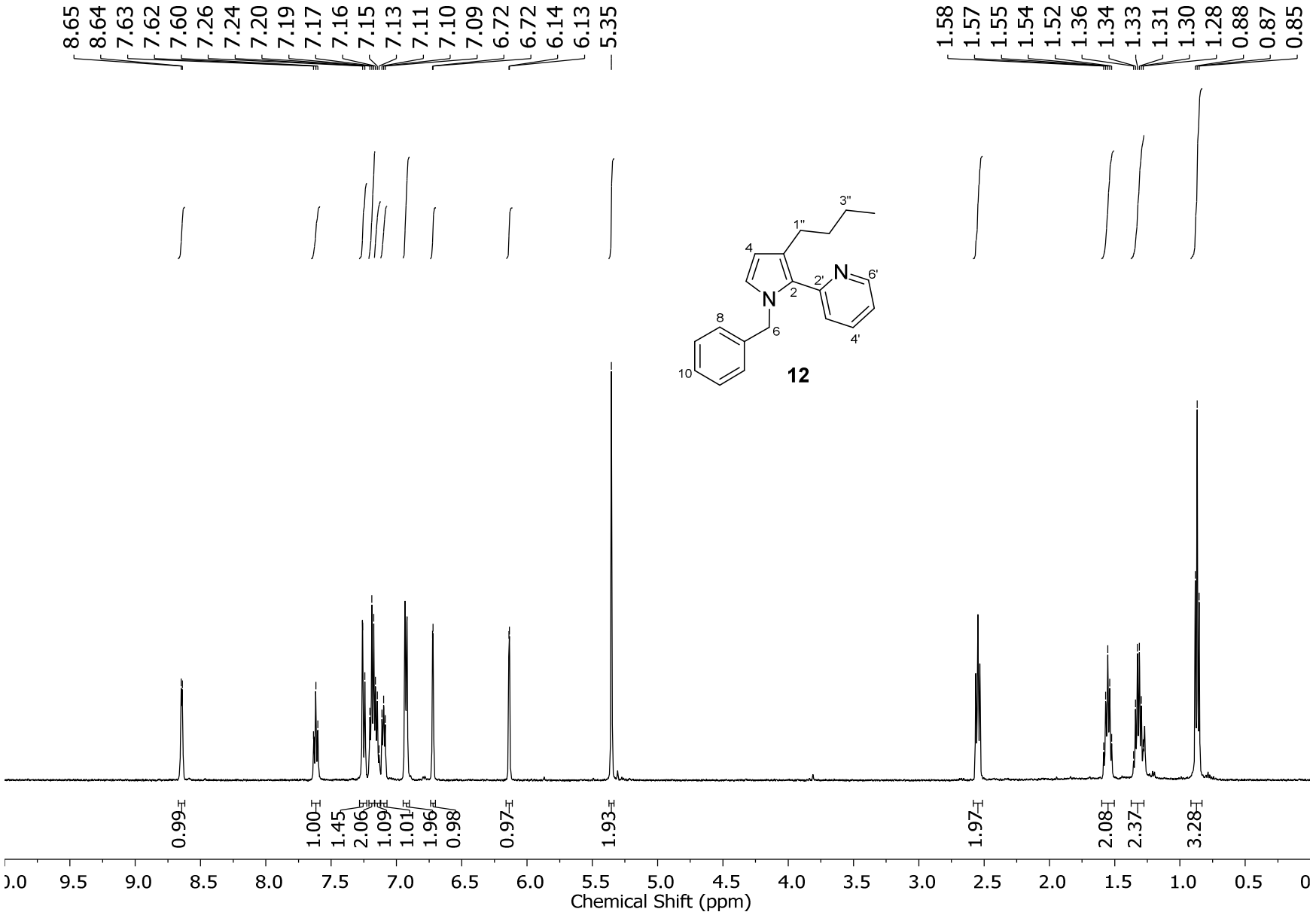

8.73
8.72
7.89
7.87
7.84
7.83
7.74
7.74
7.72
7.72
7.71
7.71
7.56
7.54
7.43
7.42
7.40
7.40
7.38
7.37
7.30
7.29
7.28
7.25
7.24
7.23
7.22
7.21
7.20
7.19
3.51
3.50
3.48
3.07
3.05
3.04
5''
4
1''
3''
6
N
6'
2'
7a
S
2
4'
5j
1.00
1.10
1.15
1.10
1.09
2.24
7.70
2.19
2.18
Chemical Shift (ppm)

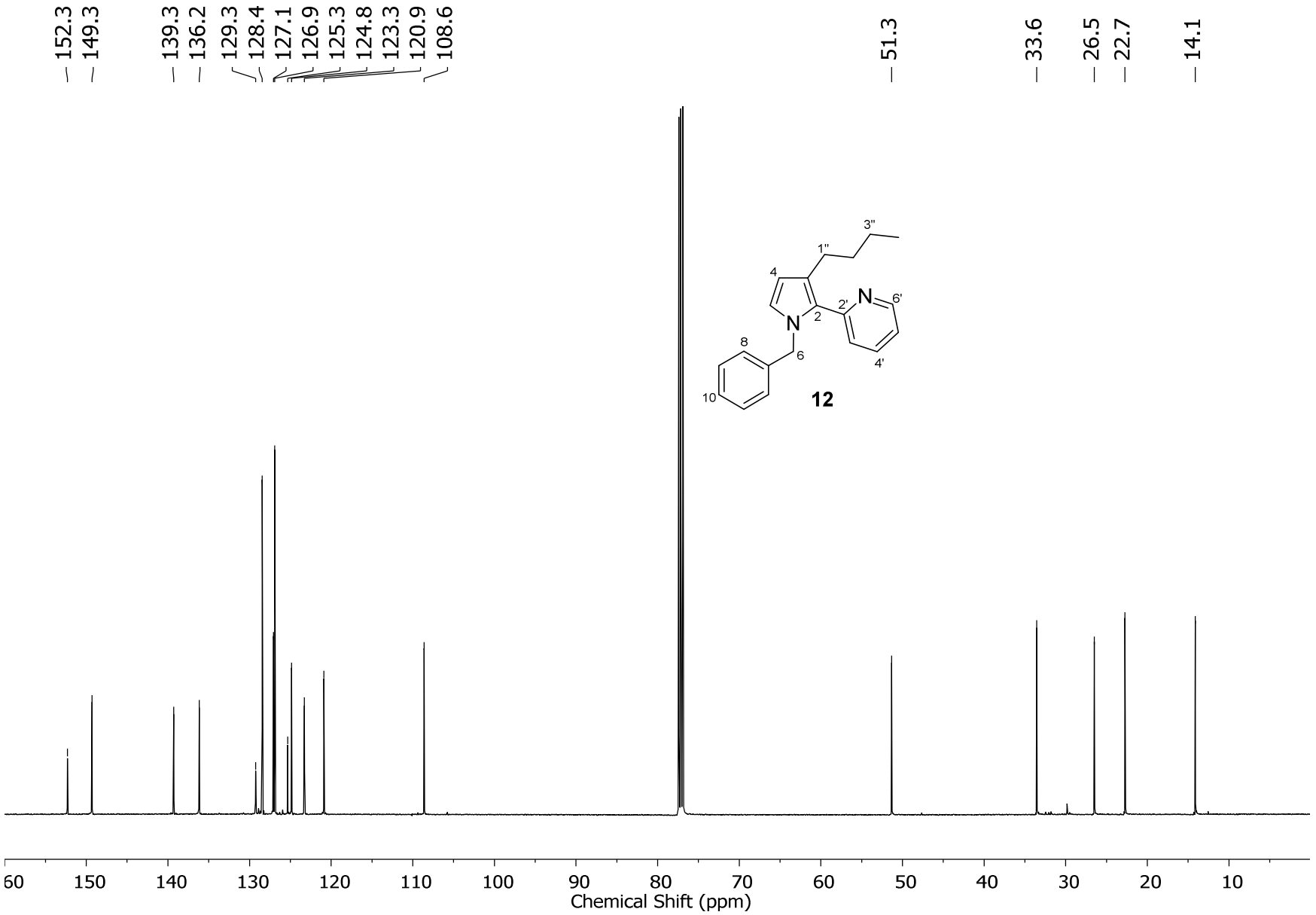

153.6
149.8
141.9
140.9
139.7
138.3
136.6
134.3
128.6
128.5
126.2
125.1
124.4
123.0
122.6
122.5
122.2
36.1
29.5
5''
3''
1''
4
6
7a
S
2
2'
N
6'
4'
5j
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

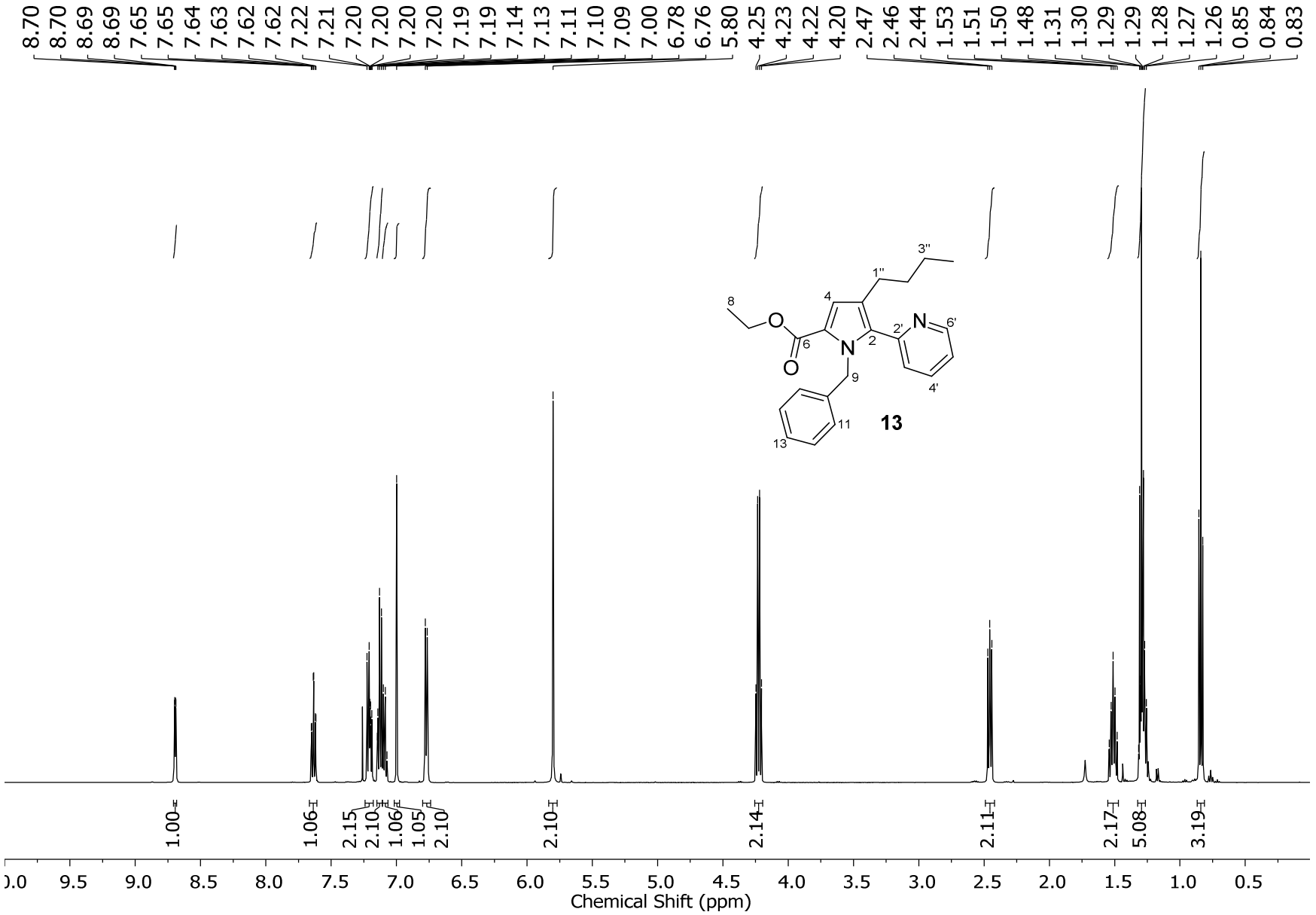

8.68
7.73
7.31
7.28
7.26
7.20
4.12
2.40
1.40
1.21
1.11
0.78
0.93
0.99
0.97
1.00
0.92
1.99
1.98
2.04
2.10
3.11
2.97
Chemical Shift (ppm)

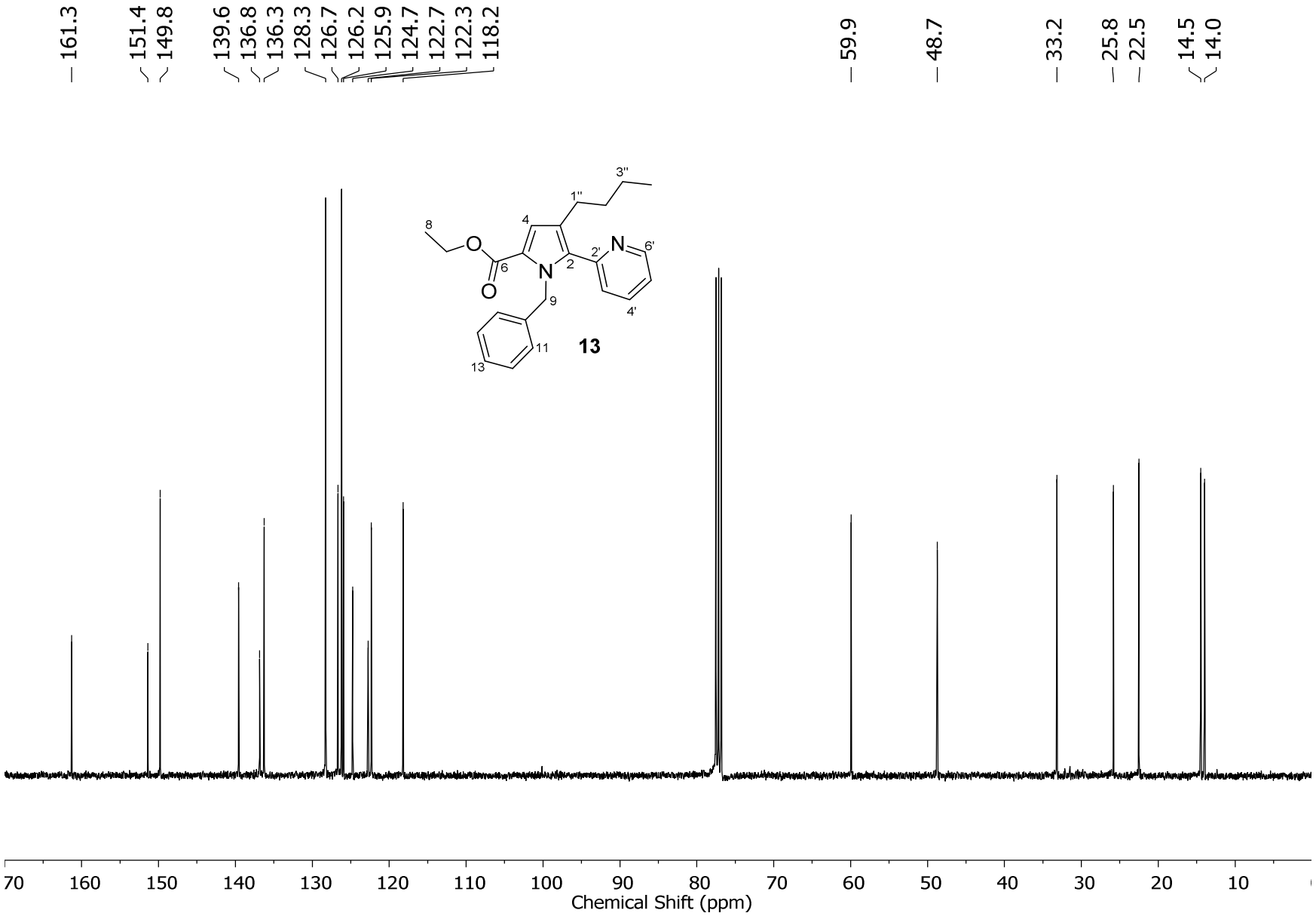
9

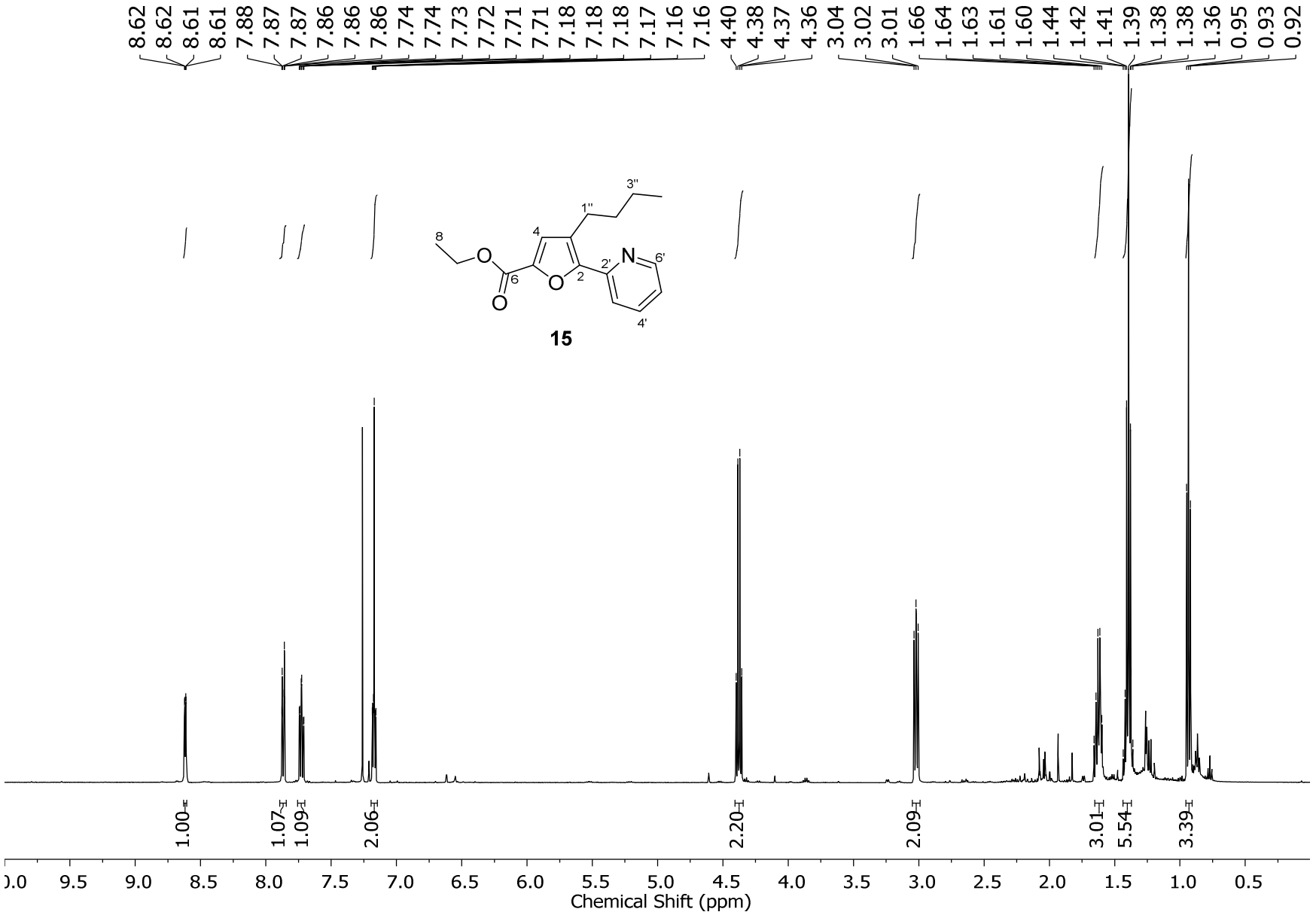

162.0
155.5
149.3
146.8
144.4
135.7
130.6
126.4
125.1
122.3
60.9
31.9
28.8
22.3
14.1
13.9
6'
N
4'
3"
1"
2'
4
8
O
S
2
6
O
9
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

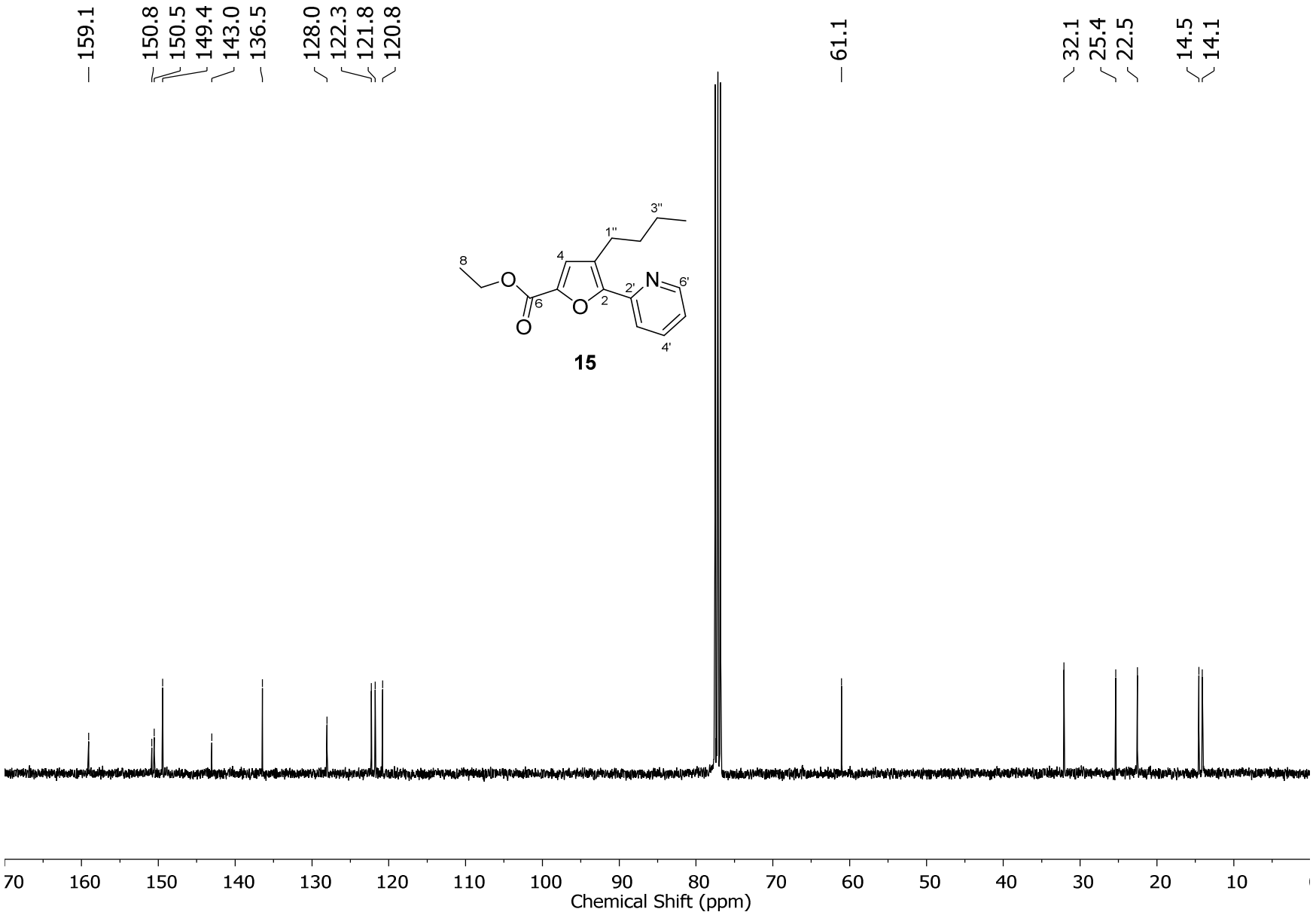

8.65
8.64
7.63
7.62
7.60
7.26
7.24
7.20
7.19
7.17
7.16
7.15
7.13
7.11
7.10
7.09
6.72
6.72
6.14
6.13
5.35
1.58
1.57
1.55
1.54
1.52
1.36
1.34
1.33
1.31
1.30
1.28
0.88
0.87
0.85
3"
1"
4
2
N
2'
N
6'
8
6
10
4'
12
0.99
1.00
1.45
2.06
1.09
1.01
1.96
0.98
0.97
1.93
1.97
2.08
2.37
3.28
Chemical Shift (ppm)

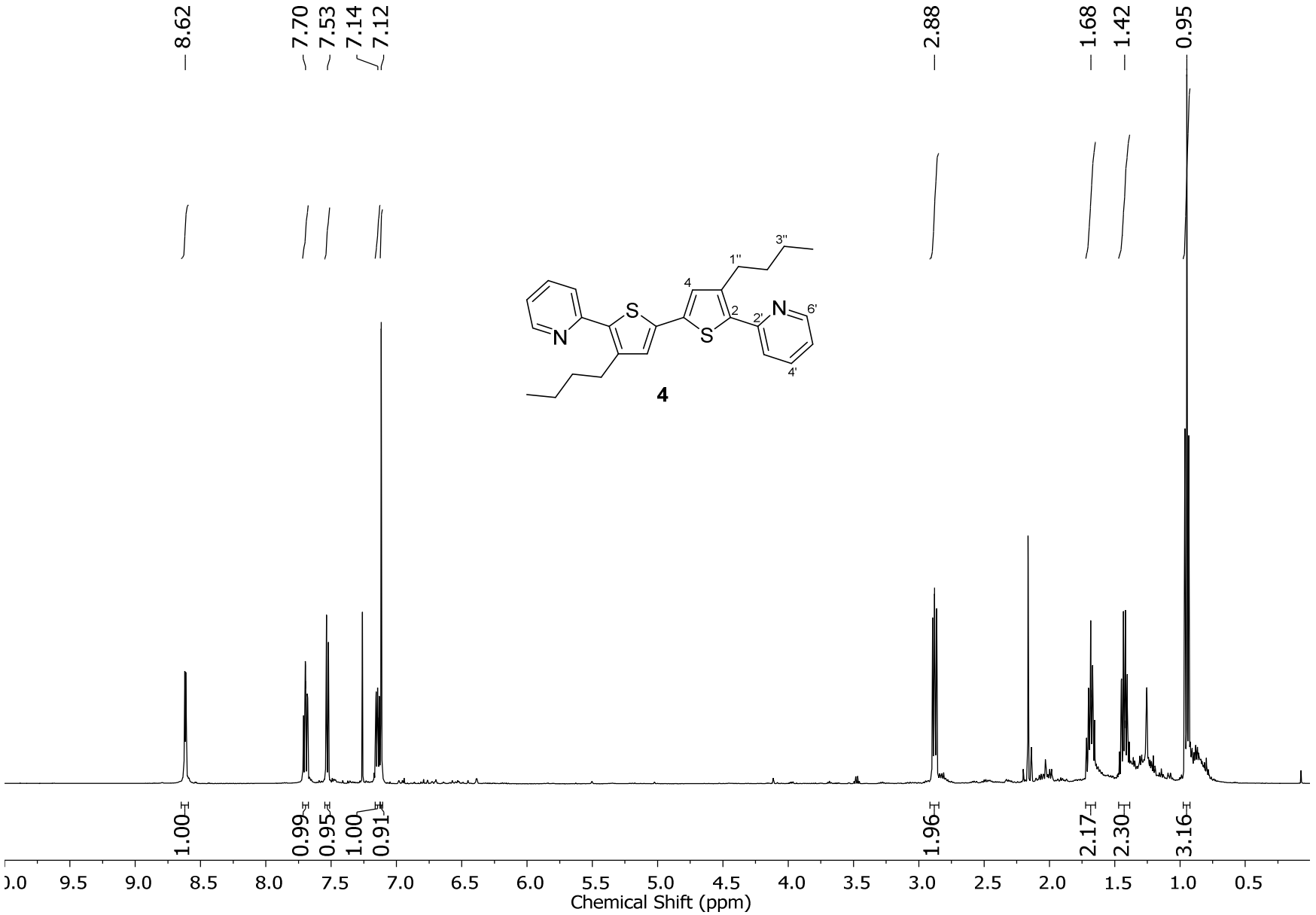

152.3
149.3
139.3
136.2
129.3
128.4
127.1
126.9
125.3
124.8
123.3
120.9
108.6
51.3
33.6
26.5
22.7
14.1
3"
1"
4
2
N
2'
N
6'
8
6
10
4'
12
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

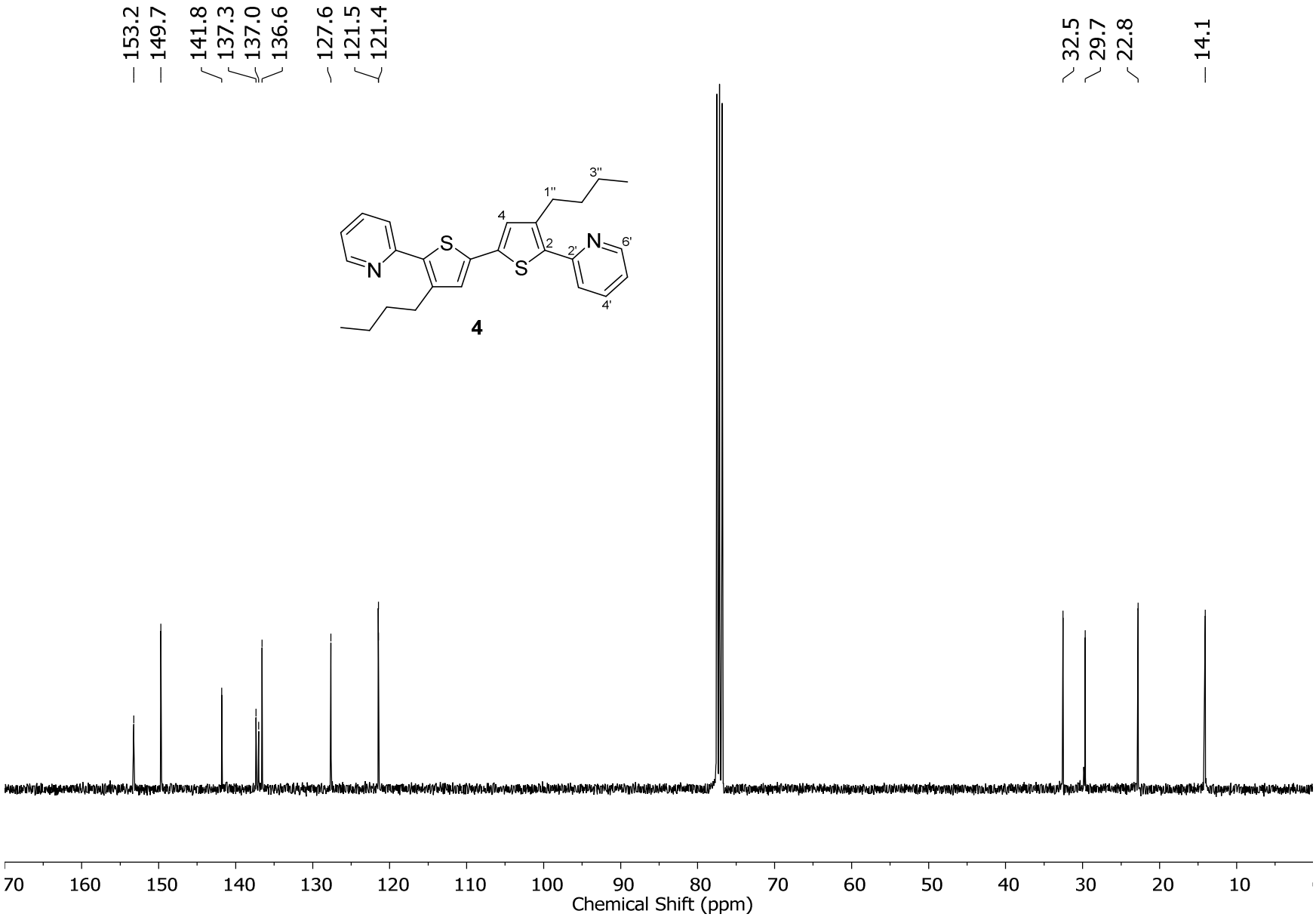

8.70 8.70 8.69 8.69 7.65 7.65 7.64 7.63 7.62 7.62 7.22 7.21 7.20 7.20 7.20 7.20 7.19 7.19 7.14 7.13 7.11 7.10 7.09 7.00 6.78 6.76 5.80 4.25 4.23 4.22 4.20 2.47 2.46 2.44 1.53 1.51 1.50 1.48 1.31 1.30 1.29 1.29 1.28 1.27 1.26 0.85 0.84 0.83
3''
1''
4
8
O
6
O
N
2
2'
N
6'
9
4'
11
13
13
1.00 1.06 2.15 2.10 1.06 1.05 2.10 2.10 2.14 2.11 2.17 5.08 3.19
Chemical Shift (ppm)


161.3
151.4
149.8
139.6
136.8
136.3
128.3
126.7
126.2
125.9
124.7
122.7
122.3
118.2
59.9
48.7
33.2
25.8
22.5
14.5
14.0
3''
1''
4
8
O
6
O
N
2
2'
N
6'
9
4'
11
13
13
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)


8.62
8.62
8.61
8.61
7.88
7.87
7.87
7.86
7.86
7.86
7.74
7.74
7.73
7.72
7.71
7.71
7.18
7.18
7.18
7.17
7.16
7.16
4.40
4.38
4.37
4.36
3.04
3.02
3.01
1.66
1.64
1.63
1.61
1.60
1.44
1.42
1.41
1.39
1.38
1.38
1.36
0.95
0.93
0.92
3''
1''
4
8
O
6
O
O
2
2'
N
6'
4'
15
1.00
1.07
1.09
2.06
2.20
2.09
3.01
5.54
3.39
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


159.1
150.8
150.5
149.4
143.0
136.5
128.0
122.3
121.8
120.8
61.1
32.1
25.4
22.5
14.5
14.1
3"
1"
4
8
O
6
O
2
2'
N
6'
O
4'
15
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)


8.62
7.70
7.53
7.14
7.12
2.88
1.68
1.42
0.95
1.00
0.99
0.95
1.00
0.91
1.96
2.17
2.30
3.16
Chemical Shift (ppm)
4


153.2
149.7
141.8
137.3
137.0
136.6
127.6
121.5
121.4
32.5
29.7
22.8
14.1
3''
1''
4
2
2'
6'
4'
S
S
N
N
4
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)