Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Enantioselective sp^3 C-H alkylation of γ-butyrolactam by a chiral Ir(I) catalyst for the synthesis of 4-substituted γ-amino acids

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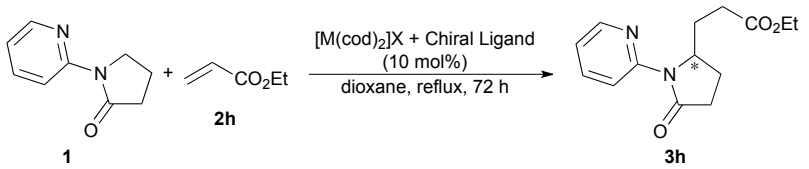
1) Experimental details and characterization data for new compounds

General information: ^{1}H NMR spectra were recorded on JEOL JNM-ECX500 (500 MHz) spectrometer. The chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) for $CDCl_3$, or external standard TMS (0 ppm) for D_2O. The peak patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in Hertz (Hz). ^{13}C NMR spectra were obtained by JEOL JNM-ECX500 (125 MHz) spectrometers and referenced to the internal solvent signals (central peak is 77.0 ppm in $CDCl_3$), or external standard TMS (0 ppm) for D_2O. $CDCl_3$ and D_2O were used as NMR solvents. High-resolution mass spectra (HRMS) were measured on a JMS-T100CS with ESI (Electro Spray Ionization) method. Optical rotations were measured on a JASCO DIP-1000 polarimeter. Preparative thin-layer chromatography (PTLC) was performed with silica gel-precoated glass plates (Merck 60 GF254) prepared in our laboratory, Flash column chromatography was performed over silica gel 200-300. All reagents were weighed and handled in air and backfilled under argon at room temperature. Unless otherwise noted, all reactions were performed under an argon atmosphere. All reagents were purchased from Aldrich, Kanto, TCI, and Wako, and used without further purification.

Experimental procedure for the synthesis of *γ*-lactam 1[1, 2]

To a dried two necked 50 mL flask CuI (2.0 mol%, 0.20 mmol, 38.1 mg) and K_2CO_3 (2.0 eq., 20 mmol, 2.8 g) were added. The reaction vessel was evacuated and backfilled with argon (×3), then 2-pyrrolidone (10.0 mmol, 851.1 mg), *N*,*N*'-dimethylethylenediamine (10 mol%, 1.0 mmol, 88.2 mg), 2-bromopyridine (1.5 eq., 15 mmol, 2.4 g) and toluene (20 mL) were added. The reaction mixture was refluxed for 24 h. After the reaction was completed, the solids were removed by celite filtration and washed with CH_2Cl_2 (5 × 5 mL). Then the solvent was evaporated, and the crude products were purified by column chromatography on silica gel (hexane/ EtOAc = 3/1 to 2/1) to give pure *γ*-lactam **1** (1.62 g, quant.).

Optimization of chiral catalyst



Entry[a]	$[M(cod)_2]X$	Chiral Ligand	Yield / %	Ee / %
1	$[Rh(cod)_2]BF_4$	(*S*)-tolBINAP	N.R.	-
2	$[Rh(cod)_2]OTf$	(*S*)-tolBINAP	N.R.	-
3	$[Ir(cod)_2]BF_4$	(*S*)-tolBINAP	87	91
4	$[Ir(cod)_2]BARF$	(*S*)-tolBINAP	36	90
5	$[Ir(cod)_2]OTf$	(*S*)-tolBINAP	trace	-
6	$[Ir(cod)_2]BF_4$	(*S*)-xyl-BINAP	15	91
7	$[Ir(cod)_2]BF_4$	(*S*)-H_8-BINAP	2	91
8	$[Ir(cod)_2]BF_4$	(*R*)-DM-H_8-BINAP	35	-6
9	$[Ir(cod)_2]BF_4$	(*S*)-SEGPHOS	trace	-
10	$[Ir(cod)_2]BF_4$	(*S*,*S*)-Me-DUPHOS	trace	-
11	$[Ir(cod)_2]BF_4$	(*S*)-DIFLUORPHOS	3	63
12	$[Ir(cod)_2]BF_4$	(*S*)-C_3-TUNEPHOS	9	84

[a] γ-Lactam **1**/ethyl acrylate **2h** was 1/4. The initial substrate concentration was 0.5 M.

General procedure for the enantioselective C-H alkylation of *γ*-lactams 1

γ-Lactam **1** (0.20 mmol, 32.4 mg), (*S*)- tolBINAP (10 mol%, 13.6 mg) and $[Ir(cod)_2]BF_4$ (10 mol%, 10.0 mg) were placed in a dried sealed tube, then capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon (×3), then alkene **2** (8.0 eq., 1.60 mmol) and degassed 1,4-dioxane (0.1 mL) was added, unless otherwise noted (entries 2 and 3 in Table 2). The rubber septum was rapidly changed with a screw cap flowing argon, and then refluxed. After the reaction was complete, the reaction mixture was cooled to room temperature and the crude products were purified by preparative TLC to give pure product **3**.

General procedure for the transformation of *γ*-lactam derivatives to *γ*-amino acid derivatives[3]

γ-Lactam derivatives **3** (0.20 mmol) and $Pd(OH)_2/C$ (20% Pd, wetted with ca.50% water, 20 mol%, 56.2 mg) were placed in a dried Schlenk tube capped with a rubber septum, then EtOH (1.8 mL) and 1.25 M HCl in EtOH (0.2 mL) were added. The reaction vessel was flushed with H_2 (× 3), then the mixture was stirred at room temperature for 24 h. The solids were removed by celite filtration and washed with CH_2Cl_2 (5 × 2 mL). Then the solvent was evaporated, and the crude products were obtained.

The crude products were placed in a dried two necked 30 mL flask. The reaction vessel was evacuated and backfilled with argon (× 3), then $NaBH_4$ (4.0 eq., 0.80 mmol, 30.4 mg) and MeOH (2.0 mL) were added carefully. The mixture was stirred at room temperature for 1 h. After the reaction was complete, the solvent was evaporated. The residue was purified by preparative TLC and the desired product **4** was obtained.

Next, a round-bottom 30 mL flask was charged with the *γ*-lactam **4** (0.1 mmol) and 6 N HCl (2.0 mL). The solution was heated to 100 °C and stirred overnight. After cooled at room temperature, the solvent was removed *in vacuo*. EtOAc (2.0 mL) was added to the reaction vessel, then the mixture was suspended by sonication and stirred at room temperature. After 1 h, the mixture was filtered and washed by EtOAc (3 × 1 mL). The solid product **5** was obtained by filter paper washed with MeOH (5 × 1 mL) and dried.

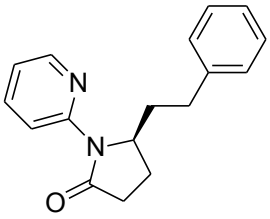
Experimental procedure for the synthesis of dihydro-pyrrolam A 7[3-5]

γ-Lactam derivatives (*S*)-**3h** (0.20 mmol, 52.4 mg) and $Pd(OH)_2/C$ (20% Pd, wetted with ca.50% water, 20 mol%, 56.2 mg) were placed in a dried Schlenk tube capped with a rubber septum, then EtOH (1.8 mL) and 1.25 M HCl in EtOH (0.2 mL) were added. The reaction vessel was flushed H_2 (× 3), then the mixture was stirred at room temperature for 24 h under H_2. The residue was removed by celite filtration and washed with CH_2Cl_2 (5 × 2 mL). The solvent was evaporated, and the crude products were obtained.

The crude products were placed in a dried two necked 30 mL flask. The reaction vessel was evacuated and backfilled with argon (× 3), the reaction vessel was cooled at 0 °C. $LiAlH_4$ (2.4 eq., 0.48 mmol, 18.2 mg) and THF (1.0 mL) was added carefully. Then the mixture was stirred at room temperature for 2 h. The reaction was quenched by addition of $Na_2SO_4 \bullet 10H_2O$, then the solids were filtered and washed by CH_2Cl_2 (8 × 2 mL). The solvent was evaporated to give the crude solid products.

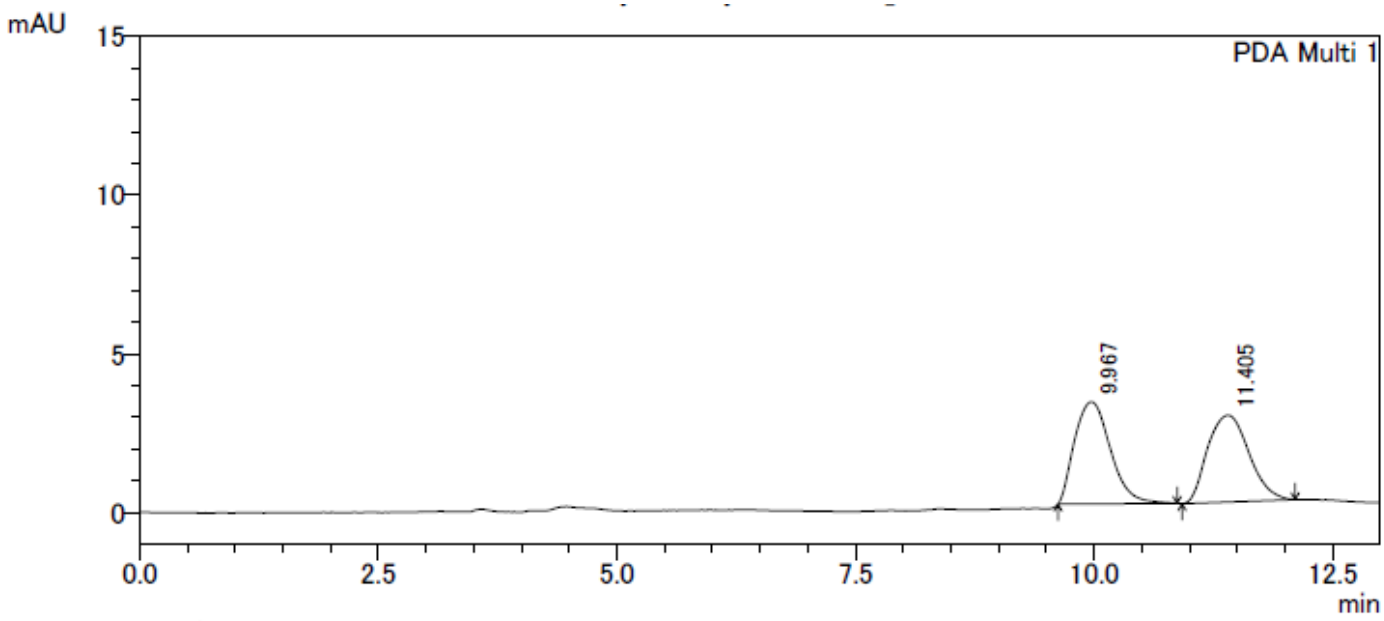
A dried Schlenk tube was charged with the crude solids and anhydrous CH_2Cl_2 (2.0 mL). Triethylamine (4.0 eq., 0.8 mmol) and *N, N*-dimethyl-4-aminopyridine (3 mol%, 2.1 mg) were added in sequence to the solution. After cooled to 0 °C, *p*-toluenesulfonyl chloride (3.0 eq., 0.6 mmol, 114.4 mg) was added instantly. The mixture was stirred at 0 °C for 15 min, and then warmed to room temperature overnight. After the reaction was completed, saturated $NaHCO_3$ aq. was added to the solution. The mixture was extracted with CH_2Cl_2 (4 × 2 mL) and the resulting solution was dried with Na_2SO_4. After evaporation of the solution, the residue was purified by preparative TLC (CH_2Cl_2/MeOH = 95/5, Rf = 0.5) and the desire solid **6** was afforded (35.1 mg, 59%).

γ-Lactam derivative **6** (0.10 mmol, 29.7 mg) in THF (2.0 mL) was placed in a dried Schlenk tube. After the solution was cooled to 0 °C, Sodium hydride (1.1 eq., 0.11 mmol, 4.4 mg, 60 % dispersion in mineral oil) was added instantly under stirred. The reaction mixture was stirred at room temperature overnight. After the reaction was completed, the reaction mixture was cooled to 0 °C and quenched with saturated NH_4Cl aq. Solution. The mixture was extracted with EtOAc (5 × 2 mL) and the organic layer was dried over Na_2SO_4. After concentration under reduced pressure, the crude products were isolated by column chromatography on silica gel (EtOAc only) to give dihydro-pyrrolam A **7** (8.0 mg, 68%). $[\alpha]^{24}_D$ = +30.3 (*c* 0.27, $CHCl_3$).



5-Phenethyl-1-(pyridin-2-yl)pyrrolidin-2-one (3a).

Isolated by preparative TLC (hexane/EtOAc = 2/1, Rf = 0.5). The title compound was obtained as yellow oil (85%). ^{1}H NMR δ 8.37-8.35 (m, 1H), 8.21-8.19 (m, 1H), 7.69-7.66 (m, 1H), 7.27-7.24 (m, 2H, overlap with $CHCl_3$), 7.18-7.14 (m, 3H), 7.03-7.01 (m, 1H), 4.87-4.82 (m, 1H), 2.79-2.65 (m, 3H), 2.60-2.53 (m, 1H), 2.32-2.19 (m, 2H), 1.97-1.91 (m, 1H), 1.84-1.76 (m, 1H); ^{13}C NMR δ 174.7, 151.1, 147.6, 141.3, 137.5, 128.3, 128.2, 125.9, 119.6, 116.4, 57.8, 34.5, 32.1, 31.6, 22.9. HRMS(ESI) calcd for $C_{17}H_{18}N_2NaO$ (M+Na): 289.1311; found: 289.1309. $[\alpha]^{31}_{D}$ = +64.9 (*c* 1.02, $CHCl_3$, 82% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 12.0 min for major isomer and 10.5 min for minor isomer).



1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

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1	9.967	84534	3224	50.555	54.066
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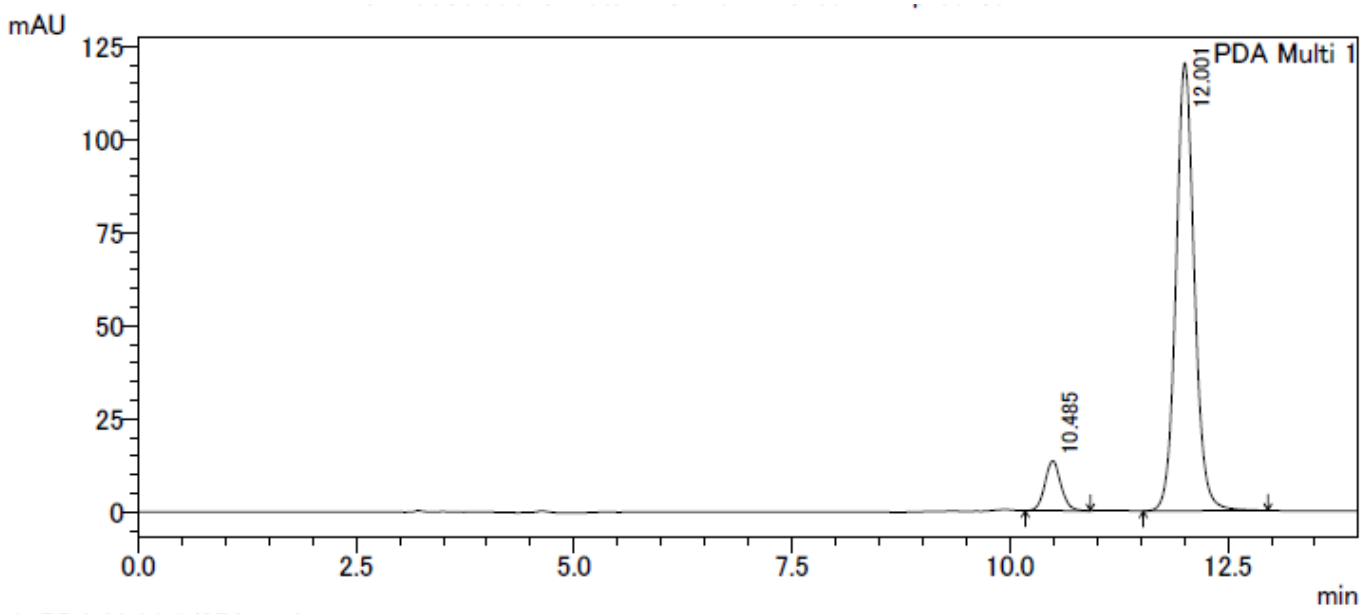
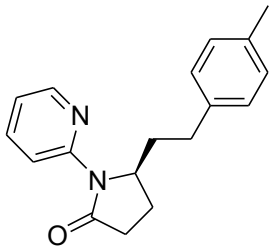
合計		167213	5962	100.000	100.000



ピークテーブル

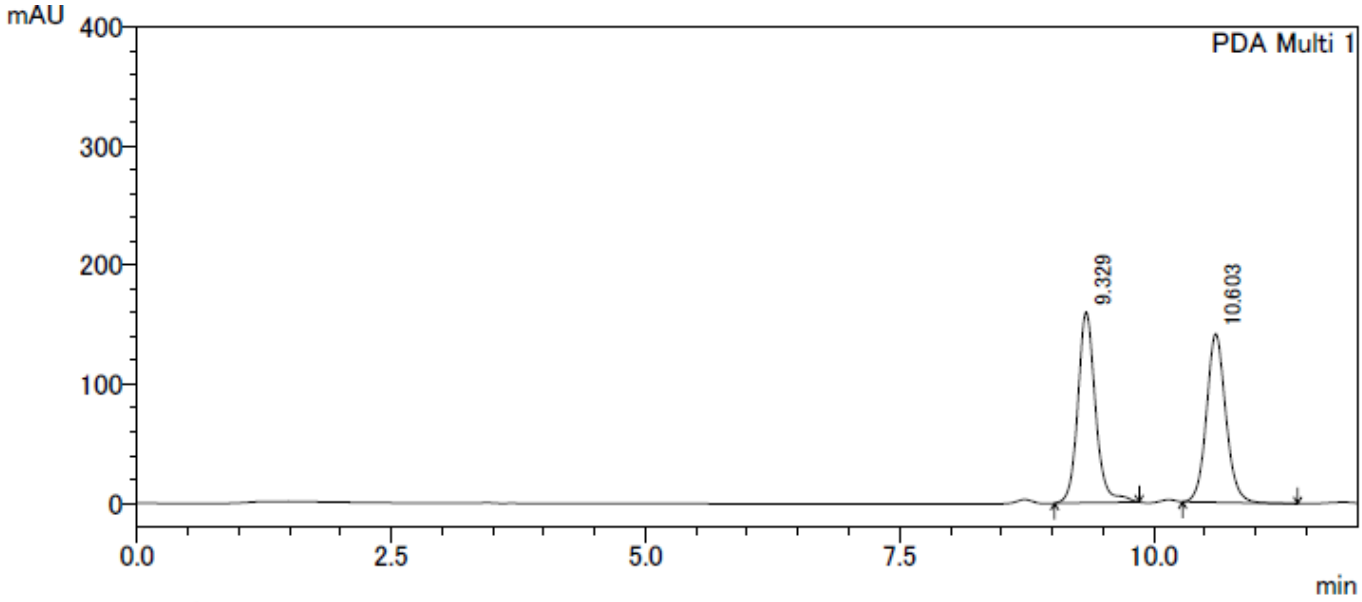
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	10.485	170961	13373	8.819	10.003
2	12.001	1767546	120307	91.181	89.997
合計		1938508	133680	100.000	100.000



5-(4-Methylphenethyl)-1-(pyridin-2-yl)pyrrolidin-2-one (3b).

Isolated by preparative TLC (hexane/EtOAc = 2/1, Rf = 0.6). The title compound was obtained as white solid (56%). Mp 66 °C, ^{1}H NMR δ 8.37-8.35 (m, 1H), 8.20-8.18 (m, 1H), 7.69-7.66 (m, 1H), 7.07-6.97 (m, 5H), 4.86-4.81 (m, 1H), 2.79-2.71 (m, 1H), 2.64-2.53 (m, 3H), 2.32-2.26 (m, 4H), 2.24-2.16 (m, 1H), 1.96-1.90 (m, 1H), 1.81-1.75 (m, 1H); ^{13}C NMR δ 174.5, 150.9, 147.4, 138.0, 137.3, 135.1, 128.8, 127.8, 119.4, 116.3, 57.6, 34.4, 31.9, 30.9, 22.7, 20.7. HRMS(ESI) calcd for $C_{18}H_{20}N_2NaO$ (M+Na): 303.1468; found: 303.1467. $[\alpha]^{29}_{D}$ = +45.5 (*c* 1.40, $CHCl_3$, 84% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 10.7 min for major isomer and 9.3 min for minor isomer).



1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

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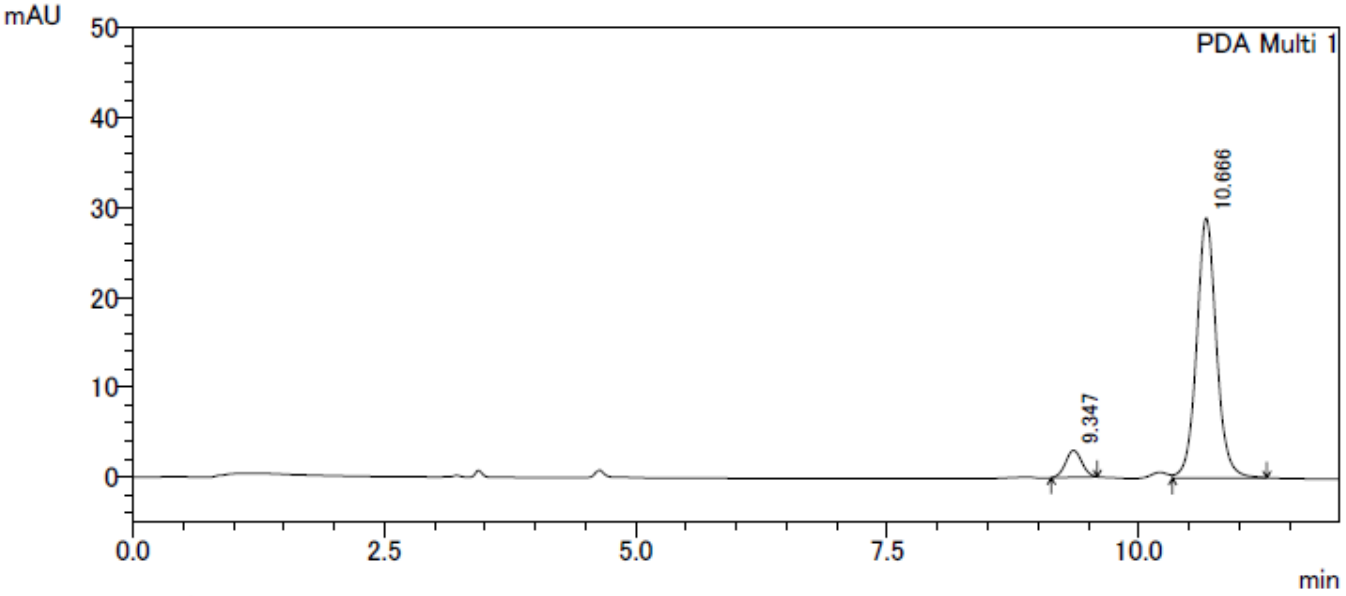
1	9.329	1941835	160530	50.820	53.166
2	10.603	1879158	141412	49.180	46.834
合計		3820993	301942	100.000	100.000

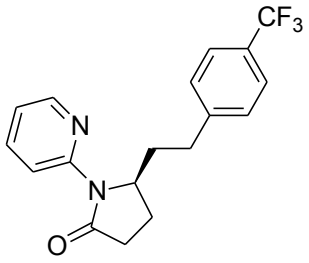


1 PDA Multi 1/254nm 4nm

ピークテーブル

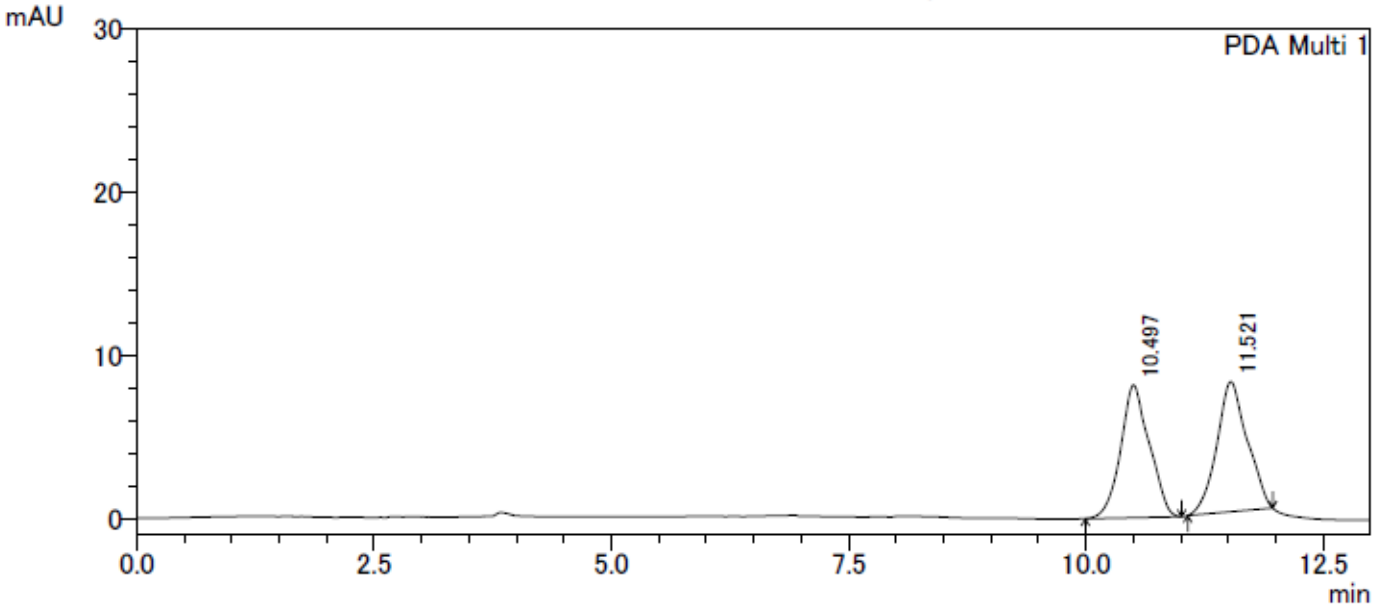
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	9.347	33774	3001	7.828	9.388
2	10.666	397653	28965	92.172	90.612
合計		431427	31965	100.000	100.000



1-(Pyridin-2-yl)-5-(4-(trifluoromethyl)phenethyl)pyrrolidin-2-one (3c).

Isolated by twice preparative TLC (hexane/EtOAc = 2/1, Rf = 0.6). The title compound was obtained as yellow oil (87%). ^{1}H NMR δ 8.35-8.34 (m, 1H), 8.22-8.20 (m, 1H), 7.70-7.66 (m, 1H), 7.52-7.50 (m, 2H), 7.28-7.26 (m, 2H), 7.04-7.02 (m, 1H), 4.87-4.82 (m, 1H), 2.81-2.72 (m, 3H), 2.62-2.55 (m, 1H), 2.34-2.21 (m, 2H), 1.97-1.92 (m, 1H), 1.88-1,80 (m, 1H); ^{13}C NMR δ 174.6, 151.1, 147.6, 145.4, 137.6, 128.6, 128.3 (d, $J_{C\text{-}F}$ = 32.2 Hz, 1C) , 125.3 (q, $J_{C\text{-}F}$ = 3.6 Hz, 1C), 119.7, 116.3, 57.6, 34.2, 32.1, 31.5, 22.9 (A pair of peaks at the aromatic religion was overlapped). HRMS(ESI) calcd for $C_{18}H_{17}F_3N_2NaO$ (M+Na): 357.1185; found: 357.1191. $[\alpha]^{30}_{D}$ = +54.2 (*c* 2.72, $CHCl_3$, 85% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 13.0 min for major isomer and 12.1 min for minor isomer).



1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

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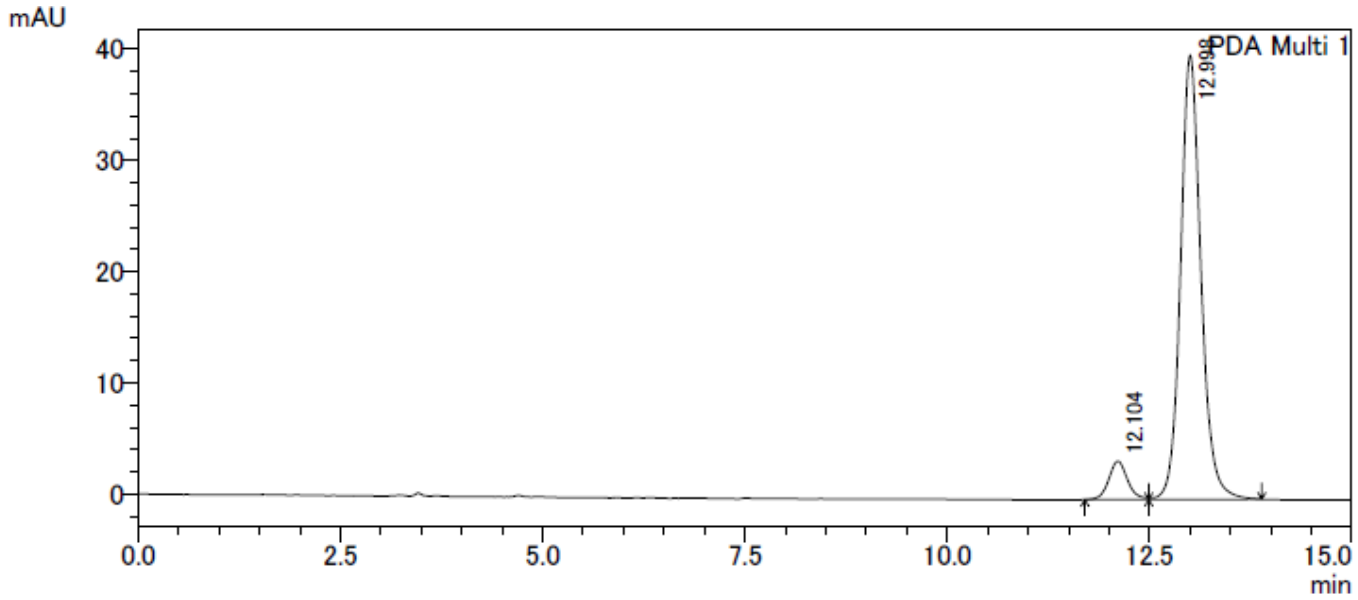
1	10.497	172306	8148	49.164	50.522
2	11.521	178169	7980	50.836	49.478
合計		350475	16127	100.000	100.000



1 PDA Multi 1/254nm 4nm

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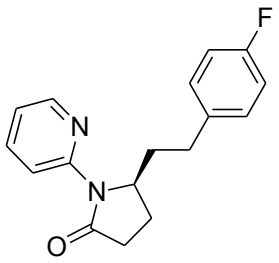
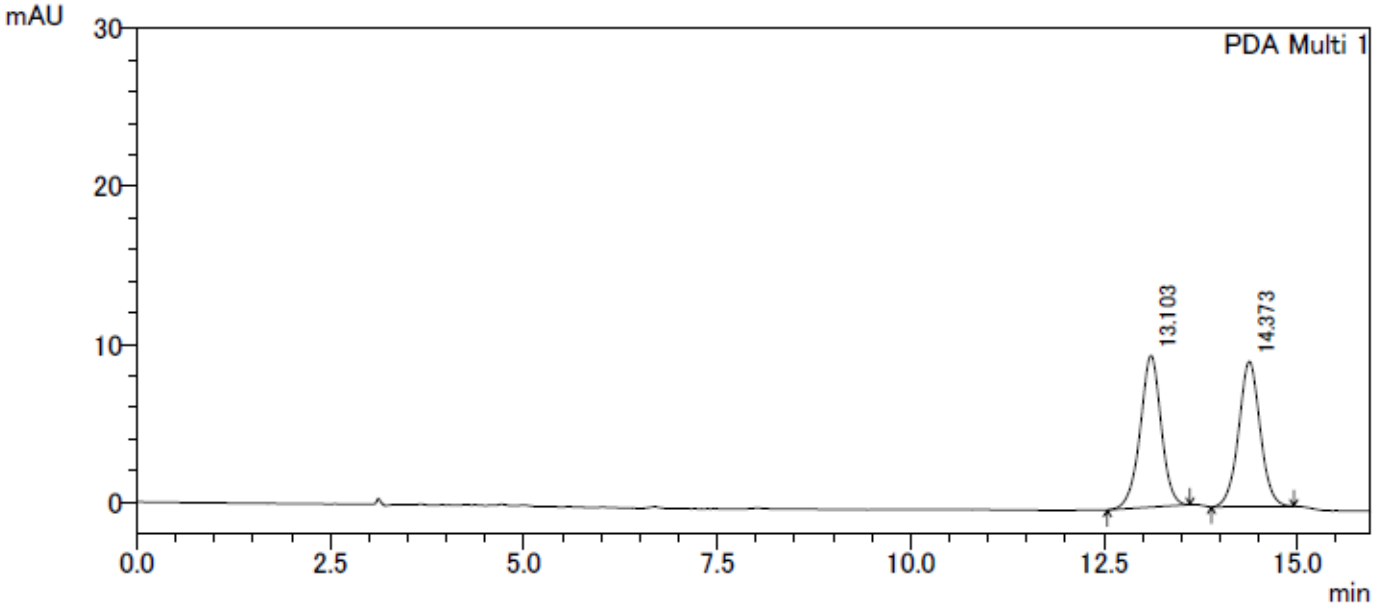
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	12.104	55763	3448	7.366	7.941
2	12.998	701214	39968	92.634	92.059
合計		756976	43416	100.000	100.000



5-(4-Fluorophenethyl)-1-(pyridin-2-yl)pyrrolidin-2-one (3d).

Isolated by twice preparative TLC (hexane/EtOAc = 2/1, Rf = 0.6). The title compound was obtained as white solid (60%). Mp 64 °C, ^{1}H NMR δ 8.36-8.35 (m, 1H), 8.22-8.20 (m, 1H), 7.70-7.66 (m, 1H), 7.12-7.09 (m, 2H), 7.04-7.01 (m, 1H), 6.96-6.91 (m, 2H), 4.85-4.80 (m, 1H), 2.80-2.71 (m, 1H), 2.66-2.53 (m, 3H), 2.33-2.16 (m, 2H), 1.96-1.89 (m, 1H), 1.83-1,73 (m, 1H); ^{13}C NMR δ 174.7, 160.3, 151.2, 147.6, 137.6, 136.9 (d, $J_{C\text{-}F}$ = 2.4 Hz, 1C), 129.5 (d, $J_{C\text{-}F}$ = 7.2 Hz, 1C), 119.7, 116.4, 115.0 (d, $J_{C\text{-}F}$ = 21.5 Hz, 1C) 57.7, 34.6, 32.1, 30.8, 22.9. HRMS(ESI) calcd for $C_{17}H_{17}FN_2NaO$ (M+Na): 307.1217; found: 307.1217. $[\alpha]^{30}_{D}$ = +60.7 (*c* 1.30, $CHCl_3$, 83% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 14.4 min for major isomer and 12.9 min for minor isomer).



1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

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1	13.103	181826	9616	50.438	51.081
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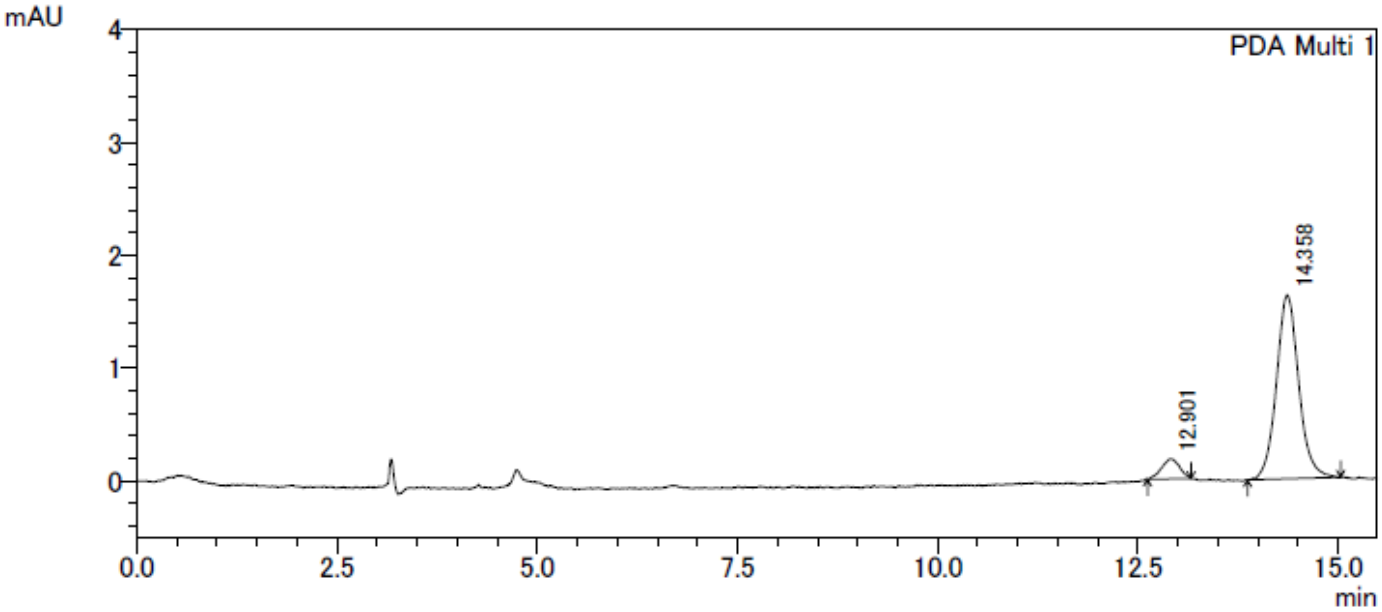
合計		360498	18825	100.000	100.000



1 PDA Multi 1/254nm 4nm

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PDA Ch1 254nm 4nm

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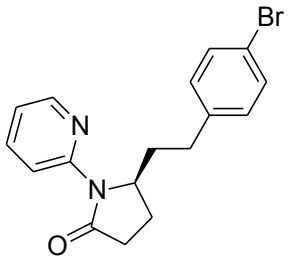
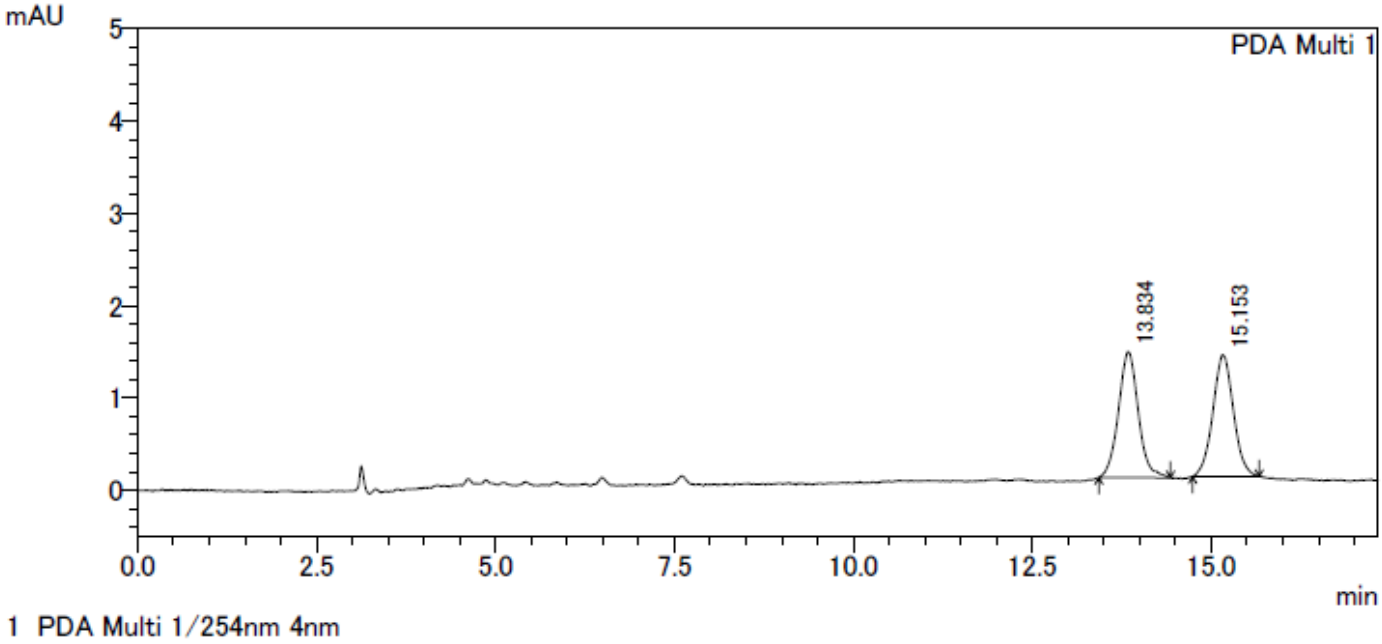
合計		34241	1805	100.000	100.000



5-(4-Bromophenethyl)-1-(pyridin-2-yl)pyrrolidin-2-one (3e).

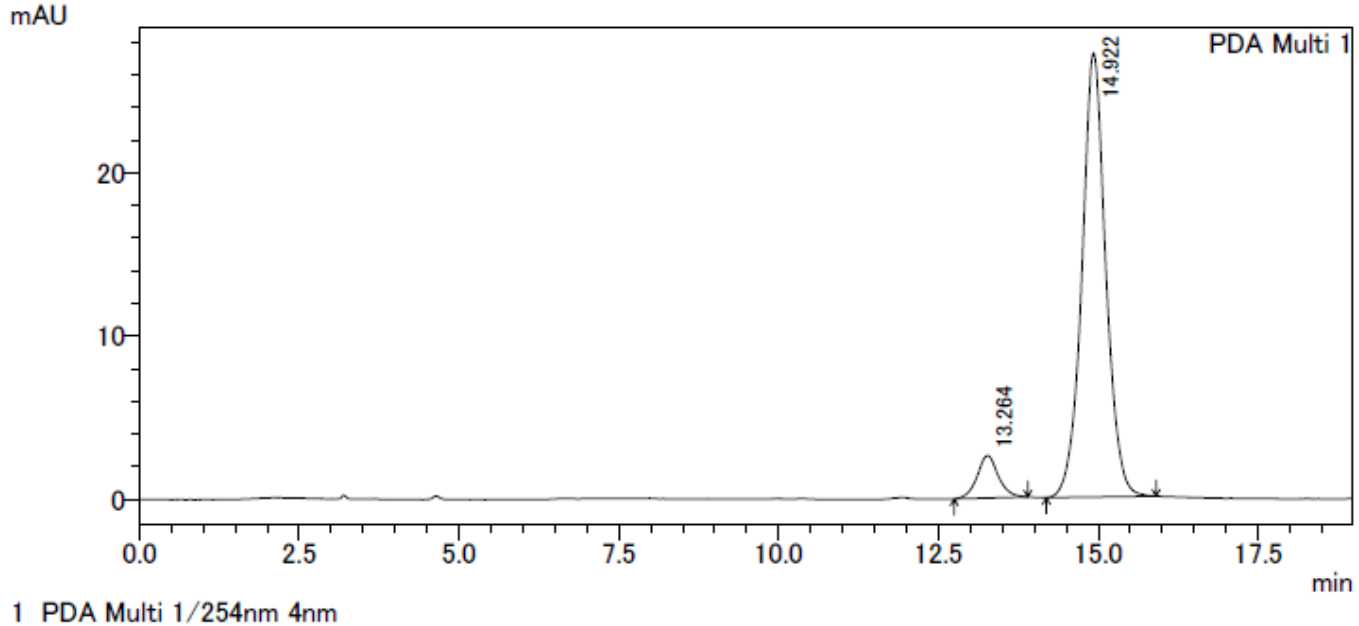
Isolated by twice preparative TLC (After hexane/EtOAc = 3/1, Rf = 0.6, EtOAc only, Rf = 0.7). The title compound was obtained as yellow oil (50%). ^{1}H NMR δ 8.35-8.34 (m, 1H), 8.21-8.20 (m, 1H), 7.69-7.66 (m, 1H), 7.37-7.35 (m, 2H), 7.03-7.01 (m, 3H), 4.84-4.79 (m, 1H), 2.79-2.71 (m, 1H), 2.64-2.53 (m, 3H), 2.32-2.16 (m, 2H), 1.95-1.89 (m, 1H), 1.82-1.74 (m, 1H); ^{13}C NMR δ 174.6, 151.1, 147.5, 140.2, 137.6, 131.4, 130.0, 119.6, 116.3, 57.6, 34.3, 32.1, 31.0, 22.9 (A pair of peaks at the aromatic religion was overlapped). HRMS(ESI) calcd for $C_{17}H_{17}BrN_2NaO$ (M+Na): 367.0421; found: 367.0416. $[\alpha]^{32}_{D}$ = +48.6 (*c* 1.39, $CHCl_3$, 84% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 14.9 min for major isomer and 13.3 min for minor isomer).



ピークテーブル

PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	13.834	26316	1365	49.924	50.855
2	15.153	26396	1319	50.076	49.145
合計		52711	2684	100.000	100.000

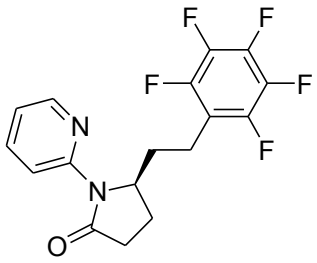


1 PDA Multi 1/254nm 4nm

ピークテーブル

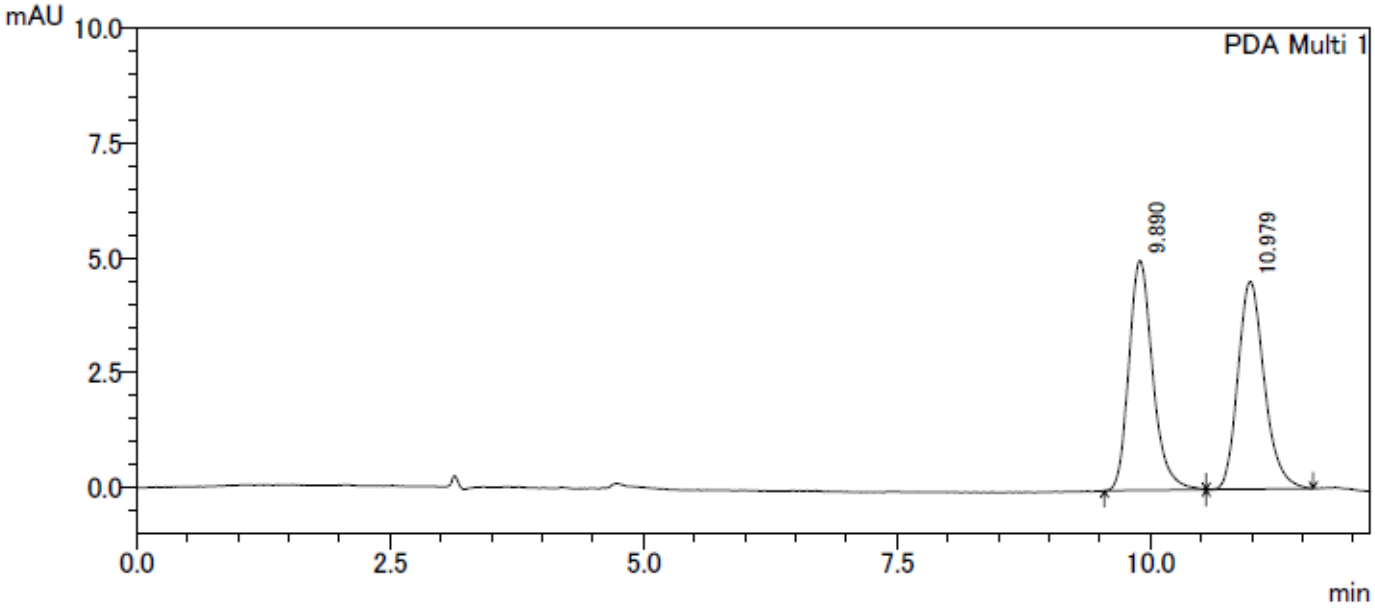
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	13.264	59778	2595	7.820	8.718
2	14.922	704668	27172	92.180	91.282
合計		764446	29767	100.000	100.000



5-(2-(Pentafluorophenyl)ethyl)-1-(pyridin-2-yl)pyrrolidin-2-one (3f).

Isolated by preparative TLC (hexane/EtOAc = 2/1, Rf = 0.7). The title compound was obtained as white solid (69%). Mp 94 °C, ^{1}H NMR δ 8.29-8.28 (m, 1H), 8.23-8.21 (m, 1H), 7.70-7.66 (m, 1H), 7.04-7.01 (m, 1H), 4.79-4.74 (m, 1H), 2.82-2.71 (m, 3H), 2.64-2.57 (m, 1H), 2.38-2.30 (m, 1H), 2.20-2.14 (m, 1H), 2.01-1.96 (m, 1H), 1.84-1.77 (m, 1H); ^{13}C NMR δ 174.5, 150.9, 147.5, 146.0, 144.0, 137.6, 136.4, 119.7, 116.0, 114.2, 57.1, 32.1, 32.0, 22.6, 18.4. HRMS(ESI) calcd for $C_{17}H_{13}F_5N_2NaO$ (M+Na): 379.0840; found: 379.0841. $[\alpha]^{28}_{D}$ = +58.7 (*c* 2.28, $CHCl_3$, 94% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 11.1 min for major isomer and 10.0 min for minor isomer).

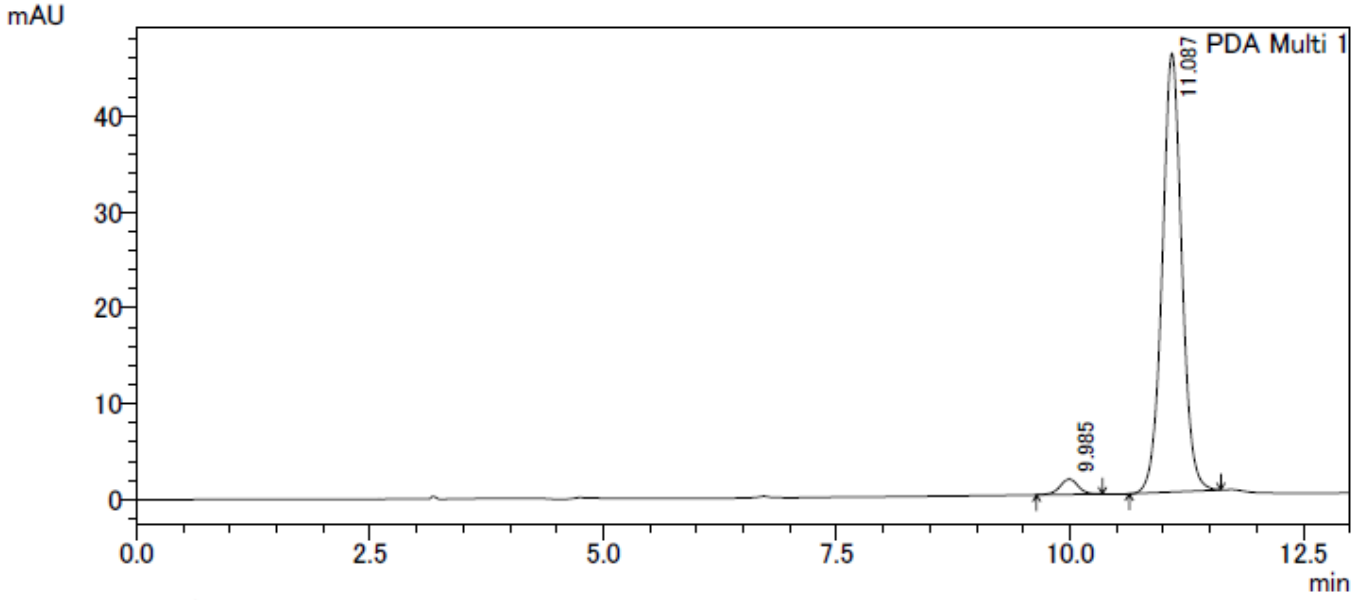


1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	9.890	82008	5007	49.938	52.513
2	10.979	82211	4528	50.062	47.487
合計		164218	9534	100.000	100.000

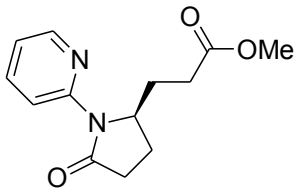


1 PDA Multi 1/254nm 4nm

ピークテーブル

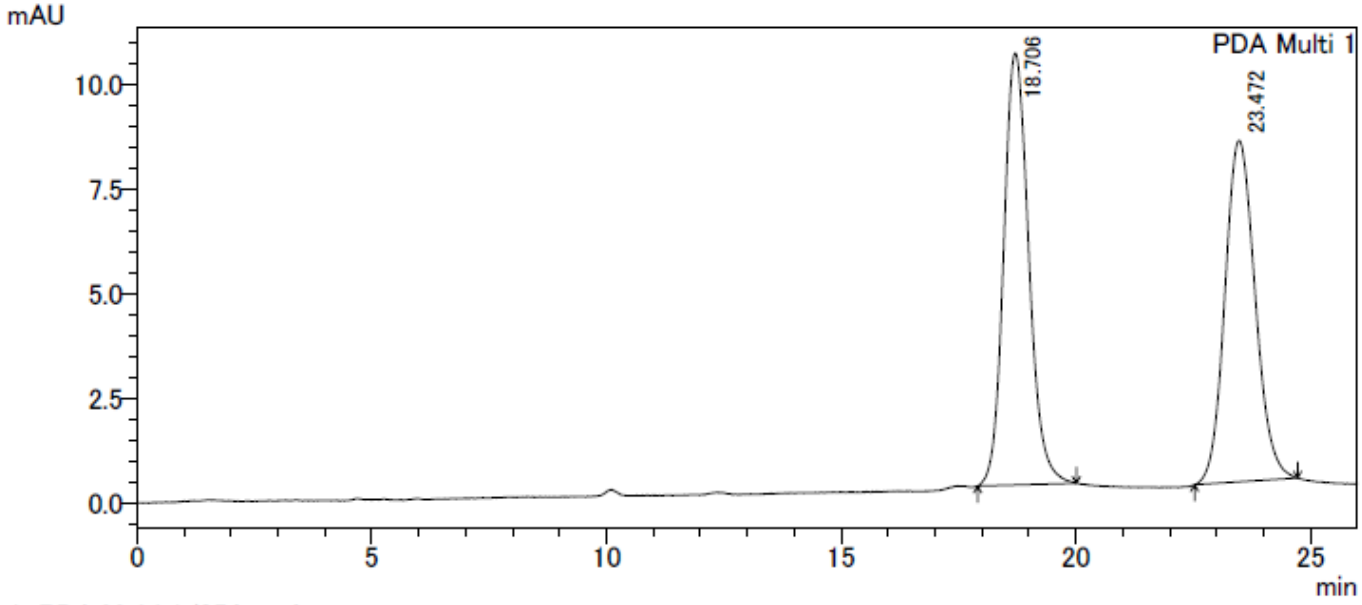
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	9.985	21953	1640	3.185	3.459
2	11.087	667278	45779	96.815	96.541
合計		689232	47419	100.000	100.000



Methyl 3-(5-oxo-1-(pyridin-2-yl)pyrrolidin-2-yl)propanoate (3g).

Isolated by preparative TLC (hexane/EtOAc = 1/1, Rf = 0.3). The title compound was obtained as yellow oil (82%). ^{1}H NMR δ 8.36-8.34 (m, 1H), 8.24-8.22 (m, 1H), 7.70-7.67 (m, 1H), 7.04-7.02 (m, 1H), 4.86-4.82 (m, 1H), 3.65 (s, 3H), 2.79-2.72 (m, 1H), 2.58-2.52 (m, 1H), 2.42-2.15 (m, 4H), 1.93-1.83 (m, 2H); ^{13}C NMR δ 174.7, 173.4, 151.2, 147.7, 137.7, 119.8, 116.3, 57.2, 51.8, 32.1, 30.3, 28.5, 23.0. HRMS(ESI) calcd for $C_{13}H_{16}N_2NaO_3$ (M+Na): 271.1053; found: 271.1053. $[\alpha]^{24}_{D}$ = +55.9 (*c* 1.70, $CHCl_3$, 91% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 23.9 min for major isomer and 19.1 min for minor isomer).

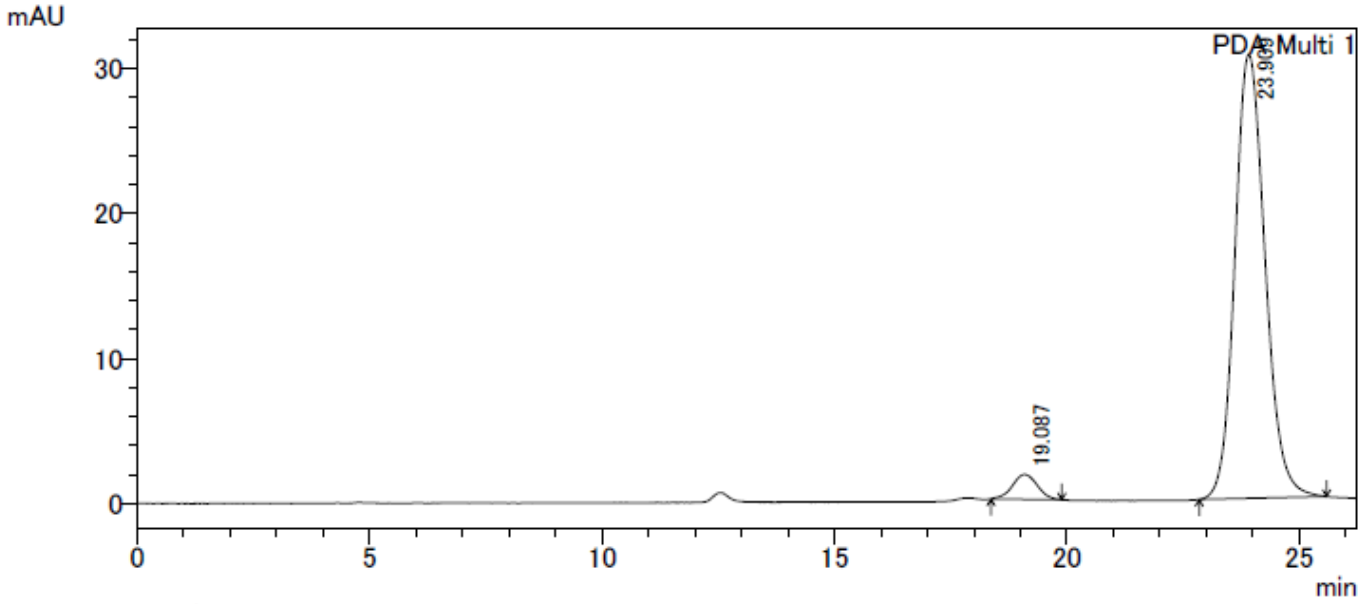


1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

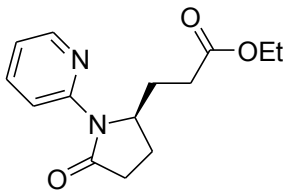
ピーク#	保持時間	面積	高さ	面積%	高さ%
1	18.706	384826	10338	51.195	55.850
2	23.472	366867	8172	48.805	44.150
合計		751693	18510	100.000	100.000



ピークテーブル

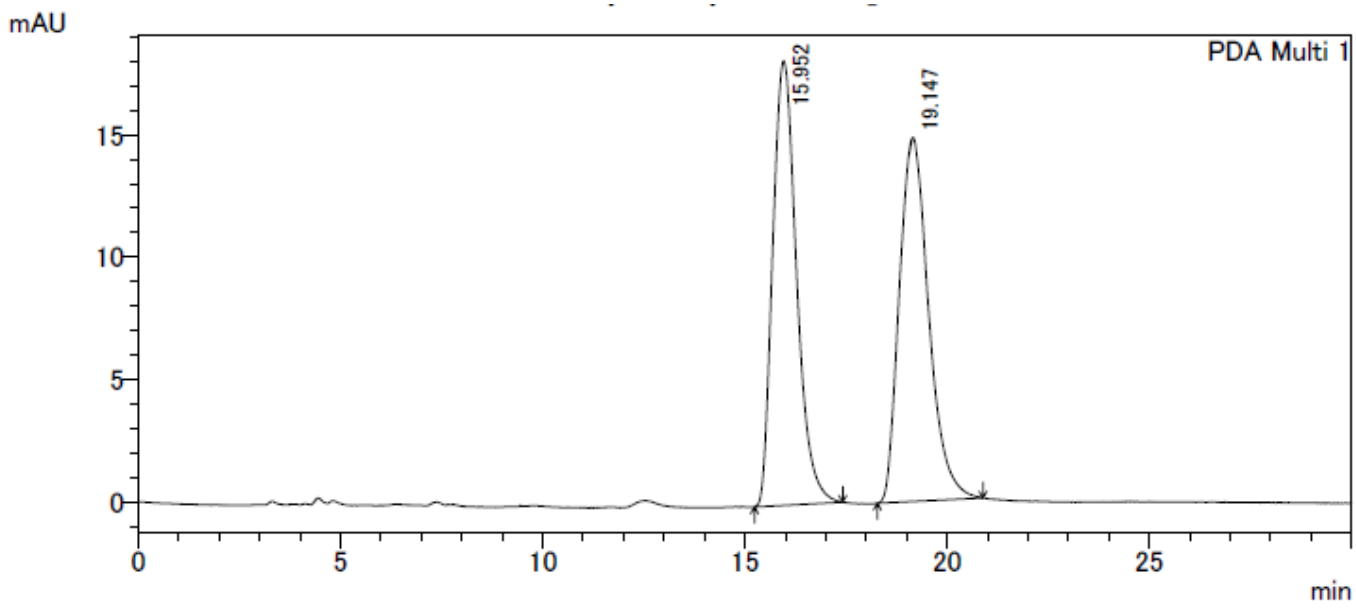
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	19.087	64340	1731	4.430	5.345
2	23.909	1387919	30660	95.570	94.655
合計		1452259	32392	100.000	100.000



Ethyl 3-(5-oxo-1-(pyridin-2-yl)pyrrolidin-2-yl)propanoate (3h).

Isolated by preparative TLC (hexane/EtOAc = 2/1, Rf = 0.3). The title compound was obtained as yellow oil (87%). ^{1}H NMR δ 8.36-8.35 (m, 1H), 8.24-8.22 (m, 1H), 7.71-7.67 (m, 1H), 7.04-7.02 (m, 1H), 4.87-4.83 (m, 1H), 4.13-4.09 (m, 2H), 2.79-2.72 (m, 1H), 2.59-2.52 (m, 1H), 2.39-2.16 (m, 4H), 1.92-1.85 (m, 2H), 1.26-1.22 (m, 3H); ^{13}C NMR δ 174.8, 173.1, 151.3, 147.8, 137.8, 119.9, 116.4, 60.7, 57.3, 32.2, 30.7, 28.6, 23.0, 14.3. HRMS(ESI) calcd for $C_{14}H_{18}N_2NaO_3$ (M+Na): 285.1210; found: 285.1208. $[\alpha]^{27}_{D}$ = +63.4 (*c* 1.87, $CHCl_3$, 91% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 18.4 min for major isomer and 15.7 min for minor isomer).

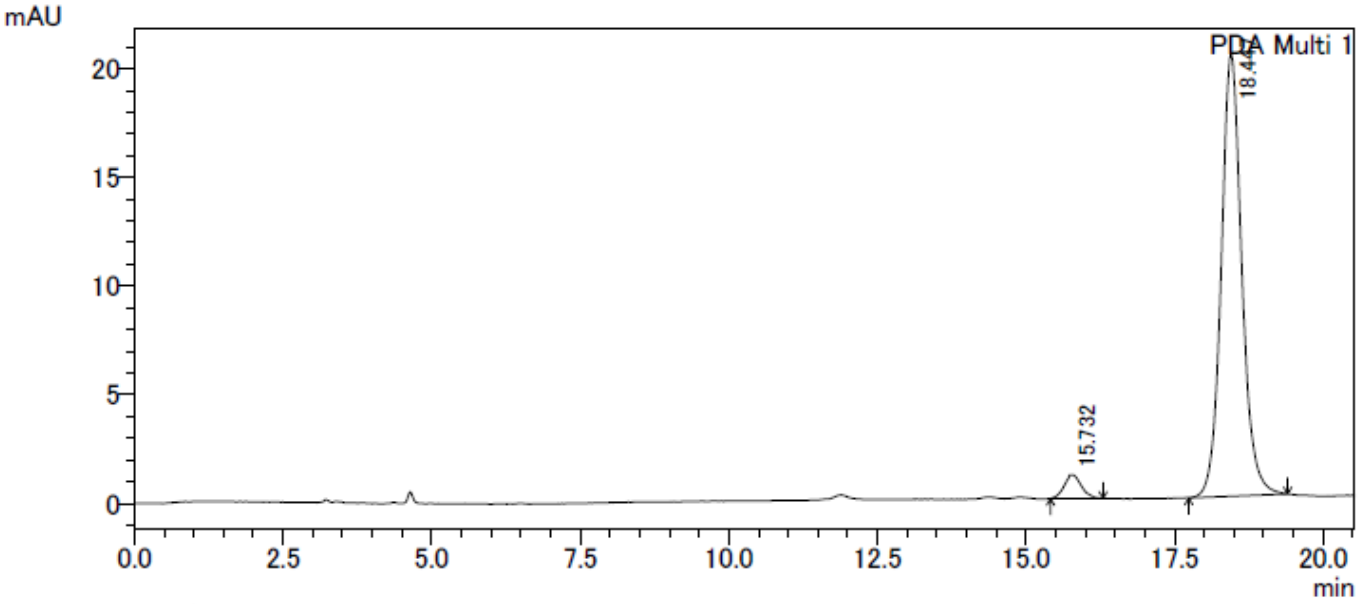


1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	15.952	742951	18158	49.821	54.996
2	19.147	748296	14859	50.179	45.004
合計		1491247	33018	100.000	100.000

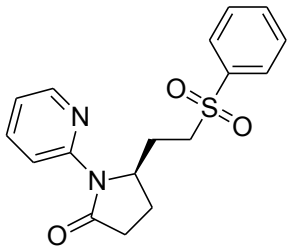


1 PDA Multi 1/254nm 4nm

ピークテーブル

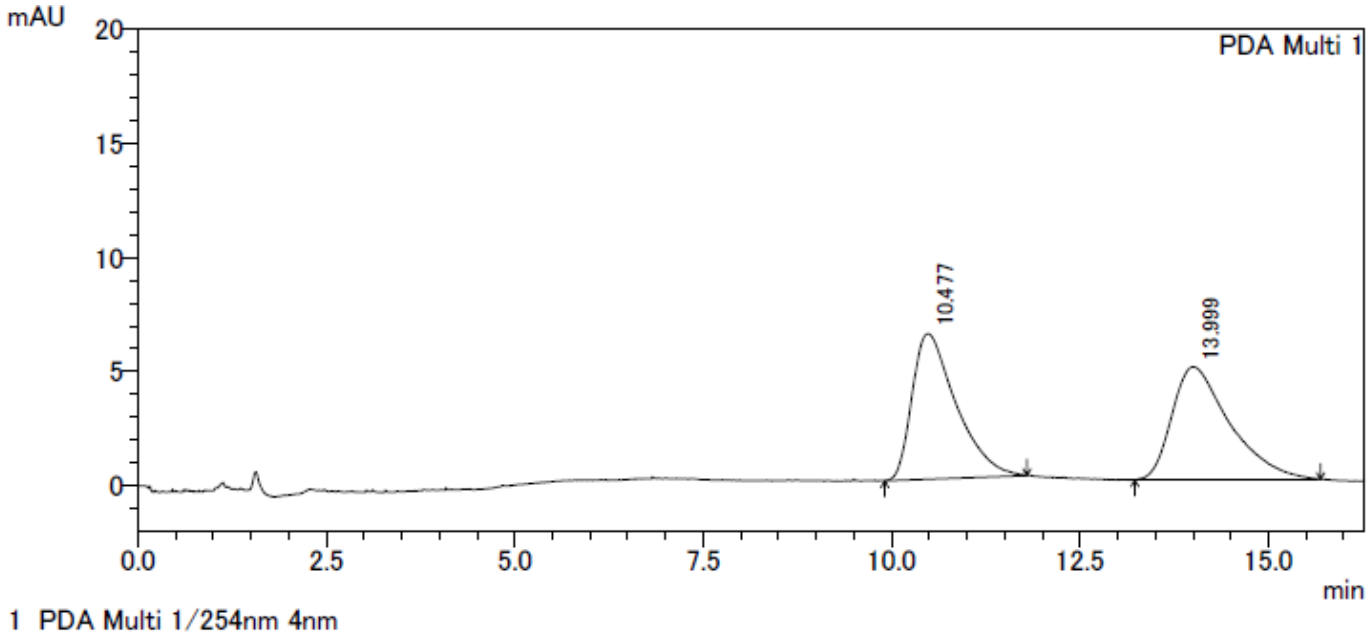
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	15.732	21688	1081	4.235	5.047
2	18.447	490412	20343	95.765	94.953
合計		512100	21425	100.000	100.000



5-(2-(Phenylsulfonyl)ethyl)-1-(pyridin-2-yl)pyrrolidin-2-one (3i).

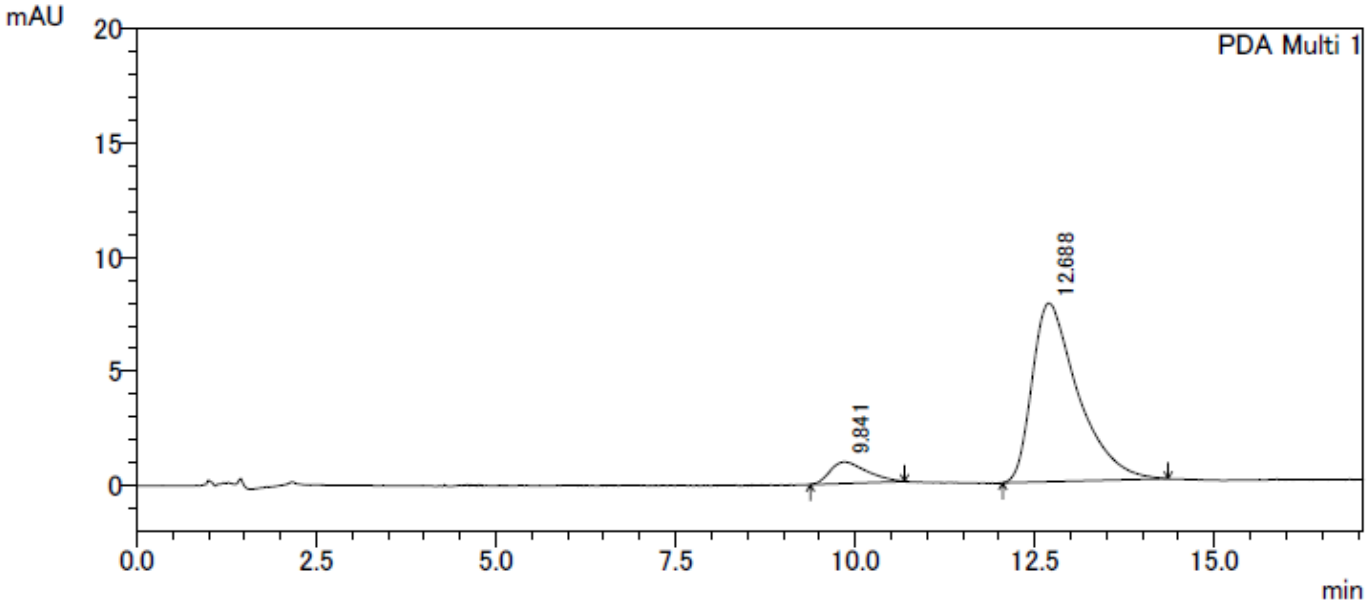
Isolated by preparative TLC (hexane/EtOAc = 1/2, Rf = 0.5). The title compound was obtained as yellow oil (70%). ^{1}H NMR δ 8.22-8.18 (m, 2H), 7.87-7.85 (m, 2H), 7.68-7.62 (m, 2H), 7.55-7.52 (m, 2H), 7.02-6.99 (m, 1H), 4.83-4.80 (m, 1H), 3.21-3.07 (m, 2H), 2.72-2.65 (m, 1H), 2.57-2.51 (m, 1H), 2.32-2.22 (m, 2H), 2.03-1.96 (m, 1H), 1.83-1.77 (m, 1H); ^{13}C NMR δ 174.3, 150.6, 147.4, 138.6, 137.7, 133.7, 129.2, 128.0, 119.8, 115.9, 56.1, 52.6, 31.7, 26.5, 22.8. HRMS(ESI) calcd for $C_{17}H_{18}N_2NaO_3S$ (M+Na): 353.0930; found: 353.0926. $[\alpha]^{29}_{D}$ = +53.4 (*c* 1.96, $CHCl_3$, 82% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IC: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/DCM = 1/1, flow rate: 4.0 mL/min, retention time: 12.7 min for major isomer and 9.8 min for minor isomer).



ピークテーブル

PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	10.477	259231	6377	49.589	56.303
2	13.999	263527	4949	50.411	43.697
合計		522758	11326	100.000	100.000

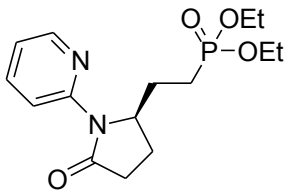


1 PDA Multi 1/254nm 4nm

ピークテーブル

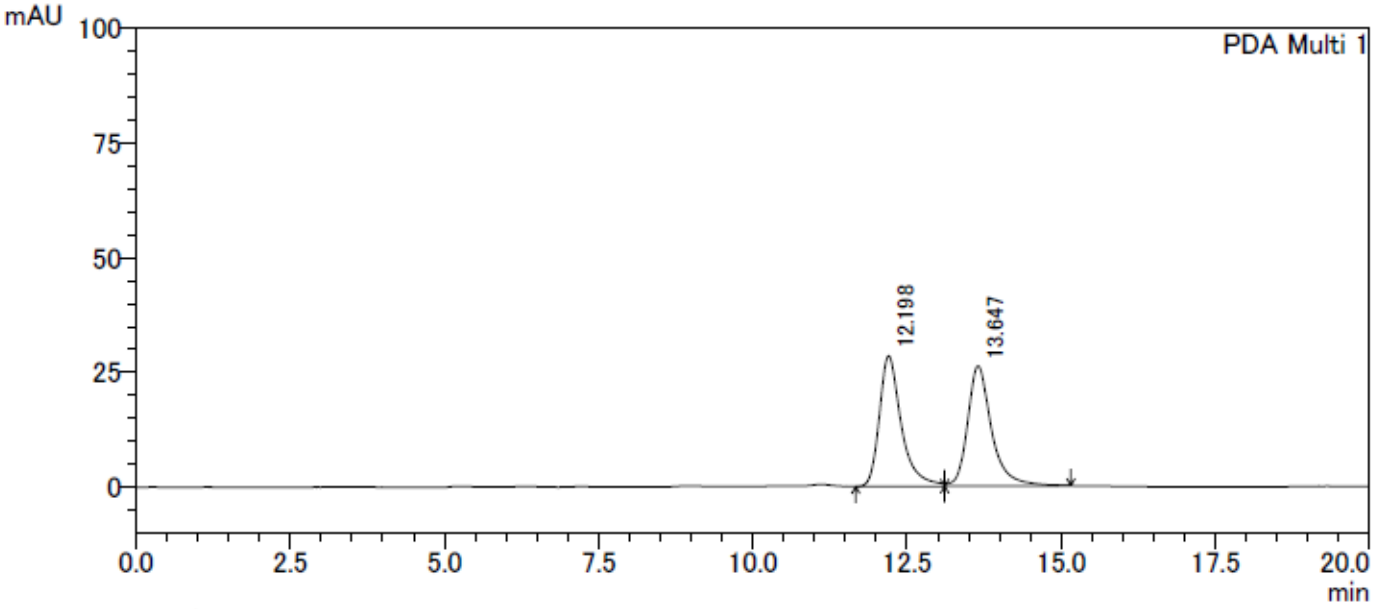
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	9.841	33758	956	8.842	10.891
2	12.688	348047	7821	91.158	89.109
合計		381805	8777	100.000	100.000



Diethyl 2-(5-oxo-1-(pyridin-2-yl)pyrrolidin-2-yl)ethylphosphonate (3j).

Isolated by preparative TLC (MeOH/EtOAc = 1/9, Rf = 0.4). The title compound was obtained as yellow oil (65%). ^{1}H NMR δ 8.36-8.34 (m, 1H), 8.23-8.22 (m, 1H), 7.72-7.68 (m, 1H), 7.06-7.03 (m, 1H), 4.85-4.80 (m, 1H), 4.12-3.96 (m, 4H), 2.78-2.70 (m, 1H), 2.60-2.54 (m, 1H), 2.32-2.24 (m, 1H), 2.19-2.13 (m, 1H), 1.91-1.69 (m, 4H), 1.30-1.26 (q, *J* = 7.2 Hz, 6H); ^{13}C NMR δ 174.5, 150.9, 147.5, 137.6, 119.7, 116.2, 61.6, 61.5, 57.8, 57.7, 31.9, 25.9, 25.8, 22.3, 22.1, 20.9, 16.3, 16.3, 16.3, 16.3. HRMS(ESI) calcd for $C_{15}H_{23}N_2NaO_4P$ (M+Na): 349.1288; found: 349.1291. $[\alpha]^{30}_{D}$ = +32.2 (*c* 1.65, $CHCl_3$, 76% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 1/1, flow rate: 0.5 mL/min, retention time: 13.4 min for major isomer and 11.9 min for minor isomer).

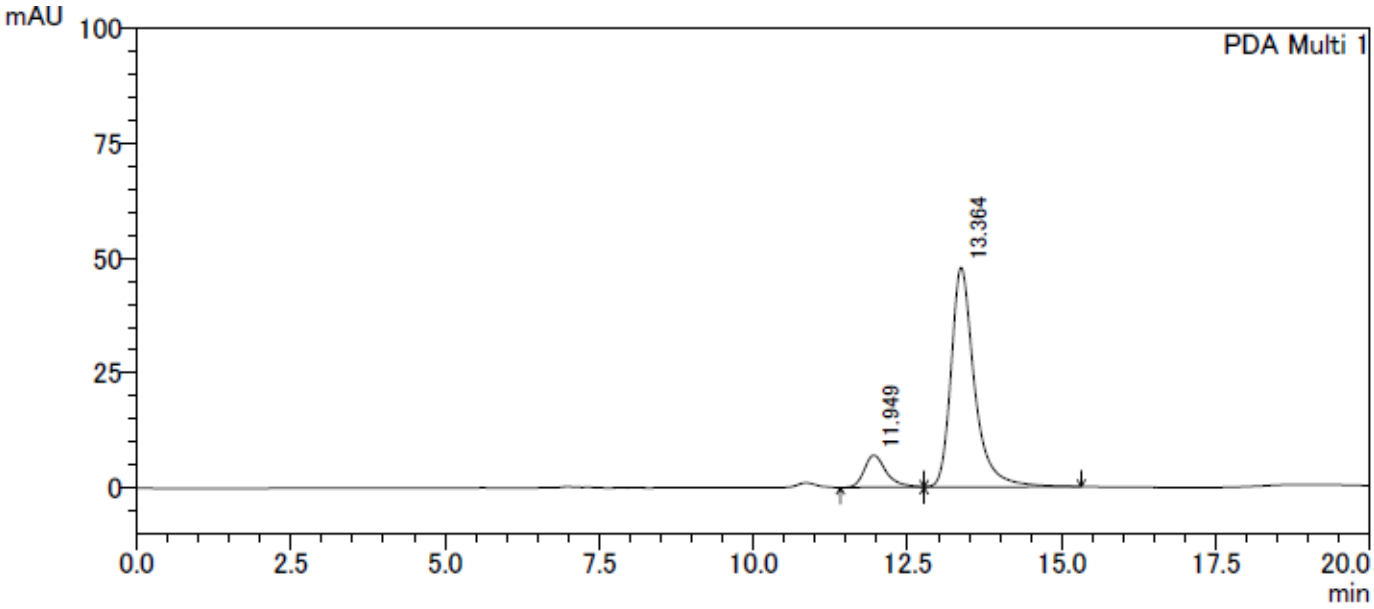


1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	12.198	705358	28467	49.844	52.082
2	13.647	709775	26191	50.156	47.918
合計		1415132	54658	100.000	100.000

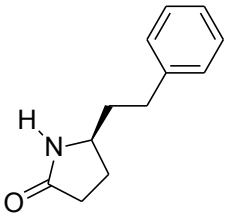


1 PDA Multi 1/254nm 4nm

ピークテーブル

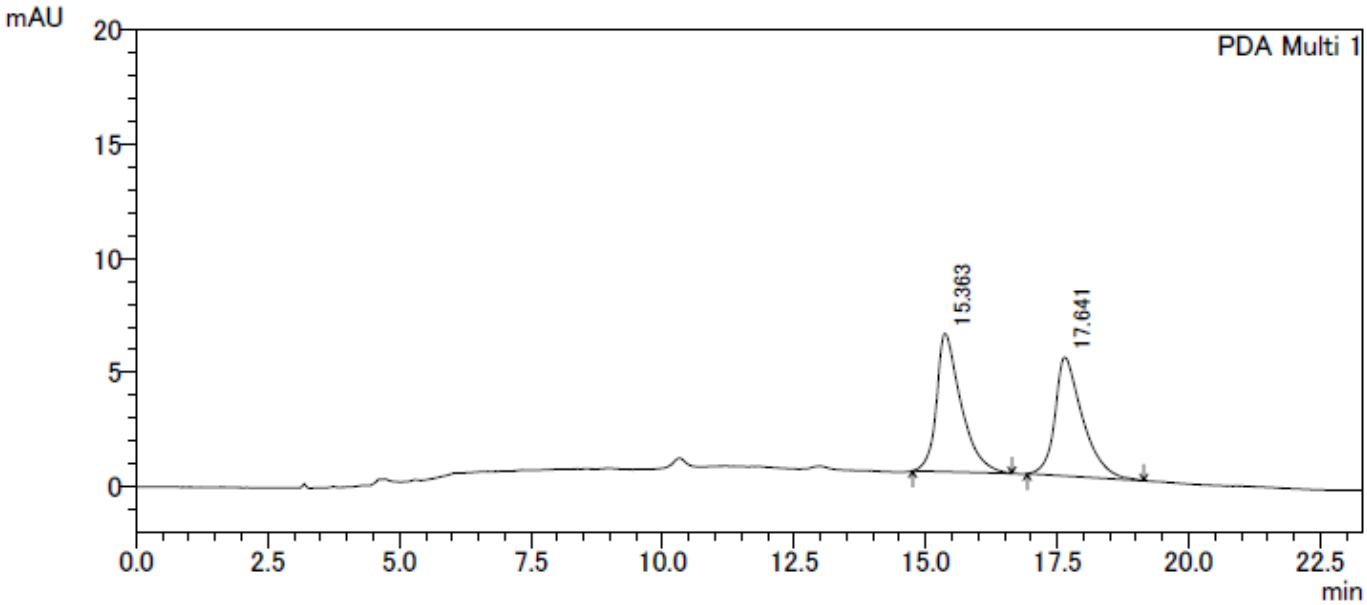
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	11.949	174690	6998	12.117	12.762
2	13.364	1267011	47836	87.883	87.238
合計		1441701	54834	100.000	100.000



(*S*)-5-Phenethylpyrrolidin-2-one (4a).

The title compound was obtained as white solid (86%). Mp 66 °C, ^{1}H NMR δ 7.31-7.17 (m, 5H, overlap with $CHCl_3$), 6.49 (br, 1H), 3.68-3.62 (m, 1H), 2.69-2.65 (m, 2H), 2.39-2.23 (m, 3H), 1.91-1.71 (m, 3H); ^{13}C NMR δ 178.3, 141.0, 128.6, 128.3, 126.2, 54.0, 38.4, 32.3, 30.1, 27.4. HRMS(ESI) calcd for $C_{12}H_{15}NNaO$ (M+Na): 212.1046; found: 212.1046. $[\alpha]^{21}_{D}$ = -22.2 (*c* 1.35, $CHCl_3$, 82% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IA: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 19/1, flow rate: 1.0 mL/min, retention time: 17.9 min for major isomer and 15.9 min for minor isomer).

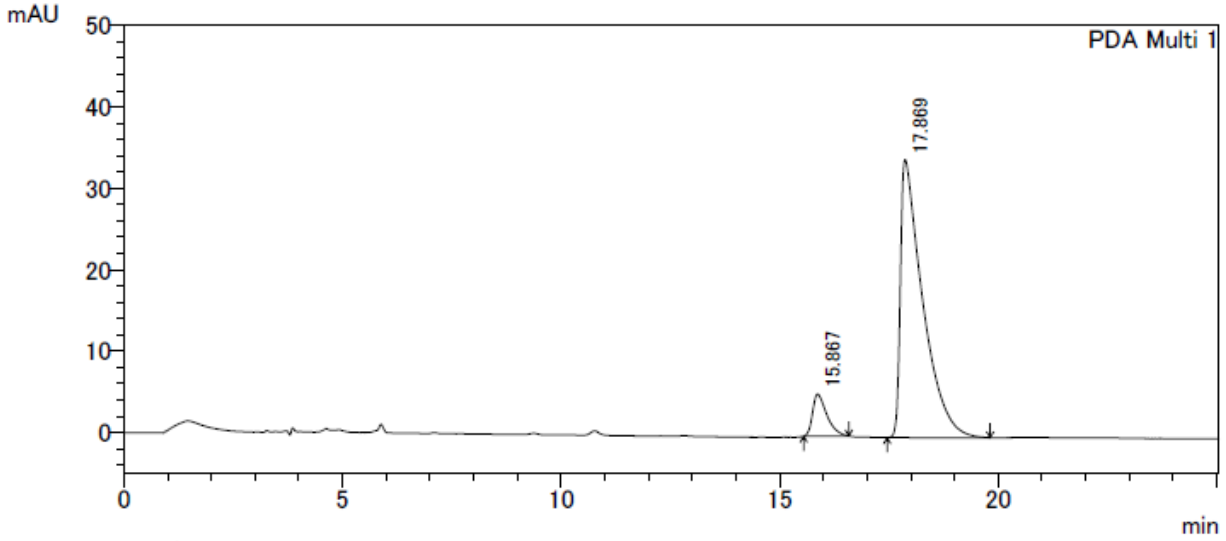


1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

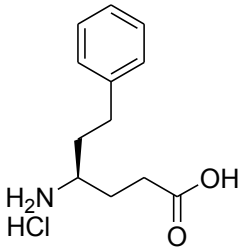
ピーク#	保持時間	面積	高さ	面積%	高さ%
1	15.363	197331	6070	50.821	53.893
2	17.641	190959	5193	49.179	46.107
合計		388290	11264	100.000	100.000



1 PDA Multi 1/254nm 4nm

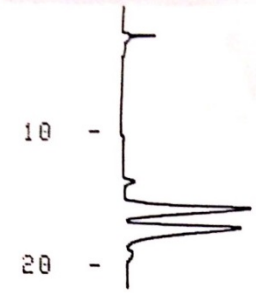
PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	15.867	117251	5172	8.832	13.152
2	17.869	1210275	34155	91.168	86.848
合計		1327526	39328	100.000	100.000



4-Amino-6-phenylhexanoic acid (5a).

The title compound was obtained as white solid (86%). Mp 157 °C, ^{1}H NMR δ 7.37-7.34 (m, 2H), 7.29-7.25 (m, 3H), 3.32-3.28 (m, 1H), 2.74-2.69 (m, 2H), 2.50-2.47 (m, 2H), 2.04-1.93 (m, 4H); ^{13}C NMR δ 176.9, 140.7, 128.8, 128.4, 126.5, 50.6, 33.4, 30.5, 29.5, 26.8. HRMS(ESI) calcd for $C_{12}H_{18}NO_2$ (M+H): 208.1332; found: 208.1333. $[\alpha]^{27}_{D}$ = -4.3 (*c* 1.20, H_2O, 82% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak ZWIX(+): 4.6 x 250 mm, 254 nm UV detector, rt, eluent: MeOH//H_2O = 49/49/2, flow rate: 1.0 mL/min, retention time: 15.9 min for major isomer and 17.5 min for minor isomer).



CHROMATOPAC C-R6A FILE 1
SAMPLE NO 0 METHOD 841
REPORT NO 85

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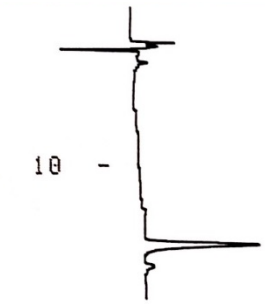

CHROMATOPAC C-R6A FILE 1
SAMPLE NO 0 METHOD 841
REPORT NO 98

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
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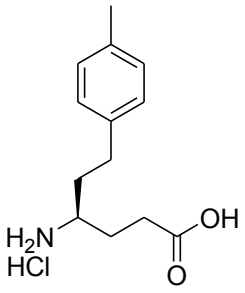
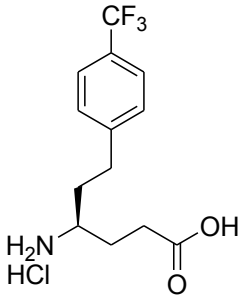


4-Amino-6-*p*-tolylhexanoic acid (5b).

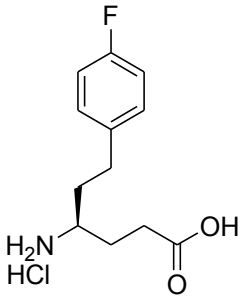
The title compound was obtained as white solid (71%). Mp 146 °C, ^{1}H NMR δ 7.22-7.21 (m, 4H), 3.33-3.30 (m, 1H), 2.72-2.68 (m, 2H), 2.52-2.49 (m, 2H), 2.31 (s, 3H), 2.03-1.94 (m, 4H); ^{13}C NMR δ 177.0, 137.6, 136.4, 129.3, 128.4, 50.6, 33.5, 30.0, 29.6, 26.8, 20.0. HRMS(ESI) calcd for $C_{13}H_{20}NO_2$ (M+H): 222.1489;

found: 222.1490. $[\alpha]^{25}_D$ = -5.2 (*c* 0.57, H_2O).



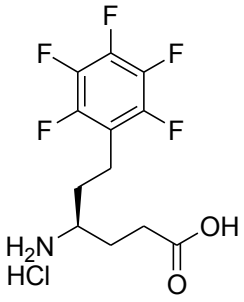
4-Amino-6-(4-(trifluoromethyl)phenyl)hexanoic acid (5c).

The title compound was obtained as white solid (79%). Mp 174 °C, ^{1}H NMR δ 7.49-7.47 (d, *J* = 8.2 Hz, 2H), 7.29-7.27 (d, *J* = 8.0 Hz, 2H), 3.27-3.24 (m, 1H), 2.74-2.62 (m, 2H), 2.42-2.39 (t, *J* = 7.5 Hz, 2H), 1.94-1.84 (m, 4H); ^{13}C NMR δ 176.6, 144.8, 128.7, 127.8, 125.3 (q, J_{C-F} = 3.9 Hz, 1C), 123.2, 33.1, 30.4, 29.4, 26.7. HRMS(ESI) calcd for $C_{13}H_{17}F_3NO_2$ (M+H): 276.1207; found: 276.1206. $[\alpha]^{28}_D$ = -5.0 (*c* 2.20, H_2O).



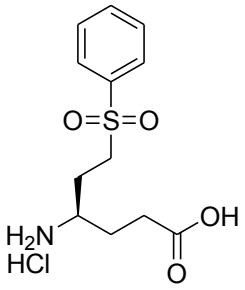
4-Amino-6-(4-fluorophenyl)hexanoic acid (5d).

The title compound was obtained as white solid (93%). Mp 161 °C, ^{1}H NMR δ 7.28-7.25 (m, 2H), 7.09-7.06 (m, 2H), 3.33-3.27 (m, 1H), 2.77-2.66 (m, 2H), 2.48 (t, *J* = 7.5 Hz, 2H), 2.04-1.87 (m, 4H); ^{13}C NMR δ 177.1, 162.2, 160.3, 136.4, 136.3, 129.9, 129.9, 115.2 (d, J_{C-F} = 10.7 Hz, 1C), 50.6, 33.5, 29.7, 29.6, 26.8. HRMS(ESI) calcd for $C_{12}H_{17}FNO_2$ (M+H): 226.1238; found: 226.1239. $[\alpha]^{30}_D$ = -3.7 (*c* 0.64, H_2O).



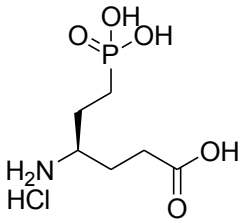
4-Amino-6-(pentafluorophenyl)hexanoic acid (5f).

The title compound was obtained as yellow paste (71%). Mp decomp (> 210 °C). ^{1}H NMR δ 3.42-3.39 (m, 1H), 2.91-2.87 (m, 2H), 2.58-2.55 (t, *J* = 7.5 Hz, 2H), 2.12-1.96 (m, 4H); ^{13}C NMR δ 176.8, 145.9, 143.9, 138.2, 136.3, 113.2, 50.6, 31.0, 29.5, 26.7, 17.7. HRMS(ESI) calcd for $C_{12}H_{13}F_5NO_2$ (M+H): 298.0861; found: 298.0860. $[\alpha]^{29}_D$ = -2.3 (*c* 0.81, H_2O).



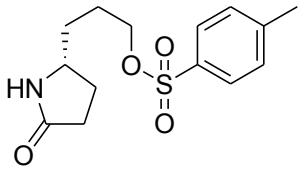
4-Amino-6-(phenylsulfonyl)hexanoic acid (5i).

The title compound was obtained as brown paste (64%). Mp decomp (> 210 °C). ^{1}H NMR δ 7.81 (d, *J* = 7.8 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 2H), 3.41-3.38 (m, 2H), 3.31-3.29 (m, 1H), 2.31-2.29 (m, 2H), 1.92-1.88 (m, 2H), 1.79-1.73 (m, 2H); ^{13}C NMR δ 176.5, 136.2, 135.0, 129.8, 127.8, 51.0, 49.5, 29.2, 26.4, 25.0. HRMS(ESI) calcd for $C_{12}H_{18}NO_4S$ (M+H): 272.0951; found: 272.0951. $[\alpha]^{32}_D$ = -3.1 (c 2.40, H_2O).



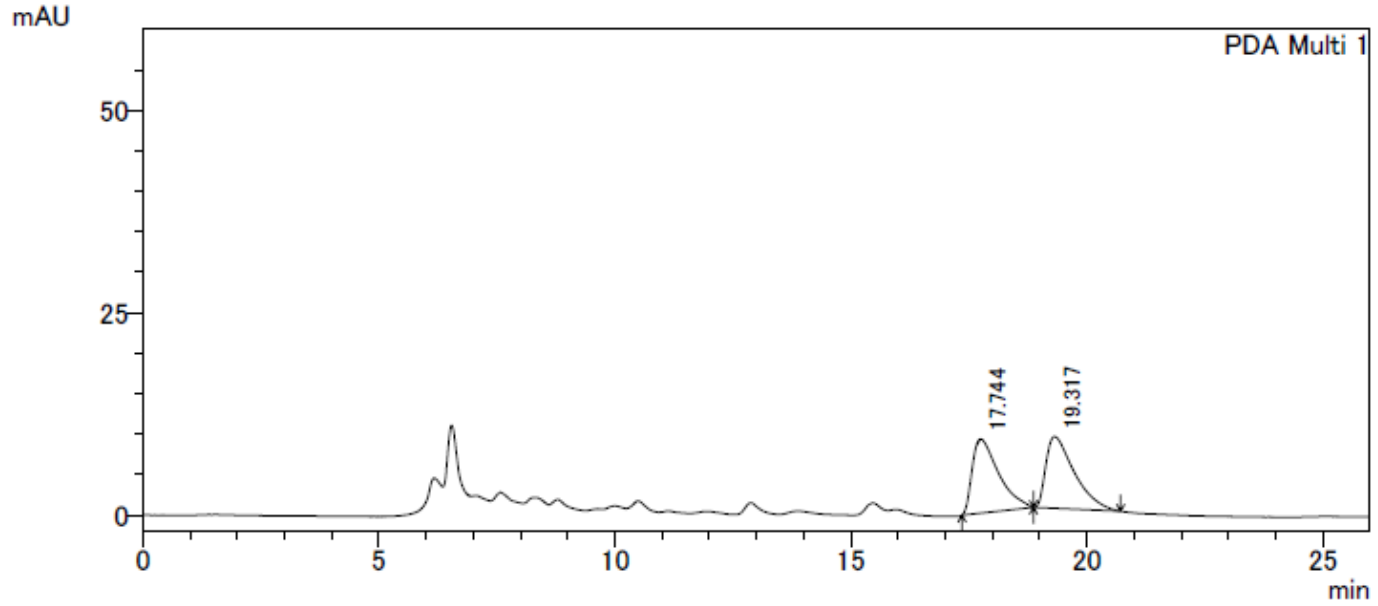
4-Amino-6-phosphonohexanoic acid (5j).

The title compound was obtained as yellow paste (56%). Mp decomp (> 210 °C). ^{1}H NMR δ 3.38-3.35 (m, 1H), 2.53-2.50 (m, 2H), 2.01-1.84 (m, 4H), 1.70-1.65 (m, 2H); ^{13}C NMR δ 176.8, 51.6, 29.5, 28.7, 26.6, 25.8. HRMS(ESI) calcd for $C_6H_{14}NO_5P$ (M+H): 212.0682; found: 212.0683. $[\alpha]^{32}_D$ = -1.2 (*c* 1.12, H_2O).



3-(5-Oxopyrrolidin-2-yl)propyl 4-methylbenzenesulfonate (6).

The title compound was obtained as white solid (59%). Mp 86 °C, ^{1}H NMR δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.50 (br, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 4.05-4.02 (m, 2H), 3.61-3.57 (m, 1H), 2.45-2.42 (m, 3H), 2.34-2.19 (m, 3H), 1.75-1.61 (m, 3H), 1.56-1.51 (m, 1H); ^{13}C NMR δ 178.6, 144.8, 132.8, 129.8, 127.7, 70.0, 53.9, 32.5, 30.1, 26.8, 25.2, 21.5. HRMS(ESI) calcd for $C_{14}H_{19}NNaO_4S$ (M+Na): 320.0927; found: 320.0926. $[\alpha]^{28}_D$ = -23.7 (*c* 4.20, $CHCl_3$, 90% ee). Ee was determined by HPLC analysis using a chiral column (Daicel Chiralpak IB: 4.6 x 250 mm, 254 nm UV detector, rt, eluent: hexane/2-propanol = 1/1, flow rate: 0.5 mL/min, retention time: 17.2 min for major isomer and 19.4 min for minor isomer).

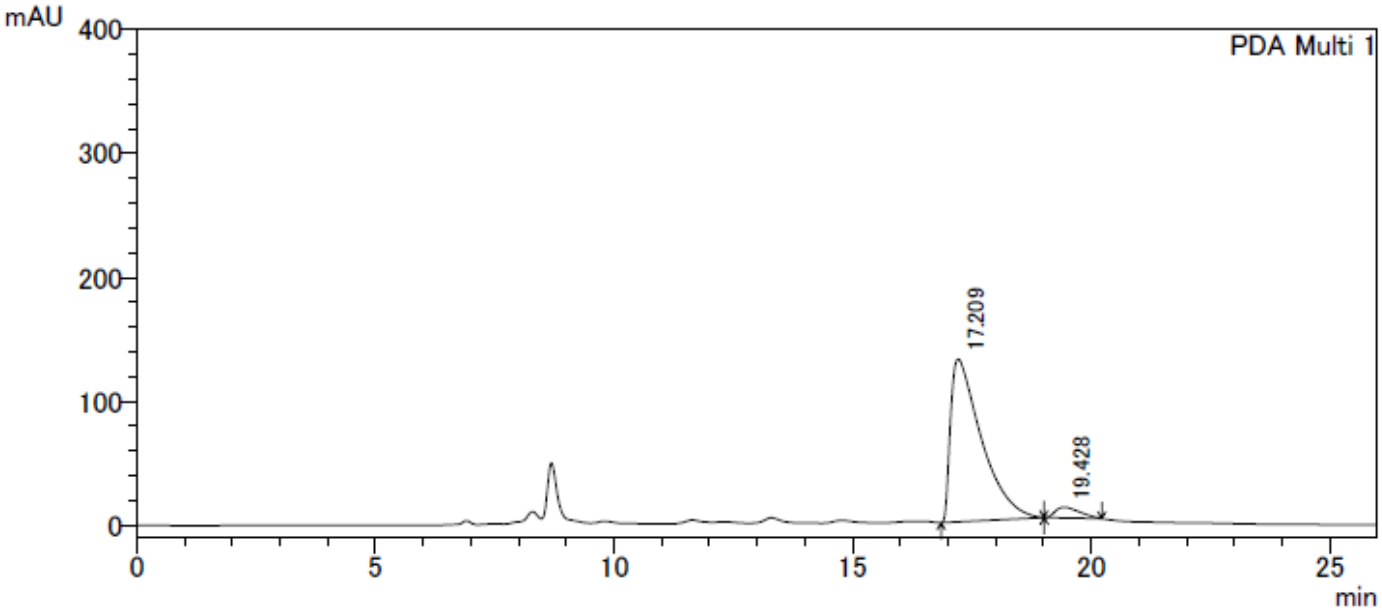


1 PDA Multi 1/254nm 4nm

ピークテーブル

PDA Ch1 254nm 4nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	17.744	355559	9163	48.904	50.826
2	19.317	371497	8865	51.096	49.174
合計		727055	18028	100.000	100.000



1 PDA Multi 1/254nm 4nm

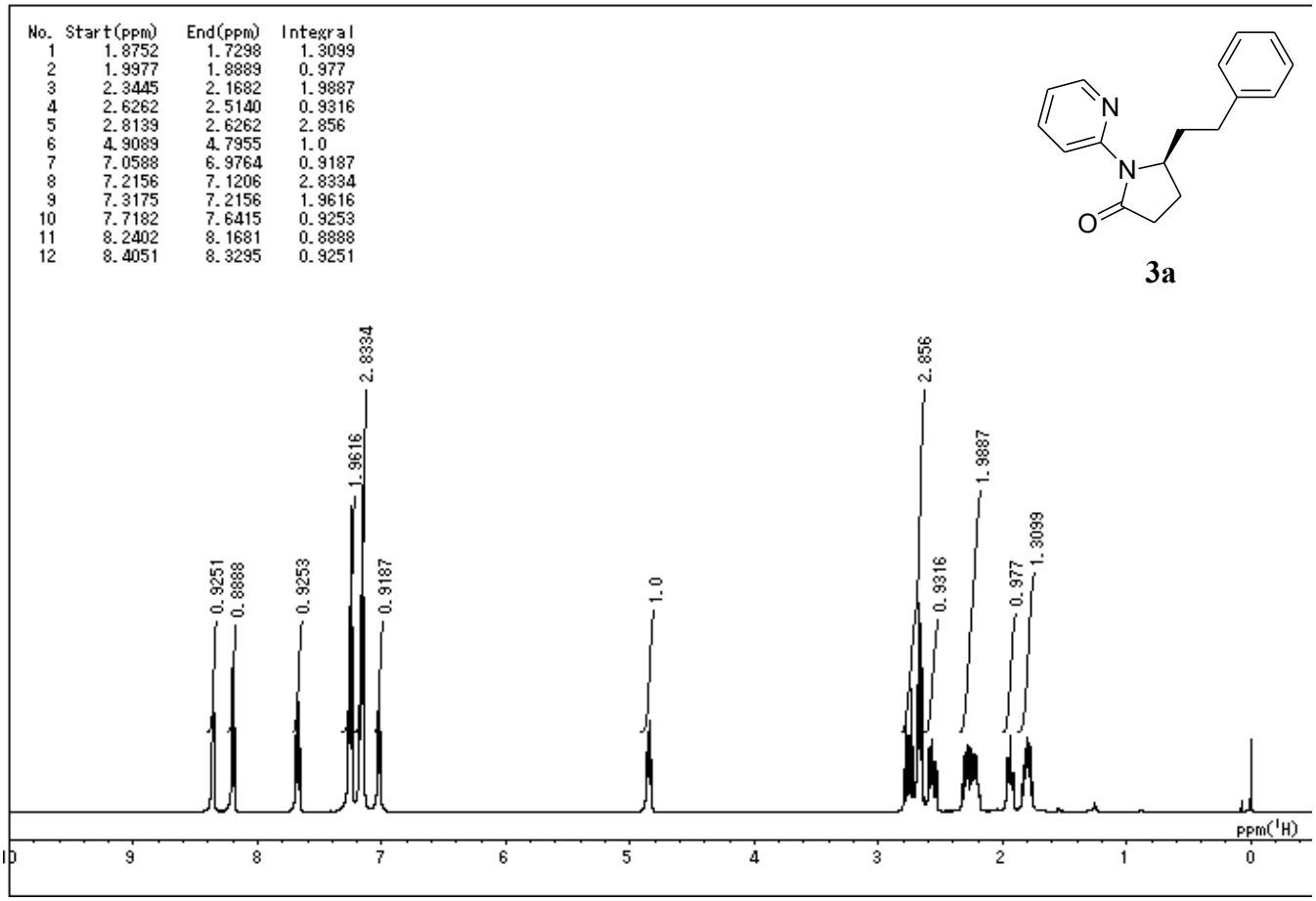
ピークテーブル

PDA Ch1 254nm 4nm

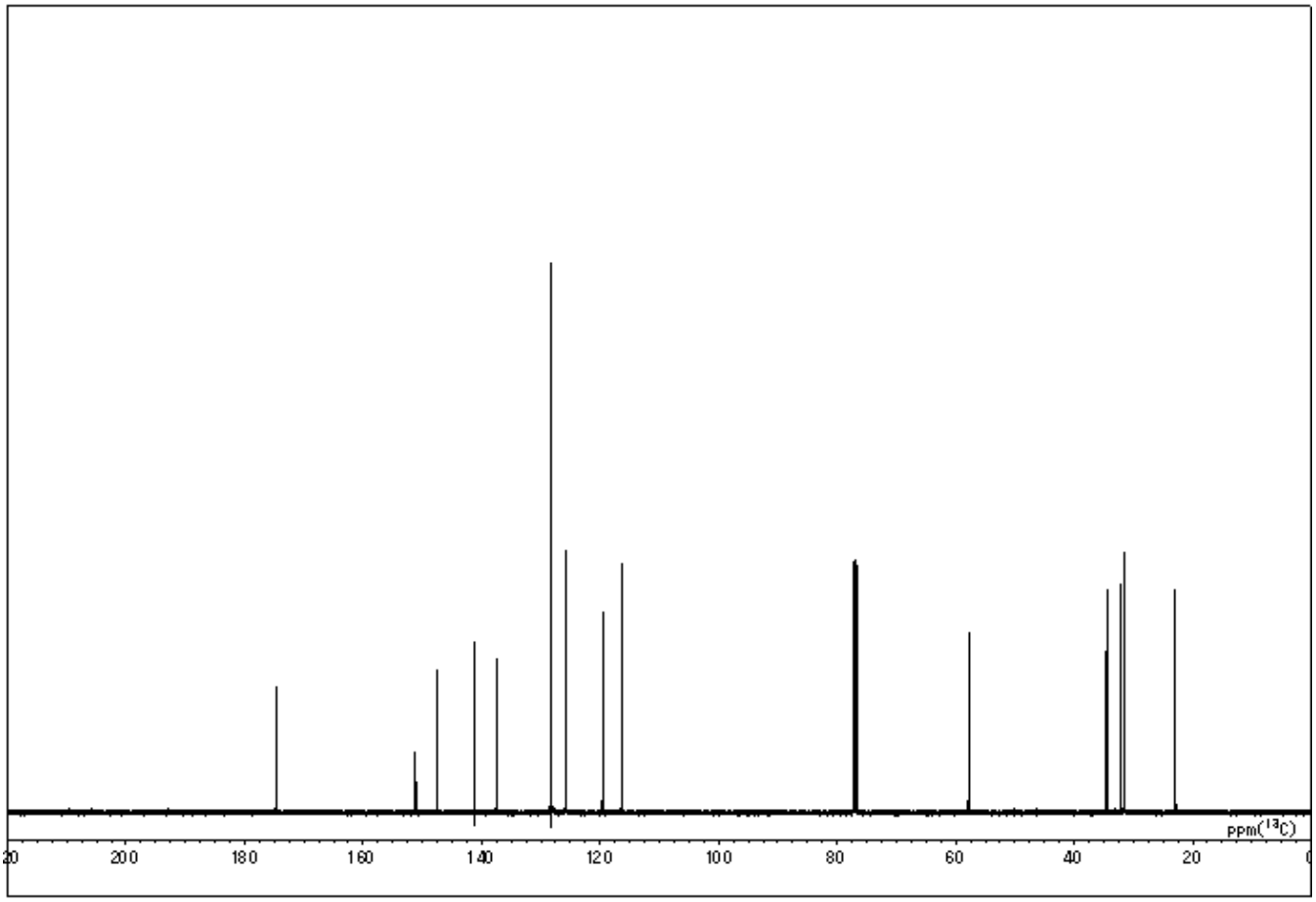
ピーク#	保持時間	面積	高さ	面積%	高さ%
1	17.209	5920300	131599	95.010	93.829
2	19.428	310968	8655	4.990	6.171
合計		6231269	140254	100.000	100.000

2) ^{1}H NMR and ^{13}C NMR spectra for new compounds

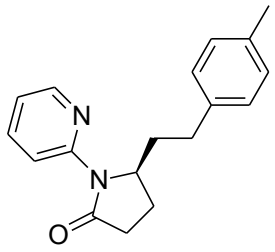
No.	Start(ppm)	End(ppm)	Integral
1	1.8752	1.7298	1.3099
2	1.9977	1.8889	0.977
3	2.3445	2.1682	1.9887
4	2.6262	2.5140	0.9316
5	2.8139	2.6262	2.856
6	4.9089	4.7955	1.0
7	7.0588	6.9764	0.9187
8	7.2156	7.1206	2.8334
9	7.3175	7.2156	1.9616
10	7.7182	7.6415	0.9253
11	8.2402	8.1681	0.8888
12	8.4051	8.3295	0.9251



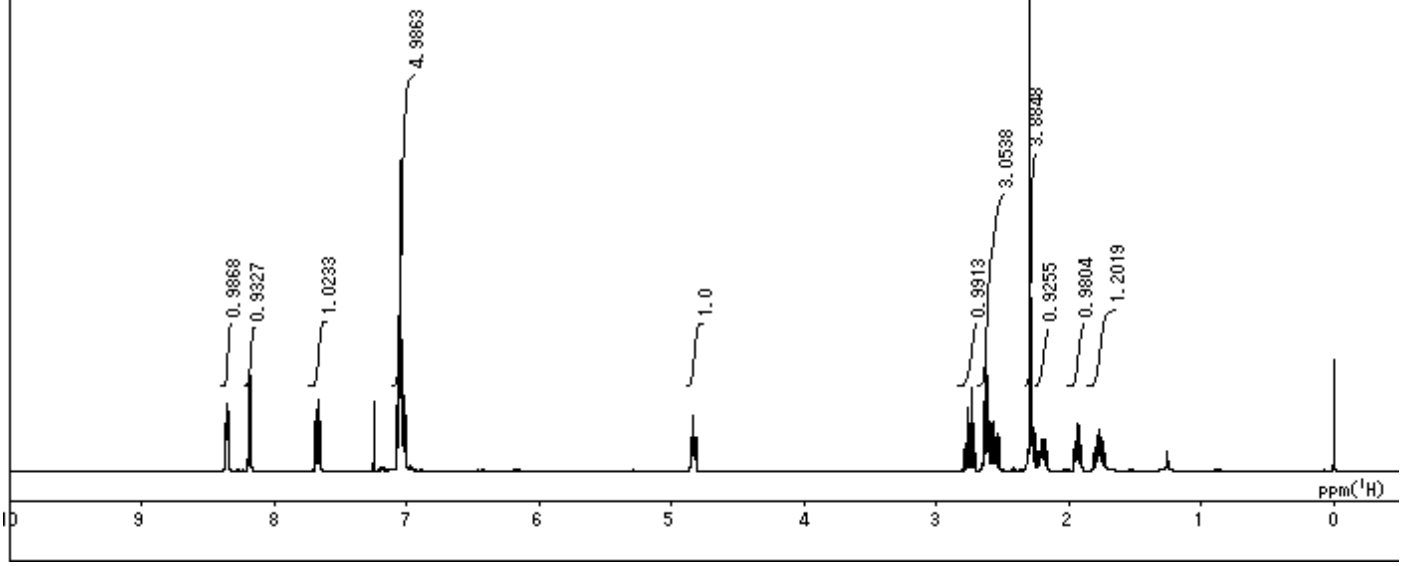
3a

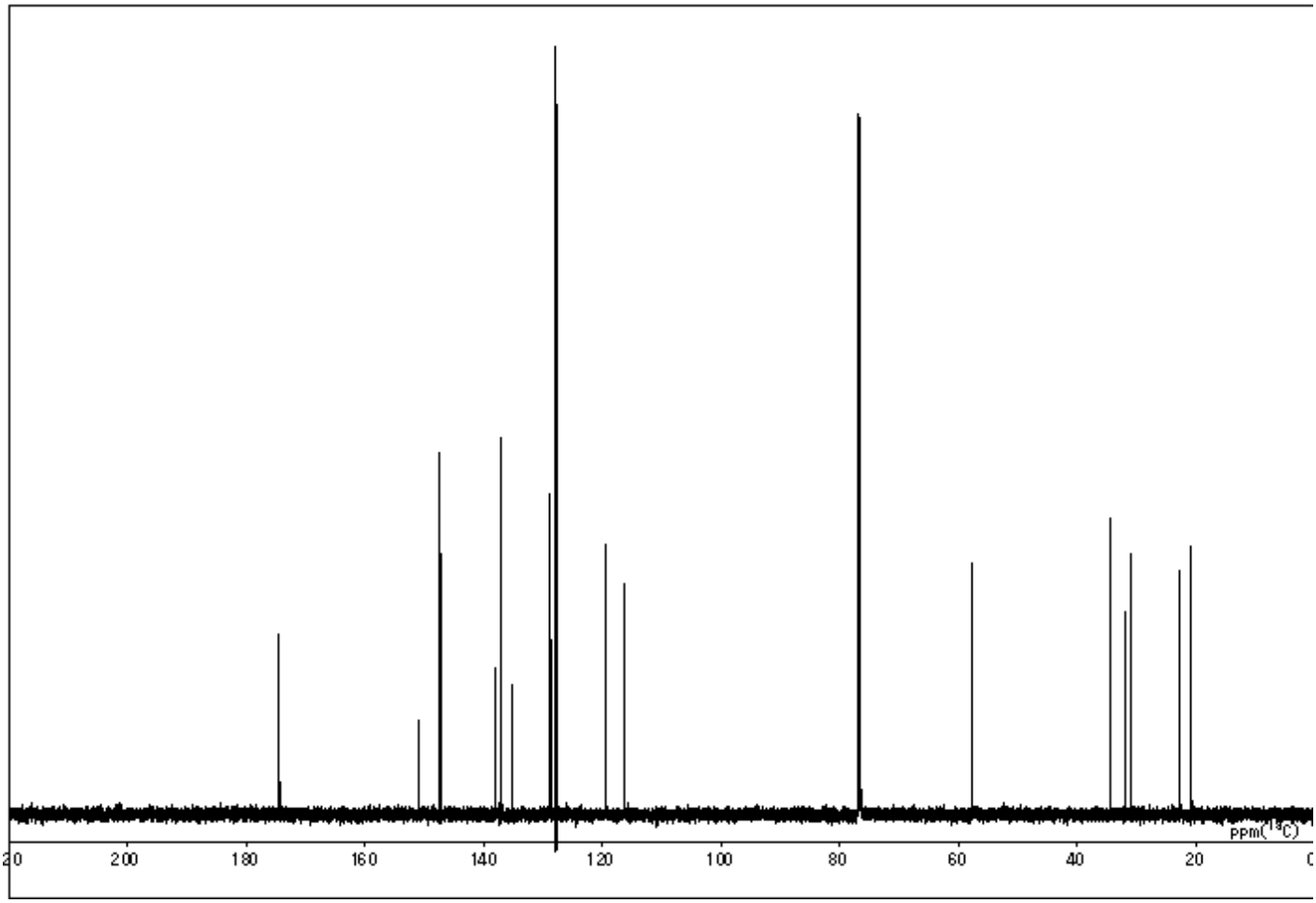


No.	Start(ppm)	End(ppm)	Integral
1	1.8639	1.6429	1.2019
2	2.0173	1.8730	0.9804
3	2.2462	2.1489	0.9255
4	2.3344	2.2462	3.8848
5	2.6893	2.4843	3.0538
6	2.8415	2.6893	0.9913
7	4.8907	4.7545	1.0
8	7.1104	6.9319	4.9863
9	7.7389	7.5867	1.0233
10	8.2323	8.1304	0.9327
11	8.4029	8.3090	0.9868

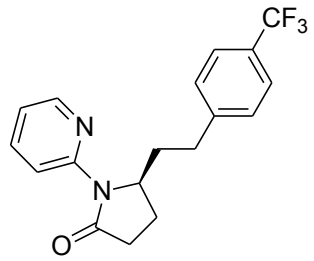


3b





No.	Start(ppm)	End(ppm)	Integral
1	1.8888	1.7754	0.9774
2	1.9872	1.8991	0.9863
3	2.3570	2.1933	2.0525
4	2.6340	2.5367	1.0101
5	2.8218	2.6844	3.1308
6	4.8847	4.8034	1.0
7	7.0701	6.9842	1.0165
8	7.3105	7.2223	2.1395
9	7.5429	7.4662	1.9978
10	7.7157	7.6402	0.9863
11	8.2435	8.1679	0.9738
12	8.3717	8.3099	0.9996



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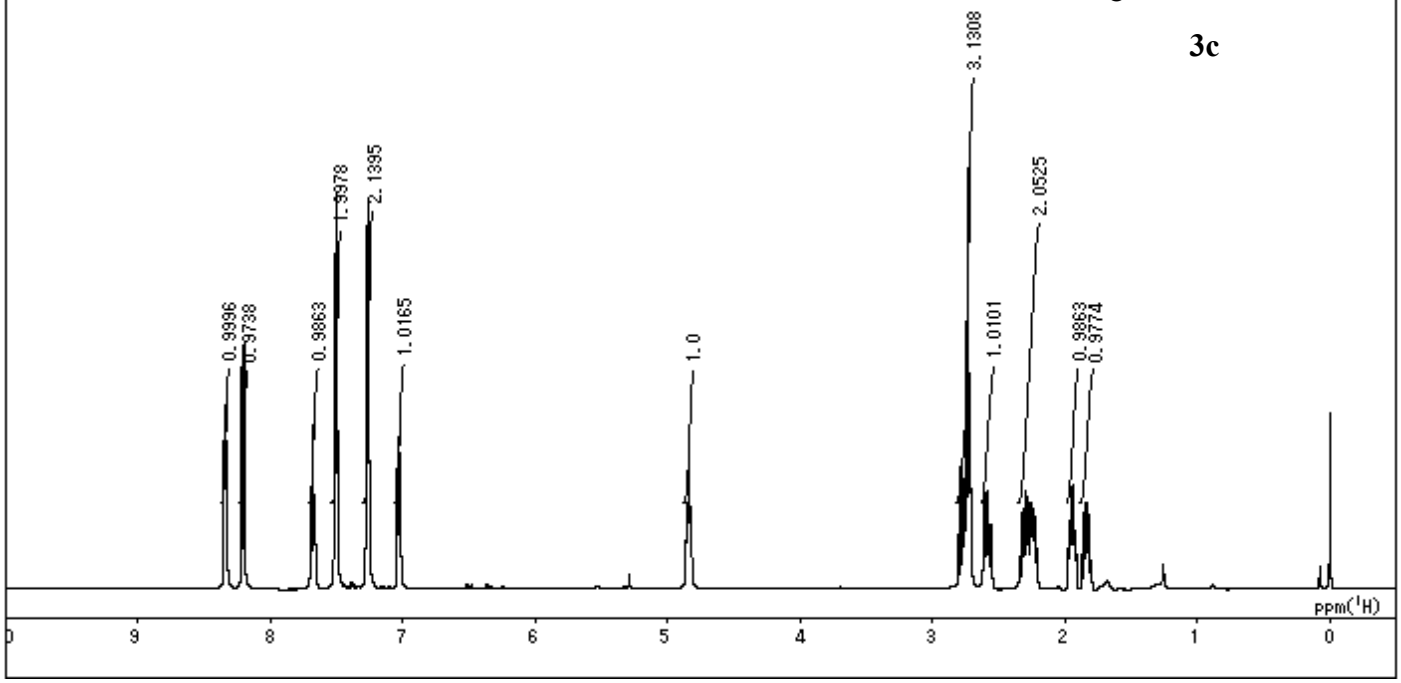
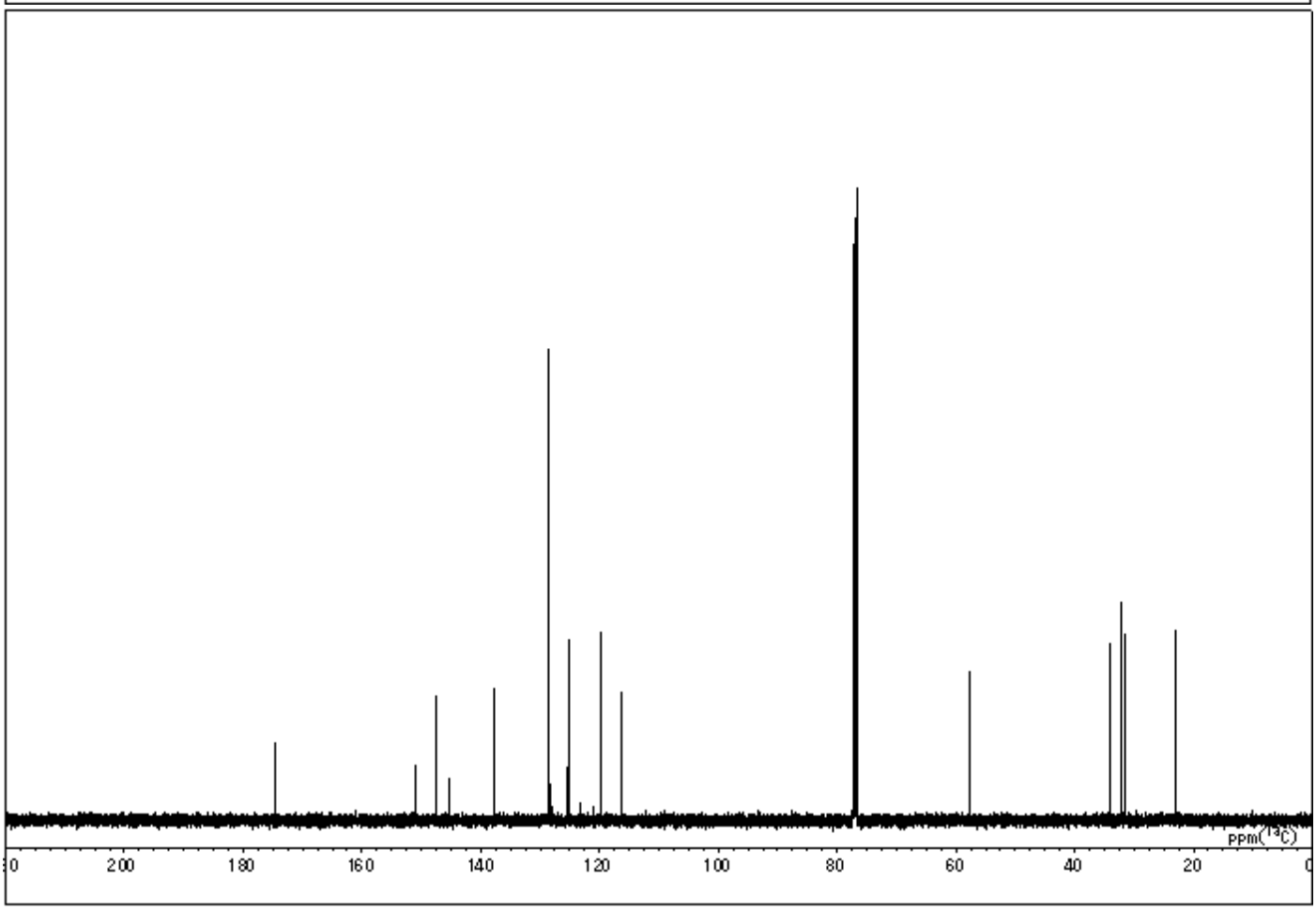
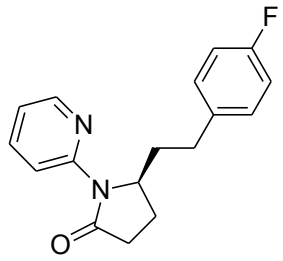
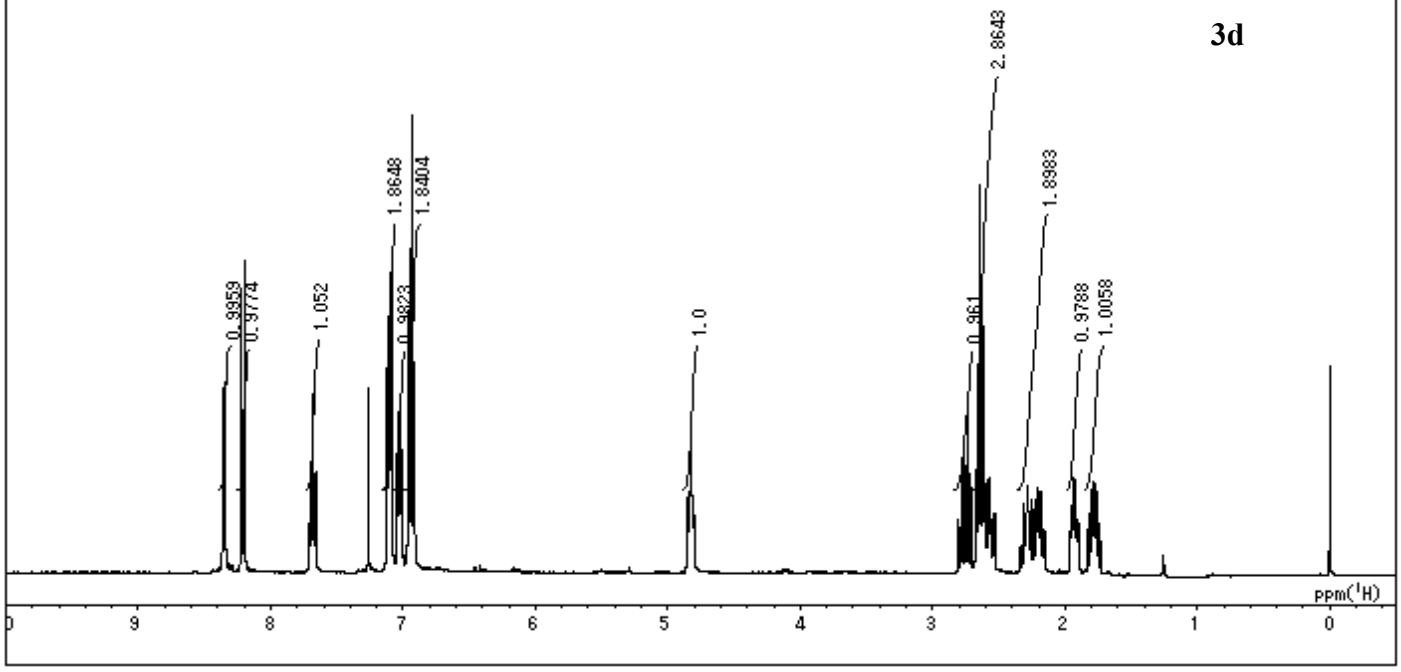


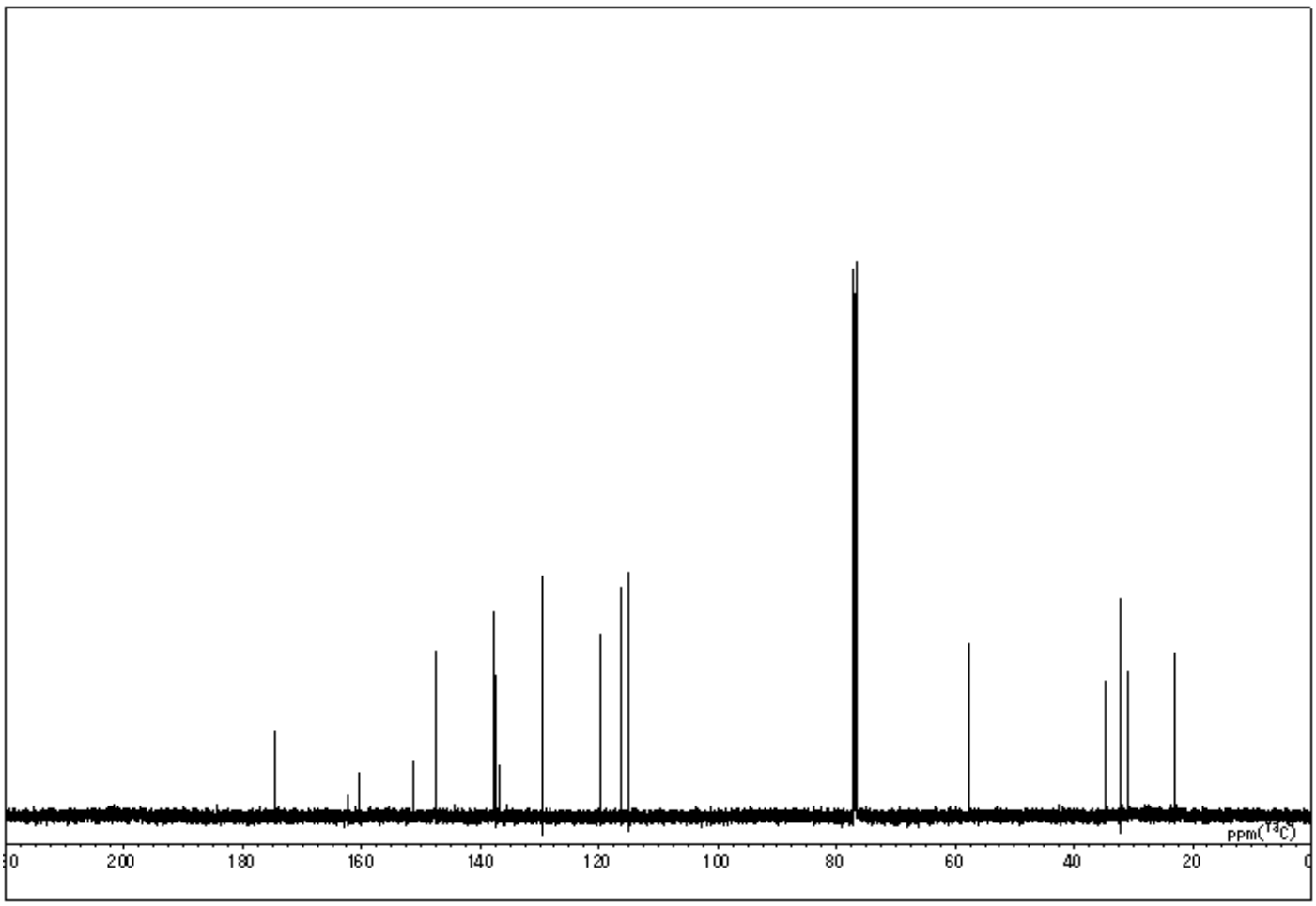


No.	Start(ppm)	End(ppm)	Integral
1	1.8448	1.7028	1.0058
2	1.9846	1.8712	0.9788
3	2.3523	2.1186	1.8983
4	2.6902	2.5046	2.8643
5	2.8391	2.6902	0.961
6	4.8907	4.7670	1.0
7	6.9950	6.8587	1.8404
8	7.0603	6.9870	0.9823
9	7.1542	7.0603	1.8648
10	7.7338	7.6170	1.052
11	8.2504	8.1542	0.9774
12	8.3936	8.2917	0.9959

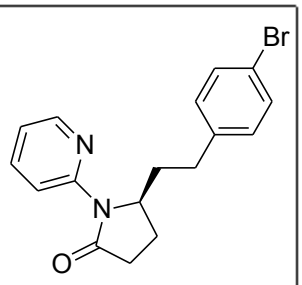


3d





No.	Start(ppm)	End(ppm)	Integral
1	1.8370	1.7191	1.1134
2	1.9595	1.8690	0.9971
3	2.3338	2.1404	2.0271
4	2.6612	2.5078	3.0617
5	2.8089	2.6956	1.0377
6	4.8547	4.7768	1.0
7	7.0618	6.9805	3.0304
8	7.4030	7.3320	1.9525
9	7.7189	7.6308	1.0383
10	8.2398	8.1643	0.9713
11	8.3795	8.3039	0.9936



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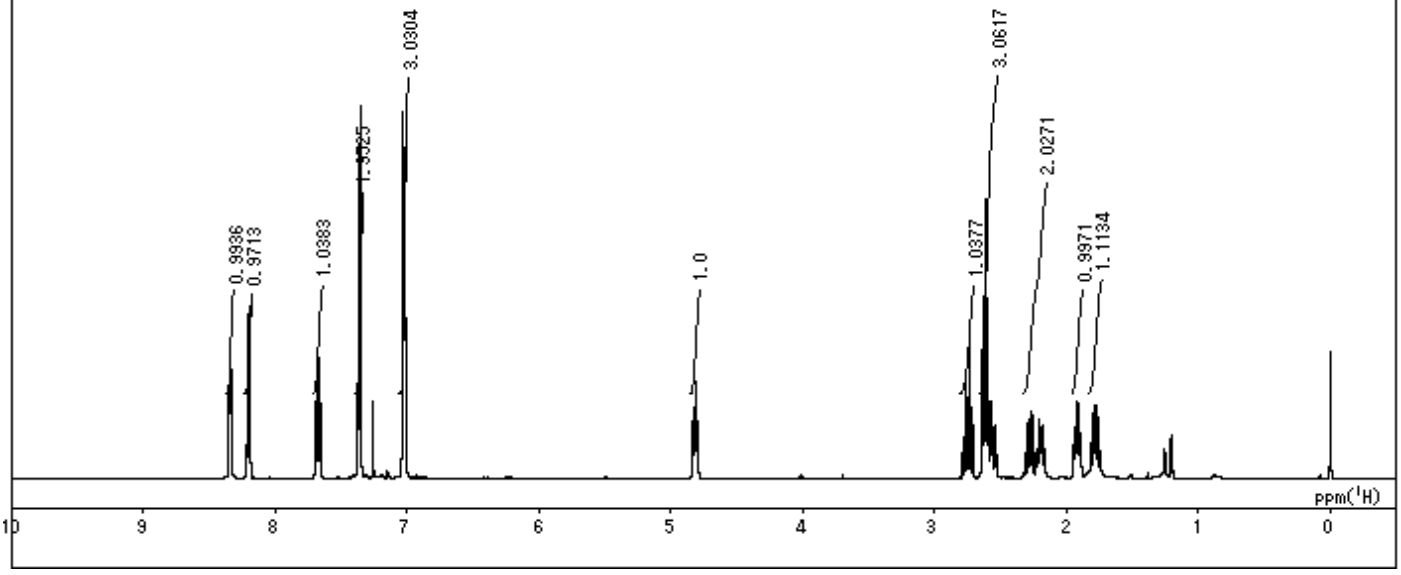
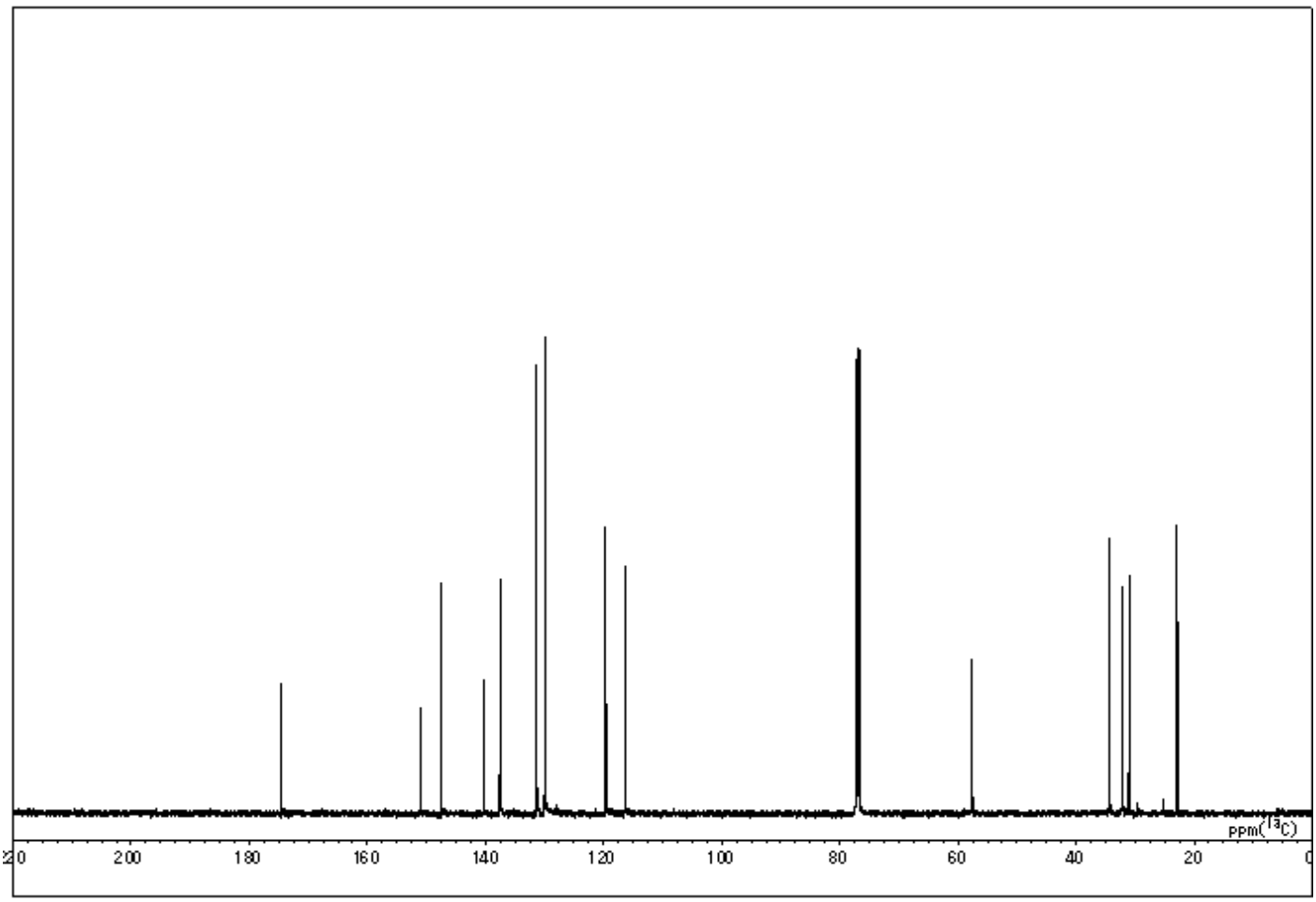
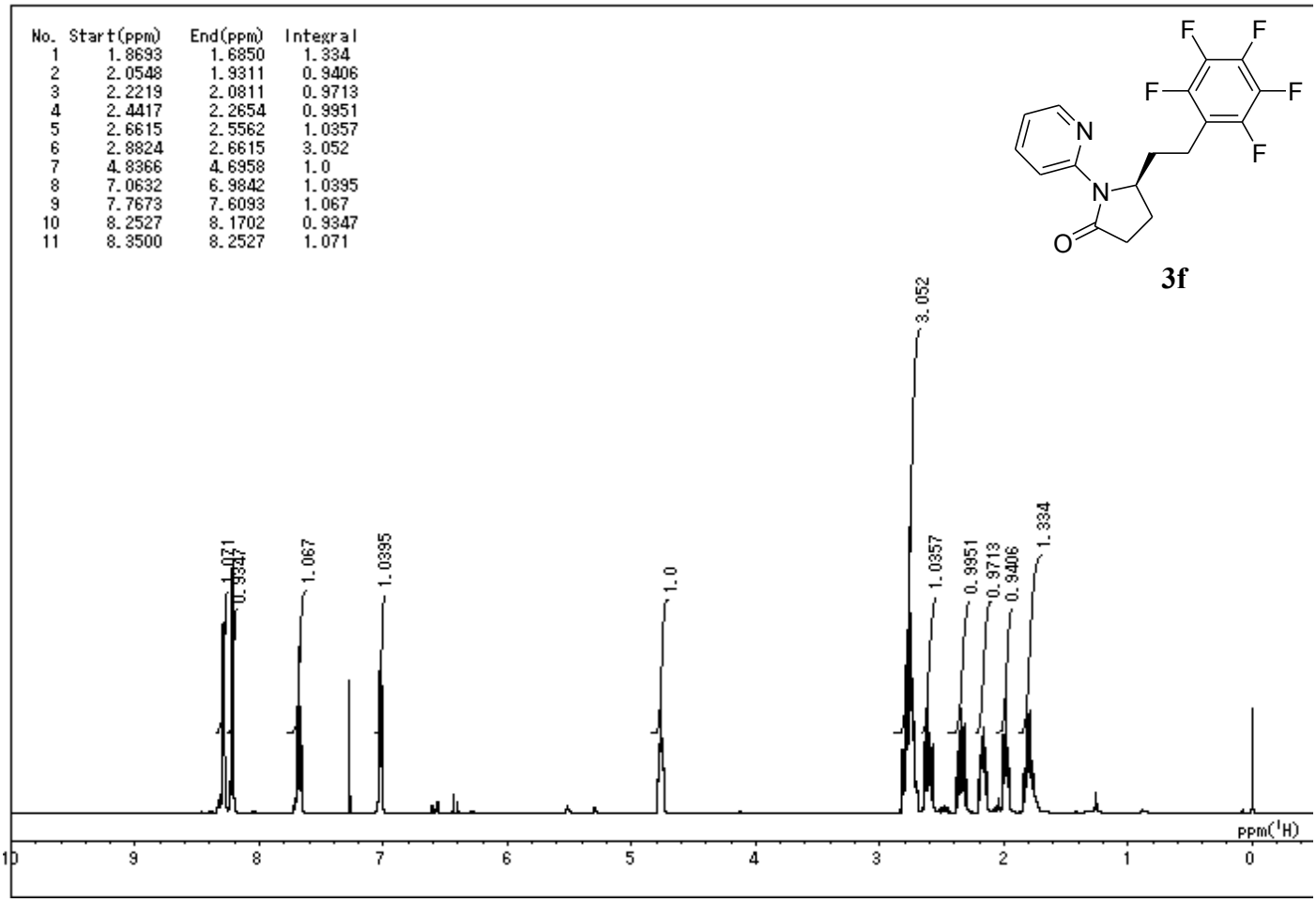




No.	Start(ppm)	End(ppm)	Integral
1	1.8693	1.6850	1.334
2	2.0548	1.9311	0.9406
3	2.2219	2.0811	0.9713
4	2.4417	2.2654	0.9951
5	2.6615	2.5562	1.0357
6	2.8824	2.6615	3.052
7	4.8366	4.6958	1.0
8	7.0632	6.9842	1.0395
9	7.7673	7.6093	1.067
10	8.2527	8.1702	0.9347
11	8.3500	8.2527	1.071



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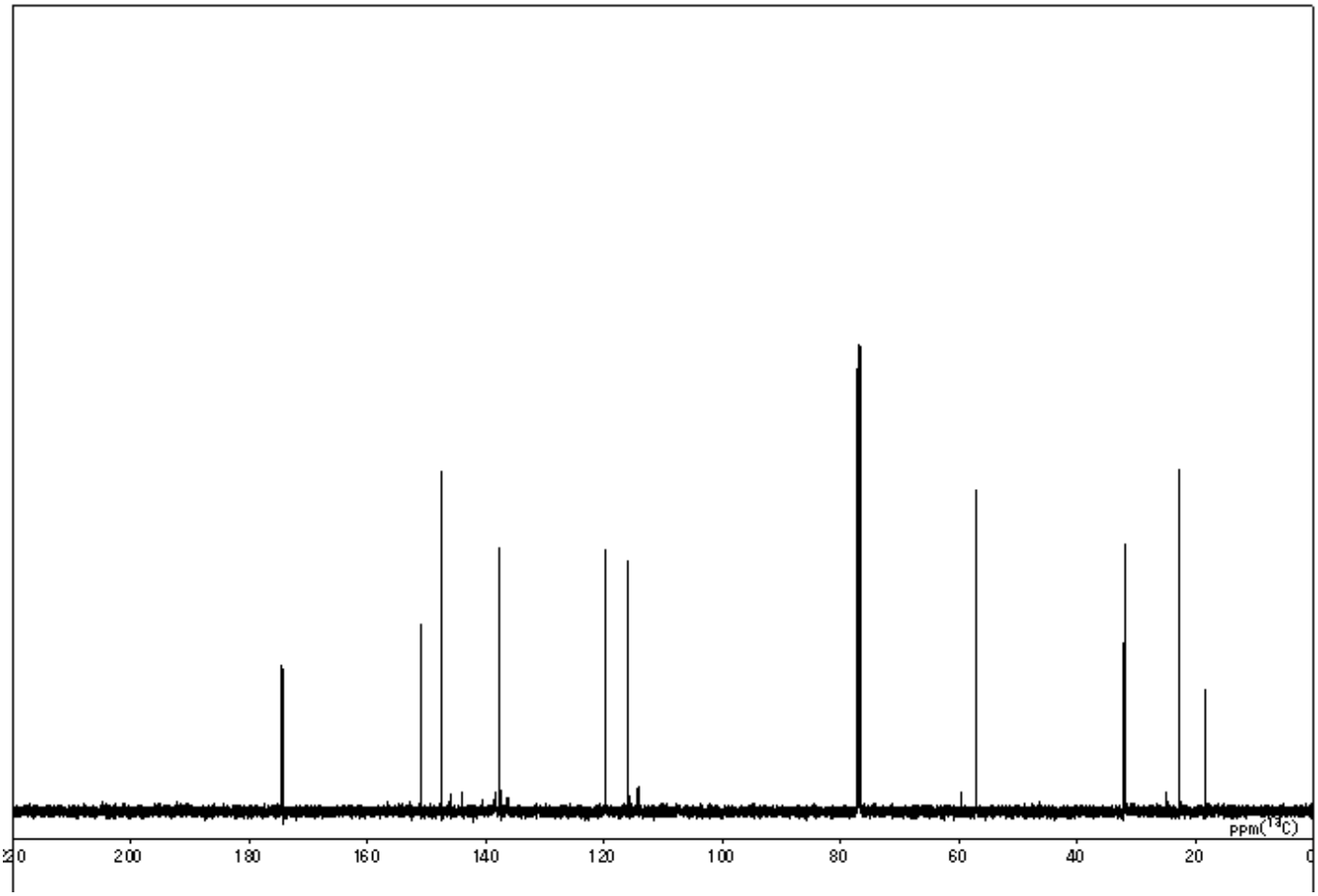

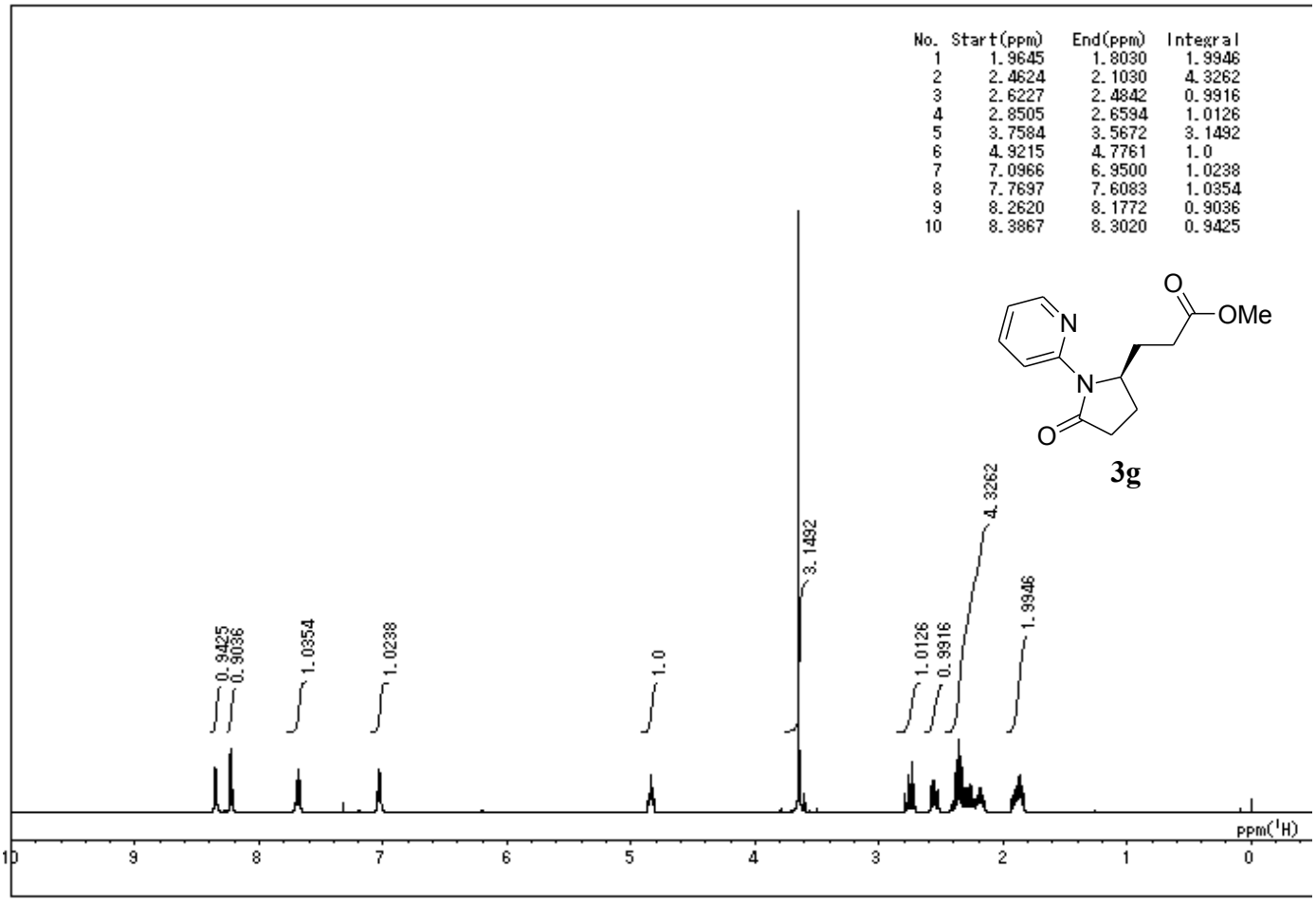
No. Start(ppm) End(ppm) Integral
1 1.9645 1.8030 1.9946
2 2.4624 2.1030 4.3262
3 2.6227 2.4842 0.9916
4 2.8505 2.6594 1.0126
5 3.7584 3.5672 3.1492
6 4.9215 4.7761 1.0
7 7.0966 6.9500 1.0238
8 7.7697 7.6083 1.0354
9 8.2620 8.1772 0.9036
10 8.3867 8.3020 0.9425
O
OMe
N
N
O
3g
0.9425
0.9036
1.0354
1.0238
1.0
3.1492
1.0126
0.9916
4.3262
1.9946
ppm(¹H)
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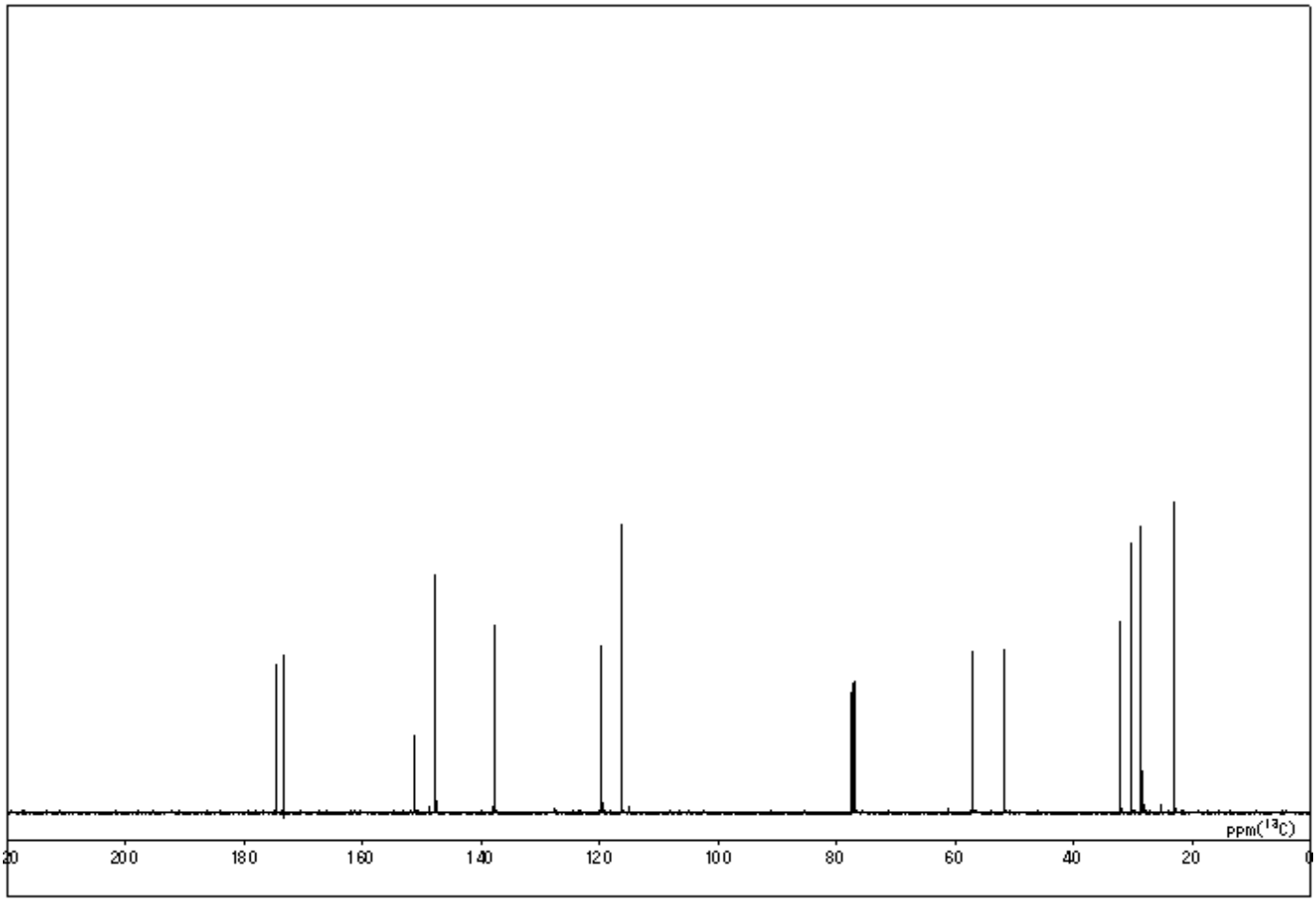
9
8
7
6
5
4
3
2
1
0


ppm(¹³C)
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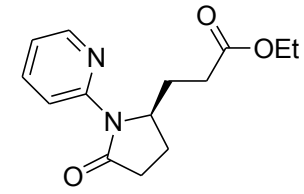
180
160
140
120
100
80
60
40
20
0

No.	Start(ppm)	End(ppm)	Integral
1	1.2797	1.2076	3.0
2	1.9460	1.8166	1.9949
3	2.4131	2.1486	4.0579
4	2.6100	2.5081	0.9821
5	2.8138	2.6993	0.9901
6	4.1623	4.0627	1.9543
7	4.8870	4.8034	0.9766
8	7.0632	6.9968	0.975
9	7.7261	7.6494	0.9711
10	8.2572	8.1989	0.9193
11	8.3843	8.3305	0.9322



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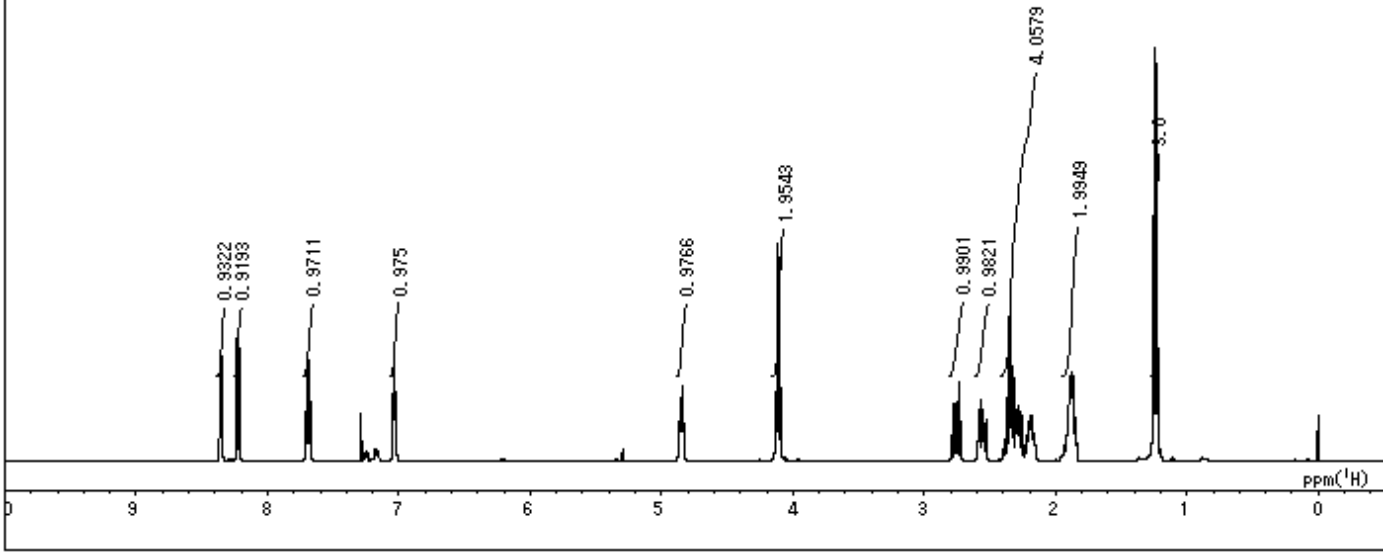
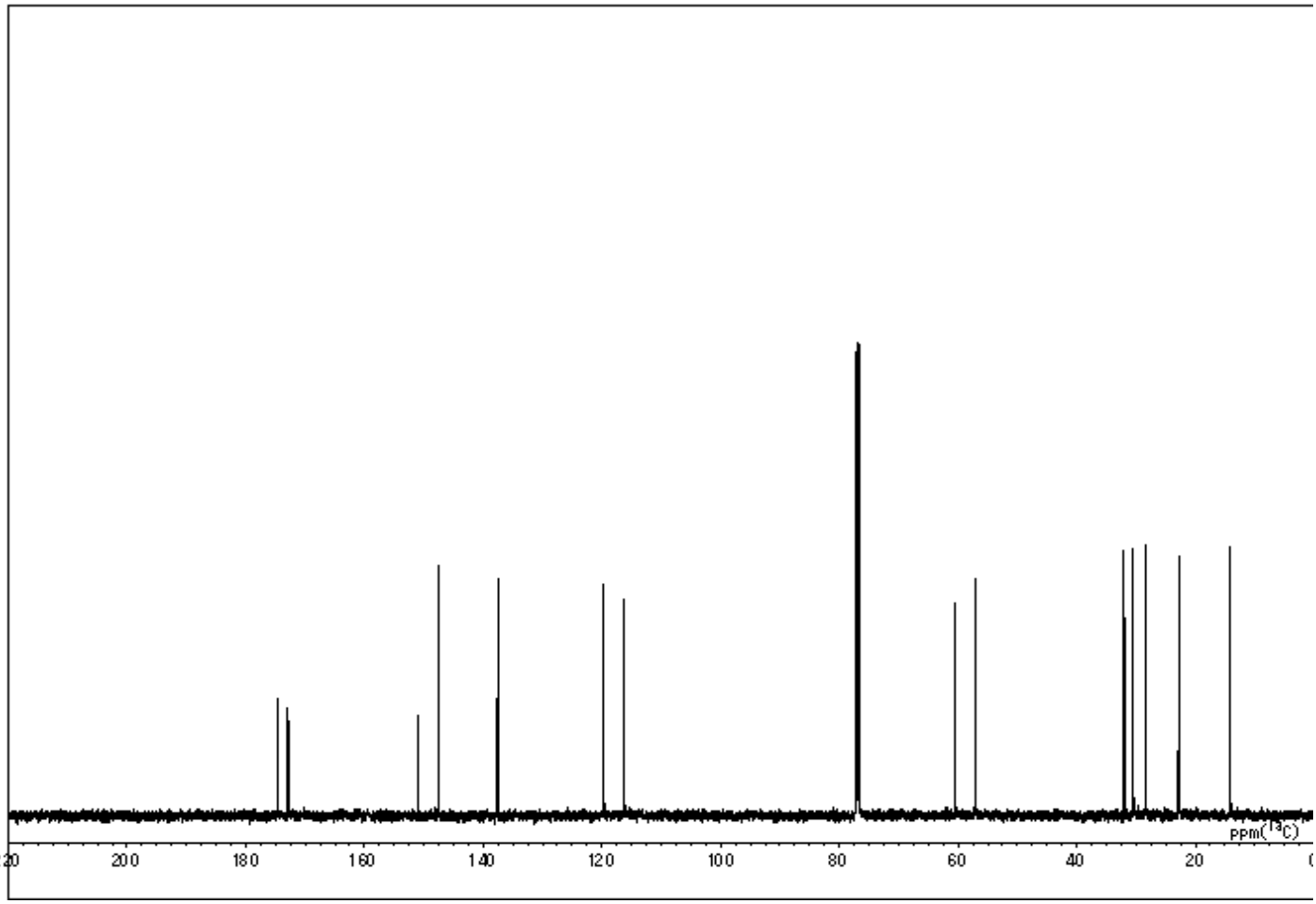
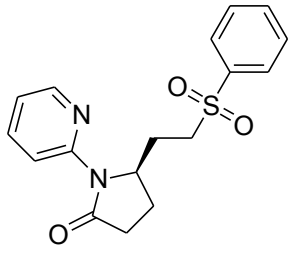
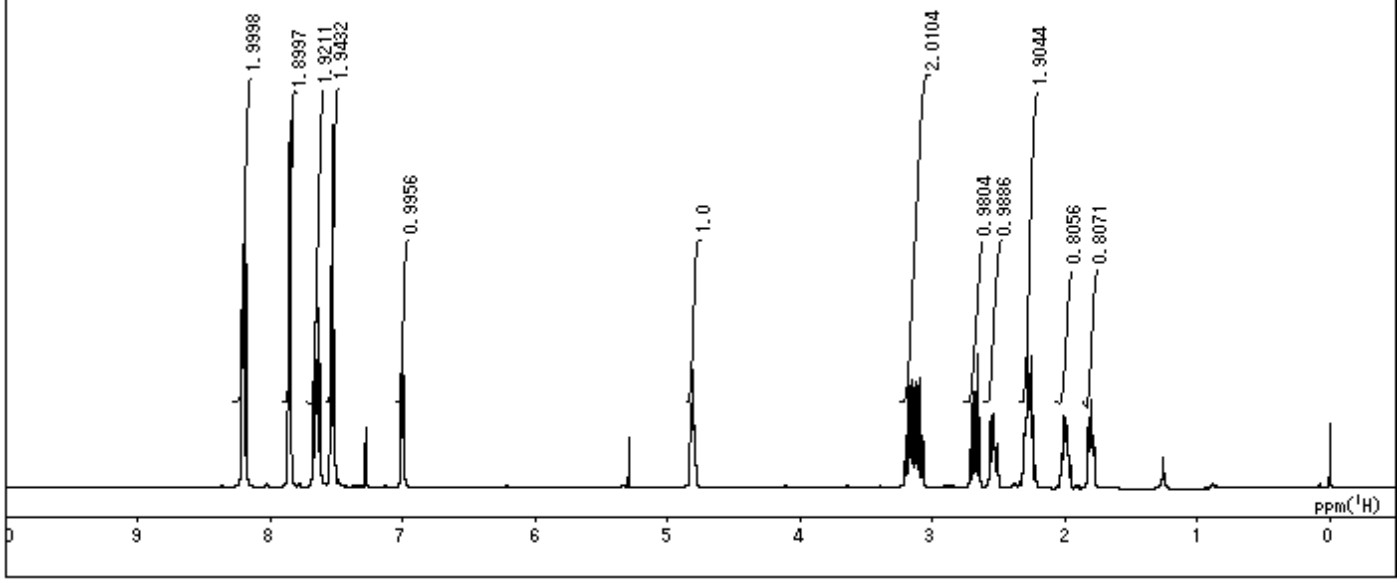


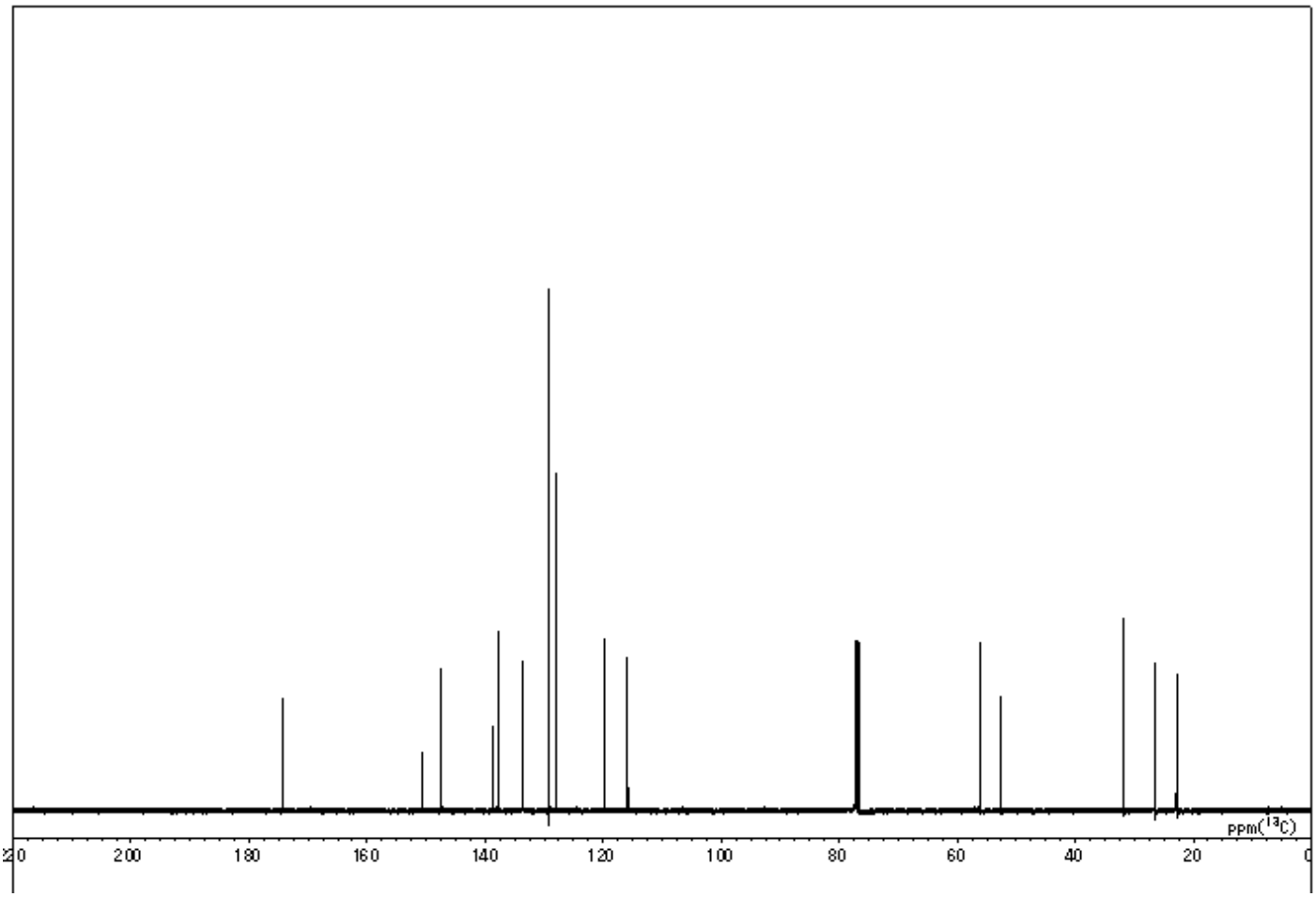


No.	Start(ppm)	End(ppm)	Integral
1	1.8626	1.7401	0.8071
2	2.0652	1.9427	0.8056
3	2.3468	2.1888	1.9044
4	2.6113	2.4705	0.9886
5	2.7693	2.6113	0.9804
6	3.2455	3.0074	2.0104
7	4.8562	4.7417	1.0
8	7.0565	6.9420	0.9956
9	7.5854	7.4789	1.9432
10	7.7342	7.5934	1.9211
11	7.9105	7.7869	1.8997
12	8.2803	8.1395	1.9998

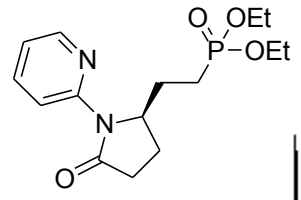


3i





No.	Start(ppm)	End(ppm)	Integral
1	1.3244	1.2076	6.2202
2	1.9243	1.6426	3.9202
3	2.2185	2.0891	0.7016
4	2.3432	2.2185	0.9973
5	2.6214	2.5138	0.9919
6	2.8035	2.6752	1.0234
7	4.1383	3.9517	4.0238
8	4.8652	4.7874	1.0
9	7.0747	7.0025	1.0598
10	7.7398	7.6516	1.0048
11	8.2481	8.1863	0.9487
12	8.3786	8.3259	1.0208



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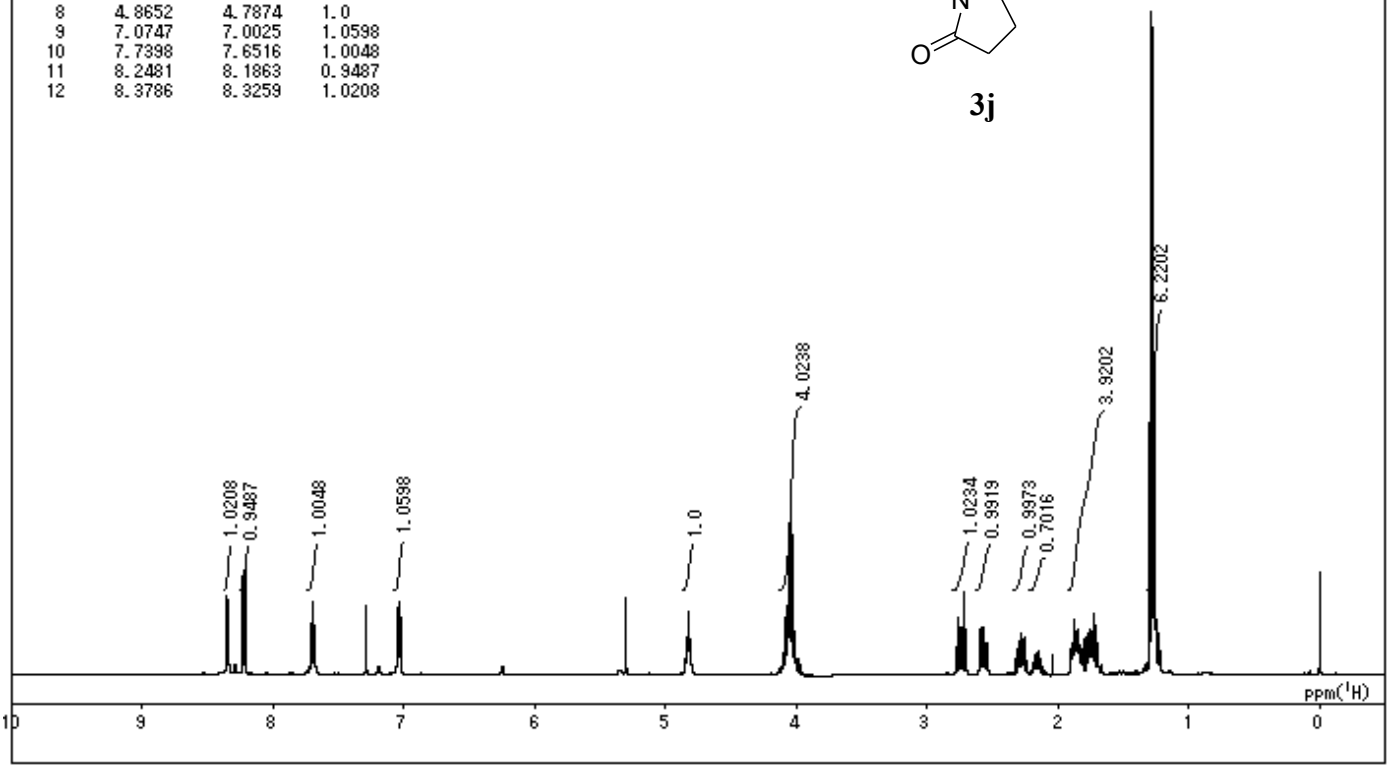
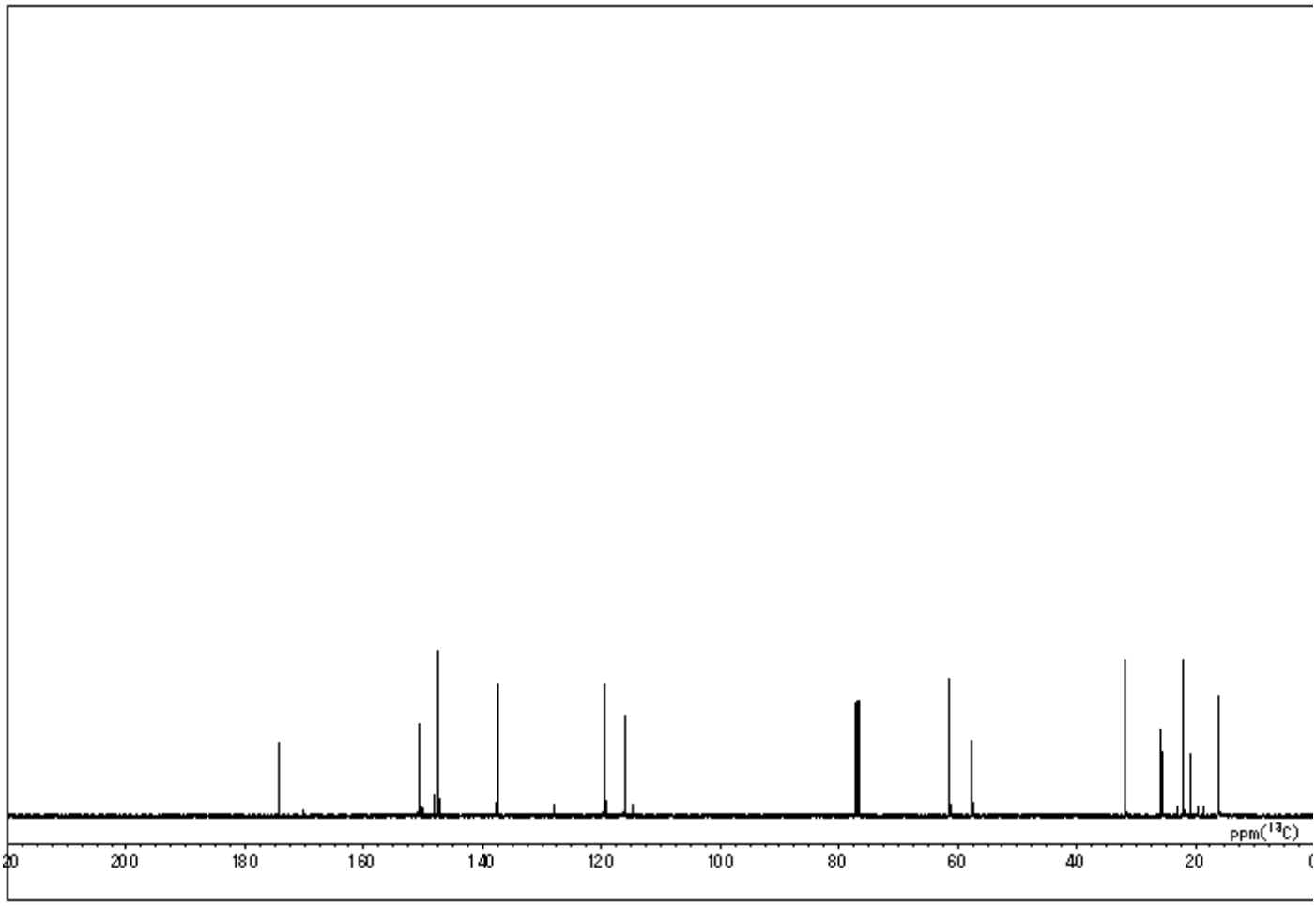
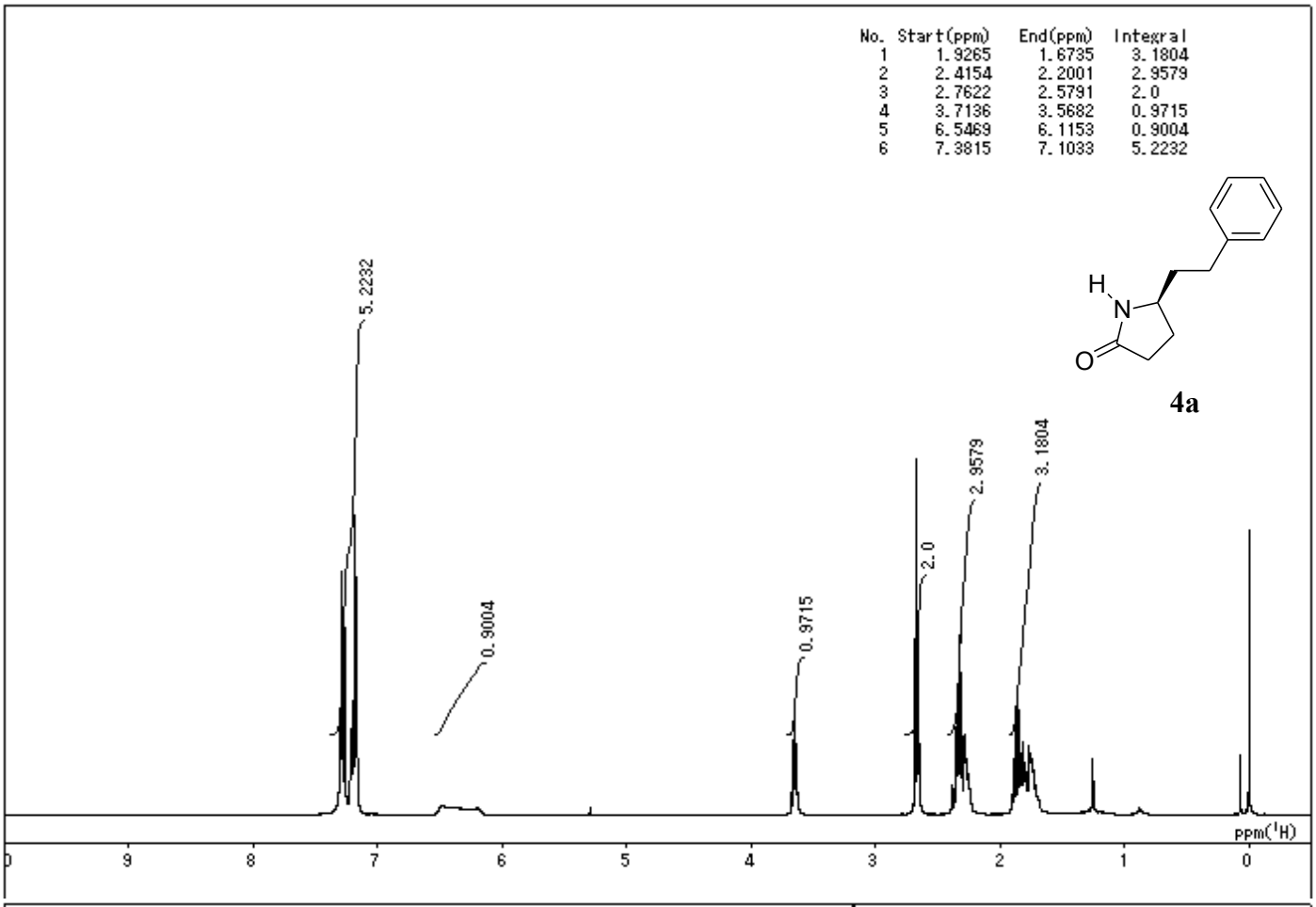
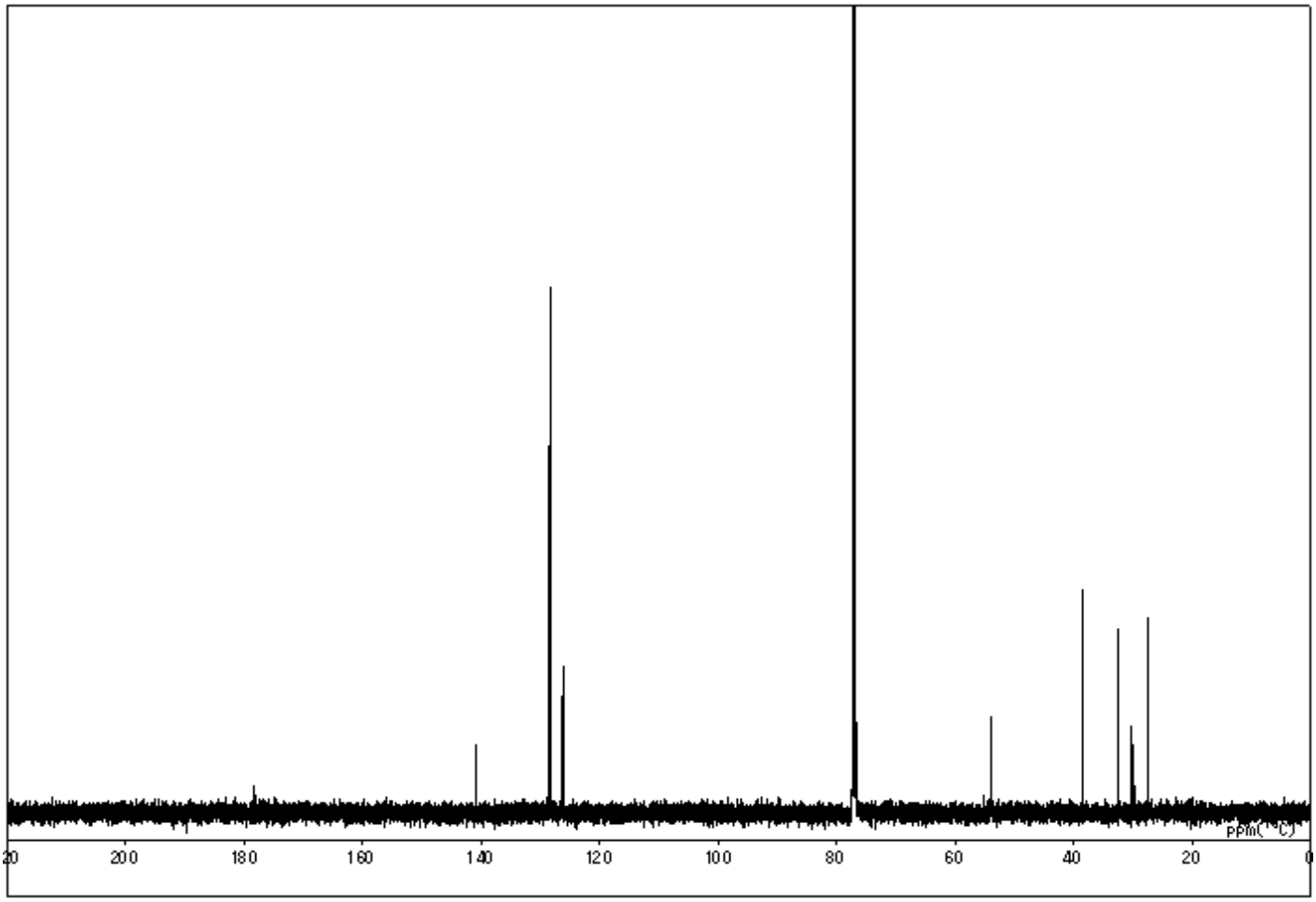
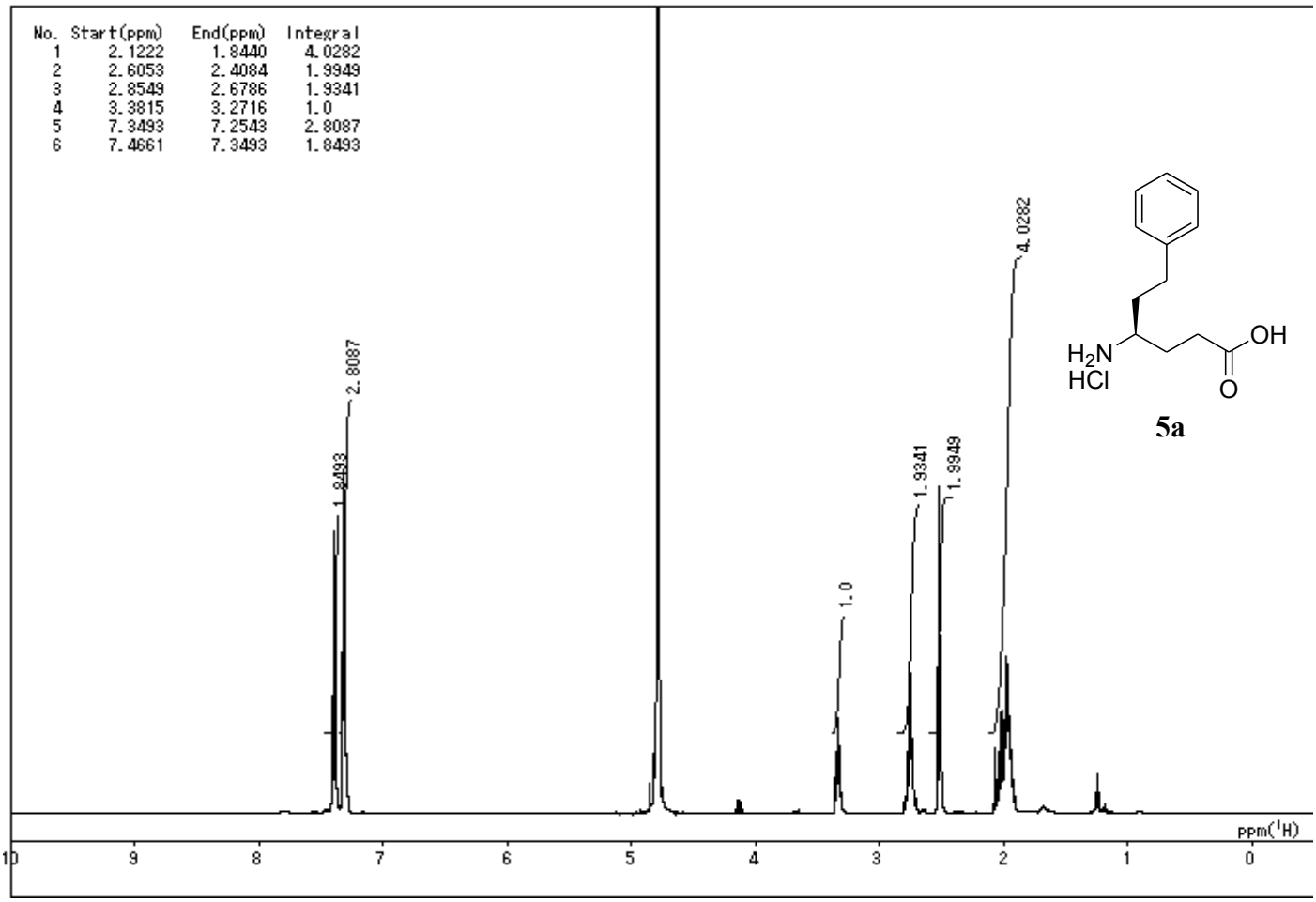




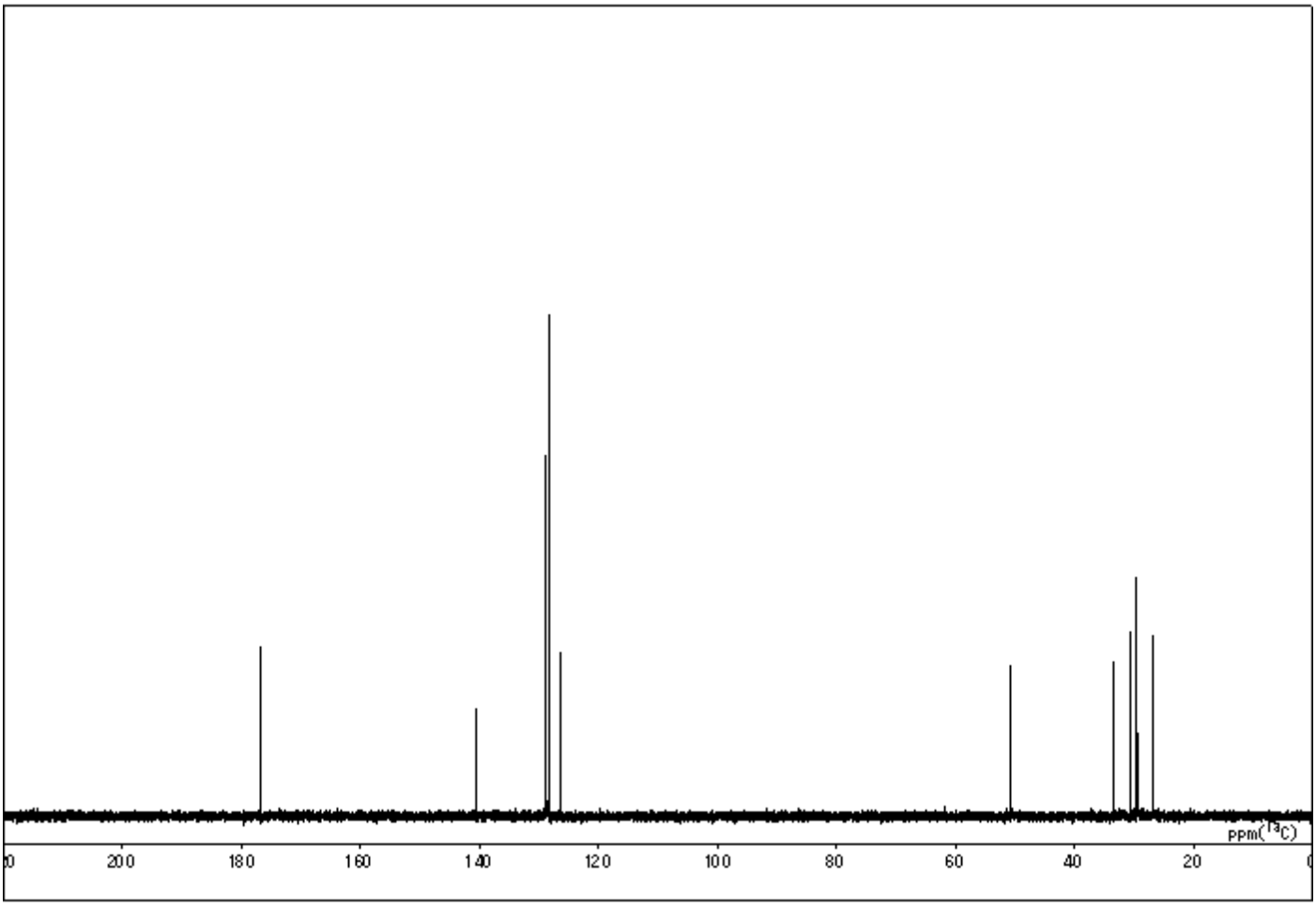

No. Start(ppm) End(ppm) Integral
1 1.9265 1.6735 3.1804
2 2.4154 2.2001 2.9579
3 2.7622 2.5791 2.0
4 3.7136 3.5682 0.9715
5 6.5469 6.1153 0.9004
6 7.3815 7.1033 5.2232
5.2232
0.9004
0.9715
2.0
2.9579
3.1804
H
N
O
4a
ppm(¹H)

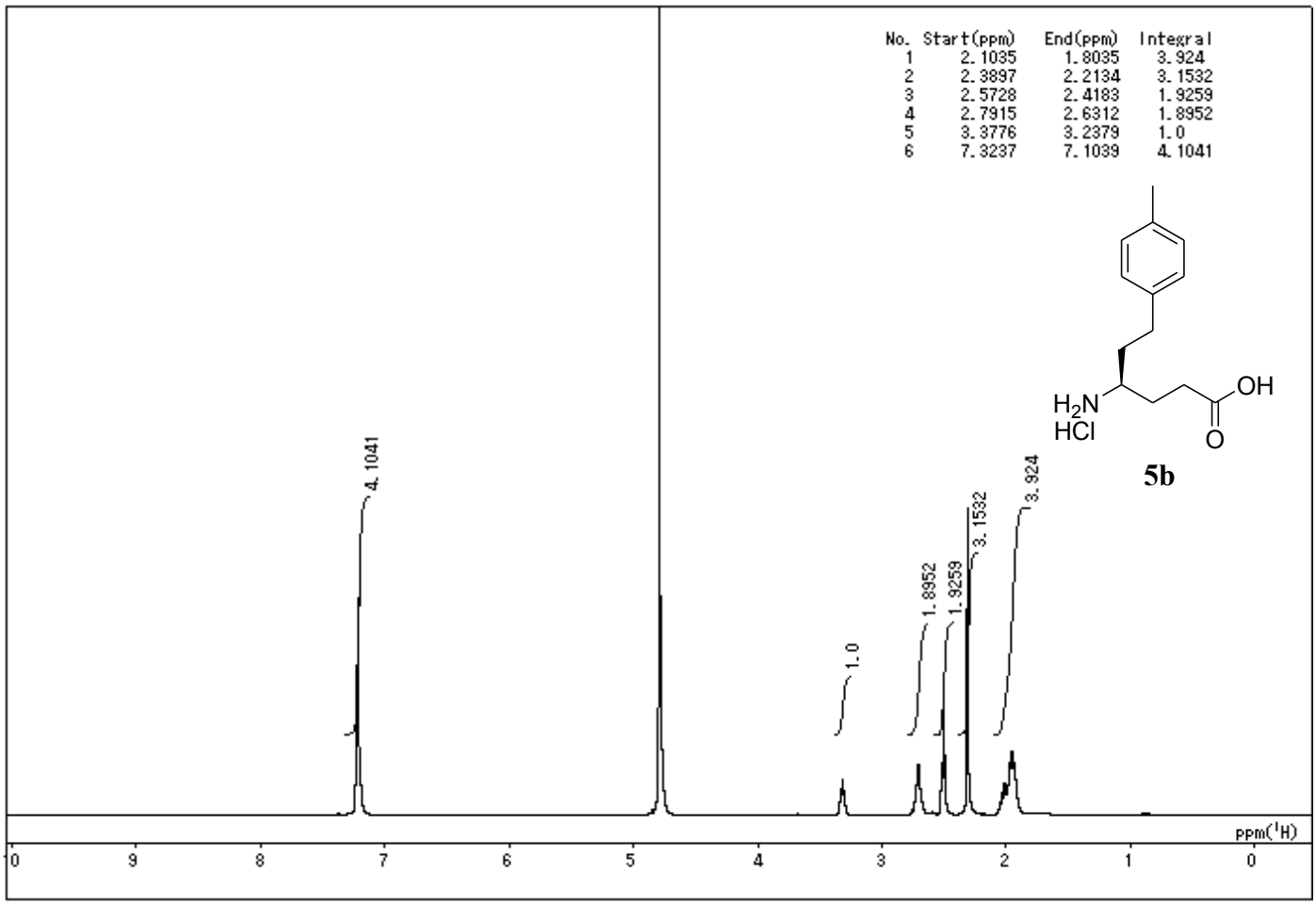

ppm(¹³C)

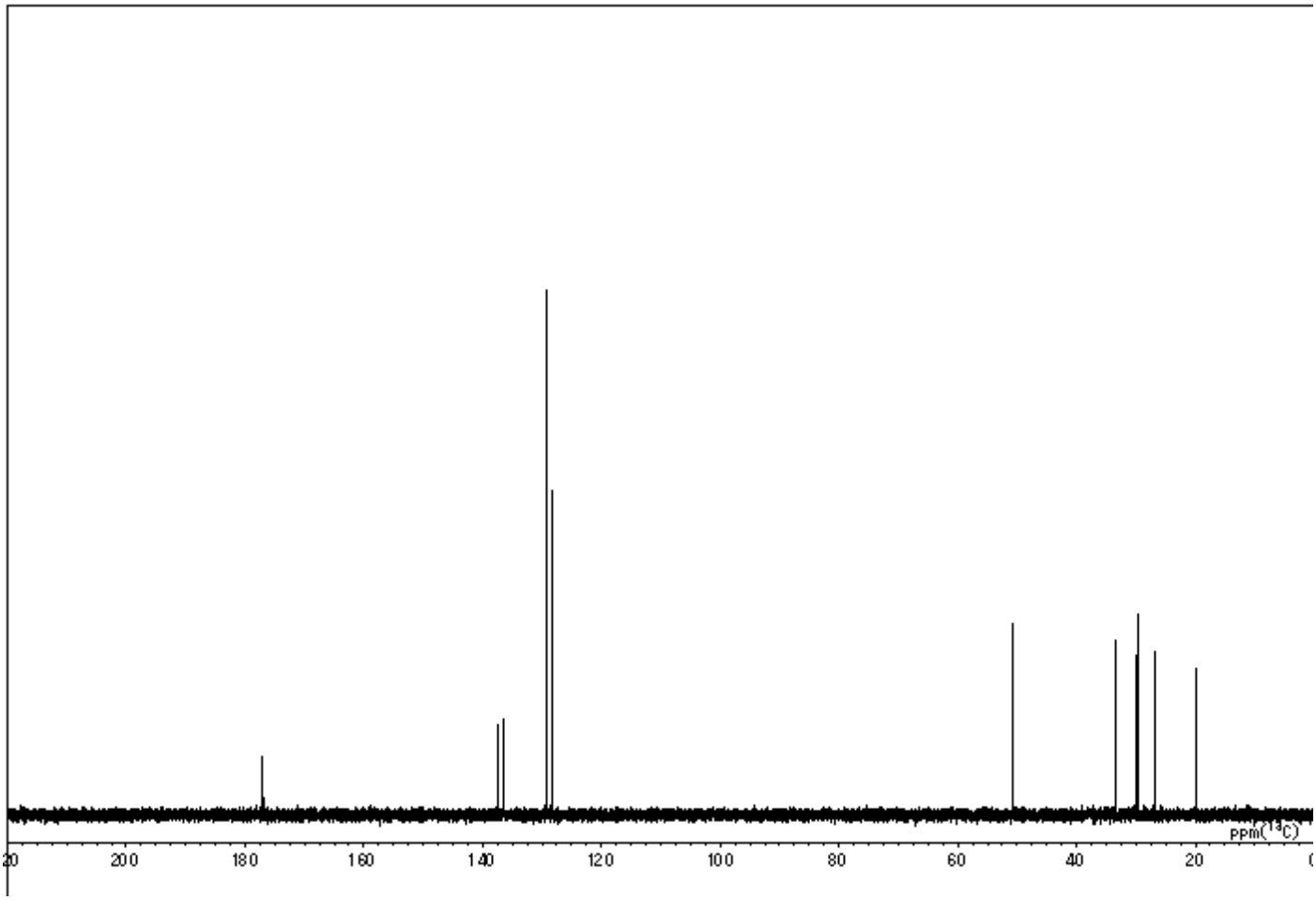
No.	Start(ppm)	End(ppm)	Integral
1	2.1222	1.8440	4.0282
2	2.6053	2.4084	1.9949
3	2.8549	2.6786	1.9341
4	3.3815	3.2716	1.0
5	7.3493	7.2543	2.8087
6	7.4661	7.3493	1.8493

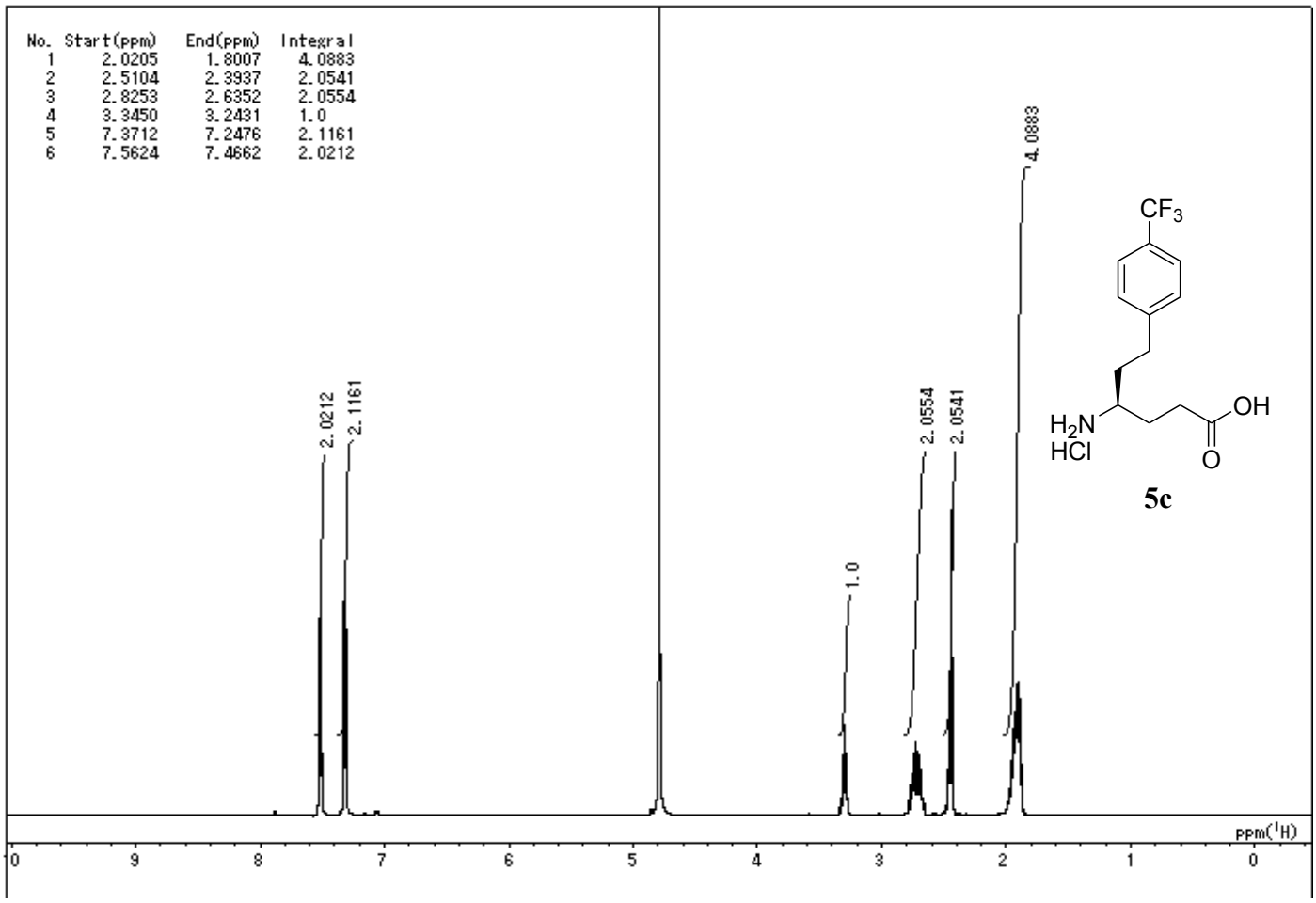


5a

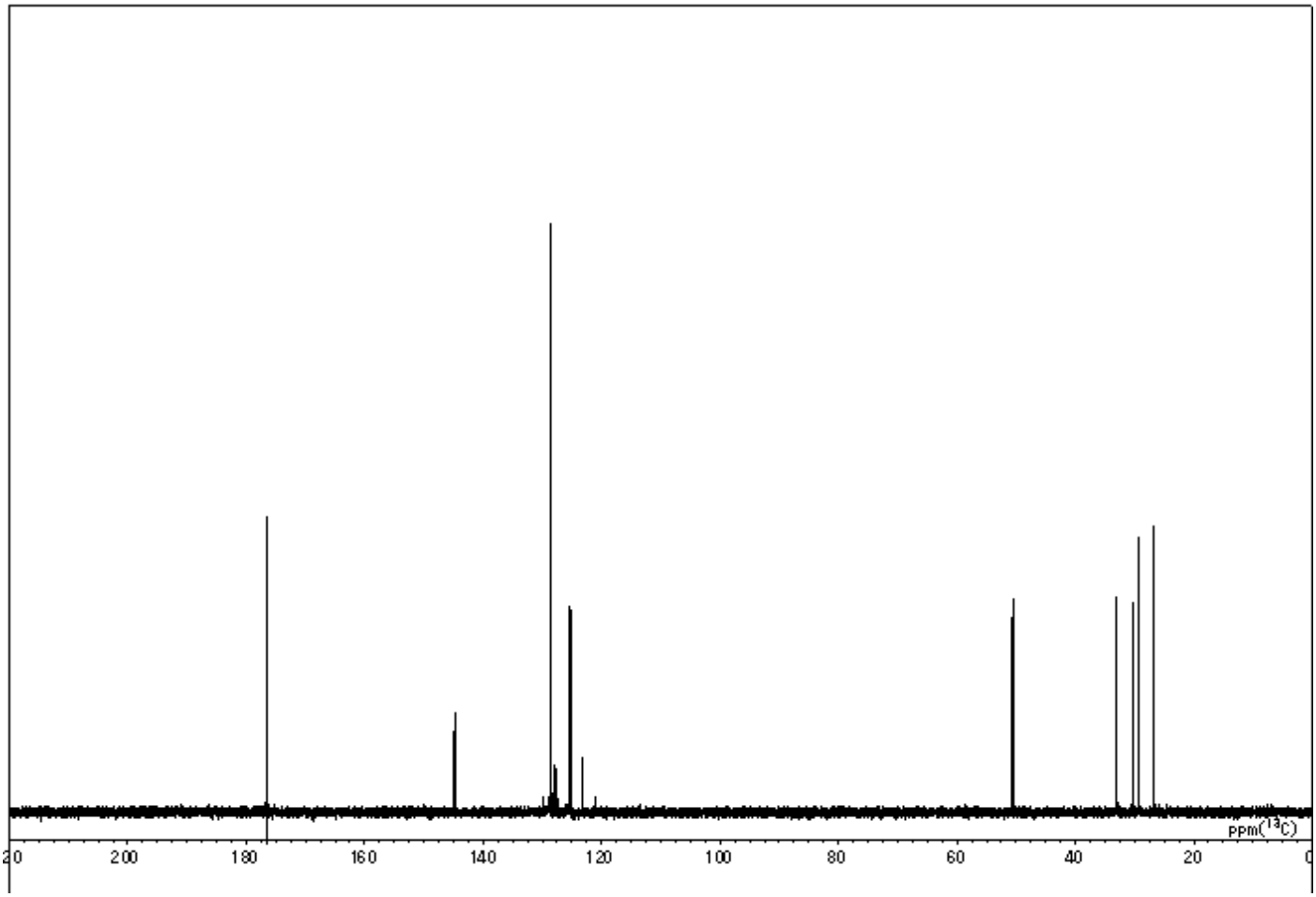


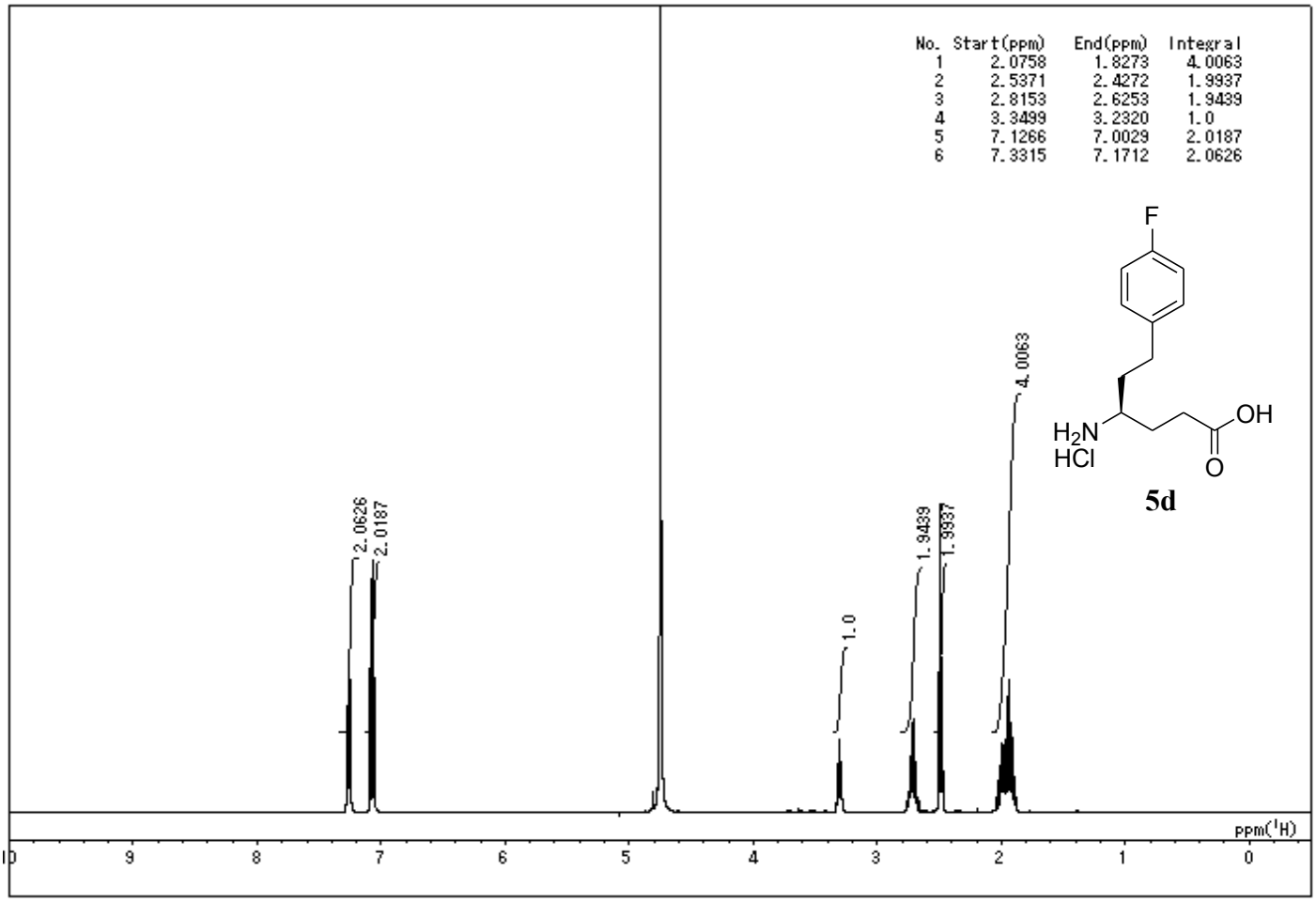

No. Start(ppm) End(ppm) Integral
1 2.1035 1.8035 3.924
2 2.3897 2.2134 3.1532
3 2.5728 2.4183 1.9259
4 2.7915 2.6312 1.8952
5 3.3776 3.2379 1.0
6 7.3237 7.1039 4.1041
H2N
HCl
OH
O
5b
4.1041
1.0
1.8952
1.9259
3.1532
3.924
ppm(1H)

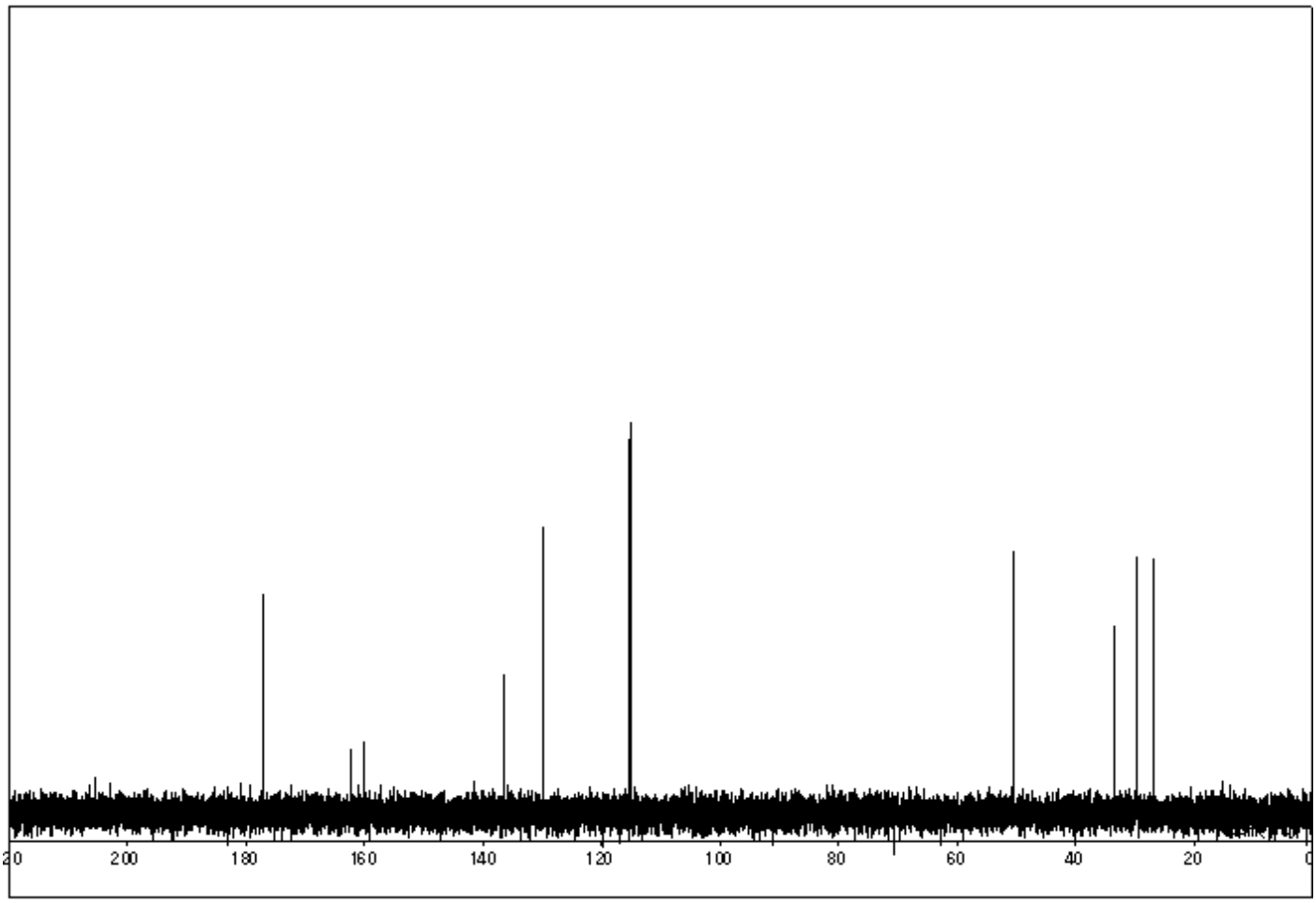

ppm(13C)

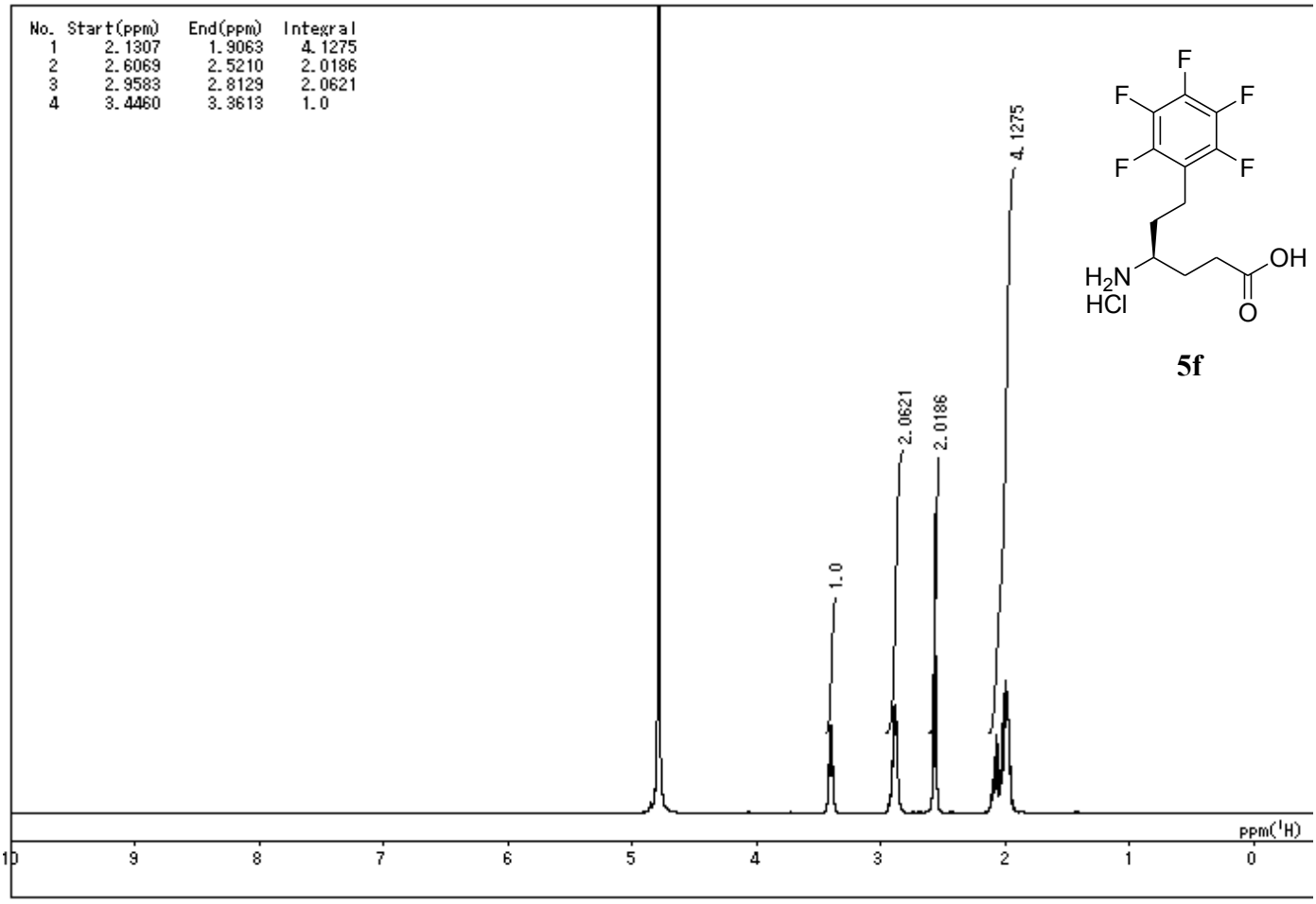

No. Start(ppm) End(ppm) Integral
1 2.0205 1.8007 4.0883
2 2.5104 2.3937 2.0541
3 2.8253 2.6352 2.0554
4 3.3450 3.2431 1.0
5 7.3712 7.2476 2.1161
6 7.5624 7.4662 2.0212
2.0212
2.1161
1.0
2.0554
2.0541
4.0883
CF3
H2N
HCl
OH
O
ppm(1H)

5c

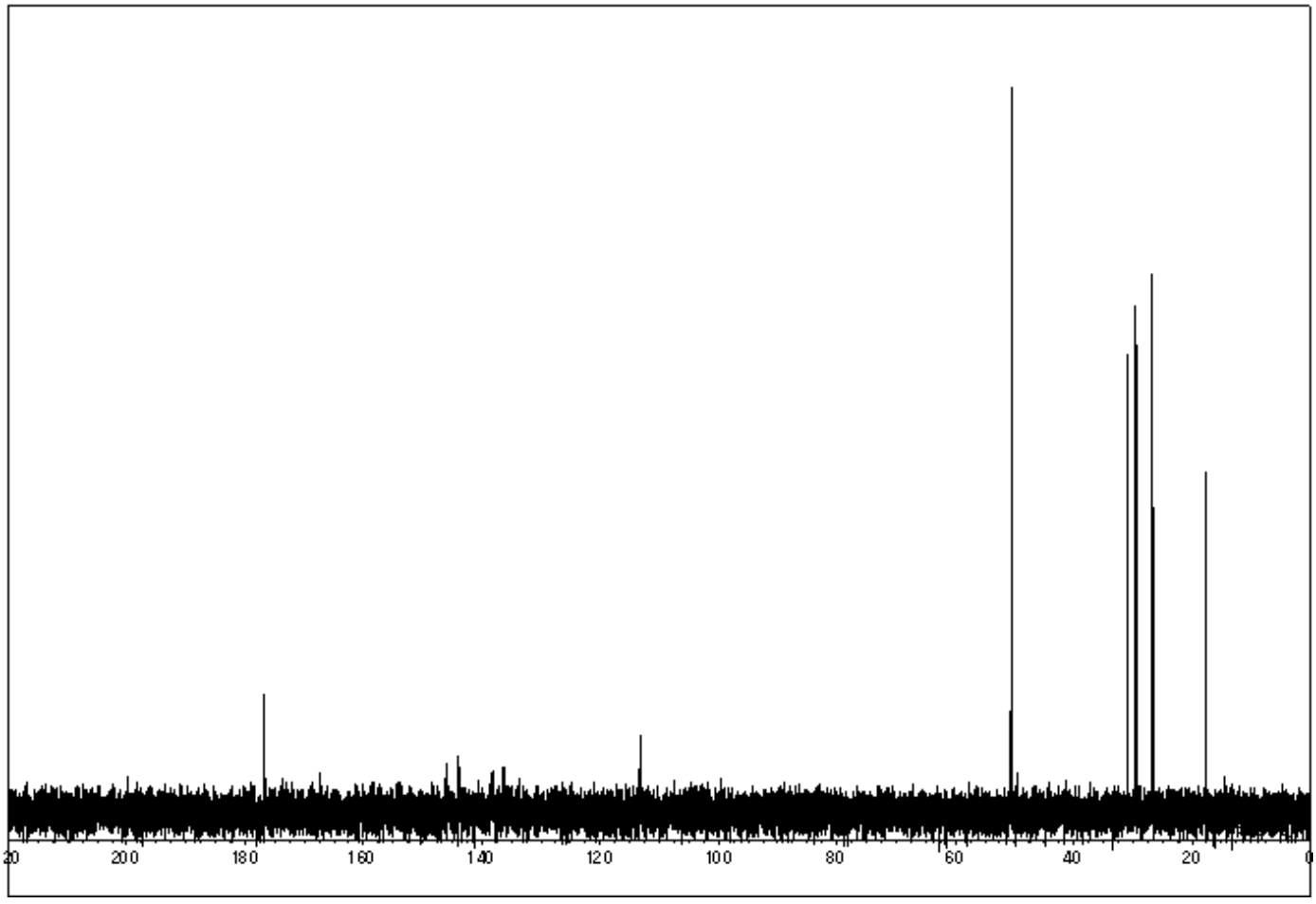

ppm(13C)

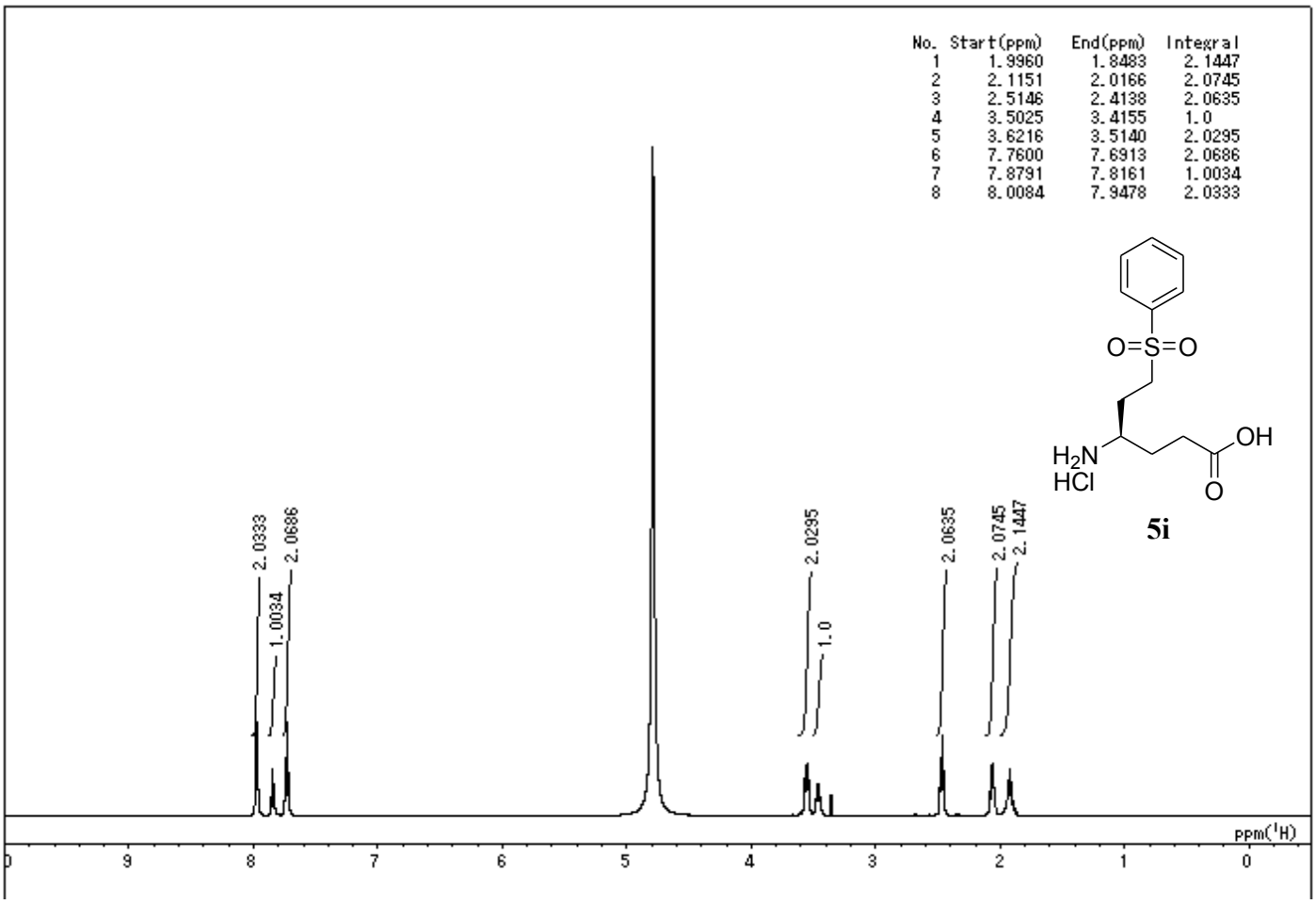

No. Start(ppm) End(ppm) Integral
1 2.0758 1.8273 4.0063
2 2.5371 2.4272 1.9937
3 2.8153 2.6253 1.9439
4 3.3499 3.2320 1.0
5 7.1266 7.0029 2.0187
6 7.3315 7.1712 2.0626
F
OH
H2N
HCl
O
5d
2.0626
2.0187
1.0
1.9439
1.9937
4.0063
ppm(1H)



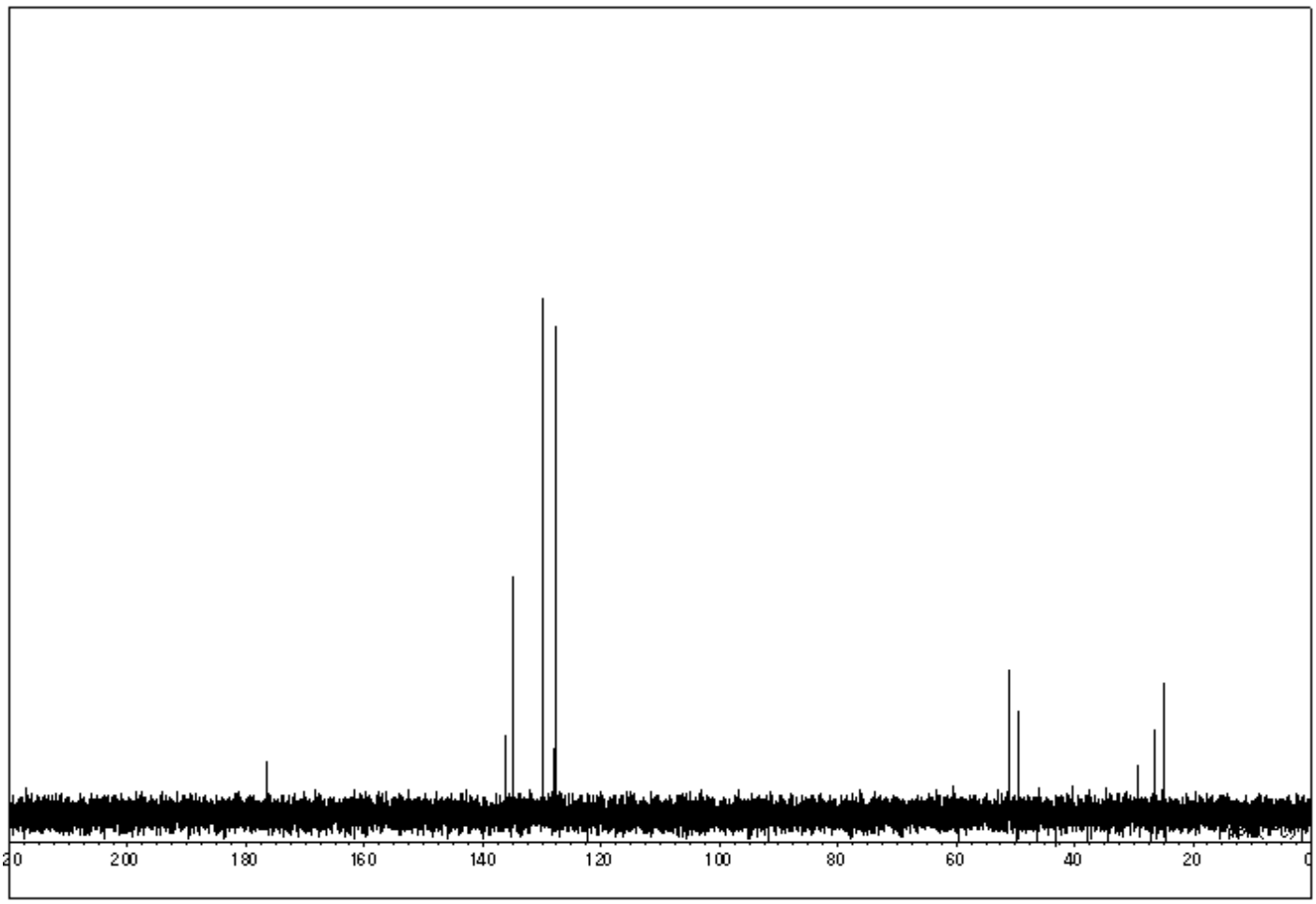

No. Start(ppm) End(ppm) Integral
1 2.1307 1.9063 4.1275
2 2.6069 2.5210 2.0186
3 2.9583 2.8129 2.0621
4 3.4460 3.3613 1.0
4.1275
2.0621
2.0186
1.0
F
F
F
F
F
H2N
HCl
OH
O
ppm(1H)
10
9
8
7
6
5
4
3
2
1
0

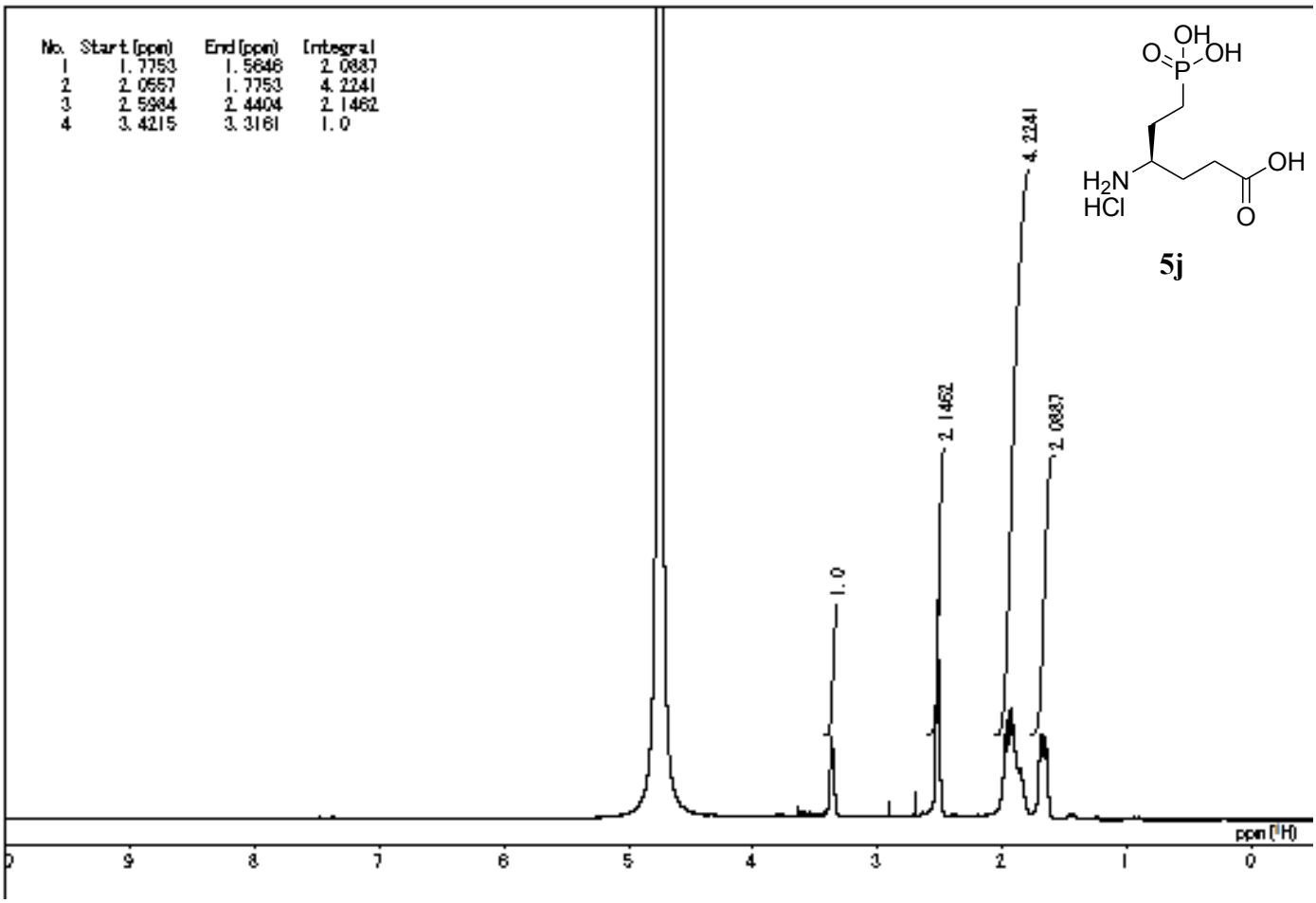
5f

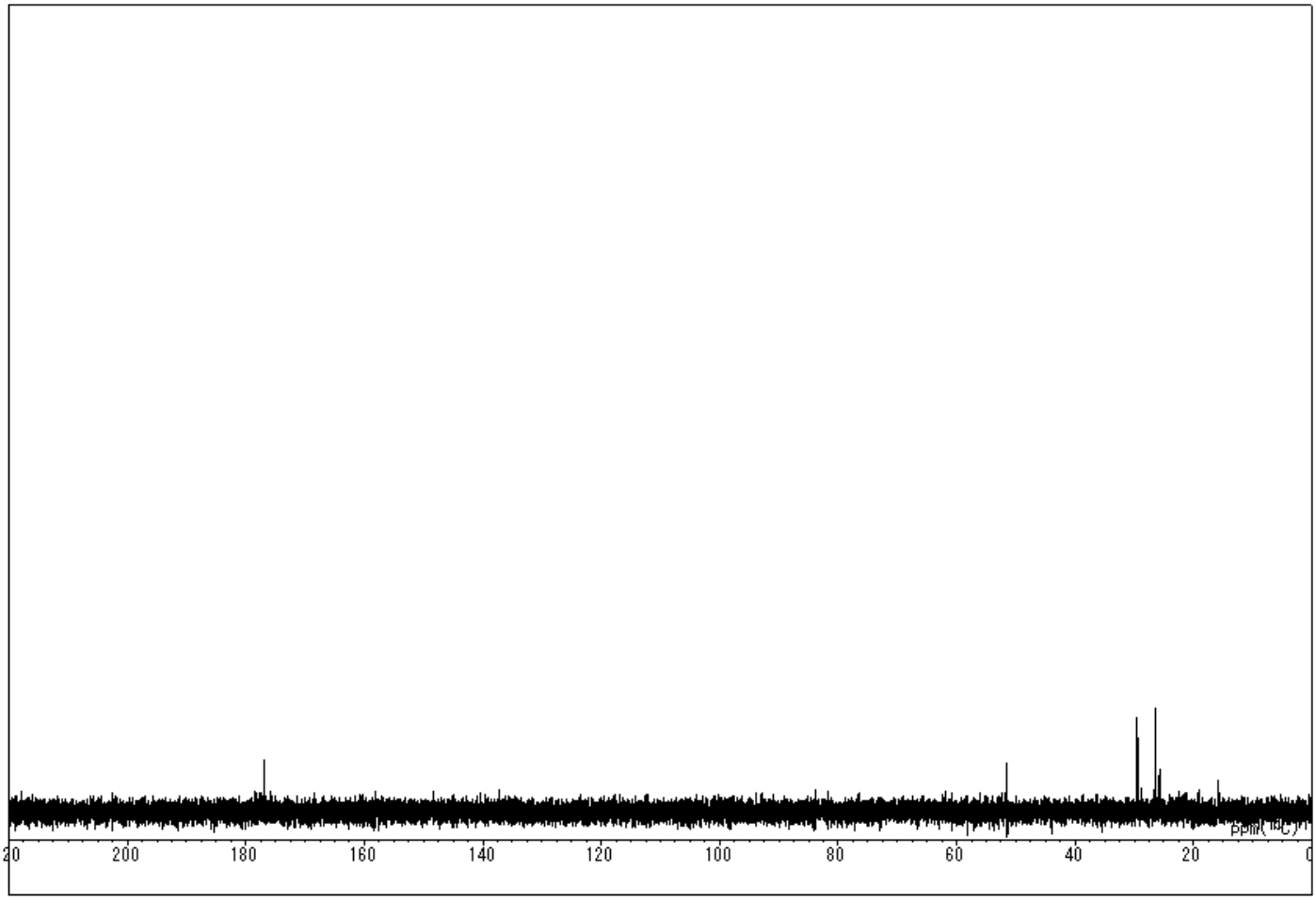

200
180
160
140
120
100
80
60
40
20
0


No. Start(ppm) End(ppm) Integral
1 1.9960 1.8483 2.1447
2 2.1151 2.0166 2.0745
3 2.5146 2.4138 2.0635
4 3.5025 3.4155 1.0
5 3.6216 3.5140 2.0295
6 7.7600 7.6913 2.0686
7 7.8791 7.8161 1.0034
8 8.0084 7.9478 2.0333
O=S=O
OH
H2N
HCl
O
2.0333
2.0686
1.0034
2.0295
1.0
2.0635
2.0745
2.1447
ppm(1H)

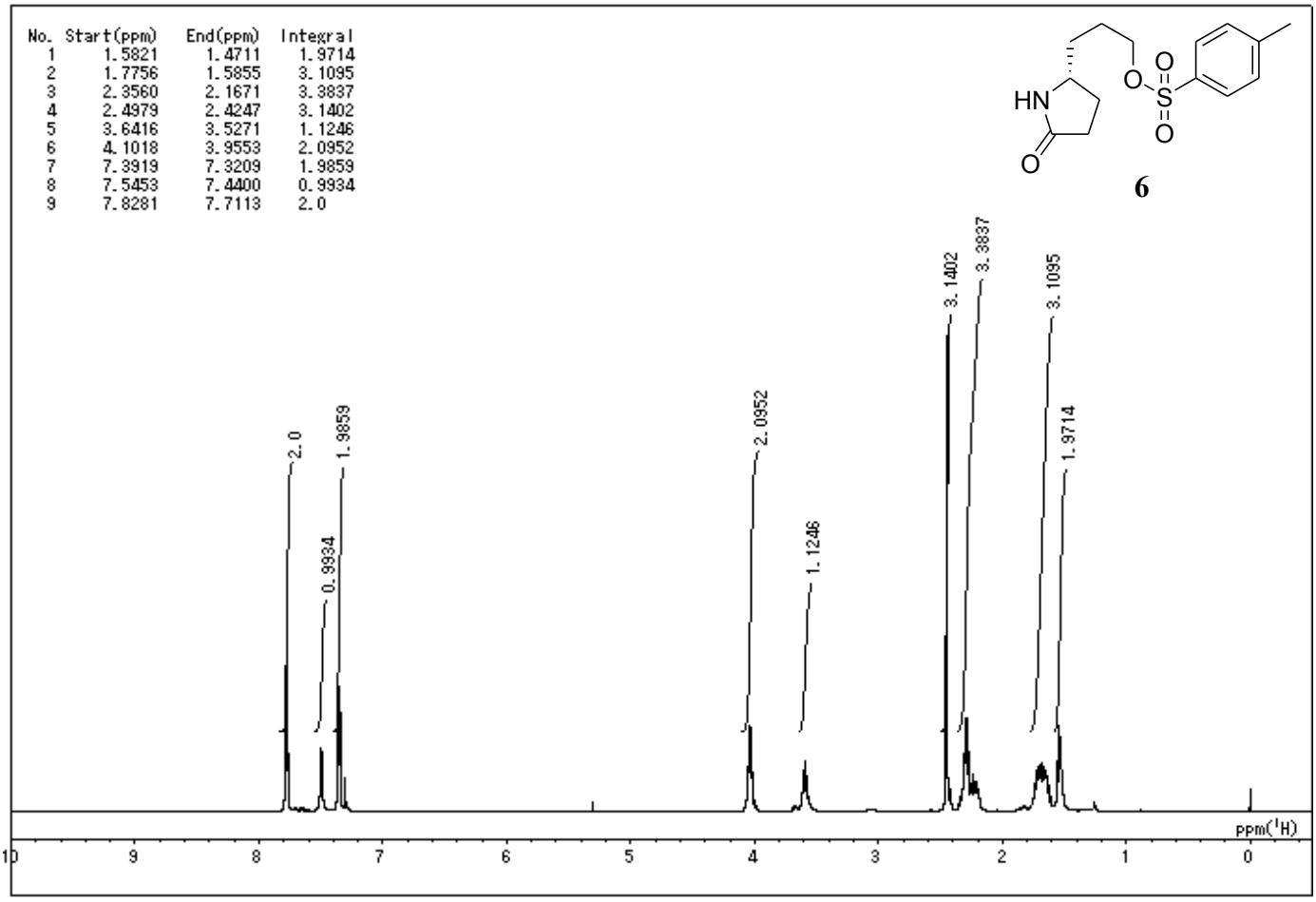
5i

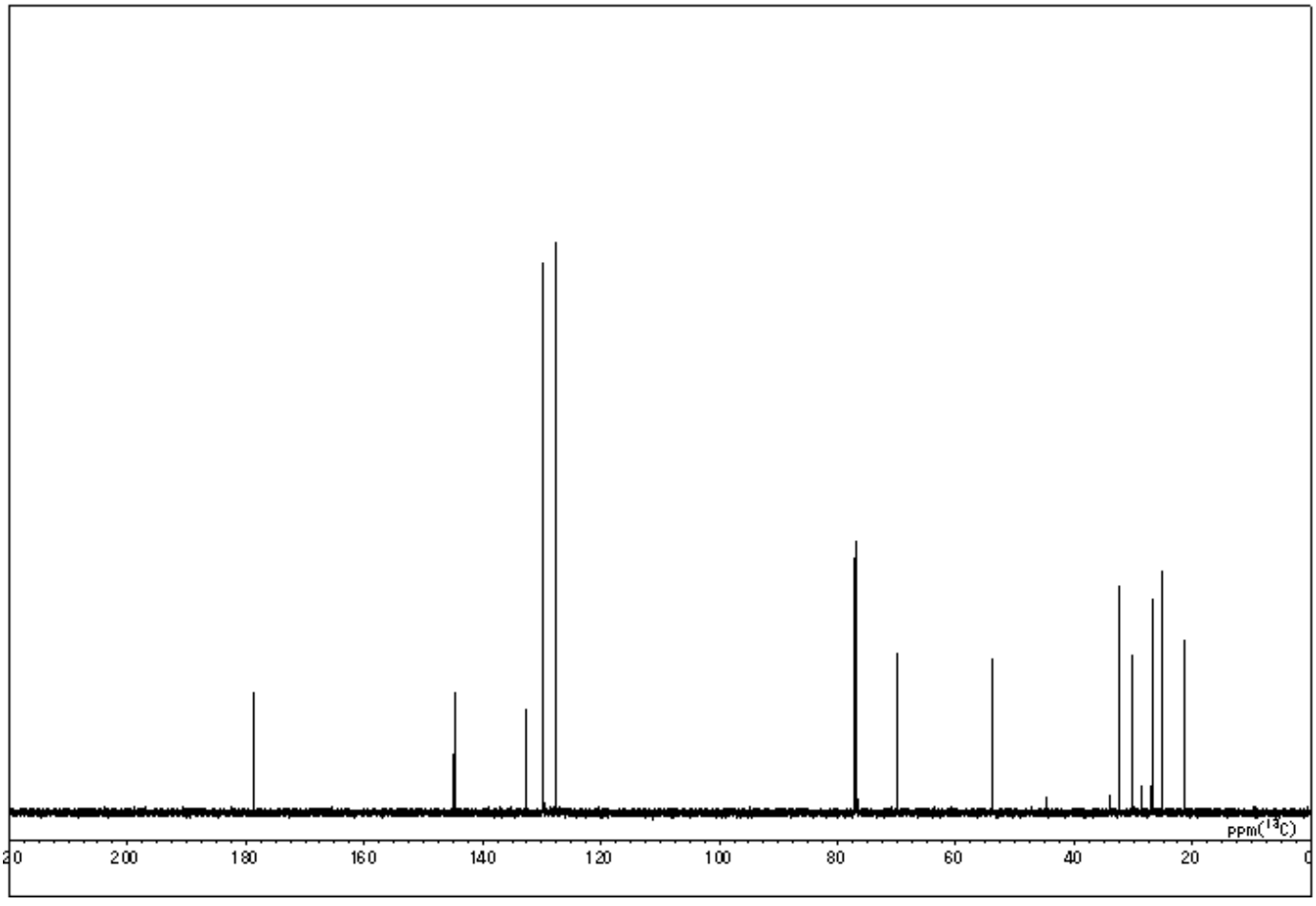



No. Start (ppm) End (ppm) Integral
1 1.7753 1.5646 2.0887
2 2.0557 1.7753 4.2241
3 2.5984 2.4404 2.1462
4 3.4215 3.3161 1.0
OH
O
P
OH
H2N
HCl
OH
O
5j
4.2241
2.1462
2.0887
1.0
ppm (1H)
9
8
7
6
5
4
3
2
1
0


200
180
160
140
120
100
80
60
40
20

No.	Start(ppm)	End(ppm)	Integral
1	1.5821	1.4711	1.9714
2	1.7756	1.5855	3.1095
3	2.3560	2.1671	3.3837
4	2.4979	2.4247	3.1402
5	3.6416	3.5271	1.1246
6	4.1018	3.9553	2.0952
7	7.3919	7.3209	1.9859
8	7.5453	7.4400	0.9934
9	7.8281	7.7113	2.0





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