Supporting Information

Catalytic enantioselective synthesis of 2-(2-hydroxyethyl)indole scaffolds via consecutive intramolecular amido-cupration of allenes and asymmetric addition of carbonyl compounds

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1. General:

Unless otherwise noted, all the reactions were performed in a flame-dried 20 mL test tube with a Teflon-coated magnetic stirring bar fitted with a 3-way glass stopcock. Air- and moisture-sensitive liquids were transferred via a gas-tight syringe and stainless-steel needle and reactions were run under argon atmosphere. All reaction work-up and purification procedures were carried out with reagent-grade solvents in air at ambient temperature. Column chromatographic purifications were performed with silica gel Merck 60 (230-400 mesh ASTM). The absolute configuration of product **3aa** was determined (see S48). For other products, the absolute configuration was tentatively assigned from the analogy to **3aa**.

Instrumentation:

^{1}H and ^{13}C NMR spectra were recorded on JEOL ECX500 (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) and JEOL ECS400 (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) spectrometers. Chemical shifts were reported in ppm in the scale relative to the solvent used as an internal reference for ^{1}H (δ = 7.26 ppm for $CDCl_3$, 2.05 ppm for acetone-d_6, and 3.31 for CD_3OD) and ^{13}C NMR (δ = 77.00 ppm for $CDCl_3$, 206.26 ppm for acetone-d_6 and 49.0 ppm for CD_3OD). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, td = triplet of doublet, m = multiplet), coupling constants (Hz) and integration. Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. Optical rotations were measured on a JASCO P-1010 polarimeter. ESI-mass spectra were measured on JEOL JMS-T100LC AccuTOF spectrometer (for High resolution mass spectra). The enantiomeric excesses (*ee*'s) were determined by high-performance liquid chromatography analysis conducted by JASCO HPLC systems (pump: PU-2080; detector: UV-2075, measured at 254 nm; chiral column; mobile phase: 2-propanol/^{n}hexane, ethanol/^{n}hexane).

Materials:

All non-commercially available compounds were prepared and characterized as described below. Other reagents were purchased from Aldrich chemical company, Tokyo Chemical Industry Co., Ltd. (TCI), Kanto Chemical Co., Inc., and Wako Pure Chemical Industries, Ltd. and used without further purification.

(*S, S*)-Ph-BPE was purchased from Aldrich chemical company.

Mesitylcopper was prepared by following the reported procedure.[1]

1, 3- Bis(diphenylphosphino)propane (dppp)was purchased from Wako Pure chemical industries.

All aliphatic and aromatic aldehydes and ketones were purchased from commercial sources and further purified by distillation/crystallization.

2-Iodo-5-methoxyaniline was prepared from 4-methoxy-2-nitroaniline in 69% yield.[2,3]

2-Iodo-3-methylaniline was prepared from 2-iodo-3-nitroaniline in 99% yield.[2]

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[1]T. Tsuda, K. Watanabe, K. Miyata, H. Yamamoto, T. Saegusa. *Inorg. Chem*. **1981**, *20*, 2728-2730.
[2]A. Wetzel, F. Gagosz. *Angew. Chem. Intl. Ed*. **2011**, *50*, 7354
[3]C. Ma, X. Liu, X. Li, J. Flippen-Anderson, S. Y, J. Cook, *J. Org. Chem*. **2001**, *66*, 4525-4542.

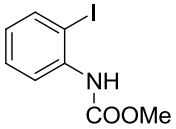
***N*-(2-iodophenyl)acetamide** and *tert*-butyl 2-iodophenylcarbamate were synthesized by using the reported procedure.[4,5]

2. *N*-Protection of *o*-Iodoanilines to carbamates and characterization:

General procedure for the synthesis of *N*-methylcarbamate:

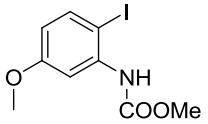
To a stirred solution of *o*-iodoaniline (5g, 22.82 mmol) in pyridine (40 mL) at 0 °C was added methyl chloroformate (2.65 mL, 34.2 mmol) dropwise *via* syringe over 10 min. The solution was slowly warmed to room temperature and stirred for 12 h. The mixture was recooled to 0 °C, and a second portion of methyl chloroformate (2.65 mL, 34.2 mmol) was added in the same manner. The mixture was stirred at room temperature for further 12 h. The reaction completion was confirmed by TLC analysis, and the reaction was quenched with water. The mixture was extracted with EtOAc (100 mL×3), and the combined organic layers were washed sequentially with water, sat. $CuSO_4$ solution, 0.3 N HCl and brine. After dried over Na_2SO_4, solvents were evaporated under vacuum. The crude residue was purified by silica gel column chromatography.

Methyl 2-iodophenylcarbamate (17):



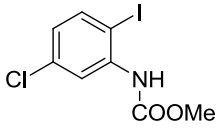
Yield: 94%; White solid; R_f = 0.33 (Ethyl acetate: Hexane (1.5:8.5)); IR (thin film): ν 3387, 2947, 1715, 1520, 1437 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.03 (d, *J* = 8 Hz, 1H), 7.73 (dd, *J* = 8 Hz, 1.7 Hz, 1H), 7.33-7.29 (m, 1H), 6.97 (brs, 1H), 6.79-6.76 (m, 1H), 3.7 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ153.6, 138.7, 138.1, 129.1 124.9, 120.2, 88.8, 52.4; HRMS (ESI): calcd for $C_8H_8INO_2$ *m/z* 299.9497 $[M+Na]^+$, Found 299.9505.

Methyl 2-iodo-5-methoxyphenyl carbamate (18):



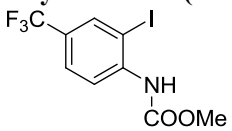
Yield: 88.6%; White solid; R_f = 0.45 (Ethyl acetate: Hexane (2:8)); IR (thin film): ν 3385, 2948, 1710, 1521, 1217 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.75 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 6.96 (brs, 1H), 6.41 (dd, *J* = 8.59 Hz, 2.86 Hz, 1H), 3.78 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ160.5, 153.6, 139.0, 138.6, 111.8, 105.3, 55.3, 52.4; HRMS (ESI): calcd for $C_9H_{10}INO_3$ *m/z* 329.96031$[M+Na]^+$, Found 329.9591.

Methyl 5-chloro-2-iodophenyl carbamate (19):



Yield: 94%; White fluffy solid; R_f = 0.26 (Ethyl acetate: Hexane (0.5:9.5)); IR (thin film): ν 3282, 2965, 1698, 1540, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ8.15 (brs, 1H), 7.66-7.63 (m, 1H), 6.97 (brs, 1H), 6.82-6.80 (m, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ153.4, 139.33, 139.31, 135.5, 125.0, 119.91, 85.2, 52.7; HRMS (ESI): calcd for $C_8H_7ClNO_2$ *m/z* 333.9108 $[M+Na]^+$, Found 333.9115.

Methyl 2-iodo-4-(trifluromethyl)phenylcarbamate (20):



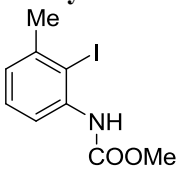
Yield: 93%; White fluffy solid; R_f = 0.25 (Ethyl acetate: Hexane (0.5:9.5)); IR (thin film): ν 3391, 2961, 2369, 1700, 1540, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.23 (d, *J* = 8.59 Hz, 1H), 7.99 (d, 1H, *J* = 1.14 Hz, 1H), 7.59 (dd, *J*=

[4]C. Gimbert, A. Vallribera, *Org. Lett*. **2009**, *11*, 269-271

[5]K. Hiroya, S. Itoh, T, Sakamoto. *J. Org. Chem*. **2004**, *69*, 1126-1136.

8.59 Hz, 1.7 Hz, 1H), 7.15 (brs, 1H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.4, 141.0, 135.8 (q, $^3J_{CF}$ 3.6 Hz), 126.8 (q, $^2J_{CF}$ 33.5 Hz), 126.4 (q, $^3J_{CF}$ 3.6 Hz), 121.8 (q, $^2J_{CF}$ 272 Hz), 118.9, 87.1, 52.8; HRMS (ESI): calcd for $C_9H_7F_3INO_2$ *m/z* 367.9371 $[M+Na]^+$, Found 367.9371.

Methyl 2-iodo-3-methylphenylcarbamate (21):



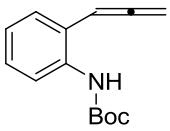
Yield: 93.5%; White solid; R_f = 0.25 (Ethyl acetate: Hexane (0.5:9.5)); IR (thin film): ν 3396, 2930, 2369, 1705, 1213, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, *J* = 8 Hz, 1H), 7.27-7.24 (m, 1H), 7.19 (brs, 1H), 7.02 (d, *J* = 7.4 Hz, 1H), 3.85 (s, 3H), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.8, 142.1, 138.3, 128.43, 124.8, 117.5, 96.63, 52.38, 29.59; HRMS (ESI): calcd for $C_9H_{10}INO_2$*m/z* 313.9654 $[M+Na]^+$, Found 313.9652.

3. Palladium(0)-catalyzed coupling reaction of iodoanilides with allenylstannane:[6]

General procedure for the preparation of 2-allenylanilides:

The solution of *N*-Boc iodoanilide(1.5 g, 4.7 mmol) and allenylstannane (2.32 g,7.05 mmol) in anhydrous DMF (40 mL) was degassed and purged with argon gas. Tris(2-furyl)phosphine (0.218 g, 0.94 mmol), $Pd_2(dba)_3$(0.145 g, 0.141mmol) and CuI (0.09 g, 0.47 mmol) were added to the reaction mixture at rt under argon atmosphere. The reaction mixture was stirred at rt for allotted time, quenched by addition of 10% aqueous NH_3 solution and extracted with diethyl ether. The combined extracts were washed with water, brine, dried over sodium sulfate and concentrated under vacuum.

***tert*-butyl 2-(propa-1,2-dienyl)phenylcarbamate (22):**



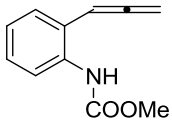
Reaction carried out in 4.7 mmol scale;

Time required for completion of reaction: 3 h

Purified by silica gel column chromatography (Et_2O:Hexane (0.5:9.5))

Isolated yield: 2.759 g, (81%); colorless liquid; R_f = 0.37 (Ethyl acetate: Hexane (1:9); IR (thin film): ν 3387, 2977, 1943, 1710, 1520, 1156, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.83 (brs, 1H), 7.23-7.20 (m, 2H), 7.10 (brs, 1H), 7.04 (td, *J* = 7.45 Hz, 1.15 Hz, 1H), 6.28 (t, *J* = 6.87, 1H), 5.19 (d, *J* = 6.87 Hz, 2H), 1.52 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.9, 152.9, 135.5, 128.6, 127.7, 123.7, 122.9, 121.8, 90.5, 80.2, 78.4, 28.2; HRMS (ESI): calcd for $C_{14}H_{17}NO_2$ *m/z* 254.1157 $[M+Na]^+$, Found 254.1150.

Methyl 2-(propa-1,2-dienyl)phenylcarbamate (1a):



Reaction carried out in 5.41 mmol scale;

Time required for completion of reaction: 3 h

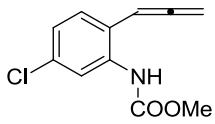
Purified by silica gel column chromatography (EtOAc: Hexane (1:9))

Isolated yield: 0.921 g (90%); white solid; R_f = 0.34 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3313, 2947, 1941, 1716, 1523, 1225, 1060, 757 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.82 (brs, 1H), 7.31 (brs, 1H), 7.24-7.21 (m, 2H), 7.07 (t, *J* = 7.45 Hz, 1H), 6.28 (t, *J* = 6.87 Hz, 1H), 5.2 (d, *J* = 6.87 Hz, 2H), 3.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.8, 154.3, 135.1, 128.7, 127.8, 124.1, 90.5,

[6]C. Mukai, Y. Takahashi. *Org. Lett*. **2005**, *7*, 5793-5796

78.7, 52.3; HRMS (ESI): calcd for $C_{11}H_{11}NO_2$ *m/z* 212.0687 $[M+Na]^+$, Found 212.0686.

Methyl 5-chloro-2-(propa-1,2-dienyl)phenylcarbamate (1b):



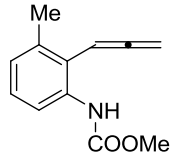
Reaction carried out in 6.42 mmol scale;

Time required for completion of reaction: 3.5 h

Purified by silica gel column chromatography (EtOAc: Hexane (1:9))

Isolated yield: 1.249g (87%); yellow solid; R_f = 0.17 (Ethyl acetate: Hexane (1:9); IR (thin film): ν 3383, 2961, 2321, 1941, 1709, 1521, 1224, 1058, 868 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.96 (brs, 1H), 7.41-7.4(m, 1H), 7.1-7.07 (m, 1H), 7.01 (dd, *J* = 8 Hz, 1.72 Hz, 1H), 6.22 (t, *J* = 6.87 Hz, 1H), 5.23 (d, *J* = 6.87 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.8, 153.8, 136.4, 133.5, 129.8, 123.9, 121.1, 99.8, 90.2, 79.3, 52.55; HRMS (ESI): calcd for $C_{11}H_{10}ClNO_2$ *m/z*246.0298 $[M+Na]^+$, Found 246.0286.

Methyl 3-methyl-2-(propa-1,2-dienyl)phenylcarbamate (1c):



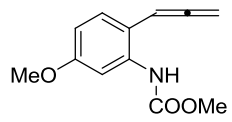
Reaction carried out in 4.8 mmol scale;

Duration of reaction: 2 days at rt

Purified by silica gel column chromatography (Et_2O: Hexane (1:9))

Isolated yield: 0.53 g (37%) 63% (brsm); liquid; R_f = 0.45 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3380, 2369, 1915, 1716, 1540, 656 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.8 (brs, 1H), 7.32-7.34 (m, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 7.45 Hz, 1H), 6.25 (t, *J* = 7.45 Hz, 1H), 5.09 (d, *J* = 6.87 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.4, 154.1, 136.6, 135.8, 127.6, 125.6, 124.7, 118.6, 87.2, 76.7, 52.2, 20.8; HRMS (ESI): calcd for $C_{12}H_{13}NO_2$ *m/z* 226.0844 $[M+Na]^+$, Found 226.0844.

Methyl 5-methoxy-2-(propa-1,2-dienyl)phenylcarbamate (1e):



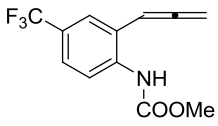
Reaction carried out in 8.14 mmol scale;

Duration of the reaction: 12 h

Purified by silica gel column chromatography (EtOAc: Hexane (1.5:8.5))

Isolated yield: 0.95 g (53%) (76%, brsm); white solid; R_f = 0.3 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3382, 3008, 2953, 1941, 1710, 1531, 1228, 1059, 765; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.6 (brs, 1H), 7.51 (brs, 1H), 7.06 (d, *J* = 8.59 Hz, 1H), 6.61 (dd, *J* = 8.59 Hz, 2.29 Hz, 1H), 6.23 (t, *J* = 6.87 Hz, 1H), 5.2 (d, *J* = 6.87 Hz, 2H), 3.8 (s, 3H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.2, 159.5, 154.0, 136.8, 129.9, 113.9, 110.3, 105.8, 90.6, 79.0, 55.3, 52.3; HRMS (ESI): calcd for $C_{12}H_{13}NO_3$ *m/z* 242.0793 $[M+Na]^+$, Found 242.0787.

Methyl 2-(propa-1,2-dienyl)-4-(trifluromethyl)phenylcarbamate (1d):



Reaction carried out in 5.79 mmol scale;

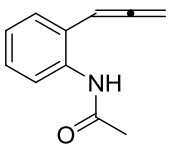
Time required for completion of reaction: 3.5 h

Purified by silica gel column chromatography (EtOAc: Hexane (1:9))

Isolated yield: 1.2 g (81%); white fluffy solid; R_f = 0.36 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3273, 2961, 2365, 1960, 1700, 1540, 1213, 769 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.1 (d, *J* = 8.59 Hz, 1H), 7.56 (brs, 1H), 7.42-7.47(m, 2H), 6.28 (t, *J* = 6.87 Hz, 1H), 5.29 (d, *J* = 7.45 Hz, 2H), 3.79 (s,

3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.9, 153.8, 138.5, [(127.2, 125.0, 122.9, 120.7) (q, $^1J_{CF}$ 272 Hz)], 125.97 (q, $^3J_{CF}$ 3.6 Hz), [(125.9, 125.7, 125.4, 125.2) (q, $^2J_{CF}$ 32 Hz)], 124.8 (q, $^2J_{CF}$ 3.6 Hz), 122.0, 120.5, 90.1, 79.7, 52.6; HRMS (ESI): calcd for $C_{12}H_{10}F_3NO_2$ *m/z* 280.0561 $[M+Na]^+$, Found 280.0563.

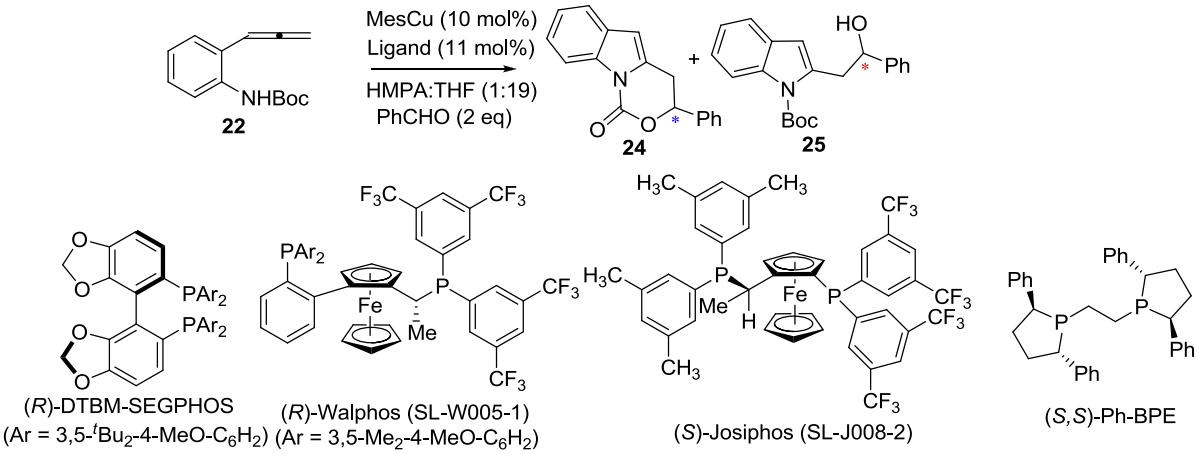
Preparation of *N*-(2-(propa-1,2-dienyl)phenyl)acetamide (23):[7]



Procedure: *N*-(2-iodophenyl)acetamide (2 g, 7.66 mmol) was added to a suspension of $[Pd(PPh_3)_4]$ (0.354g, 0.3 mmol) and lithium iodide (3 g, 22.9 mmol) in DMF (45 mL) under argon atmosphere. After 10 min, the allenylindium reagent, which was generated from propargyl bromide (0.86 mL, 11.49 mmol) and indium (1.93 g, 16.8 mmol) in DMF (25 mL) was added, and the reaction mixture was stirred at 90 to 100 °C for 1 h 15 min. The reaction mixture was cooled to room temperature and quenched slowly with sat. $NaHCO_3$ solution. The reaction mixture was extracted with diethyl ether. Combined organic layers were washed with water, brine, dried over sodium sulfate and concentrated under vacuum. Purification by silica gel column chromatography (EtOAc: hexane 4:6) afforded white fluffy solid (0.748 g, 56.6%). R_f = 0.27 (Ethyl acetate: Hexane (1:1); IR (thin film): ν 3221, 3025, 2369, 1646, 1541, 858 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.97 (brs, 1H), 7.85 (d, *J* = 6.3 Hz, 1H), 7.23-7.19 (m, 2H), 7.09 (t, *J* = 7.45 Hz, 1H), 6.29 (t, *J* = 6.87 Hz, 1H), 5.19 (d, *J* = 6.87 Hz, 2H), 2.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 210.1, 168.4, 135.0, 128.7, 127.8, 125.0, 123.7, 123.6, 90.9, 78.4, 24.0; HRMS (ESI): calcd for $C_{11}H_{11}NO$ *m/z* 196.0738 $[M+Na]^+$, Found 196.0732.

4. Catalytic tandem amido-cupration of allene and asymmetric allylation: Optimization of reaction conditions:

4-1. Ligand screening:



[7]K. Lee, D. Seomoon, P. H. Lee. *Angew. Chem. Int. Ed*. **2002**, *41*, 3901-3903

Entry	Ligand	Yield (**24**/**25**) (%)[a]	*ee* (**24**/**25**) (%)[b]
1	(*R*)-DTBM-SEGPHOS	24/40	41/n.d
2	(*R*)-Walphos	60/25	56/n.d
3	(*S*)-Josiphos	58/28	71/n.d
4	**(*S, S*)-Ph-BPE**	52/28	82/ >99

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *tert*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

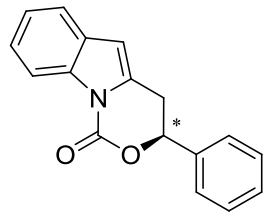
Experimental procedure:

To a flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (3.64 mg, 0.02 mmol, 10 mol%), and ligand (0.022 mmol, 11 mol%) under nitrogen atmosphere in a glove box. Anhydrous THF (418 μL) and HMPA (33 μL) were added, and the mixture was stirred at ambient temperature for 10 minutes. To the stirred solution, benzaldehyde (40 μL, 0.4 mmol) and 1 M solution of allenylanilide (**22**) (46.22 mg, 200 μL, 0.2 mmol) were added sequentially. The resulting solution was stirred at the same temperature for 44 h. Quenched with sat. NH_4Cl solution, products were extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum.

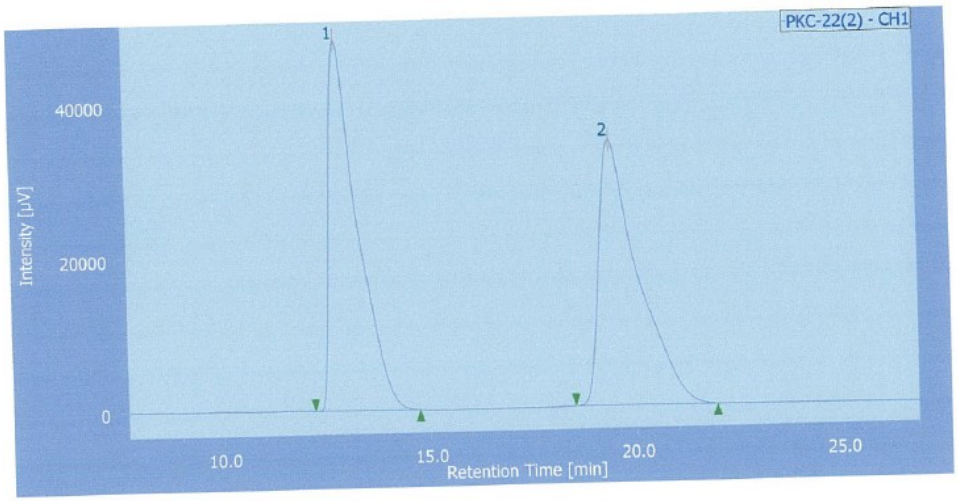
The racemic sample was prepared by performing reaction with achiral ligand 1,3-bis(diphenylphosphino)propane (dppp).

Ligand screening revealed that (*S,S*)-Ph-BPE was the best ligand for this asymmetric transformation.

3-Phenyl-3,4-dihydro-1*H*-[1,3]oxazino[3,4-a]indol-1-one (24):

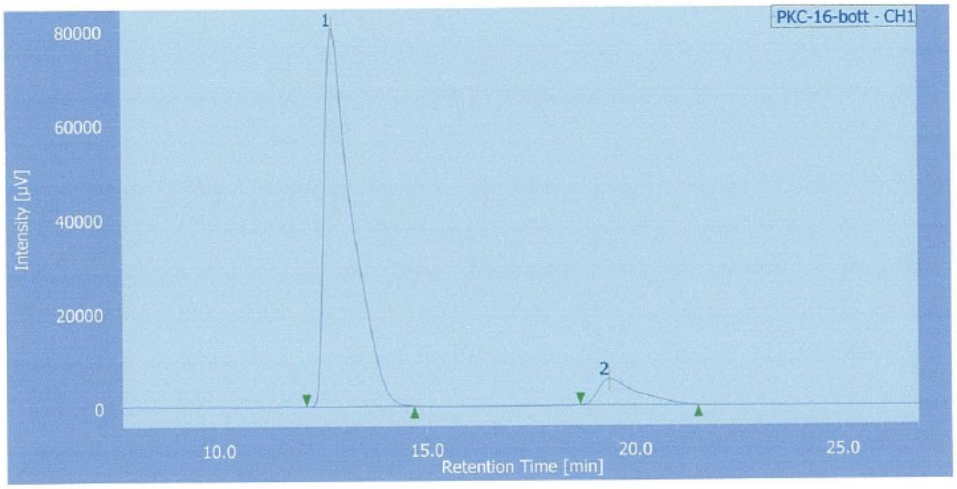


Purified by silica gel column chromatography (EtOAc: Hexane (1:9); white solid; R_f = 0.35 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3021, 2369, 1739, 1535, 1213, 1104, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.31 (d, *J* = 8.59 Hz, 1H), 7.54 (d, *J* = 8.02 Hz, 1H), 7.43-7.39 (m, 5H), 7.34 (t, *J* = 7.45 Hz, 1H), 7.29 (t, *J* = 7.45 Hz, 1H), 6.42 (s, 1H), 5.59 (dd, *J* = 10.8 Hz, 3.4 Hz, 1H), 3.43-3.31 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 147.8, 137.0, 135.1, 132.7, 129.4, 129.0, 128.8, 125.9, 124.4, 123.8, 120.3, 115.3, 104.5, 79.8, 30.3; HRMS (ESI): calcd for $C_{17}H_{13}NO_2$ *m/z* 286.08440 $[M+Na]^+$, Found 286.0850. Specific optical rotation $[\alpha]_D^{24}$ = -108.8 (*c* = 1.21, $CHCl_3$) for an enantiomerically enriched sample of 82% *ee*. Enantiomeric excess was determined by HPLC analysis in comparision with authentic racemic material; Chiralcel OD-H; Mobile phase: Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm, t_r = 12.7 min (major), 19.3 min (minor).



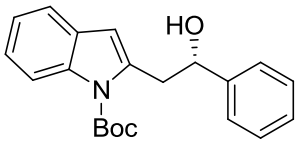
判定式

#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	12.833	2239636	48172	49.957	58.258	N/A	1931	4.809	2.189	
2	Unknown	1	19.425	2243528	34516	50.043	41.742	N/A	2417	N/A	2.022	

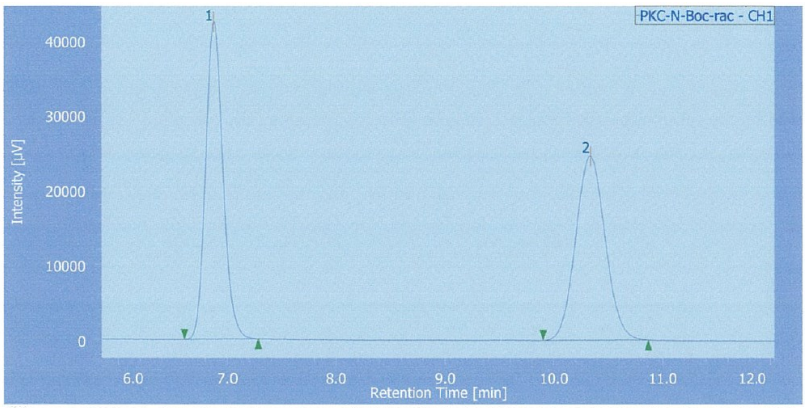


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	12.750	3753996	80293	91.276	93.560	N/A	1903	4.842	2.219	
2	Unknown	1	19.392	358812	5526	8.724	6.440	N/A	2406	N/A	2.057	

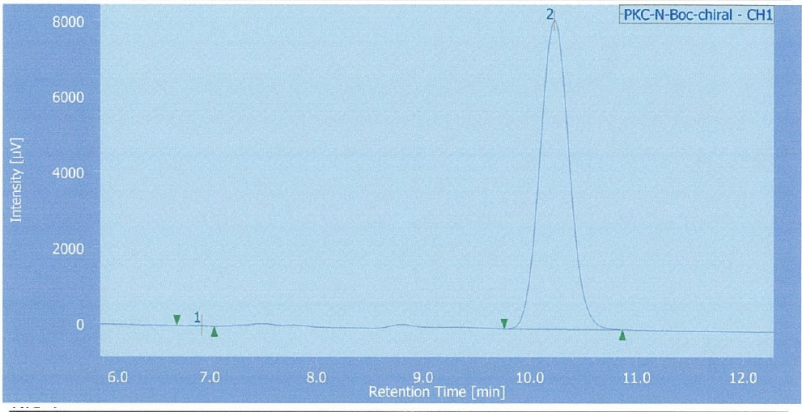
(*S*)-*tert*-butyl-2-(2-hydroxy-2-phenylethyl)-1*H*-indole-1-carboxylate (25):



Purified by silica gel column chromatography (EtOAc: Hexane (1:9); colorless liquid; R_f = 0.33 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3403, 2978, 2369, 1734, 1456, 1155, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.03 (d, *J* = 8.98 Hz, 1H), 7.48-7.45 (m, 3H), 7.39-7.19 (m, 5H), 6.43 (s, 1H), 5.09-5.05 (m, 1H), 3.62 (dd, *J* = 14.8 Hz, 4.04 Hz, 1H), 3.33 (dd, *J* = 14.8 Hz, 8.98 Hz, 1H), 2.67-2.65 (m, 1H), 1.72 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.0, 143.9, 138.0, 136.4, 129.0, 128.3, 127.4, 125.7, 123.6, 122.7, 120.0, 115.6, 110.0, 84.3, 73.15, 39.8, 28.2; HRMS (ESI): calcd for $C_{21}H_{23}NO_3$ *m/z* 360.15756 $[M+Na]^+$, Found 360.1562. Specific optical rotation $[\alpha]_D^{24}$ = -14.2 (*c* = 0.77, $CHCl_3$) (>99% *ee*); HPLC analysis: (column - ChiralpakIA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 6.9 min (minor), t_r = 10.2 min (major).



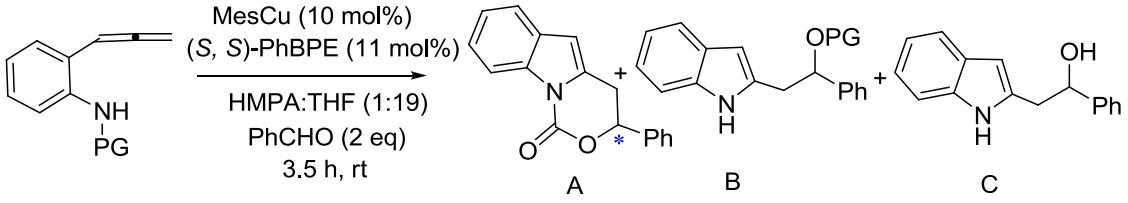
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	6.875	467320	42377	50.082	63.286	N/A	9127	8.783	1.149	
2	Unknown	1	10.333	465788	24584	49.918	36.714	N/A	6787	N/A	1.062	

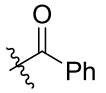
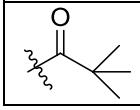


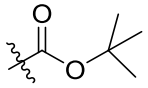
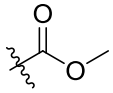
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	6.925	109	16	0.070	0.192	N/A	28331	9.867	0.757	
2	Unknown	1	10.225	155631	8149	99.930	99.808	N/A	6530	N/A	1.070	

4-2. Tuning of enantiomeric excess and yield by switching different protecting groups in allenylanilide:

The reactions were performed using (*S, S*)-PhBPE (11 mol%) and MesCu (10 mol%) in a HMPA:THF(1:19) solvent system (0.3 M concentration) (0.2 mmol scale).



-PG	Yield (%)[a]				*ee*(%)[b]	Inference
	A	B	C	Total	A/B/C	
				-	-	No reaction (SM recovered)
				-	-	No reaction (SM recovered)

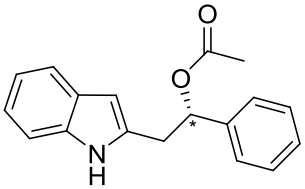
		60		60	-/68/-	-*N* to *O*-acyl migration
	52	28	-	80	82/>99/-	
	70	14	11	95	86/85/nd	

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

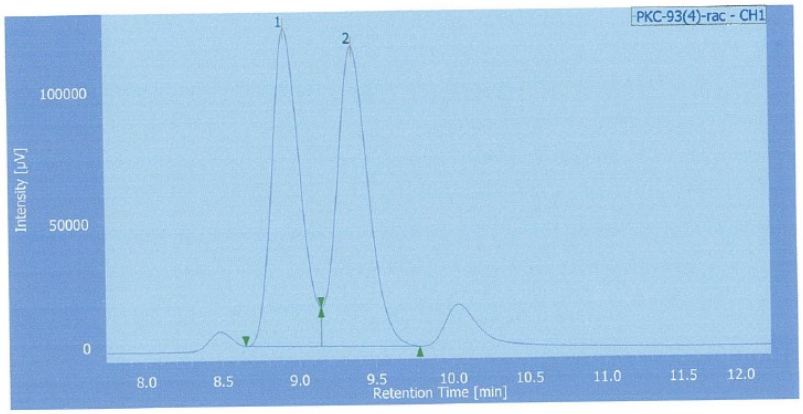
The racemic sample was prepared by performing the reaction with achiral ligand 1,3-bis(diphenylphosphino)propane (dppp).

N-COOMe (-PG) substrate showed the best result in terms of yield and enantioselectivity {Further, the ligand screening with this substrate was carried out and found the optimum result in case of (*S, S*)-Ph-BPE }.

(*S*)-2-(1*H*-indol-2-yl)-1-phenylethyl acetate (26):

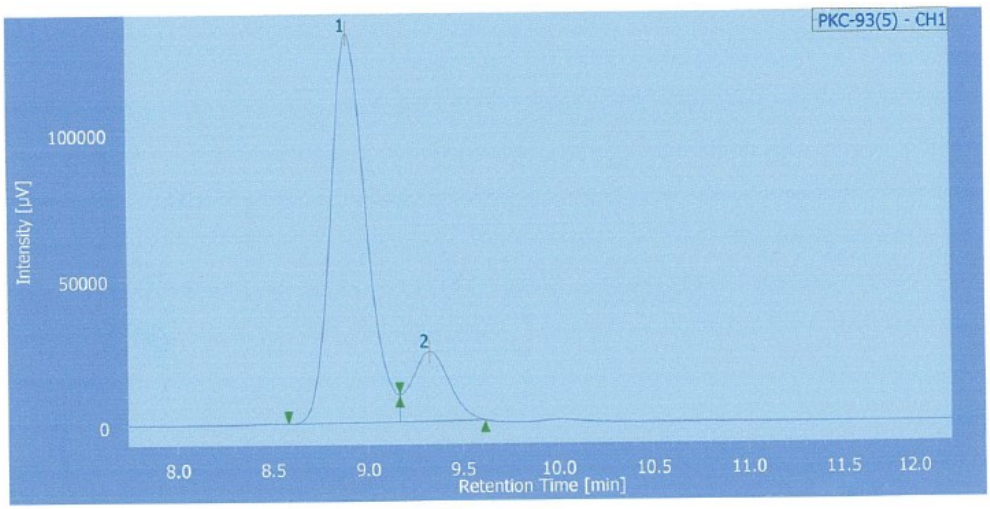


Purified by silica gel column chromatography (EtOAc: Hexane (1:9); liquid; R_f = 0.25 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3395, 1717, 2943, 1238, 1024, 750cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.87 (brs, 1H), 7.52 (d, *J* = 6.87 Hz, 1H), 7.36-7.30 (m, 5H), 7.27-7.25 (m, 1H), 7.14-7.11 (m, 1H), 7.08-7.05 (m, 1H), 6.24-6.23(m, 1H), 6.03 (t, *J* = 6.87 Hz, 1H), 3.36 (dd, *J* = 15.4 Hz, 6.3 Hz, 1H), 3.25 (dd, *J* = 15.4 Hz, 6.3 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ170.1, 139.6, 136.0, 134.1, 128.6, 128.4, 128.3, 126.4, 121.4, 120.0, 119.6, 110.4, 101.9, 75.3, 35.7, 21.2; HRMS (ESI): calcd for $C_{18}H_{17}NO_2$ *m/z* 302.1157 $[M+Na]^+$, Found 302.1153. Specific optical rotation $[\alpha]_D^{24}$ = -17.0 (*c* = 0.56, $CHCl_3$) (68% *ee*); HPLC analysis: (column - Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 8.9 min (major), 9.3 min (minor)



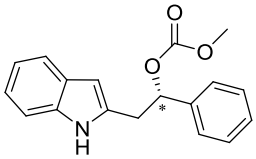
判定式

#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.917	1544904	121245	48.937	51.486	N/A	11180	1.259	N/A	
2	Unknown	1	9.358	1612008	114245	51.063	48.514	N/A	10461	N/A	N/A	

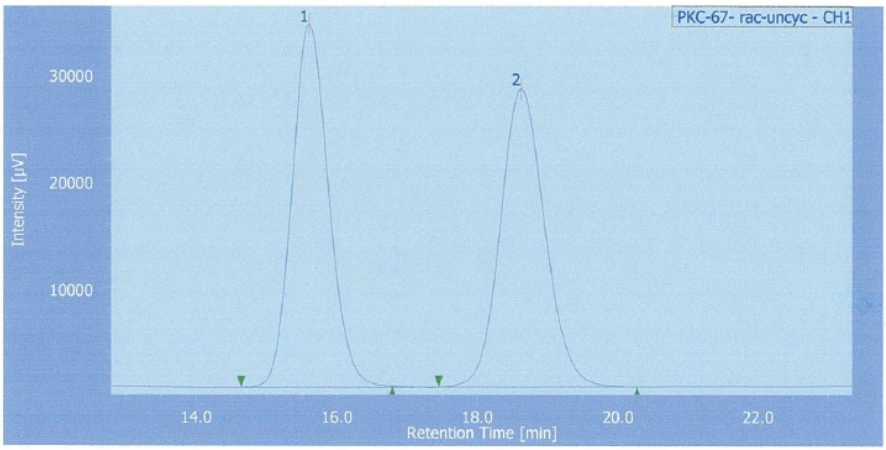


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.900	1720866	133077	84.089	84.855	N/A	11174	1.188	N/A	
2	Unknown	1	9.325	325620	23751	15.911	15.145	N/A	9612	N/A	N/A	

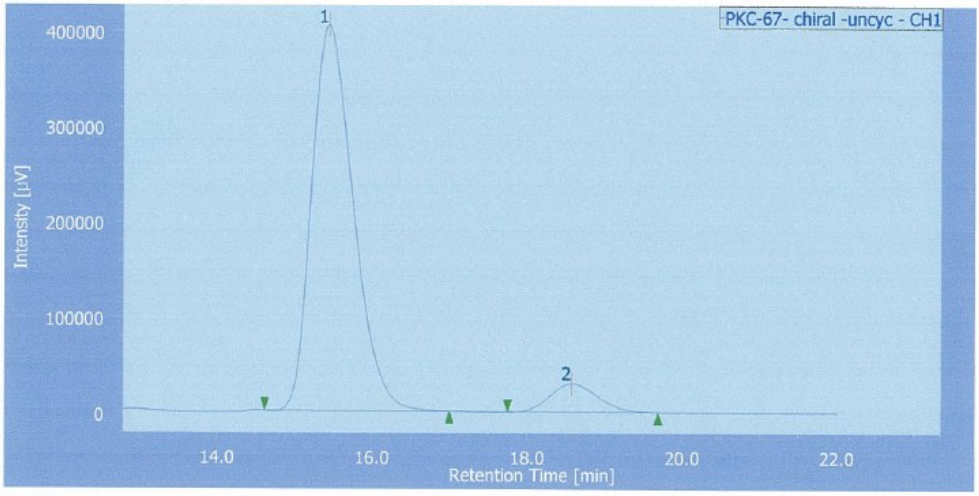
(*S*)-Methyl 2-(2-hydroxy-2-phenylethyl)-1*H*-indole-1-carboxylate (27):



Purified by silica gel column chromatography (EtOAc: Hexane (1:9); R_f = 0.25 (Ethyl acetate: Hexane (2:8)); IR (thin film): ν 3397, 2961, 2369, 1748, 1268 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.0 (brs, 1H), 7.52 (d, *J* = 7.18 Hz, 1H), 7.36-7.28 (m, 6H), 7.13 (td, *J* = 7.18 Hz, 1.35 Hz, 1H), 7.07 (td, *J* = 8.07 Hz, 1.35 Hz, 1H), 6.27 (s, 1H), 5.82 (dd, *J* = 7.63 Hz, 5.38 Hz, 1H), 3.74 (s, 3H), 3.39 (dd, *J* = 15.2 Hz, 7.6 Hz, 1H), 3.25 (dd, *J* = 14.8 Hz, 5.38 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 154.8, 139.1, 136.1, 134.0, 128.6, 128.5, 128.3, 126.3, 121.4, 120.1, 119.6, 110.5, 102.0, 79.6, 54.9, 35.7; HRMS (ESI): calcd for $C_{18}H_{17}NO_3$ *m/z* 318.11061 $[M+Na]^+$, Found 318.1113. Specific optical rotation $[\alpha]_D^{24}$ = -5.2 (*c* = 0.15, $CHCl_3$) (85% *ee*); HPLC analysis: (column –Chiralcel OD-H; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 15.4 min (major), 18.5 min (minor).

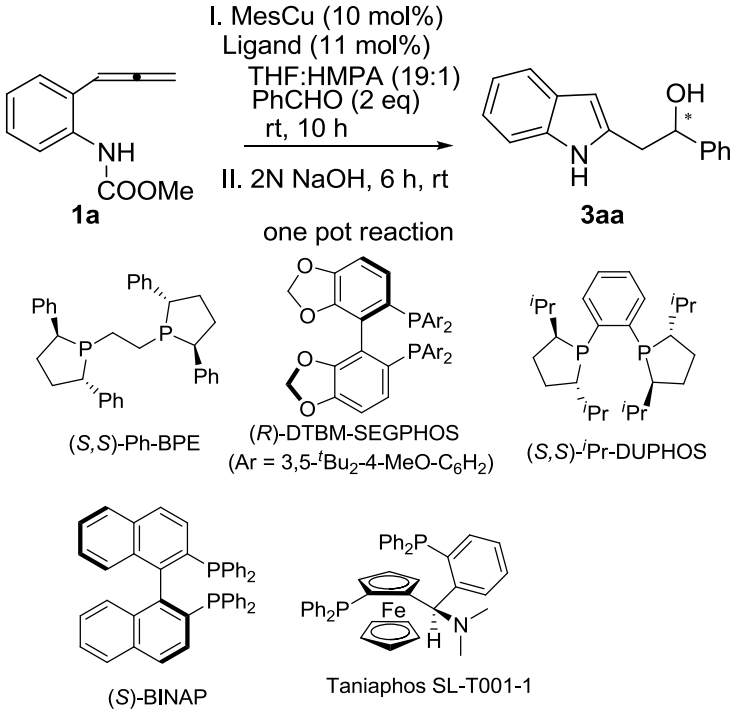


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	15.608	1226286	33870	50.119	54.892	N/A	4338	2.890	1.116	
2	Unknown	1	18.625	1220477	27832	49.881	45.108	N/A	4230	N/A	1.111	



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	15.433	15061553	403799	92.355	93.282	N/A	3958	2.964	1.333	
2	Unknown	1	18.575	1246786	29080	7.645	6.718	N/A	4218	N/A	1.178	

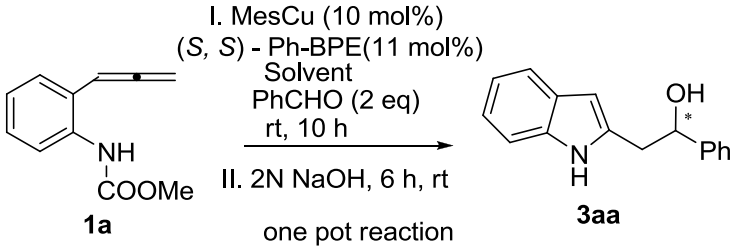
4-3. Ligand screening with the –*N*-COOMe allenylaninilide substrate (1a):



Entry	Ligand	Yield (%)[a]	*ee* (%)[b]
1	**(*S, S*)-Ph-BPE**	**85**	**88**
2	(*R*)-DTBM-SEGPHOS	51	67
3	(*S,S*),iPr-Duphos	90	45
4	(*S*)-BINAP	94	42
5	Taniaphos	86	29

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

4-4. Solvent screening:



Entry	Solvent	Yield (%)[a]	*ee* (%)[b]	Entry	Solvent	Yield (%)[a]	*ee* (%)[b]
1	DMF	92	82	7	TBME	74	86
2	DME	82	85	8	THF	89	87
3	CH_2Cl_2	60	80	9	THF:HMPA (19:1)	90	87
4	$^{i}Pr_2O$	50	84	10	Dioxane:HMPA (2:1)	92	89
5	**Dioxane**	**93**	**88**	11[c]	DMPU	50	91
6	Toluene	50	88	**12[c]**	**Dioxane**	**92**	**91**

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis. [c]Reaction carried out at 15 °C.

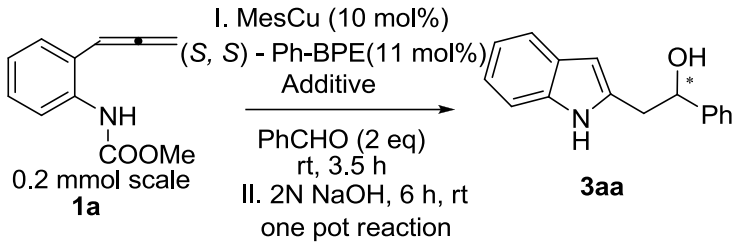
Inference: Dioxane showed the best result in this asymmetric transformation.

Experimental procedure:

A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (3.64 mg, 0.02 mmol, 10 mol%) and (*S, S*)-Ph-BPE (11.14 mg, 0.022 mmol, 11 mol%) under argon atmosphere. The anhydrous solvent (470 µL) was added, and the mixture was stirred at ambient temperature for 15 minutes. To the stirred solution, benzaldehyde (40 μL, 0.4 mmol) and 1.04 M solution of allenylanilide (**1a**) (37.8 mg, 192 μL, 0.2 mmol) were added sequentially. After stirring for 10 h at room temperature, the reaction was diluted with THF/dioxane (2.5 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 6 h, extracted the suspension with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum.

4-5. Effect of additives:

The effect of molecular sieves, alcohol and water on yield and enantioselectivity were examined, and results are illustrated below.

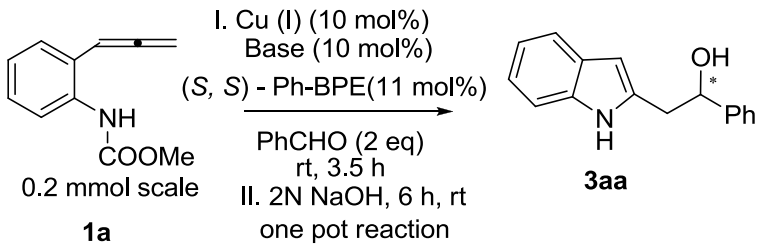


Entry	Additive	[a]Yield (%)	[b]*ee* (%)
1	-	93	88
2	MS 3A (50 mg)	91	88
3	MS 4A (50 mg)	95	88
4	MS 5A (50 mg)	97	88
5	MS 13X (50 mg)	97	88
6	EtOH (100 mol%)	86	87
7	H_2O (40 mol%)	75	89

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

4-6. Effect of copper source and base:

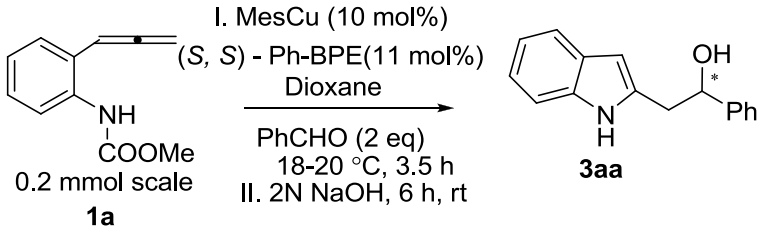
Several copper sources and bases were screened, and the results obtained are shown below.



Entry	Cu(I)	Base	Yield (%)[a]	*ee* (%)[b]
1	**MesCu**	**-**	**93**	**88**
2	$Cu(CH_3CN)_4BF_4$	LiO^{t}Bu	82	82
3	$Cu(CH_3CN)_4PF_6$	LiO^{t}Bu	77	75
4	CuOAc	LiO^{t}Bu	75	88
5	-	LiO^{t}Bu	5	-
6	CuOTf.1/2Toluene	LiO^{t}Bu	72	84
7	Cu(I)-3-methylsalicylate	LiO^{t}Bu	88	87

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

4-7. Effect of concentration on chemical yield and enantioselectivity:



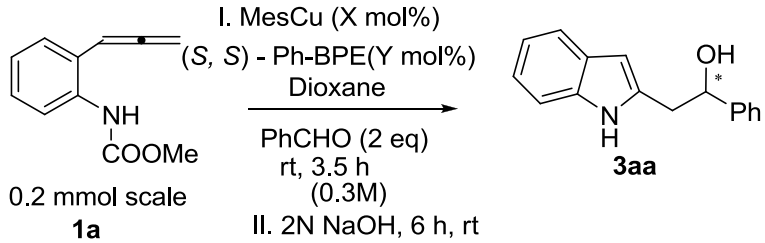
The reactions were conducted at different concentrations. The chemical yield and enantioselectivity are shown below.

Entry	Concentration (M)	Yield (%)[a]	*ee* (%)[b]
1	0.1	92	90
2	**0.3**	**91**	**91**
3	0.6	86	91
4	0.9	85	90

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

4-8. Catalyst loading:

The amount of catalyst required to procure optimum result in the desired transformation was measured and shown below.

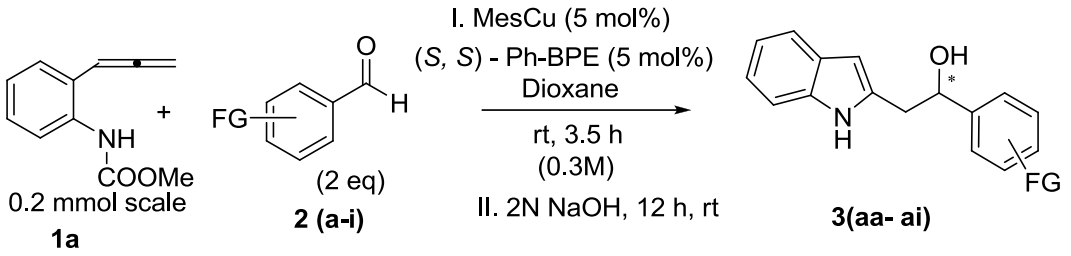


Entry	MesCu (mol%)	(S, S)-Ph-BPE (mol%)	Yield (%)[a]	*ee* (%)[b]
1	10	-	No reaction	
2	3	3	81	90
3	**5**	**5**	**96**	**89**
4	7	7	97	90
5	10	10	93	88

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

5. General Procedure for constructing 2-(2-hydroxyethyl)indoles: Reaction of allenyl anilides with aromatic aldehydes:

General procedure for constructing 2-(2-hydroxyethyl)indoles): (Condition A)

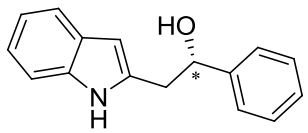


A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (1.82 mg, 0.01 mmol, 5 mol%) and (*S, S*)-PhBPE (5.06 mg, 0.01 mmol, 5 mol%) under argon atmosphere. Anhydrous dioxane (480 μL) was added, and the mixture was stirred at ambient temperature for 15 minutes. To the stirred solution, aromatic aldehyde (0.4 mmol) and 1.1 M solution of allenylanilide (**1a**) (37.8 mg, 181 μL, 0.2 mmol) were added sequentially. After stirring for 3.5 h at room temperature, the reaction was diluted with dioxane (2.5 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 12 h, and products were extracted with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compounds.

The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (*S, S*)-Ph-BPE.

The absolute configuration for all the compounds were assigned based on analogy of **3aa** (see- page S48-S51)

(*S*)-2-(1*H*-indol-2-yl)-1-phenylethanol (3aa):

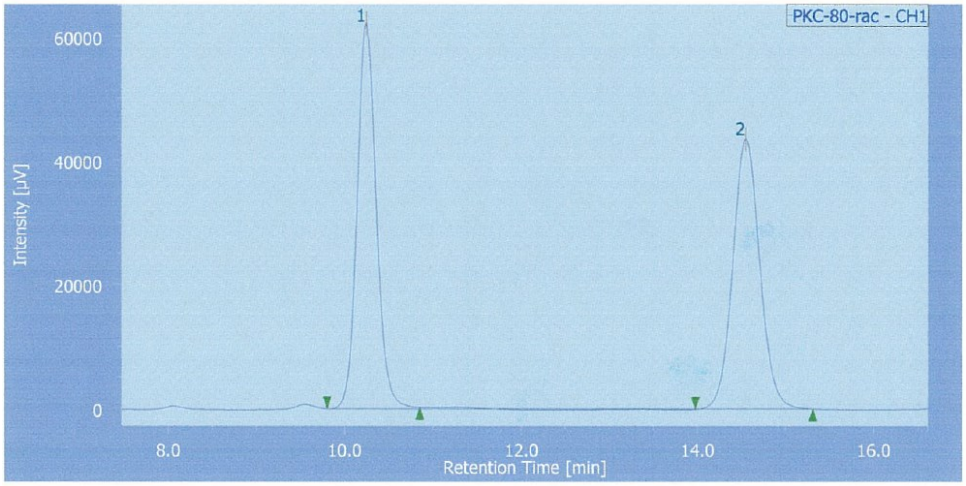


Purified by silica gel column chromatography (EtOAc: Hexane (2:8); white solid;

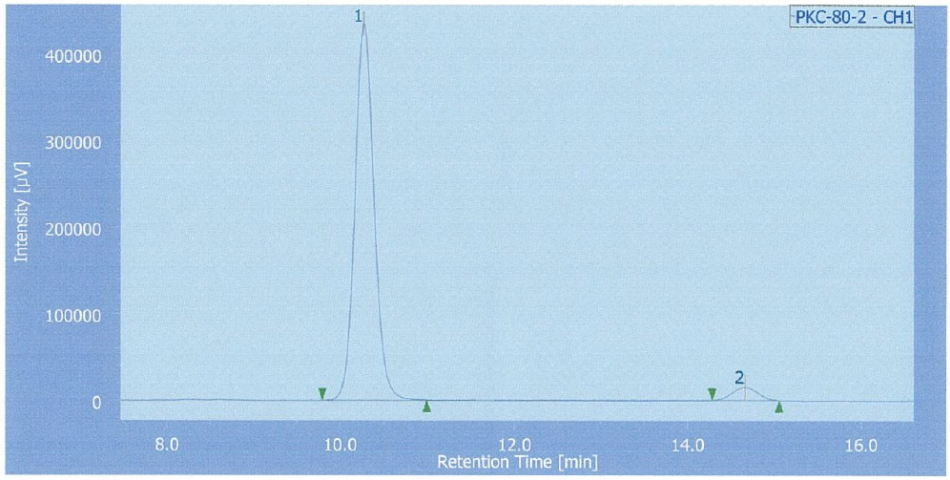
(Yield, *ee*) (%): 96%, 89% (reaction conducted at rt)

: 92%, 91% (reaction conducted at 15 °C)

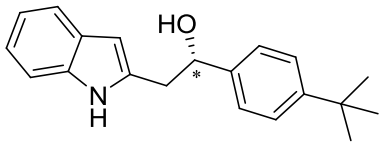
R_f = 0.33 (Ethyl acetate: Hexane (3:7)); IR (thin film): ν 3410, 3021, 2369, 1215, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.49 (brs, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.41-7.31 (m, 6H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 7.45 Hz, 1H), 6.3 (s, 1H), 5.0-4.98 (m, 1H), 3.17 (d, *J* = 6.3 Hz, 2H), 2.28 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.5, 136.17, 136.13, 128.6, 128.3, 127.9, 125.6, 121.3, 119.9, 119.5, 110.5, 101.0, 74.3, 37.8; HRMS (ESI): calcd for $C_{16}H_{15}NO$ *m/z* 260.1051 $[M+Na]^+$, Found 260.1040. Specific optical rotation $[\alpha]_D^{20}$ = - 48.0 (*c* = 0.5, $CHCl_3$) (91% *ee*); HPLC analysis: (91% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 10.2 min (major), 14.6 min (minor).



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.250	937882	62103	50.411	58.806	N/A	11217	9.193	1.079	
2	Unknown	1	14.550	922578	43503	49.589	41.194	N/A	11162	N/A	1.062	



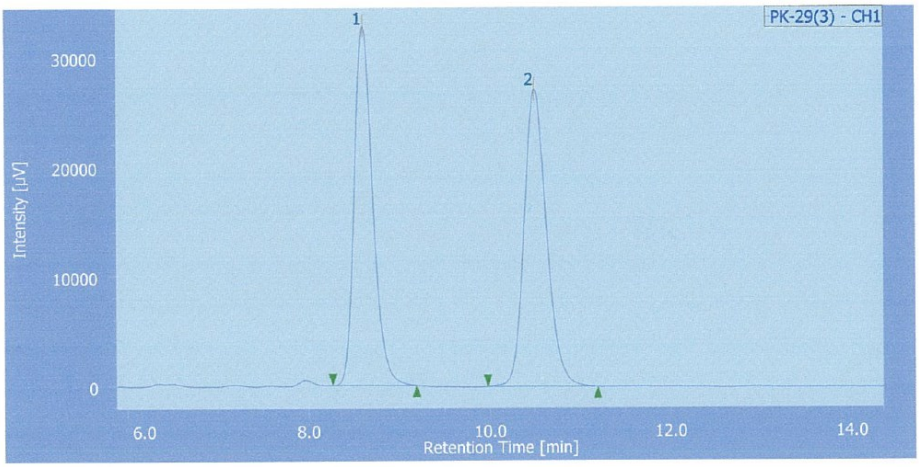
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.267	6601972	434678	95.598	96.659	N/A	11074	9.422	1.120	
2	Unknown	1	14.658	304000	15024	4.402	3.341	N/A	11596	N/A	1.014	



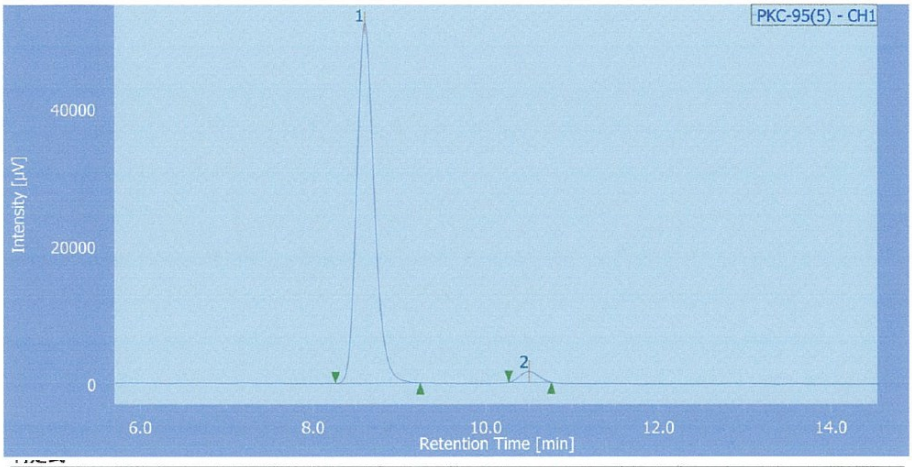
(*S*)-1-(4-*tert*-butylphenyl)-2-(1*H*-indol-2-yl)ethanol (3ab):

Purified by silica gel column chromatography (EtOAc: Hexane (2:8); white solid; Yield: 89 %;

R_f = 0.23 (Ethyl acetate: Hexane (2:8); IR (thin film): ν 3504, 3278, 2956 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.5 (brs, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.42-7.40 (m, 2H), 7.34-7.31 (m, 3H), 7.14 (t, *J* = 6.87 Hz, 1H), 7.08 (t, *J* = 6.87 Hz, 1H), 6.30 (s, 1H), 4.99 (dd, *J* = 8.59 Hz, 4.0 Hz, 1H), 3.22-3.13 (m, 2H), 2.2 (brs, 1H), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.0, 140.6, 136.5, 136.1, 128.3, 125.5, 125.4, 121.2, 119.9, 119.5, 110.5, 100.9, 74.2, 37.6, 34.5, 31.3; HRMS (ESI): calcd for $C_{20}H_{23}NO$ *m/z* 316.1677 $[M+Na]^+$, Found 316.1678. Specific optical rotation $[\alpha]_D^{24}$ = - 26.9 (*c* = 0.57, $CHCl_3$) (94% *ee*); HPLC analysis: (94% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 8.6 min (major), 10.5 min (minor).

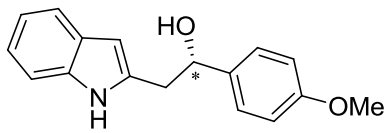


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.608	462410	32760	49.662	54.741	N/A	8946	4.681	1.186	
2	Unknown	1	10.500	468706	27085	50.338	45.259	N/A	8853	N/A	1.158	



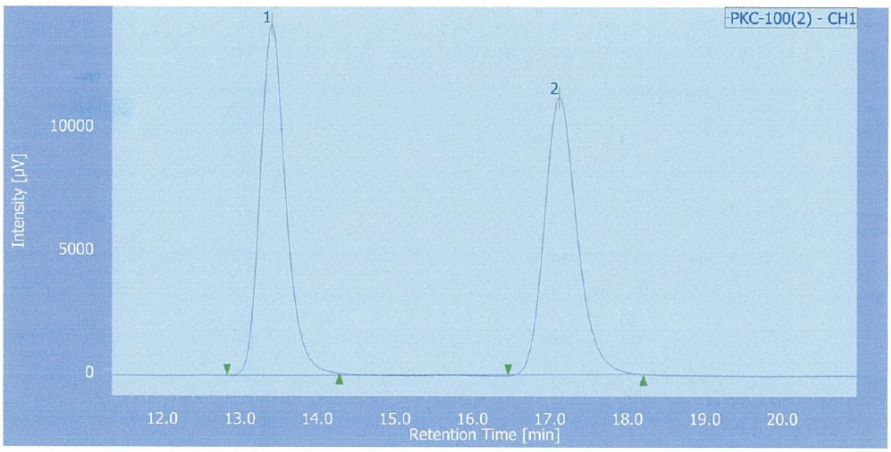
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.600	740026	52387	96.991	97.131	N/A	8922	4.926	1.196	
2	Unknown	1	10.500	22961	1547	3.009	2.869	N/A	10529	N/A	1.057	

(*S*)-2-(1*H*-indol-2-yl)-1-(4-methoxyphenyl)ethanol (3ac):

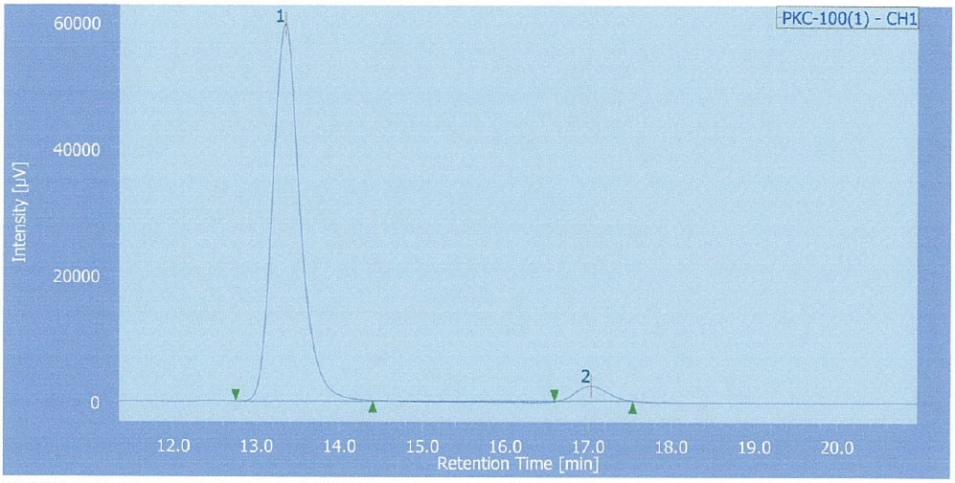


Purified by silica gel column chromatography (EtOAc: Hexane (3:7); white solid; Yield: 80 %;

R_f = 0.23 (Ethyl acetate: Hexane 3:7); IR (thin film): ν 3252, 2930, 2369, 1034, 749 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.52 (brs, 1H), 7.57 (d, *J* = 7.4 Hz, 1H), 7.33-7.27 (m, 3H), 7.16 (t, *J* = 8.02 Hz, 1H), 6.92-6.89 (m, 2H), 6.29 (s, 1H), 4.93 (dd, *J* = 8.0 Hz, 4.58 Hz, 1H), 3.82 (s, 1H), 3.18-3.11 (m, 2H), 2.29 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.2, 136.3, 136.0, 135.7, 128.3, 121.2, 119.8, 119.5, 113.9, 110.5, 100.9, 73.9, 55.2, 37.7; HRMS (ESI): calcd for $C_{17}H_{17}NO_2$ *m/z* 290.1157 $[M+Na]^+$, Found 290.1153. Specific optical rotation $[\alpha]_D^{24}$ = - 34.6 (*c* = 1.09, $CHCl_3$) (91% *ee*); HPLC analysis: (91.4% *ee*); (Column – Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 13.3 min (major), 17.0 min (minor).

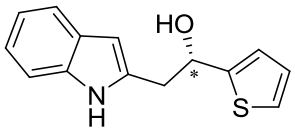


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	13.408	329666	14234	50.205	55.893	N/A	8246	5.548	1.247	
2	Unknown	1	17.117	326971	11233	49.795	44.107	N/A	8339	N/A	1.222	



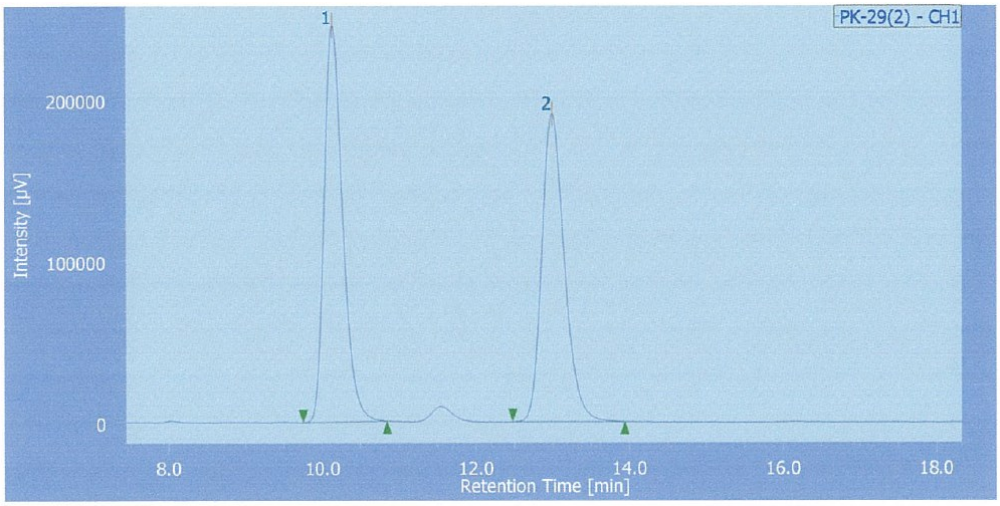
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	13.333	1372605	59670	95.708	96.152	N/A	8287	5.753	1.275	
2	Unknown	1	17.033	61548	2388	4.292	3.848	N/A	9372	N/A	1.122	

(*S*)-2-(1H-indol-2-yl)-1-(thiophene-2-yl)ethanol (3ad):

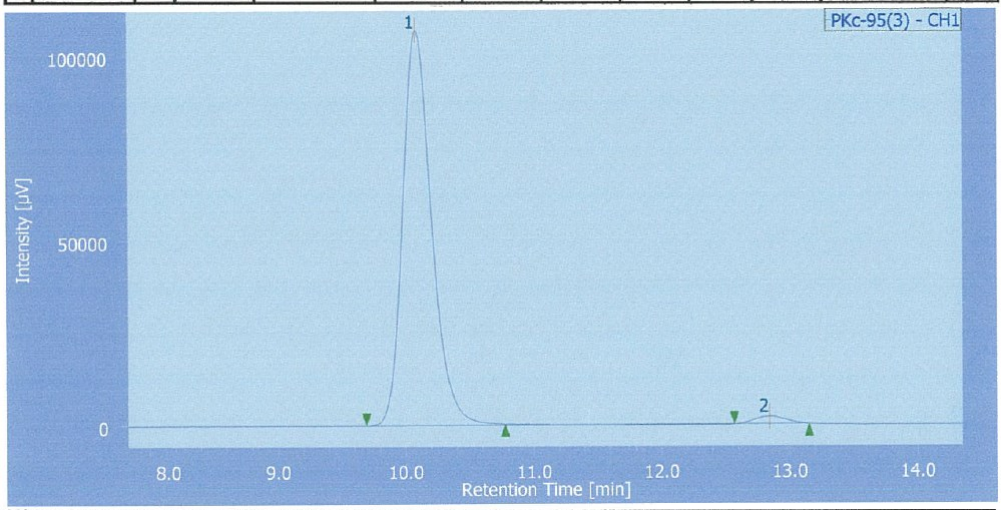


Purified by silica gel column chromatography (EtOAc: Hexane (2:8); white solid; Yield: 98 %;

R_f = 0.16 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3393, 3100, 2369, 1540, 1032, 705 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.5 (brs, 1H), 7.56 (d, *J* = 7.45 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.29 (dd, *J* = 5.16 Hz, 1.15 Hz, 1H), 7.15 (td, *J* = 8.0 Hz, 1.15 Hz, 1H), 3.33-3.25 (m, 2H), 2.43 (d, *J* = 3.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 147.1, 136.1, 135.4, 128.2, 126.8, 125.0, 124.0, 121.4, 119.9, 119.6, 110.6, 101.4, 70.1, 37.9; HRMS (ESI): calcd for $C_{14}H_{13}NOS$ *m/z* 266.0616 $[M+Na]^+$, Found 266.0613. Specific optical rotation $[\alpha]_D^{24}$ = - 25.1 (*c* = 0.73, $CHCl_3$) (96% *ee*); HPLC analysis: (96% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 10.0 min (major), 12.8 min (minor).

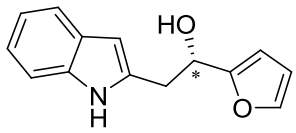


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.133	4049489	245195	51.108	56.275	N/A	9235	6.067	1.293	
2	Unknown	1	12.992	3873896	190511	48.892	43.725	N/A	9873	N/A	1.208	



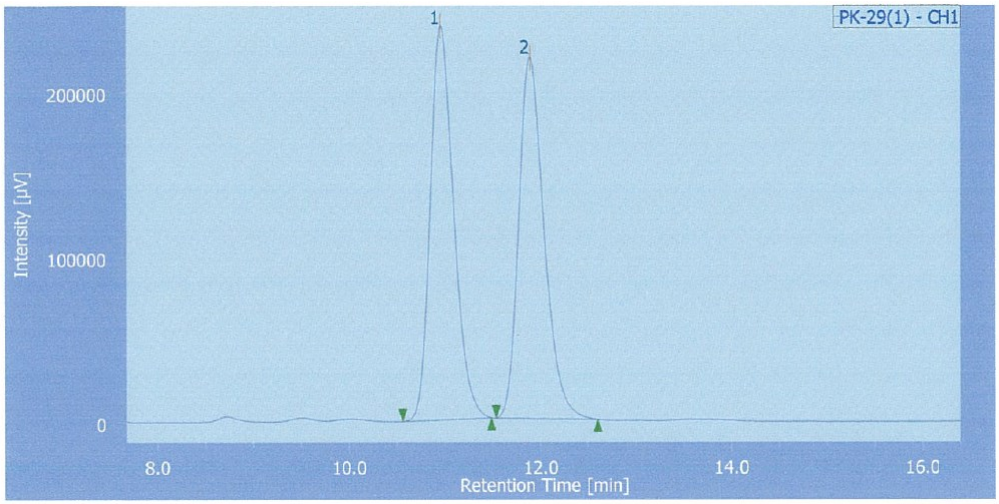
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.083	1666994	106829	98.074	98.217	N/A	10205	6.399	1.213	
2	Unknown	1	12.842	32737	1940	1.926	1.783	N/A	12192	N/A	1.088	

(*S*)-1-(furan-2-yl)-2-(1*H*-indol-2-yl)ethanol (3ae):

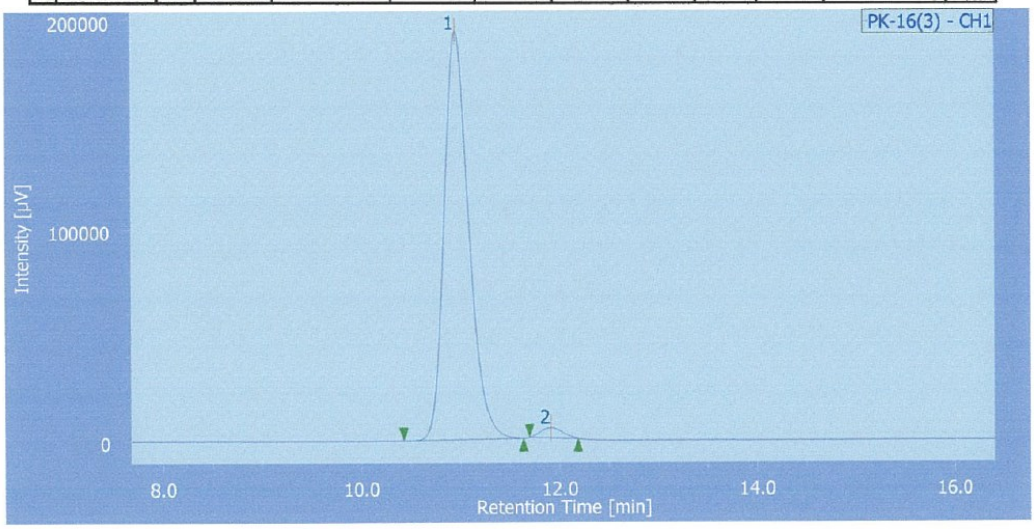


Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 94 %;

R_f = 0.38 (Ethyl acetate: Hexane 4:6); IR (thin film): ν 3408, 2926, 2360, 1507, 1022 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.46 (brs, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 1.72 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H, 7.16-7.13 (m, 1H), 6.36 (m, 1H), 6.32 (d, *J* = 1.1 Hz, 1H), 6.27 (d, *J* = 4.0 Hz, 1H), 5.03-5.0 (m, 1H), 3.31 (d, *J* = 5.7 Hz, 2H), 2.38 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 155.4, 142.1, 136.1, 135.3, 128.2, 121.3, 119.9, 119.6, 110.6, 106.4, 101.2, 67.6, 34.2; HRMS (ESI): calcd for $C_{14}H_{13}NO_2$ *m/z* 250.0844 $[M+Na]^+$, Found 250.833. Specific optical rotation $[\alpha]_D^{24}$ = - 16.96 (*c* = 0.88, $CHCl_3$) (95.77% *ee*); HPLC analysis: (96% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 10.9 min (major), 11.9 min (minor).

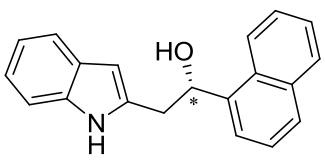


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.958	4043131	238866	49.990	52.199	N/A	9931	2.039	1.218	
2	Unknown	1	11.892	4044740	218738	50.010	47.801	N/A	9905	N/A	1.259	



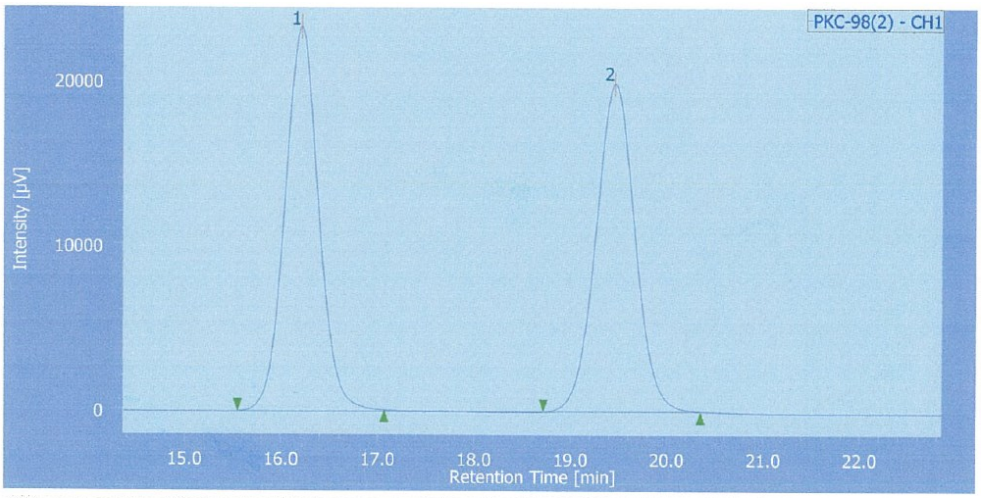
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.950	3326539	193266	97.888	97.616	N/A	9725	2.216	1.228	
2	Unknown	1	11.908	71762	4719	2.112	2.384	N/A	12679	N/A	1.124	

(*S*)-2-(1*H*-indol-2-yl)-1-(napthalen-1-yl)ethanol (3af):

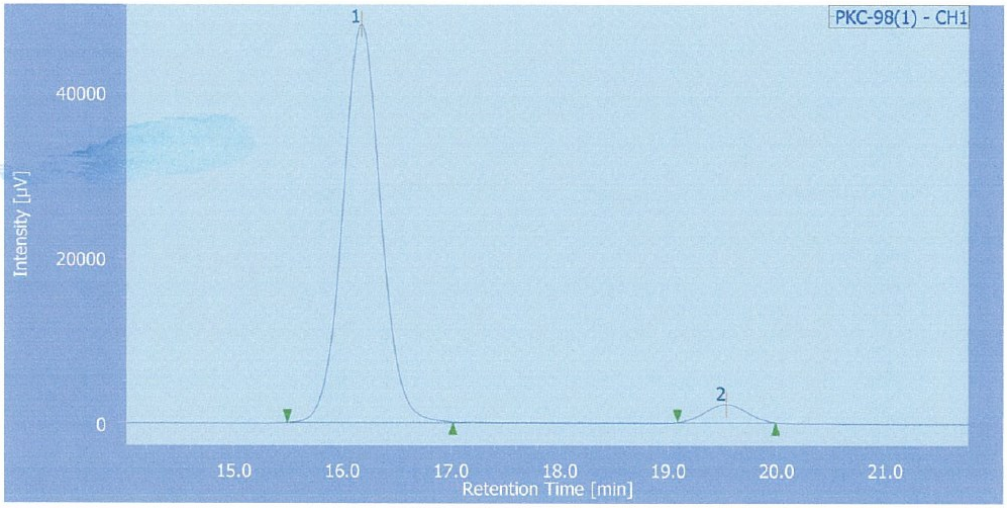


Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 85 %;

R_f = 0.3 (Ethyl acetate: Hexane 3:7); IR (thin film): ν 3440, 3017, 2361, 1540, 1214, 757 cm^{-1}; ^1H NMR (CD_3COCD_3, 500 MHz): δ 10.04 (brs, 1H), 7.91 (s, 1H), 7.86 (m, 3H), 7.59 (dd, *J* = 8.59 Hz, 1.72 Hz, 1H), 7.49-7.44 (m, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 7.45 Hz, 1H), 7.03-7.00 (m, 1H), 6.96-6.93 (m, 1H), 6.22 (s, 1H), 5.27-5.23 (m, 1H), 3.3-3.2 (m, 2H); ^{13}C NMR (CD_3COCD_3, 125 MHz): δ 143.8, 138.0, 134.3, 133.9, 129.8, 128.8, 128.6, 128.5, 126.8, 126.5, 125.3, 125.2, 121.3, 120.3, 119.7, 111.5, 101.2, 74.3, 39.3; HRMS (ESI): calcd for $C_{20}H_{17}NO$ *m/z* 310.1207 $[M+Na]^+$, Found 310.1208. Specific optical rotation $[\alpha]_D^{24}$ = - 5.9 (*c* = 0.39, CH_3CN) (91% *ee*); HPLC analysis: (91% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 16.1 min (major), 19.5 min (minor).

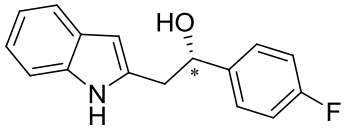


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	16.208	567493	23343	50.256	53.996	N/A	10672	4.778	1.061	
2	Unknown	1	19.458	561712	19888	49.744	46.004	N/A	11172	N/A	1.033	



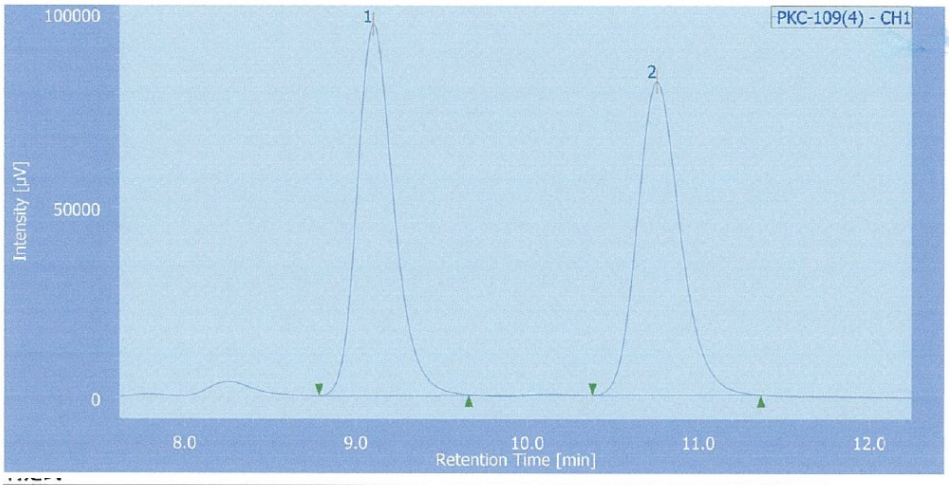
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	16.175	1175367	48099	95.322	95.653	N/A	10441	4.977	1.053	
2	Unknown	1	19.533	57677	2186	4.678	4.347	N/A	11780	N/A	0.999	

(*S*)-1-(4-Fluorophenyl)-2-(1*H*-indol-2-yl)ethanol (3ag):

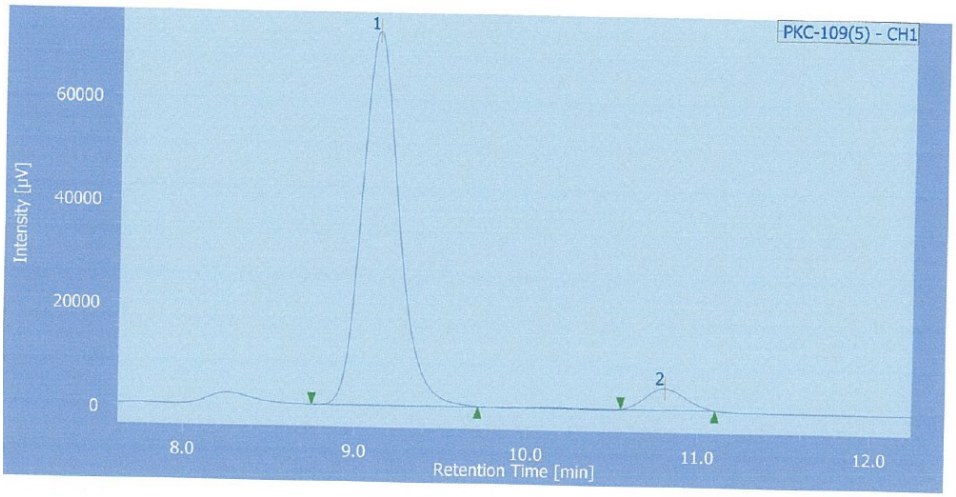


Purified by silica gel column chromatography (EtOAc: Hexane 2:8); Solid; Yield: 97 %;

R_f = 0.29 (Ethyl acetate: Hexane 3:7); IR (thin film): ν 3399, 3021, 2365, 1540, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.47 (brs, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.36-7.32 (m, 3H), 7.18-7.14 (m, 1H), 7.11-7.03 (m, 3H), 6.28 (s, 1H), 4.98 (t, *J* = 6.3 Hz, 1H), 3.14-3.13 (m, 2H), 2.25 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.3, 161.3, ($^1J_{CF}$ 243.5 Hz), 139.33, 139.31 ($^4J_{CF}$, 3.59 Hz), 136.1, 135.8, 128.3, 127.38, 127.32 ($^3J_{CF}$, 8.4), 121.4, 119.9, 119.6, 115.55 ($^2J_{CF}$ 21.5), 110.5, 101.2, 73.6, 37.9; HRMS (ESI): calcd for $C_{16}H_{14}NOF$ *m/z* 278.0957 $[M+Na]^+$, Found 278.0960. Specific optical rotation $[\alpha]_D^{24}$ = - 43.4 (*c* = 0.8, $CHCl_3$) (89% *ee*); HPLC analysis: (89% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 9.1 min (major), 10.8 min (minor).

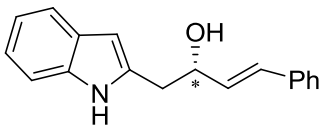


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	9.100	1449767	97649	50.206	54.238	N/A	9098	3.989	1.265	
2	Unknown	1	10.758	1437859	82388	49.794	45.762	N/A	9065	N/A	1.201	

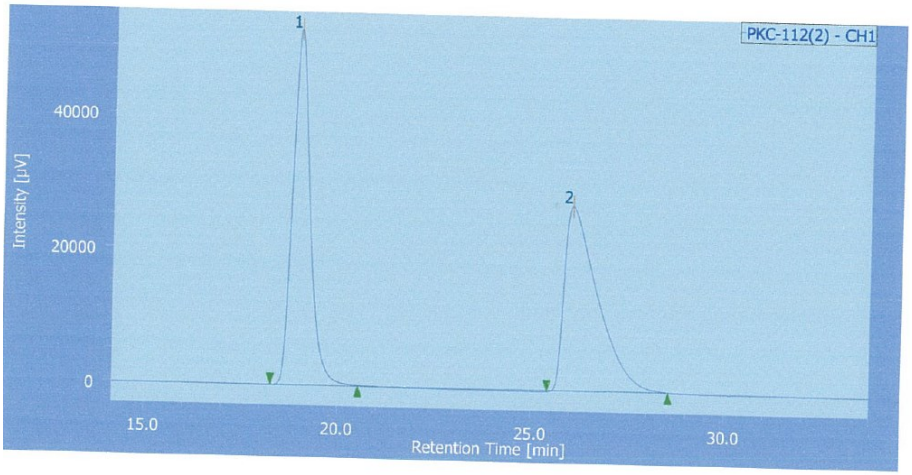


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	9.125	1079265	72255	94.313	94.619	N/A	9062	4.133	1.231	
2	Unknown	1	10.808	65079	4109	5.687	5.381	N/A	9953	N/A	1.074	

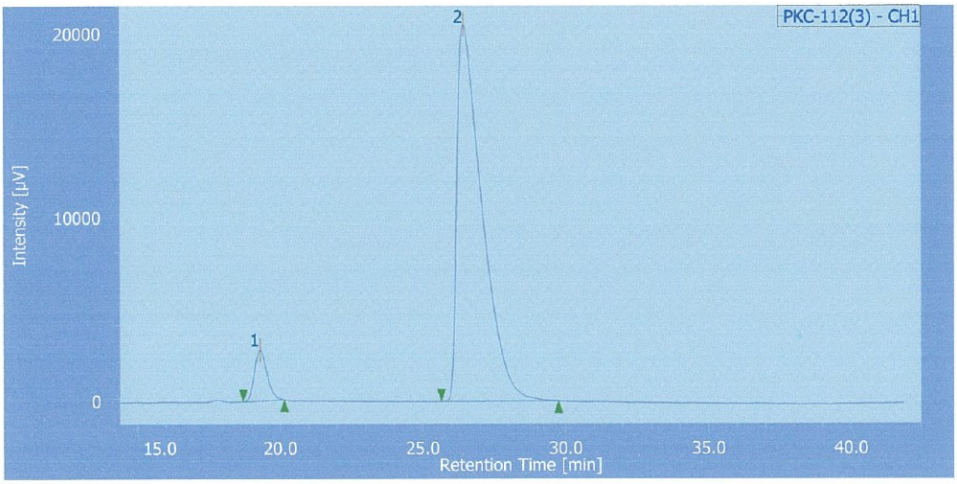
(*S*)-(*E*)-1-(1*H*-indol-2-yl)-4-phenylbut-3-en-2-ol (3aj):



Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 97 %; R_f = 0.3 (Ethyl acetate: Hexane 3:7); IR (thin film): ν 3412, 3021, 2369, 1716, 1455, 970, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.59 (brs, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.39-7.26 (m, 6H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 16 Hz, 1H), 6.33 (m, 1H), 6.30 (dd, *J* = 16 Hz, 6.87 Hz, 1H), 4.61- 4.64 (m, 1H), 3.15 (dd, *J* = 14.9, 3.4 Hz, 1H), 3.04 (dd, *J* = 14.9 Hz, 8.0 Hz, 1H), 2.05 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.2, 136.1, 135.8, 131.2, 130.8, 128.6, 128.3, 127.9, 126.5, 121.3, 119.9, 119.6, 110.6, 101,19, 72.8, 35.9; HRMS (ESI): calcd for $C_{18}H_{17}NO$ *m/z* 286.12078 $[M+Na]^+$, Found 286.1209. Specific optical rotation $[\alpha]_D^{24}$ = - 31.3 (*c* = 0.36, $CHCl_3$) (87% *ee*); HPLC analysis: (87% *ee*); (Column –Chiralpak IB; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 19.3 min (major), 26.4 min (minor).

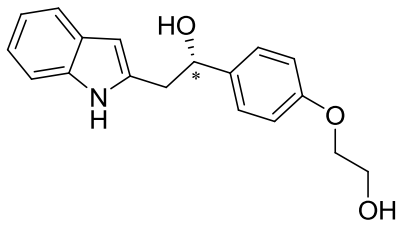


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	18.933	1668874	52823	50.405	65.873	N/A	8732	6.013	1.505	
2	Unknown	1	26.025	1642031	27366	49.595	34.127	N/A	4483	N/A	2.757	



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	19.300	84501	2779	6.366	11.948	N/A	9522	6.072	1.241	
2	Unknown	1	26.433	1242863	20483	93.634	88.052	N/A	4567	N/A	2.520	

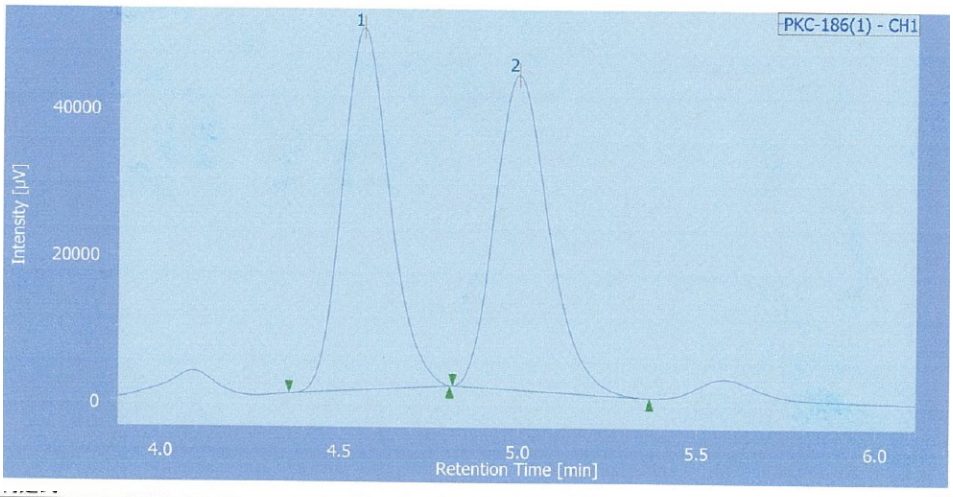
(*S*)-1-(4-(2-hydroxyethoxy)phenyl)-2-(1*H*-indol-2-yl)ethanol (3ai):



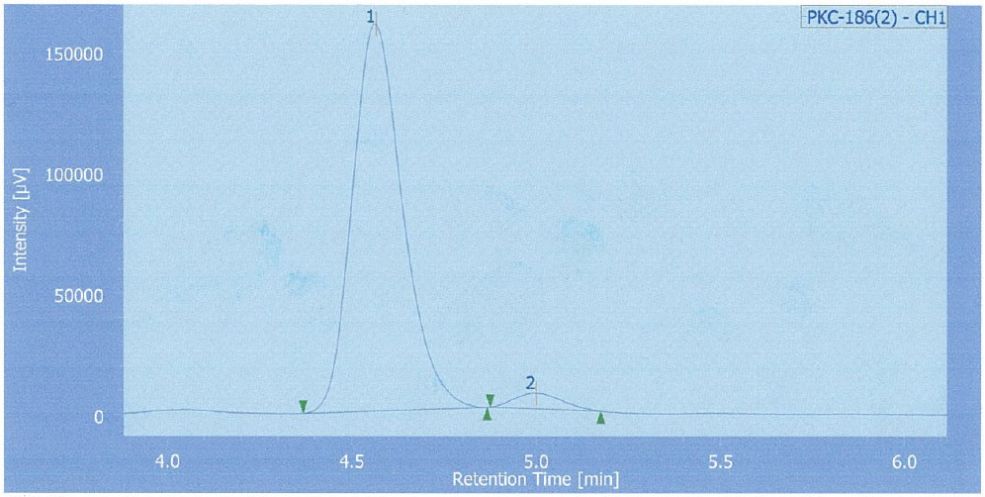
The procedure for the synthesis of this molecule is as same as the general procedure mentioned above (Condition A), but the solvent used for the reaction is (Dioxane: HMPA (10:1)) and stirred the reaction for 5h at rt.

Purified by silica gel column chromatography (Acetone: Hexane 3:7); white solid; Yield: 85 %; R_f = 0.21 (Acetone: Hexane 1:1); IR (thin film): ν 3410, 3017, 2369, 1540, 1215, 757 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz): δ 7.36 (d, *J* = 8.0 Hz, 1H), 7.25-7.22 (m, 3H), 6.97 (td, *J* = 7.2 Hz, 1.4 Hz, 1H), 6.92-6.83 (m, 3H), 6.07 (s, 1H), 4.93 (t, *J* = 6.3 Hz, 1H), 3.97 (t, *J* = 4.5 Hz, 2H), 3.19-3.13 (m, 1H), 3.08-3.03 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz): δ 159.8, 138.2, 137.9, 137.7, 130.2, 128.4, 121.5, 120.5, 119.9, 115.4, 111.6, 101.3, 74.7, 70.6, 61.8, 39.4; HRMS (ESI): calcd for $C_{18}H_{19}NO_3$ *m/z* 320.1263 $[M+Na]^+$, Found 320.1263. Specific optical rotation $[\alpha]_D^{24}$ = - 29.9 (*c* = 0.88, $CHCl_3$) (93% *ee*); HPLCanalysis: (93%

ee); (Column –Chiralpak IA; Hexane/2-propanol = 1/2, flow rate 1.0 mL/min, detection at 254 nm), t_r = 4.5 min (major), 5.0 min (minor).

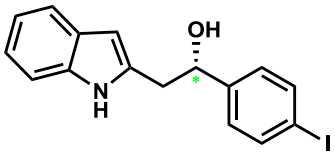


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	4.567	458615	49310	50.425	53.467	N/A	5612	1.676	1.176	
2	Unknown	1	5.000	450881	42915	49.575	46.533	N/A	5299	N/A	1.245	

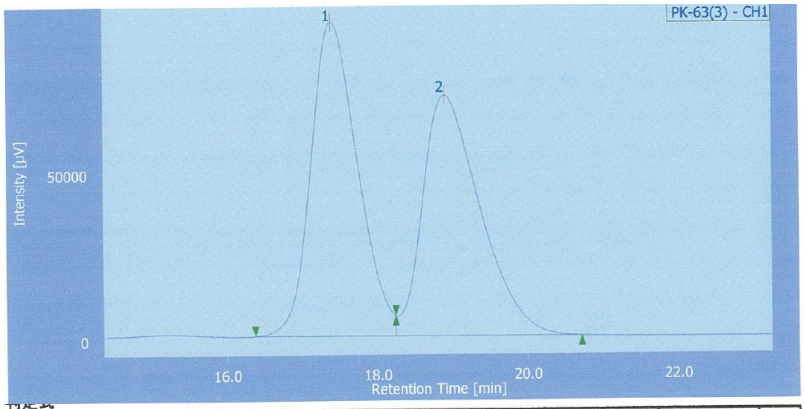


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	4.567	1517632	159744	96.347	96.133	N/A	5461	1.757	1.198	
2	Unknown	1	5.000	57536	6426	3.653	3.867	N/A	6531	N/A	1.179	

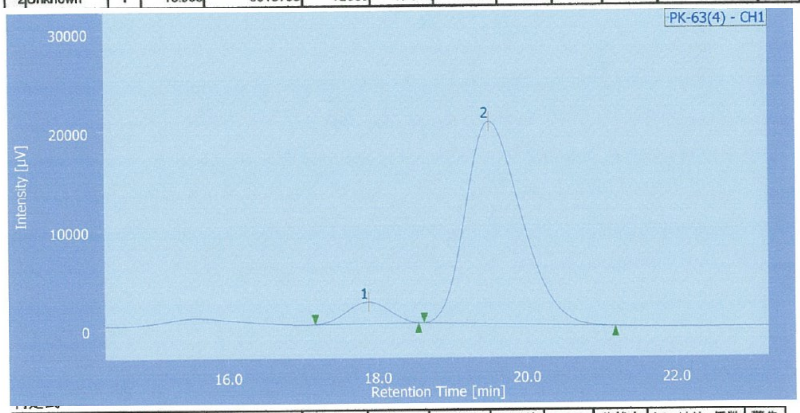
(*S*)-2-(1H-indol-2-yl)-1-(4-iodophenyl)ethanol (3ah):



Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); White solid; Yield: 79%; R_f = 0.25 (EtOAc: Hexane 3:7); IR (thin film): ν 3440, 3019, 2359, 1621, 1215, 756; ^{1}H NMR (CD_3COCD_3, 500 MHz): δ 9.95 (brs, 1H), 7.67 (d, *J* = 8 Hz, 2H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.18 (s, 1H), 5.07-5.04 (m, 1H), 4.68 (s, 1H), 3.17-3.10 (m, 2H); ^{13}C NMR (CD_3COCD_3, 125 MHz): δ 146.2, 138, 137.59, 137.54, 129.7, 129.1, 121.1, 121.3, 120.3, 119.7, 111.6, 101.4, 92.7, 73.7, 39.3; HRMS (ESI): calcd for $C_{16}H_{14}IN_1O_1$ *m/z* 386.0018 $[M+Na]^+$, Found 386.0040; Specific optical rotation $[\alpha]_D^{20}$ = -18 (*c* = 1.08, $CHCl_3$) (for 85% *ee*); HPLC analysis: (85% *ee*): (Column –Chiralcel OD-H; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 17.8 min (minor), 19.5 min (major).



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	17.400	4047975	94084	51.490	56.625	N/A	3753	1.193	N/A	
2	Unknown	1	18.900	3813709	72069	48.510	43.375	N/A	2978	N/A	N/A	

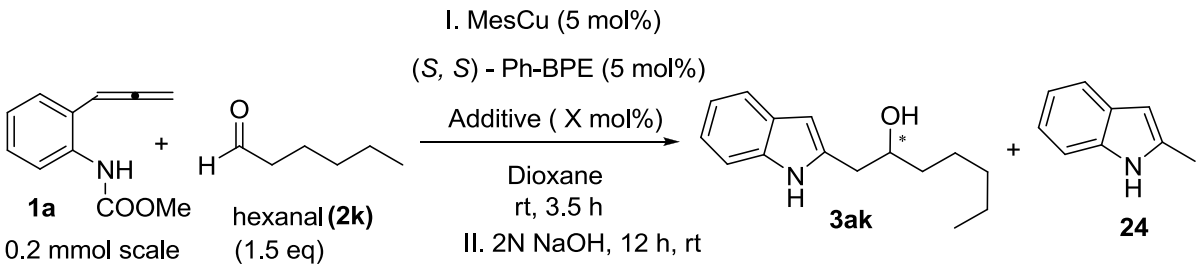


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	17.883	86024	2183	7.551	9.662	N/A	4340	1.328	0.981	
2	Unknown	1	19.508	1053143	20408	92.449	90.338	N/A	3254	N/A	1.265	

6. Reactions of allenyl anilides with aliphatic aldehydes: Screening of additives

Due to the lower electrophilicity (low reactivity) of aliphatic aldehydes, allylation proceeded to procure desired product only in low to moderate yield. To improve the yield, we envisioned that adding additional Lewis acids could enhance the electrophilicity of the aliphatic aldehyde and could accelerate the rate of the reaction. We also speculated that these additives could improve the turnover of the Cu-catalyst. Considering these aspects, we examined additive effect in the reaction of an aliphatic aldehyde (hexanal)(**2k**) and allenylanilide (**1a**). It was found that magnesium isopropoxide profoundly accelerated the rate of the reaction, resulting the desired product in good yield.

Screening of Additives:



Experimental procedure: A flame-dried 20 mL test tube equipped with magnetic stirring bar and a

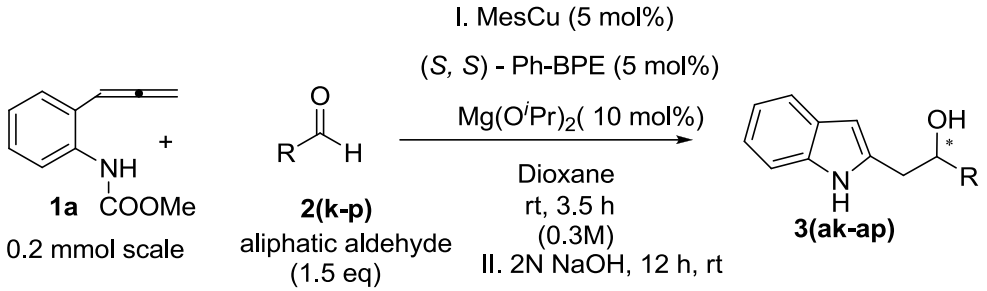
3-way glass stopcock was charged with mesitylcopper (1.8 mg, 0.01 mmol, 5 mol%), additive (5-10 mol%) and (*S, S*)-PhBPE (5.1 mg, 0.01 mmol, 5 mol%) under argon atmosphere. Anhydrous dioxane (480 μL) was added, and the mixture was stirred at ambient temperature for 20 minutes. To the stirred solution, hexanal (2k) (0.3mmol) and 1.1 M solution of allenylanilide (**1a**) (38 mg, 181 μL, 0.2 mmol) in dioxane were added sequentially. After stirring for 3.5 h at room temperature, the reaction was diluted with dioxane (2.5 mL) and quenched with 2N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 12 h, and products were extracted with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compound (**3ak**).

The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (*S, S*)-Ph-BPE.

Entry	Additive (X mol%)	Yield (%)[a]	*ee* (%)[b]	Yield **(bb)**(%)[a]
0	-	9	94	83
1	$Al(O^tBu)_3$ (5 mol%)	30	94	60
2	$Zr(O^iPr)_4$ (5 mol%)	46	94	50
3	$Ba(O^iPr)_2$ (5 mol%)	14	94	75
4	$Y(O^iPr)_2$ (5 mol%)	27	95	62
5	$La(O^iPr)_3$ (5 mol%)	50	95	42
6	$Yb(O^iPr)_3$ (5 mol%)	53	94	41
7	$Sm(O^iPr)_3$ (5 mol%)	45	94	51
8	**$Mg(O^iPr)_2$ (5 mol%)**	**58**	**94**	34
9	**$Mg(O^iPr)_2$ (10 mol%)**	**75**	**92**	22
10	**$Mg(O^iPr)_2$ (20 mol%)**	**78**	**92**	20
[c]11	$Mg(O^iPr)_2$ (10 mol%)	-	-	-
12	$Mg(OEt)_2$ (5 mol%)	60	91	33

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis. [c]The reaction was performed without MesCu and observed no reaction.

7. General procedure for the reaction of allenyl anilides with aliphatic aldehydes:



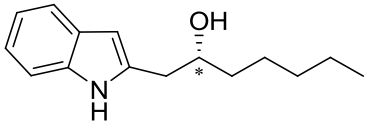
General procedure (Condition B):

A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (1.8 mg, 0.01 mmol, 5 mol%), magnesium isopropoxide (2.8 mg, 0.02 mmol, 10 mol%) and (*S, S*)-PhBPE (5.1 mg, 0.01 mmol, 5 mol%) under an argon atmosphere. Anhydrous dioxane (480 μL) was added, and the mixture was stirred at ambient temperature for 20 minutes. To the stirred solution, aliphatic aldehyde (0.3 mmol) and 1.1 M solution of allenylanilide (**1a**) (37.8 mg, 181 μL, 0.2 mmol) in dioxane were added sequentially. After stirring for 3.5 h at room temperature, the reaction was diluted with dioxane (2.5 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 12 h, and products were extracted with ethyl acetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compound.

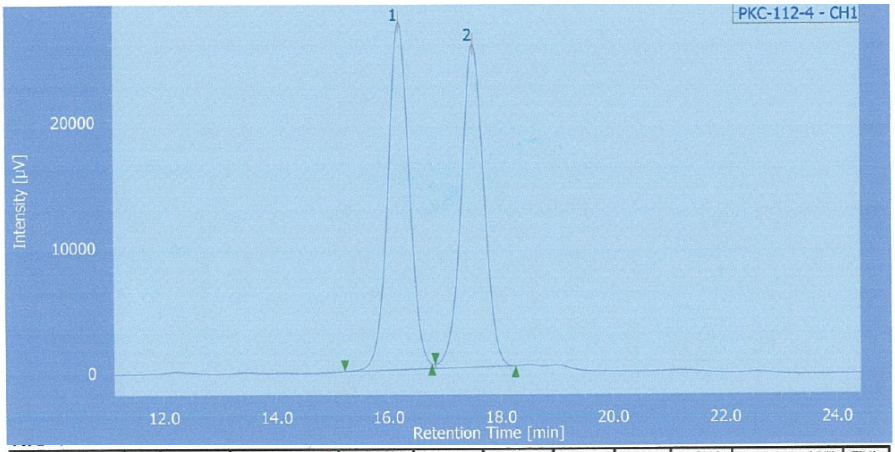
The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (*S, S*)-Ph-BPE.

The absolute configuration of all the secondary alcohols (**3ak-3ap**) were assigned based on analogy of **3aa** (see page S48-S51)

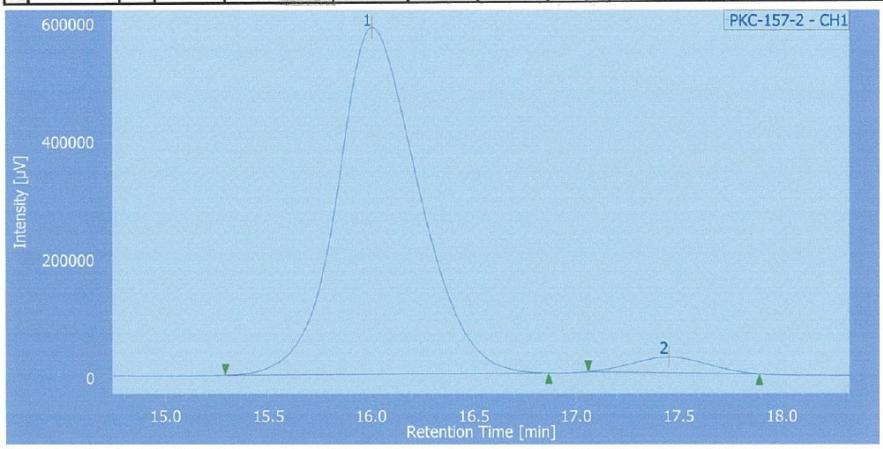
(*S*)-1-(1H-indol-2-yl)heptan-2-ol (3ak):



Purified by silica gel column chromatography (EtOAc: Hexane 2:8); yellow liquid; Yield: 73 %; R_f = 0.2 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3456, 3408, 3019, 2399, 1214cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.55 (brs, 1H), 7.55 (d, *J* = 8.02 Hz, 1H), 7.32 (d, *J* = 8.02 hz, 1H), 7.15-7.12 (m, 1H), 7.10-7.06 (m, 1H), 6.28 (s, 1H), 3.97-3.92 (m, 1H), 3.02-2.98 (dd, *J* = 14.89 Hz, 2.86 Hz, 1H), 2.81 (dd, *J* = 15.47 Hz, 8.02 Hz, 1H), 1.81 (brs, 1H), 1.55-1.26 (m, 8H), 0.9 (t, *J* = 6.87 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ136.6, 136.1, 128.4, 121.1, 119.8, 119.5, 110.5, 100.8, 71.8, 37.0, 35.5, 31.7, 25.3, 22.5, 14.0; HRMS (ESI): calcd for $C_{15}H_{21}NO$ *m/z* 254.1521 $[M+Na]^+$, Found 254.1509. Specific optical rotation $[\alpha]_D^{24}$ = - 15.0 (*c* = 0.48, $CHCl_3$) (92% *ee*); HPLC analysis: (92% *ee*); (Column – Chiralpak IA; Hexane/2-propanol = 20/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 16.0 min (major), 17.4 min (minor).

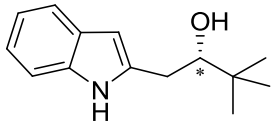


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	16.200	731755	27688	50.421	51.822	N/A	8987	1.873	0.976	
2	Unknown	1	17.517	719549	25740	49.579	48.178	N/A	9312	N/A	0.959	



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	16.008	16221882	587461	96.115	95.737	N/A	8173	2.062	1.130	
2	Unknown	1	17.450	655615	26162	3.885	4.263	N/A	10114	N/A	1.047	

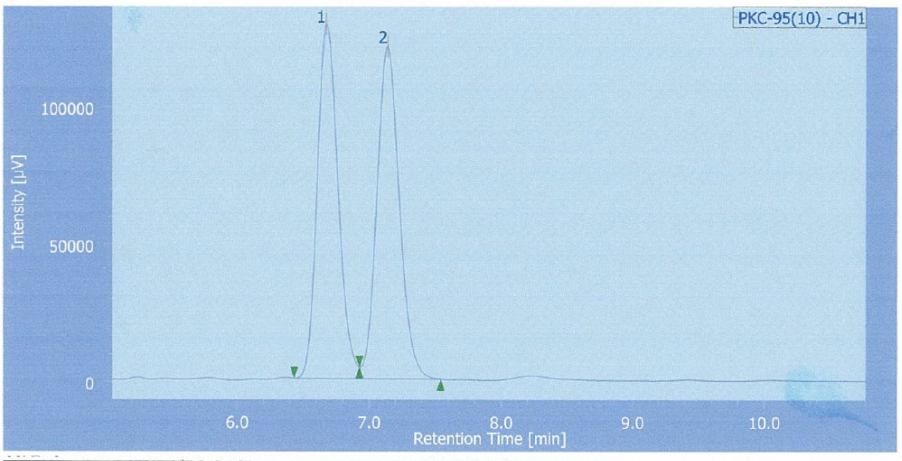
(*S*)-1-(1*H*-indol-2-yl)-3,3-dimethylbutan-2-ol (3al):



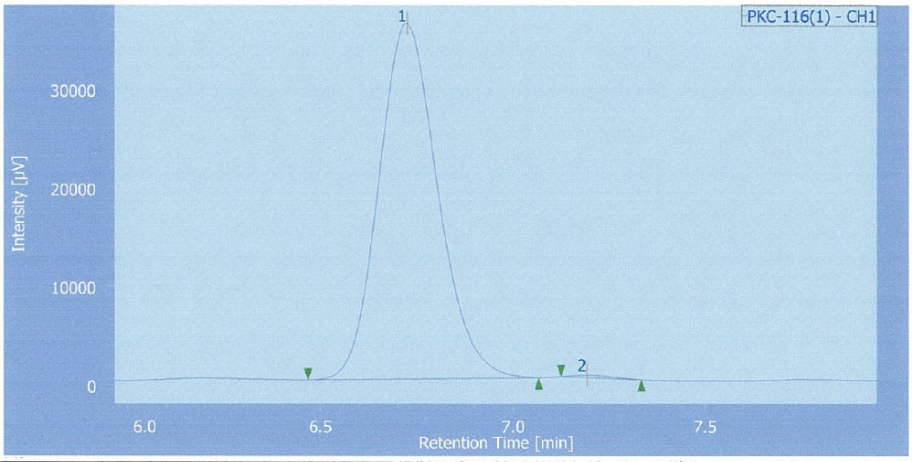
Purified by silica gel column chromatography (EtOAc: Hexane 1:9); white solid;

(Yield, *ee*) : (75%, 99%) [Reaction carried out without additive]

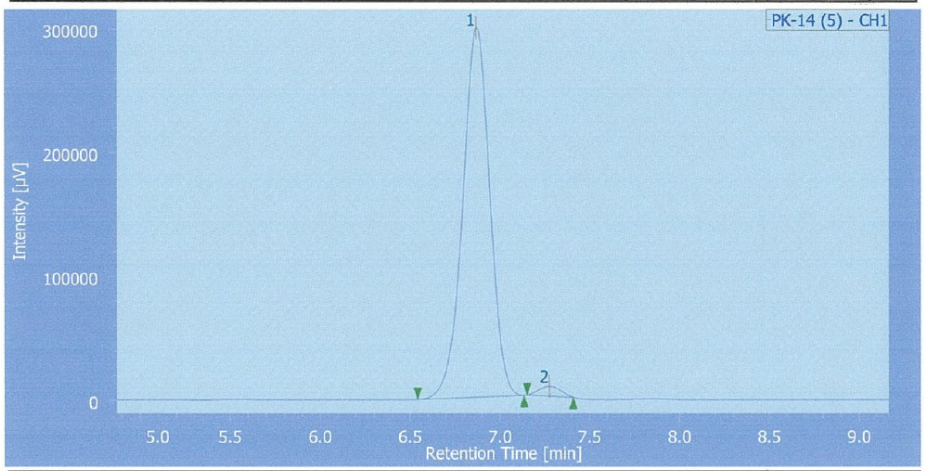
(Yield, *ee*): (95%, 96%) [Reaction carried out with additive $Mg(O^iPr)_2$ (10 mol%)] R_f = 0.35 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3417, 2960, 2369 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 8.61 (brs, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.15-7.12 (m, 1H), 7.10-7.07(m, 1H), 6.29 (s, 1H), 3.56-3.53(m, 1H), 3.01(d, *J* = 14.9 Hz, 1H), 2.72 (dd, *J* = 14.9 Hz, 10.3 Hz, 1H), 1.89 (d, *J* = 4 Hz, 1H), 1.0 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 137.9, 136.0, 128.4, 121.1, 119.7, 119.5, 110.4, 100.2, 79.8, 34.9, 30.4, 25.5; HRMS (ESI): calcd for $C_{14}H_{19}NO$ *m/z* 240.1364 $[M+Na]^+$, Found 240.1352. Specific optical rotation $[\alpha]_D^{24}$ = - 32.6 (*c* = 0.63, $CHCl_3$) (99% *ee*); HPLC analysis: (99% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 6.7 min (major), 7.1 min (minor).



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	6.675	1408709	128896	49.584	51.612	N/A	8654	1.570	1.205	
2	Unknown	1	7.142	1432325	120843	50.416	48.388	N/A	8554	N/A	1.102	

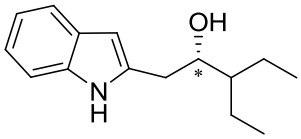


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	6.725	383455	36075	99.540	99.325	N/A	9382	1.947	1.132	
2	Unknown	1	7.192	1772	245	0.460	0.675	N/A	20117	N/A	1.493	



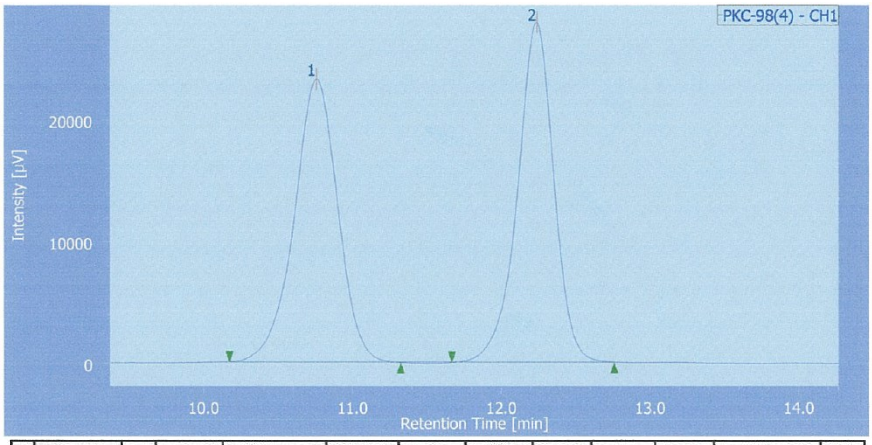
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	6.867	3129503	298250	97.941	97.454	N/A	10123	1.599	0.970	
2	Unknown	1	7.275	65798	7791	2.059	2.546	N/A	14820	N/A	1.035	

(*S*)-3-ethyl-1-(1*H*-indol-2-yl)pentan-2-ol (3am):

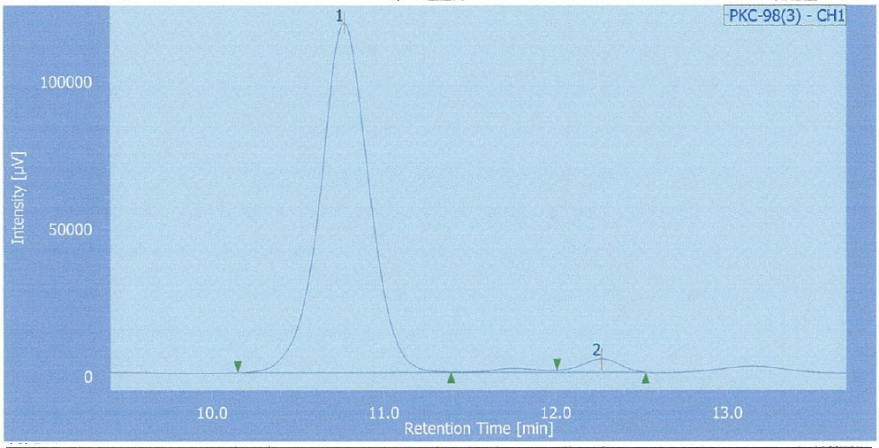


Purified by silica gel column chromatography (EtOAc: Hexane 1:9); yellow liquid; Yield: 89 %; R_f = 0.28 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3403, 2962, 2874, 2365, 1685, 1457, 1289, 1014 cm^{-1}; ^1H NMR

($CDCl_3$, 500 MHz): δ 8.61 (brs, 1H), 7.14 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.08 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 6.29 (s, 1H), 3.95-3.92 (m, 1H), 2.95 (dd, *J* = 15.1 Hz, 2.2 Hz, 1H), 2.86 (dd, *J* = 15.1Hz, 9 Hz, 1H), 1.7 (brs, 1H), 1.55-1.49(m, 2H), 1.46-1.31(m, 3H), 0.96-0.93(m, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 137.4, 136.0, 128.4, 121.1, 119.7, 119.5, 110.5, 100.5, 73.3, 46.3, 32.6, 21.7, 11.4; HRMS (ESI): calcd for $C_{14}H_{19}NO$ *m/z* 254.1521 $[M+Na]^+$, Found 240.1508. Specific optical rotation $[\alpha]_D^{24}$ = - 40.5 (*c* = 1.76, $CHCl_3$) (94% *ee*); HPLC analysis: (94% *ee*); (Column –Chiralpak IA; Hexane/Ethanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 10.7 min (major), 12.2 min (minor).

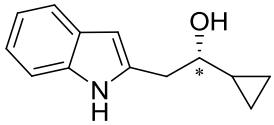


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.758	472843	23231	49.937	45.423	N/A	6781	3.123	0.940	
2	Unknown	1	12.242	474028	27913	50.063	54.577	N/A	12969	N/A	0.906	



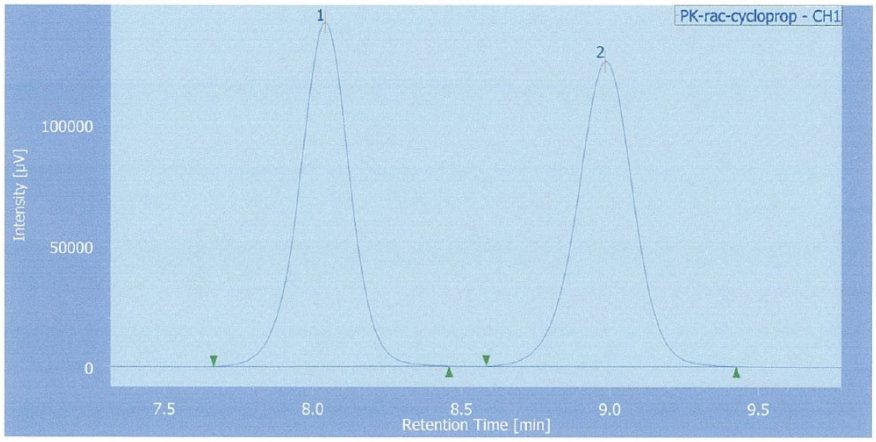
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.775	2339706	118499	97.102	96.371	N/A	7343	3.259	0.977	
2	Unknown	1	12.267	69826	4463	2.898	3.629	N/A	13991	N/A	N/A	

(*S*)-1-cyclopropyl-2-(1*H*-indol-2-yl)ethanol (3an):

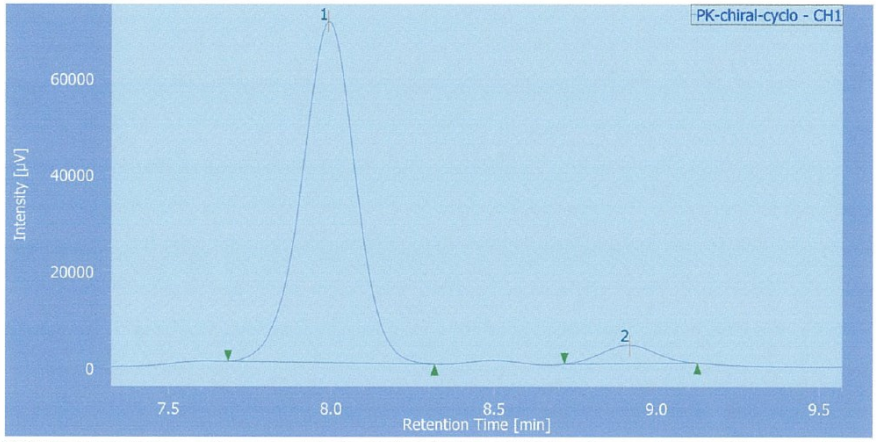


Purified by silica gel column chromatography (EtOAc: Hexane 2:8); colorless liquid; Yield: 95 %; R_f = 0.34 (Ethyl acetate: Hexane 4:6); IR (thin film): ν 3408, 3006, 2900, 2369, 1456, 1027, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.69 (brs, 1H), 8.56 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 3.19-3.12 (m, 2H), 3.02-2.97 (dd, *J* = 14.8, 7.5 Hz, 1H), 1.98 (brs, 1H), 1.02-0.96 (m, 1H), 0.62-0.52 (m, 2H), 0.37-0.32 (m, 1H), 0.3-0.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.8, 136.0, 128.3, 121.0, 119.7, 119.4, 110.5, 100.6, 35.0, 17.4, 3.1, 2.7; HRMS (ESI): calcd for $C_{13}H_{15}NO$ *m/z* 224.1051 $[M+Na]^+$, Found 224.1040. Specific optical rotation

$[\alpha]_D^{21}$ = + 3.1 (*c* = 1.45, $CHCl_3$) (90% *ee*); HPLC analysis: (90% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 8.0 min (major), 8.9 min (minor).

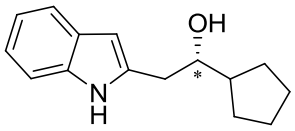


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.042	1694186	142241	50.026	53.004	N/A	11101	2.904	0.963	
2	Unknown	1	8.983	1692457	126117	49.974	46.996	N/A	10848	N/A	0.970	

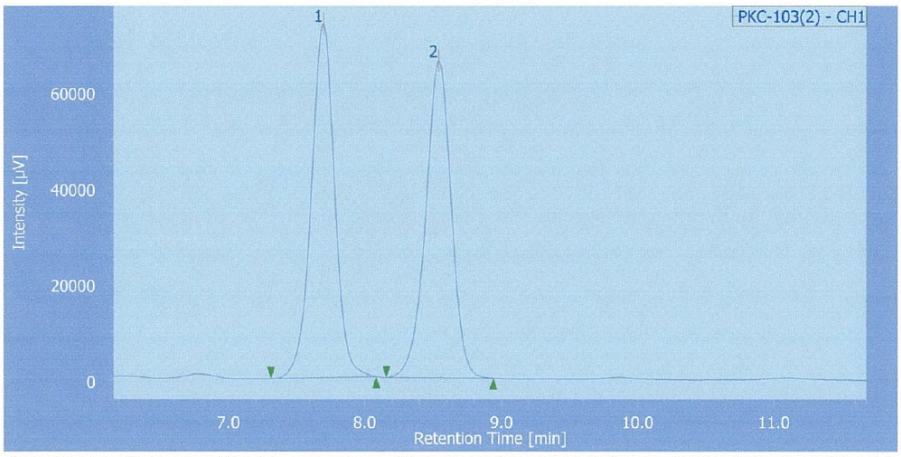


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.992	818660	70623	94.888	94.855	N/A	11314	3.024	0.973	
2	Unknown	1	8.917	44103	3831	5.112	5.145	N/A	12994	N/A	1.016	

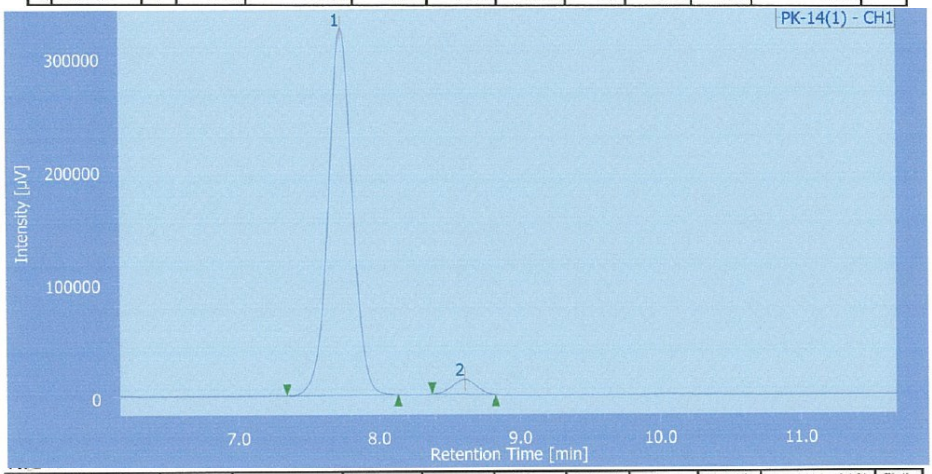
(*S*)-1-cyclopentyl-2-(1*H*-indol-2-yl)ethanol (3ap):



Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 82 %; R_f = 0.21 (Ethyl acetate: Hexane 2:8); IR (thin film): ν3400, 2369, 1540, 1215, 760cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.64 (brs, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.14 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.08 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 6.28 (s, 1H), 3.73-3.70 (m, 1H), 3.05 (dd, *J* = 15.1 Hz, 2.9 Hz, 1H), 2.83 (dd, *J* = 15.3 Hz, 8.0 Hz, 1H), 1.94-1.76 (m, 4H), 1.69-1.53 (m, 4H), 1.41-1.35 (m, 1H), 1.29-1.23 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.9, 136.0, 128.3, 121.0, 119.7, 119.4, 110.5, 100.7, 76.3, 45.6, 34.4, 29.1, 25.5; HRMS (ESI): calcd for $C_{15}H_{19}NO$ *m/z* 252.1364 $[M+Na]^+$, Found 252.1354; Specific optical rotation $[\alpha]_D^{24}$ = - 13.0 (*c* = 0.52, $CHCl_3$) (92% *ee*); HPLC analysis: (92% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 7.7 min (major), 8.6 min (minor).

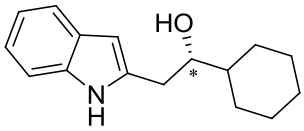


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.700	875684	73764	50.436	52.771	N/A	10371	2.643	0.955	
2	Unknown	1	8.542	860557	66017	49.564	47.229	N/A	10326	N/A	0.948	

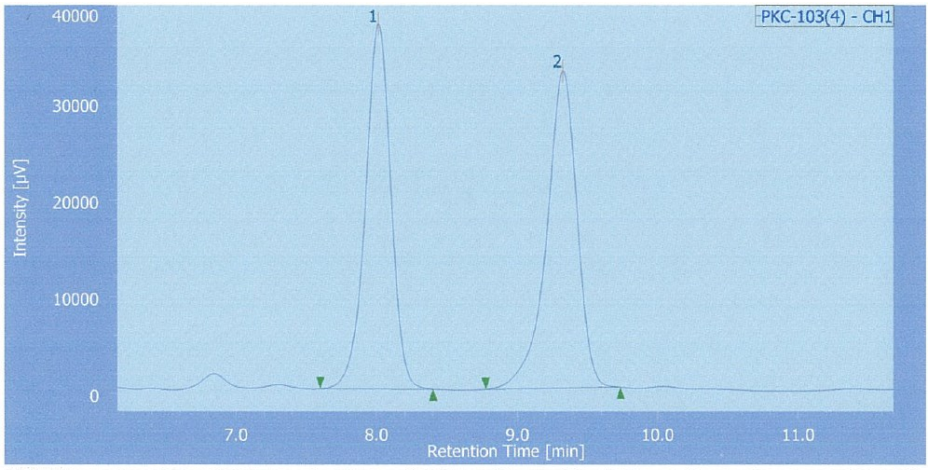


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.733	3829823	324494	96.026	96.100	N/A	10381	2.797	0.959	
2	Unknown	1	8.608	158500	13170	3.974	3.900	N/A	11313	N/A	0.951	

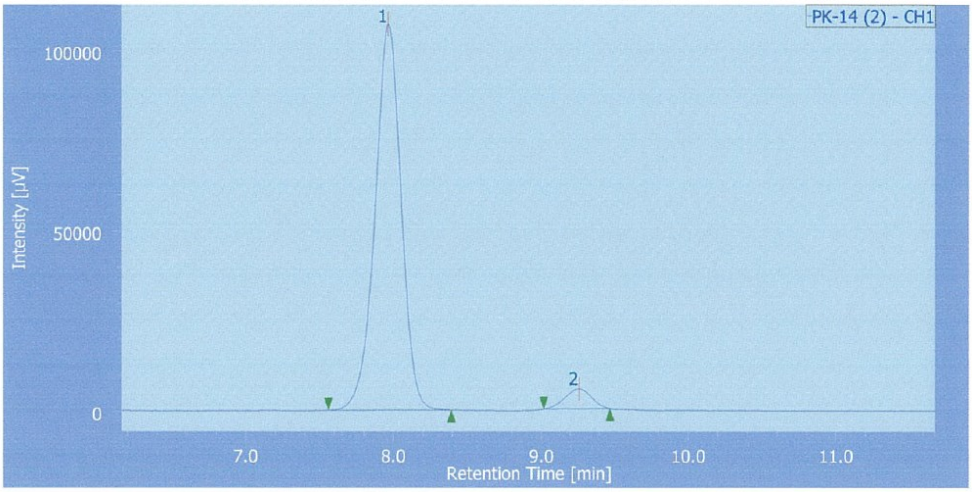
(*S*)-1-cyclohexyl-2-(1*H*-indol-2-yl)ethanol (3ao):



Purified by silica gel column chromatography (EtOAc: Hexane 2:8); white solid; Yield: 89%; R_f = 0.24 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3300, 2921, 2369, 1540, 1025cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.62 (brs, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.14 (td, *J* = 7.4 Hz, 1.2 Hz, 1H), 7.09 (td, *J* = 7.4 Hz, 1.2 Hz, 1H), 6.28 (s, 1H), 3.66 (m, 1H), 3.0 (dd, *J* = 15.2 Hz, 2.9 Hz, 1H), 2.85 (dd, *J* = 15.2 Hz, 8.6 Hz, 1H), 1.92-1.86 (m, 2H), 1.82-1.76 (m, 3H), 1.71-1.68 (m, 1H), 1.44-1.37 (m, 1H), 1.30-1.14 (m, 3H), 1.13-1.02 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 137.2, 136.0, 128.4, 121.0, 119.7, 119.4, 110.5, 100.6, 76.17, 43.0, 32.6, 29.0, 26.3, 25.9; HRMS (ESI): calcd for $C_{16}H_{21}NO$ *m/z* 266.1521 $[M+Na]^+$, Found 266.1515; Specific optical rotation $[\alpha]_D^{21}$ = - 18.6 (*c* = 0.79, $CHCl_3$)(90% *ee*); HPLC analysis: (90% *ee*): (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 7.9 min (major), 9.2 min (minor)



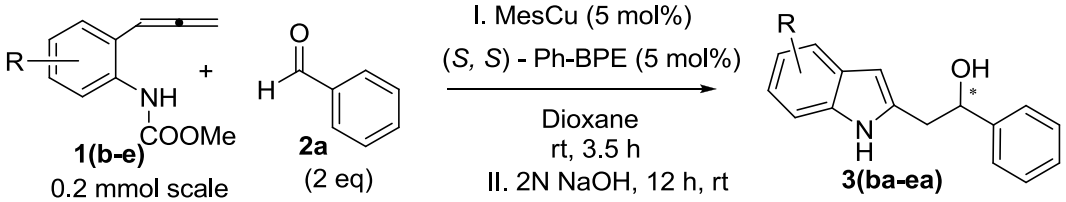
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.017	473036	37744	49.052	53.538	N/A	9925	3.767	0.929	
2	Unknown	1	9.325	491330	32755	50.948	46.462	N/A	9911	N/A	0.847	



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.967	1316898	106950	95.044	95.130	N/A	10131	3.943	0.946	
2	Unknown	1	9.258	68666	5475	4.956	4.870	N/A	11846	N/A	0.930	

8. Allenyl anilide substrate scope: Reactions of various allenyl anilides with aromatic aldehydes

The reaction of aromatic aldehyde and alleneylanilides having different electron donating or electron withdrawing substituents on the aromatic ring were examined under conditions A and B. The results obtained are shown below.

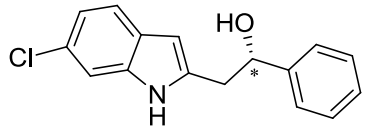


Condition A: Without additive

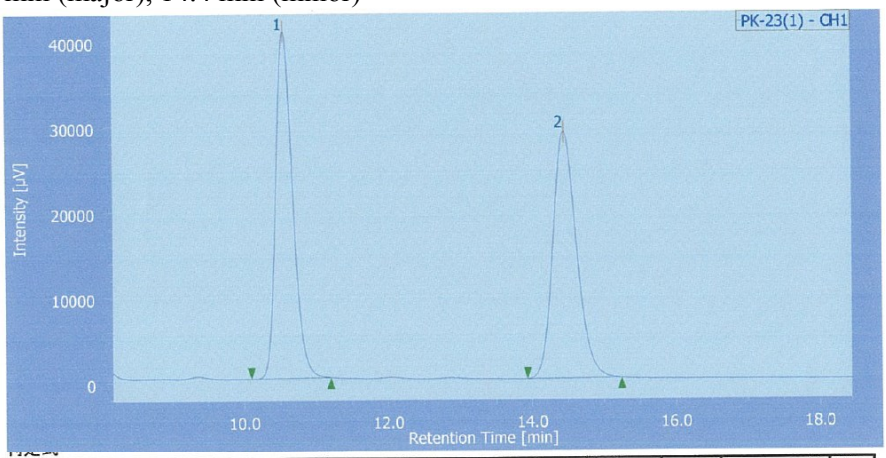
Condition B: With additive ($Mg(O^iPr)_2$(10 mol%)

The absolute configuration of all the secondary alcohols were assigned based on analogy of **3aa** (see page S48-S51)

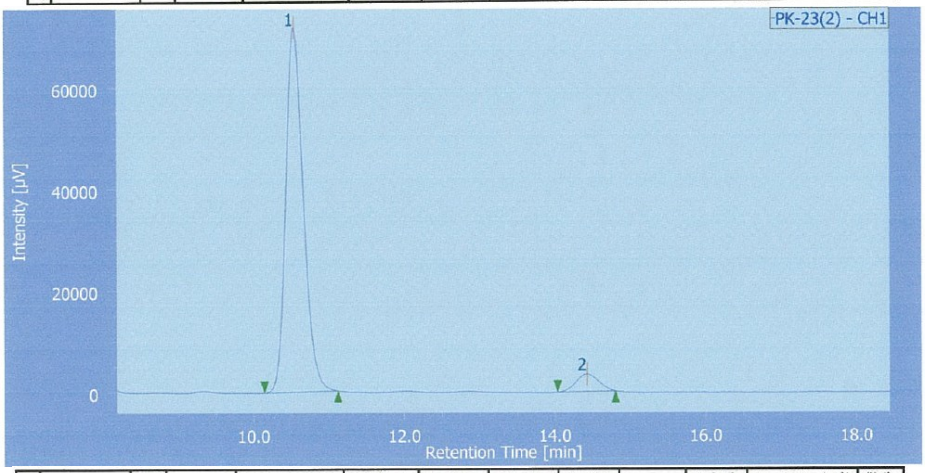
(S)-2-(6-chloro-1*H*-indol-2-yl)-1-phenylethanol (3ba):



(Reaction condition : B) Purified by silica gel column chromatography (EtOAc: Hexane 1.5:8.5); white solid; Yield: 84%; R_f = 0.23 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3252, 3021, 2369, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.59 (brs, 1H), 7.43 (d, J = 8.6 Hz, 1H), 7.40-7.29 (m, 6H), 7.05 (dd, J = 8.6 Hz, 1.7 Hz, 1H), 6.24 (s, 1H), 5.02-4.99 (m, 1H), 3.19-3.12 (m, 2H), 2.28 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.4, 137.1, 136.4, 128.7, 128.1, 127.0, 126.8, 125.6, 120.6, 120.2, 110.5, 101.0, 74.4, 37.6; HRMS (ESI): calcd for $C_{16}H_{14}ClNO$ *m/z* 294.0662 $[M+Na]^+$, Found 294.0674; Specific optical rotation $[\alpha]_D^{21}$ = - 40.8 (c = 0.54, $CHCl_3$) (90% *ee*); HPLC analysis: (90% *ee*): (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 10.5 min (major), 14.4 min (minor)

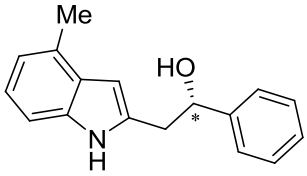


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.558	662316	40592	50.114	58.448	N/A	10027	7.688	1.179	
2	Unknown	1	14.450	659315	28857	49.886	41.552	N/A	9490	N/A	1.154	



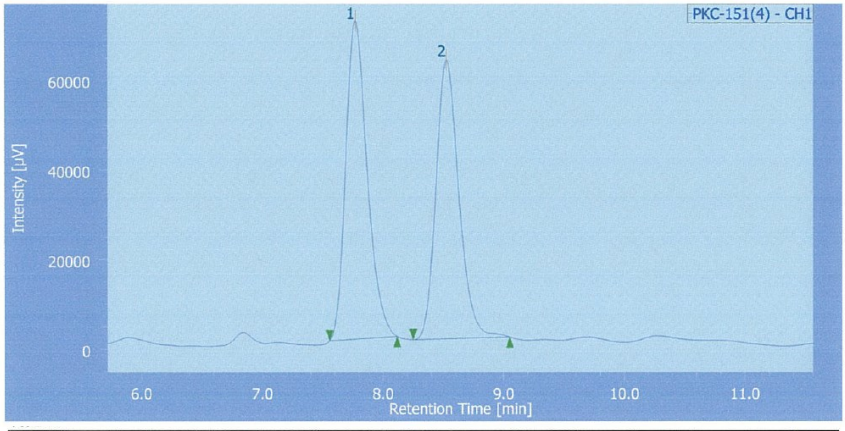
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.542	1175840	71849	94.306	95.468	N/A	9913	7.878	1.157	
2	Unknown	1	14.425	70989	3410	5.694	4.532	N/A	10431	N/A	1.021	

(*S*)-2-(4-methyl-1*H*-indol-2-yl)-1-phenylethanol (3ca):

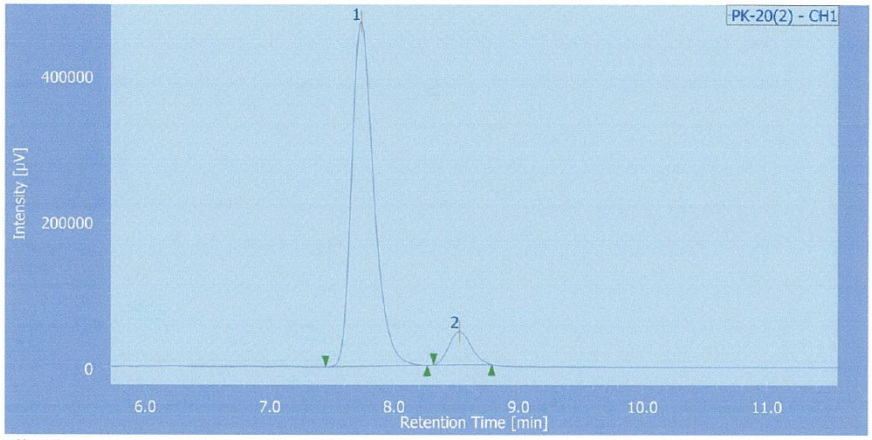


(Reaction condition: B); Purified by silica gel column chromatography (EtOAc: Hexane 1.5:8.5); Yellow liquid; Yield: 91%; R_f = 0.26 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3404, 2917, 2369, 1540, 1039, 766cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.47 (brs, 1H), 7.42-7.34 (m,

5H), 7.18 (d, J = 8.0 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 7.5 Hz, 1H), 6.3 (s, 1H), 4.97 (t-like, J = 6.3 Hz, 1H), 3.17 (brd, J = 5.7 Hz, 2H), 2.55 Hz, (s, 3H), 2.33 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.6, 135.7, 135.5, 129.4, 128.6, 128.1, 127.9, 125.6, 121.4, 119.7, 108.2, 99.6, 74.3, 37.9, 18.7;HRMS (ESI): calcd for $C_{17}H_{17}NO$ *m/z* 274.1207 $[M+Na]^+$, Found 274.1204; Specific optical rotation $[\alpha]_D^{21}$ = - 31.3 (c = 1.62, $CHCl_3$) (83% *ee*); HPLC analysis: (83% *ee*): (Column – Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 7.7 min (major), 8.5 min (minor)

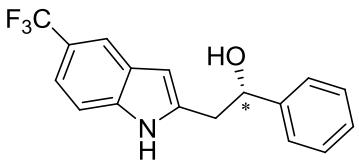


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.775	875205	71121	51.593	53.317	N/A	9471	2.279	1.236	
2	Unknown	1	8.525	821166	62272	48.407	46.683	N/A	10035	N/A	1.204	



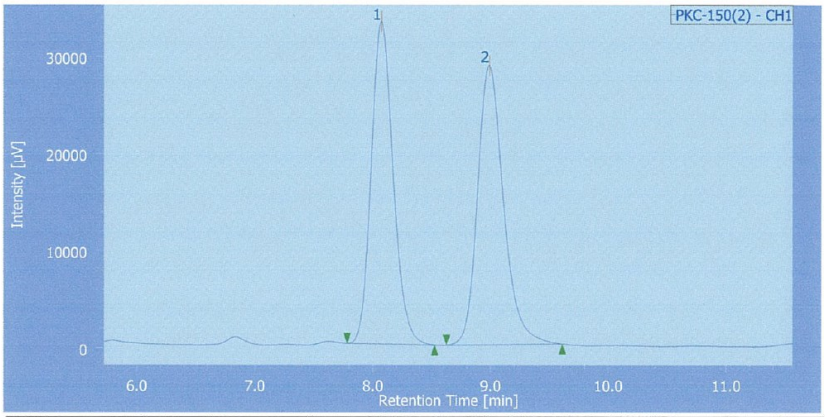
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.733	5836889	471792	91.305	91.253	N/A	9465	2.449	1.340	
2	Unknown	1	8.525	555851	45226	8.695	8.747	N/A	10663	N/A	1.120	

(*S*)-1-phenyl-2-(5-trifluoromethyl)-1*H*-indol-2-yl)ethanol (3da):

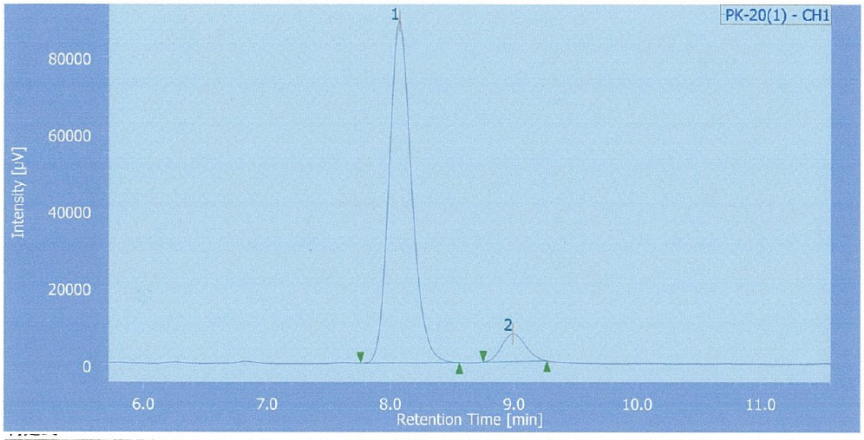


(Reaction condition: B); Purified by silica gel column chromatography (EtOAc: Hexane 1:9); White solid; Yield: 83%; R_f = 0.21 (Ethyl acetate: Hexane 2:8); IR (thin film): ν 3350, 2365, 1540, 1039, 766cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.85 (brs, 1H), 7.84(s, 1H), 7.14-7.33 (m, 7H), 6.34 (s, 1H), 5.04-5.02 (m, 1H), 3.23-3.15 (m, 2H), 2.31(brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.3, 138.2, 137.4, 128.7, 128.2, 127.6, 125.6, (126.5, 124.3, 122.2 $^1J_{CF}$ 271 Hz), (122.0, 121.7, 121.5 $^2J_{CF}$ 32 Hz), 118.0(q, $^3J_{CF}$ 3.6 Hz), 117.6 (q, $^3J_{CF}$ 3.6 Hz), 110.7, 101.7, 74.4, 37.5; HRMS (ESI): calcd for $C_{17}H_{14}F_3NO$ *m/z* 328.0925 $[M+Na]^+$, Found -328.0931; Specific optical rotation $[\alpha]_D^{23}$ = - 37.3 (c = 0.53, $CHCl_3$) (84%*ee*); HPLC analysis: (84% *ee*): (Column –

Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 8.0 min (major), 8.9 min (minor).

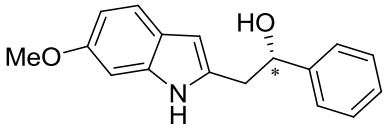


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.075	427064	33184	49.423	53.611	N/A	9285	2.550	1.155	
2	Unknown	1	8.992	437041	28714	50.577	46.389	N/A	8694	N/A	1.231	

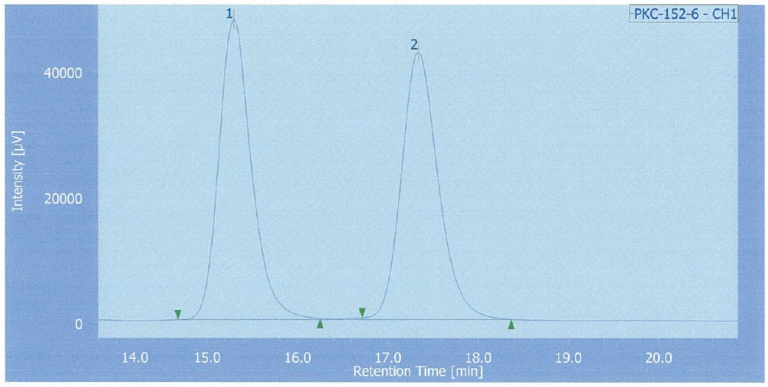


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.075	1123844	88777	92.093	92.532	N/A	9721	2.668	1.167	
2	Unknown	1	8.992	96493	7165	7.907	7.468	N/A	9907	N/A	1.096	

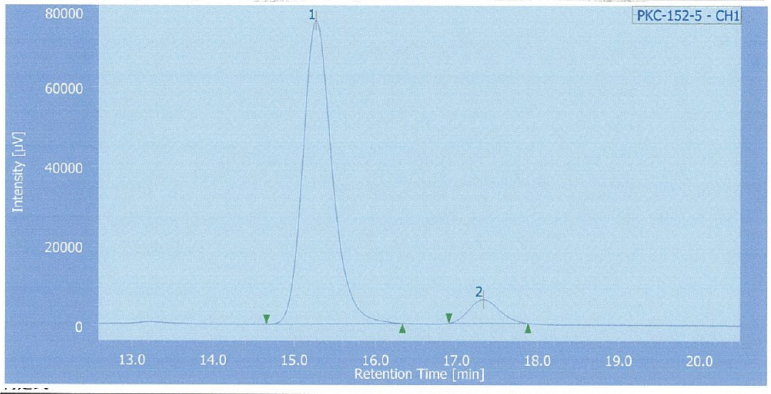
(*S*)-2-(6-methoxy-1*H*-indol-2-yl)-1-phenylethanol (3ea):



(Reaction condition: A); Purified by silica gel column chromatography (Et_2O: Hexane 4:6); Liquid; Yield: 70%; R_f = 0.27 (Diethyl ether: Hexane 6:4); IR (thin film): ν 3448, 3021, 2369, 1215, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.39 (brs, 1H), 7.42-7.31(m, 5H), 6.82 (d, J = 2.2 Hz, 1H), 6.76 (dd, J = 8.5 Hz, 2.2 Hz, 1H), 6.21 (s, 1H), 4.97 (t, J = 5.8 Hz, 1H), 3.84 (s, 3H), 3.13 (d, J = 5.8 Hz, 2H), 2.33 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.9, 143.6, 136.8, 134.9, 128.6, 127.9, 125.6, 122.5, 120.4, 109.2, 100.8, 94.4, 74.3, 55.6, 37.9; HRMS (ESI): calcd for $C_{17}H_{17}NO_2$ *m/z* 290.1157 $[M+Na]^+$, Found 290.1167; Specific optical rotation $[\alpha]_D^{24}$ = - 23.5 (c = 1.19, $CHCl_3$) (85% *ee*); HPLC analysis: (85% *ee*): (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 15.2 min (major), 17.3 min (minor).



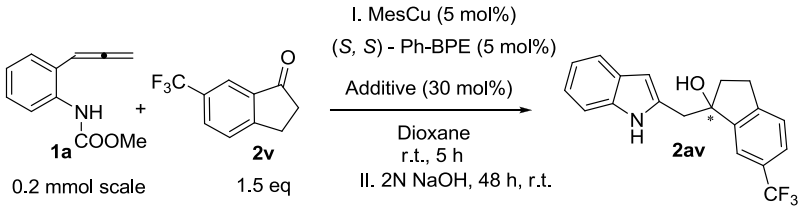
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	15.292	1194346	47726	49.904	52.907	N/A	9126	3.008	1.234	
2	Unknown	1	17.342	1198929	42481	50.096	47.093	N/A	9118	N/A	1.175	



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	15.267	1914562	76311	92.511	92.767	N/A	9064	3.086	1.230	
2	Unknown	1	17.333	154985	5950	7.489	7.233	N/A	9772	N/A	1.125	

9. Reaction of allenyl anilide with ketones-Additive effect and general procedure

Additive effect: In the reaction between allenyl anilide and ketones, protonation of the *in situ*-generated allylcopper species was predominant over nucleophilic addition to carbonyl group due to the lower electrophilicity of ketones. Thus, the additive effect in this key transformation was examined and the results are summarized in the table below. Here again, the magnesium isopropoxide was proved to be the best among other additives.

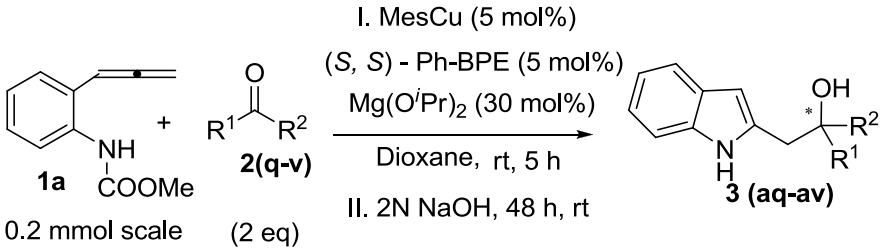


Entry	Additive (30 mol%)	Yield (%)[a]	*ee* (%)[b]
1	-	40	73
2	**$Mg(O^iPr)_2$**	**83**	**78**
3	$Al(O^iPr)_2$	75	76
4	KO^tBu	39	12
5	$MgBr_2$	0	-

6	$Ca(O^iPr)_2$	26	63
7	$La(O^iPr)_2$	25	76

[a]Yield determined by ^{1}H NMR spectrum of the crude products using *t*-Butyl methyl ether as an internal standard. [b]Enantiomeric excess was determined by chiral HPLC analysis.

9-1. General procedure for reaction between allenyl anilide and ketones:

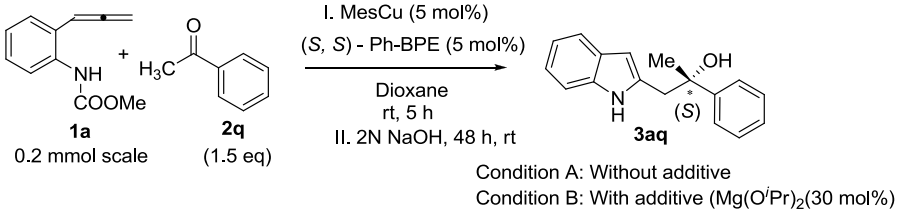


A flame-dried 20 mL test tube equipped with magnetic stirring bar and a 3-way glass stopcock was charged with mesitylcopper (1.8 mg, 0.01 mmol, 5 mol%), (*S, S*)-PhBPE (5.0 mg, 0.01 mmol, 5 mol%) and $Mg(O^iPr)_2$ (8.5 mg, 0.06 mmol, 30 mol%) under argon atmosphere. Anhydrous dioxane (480 µL) was added, and the mixture was stirred at ambient temperature for 45 minutes. To the stirred solution, ketone (0.3 mmol) and 1.1 M solution of allenyl anilide (**1a**) (37.8 mg, 181 µL, 0.2mmol) were added sequentially. After stirring for 5 h at room temperature, the reaction was diluted with THF (3 mL) and quenched with 2 N NaOH (3 mL) solution. The reaction mixture was stirred vigorously for 48 h, and products were extracted with ethyl acetate (20 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography afforded the desired compounds.

The racemic sample was prepared following the above procedure using 1,3-bis(diphenylphosphino)propane as an achiral ligand instead of (*S, S*)-Ph-BPE.

The absolute configuration of the major enantiomer of obtained tertiary alcohols can be assigned by analogy of **3aa** (See page S48-S51)

(*S*)-1-(1*H*-indol-2-yl)-2-phenylpropan-2-ol (3aq):

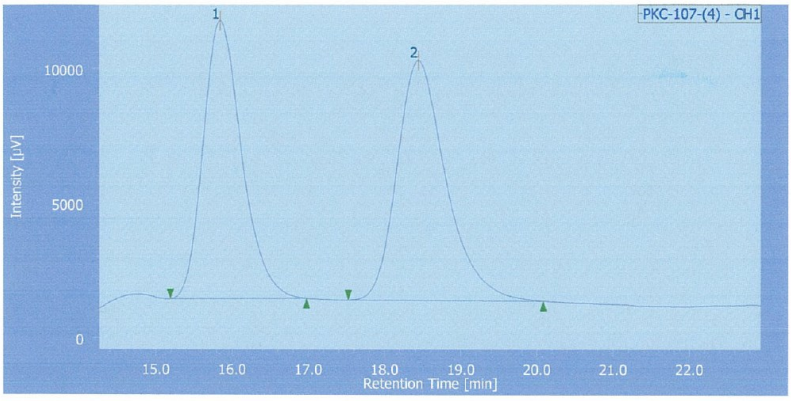


Reaction condition- A (Without additive): 53% yield, 83% *ee*

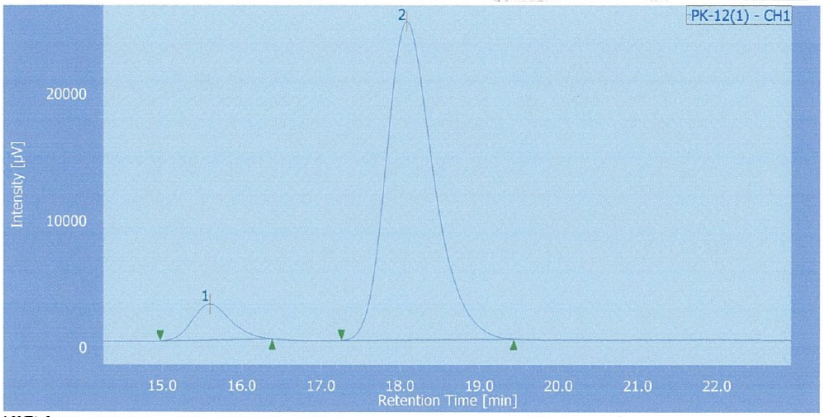
Reaction condition- B: 64% yield, 73% *ee*

Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; R_f = 0.23 (EtOAc: Hexane 2:8); IR (thin film): ν 3410, 3072. 2342, 1455, 1288 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500

MHz): δ 8.18 (brs, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.39-7.36 (m, 2H), 7.31-7.28 (m, 2H), 7.25-7.23 (m, 2H), 7.12 (td, *J* = 7.5 Hz, 1.2Hz, 1H), 7.06 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 6.26 (s, 1H), 3.32 (d, *J* = 14.9 Hz, 1H), 3.17 (d, *J* = 14.9 Hz, 1H), 2.14 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 147.5, 136.1, 135.0, 128.1, 127.1, 124.6, 121.2, 119.8, 119.4, 110.5, 102.6, 74.7, 42.9, 29.3; HRMS (ESI): calcd for $C_{17}H_{17}NO$ *m/z* 274.1208 $[M+Na]^+$, Found 274.1200; Specific optical rotation $[\alpha]_D^{24}$ = - 42.6 (*c* = 0.8, $CHCl_3$) (83% *ee*); HPLC analysis: (83% *ee*): (Column –Chiralcel OD-H; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 15.6 min (minor), 18.0 min (major).

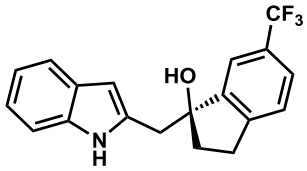


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	15.850	361062	10307	47.673	53.704	N/A	4867	2.546	1.252	
2	Unknown	1	18.442	396317	8885	52.327	46.296	N/A	4245	N/A	1.320	



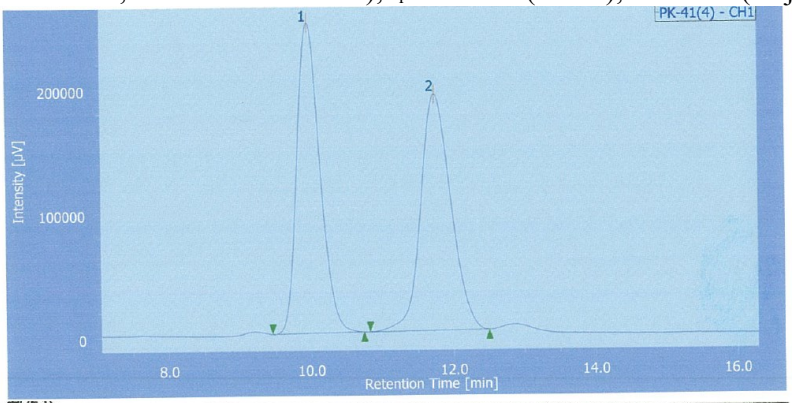
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	15.600	95206	2834	8.386	10.150	N/A	4982	2.548	1.188	
2	Unknown	1	18.083	1040043	25088	91.614	89.850	N/A	4566	N/A	1.279	

(*S*)-1-((1*H*-indol-2-yl)methyl)-6-(trifluoromethyl)-2,3-dihydro-1H-inden-1-ol (3av):

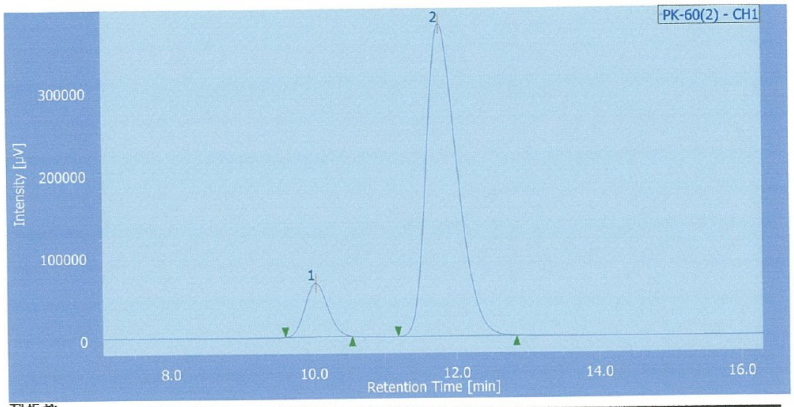


Reaction condition : B; Purified by silica gel column chromatography (Ethyl acetate: Hexane 15:85); Yellow liquid; Yield: 83%; R_f = 0.23 (EtOAc: Hexane 2:8); IR (thin film): ν 3448, 3019, 2921, 2359, 1621, 1215, 1123, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.66 (brs, 1H), 7.57 (d, *J* = 8 Hz, 2H), 7.52 (s, 1H), 7.36-7.34(m, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 6.26 (s, 1H), 3.31 (d, *J* = 14.9 Hz, 1H), 3.06-2.99 (m, 2H), 2.89-2.83 (m, 1H), 2.45-2.40 (m, 1H), 2.19 (s, 1H), 2.04-1.98 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 147.8, 146.7, 136.2, 135.1, (129.9, 129.6, 129.4, 129.1) ($^2J_{CF}$ 32 Hz), 128.1, (127.5, 125.3, 123.1, 121.0) ($^1J_{CF}$ 272 Hz), 125.7 (q, $^3J_{CF}$ 3.6 Hz), 125.4, 121.4, 119.96 (q, $^3J_{CF}$ 3.6 Hz), 119.9, 119.6, 110.6, 102.3, 83.4, 39.8, 38.6, 29.2; HRMS (ESI): calcd for

$C_{19}H_{16}F_3N_1O_1$ *m/z* 354.1082 $[M+Na]^+$, Found 354.1082; Specific optical rotation $[\alpha]_D^{24}$ = -13.8 (*c* = 1.76, $CHCl_3$) (for 77% *ee*); HPLC analysis: (77% *ee*): (Column –Chiralcel OD-H; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 10 min (minor), 11.7 min (major).

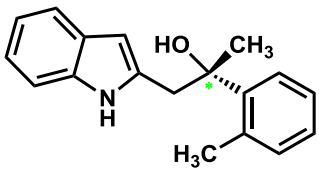


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	9.967	5565133	249923	49.787	56.798	N/A	4628	2.626	1.163	
2	Unknown	1	11.742	5612802	190099	50.213	43.202	N/A	3726	N/A	1.088	

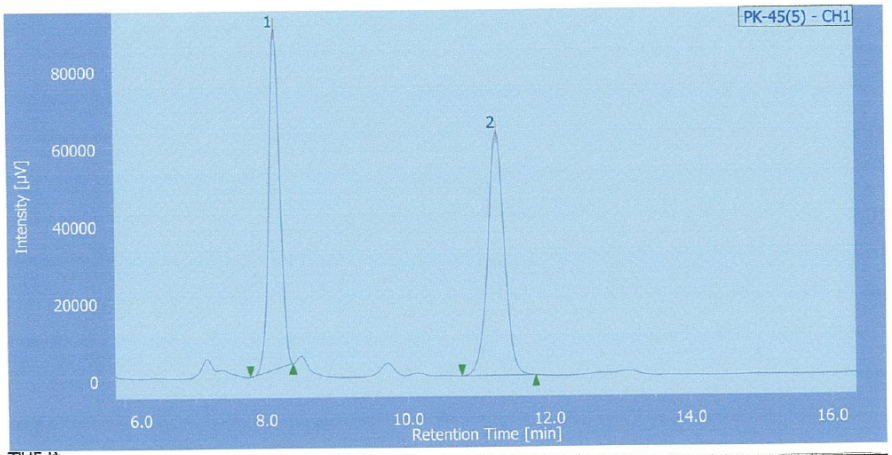


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	10.033	1433608	64987	11.247	14.656	N/A	4660	2.537	1.095	
2	Unknown	1	11.775	11312548	378414	88.753	85.344	N/A	3568	N/A	1.311	

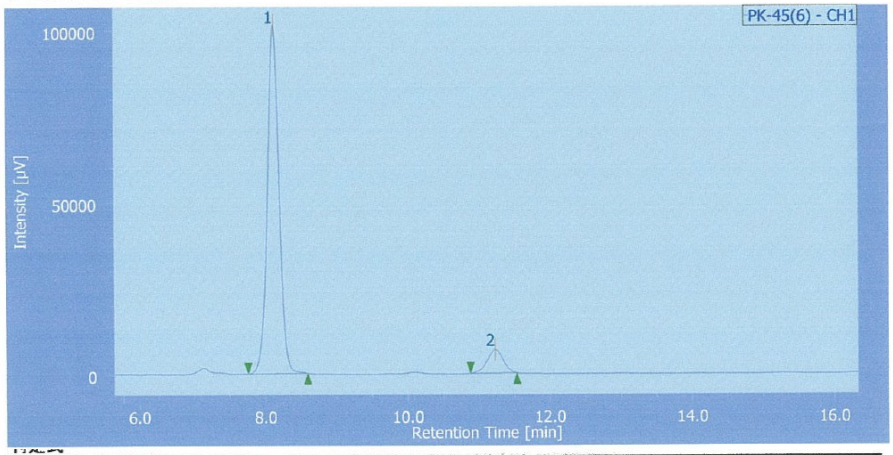
(*S*)-1-(1*H*-indol-2-yl)-2-o-tolylpropan-2-ol (3ar):



Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 57%; R_f = 0.26 (EtOAc: Hexane 2:8); IR (thin film): ν 3446, 3019, 2399, 1652, 1215, 1094, 929, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.26 (brs, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.26-7.16 (m, 4H), 7.12 (t, *J* = 8 Hz, 1H), 7.06 (t, *J* = 8 Hz, 1H), 6.28 (s, 1H), 3.5 (d, *J* = 14.9 Hz, 1H), 3.2 (d, *J* = 14.9 Hz, 1H), 2.65 (s, 3H), 2.10 (s, 1H), 1.66 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 144.5, 136.2, 135.3, 135.2, 132.9, 128.1, 127.4, 126.0, 125.8, 121.2, 119.8, 119.4, 110.5, 102.5, 75.9, 40.7, 28.7, 22.5; HRMS (ESI): calcd for $C_{18}H_{19}N_1O_1$ *m/z* 288.1364 $[M+Na]^+$, Found 288.1362; Specific optical rotation $[\alpha]_D^{24}$ = -23.8 (*c* = 0.65, $CHCl_3$) (for 83% *ee*); HPLC analysis: (83% *ee*): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 8.1 min (major), 11.2 min (minor).

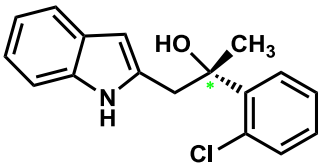


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.142	966464	87827	48.641	58.273	N/A	12833	8.925	0.931	
2	Unknown	1	11.267	1020485	62888	51.359	41.727	N/A	11813	N/A	0.950	

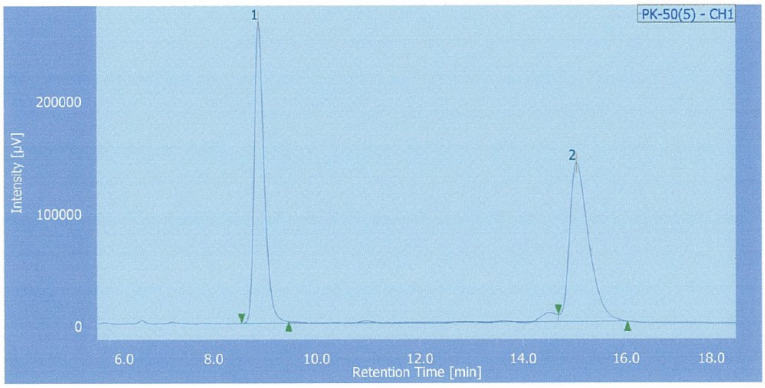


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.125	1149840	101401	91.501	93.704	N/A	12560	8.875	0.923	
2	Unknown	1	11.225	106796	6813	8.499	6.296	N/A	11964	N/A	0.951	

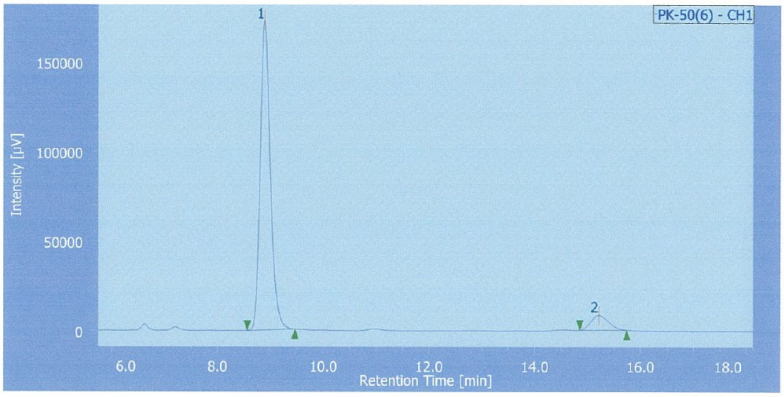
(*S*)-2-(2-chlorophenyl)-1-(1*H*-indol-2-yl)propan-2-ol (3as):



Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 67%; R_f = 0.25 (EtOAc: Hexane 2:8); IR (thin film): ν 3462, 3019, 2399, 1215, 1034 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.24 (brs, 1H), 7.66-7.64 (m, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.42-7.40 (m, 3H), 7.10 (t, J = 7.5 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.28 (s, 1H), 3.8 (d, *J* = 14.9 Hz, 1H), 3.4 (d, *J* = 14.9 Hz, 1H), 2.76 (s, 1H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.2, 136.2, 134.9, 131.4, 130.6, 128.6, 128.2, 127.6, 127.2, 121.2, 119.8, 119.4, 110.5, 102.5, 75.2, 39.2, 27.6; HRMS (ESI): calcd for $C_{17}H_{16}ClN_1O_1$ *m/z* 308.0818 $[M+Na]^+$, Found 308.0813; Specific optical rotation $[\alpha]_D^{24}$ = -62.8 (*c* = 0.85, $CHCl_3$) (85% *ee*); HPLC analysis: (85% *ee*): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 8.9 min (major), 15.2 min (minor).

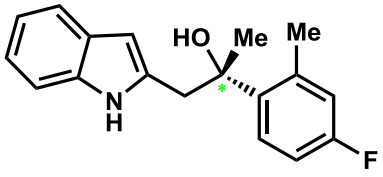


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.883	3717141	269439	50.331	65.653	N/A	10136	12.143	1.248	
2	Unknown	1	15.042	3668310	140962	49.669	34.347	N/A	8209	N/A	1.501	

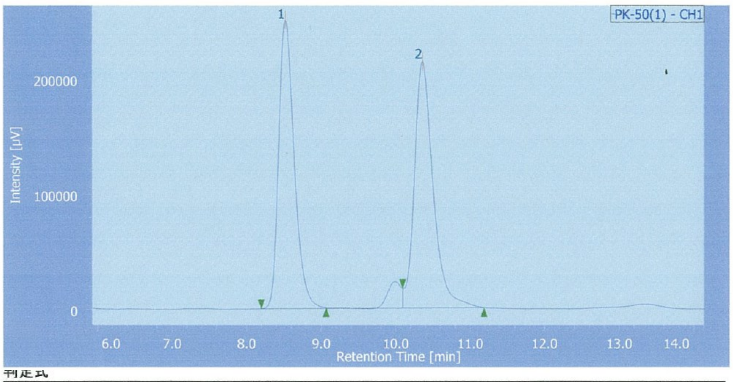


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.892	2350130	172819	92.582	95.481	N/A	10287	13.115	1.230	
2	Unknown	1	15.208	188313	8180	7.418	4.519	N/A	9779	N/A	1.225	

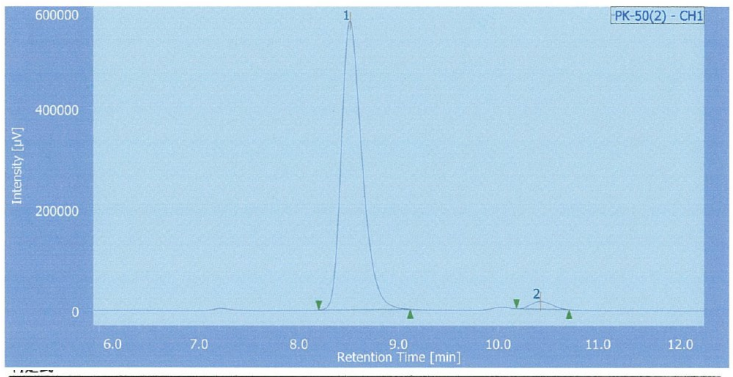
(*S*)-2-(4-Fluoro-2-methyl phenyl)-1-(1*H*-indol-2-yl)propan-2-ol (3au):



Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 62%; R_f = 0.23 (EtOAc: Hexane 2:8); IR (thin film): ν 3455, 3019, 2399, 1215, 1094, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.30 (brs, 1H), 7.53 (d, *J* = 8 Hz, 1H), 7.45-7.42 (m, 1H), 7.28 (d, *J* = 8 Hz, 1H), 7.14-7.05 (m, 2H), 6.92-6.82 (m, 2H), 6.26 (s, 1H), 3.46 (d, *J* = 14.9 Hz, 1H), 3.17 (d, *J* = 14.9 Hz, 1H), 2.63 (s, 1H), 1.64 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ (162.5, 160.6 $^1J_{CF}$ 245.9 Hz), 140.3, 137.9, 137.8 ($^3J_{CF}$ 7.2 Hz), 136.2, 135.1, 128.1, (127.6, 127.5 $^3J_{CF}$ 8.4 Hz), 121.3, 119.8, 119.5, (119.2, 119.1 $^2J_{CF}$ 20.4 Hz), (112.3, 112.2 $^2J_{CF}$ 20.4 Hz), 110.5, 102.5, 75.6, 40.8, 29.0, 22.5; HRMS (ESI): calcd for $C_{18}H_{18}FN_1O_1$ *m/z* 306.127 $[M+Na]^+$, Found 306.1289; Specific optical rotation $[\alpha]_D^{24}$ = -22.2 (*c* = 0.75, $CHCl_3$) (95% *ee*); HPLC analysis: (95% *ee*): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 8.5 min (major), 10.4 min (minor).

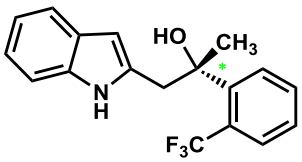


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.525	3611441	250522	49.147	53.969	N/A	8486	4.570	1.284	
2	Unknown	1	10.358	3736765	213678	50.853	46.031	N/A	9104	N/A	N/A	

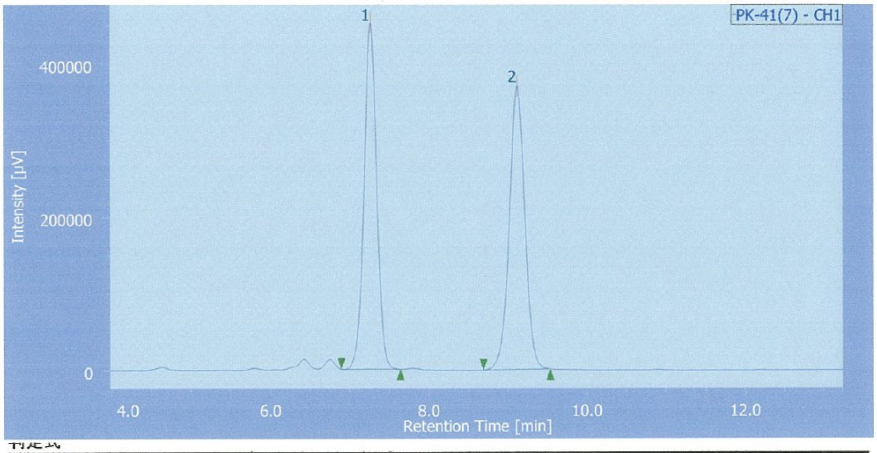


#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	8.517	8295793	572092	97.432	97.404	N/A	8235	4.990	1.330	
2	Unknown	1	10.425	218673	15249	2.568	2.596	N/A	11349	N/A	1.141	

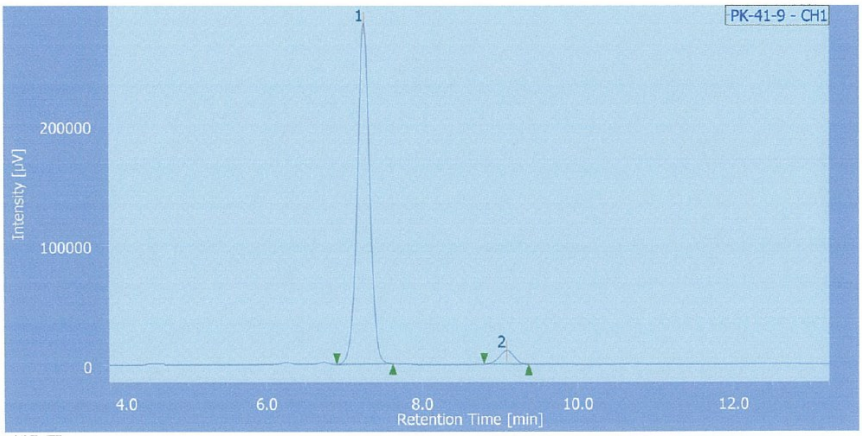
(*S*)-1-(1*H*-indol-2-yl)-2-(2-(trifluoromethyl) phenyl) propan-2-ol (3at):



Purified by silica gel column chromatography (Ethyl acetate: Hexane 2:8); Yellow liquid; Yield: 66%; R_f = 0.26 (EtOAc: Hexane 2:8); IR (thin film): ν 3447, 3019, 2358, 1551, 1215, 1122 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.52 (brs, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 8 Hz, 1H), 7.53-7.48 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 8 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.27 (s, 1H), 3.51 (d, *J* = 14.9 Hz, 1H), 3.22 (d, *J* = 14.9 Hz, 1H), 2.39 (s, 1H), 1.7 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 146.4, 136.2, 134.8, 131.6, 128.3, 128.2, 128.1, 127.2, (127.5, 127.2, 127.0, 126.7) ($^2J_{CF}$ 31 Hz), (128.1, 126.0, 123.8, 121.6) ($^1J_{CF}$ 272 Hz), 121.3, 119.8, 119.4, 110.5, 102.5, 75.9, 42.4, 30.5; HRMS (ESI): calcd for $C_{18}H_{16}F_3N_1O_1$ *m/z* 342.1082 $[M+Na]^+$, Found 342.1070; Specific optical rotation $[\alpha]_D^{24}$ = - 25.9 (*c* = 0.67, $CHCl_3$) (91% *ee*); HPLC analysis: (91% *ee*): (Column –Chiralpak IA; Hexane/2-propanol = 9/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 7.2 min (major), 9 min (minor).



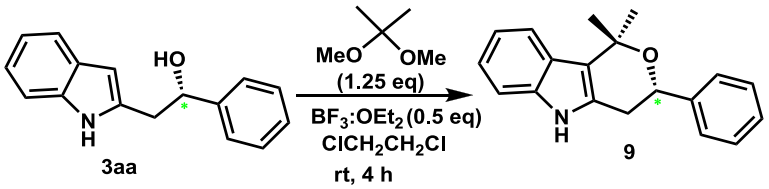
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.267	5019664	452930	49.992	55.009	N/A	10319	5.853	0.968	
2	Unknown	1	9.117	5021294	370451	50.008	44.991	N/A	10999	N/A	0.975	



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	7.258	3137836	284959	95.603	96.253	N/A	10440	5.855	0.949	
2	Unknown	1	9.083	144318	11094	4.397	3.747	N/A	11361	N/A	0.953	

10. Applications: Towards the syntheses of tetrahydropyranoindoles and spiroxindole:-

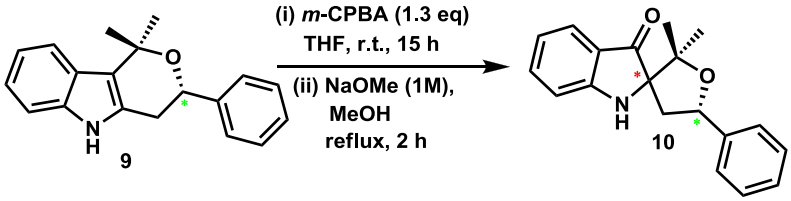
10-1. Synthesis of (*S*)-1, 1-dimethyl-3-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indole (9):



To a stirred solution of (*S*)-2-(1*H*-indol-2-yl)-1-phenylethanol (**3aa**) (60 mg, 0.252 mmol) in anhydrous 1,2-dichloroethane (3 mL) was added 2, 2-dimethoxypropane (39 µL, 0.316 mmol) followed by boron trifluoride-etherate complex (16.8 μL, 0.136 mmol) at ambient temperature under argon atmosphere. The resulting reaction mixture was stirred at room temperature for 4 h and the mixture was slowly quenched with sat. *aq*. $NaHCO_3$ solution (5 mL). The reaction mixture was extracted with ethylacetate (10 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / *n*-hexane 1/9) afforded colorless sticky liquid (69.2 mg, 99%); R_f =

0.36 (EtOAc: Hexane 2:8); IR (thin film): ν 3405, 3018, 2977, 2360, 1457, 1216, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.57 (brs, 1H), 7.4-7.37 (m, 3H), 7.27-7.25 (m, 2H), 7.2-7.14(m, 2H), 7.07-6.98 (m, 2H), 4.83-4.81 (m, 1H), 2.81 (dd, *J* = 10.3 Hz, 15.5 Hz, 1H), 2.66 (dd, *J* = 3.4 Hz, 15.5 Hz, 1H), 1.61 (s, 3H), 1.57 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 142.3, 135.8, 130.5, 128.4, 127.6, 126.3, 124.5, 121.1, 119.4, 118.7, 116.5, 110.9, 74.7, 70.7, 31.6, 29.9, 26.5; HRMS (ESI): calcd for $C_{19}H_{19}NO$ *m/z* 300.13643 $[M+Na]^+$, Found 300.1364; Specific optical rotation $[\alpha]_D^{24}$ = - 66.1 (*c* = 1.04, $CHCl_3$) (91% *ee*).

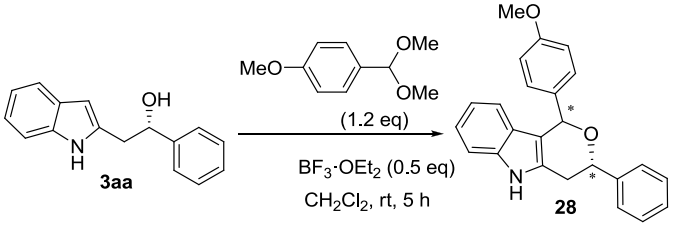
10-2. 2,2-dimethyl-5-phenyl-4,5-dihydro-2H-spiro[furan-3,2'-indolin]-3-one (10)



To a stirred solution of **9** (80.7 mg, 0.29 mmol) in tetrahydrofuran (8 mL) was added *m*-CPBA (66 mg, 0.37 mmol) at room temperature and stirred for 15 h. The reaction mixture was quenched with saturated sodium thiosulfite solution, extracted with ethyl acetate (20 mL×3) and washed the organic layer with water, brine and dried over sodium sulfate and concentrated.

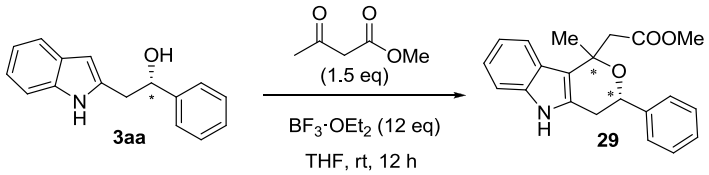
The crude residue was dissolved in 1M MeONa/MeOH (15 mL) solution, refluxed for 2 h and cooled to room temperature, quenched the reaction with 3 N HCl. Products were extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / *n*-hexane 2/8) afforded **10** as liquid (58 mg, 68%); *dr* : 6:4; R_f = 0.38 and 0.34 (diastereomeric mixture) (EtOAc: Hexane 2:8); IR (thin film): ν 3355, 3011, 2358, 1683, 1617, 1216, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) (diastereomeric mixture): δ 7.6 (d, *J* = 7.45 Hz, 1H), 7.48-7.35 (m, 5H), 7.31-7.26 (m, 1H), 6.91-6.79 (m, 2H), 5.48-5.45 (m, 0.6H), 5.27-5.23 (m, 0.4 H), 5.1 (brs, 0.4 H), 4.79 (brs, 0.6H), 3.03 (dd, *J* = 13.1 Hz, 8.6 Hz, 0.6 H), 2.72 (dd, *J* = 13.1 Hz, 10.3 Hz, 0.4 H), 2.43 (dd, *J* = 13.1 Hz, 6,87 Hz, 0.4H), 2.2 (dd, *J* = 13.1 Hz, 6.3 Hz, 0.6 H), 1.64 (brs, 1H), 1.43 (s, 3H), (1.33, 1.30) (2s, 3H);); ^{13}C NMR ($CDCl_3$, 125 MHz) (diastereomeric mixture) : δ 200.1 (199.5), 159.4, 142.8 (142.1), 137.19 (137.15), 128.5 (128.3), 127.4 (127.3), 125.8 (125.3), 124.5 (124.4), 120.9 (120.6), 118.8 (118.7), 111.68 (111.64), 84.89 (84.7), 78.1 (77.0), 76.5 (76.1), 44.9 (44.0), 25.7 (24.0), 23.3 (22.7); HRMS (ESI): calcd for $C_{19}H_{19}NO_2$ *m/z* 316.1314 $[M+Na]^+$, Found 316.1309.

10-3. Synthesis of 1-(4-methoxyphenyl)-3-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indole (28):



To a stirred solution of 2-(1*H*-indol-2-yl)-1-phenylethanol (**3aa**) (30 mg, 0.13 mmol) in anhydrous CH_2Cl_2 (3 mL) at 0 °C under argon atmosphere was added *p*-anisaldehyde dimethylacetal (27 µL, 0.16 mmol) followed by boron trifluoride-etherate complex (8.4 μL, 0.068 mmol). The resulting reaction mixture was warmed to room temperature and stirred for 5 h. The reaction mixture was slowly quenched with sat. aq. $NaHCO_3$ solution (5 mL). Products were extracted with dichloromethane (5 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / *n*-hexane 2/8) afforded yellow liquid (39 mg, 87%); R_f = 0.26 (EtOAc: Hexane 2:8); IR (thin film): ν 3396, 2921, 2360, 1508, 1247 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) (diastreomeric mixture in the ratio 6: 4): δ 8.0 (7.94) (brs, 1H), 7.5 (d, *J* = 7.4 Hz, 1H), 7.42-7.27 (m, 7H), 7.19-7.16 (m, 1H), 7.11-7.03 (m, 1H), 6.91-6.77 (m, 3H), 6.18 (6.0) (s, 1H), 5.02 (dd, *J* = 10.8 Hz, 3.4 Hz, 0.6 H), 4.85 (dd, *J* = 10.3 Hz, 4.0 Hz, 0.4 H), 3.81 (3.79) (s, 3H), 3.23-3.12 (m, 1H), 3.05-3.0 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) (diastereomeric mixture): δ 159.5 (159.8), 142.0 (141.7), 135.8 (135.7), 133.3 (133.2), 132.7 (132.3), 130.08 (130.04), 128.4 (128.3), 127.68 (127.63), 126.3 (126.1), 125.9 (125.1), 121.5 (121.3), 119.7 (119.5), 119.0 (118.8), 113.7 (113.4), 111.7 (110.7), 110.6 (110.1), 78.1 (77.2), 74.0 (69.4), 55.22 (55.20), 31.9 (30.6); HRMS (ESI): calcd for $C_{24}H_{21}NO_2$ *m/z* 378.147 $[M+Na]^+$, Found 378.1460.

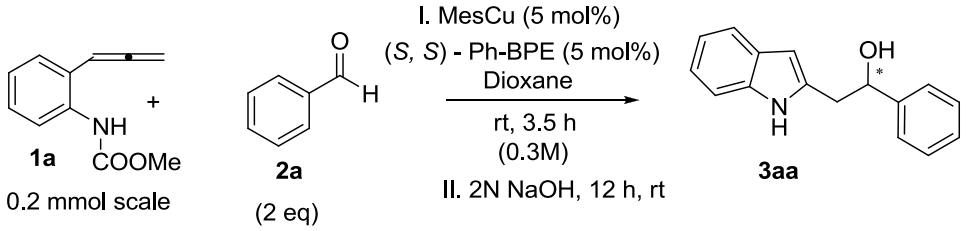
10-4. Methyl 2-(1-methyl-3-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indol-1-yl)acetate (29):



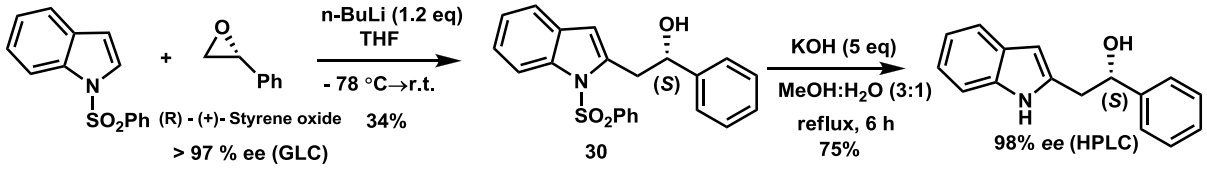
To a stirred solution of 2-(1*H*-indol-2-yl)-1-phenylethanol (**3aa**) (30 mg, 0.126 mmol) in anhydrous THF (5 mL) at rt under argon atmosphere was added methyl acetoacetate (20.4 µL, 0.189 mmol) followed by boron trifluoride-etherate complex (187 µL, 1.51 mmol). After stirring for 12 h at room temperature, the reaction was cautiously quenched with sat. aq. $NaHCO_3$ solution (5 mL), and products were extracted with dichloromethane (5 mL × 3). The combined organic extracts were washed with water and brine, dried over sodium sulfate, passed through a pad of celite, and concentrated under vacuum. Purification by silica gel column chromatography (Ethyl acetate / *n*-hexane 2/8) afforded **29** as colorless liquid (39 mg, 92%); R_f = 0.18 (EtOAc: Hexane 2:8); IR (thin film): ν 3397, 2947, 2365, 1732, 1456, 1326, 1219, 746 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) (diastreomeric mixture in the ratio 6: 4): δ 7.96 (7.91) (brs, 1H), 7.54-7.48 (m, 3H), 7.42-7.39 (m, 2H), 7.35-7.32 (m, 2H), 7.18-7.12 (m, 2H), 5.11 (4.96) (dd, *J* = 10.8 Hz, 3.4 Hz, 1H), 3.6 (s, 3H), 3.17-3.12 (m, 1H), 3.09-2.84 (m, 3H), 1.89 (1.83) (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) (distereomeric mixture): δ 170.9 (170.8), 142.3 (141.5), 135.8, 131.3 (130.87), 128.4 (128.3), 127.6 (127.5), 126.3 (125.9), 124.3 (124.0), 121.4 (121.3), 119.7 (119.6), 118.6 (118.3), 115.5 (114.1), 111.07 (111.01), 75.4 (75.3), 70.9 (70.7), 51.5 (51.2), 46.72 (43.83), 32.07 (30.54), 27.18 (25.37); HRMS (ESI): calcd for $C_{21}H_{21}NO_3$ *m/z* 358.1419 $[M+Na]^+$, Found 358.1401.

11. Confirmation of the absolute configuration of 3aa:

The reaction of allenyl anilide (**1a**) (0.2 mmol scale) with benzaldehyde (**2a**) (2 eq) in presence of 5 mol% of copper catalyst [MesCu (5 mol%) and (*S, S*)-Ph-BPE (5 mol%) as chiral ligand] in dioxane (0.3 molar concentration) at room temperature afforded **3aa** as a white solid (92%, 91% ee).



The absolute configuration of the obtained product (**3aa**) was confirmed by comparing the HPLC data and specific optical rotation of the product obtained using two step synthetic protocol[8] as shown below.



Experimental procedure:

(*S*)-1-phenyl-2-(1-(phenylsulfonyl)-1H-indol-2-yl)ethanol (30):

To a solution of 1-phenylsulfonylindole (1 g, 3.88 mmol) in dry THF (15 mL) was added dropwise *n*-butyllithium (2.9 mL, 1.6 M in hexane, 4.66 mmol) over 10 min under argon at – 78 °C. The mixture was stirred for 1.5 h at -78 °C and then allowed to warm slowly to 0 °C over 1 h. The solution was again cooled to -78 °C and (*R*)- (+)- styrene oxide (0.44 mL, 3.88 mmol) was added drop by drop. The reaction mixture was allowed slowly to warm up to room temperature overnight and quenched with saturated aqueous solution of ammonium chloride (10 mL). Products were extracted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated under high vacuum. The crude mixture was purified by silica gel column chromatography (Ethyl acetate / *n*-hexane 2/8) afforded the desired compound as a liquid (501 mg, 34%); IR (thin film): ν 3584, 3063, 1592, 1449, 1366, 1175, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.20 (d, *J* = 8.0 Hz, 1H), 7.73-7.71 (m, 2H), 7.51-7.48 (m, 3H), 7.44-7.36 (m, 5H), 7.32-7.29 (m, 2H), 7.25-7.22 (m, 1H), 8.51 (s, 1H), 5.23 (dd, *J* = 9.1Hz, 3.4 Hz, 1H), 3.55 (dd, *J* = 14.5 Hz, 2.9 Hz, 1H), 3.25 (dd, *J* = 14.5 Hz, 8.6 Hz, 1H), 2.25 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.7, 138.6, 137.8, 137.4, 133.7, 129.6, 129.2, 128.4, 127.6, 126.1, 125.7, 124.4, 123.8, 120.4, 115.0, 112.2, 73.0, 39.8; HRMS (ESI): calcd for $C_{22}H_{19}NO_3S$ *m/z* 400.0983 $[M+Na]^+$, Found 400.0989.

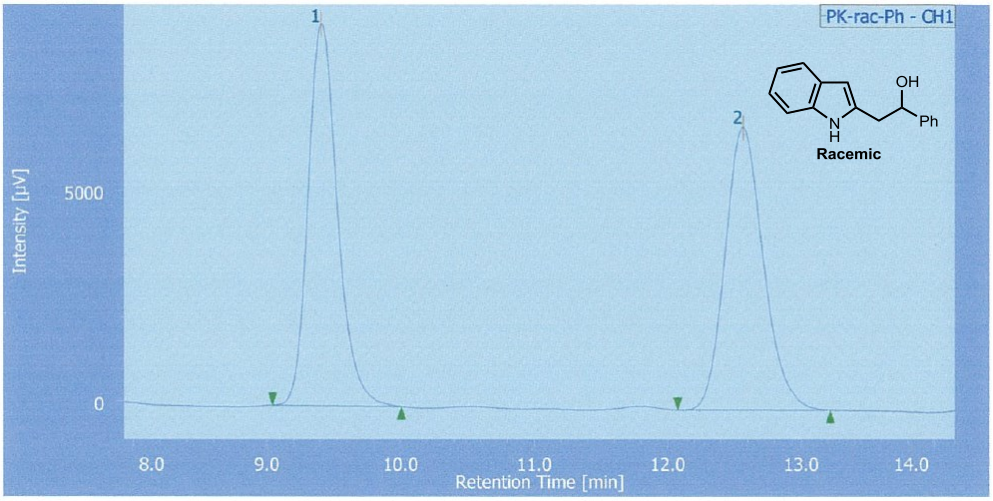
[8] Wang, J-C.; Just, G. J. Org. Chem. 1999, 64, 8090-8097

(*S*)-2-(1*H*-indol-2-yl)-1-phenylethanol:

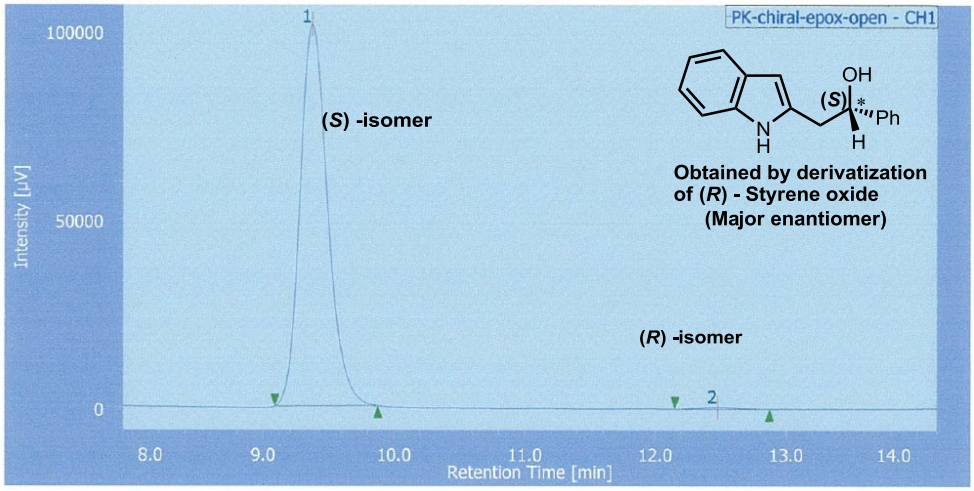
To a solution of (*S*)-1-phenyl-2-(1-(phenylsulfonyl)-1H-indol-2-yl)ethanol (**30**) (0.45 g, 1.192 mmol) in 6 mL of methanol/water (3;1) containing KOH (335 mg, 5.96 mmol) was refluxed for 7 h and the reaction was quenched with *sat*. *aq*. ammonium chloride solution. The reaction mixture was extracted with ethylacetate and the combined extracts were washed with water and brine, dried over anhydrous sodium sulfate, concentrated under high vacuum. Purified by silica gel column chromatography (EtOAc: Hexane (2:8); white solid; (212 mg, 75%)

All the spectroscopic data were in good agreement with the sample (**3aa**) obtained *via* key transformation. Specific optical rotation $[\alpha]_D^{20}$ = -52 (*c* = 0.5, $CHCl_3$) (98% *ee*); HPLC analysis: (98% *ee*); (Column –Chiralpak IA; Hexane/2-propanol = 5/1, flow rate 1.0 mL/min, detection at 254 nm), t_r = 9.37 min (major), 12.47 min (minor).

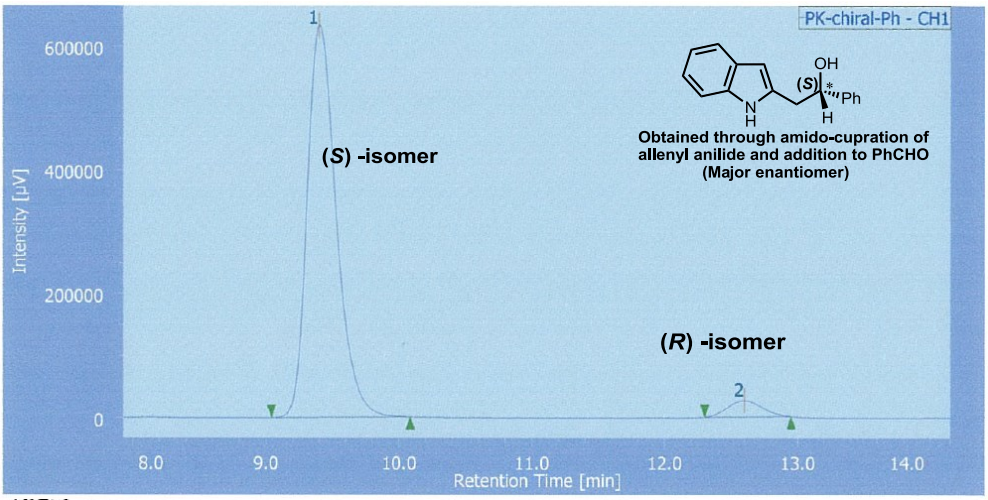
The specific optical rotation and HPLC chromatograms comparision of **3aa** obtained by amido-cupration-asymmetric allylation {(*S, S*)-Ph-BPE} method and derivatization of (*R*)-(+)-styrene oxide unambiguously revealed that the obtained compound (**3aa**) has (*S*)-configuration.



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	9.408	138626	9055	50.746	57.440	N/A	9209	6.933	1.224	
2	Unknown	1	12.567	134553	6709	49.254	42.560	N/A	9296	N/A	1.153	

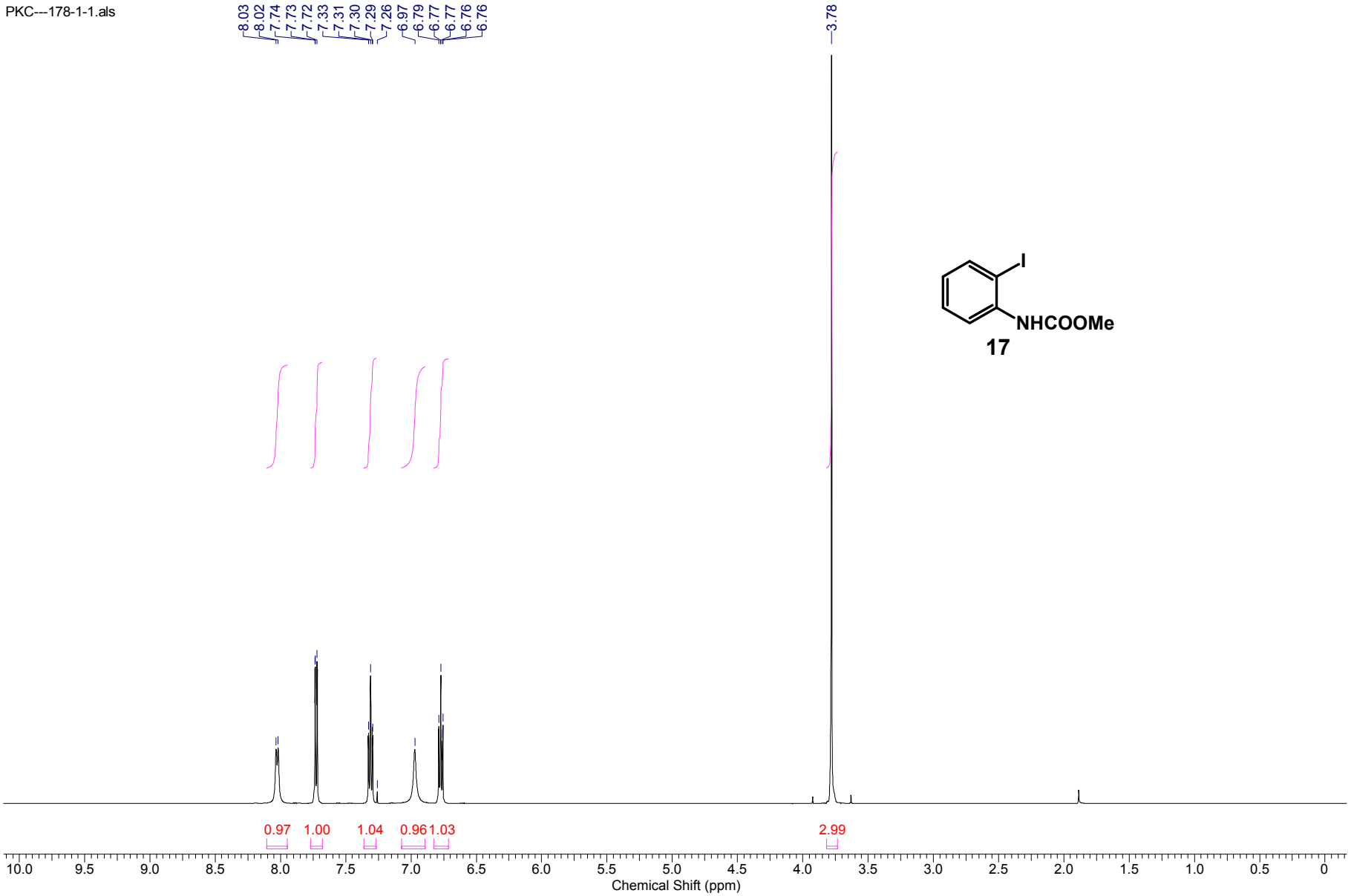


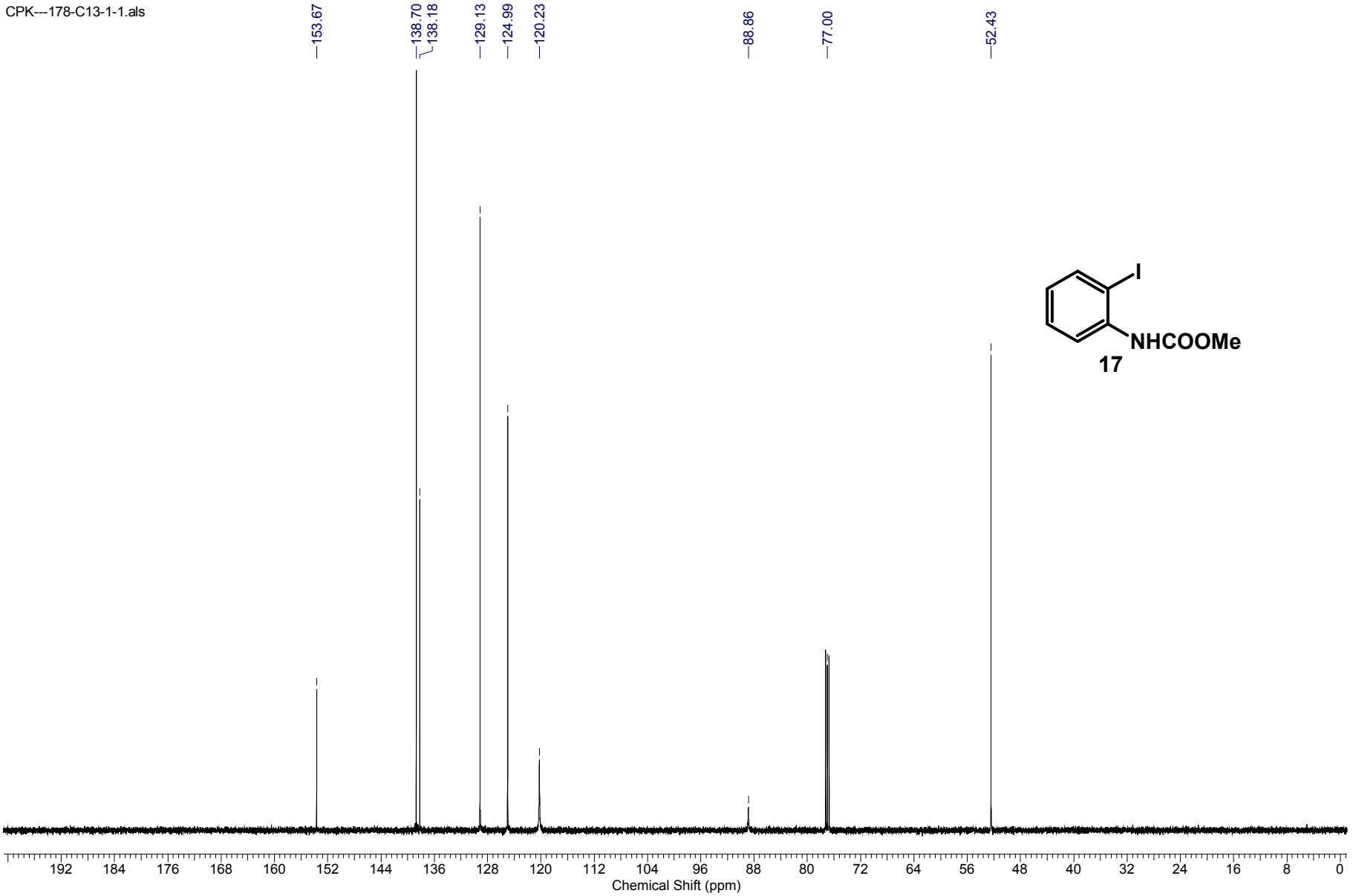
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	9.375	1479373	101230	99.452	99.551	N/A	9812	7.293	1.213	
2	Unknown	1	12.475	8144	457	0.548	0.449	N/A	11094	N/A	1.138	

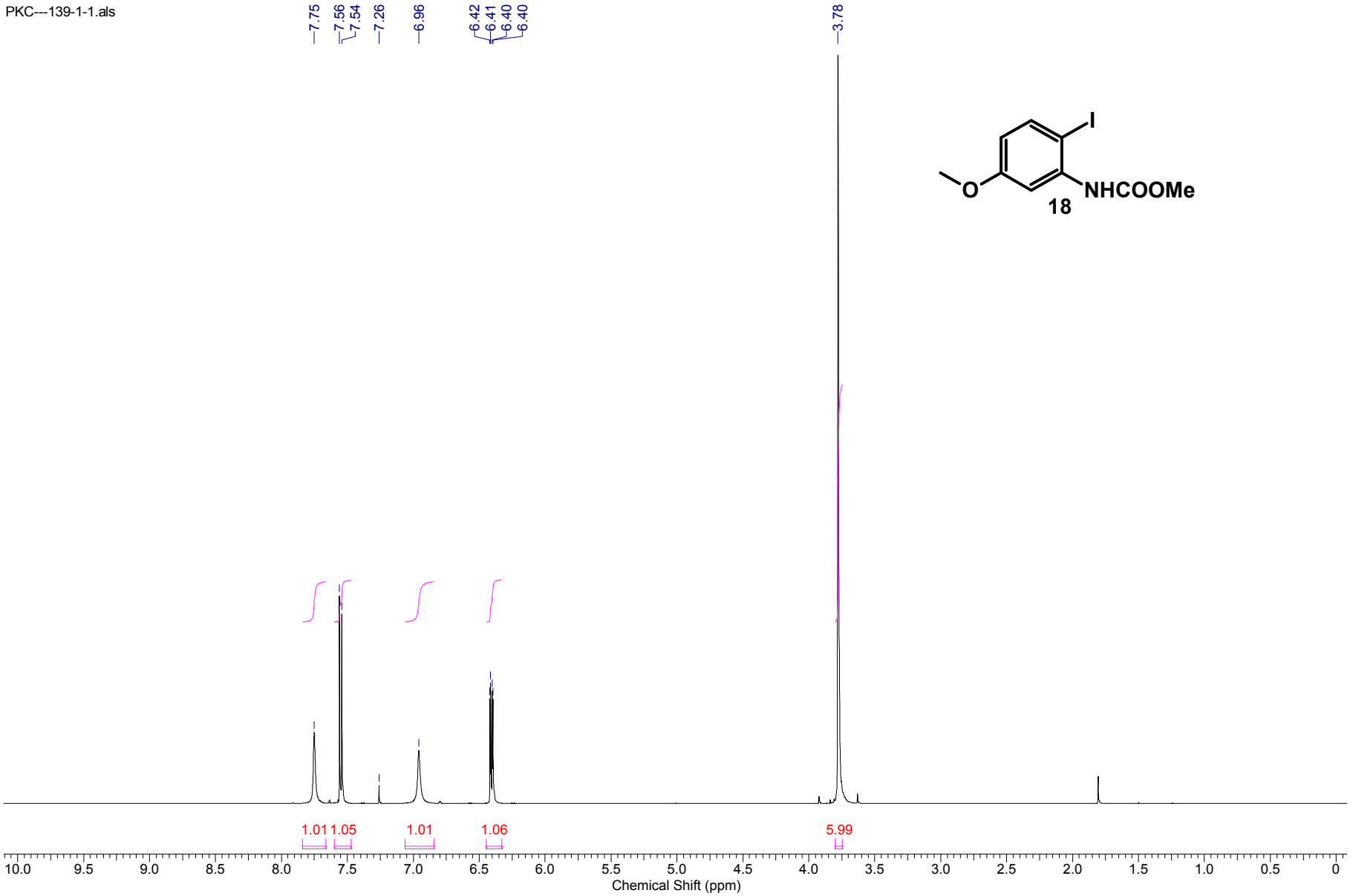


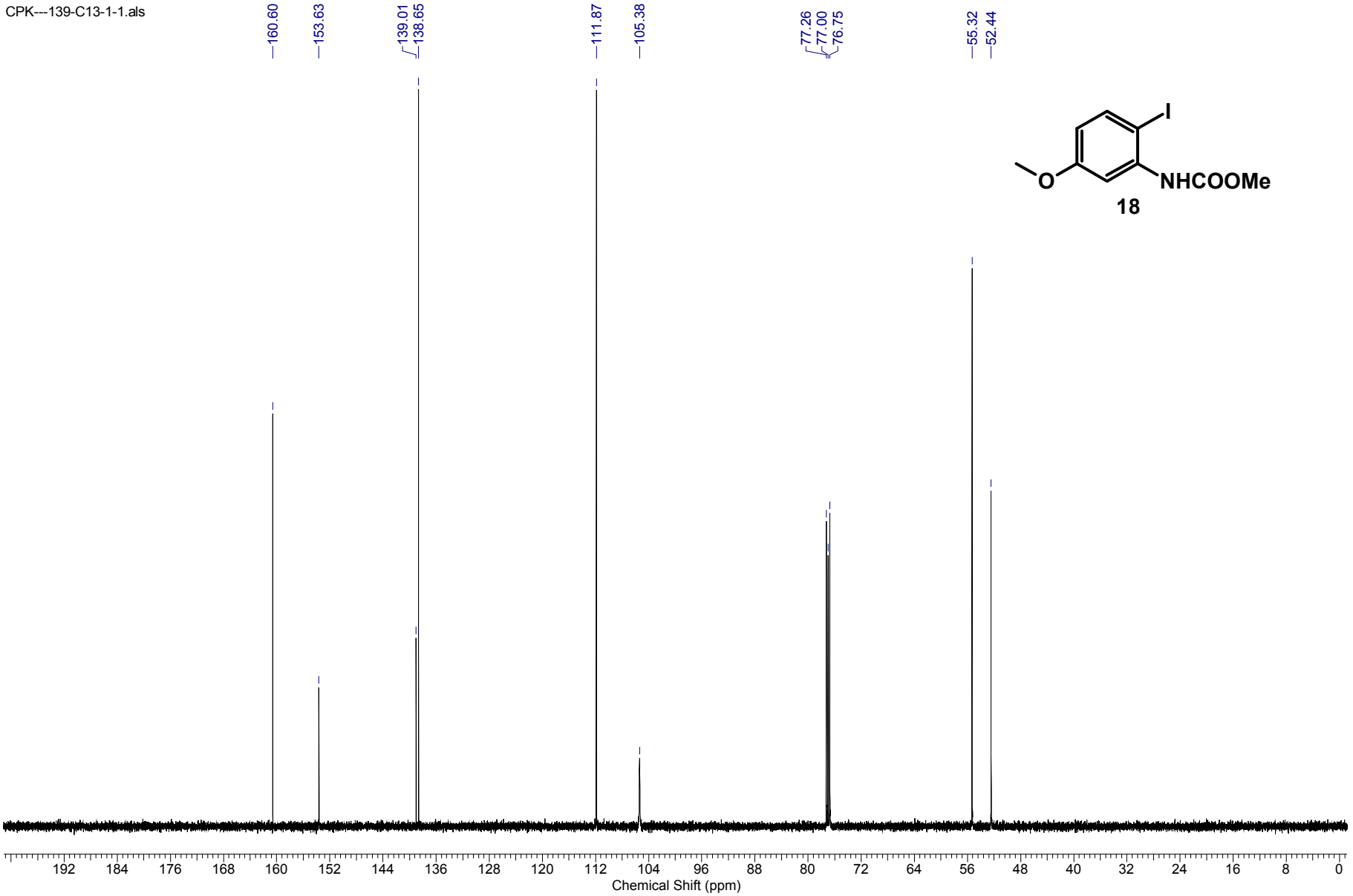
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	9.400	9552410	632384	95.230	95.994	N/A	9329	7.281	1.319	
2	Unknown	1	12.600	478468	26391	4.770	4.006	N/A	10490	N/A	1.086	

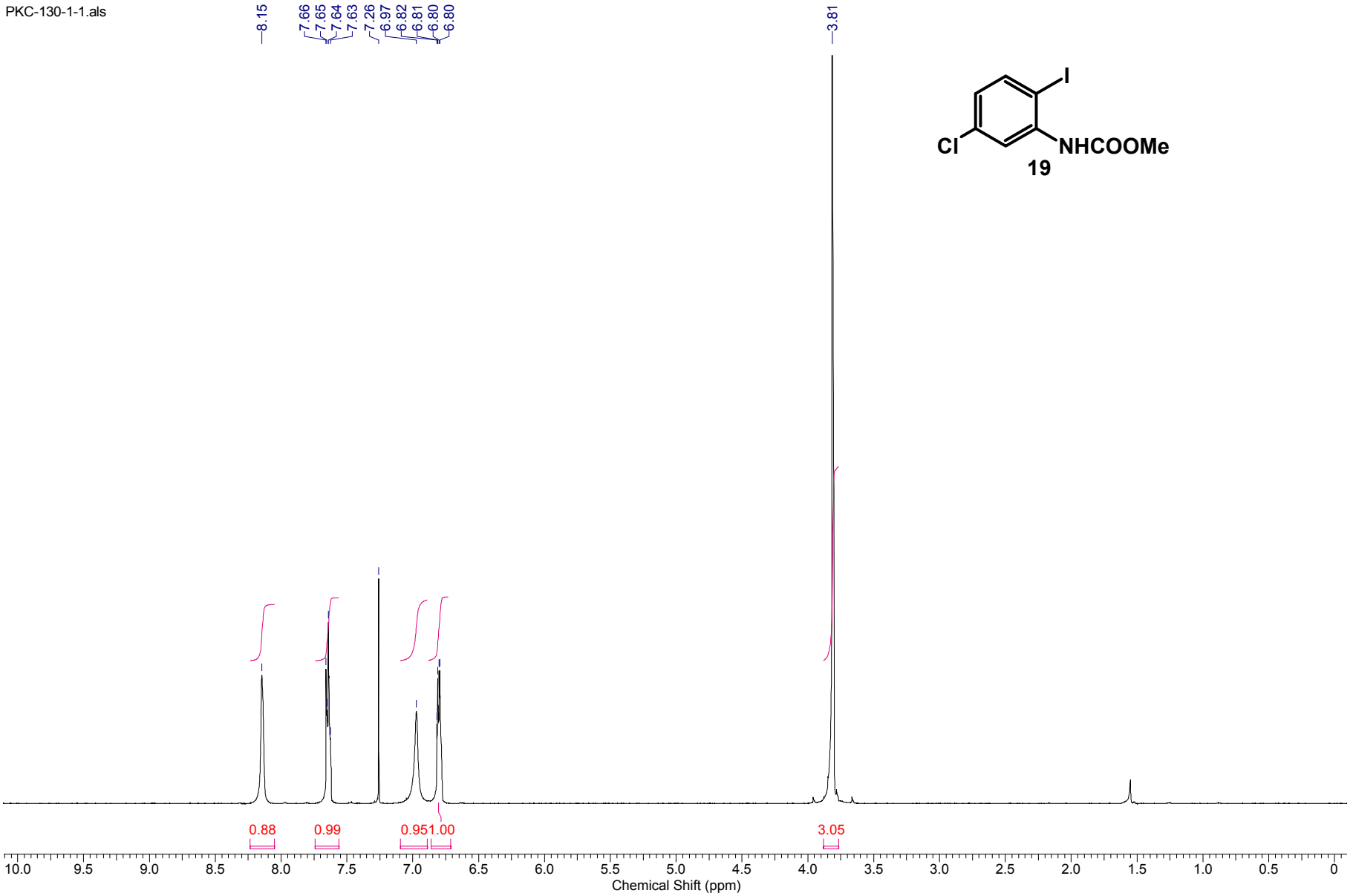
12. NMR spectra of new compounds:

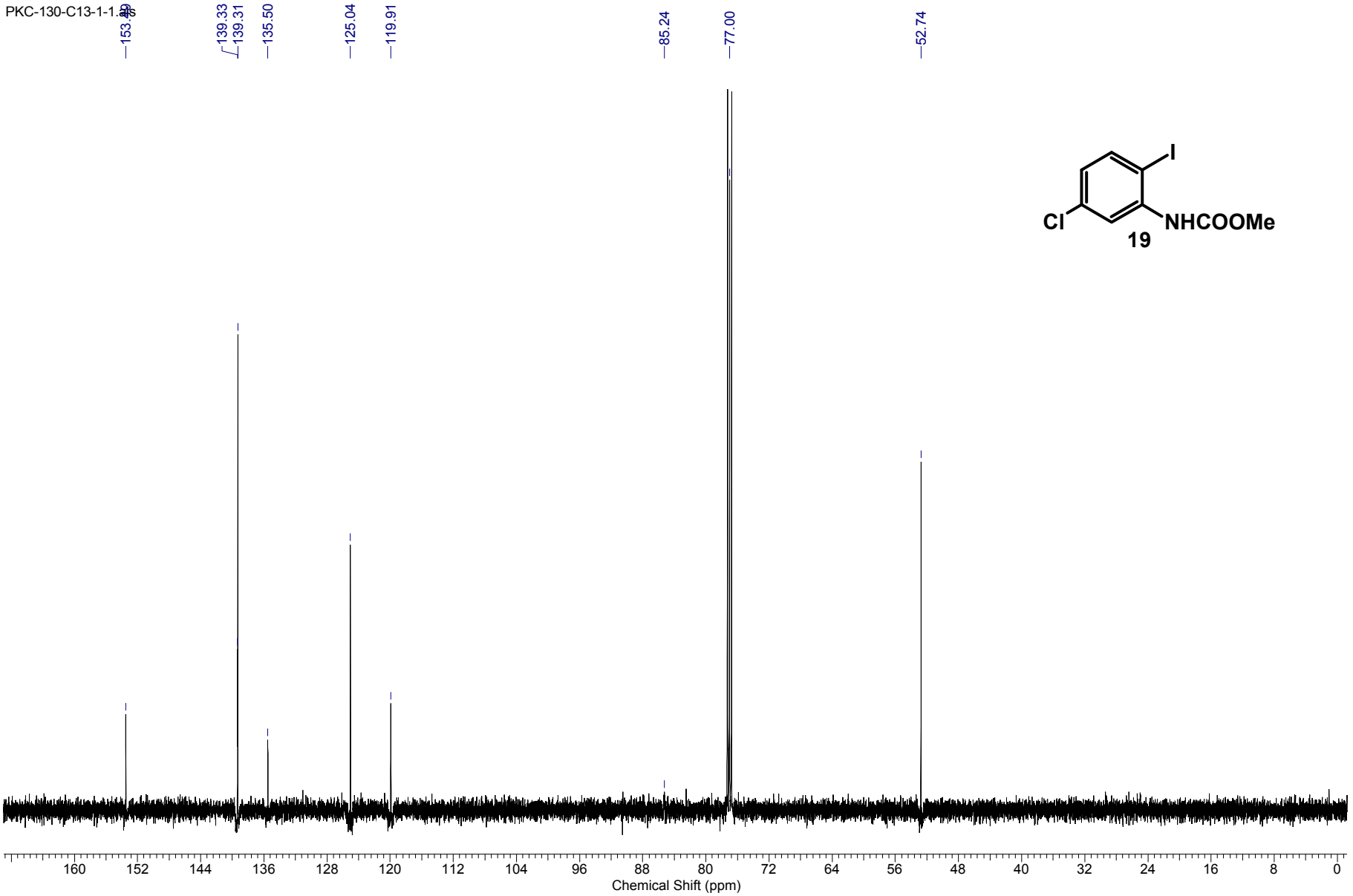

PKC---178-1-1.als
8.03
8.02
7.74
7.73
7.72
7.33
7.31
7.30
7.29
7.26
6.97
6.79
6.77
6.77
6.76
6.76
3.78
I
NHCOOMe
17
0.97
1.00
1.04
0.96
1.03
2.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

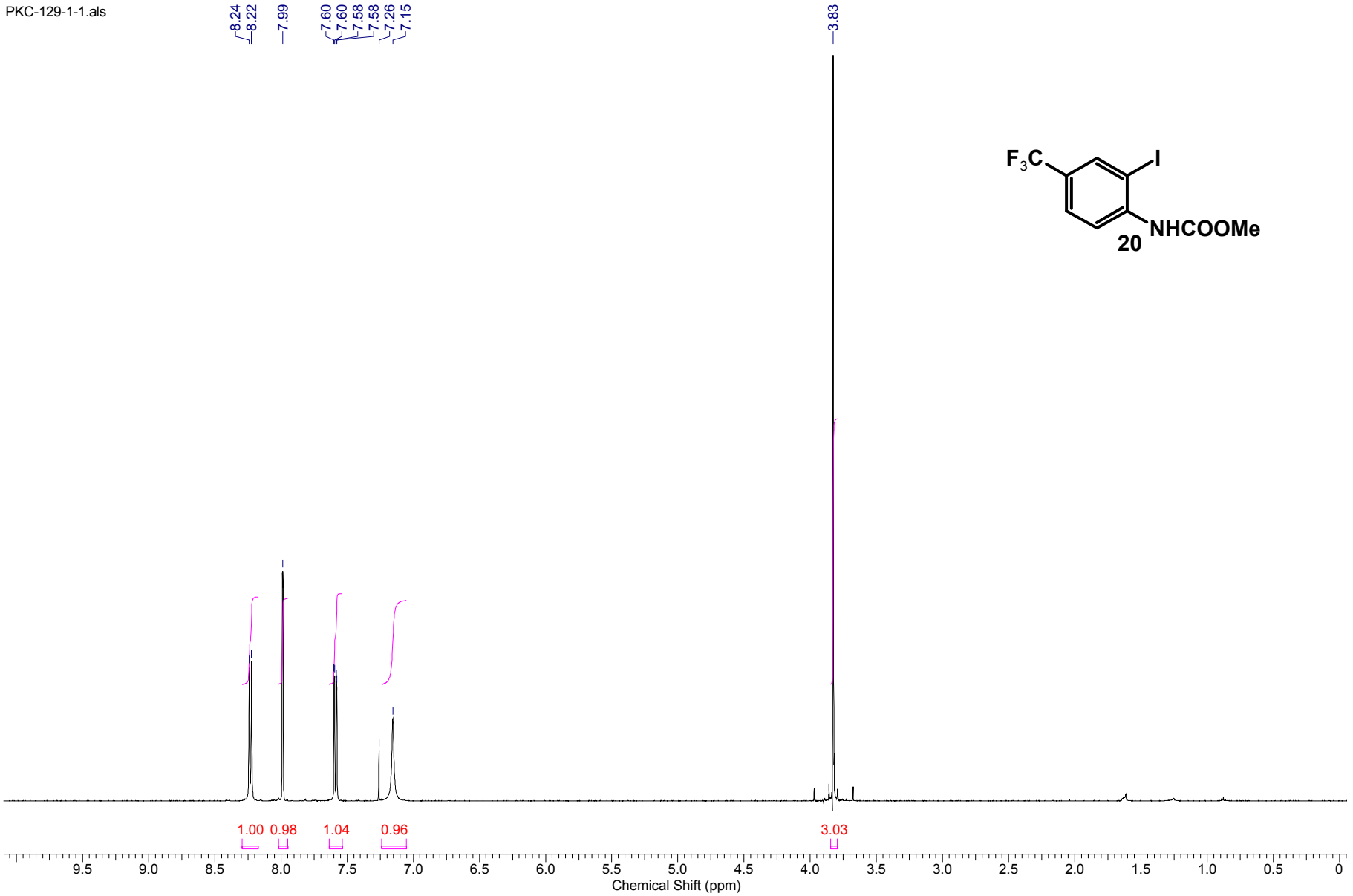

CPK---178-C13-1-1.als
153.67
138.70
138.18
129.13
124.99
120.23
88.86
77.00
52.43
I
NHCOOMe
17
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

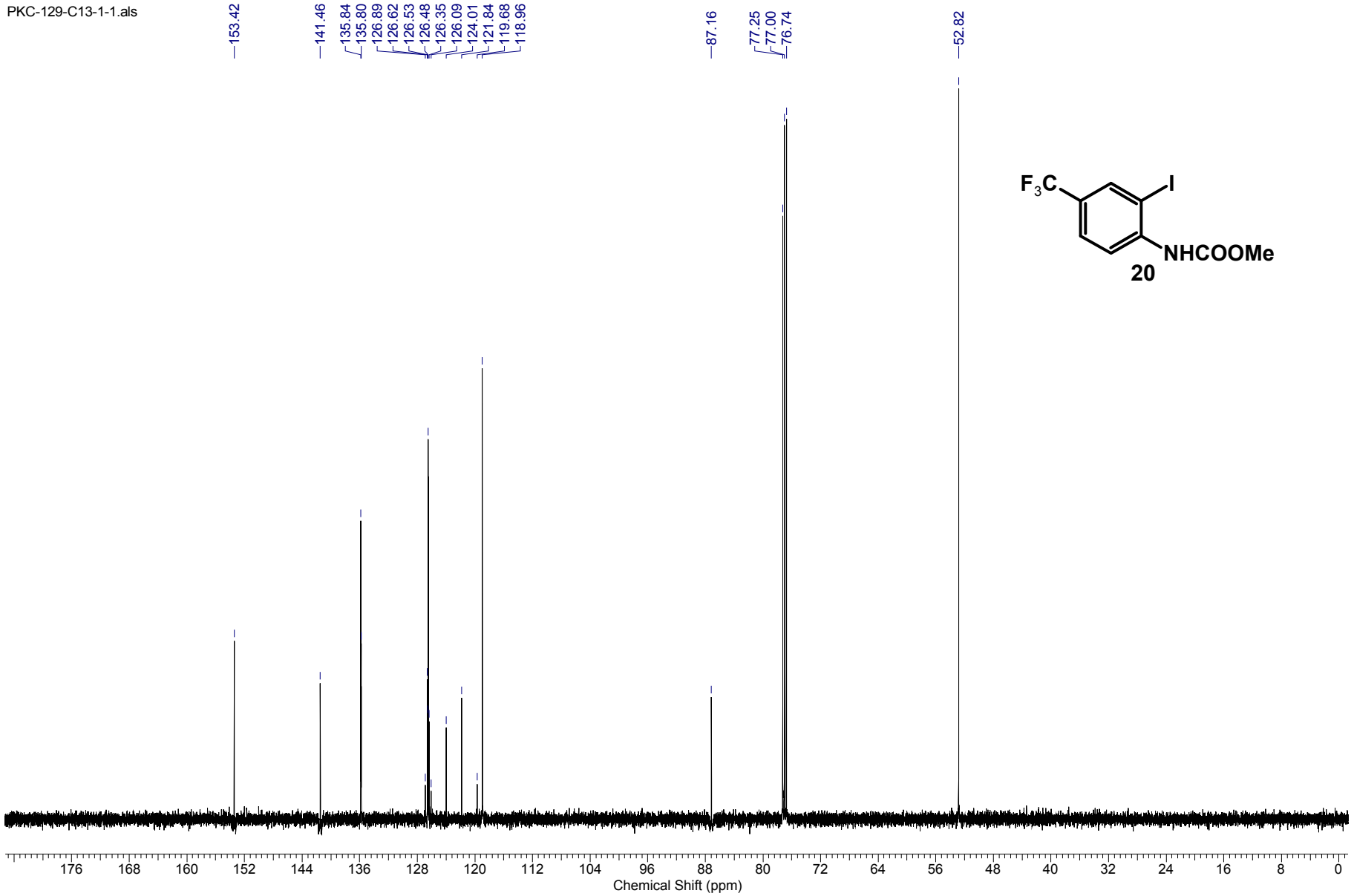

PKC---139-1-1.als
7.75
7.56
7.54
7.26
6.96
6.42
6.41
6.40
6.40
3.78
I
O
NHCOOMe
18
1.01
1.05
1.01
1.06
5.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

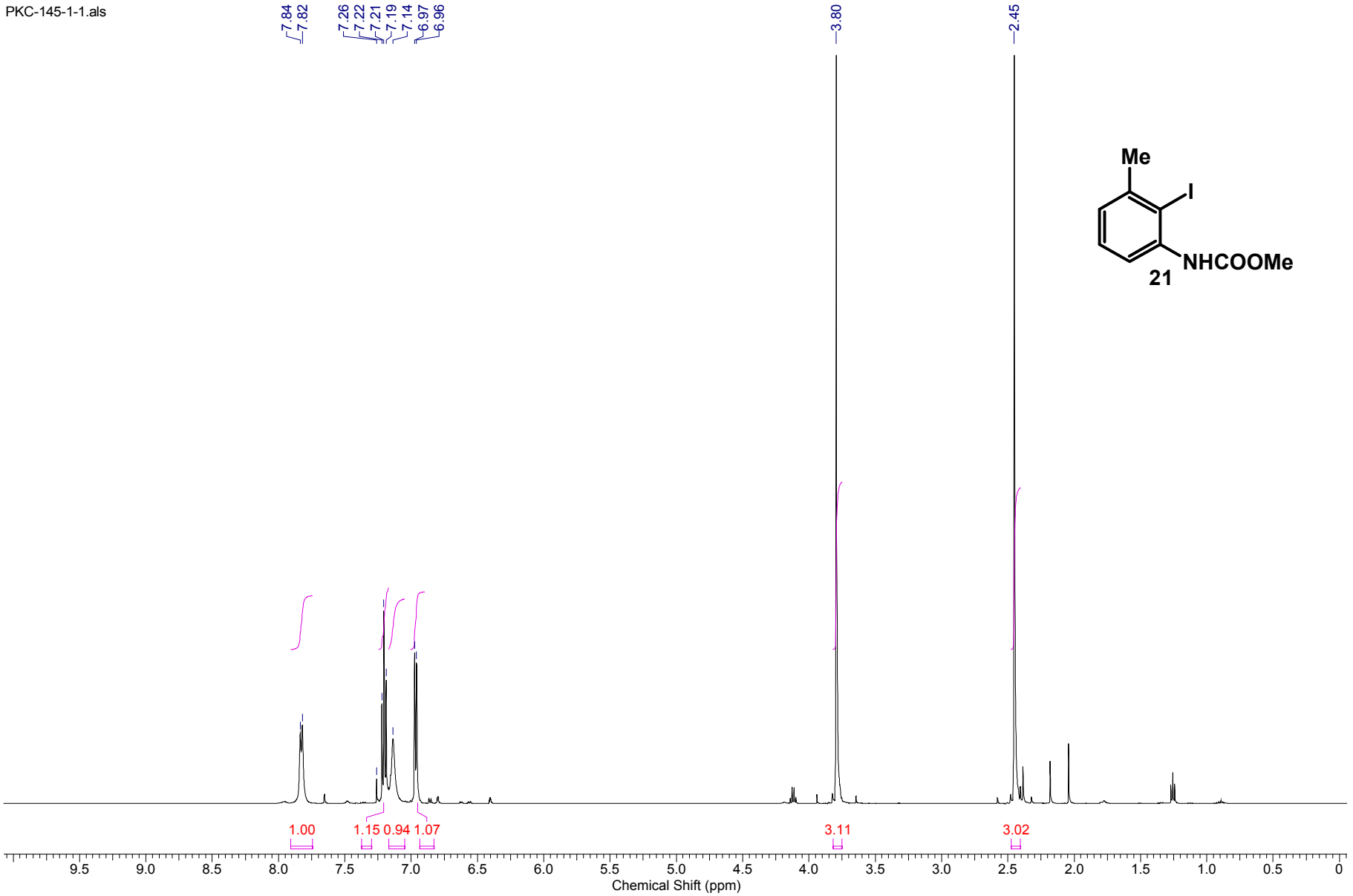

CPK---139-C13-1-1.als
160.60
153.63
139.01
138.65
111.87
105.38
77.26
77.00
76.75
55.32
52.44
I
O
NHCOOMe
18
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

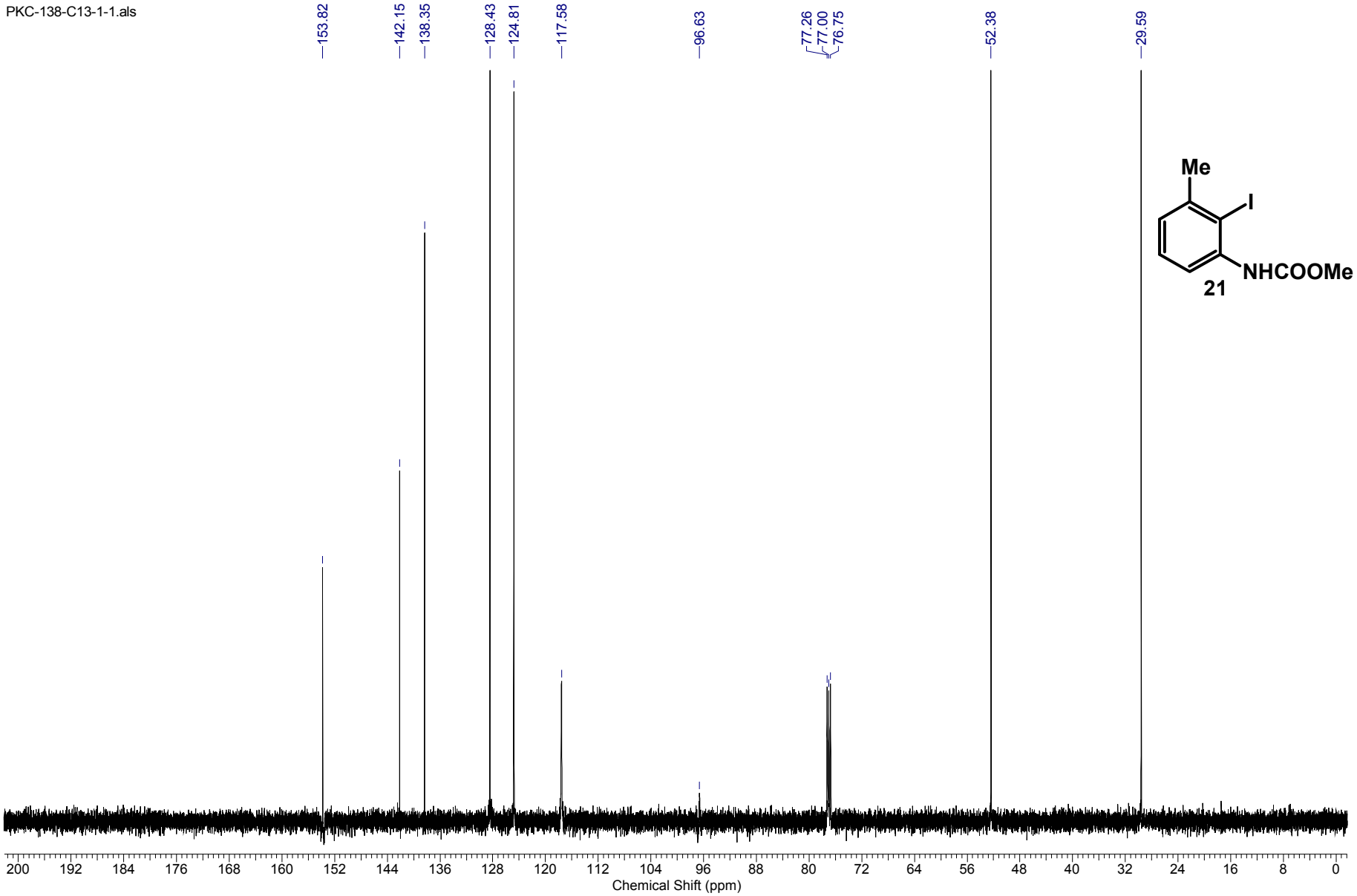

PKC-130-1-1.als
8.15
7.66
7.65
7.64
7.63
7.26
6.97
6.82
6.81
6.80
6.80
3.81
Cl
I
NHCOOMe
19
0.88
0.99
0.95
1.00
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

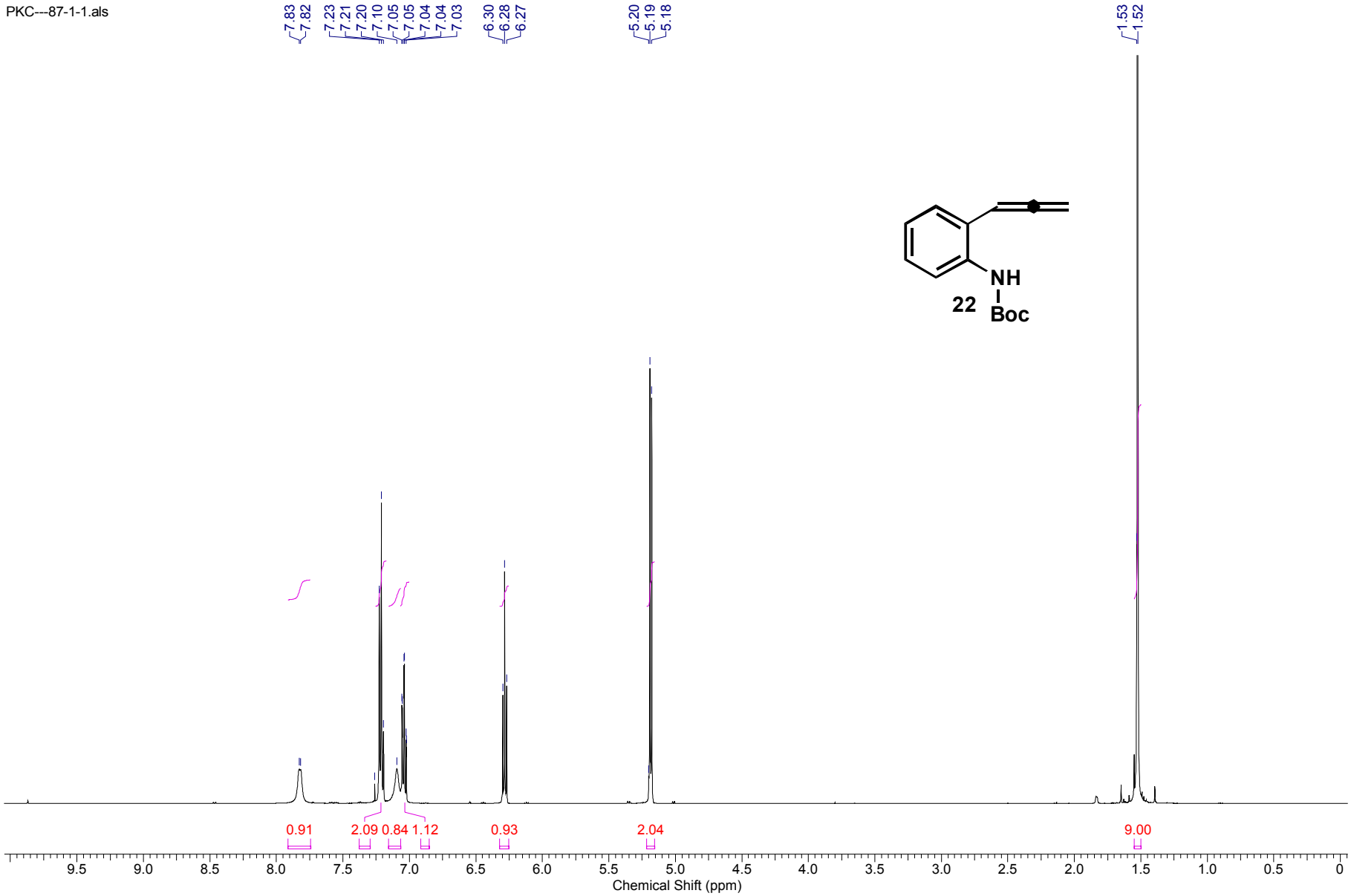

PKC-130-C13-1-1.4s
153.40
139.33
139.31
135.50
125.04
119.91
85.24
77.00
52.74
Cl
I
NHCOOMe
19
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

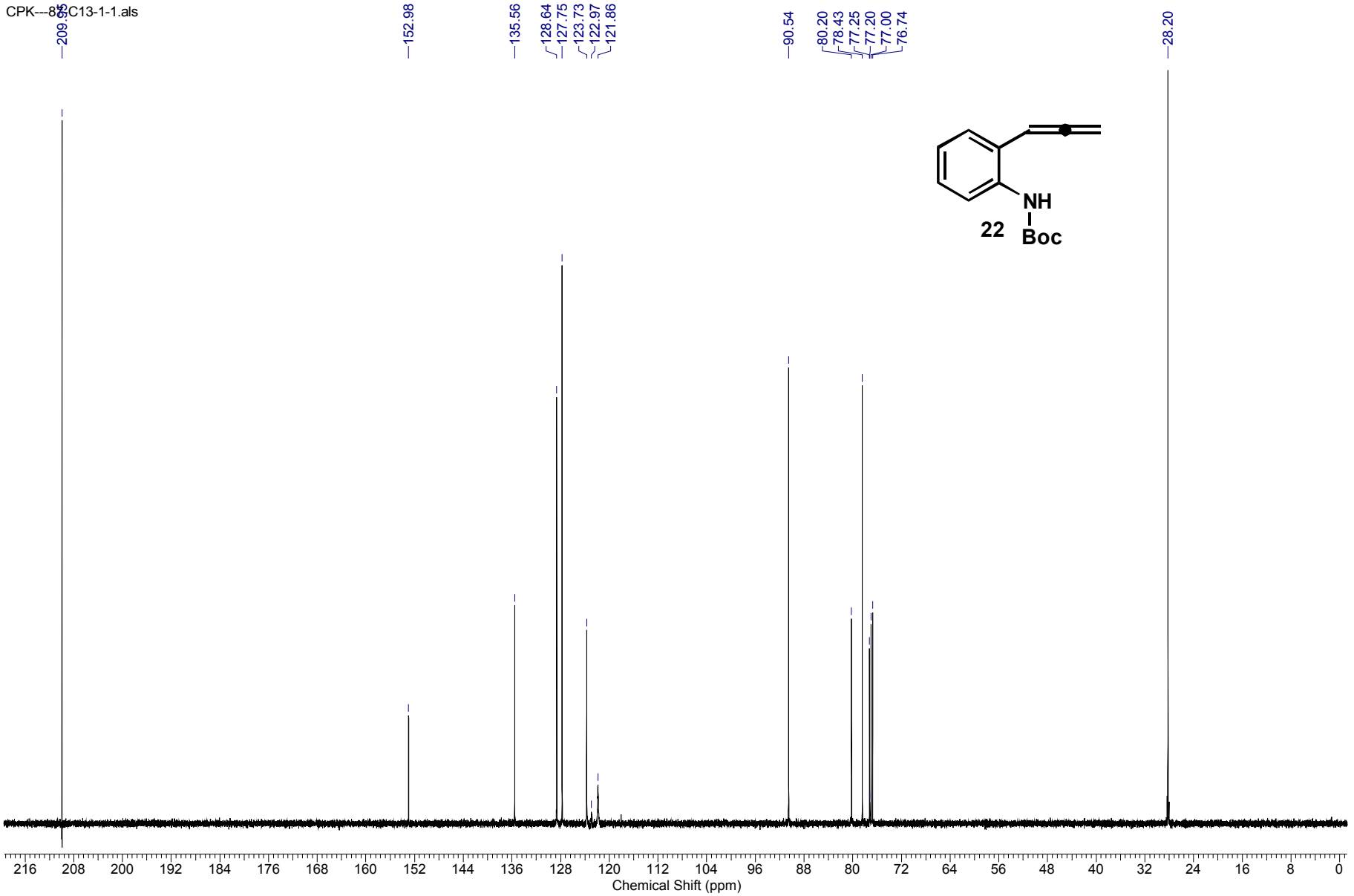

PKC-129-1-1.als
8.24
8.22
7.99
7.60
7.60
7.58
7.58
7.26
7.15
3.83
F3C
I
NHCOOMe
20
1.00
0.98
1.04
0.96
3.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

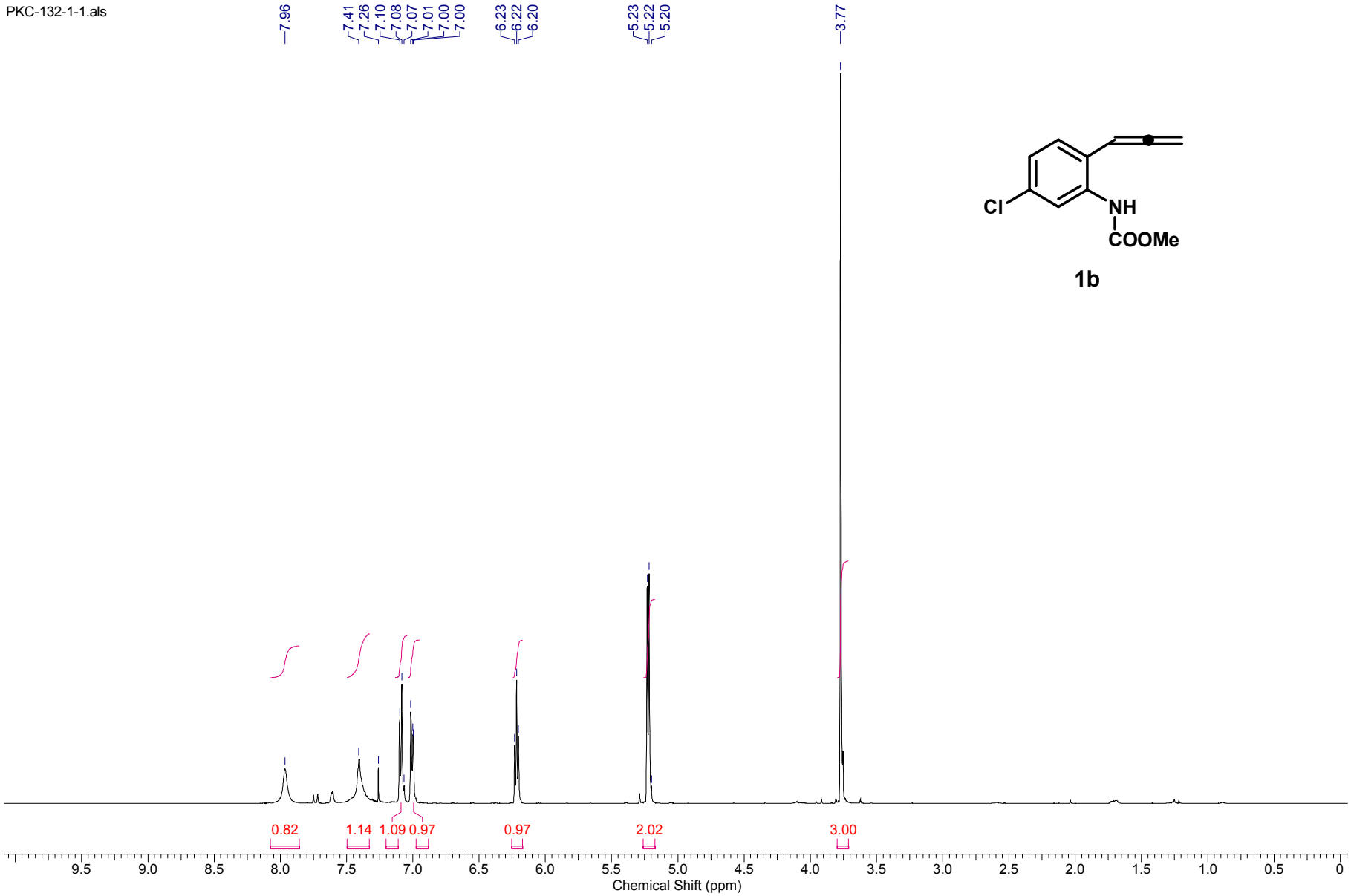

PKC-129-C13-1-1.als
153.42
141.46
135.84
135.80
126.89
126.62
126.53
126.48
126.35
126.09
124.01
121.84
119.68
118.96
87.16
77.25
77.00
76.74
52.82
F3C
I
NHCOOMe
20
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

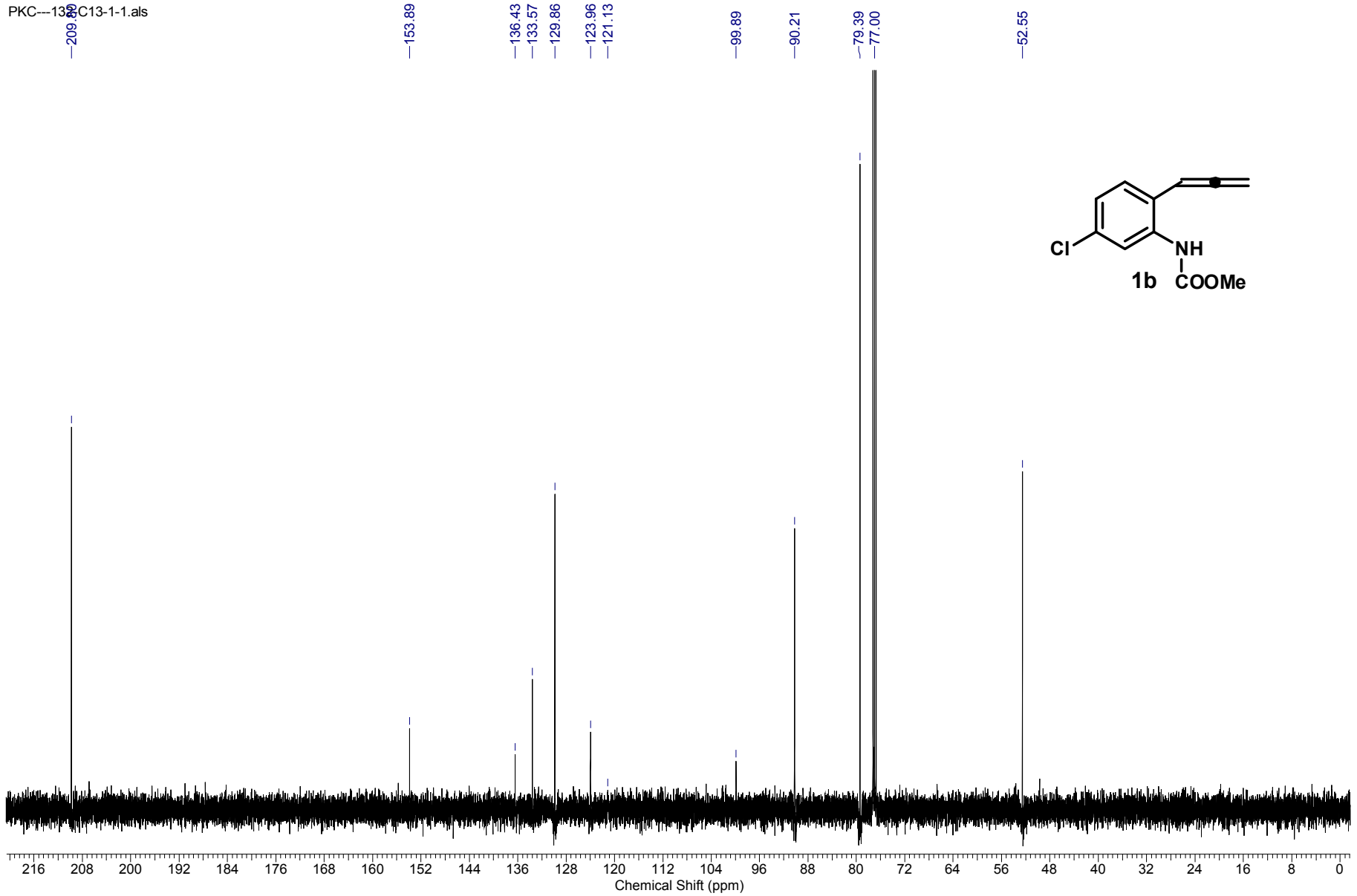

PKC-145-1-1.als
7.84
7.82
7.26
7.22
7.21
7.19
7.14
6.97
6.96
3.80
2.45
Me
I
NHCOOMe
21
1.00
1.15
0.94
1.07
3.11
3.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

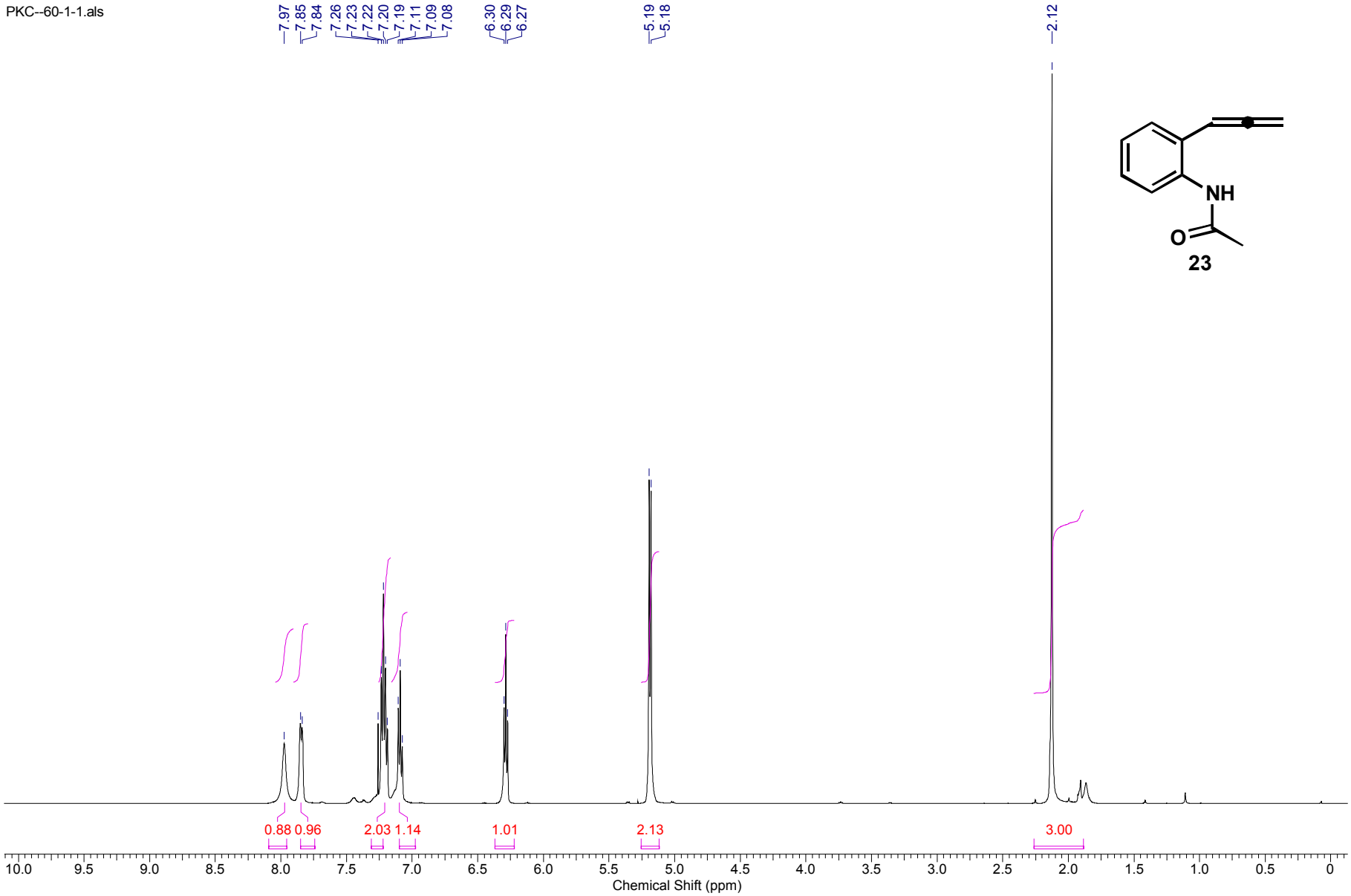

PKC-138-C13-1-1.als
153.82
142.15
138.35
128.43
124.81
117.58
96.63
77.26
77.00
76.75
52.38
29.59
Me
I
NHCOOMe
21
200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

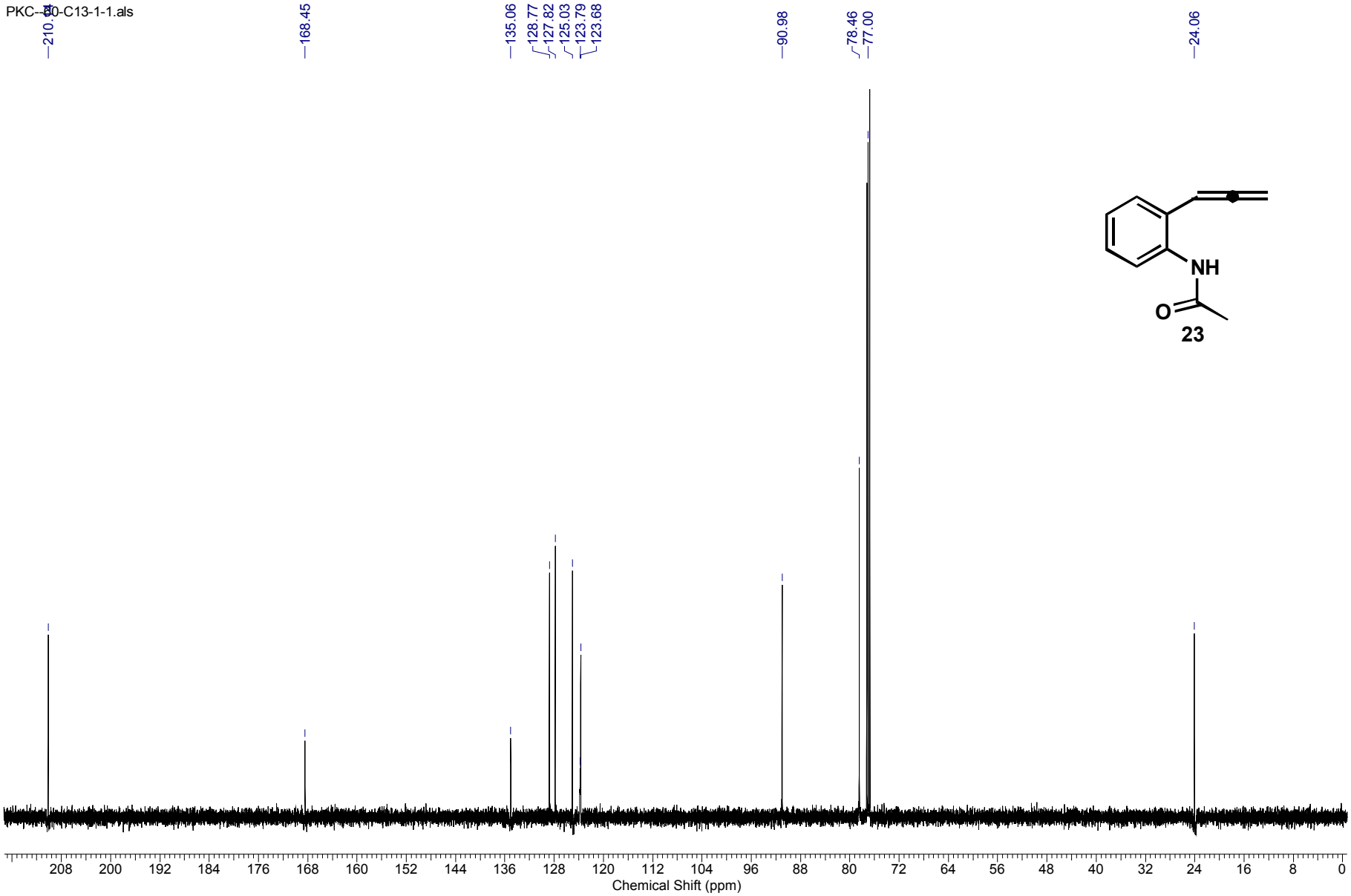

PKC---87-1-1.als
7.83
7.82
7.23
7.21
7.20
7.10
7.05
7.05
7.04
7.04
7.03
6.30
6.28
6.27
5.20
5.19
5.18
1.53
1.52
NH
Boc
22
0.91
2.09
0.84
1.12
0.93
2.04
9.00
Chemical Shift (ppm)

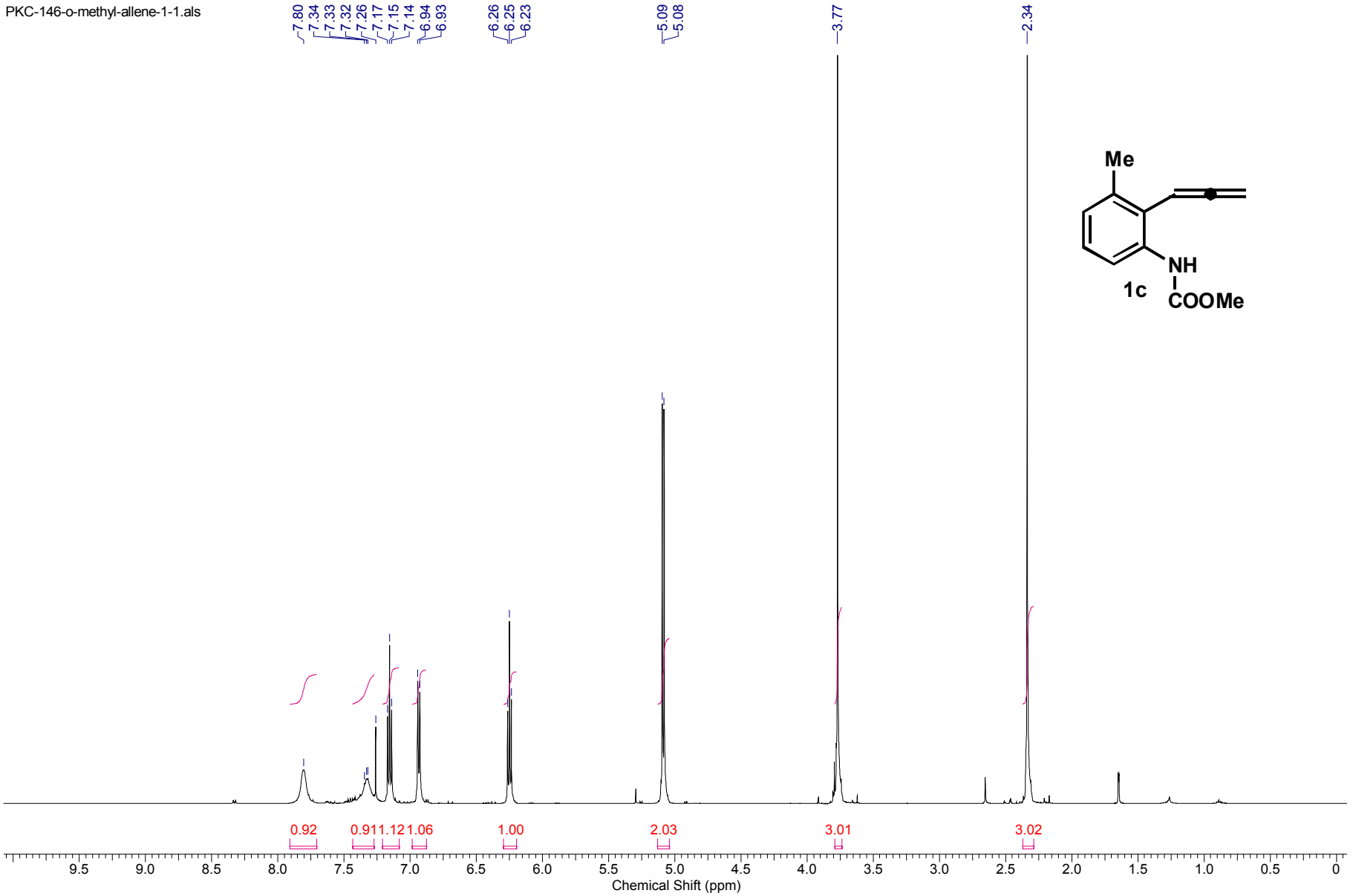

CPK---8-13C13-1-1.als
209.95
152.98
135.56
128.64
127.75
123.73
122.97
121.86
90.54
80.20
78.43
77.25
77.20
77.00
76.74
28.20
NH
Boc
22
216 208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

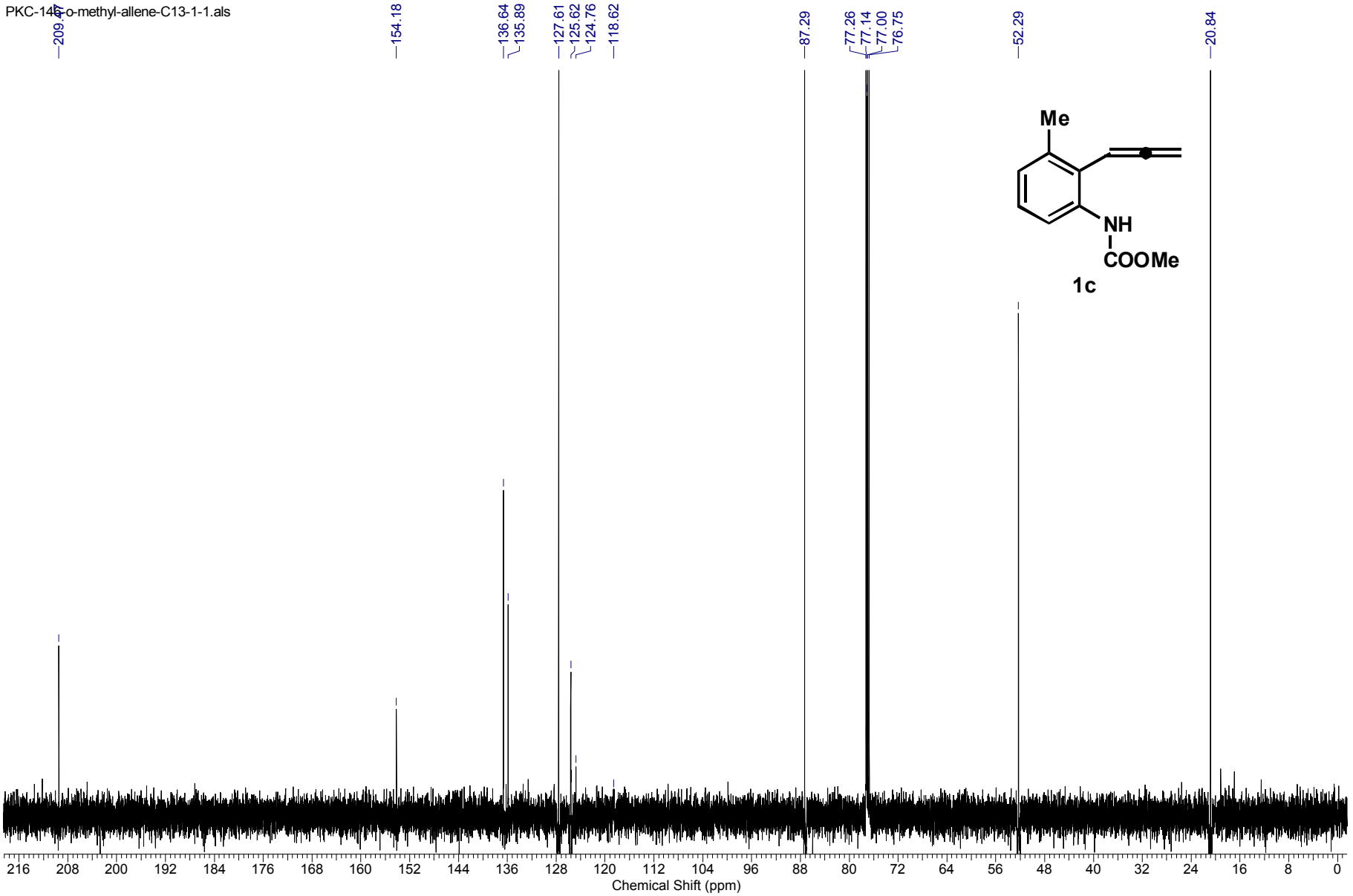

PKC-132-1-1.als
7.96
7.41
7.26
7.10
7.08
7.07
7.01
7.00
7.00
6.23
6.22
6.20
5.23
5.22
5.20
3.77
Cl
NH
COOMe
1b
0.82
1.14
1.09
0.97
0.97
2.02
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

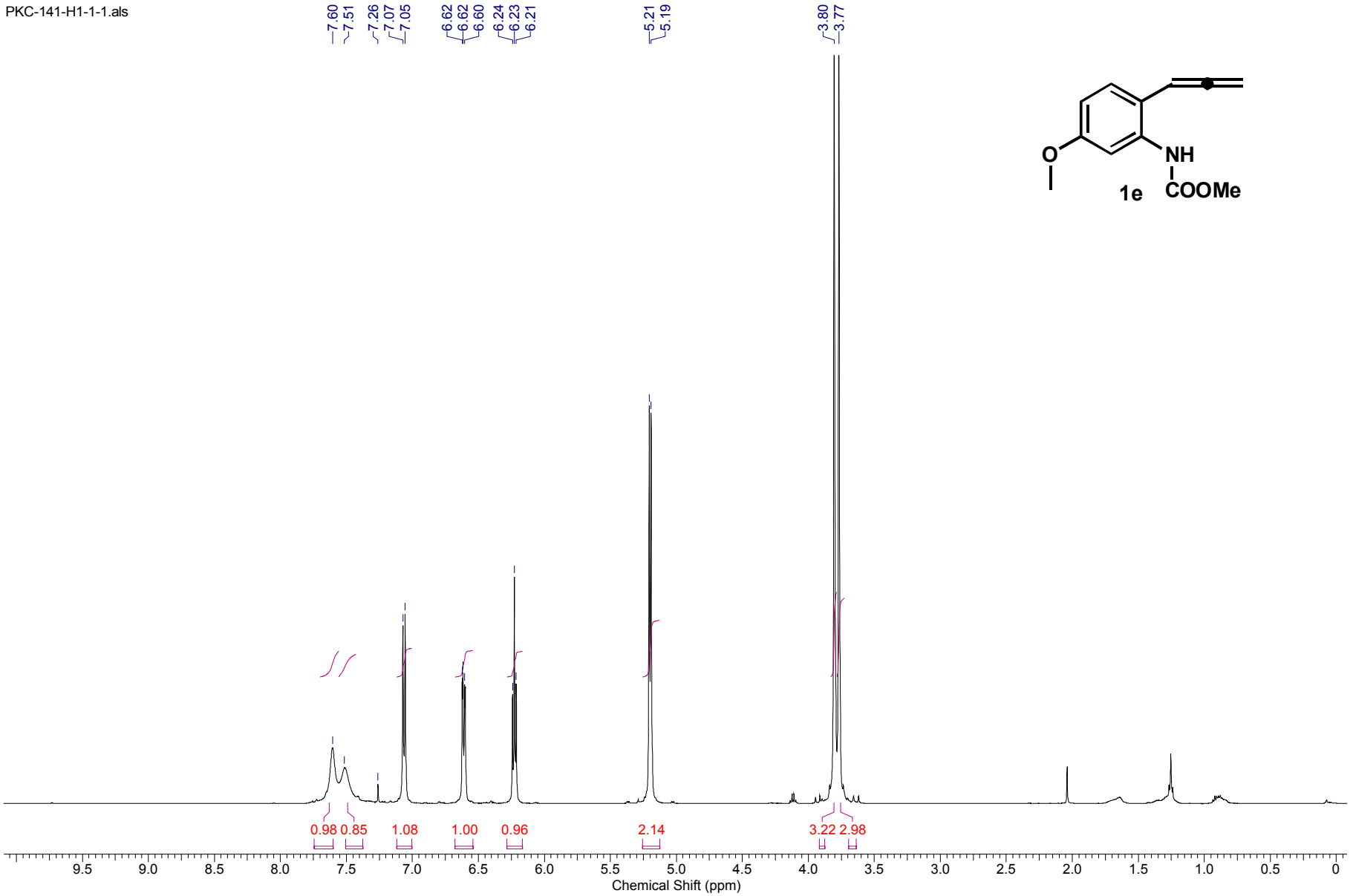

PKC---13-C13-1-1.als
209.80
153.89
136.43
133.57
129.86
123.96
121.13
99.89
90.21
79.39
77.00
52.55
Cl
NH
COOMe
1b
216 208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

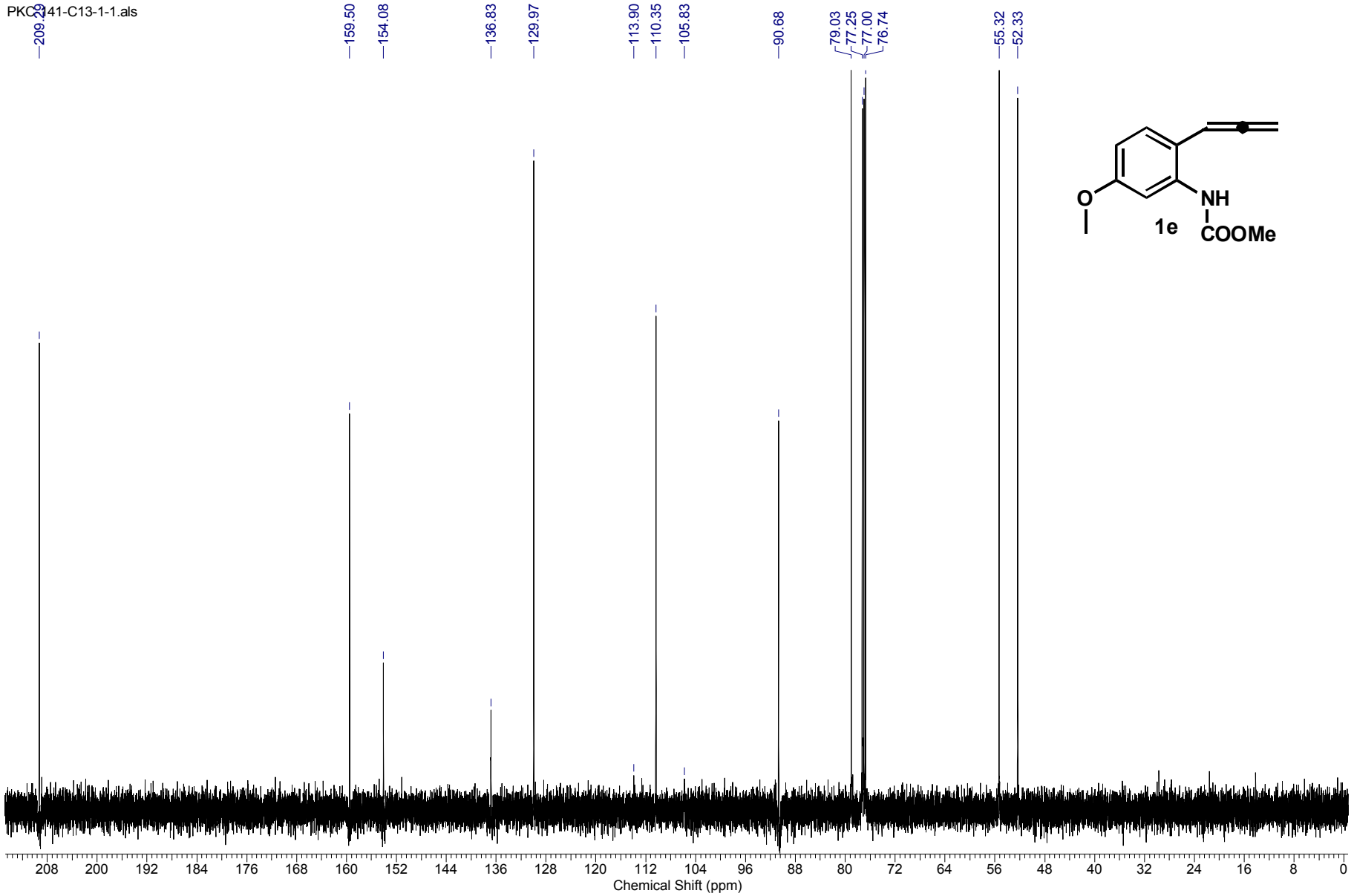

PKC--60-1-1.als
7.97
7.85
7.84
7.26
7.23
7.22
7.20
7.19
7.11
7.09
7.08
6.30
6.29
6.27
5.19
5.18
2.12
NH
O
23
0.88
0.96
2.03
1.14
1.01
2.13
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

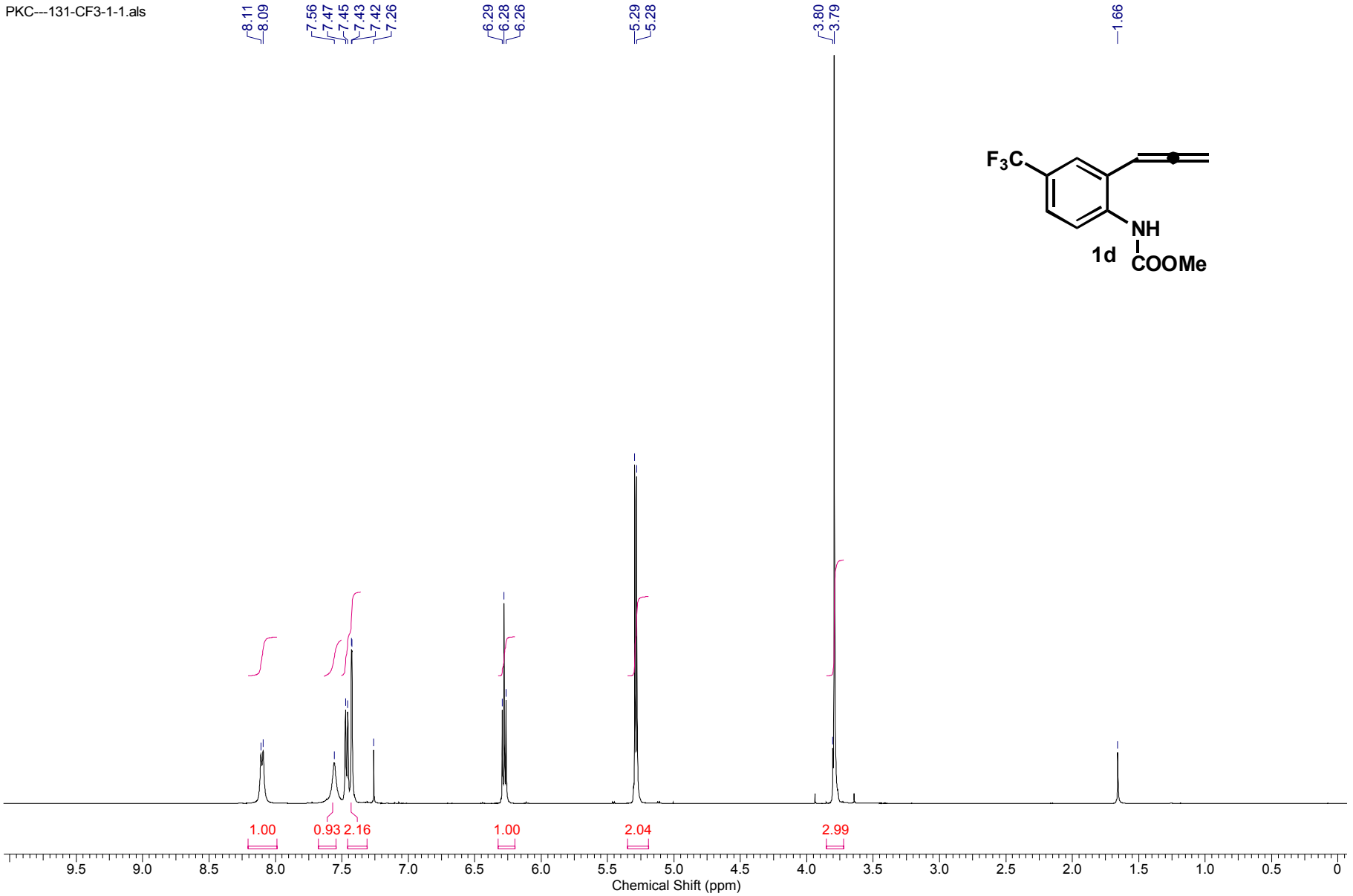

PKC--30-C13-1-1.als
210.31
168.45
135.06
128.77
127.82
125.03
123.79
123.68
90.98
78.46
77.00
24.06
NH
O
23
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

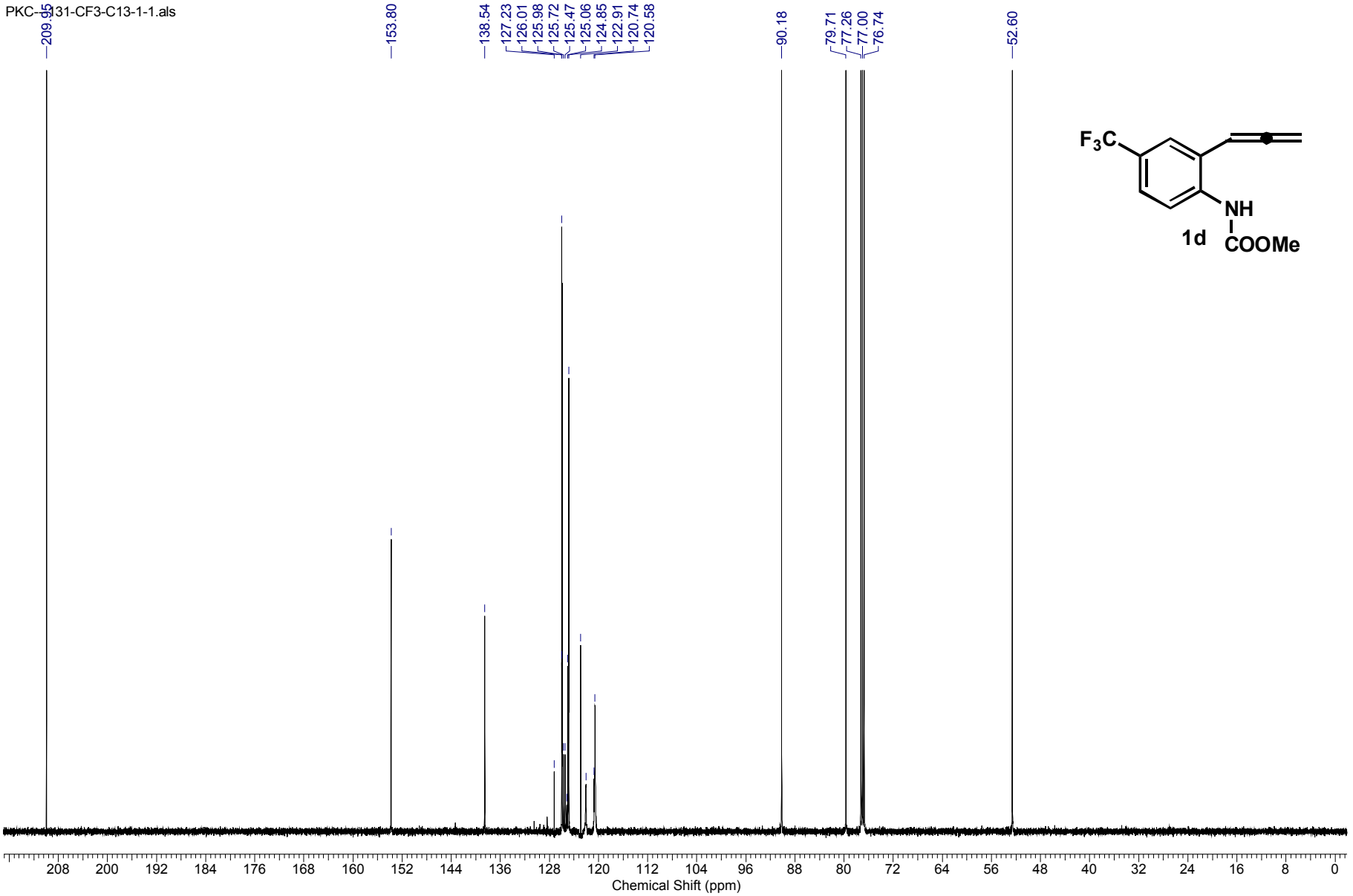

PKC-146-o-methyl-allene-1-1.als
7.80
7.34
7.33
7.32
7.26
7.17
7.15
7.14
6.94
6.93
6.26
6.25
6.23
5.09
5.08
3.77
2.34
Me
NH
COOMe
1c
0.92
0.91
1.12
1.06
1.00
2.03
3.01
3.02
Chemical Shift (ppm)

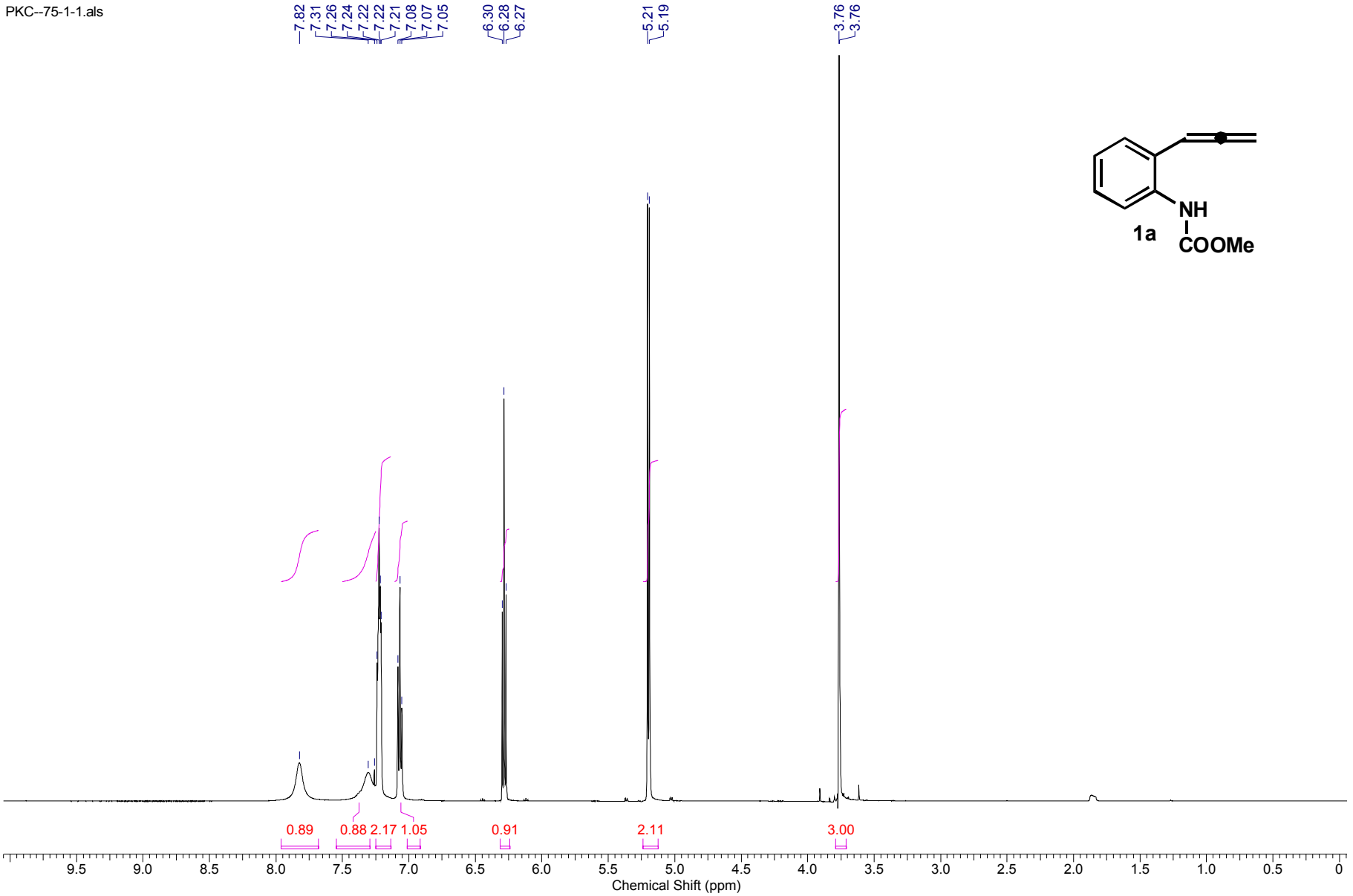

PKC-146-o-methyl-allene-C13-1-1.als
209.47
154.18
136.64
135.89
127.61
125.62
124.76
118.62
87.29
77.26
77.14
77.00
76.75
52.29
20.84
Me
NH
COOMe
1c
216 208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

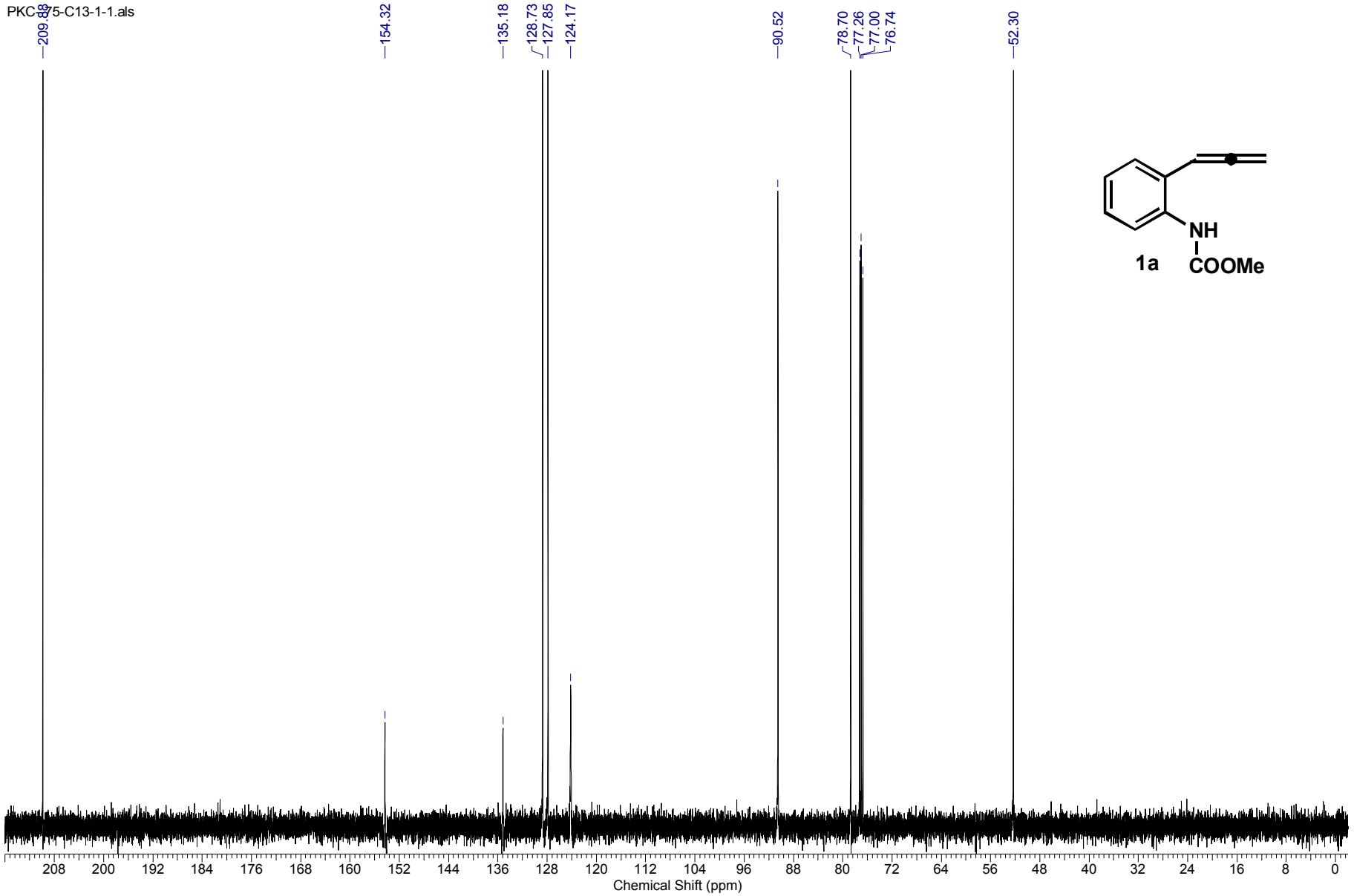

PKC-141-H1-1-1.als
7.60
7.51
7.26
7.07
7.05
6.62
6.62
6.60
6.24
6.23
6.21
5.21
5.19
3.80
3.77
O
NH
COOMe
1e
0.98 0.85 1.08 1.00 0.96 2.14 3.22 2.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

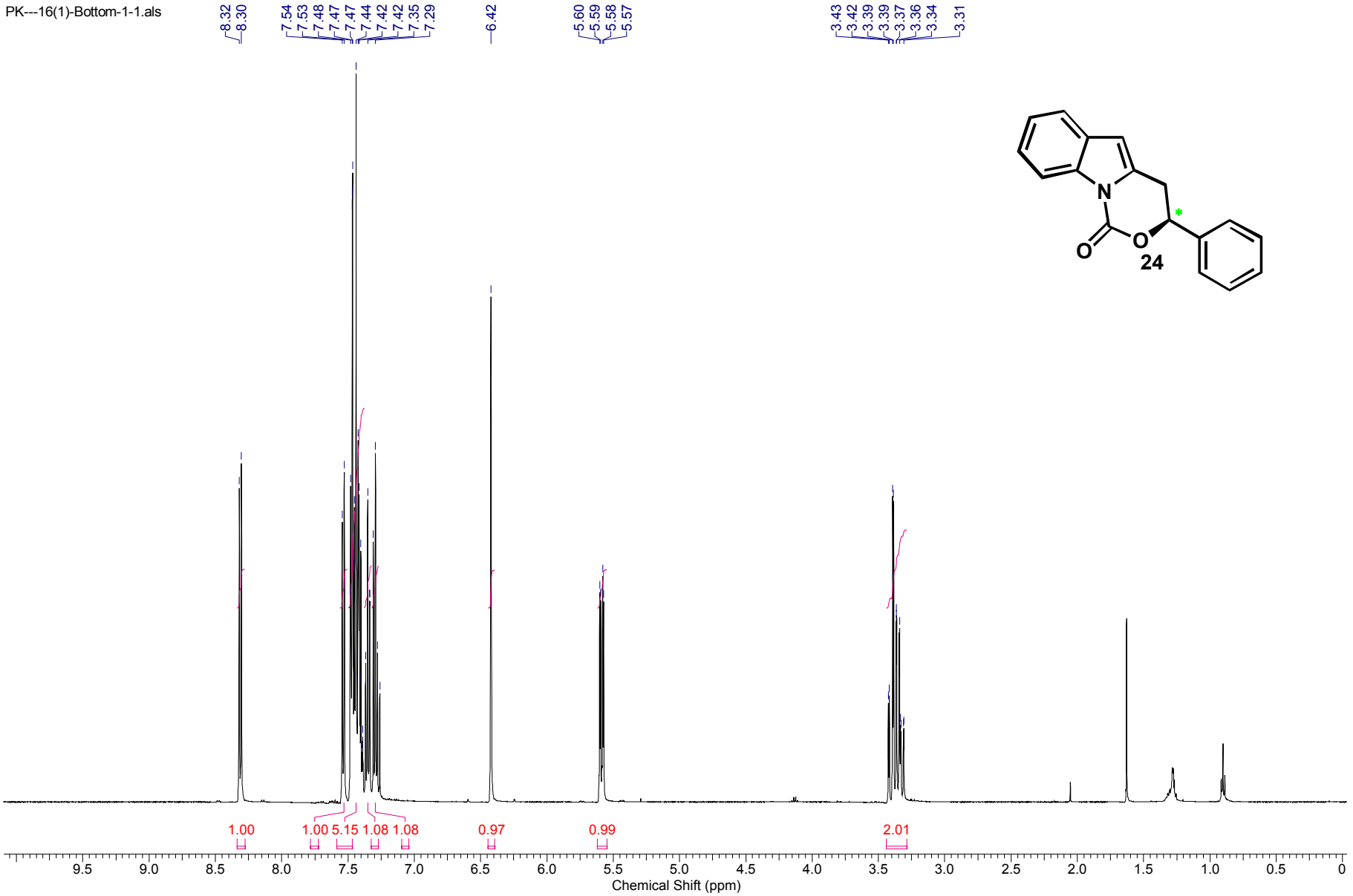

PKC241-C13-1-1.als
209.29
159.50
154.08
136.83
129.97
113.90
110.35
105.83
90.68
79.03
77.25
77.00
76.74
55.32
52.33
O
NH
COOMe
1e
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

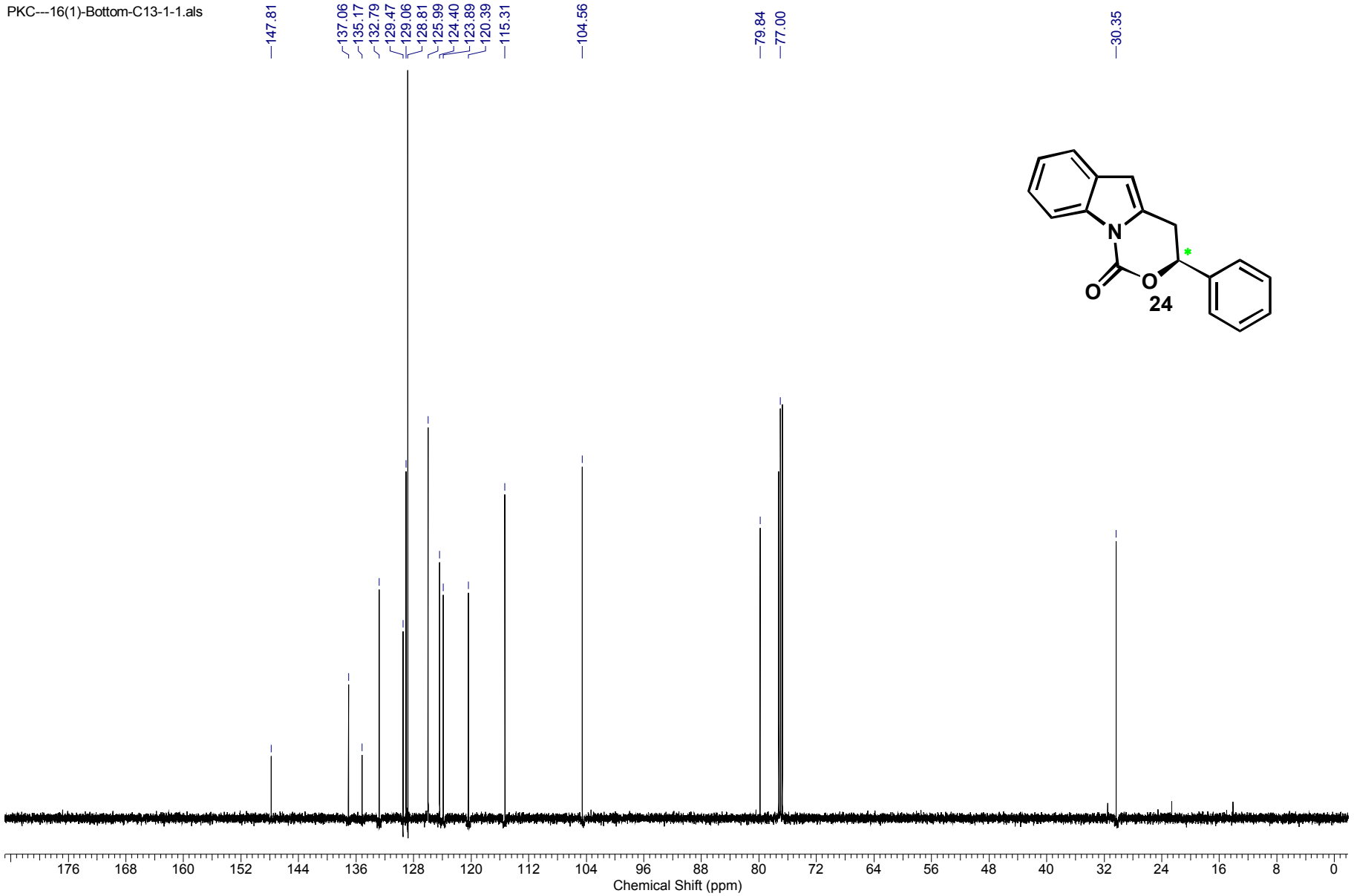

PKC---131-CF3-1-1.als
8.11
8.09
7.56
7.47
7.45
7.43
7.42
7.26
6.29
6.28
6.26
5.29
5.28
3.80
3.79
1.66
F3C
NH
COOMe
1d
1.00
0.93
2.16
1.00
2.04
2.99
Chemical Shift (ppm)

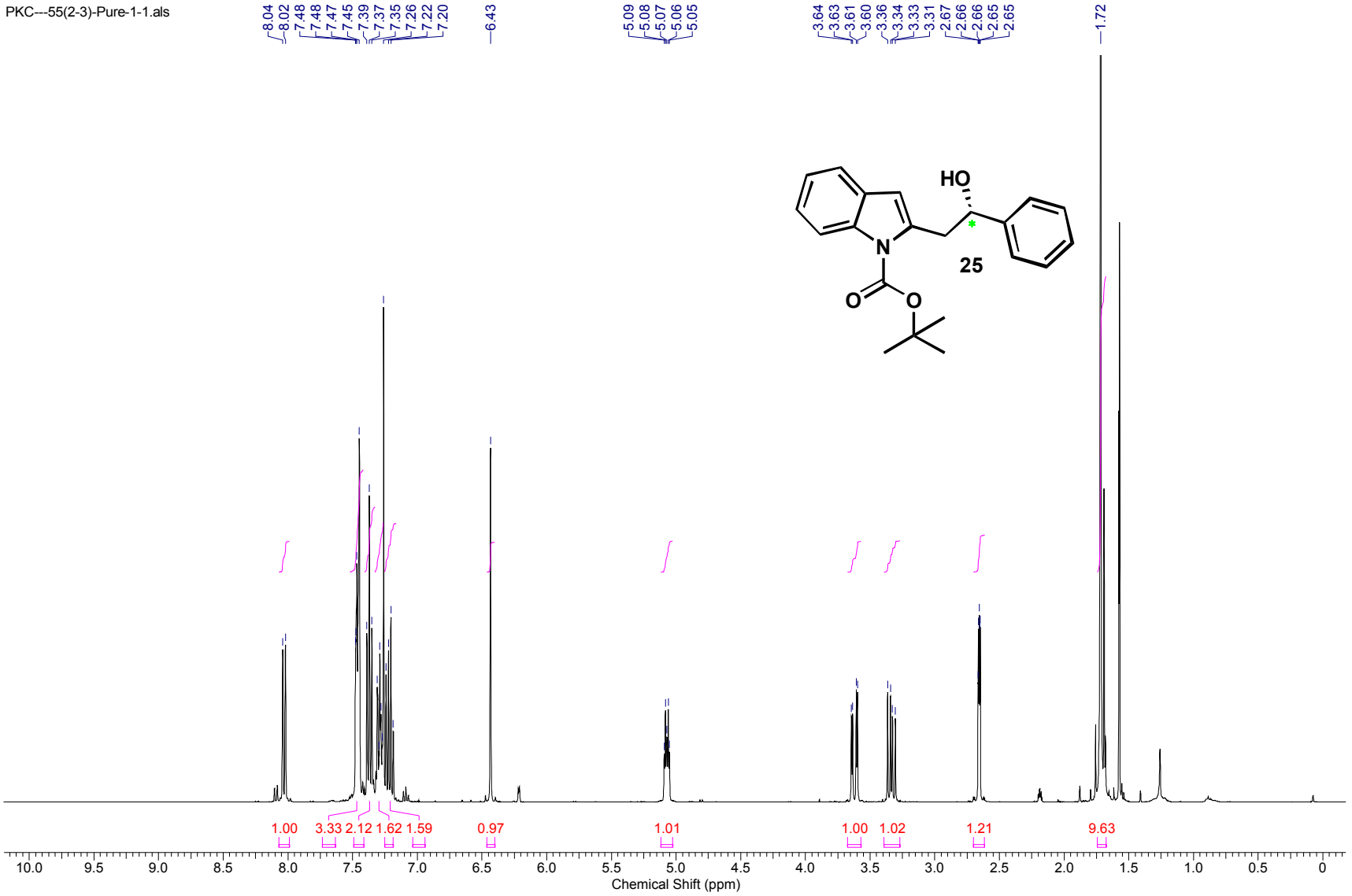

PKC-5131-CF3-C13-1-1.als
209.95
153.80
138.54
127.23
126.01
125.98
125.72
125.47
125.06
124.85
122.91
120.74
120.58
90.18
79.71
77.26
77.00
76.74
52.60
F3C
NH
COOMe
1d
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

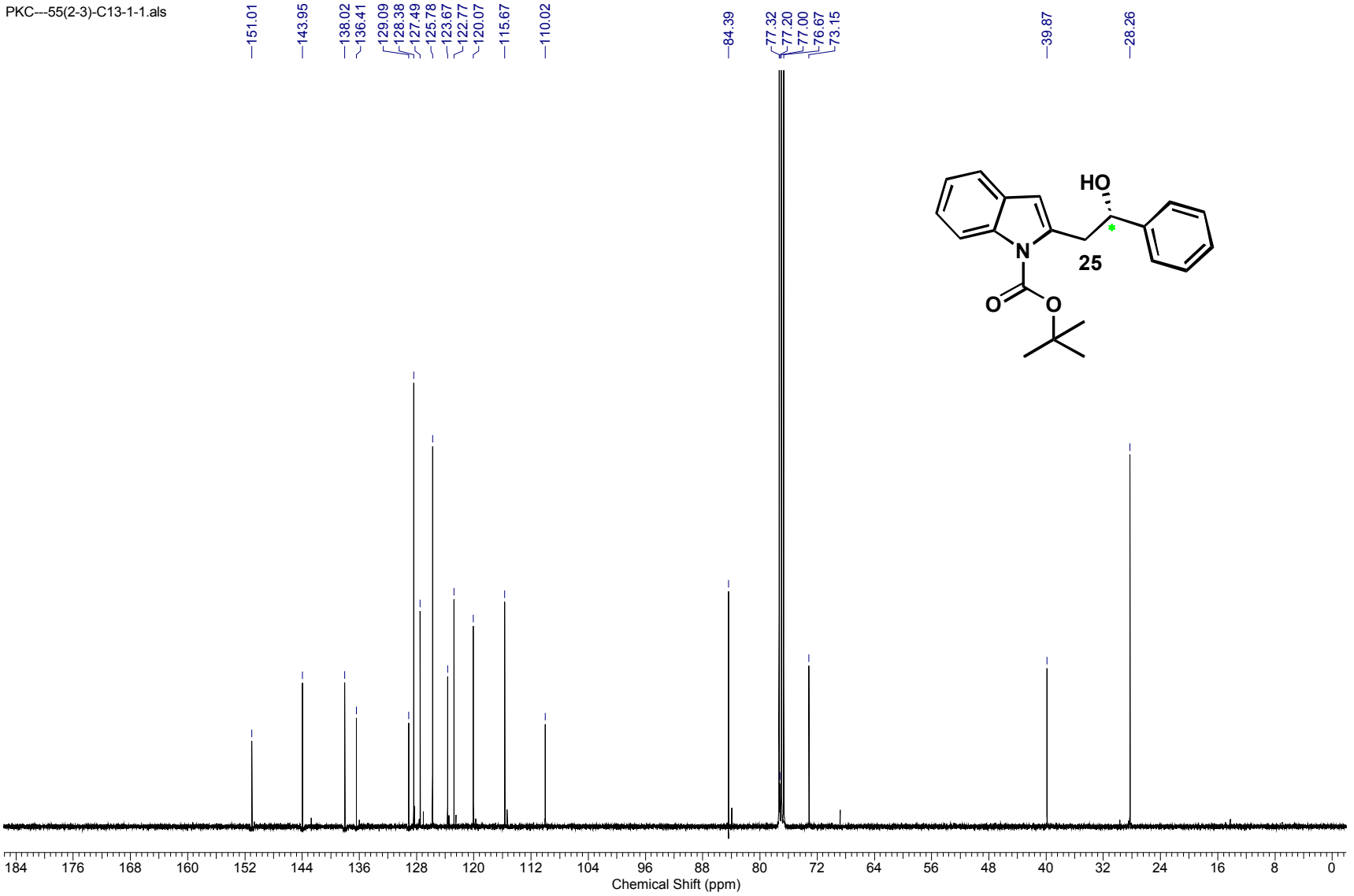

PKC--75-1-1.als
7.82
7.31
7.26
7.24
7.22
7.22
7.21
7.08
7.07
7.05
6.30
6.28
6.27
5.21
5.19
3.76
3.76
NH
COOMe
1a
0.89
0.88
2.17
1.05
0.91
2.11
3.00
Chemical Shift (ppm)

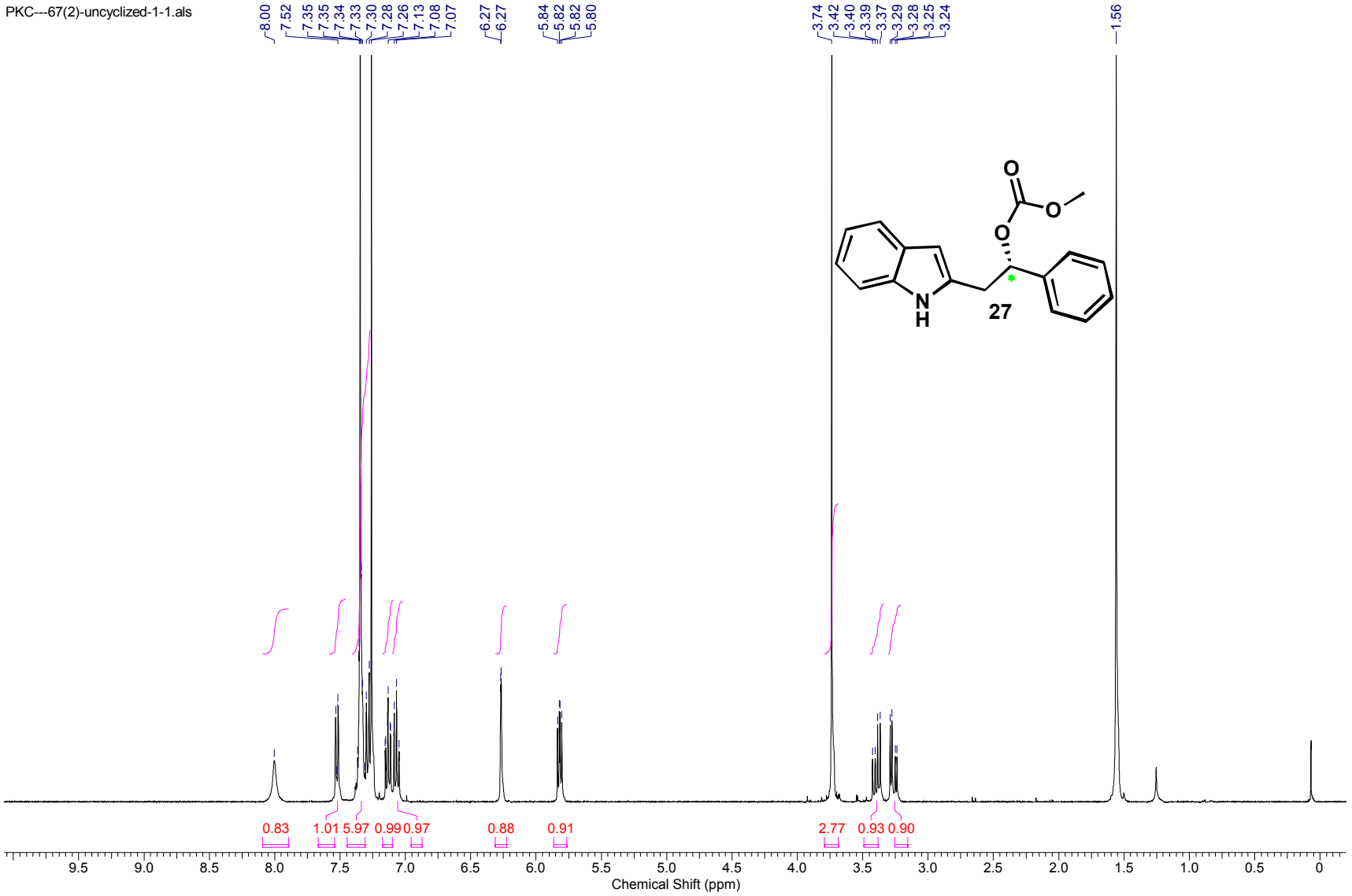

PKC-75-C13-1-1.als
209.88
154.32
135.18
128.73
127.85
124.17
90.52
78.70
77.26
77.00
76.74
52.30
NH
COOMe
1a
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

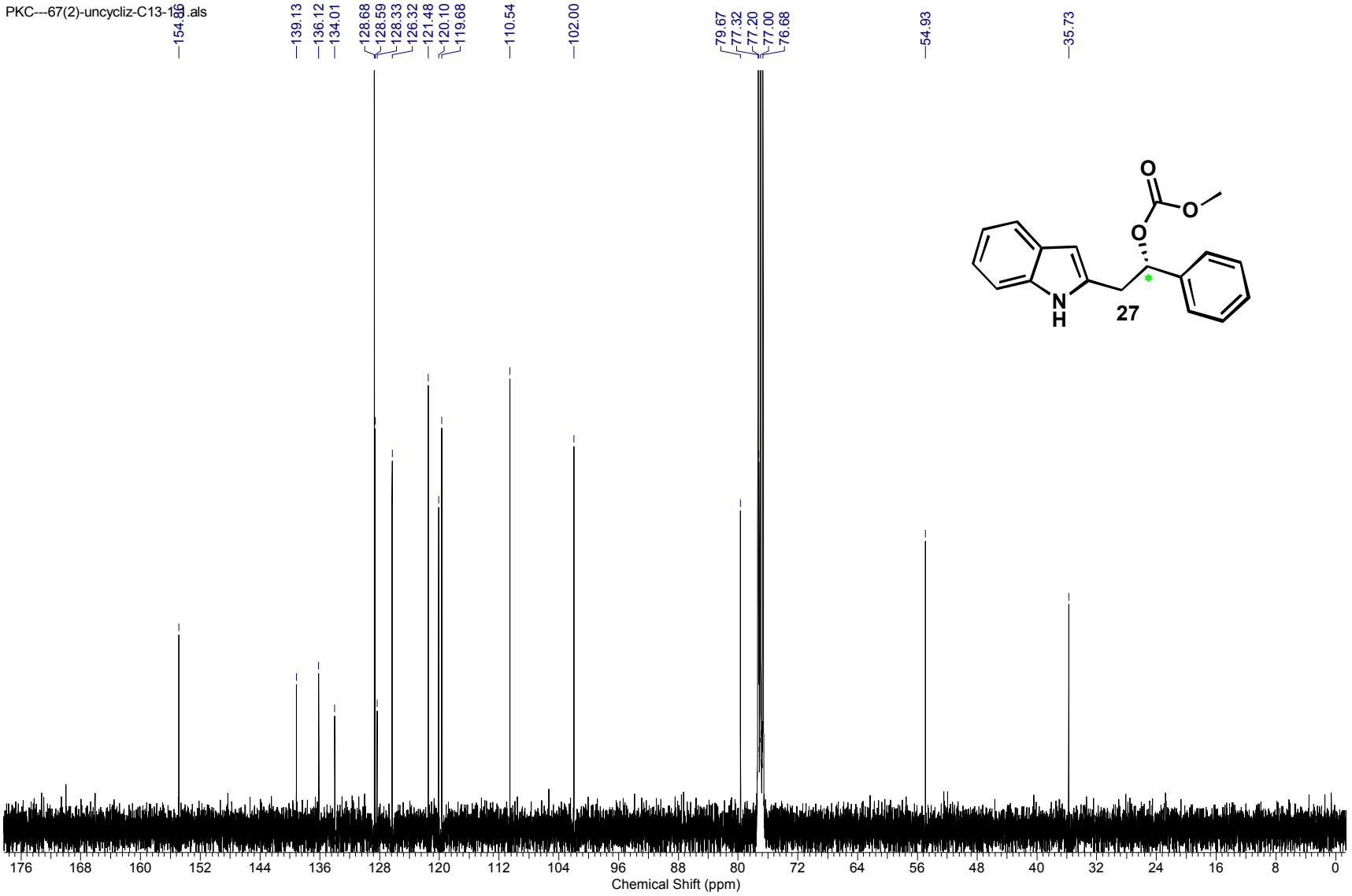

PK---16(1)-Bottom-1-1.als
8.32
8.30
7.54
7.53
7.48
7.47
7.47
7.44
7.42
7.42
7.35
7.29
6.42
5.60
5.59
5.58
5.57
3.43
3.42
3.39
3.39
3.37
3.36
3.34
3.31
N
O
O
*
24
1.00
1.00
5.15
1.08
1.08
0.97
0.99
2.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

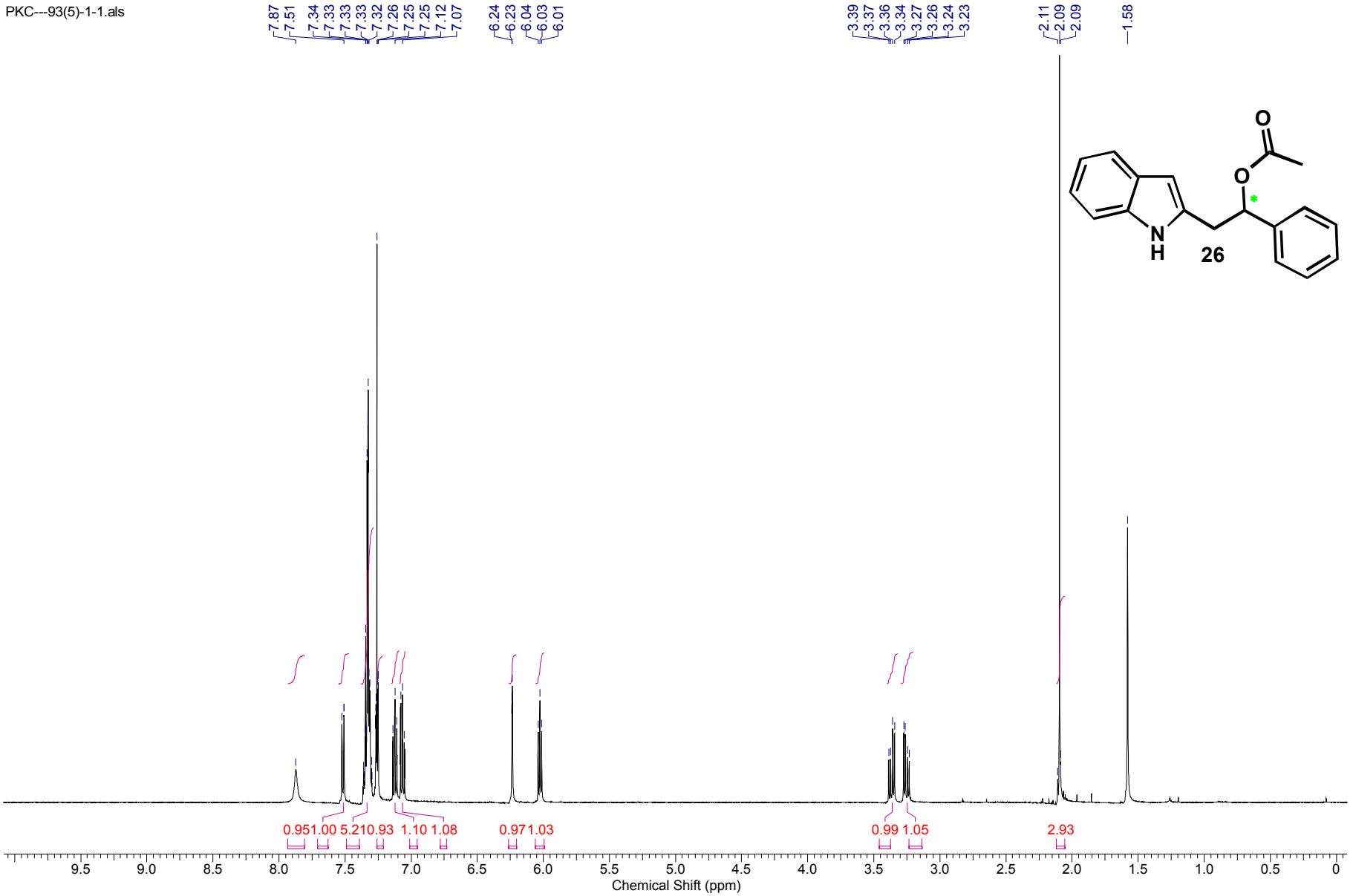

PKC---16(1)-Bottom-C13-1-1.als
147.81
137.06
135.17
132.79
129.47
129.06
128.81
125.99
124.40
123.89
120.39
115.31
104.56
79.84
77.00
30.35
N
O
O
24
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

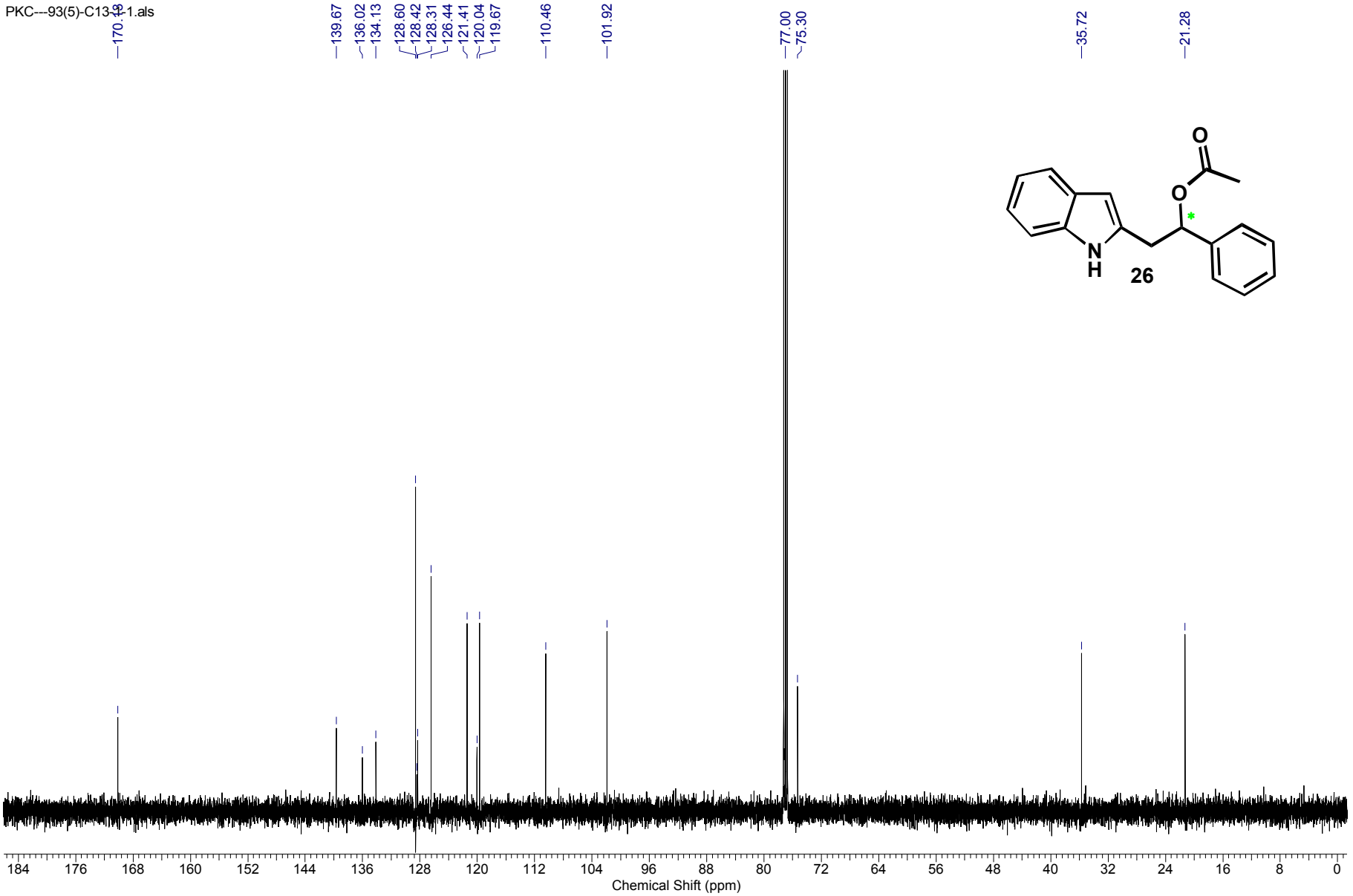

PKC---55(2-3)-Pure-1-1.als
8.04
8.02
7.48
7.48
7.47
7.45
7.39
7.37
7.35
7.26
7.22
7.20
6.43
5.09
5.08
5.07
5.06
5.05
3.64
3.63
3.61
3.60
3.36
3.34
3.33
3.31
2.67
2.66
2.66
2.65
2.65
1.72
HO
N
O
O
25
1.00
3.33
2.12
1.62
1.59
0.97
1.01
1.00
1.02
1.21
9.63
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

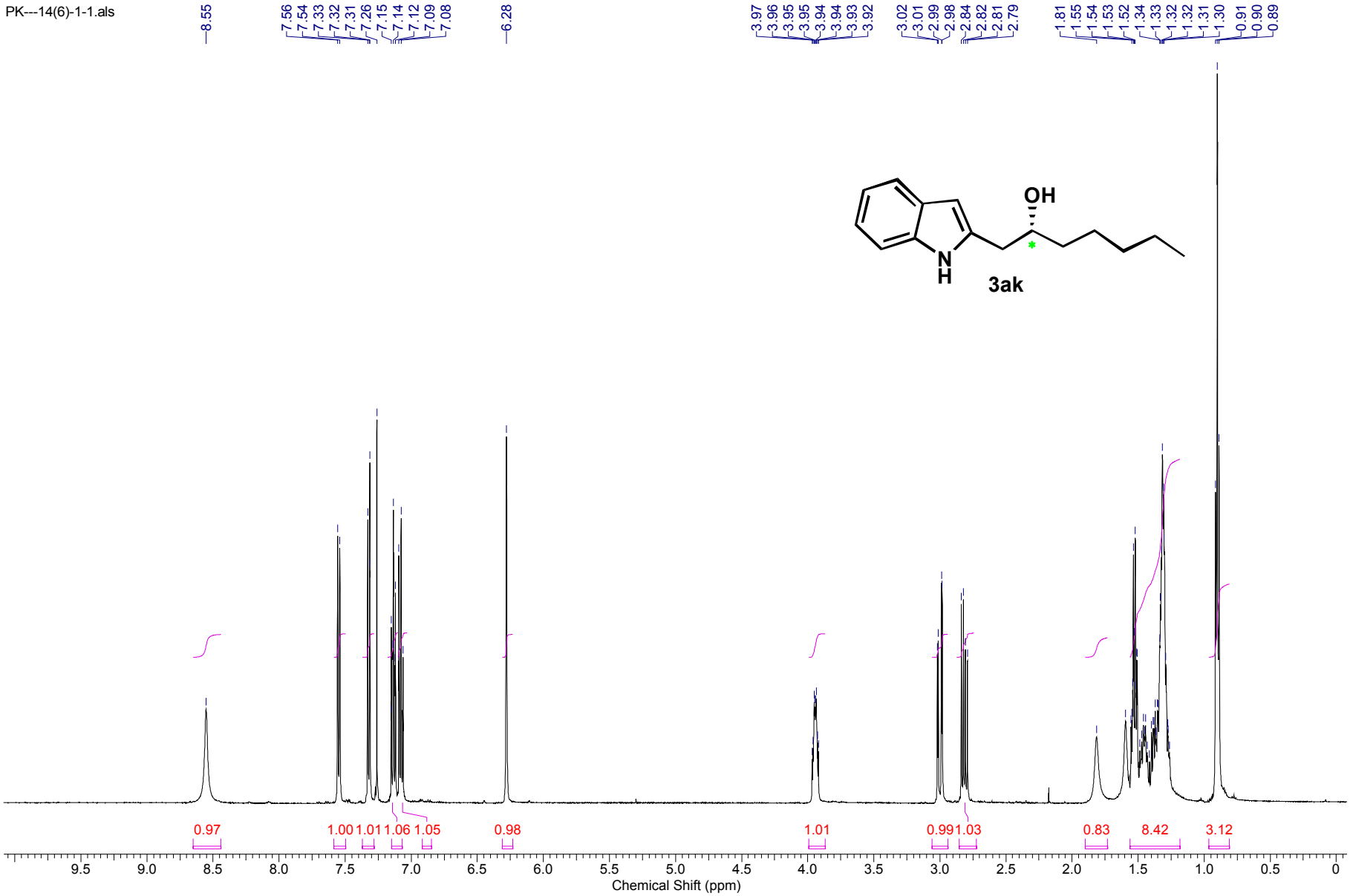

PKC---55(2-3)-C13-1-1.als
151.01
143.95
138.02
136.41
129.09
128.38
127.49
125.78
123.67
122.77
120.07
115.67
110.02
84.39
77.32
77.20
77.00
76.67
73.15
39.87
28.26
HO
N
O
O
25
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

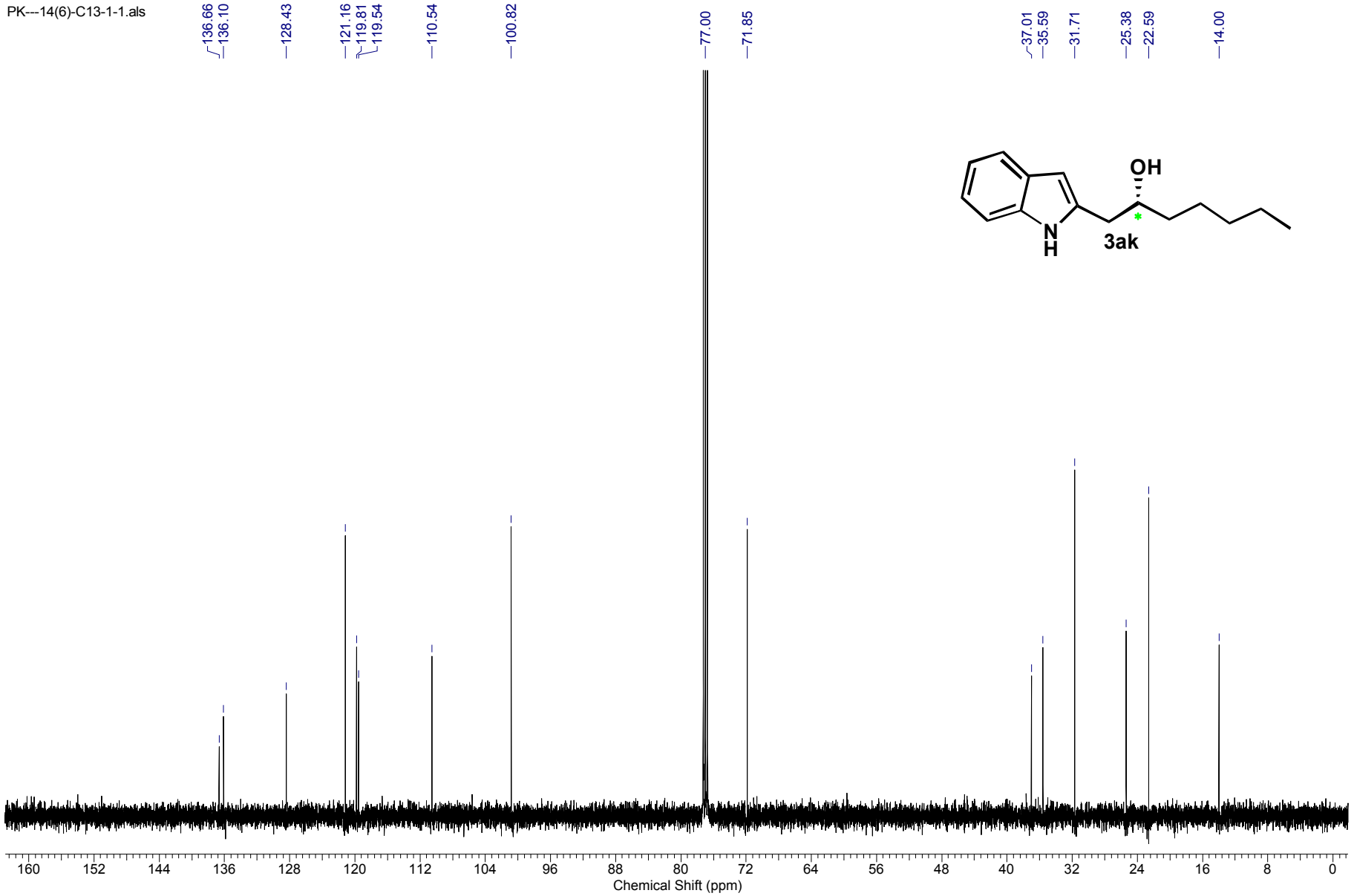

PKC---67(2)-uncyclized-1-1.als
8.00
7.52
7.35
7.35
7.34
7.33
7.30
7.28
7.26
7.13
7.08
7.07
6.27
6.27
5.84
5.82
5.82
5.80
3.74
3.42
3.40
3.39
3.37
3.29
3.28
3.25
3.24
1.56
O
O
O
N
H
27
0.83
1.01
5.97
0.99
0.97
0.88
0.91
2.77
0.93
0.90
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

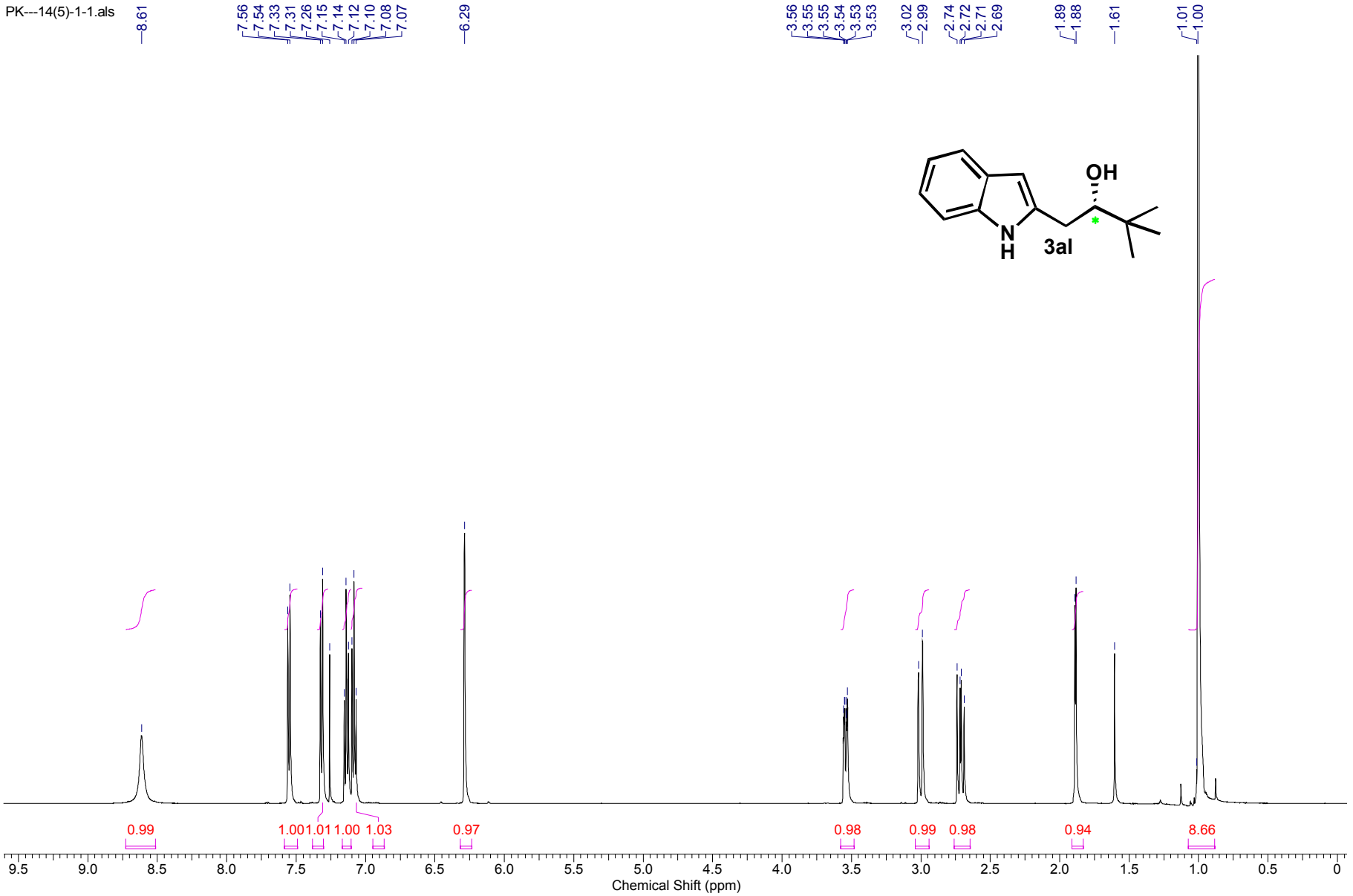

PKC---67(2)-uncycliz-C13-16.als
154.86
139.13
136.12
134.01
128.68
128.59
128.33
126.32
121.48
120.10
119.68
110.54
102.00
79.67
77.32
77.20
77.00
76.68
54.93
35.73
O
O
O
N
H
27
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

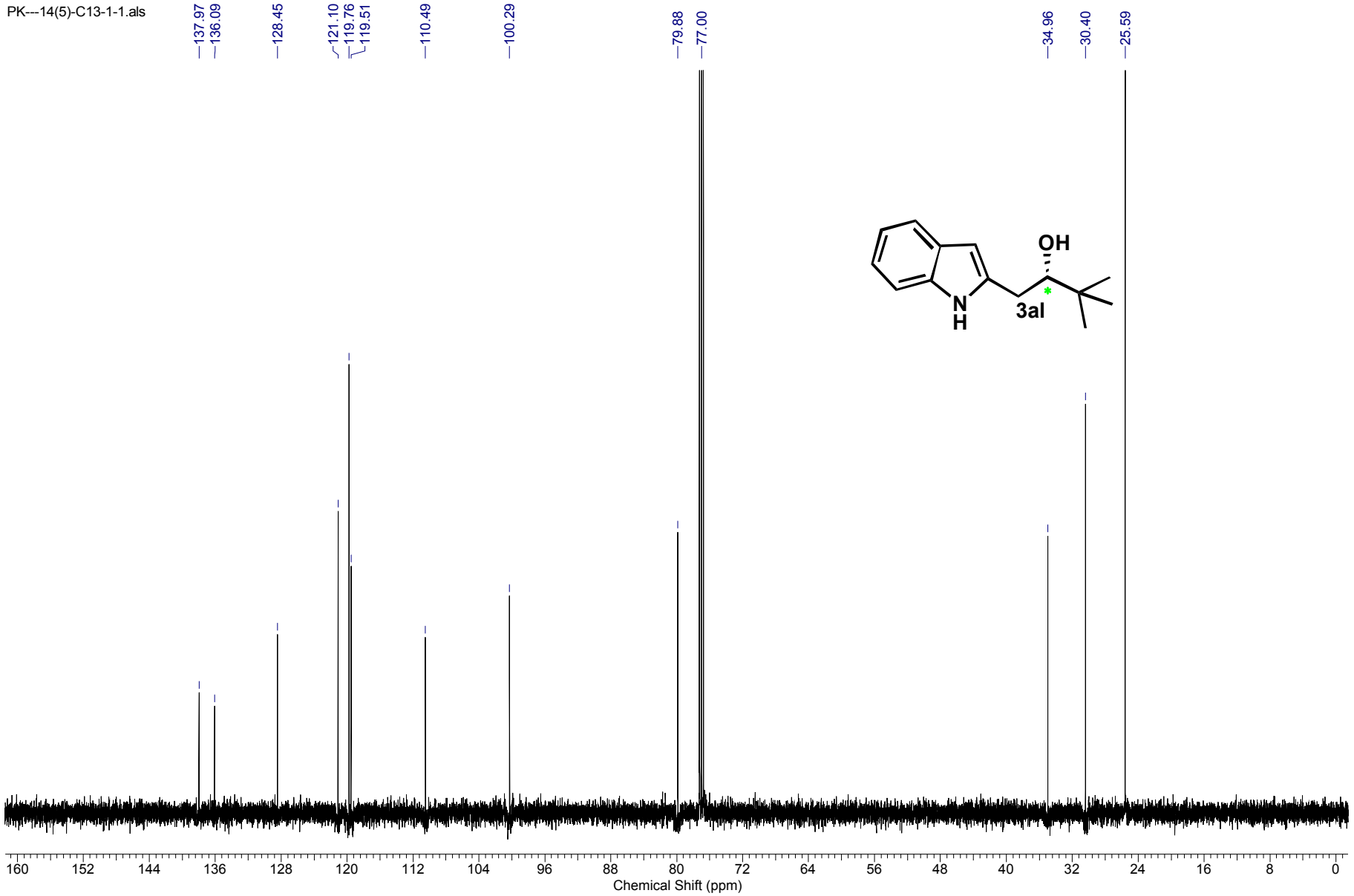

PKC---93(5)-1-1.als
7.87
7.51
7.34
7.33
7.33
7.33
7.32
7.26
7.25
7.25
7.12
7.07
6.24
6.23
6.04
6.03
6.01
3.39
3.37
3.36
3.34
3.27
3.26
3.24
3.23
2.11
2.09
2.09
1.58
O
O
N
H
26
0.95 1.00 5.21 0.93 1.10 1.08
0.97 1.03
0.99 1.05
2.93
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

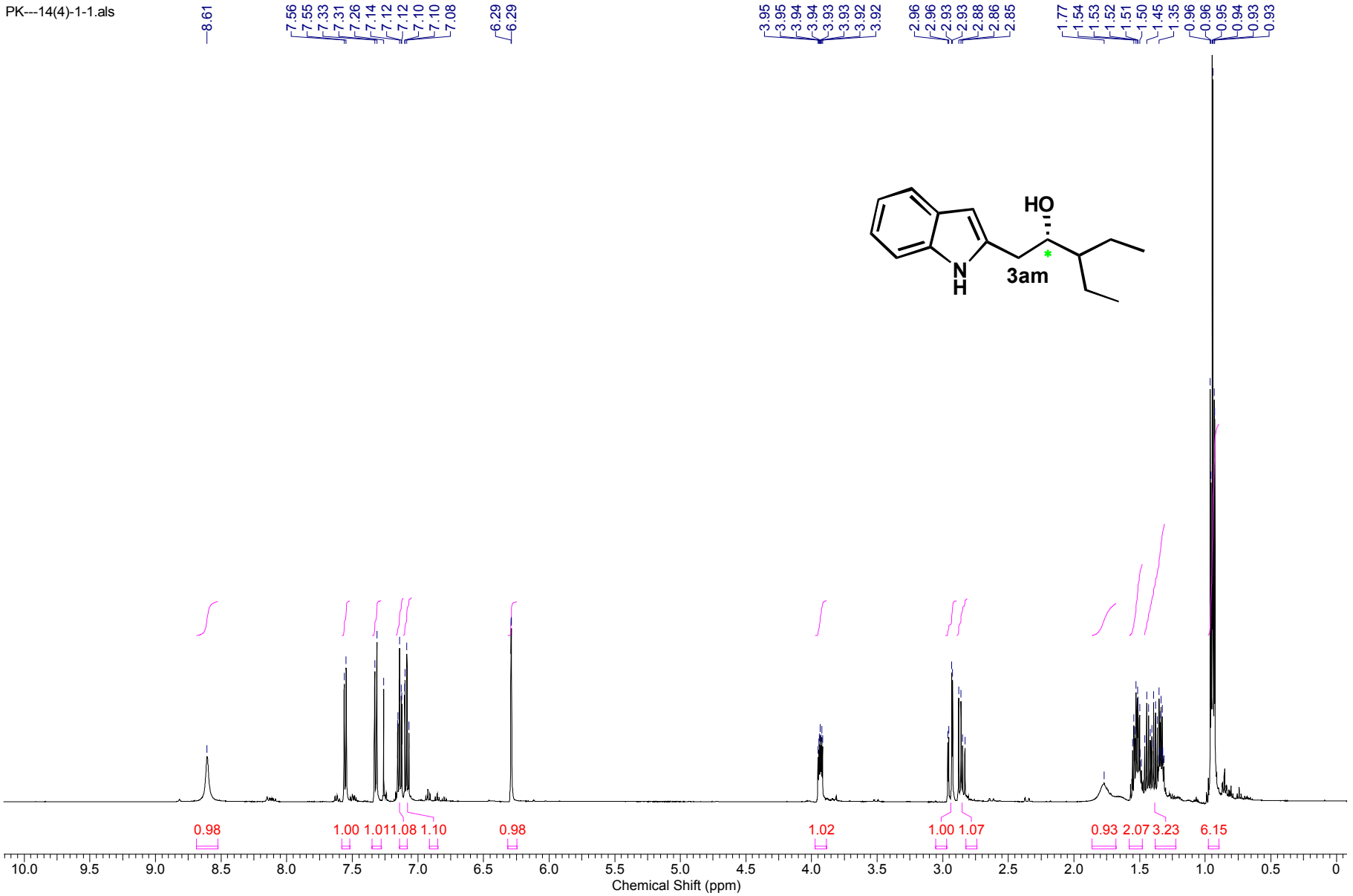

PKC---93(5)-C13-1-1.als
170.19
139.67
136.02
134.13
128.60
128.42
128.31
126.44
121.41
120.04
119.67
110.46
101.92
77.00
75.30
35.72
21.28
O
O
*
N
H
26
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

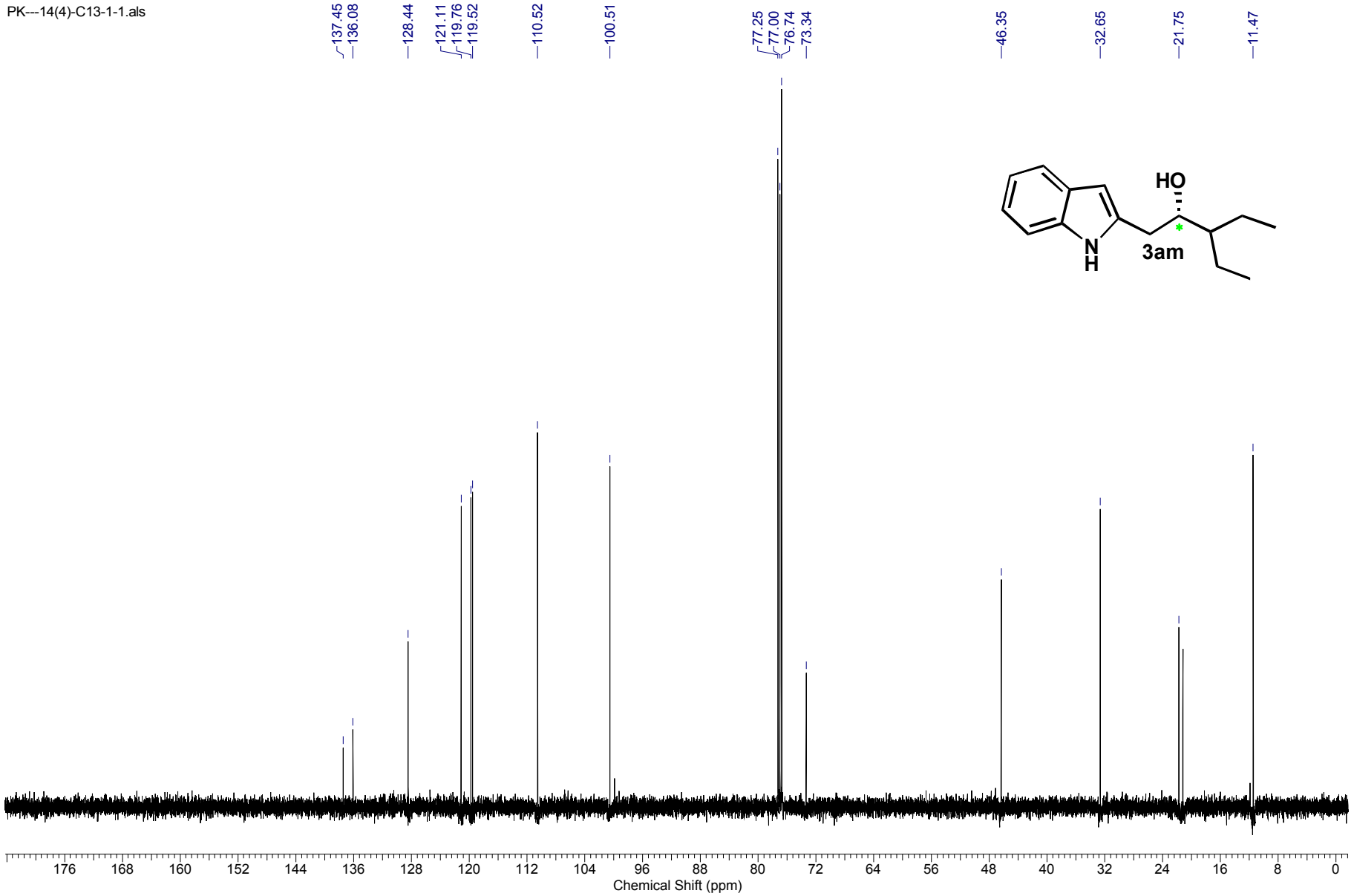

PK---14(6)-1-1.als
8.55
7.56
7.54
7.33
7.32
7.31
7.26
7.15
7.14
7.12
7.09
7.08
6.28
3.97
3.96
3.95
3.95
3.94
3.94
3.93
3.92
3.02
3.01
2.99
2.98
2.84
2.82
2.81
2.79
1.81
1.55
1.54
1.53
1.52
1.34
1.33
1.32
1.32
1.31
1.30
0.91
0.90
0.89
OH
N
H
3ak
0.97
1.00
1.01
1.06
1.05
0.98
1.01
0.99
1.03
0.83
8.42
3.12
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)

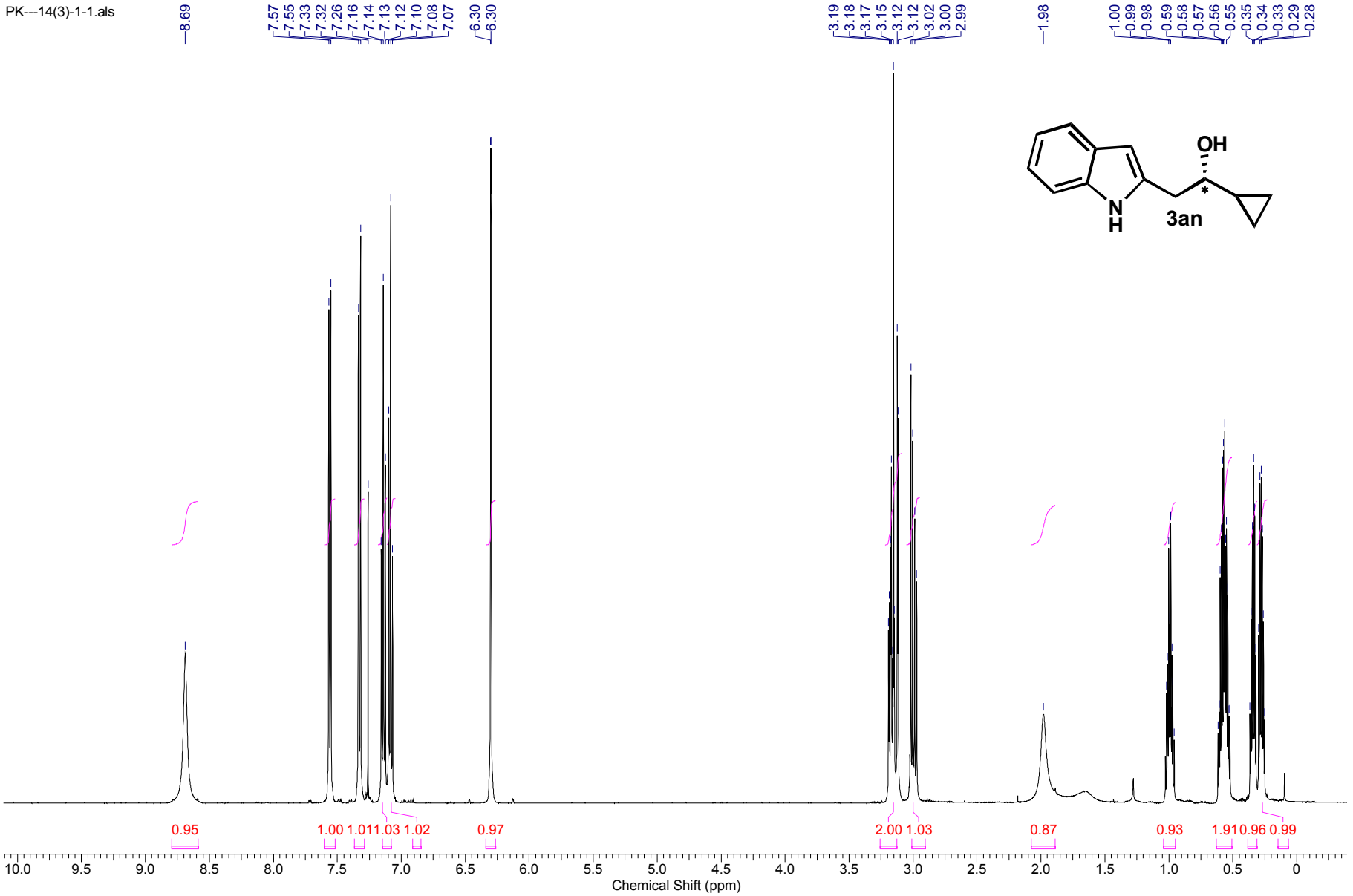

PK---14(6)-C13-1-1.als
136.66
136.10
128.43
121.16
119.81
119.54
110.54
100.82
77.00
71.85
37.01
35.59
31.71
25.38
22.59
14.00
OH
N
H
3ak
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

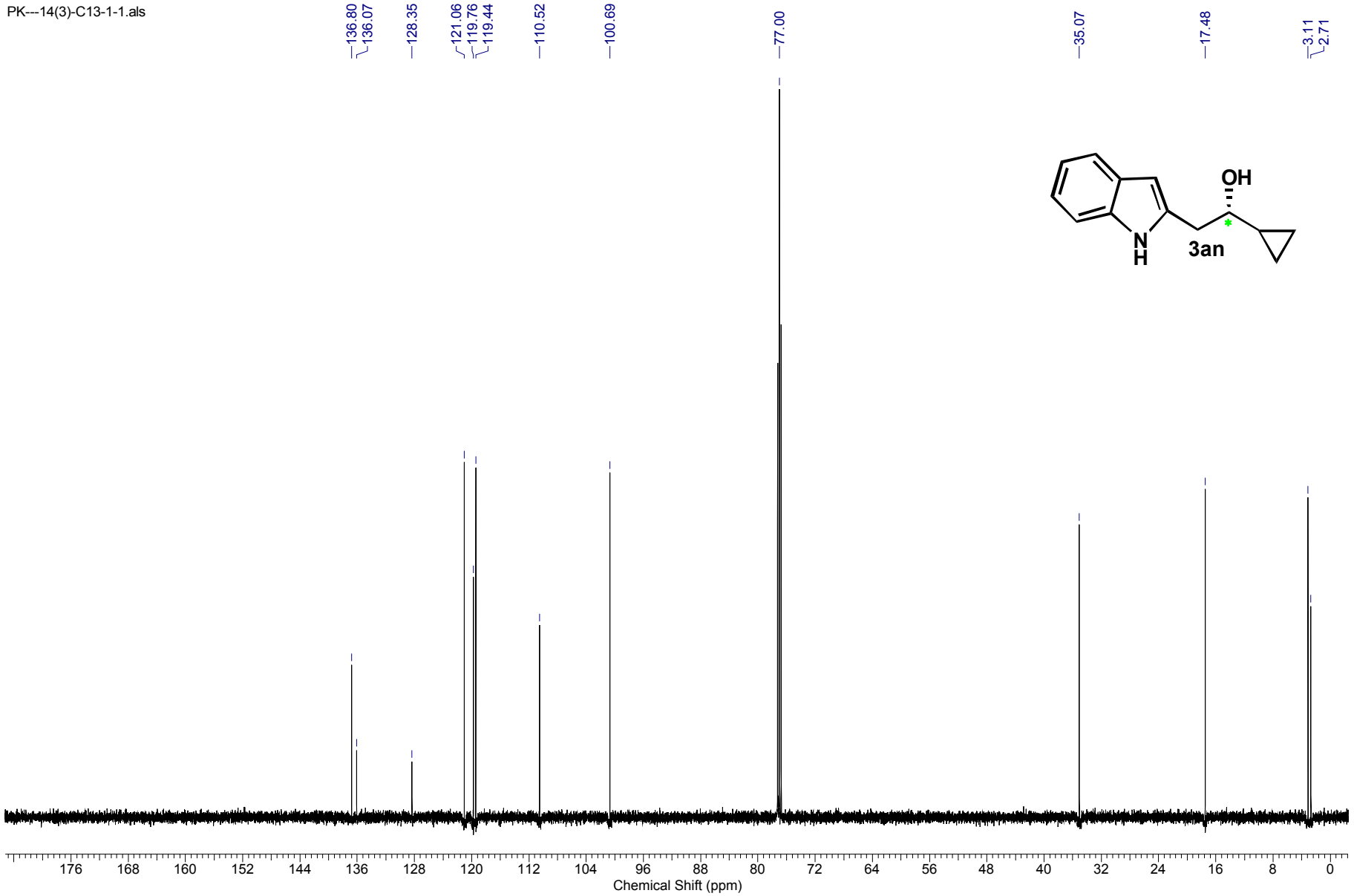

PK---14(5)-1-1.als
8.61
7.56
7.54
7.33
7.31
7.26
7.15
7.14
7.12
7.10
7.08
7.07
6.29
3.56
3.55
3.55
3.54
3.53
3.53
3.02
2.99
2.74
2.72
2.71
2.69
1.89
1.88
1.61
1.01
1.00
OH
N
H
3al
0.99
1.00
1.01
1.00
1.03
0.97
0.98
0.99
0.98
0.94
8.66
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

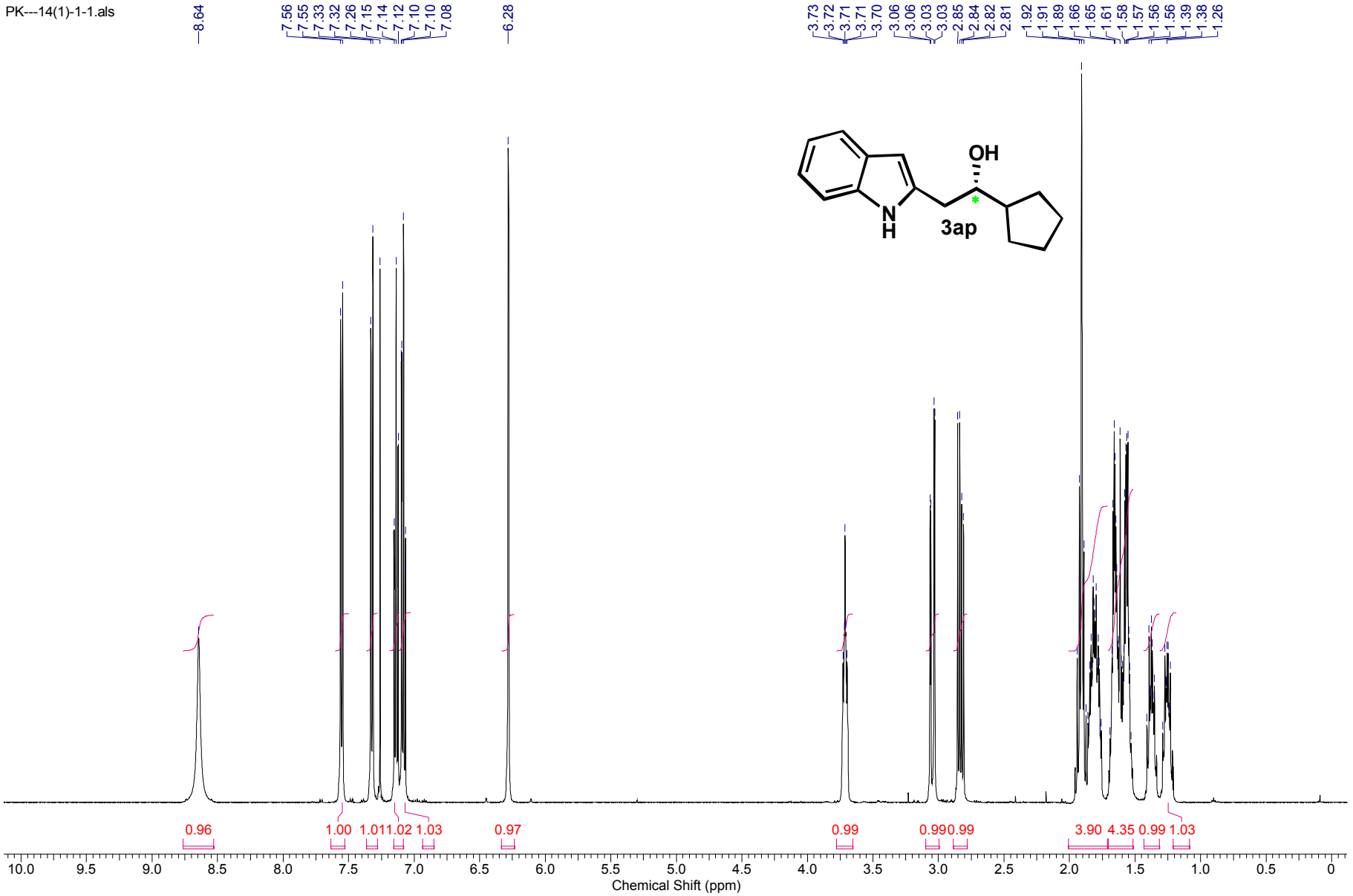

PK---14(5)-C13-1-1.als
137.97
136.09
128.45
121.10
119.76
119.51
110.49
100.29
79.88
77.00
34.96
30.40
25.59
OH
N
H
3al
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

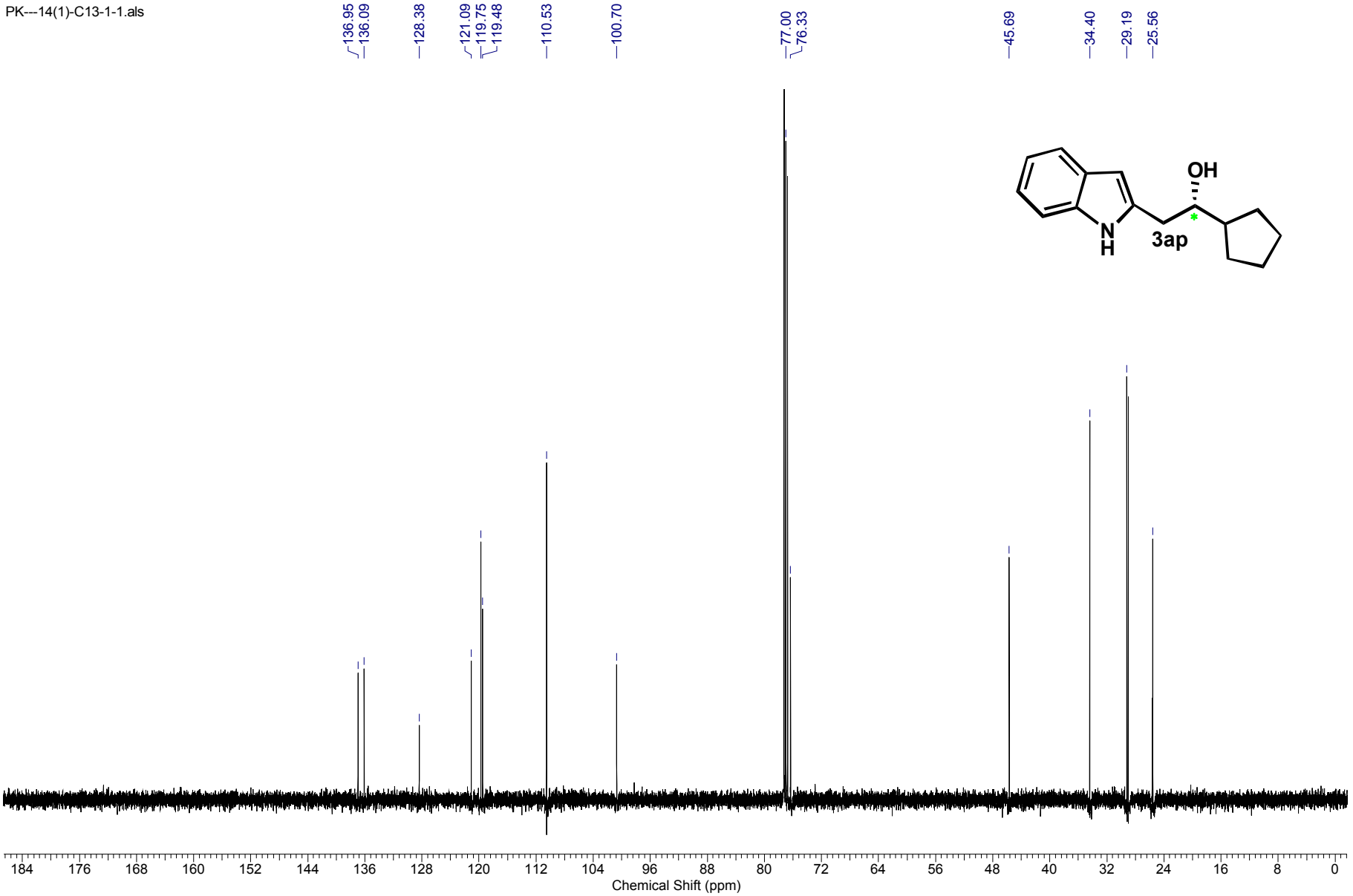

PK---14(4)-1-1.als
8.61
7.56
7.55
7.33
7.31
7.26
7.14
7.12
7.12
7.10
7.10
7.08
6.29
6.29
3.95
3.95
3.94
3.94
3.93
3.93
3.92
3.92
2.96
2.96
2.93
2.93
2.88
2.86
2.85
1.77
1.54
1.53
1.52
1.51
1.50
1.45
1.35
0.96
0.96
0.95
0.94
0.93
0.93
HO
N
H
3am
0.98
1.00
1.01
1.08
1.10
0.98
1.02
1.00
1.07
0.93
2.07
3.23
6.15
10.0
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)

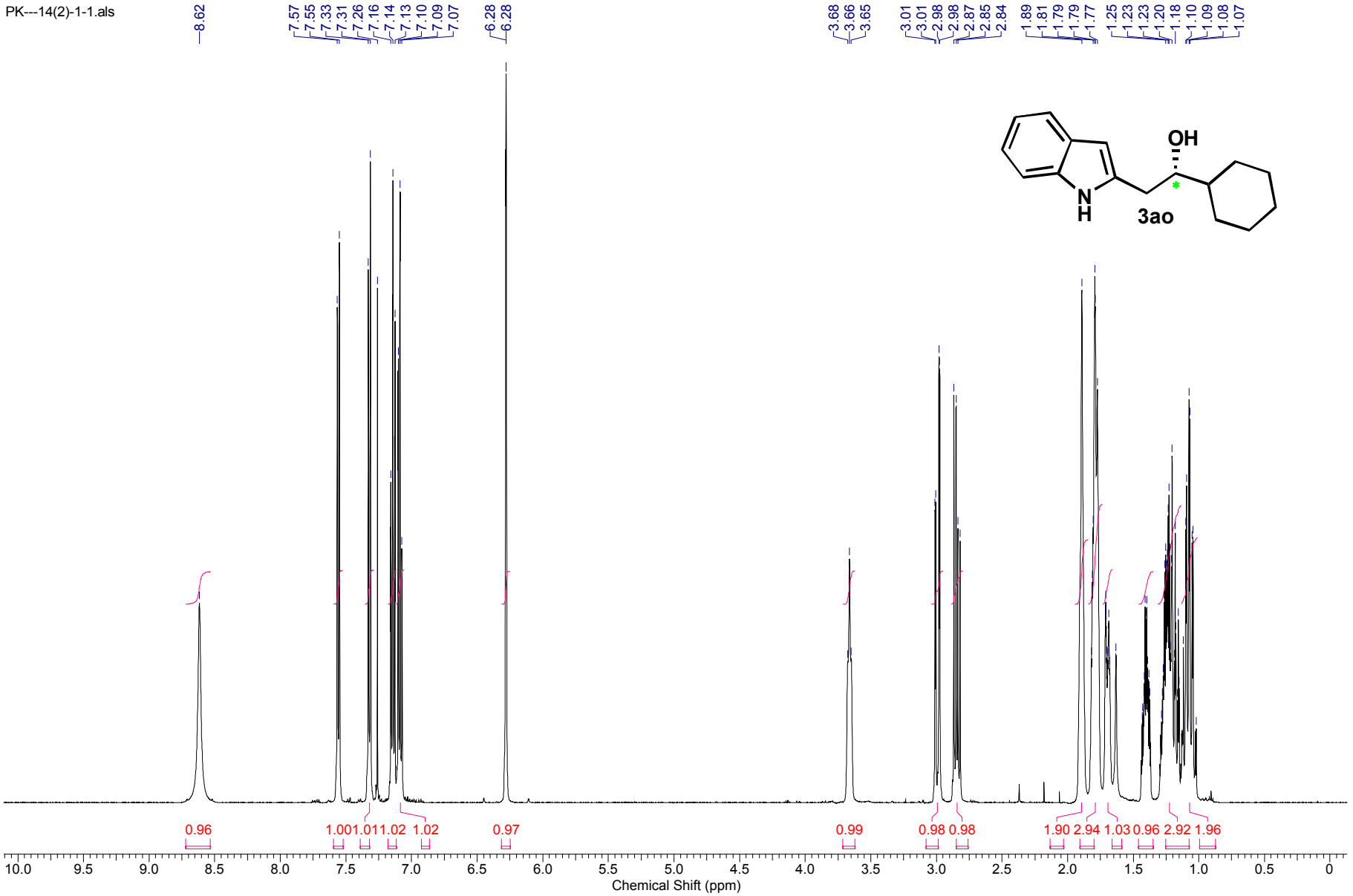

PK---14(4)-C13-1-1.als
137.45
136.08
128.44
121.11
119.76
119.52
110.52
100.51
77.25
77.00
76.74
73.34
46.35
32.65
21.75
11.47
HO
N
H
3am
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

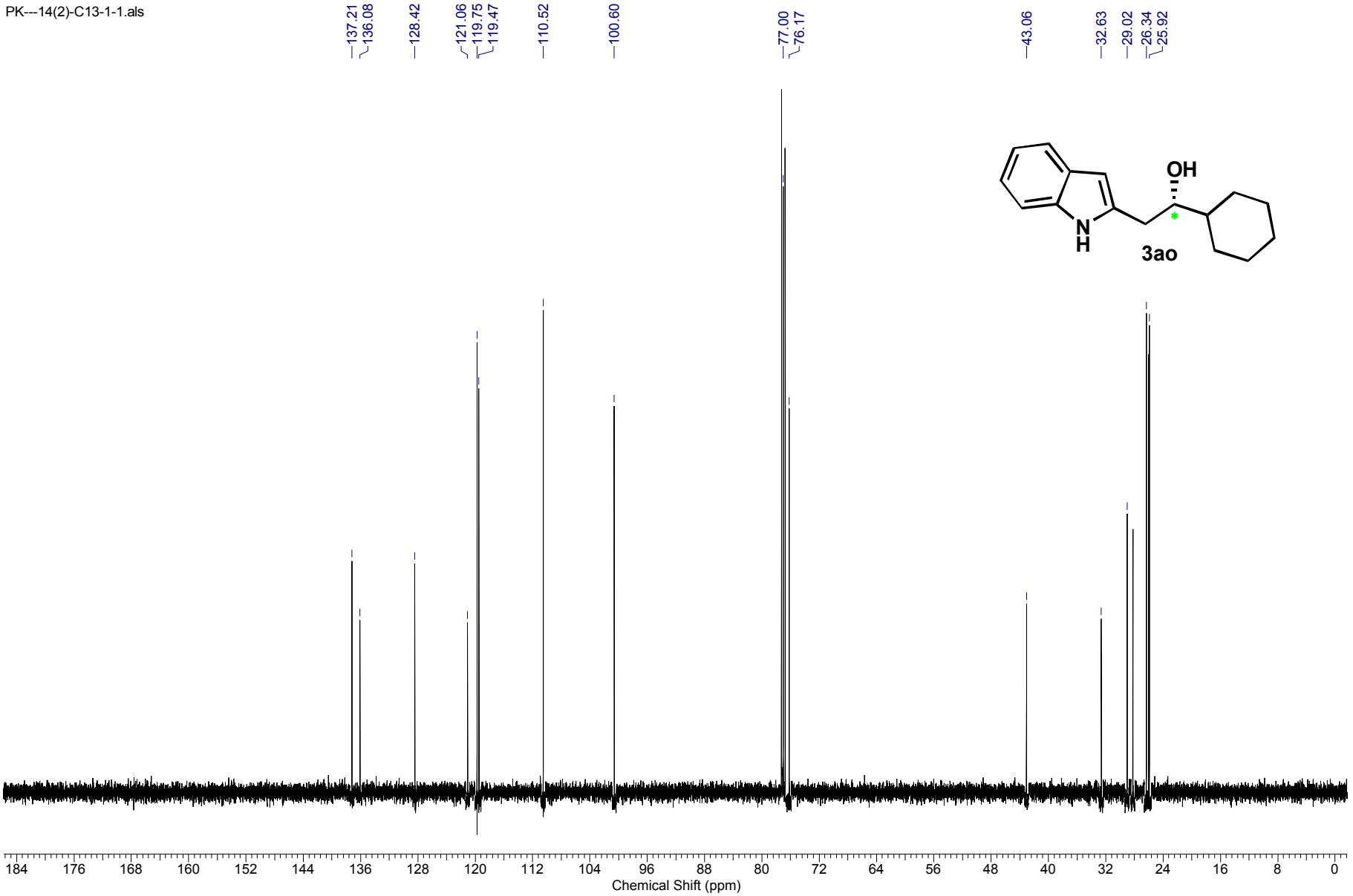

PK---14(3)-1-1.als
8.69
7.57
7.55
7.33
7.32
7.26
7.16
7.14
7.13
7.12
7.10
7.08
7.07
6.30
6.30
3.19
3.18
3.17
3.15
3.12
3.12
3.02
3.00
2.99
1.98
1.00
0.99
0.98
0.59
0.58
0.57
0.56
0.55
0.35
0.34
0.33
0.29
0.28
OH
N
H
3an
0.95
1.00
1.01
1.03
1.02
0.97
2.00
1.03
0.87
0.93
1.91
0.96
0.99
10.0
9.5
9.0
8.5
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)

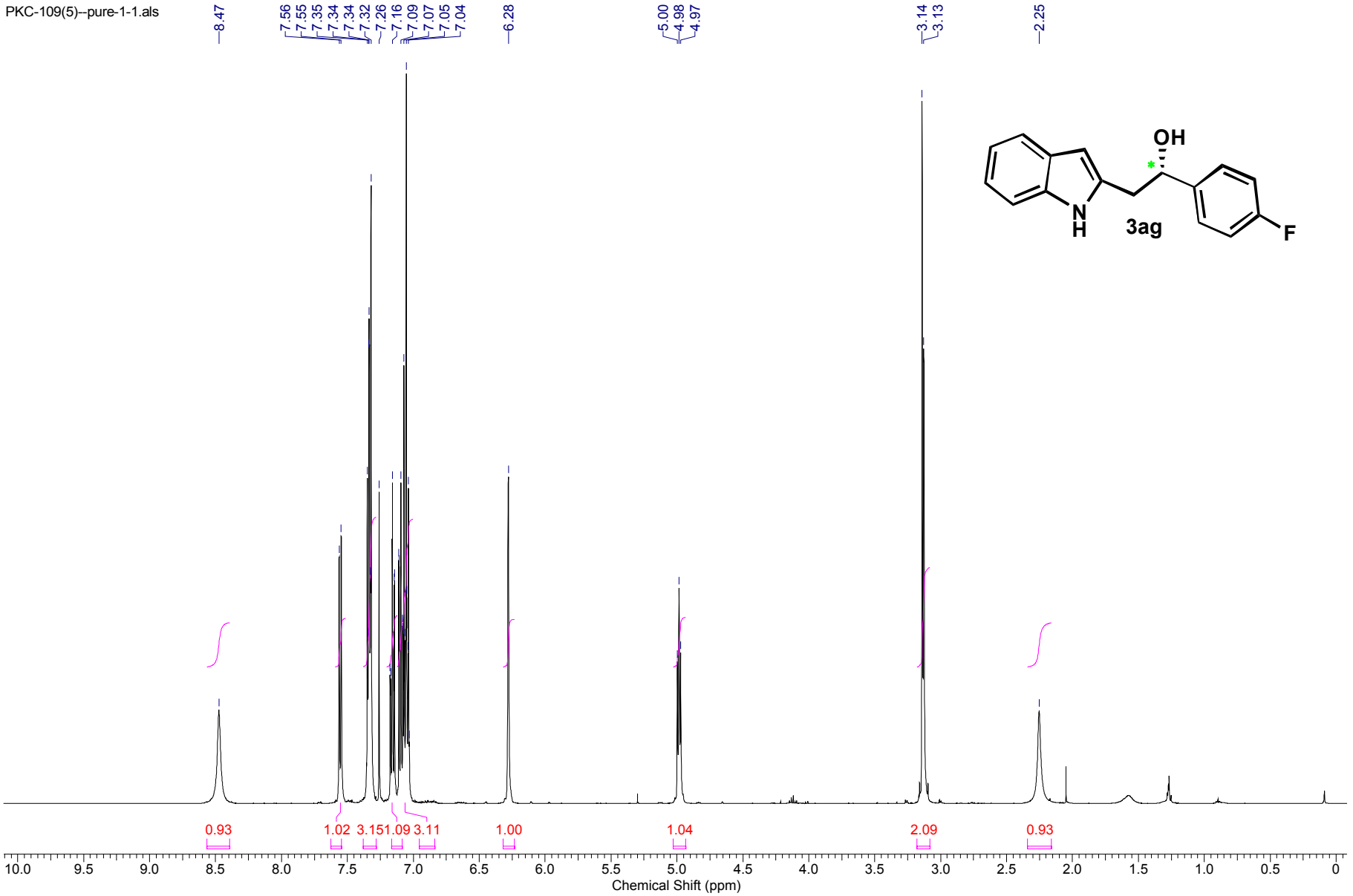

PK---14(3)-C13-1-1.als
136.80
136.07
128.35
121.06
119.76
119.44
110.52
100.69
77.00
35.07
17.48
3.11
2.71
OH
N
H
3an
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

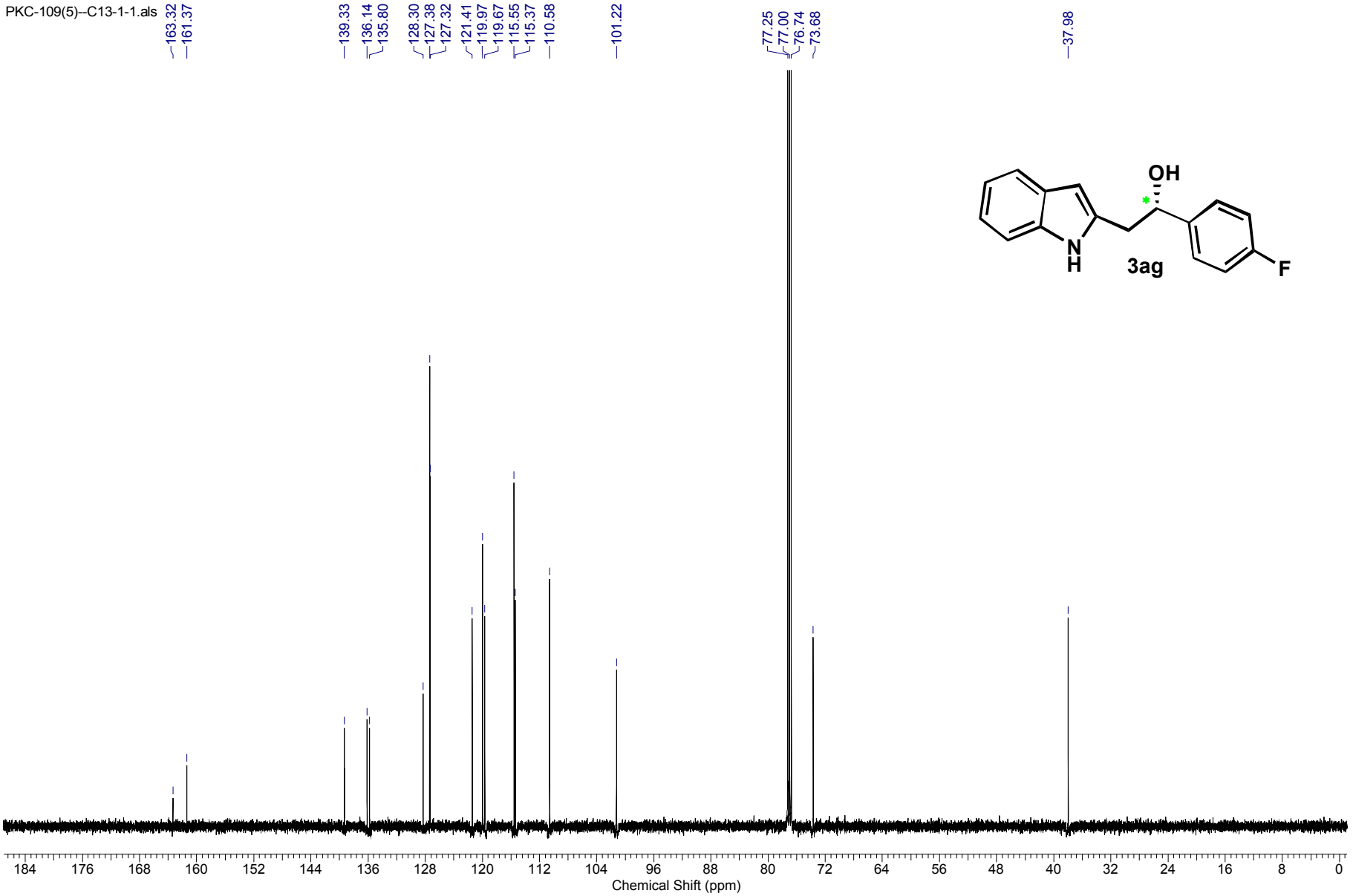

PK---14(1)-1-1.als
8.64
7.56
7.55
7.33
7.32
7.26
7.15
7.14
7.12
7.10
7.10
7.08
6.28
3.73
3.72
3.71
3.71
3.70
3.06
3.06
3.03
3.03
2.85
2.84
2.82
2.81
1.92
1.91
1.89
1.66
1.65
1.61
1.58
1.57
1.56
1.56
1.39
1.38
1.26
OH
N
H
3ap
0.96
1.00
1.01
1.02
1.03
0.97
0.99
0.99
0.99
3.90
4.35
0.99
1.03
10.0
9.5
9.0
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)

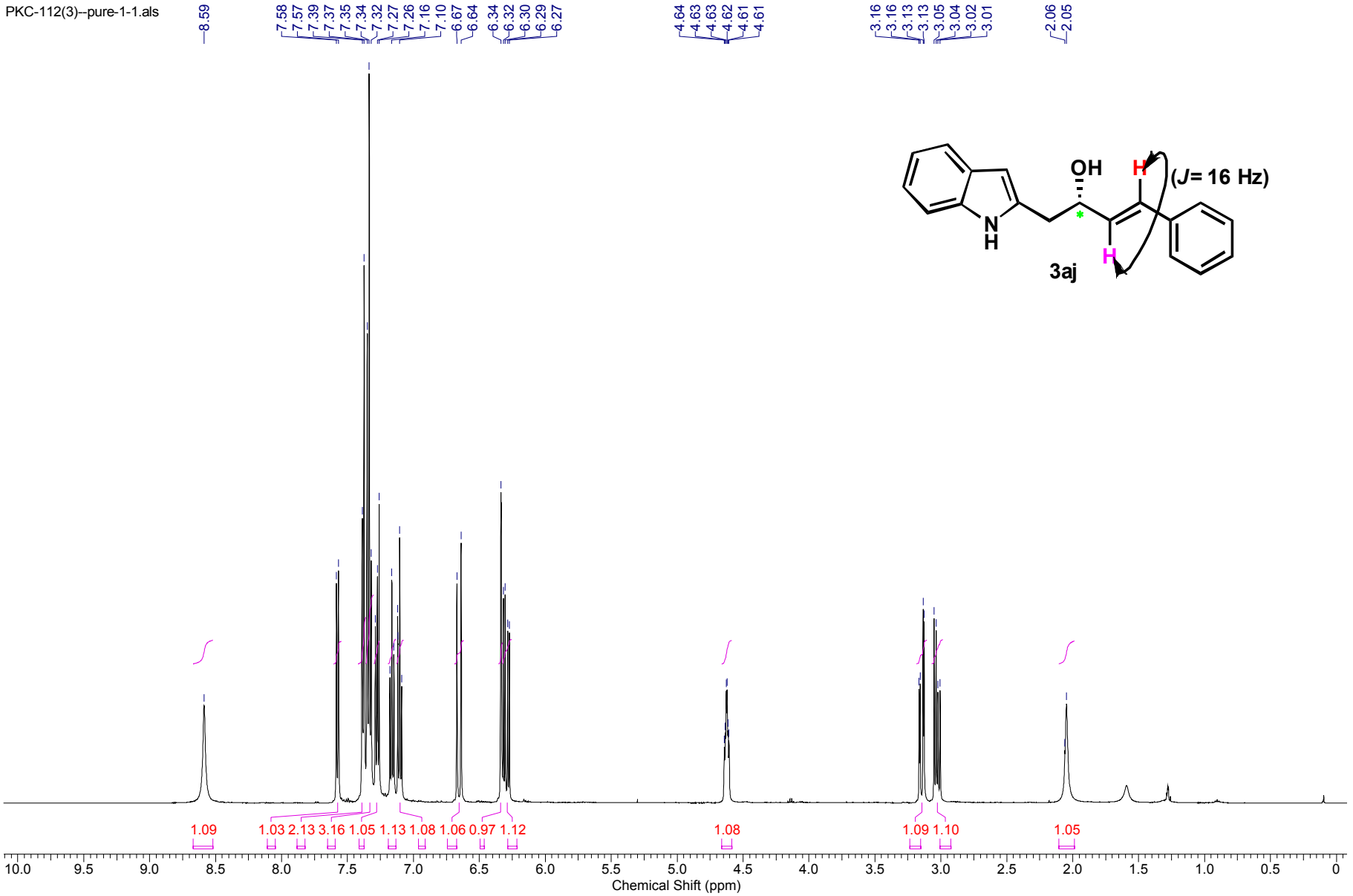

PK---14(1)-C13-1-1.als
136.95
136.09
128.38
121.09
119.75
119.48
110.53
100.70
77.00
76.33
45.69
34.40
29.19
25.56
OH
N
H
3ap
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

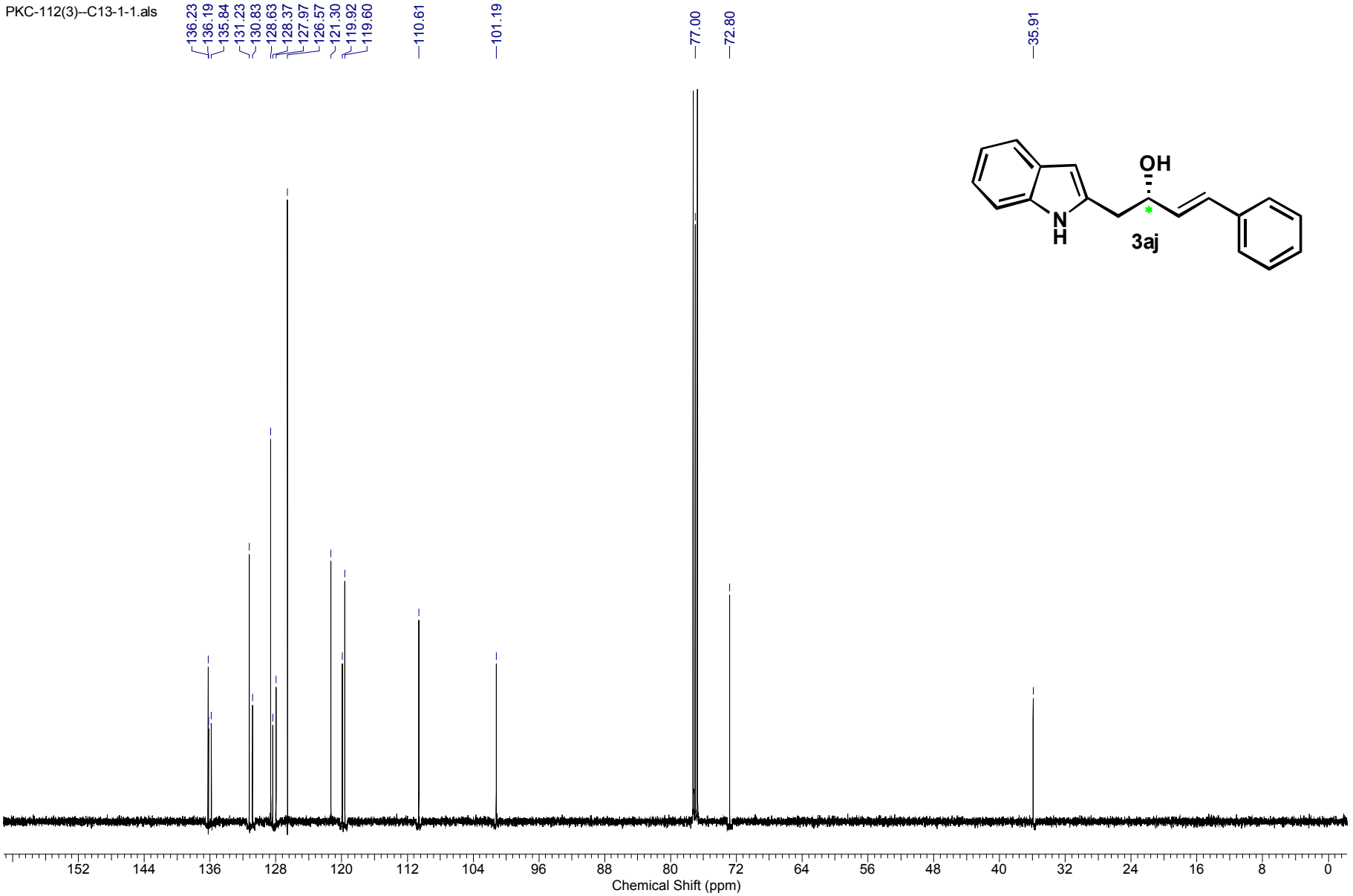

PK---14(2)-1-1.als
8.62
7.57
7.55
7.33
7.31
7.26
7.16
7.14
7.13
7.10
7.09
7.07
6.28
6.28
3.68
3.66
3.65
3.01
3.01
2.98
2.98
2.87
2.85
2.84
1.89
1.81
1.79
1.79
1.77
1.25
1.23
1.23
1.20
1.18
1.10
1.09
1.08
1.07
OH
N
H
3ao
0.96
1.00
1.01
1.02
1.02
0.97
0.99
0.98
0.98
1.90
2.94
1.03
0.96
2.92
1.96
10.0
9.5
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)

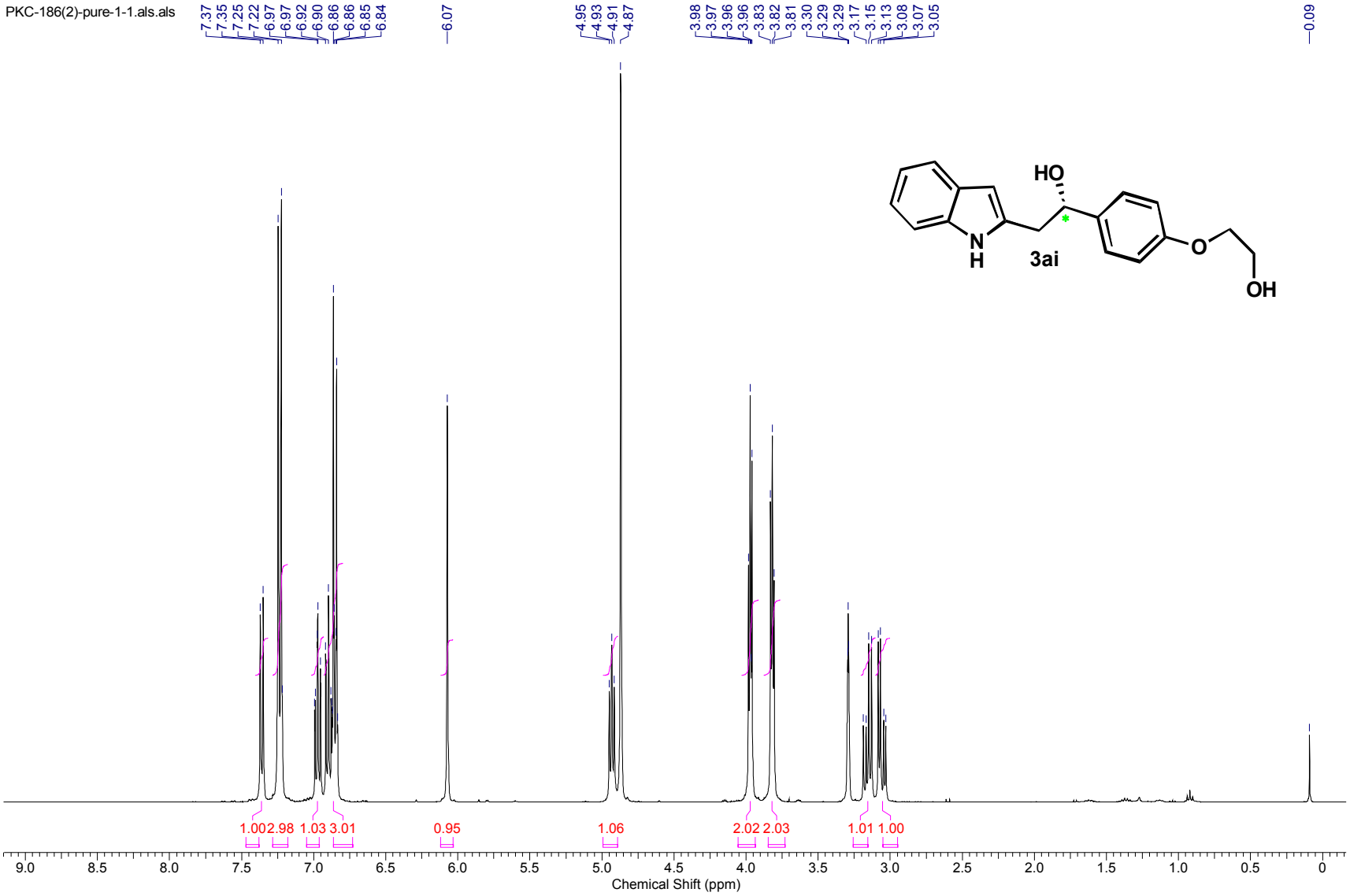

PK---14(2)-C13-1-1.als
137.21
136.08
128.42
121.06
119.75
119.47
110.52
100.60
77.00
76.17
43.06
32.63
29.02
26.34
25.92
OH
N
H
3ao
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

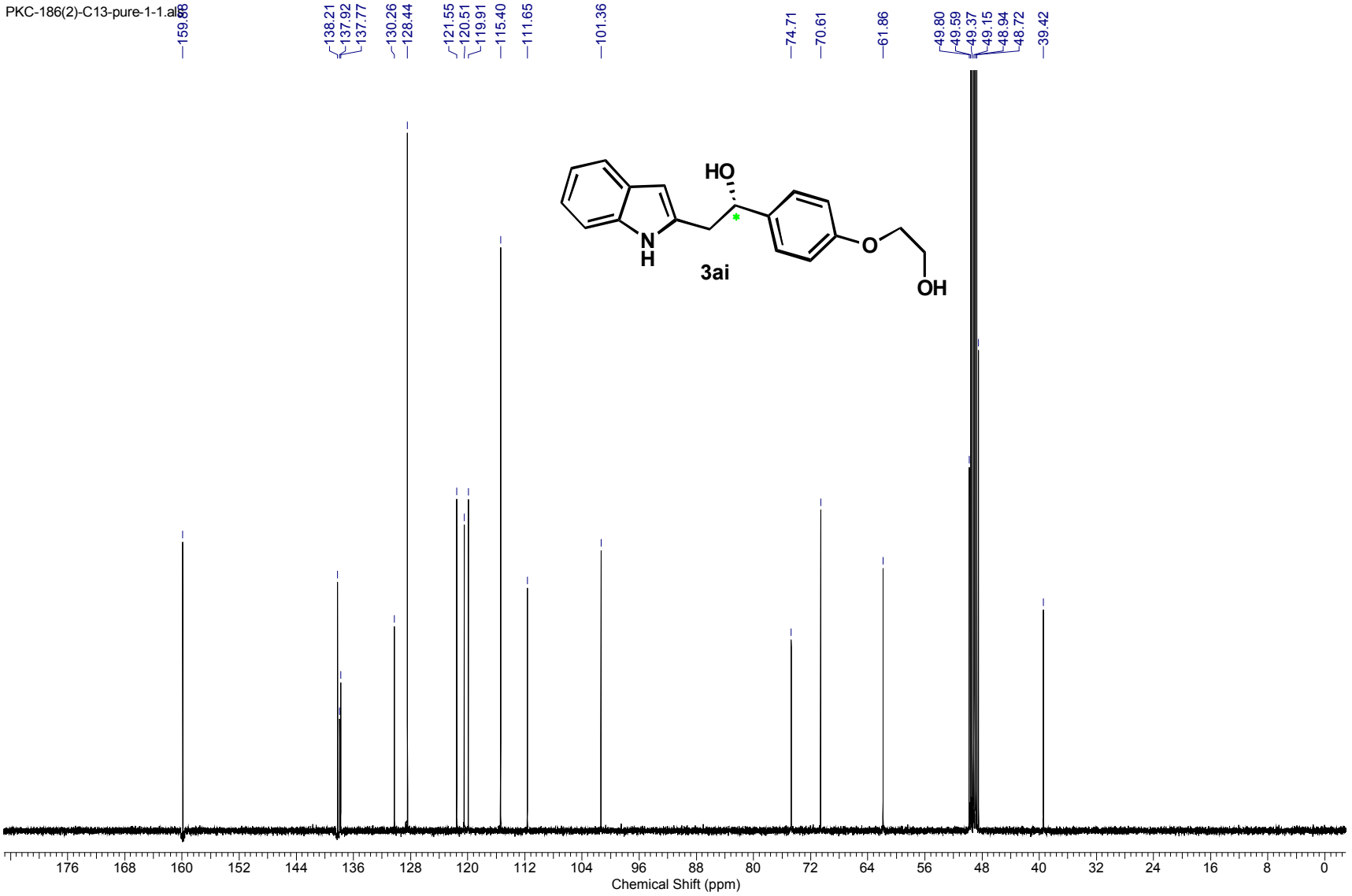

PKC-109(5)--pure-1-1.als
8.47
7.56
7.55
7.35
7.34
7.34
7.32
7.26
7.16
7.09
7.07
7.05
7.04
6.28
5.00
4.98
4.97
3.14
3.13
2.25
OH
N
H
3ag
F
0.93
1.02
3.15
1.09
3.11
1.00
1.04
2.09
0.93
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

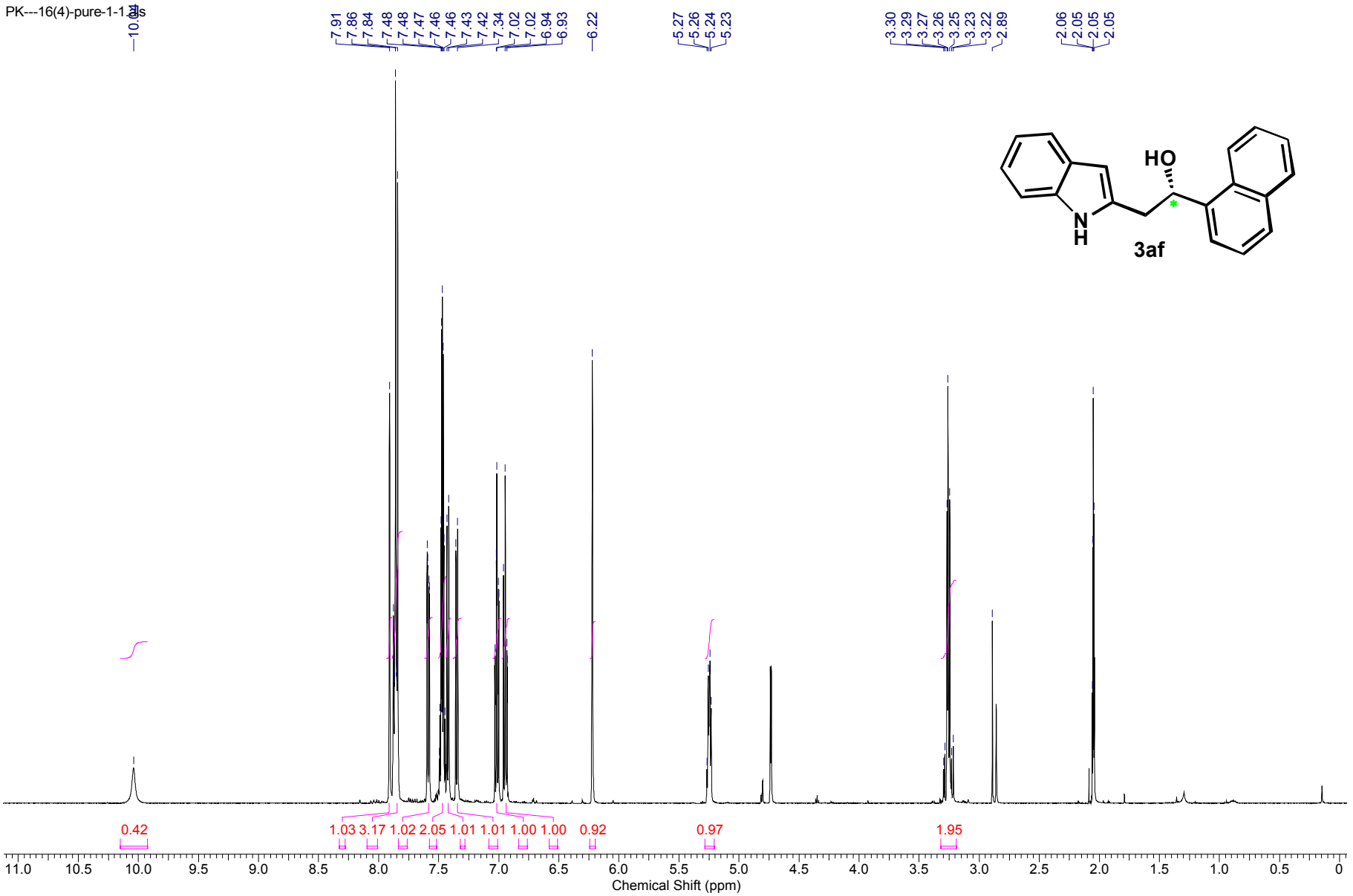

PKC-109(5)--C13-1-1.als
163.32
161.37
139.33
136.14
135.80
128.30
127.38
127.32
121.41
119.97
119.67
115.55
115.37
110.58
101.22
77.25
77.00
76.74
73.68
37.98
OH
N
H
3ag
F
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

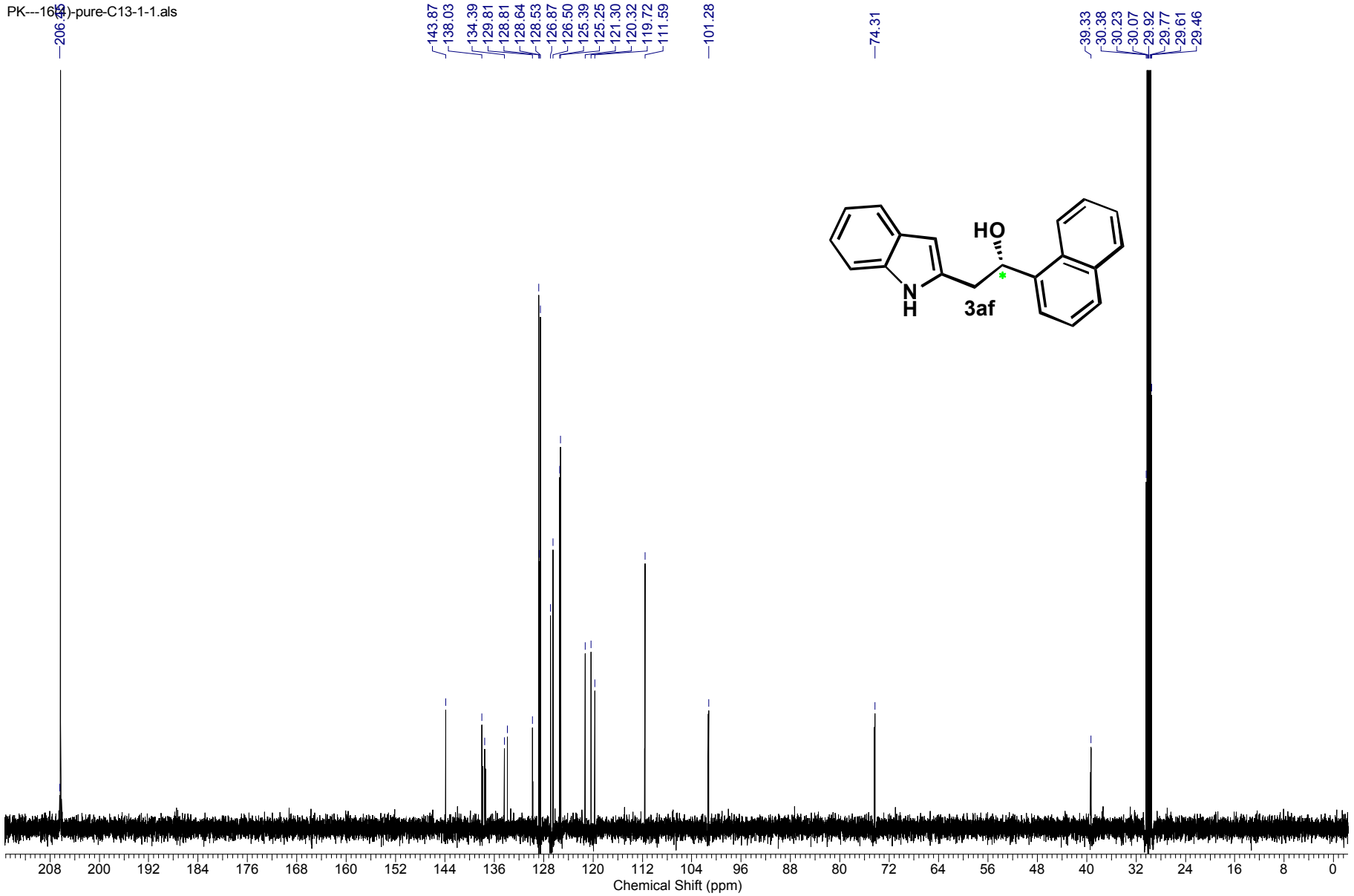

PKC-112(3)--pure-1-1.als
8.59
7.58
7.57
7.39
7.37
7.35
7.34
7.32
7.27
7.26
7.16
7.10
6.67
6.64
6.34
6.32
6.30
6.29
6.27
4.64
4.63
4.62
4.61
4.61
3.16
3.16
3.13
3.13
3.05
3.04
3.02
3.01
2.06
2.05
OH
H
(J= 16 Hz)
N
H
H
3aj
1.09
1.03
2.13
3.16
1.05
1.13
1.08
1.06
0.97
1.12
1.08
1.09
1.10
1.05
10.0
9.5
9.0
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)

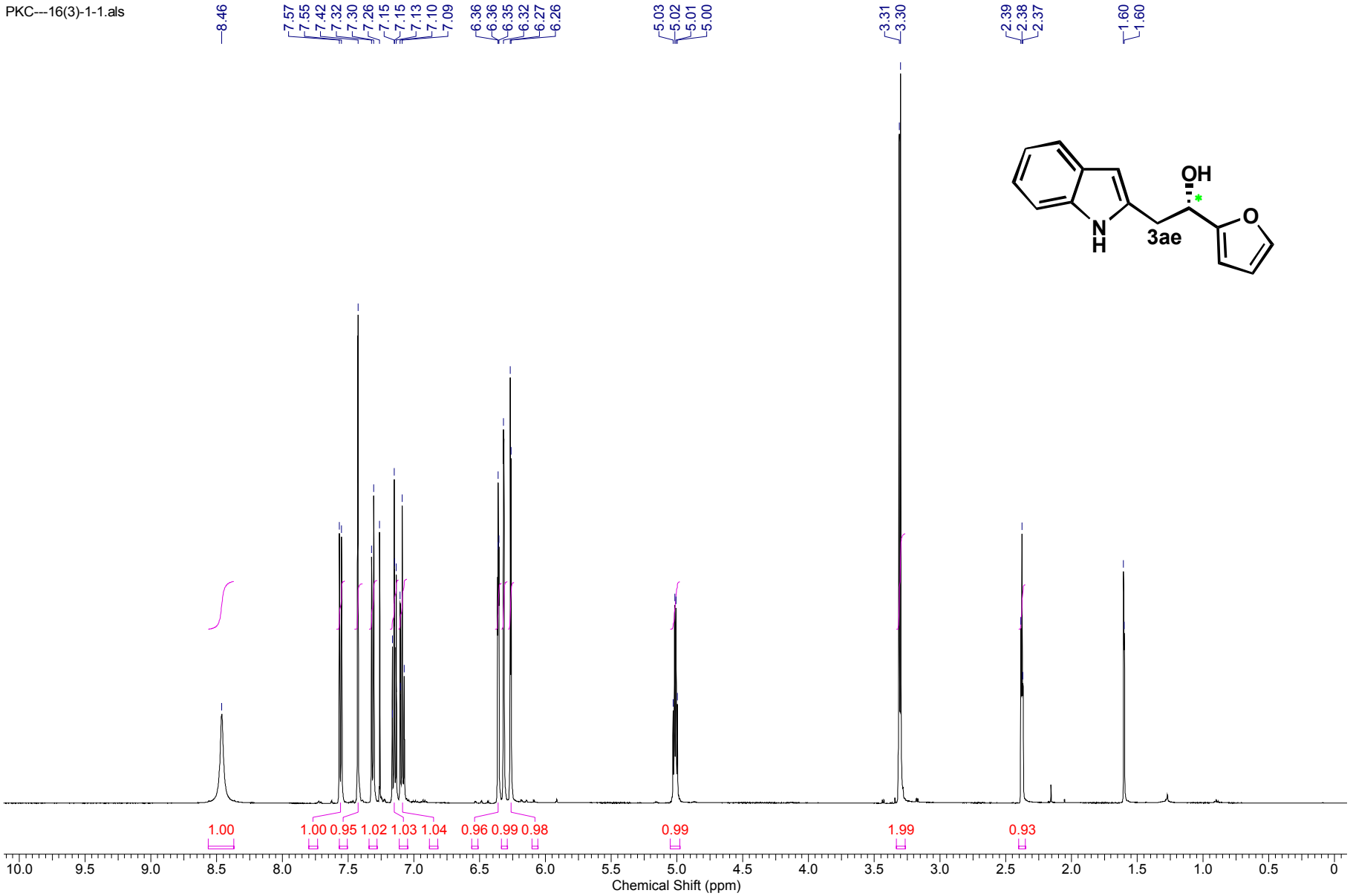

PKC-112(3)--C13-1-1.als
136.23
136.19
135.84
131.23
130.83
128.63
128.37
127.97
126.57
121.30
119.92
119.60
110.61
101.19
77.00
72.80
35.91
OH
N
H
3aj
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

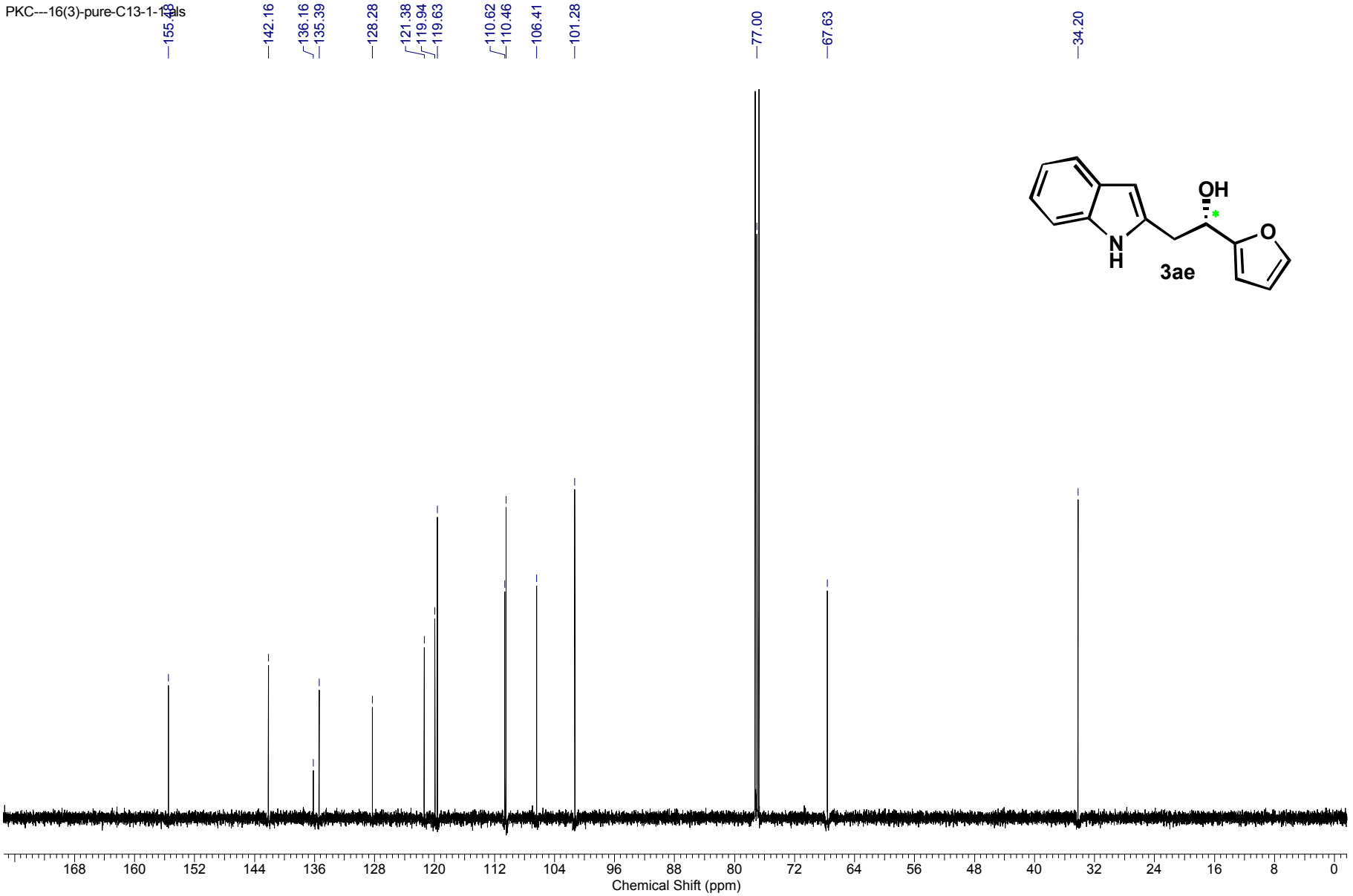

PKC-186(2)-pure-1-1.als.als
7.37
7.35
7.25
7.22
6.97
6.97
6.92
6.90
6.86
6.86
6.85
6.84
6.07
4.95
4.93
4.91
4.87
3.98
3.97
3.96
3.96
3.83
3.82
3.81
3.30
3.29
3.29
3.17
3.15
3.13
3.08
3.07
3.05
0.09
HO
N
H
3ai
O
OH
1.00 2.98 1.03 3.01
0.95
1.06
2.02 2.03
1.01 1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

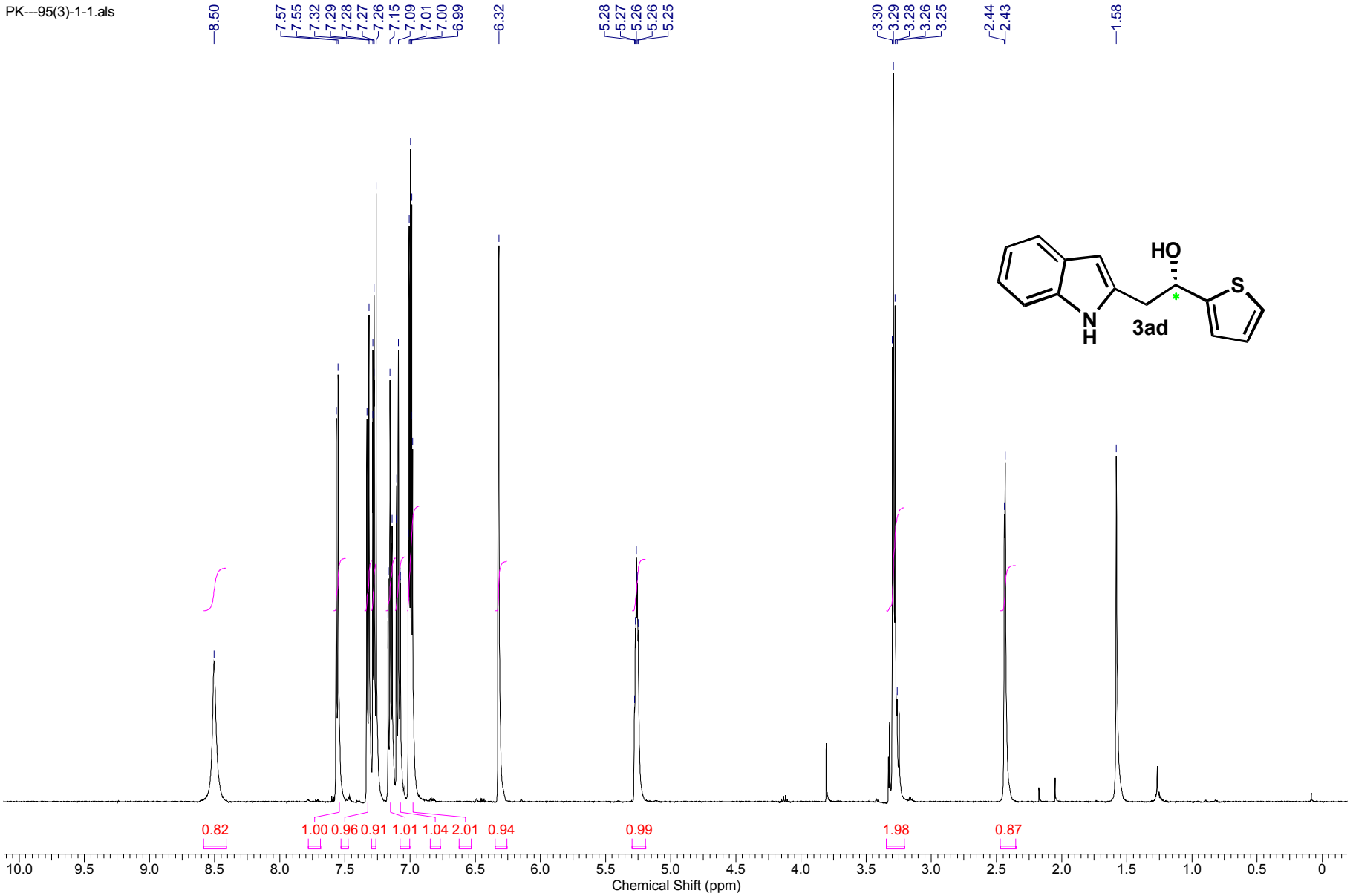

PKC-186(2)-C13-pure-1-1.als
159.98
138.21
137.92
137.77
130.26
128.44
121.55
120.51
119.91
115.40
111.65
101.36
74.71
70.61
61.86
49.80
49.59
49.37
49.15
48.94
48.72
39.42
HO
N
H
O
OH
3ai
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

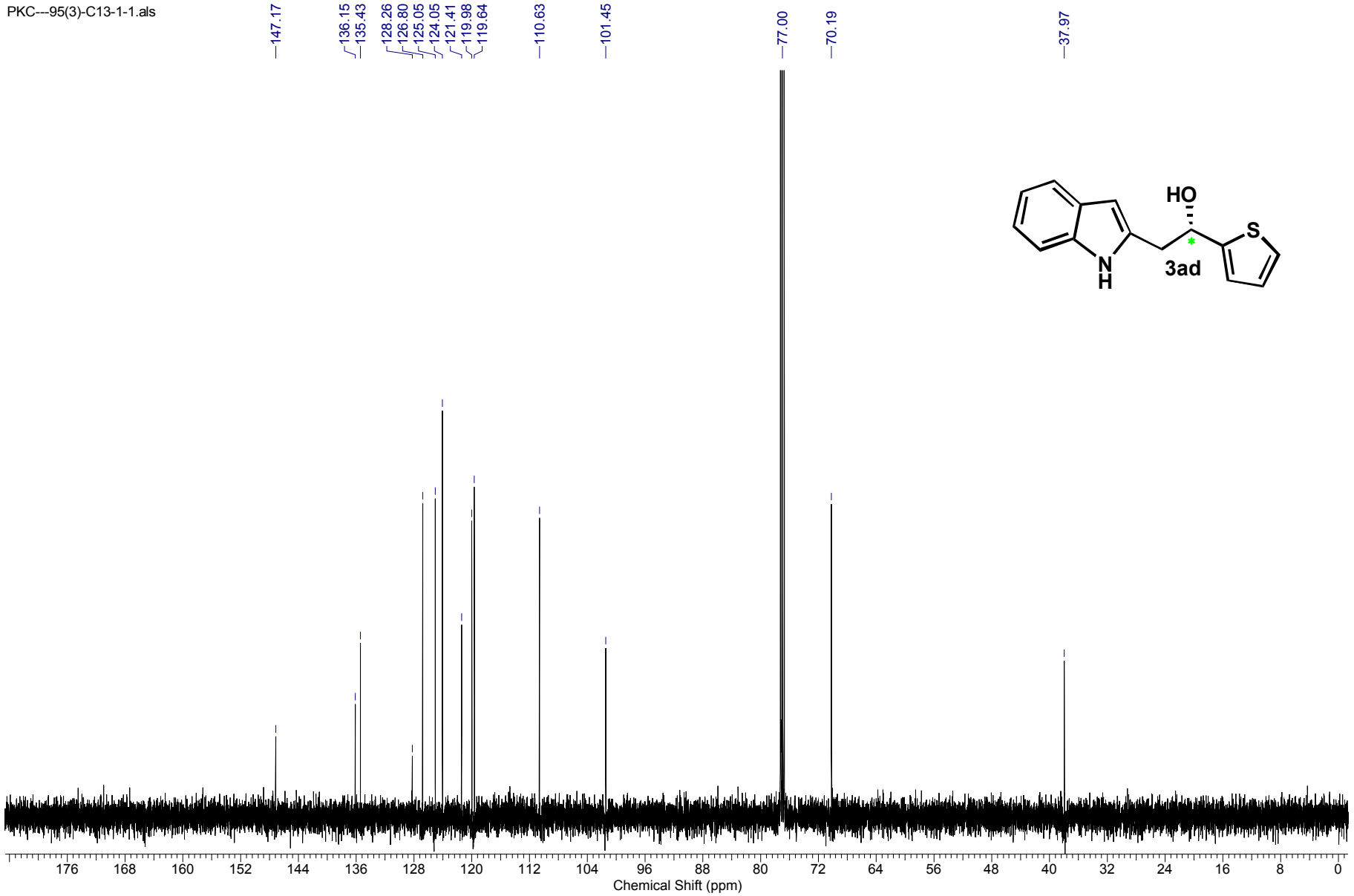

PK---16(4)-pure-1-1.1ds
10.04
7.91
7.86
7.84
7.48
7.48
7.47
7.46
7.46
7.43
7.42
7.34
7.02
7.02
6.94
6.93
6.22
5.27
5.26
5.24
5.23
3.30
3.29
3.27
3.26
3.25
3.23
3.22
2.89
2.06
2.05
2.05
2.05
HO
N
H
3af
0.42
1.03
3.17
1.02
2.05
1.01
1.01
1.00
1.00
0.92
0.97
1.95
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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)

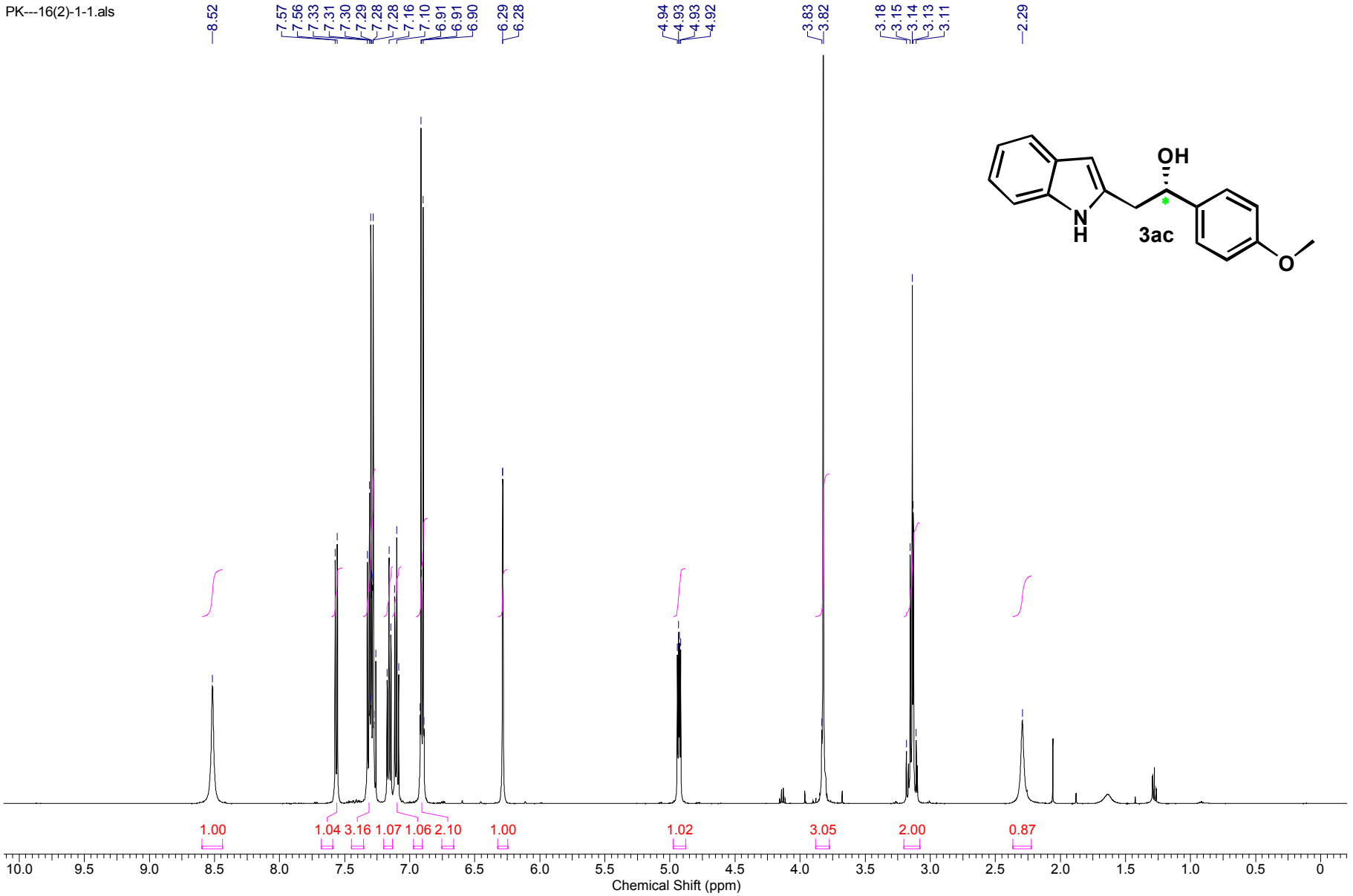

PK---1642)-pure-C13-1-1.als
206.62
143.87
138.03
134.39
129.81
128.81
128.64
128.53
126.87
126.50
125.39
125.25
121.30
120.32
119.72
111.59
101.28
74.31
39.33
30.38
30.23
30.07
29.92
29.77
29.61
29.46
HO
N
H
3af
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

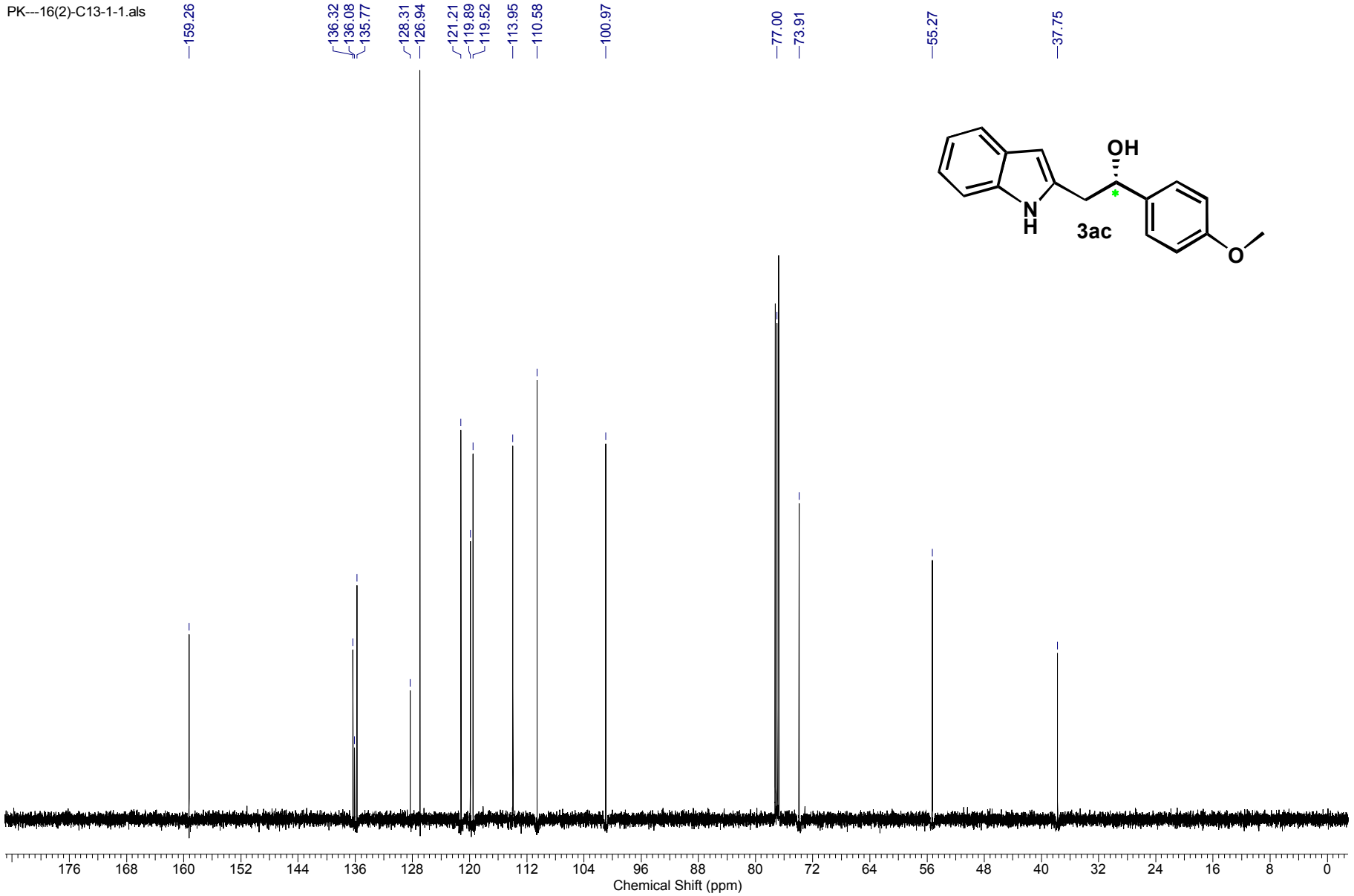

PKC---16(3)-1-1.als
8.46
7.57
7.55
7.42
7.32
7.30
7.26
7.15
7.15
7.13
7.10
7.09
6.36
6.36
6.35
6.32
6.27
6.26
5.03
5.02
5.01
5.00
3.31
3.30
2.39
2.38
2.37
1.60
1.60
OH
N
H
O
3ae
1.00
1.00 0.95 1.02 1.03 1.04
0.96 0.99 0.98
0.99
1.99
0.93
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

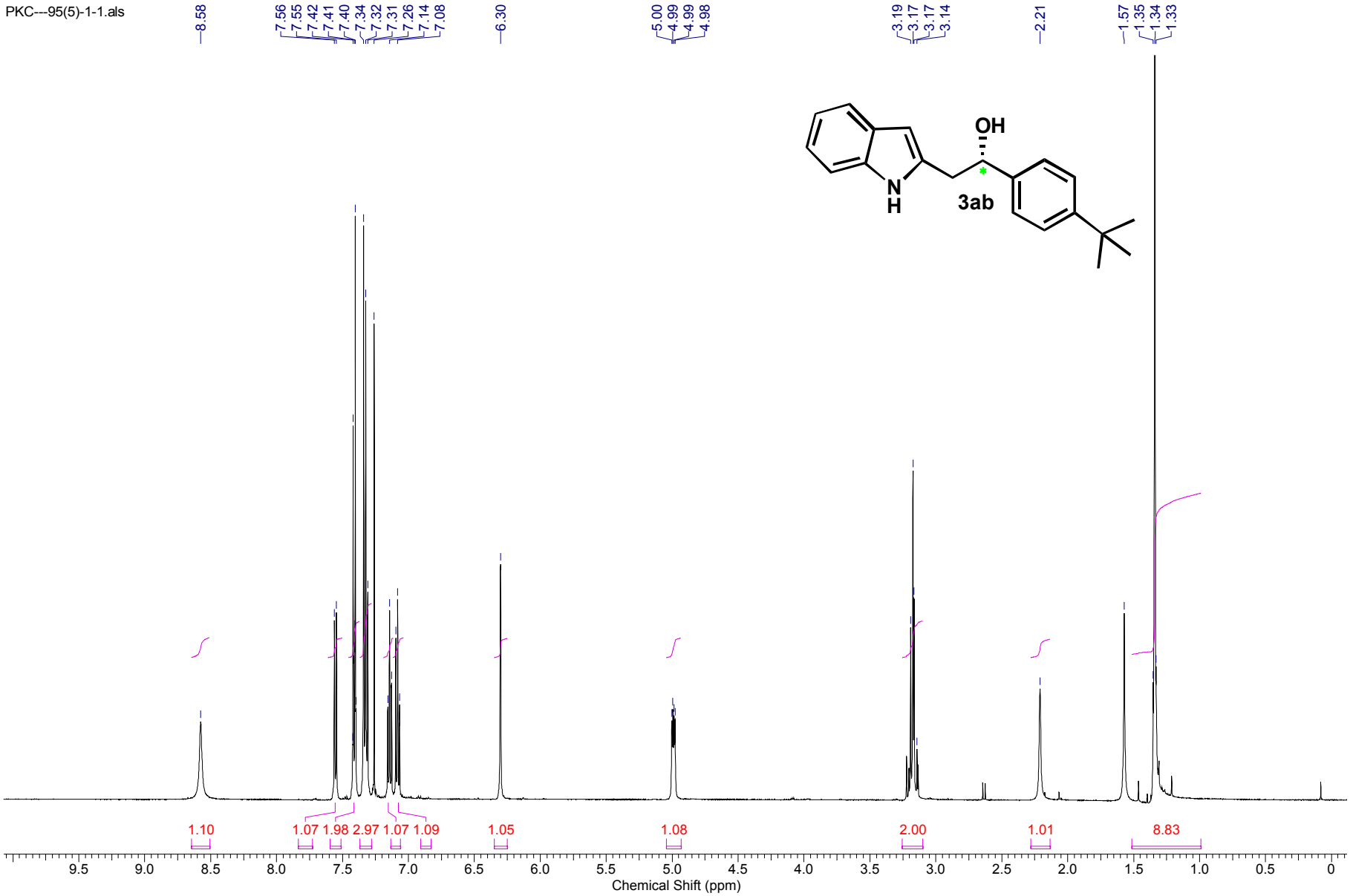

PKC---16(3)-pure-C13-1-1als
155.48
142.16
136.16
135.39
128.28
121.38
119.94
119.63
110.62
110.46
106.41
101.28
77.00
67.63
34.20
OH
N
H
O
3ae
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

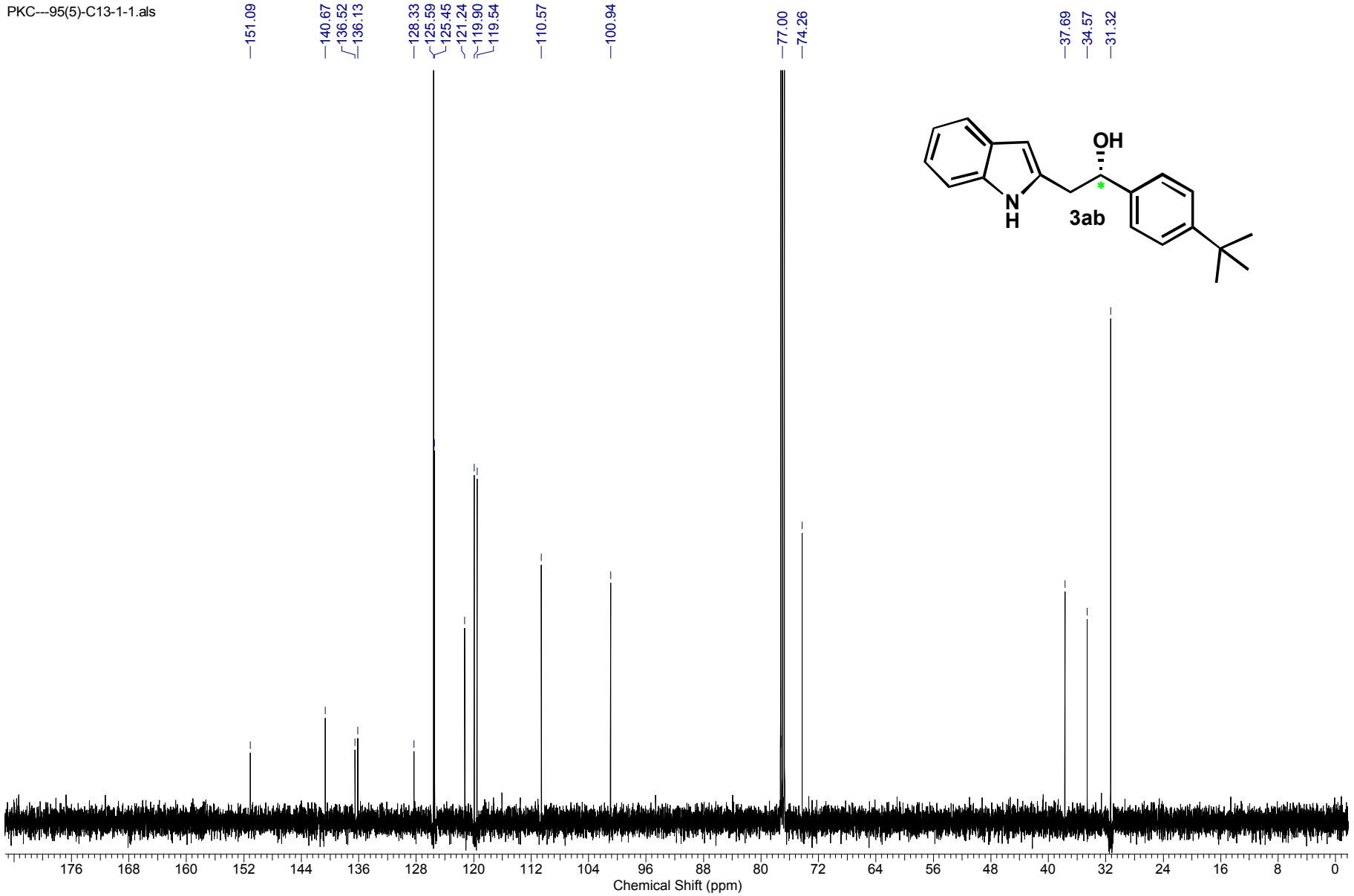

PK---95(3)-1-1.als
8.50
7.57
7.55
7.32
7.29
7.28
7.27
7.26
7.15
7.09
7.01
7.00
6.99
6.32
5.28
5.27
5.26
5.26
5.25
3.30
3.29
3.28
3.26
3.25
2.44
2.43
1.58
HO
S
N
H
3ad
0.82
1.00
0.96
0.91
1.01
1.04
2.01
0.94
0.99
1.98
0.87
Chemical Shift (ppm)

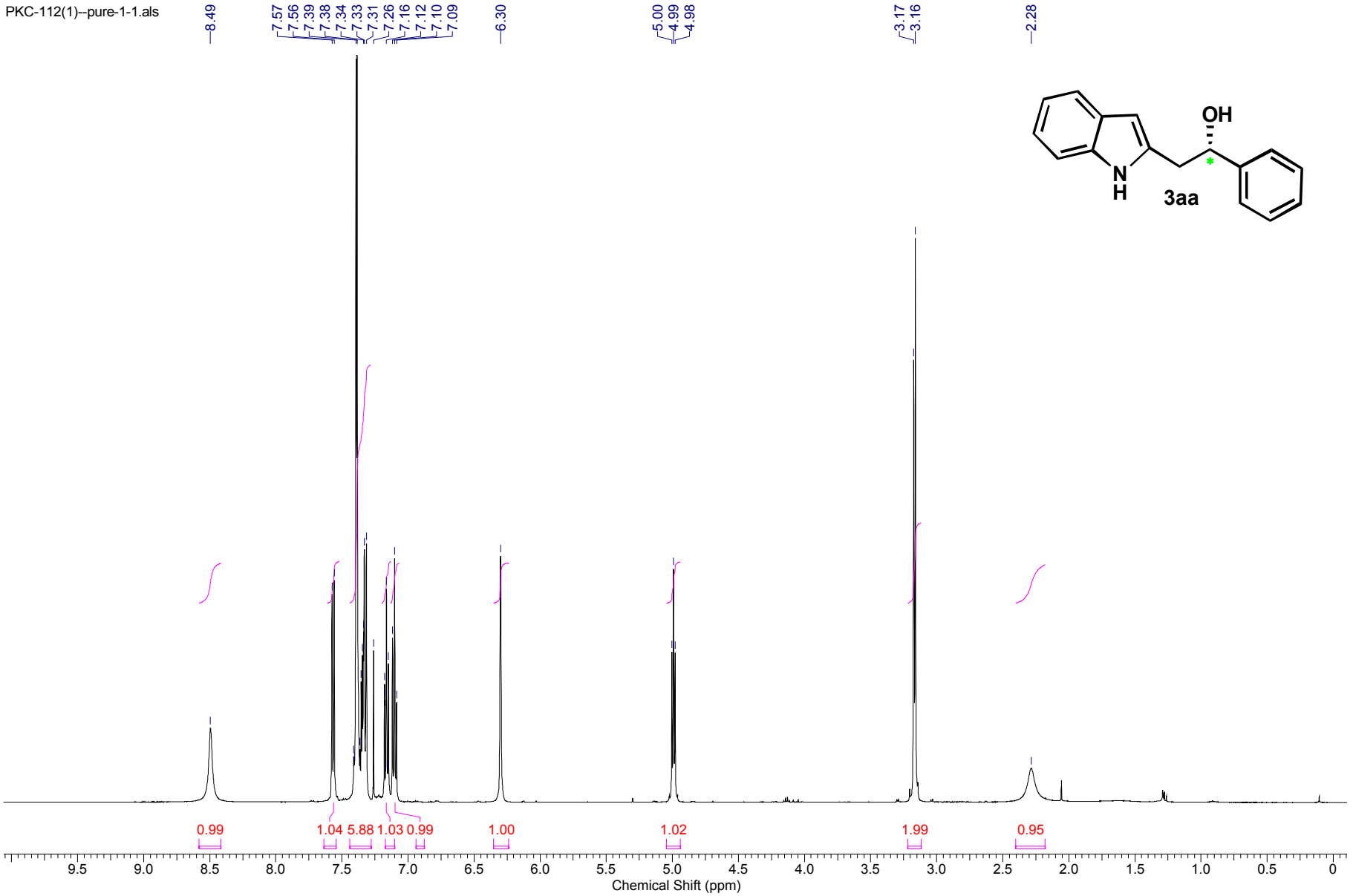

PKC---95(3)-C13-1-1.als
147.17
136.15
135.43
128.26
126.80
125.05
124.05
121.41
119.98
119.64
110.63
101.45
77.00
70.19
37.97
HO
S
N
H
3ad
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

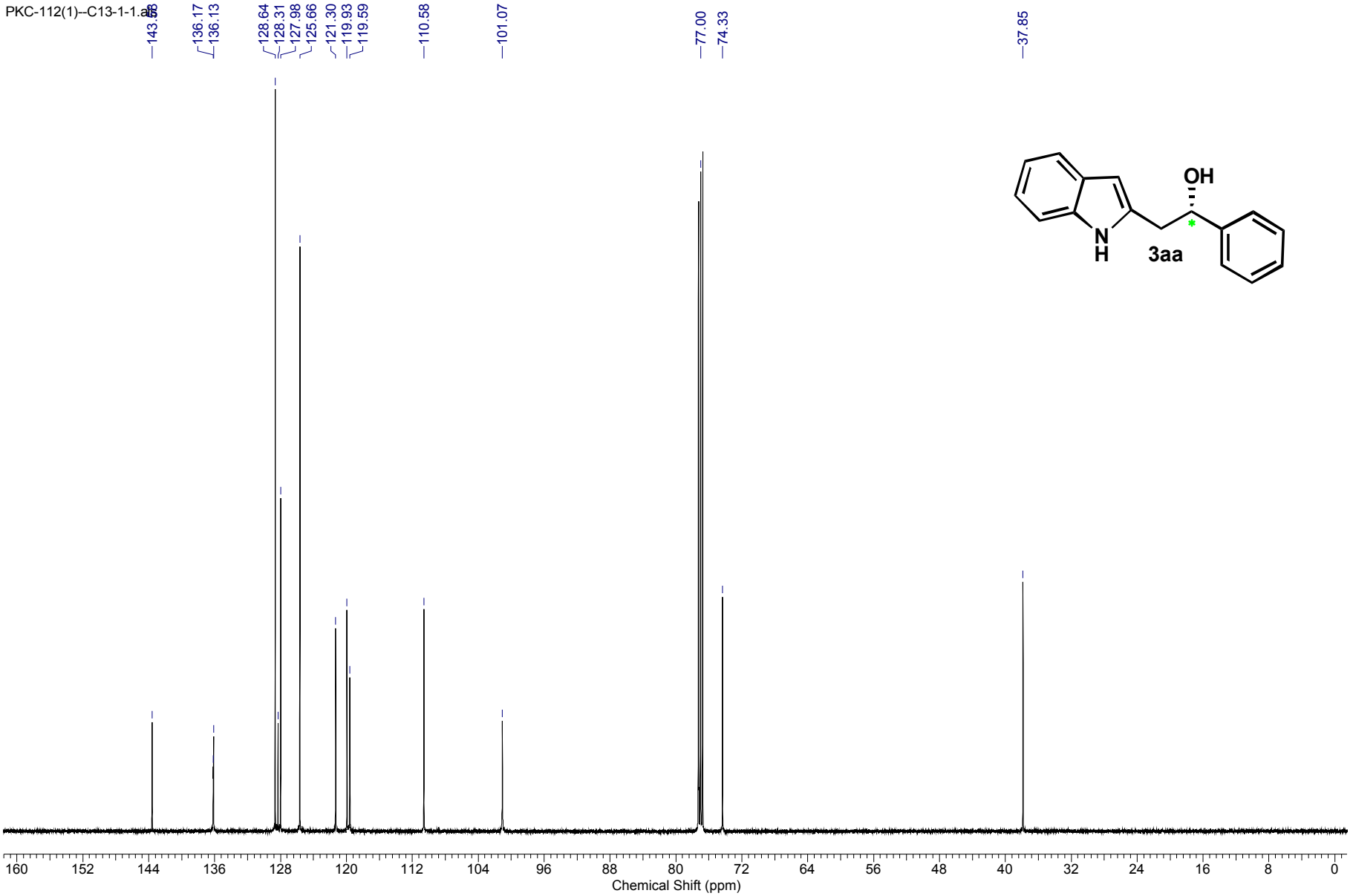

PK---16(2)-1-1.als
8.52
7.57
7.56
7.33
7.31
7.30
7.29
7.28
7.28
7.16
7.10
6.91
6.91
6.90
6.29
6.28
4.94
4.93
4.93
4.92
3.83
3.82
3.18
3.15
3.14
3.13
3.11
2.29
OH
N
H
3ac
O
1.00
1.04
3.16
1.07
1.06
2.10
1.00
1.02
3.05
2.00
0.87
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

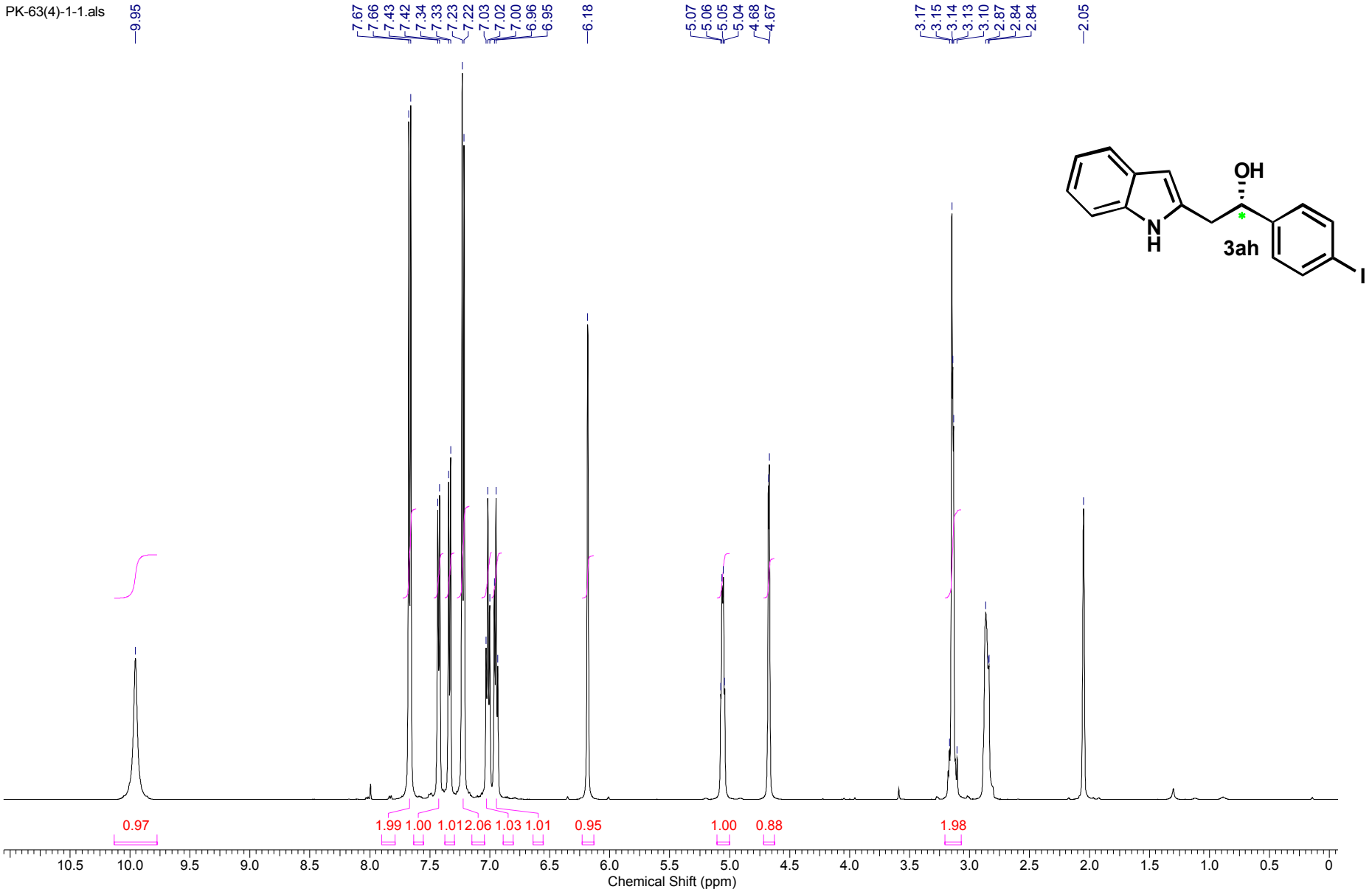

PK---16(2)-C13-1-1.als
159.26
136.32
136.08
135.77
128.31
126.94
121.21
119.89
119.52
113.95
110.58
100.97
77.00
73.91
55.27
37.75
OH
N
H
3ac
O
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

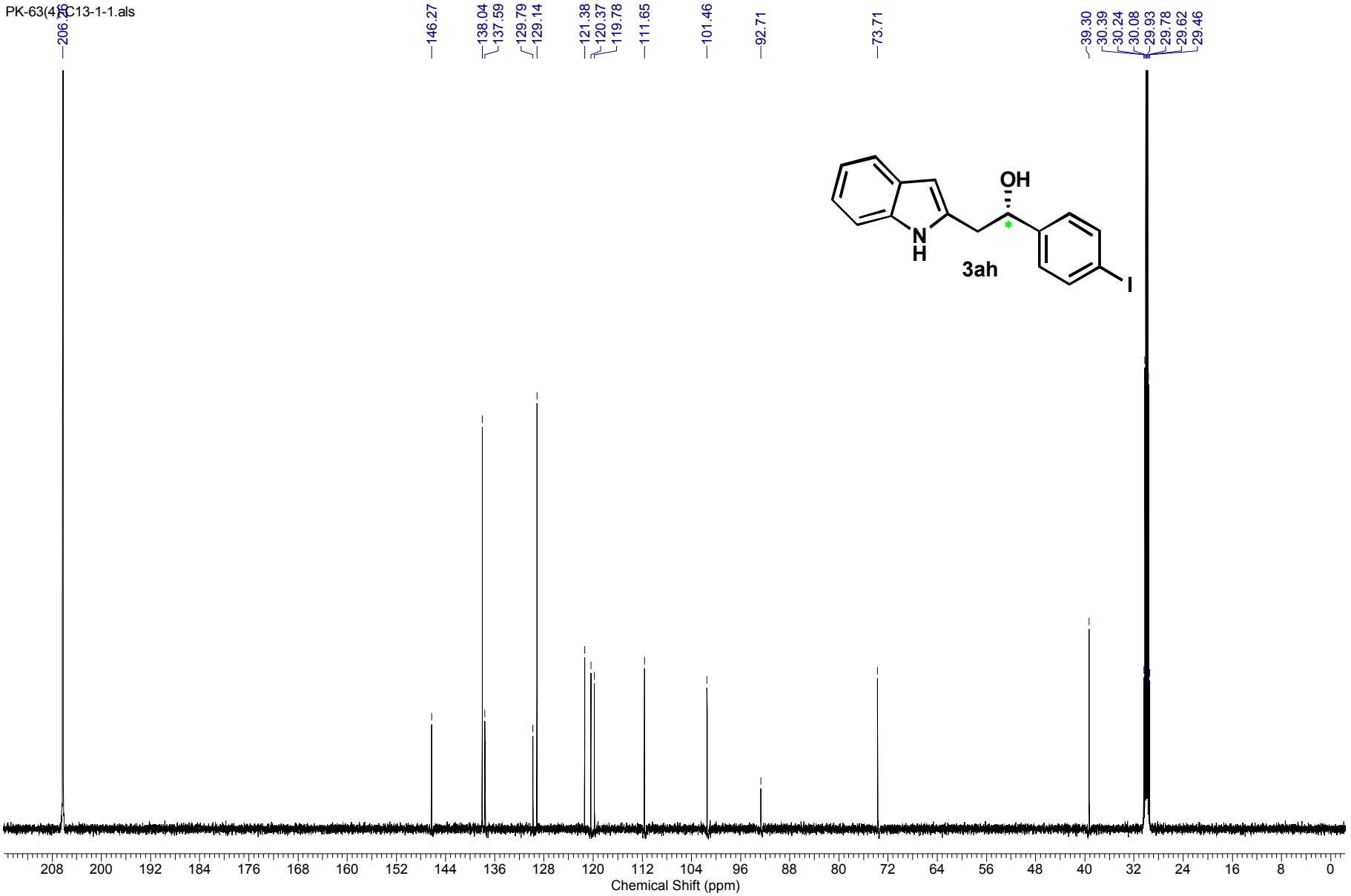

PKC---95(5)-1-1.als
8.58
7.56
7.55
7.42
7.41
7.40
7.34
7.32
7.31
7.26
7.14
7.08
6.30
5.00
4.99
4.99
4.98
3.19
3.17
3.17
3.14
2.21
1.57
1.35
1.34
1.33
OH
N
H
3ab
1.10
1.07
1.98
2.97
1.07
1.09
1.05
1.08
2.00
1.01
8.83
Chemical Shift (ppm)

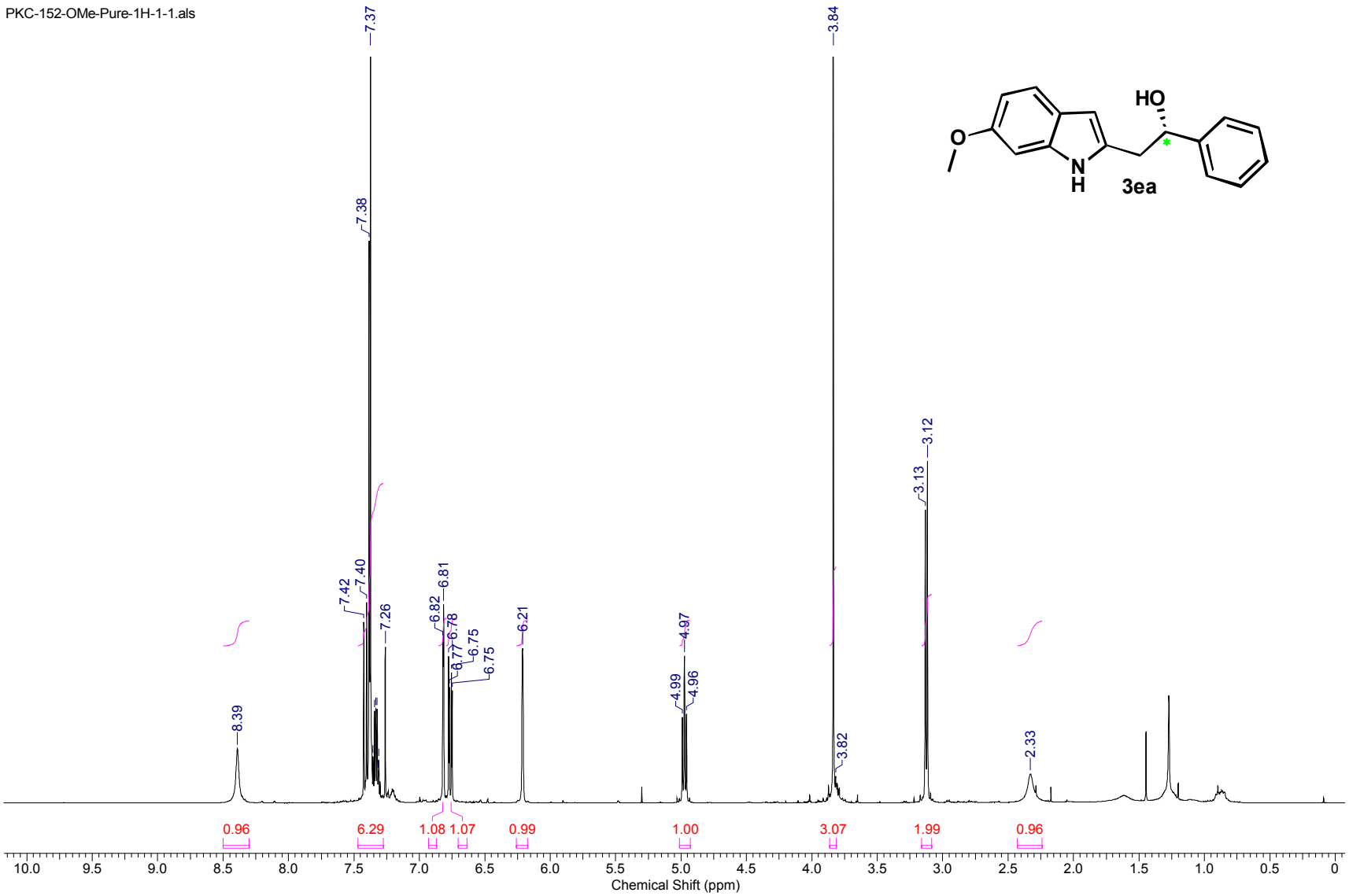

PKC---95(5)-C13-1-1.als
151.09
140.67
136.52
136.13
128.33
125.59
125.45
121.24
119.90
119.54
110.57
100.94
77.00
74.26
37.69
34.57
31.32
OH
N
H
3ab
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

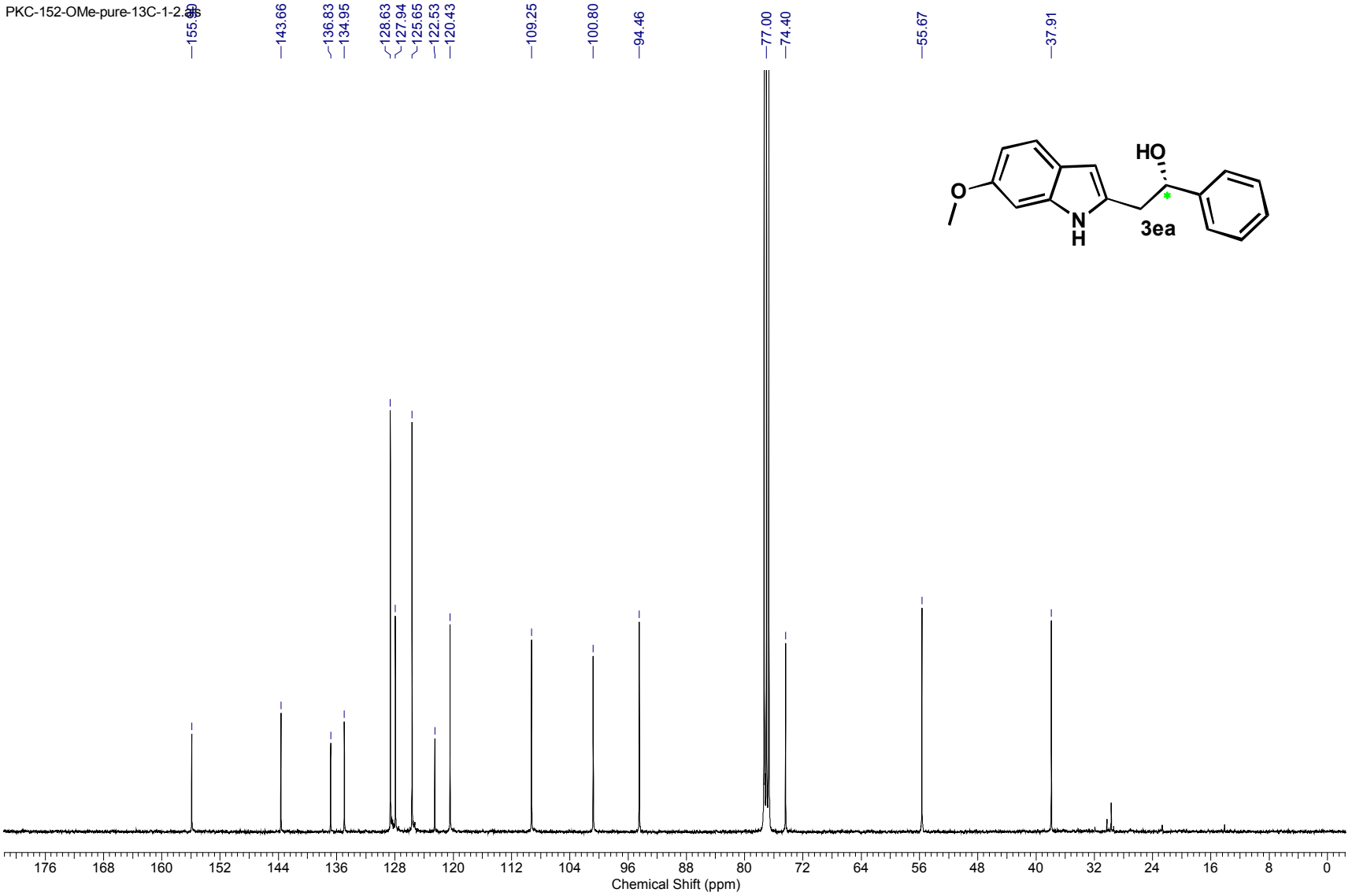

PKC-112(1)--pure-1-1.als
8.49
7.57
7.56
7.39
7.38
7.34
7.33
7.31
7.26
7.16
7.12
7.10
7.09
6.30
5.00
4.99
4.98
3.17
3.16
2.28
OH
N
H
3aa
0.99
1.04
5.88
1.03
0.99
1.00
1.02
1.99
0.95
Chemical Shift (ppm)

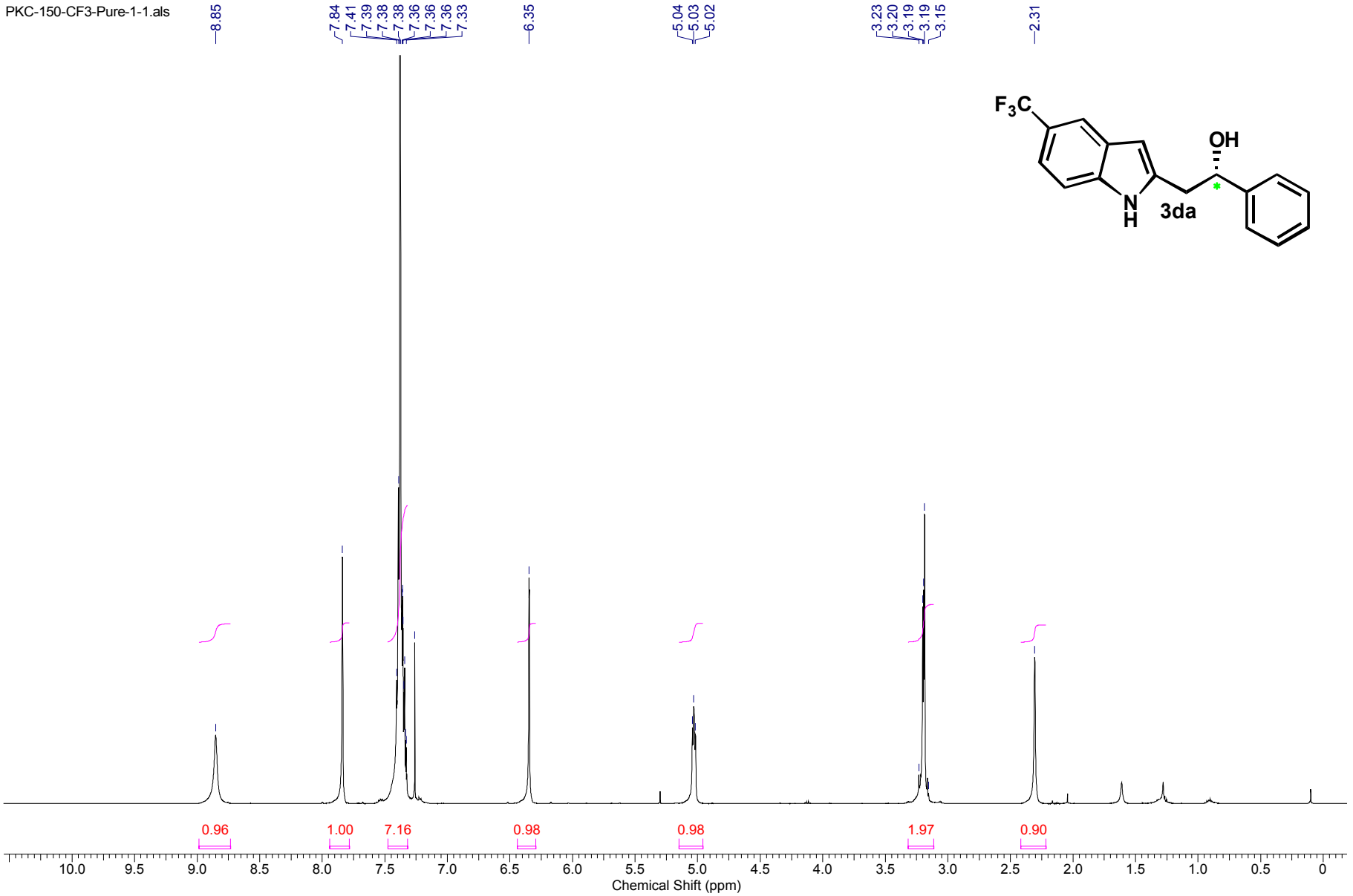

PKC-112(1)--C13-1-1.als
143.88
136.17
136.13
128.64
128.31
127.98
125.66
121.30
119.93
119.59
110.58
101.07
77.00
74.33
37.85
OH
N
H
3aa
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

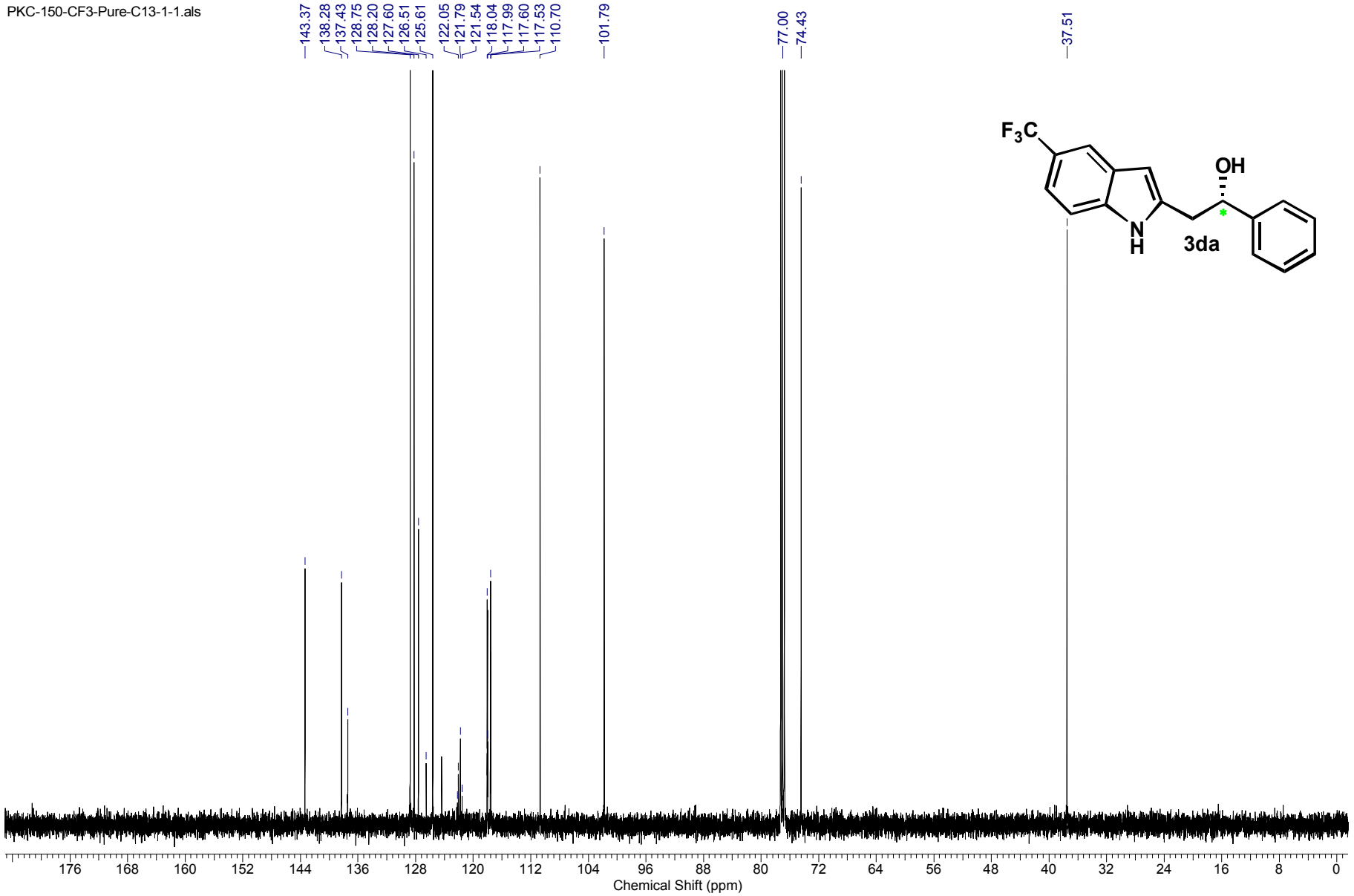

PK-63(4)-1-1.als
9.95
7.67
7.66
7.43
7.42
7.34
7.33
7.23
7.22
7.03
7.02
7.00
6.96
6.95
6.18
5.07
5.06
5.05
5.04
4.68
4.67
3.17
3.15
3.14
3.13
3.10
2.87
2.84
2.84
2.05
OH
N
H
3ah
I
0.97
1.99
1.00
1.01
2.06
1.03
1.01
0.95
1.00
0.88
1.98
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

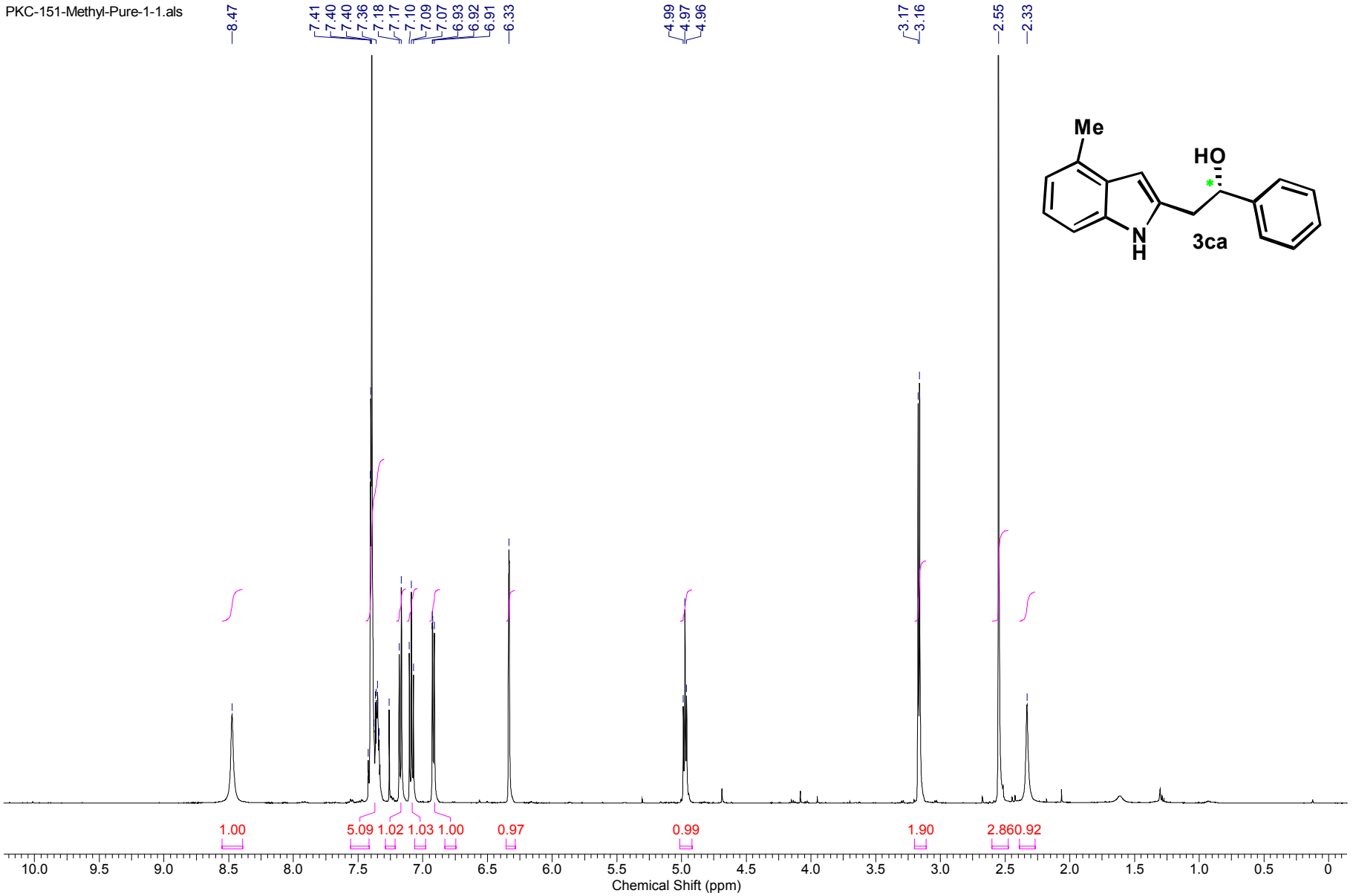

PK-63(4)C13-1-1.als
206.26
146.27
138.04
137.59
129.79
129.14
121.38
120.37
119.78
111.65
101.46
92.71
73.71
39.30
30.39
30.24
30.08
29.93
29.78
29.62
29.46
OH
N
H
3ah
I
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

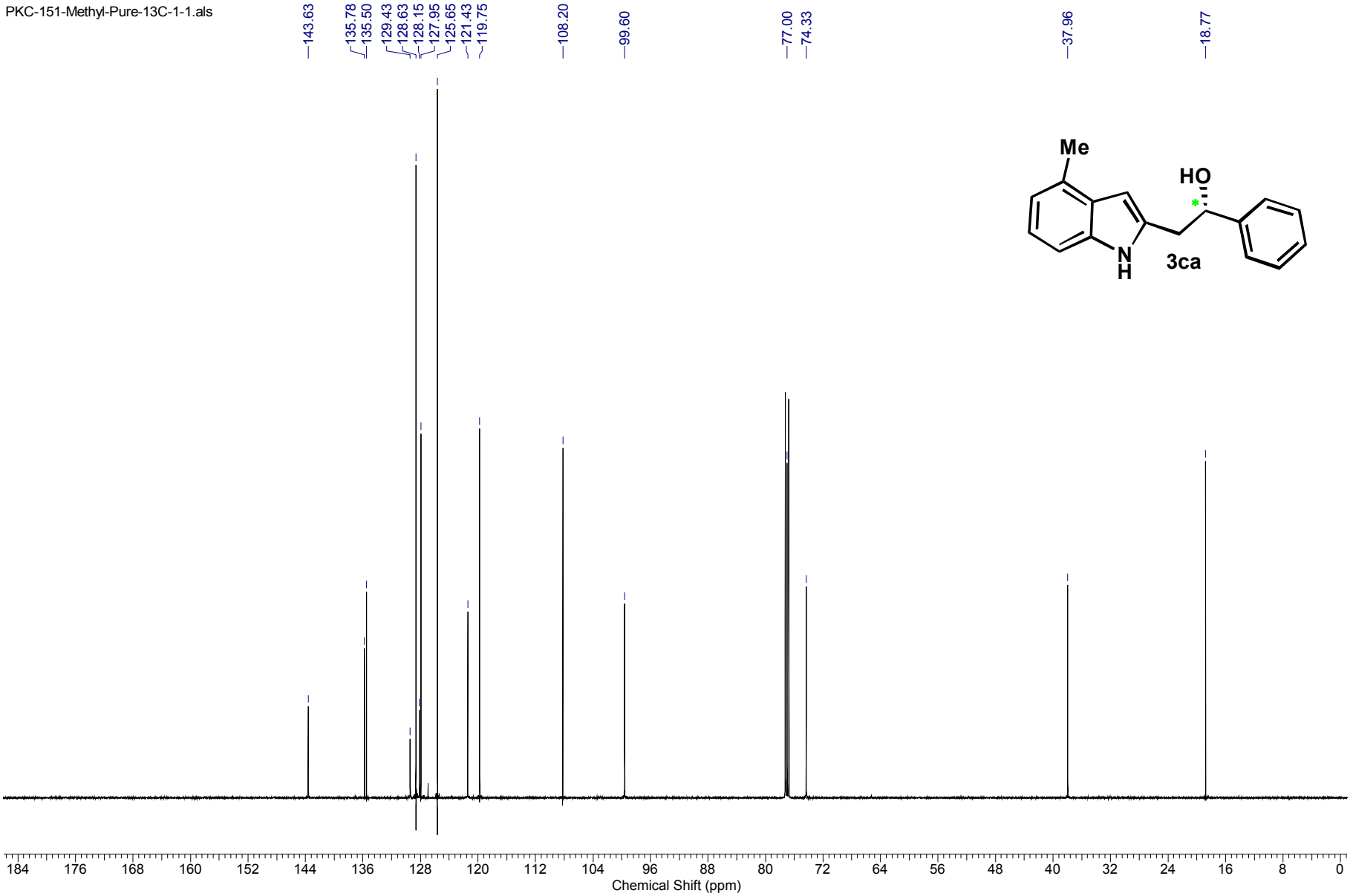

PKC-152-OMe-Pure-1H-1-1.als
7.37
3.84
7.38
HO
O
N
H
3ea
7.42
7.40
6.82
6.81
7.26
6.78
6.77
6.75
6.75
6.21
4.97
4.99
4.96
3.13
3.12
8.39
3.82
2.33
0.96
6.29
1.08
1.07
0.99
1.00
3.07
1.99
0.96
Chemical Shift (ppm)

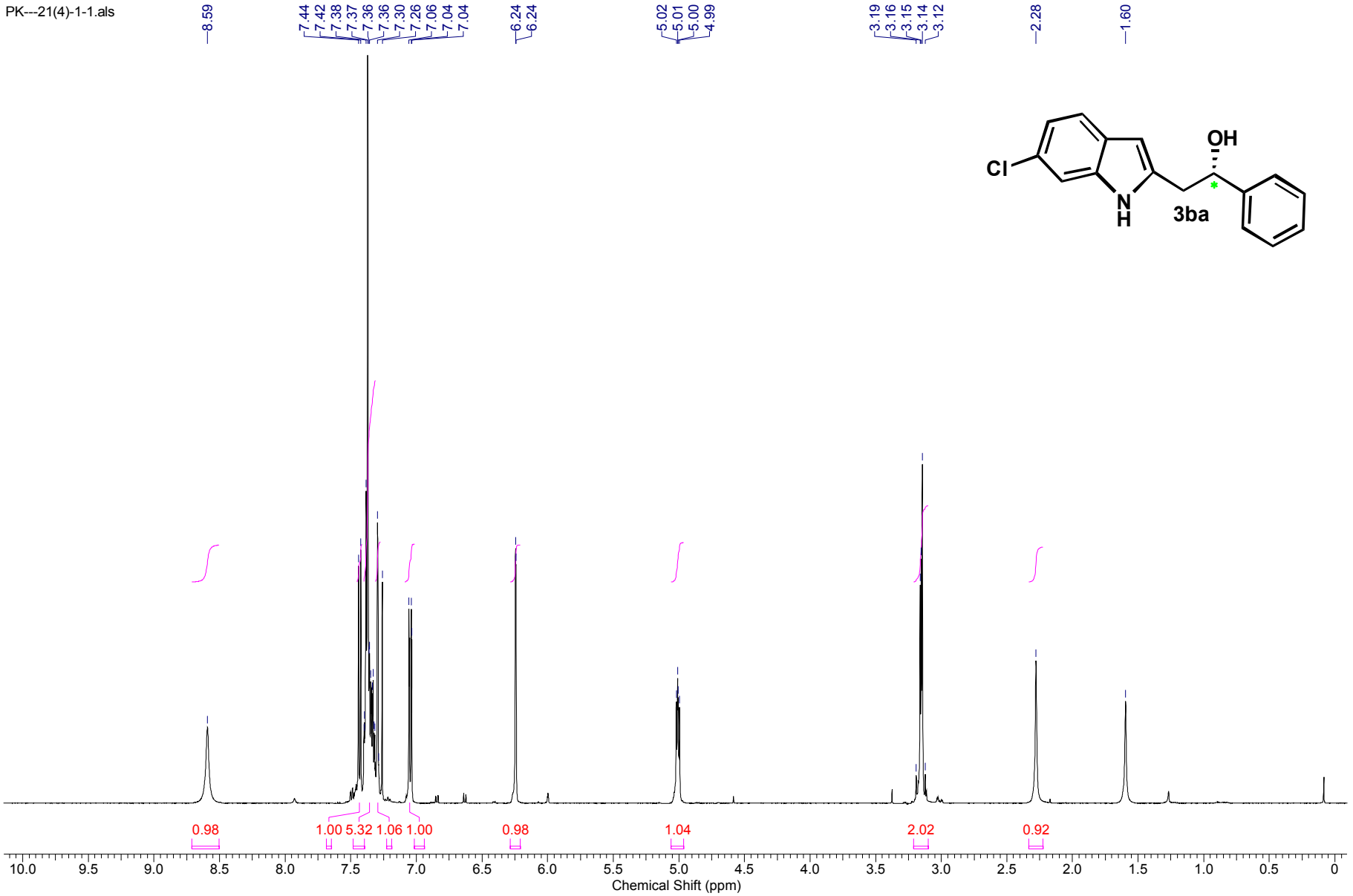

PKC-152-OMe-pure-13C-1-2.as
155.40
143.66
136.83
134.95
128.63
127.94
125.65
122.53
120.43
109.25
100.80
94.46
77.00
74.40
55.67
37.91
HO
O
N
H
3ea
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

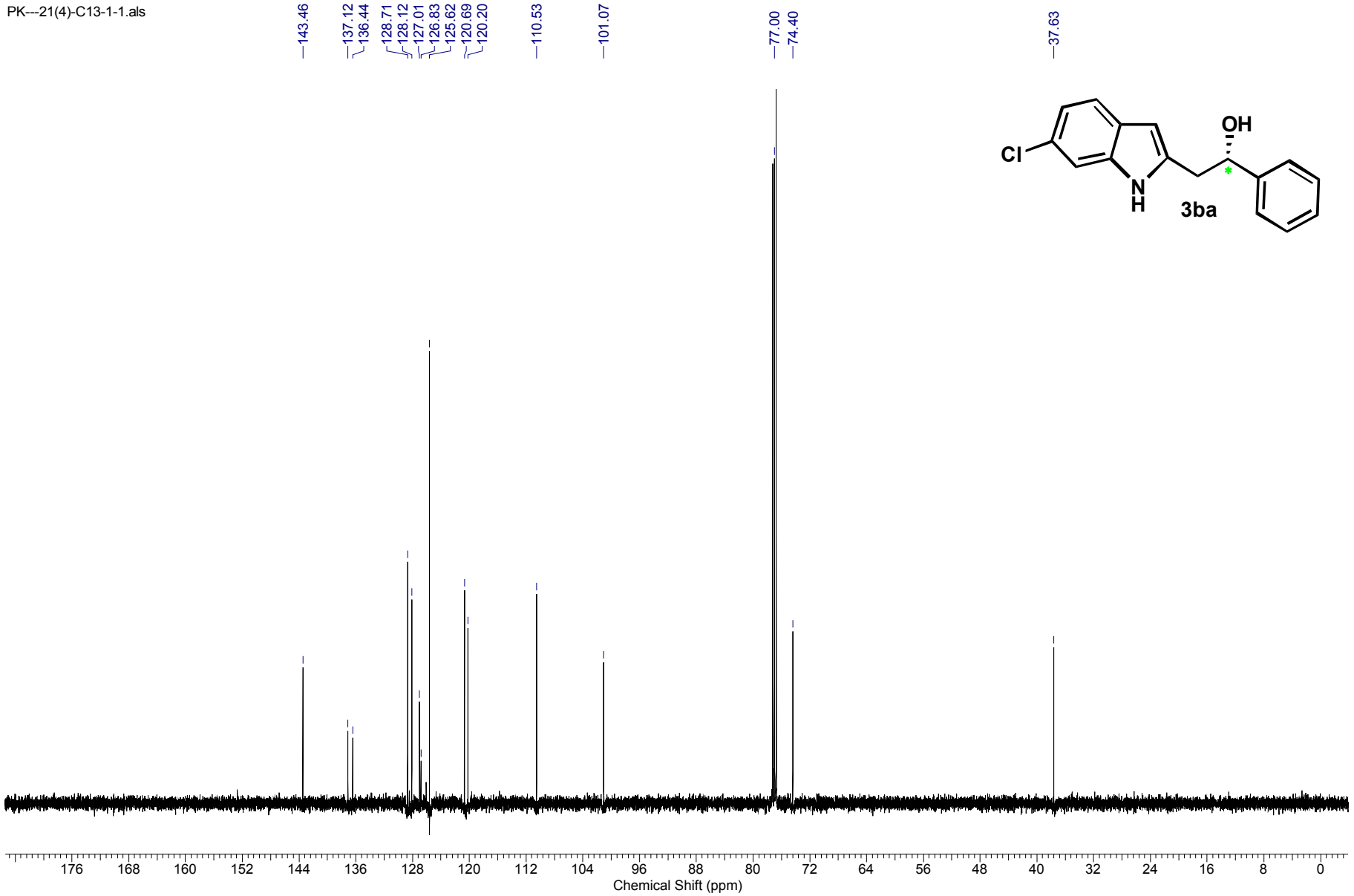

PKC-150-CF3-Pure-1-1.als
8.85
7.84
7.41
7.39
7.38
7.38
7.36
7.36
7.36
7.33
6.35
5.04
5.03
5.02
3.23
3.20
3.19
3.19
3.15
2.31
F3C
OH
N
H
3da
0.96
1.00
7.16
0.98
0.98
1.97
0.90
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

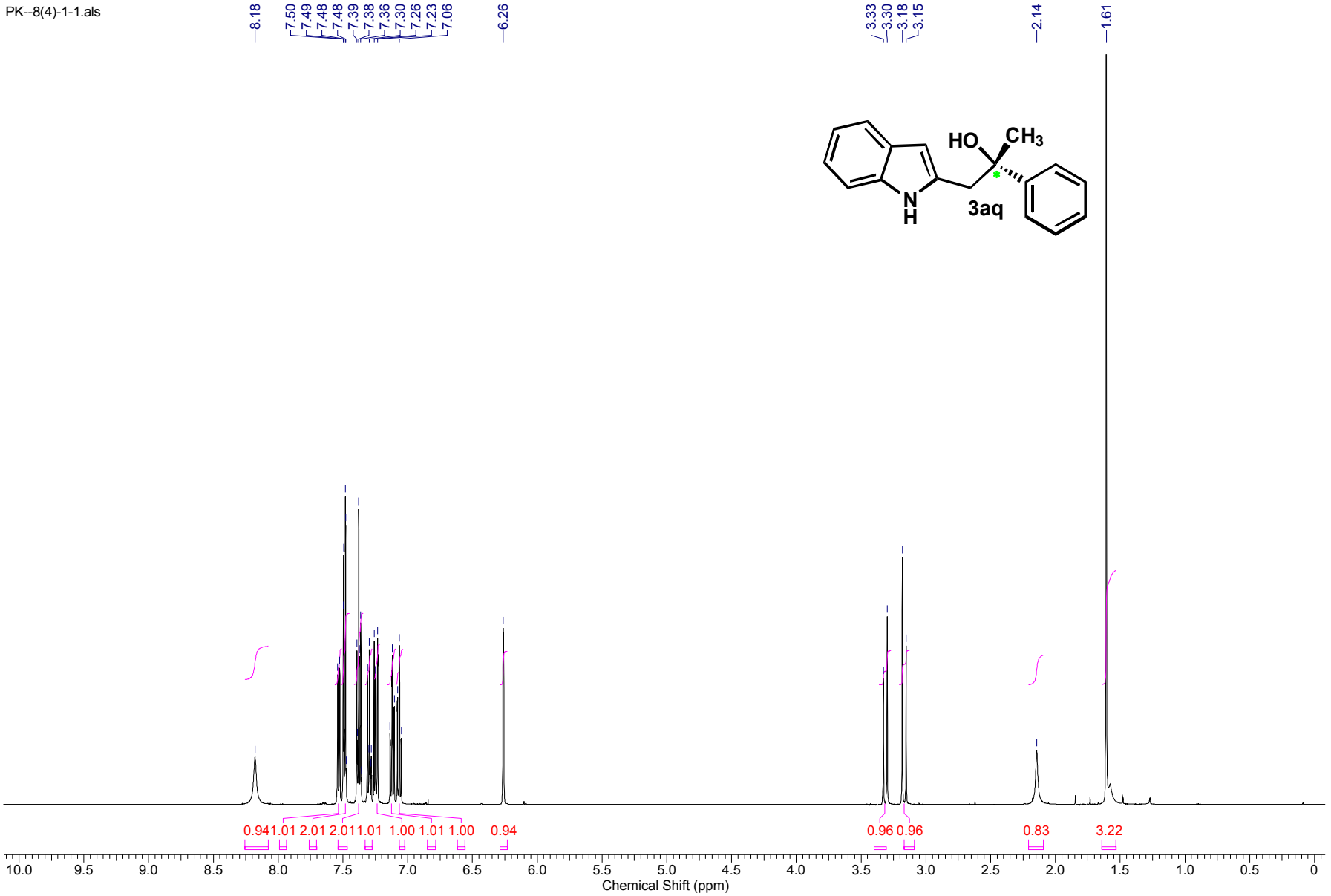

PKC-150-CF3-Pure-C13-1-1.als
143.37
138.28
137.43
128.75
128.20
127.60
126.51
125.61
122.05
121.79
121.54
118.04
117.99
117.60
117.53
110.70
101.79
77.00
74.43
37.51
F3C
OH
N
H
3da
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

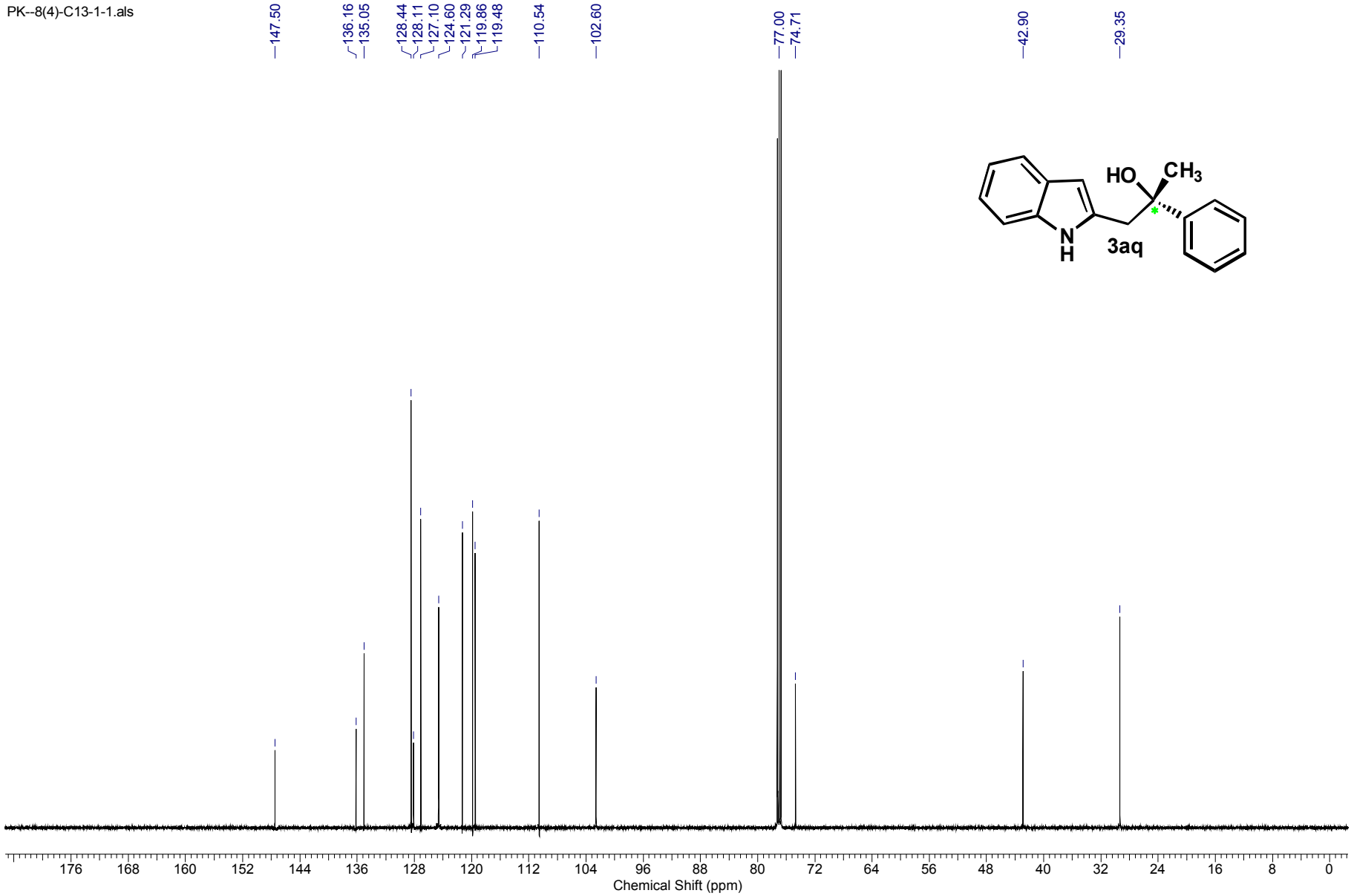

PKC-151-Methyl-Pure-1-1.als
8.47
7.41
7.40
7.40
7.36
7.18
7.17
7.10
7.09
7.07
6.93
6.92
6.91
6.33
4.99
4.97
4.96
3.17
3.16
2.55
2.33
Me
HO
N
H
3ca
1.00
5.09
1.02
1.03
1.00
0.97
0.99
1.90
2.86
0.92
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

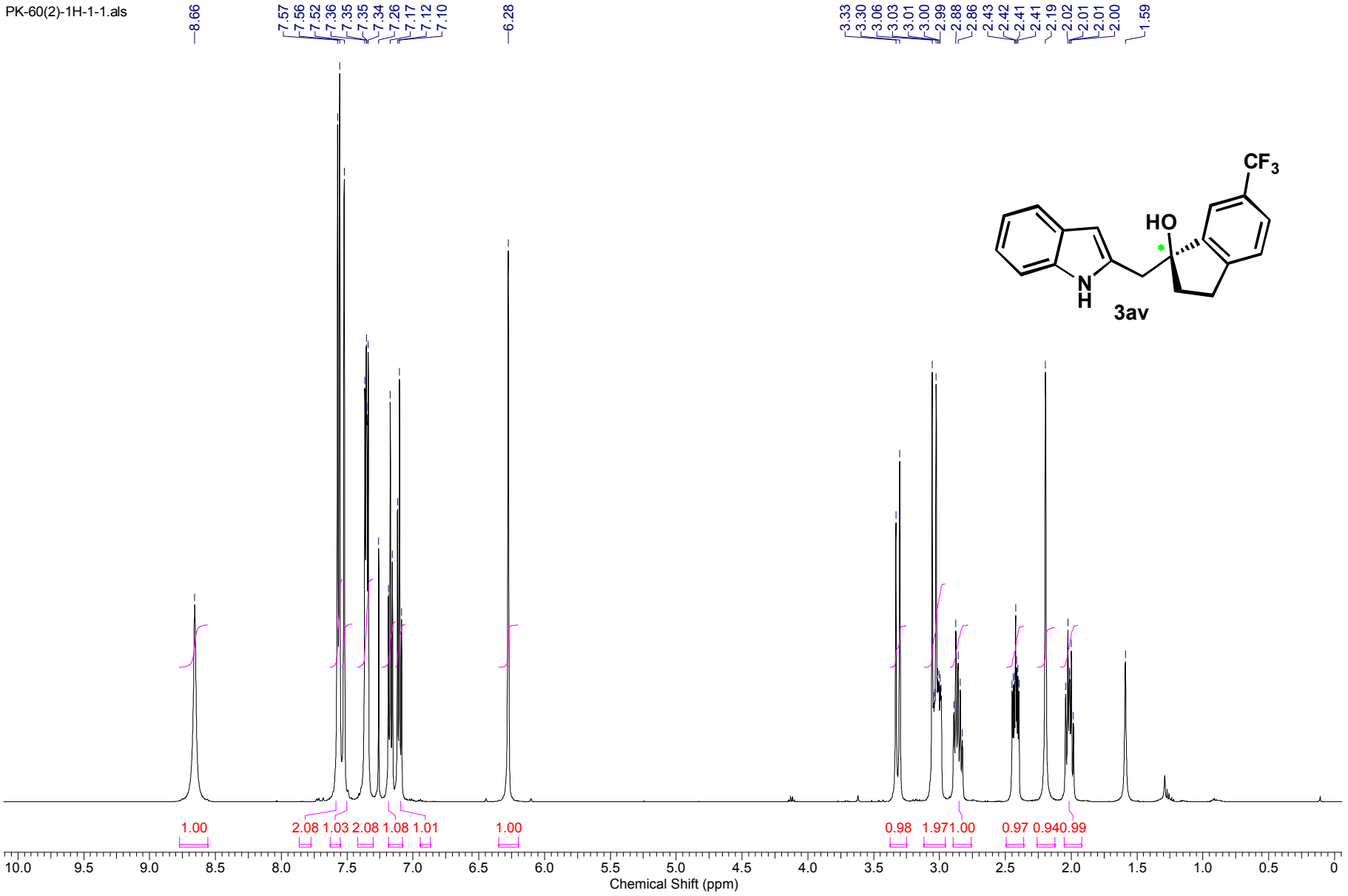

PKC-151-Methyl-Pure-13C-1-1.als
143.63
135.78
135.50
129.43
128.63
128.15
127.95
125.65
121.43
119.75
108.20
99.60
77.00
74.33
37.96
18.77
Me
HO
N
H
3ca
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

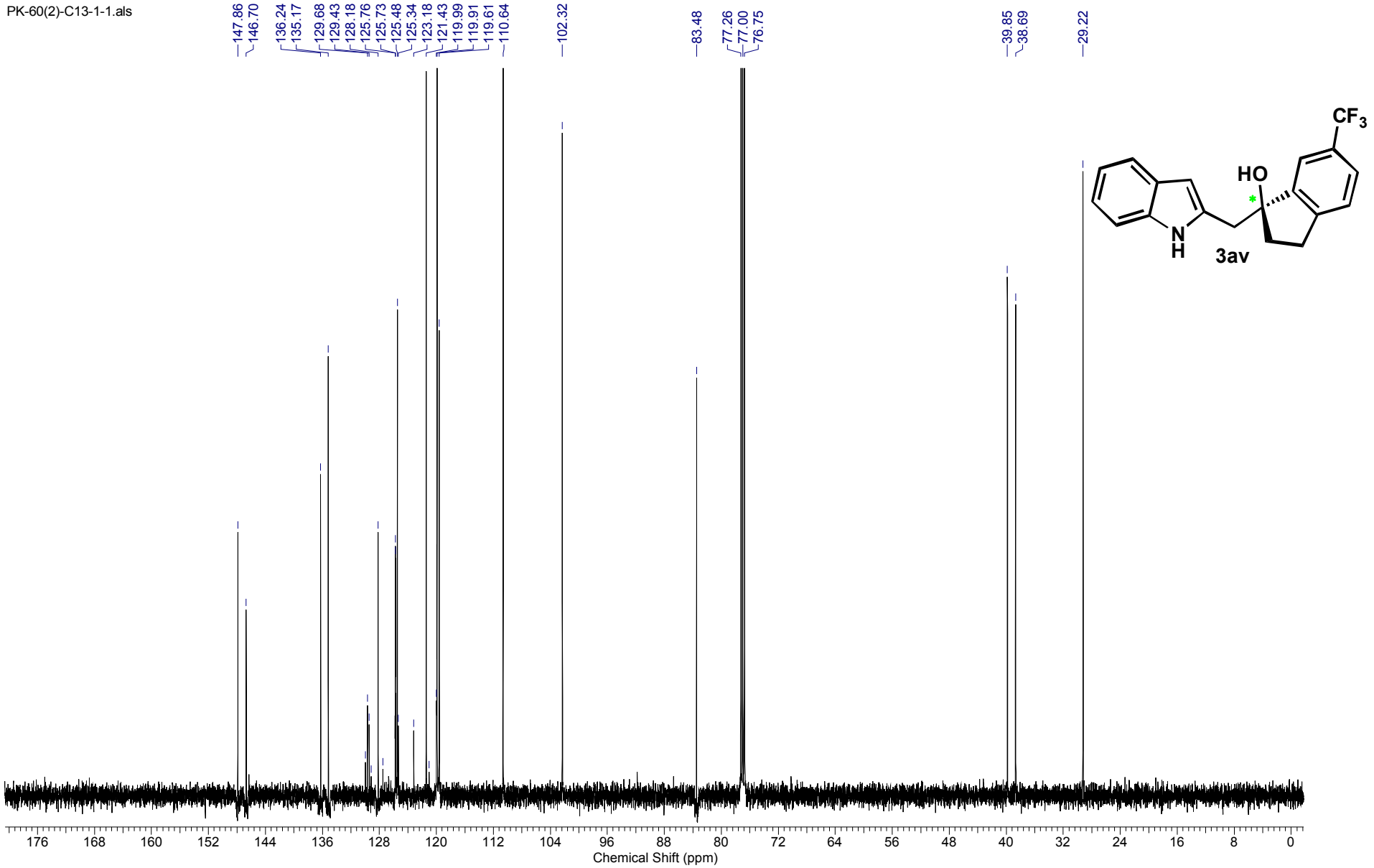

PK---21(4)-1-1.als
8.59
7.44
7.42
7.38
7.37
7.36
7.36
7.30
7.26
7.06
7.04
7.04
6.24
6.24
5.02
5.01
5.00
4.99
3.19
3.16
3.15
3.14
3.12
2.28
1.60
Cl
N
H
OH
3ba
0.98
1.00
5.32
1.06
1.00
0.98
1.04
2.02
0.92
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

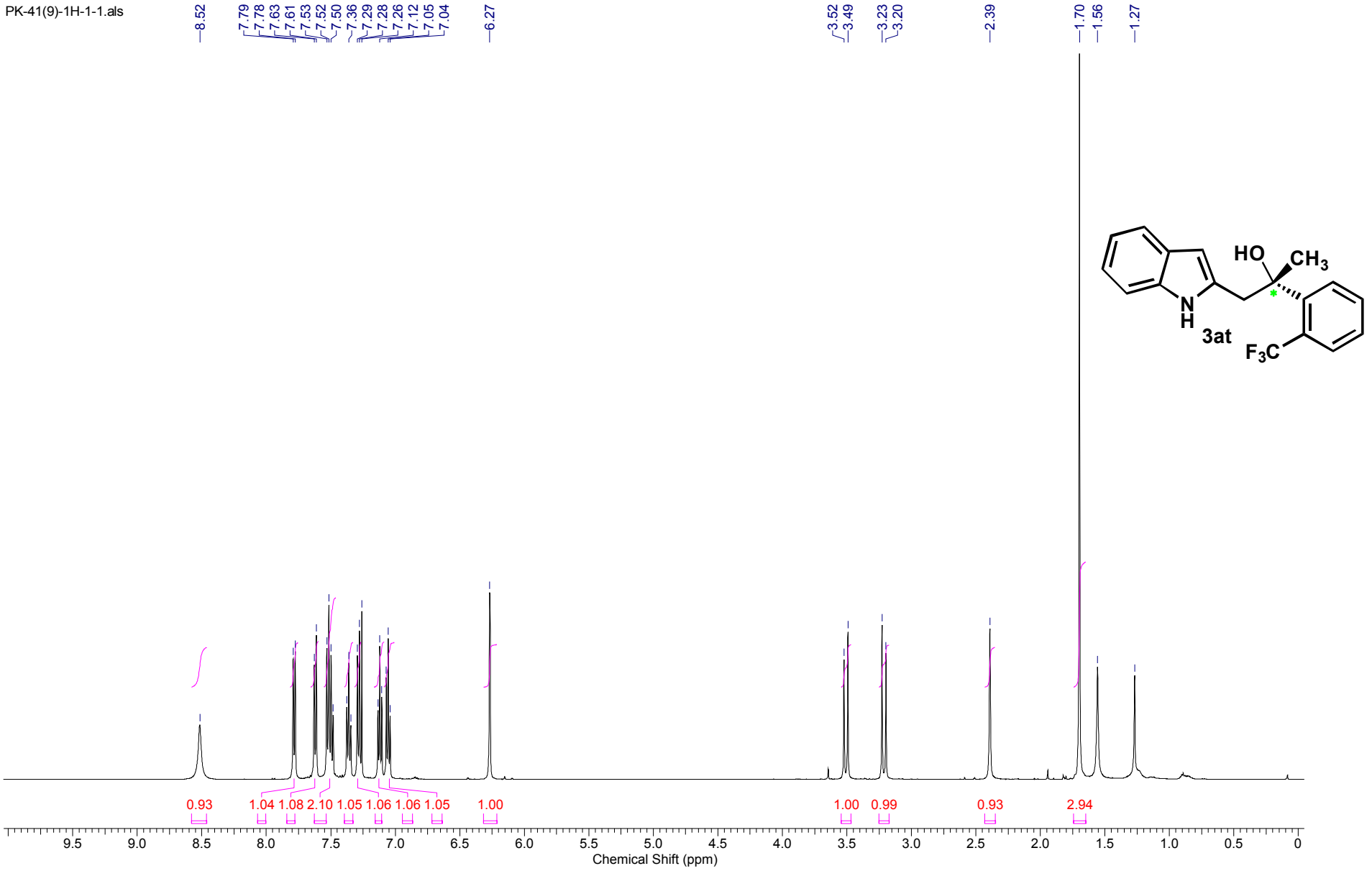

PK---21(4)-C13-1-1.als
143.46
137.12
136.44
128.71
128.12
127.01
126.83
125.62
120.69
120.20
110.53
101.07
77.00
74.40
37.63
Cl
OH
N
H
3ba
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

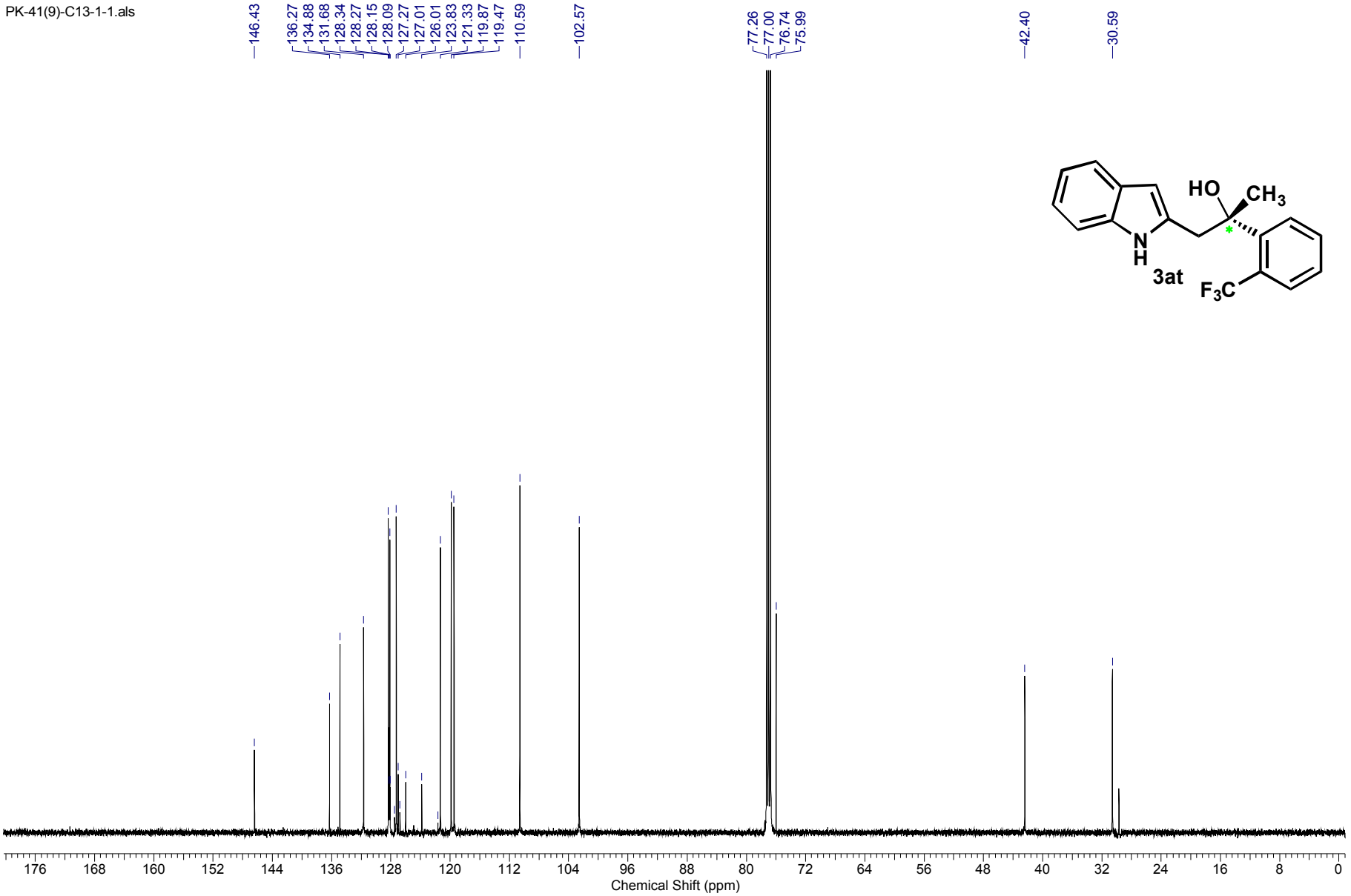

PK--8(4)-1-1.als
8.18
7.50
7.49
7.48
7.48
7.39
7.38
7.36
7.30
7.26
7.23
7.06
6.26
3.33
3.30
3.18
3.15
2.14
1.61
HO
CH3
N
H
3aq
0.94
1.01
2.01
2.01
1.01
1.00
1.01
1.00
0.94
0.96
0.96
0.83
3.22
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

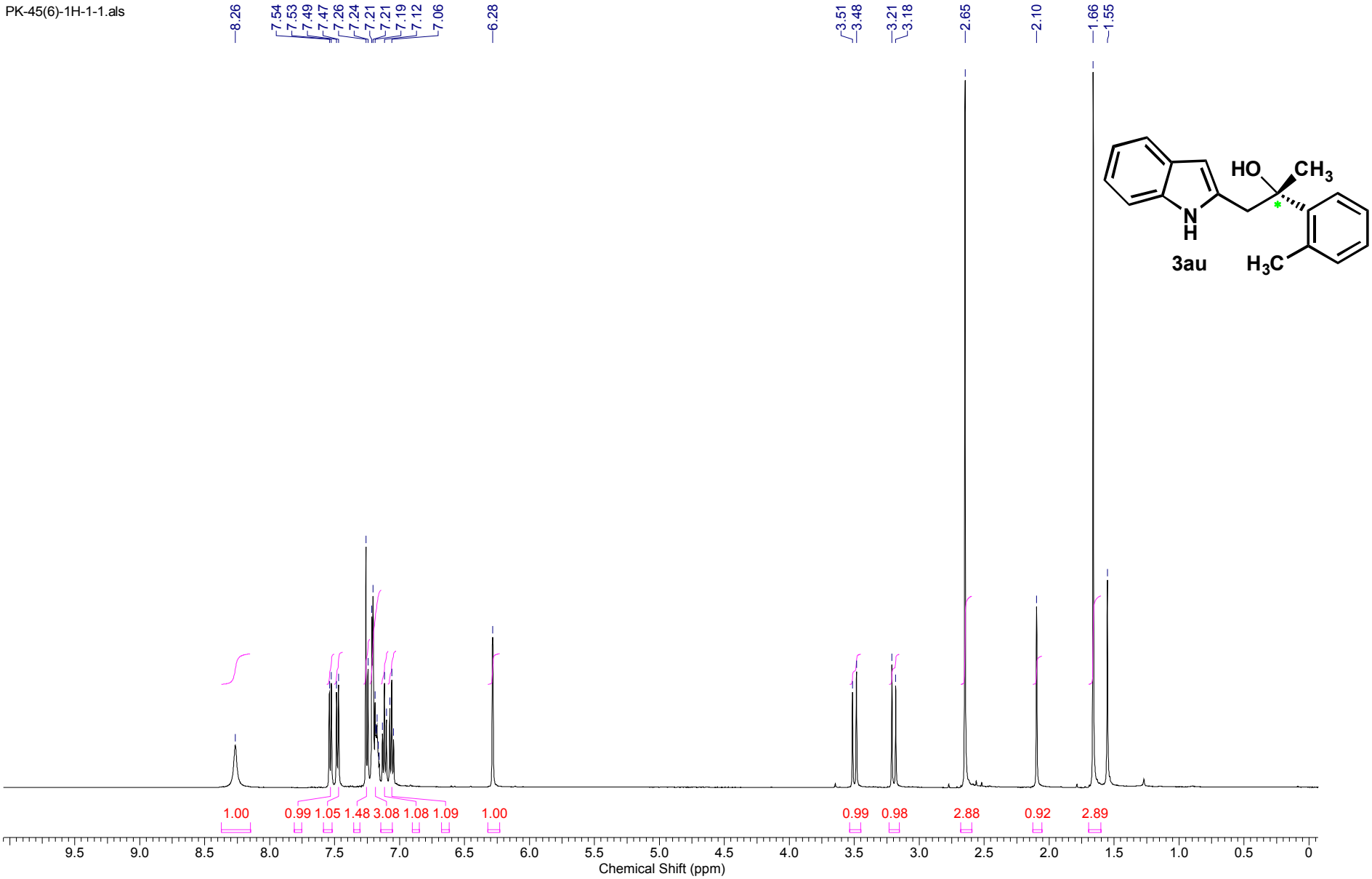

PK--8(4)-C13-1-1.als
147.50
136.16
135.05
128.44
128.11
127.10
124.60
121.29
119.86
119.48
110.54
102.60
77.00
74.71
42.90
29.35
HO
CH3
N
H
3aq
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

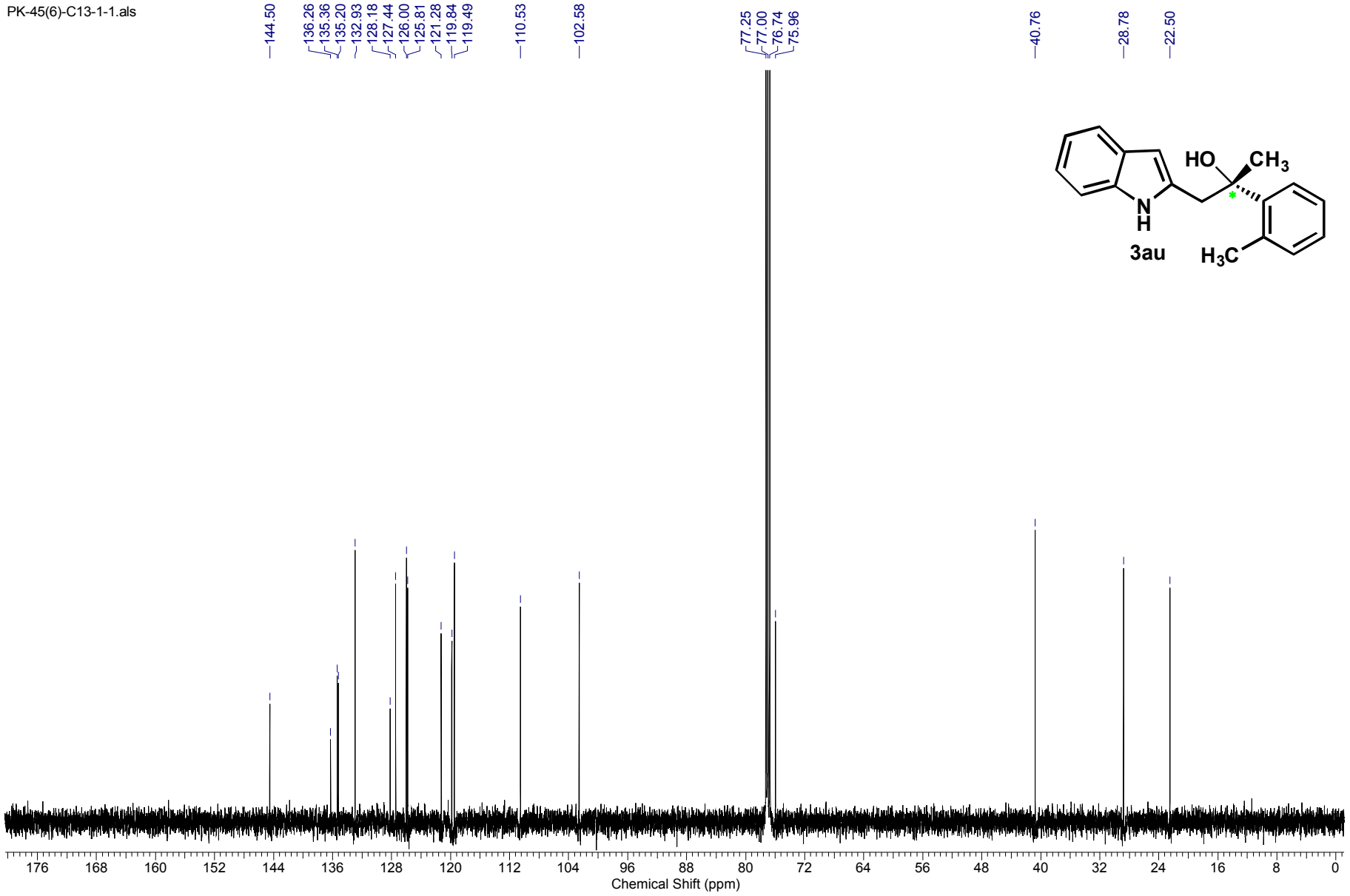

PK-60(2)-1H-1-1.als
8.66
7.57
7.56
7.52
7.36
7.35
7.35
7.34
7.26
7.17
7.12
7.10
6.28
3.33
3.30
3.06
3.03
3.01
3.00
2.99
2.88
2.86
2.43
2.42
2.41
2.41
2.19
2.02
2.01
2.01
2.00
1.59
CF3
HO
N
H
3av
1.00
2.08
1.03
2.08
1.08
1.01
1.00
0.98
1.97
1.00
0.97
0.94
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

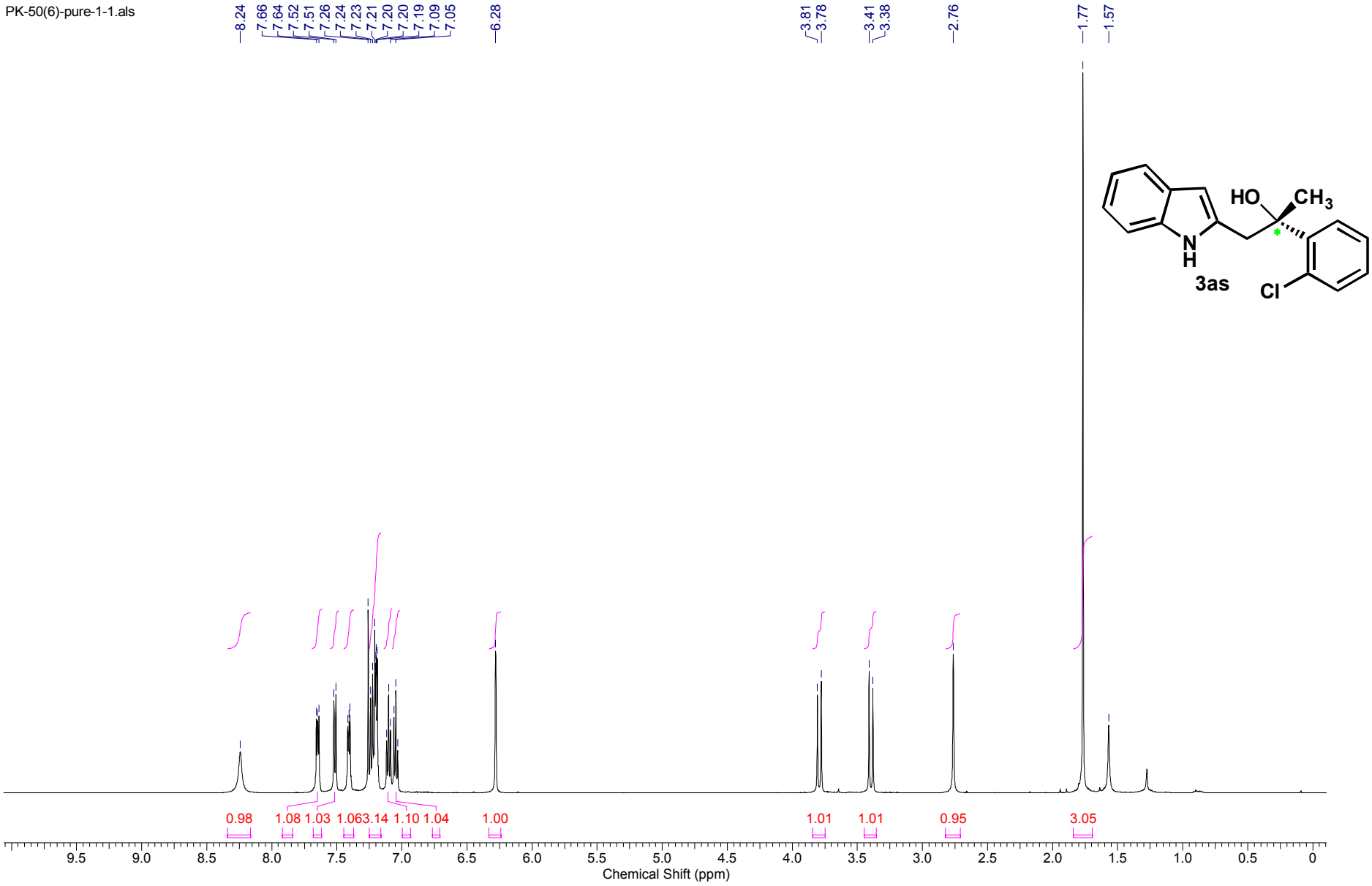

PK-60(2)-C13-1-1.als
147.86
146.70
136.24
135.17
129.68
129.43
128.18
125.76
125.73
125.48
125.34
123.18
121.43
119.99
119.91
119.61
110.64
102.32
83.48
77.26
77.00
76.75
39.85
38.69
29.22
CF3
HO
N
H
3av
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

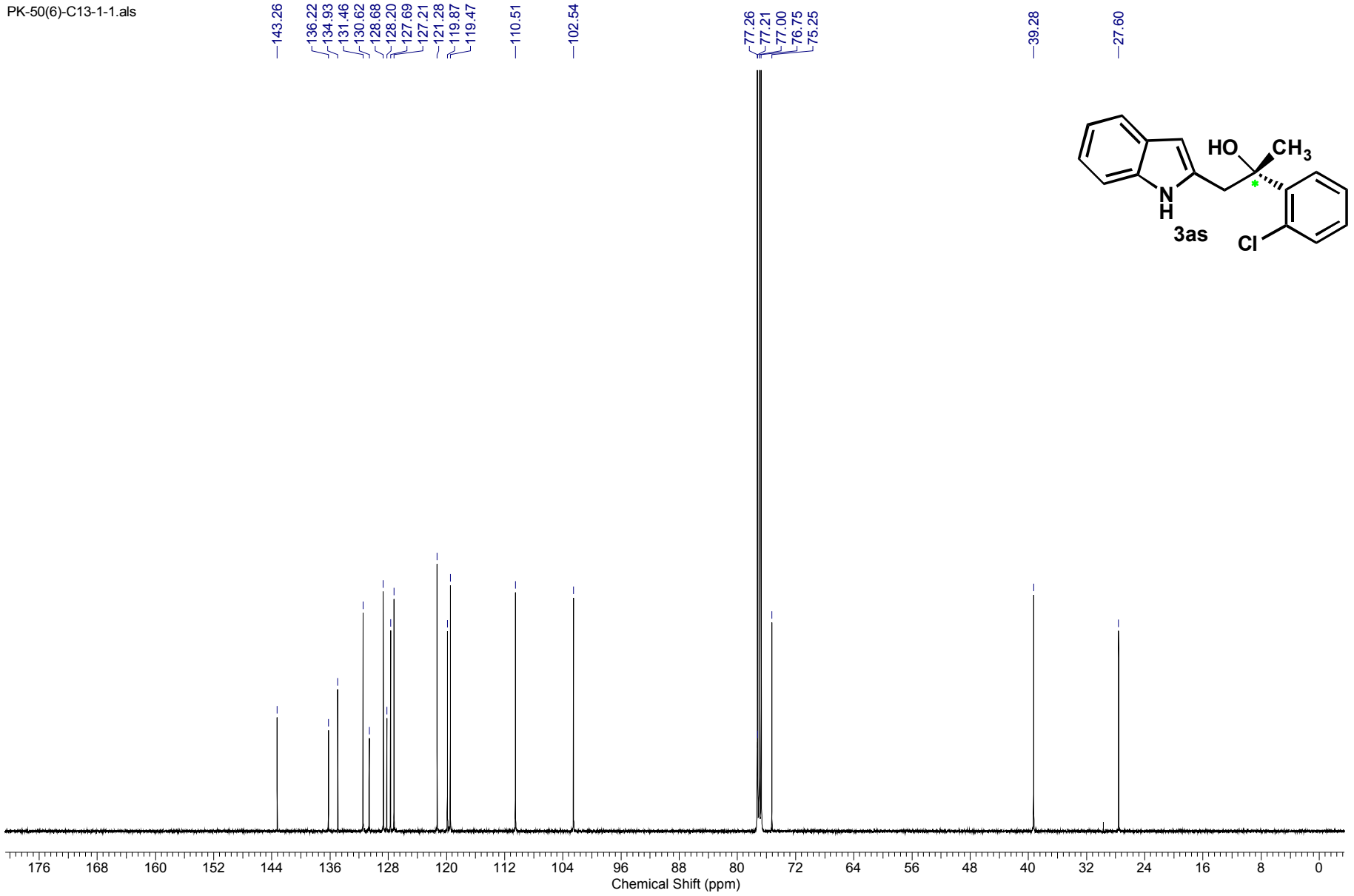

PK-41(9)-1H-1-1.als
8.52
7.79
7.78
7.63
7.61
7.53
7.52
7.50
7.36
7.29
7.28
7.26
7.12
7.05
7.04
6.27
3.52
3.49
3.23
3.20
2.39
1.70
1.56
1.27
HO
CH3
N
H
3at
F3C
0.93
1.04
1.08
2.10
1.05
1.06
1.06
1.05
1.00
1.00
0.99
0.93
2.94
Chemical Shift (ppm)

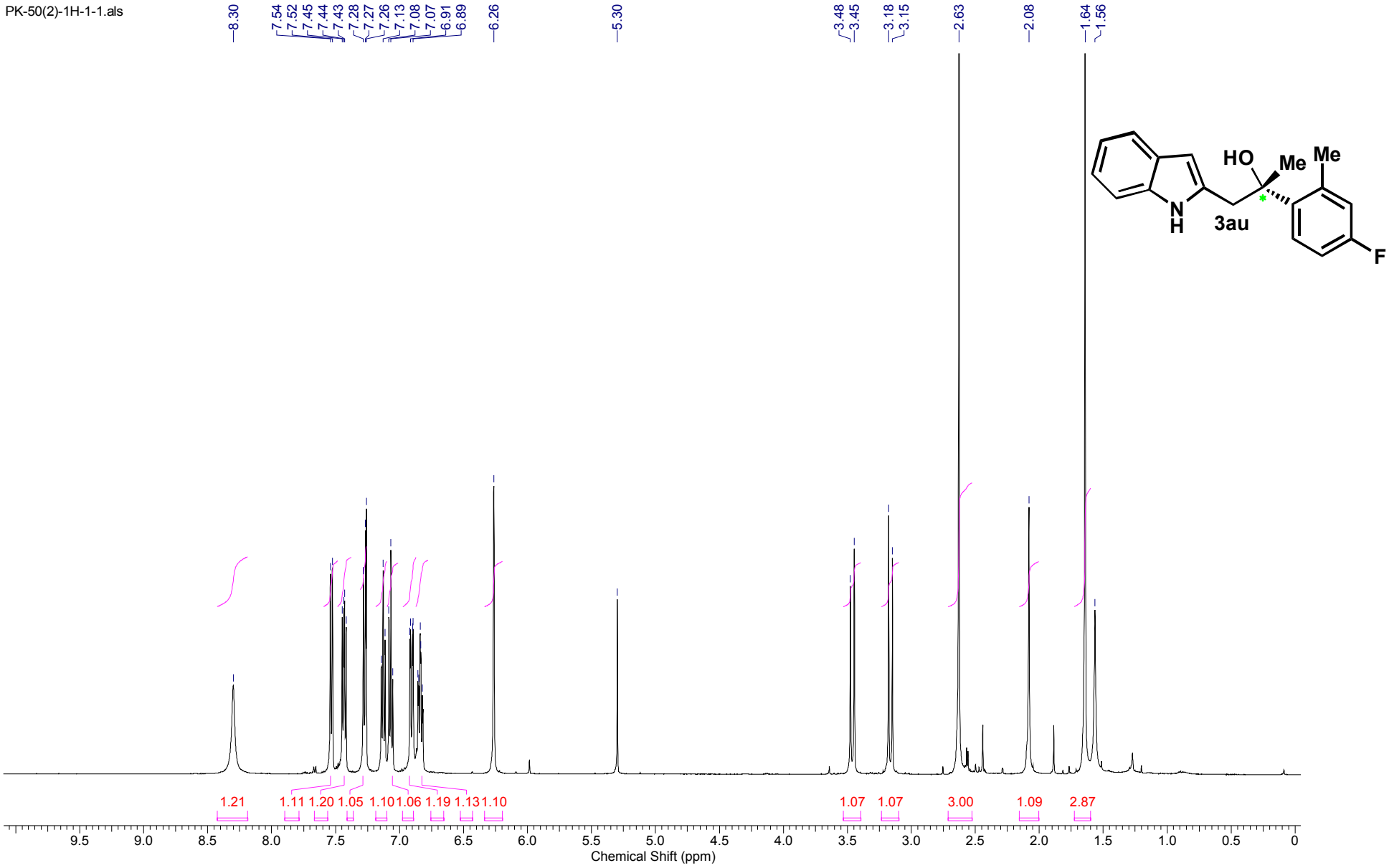

PK-41(9)-C13-1-1.als
146.43
136.27
134.88
131.68
128.34
128.27
128.15
128.09
127.27
127.01
126.01
123.83
121.33
119.87
119.47
110.59
102.57
77.26
77.00
76.74
75.99
42.40
30.59
HO
CH3
N
H
3at
F3C
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

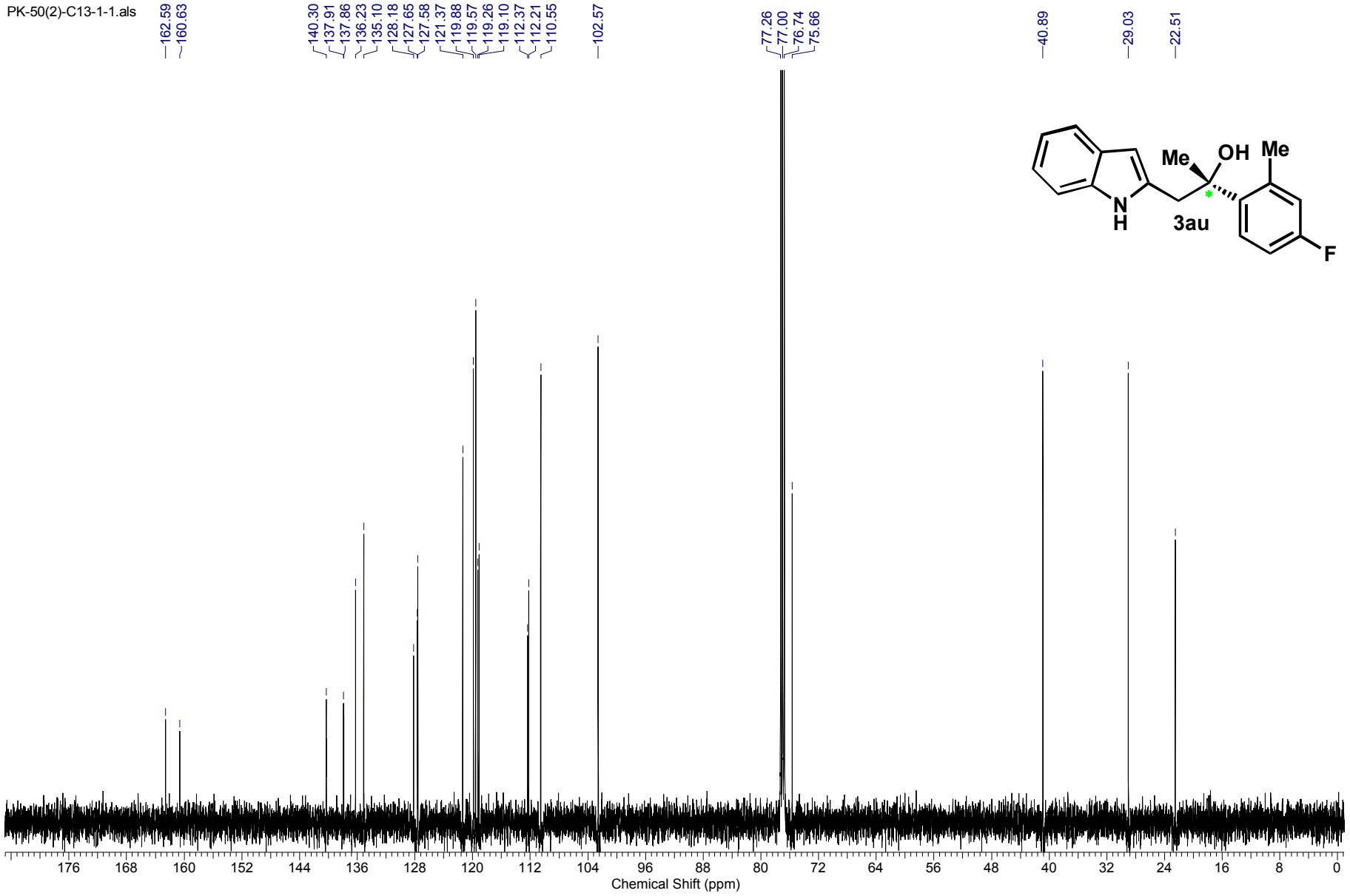

PK-45(6)-1H-1-1.als
8.26
7.54
7.53
7.49
7.47
7.26
7.24
7.21
7.21
7.19
7.12
7.06
6.28
3.51
3.48
3.21
3.18
2.65
2.10
1.66
1.55
HO
CH3
N
H
3au
H3C
1.00
0.99
1.05
1.48
3.08
1.08
1.09
1.00
0.99
0.98
2.88
0.92
2.89
Chemical Shift (ppm)

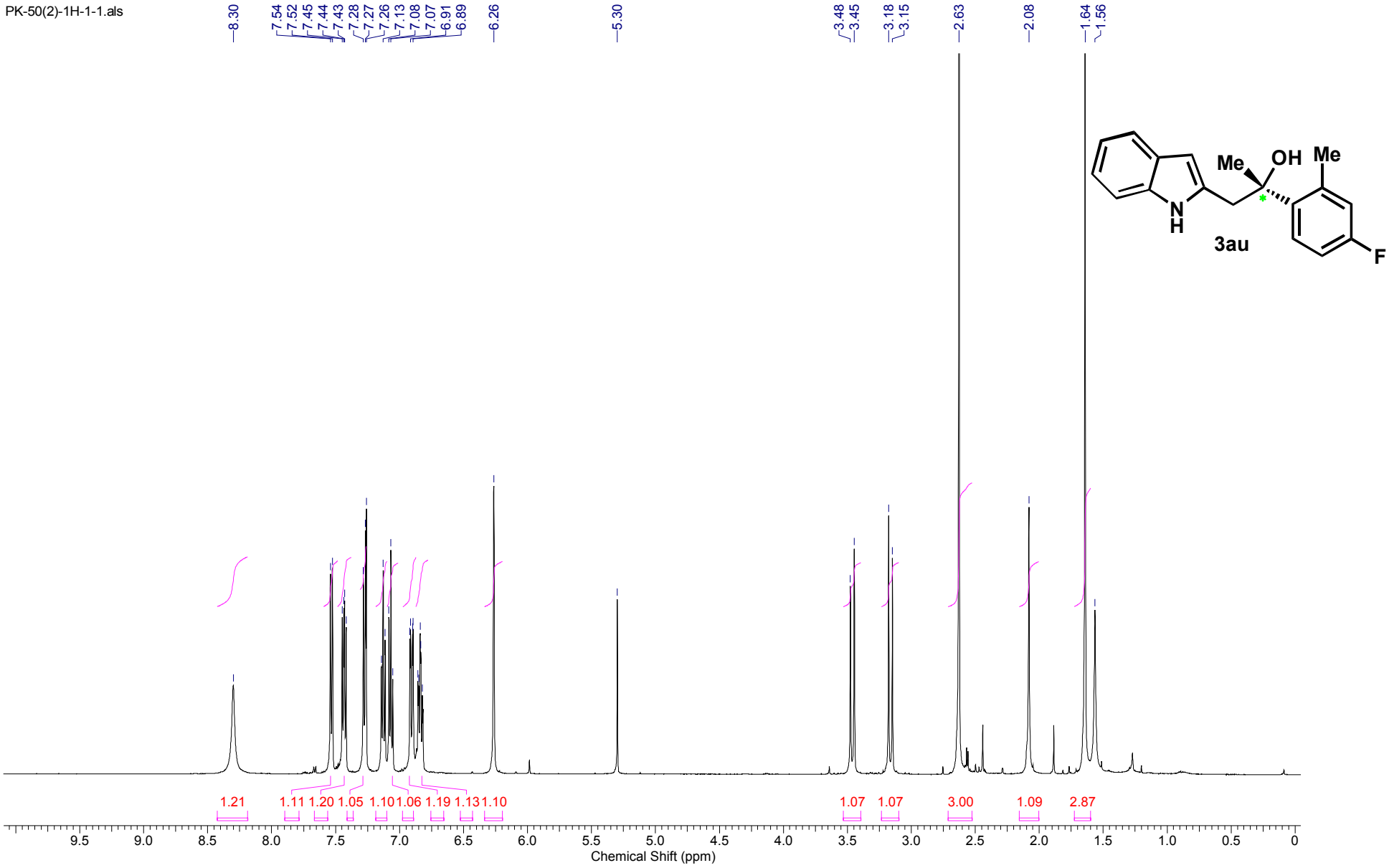

PK-45(6)-C13-1-1.als
144.50
136.26
135.36
135.20
132.93
128.18
127.44
126.00
125.81
121.28
119.84
119.49
110.53
102.58
77.25
77.00
76.74
75.96
40.76
28.78
22.50
HO
CH3
N
H
3au
H3C
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

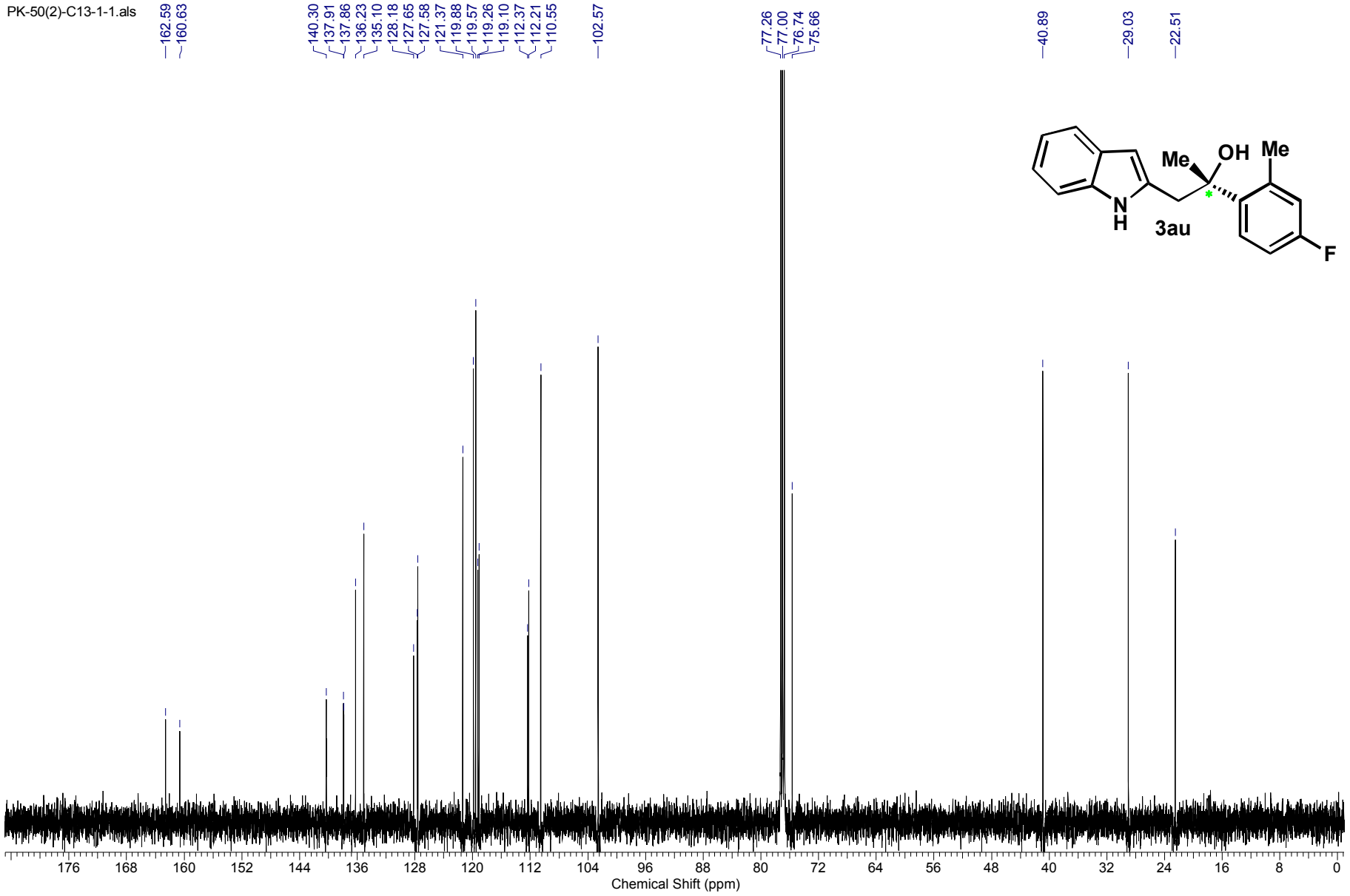

PK-50(6)-pure-1-1.als
8.24
7.66
7.64
7.52
7.51
7.26
7.24
7.23
7.21
7.20
7.20
7.19
7.09
7.05
6.28
3.81
3.78
3.41
3.38
2.76
1.77
1.57
HO
CH3
N
H
Cl
3as
0.98
1.08
1.03
1.06
3.14
1.10
1.04
1.00
1.01
1.01
0.95
3.05
Chemical Shift (ppm)

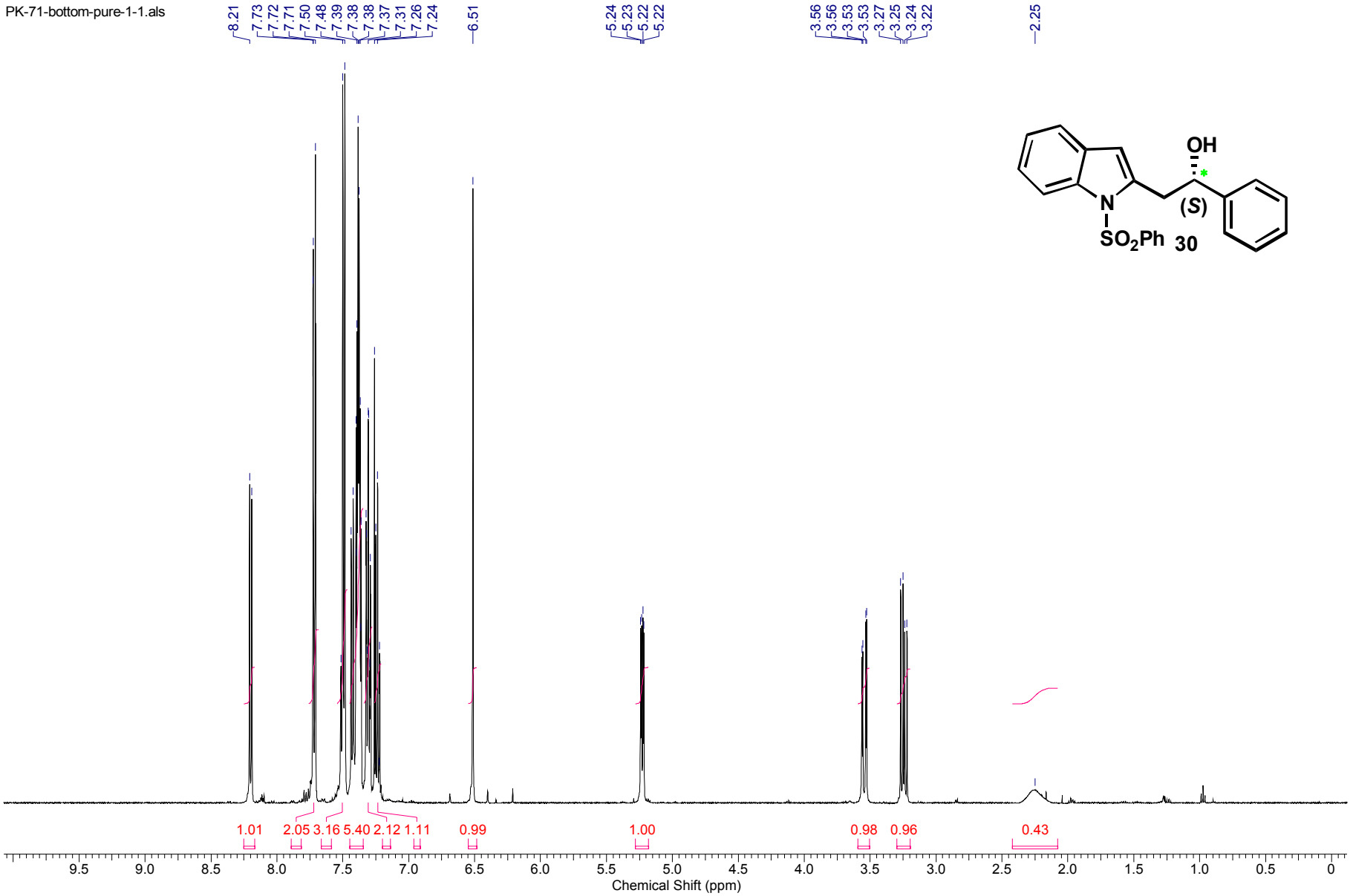

PK-50(6)-C13-1-1.als
143.26
136.22
134.93
131.46
130.62
128.68
128.20
127.69
127.21
121.28
119.87
119.47
110.51
102.54
77.26
77.21
77.00
76.75
75.25
39.28
27.60
HO
CH3
N
H
3as
Cl
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

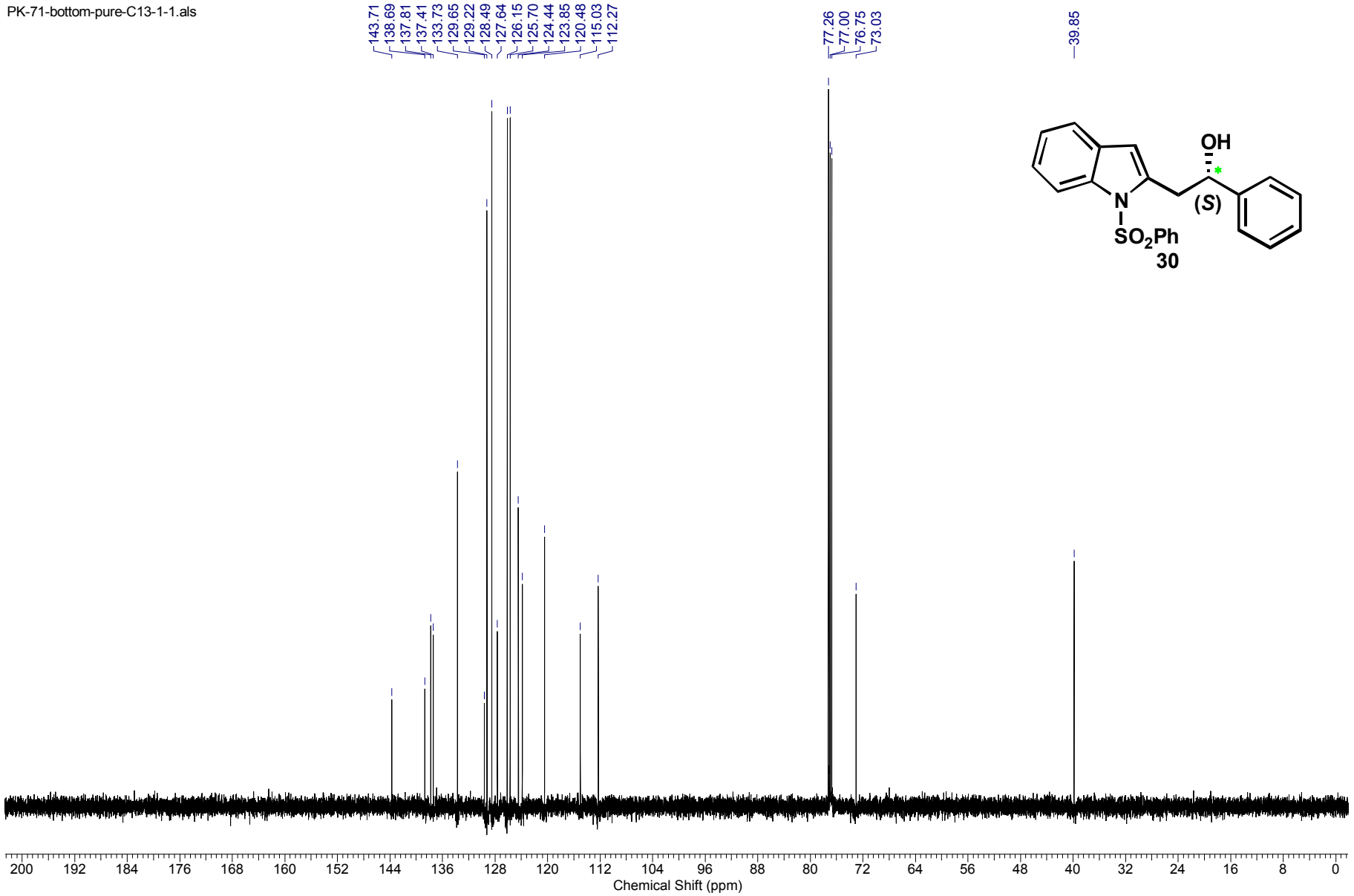

PK-50(2)-1H-1-1.als
8.30
7.54
7.52
7.45
7.44
7.43
7.28
7.27
7.26
7.13
7.08
7.07
6.91
6.89
6.26
5.30
3.48
3.45
3.18
3.15
2.63
2.08
1.64
1.56
HO
Me
Me
N
H
3au
F
1.21
1.11
1.20
1.05
1.10
1.06
1.19
1.13
1.10
1.07
1.07
3.00
1.09
2.87
Chemical Shift (ppm)

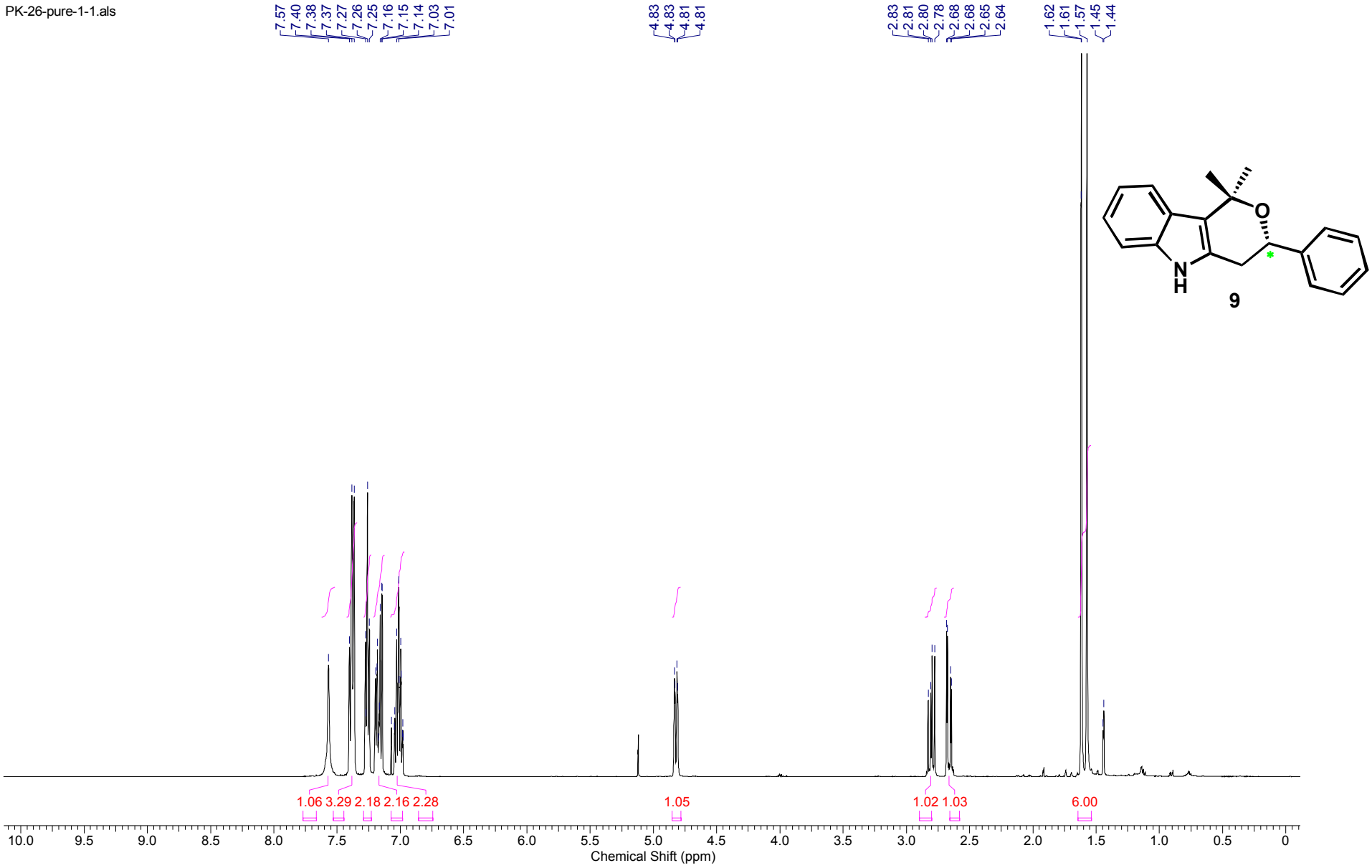

PK-50(2)-C13-1-1.als
162.59
160.63
140.30
137.91
137.86
136.23
135.10
128.18
127.65
127.58
121.37
119.88
119.57
119.26
119.10
112.37
112.21
110.55
102.57
77.26
77.00
76.74
75.66
40.89
29.03
22.51
Me
OH
Me
N
H
3au
F
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

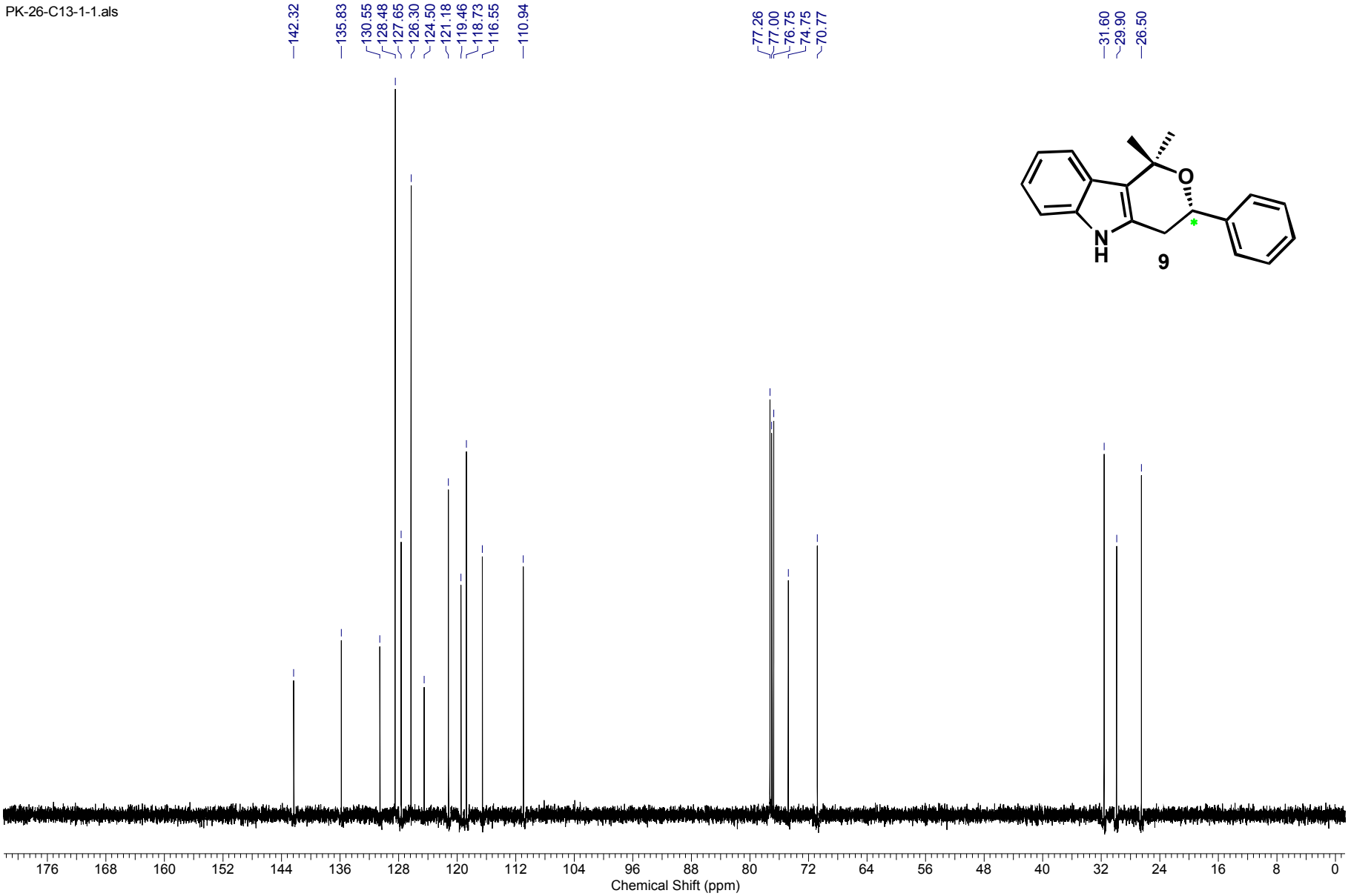

PK-50(2)-1H-1-1.als
8.30
7.54
7.52
7.45
7.44
7.43
7.28
7.27
7.26
7.13
7.08
7.07
6.91
6.89
6.26
5.30
3.48
3.45
3.18
3.15
2.63
2.08
1.64
1.56
Me
OH
Me
N
H
F
3au
1.21
1.11
1.20
1.05
1.10
1.06
1.19
1.13
1.10
1.07
1.07
3.00
1.09
2.87
Chemical Shift (ppm)

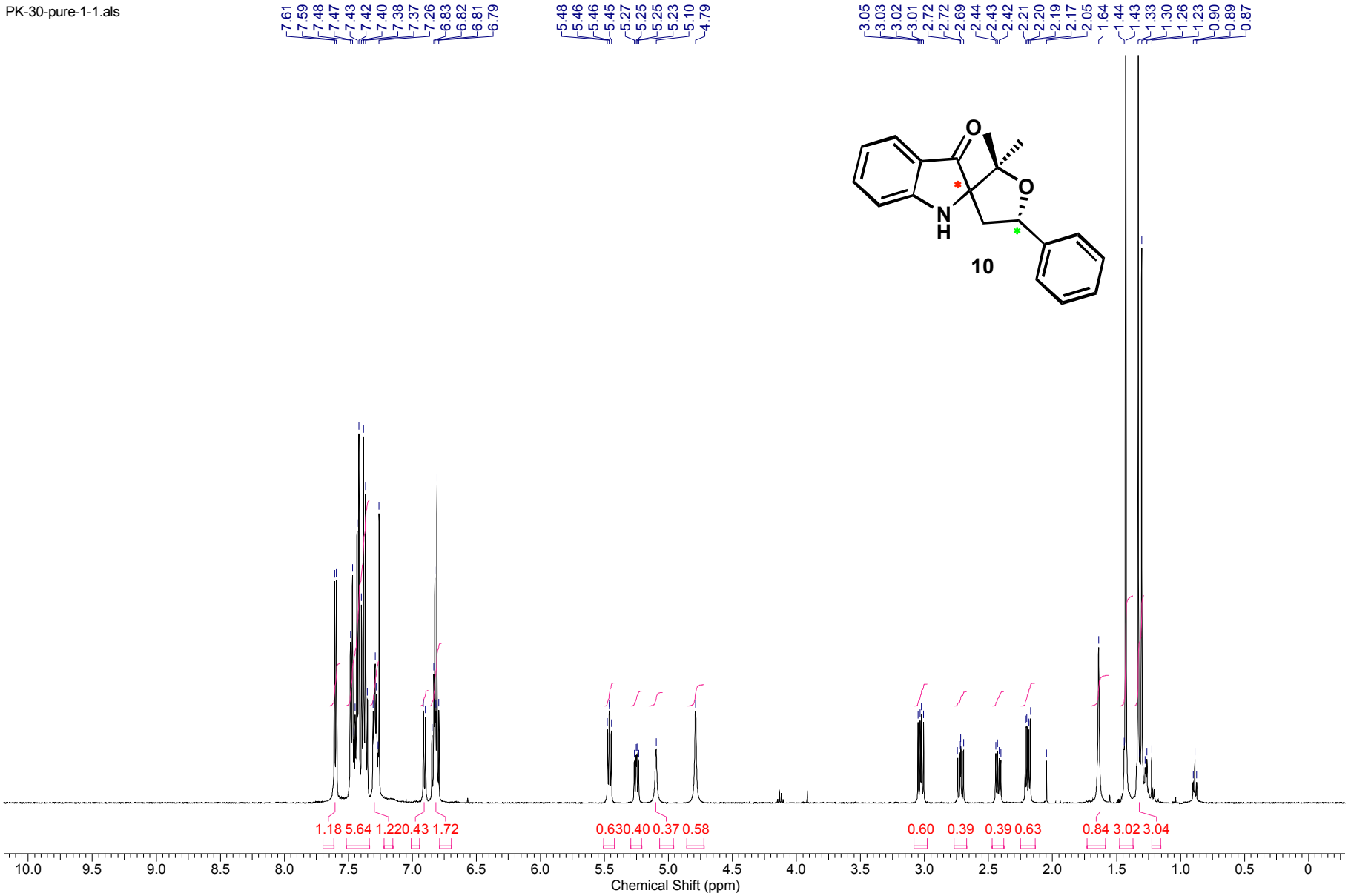

PK-50(2)-C13-1-1.als
162.59
160.63
140.30
137.91
137.86
136.23
135.10
128.18
127.65
127.58
121.37
119.88
119.57
119.26
119.10
112.37
112.21
110.55
102.57
77.26
77.00
76.74
75.66
40.89
29.03
22.51
Me
OH
Me
N
H
3au
F
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

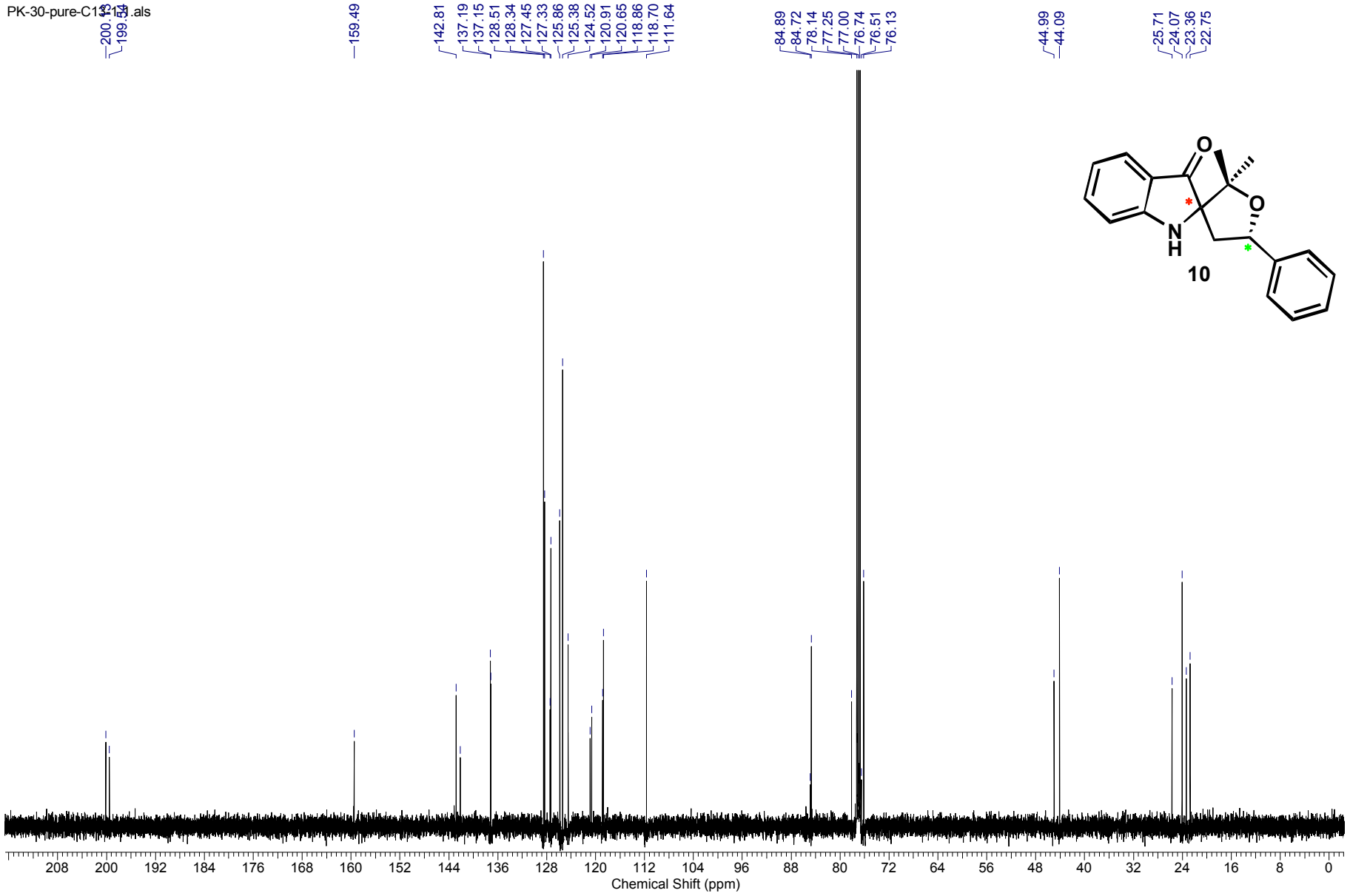

PK-71-bottom-pure-1-1.als
8.21
7.73
7.72
7.71
7.50
7.48
7.39
7.38
7.38
7.37
7.31
7.26
7.24
6.51
5.24
5.23
5.22
5.22
3.56
3.56
3.53
3.53
3.27
3.25
3.24
3.22
2.25
OH
N
(S)
SO2Ph
30
1.01
2.05
3.16
5.40
2.12
1.11
0.99
1.00
0.98
0.96
0.43
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

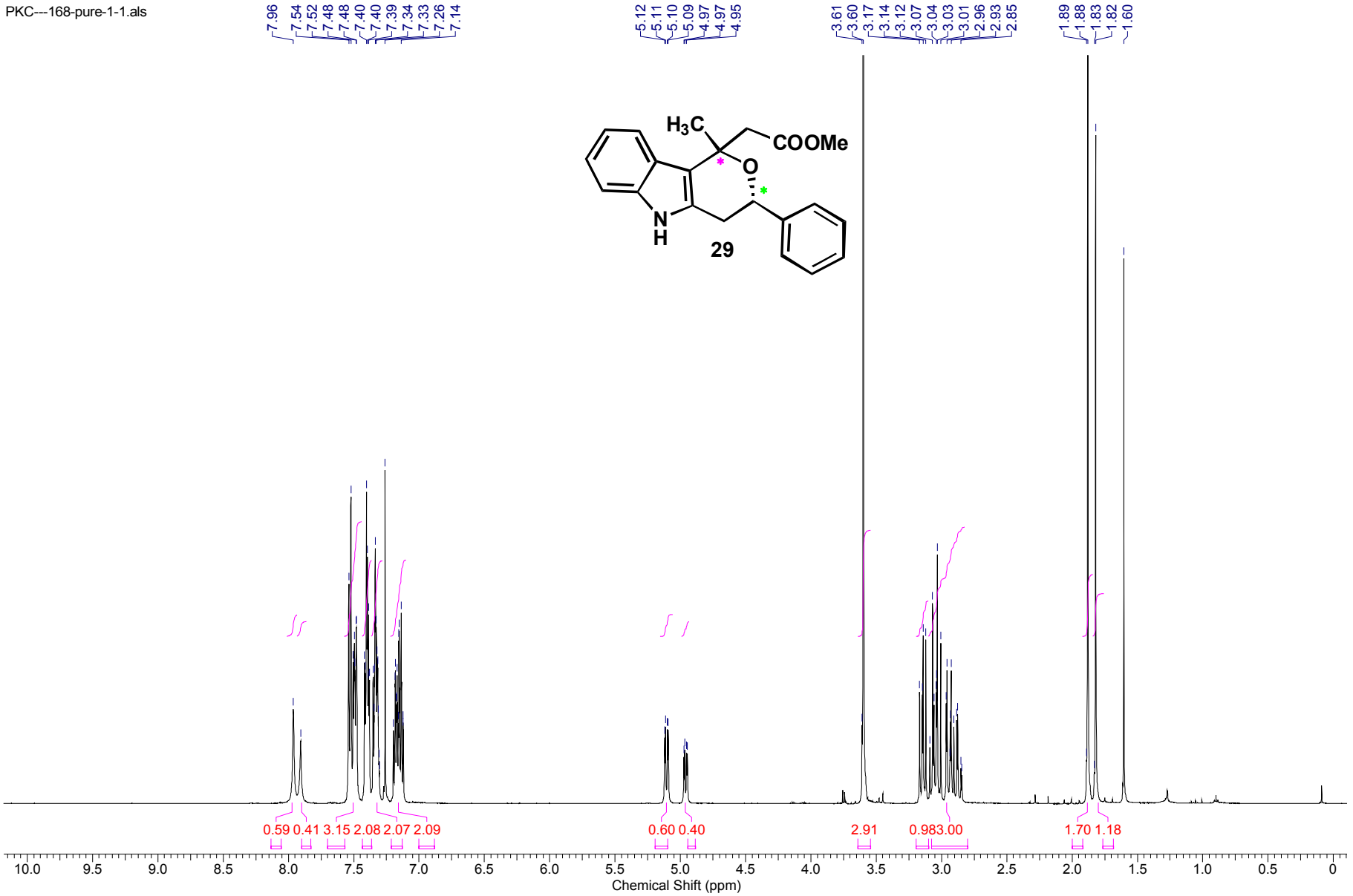

PK-71-bottom-pure-C13-1-1.als
143.71
138.69
137.81
137.41
133.73
129.65
129.22
128.49
127.64
126.15
125.70
124.44
123.85
120.48
115.03
112.27
77.26
77.00
76.75
73.03
39.85
OH
N
(S)
SO2Ph
30
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

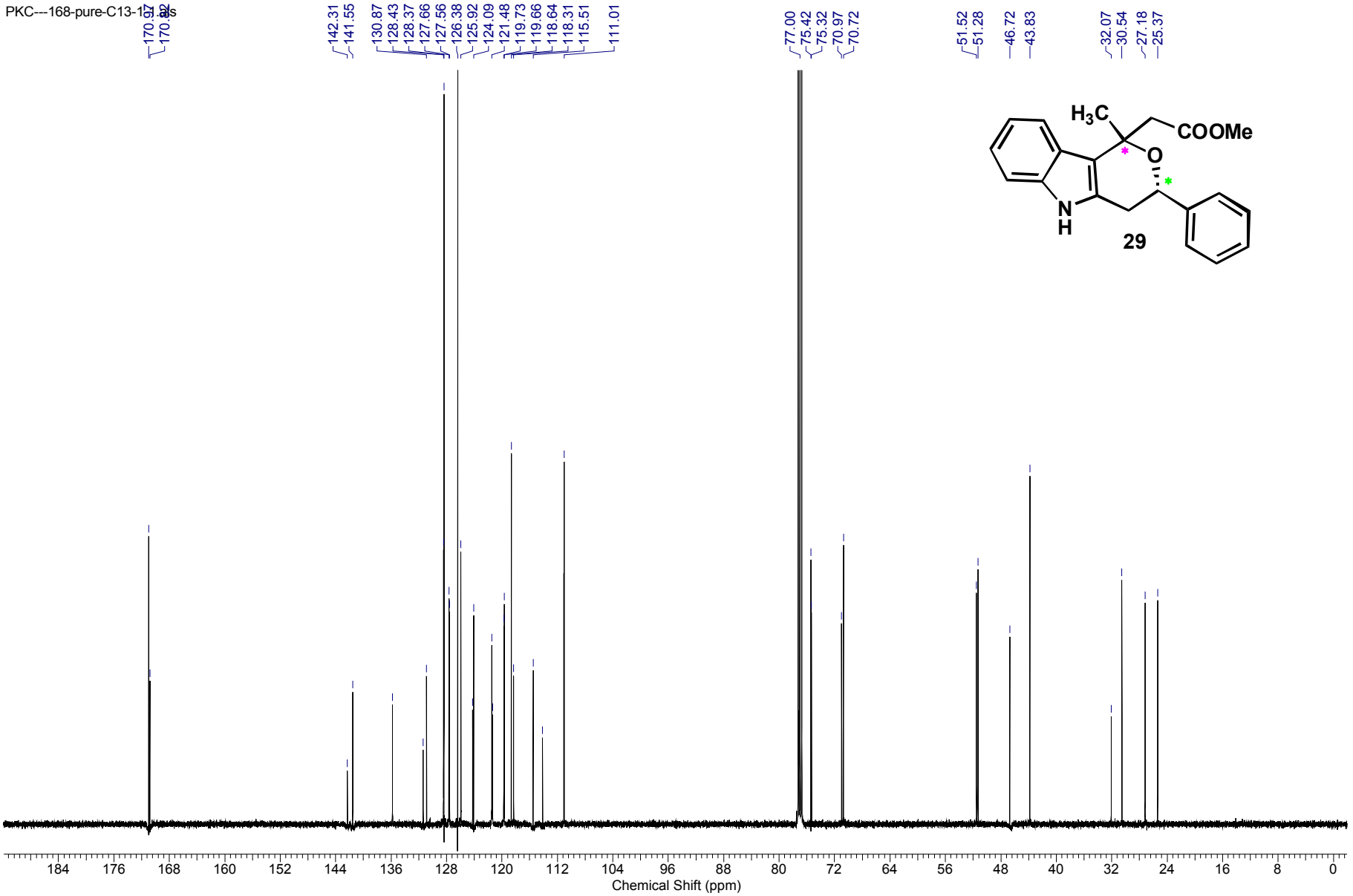

PK-26-pure-1-1.als
7.57
7.40
7.38
7.37
7.27
7.26
7.25
7.16
7.15
7.14
7.03
7.01
4.83
4.83
4.81
4.81
2.83
2.81
2.80
2.78
2.68
2.68
2.65
2.64
1.62
1.61
1.57
1.45
1.44
O
N
H
9
1.06 3.29 2.18 2.16 2.28
1.05
1.02 1.03
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

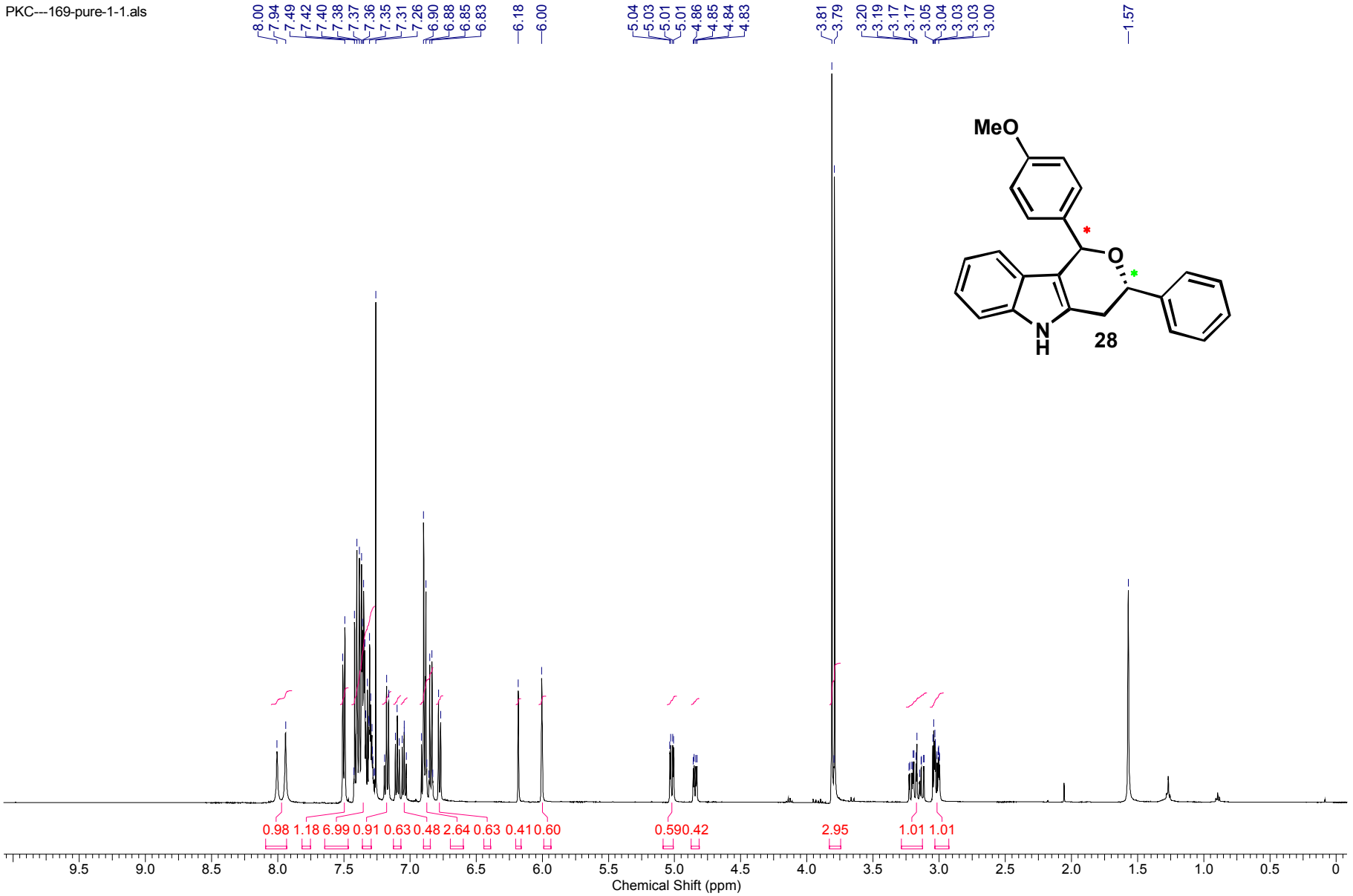

PK-26-C13-1-1.als
142.32
135.83
130.55
128.48
127.65
126.30
124.50
121.18
119.46
118.73
116.55
110.94
77.26
77.00
76.75
74.75
70.77
31.60
29.90
26.50
O
N
H
9
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

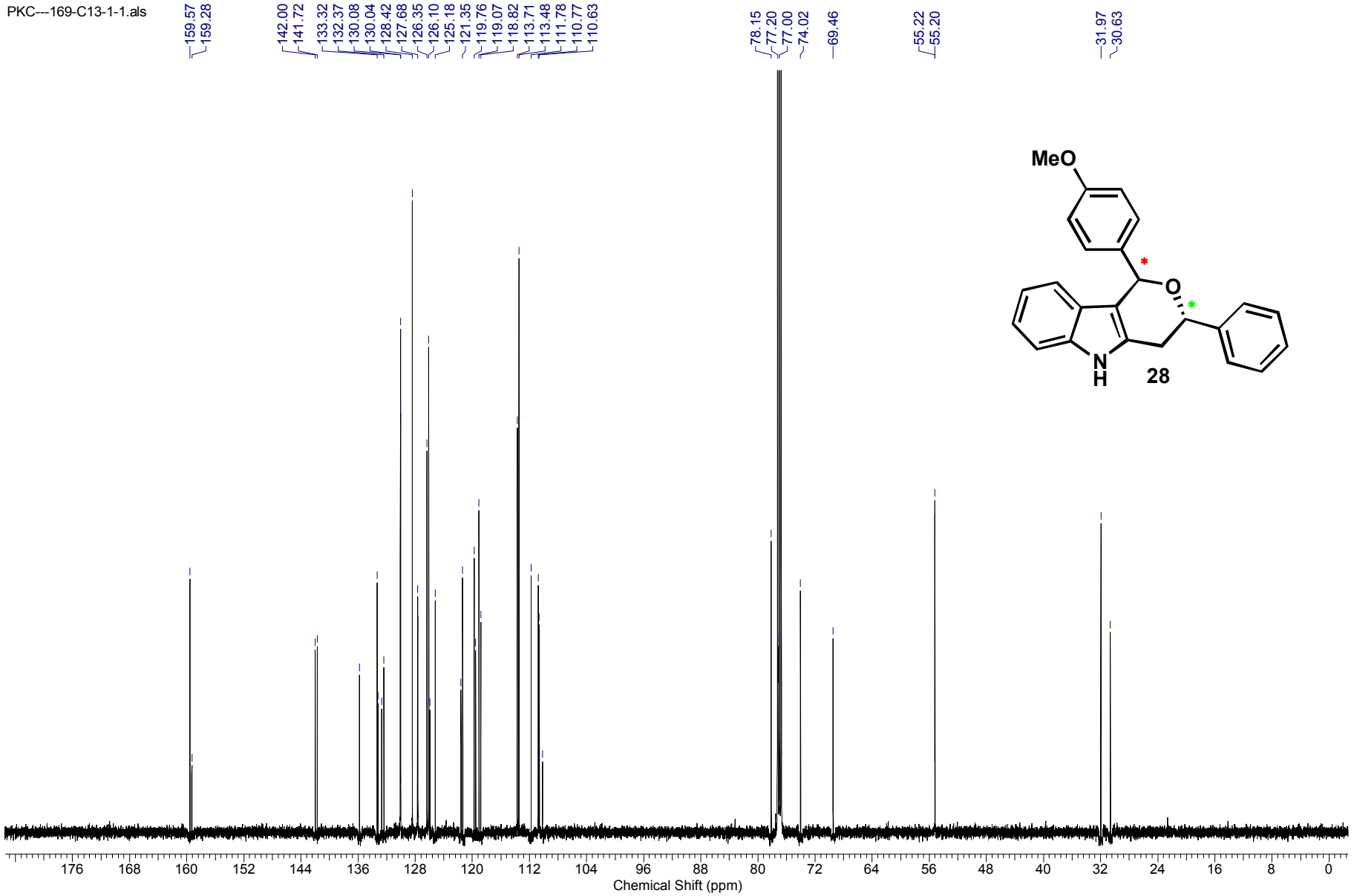

PK-30-pure-1-1.als
7.61 7.59 7.48 7.47 7.43 7.42 7.40 7.38 7.37 7.26 6.83 6.82 6.81 6.79
5.48 5.46 5.46 5.45 5.27 5.25 5.25 5.23 5.10 4.79
3.05 3.03 3.02 3.01 2.72 2.72 2.69 2.44 2.43 2.42 2.21 2.20 2.19 2.17 2.05 1.64 1.44 1.43 1.33 1.30 1.26 1.23 0.90 0.89 0.87
O
O
N
H
10
1.18 5.64 1.22 0.43 1.72
0.63 0.40 0.37 0.58
0.60 0.39 0.39 0.63
0.84 3.02 3.04
10.0 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)


PK-30-pure-C13-1H.als
200.13
199.54
159.49
142.81
137.19
137.15
128.51
128.34
127.45
127.33
125.86
125.38
124.52
120.91
120.65
118.86
118.70
111.64
84.89
84.72
78.14
77.25
77.00
76.74
76.51
76.13
44.99
44.09
25.71
24.07
23.36
22.75
O
O
N
H
10
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


PKC---168-pure-1-1.als
7.96 7.54 7.52 7.48 7.48 7.40 7.40 7.39 7.34 7.33 7.26 7.14
5.12 5.11 5.10 5.09 4.97 4.97 4.95
3.61 3.60 3.17 3.14 3.12 3.07 3.04 3.03 3.01 2.96 2.93 2.85
1.89 1.88 1.83 1.82 1.60
H3C
COOMe
O
N
H
29
0.59 0.41 3.15 2.08 2.07 2.09
0.60 0.40
2.91
0.98 3.00
1.70 1.18
10.0 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)


PKC---168-pure-C13-1
170.97
170.42
142.31
141.55
130.87
128.43
128.37
127.66
127.56
126.38
125.92
124.09
121.48
119.73
119.66
118.64
118.31
115.51
111.01
77.00
75.42
75.32
70.97
70.72
51.52
51.28
46.72
43.83
32.07
30.54
27.18
25.37
H3C
COOMe
O
N
H
29
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


PKC---169-pure-1-1.als
8.00
7.94
7.49
7.42
7.40
7.38
7.37
7.36
7.35
7.31
7.26
6.90
6.88
6.85
6.83
6.18
6.00
5.04
5.03
5.01
5.01
4.86
4.85
4.84
4.83
3.81
3.79
3.20
3.19
3.17
3.17
3.05
3.04
3.03
3.03
3.00
1.57
MeO
O
N
H
28
0.98 1.18 6.99 0.91 0.63 0.48 2.64 0.63 0.41 0.60
0.59 0.42
2.95
1.01 1.01
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)


PKC---169-C13-1-1.als
159.57
159.28
142.00
141.72
133.32
132.37
130.08
130.04
128.42
127.68
126.35
126.10
125.18
121.35
119.76
119.07
118.82
113.71
113.48
111.78
110.77
110.63
78.15
77.20
77.00
74.02
69.46
55.22
55.20
31.97
30.63
MeO
O
N
H
28
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)