Catalytic Asymmetric Hydrogenation of Quinoline Carbocycles: Unusual Chemoselectivity in Hydrogenation of Quinolines

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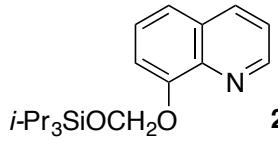
General and Materials. All NMR spectra were measured with Bruker AVANCE 400 or AVANCE III HD 400 Nanobay (9.4 T magnet) spectrometer at ambient temperature. In ^{1}H NMR spectra, chemical shifts (ppm) referenced to internal tetramethylsilane (0.00 ppm in $CDCl_3$). In ^{13}C NMR spectra, chemical shifts (ppm) referenced to the carbon signal of the deuterated solvents (77.0 ppm in $CDCl_3$). IR spectra and melting points were measured with JASCO FT/IR-4100 and Büchi Melting Point B-545, respectively. Elemental analyses and high-resolution mass spectra (FAB) were performed by Service Centre of Elementary Analysis of Organic Compounds and Network Joint Research Center for Materials and Devices (Institute for Materials Chemistry and Engineering, Kyushu University), respectively. Column chromatographies were performed with silica gel 60 (230–400 mesh, Merck).

Ethyl acetate (EtOAc) was dried with phosphorus pentoxide. 2-Propanol (*i*-PrOH), triethylamine (Et_3N), and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) were dried with calcium hydride. These solvents and reagents were distilled under nitrogen atmosphere. Dry *N*,*N*-dimethylformamide (DMF, Aldrich) was purchased. Toluene (Guaranteed Reagent) and tetrahydrofuran (THF) (HPLC grade, without inhibitor) were deoxidized by purging with nitrogen for 30 min and dried with an alumina and copper column system (GlassContour Co.). Ru(η^3-methallyl)$_2$(cod),[1] (*S*,*S*)-(*R*,*R*)-PhTRAP (**1**),[2] {Ru(*p*-cymene)[(*S*,*S*)-(*R*,*R*)-PhTRAP]}Cl,[3] 8-phenylquinoline (**2k**),[4] 8-(trifluoromethanesulfoxy)quinoline,[4] and 8-phenyl-5,6,7,8-tetrahydroquinolin-8-ol[5] were prepared according to literature procedures. 2-Phenylquinoline (**2a**), methyl quinoline-6-carboxylate (**2b**), 6-isopropylquinoline (**2c**), 3-methoxyquinoline (**2d**), 4-methoxyquinoline (**2e**), 5-methoxyquinoline (**2f**), 6-methoxyquinoline (**2g**), 7-methoxyquinoline (**2h**), 8-methoxyquinoline (**2i**), 8-methylquinoline (**2o**), 8-hydroxyquinoline, dry sodium hydride, (triisopropylsilyloxy)methyl chloride, 4-methoxyphenylboronic acid, lithium chloride, tetrakis(triphenylphosphine)palladium(0) [Pd(PPh$_3$)$_4$], 4-(trifluoromethyl)phenylboronic acid, 2-methylphenylboronic acid, sodium carbonate (Na_2CO_3), palladium(II) acetate [Pd(OAc)$_2$], 1,1'-bis(diphenylphosphino)ferrocene (DPPF), 0.5 *M* solution of cyclohexylzinc bromide in THF, 1.0 *M* solution of tetrabutylammonium fluoride (TBAF) in THF, acetic acid (AcOH), and methanesulfonic acid (MsOH) were purchased and used without further purification.

Preparation of Substrates 2

8-[(Triisopropylsilyloxy)methoxy]quinoline (2j).

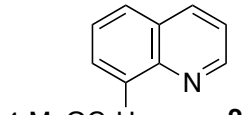


2j

8-Hydroxyquinoline (726 mg, 5.0 mmol) was placed in a three-neck flask, which was equipped with a stirring bar, rubber septum, three-way stopcock, and dropping funnel having a rubber septum. In the dropping funnel, dry sodium hydride (138 mg, 5.8 mmol) and a stirring bar were placed. After the reaction vessel was evacuated and charged with nitrogen gas three times, dry DMF (12 mL × 2) was added into the flask and dropping funnel. After the flask was immersed in an ice-bath, the suspension of NaH was added dropwise to the solution of 8-hydroxyquinoline at 0°C for 20 min. To the resulting

solution was added (triisopropylsilyloxy)methyl chloride (1.4 mL, *d* 0.96 g/mL, 6.0 mmol) with a syringe through the septum. The reaction mixture was stirred at 0°C for 5 min and at ambient temperature for 12 h. After water was added, the resulting mixture was extracted three times with Et_2O. The combined organic layer was dried over Na_2SO_4, and then evaporated under reduced pressure after filtration. The residue was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/3) to give **2j** (1.40 g, 84%) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.07 (d, *J* = 7.3 Hz, 18H), 1.20 (septet, *J* = 7.3 Hz, 3H), 5.75 (s, 2H), 7.38 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.40–7.49 (m, 2H), 7.52 (dd, *J* = 1.7, 7.5 Hz, 1H), 8.10 (dd, *J* = 1.5, 8.1 Hz, 1H), 8.93 (dd, *J* = 1.7, 4.3 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 11.8, 17.7, 88.6, 112.3, 120.4, 121.3, 126.6, 129.3, 135.7, 140.3, 149.2, 153.6; IR (neat) 2946, 2867, 1496, 1467, 1378, 1250, 1158, 1064, 984, 789, 755 cm^{-1}; Anal. Calcd for $C_{19}H_{29}NO_2Si$: C, 68.83; H, 8.82; N, 4.22. Found: C, 68.70; H, 8.84; N, 4.09.

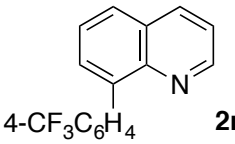
8-(4-Methoxyphenyl)quinoline [57479-35-3] (2l).[6]



2l

8-(Trifluoromethanesulfoxy)quinoline (1.39 g, 5.0 mmol), 4-methoxyphenylboronic acid (790 mg, 5.2 mmol), lithium chloride (636 mg, 15 mmol), and $Pd(PPh_3)_4$ (289 mg, 0.25 mmol) were placed in a 50 mL two-neck flask, which was equipped with a stirring bar, rubber septum, and Dimroth condenser having a three-way stopcock. After the reaction vessel was evacuated and charged with nitrogen gas three times, dry toluene (18 mL) and freshly prepared 1 *M* aqueous solution of Na_2CO_3 (3.2 mL, 3.2 mmol) were added into the flask, and then the resulting mixture was stirred under reflux for 60 h. After cooled to ambient temperature, the mixture was washed with water. The aqueous layer was extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, and then evaporated under reduced pressure after filtration. The residue was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/20) to give **2l** (892 mg, 76%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.87 (s, 3H), 7.04 (d, *J* = 8.7 Hz, 2H), 7.39 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 2H), 7.71 (dd, *J* = 1.4, 7.1 Hz, 1H), 7.78 (dd, *J* = 1.3, 8.1 Hz, 1H), 8.17 (dd, *J* = 1.7, 8.2 Hz, 1H), 8.95 (dd, *J* = 1.7, 4.2 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 55.3, 113.5, 120.9, 126.3, 127.0, 128.8, 129.9, 131.7, 131.9, 136.2, 140.5, 146.1, 150.1, 159.0.

8-[4-(Trifluoromethyl)phenyl]quinoline [1275591-20-2] (2m).[7]

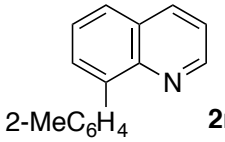


2m

The procedure for preparing **2l** was followed with use of 4-(trifluoromethyl)phenylboronic acid (985 mg, 5.2 mmol). The reaction mixture was stirred under reflux for 32 h. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/20) to give **2m** (508 mg,

37%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.42 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.70–7.77 (m, 3H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.86 (dd, *J* = 1.2, 8.1 Hz, 1H), 8.21 (dd, *J* = 1.6, 8.3 Hz, 1H), 8.94 (dd, *J* = 1.7, 4.2 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 121.2, 124.4 (q, *J* = 272 Hz), 124.9 (q, *J* = 4 Hz), 126.3, 128.3, 128.7, 129.3 (q, *J* = 32 Hz), 130.4, 130.9, 136.3, 139.4, 143.2, 145.7, 150.5.

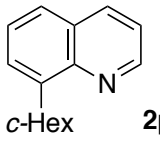
8-(2-Methylphenyl)quinoline [57479-11-5] (2n).[8]



2n

The procedure for preparing **2l** was followed with use of 2-methylphenylboronic acid (714 mg, 5.3 mmol). The reaction mixture was stirred under reflux for 22 h. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/5) to give **2n** (972 mg, 89%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.04 (s, 3H), 7.27–7.36 (m, 5H), 7.53–7.59 (m, 2H), 7.80 (dd, *J* = 3.0, 6.6 Hz, 1H), 8.14 (dd, *J* = 1.6, 8.2 Hz, 1H), 8.89 (dd, *J* = 1.7, 4.2 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 20.4, 120.8, 125.3, 126.0, 127.4, 127.6, 128.3, 129.7, 130.1, 130.3, 136.0, 136.8, 139.8, 141.4, 146.5, 150.3.

8-Cyclohexylquinoline [1539656-77-3] (2p).



2p

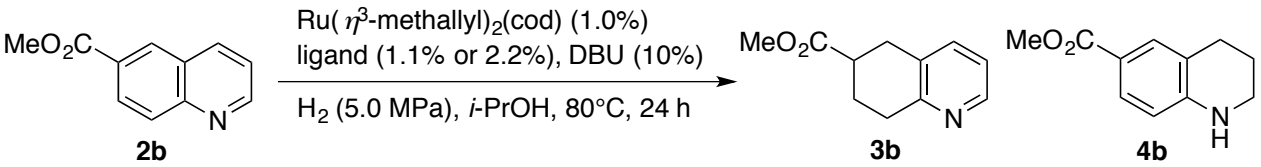
In a nitrogen-filled drybox, $Pd(OAc)_2$ (112 mg, 0.50 mmol) and DPPF (306 mg, 0.55 mmol) were placed in a 5 mL screw-capped vial equipped with a stirring bar. After dry THF (5.0 mL) was added, the vial was sealed with a screw cap containing a PTFE/silicone septum and then removed from the drybox. The solution was stirred at ambient temperature for 10 min. 8-(Trifluoromethanesulfoxy)quinoline (1.39 g, 5.0 mmol) was placed in a 100 mL two-neck flask, which was equipped with a stirring bar, rubber septum, and Dimroth condenser having a three-way stopcock. After the reaction vessel was evacuated and charged with nitrogen gas three times, the catalyst solution prepared above was transferred through a cannula into the flask, and a 0.5 *M* solution of cyclohexylzinc bromide in THF (55 mL, 28 mmol) was added with a syringe to the solution. The mixture was stirred under reflux for 60 h. After cooled to ambient temperature, the mixture was washed with water. The aqueous layer was extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, and then evaporated under reduced pressure after filtration. The residue was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/20) to give **2p** (837 mg, 79%) as pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.26–1.39 (m, 1H), 1.45–1.79 (m, 4H), 1.78–1.92 (m, 3H), 1.97–2.05 (m, 2H), 4.04 (tt, *J* = 3.3, 11.8 Hz, 1H), 7.33 (dd, *J* = 4.1, 8.2 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 8.08 (dd, *J* = 1.6, 8.2 Hz, 1H), 8.93 (dd, *J* = 1.7,

4.1 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 26.5, 27.0, 34.1, 37.1, 120.6, 125.4, 125.7, 126.4, 128.3, 136.3, 146.1, 146.6, 149.1; IR (neat) 2925, 2849, 1496, 1447, 826, 795 cm^{-1}; Anal. Calcd for $C_{15}H_{17}N$: C, 85.26; H, 8.11; N, 6.63. Found: C, 85.32; H, 8.06; N, 6.55.

Catalytic Asymmetric Hydrogenation of Quinolines 2

Procedure A: General Procedure for the Optimization of the Hydrogenation of 2b (Table 1). Ru(η^3-methallyl)$_2$(cod) (1.6 mg, 50 μmol) and (*S*,*S*)-(*R*,*R*)-PhTRAP (**1**) (4.4 mg, 5.5 μmol) were placed in a 2.0 mL Schlenk tube, which was equipped with a stirring bar, rubber septum and three-way stopcock. After the reaction vessel was evacuated and charged with nitrogen gas three times, a solvent (1.0 mL) and a base (50 μmol, if liquid) were added into the Schlenk tube through the septum by using a syringe. The catalyst solution was stirred for 10 min at ambient temperature. Methyl quinoline-6-carboxylate (**2b**) (93.6 mg, 0.50 mmol), a base (50 μmol, if solid), and a stirring bar were placed in a 50 mL test tube, which was sealed with a rubber septum, and then the tube was evacuated and charged with nitrogen gas three times. The catalyst solution was transferred through a cannula into the test tube. After the septum was removed, the test tube was quickly inserted into the nitrogen-purged stainless autoclave, and then the autoclave was sealed immediately. Hydrogen gas was introduced into the autoclave until the pressure gauge indicated over 5.0 MPa, and then the pressure was carefully released to 0.1 MPa. This procedure was repeated twice, and finally the inside of the autoclave was pressurized with hydrogen to 5.0 MPa. The mixture was vigorously stirred at 80°C for 24 h. The autoclave was cooled to room temperature, and then excess hydrogen gas was released carefully. The reaction mixture was evaporated under reduced pressure. The residue was analyzed with ^{1}H NMR in order to determine its composition, and then purified with a flash column chromatography (EtOAc/hexane = 2/1) on silica gel to give the desired 5,6,7,8-tetrahydroquinoline-6-carboxylate **3b**. Results of the selected experiments are shown in Tables 1 and S-1.

Table S-1. Effect of ligand on the ruthenium-catalyzed hydrogenation of **2b**.[a]

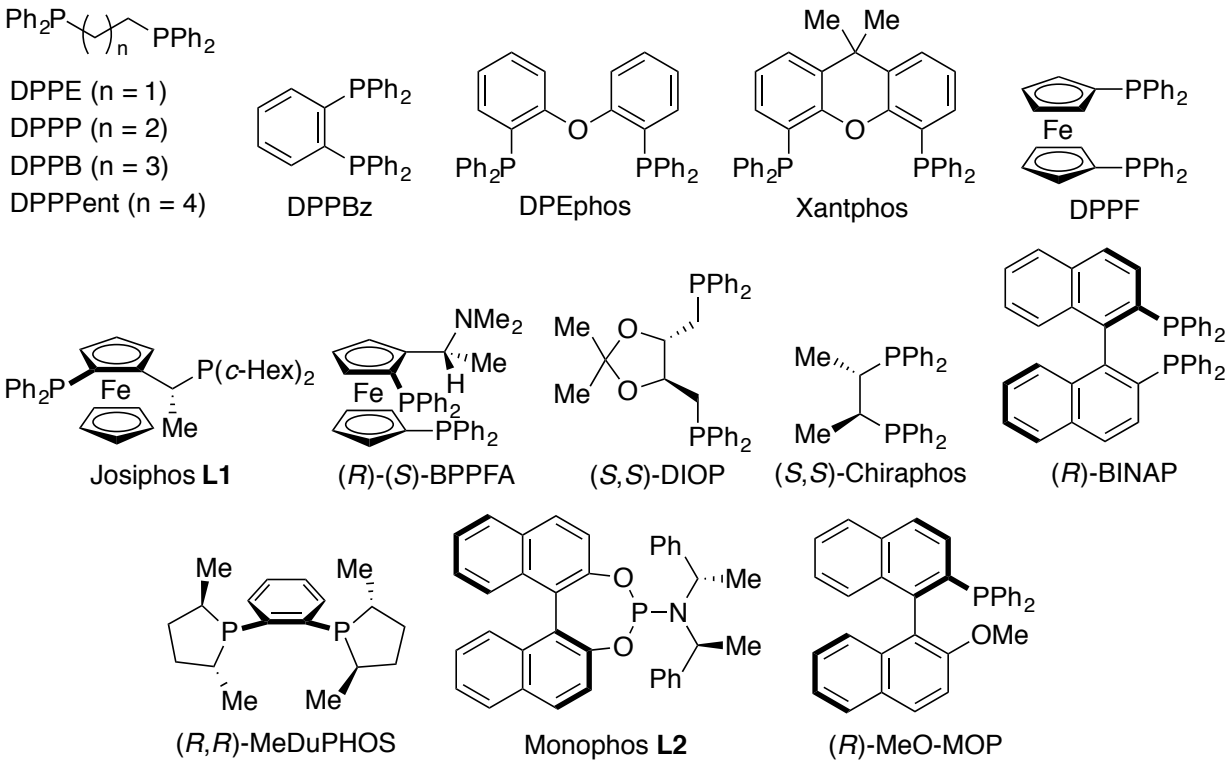


2b **3b** **4b**

entry	ligand	conv. (%)[b,c]	**3b**:**4b**[b]
1	DPPE	>99	1:99
2	DPPP	>99	2:98
3	DPPB	>99	3:97
4	DPPPent	>99	5:95
5	DPPBz	>99	1:99
6	DPEphos	58	3:97
7	Xantphos	>99	13:87

8	DPPF	64	19:81
9[d]	P(*c*-Hex)$_3$	49	33:67
10[d]	PPh_3	>99	34:66
11	Josiphos **L1**	>99	4:96
12	(*R*)-(*S*)-BPPFA	>99	4:96
13	(*S*,*S*)-DIOP	>99	3:97
14	(*S*,*S*)-Chiraphos	72	2:98
15	(*R*)-BINAP	68	4:96
16	(*R*,*R*)-Me-DuPHOS	>99	2:98
16[d]	Monophos **L2**	>99	2:98
17[d]	(*R*)-MeO-MOP	96	25:75[e]
18	(*S*,*S*)-(*R*,*R*)-PhTRAP (**1**)	>99	85:15[f]

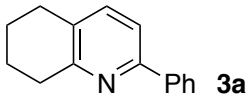
[a] Reactions were conducted on a 0.50 mmol scale in 1.0 mL of *i*-PrOH under 5.0 MPa of H_2 at 80°C for 24 h. The ratio of **2b**:Ru(η^3-methallyl)$_2$(cod):ligand:DBU was 100:1.0:1.1:10 unless otherwise noted. [b] Determined by ^{1}H NMR analysis. [c] A small amount of isopropyl ester was formed. [d] The ratio of Ru(η^3-methallyl)$_2$(cod):ligand was 1.0:2.2. [e] **3b** was obtained with 25% ee. [f] **3b** was obtained with 35% ee.



Procedure B: General Procedure for the Catalytic Asymmetric Hydrogenation of Quinolines 2 (Tables 2 and 3). Ru(η^3-methallyl)$_2$(cod) (1.6 mg, 50 μmol) and (*S*,*S*)-(*R*,*R*)-PhTRAP (**1**) (4.4 mg, 5.5 μmol) were placed in a 2.0 mL Schlenk tube, which was equipped with a stirring bar, rubber septum and three-way stopcock. After the reaction vessel was evacuated and charged with nitrogen gas three times, dry *i*-PrOH or EtOAc (1.0 mL) was added into the Schlenk tube through the septum by using a syringe.

The catalyst solution was stirred for 10 min at ambient temperature. A quinoline **2** (0.25 mmol), K_2CO_3 (6.9 mg, 50 μmol), and a stirring bar were placed in a 50 mL test tube, which was sealed with a rubber septum, and then the tube was evacuated and charged with nitrogen gas three times. The catalyst solution was transferred through a cannula into the test tube. After the septum was removed, the test tube was quickly inserted into the nitrogen-purged stainless autoclave, and then the autoclave was sealed immediately. Hydrogen gas was introduced into the autoclave until the pressure gauge indicated over 5.0 MPa, and then the pressure was carefully released to 0.1 MPa. This procedure was repeated twice, and finally the inside of the autoclave was pressurized with hydrogen to 5.0 MPa. The mixture was vigorously stirred for 24 h. The autoclave was cooled to room temperature, and then excess hydrogen gas was released carefully. The reaction mixture was evaporated under reduced pressure. The residue was purified with a flash column chromatography on silica gel to give the desired 5,6,7,8-tetrahydrouquinoline **3**.

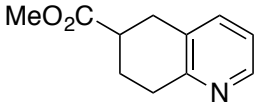
2-Phenyl-5,6,7,8-tetrahydroquinoline [1570-04-3] (3a) (eq 1).[9]



3a

Procedure A was followed with use of Et_3N (7.0 μL, *d* 0.726 g/mL, 50 μmol) and EtOAc. 2-Phenylquinoline (**2a**) (102 mg, 0.50 mmol) was used in place of **2b**. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/20) to give **3a** (101 mg, 97%) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.80–1.88 (m, 2H), 1.89–1.97 (m, 2H), 2.80 (t, J = 6.3 Hz, 2H), 3.00 (t, J = 6.3 Hz, 2H), 7.34–7.47 (m, 5H), 7.94 (d, J = 7.8 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 22.8, 23.2, 28.5, 32.8, 117.9, 126.8, 128.3, 128.6, 130.7, 137.4, 139.9, 154.6, 157.2.

(–)-Methyl 5,6,7,8-tetrahydroquinoline-6-carboxylate [76384-36-6] (3b) (Table 1, entry 6).[10]

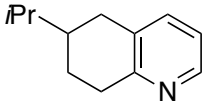


3b

Procedure A was followed with use of methyl quinoline-6-carboxylate (**2b**) (94.0mg, 0.50 mmol), Cs_2CO_3 (16.3 mg, 50 μmol), and EtOAc. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/3) to give **3b** (82.9 mg, 86%) as pale yellow oil: $[\alpha]_D^{26}$ = –18.7 (*c* 1.12, $CHCl_3$) (for 35% ee of **3b**); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.93–2.05 (m, 1H), 2.26–2.34 (m, 1H), 2.75–2.83 (m, 1H), 2.91–3.10 (m, 4H), 3.74 (s, 3H), 7.05 (dd, J = 4.7, 7.6 Hz, 1H), 7.39 (d, J = 7.6 Hz, 1H), 8.37 (d, J = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 25.7, 30.8, 31.4, 39.2, 51.8, 121.1, 130.0, 136.7, 147.2, 155.9, 175.2.

The enantiomeric excess of **3b** was determined to be 31% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10 or 30% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (+) t_1 = 9.5 min, (–) t_2 = 10.8 min (30% 2-propanol in hexane).

(–)-6-Isopropyl-5,6,7,8-tetrahydroquinoline [76384-36-6] (3c) (Table 1, entry 12).[11]

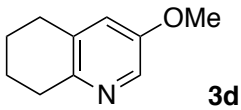


3c

Procedure A was followed with use of DBU (7.5 μL, *d* 1.018 g/mL, 50 μmol) and *i*-PrOH. 6-Isopropylquinoline (**2c**) (85.8 mg, 0.50 mmol) was used in place of **2b**. The reaction was conducted for 48 h. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/10 to 1/3) to give **3c** (29.0 mg, 33%) as colorless oil and 6-isopropyl-1,2,3,4-tetrahydroquinoline (**4c**) (40.0 mg, 46%) as colorless oil. **3c**: $[\alpha]_D^{25}$ = –64.9 (*c* 1.17, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.976 (d, *J* = 6.7 Hz, 3H), 0.981 (d, *J* = 6.7 Hz, 3H), 1.44–1.69 (m, 3H), 1.99–2.09 (m, 1H), 2.53 (dd, *J* = 10.3, 16.3 Hz, 1H), 2.78 (dd, *J* = 4.2, 16.3 Hz, 1H), 2.83–2.95 (m, 1H), 2.98–3.07 (m, 1H), 7.01 (dd, *J* = 4.7, 7.6 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 8.34 (d, *J* = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 19.7, 19.8, 26.4, 32.0, 32.4, 32.7, 40.3, 120.8, 132.1, 136.9, 146.7, 157.4. **4c**: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.19 (d, *J* = 6.9 Hz, 6H), 1.90–1.97 (m, 2H), 2.68–2.81 (m, 3H), 3.27 (t, *J* = 5.5 Hz, 2H), 3.71 (br, 1H), 6.43 (d, *J* = 8.0 Hz, 1H), 6.80–6.86 (m, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 22.4, 24.3, 27.0, 33.2, 42.1, 114.4, 121.4, 124.6, 127.4, 137.6, 142.7; IR (neat) 3402, 2954, 2865, 1616, 1511, 1297, 813 cm^{-1}; Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.11; H, 9.80; N, 7.89.

The enantiomeric excess of **3c** was determined to be 62% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (+) t_1 = 15.2 min, (–) t_2 = 18.2 min.

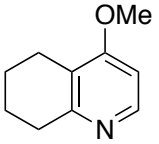
3-Methoxy-5,6,7,8-tetrahydroquinoline [405174-69-8] (3d) (Table 2, entry 1).[10]



3d

Procedure B was followed with use of 3-methoxyquinoline (**2d**) (40.2 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 80°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3d** (37.4 mg, 91%) as pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.75–1.83 (m, 2H), 1.83–1.91 (m, 2H), 2.75 (t, *J* = 6.2 Hz, 2H), 2.85 (t, *J* = 6.4 Hz, 2H), 3.81 (s, 3H), 6.88 (d, *J* = 2.6 Hz, 1H), 8.07 (d, *J* = 2.6 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 22.6, 23.3, 29.0, 31.6, 55.5, 121.1, 132.5, 134.5, 149.4, 153.7.

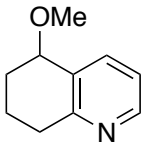
4-Methoxy-5,6,7,8-tetrahydroquinoline [860202-86-4] (3e) (Table 2, entry 2).[12]



3e

Procedure B was followed with use of 4-methoxyquinoline (**2e**) (39.8mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 80°C. The crude product was purified with a flash column chromatography on silica gel (MeOH/EtOAc = 1/10) to give **3e** (40.4 mg, 99%) as pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.73–1.88 (m, 4H), 2.62 (t, J = 6.2 Hz, 2H), 2.87 (t, J = 6.2 Hz, 2H), 3.83 (s, 3H), 6.57 (d, J = 5.6 Hz, 1H), 8.26 (d, J = 5.6 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 22.06, 22.13, 22.7, 32.4, 55.0, 103.0, 121.0, 147.8, 157.8, 163.4.

(+)-5-Methoxy-5,6,7,8-tetrahydroquinoline (3f) (Table 2, entry 3).

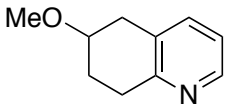


3f

Procedure B was followed with use of 5-methoxyquinoline (**2f**) (40.0 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 80°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3f** (16.5 mg, 40%) as colorless oil: $[\alpha]_D^{25}$ = +1.8 (*c* 1.11, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.77–1.87 (m, 1H), 1.94–2.14 (m, 3H), 2.87 (dt, J = 17.8, 6.8 Hz, 1H), 2.99 (dt, J = 17.8, 6.2 Hz, 1H), 3.46 (s, 3H), 4.34 (t, J = 5.2 Hz, 1H), 7.11 (dd, J = 4.7, 7.6 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 8.44 (dd, J = 1.3, 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 18.4, 26.9, 32.1, 56.2, 76.5, 121.1, 132.2, 136.8, 148.6, 157.5; IR (neat) 2940, 1576, 1443, 1351, 1087, 803 cm^{-1}; HRMS (FAB) Calcd for $C_{10}H_{14}NO$: 164.1075. Found: m/z = 164.1055 ($[M+H]^+$).

The enantiomeric excess of **3f** was determined to be 42% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (+) t_1 = 10.1 min, (–) t_2 = 13.7 min.

(+)-6-Methoxy-5,6,7,8-tetrahydroquinoline [75414-06-1] (3g) (Table 2, entry 4).[13]

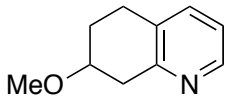


3g

Procedure B was followed with use of 6-methoxyquinoline (**2g**) (39.7 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 80°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3g** (32.0 mg, 79%) as pale yellow oil: $[\alpha]_D^{25}$ = +6.3 (*c* 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.96–2.06 (m, 1H), 2.08–2.17 (m, 1H), 2.83 (dd, J = 6.7, 16.7 Hz, 1H), 2.92 (dt, J = 17.6, 6.9 Hz, 1H), 3.01–3.14 (m, 2H), 3.43 (s, 3H), 3.69–3.75 (m, 1H), 7.04 (dd, J = 4.7, 7.6 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 8.37 (d, J = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.0, 29.4, 34.4, 55.9, 74.6, 121.1, 129.4, 137.2, 147.1, 156.4.

The enantiomeric excess of **3g** was determined to be 58% ee by the HPLC analysis with Chiralpak AS-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (–) t_1 = 14.1 min, (+) t_2 = 18.4 min.

(–)-7-Methoxy-5,6,7,8-tetrahydroquinoline (3h) (Table 2, entry 5).

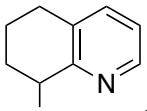


3h

Procedure B was followed with use of 7-methoxyquinoline (**2h**) (39.8 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 80°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3h** (34.1 mg, 84%) as pale yellow oil: $[\alpha]_D^{25}$ = –9.6 (*c* 1.11, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.89–1.98 (m, 1H), 1.99–2.07 (m, 1H), 2.74 (dt, *J* = 16.9, 6.6 Hz, 1H), 2.93 (dt, *J* = 16.9, 6.6 Hz, 1H), 3.00 (dd, *J* = 6.2, 17.3 Hz, 1H), 3.21 (dd, *J* = 4.8, 17.3 Hz, 1H), 3.43 (s, 3H), 3.76–3.82 (m, 1H), 7.04 (dd, *J* = 4.7. 7.7 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 8.37 (d, *J* = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 25.1, 27.0, 38.0, 55.9, 75.1, 121.1, 131.3, 136.2, 147.2, 154.9; IR (neat) 2930, 1577, 1446, 1096, 790 cm^{-1}; HRMS (FAB) Calcd for $C_{10}H_{14}NO$: 164.1075. Found: *m*/*z* = 164.1102 ([M+H]$^+$).

The enantiomeric excess of **3h** was determined to be 37% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% or 20% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (–) t_1 = 9.4 min, (+) t_2 = 11.3 min (20% 2-propanol in hexane).

(+)-8-Methoxy-5,6,7,8-tetrahydroquinoline [75414-07-2] (3i) (Table 2, entry 9).[13]

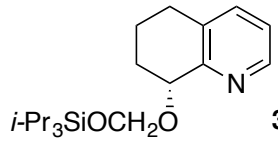


3i

Procedure B was followed with use of 8-methoxyquinoline (**2i**) (159 mg, 1.0 mmol). The reaction was conducted in EtOAc (1.0 mL) at 60°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3i** (154 mg, 94%) as pale yellow oil: $[\alpha]_D^{24}$ = +37.6 (*c* 1.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.72–1.90 (m, 2H), 1.95–2.07 (m, 1H), 2.20–2.29 (m, 1H), 2.72 (ddd, *J* = 5.8, 10.1, 17.0 Hz, 1H), 2.84 (dt, *J* = 17.0, 4.7 Hz, 1H), 3.54 (s, 3H), 4.36 (t, *J* = 3.8 Hz, 1H), 7.14 (dd, *J* = 4.7, 7.7 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 8.48 (d, *J* = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 17.5, 27.5, 28.4, 57.0, 77.6, 122.8, 132.9, 137.2, 147.2, 155.2.

The enantiomeric excess of **3i** was determined to be 82% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% or 20% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 275 nm detection, (+) t_1 = 8.7 min, (–) t_2 = 10.2 min (20% 2-propanol in hexane).

(+)-8-[(Triisopropylsilyloxy)methoxy]-5,6,7,8-tetrahydroquinoline (3j) (Table 3, entry 1).



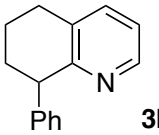
3j

Procedure B was followed with use of 8-[(triisopropylsilyloxy)methoxy]quinoline (**2j**) (78.8 mg, 0.24 mmol). The reaction was conducted in EtOAc at 60°C. The crude product was purified with a flash

column chromatography on silica gel (EtOAc/hexane = 1/3) to give **3j** (77.2 mg, 97%) as colorless oil: $[\alpha]_D^{26}$ = +33.4 (*c* 1.04, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 1.02–1.18 (m, 21H), 1.73–1.82 (m, 1H), 1.89–1.98 (m, 1H), 2.01–2.14 (m, 1H), 2.29–2.38 (m, 1H), 2.71 (ddd, *J* = 5.9, 10.0, 16.9 Hz, 1H), 2.83 (dt, *J* = 16.9, 4.8 Hz, 1H), 4.76 (t, *J* = 4.0 Hz, 1H), 5.19 (d, *J* = 4.9 Hz, 1H), 5.34 (d, *J* = 4.9 Hz, 1H), 7.11 (dd, *J* = 4.7, 7.7 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 8.44 (d, *J* = 4.7 Hz, 1H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 12.0, 17.85, 17.89, 28.3, 30.3, 74.8, 90.0, 122.6, 132.8, 137.0, 147.2, 155.9; IR (neat) 2944, 2867, 1500, 1470, 1376, 1318, 1251, 1156, 1084, 1061, 984 cm^{-1}; Anal. Calcd for $C_{19}H_{33}NO_2Si$: C, 68.01; H, 9.91; N, 4.17. Found: C, 67.99; H, 9.93; N, 4.05.

The enantiomeric excess of **3j** was determined to be 81% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 1% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (+) t_1 = 9.3 min, (–) t_2 = 10.9 min.

(+)-8-Phenyl-5,6,7,8-tetrahydroquinoline [56826-78-9] (3k) (Table 3, entry 2).[13]

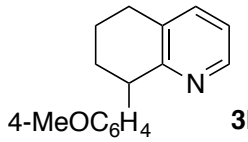


3k

Procedure B was followed with use of 8-phenylquinoline (**2k**) (52.3 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 40°C for 48 h. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/5) to give **3k** (46.5 mg, 87%) as colorless oil: $[\alpha]_D^{24}$ = +34.5 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 1.65–1.76 (m, 1H), 1.78–1.90 (m, 1H), 1.92–2.02 (m, 1H), 2.17–2.27 (m, 1H), 2.79 (dt, *J* = 17.0, 6.7 Hz, 1H), 2.88 (dt, *J* = 17.0, 6.1 Hz, 1H), 4.30 (t, *J* = 6.1 Hz, 1H), 6.98 (d, *J* = 7.2 Hz, 2H), 7.01 (dd, *J* = 4.8, 7.8 Hz, 1H), 7.14 (t, *J* = 7.3 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 7.8 Hz, 1H), 8.37 (d, *J* = 4.8 Hz, 1H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 19.3, 28.8, 32.7, 47.5, 121.0, 125.6, 128.0, 128.4, 132.8, 136.6, 146.2, 147.3, 158.3.

The enantiomeric excess of **3k** was determined to be 73% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (+) t_1 = 9.8 min, (–) t_2 = 10.8 min.

(+)-8-(4-Methoxyphenyl)-5,6,7,8-tetrahydroquinoline (3l) (Table 3, entry 3).



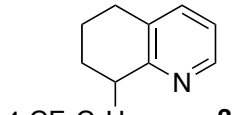
3l

Procedure B was followed with use of 8-(4-methoxyphenyl)quinoline (**2l**) (58.5 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 60°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/2) to give **3l** (56.1 mg, 94%) as colorless oil: $[\alpha]_D^{27}$ = +39.8 (*c* 1.02, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 1.67–1.78 (m, 1H), 1.80–2.00 (m, 2H), 2.16–2.26 (m, 1H), 2.81 (dt, *J* = 16.8, 6.7 Hz, 1H), 2.89 (dt, *J* = 16.8, 6.1 Hz, 1H), 3.75 (s, 3H), 4.26 (t, *J* = 6.0 Hz, 1H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 7.04 (dd, *J* = 4.6, 7.6 Hz, 1H), 7.42 (d, *J* = 7.6

Hz, 1H), 8.39 (d, J = 4.6 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 19.5, 29.0, 32.9, 46.9, 55.1, 113.6, 121.1, 129.4, 132.9, 136.7, 138.6, 147.4, 157.6, 158.7; IR (neat) 2934, 1511, 1444, 1246, 1177, 1035, 827, 796 cm^{-1}; Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.16; H, 6.89; N, 5.86.

The enantiomeric excess of **3l** was determined to be 72% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (+) t_1 = 13.7 min, (–) t_2 = 16.9 min.

(+)-8-[4-(Trifluoromethyl)phenyl]-5,6,7,8-tetrahydroquinoline (3m) (Table 3, entry 4).

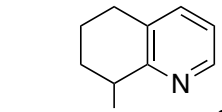


3m

Procedure B was followed with use of 8-[4-(trifluoromethyl)phenyl]quinoline (**2m**) (68.3 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 60°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/3) to give **3m** (60.8 mg, 88%) as colorless oil: $[\alpha]_D^{27}$ = +18.7 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.71–2.01 (m, 3H), 2.22–2.32 (m, 1H), 2.84 (dt, J = 17.0, 6.5 Hz, 1H), 2.92 (dt, J = 17.0, 6.5 Hz, 1H), 4.36 (t, J = 6.4 Hz, 1H), 7.08 (dd, J = 4.7, 7.7 Hz, 1H), 7.12 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 7.7 Hz, 1H), 7.52 (d, J = 8.1 Hz, 2H), 8.38 (d, J = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 19.7, 28.9, 32.9, 47.8, 121.6, 124.3 (q, J = 272 Hz), 125.2 (q, J = 4 Hz), 128.1 (q, J = 32 Hz), 128.9, 133.1, 137.0, 147.6, 150.5, 157.6; IR (neat) 2938, 1446, 1327, 1163, 1120, 1067, 833, 790 cm^{-1}; Anal. Calcd for $C_{16}H_{14}F_3N$: C, 69.30; H, 5.09; N, 5.05. Found: C, 69.32; H, 5.08; N, 5.09.

The enantiomeric excess of **3m** was determined to be 72% ee by the HPLC analysis with Chiralpak AS-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (–) t_1 = 7.9 min, (+) t_2 = 8.7 min.

(+)-8-(2-Methylphenyl)-5,6,7,8-tetrahydroquinoline (3n) (Table 3, entry 5).



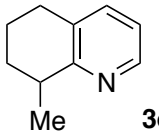
3n

Procedure B was followed with use of 8-(2-methylphenyl)quinoline (**2n**) (54.1 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 60°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/3) to give **3n** (30.8 mg, 56%) as a colorless solid: $[\alpha]_D^{25}$ = +39.0 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.66–1.77 (m, 1H), 1.81–1.94 (m, 2H), 2.13–2.22 (m, 1H), 2.39 (s, 3H), 2.80 (dt, J = 16.7, 6.8 Hz, 1H), 2.90 (dt, J = 16.7, 6.0 Hz, 1H), 4.50 (t, J = 6.1 Hz, 1H), 6.53 (d, J = 7.3 Hz, 1H), 6.97–7.08 (m, 3H), 7.15 (d, J = 7.3 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 8.37 (d, J = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 19.4, 19.5, 29.0, 30.5, 44.2, 120.9, 125.4, 125.7, 128.9, 130.4, 133.0, 135.4, 136.5, 144.3, 147.4, 158.9; IR (neat) 3045, 2940, 2857, 1571,

1489, 1443, 807, 789, 757, 729 cm^{-1}; Anal. Calcd for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 85.77; H, 7.69; N, 6.30.

The enantiomeric excess of **3n** was determined to be 41% ee by the HPLC analysis with Chiralcel OJ-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (–) t_1 = 12.2 min, (+) t_2 = 13.3 min.

(–)-8-Methyl-5,6,7,8-tetrahydroquinoline [52601-66-8] (3o) (Table 3, entry 7).[13]

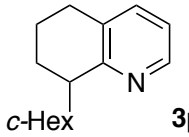


3o

Procedure B was followed with use of 8-methylquinoline (**2o**) (35.9 mg, 0.25 mmol). {Ru(*p*-cymene)[(*S*,*S*)-(*R*,*R*)-PhTRAP]}Cl (5.5 mg, 5.0 μmol) and DBU (8.2 mg, 55 μmol) were used in place of [Ru(η^3-methallyl)$_2$(cod)]–(*S*,*S*)-(*R*,*R*)-PhTRAP and K_2CO_3, respectively. The reaction was conducted in *i*-PrOH at 60°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3o** (25.9 mg, 71%) as colorless oil: $[\alpha]_D^{26}$ = –29.7 (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.37 (d, *J* = 7.1 Hz, 3H), 1.60–1.80 (m, 2H), 1.83–1.94 (m, 1H), 1.98–2.08 (m, 1H), 2.69–2.84 (m, 2H), 3.00 (sextet, *J* = 6.6 Hz, 1H), 7.01 (dd, *J* = 4.7, 7.6 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 8.39 (d, *J* = 4.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 20.0, 21.3, 29.4, 31.2, 35.6, 120.8, 131.8, 136.6, 146.9, 161.3.

The enantiomeric excess of **3o** was determined to be 79% ee by the HPLC analysis with Chiralcel OB-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (–) t_1 = 9.2 min, (+) t_2 = 10.0 min.

(–)-8-Cyclohexyl-5,6,7,8-tetrahydroquinoline [75414-11-8] (3p) (Table 3, entry 8).[13]



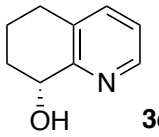
3p

Procedure B was followed with use of 8-cyclohexylquinoline (**2p**) (52.8 mg, 0.25 mmol). {Ru(*p*-cymene)[(*S*,*S*)-(*R*,*R*)-PhTRAP]}Cl (5.5 mg, 5.0 μmol) and DBU (8.2 mg, 55 μmol) were used in place of [Ru(η^3-methallyl)$_2$(cod)]–(*S*,*S*)-(*R*,*R*)-PhTRAP and K_2CO_3, respectively. The reaction was conducted in *i*-PrOH at 60°C. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3p** (46.4 mg, 86%) as colorless oil: $[\alpha]_D^{26}$ = –75.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.97–1.43 (m, 6H), 1.56–1.80 (m, 6H), 1.86–1.97 (m, 2H), 2.30–2.41 (m, 1H), 2.63–2.78 (m, 2H), 2.79–2.88 (m, 1H), 6.98 (dd, *J* = 4.8, 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 8.41 (d, *J* = 4.8 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 21.6, 24.1, 26.70, 26.73, 27.0, 27.7, 29.5, 31.5, 41.3, 45.9, 120.3, 133.2, 136.3, 146.7, 159.8.

The enantiomeric excess of **3p** was determined to be 81% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (–) t_1 = 8.1 min, (+) t_2 = 9.0 min.

Deprotection of 3j (eq 2).

(*R*)-5,6,7,8-Tetrahydroquinolin-8-ol [451466-81-2] (3q).[9]



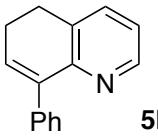
3q

Compound **3j** (81% ee, 62.0 mg, 0.18 mmol) was placed in a 2.0 mL Schlenk tube, which was equipped with a stirring bar, rubber septum and three-way stopcock. After the reaction vessel was evacuated and charged with nitrogen gas three times, a 1.0 *M* solution of TBAF in THF (0.36 mL, 0.36 mmol) was added into the tube through the septum by using a syringe.[14] The solution was stirred at ambient temperature for 5 h. After the solution was acidified with AcOH and then diluted with water, the resulting mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, and then evaporated under reduced pressure after filtration. The residue was purified with a flash column chromatography on silica gel (MeOH/EtOAc = 1/10) to give **3q** (24.7 mg, 90%) as a colorless solid: $[\alpha]_D^{24}$ = –52.0 (*c* 1.00, $CHCl_3$); lit.[9] $[\alpha]_D^{20}$ = –65 (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.75–1.88 (m, 2H), 1.95–2.06 (m, 1H), 2.23–2.34 (m, 1H), 2.74–2.90 (m, 2H), 4.11 (br, 1H), 4.71 (dd, *J* = 6.1, 7.9 Hz, 1H), 7.12 (dd, *J* = 4.8, 7.7 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 8.41 (d, *J* = 4.8 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 19.4, 28.3, 30.7, 68.9, 122.4, 131.6, 136.9, 146.7, 158.0.

The enantiomeric excess of **3q** was determined to be 80% ee by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection, (*R*) t_1 = 12.4 min, (*S*) t_2 = 15.2 min.

Mechanistic Study on the Ruthenium-Catalyzed Hydrogenation of 2.

Preparation of 8-phenyl-5,6-dihydroquinoline [343320-64-9] (5k).

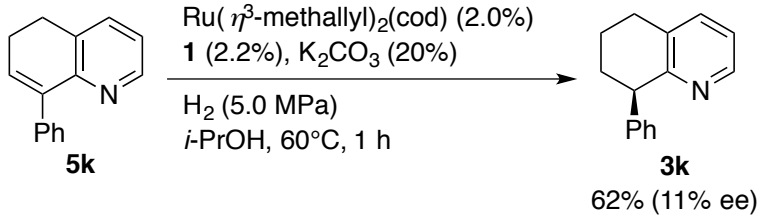


5k

MsOH (400 mg, 4.2 mmol) was placed in a 10 mL Schlenk tube, which was equipped with a stirring bar, rubber septum, and cold finger. Toluene (3.0 mL) and then 8-phenyl-5,6,7,8-tetrahydroquinolin-8-ol (225 mg, 1.0 mmol) were added into the tube. The solution was stirred under reflux for 12 h. After saturated Na_2CO_3 *aq.* was added, the mixture was extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and

then evaporated under reduced pressure after filtration. The residue was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/10) to give **5k** (202 mg, 97%) as a colorless solid: mp. 78.0–78.1°C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.46 (dt, *J* = 4.7, 8.0 Hz, 2H), 2.90 (t, *J* = 8.0 Hz, 2H), 6.43 (t, *J* = 4.7 Hz, 1H), 7.05 (dd, *J* = 4.9, 7.5 Hz, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.37 (t, *J* = 7.3 Hz, 2H), 7.41–7.47 (m, 3H), 8.40 (dd, *J* = 1.7, 4.9 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 23.0, 27.8, 121.6, 127.2, 128.0, 128.8, 132.2, 134.7, 139.5, 140.9, 147.1, 153.6; IR (neat) 3051, 2936, 2888, 2829, 1560, 1492, 1431, 796, 754, 697 cm^{-1}; Anal. Calcd for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 85.77; H, 7.69; N, 6.30.

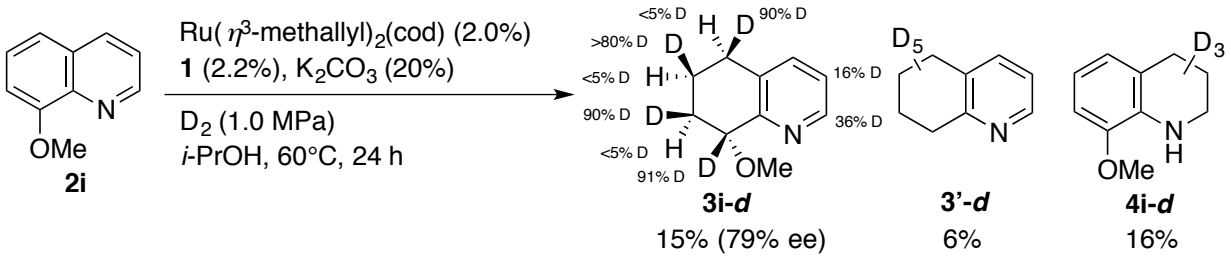
Hydrogenation of 5k (eq 3).



The procedure B for the asymmetric hydrogenation was followed with use of **5k** (51.6 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 60°C for 1 h. The ^{1}H NMR analysis of the resulting mixture was indicated that 40% of **5k** was remained. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/5) to give **3k** (32.2 mg, 62%) as colorless oil.

The enantiomeric excess of **3k** was determined to be 11% ee (–) by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection.

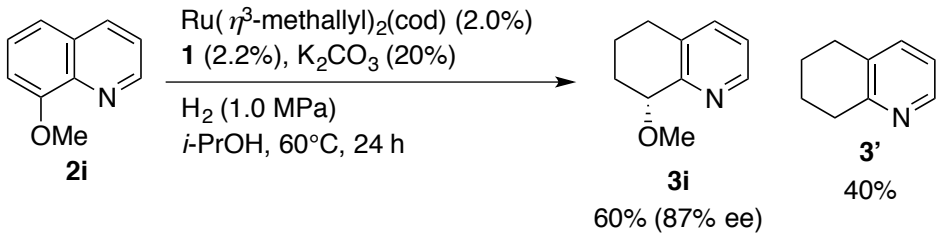
Deuteration of 2i (eq 4).



The procedure B for the asymmetric hydrogenation was followed with use of **2i** (40.0 mg, 0.25 mmol). The reaction was conducted in *i*-PrOH at 60°C under 1.0 MPa of D_2 for 24 h. The ^{1}H NMR analysis of the resulting mixture was indicated that it contained **2i** in 61%, **3i-*d*** in 15%, **3'-*d*** in 6%, and **4i-*d*** in 16%. The crude product was purified with a flash column chromatography on silica gel (EtOAc/hexane = 1/1) to give **3i-*d*** (1.5 mg, 4%) as colorless oil. The ^{1}H NMR spectrum of **3i-*d*** is given in Figure S-51. The methoxy group was used as the internal standard for calibrating the integration of each peak. In the recovered starting material, deuterium was incorporated at the 2-position in 57%.

The enantiomeric excess of **3i-*d*** was determined to be 79% ee (+) by the HPLC analysis with Chiralcel OD-H (4.6 mm ϕ × 250 mm): 10% 2-propanol in hexane, 0.5 mL/min flow, at 35°C, UV 268 nm detection.

As shown in Scheme S-1, the hydrogenation of **2i** was carried out under the above condition to compare the deuteration with the hydrogenation. The resulting mixture contains 87% ee of **3i** in 60% and **3'** in 40%. The substrate **2i** was completely consumed without formation of **4i**.



Scheme S-1. The hydrogenation of **2i** under 1.0 MPa of H_2.

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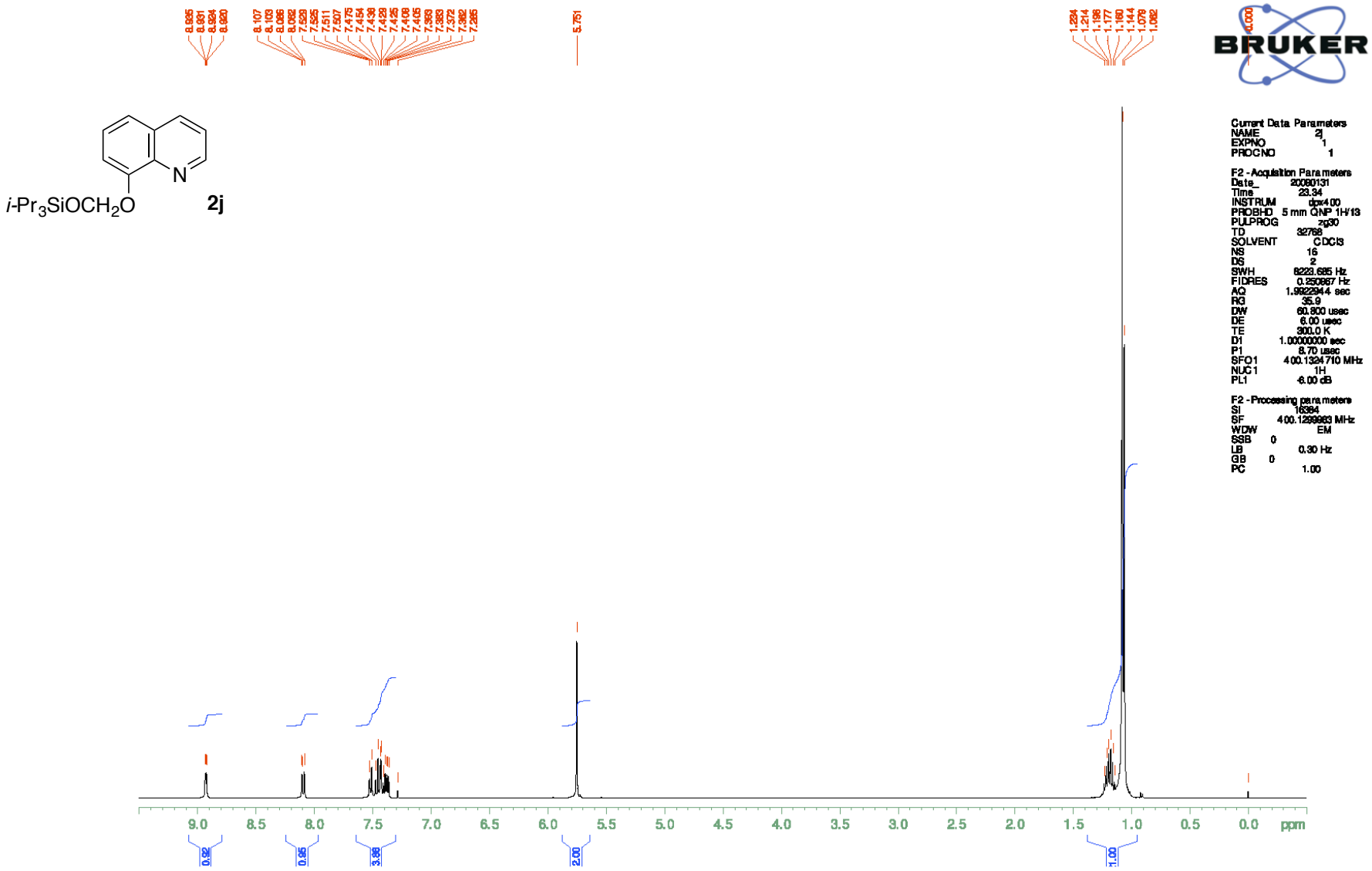


Figure S-1. ^{1}H NMR spectrum ($CDCl_3$) of **2j**.

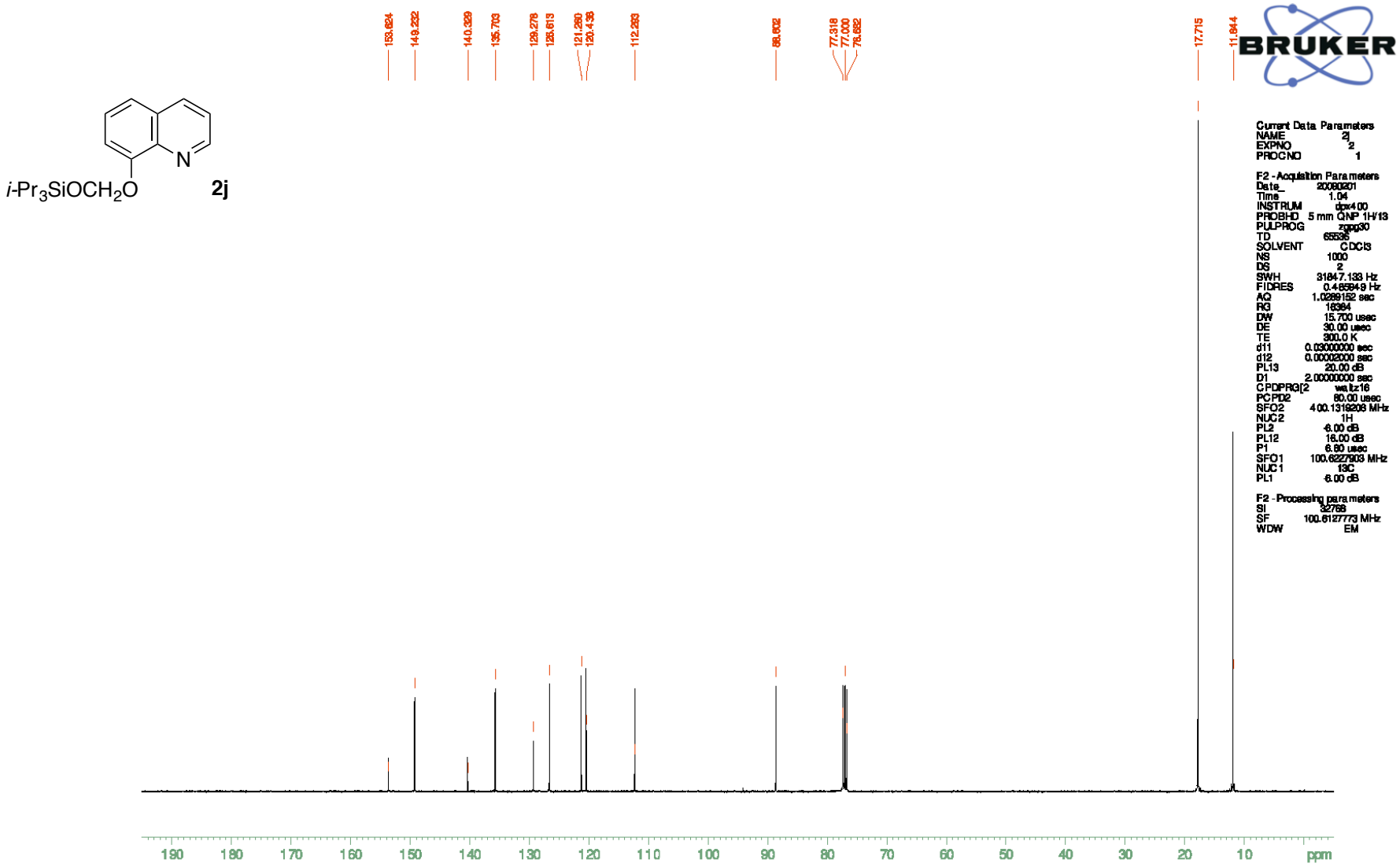


Figure S-2. ^{13}C {^{1}H} NMR spectrum ($CDCl_3$) of **2j**.

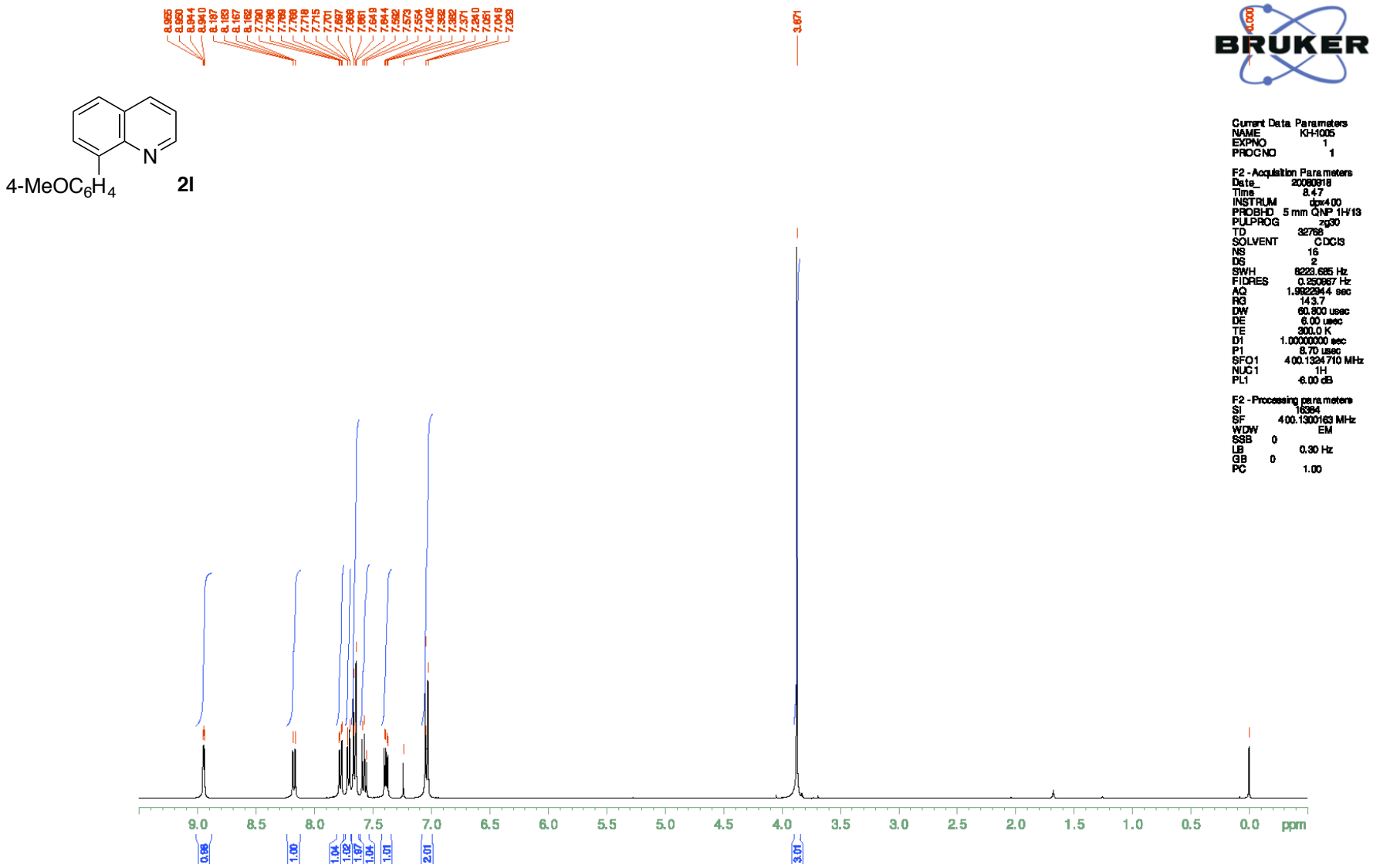


Figure S-3. ^{1}H NMR spectrum ($CDCl_3$) of **2l**.

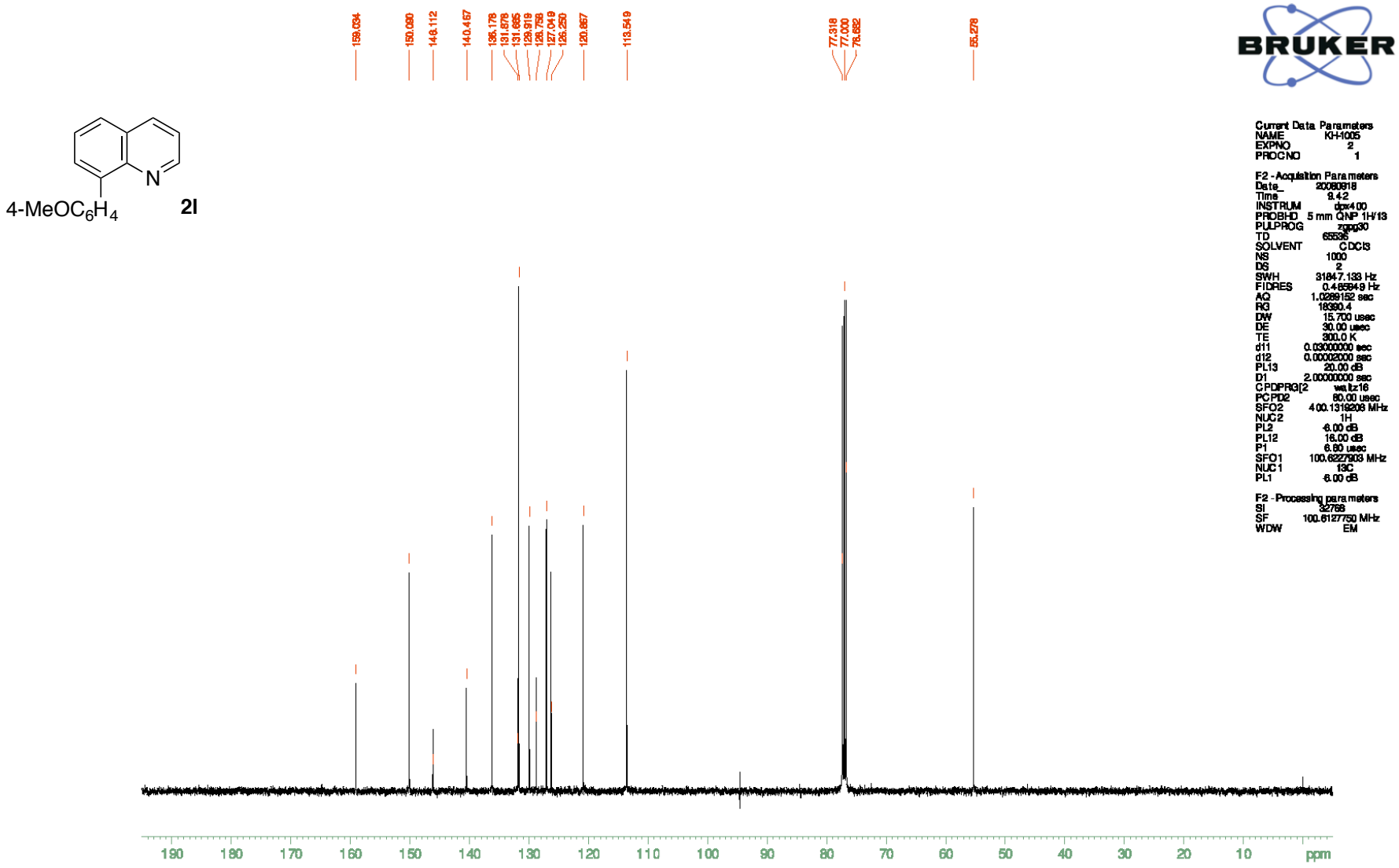


Figure S-4. ^{13}C {^{1}H} NMR spectrum ($CDCl_3$) of **2l**.

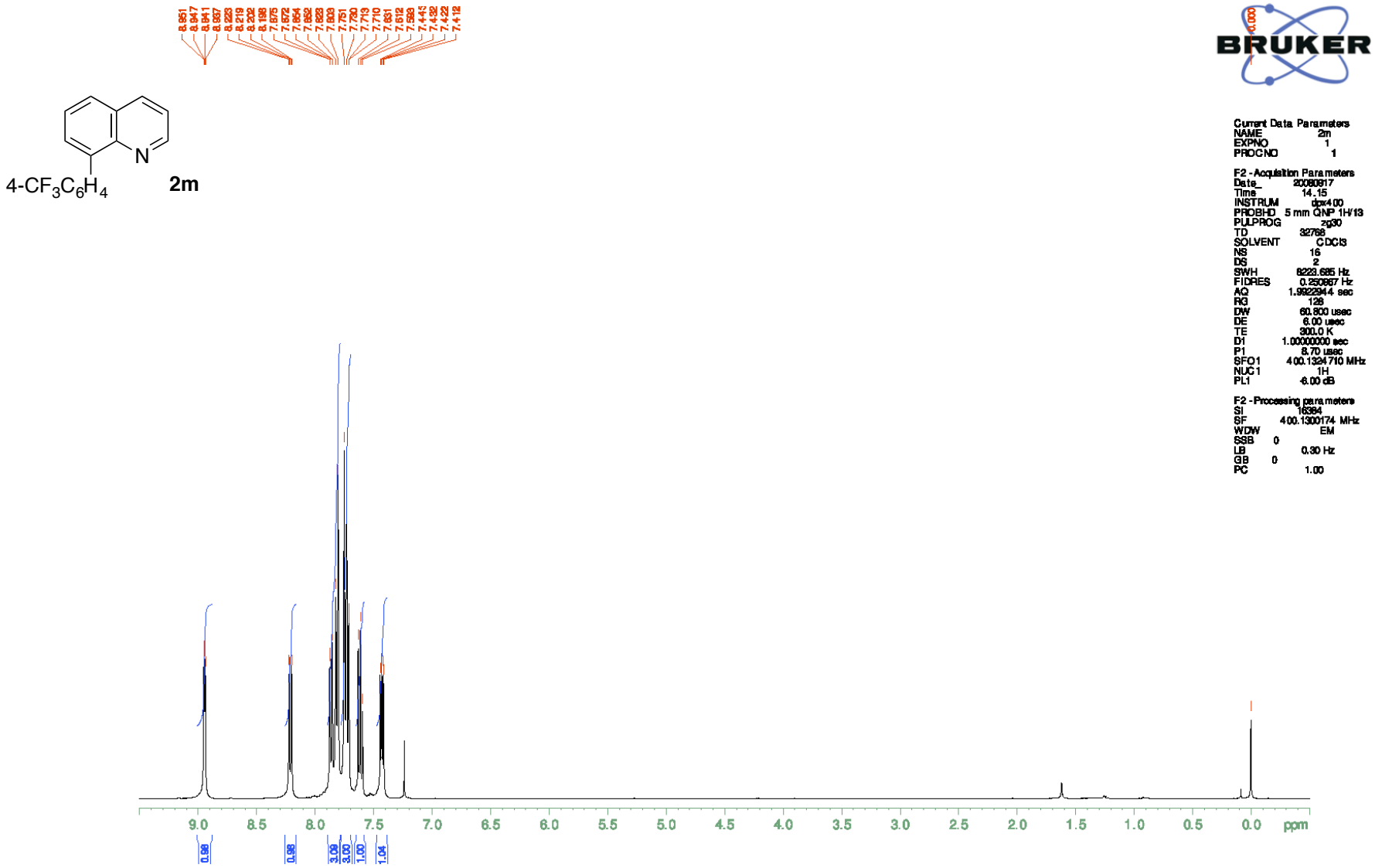


Figure S-5. ^{1}H NMR spectrum ($CDCl_3$) of **2m**.

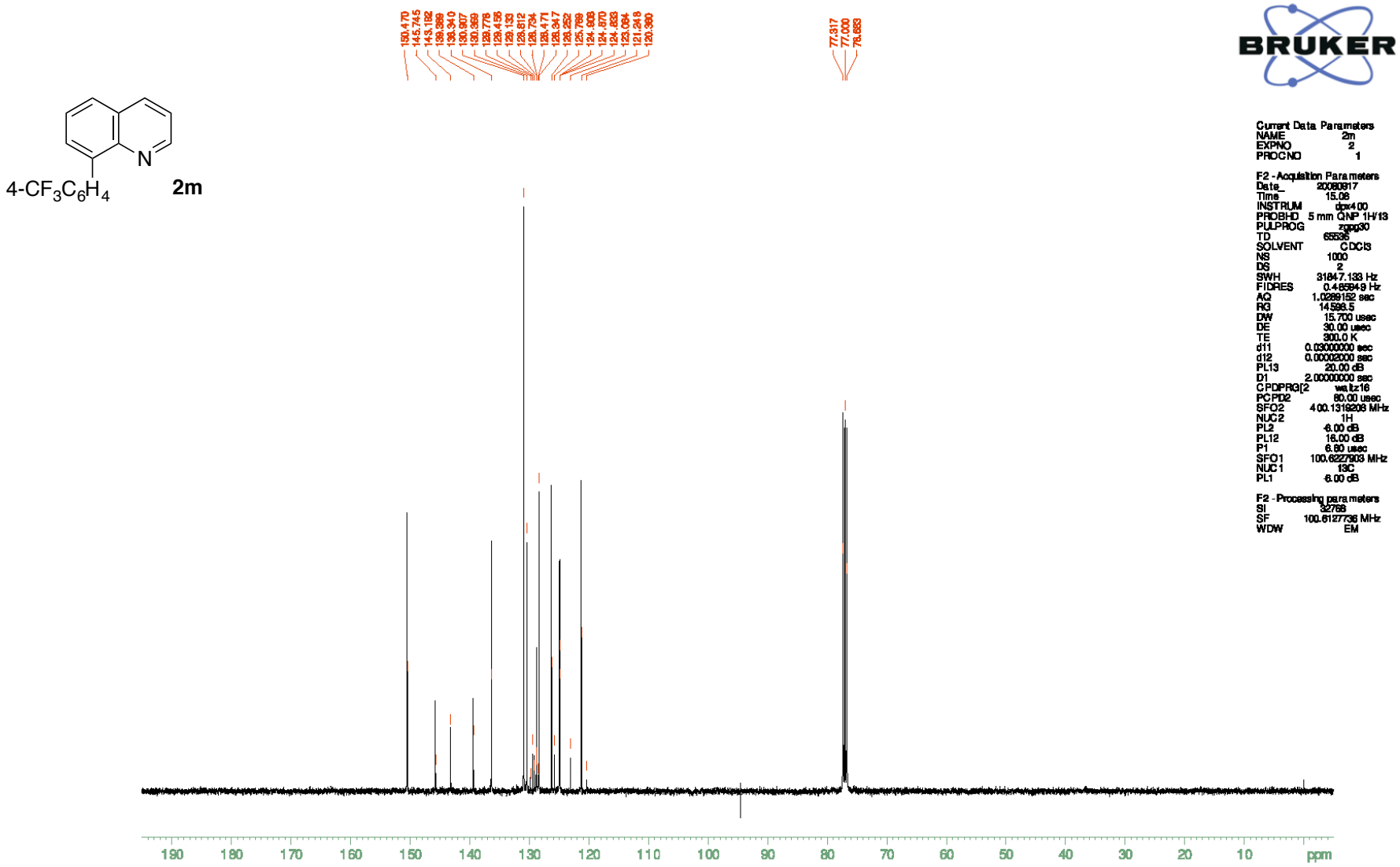


Figure S-6. ^{13}C {^{1}H} NMR spectrum ($CDCl_3$) of **2m**.

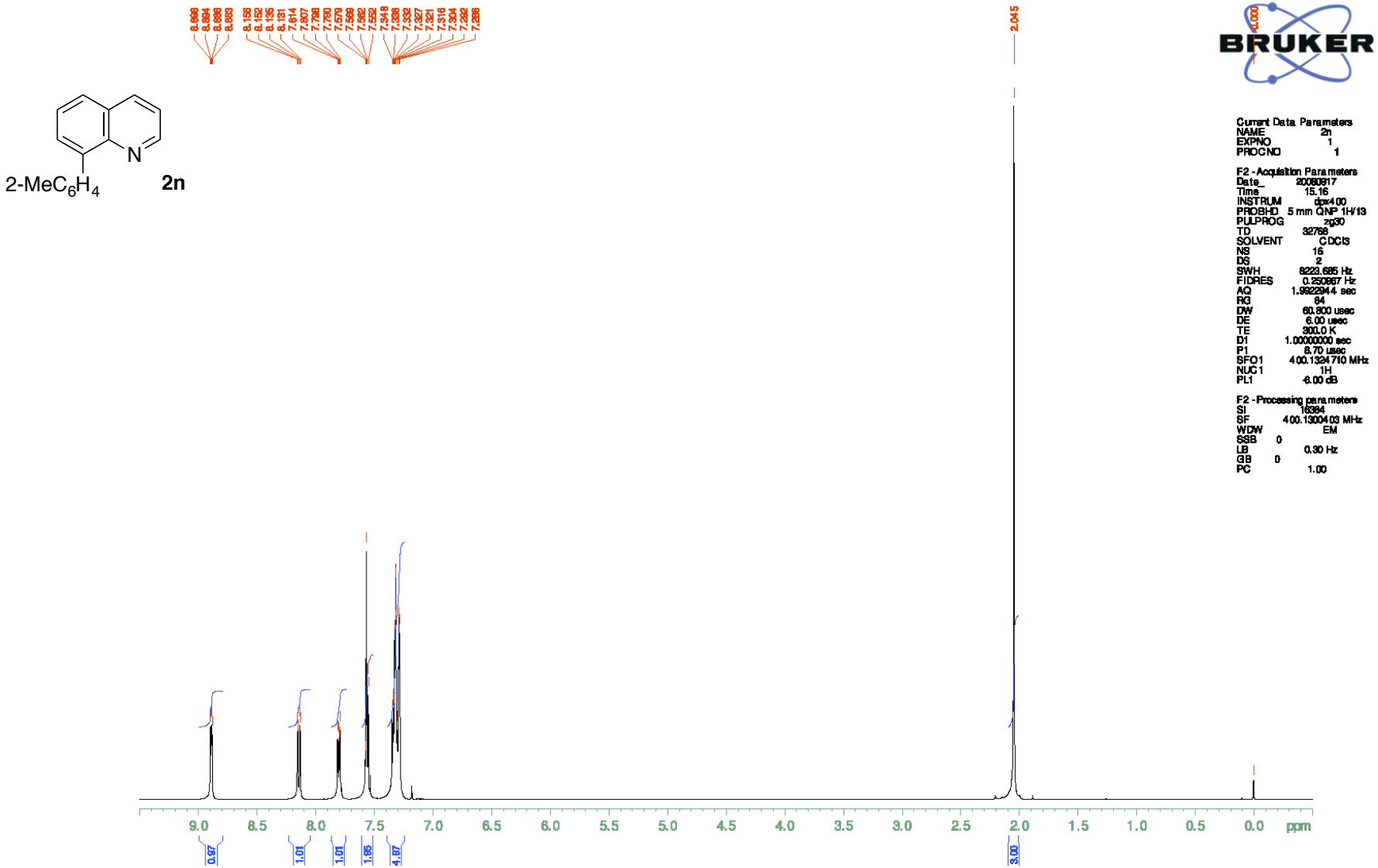


Figure S-7. ^{1}H NMR spectrum ($CDCl_3$) of **2n**.

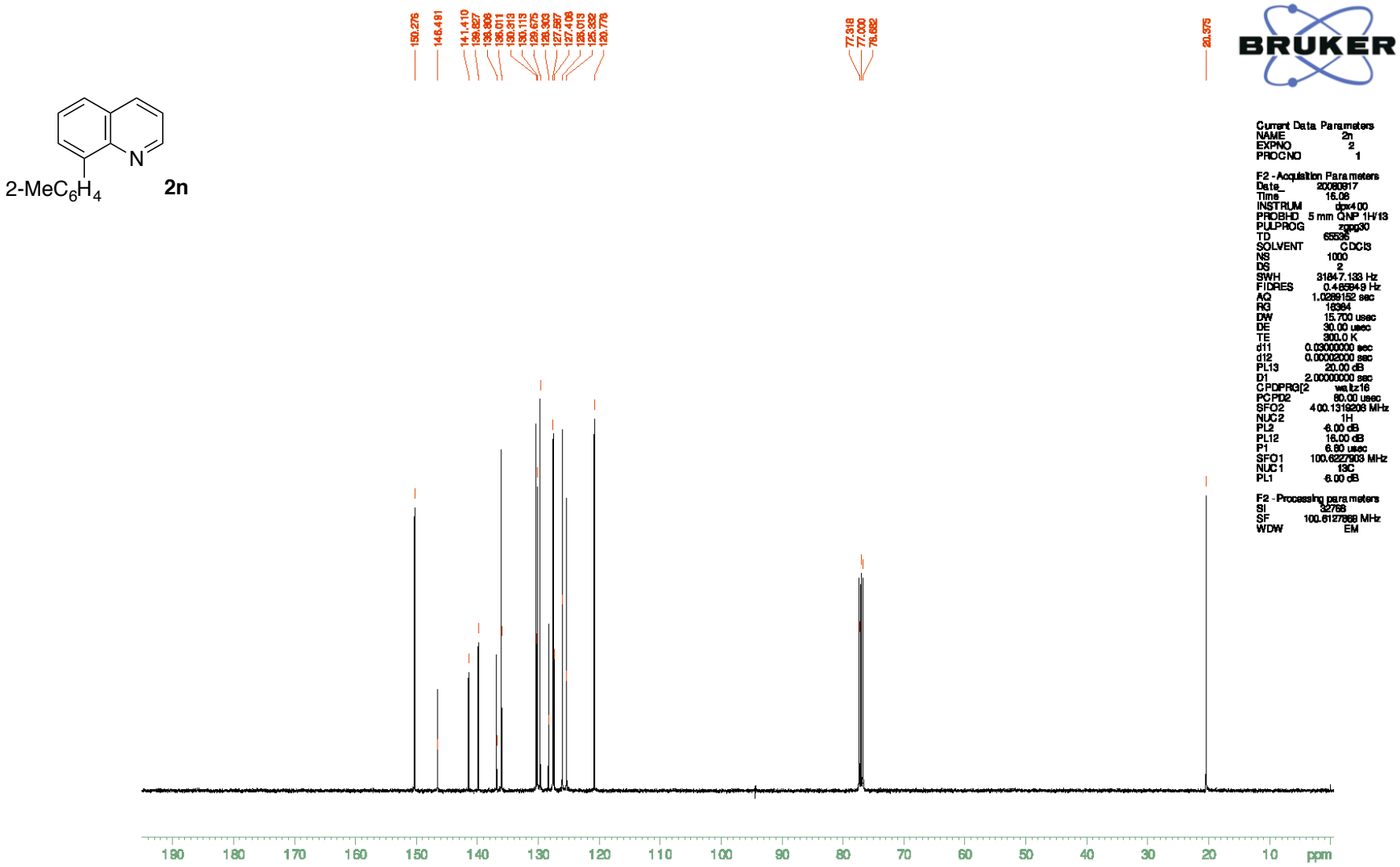


Figure S-8. ^{13}C {^{1}H} NMR spectrum ($CDCl_3$) of **2n**.

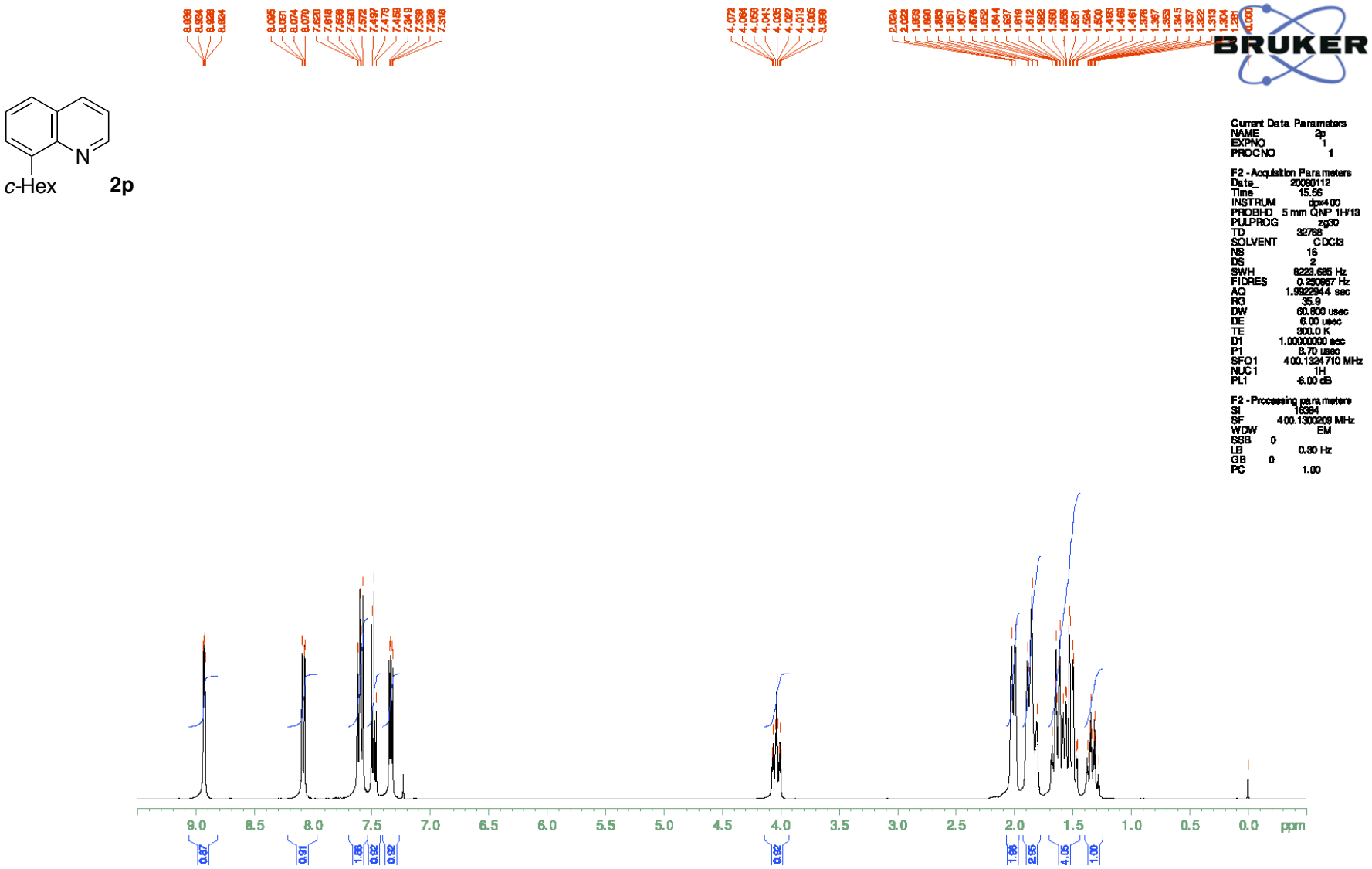


Figure S-9. ^{1}H NMR spectrum ($CDCl_3$) of **2p**.

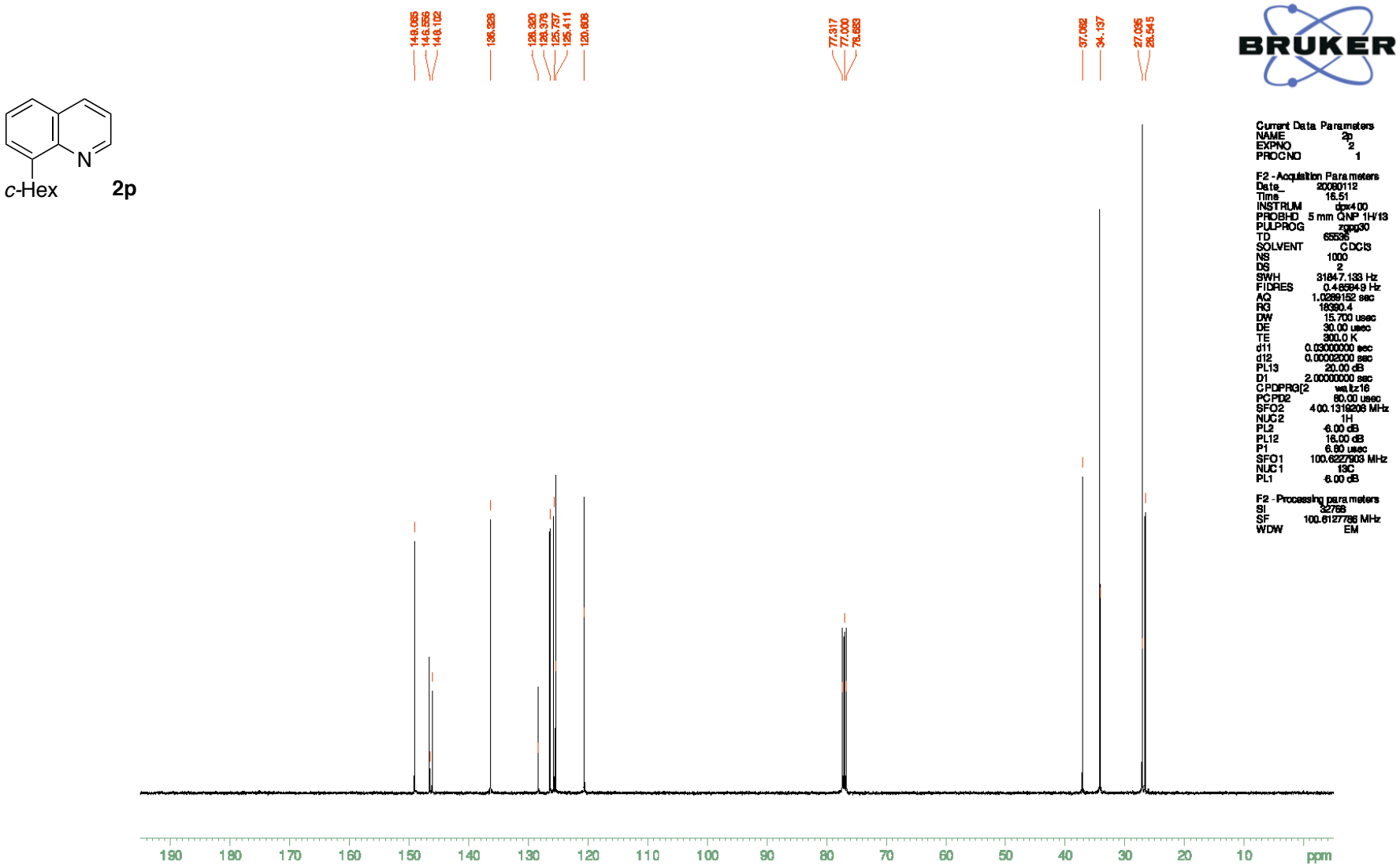


Figure S-10. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **2p**.

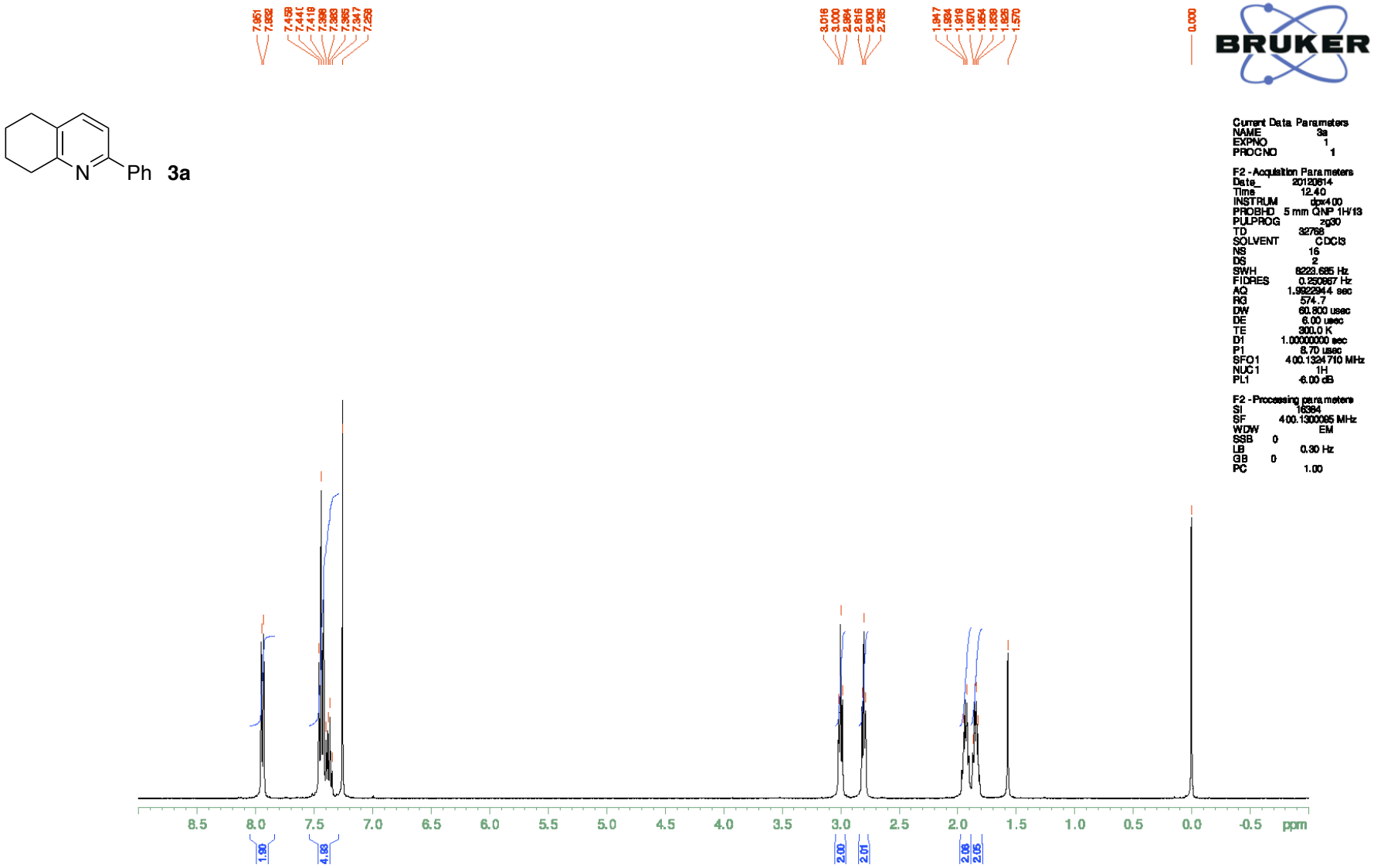


Figure S-11. ^{1}H NMR spectrum ($CDCl_3$) of **3a**.

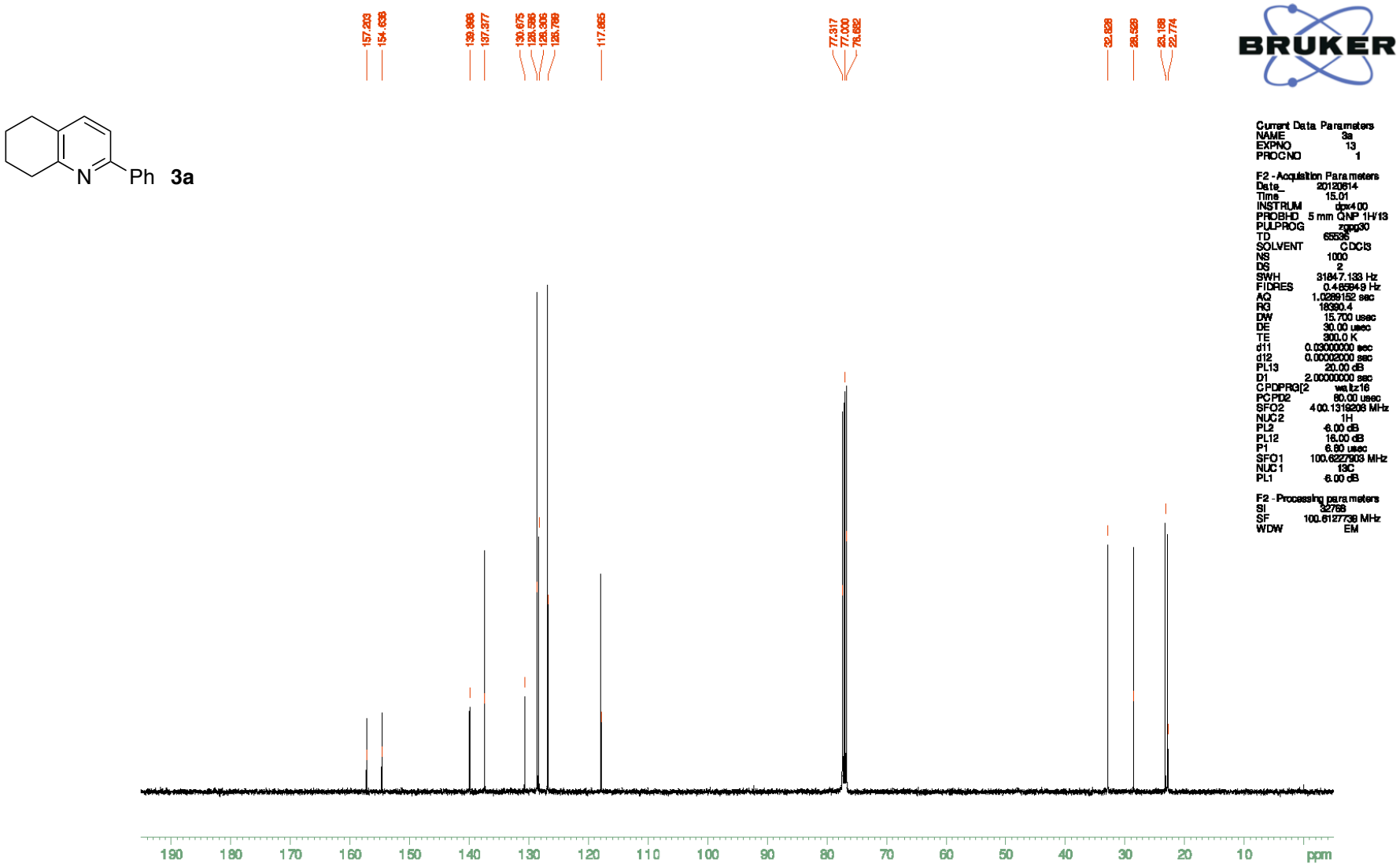


Figure S-12. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3a**.

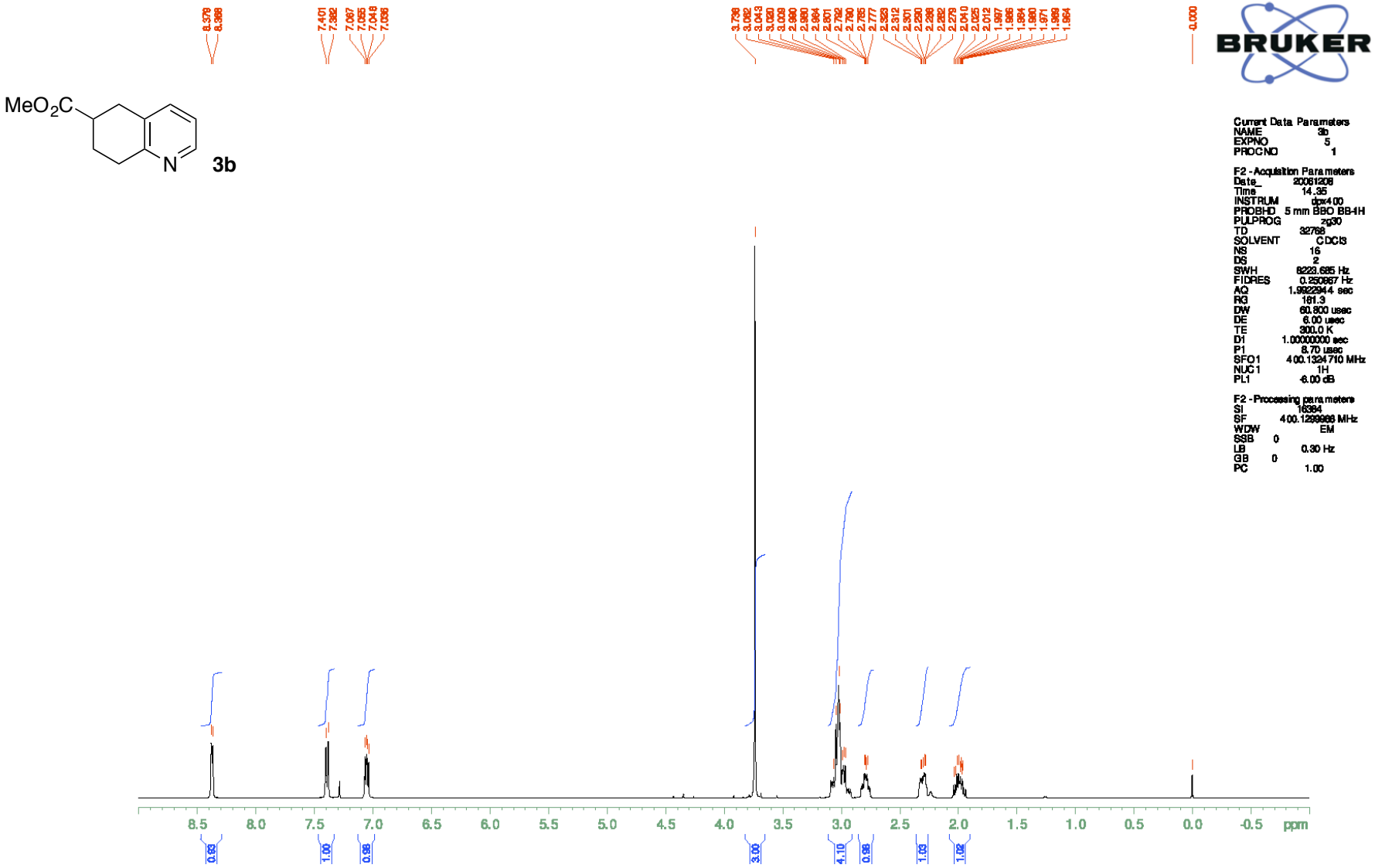


Figure S-13. ^{1}H NMR spectrum ($CDCl_3$) of **3b**.

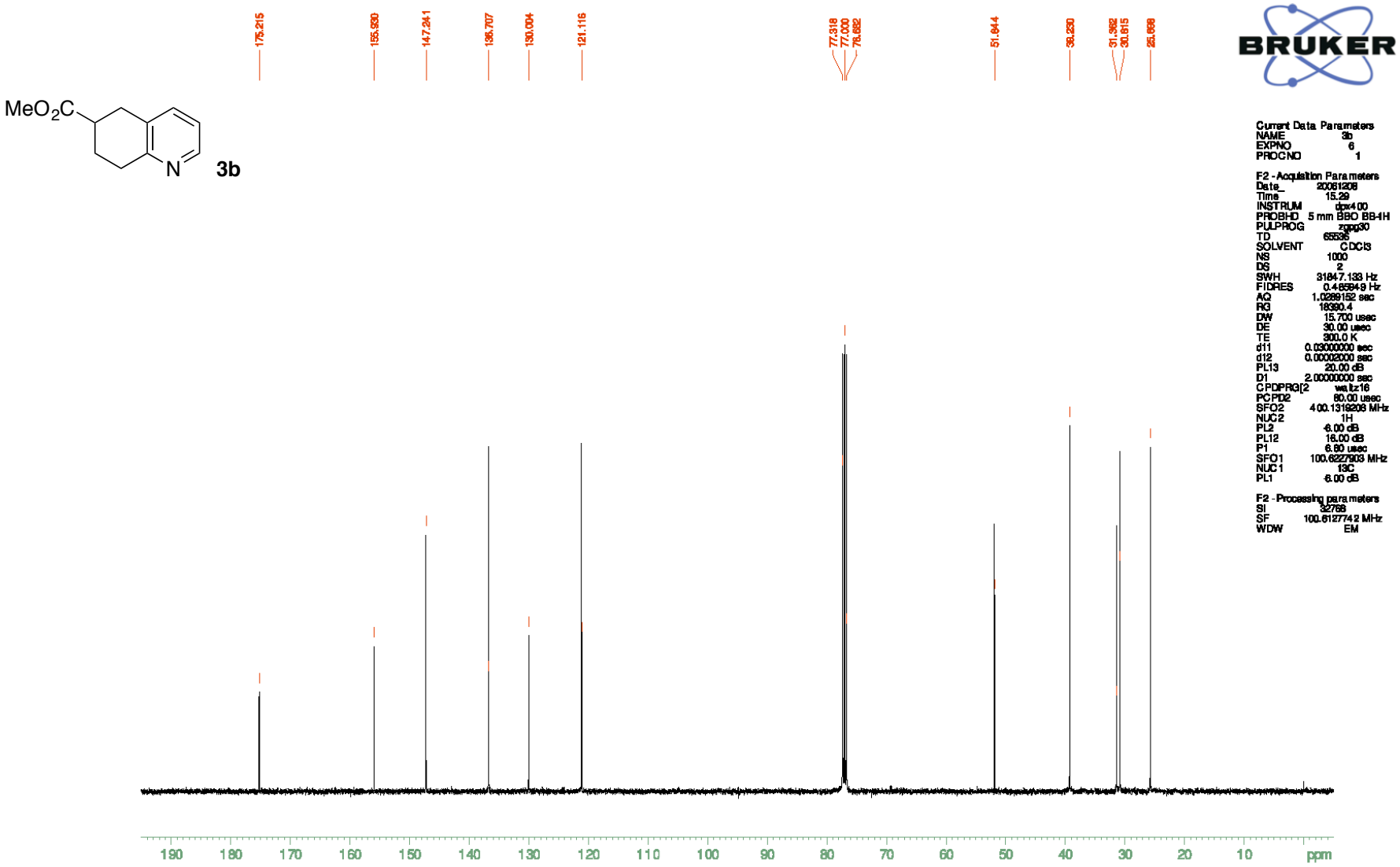


Figure S-14. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3b**.

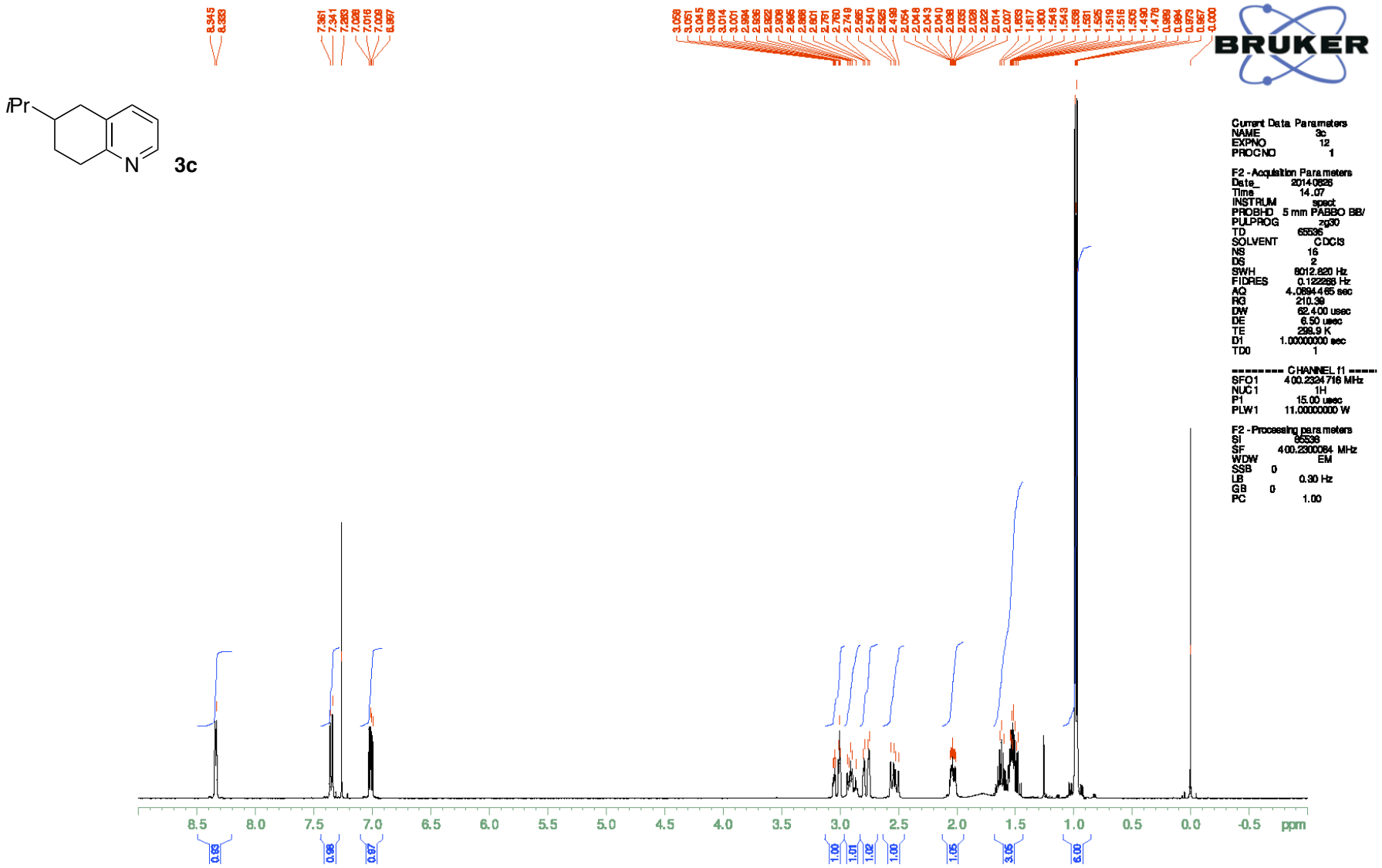


Figure S-15. ^{1}H NMR spectrum ($CDCl_3$) of **3c**.

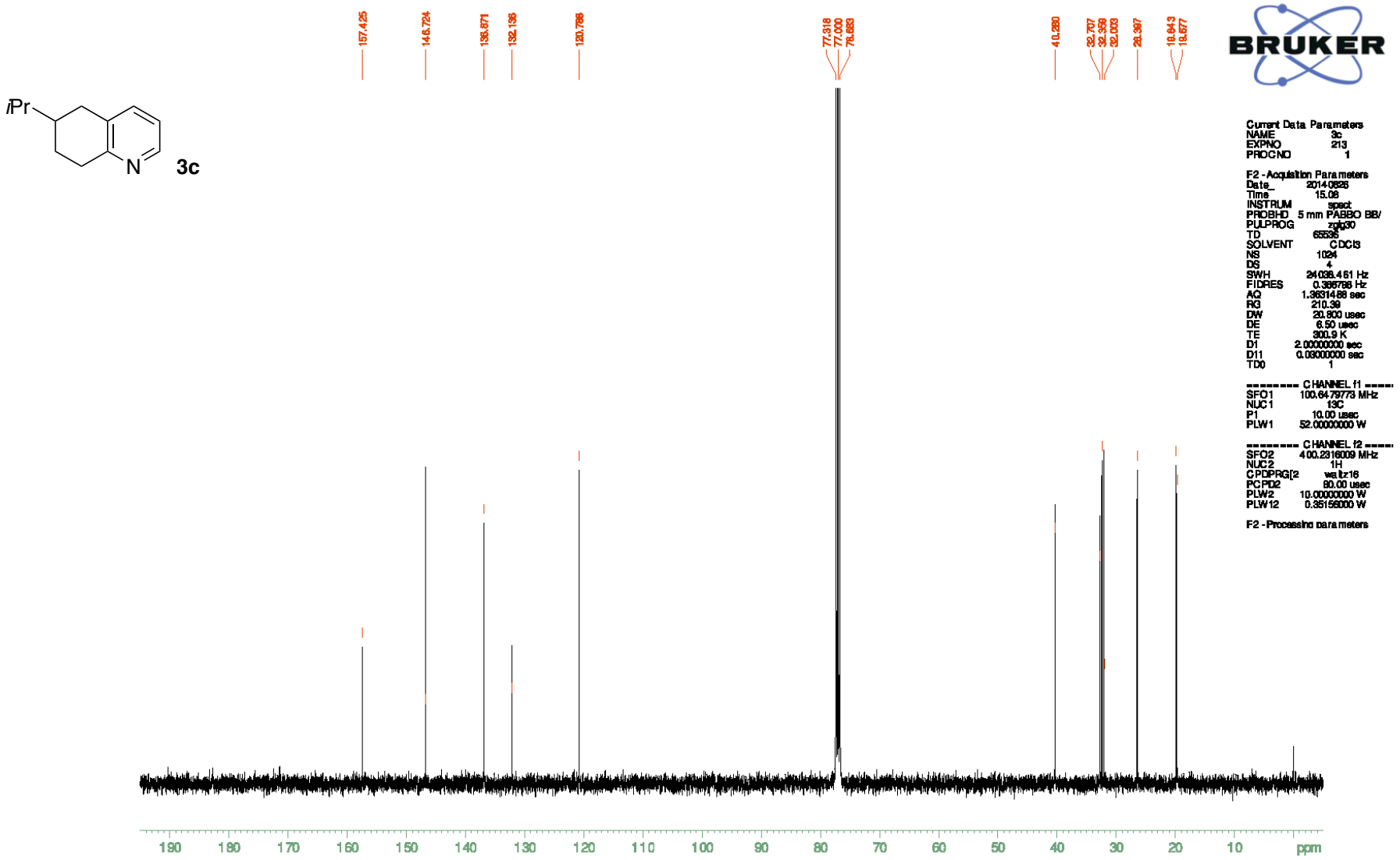


Figure S-16. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3c**.

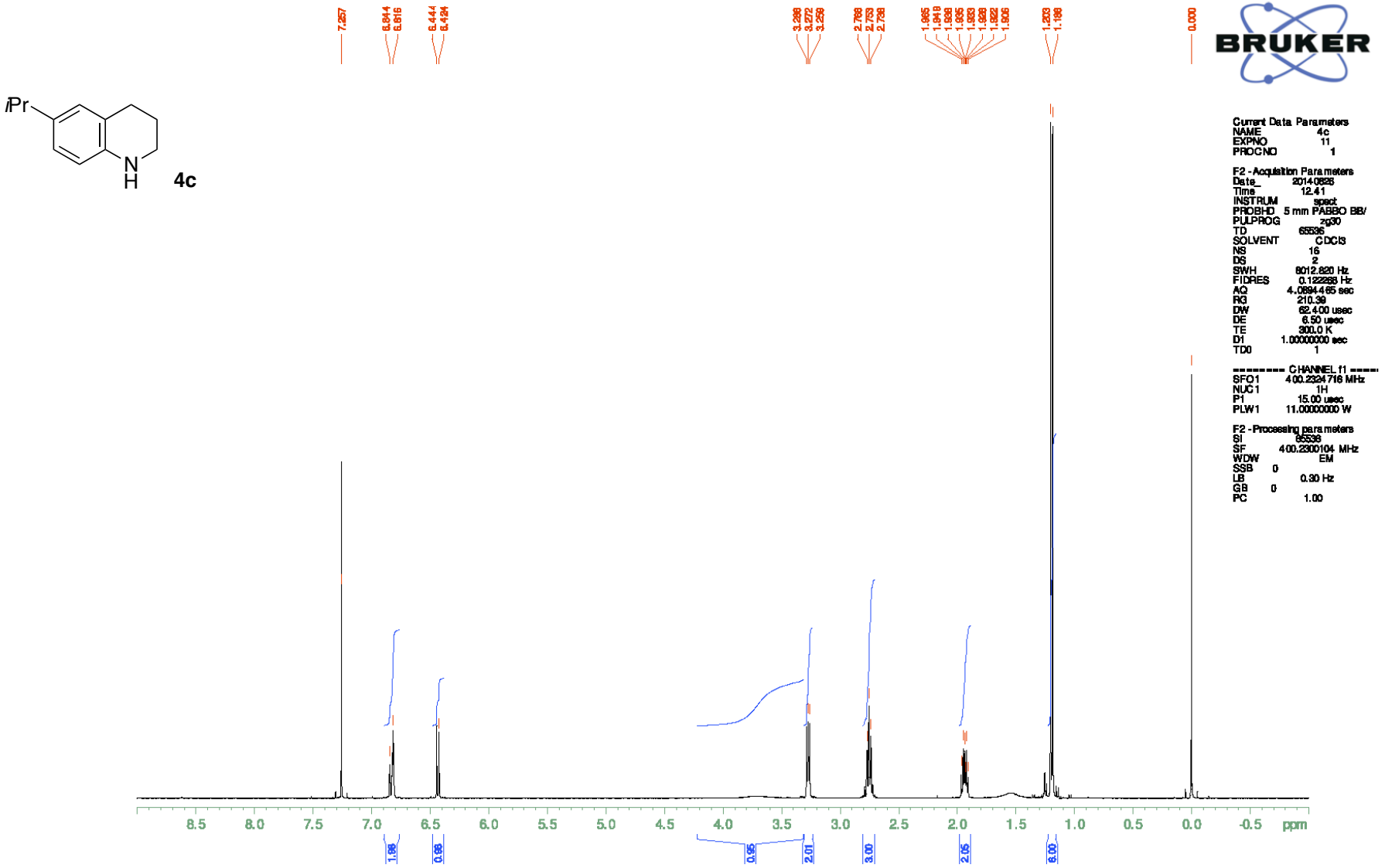


Figure S-17. ^{1}H NMR spectrum ($CDCl_3$) of **4c**.

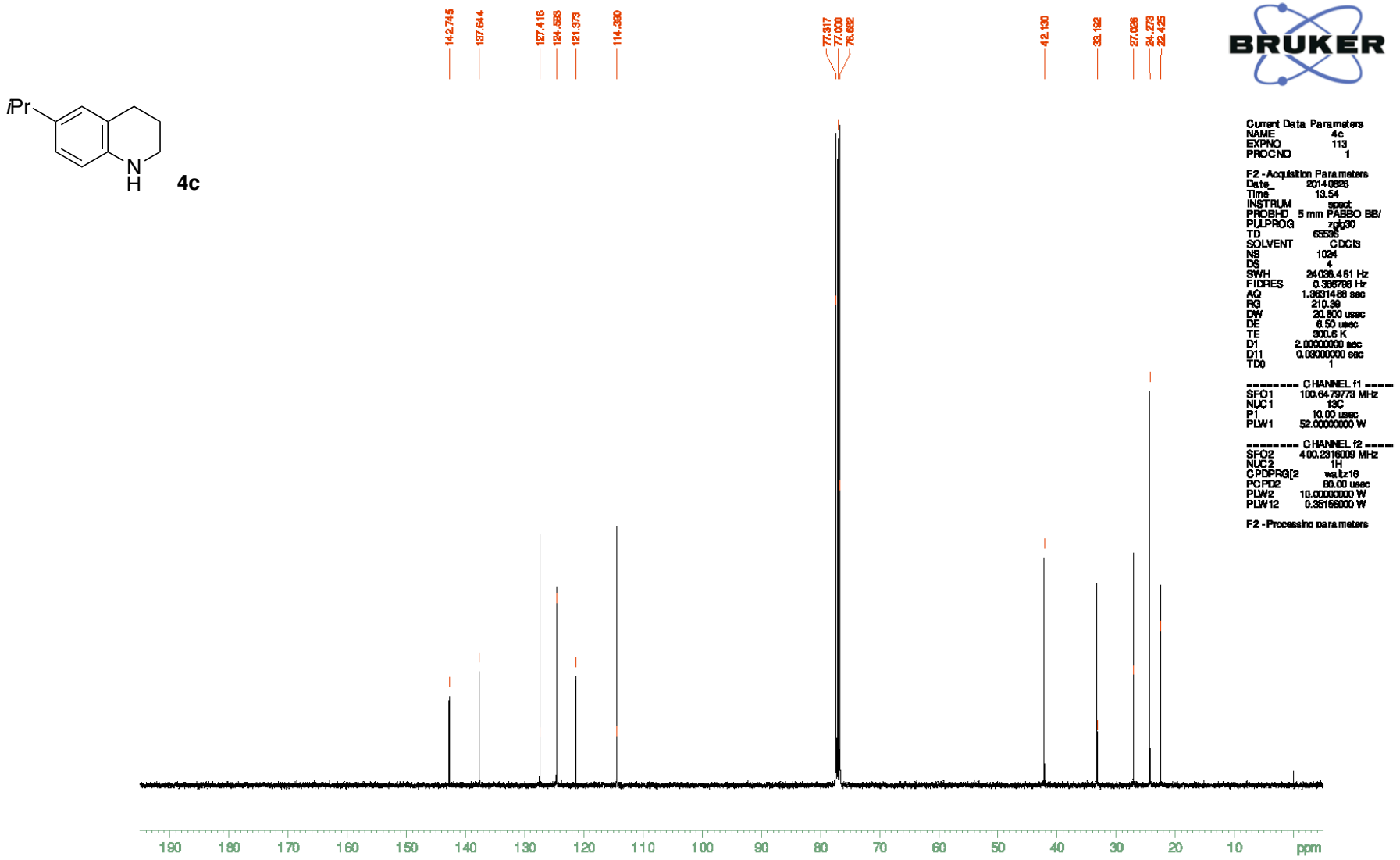


Figure S-18. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **4c**.

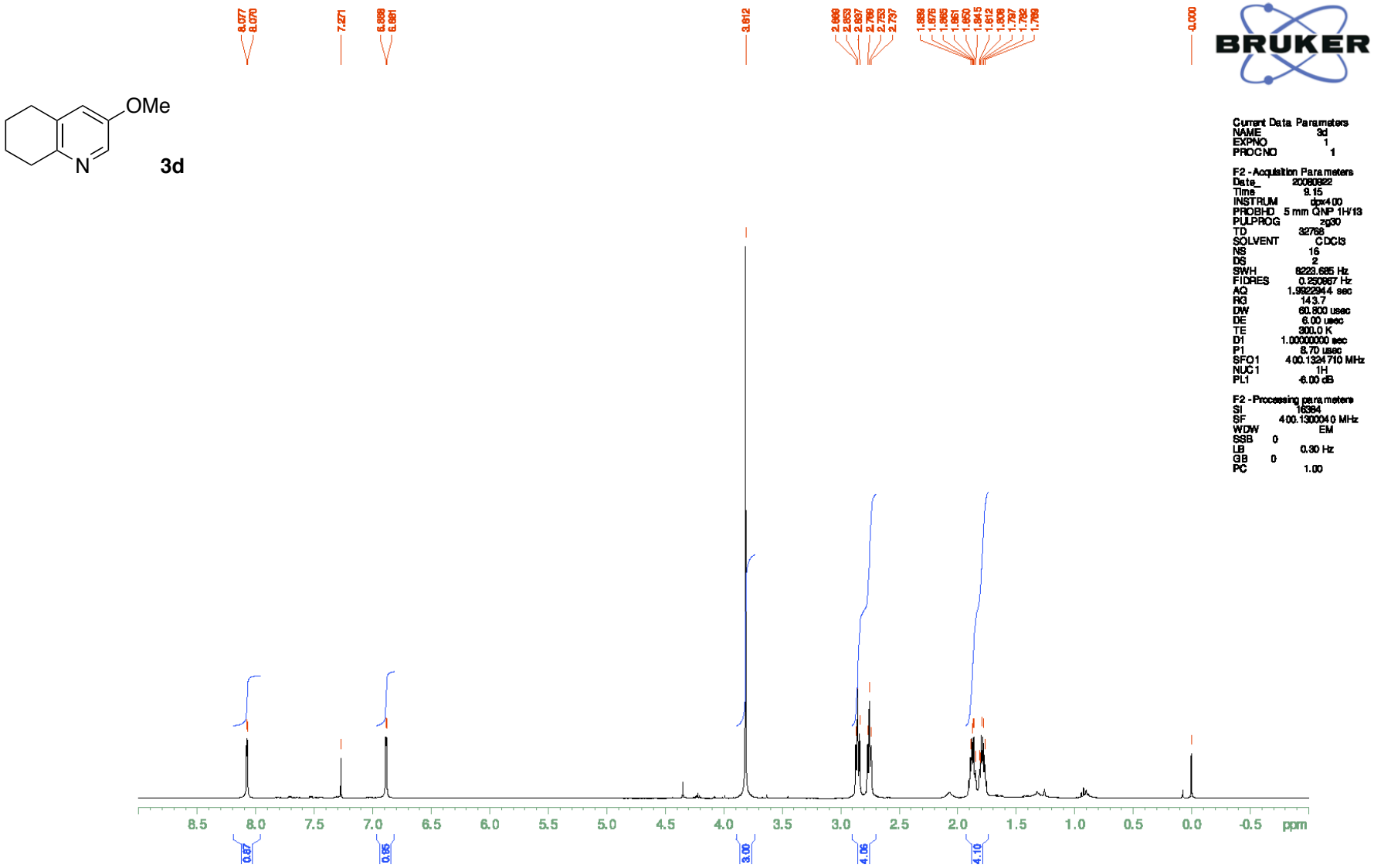


Figure S-19. ^{1}H NMR spectrum ($CDCl_3$) of **3d**.

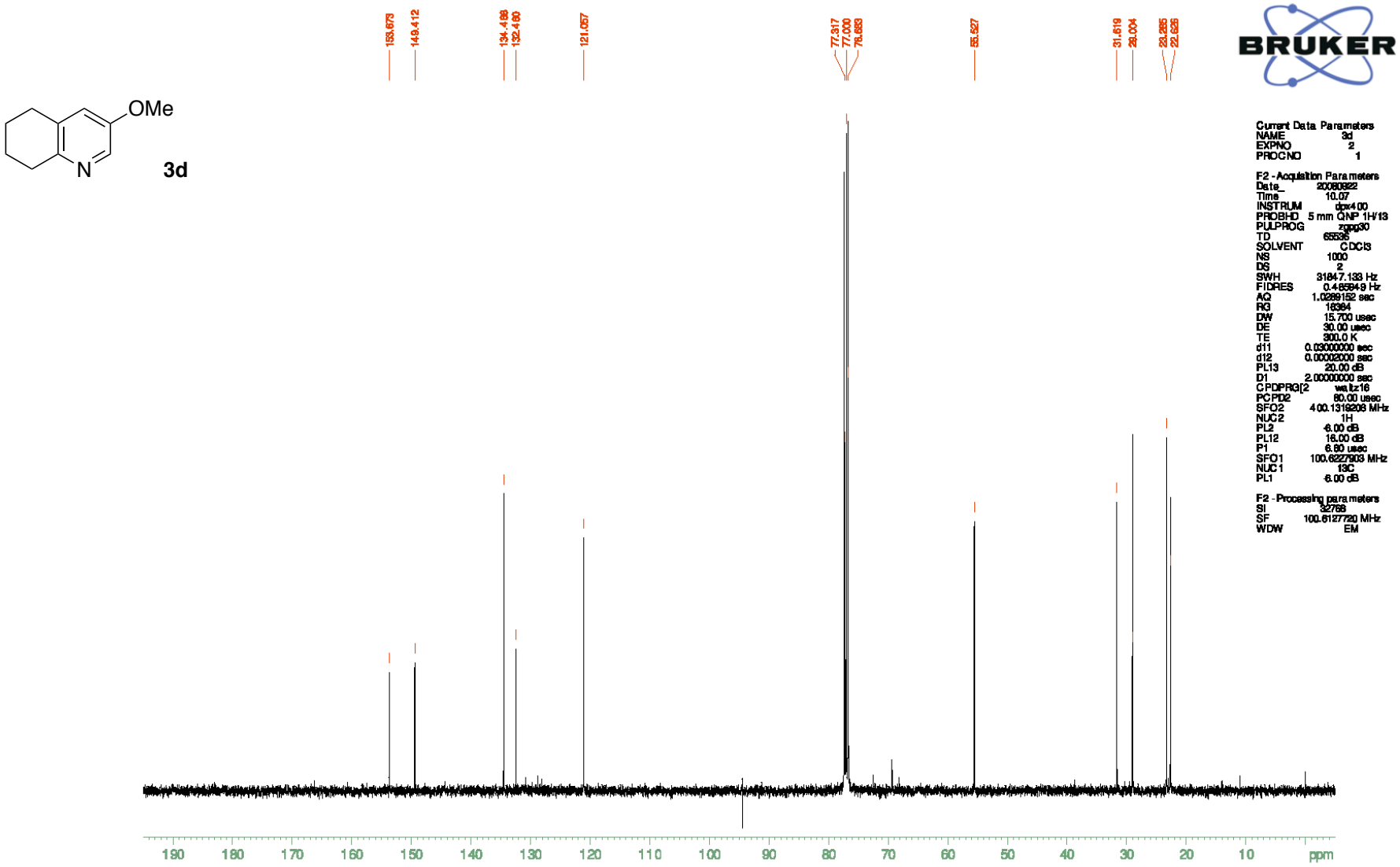


Figure S-20. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3d**.

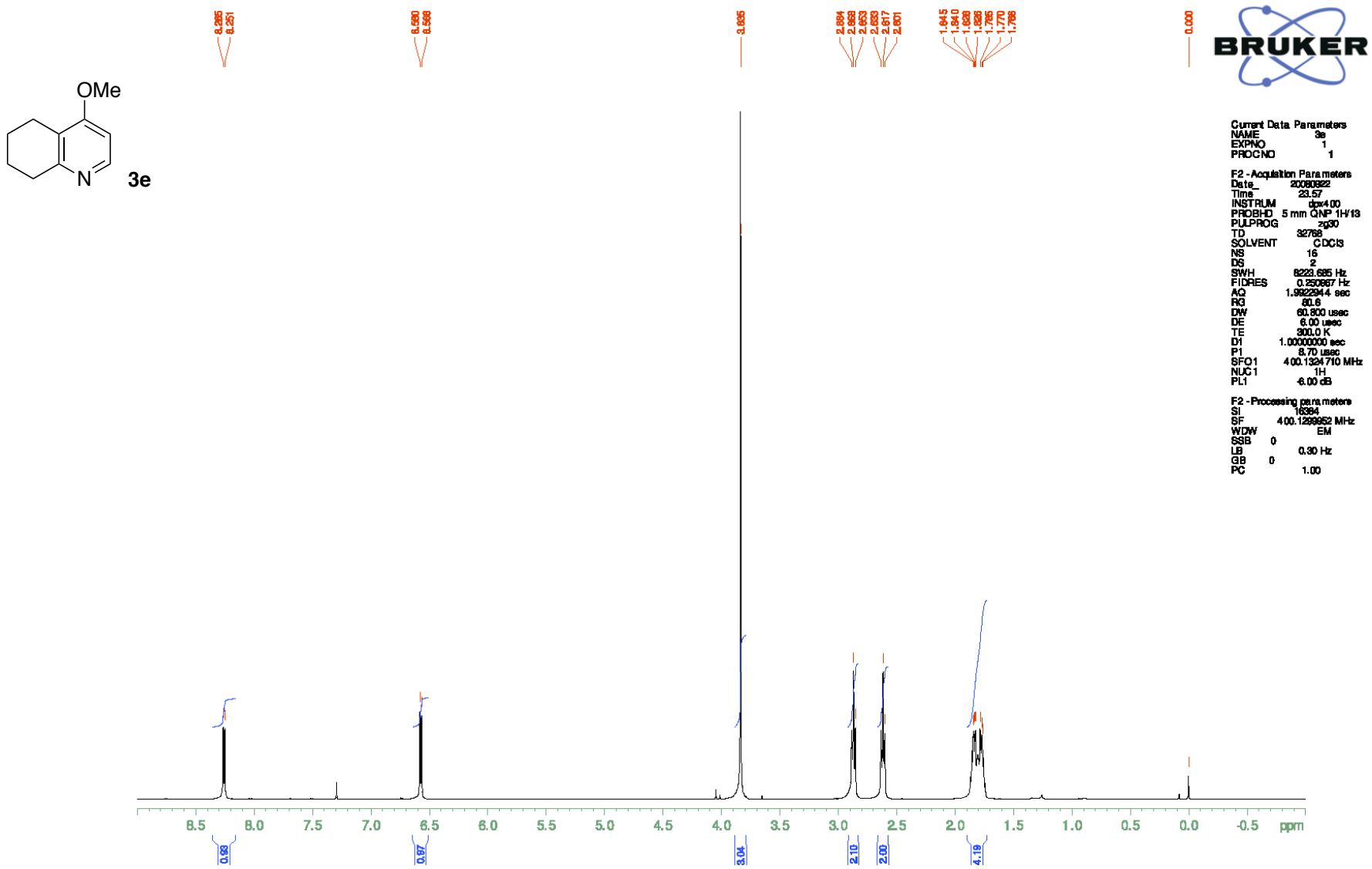


Figure S-21. ^{1}H NMR spectrum ($CDCl_3$) of **3e**.

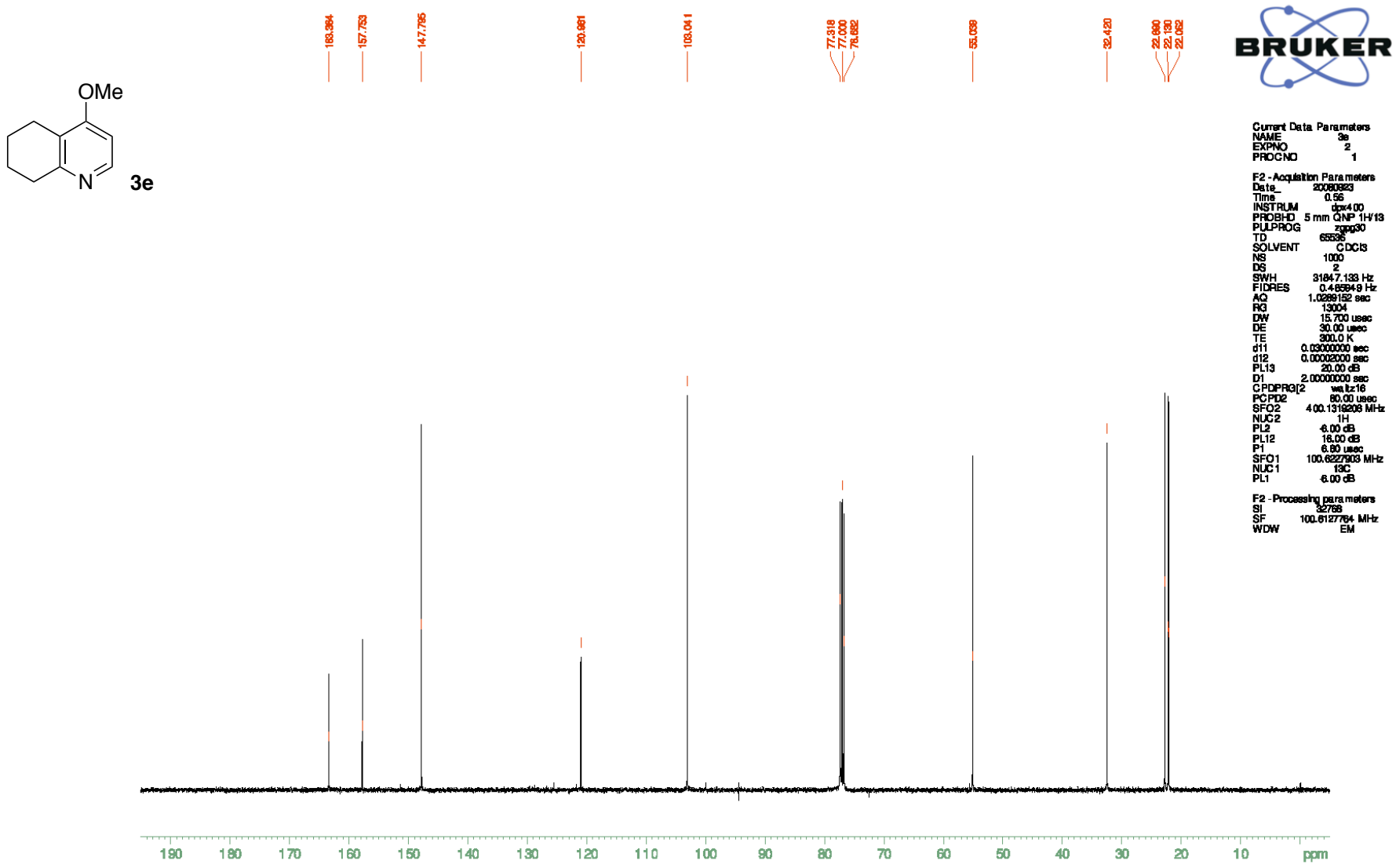


Figure S-22. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3e**.

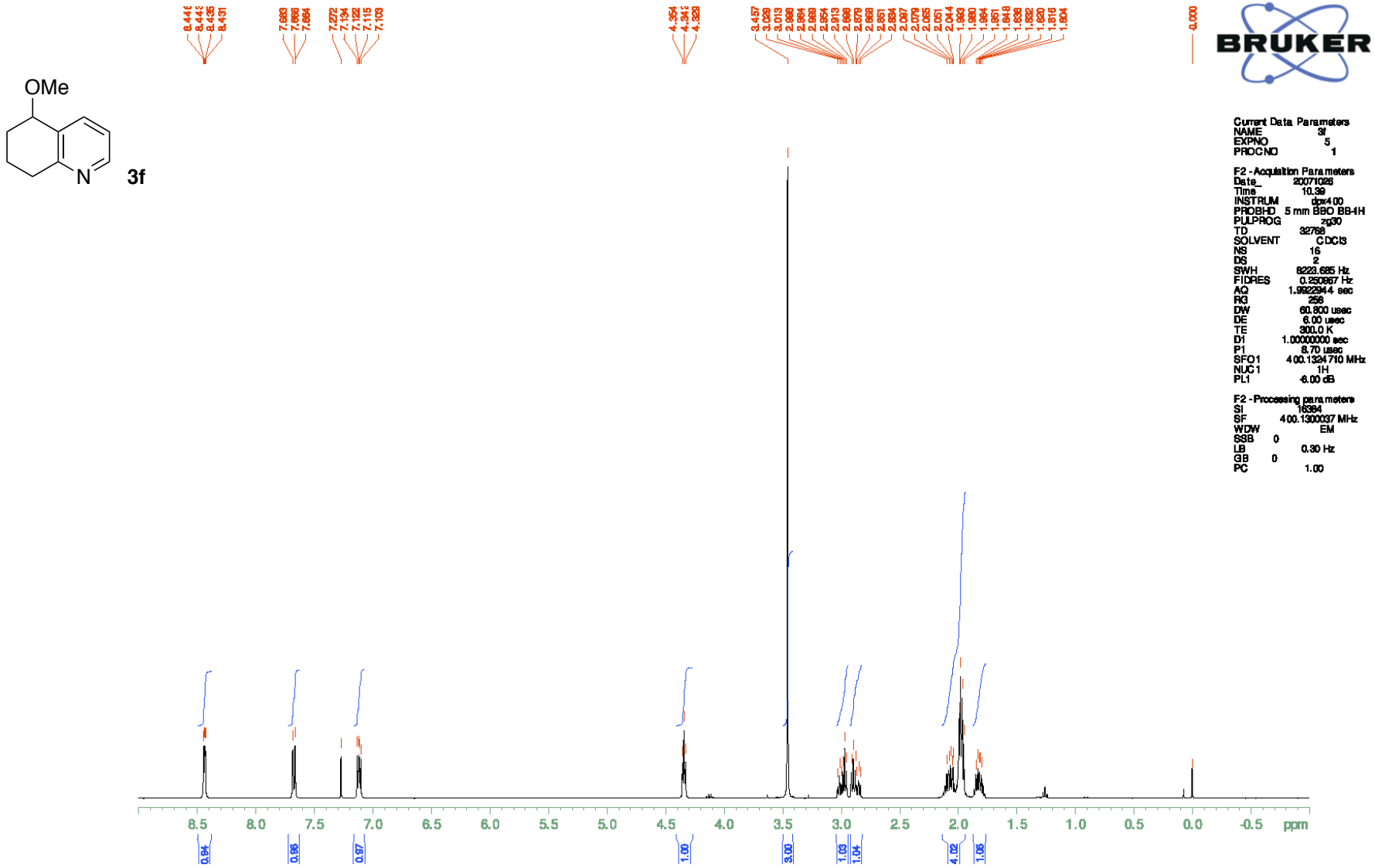


Figure S-23. ^{1}H NMR spectrum ($CDCl_3$) of **3f**.

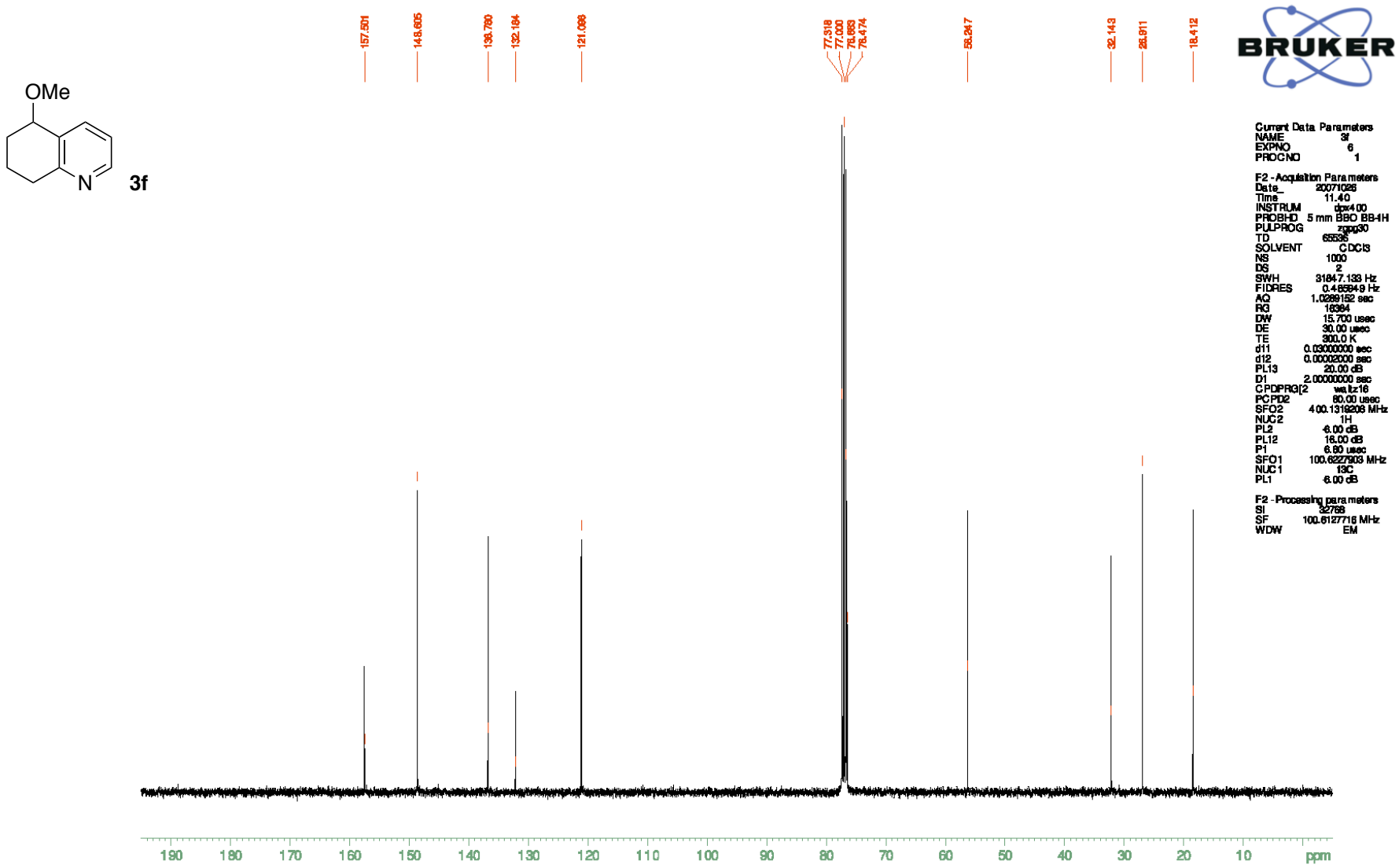


Figure S-24. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3f**.

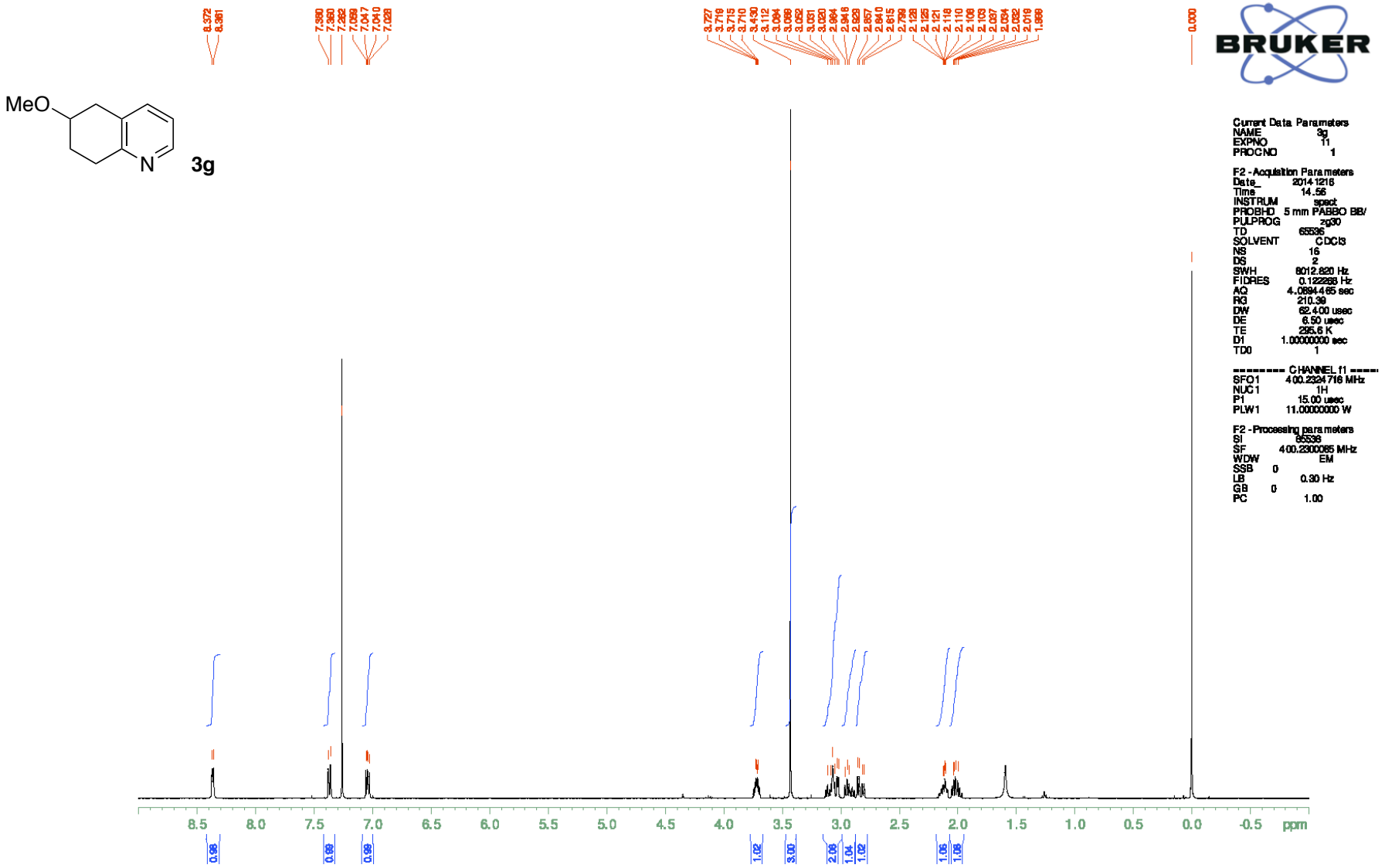


Figure S-25. ^{1}H NMR spectrum ($CDCl_3$) of **3g**.

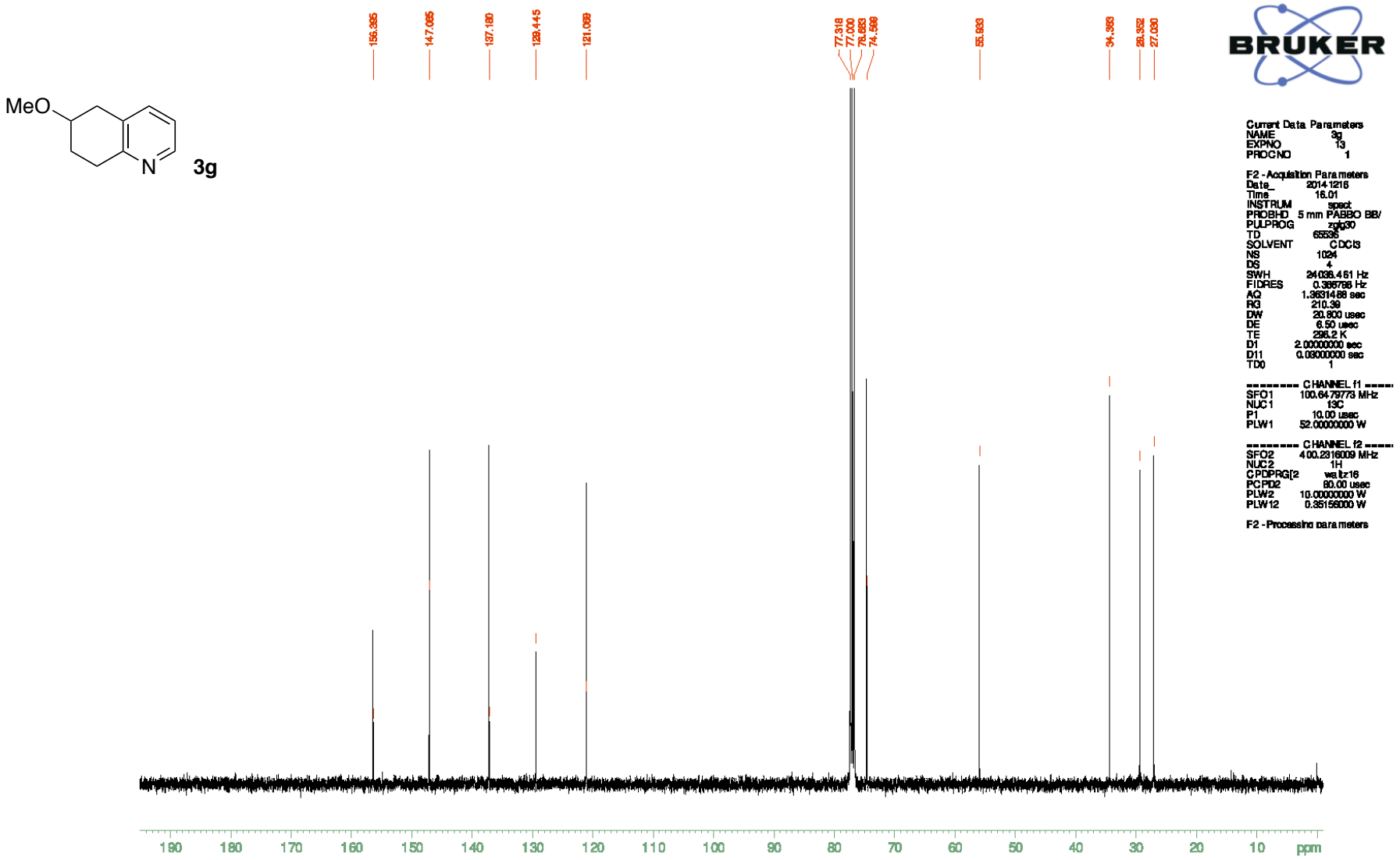


Figure S-26. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3g**.

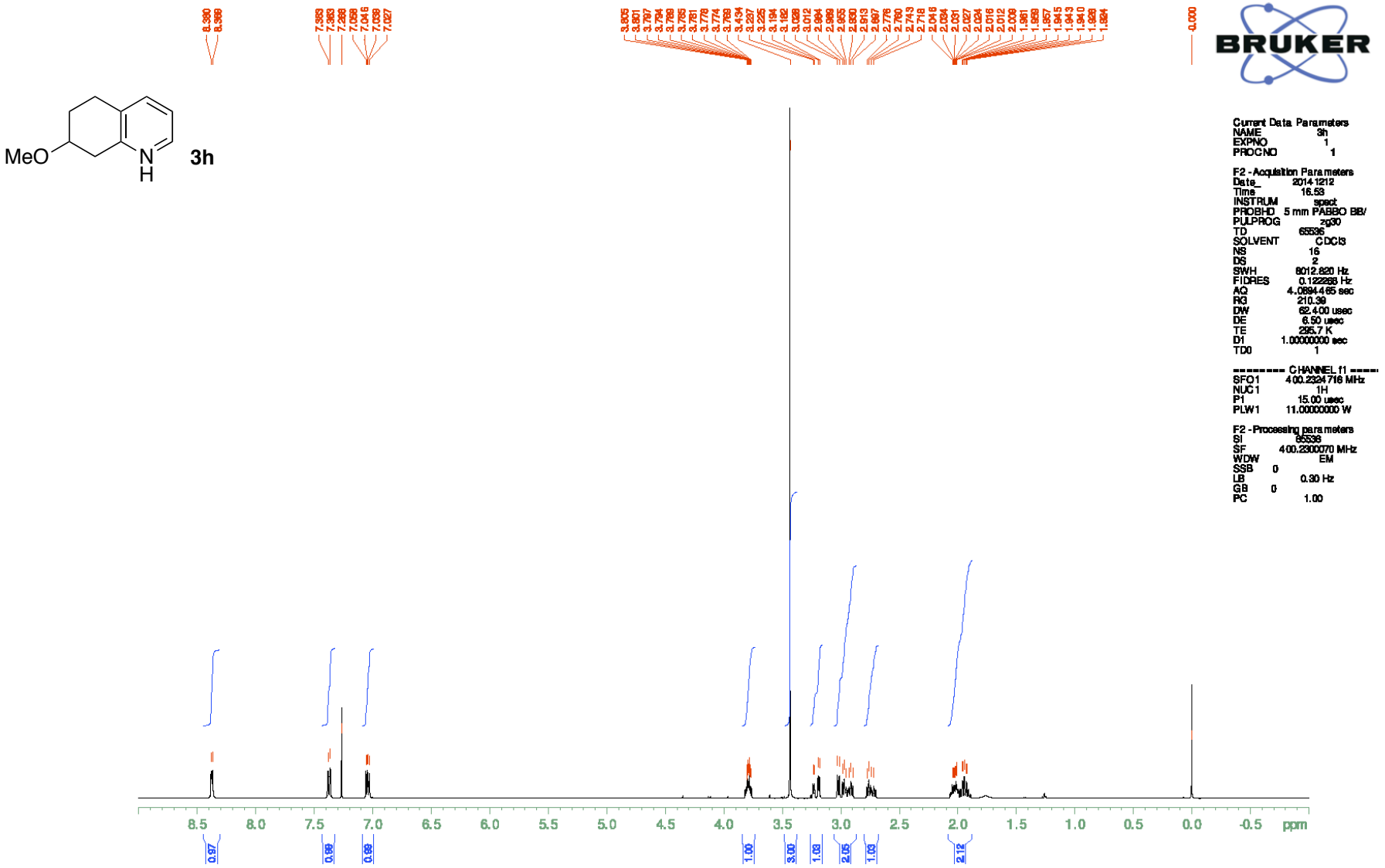


Figure S-27. ^{1}H NMR spectrum ($CDCl_3$) of **3h**.

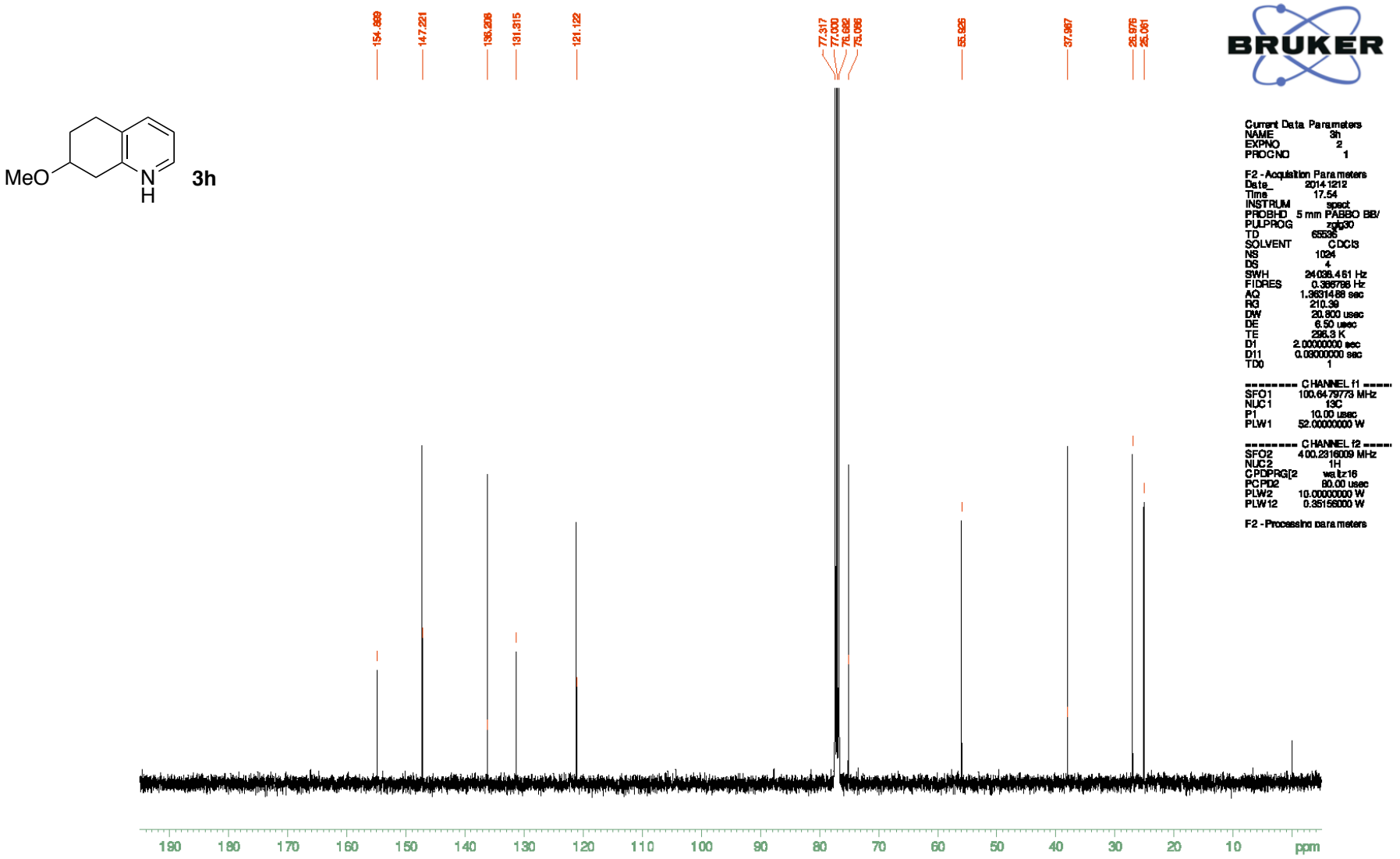


Figure S-28. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3h**.

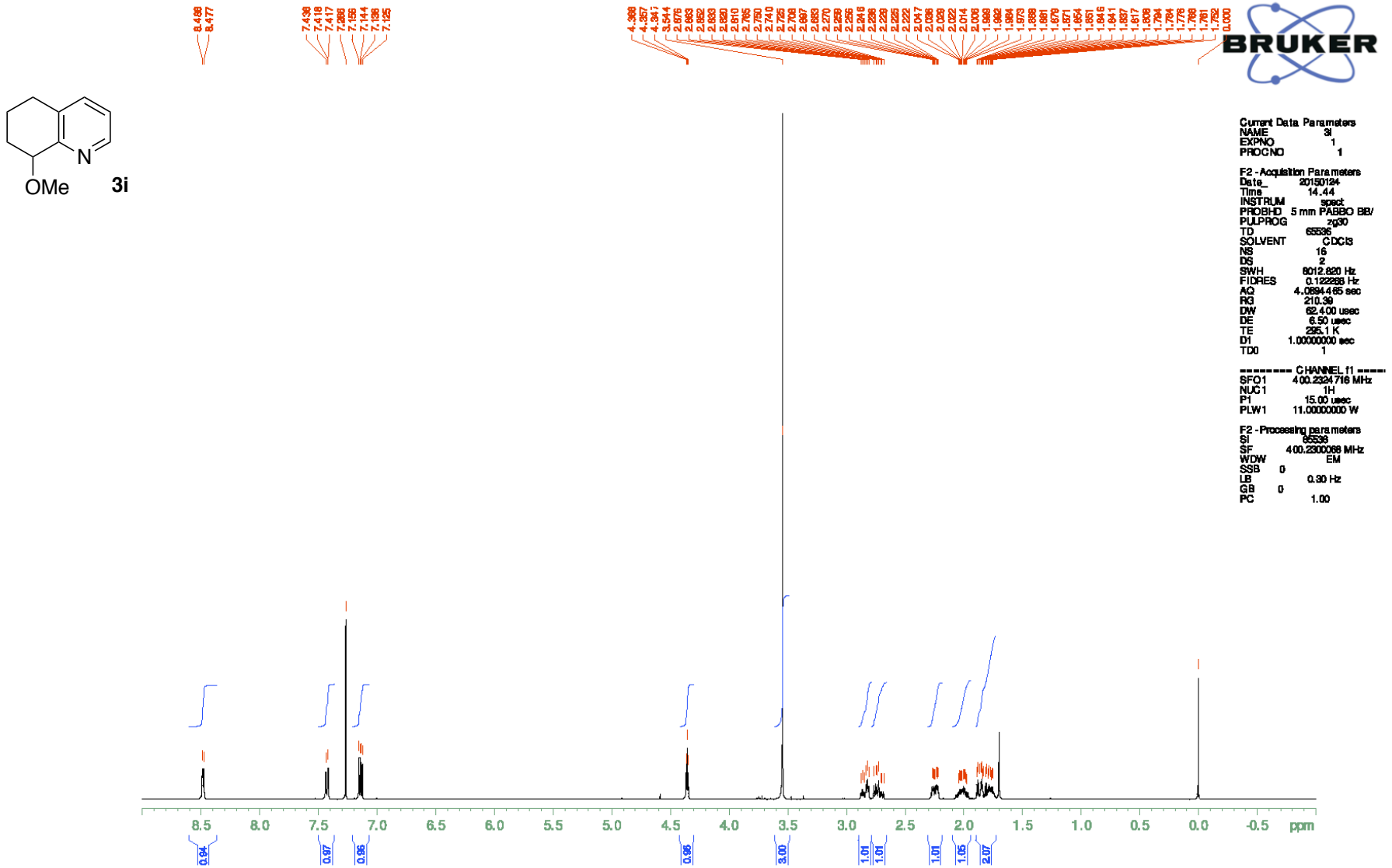


Figure S-29. ^{1}H NMR spectrum ($CDCl_3$) of **3i**.

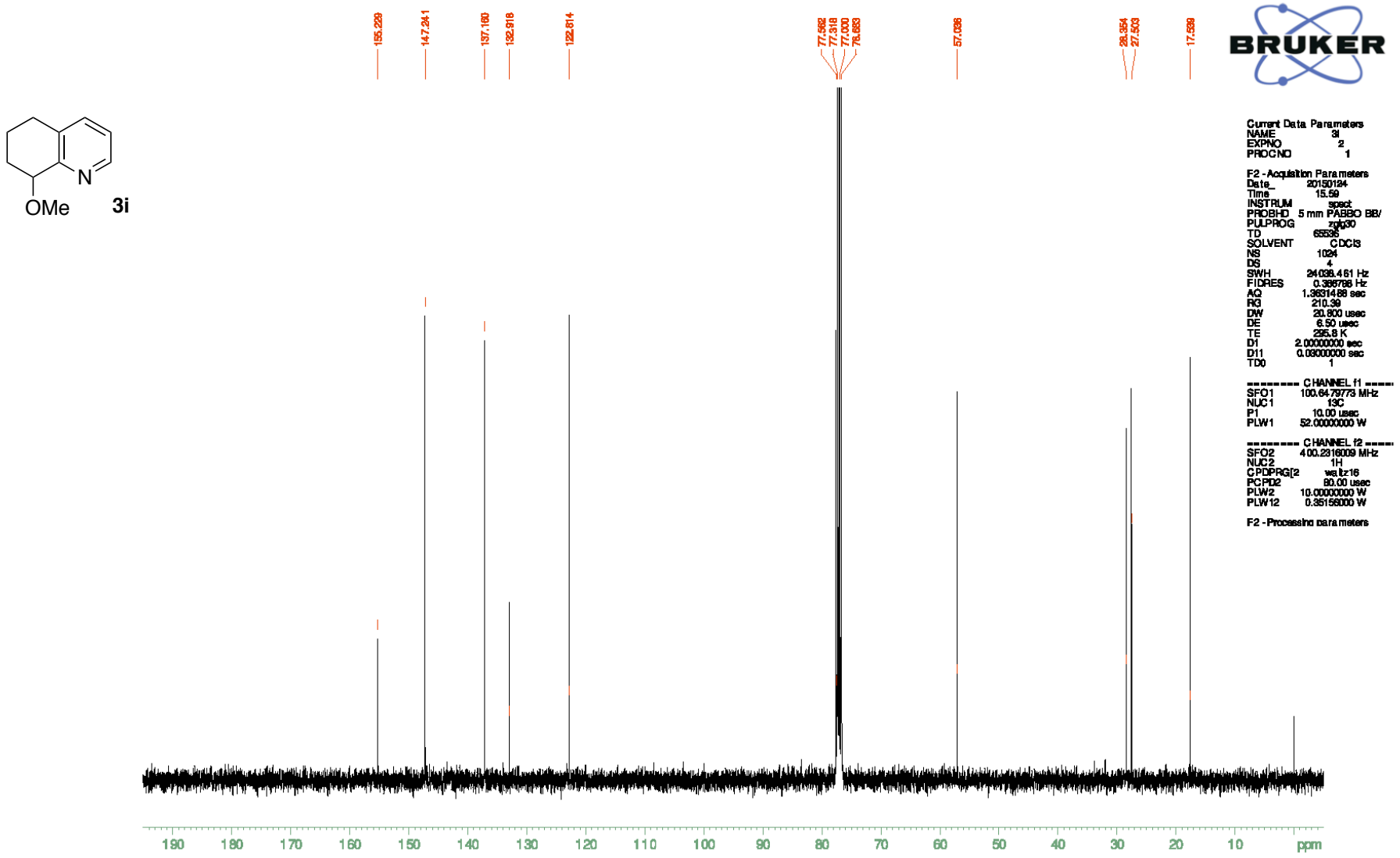
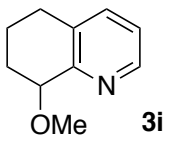
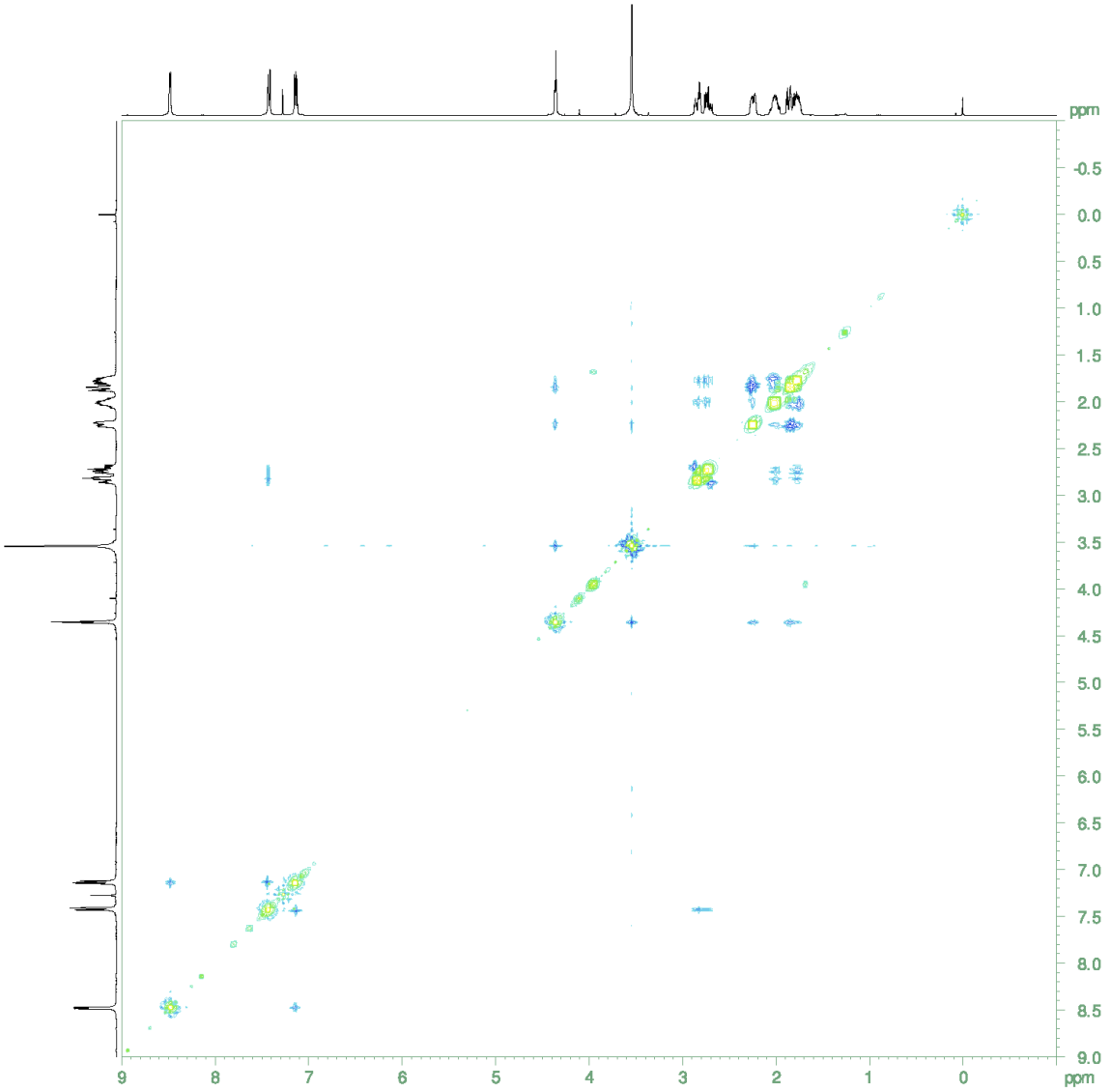


Figure S-30. ^{13}C {^{1}H} NMR spectrum ($CDCl_3$) of **3i**.



3i



Current Data Parameters
NAME 3i_NOESY
EXPNO 512
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140711
Time 21.04
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG noesygpphpp
TD 2048
SOLVENT CDCl3
NS 64
DS 32
SWH 3969.969 Hz
FIDRES 1.889633 Hz
AQ 0.2646016 sec
RG 210.39
DW 129.200 usec
DE 6.50 usec
TE 298.8 K
D0 0.00011010 sec
D1 2.00000000 sec
D8 1.00000000 sec
D11 0.03000000 sec
D12 0.00002000 sec
D16 0.00010000 sec
IN0 0.00025840 sec

======== CHANNEL f1 ========
SFO1 400.2317194 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
P17 2500.00 usec
PLW1 11.00000000 W
PLW10 3.66120005 W

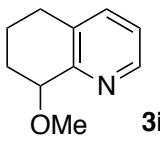
====== GRADIENT CHANNEL ===
GPNAM[1] SMSQ10.100
GPZ1 40.00 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 256
SFO1 400.2317 MHz
FIDRES 15.117068 Hz
SW 9.569 ppm
FnMODE States-TPPI

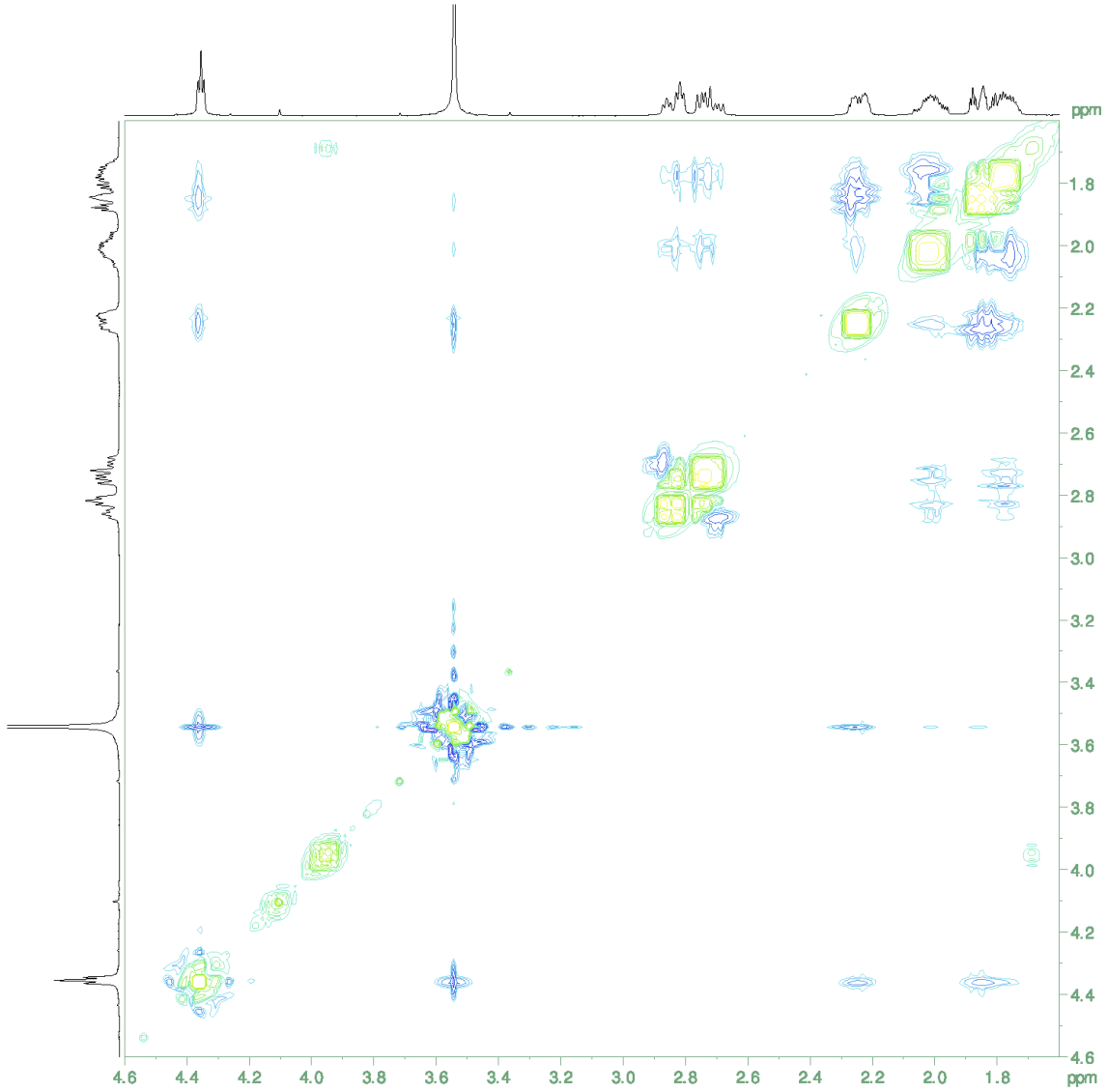
F2 - Processing parameters
SI 1024
SF 400.2300072 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
MC2 States-TPPI
SF 400.2300075 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0

Figure S-31. NOESY spectrum ($CDCl_3$) of **3i**.



3i



BRUKER

Current Data Parameters
NAME 3i_NOESY
EXPNO 512
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140711
Time 21.04
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG noesygpphpp
TD 2048
SOLVENT CDCl3
NS 64
DS 32
SWH 3969.969 Hz
FIDRES 1.889633 Hz
AQ 0.2646016 sec
RG 210.39
DW 129.200 usec
DE 6.50 usec
TE 298.8 K
D0 0.00011010 sec
D1 2.00000000 sec
D8 1.00000000 sec
D11 0.03000000 sec
D12 0.00002000 sec
D16 0.00010000 sec
IN0 0.00025840 sec

======== CHANNEL f1 ========
SFO1 400.2317194 MHz
NUC1 1H
P1 15.00 usec
P2 30.00 usec
P17 2500.00 usec
PLW1 11.00000000 W
PLW10 3.66120005 W

====== GRADIENT CHANNEL ===
GPNAM[1] SMSQ10.100
GPZ1 40.00 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 256
SFO1 400.2317 MHz
FIDRES 15.117066 Hz
SW 9.569 ppm
FnMODE States-TPPI

F2 - Processing parameters
SI 1024
SF 400.2300072 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
MC2 States-TPPI
SF 400.2300075 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0

Figure S-32. NOESY spectrum ($CDCl_3$) of **3i** (δ 1.6–4.6 ppm).

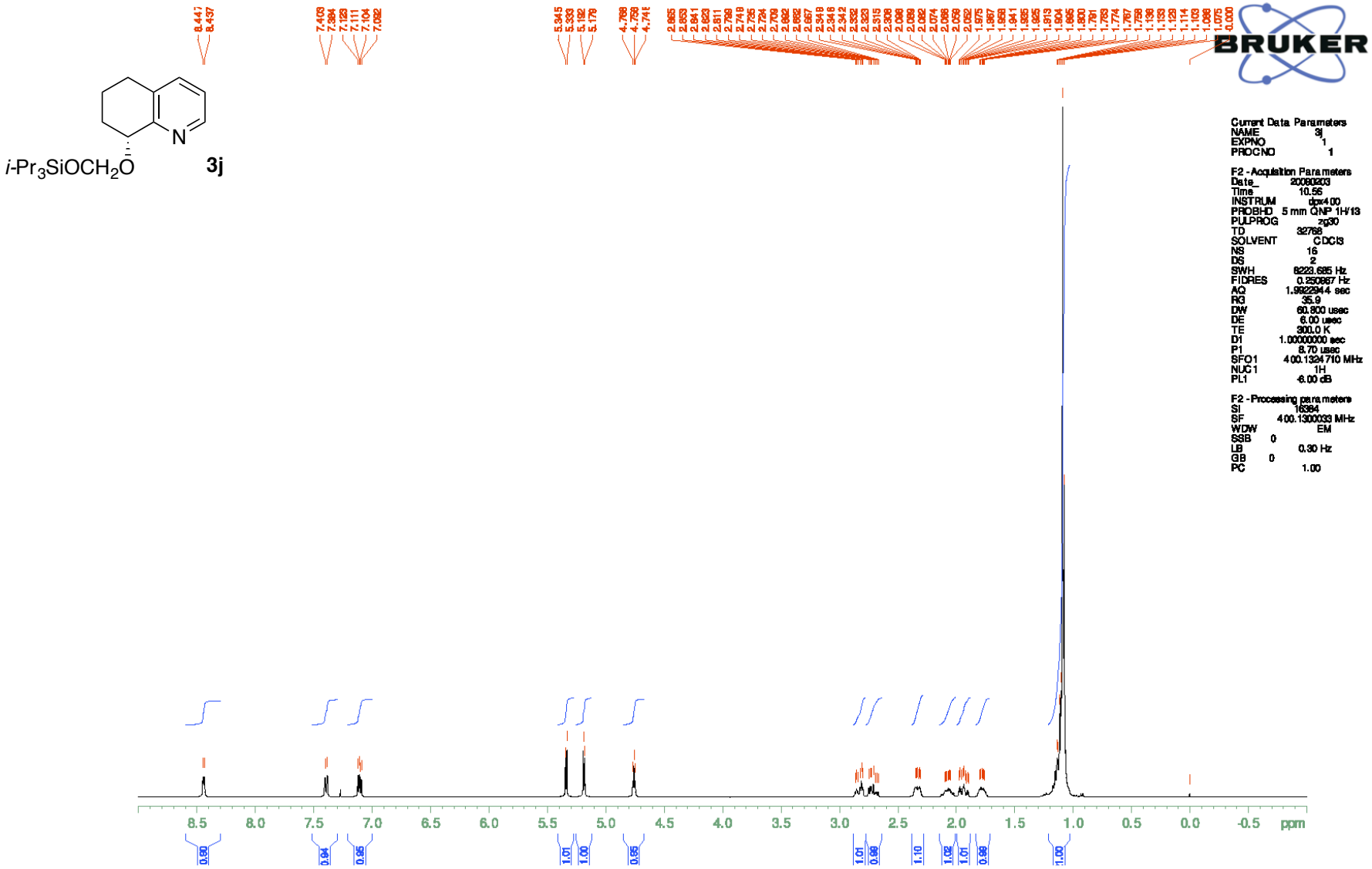


Figure S-33. ^{1}H NMR spectrum ($CDCl_3$) of **3j**.

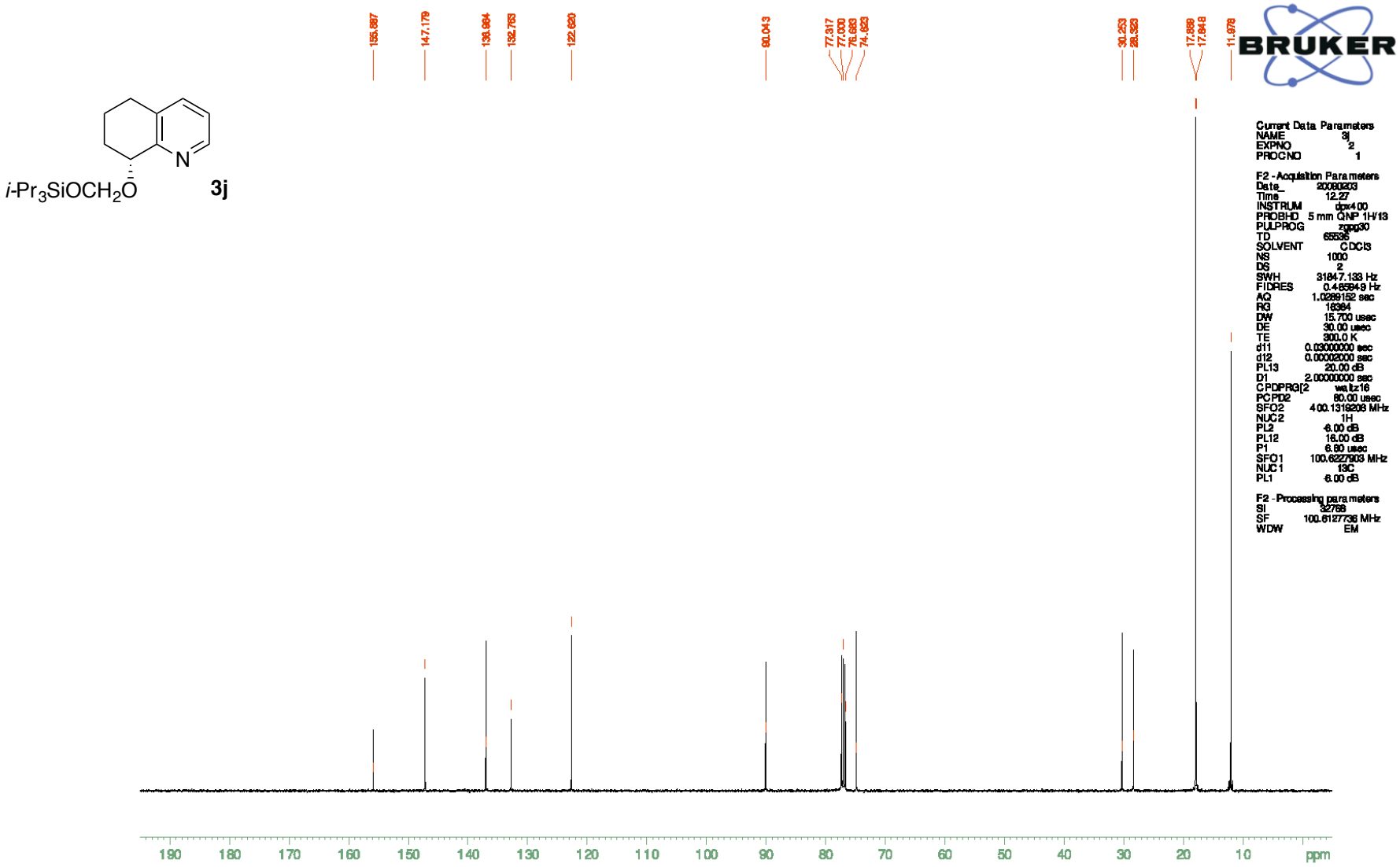


Figure S-34. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3j**.

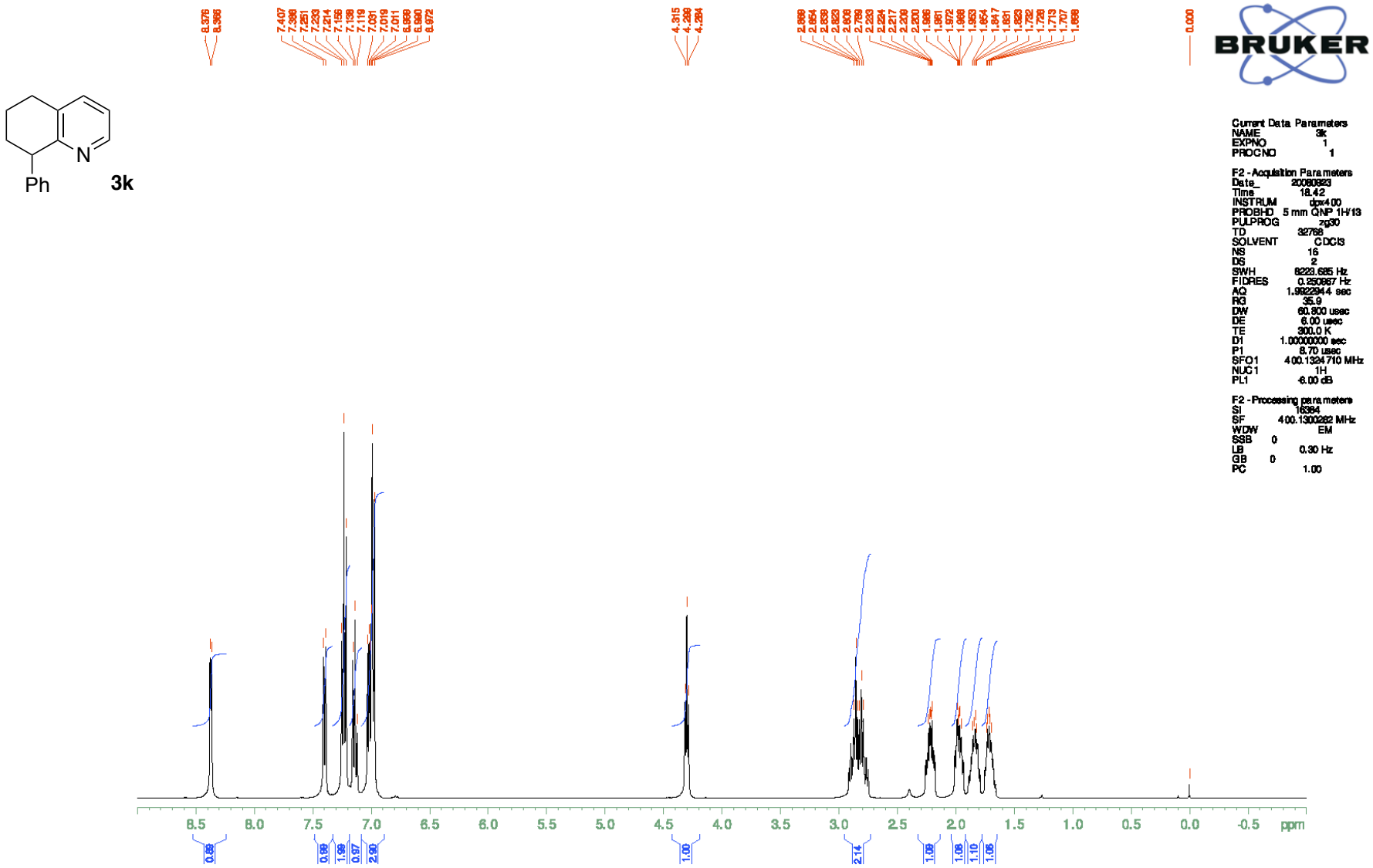


Figure S-35. ^{1}H NMR spectrum ($CDCl_3$) of **3k**.

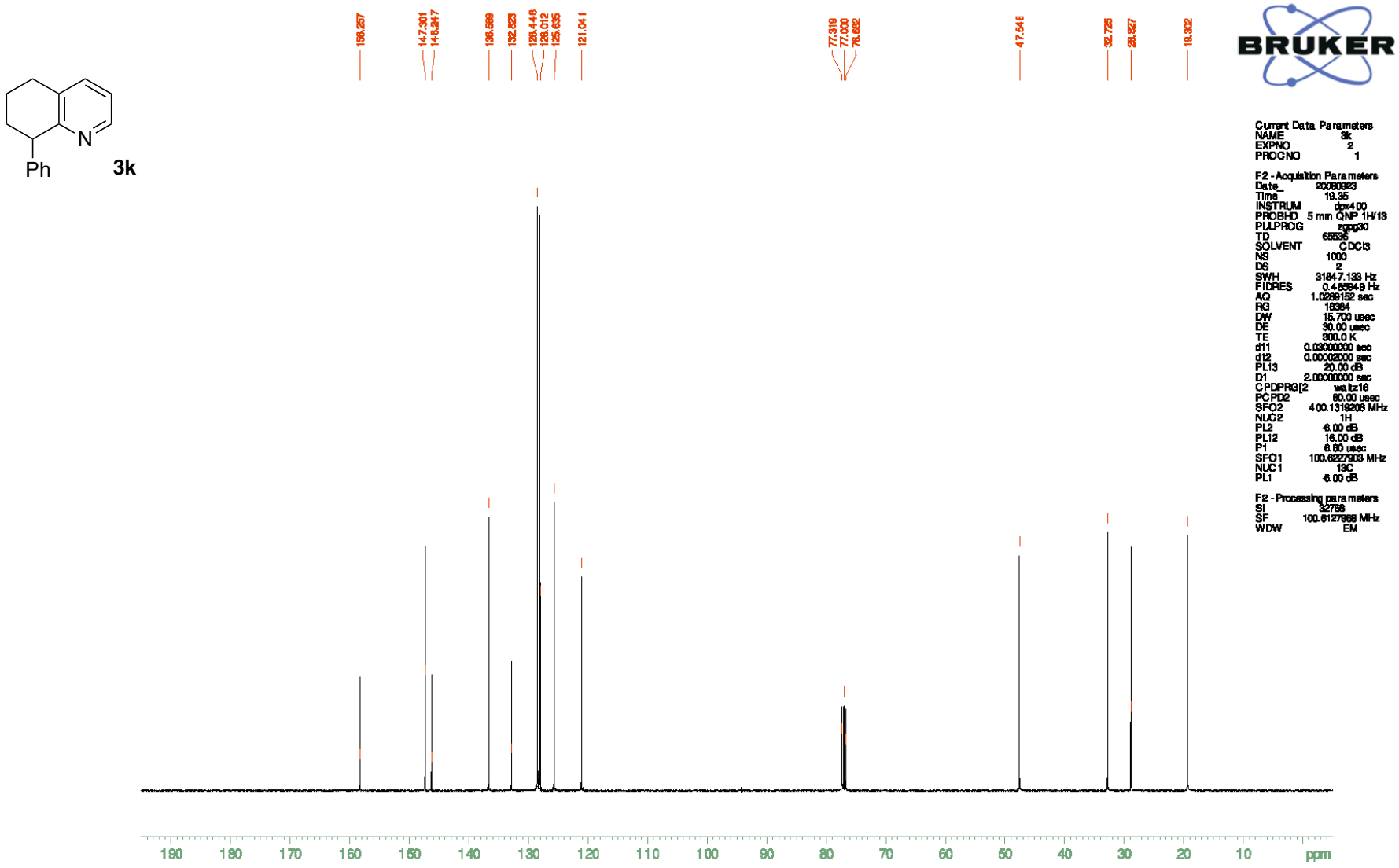


Figure S-36. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3k**.

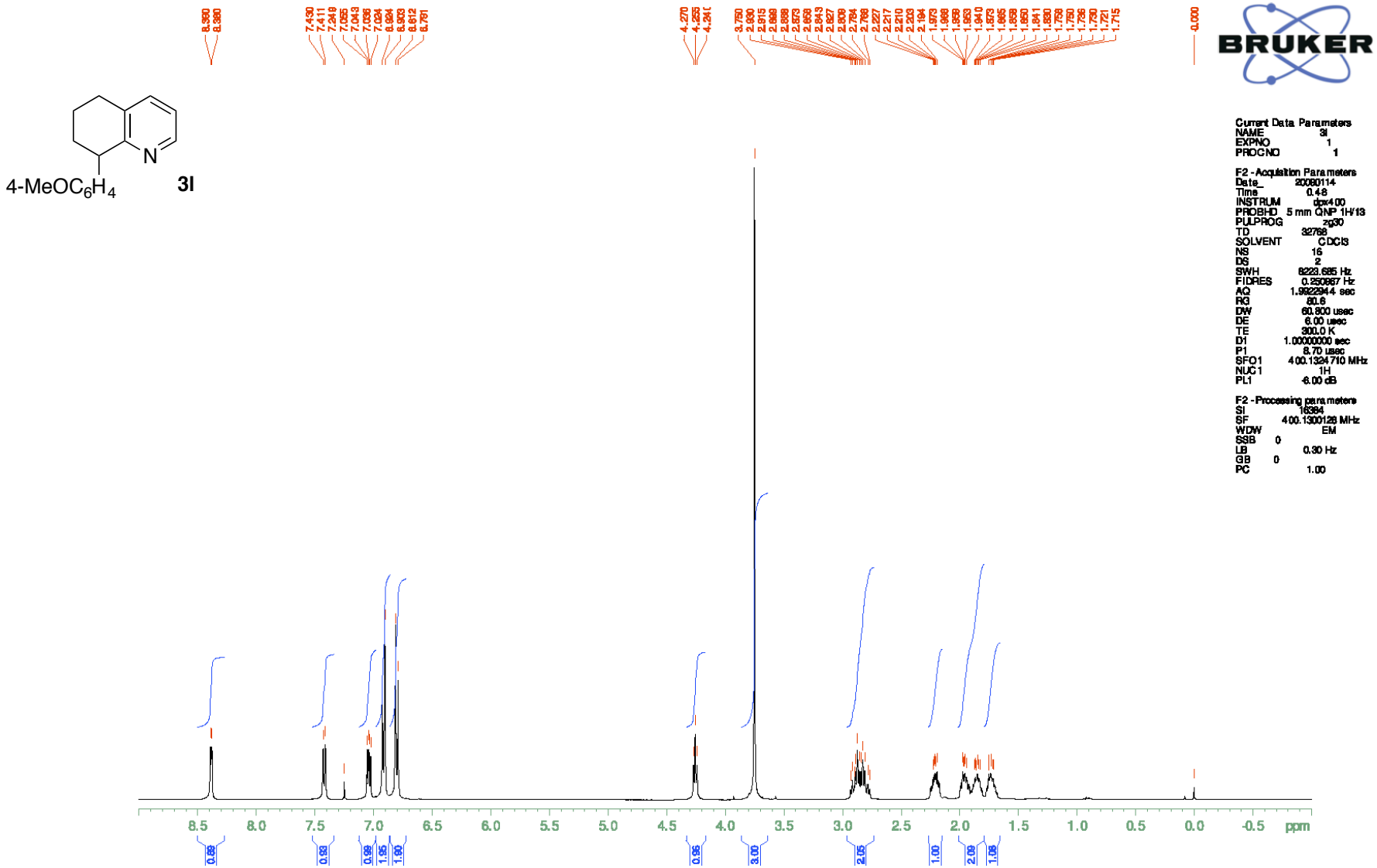


Figure S-37. ^{1}H NMR spectrum ($CDCl_3$) of **3l**.

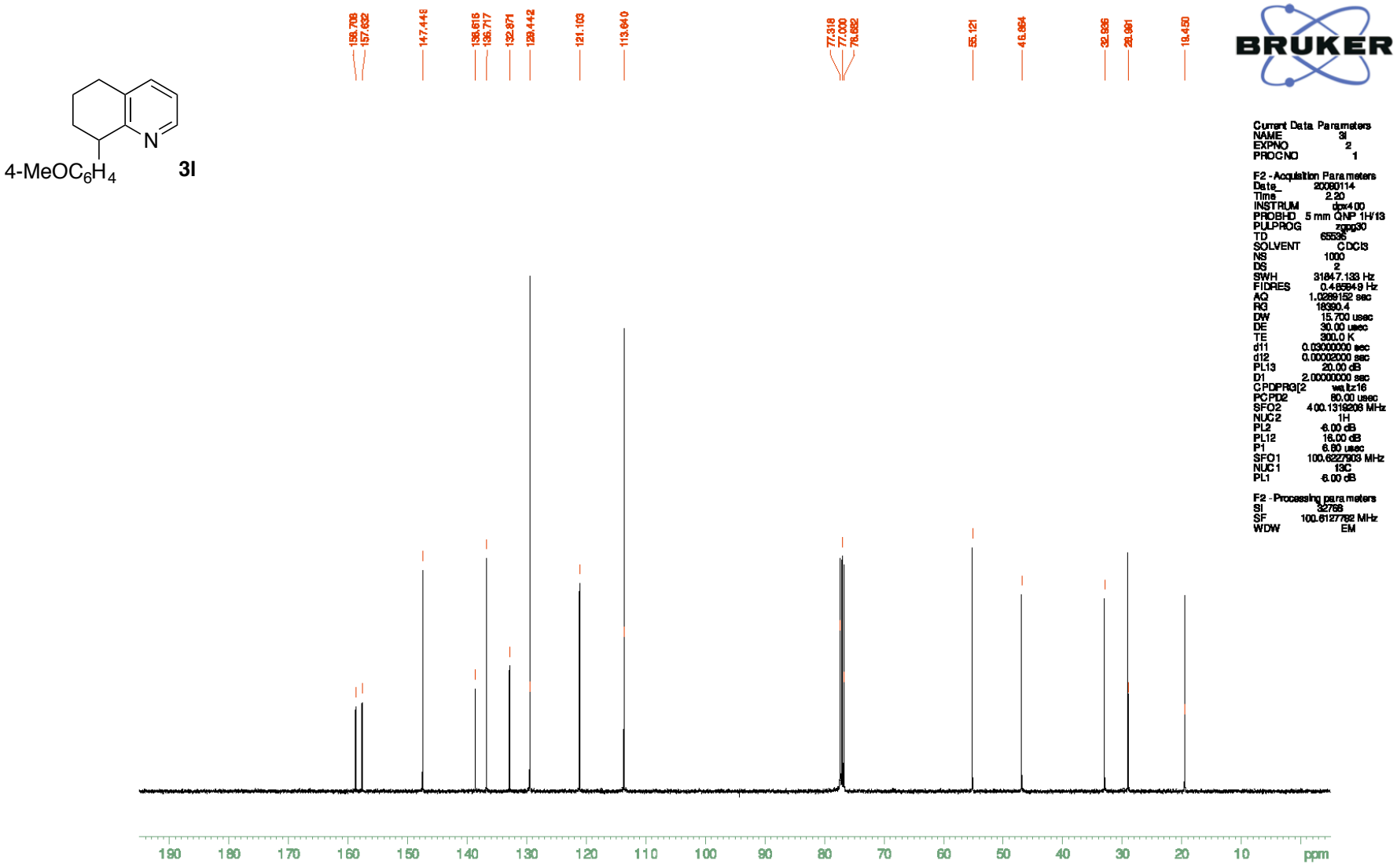


Figure S-38. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3l**.

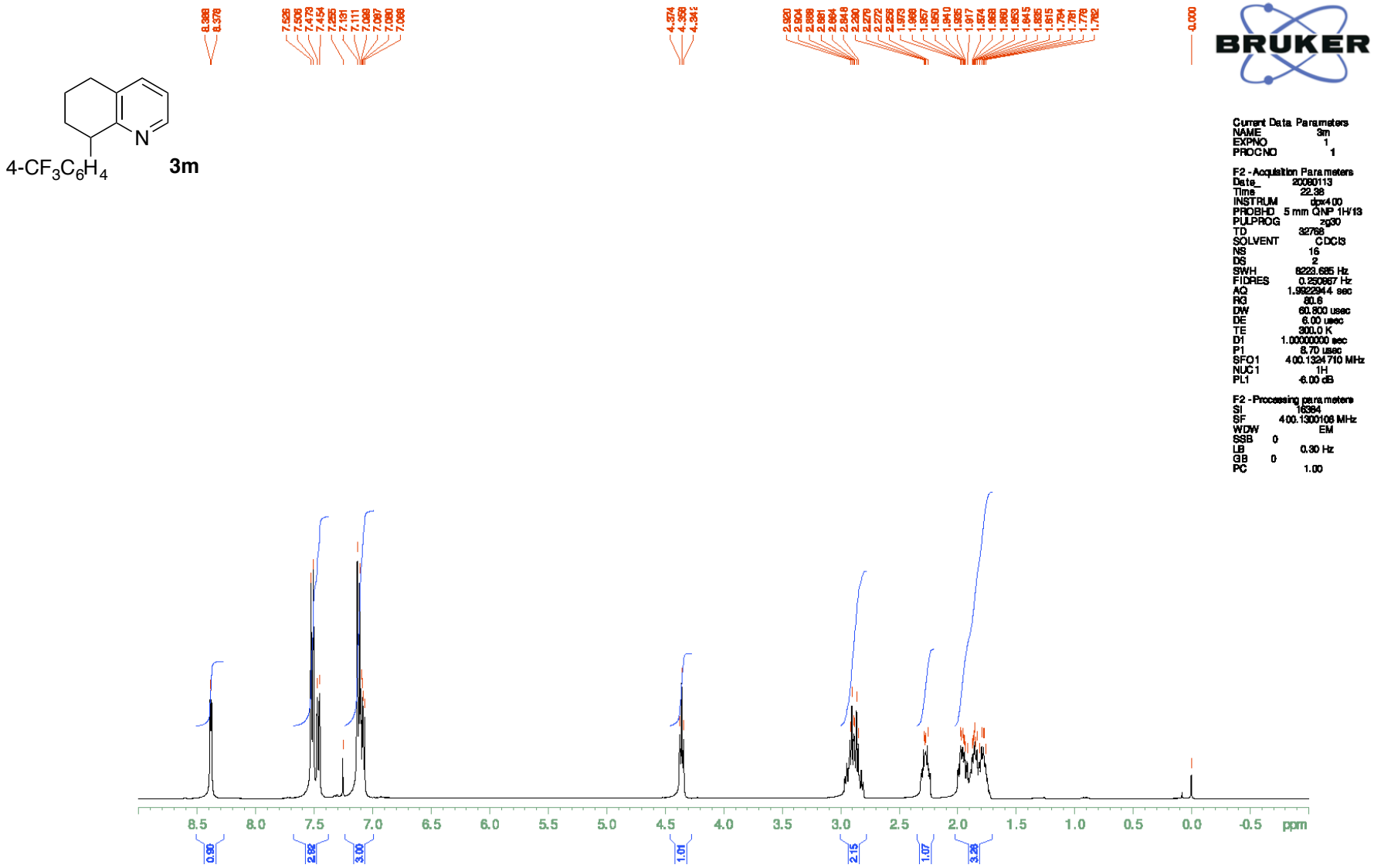


Figure S-39. ^{1}H NMR spectrum ($CDCl_3$) of **3m**.

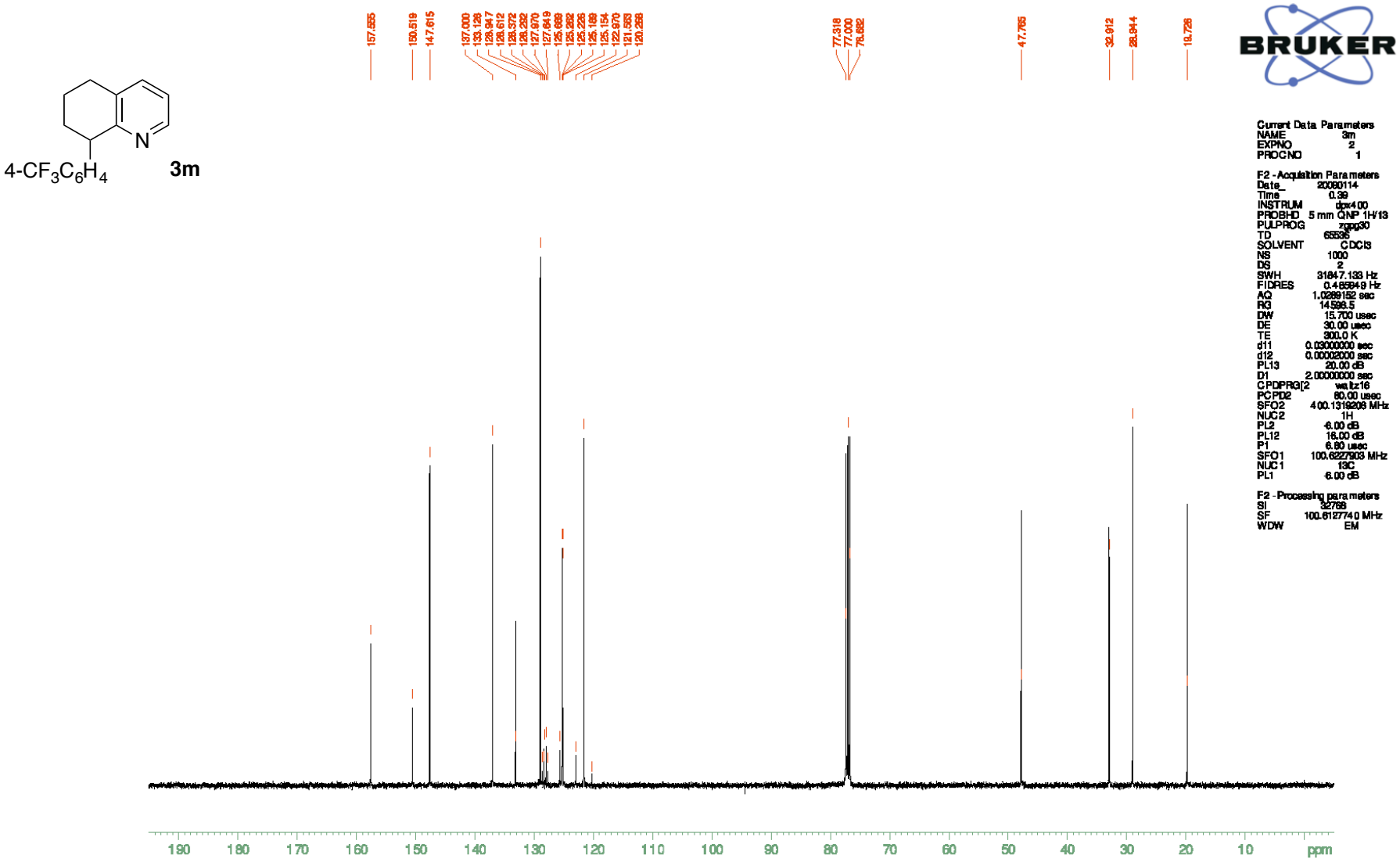


Figure S-40. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3m**.

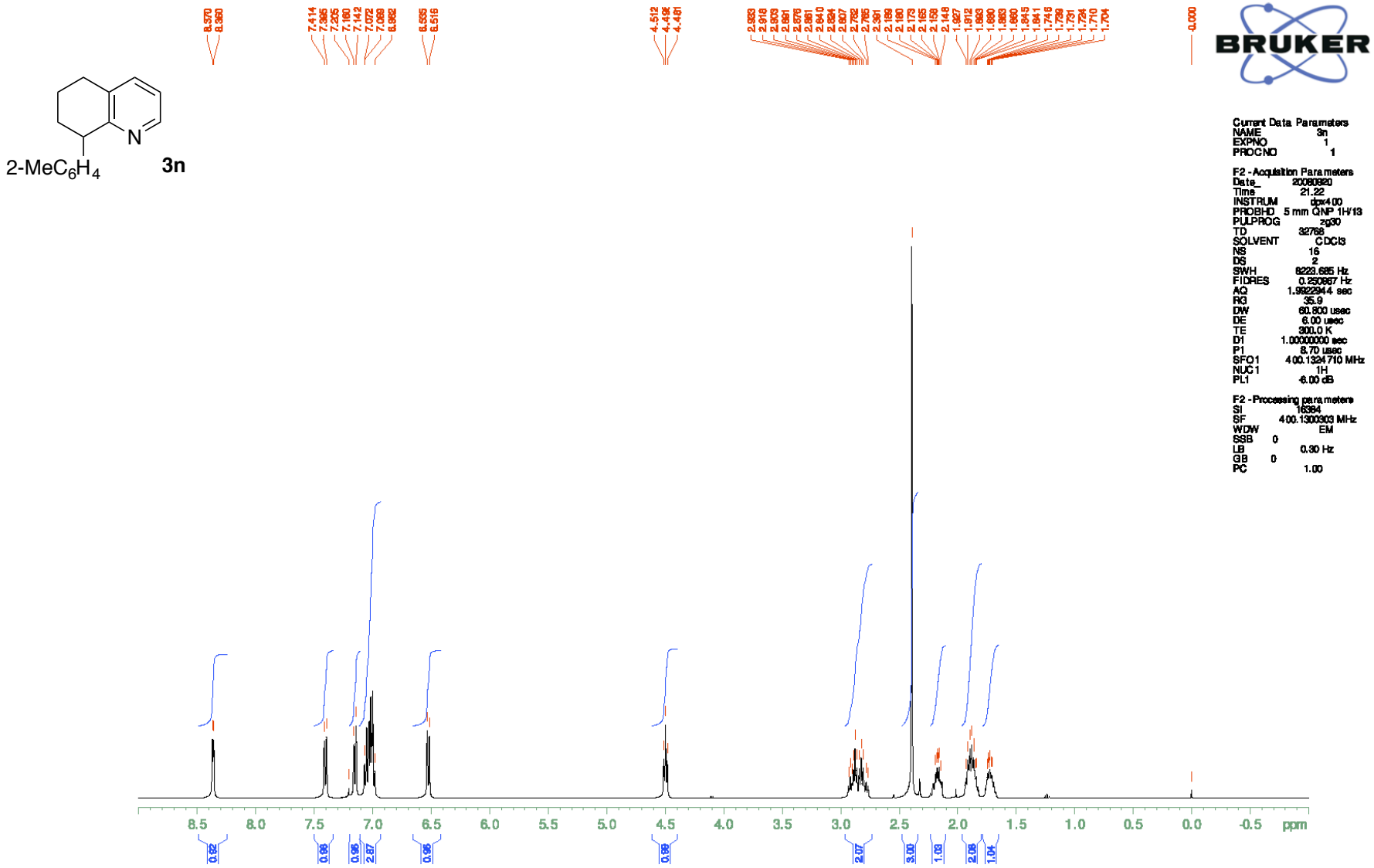


Figure S-41. ^{1}H NMR spectrum ($CDCl_3$) of **3n**.

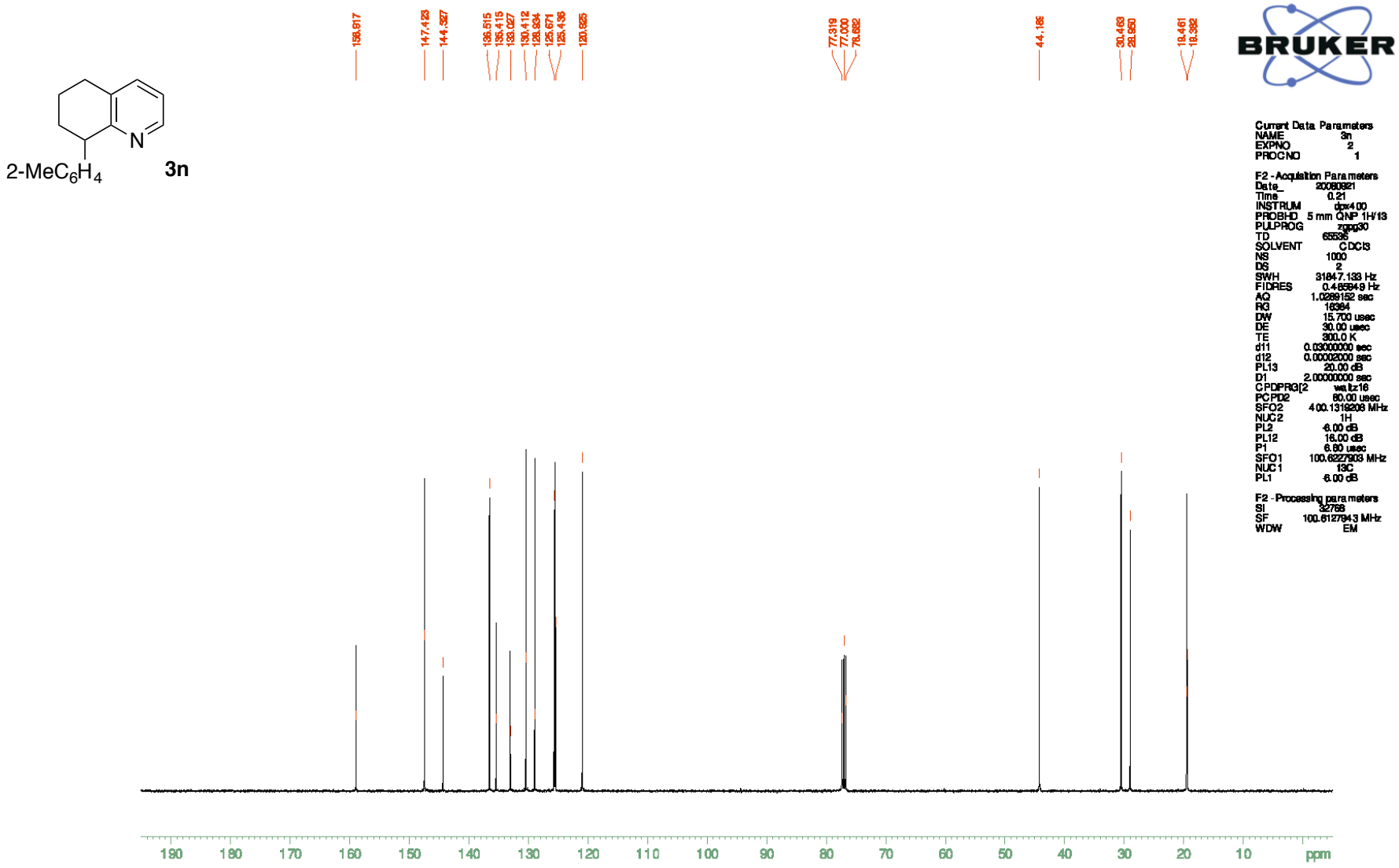


Figure S-42. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3n**.

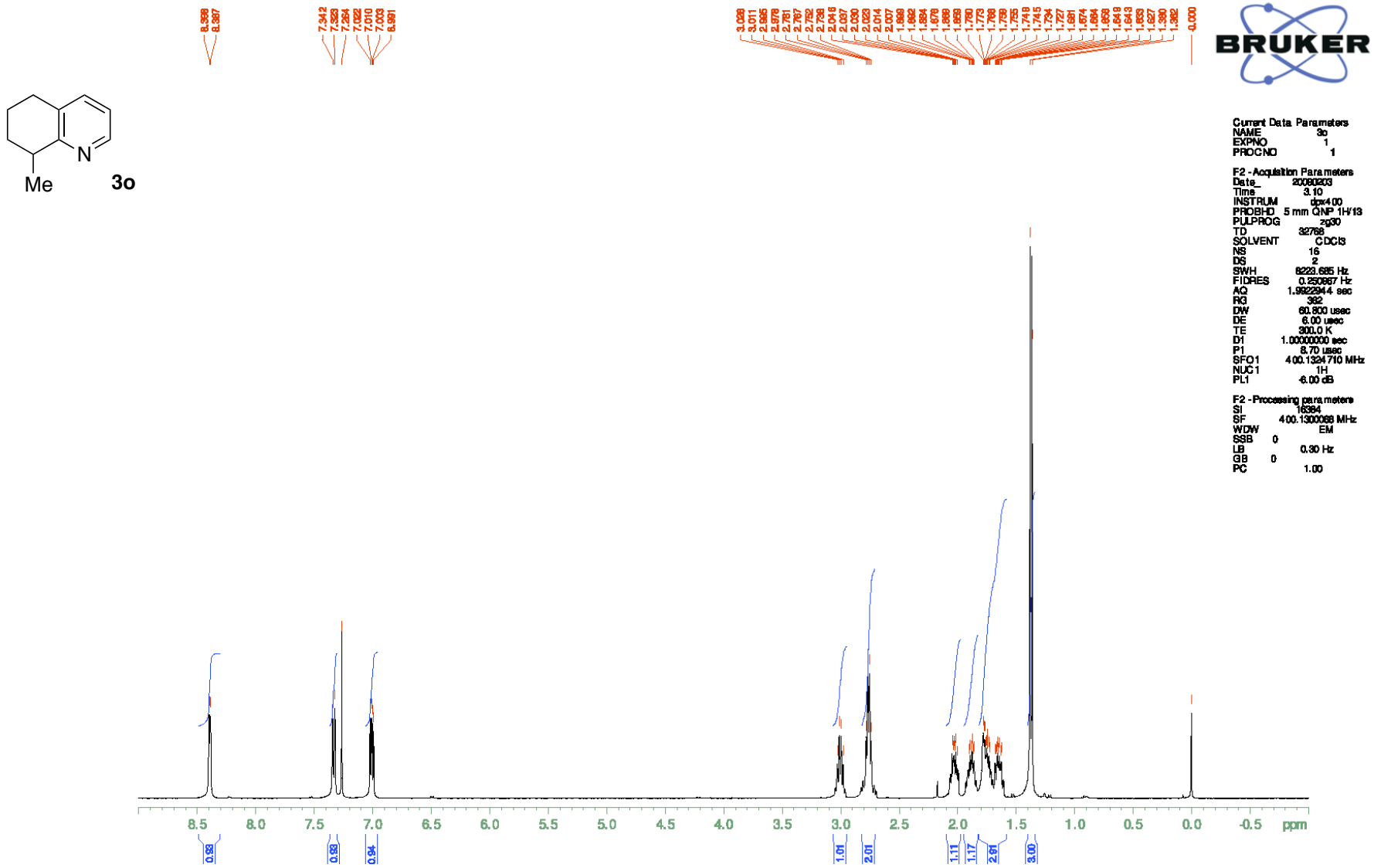


Figure S-43. ^{1}H NMR spectrum ($CDCl_3$) of **3o**.

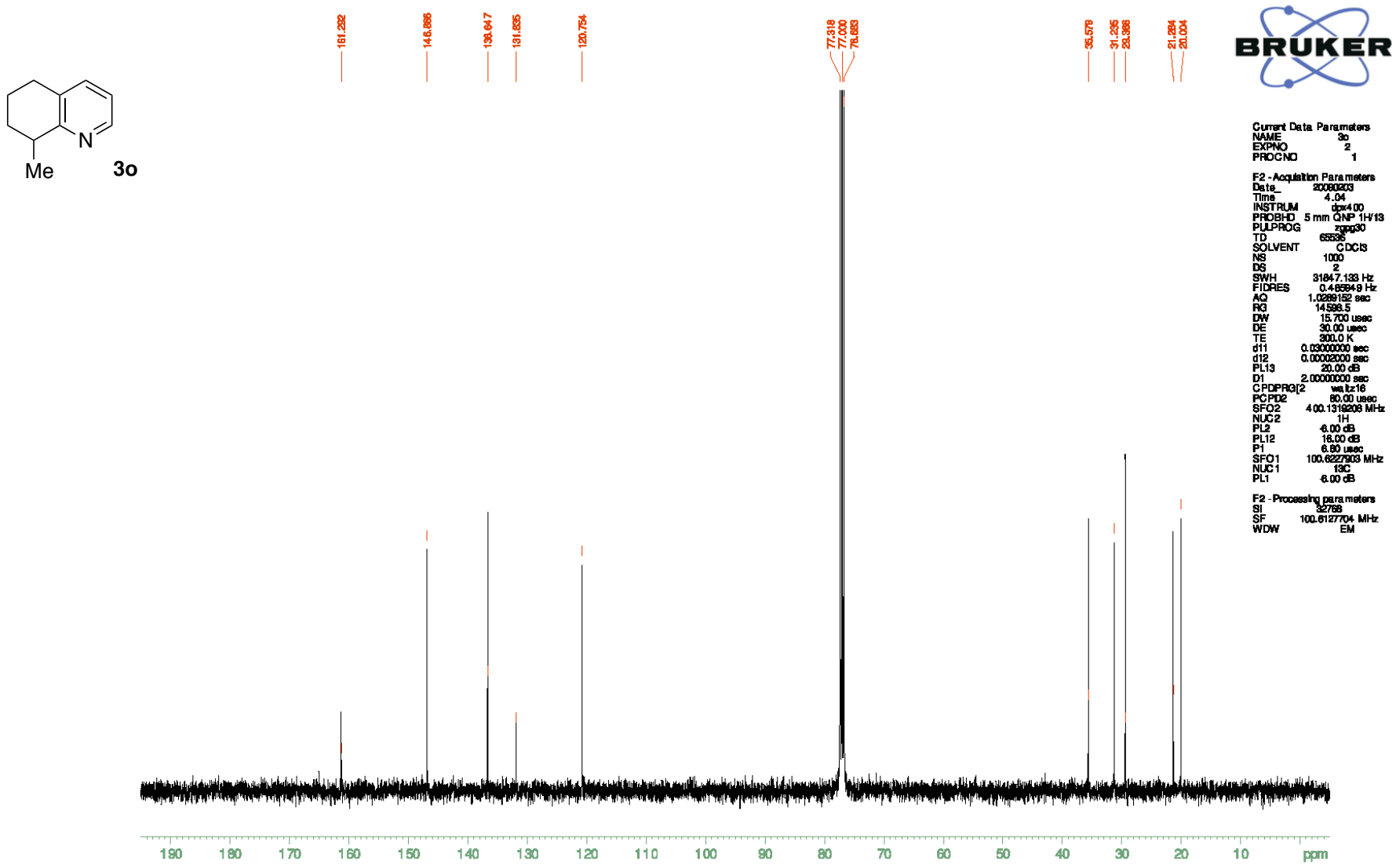


Figure S-44. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3o**.

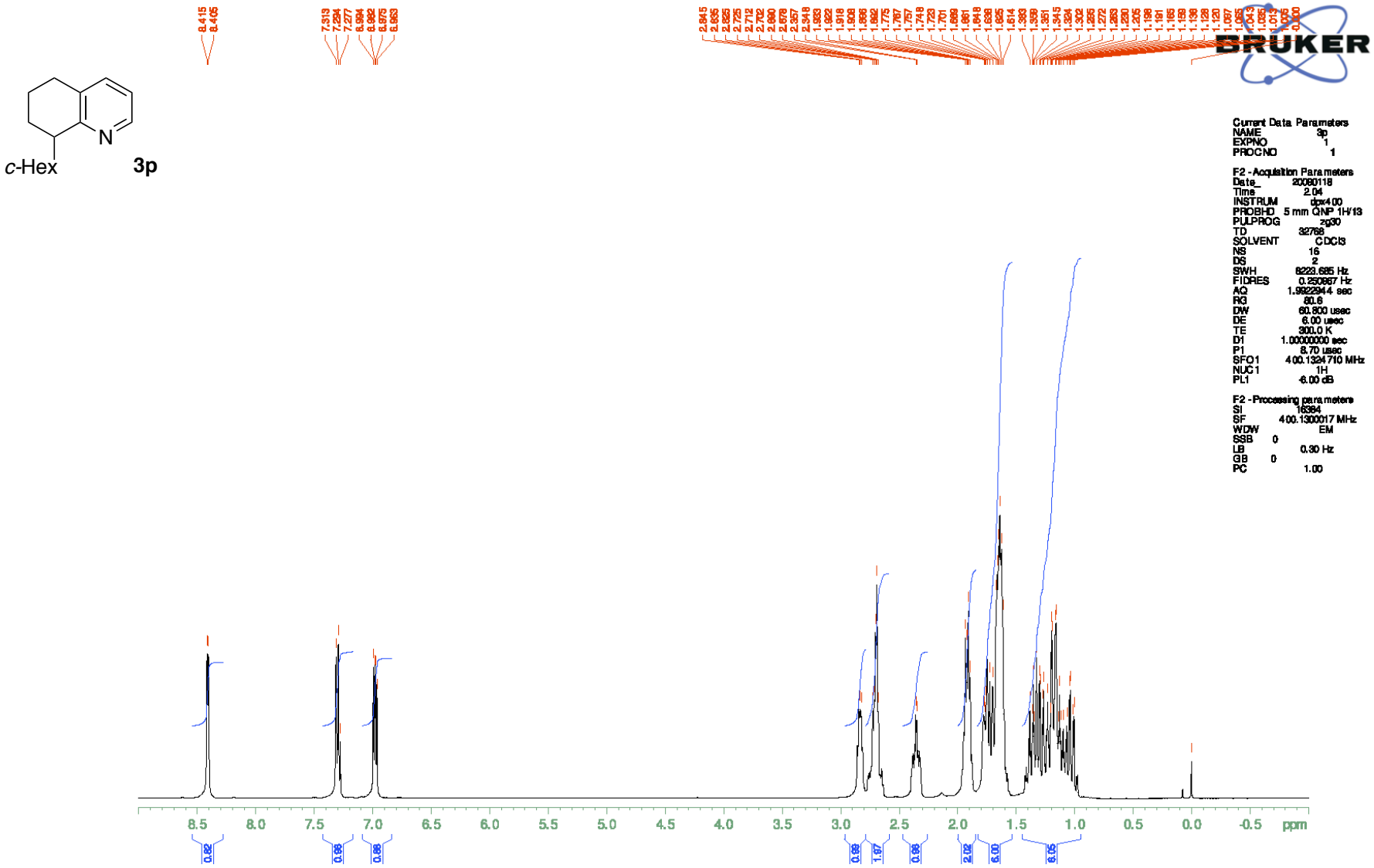


Figure S-45. ^{1}H NMR spectrum ($CDCl_3$) of **3p**.

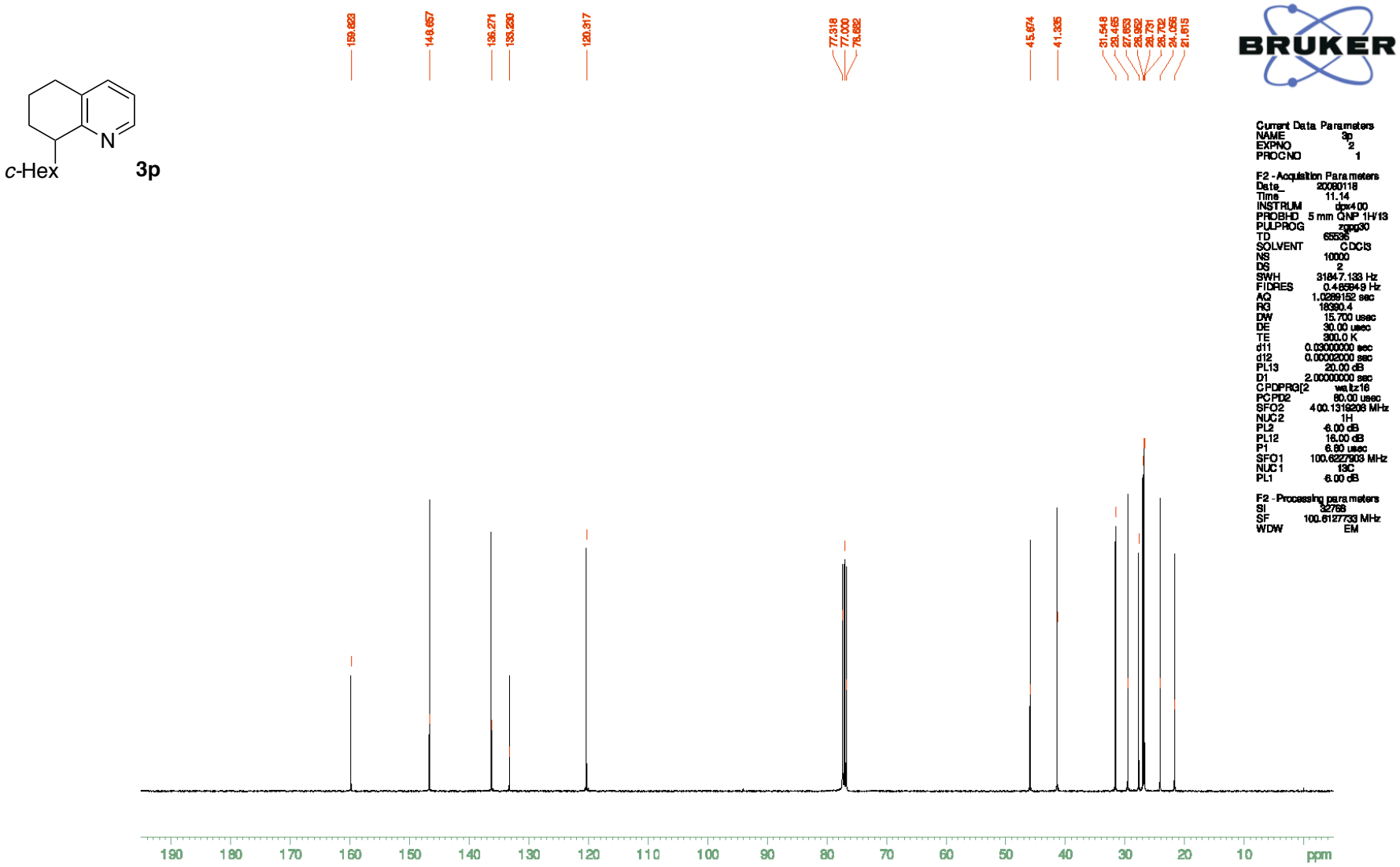


Figure S-46. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3p**.

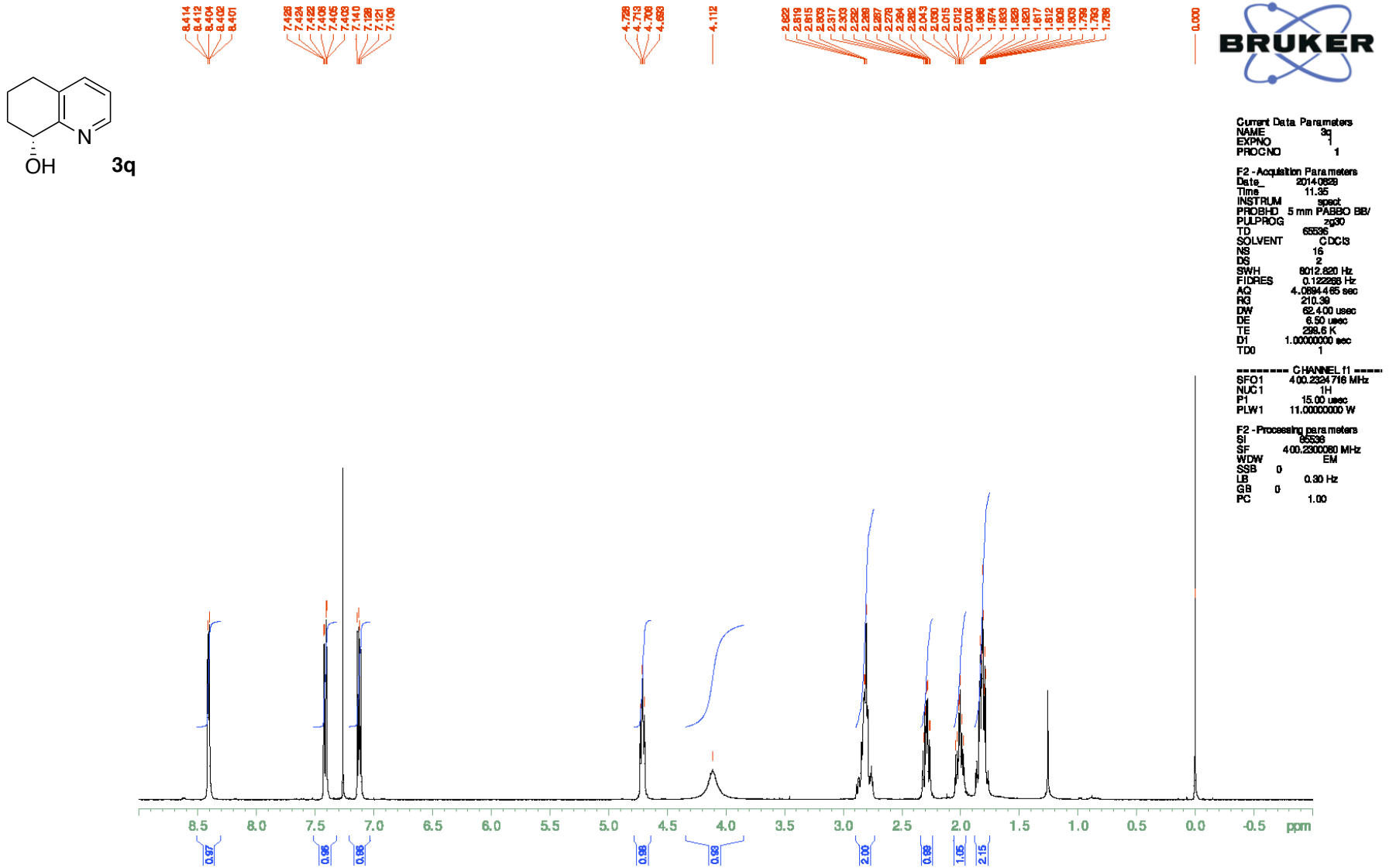


Figure S-47. ^{1}H NMR spectrum ($CDCl_3$) of **3q**.

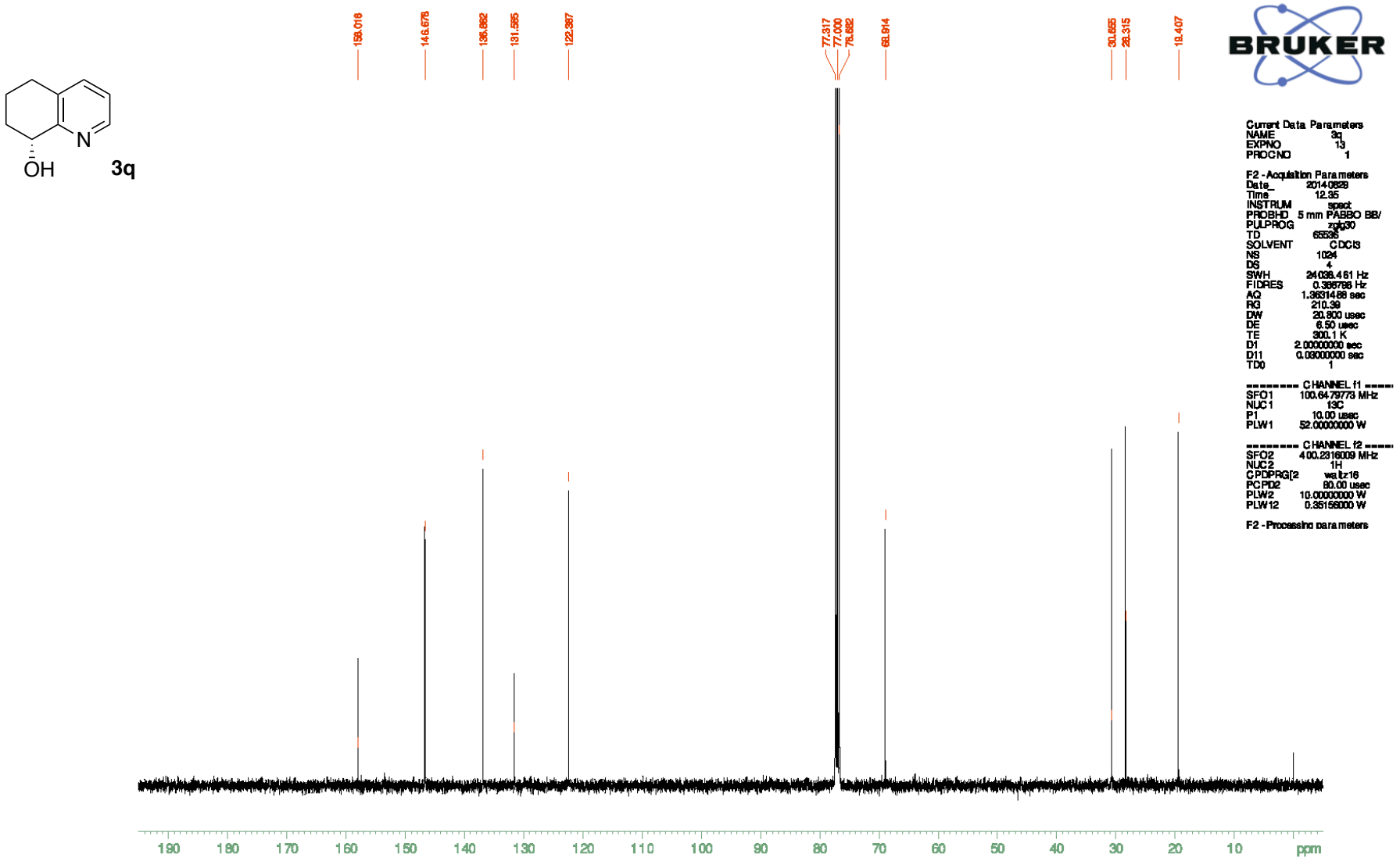


Figure S-48. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **3q**.

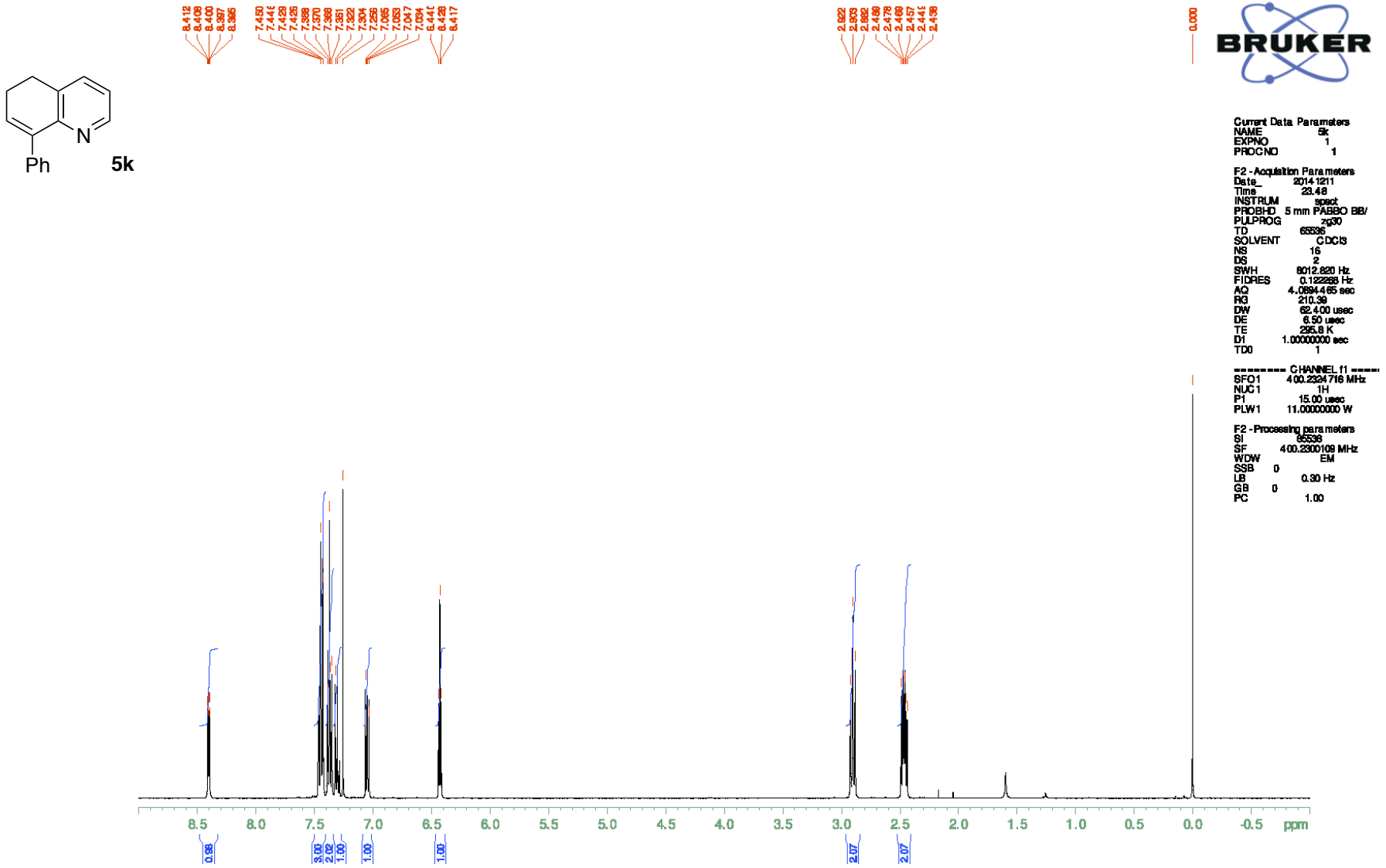


Figure S-49. ^{1}H NMR spectrum ($CDCl_3$) of **5k**.

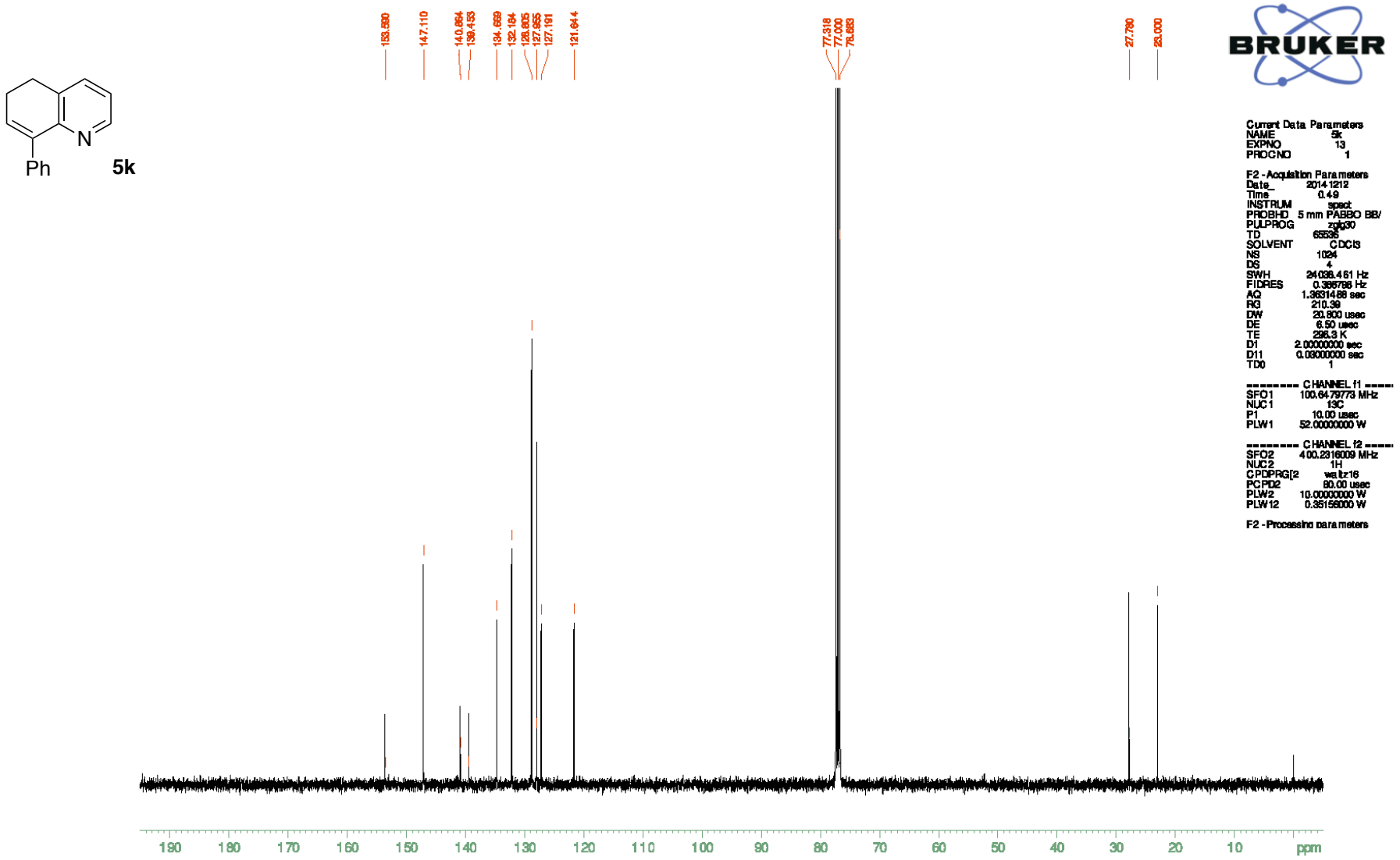


Figure S-50. ^{13}C $\{^{1}H\}$ NMR spectrum ($CDCl_3$) of **5k**.

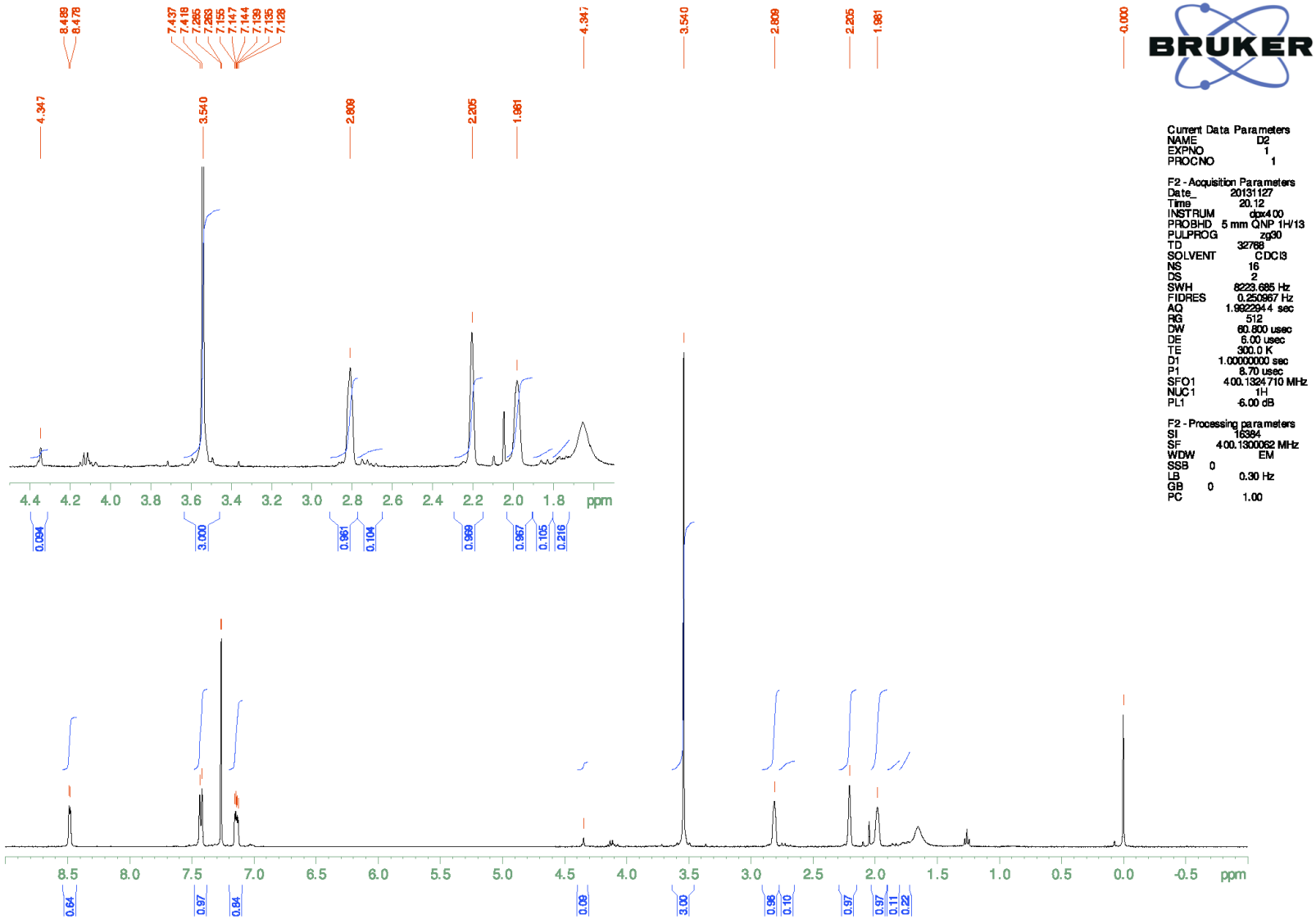


Figure S-51. ^{1}H NMR spectrum ($CDCl_3$) of **3i-*d***, which was obtained from the deuteration of **2i**.

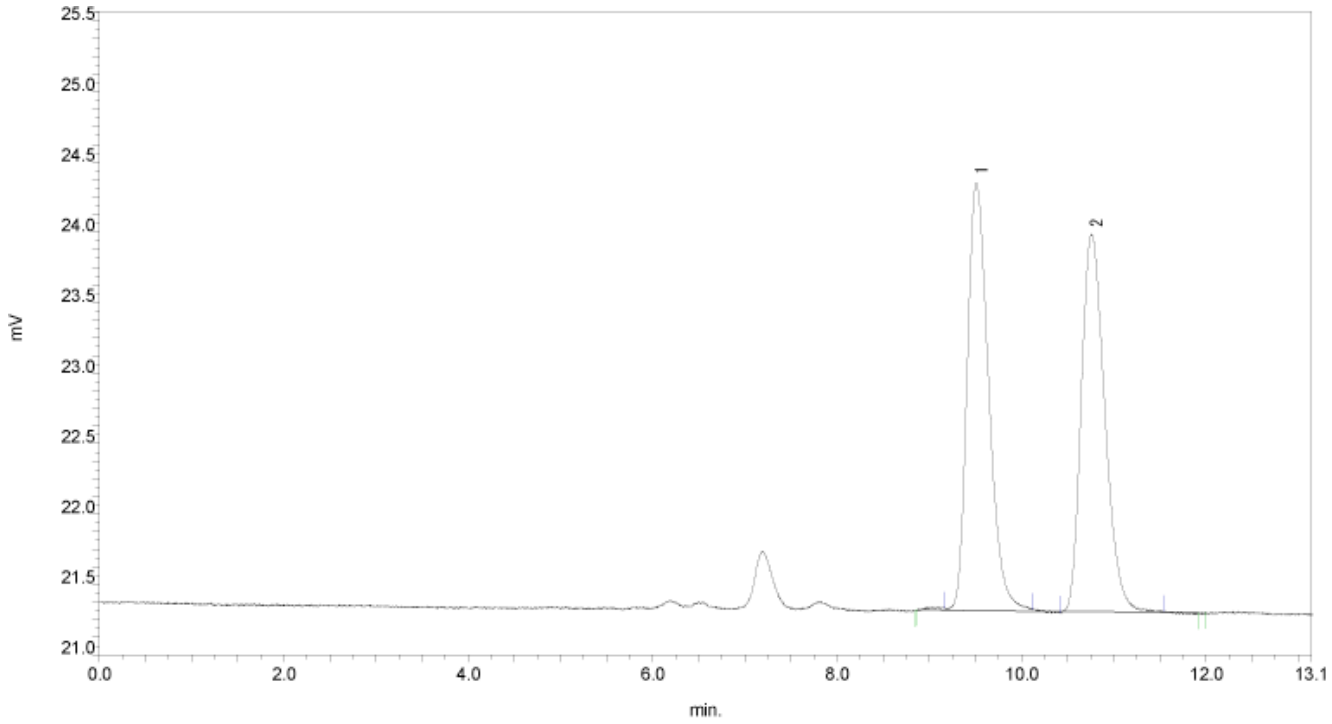
The charts of chiral HPLC analyses are given in the following pages. The translation of the Japanese words in column headings is given in figures below.

Type 1

Results 計算結果 No.	Rt(min)	Name of peak ピーク名	Integral 面積	Integral (%) 面積(%)	Height 高さ	Calibration 定量結果	NTP	Symmetry 対称性	Separation 分離度
1	9.51		49055.200	50.9759	3039	--------	7810.3	1.314	2.777
2	10.76		47177.000	49.0241	2676	--------	8384.9	1.276	------
			96232.200	100.0000	5715				

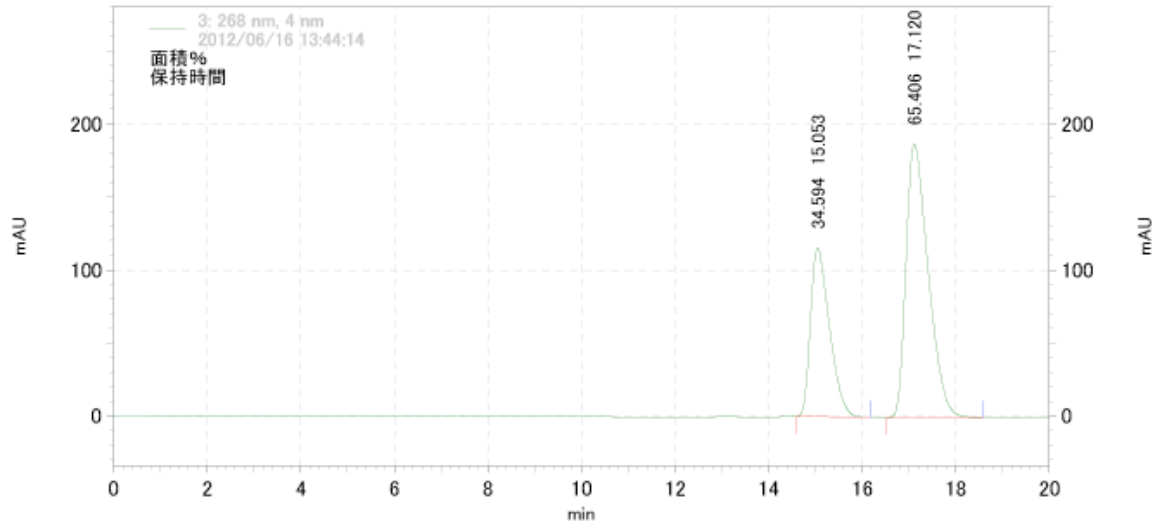
Type 2

3: 268 nm, 4 nm結果 Pk #	Results	Name of peak 名前	Retention time 保持時間	Integral 面積	Integral, % 面積%	Baseline code ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
	1		15.05	13076881	34.594	BI
	2		17.12	24723711	65.406	BI
トータル Total				37800592	100.000	



計算結果

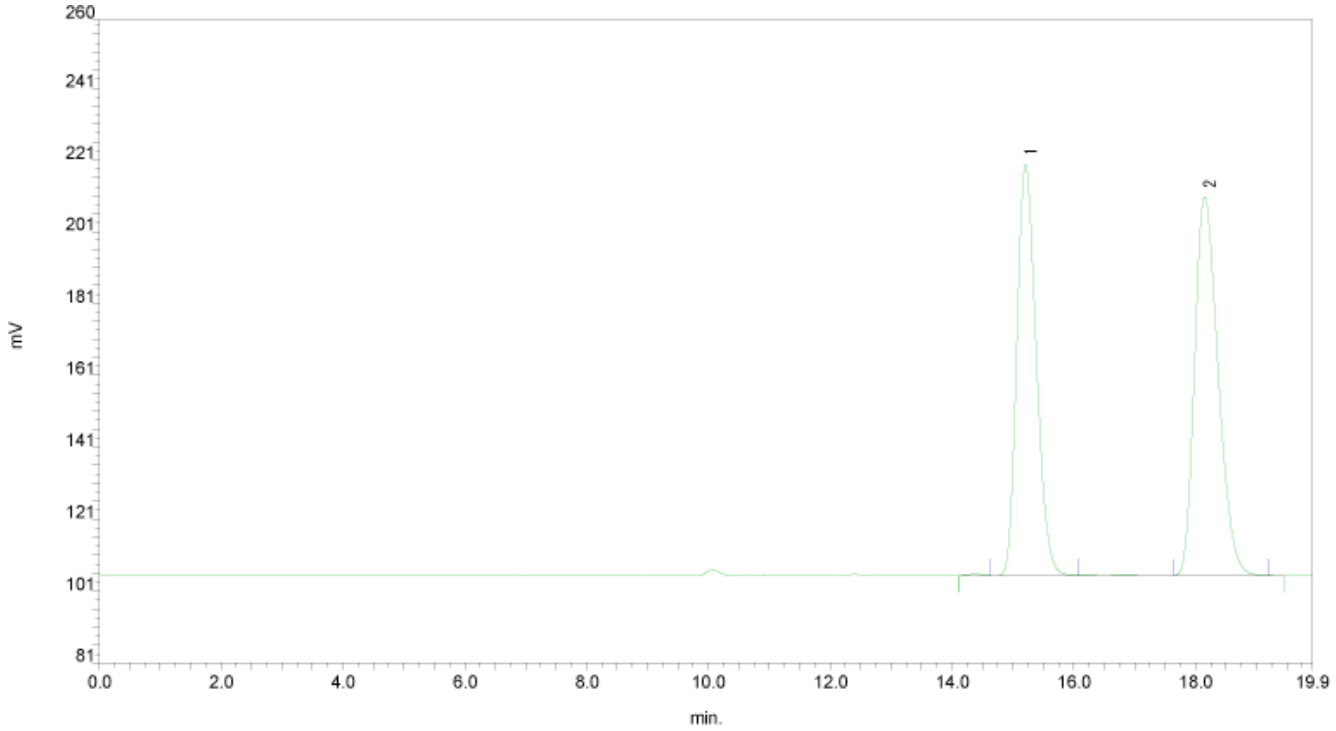
No.	Rt(min)	ﾋﾟｰｸ名	面積	面積(%)	高さ	定量結果	NTP	対称性	分離度
1	9.51		49055.200	50.9759	3039	--------	7810.3	1.314	2.777
2	10.76		47177.000	49.0241	2676	--------	8384.9	1.276	------
			96232.200	100.0000	5715				



3: 268 nm, 4 nm結果

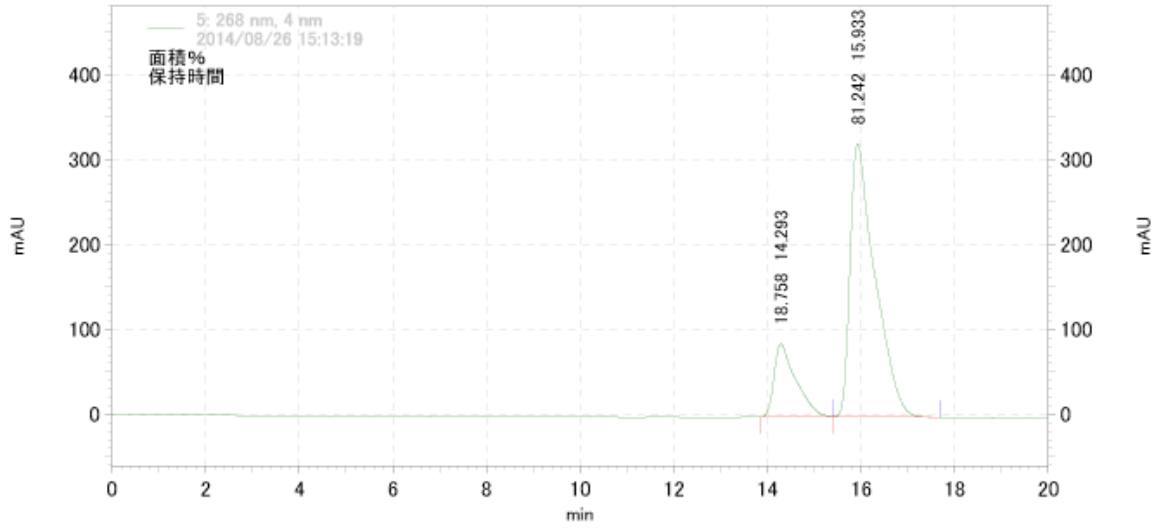
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		15.05	13076881	34.594	BI
2		17.12	24723711	65.406	BI
ﾄｰﾀﾙ			37800592	100.000	

Figure S-52. The charts of chiral HPLC analyses of racemic **3b** (upper), and the hydrogenation product obtained from entry 6 of Table 1 (lower).



計算結果

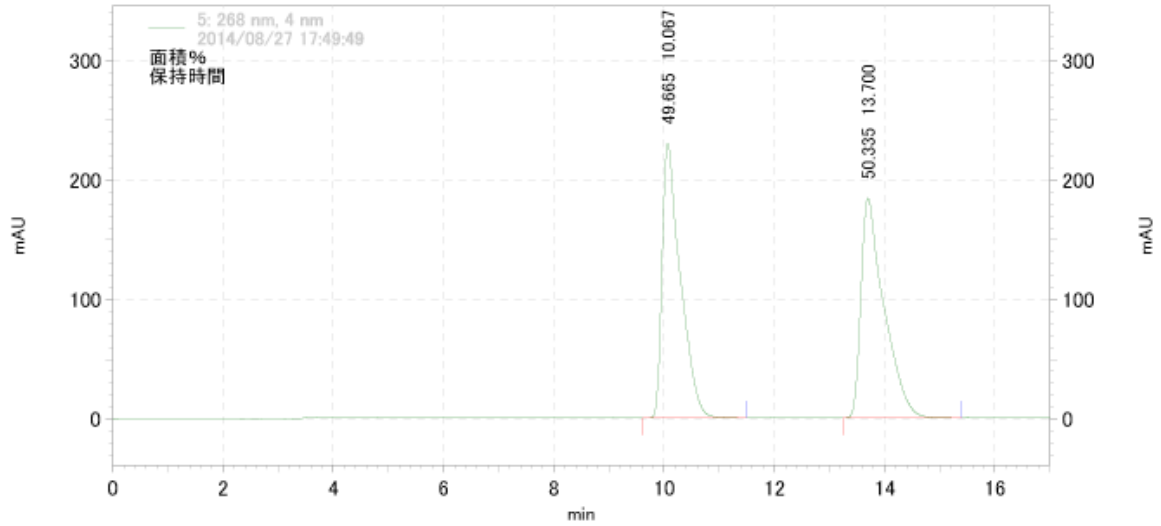
No.	Rt(min)	ピーク名	面積	面積(%)	高さ	定量結果	NTP	対称性	分離度
1	15.21		2532306.200	47.2429	114456	--------	10604.8	1.208	4.490
2	18.15		2827872.800	52.7571	105411	--------	10194.3	1.288	------
			5360179.000	100.0000	219867				



5: 268 nm, 4 nm結果

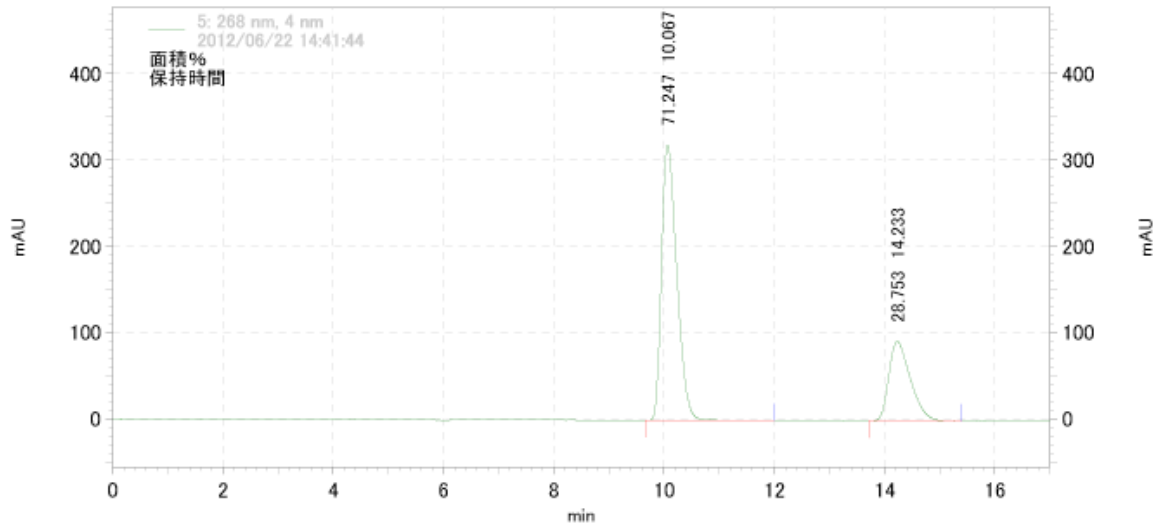
Pk #	名前	保持時間	面積	面積%	ベースラインコード
1		14.29	10971653	18.758	BV
2		15.93	47518577	81.242	VI
トータル			58490230	100.000	

Figure S-53. The charts of chiral HPLC analyses of racemic **3c** (upper), and the hydrogenation product obtained from entry 12 of Table 1 (lower).



5: 268 nm, 4 nm結果

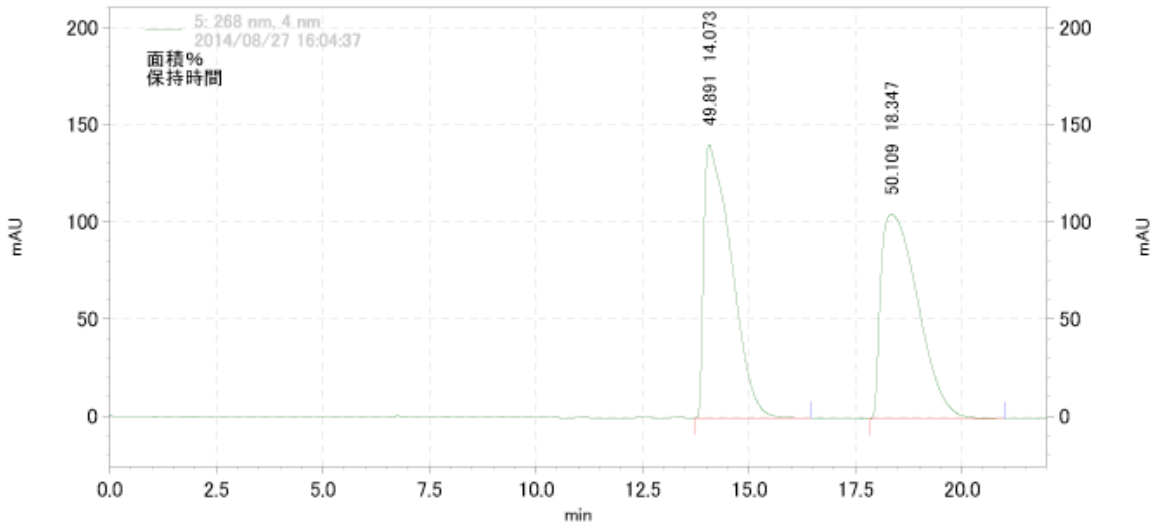
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		10.07	21121989	49.665	BI
2		13.70	21407248	50.335	BI
ﾄｰﾀﾙ			42529237	100.000	



5: 268 nm, 4 nm結果

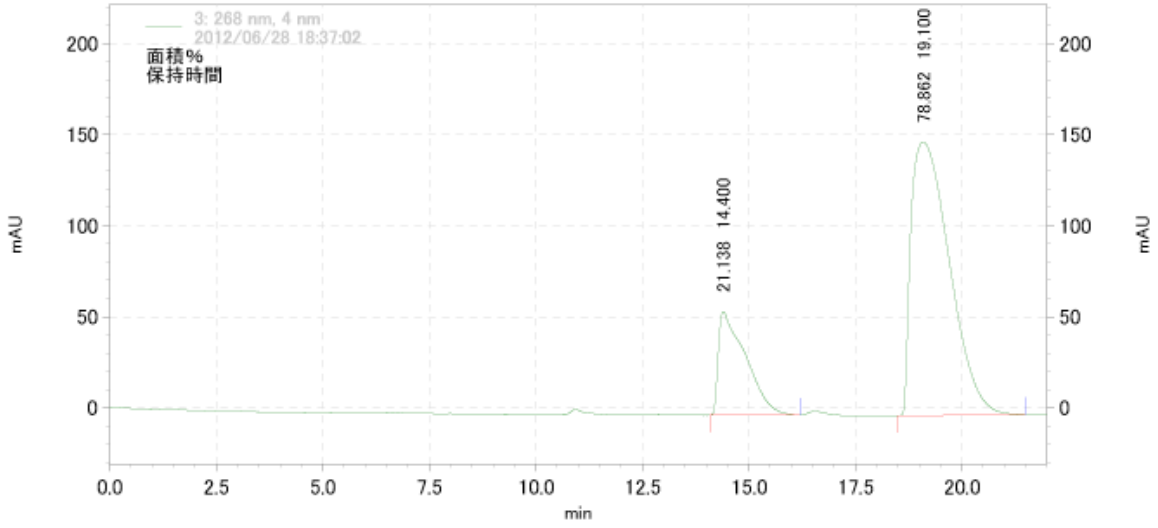
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		10.07	24592244	71.247	BI
2		14.23	9924735	28.753	BI
ﾄｰﾀﾙ			34516979	100.000	

Figure S-54. The charts of chiral HPLC analyses of racemic **3f** (upper), and the hydrogenation product obtained from entry 3 of Table 2 (lower).



5: 268 nm, 4 nm結果

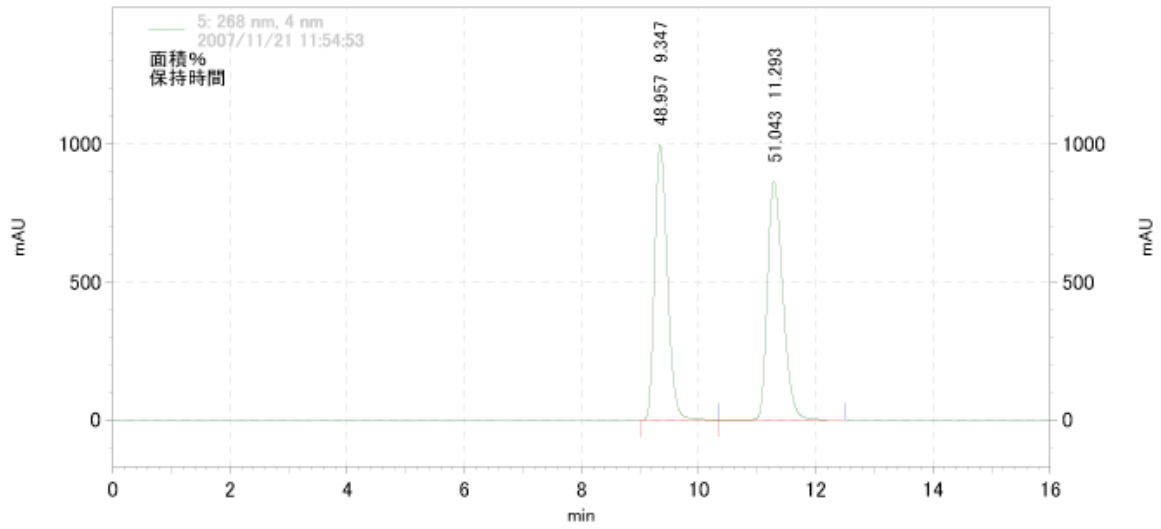
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		14.07	25312179	49.891	BI
2		18.35	25422983	50.109	BI
ﾄｰﾀﾙ			50735162	100.000	



3: 268 nm, 4 nm結果

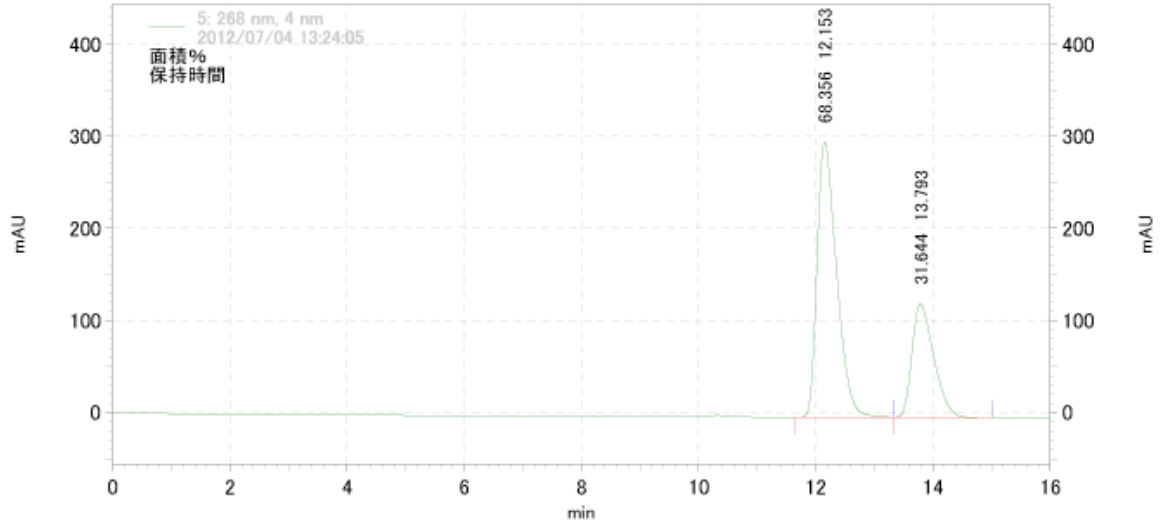
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		14.40	10095211	21.138	BB
2		19.10	37663425	78.862	II
ﾄｰﾀﾙ			47758636	100.000	

Figure S-55. The charts of chiral HPLC analyses of racemic **3g** (upper), and the hydrogenation product obtained from entry 4 of Table 2 (lower).



5: 268 nm, 4 nm結果

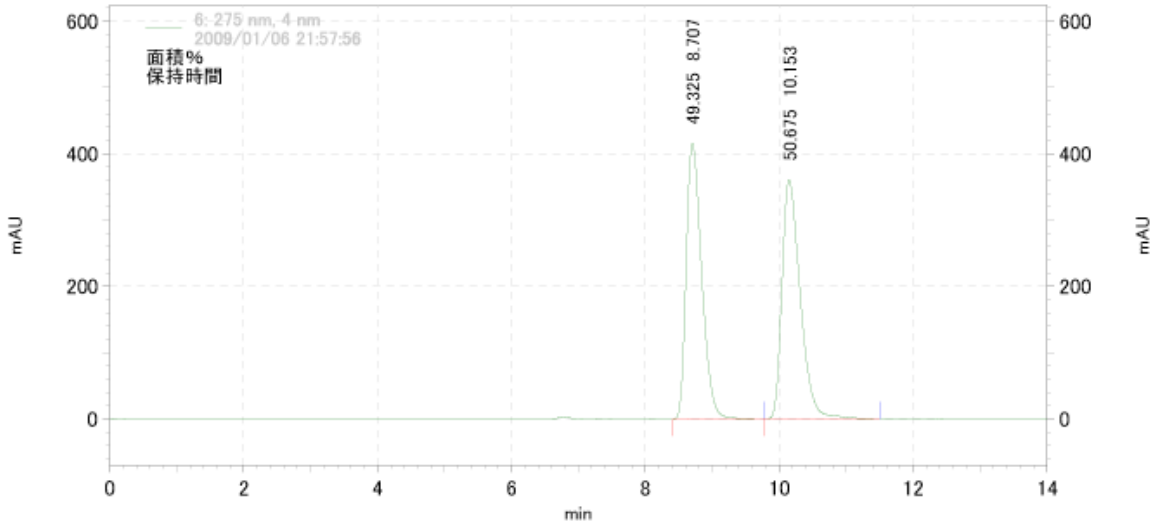
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		9.35	60797360	48.957	IV
2		11.29	63388247	51.043	VI
ﾄｰﾀﾙ			124185607	100.000	



5: 268 nm, 4 nm結果

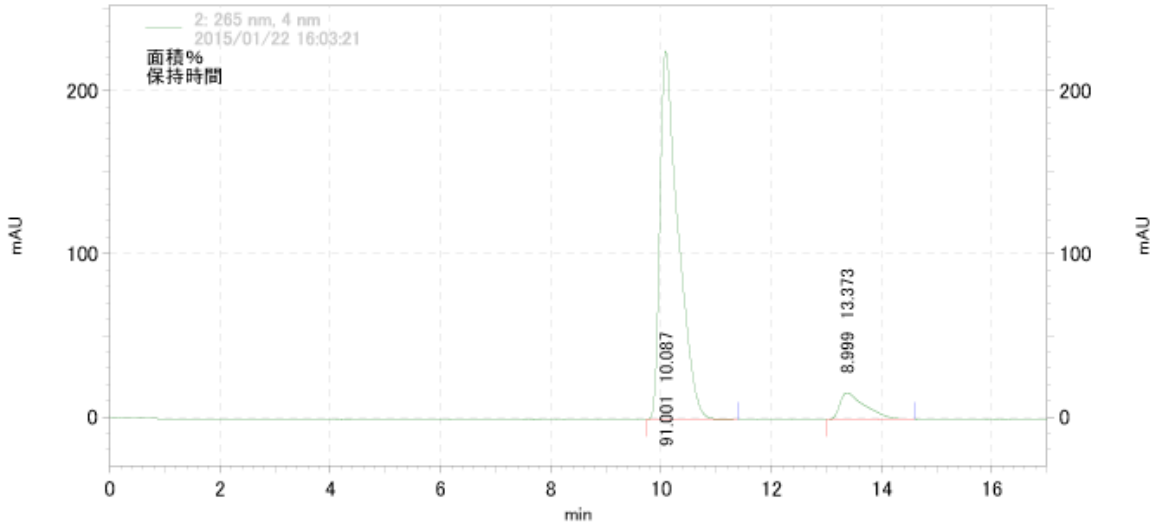
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		12.15	27610943	68.356	BV
2		13.79	12781740	31.644	VI
ﾄｰﾀﾙ			40392683	100.000	

Figure S-56. The charts of chiral HPLC analyses of racemic **3h** (upper), and the hydrogenation product obtained from entry 5 of Table 2 (lower).



6: 275 nm, 4 nm結果

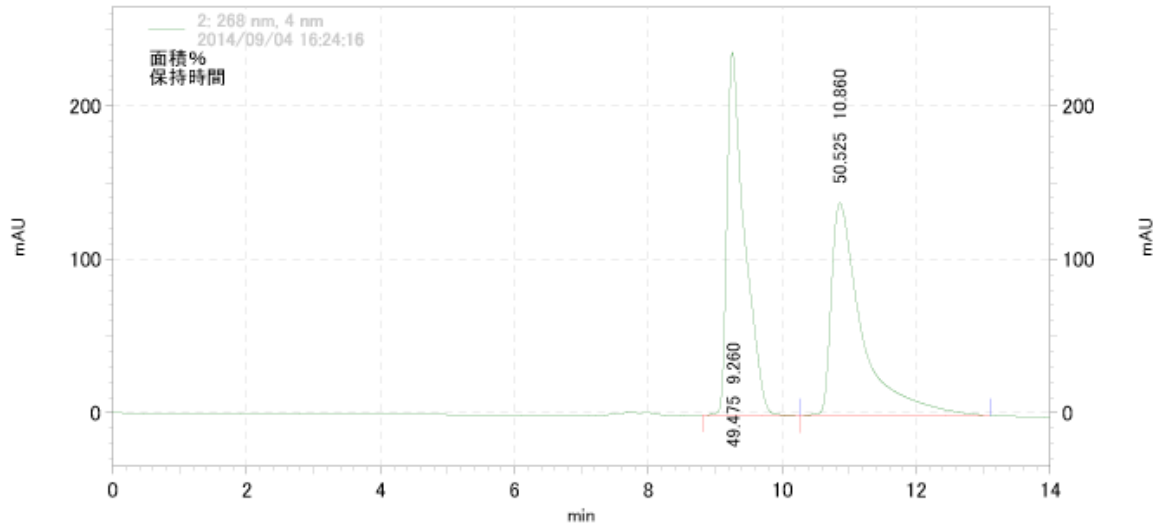
Pk #	名前	保持時間	面積	面積%	ﾍﾟｰｽﾗｲﾝｺｰﾄﾞ
1		8.71	26645406	49.325	IV
2		10.15	27374251	50.675	VI
ﾄｰﾀﾙ			54019657	100.000	



2: 265 nm, 4 nm結果

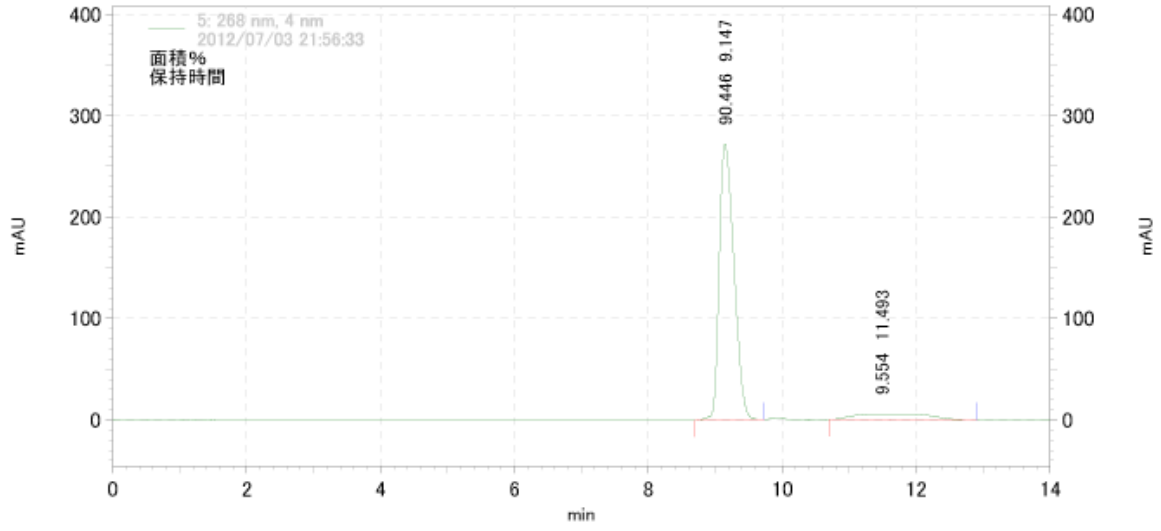
Pk #	名前	保持時間	面積	面積%	ﾍﾟｰｽﾗｲﾝｺｰﾄﾞ
1		10.09	20650078	91.001	II
2		13.37	2042084	8.999	II
ﾄｰﾀﾙ			22692162	100.000	

Figure S-57. The charts of chiral HPLC analyses of racemic **3i** (upper), and the hydrogenation product obtained from entry 8 of Table 2 (lower).



2: 268 nm, 4 nm結果

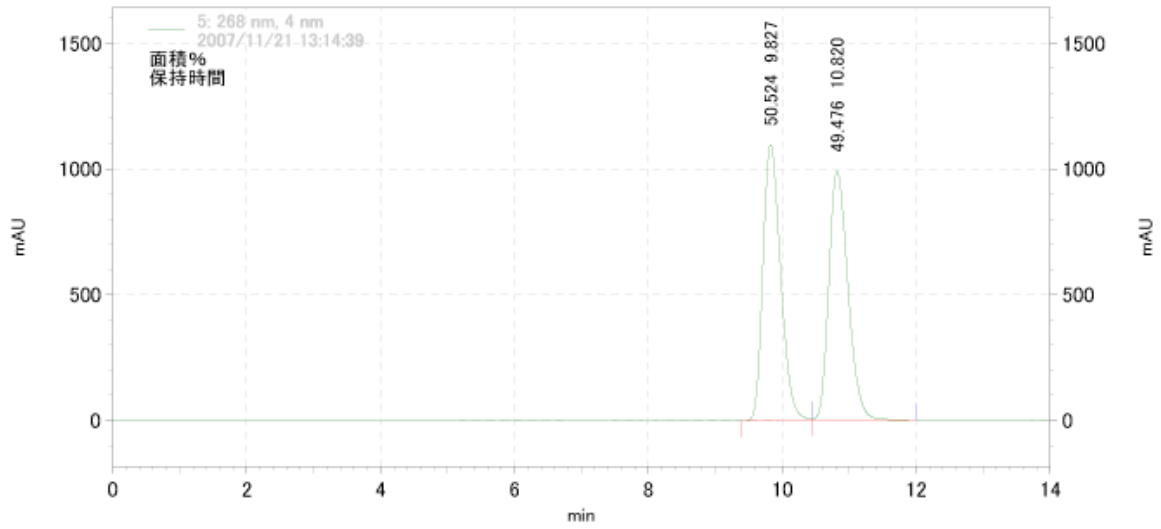
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		9.26	17349178	49.475	IB
2		10.86	17717466	50.525	BI
ﾄｰﾀﾙ			35066644	100.000	



5: 268 nm, 4 nm結果

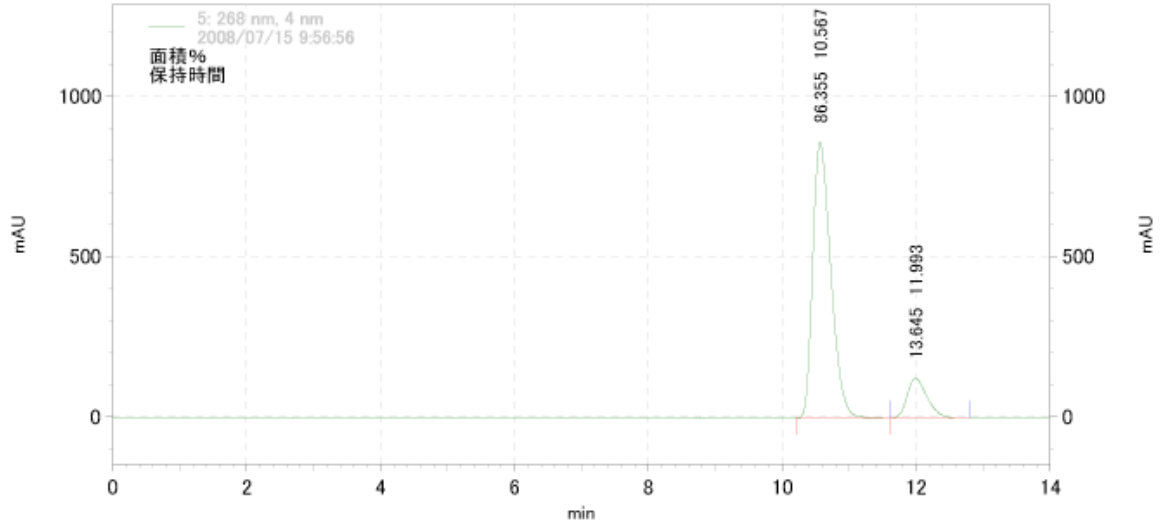
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		9.15	16568319	90.446	BB
2		11.49	1750214	9.554	II
ﾄｰﾀﾙ			18318533	100.000	

Figure S-58. The charts of chiral HPLC analyses of racemic **3j** (upper), and the hydrogenation product obtained from entry 1 of Table 3 (lower).



5: 268 nm, 4 nm結果

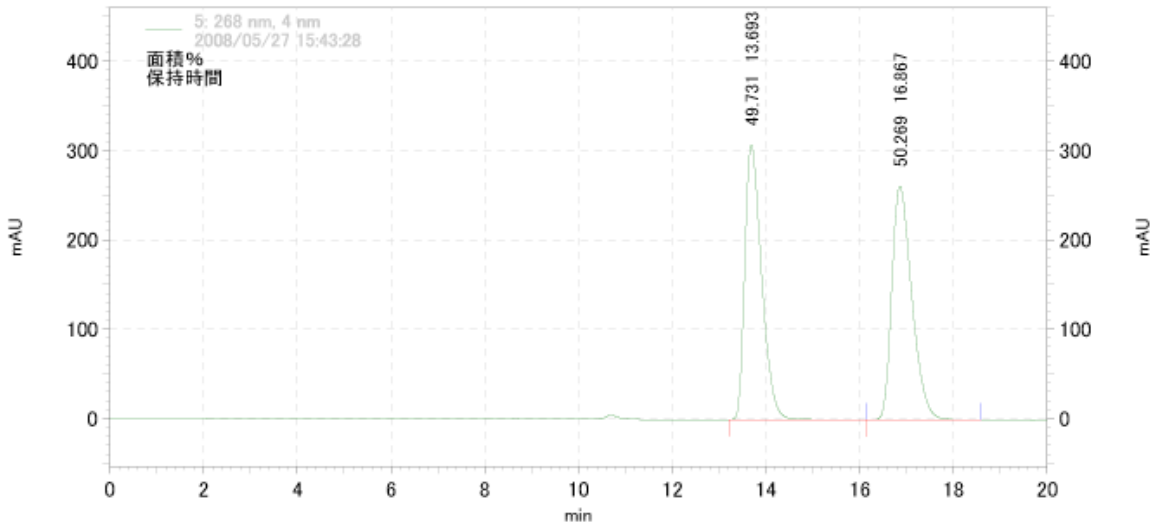
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		9.83	80492623	50.524	BV
2		10.82	78823984	49.476	VI
ﾄｰﾀﾙ			159316607	100.000	



5: 268 nm, 4 nm結果

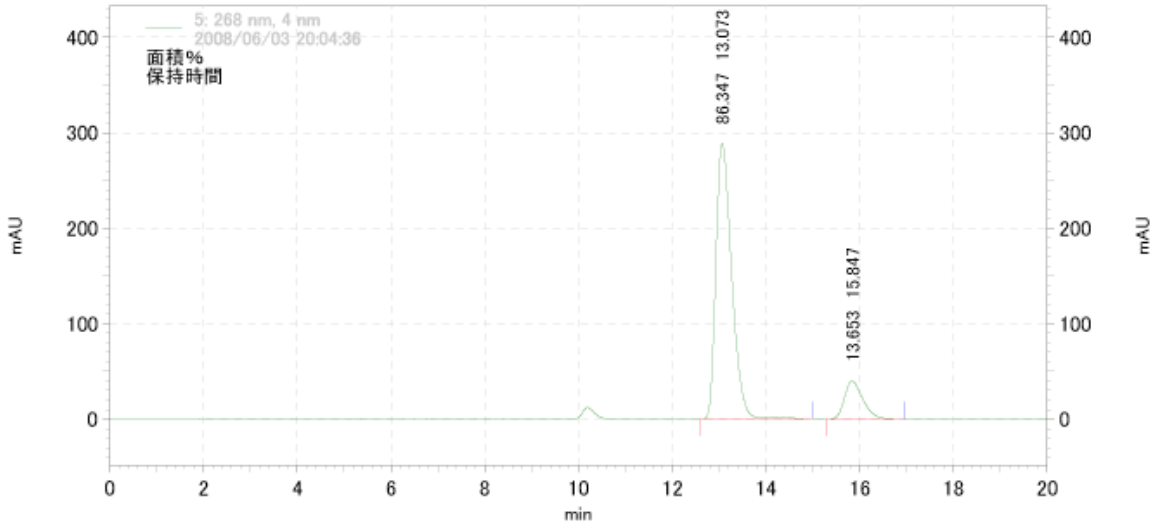
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		10.57	64248045	86.355	IV
2		11.99	10152289	13.645	VI
ﾄｰﾀﾙ			74400334	100.000	

Figure S-59. The charts of chiral HPLC analyses of racemic **3k** (upper), and the hydrogenation product obtained from entry 2 of Table 3 (lower).



5: 268 nm, 4 nm結果

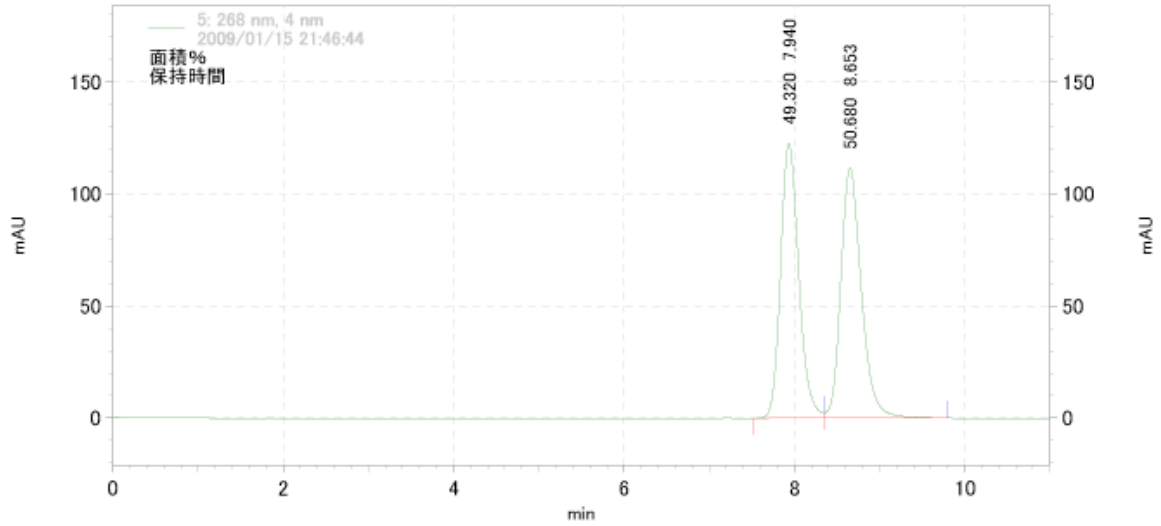
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		13.69	30681829	49.731	IB
2		16.87	31013505	50.269	BI
ﾄｰﾀﾙ			61695334	100.000	



5: 268 nm, 4 nm結果

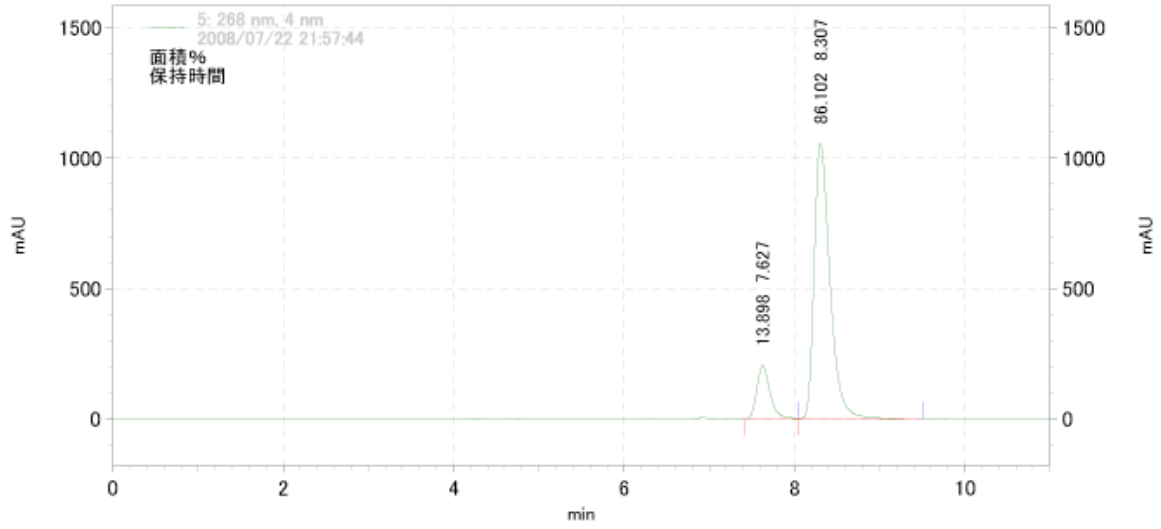
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		13.07	27030671	86.347	MM
2		15.85	4273967	13.653	BB
ﾄｰﾀﾙ			31304638	100.000	

Figure S-60. The charts of chiral HPLC analyses of racemic **3l** (upper), and the hydrogenation product obtained from entry 3 of Table 3 (lower).



5: 268 nm, 4 nm結果

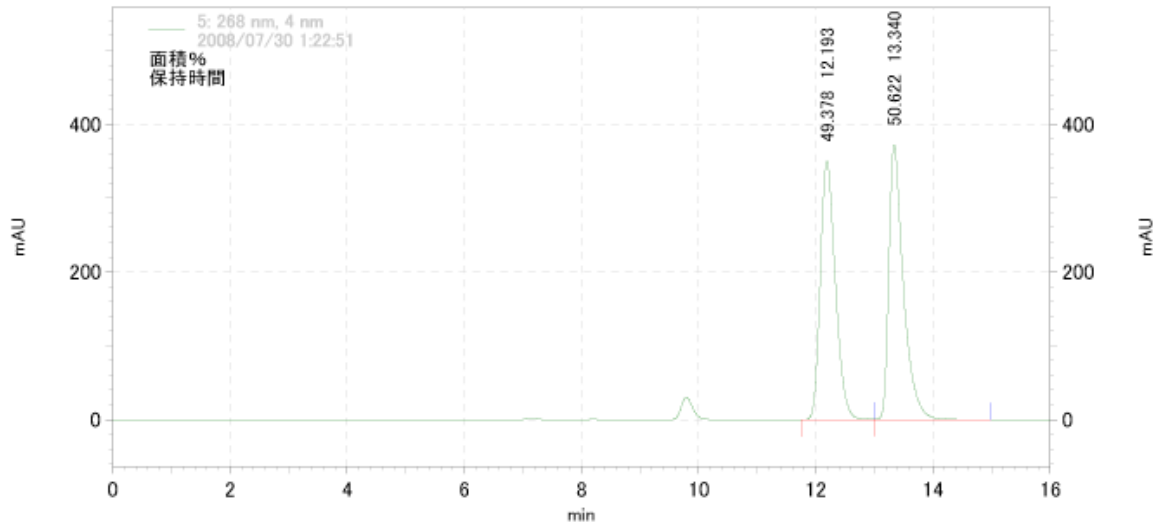
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		7.94	7276983	49.320	BV
2		8.65	7477571	50.680	VI
ﾄｰﾀﾙ			14754554	100.000	



5: 268 nm, 4 nm結果

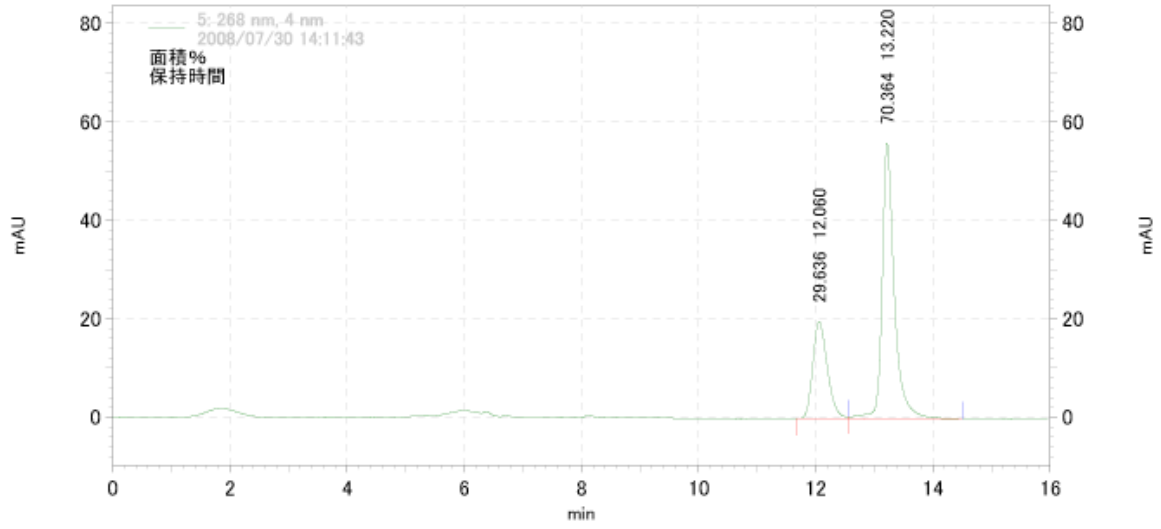
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		7.63	8811196	13.898	IV
2		8.31	54588509	86.102	VI
ﾄｰﾀﾙ			63399705	100.000	

Figure S-61. The charts of chiral HPLC analyses of racemic **3m** (upper), and the hydrogenation product obtained from entry 4 of Table 3 (lower).



5: 268 nm, 4 nm結果

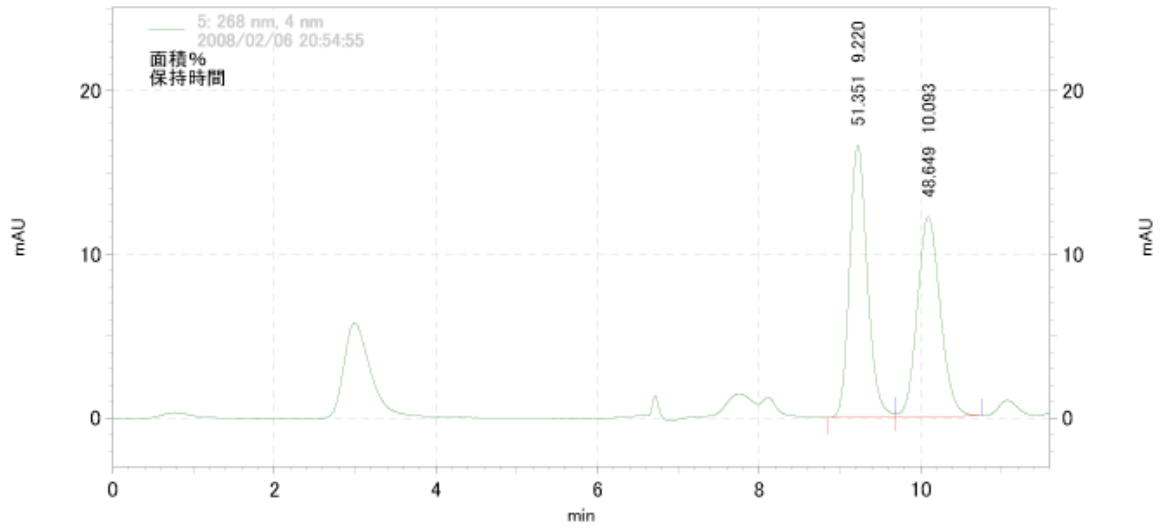
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		12.19	25114105	49.378	BV
2		13.34	25746373	50.622	VI
ﾄｰﾀﾙ			50860478	100.000	



5: 268 nm, 4 nm結果

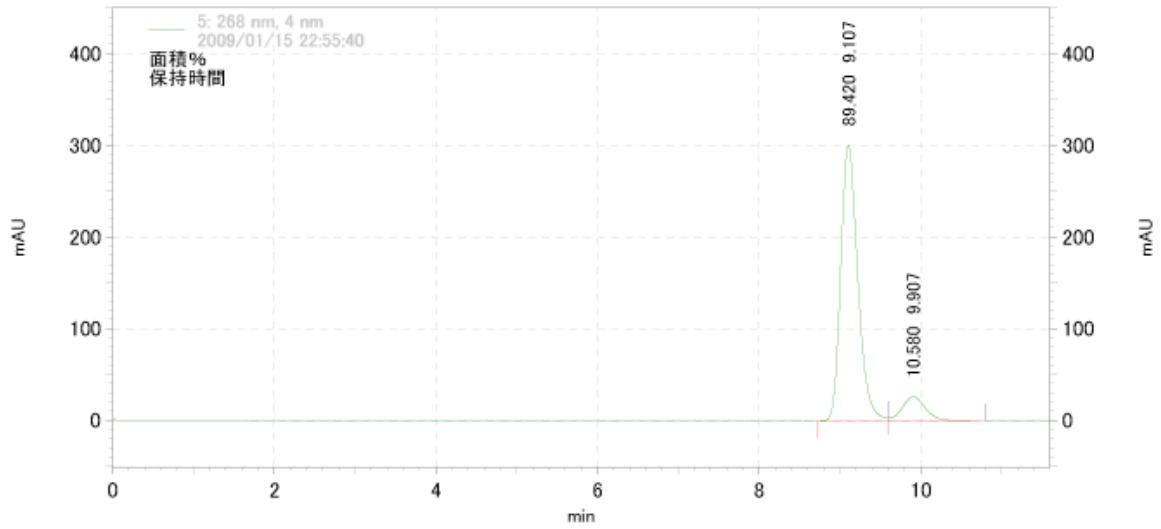
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		12.06	1364090	29.636	BV
2		13.22	3238790	70.364	VI
ﾄｰﾀﾙ			4602880	100.000	

Figure S-62. The charts of chiral HPLC analyses of racemic **3n** (upper), and the hydrogenation product obtained from entry 5 of Table 3 (lower).



5: 268 nm, 4 nm結果

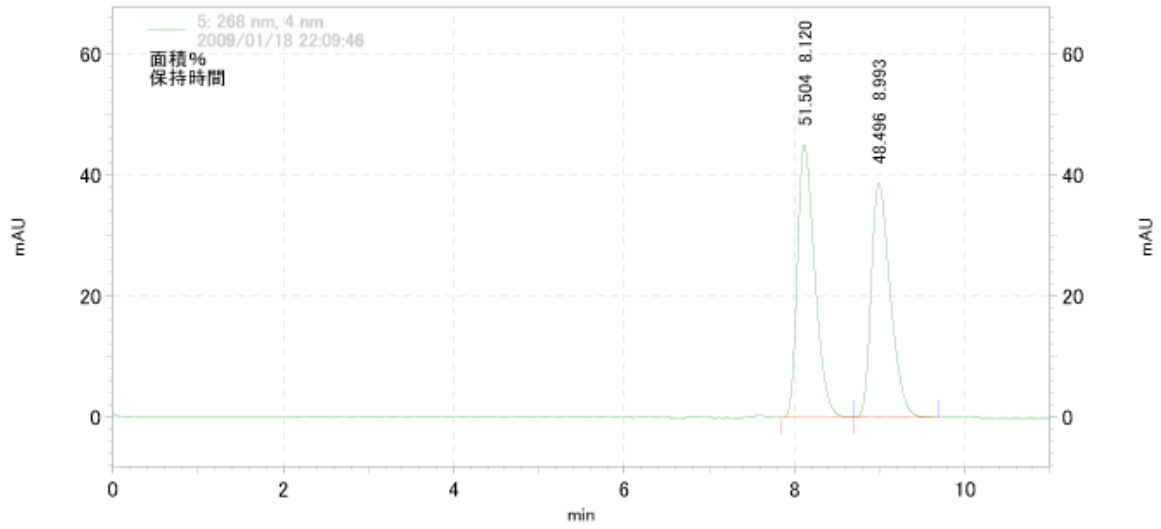
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		9.22	1017277	51.351	BV
2		10.09	963732	48.649	VB
ﾄｰﾀﾙ			1981009	100.000	



5: 268 nm, 4 nm結果

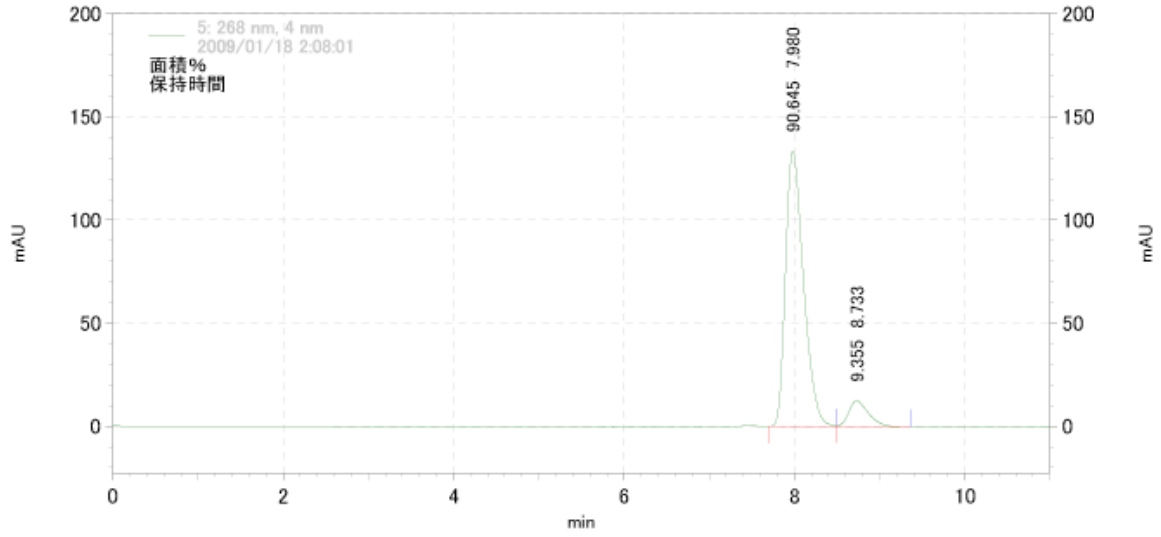
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		9.11	17620304	89.420	BV
2		9.91	2084862	10.580	VI
ﾄｰﾀﾙ			19705166	100.000	

Figure S-63. The charts of chiral HPLC analyses of racemic **3o** (upper), and the hydrogenation product obtained from entry 7 of Table 3 (lower).



5: 268 nm, 4 nm結果

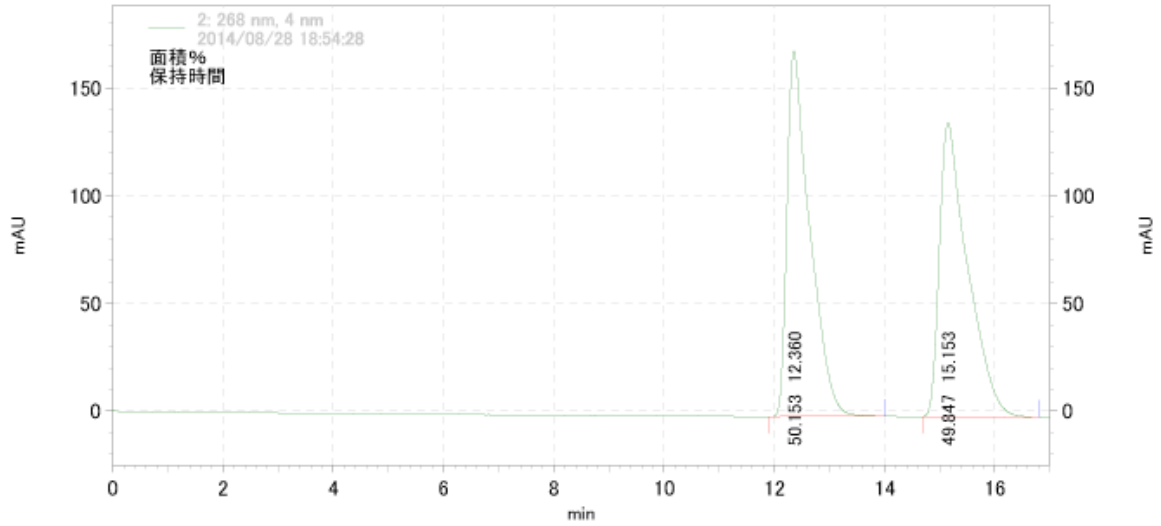
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		8.12	2562804	51.504	BV
2		8.99	2413087	48.496	VB
ﾄｰﾀﾙ			4975891	100.000	



5: 268 nm, 4 nm結果

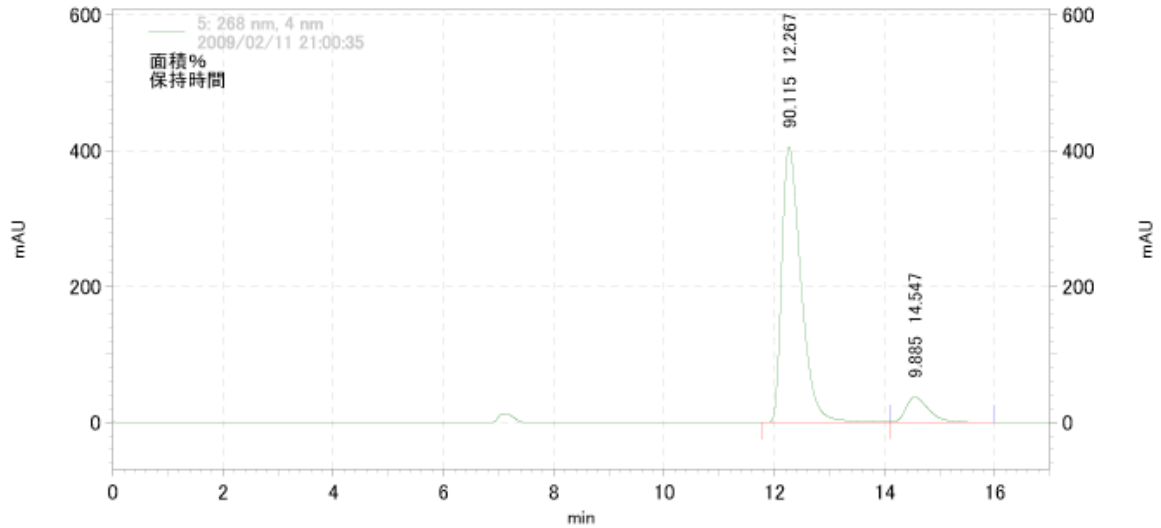
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		7.98	7835205	90.645	BV
2		8.73	808669	9.355	VB
ﾄｰﾀﾙ			8643874	100.000	

Figure S-64. The charts of chiral HPLC analyses of racemic **3p** (upper), and the hydrogenation product obtained from entry 8 of Table 3 (lower).



2: 268 nm, 4 nm結果

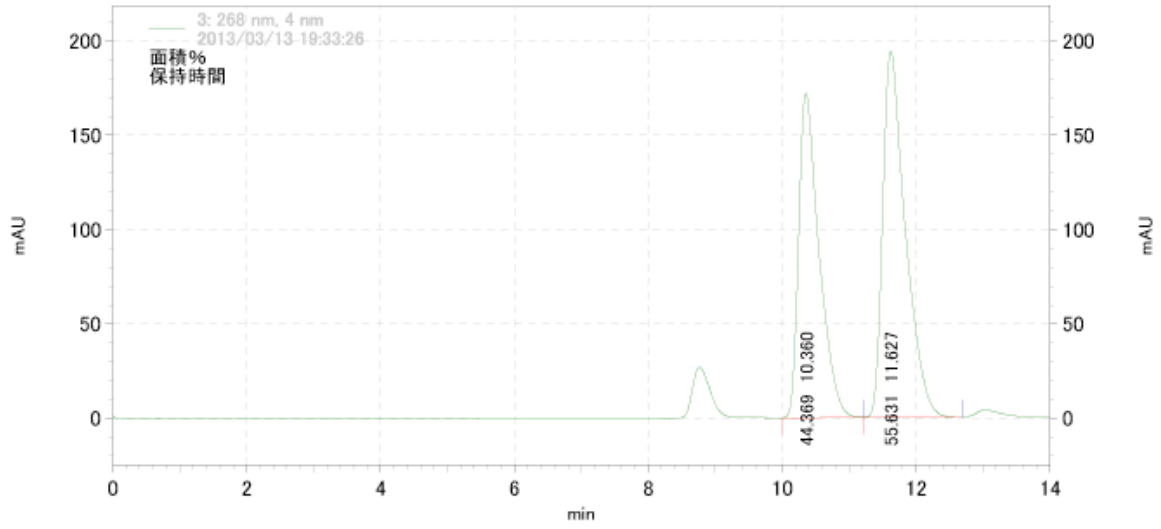
Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		12.36	19527263	50.153	BI
2		15.15	19408411	49.847	II
ﾄｰﾀﾙ			38935674	100.000	



5: 268 nm, 4 nm結果

Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		12.27	39248156	90.115	BV
2		14.55	4305492	9.885	VI
ﾄｰﾀﾙ			43553648	100.000	

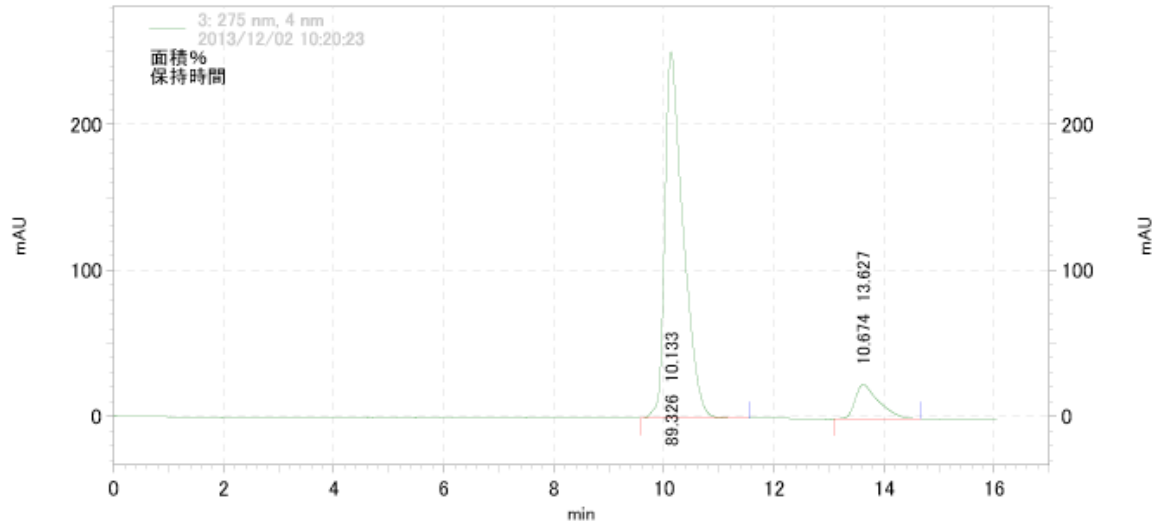
Figure S-65. The charts of chiral HPLC analyses of racemic **3q** (upper), and the product obtained from the deprotection of **3j** in eq 2 (lower).



3: 268 nm, 4 nm結果

Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		10.36	14586973	44.369	IV
2		11.63	18289526	55.631	VB
ﾄｰﾀﾙ			32876499	100.000	

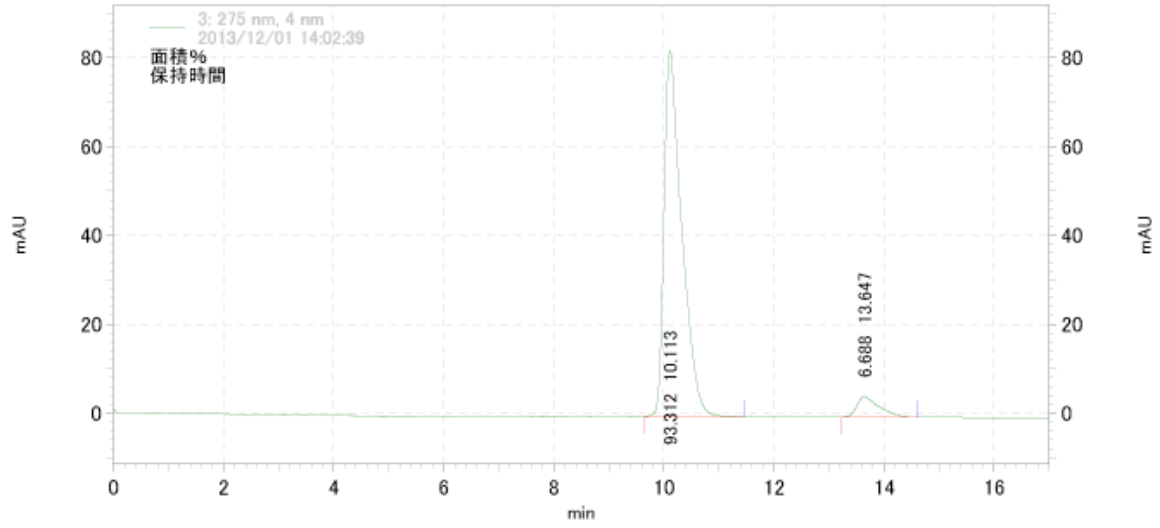
Figure S-66. The charts of chiral HPLC analyses of **3k**, which was obtained from the hydrogenation of **5k** in eq 3.



3: 275 nm, 4 nm結果

Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		10.13	23228763	89.326	BB
2		13.63	2775719	10.674	BB
ﾄｰﾀﾙ			26004482	100.000	

Figure S-67. The charts of chiral HPLC analyses of **3i-*d***, which obtained from the deuteration of **2i** in eq 4.



3: 275 nm, 4 nm結果

Pk #	名前	保持時間	面積	面積%	ﾍﾞｰｽﾗｲﾝｺｰﾄﾞ
1		10.11	7403505	93.312	BB
2		13.65	530661	6.688	BB
ﾄｰﾀﾙ			7934166	100.000	

Figure S-68. The charts of chiral HPLC analyses of **3i**, which obtained from the hydrogenation of **2i** under 1.0 MPa of H_2.