Contents

General considerations

Reactions were performed using standard glassware or were run in 2-dram vials with a PTFE/Liner screw caps and 8-dram vials using w/polyseal screw caps. Column chromatography was performed on 60Å silica gel (Dynamic Adsorbents Inc.). ^{1}H, ^{13}C, ^{19}F and 2D-NMR spectra were recorded on JEOL EC-400 or JEOL EC-500 spectrometers using residual solvent peak as a reference. Compounds for HRMS were analyzed by chemical ionization (CI) using Micromass Autospec Ultima spectrometer at the Mass Spectrometry Facility of the Department of Chemistry and Biochemistry of University of Texas-Austin. IR- spectra were obtained using a Perkin Elmer Spectrum 100 FT-IR spectrometer. Analytical thin layer chromatography was performed on silica gel IB-F (Baker-flex) by J. T. Baker. All procedures were performed under ambient air unless otherwise noted. Reagents and starting materials were obtained from commercial sources and used without further purification unless otherwise noted.

Substrate synthesis

1. Synthesis and characterization of starting amides

Amides were synthesized according to literature procedures from 8-aminoquinoline and corresponding acyl chlorides (Procedure **A**, amides: *N*-(quinolin-8-yl)benzamide, 4-trifluoromethyl-*N*-(quinolin-8-yl)benzamide, 4-bromo-*N*-(quinolin-8-yl)benzamide, 4-nitro-*N*-(quinolin-8-yl)benzamide, 2-methyl-*N*-(quinolin-8-yl)benzamide, 3-iodo-*N*-(quinolin-8-yl)benzamide, 4-methyl-*N*-(quinolin-8-yl)benzamide, *N*-(quinolin-8-yl)furan-2-carboxamide), *N*-(quinolin-8-yl)thiophene-2-carboxamide),[1] or carboxylic acids (Procedure **B**, amides: 2-methoxy-*N*-(quinolin-8-yl)benzamide and *N*-(quinolin-8-yl)cinnamamide)).[2] *N*-(Naphthalen-1-yl)picolinamide and *N*-(1-phenylethyl)picolinamide were synthesized according to Procedure **B** from picolinic acid and corresponding amine.

Procedure A:

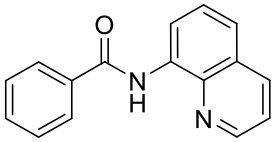
Synthesis of N-(quinolin-8-yl)benzamide is representative.

To a solution of 8-aminoquinoline (3.00 g, 21 mmol) and *N*,*N*-dimethyl-4-aminopyridine (80 mg, 0.65 mmol) in anhydrous CH_2Cl_2 (30 mL) under nitrogen Et_3N (3.3 mL, 24 mmol, 1.2 equiv)

[1] Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed*. **2013**, *52*, 4457.
[2] Tran, L. D.; Popov, I.; Daugulis, O. *J. Am. Chem. Soc*. **2012**, *134*, 18237.

was added and resulting solution was cooled to 0 °C. Benzoyl chloride (2.3 mL, 20 mmol) was added dropwise and reaction mixture was stirred at room temperature overnight. The mixture was quenched with water (30 mL) and extracted with CH_2Cl_2 (3 x 20 mL). Combined organic phase was dried over $MgSO_4$ and filtered. Concentration in vacuum followed by recrystallization from toluene afforded 4.6 g (94%) of *N*-(quinolin-8-yl)benzamide as a white solid.

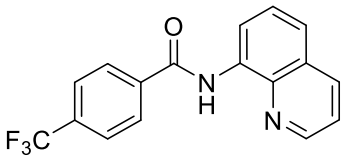
_N_-(Quinolin-8-yl)benzamide



This compound is known.[1]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.76 (s, 1H), 8.95 (dd, *J* = 7.6, 1.3 Hz, 1H), 8.85 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.14-8.04 (m, 2H), 7.68 – 7.52 (m, 5H) and 7.48 (dd, *J* = 8.2, 4.2 Hz, 1H).

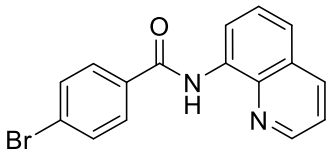
4-Trifluoromethyl-*N*-(quinolin-8-yl)benzamide



8-Aminoquinoline (3.00 g, 21 mmol), *N*,*N*-dimethyl-4-aminopyridine (80 mg, 0.65 mmol), Et_3N (3.3 mL, 24 mmol, 1.2 equiv), 4-trifluoromethylbenzoyl chloride (3.0 mL, 20 mmol), CH_2Cl_2 (30 mL). Recrystallization from hexanes/EtOAc 4:1 afforded 5.50 g (88%) of 4-trifluoromethyl-*N*-(quinolin-8-yl)benzamide as a white solid. This compound is known.[1]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.80 (s, 1H), 8.92 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.25 – 8.16 (m, 3H), 7.82 (d, *J* = 8.1 Hz, 2H), 7.65 – 7.56 (m, 2H) and 7.51 (dd, *J* = 8.3, 4.2 Hz, 1H).

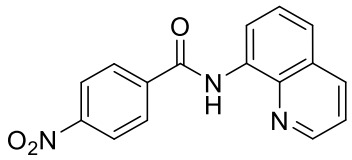
4-Bromo-*N*-(quinolin-8-yl)benzamide



8-Aminoquinoline (3.00 g, 21 mmol), *N*,*N*-dimethyl-4-aminopyridine (80 mg, 0.65 mmol), Et_3N (3.3 mL, 24 mmol, 1.2 equiv), 4-bromobenzoyl chloride (4.39 g, 20 mmol), CH_2Cl_2 (30 mL). Recrystallization from toluene afforded 5.84 g (89%) of 4-bromo-*N*-(quinolin-8-yl)benzamide as a white solid. This compound is known.[2]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.71 (s, 1H), 8.90 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.97 – 7.91 (m, 2H), 7.71 – 7.65 (m, 2H), 7.62 – 7.53 (m, 2H) and 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H).

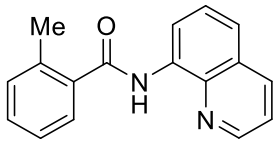
4-Nitro-*N*-(quinolin-8-yl)benzamide



8-Aminoquinoline (3.00 g, 21 mmol), *N*,*N*-dimethyl-4-aminopyridine (80 mg, 0.65 mmol), Et_3N (3.3 mL, 24 mmol, 1.2 equiv), 4-nitrobenzoyl chloride (3.71 g, 20 mmol), CH_2Cl_2 (30 mL). Recrystallization from hexanes/EtOAc 4:1 afforded 5.67 g (97%) of 4-nitro-*N*-(quinolin-8-yl)benzamide as a yellow solid. This compound is known.[3]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.83 (s, 1H), 8.91 (dd, *J* = 6.4, 2.5 Hz, 1H), 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.45 – 8.36 (m, 2H), 8.26-8.22 (m, 3H), 7.64-7.60 (m, 2H) and 7.52 (dd, *J* = 8.3, 4.2 Hz, 1H).

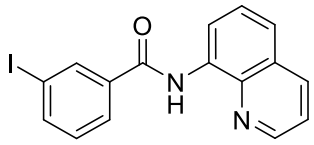
2-Methyl-*N*-(quinolin-8-yl)benzamide



8-Aminoquinoline (3.00 g, 21 mmol), *N*,*N*-dimethyl-4-aminopyridine (80 mg, 0.65 mmol), Et_3N (3.3 mL, 24 mmol, 1.2 equiv), 2-toluoyl chloride (2.6 mL, 20 mmol), CH_2Cl_2 (30 mL). Recrystallization from hexanes/EtOAc 1:1 afforded 3.91 g (75%) of 2-methyl-*N*-(quinolin-8-yl)benzamide as a white solid. This compound is known.[1]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.22 (s, 1H), 8.95 (d, *J* = 7.3 Hz, 1H), 8.78 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.41 (td, *J* = 7.5, 1.4 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 2H) and 2.61 (s, 3H).

3-Iodo-*N*-(quinolin-8-yl)benzamide



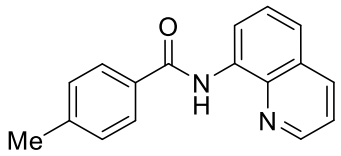
8-Aminoquinoline (1.50 g, 10.5 mmol), *N*,*N*-dimethyl-4-aminopyridine (40 mg, 0.33 mmol), Et_3N (1.65 mL, 12 mmol, 1.2 equiv), 3-iodobenzoyl chloride (2.67 g, 10 mmol), CH_2Cl_2 (15 mL). Recrystallization from hexanes/EtOAc 2:1 afforded 3.46 g (93%) of 3-iodo-*N*-(quinolin-8-yl)benzamide as a white solid. This compound is known.[4]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.67 (s, 1H), 8.90 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.41 (t, *J* = 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.02 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.91 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H) and 7.29 (t, *J* = 7.8 Hz, 1H).

[3] Truong, T.; Klimovica, K.; Daugulis, O. *J. Am. Chem. Soc*. **2013**, *135*, 9342.

[4] Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc*. **2005**, *127*, 13154.

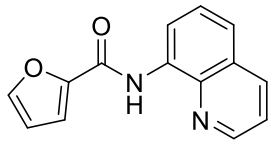
4-Methyl-*N*-(quinolin-8-yl)benzamide



8-Aminoquinoline (6.00 g, 42 mmol), *N*,*N*-dimethyl-4-aminopyridine (160 mg, 1.3 mmol), Et_3N (6.6 mL, 48 mmol, 1.2 equiv), 4-toluoyl chloride (5.3 mL, 40 mmol), CH_2Cl_2 (60 mL). Recrystallization from toluene afforded 9.0 g (86%) of amide 4-methyl-*N*-(quinolin-8-yl)benzamide as a white solid. This compound is known.[5]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.73 (s, 1H), 8.94 (dd, *J* = 7.6, 1.3 Hz, 1H), 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.02 – 7.96 (m, 2H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.53 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 2H), 2.45 (s, 3H).

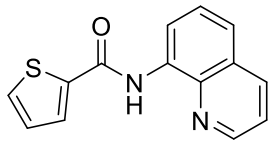
***N*-(Quinolin-8-yl)furan-2-carboxamide**



8-Aminoquinoline (1.50 g, 10.5 mmol), *N*,*N*-dimethyl-4-aminopyridine (40 mg, 0.33 mmol), Et_3N (1.65 mL, 12 mmol, 1.2 equiv), 2-furoyl chloride (1.0 mL, 10 mmol), CH_2Cl_2 (15 mL). Recrystallization from hexanes/EtOAc 4:1 afforded 1.93 g (81%) of *N*-(quinolin-8-yl)furan-2-carboxamide as a white solid. This compound is known.[1]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.77 (s, 1H), 8.96 – 8.80 (m, 2H), 8.16 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.62 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.31 (dd, *J* = 3.5, 0.7 Hz, 1H) and 6.58 (dd, *J* = 3.5, 1.7 Hz, 1H).

***N*-(Quinolin-8-yl)thiophene-2-carboxamide**



8-Aminoquinoline (1.50 g, 10.5 mmol), *N*,*N*-dimethyl-4-aminopyridine (40 mg, 0.33 mmol), Et_3N (1.65 mL, 12 mmol, 1.2 equiv), 2-thiophenecarbonyl chloride (1.1 mL, 10 mmol), CH_2Cl_2 (30 mL). Recrystallization from hexanes/EtOAc 4:1 afforded 2.33 g (92%) of *N*-(quinolin-8-yl)furan-2-carboxamide as a white solid. This compound is known.[6]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 10.61 (s, 1H), 8.90 – 8.80 (m, 2H), 8.18 (dd, J = 8.3, 1.6 Hz, 1H), 7.84 (dd, J = 3.7, 1.1 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.54 (dd, J = 8.3, 1.4 Hz, 1H), 7.48 (dd, J = 8.2, 4.2 Hz, 1H), 7.19 (dd, J = 5.0, 3.7 Hz, 1H).

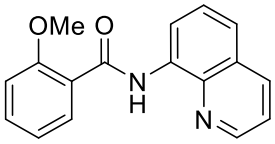
[5] Suess, A. M.; Ertem, M. Z.; Cramer, C. J.; Stahl, S. S. *J. Am.Chem. Soc.* **2013**,*135*, 9797.

Procedure B:

Synthesis of 2-methoxy-N-(quinolin-8-yl)benzamide is representative.

o-Anisic acid (2.28 g, 15 mmol, 1.5 equiv) and Et_3N (4.8 mL, 35 mmol, 3.5 equiv) were dissolved in CH_2Cl_2 (30 mL), flask was flushed with nitrogen and the resulting mixture was cooled to 0 °C. Ethyl chloroformate (1.4 mL, 15 mmol, 1.5 equiv) was added dropwise and solution was stirred at 0 °C for 30 minutes followed by dropwise addition of 8-aminoquinoline (1.44 g, 10 mmol) solution in CH_2Cl_2 (10 mL). The resulting suspension was warmed up to room temperature and stirred overnight. After completion, water (30 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The combined organic phase was dried over $MgSO_4$ and filtered, solvent was evaporated. Purification by column chromatography on silica gel (hexanes/EtOAc from 4:1 to 2:1) afforded 1.97 g (71%) of 2-methoxy-*N*-(quinolin-8-yl)benzamide as a white solid.

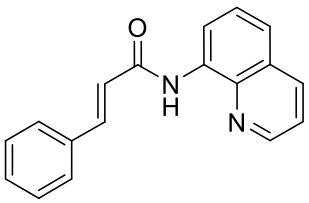
2-Methoxy-*N*-(quinolin-8-yl)benzamide



This compound is known.[5]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 12.35 (s, 1H), 9.04 (dd, *J* = 7.7, 1.1 Hz, 1H), 8.85 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.36 (dd, *J* = 7.8, 1.8 Hz, 1H), 8.15 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.57 (t, *J* = 7.9 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.43 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H) and 4.18 (s, 3H).

***N*-(Quinolin-8-yl)cinnamamide**

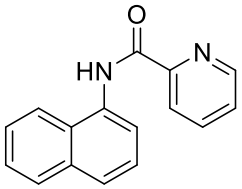


Cinnamic acid (2.22 g, 15 mmol, 1.5 equiv), Et_3N (4.8 mL, 35 mmol, 3.5 equiv), ethyl chloroformate (1.4 mL, 15 mmol, 1.5 equiv), 8-aminoquinoline (1.44 g, 10 mmol), CH_2Cl_2 (40 mL). Purification by column chromatography on silica gel (hexanes/EtOAc from 4:1 to 2:1) afforded 1.85 g (67%) of *N*-(quinolin-8-yl)cinnamamide as a white solid. This compound is known.[6]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 10.02 (s, 1H), 8.92 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.83 (d, *J* = 15.6 Hz, 1H), 7.65 – 7.51 (m, 4H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.46 – 7.38 (m, 3H) and 6.82 (d, *J* = 15.5 Hz, 1H).

[6] Ano, Y.; Tobisu, M.; Chatani, N. *Org. Lett.* **2012**, *14*, 354.

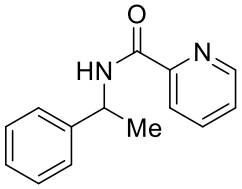
***N*-(Naphthalen-1-yl)picolinamide**



Picolinic acid (17.24 g, 140 mmol, 1.75 equiv), Et_3N (39.0 mL, 280 mmol, 3.5 equiv), ethyl chloroformate (13.4 mL, 140 mmol, 1.75 equiv), 1-naphthylamine (11.46 g, 80 mmol), CH_2Cl_2 (160 mL). Purification by column chromatography on silica gel (gradient hexanes/EtOAc from 4:1 to 1:1) afforded 12.78 g (65%) of *N*-(naphthalen-1-yl)picolinamide as a white solid. This compound is known.[7]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 10.77 (s, 1H), 8.69 (d, *J* = 4.7 Hz, 1H), 8.43 (dd, *J* = 7.5, 0.6 Hz, 1H), 8.36 (dd, *J* = 4.8, 4.0 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.96 – 7.88 (m, 2H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.62 – 7.47 (m, 4H).

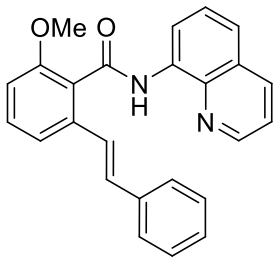
***N*-(1-Phenylethyl)picolinamide**



Picolinic acid (1.85 g, 15 mmol, 1.5 equiv), Et_3N (4.8 mL, 35 mmol, 3.5 equiv), ethyl chloroformate (1.4 mL, 15 mmol, 1.5 equiv), 1-phenethylamine (1.3 mL, 10 mmol), CH_2Cl_2 (40 mL). Purification by column chromatography on silica gel (gradient hexanes/EtOAc from 4:1 to 1:1) afforded 2.21 g (99%) of *N*-(1-phenylethyl)picolinamide as a white solid. This compound is known.[2]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.53 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 8.34 (d, *J* = 6.6 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.38 – 7.33 (m, 2H), 7.26 (tt, *J* = 6.9, 1.3 Hz, 1H), 5.38 – 5.28 (m, 1H), 1.63 (d, *J* = 6.9 Hz, 3H).

(*E*)-2-Methoxy-*N*-(quinolin-8-yl)-6-styrylbenzamide (Scheme 4)



The vial was charged with 2-methoxy-*N*-(quinolin-8-yl)benzamide (195 mg, 0.7 mmol), $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), AgOAc (175 mg, 1.05 mmol), and 2-iodostyrene (322 mg, 1.4 mmol). The resulting mixture was heated neat at 90 °C for 8 h. Reaction mixture was diluted with EtOAc (10 mL) and filtered through a pad of Celite. Filtrate was evaporated under reduced pressure. Purification by column chromatography on silica gel (toluene/EtOAc 30:1) afforded 170 mg (64%) of (*E*)-2-methoxy-*N*-(quinolin-8-yl)-6-styrylbenzamide as a white solid. This compound is known.[8]

[7] Nadres, E. T.; Santos, G. I. F.; Shabashov, D.; Daugulis, O. *J. Org. Chem*. **2013**, *78*, 9689.

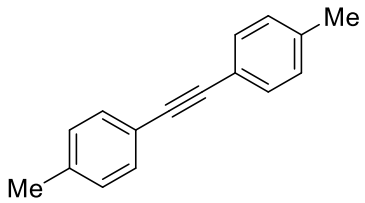
[8]Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.17 (s, 1H), 9.06 (d, *J* = 7.6 Hz, 1H), 8.71 (d, *J* = 4.2 Hz, 1H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.63 (t, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.45 – 7.11 (m, 10 H), 6.93 (dd, *J* = 6.4, 2.3 Hz, 1H), 3.87 (s, *J* = 0.7 Hz, 3H).

2. Synthesis and characterization of alkyne

Di-4-tolylacetylene was synthesized according to literature procedure by Sonogashira-type cross-coupling reaction.[9]

Di-4-tolylacetylene



Iodotoluene (3.72 g, 15 mmol), K_2CO_3 (6.22 g, 45 mmol, 3 equiv), CuBr (0.43 g, 3 mmol, 20 mol%), DBU (0.45 mL, 3 mmol, 20 mol%), tolylacetylene (2.3 mL, 18 mmol, 1.2 equiv), DMF (30 mL), 145 °C, 16 h. Column chromatography on silica gel using hexanes/EtOAc 1:1 and recrystallization from hexanes afforded 1.72 g (56%) di-4-tolylacetylene as a colorless crystalline solid. This compound is known.[8]

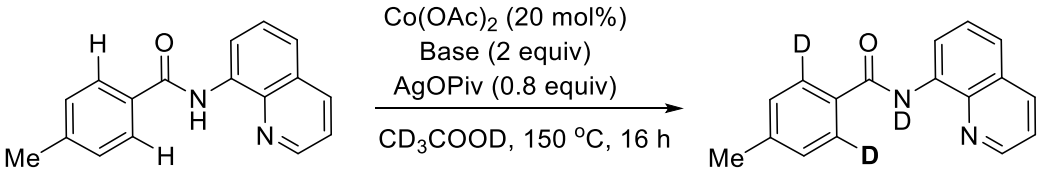
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 7.42 (d, *J* = 8.1 Hz, 4H), 7.15 (d, *J* = 7.8 Hz, 4H), 2.37 (s, 6H).

Cobalt-catalyzed sp^2 C-H functionalization

1. H/D exchange studies

General procedure for H/D exchange experiments.

2-Dram vial with a screw cap (PTFE/Liner) was charged with 4-methyl-*N*-(quinolin-8-yl)benzamide (26.2 mg, 0.1 mmol), AgOPiv (16.7 mg, 0.08 mmol, 0.8 equiv), base (0.2 mmol, 2 equiv), $Co(OAc)_2$ (4.0 mg, 0.02 mmol, 20 mol%) and CD_3COOD (0.7 mL). Resulting mixture was heated at 150 °C temperature for 16 h, cooled to room temperature and analyzed by ^{1}H-NMR spectroscopy.



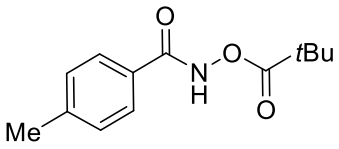
[9]Thakur, K.G.; Sekar, G. *Synthesis*, **2009**, *16*, 2785.

Table S1

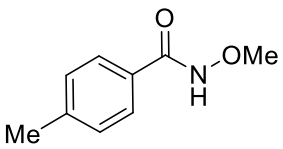
Entry	Base	H/D exchange[a], %
1	KOAc	100
2	NaOAc	110
3	CsOAc	80
4	LiOAc	105
5	CsOPiv	110
6	**NaOPiv**	**130**
7	K_2CO_3	90
8[b]	NaOAc	0

[a] H/D exchange is 200% if both *o*-hydrogens are exchanged. [b] Reaction was performed without $Co(OAc)_2$.

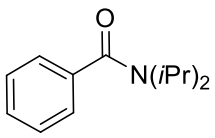
Substrates with other directing groups investigated in H/D exchange studies were not reactive and/or gave considerable amount of decomposition products.



Decomposition



Decomposition



No H/D exchange

2. Optimization of cobalt-catalyzed sp^2 C-H functionalization

2.1. Solvent

General procedure for solvent optimization experiments.

2-Dram vial with a screw cap (PTFE/Liner) was charged with 4-methyl-*N*-(quinolin-8-yl)benzamide (26.2 mg, 0.1 mmol), AgOPiv (16.7 mg, 0.08 mmol, 0.8 equiv), NaOPiv (24.8 mg, 0.2 mmol, 2 equiv), $Co(OAc)_2$ (4.0 mg, 0.02 mmol, 20 mol%), di-4-tolylacetylene (31.0 mg, 0.15 mmol, 1.5 equiv), and solvent (0.7 mL). Resulting mixture was heated at 150 °C for 12 h, cooled to room temperature and analyzed by TLC (hexanes/EtOAc 4:1, hexanes/EtOAc 1:1) and ^{1}H-NMR spectroscopy.

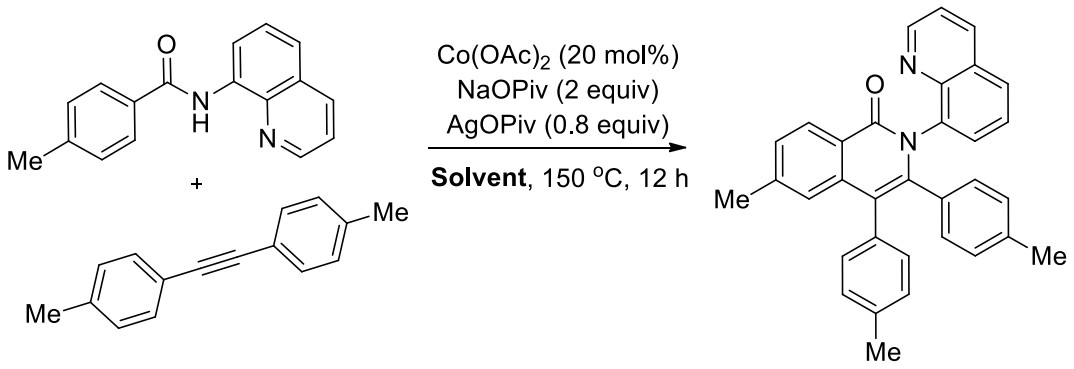


Table S2

Entry	Solvent	Substrate : Product ratio
1[a]	*o*-Dichlorobenzene	2:1 (33%)
2	DMF	>99:1
3	DMSO	>99:1
4	*n*BuOH	>99:1
5	NMP	>99:1
6	DMPU	>99:1
7[a]	**CF_3CH_2OH**	**1:>99 (63%)**
8	*N*,*N*-Dimethylacetamide	>99:1
9[a]	Toluene	3:1 (30%)
10[a]	AcOH	4:1 (18%)
11	Mesitylene	>99:1

[a] NMR yield using 1,1,2-trichloroethane as internal standard in parentheses.

2.2. Temperature

General procedure for temperature optimization experiments.

2-Dram vial with a screw cap (PTFE/Liner) was charged with 4-methyl-*N*-(quinolin-8-yl)benzamide (26.2 mg, 0.1 mmol), AgOAc (33.0 mg, 0.2 mmol, 2 equiv), NaOPiv (24.8 mg, 0.2 mmol, 2 equiv), $Co(OAc)_2$ (4.0 mg, 0.02 mmol, 20 mol%), di-4-tolylacetylene (31.0 mg, 0.15 mmol, 1.5 equiv), and CF_3CH_2OH (0.7 mL). Resulting mixture was heated at corresponding temperature for 12 – 18 h, cooled to room temperature and analyzed by TLC (hexanes/EtOAc 4:1, hexanes/EtOAc 1:1) and ^{1}H-NMR spectroscopy.

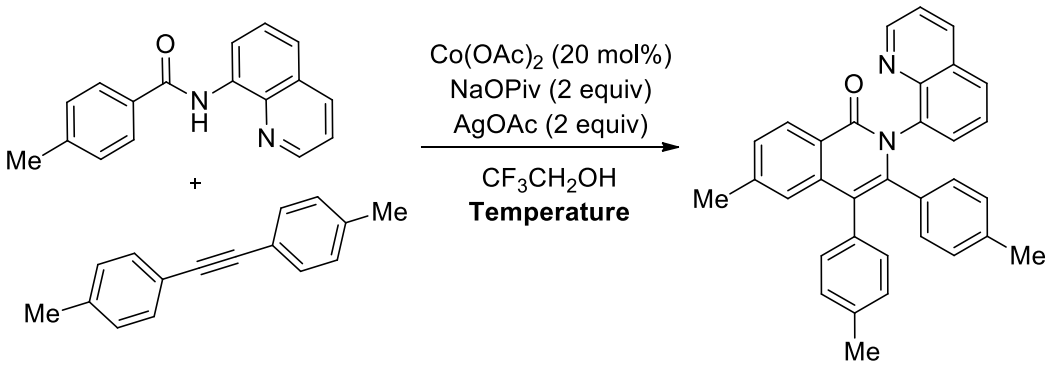


Table S3

Entry	Temperature, °C	Time, h	Substrate : Product ratio
1[a]	150	12	1:>99 (60%)
2[a]	100	12	1:>99 (58%)
3[a]	**60**	**12**	**1:>99 (60%)**
4[a,b]	**60**	**12**	**1:>99 (65%)**
5[a]	r.t.	18	4:1 (16%)

[a] NMR yield using 1,1,2-trichloroethane as internal standard in parentheses. [b] Reaction was performed using $Co(OAc)_2 \cdot 4H_2O$ (5.0 mg, 0.02 mmol, 20 mol%).

2.3. Oxidant

General procedure for oxidant optimization experiments.

2-Dram vial with a screw cap (PTFE/Liner) was charged with 4-methyl-*N*-(quinolin-8-yl)benzamide (26.2 mg, 0.1 mmol), oxidant (0.05 - 0.2 mmol, 0.5 - 2 equiv), NaOPiv (24.8 mg, 0.2 mmol, 2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (5.0 mg, 0.02 mmol, 20 mol%), di-4-tolylacetylene (20.6 mg, 0.1 mmol, 1 equiv), and CF_3CH_2OH (0.7 mL). Resulting mixture was heated at 60 °C for 2 - 16 h, cooled to room temperature and analyzed by TLC (hexanes/EtOAc 4:1, hexanes/EtOAc 1:1) and ^{1}H-NMR spectroscopy.

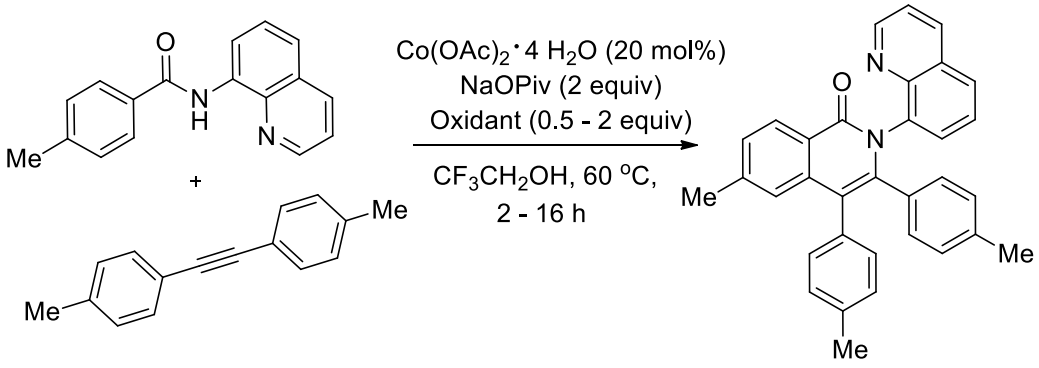


Table S4

Entry	Oxidant	Time, h	Substrate : Product ratio
1[a]	$AgNO_3$ (2 equiv)	2	1:>99 (70%)
2	$Cu(OAc)_2$ (2 equiv)	12	>99:1
3	$K_2S_2O_8$ (2 equiv)	12	>99:1
4[b]	$K_2S_2O_8$ (2 equiv)	16	>99:1
5	1,4-Benzoquinone (1 equiv)	12	>99:1
6[a,c]	$PhI(OAc)_2$ (2 equiv)	2	1:>99 (15%)
7[a,c]	$PhI(OAc)_2$ (1 equiv)	2	1:1 (11%)
8[a]	Oxone (2 equiv)	16	2:1 (33%)
9[a,b]	Oxone (2 equiv)	16	10:1 (<5%)
10[a]	Oxone (1 equiv) $Mn(OAc)_2$ (1 equiv)	16	1:4 (68%)
11[a]	Oxone (2 equiv) $Mn(OAc)_2$ (2 equiv)	16	1:4 (65%)
12[d]	Oxone (2 equiv) $Mn(OAc)_2$ (2 equiv)	16	>99:1
13[a]	**$Mn(OAc)_2$ (2 equiv)**	**16**	**1:10 (79%)**

[a] NMR yield using 1,1,2-trichloroethane as internal standard in parentheses. [b] Reaction was performed in 1 mL of MeOH/H_2O (10:1). [c] Formation of by-products was observed. [d] Reaction was performed without $Co(OAc)_2 \cdot 4H_2O$.

Reaction oxidant optimization experiments at 80 °C using 10 mol% $Co(OAc)_2 \cdot 4H_2O$ (same general procedure as for Table S4).

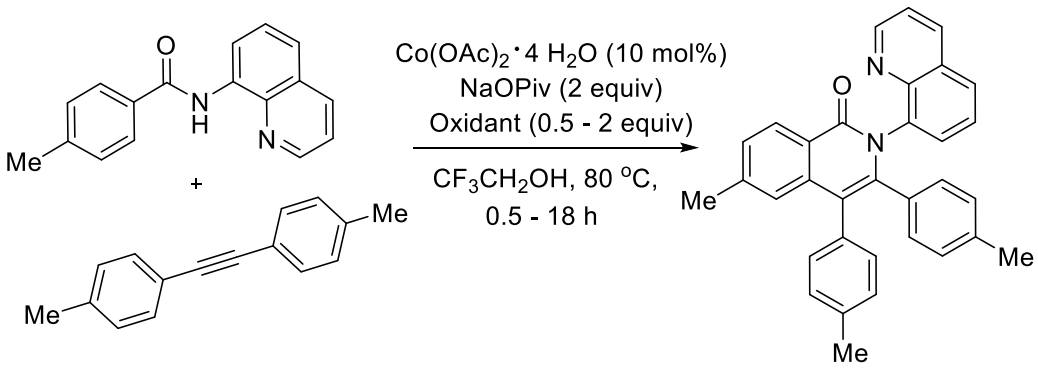


Table S5

Entry	Oxidant	Time, h	Substrate : Product ratio
1[a]	$Mn(OAc)_2$ (2 equiv)	2	1:>99 (96%)
2[a]	**$Mn(OAc)_2$ (1 equiv)**	**2**	**1:10 (87%)**
3[a]	$Mn(OAc)_2$ (0.5 equiv)	12	1:10 (85%)
4[a]	$Mn(OAc)_2$ (0.5 equiv)	2	1:2 (63%)
5[a]	$Mn(OAc)_2$ (0.5 equiv)/O_2	2	1:2 (64%)
6[b]	$Mn(OAc)_2$ (0.5 equiv)/inert atmosphere	12	>99:1
7	$Mn(OAc)_2$ (0.1 equiv)	2	>99:1
8[a]	$Mn(OAc)_3 \cdot 2\ H_2O$ (2 equiv)	2	1:5 (30%)
9[a]	$Mn(OAc)_3 \cdot 2\ H_2O$ (0.5 equiv)	0.5	3:1 (25%)
10[a]	O_2	18	1:1 (50%)

[a] NMR yield using 1,1,2-trichloroethane as internal standard in parentheses. [b] Deoxygenated CF_3CH_2OH was used under inert atmosphere.

Alkenylation Comparison with Air or Oxygen Oxidants

6-Dram vial with a screw cap (PTFE/Liner) was charged with *N*-(quinolin-8-yl)benzamide (62 mg, 0.25 mmol), $Mn(OAc)_2$ (43.5 mg, 0.25 mmol, 1 equiv), NaOPiv (24.8 mg, 0.2 mmol, 2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (5.0 mg, 0.02 mmol, 20 mol%), diphenylacetylene (53 mg, 0.3 mmol, 1.2 equiv), and CF_3CH_2OH (2.5 mL). Resulting mixture was heated at 80 °C for 8 h, cooled to room temperature and analyzed by ^{1}H-NMR spectroscopy.

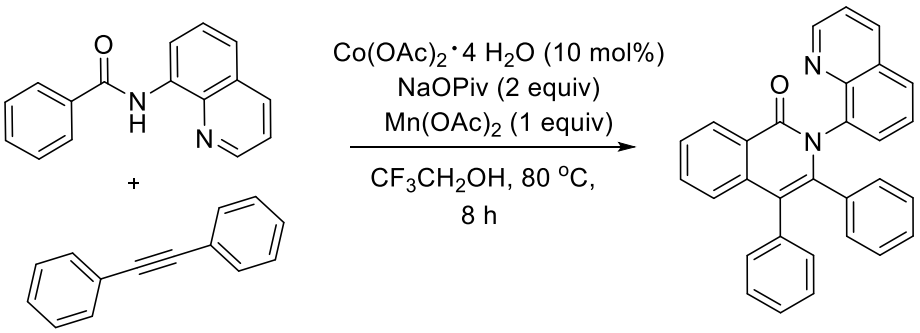


Table S6

Entry	Substrate : Product ratio	NMR yield, % [a]
1[b]	1:7	85
2[c]	1:4.3	80
3[d]	1:12	93

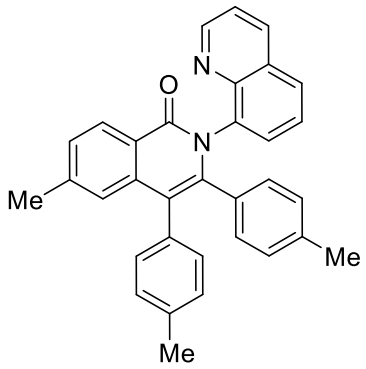
[a] NMR yield using 1,1,2-trichloroethane as internal standard. [b] Reaction vial was opened after 2, 4, and 6h. [c] Reaction was performed without opening reaction vial. [d] Reaction mixture was saturated with O_2.

3. Cobalt-catalyzed sp^2 C-H alkenylation/cyclization and characterization of products

General procedure for cobalt-catalyzed sp^2 C-H alkenylation/cyclization.

A 8 dram vial equipped with a magnetic stir bar was charged with amide (0.5 mmol), alkyne (0.6 – 0.75 mmol, 1.2 – 1.5 equiv), $Co(OAc)_2 \cdot 4H_2O$ (0.05 – 0.5 mmol, 10 mol% – 1 equiv), NaOPiv (1 mmol, 2 equiv), $Mn(OAc)_2$ (0.5 – 1.0 mmol, 1 – 2 equiv), and CF_3CH_2OH (5 mL). The reaction mixture was heated at 80 °C or 100 °C for indicated time. Reaction was monitored by TLC after 2 h, 4 h, 6 h, 12 h, and 16 h to determine the completion time. The reaction mixture was cooled to room temperature and solvent was evaporated. To the residue potassium sodium tartrate (10 mL of 1M aqueous solution) was added and mixture was extracted with CH_2Cl_2 (3 x 20 mL). Combined organic phase was dried over $MgSO_4$, filtered, and solvent was evaporated. Product was purified using column chromatography on silica gel using appropriate eluent. After purification product was dried under reduced pressure. *Note: the vessel should be opened to air several times during the reaction to ensure presence of sufficient amount of oxygen.*

6-Methyl-3,4-di-p-tolyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 1)



4-Methyl-*N*-(quinolin-8-yl)benzamide (131 mg, 0.5 mmol), di-4-tolylacetylene (124 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 12 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 221 mg (95%) of a white solid was obtained. R_f = 0.48 (hexanes/EtOAc 1:1), mp 261 – 263 °C (Et_2O).

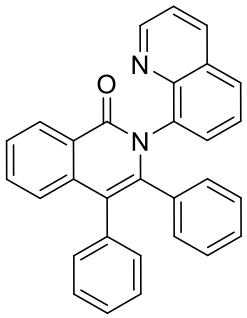
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.92 (dd, *J* = 4.0, 1.3 Hz, 1H), 8.46 (d, *J* = 8.1 Hz, 1H), 8.04 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 7.1 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.11 – 7.01 (m, 3H), 6.97 (d, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 6.61 (dd, *J* = 10.2, 8.6 Hz, 2H), 6.27 (d, *J* = 7.6 Hz, 1H), 2.39 (s, 3H), 2.28 (s, 3H), 1.93 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.7, 150.6, 144.8, 142.8, 141.9, 138.4, 137.9, 136.5, 135.9, 135.8, 133.7, 132.2, 131.6, 131.5, 130.8, 130.6, 129.5, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.3, 127.0, 125.7, 125.3, 123.3, 121.3, 118.2, 22.0, 21.2, 21.0.

HRMS calcd. for $C_{33}H_{26}N_2O$ $[M]^+$: 466.2045; found: 466.2044.

FT-IR (neat, cm^{-1}) υ 1651, 1614, 1483, 1328.

3,4-Diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 2, Entry 1)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 6 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 166 mg (78%) of a white solid was obtained. R_f = 0.34 (hexanes/EtOAc 1:1), mp 250 – 252 °C (Et_2O).

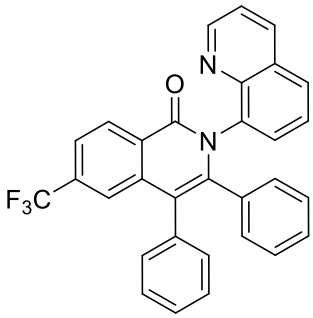
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.93 (d, *J* = 2.8 Hz, 1H), 8.61 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 9.2 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 6.9 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.40 – 7.13 (m, 9H), 6.99 (d, *J* = 7.3 Hz, 1H), 6.84 (t, *J* = 7.8 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.72 (t, *J* = 7.8 Hz, 1H), 6.49 (t, *J* = 7.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.6, 150.7, 144.6, 141.7, 138.0, 137.6, 136.4, 135.9, 134.8, 132.4, 131.7, 131.6, 130.7, 130.6, 129.6, 128.6, 128.5, 128.3, 127.9, 127.7, 127.1, 126.7, 126.6, 126.5, 126.3, 125.6, 125.5, 125.4, 121.4, 118.4.

HRMS calcd. for $C_{30}H_{20}N_2O$ $[M]^+$: 424.1576; found: 424.1577.

FT-IR (neat, cm^{-1}) υ 1652, 1332.

3,4-Diphenyl-2-(quinolin-8-yl)-6-(trifluoromethyl)isoquinolin-1(*2H*)-one (Table 2, Entry 2)



4-Trifluoromethyl-*N*-(quinolin-8-yl)benzamide (158 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 6 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 171 mg (70%) of a white solid was obtained. R_f = 0.60 (hexanes/EtOAc 1:1), mp 243 – 245 °C (Et_2O).

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.94 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.70 (d, *J* = 8.6 Hz, 1H), 8.06 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.73 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.60 (s, 1H), 7.50 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.30 – 7.16 (m, 5H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.85 (t, *J* = 7.5 Hz, 1H), 6.77 – 6.71 (m, 2H), 6.51 (t, *J* = 7.5 Hz, 1H).

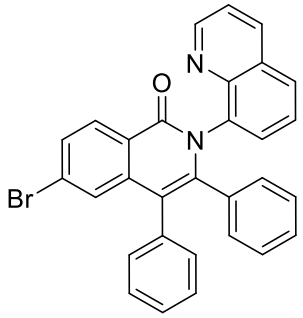
^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 161.9, 150.8, 144.4, 143.4, 138.2, 137.1, 136.1, 135.4, 134.3, 134.0 (q, J_{C-F} = 32.4 Hz), 131.6, 131.4, 130.7, 130.5, 129.5, 129.4, 128.8, 128.7, 128.3, 128.1, 127.6, 127.5, 127.2, 126.7, 126.5, 125.7, 123.8 (q, J_{C-F} = 272.3 Hz), 122.8 (m), 122.6 (m), 121.6, 118.2.

^{19}F-NMR (470 MHz, $CDCl_3$, ppm) δ -62.75.

HRMS calcd. for $C_{31}H_{19}N_2OF_3$ $[M]^+$: 492.1449; found: 492.1452.

FT-IR (neat, cm^{-1}) υ 1655, 1315, 1306, 1169, 1135, 1072.

6-Bromo-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 2, Entry 3)



4-Bromo-*N*-(quinolin-8-yl)benzamide (164 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 6 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 182 mg (73%) of a white solid was obtained. R_f = 0.48 (hexanes/EtOAc 1:1), mp 307 – 309 °C (Et_2O).

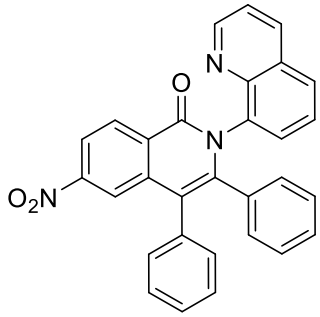
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.93 (d, *J* = 2.8 Hz, 1H), 8.44 (d, *J* = 8.6 Hz, 1H), 8.04 (d, *J* = 8.6 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.49 (d, *J* = 7.0 Hz, 1H), 7.46 (s, 1H), 7.39 – 7.34 (m, 2H), 7.29 – 7.14 (m, 5H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.76 – 6.70 (m, 2H), 6.49 (t, *J* = 8.0 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.2, 150.8, 144.5, 143.3, 139.6, 137.3, 136.0, 135.7, 134.5, 131.6, 131.4, 130.7, 130.5, 130.2, 129.9, 129.5, 128.7, 128.2, 128.0, 127.9, 127.8, 127.3, 127.0, 126.6, 126.4, 125.7, 124.2, 121.5, 117.5.

HRMS calcd. for $C_{30}H_{19}N_2O^{79}Br$ $[M]^+$: 502.0681; found: 502.0676.

FT-IR (neat, cm^{-1}) υ 1653, 1592, 1320.

6-Nitro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 2, Entry 4)



4-Nitro-*N*-(quinolin-8-yl)benzamide (147 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 6 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 183 mg (78%) of a yellow solid was obtained. R_f = 0.40 (hexanes/EtOAc 1:1), mp 275 – 277 °C (Et_2O).

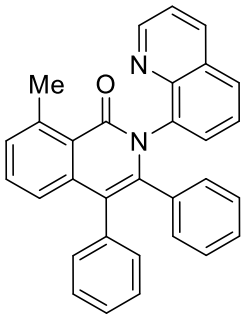
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.93 (dd, *J* = 4.6, 1.7 Hz, 1H), 8.73 (d, *J* = 8.6 Hz, 1H), 8.26 (dd, *J* = 8.6, 2.3 Hz, 1H), 8.18 (d, *J* = 2.2 Hz, 1H), 8.08 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.69 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.50 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.31 – 7.15 m, 5H), 6.97 (d, *J* = 8.0, 1H), 6.86 (t, *J* = 8.6 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 1H), 6.52 (t, *J* = 7.5 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 161.5, 150.9, 150.5, 144.4, 144.3, 138.9, 136.9, 136.1, 135.0, 134.1, 131.6, 131.3, 130.5, 130.4, 129.4, 129.1, 129.0, 128.7, 128.5, 128.3, 127.6, 127.5, 126.8, 126.6, 125.7, 124.0, 121.7, 121.2, 120.2, 118.3.

HRMS calcd. for $C_{30}H_{19}N_3O_3$ $[M]^+$: 469.1426; found: 469.1425.

FT-IR (neat, cm^{-1}) υ 1662, 1522, 1339.

8-Methyl-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 2, Entry 5)



2-Methyl-*N*-(quinolin-8-yl)benzamide (131 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 6 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 188 mg (86%) of a white solid was obtained. R_f = 0.60 (hexanes/EtOAc 1:1), mp 166 – 168 °C (Et_2O).

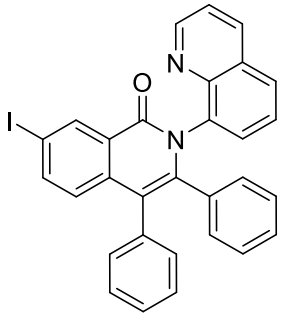
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.95 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.02 (d, *J* = 6.8 Hz, 1H), 7.63 (d, *J* = 8.6 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.35 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.24 – 7.12 (m, 6H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.83 (t, *J* = 6.9 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.70 (t, *J* = 7.5 Hz, 1H), 6.48 (t, *J* = 7.5 Hz, 1H), 3.00 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 163.4, 150.6, 144.7, 142.4, 141.7, 139.9, 138.0, 137.2, 135.9, 134.9, 131.8, 131.7, 131.5, 130.9, 130.6, 129.9, 129.6, 128.7, 128.3, 127.9, 127.7, 127.0, 126.5, 126.4, 126.2, 125.7, 124.0, 121.4, 118.4, 24.3.

HRMS calcd. for $C_{31}H_{22}N_2O$ $[M]^+$: 438.1732; found: 438.1733.

FT-IR (neat, cm^{-1}) υ 1652, 1595, 1489, 1335, 1304, 1239.

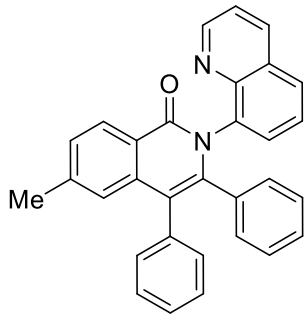
5-Iodo-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 2, Entry 6)



3-Iodo-*N*-(quinolin-8-yl)benzamide (187 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 6 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 231 mg (84%) of a white solid was obtained. R_f = 0.68 (hexanes/EtOAc 1:1), mp 257 – 259 °C (Et_2O).

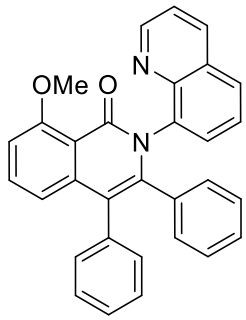
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.94 (dd, *J* = 4.6, 1.7 Hz, 1H), 8.92 (d, *J* = 1.7 Hz, 1H), 8.05 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.85 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.66 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.48 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.21 – 7.26 (m, 2H), 7.18 – 7.11 (m, 3H), 7.05 (d, *J* = 8.6 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.84 (t, *J* = 6.9 Hz, 1H), 6.75 – 6.70 (m, 2H), 6.49 (t, *J* = 7.5 Hz, 1H).
^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 161.3, 150.7, 144.4, 142.6, 141.0, 137.3, 137.2, 137.1, 136.1, 135.9, 134.5, 131.6, 131.4, 130.7, 130.5, 129.5, 128.7, 128.6, 128.1, 127.8, 127.4, 127.3, 127.1, 126.9, 126.7, 126.4, 125.7, 121.5, 118.1, 91.6.
HRMS calcd. for $C_{30}H_{19}N_2OI$ $[M]^+$: 550.0542; found: 550.0542.
FT-IR (neat, cm^{-1}) υ 1652, 1591, 1490, 1470, 1322.

6-Methyl-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one



4-Methyl-*N*-(quinolin-8-yl)benzamide (131 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 7 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 174 mg (80%) of a white solid was obtained. R_f = 0.35 (hexanes/EtOAc 1:1), mp 285 – 287 °C (Et_2O).
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.95 (d, *J* = 2.9 Hz, 1H), 8.50 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.33 (m, 3H), 7.28 – 7.23 (m, 2H), 7.19 – 7.13 (m, 3H), 7.10 (s, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.70 (t, *J* = 7.5 Hz, 1H), 6.48 (t, *J* = 7.5 Hz, 1H) and 3.06 (s, 3H).
^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.6, 150.6, 144.5, 142.9, 141.8, 138.1, 137.6, 136.6, 136.0, 134.9, 131.8, 131.6, 130.9, 130.7, 129.7, 128.6, 128.4, 128.3, 128.1, 127.9, 127.6, 127.0, 126.6, 126.5, 126.3, 125.7, 125.2, 123.4, 121.4, 118.3 and 22.0.
HRMS calcd. for $C_{31}H_{22}N_2O$ $[M]^+$: 438.1732; found: 438.1730.
FT-IR (neat, cm^{-1}) υ 1652, 1613, 1491, 1480, 1325.

8-Methoxy-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 2, Entry 7)



2-Methoxy-*N*-(quinolin-8-yl)benzamide (139 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 18 h, 80 °C. After column chromatography (hexanes/EtOAc 2:1, followed by EtOAc, then EtOAc/MeOH

95:5) 169 mg (74%) of a white solid was obtained. R_f = 0.24 (EtOAc), mp 244 – 246 °C (Et_2O).

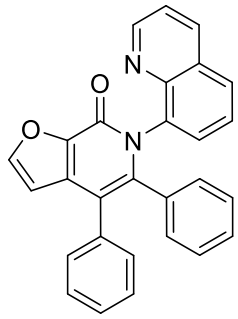
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.91 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.00 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.60 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.32 (dd, *J* = 8.6, 4.0 Hz, 1H), 7.26 -7.10 (m, 5H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.82 (t, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.69 (t, *J* = 7.5 Hz, 1H), 6.47 (t, *J* = 8.0 Hz, 1H), 3.95 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 161.5, 161.0, 150.5, 144.9, 142.6, 141.3, 138.0, 137.2, 135.8, 134.9, 132.8, 131.9, 131.8, 131.0, 130.5, 129.5, 128.4, 128.2, 127.9, 127.7, 127.0, 126.5, 126.4, 126.3, 125.5, 121.2, 117.9, 117.6, 115.1, 108.1, 56.1.

HRMS calcd. for $C_{31}H_{22}N_2O_2$ $[M]^+$: 454.1681; found: 454.1678.

FT-IR (neat, cm^{-1}) υ 1654, 1597, 1556, 1491, 1471, 1266, 1095.

4,5-Diphenyl-6-(quinolin-8-yl)furo[2,3-c]pyridin-7(*6H*)-one (Table 2, Entry 8)



N-(Quinolin-8-yl)furan-2-carboxamide (119 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (hexanes/EtOAc 2:1, followed by EtOAc, then EtOAc/MeOH 95:5) 168 mg (81%) of a white solid was obtained. R_f = 0.40 (EtOAc), mp 269 – 271 °C (Et_2O).

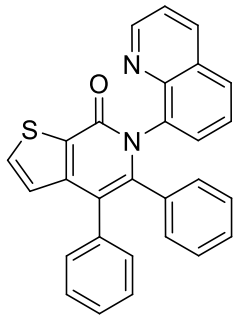
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.93 (d, *J* = 3.7 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 0.9 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.21 – 7.10 (m, 5H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.86 (t, *J* = 7.3 Hz, 1H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.62 (d, *J* = 0.9 Hz, 1H), 6.53 (t, *J* = 7.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 153.5, 150.8, 148.2, 144.6, 142.4, 142.2, 136.9, 136.2, 136.0, 134.5, 134.3, 131.0, 131.0, 130.3, 130.2, 128.8, 128.7, 127.9, 127.5, 126.8, 126.6, 126.5, 125.7, 121.5, 114.6, 107.7.

HRMS calcd. for $C_{28}H_{18}N_2O_2$ $[M]^+$: 414.1368; found: 414.1361.

FT-IR (neat, cm^{-1}) υ 1674, 1493.

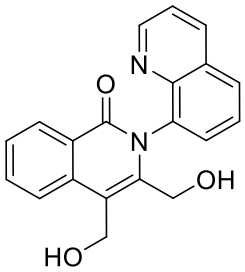
4,5-Diphenyl-6-(quinolin-8-yl)thieno[2,3-c]pyridin-7(6H)-one (Table 2, Entry 9)



N-(Quinolin-8-yl)thiophene-2-carboxamide (127 mg, 0.5 mmol), diphenylacetylene (107 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 20 h, 80 °C. After column chromatography (hexanes/EtOAc 4:1 to 1:1, followed by EtOAc) 185 mg (86%) of a white solid was obtained. This compound is known.[10]

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.93 – 8.88 (m, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.74 – 7.60 (m, 2H), 7.50 (d, *J* = 7.0 Hz, 1H), 7.43 – 7.31 (m, 2H), 7.31 – 7.09 (m, 5H), 7.05 (d, *J* = 5.0 Hz, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.85 (t, *J* = 7.2 Hz, 1H), 6.81 – 6.72 (m, 2H), 6.52 (t, *J* = 7.2 Hz, 1H).

3,4-Bis(hydroxymethyl)-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 3, Entry 1)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), 2-butyne-1,4-diol (52 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (hexanes/EtOAc 2:1, followed by EtOAc, then EtOAc/MeOH 95:5) 158 mg (95%) of a white solid was obtained. R_f = 0.20 (EtOAc), mp 196 – 198 °C (Et_2O).

^{1}H-NMR (500 MHz, DMSO-d_6, ppm) δ 8.80 (d, *J* = 4.0 Hz, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 7.5 Hz, 1H), 8.15 (d, *J* = 6.9 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.77 (t, *J* = 8.0 Hz, 1H), 7.58 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.57 (t, *J* = 6.9 Hz, 1H), 5.12 (t, *J* = 5.7 Hz, 1H), 4.95 (t, *J* = 5.2 Hz, 1H), 4.88 – 4.78 (m, 2H), 4.53 (dd, *J* = 13.2, 4.6 Hz, 1H), 3.56 (dd, *J* = 12.6, 5.7 Hz, 1H).

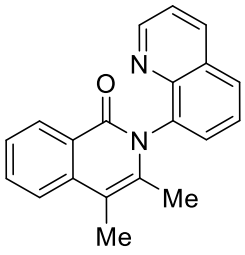
^{13}C-NMR (125 MHz, DMSO-d_6, ppm) δ 161.9, 151.1, 144.1, 141.4, 137.1, 136.5, 136.1, 132.6, 131.2, 129.1, 128.6, 127.3, 126.7, 126.4, 125.5, 124.6, 122.0, 114.5, 56.8, 56.2.

HRMS calcd. for $C_{20}H_{16}N_2O_3$ $[M]^+$: 332.1161; found: 332.1160.

FT-IR (neat, cm^{-1}) υ 1633, 1609, 1589, 1576, 1393, 1336, 1043, 1016.

[10] Srinivasarao, A.; Kumara Swamy, K.C. *J. Org. Chem.* **2014**, *79*, 3963.

3,4-Dimethyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 3, Entry 2)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), 2-butyne (47 µl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 144 mg (96%) of a white solid was obtained. R_f = 0.22 (hexanes/EtOAc 1:1), mp 234 – 236 °C (Et_2O).

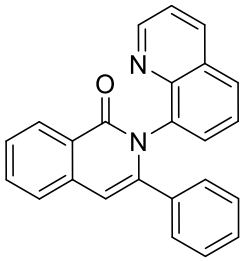
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.86 (d, *J* = 2.9 Hz, 1H), 8.50 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 6.9 Hz, 1H), 7.95 – 7.90 (m, 1H), 7.75 – 7.62 (m, 4H), 7.45 (t, *J* = 6.9 Hz, 1H), 7.38 (dd, *J* = 8.0, 4.0 Hz, 1H), 2.36 (s, 3H), 1.95 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.9, 151.1, 144.4, 138.0, 137.7, 136.1, 136.0, 132.2, 129.7, 129.2, 128.8, 128.2, 126.2, 125.4, 124.9, 122.7, 121.6, 108.5, 17.6, 13.7.

HRMS calcd. for $C_{20}H_{16}N_2O$ $[M]^+$: 300.1263; found: 300.1257.

FT-IR (neat, cm^{-1}) υ 1645, 1609, 1592, 1487, 1330.

3-Phenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 3, Entry 3)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), phenyl acetylene (66 µl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 166 mg (95%) of a white solid was obtained. R_f = 0.32 (hexanes/EtOAc 1:1), mp 207 – 209 °C (Et_2O).

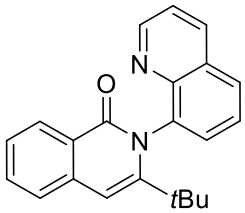
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.89 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.52 (d, *J* = 8.0 Hz, 1H), 8.04 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 8.6, 4.6 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.98 – 6.93 (m, 2H), 6.66 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 163.1, 150.7, 144.6, 144.3, 137.2, 137.1, 136.1, 135.9, 132.5, 130.5, 128.6, 128.5, 128.2, 128.7, 127.1, 126.5, 126.0, 125.6, 125.3, 121.3, 107.2.

HRMS calcd. for $C_{24}H_{16}N_2O$ $[M]^+$: 348.1263; found: 348.1262.

FT-IR (neat, cm^{-1}) υ 1651, 1615.

3-Tert-butyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 3, Entry 4)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), 3,3-dimethyl-1-butyne (73 μl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 119 mg (73%) of a white solid was obtained. R_f = 0.44 (hexanes/EtOAc 1:1), mp 174-176 °C (Et_2O).

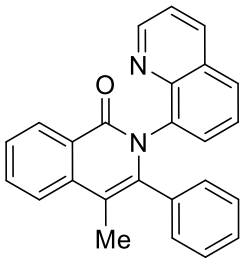
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.83 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.18 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.95 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.80 (dd, 1H, *J* = 7.5, 1.7 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.6 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.36 (dd, *J* = 8.6, 4.0 Hz, 1H), 6.82 (s, 1H), 1.06 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 165.0, 151.4, 150.9, 146.2, 139.0, 137.2, 136.0, 132.3, 131.7, 129.1, 128.9, 127.9, 126.2, 126.1, 125.5, 124.5, 121.5, 104.2, 36.5, 31.1.

HRMS calcd. for $C_{22}H_{21}N_2O$ $[M+H]^+$: 329.1654; found: 329.1658.

FT-IR (neat, cm^{-1}) υ 1651, 1614, 1594, 1562, 1358, 1343, 1167.

4-Methyl-3-phenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 3, Entry 5)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), 1-phenyl-1-propyne (75 μl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 172 mg (95%, 14:1 mixture of isomers inseparable by flash column chromatography, structure of major isomer shown) of a white solid was obtained. R_f = 0.28 (hexanes/EtOAc 1:1), mp 211-213 °C (Et_2O).

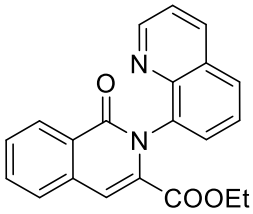
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.89 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.62 (d, *J* = 7.5 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.80 (t, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 8.6 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 6.9 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.31 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 6.9 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 2.14 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.4, 150.6, 144.5, 140.7, 137.9, 137.7, 135.8, 135.3, 132.4, 130.7, 130.2, 129.0, 128.5, 128.4, 128.3, 127.6, 127.2, 126.9, 126.3, 125.7, 125.5, 123.4, 121.2, 109.9, 14.7.

HRMS calcd. for $C_{25}H_{18}N_2O$ $[M]^+$: 362.1419; found: 362.1420.

FT-IR (neat, cm^{-1}) υ 1648, 1612, 1590, 1484, 1332.

Ethyl 1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-3-carboxylate (Table 3, Entry 6, major regioisomer)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), ethyl propiolate (61 μl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 142 mg (82%) of major regioisomer was obtained as a white solid. R_f = 0.32 (hexanes/EtOAc 1:1), mp 187-189 °C (Et_2O).

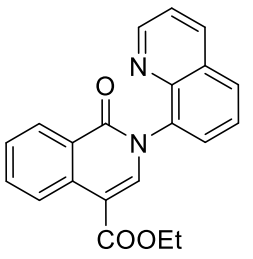
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.83 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.48 (d, *J* = 7.5 Hz, 1H), 8.18 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.78 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.44 (s, 1H), 7.36 (dd, *J* = 8.0, 4.0 Hz, 1H), 3.85 (q, *J* = 7.5 Hz, 2H), 0.79 (t, *J* = 6.9 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.4, 162.1, 150.5, 144.3, 137.1, 136.0, 135.1, 134.2, 132.8, 129.0, 128.8, 128.7, 128.4, 128.3, 127.4, 127.3, 125.8, 121.2, 111.6, 61.2, 13.2.

HRMS calcd. for $C_{21}H_{16}N_2O_3$ $[M]^+$: 344.1161; found: 344.1157.

FT-IR (neat, cm^{-1}) υ 1711, 1660, 1397, 1319, 1259, 1211, 1163.

Ethyl 1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carboxylate (Table 3, Entry 6, minor regioisomer)



In addition to the major isomer described above, 23 mg (13%) of minor regioisomer was obtained as a white solid. R_f = 0.49 (hexanes/EtOAc 1:1), mp 180-182 °C (Et_2O).

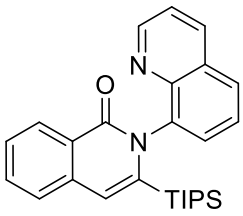
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.93 (d, *J* = 8.6 Hz, 1H), 8.90 (dd, *J* = 4.6, 1.7 Hz, 1H), 8.51 (d, *J* = 6.9 Hz, 1H), 8.27 (dd, *J* = 8.0, 1.7 Hz, 1H), 8.26 (s, 1H), 8.00 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.84 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.80 (t, *J* = 8.6 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.48 (dd, *J* = 8.6, 4.0 Hz, 1H), 4.34 (q, *J* = 6.9 Hz, 2H), 1.33 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 165.4, 162.5, 151.4, 143.6, 141.4, 137.9, 136.2, 134.8, 133.3, 129.6, 129.4, 128.8, 128.5, 127.2, 126.2, 125.8, 125.5, 122.1, 106.6, 60.6, 14.4.

HRMS calcd. for $C_{21}H_{16}N_2O_3$ $[M]^+$: 344.1161; found: 344.1159.

FT-IR (neat, cm^{-1}) υ 1707, 1661, 1613, 1488, 1309, 1244, 1186, 1153, 1101, 1052.

2-(Quinolin-8-yl)-3-(triisopropylsilyl)isoquinolin-1(*2H*)-one (Table 3, Entry 7)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), (triisopropylsilyl)acetylene (135 µl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv) and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 136 mg (64%) of a yellow oil was obtained. R_f = 0.51 (hexanes/EtOAc 1:1).

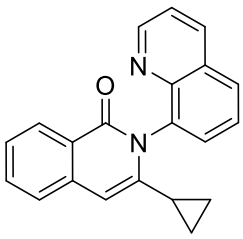
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.83 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.21 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.77 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.39 (dd, *J* = 8.6, 4.6 Hz, 1H), 6.93 (s, 1H), 0.97 (d, *J* = 7.5 Hz, 9H), 0.76 (d, *J* = 7.5 Hz, 9H), 0.61 (sep, *J* = 6.9 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 164.3, 151.0, 145.5, 143.6, 140.1, 136.5, 136.0, 132.3, 130.0, 129.3, 129.2, 128.0, 127.2, 126.3, 126.1, 125.8, 121.8, 117.7, 19.3, 18.7, 12.4.

HRMS calcd. for $C_{27}H_{32}N_2OSi$ $[M]^+$: 428.2284; found: 428.2285.

FT-IR (neat, cm^{-1}) υ 2947, 2867, 1652, 1610, 1497, 1461, 1355, 1337, 1174, 1019.

3-Cyclopropyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (Table 3, Entry 8)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), cyclopropyl acetylene (40 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 16 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 4:1 to 1:1, then EtOAc) 131 mg (84%, 13:1 mixture of isomers inseparable by flash column chromatography, structure of major isomer shown) of a white solid was obtained. R_f = 0.32 (hexanes/EtOAc 1:1), mp 194-196 °C (Et_2O).

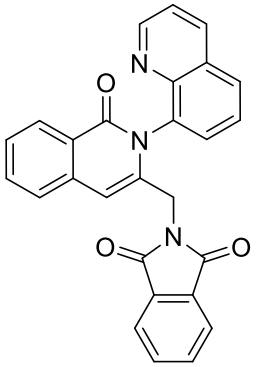
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.87 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 8.22 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.95 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.74 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.70 – 7.61 (m, 2H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.45 – 7.39 (m, 2H), 6.43 (s, 1H), 1.25 – 1.19 (m, 1H), 0.71 – 0.65 (m, 1H), 0.63 – 0.57 (m, 1H), 0.51 – 0.45 (m, 1H), 0.34 – 0.28 (m, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 163.6, 151.1, 145.1, 144.6, 137.5, 137.0, 136.1, 132.3, 130.1, 129.2, 128.9, 128.1, 126.1, 125.9, 125.6, 125.0, 121.6, 103.0, 14.6, 7.9, 6.4.

HRMS calcd. for $C_{21}H_{16}N_2O$ $[M]^+$: 312.1263; found: 312.1257.

FT-IR (neat, cm^{-1}) υ 1652, 1616, 1595, 1559, 1495, 1391, 1179.

2-((1-Oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)methyl)isoindoline-1,3-dione (Table 3, Entry 9)



N-(Quinolin-8-yl)benzamide (124 mg, 0.5 mmol), 2-(prop-2-ynyl)isoindoline-1,3-dione (111 mg, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv) and CF_3CH_2OH (5 mL), 18 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 2:1 to 1:1, then EtOAc) 199 mg (93%, 7:1 mixture of isomers inseparable by flash column chromatography, structure of major isomer shown) of a white solid was obtained. R_f = 0.59 (EtOAc), mp 232-234 °C (Et_2O).

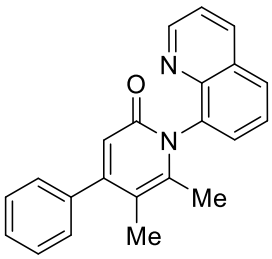
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.70 (d, *J* = 3.9 Hz, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.81 – 7.60 (m, 8H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.24 (dd, *J* = 8.2, 4.1 Hz, 1H), 6.65 (s, 1H), 4.55 (d, *J* = 16.0 Hz, 1H), 4.35 (d, *J* = 16.0 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 166.8, 151.4, 136.9, 136.7, 136.1, 135.4, 134.0, 132.6, 131.6, 130.5, 129.7, 129.5, 128.2, 126.9, 126.7, 126.6, 126.1, 125.5, 123.3, 121.7, 119.9, 106.2, 39.7.

HRMS calcd. for $C_{27}H_{18}N_3O_3$ $[MH]^+$: 432.1348; found: 432.1339.

FT-IR (neat, cm^{-1}) υ 1709, 1660, 1628, 1411, 1390, 1351, 1335, 1319.

5,6-Dimethyl-4-phenyl-1-(quinolin-8-yl)pyridin-2(*1H*)-one (4, Scheme 1)



N-(Quinolin-8-yl)cinnamamide (137 mg, 0.5 mmol), 2-butyne (47 μl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv), and CF_3CH_2OH (5 mL), 18 h, 80 °C. After column chromatography (hexanes/EtOAc 2:1, followed by EtOAc, then EtOAc/MeOH 95:5) 122 mg (75%) of a yellow oil was obtained. R_f = 0.27 (EtOAc).

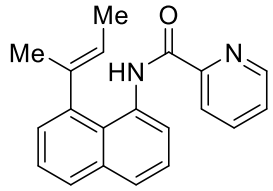
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.94 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.22 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.94 (dd, *J* = 5.7, 3.8 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.47 – 7.34 (m, 6H), 6.58 (s, 1H), 2.00 (s, 3H), 1.90 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 155.7, 151.3, 143.8, 143.7, 139.5, 137.1, 136.4, 129.3, 129.2, 128.2, 128.1, 127.8, 126.4, 121.8, 118.0, 111.5, 18.0, 15.8.

HRMS calcd. for $C_{22}H_{18}N_2O$ $[M]^+$: 326.1419; found: 326.1413.

FT-IR (neat, cm^{-1}) υ 1652, 1583, 1567, 1517, 1494, 1343.

(*E*)-*N*-(8-(But-2-en-2-yl)naphthalen-1-yl)picolinamide (6, Scheme 2)



N-(Naphthalen-1-yl)picolinamide (124 mg, 0.5 mmol), 2-butyne (59 µl, 0.75 mmol, 1.5 equiv), $Co(OAc)_2 \cdot 4H_2O$ (37 mg, 0.15 mmol, 30 mol%), NaOPiv (124 mg, 1.0 mmol, 2 equiv), and CF_3CH_2OH (5 mL), 36 h, 100 °C. After column chromatography (gradient hexanes/EtOAc from 20:1 to 1:1) 72 mg (48%) of a yellow oil was obtained. R_f = 0.30 (hexanes/EtOAc 8:1).

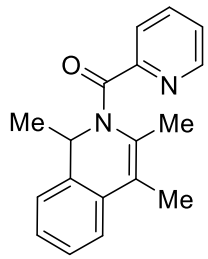
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.65 (d, *J* = 4.0 Hz, 1H), 8.45 (d, *J* = 7.5 Hz, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 7.92 (td, *J* = 7.5, 1.7 Hz, 1H), 7.77 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.50 (ddd, *J* = 7.5, 4.6, 1.2 Hz, 1H), 7.40 (t, *J* = 8.6 Hz, 1H), 7.20 (dd, *J* = 7.5, 1.7 Hz, 1H), 5.82 (q, *J* = 6.9 Hz, 1H), 1.90 (s, 3H), 1.86 (d, *J* = 6.3 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 162.4, 150.6, 147.9, 141.3, 139.3, 137.5, 135.3, 133.3, 128.3, 128.1, 126.3, 125.9, 125.5, 125.4, 125.2, 124.5, 122.8, 120.9, 19.5, 14.6.

HRMS calcd. for $C_{20}H_{18}N_2O$ $[M]^+$: 302.1419; found: 302.1412.

FT-IR (neat, cm^{-1}) υ 3262, 1678, 1519, 1492, 1465, 1429, 1347.

Pyridin-2-yl(1,3,4-trimethylisoquinolin-2(*1H*)-yl)methanone (8, Scheme 2)



N-(1-Phenylethyl)picolinamide (113 mg, 0.5 mmol), 2-butyne (59 µl, 0.75 mmol, 1.5 equiv), $Co(OAc)_2 \cdot 4H_2O$ (125 mg, 0.5 mmol, 1 equiv), NaOPiv (124 mg, 1.0 mmol, 2 equiv), $Mn(OAc)_2$ (173 mg, 1.0 mmol, 2 equiv), and CF_3CH_2OH (5 mL), 36 h, 100 °C. After column chromatography (hexanes/EtOAc 4:1) 61 mg (44%) of a yellow oil was obtained. R_f = 0.59 (hexanes/EtOAc 1:1).

^{1}H-NMR (500 MHz, toluene-d_8, 60 °C, ppm) δ 8.25 (s, 1H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.08 – 6.93 (m, 4H), 6.87 (t, *J* = 6.8 Hz, 1H), 6.71 – 6.52 (m, 2H), 5.74 – 5.22 (m, 1H), 2.27 – 1.91 (m, 3H), 1.88 (s, 3H), 1.42 (s, 3H).

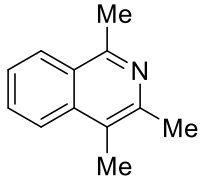
^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 155.9, 148.8, 137.4, 136.7, 132.6, 128.6, 127.3, 126.7, 126.2, 124.8, 124.2, 123.0, 120.0, 19.8, 19.6, 13.8.

HRMS calcd. for $C_{18}H_{19}N_2O$ $[MH]^+$: 279.1497; found: 279.1496.

FT-IR (neat, cm^{-1}) υ 1644, 1436, 1393, 1355, 1340, 1243, 1185.

Removal of directing group

1,3,4-Trimethylisoquinoline (9, Scheme 3)

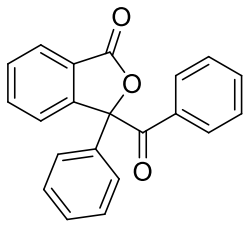


To a solution of pyridin-2-yl(1,3,4-trimethylisoquinolin-2(*1H*)-yl)methanone (67 mg, 0.24 mmol) in MeOH (3 mL) NaOH (3 mL of a 2N aqueous solution) was added and resulting mixture was stirred at 80 °C for 12 h. Reaction mixture was cooled to room temperature and solvent was evaporated under reduced pressure. Purification using column chromatography on silica gel (gradient hexanes/EtOAc from 2:1 to 1:1) afforded 38 mg (93%) of 1,3,4-trimethylisoquinoline as a yellow oil.

^{1}H-NMR (400 MHz, DMSO-d_6, ppm) δ 8.14 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.80 – 7.71 (m, 1H), 7.60 – 7.55 (m, 1H), 3.36 (s, 3H), 2.81 (s, 3H), 2.57 (s, 3H).

^{13}C-NMR (100 MHz, DMSO-d_6, ppm) δ 154.8, 147.4, 135.3, 129.9, 126.0, 125.6, 125.2, 123.5, 121.6, 22.6, 22.0, 13.5.

3-Benzoyl-3-phenylisobenzofuran-1(3H)-one (10, Scheme 3)



To a suspension of 3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(*2H*)-one (189 mg, 0.45 mmol) in MeCN/H_2O (1:1, 9 mL) CAN (987 mg, 1.8 mmol, 4 equiv) was added. Resulting solution was stirred at room temperature for 4 h. Reaction mixture was diluted with H_2O (10 mL), extracted with EtOAc (3 x 10 mL). Combined organic phase was dried over $MgSO_4$, filtered, and solvent was evaporated. After column chromatography (hexanes/EtOAc 4:1) 69 mg (49%) of 3-benzoyl-3-phenylisobenzofuran-1(3H)-one was obtained as a white solid. This compound is known. [11]

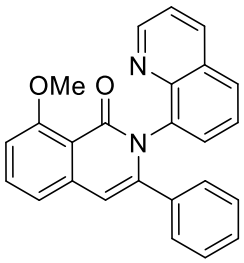
^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.04 – 7.95 (m, 2H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.61 – 7.57 (m, 2H), 7.56 – 7.49 (m, 2H), 7.42 – 7.33 (m, 5H).

^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 193.3, 169.2, 149.7, 137.5, 134.4, 134.1, 133.6, 130.9, 129.7, 129.4, 129.0, 128.3, 125.8, 125.4, 124.0, 123.6, 92.5.

[11] Hauser, C. R.; Van Eenam, D. N. *J. Org. Chem.* **1958**, *23*, 865.

Synthesis of 8-methoxy-3-phenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one

8-Methoxy-3-phenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (13, Scheme 4)

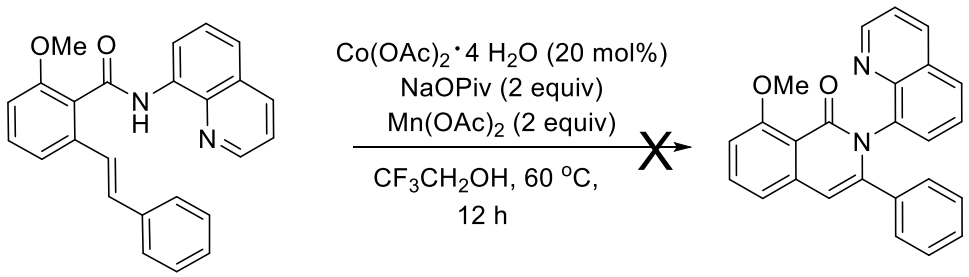


This compound was prepared according to general procedure. 2-Methoxy-*N*-(quinolin-8-yl)benzamide (139 mg, 0.5 mmol), phenyl acetylene (66 μl, 0.6 mmol, 1.2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (12.5 mg, 0.05 mmol, 10 mol%), NaOPiv (124 mg, 1 mmol, 2 equiv), $Mn(OAc)_2$ (87 mg, 0.5 mmol, 1 equiv) and CF_3CH_2OH (5 mL), 12 h, 80 °C. After column chromatography (gradient hexanes/EtOAc from 3:1 to EtOAc) 134 mg (71%) of a white solid was obtained.

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.89 (s, 1H), 8.05 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 3.0 Hz, 1H), 7.42 – 7.29 (m, 2H), 7.27 – 7.08 (m, 5H), 7.05 – 6.83 (m, 3H), 6.53 (s, 1H), 3.93 (s, 3H).

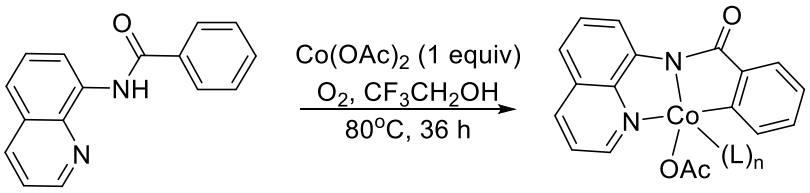
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 161.4, 161.0, 150.8, 145.1, 145.0, 140.4, 137.6, 136.2, 135.9, 133.4, 131.0, 128.7, 128.6, 128.4, 128.0, 127.9, 127.2, 125.7, 121.3, 118.5, 108.1, 107.1, 56.0.

Cyclization of (E)-2-methoxy-N-(quinolin-8-yl)-6-styrylbenzamide (Scheme 4).



2-Dram vial with a screw cap (PTFE/Liner) was charged with (*E*)-2-methoxy-*N*-(quinolin-8-yl)-6-styrylbenzamide (38.0 mg, 0.1 mmol), $Mn(OAc)_2$ (36.0 mg, 0.2 mmol, 2 equiv), NaOPiv (24.8 mg, 0.2 mmol, 2 equiv), $Co(OAc)_2 \cdot 4H_2O$ (5.0 mg, 0.02 mmol, 20 mol), and CF_3CH_2OH (1 mL). Resulting mixture was heated at 60 °C for 12 h, cooled to room temperature. Solvent was evaporated and crude mixture was analyzed by ^{1}H-NMR spectroscopy using 1,1,2-trichloroethane as an internal standard (9.3 μl, 0.1 mmol, 1 equiv).

Isolation of a presumed reaction intermediate

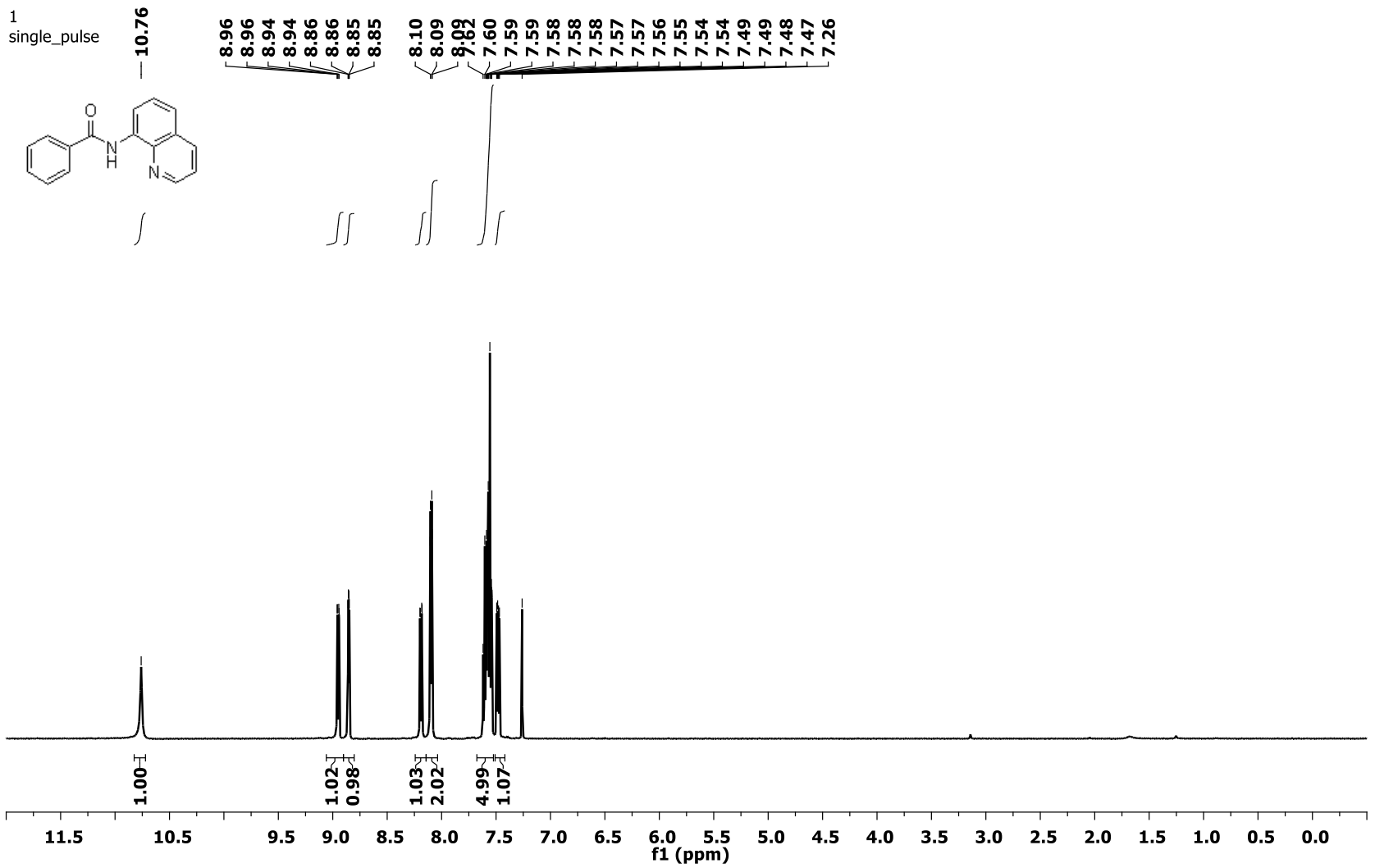


A 8 dram vial equipped with a magnetic stir bar was charged with *N*-(quinolin-8-yl)benzamide (124 mg, 0.5 mmol), $Co(OAc)_2$ (88.5 mg, 0.5 mmol, 1 equiv), NaOPiv (1 mmol, 2 equiv), and CF_3CH_2OH (5 mL). Reaction mixture was saturated with O_2 and heated at 80 °C for 36 h. Mixture was cooled to room temperature and solvent was evaporated. After column chromatography on silica gel (gradient hexanes/EtOAc from 2:1 to 1:1, then EtOAc), 89 mg of product as yellow oil was obtained. The NMR is consistent with a Co(III) species and C-H activation of phenyl ring.

^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 8.82 (d, *J* = 4.8 Hz, 1H), 8.48 (d, *J* = 7.7 Hz, 1H), 8.30 (d, *J* = 8.1 Hz, 1H), 7.67 (dd, *J* = 8.2, 5.0 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 6.56 (d, *J* = 7.5 Hz, 1H), 6.50 (d, *J* = 7.5 Hz, 1H), 6.43 (t, *J* = 7.4 Hz, 1H), 6.28 (t, *J* = 7.4 Hz, 1H), 0.47 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 200.4, 178.7, 150.5, 148.8, 147.4, 141.0, 138.7, 138.5, 129.6, 128.0, 127.4, 126.8, 125.0, 123.7, 121.8, 120.1, 117.6, 25.3.

NMR spectra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7.55
7.54
7.54
7.49
7.49
7.48
7.47
7.26
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H
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1.03
2.02
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1.07
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10.5
9.5
9.0
8.5
8.0
7.5
7.0
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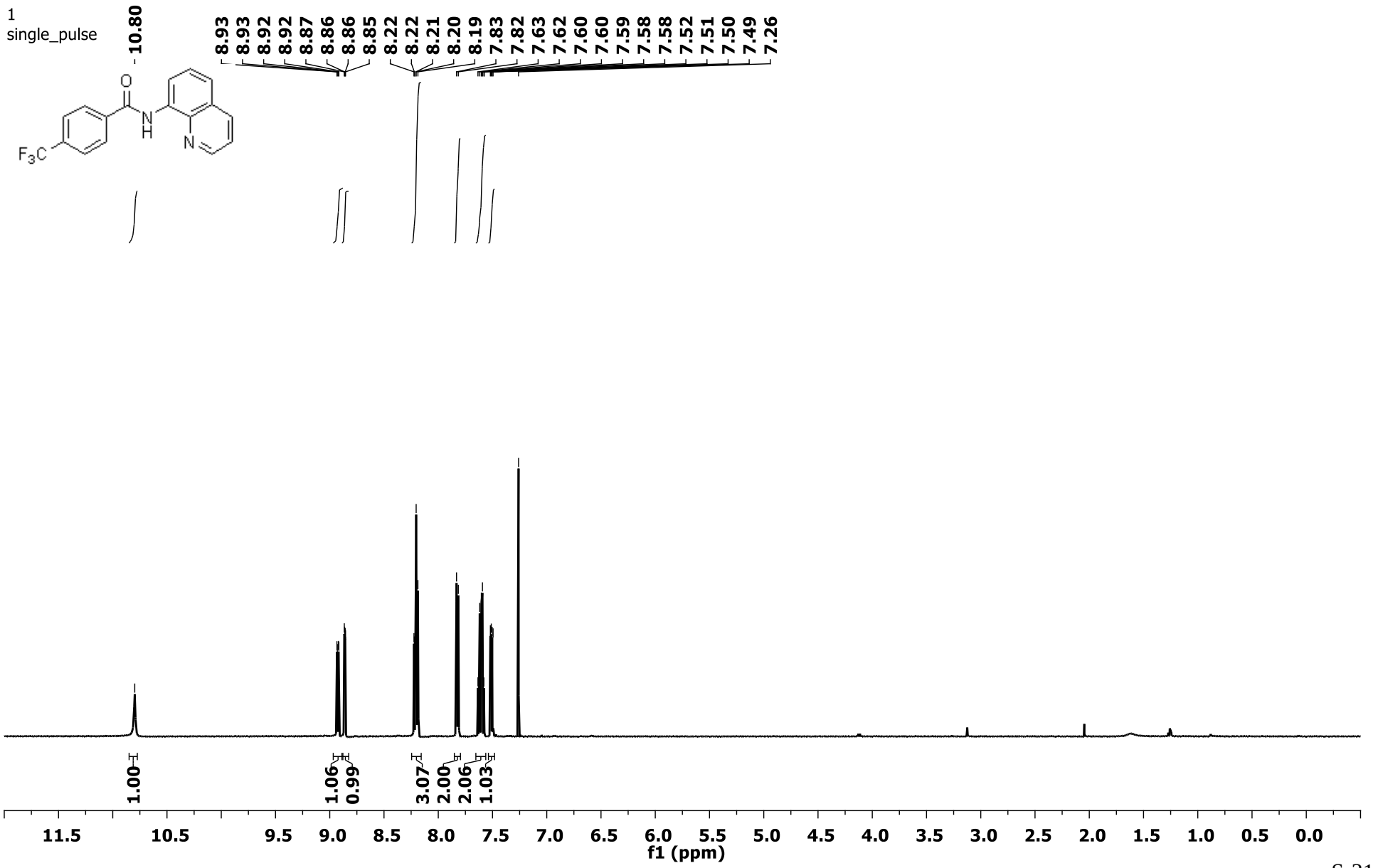
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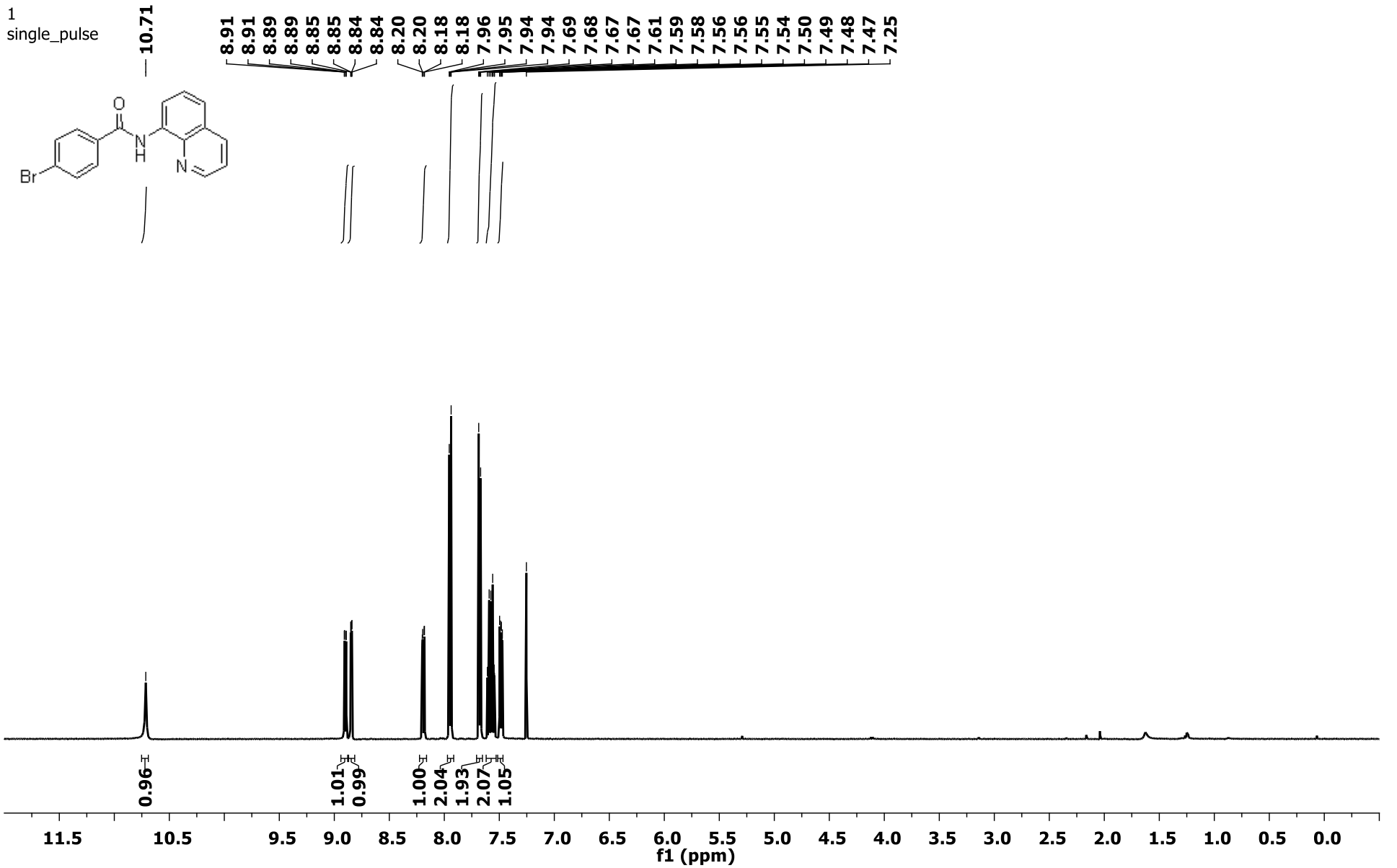
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7.94
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7.67
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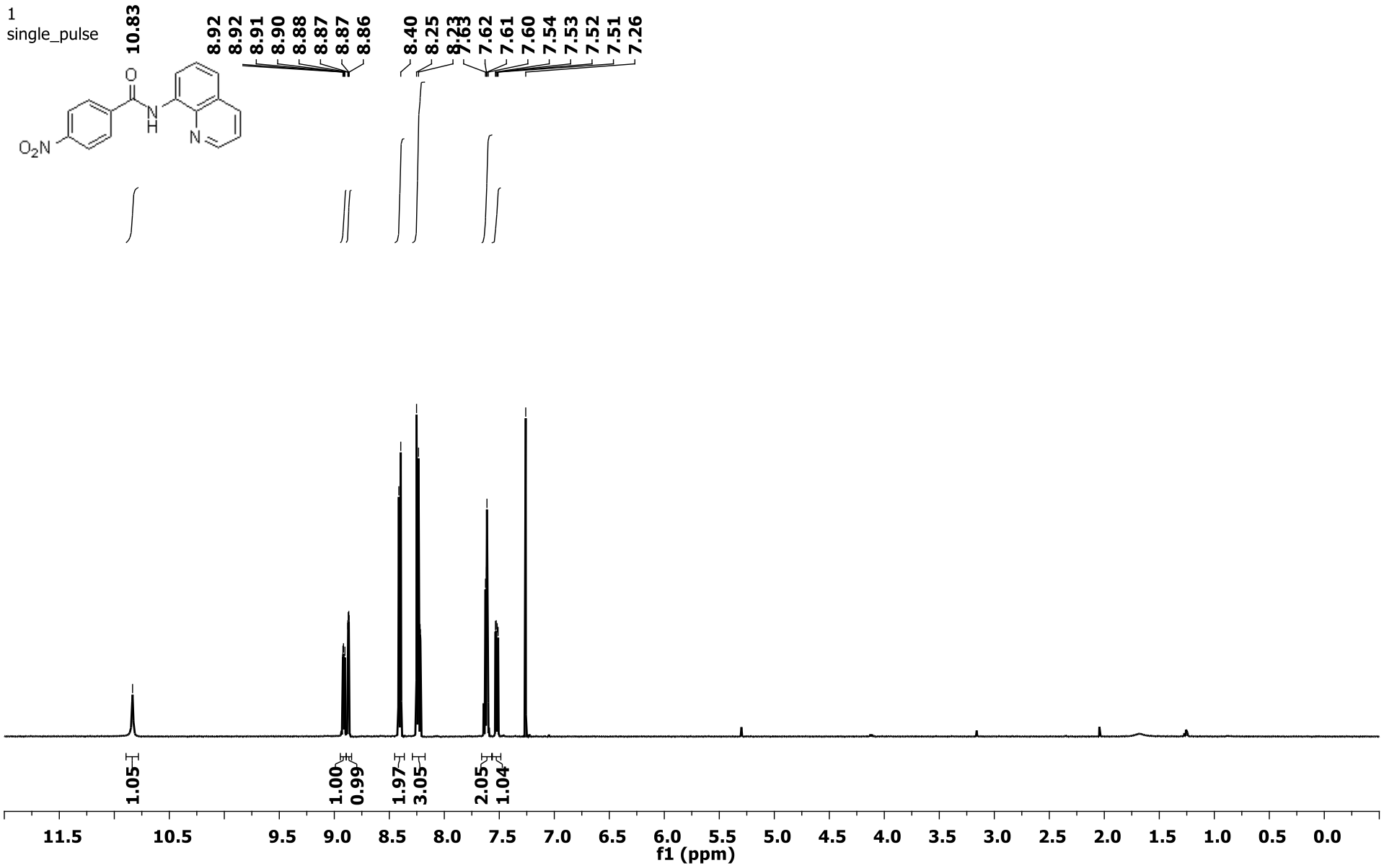
f1 (ppm)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7.51
7.26
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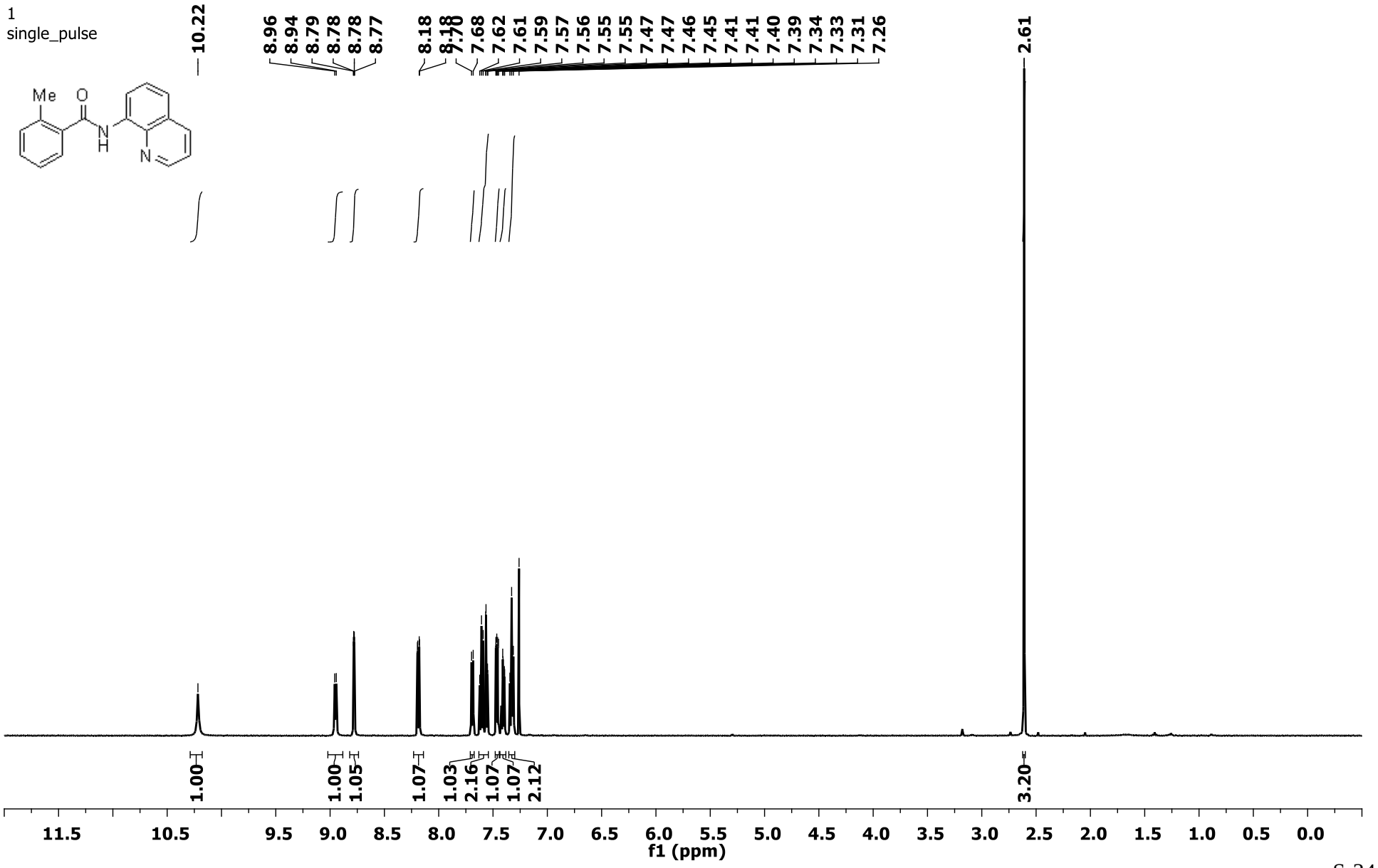
f1 (ppm)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1.07
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
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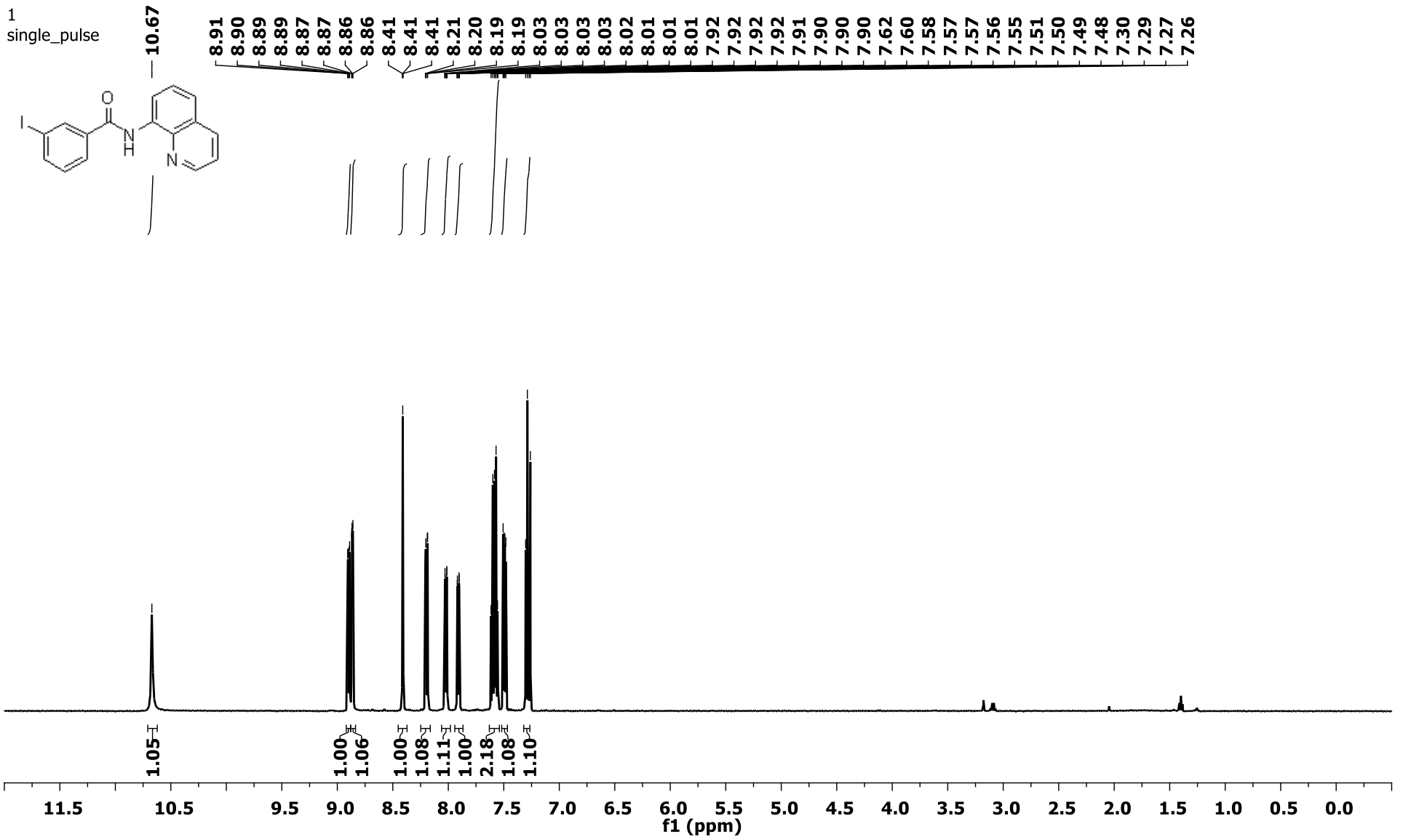
0.0
f1 (ppm)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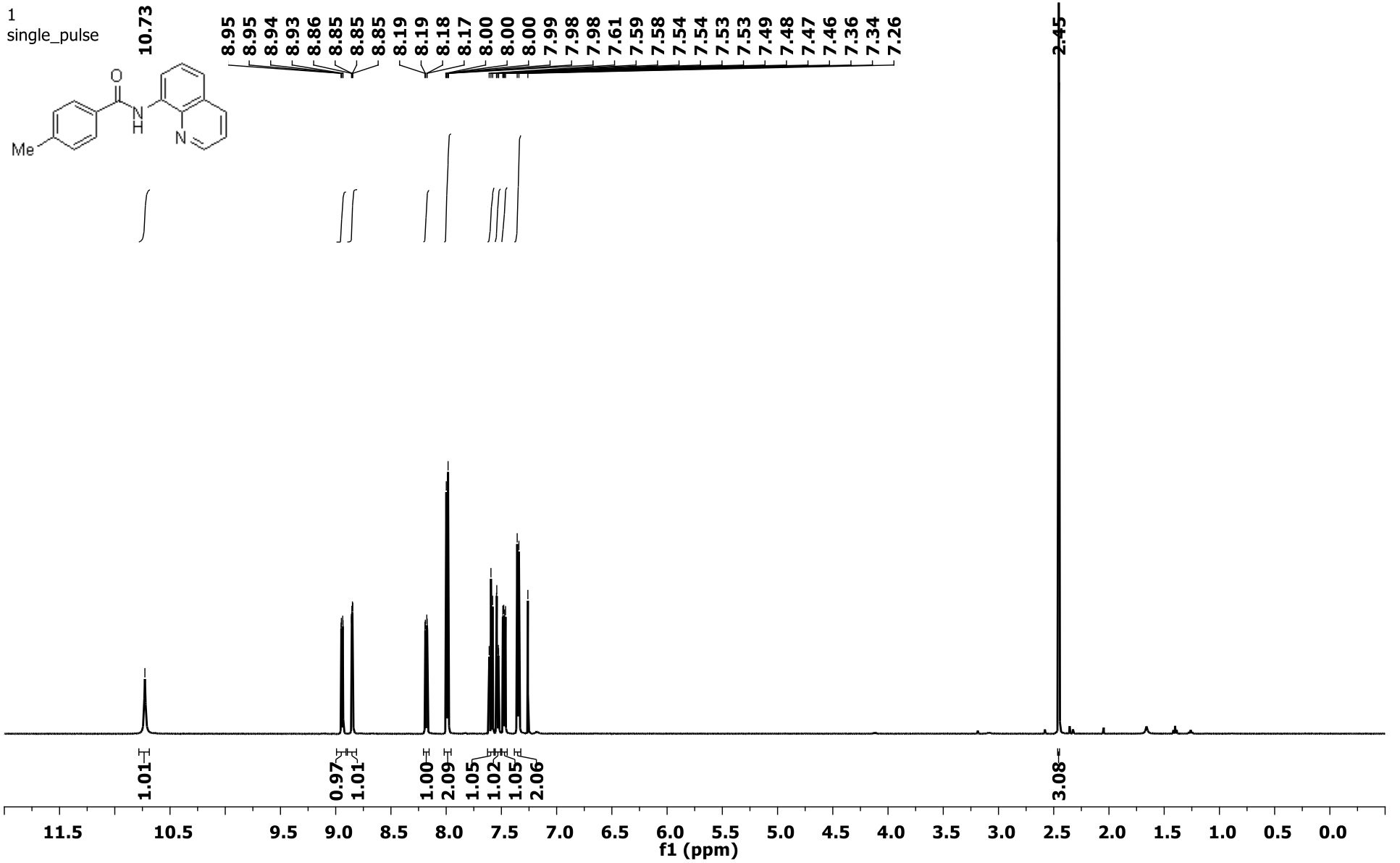
1.05 1.00 1.06 1.00 1.08 1.11 1.00 2.18 1.08 1.10
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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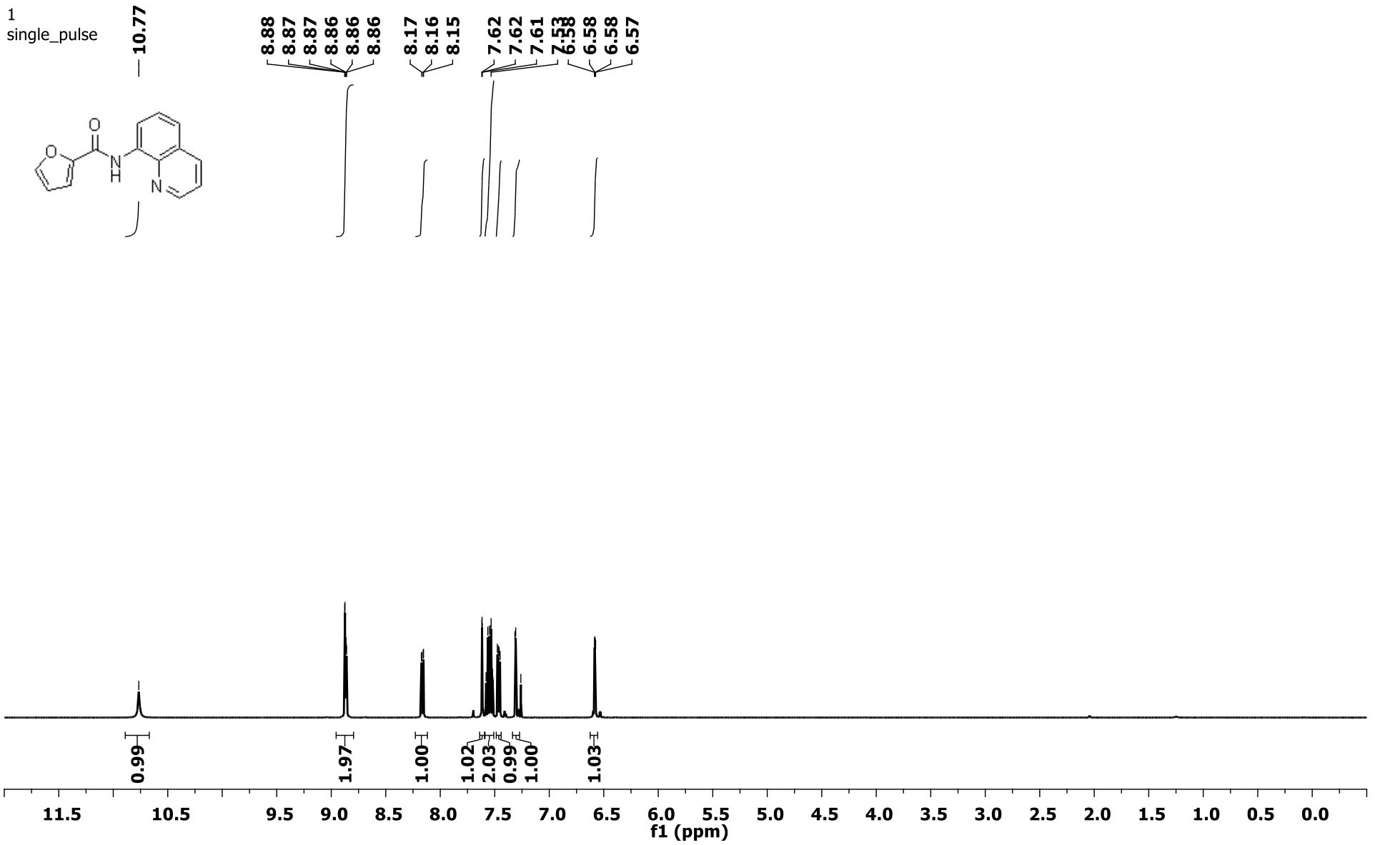
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6.57
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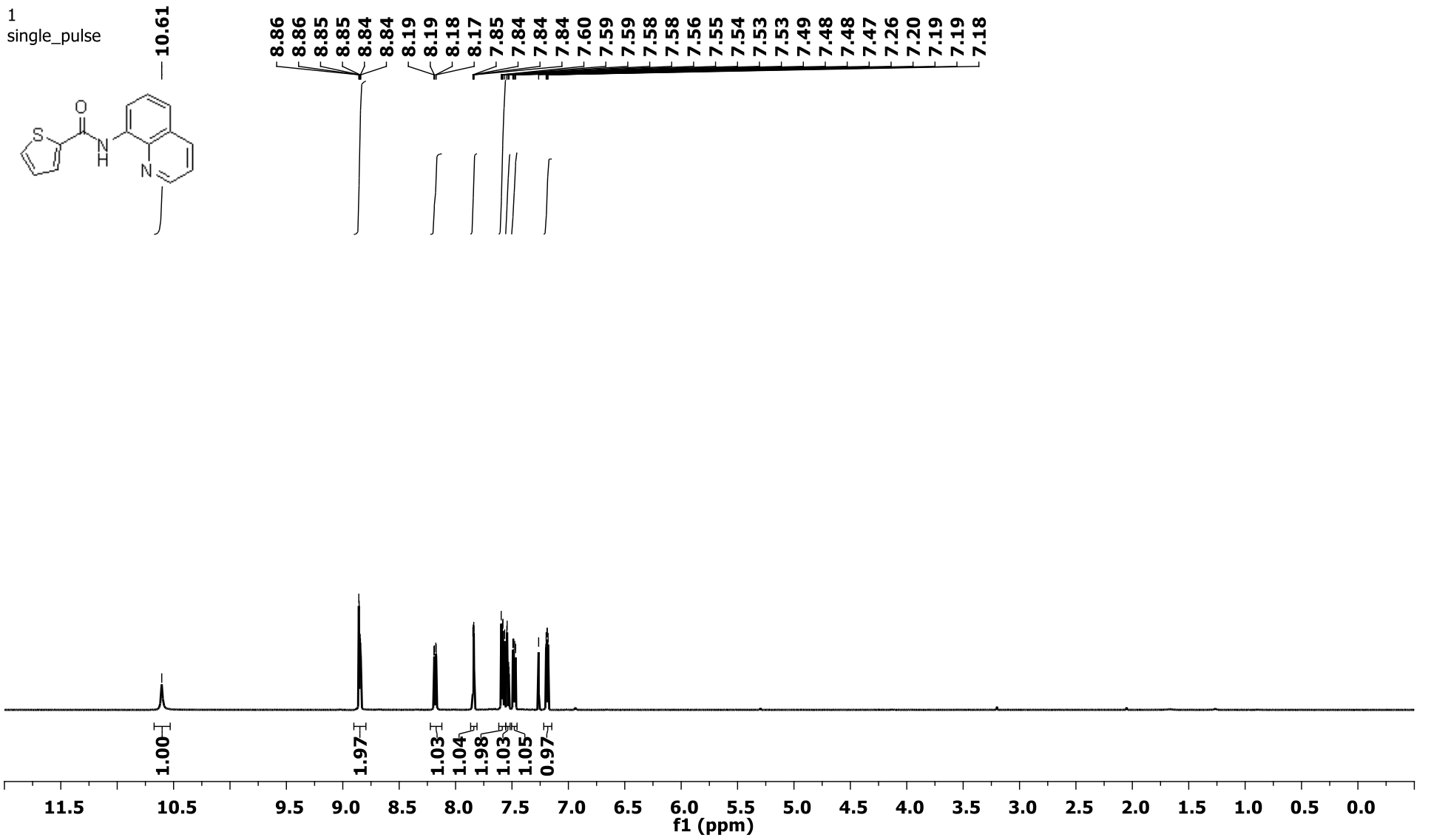
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1.03
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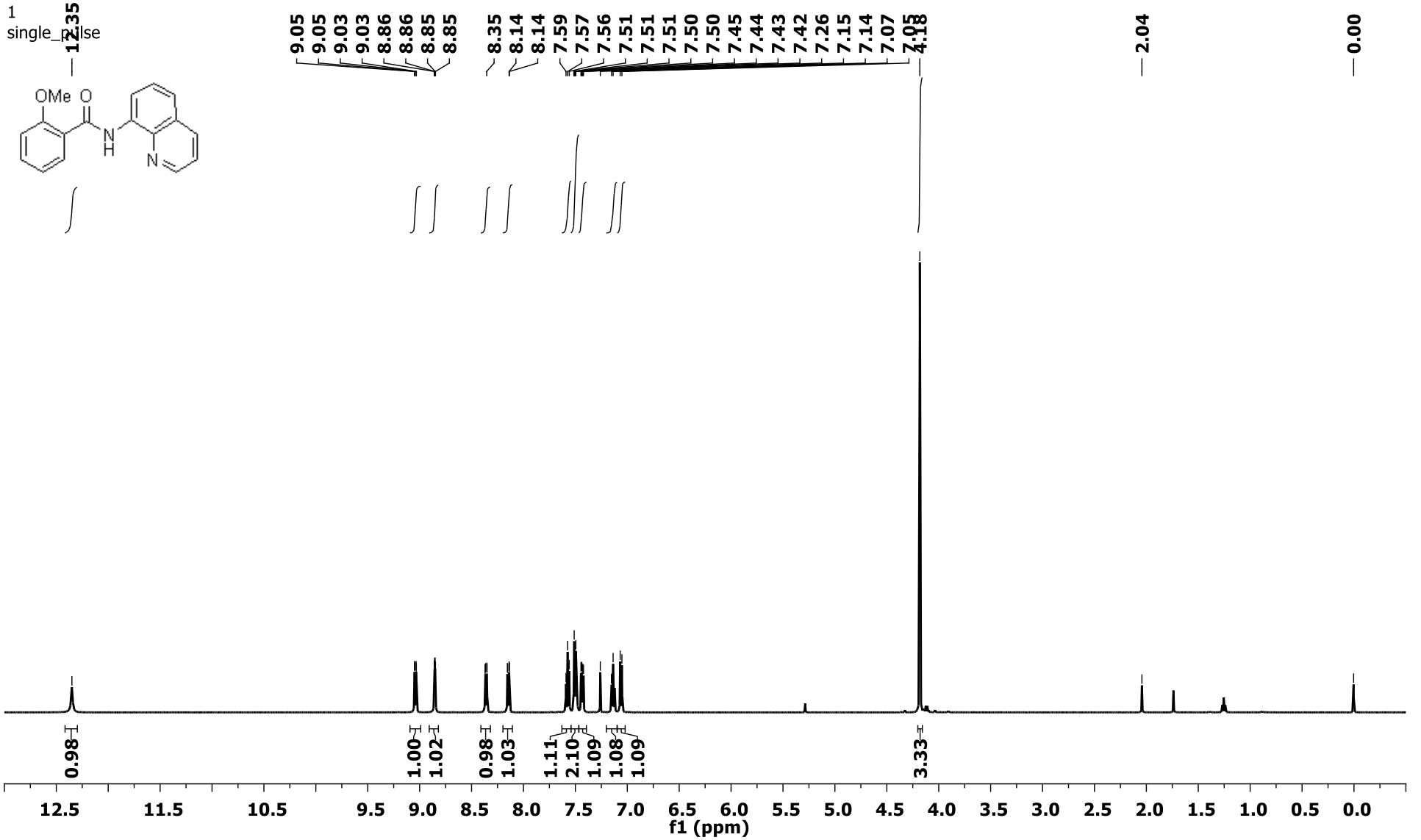
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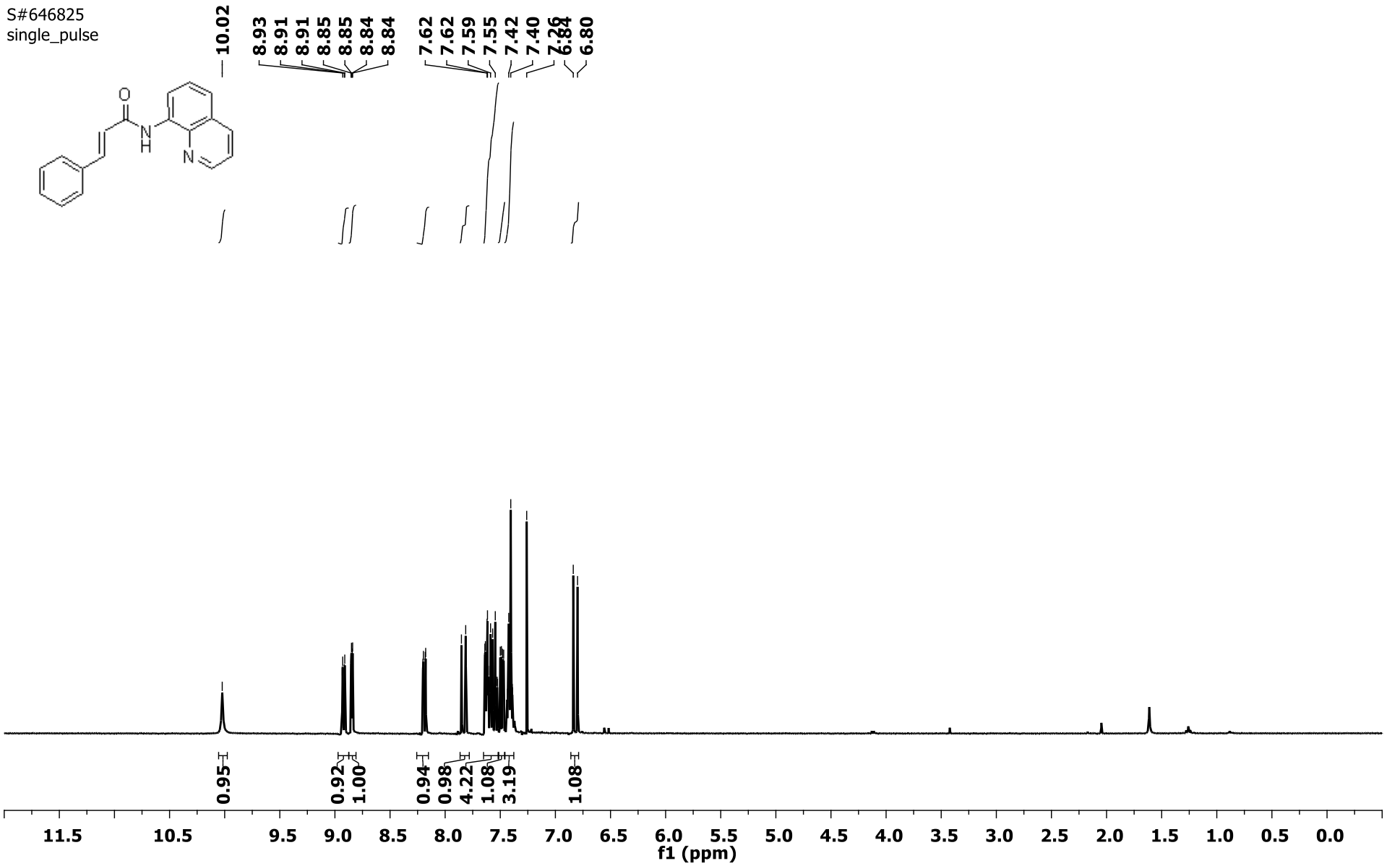
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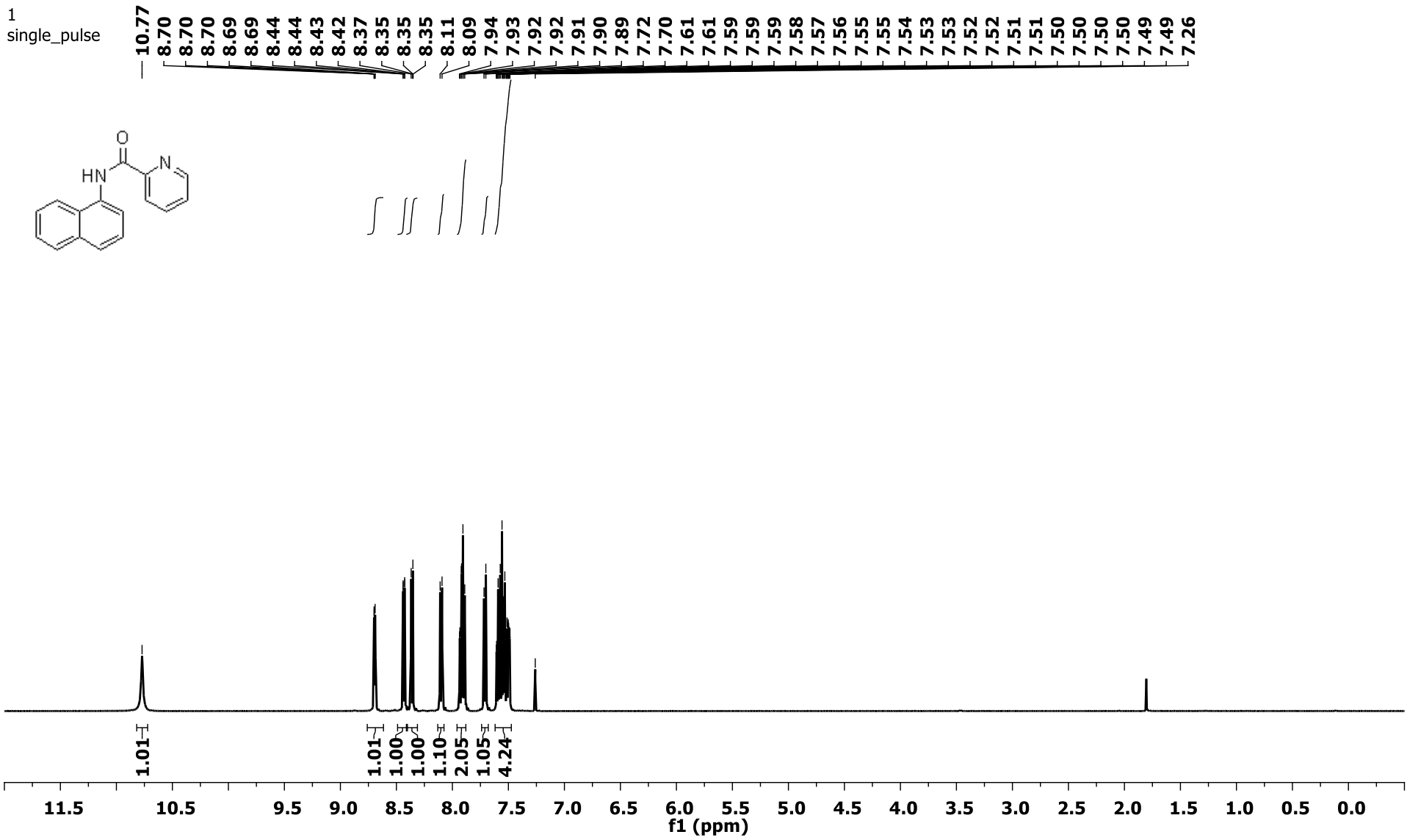
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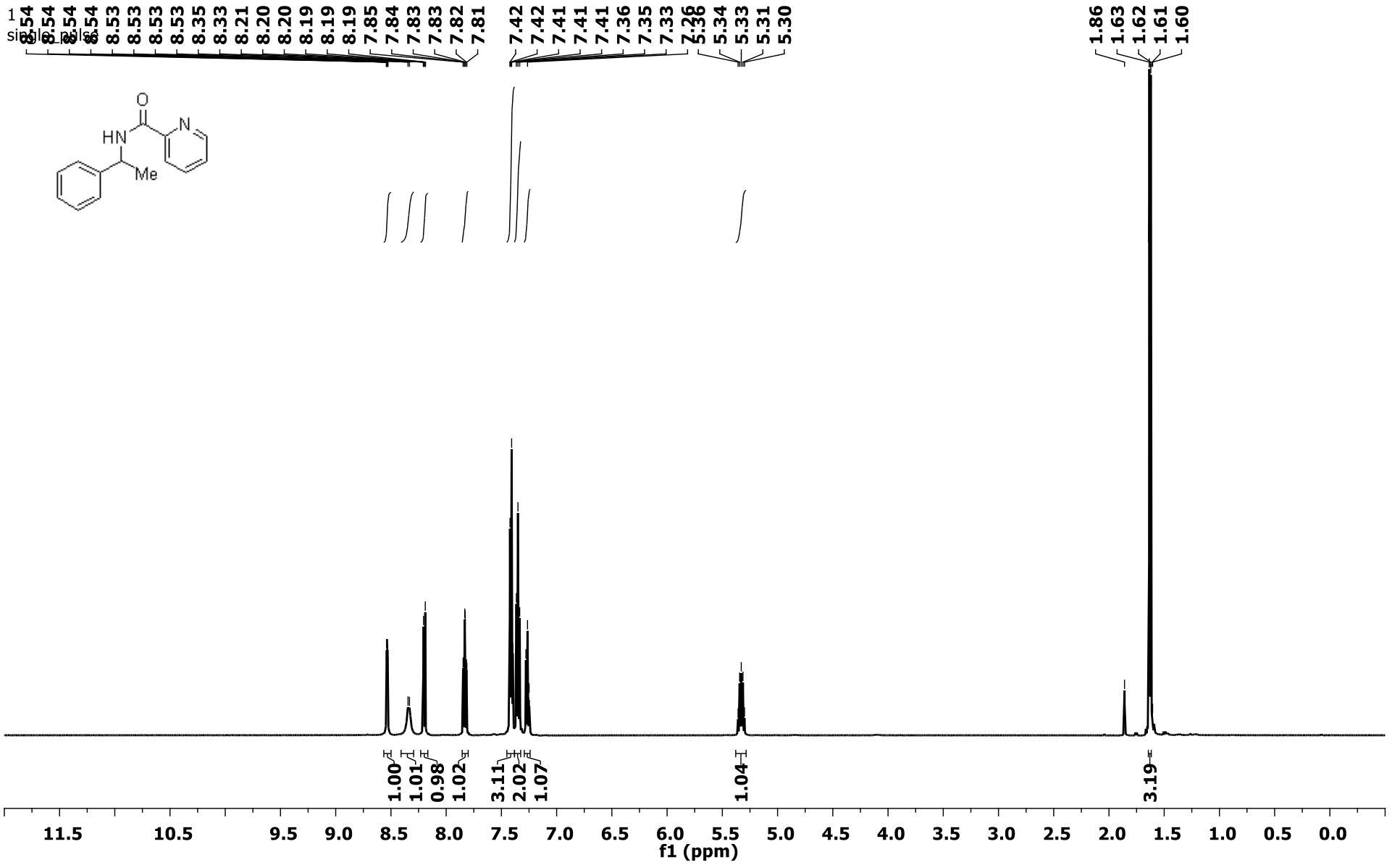
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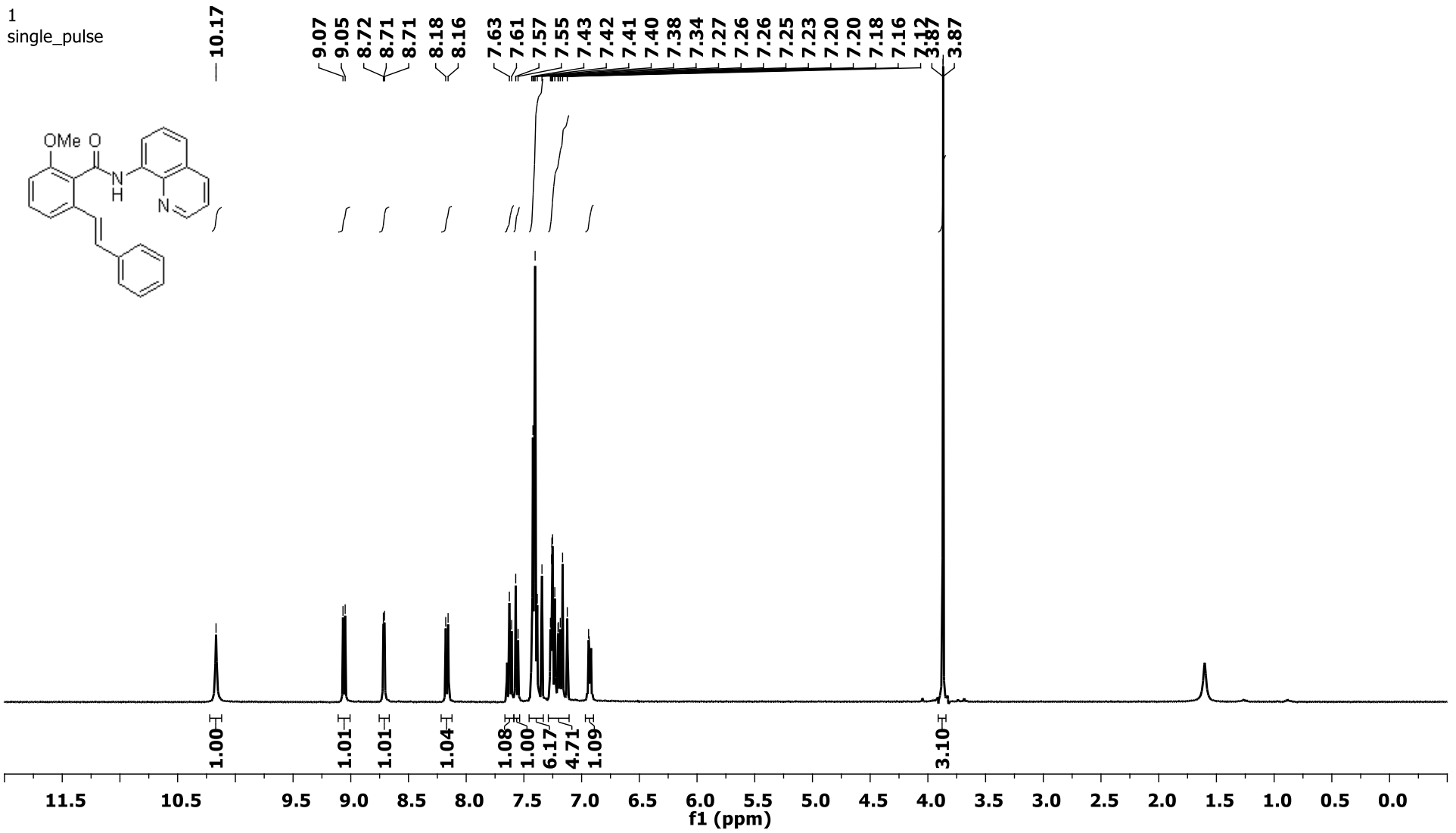
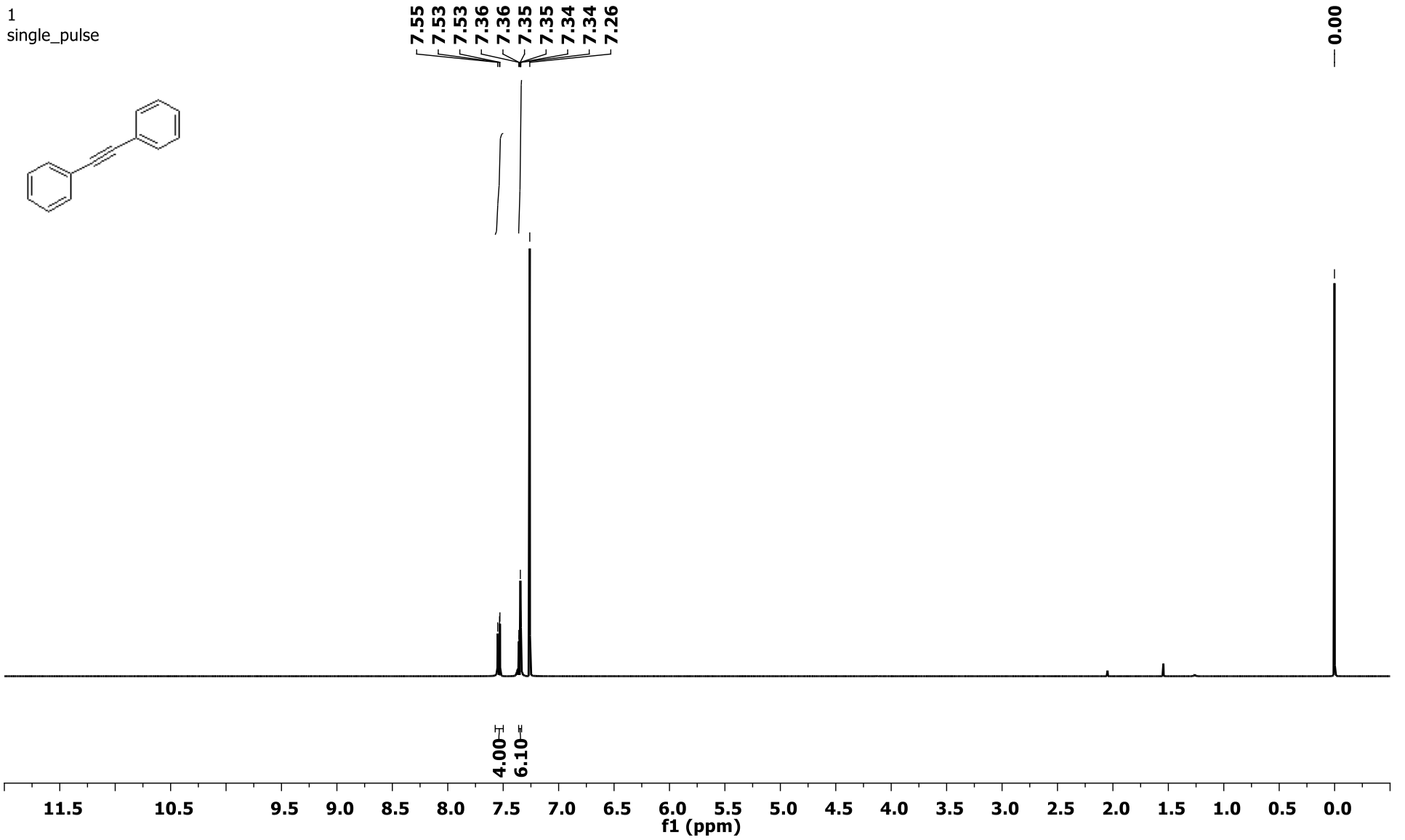
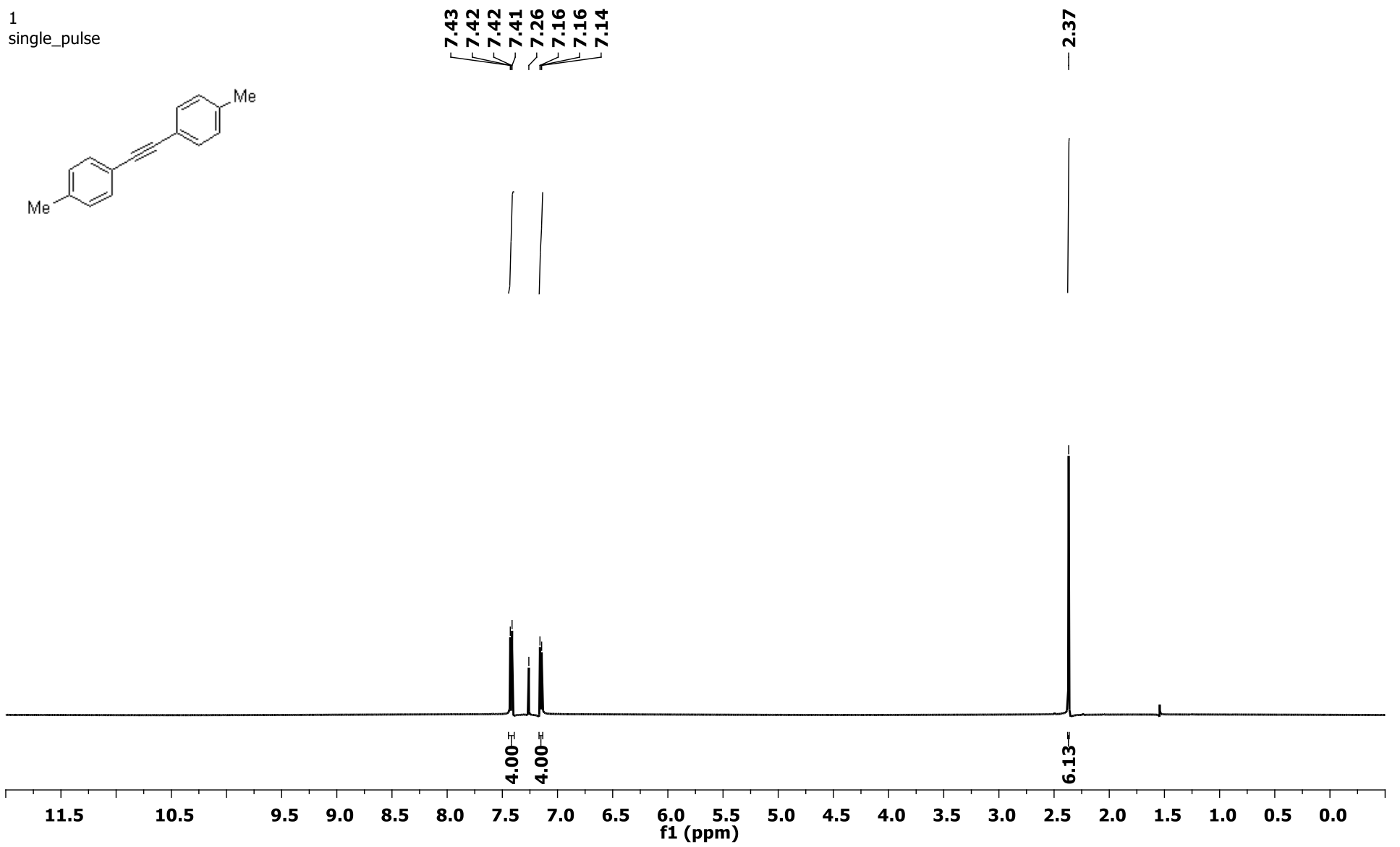
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


1
single_pulse
10.17
9.07
9.05
8.72
8.71
8.71
8.18
8.16
7.63
7.61
7.57
7.55
7.43
7.42
7.41
7.40
7.38
7.34
7.27
7.26
7.26
7.25
7.23
7.20
7.20
7.18
7.16
3.87
3.87
OMe O
N
H
N
1.00
1.01
1.01
1.04
1.08
1.00
6.17
4.71
1.09
3.10
11.5
10.5
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
0.0
f1 (ppm)


1
single_pulse
7.55
7.53
7.53
7.36
7.36
7.35
7.35
7.34
7.34
7.26
0.00
4.00
6.10
11.5
10.5
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
0.0
f1 (ppm)


1
single_pulse
Me
Me
7.43
7.42
7.42
7.41
7.26
7.16
7.16
7.14
2.37
4.00
4.00
6.13
11.5
10.5
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
0.0
f1 (ppm)

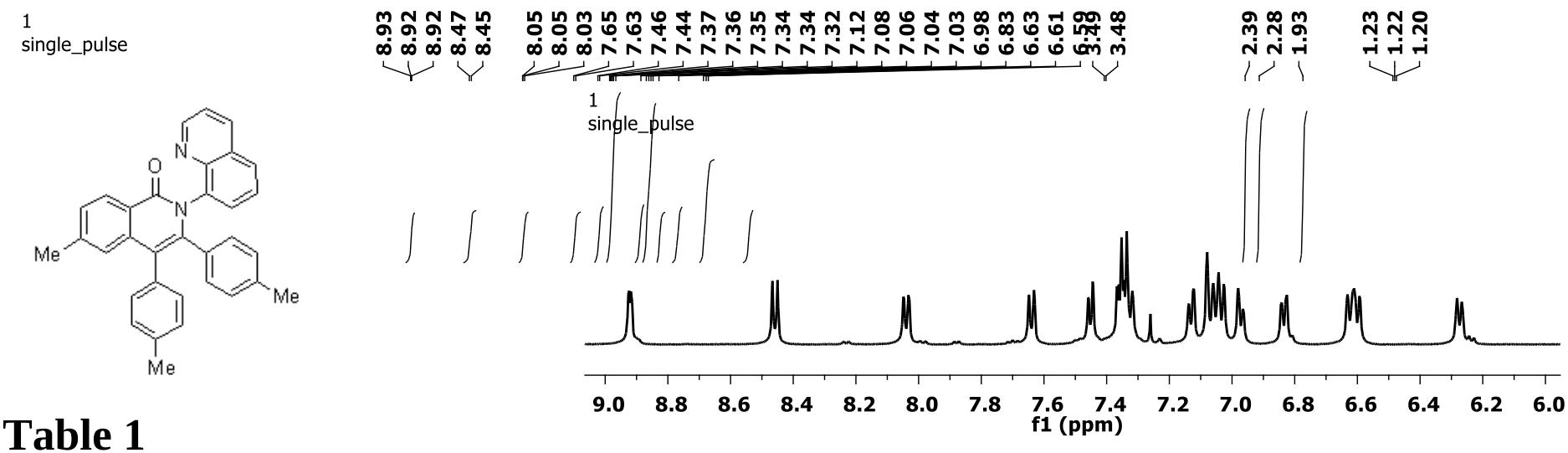
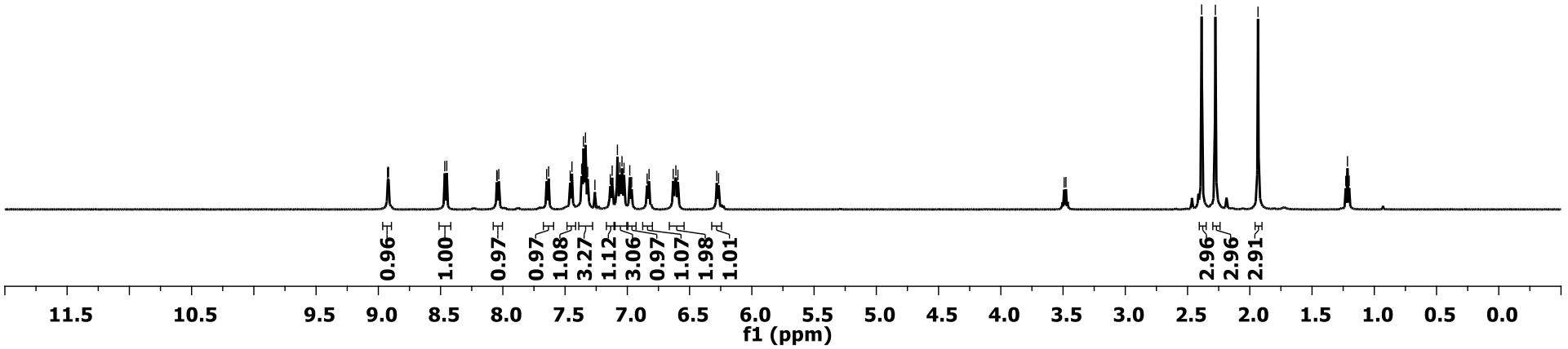

1
single_pulse
8.93
8.92
8.92
8.47
8.45
8.05
8.05
8.03
7.65
7.63
7.46
7.44
7.37
7.36
7.35
7.34
7.34
7.32
7.12
7.08
7.06
7.04
7.03
6.98
6.83
6.63
6.61
6.59
3.49
3.48
2.39
2.28
1.93
1.23
1.22
1.20
1
single_pulse
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
f1 (ppm)
O
N
N
Me
Me
Me

Table 1


0.96
1.00
0.97
0.97
1.08
3.27
1.12
3.06
0.97
1.07
1.98
1.01
2.96
2.96
2.91
11.5
10.5
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
0.0
f1 (ppm)

1
single pulse decoupled gated NOE

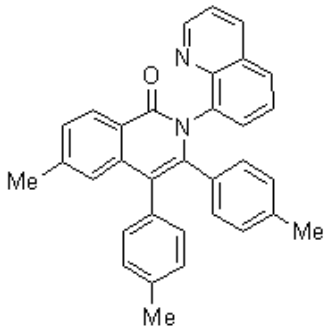


Table 1

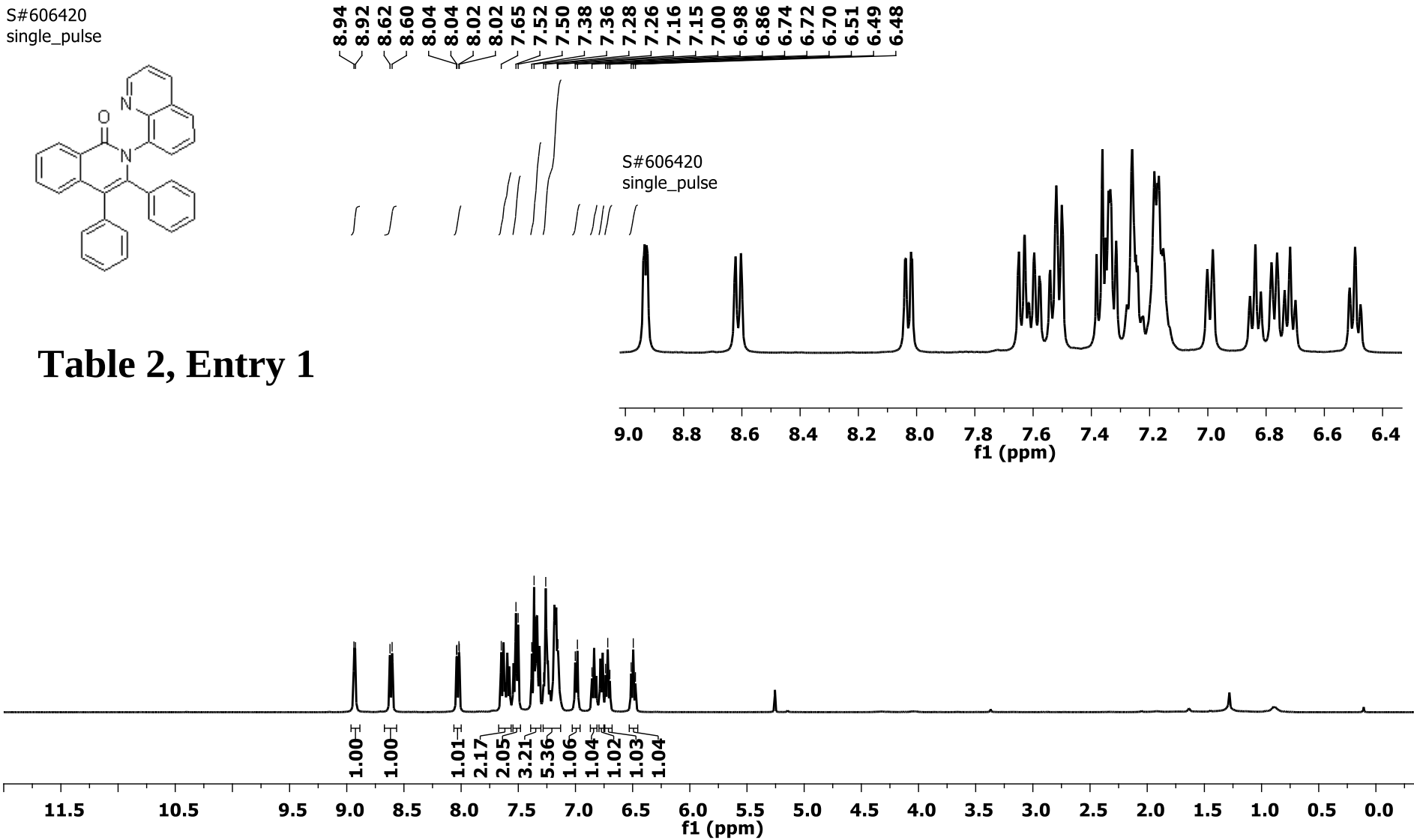


Table 2, Entry 1

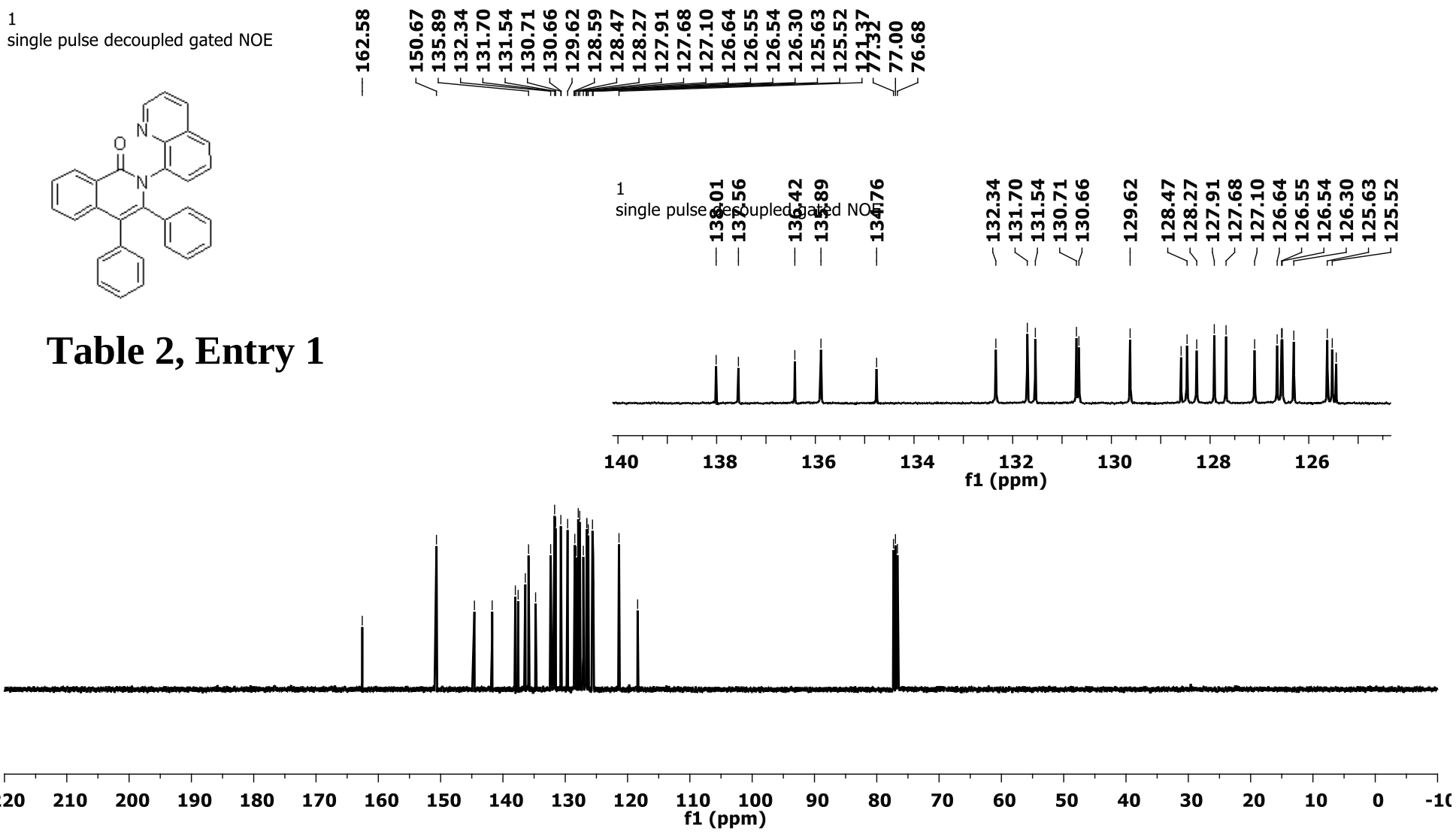


Table 2, Entry 1

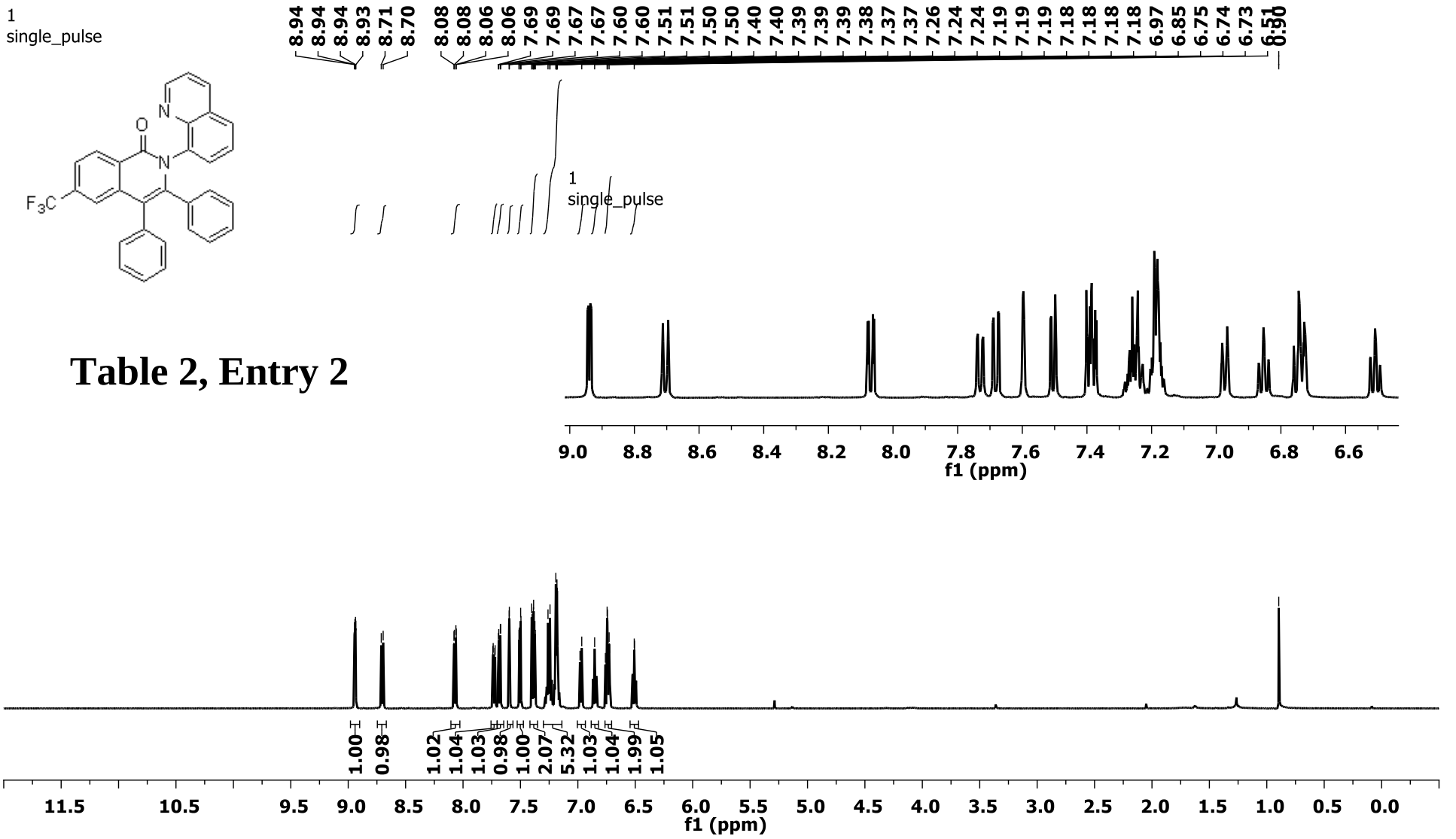


Table 2, Entry 2

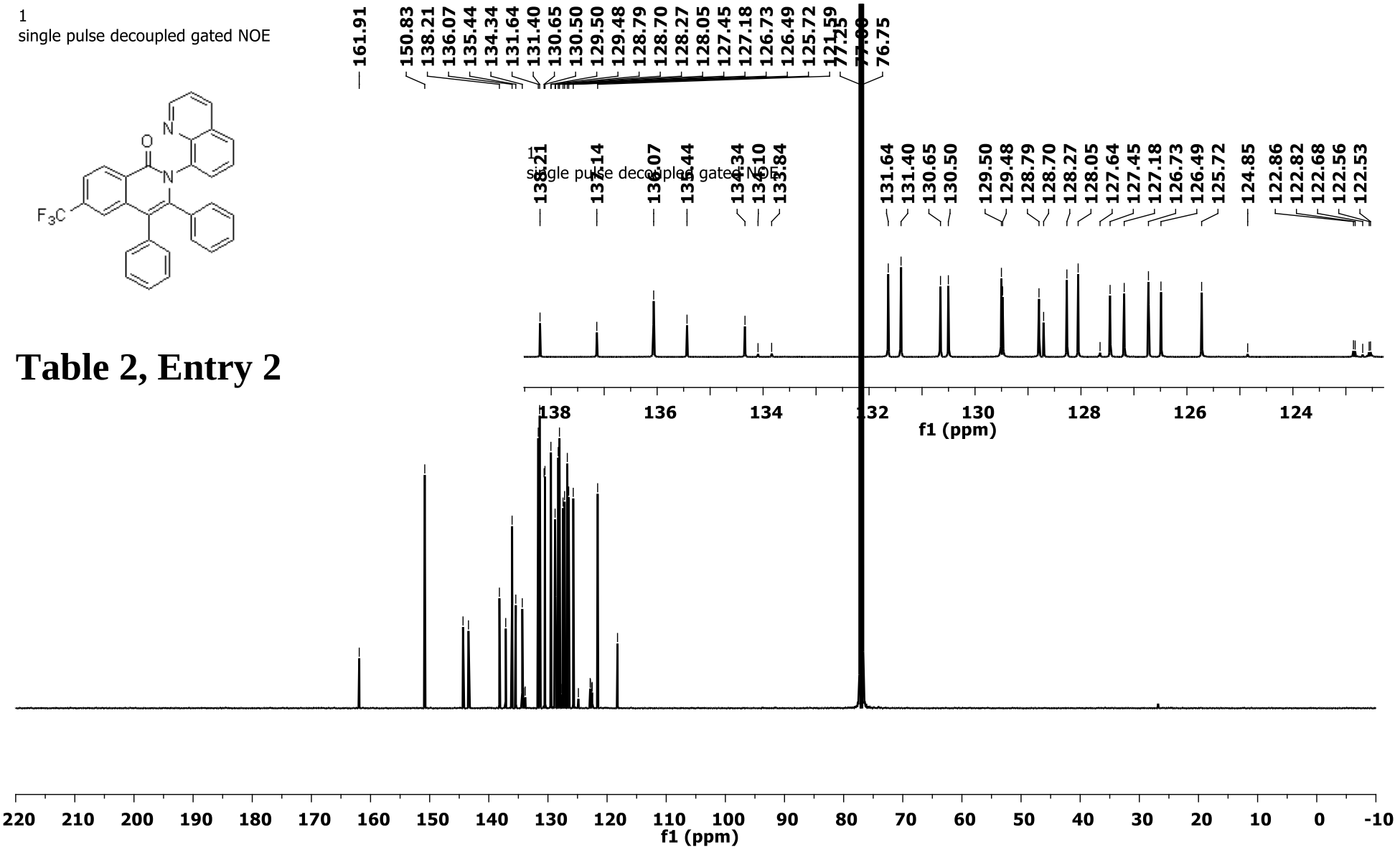


Table 2, Entry 2

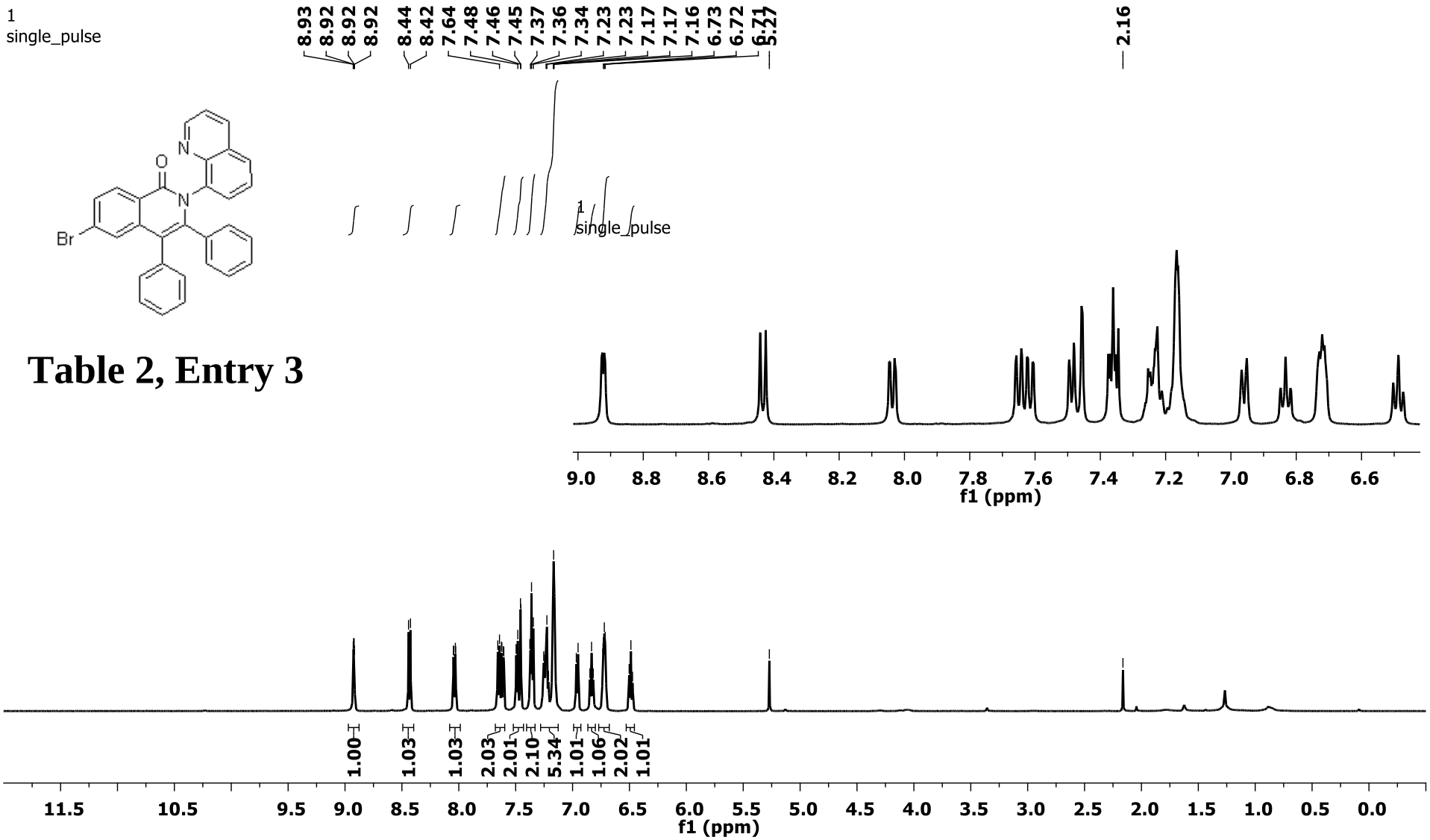


Table 2, Entry 3

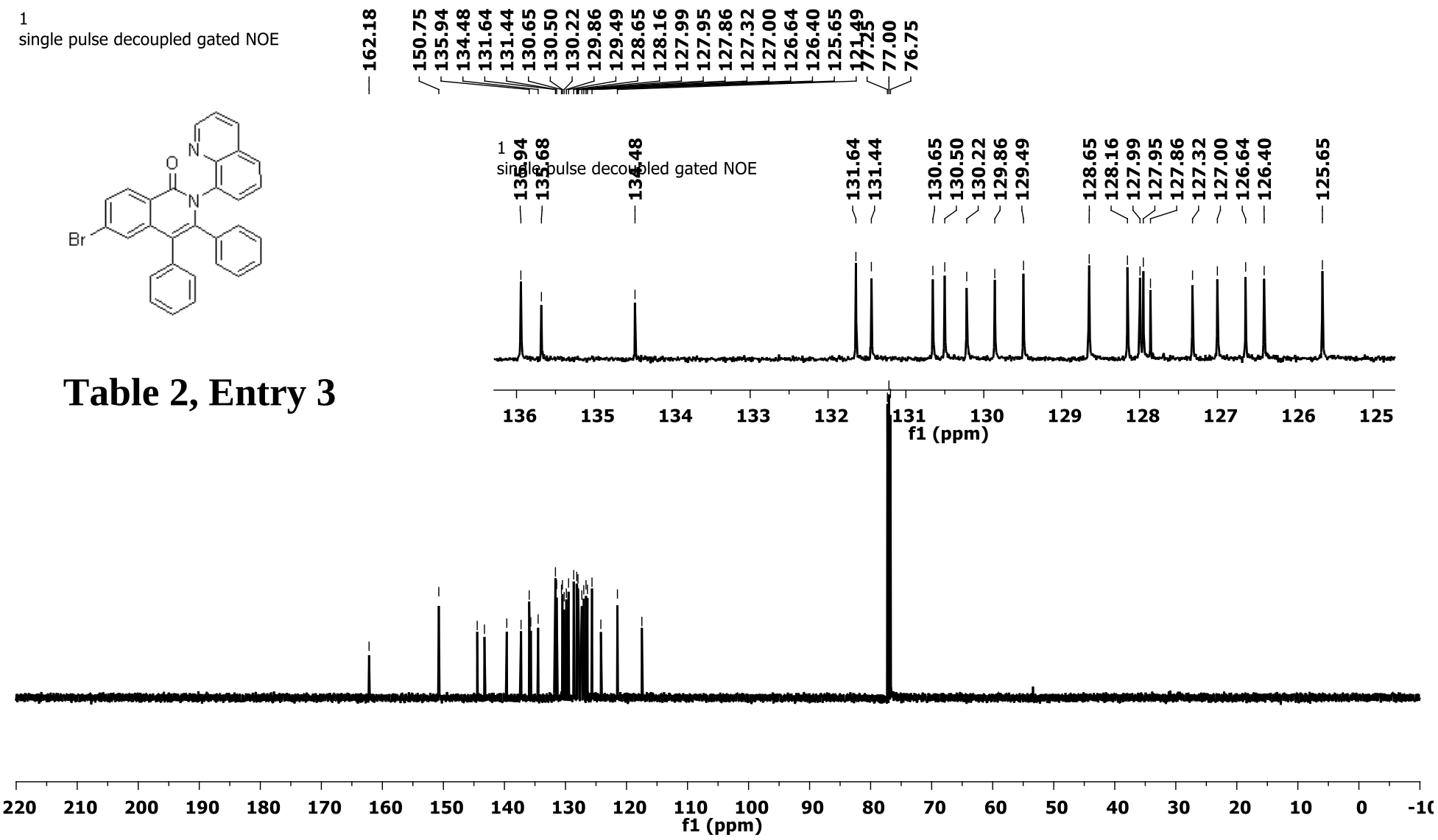


Table 2, Entry 3

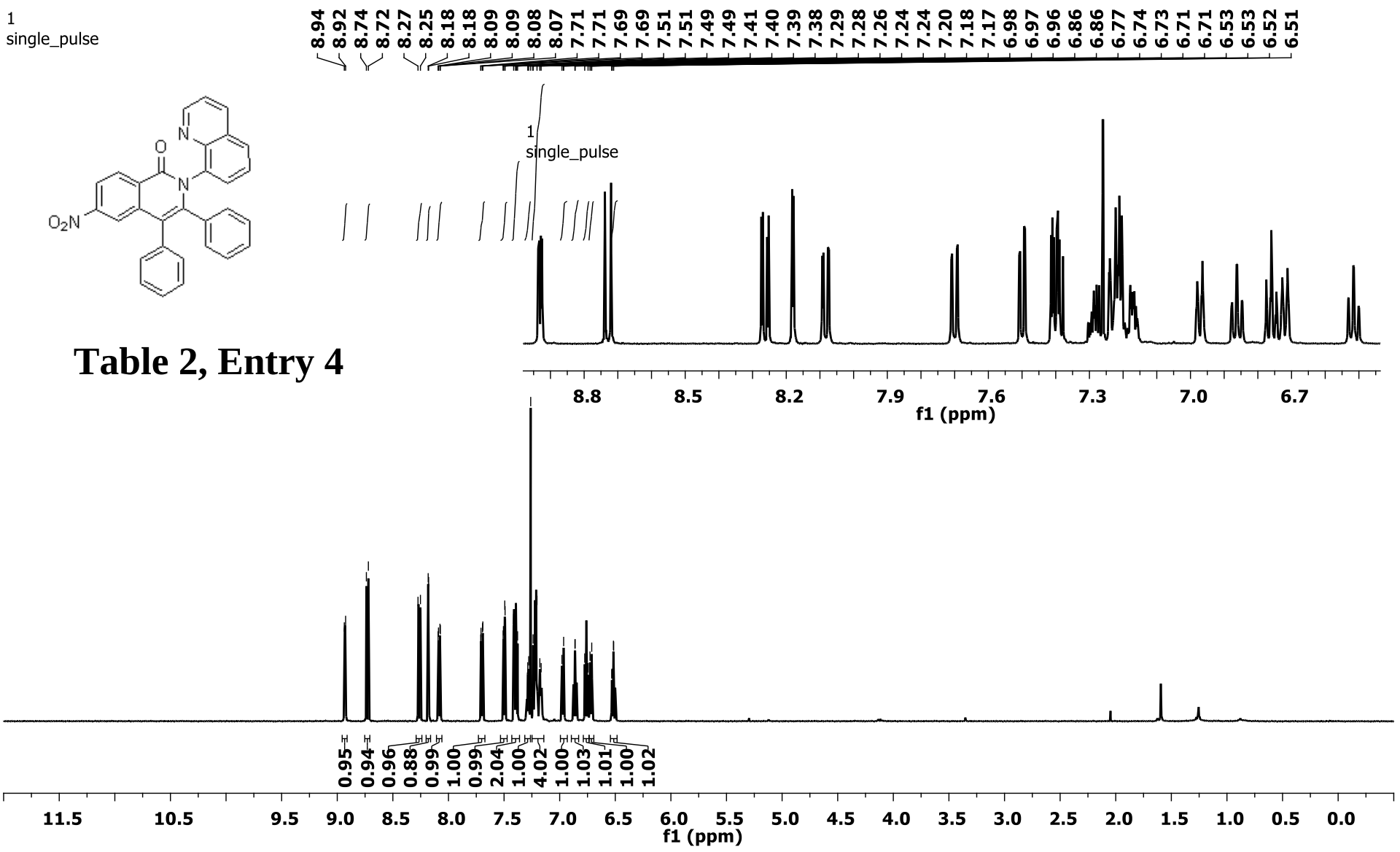


Table 2, Entry 4

1
single pulse decoupled gated NOE

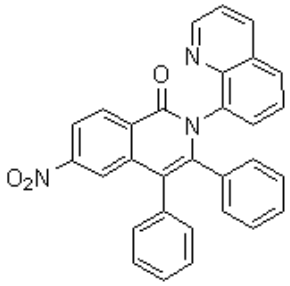
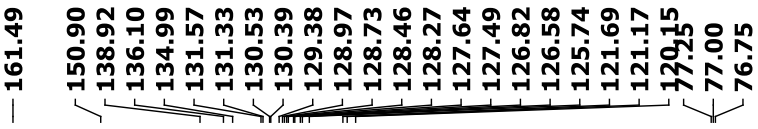
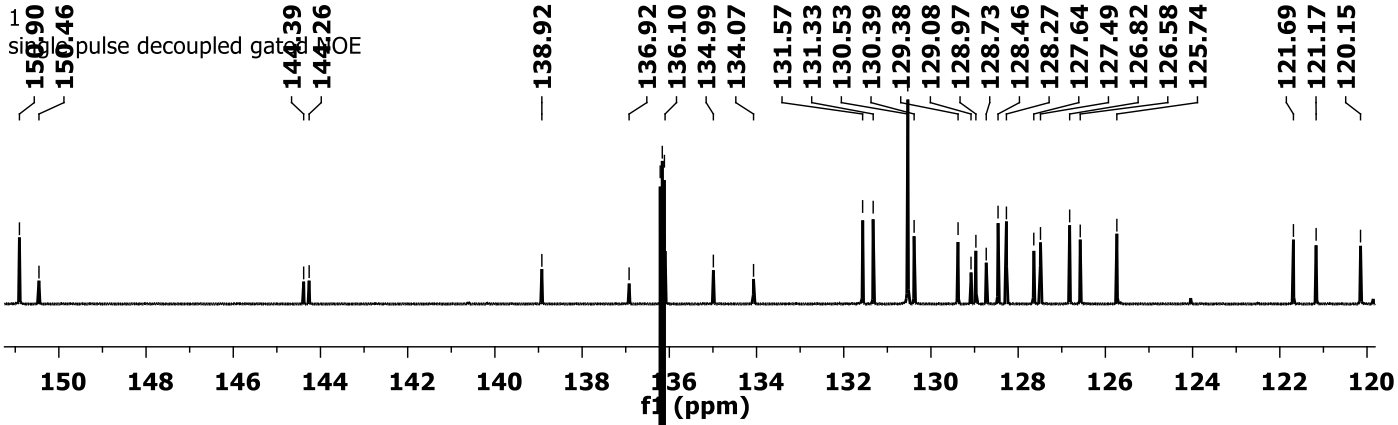
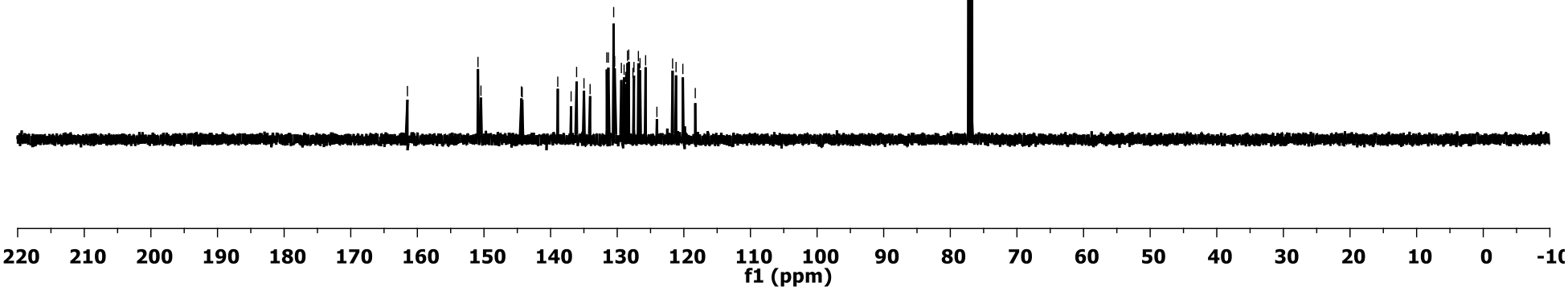


Table 2, Entry 4







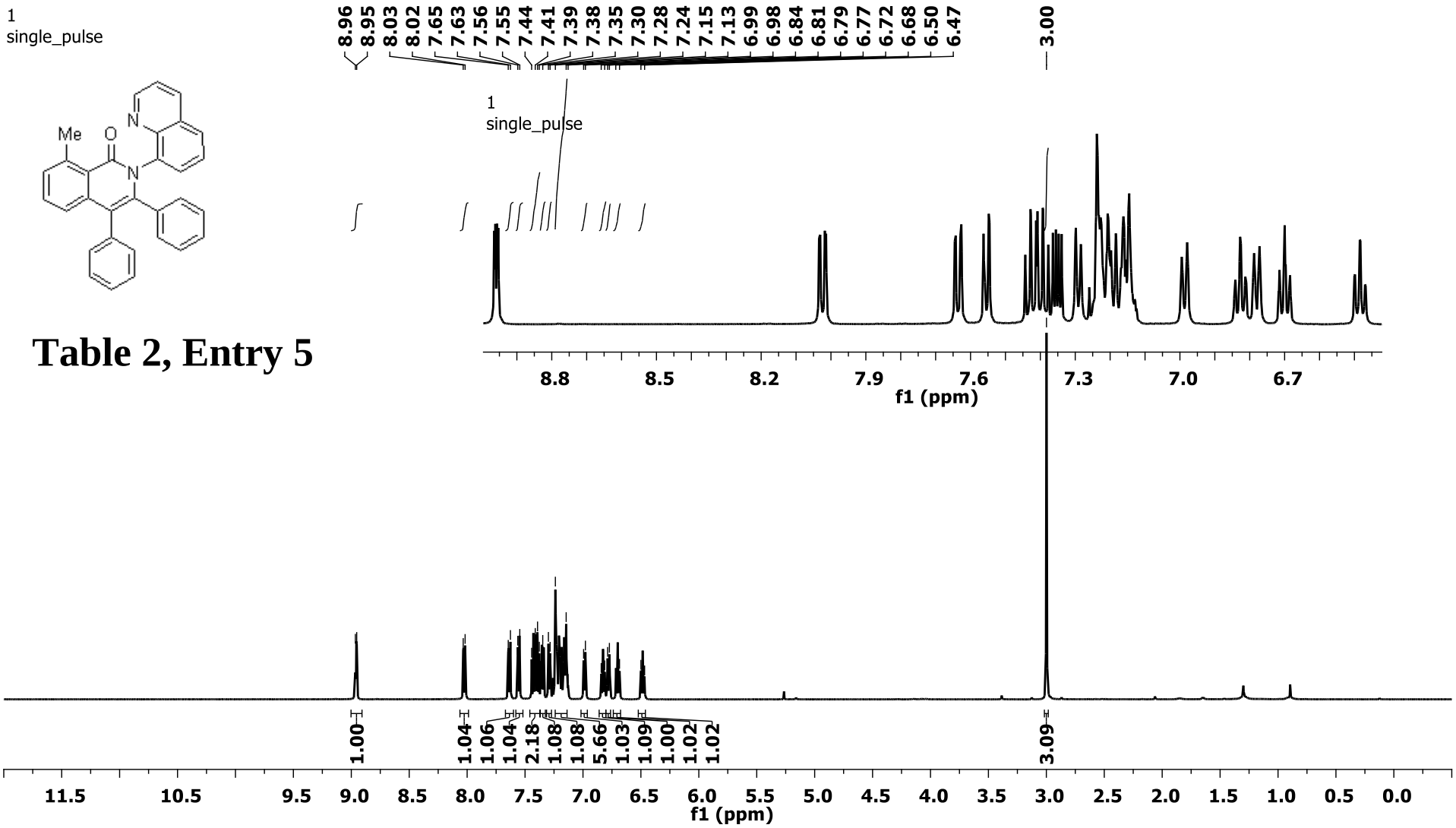


Table 2, Entry 5

1
single pulse decoupled gated NOE

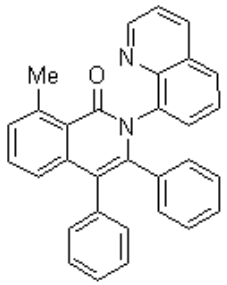
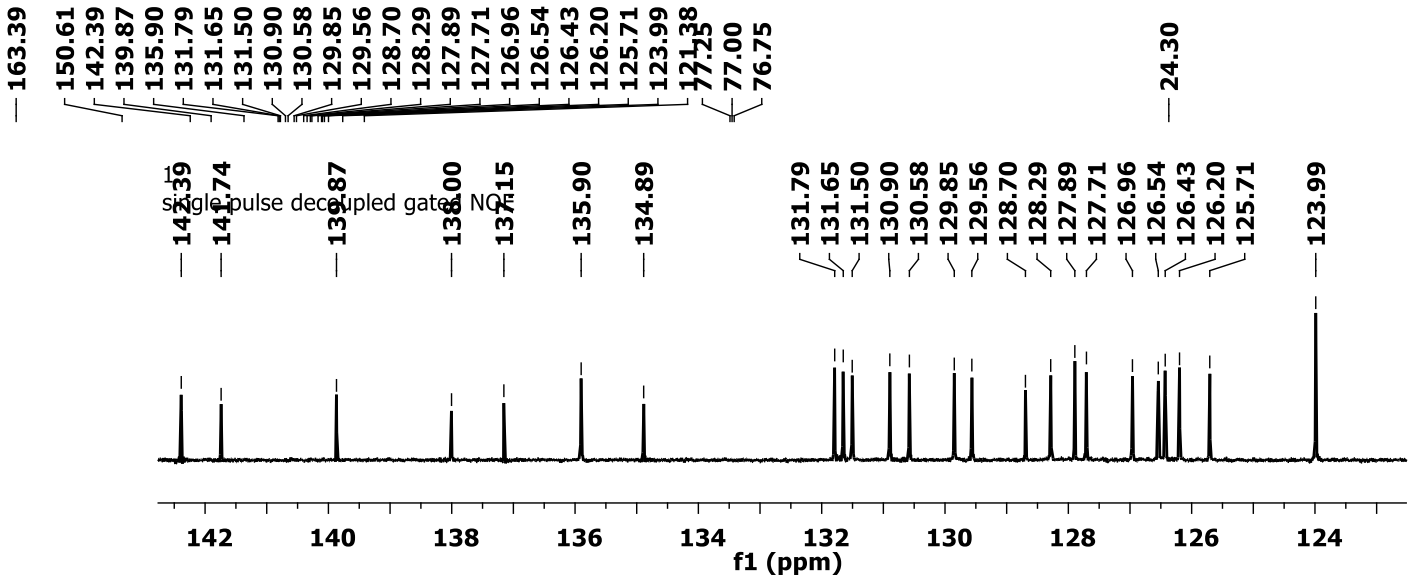
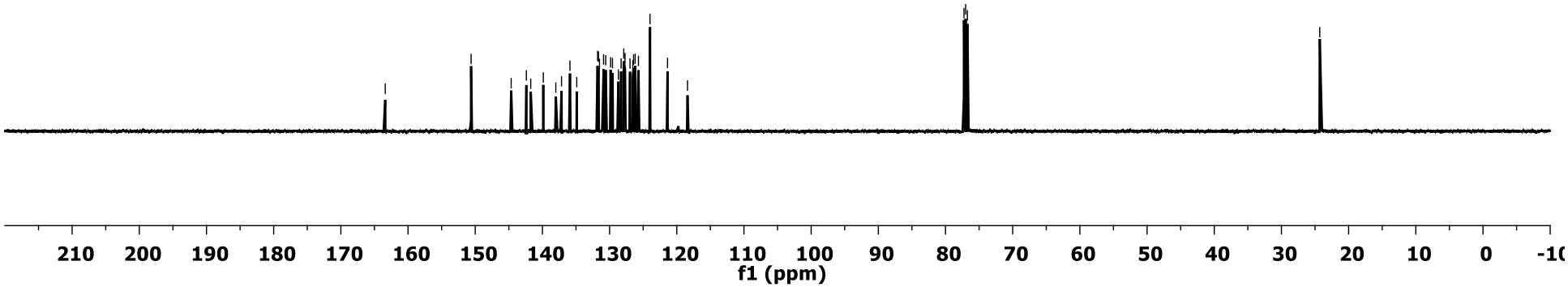
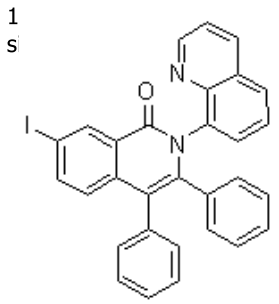


Table 2, Entry 5







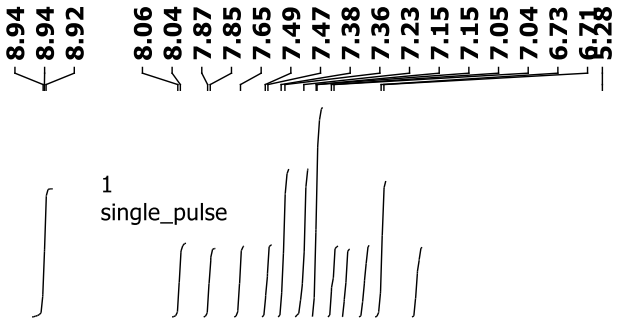
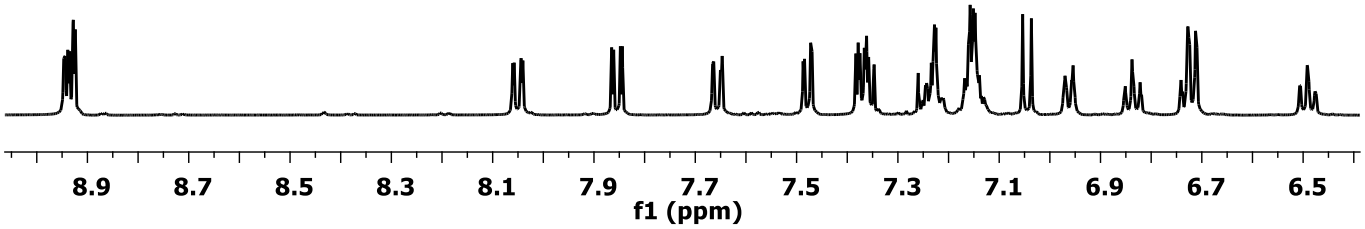
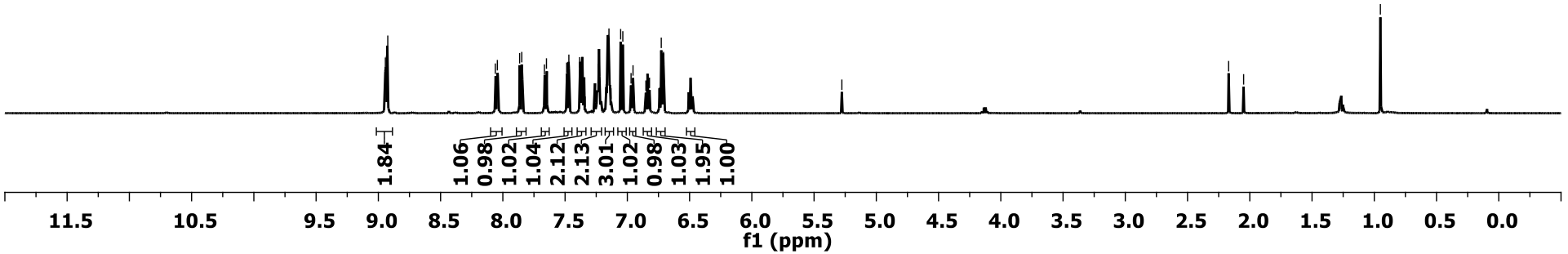
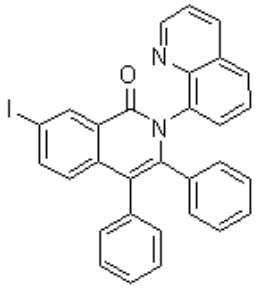


Table 2, Entry 6





1
single pulse decoupled gated NOE



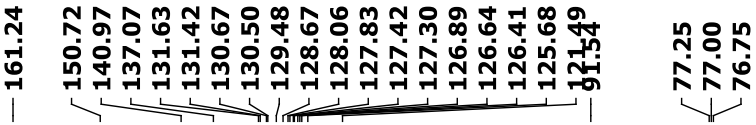
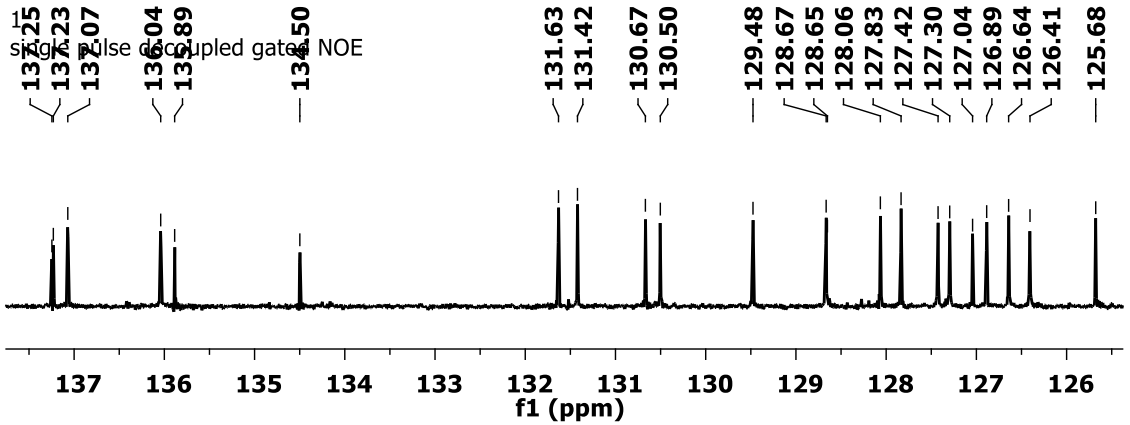
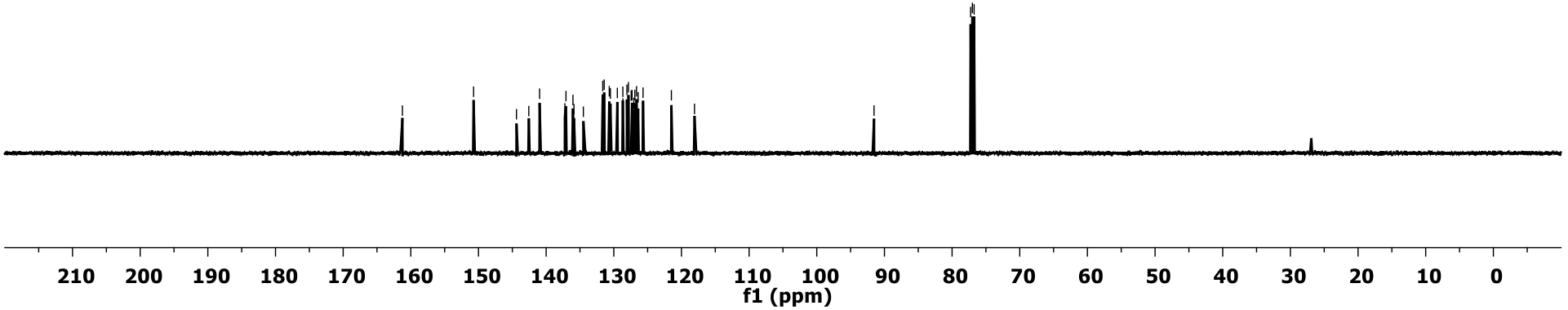
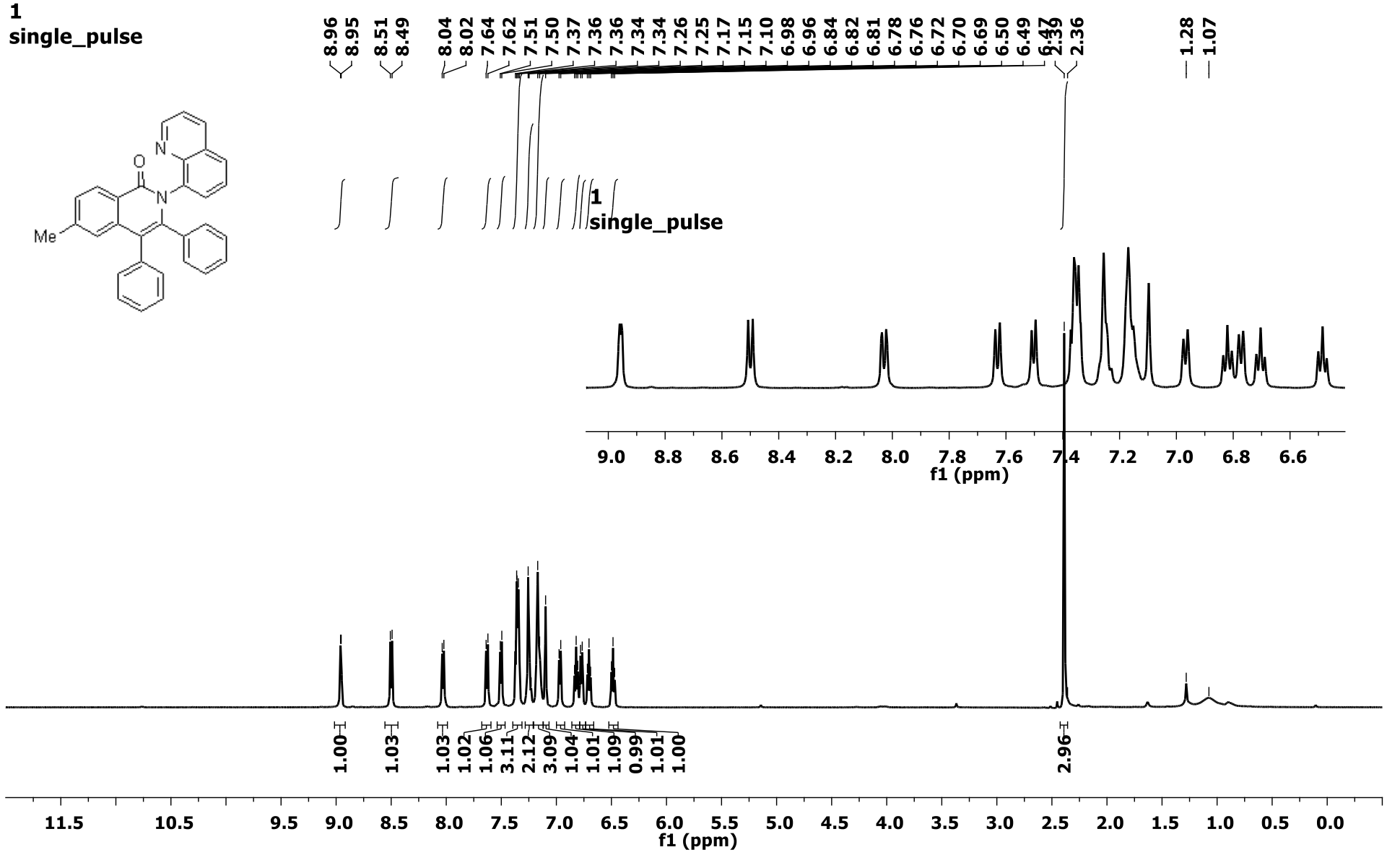
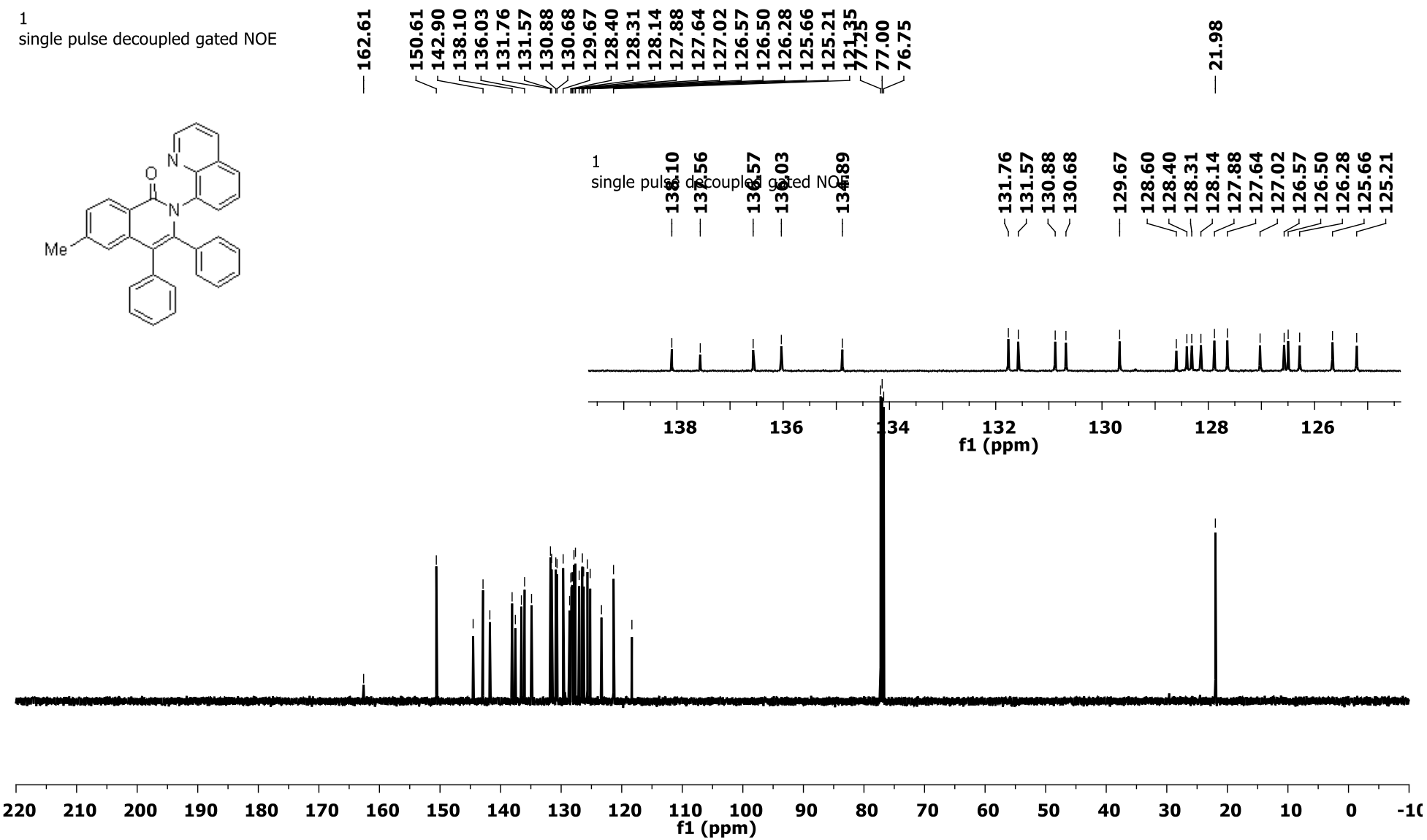


Table 2, Entry 6






1
single_pulse
8.96
8.95
8.51
8.49
8.04
8.02
7.64
7.62
7.51
7.50
7.37
7.36
7.36
7.34
7.34
7.26
7.25
7.17
7.15
7.10
6.98
6.96
6.84
6.82
6.81
6.78
6.76
6.72
6.70
6.69
6.50
6.49
6.47
2.39
2.36
1.28
1.07
N
O
N
Me
1
single_pulse
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
f1 (ppm)
1.00
1.03
1.03
1.02
1.06
3.11
2.12
3.09
1.04
1.01
1.09
0.99
1.01
1.00
2.96
11.5
10.5
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
0.0
f1 (ppm)


1
single pulse decoupled gated NOE
162.61
150.61
142.90
138.10
136.03
131.76
131.57
130.88
130.68
129.67
128.40
128.31
128.14
127.88
127.64
127.02
126.57
126.50
126.28
125.66
125.21
121.35
77.25
77.00
76.75
21.98
N
O
N
Me
1
single pulse decoupled gated NOE
138.10
137.56
136.57
136.03
134.89
131.76
131.57
130.88
130.68
129.67
128.60
128.40
128.31
128.14
127.88
127.64
127.02
126.57
126.50
126.28
125.66
125.21
138
136
134
132
130
128
126
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

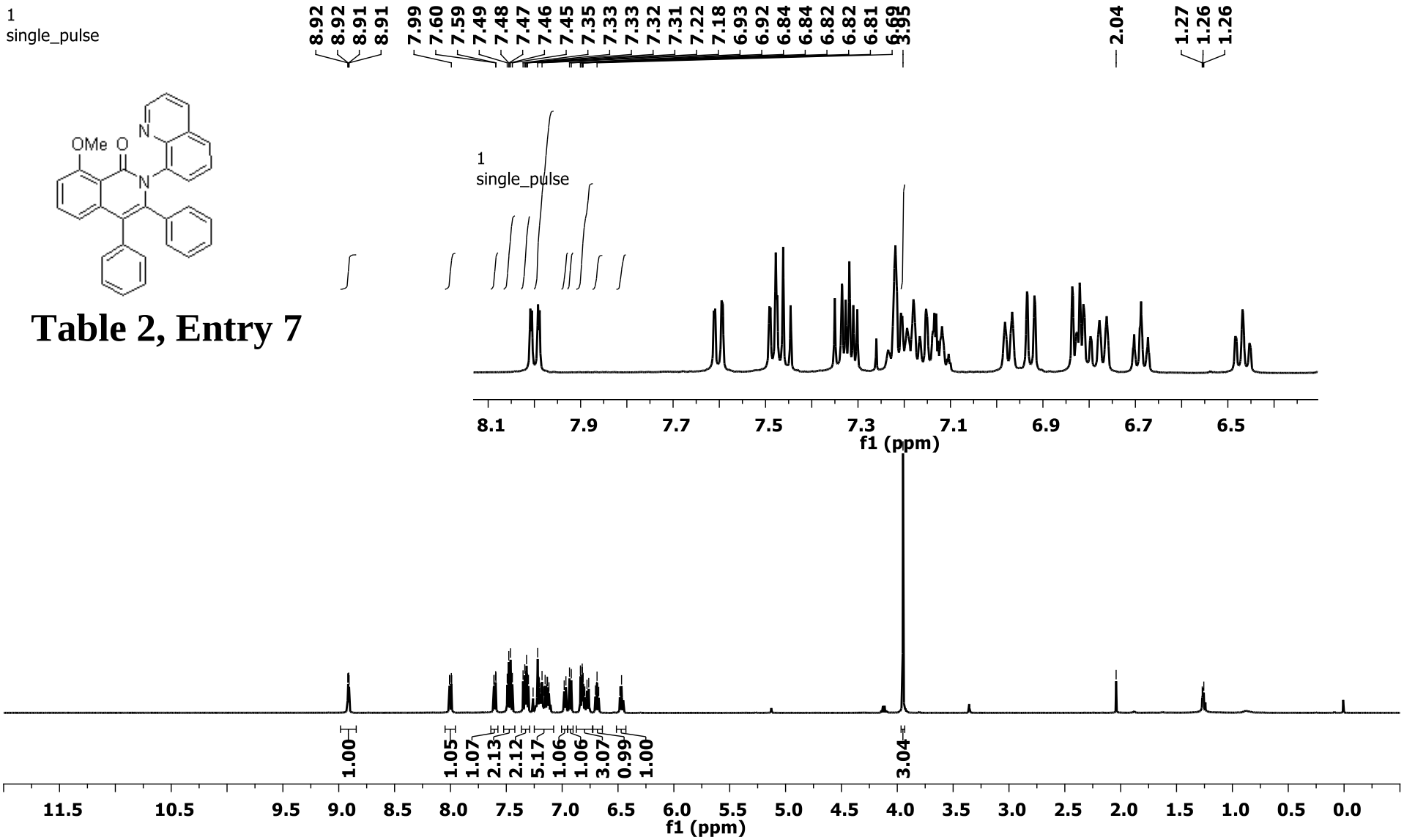
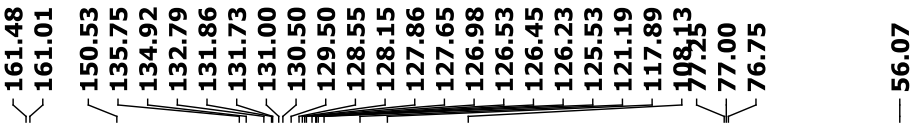


Table 2, Entry 7

1
single pulse decoupled gated NOE



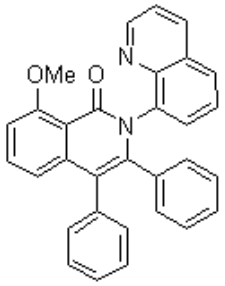
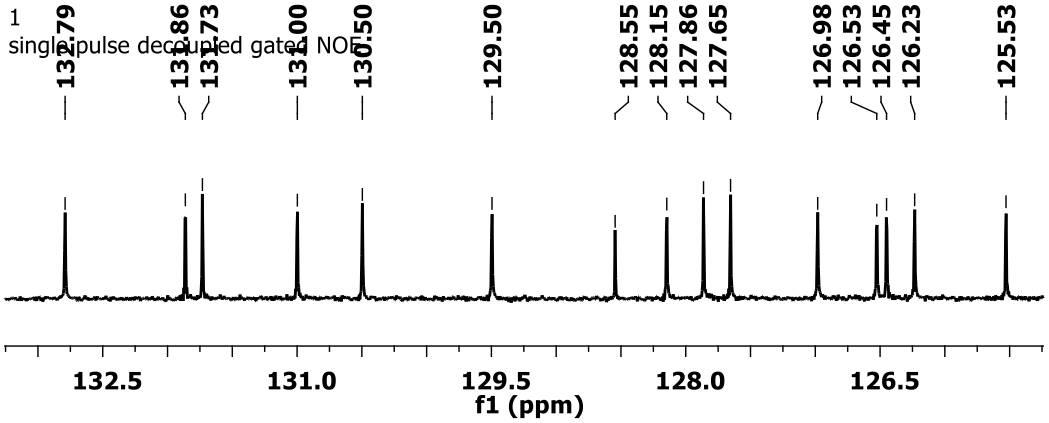
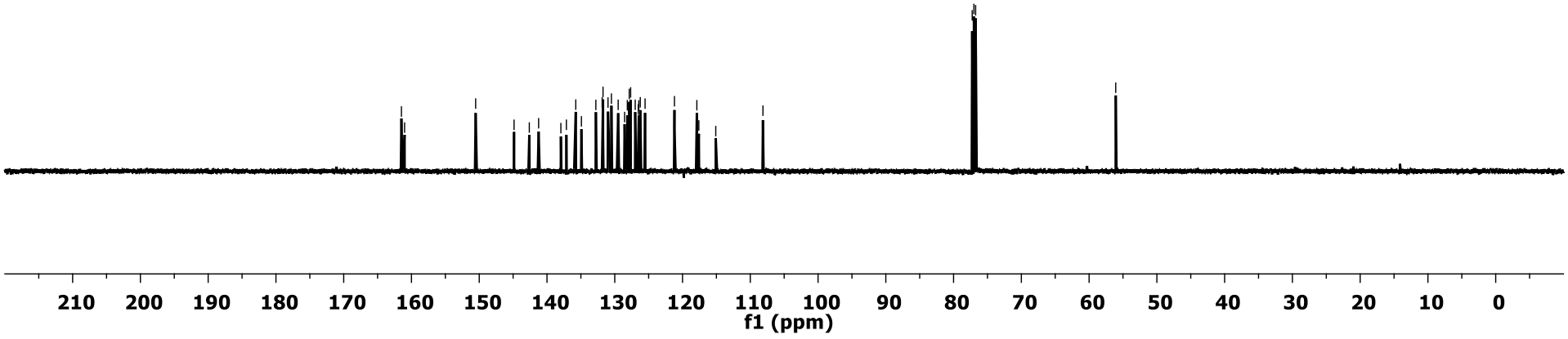


Table 2, Entry 7





S#655310
single_pulse

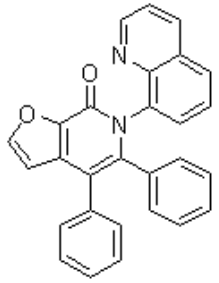


Table 2, Entry 8

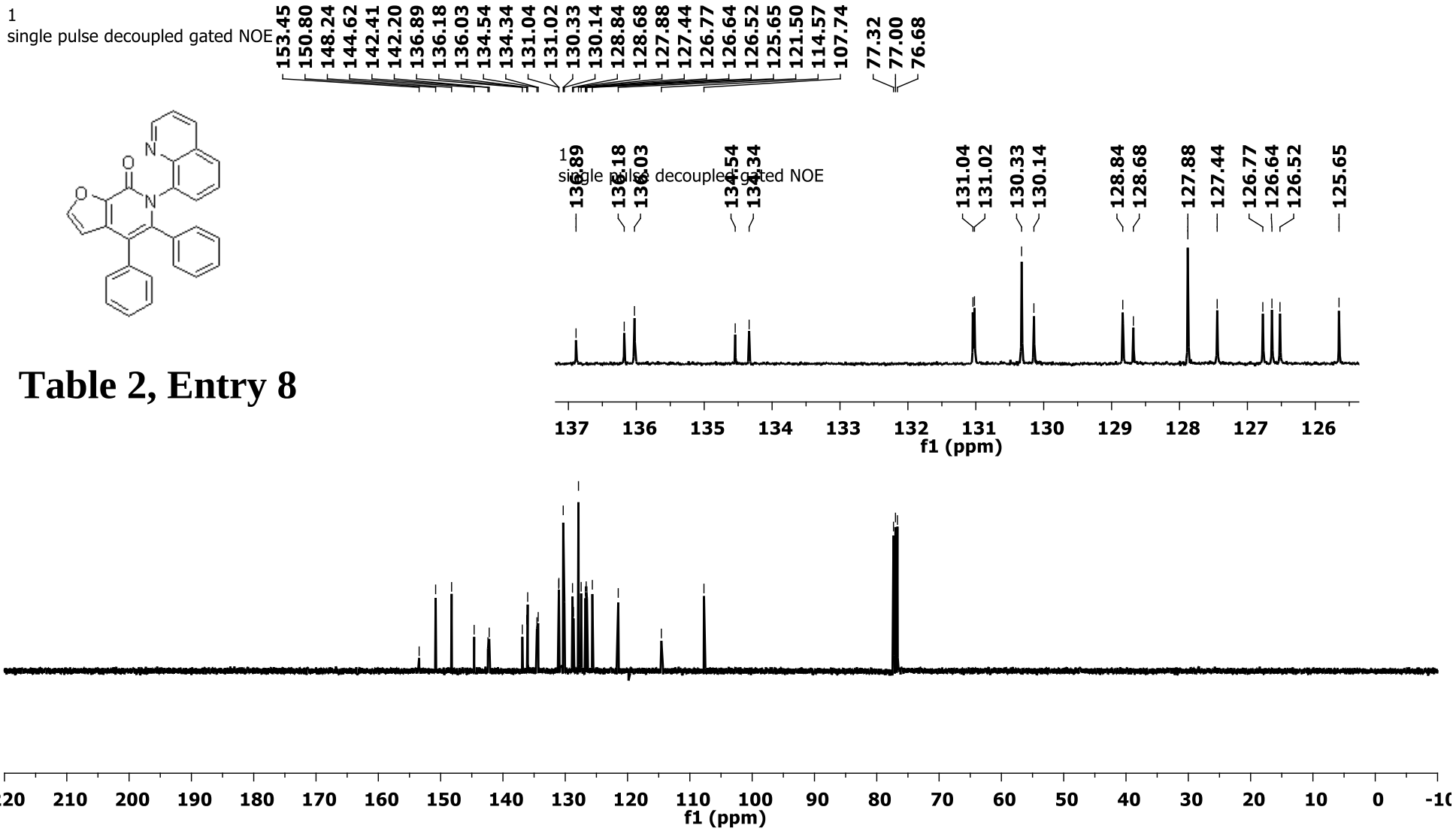


Table 2, Entry 8

1
single_pulse

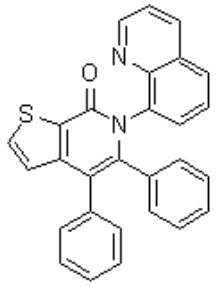
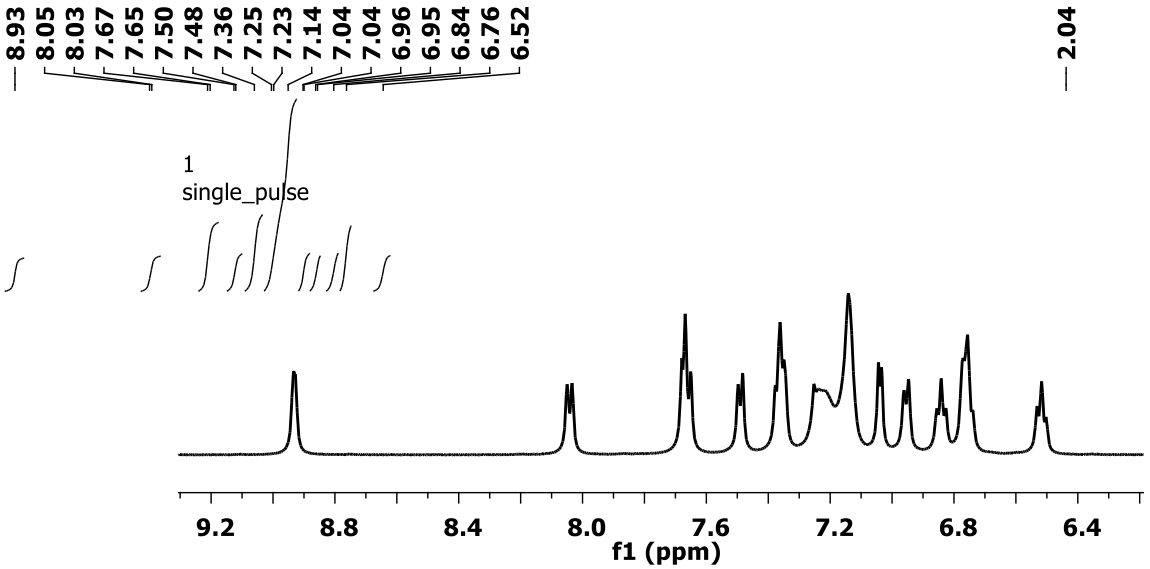
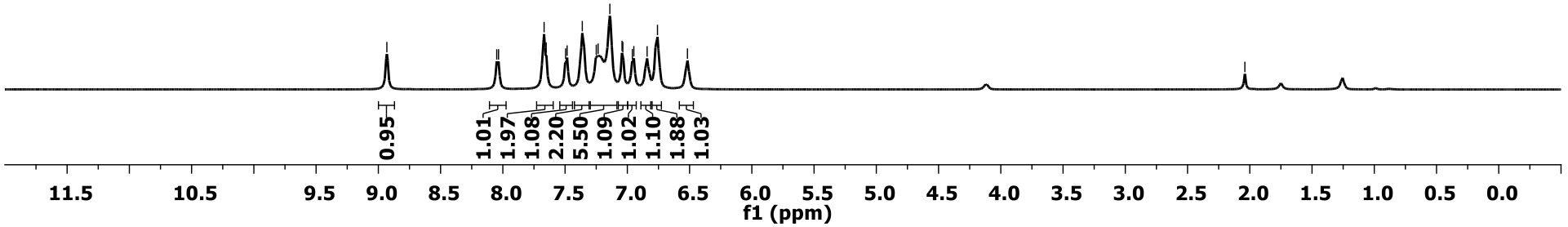


Table 2, Entry 9





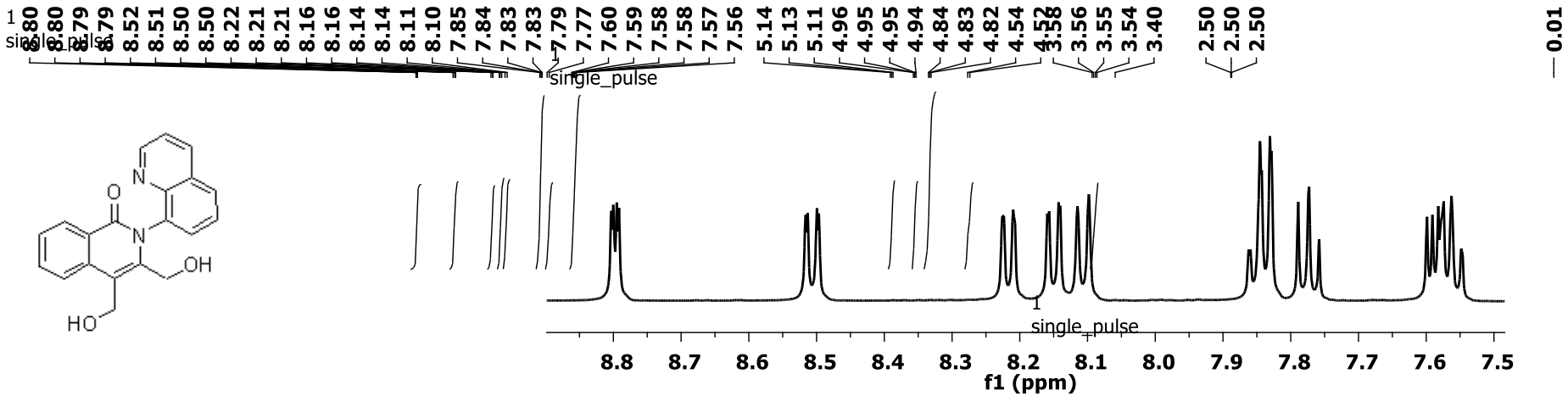
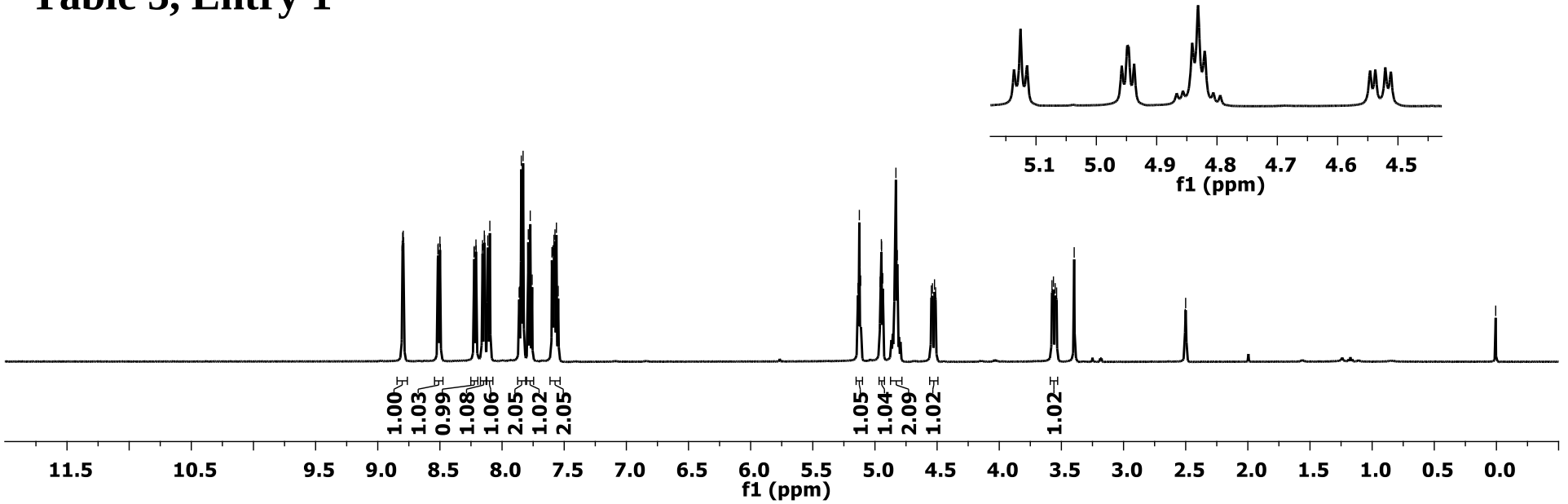


Table 3, Entry 1



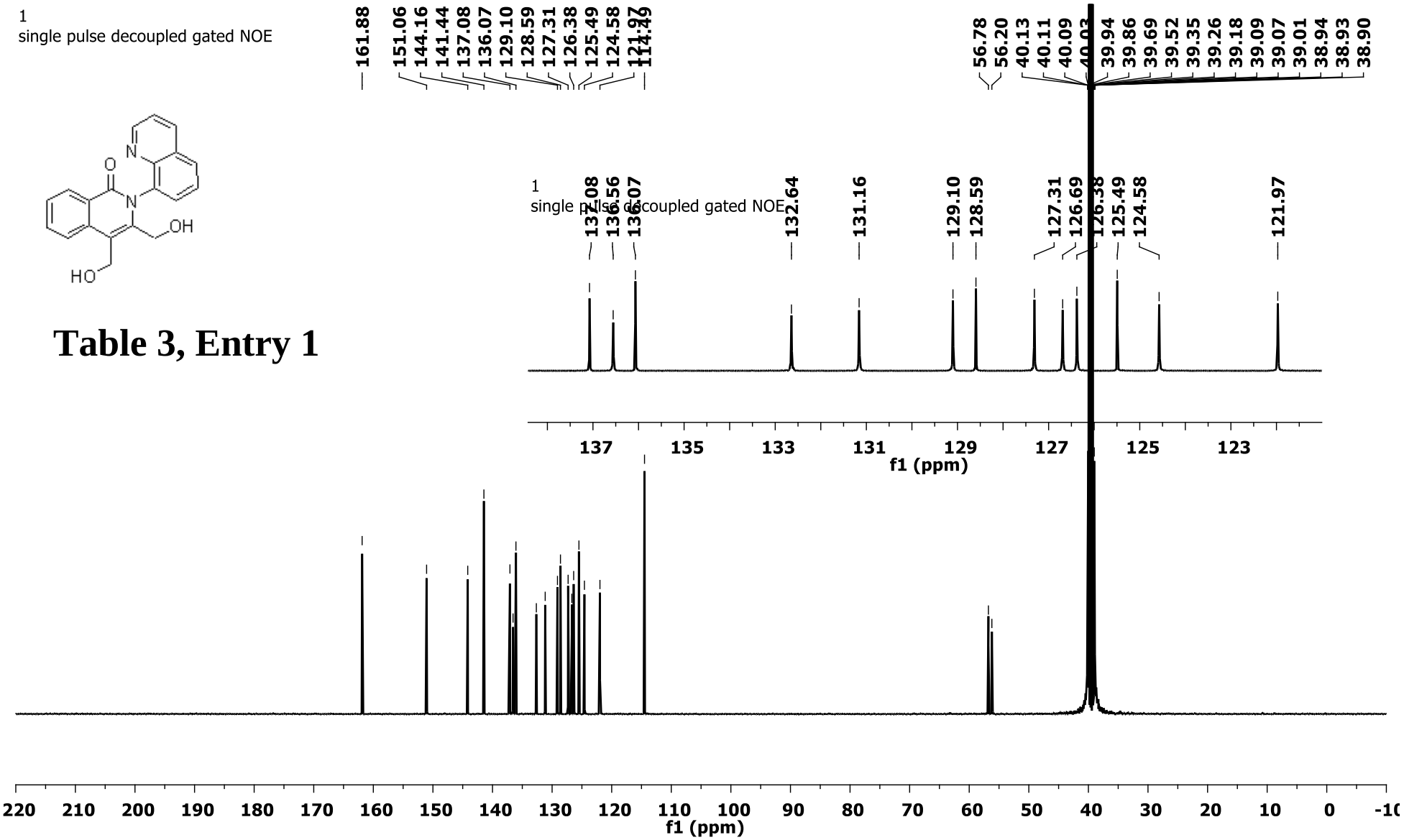
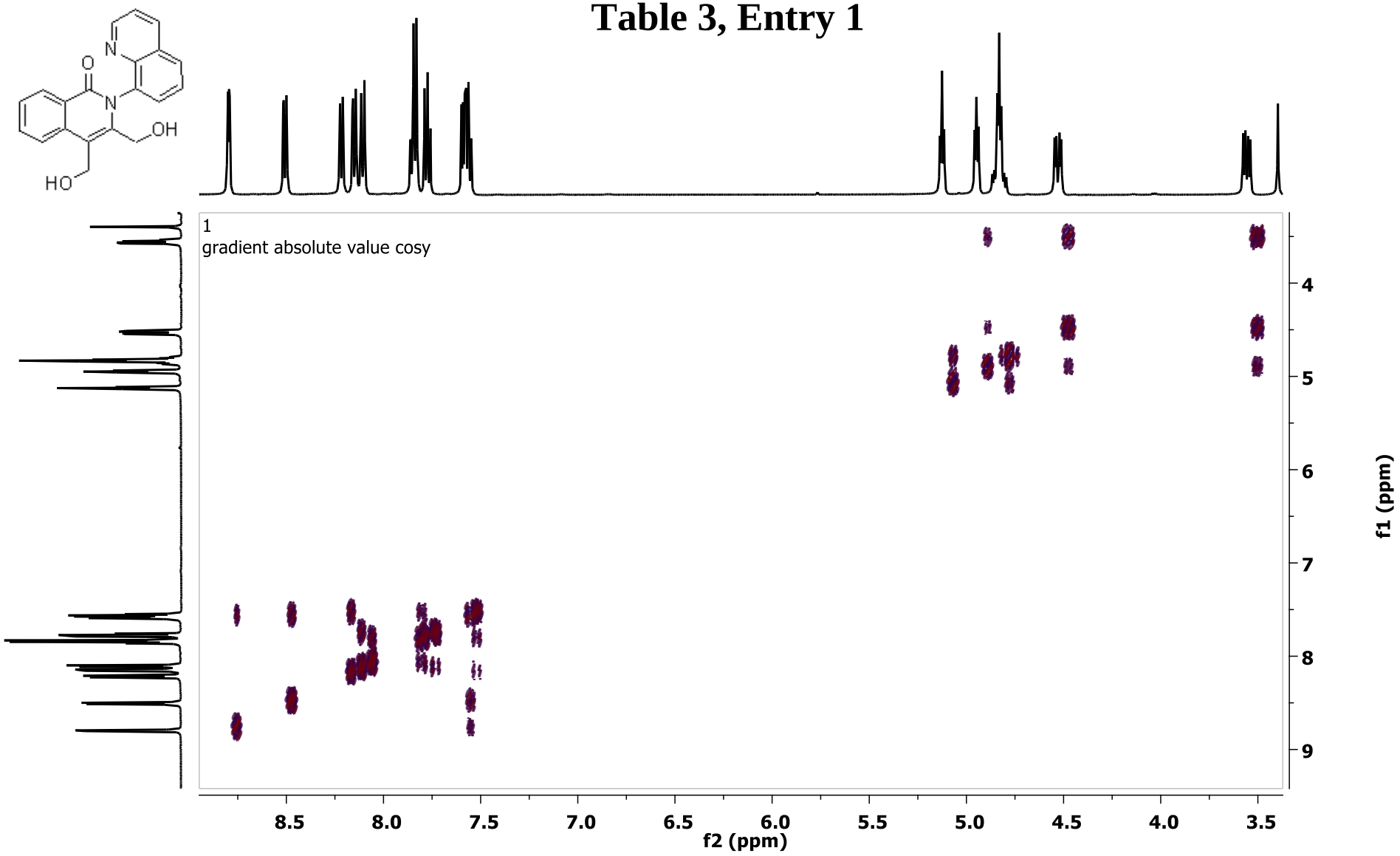

1
single pulse decoupled gated NOE
161.88
151.06
144.16
141.44
137.08
136.07
129.10
128.59
127.31
126.38
125.49
124.58
121.97
114.49
56.78
56.20
40.13
40.11
40.09
40.03
39.94
39.86
39.69
39.52
39.35
39.26
39.18
39.09
39.07
39.01
38.94
38.93
38.90
O
N
N
OH
HO
Table 3, Entry 1
1
single pulse decoupled gated NOE
137.08
136.56
136.07
132.64
131.16
129.10
128.59
127.31
126.69
126.38
125.49
124.58
121.97
137
135
133
131
129
127
125
123
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Table 3, Entry 1



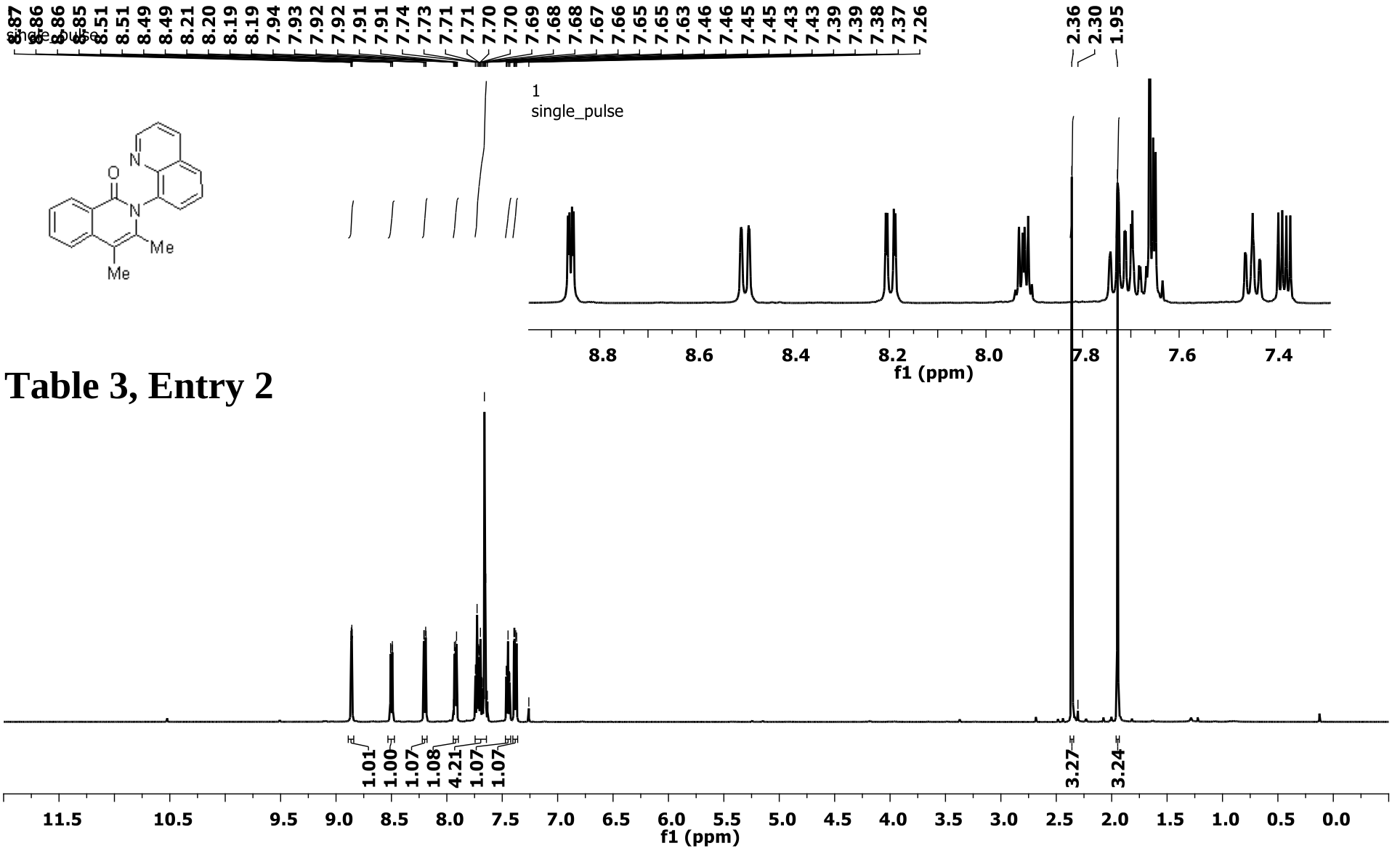


Table 3, Entry 2

1
single pulse decoupled gated NOE

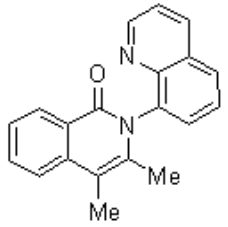
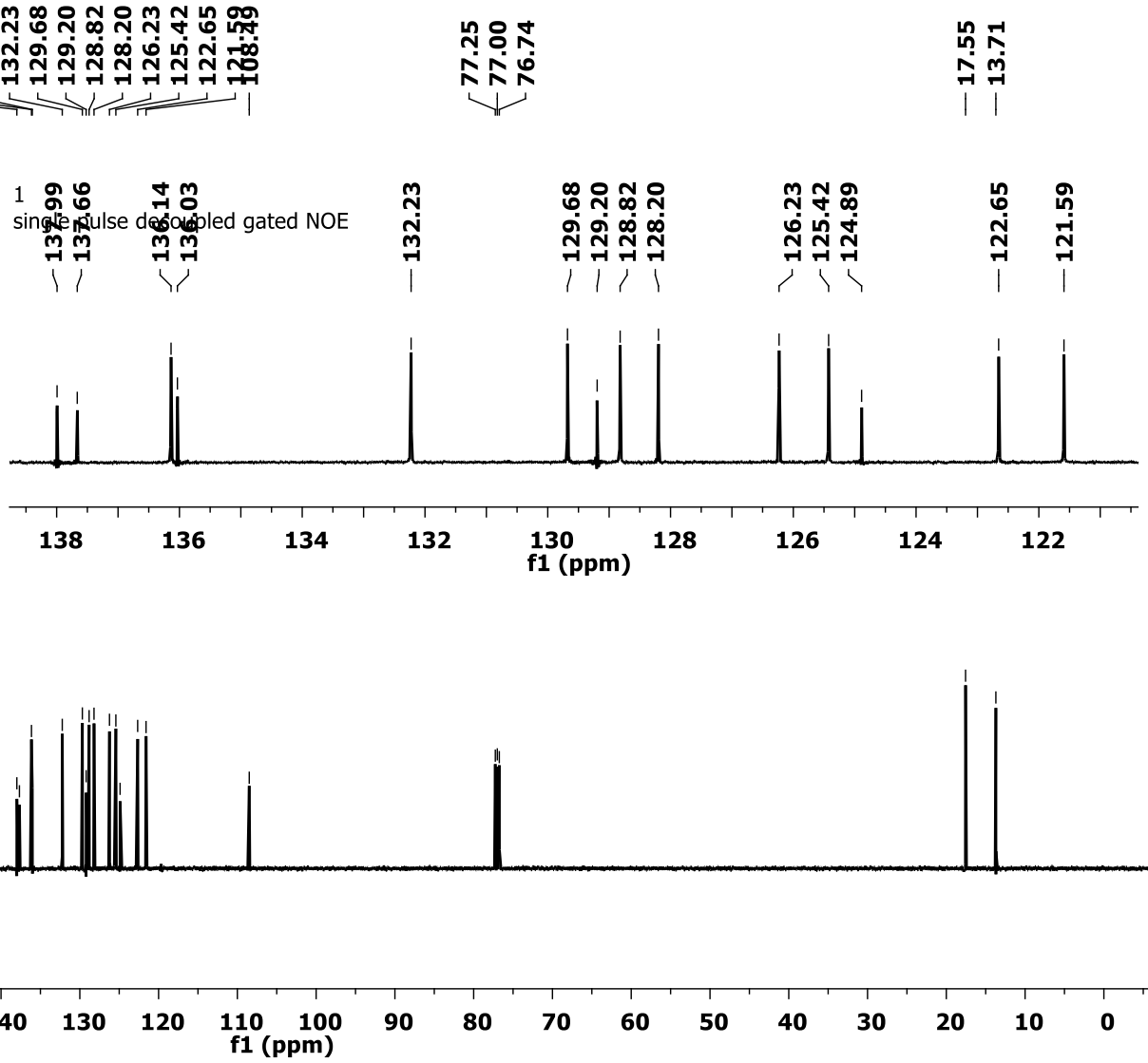


Table 3, Entry 2



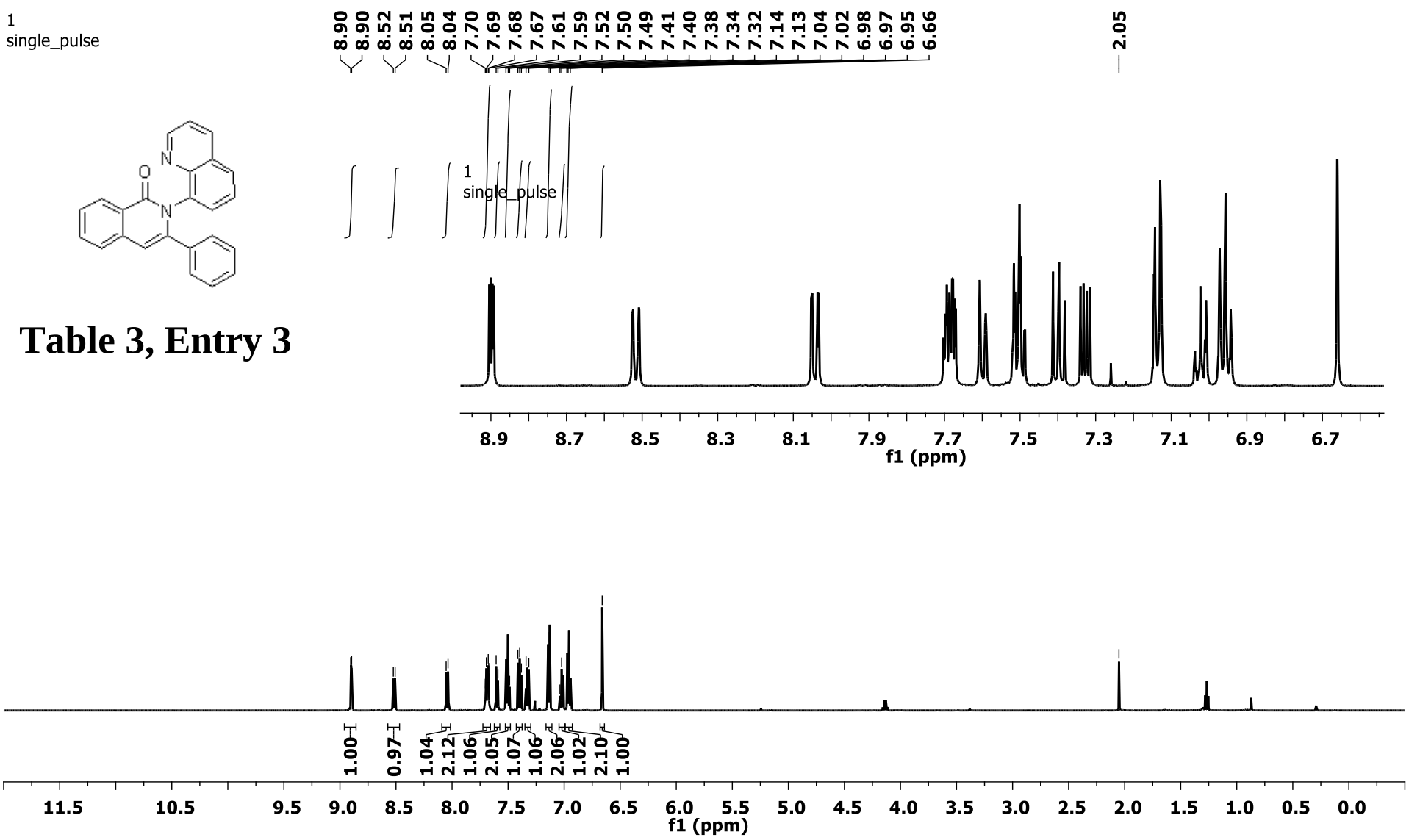


Table 3, Entry 3

1
single pulse decoupled gated NOE

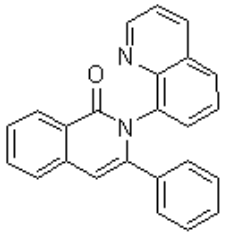


Table 3, Entry 3

Table 3, Entry 3

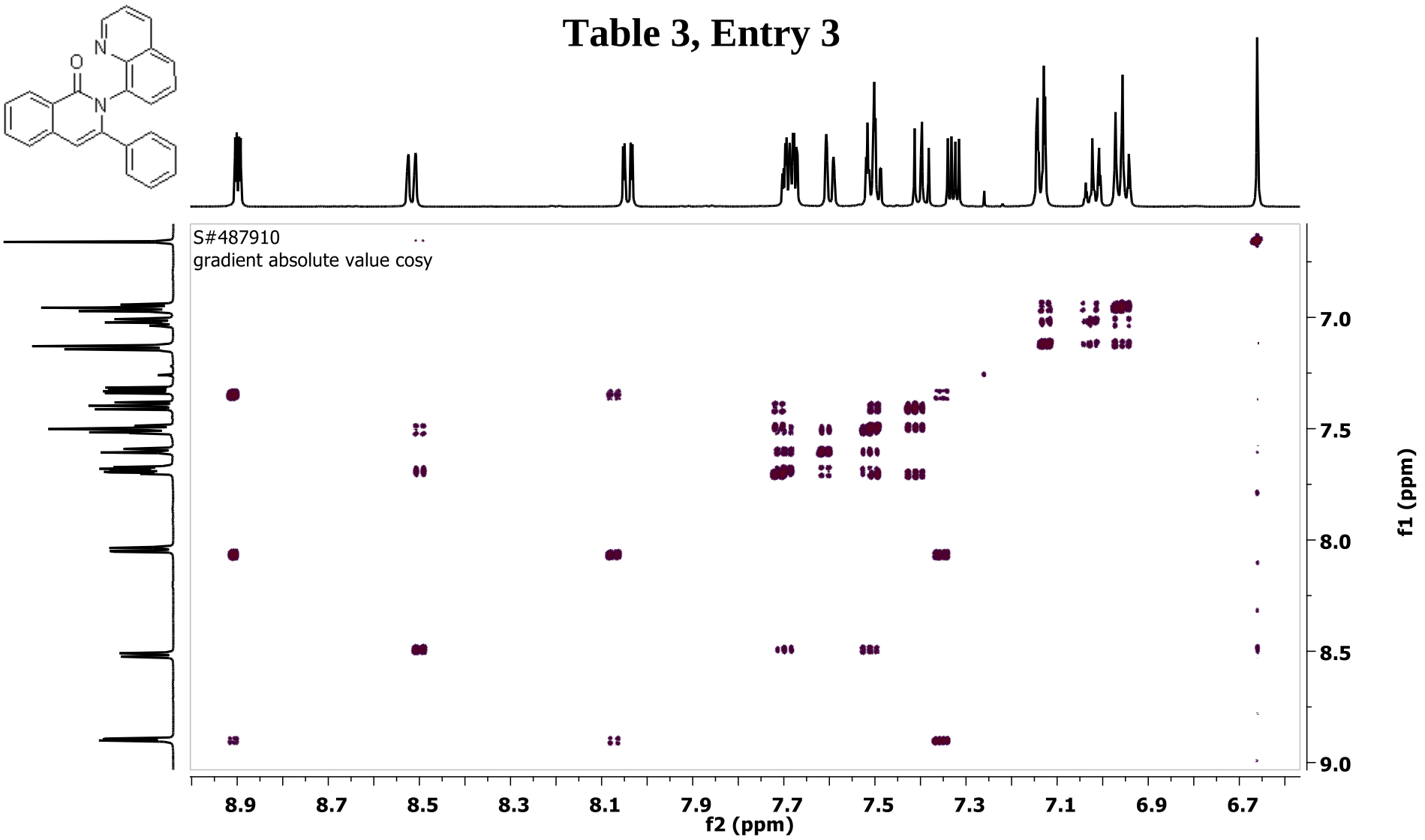
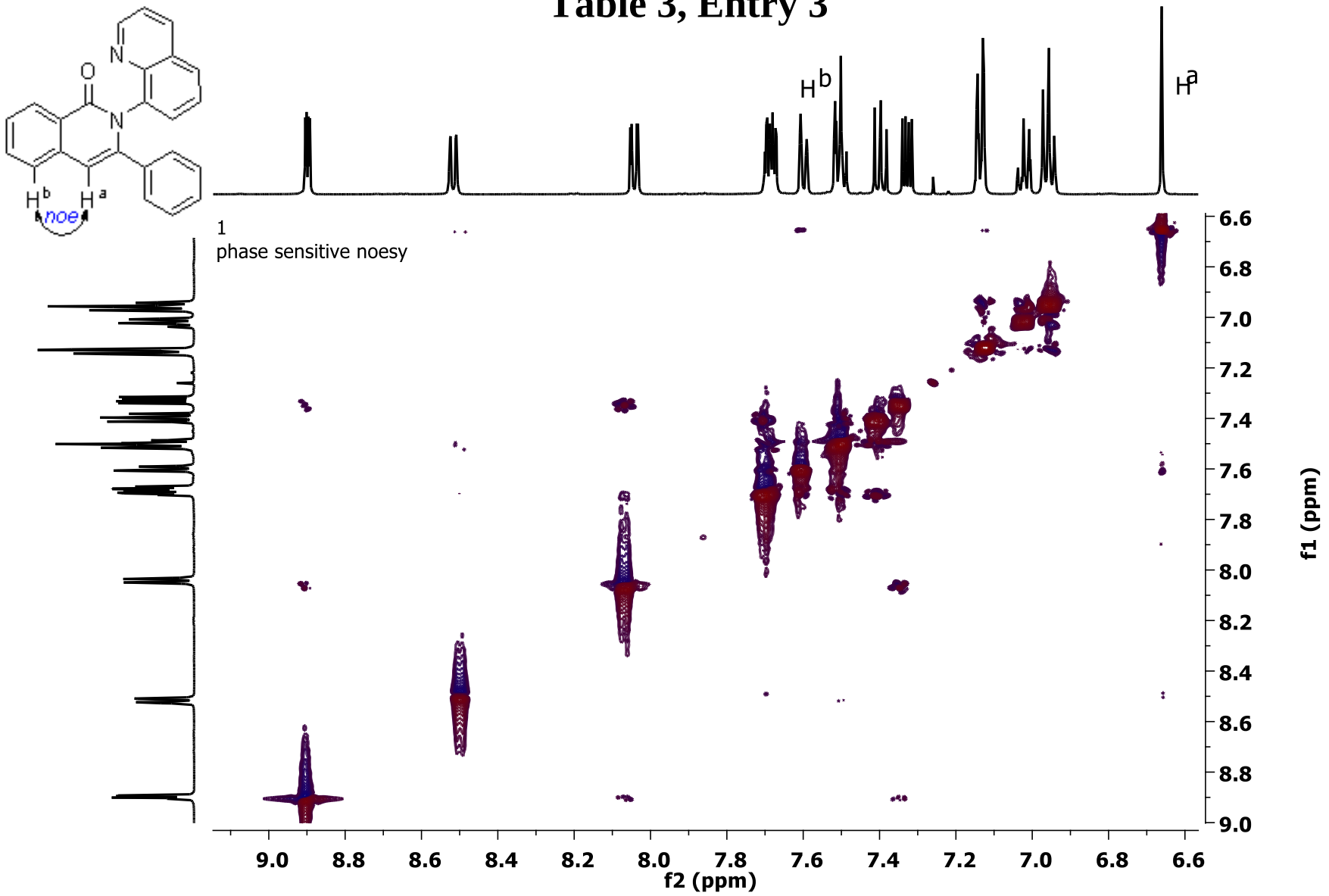


Table 3, Entry 3



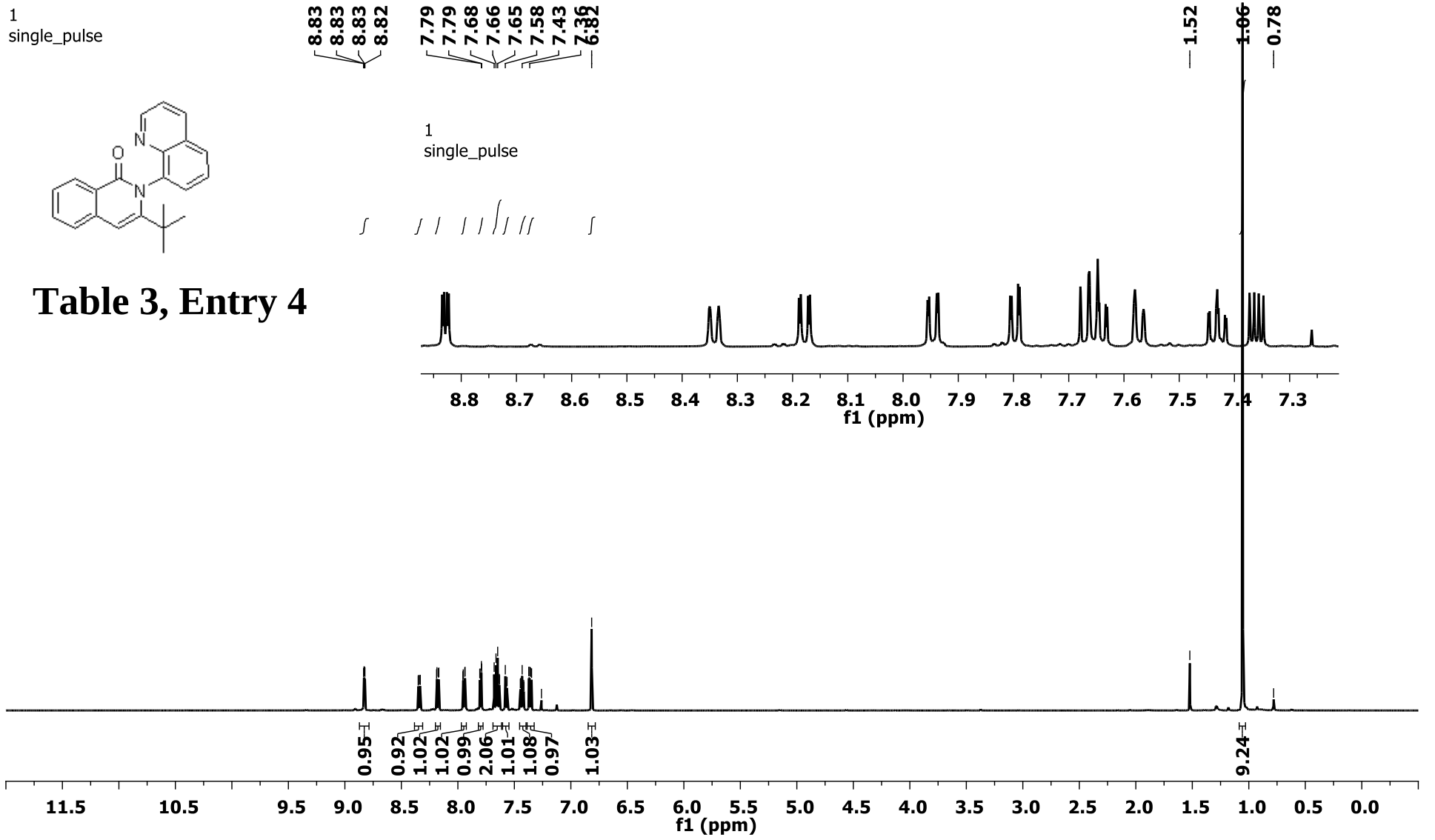


Table 3, Entry 4

1
single pulse decoupled gated NOE

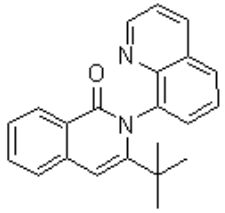


Table 3, Entry 4

Table 3, Entry 4

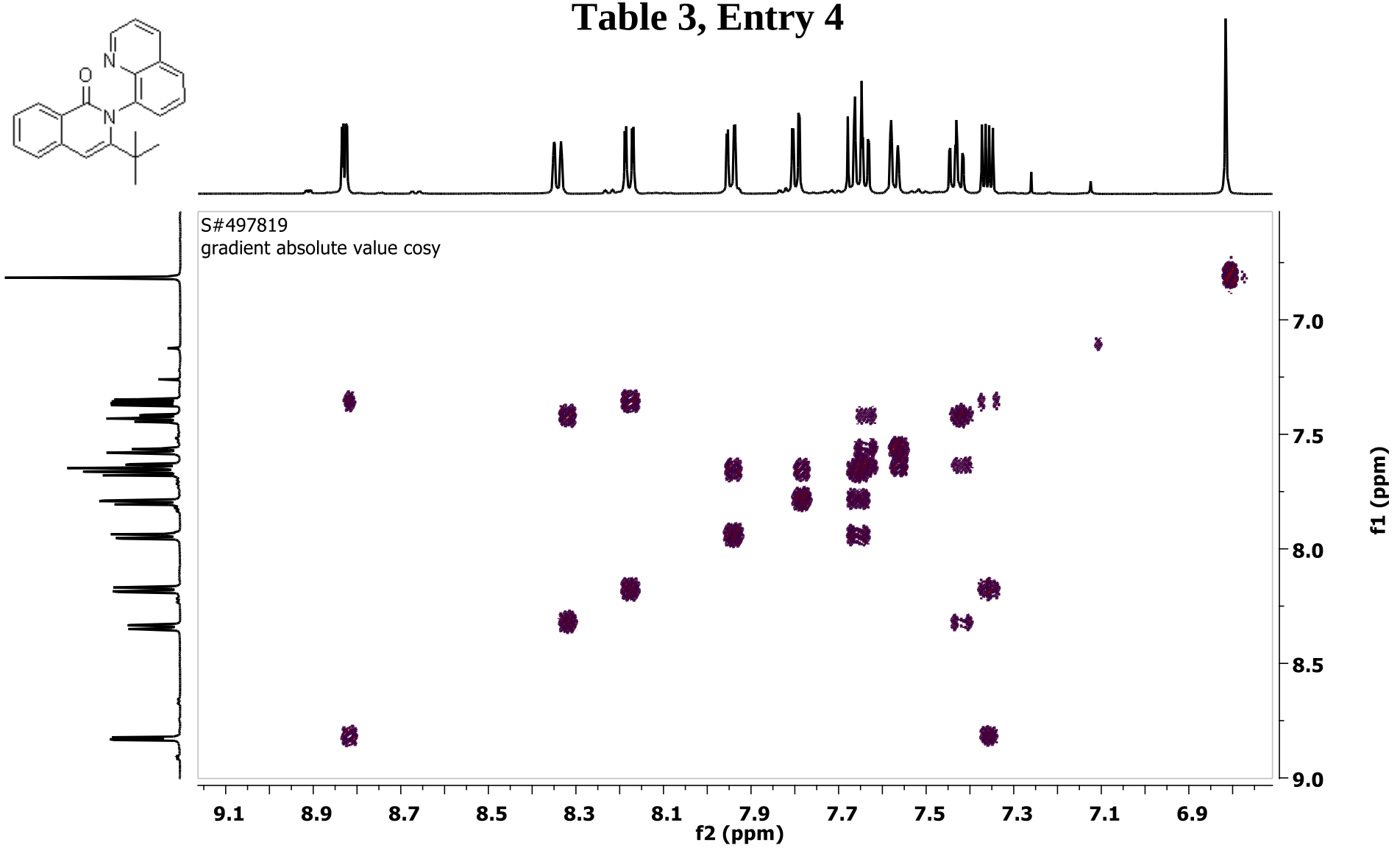
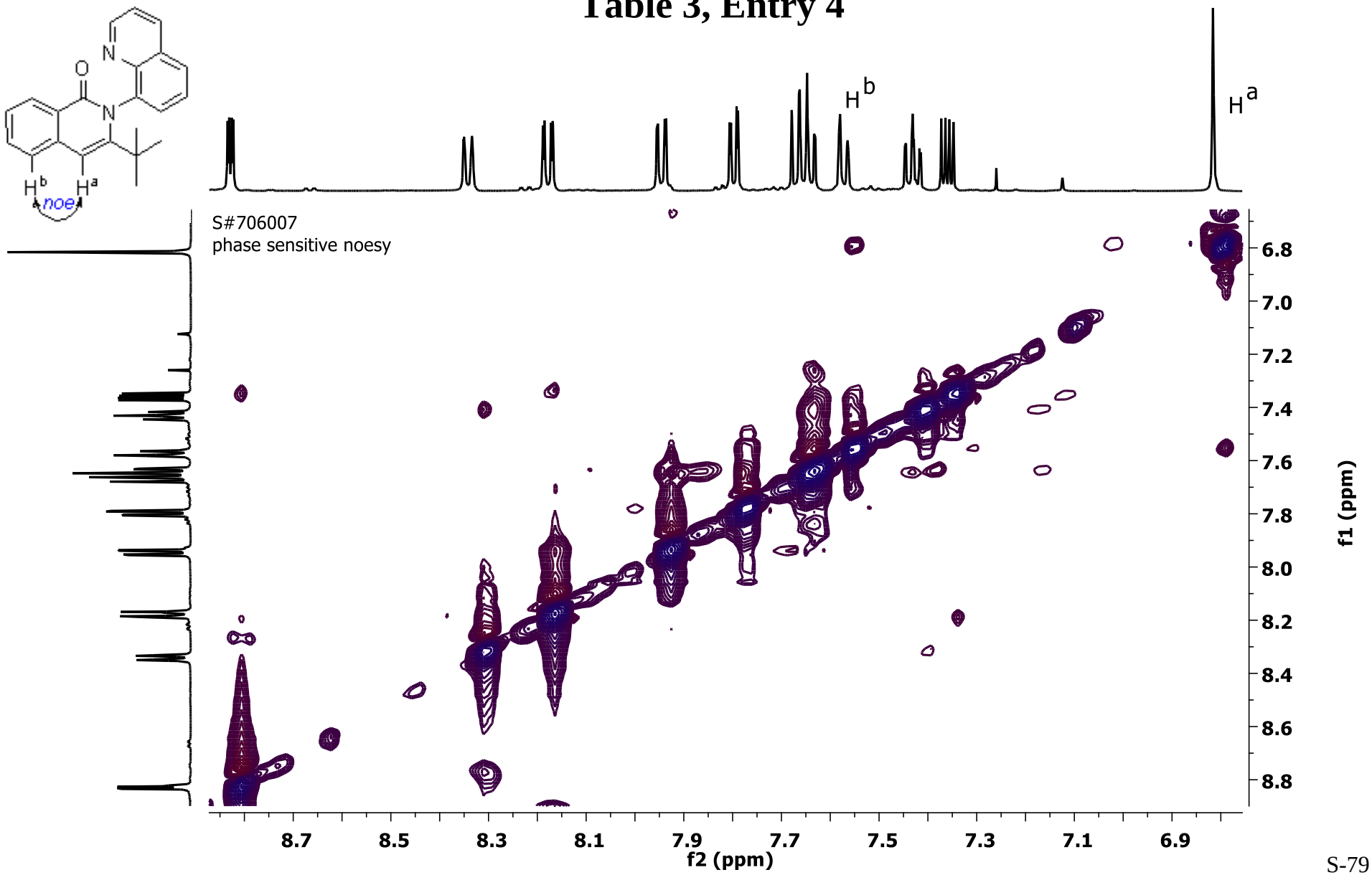


Table 3, Entry 4



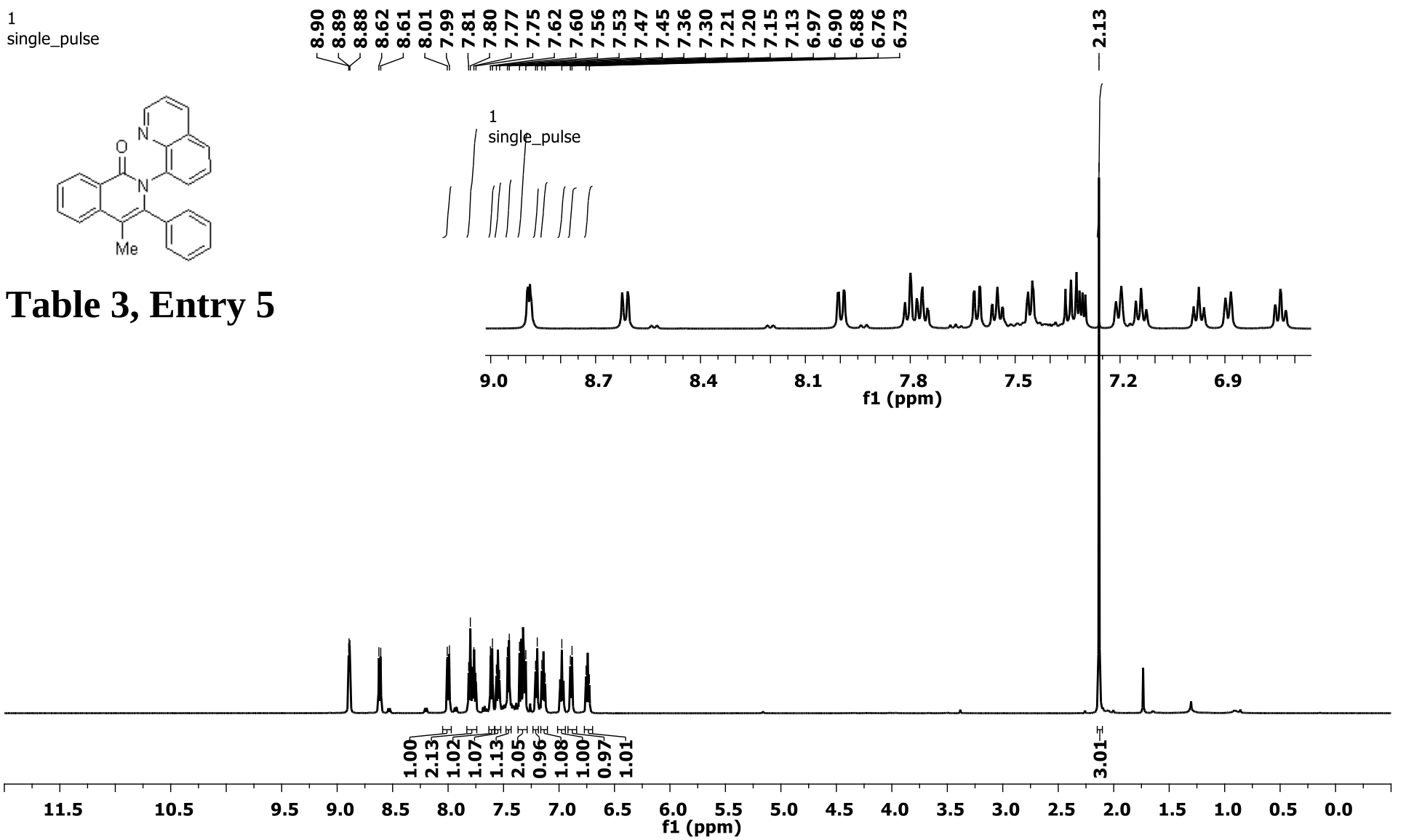


Table 3, Entry 5

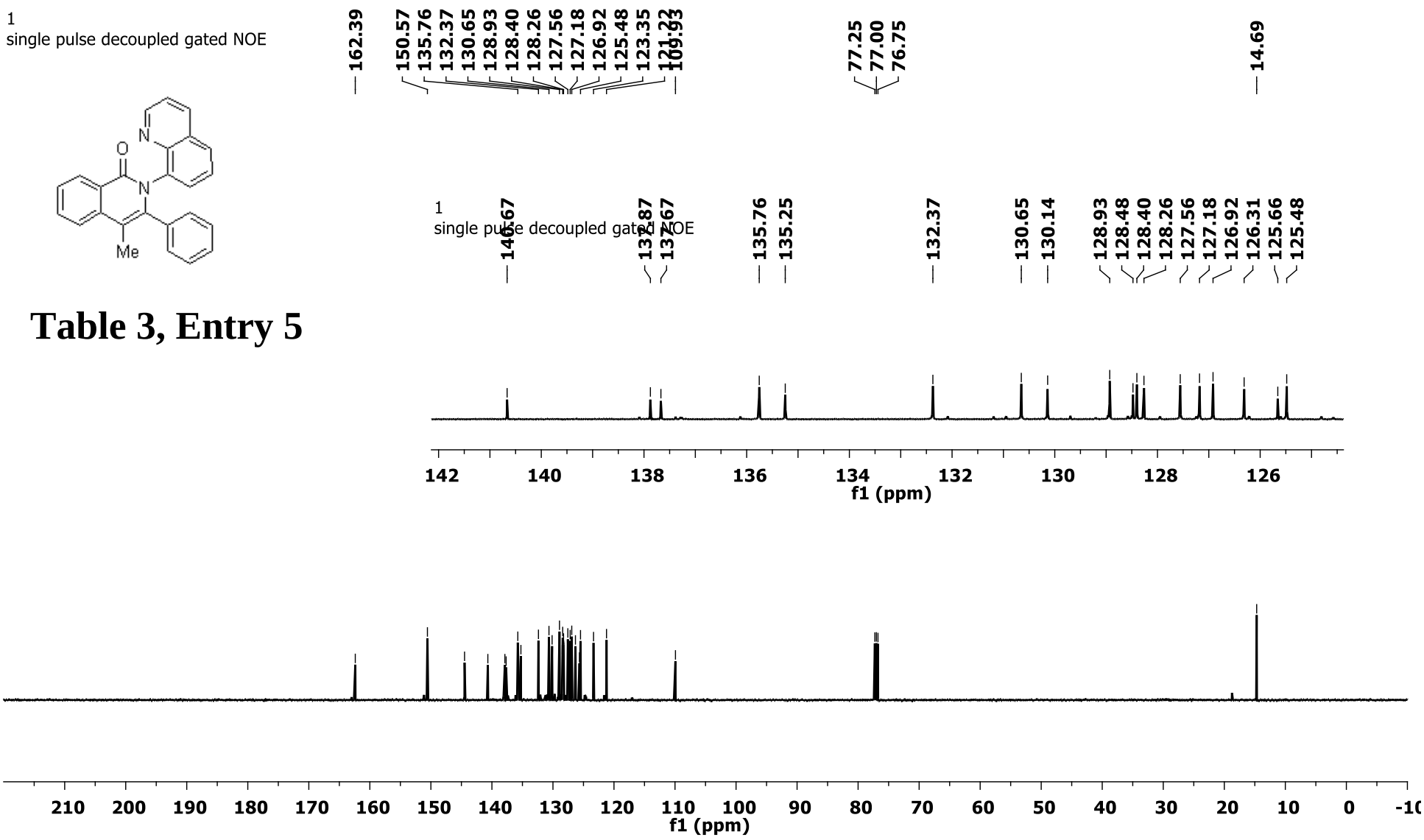


Table 3, Entry 5

Table 3, Entry 5

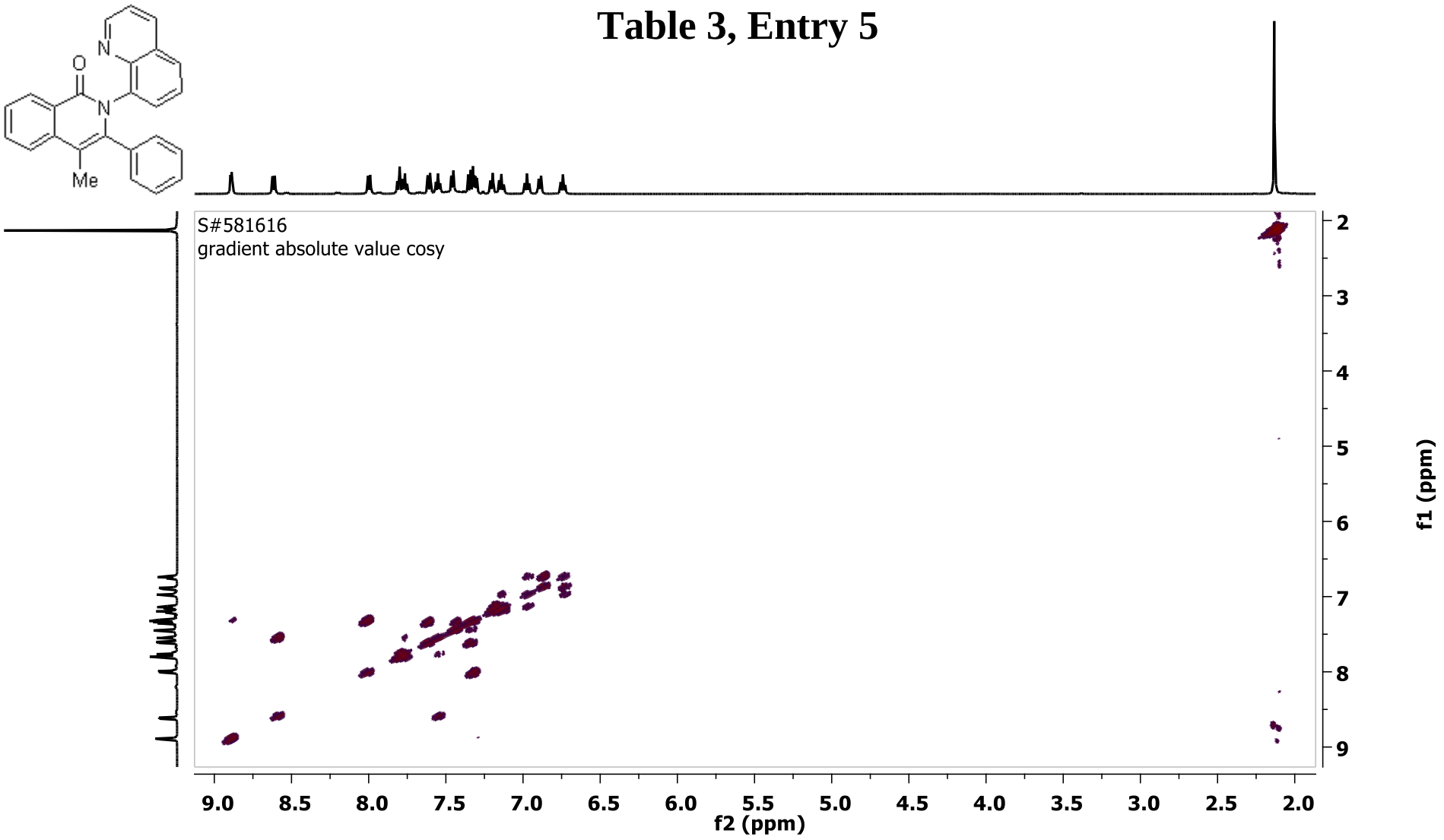
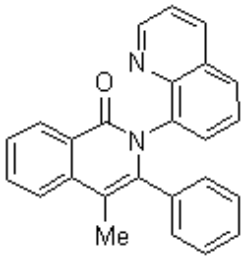


Table 3, Entry 5



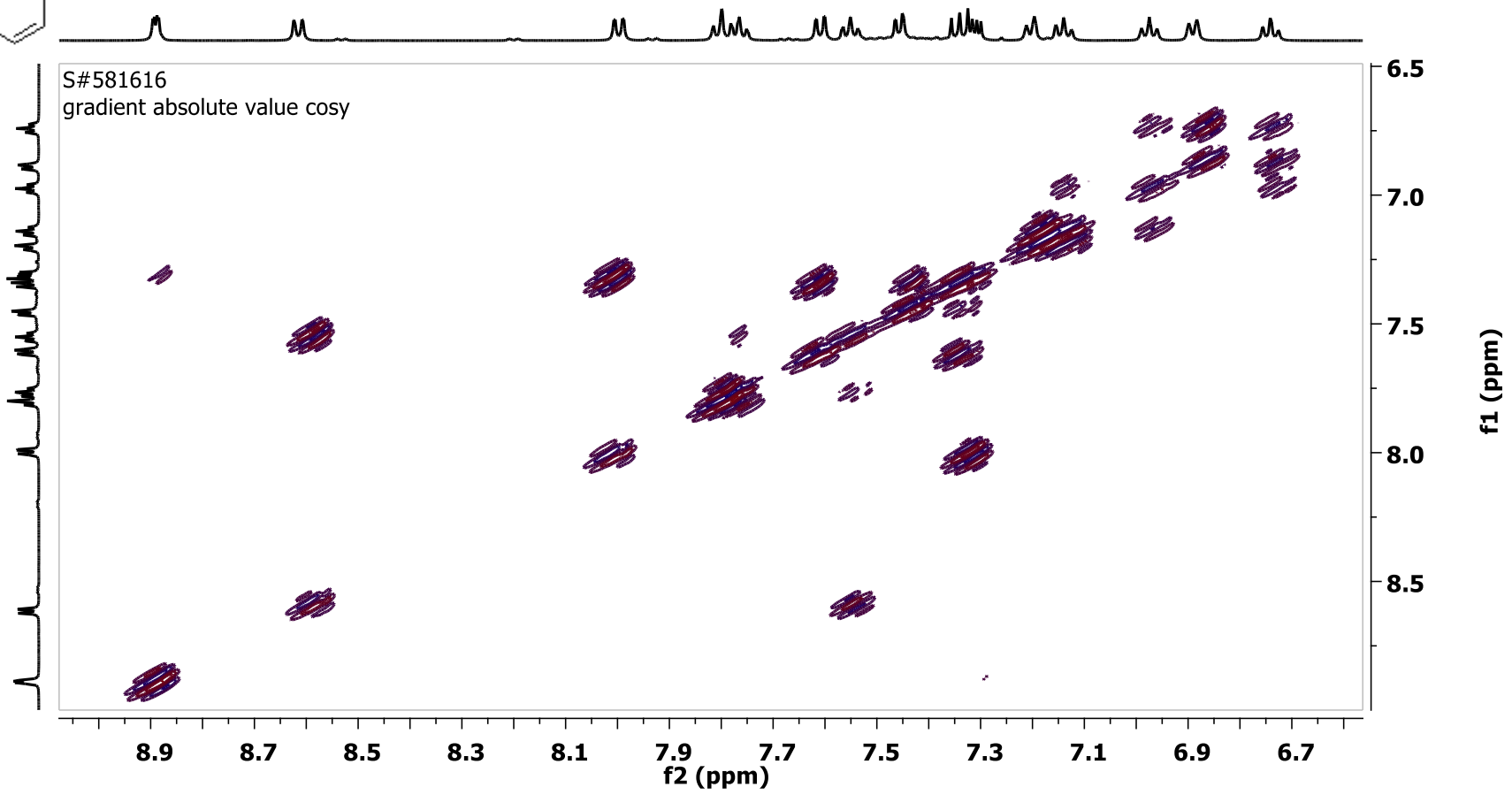
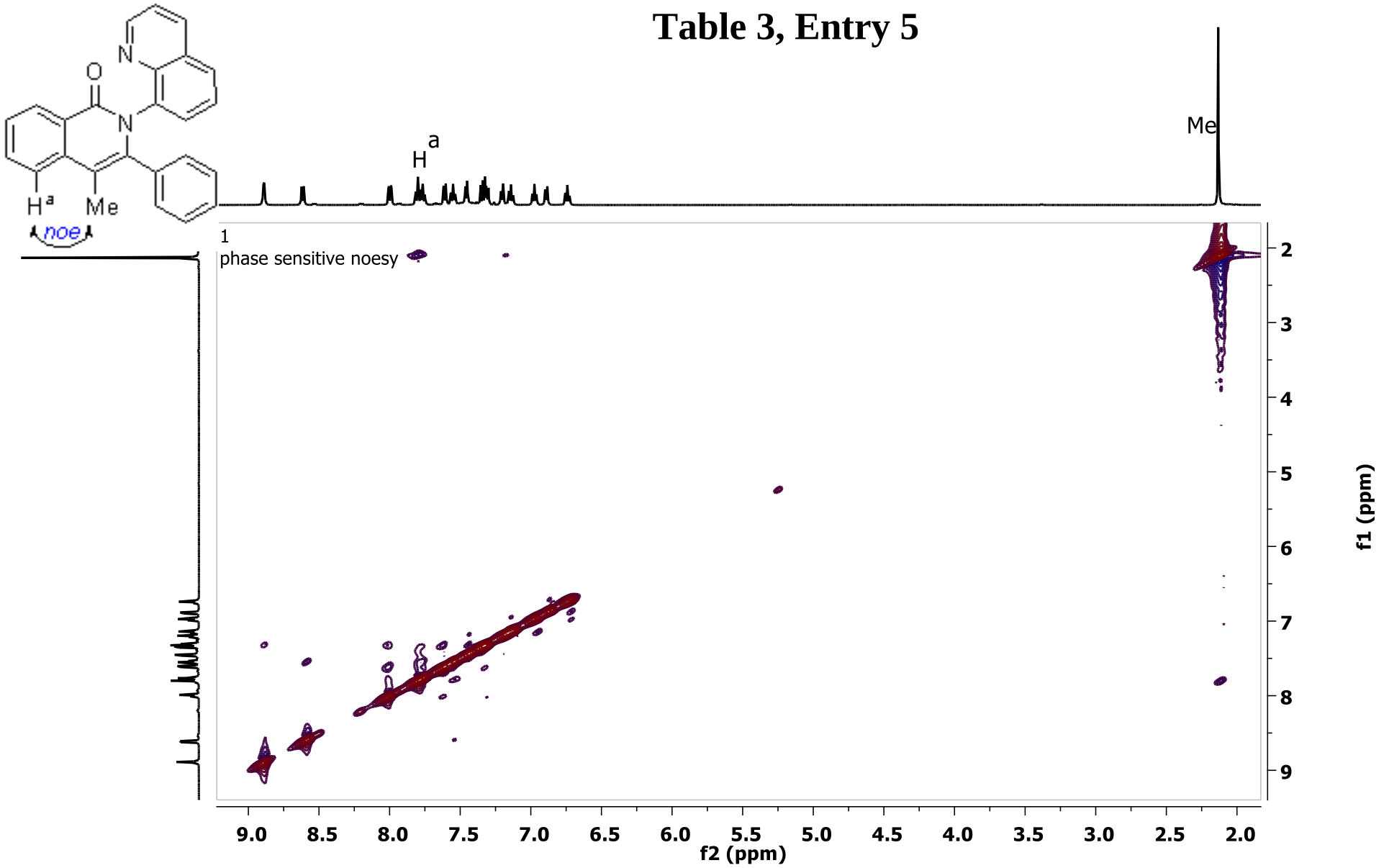


Table 3, Entry 5



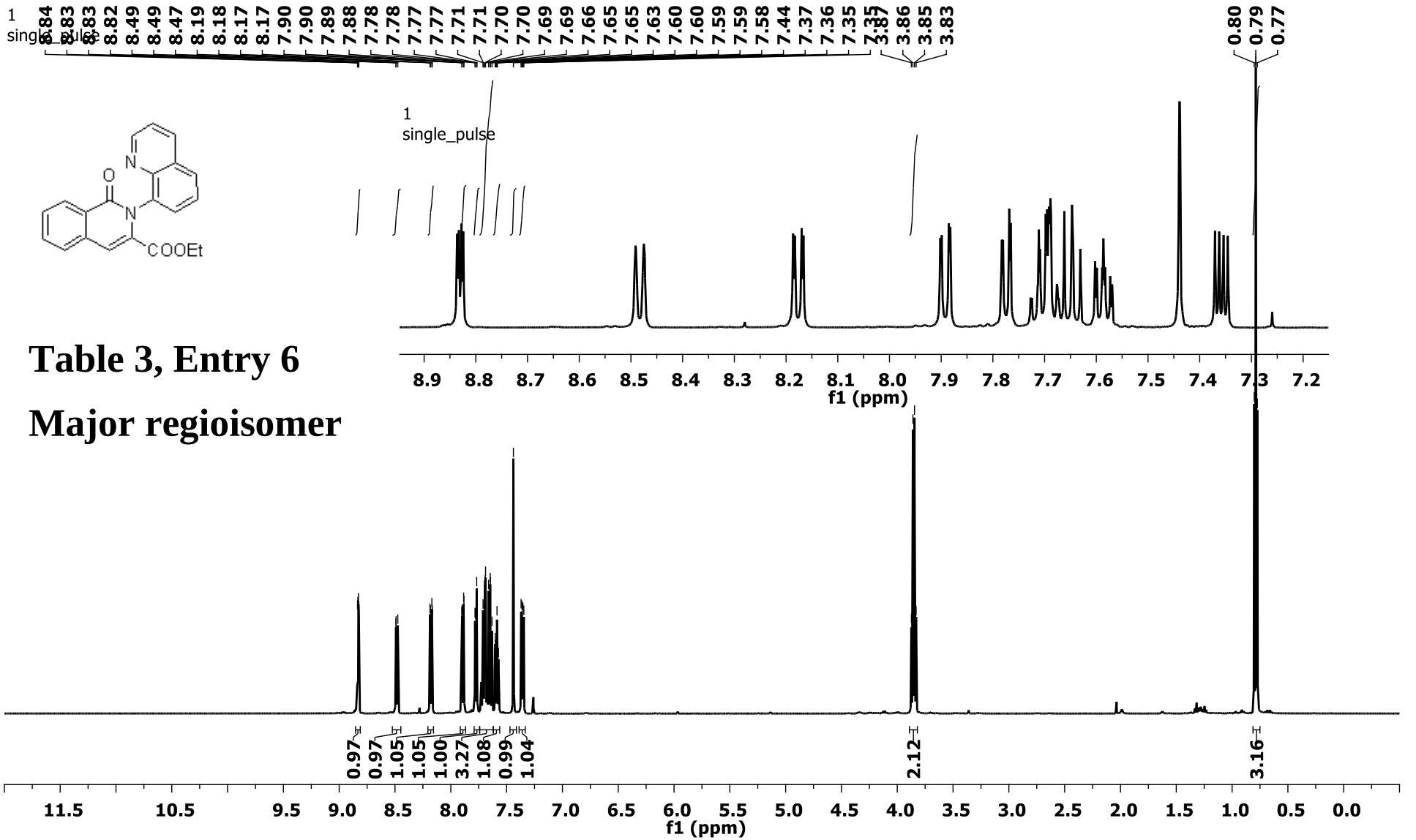


Table 3, Entry 6

Major regioisomer

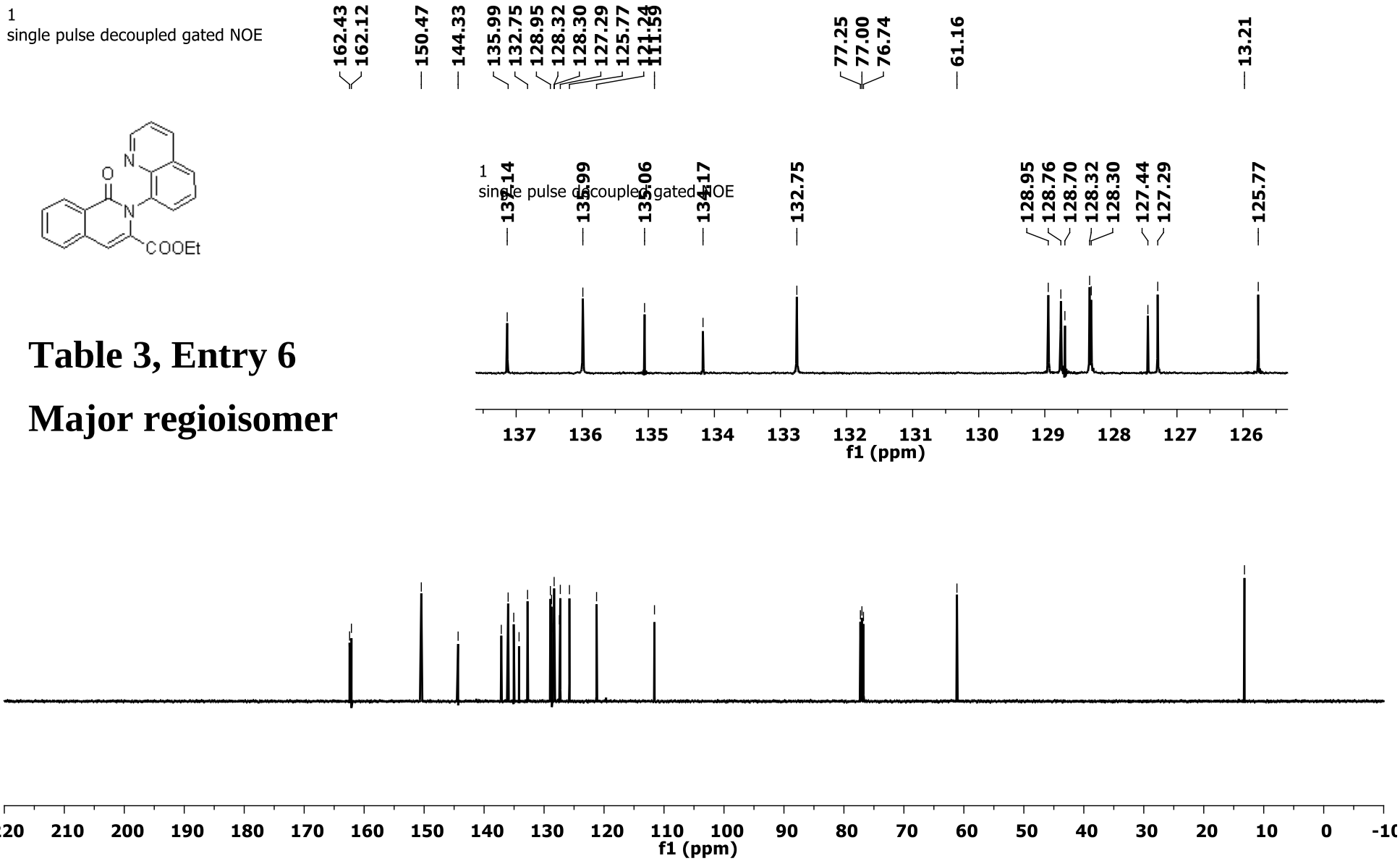
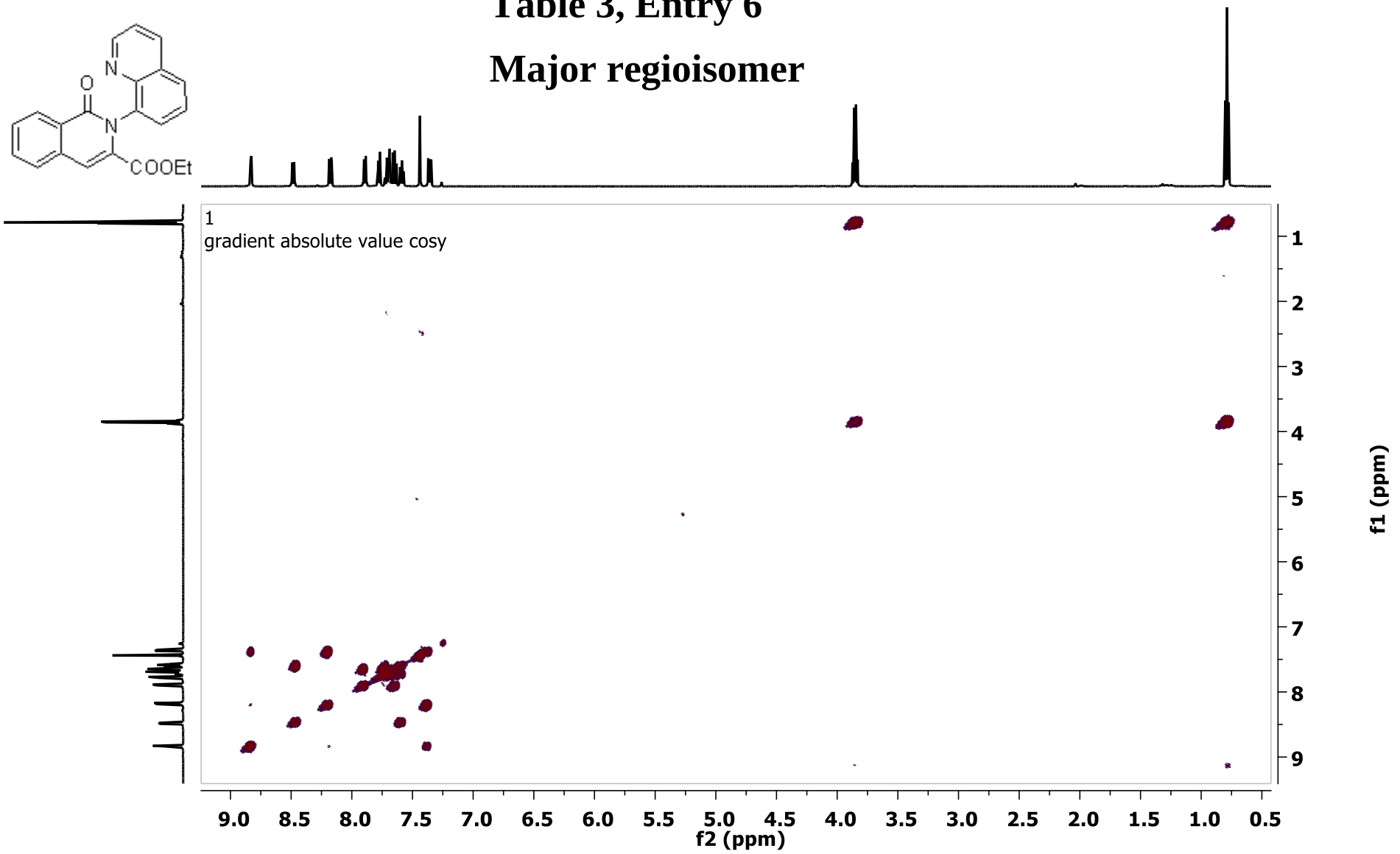


Table 3, Entry 6

Major regioisomer

Table 3, Entry 6

Major regioisomer



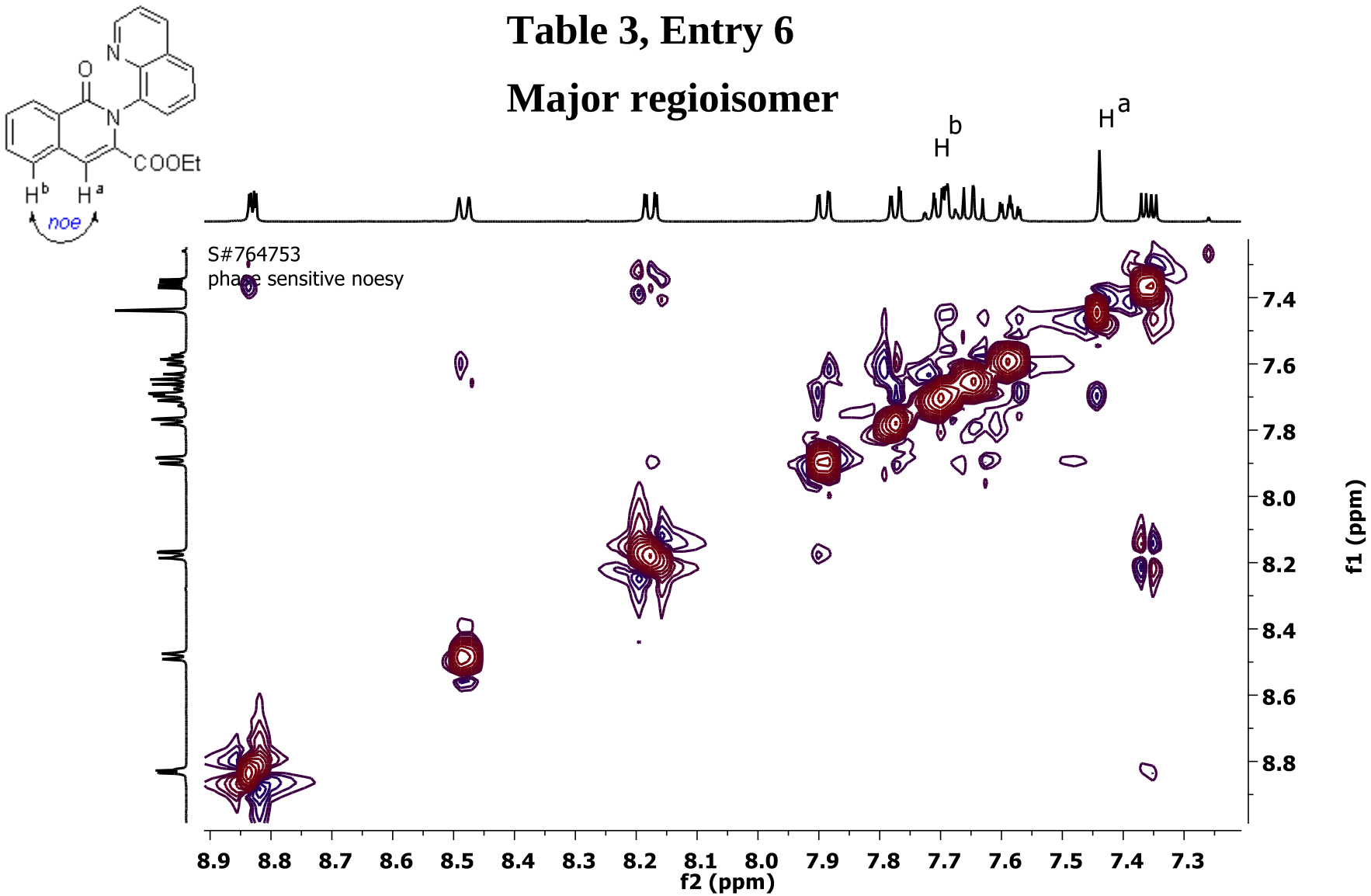
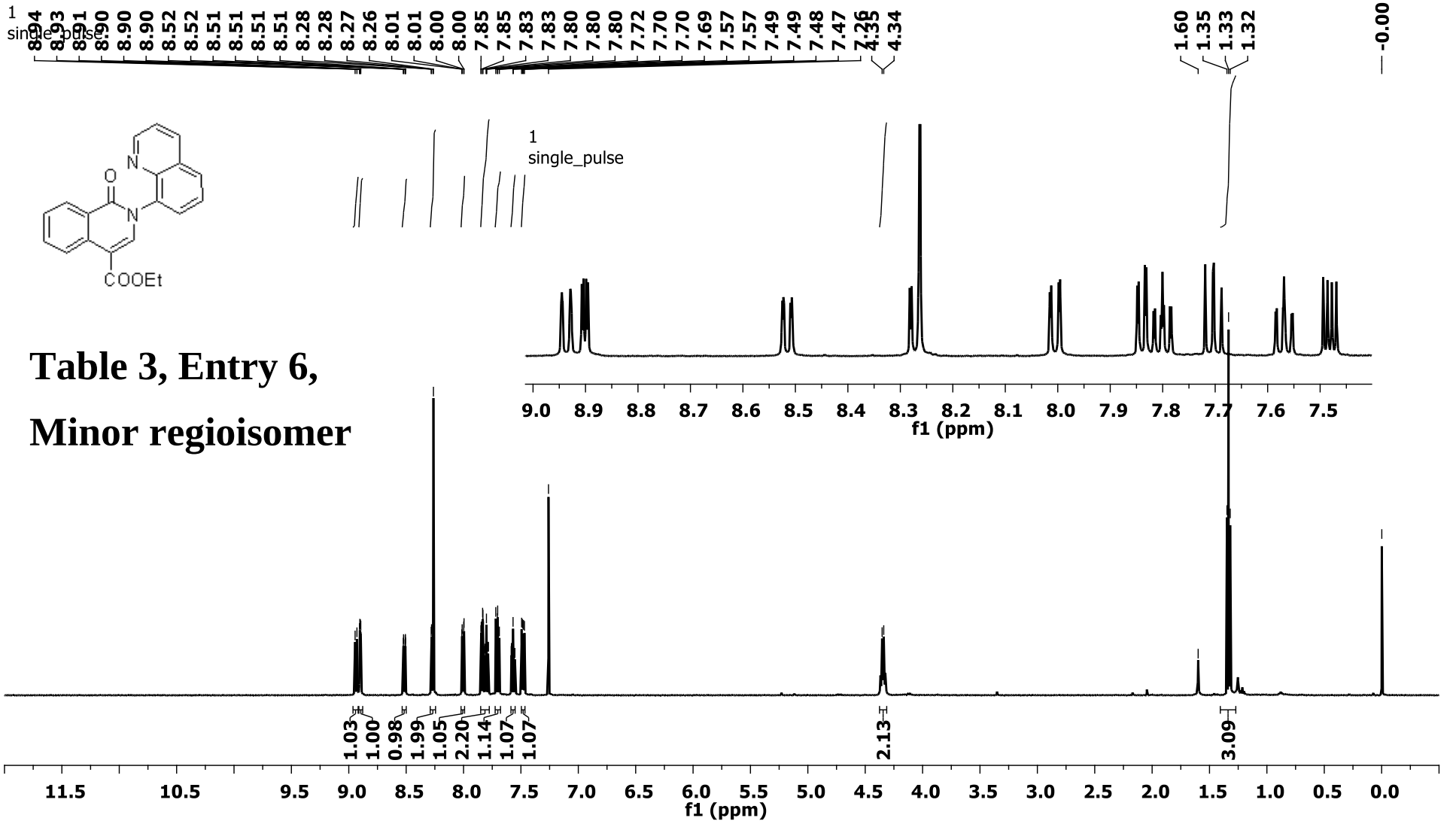


Table 3, Entry 6
Major regioisomer
O
N
N
COOEt
H b
H a
noe
H b
H a
S#764753
phase sensitive noesy
8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f2 (ppm)
7.4 7.6 7.8 8.0 8.2 8.4 8.6 8.8
f1 (ppm)


1
single_pulse
8.94 8.93 8.91 8.90 8.90 8.90 8.52 8.52 8.51 8.51 8.51 8.51 8.28 8.28 8.27 8.26 8.01 8.01 8.00 8.00 7.85 7.85 7.83 7.83 7.80 7.80 7.80 7.72 7.70 7.70 7.69 7.57 7.57 7.49 7.49 7.48 7.47 7.26 4.35 4.34
1.60 1.35 1.33 1.32
-0.00
O
N
N
COOEt
Table 3, Entry 6,
Minor regioisomer
f1 (ppm)
1.03 1.00 0.98 1.99 1.05 2.20 1.14 1.07 1.07 2.13 3.09
f1 (ppm)

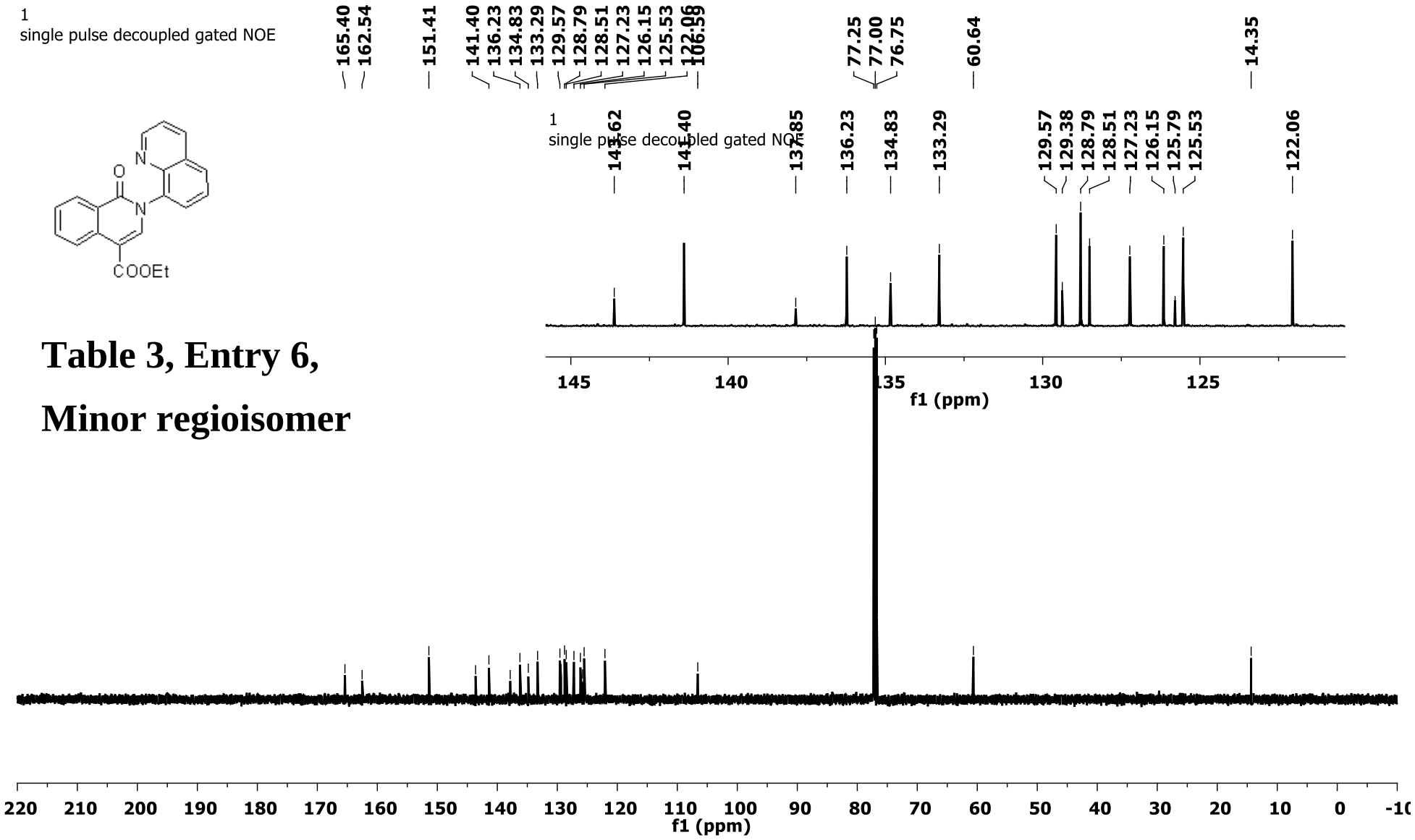


Table 3, Entry 6,

Minor regioisomer

Table 3, Entry 6,

Minor regioisomer

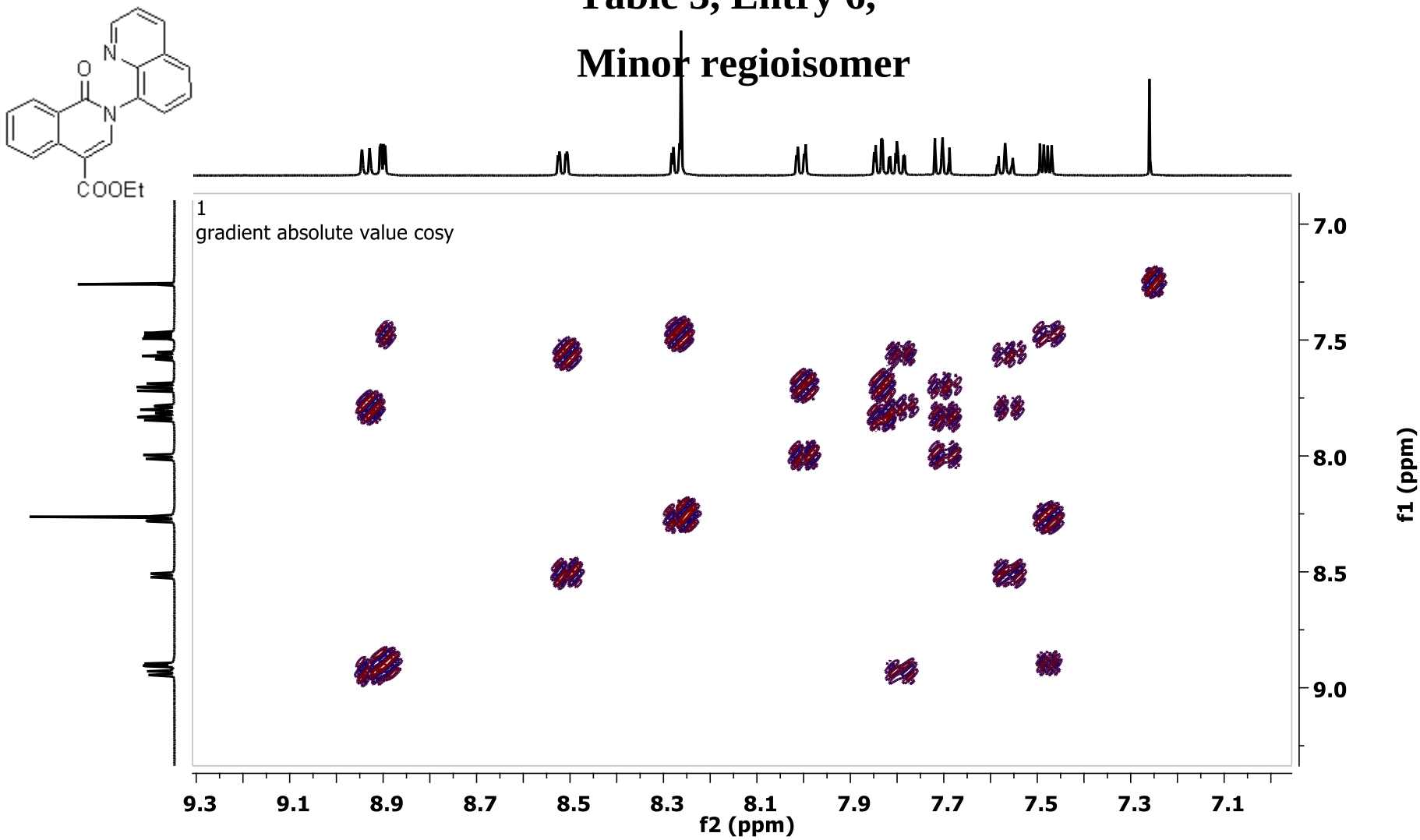
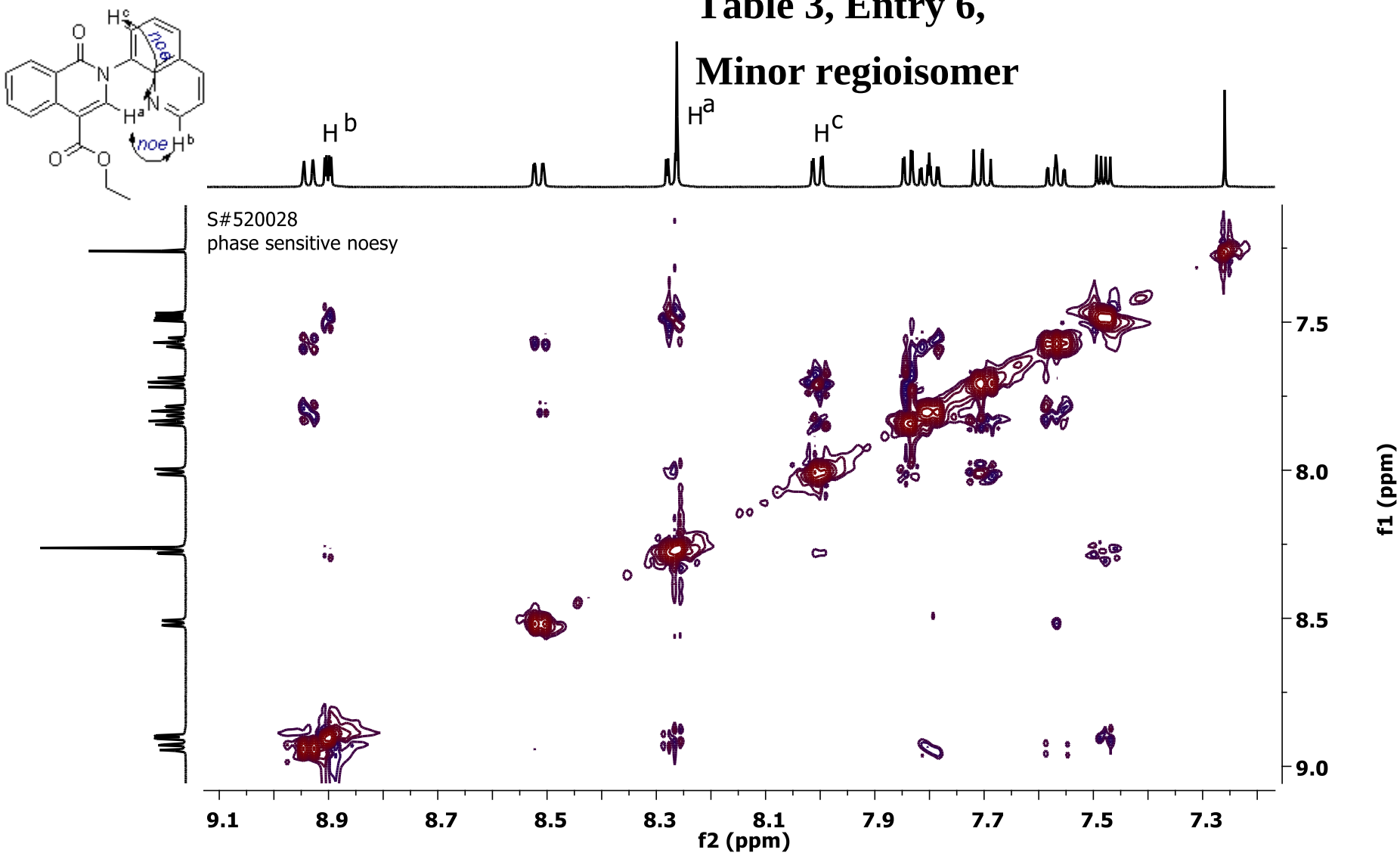


Table 3, Entry 6,

Minor regioisomer



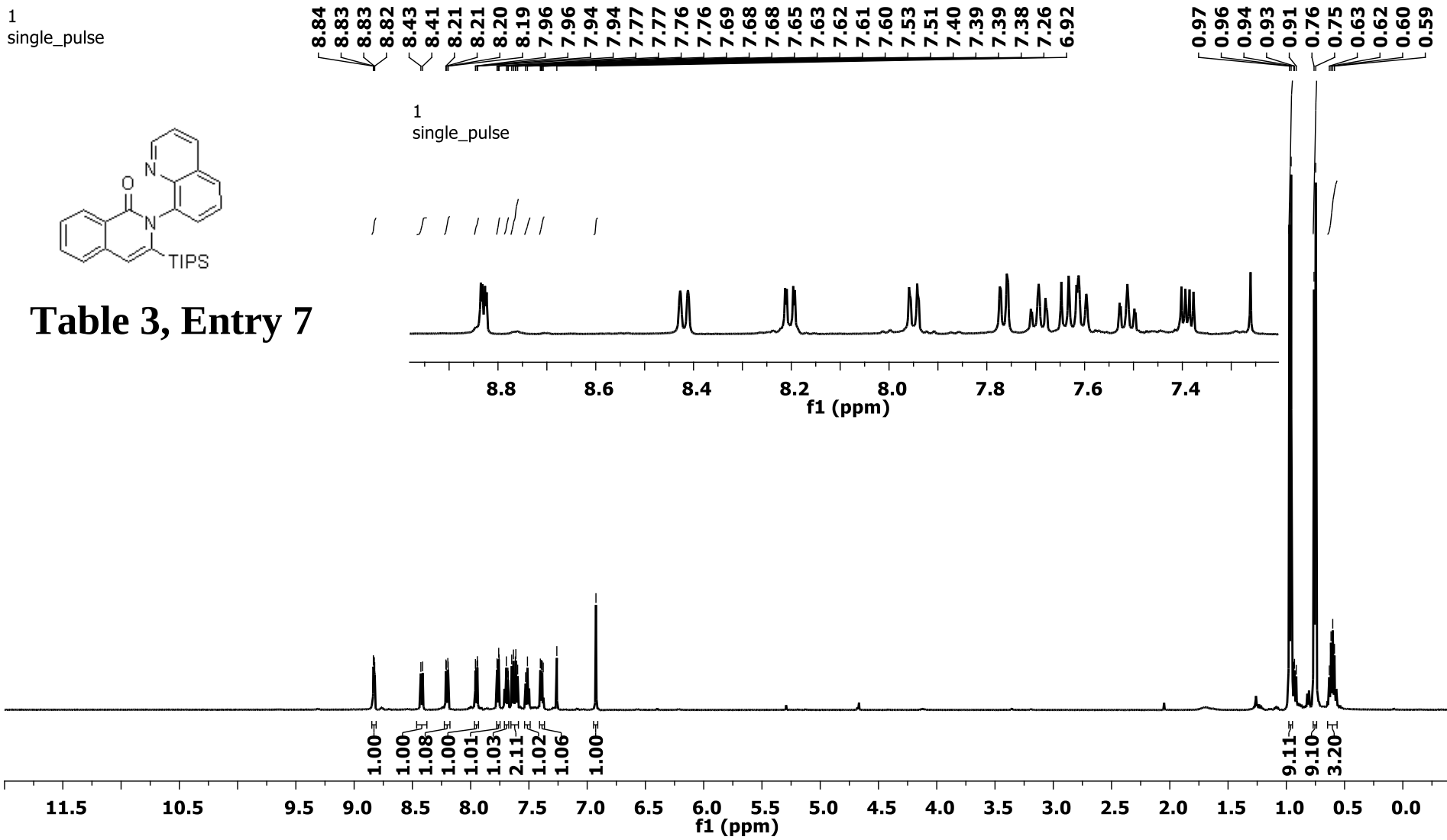


Table 3, Entry 7

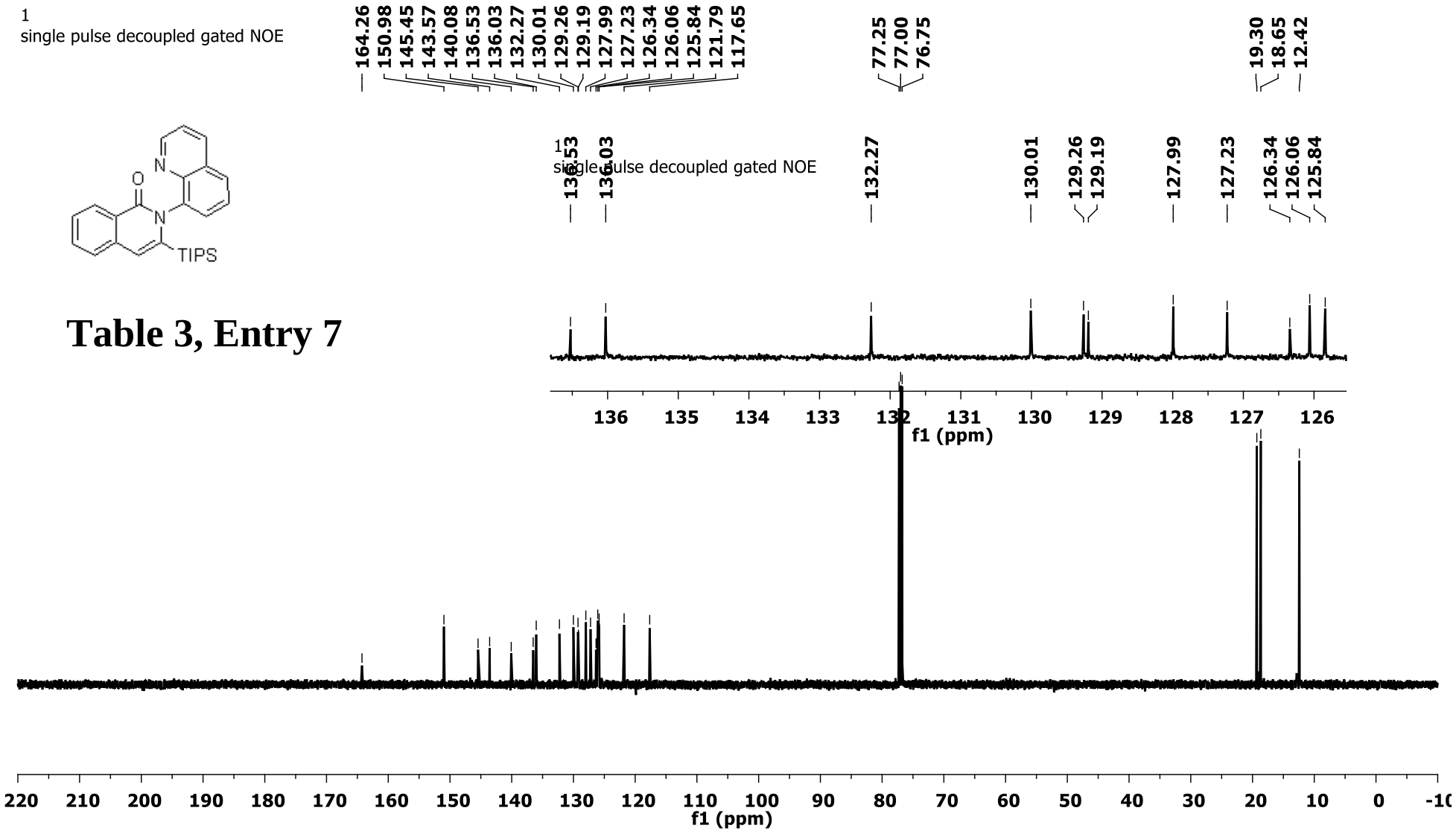


Table 3, Entry 7

Table 3, Entry 7

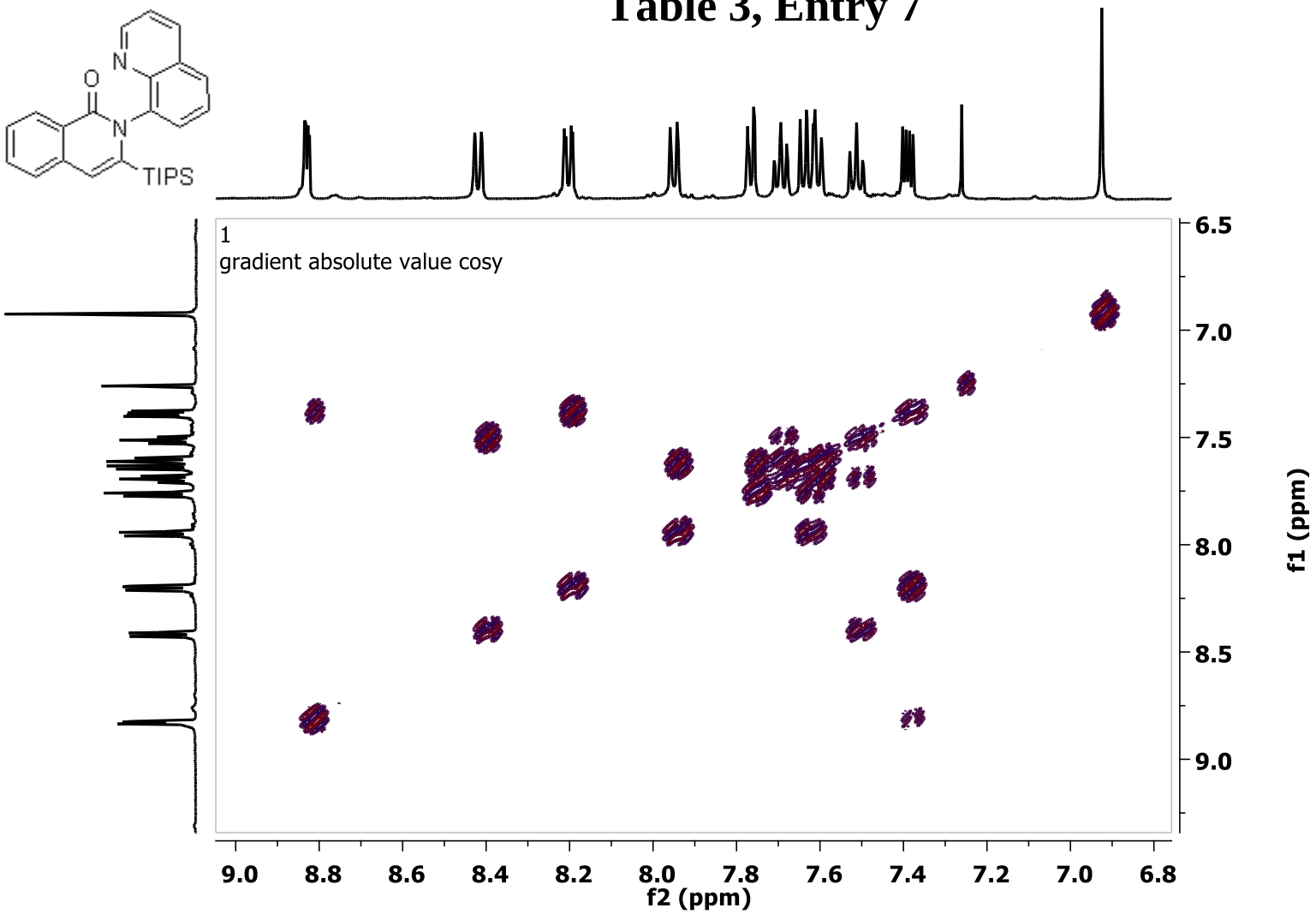
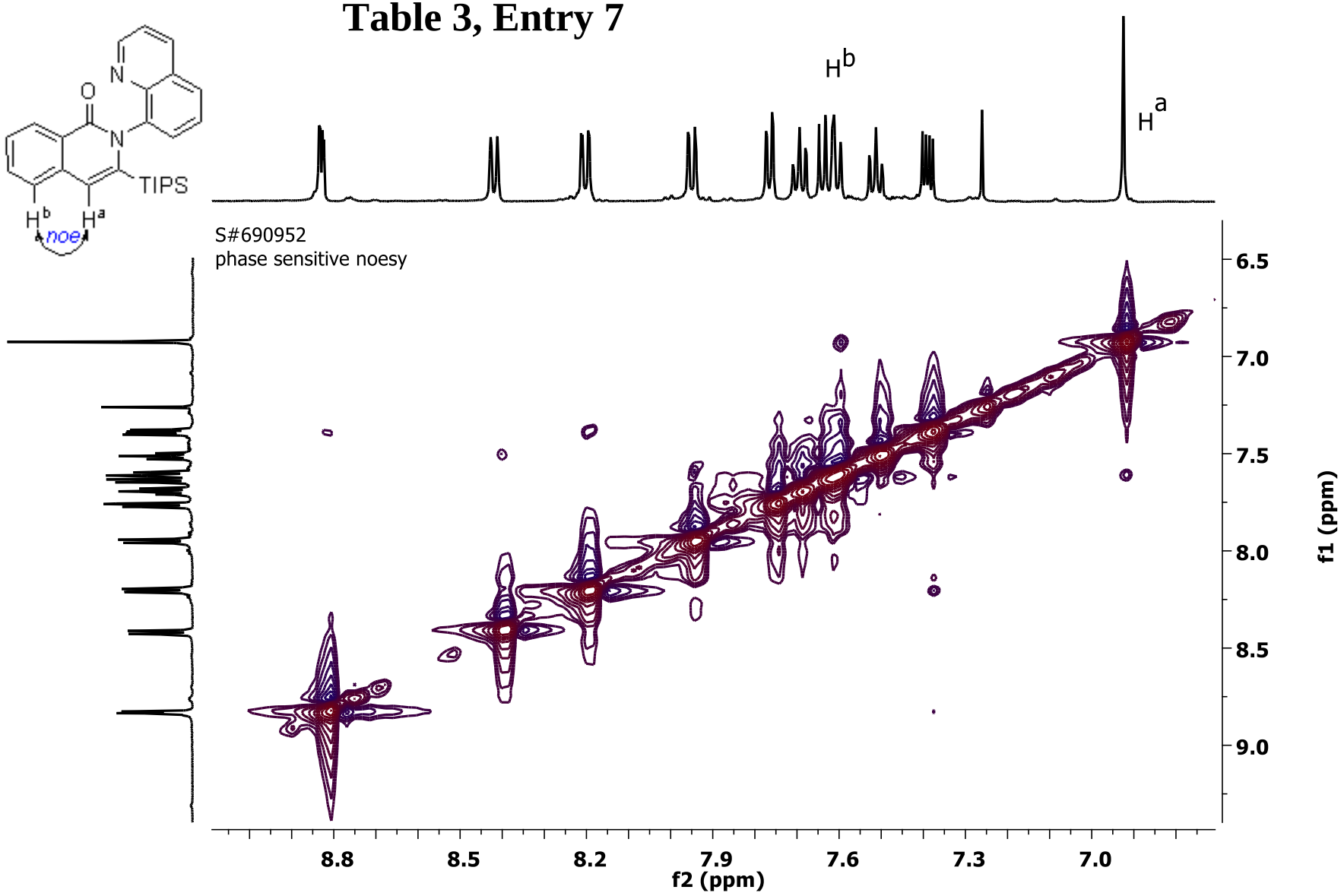


Table 3, Entry 7



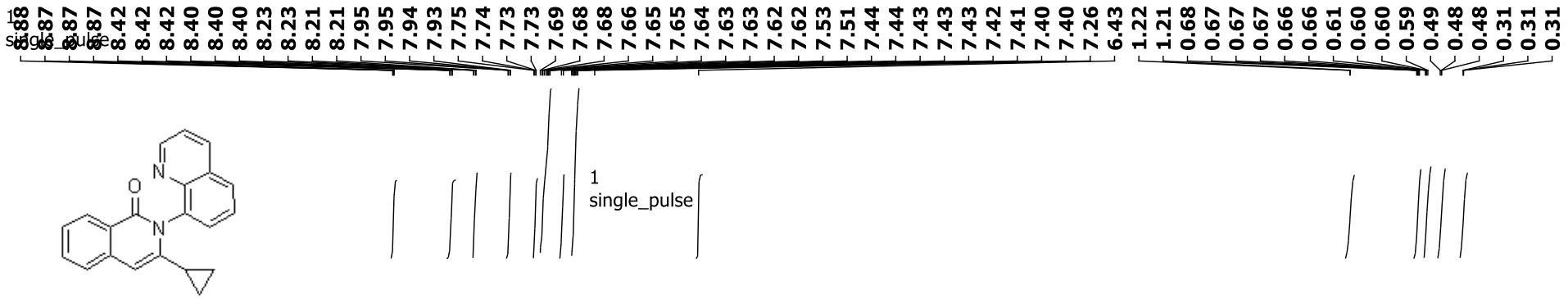
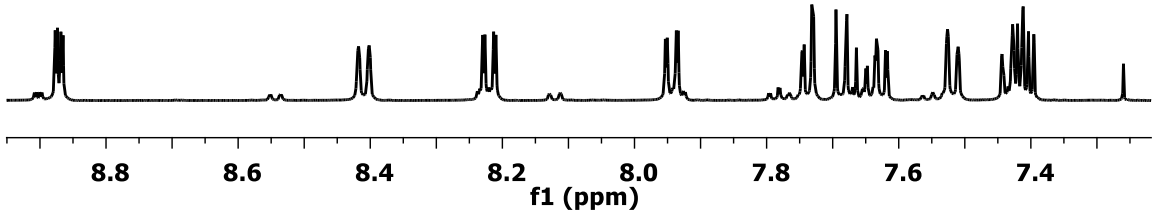
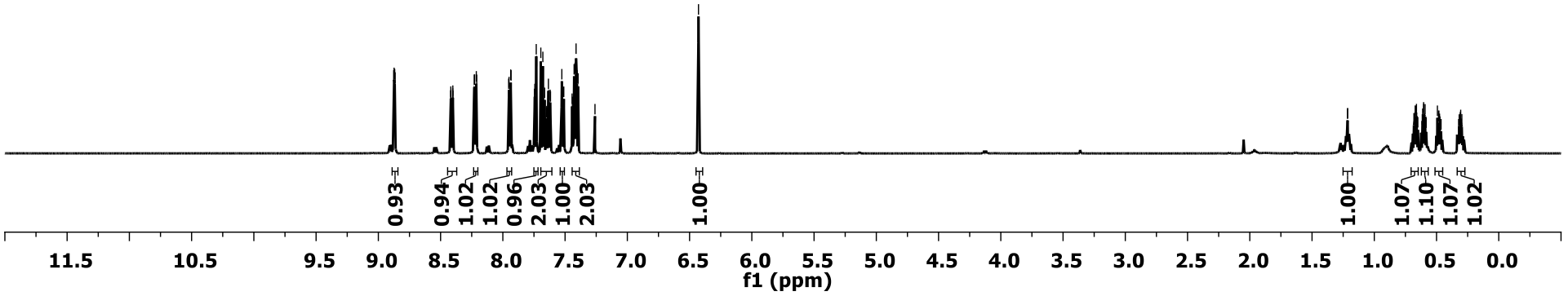


Table 3, Entry 8





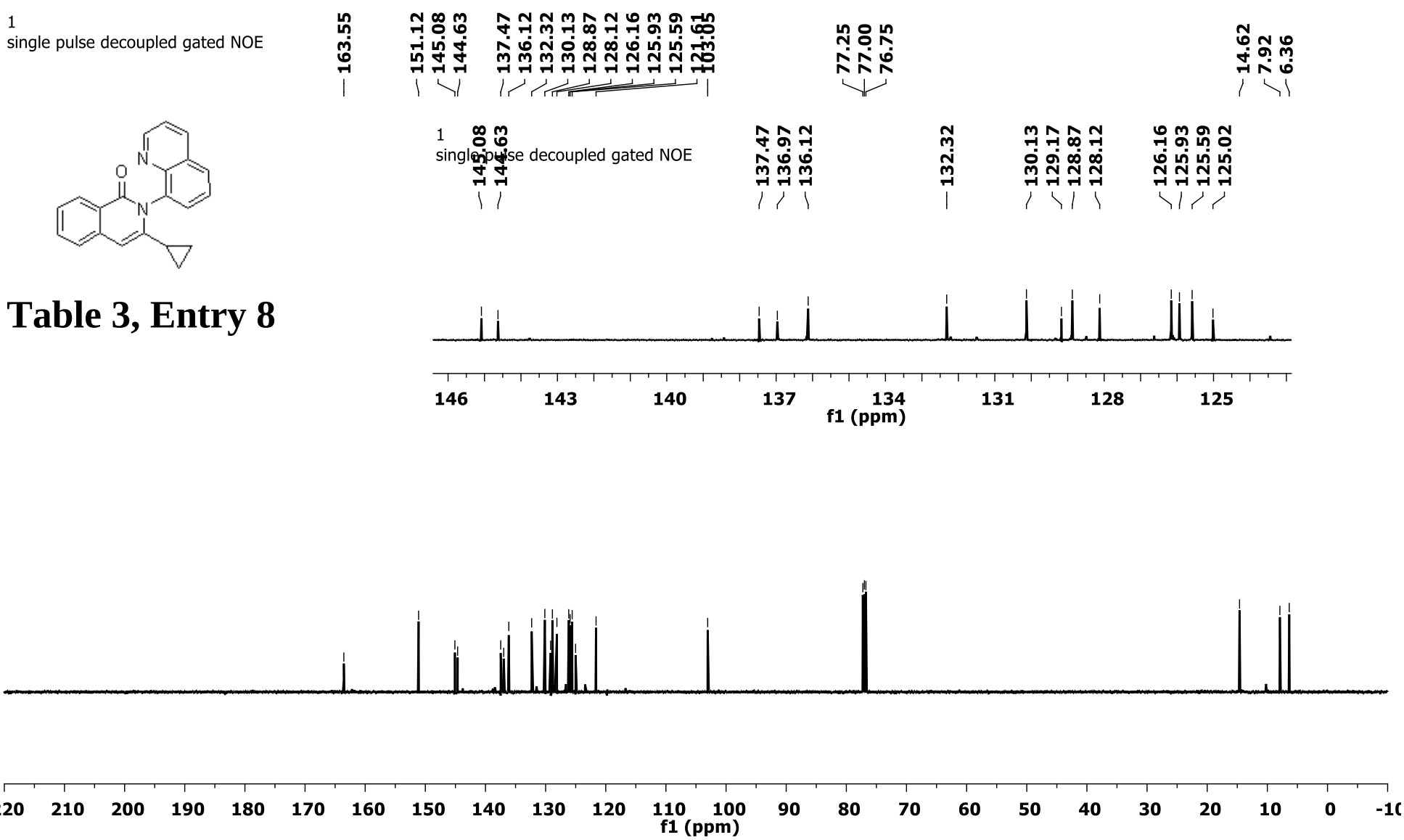


Table 3, Entry 8

Table 3, Entry 8

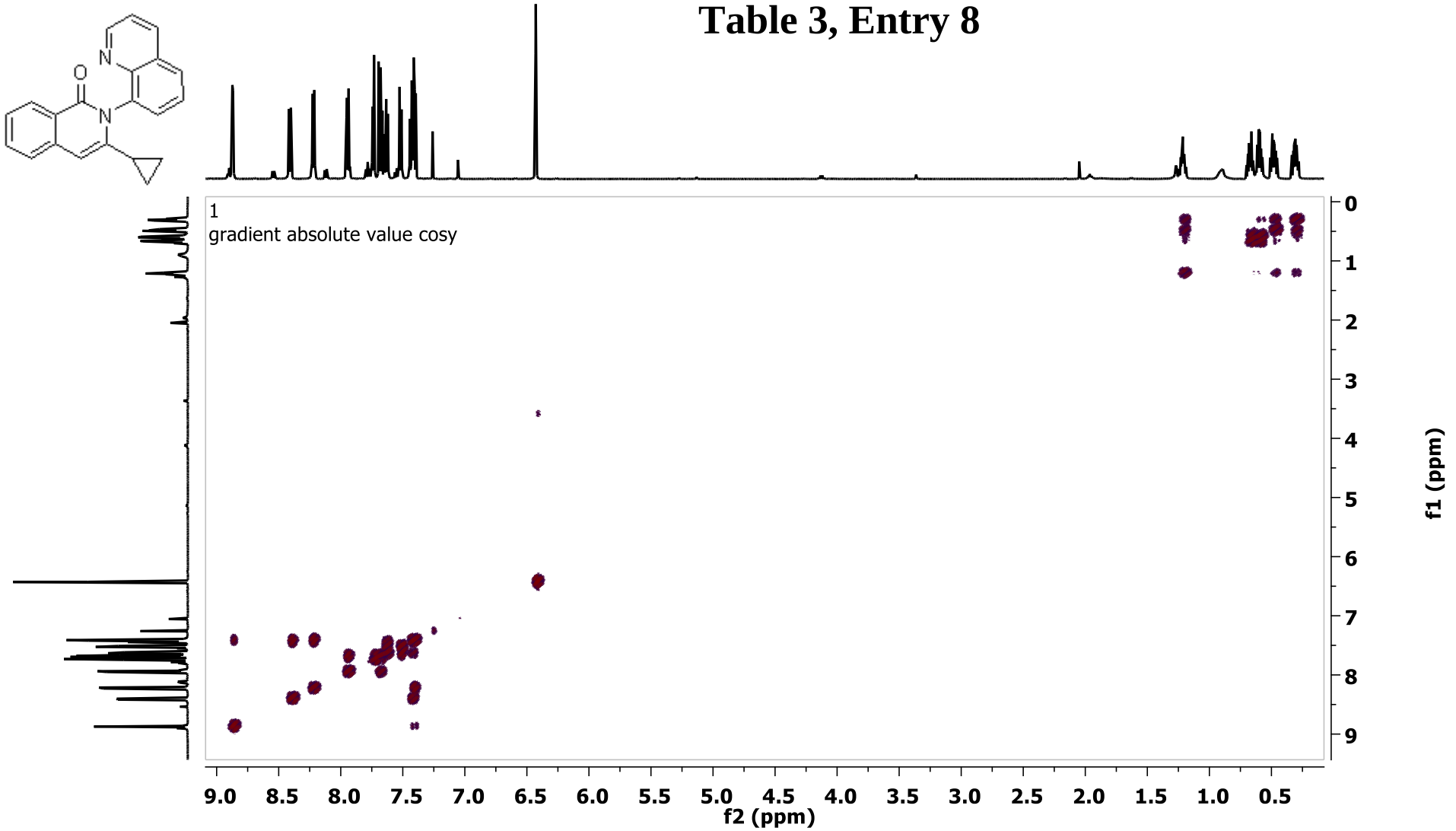
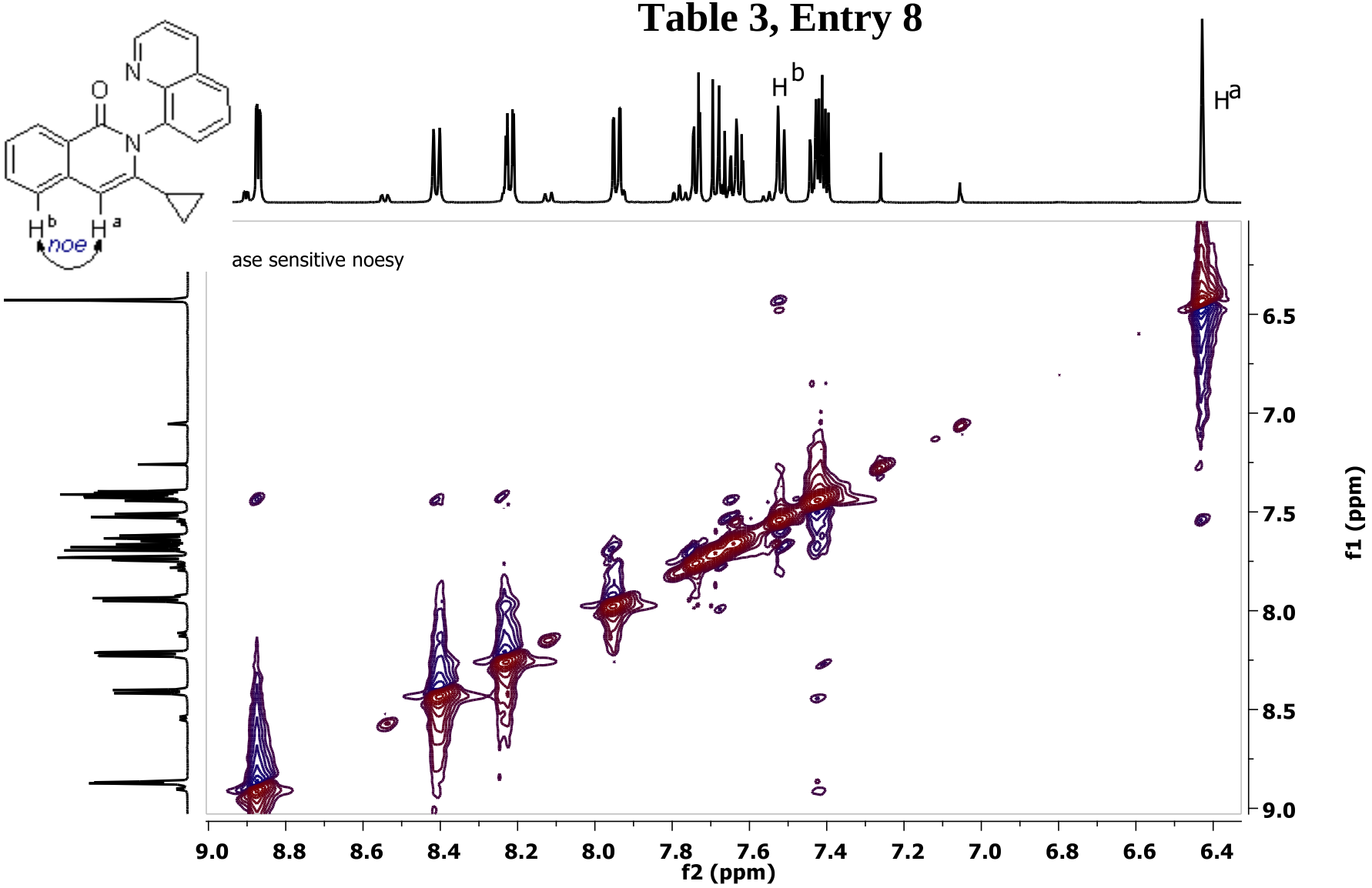


Table 3, Entry 8



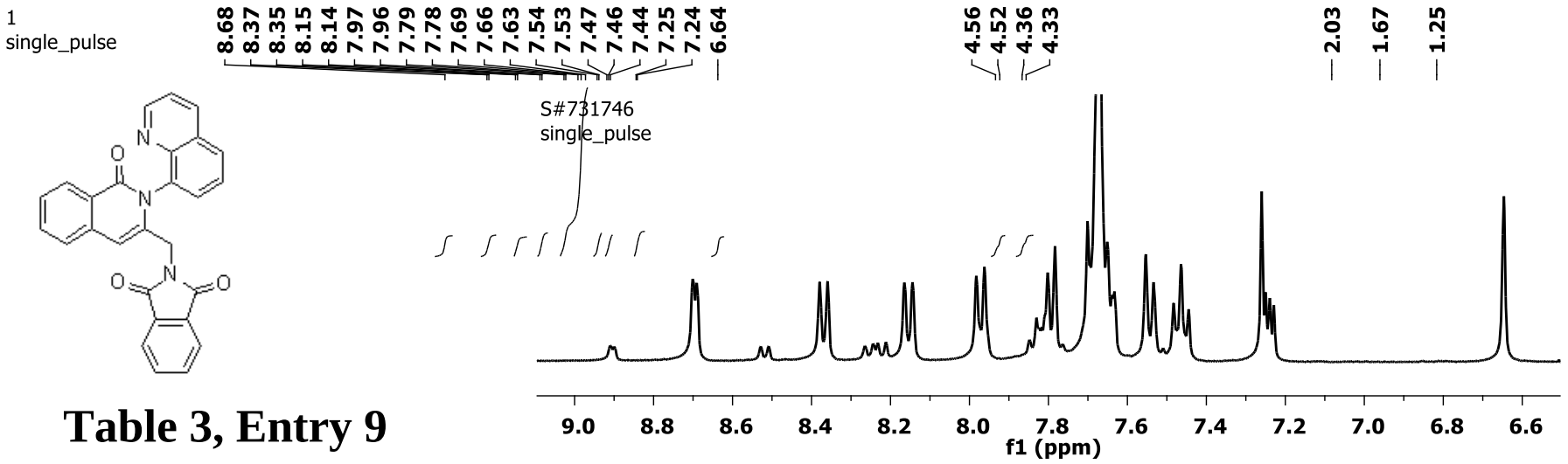
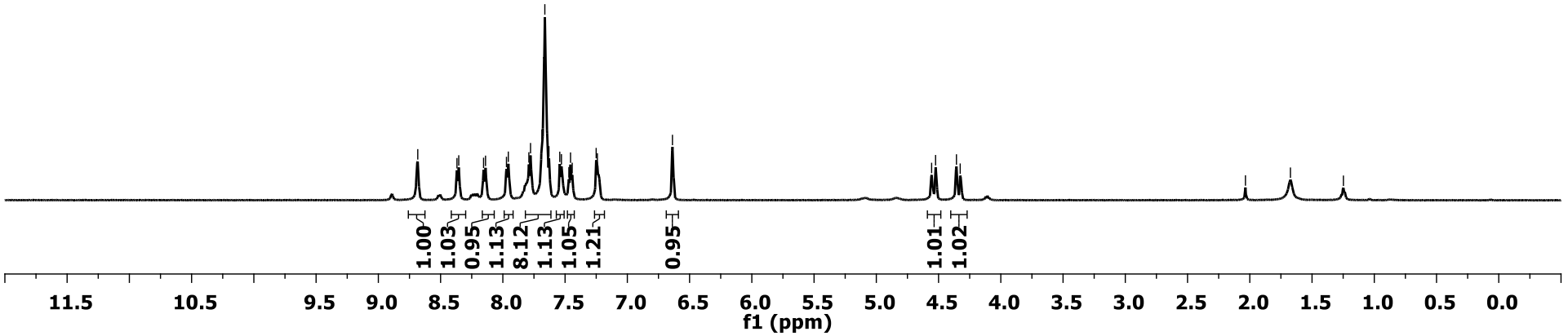


Table 3, Entry 9



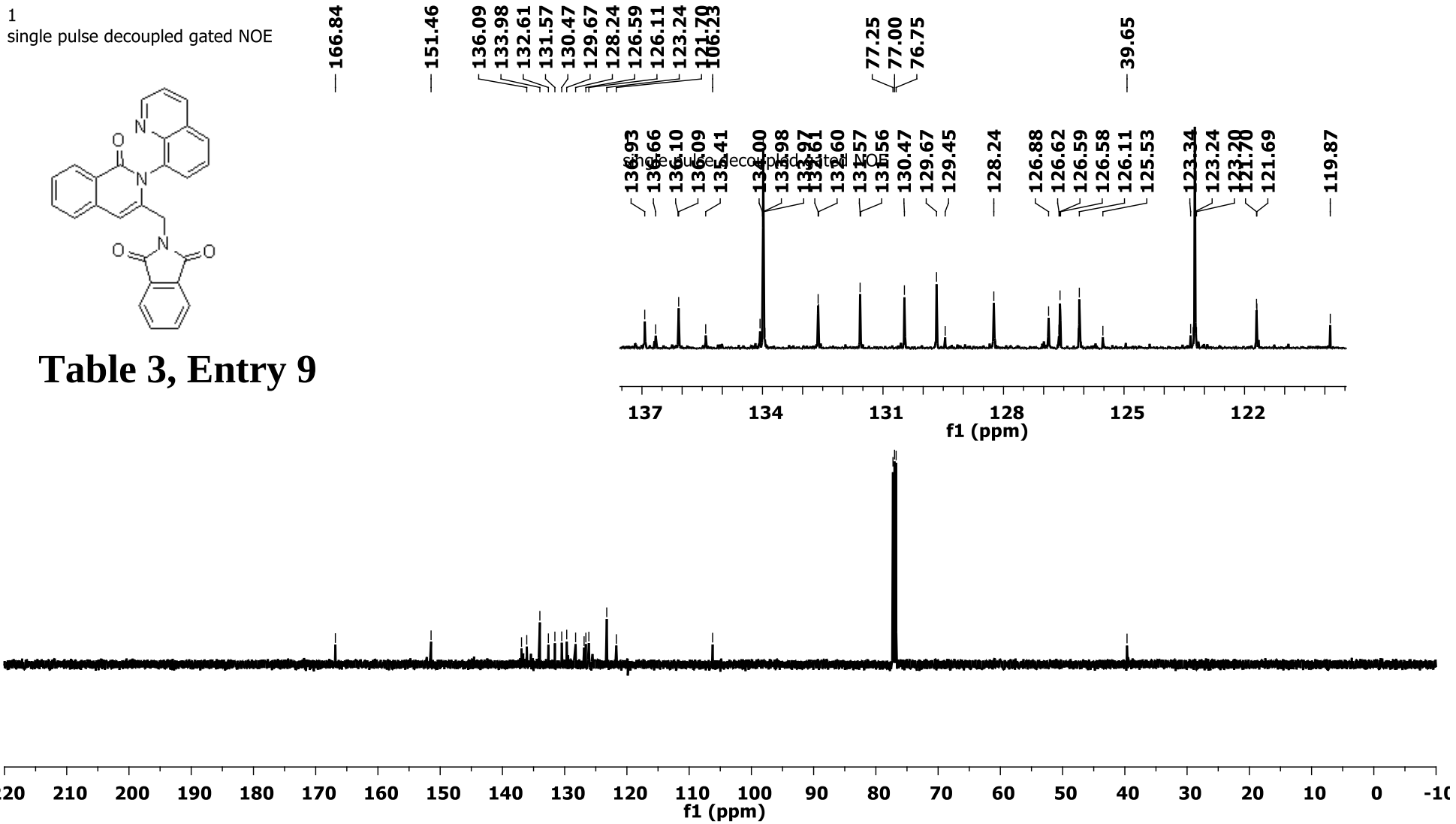


Table 3, Entry 9

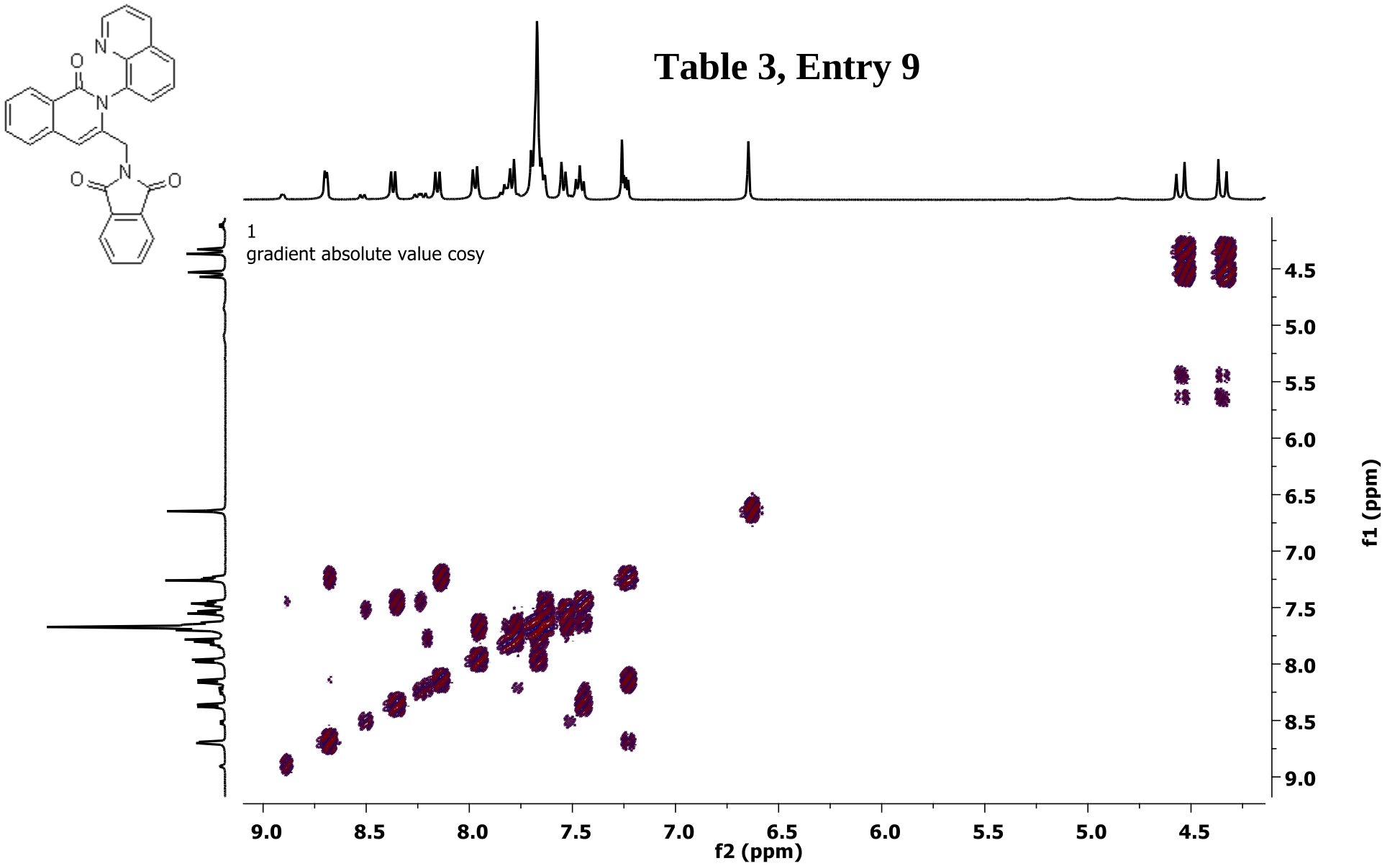
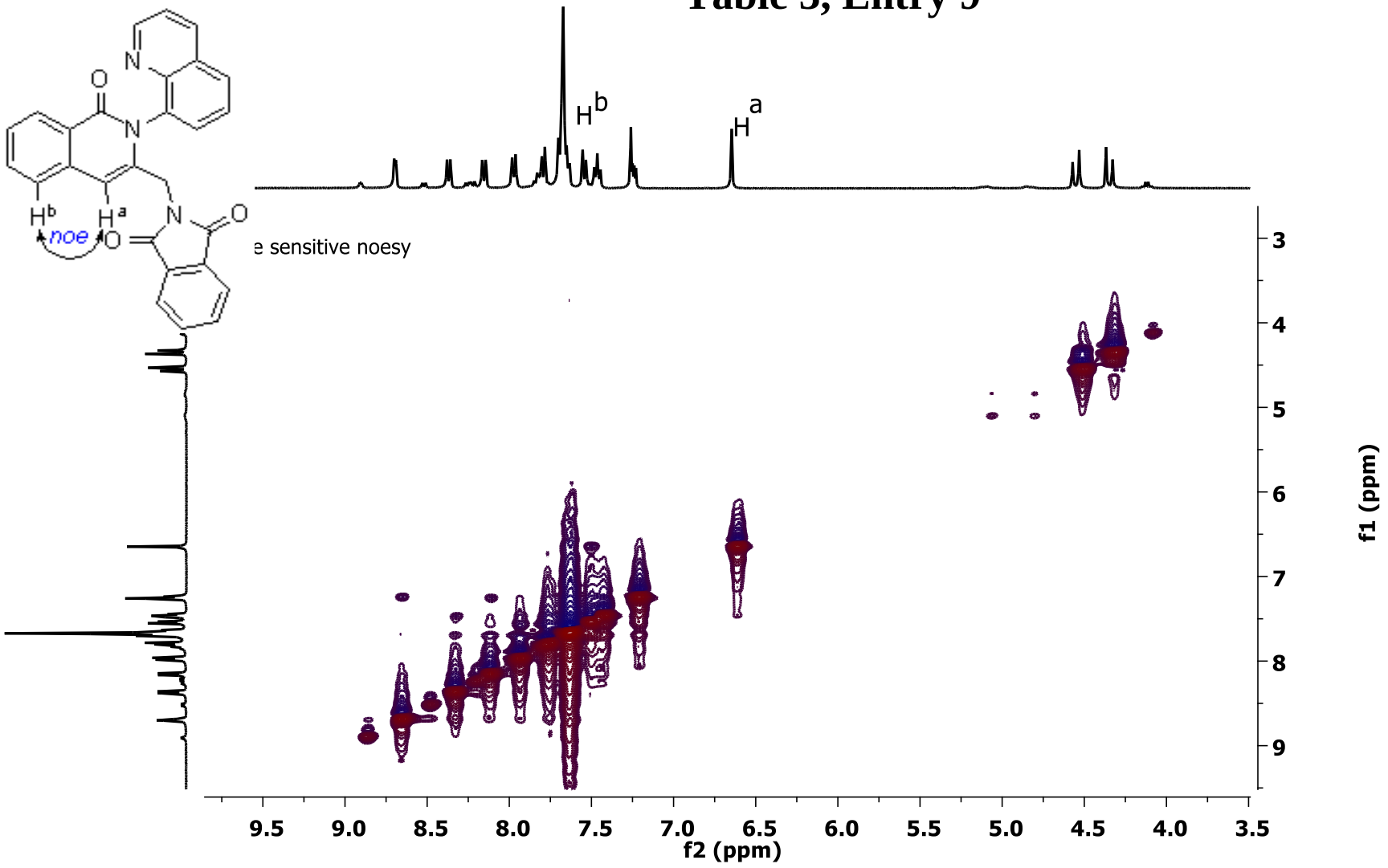
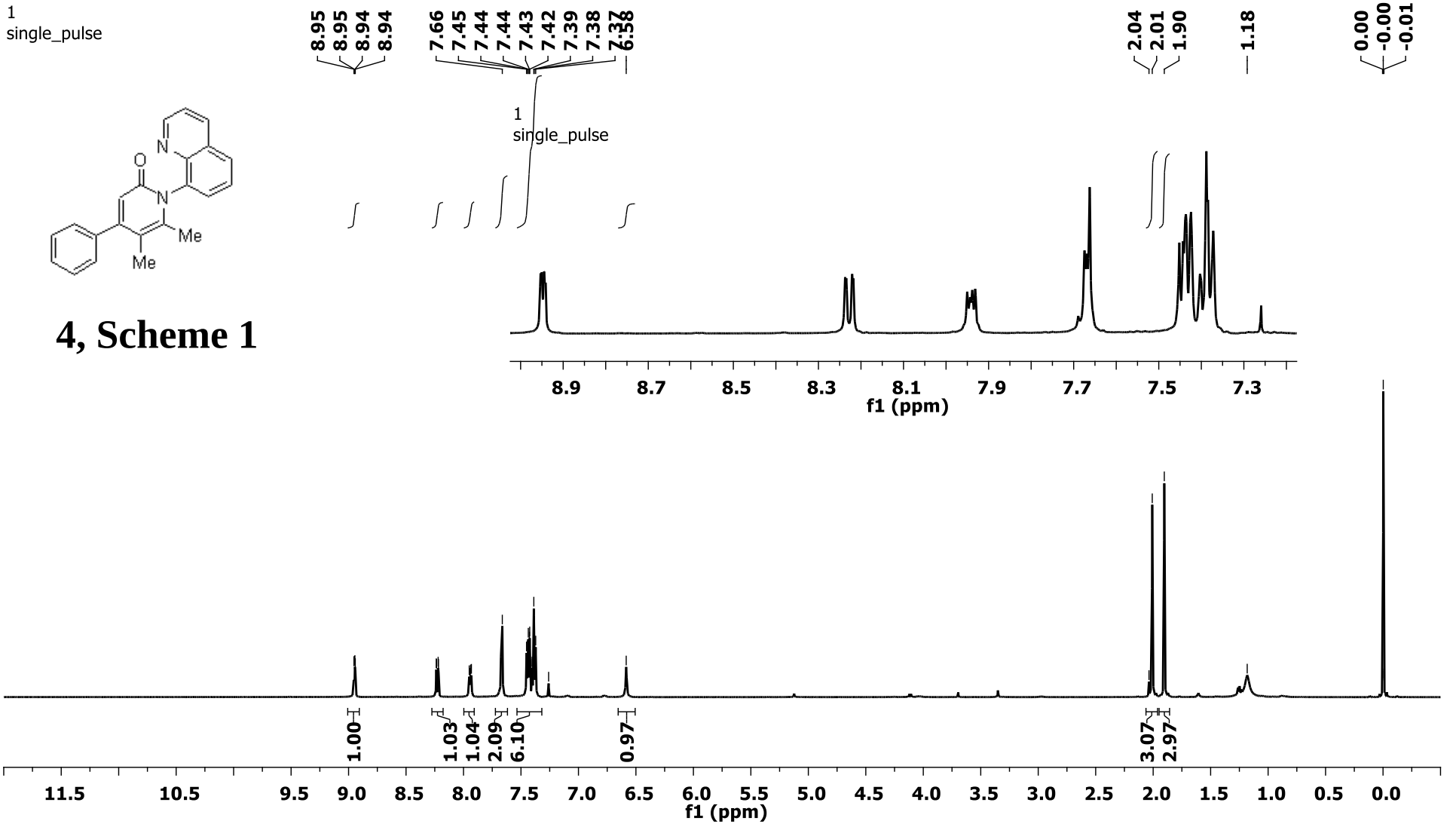


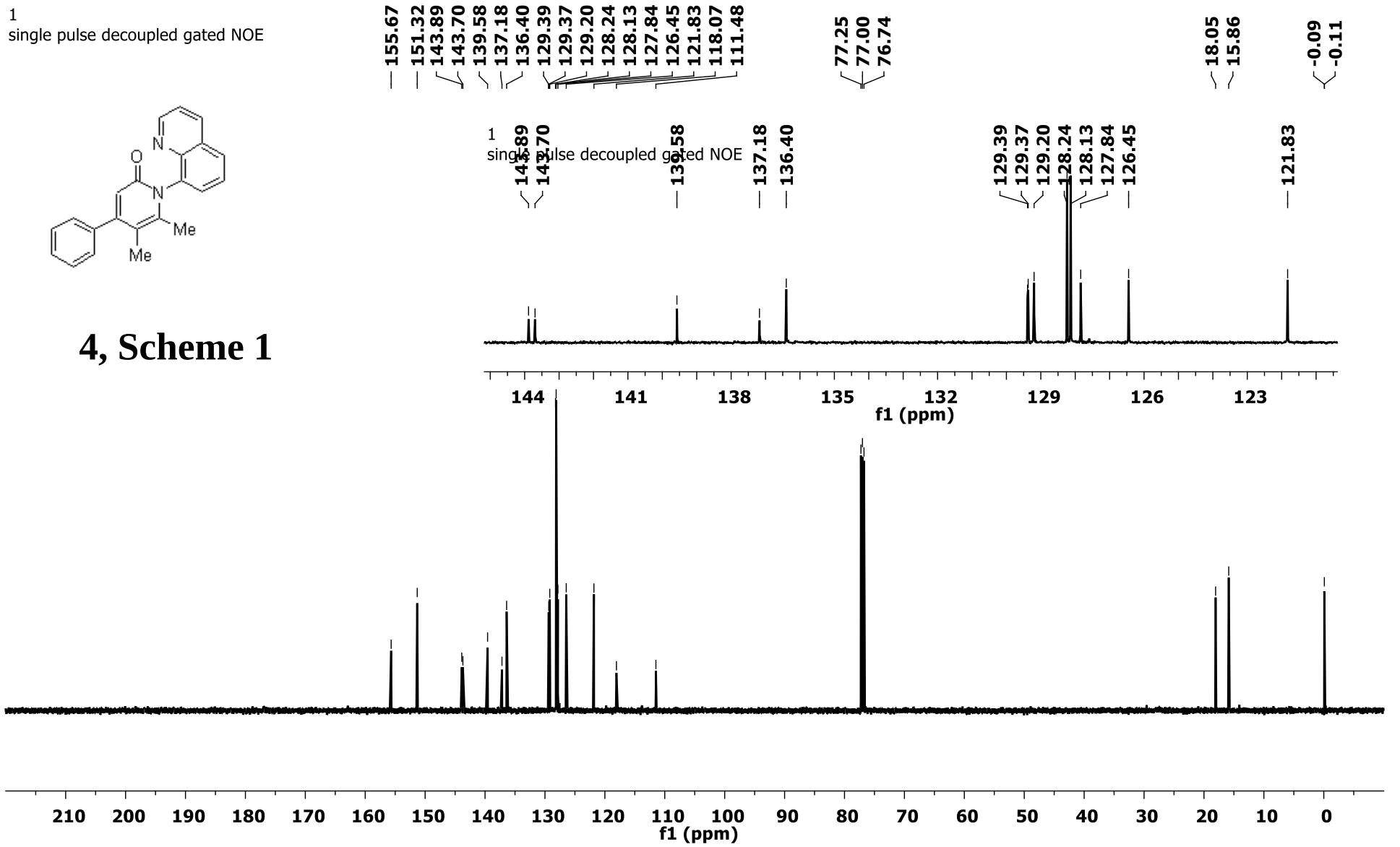
Table 3, Entry 9
1
gradient absolute value cosy
f1 (ppm)
f2 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5

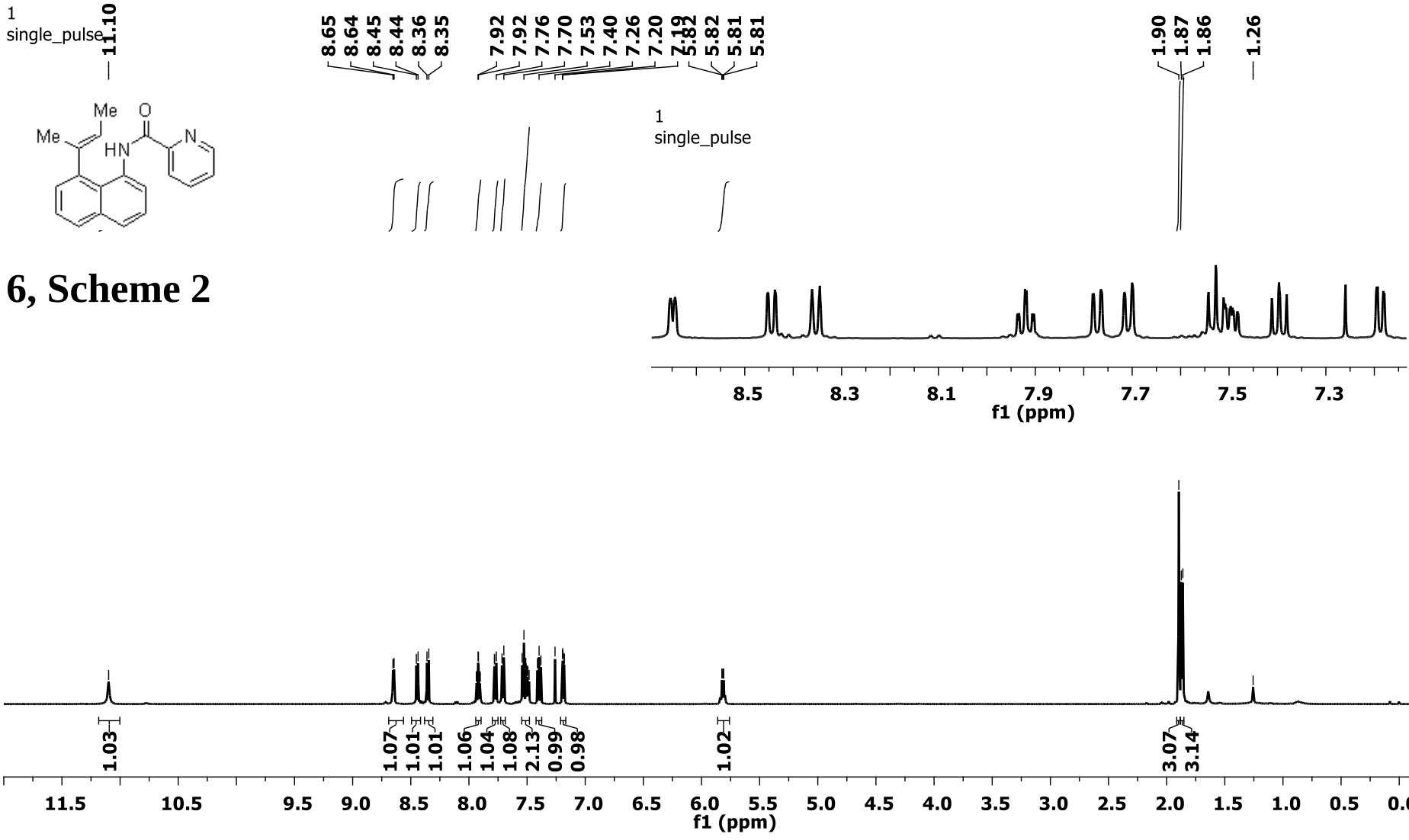
Table 3, Entry 9



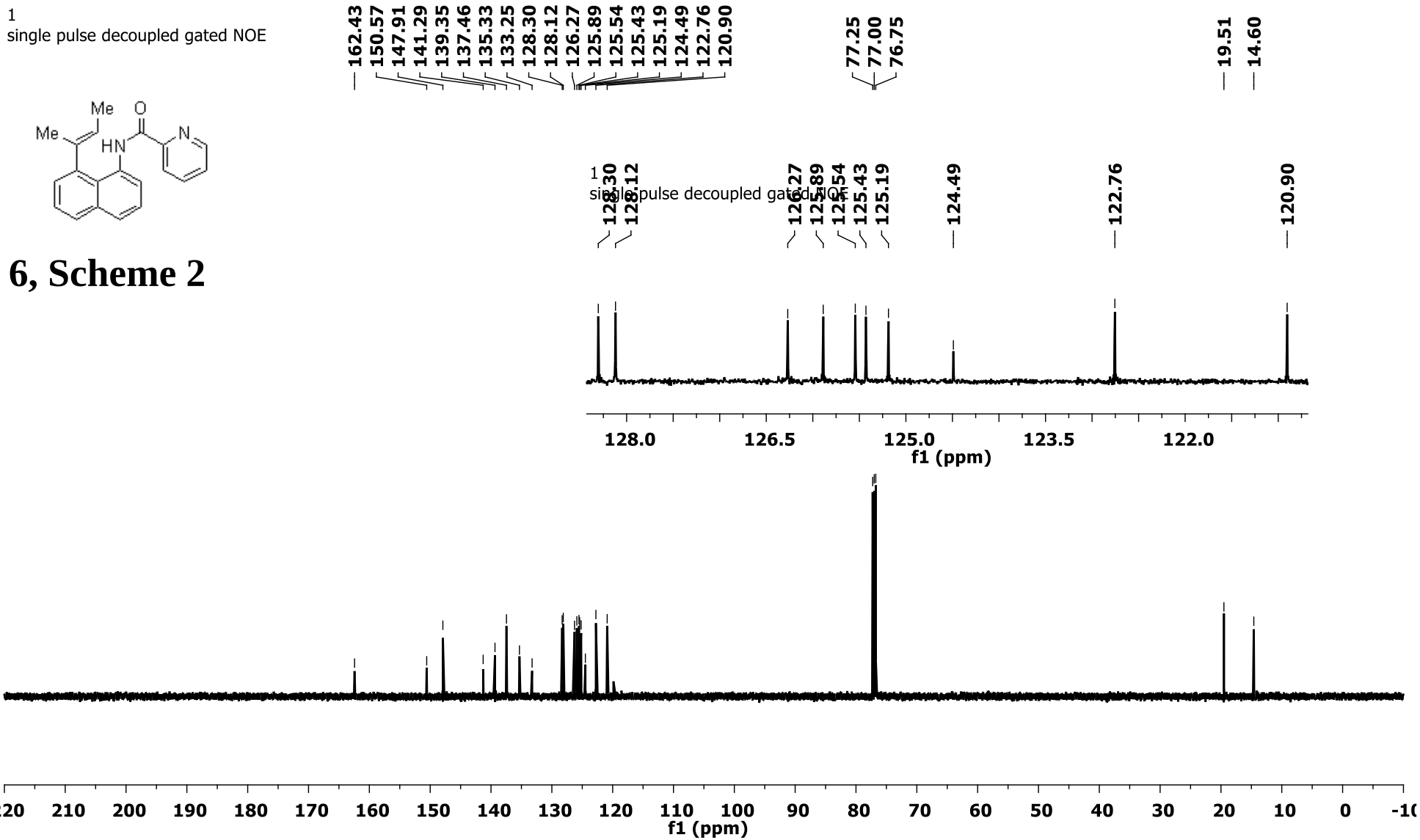

1
single_pulse
8.95
8.95
8.94
8.94
7.66
7.45
7.44
7.44
7.43
7.42
7.39
7.38
7.37
6.58
2.04
2.01
1.90
1.18
0.00
-0.00
-0.01
N
O
N
Me
Me
1
single_pulse
8.9
8.7
8.5
8.3
8.1
7.9
7.7
7.5
7.3
f1 (ppm)
1.00
1.03
1.04
2.09
6.10
0.97
3.07
2.97
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

4, Scheme 1


1
single pulse decoupled gated NOE
155.67
151.32
143.89
143.70
139.58
137.18
136.40
129.39
129.37
129.20
128.24
128.13
127.84
126.45
121.83
118.07
111.48
77.25
77.00
76.74
18.05
15.86
-0.09
-0.11
O
N
N
Me
Me
4, Scheme 1
1
single pulse decoupled gated NOE
144
141
138
135
132
129
126
123
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

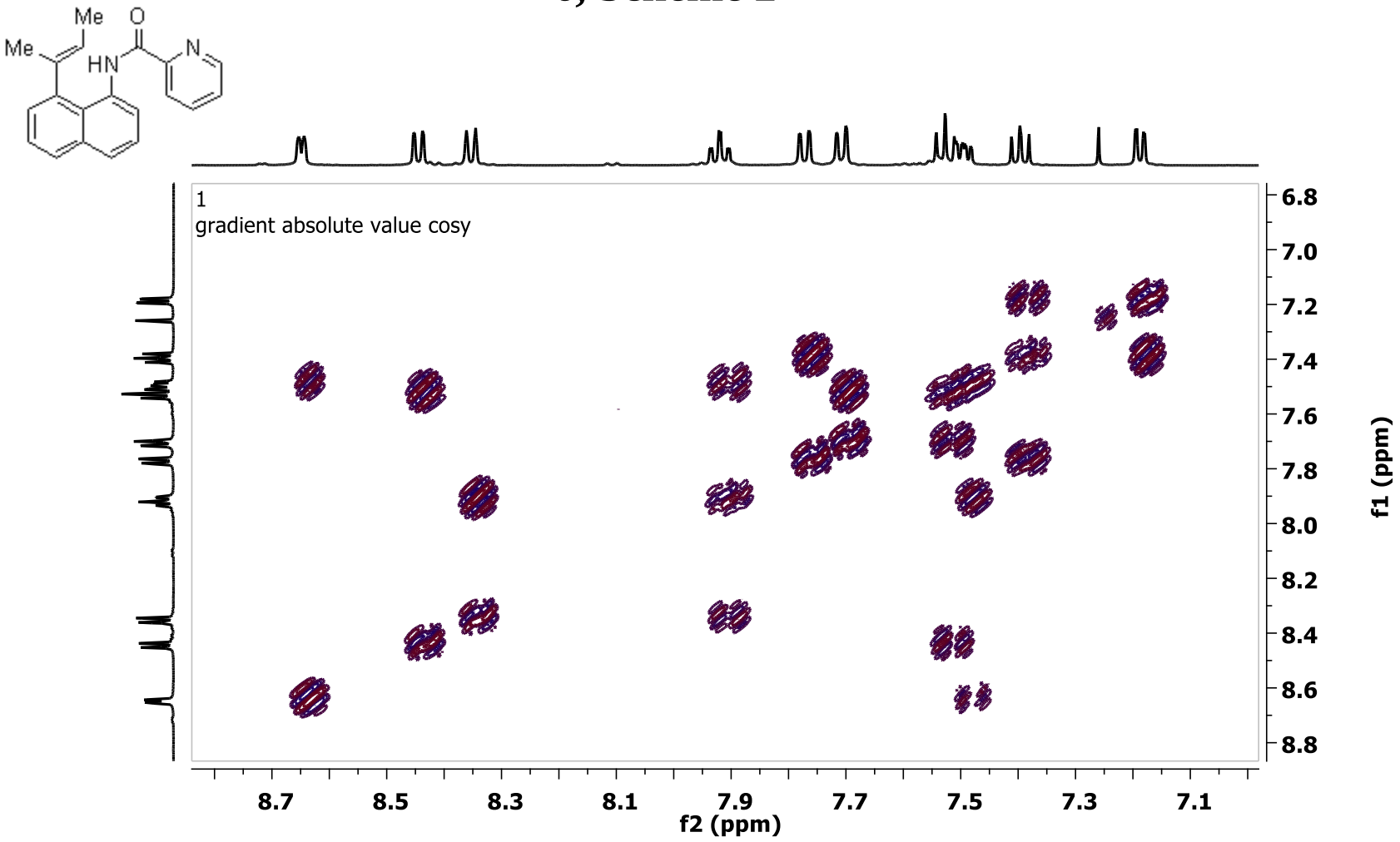

1
single_pulse
11.10
8.65
8.64
8.45
8.44
8.36
8.35
7.92
7.92
7.76
7.70
7.53
7.40
7.26
7.20
7.19
5.82
5.81
5.81
1.90
1.87
1.86
1.26
Me
O
Me
HN
N
1
single_pulse
8.5
8.3
8.1
7.9
7.7
7.5
7.3
f1 (ppm)
1.03
1.07
1.01
1.01
1.06
1.04
1.08
2.13
0.99
0.98
1.02
3.07
3.14
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

6, Scheme 2

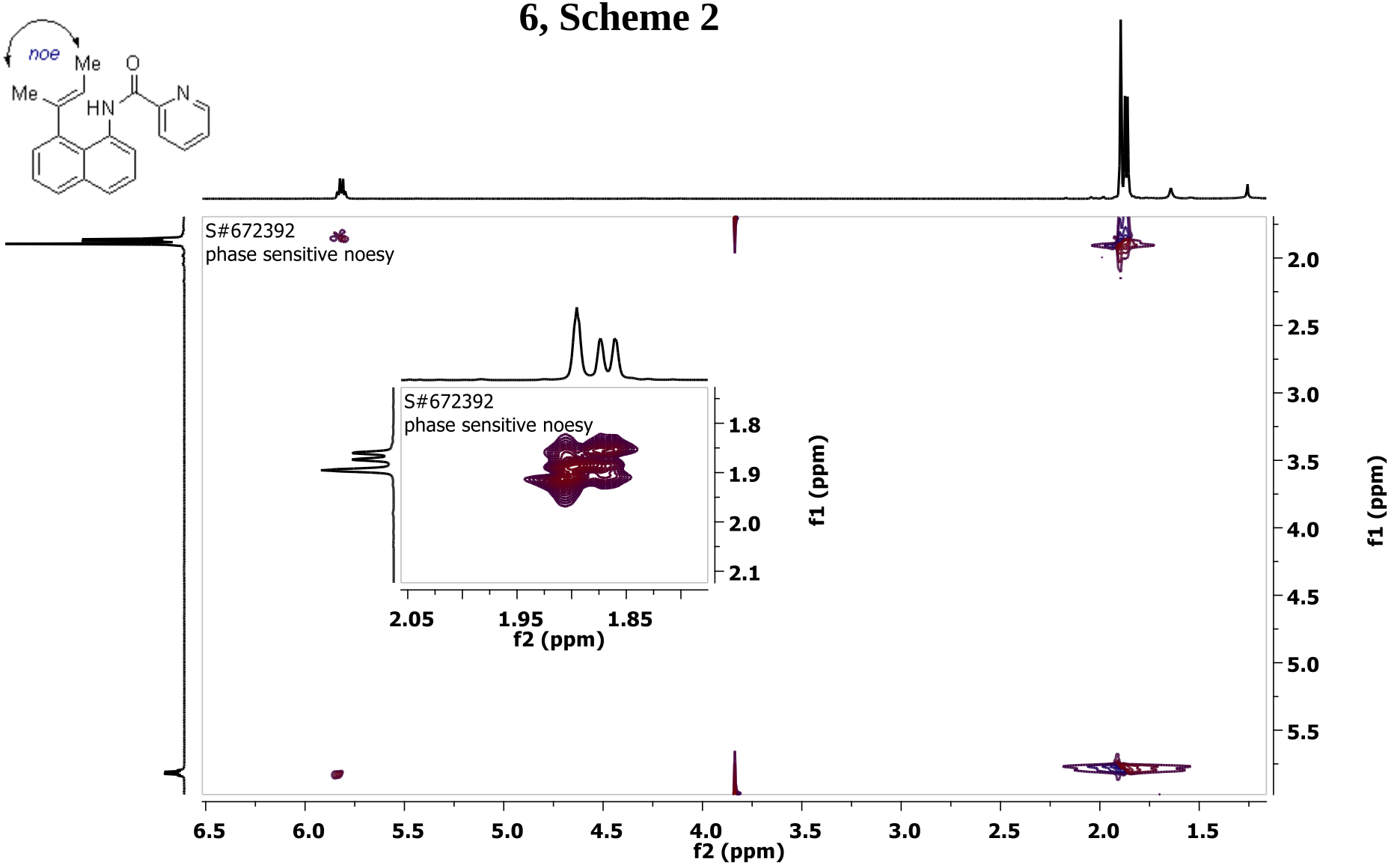

1
single pulse decoupled gated NOE
162.43
150.57
147.91
141.29
139.35
137.46
135.33
133.25
128.30
128.12
126.27
125.89
125.54
125.43
125.19
124.49
122.76
120.90
77.25
77.00
76.75
19.51
14.60
Me
O
Me
HN
N
1
single pulse decoupled gated NOE
128.30
128.12
126.27
125.89
125.54
125.43
125.19
124.49
122.76
120.90
128.0
126.5
125.0
123.5
122.0
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

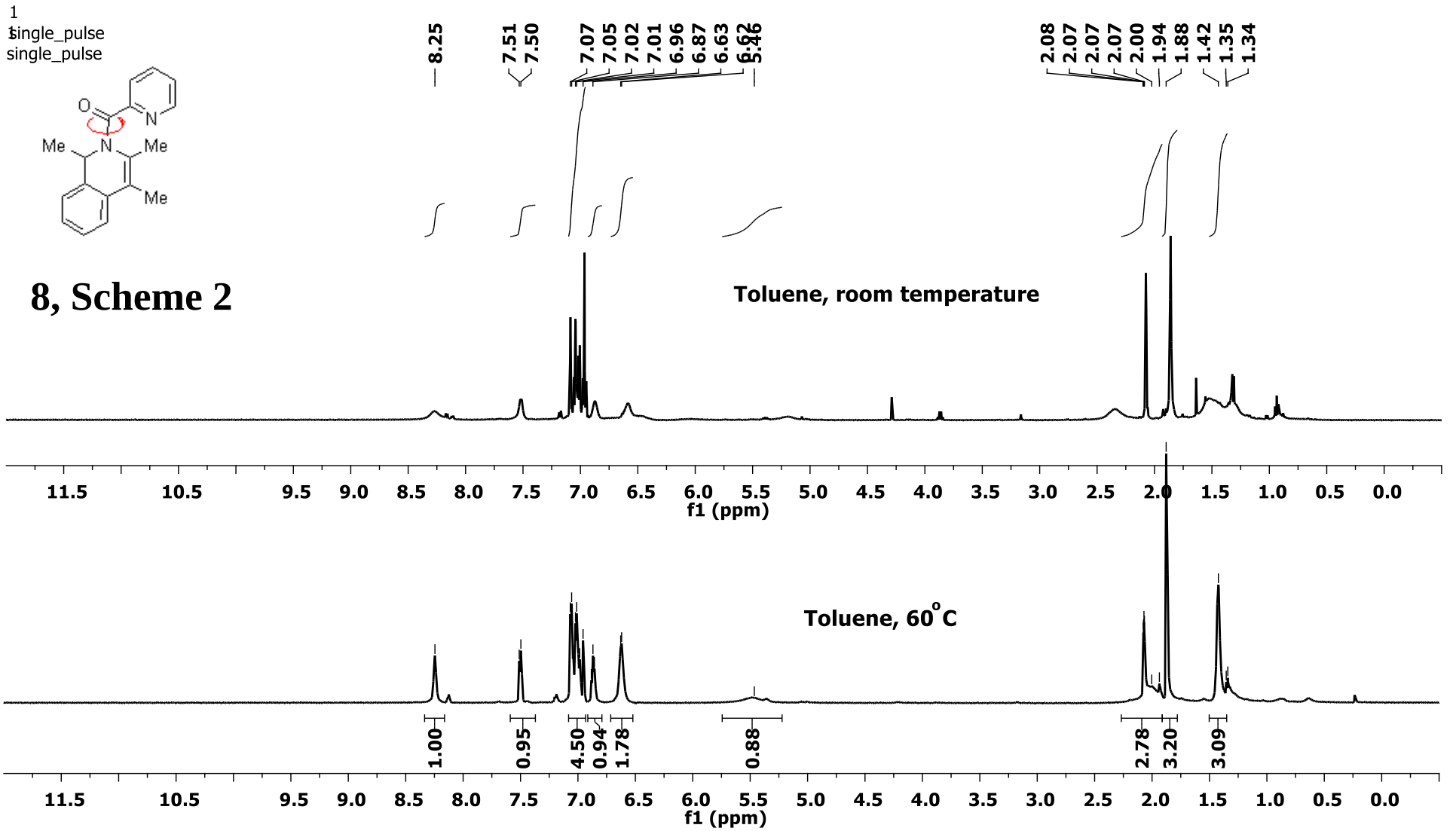
6, Scheme 2

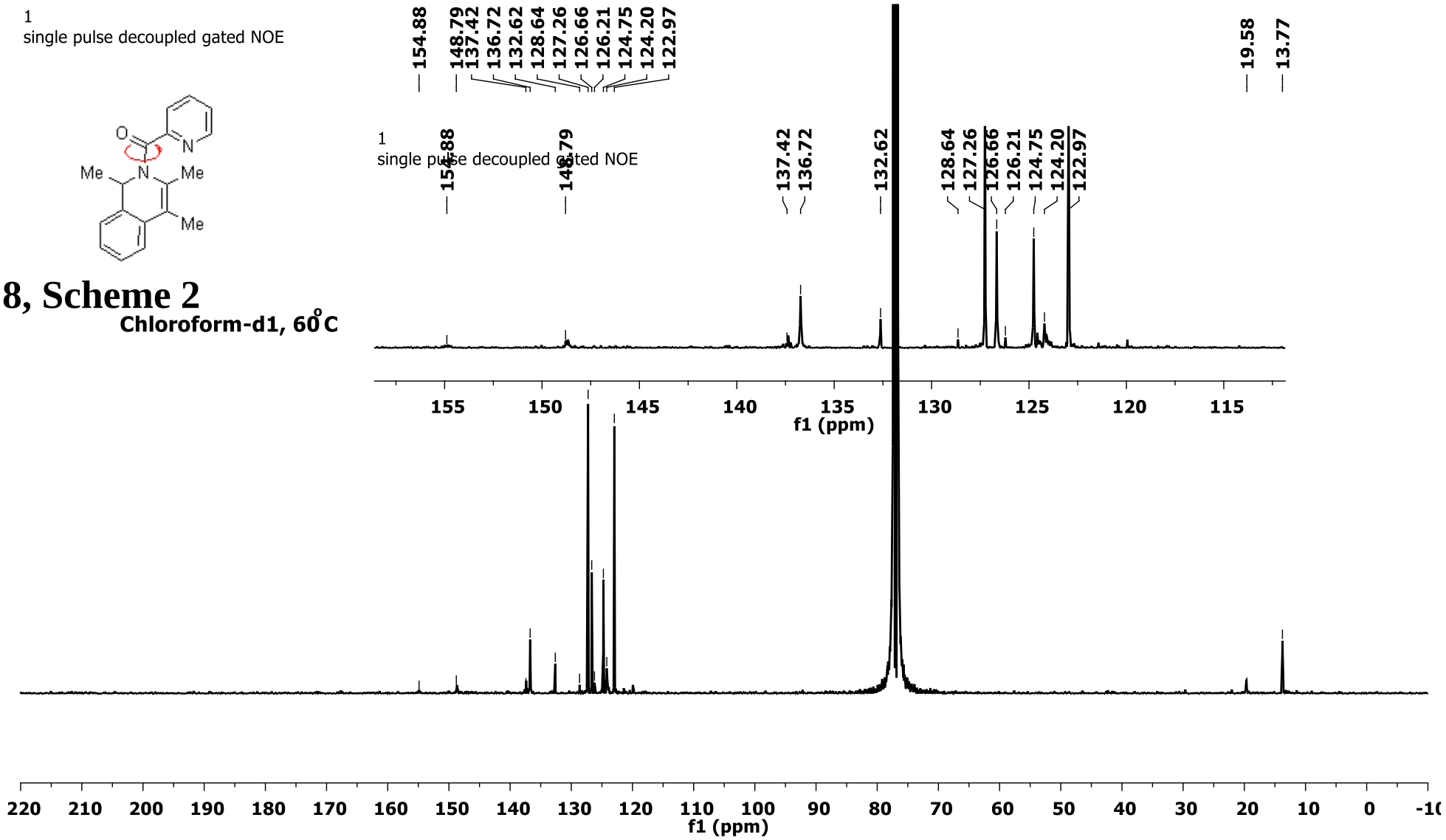
6, Scheme 2

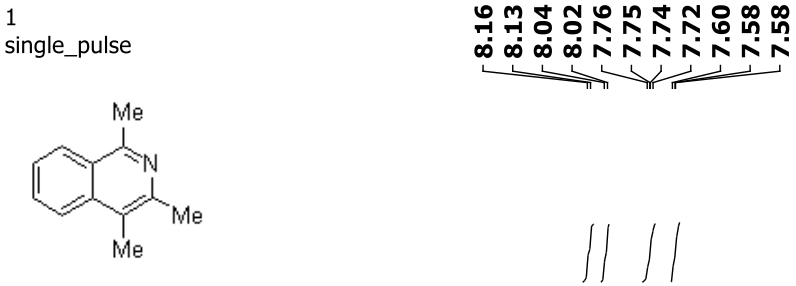

Me
O
Me
HN
N
1
gradient absolute value cosy
6.8
7.0
7.2
7.4
7.6
7.8
8.0
8.2
8.4
8.6
8.8
f1 (ppm)
8.7
8.5
8.3
8.1
7.9
7.7
7.5
7.3
7.1
f2 (ppm)

6, Scheme 2

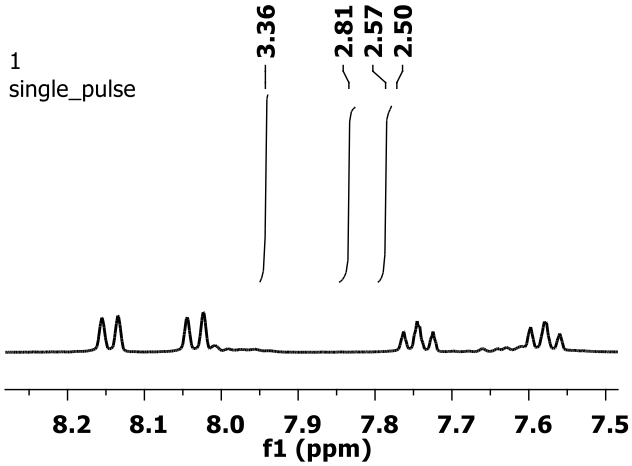

noe
Me
O
Me
HN
N
S#672392
phase sensitive noesy
S#672392
phase sensitive noesy
1.8
1.9
2.0
2.1
2.05
1.95
1.85
f2 (ppm)
f1 (ppm)
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
f1 (ppm)
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f2 (ppm)

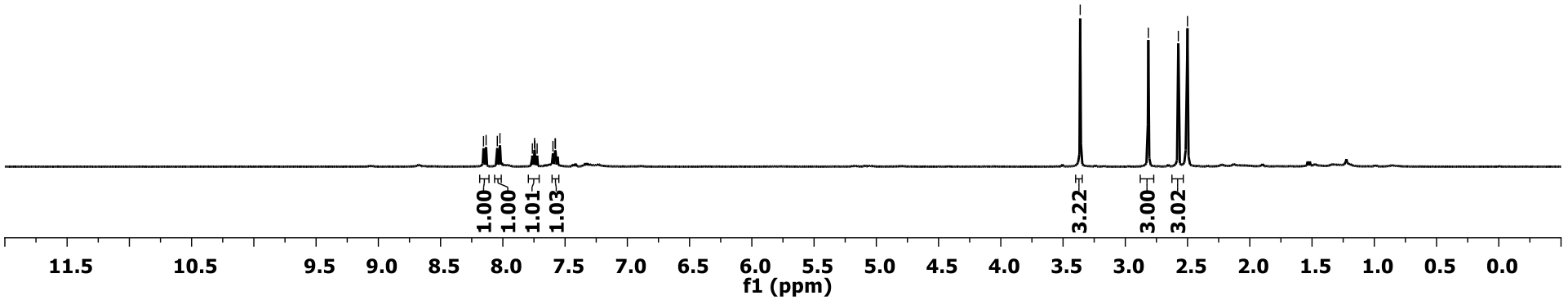

1
single_pulse
single_pulse
8.25
7.51
7.50
7.07
7.05
7.02
7.01
6.96
6.87
6.63
6.62
5.46
2.08
2.07
2.07
2.07
2.00
1.94
1.88
1.42
1.35
1.34
O
N
Me
N
Me
Me
8, Scheme 2
Toluene, room temperature
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
Toluene, 60°C
1.00
0.95
4.50
0.94
1.78
0.88
2.78
3.20
3.09
11.5
10.5
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
0.0
f1 (ppm)


1
single pulse decoupled gated NOE
154.88
148.79
137.42
136.72
132.62
128.64
127.26
126.66
126.21
124.75
124.20
122.97
19.58
13.77
O
N
Me
N
Me
Me
8, Scheme 2
Chloroform-d1, 60°C
1
single pulse decoupled gated NOE
154.88
148.79
137.42
136.72
132.62
128.64
127.26
126.66
126.21
124.75
124.20
122.97
155
150
145
140
135
130
125
120
115
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

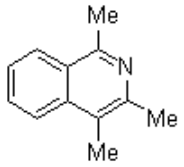

1
single_pulse
Me
N
Me
Me
8.16
8.13
8.04
8.02
7.76
7.75
7.74
7.72
7.60
7.58
7.58

9, Scheme 3

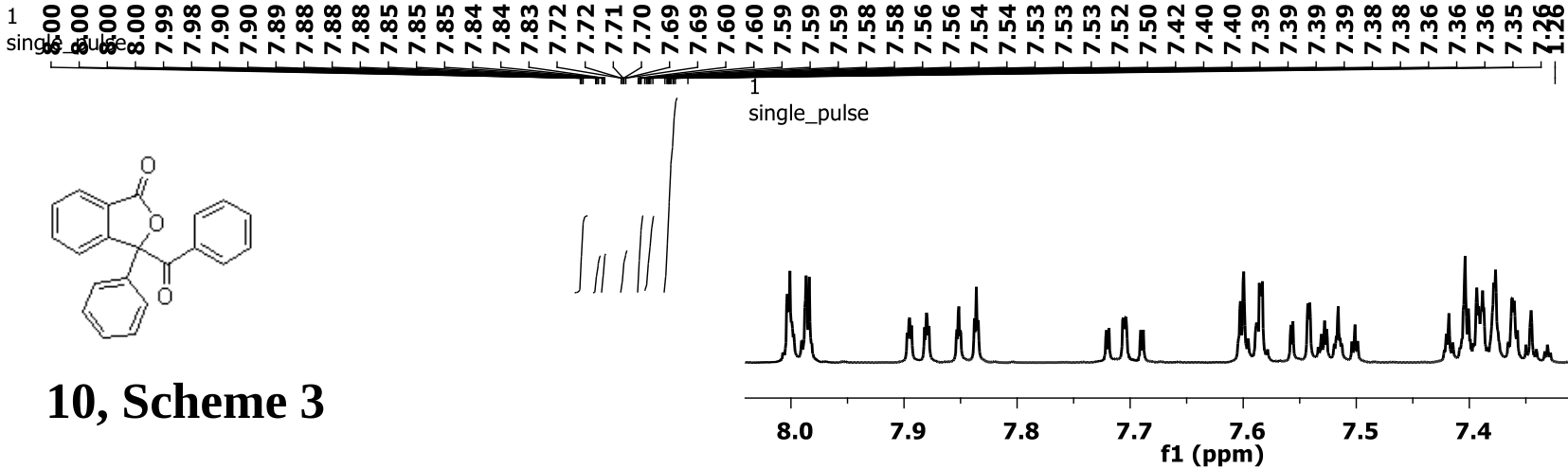

1
single_pulse
3.36
2.81
2.57
2.50
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
f1 (ppm)


1.00
1.00
1.01
1.03
3.22
3.00
3.02
11.5
10.5
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
0.0
f1 (ppm)

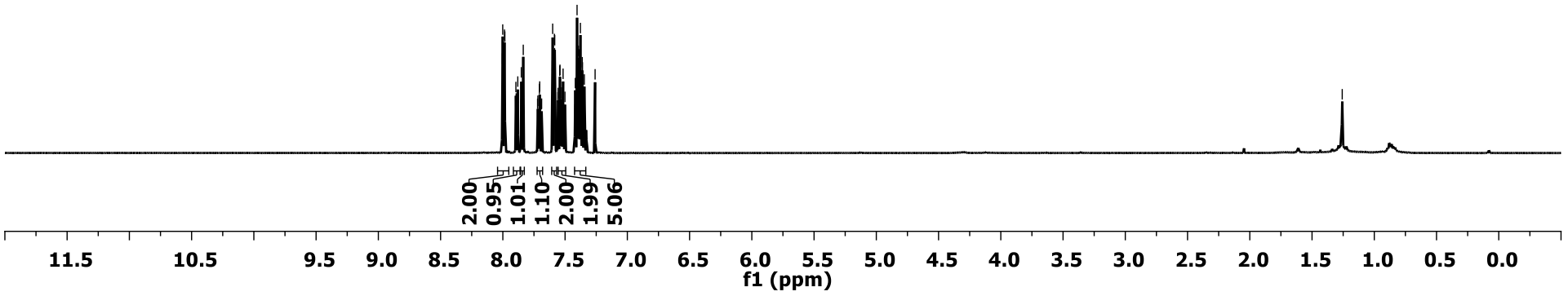
1
single pulse decoupled gated NOE

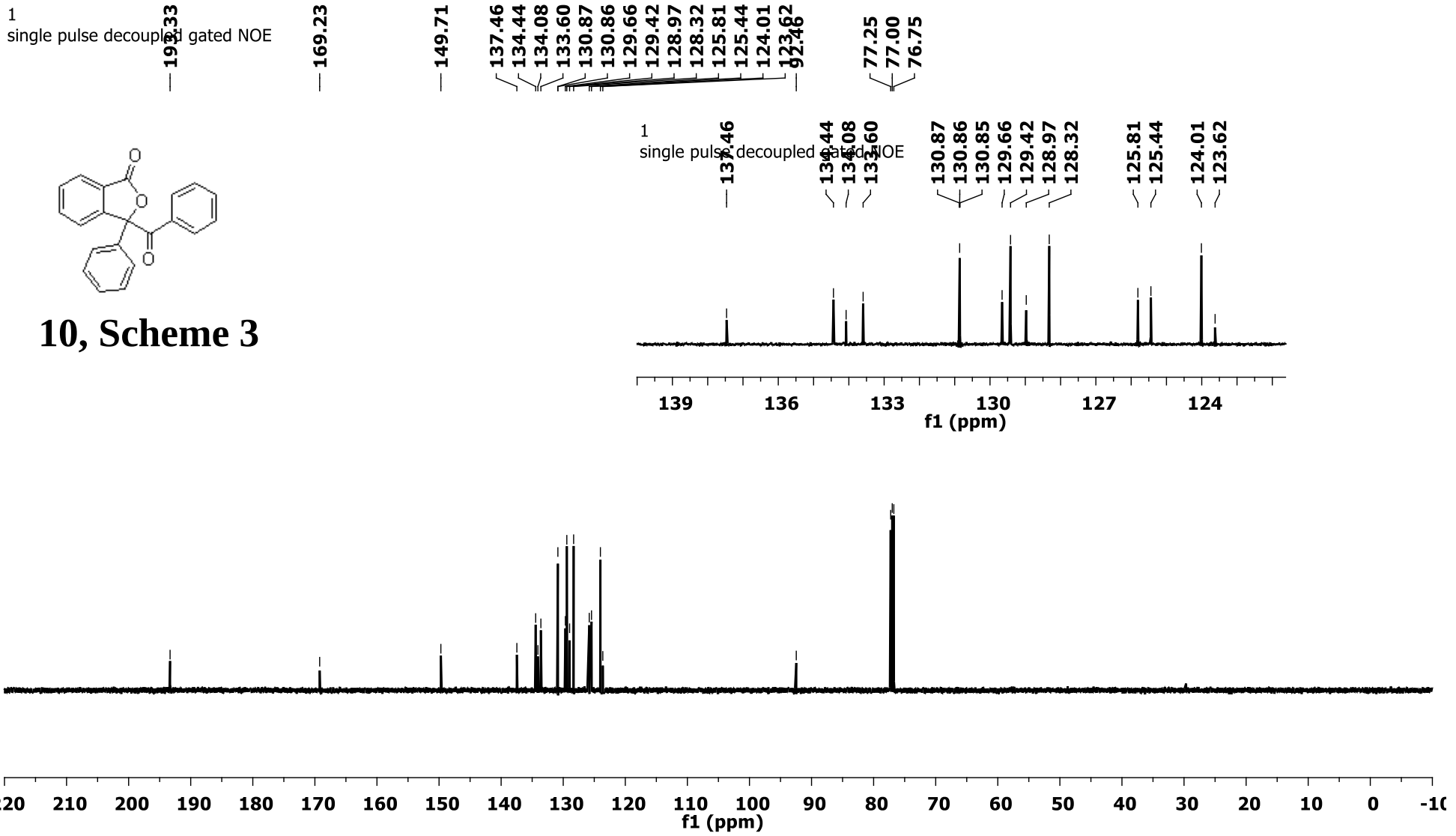


9, Scheme 3

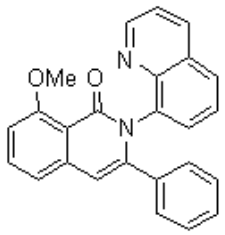

1
single_pulse
8.00 8.00 8.00 8.00 7.99 7.98 7.90 7.90 7.89 7.88 7.88 7.88 7.85 7.85 7.85 7.84 7.84 7.83 7.72 7.72 7.71 7.70 7.69 7.69 7.60 7.60 7.59 7.59 7.59 7.58 7.58 7.56 7.56 7.54 7.54 7.53 7.53 7.53 7.52 7.50 7.42 7.40 7.40 7.39 7.39 7.39 7.39 7.38 7.38 7.36 7.36 7.36 7.35 7.26 1.26
1
single_pulse
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)

10, Scheme 3

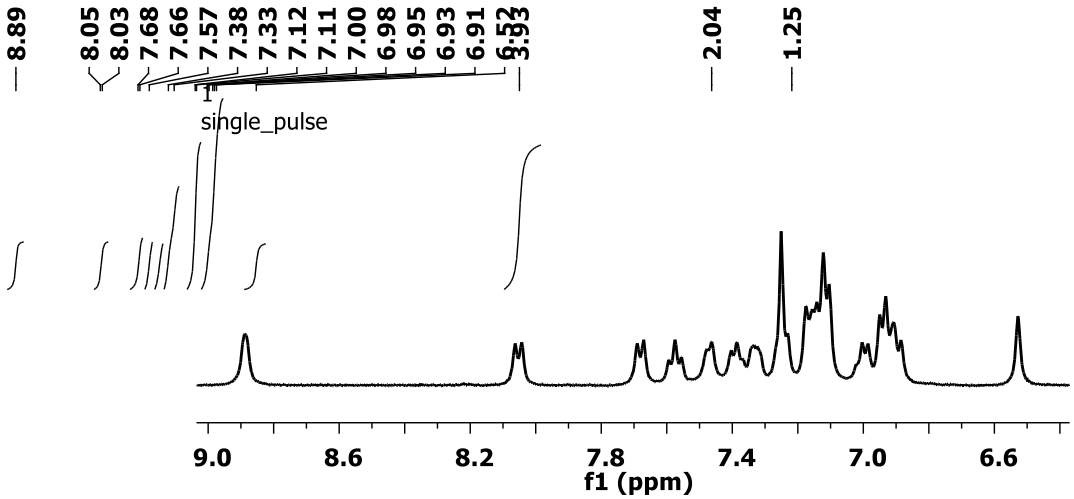

2.00 0.95 1.01 1.10 2.00 1.99 5.06
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

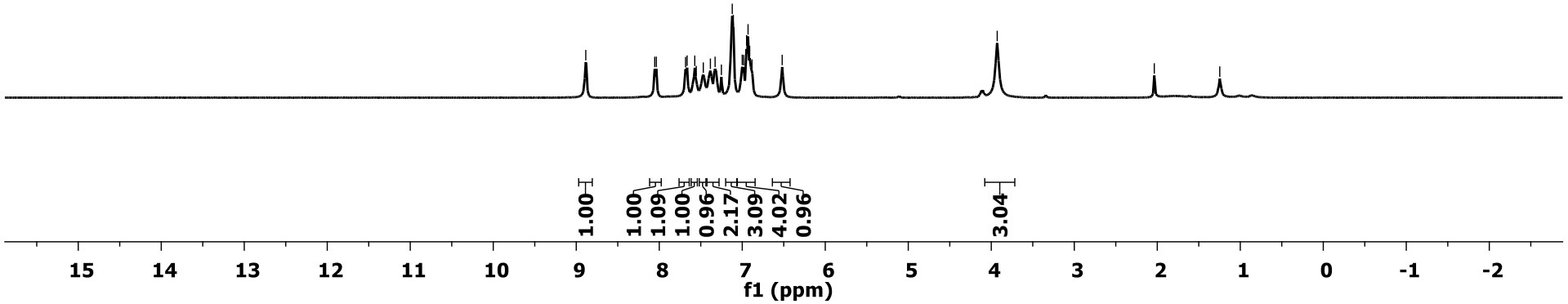

1
single pulse decoupled gated NOE
193.33
169.23
149.71
137.46
134.44
134.08
133.60
130.87
130.86
129.66
129.42
128.97
128.32
125.81
125.44
124.01
123.62
92.46
77.25
77.00
76.75
O
O
O
O
10, Scheme 3
1
single pulse decoupled gated NOE
137.46
134.44
134.08
133.60
130.87
130.86
130.85
129.66
129.42
128.97
128.32
125.81
125.44
124.01
123.62
139
136
133
130
127
124
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

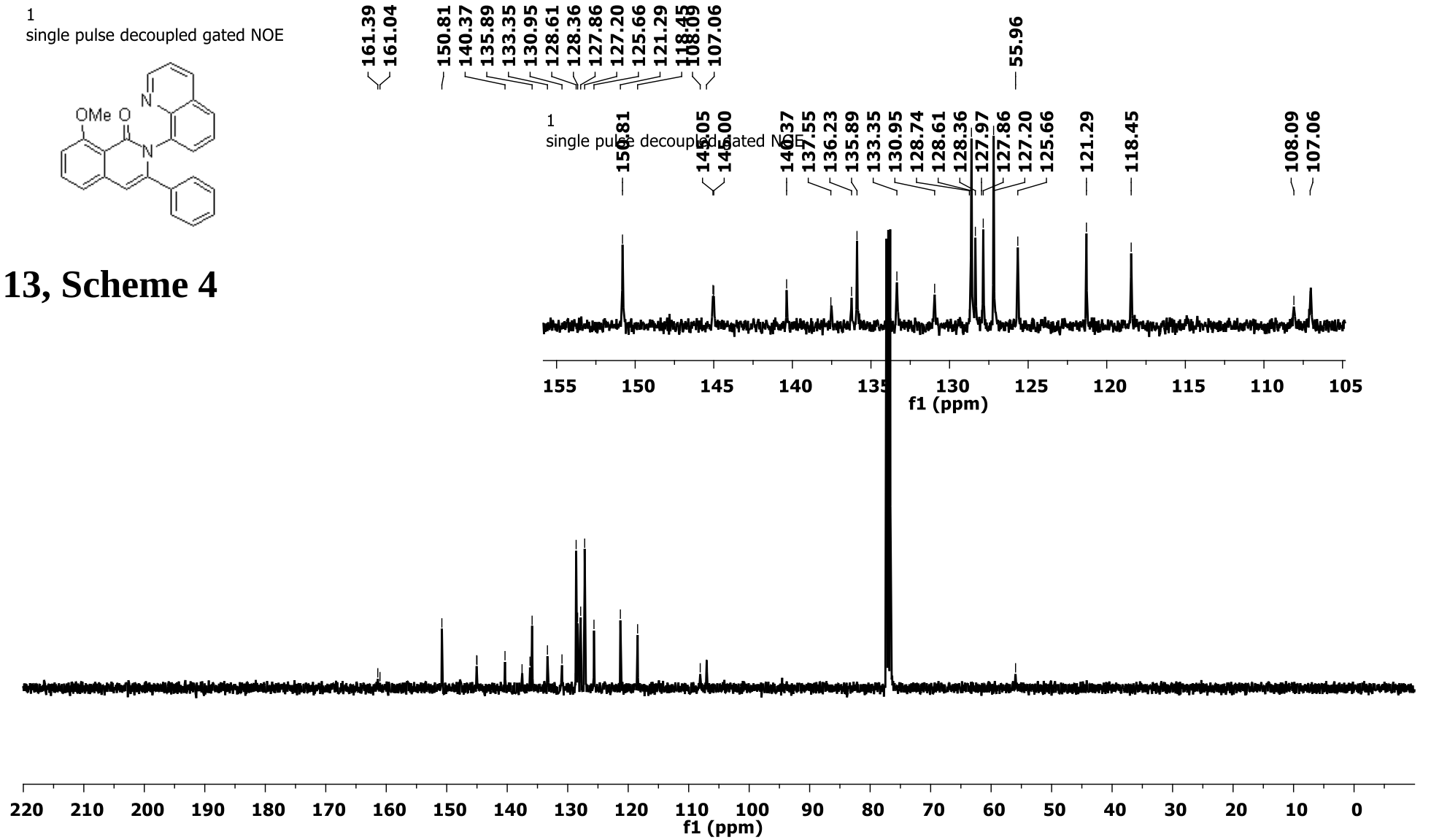
S#507449
single_pulse



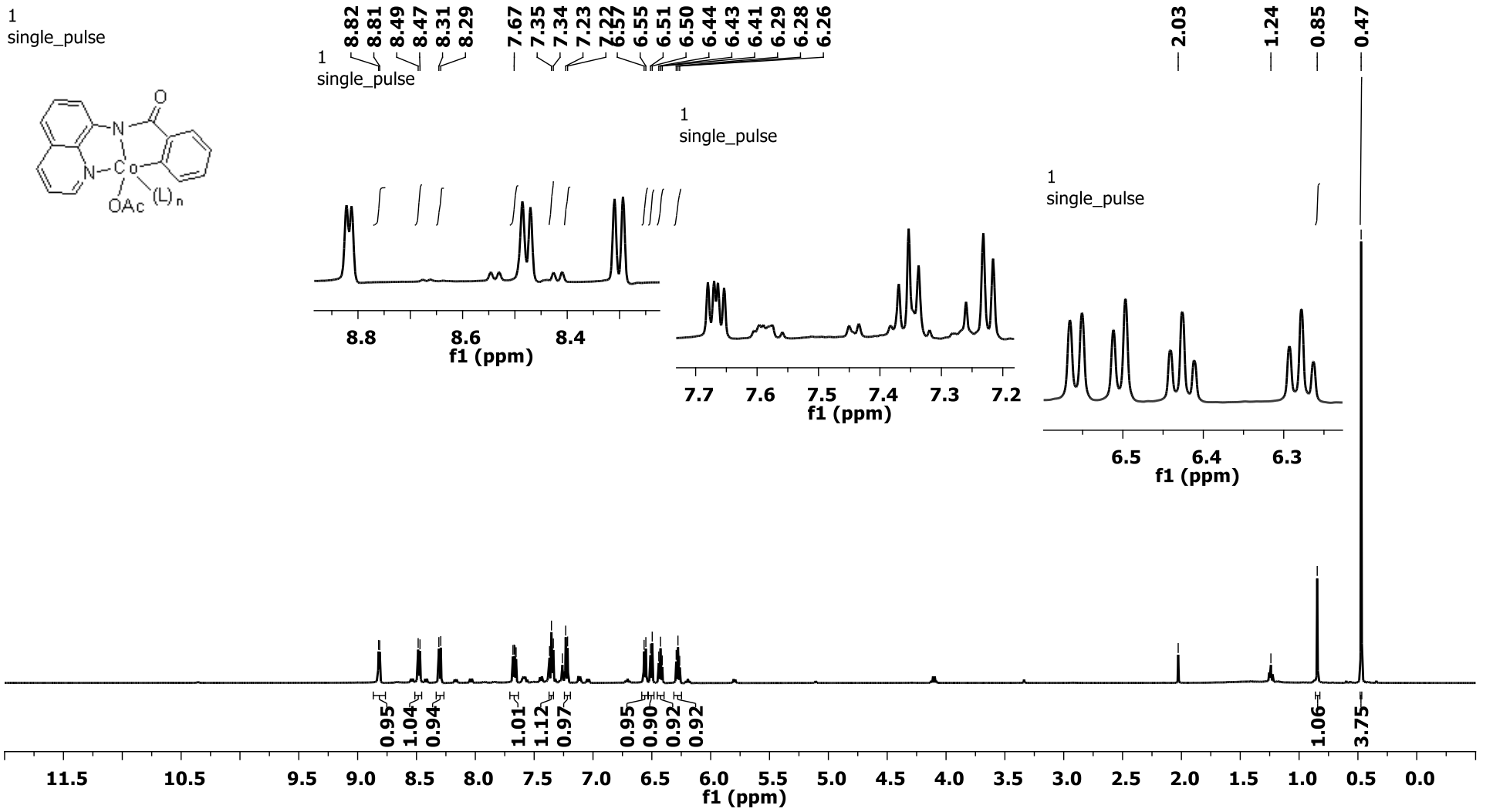
13, Scheme 4

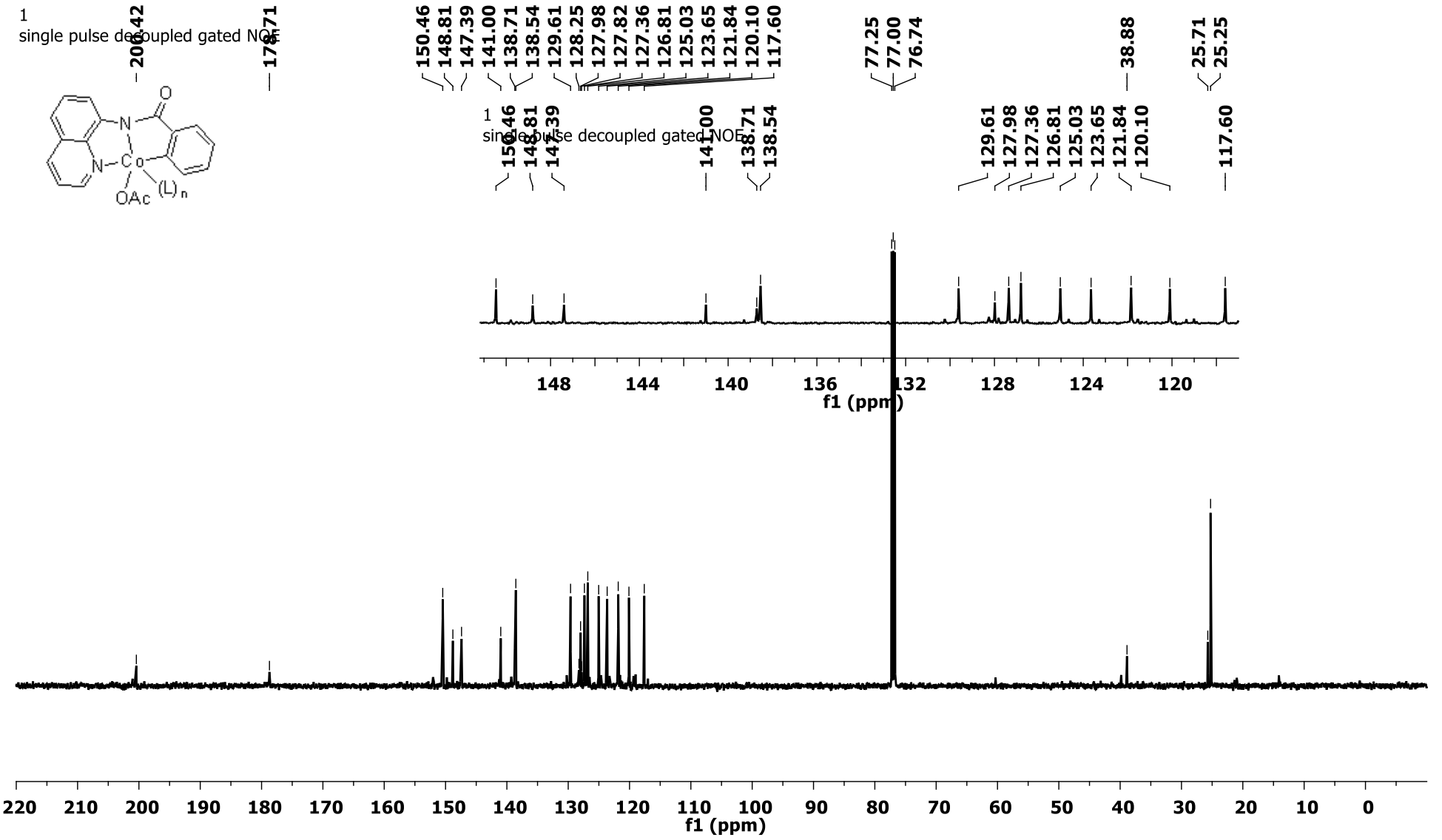





1
single pulse decoupled gated NOE
OMe O
N
N
161.39
161.04
150.81
140.37
135.89
133.35
130.95
128.61
128.36
127.86
127.20
125.66
121.29
118.45
108.09
107.06
55.96
1
single pulse decoupled gated NOE
150.81
145.05
146.00
140.37
137.55
136.23
135.89
133.35
130.95
128.74
128.61
128.36
127.97
127.86
127.20
125.66
121.29
118.45
108.09
107.06
155 150 145 140 135 130 125 120 115 110 105
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

13, Scheme 4


1
single_pulse
8.82
8.81
8.49
8.47
8.31
8.29
7.67
7.35
7.34
7.23
7.22
6.57
6.55
6.51
6.50
6.44
6.43
6.41
6.29
6.28
6.26
2.03
1.24
0.85
0.47
f1 (ppm)
0.95
1.04
0.94
1.01
1.12
0.97
0.95
0.90
0.92
0.92
1.06
3.75


1
single pulse decoupled gated NOE
206.42
178.71
150.46
148.81
147.39
141.00
138.71
138.54
129.61
128.25
127.98
127.82
127.36
126.81
125.03
123.65
121.84
120.10
117.60
77.25
77.00
76.74
38.88
25.71
25.25
O
N
N
Co
OAc
(L)n
1
single pulse decoupled gated NOE
150.46
148.81
147.39
141.00
138.71
138.54
129.61
127.98
127.36
126.81
125.03
123.65
121.84
120.10
117.60
148
144
140
136
132
128
124
120
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)