SUPPORTING INFORMATION

Palladium-Catalyzed, Aminoquinoline-Directed Arylation of Phosphonamidate and Phosphinic Amide sp^3 C-H Bonds

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I. General considerations

Reactions were run in either 1 or 2-dram vials with PTFE/Liner screw caps. Column chromatography was performed on 60Å silica gel (Dynamic Adsorbents Inc.). The ^{1}H, ^{13}C, ^{31}P, and ^{19}F spectra were recorded on JEOL EC-400, JEOL EC-500, or JEOL EC-600 spectrometers using residual solvent peak as a reference. Compounds for HRMS were analyzed by positive mode electrospray ionization (ESI) using Agilent QTOF mass spectrometer at the Mass Spectrometry Facility (MSF) of the Department of Chemistry and Biochemistry, University of Texas-Austin.

II. Materials

tert-Butyl(4-iodophenoxy)dimethylsilane,[1] *N*-(4-iodophenyl)pivalamide,[2] 3-iodo-1-tosyl-1*H*-indole,[3] 3-iodoquinoline,[4] and 3-(triisopropylsilyl)prop-2-yn-1-ol[5] were synthesized following known procedures. Diethyl ethylphosphonate, ethylphosphonic dichloride, 4-iodotoluene, 1-chloro-4-iodobenzene, 4-iodoanisole, ethyl 4-iodobenzoate, 3-iodotoluene, 3,5-bis(trifluoromethyl)iodobenzene, and 2-iodothiophene were obtained from commercial sources and used without further purification. Chlorodiethylphosphine (Alfa Aesar), Cs_3PO_4 (City Chemical), and CsOAc (Alfa Aesar) were obtained from commercial sources and were stored in glovebox. Dry CH_2Cl_2 and THF were used directly from solvent system. 1,2-Dichlorobenzene (Aldrich) was stored with molecular sieves in a dark bottle. Other reagents are commercially available and were used without further purification.

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[1] T. Ogawa, K. Ohta, T. Iijima, T. Suzuki, S. Ohta and Y. Endo, *Bioorgan. Med. Chem.*, 2009, **17**, 1109.

[2] P. S. Fier and J. F. Hartwig, *J. Am. Chem. Soc.*, 2012, **134**, 5524.

[3] B. O. A. Tasch, D. Antovic, E. Merkul and T. J. J. Müller, *Eur. J. Org. Chem.*, 2013, 4564.

[4] G. Chen, T. Shigenari, P. Jain, Z. Zhang, Z. Jin, J. He, S. Li, C. Mapelli, M. M. Miller, M. A. Poss, P. M. Scola, K.-S. Yeung and J.-Q. Yu, *J. Am. Chem. Soc.* 2015, **137**, 3338.

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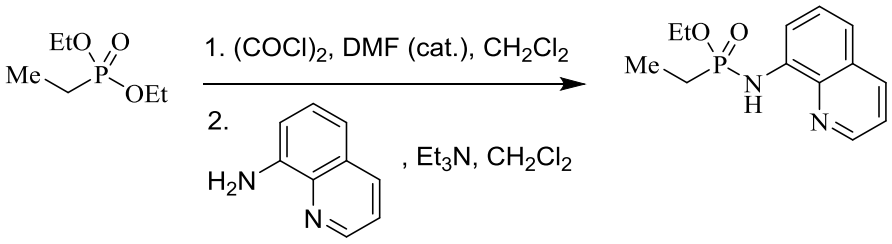
III. Synthesis of phosphonamidate and phosphonic amide starting materials

Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (1, Table 1)



A 50 mL oven-dried round bottom flask was charged diethyl ethylphosphonate (3.24 mL, 20 mmol, 1 equiv), DMF (5 drops), and CH_2Cl_2 (20 mL). The solution was kept under nitrogen and placed into an ice/water bath, followed by slow addition of oxalyl chloride (5.23 mL, 60 mmol, 3 equiv) over 5 min. The solution was kept at 0 °C for 30 min, warmed to room temperature, and stirred overnight. After completion, the crude mixture was evaporated under vacuum to remove solvent and excess oxalyl chloride. Toluene (10 mL) was added and the mixture was concentrated again.

The crude ethyl ethylphosphonochloridate was then dissolved in CH_2Cl_2 (10 mL). Resulting solution was kept under nitrogen and placed into an ice/water bath followed by slow addition of Et_3N (3.5 mL, 25 mmol, 1.25 equiv) over 5 min. The brownish solution was vigorously stirred for 30 min then warmed to room temperature for 1 h. The mixture was placed into an ice/water bath again, followed by slow addition of CH_2Cl_2 (10 mL) solution of 8-aminoquinoline (2.88 g, 20 mmol, 1 equiv) under nitrogen over 5 min. The suspension was stirred at room temperature overnight. The reaction was quenched by adding saturated aqueous NH_4Cl solution (30 mL) followed by extraction with CH_2Cl_2 (3 x 30 mL). Combined organic phase was dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (gradient hexanes/EtOAc from 1:1 to 1:2, then EtOAc:MeOH 100:1) afforded 3.71 g (70% over 2 steps) of ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate as an orange oil.

R_f = 0.25 (hexanes/EtOAc 1:1)

^{1}H NMR (600 MHz, $CDCl_3$, ppm) δ 8.77 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.10 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.34 (d, *J* = 8.1 Hz,

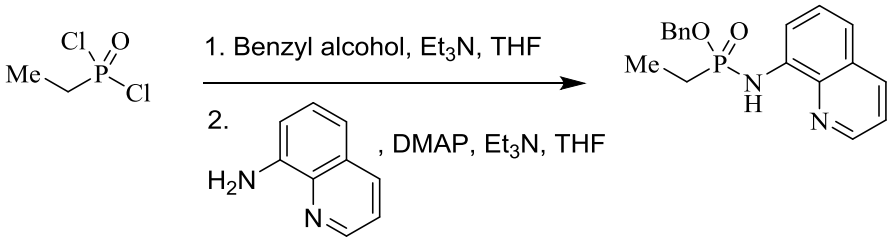
1H), 4.26 (dp, *J* = 10.1, 7.2 Hz, 1H), 4.09 (dp, *J* = 10.1, 7.2 Hz, 1H), 2.04 – 1.90 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.16 (dt, *J* = 20.2, 7.7 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, ppm) δ 148.2, 138.6 (d, J_{C-P} = 7.8 Hz), 138.0, 136.3, 128.6, 127.3, 121.9, 119.2, 111.8, 60.5 (d, J_{C-P} = 7.2 Hz), 19.7 (d, J_{C-P} = 131.1 Hz), 16.5 (d, J_{C-P} = 6.4 Hz), 6.4 (d, J_{C-P} = 5.8 Hz).

^{31}P NMR (243 MHz, $CDCl_3$, ppm) δ 32.6.

HR-MS (ESI) calcd. for $C_{13}H_{17}N_2O_2P$ $[M+H]^+$ 265.1100; found: 265.1103.

Benzyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (3, Scheme 2)



In a 100 mL flame-dried Schlenk flask, ethylphosphonic dichloride (1.0 mL, 9.86 mmol, 1 equiv) was dissolved in THF (10 mL). The solution was placed into an ice/water bath, followed by slow addition of a THF (10 mL) solution of benzyl alcohol (1.0 mL, 10 mmol, 1.01 equiv) and Et_3N (1.4 mL, 10 mmol, 1.01 equiv) via cannula. The resulting mixture was vigorously stirred at 0 °C for 30 min then warmed to room temperature and stirred for 6 h. Precipitate appeared during stirring.

The suspension was then placed back into an ice/water bath, followed by slow addition of a THF (10 mL) solution of 8-aminoquinoline (2.16 g, 15 mmol, 1.52 equiv), 4-dimethylaminopyridine (122 mg, 1 mmol, 10 mol%), and Et_3N (2.8 mL, 20 mmol, 2.03 equiv) via cannula over 15 min. Resulting mixture was warmed to room temperature and stirred overnight. The reaction was quenched by adding saturated aqueous NH_4Cl solution (30 mL) followed by extraction with CH_2Cl_2 (3 x 30 mL). Combined organic phase was dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (gradient hexanes/EtOAc 3:1 to 2:3) afforded 1.1 g (34%) of benzyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate as a light yellow oil.

R_f = 0.34 (hexanes/EtOAc 1:1)

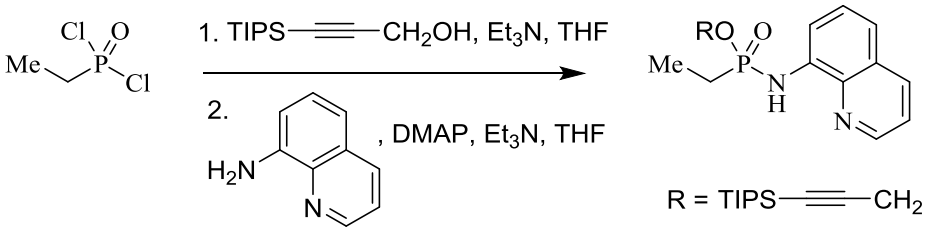
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.50 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.47 – 7.27 (m, 8H), 5.26 (dd, *J* = 12.1, 7.0 Hz, 1H), 5.07 – 4.97 (m, 1H), 2.11 – 1.95 (m, 2H), 1.30 – 1.12 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.2, 138.6 (d, J_{C-P} = 8.1 Hz), 137.7, 136.3, 128.6, 128.4, 128.3, 128.0, 127.2, 122.0, 119.4, 112.0, 65.9 (d, J_{C-P} = 6.6 Hz), 19.8 (d, J_{C-P} = 130.2 Hz), 6.5 (d, J_{C-P} = 5.8 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 33.4.

HR-MS (ESI) calcd. for $C_{18}H_{19}N_2O_2P$ $[M+H]^+$ 327.1257; found: 327.1257.

3-(Triisopropylsilyl)prop-2-yn-1-yl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (5, Scheme 2)



In a 100 mL flame-dried Schlenk flask, ethylphosphonic dichloride (1.0 mL, 9.86 mmol, 1 equiv) was dissolved in THF (10 mL). The solution was placed into an ice/water bath, followed by slow addition of a THF (10 mL) solution of 3-(triisopropylsilyl)prop-2-yn-1-ol (2.12 g, 10 mmol, 1.01 equiv) and Et_3N (1.4 mL, 10 mmol, 1.01 equiv) via cannula. The resulting mixture was vigorously stirred at 0 °C for 30 min then warmed to room temperature and stirred for 6 h. Precipitate appeared during stirring.

The suspension was then placed back into an ice/water bath, followed by slow addition of a THF (10 mL) solution of 8-aminoquinoline (2.16 g, 15 mmol, 1.52 equiv), 4-dimethylaminopyridine (122 mg, 1 mmol, 10 mol%), and Et_3N (2.8 mL, 20 mmol, 2.03 equiv) via cannula over 15 min. Resulting mixture was warmed to room temperature and stirred overnight. The reaction was quenched by adding saturated aqueous NH_4Cl solution (30 mL) followed by extraction with

CH_2Cl_2 (3 x 30 mL). Combined organic phase was dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (gradient hexanes/EtOAc 4:1 to 1:1) afforded 2.06 g (49%) of an orange oil.

R_f = 0.66 (hexanes/EtOAc 1:1)

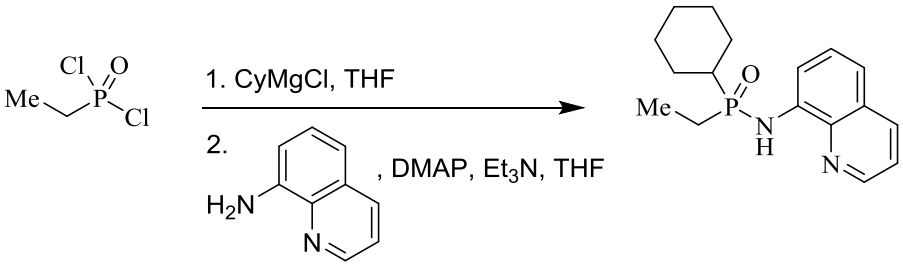
^{1}H NMR (600 MHz, $CDCl_3$, ppm) δ 8.75 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.10 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.68 (d, *J* = 9.3 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.34 (d, *J* = 8.1 Hz, 1H), 4.80 (qd, *J* = 15.8, 9.3 Hz, 2H), 2.07 – 1.96 (m, 2H), 1.17 (dt, *J* = 20.5, 7.6 Hz, 3H), 1.01 – 0.94 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.2, 138.7 (d, J_{C-P} = 8.1 Hz), 137.5, 136.2, 128.5, 127.3, 121.9, 119.4, 112.4, 101.3 (d, J_{C-P} = 7.4 Hz), 89.0, 52.7 (d, J_{C-P} = 6.0 Hz), 19.7 (d, J_{C-P} = 129.0 Hz), 18.5, 11.1, 6.4 (d, J_{C-P} = 5.9 Hz).

^{31}P NMR (243 MHz, $CDCl_3$, ppm) δ 34.2.

HR-MS (ESI) calcd. for $C_{23}H_{35}N_2O_2PSi$ $[M+H]^+$ 431.2278; found: 431.2284.

***P*-Cyclohexyl-*P*-ethyl-*N*-(quinolin-8-yl)phosphinic amide (7, Scheme 2)**



In a 100 mL flame-dried Schlenk flask, ethylphosphonic dichloride (1.0 mL, 9.86 mmol, 1 equiv) was dissolved in THF (10 mL). The solution was placed into a dry ice/acetone bath, followed by slow addition of cyclohexylmagnesium chloride (2 M Et_2O solution, 5 mL, 10 mmol, 1 equiv) via syringe over 5 min. The mixture was warmed to room temperature and stirred overnight. The flask was then placed into an ice/water bath, followed by slow addition of a THF (10 mL) solution of 8-aminoquinoline (2.16 g, 15 mmol, 1.52 equiv), 4-dimethylaminopyridine (122 mg, 1 mmol, 10 mol%), and Et_3N (2.8 mL, 20 mmol, 2.03 equiv) via cannula over 15 min.

Resulting mixture was warmed to room temperature and stirred overnight. The reaction was quenched by adding saturated aqueous NH_4Cl solution (30 mL) followed by extraction with CH_2Cl_2 (3 x 30 mL). Combined organic phase was dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (gradient hexanes/EtOAc 1:1 to 1:2, then EtOAc:MeOH 100:1) afforded 356 mg (12%) of a dark brown oil.

R_f = 0.38 (EtOAc/MeOH 100:1)

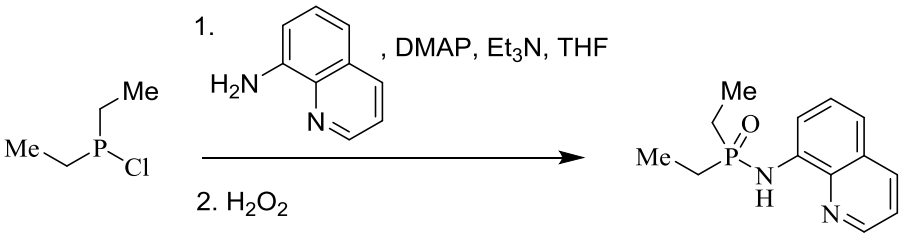
^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.73 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.82 – 7.75 (m, 1H), 7.43 – 7.36 (m, 2H), 7.33 – 7.23 (m, 2H, overlapping with $CHCl_3$ signal), 2.13 – 2.04 (m, 1H), 2.04 – 1.90 (m, 4H), 1.87 – 1.75 (m, 2H), 1.69 (bs, 1H), 1.51 – 1.46 (m, 1H), 1.47 – 1.38 (m, 1H), 1.33 – 1.17 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 147.8, 139.1, 138.7 (d, $J_{C\text{-}P}$ = 6.2 Hz), 136.4, 128.5, 127.5, 121.6, 118.7, 113.0, 37.9 (d, $J_{C\text{-}P}$ = 85.2 Hz), 26.4 (d, $J_{C\text{-}P}$ = 13.8 Hz), 25.9 (d, $J_{C\text{-}P}$ = 15.3 Hz), 25.8, 19.4 (d, $J_{C\text{-}P}$ = 82.6 Hz), 6.3 (d, $J_{C\text{-}P}$ = 5.4 Hz).

^{31}P NMR (202 MHz, $CDCl_3$, ppm) δ 46.7.

HR-MS (ESI) calcd. for $C_{17}H_{23}N_2O_2P$ $[M+H]^+$ 303.1621; found: 303.1620.

***P,P*-Diethyl-*N*-(quinolin-8-yl)phosphinic amide (9, Scheme 2)**



In a 100 mL flame-dried Schlenk flask, 8-aminoquinoline (1.56 g, 10.8 mmol, 1.5 equiv), 4-dimethylaminopyridine (44 mg, 0.36 mmol, 5 mol%), and triethylamine (2 mL, 14.5 mmol, 2 equiv) were dissolved in THF (15 mL). The solution was placed in a dry ice/acetone bath followed by slow addition of a THF (15 mL) solution of chlorodiethylphosphine (1 g, 7.23 mmol, 1 equiv) via cannula over 15 min. The mixture was vigorously stirred at -78 °C for 1 h, then warmed to room temperature and stirred overnight. The suspension was then placed into an

ice/water bath followed by slow addition of H_2O_2 (30% aqueous solution, 1 mL, 9.8 mmol, 1.35 equiv) under air over 5 min. The mixture was stirred at 0 °C for 15 min then warmed to room temperature and stirred for 30 min. The reaction was quenched by adding saturated aqueous NH_4Cl solution (30 mL) followed by extraction with CH_2Cl_2 (3 x 30 mL). Combined organic phase was dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (EtOAc then EtOAc/MeOH 10:1) afforded 1.76 g (98%) of a dark brown oil which slowly solidifies under air.

R_f = 0.16 (EtOAc/MeOH 100:1)

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.73 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.36 – 7.27 (m, 2H), 2.06 – 1.93 (m, 4H), 1.21 (dt, *J* = 18.0, 7.7 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 147.9, 138.7 (d, J_{C-P} = 8.7 Hz), 136.4, 128.6, 127.5, 121.7, 119.0, 112.8, 21.1 (d, J_{C-P} = 85.1 Hz), 6.5 (d, J_{C-P} = 4.7 Hz). One carbon signal could not be located.

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 45.5.

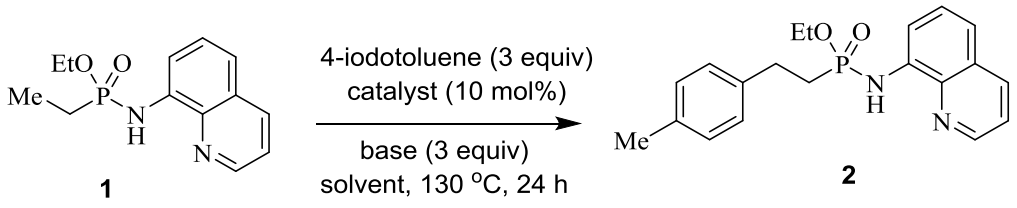
HR-MS (ESI) calcd. for $C_{13}H_{17}N_2OP$ $[M+H]^+$ 249.1151; found: 249.1155.

IV. Optimization of Phosphonamidate Arylation

General procedure for optimization experiments

A 1-dram screw cap vial equipped with a stir bar was charged with ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (26 mg, 0.1 mmol, 1 equiv), 4-iodotoluene (65 mg, 0.3 mmol, 3 equiv), catalyst (0.01 mmol, 10 mol%), base (0.3 mmol, 3 equiv), and solvent (0.5 mL). The vial was placed into a preheated oil bath (130 °C) for 24 h. The reaction was cooled to room temperature and diluted with ethyl acetate (5 mL). The resulting solution was filtered through a short plug of Celite® in ethyl acetate and concentrated under vacuum. Yields were determined by ^{1}H NMR using 1,1,2-trichloroethane internal standard.

Table S1. Optimization conditions of phosphonamidate arylation



Entry	catalyst	base	solvent	Yield of **2**, %[a]
1	$Pd(OAc)_2$	Cs_3PO_4	toluene	45
2	$Pd(OAc)_2$	Cs_3PO_4	1,2-dichlorobenzene	60
3	$Pd(OAc)_2$	Cs_3PO_4	*tert*-butylbenzene	55
4	$Pd(OAc)_2$	Cs_3PO_4	1,2-dichlorobenzene	50[b]
5	$Pd(OTFA)_2$	Cs_3PO_4	1,2-dichlorobenzene	10
6	$PdCl_2$	Cs_3PO_4	1,2-dichlorobenzene	no reaction
7	$Pd(OAc)_2$	AgOAc	1,2-dichlorobenzene	no reaction
8	$Pd(OAc)_2$	Cs_3PO_4	1,2-dichlorobenzene	73[c]
9	$Pd(OAc)_2$	Cs_3PO_4	1,2-dichlorobenzene	36[c,d]
10	none	Cs_3PO_4	1,2-dichlorobenzene	no reaction
11	$Pd(OAc)_2$	none	1,2-dichlorobenzene	no reaction

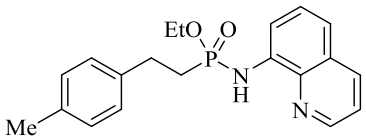
[a] ^{1}H NMR yields. [b] Temperature: 110 °C. [c] CsOAc (9.6 mg, 0.05 mmol, 50 mol%) was added. [d] 4-iodotoluene (1 equiv) was used.

V. Palladium-catalyzed arylation of phosphonamidate/phosphinic amide sp^3 C-H bonds and characterization of products

General procedure for palladium-catalyzed sp^3 C-H arylation (except substrate 9, Scheme 2)

A 2-dram screw cap vial equipped with a stir bar was charged with phosphonamidate or phosphinic amide (0.5-0.7 mmol), aryl iodide (3 equiv), $Pd(OAc)_2$ (10 mol%), and 1,2-dichlorobenzene (2.5 mL). The vial was flushed with nitrogen, capped, and placed inside a glovebox. To this mixture was added Cs_3PO_4 (3 equiv) and CsOAc (50 mol%) (no CsOAc was used for entry 6, Table 2). The sealed vial was taken out of the glovebox, stirred at room temperature for 5 min, and placed into a preheated oil bath for an appropriate time. The reaction was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was filtered through a short plug of Celite® in ethyl acetate and concentrated under vacuum. Purification by column chromatography on silica gel using appropriate eluent followed by concentrating the fraction of product and drying the residue under vacuum yielded pure product.

Ethyl *P*-(4-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 1)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 4-iodotoluene (327 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 3:1), 125 mg (71%) of a brown oil was obtained.

R_f = 0.20 (toluene/EtOAc 2:1).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.50 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.45 – f7.39 (m, 2H), 7.35 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.98 (s, 4H), 4.37 – 4.23 (m, 1H), 4.19 – 4.07 (m, 1H), 3.06 – 2.83 (m, 2H), 2.36 – 2.21 (m, 5H), 1.37 (t, *J* = 7.1 Hz, 3H).

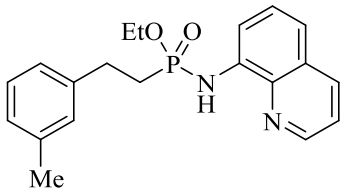
^{13}C NMR (101 MHz, $CDCl_3$, ppm) two C-P couplings could not be resolved, peaks are listed: δ 148.2, 138.6 (d, J_{C-P} = 8.2 Hz), 138.0, 137.9 (d, J_{C-P} = 17.8 Hz), 136.3, 135.7, 129.2, 128.6,

127.9, 127.2, 121.9, 119.3, 111.8, 60.6 (d, J_{C-P} = 6.9 Hz), 29.1, 27.90, 27.86, 27.84, 21.1, 16.5 (d, J_{C-P} = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.8.

HR-MS (ESI) calcd. for $C_{20}H_{23}N_2O_2P$ $[M+H]^+$ 355.1570; found: 355.1570.

Ethyl *P*-(3-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 2)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 3-iodotoluene (327 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 3:1), 112 mg (63%) of a colorless oil was obtained.

R_f = 0.23 (toluene/EtOAc 2:1).

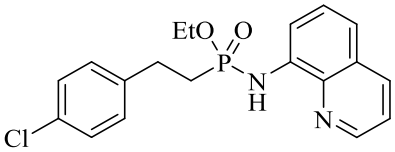
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.51 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.35 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 3H), 4.30 (dp, *J* = 10.2, 7.2 Hz, 1H), 4.23 – 4.06 (m, 1H), 3.04 – 2.81 (m, 2H), 2.35 – 2.24 (m, 2H), 2.21 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.2, 140.90 (d, J_{C-P} = 17.5 Hz), 138.6 (d, J_{C-P} = 8.3 Hz), 138.1, 137.8, 136.3, 128.9, 128.6, 128.4, 127.2, 127.0, 125.1, 122.0, 119.4, 111.8, 60.6 (d, J_{C-P} = 6.9 Hz), 28.4 (d, J_{C-P} = 128.2 Hz), 28.24 (d, J_{C-P} = 3.5 Hz), 21.4, 16.5 (d, J_{C-P} = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.7.

HR-MS (ESI) calcd. for $C_{20}H_{23}N_2O_2P$ $[M+H]^+$ 355.1570; found: 355.1564.

Ethyl *P*-(4-chlorophenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 3)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 1-chloro-4-iodobenzene (358 mg, 1.5 mmol, 3

equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 2:1), 101 mg (54%) of a brown oil was obtained.

R_f = 0.20 (toluene/EtOAc 2:1).

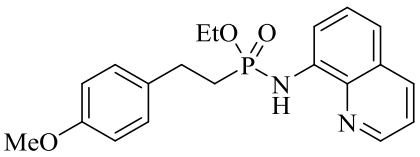
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.75 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.46 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.35 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.09 – 7.04 (m, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 4.28 (dp, *J* = 10.2, 7.1 Hz, 1H), 4.17 – 4.05 (m, 1H), 3.04 – 2.81 (m, 1H), 2.26 (dt, *J* = 16.7, 8.3 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.2, 139.2 (d, J_{C-P} = 16.2 Hz), 138.5 (d, J_{C-P} = 8.2 Hz), 137.6, 136.3, 131.9, 129.5, 128.5, 127.2, 122.0, 119.4, 111.7, 60.7 (d, J_{C-P} = 6.9 Hz), 28.0 (d, J_{C-P} = 129.1 Hz), 27.8 (d, J_{C-P} = 3.3 Hz), 16.5 (d, J_{C-P} = 6.6 Hz). One carbon signal could not be located.

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.2.

HR-MS (ESI) calcd. for $C_{19}H_{20}ClN_2O_2P$ $[M+H]^+$ 375.1024; found: 375.1023.

Ethyl *P*-(4-methoxyphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 4)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 4-iodoanisole (351 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 2:1), 126 mg (68%) of a brown oil was obtained.

R_f = 0.17 (toluene/EtOAc 2:1).

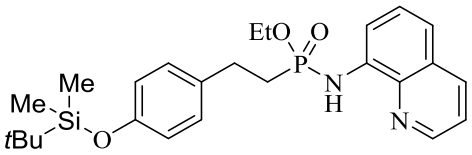
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.76 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.63 (d, *J* = 8.7 Hz, 1H), 7.49 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.35 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.73 – 6.63 (m, 2H), 4.34 – 4.22 (m, 1H), 4.17 – 4.04 (m, 1H), 3.70 (s, 3H), 3.02 – 2.81 (m, 2H), 2.32 – 2.21 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 158.0, 148.2, 138.6 (d, J_{C-P} = 8.2 Hz), 137.8, 136.2, 133.0 (d, *J* = 17.5 Hz), 129.0, 128.6, 127.2, 121.9, 119.3, 113.8, 111.8, 60.59 (d, J_{C-P} = 6.9 Hz), 55.3, 28.6 (d, J_{C-P} = 127.3 Hz), 27.5 (d, J_{C-P} = 3.5 Hz), 16.5 (d, J_{C-P} = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.7.

HR-MS (ESI) calcd. for $C_{20}H_{23}N_2O_3P$ $[M+H]^+$ 371.1519; found: 371.1513.

Ethyl *P*-(4-((*tert*-butyldimethylsilyl)oxy)phenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 5)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), *tert*-butyl(4-iodophenoxy)dimethylsilane (571 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 2:1), 105 mg (45%) of a reddish oil was obtained.

R_f = 0.22 (toluene/EtOAc 2:1).

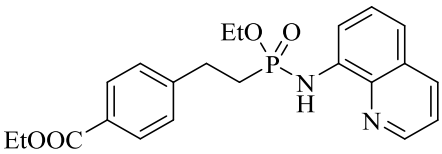
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.51 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.35 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.70 – 6.61 (m, 2H), 4.28 (dp, *J* = 10.2, 7.1 Hz, 1H), 4.17 – 4.00 (m, 1H), 3.00 – 2.79 (m, 2H), 2.33 – 2.20 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 0.94 (s, 9H), 0.12 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 154.0, 148.2, 138.6 (d, J_{C-P} = 8.0 Hz), 137.8, 136.3, 133.7 (d, J_{C-P} = 18.2 Hz), 129.0, 128.6, 127.2, 121.9, 120.1, 119.3, 111.8, 60.6 (d, J_{C-P} = 6.8 Hz), 28.67 (d, J_{C-P} = 127.2 Hz), 27.54 (d, J_{C-P} = 3.3 Hz), 25.8, 18.3, 16.5 (d, J_{C-P} = 6.7 Hz), -4.4.

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.8.

HR-MS (ESI) calcd. for $C_{25}H_{35}N_2O_3PSi$ $[M+H]^+$ 471.2227; found: 471.2237.

Ethyl 4-(2-(ethoxy(quinolin-8-ylamino)phosphoryl)ethyl)benzoate (Table 2, Entry 6)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), ethyl 4-iodobenzoate (414 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient hexanes/EtOAc from 2:1 to 1:3), 128 mg (62%) of a brown oil was obtained.

R_f = 0.14 (toluene/EtOAc 2:1).

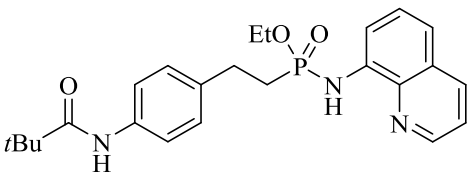
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.73 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.46 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.34 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 4.38 – 4.23 (m, 3H), 4.18 – 4.05 (m, 1H), 3.11 – 2.91 (m, 2H), 2.30 (dt, *J* = 16.7, 8.3 Hz, 2H), 1.35 (td, *J* = 7.1, 3.4 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 166.5, 148.2, 146.1 (d, J_{C-P} = 15.9 Hz), 138.5 (d, J_{C-P} = 8.1 Hz), 137.6, 136.2, 129.7, 128.6, 128.4, 128.1, 127.2, 122.0, 119.5, 111.7, 60.9, 60.7 (d, J_{C-P} = 6.8 Hz), 28.40 (d, J_{C-P} = 3.4 Hz), 27.7 (d, J_{C-P} = 129.6 Hz), 16.5 (d, J_{C-P} = 6.6 Hz), 14.4.

^{31}P NMR (243 MHz, $CDCl_3$, ppm) δ 29.0.

HR-MS (ESI) calcd. for $C_{22}H_{25}N_2O_4P$ $[M+H]^+$ 413.1625; found: 413.1631.

Ethyl *P*-(4-pivalamidophenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 7)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), *N*-(4-iodophenyl)pivalamide (455 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv),

CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient Et_2O/MeOH from 200:1 to 50:1), 154 mg (70%) of a light yellow oil was obtained.

R_f = 0.23 (Et_2O/MeOH 100:1).

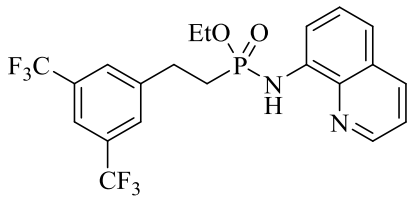
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.47 (d, *J* = 6.5 Hz, 2H), 7.43 – 7.37 (m, 2H), 7.37 – 7.30 (m, 3H), 7.00 (d, *J* = 8.4 Hz, 2H), 4.25 (dp, *J* = 10.1, 7.2 Hz, 1H), 4.09 (dp, *J* = 10.2, 7.2 Hz, 1H), 3.00 – 2.78 (m, 2H), 2.34 – 2.17 (m, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.26 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 176.7, 148.2, 138.5 (d, J_{C-P} = 8.3 Hz), 137.6, 136.6 (d, J_{C-P} = 17.6 Hz), 136.4, 136.3, 128.6, 128.4, 127.2, 121.9, 120.3, 119.4, 111.8, 60.6 (d, J_{C-P} = 6.9 Hz), 39.6, 29.0, 27.7, 16.5 (d, J_{C-P} = 6.5 Hz). One carbon signal and two C-P couplings could not be assigned.

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.6.

HR-MS (ESI) calcd. for $C_{24}H_{30}N_3O_3P$ $[M+H]^+$ 462.1917; found: 462.1922.

Ethyl *P*-(3,5-bis(trifluoromethyl)phenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 8)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 3,5-bis(trifluoromethyl)iodobenzene (510 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 2:1), 138 mg (58%) of an orange oil was obtained.

R_f = 0.47 (toluene/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.60 (d, *J* = 8.9 Hz, 1H), 7.54 (s, 3H), 7.48 – 7.39 (m, 3H), 7.36 (dd, *J* = 7.9, 1.7 Hz, 1H),

4.29 (dp, *J* = 10.2, 7.2 Hz, 1H), 4.19 – 4.06 (m, 1H), 3.22 – 3.00 (m, 2H), 2.43 – 2.26 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H).

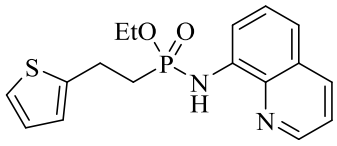
^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.3, 143.2 (d, J_{C-P} = 14.8 Hz), 138.4 (d, J_{C-P} = 8.4 Hz), 137.2 136.3, 131.6 (q, J_{C-F} = 33.2 Hz), 128.6, 128.4, 127.1, 123.2 (q, J_{C-F} = 274.1 Hz), 122.0, 120.3, 119.7, 111.6, 60.8 (d, J_{C-P} = 6.9 Hz), 28.2 (d, J_{C-P} = 3.0 Hz), 27.5 (d, J_{C-P} = 129.9 Hz), 16.4 (d, J_{C-P} = 6.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ -62.8.

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 28.0.

HR-MS (ESI) calcd. for $C_{21}H_{19}F_6N_2O_2P$ $[M+H]^+$ 477.1161; found: 477.1161.

Ethyl *N*-(quinolin-8-yl)-*P*-(2-(thiophen-2-yl)ethyl)phosphonamidate (Table 2, Entry 9)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 2-iodothiophene (315 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 3:1), 105 mg (61%) of a brown oil was obtained.

R_f = 0.41 (toluene/EtOAc 1:1).

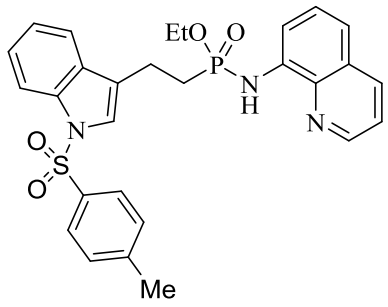
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.51 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.43 (ddd, *J* = 7.5, 5.8, 1.5 Hz, 2H), 7.36 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.03 (dd, *J* = 5.1, 1.0 Hz, 1H), 6.80 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.74 (dd, *J* = 3.5, 0.7 Hz, 1H), 4.29 (dp, *J* = 10.2, 7.2 Hz, 1H), 4.19 – 4.05 (m, 1H), 3.31 – 3.09 (m, 2H), 2.48 – 2.27 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.2, 143.8 (d, J_{C-P} = 20.6 Hz), 138.6 (d, J_{C-P} = 8.4 Hz), 137.6, 136.3, 128.6, 127.3, 126.8, 124.5, 123.5, 122.0, 119.5, 111.8, 60.7 (d, J_{C-P} = 6.8 Hz), 29.0 (d, J_{C-P} = 128.4 Hz), 22.9 (d, J_{C-P} = 2.5 Hz), 16.5 (d, J_{C-P} = 6.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 28.5.

HR-MS (ESI) calcd. for $C_{17}H_{19}N_2O_2PS$ $[M+H]^+$ 347.0978; found: 347.0973.

Ethyl *N*-(quinolin-8-yl)-*P*-(2-(1-tosyl-1*H*-indol-3-yl)ethyl)phosphonamidate (Table 2, Entry 10)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 3-iodo-1-tosyl-1*H*-indole (500 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 2:1), 171 mg (64%) of a brown oil was obtained.

R_f = 0.38 (toluene/EtOAc 1:1).

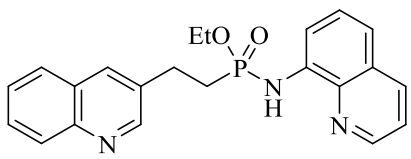
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.70 – 7.67 (m, 3H), 7.51 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.37 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.29 – 7.20 (m, 3H, overlapping with $CHCl_3$ signal), 7.18 – 7.07 (m, 3H), 4.30 (dp, *J* = 10.2, 7.2 Hz, 1H), 4.14 (dp, *J* = 10.2, 7.1 Hz, 1H), 3.12 – 2.89 (m, 2H), 2.40 – 2.30 (m, 2H), 2.28 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) One C-P coupling could not be resolved, peaks are listed. δ 148.4, 144.9, 138.6 (d, $J_{C\text{-}P}$ = 8.1 Hz), 137.6, 136.3, 135.3, 130.4, 129.9, 129.1, 128.6, 128.3, 127.2, 126.8, 124.8, 123.1, 122.7, 122.2, 122.0, 119.6, 119.3, 113.7, 111.8, 60.8 (d, $J_{C\text{-}P}$ = 6.9 Hz), 26.0 (d, $J_{C\text{-}P}$ = 129.0 Hz), 21.63, 18.1 (d, $J_{C\text{-}P}$ = 2.6 Hz), 16.5 (d, $J_{C\text{-}P}$ = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.3.

HR-MS (ESI) calcd. for $C_{28}H_{28}N_3O_4PS$ $[M+H]^+$ 534.1611; found: 534.1623.

Ethyl *P*-(2-(quinolin-3-yl)ethyl)-*N*-(quinolin-8-yl)phosphonamidate (Table 2, Entry 11)



Ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), 3-iodoquinoline (383 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5

mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient hexanes/EtOAc from 1:1 to 1:2, then EtOAc), 78 mg (40%) of a yellow oil was obtained.

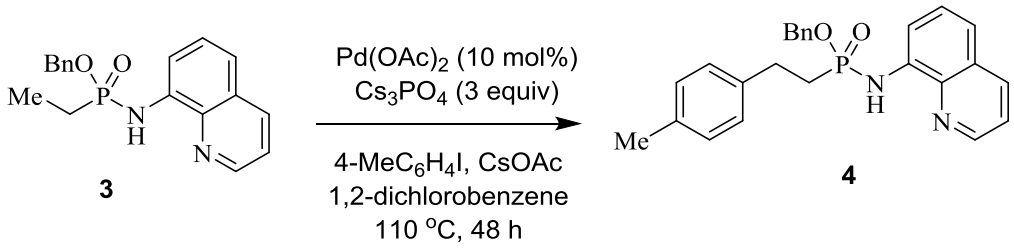
R_f = 0.17 (EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.64 (dd, *J* = 4.1, 1.7 Hz, 2H), 8.05 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 1.5 Hz, 1H), 7.67 – 7.56 (m, 3H), 7.51 – 7.30 (m, 5H), 4.39 – 4.23 (m, 1H), 4.22 – 4.04 (m, 1H), 3.29 – 3.04 (m, 2H), 2.41 (dt, *J* = 16.6, 8.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H).

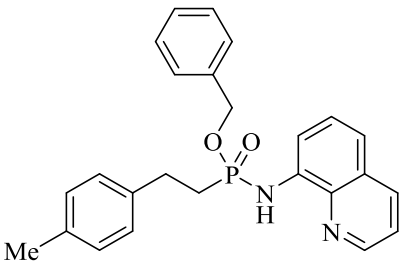
^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 151.4, 148.2, 146.8, 138.4 (d, J_{C-P} = 8.4 Hz), 137.4, 136.2, 134.3, 133.3 (d, J_{C-P} = 15.1 Hz), 129.1, 128.9, 128.5, 127.9, 127.4, 127.1, 126.7, 122.0, 119.6, 111.7, 60.8 (d, J_{C-P} = 6.9 Hz), 27.5 (d, J_{C-P} = 129.0 Hz), 25.9 (d, J_{C-P} = 3.3 Hz), 16.5 (d, J_{C-P} = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 28.7.

HR-MS (ESI) calcd. for $C_{22}H_{22}N_3O_2P$ $[M+H]^+$ 392.1522; found: 392.1523.



Benzyl *P*-(4-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (4, Scheme 2)



Benzyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (163 mg, 0.5 mmol), 4-iodotoluene (327 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 110 °C, 48 h. After column chromatography (gradient toluene/EtOAc from 20:1 to 10:1), 125 mg (60%) of an orange oil was obtained.

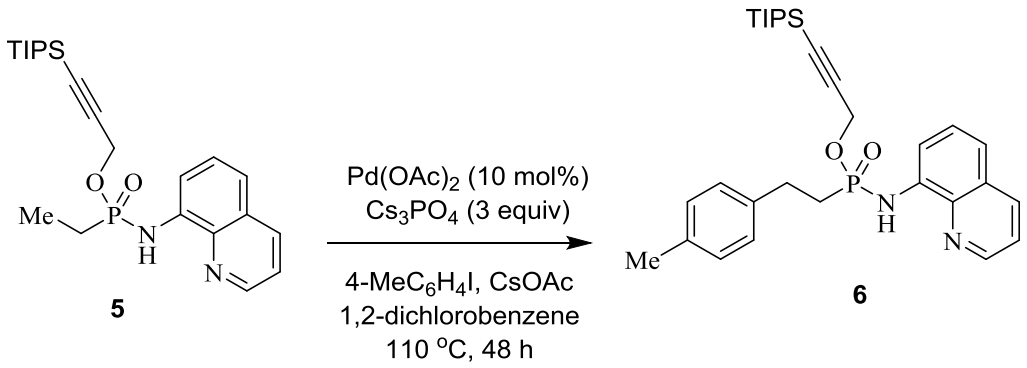
R_f = 0.2 (toluene/EtOAc 4:1)

^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.78 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.50 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.44 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.41 – 7.31 (m, 7H), 5.28 (dd, *J* = 11.7, 7.5 Hz, 1H), 5.03 (dd, *J* = 11.7, 7.0 Hz, 1H), 3.04 – 2.96 (m, 1H), 2.96 – 2.86 (m, 1H), 2.39 – 2.29 (m, 2H), 2.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 148.2, 138.6 (d, J_{C-P} = 8.0 Hz), 137.7 (d, J_{C-P} = 17.4 Hz), 137.5, 136.3, 135.8, 129.2, 128.7, 128.6, 128.5, 128.3, 128.0, 127.2, 122.0, 119.5, 112.0, 66.0 (d, J_{C-P} = 6.9 Hz), 28.6 (d, J_{C-P} = 126.7 Hz), 27.9 (d, J_{C-P} = 3.0 Hz), 21.1.

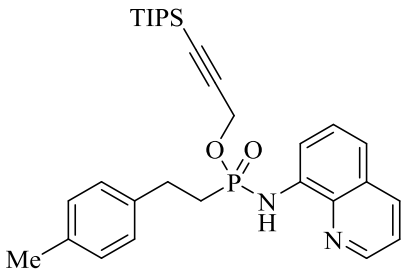
^{31}P NMR (202 MHz, $CDCl_3$, ppm) δ 30.5.

HR-MS (ESI) calcd. for $C_{25}H_{25}N_2O_2P$ $[M+H]^+$ 417.1726; found: 417.1734.



3-(Triisopropylsilyl)prop-2-yn-1-yl *P*-(4-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (6, Scheme 2)

3-(Triisopropylsilyl)prop-2-yn-1-yl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (215 mg, 0.5 mmol), 4-iodotoluene (327 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 110 °C, 48 h. After column chromatography (gradient toluene/EtOAc from 20:1 to 10:1), 114 mg (44%) of an orange oil was obtained.



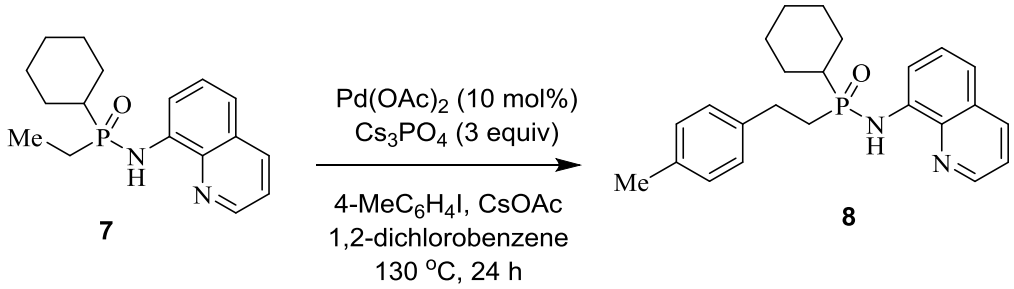
R_f = 0.23 (toluene/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.71 (d, *J* = 9.4 Hz, 1H), 7.57 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.45 – 7.34 (m, 3H), 6.97 (s, 4H), 4.93 – 4.75 (m, 2H), 3.04 – 2.82 (m, 2H), 2.41 – 2.26 (m, 2H), 2.22 (s, 3H), 0.97 (d, *J* = 3.7 Hz, 21H).

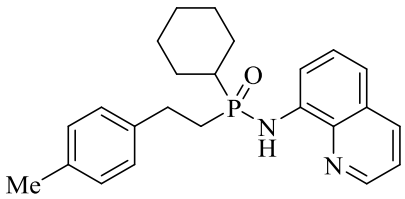
^{13}C NMR (101 MHz, $CDCl_3$, ppm) Two C-P couplings could not be resolved, peaks are listed: δ 148.1, 138.7 (d, J_{C-P} = 8.2 Hz), 137.7 (d, J_{C-P} = 17.8 Hz), 137.3, 136.2, 135.8, 129.2, 128.5, 127.9, 127.3, 121.9, 119.6, 112.5, 101.20 (d, J_{C-P} = 7.6 Hz), 89.2, 52.8 (d, J_{C-P} = 6.1 Hz), 29.1, 27.80, 27.78, 27.75, 21.0, 18.6, 11.1.

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 31.3.

HR-MS (ESI) calcd. for $C_{30}H_{41}N_2O_2PSi$ $[M+H]^+$ 521.2748; found: 521.2754.



_P_-Cyclohexyl-_P_-(4-methylphenethyl)-_N_-(quinolin-8-yl)phosphinic amide (8, Scheme 2)



P-Cyclohexyl-*P*-ethyl-*N*-(quinolin-8-yl)phosphinic amide (211 mg, 0.7 mmol), 4-iodotoluene (458 mg, 2.1 mmol, 3 equiv), $Pd(OAc)_2$ (16 mg, 0.07 mmol, 10 mol%), Cs_3PO_4 (1.04 g, 2.1 mmol, 3 equiv), CsOAc (67 mg, 0.35 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 2:1), 170 mg (62%) of a brown oil was obtained.

R_f = 0.18 (toluene/EtOAc 2:1)

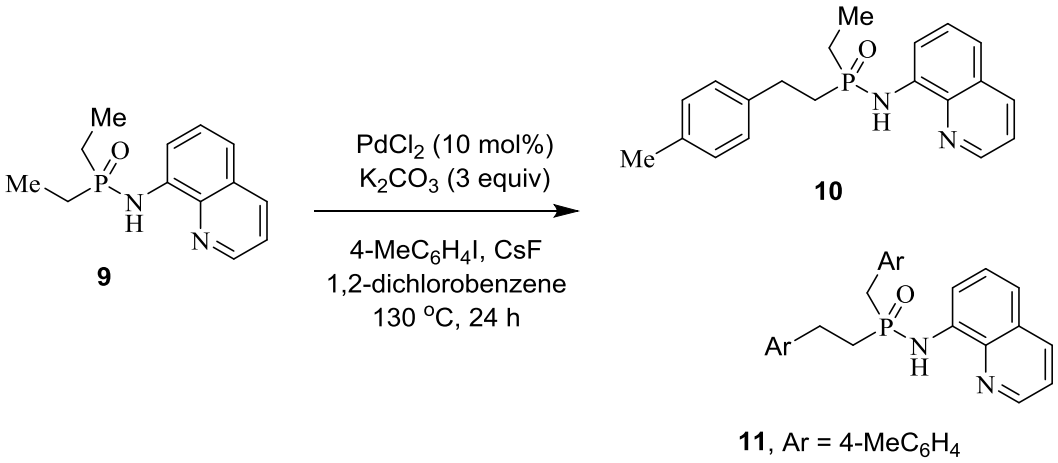
^{1}H NMR (600 MHz, $CDCl_3$, ppm) δ 8.75 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.11 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.32 (dd, *J* = 10.8, 6.2 Hz, 2H), 7.07 (dd, *J* = 8.0, 2.0 Hz, 4H), 3.05 – 2.88 (m, 2H), 2.28 (s, 3H), 2.27 – 2.20 (m, 2H), 2.09 (dd, *J* = 15.7, 5.8

Hz, 1H), 2.07 – 1.99 (m, 1H), 2.00 – 1.91 (m, 1H), 1.89 – 1.79 (m, 2H, overlapping with H_2O signal), 1.70 (bs, 1H), 1.55 – 1.47 (m, 1H), 1.47 – 1.39 (m, 1H), 1.31 – 1.18 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) One C-P coupling could not be resolved, peaks are listed: δ 147.9, 139.0, 138.8 (d, J_{C-P} = 6.2 Hz), 138.2 (d, J_{C-P} = 14.5 Hz), 136.5, 135.9, 129.3, 128.6, 128.0, 127.6, 121.7, 118.9, 113.1, 38.6 (d, J_{C-P} = 85.3 Hz), 28.6 (d, J_{C-P} = 79.0 Hz), 27.66, 27.62, 26.4 (d, J_{C-P} = 14.2 Hz), 25.9 (d, J_{C-P} = 6.1 Hz), 21.1.

^{31}P NMR (243 MHz, $CDCl_3$, ppm) δ 44.4.

HR-MS (ESI) calcd. for $C_{24}H_{29}N_2OP$ $[M+H]^+$ 393.2090; found: 393.2097.

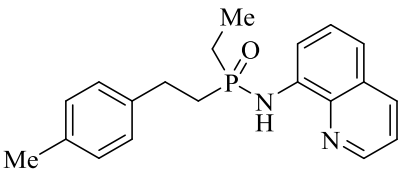


_P_-Ethyl-_P_-(4-methylphenethyl)-_N_-(quinolin-8-yl)phosphinic amide (10) and _P,P_-bis(4-methylphenethyl)-_N_-(quinolin-8-yl)phosphinic amide (11) (Scheme 2)

A 1-dram screw cap vial equipped with a stir bar was charged with *P,P*-diethyl-*N*-(quinolin-8-yl)phosphinic amide (124 mg, 0.5 mmol), 4-iodotoluene (327 mg, 1.5 mmol, 3 equiv), $PdCl_2$ (9 mg, 0.05 mmol, 10 mol%), K_2CO_3 (207 mg, 1.5 mmol, 3 equiv), and 1,2-dichlorobenzene (0.5 mL). The vial was flushed with nitrogen, capped, and placed inside a glovebox. To this mixture was added CsF (38 mg, 0.25 mmol, 50 mol%). The sealed vial was taken out of the glovebox, stirred at room temperature for 5 min, and placed into a preheated oil bath (130 °C) for 24 h. The reaction was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was filtered through a short plug of Celite® in ethyl acetate and concentrated under vacuum. Purification by column chromatography on silica gel (gradient MeOH in EtOAc from 0

to 3%) afforded 57 mg (27%) of *P*,*P*-bis(4-methylphenethyl)-*N*-(quinolin-8-yl)phosphinic amide as a brown oil and 83 mg (49%) of *P*-ethyl-*P*-(4-methylphenethyl)-*N*-(quinolin-8-yl)phosphinic amide as a brown oil.

_P_-Ethyl-_P_-(4-methylphenethyl)-_N_-(quinolin-8-yl)phosphinic amide (10, Scheme 2)



R_f = 0.43 (EtOAc/MeOH 100:1)

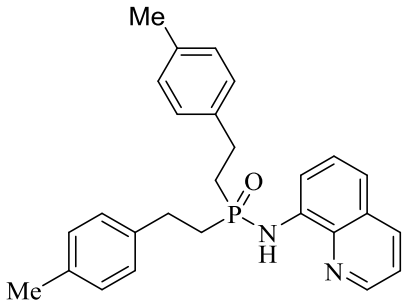
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.11 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.45 – 7.33 (m, 4H), 7.10 – 7.03 (m, 4H), 2.96 (dd, *J* = 17.7, 8.7 Hz, 2H), 2.38 – 2.22 (m, 5H), 1.99 (dq, *J* = 15.3, 7.7 Hz, 2H), 1.22 (dt, *J* = 18.2, 7.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.0, 138.7 (d, J_{C-P} = 6.6 Hz), 138.5, 137.9 (d, J_{C-P} = 14.5 Hz), 136.5, 136.0, 129.4, 128.6, 128.0, 127.5, 121.8, 119.2, 112.9, 30.2 (d, J_{C-P} = 81.9 Hz), 27.8 (d, J_{C-P} = 2.6 Hz), 22.0 (d, J_{C-P} = 85.0 Hz), 21.10, 6.5 (d, J_{C-P} = 4.9 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 43.2.

HR-MS (ESI) calcd. for $C_{20}H_{23}N_2OP$ $[M+H]^+$ 339.1621; found: 339.1622

_P,P_-Bis(4-ethylphenethyl)-_N_-(quinolin-8-yl)phosphinic amide (11, Scheme 2)



R_f = 0.7 (EtOAc/MeOH 100:1)

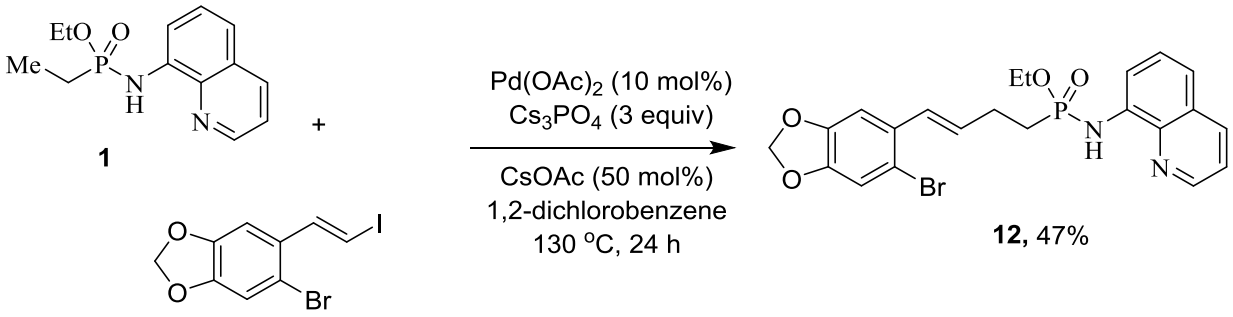
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.75 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.40 (tdd, *J* = 9.0, 8.2, 3.1 Hz, 4H), 7.05 (q, *J* = 8.2 Hz, 8H), 2.98 – 2.88 (m, 4H), 2.32 – 2.20 (m, 4H), 2.27 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.0, 138.7 (d, J_{C-P} = 6.6 Hz), 138.4, 137.8 (d, J_{C-P} = 14.3 Hz), 136.5, 136.1, 129.4, 128.6, 128.1, 127.5, 121.8, 119.3, 113.0, 31.0 (d, J_{C-P} = 81.6 Hz), 27.9 (d, J_{C-P} = 2.7 Hz), 21.1.

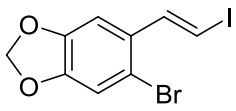
^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 40.7.

HR-MS (ESI) calcd. for $C_{27}H_{29}N_2OP$ $[M+H]^+$ 429.2090; found: 429.2098.

Scheme 3: Alkenylation of phosphonamidate 1



Synthesis of (*E*)-5-bromo-6-(2-iodovinyl)benzo[*d*][1,3]dioxole[6]



Inside glovebox, a flame-dried 100 mL Schlenk flask was charged with NaHMDS (4.4 g, 24 mmol, 3.4 equiv). Outside glovebox, THF (15 mL) was added via syringe and the mixture was stirred until a homogeneous solution was obtained. Diethyl ether (15 mL) was then added and the resulting solution was cooled to -78 °C. After 15 min, a THF (3 mL) solution of CH_2I_2 (3.21 g, 12 mmol, 1.7 equiv) was added in dark over 5 min. After 20 min, a THF (10 mL) solution of 5-bromo-6-bromomethyl-1,3-benzodioxole (2.67 g, 7 mmol, 1 equiv) was added dropwise via cannula over 10 min. After 90 min, the mixture was warmed to room temperature and stirred overnight. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (1.8 mL, 12 mmol, 1.7 equiv) was added dropwise and the suspension was stirred for an additional one hour. The reaction was diluted with Et_2O (100 mL) and filtered through a plug of Celite® in Et_2O. Solvent was removed under vacuum. Purification by column chromatography (hexanes/EtOAc 20:1) afforded 1.1g (49%) of (*E*)-5-bromo-6-(2-iodovinyl)benzo[*d*][1,3]dioxole as an off-white solid.

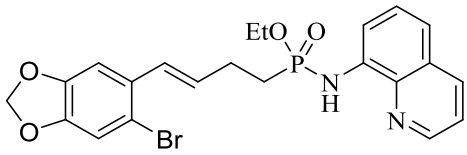
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.64 (d, *J* = 14.8 Hz, 1H), 6.97 (s, 1H), 6.86 (s, 1H), 6.67 (d, *J* = 14.9 Hz, 1H), 5.98 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.6, 147.8, 143.5, 131.1, 113.9, 112.8, 106.2, 102.1, 77.8.

HR-MS (CI) calcd. for $C_9H_6BrIO_2$ (for ^{79}Br): 351.8596; found: 351.8593.

[6] General procedure from: J. J. Mousseau, J. A. Bull and A. B. Charette, *Angew. Chem., Int. Ed.*, 2010, **49**, 1115.

Ethyl (*E*)-*P*-(4-(6-bromobenzo[*d*][1,3]dioxol-5-yl)but-3-en-1-yl)-*N*-(quinolin-8-yl)phosphonamidate (12, Scheme 3)



The general procedure for palladium-catalyzed sp^3 C-H arylation was followed: ethyl *P*-ethyl-*N*-(quinolin-8-yl)phosphonamidate (132 mg, 0.5 mmol, 1 equiv), (*E*)-5-bromo-6-(2-iodovinyl)benzo[*d*][1,3]dioxole (529 mg, 1.5 mmol, 3 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 10 mol%), Cs_3PO_4 (740 mg, 1.5 mmol, 3 equiv), CsOAc (48 mg, 0.25 mmol, 50 mol%), 1,2-dichlorobenzene (2.5 mL), 130 °C, 24 h. After column chromatography (gradient toluene/EtOAc from 4:1 to 2:1), 114 mg (47%) of a colorless oil was obtained.

R_f = 0.33 (toluene/EtOAc 2:1)

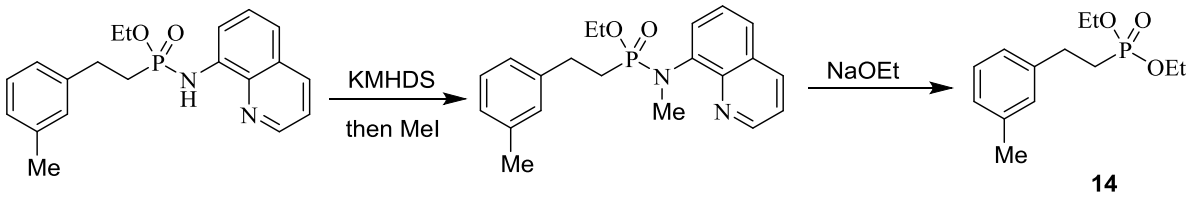
^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.74 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.57 – 7.49 (m, 1H), 7.48 – 7.31 (m, 3H), 6.90 (s, 1H), 6.70 (s, 1H), 6.59 (d, *J* = 15.6 Hz, 1H), 6.01 – 5.82 (m, 4H), 4.36 – 4.24 (m, 1H), 4.20 – 4.06 (m, 1H), 2.64 – 2.51 (m, 2H), 2.25 – 2.10 (m, 2H), 1.37 (td, *J* = 7.1, 3.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 148.2, 147.5, 138.5 (d, J_{C-P} = 8.2 Hz), 137.7, 136.2, 130.4, 130.3 (d, J_{C-P} = 15.5 Hz), 129.3, 128.6, 127.3, 121.9, 119.4, 114.1, 112.5, 111.8, 106.1, 101.7, 60.6 (d, J_{C-P} = 6.8 Hz), 26.2 (d, J_{C-P} = 129.5 Hz), 25.8 (d, J_{C-P} = 3.4 Hz), 16.5 (d, J_{C-P} = 6.7 Hz).

^{31}P NMR (162 MHz, $CDCl_3$, ppm) δ 29.9.

HR-MS (ESI) calcd. for $C_{22}H_{22}BrN_2O_4P$ $[M+H]^+$ 489.0573; found: 489.0573.

Scheme 4: Directing group removal



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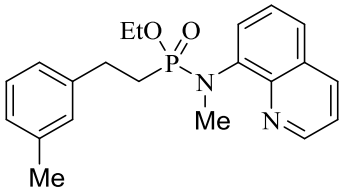
Ethyl *N*-methyl-*P*-(3-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (Scheme 4)



In a 20 mL vial, ethyl *P*-(3-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (354 mg, 1 mmol, 1 equiv) was dissolved in THF (5 mL). The vial was then placed into an ice/water bath followed by dropwise addition of a THF solution of KHMDS (1 M solution, 1.5 mL, 1.5 mmol, 1.5 equiv) via syringe. The mixture was stirred at 0 °C for 30 min, then warmed to room temperature and stirred for an additional 30 min. The vial was then placed back into the ice/water bath, followed by slow addition of methyl iodide (0.3 mL, 5 mmol, 5 equiv) over 5 min. The solution was kept at 0 °C for 2 h then warmed to room temperature and stirred for 48 h. The reaction was quenched by adding saturated aqueous solution of NH_4Cl (20 mL). The mixture was extracted with CH_2Cl_2 (3 x 20 mL). Combined organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. Purification by column chromatography (gradient hexanes/EtOAc from 2:1 to 1:2, then EtOAc) afforded 123 mg (67%) of ethyl *P*-(3-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate as a light yellow oil.

R_f = 0.23 (EtOAc 100%).

^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.90 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.14 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.68 (dt, *J* = 7.4, 1.4 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.20 – 7.13 (m, 1H), 7.00 – 6.96 (m, 3H), 4.36 – 4.21 (m, 2H), 3.32 (d, *J* = 8.2 Hz, 3H), 3.09 (tdd, *J* = 13.2, 8.6, 4.6 Hz, 1H), 2.98 – 2.87 (m, 1H), 2.37 – 2.16 (m, 5H), 1.36 (t, *J* = 7.0 Hz, 3H).

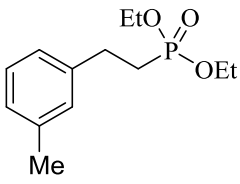
^{13}C NMR (126 MHz, $CDCl_3$, ppm) One coupling C-P could not be resolved, peaks are listed: δ 149.7 (d, J_{C-P} = 5.6 Hz), 145.9, 142.2 (d, J_{C-P} = 19.0 Hz), 141.7 (d, J_{C-P} = 2.5 Hz), 138.1, 136.4,

129.9, 129.8, 129.1, 128.5, 127.0, 126.8, 126.6, 125.2, 121.4 (d, J_{C-P} = 8.8 Hz), 59.9 (d, J_{C-P} = 7.0 Hz), 38.2, 28.8 (d, J = 129.8 Hz), 28.7, 21.5 (d, J_{C-P} = 4.6 Hz), 16.56, 16.51, 16.46.

^{31}P NMR (202 MHz, $CDCl_3$, ppm) δ 33.5.

HR-MS (ESI) calcd. for $C_{21}H_{25}N_2O_2P$ $[M+H]^+$ 369.1726; found: 369.1729.

Diethyl (3-methylphenethyl)phosphonate (14, Scheme 4)

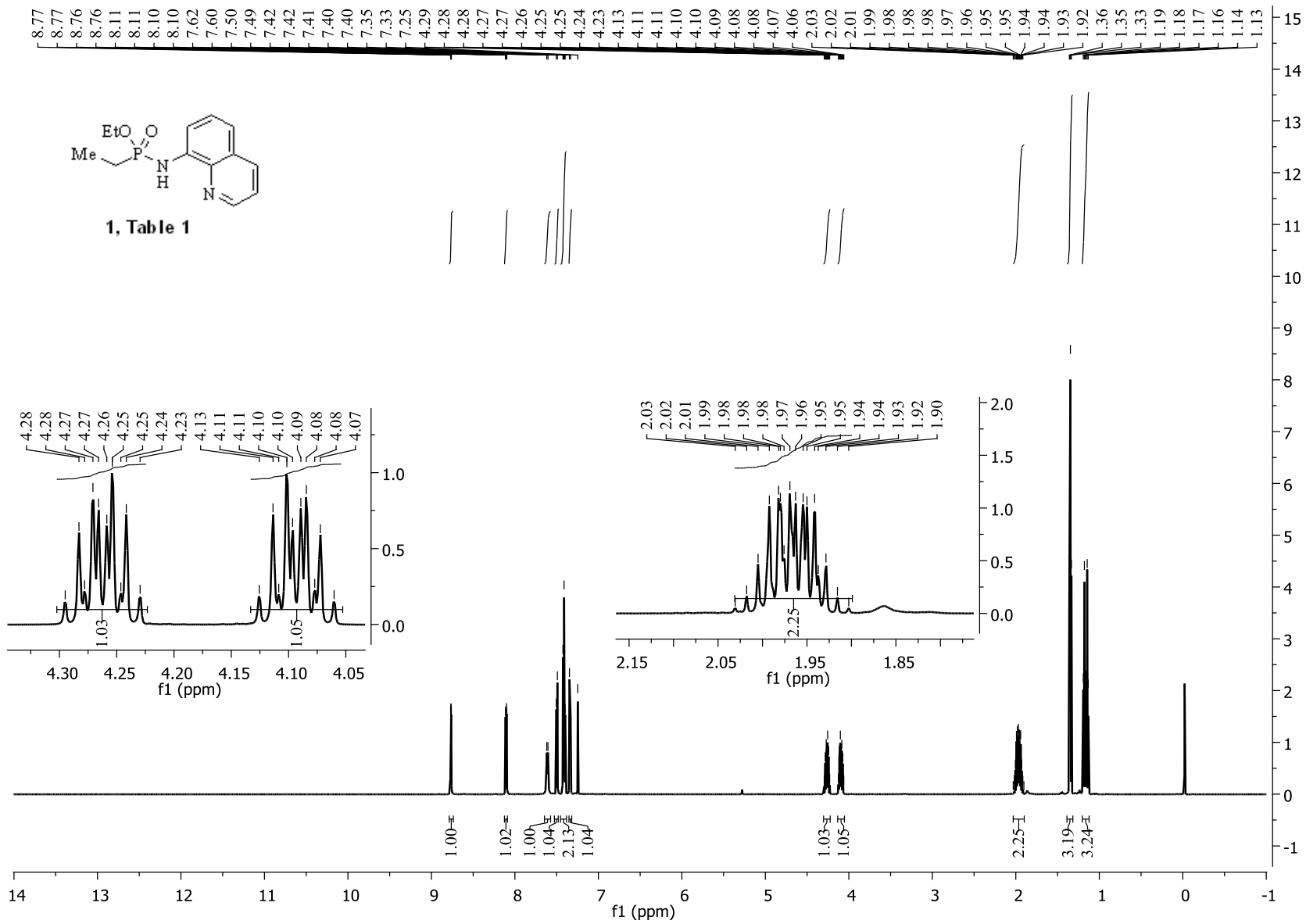


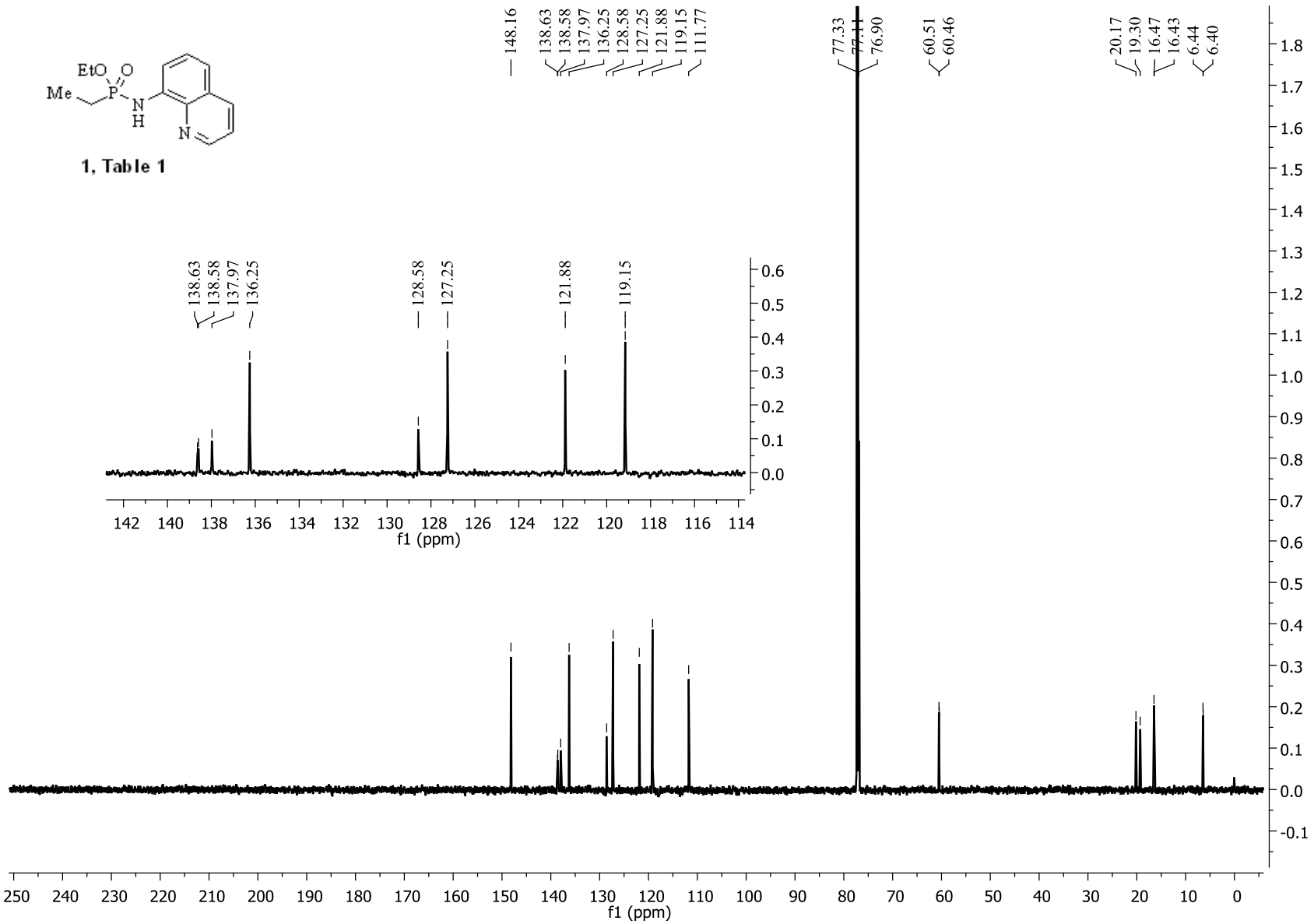
In a 20 mL vial, ethyl *P*-(3-methylphenethyl)-*N*-(quinolin-8-yl)phosphonamidate (183 mg, 0.5 mmol, 1 equiv) was dissolved in a mixture of Et_2O/EtOH (4:1 v/v, 5 mL). The vial was put inside a glovebox, and NaOEt (102 mg, 1.5 mmol) was added. The mixture was stirred at room temperature for 6 h. Reaction was quenched by adding water (20 mL) followed by extraction with EtOAc (20 mL x 3). Combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuum. Purification by column chromatography (gradient MeOH in Et_2O from 0 to 2%) afforded 102 mg (80%) of diethyl (3-methylphenethyl)phosphonate as a colorless oil. Product is visualized by $KMnO_4$ stain. This compound is known.[7]

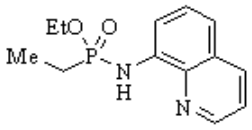
^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.16 (t, *J* = 7.4 Hz, 1H), 7.03 – 6.94 (m, 3H), 4.16 – 4.02 (m, 4H), 2.86 (dd, *J* = 17.5, 9.2 Hz, 2H), 2.30 (s, 3H), 2.07 – 1.95 (m, 2H), 1.36 – 1.24 (m, 6H).

^{31}P NMR (202 MHz, $CDCl_3$, ppm) δ 31.5.

[7] S. Kim, C.-E. Kim, B. Seo and P. H. Lee, *Org. Lett.*, 2014, **16**, 5552.







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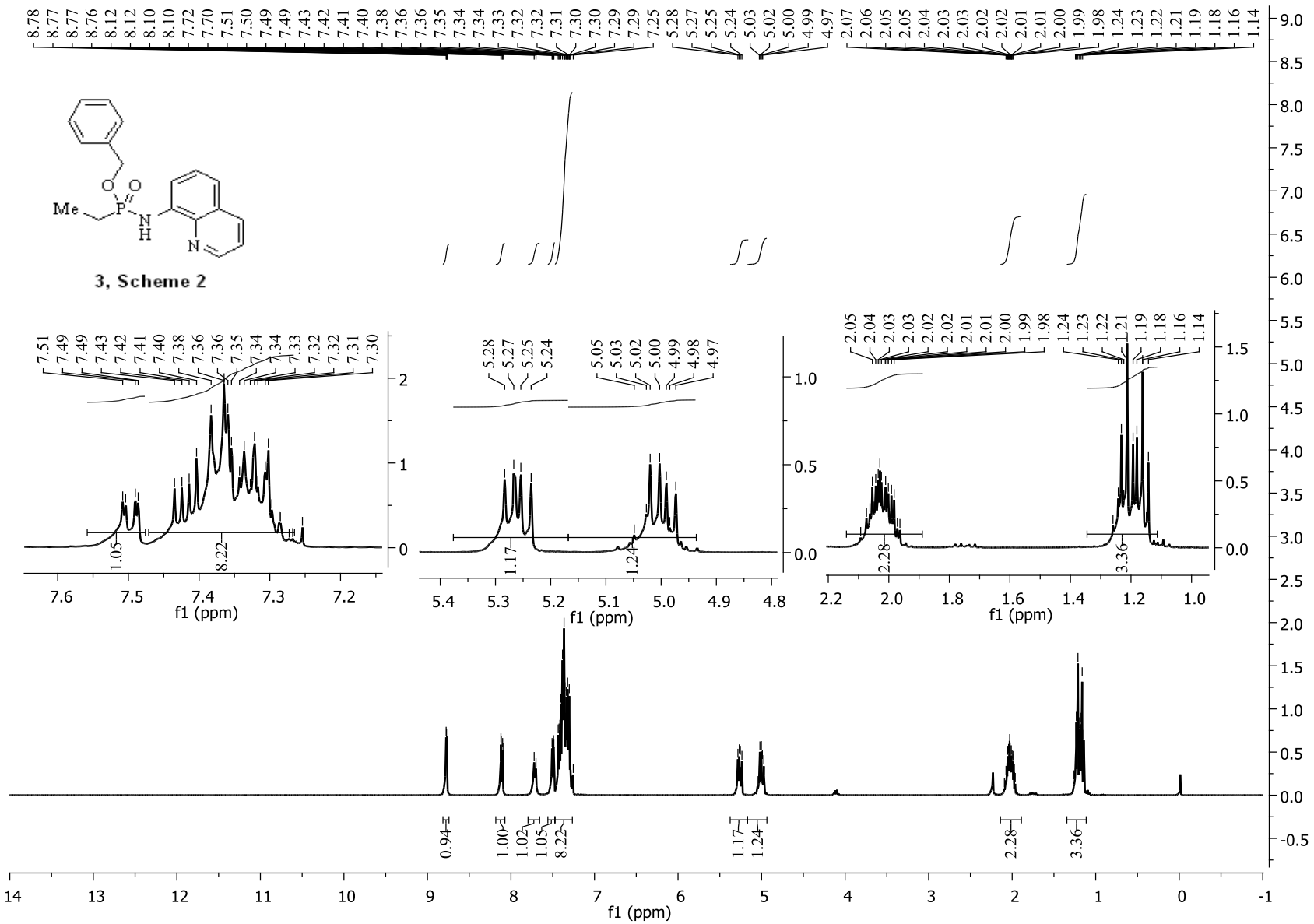
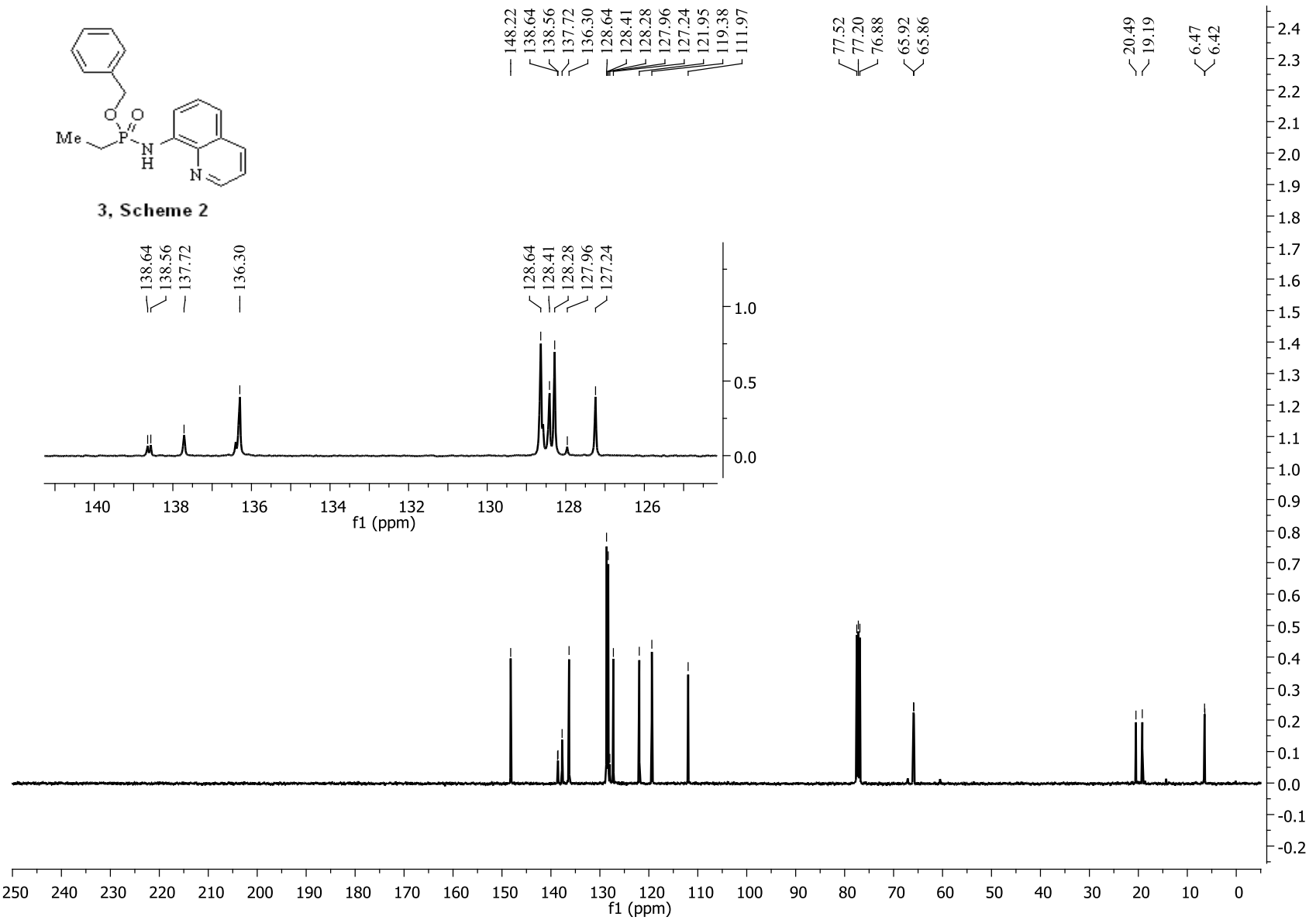
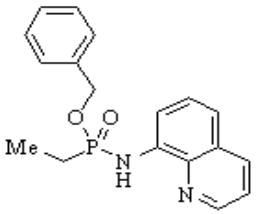
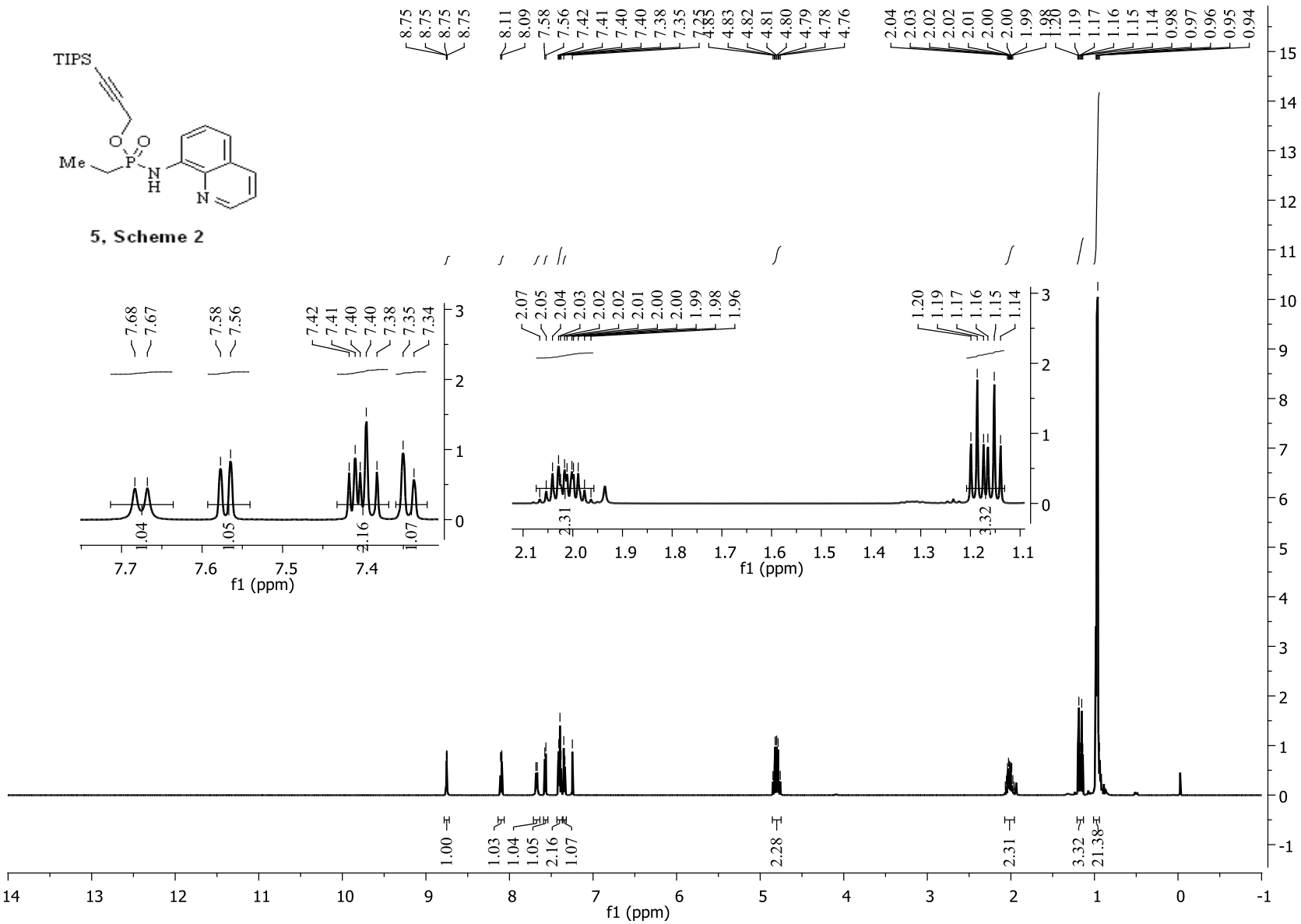
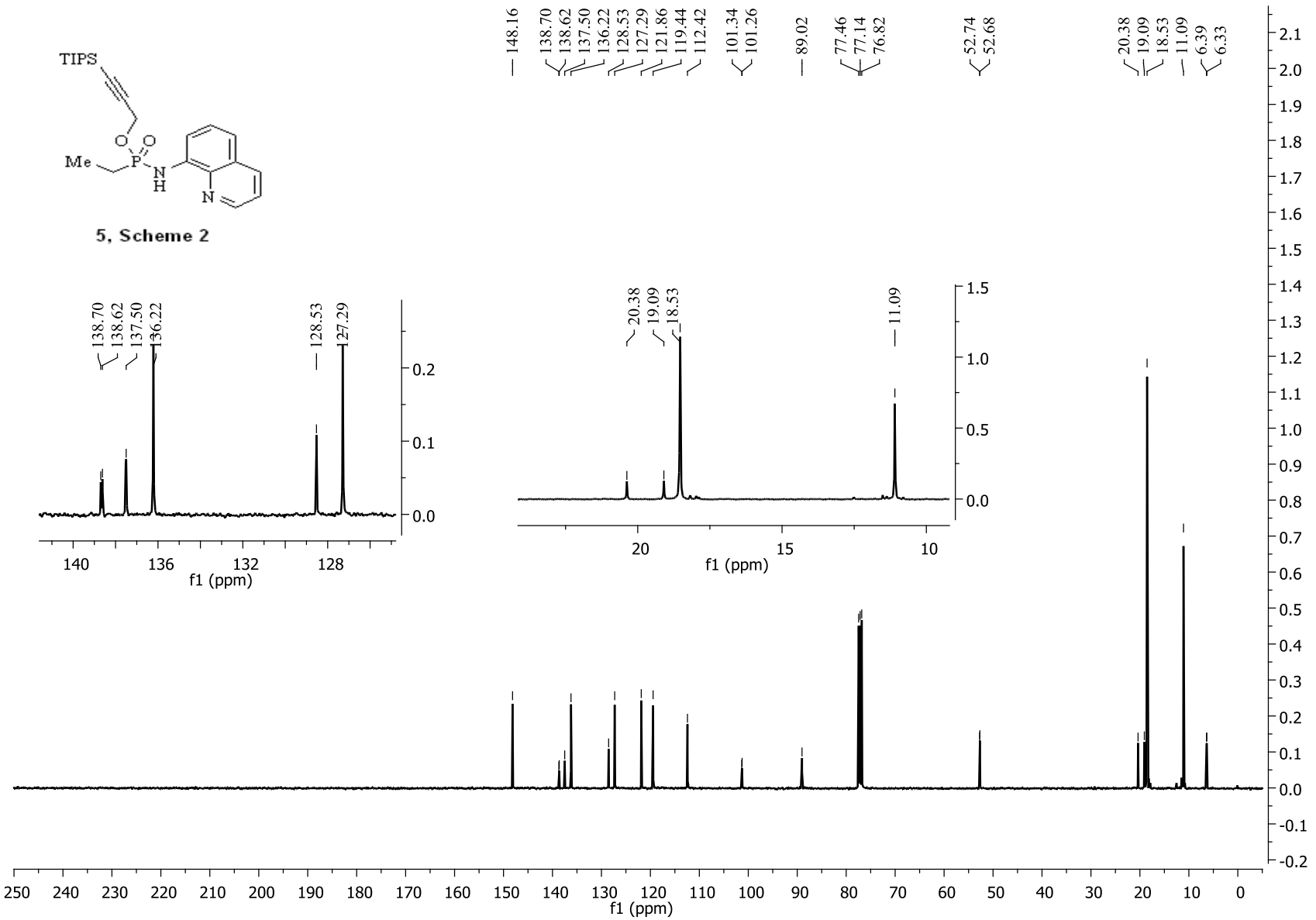


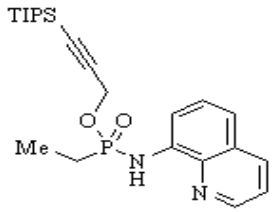




3, Scheme 2







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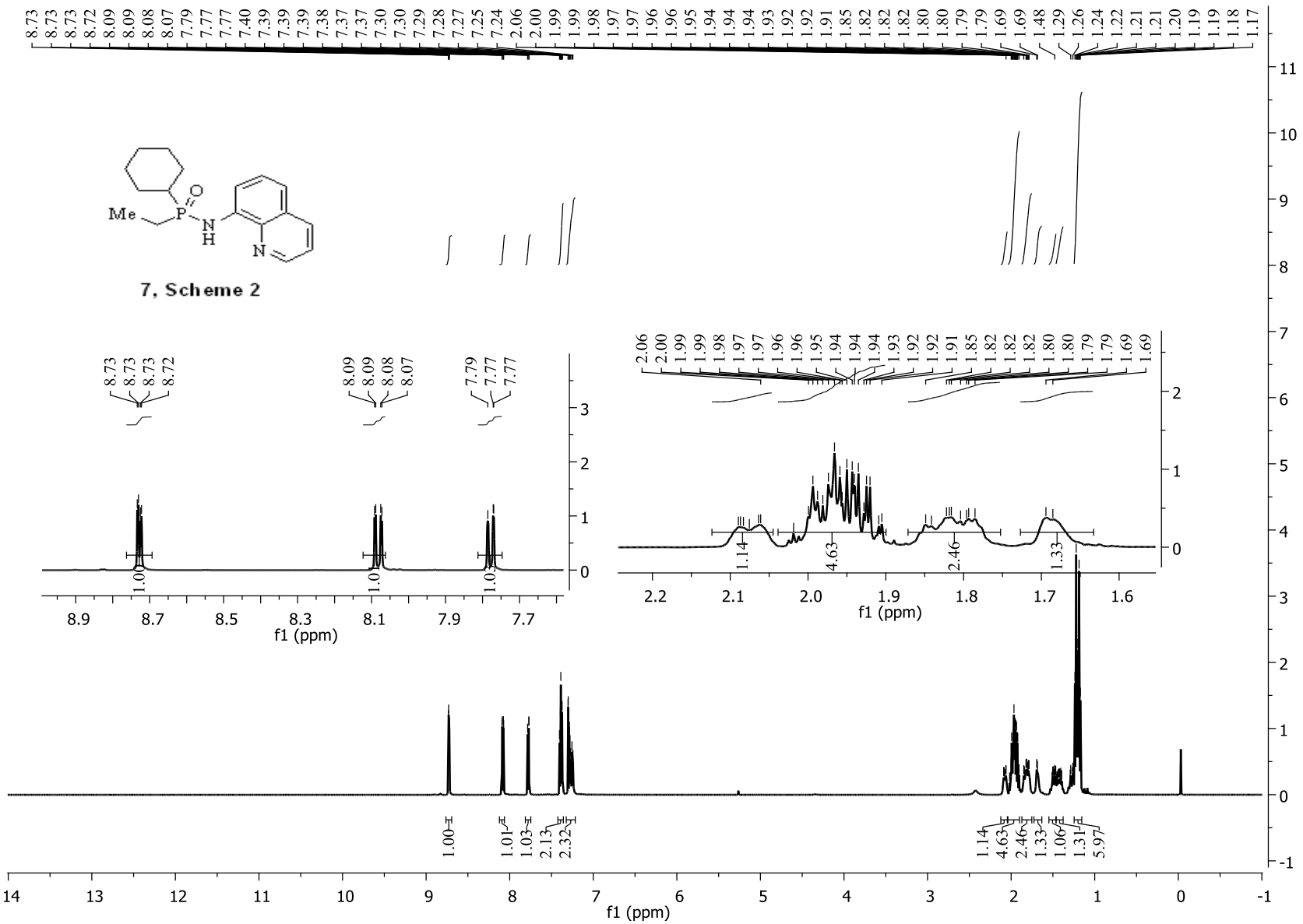
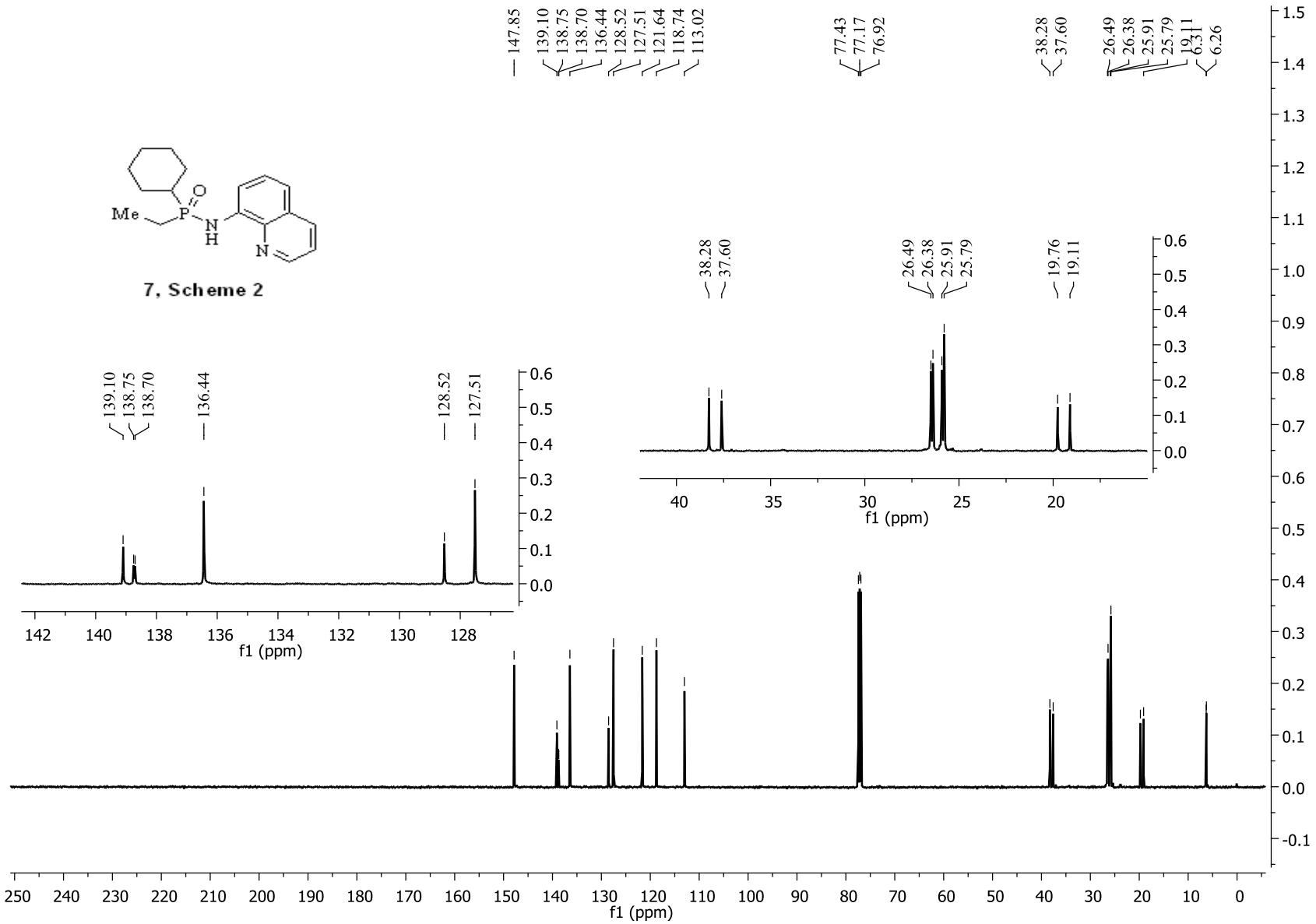
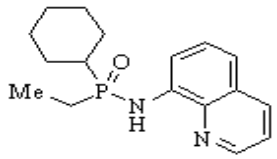
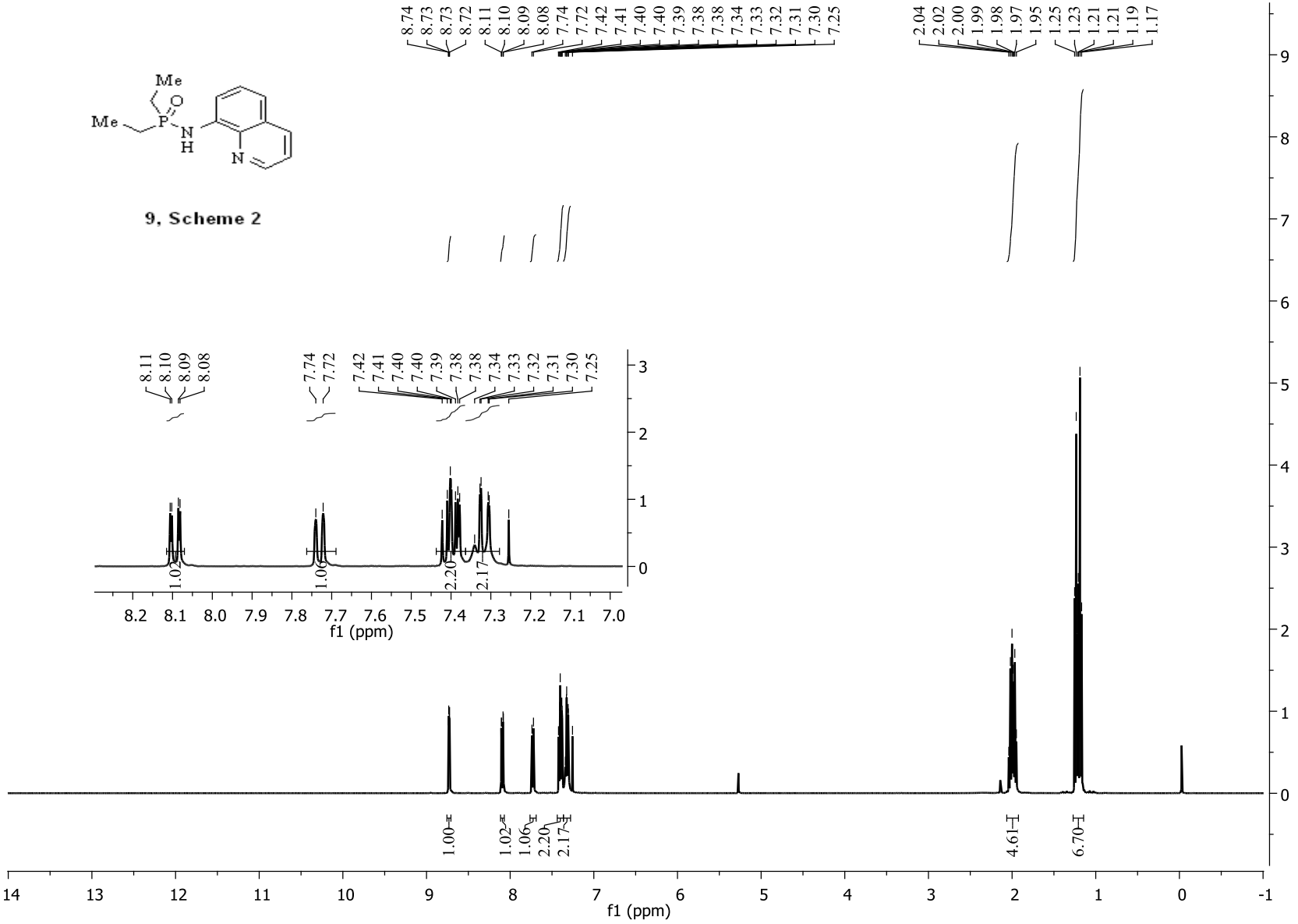
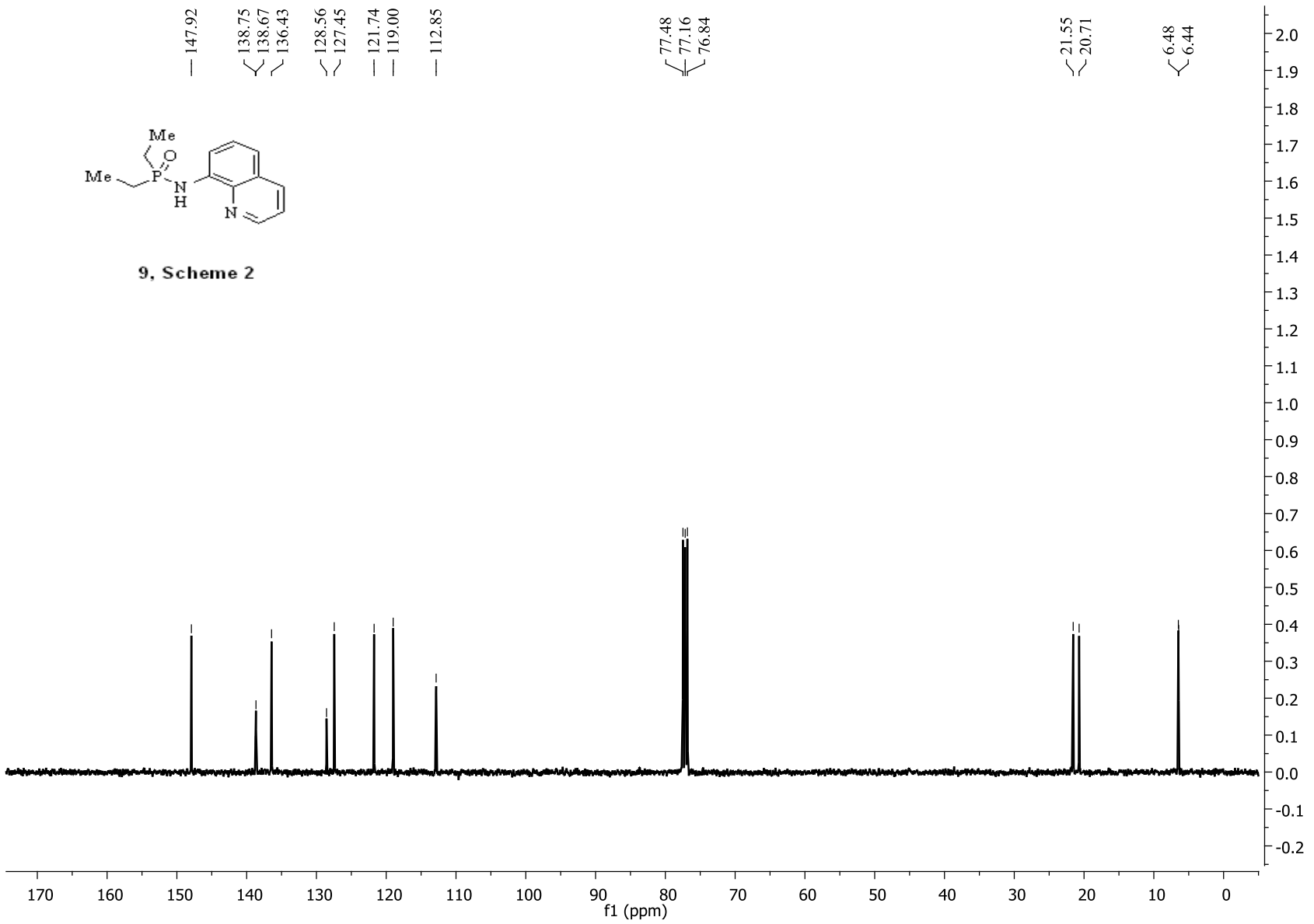


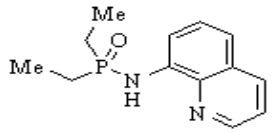




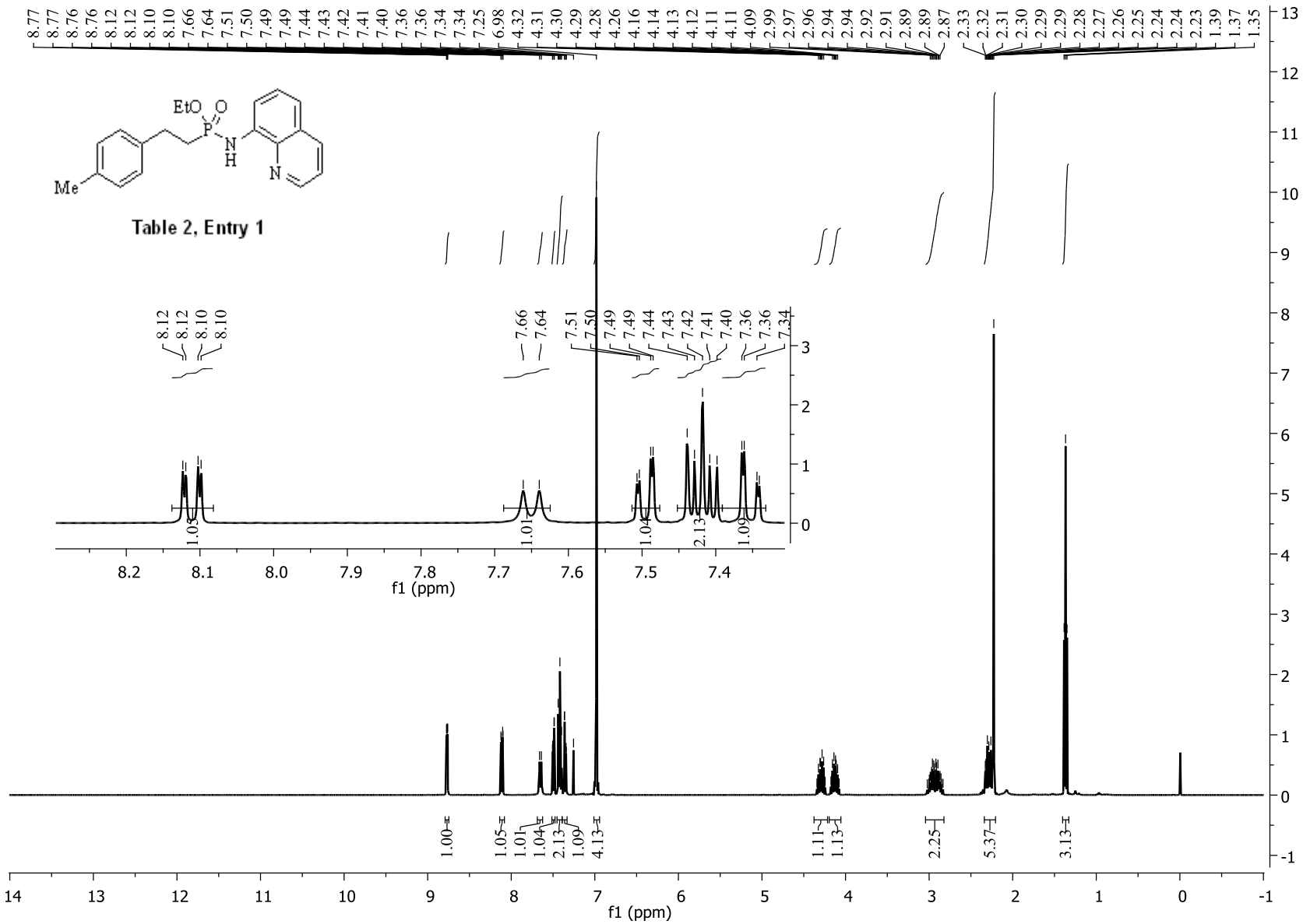
7, Scheme 2

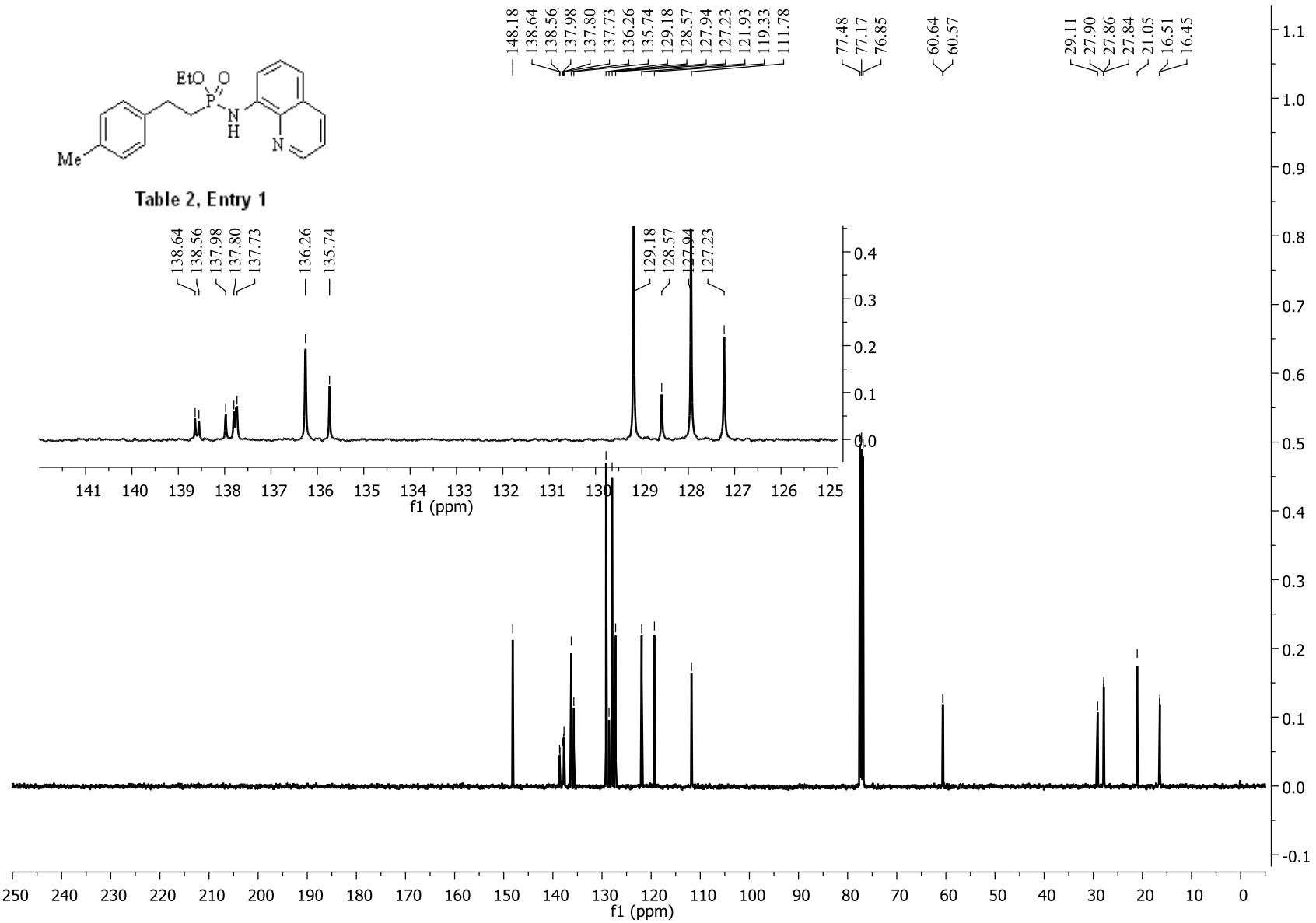


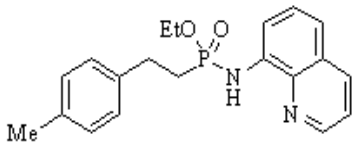




9, Scheme 2







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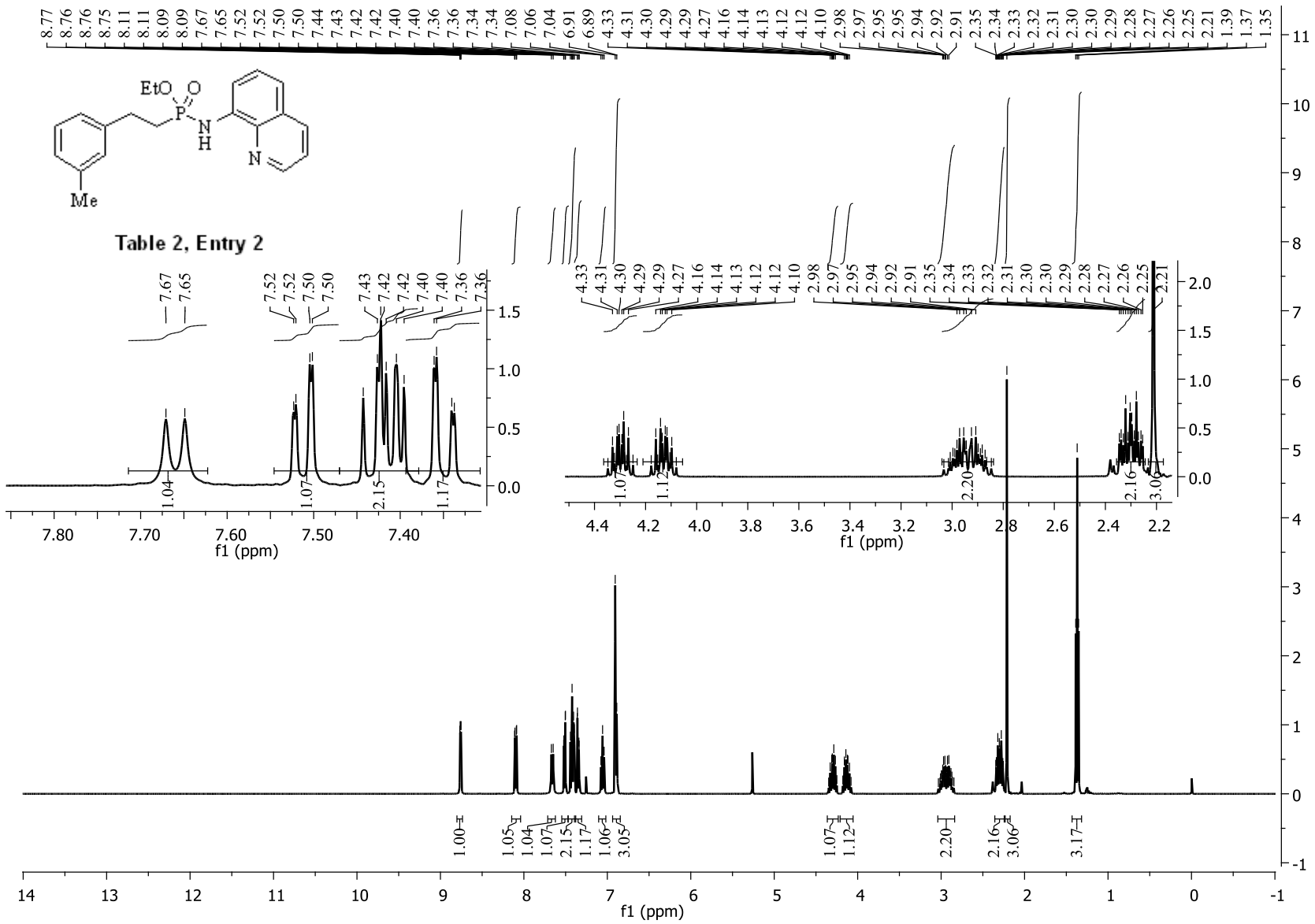

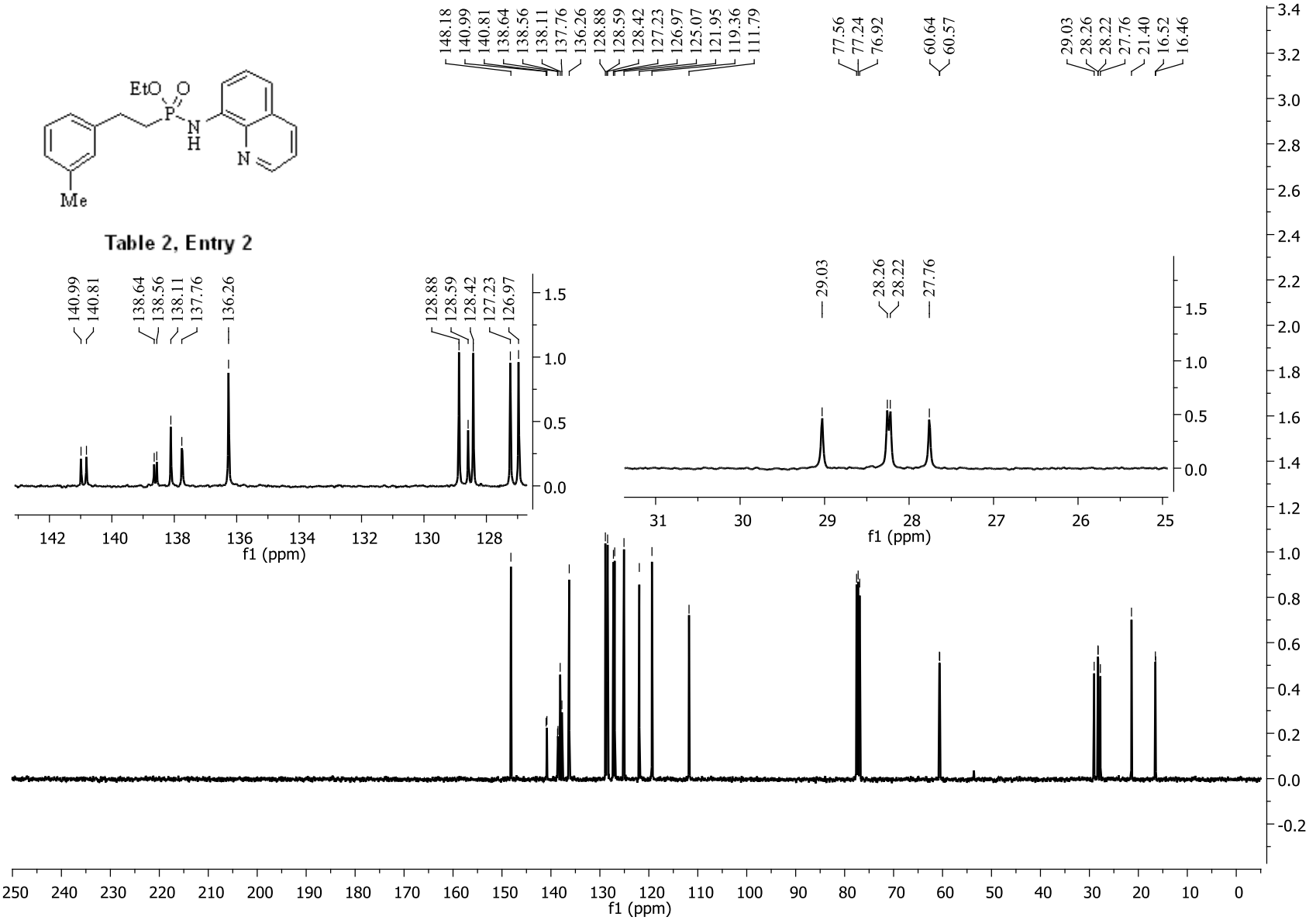

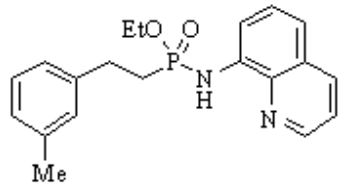

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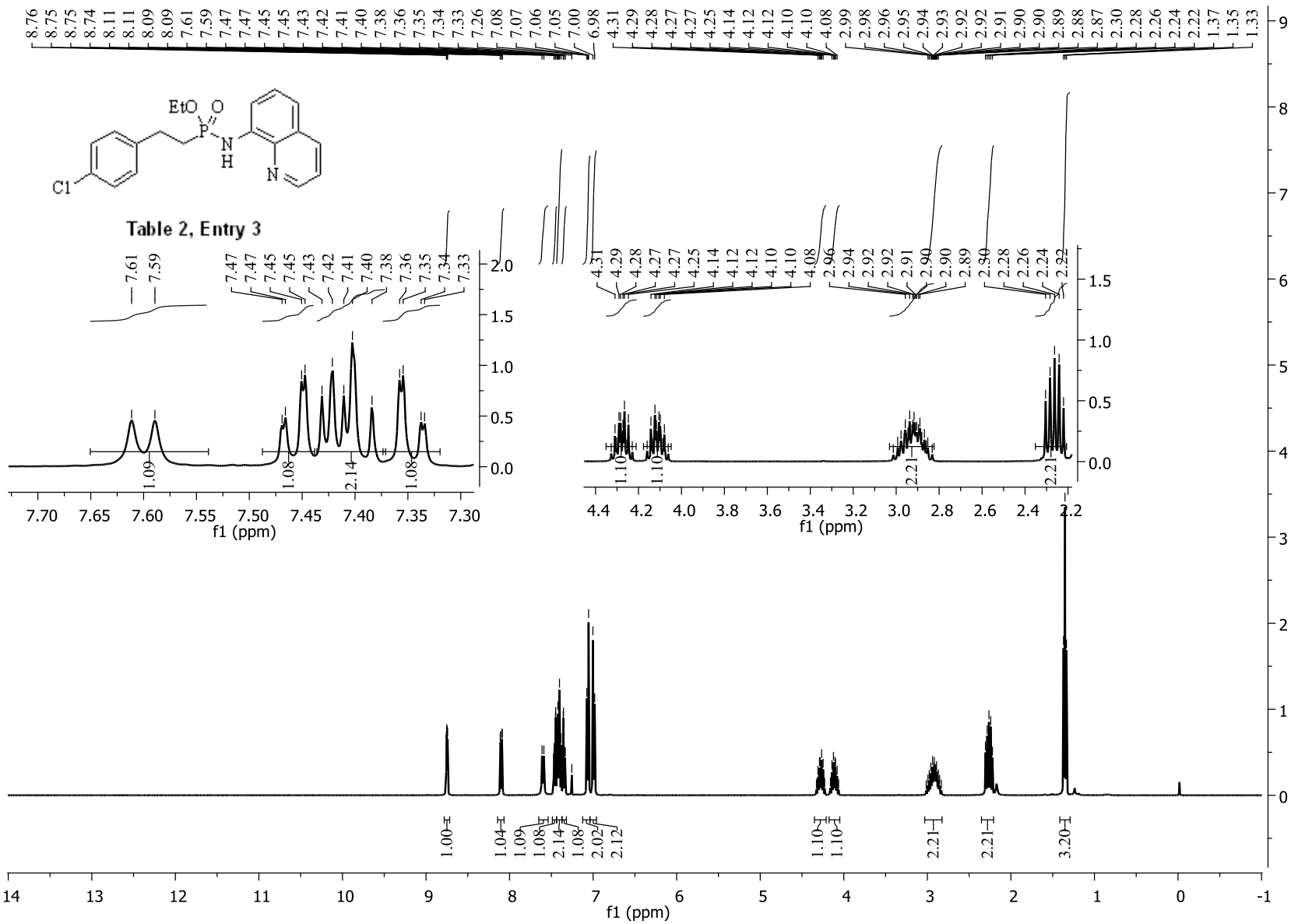

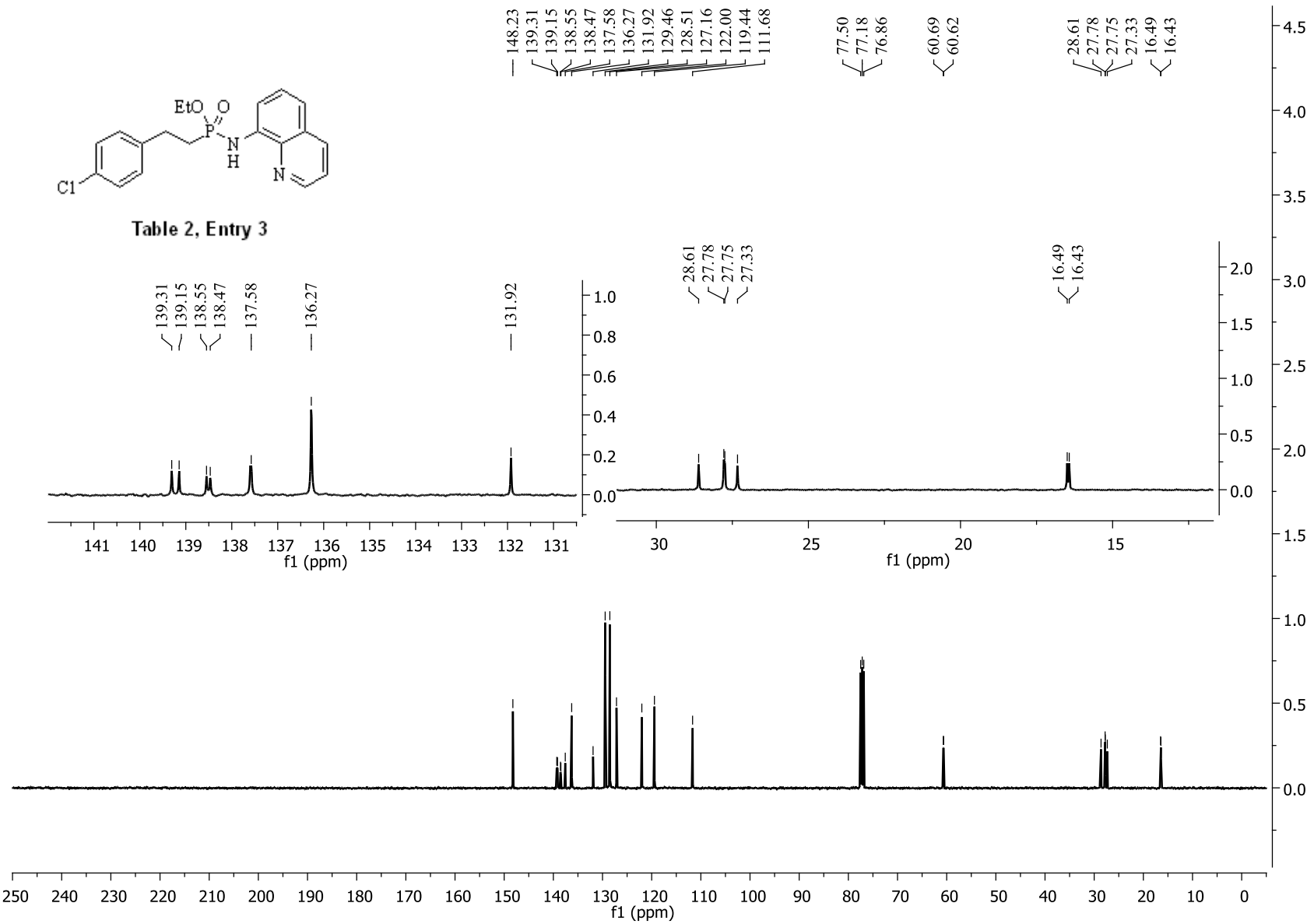

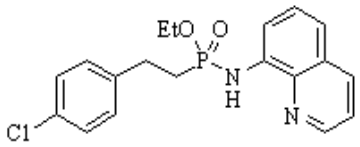

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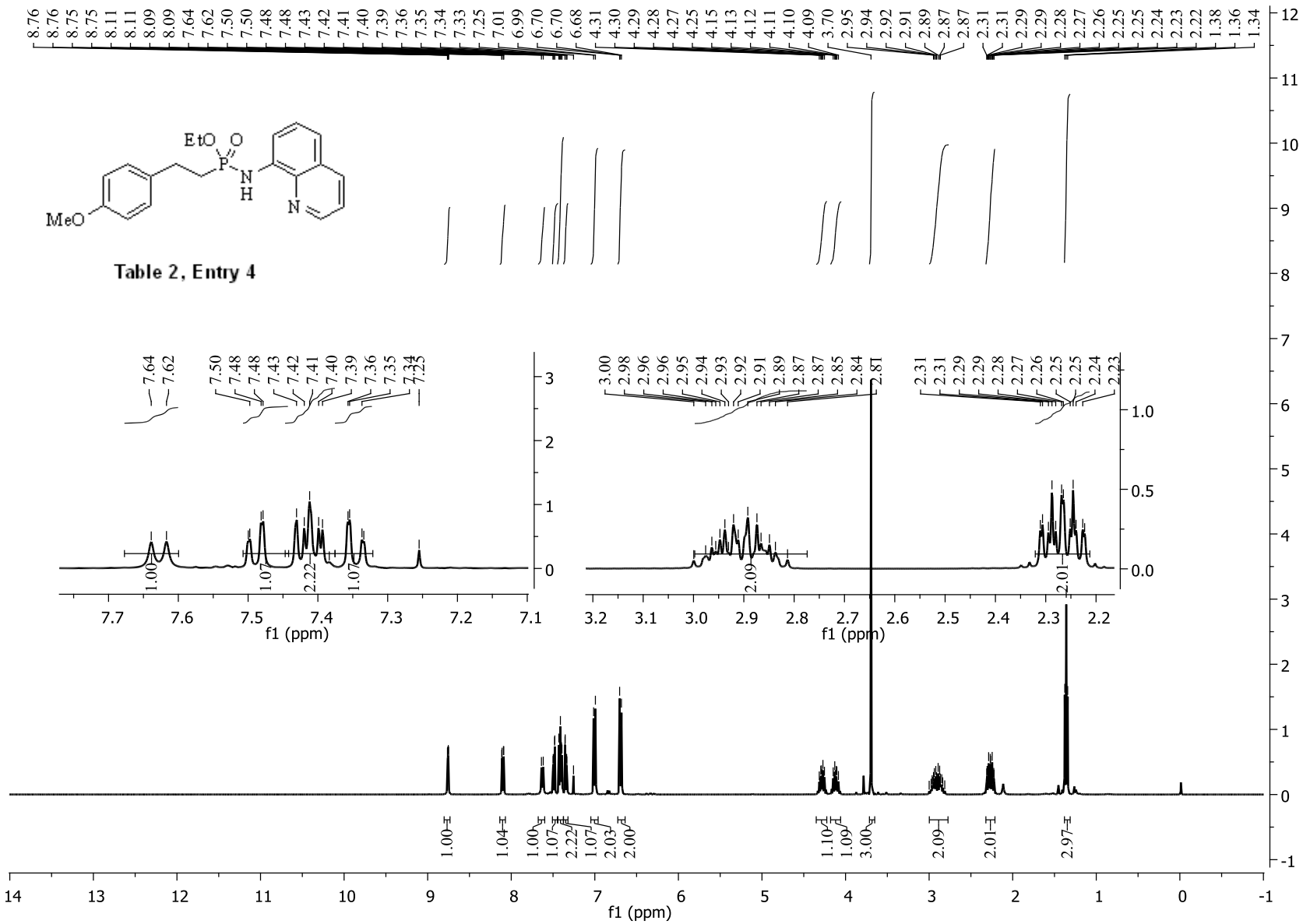

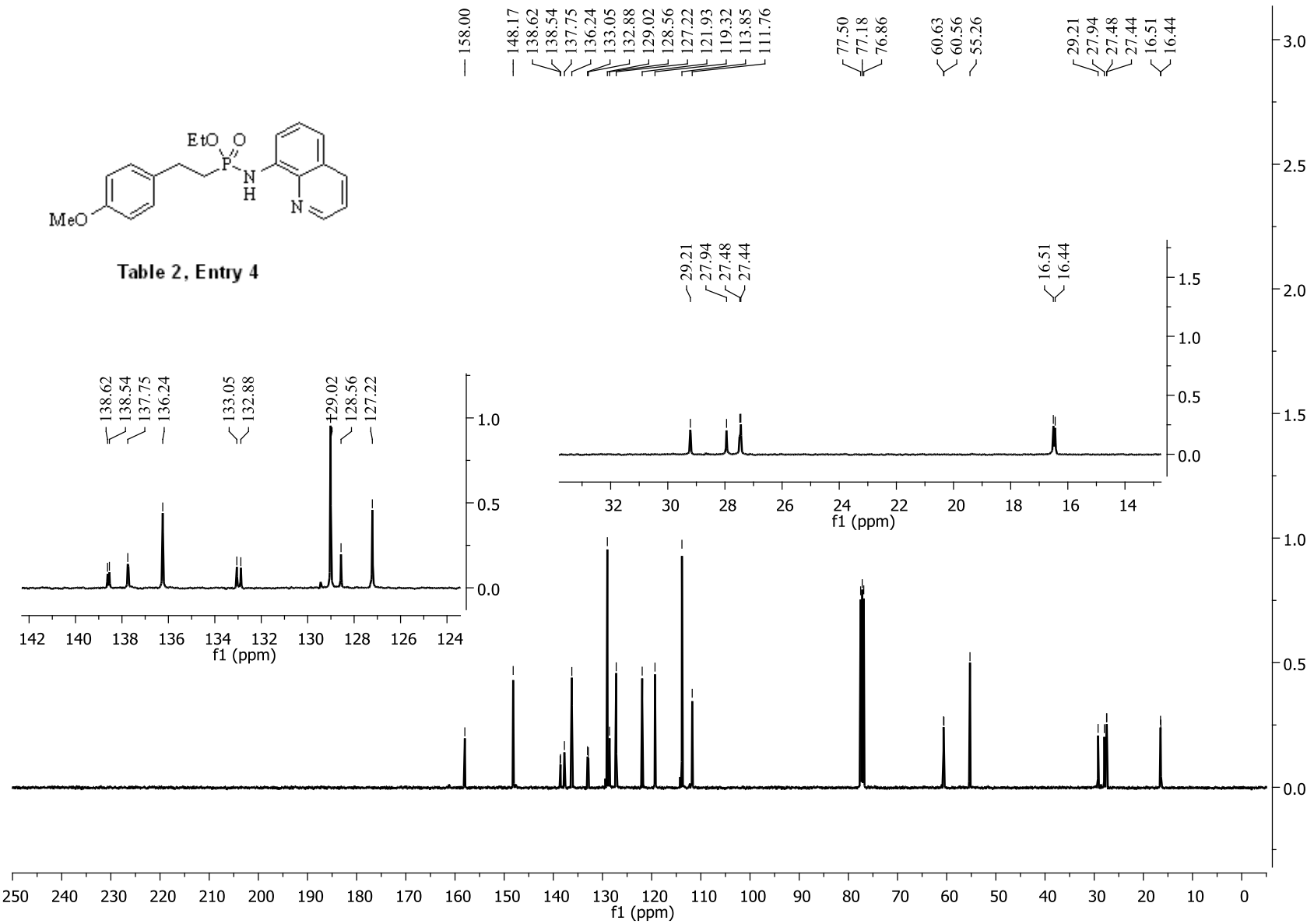

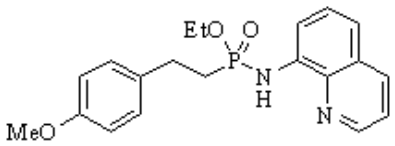

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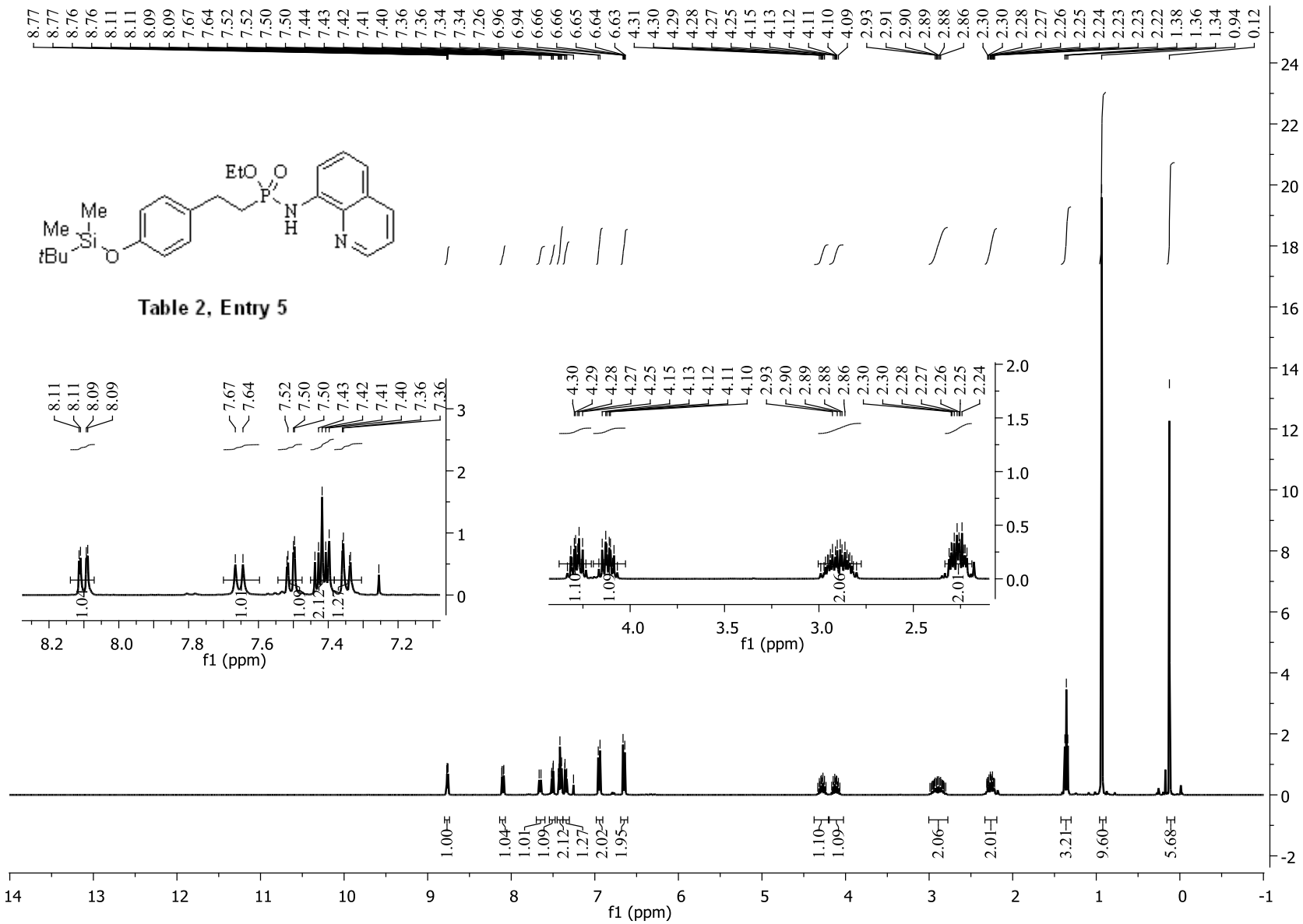

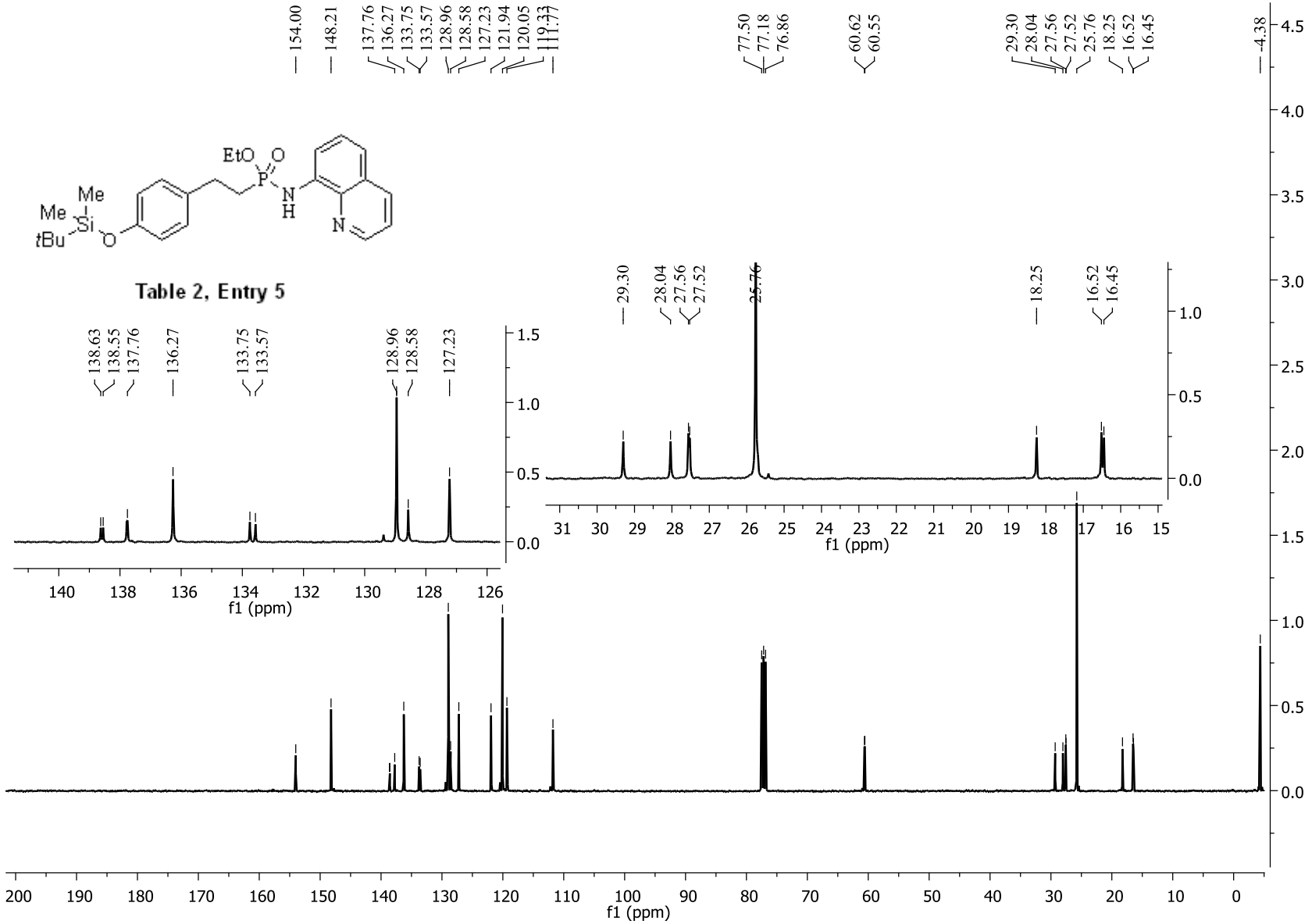

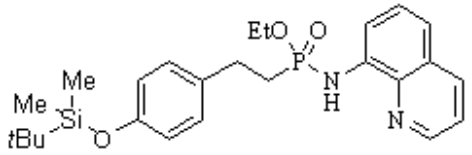

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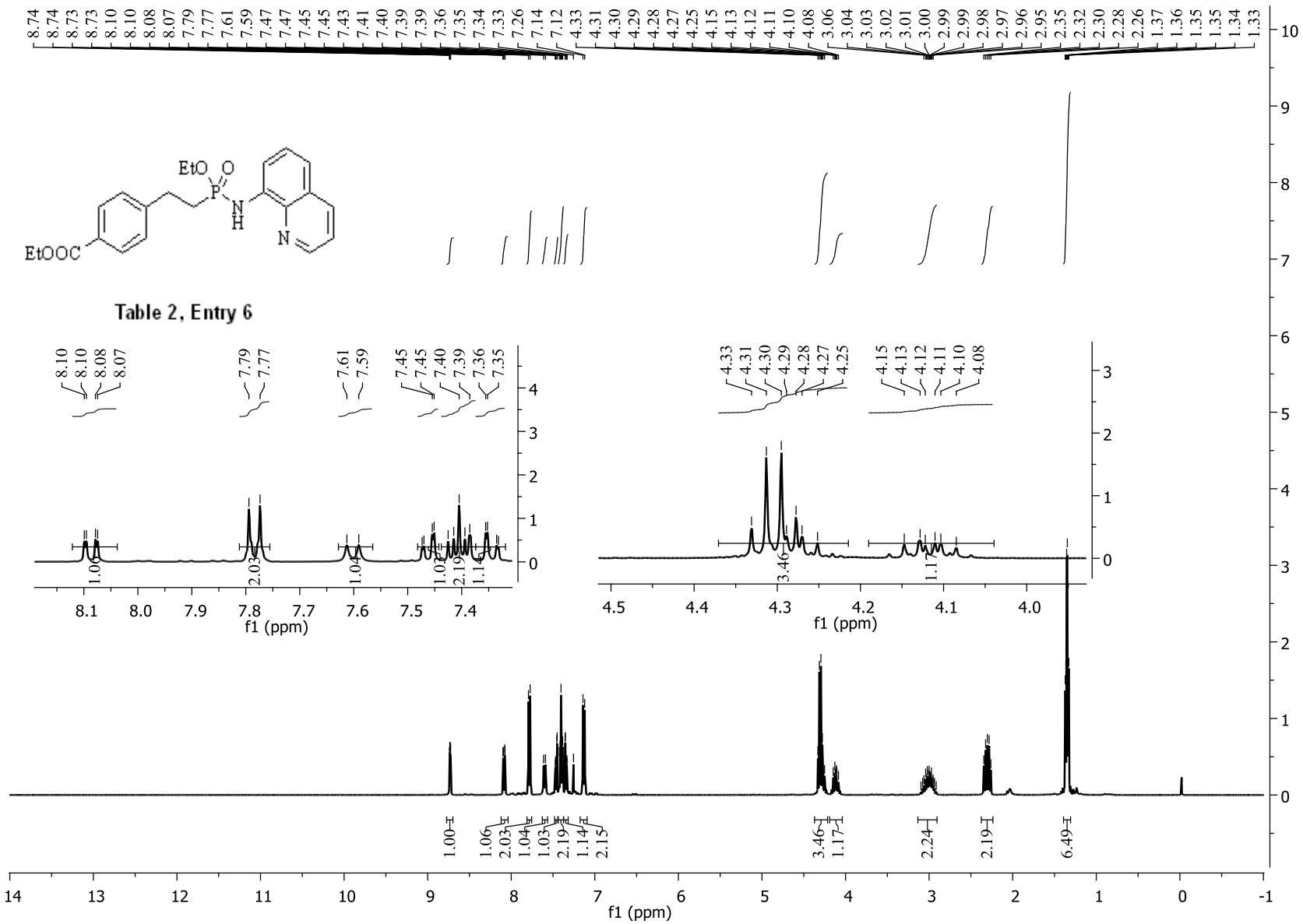

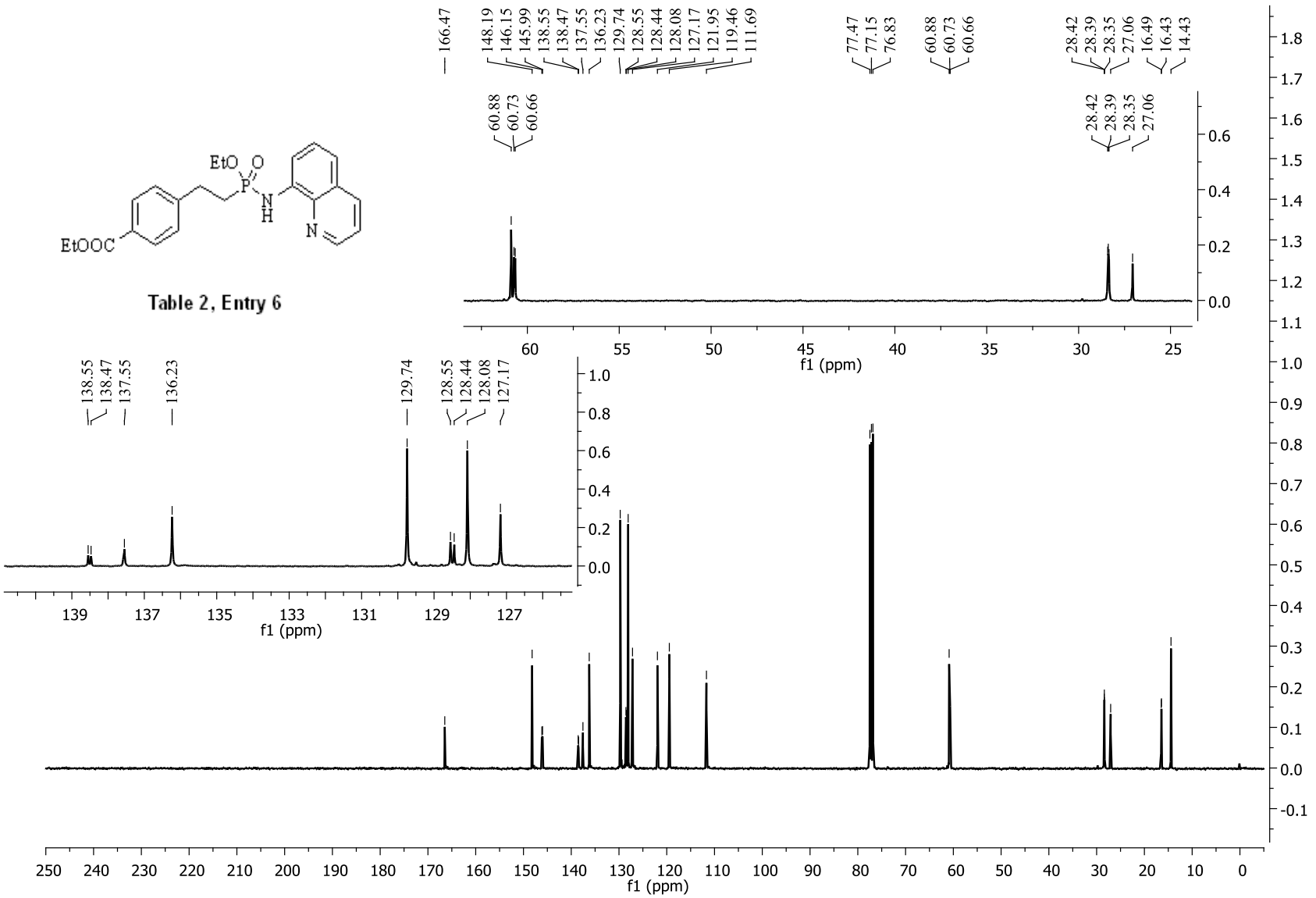

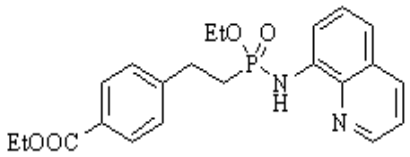

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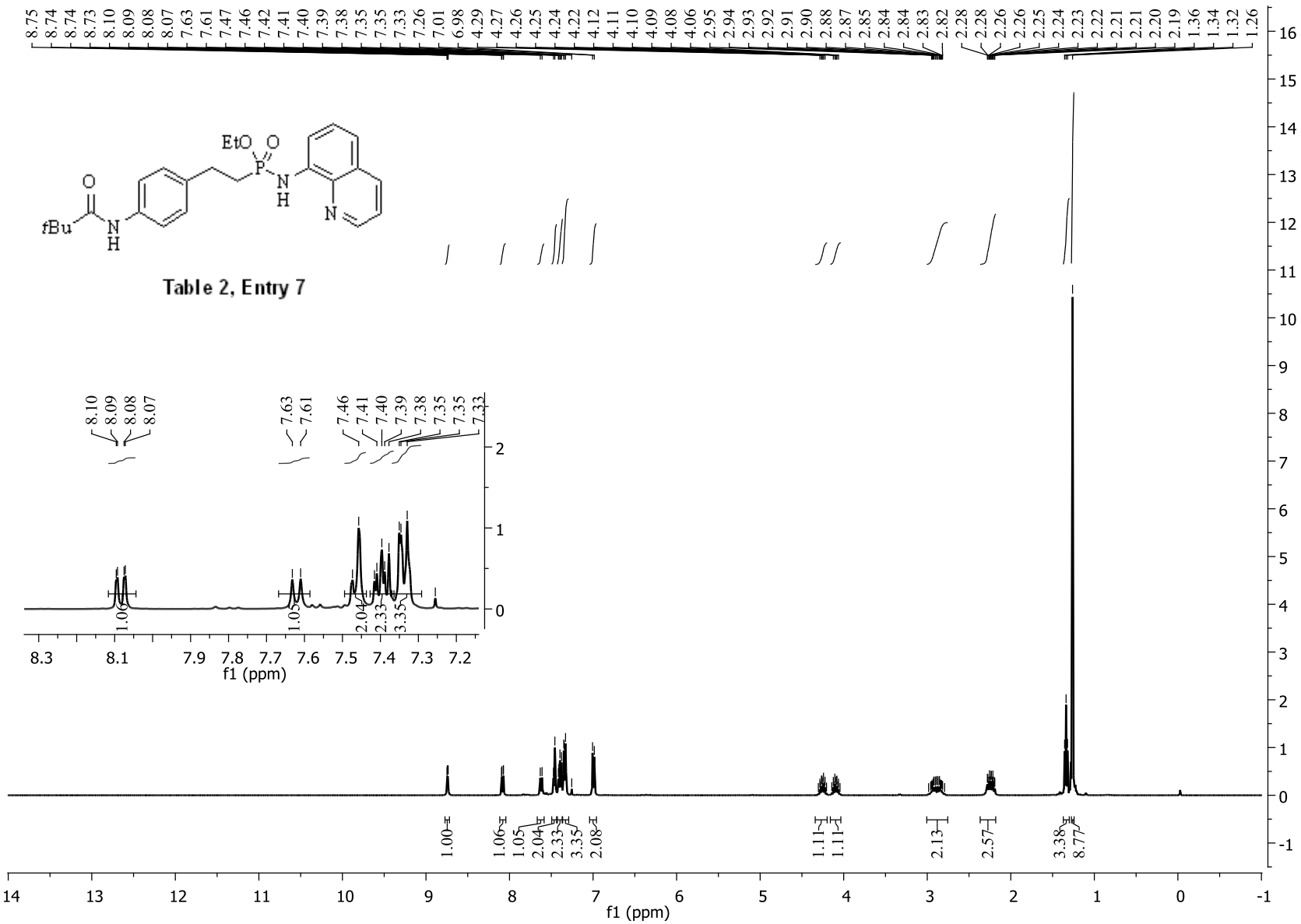

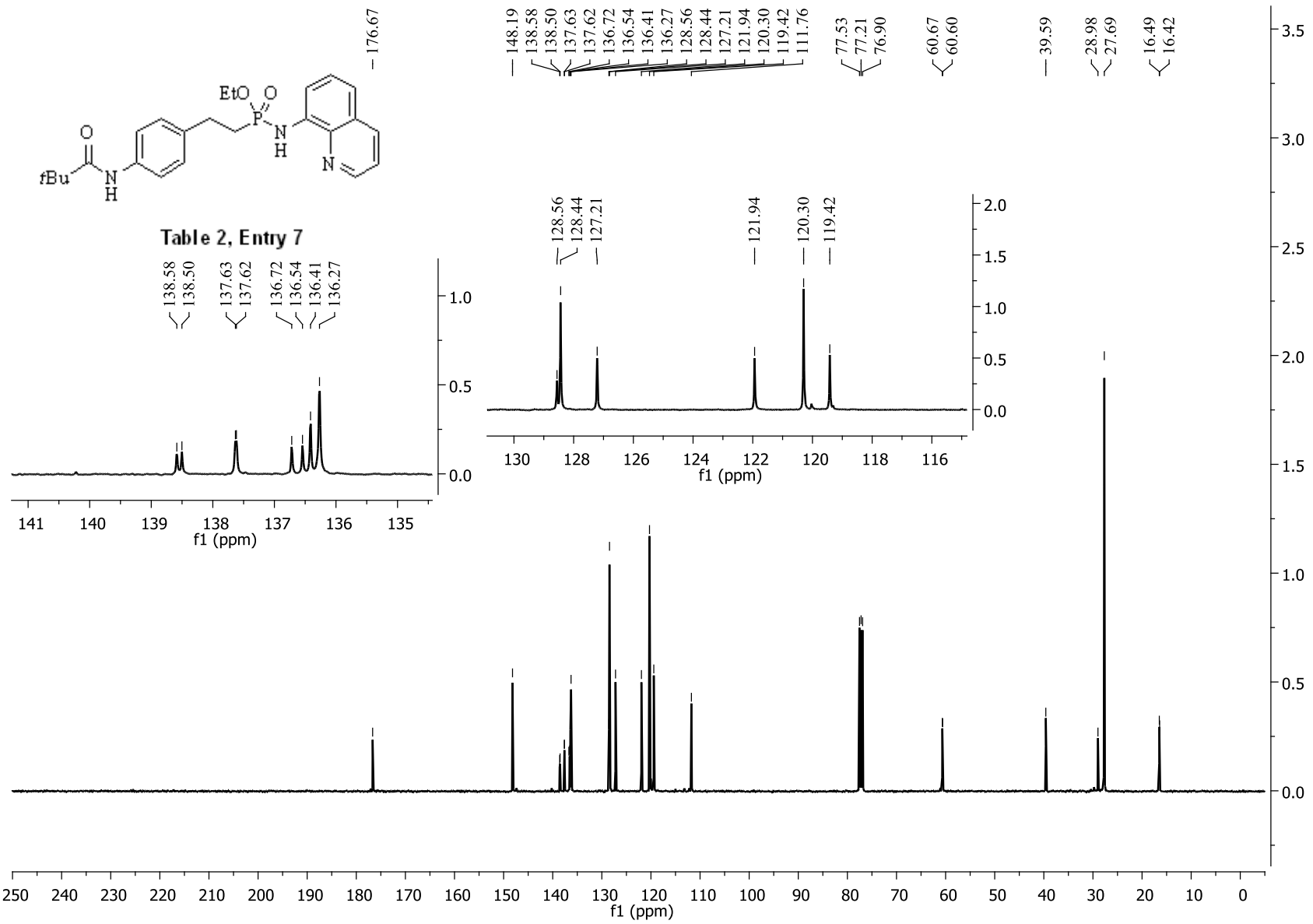

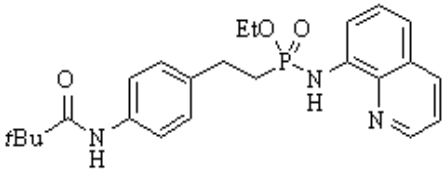

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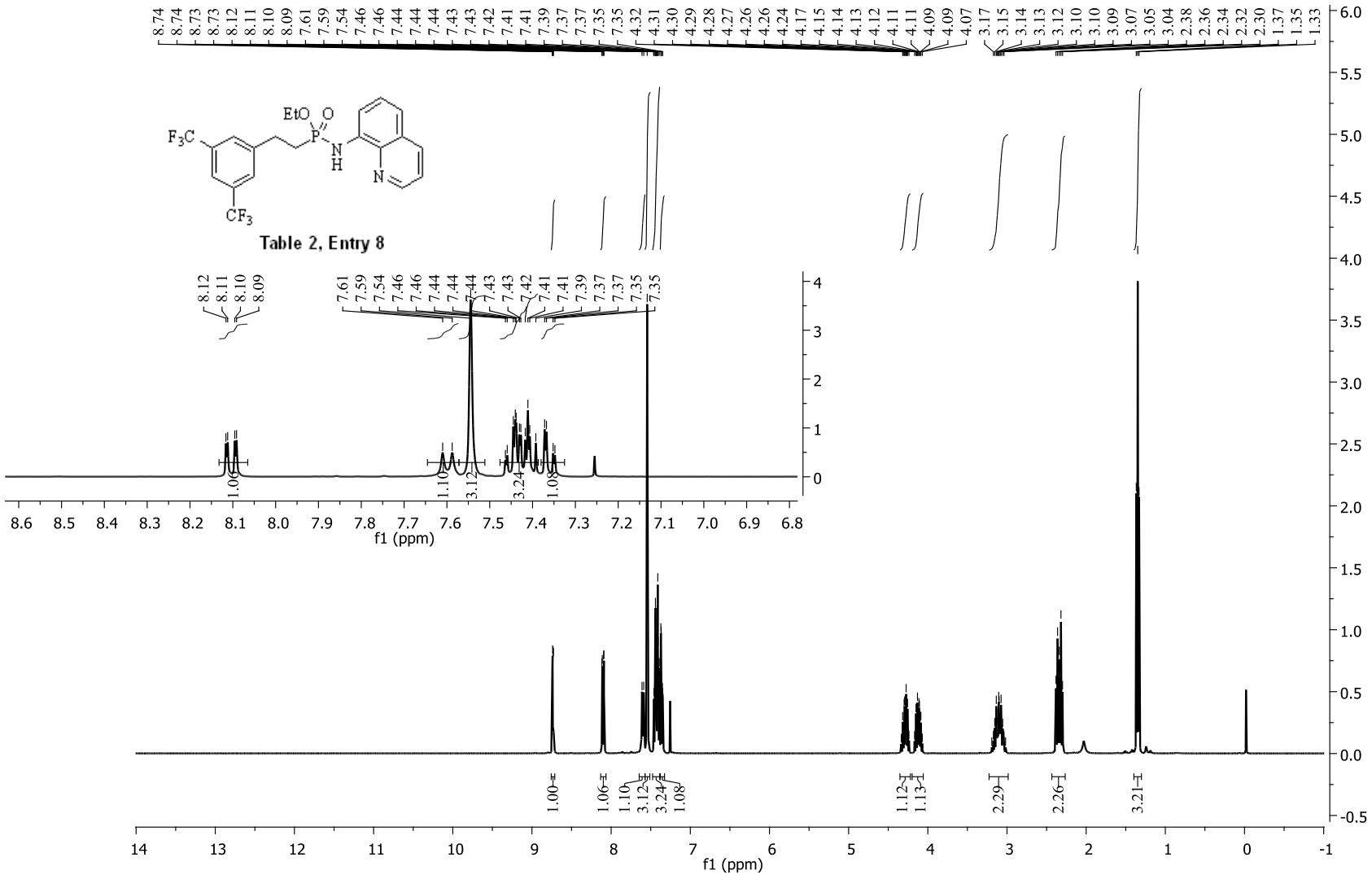

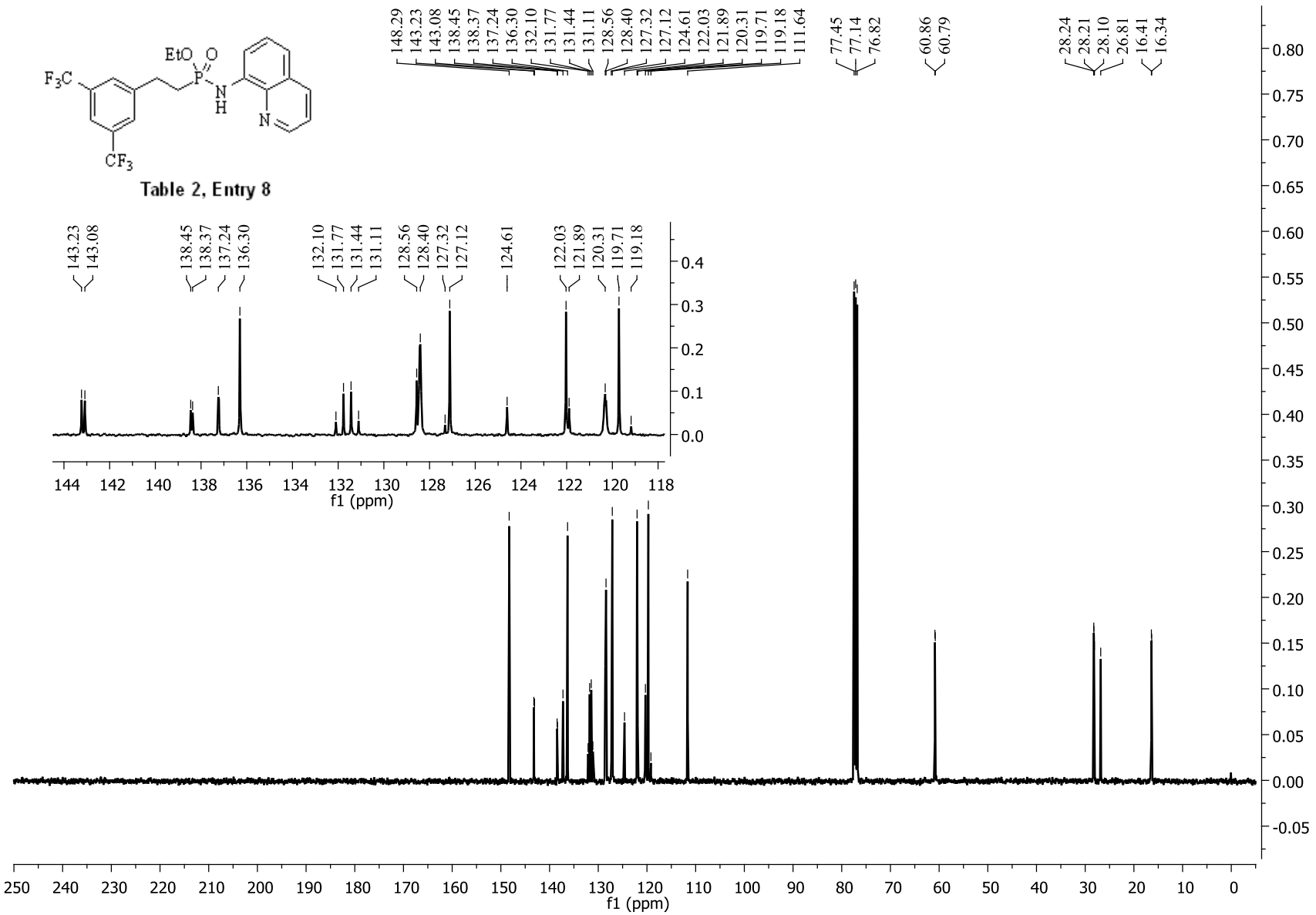

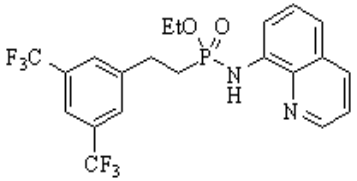

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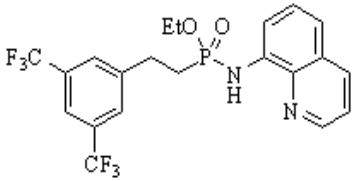

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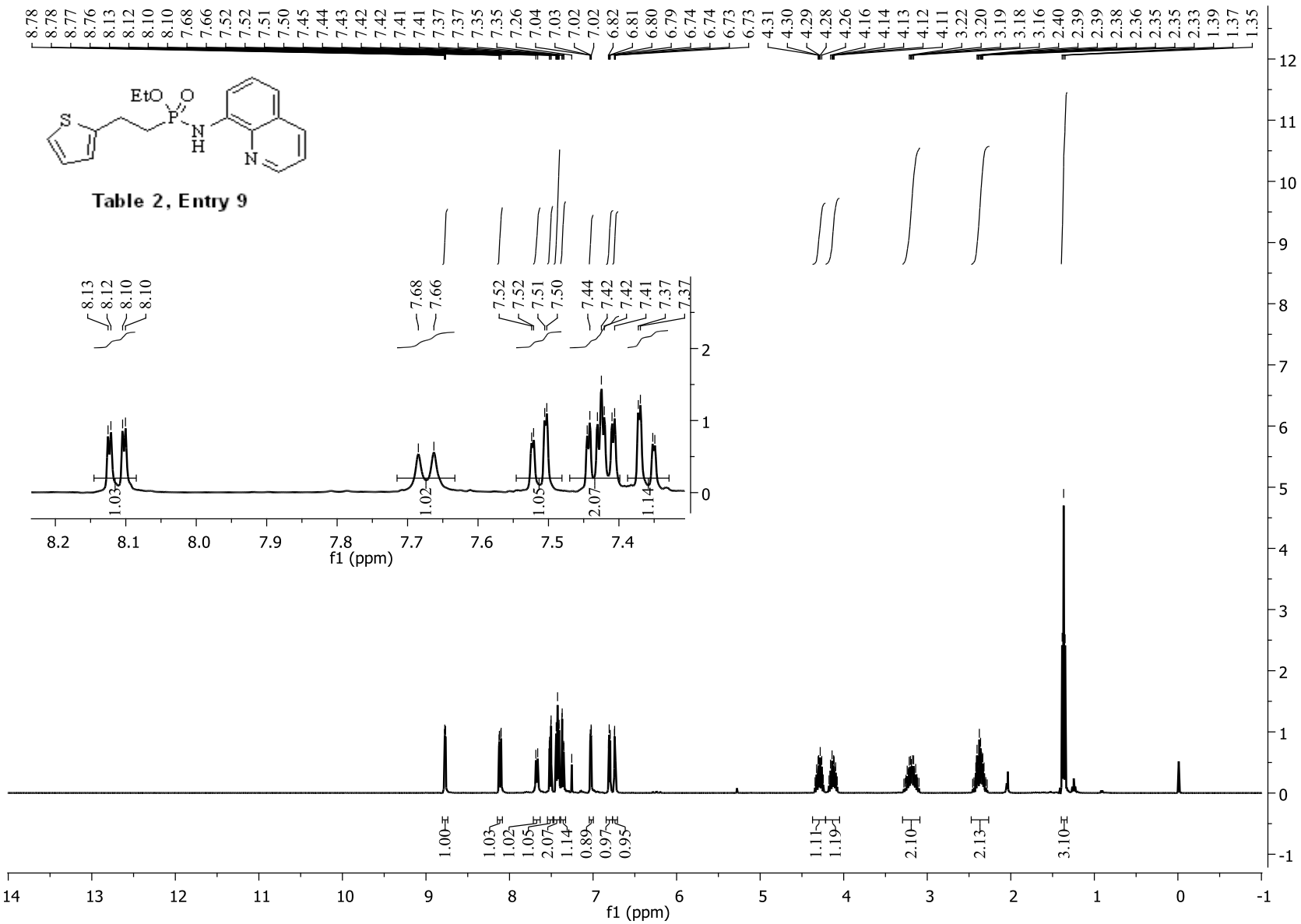

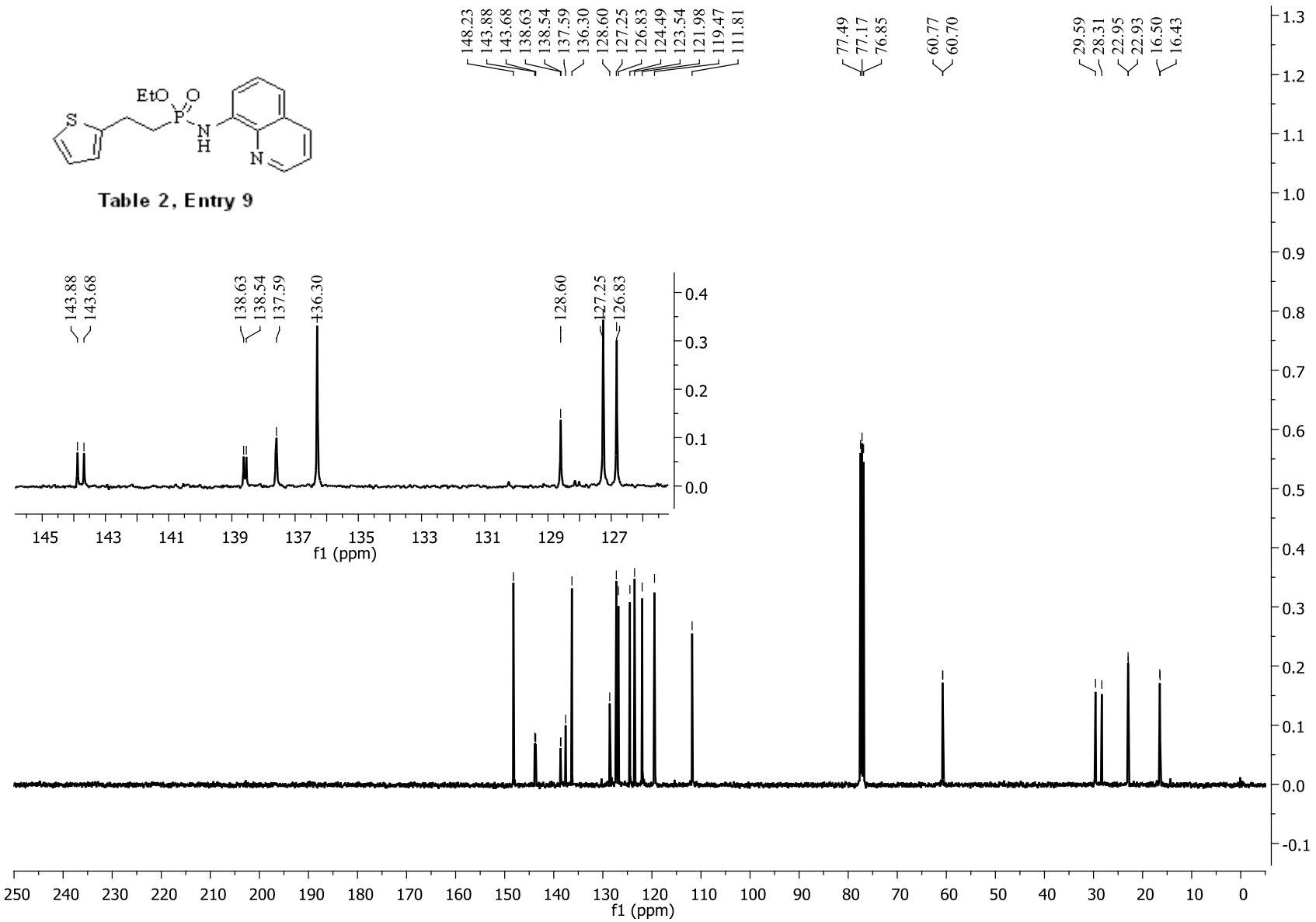

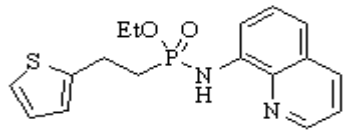

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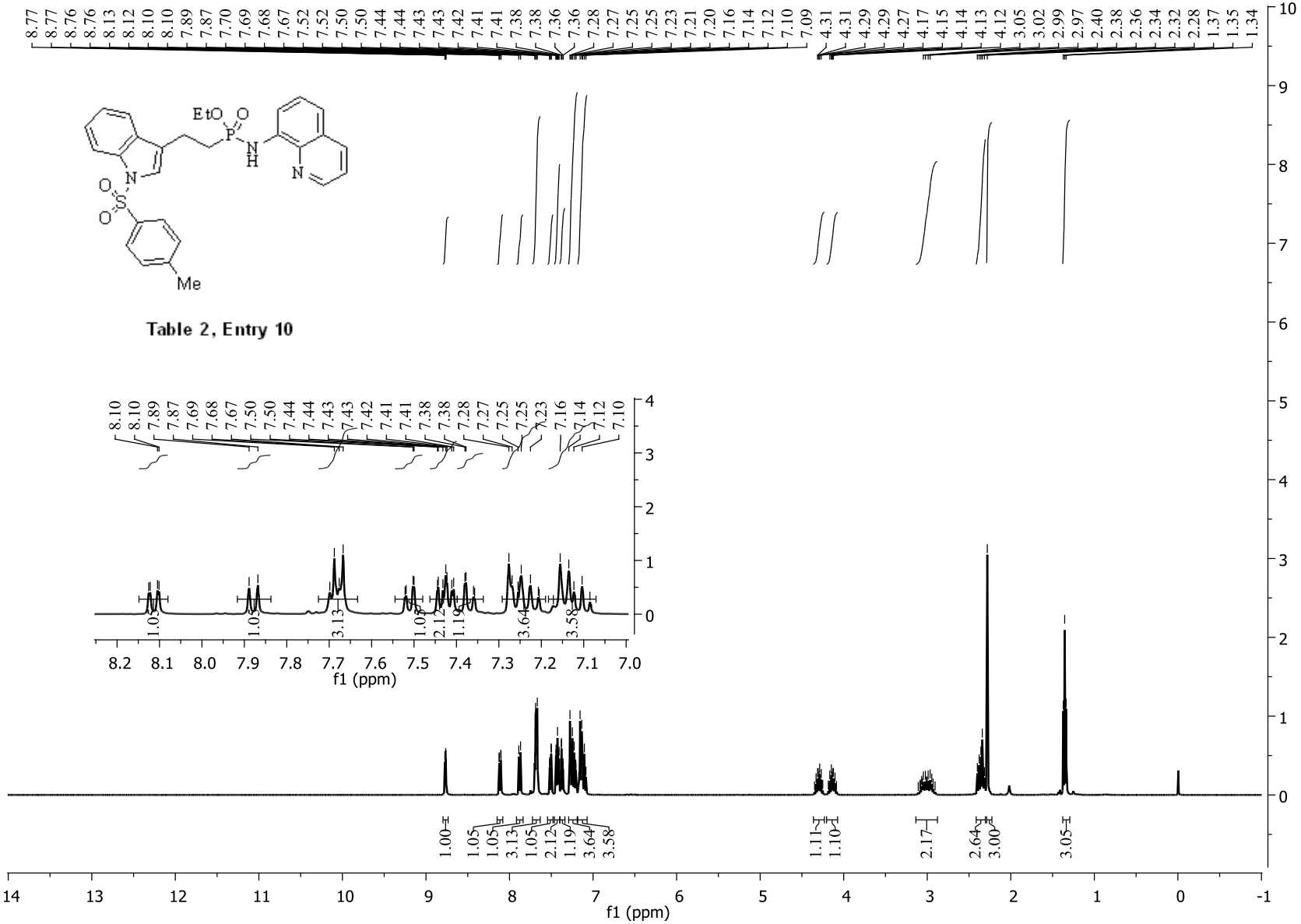

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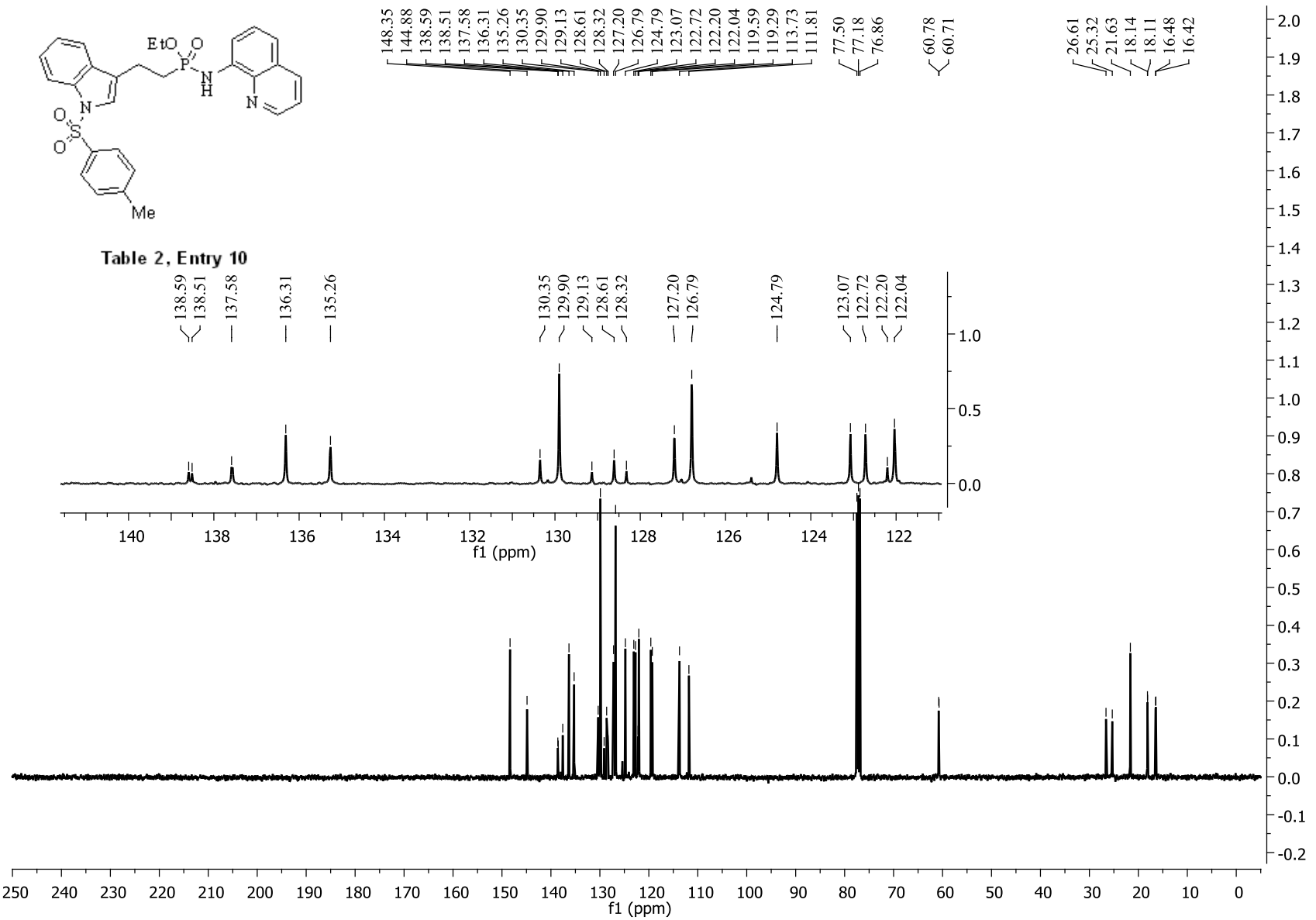

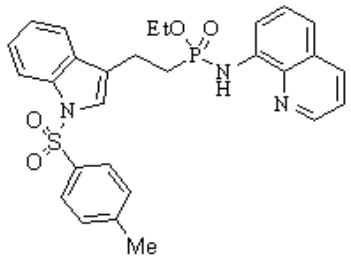

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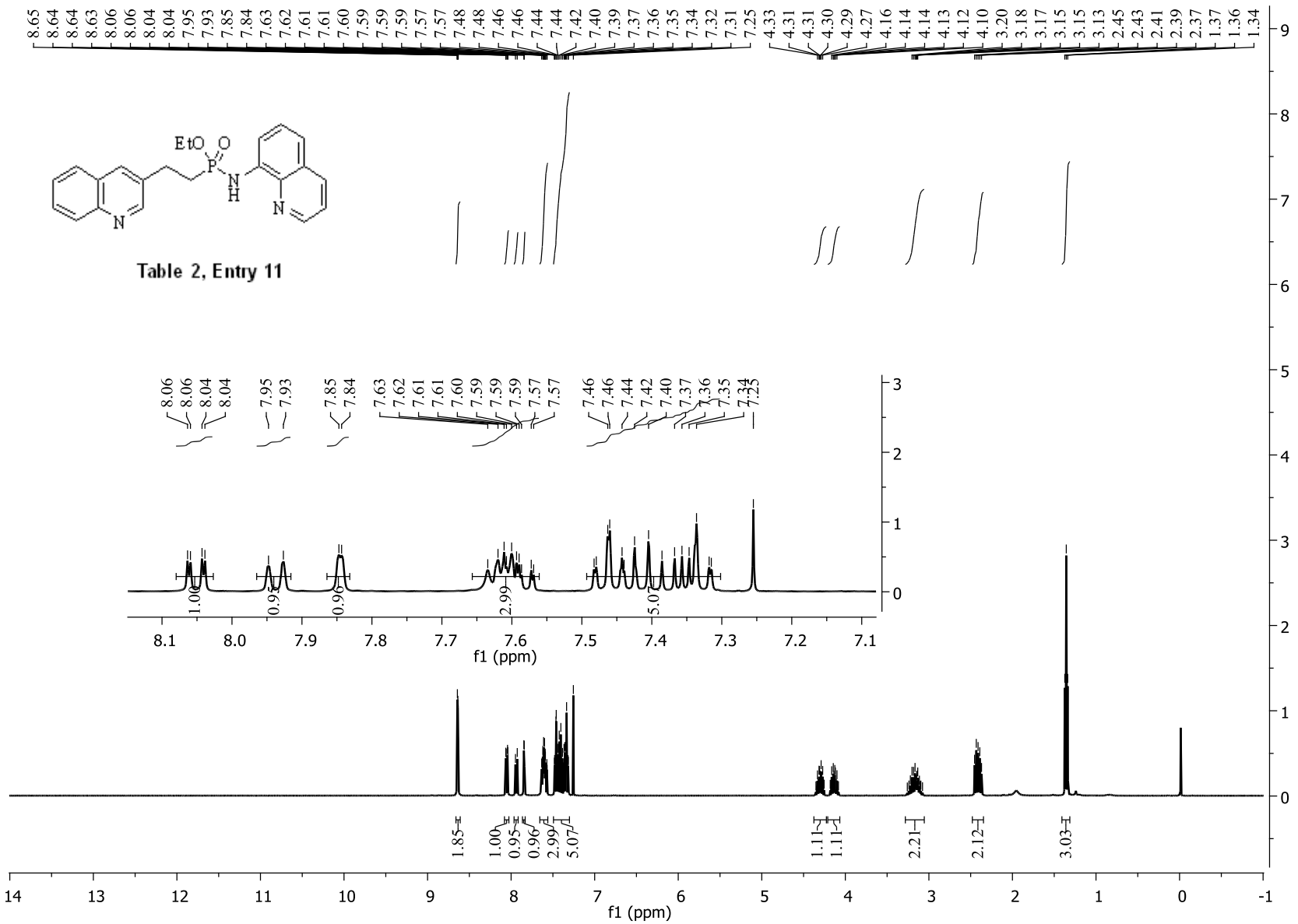

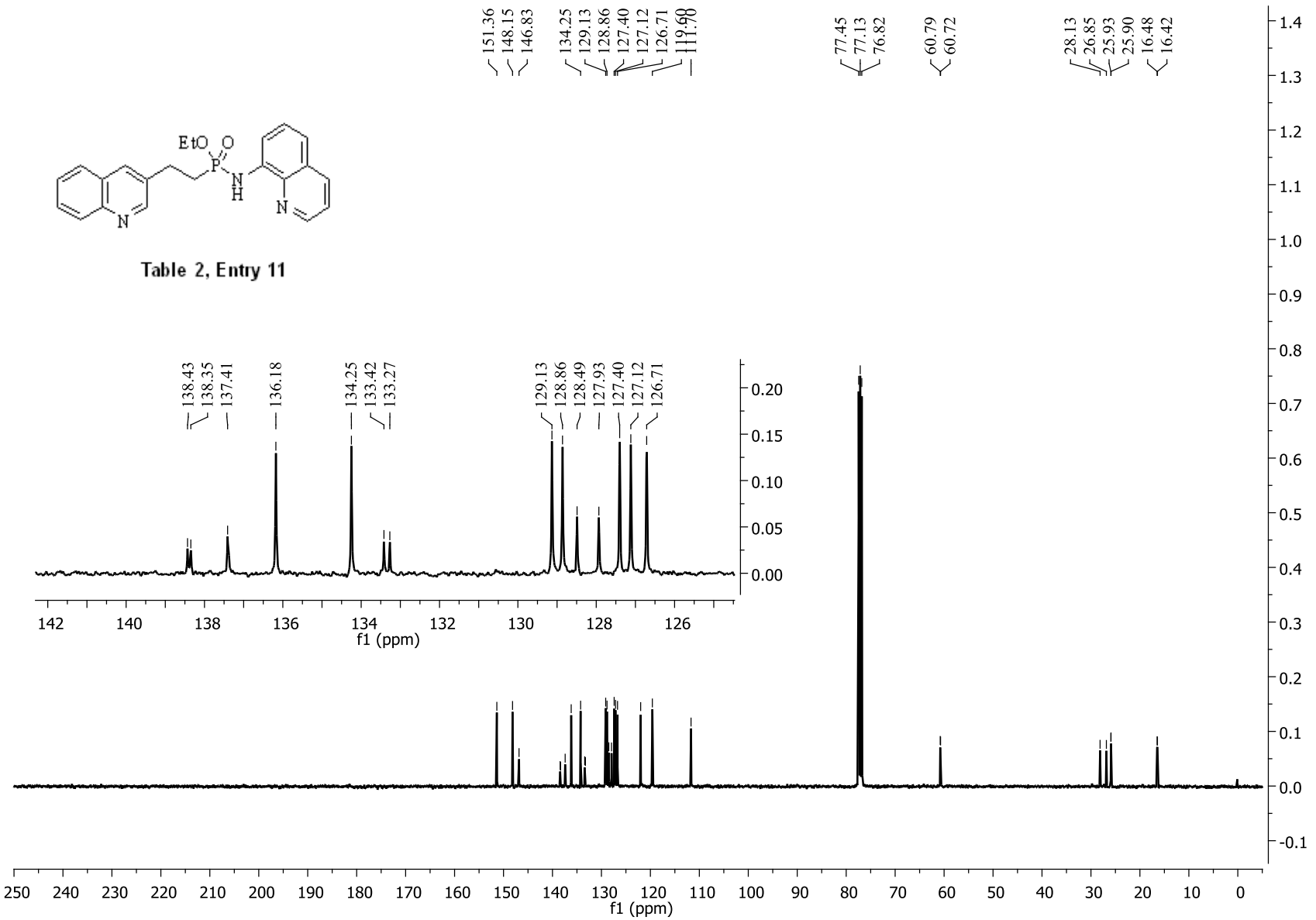

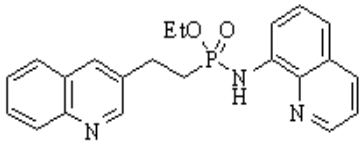

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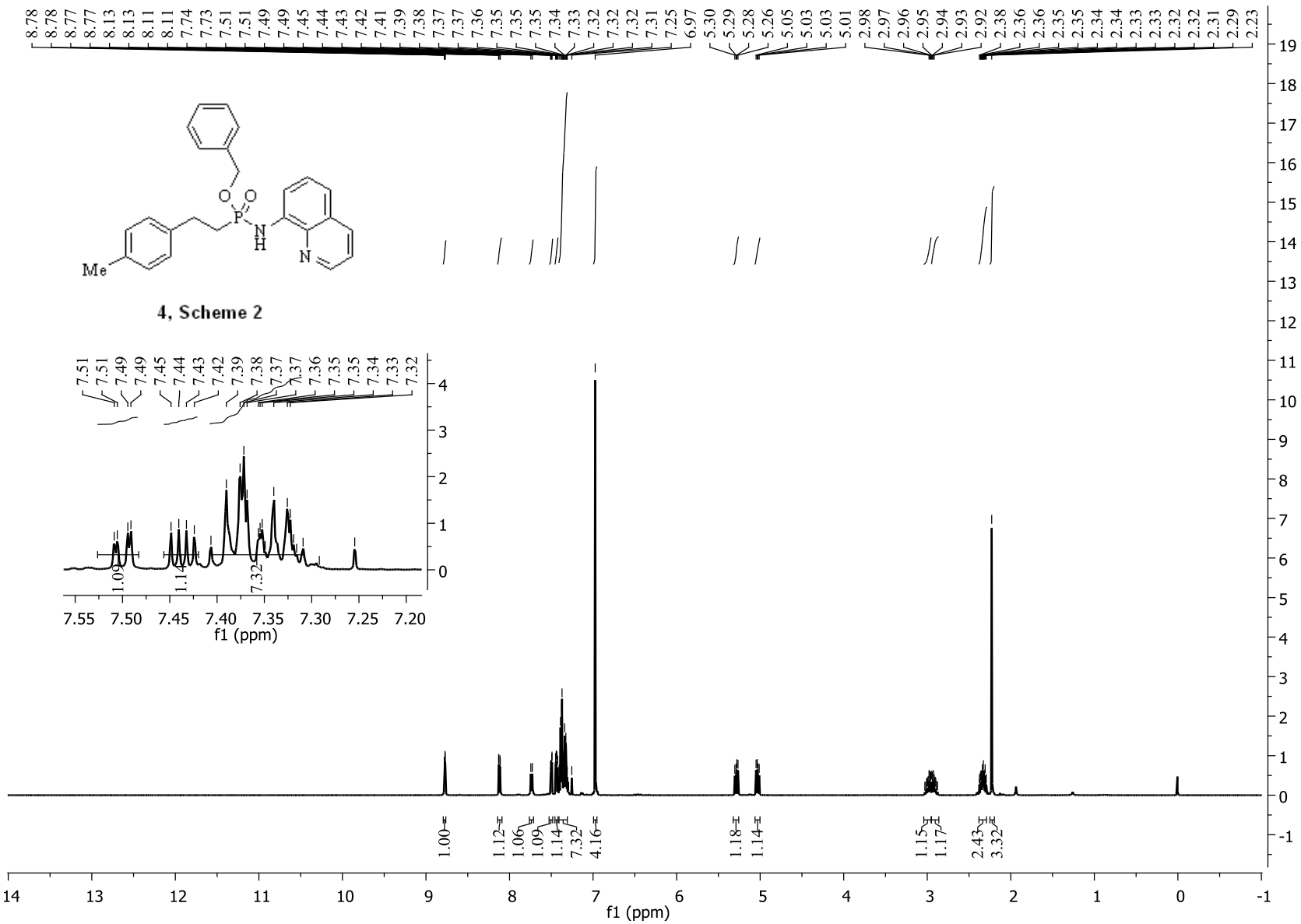
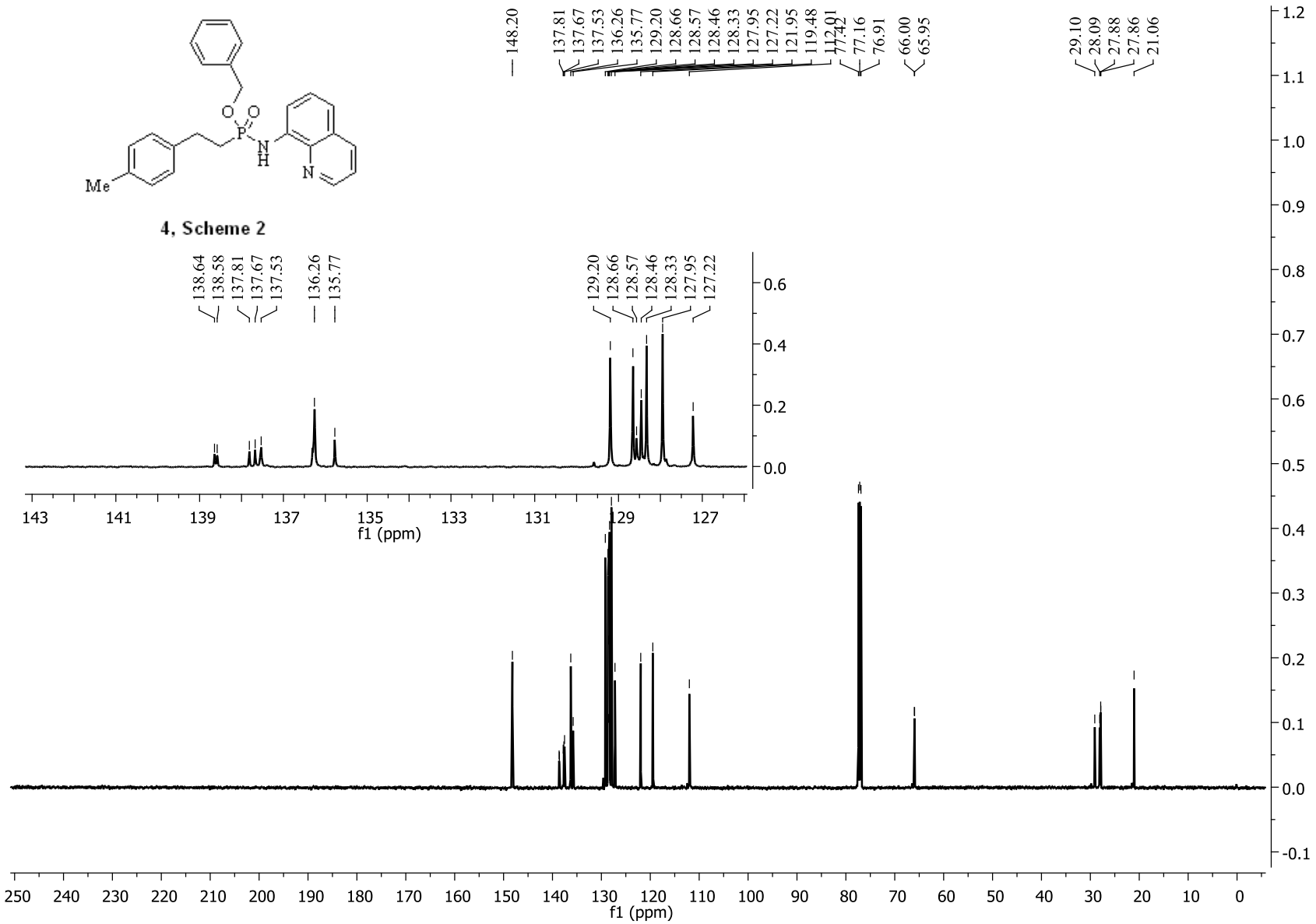
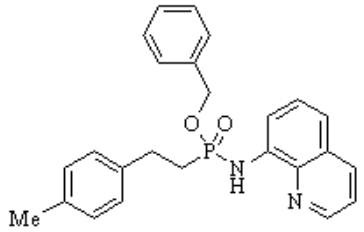
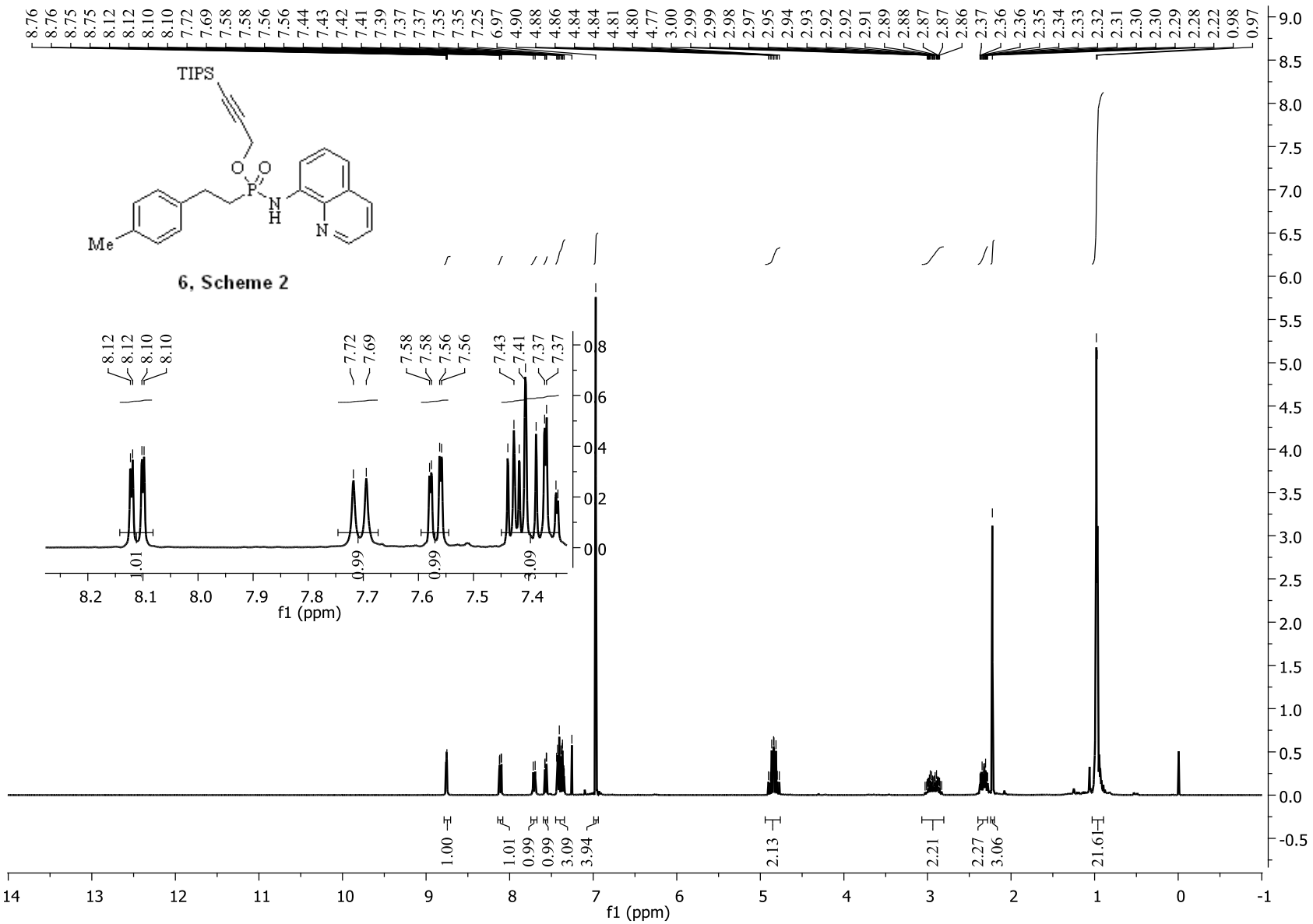
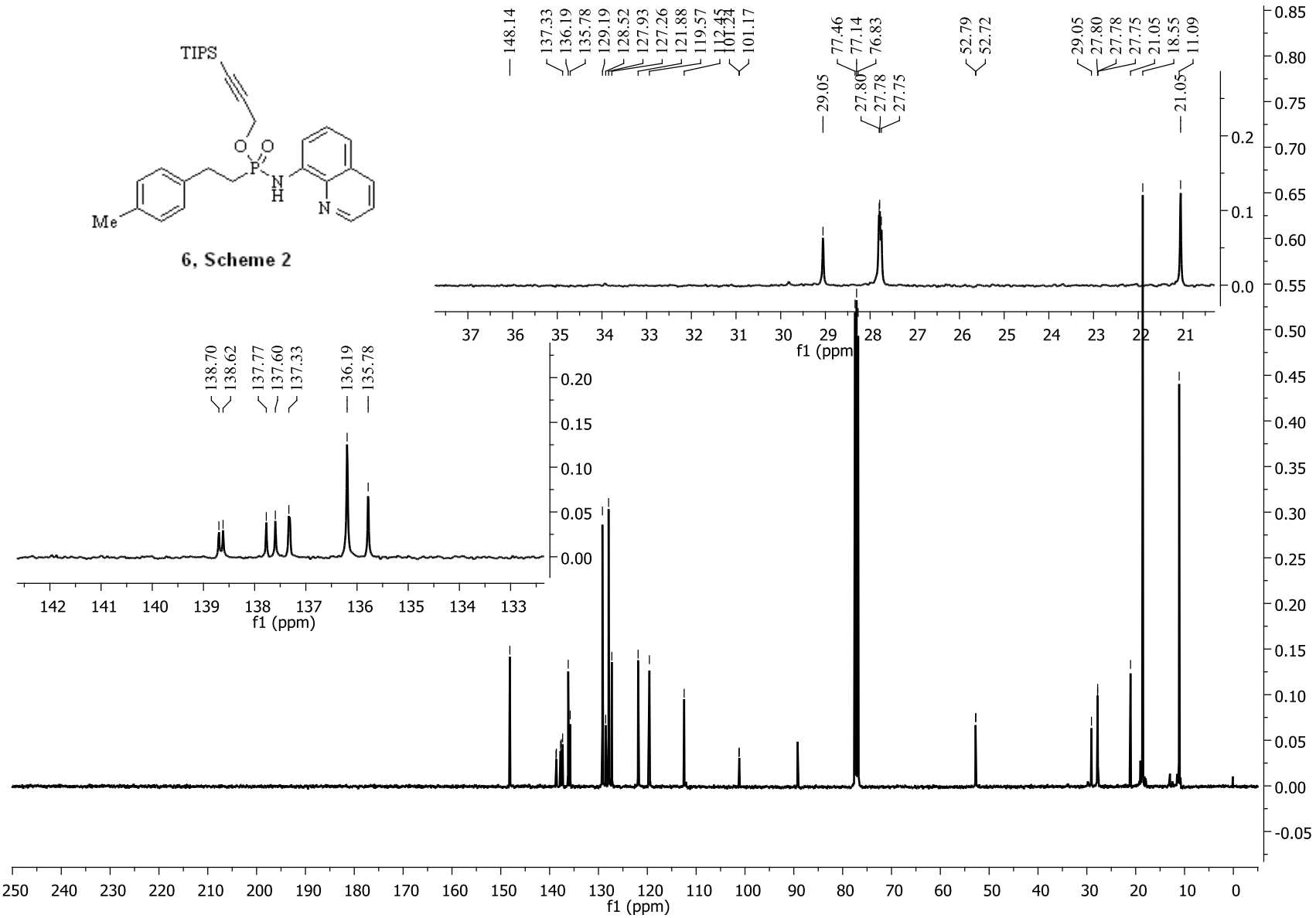


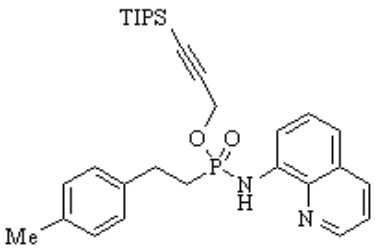




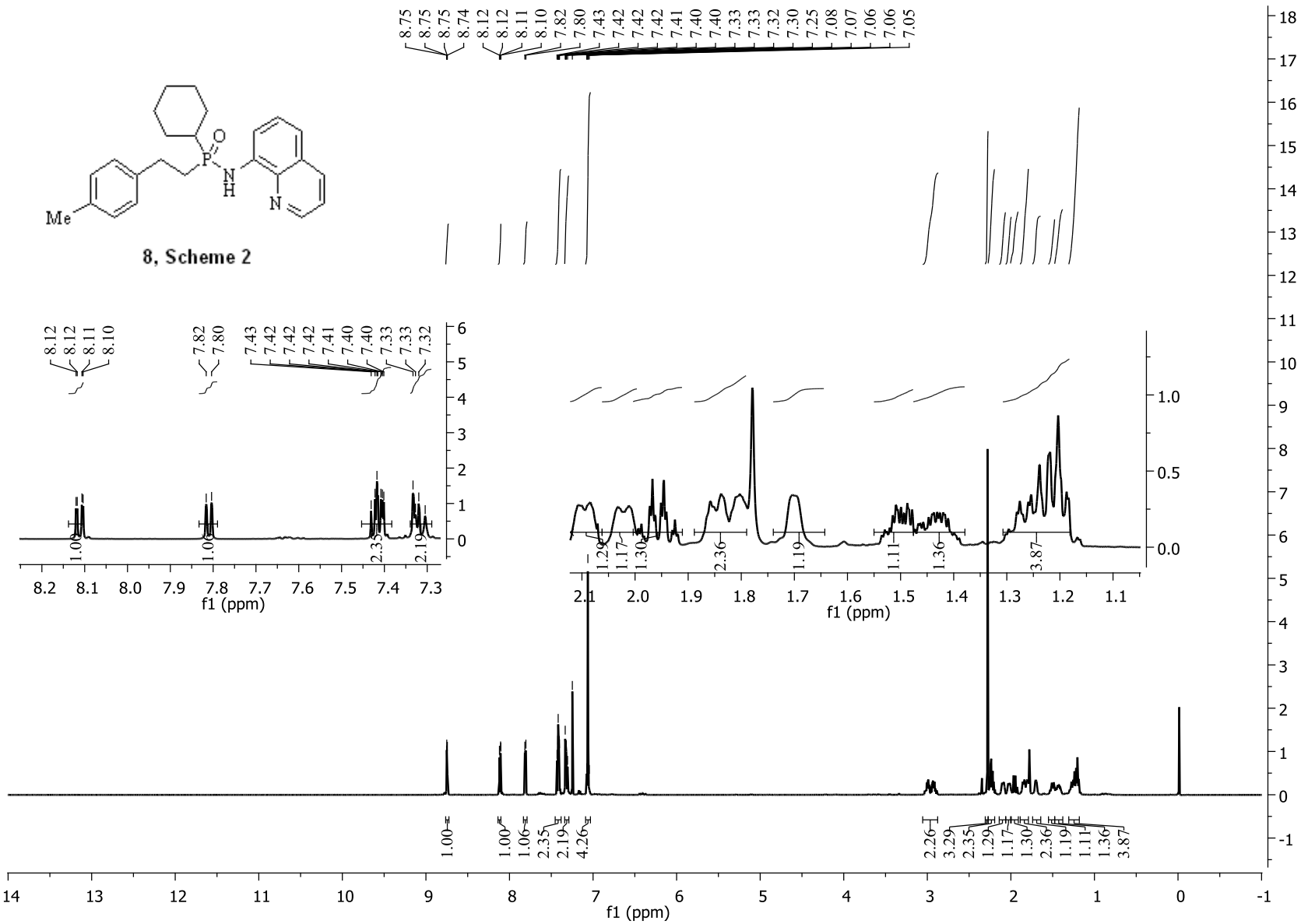
4, Scheme 2

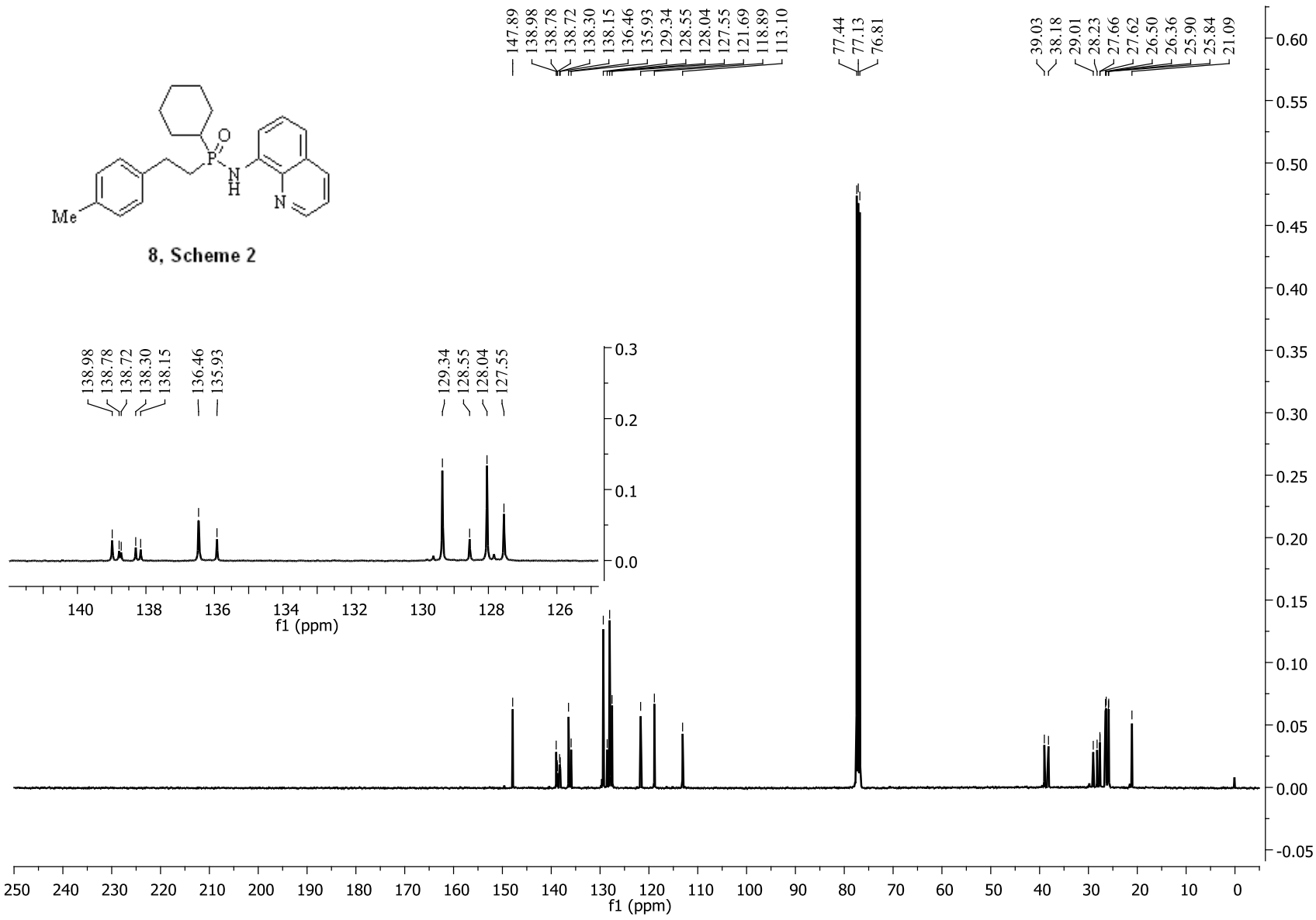


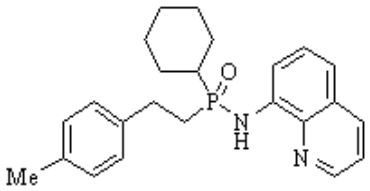




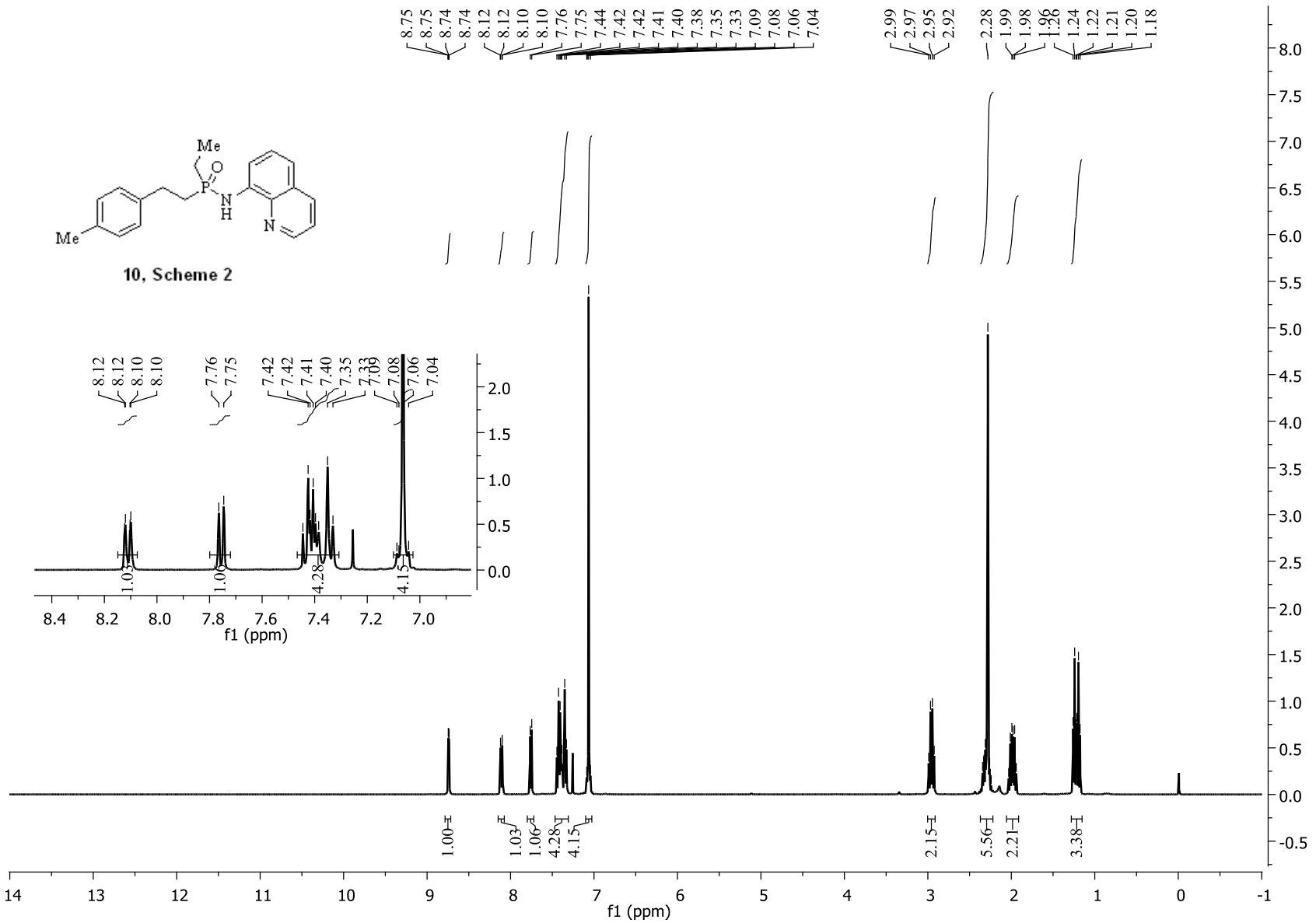
6, Scheme 2

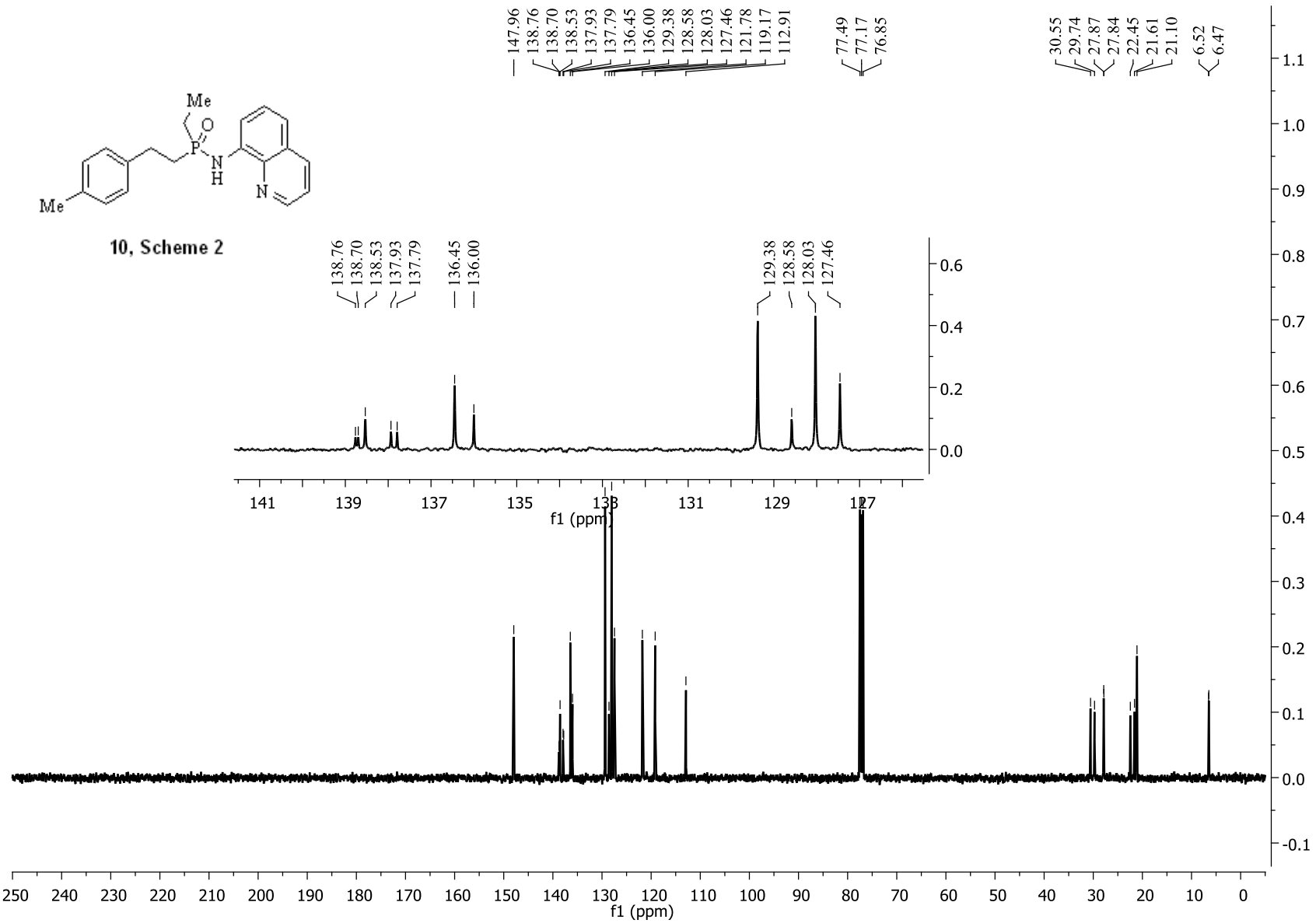


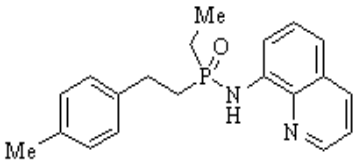




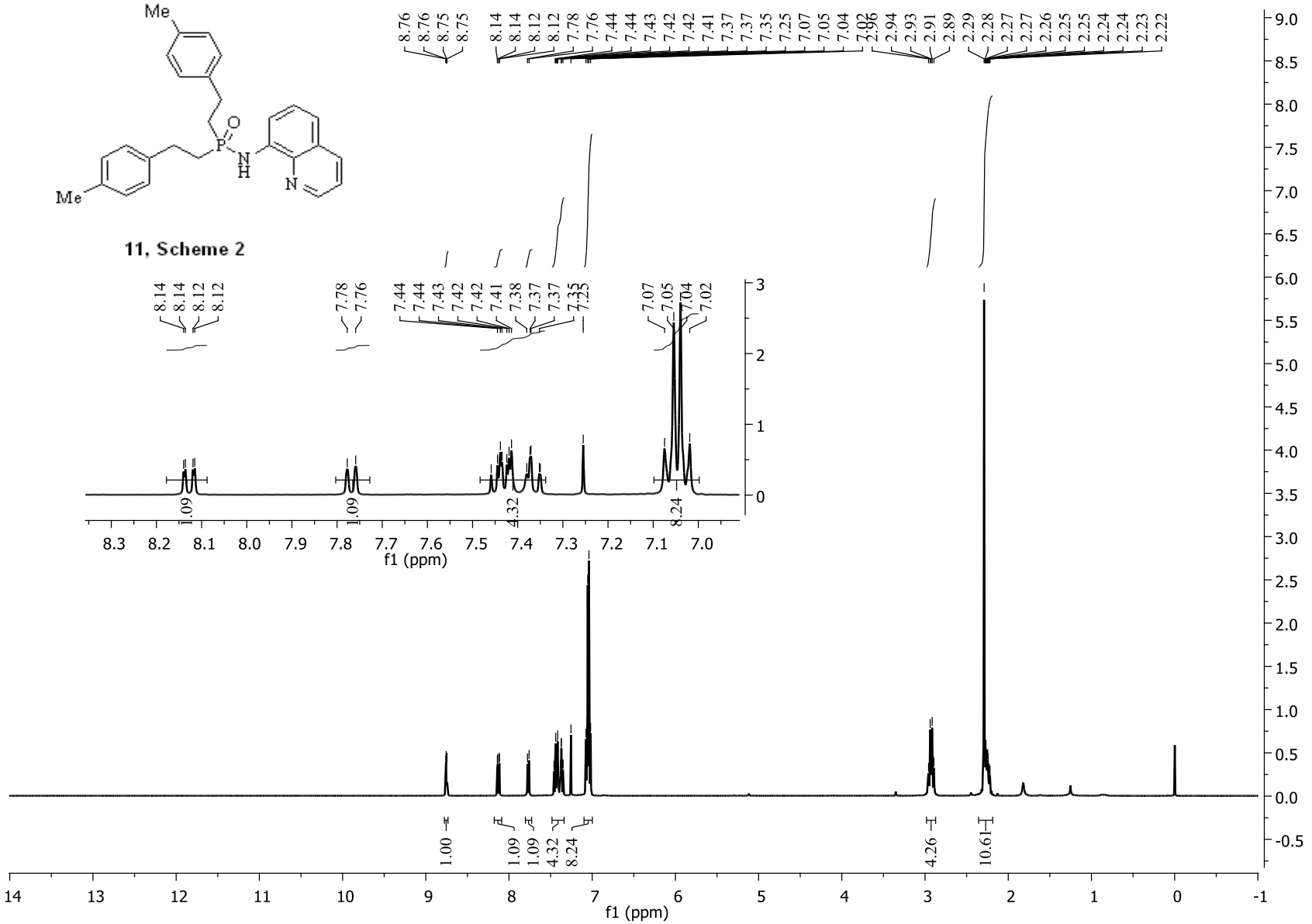
8, Scheme 2

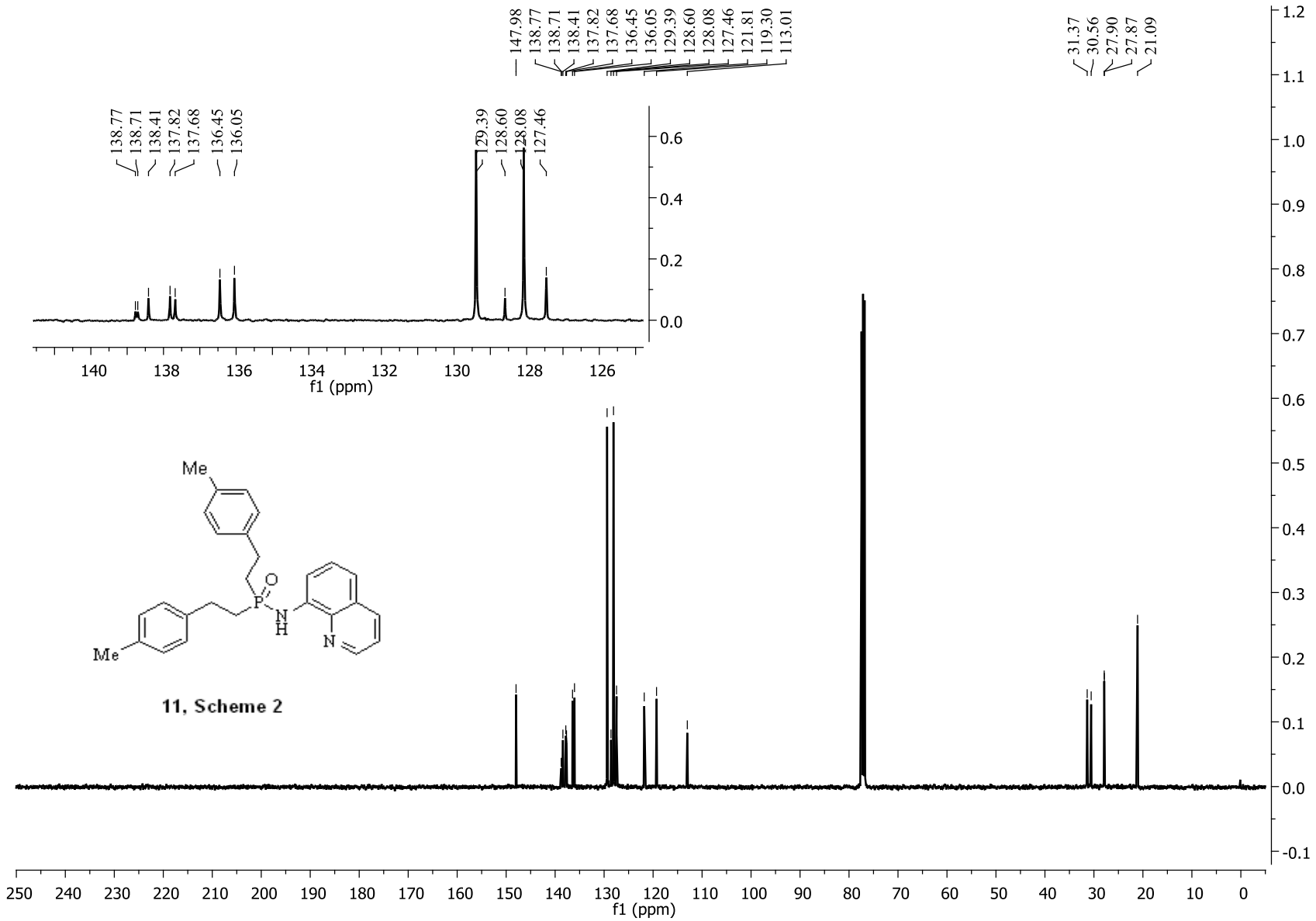


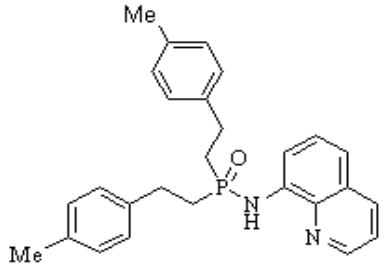




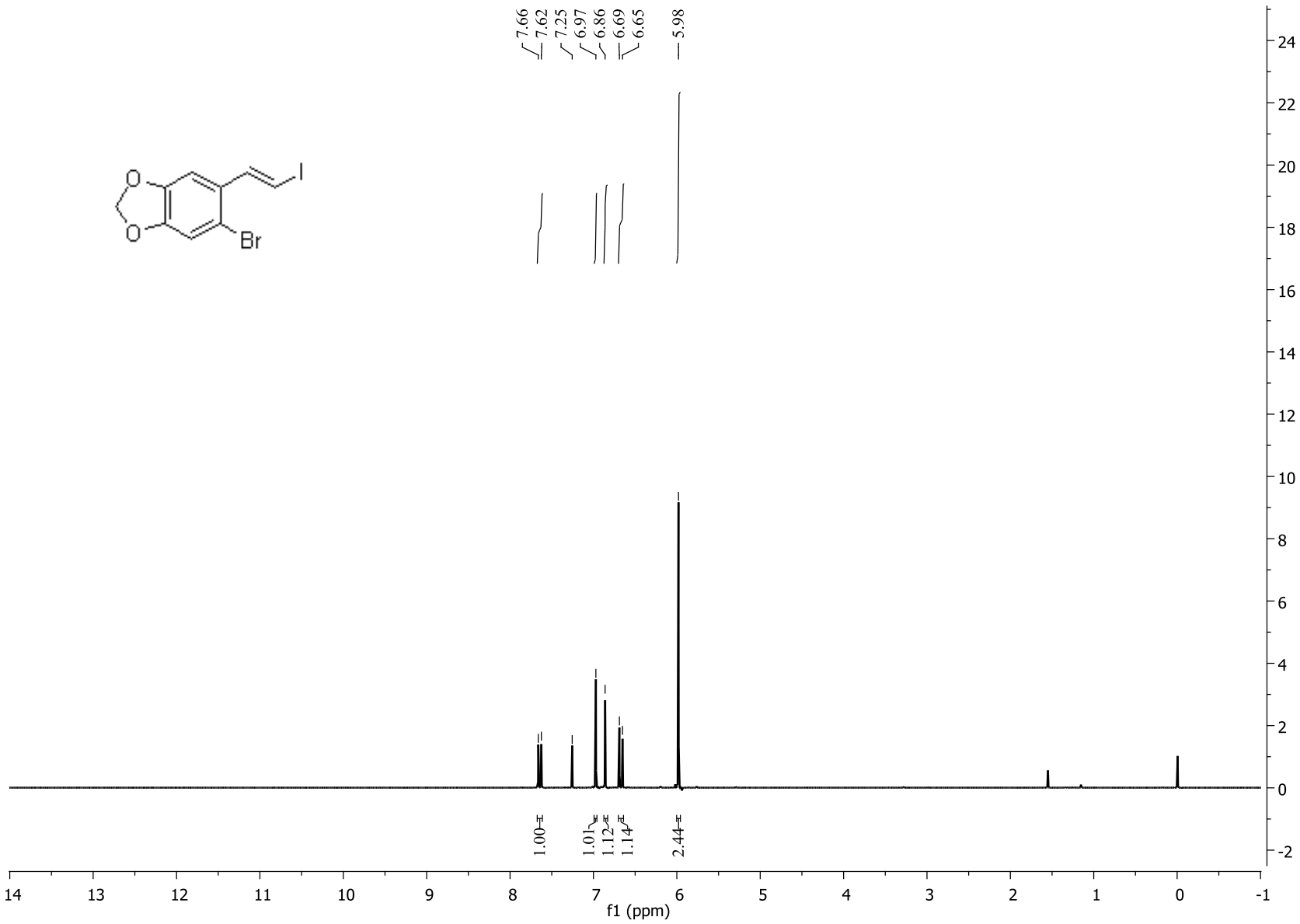
10, Scheme 2

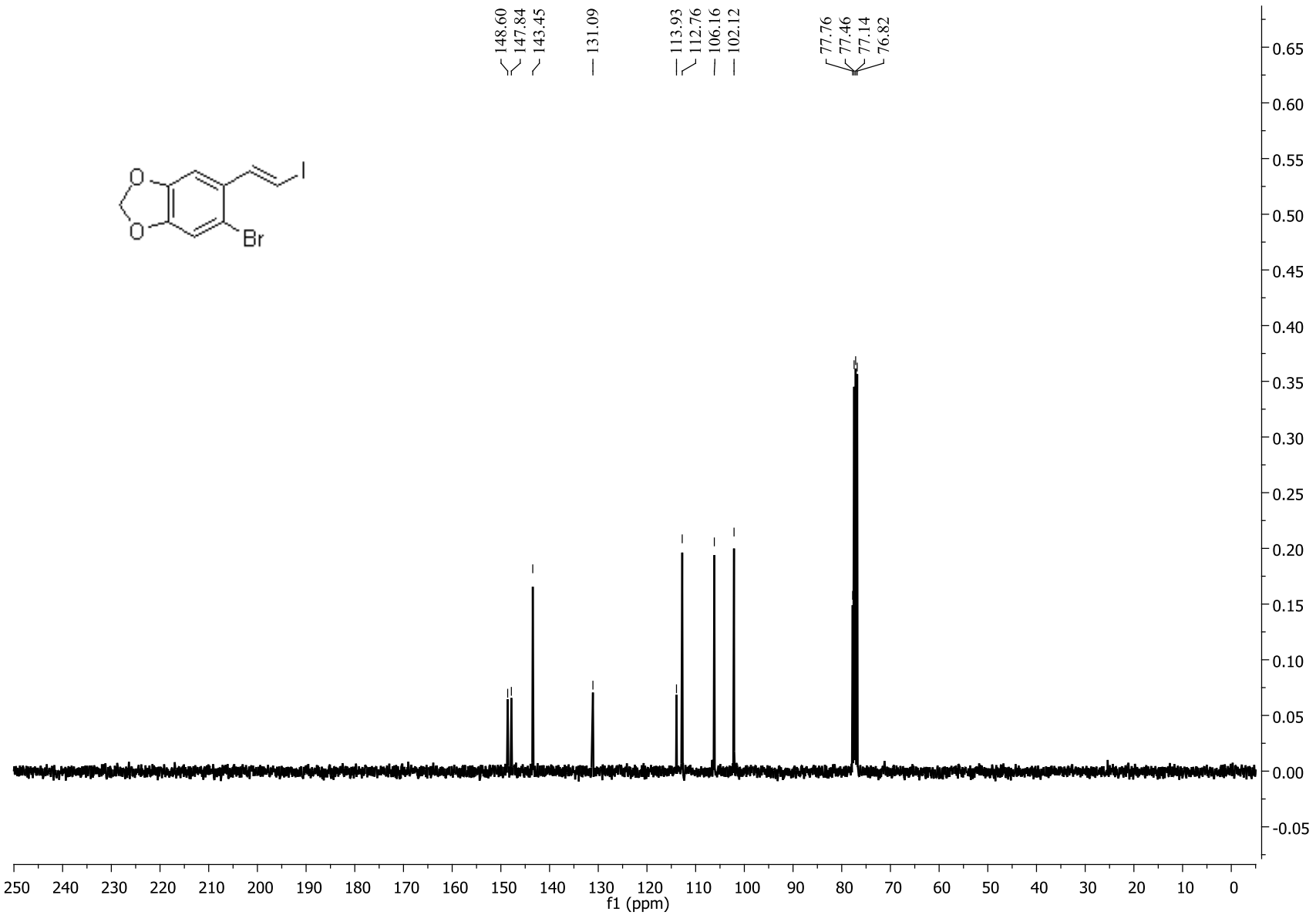


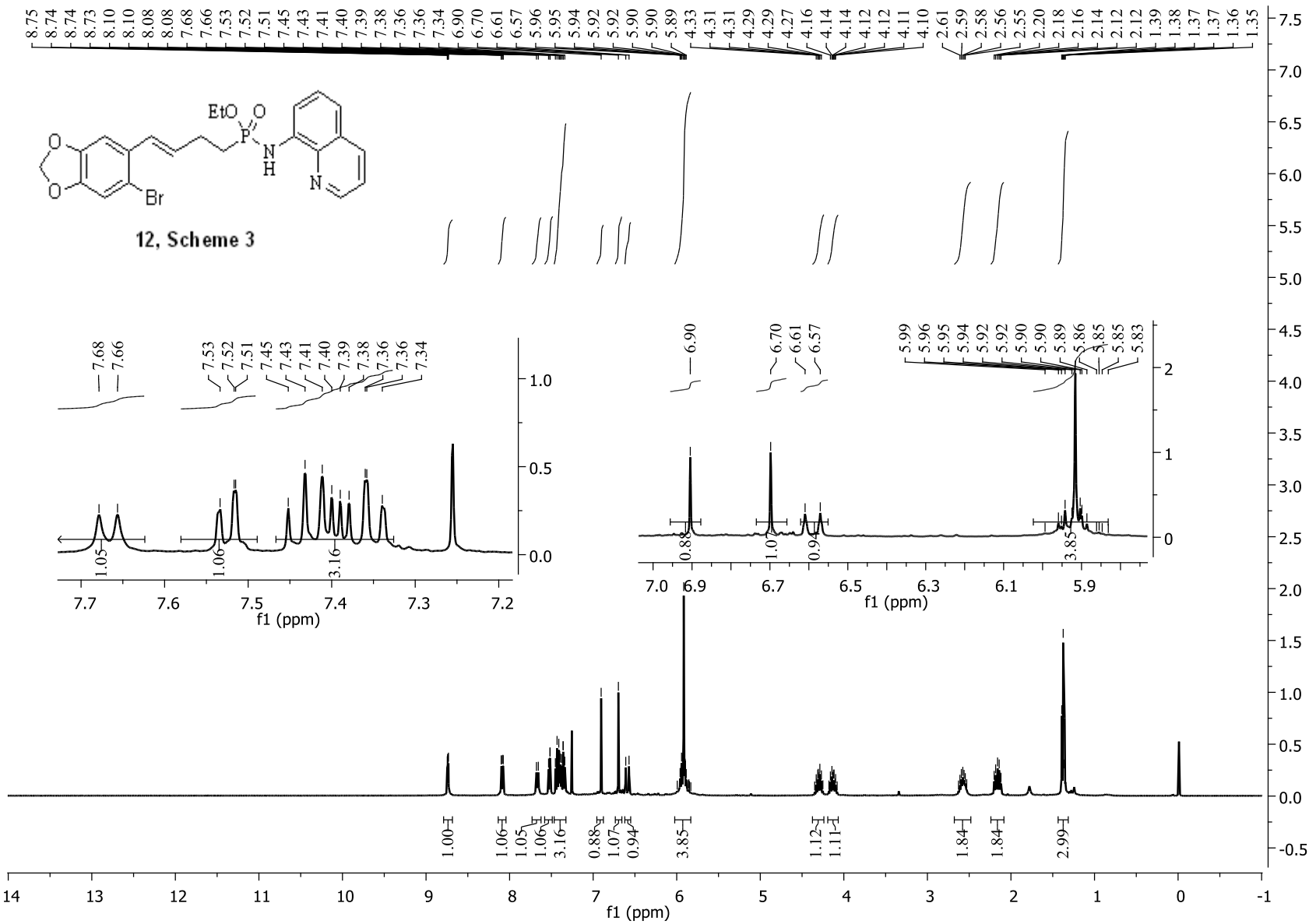


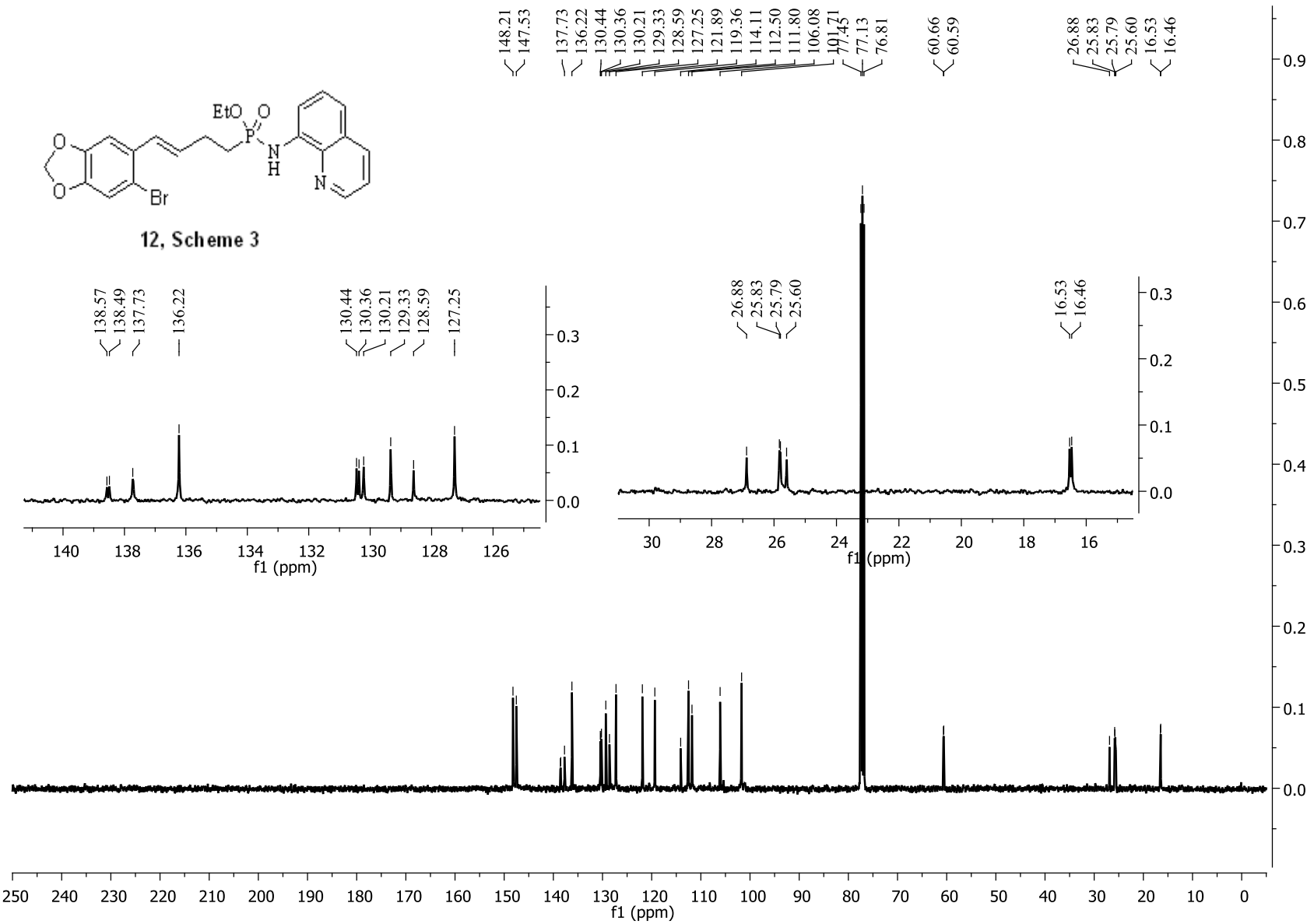


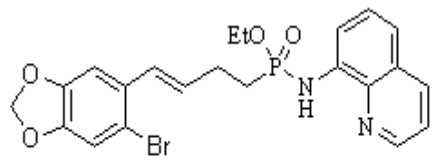
11, Scheme 2



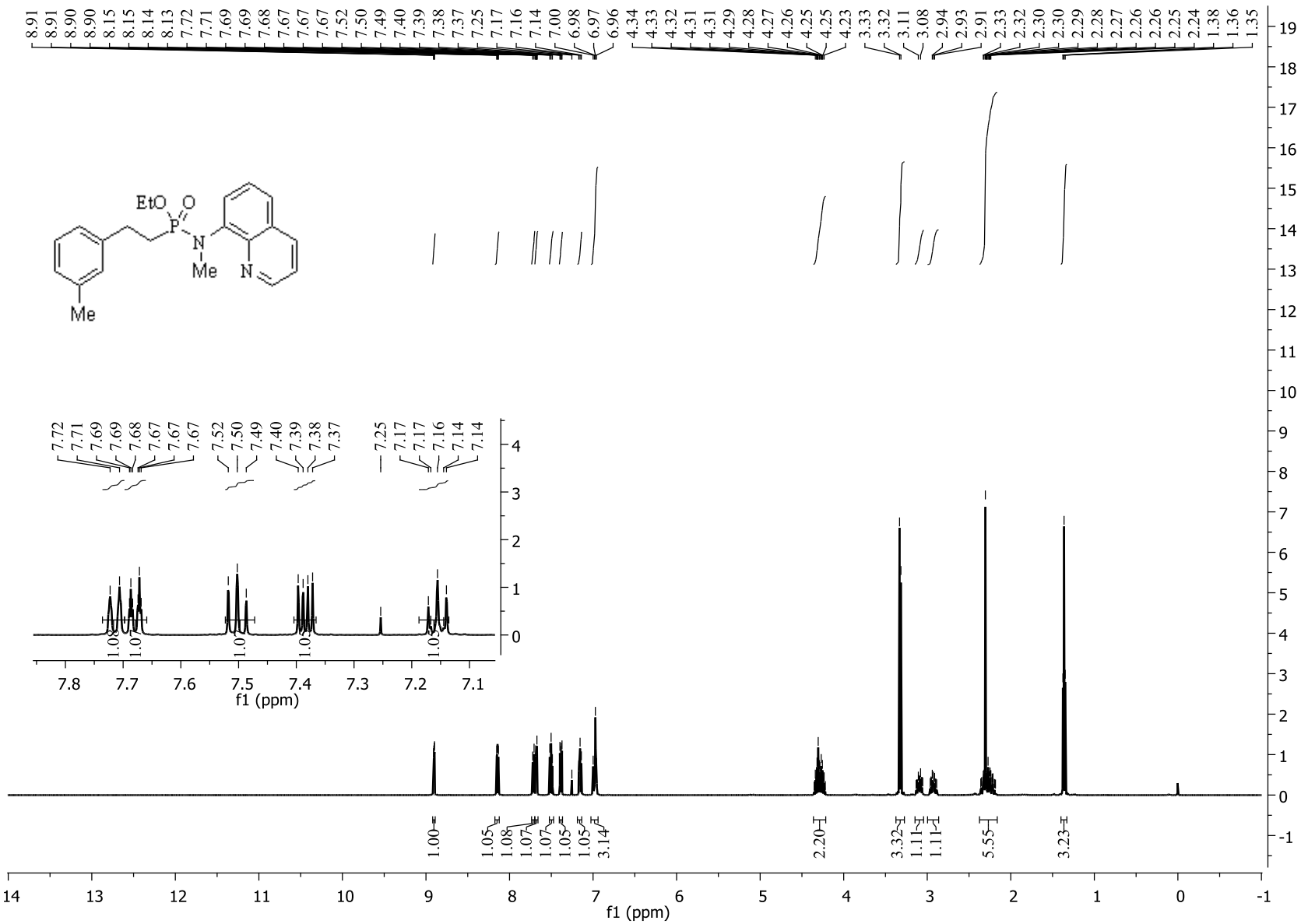


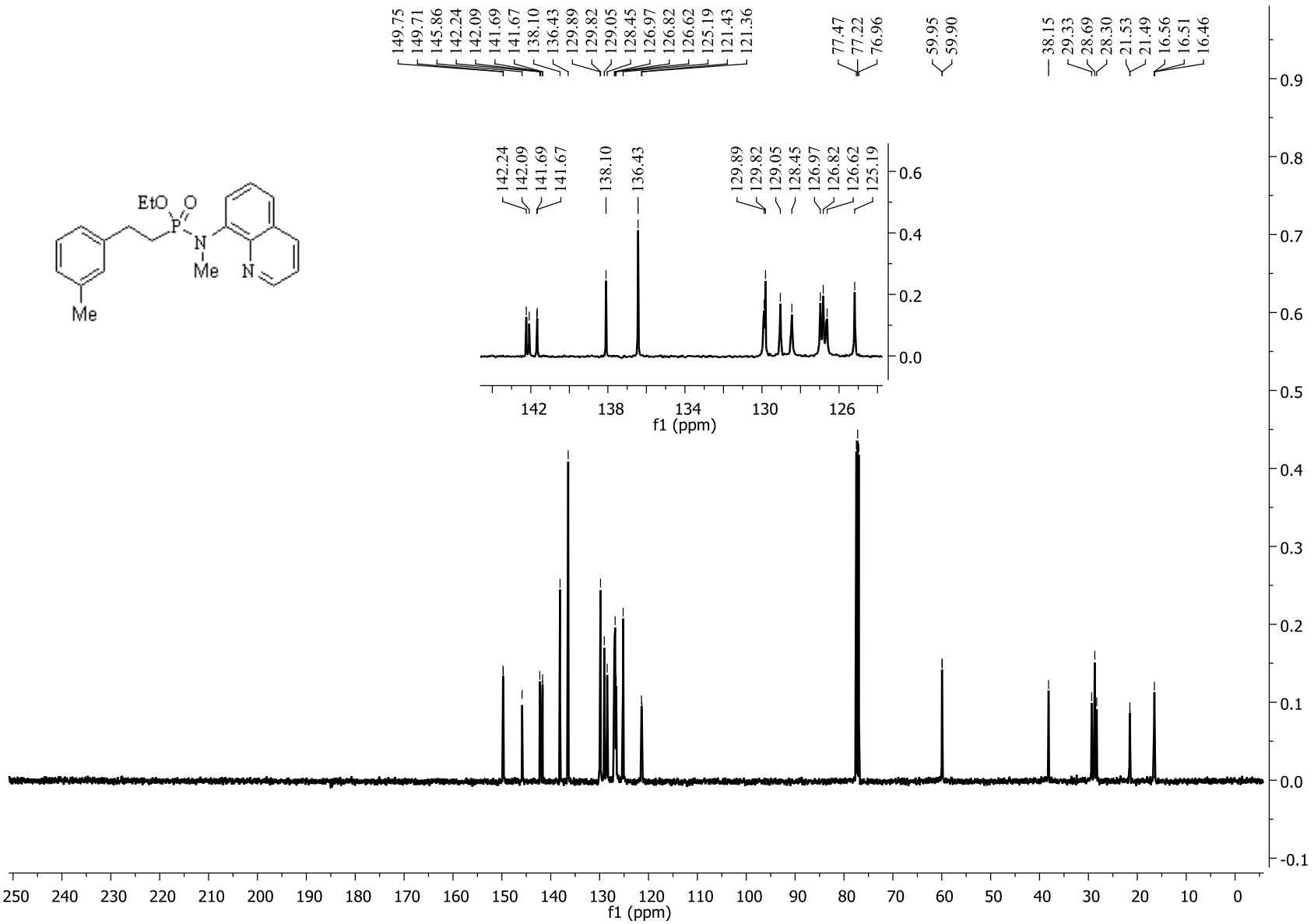


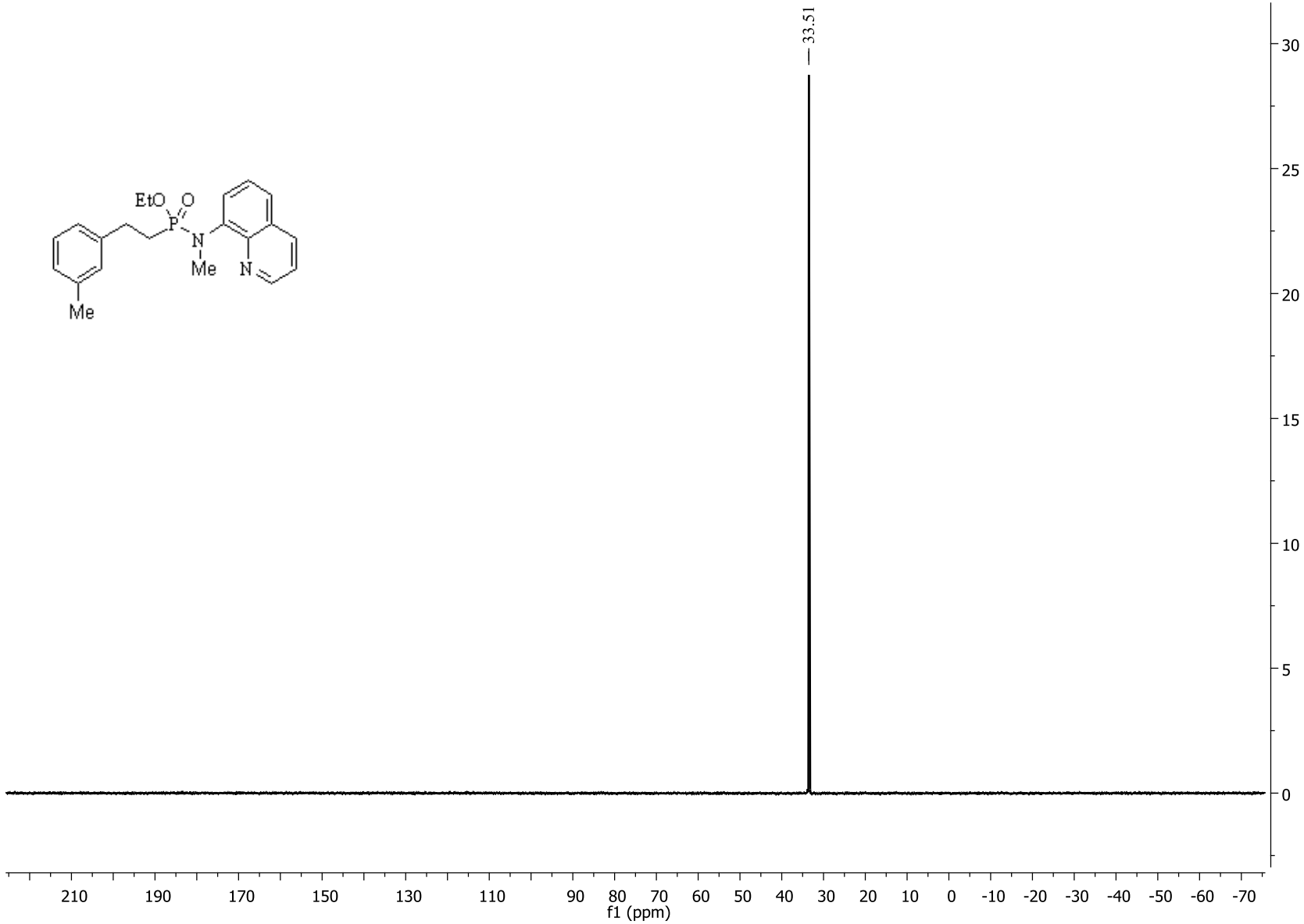


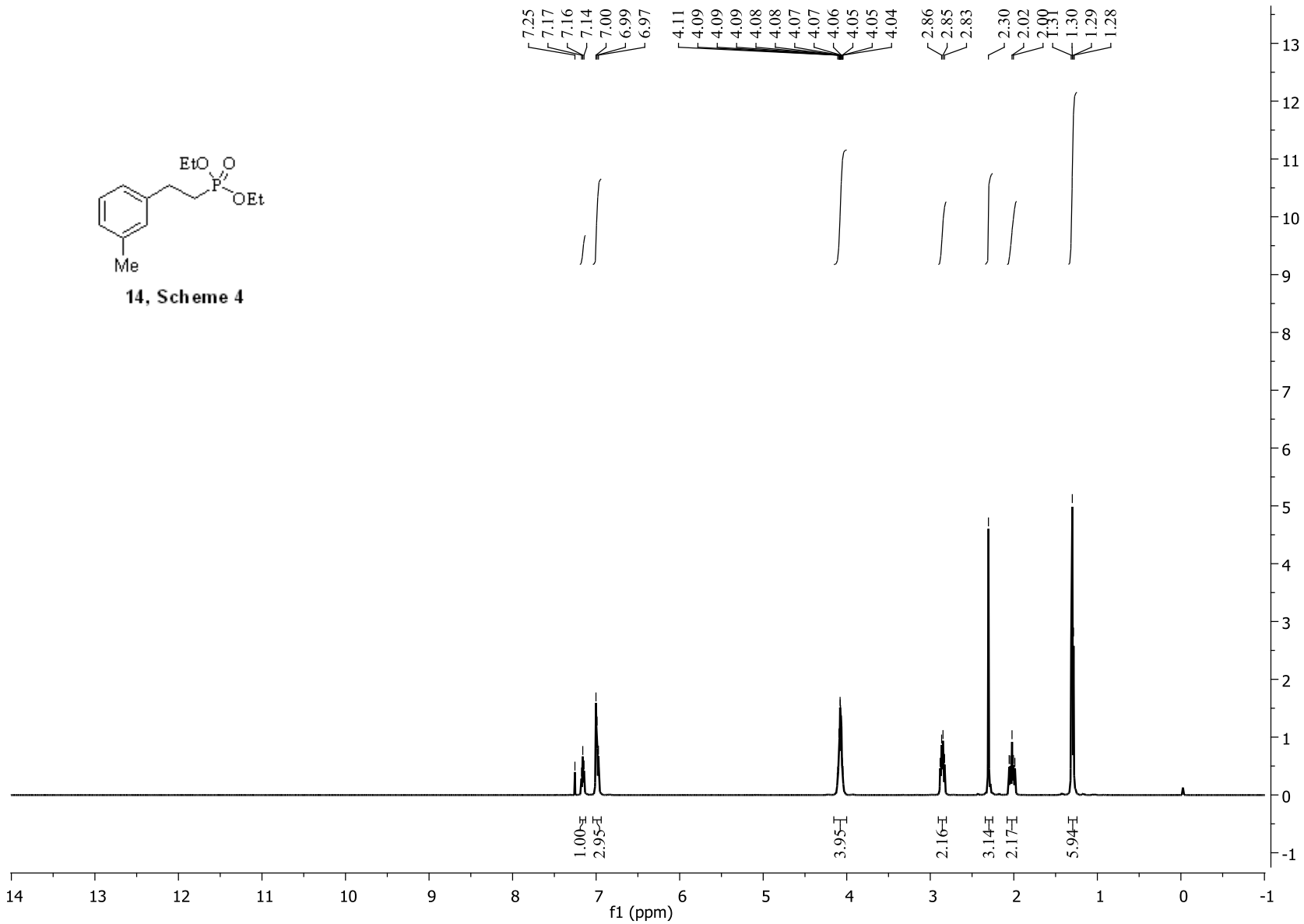


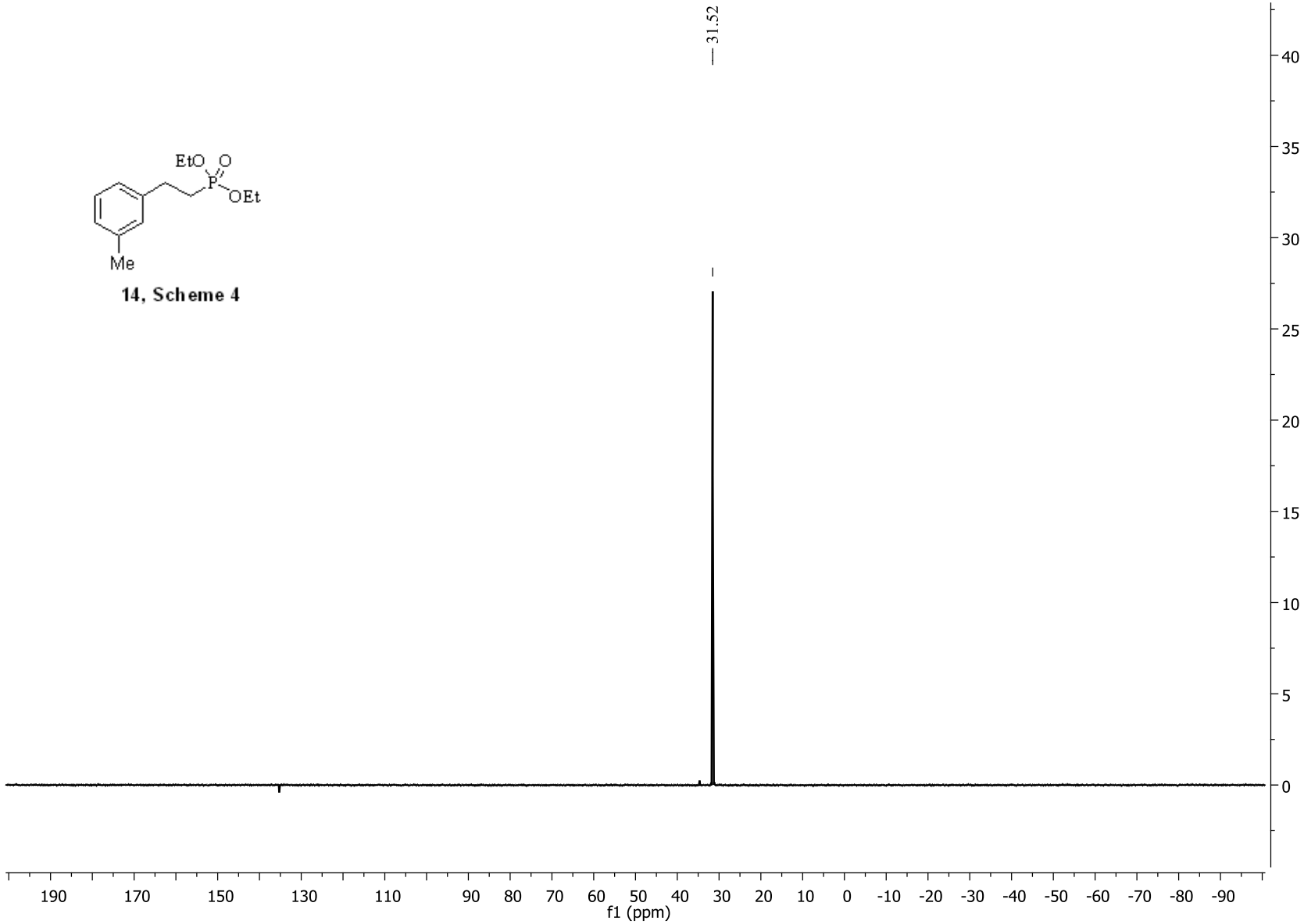
12, Scheme 3











14, Scheme 4