Axially chiral P-N ligands for the copper catalysed β-borylation of α,β-unsaturated esters.

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Supporting Information

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1. Experimental Procedures

1.1 General Experimental

All reactions were performed under anhydrous conditions and an inert atmosphere of nitrogen in the oven-dried glassware with magnetic stirring. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogenous materials, unless otherwise indicated. Reagents were used as obtained from commercial sources or purified according to the guidelines of Perrin and Armarego.[1] Evaporation in vacuo refers to the removal of volatiles on a Büchi rotary evaporator with an integrated vacuum pump. Flash chromatography was carried out using Merck Kiesegel 60 F254 (230–400 mesh) silica gel following the method of Still et al.[2] Thin-layer chromatography (TLC) was performed on Merck DC-Alufolien plates pre-coated with silica gel 60 F254. They were visualized either by quenching of ultraviolet fluorescence, or by charring with an acidic vanillin soln. (vanillin, H_2SO_4 and acetic acid in MeOH). The Microanalytical Laboratory, University College Dublin, performed elemental analyses. Electrospray mass spectra were recorded on a Micromass Quattro with electrospray probe. Exact mass ESI mass spectra (HRMS) were measured on a micromass LCT orthogonal time of flight mass spectrometer with leucine enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass. ^{1}H NMR spectra were recorded on a 300 MHz Varian-Unity spectrometer, a 400 MHz Varian-Unity spectrometer or a 500 MHz Varian-Unity spectrometer. Chemical shifts are quoted in ppm relative to tetramethylsilane and coupling constants (J) are quoted in Hz and are uncorrected. $CDCl_3$ was used as the solvent for all NMR spectra unless otherwise stated. 75.4 MHz ^{13}C spectra were recorded on a 300 MHz Varian-Unity spectrometer, 101 MHz ^{13}C spectra on a 400 MHz Varian-Unity spectrometer and 125 ^{13}C spectra on a 500 MHz Varian-Unity spectrometer. Tetramethylsilane was used as the internal standard in all ^{13}C spectra recorded. 121.4 MHz ^{31}P spectra were recorded on a 300 MHz Varian-Unity spectrometer and 162 MHz ^{31}P spectra on a 400 MHz Varian-Unity spectrometer. ^{31}P Chemical shifts are reported relative to 85% aqueous phosphoric acid (0.0 ppm). All

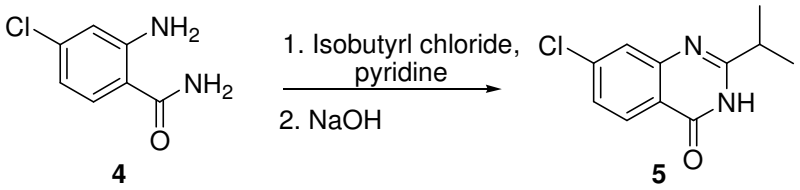
[1] D. D. Perrin, W. L. F. Armarego, *Purification of Laboratory Chemicals*, Pergamon Press: New York, 1988.

[2] W. C. Still, M. Hahn, A Mitra, *J. Org. Chem.* 1978, **43**, 2923–2925.

reaction solvents were distilled before use, unless otherwise indicated. Anhydrous solvents were obtained from a PureSolv-300-3-MD dry solvent dispenser and used without further purification unless otherwise stated. Melting points (mp) are quoted to the nearest 0.5 °C. GC and HPLC analysis was carried out using a Supelco 2-4304 beta-Dex® 120 (30 m x 0.25 mm, 0.25 mm film) and a Chiralcel OD column (0.46 cm I.D. x 25 cm) respectively. Optical rotation values were measured on a Perkin Elmer 241 Polarimeter. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}.

1.2 Synthesis and resolution of Quinazolinap 2c

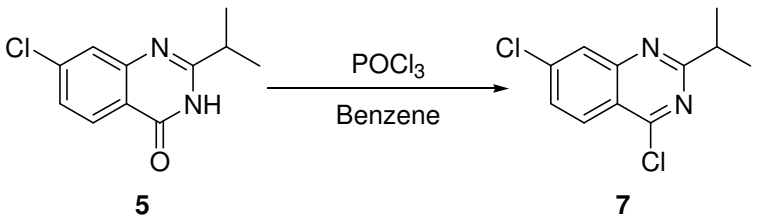
7-chloro-2-isopropylquinazolin-4(3H)-one 5



4 **5**

To a solution of 2-amino-4-chlorobenzamide **4** (15.0 g, 88 mmol) and pyridine (7.6 g, 97 mmol) in dichloromethane (150 mL) was added isobutyrl chloride (10.3 g, 97 mmol) slowly *via* syringe and stirred for 1 h. The pale yellow solid formed was filtered and taken up in a solution of aqueous NaOH (5 %, 120 mL) and heated at reflux for 30 min. The solution was cooled to room temperature and acidified to pH ~ 3 with HCl (1 M). The solid was filtered and washed with water to yield the title compound as a white fibrous solid (17.4 g, 89 %). Mp = 200 – 201 ^{o}C. ^{1}H NMR (300 MHz, [D_6]-DMSO) δ = 12.27 (br. s, 1H), 8.06 (br. s, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 1.9 Hz, 1H), 2.88 (sep., *J* = 6.9 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 6H) ppm. ^{13}C {^{1}H} NMR (125 MHz, [D_6]-DMSO) δ = 164.0, 162.0, 150.7, 139.6, 128.5, 126.9, 126.8, 120.5, 34.1, 21.0 ppm. IR (KBr): υ_{max} = 3173, 2930, 1669, 1101 cm^{-1}. $C_{11}H_{12}N_2O$ requires: C 59.33, H 4.98, N 12.55. Found: C 59.20, H 4.95, N 12.40. HRMS calcd. for $C_{11}H_{11}N_2OCl$ 222.0560, found 222.0571.

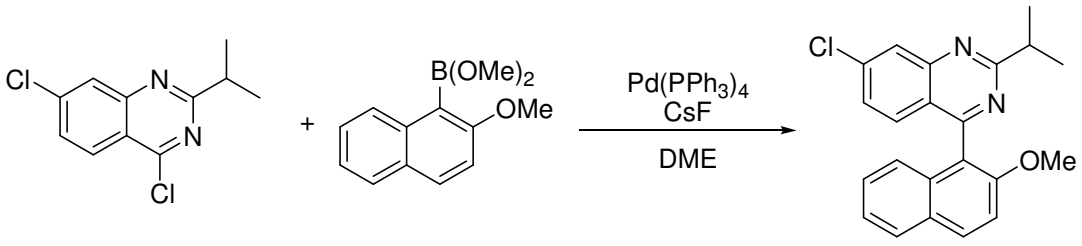
4,7-dichloro-2-isopropylquinazoline 7



5 **7**

A solution of 7-chloro-2-isopropylquinazolin-4(3H)-one (11.4 g, 51 mmol) and N,N-diethylaniline (11.4 g, 76.5 mmol) in benzene (250 mL) was azeotropically dried. To this was added $POCl_3$ (5.2 g, 34 mmol) *via* syringe and stirred at reflux for 3 h resulting in a deep red solution. The mixture was cooled to room temperature, diluted with ethyl acetate (150 mL) and washed sequentially with water (2 x 150 mL), HCl (1 M, 2 x 150 mL), water (150 mL), brine (150 mL), $NaHCO_3$ (150 mL), water (150 mL) and brine (150 mL). The solution was dried ($MgSO_4$) and volatiles removed *in vacuo* to give a red solid. This was purified by column chromatography with pentane:ethyl acetate (4:1) to yield the title compound as a low melting solid. (8.4 g, 69 %) ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.15 (d, J = 8.9, 1H), 8.00 (d, J = 1.7, 1H), 7.6 (dd, J = 8.9, 1.8, 1H), 3.31 (sep., J = 6.9 1H), 1.14 (d, J = 6.9, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 172.2, 162.1, 152.0, 140.0, 128.9, 127.5, 127.0, 120.6, 37.2, 21.4 ppm. IR (NaCl): υ_{max} = 2969, 1605, 1572, 1468, 1330, 1311 cm^{-1}. HRMS calcd. for $C_{11}H_{10}N_2Cl_2$ 240.0221, found 240.0216.

7-chloro-2-isopropyl-4-(2-methoxynaphthalen-1-yl)quinazoline 8

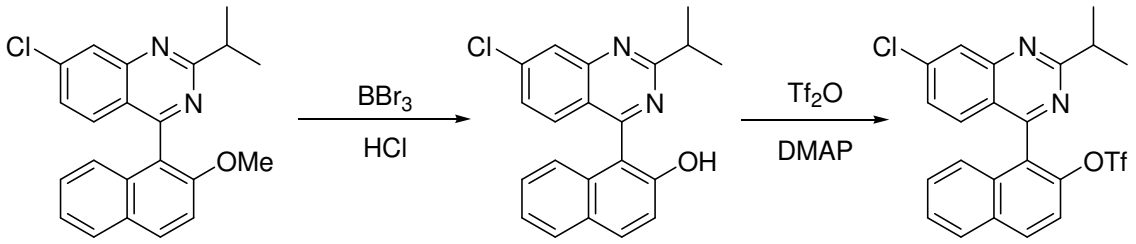


7 **12** **8**

4,7-dichloro-2-isopropylquinazoline (3.0 g, 12.4 mmol) and $Pd(PPh_3)_4$ (0.43 g, 0.37 mmol) were dissolved in DME (60 mL) to form a yellow solution. To this was added 2-methoxynaphthalen-1-ylboronic acid (2.5 g, 12.4 mmol) and caesium fluoride (3.8 g, 24.8 mmol). The mixture was stirred at 80 ^{0}C for 6 h (TLC). After cooling to room temperature, water (40 mL) and dichloromethane (40 mL) were added. The organic layer was separated and extraction was completed with further portions of dichloromethane, dried ($MgSO_4$) and reduced *in vacuo* to give a yellow oil which was purified by column chromatography pentane:ethyl acetate (2:1) to give the title compound as a white solid (2.46 g, 55 %). M.p. 128.5 – 129 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.10 (d, = 1.9 Hz, 1H), 8.03 (d, *J* = 9.1 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 9.1 Hz, 1H), 7.40-7.37 (m, 1H), 7.34 (~dt, *J* = 9.1, 1.2 Hz, 1H), 7.31 (d, *J* = 1.8 Hz, 1H), 7.29 (d, *J* = 2.1 Hz, 1H), 7.11 (d, *J* = 8.5, 1H), 3.48 (sept., *J* = 6.9, 1H), 1.51 (d, *J* = 2.4, 3H), 1.49 (d, *J* = 2.5, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.9, 167.3, 154.9, 151.7, 139.8, 133.2, 131.6, 129.4, 128.6, 128.3, 127.8, 127.8, 127.5, 124.4, 124.2, 122.3, 119.8, 113.6, 56.8, 38.3, 22.2, 21.7 ppm. . IR (KBr disc): υ_{max} =3006, 2964, 2921, 1555 and 1275.

HRMS calcd. for $C_{22}H_{19}ClN_2O$ 262.1186, found 262.1201. $C_{22}H_{19}ClN_2O$ requires C 72.82, H 5.28, N 7.72. Found C 72.72, H 5.50, N 7.57. IR (KBr disc): υ_{max} =3006, 2964, 2921, 1555 and 1275.

1-(7-chloro-2-isopropylquinazolin-4-yl)naphthalen-2-yl trifluoromethanesulfonate 10

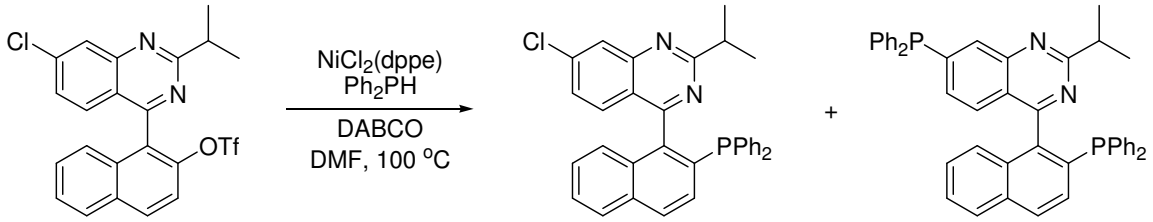


8 **9** **10**

To a solution of 7-chloro-2-isopropyl-4-(2-methoxynaphthalen-1-yl)quinazoline (2.0 g, 6.4 mmol) was added a solution of BBr_3 in dichloromethane (1 M, 12.8 mL). The resulting dark red/black solution was stirred at room temperature for 16 h. HCl (1 M, 30 mL) was added and stirred for 30 min resulting in an orange precipitate. This was filtered and dried thoroughly. A sample (100 mg) of the crude was purified for analysis. Mp = 156 – 157 ^{o}C. . ^{1}H NMR (400 MHz, $CDCl_3$); δ = 9.91 (br. s, 1H), 8.08 (d, *J* = 2.1 Hz, 1H), 7.94 (d, *J* = 8.9 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.31 – 7.26 (m, 3H), 3.45 (sept, *J* = 6.9 Hz, 1H), 1.50 (d, *J* = 6.9 Hz, 3H), 1.50 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz $CDCl_3$); δ = 171.3, 165.8, 155.3, 152.6, 140.4, 133.0, 132.3, 129.4, 128.8, 128.5, 127.8, 127.5, 126.9, 124.8, 123.8, 120.5, 119.2, 113.9, 37.7, 21.9, 21.3 ppm. HRMS calcd for $C_{21}H_{17}ClN_2O$ 348.1029, found 348.1032. IR (NaCl); 2969, 1603, 1346, 1278, 1090 cm^{-1}. The remaining crude naphtol was transferred to a suitable round bottom flask and suspended in dry dichloromethane (20 mL). N,N-dimethylaminopyridine (2.3 g, 19.2 mmol) was added to give a dark brown solution. Trifluoromethanesulfonic anhydride (2.0 g, 7.04 mmol) was added over 5 min and stirred for 16 h. The resulting solution was washed with HCl (1 M, 20 mL) and extraction completed with further portions of dichloromethane. The organic layers were combined, dried ($MgSO_4$) and reduced *in vacuo*. Purification was by column chromatography with pentane:ethyl acetate (3:1) to yield the title compound as a white solid (2.5 g, 81 % from **8**). Mp = 84.5 - 86.5 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.14 (dd, *J*=5.39, 3.67 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.62-7.59 (m, 2H), 7.46 (ddd, *J* = 8.2,

6.9, 1.1 Hz, 1H), 7.36 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.30-7.23 (m, 3H), 3.47 (sept., *J* = 6.9 Hz, 1H), 1.48 (app. t, *J* = 7.2 Hz, 6H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz $CDCl_3$) δ = 173.0, 163.3, 151.8, 144.7, 140.5, 132.69, 132.5, 132.3, 128.7, 128.6, 128.5, 128.1, 127.8, 127.7, 127.2, 126.1, 121.7, 119.6, 118.2 (q, *J* = 320 Hz) 38.3, 21.9, 21.7 ppm (one carbon signal obscured). HRMS calcd. for $C_{22}H_{17}ClN_2O_3F_3S$ 481.0601, found 481.0595 $[M+H]^+$. $C_{22}H_{16}ClF_3N_2O_3S$ requires C 54.95, H 3.35, N 5.83. Found C 54.90, H 3.51, N 5.66. IR (KBr disc): υ_{max} = 3057, 2981, 2876, 1606, 1509 and 1474.

7-chloro-4-(2-(diphenylphosphino)naphthalen-1-yl)-2-isopropylquinazoline 2c

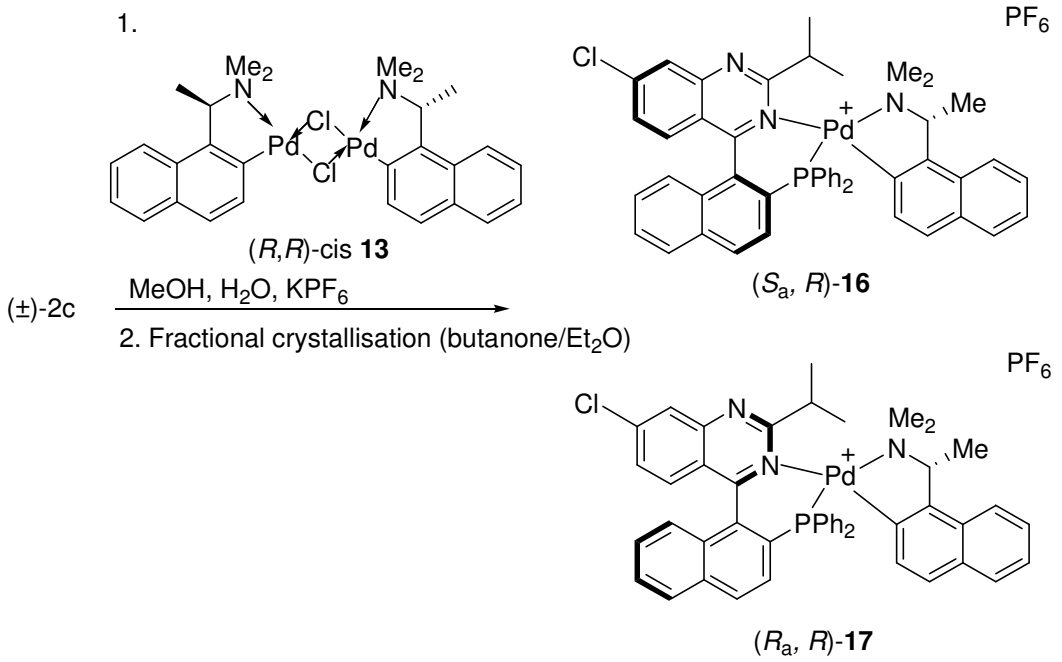


10 **2c** **11**

To a solution of $NiCl_2$(dppe) [144 mg, 0.77 mmol; dppe: 1,2-bis(diphenylphosphine)-ethane] in DMF (8 mL) was added Ph_2PH (780 mg, 4.2 mmol), and the mixture was stirred at 100 ^{0}C for 30 min. A solution of triflate **10** (2.7 g, 5.6 mmol) and DABCO (2.5 g, 22.3 mmol) in DMF (8 mL) was added *via* cannula to give initially a pale green transparent solution which over the course of 1 h became a dark brown solution. After 1 h a second portion of Ph_2PH (780 mg, 4.2 mmol) was added. After 24 h at 100 ^{o}C the solution was cooled to room temperature and filtered through Celite® the residue was reduced *in vacuo* and taken up in dichloromethane and washed with water and brine. The organic layer was dried ($MgSO_4$), and concentrated *in vacuo* to give a brown oil. Flash chromatography (silica gel, pentane/EtOAc 4:1) gave a mixture of the mono- and diphosphenylated products. These were isolated by column chromatography (silica gel, pentane/EtOAc 9:1). The monocoupled product was isolated as a white solid (980 mg, 35 %) mp 142 – 143 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.07 (d, *J* = 1.8 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.51 (dt, *J* = 7.9, 0.8 Hz, 1H), 7.36 (dd, *J* = 8.6, 3.1 Hz, 1H), 7.32 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.30 – 7.20 (m, 9H), 7.19 (d, *J* = 1.9 Hz, 1H),

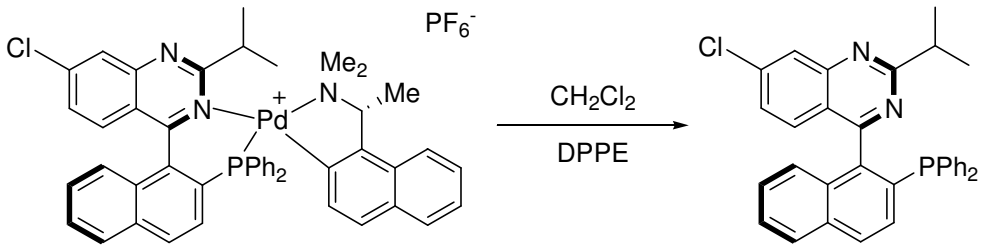
7.13 (t, *J* = 6.9 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 1H), 3.25 (sept, *J* = 6.9 Hz, 1H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.24 (d, *J* = 6.8 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz $CDCl_3$) δ = 172.4, 169.1 (d, J_{C-P} = 6.7 Hz), 151.2, 141.6 (d, J_{C-P} = 32.6 Hz), 139.6, 137.0 (d, J_{C-P} = 11.8 Hz), 136.4 (d, J_{C-P} = 11.2 Hz), 134.6 (d, J_{C-P} = 15.1 Hz), 133.7 (d, J_{C-P} = 20.2 Hz), 133.5, 133.4 (d, J_{C-P} = 19.1 Hz), 131.8 (d, J_{C-P} = 8.8 Hz), 130.0, 129.3, 127.7, 128.4(d, J_{C-P} = 6.7 Hz), 128.4, 128.3 (d, J_{C-P} = 6.7 Hz), 128.2, 128.1, 127.7, 127.6, 127.1, 127.1, 126.0, 122.1, 37.9, 21.7, 21.1 ppm. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ = 13.5 ppm. $C_{33}H_{26}ClN_2P$ requires C: 76.66, H: 5.07, N: 5.42, Cl: 6.86, P: 5.99, found; C: 76.46, H: 5.18, N: 5.29, Cl: 6.91, P: 5.81. The dicoupled product was isolated as a white solid (1.1 g, 29 %). Mp = 98 – 99 °C. ^1H NMR (400 MHz, $CDCl_3$): 7.88 (d, *J* = 7.7, 3H), 7.49 (app t, *J* = 8.0, 1H), 7.42 – 7.28 (m, 12H), 7.28 – 7.10 (m, 14H), 3.23 (sept, *J* = 6.9, 3H), 1.25 (d, *J* = 6.9, 3H) ppm. $^{31}P\{^1H\}$ NMR (243 MHz, $CDCl_3$) δ = -3.2, -13.6 ppm. IR (KBr): υ_{max} = 3048, 2957, 1601, 1555, 1475, 1089 cm^{-1}. HRMS calcd. for $C_{33}H_{27}N_2ClP$ 517.1600, found 517.1588 $[M+H]^+$. $C_{45}H_{36}N_2P_2$ requires: C 81.06, H 5.44, N 4.20. Found : C 80.80, H 5.61, N 4.48.

7-chloro-4-(2-(diphenylphosphino)naphthalen-1-yl)-2-isopropylquinazoline resolution complex



(+)-di-μ-chlorobis[(R)-dimethyl(1-(1-naphtyl)ethyl)-aminato-C_2,N]dipalladium(II) (131 mg, 0.2 mmol) and (*R,S*) 7-chloro-4-(2-(diphenylphosphino)naphthalen-1-yl)-2-isopropylquinazoline (200 mg, 0.4 mmol) were dissolved in MeOH (10 mL) and stirred for 16 h to give a yellow solution. To this was added KPF_6 (74 mg, 0.4 mmol) in water (5 mL) upon which a yellow precipitate formed. Stirring was continued for 10 min and filtered to yield a yellow powder which was shown to be a 1:1 mixture of the (*R,R*) and (*S,R*) bidentate complex (^{31}P NMR showed two peaks of equal intensity at 33.9 and 40.9 ppm). Crystallisation from butanone/diethyl ether gave a single diasteriomer (77 mg, 40 %). Mp 219.5 – 220.0 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.18 (d, *J* = 8.7 Hz, 1H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 1.9 Hz, 1H), 7.77 – 7.61 (m, 4H), 7.59 – 7.51 (m, 1H), 7.49 – 7.10 (m, 10H), 7.07 (d, *J* = 8.5 Hz, 1H), 6.88 (d, *J* = 9.1 Hz, 2H), 6.77 – 6.60 (m, 4H), 4.36 - 4.24 (m, 2H), 2.70 (d, *J* = 2.2, 3H), 2.48 (d, *J* = 3.4, 3H), 1.78 (d, *J* = 6.6, 3H), 1.60 (d, *J* = 6.6, 3H), 1.30 (d, *J* = 6.3, 3H) ppm. ^{13}C{^{1}H} NMR (150 MHz $CDCl_3$) δ = 170.5, 165.3 (d, $J_{C\text{-}P}$ = 6.2 Hz), 151.5, 150.1, 149.1, 142.8, 136.4 (d, $J_{C\text{-}P}$ = 12.3 Hz), 136.3 (d, $J_{C\text{-}P}$ = 12.3 Hz), 135.4 (d, $J_{C\text{-}P}$ = 11.2 Hz), 134.1, 132.7 (d, $J_{C\text{-}P}$ = 8.4 Hz), 132.4, 132.1, 132.0 (d, $J_{C\text{-}P}$ = 8.4 Hz), 131.7, 130.1, 129.8, 129.4, 129.1, 129.0, 128.7 (d, $J_{C\text{-}P}$ = 5.1 Hz), 127.5, 127.1, 126.8, 126.7, 128.7 (d, $J_{C\text{-}P}$ = 5.1 Hz), 127.5, 127.1, 126.8, 126.7, 126.3 (d, $J_{C\text{-}P}$ = 6.2 Hz), 125.3 (d, $J_{C\text{-}P}$ = 6.2 Hz), 125.1, 125.1, 123.8, 123.5, 123.1, 122.0, 121.3, 73.8, 51.5, 48.3, 38.2, 24.2, 23.2, 22.3 ppm. ^{31}P{^{1}H} NMR (243 MHz, $CDCl_3$) δ = 33.9 ppm. IR = 2361, 1604, 1565, 842 cm^{-1}. $C_{47}H_{42}ClF_6N_3P_2Pd$ requires: C 58.40, H 4.38, N 4.35. Found C 58.27, H 4.44, N 4.26. $[\alpha]^{21}_{D}$ = -199^{o} (*c* 1, $CHCl_3$)

Decomplexation of enantiopure 7-chloro-4-(2-(diphenylphosphino)naphthalen-1-yl)-2-isopropylquinazoline (R_a)-2c



(R_a,*R*)-**17** (R_a)-**2c**

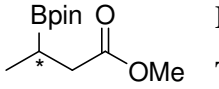
The palladium complex (313 mg, 0.4 mmol) was dissolved in dichloromethane (5 mL) and to this was added 1,2-bis(diphenylphosphine)ethane (159 mg, 0.4 mmol) and stirred for 3 h at room temperature. Solvent was removed *in vacuo* and the resulting solid was purified by column chromatography (CH_2Cl_2) to give (R_a)-7-chloro-4-(2-(diphenylphosphino)naphthalen-1-yl)-2-isopropylquinazoline as a white solid (95 %). $[\alpha]^{21}_D = +102^o$ (*c* 1, $CHCl_3$). Identical in all other respects to previously prepared racemic sample. The stereochemistry was assigned by X-ray crystallography.

General procedure for the borylation of α,β-unsaturated esters: THF (3 mL) was added to CuCl (0.010 mmol, 1 mg), NaO*t*Bu (0.015 mmol, 1.4 mg) and ligand (0.020 mmol) in a dry Schlenk tube under nitrogen. The mixture was stirred for 30 min. at room temperature, at this point bis(pinacolato)diboron (0.550 mmol, 139.7 g) was added and stirred for a further 10 mins. The α,β-unsaturated ester (0.500 mmol) was then added followed by MeOH (1 mmol, 0.040 mL). Stirring was continued for 6 h and a sample removed for ^{1}H NMR analysis.

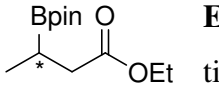
Oxidation: To the reaction vessel in which the borylation reaction was carried out was added water (2.5 mL) and sodium perborate monohydrate (2.0 mmol, 0.20 g). The reaction mixture was stirred for 12 h at room temperature at which time a further portion of water (2.5 mL) was added. The product was extracted with ethyl acetate (3 x 15 mL) and the combined organics washed with brine, dried over $MgSO_4$ and volatiles reduced *in vacuo* to give a clear oil which was used without further purification for the final derivatisation.

Acylation: The oxidised product was dissolved in dry dichloromethane (3 mL) in a dry Schlenk and to this was added triethylamine (1 mL), DMAP (6 mg, 0.05 mmol) and acetic anhydride (0.150 mL, 1.6 mmol). The mixture was heated to 50 ^{o}C for 1 h. The product was purified by silica gel chromatography to give a colourless oil. Ees were determined using GC analysis.

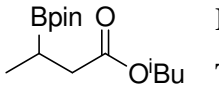
Preparation of Phenoxy derivative of the product of borylation of *t*-Butyl crotonate: (for the borylation of *t*-butyl crotonate, the acylated derivative proved inseparable by GC). The oxidised product was dissolved in THF and to this was added DMAP (19 mg, 0.26 mmol), triethylamine (174 μL, 1.25 mmol) and benzoyl chloride to give a white precipitate. Phenoxy acetic acid (95 mg, 0.625 mmol) was then added and stirred at room temperature for 1 h. The product was purified by silica gel chromatography to yield a colourless oil.



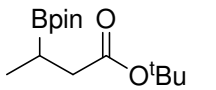
Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate: The title compound was prepared using the general procedure. ^{1}H NMR was carried out on the crude reaction mixture following removal of THF *in vacuo*. ^{1}H NMR (300 MHz, $CDCl_3$):δ = 3.58 (s, 3 H), 2.38 (dd, *J* = 16.4, 7.7 Hz, 1 H), 2.32 (dd, *J* = 16.3, 8.7 Hz, 1 H), 1.42-1.22 (m, 1 H), 1.17 (s, 12 H), 0.93 (d, *J* = 7.5) ppm.



Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate: The title compound was prepared using the general procedure. ^{1}H NMR was carried out on the crude reaction mixture following removal of THF *in vacuo*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.11 (q, *J* = 7.1 Hz, 2 H), 2.39 (dd, *J* = 16.3, 7.8 Hz, 1 H), 2.36 (dd, *J* = 16.6, 8.6 Hz), 1.45-1.30 (m, obs., 1 H), 1.23 (br. s, 15 H), 0.99 (d, *J* = 7.5 Hz, 3 H) ppm.

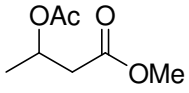


Isobutyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate: The title compound was prepared using the general procedure. ^{1}H NMR was carried out on the crude reaction mixture following removal of THF *in vacuo*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.77 (dd, *J* = 6.5, 3.6 Hz, 2 H), 2.35 (dd, *J* = 16.4, 7.6 Hz 1 H), 2.32 (dd, *J* = 16.3, 6.9 Hz, 1 H), 1.97-1.72 (m, 1 H), 1.42-1.24 (m, 1 H), 1.12 (s, 12 H), 0.93 (d, *J* =7.5, 3 H), 0.85 (d, *J* = 6.7, 6 H) ppm.

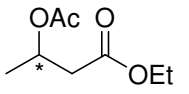


Tert-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate: The title compound was prepared using the general procedure. ^{1}H NMR was carried out on the crude reaction mixture following removal of THF *in vacuo*. ^{1}H

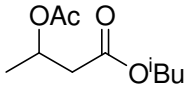
NMR (300 MHz, $CDCl_3$): δ = 2.32 (dd, *J* = 8.7, 16.6 Hz, 1 H), 2.27 (dd, *J* = 7.8, 16.6 Hz, 1 H), 1.36-1.25 (m, obs., 1 H), 1.25 (s, 12 H), 1.22 (s, 9 H), 0.97 (d, *J* = 7.44, 3 H) ppm.



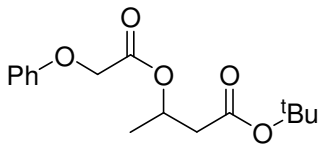
Methyl 3-acetoxybutanoate: Prepared using the general acylation procedure. Ees were determined using chiral GC; β-CD, 30 m, 80 °C, 11.4 psi, R_T = 17.4 min (*R*), 19.7 min (*S*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.31-5.18 (m, 1 H), 3.67 (s, 3 H), 2.57 (dd, *J* = 15.5, 7.5 Hz, 1 H), 2.55 (dd, *J* = 15.5, 5.8 Hz, 1 H), 2.01 (s, 3 H), 1.28 (d, *J* = 6.3 Hz, 3 H) ppm.



Ethyl 3-acetoxybutanoate: Prepared using the general acylation procedure. Ees were determined using chiral GC; β-CD, 30 m, 80 °C, 27.1 psi, R_T = 13.8 min (*R*), 14.5 min (*S*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.30-5.20 (m, 1 H), 3.60 (q, *J* = 7.28, 2 H), 2.57 (dd, *J* = 15.4, 7.4 Hz, 1 H), 2.54 (dd, *J* = 15.4, 8.0 Hz, 1 H), 2.01 (s, 3 H), 1.29 (t, *J* = 7.24 Hz, 3 H), 1.22 (d, *J* = 7.4, 3 H) ppm.



Butyl 3-acetoxybutanoate: Prepared using the general acylation procedure. Ees were determined using chiral GC; β-CD, 30 m, 100 °C, 14.5 psi, R_T = 17.9 min (*R*), 20.1 min (*S*). ^{1}H NMR (300 MHz, $CDCl_3$): δ =5.31-5.19 (m, 1 H), 3.85 (d, *J* = 6.6, 2 H), 2.56 (dd, *J* = 15.5, 7.5 Hz, 1 H), 2.54 (dd, *J* = 15.5, 5.6 Hz, 1 H), 1.99 (s, 3 H), 1.95-1.82 (m, 1 H), 1.28 (d, *J* = 6.3 Hz, 3 H), 0.90 (d, *J* = 6.7 Hz, 6 H) ppm.



***Tert*-butyl 3-(2-phenoxyacetoxy)butanoate:** Prepared as described above. Ees were determined using chiral HPLC, chiracel OD column, hexane:IPA (85:15), 1 mL/min. 220 nm. R_T = 20.7 (*S*) min, 31.8 min (*R*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (t, *J* = 7.6 Hz, 2H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 2H), 5.39 (sext, *J* = 6.6 Hz, 1H), 4.58 (s, 2H), 2.53 (dd, *J* = 15.5, 7.7 Hz, 1H), 2.50 (dd, *J* = 15.4, 7.8 Hz, 1H), 1.44 (s, 9H), 1.32 (d, *J* = 6.3 Hz, 3H) ppm.

Single Crystal X-ray Structure Data

Crystal data and structure refinement for Pd^{II} complex (S_a, *R*)-14.

Empirical formula	$C_{66}\ H_{52}\ N_4\ P_2\ Cl_4\ Cu_2$	
Formula weight	1231.94	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P–1 (#2)	
Unit cell dimensions	a = 10.7093(9) Å	α= 114.885(2)°.
	b = 12.0684(11) Å	β= 100.794(2)°.
	c = 13.4541(12) Å	γ = 96.372(2)°.
Volume	1514.0(2) $Å^3$	
Z	1	
Density (calculated)	1.351 Mg/m^3	
Absorption coefficient	0.975 mm^{-1}	
F(000)	632	
Crystal size	0.30 x 0.15 x 0.15 mm^3	
Theta range for data collection	1.73 to 22.51°.	
Index ranges	–11<=h<=11, –12<=k<=12, –14<=l<=14	
Reflections collected	9554	
Independent reflections	3953 [R(int) = 0.0228]	
Completeness to theta = 22.51°	99.8 %	
Absorption correction	Semi–empirical from equivalents	
Max. and min. transmission	0.8675 and 0.6626	
Refinement method	Full–matrix least–squares on F^2	
Data / restraints / parameters	3953 / 0 / 354	
Goodness–of–fit on F^2	1.103	
Final R indices [I>2sigma(I)]	R1 = 0.0535, wR2 = 0.1509	
R indices (all data)	R1 = 0.0666, wR2 = 0.1572	
Largest diff. peak and hole	1.391 and –0.474 e.$Å^{-3}$	

Crystal data and structure refinement for Cu^{I} complex of 2c.

The quinazoline unit showed signs of disorder in earlier stages of refinement. An attempt to refine this disorder did not lead to a chemically reasonable result, thus it was neglected in the final refinement. The residual electron density close to the isopropyl moiety is due to this unrefineable disorder: it marks the position of the minor occupied chlorine atom.

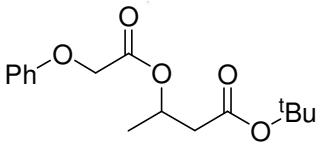
Empirical formula	$C_{66}\ H_{52}\ N_4\ P_2\ Cl_4\ Cu_2$	
Formula weight	1231.94	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P–1 (#2)	
Unit cell dimensions	a = 10.7093(9) Å	α= 114.885(2)°.
	b = 12.0684(11) Å	β= 100.794(2)°.
	c = 13.4541(12) Å	γ = 96.372(2)°.
Volume	1514.0(2) $Å^3$	
Z	1	
Density (calculated)	1.351 Mg/m^3	
Absorption coefficient	0.975 mm^{-1}	
F(000)	632	
Crystal size	0.30 x 0.15 x 0.15 mm^3	
Theta range for data collection	1.73 to 22.51°.	
Index ranges	–11<=h<=11, –12<=k<=12, –14<=l<=14	
Reflections collected	9554	
Independent reflections	3953 [R(int) = 0.0228]	
Completeness to theta = 22.51°	99.8 %	
Absorption correction	Semi–empirical from equivalents	
Max. and min. transmission	0.8675 and 0.6626	
Refinement method	Full–matrix least–squares on F^2	
Data / restraints / parameters	3953 / 0 / 354	
Goodness–of–fit on F^2	1.103	
Final R indices [I>2sigma(I)]	R1 = 0.0535, wR2 = 0.1509	
R indices (all data)	R1 = 0.0666, wR2 = 0.1572	
Largest diff. peak and hole	1.391 and –0.474 e.$Å^{-3}$	

HPLC and GC Traces

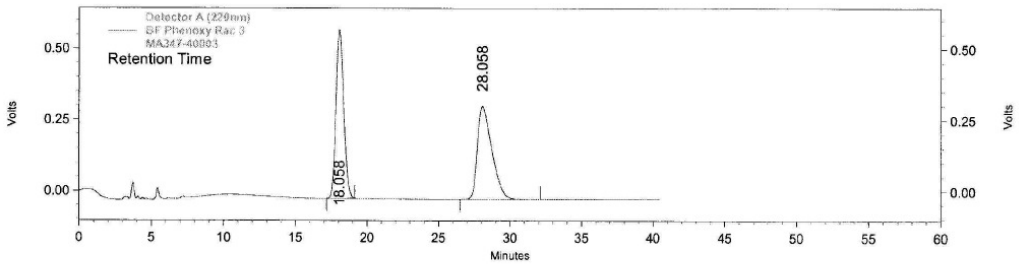
Shimadzu CLASS-VP V6.10 *Area % Report* **Page 1 of 1**

Method Name: C:\CLASS-VP\Brian\EV1.met
Data Name: C:\CLASS-VP\Billy\MA347-40003
User: System
Acquired: 20/10/2008 15:52:41
Printed: 23/10/2008 14:48:12

Racemic



Racemic



Detector A (220nm)

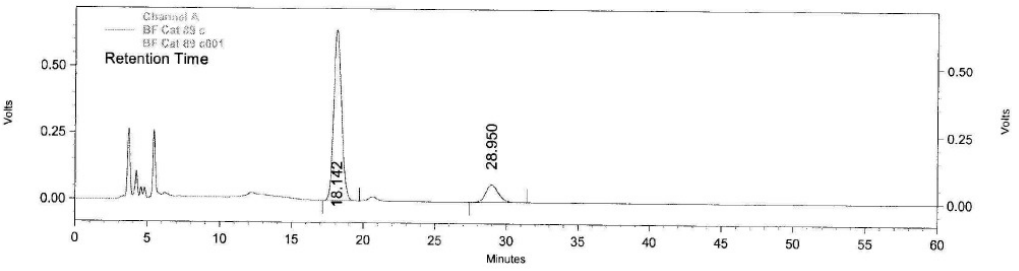
Pk #	Retention Time	Area	Area %	Height	Height %
1	18.058	22288760	49.450	593409	64.580
2	28.058	22784288	50.550	325468	35.420

Shimadzu CLASS-VP V6.10 *Area % Report* **Page 1 of 1**

Method Name: C:\CLASS-VP\Billy\tBu Phenoxy .met
Data Name: C:\CLASS-VP\Billy\BF Cat 89 c001
User: System
Acquired: 23/10/2008 16:28:22
Printed: 28/10/2008 10:37:24

S-Quinap 72 %

72 % ee



Detector A (220nm)

Pk #	Retention Time	Area	Area %	Height	Height %
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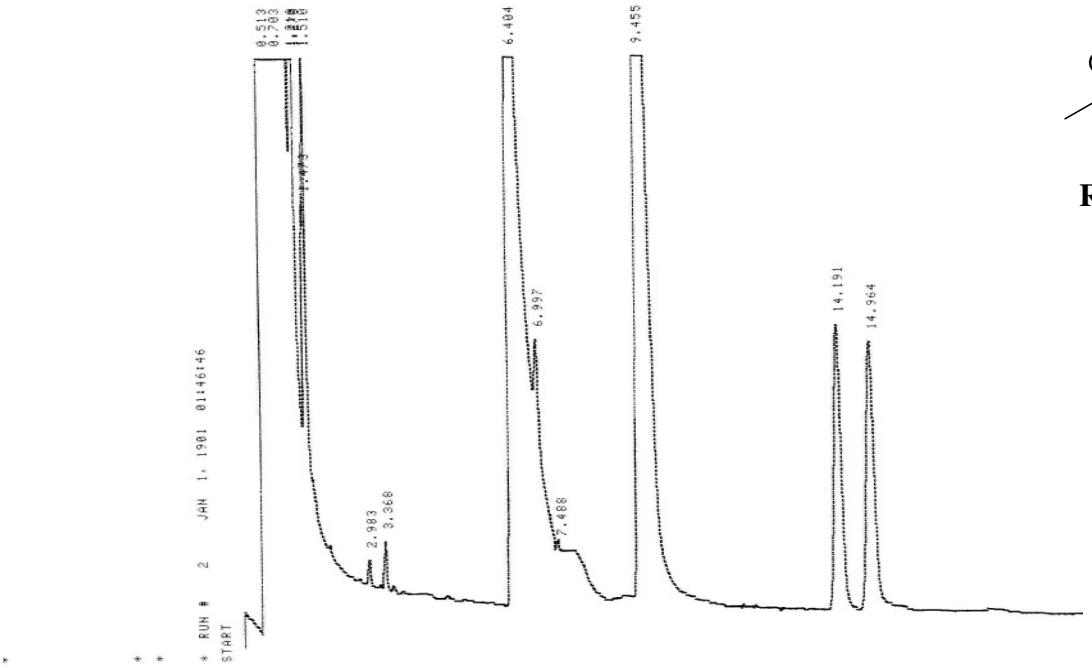
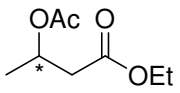
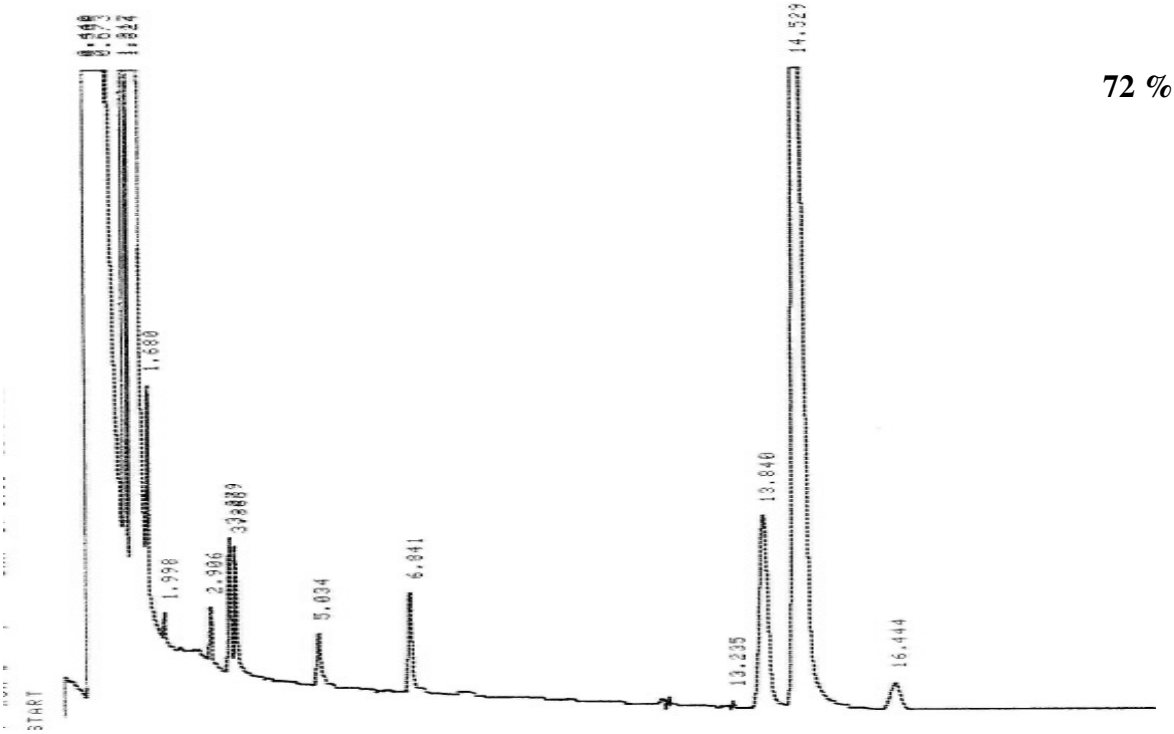
2	28.950	4059920	14.320	65866	9.353
Totals		28351012	100.000	704234	100.000

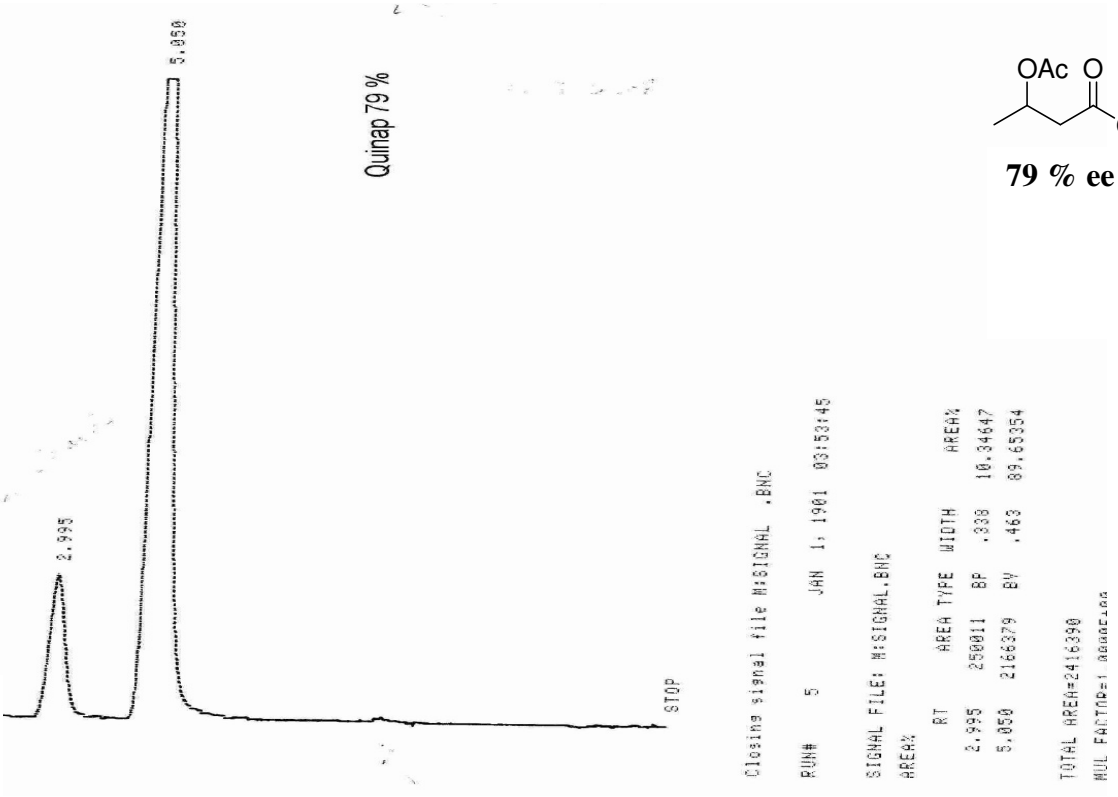




Racemic



72 % ee

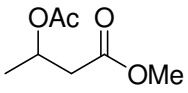


79 % ee

Start 15.0 mins…

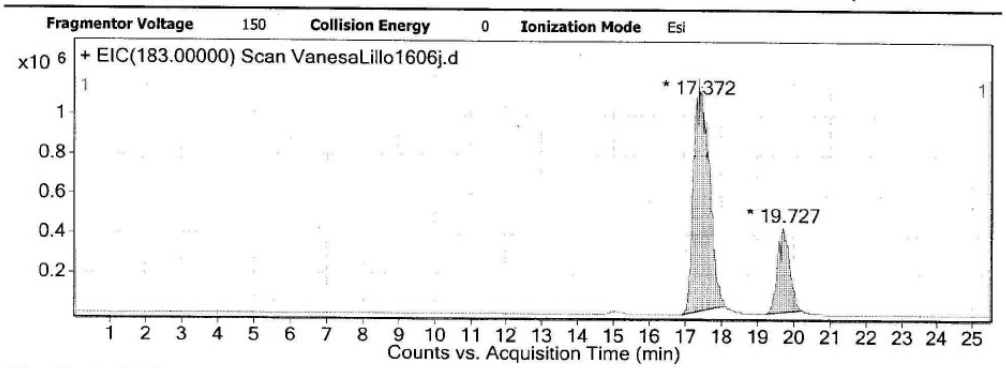
Qualitative Analysis Report

Data Filename	VanesaLillo1606j.d	**Sample Name**	BF 1.20 B (16)
Sample Type	Unavailable	**Position**	Unavailable
Instrument Name	Unavailable	**User Name**	Unavailable
Acq Method		**IRM Calibration Status**	[redacted]
DA Method	Proces_formula.m	**Comment**	-



50 % ee

User Chromatograms



Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
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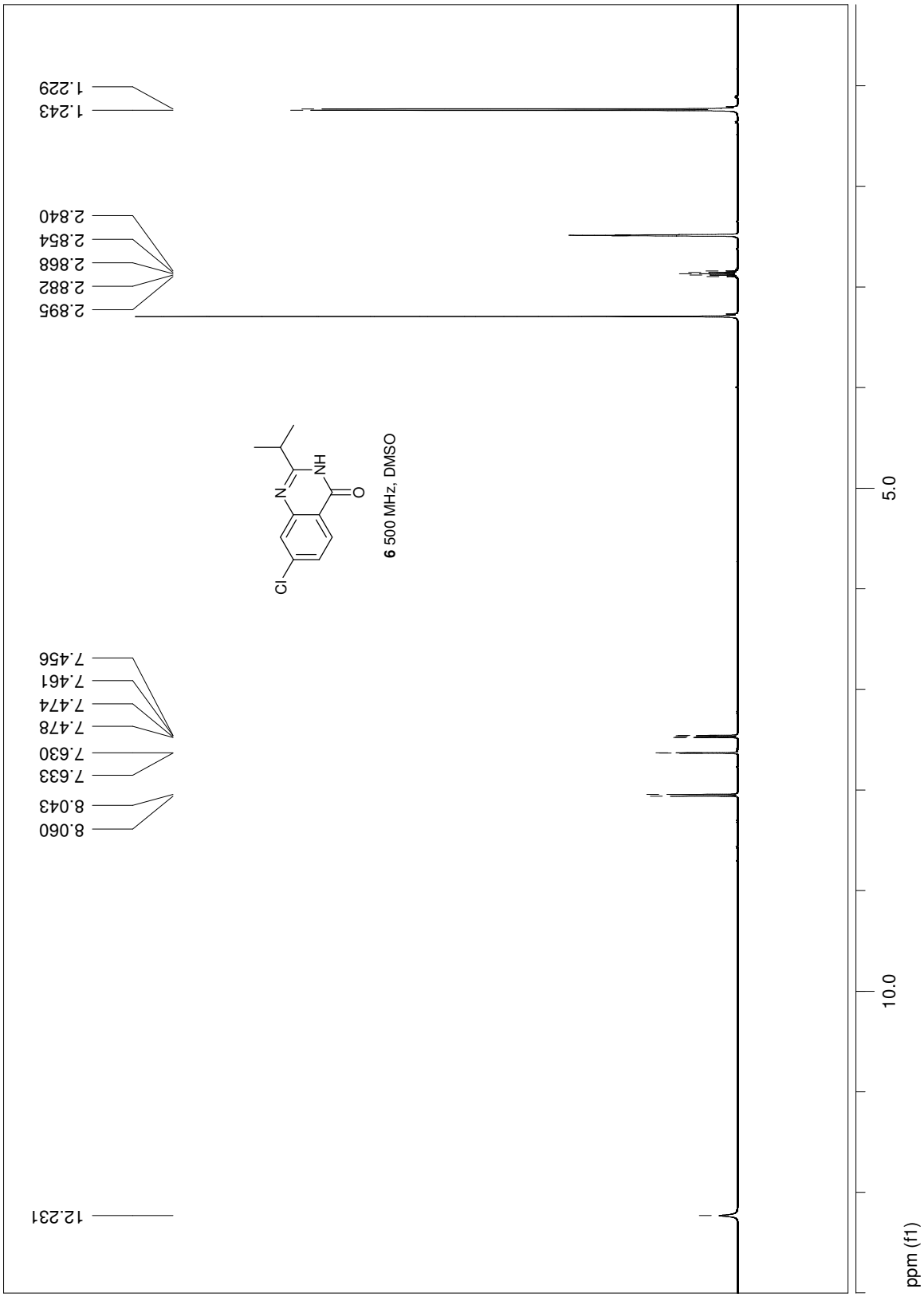
2	19.236	19.727	20.219	423434	9790051	28.55

User Spectra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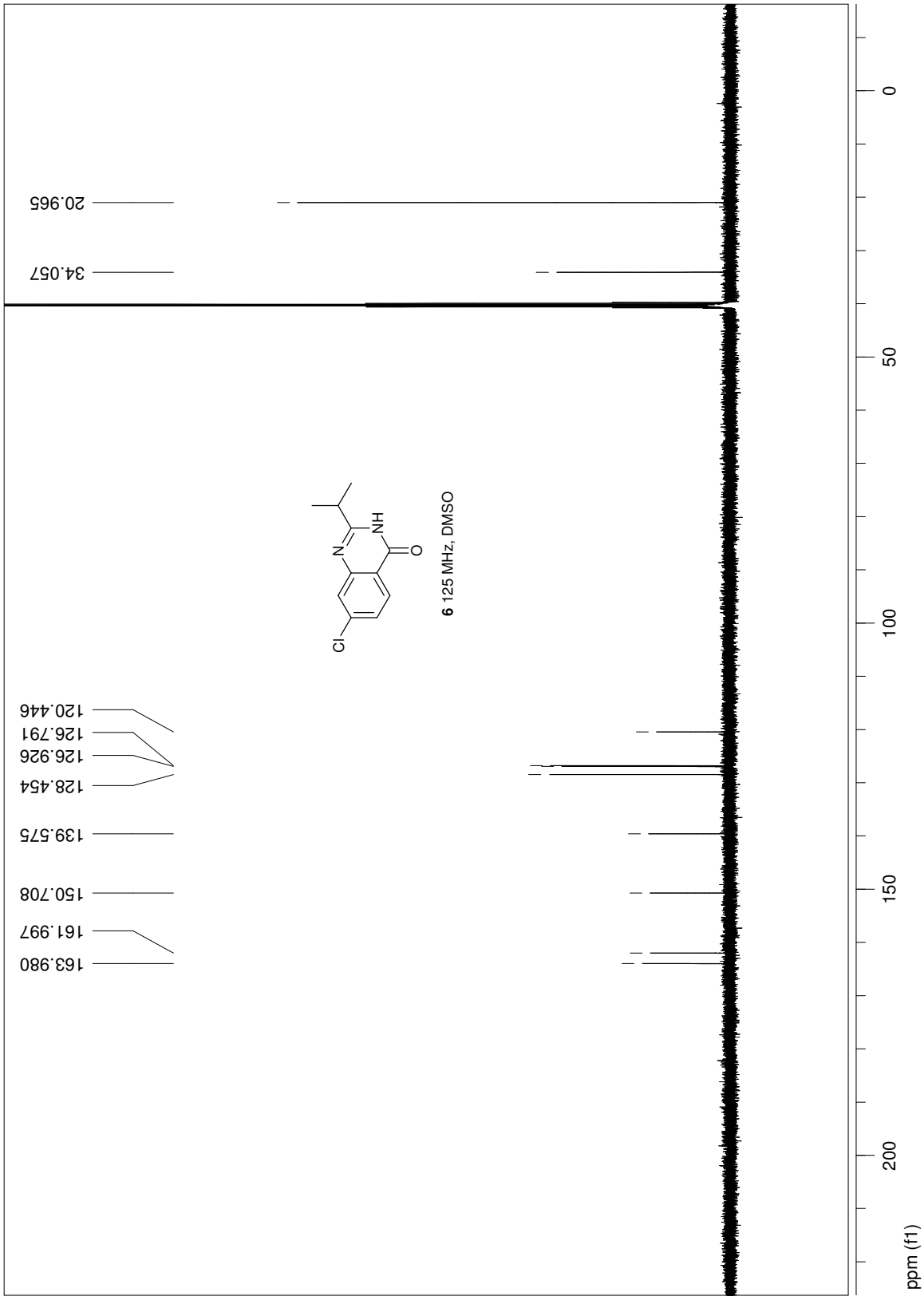
1.243
2.840
2.854
2.868
2.882
2.895
7.456
7.461
7.474
7.478
7.630
7.633
8.043
8.060
12.231
NH
N
O
Cl
6 500 MHz, DMSO
5.0
10.0
ppm (f1)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34.057
120.446
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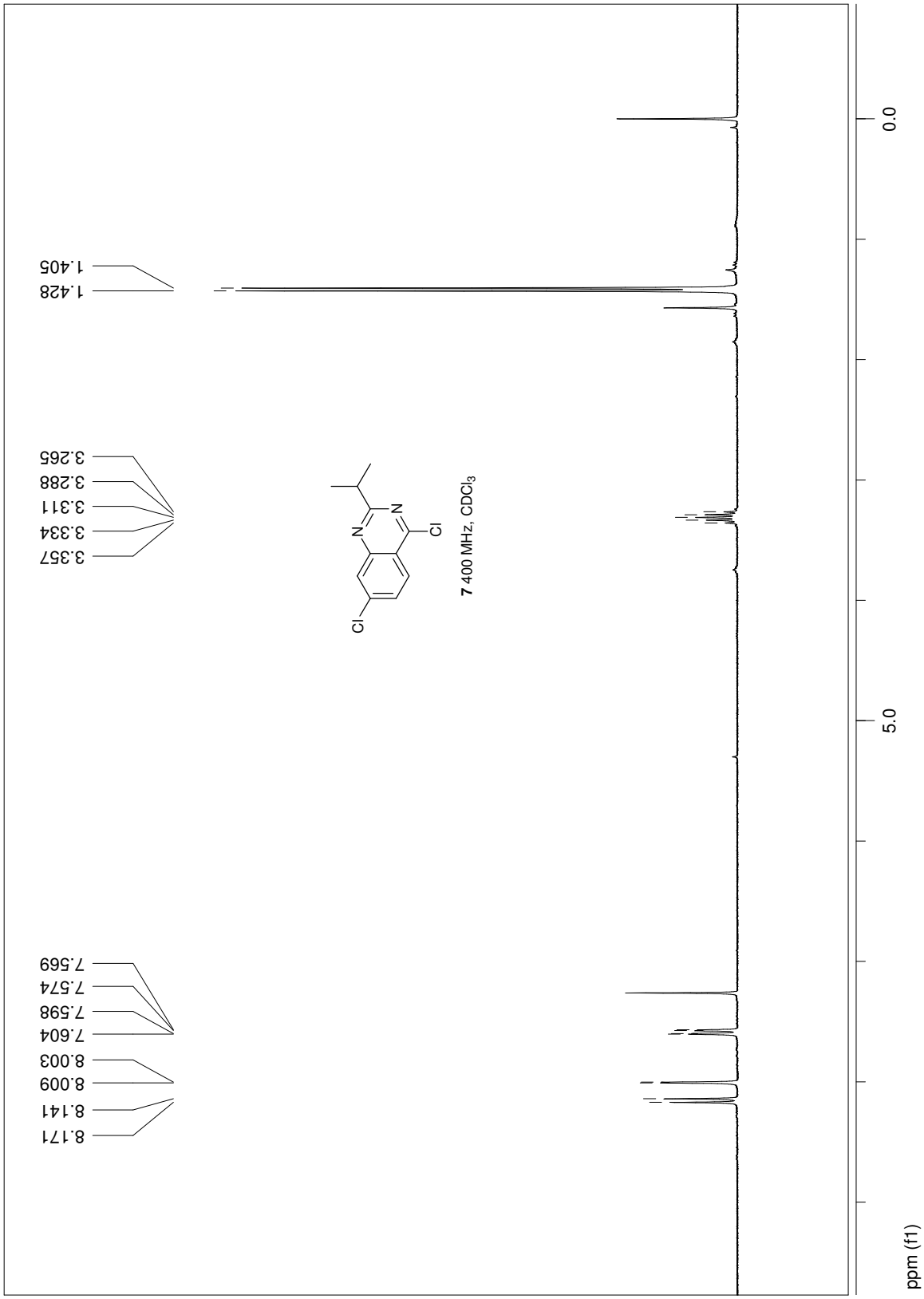
126.926
128.454
139.575
150.708
161.997
163.980
6 125 MHz, DMSO
NH
N
O
Cl
0
50
100
150
200
ppm (f1)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3.311
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7.574
7.598
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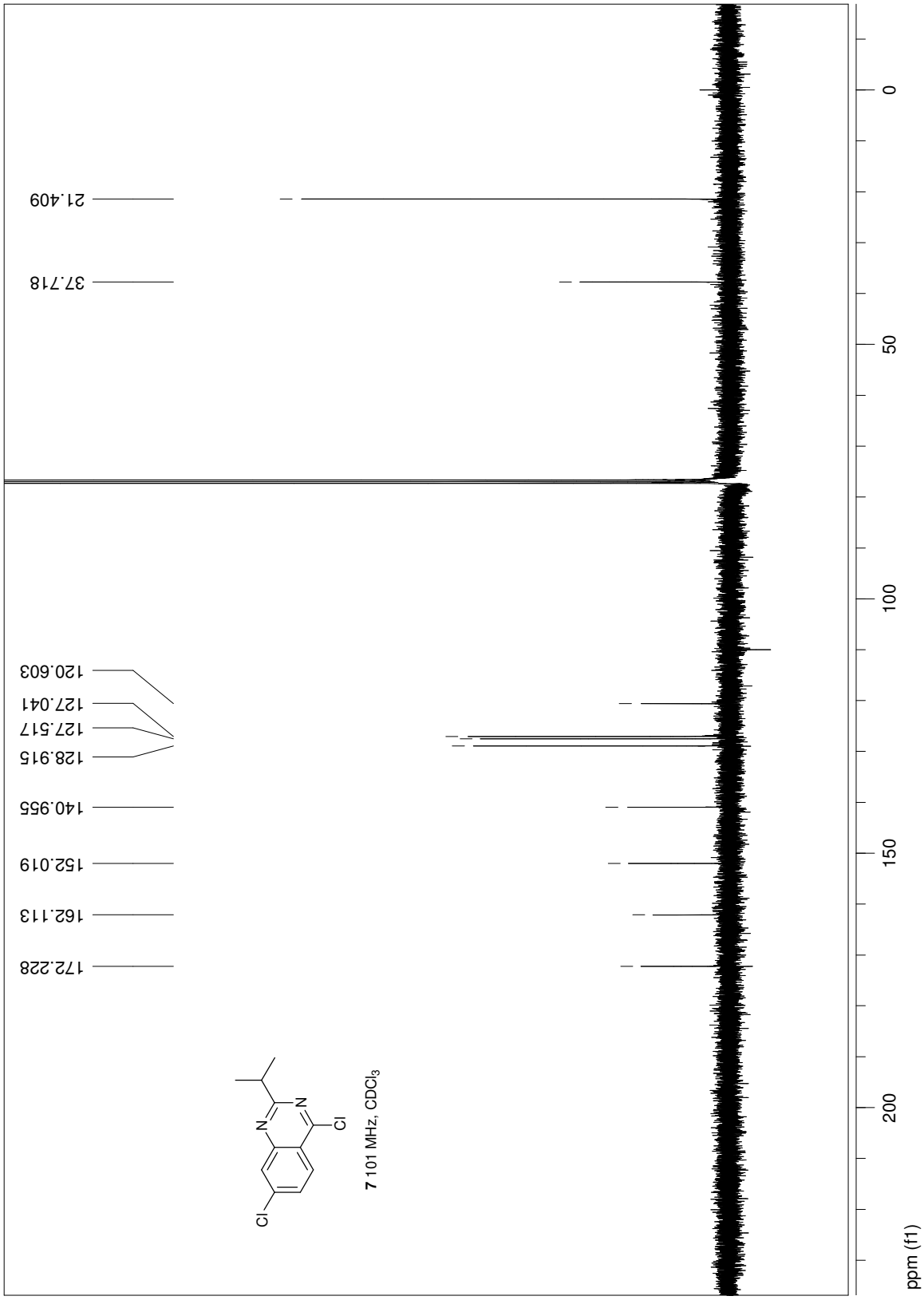
8.141
8.171
Cl
N
N
Cl
7 400 MHz, CDCl3
0.0
5.0
ppm (f1)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37.718
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127.041
127.517
128.915
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7 101 MHz, CDCl3
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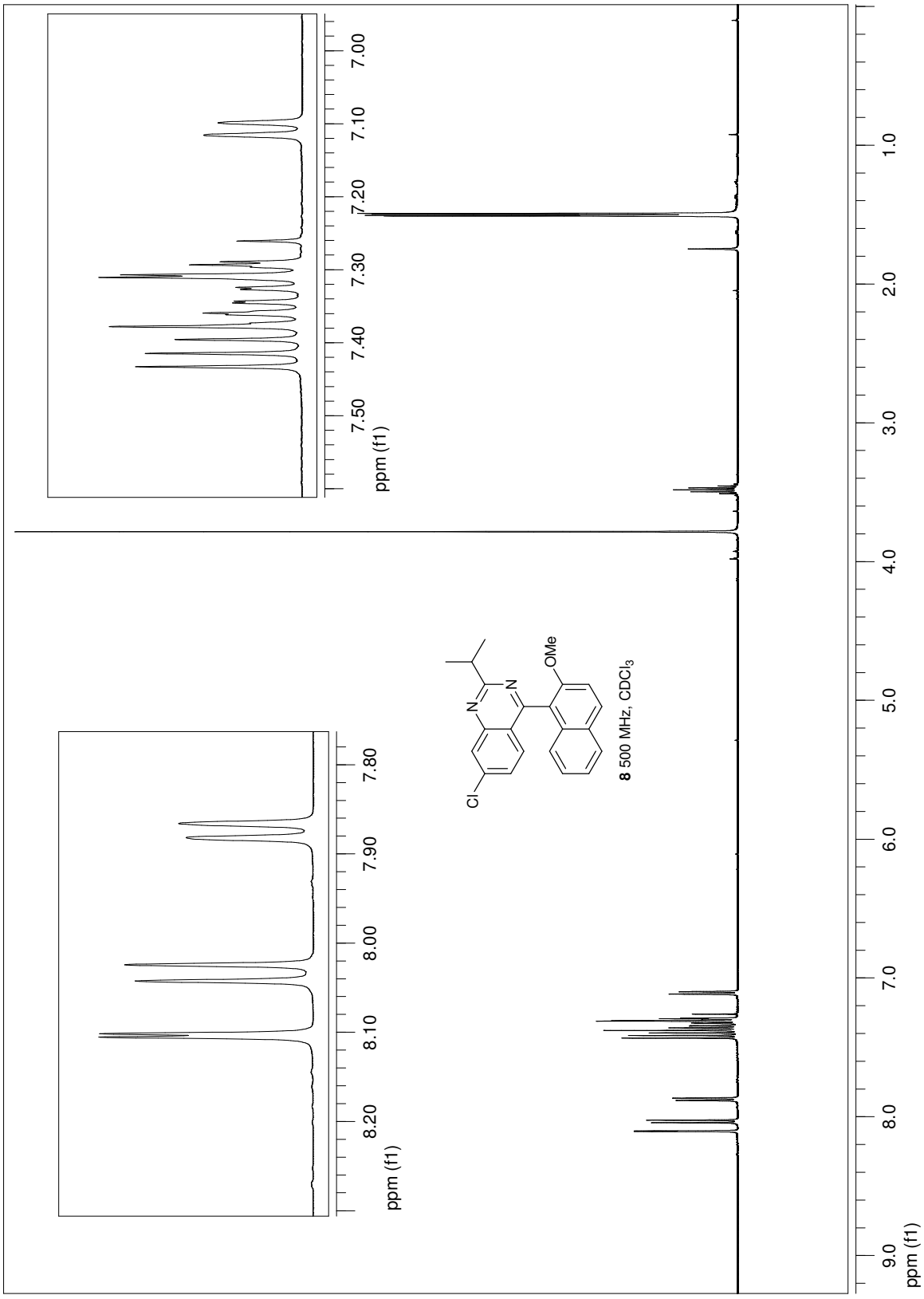
N
N
Cl
0
50
100
150
200
ppm (f1)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7.20
7.30
7.40
7.50
ppm (f1)
7.80
7.90
8.00
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8.20
OMe
N
N
Cl
8 500 MHz, CDCl3
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8.0
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6.0
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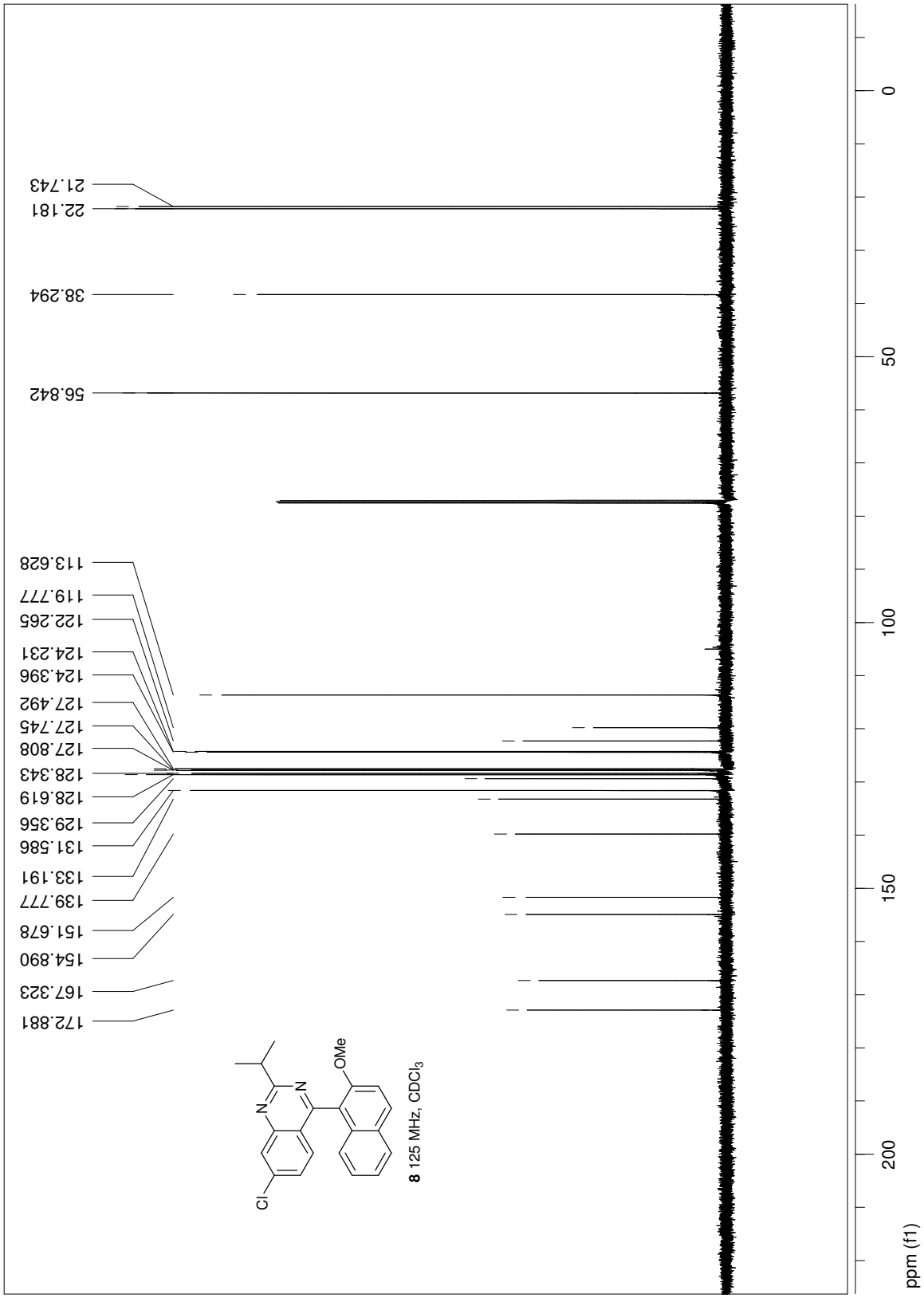
4.0
3.0
2.0
1.0
ppm (f1)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113.628
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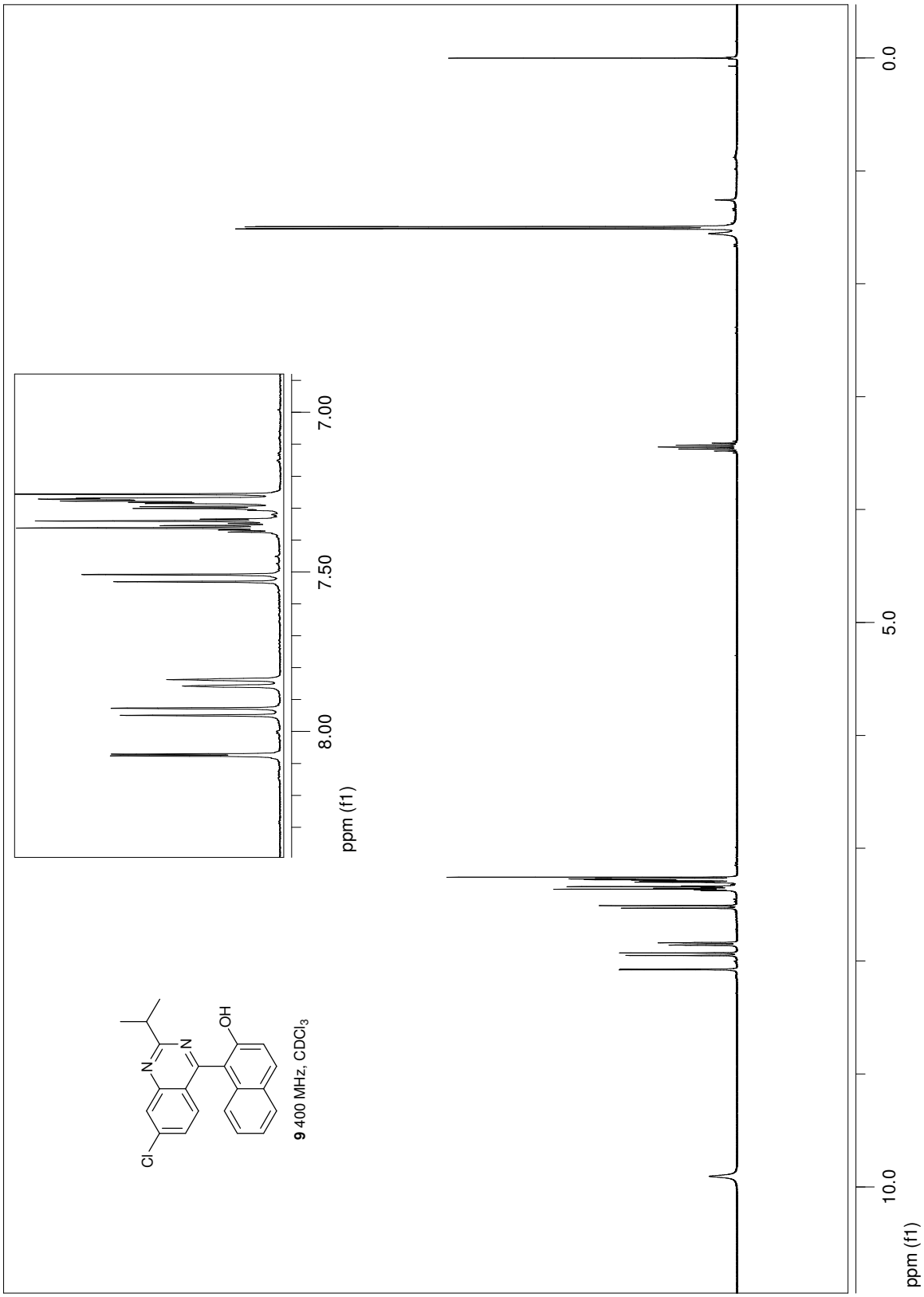
127.808
128.343
128.619
129.356
131.586
133.191
139.777
151.678
154.890
167.323
172.881
0
50
100
150
200
ppm (f1)
OMe
N
N
Cl
8 125 MHz, CDCl3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5.0
10.0
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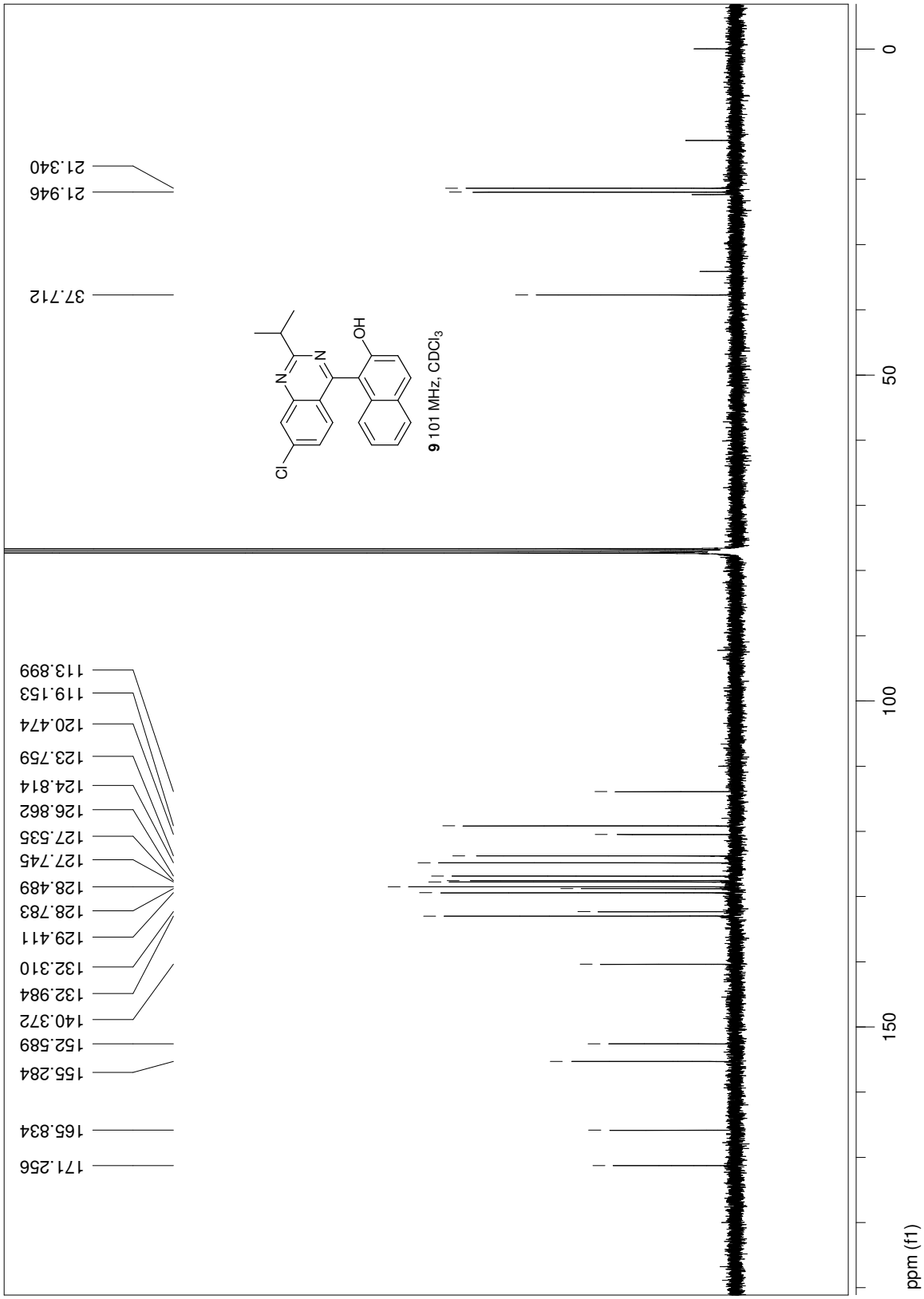
7.00
7.50
8.00
ppm (f1)
OH
N
N
Cl
9 400 MHz, CDCl3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132.310
132.984
140.372
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N
N
Cl
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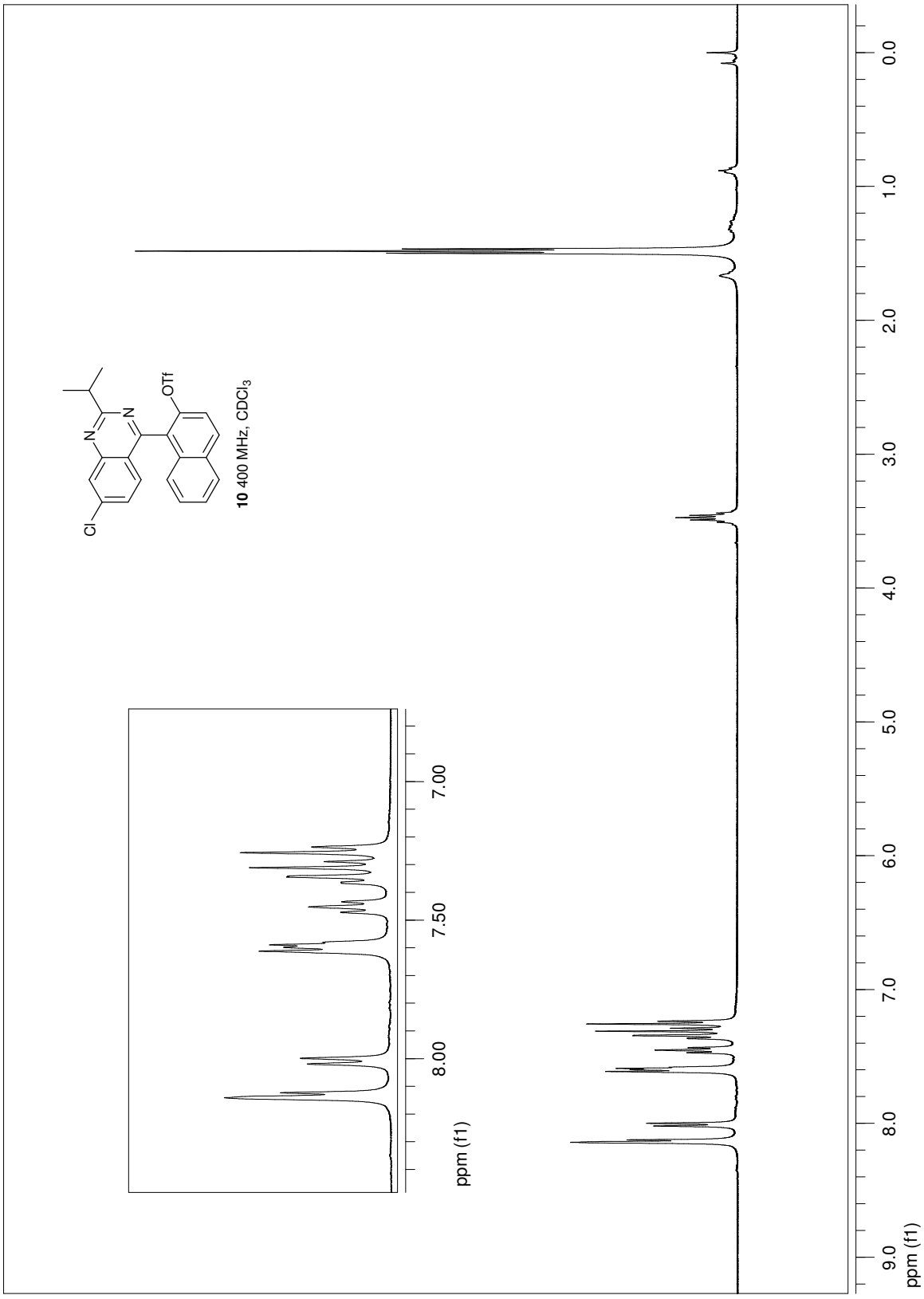
50
100
150
ppm (f1)


OTf
N
N
Cl
10 400 MHz, CDCl3
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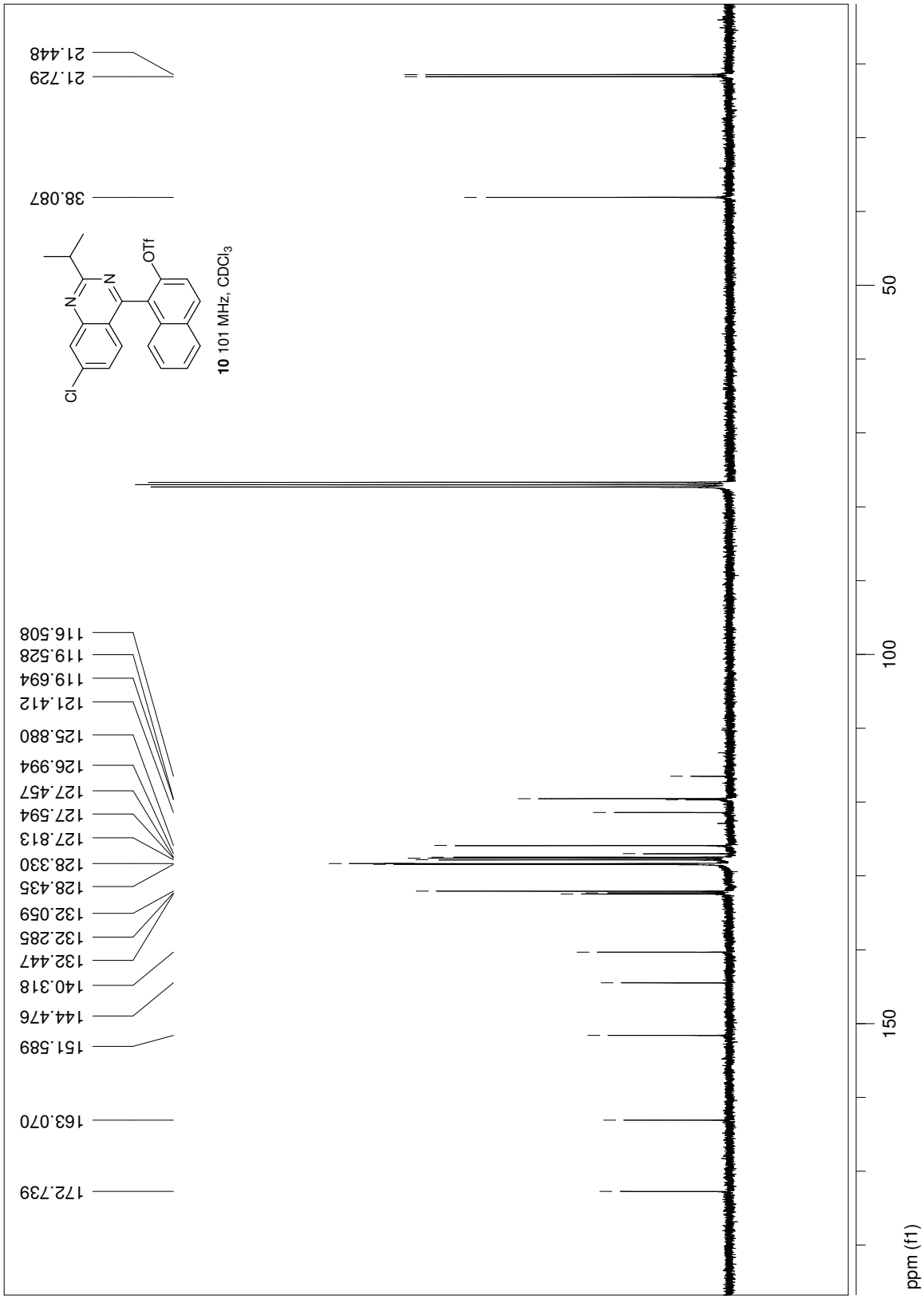
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
ppm (f1)
7.00
7.50
8.00
ppm (f1)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OTf
N
N
Cl
10 101 MHz, CDCl3
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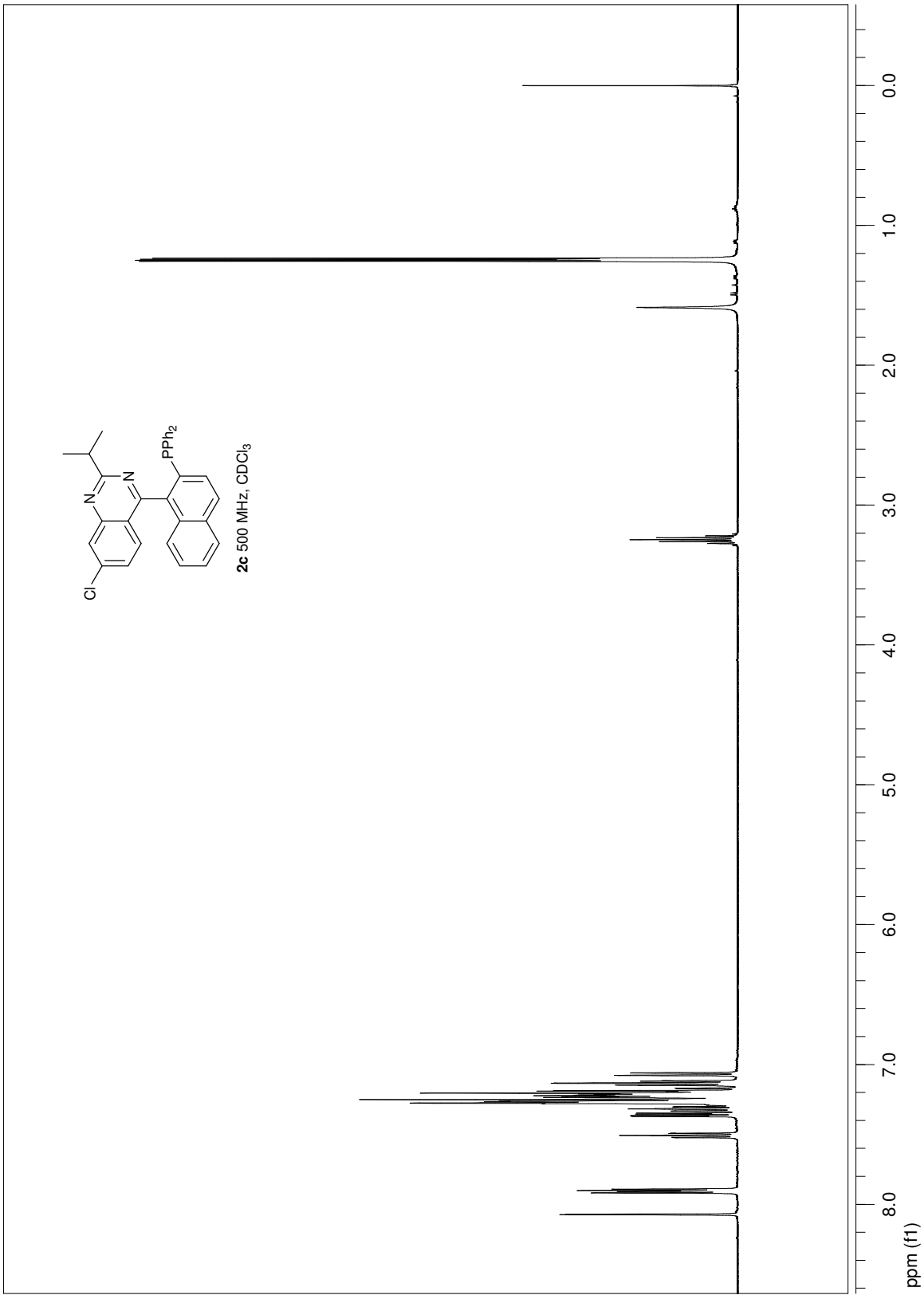
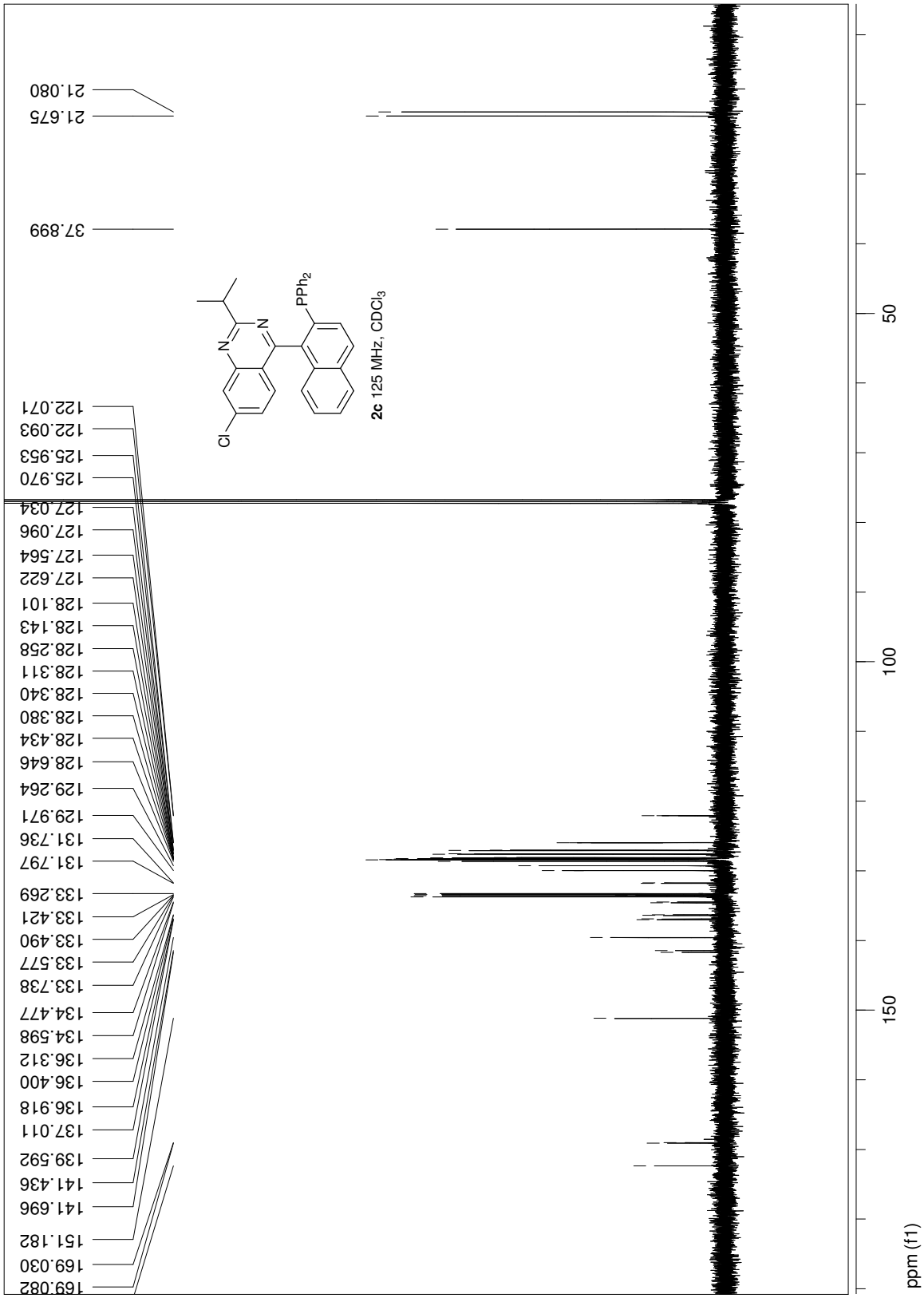
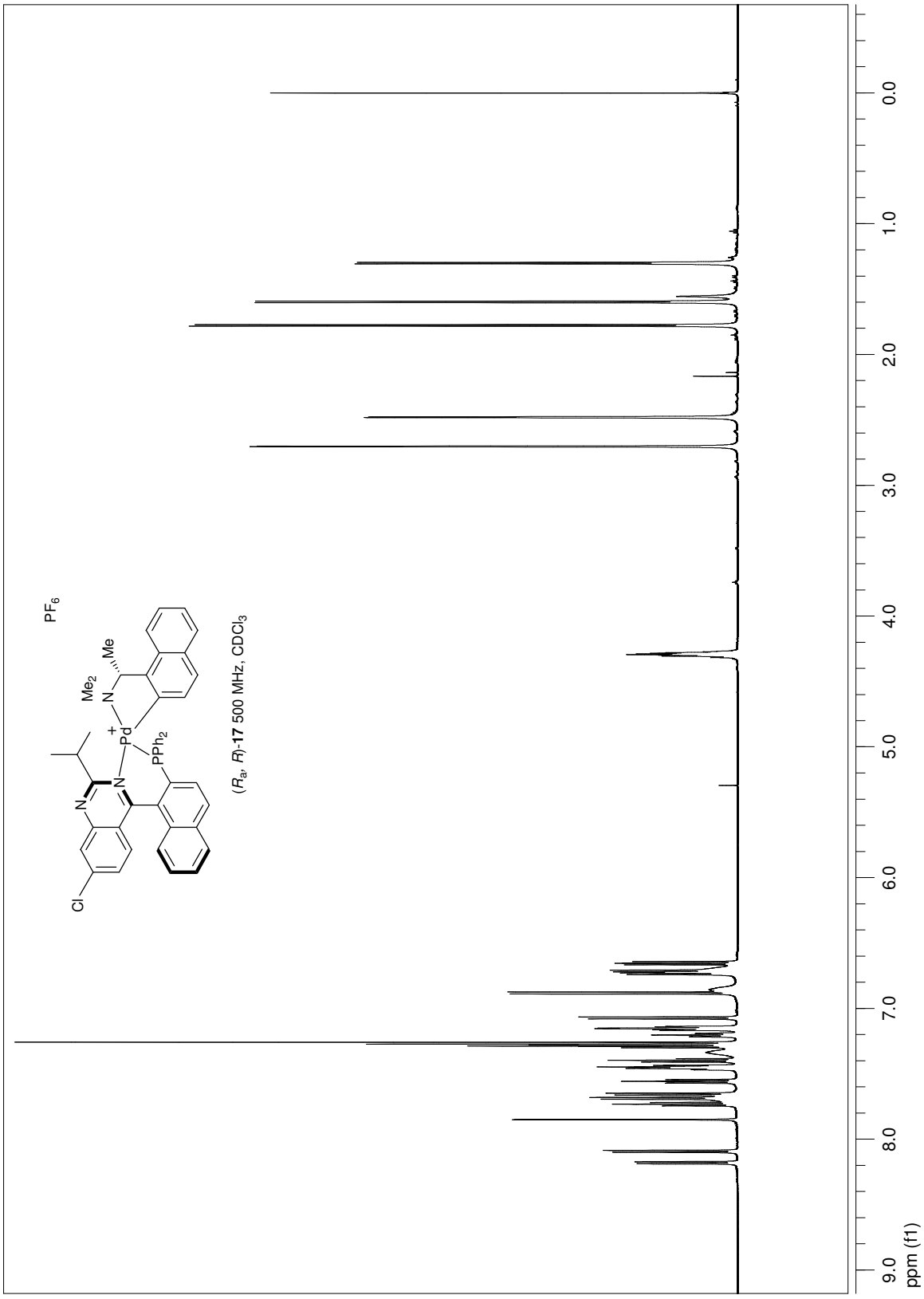
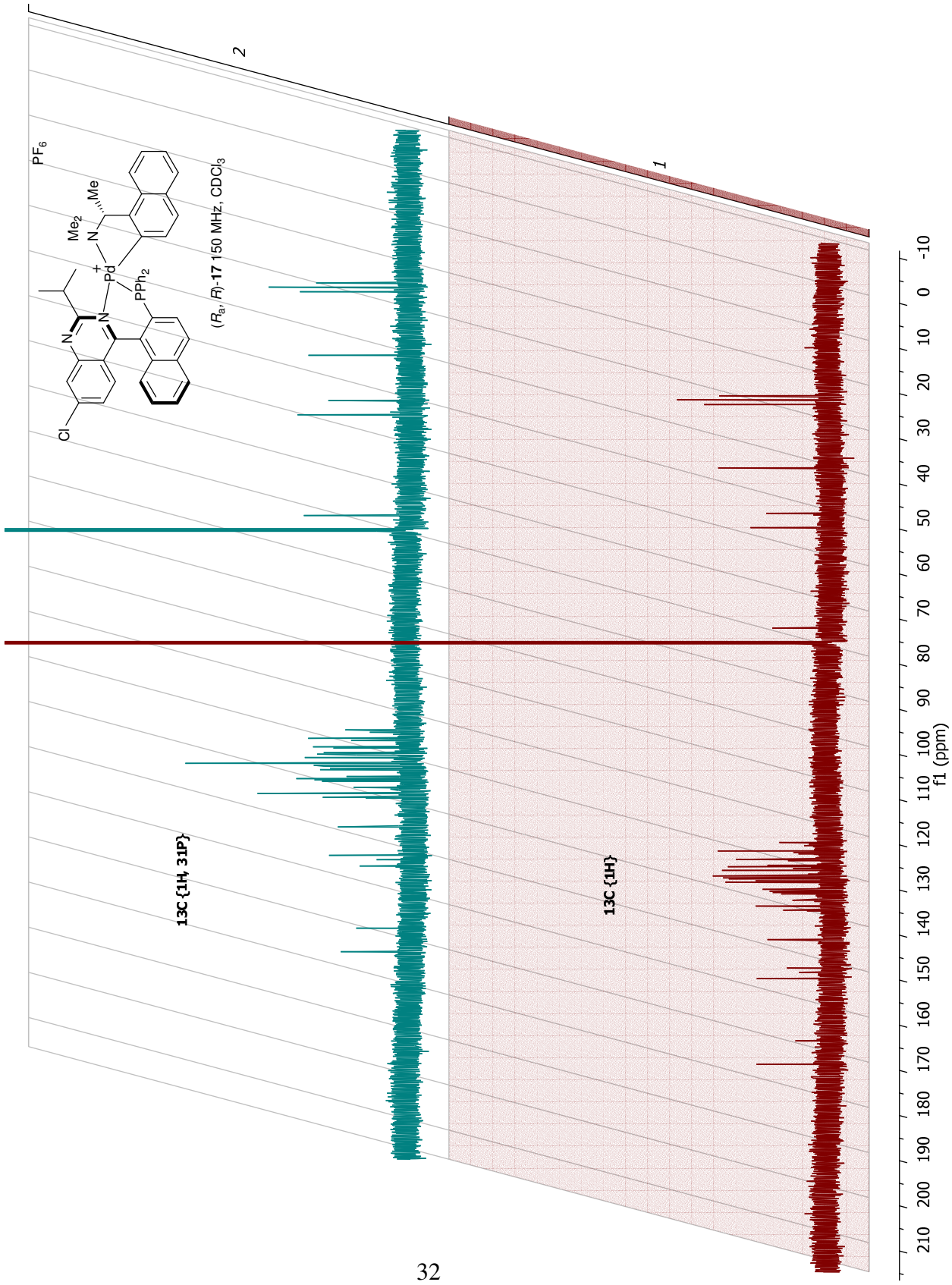
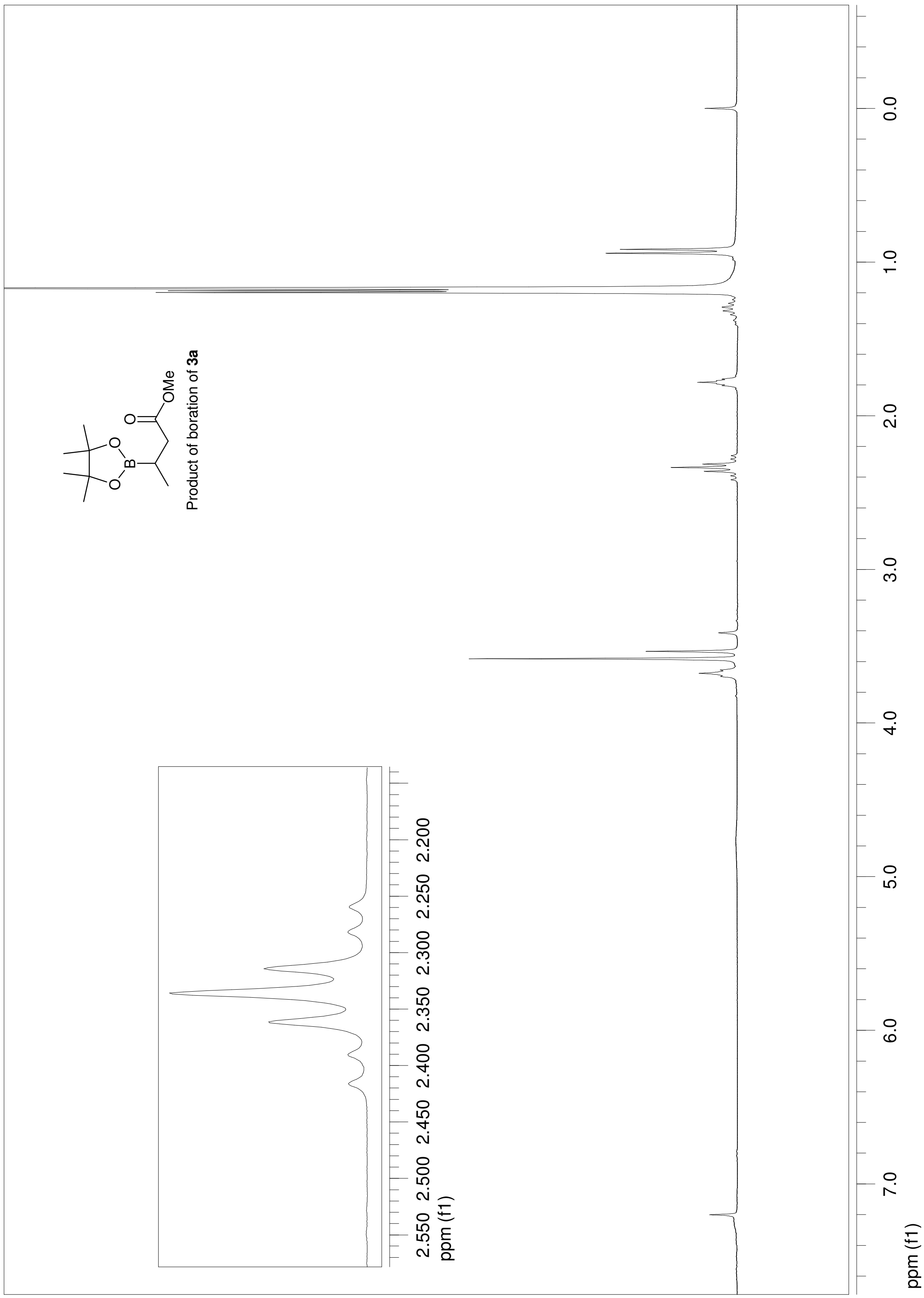
128.435
132.059
132.285
132.447
140.318
144.476
151.589
163.070
172.739
50
100
150
ppm (f1)

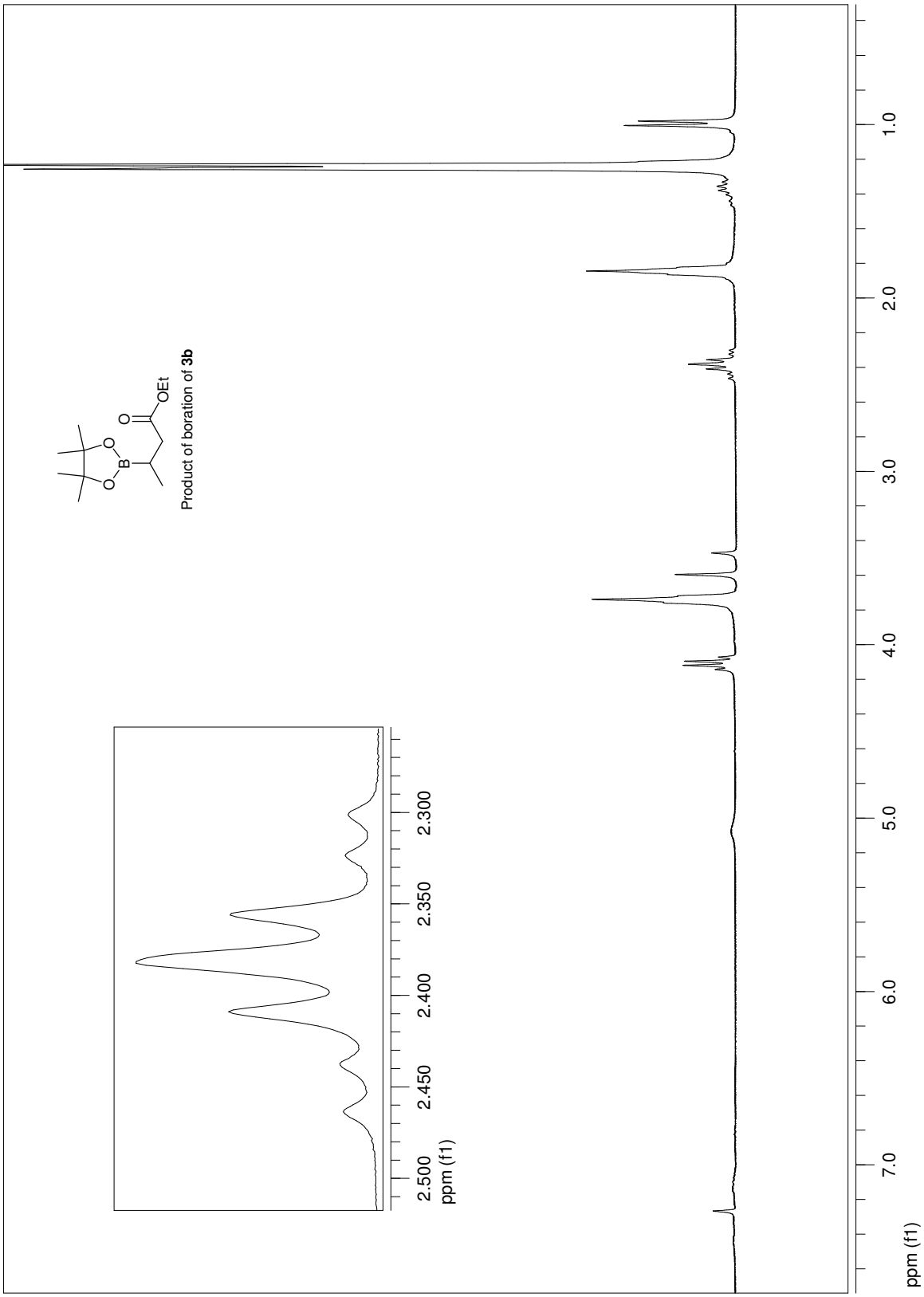

PPh2
N
N
Cl
2c 500 MHz, CDCl3
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (f1)

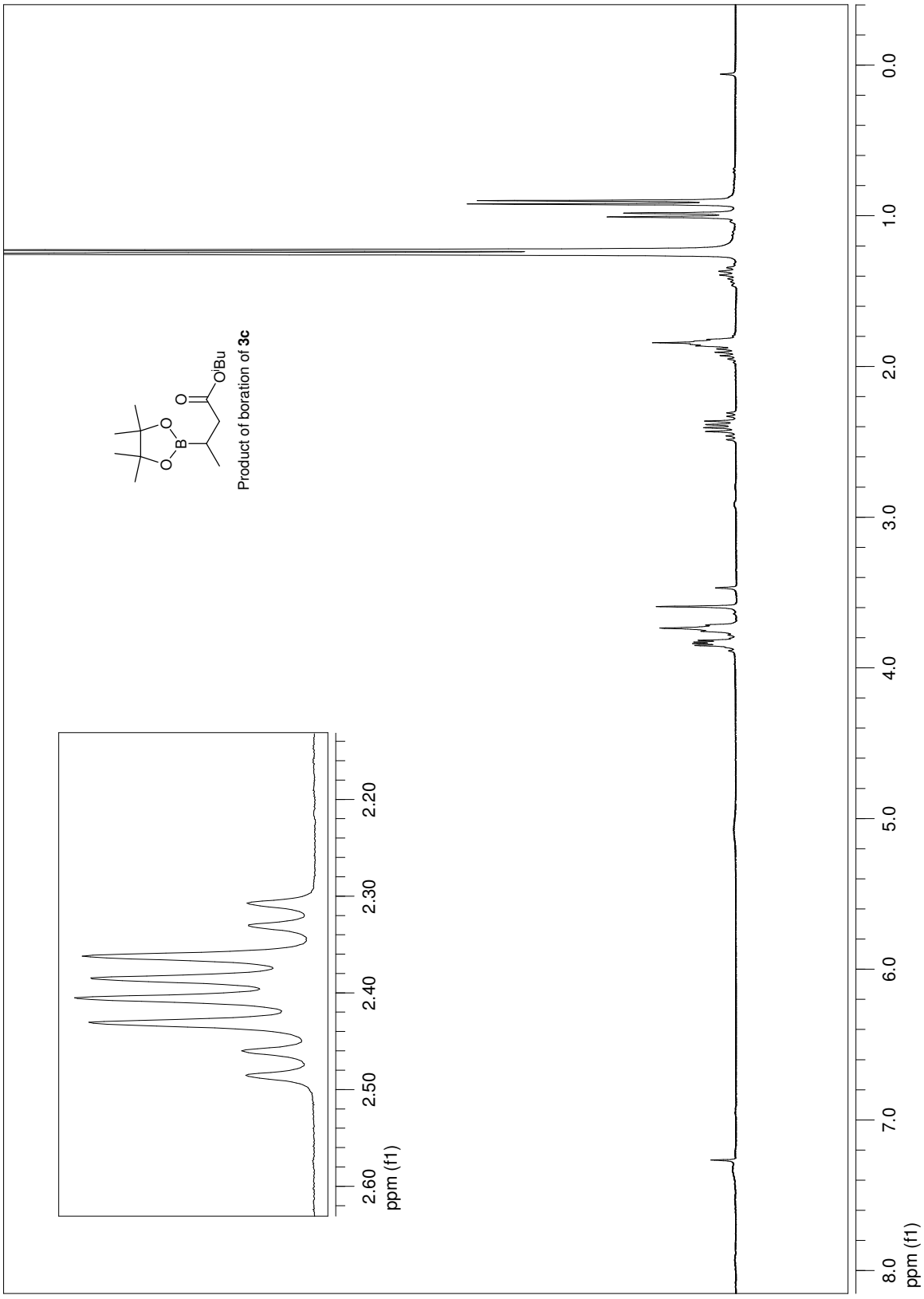

21.080
21.675
37.899
122.071
122.093
125.953
125.970
127.034
127.096
127.564
127.622
128.101
128.143
128.258
128.311
128.340
128.380
128.434
128.646
129.264
129.971
131.736
131.797
133.269
133.421
133.490
133.577
133.738
134.477
134.598
136.312
136.400
136.918
137.011
139.592
141.436
141.696
151.182
169.030
169.082
Cl
N
N
PPh2
2c 125 MHz, CDCl3
50
100
150
ppm (f1)

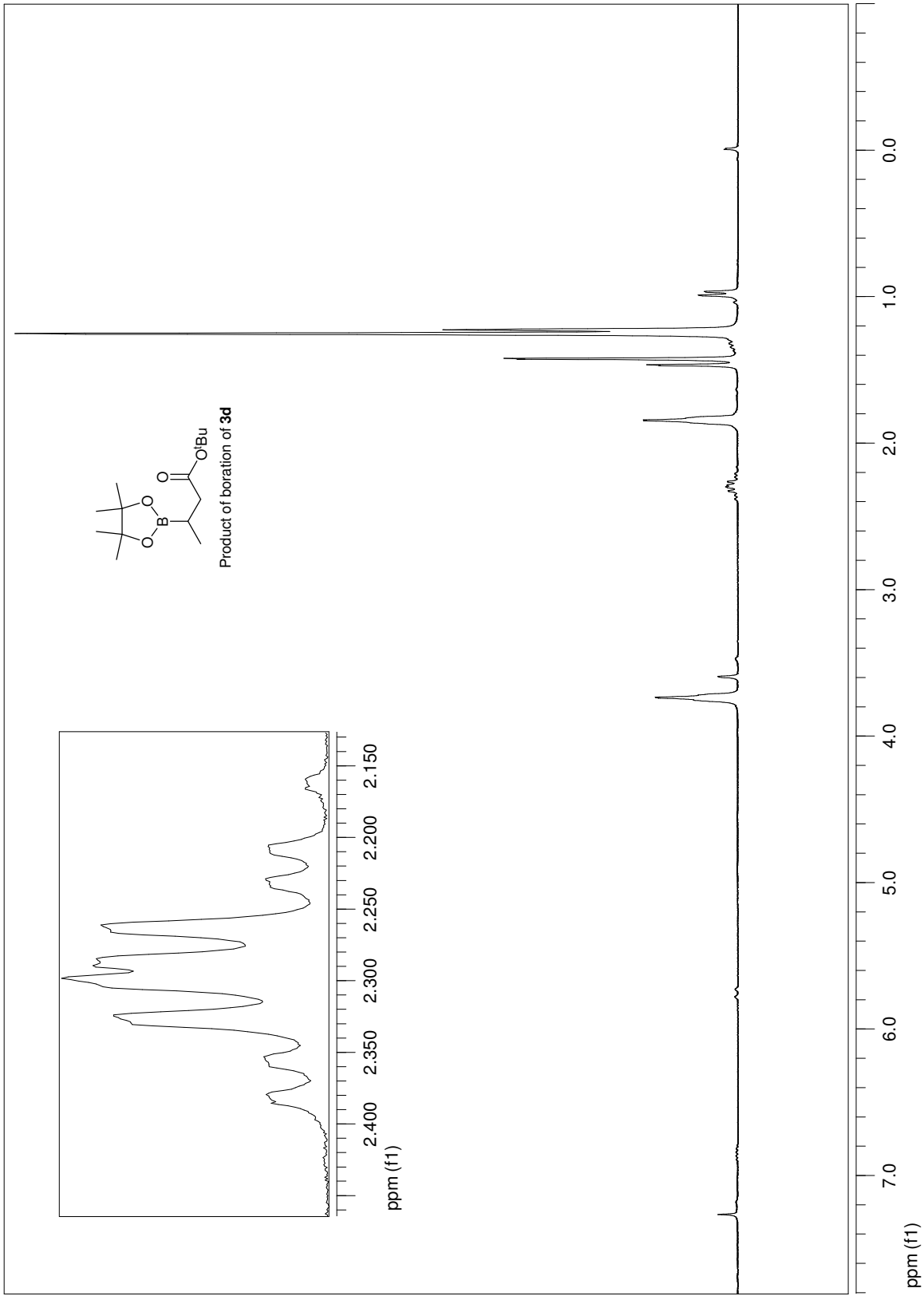

PF6
Me2
N
Me
Pd
PPh2
N
N
Cl
(Ra, R)-17 500 MHz, CDCl3
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
ppm (f1)

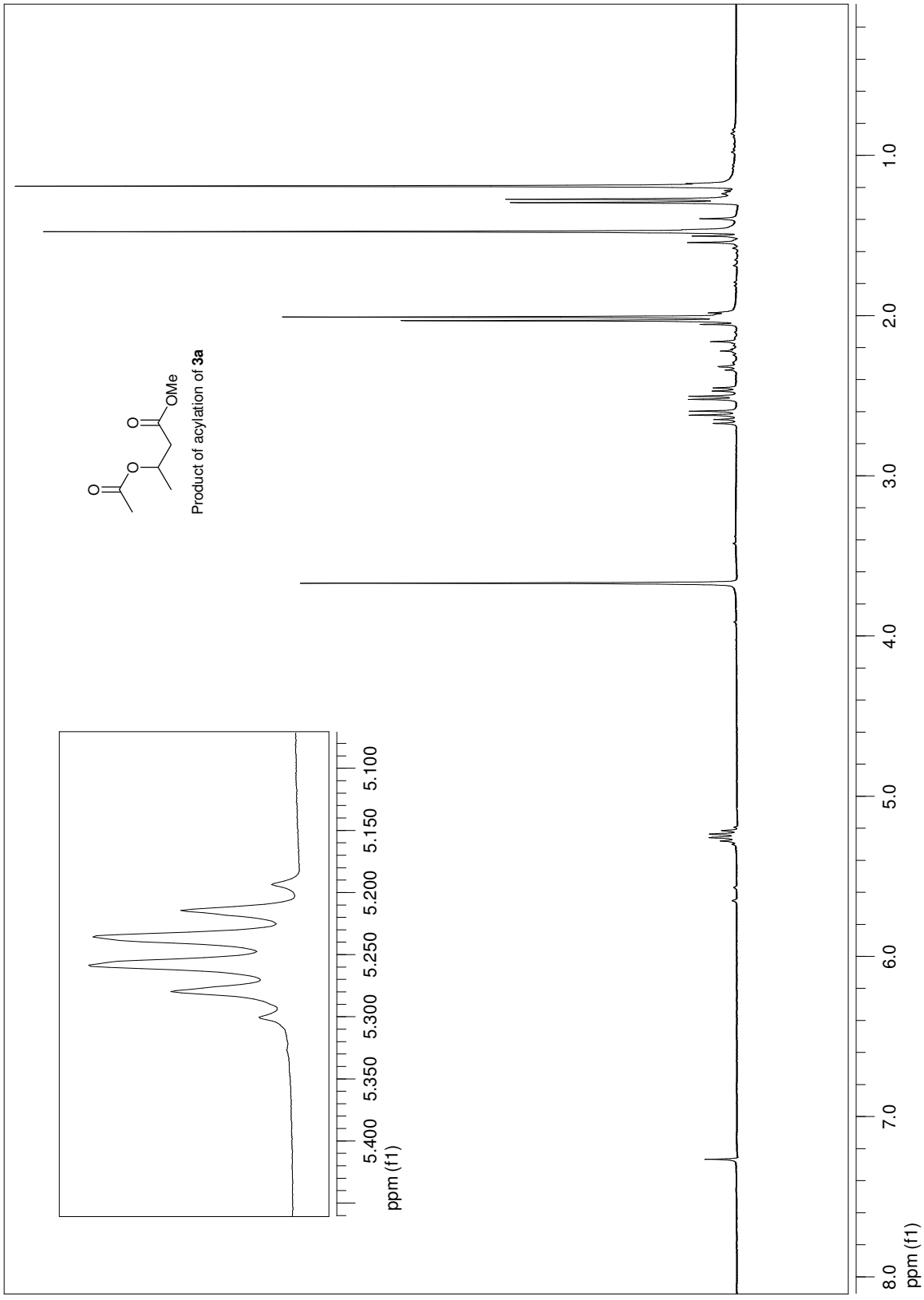

2
1
PF6
Me2
N
Me
Pd
PPh2
N
N
Cl
(Ra, R)-17 150 MHz, CDCl3
13C {1H, 31P}
13C {1H}
f1 (ppm)
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210

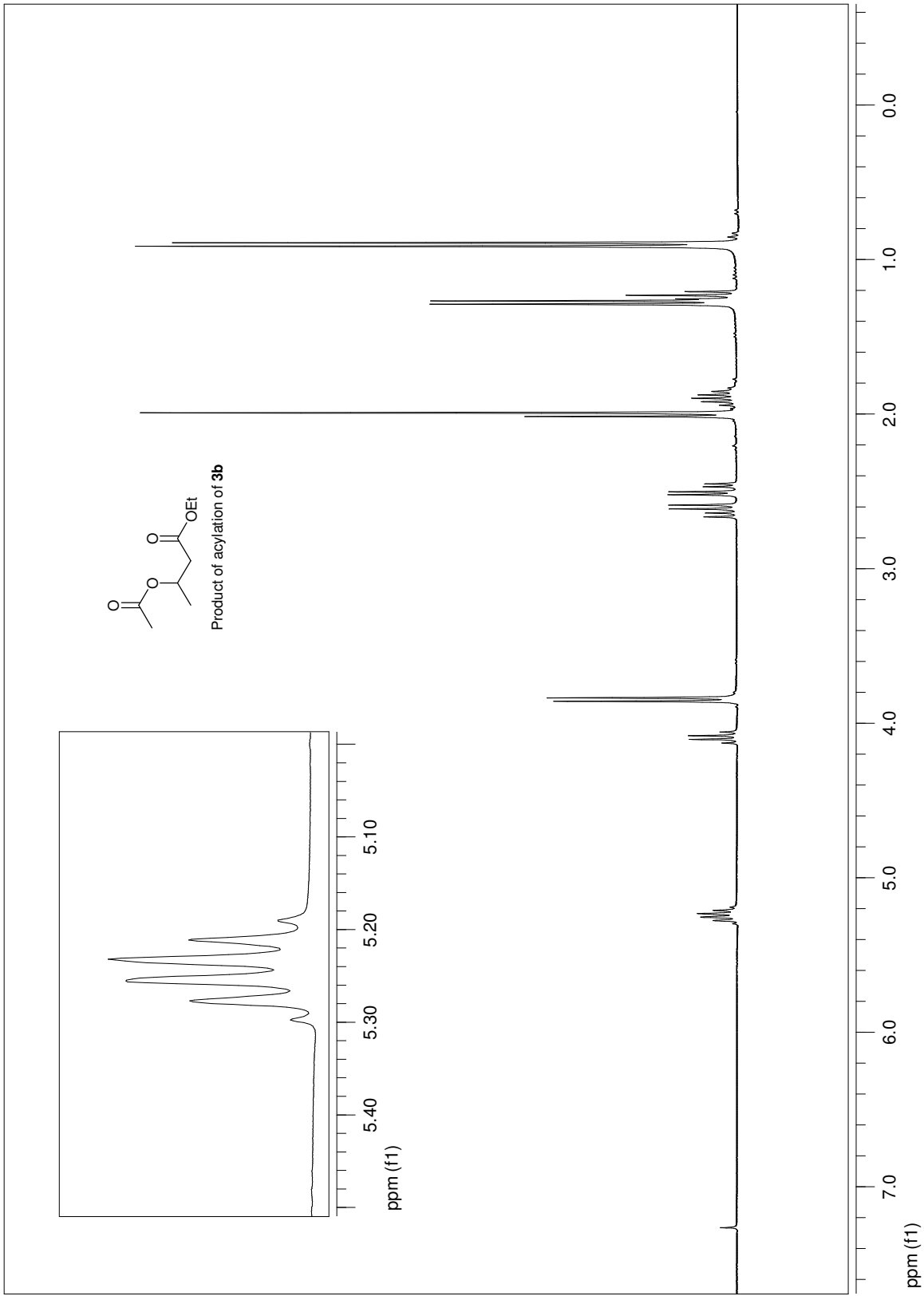

O
B
O
O
OMe
Product of boration of **3a**
2.550 2.500 2.450 2.400 2.350 2.300 2.250 2.200
ppm (f1)
7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

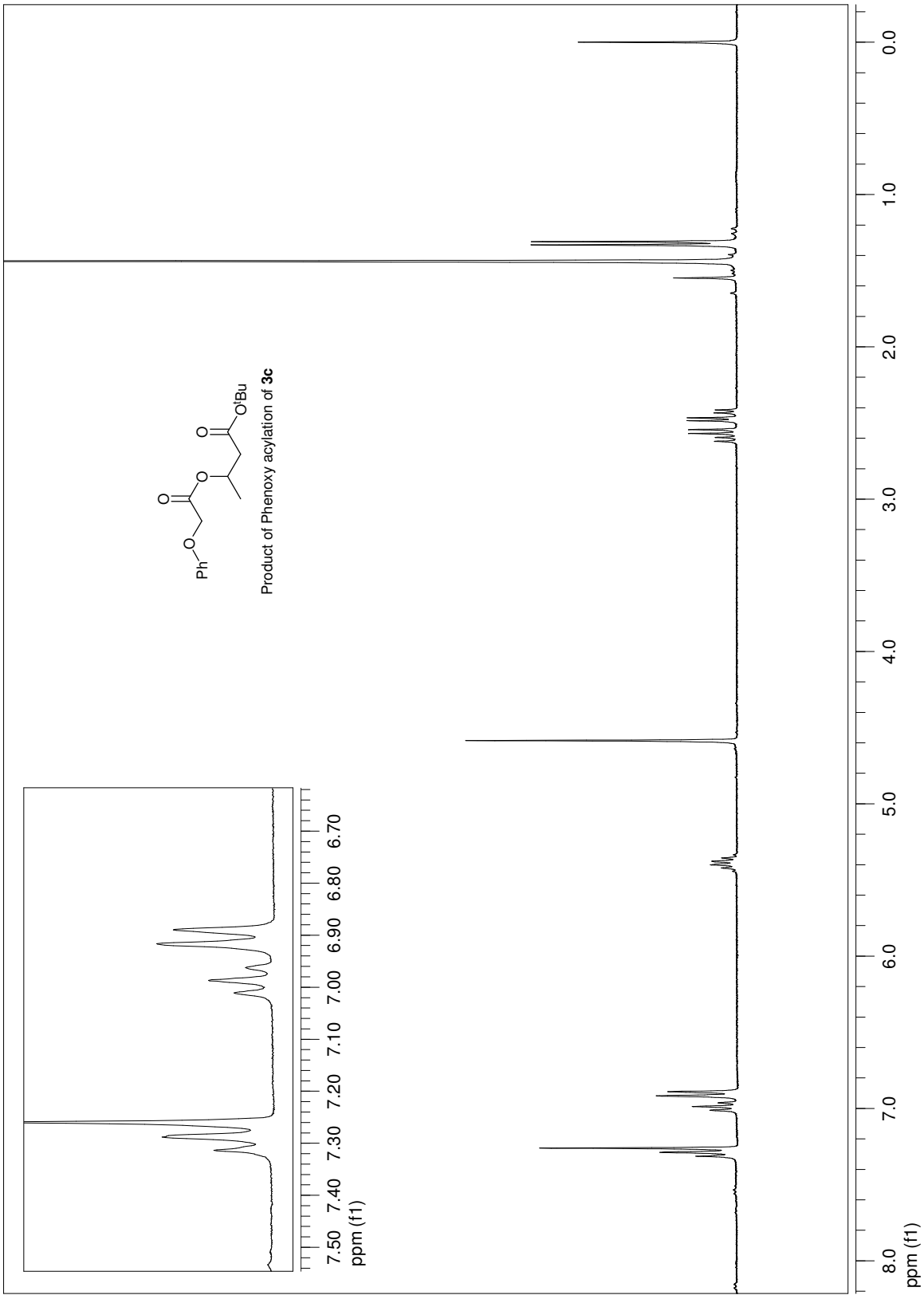

Product of boration of 3b
OEt
O
O
B
O
2.500
2.450
2.400
2.350
2.300
ppm (f1)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)


Product of boration of 3c
OiBu
O
O
B
O
2.60
2.50
2.40
2.30
2.20
ppm (f1)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


Product of boration of 3d
OtBu
O
O
O
B
2.400
2.350
2.300
2.250
2.200
2.150
ppm (f1)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


OMe
Product of acylation of 3a
5.400 5.350 5.300 5.250 5.200 5.150 5.100
ppm (f1)
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0
ppm (f1)


Product of acylation of 3b
OEt
O
O
O
ppm (f1)
5.40
5.30
5.20
5.10
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


Product of Phenoxy acylation of 3c
Ph
O
O
O
O
O
OtBu
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (f1)
6.70
6.80
6.90
7.00
7.10
7.20
7.30
7.40
7.50
ppm (f1)