

Supporting Information

Indium-Catalyzed C(sp³)-H Functionalization of 2-Methylazaarenes through Direct Benzylic Addition to Trifluoromethyl Ketones

Zaini Jamal and Yong-Chua Teo*

Natural Sciences and Science Education, National Institute of Education, Nanyang Technological University, 1 Nanyang Walk, Singapore 637616, Singapore.
Tel: (+65) 6790 3846; Fax: (+65) 6896 9414; E-mail: yongchua.teo@nie.edu.sg

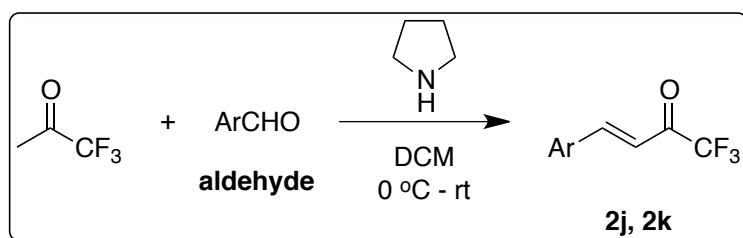
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1. General Considerations

All commercially available chemicals were used directly upon purchase from suppliers. Anhydrous solvents were used for all non-aqueous reactions and deionized water was used for aqueous reactions. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Flash chromatography was performed using Merck silica gel 60 with AR grade solvents. Columns were packed as a silica gel suspension in hexane prior to elution by the appropriate solvent system (hexane:ethyl acetate). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance DPX 400 spectrophotometer (chloroform-*d*, methanol-*d* or acetone-*d*₆ as solvent). Chemical shifts for ¹H NMR and ¹³C NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe₄ and relative to the residual signals of the appropriate solvents. Multiplicities are reported based on apparent multiplicities and given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); ddd (doublets of doublets of doublet); dddd (doublets of doublets of doublets of doublet); dt (doublets of triplet); brs (broad); or m (multiplets). Coupling constants (*J* values) are reported in unit of Hertz (Hz). Numbers of protons are reported based on the appropriate integration of the signals. Mass spectroscopy was performed using Agilent 1100 series LC/MSD.

2. Experimental Procedures for Synthesis of **2j** and **2k**

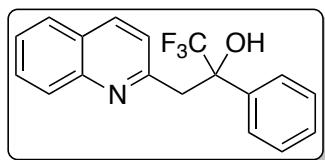


2j and **2k** were synthesized according to modified literature procedure:¹ To a 25-mL RBF equipped with a magnetic stir bar and tightly sealed with a rubber septum, 1,1,1-trifluoropropan-2-one (40 mmol, 4.0 equiv.) in DCM (10 mL) was cooled to 0 °C. With continuous stirring, pyrrolidine (10 mmol, 1.0 equiv.) was then added dropwise followed by the appropriate aldehydes (10 mmol, 1.0 equiv.). After 2 h of stirring at 0 °C, the reaction mixture was then allowed to warm up to room temperature at which stirring was continued for another 24 h. The reaction was then quenched with saturated NH₄Cl solution. The organic layer was then separated, washed with water, dried over Na₂SO₄ and concentrated under reduced pressure. The residual was then purified by flash chromatography (hexane:ethyl acetate = 100:0, 98:2). The analytically pure enone products as **2j** and **2k** were then obtained after further purification by recrystallization from hexane at 0 °C. **2j** and **2k** are known compounds whose identities were determined by comparisons of the respective ¹H NMR spectra with reported literature.¹⁻³

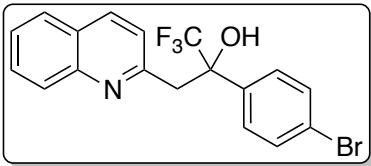
3. General Experimental Procedure for In-catalyzed Benzylic C-H Addition

To an 8-mL reaction vial equipped with a magnetic stir bar, InCl₃ (5.5 mg, 5.0 mol%), 2-methylazaarenes (0.75 mmol, 1.5 equiv.), TFMK (0.5 mmol, 1.0 equiv.) and ¹BuOH (0.5 mL) were sequentially added. The vial was then capped and placed into a pre-heated oil bath at 60 °C with vigorous stirring. After 24 h, the reaction mixture was then allowed to cool to room temperature and passed through a short pad of celite with dichloromethane washing. The crude reaction mixture was then dried over Na₂SO₄ and concentrated under reduced pressure. Purification by silica gel chromatography (hexane:ethyl acetate = 100:0, 95:5) then gave the intended addition product.

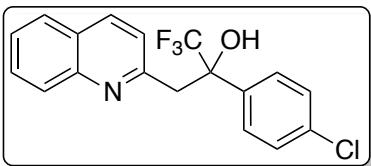
4. Characterization Data for Benzylic C-H Addition Products



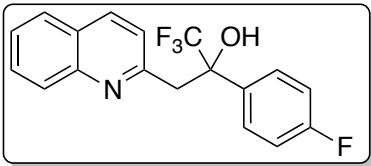
1,1,1-trifluoro-2-phenyl-3-(quinolin-2-yl)propan-2-ol (**3aa**).⁴ White solid (99 %, 158.5 mg); ¹H NMR (400 MHz, CDCl₃): δ 3.67 (d, *J* = 15.2 Hz, 1H), 3.78 (d, *J* = 15.2 Hz, 1H), 7.20 – 7.24 (m, 2H), 7.27 – 7.30 (m, 2H), 7.46 – 7.50 (m, 1H), 7.65 – 7.73 (m, 4H), 7.95 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 8.50 (s, 1H); ¹³C NMR (100 MHz, CD₃OD): δ 42.3, 78.7 (q, *J* = 30.0 Hz), 122.8 (overlapping q signal), 124.2, 125.6 (overlapping q signal), 127.8, 128.2, 128.4, 129.0, 129.1, 129.2, 129.4, 131.2, 138.3, 139.2, 147.8, 159.1; HRMS (ESI) Calcd for C₁₈H₁₅F₃NO [M+H]: 318.1105 found: 318.1107.



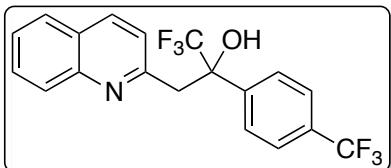
2-(4-bromophenyl)-1,1,1-trifluoro-3-(quinolin-2-yl)propan-2-ol (3ab). Off-white solid (99%, 198.0 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 3.82 (d, $J = 15.6$ Hz, 1H), 3.96 (d, $J = 15.2$ Hz, 1H), 7.46 – 7.50 (m, 2H), 7.54 – 7.58 (m, 2H), 7.70 – 7.78 (m, 3H), 7.89 (d, $J = 8.0$ Hz, 1H), 7.99 (d, $J = 8.4$ Hz, 1H), 8.29 (d, $J = 8.4$ Hz, 1H), 8.36 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.2, 78.2 (q, $J = 28.2$ Hz), 123.0, 123.9, 126.2 (q, $J = 283.2$ Hz), 127.7, 128.0, 128.88, 128.93, 130.2, 131.2, 132.0, 138.7, 139.0, 147.1, 159.1; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{14}\text{BrF}_3\text{NO} [\text{M}+\text{H}]$: 396.0211 found: 396.0208.



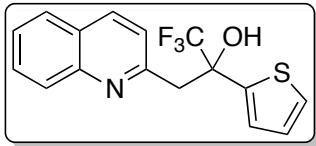
2-(4-chlorophenyl)-1,1,1-trifluoro-3-(quinolin-2-yl)propan-2-ol (3ac). White solid (99%, 179.4 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 3.82 (d, $J = 15.2$ Hz, 1H), 3.96 (d, $J = 15.2$ Hz, 1H), 7.33 (d, $J = 8.8$ Hz, 2H), 7.53 – 7.57 (m, 2H), 7.73 – 7.79 (m, 3H), 7.88 (d, $J = 8.0$ Hz, 1H), 7.98 (d, $J = 8.4$ Hz, 1H), 8.28 (d, $J = 8.4$ Hz, 1H), 8.37 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.3, 78.1 (q, $J = 28.1$ Hz), 122.0 (overlapping q signal), 123.9, 124.8 (overlapping q signal), 127.7, 128.0, 128.87, 128.92, 129.0, 129.9, 130.5 (overlapping q signal), 131.2, 134.8, 138.5, 138.7, 147.1, 159.1; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{14}\text{ClF}_3\text{NO} [\text{M}+\text{H}]$: 352.0716 found: 352.0716.



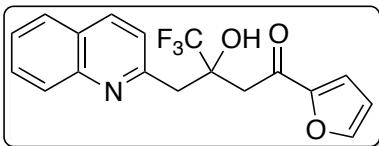
1,1,1-trifluoro-2-(4-fluorophenyl)-3-(quinolin-2-yl)propan-2-ol (**3ad**). White solid (98%, 164.1 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 3.82 (d, $J = 15.2$ Hz, 1H), 3.96 (d, $J = 15.2$ Hz, 1H), 7.03 – 7.09 (m, 2H), 7.54 – 7.58 (m, 2H), 7.74 – 7.82 (m, 3H), 7.89 (d, $J = 8.0$ Hz, 1H), 7.99 (d, $J = 8.4$ Hz, 1H), 8.29 (d, $J = 8.4$ Hz, 1H), 8.34 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.4, 78.1 (q, $J = 28.1$ Hz), 115.6 (d, $J = 21.5$ Hz), 124.0, 126.4 (q, $J = 283.1$ Hz), 127.6, 128.0, 128.9, 129.0, 130.2 (d, $J = 8.3$ Hz), 131.2, 135.7 (d, $J = 3.1$ Hz), 138.7, 147.2, 159.3, 163.5 (d, $J = 244.0$ Hz); HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{14}\text{F}_4\text{NO} [\text{M}+\text{H}]$: 336.1011 found: 336.1013.



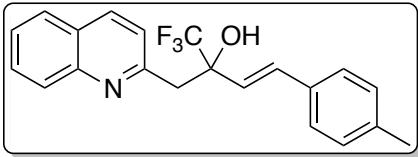
1,1,1-trifluoro-3-(quinolin-2-yl)-2-(4-(trifluoromethyl)phenyl)propan-2-ol (**3ae**). Off-white solid (98%, 188.9 mg); ^1H NMR (400 MHz, CDCl_3): δ 3.67 (d, $J = 15.2$ Hz, 1H), 3.82 (d, $J = 15.6$ Hz, 1H), 7.24 (d, $J = 8.4$ Hz, 1H), 7.51 – 7.70 (m, 3H), 7.71 – 7.74 (m, 1H), 7.77 (d, $J = 8.0$ Hz, 1H), 7.83 (d, $J = 8.0$ Hz, 2H), 7.96 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.73 (s, brs, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.2, 78.4 (q, $J = 28.1$ Hz), 123.9, 125.2 (q, $J = 269.7$ Hz), 125.9 (q, $J = 3.7$ Hz), 126.2 (q, $J = 283.3$ Hz), 127.7, 128.0, 128.9, 130.3 (overlapping q signal), 130.6 (overlapping q signal), 131.0 (overlapping q signal), 131.3, 138.8, 144.2, 147.1, 147.2, 158.9, 159.0; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{14}\text{F}_6\text{NO} [\text{M}+\text{H}]$: 386.0979 found: 386.0981.



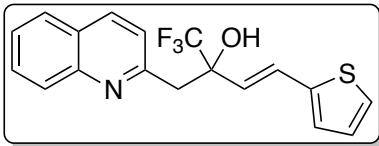
1,1,1-trifluoro-3-(quinolin-2-yl)-2-(thiophen-2-yl)propan-2-ol (**3ah**).⁴ White solid (90%, 146.0 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 3.78 (d, *J* = 15.2 Hz, 1H), 3.89 (d, *J* = 15.2 Hz, 1H), 6.92 (dd, *J*₁ = 4.8 Hz, *J*₂ = 4.0 Hz, 1H), 7.26 (d, *J* = 3.6 Hz, 1H), 7.31 (d, *J* = 4.8 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.75 – 7.79 (m, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 8.30 (d, *J* = 8.4 Hz, 1H), 8.84 (s, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 41.2, 77.8 (q, *J* = 29.5 Hz), 124.0, 125.8 (q, *J* = 282.7 Hz), 126.7, 127.2, 127.7, 127.9, 128.0, 128.90, 128.93, 131.3, 138.7, 144.4, 147.1, 159.2; HRMS (ESI) Calcd for C₁₆H₁₃F₃NOS [M+H]: 324.0670, found: 324.0673.



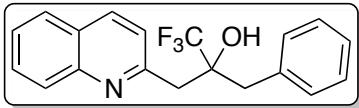
4,4,4-trifluoro-1-(furan-2-yl)-3-hydroxy-3-(quinolin-2-ylmethyl)butan-1-one (**3ai**). Yellow solid (36%, 63.1 mg, 65%, 113.6 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 3.25 (d, *J* = 14.8 Hz, 1H), 3.39 (d, *J* = 15.2 Hz, 1H), 3.51 (d, *J* = 15.2 Hz, 1H), 3.76 (d, *J* = 15.2 Hz, 1H), 6.68 (dd, *J*₁ = 3.6 Hz, *J*₂ = 2.0 Hz, 1H), 7.39 (d, *J* = 3.6 Hz, 1H), 7.55 – 7.61 (m, 2H), 7.72 – 7.77 (m, 2H), 7.83 (d, *J* = 1.2 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 8.35 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 39.7, 41.5, 76.9 (q, *J* = 27.6 Hz), 113.5, 119.8, 124.2, 127.1 (q, *J* = 284.8 Hz), 127.5, 128.0, 128.8, 129.2, 130.9, 138.3, 147.4, 148.6, 154.1, 159.4, 186.0; HRMS (ESI) Calcd for C₁₈H₁₅F₃NO₃ [M+H]: 350.1004 found: 350.1005.



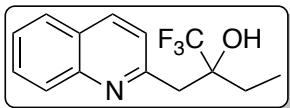
(*E*)-1,1,1-trifluoro-2-(quinolin-2-ylmethyl)-4-(*p*-tolyl)but-3-en-2-ol (**3aj**). Off-white solid (85%, 151.2 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 2.25 (s, 3H), 3.50 – 3.59 (m, 2H), 6.39 (d, J = 16.0 Hz, 1H), 6.84 (d, J = 16.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.56 – 7.60 (m, 3H), 7.76 – 7.80 (m, 1H), 7.92 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 21.2, 41.1, 77.3 (q, J = 27.9 Hz), 122.4 (overlapping q signal), 124.0, 125.2 (overlapping q signal), 126.0, 127.5, 127.6, 128.1, 128.9, 129.2, 130.1, 130.9 (overlapping q signal), 131.1, 134.0, 134.3, 138.4, 138.7, 147.5, 159.1; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{19}\text{F}_3\text{NO} [\text{M}+\text{H}]$: 358.1418 found: 358.1418.



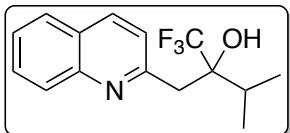
(*E*)-1,1,1-trifluoro-2-(quinolin-2-ylmethyl)-4-(thiophen-2-yl)but-3-en-2-ol (**3ak**). Off-white solid (85%, 148.8 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 3.50 – 3.59 (m, 2H), 6.23 (d, J = 15.6 Hz, 1H), 6.91 – 6.93 (m, 1H), 7.00 – 7.06 (m, 2H), 7.29 (d, J = 4.8 Hz, 1H), 7.57 – 7.60 (m, 2H), 7.70 (s, brs, 1H), 7.76 – 7.80 (m, 1H), 7.80 – 7.94 (m, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.8, 77.1 (q, J = 28.1 Hz), 123.9, 126.19, 126.22, 126.5 (q, J = 283.6 Hz), 127.53, 127.55, 128.0, 128.1, 128.5, 128.9, 129.2, 131.1, 138.5, 141.8, 147.4, 158.9; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{17}\text{F}_3\text{NOS} [\text{M}+\text{H}]$: 350.0826 found: 350.0826.



2-benzyl-1,1,1-trifluoro-3-(quinolin-2-yl)propan-2-ol (**3al**).⁴ Light yellow solid (73%, 120.4 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 3.00 (d, *J* = 14.0 Hz, 1H), 3.11 (d, *J* = 15.6 Hz, 1H), 3.22 (d, *J* = 13.6 Hz, 1H), 3.34 (d, *J* = 15.6 Hz, 1H), 7.18 – 7.22 (m, 1H), 7.25 – 7.29 (m, 2H), 7.41 – 7.44 (m, 3H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.73 – 7.77 (m, 1H), 7.91 – 7.98 (m, 3H), 8.28 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 38.7, 41.5, 77.5 (q, *J* = 25.9 Hz), 123.7, 127.4, 127.7, 127.8 (q, *J* = 286.1 Hz), 127.9, 128.81, 128.84, 128.9, 131.0, 132.2, 136.3, 138.5, 147.0, 160.1; HRMS (ESI) Calcd for C₁₉H₁₇F₃NO [M+H]: 332.1262 found: 332.1262.

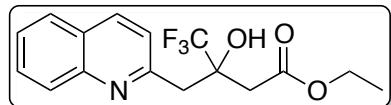


1,1,1-trifluoro-2-(quinolin-2-ylmethyl)butan-2-ol (**3am**).⁴ White solid (46%, 61.6 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 1.04 (t, *J* = 7.6 Hz, 3H), 1.74 – 1.83 (m, 2H), 3.29 – 3.38 (m, 2H), 7.35 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.77 – 7.81 (m, 1H), 8.00 (dd, *J*₁ = 21.4 Hz, *J*₂ = 8.2 Hz, 2H), 8.36 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 7.8, 28.9, 39.2, 76.9 (q, *J* = 25.8 Hz), 123.9, 127.5, 128.03 (q, *J* = 292.0 Hz), 128.01, 128.9, 129.5, 131.1, 138.4, 147.5, 160.1; HRMS (ESI) Calcd for C₁₄H₁₅F₃NO [M+H]: 270.1105 found: 270.1106.

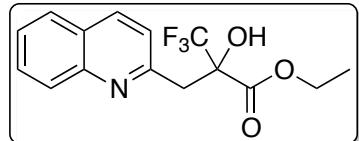


1,1,1-trifluoro-3-methyl-2-(quinolin-2-ylmethyl)butan-2-ol (**3an**). Light yellow solid (34%, 47.5 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 1.09 – 1.12 (m, 6H), 2.11 – 2.15 (m, 1H), 3.33 (s, 2H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.59 – 7.63 (m, 1H), 7.73 (s, 1H), 7.78

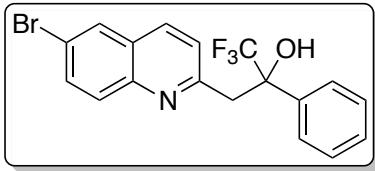
– 7.82 (m, 1H), 7.98 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.8 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 17.4, 17.9, 34.6, 36.3, 79.1 (q, J = 24.9 Hz), 123.9, 127.5, 128.0, 128.3 (q, J = 287.4 Hz), 128.9, 129.1, 131.2, 138.6, 147.3, 160.5; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{16}\text{F}_3\text{NO} [\text{M}+\text{H}]$: 284.1262 found: 284.1259.



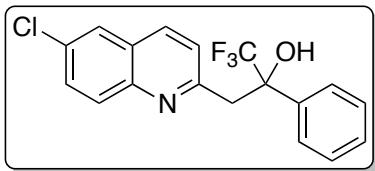
Ethyl 4,4,4-trifluoro-3-hydroxy-3-(quinolin-2-ylmethyl)butanoate (**3ao**).⁴ Colourless oil (56%, 91.8 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 1.20 (t, J = 7.2 Hz, 3H), 2.80 (s, 2H), 3.47 (d, J = 15.2 Hz, 1H), 3.79 (d, J = 15.2 Hz, 1H), 4.07 (q, J = 7.2 Hz, 2H), 7.56 (d, J = 8.4 Hz, 1H), 7.59 – 7.63 (m, 1H), 7.77 – 7.81 (m, 2H), 7.97 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 14.4, 39.1, 39.8, 61.4, 76.0 (q, J = 27.8 Hz), 124.2, 127.0 (q, J = 284.8 Hz), 127.6, 128.1, 128.9, 129.2, 131.0, 138.4, 147.4, 159.4, 170.0; HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{16}\text{F}_3\text{NO}_3 [\text{M}+\text{H}]$: 328.1160 found: 328.2306



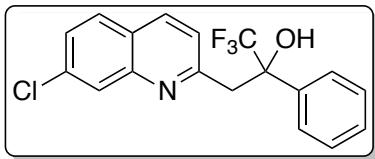
Ethyl 3,3,3-trifluoro-2-hydroxy-2-(quinolin-2-ylmethyl)propanoate (**3ap**).⁴ White solid (88%, 137.9 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 1.18 (t, J = 7.2 Hz, 3H), 3.54 (d, J = 15.2 Hz, 1H), 3.81 (d, J = 14.8 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 6.38 (s, brs, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.73 – 7.78 (m, 1H), 7.95 (t, J = 8.2 Hz, 2H), 8.30 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 14.3, 40.2, 63.2, 78.8 (q, J = 28.3 Hz), 125.1 (q, J = 283.8 Hz), 123.7, 127.4, 128.1, 128.8, 129.4, 130.7, 137.8, 147.9, 157.3, 169.3; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{14}\text{F}_3\text{NO}_3 [\text{M}+\text{H}]$: 314.1004 found: 314.1440



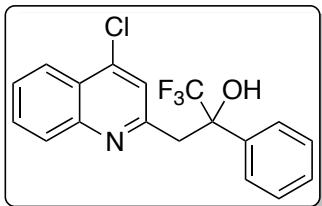
3-(6-bromoquinolin-2-yl)-1,1,1-trifluoro-2-phenylpropan-2-ol (3ba). White solid (92%, 182.0 mg); ^1H NMR (400 MHz, CDCl_3): δ 3.70 (d, $J = 15.2$ Hz, 1H), 3.79 (d, $J = 14.8$ Hz, 1H), 7.24 – 7.28 (m, 2H), 7.31 – 7.35 (m, 2H), 7.69 (d, $J = 7.6$ Hz, 2H), 7.76 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.2$ Hz, 1H), 7.84 (d, $J = 9.2$ Hz, 1H), 7.91 (d, $J = 2.0$ Hz, 1H), 7.97 (d, $J = 8.4$ Hz, 1H), 8.13 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.8, 78.2 (q, $J = 29.7$ Hz), 120.7, 124.9, 127.9, 128.5 (q, $J = 283.3$ Hz), 128.9, 129.0, 129.1, 130.8, 131.0, 134.2, 137.6, 139.3, 145.7, 160.0; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{14}\text{BrF}_3\text{NO} [\text{M}+\text{H}]$: 396.0211 found: 396.0218.



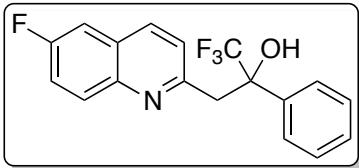
3-(6-chloroquinolin-2-yl)-1,1,1-trifluoro-2-phenylpropan-2-ol (3ca). White solid (91%, 159.8 mg); ^1H NMR (400 MHz, CDCl_3): δ 3.70 (d, $J = 15.2$ Hz, 1H), 3.81 (d, $J = 15.2$ Hz, 1H), 7.25 – 7.28 (m, 2H), 7.31 – 7.35 (m, 2H), 7.62 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.2$ Hz, 1H), 7.70 – 7.72 (m, 3H), 7.90 (d, $J = 9.2$ Hz, 1H), 7.97 (d, $J = 8.4$ Hz, 1H), 8.16 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.7, 78.3 (q, $J = 28.0$), 125.0, 126.4 (q, $J = 283.3$ Hz), 127.4, 127.9, 128.5, 128.9, 129.1, 130.9, 131.6, 132.6, 137.7, 139.3, 145.6, 159.9; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{14}\text{ClF}_3\text{NO} [\text{M}+\text{H}]$: 352.0716 found: 352.0717.



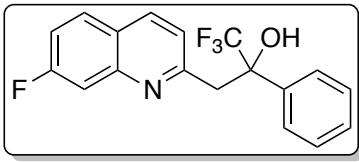
3-(7-chloroquinolin-2-yl)-1,1,1-trifluoro-2-phenylpropan-2-ol (3da). White solid (92%, 162.3 mg); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 3.82 (d, $J = 15.2$ Hz, 1H), 3.98 (d, $J = 15.2$ Hz, 1H), 7.20 – 7.24 (m, 1H), 7.28 – 7.32 (m, 2H), 7.51 (dd, $J_1 = 8.8$ Hz, $J_2 = 2.0$ Hz, 1H), 7.55 (d, $J = 8.4$ Hz, 1H), 7.76 (d, $J = 7.6$ Hz, 2H), 7.84 – 7.88 (m, 2H), 8.03 (d, $J = 1.6$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.8, 78.3 (q, $J = 27.9$ Hz), 122.2 (overlapping q signal), 124.4, 125.0 (overlapping q signal), 126.4, 127.9, 128.0, 128.2, 128.9, 129.1, 130.6, 130.7 (overlapping q signal), 136.4, 138.4, 139.3, 147.5, 160.7; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{14}\text{ClF}_3\text{NO} [\text{M}+\text{H}]$: 352.0716 found: 352.0715.



3-(4-chloroquinolin-2-yl)-1,1,1-trifluoro-2-phenylpropan-2-ol (3ea). White solid (98%, 173.1 mg); ^1H NMR (400 MHz, CDCl_3): δ 3.63 (d, $J = 15.2$ Hz, 1H), 3.75 (d, $J = 15.2$ Hz, 1H), 7.22 – 7.26 (m, 1H), 7.29 – 7.34 (m, 3H), 7.55 – 7.59 (m, 1H), 7.67 – 7.74 (m, 3H), 7.95 (d, $J = 8.4$ Hz, 1H), 8.12 (d, $J = 8.4$ Hz, 1H), 8.15 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 40.7, 78.3 (q, $J = 28.0$ Hz), 124.0, 124.6, 125.7, 126.4 (q, $J = 283.2$ Hz), 128.0, 128.8, 129.0, 129.2, 129.6, 132.2, 139.1, 143.9, 148.1, 159.4; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{14}\text{ClF}_3\text{NO} [\text{M}+\text{H}]$: 352.0716 found: 352.0716.

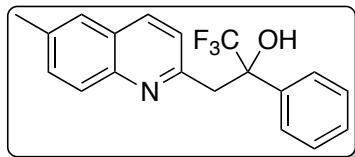


1,1,1-trifluoro-3-(6-fluoroquinolin-2-yl)-2-phenylpropan-2-ol (**3fa**). White solid (75%, 126.2 mg); ¹H NMR (400 MHz, CDCl₃): δ 3.66 (d, *J* = 15.2 Hz, 1H), 3.77 (d, *J* = 15.2 Hz, 1H), 7.21 – 7.25 (m, 2H), 7.28 – 7.36 (m, 3H), 7.45 (td, *J₁* = 8.6 Hz, *J₂* = 2.7 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.95 (dd, *J₁* = 9.2 Hz, *J₂* = 5.2 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 8.18 (s, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 40.6, 78.3 (q, *J* = 27.6 Hz), 111.8 (d, *J* = 22.0 Hz), 121.1 (d, *J* = 25.9 Hz), 122.2 (overlapping q signal), 124.9, 125.1 (overlapping q signal), 128.0, 128.6 (d, *J* = 10.2 Hz), 128.9 (d, *J* = 1.1 Hz), 129.1, 130.7 (overlapping q signal), 131.8 (d, *J* = 9.2 Hz), 138.0 (d, *J* = 4.0 Hz), 139.4, 144.4, 158.9, 161.2 (d, *J* = 244.9 Hz); HRMS (ESI) Calcd for C₁₈H₁₄F₄NO [M+H]: 336.1011 found: 336.1011.

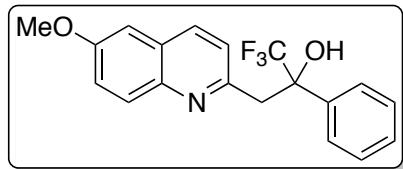


1,1,1-trifluoro-3-(7-fluoroquinolin-2-yl)-2-phenylpropan-2-ol (**3ga**). White solid (94%, 157.7 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 3.82 (d, *J* = 15.2 Hz, 1H), 3.96 (d, *J* = 15.2 Hz, 1H), 7.20 – 7.24 (m, 1H), 7.28 – 7.32 (m, 2H), 7.39 (td, *J₁* = 8.8 Hz, *J₂* = 2.8 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.69 (dd, *J₁* = 10.4 Hz, *J₂* = 2.4 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.91 – 7.98 (m, 2H), 8.26 (d, *J* = 10.8 Hz, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 40.8, 78.3 (q, *J* = 27.6 Hz), 112.5 (d, *J* = 20.8 Hz), 117.8 (d, *J* = 25.3 Hz), 122.2 (overlapping q signal), 123.5 (d, *J* = 2.2 Hz), 125.1, 127.8 (overlapping q signal), 128.0, 128.9, 129.1, 130.7 (overlapping q signal), 131.4 (d, *J* =

10.2 Hz), 138.5, 139.4, 148.1 (d, J = 12.8 Hz), 160.7, 164.3 (d, J = 247.5 Hz); HRMS (ESI) Calcd for $C_{18}H_{14}F_4NO$ [M+H]: 336.1011 found: 336.1013.

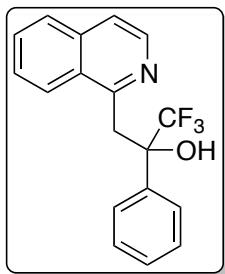


1,1,1-trifluoro-3-(6-methylquinolin-2-yl)-2-phenylpropan-2-ol (**3ha**). White solid (95%, 157.0 mg); 1H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 3H), 3.63 (d, J = 15.2 Hz, 1H), 3.75 (d, J = 14.8 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 7.19 – 7.24 (m, 1H), 7.28 – 7.30 (m, 2H), 7.47 – 7.51 (m, 2H), 7.67 (d, J = 7.6 Hz, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 8.55 (s, 1H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 21.5, 40.4, 78.3 (q, J = 27.9 Hz), 122.3 (overlapping q signal), 124.0, 125.1 (overlapping q signal), 127.5, 128.0, 128.7, 128.9, 129.0, 130.8 (overlapping q signal), 133.3, 137.5, 137.9, 139.6, 145.8, 158.4; HRMS (ESI) Calcd for $C_{19}H_{17}F_3NO$ [M+H]: 332.1262 found: 332.1262.

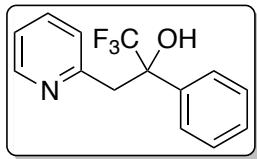


1,1,1-trifluoro-3-(6-methoxyquinolin-2-yl)-2-phenylpropan-2-ol (**3ia**). Yellow solid (58%, 100.8 mg); 1H NMR (400 MHz, $CDCl_3$): δ 3.61 (d, J = 15.2 Hz, 1H), 3.73 (d, J = 14.8 Hz, 1H), 3.86 (s, 3H), 7.00 (d, J = 2.4 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.22 – 7.34 (m, 4H), 7.67 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 9.2 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 8.50 (s, brs, 1H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 40.2, 56.0, 78.3 (q, J = 27.8 Hz), 106.3, 122.3 (overlapping q signal), 123.8, 124.2, 125.1 (overlapping q signal), 128.0, 128.9, 129.0, 129.1, 130.3, 130.8 (overlapping q signal), 137.3, 139.6,

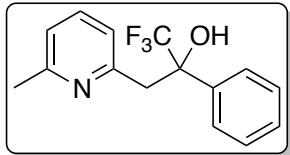
143.2, 156.5, 158.9; HRMS (ESI) Calcd for C₁₉H₁₇F₃NO₂ [M+H]: 348.1211 found: 348.1210.



1,1,1-trifluoro-3-(isoquinolin-1-yl)-2-phenylpropan-2-ol (**3ja**).⁴ White solid (99%, 156.9 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 4.00 (d, *J* = 16.0 Hz, 1H), 4.37 (d, *J* = 16.0 Hz, 1H), 7.18 – 7.21 (m, 1H), 7.25 – 7.28 (m, 2H), 7.68 (d, *J* = 5.6 Hz, 1H), 7.74 – 7.81 (m, 4H), 7.92 (d, *J* = 7.6 Hz, 1H), 8.32 (d, *J* = 5.6 Hz, 1H), 8.58 (d, *J* = 8.4 Hz, 1H), 8.80 (s, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 35.0, 78.3 (q, *J* = 27.7 Hz), 121.3, 126.1, 126.6 (q, *J* = 283.3 Hz), 127.8, 128.48, 128.52, 128.8, 129.0, 129.1, 131.9, 137.5, 140.1, 140.6, 159.0; HRMS (ESI) Calcd for C₁₈H₁₅F₃NO [M+H]: 318.1105 found: 318.1106.



1,1,1-trifluoro-2-phenyl-3-(pyridin-2-yl)propan-2-ol (**3ka**).⁴ Light yellow solid (48%, 63.7 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 3.62 (d, *J* = 14.8 Hz, 1H), 3.71 (d, *J* = 15.2 Hz, 1H), 7.22 – 7.28 (m, 2H), 7.30 – 7.34 (m, 2H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.69 – 7.74 (m, 3H), 8.01 (s, 1H), 8.43 (d, brs, *J* = 4.4 Hz, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 40.0, 78.1 (q, *J* = 27.8 Hz), 122.3 (overlapping q signal), 123.3, 125.1 (overlapping q signal), 126.0, 128.0, 128.9, 129.0, 130.8 (overlapping q signal), 138.6, 139.5, 148.8, 158.2; HRMS (ESI) Calcd for C₁₄H₁₃F₃NO [M+H]: 268.0949 found: 268.0944.



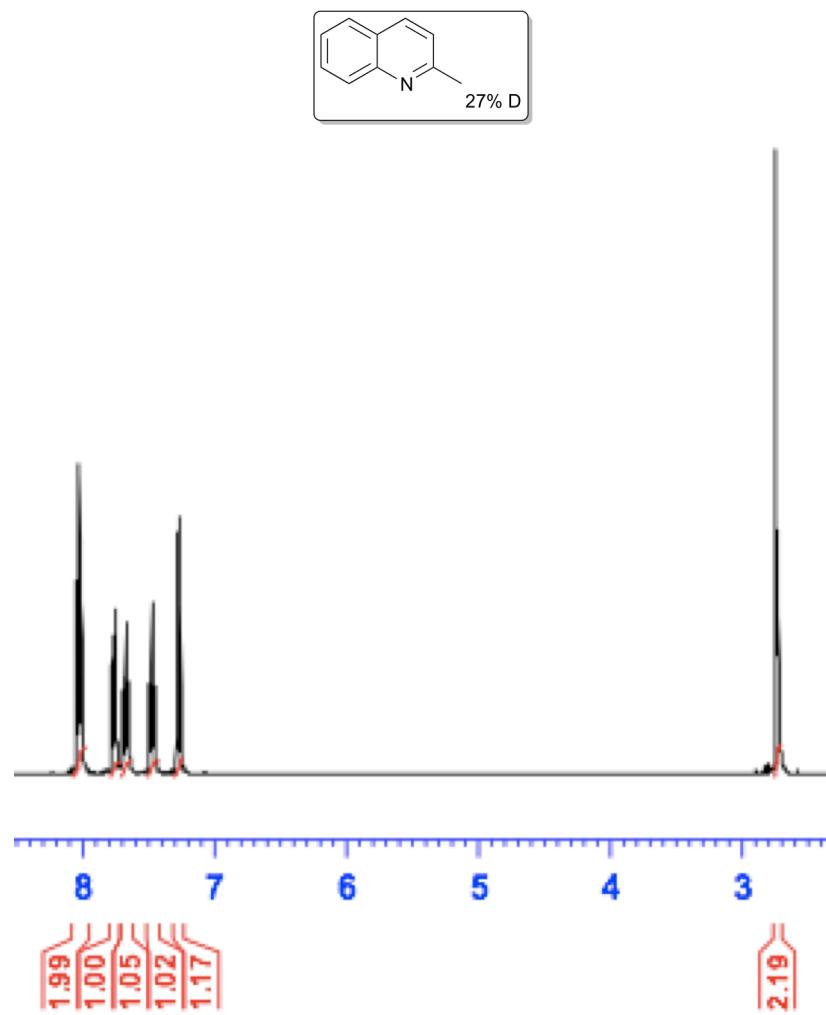
1,1,1-trifluoro-3-(6-methylpyridin-2-yl)-2-phenylpropan-2-ol (**3la**). White solid (75 %, 106 mg); ¹H NMR (400 MHz, (CD₃)₂CO): δ 2.44 (s, 3H), 3.61 (q, *J* = 15.2 Hz, 2H), 7.09 (d, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.27 (m, 1H), 7.30 – 7.34 (m, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 2H), 8.28 (s, 1H); ¹³C NMR (100 MHz, (CD₃)₂CO): δ 24.1, 39.9, 78.1 (q, *J* = 27.8 Hz), 122.3 (overlapping q signal), 122.7, 122.9, 125.1 (overlapping q signal), 128.0, 128.8, 129.0, 130.8 (overlapping q signal), 138.9, 139.7, 157.4, 157.8; HRMS (ESI) Calcd for C₁₅H₁₅F₃NO [M+H]: 282.1105 found: 282.1108.

References

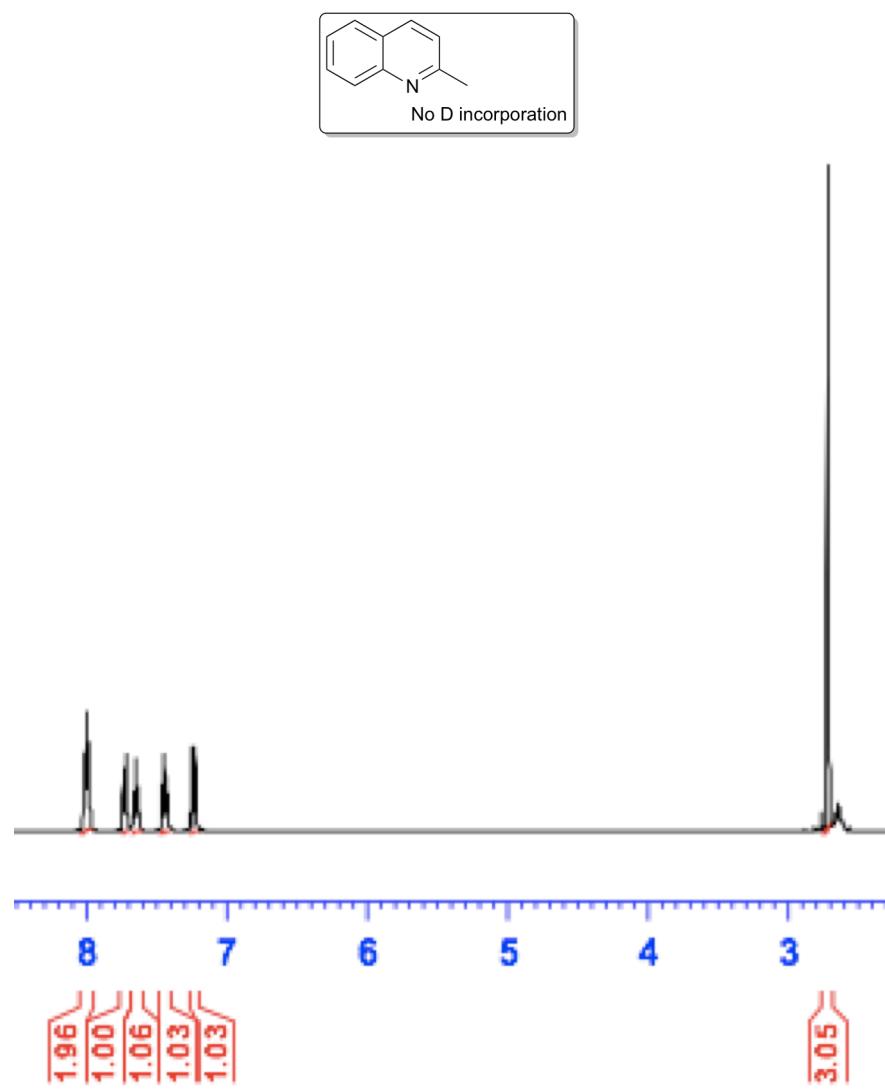
1. C. Zheng, Y. Li, Y. Yang, H. Wang, H. Cui, J. Zhang and G. Zhao, *Adv. Synth. Catal.* 2009, **351**, 1685.
2. P.-P. Yeh, D. S. B. Daniels, D. B. Cordes, A. M. Z. Slawin and A. D. Smith, *Org. Lett.* 2014, **16**, 964.
3. J. Hu, S. Chen, Y. Sun, J. Yang and Y. Rao, *Org. Lett.* 2012, **14**, 5030.
4. V. B. Graves and A. Shaikh, *Tetrahedron Lett.* 2013, **54**, 695.

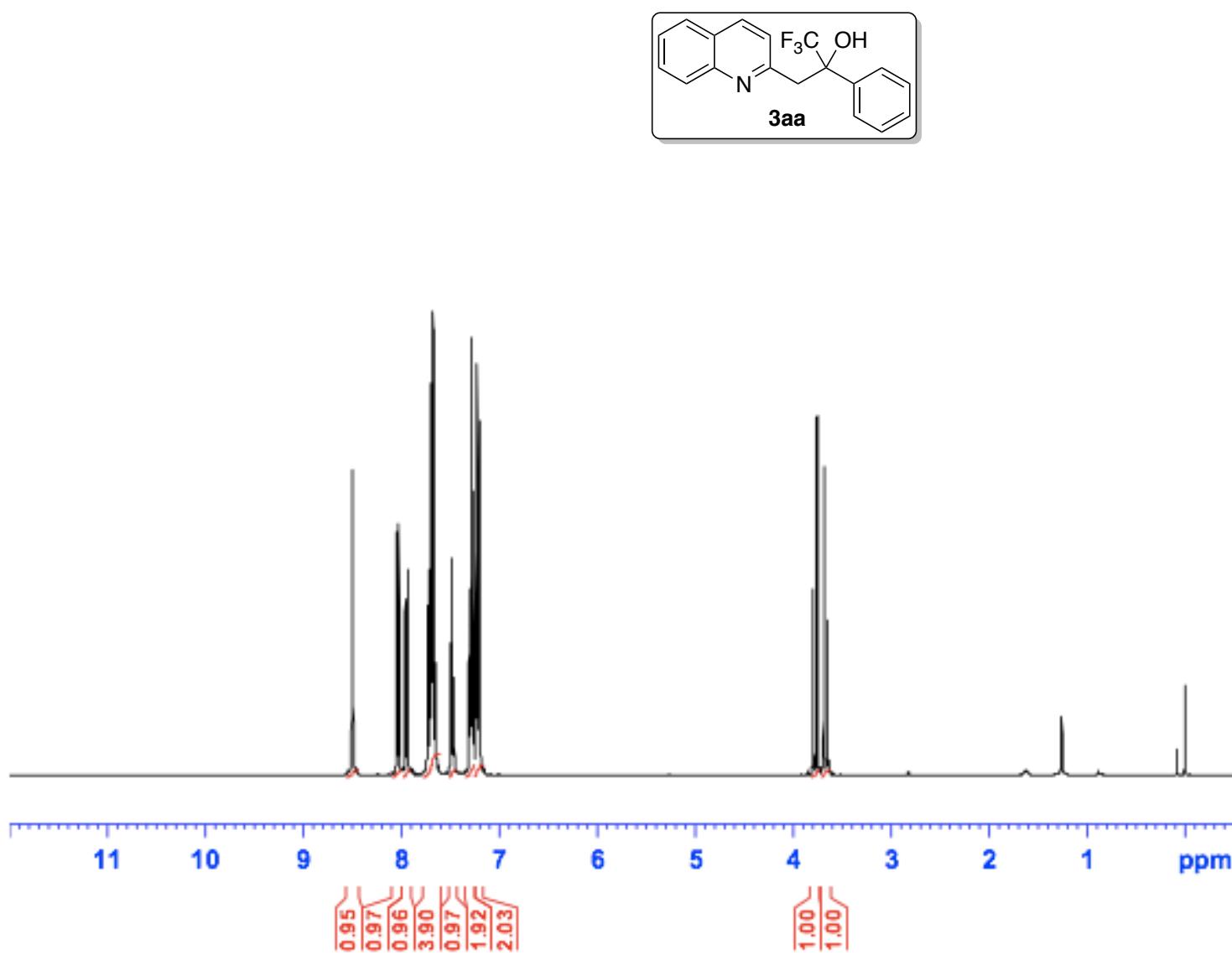
5. Deuterium Exchange Experiments

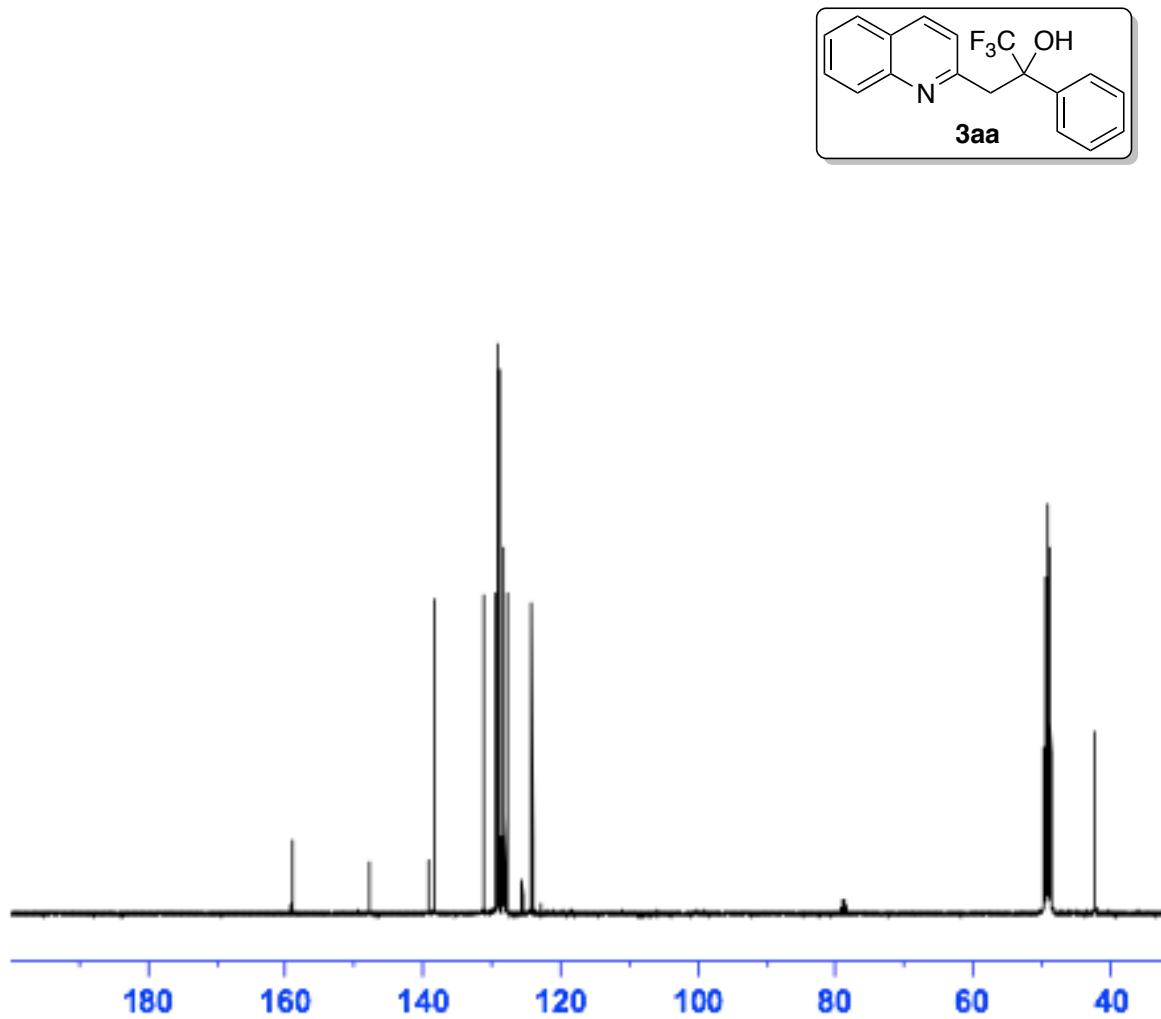
To an 8-mL reaction vial equipped with a magnetic stir bar, InCl₃ (5.5 mg, 0.025 mmol), 2-methylquinoline (102 μ L, 0.75 mmol) and D₂O (0.5 mL) were sequentially added. The vial was then capped and placed into a pre-heated oil bath at 60 °C with vigorous stirring for 24 h. With glass Pasteur pipettes, an aliquot of the mixture was then drawn and passed through a short pad of silica gel using CDCl₃. The resulting clear mixture was then analyzed by ¹H NMR spectroscopy from which the percentage of deuterium incorporation was determined to be 27%.



Similar procedure was also adopted for the control experiment conducted with omitted InCl_3 whereby no deuterium incorporation was observed.







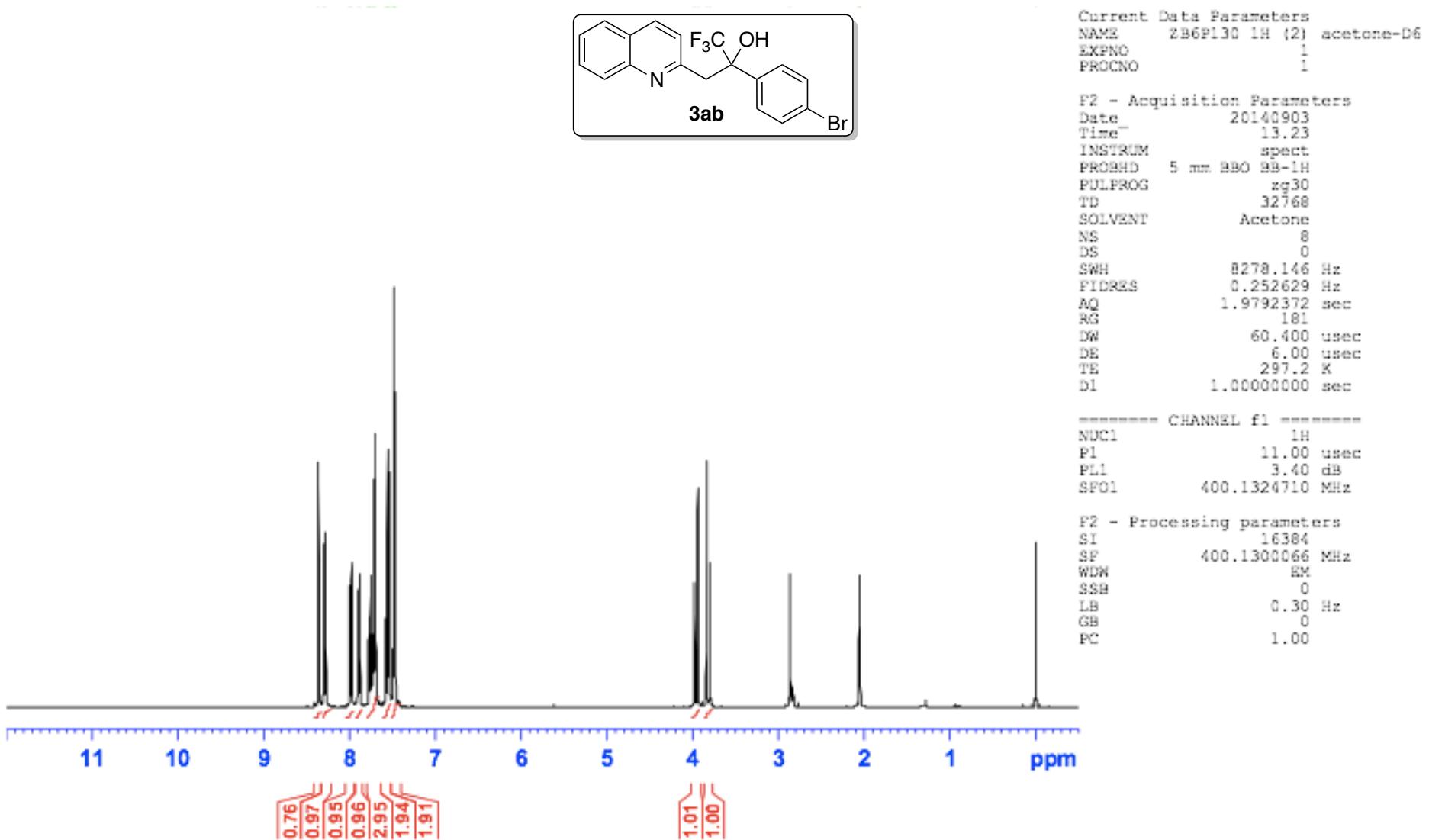
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EXPNO 1
PROCNO 1

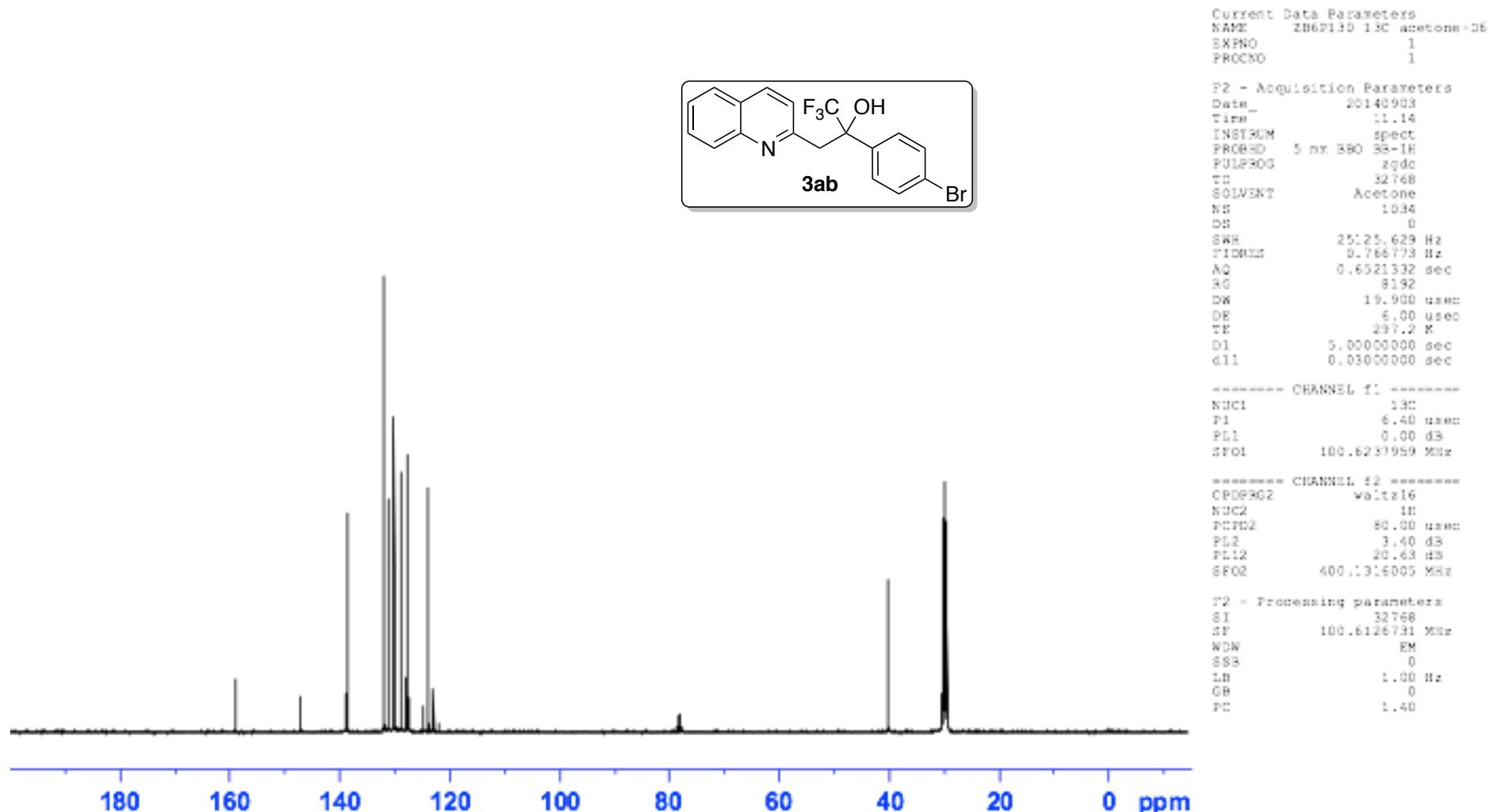
P2 - Acquisition Parameters
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Time 14.09
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TD 32768
SOLVENT MeOD
NS 505
DS 0
SWH 25125.629 Hz
FIDRES 0.766773 Hz
AQ 0.6521332 sec
RG 5792.6
DW 19.900 usec
DE 6.00 usec
TE 297.2 K
D1 5.0000000 sec
d11 0.0300000 sec

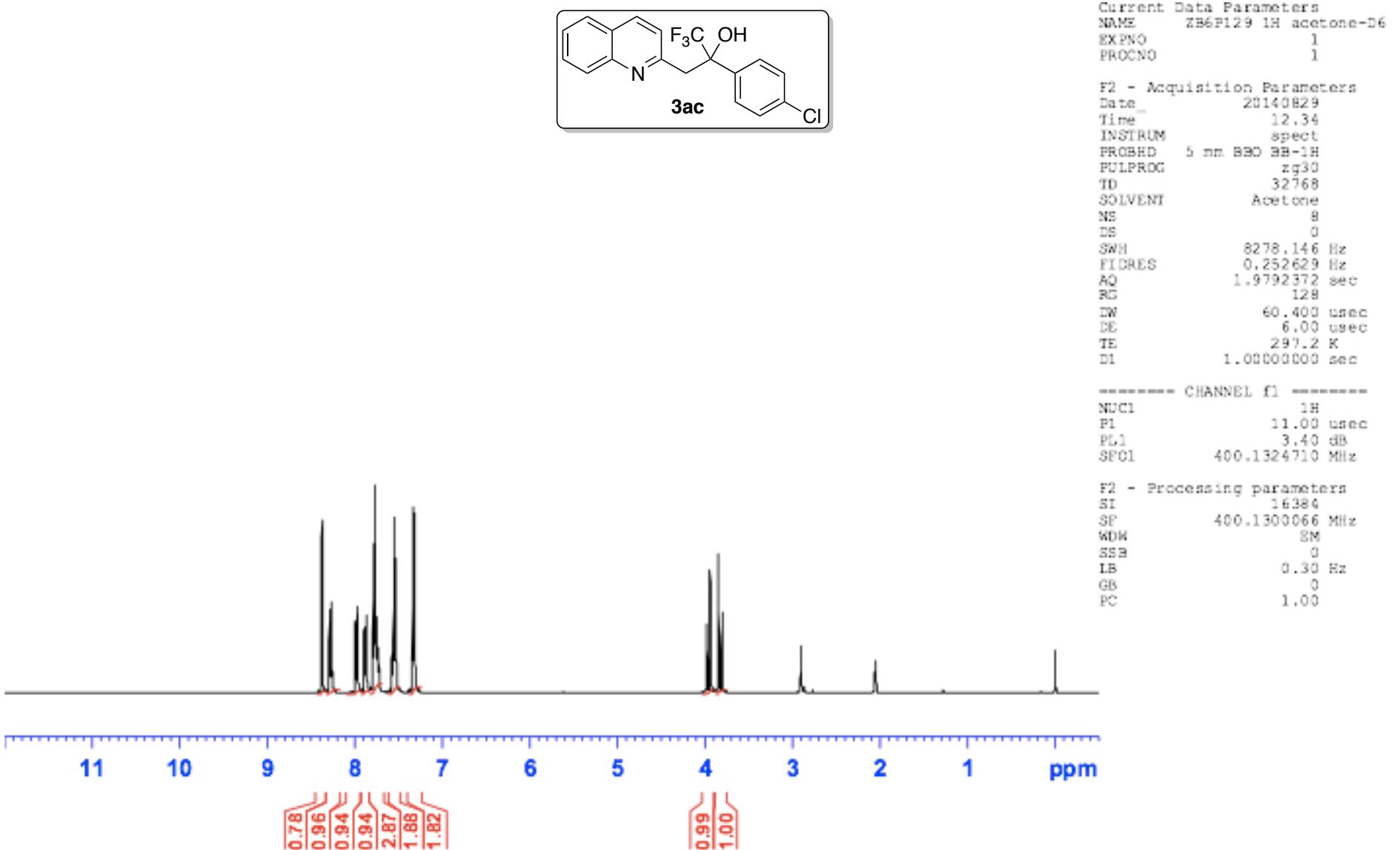
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PL1 0.00 dB
SFO1 100.6237959 MHz

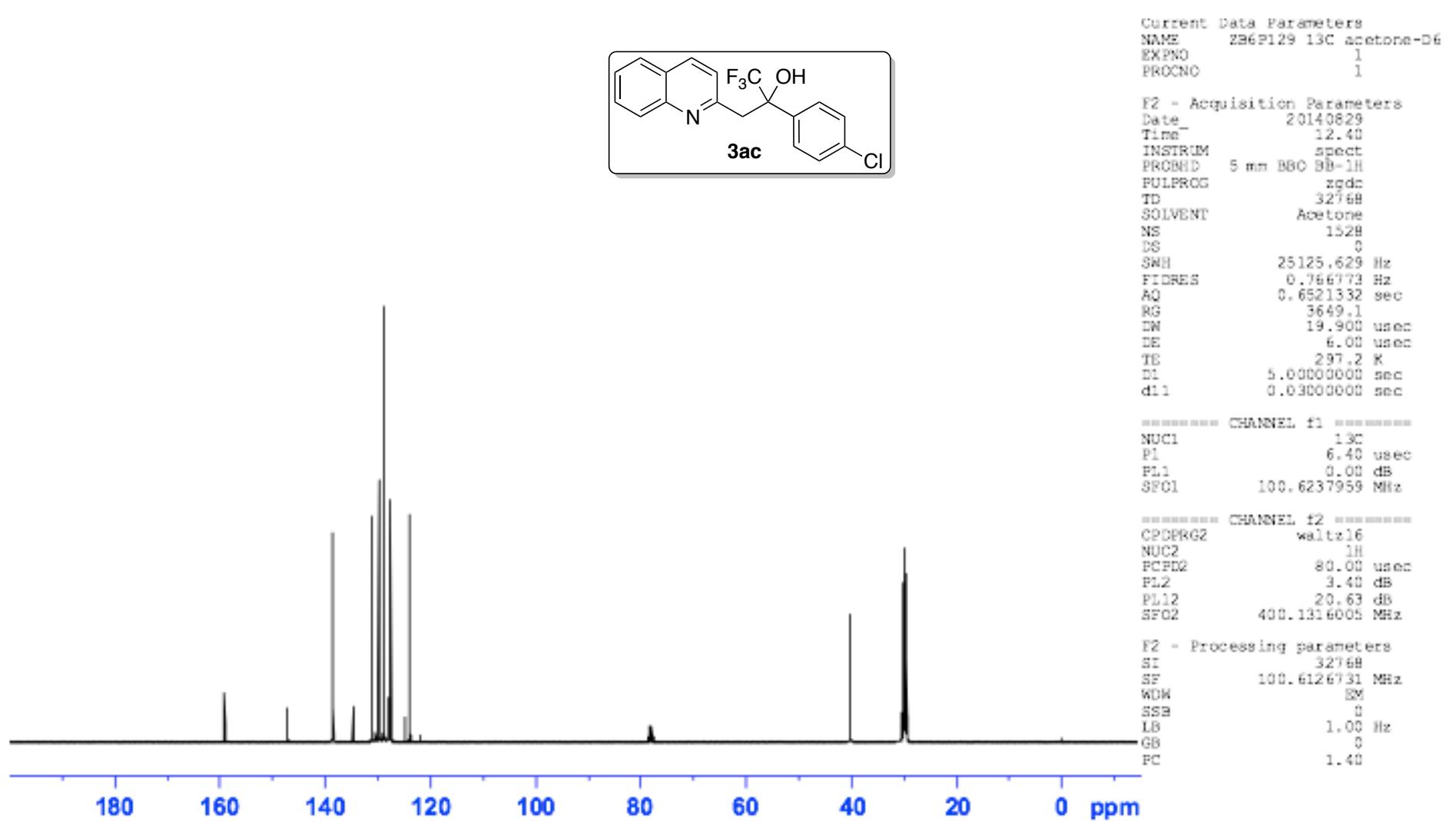
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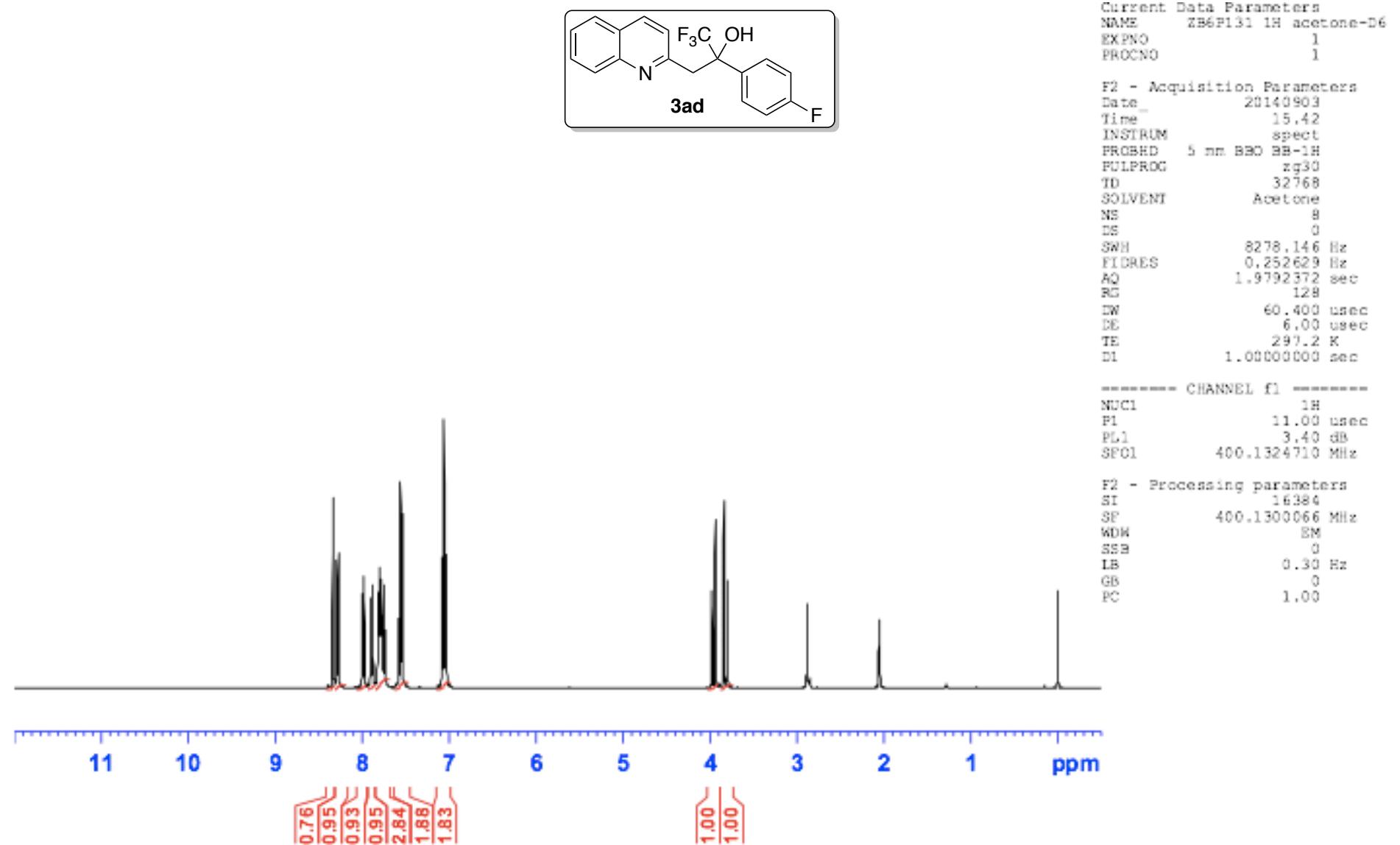
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WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

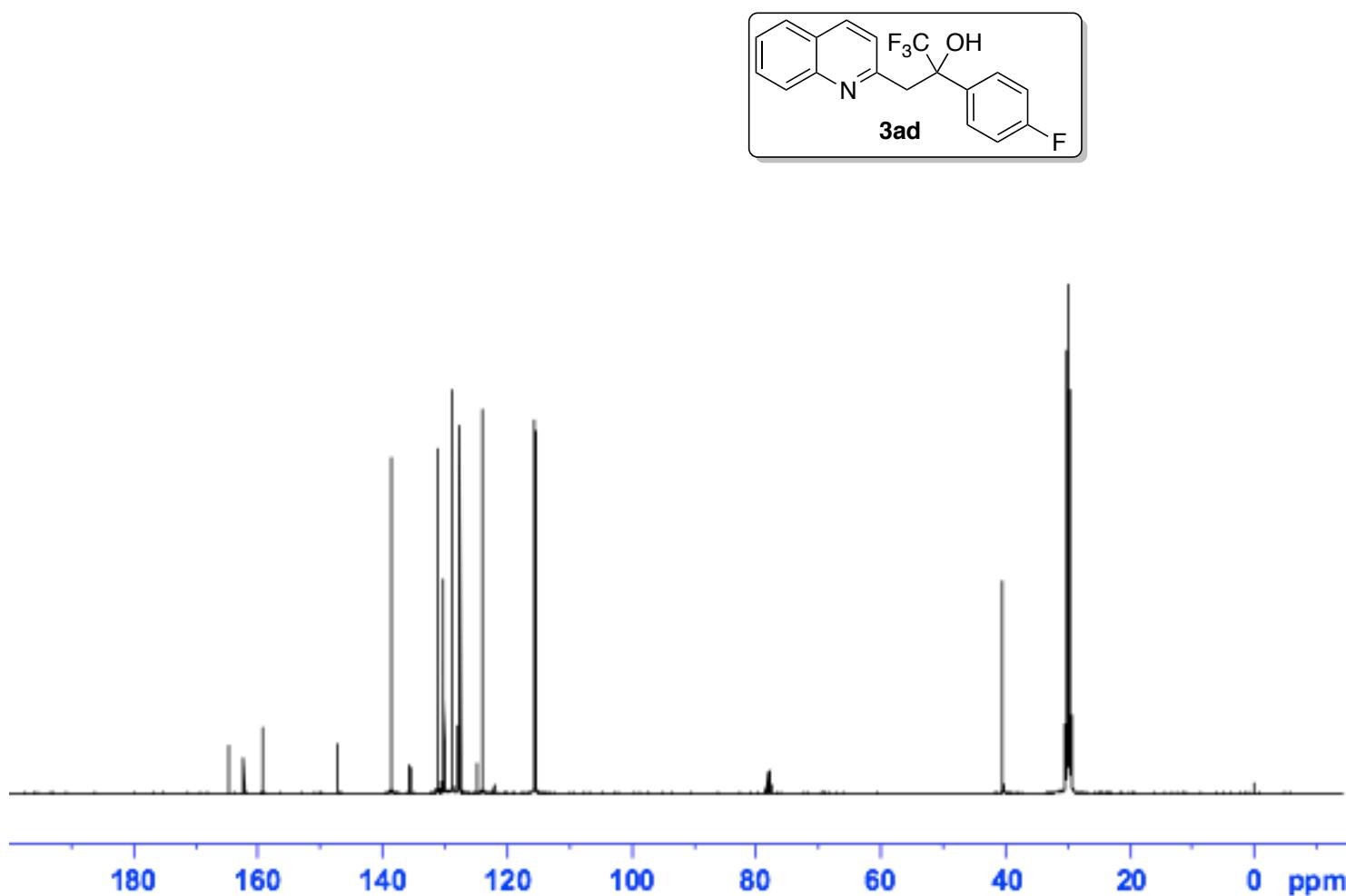












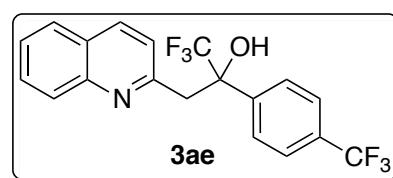
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 PROCNO 1

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 FIDRES 0.766773 Hz
 AQ 0.6521332 sec
 RG 7298.2
 DW 19.900 usec
 DE 6.00 usec
 TE 297.2 K
 D1 5.0000000 sec
 d11 0.0300000 sec

===== CHANNEL f1 =====
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 P1 6.40 usec
 PL1 0.00 dB
 SFQ1 100.6237959 MHz

===== CHANNEL f2 =====
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 NUC2 1H
 PCPD2 80.00 usec
 PL2 3.40 dB
 PL12 20.63 dB
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F2 - Processing parameters
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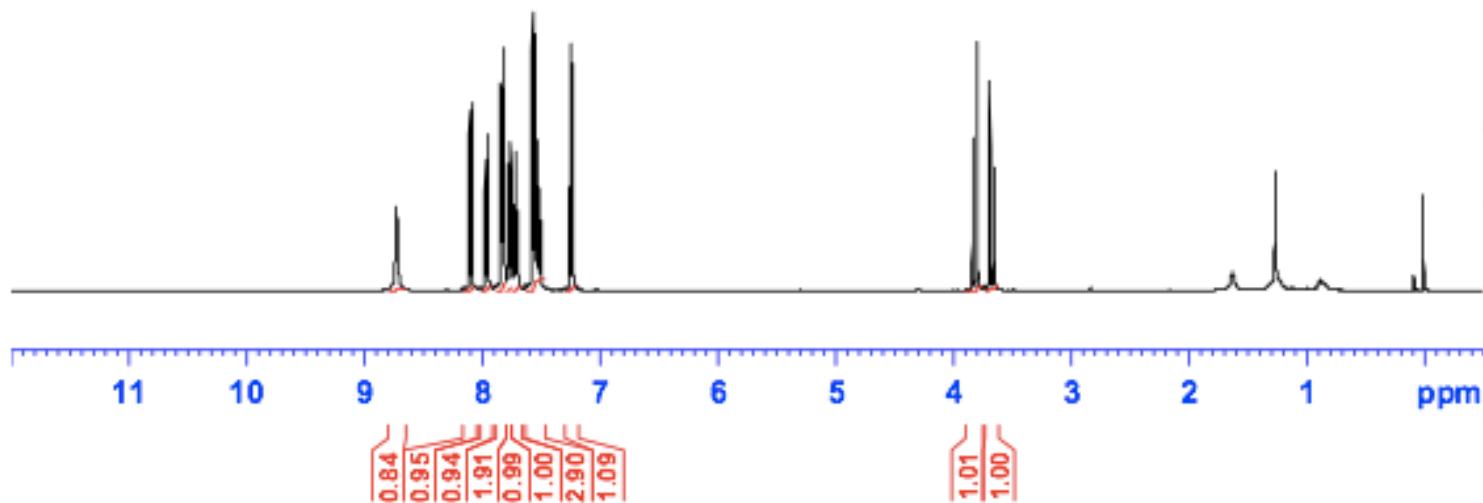


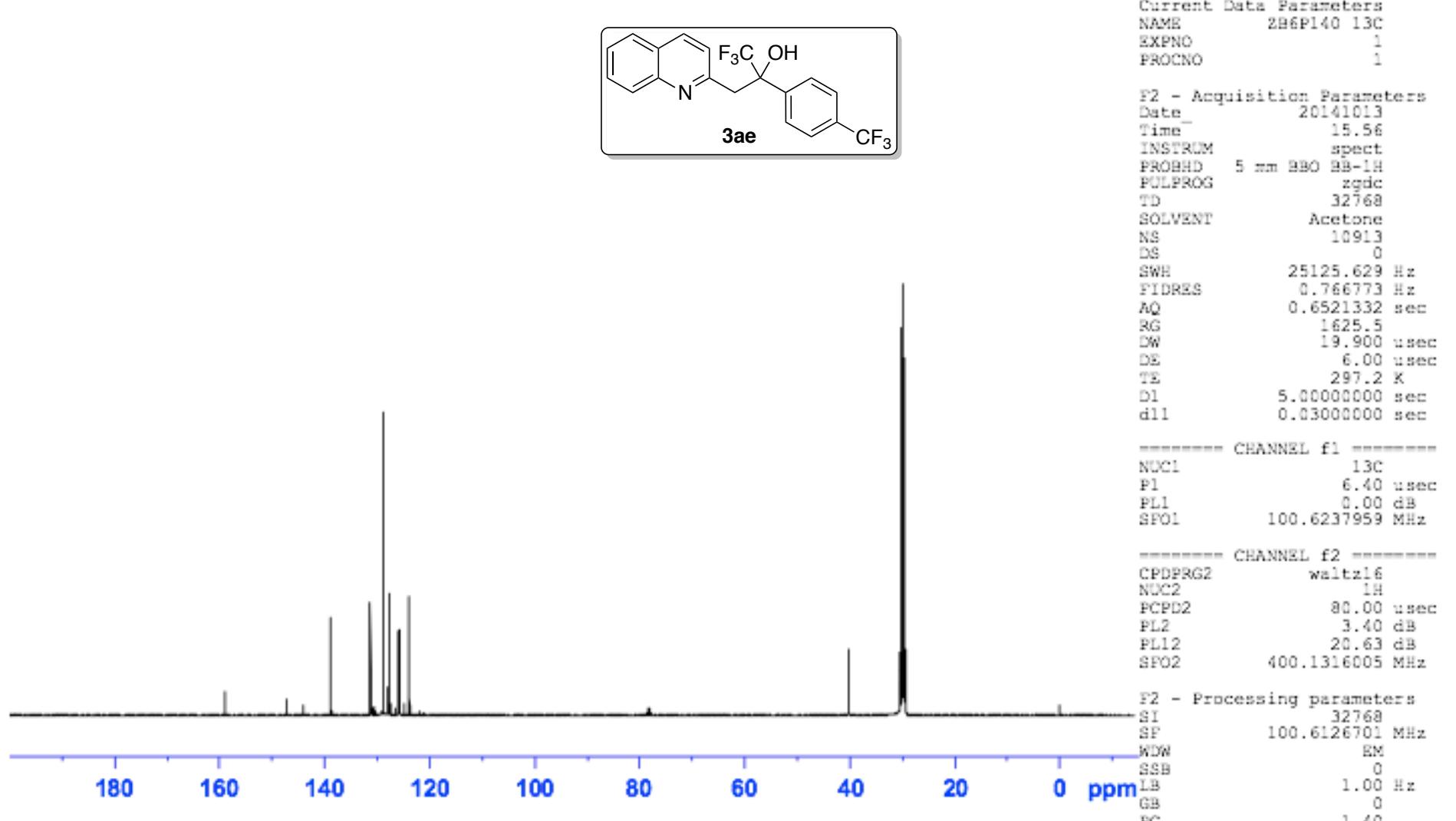
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 PROCNO 1

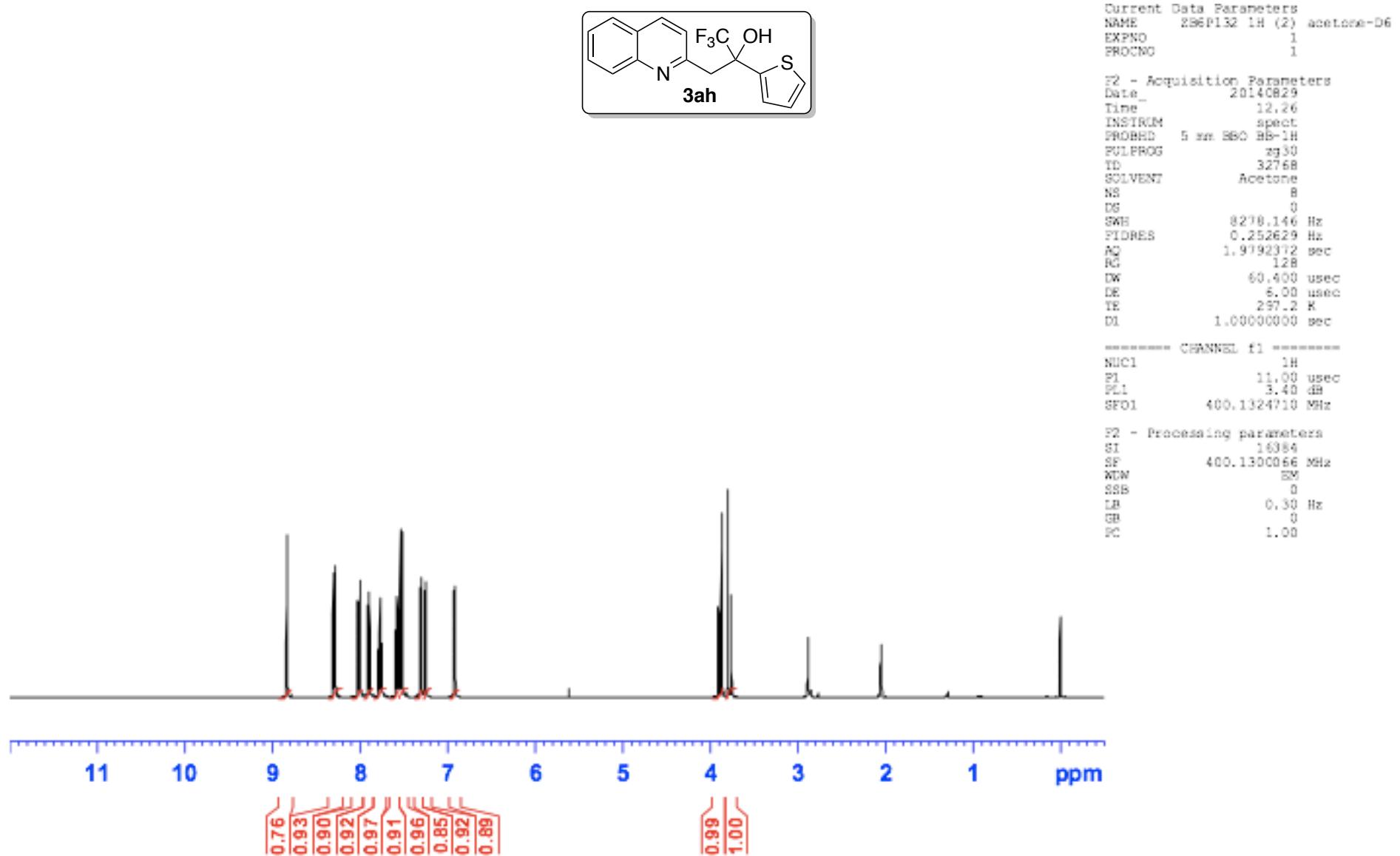
P2 - Acquisition Parameters
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 DS 0
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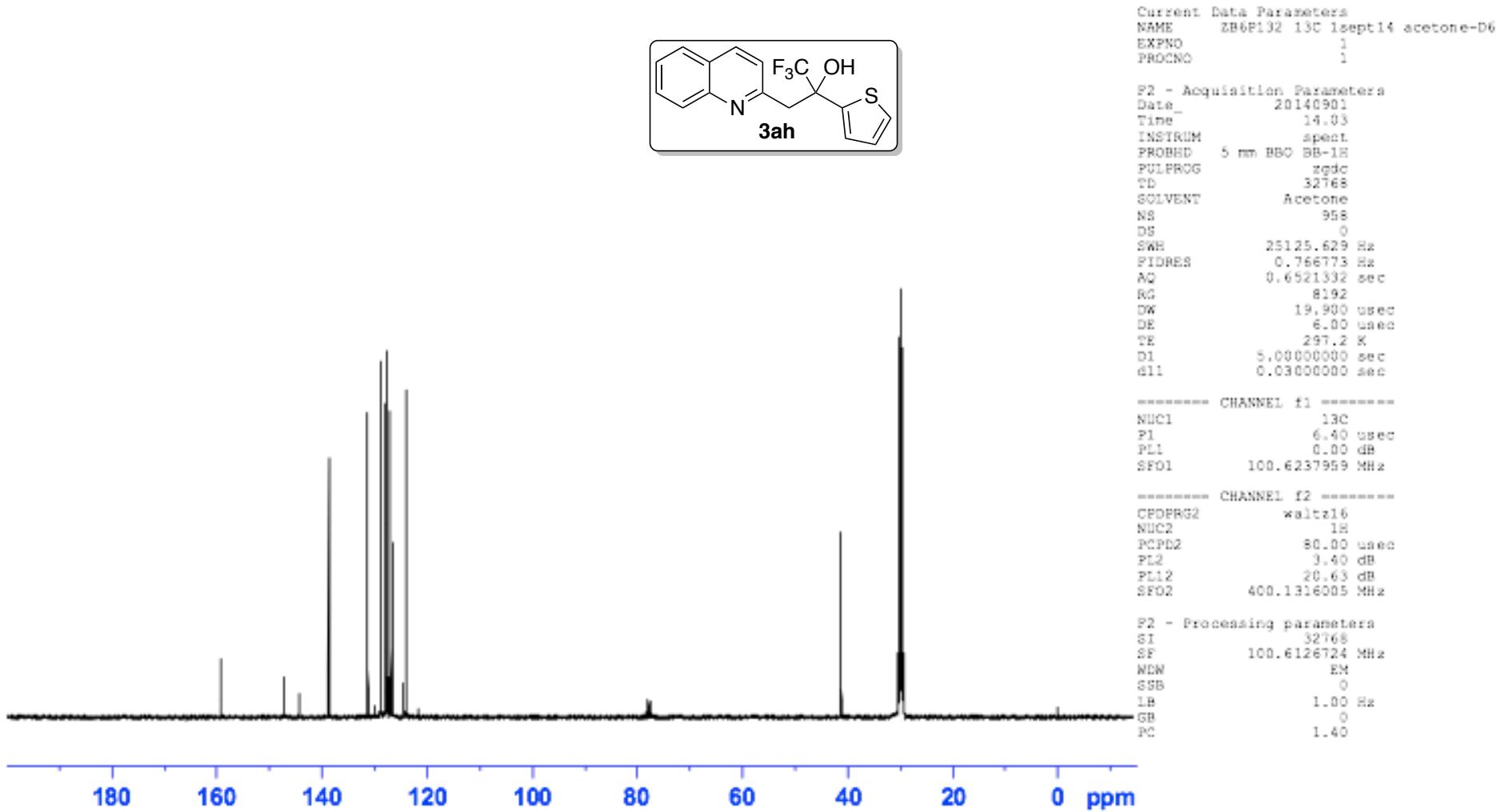
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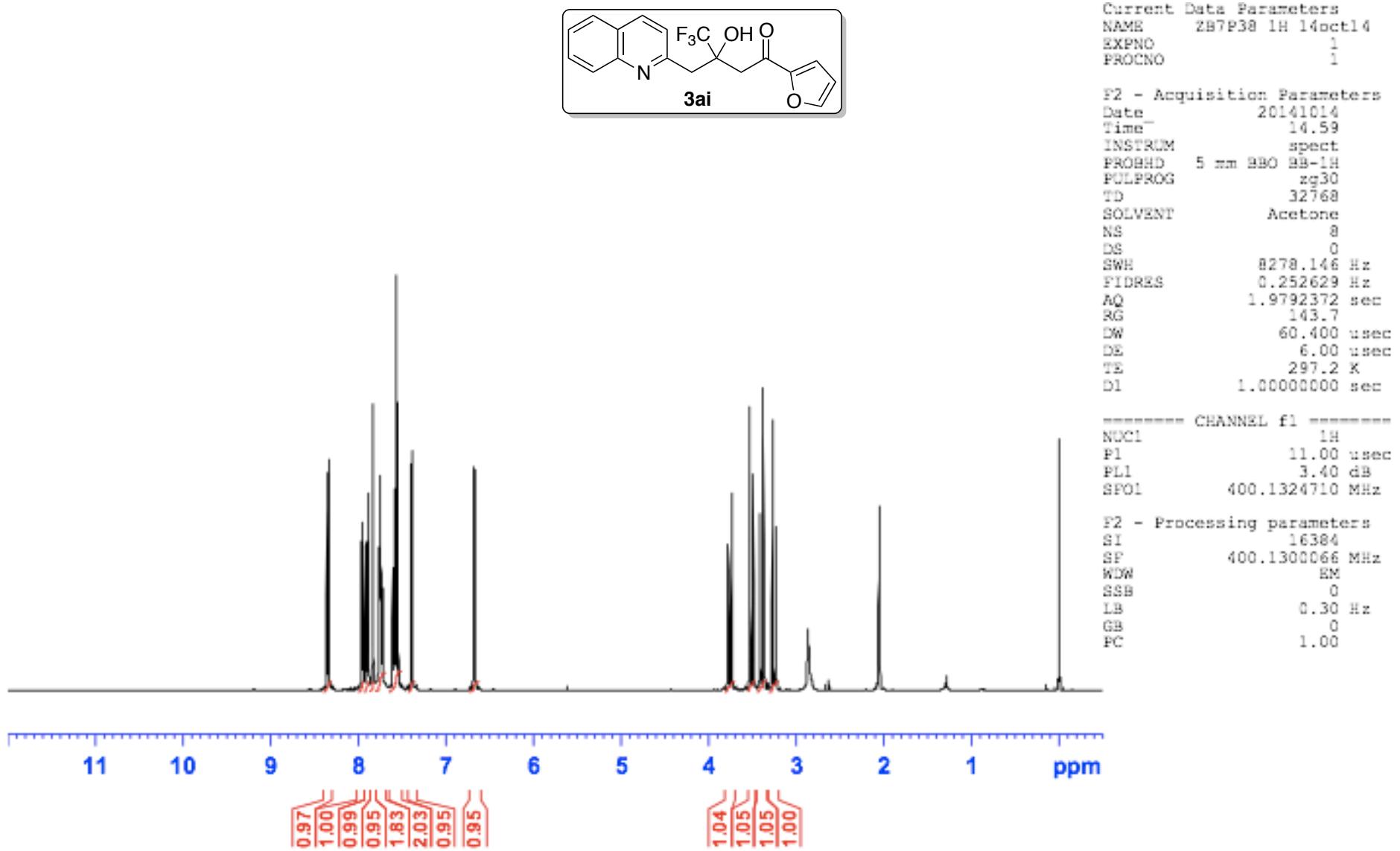
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 FC 1.00

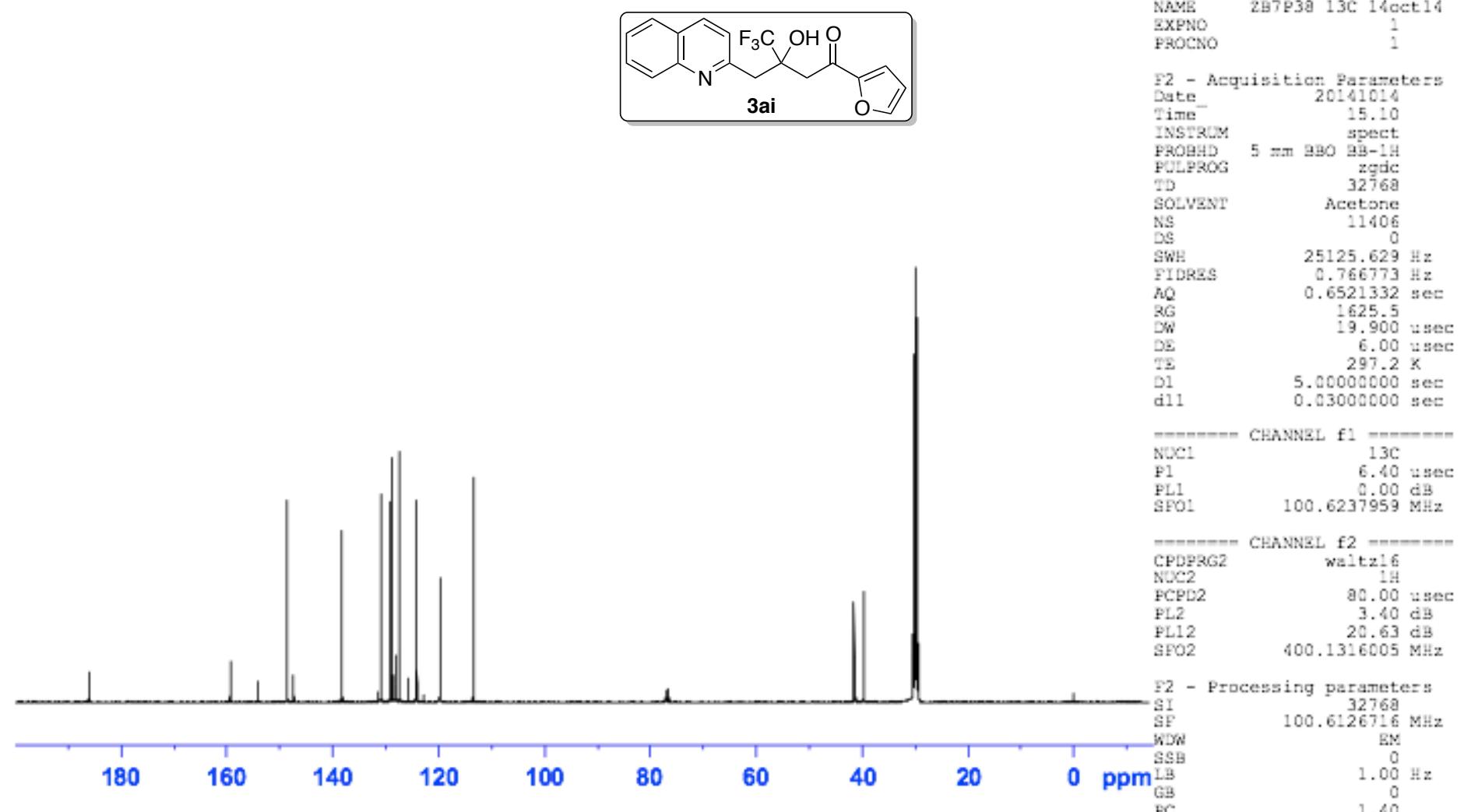


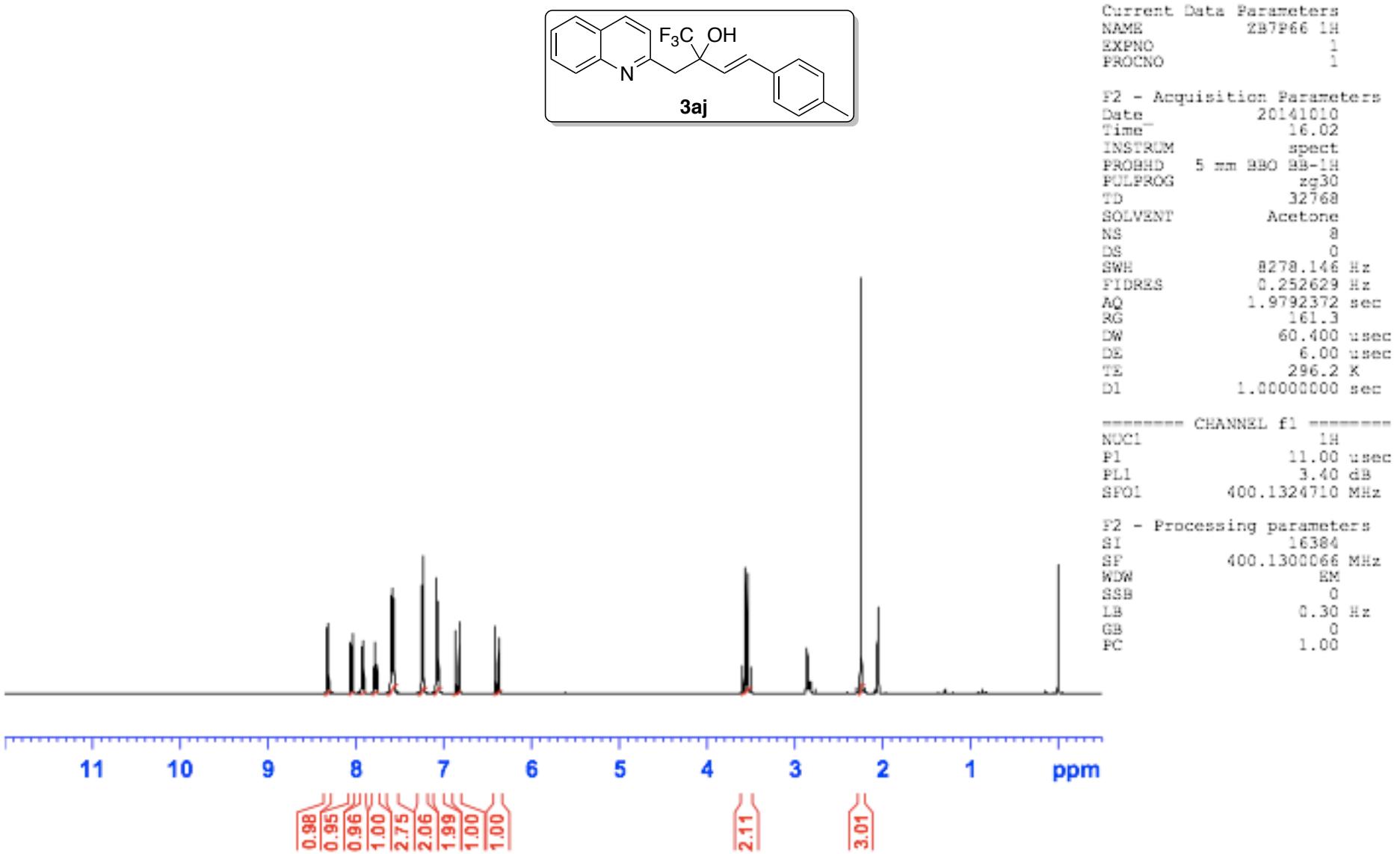


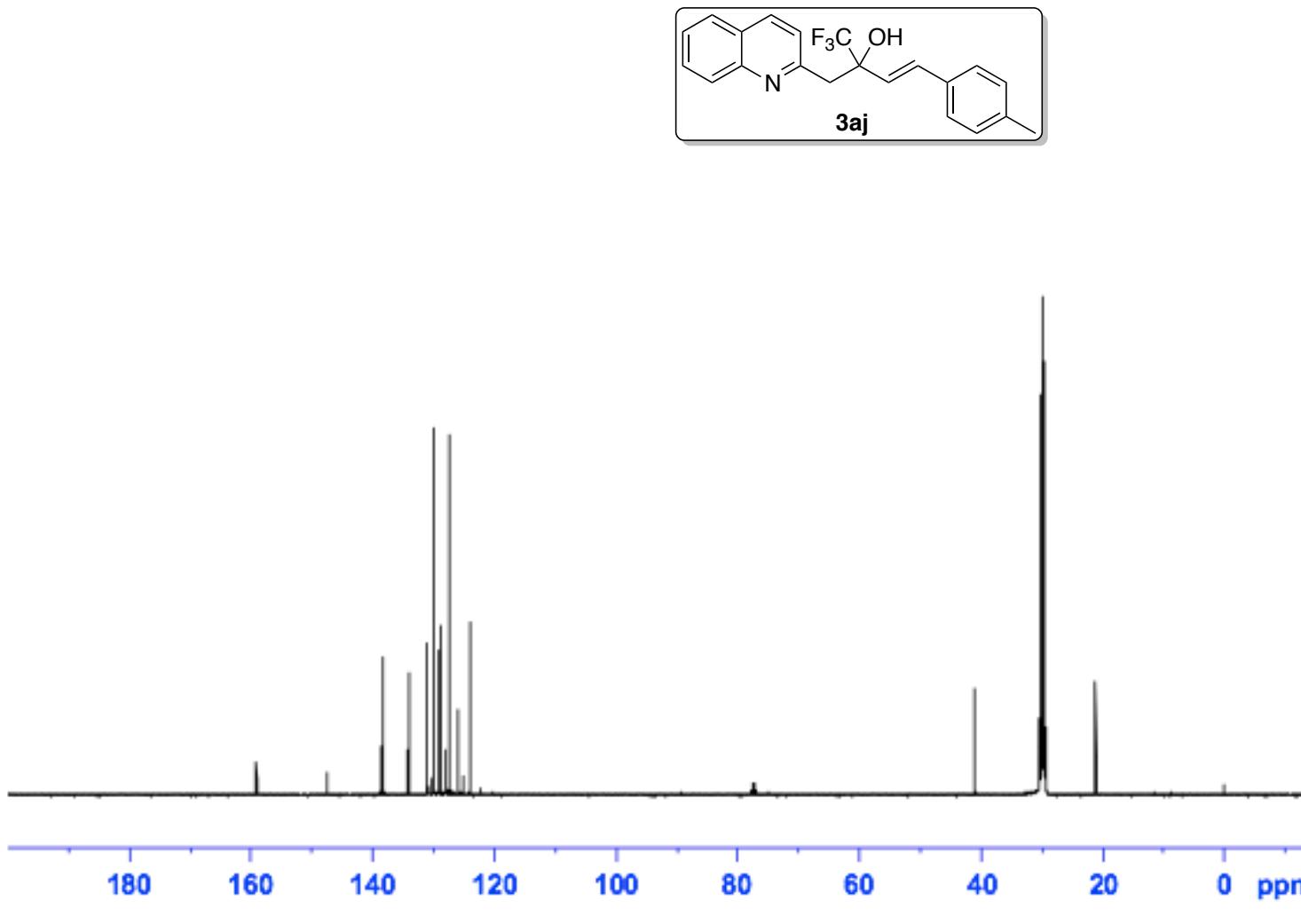


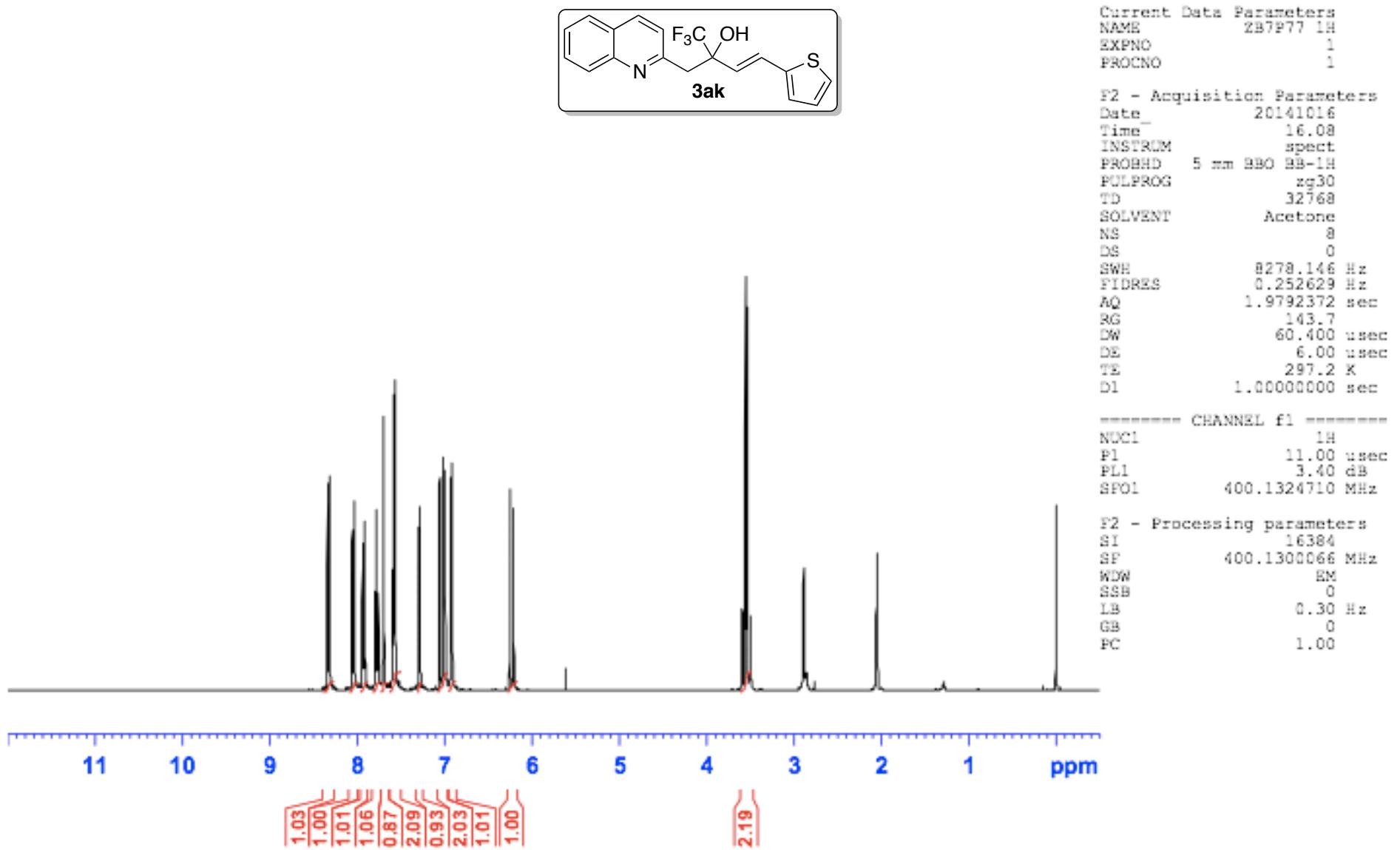


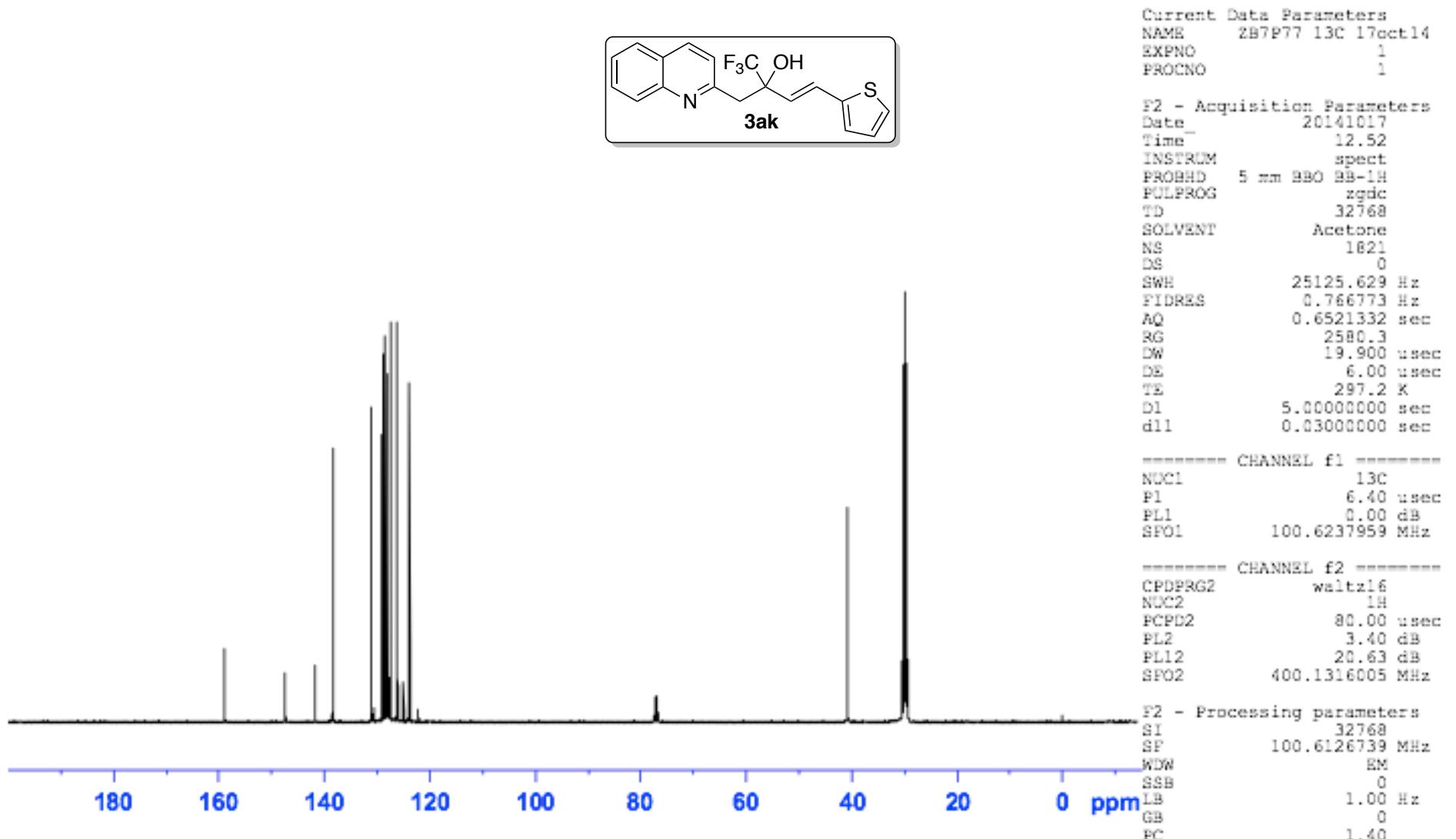


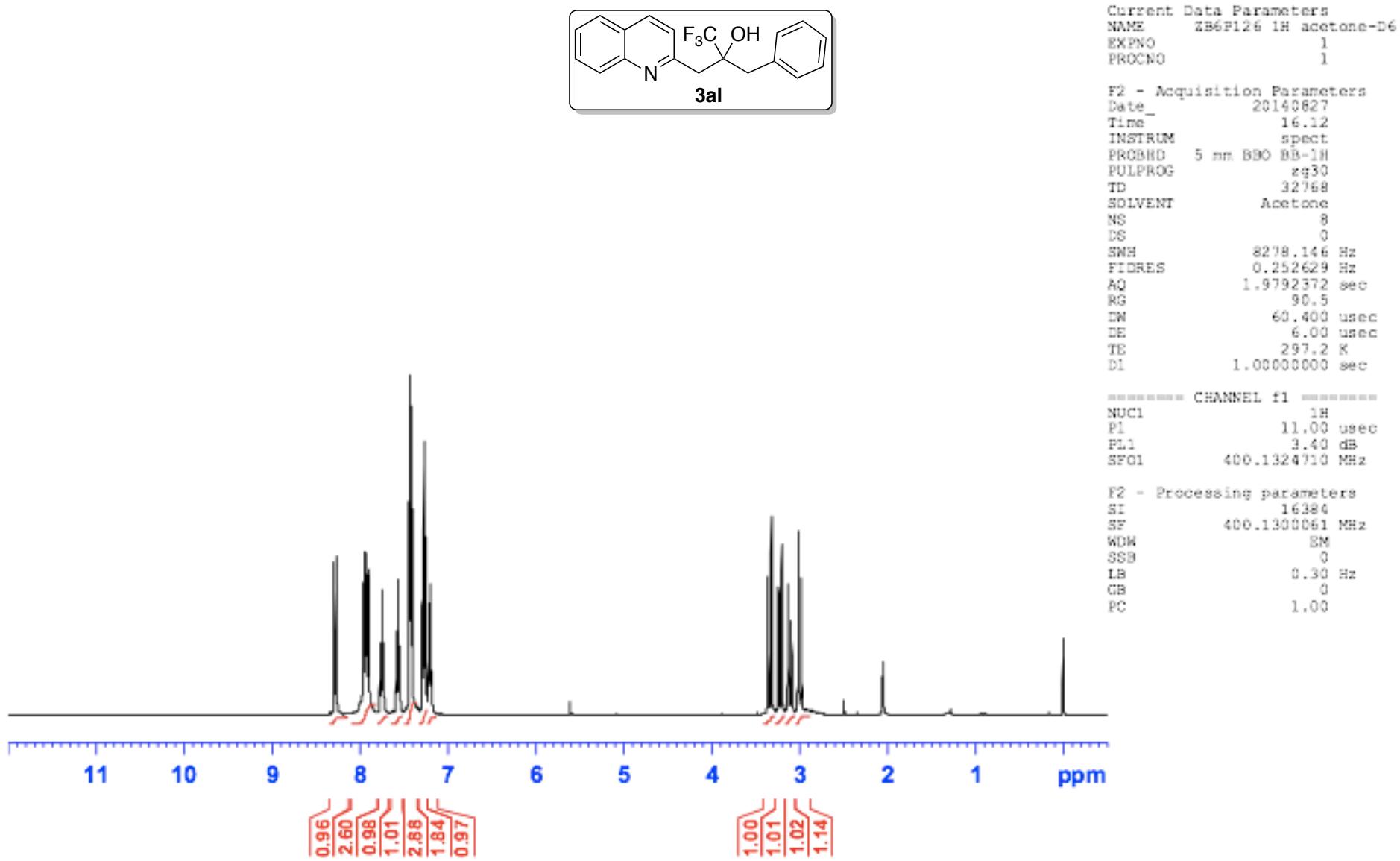


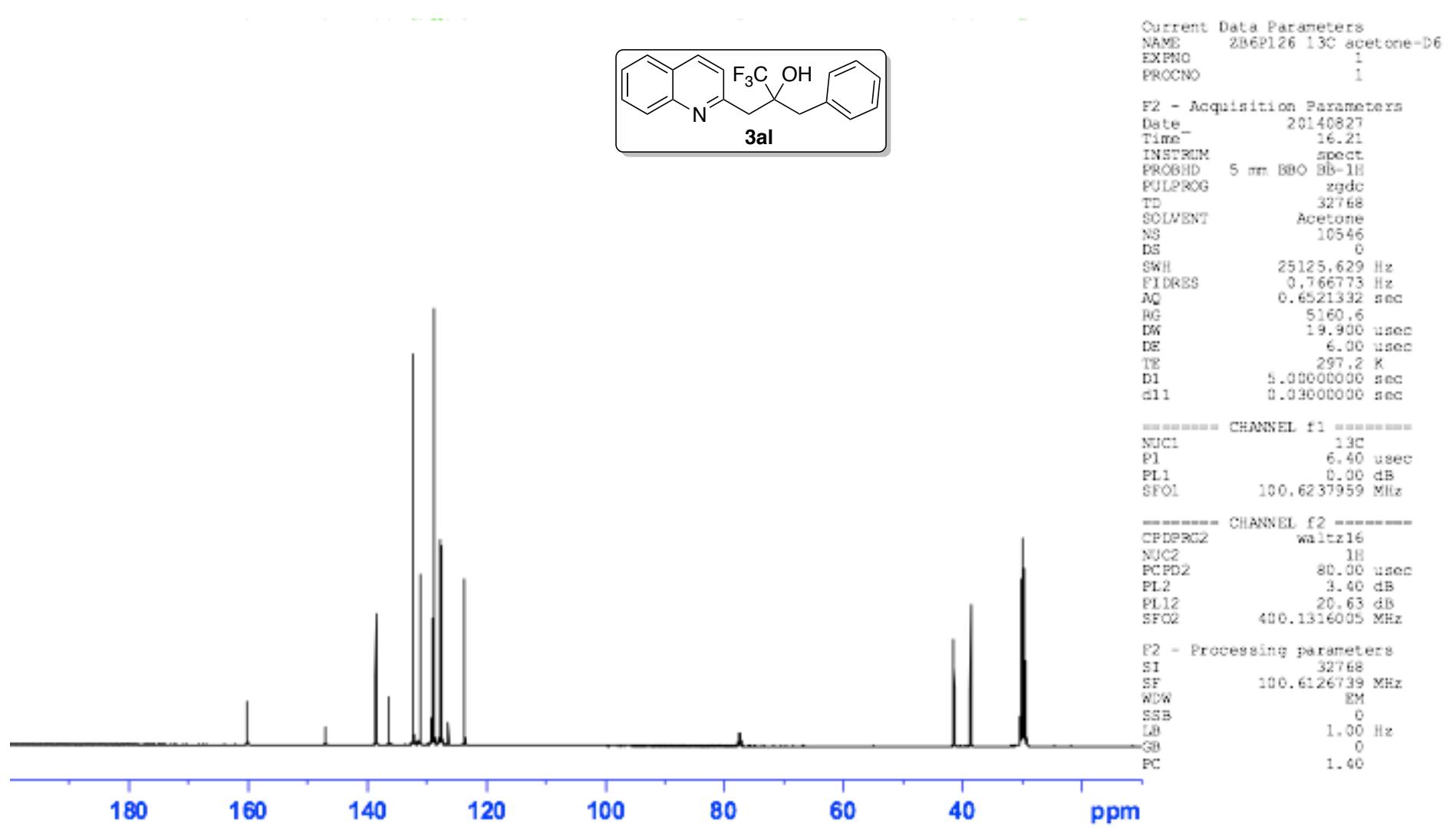


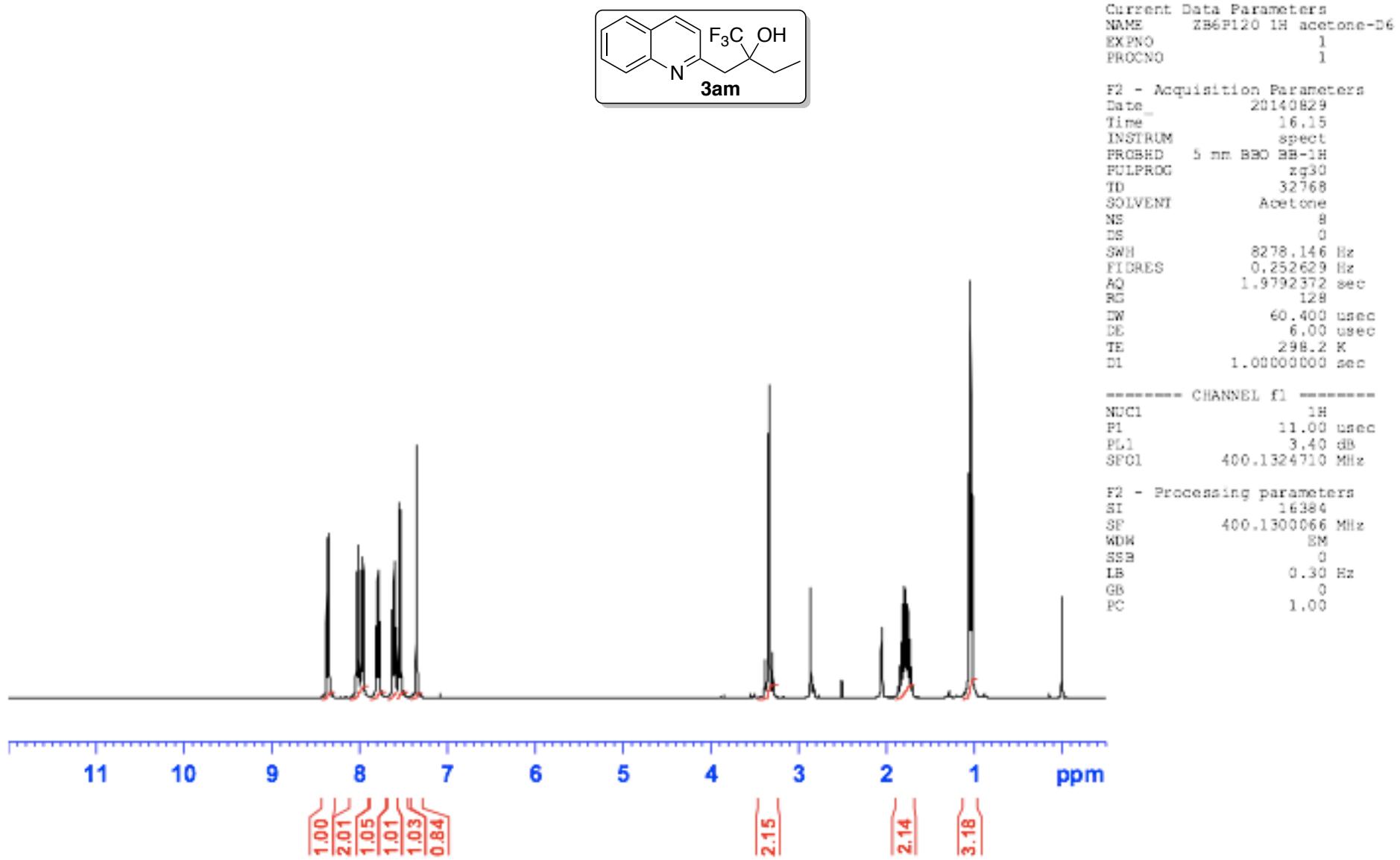


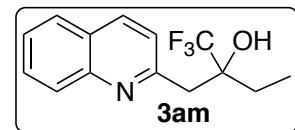
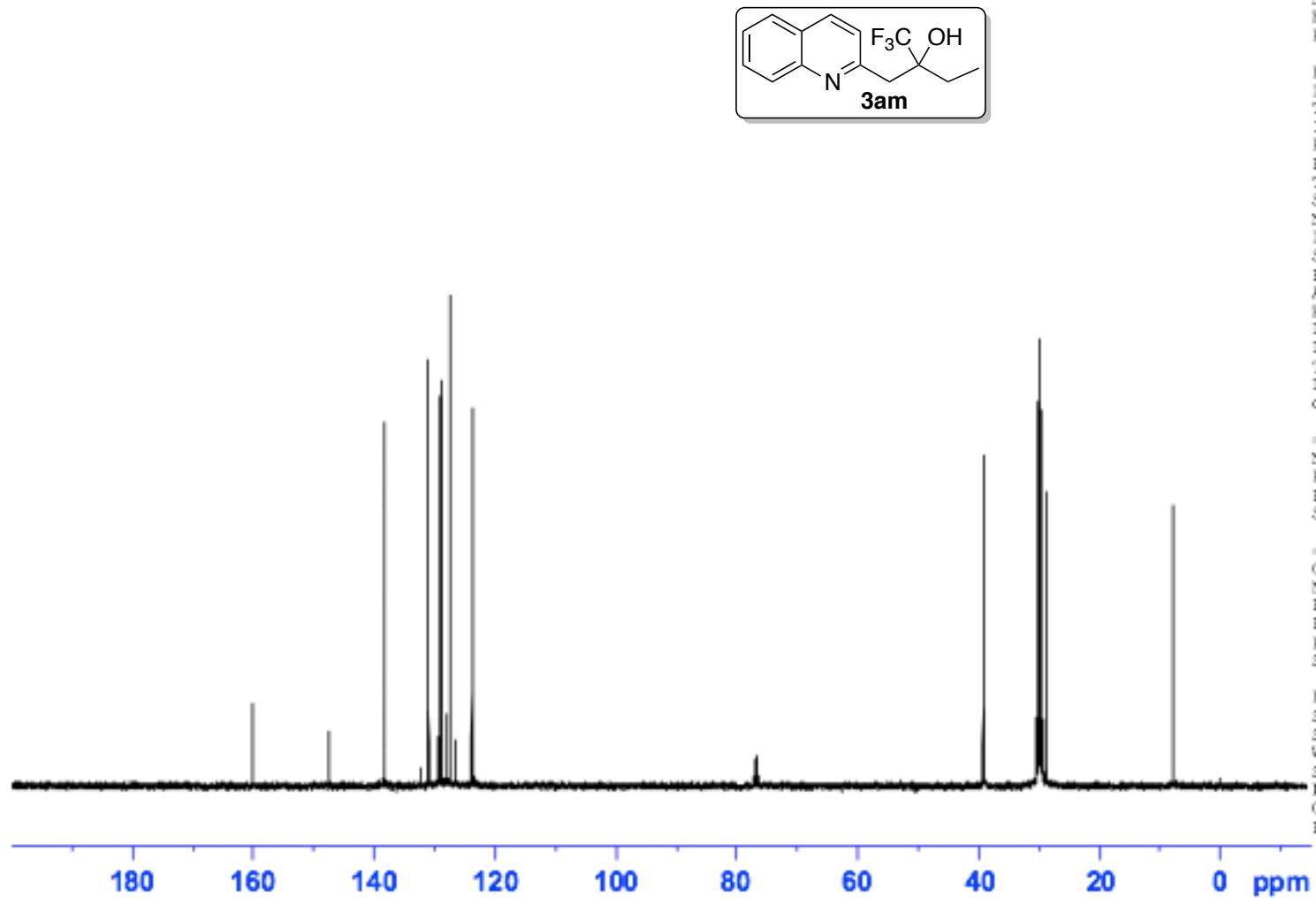


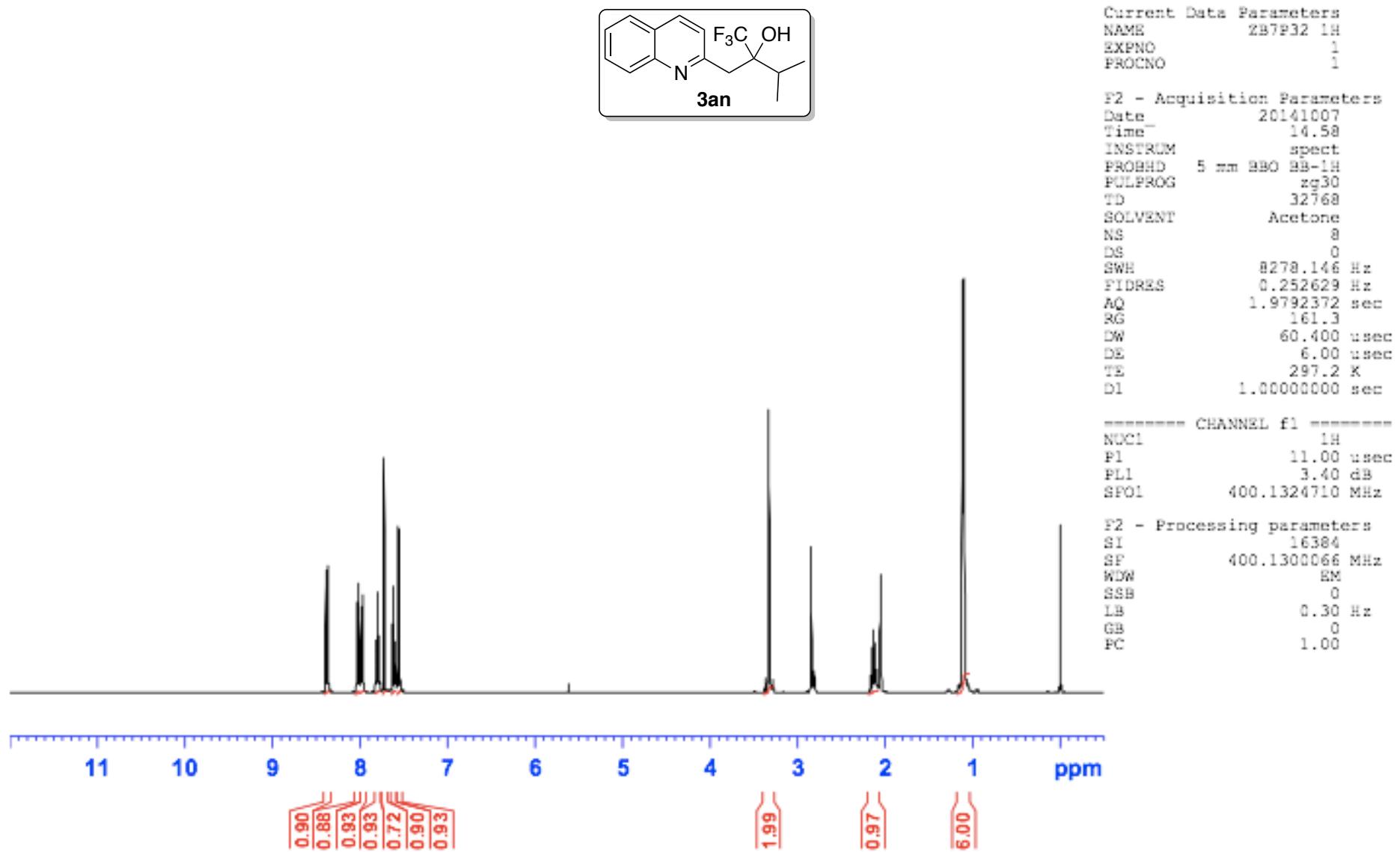


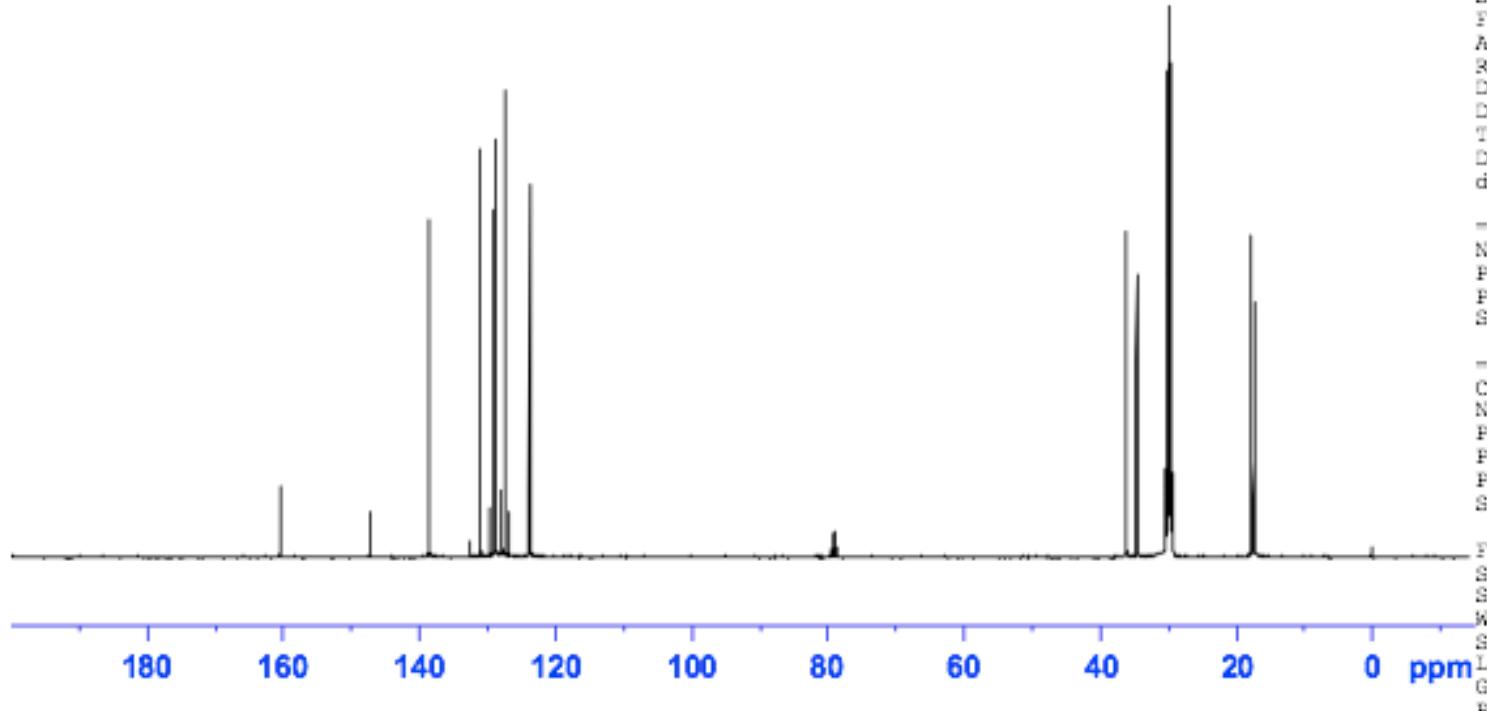












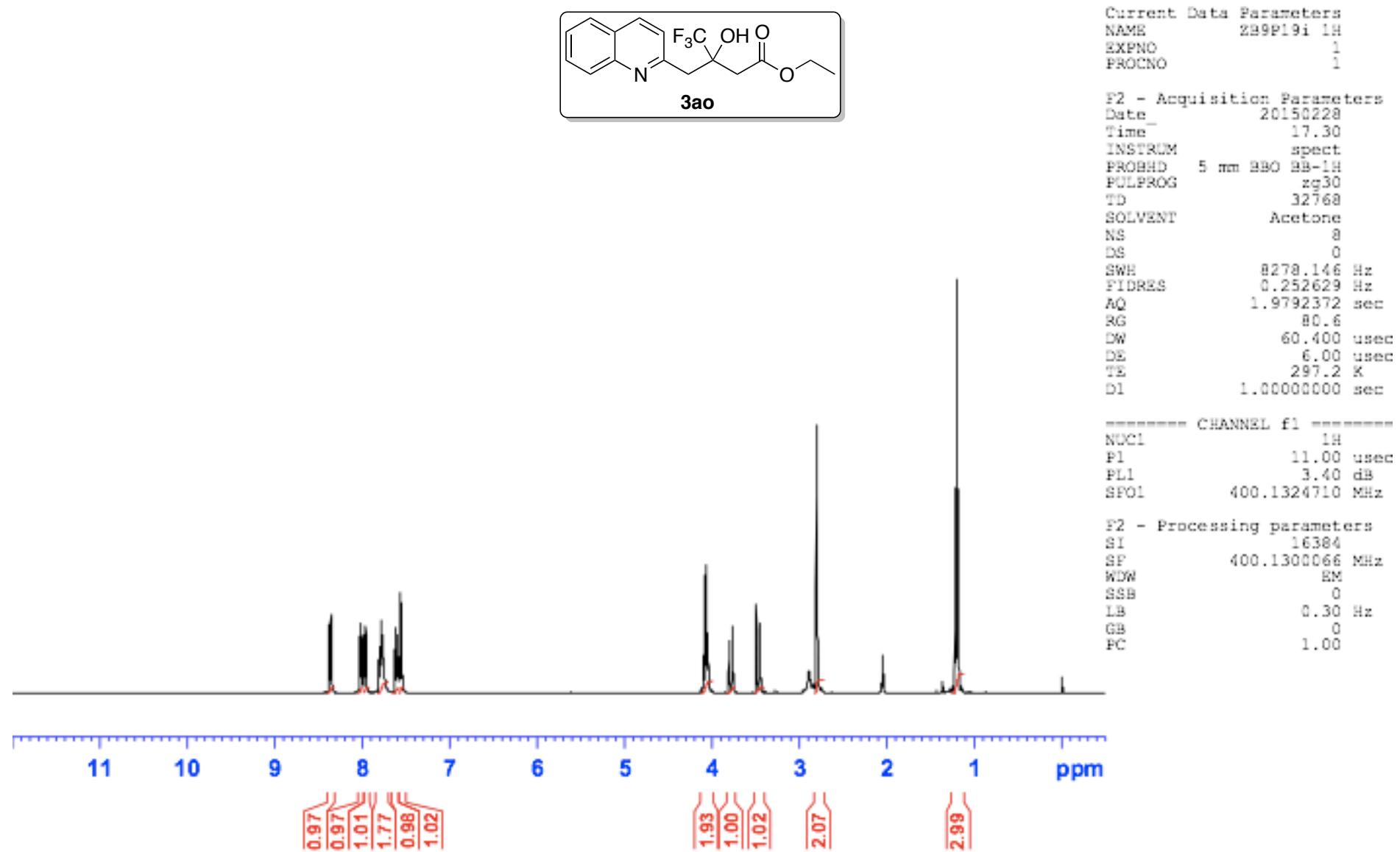
Current Data Parameters
NAME 2B7P32 13C Oct14
EXPNO 1
PROCNO 1

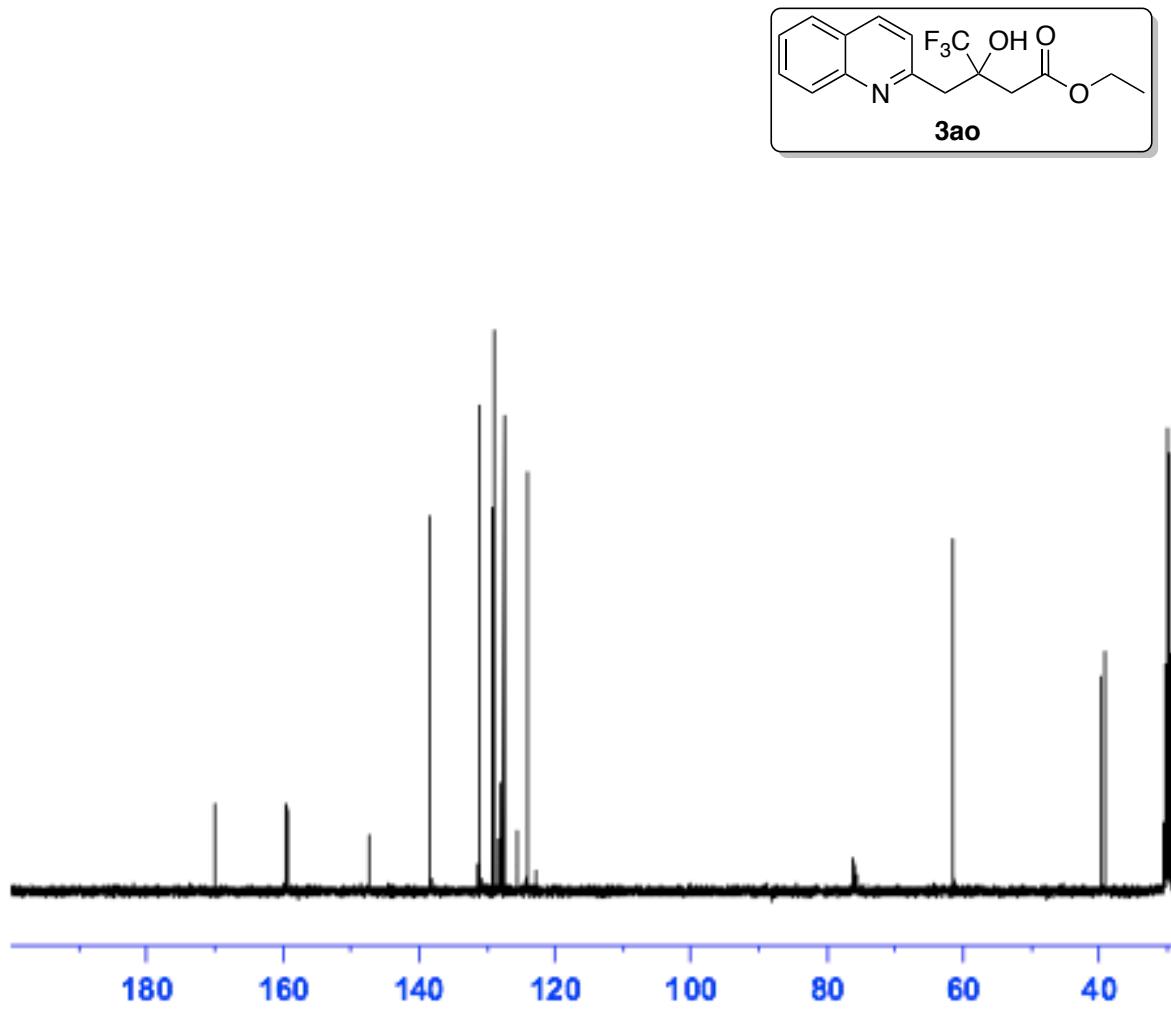
F2 - Acquisition Parameters
Date 20141008
Time 14.59
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 32768
SOLVENT Acetone
NS 11511
DS 0
SWH 25125.629 Hz
FIDRES 0.766773 Hz
AQ 0.6521332 sec
RG 6502
DW 19.900 usec
DE 6.00 usec
TE 297.2 K
D1 5.0000000 sec
d11 0.0300000 sec

----- CHANNEL f1 -----
NUC1 13C
P1 6.40 usec
PL1 0.00 dB
SPO1 100.6237959 MHz

----- CHANNEL f2 -----
CPDPFG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 3.40 dB
PL12 20.63 dB
SPO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6126716 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40





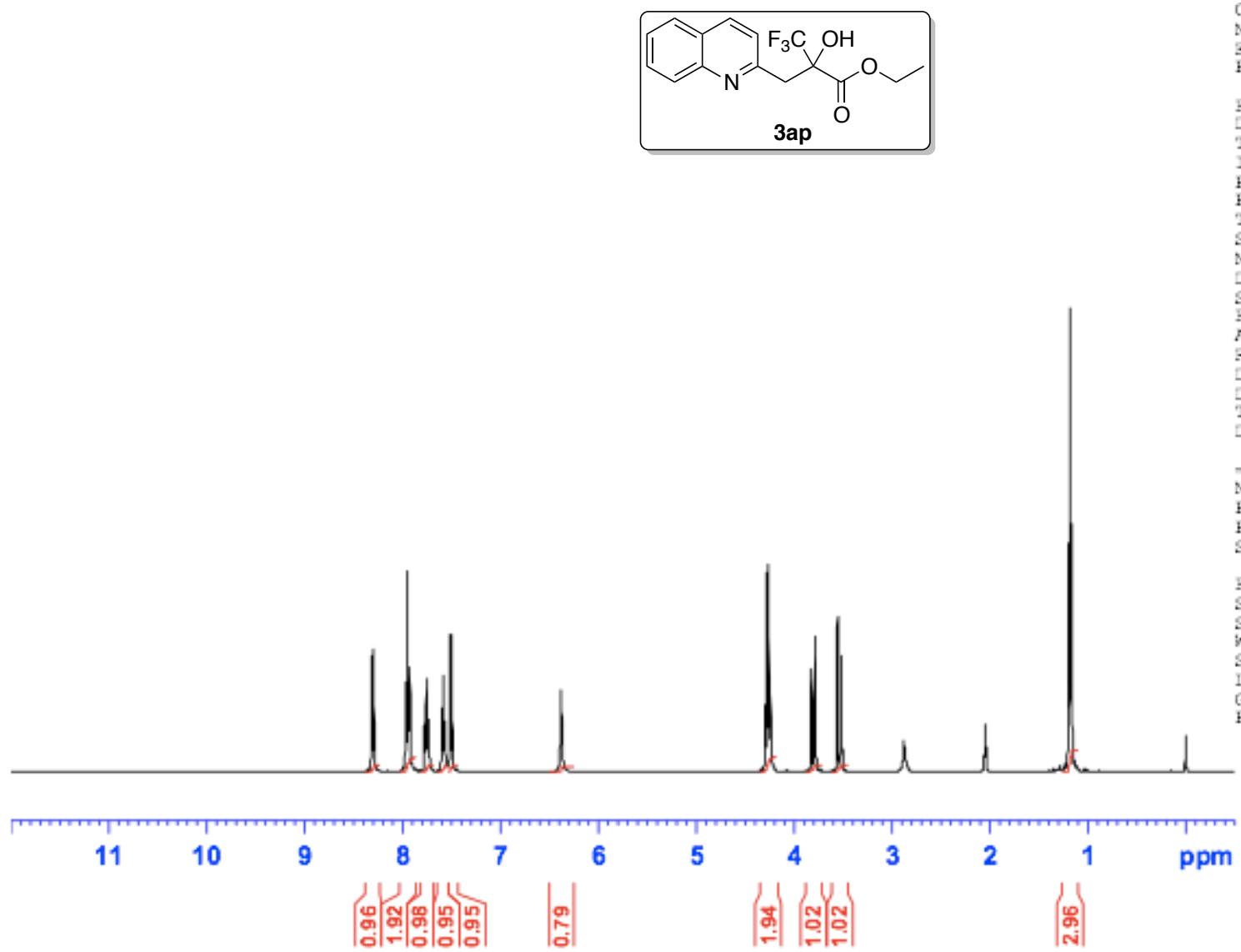
Current Data Parameters
NAME ZB9P19i 13C
EXPNO 1
PROCNO 1

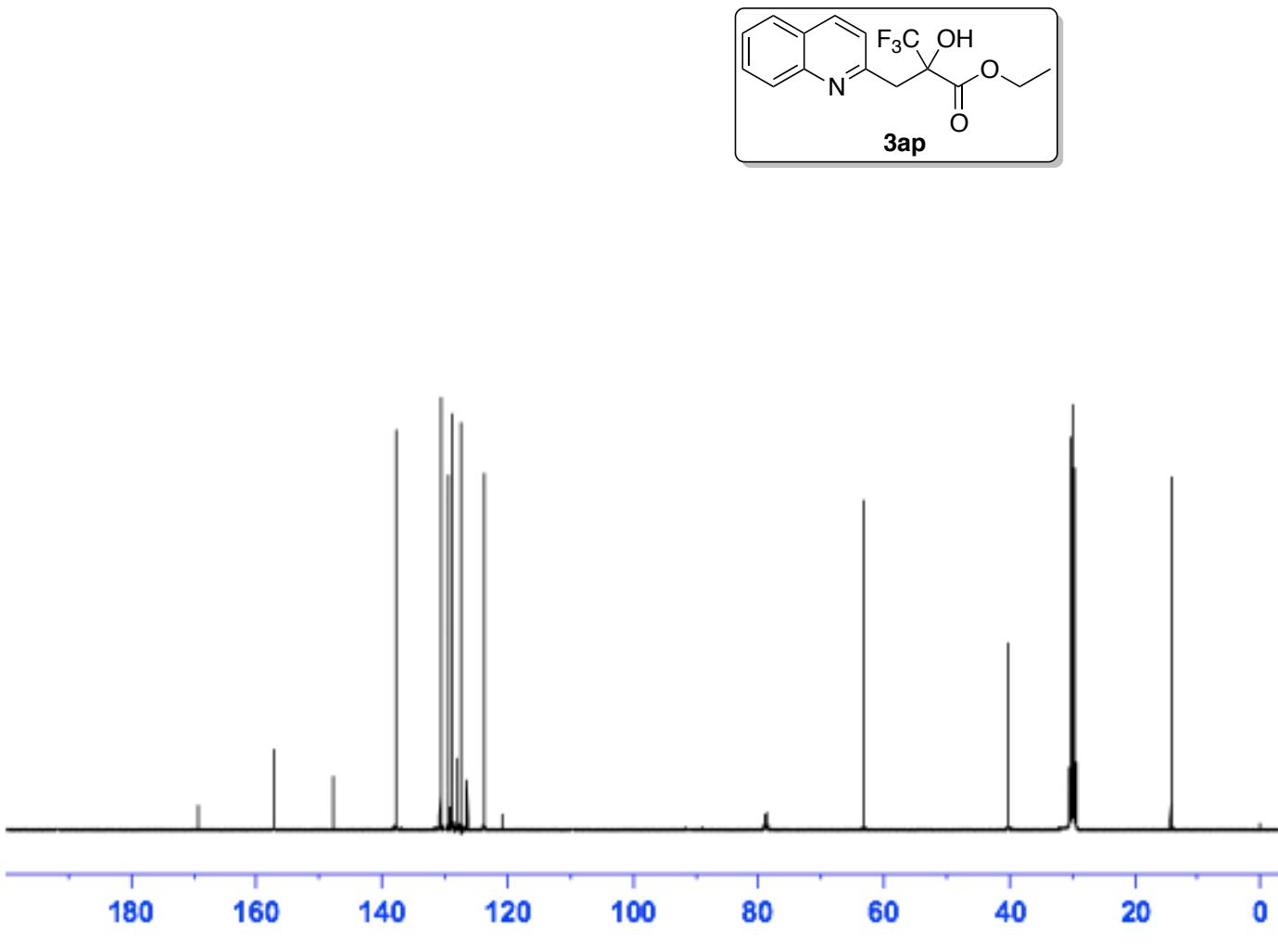
F2 - Acquisition Parameters
Date 20150228
Time 17.43
INSTRUM spect
PROBHD 5 mm BBC BB-1H
PULPROG zgdc
TD 32768
SOLVENT Acetone
NS 13711
DS 0
SWH 25125.629 Hz
FIDRES 0.766773 Hz
AQ 0.6521332 sec
RG 3649.1
DW 19.900 usec
DE 6.00 usec
TE 297.2 K
D1 5.0000000 sec
d11 0.0300000 sec

===== CHANNEL f1 =====
NUC1 13C
P1 6.40 usec
PL1 0.00 dB
SF01 100.6237959 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 3.40 dB
PL12 20.63 dB
SF02 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6126731 MHz
NDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40





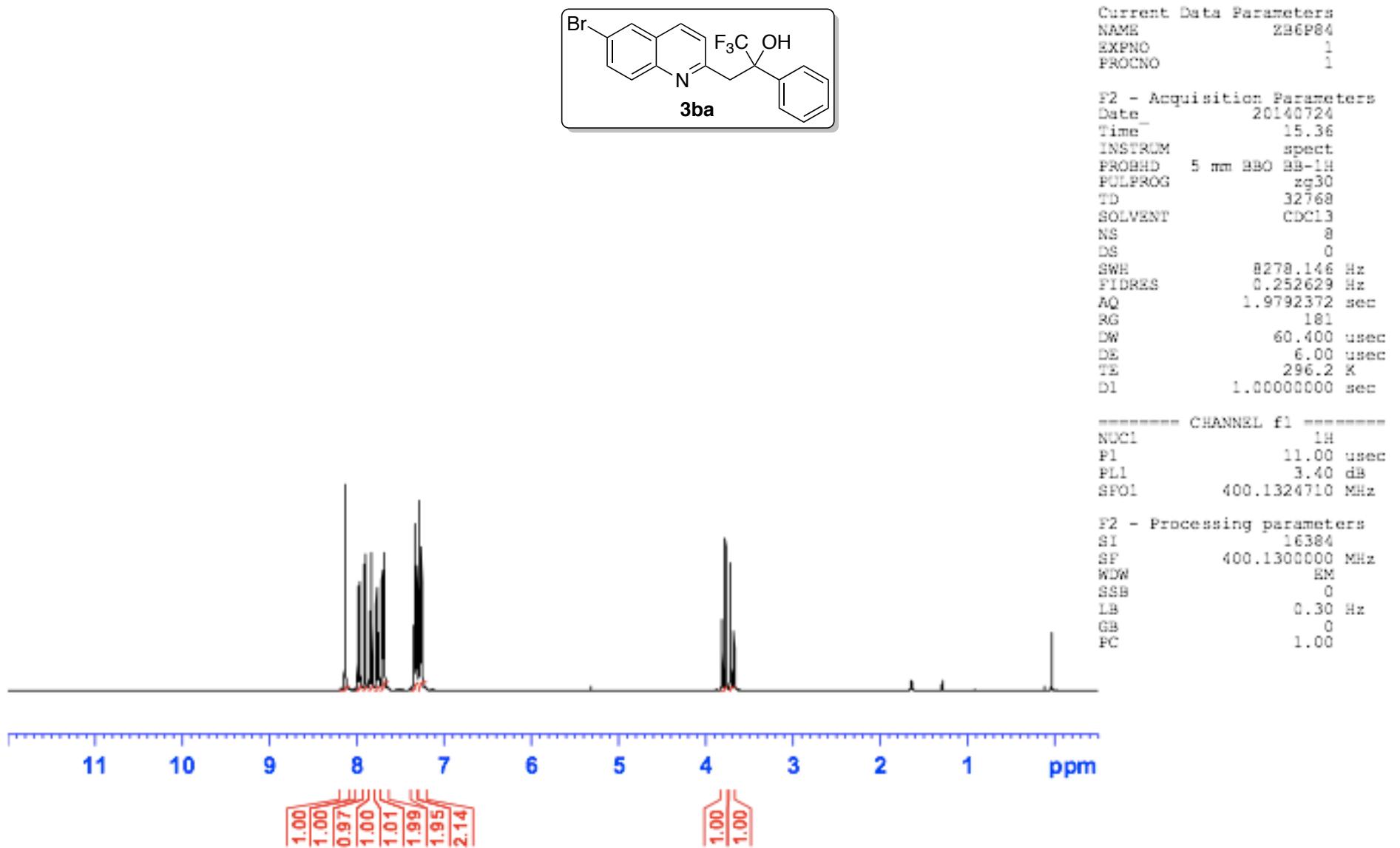
Current Data Parameters
NAME ZB9P19ii 13C
EXPNO 1
PROCNO 1

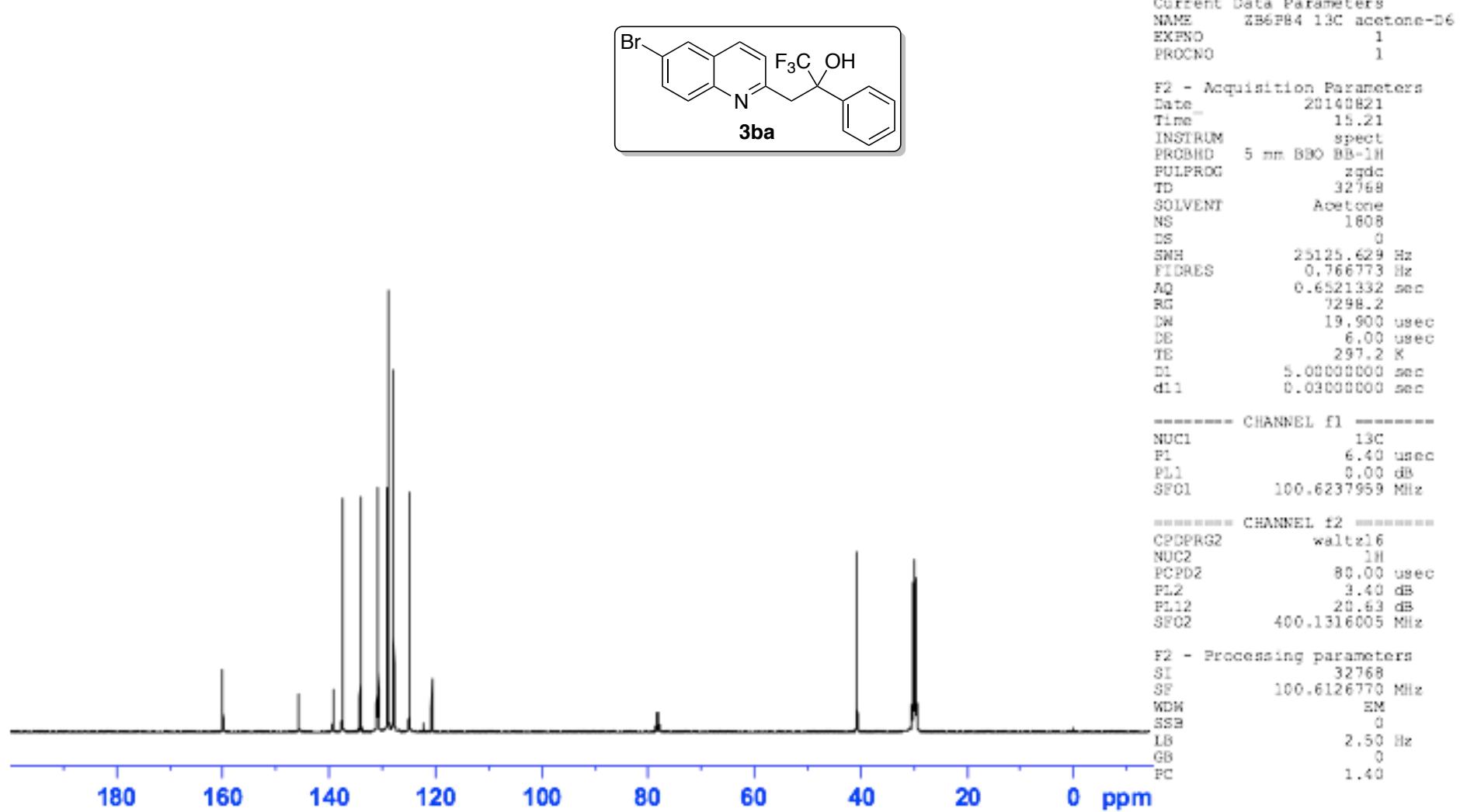
F2 - Acquisition Parameters
Date 20150228
Time 11.58
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgdic
TD 32768
SOLVENT Acetone
NS 3246
DS 0
SWE 25125.629 Hz
FIDRES 0.766773 Hz
AQ 0.6521332 sec
RG 8192
DW 19.900 usec
DE 6.00 usec
TE 297.2 K
D1 5.0000000 sec
d11 0.0300000 sec

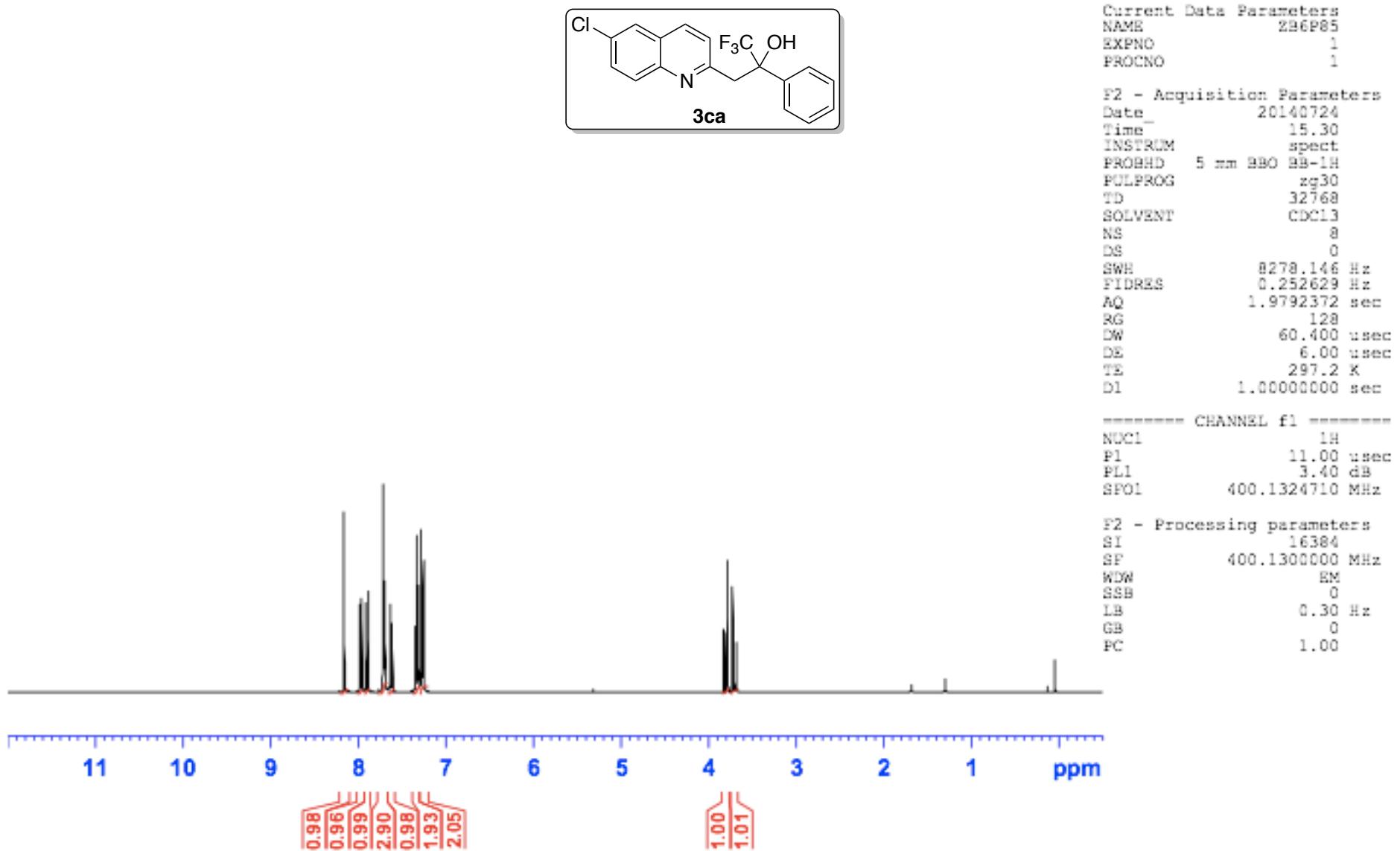
----- CHANNEL f1 -----
NUC1 13C
P1 6.40 usec
PL1 0.00 dB
SPO1 100.6237959 MHz

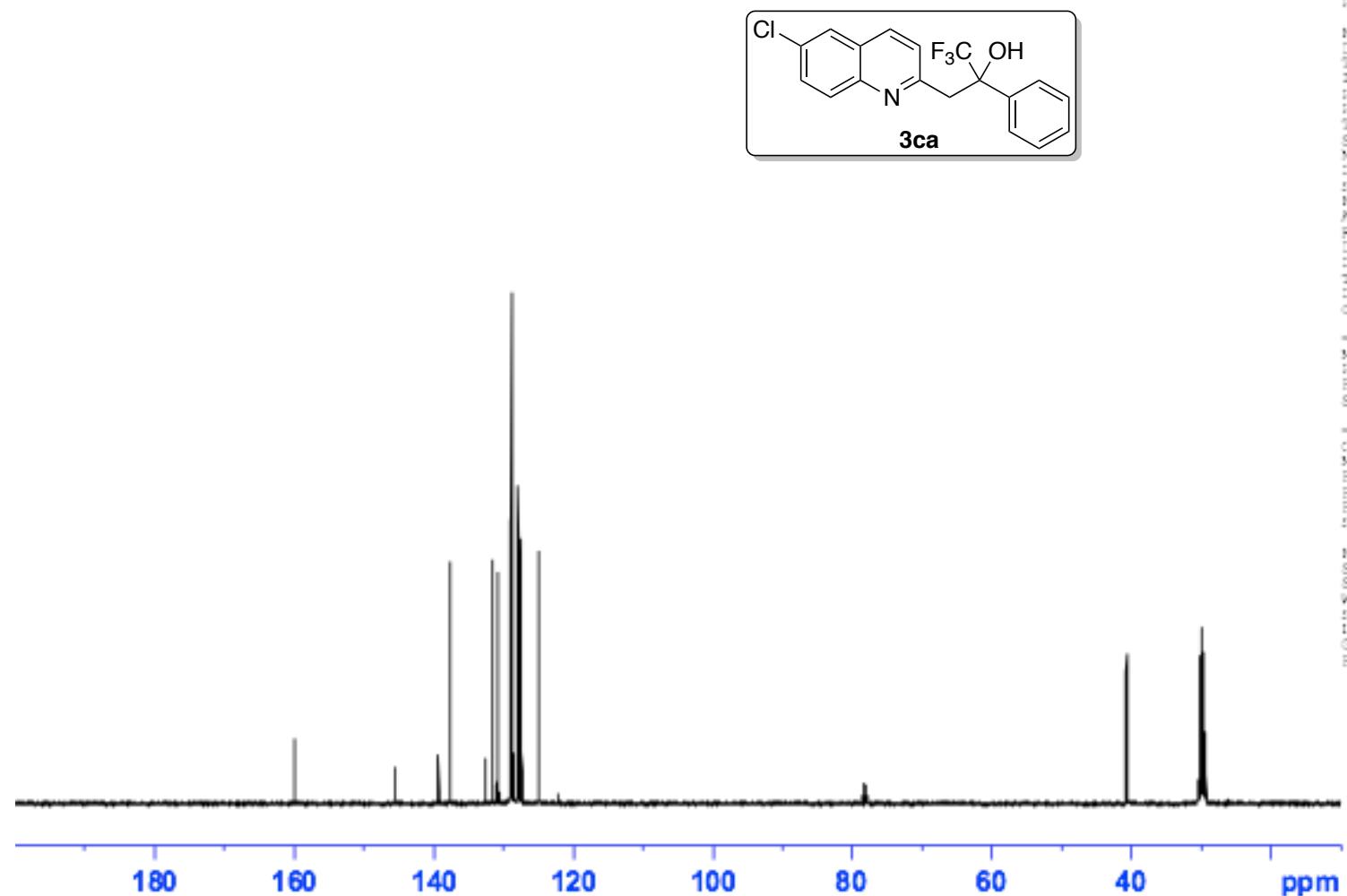
----- CHANNEL f2 -----
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 3.40 dB
PL12 20.63 dB
SPO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6126724 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40









Current Data Parameters
NAME 2B6P65 13C 23Aug14 acetone-D6
BPNR 1
PRNCNO 1

P2 = Acquisition Parameters
DATE 20140822
TIME 15:30
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpc
TD 32768
SOLVENT Acetone
NS 126
DS 0
SWH 25125.629 Hz
ETR 0.786713 Hz
AQ 0.6521332 sec
RG 5160.6
DW 19.900 usec
TE 6.00 usec
TM 298.2 K
D1 5.0000000 sec
d11 0.0300000 sec

===== CHANNEL f1 ======
NU1 13C
P1 6.40 usec
PL1 0.00 dB
SP01 100.6237939 MHz

===== CHANNEL f2 ======
CPDPNG2 waltz16
NU2 1H
PCPD2 80.00 usec
PL2 3.40 dB
PL12 20.63 dB
SP02 400.1316005 MHz

P2 = Processing parameters
S 32768
SF 100.6126754 MHz
WDW EM
SSB 0
LB 1.00 Hz
GS 0
PC 1.40

