Supporting Information

A novel procedure for the synthesis of borylated quinolines and its application in the development of potential boron-based homeodomain interacting protein kinase 2 (HIPK2) inhibitors

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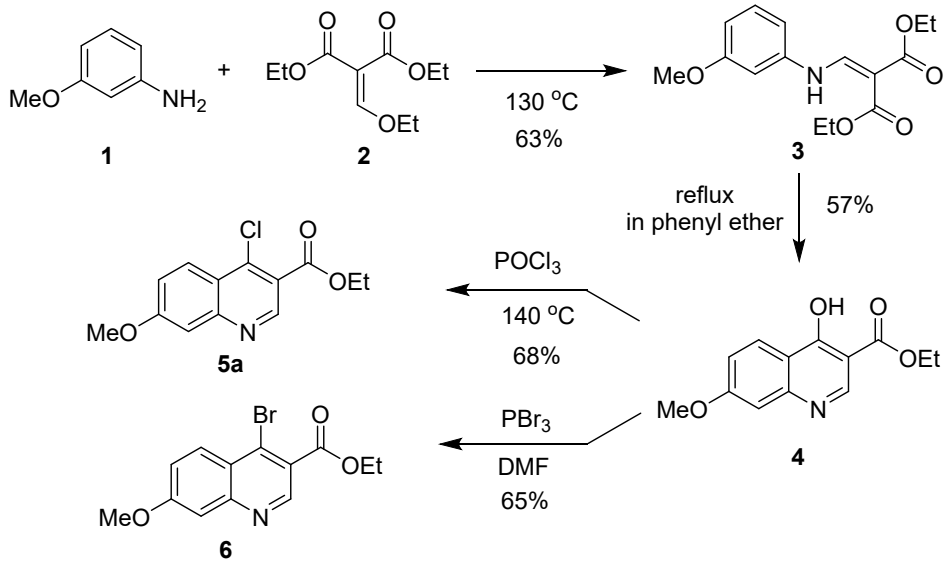
Experimental Selection

General remarks:

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz NMR and 100 MHz NMR spectrometers and $CDCl_3$, DMSO-d_6, acetone-d_6, methanol-d_4 were used as a solvent. Signal patterns are indicated as s, singlet; d, doublet; dd, doublet of doublets; t, triplet; m, multiplet; bs, broad singlet and bm, broad multiplet. Coupling constants (*J*) are given in hertz (Hz). Room temperature ranged from 25-30 °C during the reactions.

Synthesis of starting materials 5a and 6[1]



Scheme 1. Synthesis of **5a** and **6**.

Diethyl 2-(((3-methoxyphenyl)amino)methylene)malonate (3)

m-anisidine (0.028 mol) and diethyl ethoxymethylenemalonate (0.034 mol) were mixed and heated to 130 °C for 1 hr. Cooling to room temperature resulted in yellow oil that was placed in an ice bath left in refrigerator for 2 hr. The solid that formed was crystallized with hexane to give **3** (63%) as white feathery solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, J = 8.0 Hz, 3H), 1.35 (t, J = 8.0 Hz, 3H), 3.82 (s, 3H), 4.23 (q, J = 8.0 Hz, 2H), 4.28 (q, J = 8.0 Hz, 2H), 6.65 (t, J = 4.0 Hz, 1H), 6.72 (m, 2H), 7.27 (q, J = 8.0 Hz, 1H), 8.50 (d, J =12.0 Hz, 1H), 10.97 (d, J = 12.0 Hz, 1H).

Ethyl 4-hydroxy-7-methoxyquinoline-3-carboxylate (**4**)

Compound **3** (1.48 g, 5.05 mmol) was added to already refluxing (265 °C) phenyl ether (10 mL). The mixture was left to reflux for 1 hr. and then cooled to room temperature. The solid that formed was filtered and washed thoroughly with hexane to give **4** (57%) as a white powder.

^{1}H NMR (400 MHz, DMSO-d_6): δ 1.29 (t, J = 8.0 Hz, 3H), 3.86 (s, 3H), 4.20 (q, J = 8.0 Hz, 2H), 7.01 (m, 2H), 8.05 (d, J = 8.0 Hz, 1H), 8.49 (s, 1H), 12.11 (s, 1H).

Ethyl 4-chloro-7-methoxyquinoline-3-carboxylate (5a)

Compound **4** (2.75 mmol) was added to phosphorus oxychloride (2 mL) and heated at 140 °C for an hour. The mixture was then poured onto ice, neutralized with 1M NaOH resulting in a solid that was filtered, washed with water and dried to afforded **5** (68%) as yellowish solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46 (t, J = 4.0 Hz, 3H), 3.99 (s, 3H), 4.48 (q, J = 8.0 Hz, 2H), 7.33 (m, 1H), 7.44 (d, J = 2.8 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 9.17 (s, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 14.2, 55.8, 61.8, 107.6, 120.7, 121.5, 126.7, 143.4, 150.9, 151.7.

Ethyl 4-bromo-7-methoxyquinoline-3-carboxylate (6)

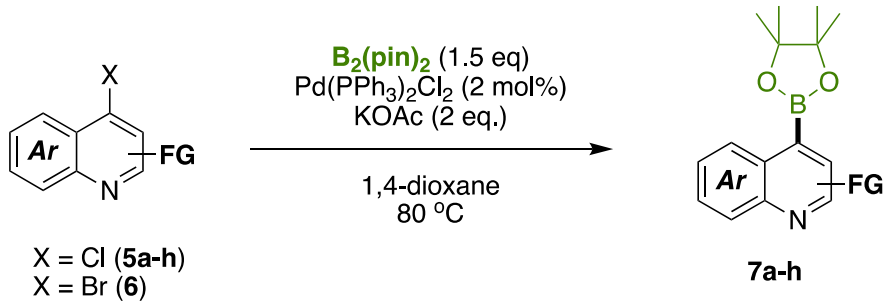
PBr_3 (3.47 mmol) was added dropwise to a suspension of a suspension of compound **4** (3.44 mmol) in DMF (6 mL) at r.t. The resulting mixture was stirred under N_2 for 30 min. and monitored by TLC until the reaction is complete. The reaction mixture was then quenched with ice water and neutralized by the addition of sat. $NaHCO_3$ and the resulted precipitate was filtered, washed with water and dried.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46 (t, J = 8.0 Hz, 3H), 3.98 (s, 3H), 4.48 (q, J = 8.0 Hz, 2H), 7.33 (m, 1H), 7.42 (d, J = 2.8 Hz, 1H), 8.29 (d, J= 8.0 Hz, 1H), 9.05 (s, 1H); ^{13}C NMR (100

MHz; $CDCl_3$): δ 14.2, 55.8, 62.0, 107.4, 121.8, 122.8, 123.7, 129.7, 134.9, 150.4, 151.3, 162.5, 165.2.

Starting material **5b-g** are commercially available and directly purchased from Fisher Scientific, USA and MilliporeSigma.

General procedure for the borylation of 4-haloquinolines to synthesize 7a-h



Compound **5** (1.0 mmol) or **6** (1.0 mmol) together with $B_2(pin)_2$ (1.5 mmol), KOAc (2.0 mmol), $Pd(PPh_3)_2Cl_2$ (2 mol%) and 1,4-dioxane (2 mL) was added into a 20 mL reaction vial under N_2. The resulting mixture was stirred at r.t. for 10 min then heat at 80 °C for about 12 h under N_2. After the reaction was completed, the reaction mixture was poured into 10 mL of ice cold water and extracted by ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by silica gel to give the boron-containing compound.

Ethyl 7-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline-3-carboxylate (7a)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (t, J = 4.0 Hz, 3H), 1.54 (s, 12H), 3.98 (s, 3H), 4.48 (q, J = 4.0 Hz, 2H), 7.27 (m, 1H), 7.45 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 9.30 (s, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 14.3, 25.4, 55.6, 61.7, 84.9, 107.7, 120.4, 124.7, 129.8, 149.2, 150.7, 162.0, 167.2; HRMS: calcd. for $C_{19}H_{24}B\ NO_5H^+$ 358.1820, found 358.1833.

Ethyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline-3-carboxylate (7b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.47 (t, J = 7.0 Hz, 3H), 1.57 (s, 12H), 4.51 (q, J = 7.0 Hz, 2H), 7.62-7.66 (m, 1H), 7.81-7.85 (m, 1H), 8.01 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 9.39 (s, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 14.3, 25.4, 62.0, 85.1, 126.8, 127.5, 128.9, 129.3, 129.6, 131.7, 148.2, 166.8; HRMS: calcd. for $C_{18}H_{22}BNO_4H^+$ 328.1715, found 328.1755.

Ethyl 8-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline-3-carboxylate (7c)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, J = 7.0 Hz, 3H), 1.47 (s, 12H), 4.03 (s, 3H), 4.41 (q, J = 7.0 Hz, 2H), 7.07-7.11 (m, 1H), 7.44-7.48 (m, 2H), 9.29 (s, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 14.3, 25.4, 56.2, 62.0, 85.1, 109.6, 120.4, 127.4, 128.4, 130.7, 132.1, 147.3, 155.4, 166.9; MS: calcd. for $C_{19}H_{24}B\ NO_5H^+$ 358.1820, found 358.1866.

Ethyl 8-cyano-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline-3-carboxylate (7d)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48 (t, J = 6.8 Hz, 3H), 1.56 (s, 12H), 4.53 (q, J = 6.8 Hz, 2H), 7.68-7.72 (m, 1H), 8.22-8.24 (m, 2H), 9.55 (s, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 14.3, 25.4, 62.4, 85.4, 113.7, 117.0, 126.5, 128.5, 129.5, 133.8, 137.0, 148.0, 150.8, 166.4; HRMS: calcd. for $C_{19}H_{21}BN_2O_4Na^+$ 375.1487, found 375.1539.

4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)quinoline (7e)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 12H), 7.59-7.63 (m, 1H), 7.69-7.73 (m, 1H), 8.10-8.15 (m, 2H), 8.65 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 24.9, 85.0, 116.8, 121.8 (q, J = 274 Hz, 1C), 124.0, 127.7, 128.4, 128.8, 130.1, 131.9, 146.5, 147.2 (t, J = 33.5 Hz, 1C); ^{19}F NMR (400 MHz, $CDCl_3$): -67.37; δ MS: calcd. for $C_{16}H_{17}BF_3NO_2Na^+$ 346.1197, found 346.2139.

8-methoxy-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (7f)

Compound **5** (1.0 mmol) or **6** (1.0 mmol) together with $B_2(pin)_2$ (1.5 mmol), KOAc (2.0 mmol), $Pd(PPh_3)_2Cl_2$ (2 mol%), Xphos (2 mol%) and 1,4-dioxane (2 mL) was added into a 20 mL reaction vial under N_2. The resulting mixture was stirred at r.t. for 10 min then heat at 80 °C for about 12 h under N_2. After the reaction was completed, the reaction mixture was poured into 10 mL of ice cold water and extracted by ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by silica gel to give the boron-containing compound.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 12H), 2.76 (s, 3H), 4.00 (s, 3H), 6.97 (d, J = 7.6 Hz, 1H), 7.35-7.39 (m, 1H), 7.72 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H) ; ^{13}C NMR (100 MHz; $CDCl_3$): δ 25.0, 56.0, 84.6, 107.7, 120, 126.2, 130.4, 154.4, 157.0; MS: calcd. for $C_{17}H_{22}BNO_3H^+$ 300.1766, found 300.2595.

4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (7h)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 12H), 7.56-7.60 (m, 1H), 7.69-7.73 (m, 1H), 7.85 (d, J = 3.6 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 8.65 (d, J = 8.4 Hz, 1H), 8.93 (d, J = 3.6 Hz, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 25.0, 84.5, 126.8, 128.4, 128.7, 129.1, 129.7, 131.1, 147.9, 149.5.

7-methoxy-[1,2]oxaborolo[4,3-c]quinolin-1(3H)-ol (9)

To a solution of compound **7** (0.5 mmol) in anhydrous EtOH (5 mL) was added $NaBH_4$ (1.25 mmol) at 0 °C. The reaction was stirred at r.t. for 30 min and extracted by ethyl acetate. The organic layer was washed with brine and dried over anhydrous Na_2SO_4. The residue after rotary evaporation was purified by silica gel.

^{1}H NMR (400 MHz; methanol-d_4): δ 3.96 (s, 3H), 5.06 (s, 2H), 7.27 (d, J = 8.0 Hz, 1H), 7.35 (s, 1H), 8.24 (d, J= 8.0 Hz, 1H), 8.57 (s, 1H); ^{13}C NMR (100 MHz; acetone-d_6 + $CDCl_3$) δ 55.8,

69.3, 101.6, 112.4, 121.3, 128.5, 144.4, 162.0; MS: calcd. for $C_{11}H_9\ BNO_3^-$ 214.0681, found 214.0606.

Potassium (3-(ethoxycarbonyl)-7-methoxyquinolin-4-yl)trifluoroborate (10)

Compound **7** (0.15g, 0.42 mmol) was added to 12 mL MeOH and then 3 M KHF_2 was added. After stirring for overnight, MeOH was evaporated to get white residue. The residue was dissolved in 10 mL acetone and filtered. The filtrate was evaporated to get white solid which was further for recrystallization in acetone and diethyl ether to get white solid.

^{1}H NMR (400 MHz; acetone-d_6): δ 1.33 (t, J= 4.0 Hz, 3H), 3.93 (s, 3H), 4.32 (q, 2H), 7.09 (d, J= 8.0 Hz, 1H), 7.27 (d, J= 4.0 Hz, 1H), 8.56 (s, 1H), 8.60 (d, J= 4.0 Hz, 1H); ^{13}C NMR (100 MHz, acetone-d_6): δ 15.5, 56.5, 62.1, 108.6, 119.1, 128.6, 131.6, 134.5, 148.7, 151.5, 161.8, 173.9; MS: calcd. for $C_{13}H_{12}BF_3NO_3^-$ 298.0868, found 298.0759.

(3-(ethoxycarbonyl)-7-methoxyquinolin-4-yl)boronic acid (11)

Compound **9** (60 mg, 0.178 mmol) and silica gel (21.3 mg, 0.356 mmol) was added to EtOAC/H_2O (1.0 mL: 1.0 mL) in one portion. The reaction mixture was stirred at r.t. until the reaction is complete (3h). The reaction was filtered to remove silica gel and the filter cake was thoroughly washed with EtOAC. The aqueous and organic layers were separated. The aqueous was extracted by EtOAC and the combined layers were dried to afford compound **10**.

^{1}H NMR (400 MHz; acetone-d_6): δ 1.33 (t, J = 8.0 Hz, 3H), 3.93 (s, 3H), 4.33 (q, 2H), 7.12 (dd, J_1 = 4.0 Hz, J_2 = 4.0 Hz, 1H). 7.31 (d, J = 4.0 Hz, 1H), 8.61 (m, 2H); ^{13}C NMR (100 MHz, acetone-d_6): δ 13.6, 54.8, 64.5, 106.0, 117.6, 124.8, 126.9, 129.8, 132.8, 146.2, 148.7, 160.4, 171.7; MS: calcd. for $C_{13}H_{13}\ BNO_5^-$ 274.0892, found 274.0777.

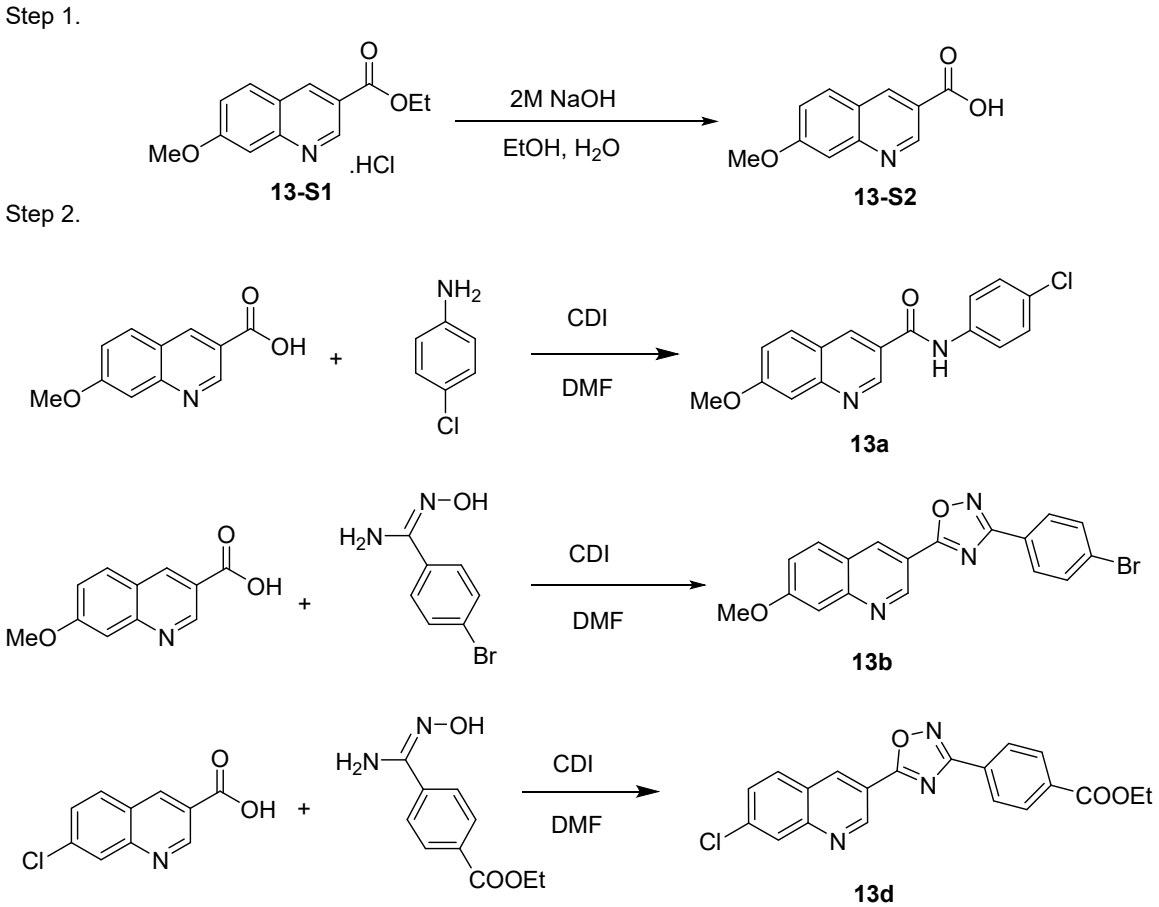
Ethyl 4-(4-cyanophenyl)-7-methoxyquinoline-3-carboxylate (12)

Compound **7a** (0.5 mmol) together with 4-chlorobenzenenitrile (0.6 mmol), K_2CO_3 (1 mmol), Pd(dppf)Cl_2 (5 mol%) and 1,4-dioxane/H_2O (19:1) (2 mL) was added into a 20 mL reaction vial under N_2. The resulting mixture was stirred at 80 ^{o}C for 16 h. After the reaction was completed, the reaction mixture was poured into 10 mL of ice cold water and extracted by ethyl acetate. The

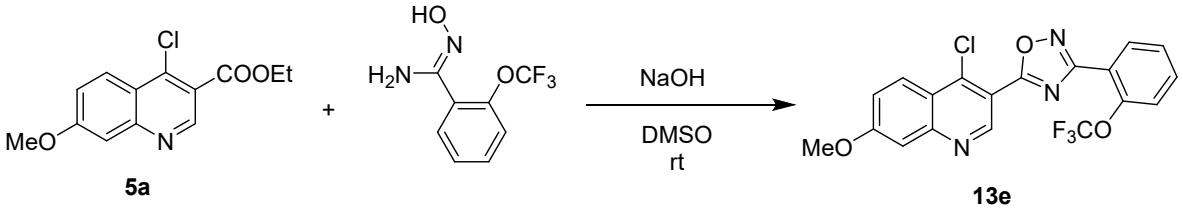
combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by silica gel to give **12** in 78% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (t, J = 7.0 Hz, 3H), 4.02 (s, 3H), 4.18 (q, J = 7.0 Hz, 2H), 7.17-7.20 (m, 1H), 7.30 (d, J = 9 Hz, 1H), 7.42 (d, J = 8 Hz, 2H), 7.59 (s, 1H), 7.83 (d, J = 8 Hz, 2H), 9.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9, 56.0, 83.8, 105.0, 119.4, 122.0, 122.6, 125.6, 130.2, 135.8, 138.4, 140.6, 146.6, 16.1, 163.5; HRMS: calcd. for $C_{20}H_{16}N_2O_3H^+$ 333.1234, found 333.1251.

Synthesis of starting materials 13a-e:



Scheme 2. Synthesis of **13a**, **13b** and **13d**[2].



Scheme 3. Synthesis of **13e**.

7-methoxyquinoline-3-carboxylic acid (**13-S**)

Compound **13-S1** (1.5 g, 5.5 mmol) was hydrolyzed in 10 mL EtOH and 2M sodium hydroxide. The reaction mixture was stirred overnight. After concentration under vacuum, the mixture was acidified with 1M HCl. The resultant solid was filtered, washed with water and dried to get a beige solid **13-S2** was obtained as a white solid.

^{1}H NMR (400 MHz, DMSO-d_6): 3.97 (s, 3H), 7.35 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 8.10 (d, J =12.0 Hz, 1H), 8.87 (s, 1H), 9.24 (s, 1H); ^{13}C NMR (100 MHz; DMSO-d_6): 55.7, 107.2, 120.1, 121.6, 121.8, 130.6, 137.8, 150.2, 151.0, 162.0, 166.5.

3-(4-bromophenyl)-5-(7-methoxyquinolin-3-yl)-1,2,4-oxadiazole (13b)

7-methoxyquinoline-3-carboxylic acid **13-S2** (2.0 mmol) and CDI (2.4 mmol) were dissolved in 15 mL DMF and stirred at r.t. for 30 min. (*E*)-4-bromo-N'-hydroxybenzimidamide (2.4 mmol, 0.54 g) was added and the reaction mixture was heated under reflux for 24 h. The mixture was poured into water (40 mL) extracted with EtOAc (3x 20 mL) and the combined layer were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel column chromatography to give the oxadiazole product as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): 9.57 (s, 1H), 8.89 (s, 1H), 8.09 (d, J = 8Hz, 2H), 7.87 (d, J= 12 Hz, 1H), 7.68 (d, J = 8 Hz, 2H), 7.51 (s, 1H), 7.33 (dd, J_1 = 8Hz, J_2 = 4 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.8, 107.7, 115.3, 121.4, 122.1, 125.6, 129.0, 129.9, 135.9, 148.6, 151.7, 162.9, 168.3, 174.4.

5-(4-chloro-7-methoxyquinolin-3-yl)-3-(2-(trifluoromethoxy)phenyl)-1,2,4-oxadiazole (13e)

In a 25 mL round bottom flask compound **5a** (1.0 mmol), N'-hydroxy-2-(trifluoromethoxy)benzimidamide (1.2 mmol) and powdered NaOH (1.5 mmol) were taken followed by addition of 5 mL DMSO. The reaction was stirred at room temperature and the progress of reaction was monitored by TLC. Upon completion the reaction mixture was poured in ice cold water (50 mL). The crude solid obtained was purified by column chromatography to obtain the desired product.

^{1}H NMR (400 MHz, DMSO-d_6): 3.99 (s, 3H), 7.41 (d, J = 7.6 Hz, 1H), 7.59-7.63 (m, 3H),7.74-7.84 (m, 2 H), 8.63 (d, J = 8.8 Hz, 1H), 9.46 (s, 1H); ^{13}C NMR (100 MHz; DMSO-d_6): 56.3, 109.2, 117.8, 119.9, 120.8, 126.0, 127.7, 131.6, 132.9, 146.2, 149.4, 151.8, 162.9.

General procedure for the borylation to synthesize compounds 14a-d

Compound **13** (1.0 mmol) together with $B_2(pin)_2$ (1.5 mmol), KOAc (2.0 mmol), $Pd(PPh_3)_2Cl_2$ (2 mol%) and 1,4-dioxane (2 mL) was added into a 20 mL reaction vial under N_2. The resulting mixture was stirred at r.t. for 10 min then heat at 80 °C for about 12 h under N_2. After the reaction was completed, the reaction mixture was poured into 10 mL of ice cold water and extracted by ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by silica gel to give the boron-containing compound.

7-methoxy-N-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)quinoline-3-carboxamide (14a)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (s, 12H), 3.89 (s, 3H), 7.19-7.24 (m, 1H), 7.50 (s, 1H), 7.72-7.78 (m, 5H), 8.73 (s, 1H), 8.95 (s, 1H), 9.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 25.4, 62.4, 85.4, 113.7, 117.0, 126.5, 128.5, 129.5, 133.8, 137.0, 148.0, 150.8, 166.4; HRMS: calcd. for $C_{23}H_{25}BN_2O_4H^+$ 405.1980, found 405.2014.

5-(7-methoxyquinolin-3-yl)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1,2,4-oxadiazole (14b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (s, 12H), 3.94 (s, 3H), 7.22-7.27 (m, 1H), 7.48-7.60 (m, 1H), 7.79-7.82 (m, 2H), 7.88-8.00 (m, 2H), 8.12 (d, J = 8.0 Hz, 1H), 8.40 (d, J = 14.8 Hz, 1H), 9.49 (d, J = 10.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9, 55.9, 84.2, 107.0, 115.4, 121.8, 122.3, 126.7, 129.1, 130.1, 132.2, 135.3, 136.5, 148.1, 163.3, 168.4, 169.1, 173.9, 174.1; HRMS: calcd. for $C_{24}H_{24}BN_3O_4H^+$ 430.1933, found 430.1973.

Ethyl 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline-3-carboxylate (15a)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 12H), 1.39 (t, J = 7.0 Hz, 3H), 4.42 (q, J = 7.0 Hz, 2H), 7.86-7.95 (m, 2H), 8.64 (s, 1H), 8.83 (s, 1H), 9.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 24.9, 61.8, 84.5, 123.9, 128.2, 128.5, 132.4, 149.3, 165.0; HRMS: calcd. for $C_{18}H_{22}BNO_4H^+$ 328.1715, found 328.1705.

Ethyl 4-(5-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinolin-3-yl)-1,2,4-oxadiazol-3-yl)benzoate (15b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24-1.26 (m, 3H), 1.37 (s, 12H), 4.38 (q, J = 7.2 Hz, 2H), 7.93-7.96 (m, 1H), 8.20-8.22 (m, 2H), 8.30-8.32 (m, 3H), 8.43 (s, 1H), 9.35 (s, 1H), 9.62 (s, 1H).
Due to low solubility in solvent 13C NMR and HRMS was not obtained for **15b**.

Potassium trifluoro(4-(5-(7-methoxyquinolin-3-yl)-1,2,4-oxadiazol-3-yl)phenyl)borate (16)

Compound **14b** (0.14 mmol) was added to 15 mL MeOH, and then 3 M KHF_2 was added, after stirring for 2h. MeOH was evaporated to get residue. The crude product was dissolved in acetone and filtered, and filtrate was evaporated to get white solid which was further for recrystallization in acetone and diethyl ether to get pure product **16**.

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.99 (3H, s), 7.42 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.54 (m, 3H), 7.90 (d, J = 8.0 Hz, 2H), 8.20 (d, J = 12.0 Hz, 1H), 9.19 (d, J = 2.0 Hz, 1H), 9.49 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 55.8, 107.4, 114.9, 120.7, 121.7, 122.6, 130.5, 132.0, 136.1, 148.1, 150.9, 162.4, 168.9, 173.6; MS: calcd. for $C_{18}H_{12}BF_3N_3O_2^-$ 370.0980, found 370.0846.

(4-(5-(7-methoxyquinolin-3-yl)-1,2,4-oxadiazol-3-yl)phenyl)boronic acid (17)

Compound **16** (0.09 mmol) and silica gel (0.18 mmol) was added H_2O/EtOAC (1.0 mL/1.0 mL) in one portion, the reaction mixture was stirred at r.t. until reaction is complete (about 24 hr). The reaction mixture was filtered to remove the silica gel and the filter cake was thoroughly washed with EtOAC, and then washed with acetone. The aqueous was extracted by EtOAC and the combined layers were dried to afford compound **17**.

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.99 (s, 3H), 7.42 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.54 (s, 1H), 8.01 (d, J = 8.0Hz, 2H) , 8.11(d, J = 8.0Hz, 2H) , 8.20 (d, J = 8.0 Hz, 1H), 8.32 (s, 2H), 9.20 (s, 1H), 9.49 (d, J = 4.0 Hz, 1H,); ^{13}C NMR (100 MHz, DMSO- d_6): δ 56.3, 107.9, 115.3, 121.4, 122.2, 126.5, 131.2, 135.3, 136.7, 148.7, 151.6, 163.0, 168.8, 174.6; HRMS: calcd. for $C_{18}H_{14}BNO_4H^+$ 348.1150, found 348.1175.

4-(5-(7-boronoquinolin-3-yl)-1,2,4-oxadiazol-3-yl)benzoic acid (18)

Compound **15b** (0.3 mmol) was hydrolyzed in 5 mL EtOH and 2M (5mL) sodium hydroxide. The reaction mixture was stirred overnight. After concentration under vacuum, the mixture was acidified with 1M HCl. The resultant solid was filtered, washed with water and dried to get a beige solid **18** was obtained as a white solid.

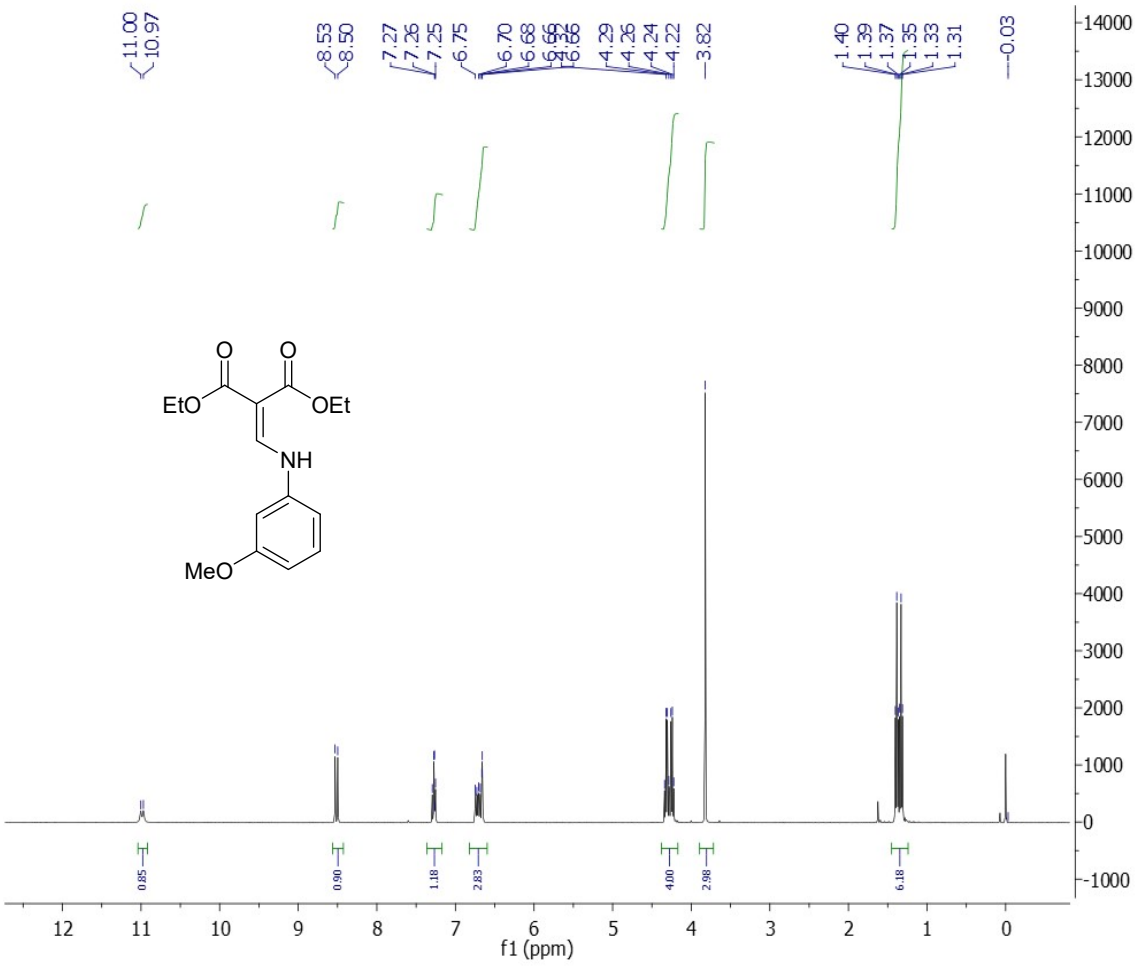
^{1}H NMR (400 MHz, DMSO-d_6 + MeOH-d_4) δ 8.13-8.23 (m, 6H), 8.54-8.60 (m, 1H), 9.17 (m, 1H), 9.52 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6 + MeOH-d_4) δ 117.6, 127.8, 128.0, 128.6, 130.2, 132.6, 133.8, 135.7, 136.9, 148.0, 148.8, 167.0, 168.2, 174.6.

(Due to low solubility of compound spectra was recorded in the DMSO-d_6 + MeOH-d_4).

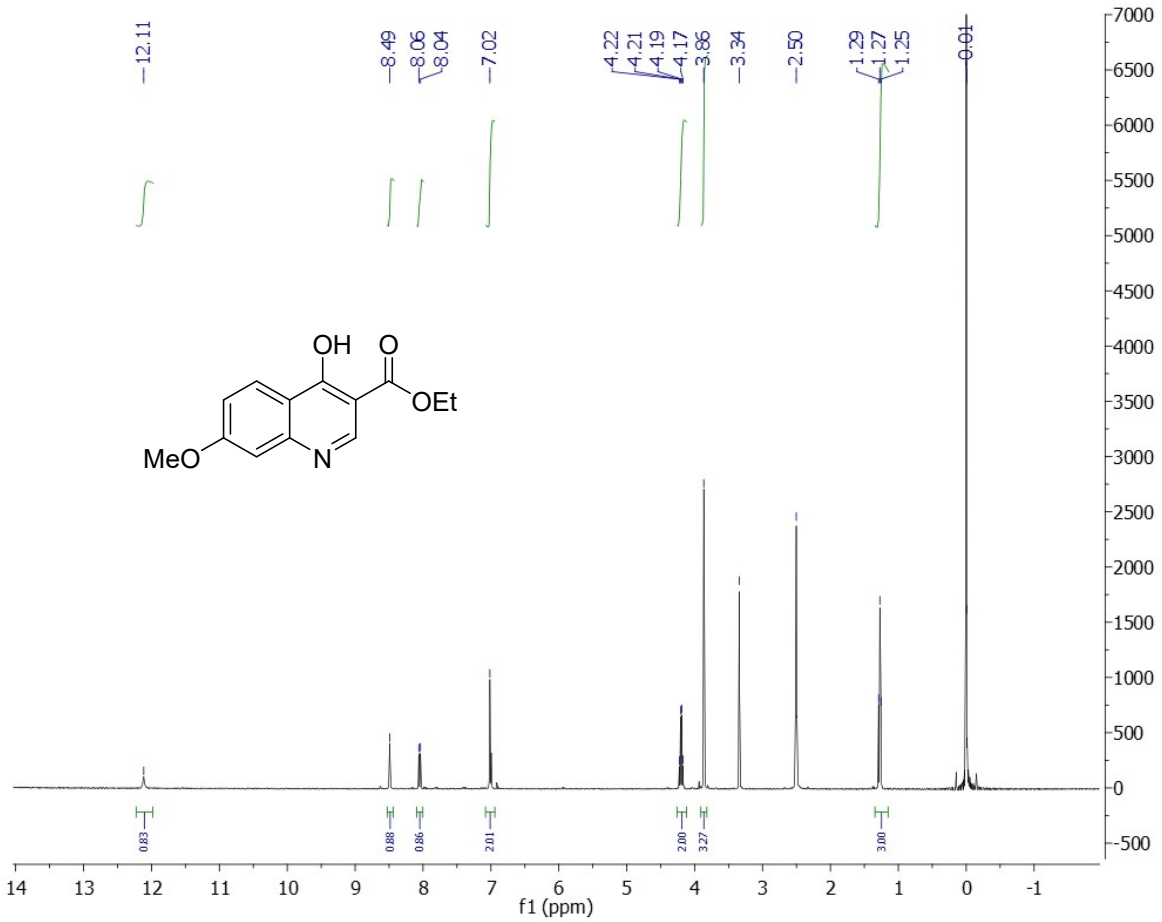
References:

1. Y. Zhang, W. A. Guiguemde, M. Sigal, F. Zhu, M. C. Connelly, S. Nwaka and R. K. Guy, *Bioorganic & medicinal chemistry*, 2010, **18**, 2756-2766.

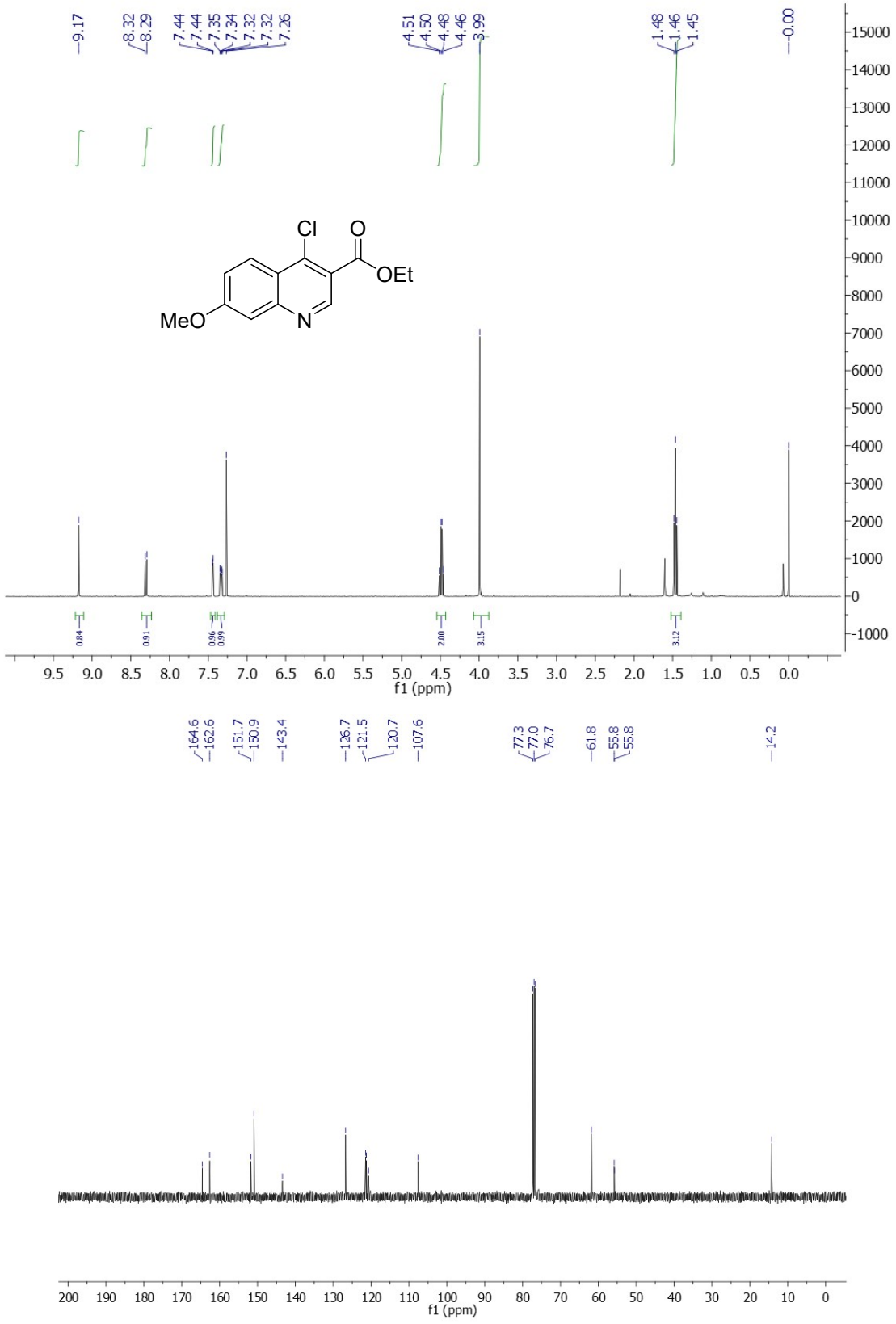
2. B. C. Das, X.-Y. Tang, P. Rogler and T. Evans, *Tetrahedron letters*, 2012, **53**, 3947-3950.



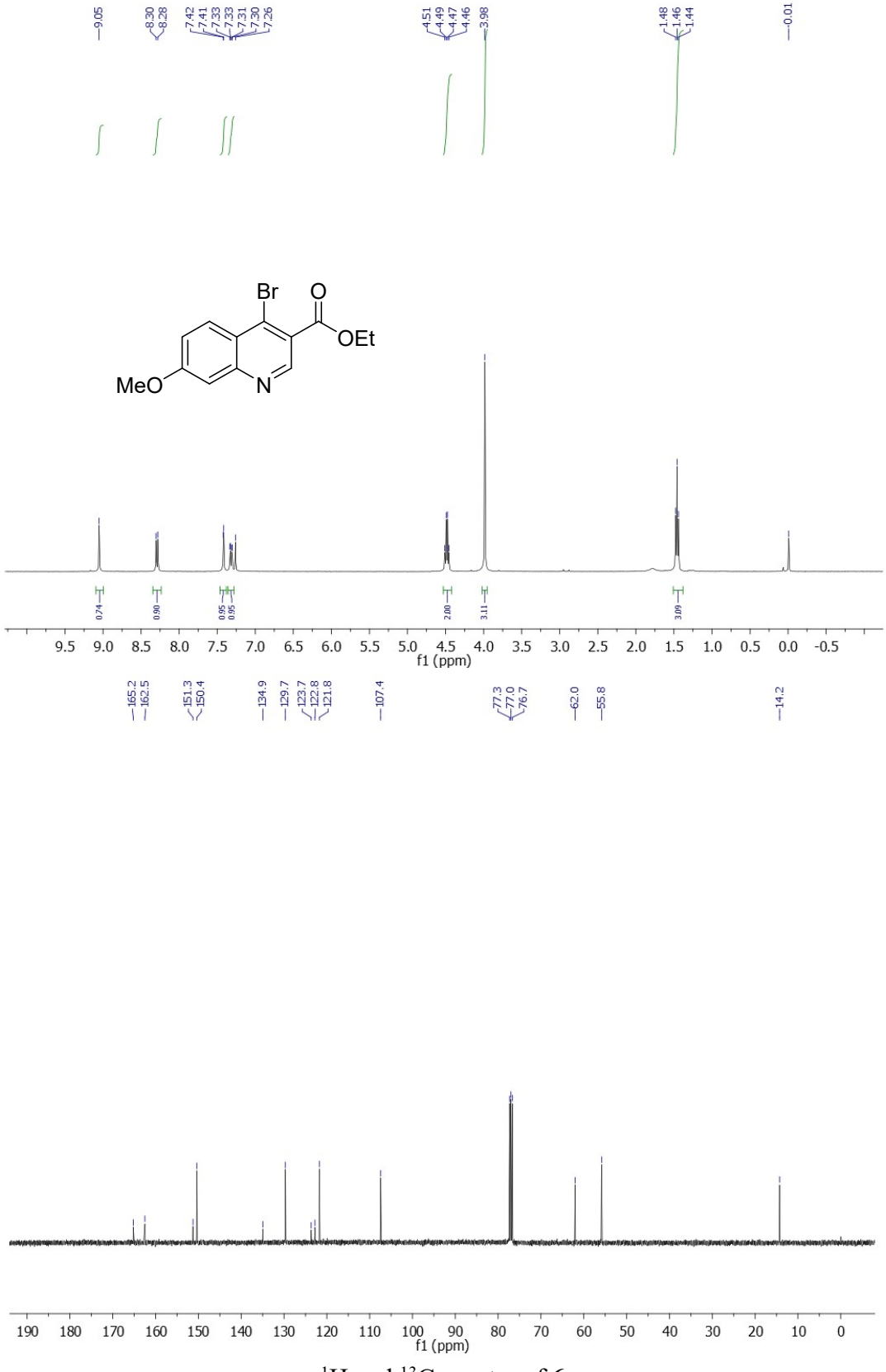
^{1}H spectrum of **3**



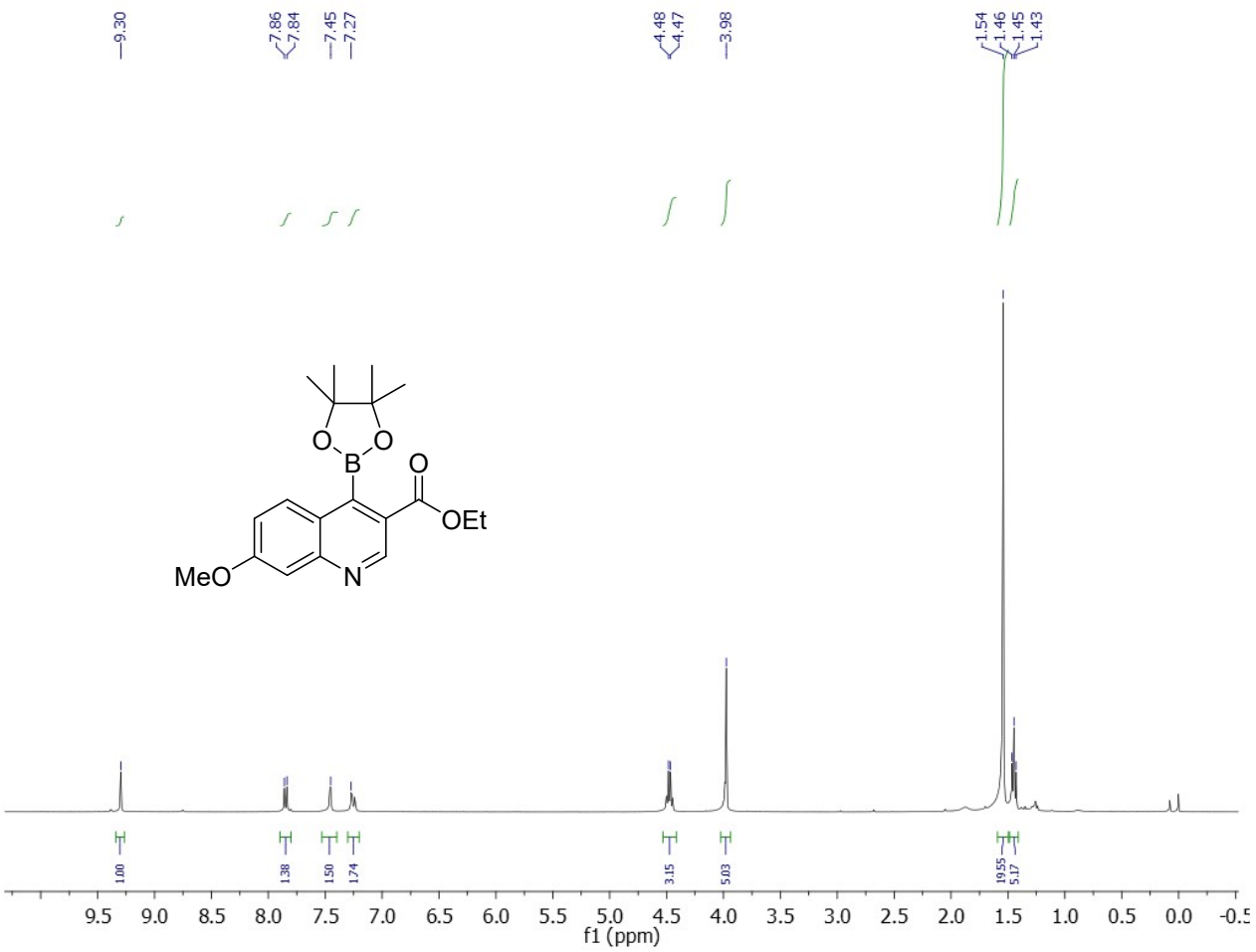
^{1}H spectrum of **4**



^{1}H and ^{13}C spectra of **5a**



^{1}H and ^{13}C spectra of **6**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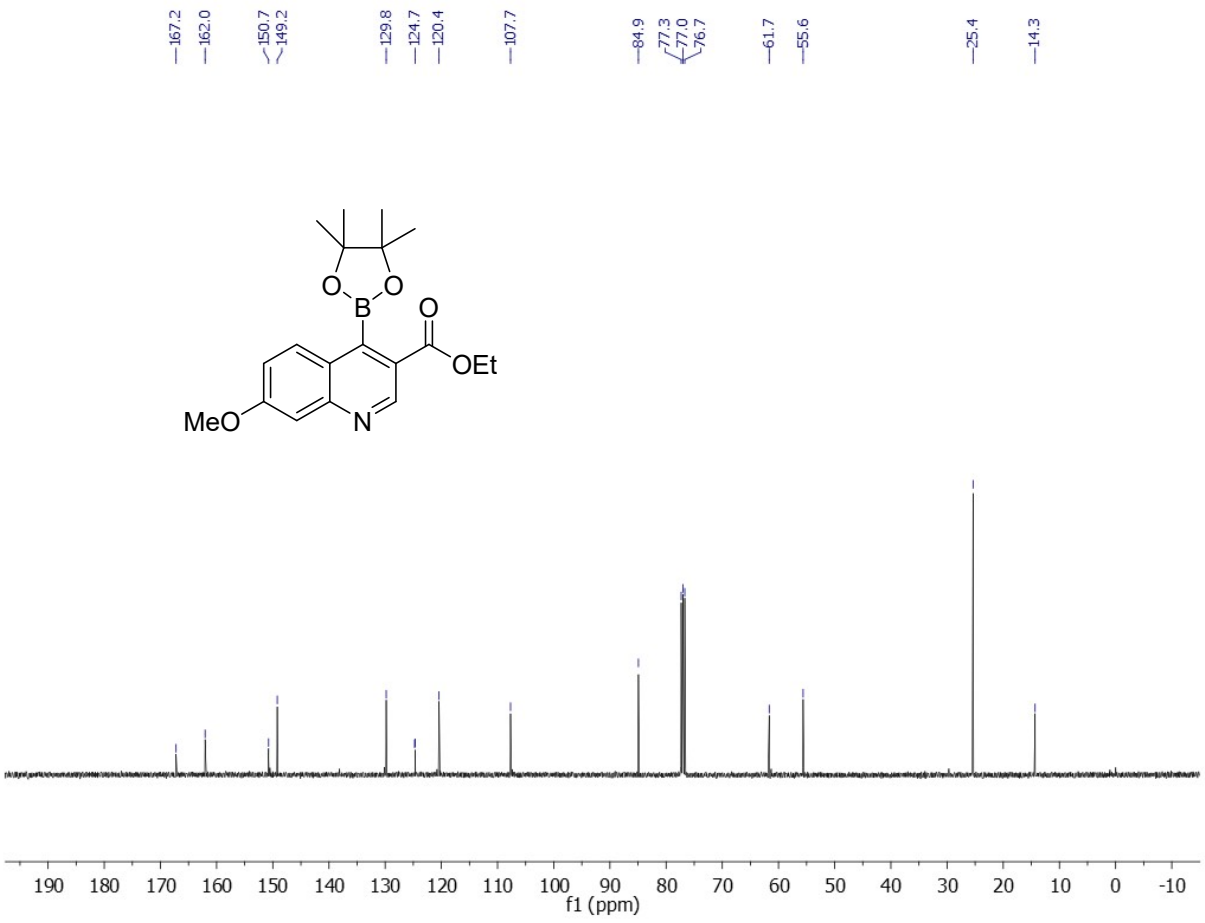
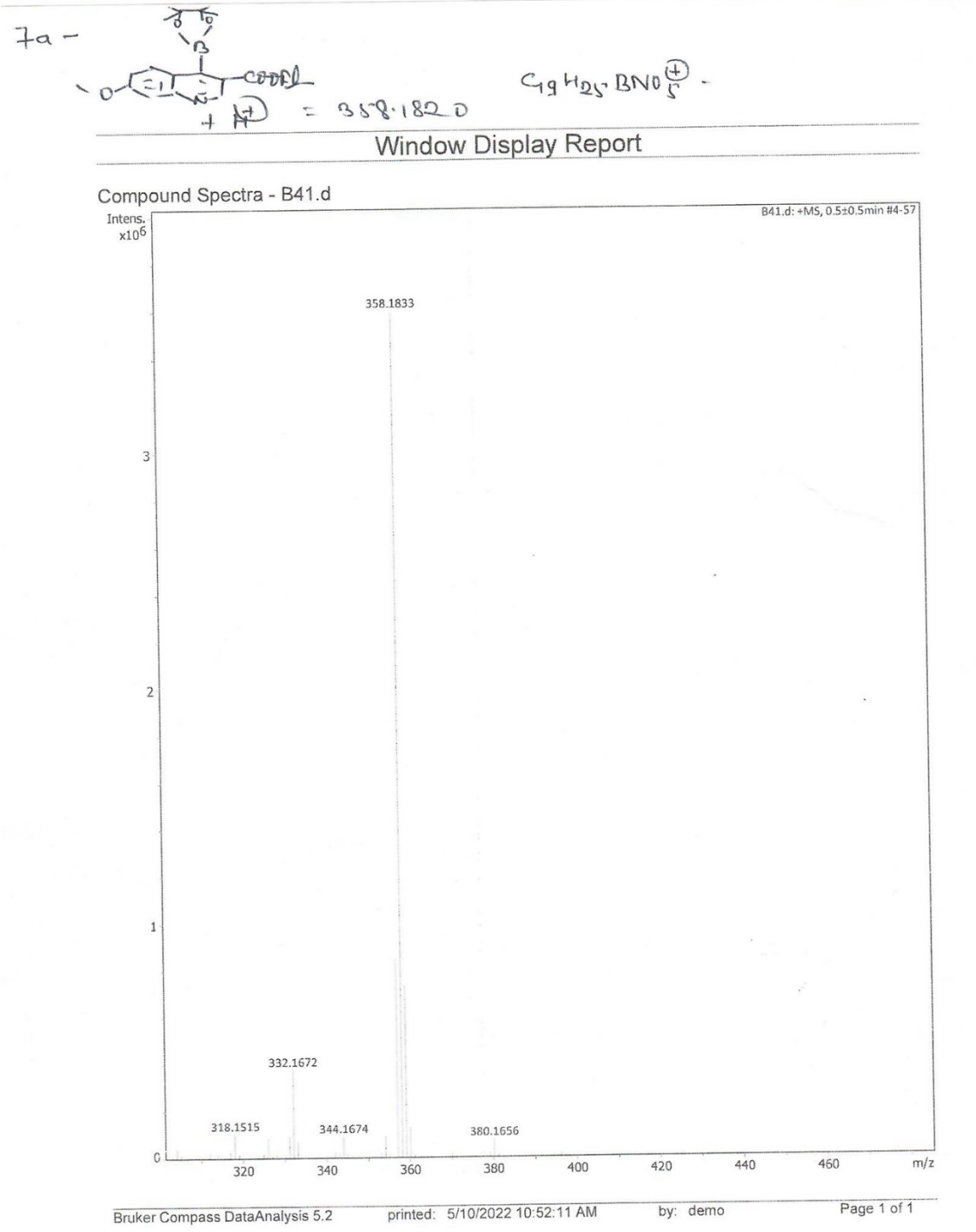
7.86
7.84
7.45
7.27
4.48
4.47
3.98
1.54
1.46
1.45
1.43
O
B
O
O
OEt
MeO
N
1.00
1.38
1.50
1.74
3.15
5.03
19.55
5.17
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

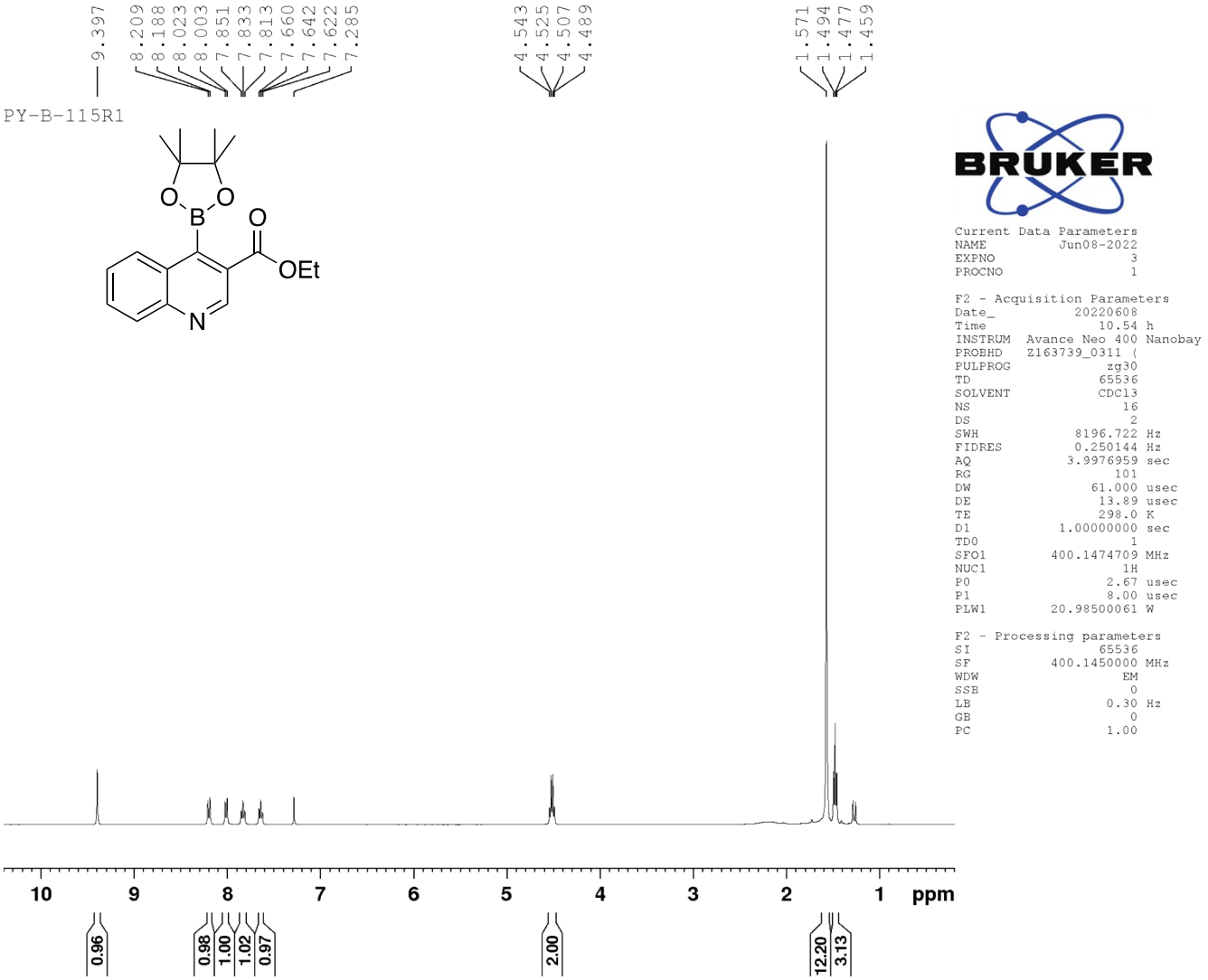
^{1}H NMR of **7a**


167.2
162.0
150.7
149.2
129.8
124.7
120.4
107.7
84.9
77.3
77.0
76.7
61.7
55.6
25.4
14.3
O
B
O
O
OEt
MeO
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

^{13}C NMR of **7a**



Mass spectrum of **7a**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8.209
8.188
8.023
8.003
7.851
7.833
7.813
7.660
7.642
7.622
7.285
4.543
4.525
4.507
4.489
1.571
1.494
1.477
1.459
PY-B-115R1
O
B
O
O
OEt
N
BRUKER
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PROCNO 1
F2 - Acquisition Parameters
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DS 2
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FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
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SF 400.1450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
ppm
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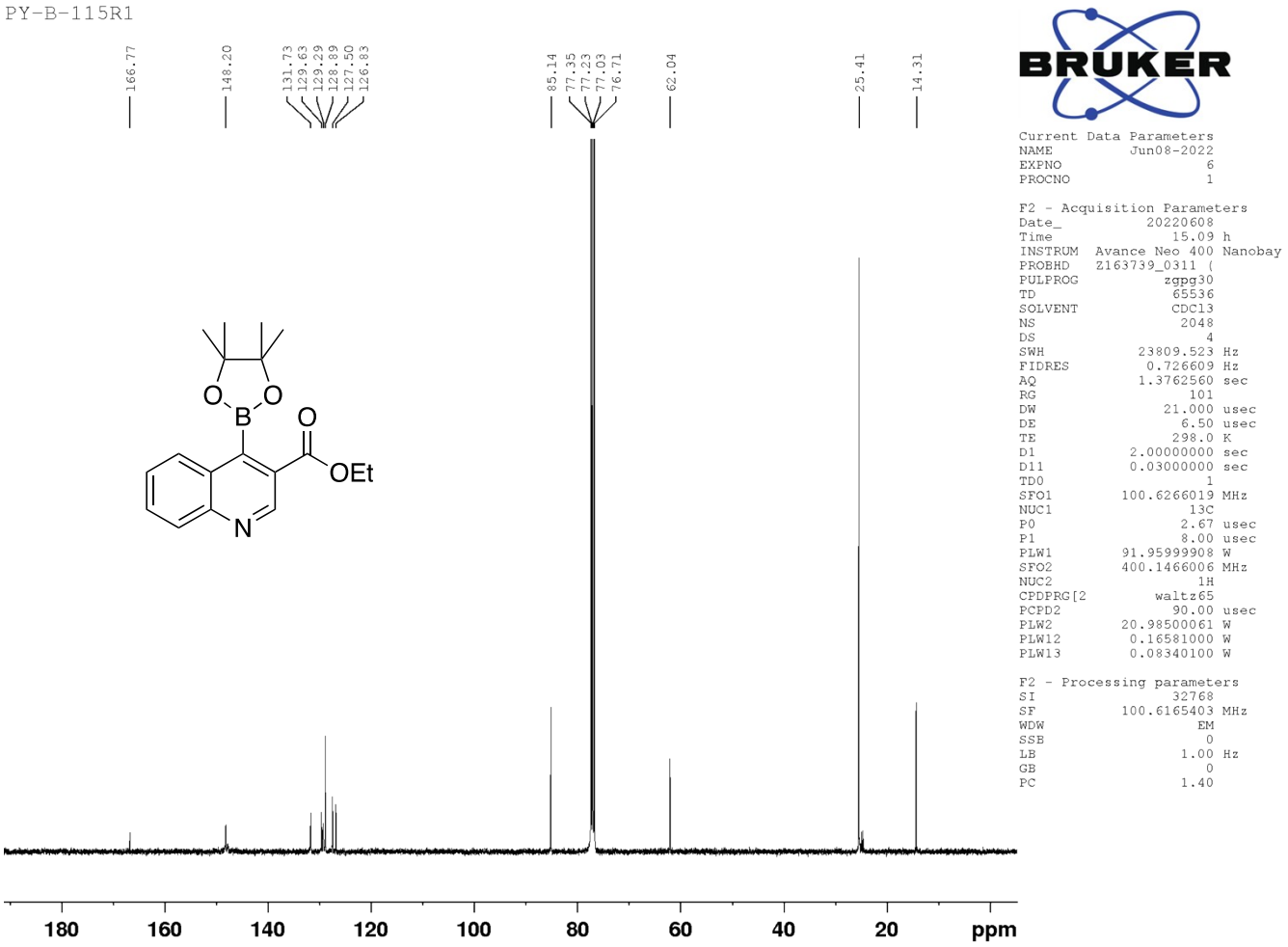
0.98
1.00
1.02
0.97
2.00
12.20
3.13

^{1}H NMR of **7b**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148.20
131.73
129.63
129.29
128.89
127.50
126.83
85.14
77.35
77.23
77.03
76.71
62.04
25.41
14.31
O
B
O
O
OEt
N
180
160
140
120
100
80
60
40
20
ppm
BRUKER
Current Data Parameters
NAME Jun08-2022
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
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Time 15.09 h
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SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
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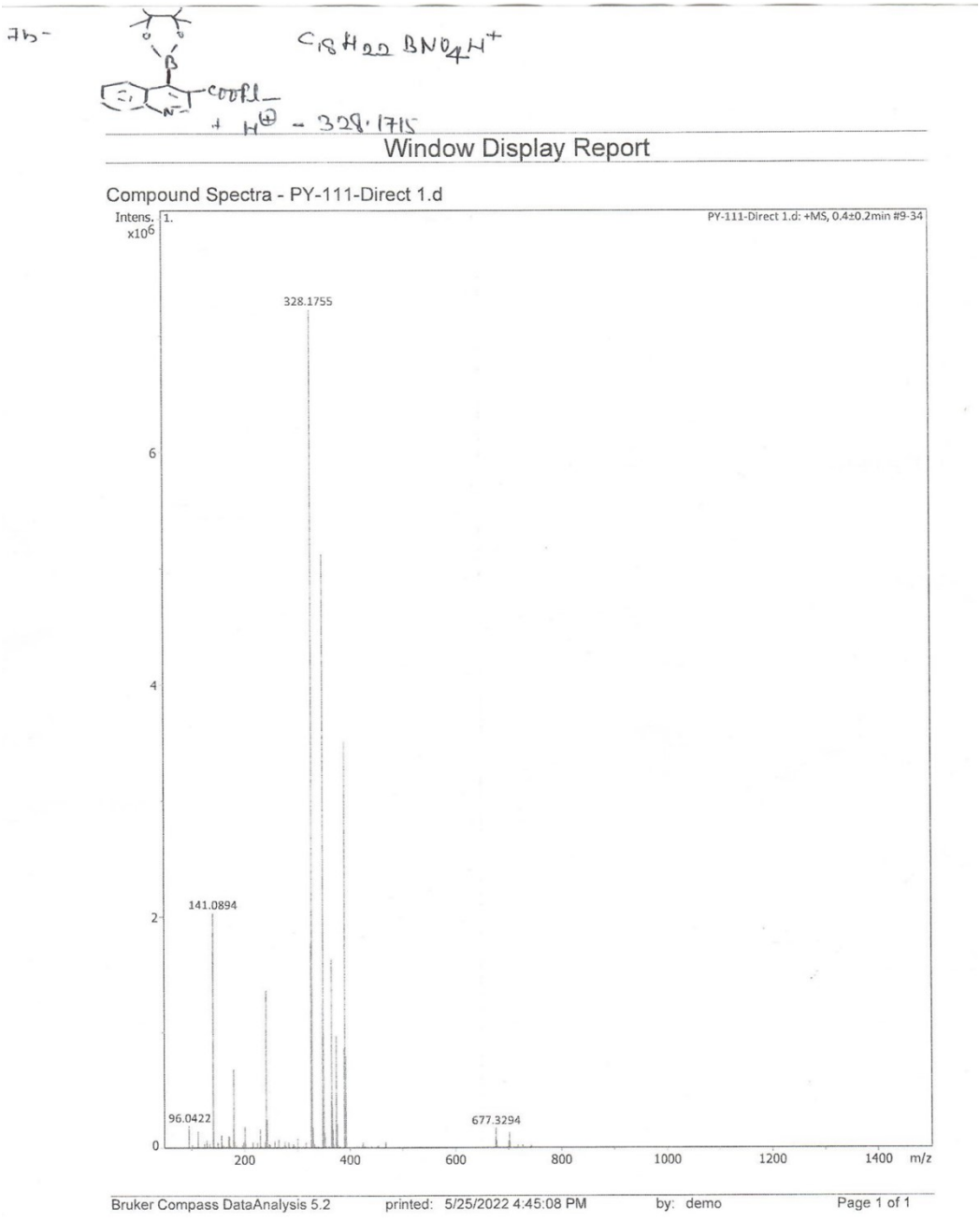
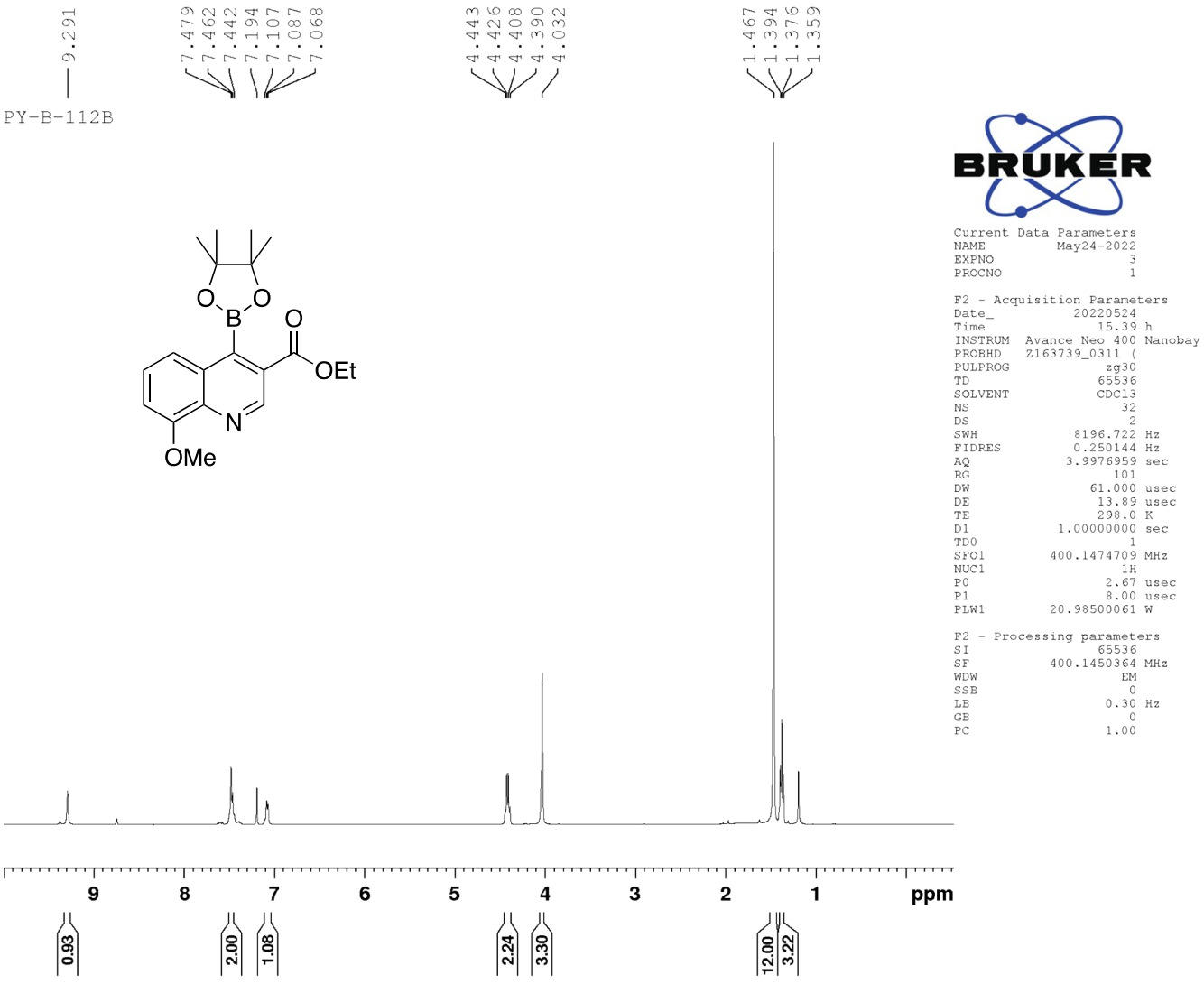
GB 0
PC 1.40

^{13}C NMR of **7b**



Mass spectrum of **7b**



BRUKER

Current Data Parameters
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PROCNO 1

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TD 65536
SOLVENT CDCl3
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DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
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P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W

F2 - Processing parameters
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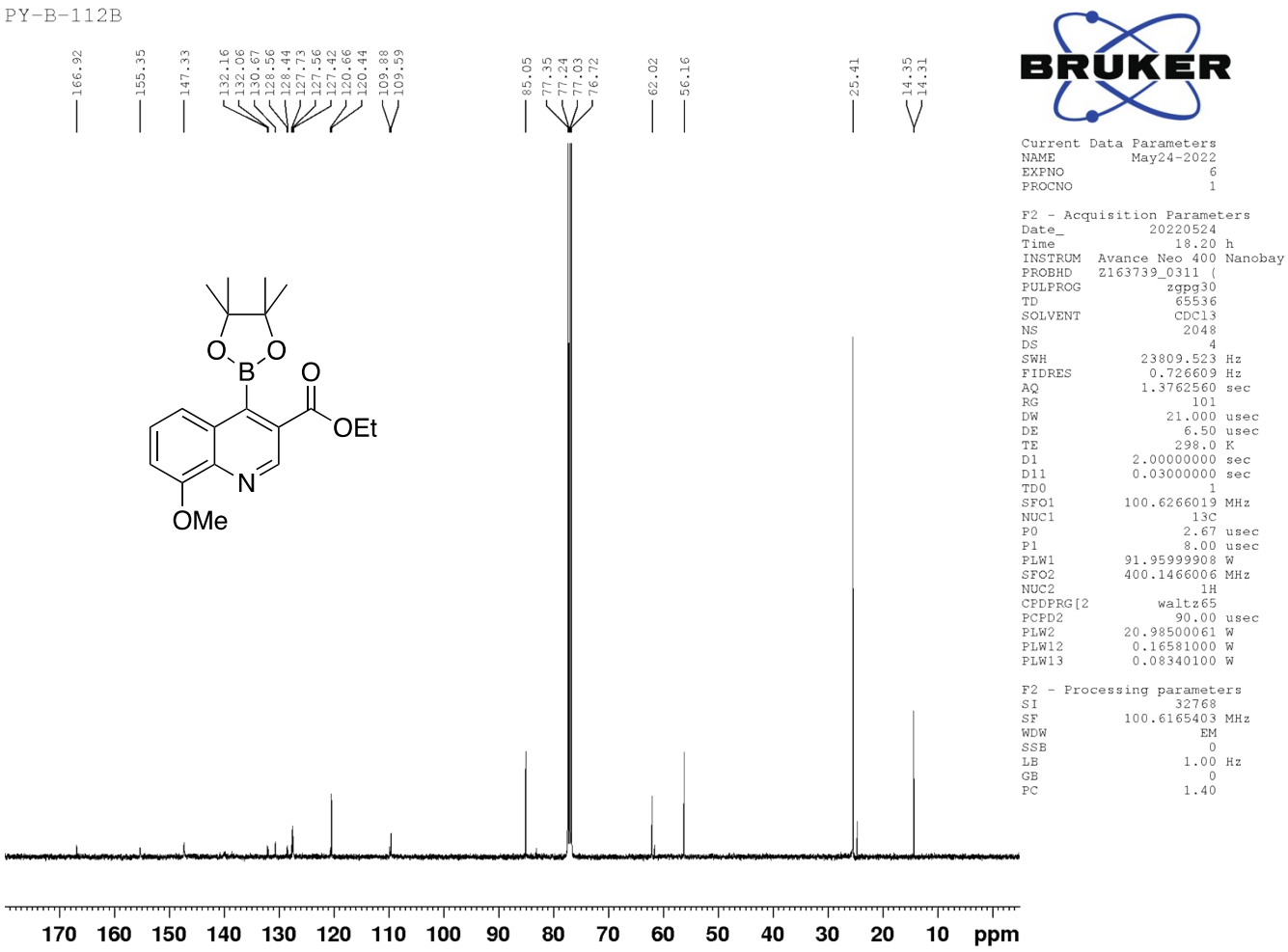
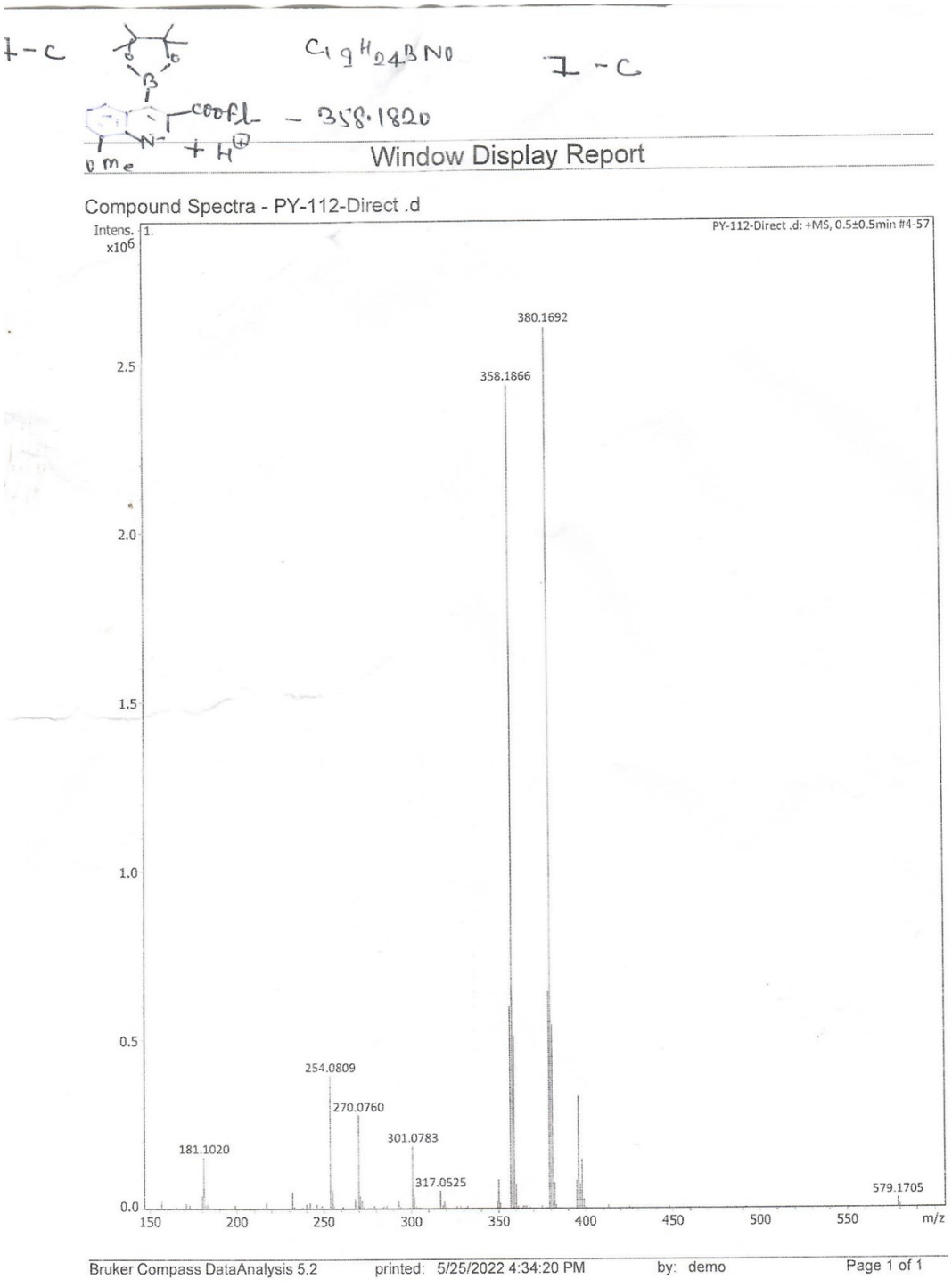
SF 400.1450364 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

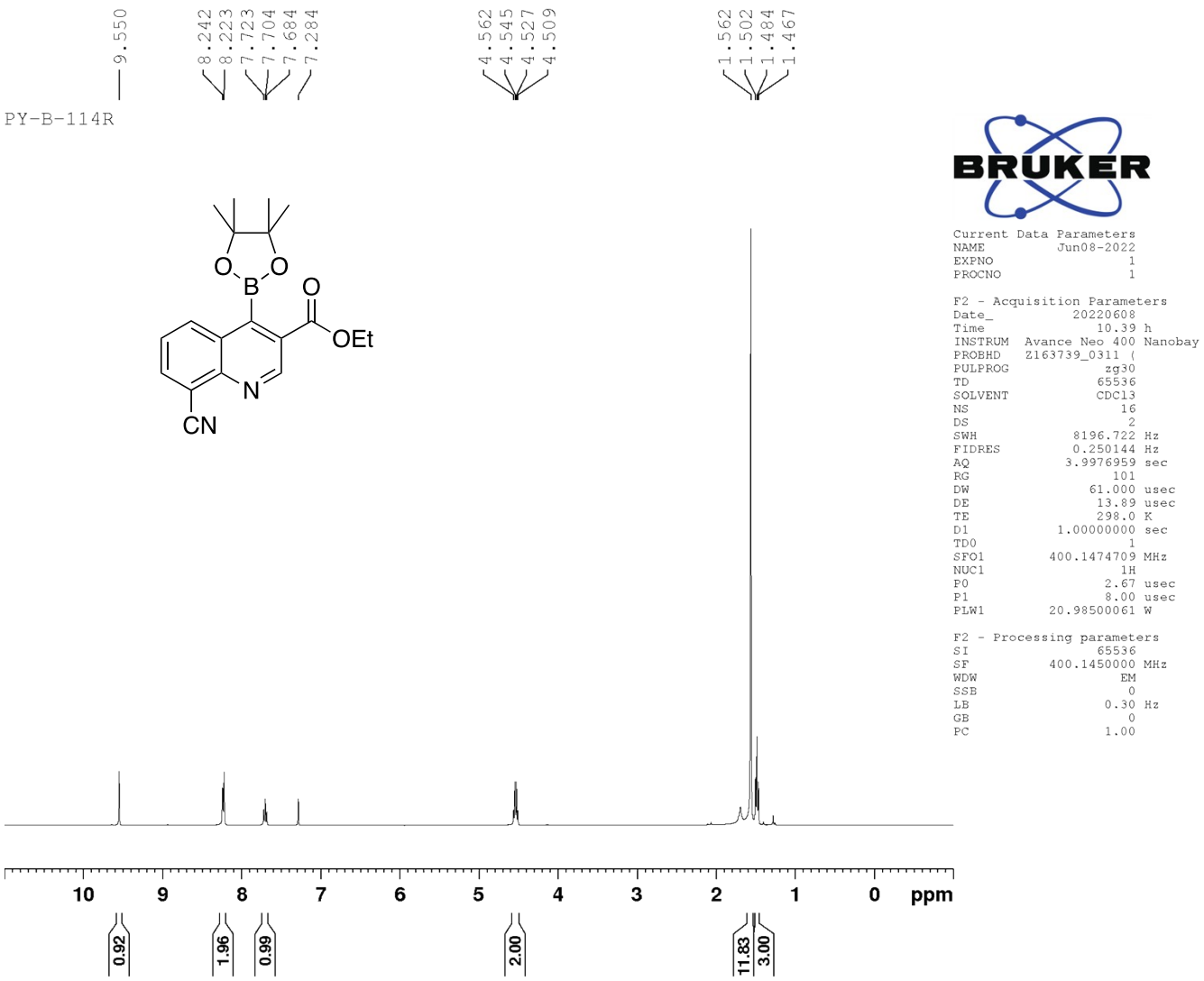
^{1}H NMR of **7c**



^{13}C NMR of **7c**



Mass spectrum of **7c**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1.484
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CN
BRUKER
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PROCNO 1
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SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
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P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
0
ppm
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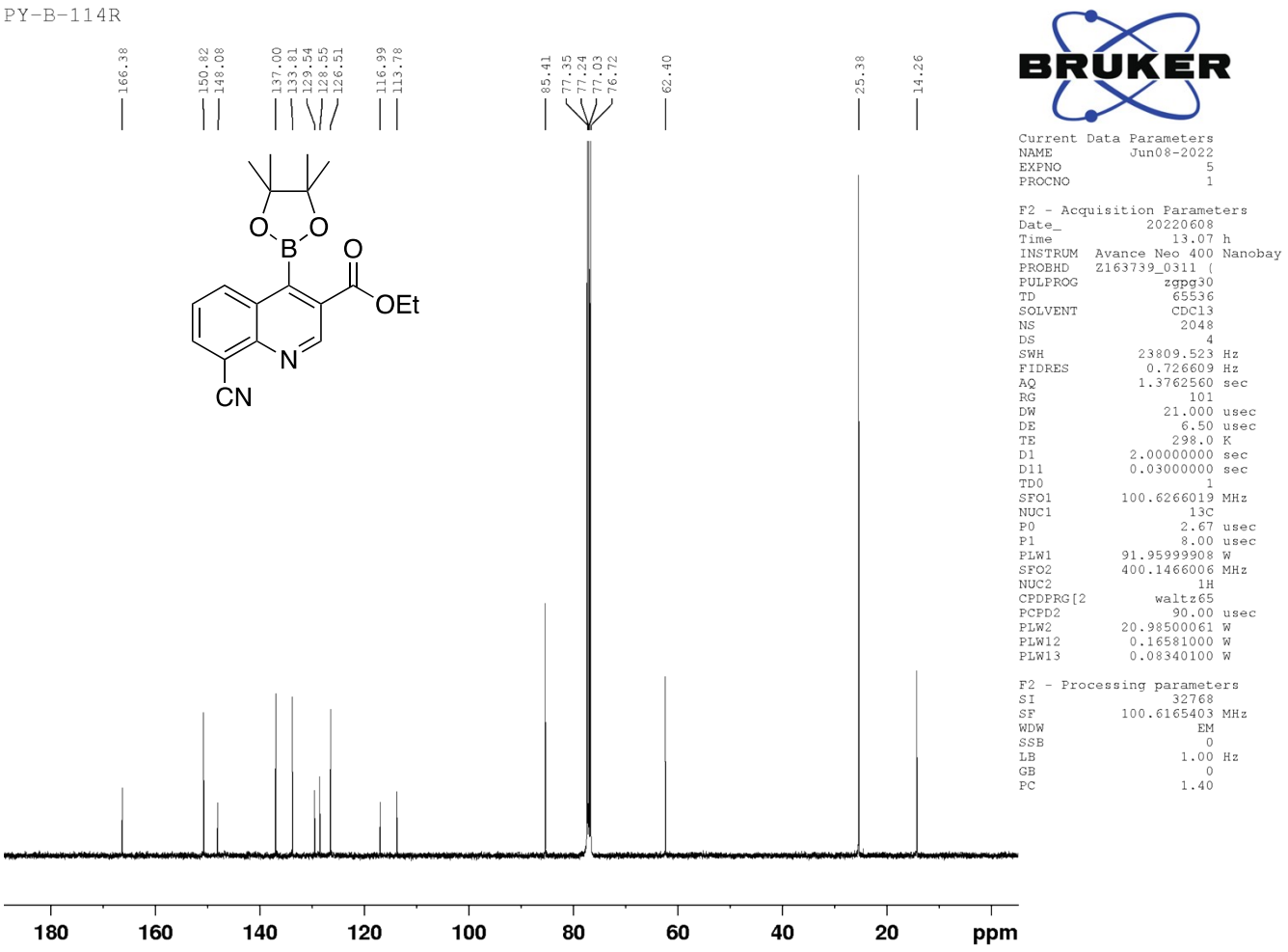
1.96
0.99
2.00
11.83
3.00

^{1}H NMR of **7d**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137.00
133.81
129.54
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126.51
116.99
113.78
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77.24
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76.72
62.40
25.38
14.26
O
B
O
O
OEt
N
CN
180
160
140
120
100
80
60
40
20
ppm
BRUKER
Current Data Parameters
NAME Jun08-2022
EXPNO 5
PROCNO 1
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Time 13.07 h
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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2048
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
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WDW EM
SSB 0
LB 1.00 Hz
GB 0
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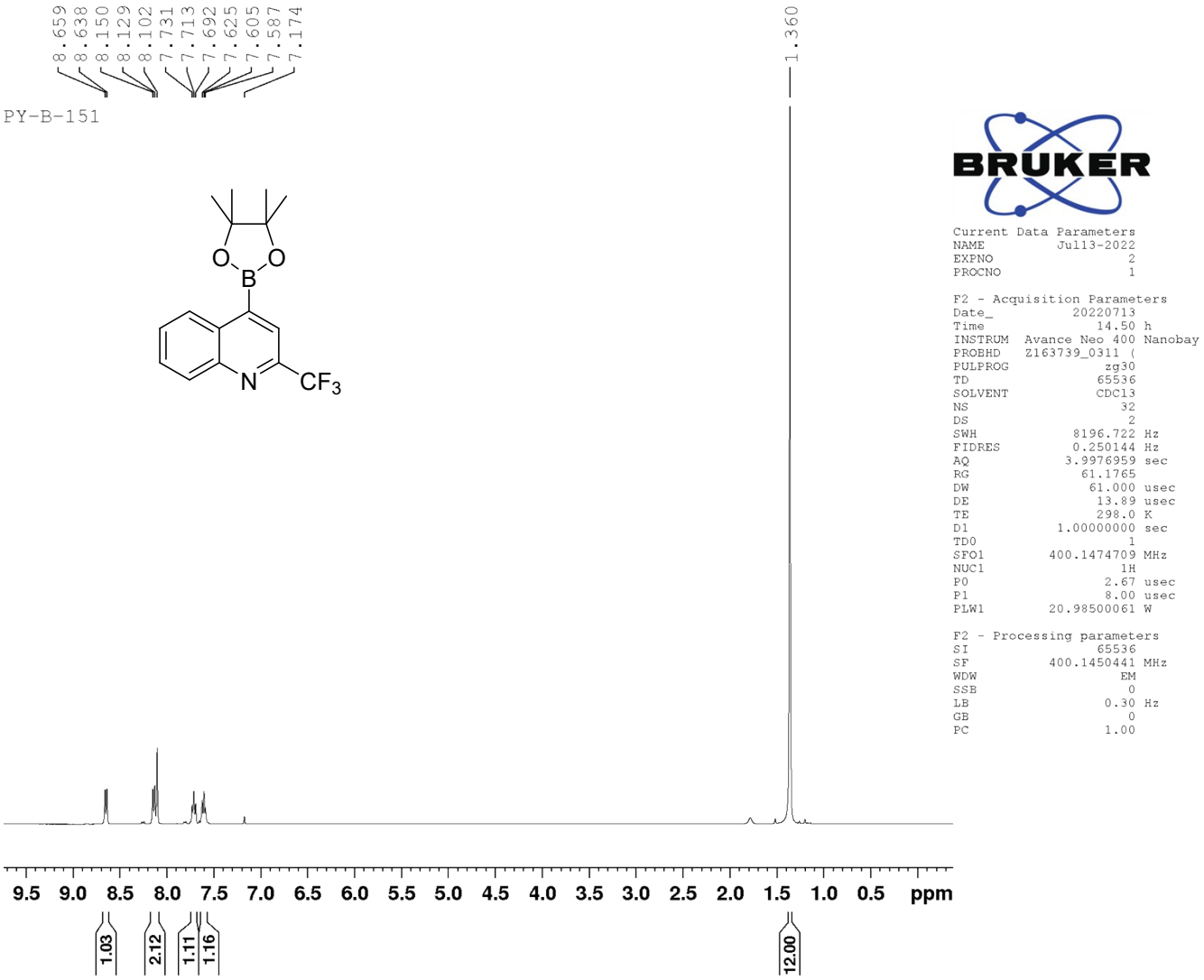
^{13}C NMR of **7d**



BRUKER

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PROCNO                 1

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TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG               61.1765
DW                61.000 usec
DE                13.89 usec
TE                298.0 K
D1            1.00000000 sec
TD0                    1
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NUC1                  1H
P0                 2.67 usec
P1                 8.00 usec
PLW1         20.98500061 W

F2 - Processing parameters
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WDW                   EM
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LB                  0.30 Hz
GB                     0
PC                  1.00
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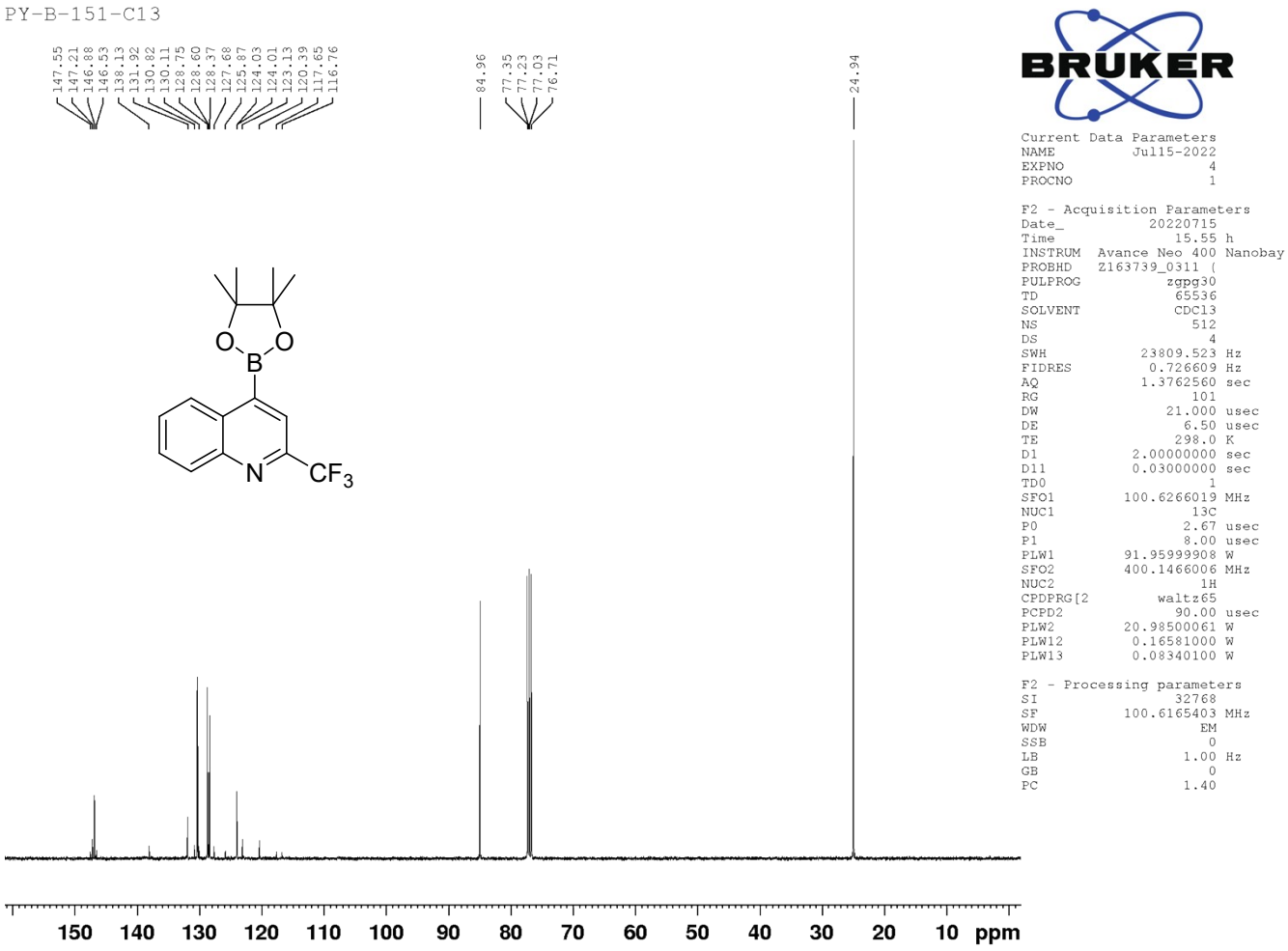
^{1}H NMR of **7e**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147.21
146.88
146.53
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131.92
130.82
130.11
128.75
128.60
128.37
127.68
125.87
124.03
124.01
123.13
120.39
117.65
116.76
84.96
77.35
77.23
77.03
76.71
24.94
O
B
O
N
CF3
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
Current Data Parameters
NAME Jul15-2022
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
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Time 15.55 h
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PROBHD Z163739_0311 (
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SOLVENT CDCl3
NS 512
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
F2 - Processing parameters
SI 32768
SF 100.6165403 MHz
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SSB 0
LB 1.00 Hz
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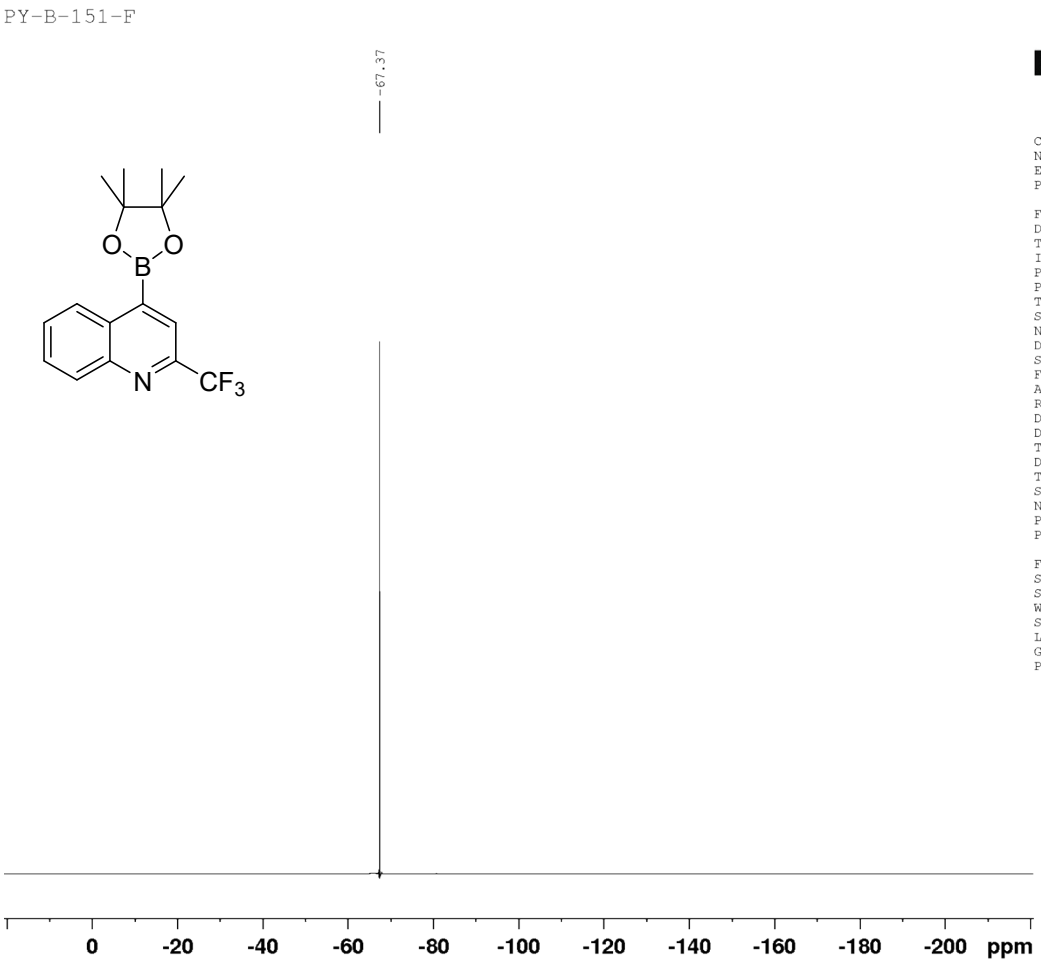
^{13}C NMR of **7e**



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SOLVENT CDCl3
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FIDRES 1.387163 Hz
AQ 0.7208960 sec
RG 101
DW 5.500 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 376.4748291 MHz
NUC1 19F
P1 12.00 usec
PLW1 30.18499947 W

F2 - Processing parameters
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SF 376.5124803 MHz
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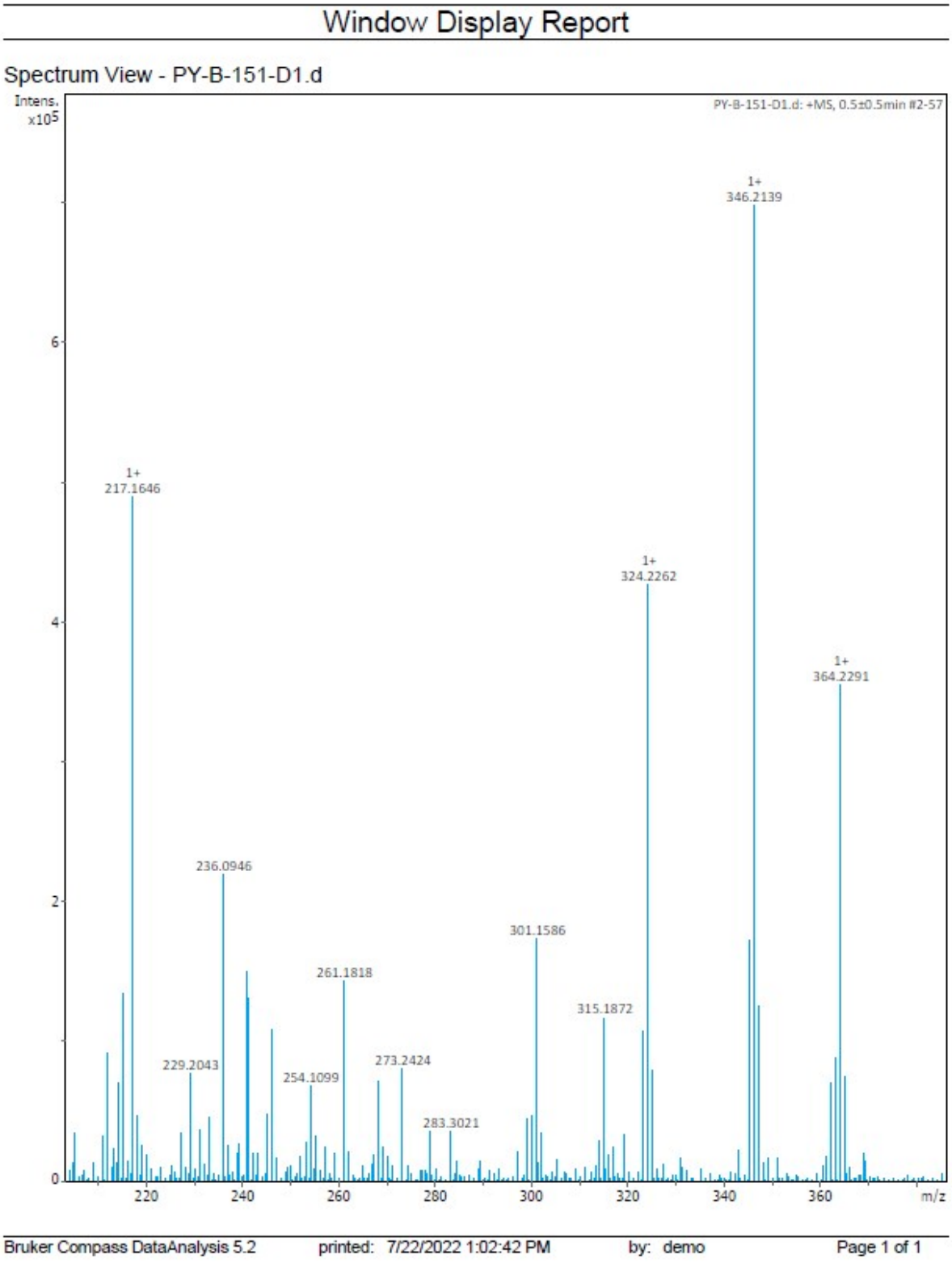
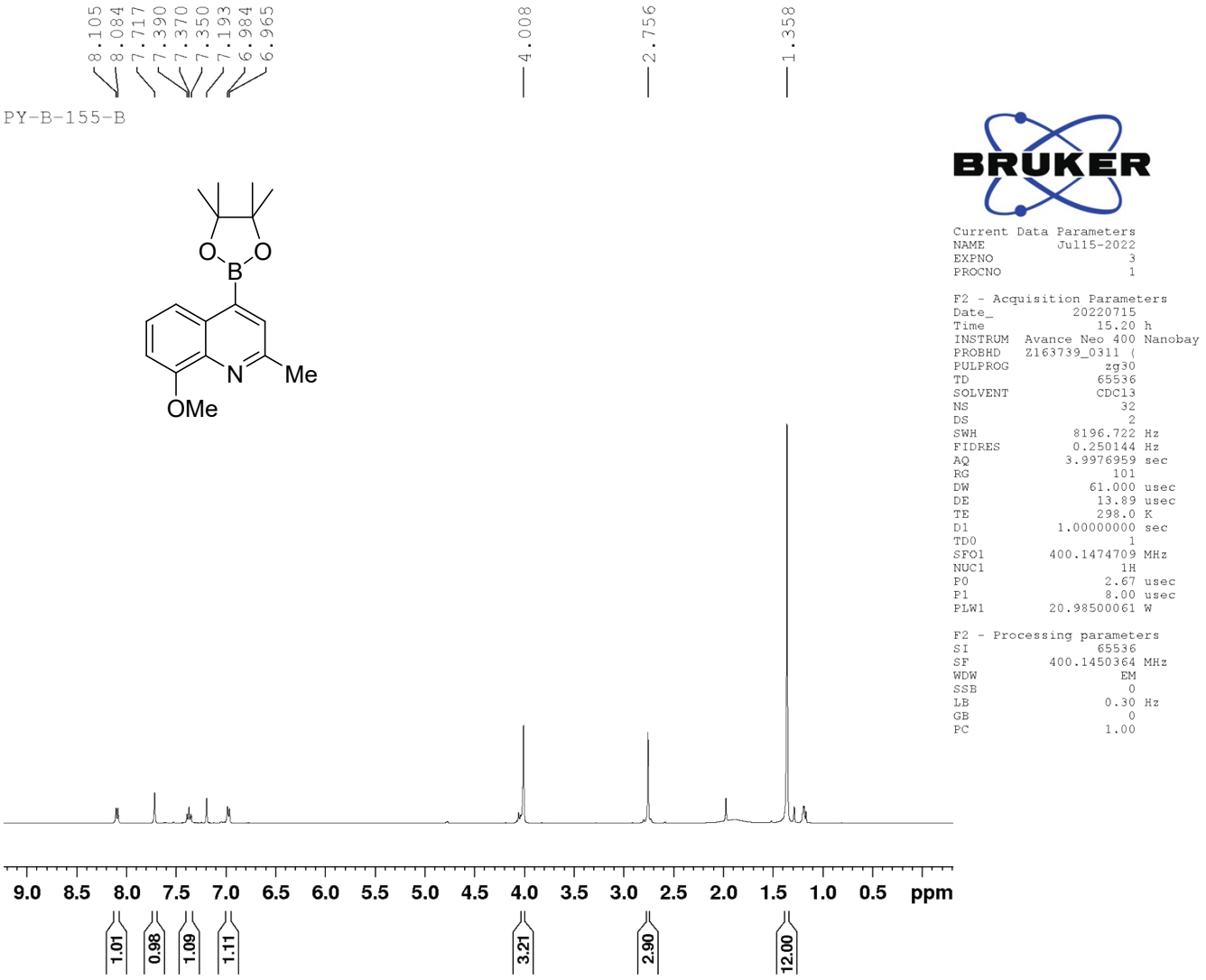
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

^{19}F NMR of **7e**



Mass spectrum of **7e**


8.105
8.084
7.717
7.390
7.370
7.350
7.193
6.984
6.965
4.008
2.756
1.358
PY-B-155-B
BRUKER
O
B
O
N
Me
OMe
Current Data Parameters
NAME Jul15-2022
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220715
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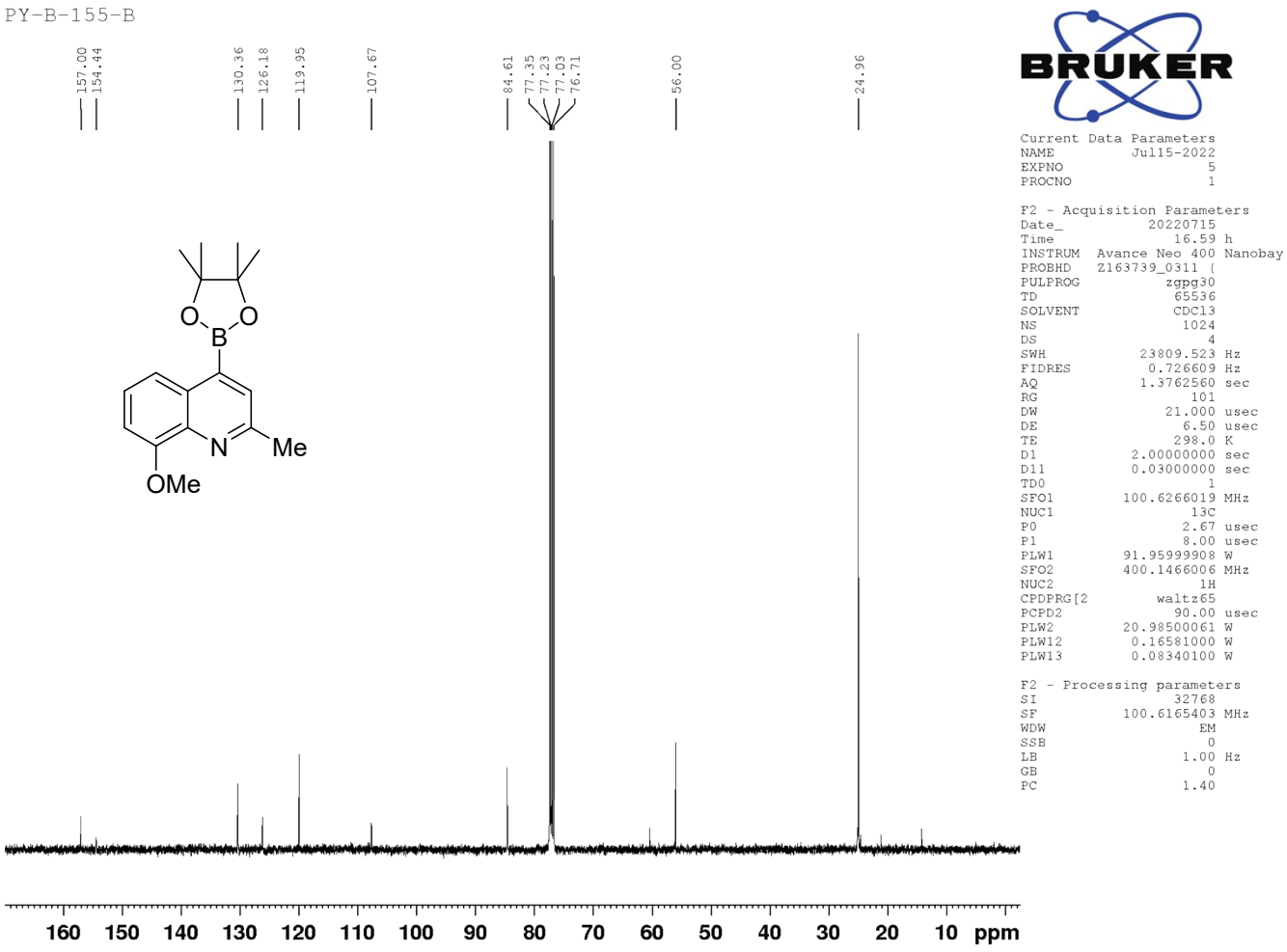
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450364 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.01
0.98
1.09
1.11
3.21
2.90
12.00

^{1}H NMR of **7f**


PY-B-155-B
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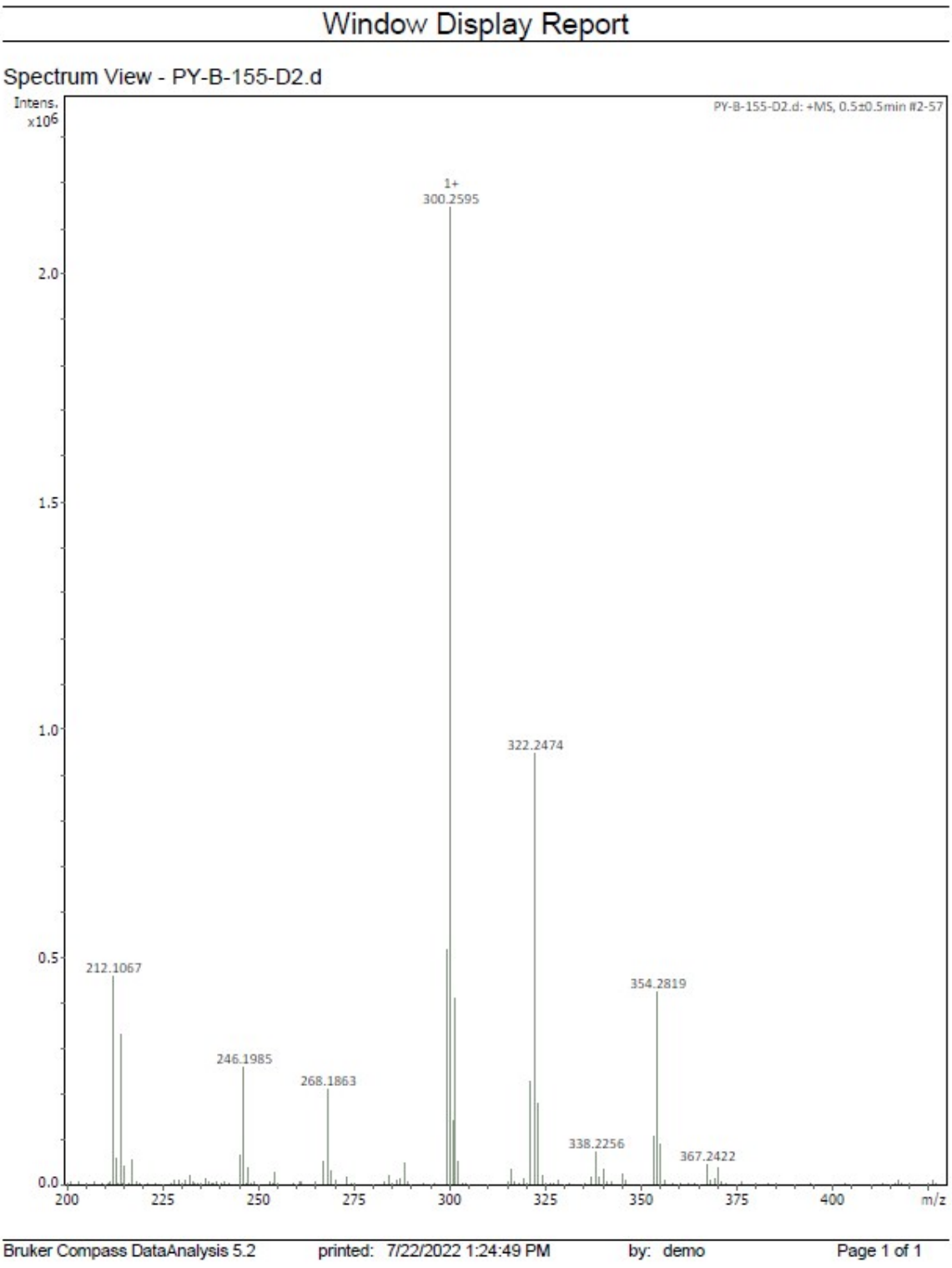
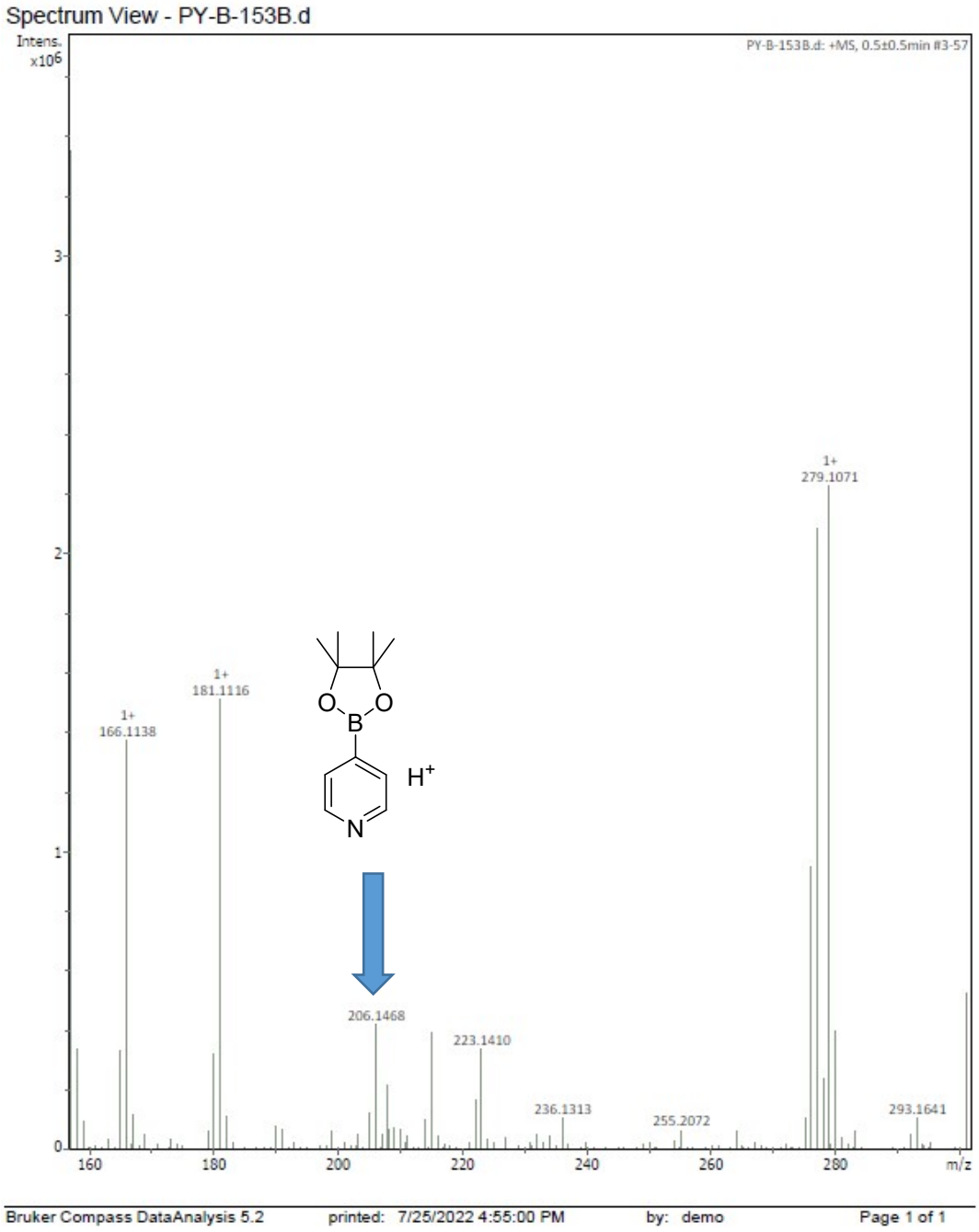
126.18
119.95
107.67
84.61
77.35
77.23
77.03
76.71
56.00
24.96
O
B
O
N
Me
OMe
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
BRUKER
Current Data Parameters
NAME Jul15-2022
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220715
Time 16.59 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
F2 - Processing parameters
SI 32768
SF 100.6165403 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

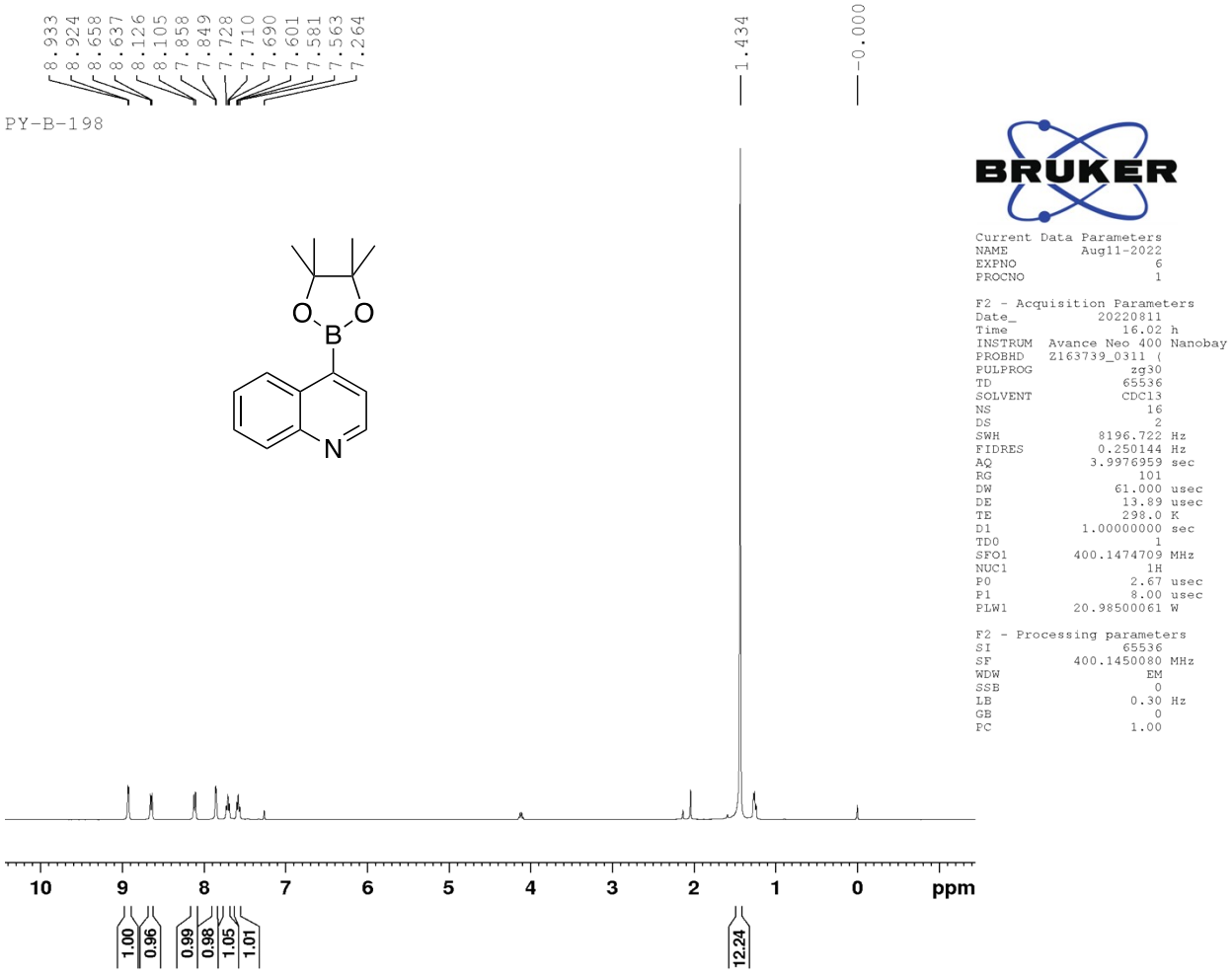
^{13}C NMR of **7f**



Mass spectrum of **7f**

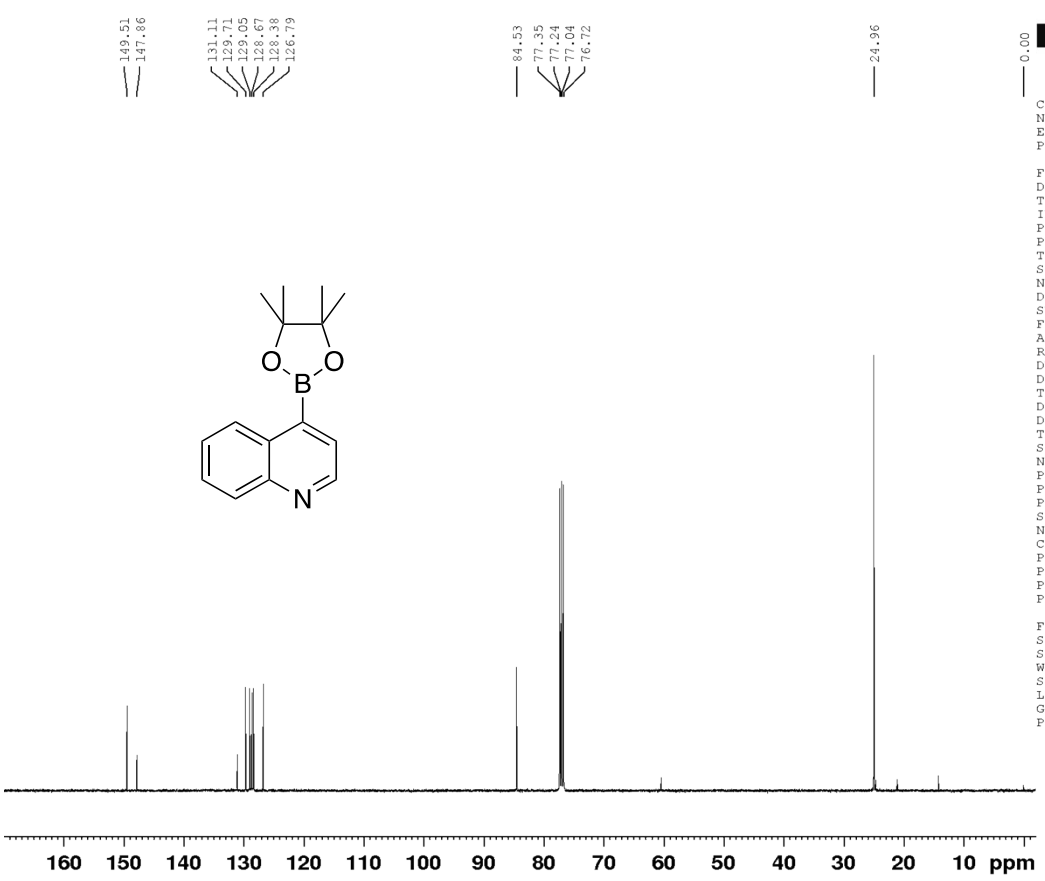


Mass spectrum of **7g**


8.933
8.924
8.658
8.637
8.126
8.105
7.858
7.849
7.728
7.710
7.690
7.601
7.581
7.563
7.264
1.434
0.000
PY-B-198
O
B
O
N
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.96
0.99
0.98
1.05
1.01
12.24
BRUKER
Current Data Parameters
NAME Aug11-2022
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220811
Time 16.02 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450080 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

^{1}H NMR of **7h**

PY-B-198

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Current Data Parameters
NAME                 Aug11-2022
EXPNO                         7
PROCNO                        1

F2 - Acquisition Parameters
Date_               20220811
Time                   17.08 h
INSTRUM  Avance Neo 400 Nanobay
PROBHD   Z163739_0311 (
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       1024
DS                          4
SWH                 23809.523 Hz
FIDRES              0.726609 Hz
AQ                  1.3762560 sec
RG                        101
DW                     21.000 usec
DE                      6.50 usec
TE                     298.0 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1
SFO1              100.6266019 MHz
NUC1                      13C
P0                      2.67 usec
P1                      8.00 usec
PLW1              91.95999908 W
SFO2              400.1466006 MHz
NUC2                      1H
CPDPRG[2              waltz65
PCPD2                  90.00 usec
PLW2              20.98500061 W
PLW12              0.16581000 W
PLW13              0.08340100 W

F2 - Processing parameters
SI                      32768
SF                100.6165403 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
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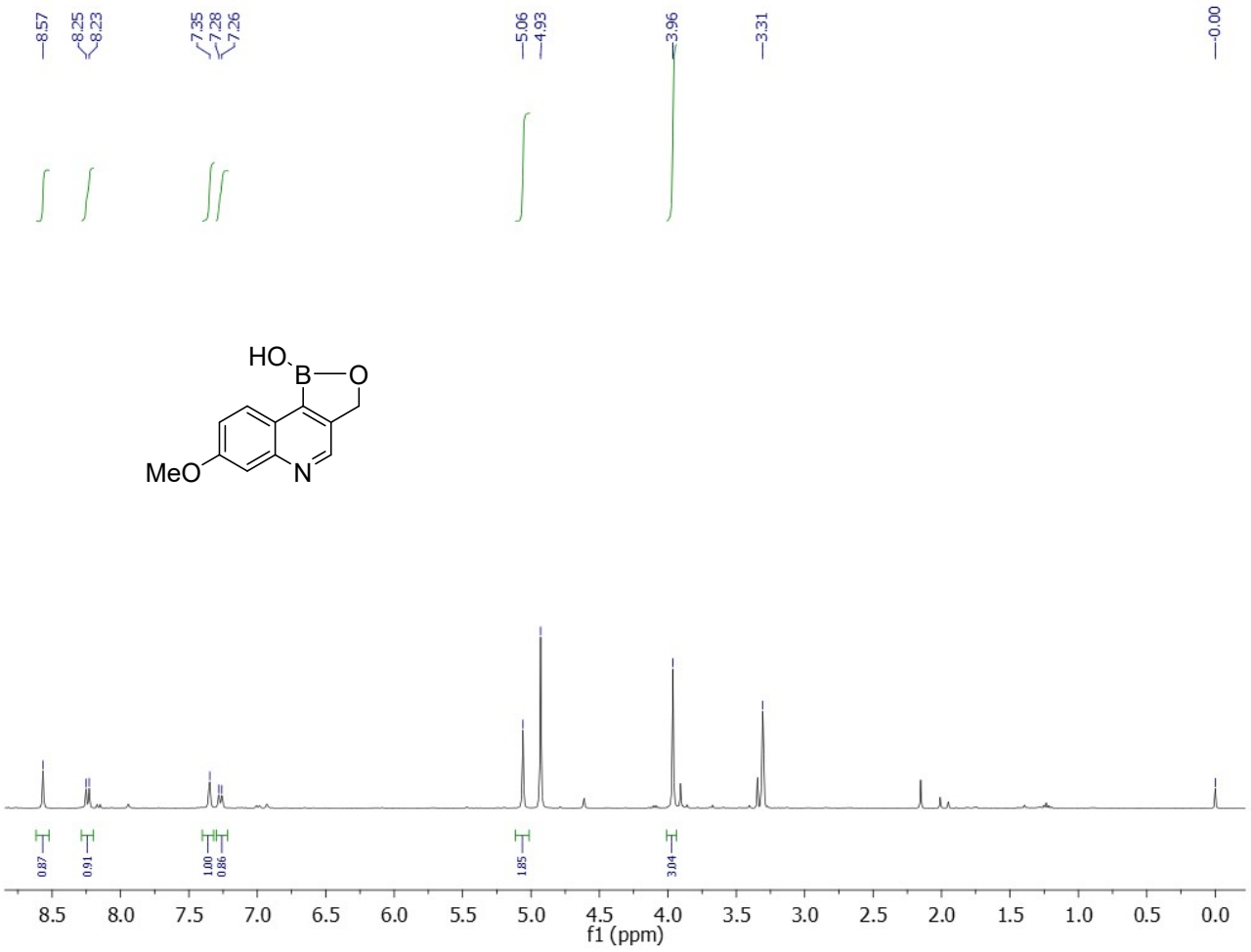
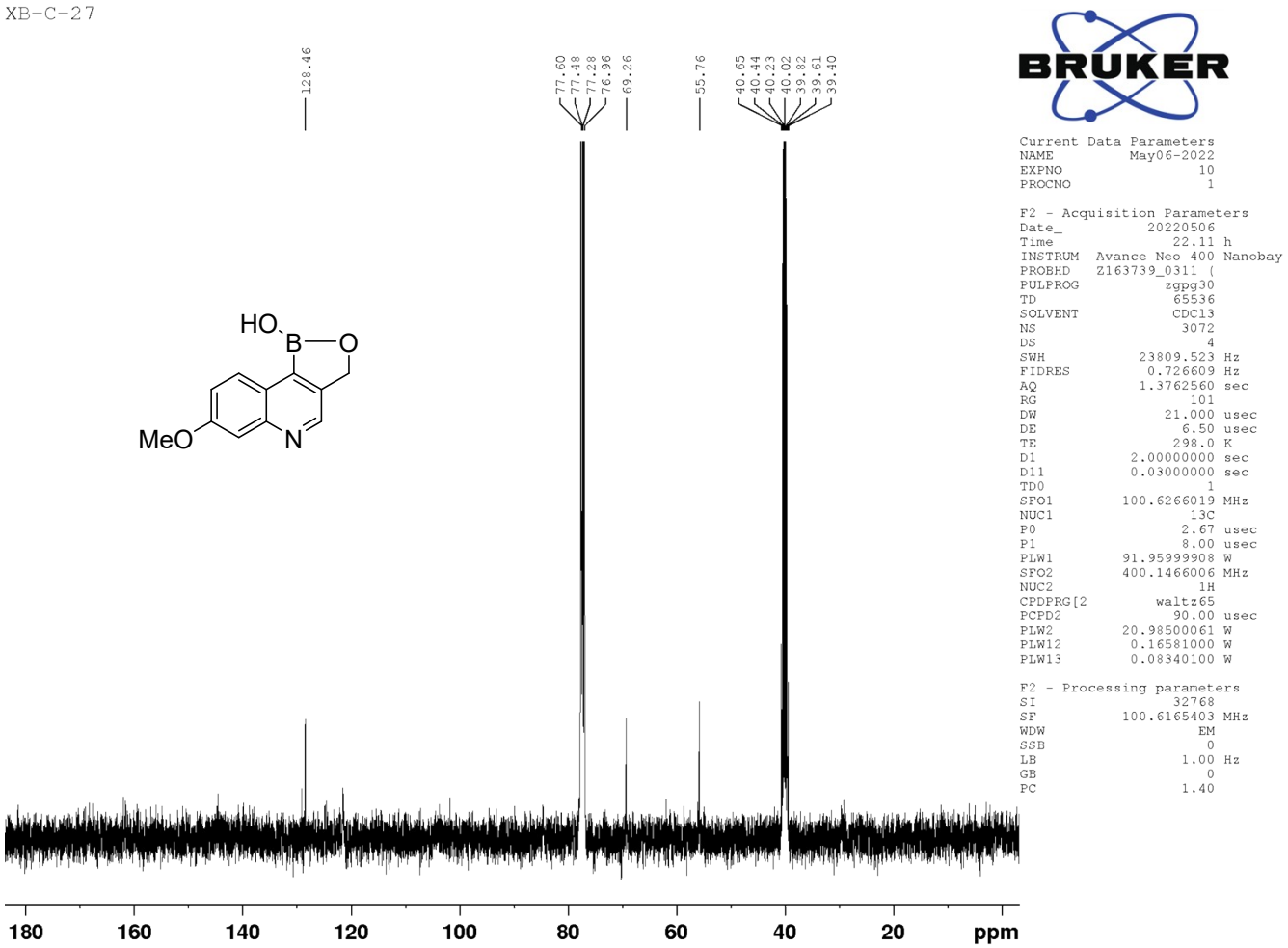
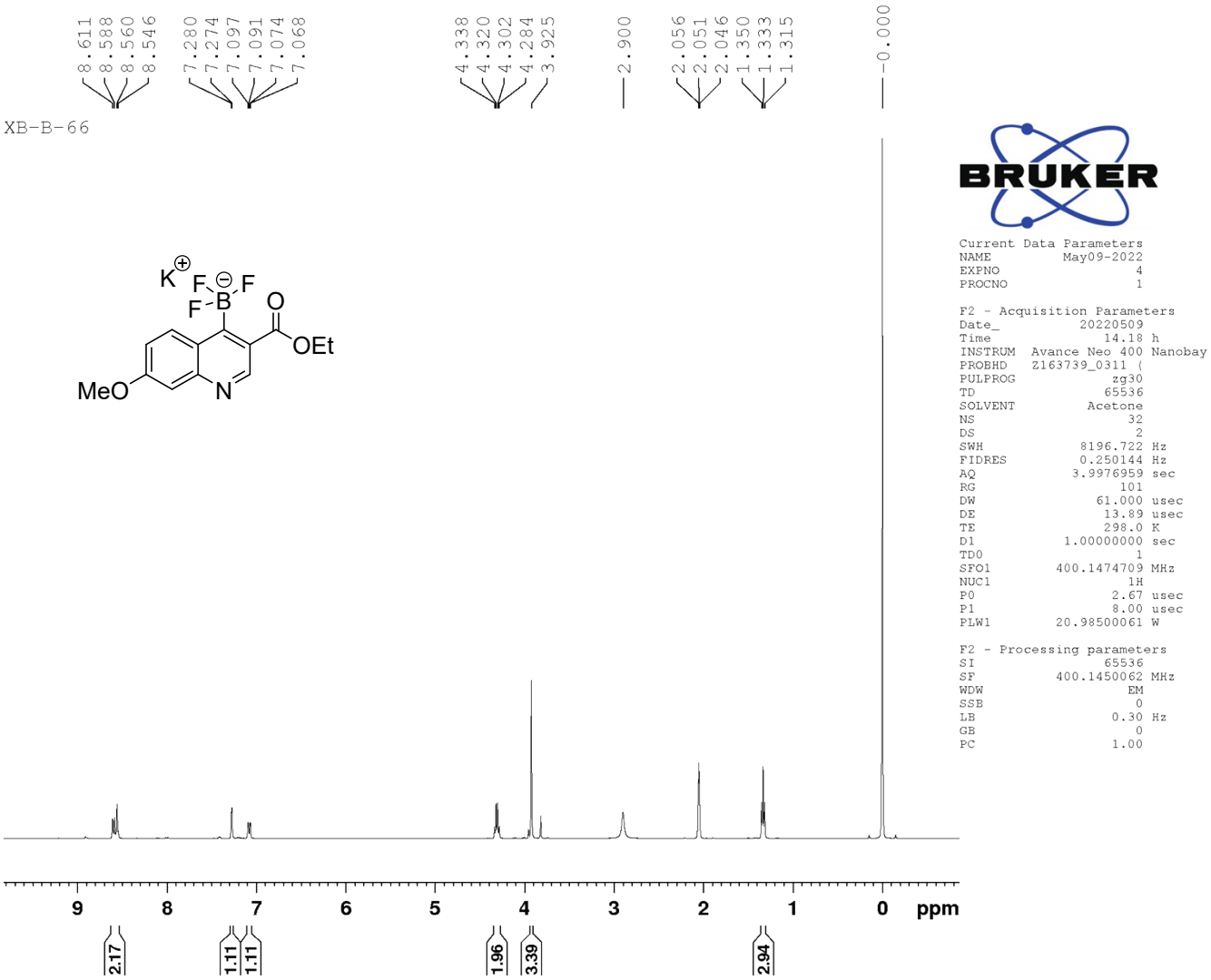

8.57
8.25
8.23
7.35
7.28
7.26
5.06
4.93
3.96
3.31
0.00
HO
B
O
MeO
N
0.87
0.91
1.00
0.86
1.85
3.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

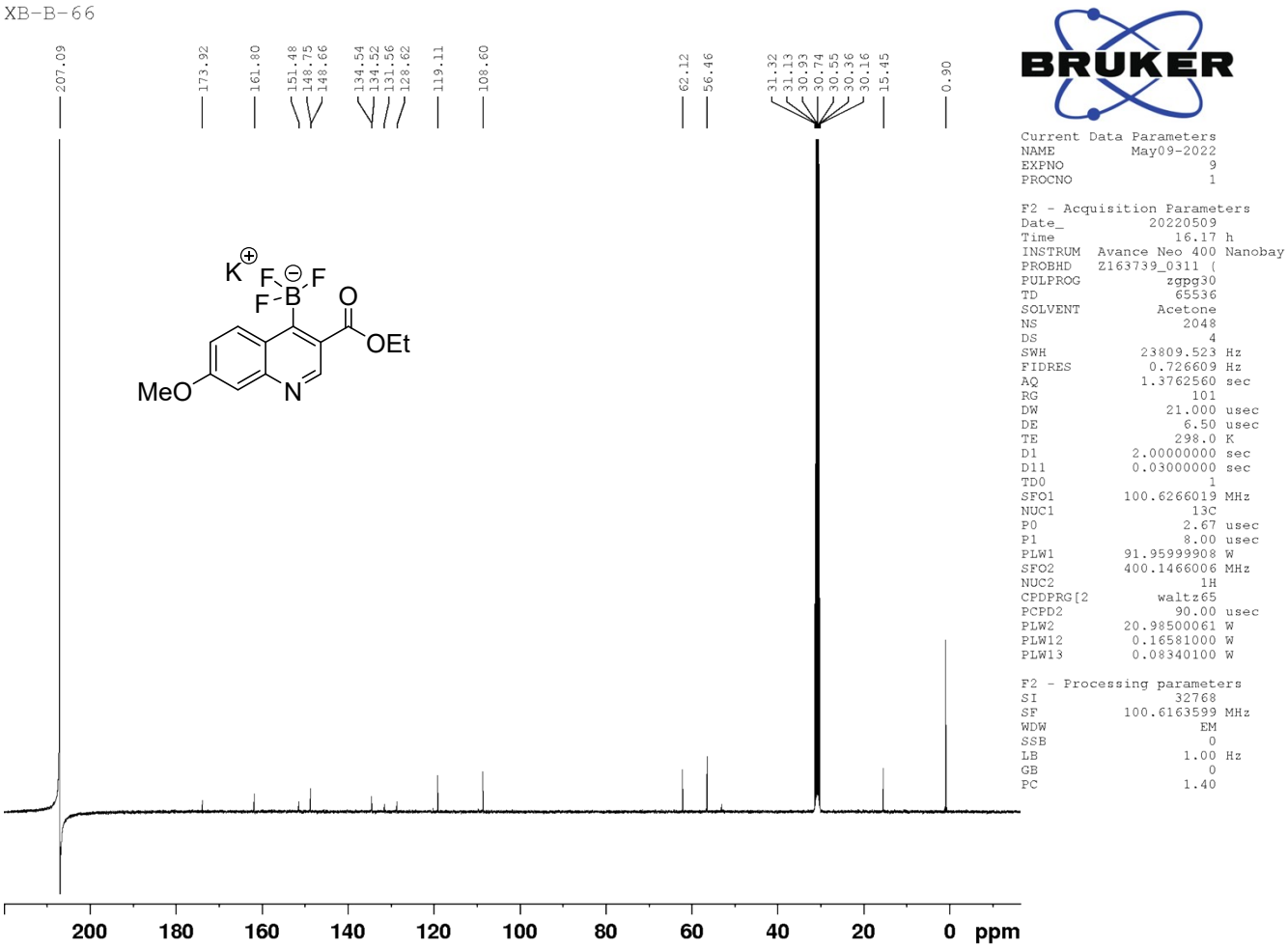
^{1}H NMR of **9**


XB-C-27
128.46
77.60
77.48
77.28
76.96
69.26
55.76
40.65
40.44
40.23
40.02
39.82
39.61
39.40
HO
B
O
MeO
N
180
160
140
120
100
80
60
40
20
ppm
BRUKER
Current Data Parameters
NAME May06-2022
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220506
Time 22.11 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3072
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
F2 - Processing parameters
SI 32768
SF 100.6165403 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

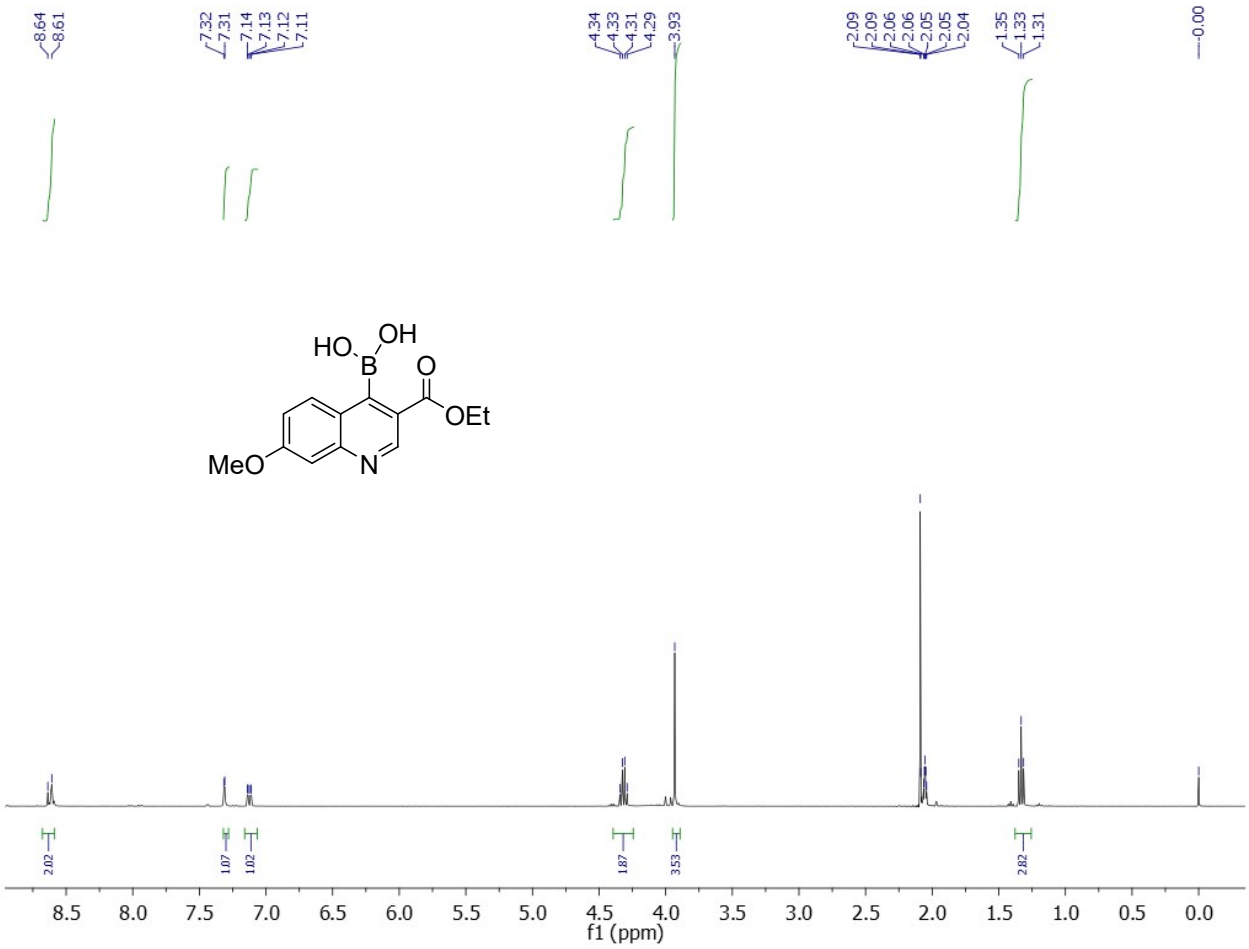
^{13}C NMR of **9**


8.611
8.588
8.560
8.546
7.280
7.274
7.097
7.091
7.074
7.068
4.338
4.320
4.302
4.284
3.925
2.900
2.056
2.051
2.046
1.350
1.333
1.315
0.000
XB-B-66
K
F
B
F
F
O
OEt
MeO
N
BRUKER
Current Data Parameters
NAME May09-2022
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 14.18 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT Acetone
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450062 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9
8
7
6
5
4
3
2
1
0
ppm
2.17
1.11
1.11
1.96
3.39
2.94

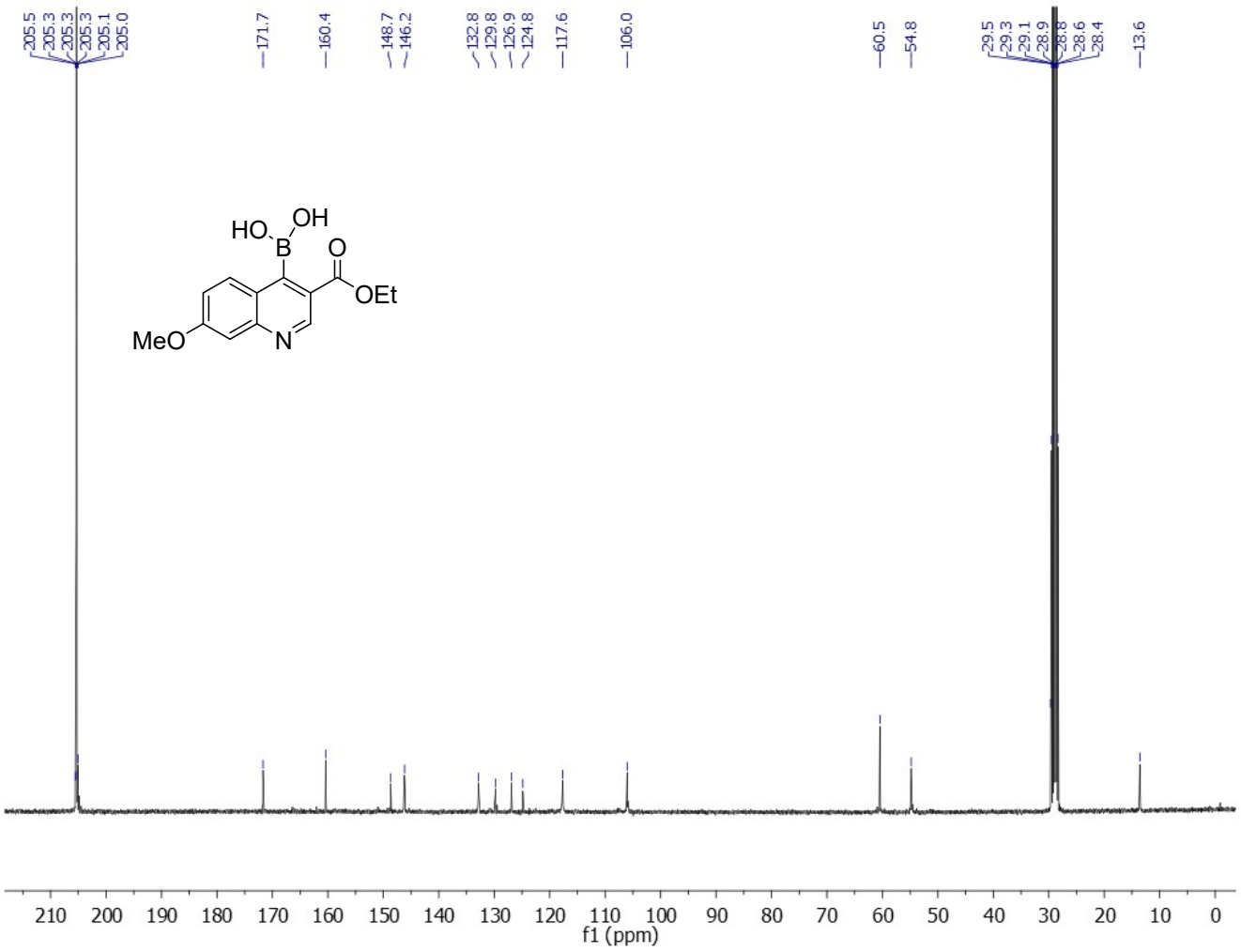
^{1}H NMR of **10**


XB-B-66
207.09
173.92
161.80
151.48
148.75
148.66
134.54
134.52
131.56
128.62
119.11
108.60
62.12
56.46
31.32
31.13
30.93
30.74
30.55
30.36
30.16
15.45
0.90
K
F
B
F
F
O
OEt
MeO
N
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
Current Data Parameters
NAME May09-2022
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 16.17 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zgpg30
TD 65536
SOLVENT Acetone
NS 2048
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
F2 - Processing parameters
SI 32768
SF 100.6163599 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

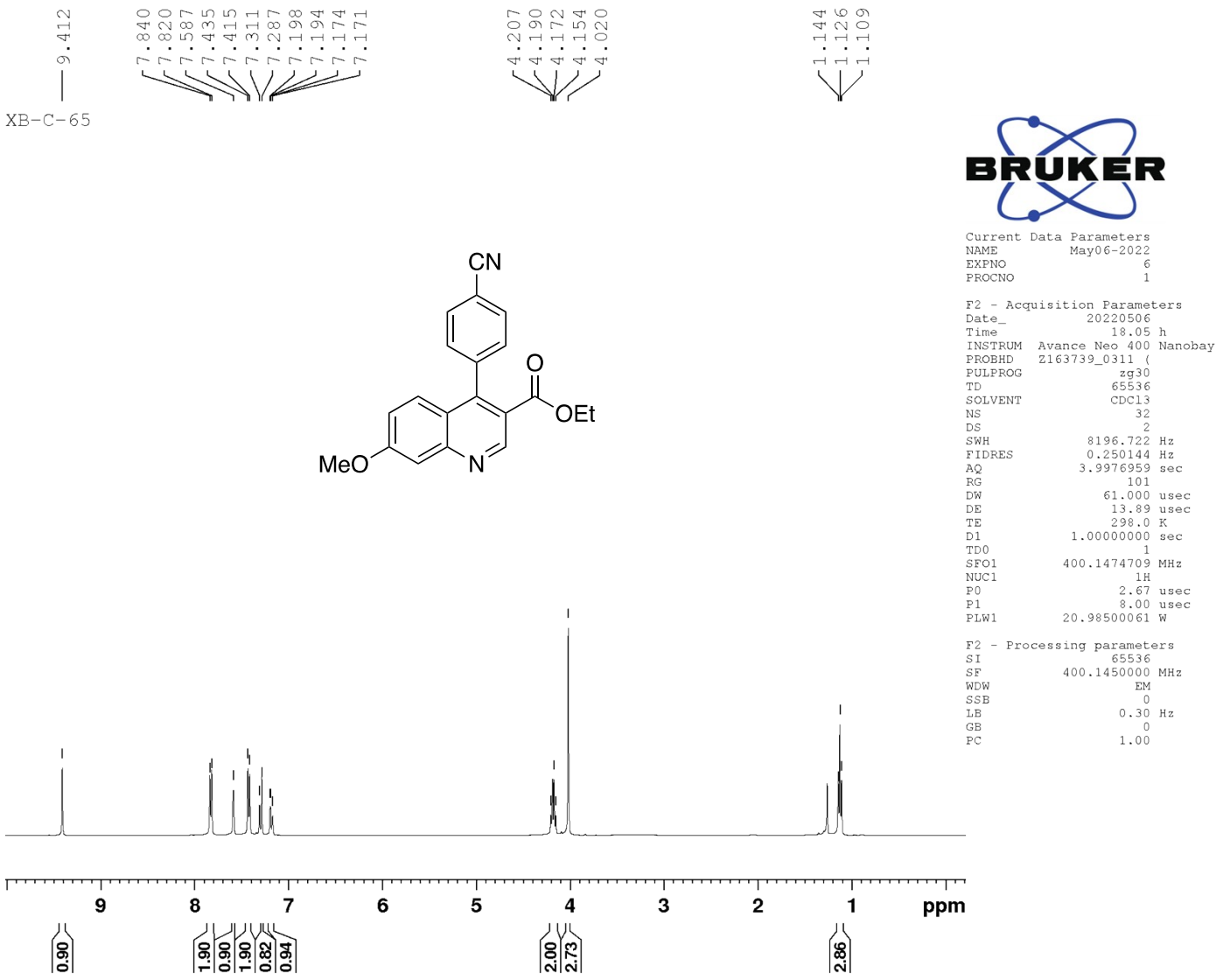
^{13}C NMR of **10**


8.64
8.61
7.32
7.31
7.14
7.13
7.12
7.11
4.34
4.33
4.31
4.29
3.93
2.09
2.09
2.06
2.06
2.05
2.05
2.04
1.35
1.33
1.31
0.00
HO
B
OH
O
OEt
MeO
N
2.02
1.07
1.02
1.87
3.53
2.82
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

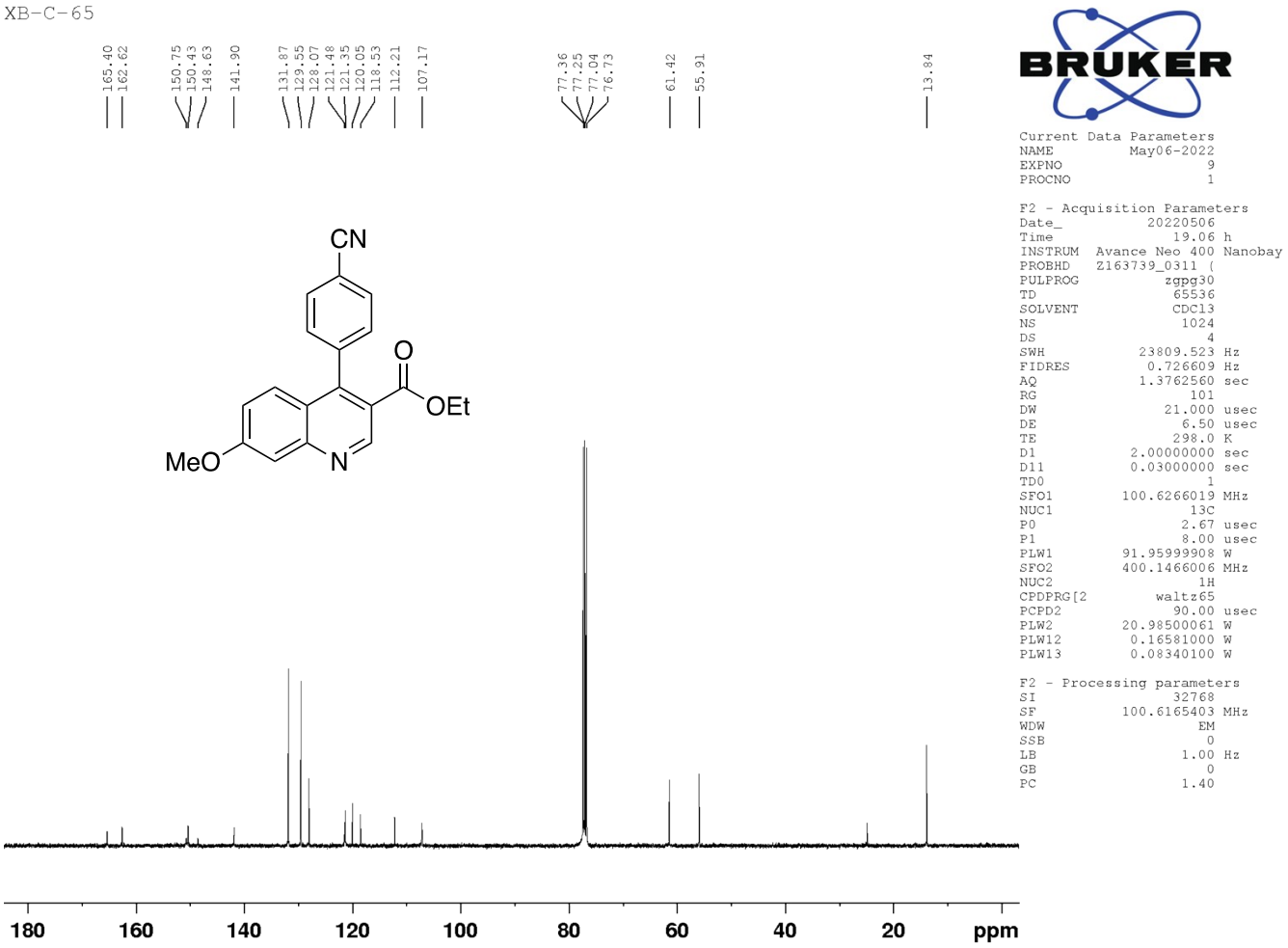
^{1}H NMR of **11**


205.5
205.3
205.3
205.3
205.1
205.0
171.7
160.4
148.7
146.2
132.8
129.8
126.9
124.8
117.6
106.0
60.5
54.8
29.5
29.3
29.1
28.9
28.8
28.6
28.4
13.6
HO
B
OH
O
OEt
MeO
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

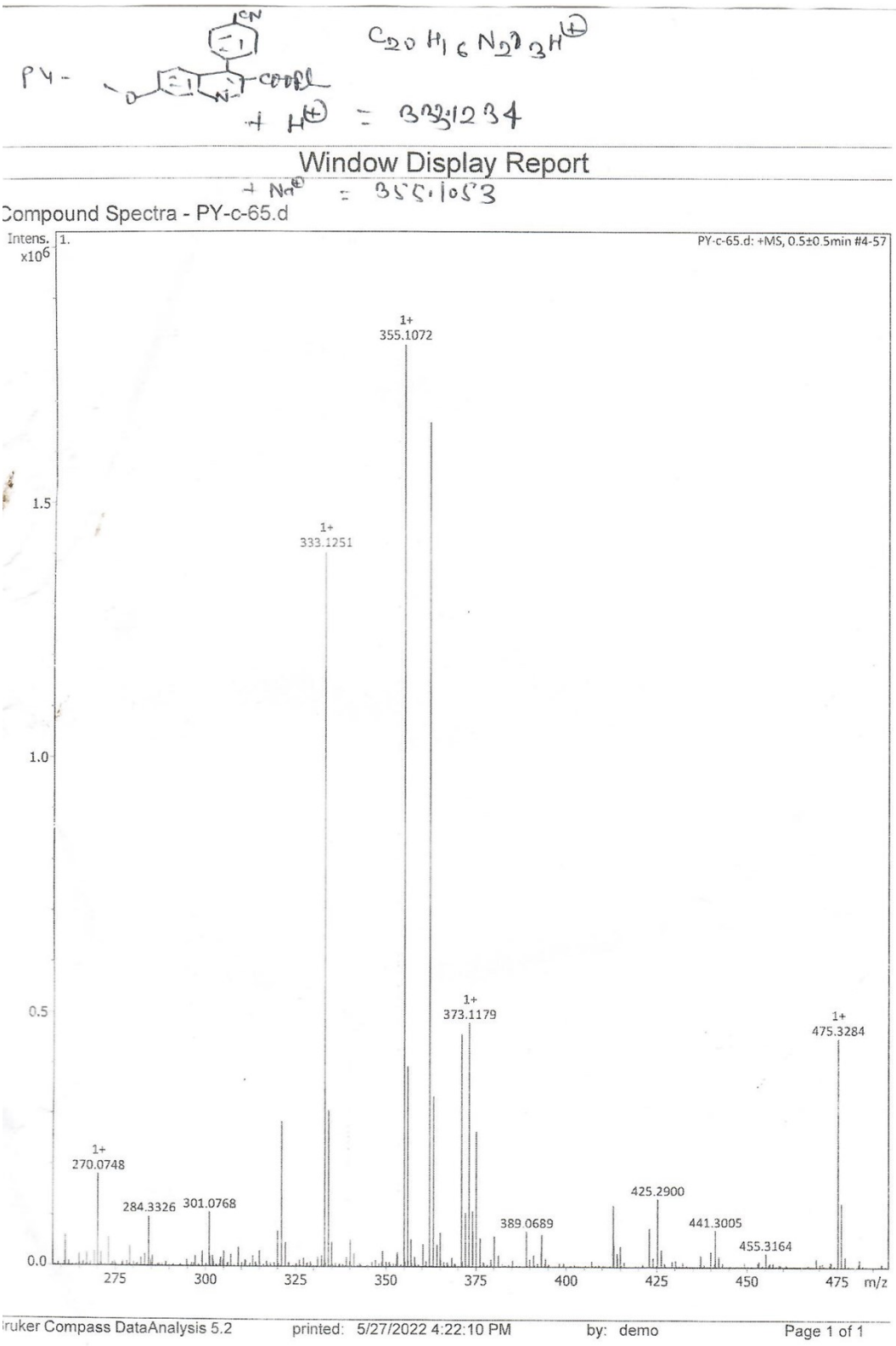
^{13}C NMR of **11**


9.412
7.840
7.820
7.587
7.435
7.415
7.311
7.287
7.198
7.194
7.174
7.171
4.207
4.190
4.172
4.154
4.020
1.144
1.126
1.109
XB-C-65
CN
O
OEt
MeO
N
BRUKER
Current Data Parameters
NAME May06-2022
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220506
Time 18.05 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9
8
7
6
5
4
3
2
1
ppm
0.90
1.90
0.90
1.90
0.82
0.94
2.00
2.73
2.86

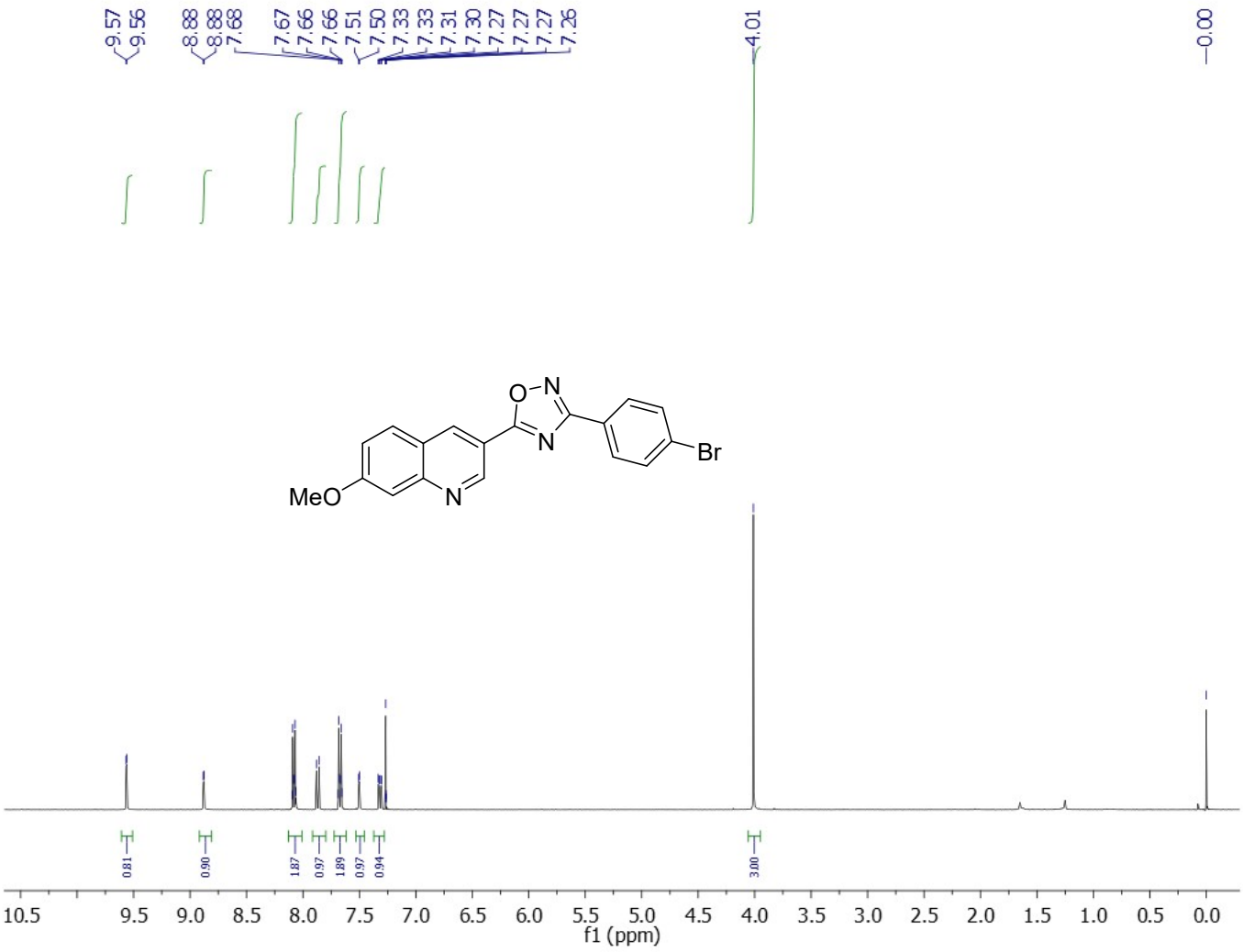
^{1}H NMR of **12**


XB-C-65
165.40
162.62
150.75
150.43
148.63
141.90
131.87
129.55
128.07
121.48
121.35
120.05
118.53
112.21
107.17
77.36
77.25
77.04
76.73
61.42
55.91
13.84
CN
O
OEt
MeO
N
180
160
140
120
100
80
60
40
20
ppm
BRUKER
Current Data Parameters
NAME May06-2022
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220506
Time 19.06 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
F2 - Processing parameters
SI 32768
SF 100.6165403 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

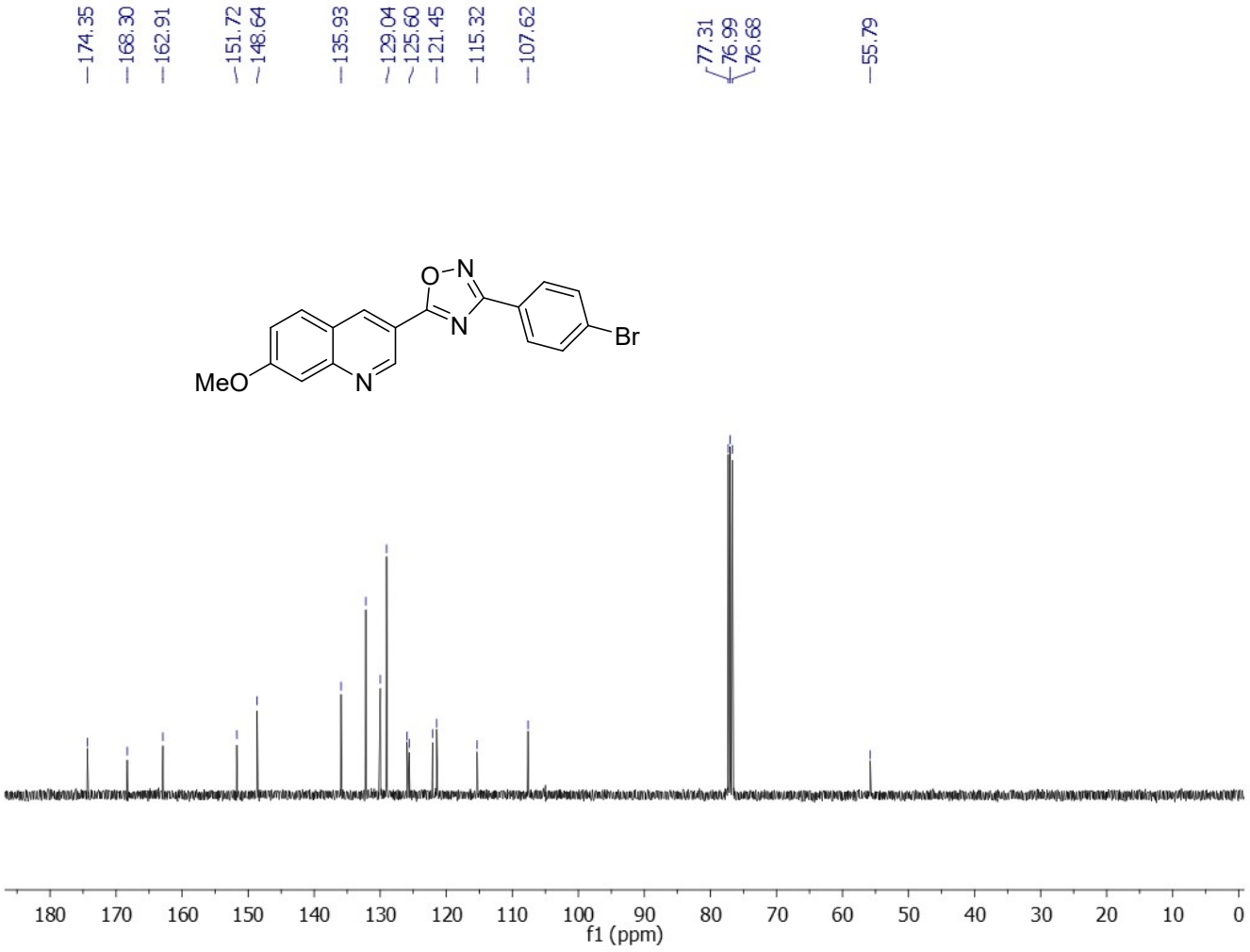
^{13}C NMR of **12**



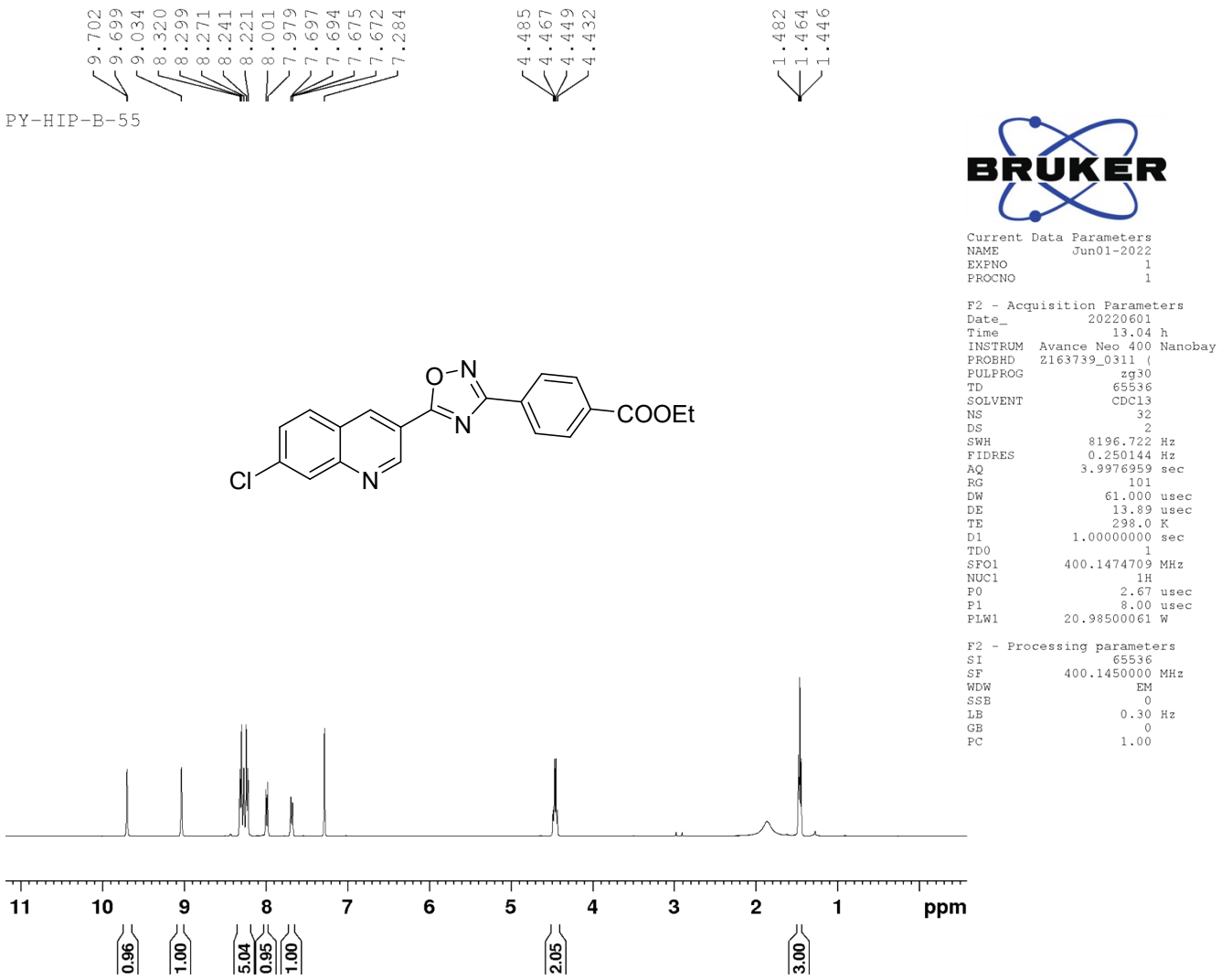
Mass spectrum of **12**


9.57
9.56
8.88
8.88
7.68
7.67
7.66
7.66
7.51
7.50
7.33
7.33
7.31
7.30
7.27
7.27
7.27
7.26
4.01
0.00
O
N
N
Br
MeO
N
0.81
0.90
1.87
0.97
1.89
0.97
0.94
3.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

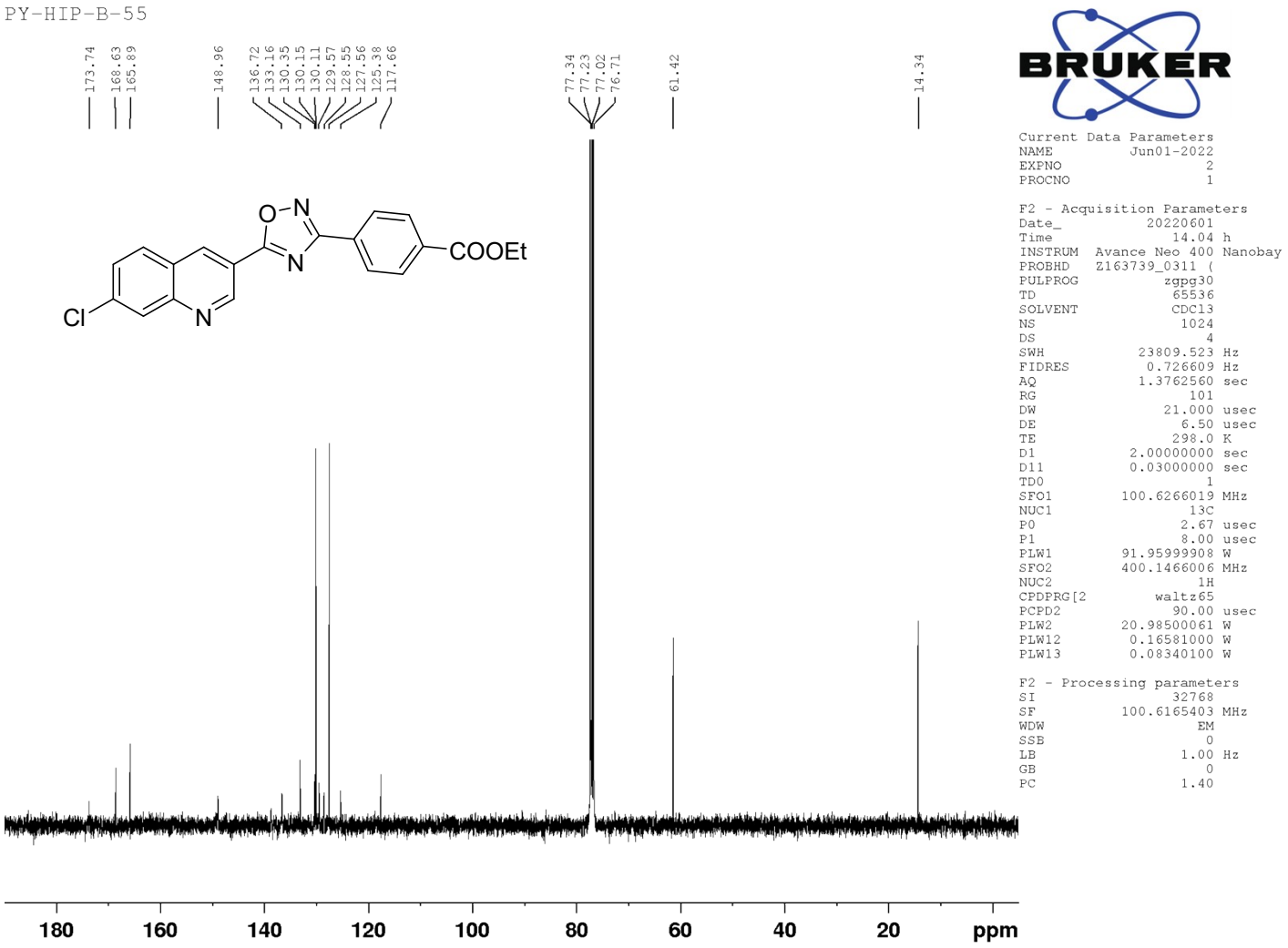
^{1}H NMR of **13b**



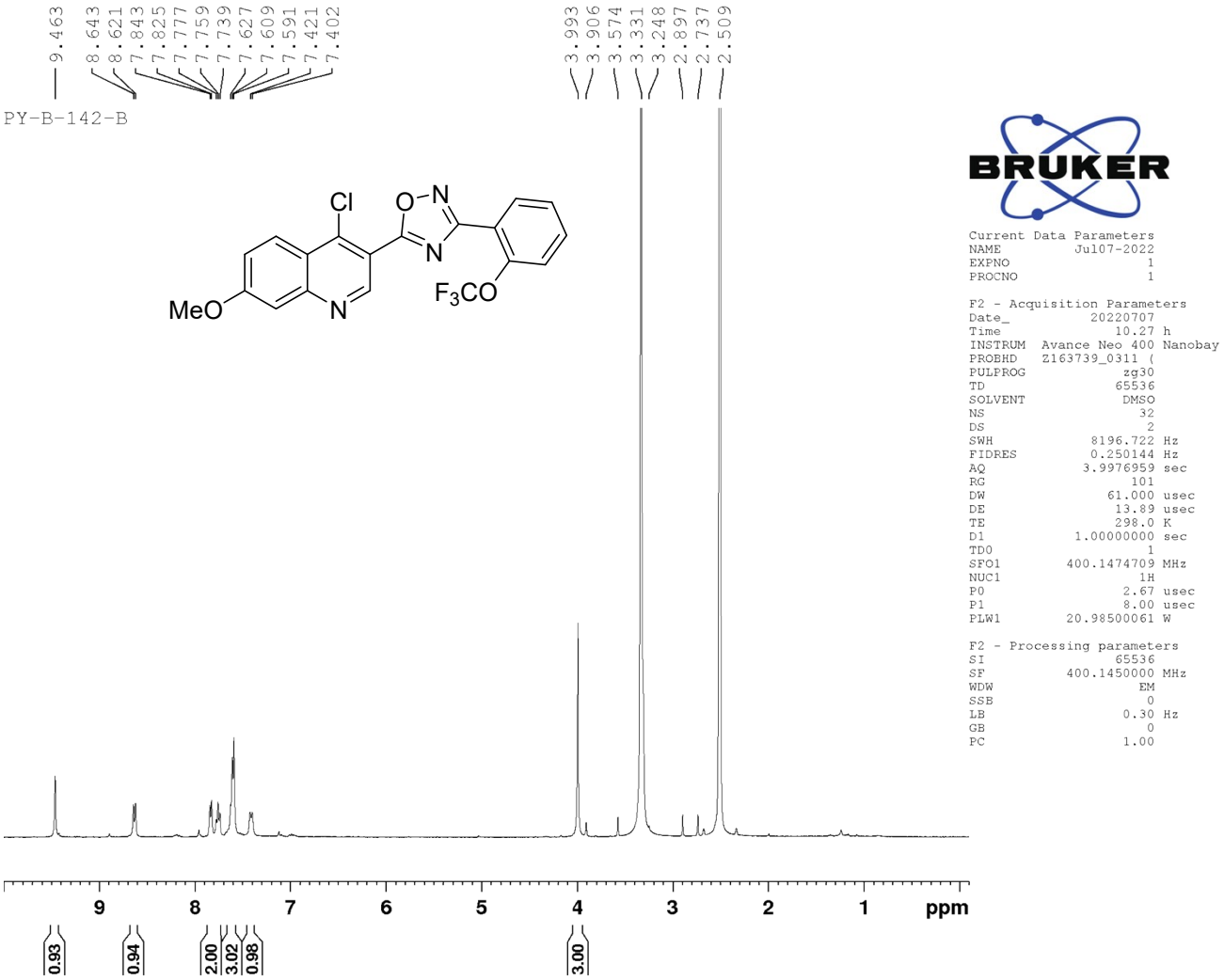
^{13}C NMR of **13b**


9.702
9.699
9.034
8.320
8.299
8.271
8.241
8.221
8.001
7.979
7.697
7.694
7.675
7.672
7.284
4.485
4.467
4.449
4.432
1.482
1.464
1.446
PY-HIP-B-55
BRUKER
Current Data Parameters
NAME Jun01-2022
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220601
Time 13.04 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
N
N
COOEt
Cl
N
11
10
9
8
7
6
5
4
3
2
1
ppm
0.96
1.00
5.04
0.95
1.00
2.05
3.00

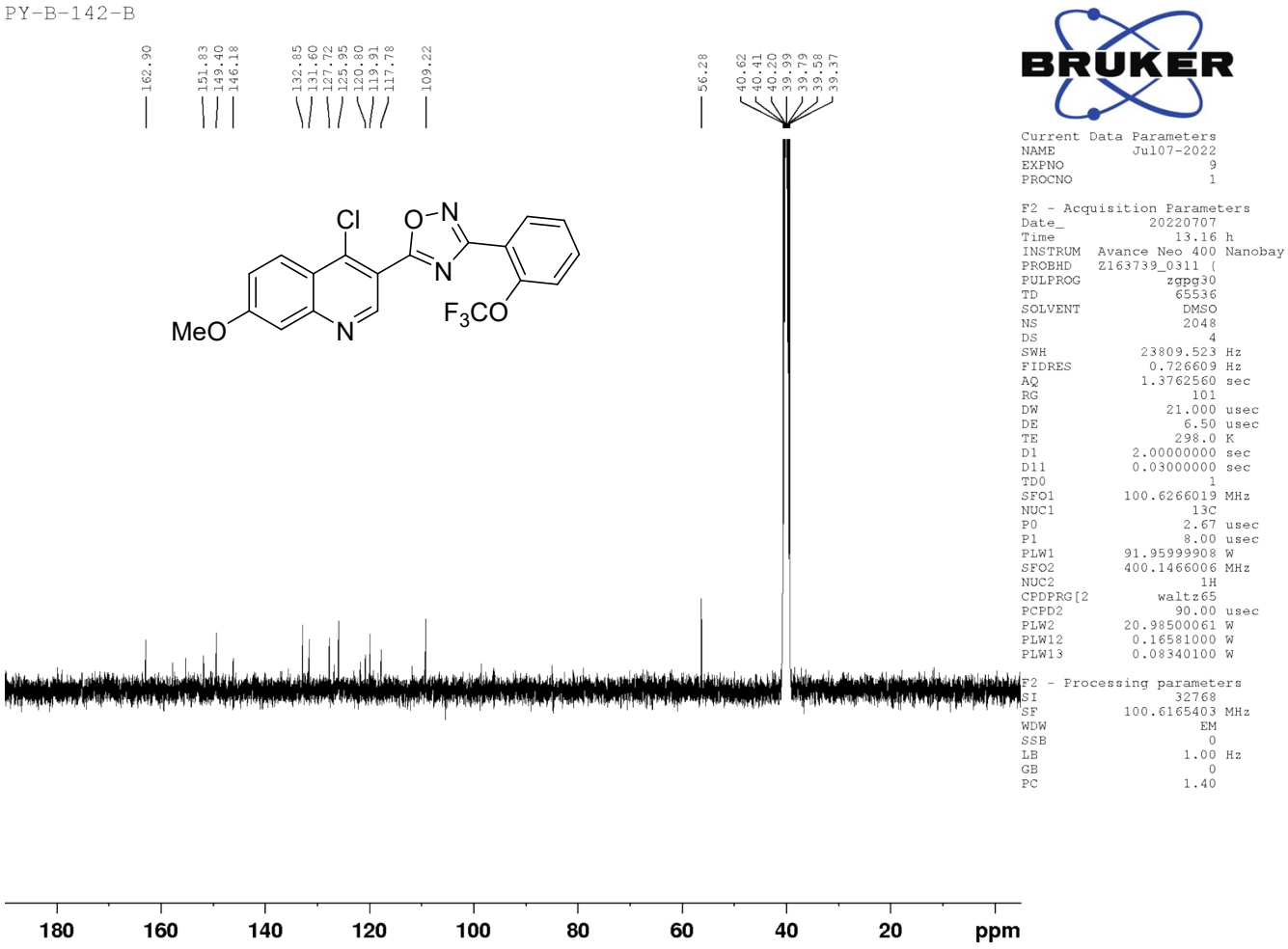
^{1}H NMR of **13d**



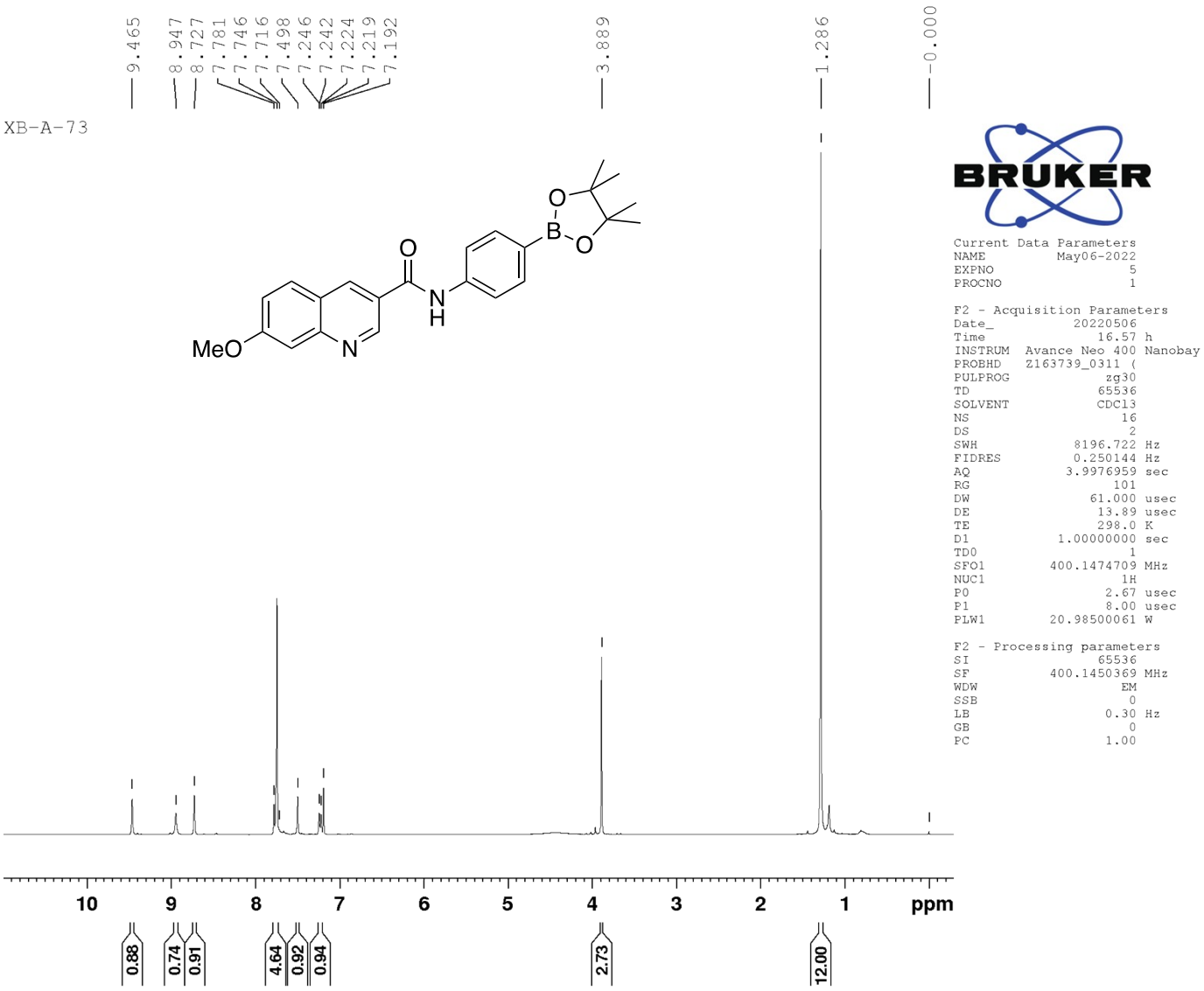
^{13}C NMR of **13d**


9.463
8.643
8.621
7.843
7.825
7.777
7.759
7.739
7.627
7.609
7.591
7.421
7.402
3.993
3.906
3.574
3.331
3.248
2.897
2.737
2.509
PY-B-142-B
Cl
O
N
N
MeO
N
F3CO
BRUKER
Current Data Parameters
NAME Jul07-2022
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220707
Time 10.27 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9
8
7
6
5
4
3
2
1
ppm
0.93
0.94
2.00
3.02
0.98
3.00

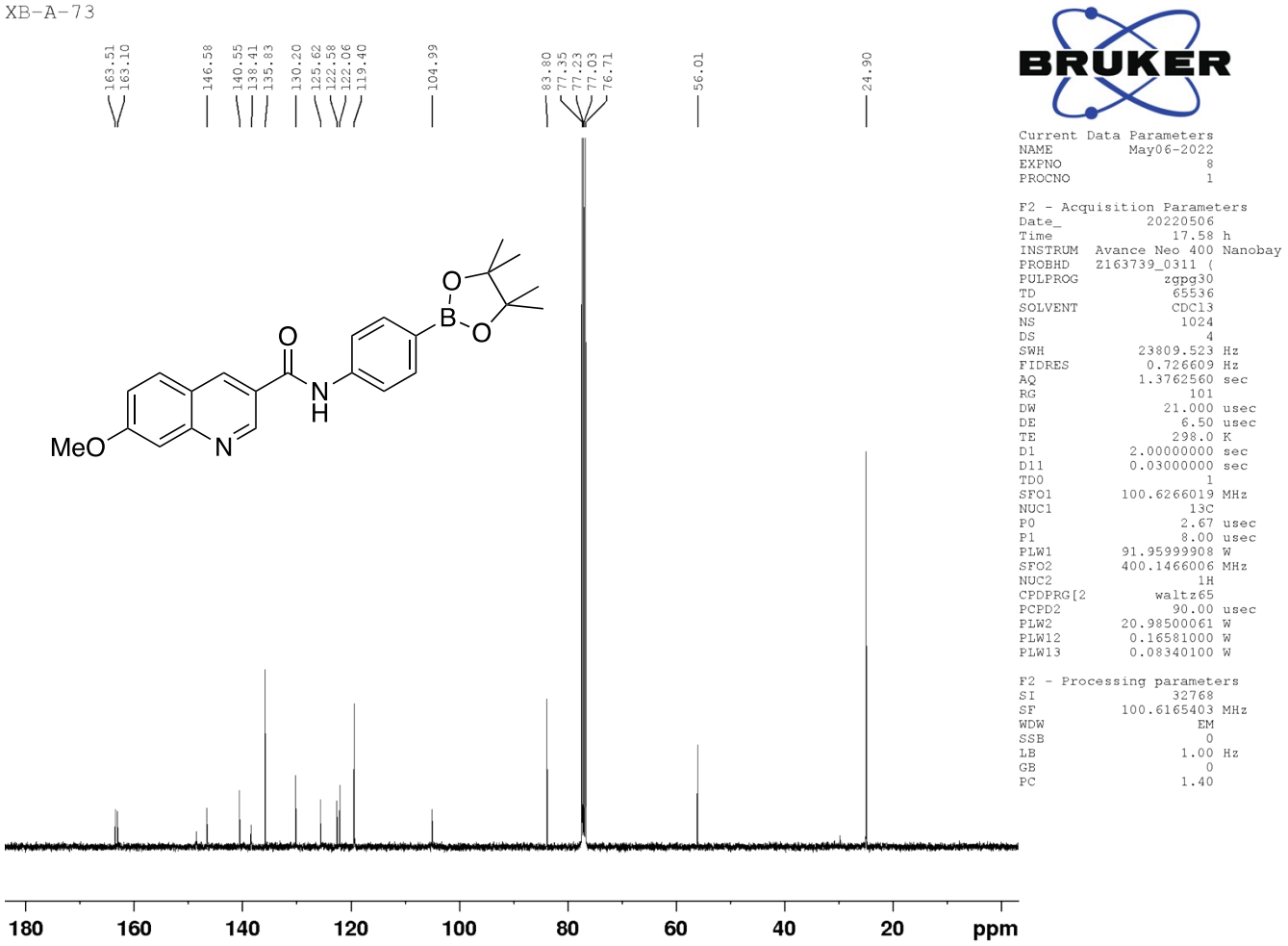
^{1}H NMR of **13e**



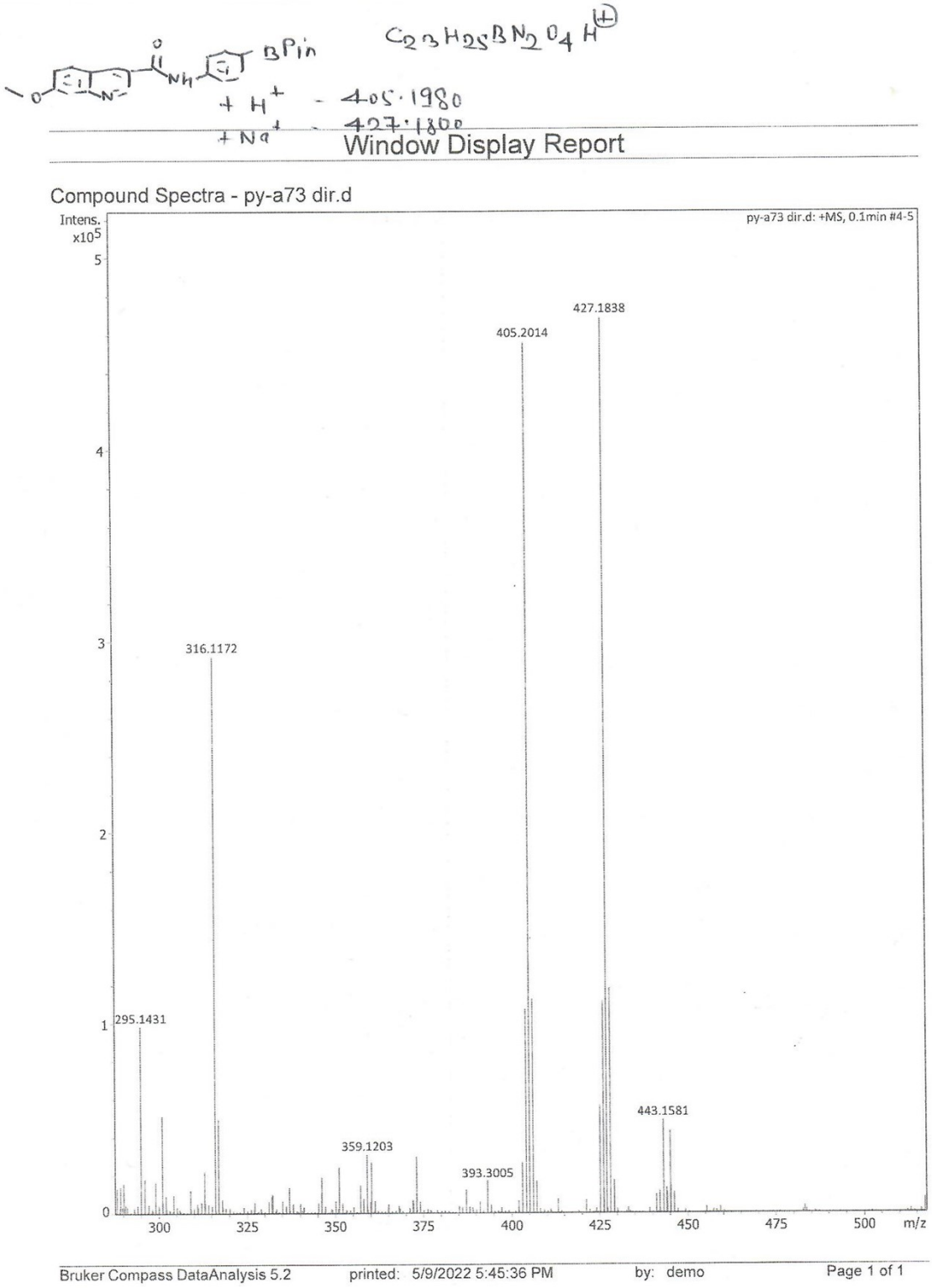
^{13}C NMR of **13e**


9.465
8.947
8.727
7.781
7.746
7.716
7.498
7.246
7.242
7.224
7.219
7.192
3.889
1.286
0.000
XB-A-73
MeO
N
O
B
O
O
N
H
Current Data Parameters
NAME May06-2022
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220506
Time 16.57 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450369 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
ppm
0.88
0.74
0.91
4.64
0.92
0.94
2.73
12.00

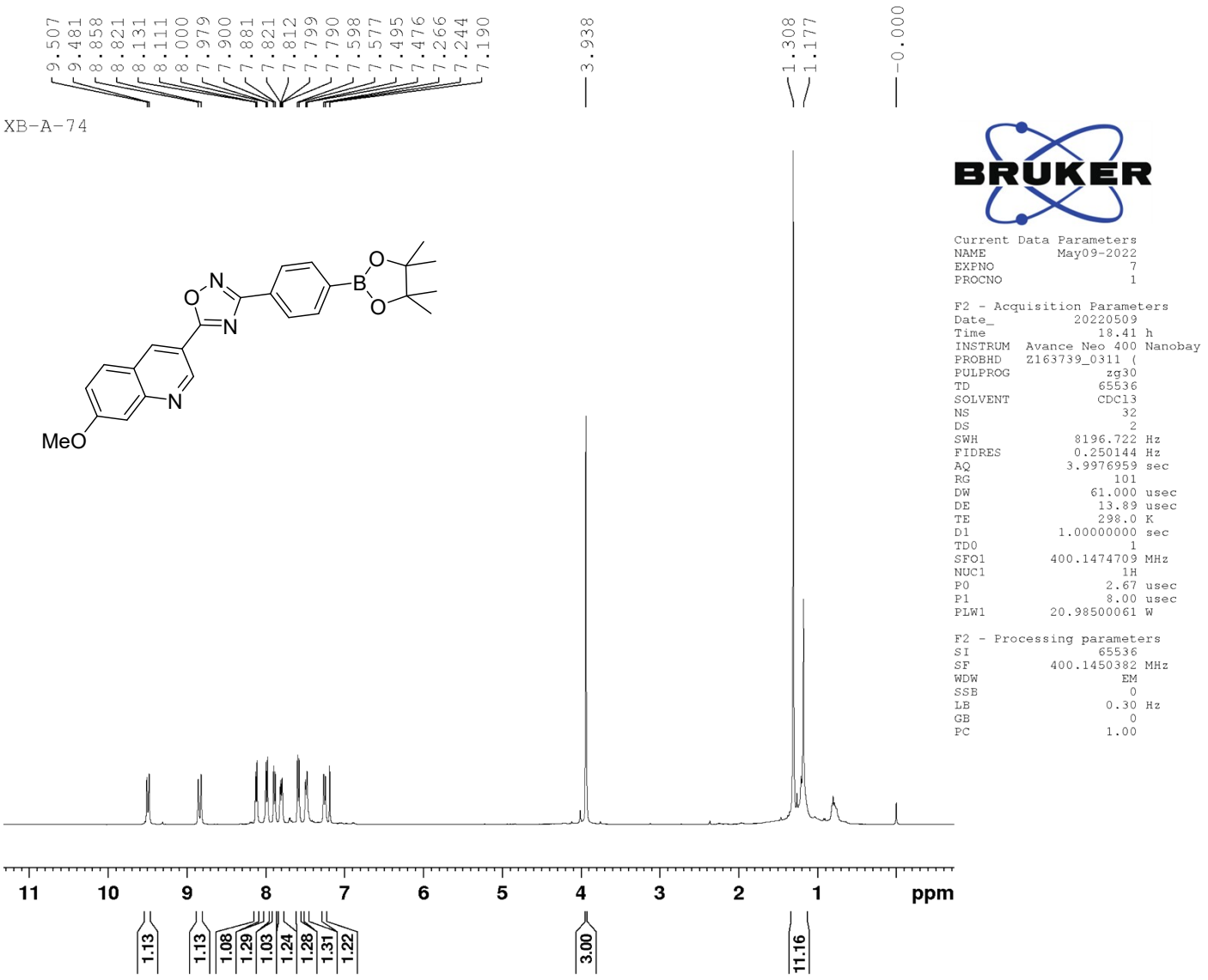
^{1}H NMR of **14a**



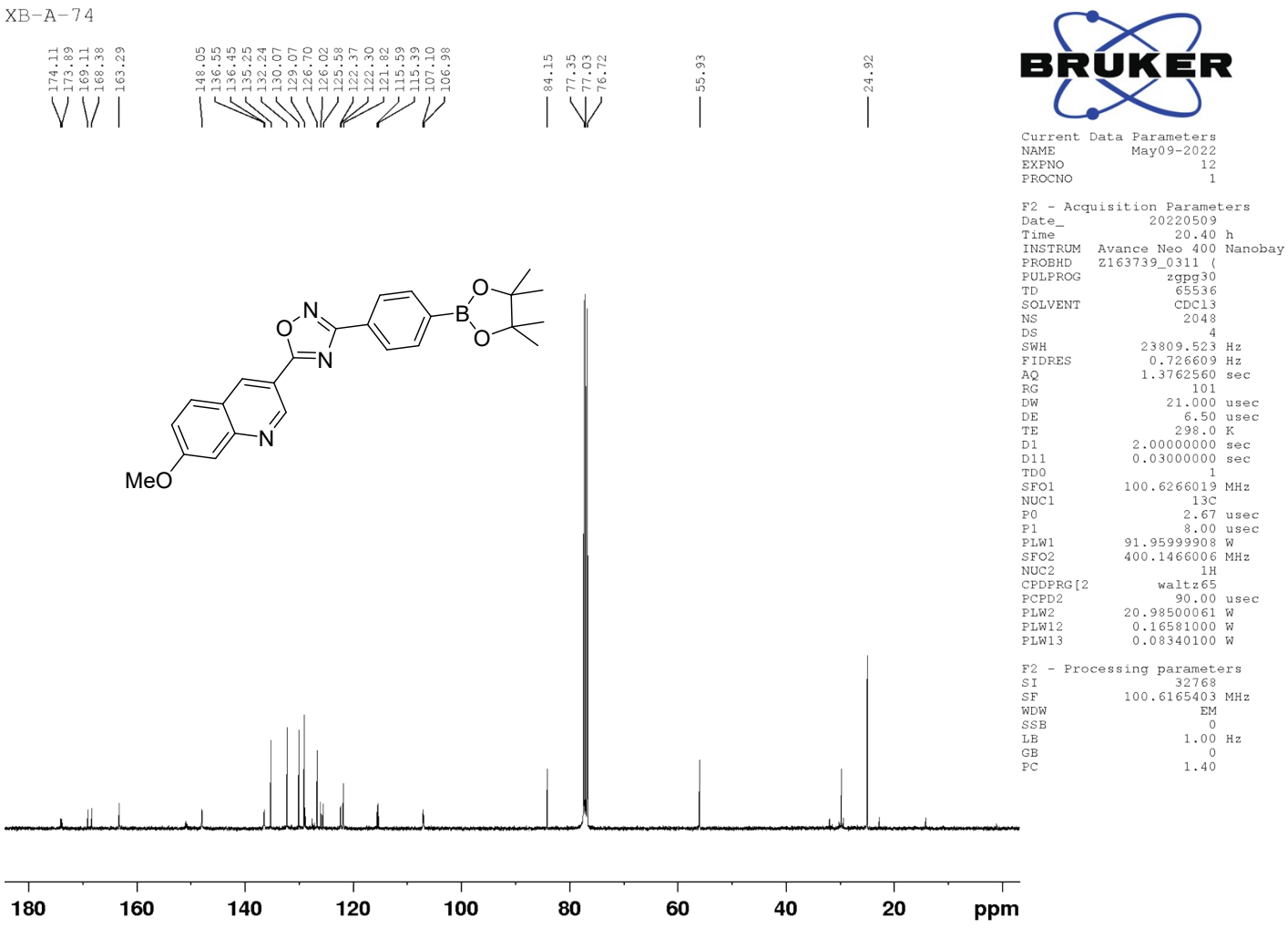
^{13}C NMR of **14a**



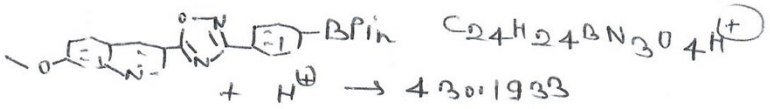
Mass spectrum of **14a**


9.507
9.481
8.858
8.821
8.131
8.111
8.000
7.979
7.900
7.881
7.821
7.812
7.799
7.790
7.598
7.577
7.495
7.476
7.266
7.244
7.190
3.938
1.308
1.177
0.000
XB-A-74
MeO
BRUKER
Current Data Parameters
NAME May09-2022
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 18.41 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450382 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.13 1.13 1.08 1.29 1.03 1.24 1.28 1.31 1.22
3.00
11.16

^{1}H NMR of **14b**

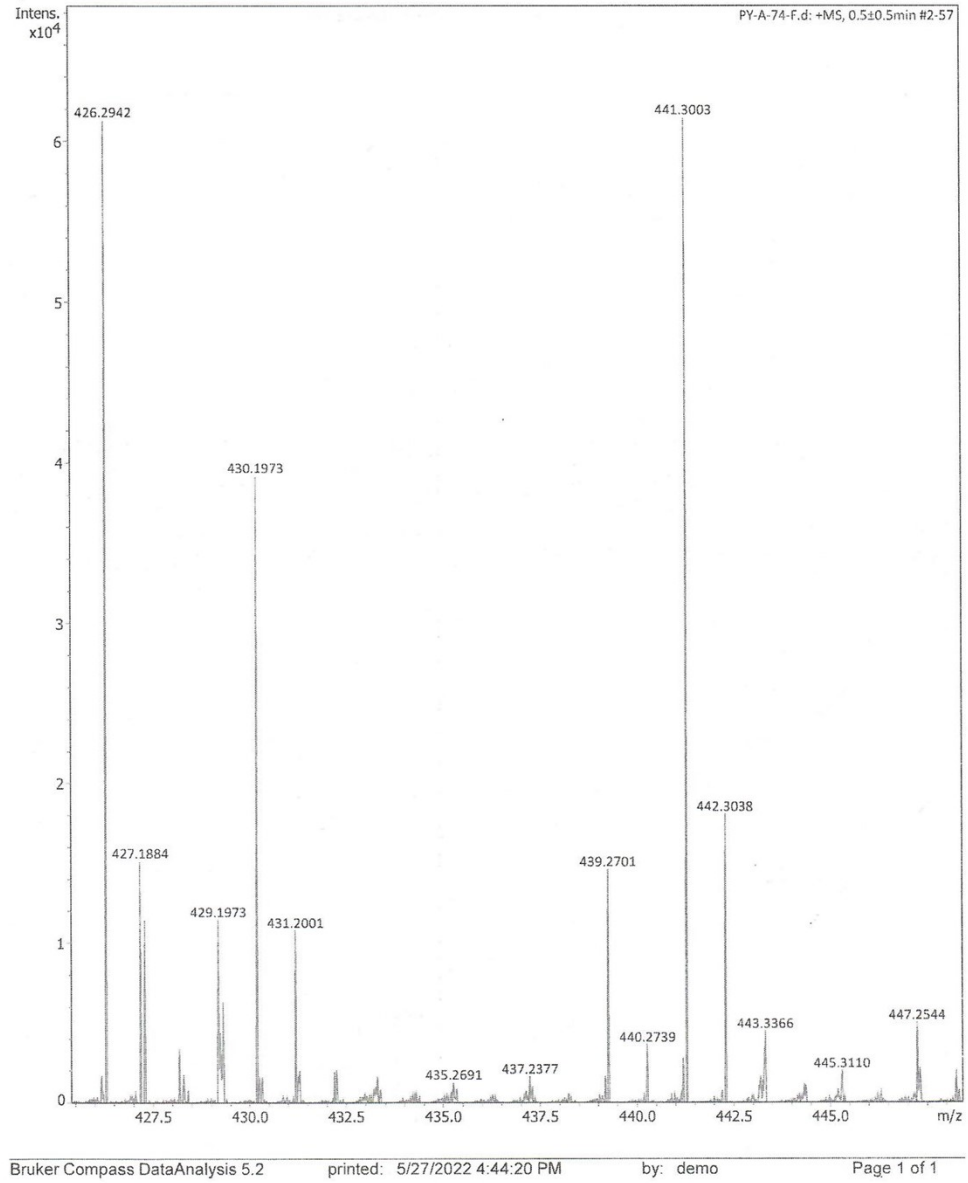


^{13}C NMR of **14b**



Window Display Report

Spectrum View - PY-A-74-F.d



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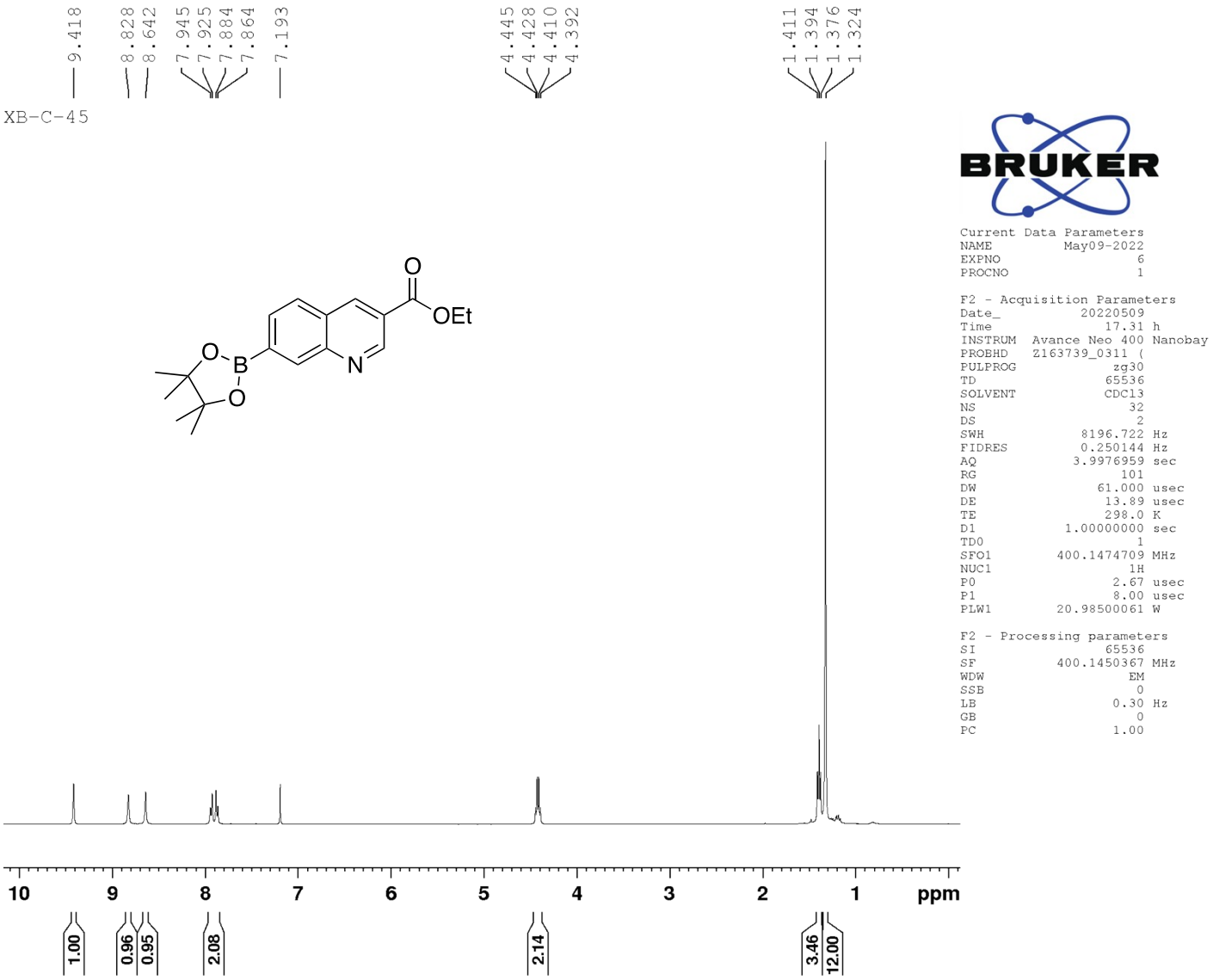
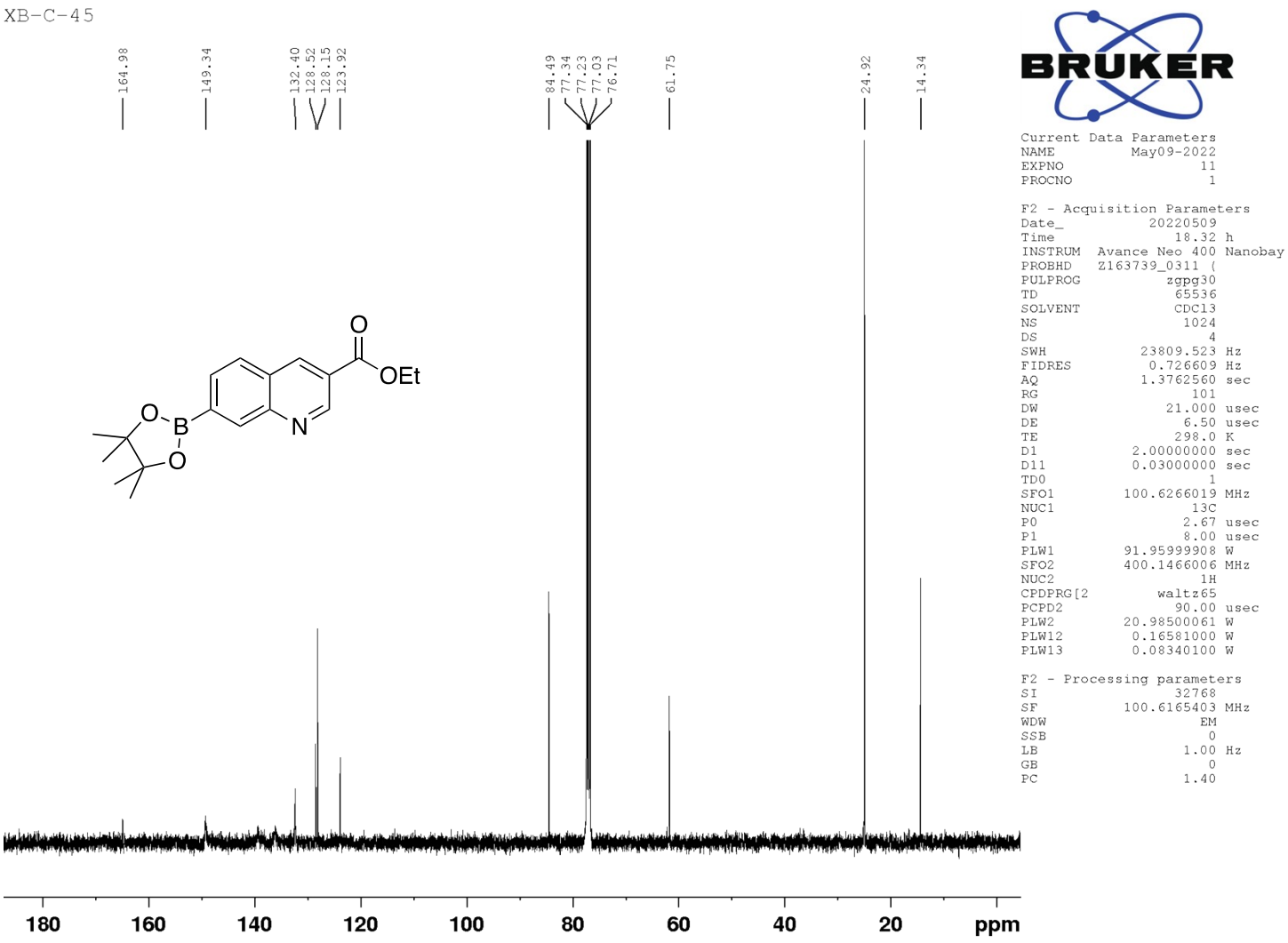
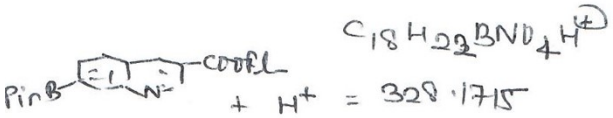
Mass spectrum of **14b**


9.418
8.828
8.642
7.945
7.925
7.884
7.864
7.193
4.445
4.428
4.410
4.392
1.411
1.394
1.376
1.324
XB-C-45
O
OEt
O
B
O
N
BRUKER
Current Data Parameters
NAME May09-2022
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 17.31 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450367 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
ppm
1.00
0.96
0.95
2.08
2.14
3.46
12.00

^{1}H NMR of **15a**

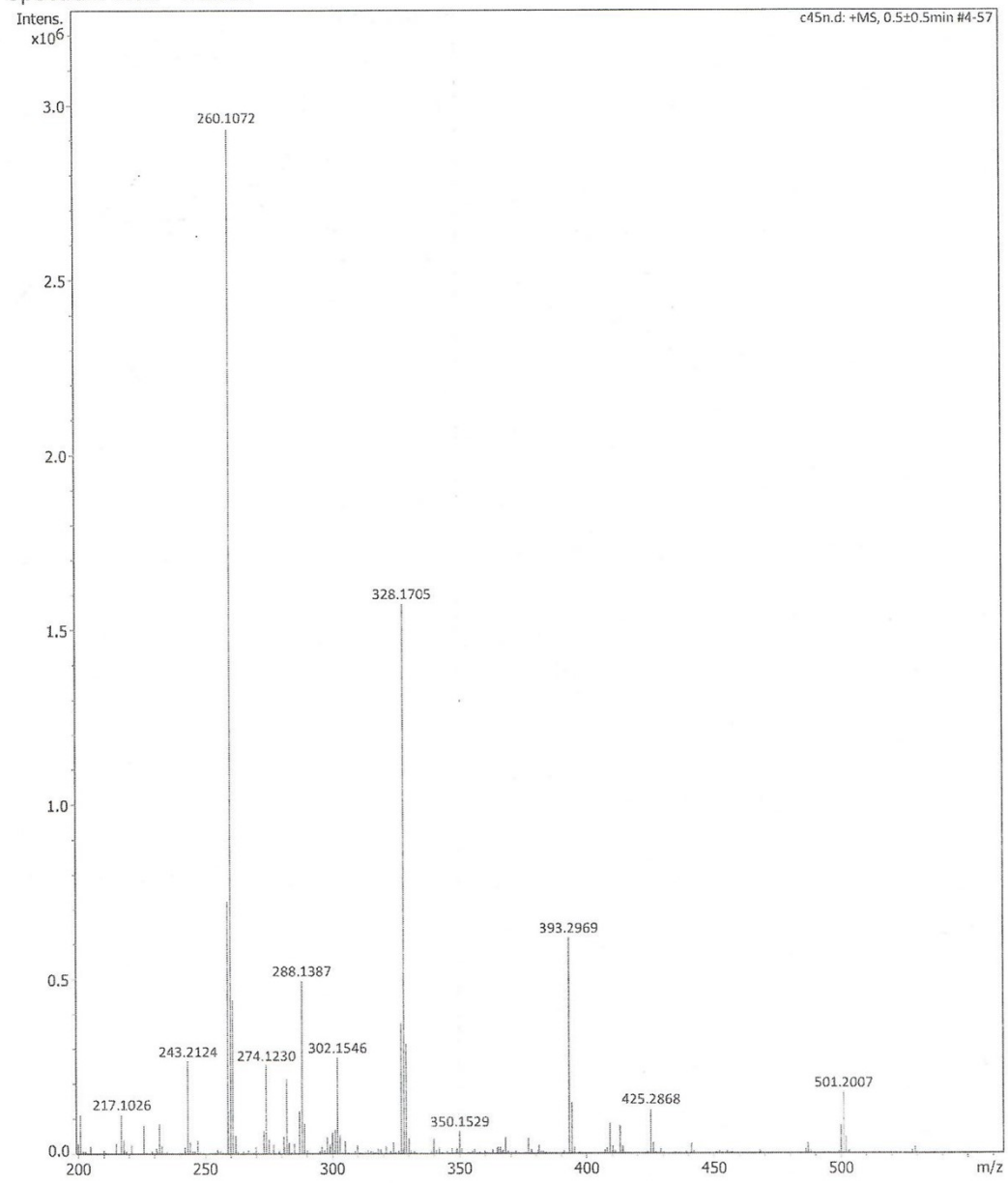


^{13}C NMR of **15a**



Window Display Report

Spectrum View - c45n.d



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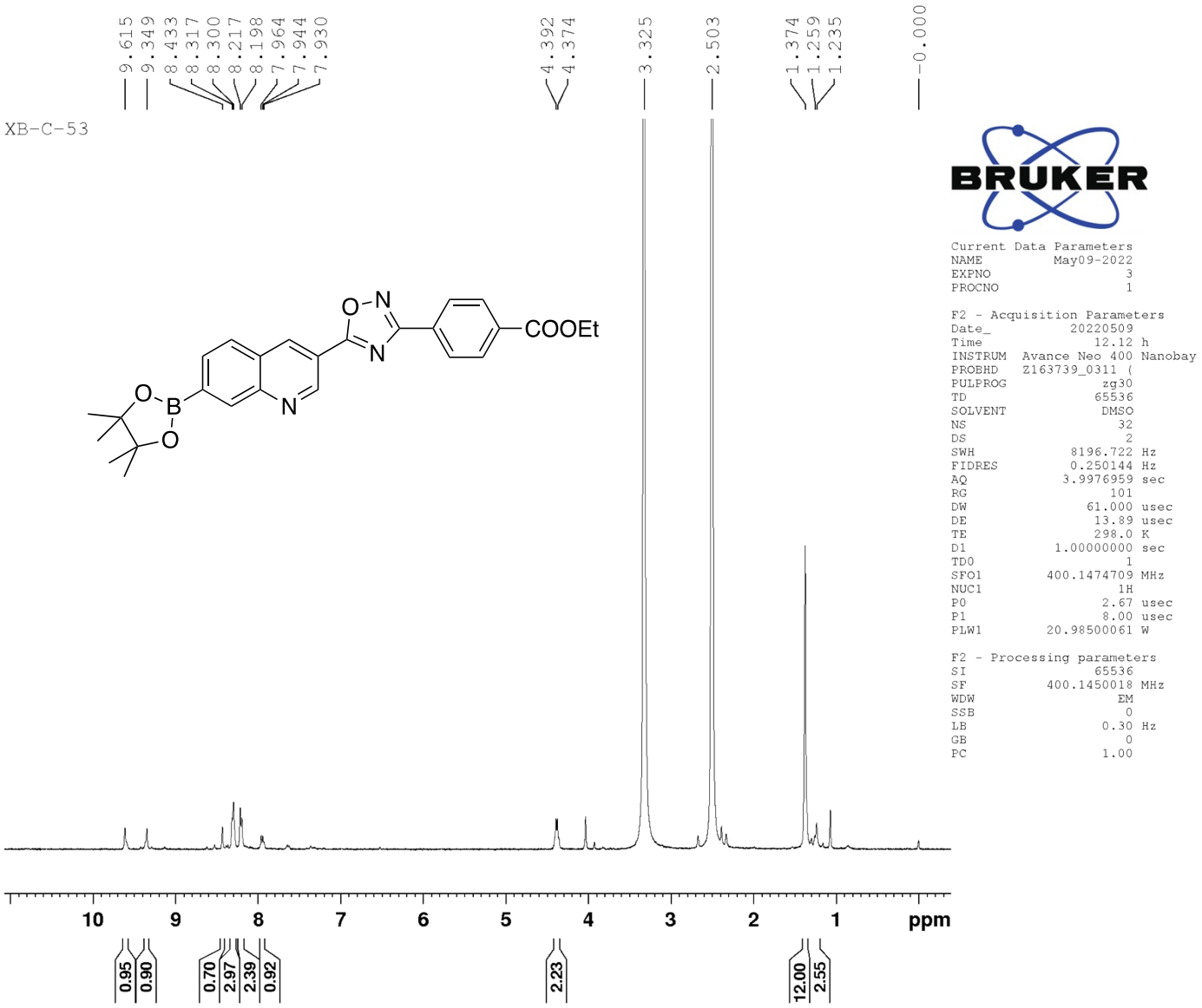
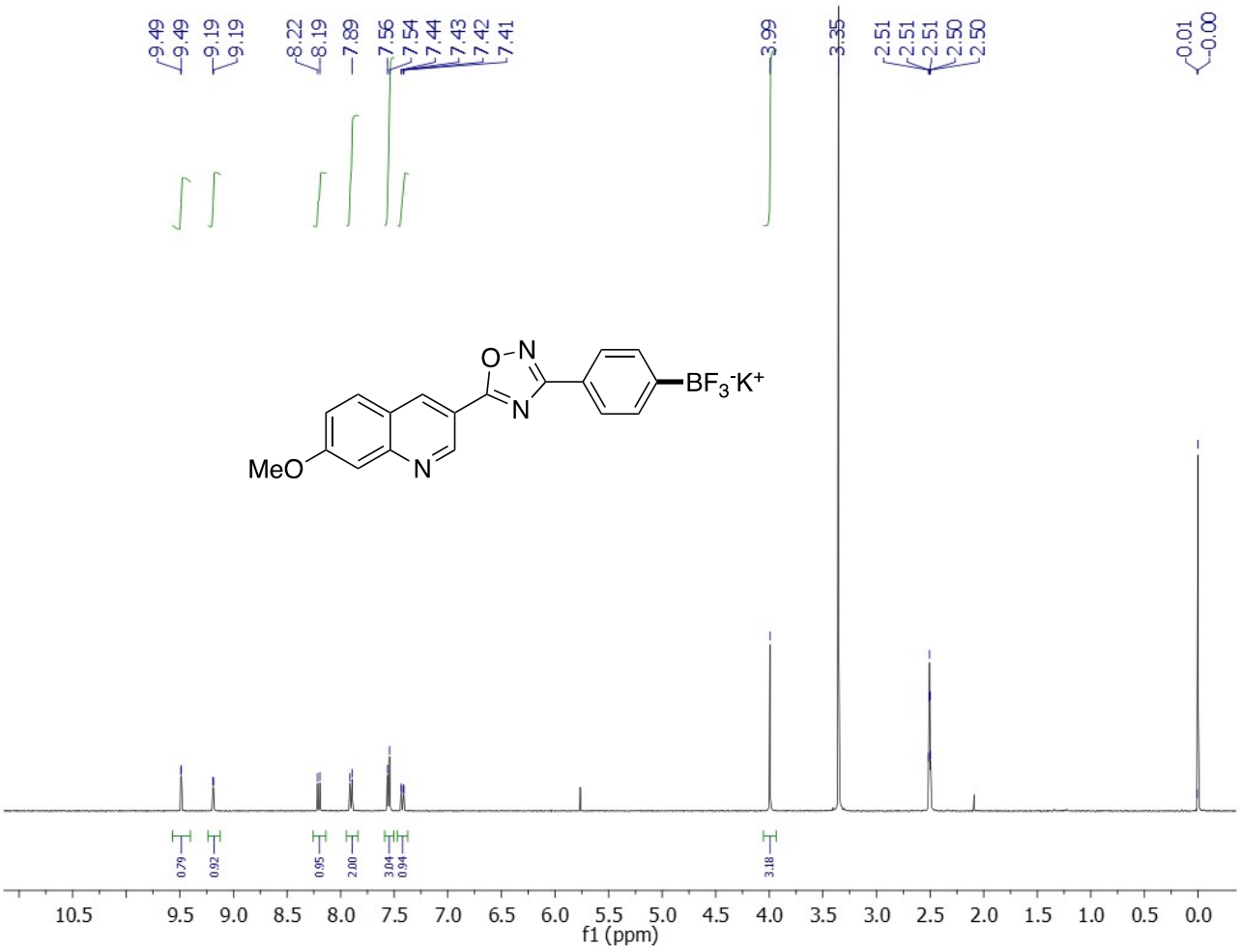
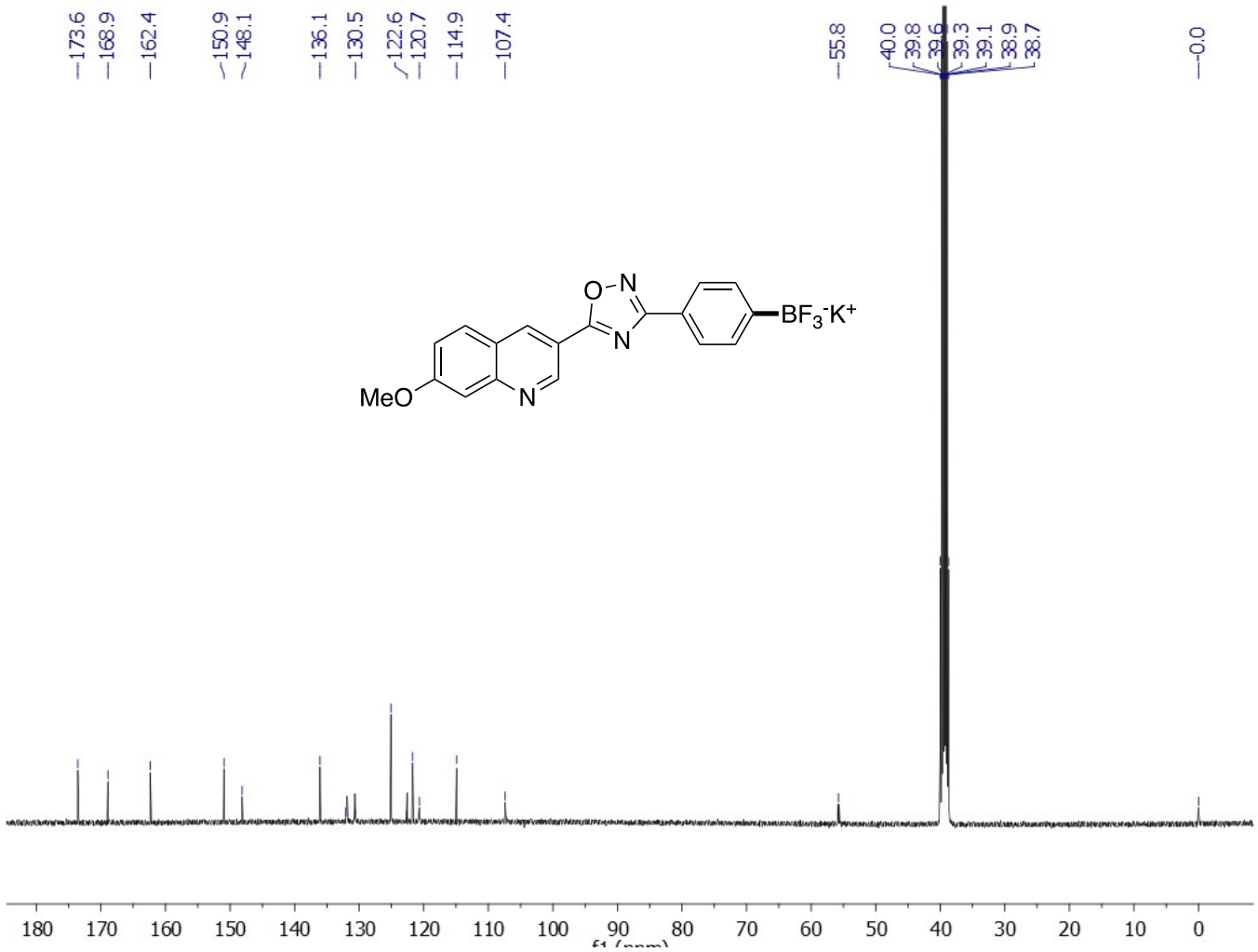
Mass spectrum of **15a**


9.615
9.349
8.433
8.317
8.300
8.217
8.198
7.964
7.944
7.930
4.392
4.374
3.325
2.503
1.374
1.259
1.235
0.000
XB-C-53
COOEt
BRUKER
Current Data Parameters
NAME May09-2022
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 12.12 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450018 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
ppm
0.95
0.90
0.70
2.97
2.39
0.92
2.23
12.00
2.55

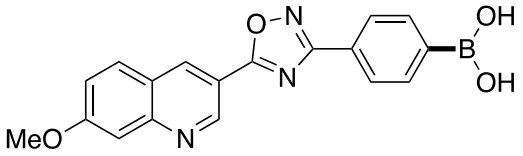
^{1}H NMR of **15b**


9.49
9.49
9.19
9.19
8.22
8.19
7.89
7.56
7.54
7.44
7.43
7.42
7.41
3.99
3.35
2.51
2.51
2.51
2.50
2.50
0.01
0.00
O
N
N
BF3-K+
MeO
N
0.79
0.92
0.95
2.00
3.04
0.94
3.18
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

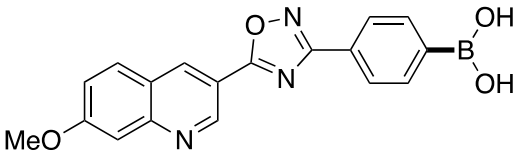
^{1}H NMR of **16**


173.6
168.9
162.4
150.9
148.1
136.1
130.5
122.6
120.7
114.9
107.4
55.8
40.0
39.8
39.6
39.3
39.1
38.9
38.7
0.0
O
N
N
BF3-K+
MeO
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

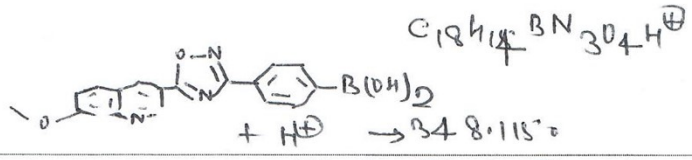
^{13}C NMR of **16**



^{1}H NMR of **17**

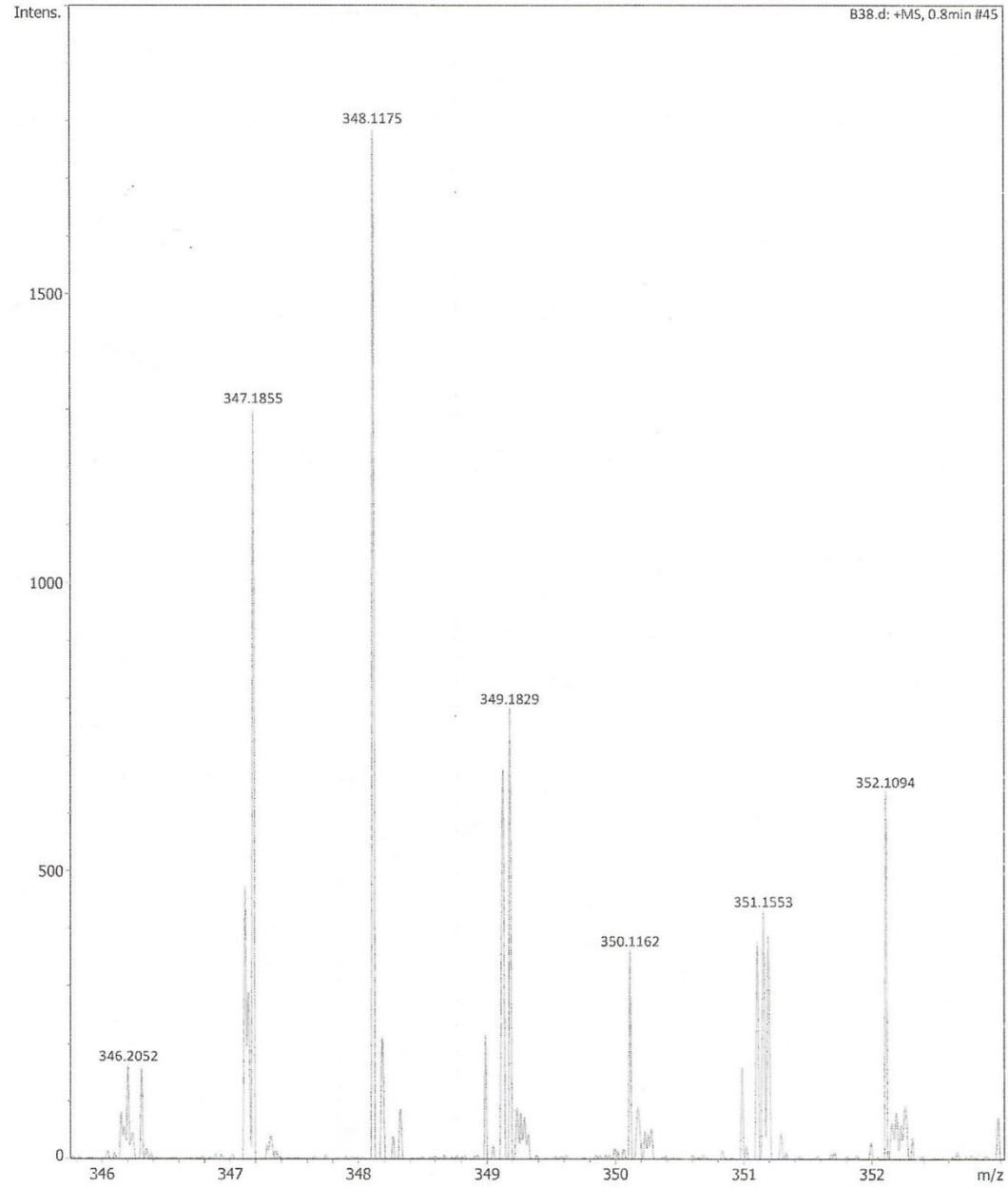


^{13}**C** NMR of **17**



Window Display Report

Compound Spectra - B38.d



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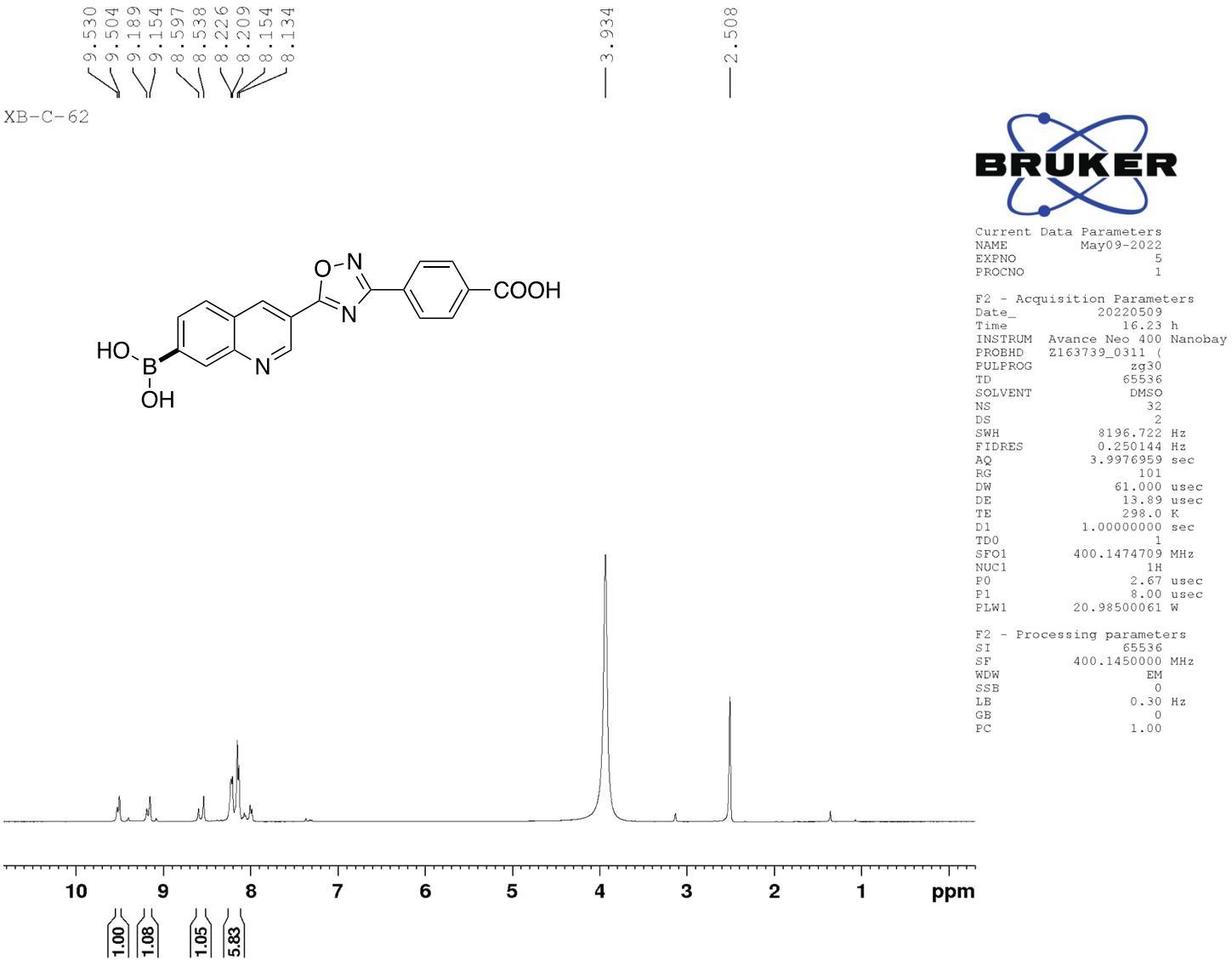
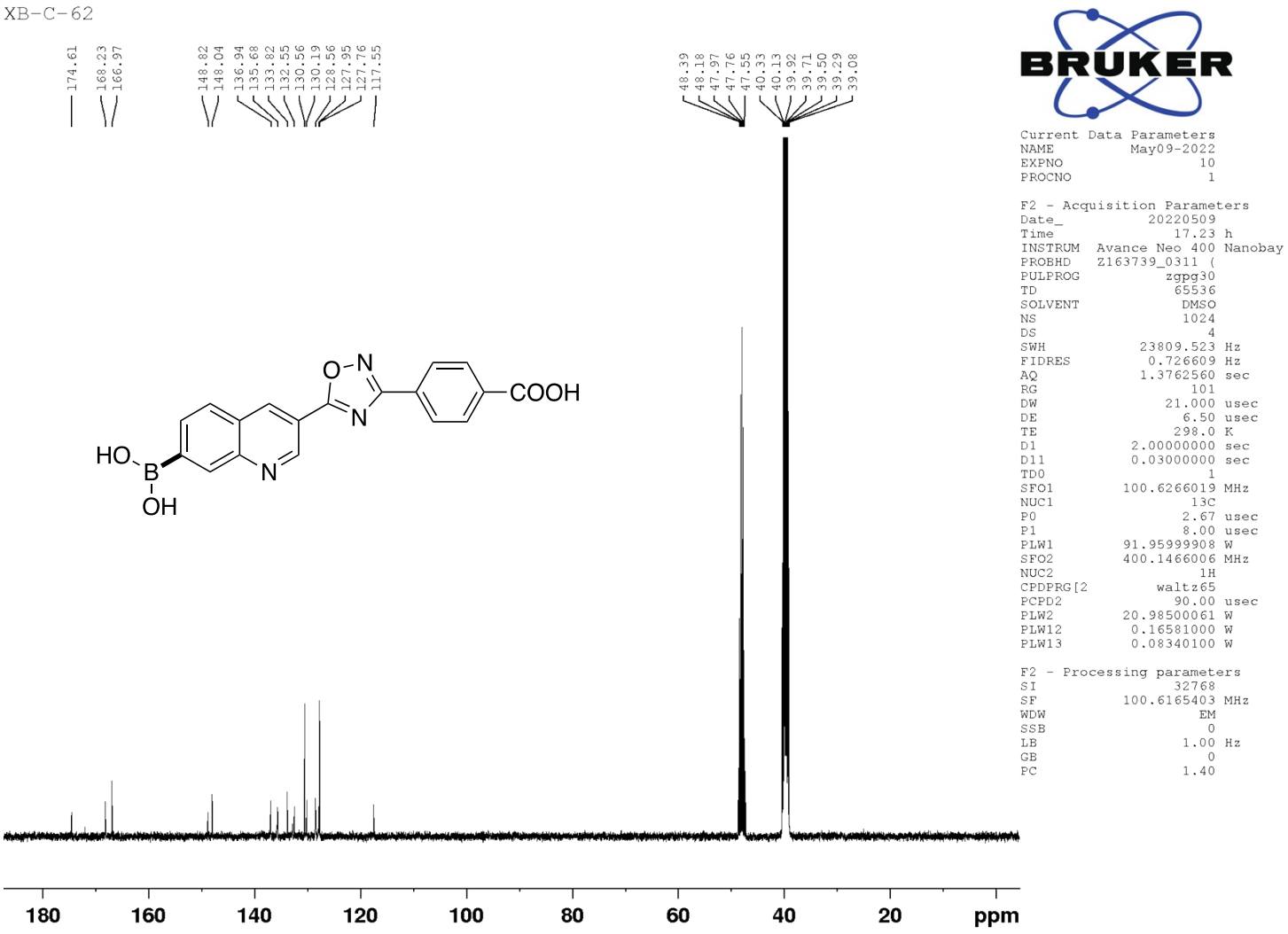
Mass spectrum of **17**


9.530
9.504
9.189
9.154
8.597
8.538
8.226
8.209
8.154
8.134
3.934
2.508
XB-C-62
BRUKER
Current Data Parameters
NAME May09-2022
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 16.23 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 32
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 13.89 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1474709 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 20.98500061 W
F2 - Processing parameters
SI 65536
SF 400.1450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
HO
B
OH
N
O
N
N
COOH
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.08
1.05
5.83

^{1}H NMR of **18**


XB-C-62
174.61
168.23
166.97
148.82
148.04
136.94
135.68
133.82
132.55
130.56
130.19
128.56
127.95
127.76
117.55
48.39
48.18
47.97
47.76
47.55
40.33
40.13
39.92
39.71
39.50
39.29
39.08
BRUKER
Current Data Parameters
NAME May09-2022
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220509
Time 17.23 h
INSTRUM Avance Neo 400 Nanobay
PROBHD Z163739_0311 (
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 23809.523 Hz
FIDRES 0.726609 Hz
AQ 1.3762560 sec
RG 101
DW 21.000 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6266019 MHz
NUC1 13C
P0 2.67 usec
P1 8.00 usec
PLW1 91.95999908 W
SFO2 400.1466006 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 90.00 usec
PLW2 20.98500061 W
PLW12 0.16581000 W
PLW13 0.08340100 W
F2 - Processing parameters
SI 32768
SF 100.6165403 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
HO
B
OH
O
N
N
N
COOH
180
160
140
120
100
80
60
40
20
ppm

^{13}C NMR of **18**