Supporting Information

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General Considerations

All reactions were carried out with commercial solvents and reagents that were used as received. Flash chromatography was carried out with Geduran® Si60 silica gel (Merck). Concentration and removal of trace solvents was done via a Büchi rotary evaporator using dry ice/acetone condenser, and vacuum applied from an aspirator or Büchi V-500 pump. All reagents and starting materials were purchased from Sigma Aldrich, Alfa Aesar, TCI America, and/or Strem, and were used without further purification. All solvents were purchased from Sigma Aldrich, EMD, Anachemia, Caledon, Fisher, or ACP and used without further purification, unless otherwise specified.

Nuclear magnetic resonance (NMR) spectra were recorded using chloroform-d ($CDCl_3$) or acetonitrile-d_3 (CD_3CN). Signal positions (δ) are given in parts per million from tetramethylsilane (δ 0) and were measured relative to the signal of the solvent (^{1}H NMR: $CDCl_3$: δ 7.26, CD_3CN: δ 1.96; ^{13}C NMR: $CDCl_3$: δ 77.16, CD_3CN: δ 118.26). Coupling constants (J values) are given in Hertz (Hz) and are reported to the

nearest 0.1 Hz. ^{1}H NMR spectral data are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet), coupling constants, number of protons. NMR spectra were recorded on a Bruker Avance 600 equipped with a QNP or TCI cryoprobe (600 MHz), Bruker 500 (500 MHz), or Bruker 400 (400 MHz). Assignments of ^{1}H and ^{13}C NMR spectra are based on analysis of ^{1}H-^{1}H COSY, HSQC, and HMBC spectra, where applicable. Methyl propiolate or 4-fluorotoluene was added to the crude reaction mixtures and used as an internal standard. Yields were then calculated following analysis of ^{1}H NMR spectra. **42**[1] was identified by comparison of its spectral data to that reported previously.

High-resolution mass spectra were performed on an Agilent 6210 TOF LC/MS, Bruker MaXis Impact TOF LC/MS, or Bruker micrOTOF-II LC mass spectrometer.

General Procedure A: Heterobenzylic monofluorination

To a solution of substrate in CH_3CN (0.1-0.25 M substrate) was added *N*-fluorobenzenesulfonimide (NFSI) (3.0 equiv.) and Li_2CO_3 (1.1 equiv.). The resulting reaction mixture was then heated to 65 °C and maintained at this temperature for 18-24 h. The reaction mixture was cooled, diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$), concentrated and the crude reaction product was purified by column chromatography on silica gel.

General Procedure B: Heterobenzylic difluorination

To a solution of substrate in CH_3CN (0.25-0.50 M substrate) was added *N*-fluorobenzenesulfonimide (NFSI) (5.0 equiv.) and Li_2CO_3 (5.0 equiv.). The resulting reaction mixture was then either heated to 75 °C and maintained at this temperature for 48 h or heated to 125 °C and maintained at this temperature for 1 h in a microwave reactor. The reaction mixture was cooled, diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$), concentrated and the crude reaction product was purified by column chromatography on silica gel.

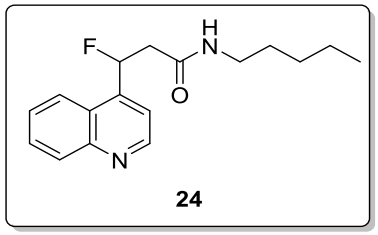
General Procedure C: Heterobenzylic trifluoromethylthiolation

To a solution of substrate in CH_3CN (0.20-0.50 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (2.4 equiv.) and Li_2CO_3 (1.1 equiv.). The resulting reaction mixture was then either heated to 75 °C and maintained at this temperature for 48 h or heated to 125 °C and maintained at this temperature for 1 h in a microwave reactor. The reaction mixture was cooled, diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$), concentrated and the crude reaction product was purified by column chromatography on silica gel.

[1] A. Haas, M. Spitzer, M. Lieb, *Chem. Ber*. **1988**, *121*, 1329-1340

Preparation and characterization of all compounds

Preparation of compound **24**



24

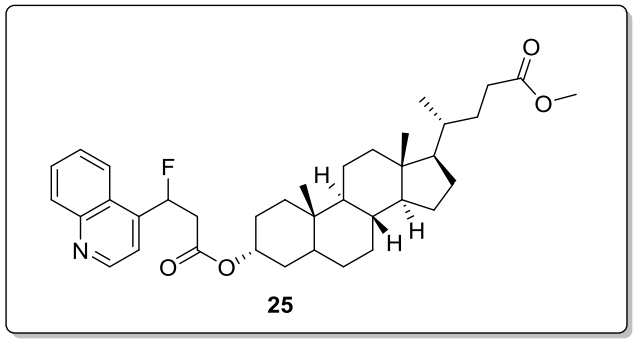
Following General Procedure **A**, to a solution of *N*-pentyl-3-(quinolin-4-yl)propenamide (0.0485 g, 0.179 mmol) in 1.2 mL of CH_3CN (0.15 M substrate) was added NFSI (0.170 g, 0.538 mmol, 3.0 equiv.) and Li_2CO_3 (0.015 g, 0.197 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 65 °C and maintained at this temperature for 24 h. Purification of the crude **24** by flash chromatography (pentane-ethyl acetate 4:6) afforded **24** (32.5 mg, 63%)

^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.95 (d, J = 4.5 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.78 (dd, J = 8.4, 7.1 Hz, 1H), 7.63 (dd, J = 8.4, 7.1 Hz, 1H), 7.55 (d, J = 4.5 Hz, 1H), 6.73 (ddd, J = 46.8, 9.1, 2.6 Hz, 1H), 5.63 (br s, 1H), 3.32 (m, 2H), 2.90 (ddd, J = 37.1, 15.4, 2.8 Hz, 1H), 2.78 (ddd, J = 17.5, 15.3, 9.1, 4.4 Hz 1H), 1.52 (m, 2H), 1.31 (m, 4H), 0.90 (dd, J = 7.3, 7.3 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 168.2, 149.8, 130.9, 130.2, 130.1, 129.9, 127.7, 124.4 (d, J = 5.1 Hz), 122.9, 116.9 (d, J = 11.4 Hz), 88.5 (d, J = 175.5 Hz), 44.5 (d, J = 24.8 Hz), 40.1, 29.3, 29.1, 22.5, 14.1; **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –183.6

HRMS (EI$^+$) calcd for $[C_{17}H_{22}FN_2O]^+$ 289.1711, found 289.1724.

Preparation of compound **25**

Following General Procedure **A**, to a solution of substrate (0.040 g, 0.070 mmol) in 0.35 mL of CH_3CN (0.20 M substrate) was added NFSI (0.066 g, 0.21 mmol, 3.0 equiv.) and Li_2CO_3 (6.0 mg, 0.077 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 65 °C and maintained at this temperature for 24 h. Purification of the crude **25** by flash chromatography (pentane-ethyl acetate 5:5) afforded **25** as a 1:1 mixture of diastereomers (37.0 mg, 90%)**.**



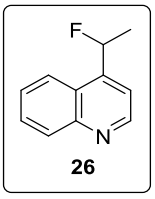
25

IR (neat): υ = 2939, 2868, 1724, 1178, 905, 730 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.96 (1H), 8.17 (1H), 7.93 (1H), 7.76 (1H), 7.62 (1H), 7.53 (1H), 6.66 (1H), 4.84 (1H), 3.66 (3H), 2.99(1H), 2.34 (1H), 2.21 (1H), 1.96 (1H), 1.91-0.98 (25H), 0.94 (3H), 0.91 (3H), 0.65 (3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 174.9, 169.0, 150.5, 148.5, 144.1, 130.8, 129.7, 127.4, 124.5, 122.7, 117.3, 87.8, 75.8, 56.6, 56.2, 51.6, 42.9, 42.4, 42.1, 42.1, 40.6, 40.3, 36.0, 35.5, 35.1, 34.7, 32.4, 32.3, 31.2, 31.2, 28.3, 27.1, 26.8, 26.7, 26.5, 24.3, 23.5, 21.0, 18.4, 12.2; **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –182.9, –182.9.

HRMS (EI$^+$) calcd for $[C_{37}H_{51}FNO_4]^+$ 592.3797, found 592.3793.

Preparation of compound **26**

Following General Procedure **A**, to a solution of 4-ethylquinoline (0.025 g, 0.159 mmol) in 1.60 mL of CH_3CN (0.10 M substrate) was added NFSI (0.150 g, 0.478 mmol, 3.0 equiv.) and Li_2CO_3 (13.0 mg, 0.175 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 65 °C and maintained at this temperature for 24 h. Purification of the crude **26** by flash chromatography (pentane-EtOAc 7:3) afforded **26** (17.3 mg, 62%).



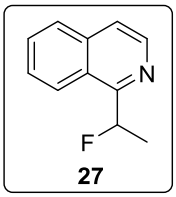
26

^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.95 (d, J = 4.5 Hz, 1H), 8.17 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.74 (dd, J = 8.2, 8.2 Hz, 1H), 7.59 (dd, J = 7.9, 7.9 Hz, 1H), 7.51 (d, J = 4.4 Hz, 1H), 6.33 (dq, J = 46.8, 6.5 Hz, 1H), 1.81 (dd, J = 24.3, 6.5 Hz, 3H) **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 150.6 (d, J = 22.5 Hz), 148.4, 146.9 (d, J = 19.1 Hz), 130.7, 129.4, 127.0, 124.7 (d, J = 4.8 Hz), 122.9, 116.6 (d, J = 10.9 Hz) 87.8 (d, J = 172.3 Hz), 22.7 (d, J = 25.1 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –176.7

HRMS (ESI^+) calcd for $[C_{11}H_{11}FN]^+$ 176.0870, found 176.0841

Preparation of compound **27**

Following General Procedure **A**, to a solution of 1-ethylisoquinoline (0.025 g, 0.159 mmol) in 1.60 mL of CH_3CN (0.25 M substrate) was added NFSI (0.150 g, 0.478 mmol, 3.0 equiv.) and Li_2CO_3 (13.0 mg, 0.175 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 24 h. Purification of the crude **27** by flash chromatography (pentane-EtOAc 85:15) afforded **27** (19.3 mg, 69%).



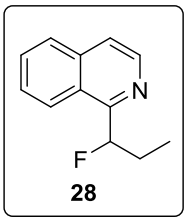
27

IR (neat): υ = 3055, 2989, 1624, 1586, 1378, 1055, 827 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.52 (d, J = 5.7 Hz, 1H), 8.38 (d, J = 8.6 Hz, 1H), 7.87 (d, J = 8.3 Hz, 1H), 7.71 (dd, J = 7.8, 7.8 Hz, 1H), 7.65 (d, J = 5.5 Hz, 1H), 7.64 (dd, J = 7.6 Hz, 1H), 6.35 (dq, J = 48.0, 6.6 Hz, 1H), 1.93 (dd, J = 24.0 Hz, 6.6 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 157.8 (d, J = 19.7 Hz), 141.5, 136.9, 130.2, 127.6 (d, J = 1.7 Hz), 127.6, 126.2, 125.3 (d, J = 5.8 Hz), 121.6 (d, J = 1.7 Hz), 91.2 (d, J = 168.2 Hz), 20.5 (d, J = 23.6 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –169.5

HRMS (EI^+) calcd for $[C_{11}H_{11}FN]^+$ 176.0870, found 176.0887

Preparation of compound **28**

Following General Procedure **A**, to a solution of 1-propylisoquinoline (0.025 g, 0.146 mmol) in 0.60 mL of CH_3CN (0.25 M substrate) was added NFSI (0.138 g, 0.438 mmol, 3.0 equiv.) and Li_2CO_3 (12.0 mg, 0.161 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 24 h. The yield for **28** (78%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash chromatography (pentane-EtOAc 85:15) provided an analytical sample of **28**.



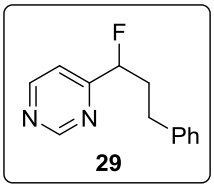
28

IR (neat): υ = 2957, 1604, 1499, 1119, 900 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.51 (d, J = 5.5 Hz, 1H), 8.37 (d, J = 8.3 Hz, 1H), 7.86 (d, J = 8.3 Hz, 1H), 7.70 (dd, J = 7.4, 7.4 Hz, 1H), 7.64 (d, J = 5.5 Hz, 1H), 7.62 (dd, J = 7.4, 7.4 Hz, 1H), 6.04 (ddd, J = 48.1, 8.6, 5.2 Hz, 1H), 2.35 (m, 1H), 2.20 (m, 1H), 1.12 (dd, J = 7.4, 7.4 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 157.4 (d, J = 19.8 Hz), 141.5, 136.8, 130.1, 127.5, 127.4 (d, J = 1.4 Hz), 126.2, 125.2 (d, J = 6.2 Hz), 121.3 (d, J = 1.4 Hz), 96.2 (d, J = 173.4 Hz), 28.2 (d, J = 22.7 Hz), 9.9 (d, J = 5.7 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –178.0

HRMS (EI^+) calcd for $[C_{12}H_{13}FN]^+$ 190.1027, found 190.1027

Preparation of compound **29**

Following General Procedure **A**, to a solution of 4-(3-phenylpropyl)pyrimidine (0.025 g, 0.126 mmol) in 1.25 mL of CH_3CN (0.10 M substrate) was added NFSI (0.238 g, 0.756 mmol, 6.0 equiv.) and Li_2CO_3 (10.0 mg, 0.139 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 125 °C and maintained at this temperature for 25 minutes in a microwave reactor. The yield for **29** (48%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 6:4) provided an analytical sample of **29**.



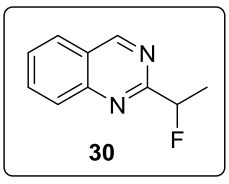
29

IR (neat): υ = 2829, 1582, 1350, 1056, 750 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.16 (s, 1H), 8.78 (d, J = 4.8 Hz, 1H), 7.52 (d, J = 4.9 Hz, 1H), 7.29 (dd, J = 7.4, 7.4 Hz, 1H), 7.22 (d, J = 7.4 Hz, 1H), 7.20 (dd, J = 7.4, 7.4 Hz, 1H), 5.49 (ddd, J = 48.4, 8.6, 2.3 Hz, 1H), 2.84 (dd, J = 8.3, 8.3 Hz, 2H), 2.39 (m, 1H), 2.22 (m, 1H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 168.8 (d, J = 26.0 Hz), 158.1 (d, J = 2.9 Hz), 157.5 (d, J = 1.6 Hz), 140.6, 128.7, 128.6, 126.4, 117.0 (d, J = 8.3 Hz), 92.5 (d, J = 175.9 Hz), 36.9 (d, J = 21.7 Hz), 31.0 (d, J = 3.2 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –193.4

HRMS (EI^+) calcd for $[C_{13}H_{14}FN_2]^+$ 217.1136, found 217.1128

Preparation of compound **30**

Following General Procedure **A**, to a solution of 2-ethylquinazoline (0.025 g, 0.158 mmol) in 0.60 mL of CH_3CN (0.25 M substrate) was added NFSI (0.100 g, 0.50 mmol, 3.0 equiv.) and Li_2CO_3 (0.026 g, 0.348 mmol, 2.2 equiv.). The resulting reaction mixture was then heated to 125 °C and maintained at this temperature for 60 minutes in a microwave reactor. The yield for **30** (72%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 7.5:2.5) provided an analytical sample of **30**.



30

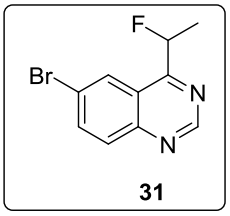
IR (neat): υ = 2959, 1620, 1585, 1490, 1379, 1077, 765 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.96 (m, 2H), 7.69 (dd, J = 7.6, 7.6 Hz, 1H), 5.91 (dq, J = 48.5, 6.6 Hz), 1H), 1.85 (dd, J = 24.1, 6.7 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 164.5 (d, J = 19.6 Hz), 161.1, 150.2, 134.7, 128.7, 128.2, 127.4,

124.2, 91.2 (d, J = 173.9 Hz), 20.9 (d, J = 24.1); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –177.1

HRMS (EI^+) calcd for $[C_{10}H_{10}FN_2]^+$ 177.0823, found 177.0817

Preparation of compound **31**

Following General Procedure **A**, to a solution of 6-bromo-4-ethylquinazoline (0.025 g, 0.106 mmol) in 1.1 mL of CH_3CN (0.10 M substrate) was added NFSI (0.040 g, 0.127 mmol, 1.2 equiv.) and Li_2CO_3 (9.0 mg, 0.117 mmol, 1.1 equiv.). The resulting reaction mixture was then left room temperature and maintained at this temperature for 96 hours. Purification of the crude **31** by flash chromatography (pentane-ethyl acetate; 85:15) afforded **31** (24.0 mg, 91%).



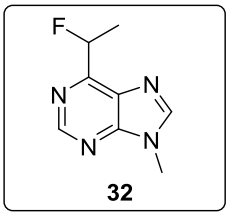
31

IR (neat): υ = 3975, 2254, 1498, 903, 726 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.32 (s, 1H), 8.01 (dd, J = 9.0, 2.0 Hz, 1H), 7.99 (d, J = 9.0 Hz, 1H), 6.18 (dq, J = 48.1, 6.9 Hz, 1H), 1.91 (dd, J = 24.2, 6.6 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 166.3 (d, J = 21.3 Hz), 154.5, 149.8, 137.7, 131.2, 127.6 (d, J = 9.2 Hz), 123.3, 122.1, 91.2 (d, J = 172.1 Hz), 20.7 (d, J = 23.1 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –174.2

HRMS (EI^+) calcd for $[C_{10}H_9BrFN_2]^+$ 254.9928, found 254.9949

Preparation of compound **32**

Following General Procedure **A**, to a solution of 6-ethyl-9-methyl-9*H*-purine (0.015 g, 0.093 mmol) in 0.40 mL of CH_3CN (0.25 M substrate) was added NFSI (0.096 g, 0.303 mmol, 3.3 equiv.) and Li_2CO_3 (8.2 mg, 0.111 mmol, 1.2 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 36 hours. Purification of the crude **32** by flash chromatography (CH_2Cl_2-MeOH 96:4) afforded **32** (11.1 mg, 70%).



32

IR (neat): υ = 2978, 2262, 1039, 832 cm^{-1};**^{1}H-NMR** (600 MHz, CD_3CN): δ 8.92 (s, 1H), 8.21 (s, 1H), 6.18 (dq, J = 47.3, 6.6 Hz, 1H), 1.81 (dd, J = 24.7, 6.7 Hz, 3H); **^{13}C-NMR** (150 MHz, CD_3CN): δ 157.5 (d, J = 19.4 Hz), 153.7, 152.8, 147.8, 131.7, 88.8 (d, J = 168.8 Hz), 30.2, 20.2 (d, J = 24.4 Hz); **^{19}F-NMR** (470 MHz, CD_3CN): δ –176.6

HRMS (EI^+) calcd for $[C_8H_{10}FN_4]^+$ 181.0884, found 181.0890

Preparation of compound **33**

Following General Procedure **B**, to a solution of 4-methylquinoline (0.030 mL, 0.226 mmol) in 0.45 mL of CH_3CN (0.50 M substrate) was added NFSI (0.357 g, 1.13 mmol, 5.0 equiv.) and Li_2CO_3 (0.084 g, 1.13 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **33** (68%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 6:4) provided an analytical sample of **33**

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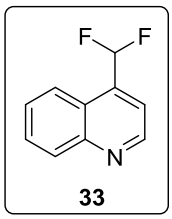


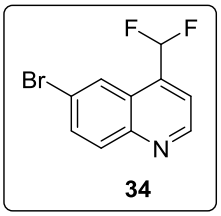
33

^{1}H-NMR (600 MHz, $CDCl_3$): δ 9.03 (d, J = 4.3 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.80 (dd, J = 7.5, 7.5 Hz, 1H), 7.67 (dd, J = 7.5 Hz, 1H). 7.60 (d, J = 4.3 Hz, 1H), 7.17 (t, J = 54.6 Hz, 1H) ; **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 150.1, 148.8, 138.0 (t, J = 21.8 Hz), 130.6, 130.1, 128.0, 124.3 (t, J = 3.1 Hz), 123.4, 118.1 (t, J = 7.7 Hz), 113.4 (t, J = 241.0 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –115.1

HRMS (EI^+) calcd for $[C_{10}H_8F_2N]^+$ 180.0619, found 180.0600.

Preparation of compound **34**

Following General Procedure **B**, to a solution of 6-bromo-4-methylquinoline (0.030 g, 0.136 mmol) in 0.30 mL of CH_3CN (0.50 M substrate) was added NFSI (0.214 g, 0.679 mmol, 5.0 equiv.) and Li_2CO_3 (0.050 g, 0.679 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **34** (64%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 6:4) provided an analytical sample of **34**.



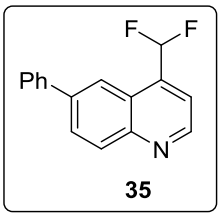
34

^{1}H-NMR (600 MHz, $CDCl_3$): δ 9.03 (d, J = 4.3 Hz, 1H), 8.26 (s, 1H), 8.08 (d, J = , 9.0 Hz, 1H), 7.88 (dd, J = 9.1, 1.8 Hz, 1H), 7.61 (d, J = 4.5 Hz, 1H), 7.10 (t, J = 54.4 Hz, 1H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 150.4, 147.4, 137.2 (t, J = 22.4 Hz), 133.7, 132.2, 126.0, 125.3 (t, J = 2.7 Hz), 122.4, 119.0 (t, J = 7.5 Hz), 113.2 (t, J = 241.1 Hz); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –114.9

HRMS (EI^+) calcd for $[C_{10}H_7BrF_2N]^+$ 257.9724, found 257.9711

Preparation of compound **35**

Following General Procedure **B**, to a solution of 4-methyl-6-phenylquinoline (0.046 g, 0.210 mmol) in 0.42 mL of CH_3CN (0.50 M substrate) was added NFSI (0.331 g, 1.05 mmol, 5.0 equiv.) and Li_2CO_3 (0.078 g, 1.05 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **35** (41%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **35**.



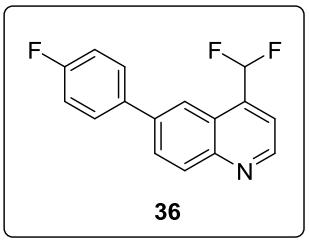
35

^{1}H-NMR (600 MHz, $CDCl_3$): δ 9.06 (d, J = 4.4 Hz, 1H), 8.31 (d, J = 8.8 Hz, 1H), 8.29 (s, 1H), 8.10 (dd, J = 8.8, 1.9 Hz, 1H), 7.77 (d, J = 7.7 Hz, 2H), 7.66 (d, J = 4.3 Hz, 1H), 7.57 (dd, J = 7.7, 7.7 Hz, 2H), 7.48 (dd, J = 7.7, 7.7 Hz, 1H), 7.25 (t, J = 54.6 Hz, 1H) ; **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 150.0, 148.1, 140.8, 140.3, 138.0 (t, J = 21.6 Hz), 130.9, 129.9, 129.2, 128.3, 127.8, 124.5 (t, J = 2.9 Hz), 121.2, 118.5 (t, J = 7.8 Hz), 113.5 (t, J = 240.8 Hz); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –115.0

HRMS (EI^+) calcd for $[C_{16}H_{12}F_2N]^+$ 256.0932, found 256.0930

Preparation of compound **36**

Following General Procedure **B**, to a solution of 4-(methyl)-6-(4-fluorophenyl)quinoline (0.035 g, 0.147 mmol) in 0.29 mL of CH_3CN (0.50 M substrate) was added NFSI (0.232 g, 0.735 mmol, 5.0 equiv.) and Li_2CO_3 (0.059 g, 0.735 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **36** (63%) was determined by analysis of a ^1H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **36**.



36

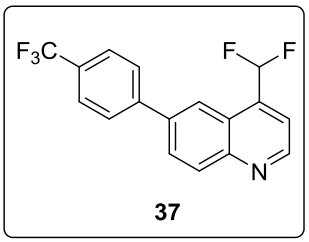
^{1}H-NMR (600 MHz, $CDCl_3$): δ 9.02 (s, 1H), 8.27 (d, J = 8.8 Hz, 1H), 8.19 (s, 1H), 8.00 (dd, J = 8.8, 1.9 Hz, 1H), 7.68 (m, 2H), 7.62 (d, J = 3.9 Hz, 1H), 7.57 (dd, J = 7.7, 7.7 Hz, 2H), 7.21 (dd, J = 8.7, 8.7 Hz, 1H), 7.19 (t, J = 54.6 Hz, 1H) ; **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 163.1 (d, J = 248.7 Hz), 150.0, 148.0, 139.8, 138.0 (t, J = 21.7 Hz), 136.4 (d, J = 3.2 Hz), 131.0, 129.8, 129.4 (d, J = 8.2 Hz) 124.5, 121.1, 118.7 (t, J = 7.0 Hz), 116.2 (d, J = 21.1 Hz), 113.6 (t, J = 241.3 Hz); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –114.2, –114.7

HRMS (EI^+) calcd for $[C_{16}H_{11}F_3N]^+$ 274.0838, found 274.0813

Melting point: 111-114 ˚C

Preparation of compound **37**

Following General Procedure **B**, to a solution of 4-methyl-6-(4-(trifluoromethyl)phenyl)quinoline (0.035 g, 0.122 mmol) in 0.24 mL of CH_3CN (0.50 M substrate) was added NFSI (0.192 g, 0.610 mmol, 5.0 equiv.) and Li_2CO_3 (0.045 g, 0.610 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temprature for 48 hours. The yield for **37** (60%) was determined by analysis of a ^1H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **37**.



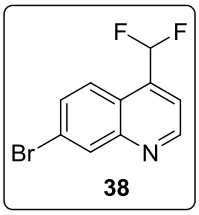
37

IR (neat): υ = 2948, 1680, 1173, 722 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.08 (s, 1H), 8.35 (d, J = 8.8 Hz, 1H), 8.29 (s, 1H), 8.06 (dd, J = 8.8, 1.8 Hz, 1H), 7.83 (d, J = 8.2 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 3.7 Hz, 1H), 7.20 (t, J = 54.7 Hz, 1H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 150.1, 147.8, 143.7, 139.6, 138.7 (t, J = 22.5 Hz), 130.8, 130.5 (q, J = 32.6 Hz), 129.9, 128.2, 126.2 (q, J = 3.7 Hz), 124.6, 124.2 (q, J = 272.4 Hz), 122.0, 119.0, 113.5 (t, J = 241.2 Hz) 121.1, 118.7 (t, J = 7.0 Hz), 116.2 (d, J = 21.1 Hz), 113.6 (t, J = 241.3 Hz); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –62.5, –114.6

HRMS (EI^+) calcd for $[C_{17}H_{11}F_5N]^+$ 324.0806, found 324.0813

Preparation of compound **38**

Following General Procedure **B**, to a solution of 7-bromo-4-methylquinoline (0.025 g, 0.113 mmol) in 0.22 mL of CH_3CN (0.50 M substrate) was added NFSI (0.178 g, 0.566 mmol, 5.0 equiv.) and Li_2CO_3 (0.042 g, 0.566 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **38** (68%) was determined by analysis of a ^1H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **38**.



38

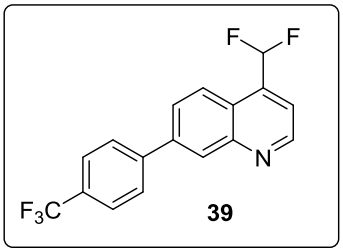
IR (neat): υ = 2971, 2254, 1604, 902, 724 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.03 (d, J = 4.3 Hz, 1H), 8.41 (d, J = 2.0 Hz, 1H), 7.99 (d, J = 9.0 Hz, 1H), 7.76 (dd, J = 9.0 Hz, 1H) 7.61 (d, J = 4.3 Hz, 1H), 7.12 (t, J = 54.2 Hz, 1 H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 151.1, 149.4, 138.2 (t, J = 22.4 Hz), 132.9, 131.5, 124.9, 124.4, 118.5 (t, J = 7.6 Hz), 113.3 (t, J = 241.3 Hz); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –114.6

HRMS (EI^+) calcd for $[C_{10}H_7BrF_2N]^+$ 257.9724, found 257.9739

Melting point: 68-72˚C

Preparation of compound **39**

Following General Procedure **B**, to a solution of 4-methyl-7-(4-(trifluoromethyl)phenyl)quinoline (0.035 g, 0.122 mmol) in 0.24 mL of CH_3CN (0.50 M substrate) was added NFSI (0.192 g, 0.61 mmol, 5.0 equiv.) and Li_2CO_3 (0.045 g, 0.61 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **39** (46%) was determined by analysis of a ^1H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **39**.



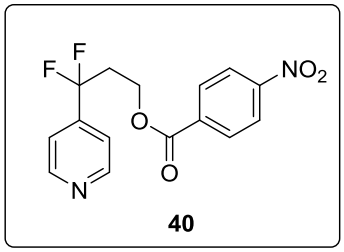
39

IR (neat): υ = 2925, 1617, 1326, 1119, 1071, 729 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.07 (d, J = 4.2 Hz, 1H), 8.44 (d, J = 1.7 Hz, 1H), 8.21 (d, J = 8.6 Hz, 1H), 7.92 (dd, J = 8.8, 1.8 Hz, 1H) 7.87 (d, J = 8.2 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H), 7.63 (ddd, J = 4.2 Hz, 1H), 7.18 (t, J = 54.5 Hz, 1H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 150.9, 148.9, 143.3, 141.3, 138.1 (t, J = 22.7 Hz), 136.0, 130.5 (q, J = 32.7), 128.5, 128.0, 127.3, 126.2 (q, J = 3.7 Hz), 124.4, 123.8 (t, J = 3.1 Hz), 118.5 (t, J = 7.9 Hz), 113.4 (t, J = 241.3 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$):δ –62.5, –114.8

HRMS (EI^+) calcd for $[C_{17}H_{11}F_5N]^+$ 324.0806, found 324.0806

Preparation of compound **40**

Following General Procedure **B**, to a solution of 3-(pyridin-4-yl)propyl 4-nitrobenzoate (0.025 g, 0.087 mmol) in 0.17 mL of ethyl acetate (0.50 M substrate) was added NFSI (0.274 g, 0.87 mmol, 10 equiv.) and Li_2CO_3 (0.033 g, 0.44 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. Purification of the crude **40** by flash chromatography (pentanes: ethyl acetate 1:1) afforded **40** (13.1 mg, 49%).



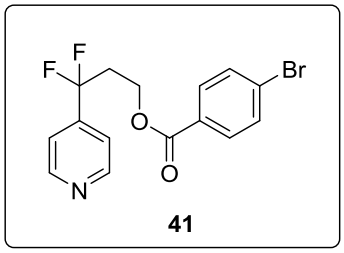
40

^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.80 (d, J = 3.8 Hz, 1H), 8.28 (d, J = 8.5 Hz, 2H), 8.05 (d, J = 8.5, 1H), 7.64 (d, J = 3.8 Hz, 2H), 4.60 (dd, J = 6.3, 6.3 Hz, 2H), 2.69 (m, J = 3.7 Hz, 2H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 164.4, 150.9, 149.4, 149.3, 135.0, 130.8, 123.8, 120.3, 120.2, 59.3, 37.8 (t, J = 26.7 Hz); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –97.9.

HRMS (EI$^+$) calcd for $[C_{15}H_{13}F_2N_2O_4]^+$ 323.0838, found 323.0845.

Preparation of compound **41**

Following General Procedure **B**, to a solution of 3-(pyridin-4-yl)propyl 4-bromobenzoate (0.025 g, 0.078 mmol) in 0.16 mL of ethyl acetate (0.50 M substrate) was added NFSI (0.247 g, 0.78 mmol, 10 equiv.) and Li_2CO_3 (0.029 g, 0.39 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. Purification of the crude **41** by flash chromatography (pentanes: ethyl acetate 1:1) afforded **41** (12.1 mg, 47%).



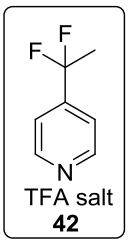
41

IR (neat): υ = 2973, 1723, 1272, 1118, 732 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.73 (d, J = 3.8 Hz, 2H), 7.68 (d, J = 7.8 Hz, 2H), 7.56 (d, J = 7.8 Hz, 2H), 7.42 (d, J = 3.8 Hz, 2H), 4.51 (t, J = 5.9 Hz, 2H), 2.66 (tt, J = 15.7, 6.2 Hz, 2H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 165.5, 150.6, 144.9 (t, J = 26.8 Hz), 131.9, 131.1, 128.6, 128.5, 120.5 (t, J = 242.9 Hz), 119.6 (t, J = 6.3 Hz), 58.8 (t, J = 5.4 Hz), 37.9 (t, J = 27.2 Hz); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –97.6

HRMS (EI$^+$) calcd for $[C_{15}H_{13}BrF_2NO_2]^+$ 356.0092, found 356.0091

Preparation of compound **42**

Following General Procedure **B**, to a solution of 4-ethylpyridine (0.025 mL, 0.22 mmol) in 0.45 mL of ethyl acetate (0.50 M substrate) was added NFSI (0.694 g, 2.20 mmol, 10 equiv.) and Li_2CO_3 (0.081 g, 1.10 mmol, 5 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **42**[1] (43%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. TFA was added to the reaction mixture prior to concentration under reduced pressure. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **42**.



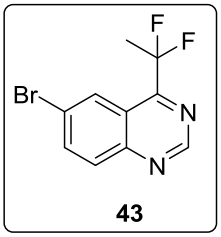
42

IR (neat): υ = 3085, 2923, 1666, 1293, 1150, 720 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 11.11 (br s, 1H), 9.02 (d, J = 6.2 Hz, 2H), 7.95 (d, J = 6.3 Hz, 2H), 2.00 (t, J = 18.4 Hz, 3H); **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –75.9, –92.2

HRMS (EI^+) calcd for $[C_7H_8F_2N]^+$ 144.0619, found 144.0623

Preparation of compound **43**

Following General Procedure **B**, to a solution of 6-bromo-4-ethylquinazoline (0.025 g, 0.106 mmol) in 0.22 mL of CH_3CN (0.50 M substrate) was added NFSI (0.100 g, 0.318 mmol, 3.0 equiv.) and Li_2CO_3 (9.0 mg, 0.117 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 125 °C and maintained at this temperature in a microwave reactor for 1 hour. The yield for **43** (74%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 8:2) provided an analytical sample of **43**.



43

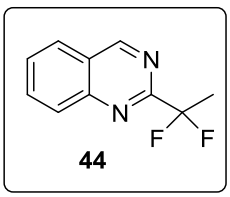
IR (neat): υ = 3059, 2976, 1394, 1117, 1036, 759 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.66 (d, J = 1.2 Hz, 1H), 8.04 (dd, J = 9.0, 1.8 Hz, 1H) 1H), 8.02 (d, J = 9.0, 1H), 2.23 (t, J = 19.4, 1H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 160.6 (d, J = 32.2 Hz), 153.8, 150.7, 138.1, 131.1, 128.5 (t, J = 6.1 Hz), 123.0 (t, J = 240.7 Hz), 123.0, 122.2, 22.7 (t, J = 25.7 Hz); **^{19}F-NMR** ($CDCl_3$): δ –84.4

HRMS (EI^+) calcd for $[C_{10}H_8BrF_2N_2]^+$ 272.9833, found 272.9833

Melting point: 86-89˚C

Preparation of compound **44**

Following General Procedure **B**, to a solution of 2-ethylquinazoline (0.025 g, 0.158 mmol) in 0.65 mL of CH_3CN (0.25 M substrate) was added NFSI (0.249 g, 0.791 mmol, 5.0 equiv.) and Li_2CO_3 (0.026 g, 0.348 mmol, 2.2 equiv.). The resulting reaction mixture was then heated to 125 °C and maintained at this temperature in a microwave reactor for 1 hour. The yield for **44** (86%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 4:6) provided an analytical sample of **44**.



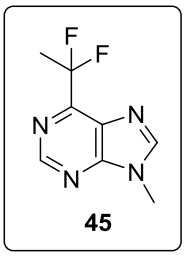
44

IR (neat): υ = 2977, 1620, 1584, 905, 729 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.52 (s, 1H), 8.17 (d, J = 8.7 Hz, 1H), 8.01 (m, 2H), 7.76 (dd, J = 7.3 Hz, 1H), 2.19 (t, J = 18.7 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 161.4, 159.3 (t, J = 28.1 Hz), 149.9, 135.0, 129.2, 129.2, 127.3, 124.7, 119.8 (t, J = 239.7 Hz), 23.4 (t, J = 26.8 Hz); **^{19}F-NMR** ($CDCl_3$): δ –92.8

HRMS (EI^+) calcd for $[C_{10}H_9F_2N_2]^+$ 195.0728, found 195.0725

Preparation of compound **45**

Following General Procedure **B**, to a solution of 6-ethyl-9-methyl-9H-purine (0.025 g, 0.169 mmol) in 0.68 mL of CH_3CN (0.25 M substrate) was added NFSI (0.266 g, 0.843 mmol, 5.0 equiv.) and Li_2CO_3 (0.027 g, 0.372 mmol, 2.2 equiv.). The resulting reaction mixture was then heated to 125 °C and maintained at this temperature in a microwave reactor for 1 hour. The yield for **45** (69%) was determined by analysis of a ^1H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:9) provided an analytical sample of **45**.



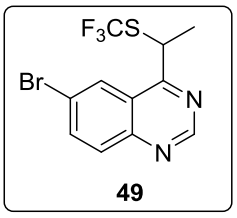
45

IR (neat): υ = 2975, 1594, 1328, 1119, 907, 731 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.05 (s, 1H), 8.19 (s, 1H), 3.96 (s, 3H) 1H), 2.20 (t, J = 19.4, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 153.7, 152.9 (t, J = 30.1 Hz), 152.1, 146.7, 130.1, 120.4 (t, J = 240.2 Hz), 30.1, 23.6 (t, J = 26.4 Hz); **^{19}F-NMR** ($CDCl_3$): δ –90.8

HRMS (EI^+) calcd for $[C_8H_9F_2N_4]^+$ 199.0790, found 199.0784

Preparation of compound **49**

Following General Procedure **C**, to a solution of 6-bromo-4-ethylquinazoline (0.025 g, 0.106 mmol) in 0.53 mL of CH_3CN (0.20 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (0.100 g, 0.252 mmol, 2.4 equiv.) and Li_2CO_3 (9.0 mg, 0.117 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. Purification of the crude **49** by flash chromatography (pentanes: ethyl acetate; 85:15) afforded **49** (33.0 mg, 92%).



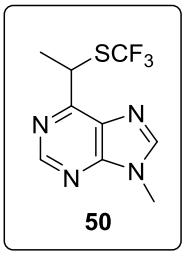
49

IR (neat): υ = 2977, 1557, 1485, 1115, 731 cm^{-1};**^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.30 (s, 1H), 8.28 (d, J = 1.8 Hz, 1H), 8.02 (dd, J = 9.0, 2.0 Hz, 1H), 8.00 (d, J = 9.0 Hz, 1H) 5.25 (q, J = 7.1 Hz, 1H), 1.94 (d, J = 7.1 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 167.9, 154.7, 149.4, 138.0, 131.6, 130.9 (q, J = 307.8 Hz), 125.9, 122.7, 122.6, 41.4, 22.9; **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –40.3

HRMS (EI^+) calcd for $[C_{11}H_9BrF_3N_2S]^+$ 336.9616, found 336.9621

Preparation of compound **50**

Following General Procedure **C**, to a solution of 6-ethyl-9-methyl-9H-purine (0.025 g, 0.169 mmol) in 0.68 mL of CH_3CN (0.25 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (0.147 g, 0.372 mmol, 2.2 equiv.) and Li_2CO_3 (0.015 g, 0.20 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 125 °C and maintained at this temperature in a microwave reactor for 50 minutes. The yield for **50** (56%) was determined by analysis of a ^1H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **50**.



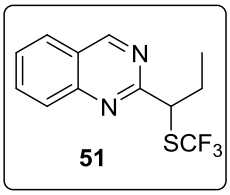
50

IR (neat): υ = 2953, 1750, 1591, 1331, 1223, 1114 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.96 (s, 1H), 8.08 (s, 1H), 5.28 (q, J = 7.1 Hz, 1H), 3.93 (s, 3H), 1.90 (d, J = 7.4, 1H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 159.9, 152.8, 152.2, 145.4, 130.9 (q, J = 304.2 Hz), 40.7 (q, J = 1.8 Hz), 30.1, 21.7; **^{19}F-NMR** ($CDCl_3$): δ –40.4

HRMS (EI^+) calcd for $[C_9H_{10}F_3N_4S]^+$ 263.0573, found 263.0573

Preparation of compound **51**

Following General Procedure **C**, to a solution of 2-propylquinazoline (0.025 g, 0.158 mmol) in 0.65 mL of CH_3CN (0.25 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (0.249 g, 0.791 mmol, 5.0 equiv.) and Li_2CO_3 (0.026 g, 0.348 mmol, 2.2 equiv.). The resulting reaction mixture was then heated to 125 °C and maintained at this temperature in a microwave reactor for 1 hour. The yield for **51** (74%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 1:1) provided an analytical sample of **51**.



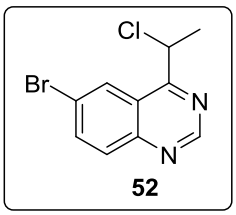
51

IR (neat): υ = 2973, 1624, 1113, 905, 731 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.52 (d, J = 5.7 Hz, 1H), 8.17 (d, J = 8.7 Hz, 1H), 7.88 (dd, J = 7.3, 7.3 Hz, 1H), 7.67 (dd, J = 7.3, 7.3 Hz, 1H), 7.62 (d, J = 5.5 Hz, 1H), 5.25 (dd, J = 5.9, 5.7 Hz, 1H), 2.42 (m, 1H), 2.32 (m, 1H), 0.91 (t, J = 7.6 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 158.7, 141.9, 136.7, 131.3 (q, J = 307.7 Hz), 130.6, 128.0, 126.0, 124.2, 120.8, 47.7, 30.0, 11.4; **^{19}F-NMR** ($CDCl_3$): δ –40.3

HRMS (EI^+) calcd for $[C_{12}H_{12}F_3N_2S]^+$ 273.0668, found 273.0688

Preparation of compound **52**

To a solution of 6-bromo-4-ethylquinazoline (0.020 g, 0.085 mmol) in 0.35 mL of CH_3CN (0.25 M substrate) was added *N*-chlorobenzenesulfonimide (0.034 g, 0.102 mmol, 1.2 equiv.) and Li_2CO_3 (6.9 mg, 0.093 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to and maintained at 75 °C for 48 hours. Purification of the crude **52** by flash chromatography (pentanes: diethyl ether; 6:4) afforded **52** (17.7mg, 78%).



52

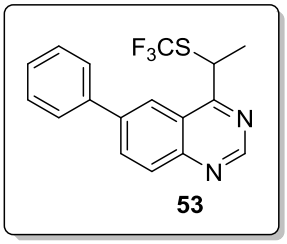
IR (neat): υ = 2925, 1558, 1484, 905, 837, 729 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.35 (s, 1H), 8.44 (d, J = 1.9 Hz, 1H), 8.01 (dd, J = 8.9, 1.9 Hz, 1H), 7.99 (d, J = 8.9 Hz, 1H) 5.75 (q, J = 6.7 Hz, 1H), 2.08 (d, J = 6.7 Hz, 3 H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 166.4, 154.8, 149.7, 137.7, 131.4, 126.7, 123.4, 122.3, 52.7, 22.1

Melting point: 107-108˚C

HRMS (EI^+) calcd for $[C_{10}H_9BrClN_2]^+$ 270.9632, found 270.9642.

Preparation of compound **53**

To a solution of 4-ethyl-6-phenylquinazoline (0.030 g, 0.128 mmol) in 0.60 mL of CH_3CN (0.20 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (0.102 g, 0.256 mmol, 2.0 equiv.) and Li_2CO_3 (10.0 mg, 0.141 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to and maintained at 75 °C for 36 hours. Purification of the crude **53** by flash chromatography (pentanes: diethyl ether; 6:4) afforded **53** (20.9 mg, 49%).



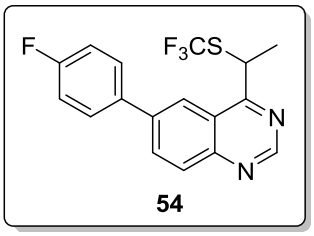
53

^{1}H-NMR (500 MHz, $CDCl_3$): δ 9.29 (s, 1H), 8.26 (d, J = 1.5 Hz, 1H), 8.21 (dd, J = 8.7, 1.5 Hz, 1H), 8.18 (d, J = 8.7 Hz, 1H) 5.42 (q, J = 7.0 Hz, 1H), 1.98 (d, J = 7.0 Hz, 3H); **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 168.7, 154.4, 150.1, 141.6, 139.7, 134.2, 131.2 (d, J = 307.6 Hz), 130.3, 129.4, 128.7, 127.7, 121.9, 121.1, 41.4, 22.9; **^{19}F-NMR** (470 MHz, $CDCl_3$): δ -40.3

HRMS (EI^+) calcd for $[C_{17}H_{14}F_3N_2S]^+$ 335.0824, found 335.0844

Preparation of compound **54**

To a solution of 4-ethyl-6-(4-fluorophenyl)quinazoline (0.030 g, 0.119 mmol) in 0.60 mL of CH_3CN (0.20 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (0.095 g, 0.240 mmol, 2.0 equiv.) and Li_2CO_3 (9.7 mg, 0.13 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to and maintained at 75 °C for 36 hours. Purification of the crude **54** by flash chromatography (pentanes: diethyl ether; 6:4) afforded **54** (33.3 mg, 79%).



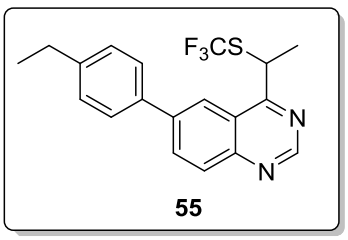
54

^{1}H-NMR (500 MHz, $CDCl_3$): δ 9.28 (s, 1H), 8.21 (d, J = 1.5 Hz, 1H), 8.19 (d, J = 8.6 Hz, 1H), 8.14 (dd, J = 8.6, 1.8 Hz, 1H), 7.67 (m, 2H), 7.24 (m, 2H) 5.40 (q, J = 7.0 Hz, 1H), 1.98 (d, J = 7.0 Hz, 3 H); **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 168.8, 160.3 (d, J = 248.5 Hz), 154.5, 150.1, 140.5, 135.8 (d, J = 2.8 Hz), 134.0, 131.1 (q, J = 307.2), 130.4, 129.4 (d, J =8.0 Hz), 121.9, 120.9, 116.4 (d, J = 21.7), 41.3, 22.9; **^{19}F-NMR** (470 MHz, $CDCl_3$): δ -40.3, -113.4

HRMS (EI^+) calcd for $[C_{17}H_{13}F_4N_2S]^+$ 353.0730, found 353.0711.

Preparation of compound **55**

To a solution of 4-ethyl-6-(4-ethylphenyl)quinazoline (0.030 g, 0.115 mmol) in 0.55 mL of CH_3CN (0.20 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (0.091 g, 0.230 mmol, 2.0 equiv.) and Li_2CO_3 (9.3 mg, 0.270 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to and maintained at 75 °C for 48 hours. Purification of the crude **55** by flash chromatography (pentanes: diethyl ether; 6:4) afforded **55** (28.3mg, 68%).



55

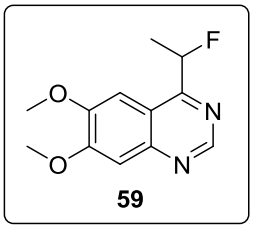
^{1}H-NMR (500 MHz, $CDCl_3$): δ 9.27 (s, 1H), 8.23 (d, J = 1.6 Hz, 1H), 8.20 (dd, J = 9.1, 1.8 Hz, 1H), 8.16 (d, J = 9.1 Hz, 1H), 7.63 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 5.41 (q, J = 7.0 Hz, 1H), 2.75 (q, J = 7.6 Hz, 2H), 1.98 (d, J = 7.0 Hz, 3H), 1.31 (t, J = 7.6Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$):

δ 168.2, 154.3, 150.0, 145.1, 141.5, 137.0, 134.2, 131.1 (q, J = 309.0 Hz), 130.2, 129.0, 127.6, 122.0, 120.7, 41.5, 28.7, 23.0, 15.7; **^{19}F-NMR** (470 MHz, $CDCl_3$): δ -40.3.

HRMS (EI^+) calcd for $[C_{19}H_{18}F_3N_2S]^+$ 363.1137, found 363.1119.

Preparation of compound **59**

Following General Procedure **A**, to a solution of quazodine (0.025 g, 0.115 mmol) in 1.2 mL of CH_3CN (0.10 M substrate) was added NFSI (0.044 g, 0.138 mmol, 1.2 equiv.) and Li_2CO_3 (10.0 mg, 0.127 mmol, 1.1 equiv.). The resulting reaction mixture was then left room temperature and maintained at this temperature for 120 hours. Purification of the crude **59** by flash chromatography (pentane-ethyl acetates; 1:1) afforded **59** (14.0 mg, 50%).



59

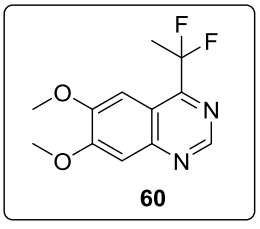
IR (neat): υ = 2957, 1617, 1501, 1233, 1133, 905, 729 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.12 (s, 1H), 7.56 (s, 1H), 7.38 (s, 1H), 6.15 (dq, J = 48.1, 6.6 Hz, 1H), 4.08 (s, 3H), 4.06 (s, 3H), 1.90 (dd, J = 24.2, 6.7 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 163.6 (d, J = 20.8 Hz), 156.1, 153.0, 150.5, 149.5, 118.2, 107.3, 102.2 (d, J = 9.2 Hz), 91.7 (d, J = 171.5 Hz), 56.6, 56.4, 20.5 (d, J = 23.2 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –174.1

HRMS (EI^+) calcd for $[C_{12}H_{14}FN_2O_2]^+$ 237.1034, found 237.1042

Melting point: 111-114˚C

Preparation of compound **60**

Following General Procedure **B**, to a solution of quazodine (0.025 g, 0.115 mmol) in 0.23 mL of CH_3CN (0.50 M substrate) was added NFSI (0.108 g, 0.344 mmol, 3.0 equiv.) and Li_2CO_3 (9.0 mg, 0.127 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 125 °C in a microwave reactor and maintained at this temperature for 1 hour. Purification of the crude **60** by flash chromatography (pentanes: ethyl acetate; 7:3) afforded **60** (17.8 mg, 62%).



60

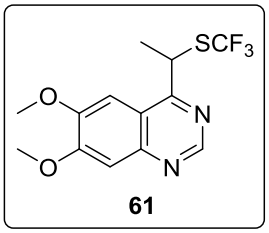
^{1}H-NMR (600 MHz, $CDCl_3$): δ 9.14 (s, 1H), 7.68 (s, 1H), 7.39 (s, 1H), 4.09 (s, 1H), 4.07 (s, 1H), 2.22 (t, J = 19.6 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$) δ 158.0 (t, J = 30.3 Hz), 156.4, 152.3, 150.9, 150.3, 123.5 (t, J = 239.9 Hz), 117.2, 107.1, 103.0, 56.6, 56.4, 22.7 (t, J = 25.5 Hz); **^{19}F-NMR** (470 MHz, $CDCl_3$): δ –85.3

HRMS (ESI^+) calcd for $[C_{12}H_{15}F_2N_2O_2]^+$ 255.0940, found 255.0949

Preparation of compound **61**

Following General Procedure **C**, to a solution of quazodine (0.025 g, 0.115 mmol) in 0.60 mL of CH_3CN (0.20 M substrate) was added *N*-trifluoromethylthiobenzenesulfonimide (0.108 g, 0.275 mmol, 2.4 equiv.) and Li_2CO_3 (9.0 mg, 0.127 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to

75 °C and maintained at this temperature for 48h. Purification of the crude **61** by flash chromatography (pentanes: ethyl acetate; 1:1) afforded **61** (34.0 mg, 94%).



61

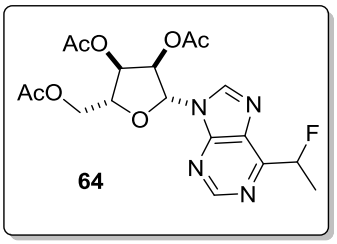
^{1}H-NMR (600 MHz, $CDCl_3$): δ 9.12 (s, 1H), 8.18 (s, 1H), 7.38 (s, 1H), 7.25 (s, 1H), 5.20, (q, J = 7.0, 1H), 4.08 (s, 3H), 4.08 (s, 3H), 1.96 (d, J = 6.9 Hz, 3H); **^{13}C-NMR** (150 MHz, MeOD): δ 164.7, 156.4, 153.4, 151.1, 149.0, 131.2 (q, J = 307.7 Hz), 117.5, 107.7, 100.7, 56.7, 56.4, 41.4, 22.4; **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –40.4

HRMS (EI$^+$) calcd for $[C_{13}H_{14}F_3N_2O_2S]^+$ 319.0723, found 319.0725

Melting point: 104-107˚C

Preparation of compound **64**

Following General Procedure **A**, to a solution of **63** (0.020 g, 0.049 mmol) in 0.20 mL of CH_3CN (0.25 M substrate) was added NFSI (0.047 g, 0.148 mmol, 3.0 equiv.) and Li_2CO_3 (4.0 mg, 0.054 mmol, 1.1 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. The yield for **64** (69%) was determined by analysis of a ^{1}H NMR spectrum (500 MHz, CD_3CN) using 4-fluorotoluene as an internal standard. Purification of the crude material by flash column chromatography (pentane-ethyl acetate; 25:75) provided an analytical sample of **64** as a 1:1 mixture of diastereomers.



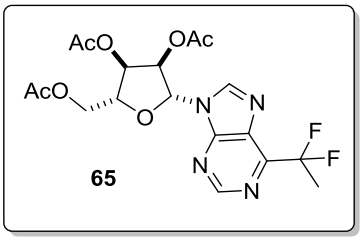
64

IR (neat): υ = 2971, 1748, 1592, 1223, 1057 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.00 (1H), 8.26 (1H), 6.25 (1H), 6.19 (1H), 5.98 (1H), 5.68 (1H), 4.48 (1H), 4.46 (1H), 4.39 (1H), 2.16 (3H), 2.12 (3H), 2.09 (3H), 1.88 (3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 170.4, 169.7, 169.5, 159.2, 152.8, 151.7, 143.4, 131.5, 88.4, 86.7, 80.6, 73.2, 70.7, 63.1, 20.9, 20.7, 20.7, 20.5; **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –180.2, 180.2.

HRMS (EI$^+$) calcd for $[C_{18}H_{22}FN_4O_7]^+$ 425.1467, found 425.1459

Preparation of compound **65**

Following General Procedure **B**, to a solution of **63** (0.010 g, 0.025 mmol) in 0.10 mL of CH_3CN (0.25 M substrate) was added NFSI (0.039 g, 0.123 mmol, 5.0 equiv.) and Li_2CO_3 (9.1 mg, 0.123 mmol, 5.0 equiv.). The resulting reaction mixture was then heated to 75 °C and maintained at this temperature for 48 hours. Purification of the crude **65** by flash chromatography (pentanes: ethyl acetate 25:75) afforded **65** (6.3 mg, 57%).



65

IR (neat): υ = 2952, 1749, 1590, 1224, 1133 cm^{-1}; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.05 (s, 1H), 8.35 (s, 1H), 6.28 (d, J = 5.1 Hz 1H), 5.98 (t, J =5.2, 5.2 Hz, 1H), 5.66 (dd, J = 5.1, 5.1 Hz, 1H), 4.49 (m, 1H), 4.46 (dd, J = 13.1, 1.8 Hz, 1H), 4.40 (dd, J = 13.1 Hz, 4.1 Hz, 1H), 2.20 (t, J = 18.8 Hz, 3H), 2.17 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ 170.3, 169.6, 169.3, 153.4 (t, J = 30.9 Hz), 152.7, 152.2, 144.3, 130.8,

120.0 (t, J = 239.6 Hz), 86.7, 80.5, 73.1, 70.6, 62.9, 23.4 (t, J = 25.9 Hz), 20.8, 20.5, 20.4; **^{19}F-NMR (**470 MHz, $CDCl_3$):δ –90.9.

HRMS (EI^+) calcd for $[C_{18}H_{21}F_2N_4O_7]^+$ 443.1373, found 443.1370

Radiochemistry

Production of $[^{18}F]F_2$ gas

$[^{18}F]F_2$ gas was produced on TRIUMF's TR13 cyclotron via the $^{18}O(p,n)^{18}F$ nuclear reaction in an aluminum-body target using two proton irradiations. First $[^{18}O]O_2$ was loaded into the target to ~270 psi and irradiated with 25 μA of 13 MeV protons for 5-10 minutes. The gas was removed under reduced pressure and cryogenically trapped for recycling. F_2 gas (3 % in Ar) was filled into the target to 14 psi and topped with Ar to 290 psi. The target was then irradiated for 2-5 min with 20 μA of 13 MeV protons. The target was emptied to the chemistry lab carried by Ar.

Synthesis of $[^{18}F]$*N*-fluorodibenzenesulfonamide ($[^{18}F]$NFSI)

Sodium dibenzenesulfonamide (40 mg, 125 μmol) was dissolved in 1 mL of 4:1 CH_3CN:H_2O and placed in a conical vial. $[^{18}F]F_2$ produced in the cyclotron target was then passed through the solution over a period of ~10 min. The waste gas was trapped by saturated KI solution. Typically 3-4 GBq was trapped in the reaction mixture. The resulting solution was then passed through a SepPak (Waters tC18 SepPak Plus Long Cartridge). The cartridge was washed with 10 mL H_2O followed by 600 μL CH_3CN. $[^{18}F]$NFSI was then eluted from the SepPak cartridge in 2.4 mL CH_3CN. Typically, 50 ± 8 μmol of purified NFSI with an activity of 0.3-0.5 GBq is produced from this process. The amount of NFSI generated in each reaction was calculated following HPLC analysis of the reaction mixture and comparison with a calibration curve prepared from NFSI.

Synthesis of $[^{18}F]$ 67

The $[^{18}F]$NFSI solution was concentrated under vacuum at 75 °C, then 360 μL CH_3CN was added. The mixture of **66** (6.70 mg, 50 μmol), Li_2CO_3 (4.2 mg, 57 μmol) and $[^{18}F]$NFSI (180 μL CH_3CN solution) were place in a 5 mL conical vial and reacted at 75 °C for 40 min. After this time, a fraction of the resulting mixture was subjected to HPLC analysis to get the radiochemical conversion (RCC). Analytical HPLC was

carried out on a Phenomenex Luna C18 (4.6 x 100 mm, 1 mL/min) using a gradient of 100% solvent A (0.1% TFA in H_2O) to 100% solvent B (0.1% TFA in CH_3CN) over 15 min. A fraction of 15 µL reaction mixture was used for the purification, the mixture was subjected to semi-preparatory HPLC purification. Semi-preparatory HPLC condition: Phenomenex Luna C18 (4.6 x 100 mm, 1 mL/min) using a gradient of 100% solvent A (0.1% TFA in H_2O) to 100% solvent B (0.1% TFA in CH_3CN) over 15 min. The radiochemical yield (RCY) is reported as a percentage and represents the total activity present in the purified ^{18}F-labeled **62** divided by the total activity present in the purified [^{18}F]NFSI x 100 (decay corrected).

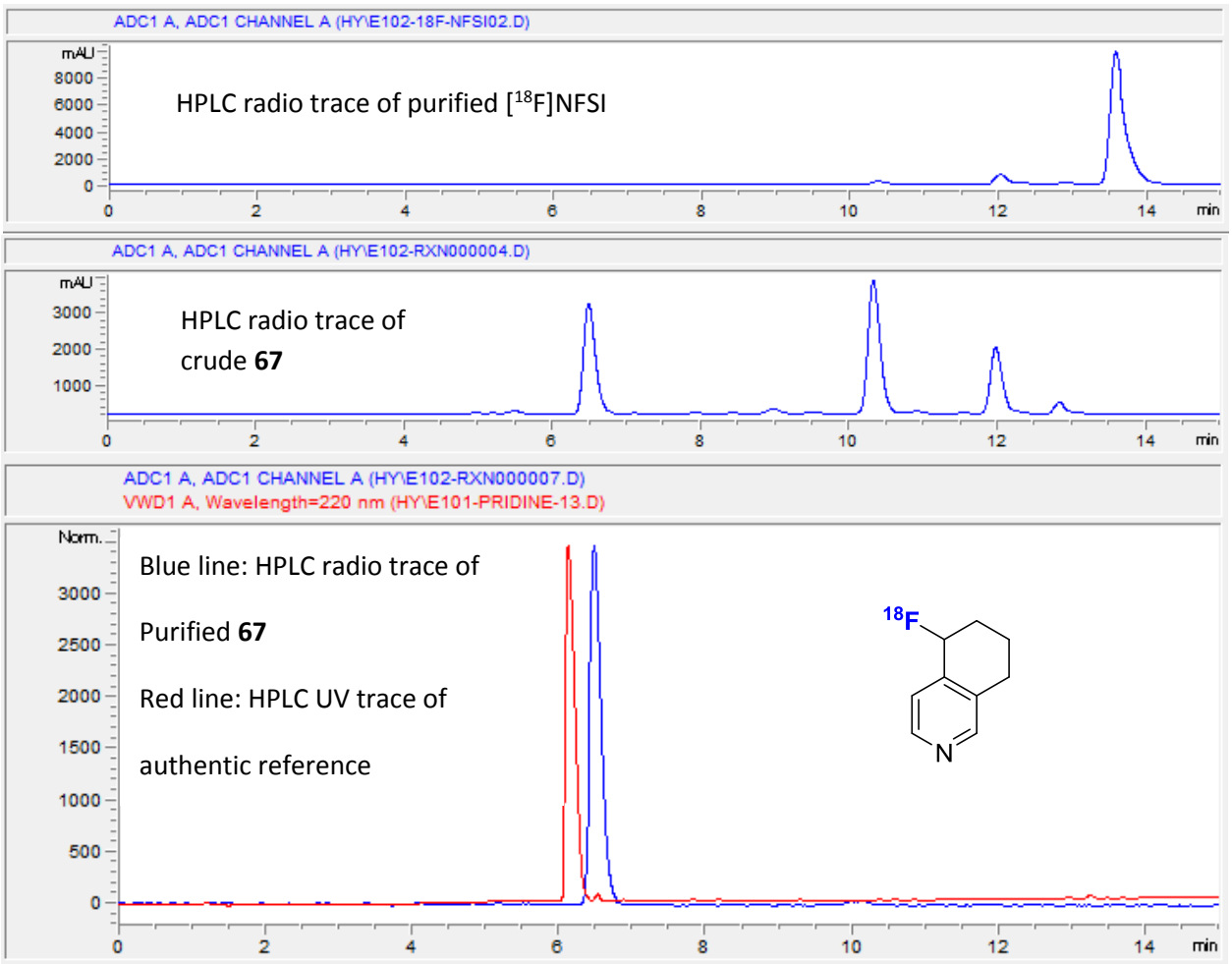
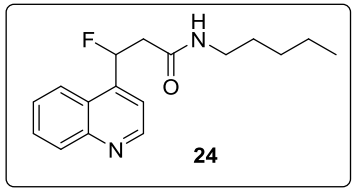
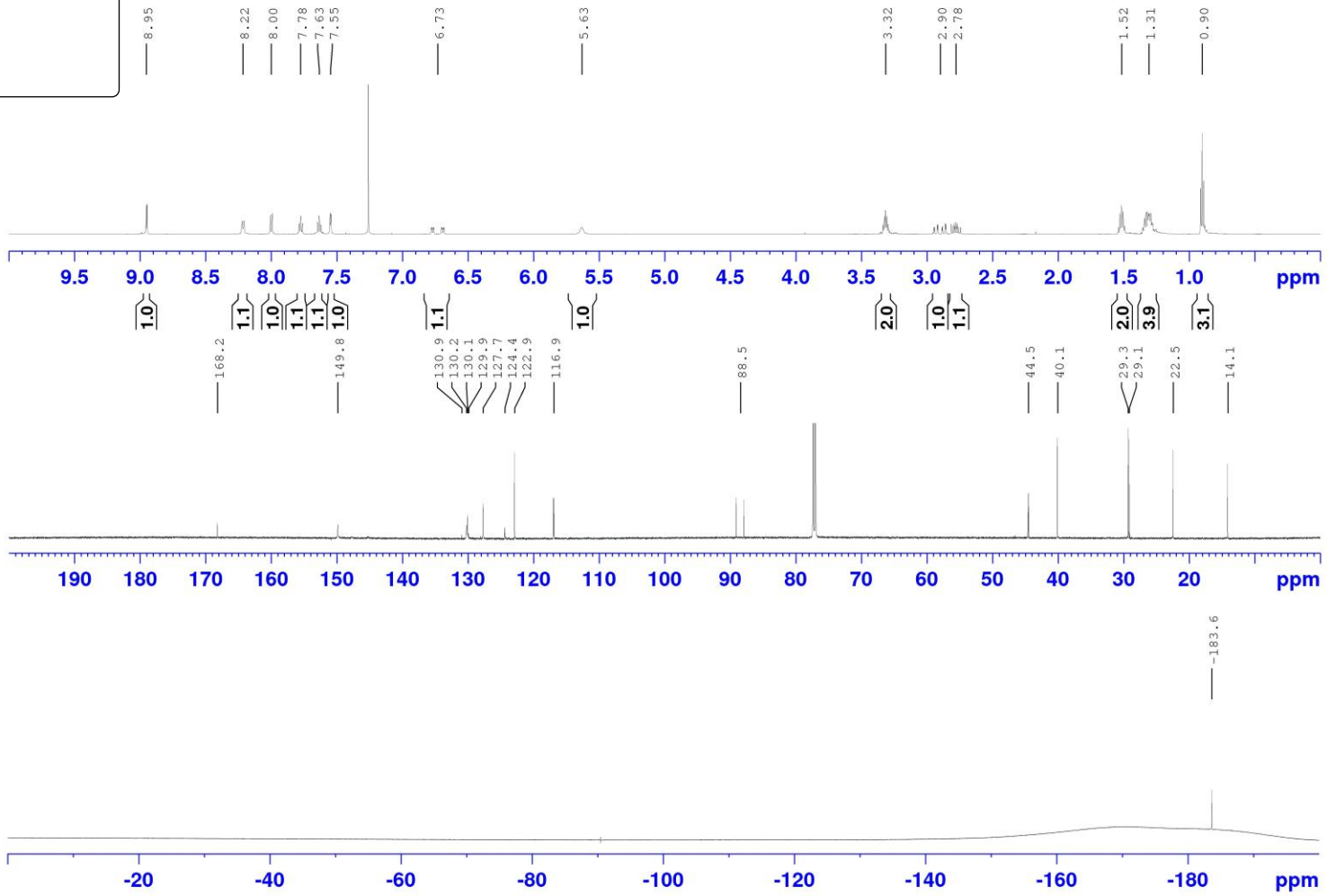


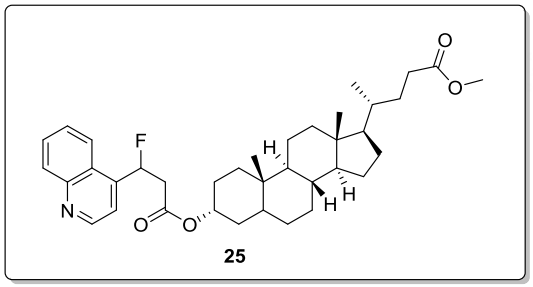
Figure S1: HPLC radio trace of purified [^{18}F]NFSI (top), HPLC radio trace of crude (middle) and HPLC radio trace of purified **67** (bottom, blue line) overlaid with HPLC UV trace (220 nm) of authentic reference (bottom, red line).

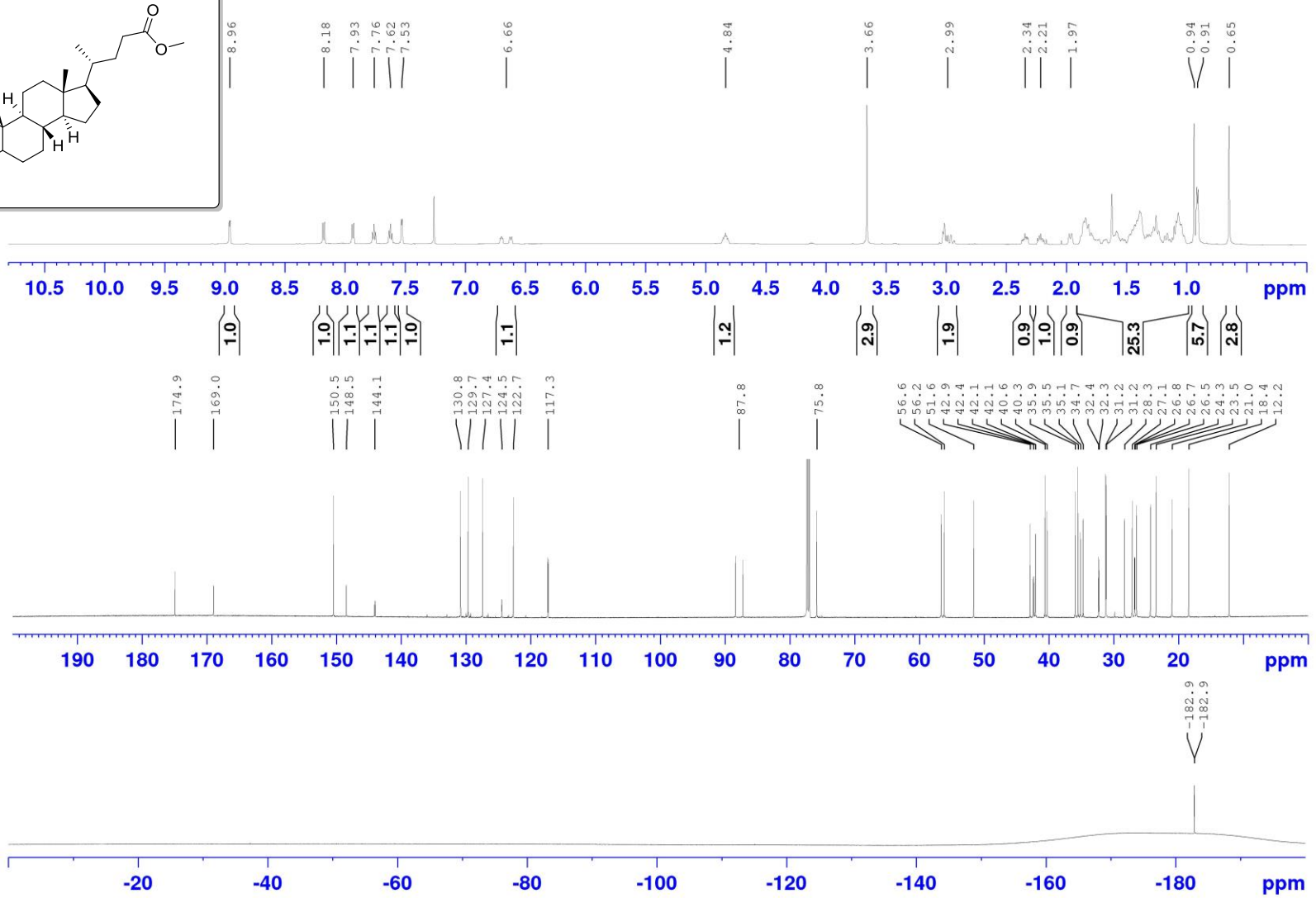
^{1}H, ^{13}C and ^{19}F NMR spectra of **24** recorded in $CDCl_3$ on a 600 MHz spectrometer



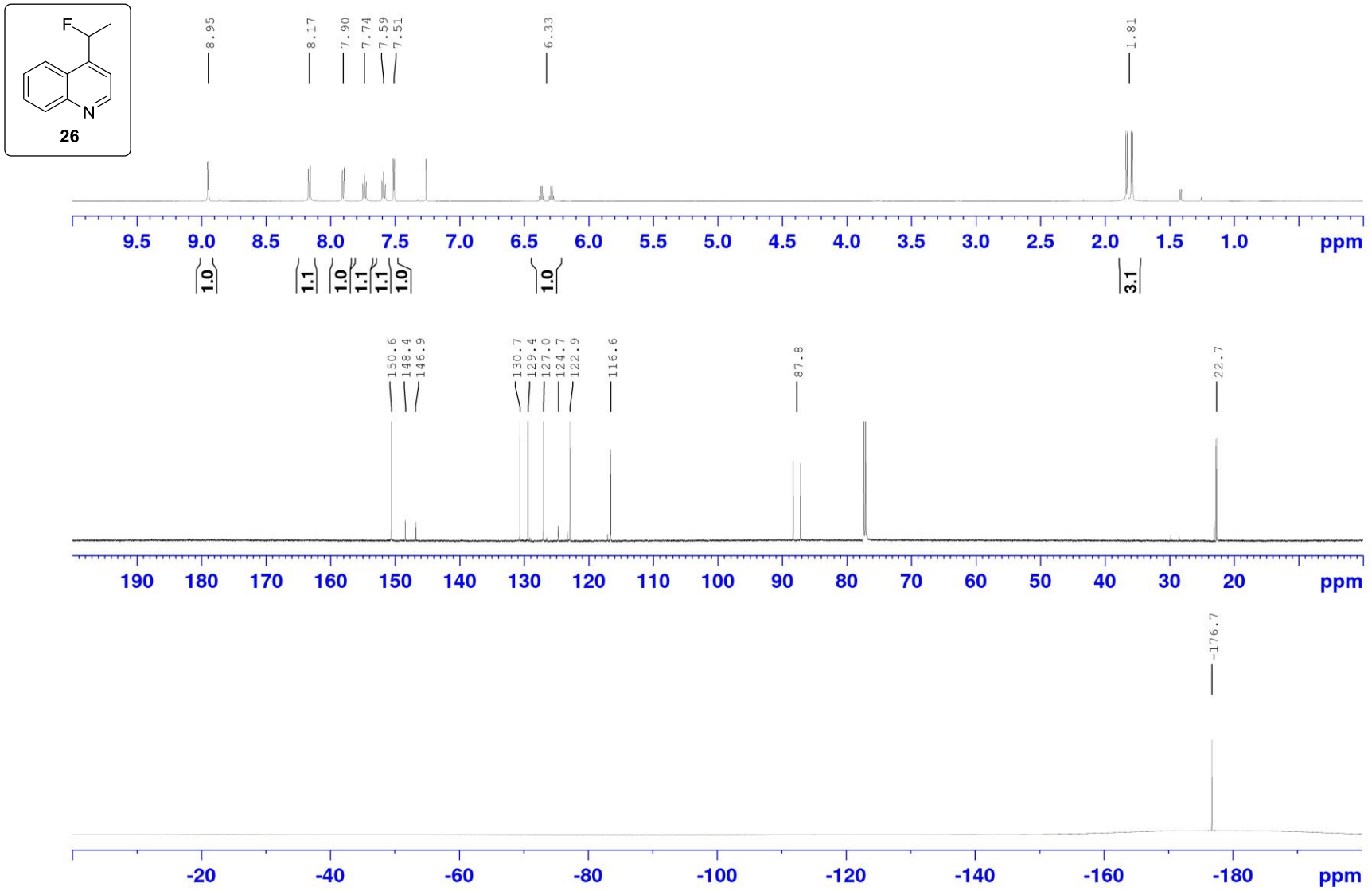


^{1}H, ^{13}C and ^{19}F NMR spectra of **25** (1:1 mixture of diastereomers) recorded in $CDCl_3$ on a 600 MHz spectrometer

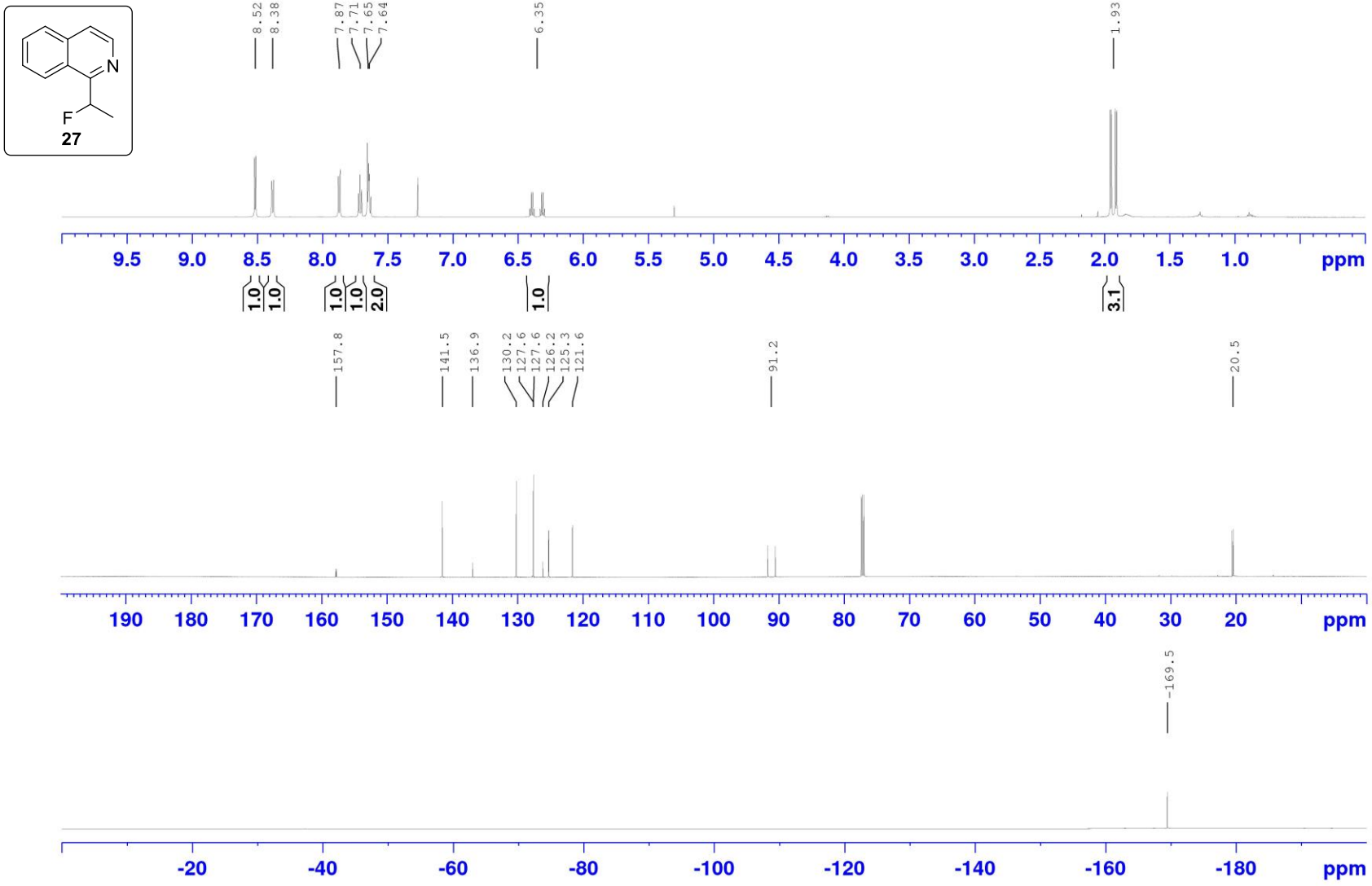




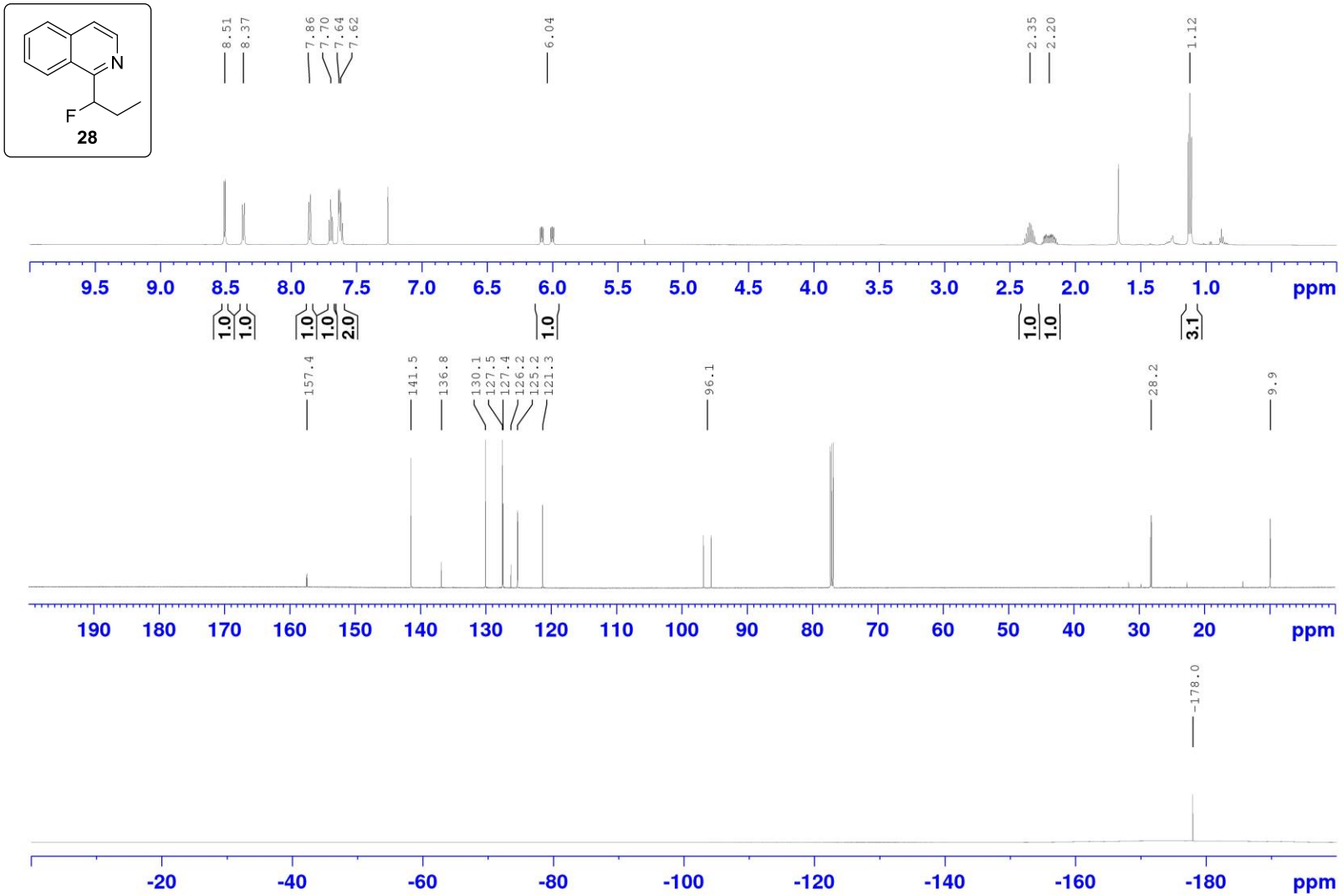
^{1}H, ^{13}C and ^{19}F NMR spectra of **26** recorded in $CDCl_3$ on a 600 MHz spectrometer



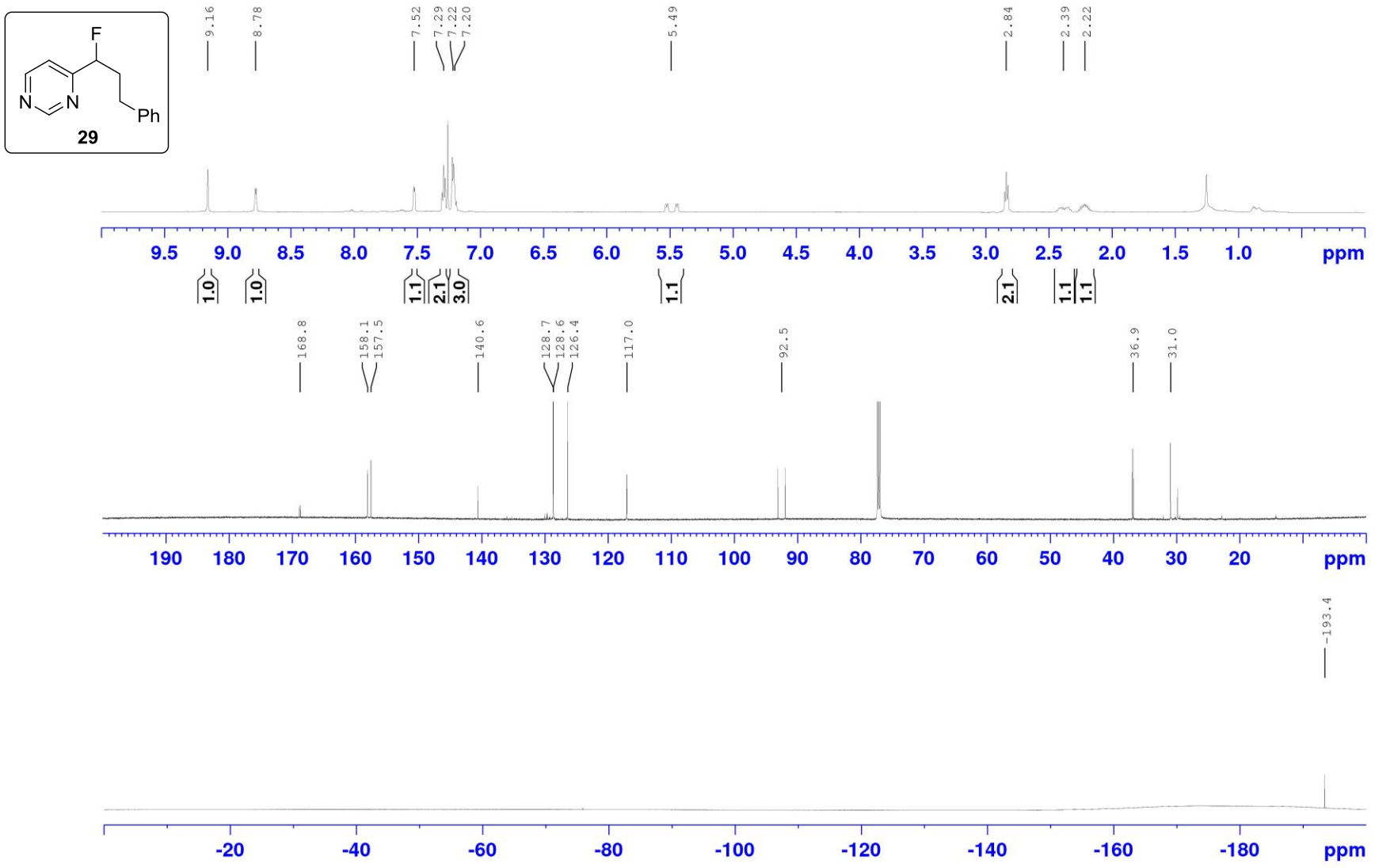
^{1}H, ^{13}C and ^{19}F NMR spectra of **27** recorded in $CDCl_3$ on a 600 MHz spectrometer



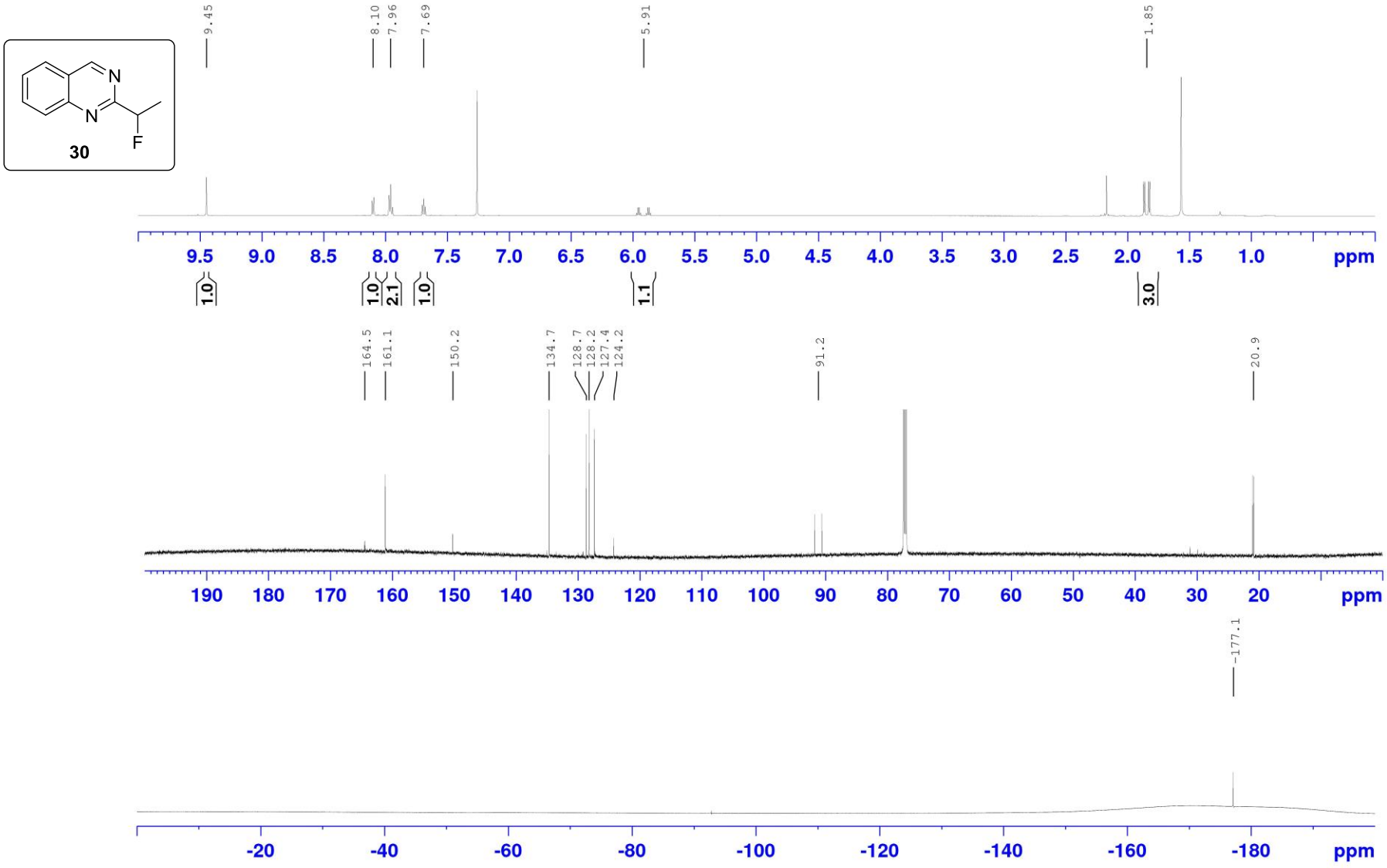
^{1}H, ^{13}C and ^{19}F NMR spectra of **28** recorded in $CDCl_3$ on a 600 MHz spectrometer



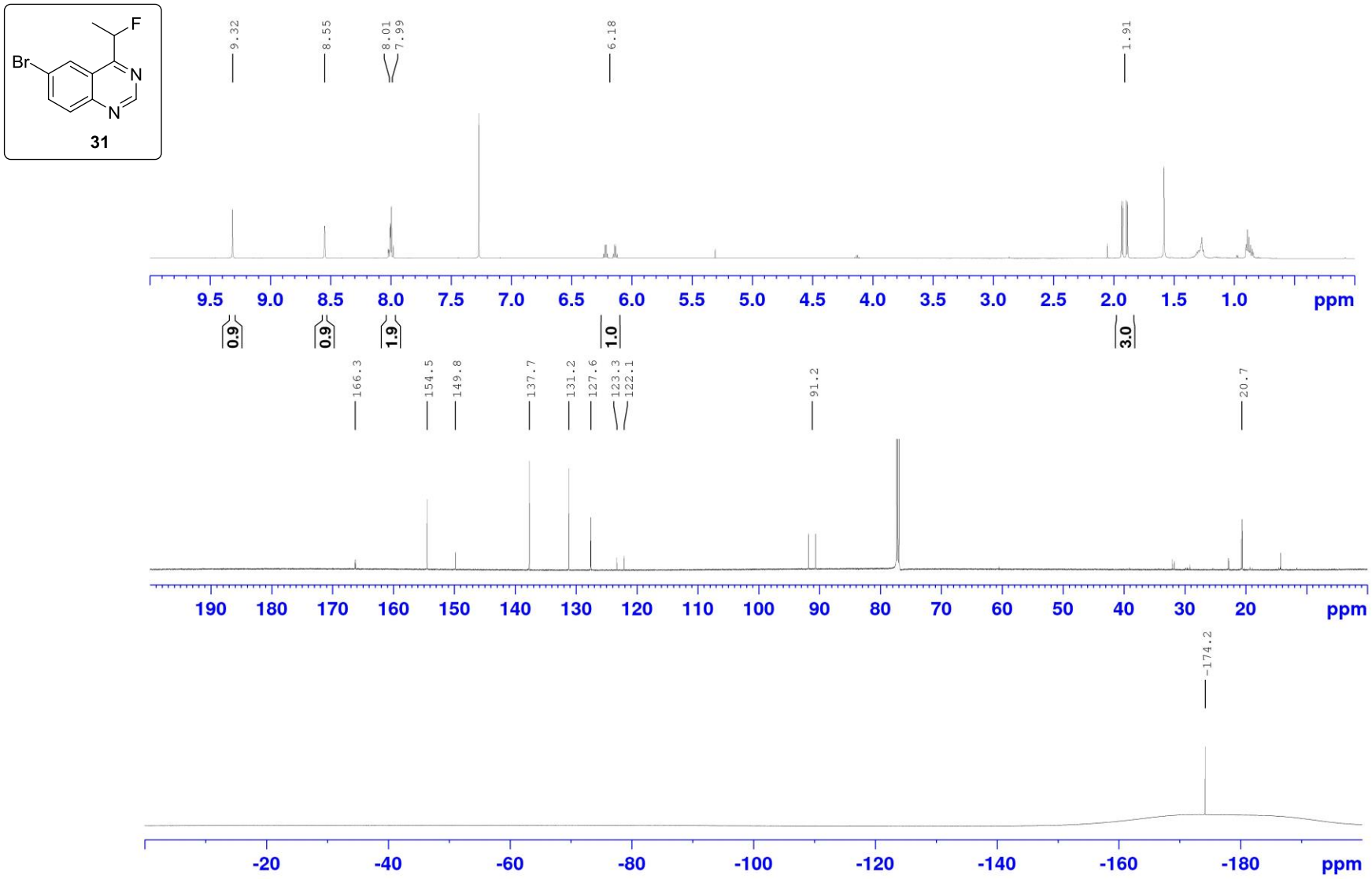
^{1}H, ^{13}C and ^{19}F NMR spectra of **29** recorded in $CDCl_3$ on a 600 MHz spectrometer



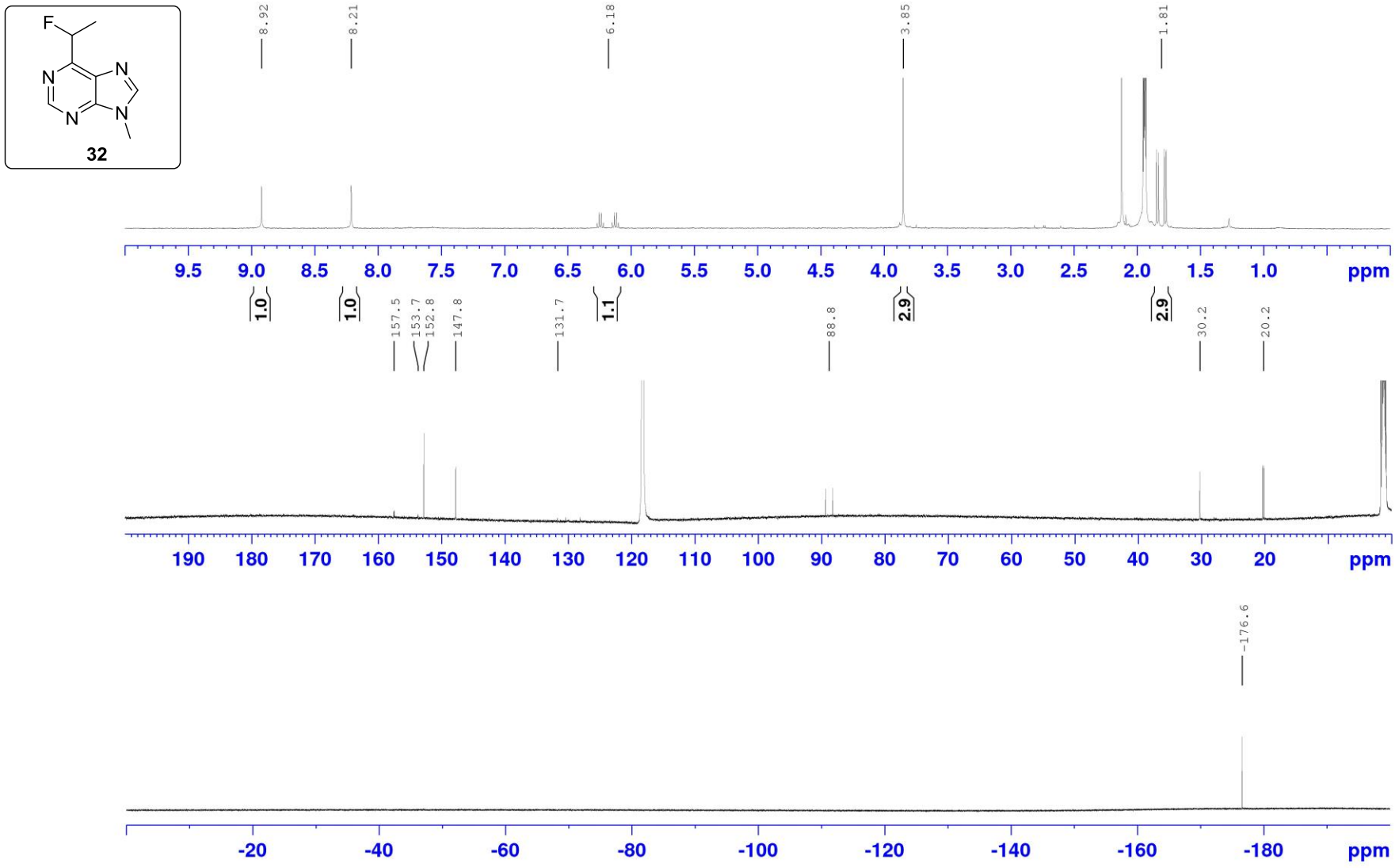
^{1}H, ^{13}C and ^{19}F NMR spectra of **30** recorded in $CDCl_3$ on a 600 MHz spectrometer



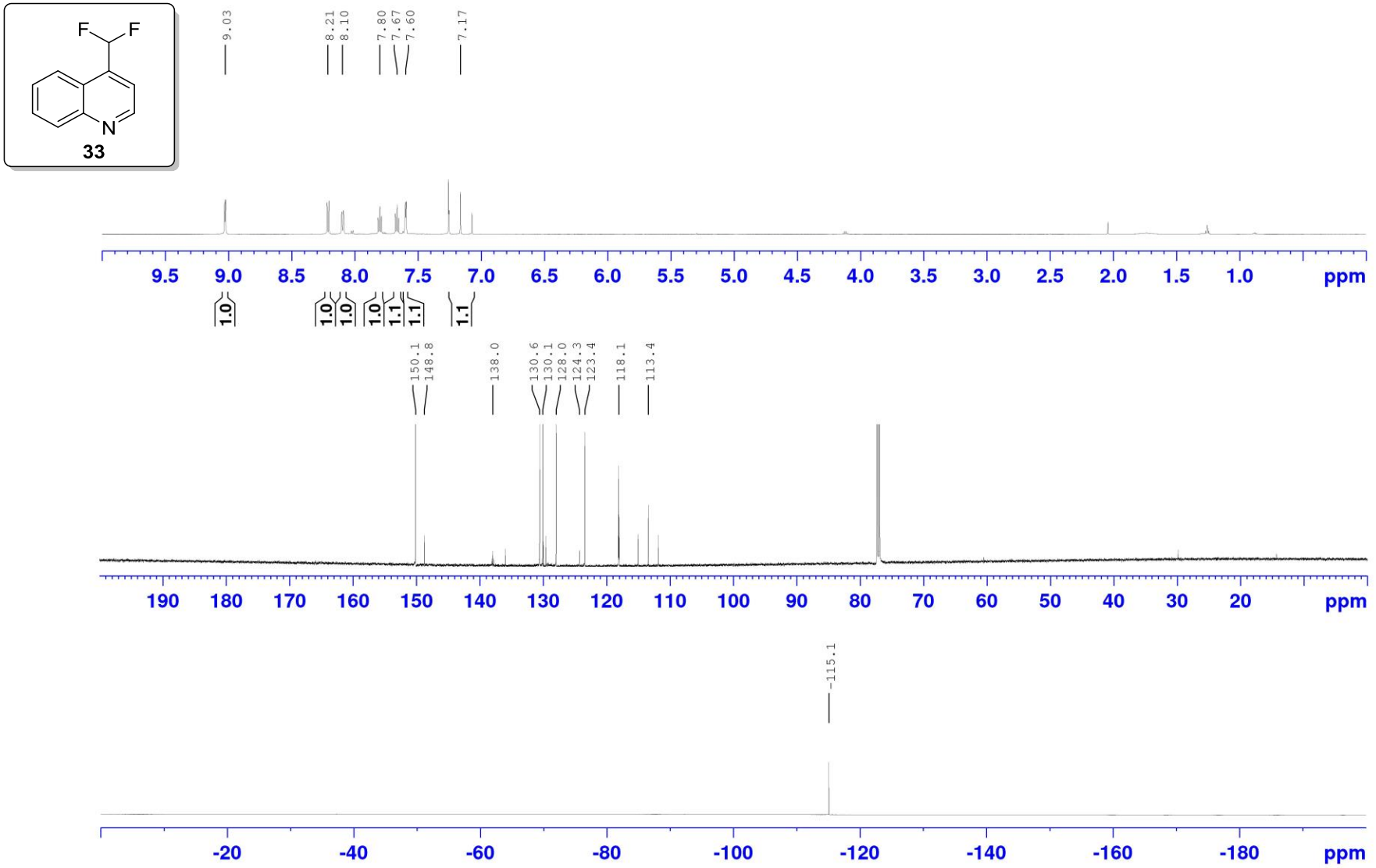
^{1}H, ^{13}C and ^{19}F NMR spectra of **31** recorded in $CDCl_3$ on a 600 MHz spectrometer



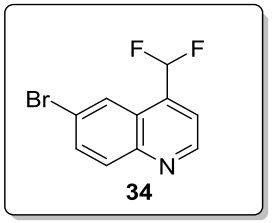
^{1}H, ^{13}C and ^{19}F NMR spectra of **32** recorded in CD_3CN on a 600 MHz spectrometer



^{1}H, ^{13}C and ^{19}F NMR spectra of **33** recorded in $CDCl_3$ on a 600 MHz spectrometer



^{1}H, ^{13}C and ^{19}F NMR spectra of **34** recorded in $CDCl_3$ on a 600 MHz spectrometer



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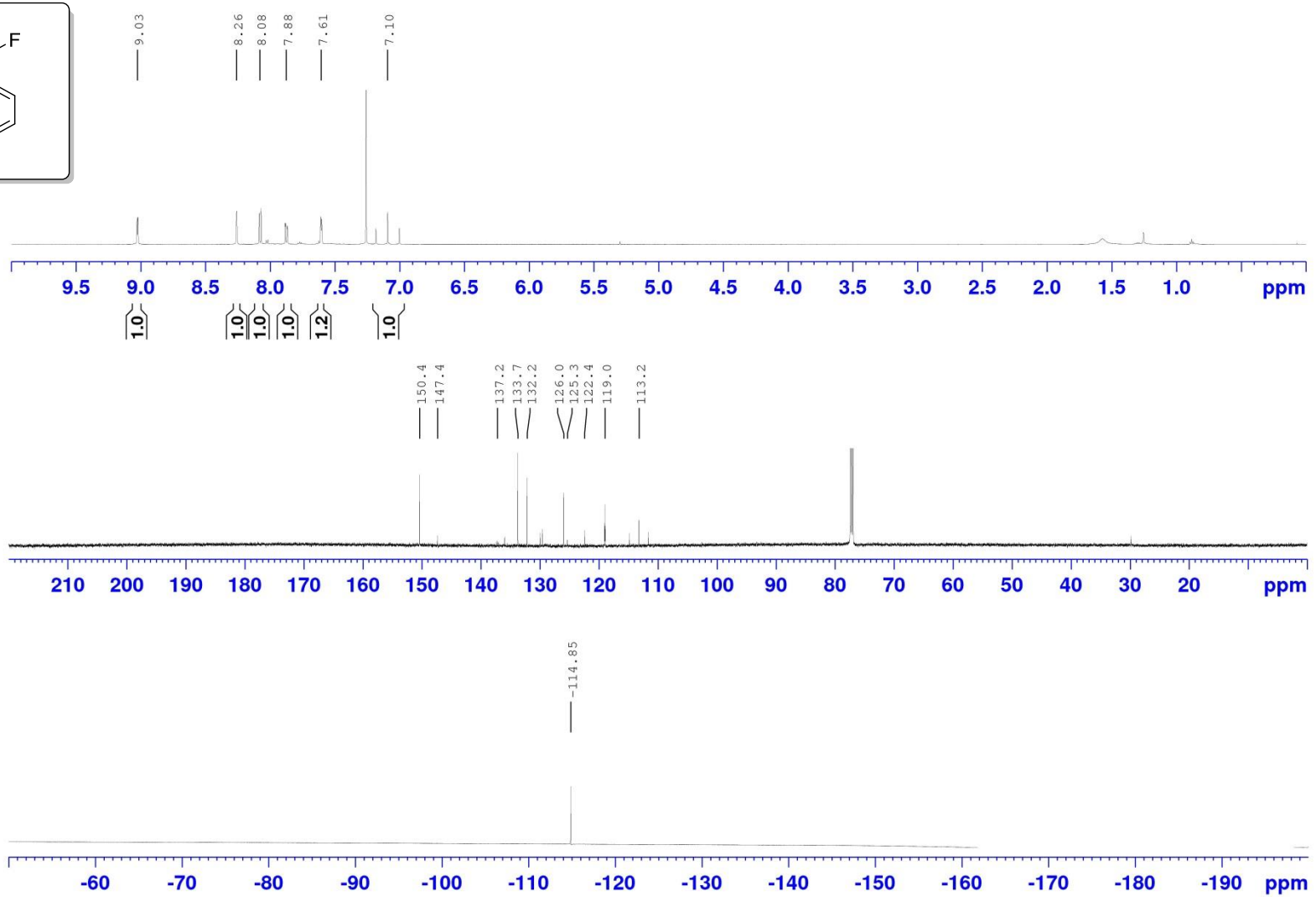
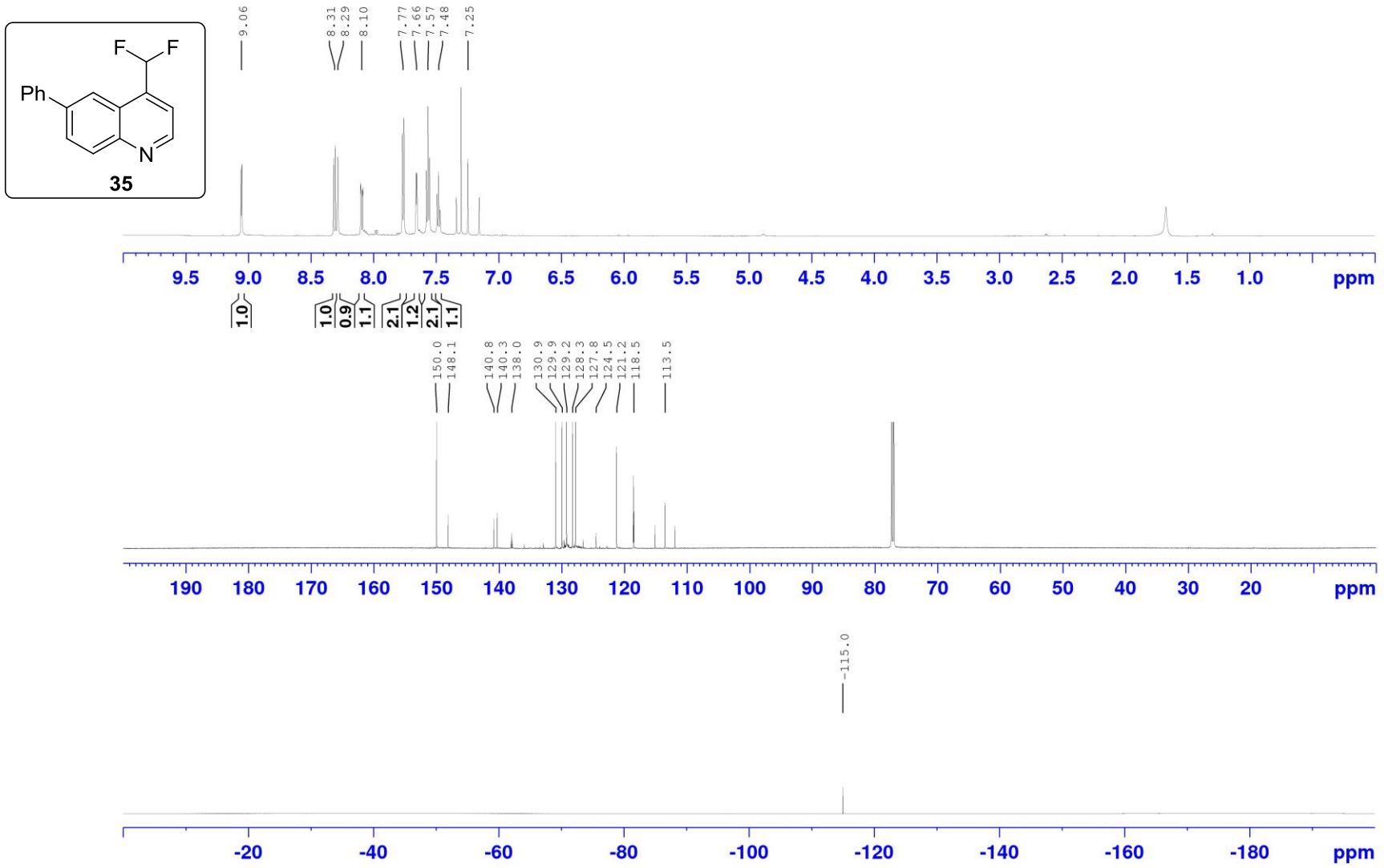
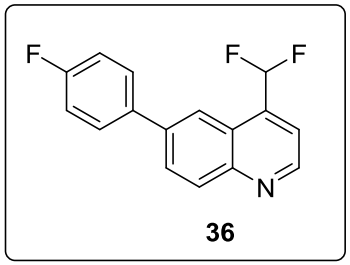


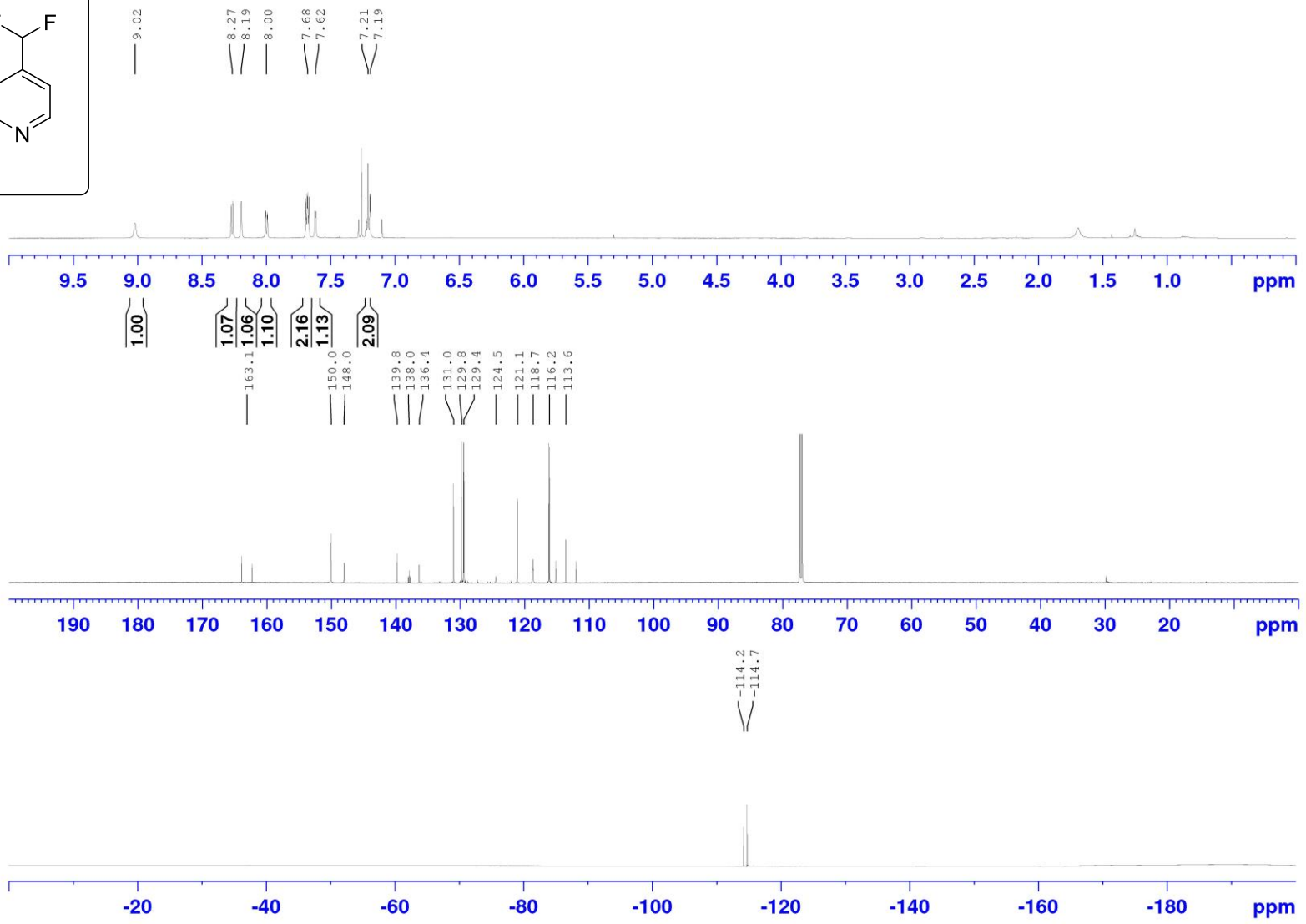
^{1}H, ^{13}C and ^{19}F NMR spectra of **35** recorded in $CDCl_3$ on a 600 MHz spectrometer



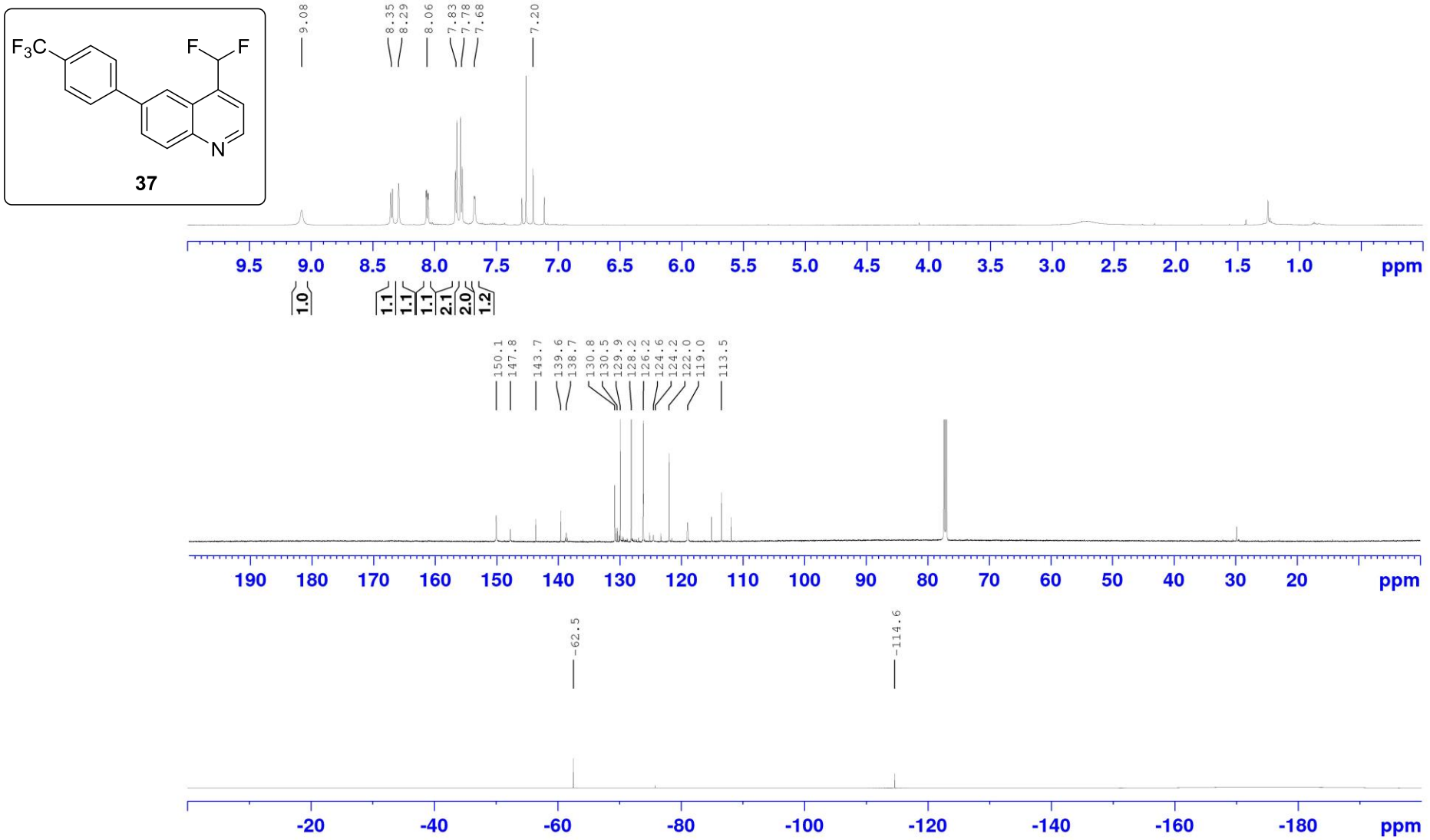
^{1}H, ^{13}C and ^{19}F NMR spectra of **36** recorded in $CDCl_3$ on a 600 MHz spectrometer



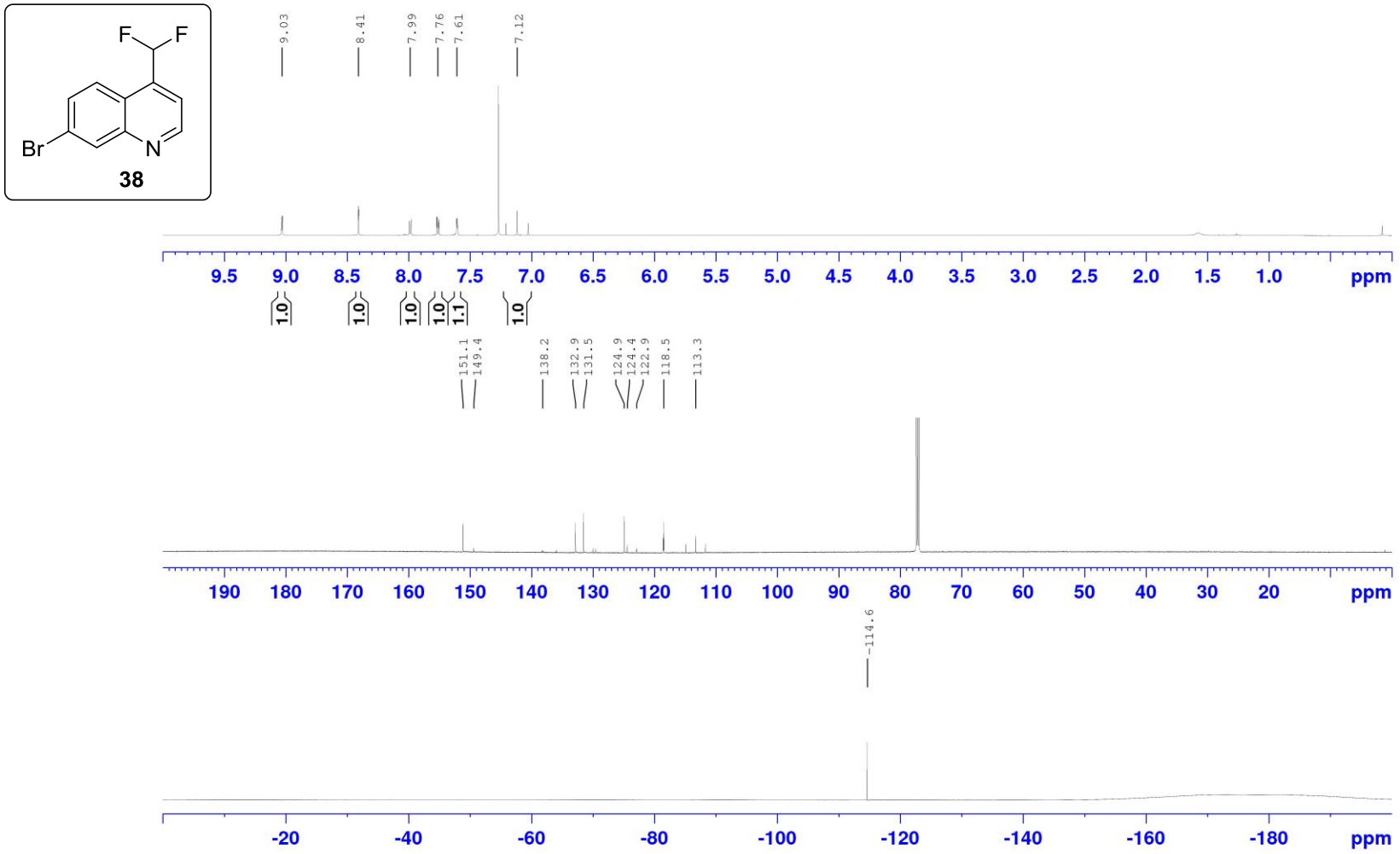
36



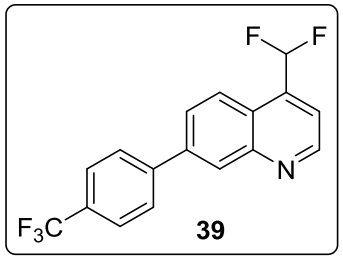
^{1}H, ^{13}C and ^{19}F NMR spectra of **37** recorded in $CDCl_3$ on a 600 MHz spectrometer

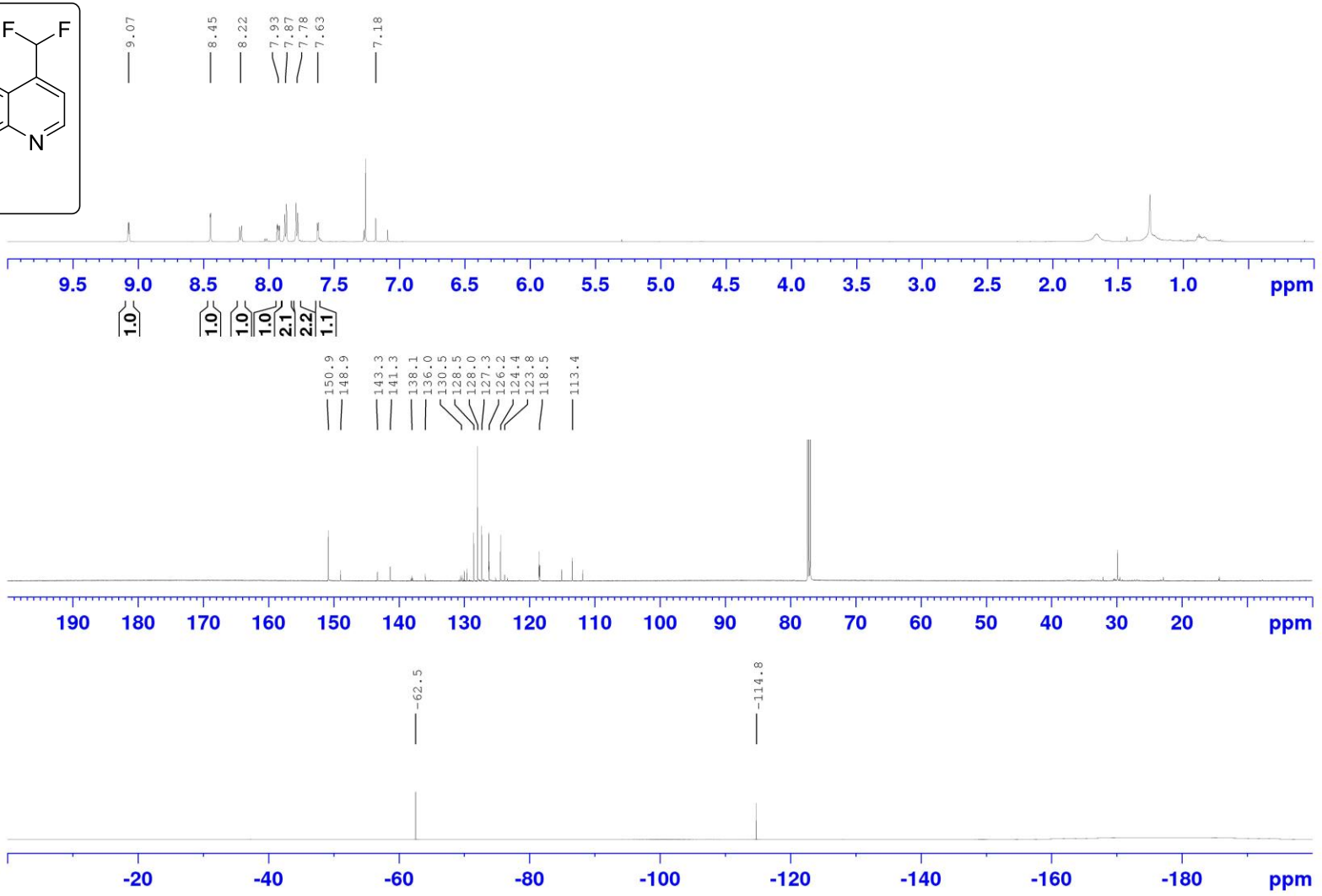


^{1}H, ^{13}C and ^{19}F NMR spectra of **38** recorded in $CDCl_3$ on a 600 MHz spectrometer

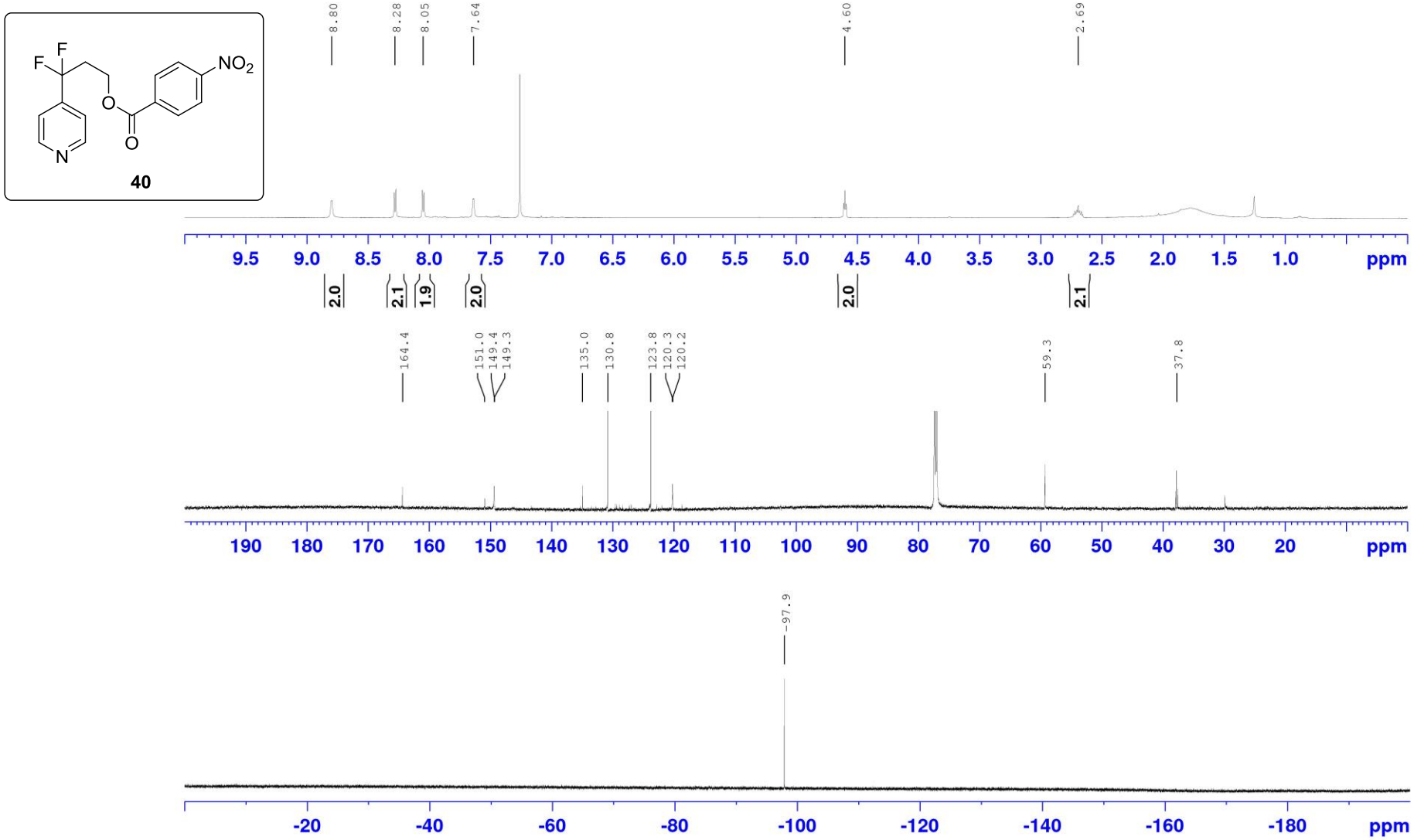


^{1}H, ^{13}C and ^{19}F NMR spectra of **39** recorded in $CDCl_3$ on a 600 MHz spectrometer

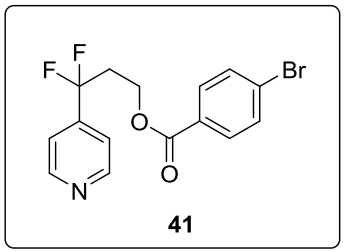




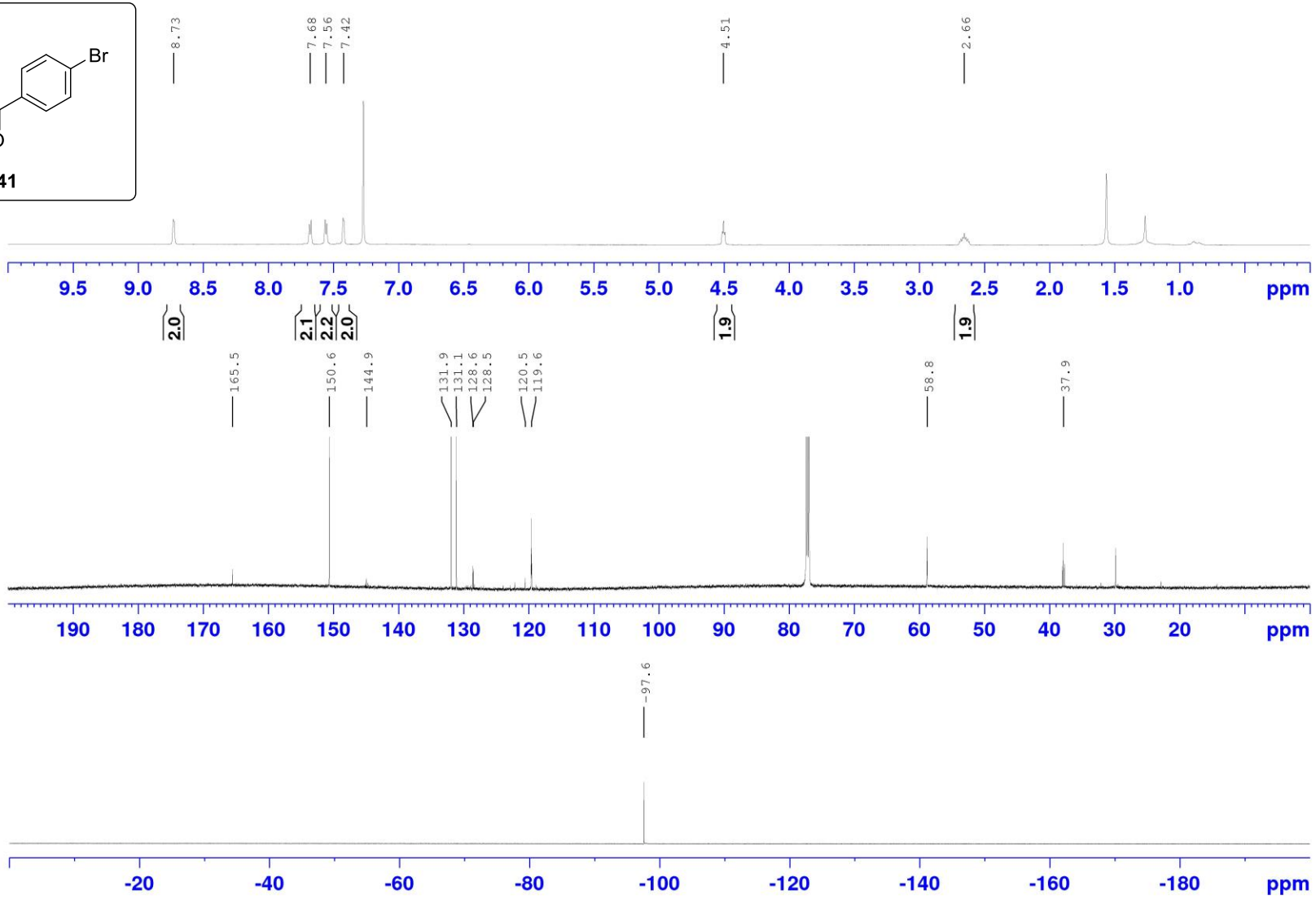
^{1}H, ^{13}C and ^{19}F NMR spectra of **40** recorded in $CDCl_3$ on a 600 MHz spectrometer



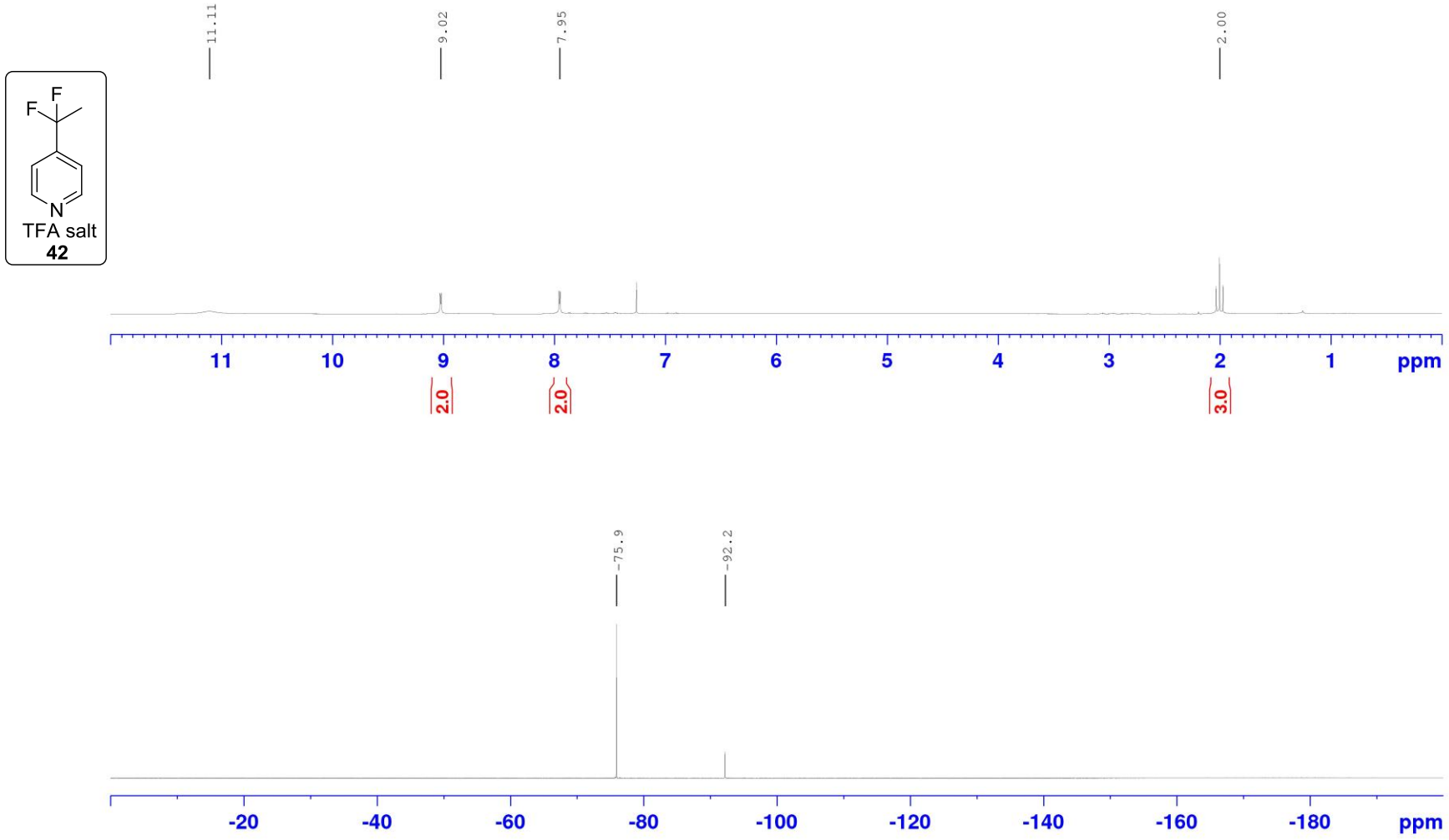
^{1}H, ^{13}C and ^{19}F NMR spectra of **41** recorded in $CDCl_3$ on a 600 MHz spectrometer



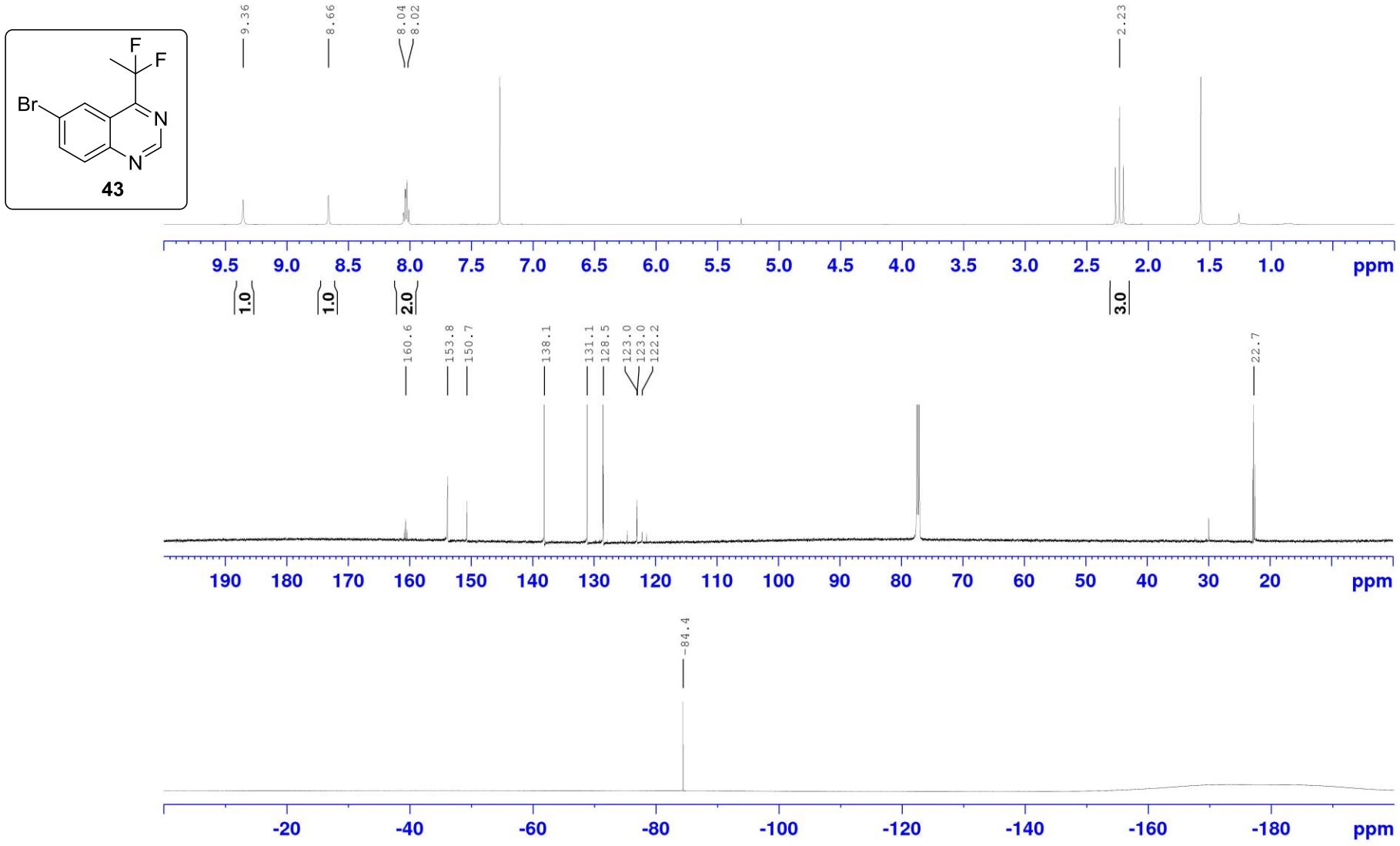
41



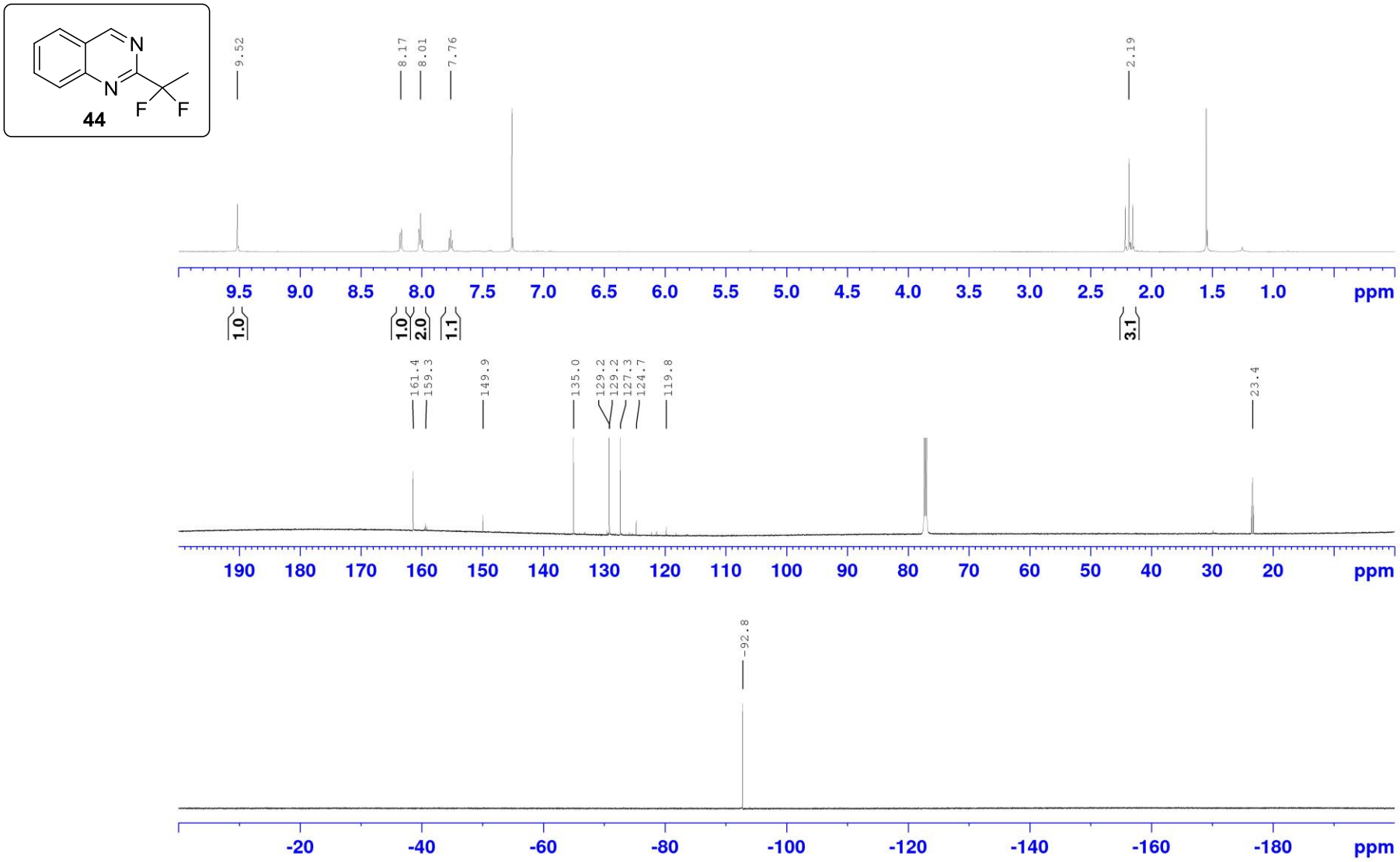
^{1}H and ^{19}F NMR spectra of **42** recorded in $CDCl_3$ on a 600 MHz spectrometer



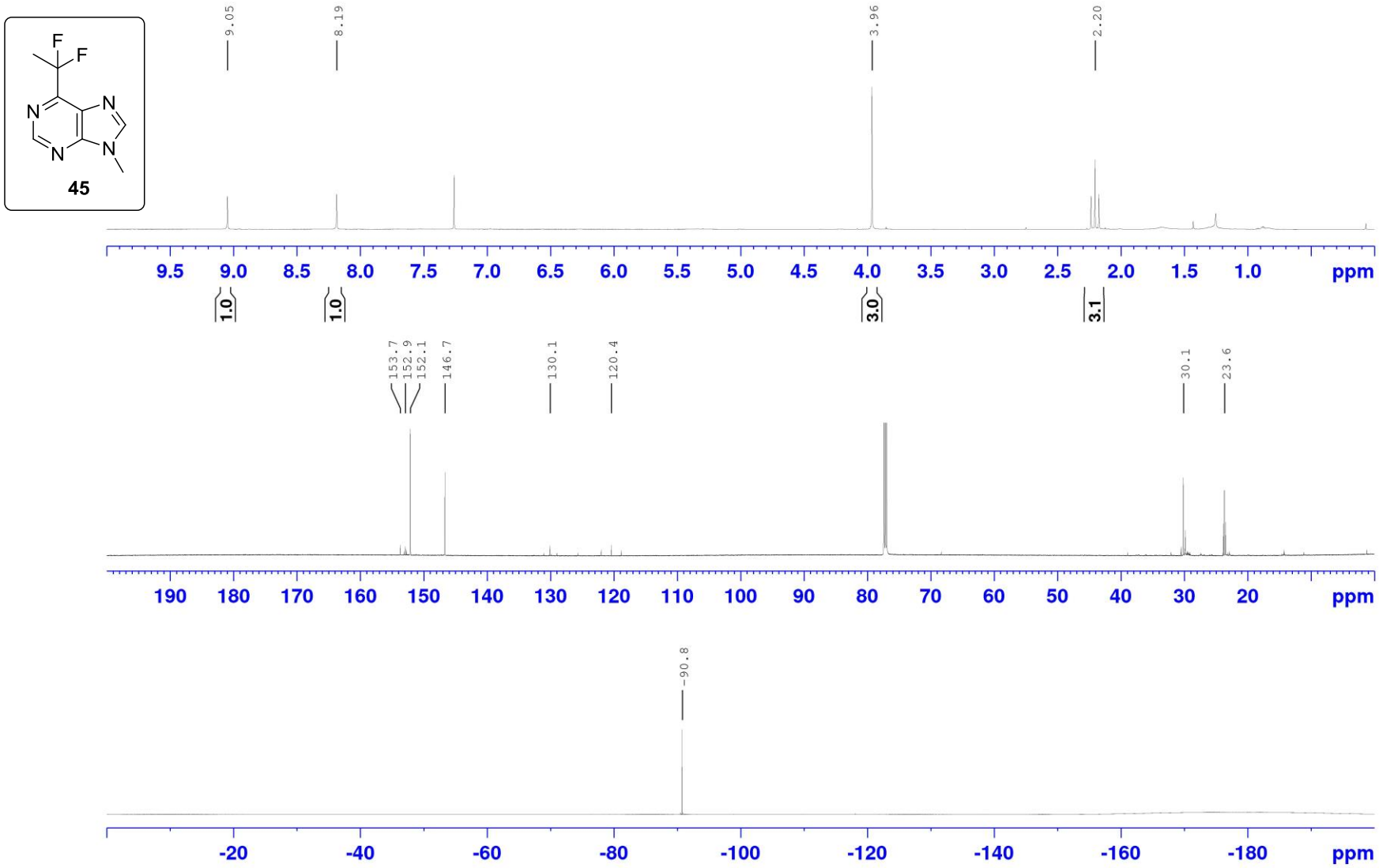
^{1}H, ^{13}C and ^{19}F NMR spectra of **43** recorded in $CDCl_3$ on a 600 MHz spectrometer



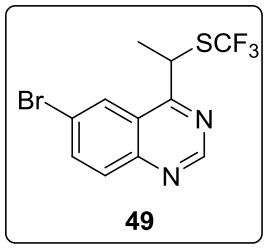
^{1}H, ^{13}C and ^{19}F NMR spectra of **44** recorded in $CDCl_3$ on a 600 MHz spectrometer



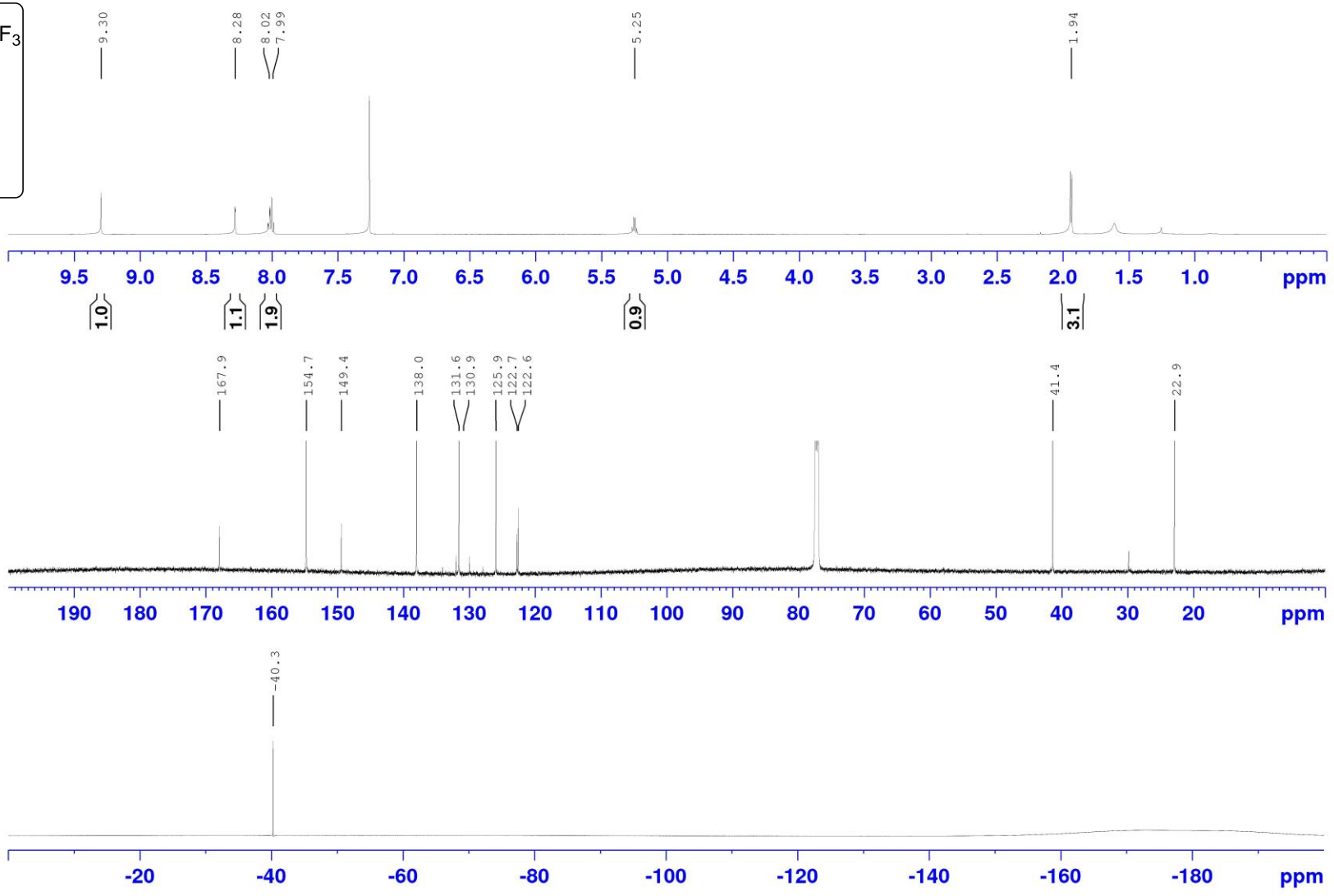
^{1}H, ^{13}C and ^{19}F NMR spectra of **45** recorded in $CDCl_3$ on a 600 MHz spectrometer



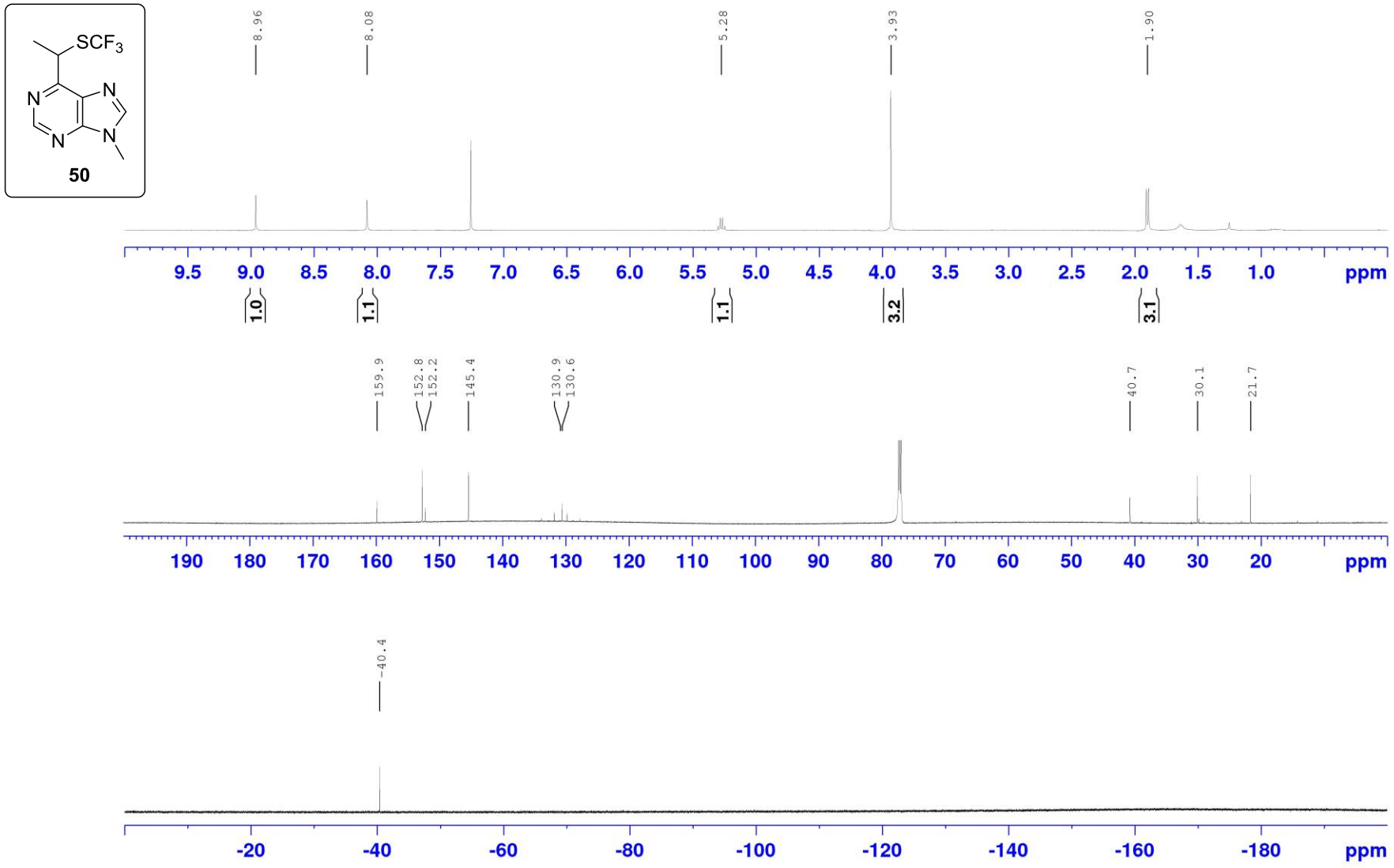
^{1}H, ^{13}C and ^{19}F NMR spectra of **49** recorded in $CDCl_3$ on a 600 MHz spectrometer



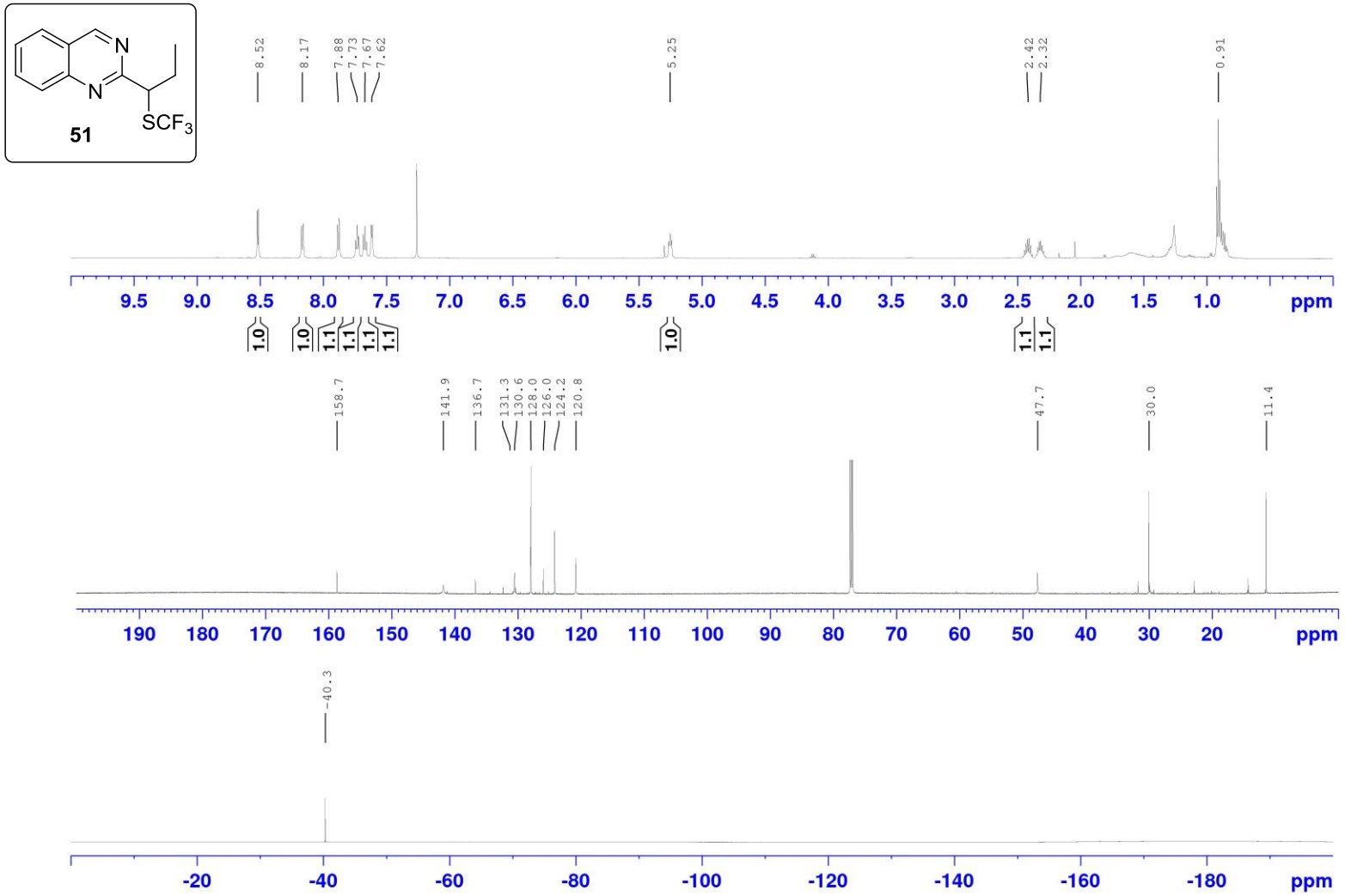
49



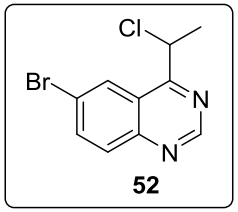
^{1}H and ^{13}C NMR spectra of **50** recorded in $CDCl_3$ on a 600 MHz spectrometer



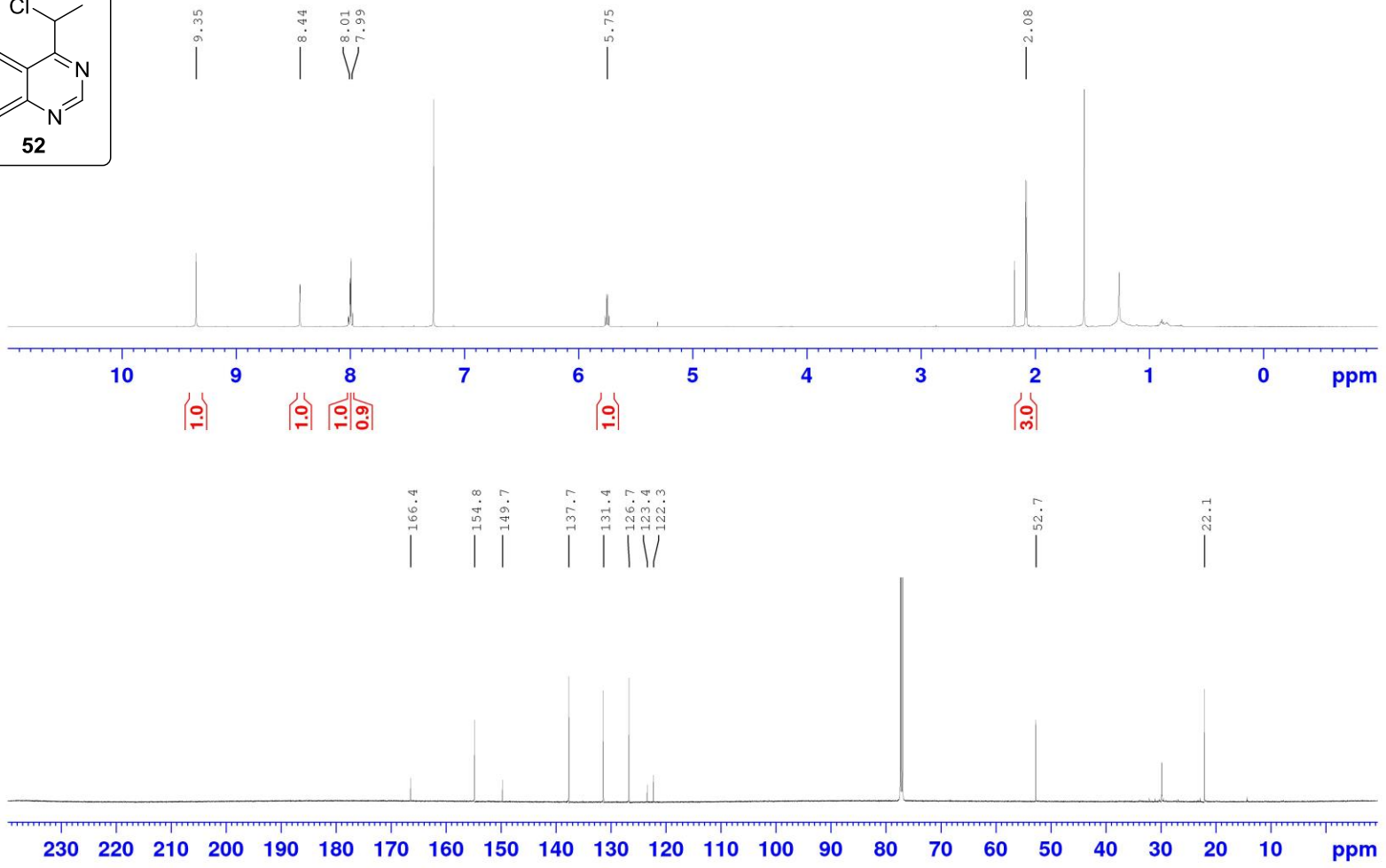
^{1}H and ^{13}C NMR spectra of **51** recorded in $CDCl_3$ on a 600 MHz spectrometer



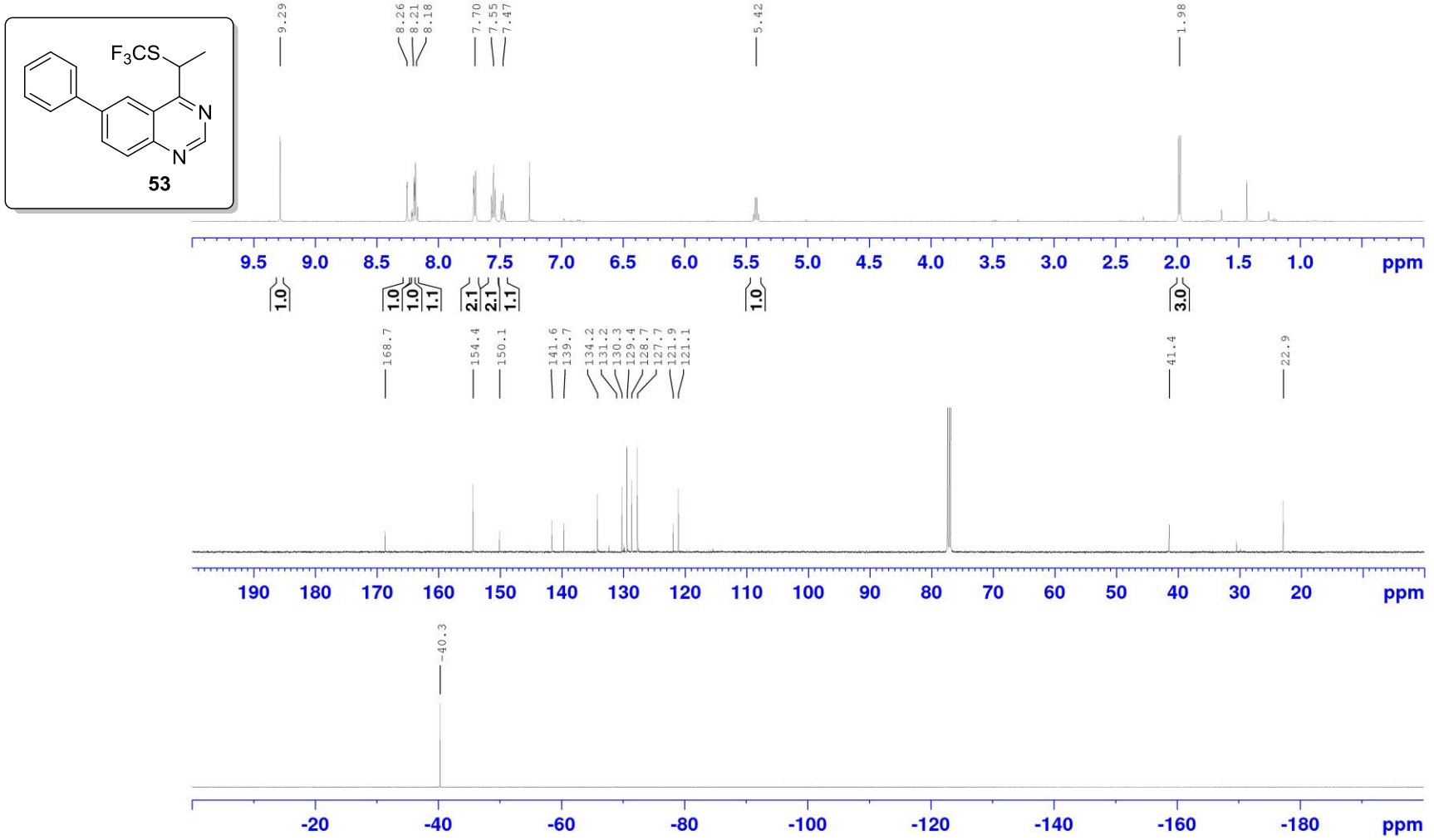
^{1}H and ^{13}C NMR spectra of **52** recorded in $CDCl_3$ on a 600 MHz spectrometer



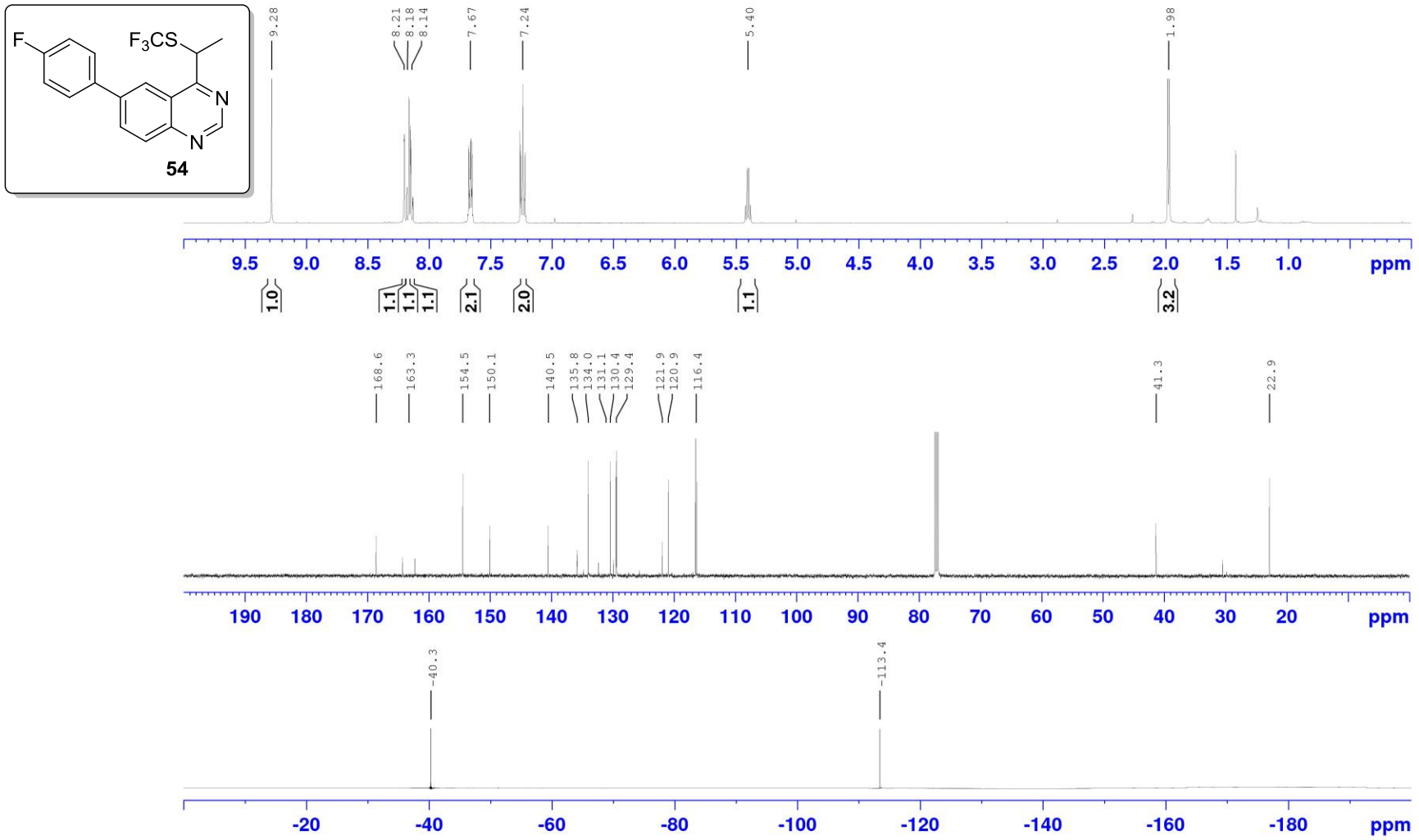
52



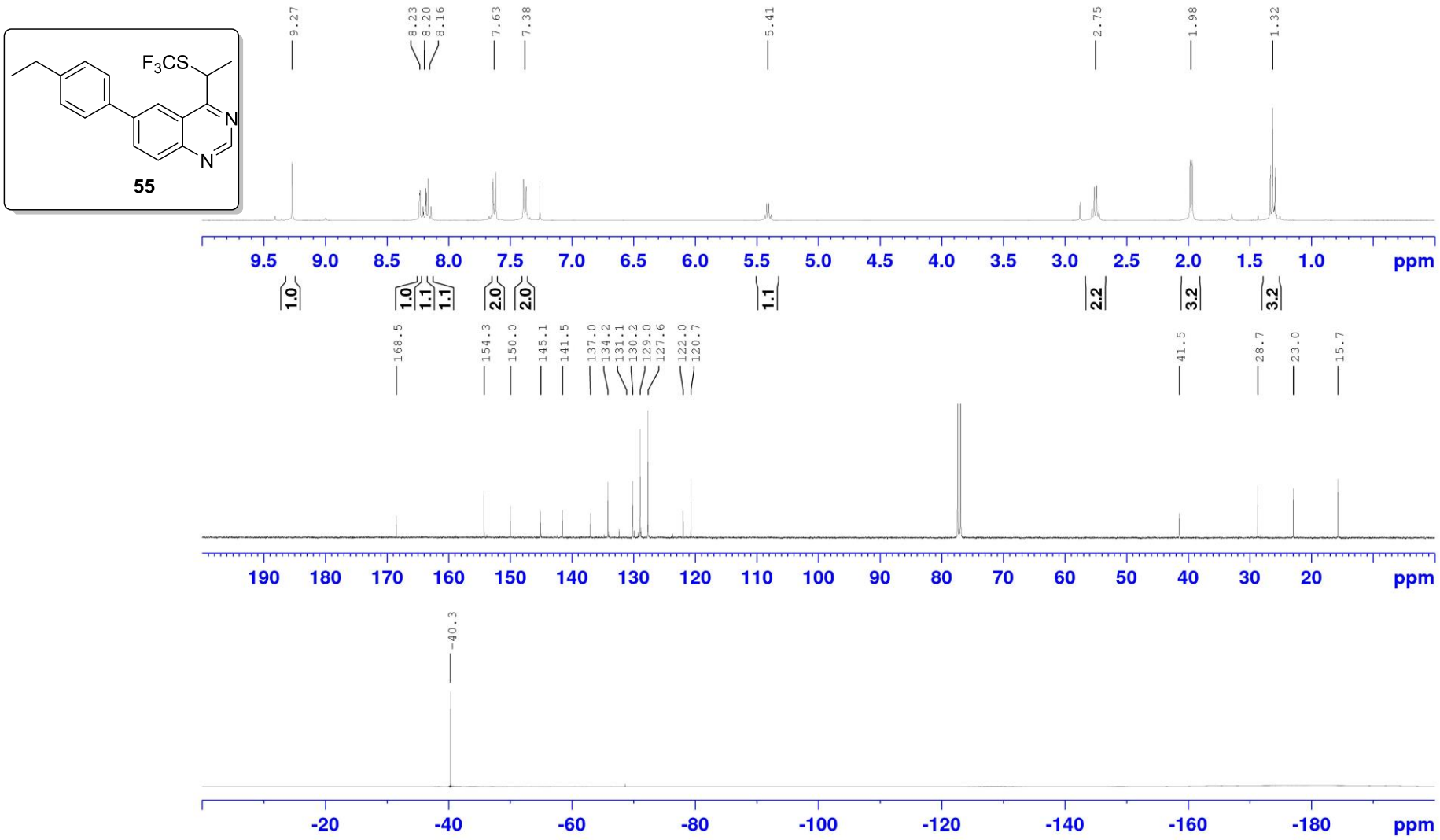
^{1}H, ^{13}C and ^{19}F NMR spectra of **53** recorded in $CDCl_3$ on a 500 MHz spectrometer



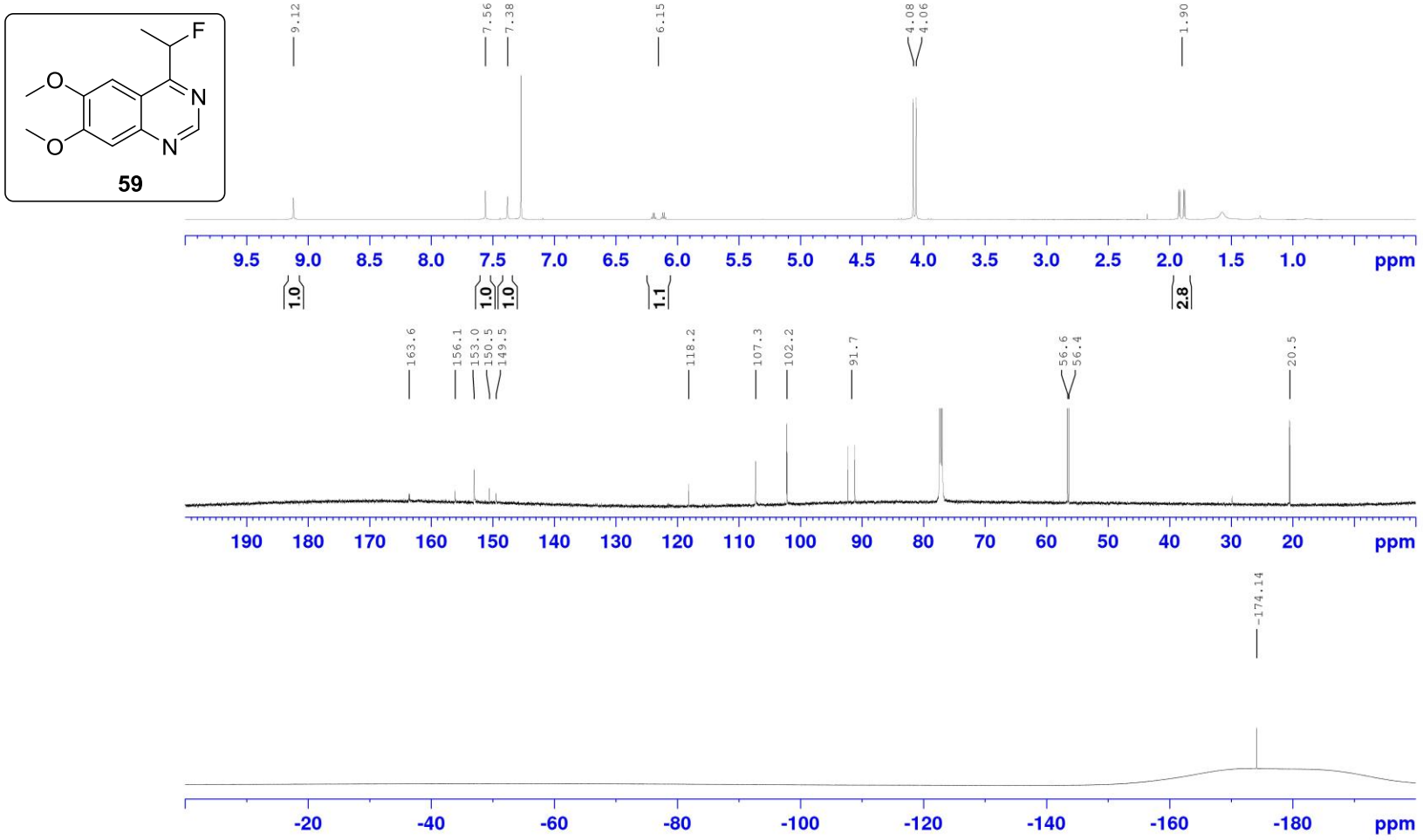
^{1}H, ^{13}C and ^{19}F NMR spectra of **54** recorded in $CDCl_3$ on a 500 MHz spectrometer



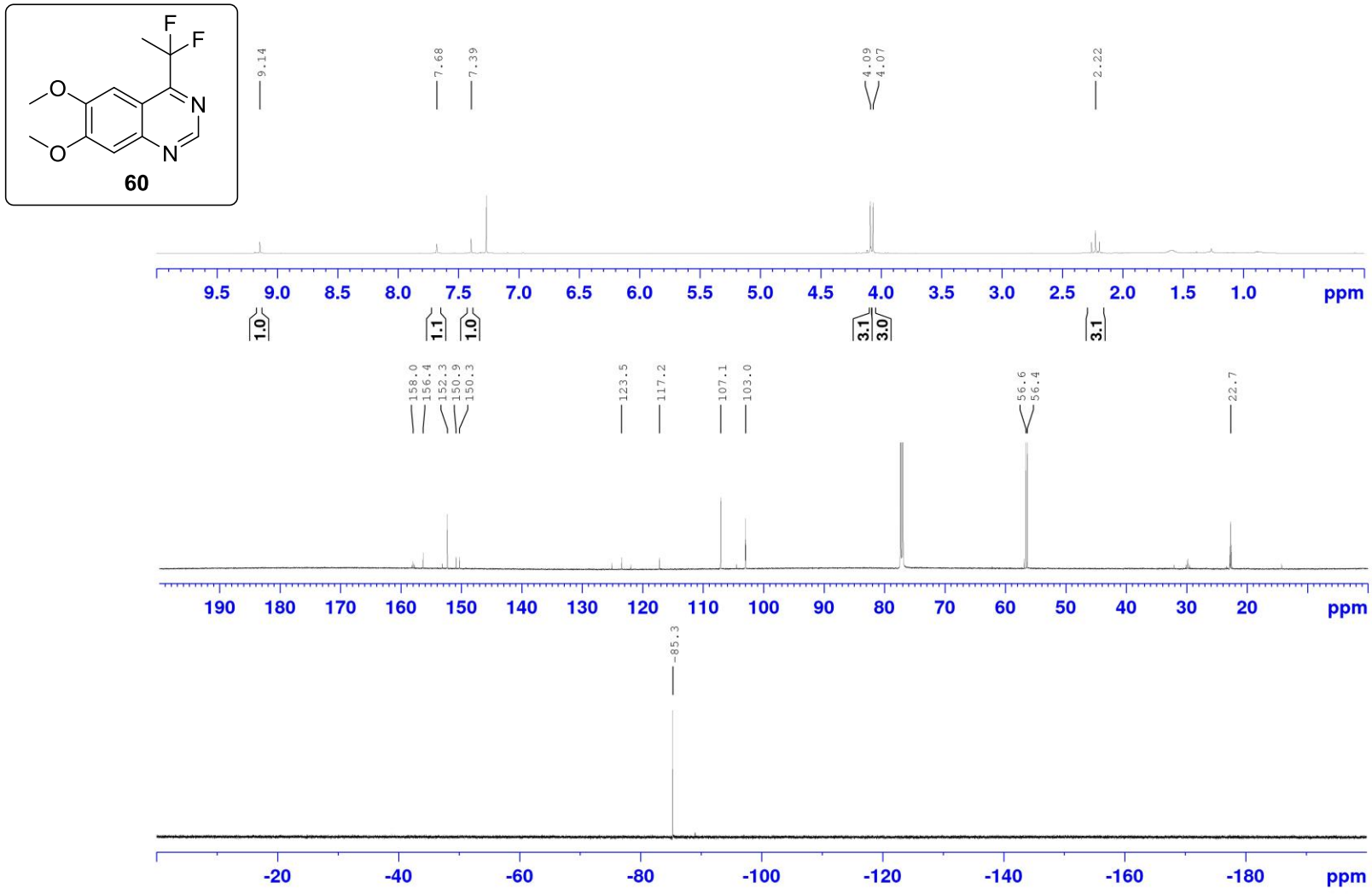
^{1}H, ^{13}C and ^{19}F NMR spectra of **55** recorded in $CDCl_3$ on a 500 MHz spectrometer



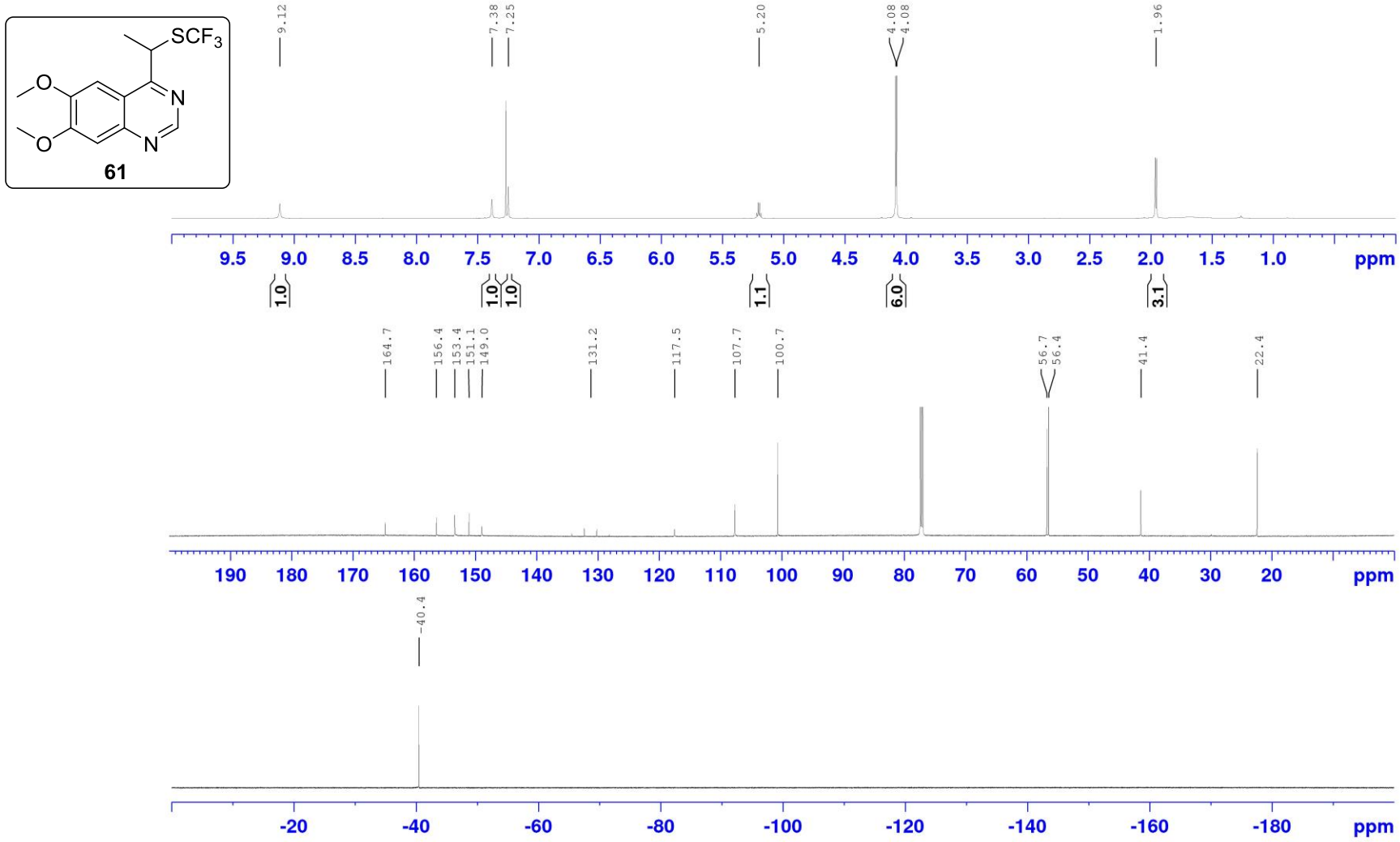
^{1}H, ^{13}C and ^{19}F NMR spectra of **59** recorded in $CDCl_3$ on a 600 MHz spectrometer



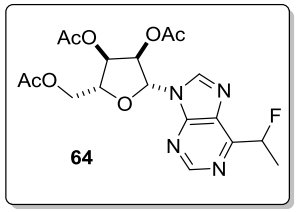
^{1}H, ^{13}C and ^{19}F NMR spectra of **60** recorded in $CDCl_3$ on a 600 MHz spectrometer

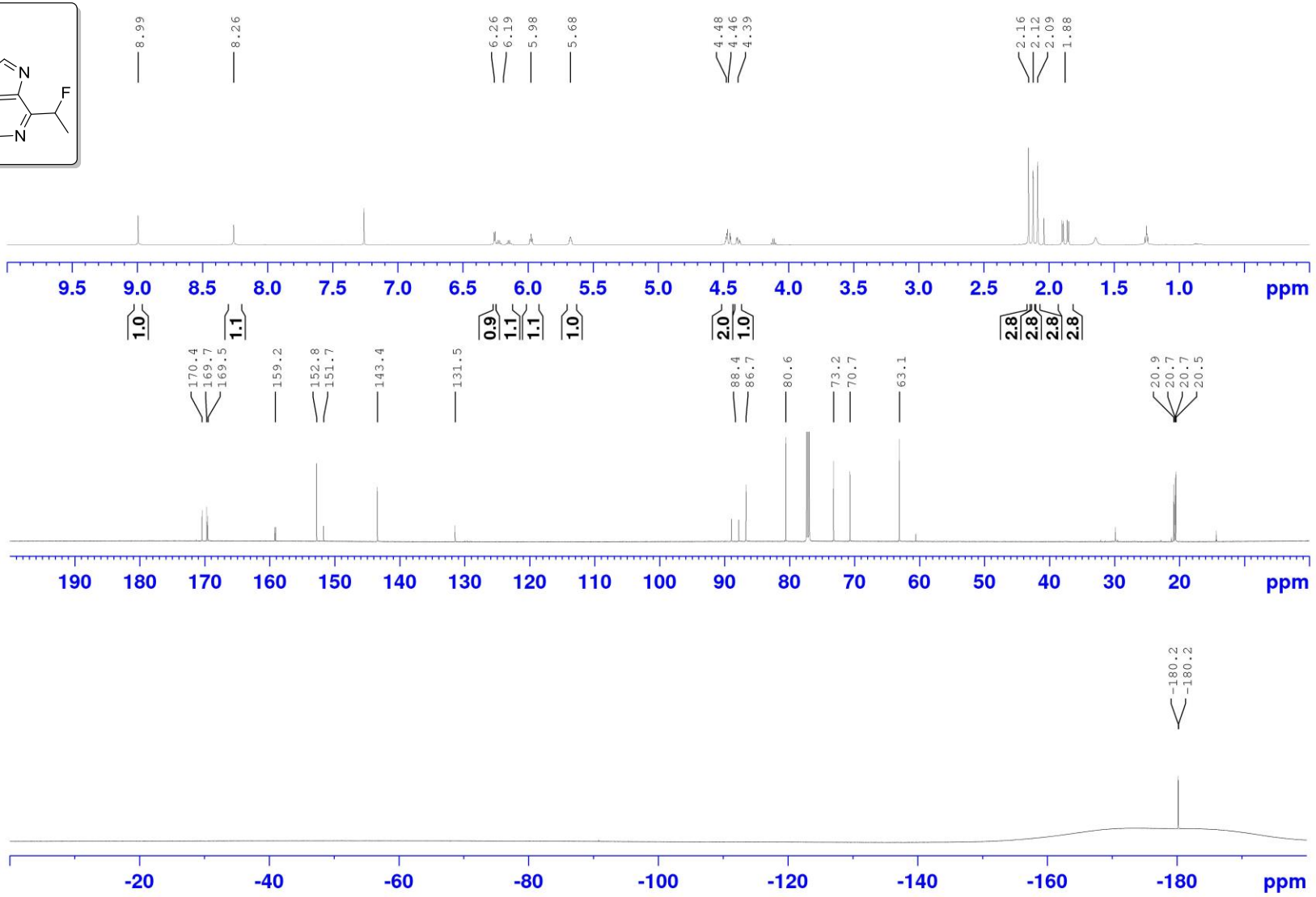


^{1}H, ^{13}C and ^{19}F NMR spectra of **61** recorded in $CDCl_3$ on a 600 MHz spectrometer



^{1}H, ^{13}C and ^{19}F NMR spectra of **64** recorded in $CDCl_3$ on a 600 MHz spectrometer





^{1}H, ^{13}C and ^{19}F NMR spectra of **65** recorded in $CDCl_3$ on a 600 MHz spectrometer