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SUPPORTING INFORMATION

A simple method for the synthesis of N-difluoromethylated pyridines and 4-pyridones/quinolones by using $BrCF_2COOEt$ as the difluoromethylation reagent.

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1.- Materials and Methods

Unless otherwise stated, common chemicals and solvents (HPLC grade or reagent grade quality) were purchased from commercial sources and used without further purification. Aluminium plates coated with a 0.2 mm thick layer of silica gel 60 F_{254} were used for thin-layer chromatography analyses (TLC), whereas flash column chromatography purification was carried out using silica gel 60 (230-400 mesh). Microwave reactions were performed in a Biotage Initiator+ Microwave System at the stated conditions. Reversed-phase high-performance liquid chromatography (HPLC) analyses were carried out on a Jupiter Proteo C_{18} column (250x4.6 mm, 90 Å 4 μm, flow rate: 1 mL/min) using linear gradients of 0.1% formic acid in H_2O (A) and 0.1% formic acid in ACN (B). Capillary electrophoresis analyses were carried out on a Hewlett Packard G1600AX-3D Capillary Electrophoresis instrument using a borate buffer solution (pH=9) as an electrolyte. Detection was performed by an UV/Vis diode-array detector operating between 190 and 600 nm. NMR spectra were recorded at 25 ºC in a 400 MHz spectrometer using the deuterated solvent as an internal deuterium lock. The residual protic signal of chloroform or DMSO was used as a reference in ^{1}H and ^{13}C NMR spectra recorded in $CDCl_3$ or DMSO-d_6, respectively. Chemical shifts are reported in part per million (ppm) in the δ scale, coupling constants in Hz and multiplicity as follows: s (singlet), d (doublet), t (triplet), q (quartet), qt (quintuplet), m (multiplet), dd (doublet of doublets), tt (triplet of triplets), td (triplet of doublets), etc. IR spectra (Attenuated Total Reflectance, ATR) were recorded on a Nicolet 6700 FT-IR ThermoScientific spectrometer and only the more representative frequencies (ν) are reported in cm^{-1}. Electrospray ionization mass spectra (ESI-MS) were recorded on an instrument equipped with single quadrupole detector coupled to an HPLC, and high-resolution (HR) ESI-MS on a LC/MS-TOF instrument.

2.- Synthesis of *N*-difluoromethylated pyridine derivatives and compound 9a

2.1. *N*-Difluoromethylation general procedure

In a typical experiment, 100 mg of the pyridine derivative were dissolved in a 1:1 (v/v) mixture of ACN (HPLC quality) and THF (previously eluted through basic aluminium oxide for chromatography, Brockmann I type, 50-200 μm, 60 Å) (20 mL). Then, 5 mol equivalents of ethyl bromodifluoroacetate (**1**) were added to the solution and left to react at 60ºC for 24 h under continuous stirring.

2.1.1. Synthesis of 1-difluoromethyl-4-dimethylaminopyridinium bromide (3)

DMAP (100 mg, 0.82 mmol) was reacted with **1** (0.54 mL, 4.1 mmol) in a 1:1 (v/v) mixture of neutralized THF and ACN (20 mL) at 60ºC for 24 h following the general procedure. After removal of the solvent under reduced pressure and precipitation with cold diethyl ether (10 mL), the expected compound was obtained as a yellowish solid (0.22 g, 92% yield).

Characterization: Yellowish solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.88 (2H, d, *J* = 8 Hz), 8.54 (1H, t, *J* = 58 Hz), 7.13 (2H, d, *J* = 8 Hz), 3.41 (6H, s). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm) 158. 2, 137.9, 111.3 (t, *J* = 262 Hz), 108.3, 41.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) -95.4 (2F, d, *J* = 58 Hz). HRMS (ESI): calc. *m/z* for $C_8H_{11}F_2N_2^+$ $[M]^+$ 173.0885; found 173.0886. HPLC: R_t = 7.7 min (analytical gradient: 0 to 25 % of B in 30 min; A: 0.1 % formic acid in H_2O, B: 0.1 % formic acid in ACN).

2.1.2. Synthesis of 1-(carboxydifluoromethyl)-4-(dimethylamino)pyridinium bromide (2b)

Following the general procedure, 120 mg of DMAP were dissolved in 20 mL of ACN (HPLC grade) and 5 mol equivalents of **1** were added. After stirring for 24 h at 60ºC, the solvent was removed under reduced pressure and an aliquot of the crude was purified by analytical reversed-phase HPLC. After lyophilisation, compound **2b** was obtained as a yellowish solid.

Characterization: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 8.26 (2H, d, *J* = 8.0 Hz), 6.89 (2H, d, *J* = 8.0 Hz), 3.23 (6H, s). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN) δ (ppm) 159.2 (t, *J* = 26 Hz), 158.5, 137.9 (t, *J* = 4.0 Hz), 114.0 (t, *J* = 286 Hz), 108.0, 41.1. ^{19}F NMR (376 MHz, CD_3CN) δ (ppm) -90.3 (s, 2F). IR (ATR) ν (cm^{-1}) 3370, 3076, 2914, 1688, 1650, 1581, 1525, 1413, 1372, 1356, 1167, 1106, 866, 829, 796, 691, 658, 571. LRMS: calc. *m/z* for $C_9H_{11}F_2N_2O_2^+$ $[M]^+$ 217.08; found 216.99. HRMS (ESI): calc. *m/z* for $C_9H_{11}F_2N_2O_2^+$ $[M]^+$ 217.0783; found 217.0787. HPLC: R_t = 12.9 min (analytical gradient: 0 to 40 % of B in 30 min; A: 0.1 % formic acid in H_2O, B: 0.1 % formic acid in ACN).

2.1.3. Synthesis of 1-(difluoromethyl)pyridinium bromide (4a)

Following the general procedure, 10 mg of pyridine were dissolved in 2 mL of ACN/THF 1:1 and 5 mol equivalents of **1** were added. After stirring for 24 h at 60ºC, the solvent was removed under reduced pressure. The reaction crude was dissolved in DMSO-d_6 and ^{1}H and ^{19}F NMR spectra were recorded to assess the conversion yield and characterize **4a**

Characterization: ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.48 (2H, m), 8.95 (1H, tt, *J* = 8, 1.2 Hz), 8.40 (2H, t, *J* = 7.2 Hz), 8.31 (1H, t, *J* = 58 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm) -96.4 (d, 2F, *J* = 58 Hz). LRMS: calc. *m/z* for $C_6H_6F_2N^+$ $[M]^+$ 130.05; found 129.9.

2.1.4. Synthesis of 1-(difluoromethyl)-2-methylpyridinium bromide (5a)

Following the same procedure as for the synthesis of **4a**, ^{1}H and ^{19}F NMR analyses were carried out with the totality of the crude after 24 h.

Characterization: ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.36 (1H, d, *J* = 7.6, 1.4 Hz), 8.78 (1H, td, *J* = 7.6, 1.4 Hz), 8.41 (1H, t, *J* = 57 Hz), 8.23 (1H, d, *J* = 7.6 Hz), 8.18 (1H, t, *J* = 7.6 Hz), 2.96 (3H, s). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm) -99.8 (2F, d, *J* = 57 Hz). LRMS: calc. *m/z* for $C_7H_8F_2N^+$ $[M]^+$ 144.06; found 143.9.

2.1.5. Synthesis of 1-(difluoromethyl)-2,6-dimethylpyridinium bromide (6a)

Following the same procedure as for the synthesis of **4a**, ^{1}H and ^{19}F NMR analyses were carried out with the totality of the crude after 24 h.

Characterization: ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.63 (1H, t, *J* = 8 Hz), 8.46 (t, 1H, *J* = 58 Hz), 8.05 (2H, d, *J* = 8 Hz), 2.08 (6H, s). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm) -98.5 (2F, d, *J* = 58 Hz). LRMS: calc. *m/z* for $C_8H_{10}F_2N^+$ $[M]^+$ 158.08; found 157.8.

2.1.6. Synthesis of 2-(cyano(1-difluoromethyl(4-pyridin-1-ium))methylene)-7-(*N*,*N*-diethylamino)-4-methyl-coumarin bromide (8b).

Following the general procedure, 2-(cyano(4-pyridine)methylene)-7-(*N*,*N*-diethylamino)-4-methyl-coumarin (**8**) (40 mg, 0.12 mmol) was reacted with 30 mol equiv. of **1** (0.32 mL, 3.6 mmol; the reagent addition was divided into three portions at t = 0, 1 h and 4 h) in a 1:1 (v/v) mixture of neutralized THF and ACN (20 mL) at 60ºC for 24 h. After evaporation under reduced pressure, compound **8b** was purified by column chromatography (silica gel, 0-8% MeOH in DCM) to give 46 mg of a dark blue solid (yield 83%).

Characterization: TLC: R_f (DCM/MeOH 9:1) 0.67. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.75 (2H, d, *J* = 8.0 Hz), 8.13 (2H, br d, *J* = 8.0 Hz), 8.03 (1H, t, *J* = 58 Hz), 7.85 (1H, d, *J* = 9.2 Hz), 7.12 (1H, dd, *J* = 9.2, 2.4 Hz), 7.08 (2H, m), 3.61 (4H, q, *J* = 7.2 Hz), 2.63 (3H, s),

1.20 (6H, t, *J* = 7.2 Hz). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-*d*$_6$) δ (ppm) 167.2, 156.3, 155.6, 152.9, 152.7, 137.5, 127.6, 118.9, 117.7, 113.4, 112.2 (t, *J* = 262 Hz), 111.7, 110.9, 96.1, 79.5, 44.5, 18.7, 12.4. ^{19}F NMR (376 MHz, DMSO-*d*$_6$) δ (ppm): -95.9 (2F, d, *J* = 58 Hz). HRMS (ESI-TOF) (*m/z*): $[M]^+$ Calcd for $C_{22}H_{22}F_2N_3O^+$, 382.1725; found, 382.1727. Analytical HPLC (10−100% B in 30 min, formic acid additive): R_t = 14.6 min.

2.1.7. Synthesis of 10-methyl-3,6-bis(dimethylamino)acridin-10-ium triflate (9a)

Acridine orange (200 mg, 0.75 mmol) was reacted with methyl trifluoromethanesulfonate (0.34 mL, 3 mmol) in DCM (100 mL) at room temperature for 24 h. After evaporation under reduced pressure, compound **9a** was purified by column chromatography (silica gel, 0-4% MeOH in DCM) to give 173 mg of an orange solid (yield 54%).

Characterization: TLC: R_f (DCM/MeOH 9:1) 0.52. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm) 8.84 (1H, s), 7.96 (2H, d, *J* = 9.2 Hz), 7.30 (2H, dd, *J* = 9.2, 2.0 Hz), 6.76 (2H, d, *J* = 2.0 Hz), 4.15 (3H, s), 3.29 (12H, s). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-*d*$_6$) δ (ppm) 155.2, 143.0, 142.4, 132.7, 116.3, 114.2, 92.9, 40.3, 35.5. HRMS (ESI-TOF) (*m/z*): $[M]^+$ Calcd for $C_{18}H_{22}N_3$, 280.1808; found, 280.1814. Analytical HPLC (10−100% B in 30 min, formic acid additive): R_t = 13 min.

2.1.8. Synthesis of 10-(difluoromethyl)-3,6-bis(dimethylamino)acridin-10-ium bromide (9b)

Following the general procedure, acridine orange (100 mg, 0.38 mmol) was reacted with 5 mol equiv. of **1** (0.25 mL, 1.9 mmol) in a 1:1 (v/v) mixture of neutralized THF and ACN (20 mL) at 60ºC for 24 h. Then, an additional amount of **1** was added (0.25 mL) and the reaction was stirred at 60ºC for 24 h. After evaporation under reduced pressure and precipitation from *tert*-butyl methyl ether, compound **9b** was purified by column chromatography (silica gel, 0-5% MeOH in DCM) to give 115 mg of a garnet/burgundy solid (yield 76%).

Characterization: TLC: R_f (DCM/MeOH 95:5) 0.28. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm) 8.80 (1H, s), 8.64 (1H, t, *J* = 55 Hz), 7.96 (2H, d, *J* = 9.2 Hz), 7.29 (2H, dd, *J* = 9.2, 2.2 Hz), 6.93 (2H, br s), 3.31 (12H, s). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-*d*$_6$) δ (ppm) 155.8, 146.2, 140.1, 134.1, 116.1, 114.3, 112.3 (t, *J* = 252 Hz), 94.4, 40.5. ^{19}F NMR (376 MHz, DMSO-*d*$_6$) δ (ppm): -102.0 (2F, d, *J* = 55 Hz). HRMS (ESI-TOF) (*m/z*): $[M]^+$ Calcd for $C_{18}H_{20}F_2N_3$, 316.1620; found, 316.1619. Analytical HPLC (10−100% B in 30 min, formic acid additive): R_t = 13.6 min.

3.- Synthesis of *N*-difluoromethylated 4-pyridone/quinolone derivatives

3.1. Synthesis of 1-(difluoromethyl)pyridin-4-one (10b)

The reaction between 4-methoxypyridine (500 mg, 4.58 mmol) and ethyl bromodifluoroacetate (6.05 mL, 45.8 mmol) was carried out following the standard procedure. After stirring at 60ºC for 24 h, the solvent was removed under reduced pressure and the product was purified by column chromatography (silica gel, 0-5% MeOH in DCM). The appropriate fractions were collected and the solvents removed in a rotary evaporator to give 365 mg (55 % yield) of a colourless oil.

Characterization: TLC: R_f (DCM/MeOH 9:1) 0.41. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.52 (2H, d, *J* = 7.8 Hz), 6.76 (1H, t, *J* = 59.6 Hz), 6.44 (2H, d, *J* = 7.8 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm) 179.9, 134.1, 119.2, 112.1 (t, *J* = 255 Hz) .^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm) -92.2 (d, 2F, *J* = 59.6 Hz). HRMS (ESI): calc. *m/z* for $C_6H_6F_2NO$ $[M+H]^+$ 146.0412; found 146.0412. HPLC: R_t = 12.4 min (analytical gradient: 0 to 40 % of B in 30 min; A: 0.1 % formic acid in H_2O, B: 0.1 % formic acid in ACN).

3.2. Synthesis of 1-(difluoromethyl)quinolin-4-one (11a)

The reaction between 4-methoxyquinoline (500 mg, 3.14 mmol) and ethyl bromodifluoroacetate (6.23 mL, 47.1 mmol) was carried out following the standard procedure (60ºC, 24 h). Then, an additional amount of ethyl bromodifluoroacetate was added (4.15 mL, 31.4 mmol). After stirring at 60ºC for 24 h, the solvent was removed under reduced pressure and the product was purified by column chromatography (silica gel, 0-1% AcOEt in DCM). The appropriate fractions were collected and the solvents removed in a rotary evaporator to give 370 mg (60 % yield) of a white solid.

Characterization: TLC: R_f (AcOEt) 0.70. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.41 (1H, d, *J* = 8.4 Hz), 7.74 (1H, d, *J* = 8.0 Hz), 7.72-7.62 (2H, m), 7.45 (1H, t, *J* = 7.4 Hz), 7.24 (1H, t, *J* = 59.5 Hz), 6.31 (1H, d, *J* = 8.0 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm) 178.6, 137.2, 136.1, 133.0, 127.4, 126.5, 125.2, 115.2 (t, *J* = 3.2 Hz), 112.3, 111.7 (t, *J* = 255 Hz).^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm) -95.3 (d, 2F, *J* = 59.5 Hz). HRMS (ESI): calc. *m/z* for $C_{10}H_8F_2NO$ $[M+H]^+$ 196.0574; found 196.0569. HPLC: R_t = 15.7 min (analytical gradient: 0 to 100 % of B in 30 min; A: 0.1 % formic acid in H_2O, B: 0.1 % formic acid in ACN).

4.- UV-HPLC-MS analysis of the N-difluoromethylation reaction of DMAP in ACN.

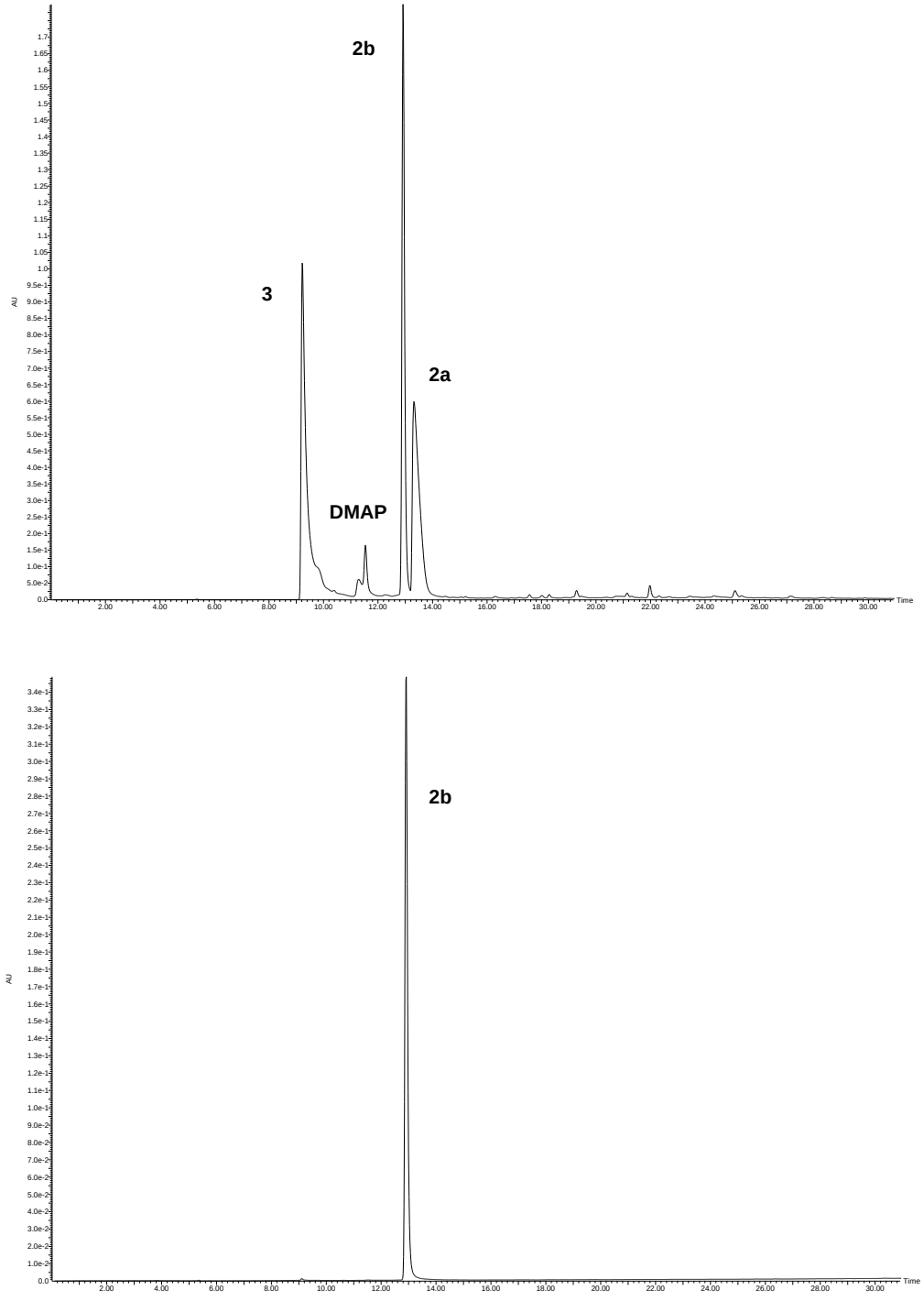

Figure S1. UV-HPLC-MS analysis of the N-difluoromethylation reaction of DMAP with **1** in ACN (HPLC quality), crude (top) and pure intermediate **2b** isolated (bottom).

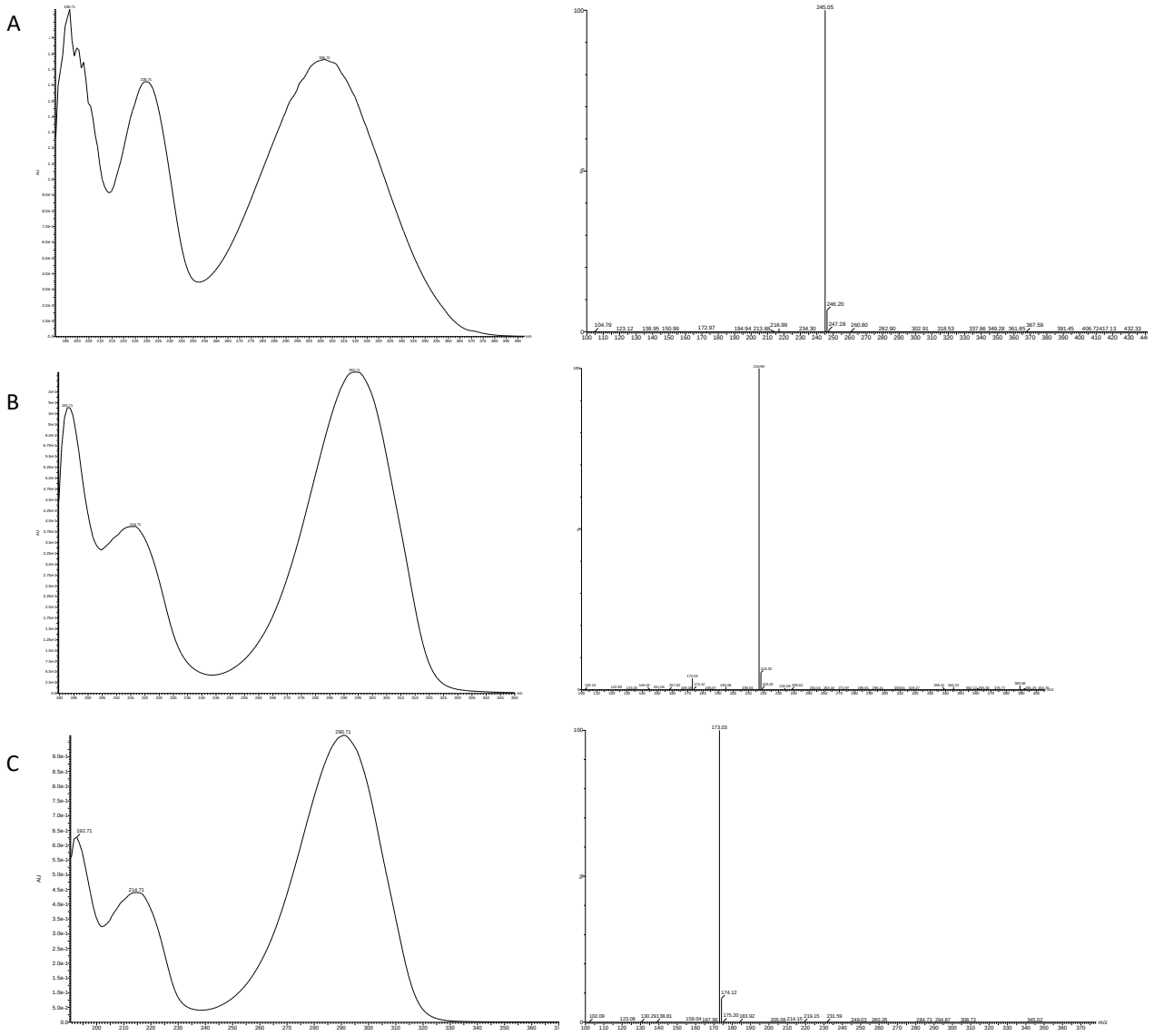

Figure S2. UV-vis spectra (left) and LR ESI-MS spectra (right) of compounds **2a** (A), **2b** (B) and **3** (C). Data was obtained from UV-HPLC-MS analysis showed in Figure S1.

Table S1. UV-vis and LR ESI-MS characterization of compounds **2a**, **2b** and **3**.[a]

Compound	λ_{max} (nm)	*m/z* (exp.)	*m/z* (calc.)
2a	307	245.05	245.11 $C_{11}H_{15}F_2N_2O_2$ $[M]^+$
2b	294	216.99	217.08 $C_9H_{11}F_2N_2O_2$ $[M]^+$
3	291	173.03	173.09 $C_8H_{11}F_2N_2$ $[M]^+$

[a] Data was collected from UV-vis and LR ESI-MS spectra showed in Figure S2.

5.- Capillary electrophoresis analysis of the N-difluoromethylation reaction of DMAP.

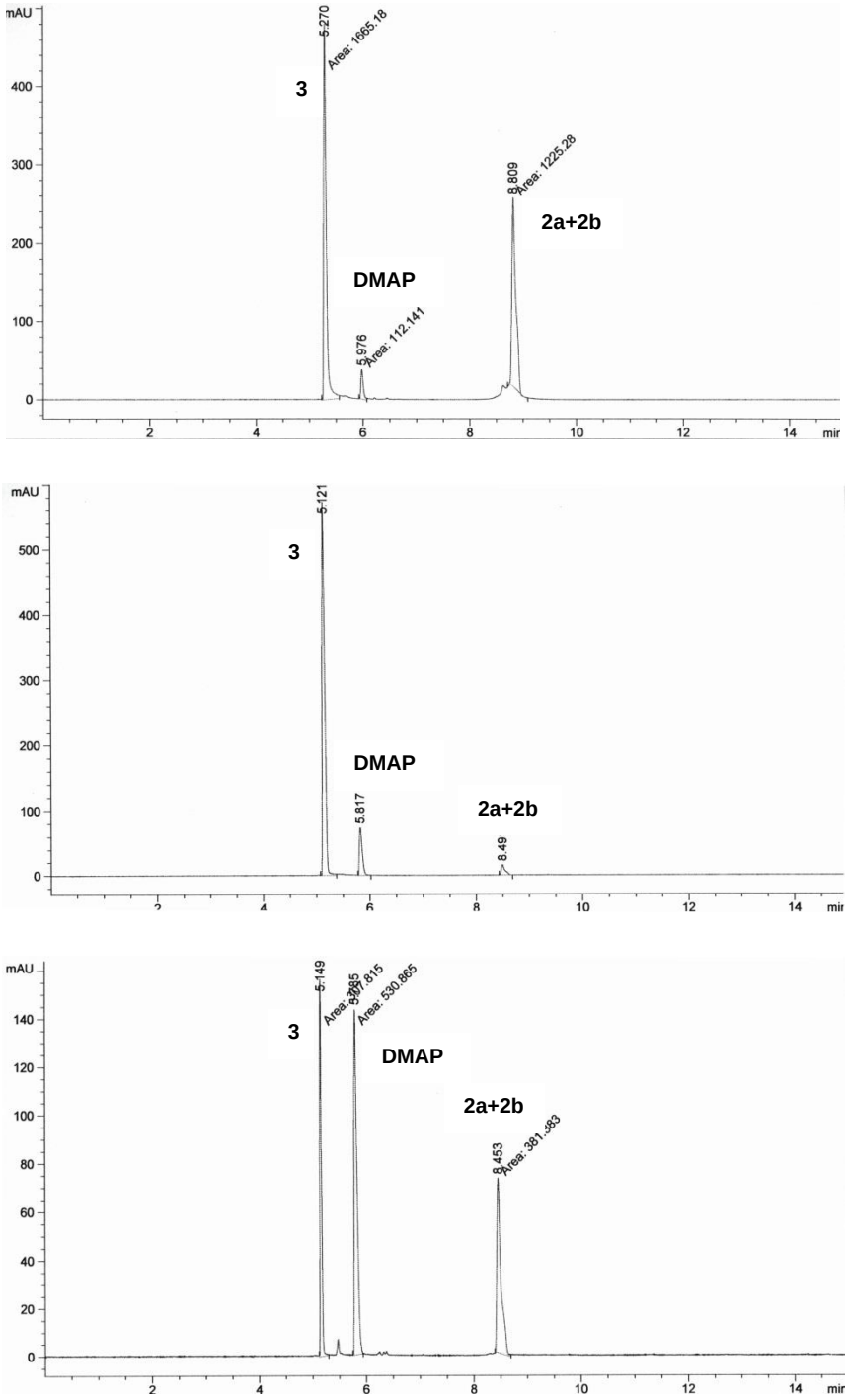

Figure S3. Electropherograms of the N-difluoromethylation reaction of DMAP with **1** in ACN (top), neutralized THF (center) and dioxane (bottom).

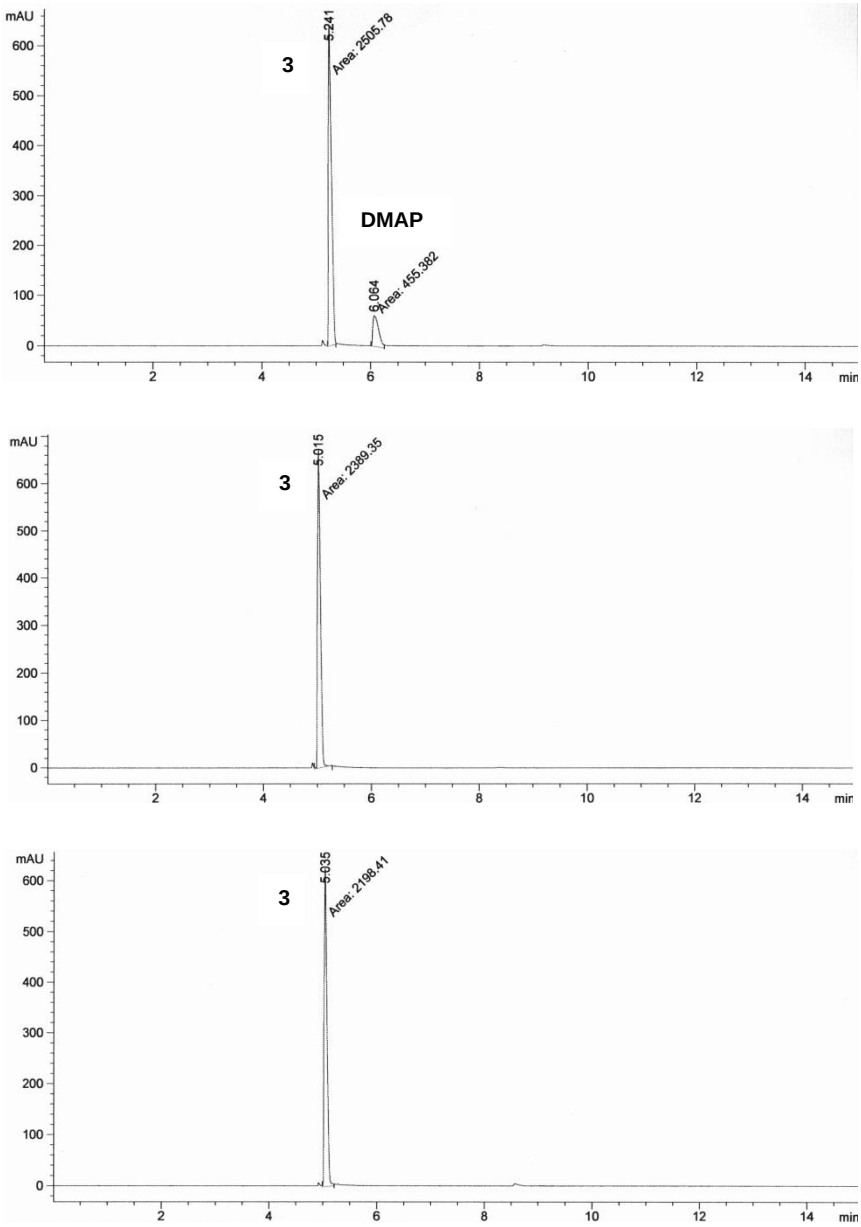

Figure S4. Electropherograms of the N-difluoromethylation reaction of DMAP with 1.1 (top), 1.5 (middle) and 3 (bottom) mol equiv. of **1** in a 1:1 mixture of neutralized THF and ACN at 60^{o}C for 24 h.

6.- ^{1}H and ^{19}F NMR and HR ESI-MS analysis of the N-difluoromethylation reaction of DMAP in CD_3CN/D_2O 98:2 (v/v).

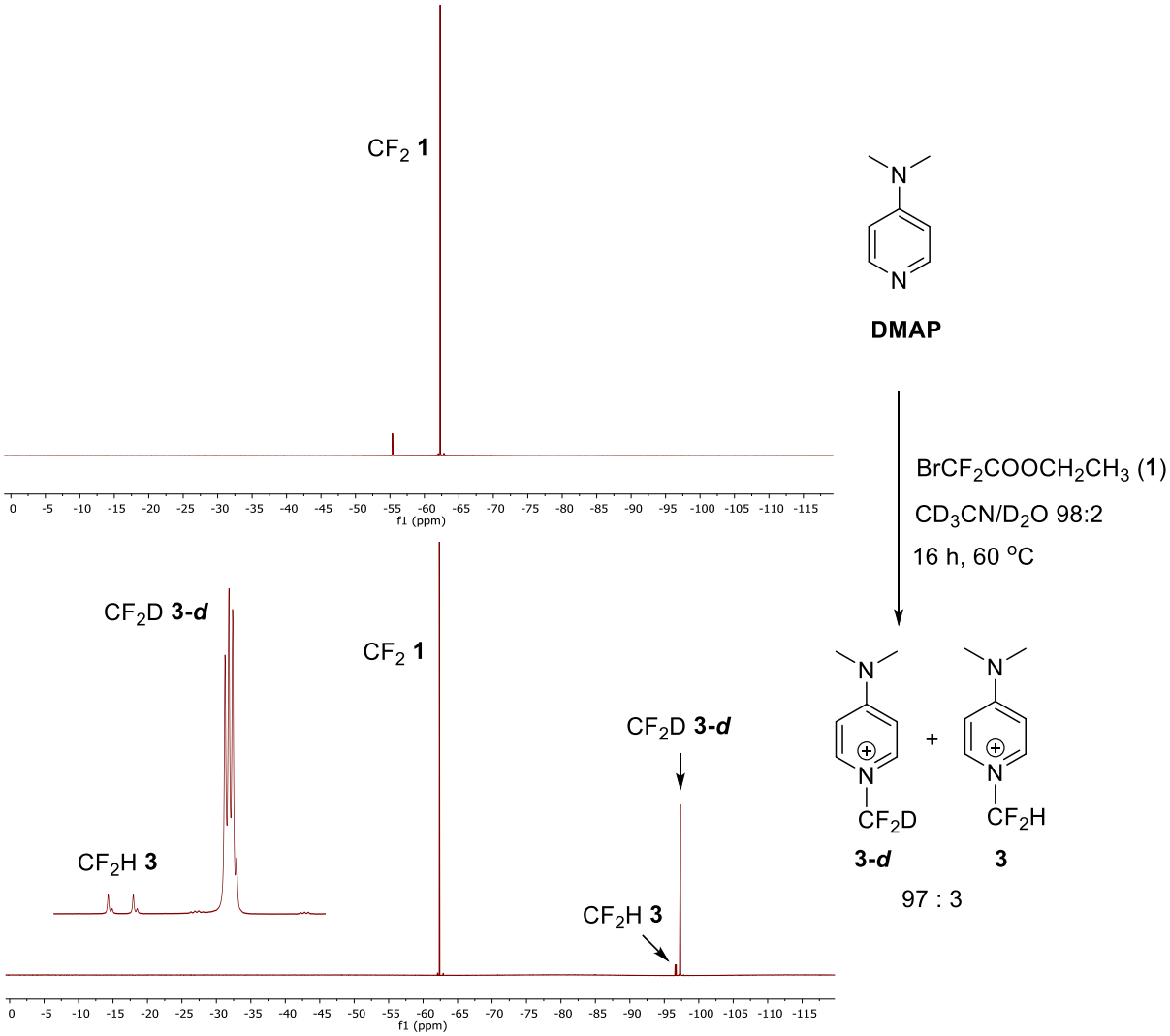

Figure S5. Top: ^{19}F NMR spectra (376 MHz) of a freshly prepared solution of DMAP (25 mg, 0.20 mmol) and ethyl bromodifluoroacetate (53 μL, 0.41 mmol) in 4 mL of a 98:2 (v/v) mixture of CD_3CN and D_2O. Bottom: ^{19}F NMR spectra (376 MHz) after heating for 16 h at 60ºC.

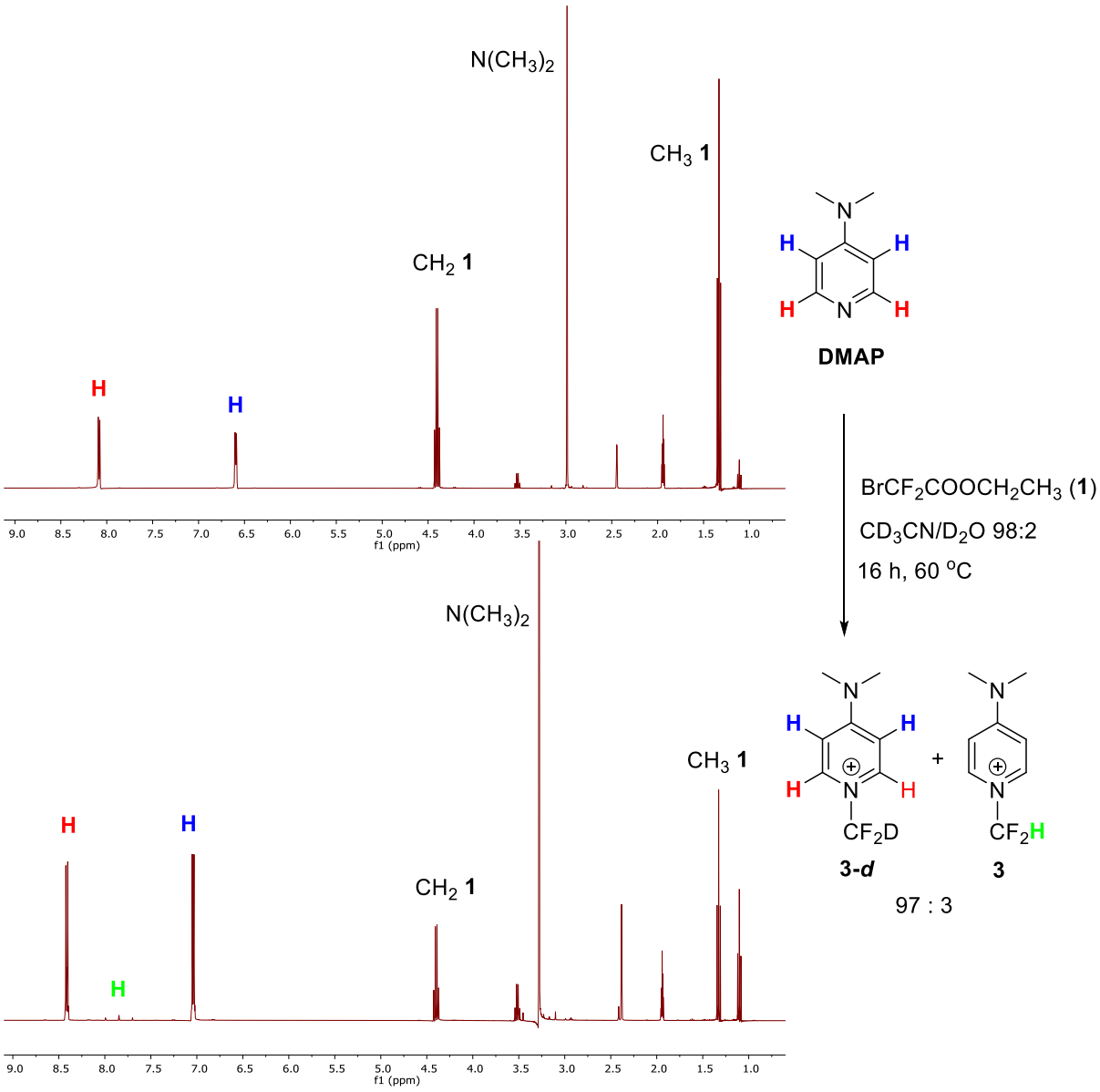

Figure S6. Top: ^{1}H NMR spectra (400 MHz) of a freshly prepared solution of DMAP (25 mg, 0.20 mmol) and ethyl bromodifluoroacetate (53 μL, 0.41 mmol) in 4 mL of a 98:2 (v/v) mixture of CD_3CN and D_2O. Bottom: ^{1}H NMR spectra (400 MHz) after heating for 16 h at 60°C.

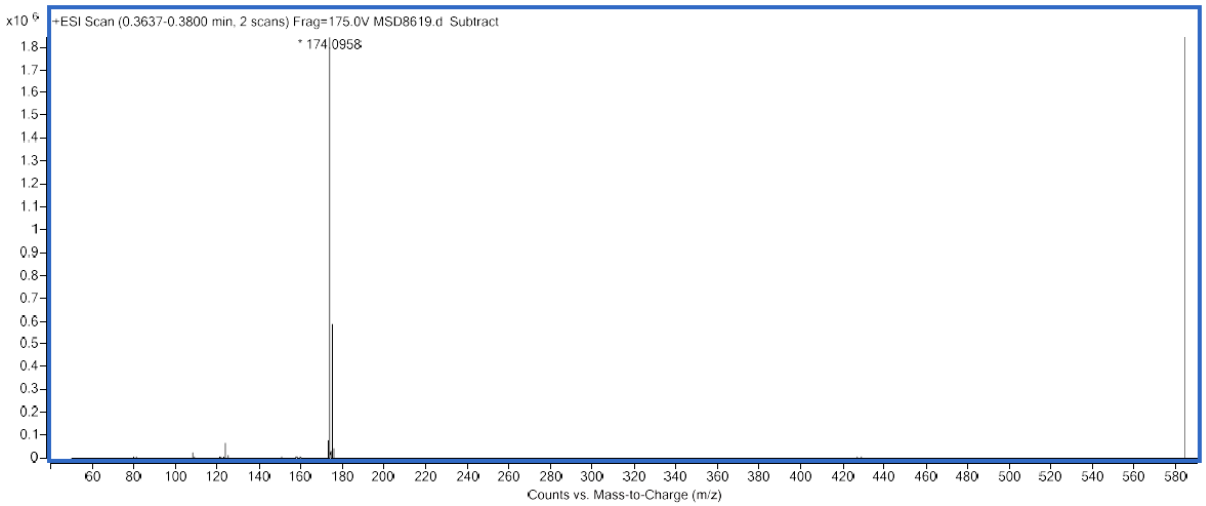

Figure S7. HR ESI-MS spectrum of reaction crude between DMAP and ethyl bromodifluoroacetate in a 98:2 (v/v) mixture of CD_3CN and D_2O after heating for 16 h at 60ºC.

Table S2. HR ESI-MS characterization of compounds **3** and **3-*d***.

Compound	*m/z* (exp.)	*m/z* (calc.)
3-*d*	174.0958	174.0948 $C_8H_{10}DF_2N_2^+$ $[M]^+$
3	173.0886	173.0885 $C_8H_{11}F_2N_2$ $[M]^+$

7.- Stability of compound 2b in CD_3CN by ^1H NMR.

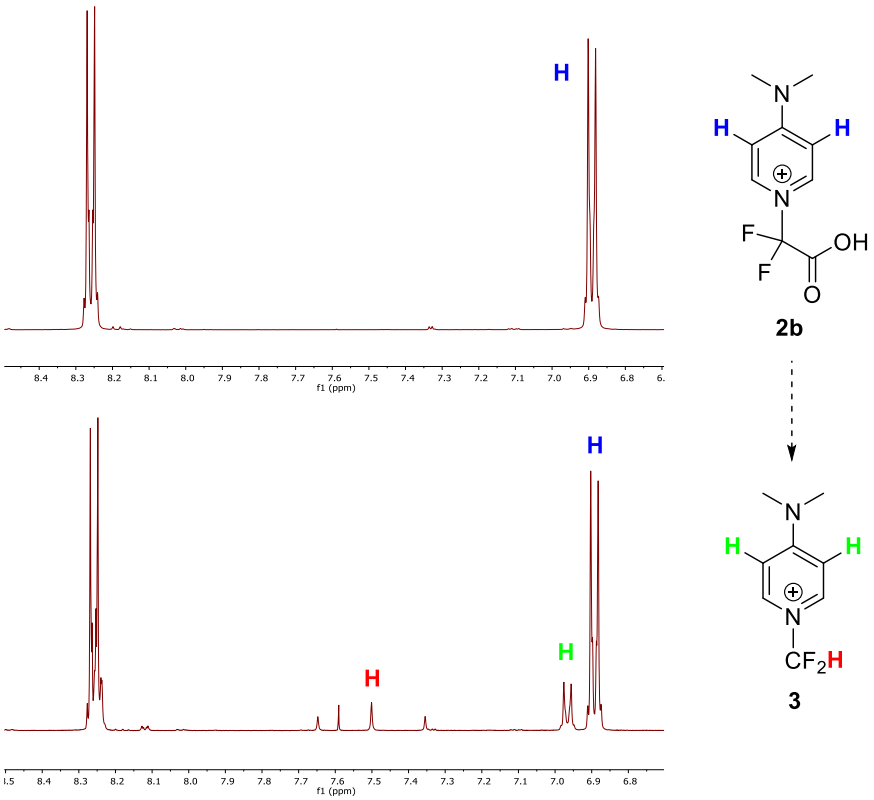

Figure S8. Comparison of the region between 6.7 and 8.5 ppm of the ^1H NMR spectra (400 MHz) of a freshly prepared solution of compound **2b** in CD_3CN (top) with the same region after standing for 96 h at room temperature (bottom).

8.- ^{1}H and ^{19}F NMR analysis of the N-difluoromethylation reaction of 4-6

Compound 4a

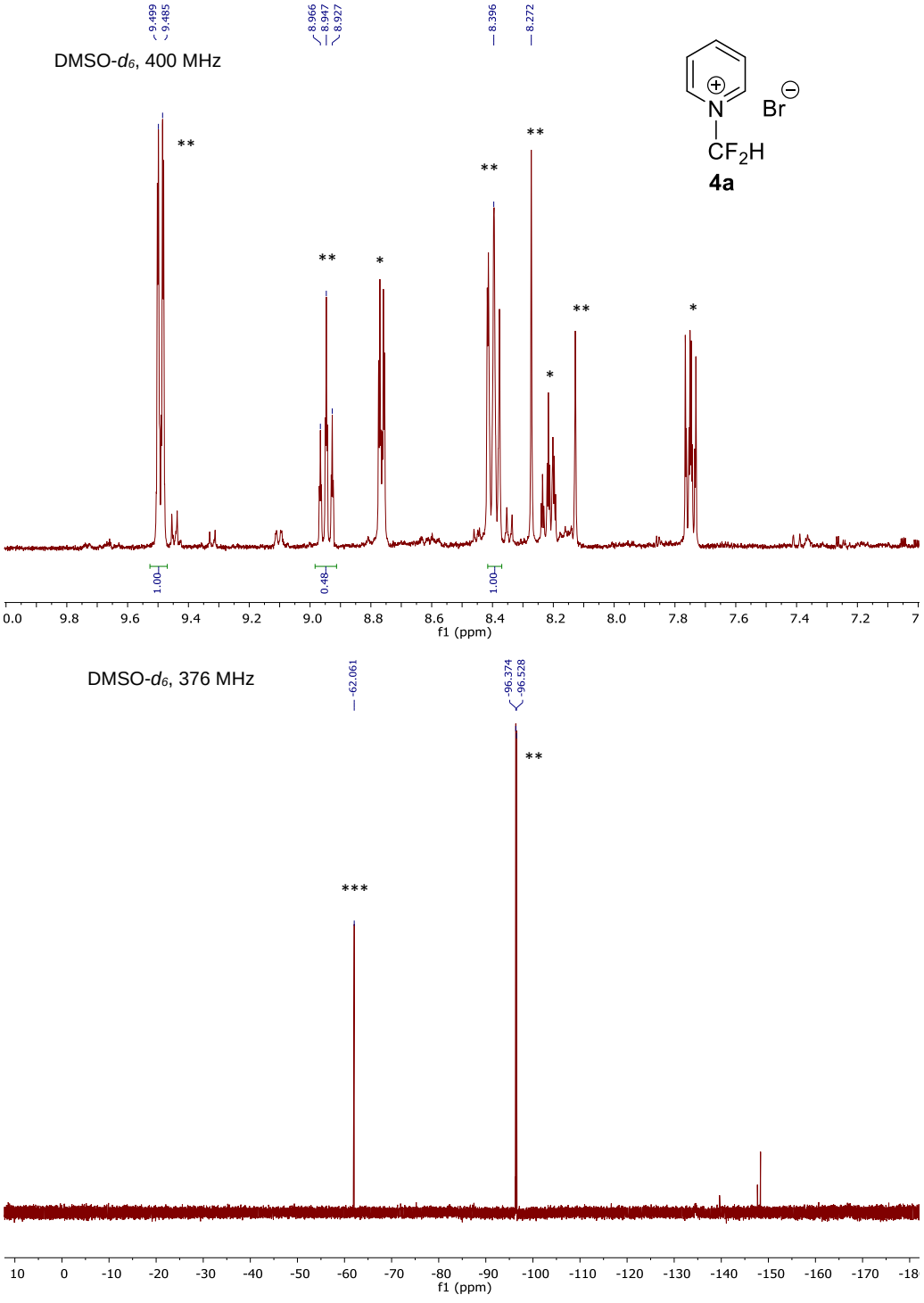

Figure S9. Aromatic region of the ^{1}H NMR (top) and ^{19}F NMR (bottom) spectra for the N-difluoromethylation reaction of pyridine (**4**) with 5 mol equiv. of **1** in a 1:1 mixture of neutralized THF and ACN at 60°C for 24 h. After removal of the solvent under reduced pressure, the reaction crude was dissolved in DMSO-*d6* to register the ^{1}H and ^{19}F NMR spectra. * = pyridine signals. ** = compound **4a** signals. *** = compound **1** signal.

Compound 5a

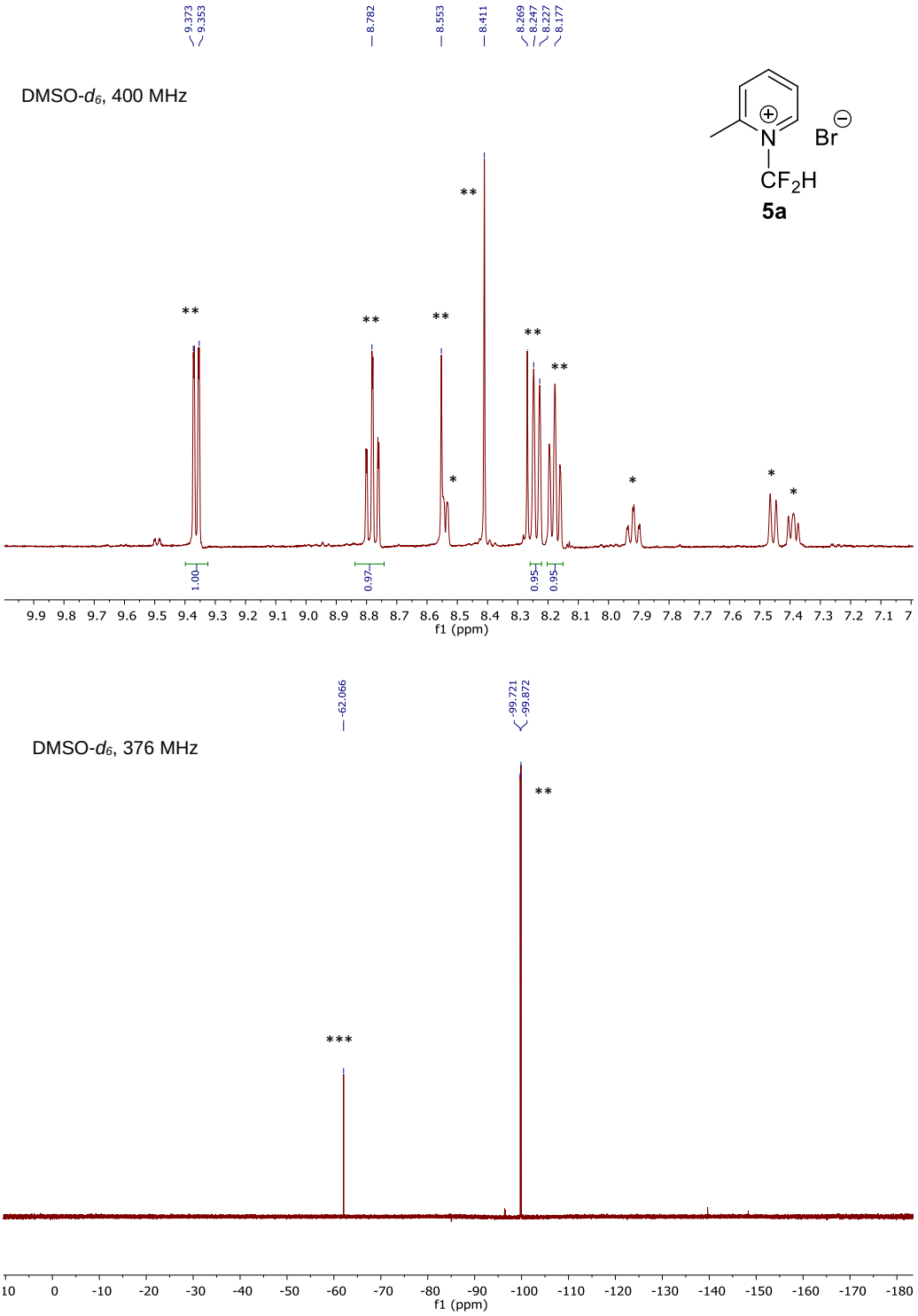

Figure S10. Aromatic region of the ^{1}H NMR (top) and ^{19}F NMR (bottom) spectra for the N-difluoromethylation reaction of 2-picoline (**5**) with 5 mol equiv. of **1** in a 1:1 mixture of neutralized THF and ACN at 60ºC for 24 h. After removal of the solvent under reduced pressure, the reaction crude was dissolved in DMSO-*d*$_6$ to register the ^{1}H and ^{19}F NMR spectra. * = 2-picoline signals. ** = compound **5a** signals. *** = compound **1** signal.

Compound 6a

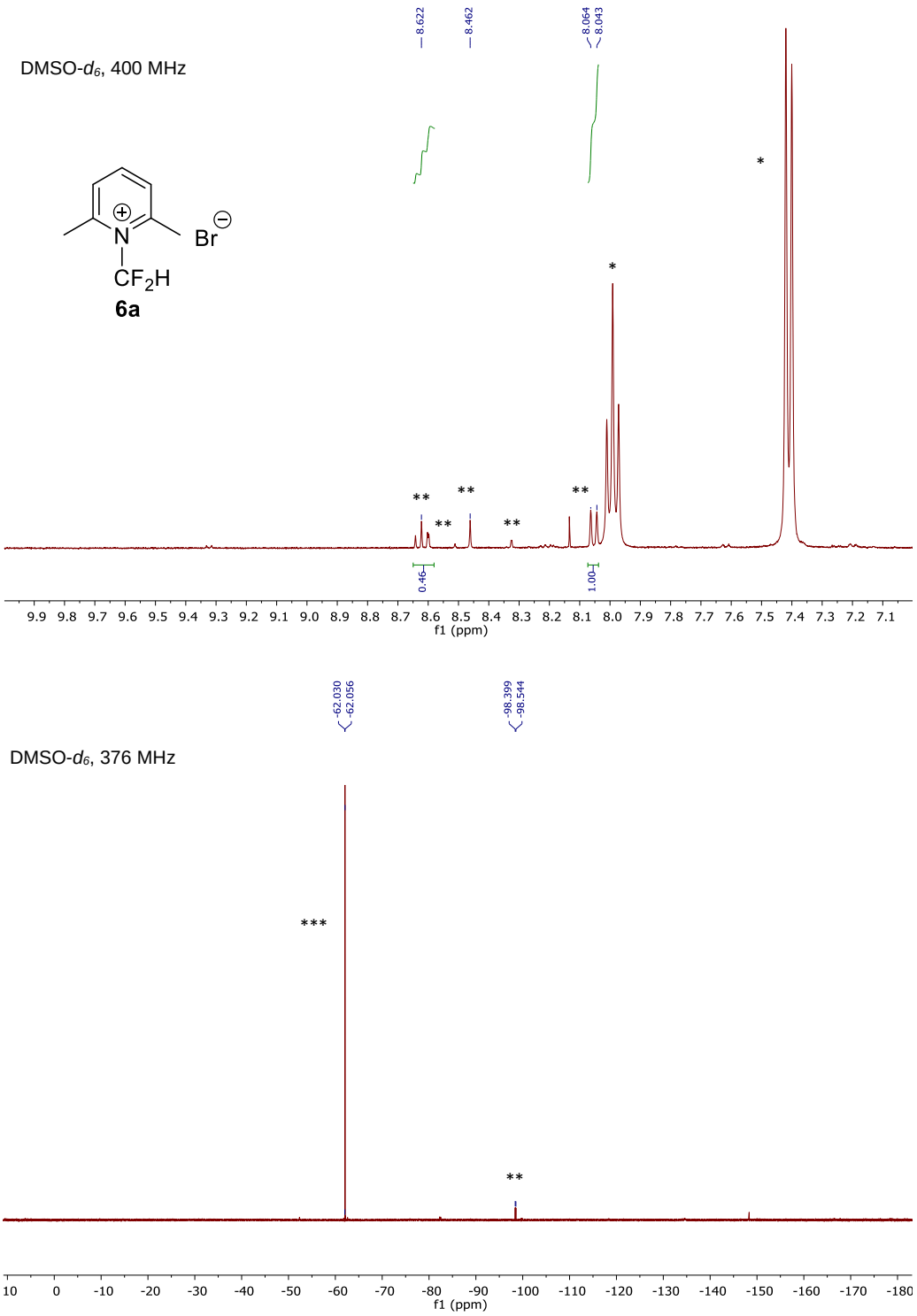

Figure S11. Aromatic region of the ^{1}H NMR (top) and ^{19}F NMR (bottom) spectra for the N-difluoromethylation reaction of 2,6-lutidine (**6**) with 5 mol equiv. of **1** in a 1:1 mixture of neutralized THF and ACN at 60ºC for 24 h. After removal of the solvent under reduced pressure, the reaction crude was dissolved in DMSO-*d*$_6$ to register the ^{1}H and ^{19}F NMR spectra. * = 2,6-lutidine signals. ** = compound **6a** signals. *** = compound **1** signal.

9.- HPLC analysis of fluorophores 8b and 9a-9b

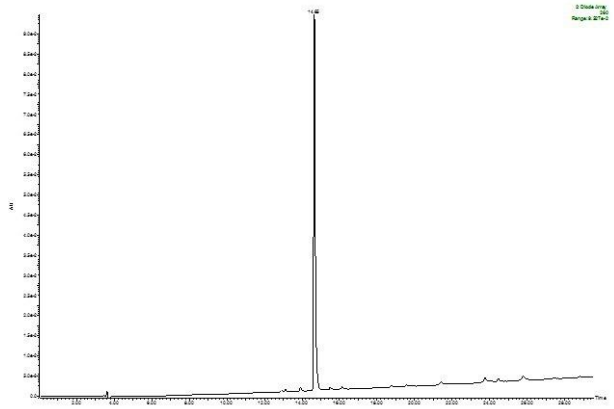

Figure S12. Reversed-phase HPLC-MS analysis of purified compound **8b**.

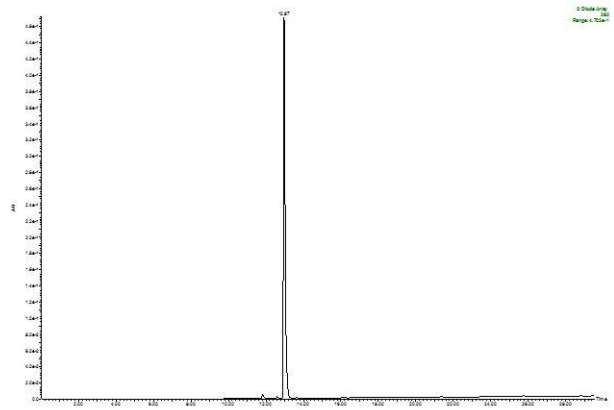

Figure S13. Reversed-phase HPLC-MS analysis of purified compound **9a**.

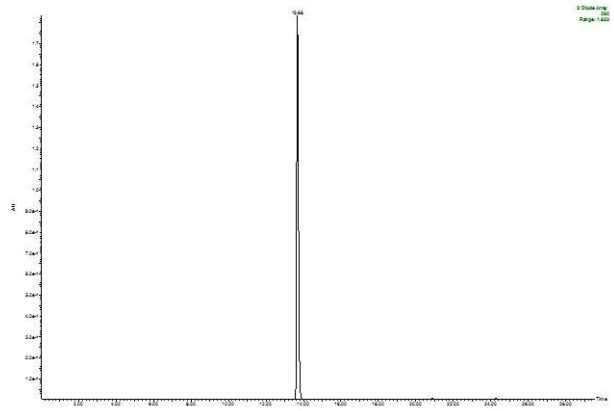

Figure S14. Reversed-phase HPLC-MS analysis of purified compound **9b**.

10.- HPLC-MS analysis of the N-difluoromethylation reaction of 10-11

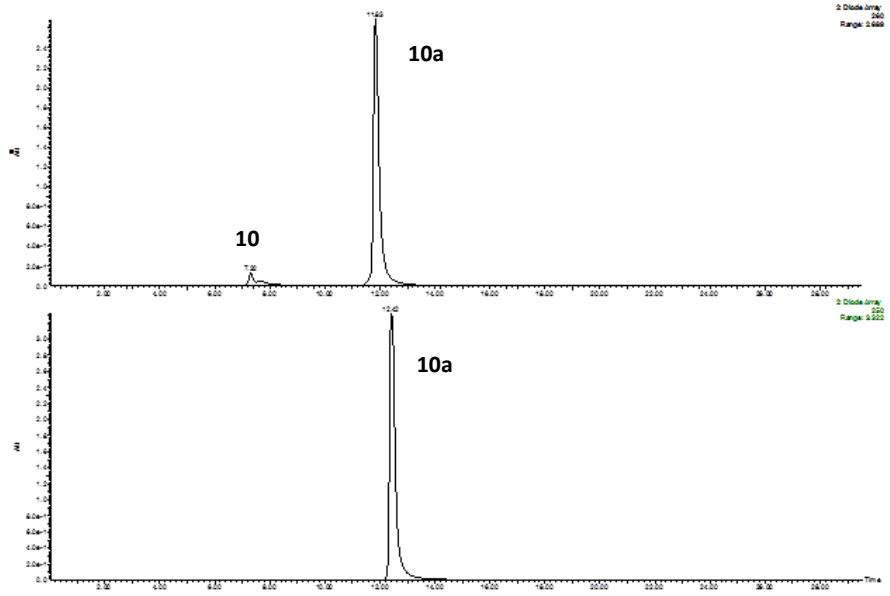

Figure S15. Reversed-phase HPLC-MS analysis for the N-difluoromethylation reaction of **10**: crude after 24 h (top) and purified compound **10b**.

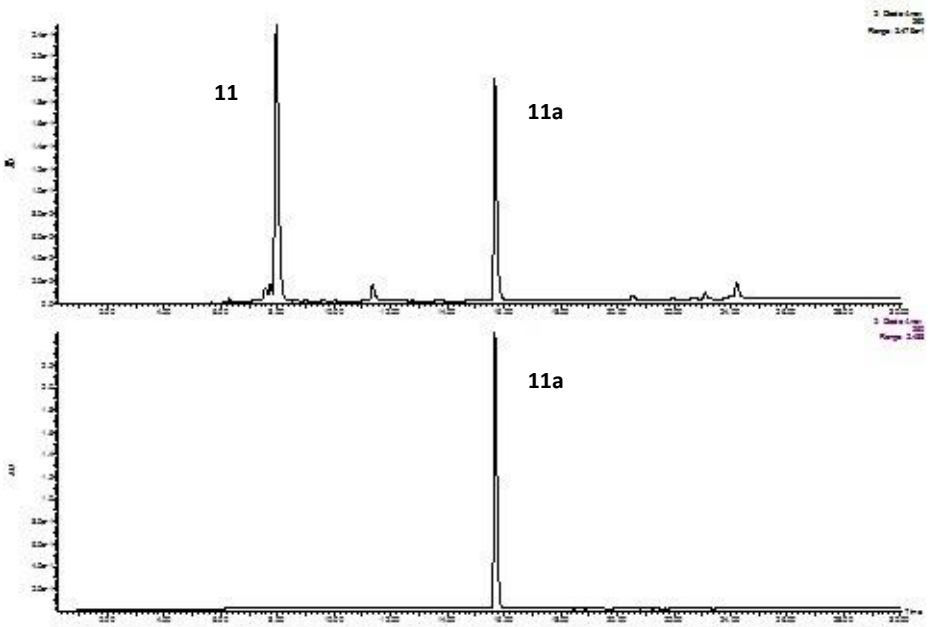

Figure S16. Reversed-phase HPLC-MS analysis for the N-difluoromethylation reaction of **11**: crude after 24 h (top) and purified compound **11a**.

11.- ^{1}H, ^{13}C and ^{19}F NMR spectra and HR ESI-MS of the compounds

Compound 2b

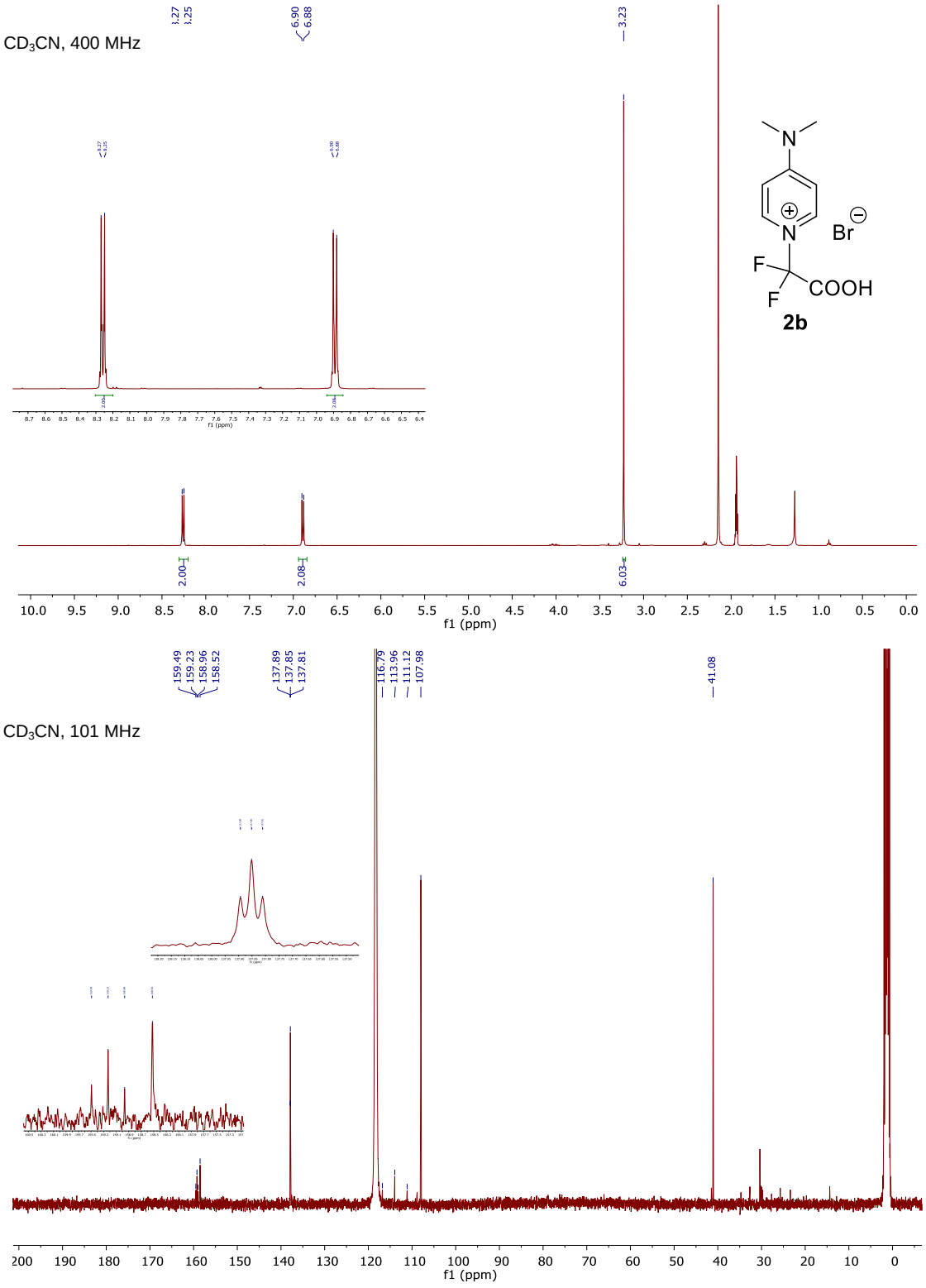

Figure S17. ^{1}H and ^{13}C NMR spectra of compound **2b** in CD_3CN.

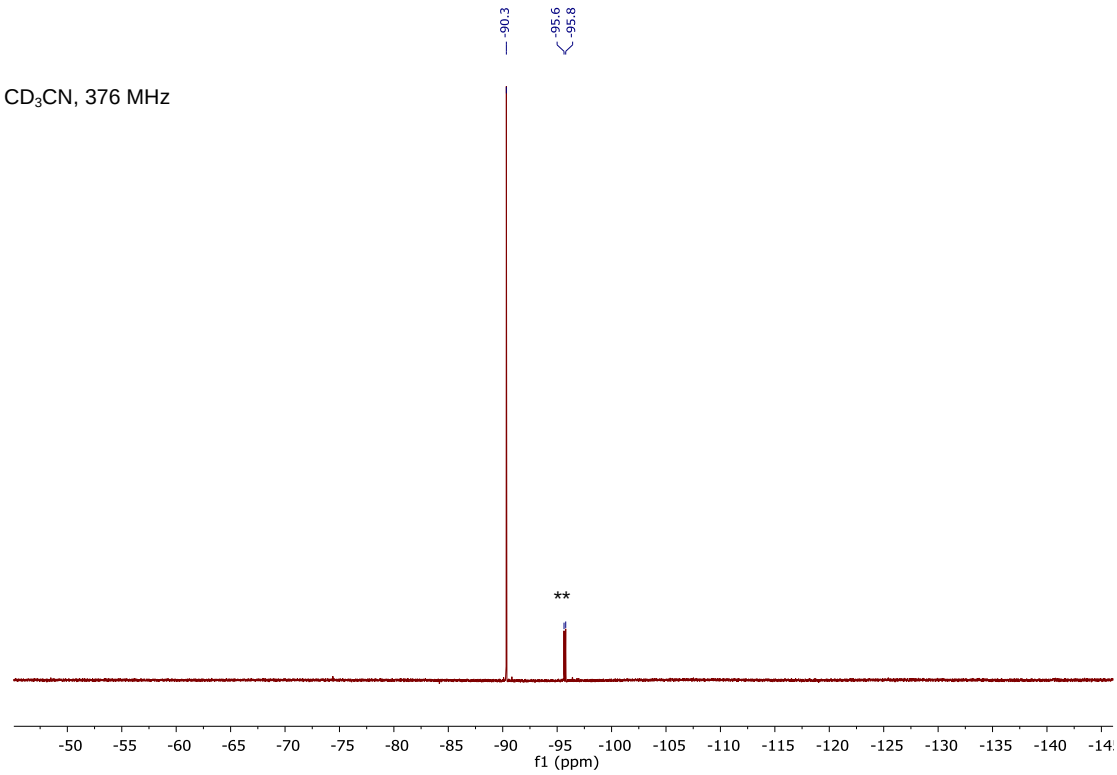

Figure S18. ^{19}F NMR spectra of compound **2b** in CD_3CN.** This doublet corresponds to the fluorine atoms of the CF_2H group in compound **3**, which was spontaneously generated from **2b** after standing in CD_3CN solution for 48 h prior to the registration of the ^{19}F NMR.

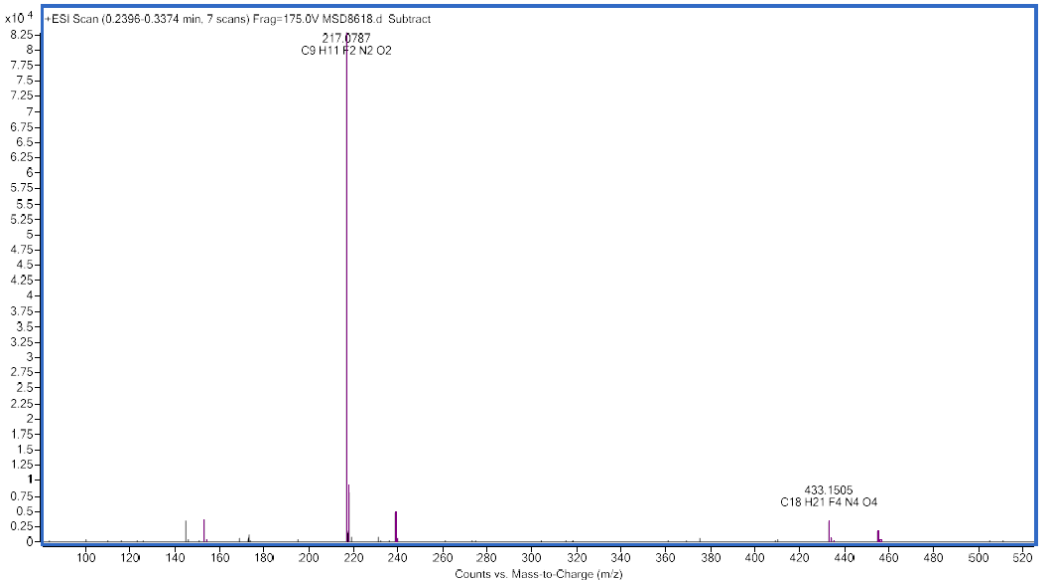

Figure S19. HR ESI-MS spectrum of compound **2b**.

Compound 3

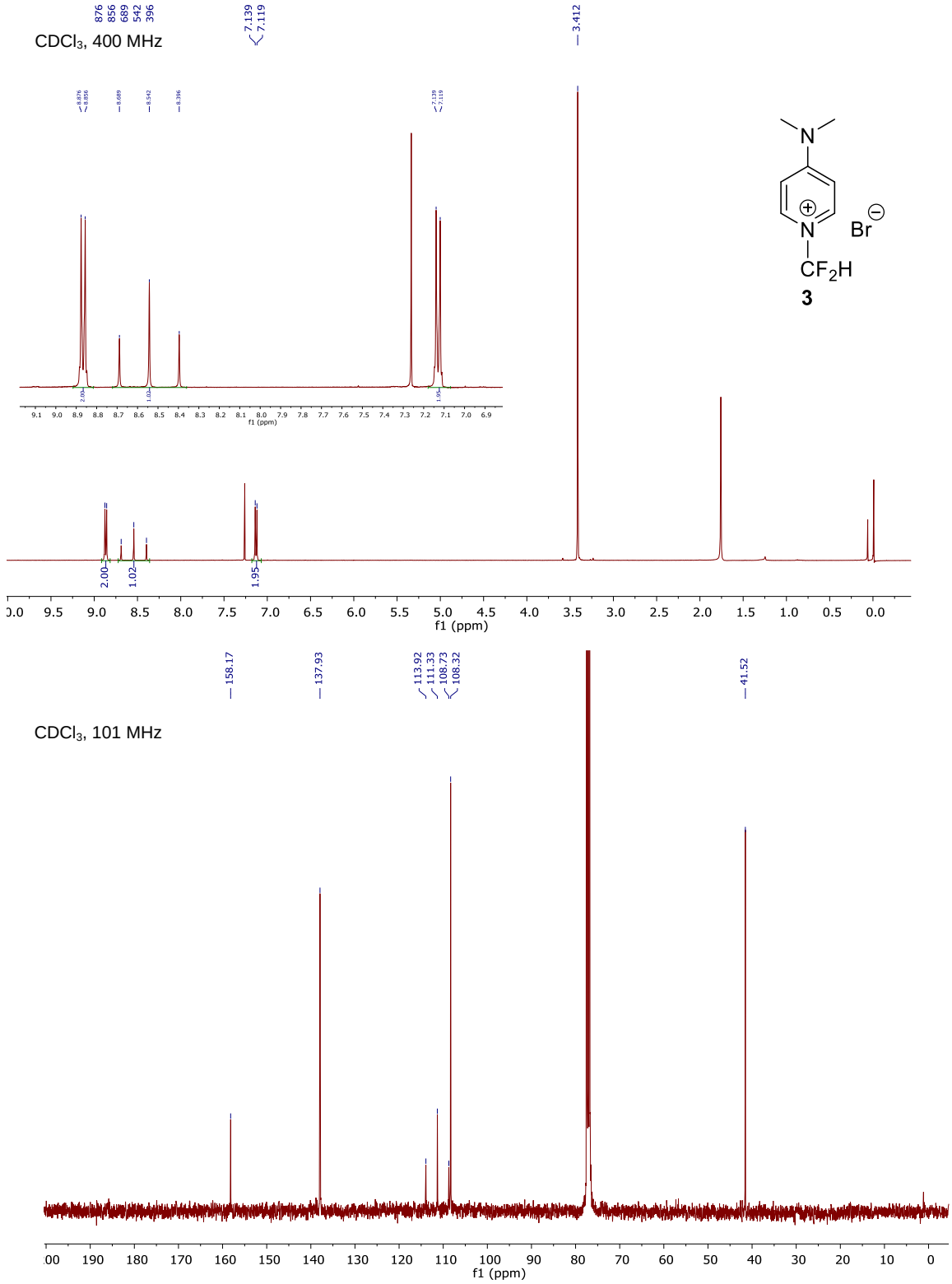

Figure S20. ^{1}H and ^{13}C NMR spectra of compound **3** in $CDCl_3$.

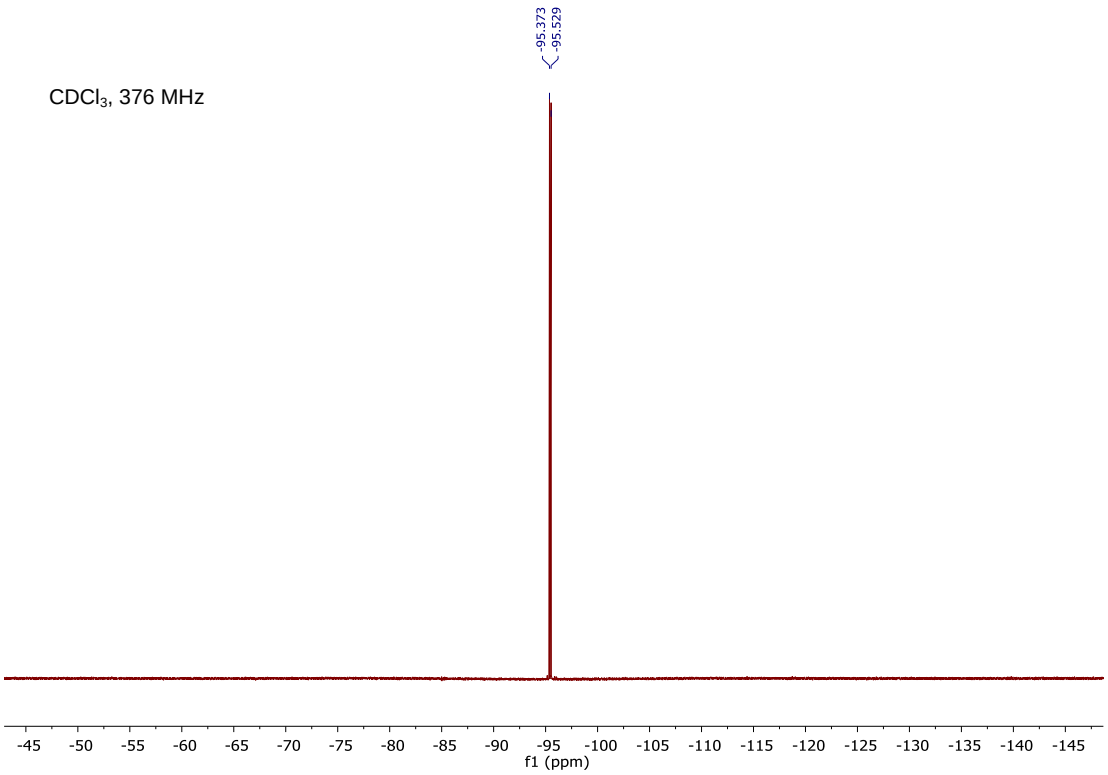

Figure S21. ^{19}F NMR spectra of compound **3** in $CDCl_3$.

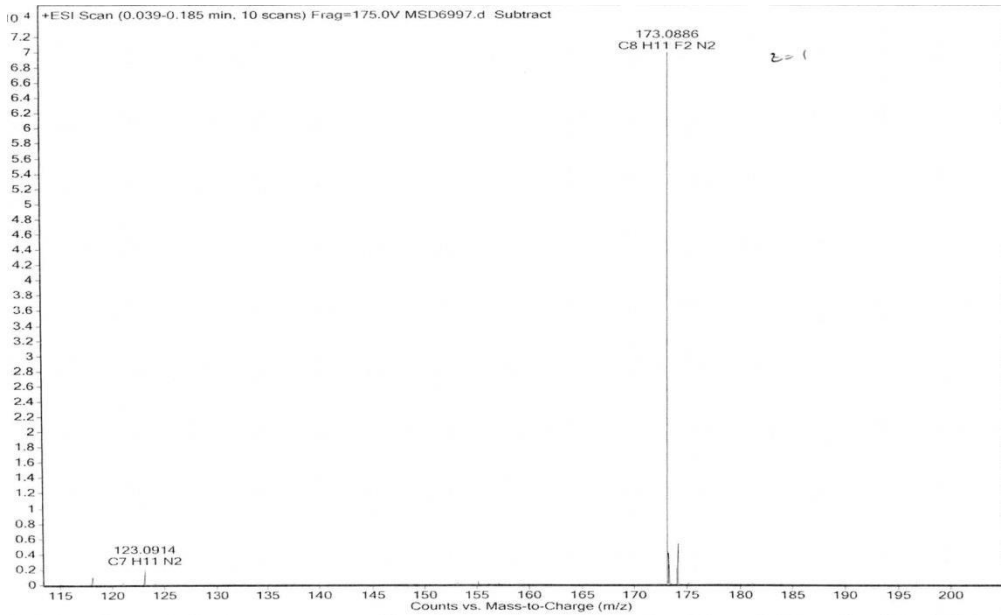

Figure S22. HR ESI-MS spectrum of compound **3**.

Compound 8b

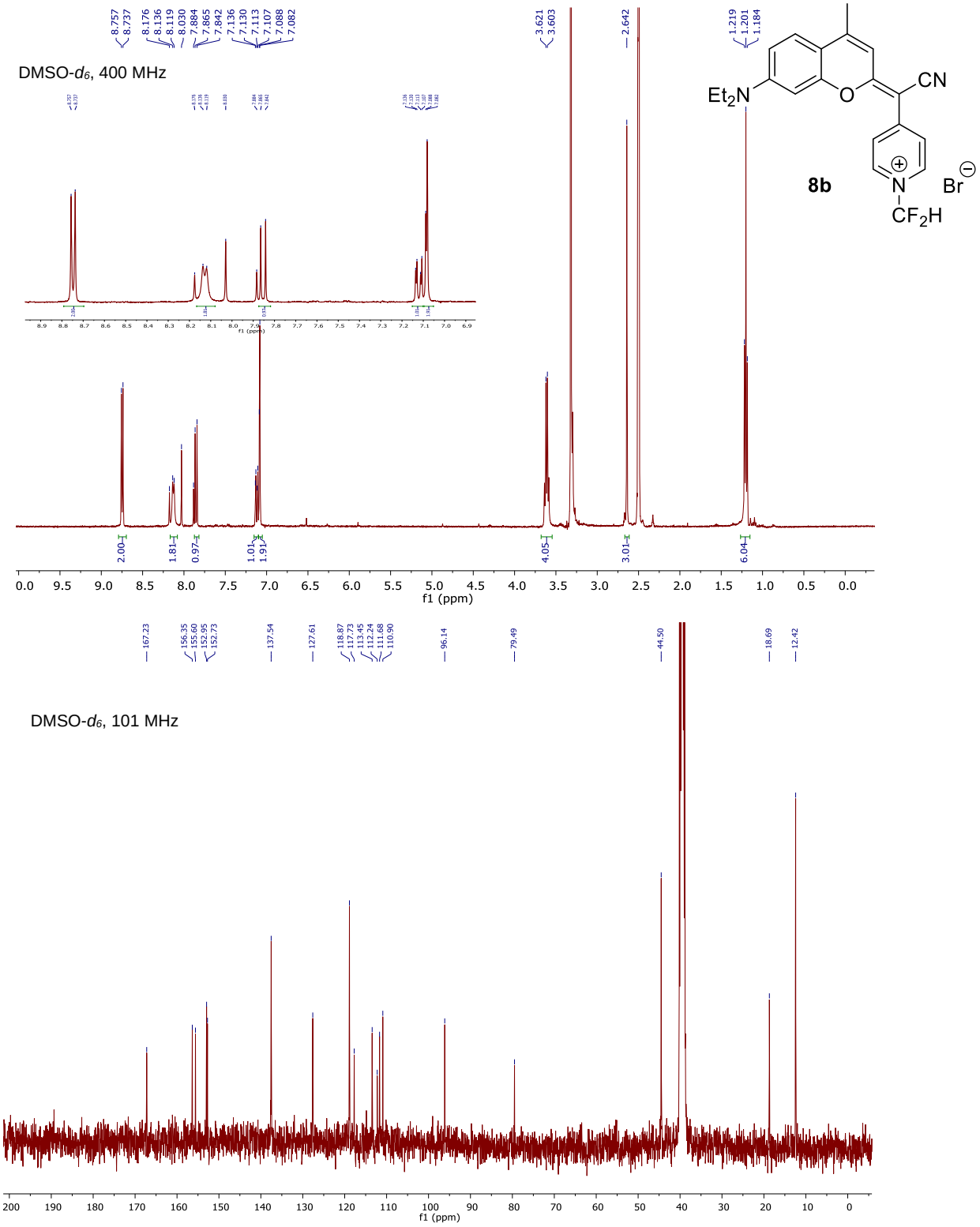

Figure S23. ^{1}H and ^{13}C NMR spectra of compound **8b** in DMSO-d_6.

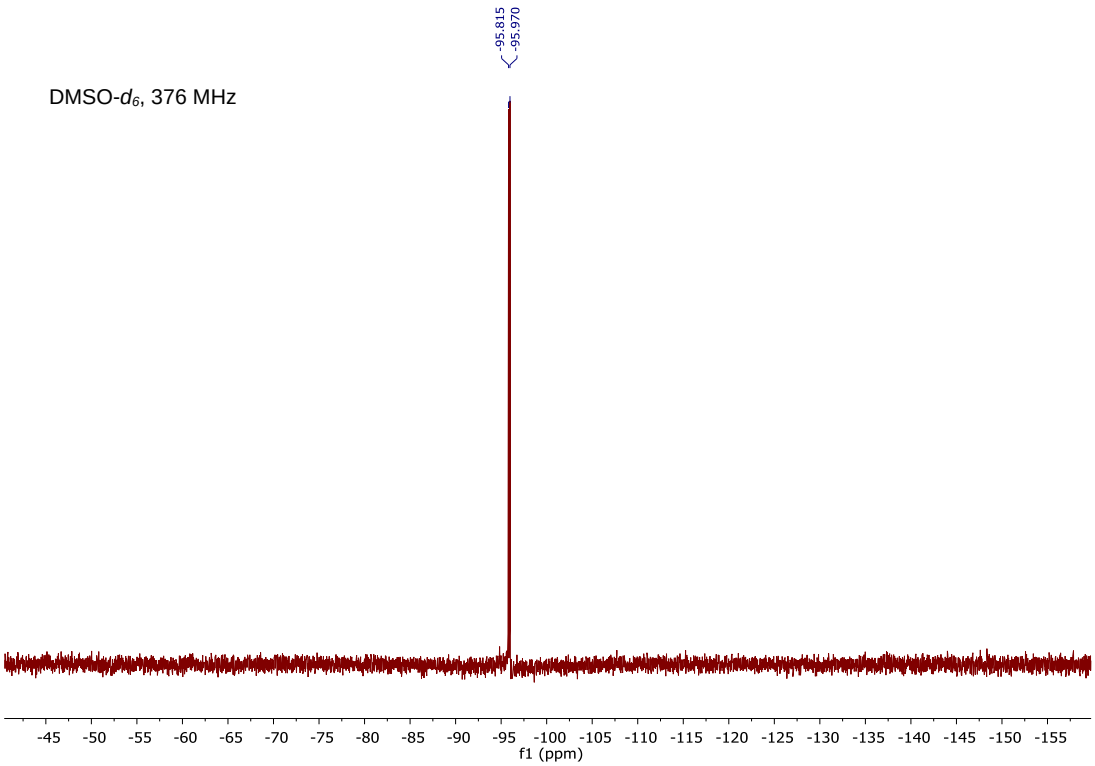

Figure S24. ^{19}F NMR spectra of compound **8b** in DMSO-d_6.

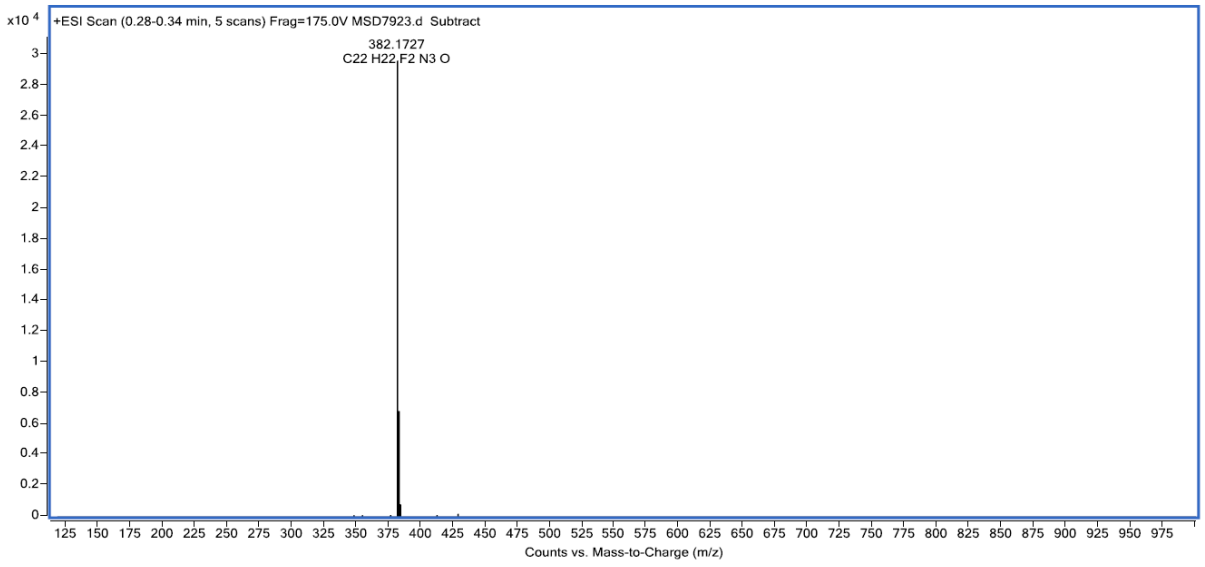

Figure S25. HR ESI-MS spectrum of compound **8b**.

Compound 9a

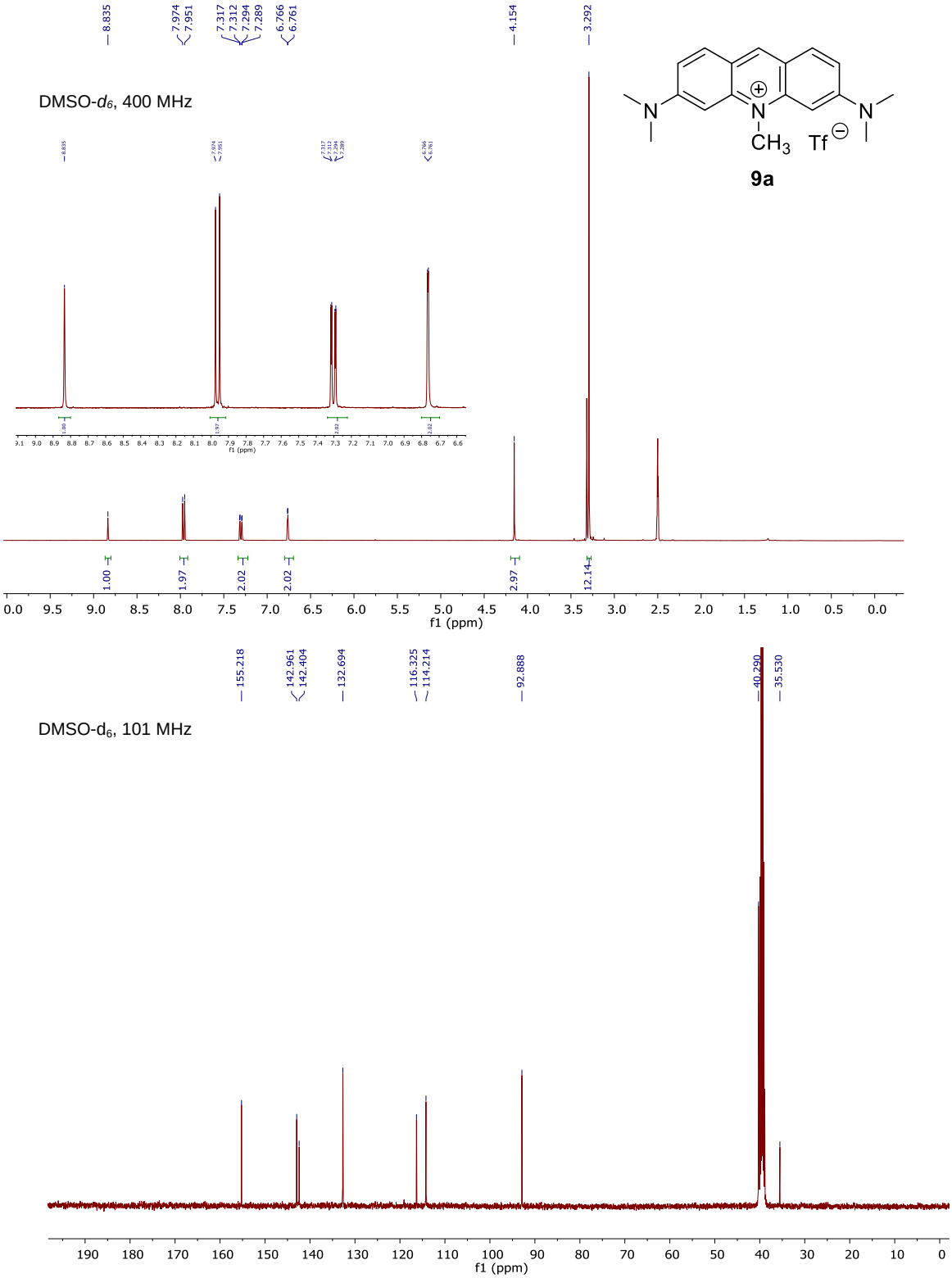

Figure S26. ^{1}H and ^{13}C NMR spectra of compound **9a** in DMSO-*d*$_6$.

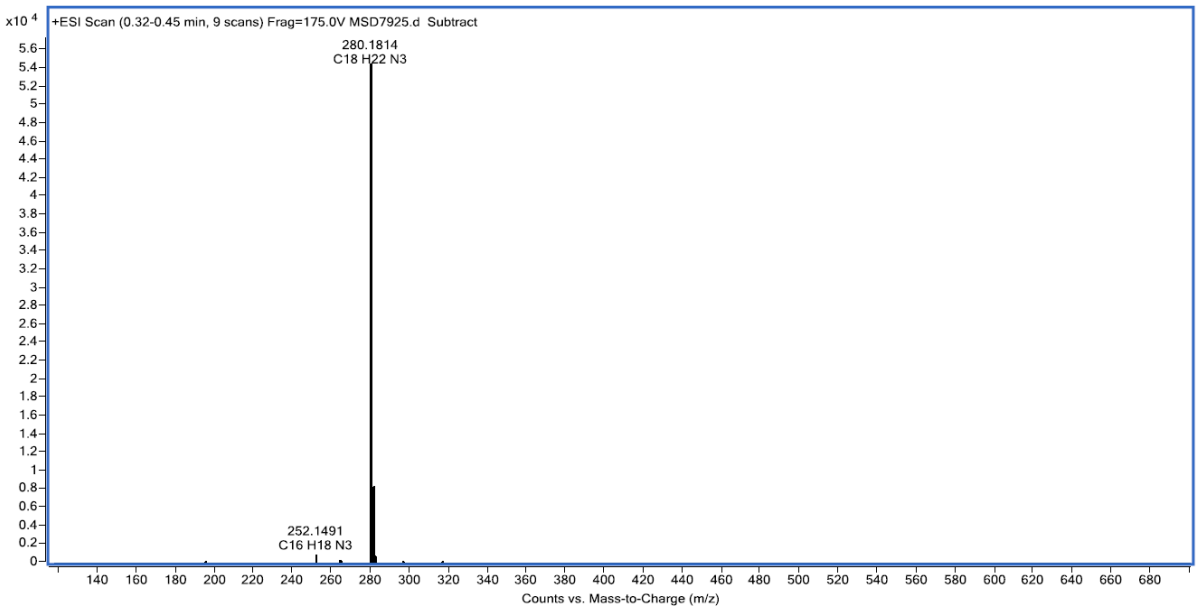

Figure S27. HR ESI-MS spectrum of compound **9a**.

Compound 9b

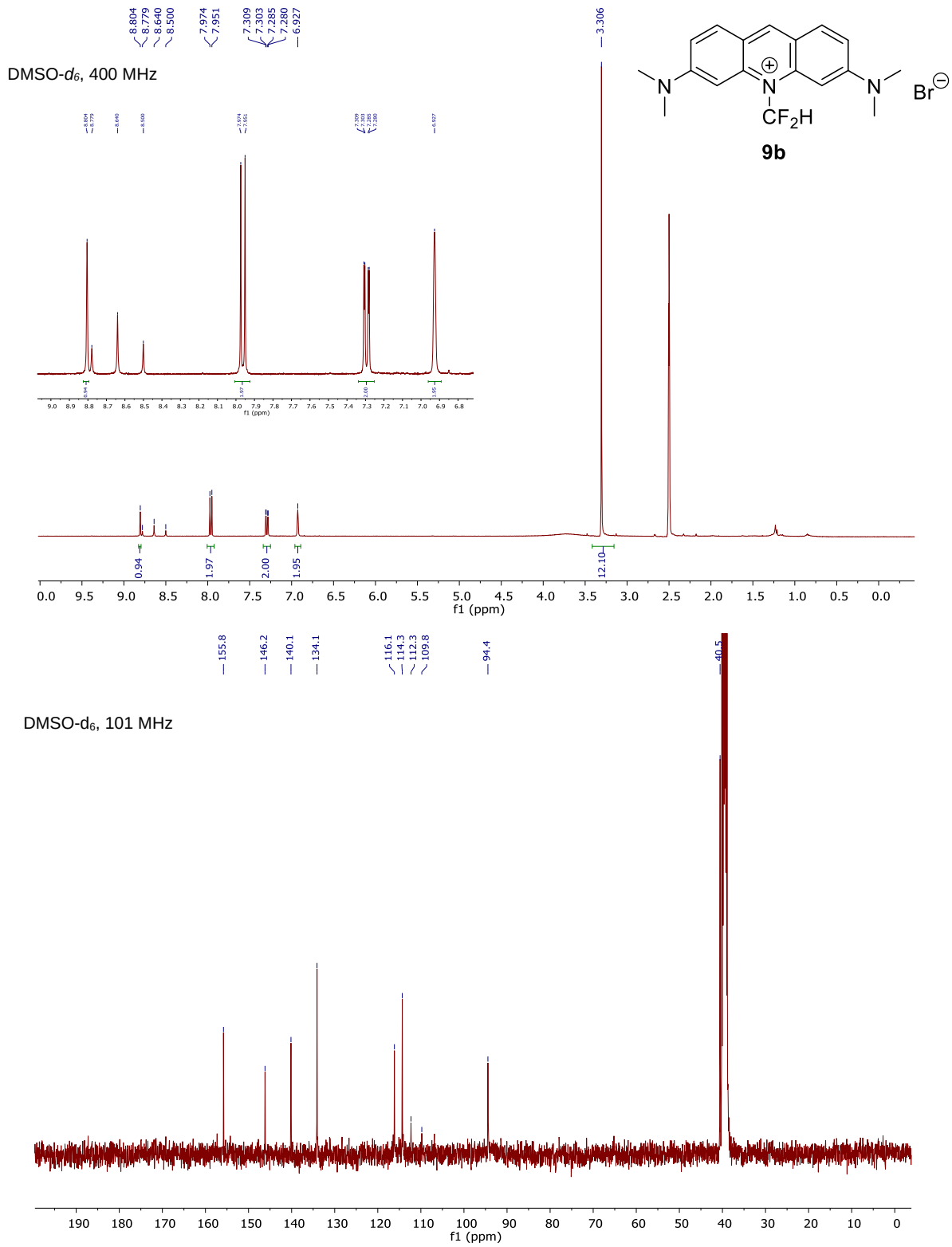

Figure S28. ^{1}H and ^{13}C NMR spectra of compound **9b** in DMSO-*d*$_6$.

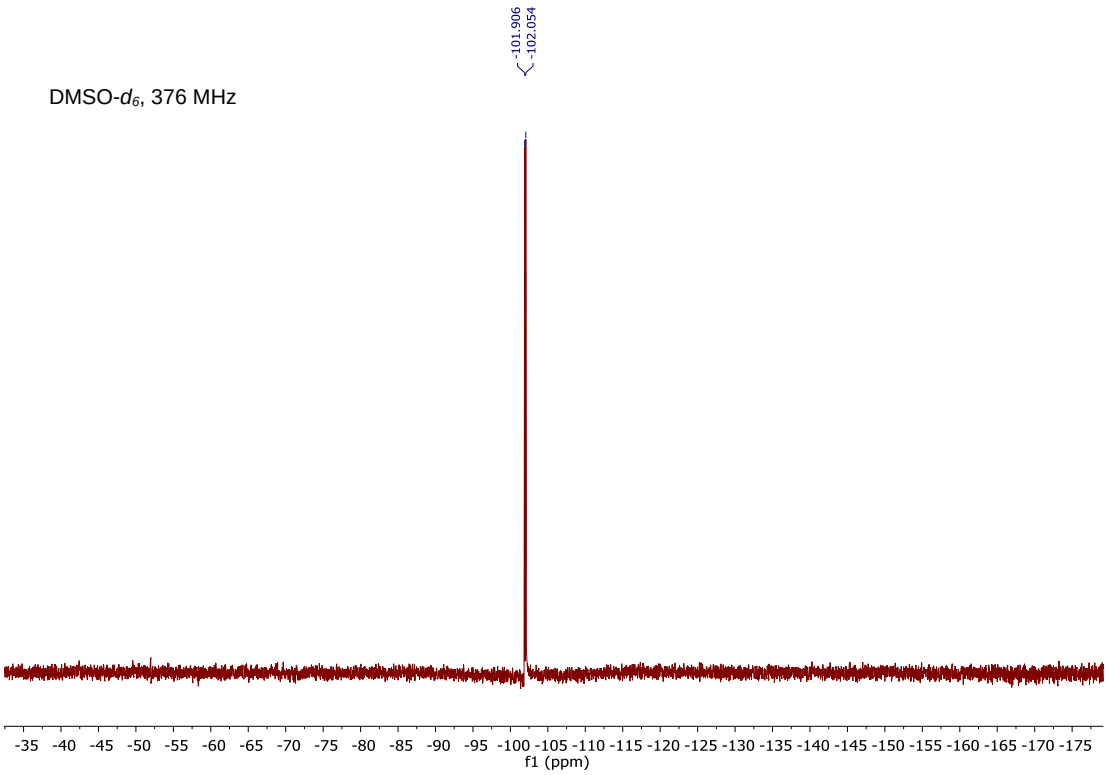

Figure S29. ^{19}F NMR spectra of compound **9b** in DMSO-d_6.

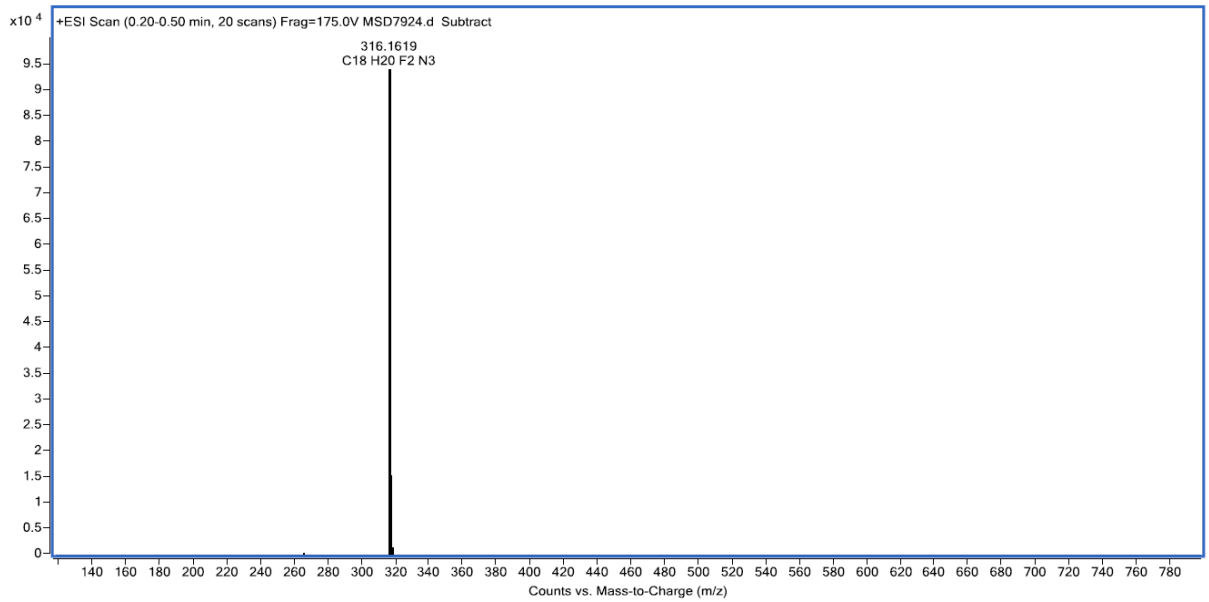

Figure S30. HR ESI-MS spectrum of compound **9b**.

Compound 10b

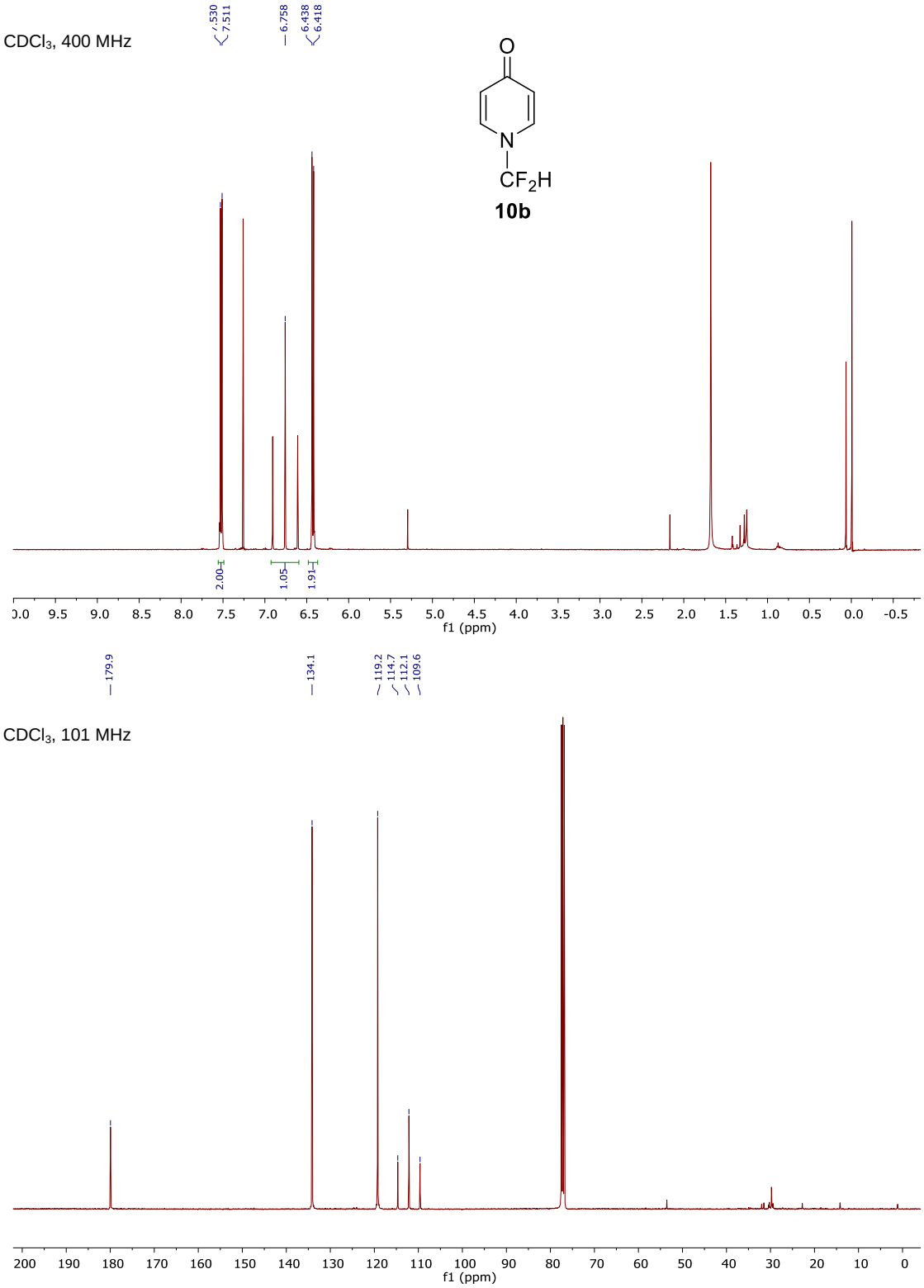

Figure S31. ^{1}H and ^{13}C NMR spectra of compound **10b** in $CDCl_3$.

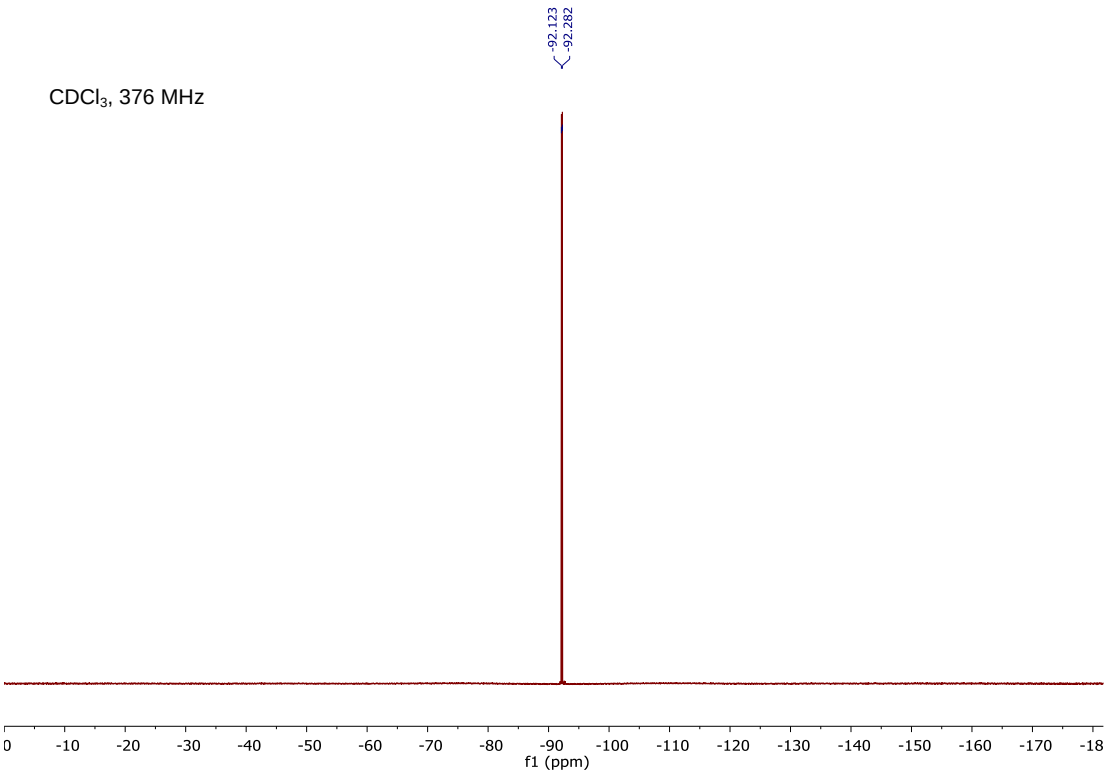

Figure S32. ^{19}F NMR spectra of compound **10b** in $CDCl_3$.

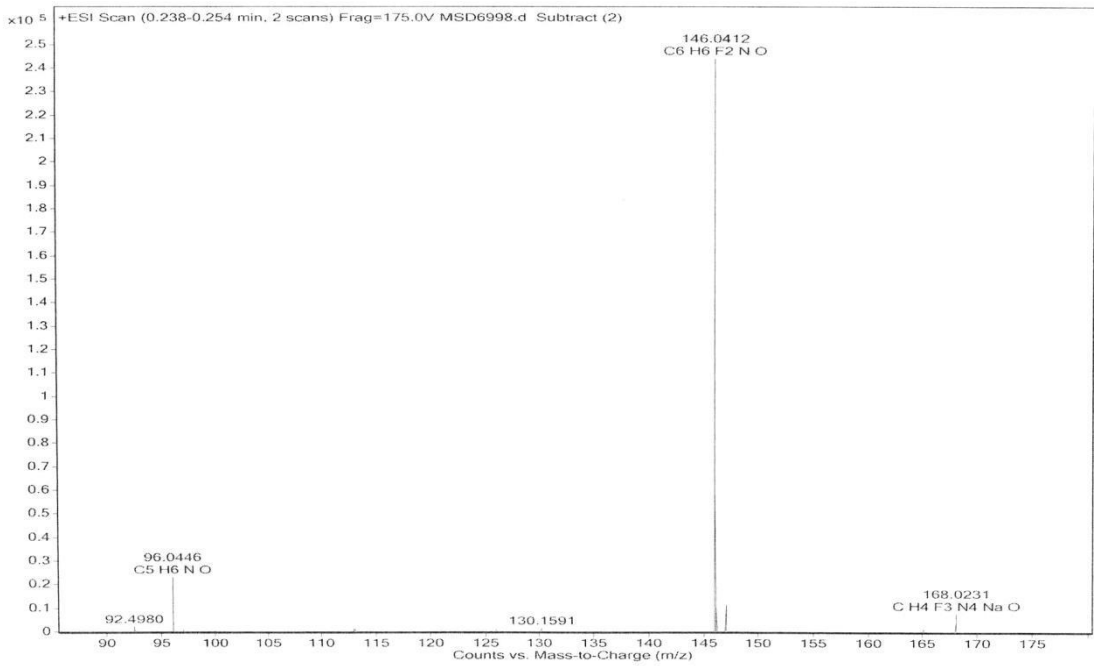

Figure S33. HR ESI-MS spectrum of compound **10b**.

Compound 11a

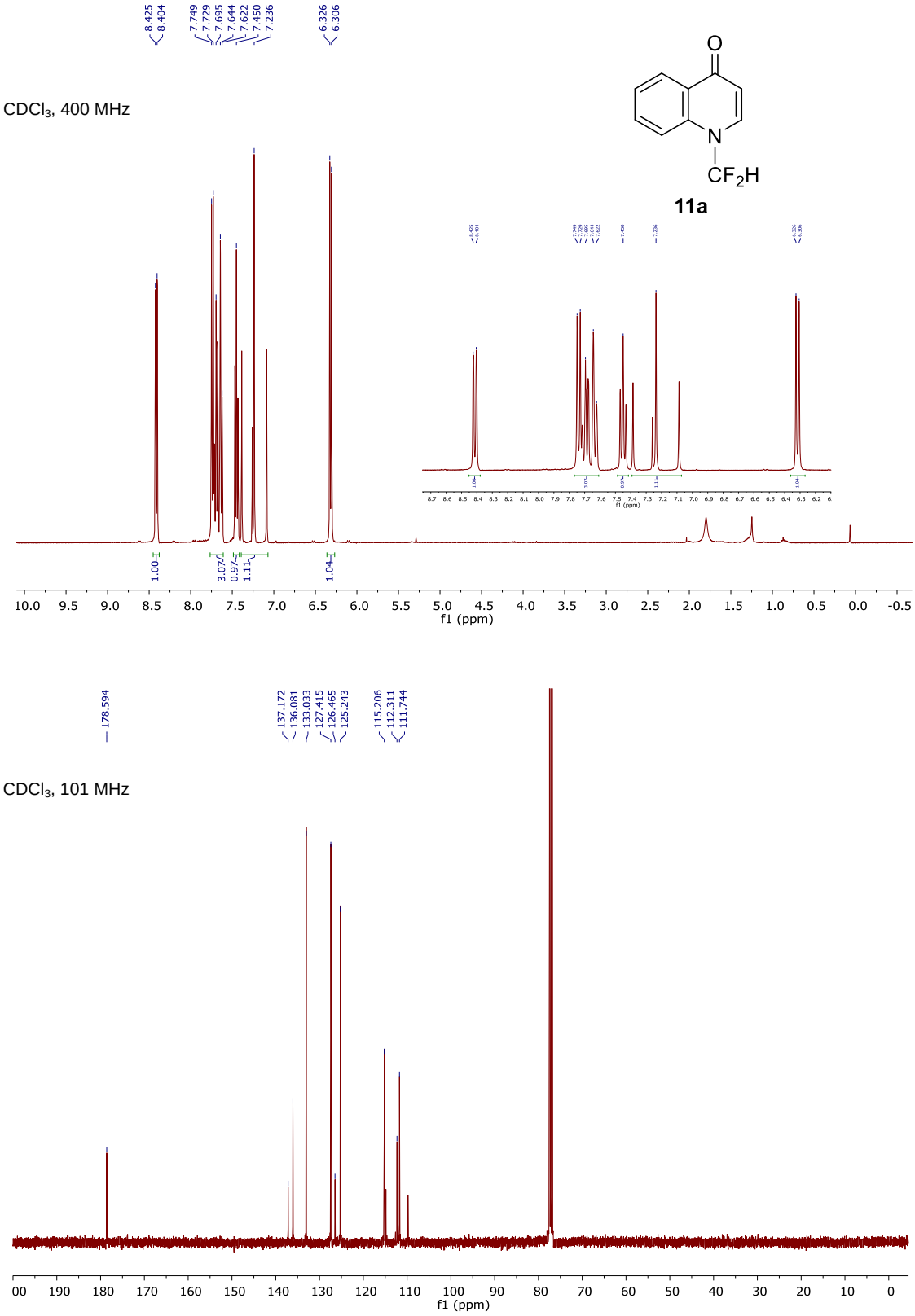

Figure S34. ^{1}H and ^{13}C NMR spectra of compound **11a** in $CDCl_3$.

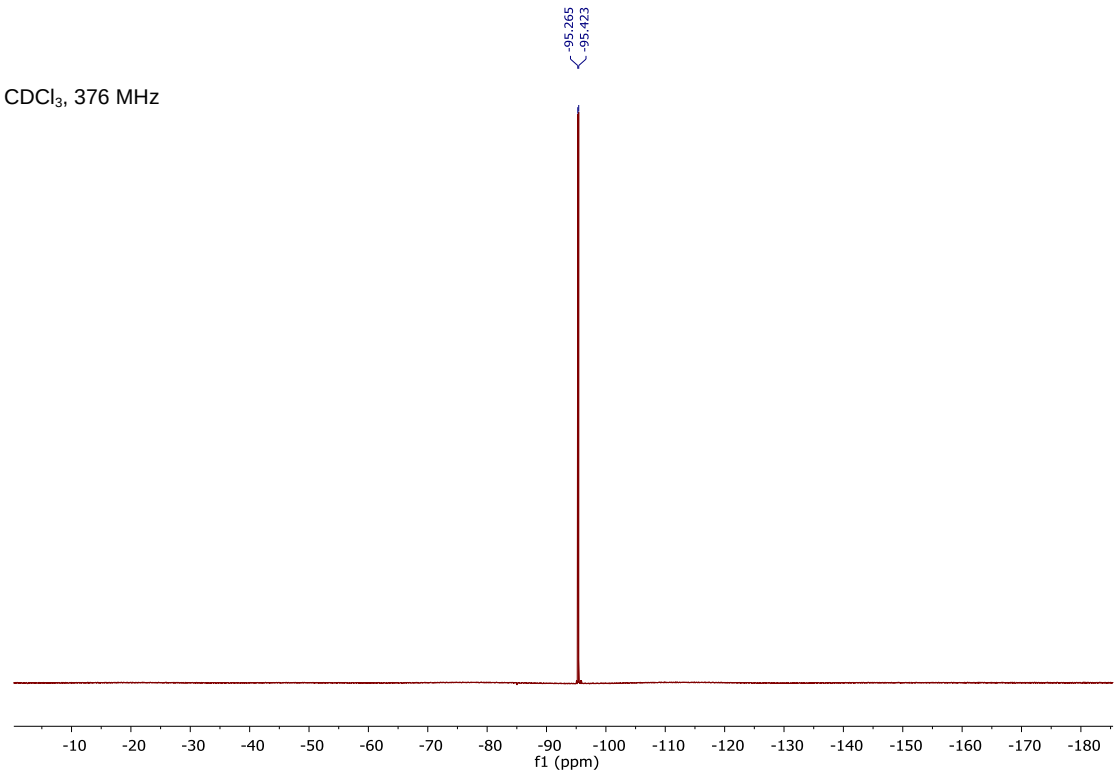

Figure S35. ^{19}F NMR spectra of compound **11a** in $CDCl_3$.

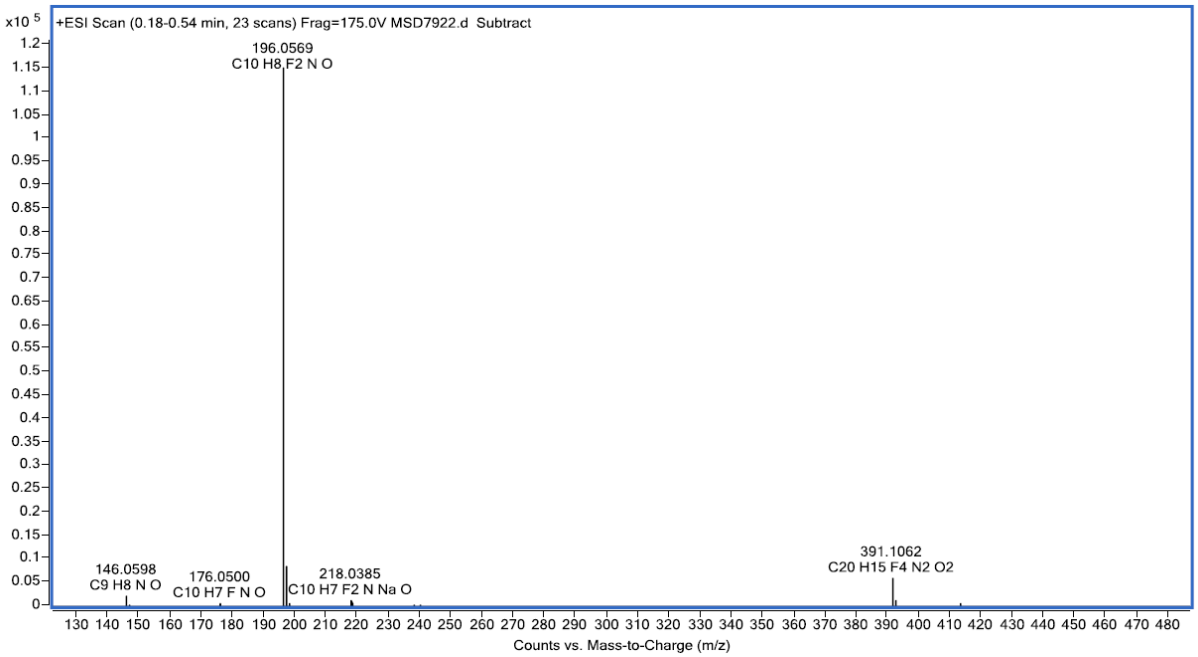

Figure S36. HR ESI-MS spectrum of compound **11a**.