Supporting Information

Hydrogen Bond Directed Photocatalytic Hydrodefluorination; Overcoming Electronic Control

Mohammad B. Khaled, Roukaya K. El Mokadem, and Jimmie D. Weaver III

Department of Chemistry, Oklahoma State University, Oklahoma 74078

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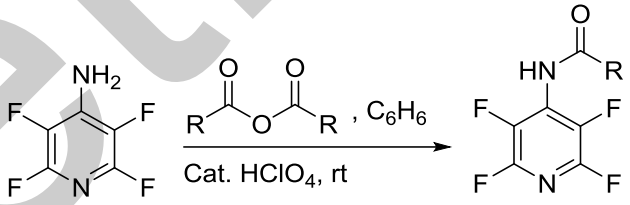
General Experimental

All reagents were obtained from commercial suppliers (Sigma-Aldrich, Oakwood chemicals, Alfa Aesar, or Matrix Scientific) and used without further purification unless otherwise noted. Acetonitrile (CH_3CN) was dried over molecular sieves. Diisopropylethylamine was distilled and stored over KOH pellets. Pentafluoroaniline (**6o**) was purchased from Sigma Aldrich. Photocatalyst tris-*fac*(2-phenyl pyridinato-C^2)iridium(III)($Ir(ppy)_3$) ($Ir(ppy)_3$) was synthesized according to literature procedure.[1] Reactions were monitored by ^{19}F NMR and GC-MS (QP 2010S Shimadzu, equipped with auto sampler). NMR spectra were obtained on a 400 MHz Bruker Avance III spectrometer or a 400 MHz Unity Inova spectrometer. ^1H and ^{19}F NMR chemical shifts are reported in ppm relative to the residual solvent peak. Purifications were carried out using Teledyne Isco Combiflash Rf 200i flash chromatograph with Sorbtech Rf normal phase silica (4 g, or 12 g columns). Substrate synthesis reactions were monitored by thin layer chromatography (TLC), obtained from Sorbent Technology, silica XHL TLC Plates with UV254, glass backed 250 µm and were visualized with ultraviolet light.

Photocatalytic Reaction Setup

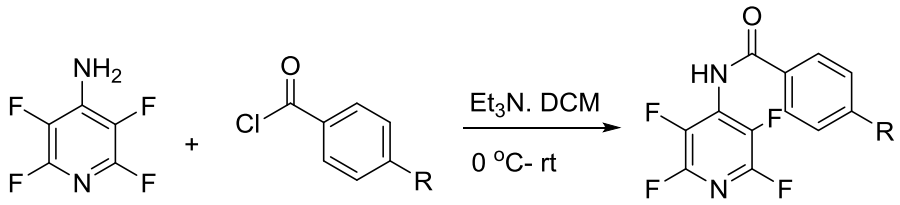
Photocatalytic reactions were carried out in a light bath as described below. Strips of blue LEDs (18 LED/ft.) were purchased from Solid Apollo. The strips (4.9 ft) were wrapped around on the walls of glass crystallization dish and secured with masking tape and then wrapped with aluminum foil. A lid which rest on the top was fashioned from cardboard and holes were made such that NMR tubes were held firmly in the cardboard lid which was placed on the top of bath. Water was added to the bath such that the tubes were submerged in the water which was maintained at 25 °C, 45 °C, or 60 °C by the aid of a thermostat controlled heating mantle.

General Procedure A. These reactions were carried out when the acid anhydride was available**.**



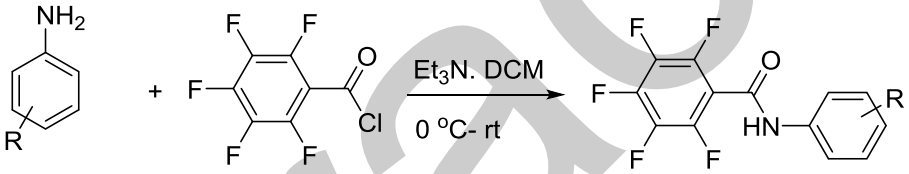
This procedure was adapted from a literature procedure.[2,3] In a 25 mL reaction flask, fluorinated starting material (1.0 equiv), acid anhydride (1.4 equiv), $HClO_4$ (0.1 equiv, 5.8 M) and benzene (0.3 M) were added and stirred at room temperature. The reaction mixture was extracted with ethyl acetate (3 x 15 mL). The combined ethyl acetate portion was washed with water (1 x 15 mL), 1 M HCl (1 x 10 mL), and brine (1 x 10 mL). The ethyl acetate portion was dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by normal phase chromatography.

General Procedure B. These reactions were carried out when the substituted benzoyl chlorides were available.



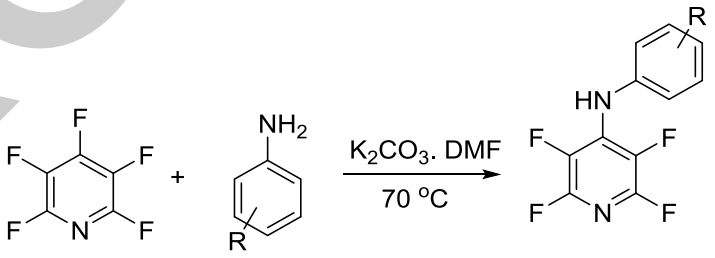
Fluorinated starting material (1.0 equiv), triethylamine (2 equiv), in DCM (0.3 M), and then substituted benzoyl chloride (2.0 equiv) were added under argon at 0 °C. This solution was stirred one hour at 0 °C, then at room temperature overnight, and subsequently poured into water (30 mL). After extraction with DCM (3 x 50 mL), and drying with anhydrous $MgSO_4$, the solvent was removed under reduced pressure. The crude material was purified by normal phase chromatography.

General Procedure C. These reactions were carried out when pentafluorobenzoyl amides were desired.



Aryl amine (1.0 equiv), triethylamine (2 equiv), in DCM (0.3 M), and then 2,3,4,5,6-pentafluorobenzoyl chloride (2.0 equiv) was added under argon at 0 °C. This solution was stirred one hour at 0 °C, then at room temperature for another 12 h, and subsequently poured into water (30 mL). After extraction with DCM (3 x 50 mL), and drying with $MgSO_4$, the solvent was removed under reduced pressure. The crude material was purified by normal phase chromatography.

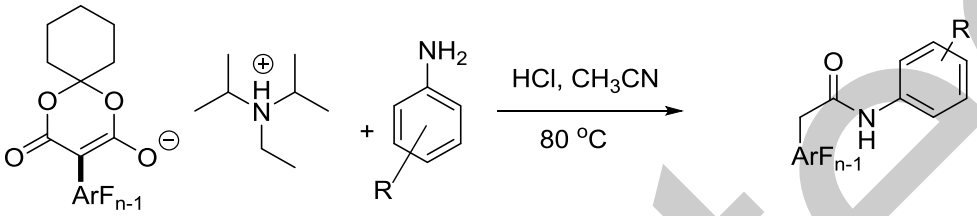
General Procedure D.



Aryl amine (1.5 equiv), K_2CO_3 (2 equiv), in DMF (0.2 M), and then pentafluoropyridine (1 equiv) were added under an atmosphere of argon at 0 °C, allowed to warm to room temperature over one hour, and then stirred at 70 °C overnight. The suspension was poured into ice water and

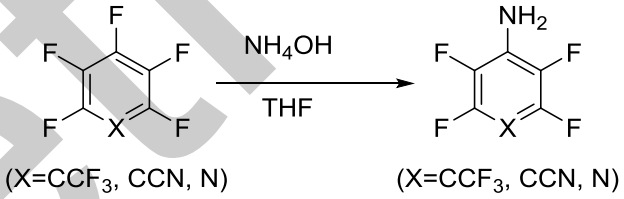
subsequently extracted with diethyl ether (2 x 60 mL). After washing the organic phase with water (3 x 15 mL), it was dried with $MgSO_4$, and the solvent was removed under reduced pressure. The crude material was purified by normal phase chromatography.

General Procedure E. The substrates are formed in a single step via the decomposition of the perfluoroarylated Meldrum's acid enolate salts

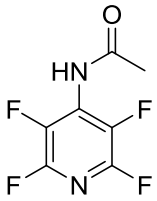


Commercially available FAYE blocks were transformed to the amide by an adaption of the literature procedure.[4] The ammonium enolate salt (1.0 equiv) and aryl amine (3.0 equiv) were dissolved in CH_3CN (0.13 M). To this solution, HCl was added (1.2 equiv, 2 M HCl in diethyl ether). The reaction flask was placed in an oil bath which was maintained at 80 °C for 12 h. After cooling the reaction mixture to room temperature, the solvent was removed under reduced pressure. This residue was poured into ice water (50 mL), and subsequently extracted with DCM (3 x 50 mL). After washing the combined organic phase with 15 mL brine, the organic layer was dried with $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude material was purified by normal phase chromatography.

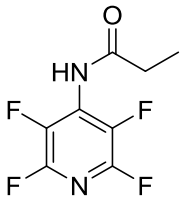
General Procedure F.



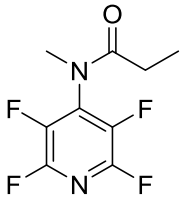
This procedure was adapted from the literature procedures.[2,3] A 50 mL flask equipped with a magnetic stirrer and condenser was charged with fluorinated arenes (pentafluoropyridine, octafluorotoluene, or 2,3,4,5,6-pentafluorobenzonitrile (1 mL), NH_4OH (4 mL, 28%w/w), and THF (15 mL). The reaction mixture was heated to reflux for 18 h. The flask was cooled to room temperature and THF was removed under reduced pressure. To the residue, was added water (10 mL) and the aqueous portion was extracted with DCM (3 x 20 mL). The combined organic phase was dried with $MgSO_4$, filtered, and concentrated under reduced pressure to furnish the corresponding amine (2,3,5,6-tetrafluoropyridin-4-amine, 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline, or 4-amino-2,3,5,6-tetrafluorobenzonitrile), which were sufficiently pure for further use.



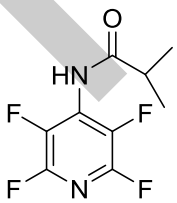
4a *N*-(perfluoropyridin-4-yl)acetamide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 3.26 mmol), acetic anhydride (0.390 mL, 4.10 mmol), $HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 6 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 4 cv and ramped to 100% EtOAc for 4-45 cv and then held at 100% EtOAc 45-48 cv) on a 12 g silica column to afford of **4a** in 29% yield (200 mg, 1.47 mmol) as a white solid which matched the literature.[5] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (s, 1H), 2.33 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.6- -90.2 (m, 2F), -145.7- -145.4 (m, 2F).



4b *N*-(perfluoropyridin-4-yl)propionamide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 3.26 mmol), propionic anhydride (0.520 mL, 4.00 mmol), conc. $HClO_4$ (17.0μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 5 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-30 cv and then held at 100% EtOAc 30-40 cv) on a 12 g silica column to afford of **4b** in 36% yield (250 mg, 1.13 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (s, 1H), 2.57 (q, *J* = 7.5 Hz, 2H), 1.30 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.1 – -90.3 (m, 2F), -145.2 – -146.4 (m, 2F).

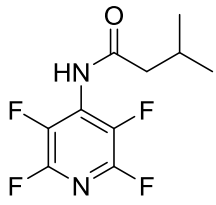


3b *N*-methyl-*N*-(perfluoropyridin-4-yl)propionamide In a 50 mL reaction flask, K_2CO_3 (0.155 g, 1.12 mmol) was suspended in anhydrous DMF (10 mL). The mixture was cooled 0 °C and a solution of **4b** (0.250 g, 1.12 mmol) in DMF (5 mL) was added dropwise. The reaction was stirred at 0 °C for 30 minutes. Then a solution of CH_3I (0.10 mL, 1.60 mmol) in anhydrous DMF (2 mL) was slowly added to the mixture. After complete addition, the reaction was warmed to room temperature and stirred overnight. Diethyl ether (60 mL) was added and the mixture was washed with water (3 × 10 mL). The organic layer was washed with brine (15 mL), dried with $MgSO_4$ and concentrated under reduced pressure to provide the crude material. The crude material was purified by flash chromatography using hexane:EtOAc (0 – 20% EtOAc for 20 cv and ramped to 100% EtOAc for 20-30 cv and then held at 100% EtOAc 30-35 cv) on a 12 g silica column to afford of **3b** in 92% yield (0.152 g, 0.640 mmol) as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.25 (s, 3H), 2.54 – 1.94 (m, 2H), 1.23 – 1.01 (m, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -87.4- -88.2 (m, 2F), -145.8 – -146.3 (m, 2F).

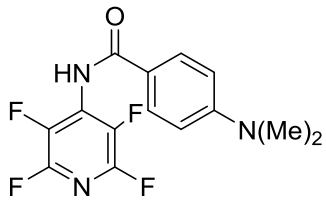


4c *N*-(perfluoropyridin-4-yl)isobutyramide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 3.26 mmol), isobutyric anhydride (0.640 mL, 4.00 mmol), conc. $HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 6 h. After workup, the crude material was purified by flash chromatography using

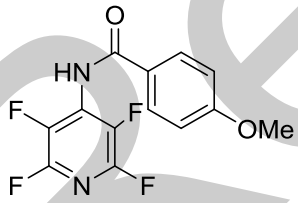
hexane:EtOAc (0 – 50% EtOAc for 10 cv and ramped to 100% EtOAc for 10-40 cv and then held at 100% EtOAc 40-45 cv) on a 12 g silica column to afford of **4c** in 45% yield (350 mg, 1.51 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.06 (d, *J* = 33.5 Hz, 1H), 2.72 (hept, *J* = 6.9 Hz, 1H), 1.34 (d, *J* = 6.9 Hz, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -88.5 – -90.3 (m, 2F), -145.3 – -147.1 (m, 2F).



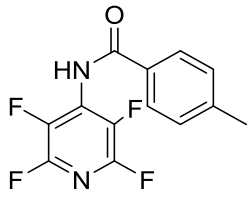
4d 3-methyl-*N*-(perfluoropyridin-4-yl)butanamide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 3.26 mmol), isovaleric anhydride (0.810 mL, 4.00 mmol), conc.$HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 5 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 10 cv and ramped to 100% EtOAc for 10-35 cv and then held at 100% EtOAc 35-45 cv) on a 12 g silica column to afford of **4d** in 58% yield (473 mg, 1.90 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.04 (d, *J* = 15.8 Hz, 1H), 2.40 (d, *J* = 7.2 Hz, 2H), 2.32 – 2.20 (m, 1H), 1.08 (d, *J* = 6.6 Hz, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -88.7 – -90.3 (m, 2F), -144.7 – -146.8 (m, 2F).



4e 4-(dimethylamino)-*N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.300 g, 1.81 mmol), 4-(dimethylamino)benzoyl chloride (0.660 g, 2.10 mmol), triethylamine (0.500 mL, 3.60 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 15 cv and ramped to 100% EtOAc for 15-45 cv and then held at 100% EtOAc 45-50 cv) on a 12 g silica column to afford of **4e** in 31% yield (176 mg, 0.560 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 7.98 (m, 2H), 6.71 – 6.67 (m, 2H), 3.10 (s, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.5 – -89.8 (m, 2F), -145.4 – -145.6 (m, 2F).

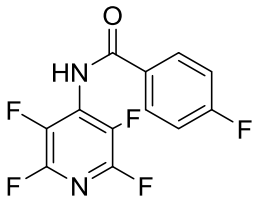


4f 4-methoxy-*N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.300 g, 1.81 mmol), 4-methoxybenzoyl chloride (0.61 g, 3.6 mmol), triethylamine (0.500 mL, 3.60 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 10 cv and ramped to 100% EtOAc for 10-45 cv and then held at 100% EtOAc 45-55 cv) on a12 g silica column to afford of **4f** in 26% yield (142 mg, 0.470 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 7.96 (m, 2H), 6.99 – 6.84 (m, 2H), 3.81 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.4 – -89.9 (m, 2F), -145.8 – -146.3 (m, 2F).

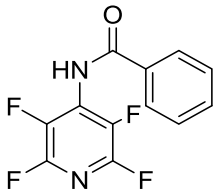


4g 4-methyl-*N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine

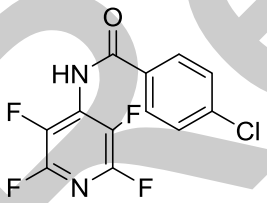
(0.300 g, 1.81 mmol), *p*-toluoyl chloride (0.560 g, 3.60 mmol), triethylamine (0.500 mL, 3.60 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-35 cv and then held at 100% EtOAc 35-55 cv) on a 12 g silica column to afford of **4g** in 45% yield (229 mg, 0.810 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 7.9 Hz, 2H), 7.67 (s, 1H), 7.28 (d, *J* = 7.9 Hz, 2H), 2.39 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -87.7 – -91.1 (m, 2F), -144.1 – -147.3 (m, 2F).



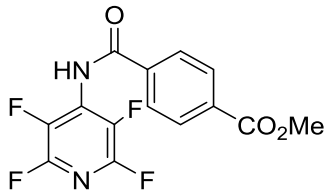
4h 4-fluoro-*N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.300 g, 1.81 mmol), 4-fluorobenzoyl chloride (0.570 g, 3.60 mmol), triethylamine (0.500 mL, 3.60 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 8 cv and ramped to 100% EtOAc for 8-42 cv and then held at 100% EtOAc 42-48 cv) on a 12 g silica column to afford of **4h** in 40% yield (210 mg, 0.730 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 – 7.67 (m, 2H), 7.16 – 6.98 (m, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -91.8 (m, 2F), -106.7 (s, 1F), -145.1 – -146.3 (m, 2F).



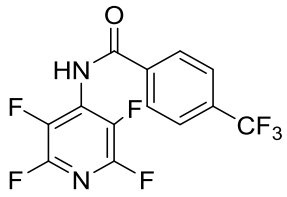
4i *N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 3.26 mmol), benzoic anhydride (0.910 mL, 4.00 mmol), conc.$HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 8 h. After workup, The crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 10 cv and ramped to 100% EtOAc for 10-37 cv and then held at 100% EtOAc 37-50 cv) on a 12 g silica column to afford of **4i** in 51% yield (460 mg, 1.70 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 – 7.95 (m, 2H), 7.76 – 7.66 (m, 2H), 7.59 (dd, *J* = 8.4, 7.1 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -88.2 – -90.4 (m, 2F), -144.5 – -146.8 (m, 2F).



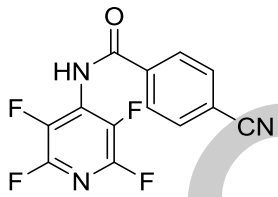
4j 4-chloro-*N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.300 g, 1.81 mmol), 4-chlorobenzoyl chloride (0.630 g, 3.60 mmol), triethylamine (0.500 mL, 3.60 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 12 cv and ramped to 100% EtOAc for 12-40 cv and then held at 100% EtOAc 40-46 cv) on a 12 g silica column to afford of **4j** in 67% yield (371 mg, 1.22 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.73 (s, 1H), 7.45 (d, *J* = 8.3 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -88.3 – -90.8 (m, 2F), -144.2 – -147.4 (m, 2F).



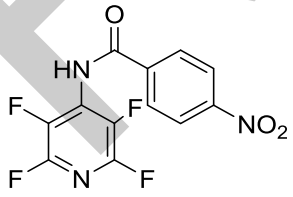
4k methyl 4-((perfluoropyridin-4-yl)carbamoyl)benzoate was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.170 g, 1.00 mmol), methyl 4-(chlorocarbonyl)benzoate (0.400 g, 2.10 mmol), triethylamine (0.250 mL, 2.10 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using (0 – 50% and to 100% EtOAc for 10-45 cv and then held at 100% EtOAc 45-58 cv) on a 12 g silica column to afford of **4k** in 44% yield (265 mg, 0.810 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 8.4 Hz, 2H), 8.03 (d, *J* = 8.4 Hz, 2H), 7.81 (s, 1H), 4.01 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.1 – -89.9 (m, , 2F), -145.4 – -145.5 (m, 2F).



4l *N*-(perfluoropyridin-4-yl)-4-(trifluoromethyl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.300 g, 1.81 mmol), 4-(trifluoromethyl)benzoyl chloride (0.410 g, 2.10 mmol), triethylamine (0.250 mL, 2.10 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-35 cv and then held at 100% EtOAc 35-42 cv) on a 12 g silica column to afford of **4l** in 50% yield (302 mg, 0.890 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.1 Hz, 2H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.76 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.19 (m, 3F), -87.6 – -90.8 (m, 2F), -143.6 – -146.4 (m, 2F).

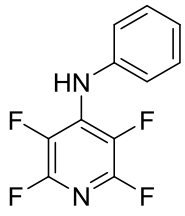


4m 4-cyano-*N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.300 g, 1.81 mmol), 4-cyanobenzoyl chloride (0.320 g, 2.10 mmol), triethylamine (0.250 mL,2.10 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 35% EtOAc for 8 cv and ramped to 100% EtOAc for 8-30 cv and then held at 100% EtOAc 30-37 cv) on a 12 g silica column to afford of **4m** in 41% yield (215 mg, 0.730 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 – 8.02 (m, 2H), 7.98 – 7.84 (m, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -87.6 – -89.4 (m, 2F), -144.7 – -146.1 (m, 2F).

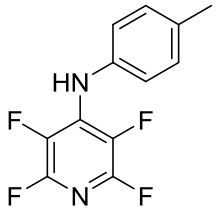


4n 4-nitro-*N*-(perfluoropyridin-4-yl)benzamide was prepared by general procedure B. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.300 g, 1.81 mmol), 4-nitrobenzoyl chloride (0.670 g, 3.60 mmol), triethylamine (0.250 mL, 2.10 mmol), and DCM (5 mL) was stirred at room temperature overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-30 cv and then held at 100% EtOAc 30-45 cv) on a 12 g silica

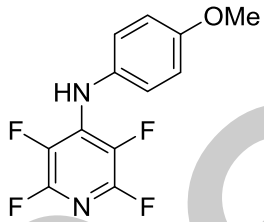
column to afford of **4n** in 19% yield (115 mg, 0.370 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 9.1 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -94.4 – -96.8 (m, 2F), -163.2 – -166.1 (m, 2F).



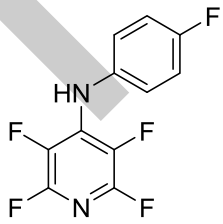
5a 2,3,5,6-tetrafluoro-*N*-phenylpyridin-4-amine was prepared by general procedure D. The mixture of the aniline (0.170 g, 1.80 mmol), K_2CO_3 (0.330 g, 2.40 mmol), pentafluoropyridine (0.200 g, 1.20 mmol), and DMF (5 mL) was stirred at 70 °C overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 10 cv and ramped to 100% EtOAc for 10-20 cv and then held at 100% EtOAc 20-30 cv) on a12 g silica column to afford of **5a** in 43% yield (188 mg, 0.780 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.24 (m, 2H), 7.21 – 7.10 (m, 1H), 7.03 (dt, *J* = 6.9, 1.5 Hz, 2H), 6.28 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -90.4 – -94.1 (m, 2F), -153.8 – -159.9 (m, 2F).



5b 2,3,5,6-tetrafluoro-*N*-(*p*-tolyl)pyridin-4-amine was prepared by general procedure D. The mixture of the *p*-toluidine (0.190 g, 1.80 mmol), K_2CO_3 (0.330 g, 2.40 mmol), pentafluoropyridine (0.200 g, 1.20 mmol), and DMF (5 mL) was stirred at 70 °C overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 8 cv and ramped to 100% EtOAc for 8-20 cv and then held at 100% EtOAc 20-33 cv) on a 12 g silica column to afford **5b** in 45% yield (201 mg, 0.780 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4, 2H), 2.39 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -88.8 – -89.2 (m, 2F), -149.8 – -150.7 (, 2F).

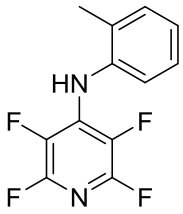


5c 2,3,5,6-tetrafluoro-*N*-(4-methoxyphenyl)pyridin-4-amine was prepared by general procedure D. The mixture of the *p*-anisidine (0.220 g, 1.80 mmol), K_2CO_3 (0.330 g, 2.40 mmol), pentafluoropyridine (0.200 g, 1.20 mmol), and DMF (5 mL) was stirred at 70 °C overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 10 cv and ramped to 100% EtOAc for 10-18 cv and then held at 100% EtOAc 10-30 cv) on a 12 g silica column to afford of **5c** in 18% yield (90.0 mg, 0.330 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.13 (d, *J* = 8.7, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.54 (s, 1H), 3.85 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -92.8 – -93.2 (m, 2F), -142.7 – -144.2 (m, 2F).



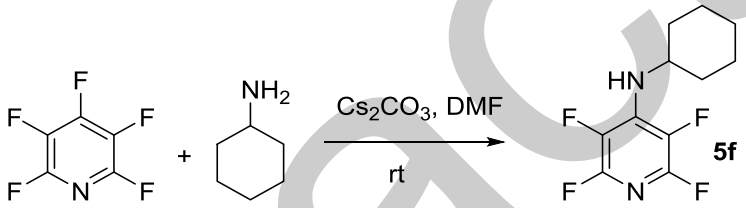
5d 2,3,5,6-tetrafluoro-*N*-(4-fluorophenyl)pyridin-4-amine was prepared by general procedure D. The mixture of the 4-fluoroaniline (0.200 g, 1.80 mmol), K_2CO_3 (0.330 g, 2.40 mmol), pentafluoropyridine (0.200 g, 1.20 mmol), and DMF (5 mL) was stirred at 70 °C overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-20 cv and then held

at 100% EtOAc 20-30 cv) on a 12 g silica column to afford of **5d** in 21% yield (103 mg, 0.390 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 – 6.95 (m, 4H), 6.19 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -86.7 (dd, *J* = 20.5, 13.3 Hz, 2F), -113.8 – -114.02 (m, 1F), -144.9 – -151.00 (m, 2F).

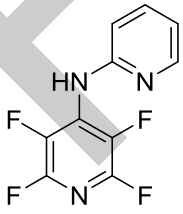


5e 2,3,5,6-tetrafluoro-*N*-(*o*-tolyl)pyridin-4-amine was prepared by general procedure D. The mixture of the *o*-toluidine (0.190 g, 1.80 mmol), K_2CO_3 (0.330 g, 2.40 mmol) pentafluoropyridine (0.200 g, 1.20 mmol), and DMF (5 mL) was stirred at 70 °C overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 6 cv and ramped to 100% EtOAc for 6-25 cv and then held at 100% EtOAc 25-35 cv) on a 12 g silica column to afford of **5e** in 22% yield (870 mg, 0.340 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.15 (m, 3H), 7.10 (dd, *J* = 7.7, 1.3 Hz, 1H), 2.07 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -87.6 – -89.6 (m, 2F), -148.7 – -150.2 (m, 2F).

5f *N*-cyclohexyl-2,3,5,6-tetrafluoropyridin-4-amine

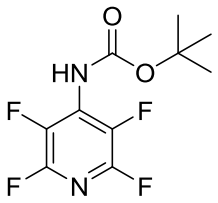


To a solution of pentafluoropyridine (2.00 g, 12.0 mmol) in anhydrous DMF (15 mL) was added Cs_2CO_3 (8.00 g, 24.5 mmol), followed by cyclohexylamine (2.70 mL, 24.0 mmol). The reaction was stirred at room temperature for 16 hours, and then diluted by adding water (50 mL). The aqueous phase was extracted with diethyl ether (3 x 30 mL). The combined organic phase was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography using hexane:EtOAc (0 – 20% EtOAc for 15 cv and ramped to 100% EtOAc for 15-18 cv and then held for 18-21 cv) on a 80 g silica column to afford of **5f** in 85% yield **(**2.50 g, 10.1 mmol). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.43 – 4.19 (m, 1H), 3.68 (d, *J* = 10.1 Hz, 1H), 1.99 (dd, *J* = 12.5, 4.4 Hz, 2H), 1.72 (dt, *J* = 13.3, 4.0 Hz, 2H), 1.60 (dd, *J* = 13.0, 8.2 Hz, 1H), 1.39 – 1.24 (m, 2H), 1.19 – 1.13 (m, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -94.5 – -95.5 (m, 2F), -164.3 – -165.3 (m, 2F).

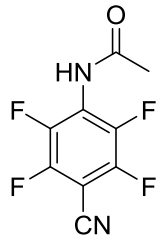


5g *N*-(perfluoropyridin-4-yl)pyridin-2-amine was prepared by general procedure D. The mixture of the pyridin-2-amine (0.170 g, 1.80 mmol), K_2CO_3 (0.330 g, 2.40 mmol), pentafluoropyridine (0.200 g, 1.20 mmol), and DMF (5 mL) was stirred at 70 °C overnight. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-35 cv and then held at 100% EtOAc 35-40 cv) on a 12 g silica column to afford of **5g** in 29% yield (117 mg, 0.480 mmol) as a yellow solid. ^{1}H

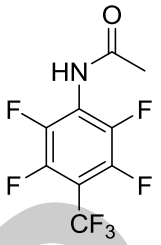
NMR (400 MHz, Acetonitrile-d_3) δ 8.23 (ddd, J = 5.0, 1.9, 0.9 Hz, 1H), 7.72 (ddd, J = 8.2, 7.3, 1.9 Hz, 1H), 7.10 – 6.99 (m, 2H). ^{19}F NMR (376 MHz, Acetonitrile-d_3) δ -95.4 – -95.7 (m, 2F), -149.6 – -150.1 (m, 2F).



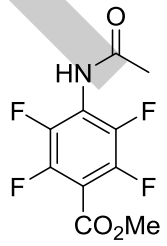
5h tert-butyl (perfluoropyridin-4-yl)carbamate was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 3.26 mmol), di-*tert*-butyl dicarbonatee (0.910 mL, 4.00 mmol), conc. $HClO_4$ (17.0 µL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 5 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 11 cv and ramped to 100% EtOAc for 11-30 cv and then held at 100% EtOAc 30-40 cv) on a 12 g silica column to afford of **5h** in 92% yield (800 mg, 3.00 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 1.49 (s, 9H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.5 – -90.8 (m, 2F), -145.6 – -146.3 (m, 2F).



6a *N*-(4-cyano-2,3,5,6-tetrafluorophenyl)acetamide was prepared by general procedure A. The mixture of the 4-amino-2,3,5,6-tetrafluorobenzonitrile (0.500 g, 2.60 mmol), acetic anhydride (0.520 mL, 4.00 mmol), conc. $HClO_4$ (17.0 µL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 8 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-20 cv and then held at 100% EtOAc 20-35 cv) on a 12 g silica column to afford of **6a** in 74% yield (450 mg, 1.92 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (s, 1H), 2.32 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -132.4 – -133.2 (m, 2F), -141.5 – -142.8 (m, 2F).

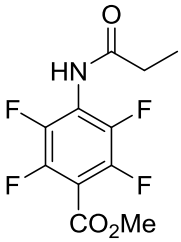


6b *N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoro-4-(trifluoromethyl) aniline (0.250 g, 1.07 mmol), acetic anhydride (0.140 mL, 1.30 mmol), conc. $HClO_4$ (17.0 µL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 7 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 8 cv and ramped to 100% EtOAc for 8-28 cv and then held at 100% EtOAc 28-38 cv) on a 12 g silica column to afford of **6b** in 87% yield (282 mg, 1.02 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 (s, 1H), 2.22 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -56.1 (s, 3F), -140.5 – -141.2 (m, 2F), -142.2 – -143.6 (m, 2F).

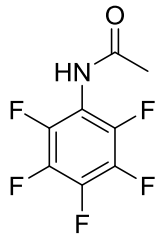


6c methyl 4-acetamido-2,3,5,6-tetrafluorobenzoate was prepared by general procedure A. The mixture of the methyl 4-amino-2,3,5,6-tetrafluorobenzoate (0.250 g, 1.12 mmol), acetic anhydride (0.130 mL, 1.30 mmol), conc. $HClO_4$ (17.0 µL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 3 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 10 cv and ramped to 100% EtOAc for 10-30

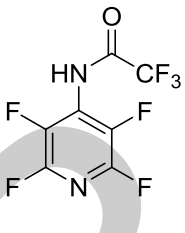
cv and then held at 100% EtOAc 30-45 cv) on a 12 g silica column to afford of **6c** in 97% yield (290 mg, 1.10 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.06 (s, 1H), 4.00 (s, 3H), 2.29 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.3 – -140.1 (m, 2F), -142.8 – -144.8 (m, 2F).



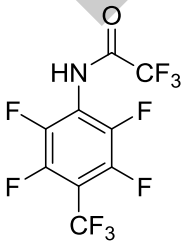
6d methyl 2,3,5,6-tetrafluoro-4-propionamidobenzoate was prepared by general procedure A. The mixture of the methyl 4-amino-2,3,5,6-tetrafluorobenzoate (0.250 g, 1.12 mmol), propionic anhydride (0.180 mL, 1.40 mmol), conc. $HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 5 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 10 cv and ramped to 100% EtOAc for 10-20 cv and then held at 100% EtOAc 25-38 cv) on a 12 g silica column to afford of **6d** in 93% yield (289 mg, 1.00 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (s, 1H), 3.90 (s, 3H), 2.43 (q, *J* = 7.5, 2H), 1.17 (t, *J* = 7.5, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.4 – -139.8 (m, 2F), -144.1 – -144.4 (m, 2F).



6e *N*-(perfluorophenyl)acetamide was prepared by general procedure A. The mixture of the 2,3,4,5,6-pentafluoroaniline (0.544 g, 2.97 mmol), acetic anhydride (0.380 mL, 3.74 mmol), conc. $HClO_4$ (17.0 μL, 0.28 mmol), and benzene (5 mL) was stirred at room temperature for 6 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 7 cv and ramped to 100% EtOAc for 7-24 cv and then held at 100% EtOAc 24-35 cv) on a 12 g silica column to afford of **6e** in 46% yield (310 mg, 1.37 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.88 (s, 1H), 2.27 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -144.9 (dd, *J* = 22.2, 5.9 Hz, 2F), -156.31 (tt, *J* = 21.6 Hz, 1F), -162.3 – 163.2 (m, 2F).

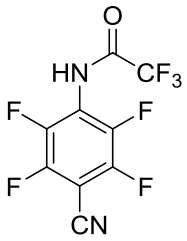


6f 2,2,2-trifluoro-*N*-(perfluoropyridin-4-yl)acetamide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 2.97 mmol), 2,2,2-trifluoroacetic anhydride (0.640 mL, 4.58 mmol), conc. $HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 6 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 8 cv and ramped to 100% EtOAc for 8-30 cv and then held at 100% EtOAc 30-55 cv) on a 12 g silica column to afford of **6f** in 49% yield (420 mg, 1.60 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -74.8 (s, 3F), -87.3 – -87.5 (m, 2F), -143.8 – -144.1 (m, 2F).

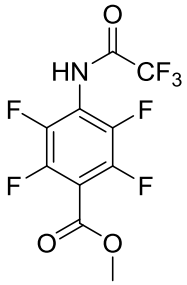


6g 2,2,2-trifluoro-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl) acetamide was prepared by general procedure A. The mixture of the 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline (0.544 g, 2.33 mmol), trifluoroacetic anhydride (0.410 mL, 2.94 mmol), conc. $HClO_4$ (17.0 μL, 0.280 mmol), and

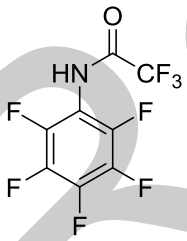
benzene (5 mL) was stirred at room temperature for 6 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-45 cv) on a 12 g silica column to afford of **6g** in 32% yield (256 mg,0.780 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -56.2 (s, 3F), -74.8 (s, 3F), -138.6 – -139.1 (m, 2F), -141.4 – -141.7 (m, 2F).



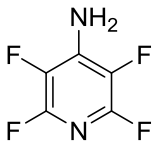
6h ***N*-(4-cyano-2,3,5,6-tetrafluorophenyl)-2,2,2-trifluoroacetamide** was prepared by general procedure A. The mixture of the 4-amino-2,3,5,6-tetrafluorobenzonitrile (0.544 g, 2.86 mmol), trifluoroacetic anhydride (0.510 mL, 3.60 mmol), conc. $HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 8 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-30 cv and then held at 100% EtOAc 30-37 cv) on a 12 g silica column to afford of **6h** in 26% yield (210 mg, 0.730 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -75.1 (s, 3F), -142.2 – -146.1 (m, 2F), -159.6 – -164.1 (m, 2F).



6i methyl 2,3,5,6-tetrafluoro-4-(2,2,2-trifluoroacetamido)benzoate was prepared by general procedure A. The mixture of the methyl 4-amino-2,3,5,6-tetrafluorobenzoate (0.544 g, 2.44 mmol), trifluoroacetic anhydride (0.430 mL, 3.07 mmol), conc. $HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 8 h. After workup, The crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 8 cv and ramped to 100% EtOAc for 8-36 cv and then held at 100% EtOAc 36-48 cv) on a 12 g silica column to afford of **6i** in 25% yield (200 mg, 0.630 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (s, 1H), 4.03 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -74.9 (s, 3F), -137.8 – -138.1 (m, 2F), -142.6 – -142.8 (m, 2F).

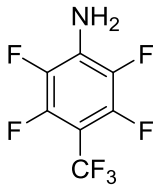


6j 2,2,2-trifluoro-*N*-(perfluorophenyl)acetamide was prepared by general procedure A. The mixture of the 2,3,4,5,6-pentafluoroaniline (0.544 g, 2.97 mmol), trifluoroacetic anhydride (0.580 mL, 4.10 mmol), the conc. $HClO_4$ (17.0 μL, 0.280 mmol), and benzene (5 mL) was stirred at room temperature for 8 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-35 cv) on a 12 g silica column to afford of **6j** in 75% yield (626 mg, 2.24 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -75.1 (s, 3F), -143.4 – -144.2 (m, 2F), -152.8 (tt, *J* = 21.5 Hz, 1F), -160.3 – -160.9 (m, 2F).

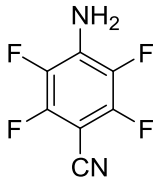


6k 2,3,5,6-tetrafluoropyridin-4-amine was prepared by general procedure F. The mixture of the pentafluoropyridine (1.00 mL, 9.00 mmol), ammonium

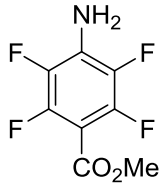
hydroxide solution (28.0-30.0% NH_3 basis, 3.00 mL), and THF (15 mL) was heated to reflux for 18 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-20 cv and then held at 100% EtOAc 20-32cv) on a 12 g silica column to afford of **6k** in 88% yield (1.33 g, 8.00 mmol) as a white solid. This compound was reported previously and the spectra matched accordingly.[9]



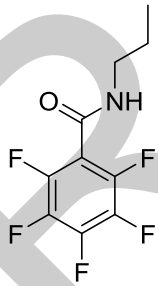
6l 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline was prepared by general procedure F. The mixture of the 1,2,3,4,5-pentafluoro-6-(trifluoromethyl)benzene (1.00 mL, 7.00 mmol), ammonium hydroxide solution (28.0-30.0% NH_3 basis, 3.00 mL), and THF (15 mL) was heated to reflux for 18 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-36 cv) on a 12 g silica column to afford of **6l** in 49% yield (0.800 g, 3.43 mmol) as a yellow liquid. This compound was reported previously and the spectra matched accordingly.[9]



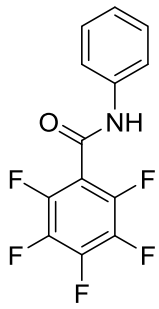
6m 4-amino-2,3,5,6-tetrafluorobenzonitrile was prepared by general procedure F. The mixture of the 2,3,4,5,6-pentafluorobenzonitrile (1.00 mL, 7.90 mmol), ammonium hydroxide solution (28.0-30.0% NH_3 basis, 3.00 mL), and THF (15 mL) was heated to reflux for 18 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 8 cv and ramped to 100% EtOAc for 8-20 cv and then held at 100% EtOAc 20-35 cv) on a 12 g silica column to afford of **6m** in 61% yield (0.920 g, 4.84 mmol) as a brown solid. This compound was reported previously and the spectra matched accordingly.[9]



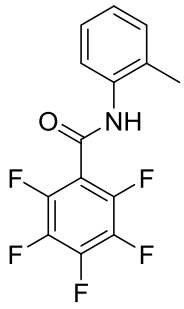
6n methyl 4-amino-2,3,5,6-tetrafluorobenzoate was reported previously and the spectra matched accordingly.[5] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.44 (s, 2H), 3.93 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -140.7 – -141.7 (m, 2F), -162.3 – 163-3 (m, 2F).



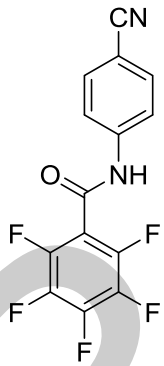
7a 2,3,4,5,6-pentafluoro-*N*-propylbenzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.500 g, 2.17 mmol), propylamine (0.710 mL, 8.70 mmol), Et_3N (1.22 mL, 8.71 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 9 cv and ramped to 100% EtOAc for 9-28 cv and then held at 100% EtOAc 28-45 cv) on a 12 g silica column to afford of **7a** in 33% yield (182 mg, 0.720 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.28 (s, 1H), 3.33 (t, *J* = 6.7 Hz, 2H), 1.56 (m, *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.4, 7.0 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -140.3 – -141.8 (m, 2F), -151.2 (tt, *J* = 20.6 Hz, 1F), -159.6 – -160.7 (m, 2F).



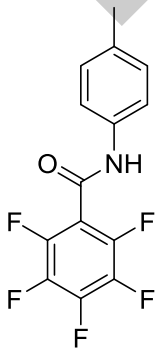
7b 2,3,4,5,6-pentafluoro-*N*-phenylbenzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.500 g, 2.17 mmol), aniline (0.400 mL, 4.35 mmol), Et_3N (0.630 mL, 4.35 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 6 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-47 cv) on a 12 g silica column to afford of **7b** in 61% yield (382 mg, 1.33 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (s, 1H), 7.60 (d, *J* = 7.4 Hz, 2H), 7.41 (dd, *J* = 8.4, 7.5 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -140.1 – -141-6 (m, 2F), -149.5 – -149.8 (m, 1F), -159.5 – 159.9 (m, 2F).



7c 2,3,4,5,6-pentafluoro-*N*-(*o*-tolyl)benzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.500 g, 2.17 mmol), *o*-toluidine (0.230 g, 2.15 mmol), Et_3N (0.630 mL, 4.35 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-20 cv and then held at 100% EtOAc 20-46 cv) on a 12 g silica column to afford of **7c** in 60% yield (392 mg, 1.30 mmol) as a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 9.53 (s, 1H), 7.63 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.43 – 6.96 (bm, 3H), 2.89 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.8 (dd, *J* = 14.3, 3.4 Hz, 2F), -149.8 – 140.1 (m, 1F), -158.3 – -161.8 (m, 2F).

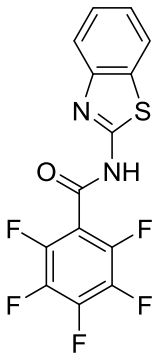


7d *N*-(4-cyanophenyl)-2,3,4,5,6-pentafluorobenzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.500 g, 2.17 mmol), 4-aminobenzonitrile (0.400 g, 3.38 mmol), Et_3N (0.630 mL, 4.35 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 9 cv and ramped to 100% EtOAc for 9-23 cv and then held at 100% EtOAc 23-45 cv) on a 12 g silica column to afford of **7d** in 25% yield (178 mg, 0.570 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (s, 1H), 7.70 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.6 (dd, *J* = 14.2, 3.6 Hz, 2F), -148.5 – -148.8 (m, 1F), -157.8 – -160.4 (m, 2F).

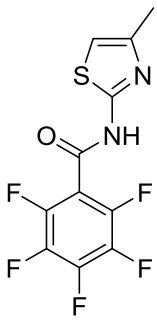


7e 2,3,4,5,6-pentafluoro-*N*-(*p*-tolyl)benzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.500 g, 2.17 mmol), *p*-toluidine (0.230 g, 2.15 mmol), Et_3N (0.630 mL, 4.35 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After

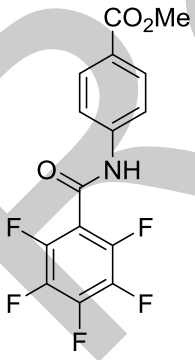
workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 6 cv and ramped to 100% EtOAc for 6-25 cv and then held at 100% EtOAc 25-38 cv) on a 12 g silica column to afford of **7e** in 23% yield (151 mg, 0.500 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 2.38 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -140.00 (dd, *J* = 14.3, 3.4 Hz, 2F), -149.81 – -150.05 (m, 1F), -155.41 – -164.13 (m, 2F).



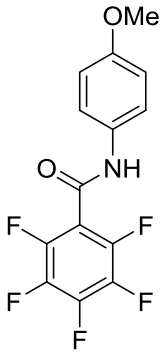
7f *N*-(benzo[d]thiazol-2-yl)-2,3,4,5,6-pentafluorobenzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.500 g, 2.17 mmol), 2-aminobenzothiazole (0.650 g, 4.33 mmol), Et_3N (0.630 mL, 4.35 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 8 cv and ramped to 100% EtOAc for 8-30 cv and then held at 100% EtOAc 30-35 cv) on a 12 g silica column to afford of **7f** in 19% yield (142 mg, 0.410 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.78 (m, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.35 (m, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -137.8 – -139.6 (m, 2F), -147.1 (tt, *J* = 21.1 Hz, 1F), -158.1 – -159.1 (m, 2F).



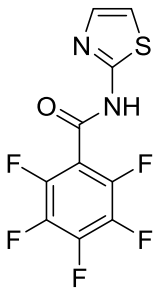
7g 2,3,4,5,6-pentafluoro-*N*-(4-methylthiazol-2-yl)benzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.360 g, 1.56 mmol), 2-amino-4-methylthiazole (0.150 g, 1.31 mmol), Et_3N (0.210 mL, 1.40 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-40 cv) on a 12 g silica column to afford of **7g** in 20% yield (102 mg,0.330 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.65 (s, 1H), 2.17 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.5 – -139.4 (m, 2F), -147.6 (tt, *J* = 21.0, 4.3 Hz, 1F), -158.8 (m, 2F).



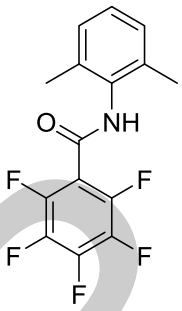
7h methyl 4-(perfluorobenzamido)benzoate was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.360 g, 1.56 mmol), methyl 4-aminobenzoate (0.200 g, 1.31 mmol), Et_3N (0.210 mL, 1.40 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 12 cv and ramped to 100% EtOAc for 12-25 cv and then held at 100% EtOAc 25-45 cv) on a 12 g silica column to afford of **7h** in 78% yield (420 mg, 1.22 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.8 Hz, 2H), 7.89 (s, 1H), 7.72 (d, *J* = 8.8 Hz, 2H), 3.95 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.74 – 140.1 (m, 2F), -148.86 – 149.4 (m, 1F), -156.45 – -162.65 (m, 2F).



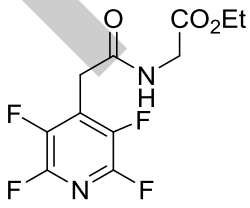
7i 2,3,4,5,6-pentafluoro-*N*-(4-methoxyphenyl)benzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.360 g, 1.56 mmol), 4-methoxyaniline (0.160 g, 1.31 mmol), Et_3N (0.210 mL, 1.41 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 5 cv and ramped to 100% EtOAc for 5-28 cv and then held at 100% EtOAc 28-40 cv) on a 12 g silica column to afford of **7i'** in 46% yield (230 mg, 0.720 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.8 (d, *J* = 17.2 Hz, 2F), -149.8 (tt, *J* = 20.8 Hz, 1F), -157.8 – -161.2 (m, 2F)



7j 2,3,4,5,6-pentafluoro-*N*-(thiazol-2-yl)benzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.360 g, 1.56 mmol), thiazol-2-amine (0.130 g, 1.31 mmol), Et_3N (0.210 mL, 1.40 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 8 cv and ramped to 100% EtOAc for 8-32 cv and then held at 100% EtOAc 32-40 cv) on a 12 g silica column to afford of **7j'** in 59% yield (271 mg, 0.920 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.00 (d, *J* = 3.5 Hz, 1H), 6.77 (d, *J* = 3.5 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.3 – -139.1 (m, 2F), -147.8 (tt, *J* = 20.8 Hz, 1F), -158.4 – -159.6 (m, 2F).

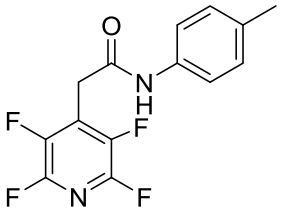


8a *N*-(2,6-dimethylphenyl)-2,3,4,5,6-pentafluorobenzamide was prepared by general procedure C. The mixture of the 2,3,4,5,6-pentafluorobenzoyl chloride (0.500 g, 2.17 mmol), 2,6-dimethylaniline (0.800 g, 6.61 mmol), Et_3N (0.630 mL, 4.35 mmol), and DCM (15 mL) was stirred one hour at 0 °C, then at room temperature for another 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-40 cv) on a 12 g silica column to afford of **8a** in 50% yield (348 mg, 1.10 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (s, 1H), 7.23 – 7.17 (m, 1H), 7.14 (d, *J* = 8.4 Hz, 2H) 2.31 (s, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.4 – -140.8 (m, 2F), -150.5 (tt, *J* = 20.5, 2.8 Hz, 1F), -158.9 – -160.5 (m, 2F).

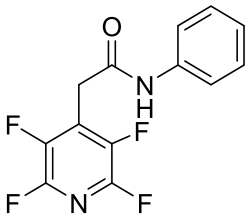


10a ethyl (2-(perfluoropyridin-4-yl)acetyl)glycinate was prepared by general procedure E. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo-3-(perfluoropyridin-4-yl)-1,5-dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.71 mmol), ethyl 2-aminoacetate hydrochloride (0.538 g, 3.85 mmol), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using

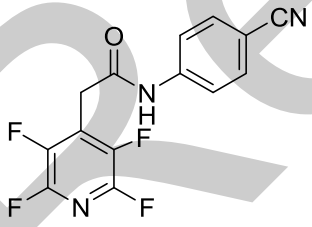
hexane:EtOAc (0 – 50% EtOAc for 7 cv and ramped to 100% EtOAc for 7-32 cv and then held at 100% EtOAc 32-48 cv) on a 12 g silica column to afford of **10a** in 32% yield (133 mg, 0.470 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.45 (s, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 4.08 (d, *J* = 5.1 Hz, 2H), 3.84 (s, 2H), 1.31 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -90.8 – -91.4 (m, 2F), -143.41 – -144.7 (m, 2F).



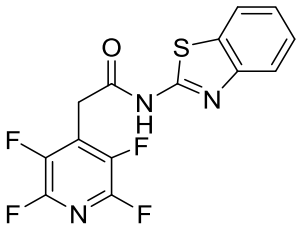
10b 2-(perfluoropyridin-4-yl)-*N*-(*p*-tolyl)acetamide was prepared by general procedure E. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo-3-(perfluoropyridin-4-yl)-1,5-dioxaspiro[5.5]undec-2-en-2-olate (0.500 g 1.71 mmol), *p*-toluidine (0.550 g, 5.13 mmol), 2 M ethereal HCl (0.9 mL), and MeCN (15 mL) was stirred at 80 ºC for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 5 cv and ramped to 100% EtOAc for 5-28 cv and then held at 100% EtOAc 28-43 cv) on a 12 g silica column to afford of **10b** in 47% yield (213 mg, 0.710 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 3.93 (s, 2H), 2.35 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -90.6 – -91.9 (m, 2F), -141.1 – -144.9 (m, 2F).



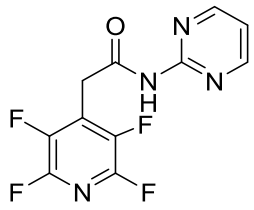
10c 2-(perfluoropyridin-4-yl)-*N*-phenylacetamide was prepared by general procedure E. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo-3-(perfluoropyridin-4-yl)-1,5-dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.71 mmol), aniline (0.480 mL, 5.13 mmol), 2 M ethereal HCl (0.9 mL), and MeCN (15 mL) was stirred at 80 ºC for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 40% EtOAc for 6 cv and ramped to 100% EtOAc for 6-25 cv and then held at 100% EtOAc 25-42cv) on a 12 g silica column to afford of **10c** in 41% yield (178 mg, 0.630 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 8.0 Hz, 2H), 7.37 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 3.96 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.2 – -90.8 (m, 2F), -142.2 – -144.2 (m, 2F).



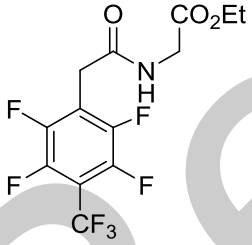
10d *N*-(4-cyanophenyl)-2-(perfluoropyridin-4-yl)acetamide was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo-3-(perfluoropyridin-4-yl)-1,5-dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.71 mmol), 4-aminobenzonitrile (0.600 g, 5.13 mmol), 2 M ethereal HCl (0.9 mL), and MeCN (15 mL) was stirred at 80 ºC for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 8 cv and ramped to 100% EtOAc for 8-25 cv and then held at 100% EtOAc 25-42 cv) on a 12 g silica column to afford of **10e** in 69% yield (319 mg, 1.03 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (bm, 5H), 3.99 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -90.1– -91.8 (m, 2F), -143.2– -144.3 (m, 2F).



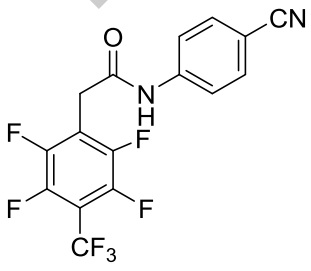
10e *N*-(benzo[d]thiazol-2-yl)-2-(perfluoropyridin-4-yl)acetamide was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo-3-(perfluoropyridin-4-yl)-1,5-dioxaspiro[5.5]undec-2-en-2-olate (0.600 g, 1.80 mmol), 2-aminobenzothiazole (0.810 g, 5.42 mmol), 2 M ethereal HCl (1 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-45 cv) on a 12 g silica column to afford of **10d** in 65% yield (402 mg, 1.20 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 – 7.82 (m, 2H), 7.54 (ddd, *J* = 8.3, 7.3, 1.3 Hz, 2H), 7.45 – 7.39 (m, 1H), 4.07 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -88.3 – -92.2 (m, 2F), -141.3 – -145.4 (m, 2F).



10f 2-(perfluoropyridin-4-yl)-*N*-(pyrimidin-2-yl)acetamide was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo-3-(perfluoropyridin-4-yl)-1,5-dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.71 mmol), 4-aminobenzonitrile (0.430 g, 5.13 mmol), 2 M ethereal HCl (0.9 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-29 cv and then held at 100% EtOAc 29-57 cv) on a 12 g silica column to afford of **10f** in 68% yield (335 mg, 1.03 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.24 (s, 1H), 8.68 (d, *J* = 4.9 Hz, 2H), 7.11 (t, *J* = 4.8 Hz, 1H), 4.61 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -91.29 – 92.2 (m, 2F), -139.37 – -151.92 (m, 2F).

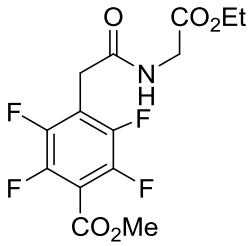


10g ethyl (2-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl) acetyl)glycinate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-(trifluoromethyl) phenyl)-1,5- dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.25 mmol), ethyl 2-aminoacetate hydrochloride (0.314 g, 2.25 mmol), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 6 cv and ramped to 100% EtOAc for 6-25 cv and then held at 100% EtOAc 25-40 cv) on a 12 g silica column to afford of **10f** in 38% yield (170 mg, 0.470 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.31 (s, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.09 (d, *J* = 4.9 Hz, 2H), 3.80 (s, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -56.4 (s, 3F), -140.2—141.7 (m, 2F), -140.6 – -140.8 (m, 2F).

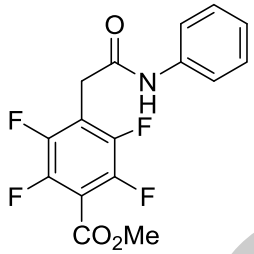


10h *N*-(4-cyanophenyl)-2-(2,3,5,6-tetrafluoro-4-(trifluoromethyl) phenyl) acetamide was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-

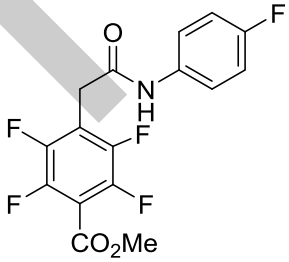
(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl) -1,5- dioxaspiro[5.5] undec-2-en-2-olate (0.500 g, 1.25 mmol), 4-aminobenzonitrile (0.440 g, 3.76 mmol), 2 M ethereal HCl (0.8 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 8 cv and ramped to 100% EtOAc for 8-28 cv and then held at 100% EtOAc 28-46 cv) on a 12 g silica column to afford of **10g** in 26% yield (122 mg, 0.490 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 (s, 1H), 7.65 – 7.53 (bm, 4H), 3.87 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -56.4 (s, 3F), -88.3 – -92.2 (m, 2F), -141.3 – -145.4 (m, 2F).



11a methyl 4-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-4-(methoxycarbonyl)phenyl)-1,5- dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.28 mmol), ethyl 2-aminoacetate hydrochloride (0.540 g, 3.85 mmol), 2 M ethereal HCl (2 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 7 cv and ramped to 100% EtOAc for 7-23 cv and then held at 100% EtOAc 23-49 cv) on a 12 g silica column to afford of **11a** in 49% yield (222 mg, 0.630 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.24 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.08 (d, *J* = 5.0 Hz, 2H), 4.00 (s, 3H), 3.77 (s, 2H), 1.31 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.6 – -140.2 (m, 2F), -141.2 – -142.9 (m, 2F).

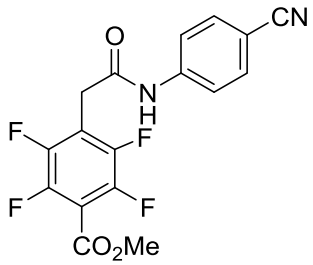


11b methyl 2,3,5,6-tetrafluoro-4-(2-oxo-2-(phenylamino)ethyl)benzoate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-4-(methoxyca rbonyl)phenyl)-1,5- dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.28 mmol), aniline (0.360 g, 3.85 mmol), 2 M ethereal HCl (0.8 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held at 100% EtOAc 25-40 cv) on a 12 g silica column to afford of **11b** in 47% yield (205 mg, 0.600 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 7.8 Hz, 2H), 7.36 (bm, 3H), 7.16 (d, *J* = 7.8 Hz, 1H), 4.01 (s, 3H), 3.89 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.1 – -139.5 (m, 2F), -140.9 – -141.4 (m, 2F).

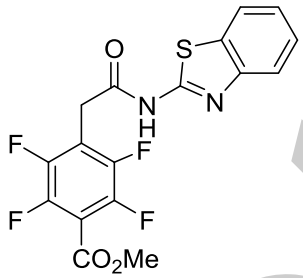


11c methyl 2,3,5,6-tetrafluoro-4-(2-((4-fluorophenyl)amino)-2-oxoethyl)benzoate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-4-(methoxycarbonyl)phenyl)-1,5- dioxaspiro[5.5]undec-2-en-2-olate (0.500 g, 1.28 mmol), 4-fluoroaniline (0.430 g, 3.85 mmol), 2 M ethereal HCl (0.8 mL), and MeCN (15 mL) was stirred at 80 °C for

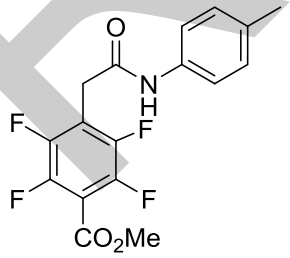
12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 5 cv and ramped to 100% EtOAc for 5-27 cv and then held at 100% EtOAc 27-49 cv) on a 12 g silica column to afford of **11c** in 73% yield (335 mg, 0.930 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.44 (m, 2H), 7.32 (s, 1H), 7.05 (m, 2H), 4.01 (s, 3H), 3.88 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -116.8 – -117.4 (m, 1F), -139.1 – -140.6 (m, 2F), -139.6 – -141.2 (m, 2F).



11d methyl 4-(2-((4-cyanophenyl)amino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-4-(methoxycarbonyl)phenyl) -1,5- dioxaspiro[5.5] undec-2-en-2-olate (0.500 g, 1.28 mmol), 4-aminobenzonitrile (0.46g, 3.85 mmol), 2 M ethereal HCl (0.8 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 6 cv and ramped to 100% EtOAc for 6-26 cv and then held at 100% EtOAc 26-45 cv) on a 12 g silica column to afford of **11d** in 53% yield (248 mg, 0.700 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.62 (bm, 5H), 4.02 (s, 3H), 3.93 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.3 – -139.7 (m, 2F), -140.8 – -141.4 (m, 2F).

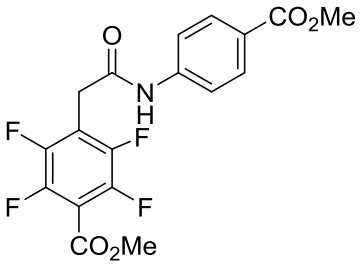


11e methyl 4-(2-(benzo[d]thiazol-2-ylamino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-4-(methoxycarbonyl)phenyl)-1,5- dioxaspiro[5.5] undec-2-en-2-olate (0.500 g, 1.28 mmol), benzo[d]thiazol-2-amine (0.580 g, 3.85 mmol), 2 M ethereal HCl (0.8 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 5 cv and ramped to 100% EtOAc for 5-32 cv and then held at 100% EtOAc 32-47 cv) on a 12 g silica column to afford of **11e** in 55% yield (110 mg, 0.280 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 12.04 (s, 1H), 7.88 (m, 2H), 7.52 (td, *J* = 7.8, 7.3, 3.1 Hz, 1H), 7.45 – 7.34 (m, 1H), 4.19 – 3.87 (m, 5H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.1 (dd, *J* = 24.7, 13.7, 2F), -140.8 (dd, *J* = 24.7, 13.7 Hz, 2F).



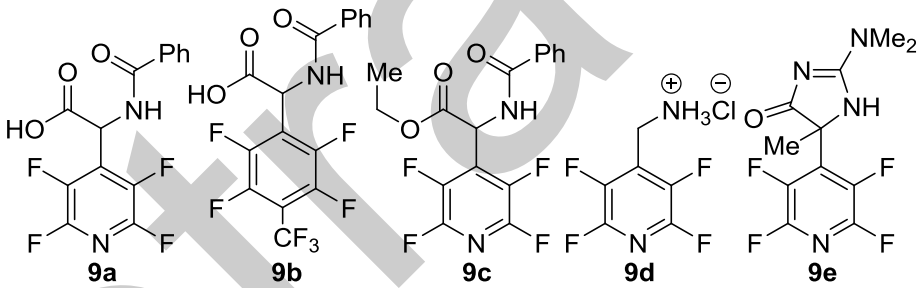
11f methyl 2,3,5,6-tetrafluoro-4-(2-oxo-2-(p-tolylamino) ethyl) benzoate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-4-(methoxycarbonyl)phenyl)-1,5- dioxaspiro[5.5] undec-2-en-2-olate (0.500 g, 1.28 mmol), *p*-toluidine (0.410 g, 3.85 mmol), 2 M ethereal HCl (0.8 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane:EtOAc (0 – 45% EtOAc for 5 cv and ramped to 100% EtOAc for 5-25 cv and then held

at 100% EtOAc 25-38 cv) on a 12 g silica column to afford of **11f** in 36% yield (167 mg, 0.470 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 3.92 (s, 3H), 3.81 (s, 2H), 2.25 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.3 – -139.7 (m, 2F), -140.8 – -141.4 (m, 2F).



F2C methyl 2,3,5,6-tetrafluoro-4-(2-((4-(methoxycarbonyl)phenyl) amino)-2-oxoethyl)benzoate was prepared by general procedure C. The mixture of the *N*-ethyl-*N*-isopropylpropan-2-aminium 4-oxo- 3-(2,3,5,6-tetrafluoro-4- (methoxycarbonyl)phenyl) -1,5- dioxaspiro [5.5]undec-2-en-2-olate (0.500 g, 1.28 mmol), *p*-toluidine (0.570 g, 3.84 mmol), 2 M ethereal HCl (0.8 mL), and MeCN (15 mL) was stirred at 80 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane :EtOAc (0 – 50% EtOAc for 10 cv and ramped to 100% EtOAc for 10-32 cv and then held at 100% EtOAc 32-54 cv) on a 12 g silica column to afford F2C in in 14% yield (71.0 mg, 0.180 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 8.7 Hz, 2H), 7.61 (d, *J* = 8.7 Hz, 2H), 4.02 (s, 2H), 3.92 (bm, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.2 – -140.1 (m, 2F), -141.2 – -142.5(m, 2F).

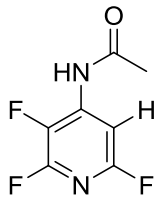
The following compounds were prepared according to the literature.[6]



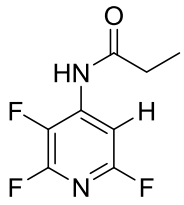
General procedure A for the photocatalytic hydrodefluorination reaction

In an NMR tube capped with NMR septa (Ace glass, part no. 9096-25) was charged tris(2-phenyl pyridinato-C 2 , *N*) Iridium(III) ($Ir(ppy)_3$) (0.250 mM, 1.00 mL in MeCN). Fluorinated starting material **1a-z** (1 equiv) and *N*, *N*-diisopropylethylamine (1.1 -3 equiv) were added and the reaction was degassed via Ar bubbling for 5-10 min, at 0 °C, to avoid evaporation of *N*, *N*-diisopropylethylamine and any other volatile starting materials and then left under positive Ar pressure by removing the exit needle and then the argon supply needle. The tube was placed in a light bath (*vide supra*) and the lower portion of the tube was submerged under the water bath which was maintained at 25 °C, 45 °C, or 60 °C via the use of a thermostated heating mantle. The reaction was monitored by ^{19}F NMR and GC-MS. After the complete consumption of starting material, the CH_3CN was removed via rotavap and the residue was treated with

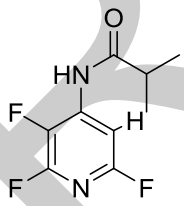
deionized water (2 mL) and extracted with EtOAc (5 x 1 mL). The combined organic portions were dried with anhydrous $MgSO_4$, filtered, concentrated in vacuo, and purified by normal phase chromatography.



4a' *N*-(2,3,6-trifluoropyridin-4-yl)acetamide was prepared by general procedure A. The mixture of **4a** (21.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 25 cv and ramped to 100% EtOAc for 25-50 cv and then held at 100% EtOAc 50-55 cv) on a 4 g silica column to afford of **4A'** in 99% yield (18.8 mg, 0.100 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (dt, *J* = 3.6, 1.1 Hz, 1H), 7.78 (s, 1H), 2.24 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -70.1 (dd, *J* = 23.0, 13.3 Hz, 1F), -88.8 (dd, *J* = 21.8, 13.5 Hz, 1F), -165.4 (ddd, *J* = 22.3, 3.4 Hz, 1F). This compound reported previously and the spectra matched accordingly.[5]

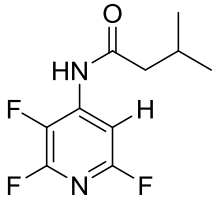


4b' *N*-(2,3,6-trifluoropyridin-4-yl)propionamide was prepared by general procedure A. The mixture of the **4b** (22.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 22 cv and ramped to 100% EtOAc for 22-45 cv and then held at 100% EtOAc 45-50 cv) on a 4 g silica column to afford **4b'** in 97% yield (19.4 mg, 0.121 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.91 (dt, *J* = 3.5, 1.1 Hz, 1H), 7.60 (s, 1H), 2.46 (q, *J* = 7.5 Hz, 2H), 1.21 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-d) δ -70.1 (dd, *J* = 22.7, 13.2 Hz, 1F), -88.7 (dd, *J* = 21.9, 13.3 Hz, 1F), -165.7 (ddd, *J* = 22.4, 3.6 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 157.3 (dd, *J* = 14.6, 3.4 Hz), 156.1 – 153.5 (m), 149.7 (dd, *J* = 18.3, 14.5 Hz), 147.3 (dd, *J* = 18.2, 14.5 Hz), 139.7, 133.4 (d, *J* = 28.1 Hz), 131.0 (dd, *J* = 28.1, 6.7 Hz), 97. 5 (dd, *J* = 45.0, 6.1 Hz), 30.9, 9.0. FT-IR cm^{-1} 3418, 3054, 2877, 1599, 1572. HRMS (ESI) calc., $C_8H_7F_3N_2O$ 204.0510, observed, 204.0513. mp 69-71 °C.

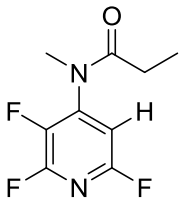


4c' *N*-(2,3,6-trifluoropyridin-4-yl)isobutyramide was prepared by general procedure A. The mixture of **4c** (24.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 10 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 20 cv and ramped to 100% EtOAc for 20-45 cv and then held at 100% EtOAc 45-50 cv) on a 4 g silica column to afford **4c'** in 93% yield (20.5 mg, 0.100 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (m, 1H), 7.74 (s, 1H), 2.66 (hept, *J* = 6.8 Hz, 1H), 1.31 (d, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -70.1 (dd, *J* = 23.0, 13.4 Hz, 1F), -88.9 (dd, *J* = 21.9, 13.2 Hz, 1F), -165.7 (ddd, *J* = 22.4, 7.0 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.5, 157.3 (dd, *J* = 14.5, 3.3 Hz), 148.5 (ddd, *J* = 240.5,

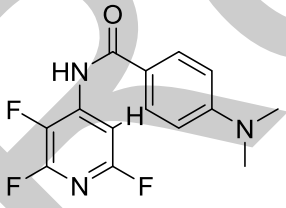
18.2, 14.5 Hz), 139.9 (ddd, *J* = 12.7, 8.1, 4.4 Hz), 132.3 (ddd, *J* = 247.9, 28.0, 6.6 Hz), 97.5 (ddd, *J* = 45.1, 5.8, 1.4 Hz), 37.0, 19.2. FT-IR cm^{-1} 3299, 3089, 2901, 1554, 1581. HRMS (ESI) calc., $C_9H_9F_3N_2O$ calc., 218.0667; observed, 218.0622. mp 73-75 °C.



4d' 3-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)butanamide was prepared by general procedure A. The mixture of the **4d** (25.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 18 cv and ramped to 100% EtOAc for 18-35 cv and then held at 100% EtOAc 35-45 cv) on a 4g silica column to afford **4d'** in 91% yield (21.0 mg, 0.0900 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 – 7.97 (m, 1H), 7.74 (s, 1H), 2.37 (d, 2H), 2.29 – 2.20 (m, 1H), 1.06 – 1.03 (m, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -70.2 (dd, *J* = 23.0, 13.4 Hz, 1F), -88.9 (dd, *J* = 21.7, 13.4 Hz, 1F), -165.4 (ddd, *J* = 22.8, 3.9 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.1, 156.1 (ddd, *J* = 241.2, 14.5, 3.2 Hz), 148.5 (ddd, *J* = 240.6, 18.2, 14.5 Hz), 139.7, 132.2 (ddd, *J* = 248.1, 27.9, 6.6 Hz), 97.5 (ddd, *J* = 45.1, 5.5, 1.3 Hz), 46.8, 26.0, 22.3. FT-IR cm^{-1} 3309, 3259, 2798, 1589, 1596. HRMS (ESI) calc., $C_{10}H_{11}F_3N_2O$ 232.0823; observed, 232.0861. mp 85-87 °C.

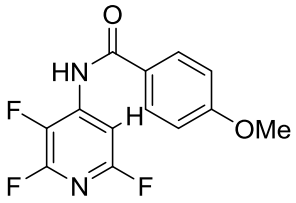


3b' *N*-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)propionamide was prepared by general procedure A. The mixture of the **4b** (24.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-35% EtOAc for 20 cv and ramped to 100% EtOAc for 20-30 cv and then held at 100% EtOAc 30-35 cv) on a 4g silica column to afford **3b'** 82% yield (18.0 mg, 0.0800 mmol) as colorless liquid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.69 (m, 1H), 3.26 (s, 3H), 2.26 (q, *J* = 7.4 Hz, 2H), 1.09 (t, *J* = 7.4 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -73.8 – -74.7 (m, 1F), -89.1 – -89.9 (m, 1F), -151.4 – -152.3 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.0, 154.5 (d, *J* = 14.7 Hz), 152.1 (d, *J* = 14.7 Hz), 149.6 (d, *J* = 16.2 Hz), 147.1, 144.0, 138.1 (d, *J* = 18.0 Hz), 103.8 (dd, *J* = 38.4, 6.3 Hz), 34. 8 (d, *J* = 2.4 Hz), 25.3 (d, *J* = 1.8 Hz), 7.2. FT-IR cm^{-1}, 1672, 1583, 1365, 1218. HRMS (ESI) calc., $C_9H_9F_3N_2O$ 218.0667; observed 218.0632.

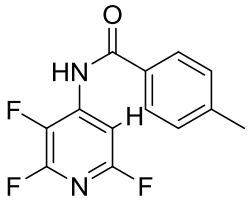


4e' 4-(dimethylamino)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4e** (31.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 20 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 25 cv and ramped to 100% EtOAc for 25-40 cv and then held at 100% EtOAc 40-50 cv) on a 4g silica column to afford **4e'** in 78% yield (23.0 mg, 0.0800 mmol) as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 (s, 1H), 8.03 (d, *J* = 3.4 Hz, 1H), 7.71 (d, *J* = 9.0 Hz, 2H), 6.64 (d, *J* = 9.0 Hz, 2H), 3.01 (s, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -70.4 (dd, *J* = 22.6, 13.2 Hz, 1F), -89.5 (dd, *J* = 22.0, 13.3 Hz, 1F), -166.2 (ddd, *J* = 22.4, 3.5 Hz, 1F). ^{13}C NMR (101 MHz,

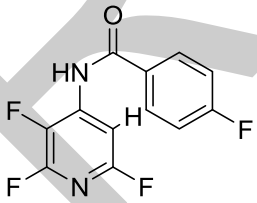
Acetone-d_6) δ 167.2, 161.9, 159.5, 156.5 (dd, *J* = 240.7, 12.3 Hz), 150.3 (dt, *J* = 242.1, 17.1 Hz), 143.6 (ddd, *J* = 250.7, 25.3, 6.4 Hz), 143.7 – 143.3 (m), 137.0 (d, *J* = 2.8 Hz), 122.9 (d, *J* = 7.8 Hz), 116.9 (d, *J* = 22.5 Hz), 110.6 (dd, *J* = 38.8, 5.8 Hz). 37.7. HRMS (ESI) calc., $C_{14}H_{12}F_3N_3O$ 295.0932; observed 295.0986. mp 122-125 ºC.



4f' 4-methoxy-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4f** (30.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 ºC for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-45% EtOAc for 25 cv and ramped to 100% EtOAc for 25-45 cv and then held at 100% EtOAc 45-50 cv) on a 4g silica column to afford **4f'** in 85% yield (24.0 mg, 0.0900 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 8.03 (m, 1H), 7.88 – 7.74 (m, 2H), 7.04 – 6.90 (m, 2H), 3.83 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -69.9 (dd, *J* = 22.7, 13.0 Hz), -88.8 (dd, *J* = 21.6, 13.4 Hz), -165.6 (appt, *J* = 22.4 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.9, 153.5, 131.4 (d, *J* = 242.6 Hz), 129.2, 118.6, 114.7 – 107.6 (dd, *J* = 45.2, 4.9 Hz), 97.1, 40.1. FT-IR cm^{-1} 3163, 3078, 2271, 1665, 1234. HRMS (ESI) calc., $C_{13}H_9F_3N_2O_2$ 282.0616; observed 282.0696. mp 117-119 ºC.

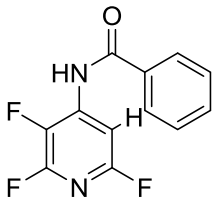


4g' 4-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4g** (28.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 ºC for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-45% EtOAc for 20 cv and ramped to 100% EtOAc for 20-45 cv and then held at 100% EtOAc 45-50 cv) on a 4g silica column to afford **4g'** in 86% yield (24.0 mg, 0.0900 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.36 (s, 1H), 8.13 (d, *J* = 3.5 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.37 (d, *J* = 7.8 Hz, 2H), 2.48 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -69.7 (dd, *J* = 23.1, 13.1 Hz, 1F), -88.5 (dd, *J* = 21.9, 13.2 Hz, 1F), -164.1 – -166.9 (ddd, *J* = 22.5, 18.7, 3.7 Hz, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 167. 9, 157.4 (ddd, *J* = 237.3, 15.4, 3.3 Hz), 150.7 (ddd, *J* = 237.0, 18.9, 14.8 Hz), 145.4, 143.1 (ddd, *J* = 13.4, 8.8, 4.7 Hz), 136.5 (dd, *J* = 28.0, 6.6 Hz), 134.0 (dd, *J* = 28.1, 6.6 Hz), 132.3, 131.0, 1230.0, 100.0 (dd, *J* = 45.1, 5.5 Hz), 22.39. FT-IR cm^{-1} 3459, 3201, 2522, 1682, 1211. HRMS (ESI) calc., $C_{13}H_9F_3N_2O$ 266.0667; observed 266.0692. mp 133-135 ºC

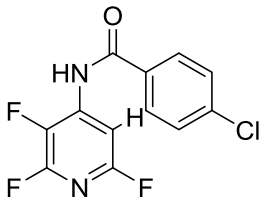


4h' 4-fluoro-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4h** (29.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 ºC for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-45% EtOAc for 25 cv and ramped to 100% EtOAc for 25-35 cv and then held at 100% EtOAc 35-45 cv) on a 4g silica column to afford **4h'** in 83% yield (23.0 mg, 0.0900 mmol) as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ

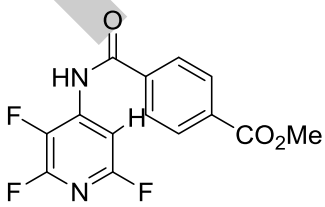
8.25 (s, 1H), 8.01 (m, H), 7.85 (dd, *J* = 8.8, 5.1 Hz, 2H), 7.17 (dd, *J* = 8.5 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -69.5 (dd, *J* = 23.1, 13.3 Hz, 1F), -88.4 (dd, *J* = 21.9, 13.4 Hz, 1F), -104.2—104.5 (m, 1F), -165.1 (ddd, *J* = 22.5, 3.5 Hz, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 168.2, 159.6 – 155.1 (m), 152.9, 150.6 – 147.2 (m), 143.2, 135.2, 134.6, 130.4, 129.9, 100.2 (dd, *J* = 45.4, 5.4 Hz). FT-IR cm^{-1} 3458, 3284, 2827, 1610, 1189. HRMS (ESI) calc., $C_{12}H_6F_4N_2O$ 270.0416; observed 270.0456. mp 112-116 °C.



4i' *N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4i** (24.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 19 cv and ramped to 100% EtOAc for 19-34 cv and then held at 100% EtOAc 34-40 cv) on a 4g silica column to afford **4i'** in 99% yield (24.0 mg, 1.00 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (s, 1H), 8.08 – 8.03 (m, 1H), 7.88 – 7.80 (m, 2H), 7.66 – 7.55 (m, 1H), 7.50 (dd, *J* = 8.3, 6.9 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -70.2 (dd, *J* = 23.0, 13.4 Hz, 1F), -88.9 (dd, *J* = 21.7, 13.4 Hz, 1F), -165.5 (ddd, *J* = 22.1, 3.6Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.3, 160.9 – 152.8 (m), 148.5 (ddd, *J* = 240.9, 18.2, 14.5 Hz), 139.9, 133.9 (dd, *J* = 28.1, 6.5 Hz), 133.3, 132.7, 131.4 (dd, *J* = 28.0, 6.6 Hz), 129.2, 127.3, 97.6 (dd, *J* = 45.2, 5.7 Hz). FT-IR cm^{-1} 3298, 3149, 2798, 1672, 1192. HRMS (ESI) calc., $C_{12}H_7F_3N_2O$ 252.0510; observed, 252.0547. mp-99-101 °C.

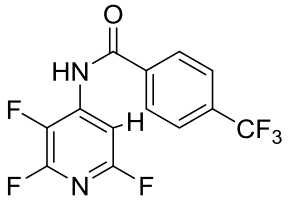


4j' 4-chloro-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4j** (30.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 20 cv and ramped to 100% EtOAc for 20-35 cv and then held at 100% EtOAc 35-40 cv) on a 4g silica column to **4j'** in 74% yield (20.0 mg, 0.0700 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -69.7 (dd, *J* = 23.1, 13.1 Hz, 1F), -88.5 (dd, *J* = 21.9, 13.2 Hz, 1F), -165.8 (ddd, *J* = 22.5, 3.7 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.2, 156.1 (d, *J* = 241.6 Hz), 150.7 – 146.6 (m), 139.9, 133.9 (dd, *J* = 28.0, 6.7 Hz), 131.4 (dd, *J* = 28.5, 6.9 Hz), 129.2, 127.3, 97.6 (dd, *J* = 44.9, 5.7 Hz). FT-IR cm^{-1} 3498, 3245, 2434, 1699, 1216. HRMS (ESI) calc., $C_{12}H_7F_3N_2O$ 252.0510; observed, 252.0547. mp-99-101 °C. The product formed after second HDCl.

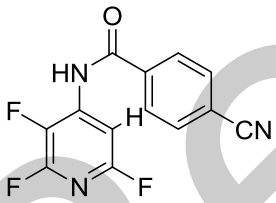


4k' methyl 4-((2,3,6-trifluoropyridin-4-yl)carbamoyl)benzoate was prepared by general procedure A. The mixture of the **4k** (33.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed

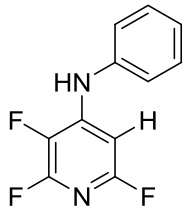
in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-45% EtOAc for 25 cv and ramped to 100% EtOAc for 25-45 cv and then held at 100% EtOAc 45-55 cv) on a 4g silica column to afford **4k'** in 86% yield (27.0 mg, 0.0900 mmol) as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 – 7.61 (m, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.1 Hz, 2H), 3.75 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -74.3 (dd, *J* = 25.5, 13.6 Hz, 1F), -88.4 (dd, *J* = 23.1, 13.7 Hz, 1F), -146.3 (ddd, *J* = 25.5, 22.9 Hz, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 166.0, 165.8, 156.2 – 153.4 (m), 151.2 – 146.9 (m), 143.1, 143.0 – 140.3 (m), 141.3 (d, *J* = 11.7 Hz), 130. (d, *J* = 2.2 Hz), 125.2, 118.6 (d, *J* = 2.0 Hz), 108.9 (dd, *J* = 38.8, 5.6 Hz), 51.2 (d, *J* = 2.0 Hz). FT-IR cm^{-1} 3400, 3026, 2817, 1739, 1695. HRMS (ESI) calc., $C_{14}H_9F_3N_2O_3$ 310.0565; observed, 310.0591. mp-128-131°C.



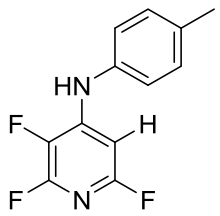
4l' 4-(trifluoromethyl)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4l** (34.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 25 cv and ramped to 100% EtOAc for 25-34 cv and then held at 100% EtOAc 34-45 cv) on a 4g silica column to afford **4l'** in 99% yield (32.0 mg, 0.100 mmol) as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 26.5 Hz, 1H), 8.08 – 7.92 (m, 2H), 7.73 (dd, *J* = 17.3, 7.9 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.2 (s, 3F), -69.3 (dd, *J* = 23.2, 12.9 Hz, 1F), -87.9 (dd, *J* = 21.9, 13.1 Hz, 1F), -164.7 (ddd, *J* = 22.6 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.2, 156.6 (dd, *J* = 242.2, 14.0 Hz), 151.4 – 146.3 (m), 144.3, 141.2 – 134.1 (m), 136.0, 129.9, 127.8, 127.3, 126.3, 99.4 – 95.7 (m). FT-IR cm^{-1} 3421, 3001, 2838, 1771, 1322. HRMS (ESI) calc., $C_{13}H_6F_6N_2O$ 320.0384; observed, 320.0351. mp-110-112°C



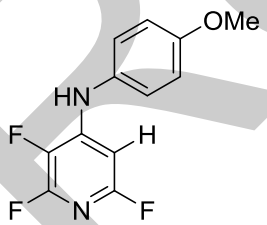
4m' 4-cyano-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide was prepared by general procedure A. The mixture of the **4m** (30.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-45% EtOAc for 20 cv and ramped to 100% EtOAc for 20-45 cv and then held at 100% EtOAc 45-50 cv) on a 4g silica column to afford **-4m'** in 81% yield (23.0 mg, 0.0800 mmol) as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -69.7 (dd, *J* = 23.1, 13.1 Hz, 1F), -88.5 (dd, *J* = 21.9, 13.2 Hz, 1F), -165.63 (ddd, *J* = 22.4 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.1, 156.1 (d, *J* = 223.6 Hz), 148.6 (d, *J* = 255.1 Hz), 144.3, 140.1, 132.7 (d, *J* = 254.8 Hz), 129.9, 129.9, 127.6, 127.3, 97.6 (d, *J* = 45.3 Hz). FT-IR cm^{-1} 3342, 3165, 2421, 1623, 1276. HRMS (ESI) calc., $C_{13}H_6F_3N_3O$ 277.0463; observed, 277.0419. mp-104-107 °C



5a' 2,3,6-trifluoro-*N*-phenylpyridin-4-amine was prepared by general procedure A. The mixture of the **5a** (24.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 18 cv and ramped to 100% EtOAc for 18-35 cv and then held at 100% EtOAc 35-40 cv) on a 4g silica column to afford **5a'** in 76% yield (17.0 mg, 0.0800 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.03 (m, 3H), 6.46 (s, 1H), 6.33 (d, *J* = 4.1 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.3 (dd, *J* = 21.1, 12.9 Hz, 1F), -92.1 (dd, *J* = 21.2, 12.9 Hz, 1F), -171.4 (ddd, *J* = 21.1, 3.7 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.6 (ddd, *J* = 237.9, 16.8, 2.9 Hz), 149.4 (ddd, *J* = 237.9, 19.8, 13.7 Hz), 146.7 (ddd, *J* = 13.7, 8.9, 5.4 Hz), 137.6, 131.6 (ddd, *J* = 244.1, 27.8, 6.2 Hz), 129.7, 126.7, 123.2, 89.9 (dd, *J* = 44.4, 4.6 Hz). FT-IR cm^{-1} 3296, 3106, 2984, 1646, 1480. HRMS (ESI) calc., $C_{11}H_7F_3N_2$ 224.0561; observed, 224.0585. mp-87-89 °C.

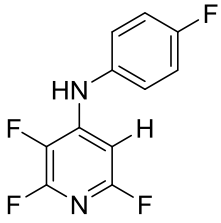


5b' 2,3,6-trifluoro-*N*-(*p*-tolyl)pyridin-4-amine was prepared by general procedure A. The mixture of the **5b** (26.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 30 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 20 cv and ramped to 100% EtOAc for 20-30 cv and then held at 100% EtOAc 30-40 cv) on a 4g silica column to afford **5b'** in 79% yield (19.0 mg, 0.0800 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 – 7.11 (m, 2H), 7.04 (d, *J* = 8.2 Hz, 2H), 6.37 (s, 1H), 6.23 (d, *J* = 4.1 Hz, 1H), 2.30 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.5 (dd, *J* = 21.0, 12.8 Hz, 1F), -92.5 (dd, *J* = 21.1, 12.8 Hz, 1F), -171.9 (ddd, *J* = 21.1, 3.8 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.8 (ddd, *J* = 237.6, 16.7, 2.9 Hz), 149.2 (ddd, *J* = 237.5, 19.9, 13.7 Hz), 146.6 (ddd, *J* = 12.4, 8.9, 5.4 Hz), 136.4, 134.7, 132.6 (dd, *J* = 28.0, 5.8 Hz), 130.5, 130.4 – 129.9 (m), 123.8, 89.3 (dd, *J* = 44.5, 4.5 Hz), 21.0. FT-IR cm^{-1} 3281, 3187, 2898, 1620, 1458. HRMS (ESI) calc., $C_{12}H_9F_3N_2$ 238.0718; observed, 238.0774. mp-76-79 °C.

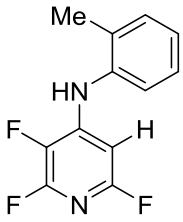


5c' 2,3,6-trifluoro-*N*-(4-methoxyphenyl)pyridin-4-amine was prepared by general procedure A. The mixture of the **5c** (27.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 26 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 25cv and ramped to 100% EtOAc for 25-35 cv and then held at 100% EtOAc 35-40 cv) on a 4g silica column to afford **5c'** in 41% yield (10.0 mg, 0.0400 mmol) as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.08 (d, *J* = 8.9 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 6.39 (s, 1H), 6.06 (d, *J* = 4.2 Hz, 1H), 3.75 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.8 (dd, *J* = 20.9, 12.7 Hz, 1F), -

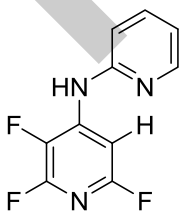
93.0 (dd, *J* = 21.0, 12.7 Hz, 1F), -172.5 (ddd, *J* = 20.9, 3.7 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.8, 156.48 (dd, *J* = 237.3, 16.9 Hz), 149.1 (ddd, *J* = 237.0, 20.0, 13.6 Hz), 147.7 (ddd, *J* = 12.2, 9.0, 5.4 Hz), 132.4 – 130.1 (m), 126.7, 115.1, 89.2 (dd, *J* = 44.3, 4.5 Hz), 55.5. FT-IR cm^{-1} 3427, 3210, 2776, 1676, 1428. HRMS (ESI) calc., $C_{12}H_9F_3N_2O$ 254.0667; observed, 254.0623. mp-81-83 °C.



5d' 2,3,6-trifluoro-*N*-(4-fluorophenyl)pyridin-4-amine was prepared by general procedure A. The mixture of the **5d** (26.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 22 cv and ramped to 100% EtOAc for 22-36 cv and then held at 100% EtOAc 36-45 cv) on a 4g silica column to afford **5d'** in 69% yield (17.0 mg, 0.0700 mmol) as yellow solid. ^{1}H NMR (400 MHz, Benzene-d_6) δ 7.17 (dd, *J* = 8.0, 4.7 Hz, 2H), 7.13 – 7.04 (dd, *J* = 8.0, 4.8 Hz 2H), 6.34 (s, 1H), 6.16 (d, *J* = 3.8 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -71.7 (dd, *J* = 21.8, 13.2 Hz, 1F), -85.2 (dd, *J* = 21.5, 12.9 Hz, 1F), -113.2 (tt, *J* = 12.8, 7.3, 4.1 Hz, 1F), -162.8 (ddd, *J* = 21.6, 3.5 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.4, 155.3, 153.4 – 149.6 (m), 146.2 (ddd, *J* = 237.4, 17.7, 13.5 Hz), 142.7 (d, *J* = 2.3 Hz), 130.8 (ddd, *J* = 247.3, 29.6, 5.5 Hz), 116.2 (d, *J* = 7.7 Hz), 115.7 (d, *J* = 22.2 Hz), 97.5 (dd, *J* = 38.4, 5.1 Hz). FT-IR cm^{-1} 3427, 3210, 2776, 1676, 1428. HRMS (ESI) calc., $C_{11}H_6F_4N_2$ 242.0467; observed, 242.0489. mp-73-75 °C

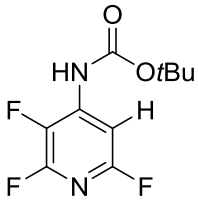


5e' 2,3,6-trifluoro-*N*-(*o*-tolyl)pyridin-4-amine was prepared by general procedure A. The mixture of the **5e** (26.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 30 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 20 cv and ramped to 100% EtOAc for 20-30cv and then held at 100% EtOAc 30-38 cv) on a 4g silica column to afford **5e'** in 68% yield (16.0 mg, 0.0700 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 – 7.16 (m, 3H), 7.09 (d, *J* = 7.8 Hz, 1H), 6.07 (s, 1H), 5.89 (d, *J* = 4.3 Hz, 1H), 2.05 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -71.6 (dd, *J* = 22.9, 13.0 Hz, 1F), -87.1 (dd, *J* = 21.3, 13.1 Hz, 1F), -172.4 (ddd, *J* = 21.1, 3.9 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.6 (dd, *J* = 236.9, 16.8 Hz), 149.5, 147.2 (d, *J* = 17.2 Hz), 142.9 (d, *J* = 6.1 Hz), 136.8 (d, *J* = 2.3 Hz), 132.9 (d, *J* = 1.4 Hz), 130.7, 126.9, 126.5, 124.5 (d, *J* = 4.2 Hz), 99.4 (d, *J* = 42.6 Hz), 17.8. FT-IR cm^{-1} 3401, 3277, 2325, 1626, 1397. HRMS (ESI) calc., $C_{12}H_9F_3N_2$ 238.0718; observed, 242.0699. mp-82-84 °C

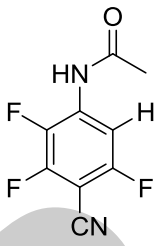


5g' *N*-(2,3,6-trifluoropyridin-4-yl)pyridin-2-amine was prepared by general procedure A. The mixture of the **5g** (24.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the

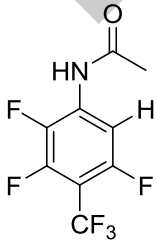
crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 25 cv and ramped to 100% EtOAc for 25-42cv and then held at 100% EtOAc 42-50 cv) on a 4g silica column to afford **5g'** in 71 % yield (17.0 mg, 0.0800 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (dd, *J* = 5.2, 1.8 Hz, 1H), 8.07 (d, *J* = 4.0 Hz, 1H), 7.62 (td, *J* = 7.8, 1.9 Hz, 1H), 7.06 – 6.91 (m, 2H), 6.82 (d, *J* = 8.3 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -71.5 (dd, *J* = 21.5, 13.3 Hz, 1F), -91.6 (dd, *J* = 21.3, 13.1 Hz, 1F), -169.2 (ddd, *J* = 21.7, 4.0 Hz, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 161.6, 155.1 – 151.9 (m), 149.5, 148.1 (dd, *J* = 12.1, 6.0 Hz), 147.4 (dd, *J* = 18.7, 13.4 Hz), 138.7, 132.3 (ddd, *J* = 246.1, 29.7, 5.2 Hz), 114.1, 109.8, 98.3 (dd, *J* = 38.6, 4.7 Hz). FT-IR cm^{-1} 3447, 3251, 2872, 1690, 1312. HRMS (ESI) calc., $C_{10}H_6F_3N_3$ 225.0514; observed, 225.0556. mp-76-78 °C.



5h' tert-butyl (2,3,6-trifluoropyridin-4-yl)carbamate was prepared by general procedure A. The mixture of the **5h** (27.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 10 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-45% EtOAc for 20 cv and ramped to 100% EtOAc for 20-40v and then held at 100% EtOAc 40-45 cv) on a 4g silica column to afford **5h'** in 98% yield (24.4 mg, 0.100 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.73 (s, 1H), 1.49 (s, 9H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.2 (dd, *J* = 24.1, 14.5 Hz), -86.5 (dd, *J* = 21.9, 13.9 Hz), -152.2 (ddd, *J* = 24.7, 21.8, 3.5 Hz). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.5 (ddd, *J* = 244.0, 14.2, 3.7 Hz), 149.3 (d, *J* = 245.4), 149.1, 141.5 (d, *J* = 4.4 Hz), 138.8 (ddd, *J* = 257.4, 26.0, 7.7 Hz), 106.8 (ddd, *J* = 39.2, 6.5, 2.4 Hz), 85.1, 27.7. FT-IR cm^{-1} 3391, 3002, 1682, 1295. HRMS (ESI) calc., $C_9H_5F_3N_2O$ 248.0773; observed 248.0761. mp-79-81 °C.

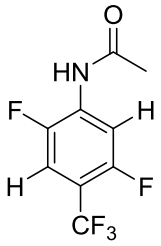


6a' *N*-(4-cyano-2,3,5-trifluorophenyl)acetamide was prepared by general procedure A. The mixture of the **6a** (23.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-40% EtOAc for 20 cv and ramped to 100% EtOAc for 20-40v and then held at 100% EtOAc 40-46 cv) on a 4g silica column to afford **6a'** in 96% yield (20.0 mg, 0.0900 mmol) as white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 (ddd, *J* = 8.5, 5.0, 2.3 Hz, 1H), 6.93 (s, 1H), 2.21 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -119.8 (ddd, *J* = 13.2, 8.5, 2.3 Hz), -132.6 (ddd, *J* = 18.7, 13.0, 4.9 Hz), -133.7 (dd, *J* = 20.2 Hz). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.4, 153.3, 150.5, 147.9, 144.5, 114.2, 111.7, 23.2. FT-IR cm^{-1} 3346, 3112, 2249, 1732, 1346. HRMS (ESI) calc., $C_9H_5F_3N_2O$ 214.0354; observed 214.0373. mp-73-75 °C.

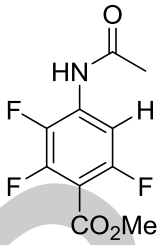


6b' *N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide was prepared by general procedure A. The mixture of the **6b** (28.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in

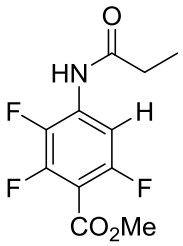
MeCN) was placed in the light bath under 45 °C for 8 h. Careful monitoring of the reaction is essential to prevent formation of the di-HDF product, see below. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 40% EtOAc for 5 cv and ramped slowly to 100% EtOAc for 5-45 cv and then held at 100% EtOAc 45-48 cv) on a 4g silica column to afford **6b** in 91% yield (21.0 mg, 0.0800 mmol) as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (ddd, *J* = 8.7, 5.5, 2.3 Hz, 1H), 6.99 (s, 1H), 2.20 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -61.2 (d, *J* = 12.9 Hz, 3F), -120.7 (dd, *J* = 14.2, 9.1 Hz, 1F), -135.2 (dd, *J* = 20.6 Hz, 1F), -143.1 (ddd, *J* = 14.1, 7.4 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7 (d, *J* = 28.3 Hz), 153.2, 149.3 (d, *J* = 320.4 Hz), 145.4 (d, *J* = 261.0 Hz), 142.2 (d, *J* = 250.7 Hz), 129.8 (d, *J* = 32.4 Hz), 119.4, 108.5 (d, *J* = 25.1 Hz), 29.7. FT-IR cm^{-1} 3309, 3019, 2188, 1612, 1324. HRMS (ESI) calc., $C_9H_5F_6NO$ 257.0275; observed 257.0274. mp 88-91 °C.



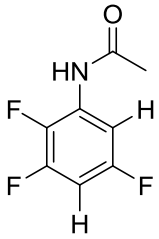
6b'' *N*-(2,5-difluoro-4-(trifluoromethyl)phenyl)acetamide was prepared by general procedure A. The mixture of the **6b** (28.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 50% EtOAc for 25 cv and ramped slowly to 100% EtOAc for 25-55 cv and then held at 100% EtOAc for 55-58 cv) on a 4g silica column to afford **6b''** in 74% yield (17.0 mg, 0.0700 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.33 (dd, *J* = 12.1, 6.3 Hz, 1H), 7.43 (s, 1H), 7.26 (dd, *J* = 10.5, 6.1 Hz, 1H), 2.20 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -61.0 (d, *J* = 12.8 Hz, 3F), -116.5 (dd, *J* = 15.5, 6.5 Hz, 1F), -135.98 (d, *J* = 8.8 Hz, 1F). This compound reported previously and the spectra matched accordingly.[5]



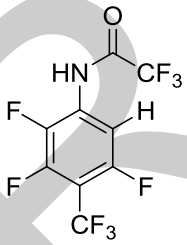
6c' methyl 4-acetamido-2,3,6-trifluorobenzoate was prepared by general procedure A. The mixture of the **6c** (27.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 45% EtOAc for 20 cv and ramped slowly to 100% EtOAc for 22-45 cv and then held at 100% EtOAc for 45-50 cv) on a 4g silica column to afford **6c'** in 97% yield (24.0 mg, 0.100 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (ddd, *J* = 9.9, 5.6, 2.2 Hz, 1H), 6.91 (s, 1H), 3.88 (s, 3H), 2.19 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -122.5 (dd, *J* = 14.7, 9.8 Hz), -136.6 (dd, *J* = 16.3 Hz), -136.9 (ddd, *J* = 15.8, 7.5 Hz). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.9, 162.8, 151.6 (d, *J* = 249.9 Hz), 148.2 (d, *J* = 119.5 Hz), 145.6 (d, *J* = 129.5 Hz), 119.9, 117.3 (t, *J* = 8.8 Hz), 112.4 (dd, *J* = 24.2, 3.7 Hz), 52.9, 29.7. FT-IR cm^{-1} 3376, 3212, 2965, 1678, 1592, 937. HRMS (ESI) calc., $C_{11}H_{10}F_3NO_3$ 261.0613; observed 261.0651. mp-81-83 °C



6d' methyl 2,3,6-trifluoro-4-propionamidobenzoate was prepared by general procedure A. The mixture of the **6d** (28.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 40% EtOAc for 20 cv and ramped slowly to 100% EtOAc for 20-40 cv and then held at 100% EtOAc for 40-45 cv) on a 4g silica column to afford **6d'** in 93% yield (23.0 mg, 0.0900 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (ddd, *J* = 9.8, 5.6, 2.3 Hz, 1H), 6.84 (s, 1H), 3.88 (s, 3H), 2.43 (q, *J* = 7.5 Hz, 2H), 1.21 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -122.6 (dd, *J* = 14.7, 9.8 Hz, 1F), -136.6 (dd, *J* = 20.6 Hz, 1F), -137.1 (ddd, *J* = 20.4, 14.6, 5.7 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.5, 162.8, 153.6 – 150.1 (m), 149.4 – 147.2 (m), 147.0 – 144.7 (m), 119.9 (d, *J* = 17.9 Hz), 117.0, 112.5 (d, *J* = 3.7 Hz), 52.9, 29.4, 9.39. FT-IR cm^{-1} 3324, 3281, 2248, 1767, 1006. HRMS (ESI) calc., $C_{11}H_{10}F_3NO_3$ 261.0613; observed 261.0651. mp-81-83 °C

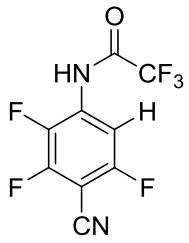


6e' methyl 2,3,6-trifluoro-4-propionamidobenzoate was prepared by general procedure A. The mixture of the **6e** (23.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 35% EtOAc for 18 cv and ramped slowly to 100% EtOAc for 18-35 cv and then held at 100% EtOAc for 35-40 cv) on a 4g silica column to afford **6e'** in 86% yield (16.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 17.0 Hz, 1H), 7.30 (s, 1H), 6.92 (ddd, *J* = 9.8, 7.1, 2.7 Hz, 1H), 1.97 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.3 (ddd, *J* = 16.0, 7.9, 4.0 Hz, 1F), -131.9 (ddd, *J* = 22.5, 9.5, 4.0 Hz, 1F), -143.3 – -144.6 (m, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 175.6, 161.5 (ddd, *J* = 244.1, 9.7, 2.6 Hz), 155.6 – 152.8 (m), 152.7, 152.83 – 150.0 (m), 130.4 – 122.1 (m), 110.4 (ddd, *J* = 28.7, 21.3, 2.0 Hz), 38.0 (d, *J* = 2.3 Hz). FT-IR cm^{-1} 3261, 3187, 2881, 1573, 1526. HRMS (ESI) calc., $C_8H_6F_3NO$ 189.0401; observed 189.0393. mp-111-113 °C.

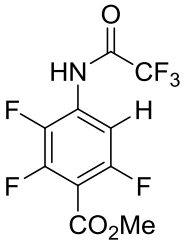


6g' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide was prepared by general procedure A. The mixture of the **6g** (33.0 mg, 0.100 mmol), N-ethyl morpholine (22.0 uL, 0.200 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 76 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 45% EtOAc for 25 cv and ramped slowly to 100% EtOAc for 25-40 cv and then held at 100% EtOAc for 40-55 cv) on a 4g silica column to afford **6g'** in 75% yield (23.0 mg, 0.0700 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.24 (ddd, *J* = 8.4, 5.4, 2.3 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -61.3 (s, 3F), -74.9 (s, 3F), -119.3 (dd, *J* = 14.5, 8.9 Hz, 1F), -133.8 (dd, *J* = 20.5, 2.3 Hz, 1F), -141.5 – -142.7 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.8 (d, *J* =

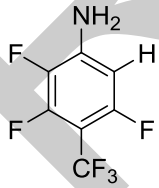
40.3 Hz), 152.4, 150.9, 145.1, 144.3, 120.7 (d, *J* = 21.8 Hz), 112.5 (dd, *J* = 26.0, 3.8 Hz), 101.1. FT-IR cm^{-1} 3342, 3199, 2246, 1687, 1451. HRMS (ESI) calc., $C_9H_2F_9NO$ 310.9993; observed 310.9946. mp-122--124 °C.



6h' *N*-(4-cyano-2,3,5-trifluorophenyl)-2,2,2-trifluoroacetamide was prepared by general procedure A. The mixture of the **6h** (29.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 59 h. After workup, The crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 40% EtOAc for 20 cv and ramped slowly to 100% EtOAc for 20-40 cv and then held at 100% EtOAc for 40-46 cv) on a 4g silica column to afford **6h'** in 75% yield (17.0 mg, 0.0600 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (s, 1H), 7.26 (ddd, *J* = 8.4, 4.9, 2.4 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -74.8 (s, 3F), -118.4 (dd, *J* = 13.6, 8.2 Hz, 1F), -131.4 (dd, *J* = 13.6, 4.8 Hz, 1F), -132.5 (ddd, *J* = 19.9, 2.5 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.6 (d, *J* = 39.8 Hz), 153.5, 150.9, 147.8, 144.8, 116.4 (d, *J* = 27.4 Hz), 114.6 (dd, *J* = 25.0, 4.3 Hz), 111.1. FT-IR cm^{-1} 3312, 3234, 2428, 1426, 1262. HRMS (ESI) calc., $C_9H_2F_6N_2O$ 268.0071; observed 268.0028. mp-114--116 °C

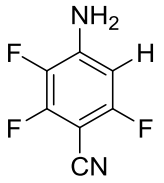


6i' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide was prepared by general procedure A. The mixture of the **6i** (32.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 40 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 40% EtOAc for 22 cv and ramped slowly to 100% EtOAc for 22-45 cv and then held at 100% EtOAc for 45-55 cv) on a 4g silica column to afford **6i'** in 70% yield (21.0 mg, 0.0700 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (s, 1H), 7.54 (ddd, *J* = 9.7, 5.5, 2.4 Hz, 1H), 3.91 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -74.9 (s, 3F), -121.39 (dd, *J* = 15.3, 9.6 Hz, 1F), -135.2 (dd, *J* = 20.5, 2.4 Hz, 1F), -135.8 (ddd, *J* = 20.5, 15.2, 5.5 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.4, 154.9, 154.5, 152.8, 150.9, 148.9 (d, *J* = 12.5 Hz), 147.9 (d, *J* = 19.9 Hz), 146.5 – 145.9 (m), 145.1, 119.4, 116.7, 112.9 (dd, *J* = 23.6, 4.0 Hz), 53.2. FT-IR cm^{-1} 3431, 3305, 2272, 1681, 1283. HRMS (ESI) calc., $C_{10}H_5F_6NO_3$ 301.0174; observed 301.0139. mp-143--145 °C.

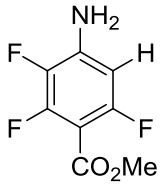


6l' 2,3,5-trifluoro-4-(trifluoromethyl)aniline was prepared by general procedure A. The mixture of the **6l** (23.0 mg, 0.100 mmol), *N*-ethyl morpholine (22.0 uL, 0.200 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 30 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 40% EtOAc for 18 cv and ramped slowly to 100% EtOAc for 18-40 cv and then held at 100% EtOAc for 40-45 cv) on a 4g silica column to afford **6l'** in 73% yield (16.0 mg, 0.0700 mmol) as a yellow liquid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (t, *J* = 7.3 Hz, 1H),

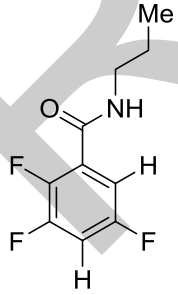
3.03 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -61.0 (s, 3F), -122.10 (m, 1F), -137.00 – -138.20 (m, 1F), -140.3 – -142.7 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 132.9 (d, *J* = 47.9 Hz), 129.2 (d, *J* = 30.8 Hz), 127.5 (d, *J* = 34.9 Hz), 122.5, 108.4, 28.01. FT-IR cm^{-1} 3493, 3289, 1642, 1312, 1283. HRMS (ESI) calc., $C_7H_3F_6N$ 215.0170; observed 215.0176.



6m' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide was prepared by general procedure A. The mixture of the **6m** (19.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 14 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 1 cv, slowly ramped to 12% EtOAc for 1- 12 cv, to 20% EtOAc for 12-26 cv, to 25% EtOAc for 26-32 cv then ramped to 100% EtOAc for 32-34 cv, then held at 100% EtOAc 34- 40 cv) on a 4g silica column to afford **6m'** in 97% yield (17.0 mg, 0.100 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.07 (s, 1H), 6.97 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -135.1 – -135.9 (m, 2F), -154.2 (dd, *J* = 19.0, 12.2 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.4, 154.9, 154.5, 152.8, 150.3, 148.6 (d, *J* = 12.5 Hz), 147.6 (d, *J* = 19.9 Hz), 146.5 – 145.9 (m), 145.1, 119.4, 116.7, 112.7 (dd, *J* = 23.6, 4.0 Hz), 53.2. FT-IR cm^{-1} 3414, 3357, 2924, 2234, 1642. This compound reported previously and the spectra matched accordingly.[5]

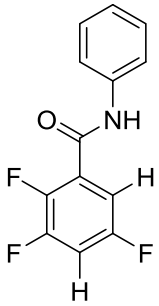


6n' methyl 4-amino-2,3,6-trifluorobenzoate was prepared by general procedure A. The mixture of the **6n** (22.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-10% EtOAc for 25 cv and ramped to 100% EtOAc for 10-52 cv and then held at 100% EtOAc 52-57 cv) on a 12 g silica column to afford **6n'** in 99% yield (20.0 mg, 0.100 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (ddd, *J* = 11.1, 5.7, 2.2 Hz, 1H), 4.22 (s, 2H), 3.83 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -137.8 (dd, *J* = 11.3 Hz, 1F), -138.8 (dd, *J* = 19.3, 12.9, 1F), -156.0 (ddd, *J* = 19.9, 10.3, 2.4 Hz, 1F). FT-IR cm^{-1} 3403, 3050, 2984, 1732, 1551, 1642. This compound reported previously and the spectra matched accordingly.[5]

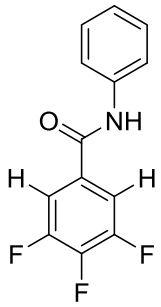


7a' 2,3,5-trifluoro-*N*-propylbenzamide was prepared by general procedure A. The mixture of the **7a** (25.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0-15% EtOAc for 25 cv and ramped to 100% EtOAc for 25-38 cv and then held at 100% EtOAc 38-46 cv) on a 4 g silica column to afford **7a'** in yield of 54% (12.0 mg, 0.0600 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (ddt, *J* = 8.4, 5.1, 3.0 Hz, 1H), 6.99 (dtd, *J* = 9.6, 6.9, 3.2 Hz, 1H), 6.57 (s, 1H), 3.38 (d, *J* = 6.7 Hz, 2H), 1.59 (q, *J* = 7.3 Hz, 2H), 0.96 – 0.91 (m, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.1 – -114.1

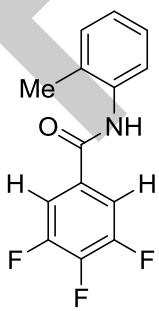
(m, 1F), -131.2 – -134.1 (m, 1F), -144.82 – -145.0 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.0, 159.2 – 155.4 (m), 150.3 (ddd, *J* = 252.6, 16.8, 11.9 Hz), 147.8 – 143.4 (m), 126.6 – 121.5 (m), 112.8 (dd, *J* = 25.4, 3.6 Hz), 108.3 (dd, *J* = 27.6, 20.9 Hz), 42.0, 22.6, 11.3 (d, *J* = 2.1 Hz). FT-IR cm^{-1} 3386, 3207, 2894, 1783, 1492. HRMS (ESI) calc., $C_{10}H_{10}F_3NO$ 217.0714; observed 217.0760. mp-130-133 °C.



7b' 2,3,5-trifluoro-*N*-phenylbenzamide was prepared by general procedure A. The mixture of the **7b** (29.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 8% EtOAc for 5 cv and ramped to 100% EtOAc for 8-20 cv and then held at 100% EtOAc 20-25 cv) on a 4 g silica column to afford **7b'** in 67% yield (17.0 mg, 0.0700 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 14.0 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 2H), 7.33 (dd, *J* = 9.4, 6.5 Hz, 2H), 7.16 – 7.11 (m, 1H), 7.07 (ddt, *J* = 9.9, 6.5, 3.4 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.4 – -113.2 (m, 1F), -131.9 – -132.5 (m, 1F), -141.9 – -146.7 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.9, 156.4, 150.6 (d, *J* = 253.1 Hz), 145.4 (d, *J* = 244.9 Hz), 137.0, 129.2, 125.7, 124.2 (d, *J* = 10.7 Hz), 120.6, 113.2. FT-IR cm^{-1} 3412, 3263, 2789, 1704, 1261. HRMS (ESI) calc., $C_{13}H_8F_3NO$ 251.0558; observed 251.0509. mp-117-119 °C.

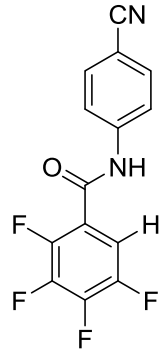


7b'' 2,3,5-trifluoro-*N*-phenylbenzamide was prepared by general procedure A. The mixture of the **7b** (29.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 25 °C for 12 h. After workup, the crude material was purified by flash chromatographyusing hexane : ethyl acetate (0 – 10% EtOAc for 5 cv and ramped to 100% EtOAc for 8-20 cv and then held at 100% EtOAc 20-32 cv) on a 4 g silica column to afford **7b'** in 56% yield (14.0 mg, 0.0600 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.42 (m, 5H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.13 (t, *J* = 7.5 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -129.7 – -133.1 (m, 2F), -154.1 – -155.0 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.4, 150.2 (dd, *J* = 253.1, 10.6 Hz), 141.1 (d, *J* = 258.1 Hz), 136.0, 129.2, 128.2, 124.2, 119.3, 110.8 (d, *J* = 22.8 Hz). FT-IR cm^{-1} 3489, 3239, 2745, 1723, 1286. HRMS (ESI) calc., $C_{13}H_8F_3NO$ 251.0558; observed 251.0529. mp-114-117 °C.

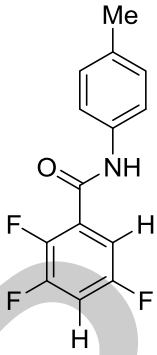


7c' 3,4,5-trifluoro-*N*-(o-tolyl)benzamide was prepared by general procedure A. The mixture of the **7c** (30.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatographyusing hexane : ethyl acetate (0 – 8% EtOAc for 8 cv and ramped to 100% EtOAc for 8-20 cv and then held at 100% EtOAc 20-34 cv) on a

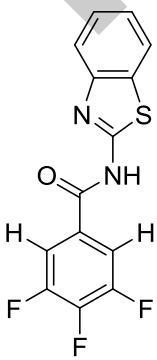
4 g silica column to afford **7g'** in 63% yield (17.0 mg,0.0600 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 7.9 Hz, 1H), 7.46 (t, *J* = 6.7 Hz, 2H), 7.18 (d, *J* = 7.2 Hz, 3H), 7.09 (t, *J* = 7.5 Hz, 1H), 2.26 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -130.0 – -132.8 (m, 2F), -154.2 – -155.2 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.5, 151.2 (d, *J* = 246.0 Hz), 142.1 (d, *J* = 258.6 Hz), 134.9, 130.7, 129.7, 127.0, 126.1, 125.9, 123.4, 111.8 (d, *J* = 22.6 Hz), 29.7. FT-IR cm^{-1} 3453, 3229, 2714, 1666, 1239. HRMS (ESI) calc., $C_{14}H_{10}F_3NO$ 265.0714; observed 265.0762. mp-115-117 °C.



7d' *N*-(4-cyanophenyl)-2,3,4,5-tetrafluorobenzamide was prepared by general procedure A. The mixture of the **7d** (31.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 6 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 18 cv, slowly ramped to 20% EtOAc for 18-22 cv and then ramped to 100% EtOAc for 22-26 cv, then held at 100% EtOAc 36- 45 cv), on a 4 g silica column to afford **7g'** in 72% yield (20.0 mg,0.0700 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 14.5 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 8.7 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -133.9 – -135.97 (m, 1F), -138.6 – -139.2 (m, 1F), -146.0 – -147.1 (m, 1F), -151.5 – -153.8 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.5, 150.8 – 145.5 (m), 144.7 (d, *J* = 15.0 Hz), 140.9, 142.8 – 139.1 (m), 133.4, 120.4 (d, *J* = 5.1 Hz), 118.4, 117.0 (d, *J* = 6.1 Hz), 113.3 (d, *J* = 21.6 Hz), 111.4 – 109.1 (m), 108.5. FT-IR cm^{-1} 3435, 3219, 2231, 1682, 1221. HRMS (ESI) calc., $C_{14}H_6F_4N_2O$ 294.0416; observed 294.0486. mp-120-123 °C.

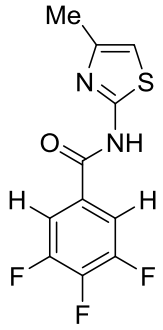


7e' 2,3,5-trifluoro-*N*-(*p*-tolyl)benzamide was prepared by general procedure A. The mixture of the **7e** (30.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 18 cv, slowly ramped to 20% EtOAc for 18-26 cv and then ramped to 100% EtOAc for 26-33 cv, then held at 100% EtOAc 38 46 cv), on a 4 g silica column to afford **7h'** in yield of 68% (18.0 mg, 0.0700 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 14.1 Hz, 1H), 7.58 (dddd, *J* = 8.5, 5.2, 3.3, 2.1 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 7.09 – 7.00 (m, 1H), 2.28 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.5 – -113.1 (m, 1F), -127.4 – -138.1 (m, 1F), -139.6 – -150.2 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.9, 135.1, 134.5, 129.6 (d, *J* = 4.0 Hz), 124.2, 120.6, 113.0 (d, *J* = 22.6 Hz), 111.4 – 103.0 (m), 20.9. FT-IR cm^{-1} 3449, 3251, 2214, 1697, 1281. HRMS (ESI) calc., $C_{14}H_{10}F_3NO$ 265.0714; observed 265.0772. mp-112-114 °C.

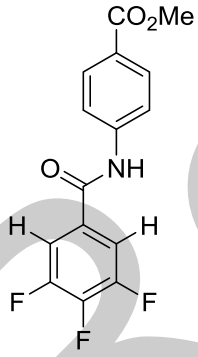


7f' *N*-(benzo[d]thiazol-2-yl)-3,4,5-trifluorobenzamide was prepared by general procedure A. The mixture of the **7f** (34.0 mg, 0.100 mmol), DIPEA (54.0 uL,

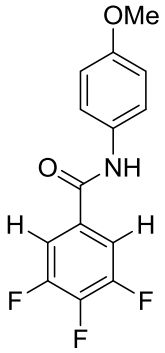
0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 10 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 19 cv, slowly ramped to 20% EtOAc for 19-22 cv and then ramped to 100% EtOAc for 22-24 cv, then held at 100% EtOAc 34- 45 cv), on a 4 g silica column to afford **7f'** in 62% yield (19.0 mg,0.0600 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.10 (s, 4H), 7.51 (s, 1H), 7.39 (d, J = 7.3 Hz, 2H). ^{19}F NMR (376 MHz, Acetone-d_6) δ -130.1 – -145.0 (m, 2F), -156.3 – -157. 2 (m, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 151.8 (d, J = 250.4 Hz), 148.2– 143.5 (m), 130.2, 127.1, 125.0, 122.9, 121.1, 114.3 (d, J = 24.5 Hz). FT-IR cm^{-1} 3473, 3044, 1681, 1514, 823. HRMS (ESI) calc., $C_{14}H_7F_3N_2OS$ 308.0231; observed 308.0288. mp-119-123 °C.



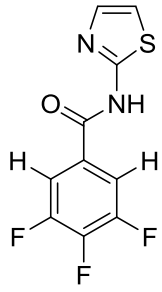
7g' 3,4,5-trifluoro-*N*-(4-methylthiazol-2-yl)benzamide was prepared by general procedure A. The mixture of the **7g** (31.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 10% EtOAc for 8 cv and ramped to 100% EtOAc for 8-20 cv and then held at 100% EtOAc 20-38 cv) on a 4 g silica column to afford **7c'** in 60% yield (16.0 mg, 0.0600 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.74 – 7.49 (m, 2H), 6.55 (d, J = 14.7 Hz, 1H), 2.25 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-d) δ -131.3 (dd, J = 20.3, 7.7 Hz, 2F), -152.5 – -152.1 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-d) δ 162.1, 158.4, 152.4 – 151.2 (m), 146.3 (d, J = 249.3 Hz), 142.6, 140.4, 116.3 (d, J = 7.2 Hz), 33.6. FT-IR cm^{-1} 3482, 3199, 2732, 1714, 1261. HRMS (ESI) calc., $C_{11}H_7F_3N_2OS$ 272.0231; observed 272.0278. mp-129-132 °C.



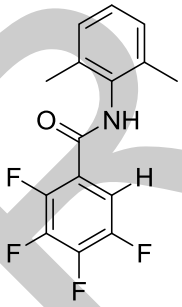
7h' methyl 4-(3,4,5-trifluorobenzamido)benzoate was prepared by general procedure A. The mixture of the **7h** (34.0 mg, 0.100 mmol), DIPEA (35.0 uL, 0.200 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 25 °C for 10 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 15 cv, slowly ramped to 20% EtOAc for 15-28 cv and then ramped to 100% EtOAc for 28-38 cv, then held at 100% EtOAc 38 50 cv), on a 4 g silica column to afford **7h'** in 81% yield (25.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.23 – 7.63 (m, 6H), 3.88 (d, J = 1.6 Hz, 3H). ^{19}F NMR (376 MHz, Acetone-d_6) δ -135.2 (dd, J = 19.9, 8.6 Hz), -157.8 – - 158.7 (m, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 167.6 (d, J = 6.2 Hz), 164.2, 151.3 (d, J = 10.7 Hz), 145.9 – 142.8 (m), 132.1 (d, J = 13.1 Hz), 129.3 – 126.7 (m), 122.8 – 119.3 (m), 114.4 (d, J = 22.8 Hz), 113.7 (d, J = 21.3 Hz), 110.0 (d, J = 27.8 Hz), 53.1 (d, J = 3.9 Hz). FT-IR cm^{-1} 3475, 3022, 1741, 1664, 1206. HRMS (ESI) calc., $C_{15}H_{10}F_3NO_3$ 309.0613; observed 309.0627. mp-115-119 °C



7i' 3 2,3,4,5,6-pentafluoro-*N*-(4-methoxyphenyl)benzamide was prepared by general procedure A. The mixture of the **7i** (32.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.25 mM, 1 mL in MeCN) was placed in the light bath under 25 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 20 cv, slowly ramped to 20% EtOAc for 20-25 cv and then ramped to 100% EtOAc for 25-35 cv, then held at 100% EtOAc 35-45 cv), on a 4 g silica column to afford **7i** in 75% yield (21.0 mg,0.700 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.91 – 7.78 (m, 2H), 7.73 – 7.66 (m, 2H), 6.99 – 6.91 (m, 2H), 3.80 (d, *J* = 1.8 Hz, 3H). ^{19}F NMR (376 MHz, Acetone-d_6) δ -135.5 (dd, *J* = 19.9, 8.7 Hz, 2F), -158.7 – -159.3 (m, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 163.4, 158.3, 152.5 (d, *J* = 239.2 Hz), 143.2 (d, *J* = 254.4 Hz), 133.6, 123.7, 123.1, 115.5, 114.1 (d, *J* = 22.5 Hz), 56.5. FT-IR cm^{-1} 3461, 3050, 2821, 1685, 1211. HRMS (ESI) calc., $C_{14}H_{10}F_3NO_2$ 281.0664; observed 281.0612. mp-124-126 °C.

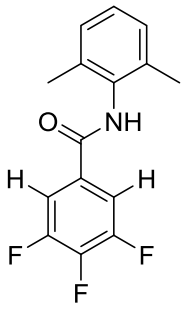


7j' 3,4,5-trifluoro-*N*-(thiazol-2-yl)benzamide was prepared by general procedure A. The mixture of the **7j** (29.0 mg, 0.100 mmol), DIPEA (35.0 uL, 0.200 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 25 °C for 10 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 15 cv, slowly ramped to 20% EtOAc for 15-25 cv and then ramped to 100% EtOAc for 25-30 cv, then held at 100% EtOAc 35 45 cv), on a 4 g silica column to afford **7i'** in 77% yield (20.0 mg, 0.0800 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 – 7.49 (m, 2H), 6.55 (d, *J* = 14.7 Hz, 1H), 2.25 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -131.1 (dd, *J* = 20.2, 7.3 Hz, 2F), -152.2 – -153.6 (m, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 163.3, 159.9, 154.7 – 149.6 (m), 143.0 (d, *J* = 255.8 Hz), 137.6, 114.5, 113.9 (d, *J* = 6.5 Hz), 113.8 (d, *J* = 6.2 Hz). FT-IR cm^{-1} 3419, 3225, 1714, 1315, 1423. HRMS (ESI) calc., $C_{10}H_5F_3N_2OS$ 258.0075; observed 258.0061. mp-120-123 °C

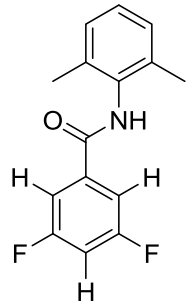


8a' *N*-(2,6-dimethylphenyl)-2,3,4,5-tetrafluorobenzamide was prepared by general procedure A. The mixture of the **8a** (32.0 mg, 0.100 mmol), DIPEA (20.0 uL, 0.120 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 23 °C for 7 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 18% EtOAc for 18-25 cv and then ramped to 100% EtOAc for 25-42 cv, then held at 100% EtOAc 42 50 cv), on 4 g silica column to afford **8a'** in 88% yield (26.0 mg, 0.0700 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (dddd, *J* = 10.7, 8.6, 6.5, 2.5 Hz, 1H), 7.78 (d, *J* = 12.5 Hz, 1H), 7.25 – 7.12 (m, 3H), 2.30 (s, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -136.2 (dddd, *J* = 21.5, 13.6, 10.7, 3.3 Hz, 1F), -138.9 (ddd, *J* = 16.4, 12.9, 6.5 Hz, 1F), -148.5 – 149.1 (m, 1F), -153.6 (dd, *J* = 22.6, 19.6 Hz, 1F). ^{13}C NMR (101 MHz,

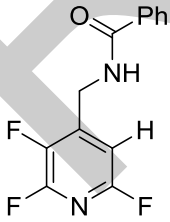
DMSO-d_6) δ 159.7, 149.5 – 147.0 (m), 146.5 – 144.5 (m), 143.9 – 142.1 (m), 141.5 – 139.4 (m), 136.1 (d, J = 1.6 Hz), 134.7, 133.3, 128.3, 127.7, 115.5 – 108.4 (m), 18.0. FT-IR cm^{-1} 3460, 3276, 2209, 1651, 1220. HRMS (ESI) calc., $C_{15}H_{11}F_4NO$ 297.0777; observed 297.0801. mp-135-137 °C.



8a''*N*-(2,6-dimethylphenyl)-3,4,5-trifluorobenzamide was prepared by general procedure A. The mixture of the **8a** (32.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 15% EtOAc for 15-25 cv and then ramped to 100% EtOAc for 25-35 cv, then held at 100% EtOAc 35 40 cv), on a 4 g silica column to afford **8a''** in 87% yield (24.0 mg, 0.0900 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.60 (dd, J = 7.6, 6.4 Hz, 2H), 7.26 (s, 1H), 7.22 – 7.13 (m, 3H), 2.29 (s, 6H). ^{19}F NMR (376 MHz, Chloroform-d) δ -131.7 (dd, J = 20.0, 7.5 Hz, 2F), -154.3 – -155.3 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-d) δ 156.7, 148.6 – 146.4 (m), 144.5 (d, J = 20.7 Hz), 142.2 (d, J = 14.4 Hz), 135.6, 132.3, 128.3 (d, J = 18.0 Hz), 117.2, 107.6, 18.3. FT-IR cm^{-1} 3423, 3191, 2293, 1729, 1267. HRMS (ESI) calc., $C_{15}H_{12}F_3NO$ 279.0871; observed 279.0818. mp-128-131 °C.

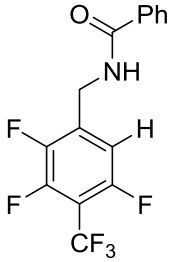


8a''' *N*-(2,6-dimethylphenyl)-3,5-difluorobenzamide was prepared by general procedure A. The mixture of the **8a** (32.0 mg, 0.100 mmol), DIPEA (100 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 60 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 16% EtOAc for 16-24 cv and then ramped to 100% EtOAc for 24-40 cv, then held at 100% EtOAc 40 45 cv), on a 4 g silica column to afford **8a'''** in 96% yield (25.0 mg, 0.0700 mmol) as a white solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.83 – 7.50 (m, 2H), 7.27 (tt, J = 9.0, 2.4 Hz, 1H), 7.11 (d, J = 3.2 Hz, 3H), 2.24 (s, 6H). ^{19}F NMR (376 MHz, Acetone-d_6) δ -110.2 (d, J = 8.2 Hz, 2F). ^{13}C NMR (101 MHz, Chloroform-d) δ 164.3, 137.7, 135.4, 133.1, 128.4, 127.8, 112.0 (d, J = 22.6 Hz), 110.3, 107.2 (d, J = 50.5 Hz), 18.4. FT-IR cm^{-1} 3487, 3213, 2221, 1760, 1291. HRMS (ESI) calc., $C_{15}H_{13}F_2NO$ 261.0965; observed 261.0931. mp-119-123 °C.

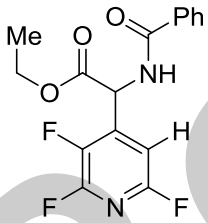


9a' *N*-((2,3,6-trifluoropyridin-4-yl)methyl)benzamide was prepared by general procedure A. The mixture of the **9a** (33.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 15% EtOAc for 15-25 cv and then ramped to 100% EtOAc for 25-35 cv, then held at 100% EtOAc 35 45 cv), on a 4 g silica column to afford **9a'** in 79% yield (19.0 mg, 0.0700 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-d) δ

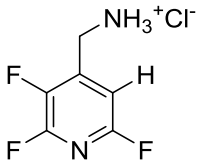
7.78 – 7.68 (m, 2H), 7.58 – 7.45 (m, 1H), 7.40 (dd, *J* = 8.4, 6.9 Hz, 2H), 6.79 (t, *J* = 3.0 Hz, 1H), 6.67 (s, 1H), 4.68 (d, *J* = 6.2 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.4 (ddd, *J* = 26.9, 12.6, 2.8 Hz, 1F), -88.2 (dd, *J* = 22.2, 12.7 Hz, 1F), -152.4 (ddd, *J* = 25.9, 22.1, 3.2 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7, 155.3 (d, *J* = 235.6 Hz), 150.2, 143.5 (d, *J* = 7.2 Hz), 143.1 – 138.0 (m), 133.1, 132.3, 128.8, 127.1, 106.1 (dd, *J* = 38.6, 5.9 Hz), 37.3. FT-IR cm^{-1} 3490, 3369, 2292, 1651, 1273. HRMS (ESI) calc., $C_{13}H_9F_3N_2O$ 266.0667; observed 266.0327. mp-75-78 ^{o}C. The hydrolysis of acid observed during the HDF reaction



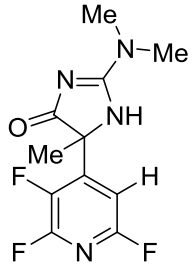
9b' *N*-(2,3,5-trifluoro-4-(trifluoromethyl)benzyl)benzamide was prepared by general procedure A. The mixture of the **9b** (40.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 ^{o}C for 12 h. After workup, the crude material was purified by flash chromatography using hexane: ethyl acetate (0% for 10 cv, slowly ramped to 18% EtOAc for 18-29 cv and then ramped to 100% EtOAc for 29-47 cv, then held at 100% EtOAc 47 55 cv), on a 4 g silica column to afford **9b'** in 80% yield (24.0 mg, 0.0700 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.74 (m, 2H), 7.58 – 7.51 (m, 1H), 7.49 – 7.43 (m, 2H), 7.18 (ddd, *J* = 8.8, 4.9, 2.2 Hz, 1H), 6.64 (s, 1H), 4.80 (d, *J* = 6.2 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -61.4 (s, 3F), -113.9 – -118.2 (m, 1F), -134.0 – -135.4 (m, , 1F), -142.5 – -143. 9 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.6, 167.2, 157.1, 154.6, 149.9 (d, *J* = 253.1 Hz), 144.9 (d, *J* = 250.0 Hz), 133.4, 131.9, 128.7, 126.9, 122.4 – 117.3 (m), 112.4 – 103.7 (m), 32.3. FT-IR cm^{-1} 3440, 3322, 2273, 1659, 1248. HRMS (ESI) calc.$C_{15}H_9F_6NO$ 333.0588; observed 333.0581. mp-68-71 ^{o}C. The hydrolysis of acid observed during the HDF reaction.



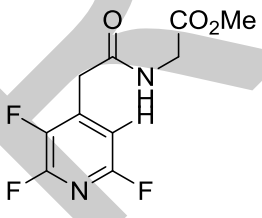
9c' ethyl 2-benzamido-2-(2,3,6-trifluoropyridin-4-yl)acetate was prepared by general procedure A. The mixture of the **9c** (36.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 ^{o}C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 15% EtOAc for 15-30 cv and then ramped to 100% EtOAc for 30-40 cv, then held at 100% EtOAc 40 45 cv), on a 4 g silica column to afford **9c'** in 94% yield (32.0 mg, 0.0900 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 – 7.71 (m, 2H), 7.55 – 7.47 (m, 1H), 7.47 – 7.37 (m, 2H), 7.32 (d, *J* = 5.8 Hz, 1H), 6.85 (t, *J* = 3.0 Hz, 1H), 5.87 (d, *J* = 5.8 Hz, 1H), 4.30 – 4.17 (m, 2H), 1.20 (d, *J* = 7.2 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -71.8 (ddd, *J* = 26.1, 12.6, 2.8 Hz, 1F), -86.5 (dd, *J* = 21.9, 12.7 Hz, 1F), -147.6 – -158.9 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.1, 166.6, 157.0 – 153.7 (m), 151.3 – 148.0 (m), 142.1 (d, *J* = 48.0 Hz), 132.5, 128.8, 127.6, 127.7, 109.9, 106.9 (d, *J* = 38.6 Hz), 63.7, 29.70, 13.9. FT-IR cm^{-1} 3477, 3325, 2300, 1650, 1229. HRMS (ESI) calc., $C_{16}H_{13}F_3N_2O_3$ 338.0878; observed 338.0879. mp 91-93 ^{o}C.



9d' (2,3,6-trifluoropyridin-4-yl)methanaminium chloride was prepared by general procedure A. The mixture of the **9c** (22.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 15% EtOAc for 10-15 cv and then ramped to 100% EtOAc for 15-25 cv, then held at 100% EtOAc 25 35 cv), on a 4 g silica column to afford **9c'** in 96% yield (19.0 mg, 0.0900 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.74 (t, *J* = 3.0 Hz, 1H), 3.70 (m, 5H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -77.3 (dd, *J* = 26.3, 13.1 Hz), -91.6 (dd, *J* = 21.8, 12.9 Hz), -154.5 (ddd, *J* = 25.4, 21.5, 3.1 Hz). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.9 (ddd, *J* = 244.5, 12.5, 2.8 Hz), 150.5 – 147.6 (m), 140.3 (dd, *J* = 25.3, 6.6 Hz), 138.7 (ddd, *J* = 13.9, 8.6, 3.0 Hz), 108.0 (dd, *J* = 38.3, 6.0 Hz), 52.7. FT-IR cm^{-1} 3498, 3323, 23008, 1652, 1239. HRMS (ESI) calc., $C_6H_6ClF_3N_2$ 198.0172; observed 198.0172. mp 161-162 °C.

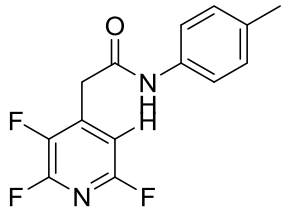


9e' 2-(dimethylamino)-5-methyl-5-(2,3,6-trifluoropyridin-4-yl)-1,5-dihydro-4H-imidazol-4-one was prepared by general procedure A. The mixture of the **9e** (29.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 15% EtOAc for 15-28 cv and then ramped to 100% EtOAc for 28-45 cv, then held at 100% EtOAc 45 58 cv), on a 4g silica column to afford **9d'** in 75% yield (26.0 mg, 0.100 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 2.7 Hz, 1H), 6.74 (s, 1H), 3.09 (d, *J* = 49.8 Hz, 6H), 1.70 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -71.7 (dd, *J* = 26.1, 12.9 Hz, 1F), -88. 0 (dd, *J* = 22.5, 12.9 Hz, 1F), -149.2 (ddd, *J* = 25.9, 22.3, 3.5 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 186.2, 169.4, 159.0 – 153.5 (m), 149.5 (dd, *J* = 245.5, 17.3 Hz), 144.7 (d, *J* = 8.8 Hz), 143.7 – 138.6 (m), 105.0 (dd, *J* = 39.9, 5.9 Hz), 65.5 (d, *J* = 2.5 Hz), 37.6 (d, *J* = 243.5 Hz), 24.9. FT-IR cm^{-1} 3408, 3050, 2300, 1686, 1327. HRMS (ESI) calc., $C_{11}H_{11}F_3N_4O$ 272.0885; observed 272.0847. mp-102-104 °C.

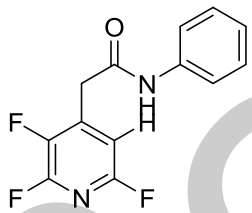


10a' methyl(2-(2,3,6-trifluoropyridin-4-yl)acetyl)glycinate was prepared by general procedure A. The mixture of the **10a** (29.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 12% EtOAc for 15-25 cv and then ramped to 100% EtOAc for 25-36 cv, then held at 100% EtOAc 36 43 cv), on a 4 g silica column to afford **10a'** in 82% yield (23.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.83 (t, *J* = 3.0 Hz, 1H), 6.44 (s, 1H), 4.16

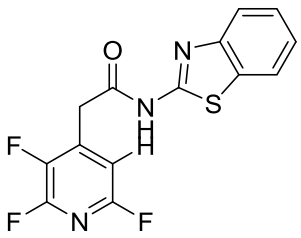
(d, *J* = 7.2 Hz, 2H), 3.98 (d, *J* = 5.2 Hz, 2H), 3.65 (d, *J* = 1.3 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -73.2 (ddd, *J* = 26.1, 13.0, 2.7 Hz, 1F), -87.8 (dd, *J* = 22.0, 12.9 Hz, 1F), -150.8 (ddd, *J* = 25.8, 21.8, 3.1 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.5, 167.1, 155.0 (ddd, *J* = 244.6, 12.5, 3.0 Hz), 148.9 (ddd, *J* = 245.9, 17.3, 15.7 Hz), 141.4 (ddd, *J* = 252.5, 25.2, 6.6 Hz), 139.6 (ddd, *J* = 13.8, 8.6, 2.9 Hz), 108.1 (dd, *J* = 38.3, 6.0 Hz), 61.8, 41.6, 35.4 (d, *J* = 2.5 Hz), 14.1. FT-IR cm^{-1} 3437, 3314, 2216, 1710, 1296. HRMS (ESI) calc., $C_{10}H_9F_3N_2O_3$ 262.0565; observed 262.0543. mp-97-100 °C



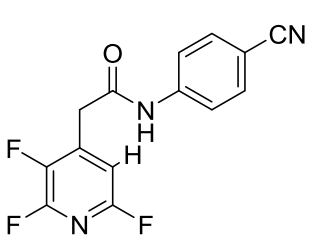
10b' ***N*-(*p*-tolyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide** was prepared by general procedure A. The mixture of the **10b'** (30.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 16 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 % for 10 cv, slowly ramped to 14% EtOAc for 14-22 cv and then ramped to 100 % EtOAc for 22-35 cv, then held at 100% EtOAc 35 40 cv), on a 4 g silica column to afford **10b'** in 86% yield (24.0 mg, 0.0900 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (s, 1H), 7.29 (s, 2H), 7.07 – 7.04 (m, 2H), 6.85 (t, *J* = 3.0 Hz, 1H), 3.71 (d, *J* = 1.3 Hz, 2H), 2.24 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.9 (ddd, *J* = 26.0, 12.7, 2.6 Hz, 1F), -87.5 (dd, *J* = 22.2, 12.8 Hz, 1F), -150.1 – -152. 2 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.7, 156.2, 150.1 (d, *J* = 16.9 Hz), 147.7 (d, *J* = 17.1 Hz), 142.7 (d, *J* = 24.9 Hz), 140.6 – 139.8 (m), 139.4, 134.6 (d, *J* = 54.4 Hz), 129.6 (d, *J* = 2.3 Hz), 120.2, 111.8, 108.1 (dd, *J* = 38.4, 5.9 Hz), 36.7, 20.9. FT-IR cm^{-1} 3471, 3361, 3010, 1726, 1211. HRMS (ESI) calc., $C_{14}H_{11}F_3N_2O$ 280.0823; observed 280.0792. mp-137-140 °C.



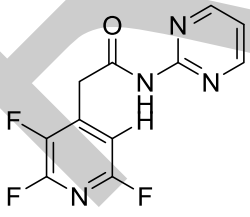
10c' *N*-phenyl-2-(2,3,6-trifluoropyridin-4-yl)acetamide was prepared by general procedure A. The mixture of the **10c** (28.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 14 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 15% EtOAc for 15-25 cv and then ramped to 100% EtOAc for 25-35 cv, then held at 100% EtOAc 35 44 cv), on a 4 g silica column to afford **10c'** in 75% yield (22.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 7.7 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 3.0 Hz, 1H), 3.74 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.7 (dd, *J* = 26.5, 13.0 Hz, 1F), -87.3 (dd, *J* = 21.9, 12.8 Hz, 1F), -148.8 – -155.9 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.7, 155.2 (d, *J* = 241.9 Hz), 149.2 (d, *J* = 245.9 Hz), 141.5 (d, *J* = 226.5 Hz), 139.3, 136.9, 129.1, 125.1, 120.1, 108.2 (dd, *J* = 38.4, 6.0 Hz), 36.9. FT-IR cm^{-1} 3467, 3361, 3230, 1701, 1222. HRMS (ESI) calc., $C_{13}H_9F_3N_2O$ 266.0667; observed 266.0638. mp-133-135 °C.



10d' ***N*-(benzo[d]thiazol-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide** was prepared by general procedure A. The mixture of the **10d** (34.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 18 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 13% EtOAc for 15-25 cv and then ramped to 100% EtOAc for 25-40 cv, then held at 100% EtOAc 40 48 cv), on a 4 g silica column to afford **10d'** in 58% yield (19.0 mg, 0.0600 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.41 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.36 – 7.27 (m, 1H), 6.83 (t, *J* = 3.0 Hz, 1H), 3.88 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -71.9 – -73.2 (m, 1F), -86.7 (dd, *J* = 21.9, 12.8 Hz, 1F), -150.1 (ddd, *J* = 25.7, 21.8, 3.1 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.4, 158.4, 155.1 (d, *J* = 230.3 Hz), 147.5, 141.7 (d, *J* = 253.4 Hz), 138.6 – 133.1 (m), 131.9, 126.7, 124.6, 124.5, 121.7, 120.6, 108.2 (dd, *J* = 38.6, 6.1 Hz), 35.6. FT-IR cm^{-1} 3413, 3301, 3230, 1719, 1700. HRMS (ESI) calc., $C_{14}H_8F_3N_3OS$ 323.0340; observed 323.0347. mp-141-144 °C.

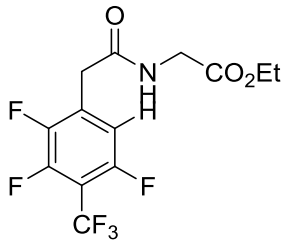


10e' ***N*-(4-cyanophenyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide** was prepared by general procedure A. The mixture of the **10e** (31.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 15% EtOAc for 15-28 cv and then ramped to 100% EtOAc for 28-38 cv, then held at 100% EtOAc 38 45 cv), on a 4 g silica column to afford **10e'** in 79% (20.0 mg, 0.0700 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 (s, 1H), 7.58 (d, *J* = 6.4 Hz, 4H), 6.85 (s, 1H), 3.79 (d, *J* = 1.3 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -72.4 (dd, *J* = 26.3, 12.7 Hz, 1F), -86.9 (dd, *J* = 22.0, 12.7 Hz, 1F), -147.5 – -154.1 (m, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 168.1, 156.5 (ddd, *J* = 241.3, 12.9, 2.8 Hz), 150.3 (dt, *J* = 241.9, 16.7 Hz), 144.7, 142.9 (ddd, *J* = 14.0, 9.0, 2.9 Hz), 145.1 – 142.1 (m), 134.9, 121.2, 120.2, 110.7 (dd, *J* = 38.8, 5.8 Hz), 108.3, 37.9. FT-IR cm^{-1} 3413, 3041, 1668, 1265, 899. HRMS (ESI) calc., $C_{14}H_8F_3N_3O$ 291.0619; observed 291.0678. mp-137-140 °C.

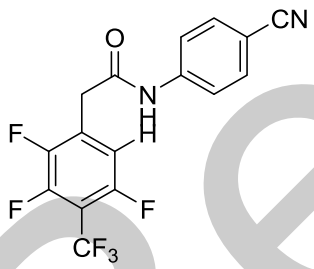


10f' ***N*-(pyrimidin-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide** was prepared by general procedure A. The mixture of the **10f** (29.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in 1:1 v/v MeCN:DMSO) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 16% EtOAc for 16-25 cv and then ramped to 100% EtOAc for 25-50 cv, then held at 100% EtOAc 50 58 cv), on a 4 g silica column to afford **10f'** in 93% yield (25.0 mg, 0.0900

mmol) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.02 (s, 1H), 8.69 (dd, J = 4.8, 1.3 Hz, 2H), 7.31 (d, J = 2.8 Hz, 1H), 7.22 (td, J = 4.9, 1.3 Hz, 1H), 4.21 (s, 2H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -75.4 (dd, J = 26.0, 13.4 Hz, 1F), -91.2 (dd, J = 23.3, 13.5 Hz, 1F), -140.4 – -158.3 (m, 1F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.9, 158.9, 157.8, 156.3 – 152.5 (m), 150.1 – 146.3 (m), 143.5 – 142.7 (m), 142.7 – 139.9 (m), 117.4, 109.9 (dd, J = 38.2, 5.5 Hz), 37.2. FT-IR cm^{-1} 3492, 3060, 2847, 1658, 1158. HRMS (ESI) calc., $C_{11}H_7F_3N_4O$ 343.0643; observed 343.0681. mp-146-149 °C

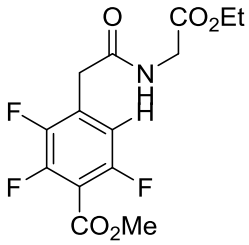


10g' ethyl (2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetyl) glycinate was prepared by general procedure A. The mixture of the **10g** (34.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 12 cv, slowly ramped to 15% EtOAc for 15-30 cv and then ramped to 100% EtOAc for 30-38 cv, then held at 100% EtOAc 38-44 cv), on a 4 g silica column to afford **10g'** in 77% yield (26.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.73 – 7.65 (m, 2H), 7.37 (td, J = 7.7, 7.2, 2.0 Hz, 2H), 7.09 (ddd, J = 8.7, 4.9, 2.3 Hz, 1H), 6.54 (s, 1H), 4.71 (d, J = 6.3 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-d) δ -61.3 (s, 3F), -113.3 – -118.8 (m, 1F), -133.4 – -134.8 (m, 1F), -142.9 – -144.1 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.5, 166.8, 155.8 (d, J = 241.2 Hz), 149.9 (d, J = 252.4 Hz), 144.9 (dd, J = 255.0, 19.1 Hz), 125.1, 119.9 (d, J = 23.6 Hz), 117.4 (d, J = 15.9 Hz), 108.5 (d, J = 27.5 Hz), 61.8, 41.7, 30.0, 14.1. FT-IR cm^{-1} 3481, 3001, 2914, 1744, 1667, 1333. HRMS (ESI) calc., $C_{13}H_{11}F_6NO_3$ 343.0643; observed 343.0681. mp-111-114 °C

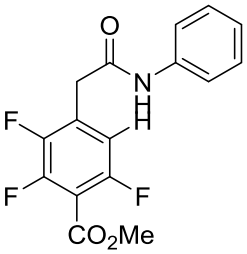


10h' *N*-(4-cyanophenyl)-2-(2,3,5-trifluoro-4-(trifluoromethyl) phenyl) acetamide was prepared by general procedure A. The mixture of the **10h** (38.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 45 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 15% EtOAc for 15-28 cv and then ramped to 100% EtOAc for 28-38 cv, then held at 100% EtOAc 38-50 cv), on a 4 g silica column to afford **10g'** in 79% yield (29.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.73 – 7.65 (m, 2H), 7.37 (td, J = 7.7, 7.2, 2.0 Hz, 2H), 7.09 (ddd, J = 8.7, 4.9, 2.3 Hz, 1H), 6.54 (s, 1H), 4.71 (d, J = 6.3 Hz, 2H). ^{19}F NMR (376 MHz, Chloroform-d) δ -61.3 (s, 3F), -113.3 – -118.8 (m, 1F), -133.4 – -134.3 (m, 1F), -142.9 – -144.5 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-d) δ 167.2 – 167.1 (m), 155.9 (d, J = 248.0 Hz), 151.7 (d, J = 232.7 Hz), 149.4 – 146.1 (m), 133.5 – 133.3 (m), 133.2, 132.1, 132.1 – 131.9 (m), 128.7, 128.7 – 128.6 (m), 127.8 – 126.2 (m), 120.2, 108.8 (d, J = 27.7 Hz), 32.8, 27.3 (m). FT-IR cm^{-1} 3453,

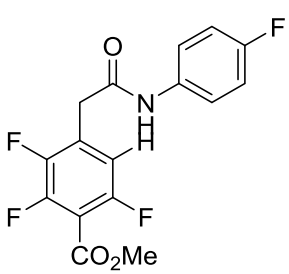
3010, 2229, 1675, 1229, 1158. HRMS (ESI) calc., $C_{16}H_8F_6N_2O$ 358.0541; observed 358.0545. mp-144-147 °C.



11a' methyl 4-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate was prepared by general procedure A. The mixture of the **11a** (35.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 23 °C for 24 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 12% EtOAc for 12-30 cv and then ramped to 100% EtOAc for 30-45 cv, then held at 100% EtOAc 45-50 cv), on a 4 g silica column to afford **11a'** in 81% yield (27.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.44 (m, 1H), 6.21 (s, 1H), 4.24 (dd, *J* = 7.1, 1.4 Hz, 2H), 4.07 (dd, *J* = 5.1, 1.4 Hz, 2H), 3.99 – 3.95 (m, 3H), 3.75 (d, *J* = 1.5 Hz, 2H), 1.34 – 1.29 (m, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -117.7 – -119.1 (m, 1F), -134.6 – -134.6 (m, 1F), -138.6 (ddd, *J* = 20.7, 16.1, 5.1 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.6, 167.0, 162.9 (d, *J* = 3.0 Hz), 155.6 (ddd, *J* = 246.2, 6.4, 3.5 Hz), 151.3 – 148.5 (m), 147.1 (ddd, *J* = 260.1, 14.4, 3.7 Hz), 119.3, 117.7 (dd, *J* = 22.2, 16.9 Hz), 112.4 (dd, *J* = 26.2, 3.8 Hz), 61.7, 52.8, 41.7, 30.2 (d, *J* = 1.9 Hz), 14.1. FT-IR cm^{-1} 3449, 3076, 2836, 1701, 1112. HRMS (ESI) calc., $C_{14}H_{14}F_3NO_5$ 333.0824; observed 333.0852. mp-112-114 °C

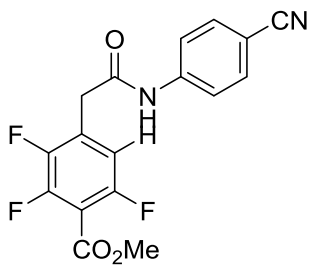


11b' methyl 2,3,6-trifluoro-4-(2-oxo-2-(phenylamino)ethyl)benzoate was prepared by general procedure A. The mixture of the **11b** (34.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 23 °C for 19 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 12 % EtOAc for 12-25 cv and then ramped to 100% EtOAc for 25-35 cv, then held at 100% EtOAc 35-43 cv), on a 4 g silica column to afford **11b'** in 83% yield (26.0 mg, 0.0800 mmol) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 7.57 (dt, *J* = 8.3, 1.7 Hz, 3H), 7.32 (ddd, *J* = 9.4, 7.4, 2.1 Hz, 2H), 7.11 – 7.02 (m, 1H), 4.00 – 3.82 (m, 5H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -118.1– -119.2 (m, 1F), -135.5 – -136.8 (m, 1F), -141.02 – 142.5 (m, 1F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.2, 162.6 (d, *J* = 3.1 Hz), 157.8 – 154.4 (m), 152.3 – 148.3 (m), 148.1 – 144.8 (m), 139.2, 129.2, 123.9, 119.6 (d, *J* = 4.6 Hz), 119.0 (t, *J* = 9.1 Hz), 112.4 (dd, *J* = 26.4, 3.7 Hz), 53.4, 31.0. FT-IR cm^{-1} 3488, 3076, 2867, 1753, 1100. HRMS (ESI) calc., $C_{16}H_{12}F_3NO_3$ 323.0769; observed 323.0718. mp-128-131 °C.

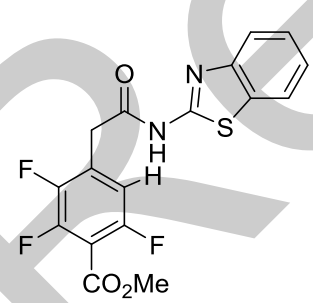


11c' methyl 2,3,6-trifluoro-4-(2-((4-fluorophenyl)amino)-2-oxoethyl)benzoate was prepared by general procedure A. The mixture of the **11f** (36.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and

1 mL of photocatalyst stock solution (0.250 mM, 1 mL in 1:1 v/v MeCN:DMSO) was placed in the light bath under 23 °C for 12 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 12% EtOAc for 12-24 cv and then ramped to 100% EtOAc for 24-34 cv, then held at 100% EtOAc 34-40 cv), on a 4 g silica column to afford **11c'** in 85% yield (28.0 mg, 0.0700 mmol) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.41 (s, 1H), 7.58 (dt, J = 12.0, 6.0 Hz, 3H), 7.15 (t, J = 8.9 Hz, 2H), 3.96 – 3.83 (m, 5H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -117.5 – -118.3 (m, 1F), -119.0 – -120.5 (m, 1F), -135.5 – -136.6 (m, 1F), -140.9 – -141.2 (m, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 165.6, 162.2, 159.2, 156.9, 155.4 (d, J = 241.9 Hz), 149.4 (d, J = 239.5 Hz), 146.1 (d, J = 252.6 Hz), 135.2, 131.3, 120.9, 115.2, 112.1, 52.9, 30.5. FT-IR cm^{-1} 3486, 3312, 2895, 1668, 1159. HRMS (ESI) calc., $C_{16}H_{11}F_4NO_3$ 341.0675; observed 341.0677. mp-127-130 °C.

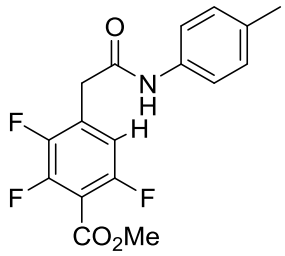


11d' methyl 4-(2-((4-cyanophenyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate was prepared by general procedure A. The mixture of the **11d** (37.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in 1:1 v/v MeCN:DMSO) was placed in the light bath under 23 °C for 15 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0% for 10 cv, slowly ramped to 12% EtOAc for 12-20 cv and then ramped to 100% EtOAc for 20-42 cv, then held at 100% EtOAc 42-55cv), on a 4 g silica column to afford **11d'** in 82% yield (29.0 mg, 0.0800 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.68 – 7.63 (m, 4H), 7.54 (ddd, J = 9.2, 5.1, 2.3 Hz, 1H), 3.99 (s, 3H), 3.90 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-d) δ -117.3 – -119.3 (m, 1F), -134.5 – -135-8 (m, 1F), -138.2 (ddd, J = 20.6, 16.1, 5.1 Hz, 1F). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.5, 162.8, 154.3 (d, J = 9.8 Hz), 152.9, 151.5 – 148.6 (m), 148.4 – 145.5 (m), 141.3, 133.36, 119.6, 118.6, 116.8 (d, J = 38.7 Hz), 112.6 (d, J = 26.1 Hz), 107.8, 53.0, 31.6. FT-IR cm^{-1} 3379, 3301, 2867, 1719, 1263. HRMS (ESI) calc., $C_{17}H_{11}F_3N_2O_3$ 348.0722; observed 348.0745. mp-128-131 °C

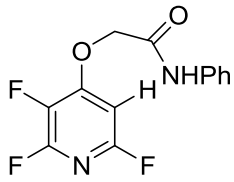


11e' methyl 4-(2-(benzo[d]thiazol-2-ylamino)-2-oxoethyl)-2,3,6-trifluorobenzoate was prepared by general procedure A. The mixture of the **11e** (40.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN) was placed in the light bath under 23 °C for 19 h. After workup, the crude material was purified by flash chromatography using hexane: ethyl acetate (0% for 10 cv, slowly ramped to 14% EtOAc for 14-25 cv and then ramped to 100% EtOAc for 25-45 cv, then held at 100% EtOAc 45-55cv) on a 4 g silica column to afford **11e'** in 76% yield (29.0 mg, 0.0800 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.79 – 7.71 (m, 2H), 7.67 – 7.48 (m, 1H), 7.48 – 7.35 (m, 2H), 3.89 (s, 3H), 3.87 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-d) δ -118.1 (dd, J = 16.0, 9.2 Hz, 1F), -134.2 – -135.6 (m, 1F), 138.2 (ddd, J = 20.8, 16.2, 5.0 Hz, 1F). ^{13}C NMR

(101 MHz, Chloroform-*d*) δ 166.9, 166.0, 164.2 – 162.1 (m), 158.9, 158.7, 157.1 (d, *J* = 63.8 Hz), 155.7 (d, *J* = 142.0 Hz), 147.7, 132.0, 126.6, 124.4, 121.8, 120.5, 116.3, 112.6 (d, *J* = 29.7 Hz), 52.7, 30.5. FT-IR cm^{-1} 3425, 3351, 2798, 1729, 1142. HRMS (ESI) calc., $C_{17}H_{11}F_3N_2O_3$ 348.0722; observed 348.0745. mp-128-131 ºC



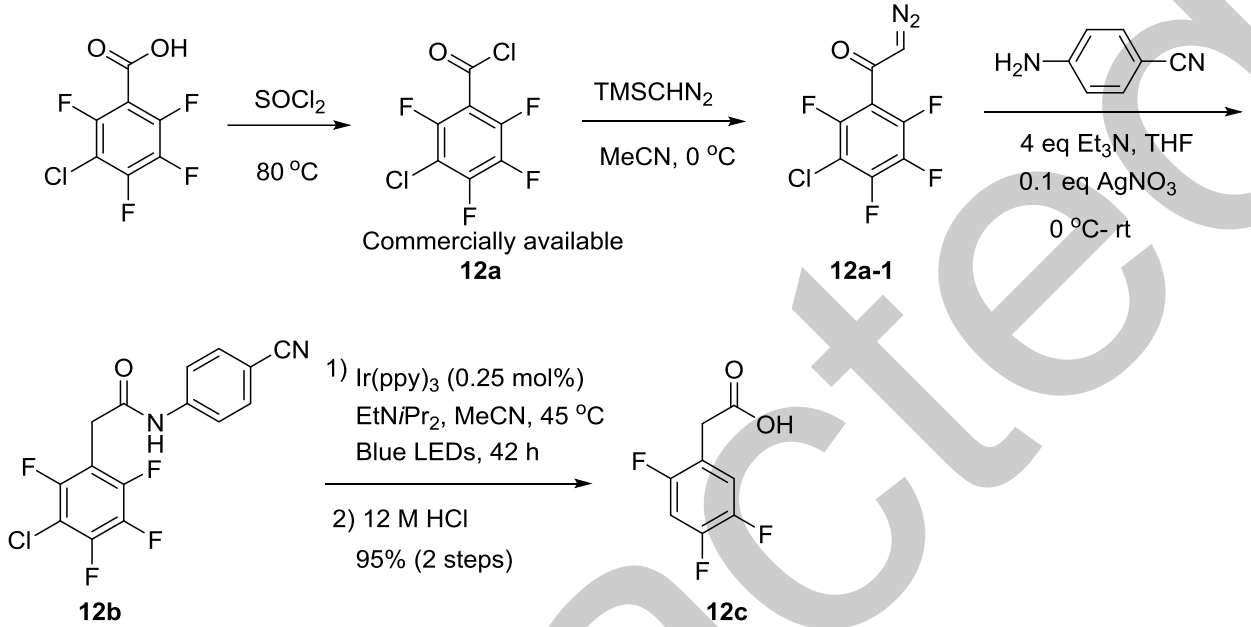
11f' methyl 2,3,6-trifluoro-4-(2-oxo-2-(*p*-tolylamino)ethyl)benzoate was prepared by general procedure A. The mixture of the **11f** (36.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in 1:1 v/v MeCN:DMSO) was placed in the light bath under 23 ºC for 16 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 8% EtOAc for 5 cv and ramped to 100% EtOAc for 8-20 cv and then held at 100% EtOAc 20-25 cv) on a 4 g silica column to afford **11f'** in 79% yield (25.0 mg, 0.0700 mmol) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.38 (m, 1H), 7.28 (dd, *J* = 8.6, 3.1 Hz, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 3.89 (s, 3H), 3.74 (s, 2H), 2.24 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -118.4 (dd, *J* = 16.1, 8.9 Hz, 1F), -134.6 – -135.0 (m, 1F), -138.5 (ddd, *J* = 20.9, 16.0, 5.1 Hz, 1F). ^{13}C NMR (101 MHz, Acetone-d_6) δ 167.1, 164.1, 159.5 – 155.8 (m), 153.7 – 150.2 (m), 150.1 – 146.5 (m), 138.3, 134.7, 130.9, 122.1 (d, *J* = 25.8 Hz), 121.0, 119.06 (d, *J* = 26.9 Hz), 113.6 (d, *J* = 30.3 Hz), 54.0, 32.3, 21.7. FT-IR cm^{-1} 3461, 3011, 2850, 1773, 1671. HRMS (ESI) calc., $C_{17}H_{14}F_3NO_3$ 337.0926; observed 337.0912. mp-92-95 ºC.



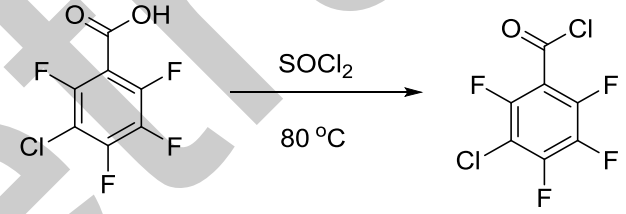
E11' *N*-phenyl-2-((2,3,6-trifluoropyridin-4-yl)oxy)acetamide was prepared by general procedure A. The mixture of the **E11** (30.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in 1mL MeCN) was placed in the light bath under 23 ºC for 79 h. After workup, the crude material was purified by flash chromatography using hexane : ethyl acetate (0 – 10% EtOAc for 6 cv and ramped to 100% EtOAc for 10-25 cv and then held at 100% EtOAc 25-35 cv) on a 4 g silica column to afford **E11'** in 38% yield (11.0 mg, 0.0390 mmol) as a brown solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 7.7 Hz, 1H), 7.50 (d, *J* = 7.7 Hz, 2H), 7.35 (s, 2H), 7.16 (d, *J* = 7.8 Hz, 1H), 3.98 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -76.3 (dd, *J* = 26.3, 12.7 Hz), -90.8 (dd, *J* = 22.0, 12.7 Hz), -151.2 – -160.3 (m, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7, 159.4 (d, *J* = 230.5 Hz), 153.5 (d, *J* = 239.5 Hz), 151.0 (d, *J* = 236.2 Hz), 145.6, 142.2, 132.2, 128.2, 123.1, 111.23 (dd, *J* = 398.3, 6.0 Hz), 39.8. FT-IR cm^{-1} 3456, 3379, 3253, 1692, 1201. HRMS (ESI) calc., $C_{13}H_9F_3N_2O_2$ 282.0616; observed 282.0598. mp-87-89 ºC.

Synthesis of key fluorinated starting material for Januvia

Scheme 1 Synthesis of 2,4,5-trifluorophenylacetic acid via first approach



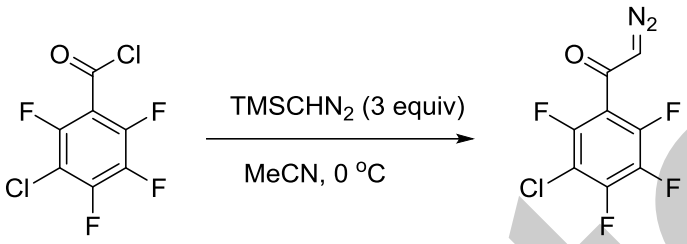
12a 3-chloro-2,4,5,6-tetrafluorobenzoyl chloride



Under an atmosphere of argon and anhydrous conditions, to commercially available 3-chloro-2,4,5,6-tetrafluorobenzoic acid (300 mg, 1.32 mmol) in a 25 mL round-bottomed flask equipped with a reflux condenser was added, excess thionyl chloride (2 mL). The mixture was gently stirred and refluxed at 80 °C in an oil bath for 2 h. After cooling the reaction mixture to room temperature, excess thionyl chloride was evaporated under vacuum (278 mTorr) for 36 minutes leaving a pale yellow benzoyl chloride residue in the flask. The product is moderately volatile

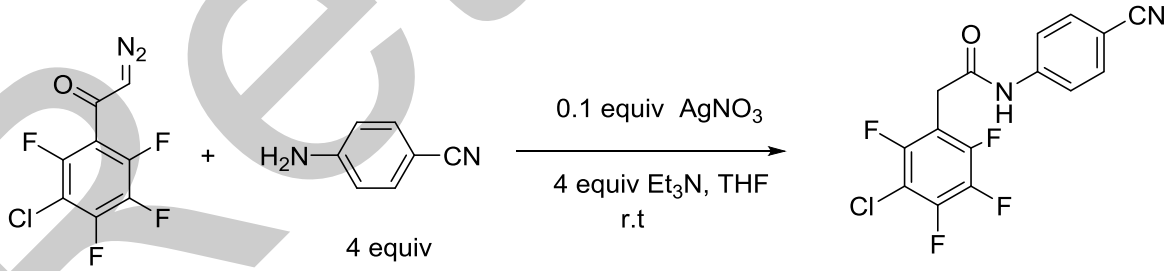
and care should be taken not to evaporate it. The product was taken up to the next step without any further purification.

12a-1 1-(3-chloro-2,4,5,6-tetrafluorophenyl)-2-diazoethan-1-one



Under an atmosphere of argon and anhydrous conditions, **12a** was dissolved in MeCN (5 mL) in a dry 25 mL round bottom flask. Trimethylsilyl diazomethane (2 M solution in diethyl ether, 2 mL, 3.9 mmoles, 3 equiv) was added dropwise via syringe to reaction mixture at 0 °C over 15 minutes. After stirring at 0 °C for 30 minutes, the yellow solution was stirred at ambient temperature for 7 h. The MeCN and resulting residue were then removed under reduced pressure (278 mTorr). The product, **12a**, was used in the next step of the sequence without further purification.

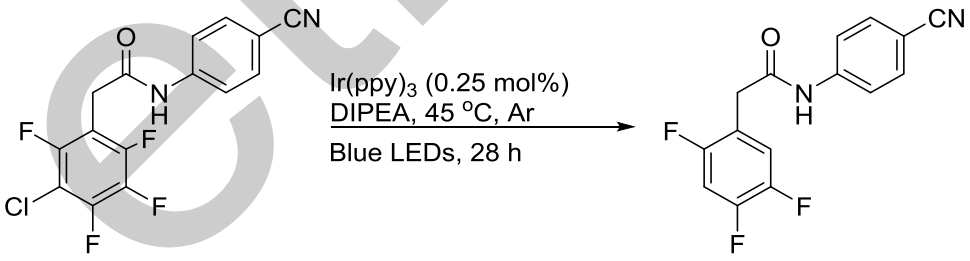
12b 2-(3-chloro-2,4,5,6-tetrafluorophenyl)-*N*-(4-cyanophenyl)acetamide



Under an atmosphere of argon and anhydrous conditions, in a 25 mL round bottom flask equipped with a magnetic stir bar, and previously synthesized **12a-1** (320 mg, 1.27 mmol) was added THF (10 mL) and 4-aminobenzonitrile (600 mg, 5mmol, 4 equiv), then triethylamine (0.7

mL, 5 mmol, 4 equiv) was added slowly, at 0 °C, with constant stirring, after which all of the solid material was dissolved. Silver nitrate powder (22 mg, 0.13 mmol, 0.1 equiv) was added into the reaction mixture. Aluminum foil was used to cover the reaction flask. The reaction mixture was sonicated for 1.5 hours and then the mixture was stirred at ambient temperature for another 2.4 h. The reaction was quenched by the addition of 1M HCl (8 mL). and then extracted with Et_2O (3 x 20 mL) and the combined organic layers washed with brine, dried over $MgSO_4$, filtered, and evaporated to dryness under reduced pressure to afford **12b** as a yellow powder in 97 % yield (421 mg, 1.2 mmol). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (s, 4H), 7.54 (s, 1H), 3.86 (s, 2H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -120.23 (d, *J* = 9.5 Hz), -132.84 (dd, *J* = 21.2, 4.5 Hz), -136.54 (dd, *J* = 21.8, 4.5 Hz), -161.38 (d, *J* = 9.6 Hz). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.10, 152.66 (d, *J* = 249.3 Hz), 148.80 (d, *J* = 164.0 Hz), 146.32 (d, *J* = 147.0 Hz), 143.34, 137.57 (d, *J* = 227.2 Hz), 133.85, 119.65, 119.40, 111.17 – 110.14 (m), 106.22 (ddd, *J* = 23.5, 18.1, 5.5 Hz), 105.82, 30.76. FT-IR cm^{-1} 3446, 3020, 1678, 1211, 713. HRMS (ESI) calc., $C_{17}H_{14}F_3NO_3$ 342.6776; observed 342.6758. mp-151-152 °C.

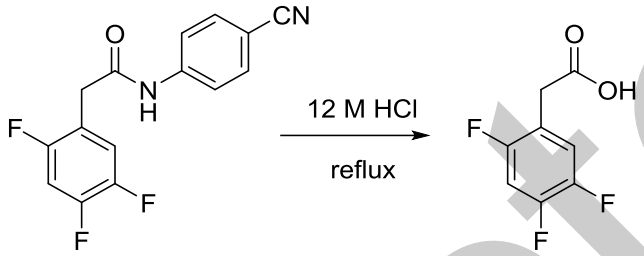
12b-1 *N*-(4-cyanophenyl)-2-(2,4,5-trifluorophenyl)acetamide



An NMR tube capped with NMR septa (Ace glass, part no. 9096-25) was charged with ($Ir(ppy)_3$) (0.25 mM, 1 mL in MeCN), **12b** (34 mg, 0.1 mmol, 1 equiv) and *N*, *N*-diisopropylethylamine (2 equiv), and the tube was capped and the reaction was degassed at 0 °C to avoid evaporation of *N*, *N*-diisopropylethylamine during the degassing process (Ar bubbling for 10 min). The NMR tube

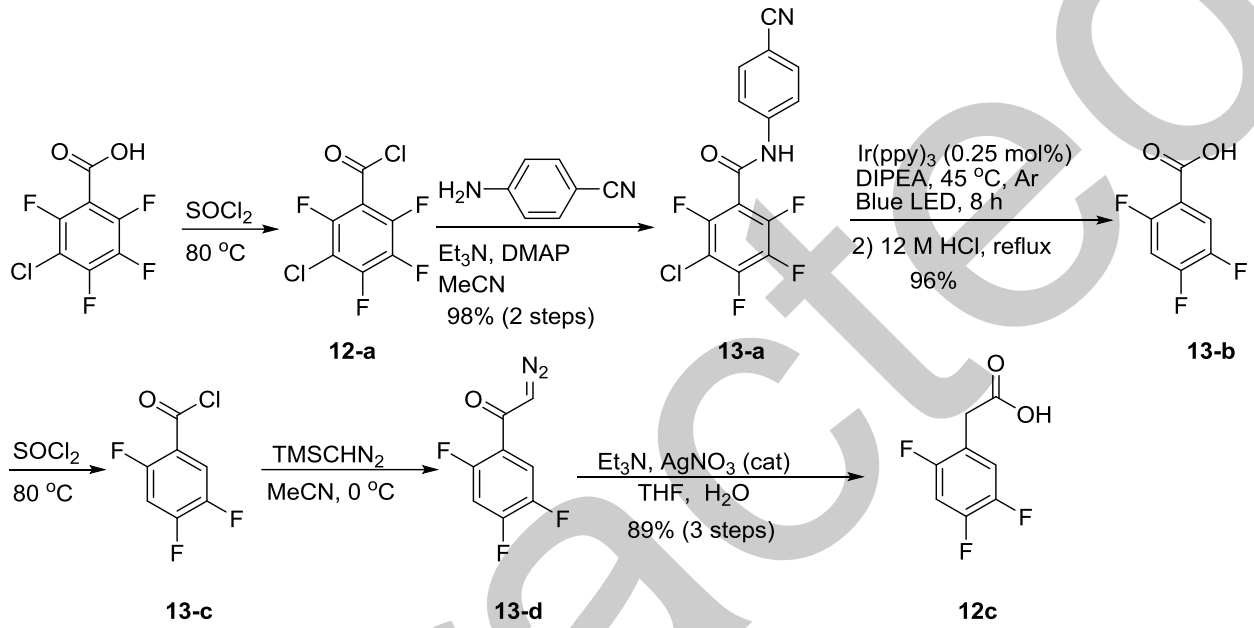
was placed in a light bath (vide supra) and the lower portion of the tube was submerged under the water bath which was maintained at 45 °C. The reaction was monitored by ^{19}F NMR. After the complete conversion starting material to product, the CH_3CN was removed via rotavap and the residue was used in the subsequent reaction without further purification.

12c 2,4,5-trifluorophenylacetic acid

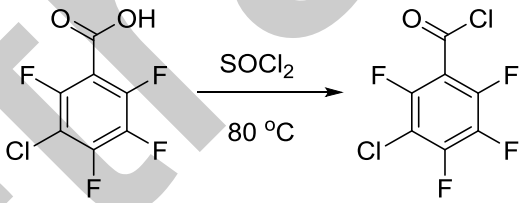


In an NMR tube capped with NMR septa (Ace glass, part no. 9096-25) was charged with **12b-1** and 12 M HCl. The NMR tube was placed in an oil bath and heated to 80 °C for 5 h. The reaction mixture was cooled to room temperature and then the aqueous phase was extracted with dichloromethane (3 x 8 mL), the combined organic layers were then treated with 1 M NaOH (3 x 8 mL). The combined aqueous layers residue were acidified with 2 M HCl and then extracted with chloroform (3 x10 mL). The combined layers were dried with anhydrous magnesium sulfate, and concentrated under reduced pressure to furnish a white powder in 95% yield (18 mg, 0.09 mmol).

Scheme 2 Synthesis of 2,4,5-trifluorophenylacetic acid via dehalogenation then homologation

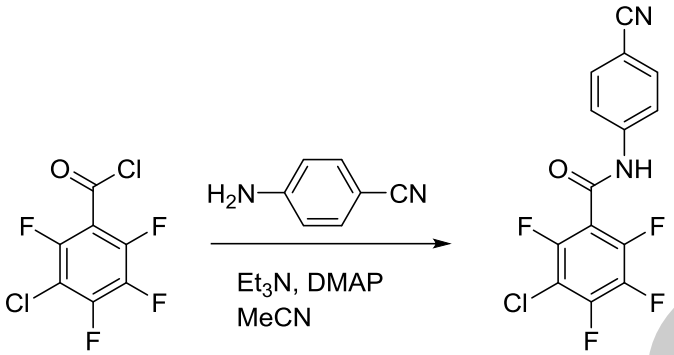


12a 3-chloro-2,4,5,6-tetrafluorobenzoyl chloride



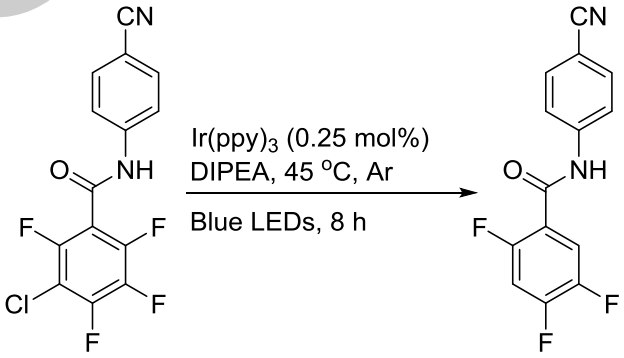
The compound was prepared as described above.

13-a 3-chloro-*N*-(4-cyanophenyl)-2,4,5,6-tetrafluorobenzamide



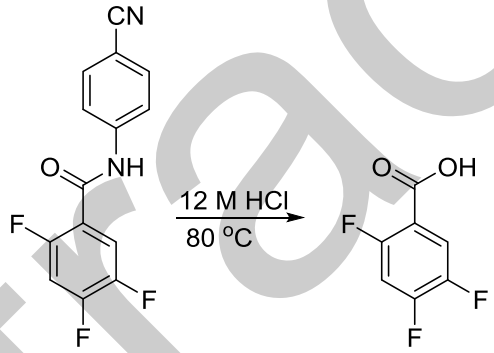
Under an atmosphere of argon and anhydrous conditions, an ice-cooled 25 mL round-bottomed flask containing a solution of and 4-aminobenzonitrile (576 mg, 4.87 mmol, 1.20 equiv) and a catalytic amount of DMAP (20 mg) in dry THF (20 mL) were added. Then triethylamine (680 µL, 4.87 mmol, 1.20 equiv) and the **12a** (4.80 mmol, 1.0 equiv). After 10 min, the ice bath was removed and the reacting mixture was allowed to warm to room temperature (10 h). After this time, the resulting mixture was poured into saturated NH_4Cl solution (20 mL). The layers were separated and the amide extracted from the aqueous layer Et_2O (3 x 20 mL). The combined organic phases were washed with 1 M HCl (12 mL), brine (20 mL), dried over $MgSO_4$ (4 g), filtered, and evaporated to dryness under reduced pressure to furnish the product as a yellow powder in 98% yield (1.30 g, 3.7 mmol).

13a-1 2,4,5-trifluorobenzoic acid



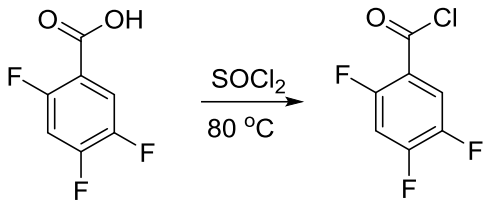
In an NMR tube capped with NMR septa (Ace glass, part no. 9096-25) was charged with ($Ir(ppy)_3$) (0.25 mM, 1 mL in MeCN), **13a** (33 mg, 0.1 mmol, 1 equiv), and *N, N*-diisopropylethylamine (2 equiv) and the reaction was degassed at 0 °C to avoid evaporation of *N, N*-diisopropylethylamine during the degassing process (Ar bubbling for 10 min). The NMR tube was placed in a light bath (vide supra) and the lower portion of the tube was submerged under the water bath which was maintained at 45 °C. The reaction was monitored by ^{19}F NMR, and after the complete consumption of starting material, the CH_3CN was removed via rotavap and the residue was used in the following steps without further purification.

13-b 2,4,5-trifluorobenzoic acid



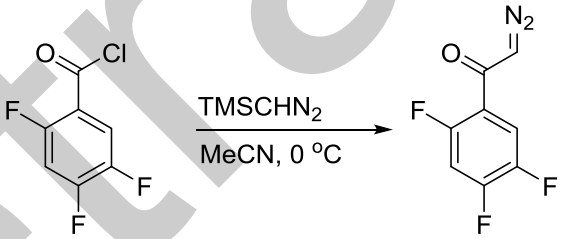
In an NMR tube capped with NMR septa (Ace glass, part no. 9096-25) was charged with **13a-1** and 12 M HCl. The NMR tube was placed in an oil bath and heated to 80 °C for 5 h. The reaction mixture was cooled to room temperature and the aqueous phase was extracted with dichloromethane (3 x 8 mL), the combined organic layers were then treated with 1 M NaOH (3 x 8 mL). The combined aqueous layers residues were acidified with 2 M HCl, and the aqueous phase was extracted with chloroform (3 x10 mL). The combined organic layers were dried with anhydrous magnesium sulfate and condensed under pressure to furnish the product as a pale yellow oil in 96% yield (17 mg, 0.10 mmol).

13-c 2,4,5-trifluorobenzoyl chloride



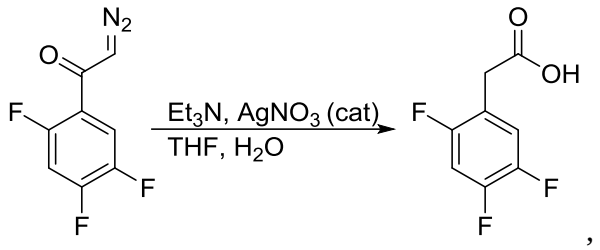
To **13b** (80 mg, 0.45 mmol) in a 5 mL round-bottomed flask and equipped with a reflux condenser was added excess thionyl chloride (2 mL). The mixture was gently stirred and refluxed at 80 °C in an oil bath for 2 h. After cooling the reaction mixture to room temperature, excess thionyl chloride was evaporated under vacuum (780 mmHg) for 36 minutes leaving the benzoyl chloride as a pale yellow residue. The product was taken to next step without any further purification.

13-d 2-diazo-1-(2,4,5-trifluorophenyl)ethan-1-one



Under an atmosphere of argon and anhydrous conditions, **13c** (87 mg, 0.45 mmol) was dissolved in MeCN (5 mL) in a 25 mL round bottom flask. Trimethylsilyl diazomethane (2M solution in diethyl ether, 0.67 mL, 1.3 mmoles, 3 equiv) was added dropwise via syringe to reaction mixture at 0 °C, over 15 minutes. After stirring at 0 °C for 30 minutes, the yellow solution was allowed to warm to ambient temperature (6 h). The MeCN and resulting residue were then removed under reduced pressure (278 mTorr). **13-d** intermediate was used in the next step of the reaction without further purification.

12c 2-(2,4,5-trifluorophenyl)acetic acid



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Under an atmosphere of argon and anhydrous conditions, a 25 mL round bottom flask equipped with a magnetic stir bar and **13d** (89 mg, 1.27 mmol), was charged with THF (4 mL). Then triethylamine (0.25 mL, 1.8 mmol, 4 equiv) was added slowly at 0 ^{o}C with constant stirring, after which all of the solid material was dissolved. Silver nitrate powder (7.5 mg, 0.13 mmol, 0.1 equiv) was added into the reaction mixture. Aluminum foil was used to cover the reaction flask, and after the reaction mixture was sonicated for 1.5 h, H_2O (0.03 mL, 1.8 mmol, 4 equiv) was added dropwise over 10 minutes. Then, the mixture was stirred at ambient temperature for another 3 h before the reaction was quenched by addition of 1M HCl (8 mL). The mixture was extracted with Et_2O (3 x 20 mL) and the combined organic layers washed with brine and dried over $MgSO_4$. Filtration and concentration followed by purification by flash column chromatography (SiO_2, 20% ethyl acetate/ hexanes) afforded the 2-(2,4,5-trifluorophenyl)acetic acid as a yellow oil in 89 % yield (75 mg, 1.2 mmol).

The most common synthesis based on literature searching proceeds through this route. Yields and references for each step are shown below in the Scheme.

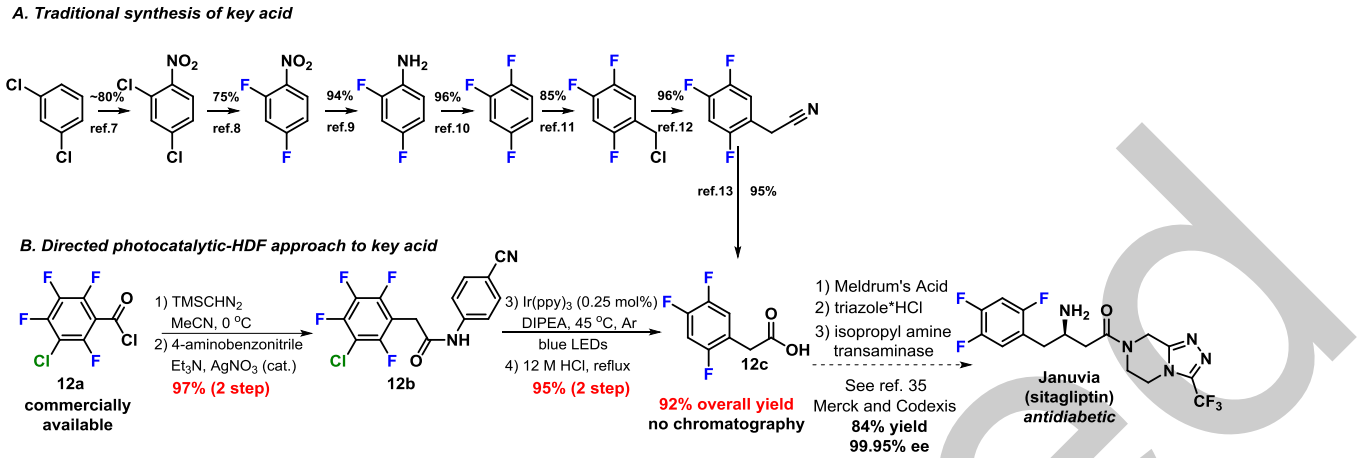
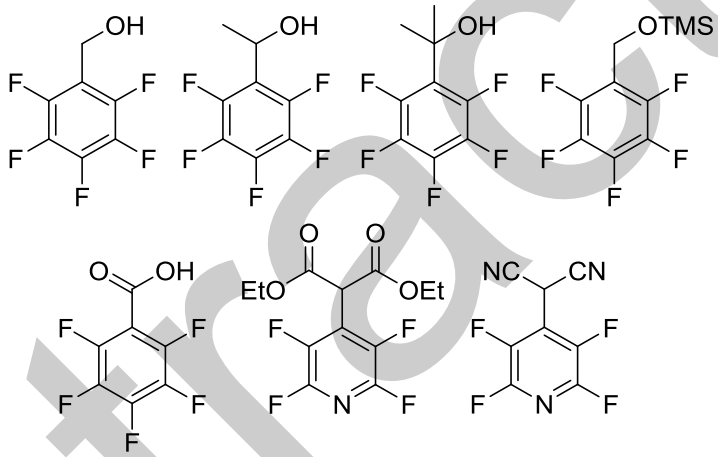


Table 1 Potential substrates that did not undergo directed photo-HDF under standard reaction conditions.



pK_a determination procedure:

- Apparatus

50 mL Burette Vernier

Hanna Instruments HI98103 Checker pH Tester

250 mL beakers (2)

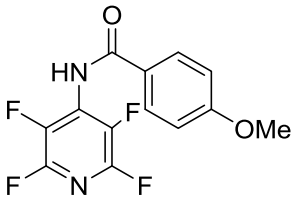
Stir bar and stir plate

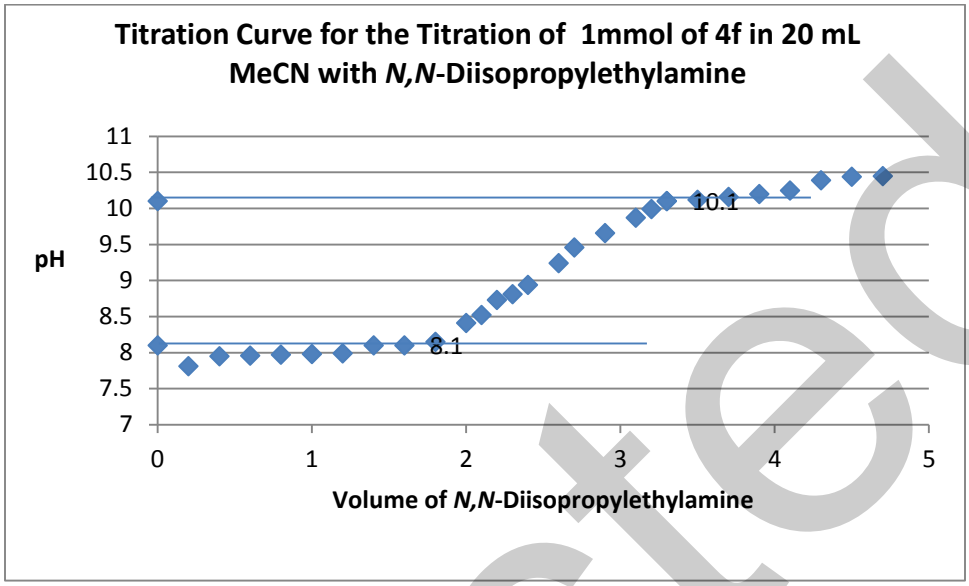
DI water

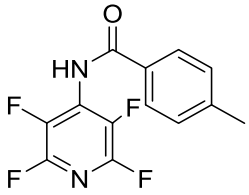
Ring stand, burette clamp, clamp for pH Tester

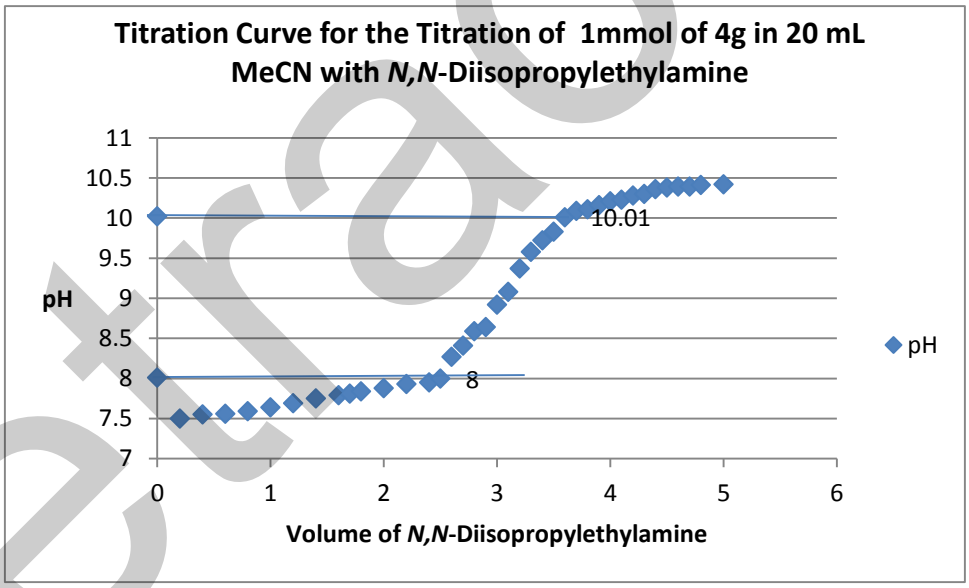
Calibrate the pH tester using buffer solution (pH=10, 7). Fill the burette with neat *N*,*N*-diisopropylethylamine. Add (1 mmol fluorinated compound in 20 mL MeCN) into a 250 mL beaker. Titrate the solution by adding the *N*,*N*-diisopropylethylamine as the titrant in 0.2–0.4 mL increments, and stir. Measure and record the pH of the solution in the beaker after 3-10 minutes of stirring. After each measurement, rinse the pH probe with DI water and MeCN and replace the probe into a pH 7.0 buffered solution. Keep recording the pH until the change between readings becomes very slight. At the equivalence point, the volume of base added is just enough to exactly neutralize all of the acid. A plot of the pH vs. the volume will reveal the equivalence point and allow the pKa to be determined. The measured pH is equal to pK_a, at exactly one-half the volume of the equivalence point. The procedure modified from literature procedures.[14]

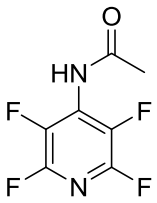
The titration curves of the selected compounds

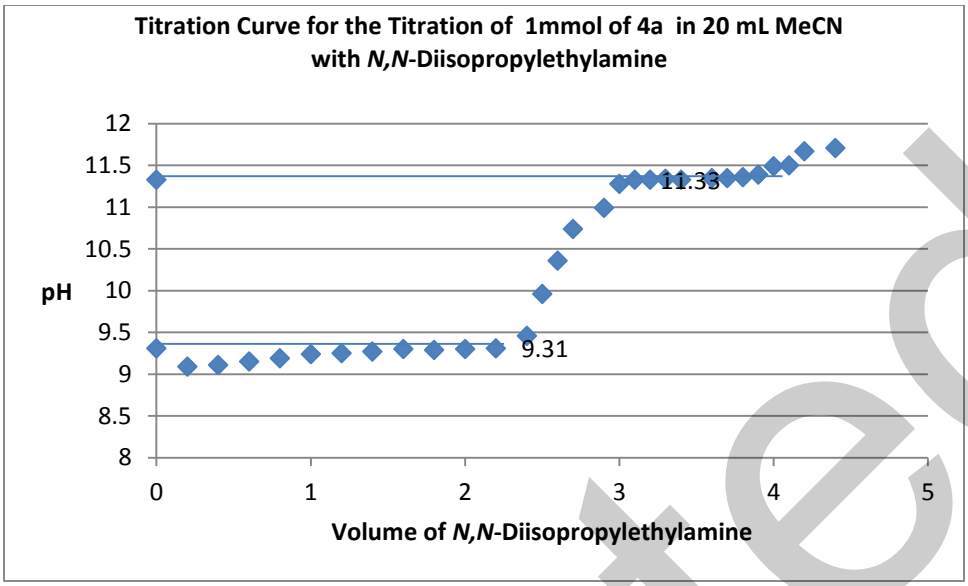


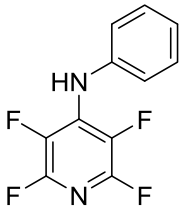


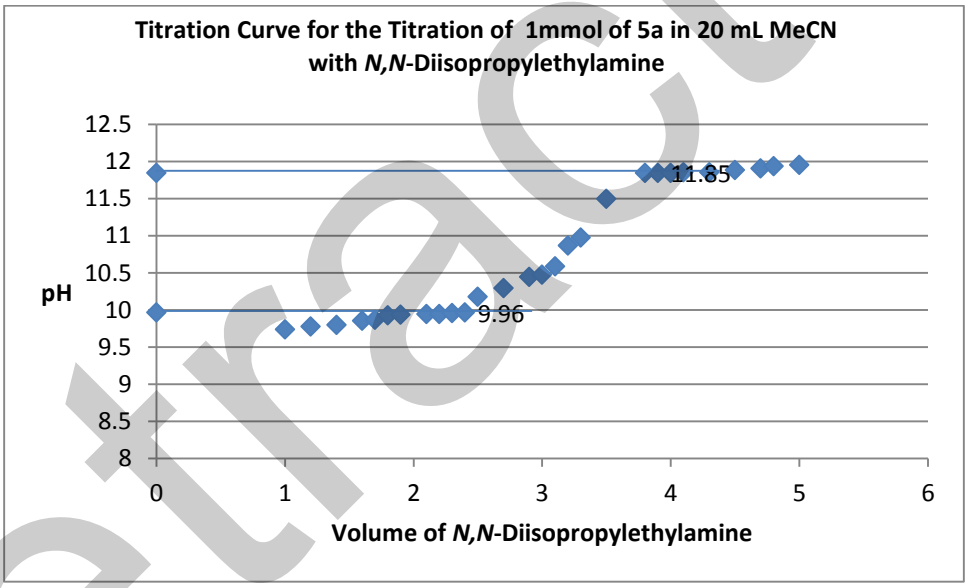


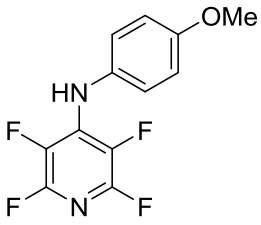


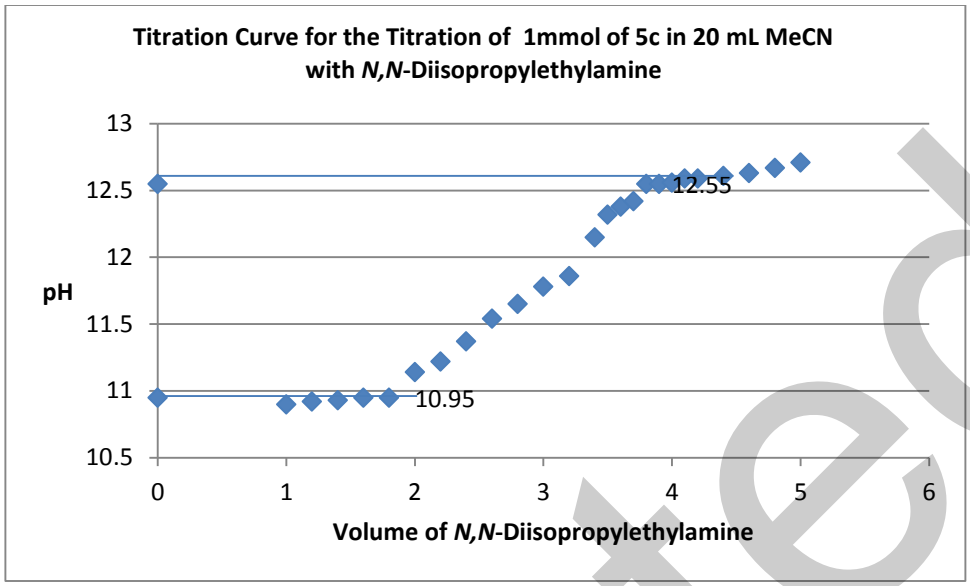

O
HN
F
F
F
F
N

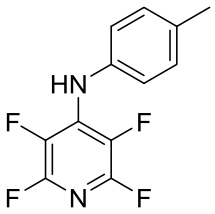

Titration Curve for the Titration of 1mmol of 4a in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12
11.5
11
10.5
10
9.5
9
8.5
8
11.33
9.31
0
1
2
3
4
5
Volume of N,N-Diisopropylethylamine

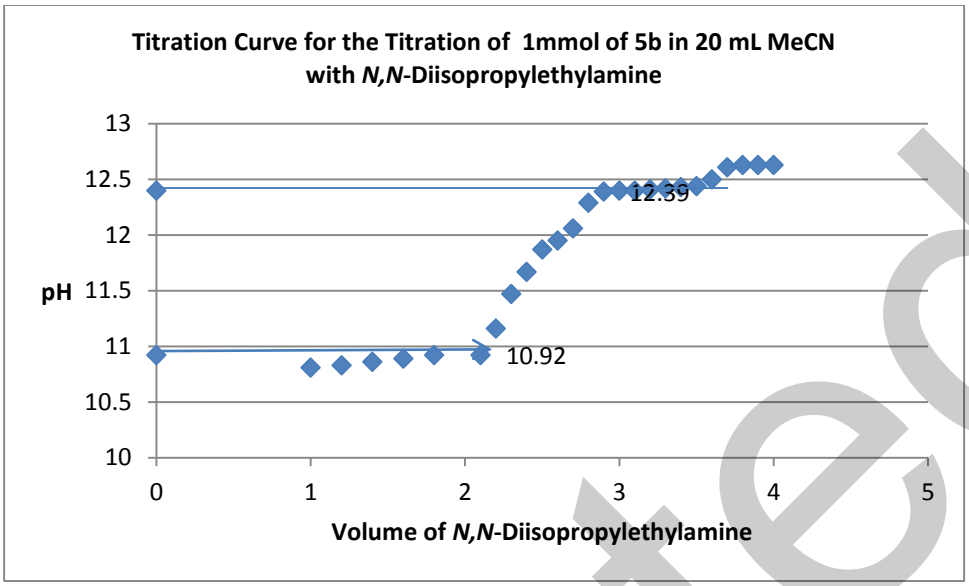

HN
F
F
F
F
N

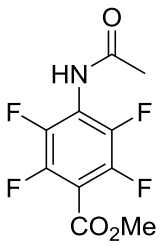

Titration Curve for the Titration of 1mmol of 5a in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12.5
12
11.5
11
10.5
10
9.5
9
8.5
8
11.85
9.96
0
1
2
3
4
5
6
Volume of N,N-Diisopropylethylamine

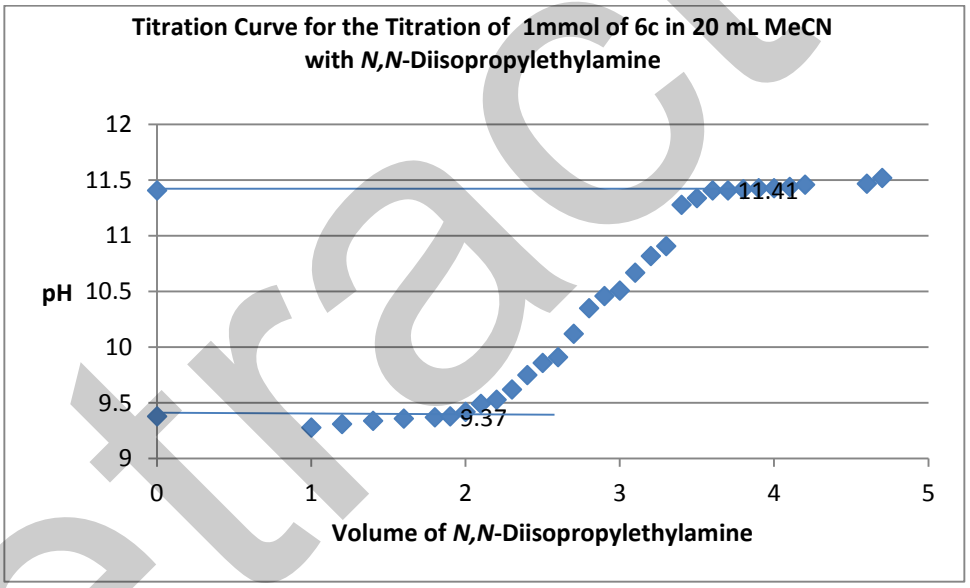

OMe
HN
F
F
F
N
F

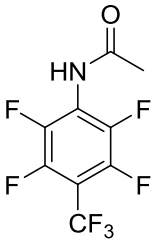

Titration Curve for the Titration of 1mmol of 5c in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13
12.5
12
11.5
11
10.5
0
1
2
3
4
5
6
12.55
10.95
Volume of N,N-Diisopropylethylamine

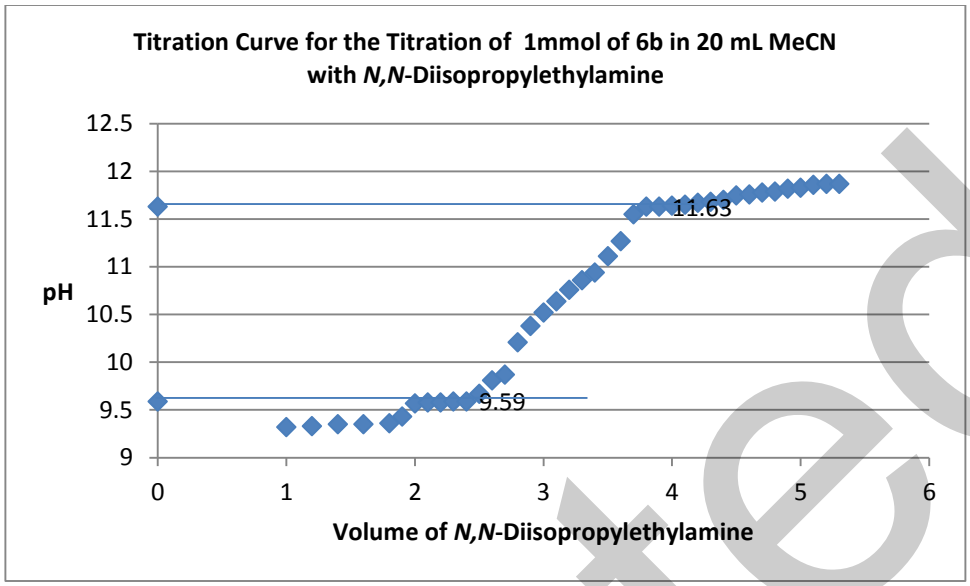

HN
F
F
F
N
F

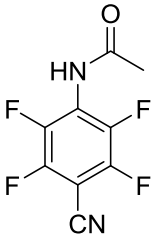

Titration Curve for the Titration of 1mmol of 5b in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13
12.5
12
11.5
11
10.5
10
0
1
2
3
4
5
12.39
10.92
Volume of N,N-Diisopropylethylamine

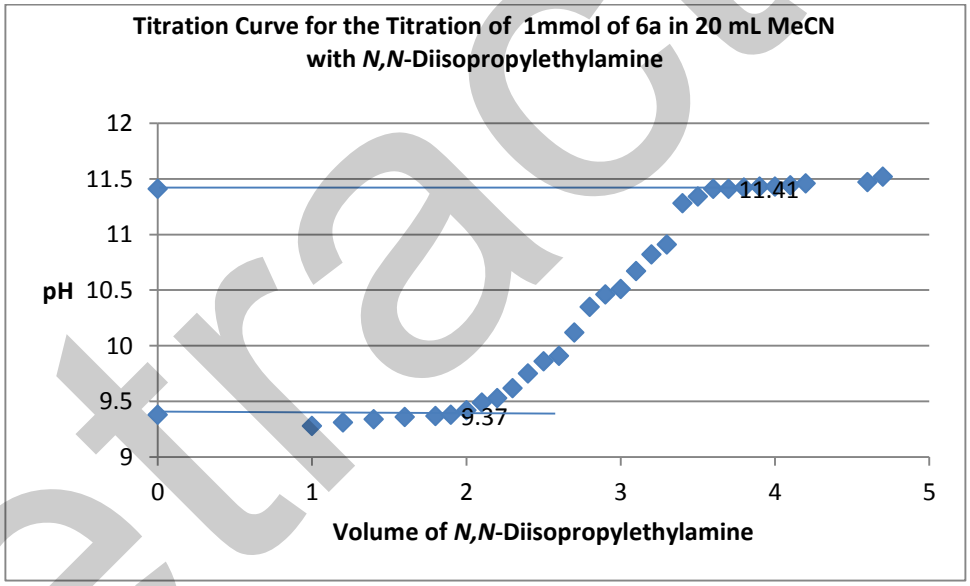

O
HN
F
F
F
F
CO2Me

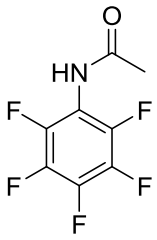

Titration Curve for the Titration of 1mmol of 6c in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
11.41
9.37
Volume of N,N-Diisopropylethylamine

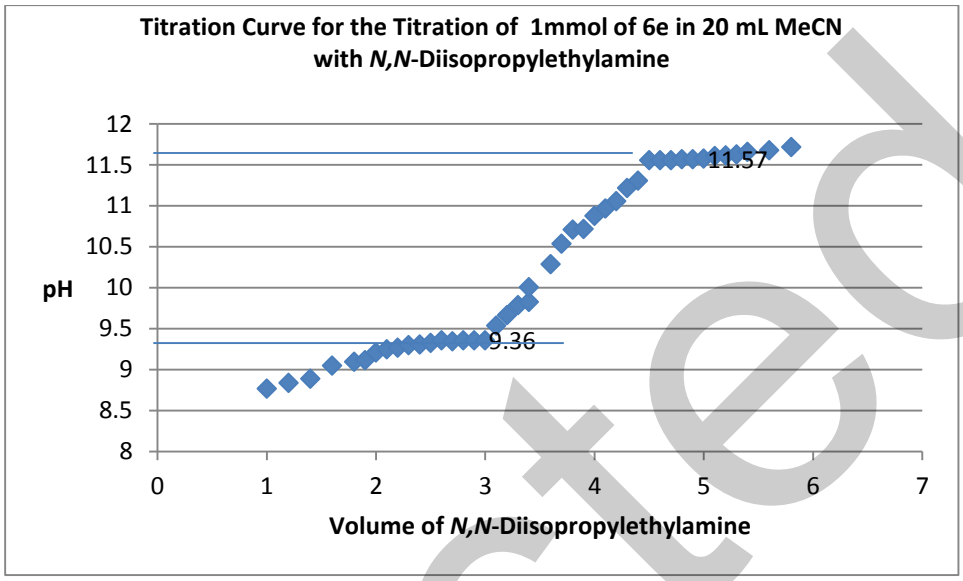

O
HN
F
F
F
F
CF3

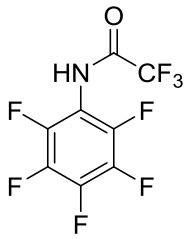

Titration Curve for the Titration of 1mmol of 6b in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12.5
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
6
11.63
9.59
Volume of N,N-Diisopropylethylamine

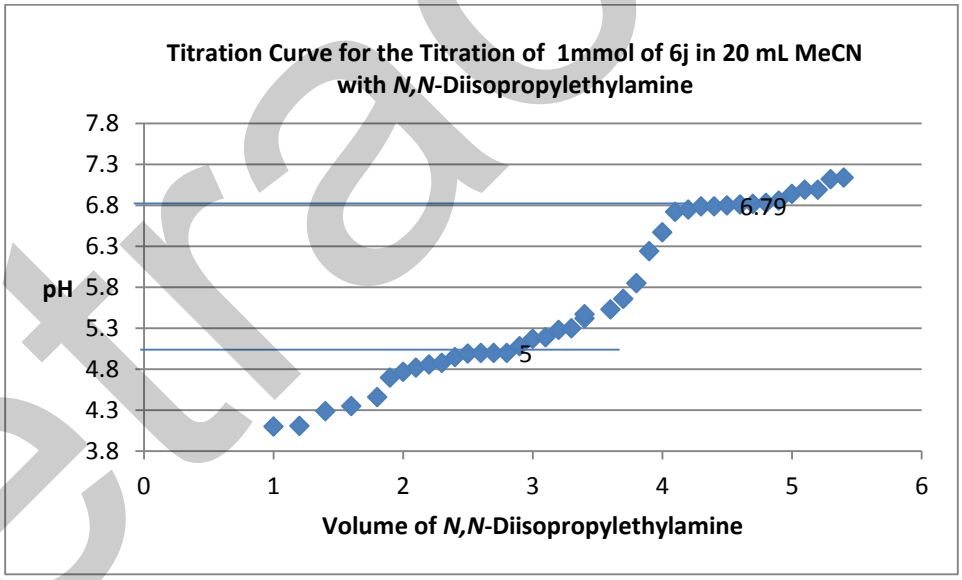

O
HN
F
F
F
F
CN

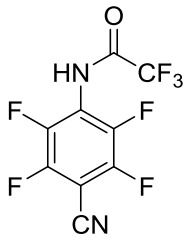

Titration Curve for the Titration of 1mmol of 6a in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
11.41
9.37
Volume of N,N-Diisopropylethylamine

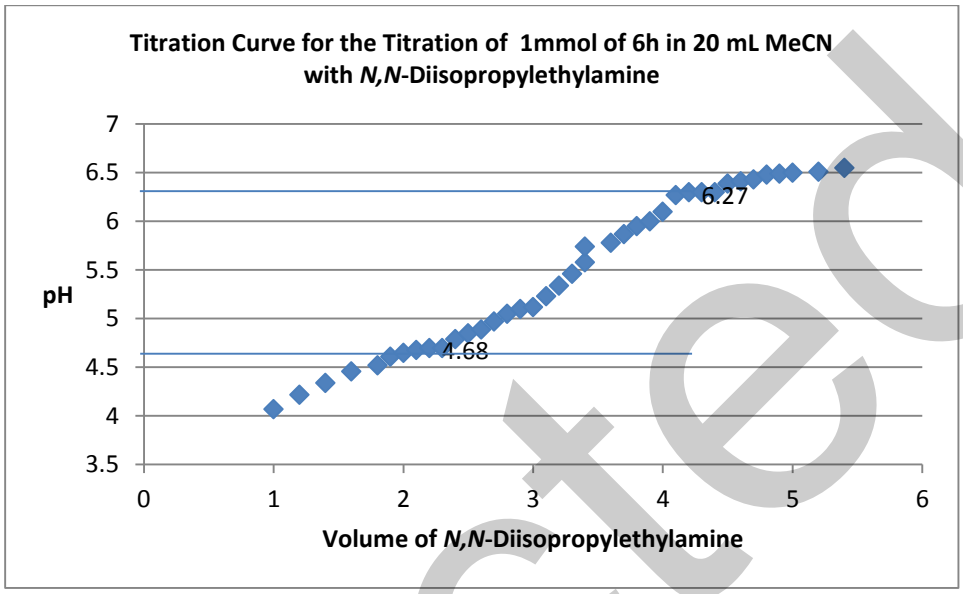

O
HN
F
F
F
F
F

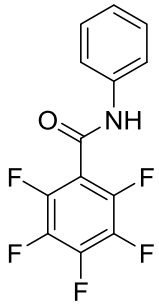

Titration Curve for the Titration of 1mmol of 6e in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12
11.5
11
10.5
10
9.5
9
8.5
8
0
1
2
3
4
5
6
7
11.57
9.36
Volume of N,N-Diisopropylethylamine

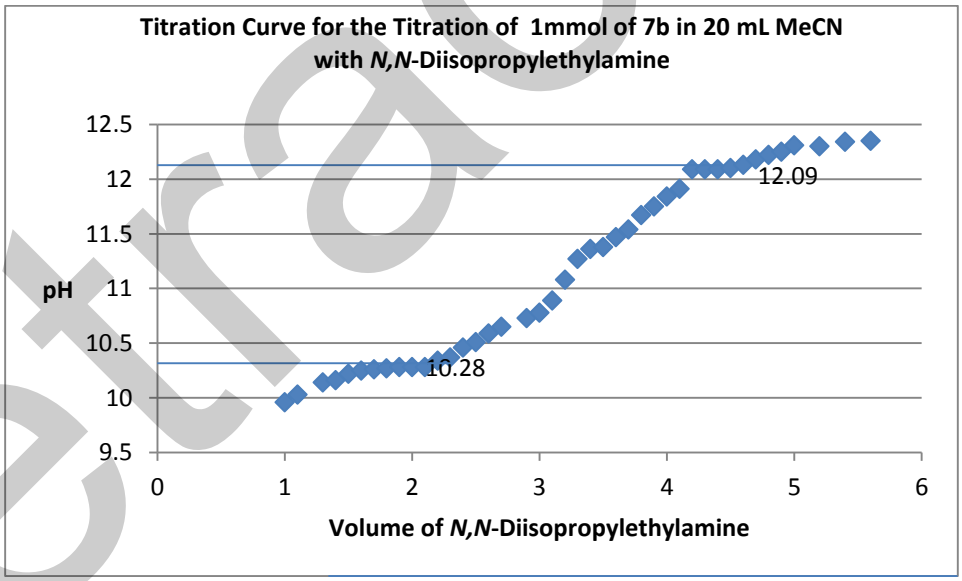

O
HN
CF3
F
F
F
F
F

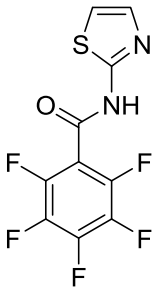

Titration Curve for the Titration of 1mmol of 6j in 20 mL MeCN with N,N-Diisopropylethylamine
pH
7.8
7.3
6.8
6.3
5.8
5.3
4.8
4.3
3.8
0
1
2
3
4
5
6
6.79
5
Volume of N,N-Diisopropylethylamine

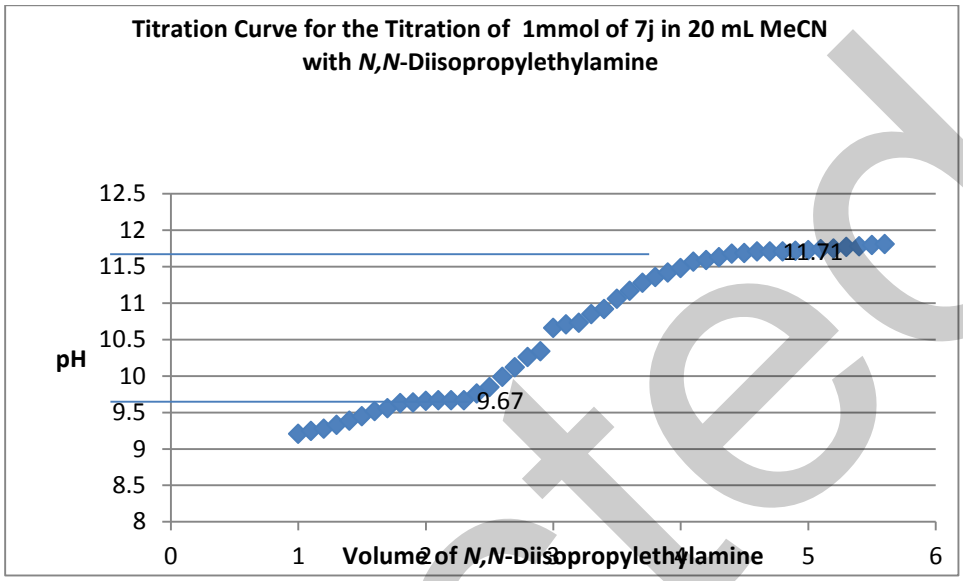

O
HN
CF3
F
F
F
F
CN

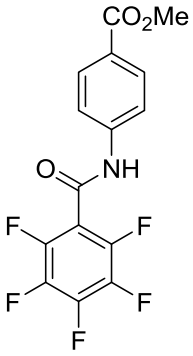

Titration Curve for the Titration of 1mmol of 6h in 20 mL MeCN with N,N-Diisopropylethylamine
pH
7
6.5
6
5.5
5
4.5
4
3.5
0
1
2
3
4
5
6
6.27
4.68
Volume of N,N-Diisopropylethylamine

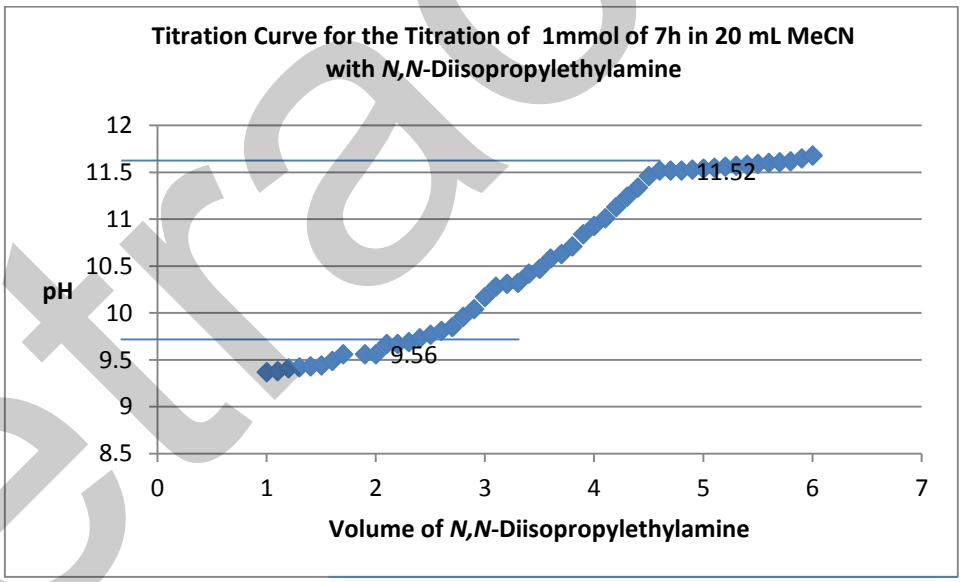

O
NH
F
F
F
F
F

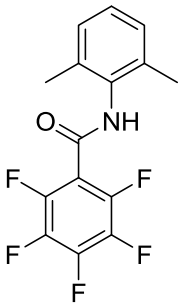

Titration Curve for the Titration of 1mmol of 7b in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12.5
12
11.5
11
10.5
10
9.5
0
1
2
3
4
5
6
12.09
10.28
Volume of N,N-Diisopropylethylamine

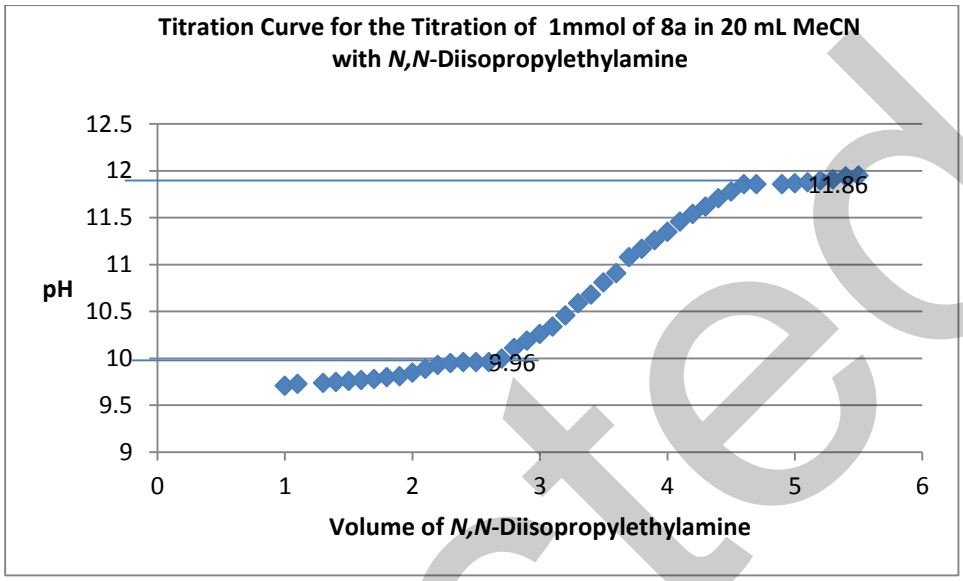

S
N
O
NH
F
F
F
F
F

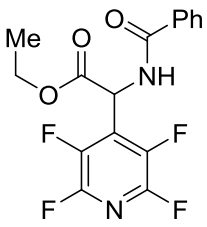

Titration Curve for the Titration of 1mmol of 7j in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12.5
12
11.5
11
10.5
10
9.5
9
8.5
8
0
1
2
3
4
5
6
11.71
9.67
Volume of N,N-Diisopropylethylamine

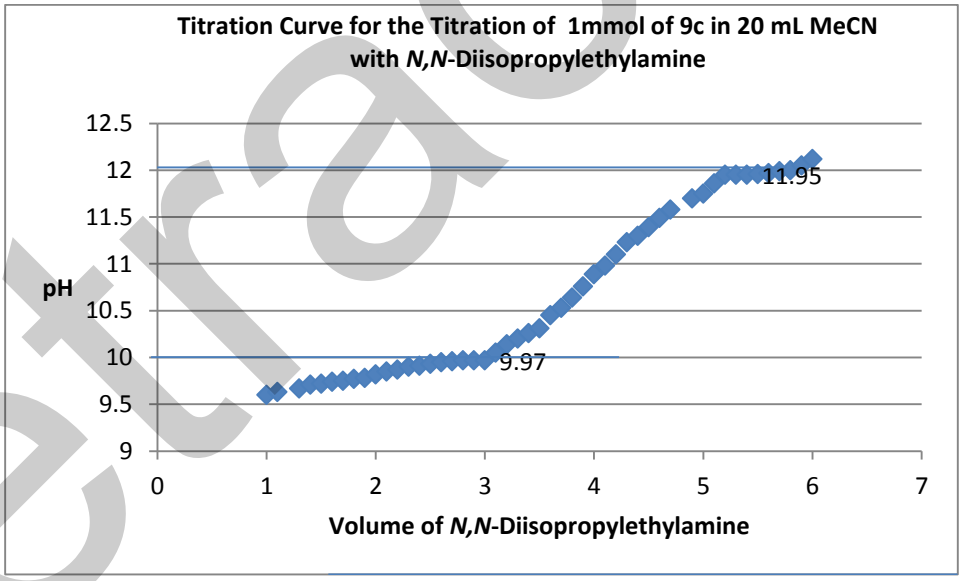

CO2Me
O
NH
F
F
F
F
F

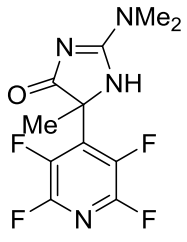

Titration Curve for the Titration of 1mmol of 7h in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12
11.5
11
10.5
10
9.5
9
8.5
0
1
2
3
4
5
6
7
11.52
9.56
Volume of N,N-Diisopropylethylamine

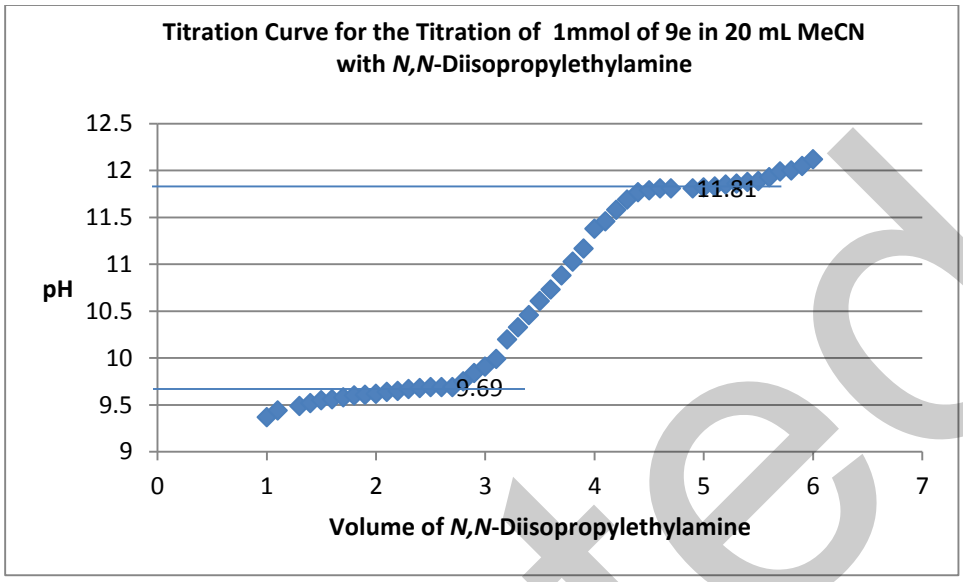

O
NH
F
F
F
F
F

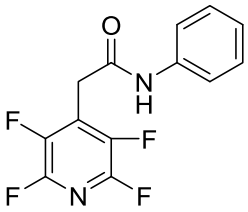

Titration Curve for the Titration of 1mmol of 8a in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12.5
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
6
11.86
9.96
Volume of N,N-Diisopropylethylamine

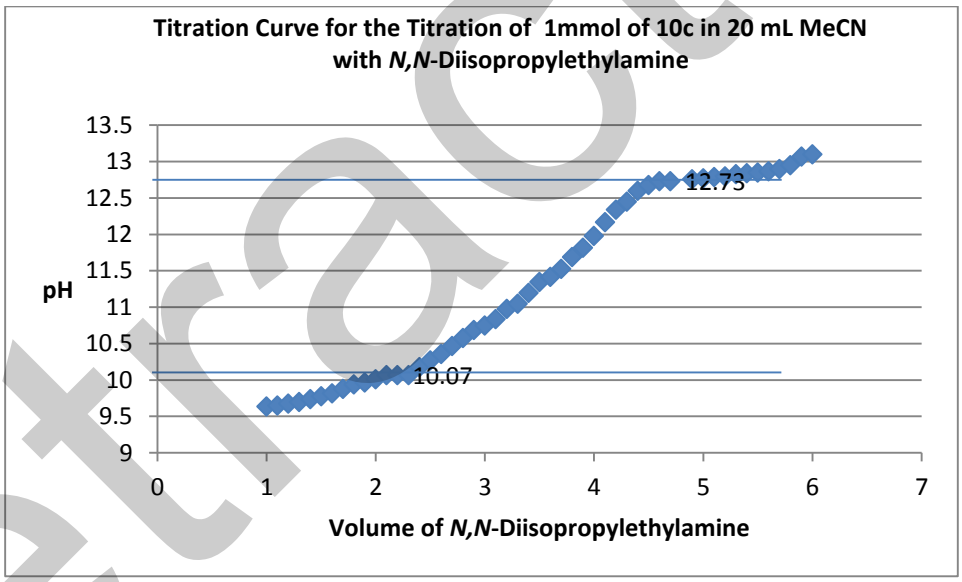

Me
O
O
Ph
NH
F
F
F
F
N

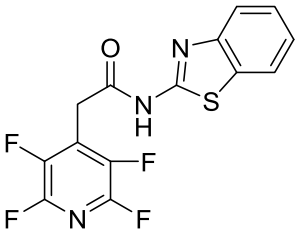

Titration Curve for the Titration of 1mmol of 9c in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12.5
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
6
7
11.95
9.97
Volume of N,N-Diisopropylethylamine

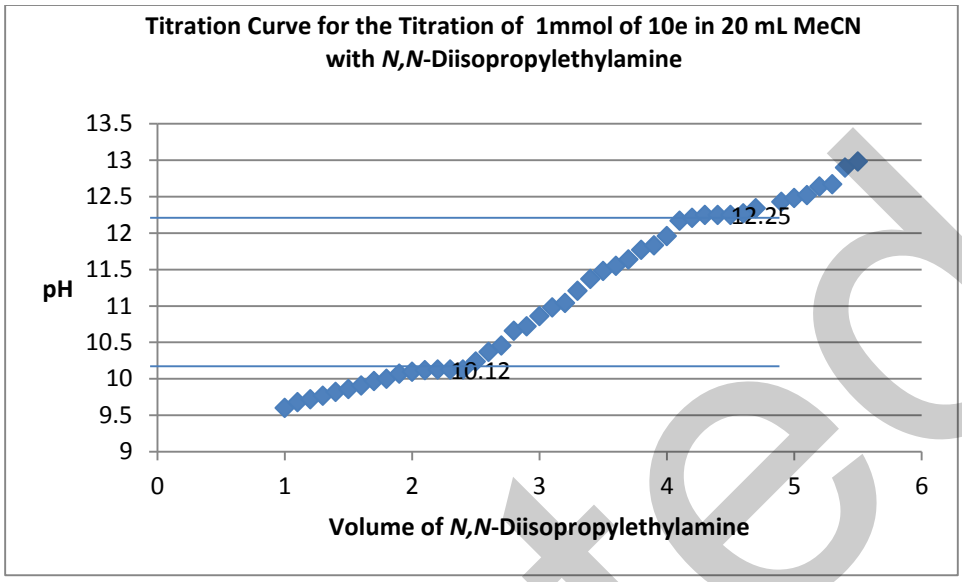

NMe2
N
O
NH
Me
F
F
F
N
F

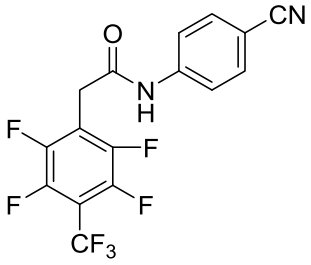

Titration Curve for the Titration of 1mmol of 9e in 20 mL MeCN with N,N-Diisopropylethylamine
pH
12.5
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
6
7
11.81
9.69
Volume of N,N-Diisopropylethylamine

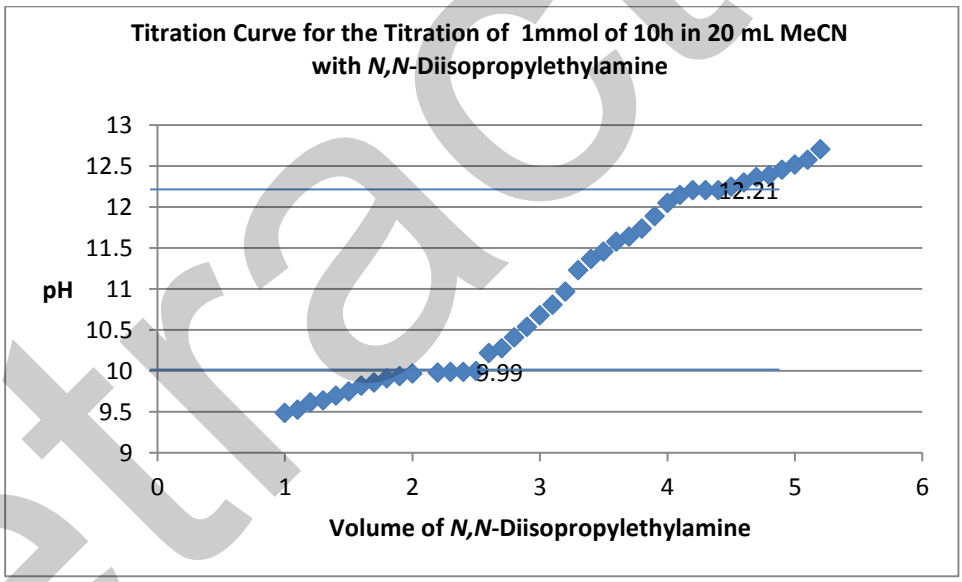

O
N
H
F
F
F
N
F

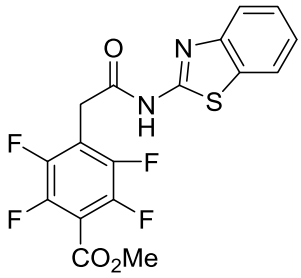

Titration Curve for the Titration of 1mmol of 10c in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13.5
13
12.5
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
6
7
12.73
10.07
Volume of N,N-Diisopropylethylamine

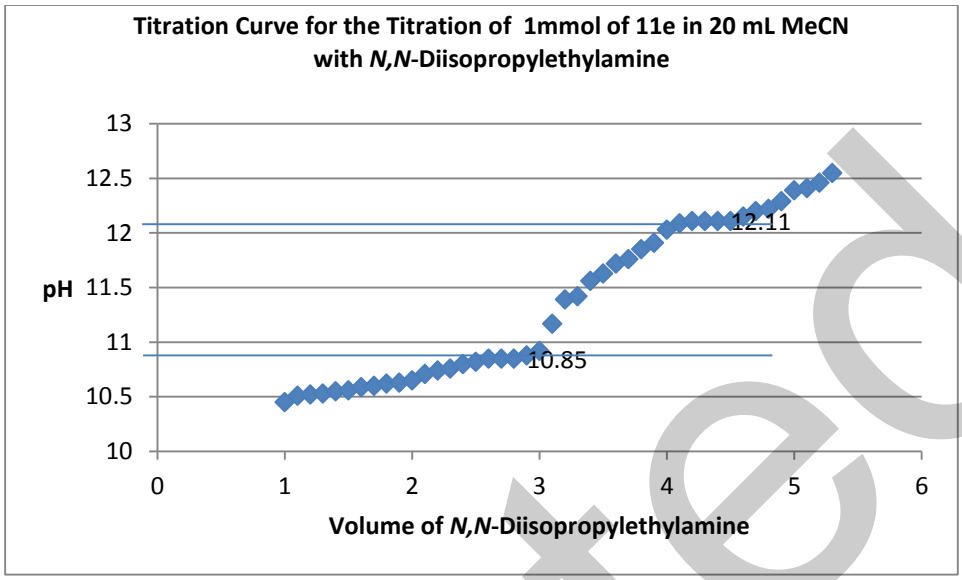

O
N
H
N
S
F
F
F
N
F

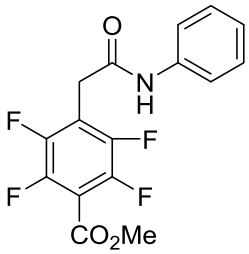

Titration Curve for the Titration of 1mmol of 10e in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13.5
13
12.5
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
6
12.25
10.12
Volume of N,N-Diisopropylethylamine

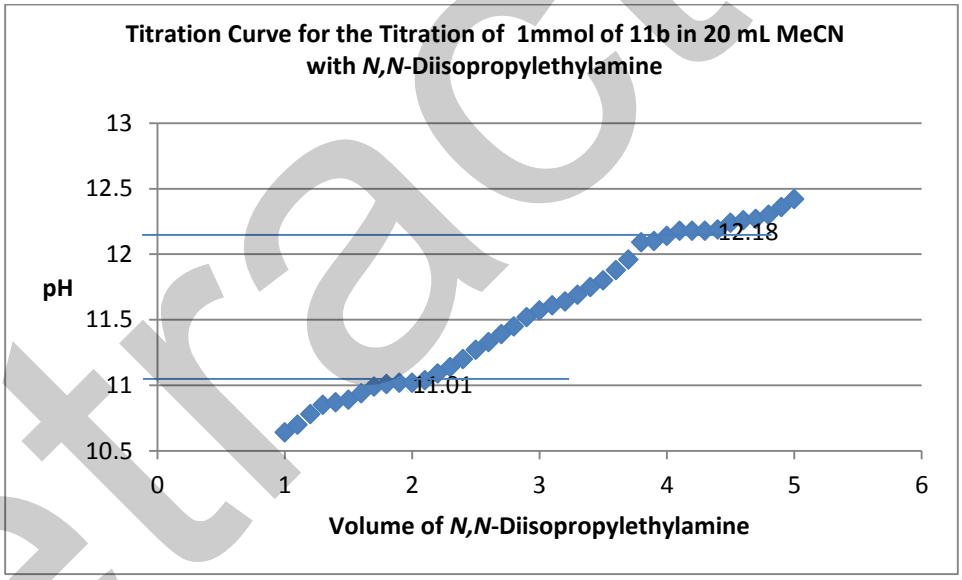

O
N
H
CN
F
F
F
F
CF3

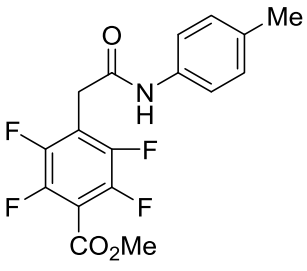

Titration Curve for the Titration of 1mmol of 10h in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13
12.5
12
11.5
11
10.5
10
9.5
9
0
1
2
3
4
5
6
12.21
9.99
Volume of N,N-Diisopropylethylamine

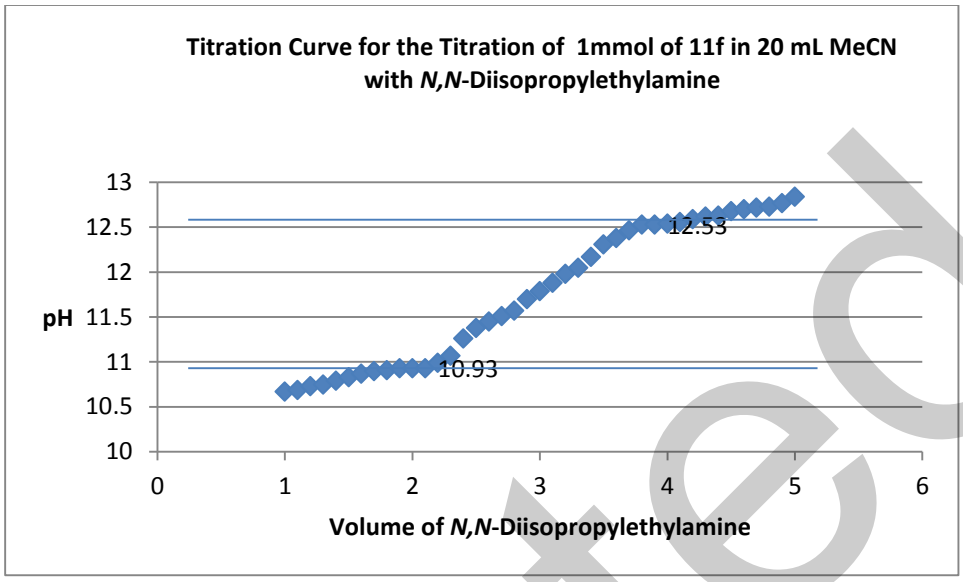

O
N
N
H
S
F
F
F
F
CO2Me

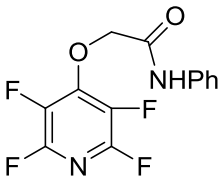

Titration Curve for the Titration of 1mmol of 11e in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13
12.5
12
11.5
11
10.5
10
0
1
2
3
4
5
6
12.11
10.85
Volume of N,N-Diisopropylethylamine


O
N
H
F
F
F
F
CO2Me


Titration Curve for the Titration of 1mmol of 11b in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13
12.5
12
11.5
11
10.5
0
1
2
3
4
5
6
12.18
11.01
Volume of N,N-Diisopropylethylamine


Me
O
N
H
F
F
F
F
CO_2Me


Titration Curve for the Titration of 1mmol of 11f in 20 mL MeCN with N,N-Diisopropylethylamine
pH
13
12.5
12
11.5
11
10.5
10
0
1
2
3
4
5
6
12.53
10.93
Volume of N,N-Diisopropylethylamine


O
O
NHPh
F
F
F
N
F

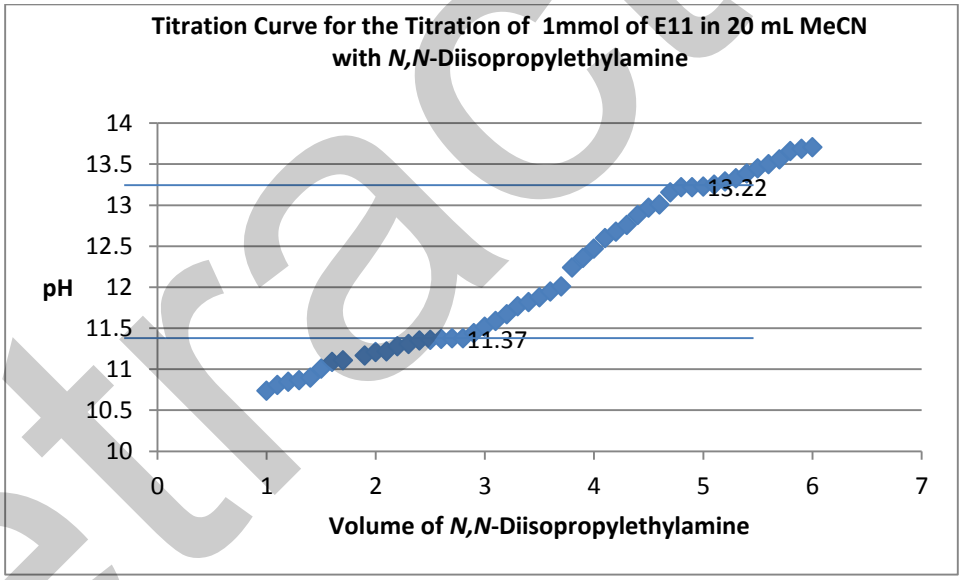
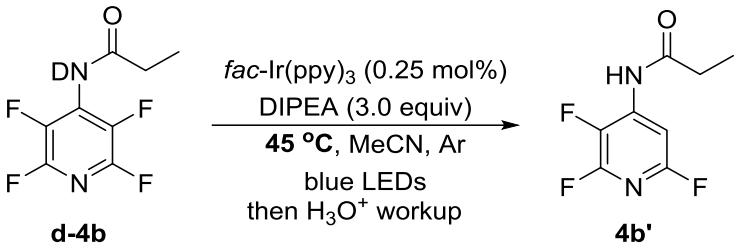
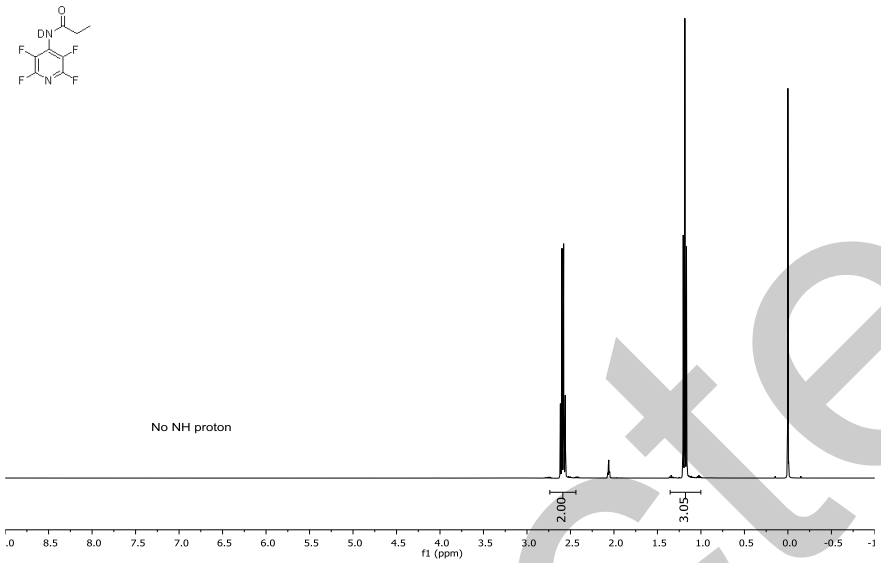

Titration Curve for the Titration of 1mmol of E11 in 20 mL MeCN with N,N-Diisopropylethylamine
pH
14
13.5
13
12.5
12
11.5
11
10.5
10
0
1
2
3
4
5
6
7
13.22
11.37
Volume of N,N-Diisopropylethylamine

Photo-HDF reaction of *N*-(perfluoropyridin-4-yl)propionamide-*N*-d (d-4b)



d-4b was synthesized by dissolving **4b** in DCM and subjecting to successive washes with D_2O until the NH could no longer be detected by 1H NMR. At this point, the solvent was removed and d-4b was subjected to standard photo-HDF reaction conditions. **4b'** was prepared by general procedure A. The mixture of the **4b-deuterated** (22.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN)was placed in the light bath under 45 ^oC for 14 h. After the complete consumption of starting material, the CH_3CN was removed via rotavap and the residue was treated with 0.1 M of HCl (2 mL) (let it stir for 30 minutes) and then extracted with EtOAc (5 x 1 mL). The combined organic portions were dried with anhydrous $MgSO_4$, filtered, concentrated in vacuo, and purified by normal phase chromatography. Deuterium incorporation was then determined by comparison of the aryl-H integration to the amide and ethyl signals. No appreciable difference was observed. Therefore, we concluded that the acidic NH does not serve as the H-atom source.

d-4b ^{1}HNMR



d-4b'

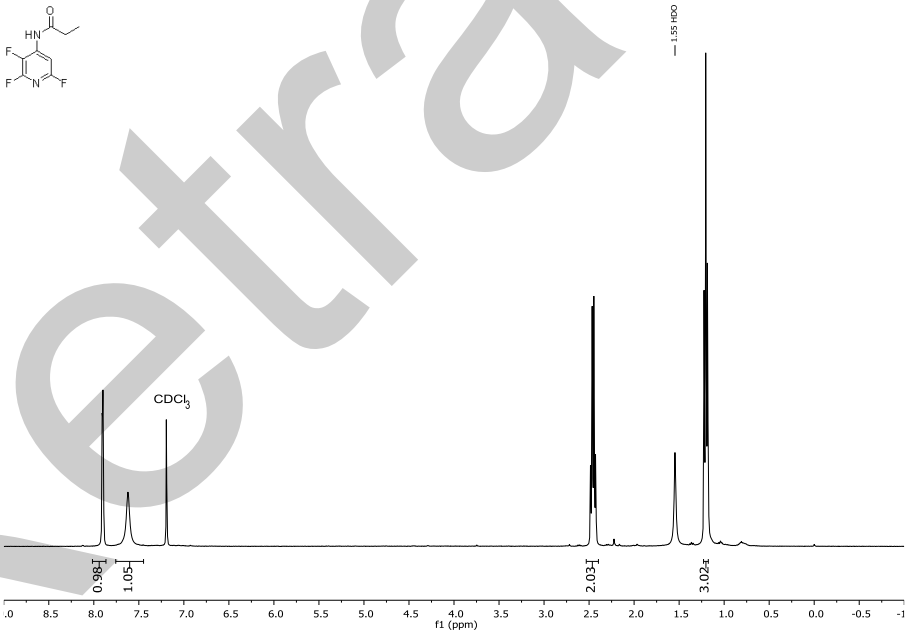
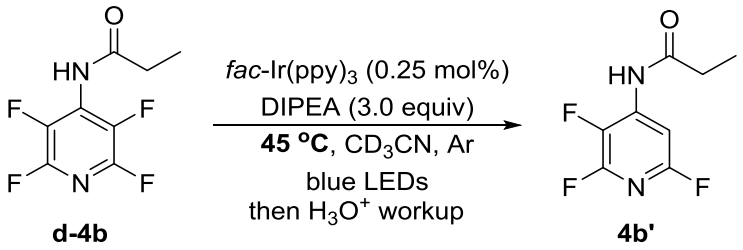
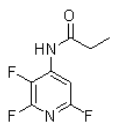


Photo-HDF reaction of 4b *N*-(perfluoropyridin-4-yl)propionamide (4b')



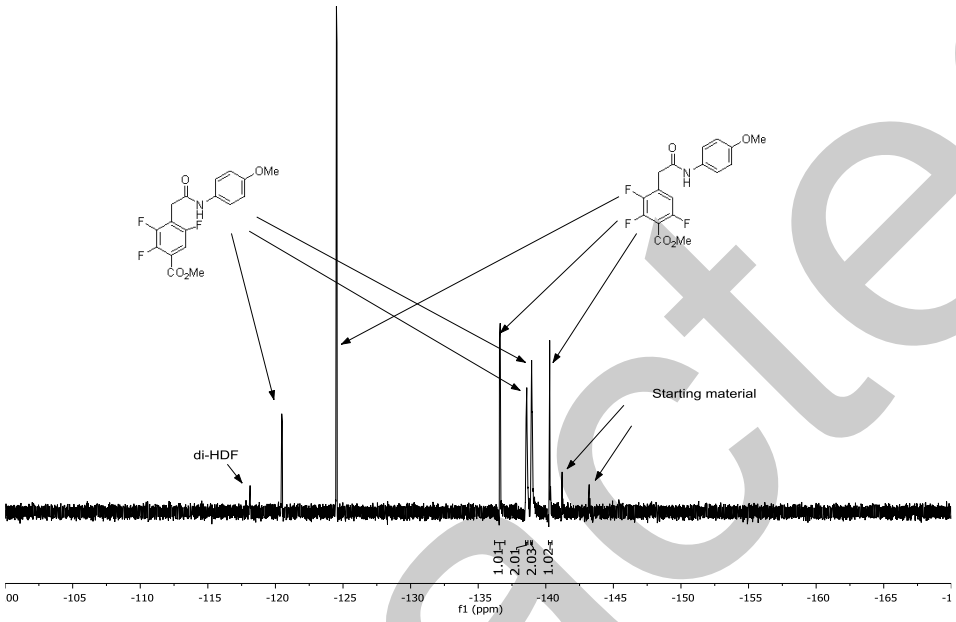
4b' was prepared by general procedure A. The mixture of the **4b** (221.0 mg, 0.100 mmol), DIPEA (54.0 uL, 0.300 mmol), and 1 mL of photocatalyst stock solution (0.250 mM, 1 mL in MeCN)was placed in the light bath under 45 ^{o}C for 13 h. After the complete consumption of starting material, the CD_3CN was removed via rotavap and the residue was treated with 0.1 M of HCl (2 mL) (let it stir for 30 minutes) and then extracted with EtOAc (5 x 1 mL). The combined organic portions were dried with anhydrous $MgSO_4$, filtered, concentrated in vacuo, and purified by normal phase chromatography. Deuterium incorporation was then determined by comparison of the aryl-H integration to the amide and ethyl signals. No noticeable difference was observed. Therefore, we concluded that the CD_3CN does not serve as the H-atom source.



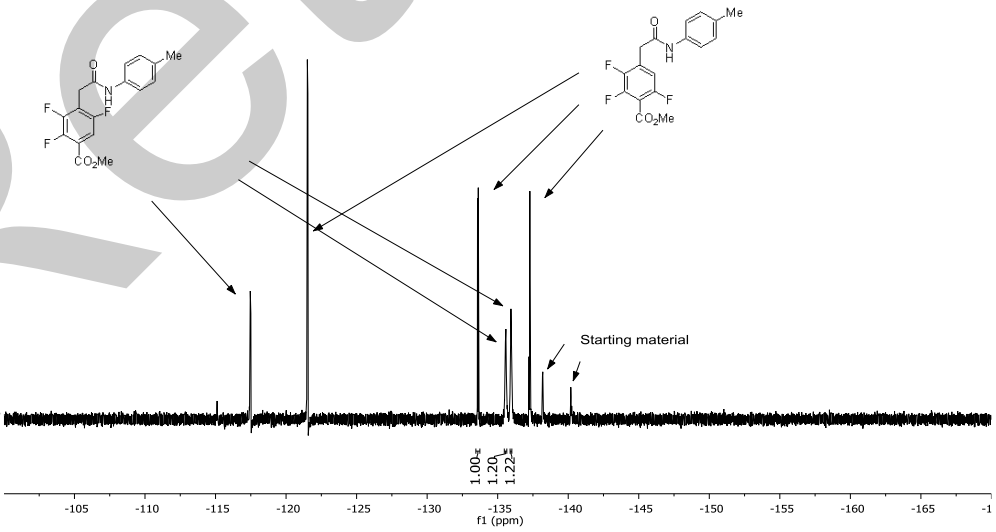
use CD_3CN as solvent

The following spectra were used in the intramolecular competition experiment used to generate Figure 3. The integrations were used to generate the product ratios.

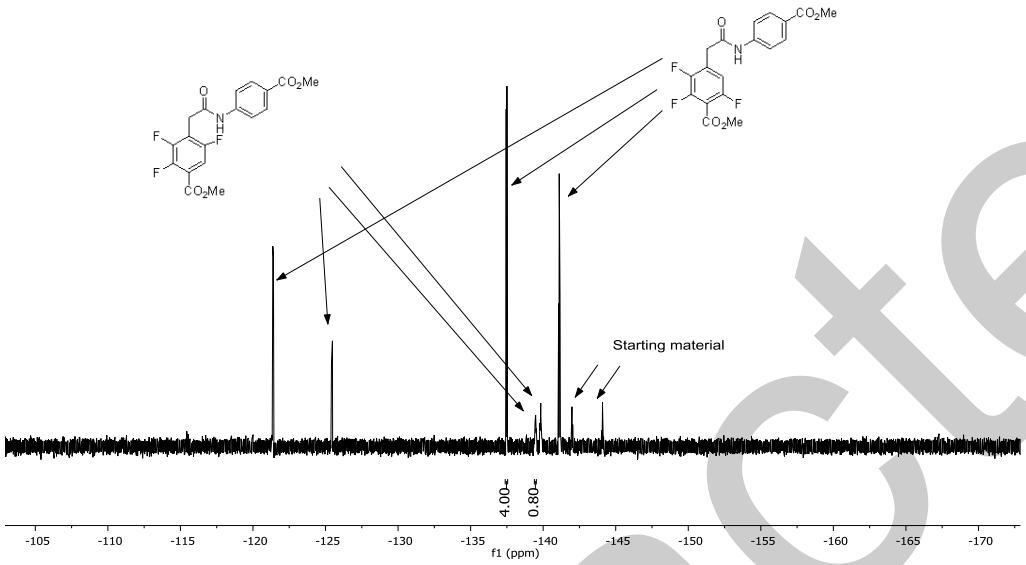
F2(a') and F2(a'') ^{19}F NMR (376 MHz, Benzene-d_6)



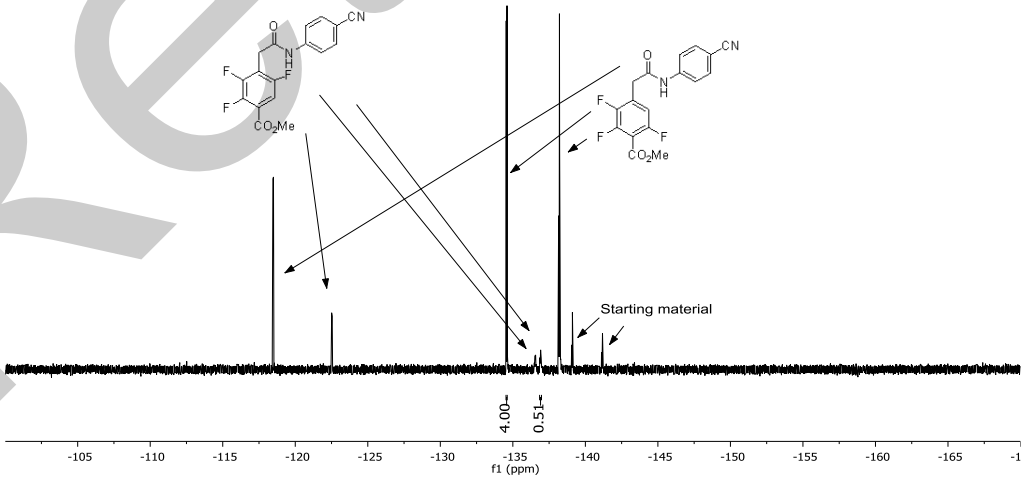
F2(b') and F2(b'') ^{19}F NMR (376 MHz, Benzene-d_6)



F2(c') and F2(c'') ^{19}F NMR (376 MHz, Benzene d_6)



F2(d') and F2(d'') ^{19}F NMR (376 MHz, Benzene-d_6)



Confirm the correlation of regioselectivity

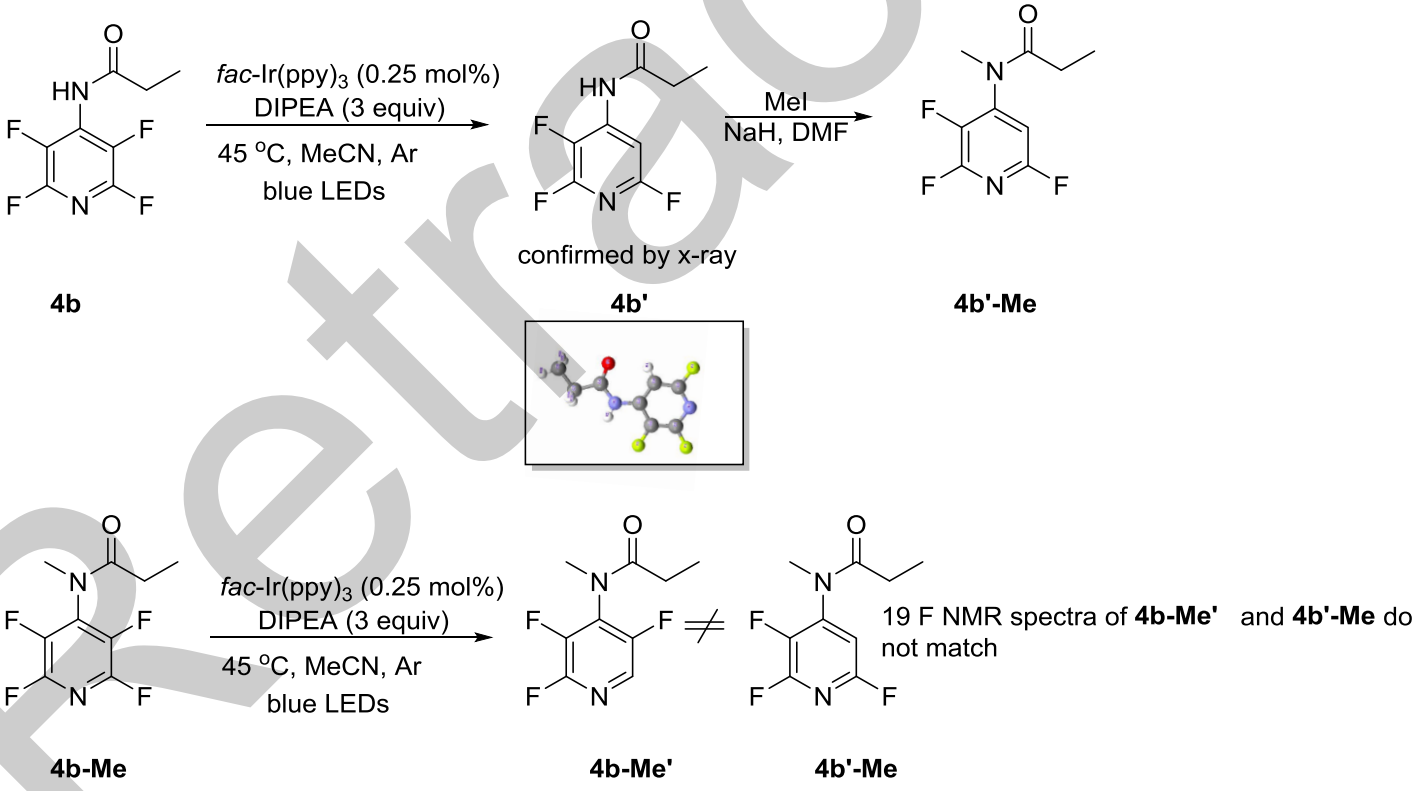
General procedure G: This procedure carried out for the following substrates (**4b**, **6a**, **6b**, **6c**, **7b**, **9c**, **10d**, **10g**, and **11b**).

For example, Compound **4b** undergoes Photo-HDF reaction to furnish **4b'**. Methylation of **4b'** using MeI furnished methylated **4b'** that's having different ^{19}F NMR shift compare with photo-HDF product of already methylated **4b**. The ^{19}F NMR spectra's for both products (**4b'-Me & 4b-Me'**) did not match.

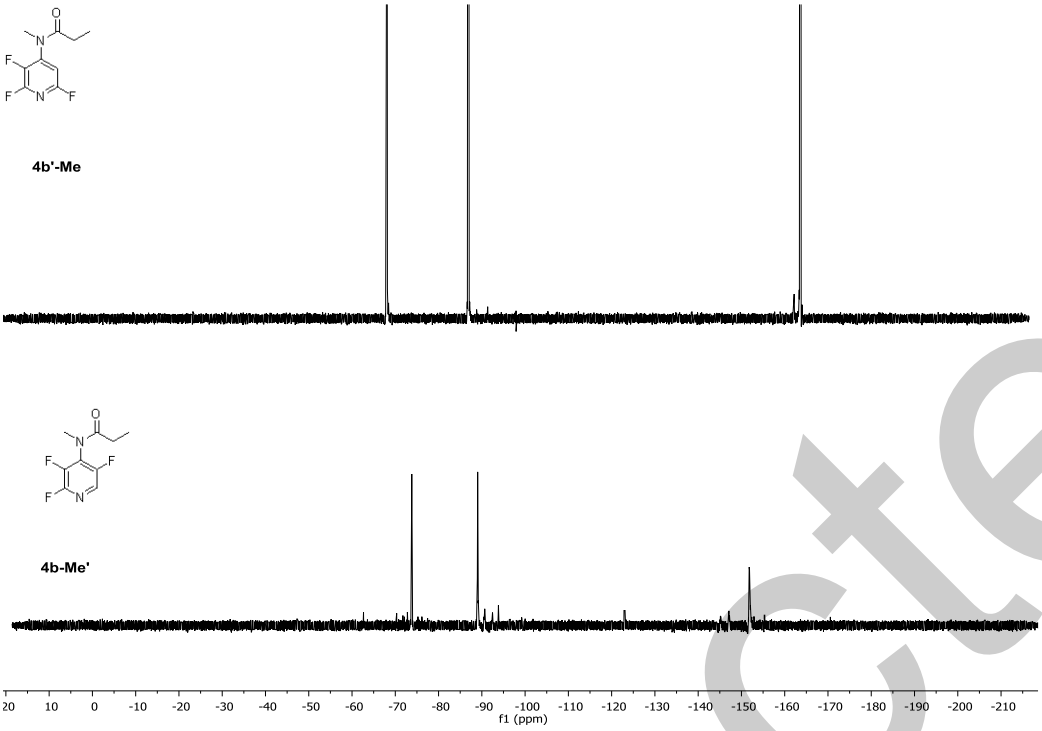
General Procedure H: This procedure carried out for the following substrates **(6l**, **6m,** and **6n).**

For example, Compound **6l** undergo Photo-HDF reaction to furnish **6l'**. Acetylation of **6l'** using acetic anhydride furnished acylated **6l**' that's having same ^{19}F shift compare with photo-HDF product of already acylated **6b**. The ^{19}F NMR spectra's for both products (**6b'**, **6b'** from late acylation) did match.

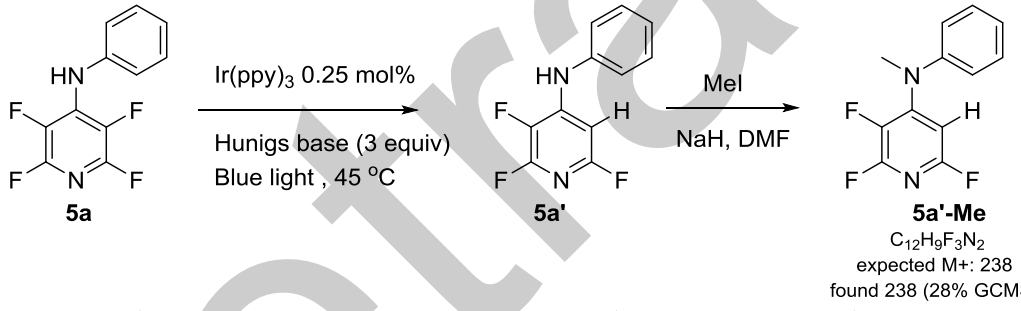
Confirmation of fluorine regiochemistry via synthesis of 4b'-Me & 4b-Me' in CD_3CN

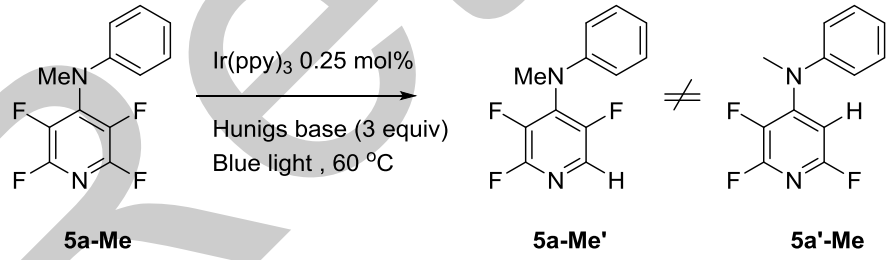


Crude ^{19}F NMR spectra for 4b'-Me & 4b-Me' in CD_3CN



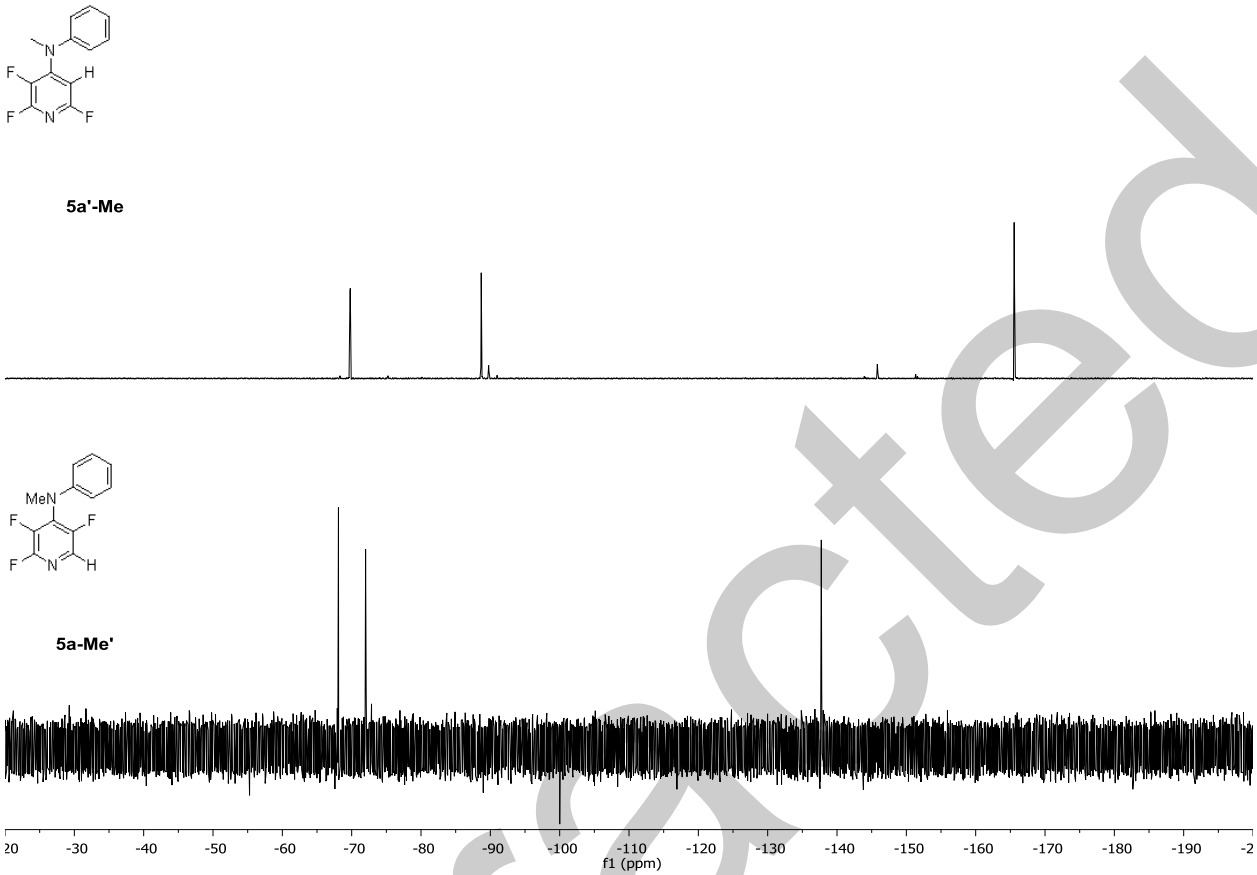
Confirmation of fluorine regiochemistry via synthesis of 6a'-Me & 6a-Me' in CD_3CN



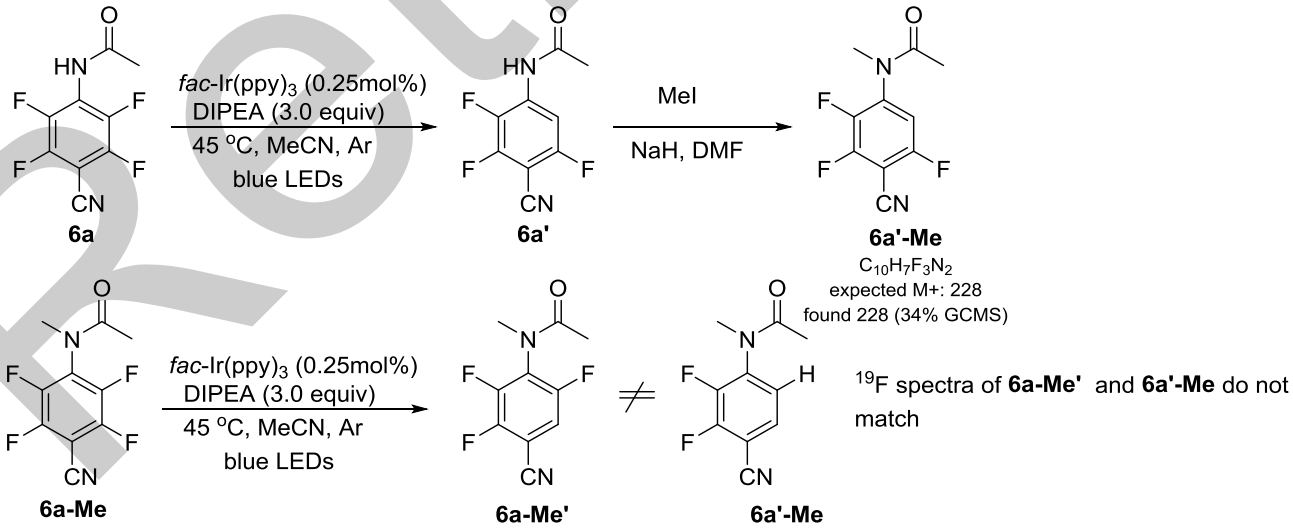


^{19}F spectra of **5a-Me'** and **5a'-Me** do not match

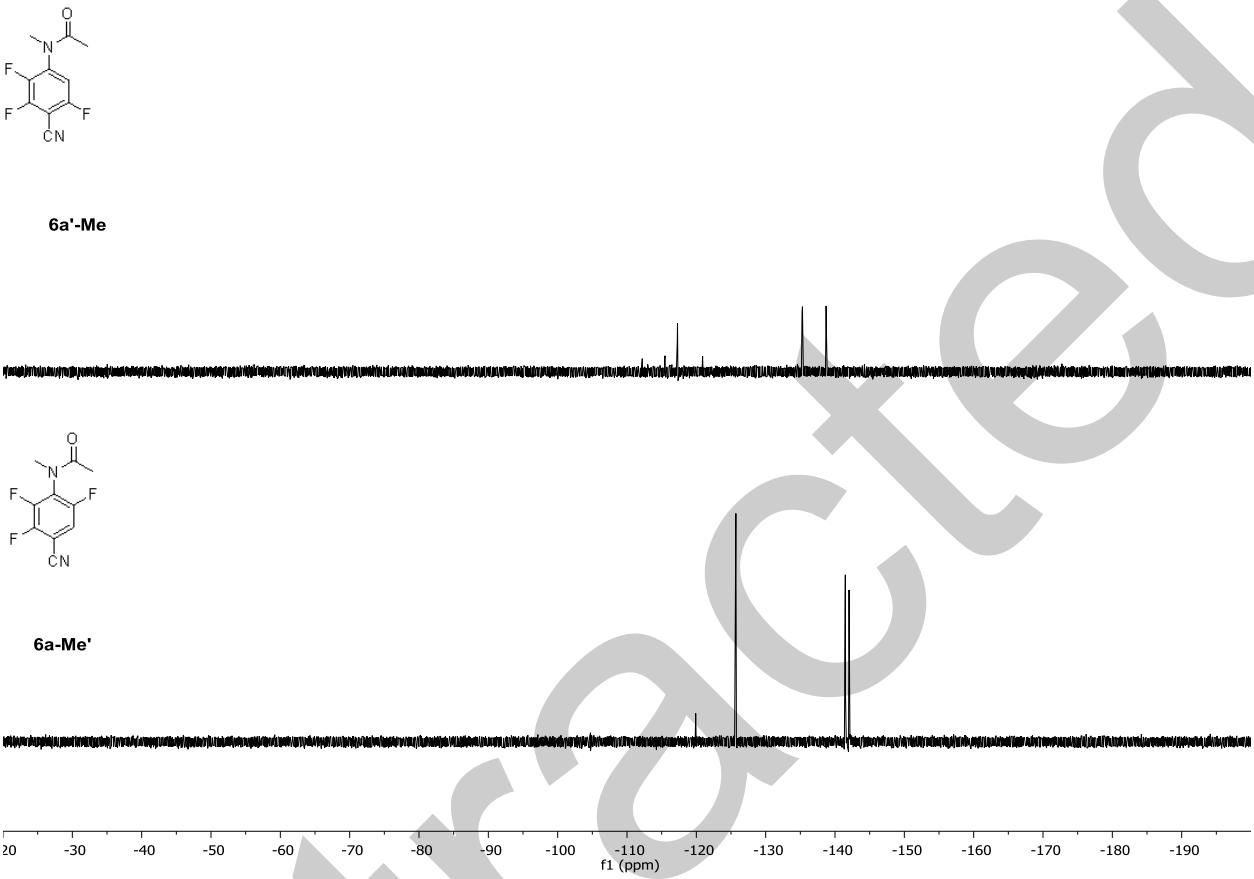
Crude ^{19}F NMR spectra for 5a'-Me & 5a-Me' in CD_3CN



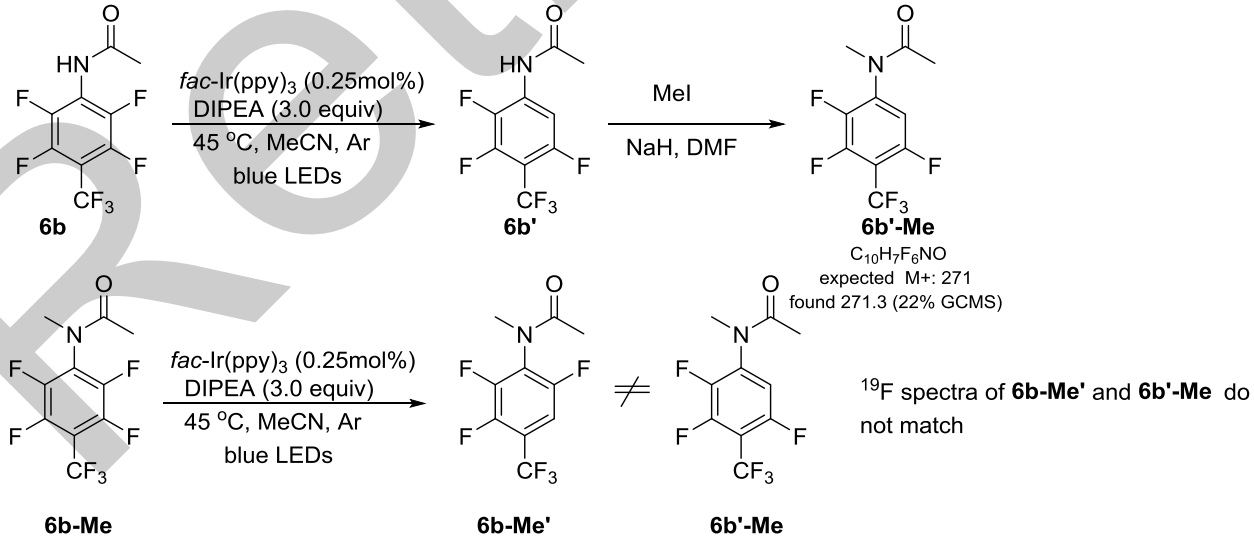
Confirmation of fluorine regiochemistry via synthesis of 6a'-Me & 6a-Me' in CD_3CN



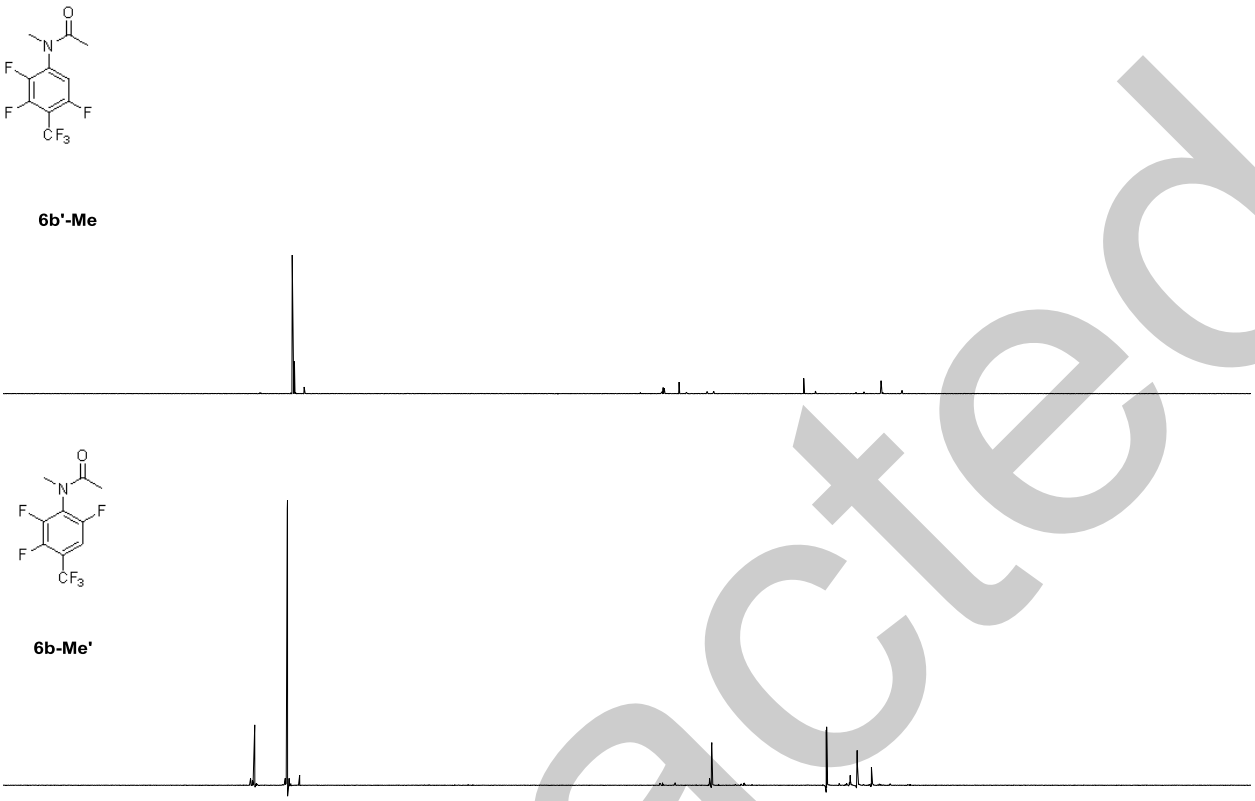
Crude ^{19}F NMR spectra for 6a'-Me & 6a-Me' in CD_3CN



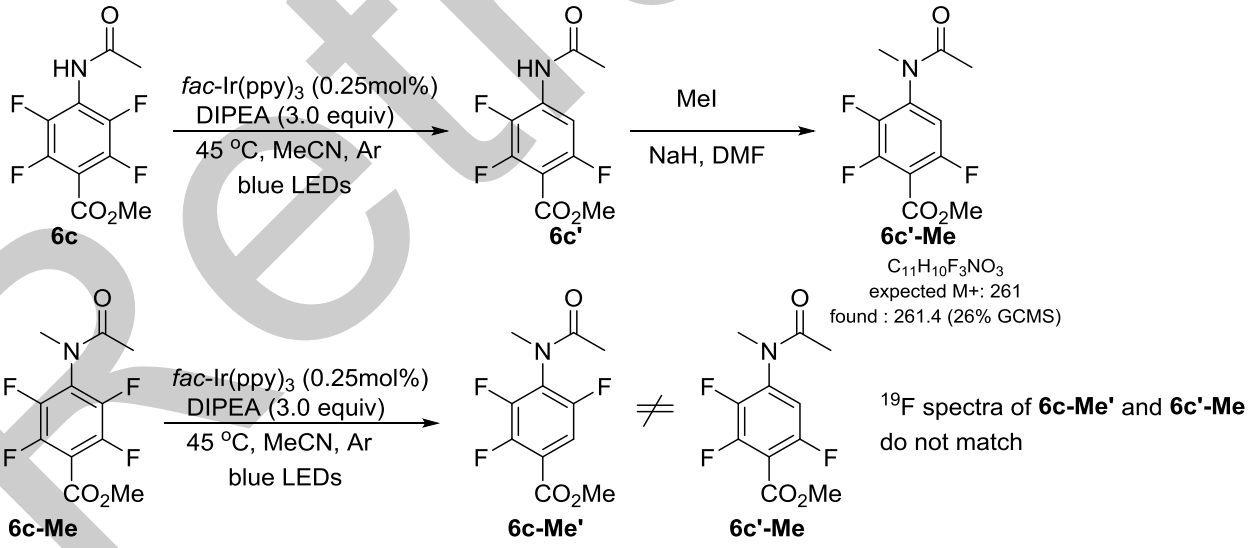
Confirmation of fluorine regiochemistry via synthesis 6b'-Me & 6b-Me' in CD_3CN



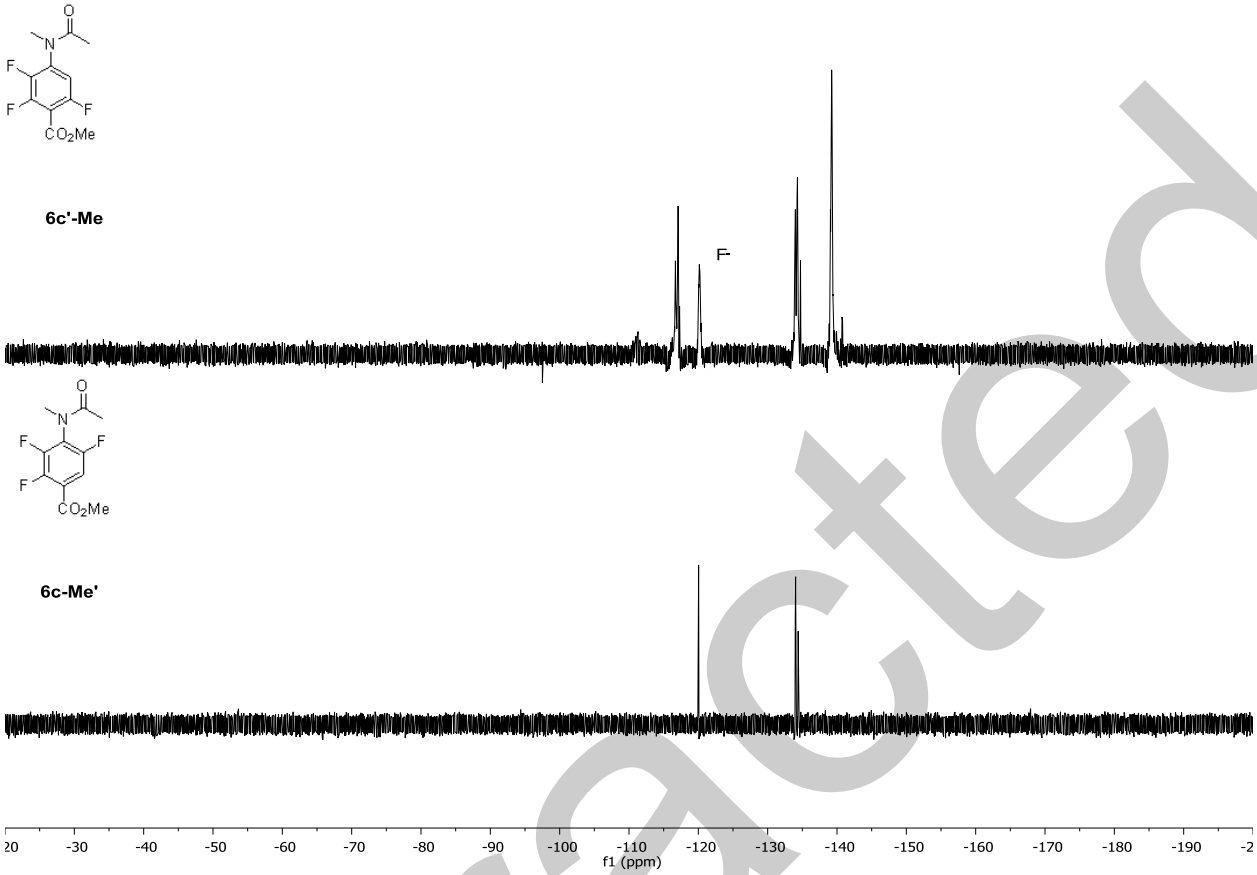
Crude ^{19}F NMR spectra for 6b'-Me & 6b-Me' in CD_3CN



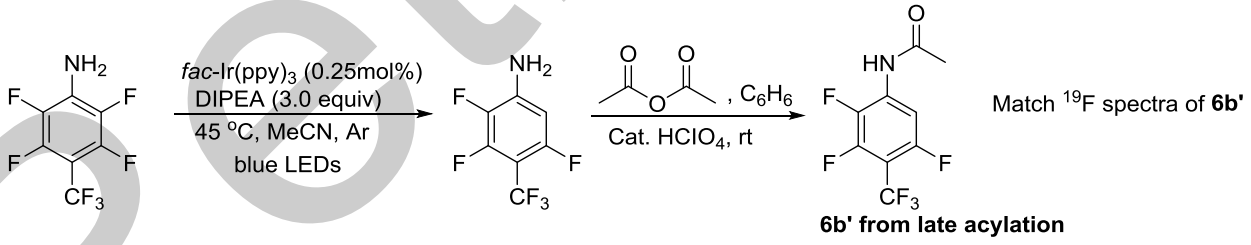
Confirmation of fluorine regiochemistry via synthesis 6c'-Me & 6c-Me' in CD_3CN



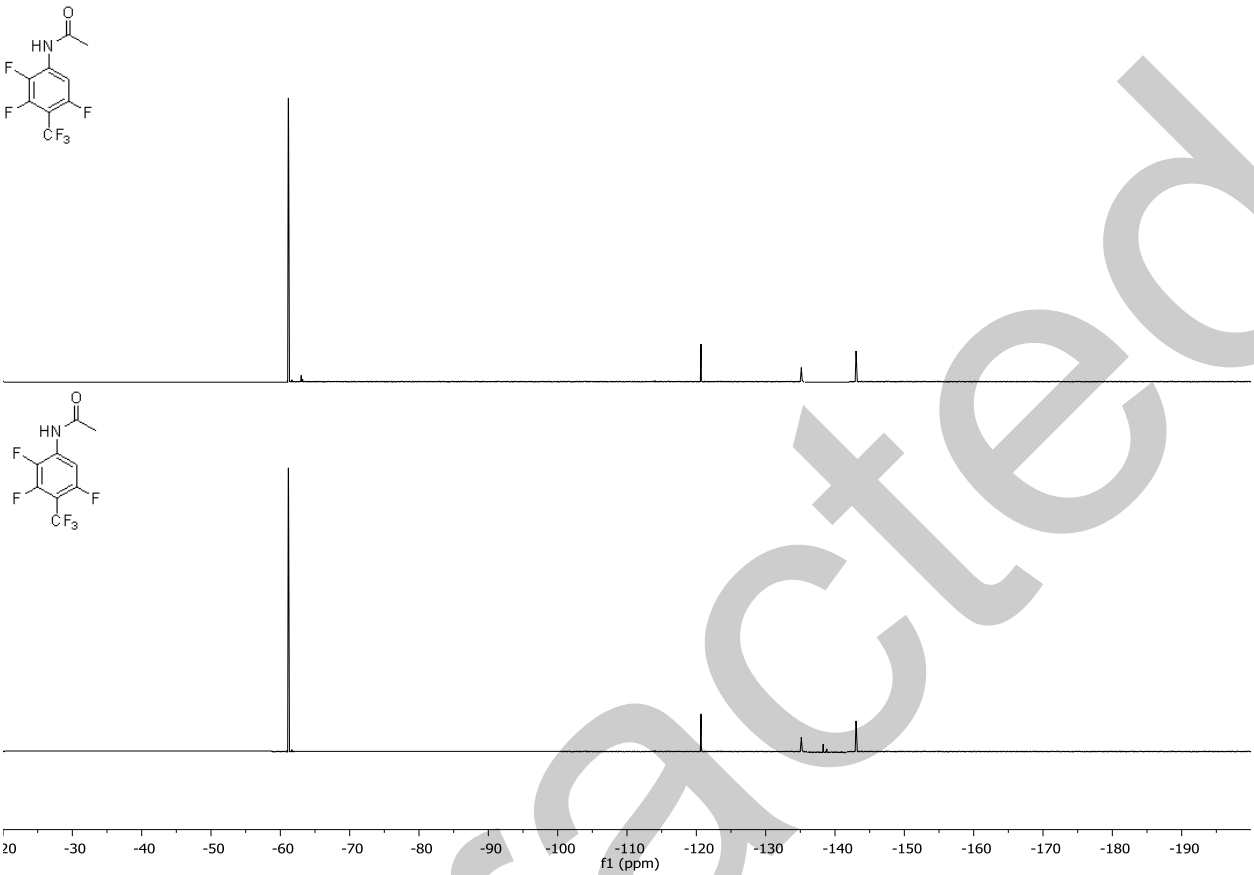
Crude ^{19}F NMR spectra for 6c'-Me & 6c-Me' in CD_3CN



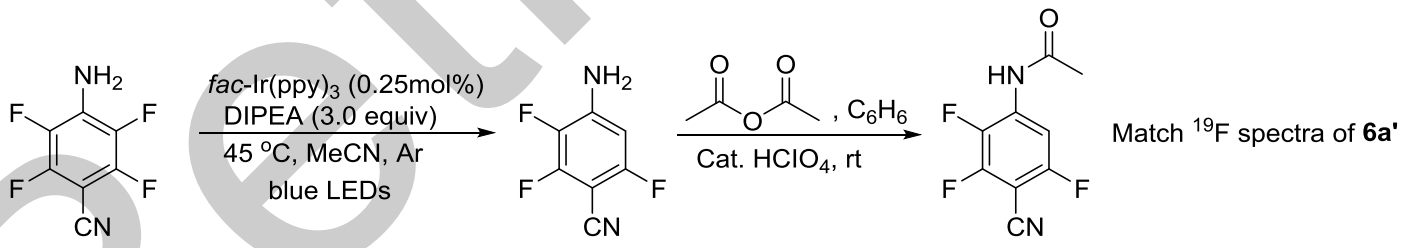
Confirmation of fluorine regiochemistry of 6l via synthesis of 6b' & 6b' late acylation in CD_3CN



Crude ^{19}F NMR spectra for 6b' & 6b' from late acylation in CD_3CN



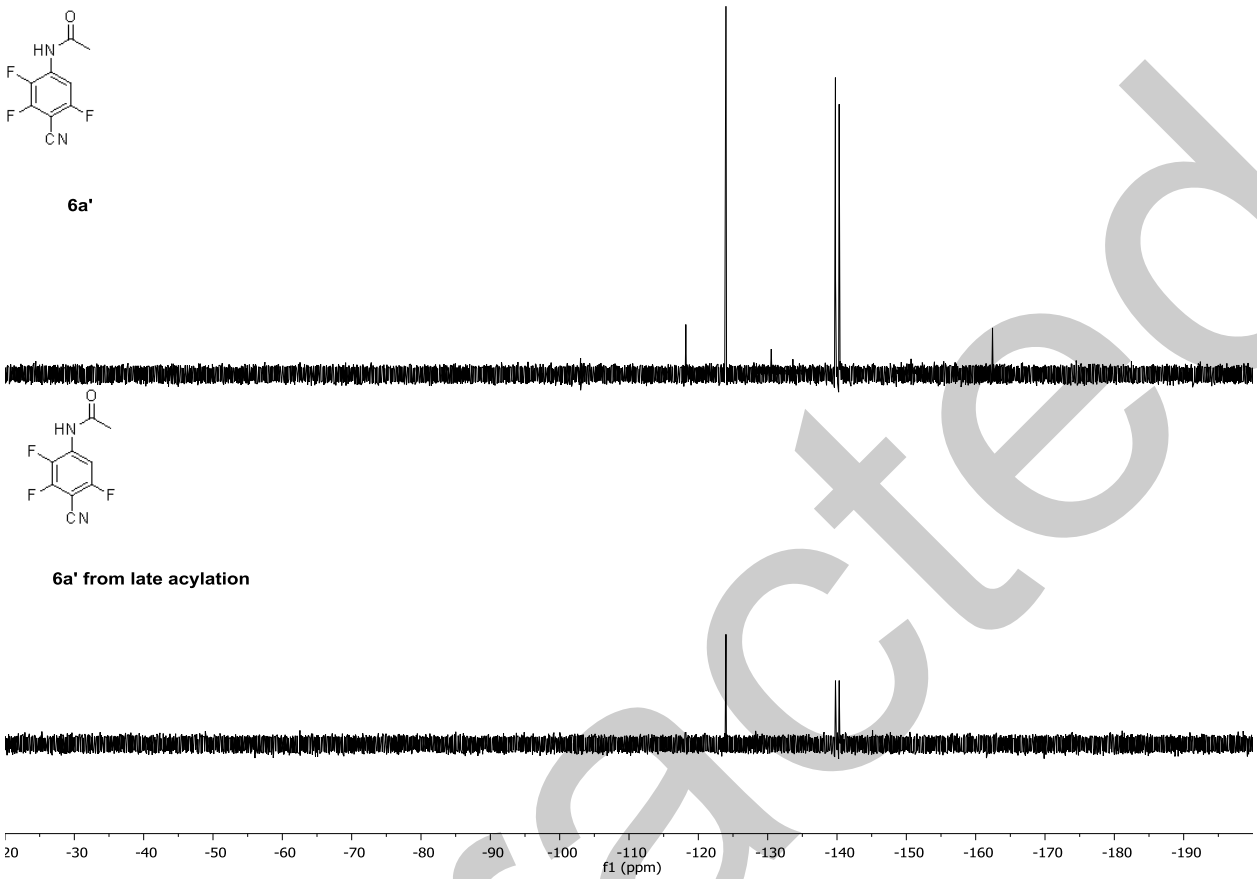
Confirmation of fluorine regiochemistry of 6m via synthesis of 6a' & 6a' late acylation in CD_3CN



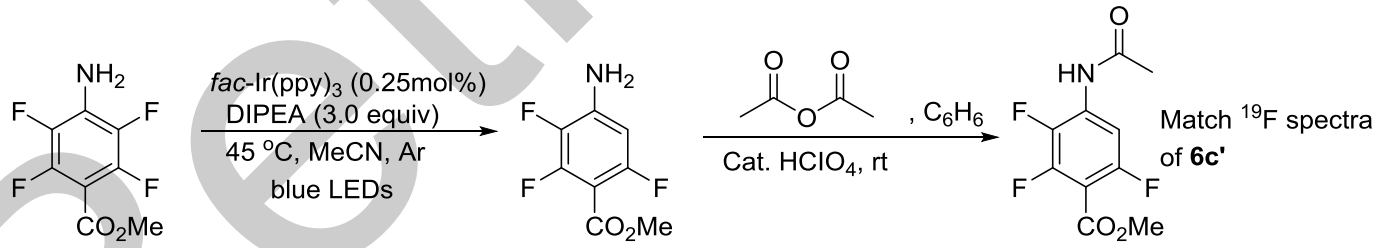
Match ^{19}F spectra of **6a'**

6a' from late acylation

Crude ^{19}F NMR spectra for 6a' & 6a' from late acylation in CD_3CN

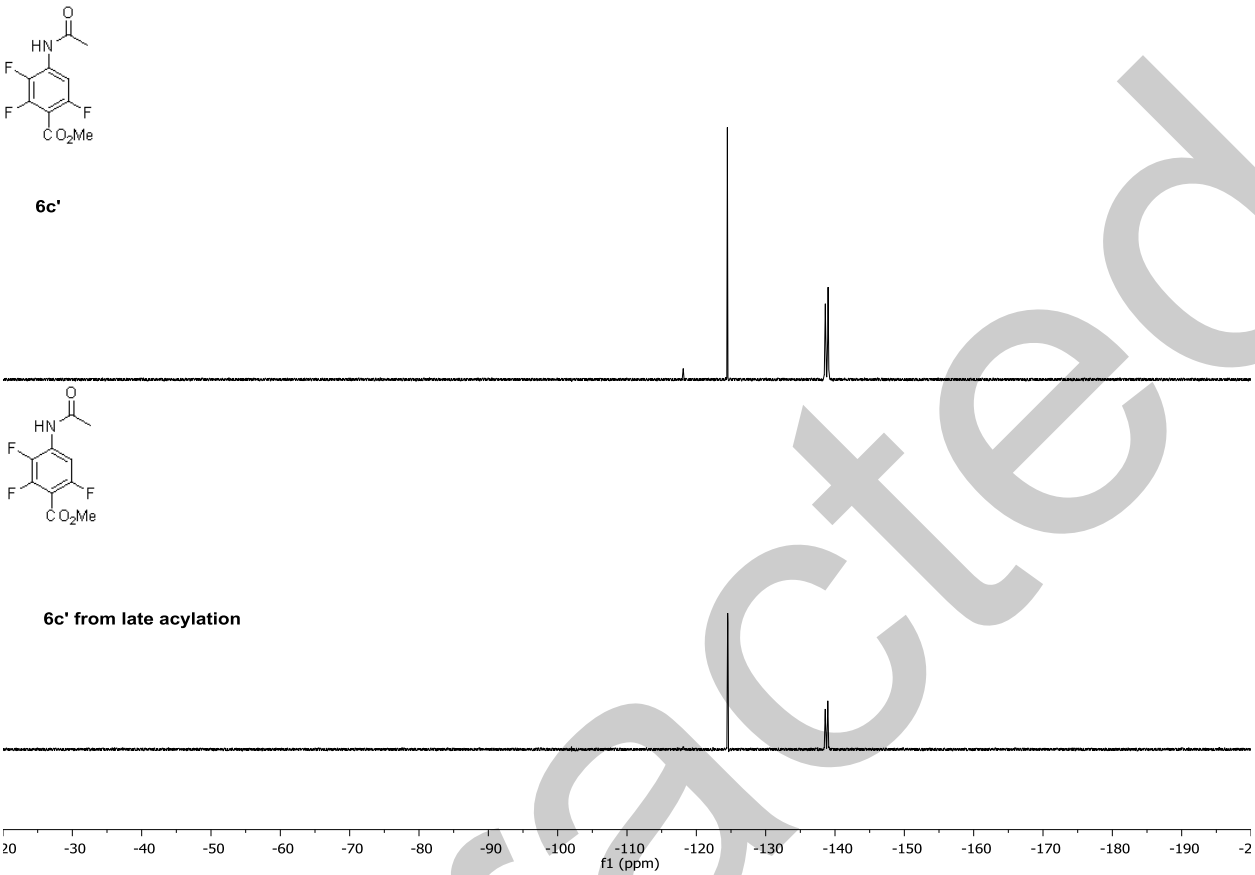


Confirmation of fluorine regiochemistry of 6n via synthesis of 6c' & 6c' from late acylation in CD_3CN

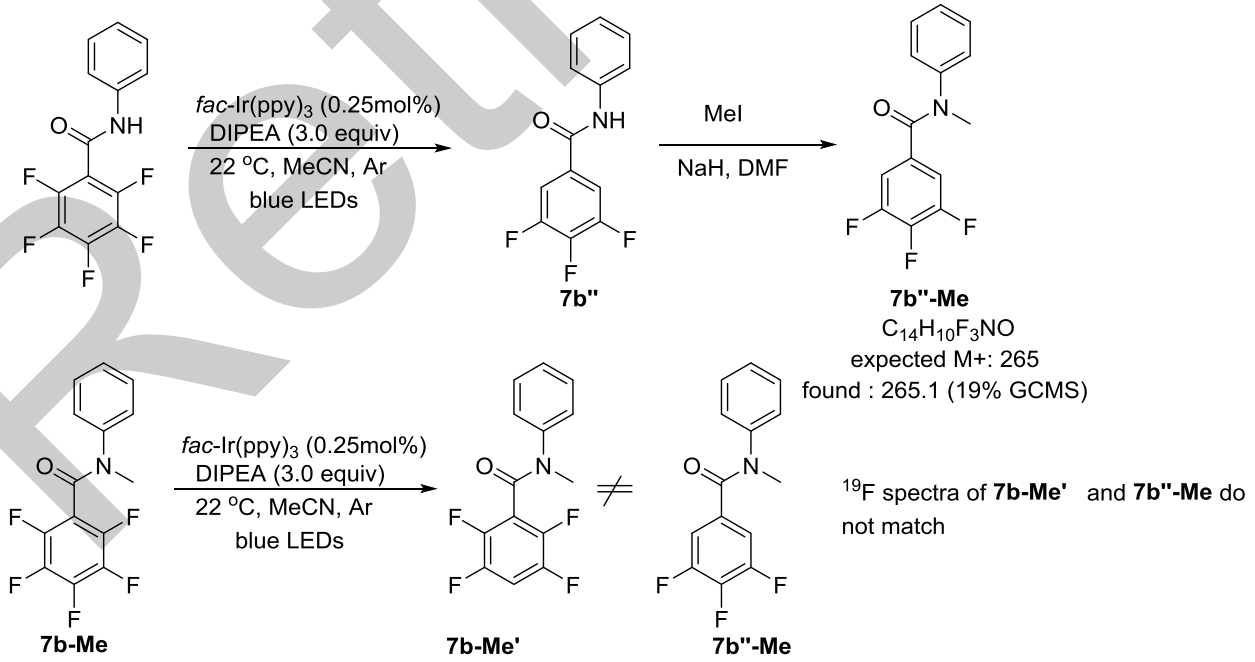


6c' from late acylation

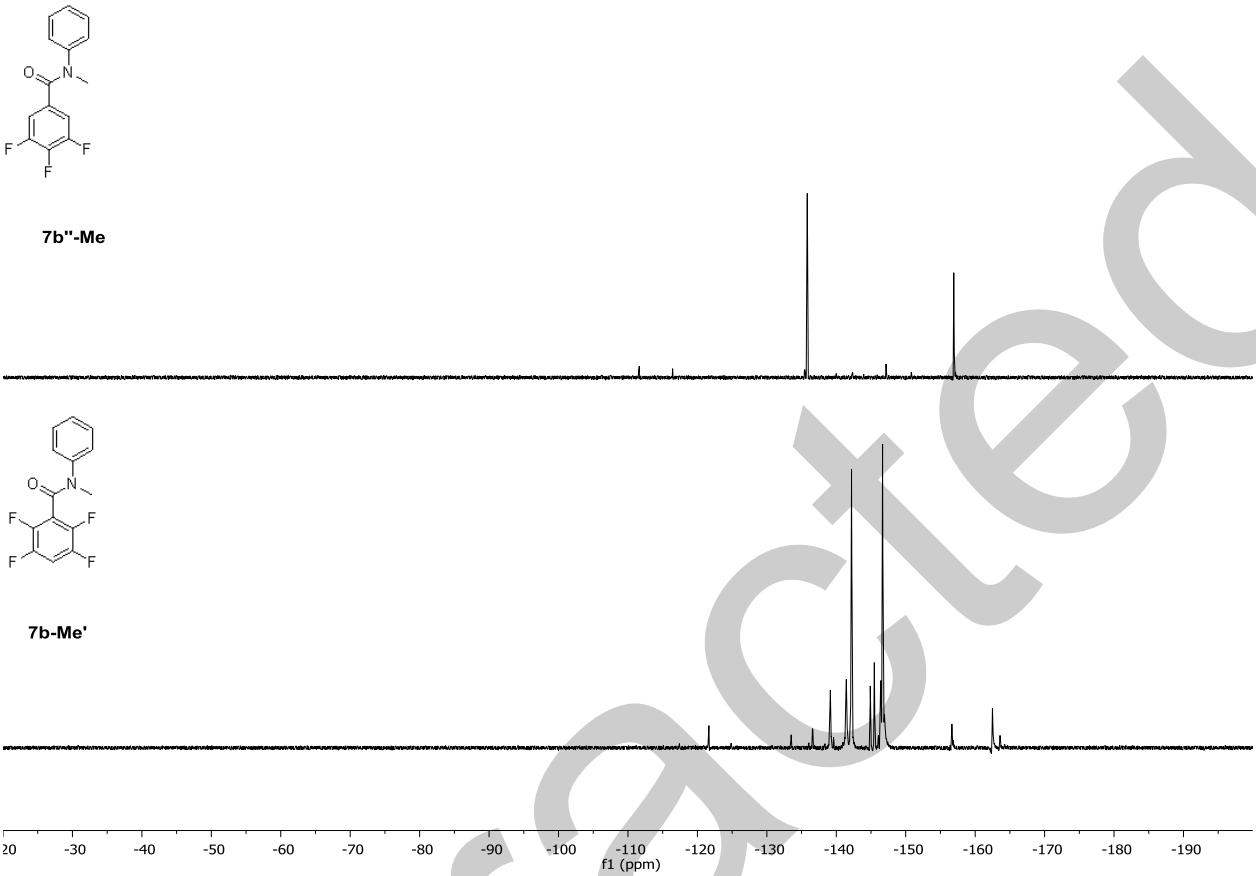
Crude ^{19}F NMR spectra for 6c' & 6c' from late acylation in CD_3CN



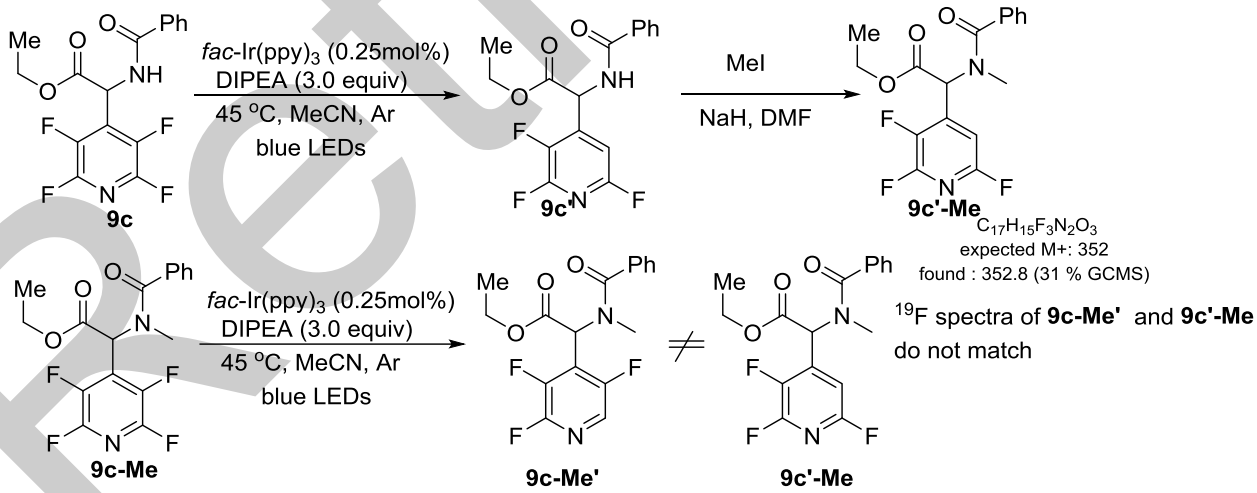
Confirmation of fluorine regiochemistry via synthesis of 7b''-Me & 7b-Me' in CD_3CN



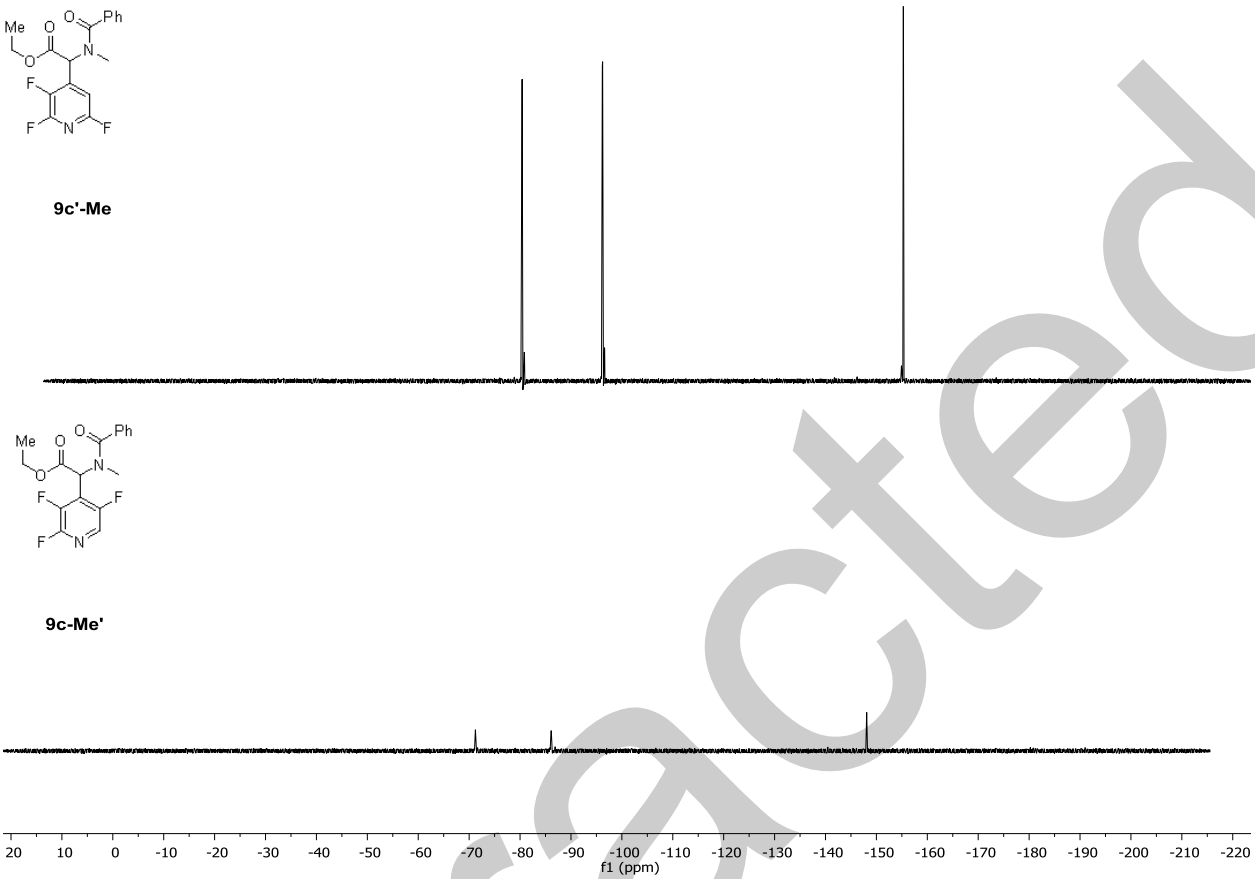
Crude ^{19}F NMR spectra for 7b''-Me & 7b-Me' in CD_3CN



Confirmation of fluorine regiochemistry via synthesis of 9c'-Me & 9c-Me' in CD_3CN



Crude ^{19}F NMR spectra for 9c'-Me & 9c-Me' in CD_3CN



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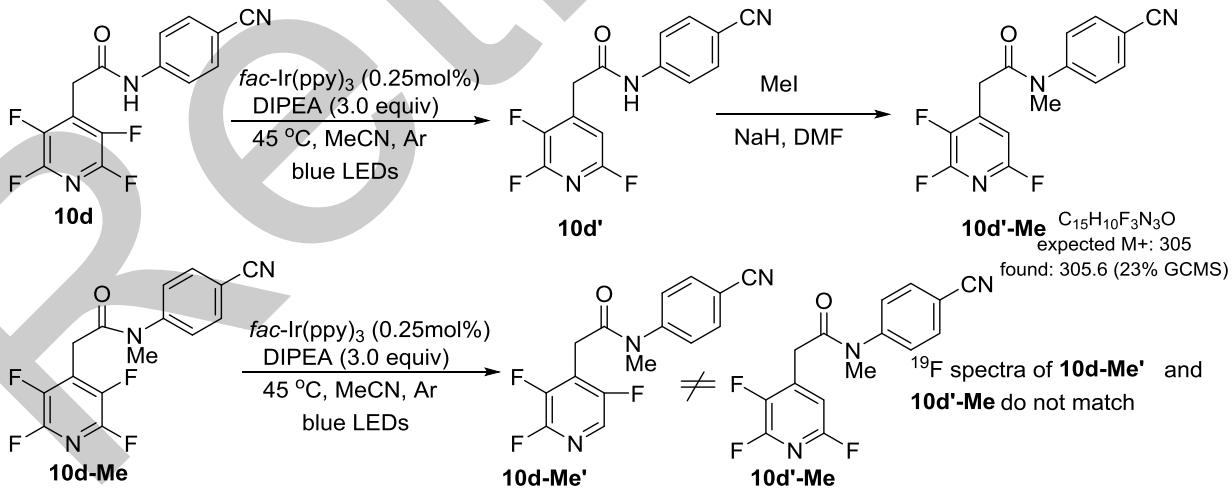
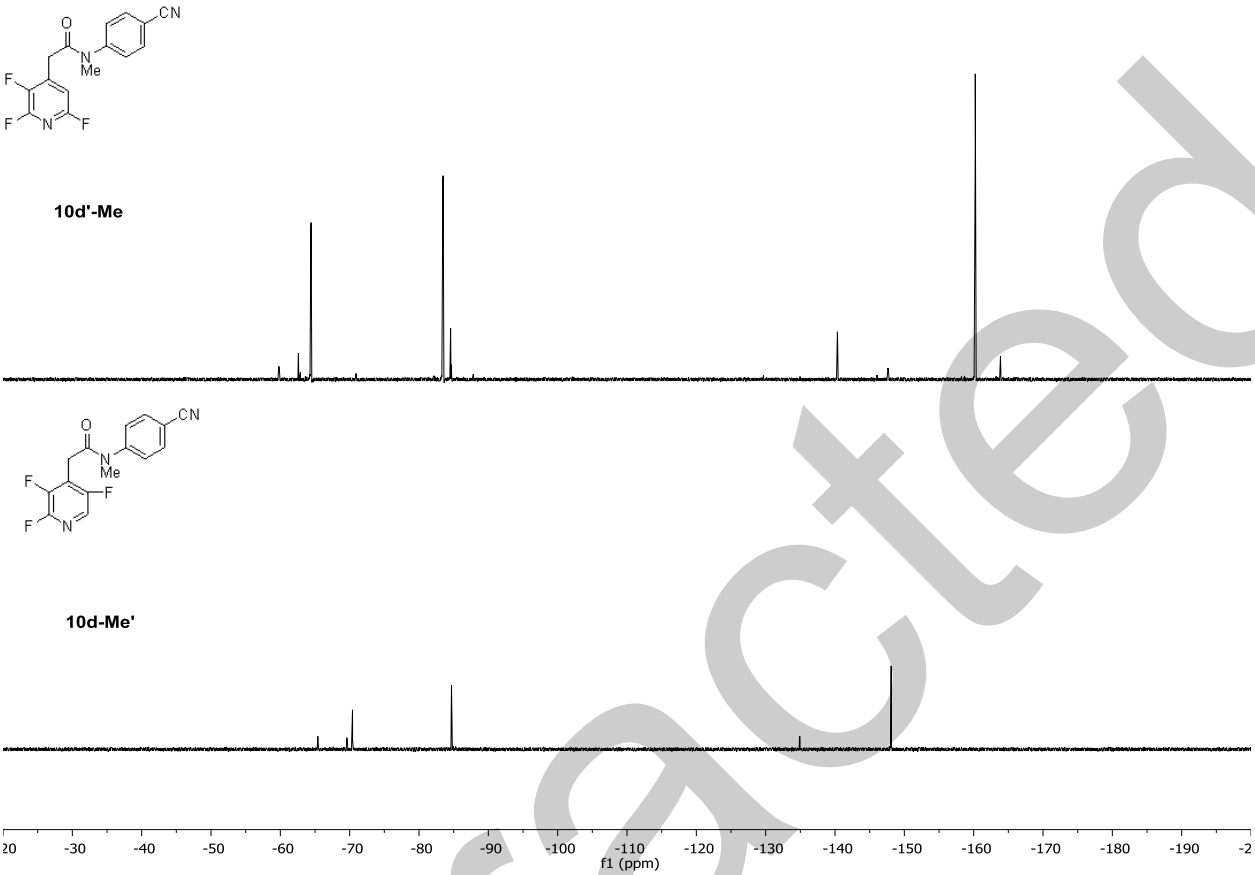
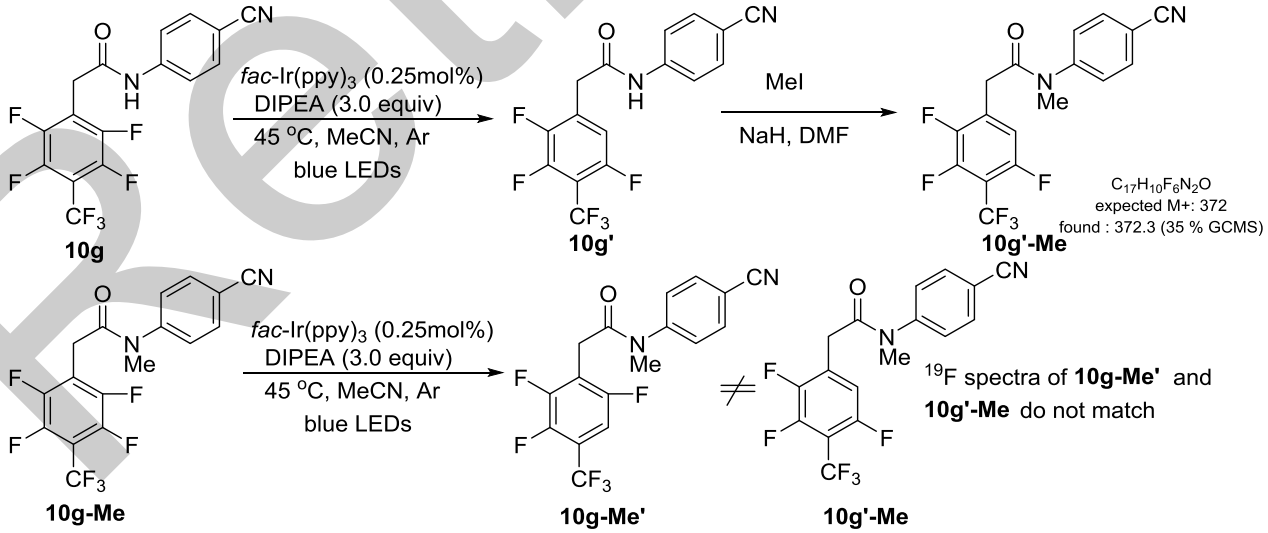


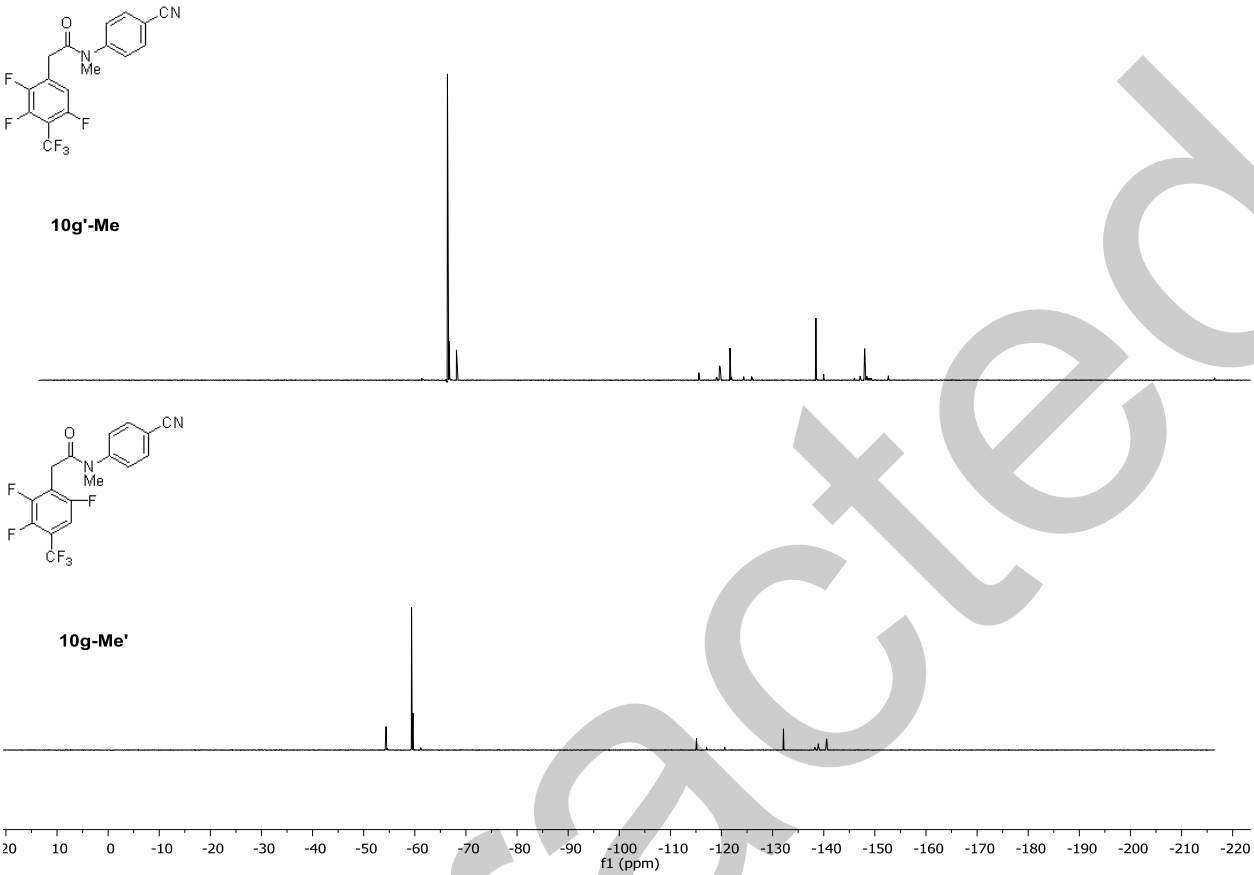
Crude ^{19}F NMR spectra for 10d'-Me & 10d-Me' in CD_3CN



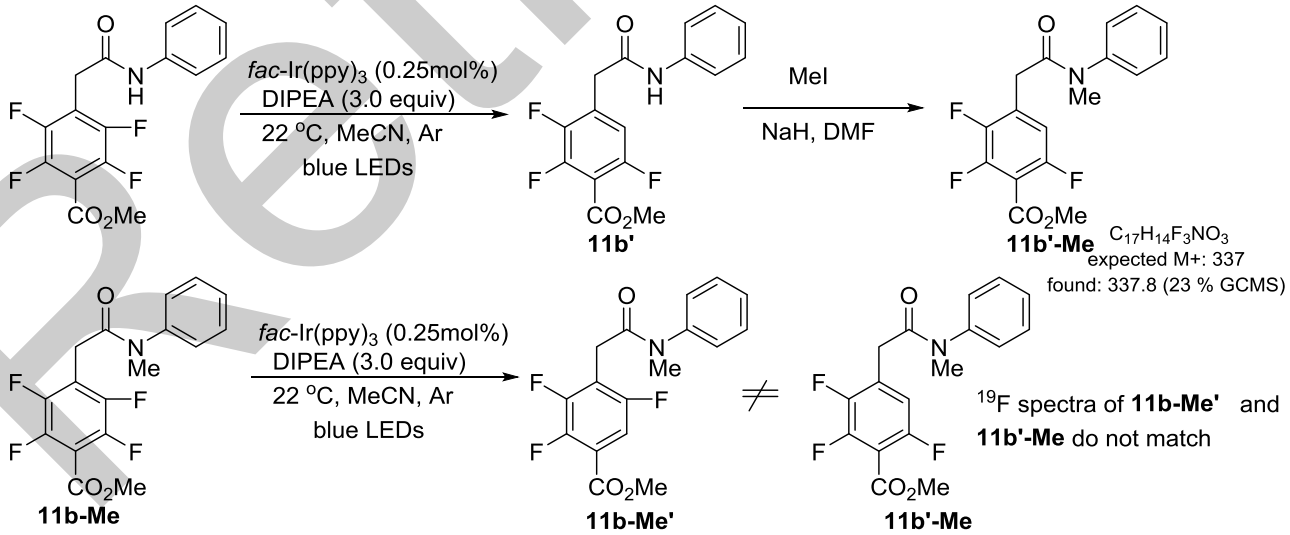
Confirmation of fluorine regiochemistry via synthesis of 10g'-Me & 10g-Me' in CD_3CN



Crude ^{19}F NMR spectra for 10g'-Me & 10g-Me' in CD_3CN



Confirmation of fluorine regiochemistry via synthesis of ^{19}F NMR spectra for 11b'-Me & 11b-Me' in CD_3CN



Crude ^{19}F NMR spectra for 11b'-Me & 11b-Me' in CD_3CN

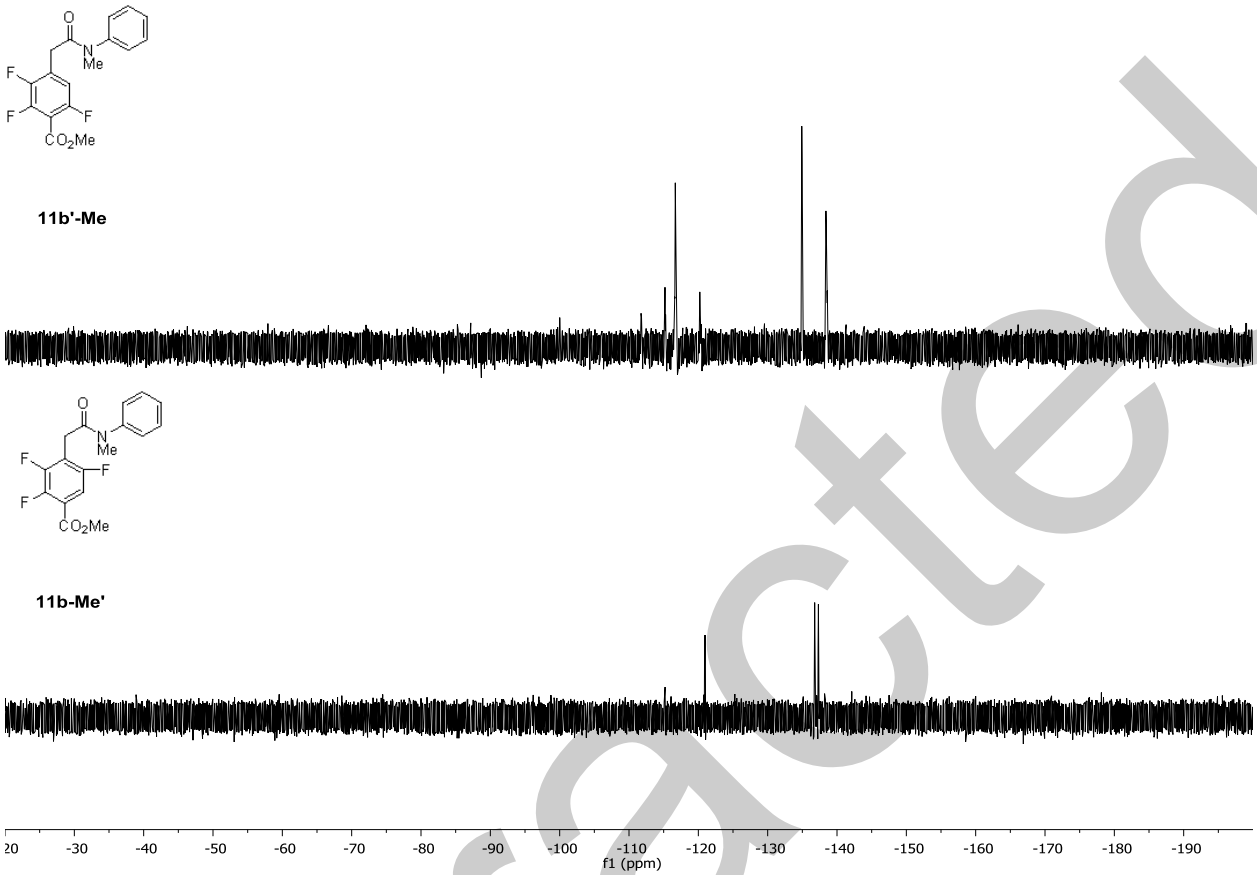


Photo-HDF 7a reaction

Evidence that the para-HDF occurs first is seen in that early in the reaction it is the dominant product. Ultimately, this product is consumed to form di-HDF product, which is only a minor product in the spectrum below. Acetonitrile was removed under reduced pressure and then the crude was dissolved in $CDCl_3$ for NMR analysis.

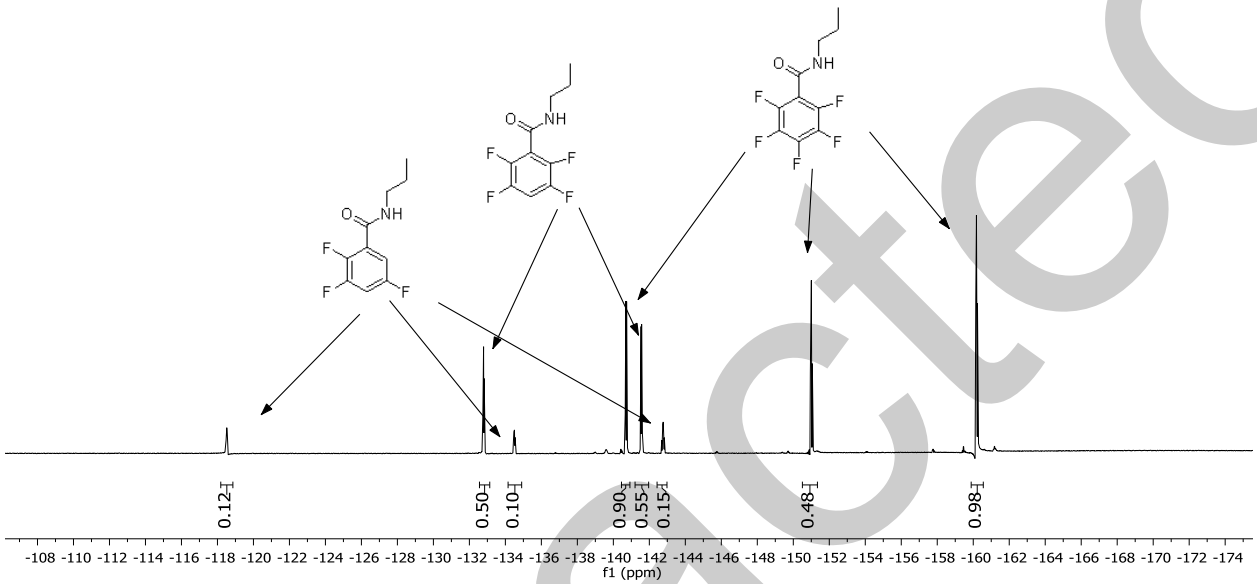
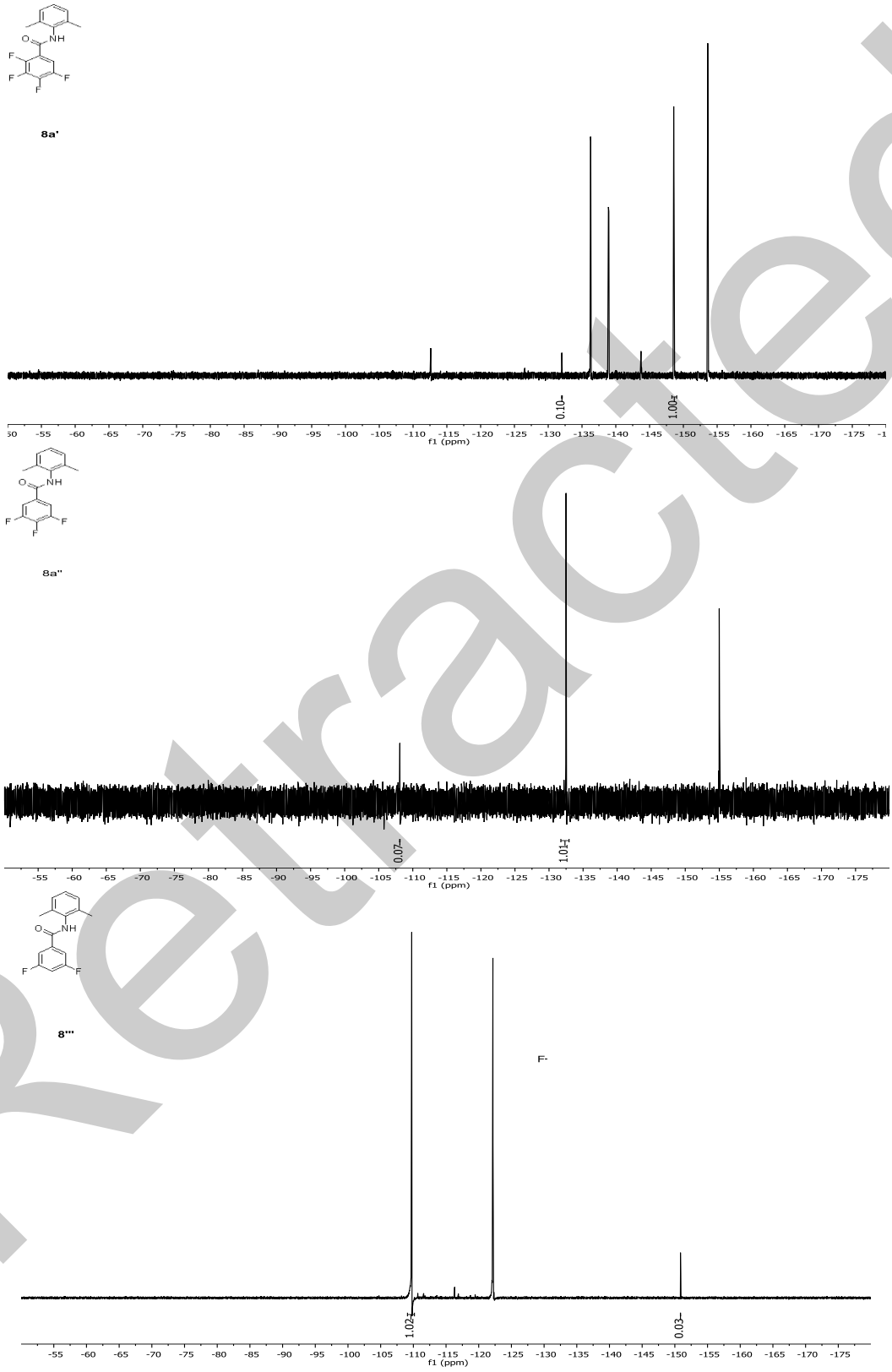

0.12
0.50
0.10
0.90
0.55
0.15
0.48
0.98
-108 -110 -112 -114 -116 -118 -120 -122 -124 -126 -128 -130 -132 -134 -136 -138 -140 -142 -144 -146 -148 -150 -152 -154 -156 -158 -160 -162 -164 -166 -168 -170 -172 -174
f1 (ppm)

Photo-HDF 8a reaction: ^{19}FNMR for the crude 8a', 8a'', 8a'''



Model Calculations

It was expected that the bulky amide would lead to greater thermal control as a result of steric decompression which occurs when rotation about the N-CO bond occurs, and that this was facilitated by sterically large aryl substituents. This is supported by MM2 calculations (below). Minimization of the bulky dimethyl structure (Fig **1a**) gives a dihedral angle O-C-N-H that is 26^{o} which positions the acidic proton further below the plane of the fluoroarene and is seen more clearly in the second image (Fig **1b**). In comparison, the same O-C-N-H dihedral angle of the di-H structure (Fig **1c**) is only 12^{o}. As a consequence, the acidic proton is not as far below the plane.

A similar assessment, after directed mono-HDF has occurred, indicates that the bulky amide will maintain a substantial deviation from planarity, with an O-C-N-H dihedral angle of 25^{o} (Figure **1d**, bottom left), whereas the less bulky amide results in only 10^{o} deviation from planarity (figure **1e**, bottom right).

While not shown, the calculations also suggest that there would be some rotation about the *N*-aryl bond for the bulky amide, 13^{o} (left), and 1^{o} (right) for the simple phenyl amide. It is not impossible that this difference also plays a role, but we believe it is the OC-NH rotation that is primarily responsible for the greater control, which is of course, a result of faster directed-HDF compared to electronically controlled HDF.

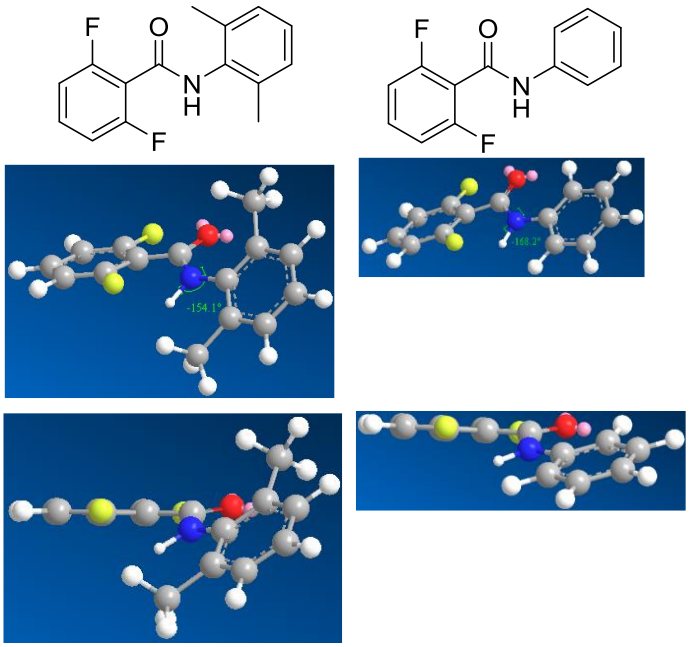


Figure 1a (top), Figure 1b (bottom) Figure 1c (top), Figure 1d (bottom)

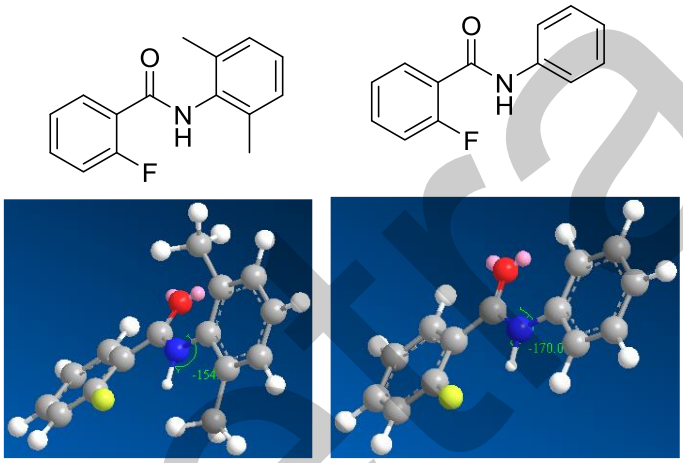


Figure 1d Figure 1e

,

Figure 1

A pseudo-Hammett plot of the directed photo-HDF study

Six NMR reactions for substrates **4e**, **4f**, **4i**, **4h**, **4k**, **4l** were set up as below. In an NMR tubes capped with NMR septa (Ace glass, part no. 9096-25) was charged tris(2- phenyl pyridinato--C^2,*N*) Iridium(III) ($Ir(ppy)_3$) (0.25 mol% catalyst solution in 1mL MeCN). **4e**, **4f**, **4i**, **4h**, **4k**, **4l** (1 equiv, 0.1 mmol) and *N*, *N*-diisopropylethylamine (3 equiv) were added to each of them. The reactions were degassed via Ar bubbling for 10 min at 0 ^oC, to avoid evaporation of *N*, *N*-diisopropylethylamine and any other volatile starting materials, and then left under positive Ar pressure by removing the exit needle and then the argon supply needle. After finishing degassing all the NMR tubes, all the NMR tubes were placed in a light bath simultaneously and the lower portion of the tubes were submerged under the water bath which was maintained at 45 ^oC. The NMR tubes were taken out from light bath at 0 min, 30 min, 1 h, 2 h, 3 h, 4 h, 6 h, 8h, 9h, 10h, and 24 h intervals and wrapped with aluminum foil to block the light during transport to the NMR. ^{19}F NMR spectra were recorded and conversions (Figure **1**) and rate of product formation were calculated by integrating NMR signals of reactant and product. At low conversion (ca. 20%), an average rate was determined and a Hammett plot was constructed.

Catalyst turnover experiment and calculation

To assess the catalalyst robustness the following TON experiment was carried out using 3-methyl-*N*-(perfluoropyridin-4-yl)butanamide (**4d**) as the substrate. An NMR tube was charged with tris(2- phenyl pyridinato-C^2,*N*) Iridium(III) ($Ir(ppy)_3$) (0.00000244 mmol in 1 mL of MeCN) The catalyst solution was made as follows. 16.0 mg of $Ir(ppy)_3$ was dissolved in 100.0 mL of MeCN, and 1.00 mL of the resulting solution was diluted with 9.00 mL of MeCN, and then 1.00 mL of this solution was further diluted with 9.00 mL of MeCN, to give the stock

solution which was used above) and fitted with rubber septum (Ace glass, part no. 9096-25), **4d** (0.100 mmol, 25.0 mg, 1.00 equiv) and *N*,*N*- diisopropylethylamine (0.300 mmol, 54.1µL, 3.00 equiv) were added. The reaction was degassed via Ar bubbling (at 0 °C) for 10 min and septum was parafilmed tightly to avoid exposure to air. The tube was placed in a light bath (description above) and the lower portion of the tube was submerged under the water bath which was maintained at 45 °C. The reaction progress was monitored periodically by ^{19}F NMR. After 48 h, 76 h, 120 h, the NMR tube was degassed via Ar bubbling for 10 min in an ice bath and the septum was again parafilmed. After X h and ~80% conversion, an additional 1.00 equiv of **4b** and 3.00 equiv. of DIPEA were added, and then degassed as previously described. After 158 hours no noticeable product formation difference was observed in the ^{19}F NMR. Therefore, we stopped the reaction. The overall conversion was 64%.

Total substrate 0.200 mmol **4b**

Total catalyst 0.00000244 mmol $Ir(ppy)_3$

Max turnover number= 0.200 mmol/0.00000244 mmol = 81,967 TON

81,967 TON * 64% conv. = 52,459 TON, or 52,500 TON

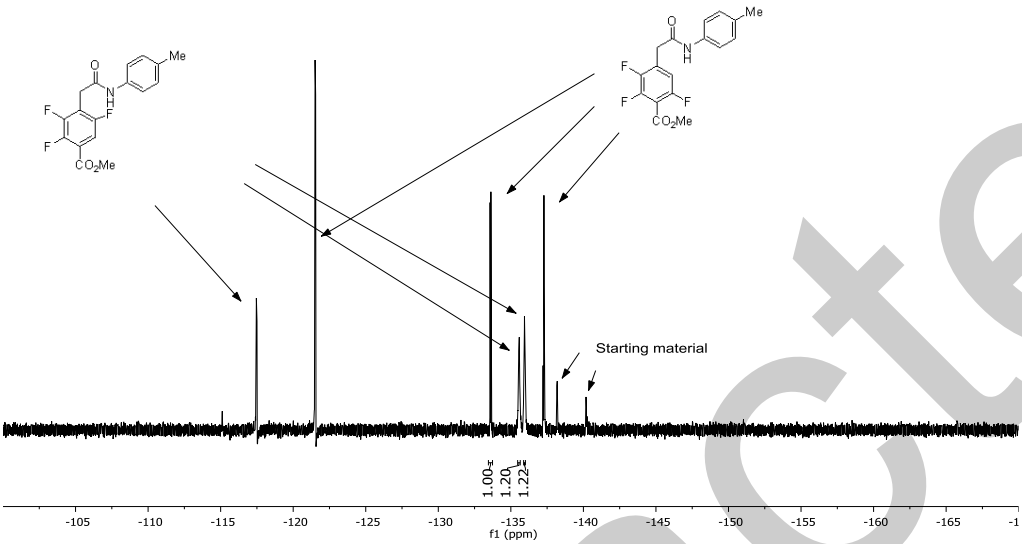
Assessing the temperature effect with respect to 7b

To assess the temperature effect, two NMR reactions for substrate **7b** were set up as below. In an two NMR tubes capped with NMR septa (Ace glass, part no. 9096-25) was charged tris(2-phenyl pyridinato-C 2 , N) Iridium(III) ($Ir(ppy)_3$) (0.25 mol% catalyst solution in 1mL MeCN). **7b** (1 eq, 29.0 mg, 0.100 mmol) and *N, N*-diisopropylethylamine (3 eq) were added for each of them. The reactions was degassed via Ar bubbling for 10 min at 0 °C, to avoid evaporation of *N*,

N-diisopropylethylamine and any other volatile starting materials and then left under positive Ar pressure by removing the exit needle and then the argon supply needle. After finishing degassing the two NMR tubes, the first NMR tube was placed in light bath at 45 °C, and the second one was placed in light bath at 23 °C. ^{19}F NMR spectra were recorded at 1 h, 3 h, 6 h, 8 h, 10 h, and 12 h. Ultimately, the first NMR reaction carried out to furnish **7b'** product during the reaction time. In contrast, the second NMR reaction carried out to furnish **7b''** during the reaction time.

The same procedure above was used to assess the temperature effect on the regioselectivity of benzoate motif (**11 a-f**). For example, In an two NMR tubes capped with NMR septa (Ace glass, part no. 9096-25) was charged tris(2- phenyl pyridinato-C^2,*N*) Iridium(III) ($Ir(ppy)_3$) (0.25 mol% catalyst solution in 1mL MeCN). **11f** (1 equiv, 36.0 mg, 0.100 mmol) and *N*, *N*-diisopropylethylamine (3 equiv) were added for each of them. The reactions was degassed via Ar bubbling for 10 min at 0 °C, and then left under positive Ar pressure by removing the exit needle and then the argon supply needle. After finishing degassing the two NMR tubes, the first NMR tube was placed in light bath at **45 °C**, and the second one was placed in light bath at **23 °C**. ^{19}F NMR spectra were recorded at 2 h, 5 h, 6 h, 7 h, 10 h, 14 h, and 16h. In the reaction run at 45 °C, two regioisomers formed with some starting material leftover, and as time progressed di-HDF product was also detected. In the 23 °C reaction, exclusivly one product formed as the reaction proceeded (94% yield).

F2b ^{1}H NMR (400 MHz, benzene-d_6)



^{1}H NMR (400 MHz, benzene-d_6)

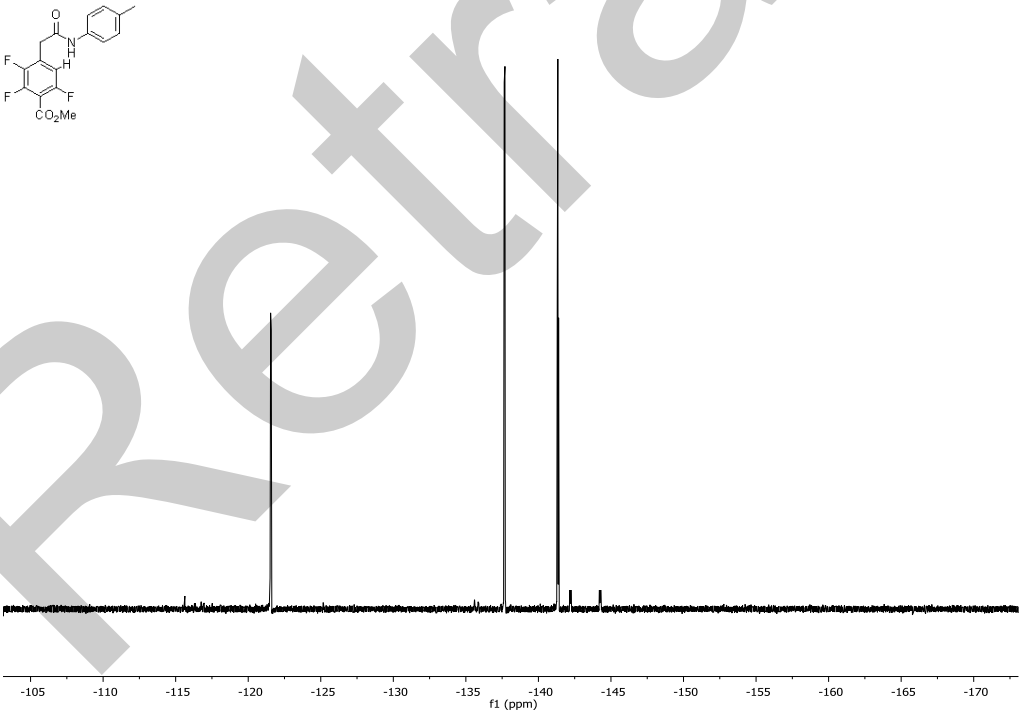
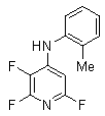


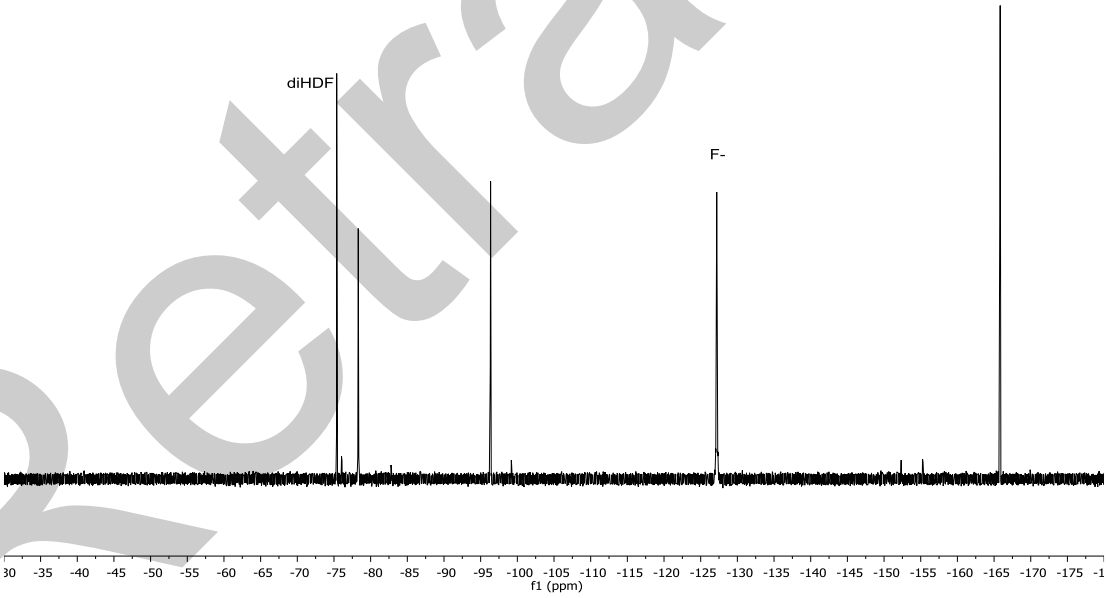
Table 2. The reactions that furnished relatively moderate yields due to over reduction.

Compound	Major over reduction
4e, 4j, 5a, 5b, 5c, 5d, 5e, 5g, 6g, 6h, 6i, 6l, 9a, 9b, 10b, 10d, 10g, 10h. 11e	**Di HDF**
7a, 7b, 7b'', 7c, 7d, 7e, 7f, 7g	**Tri HDF**

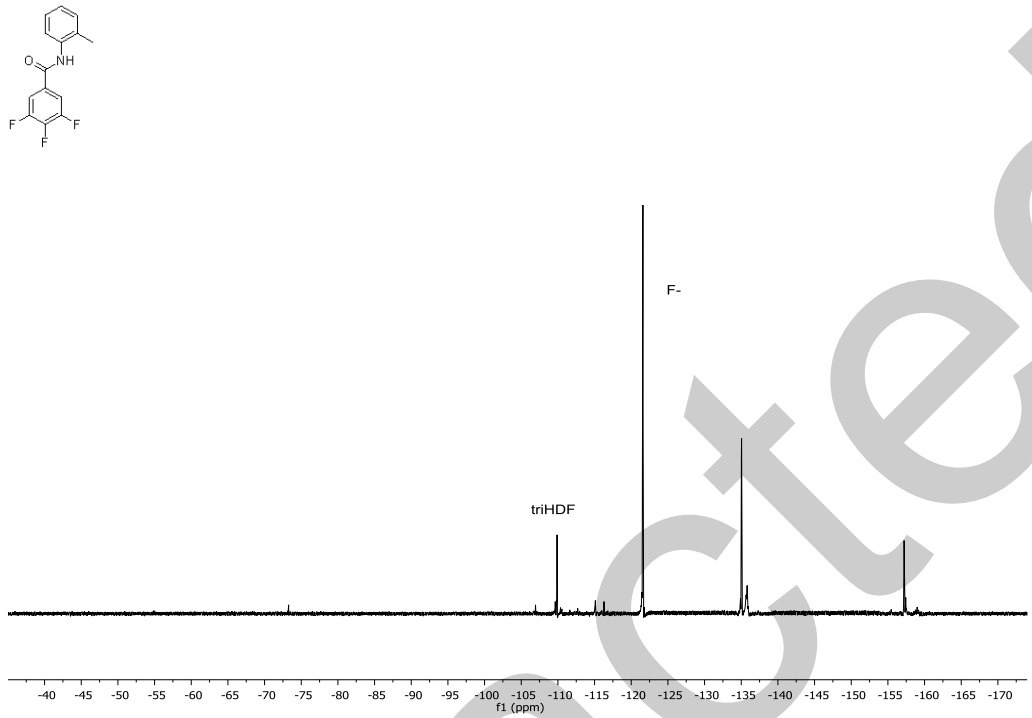
For examples:

^{19}F NMR spectra for crude product 5e

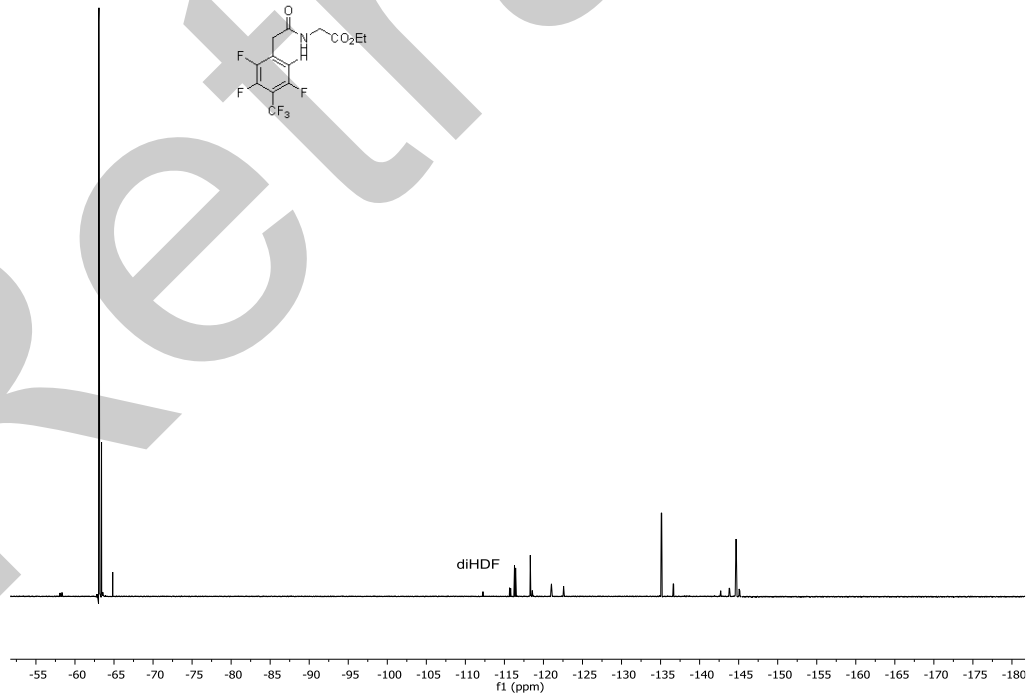




^{19}F NMR spectra for crude product 7c



^{19}F NMR spectra for crude product 10g



Stacked ^{1}H NMR spectra of 6f & 4b with different amount of DIPEA

The present data represents amide proton titration-shifts caused by addition of DIPEA base. For compound 6f , the amide proton shift prior to any addition of DIPEA was approximately 10.65 ppm. With incremental addition of DIPEA the figure **2a** shows that the amide proton shifted to the high field. Upon addition of 120 µL of added DIPEA the amide signal has completely shifted to the deprotonated compound. For compound 4b : the amide proton shift prior any addition of DIPEA was shift approximately 9.42 ppm . With addition of DIPEA the amide proton shift with observed broadening of the peak because of rapid proton exchange with DIPEA base. After addition of 120 µL the broad signal is observed approximately 6.40 ppm as shown in figure **2b**.

Figure 2a: Titration of 6f with DIPEA : Dissolve **6f** in 1 mL 1:1 v/v $CDCl_3$: MeCN , Then add DIPEA by 50 µL syringe at 23 ºC.

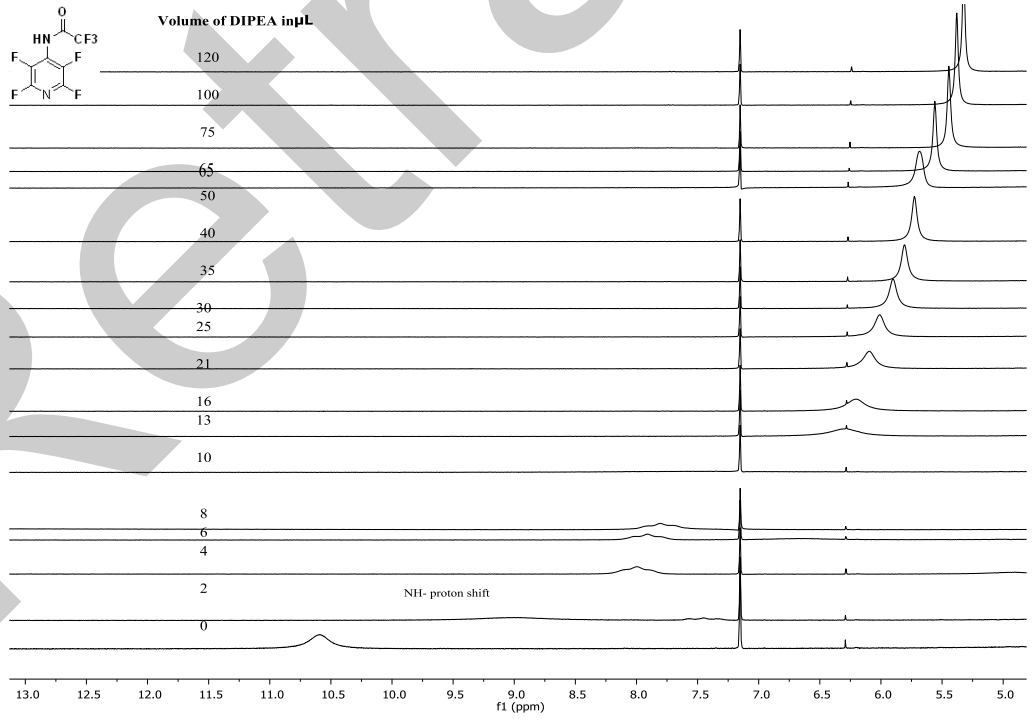
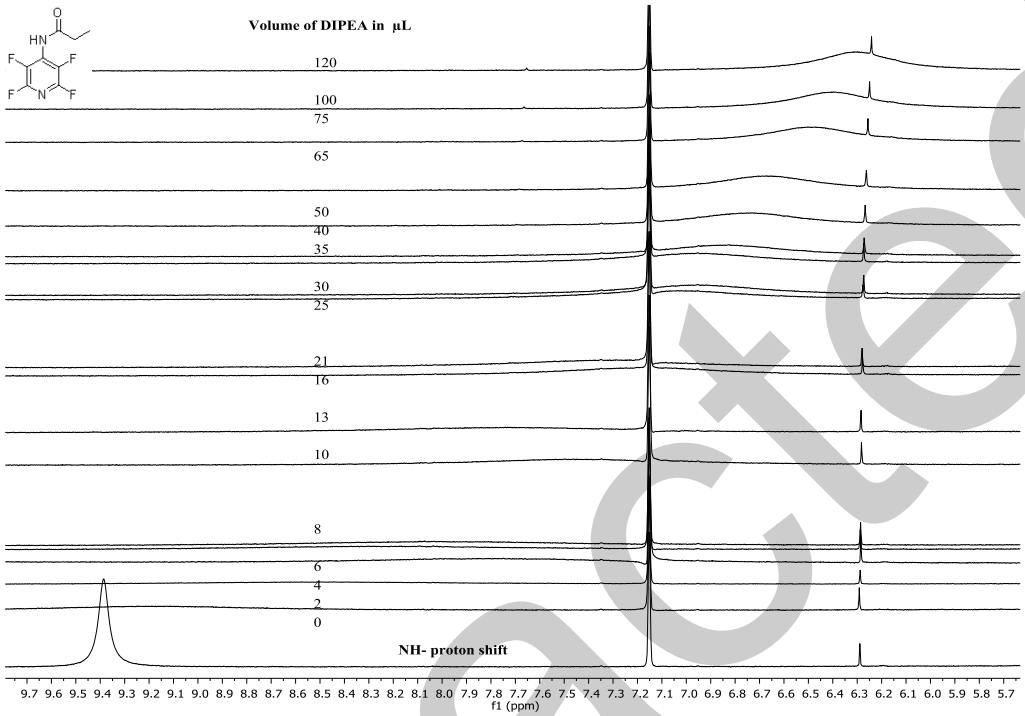


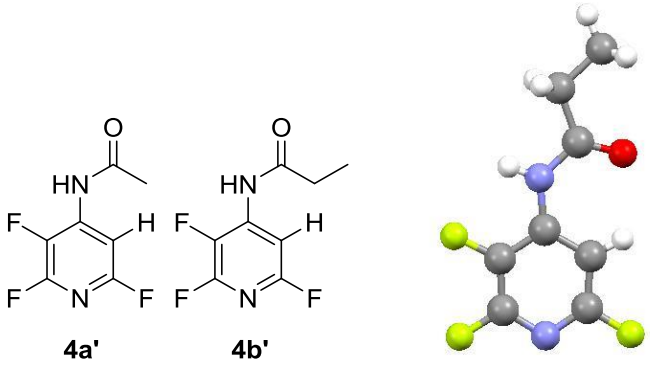
Figure 2b: Titration of 4b f with DIPEA : Dissolve 0.1 mmol of **4b** in 1 mL 1:1 v/v $CDCl_3$: MeCN , Then add DIPEA by 50 µL syringe at 23 ºC.

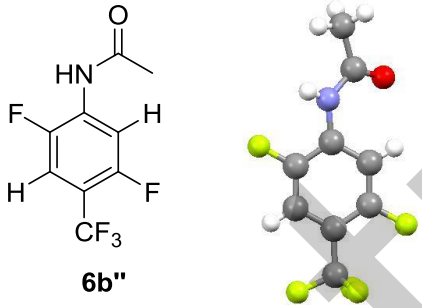


12. Single-crystal X-ray crystallography

The crystal structure of compound **4a** is shown below (Supplementary Fig. SI-1). For compound **4a**, **4b**, and **6b''** crystal were removed from the crystallization vial and immediately coated with Non-drying Immersion Oil for Microscopy (Type B, Formula Code: 1248) on a glass slide. A suitable crystal was mounted in oil on a MiTeGen loop and cooled to 100 K in a stream of cold N_2 using Bruker Kryoflex low temperature device. X-ray diffraction data for all complexes were collected on a Bruker Smart APEX II diffractometer with a CCD detector using combinations of φ and ω scans with Mo(Kα) radiation (λ = 0.71073 Å). Unit cell determination and data collection were done under APEX2 software package,[15] while data integration employed the Bruker SAINT software package.[16] Multi-scan absorption corrections were done by using SADABS.[17] All structures were solved by

direct methods and refined by full-matrix least-squares on F_2 using the SHELXTL suite.[18] The non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed geometrically and refined using the riding model. Images were generated by using Mercury CSD software.





Supplementary Fig. SI-1 X-ray crystal structure of compounds 4a', 4b', and 6b''

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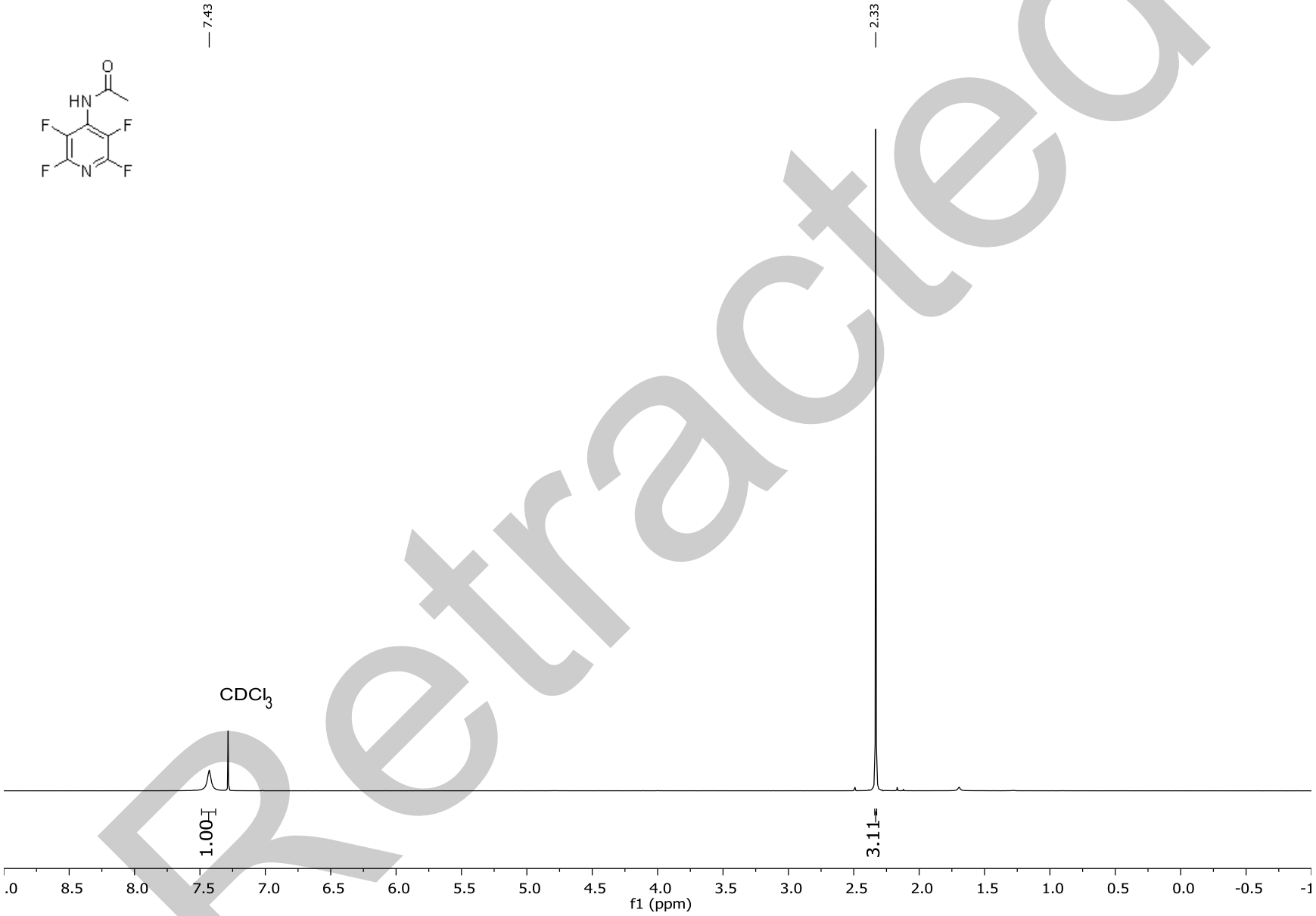
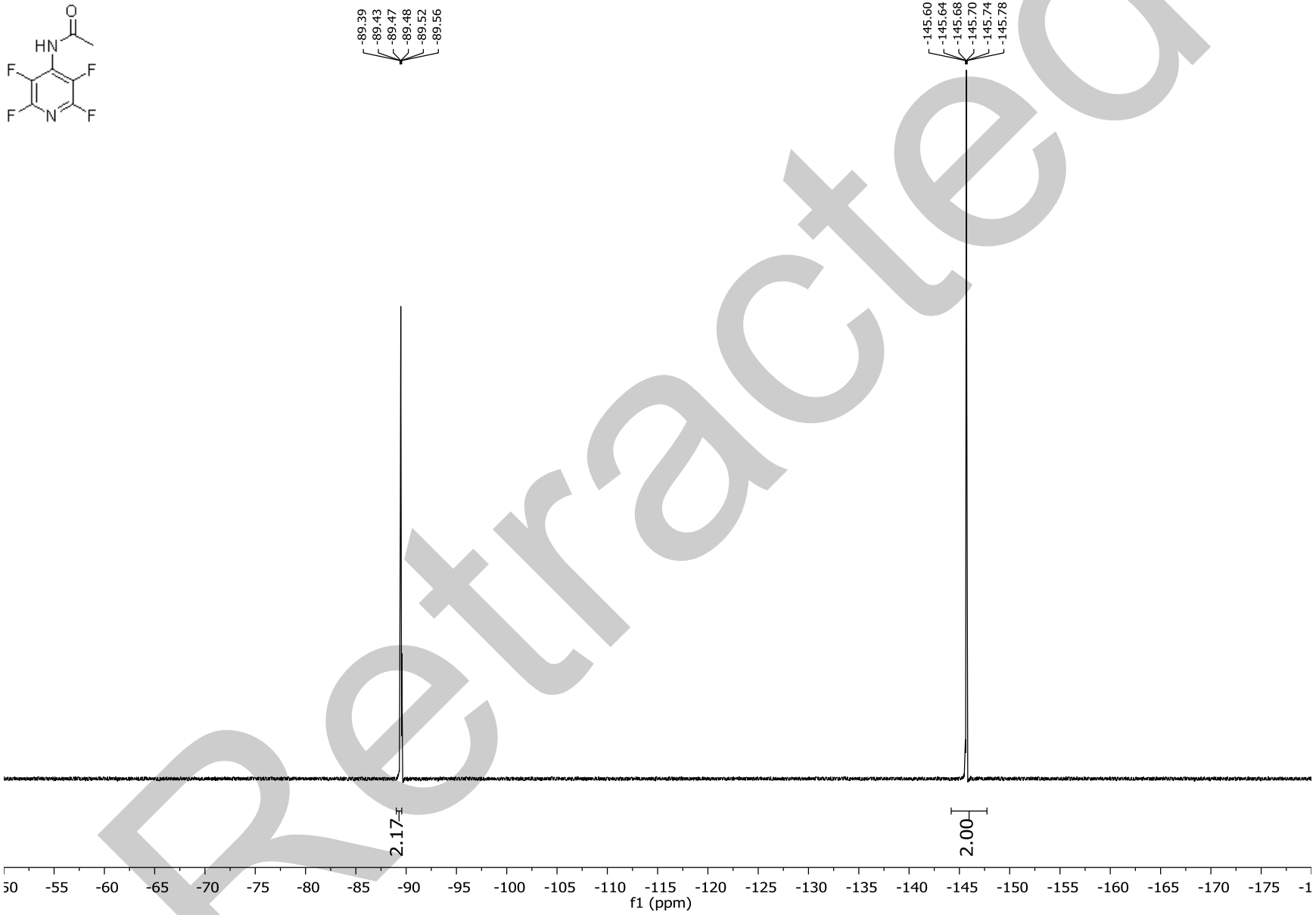
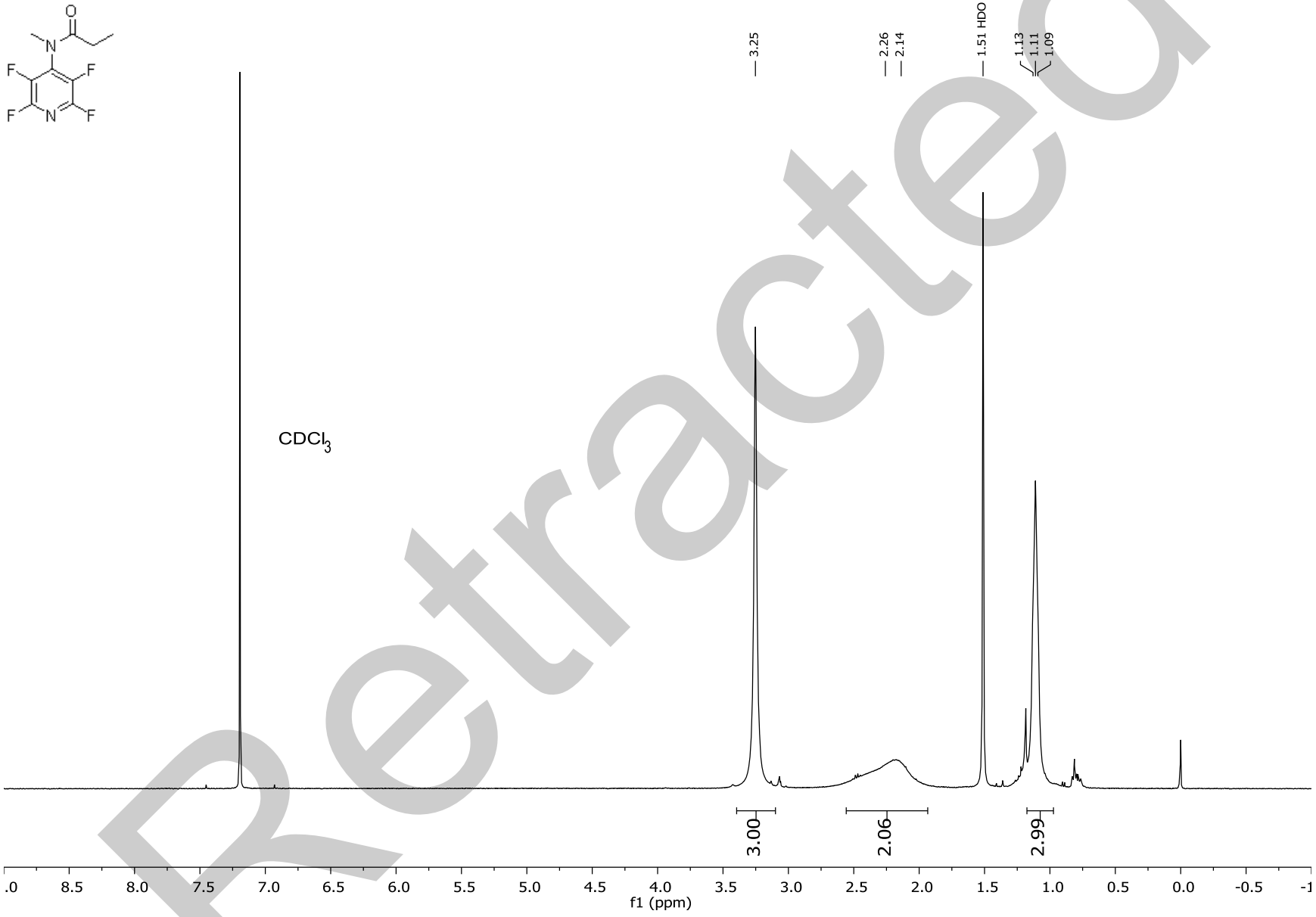
4a *N*-(perfluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



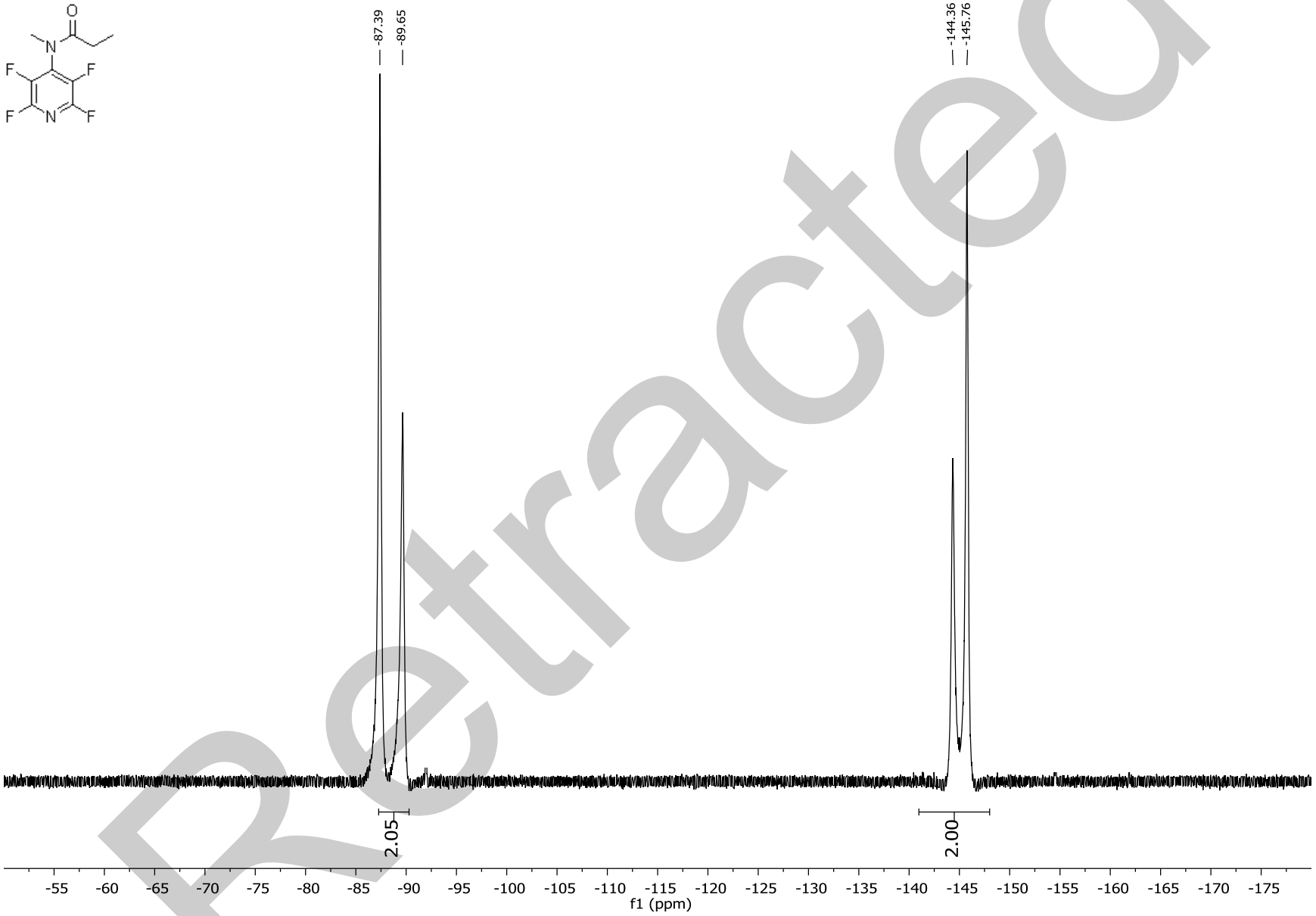
4a *N*-(perfluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



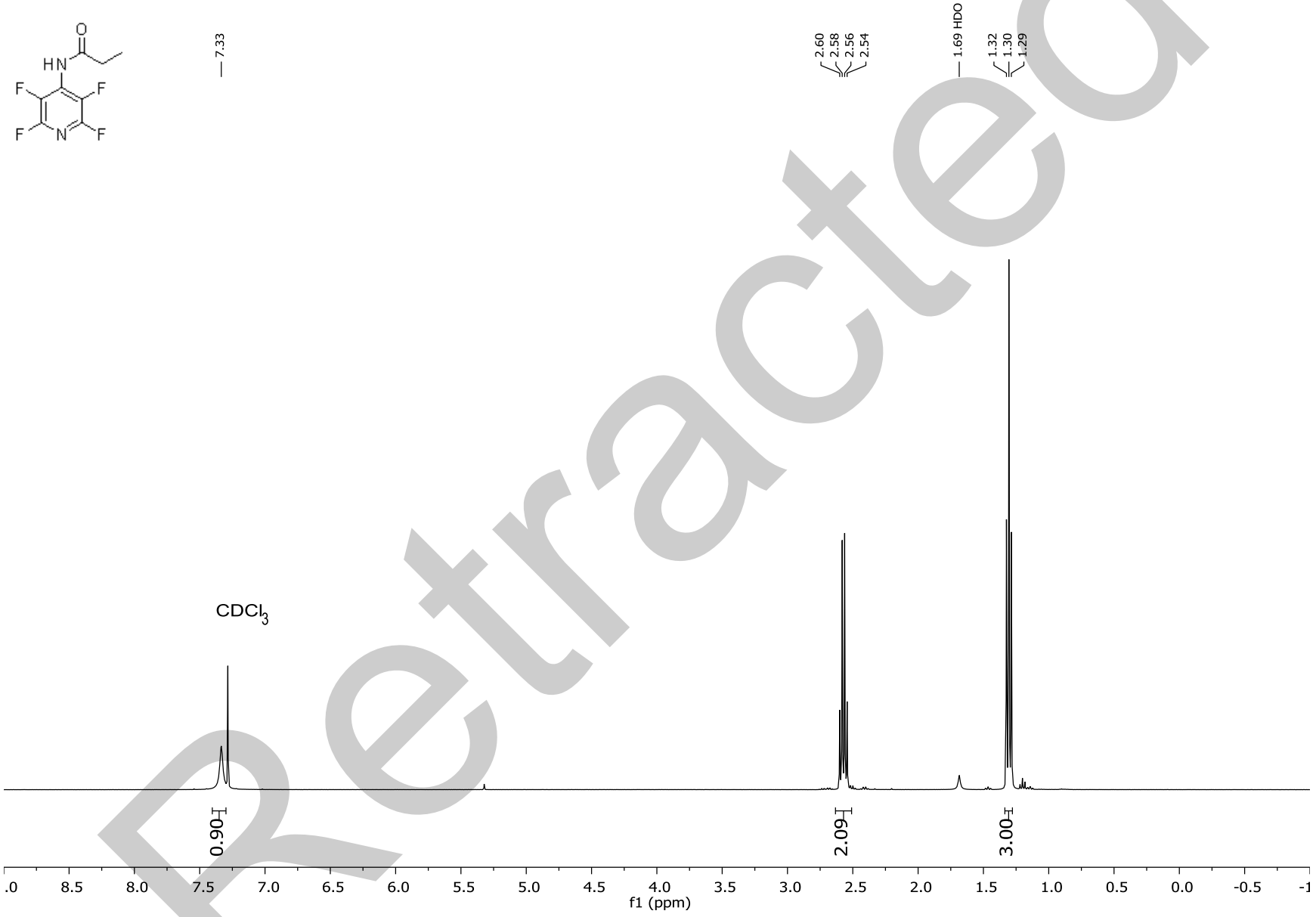
3b *N*-methyl-*N*-(perfluoropyridin-4-yl)propionamide. ^{1}H NMR (400 MHz, $CDCl_3$)



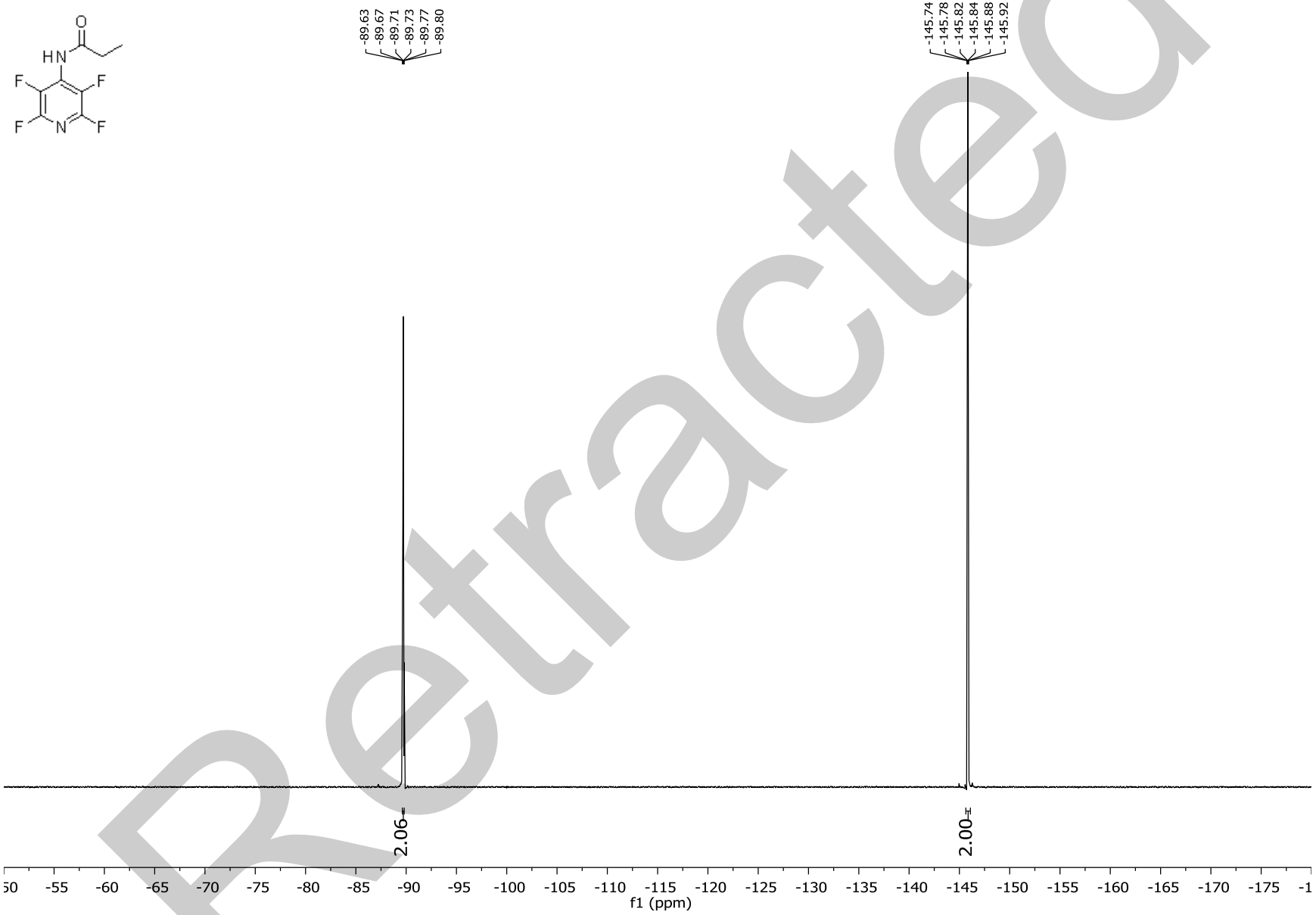
3b *N*-methyl-*N*-(perfluoropyridin-4-yl)propionamide. ^{19}F NMR (376 MHz, $CDCl_3$)



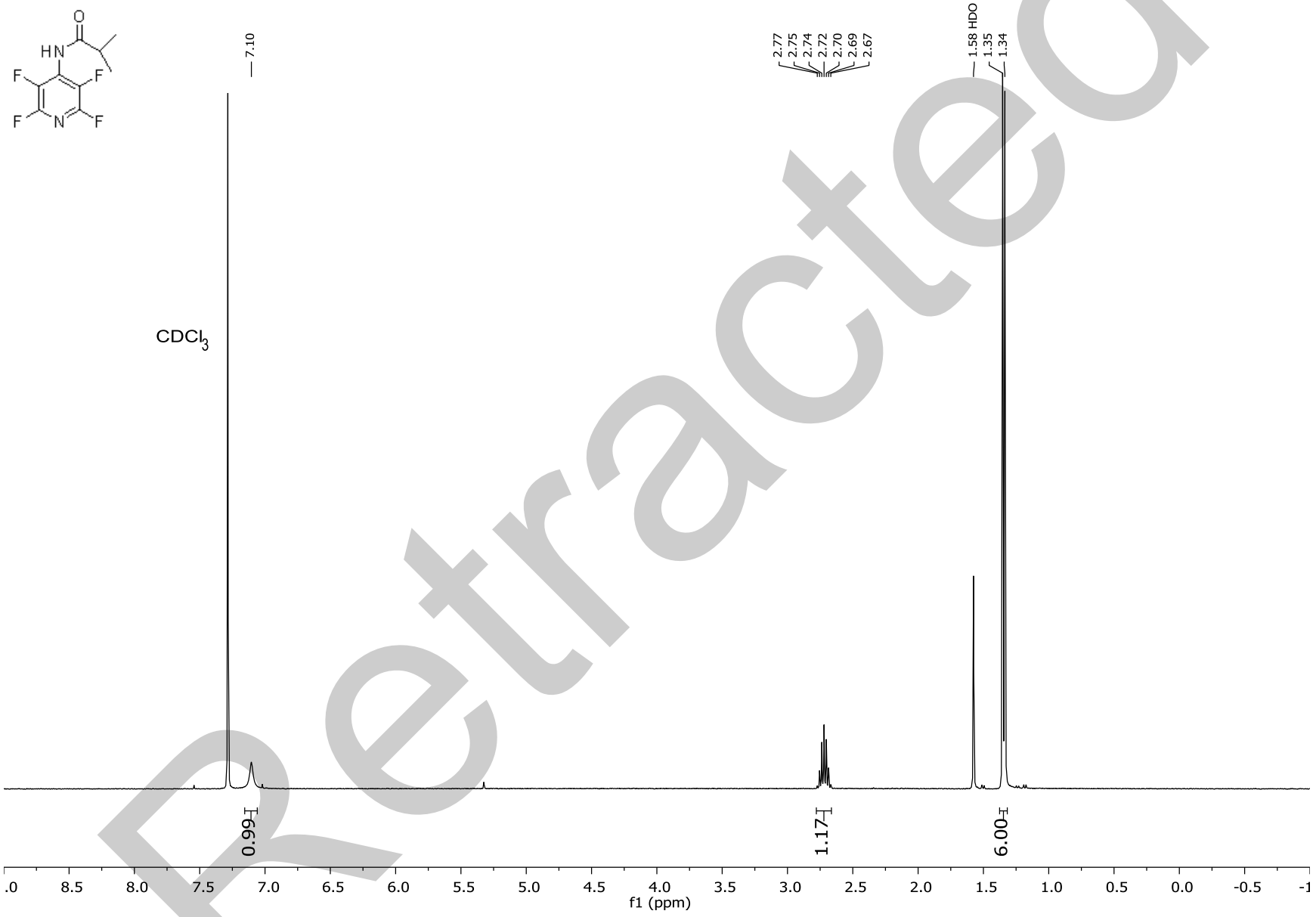
4b *N*-(perfluoropyridin-4-yl)propionamide ^{1}H NMR (400 MHz, $CDCl_3$)



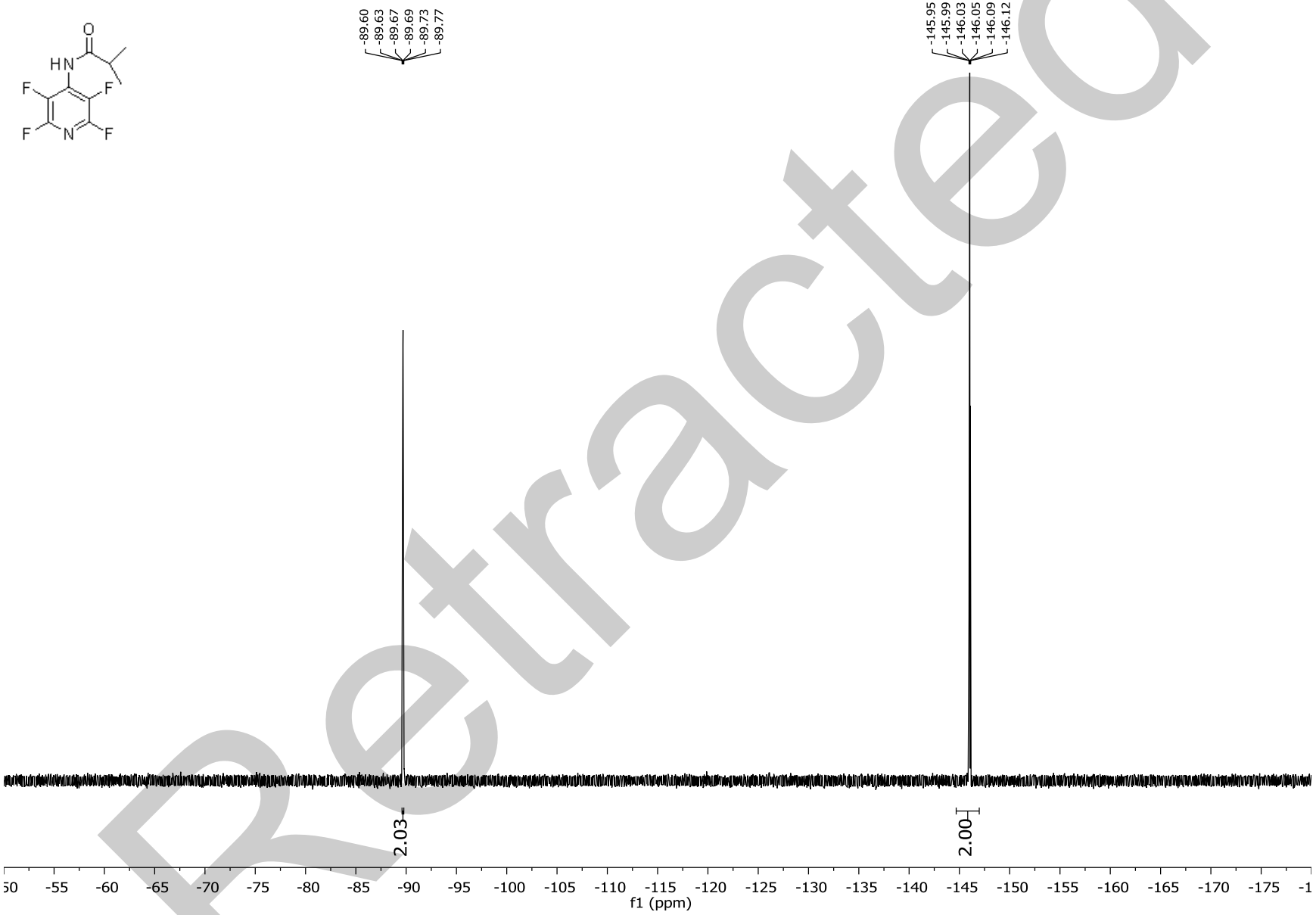
4b *N*-(perfluoropyridin-4-yl)propionamide ^{19}F NMR (376 MHz, $CDCl_3$)



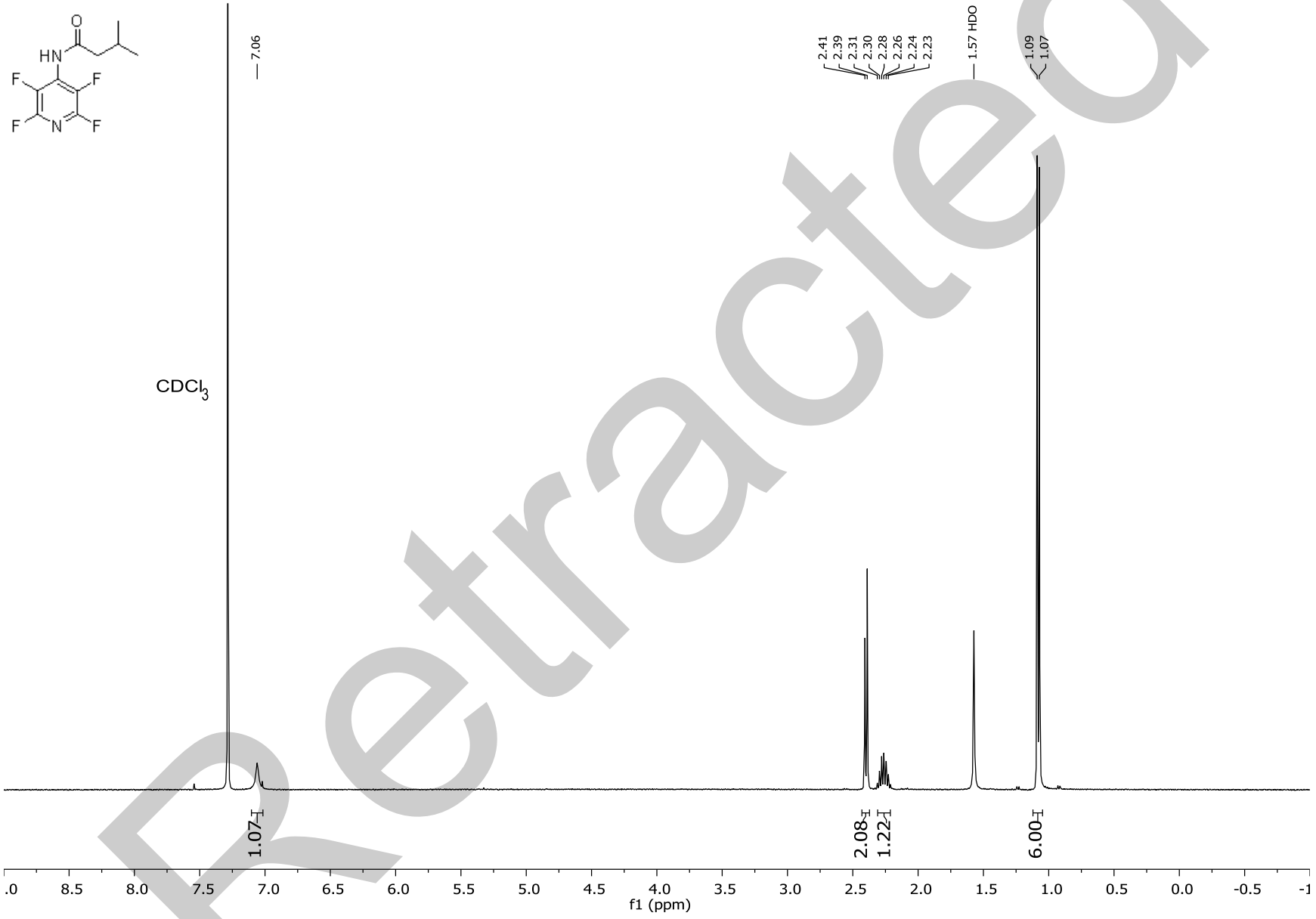
4c *N*-(perfluoropyridin-4-yl)isobutyramide ^{1}H NMR (400 MHz, $CDCl_3$)



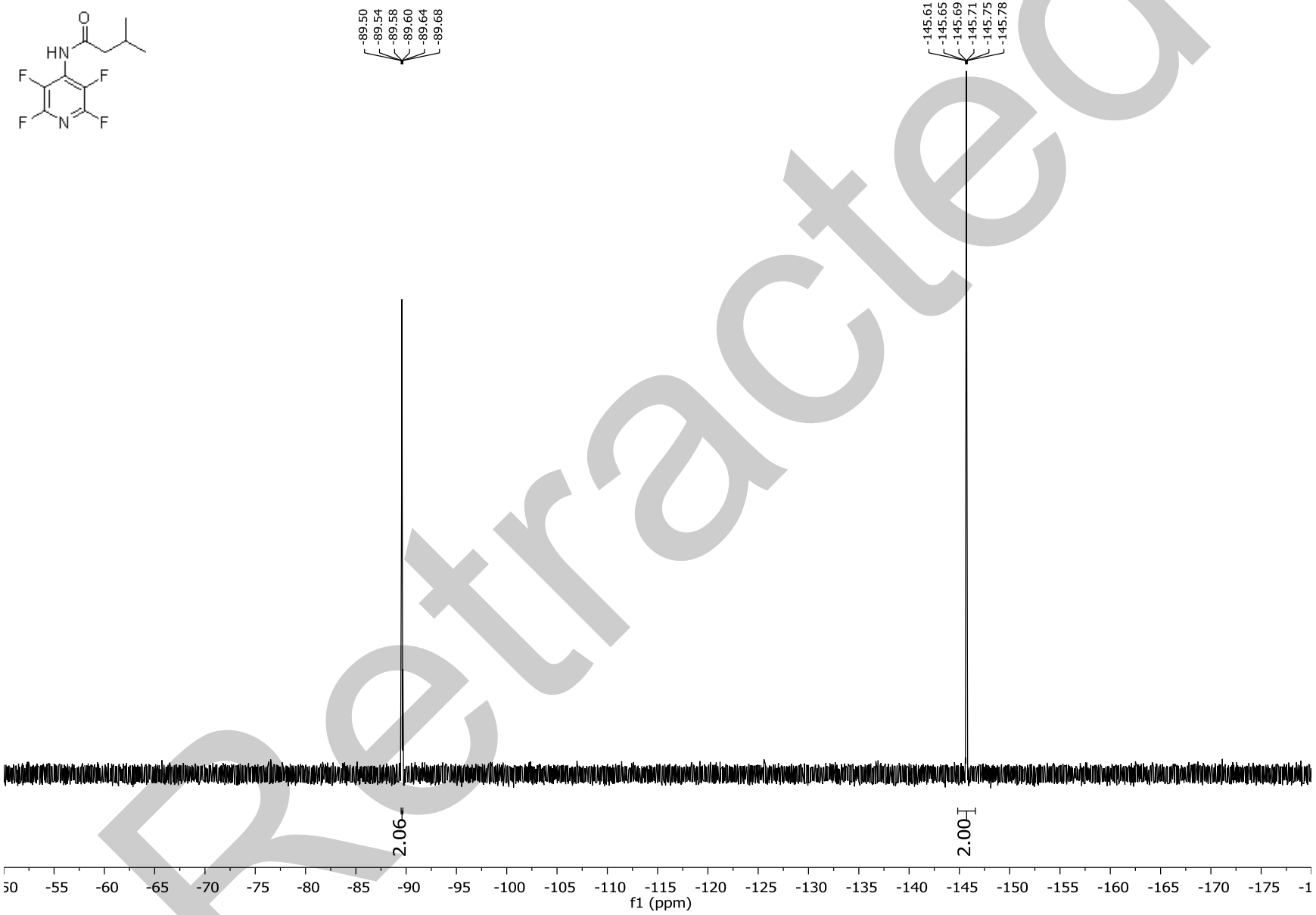
4c *N*-(perfluoropyridin-4-yl)isobutyramide ^{19}F NMR (376 MHz, $CDCl_3$)



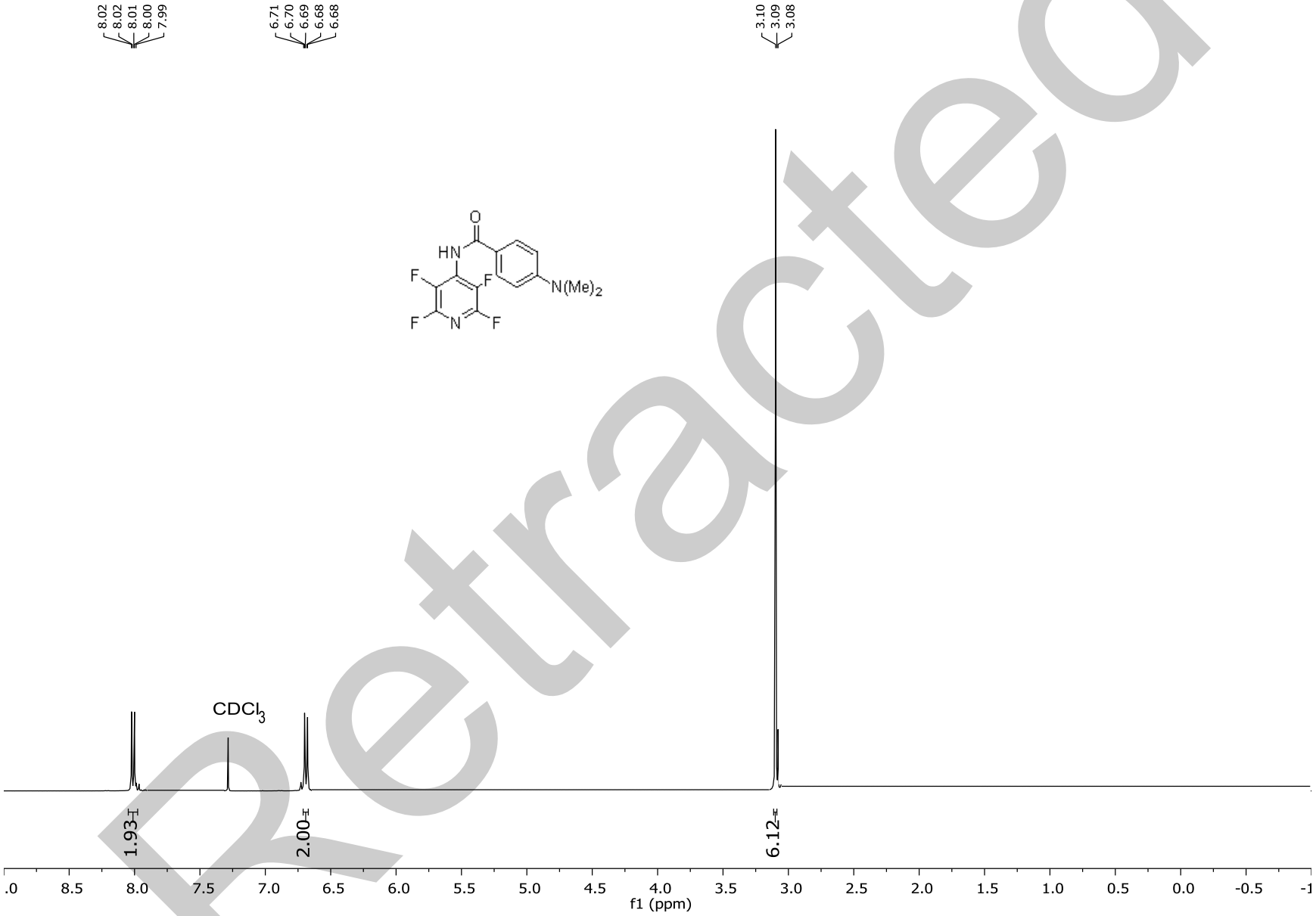
4d 3-methyl-*N*-(perfluoropyridin-4-yl) ^{1}H NMR (400 MHz, $CDCl_3$)



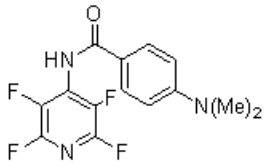
4d 3-methyl-*N*-(perfluoropyridin-4-yl)butanamide ^{19}F NMR (376 MHz, $CDCl_3$)



4e 4-(dimethylamino)-*N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)

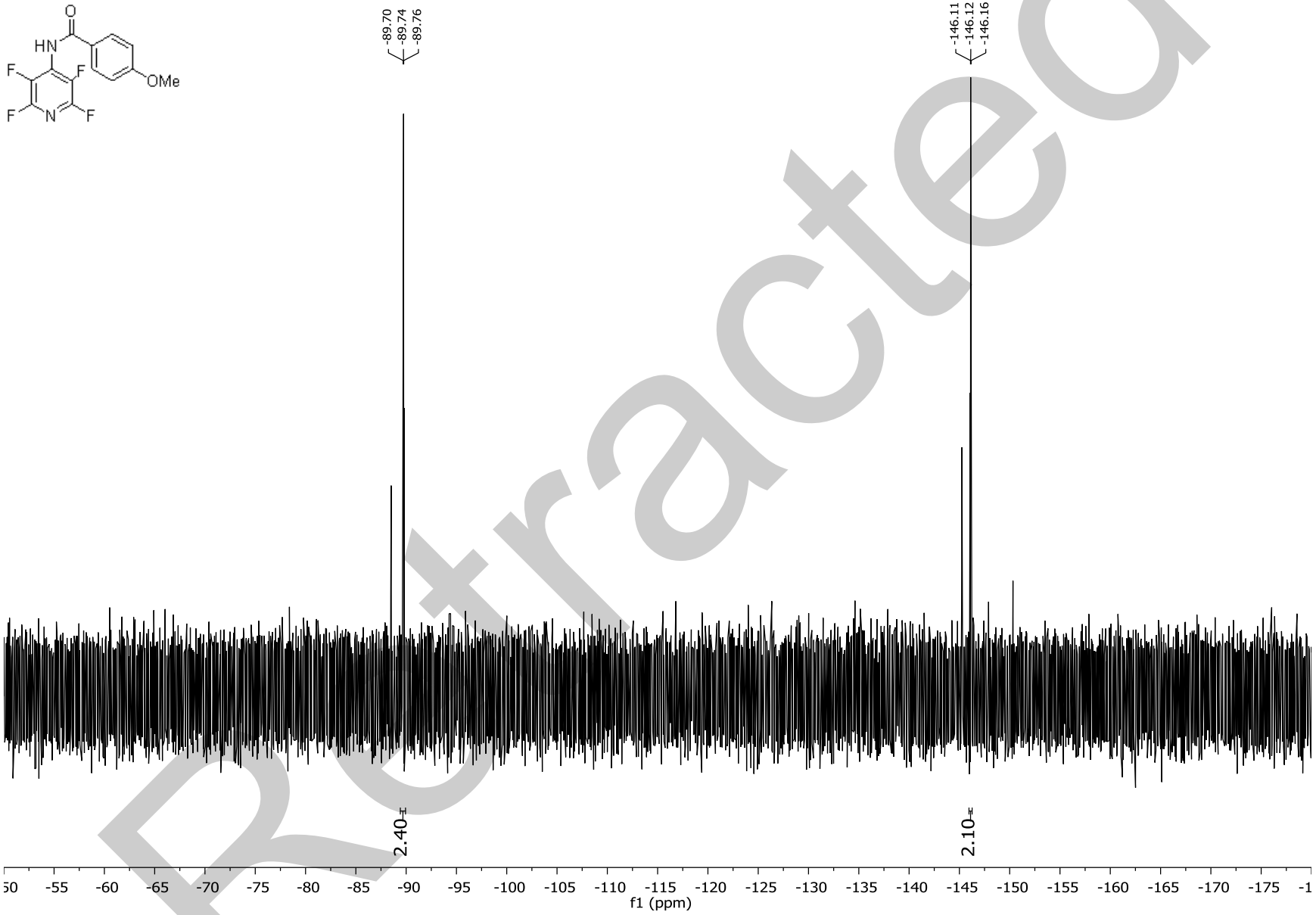


4e 4-(dimethylamino)-*N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)

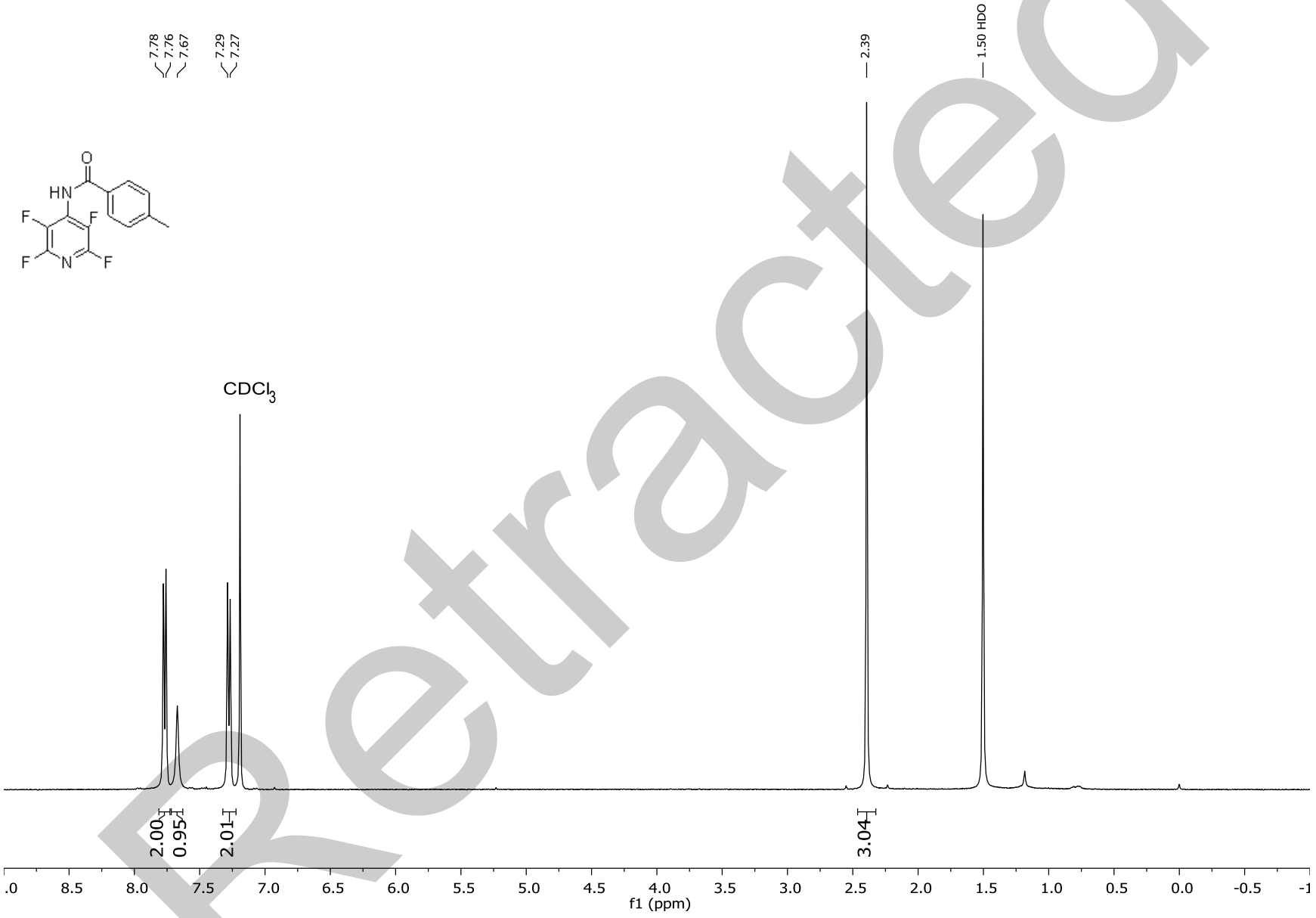


4f 4-methoxy-*N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)

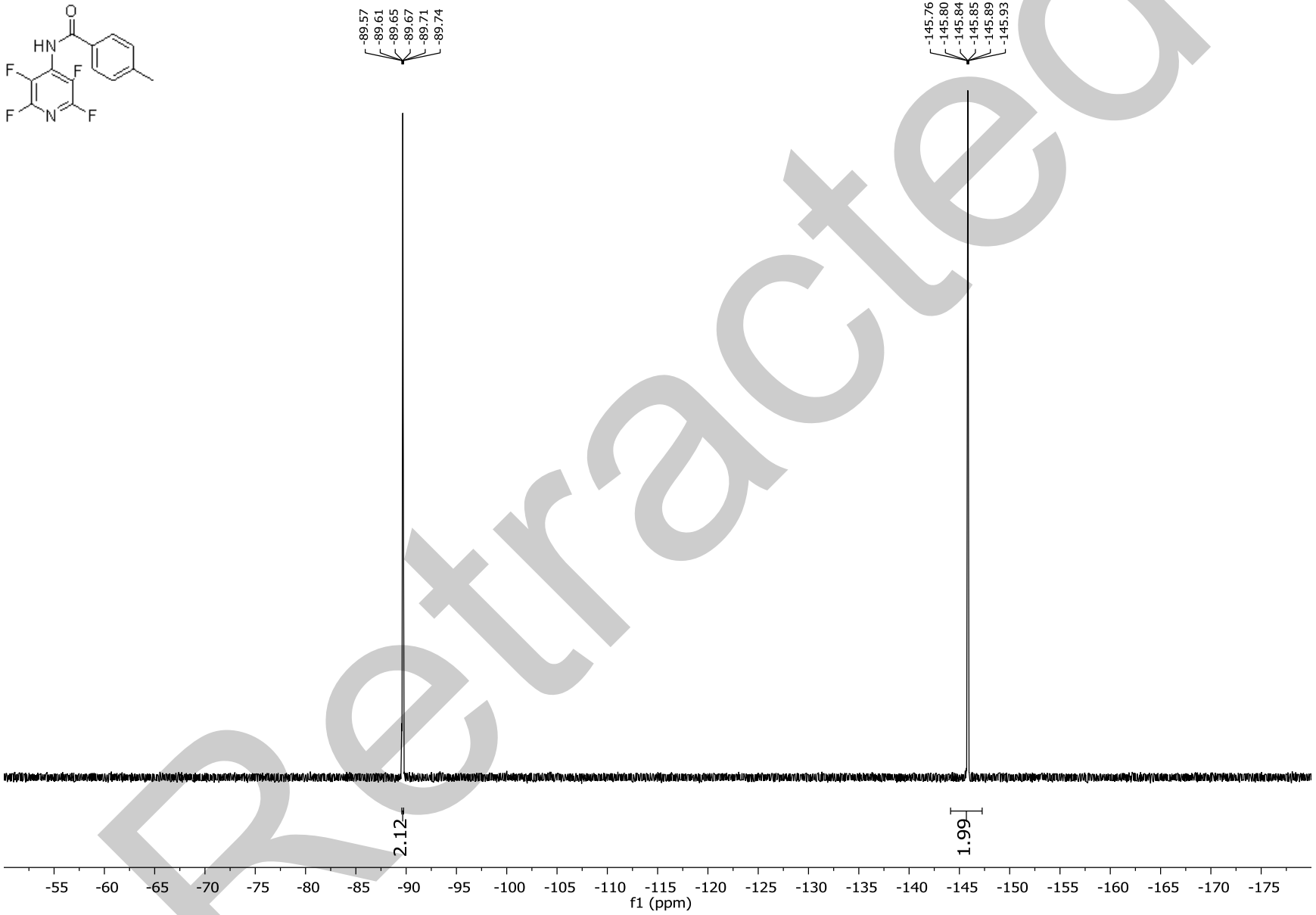
4f 4-methoxy-*N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



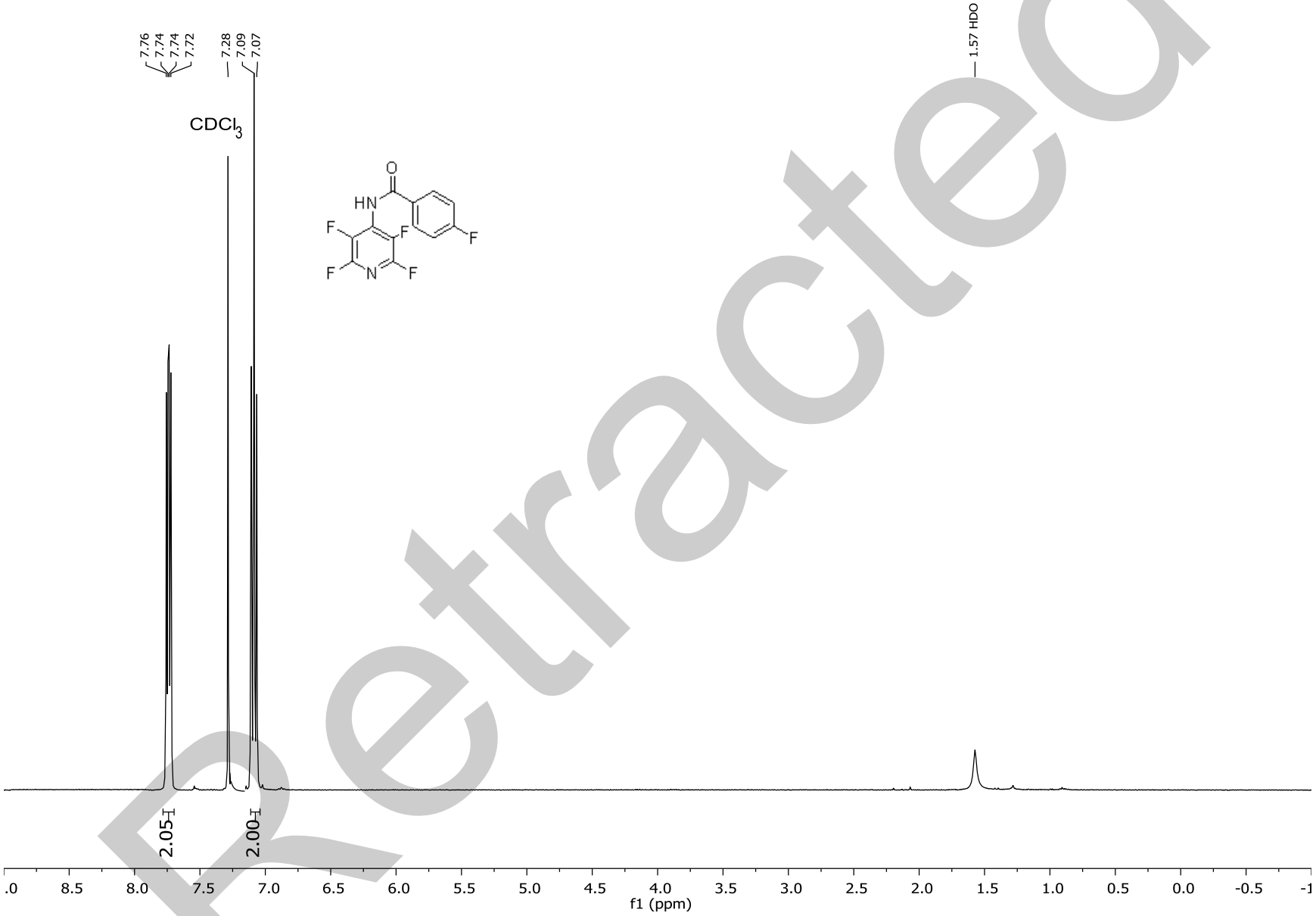
4g 4-methyl-*N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



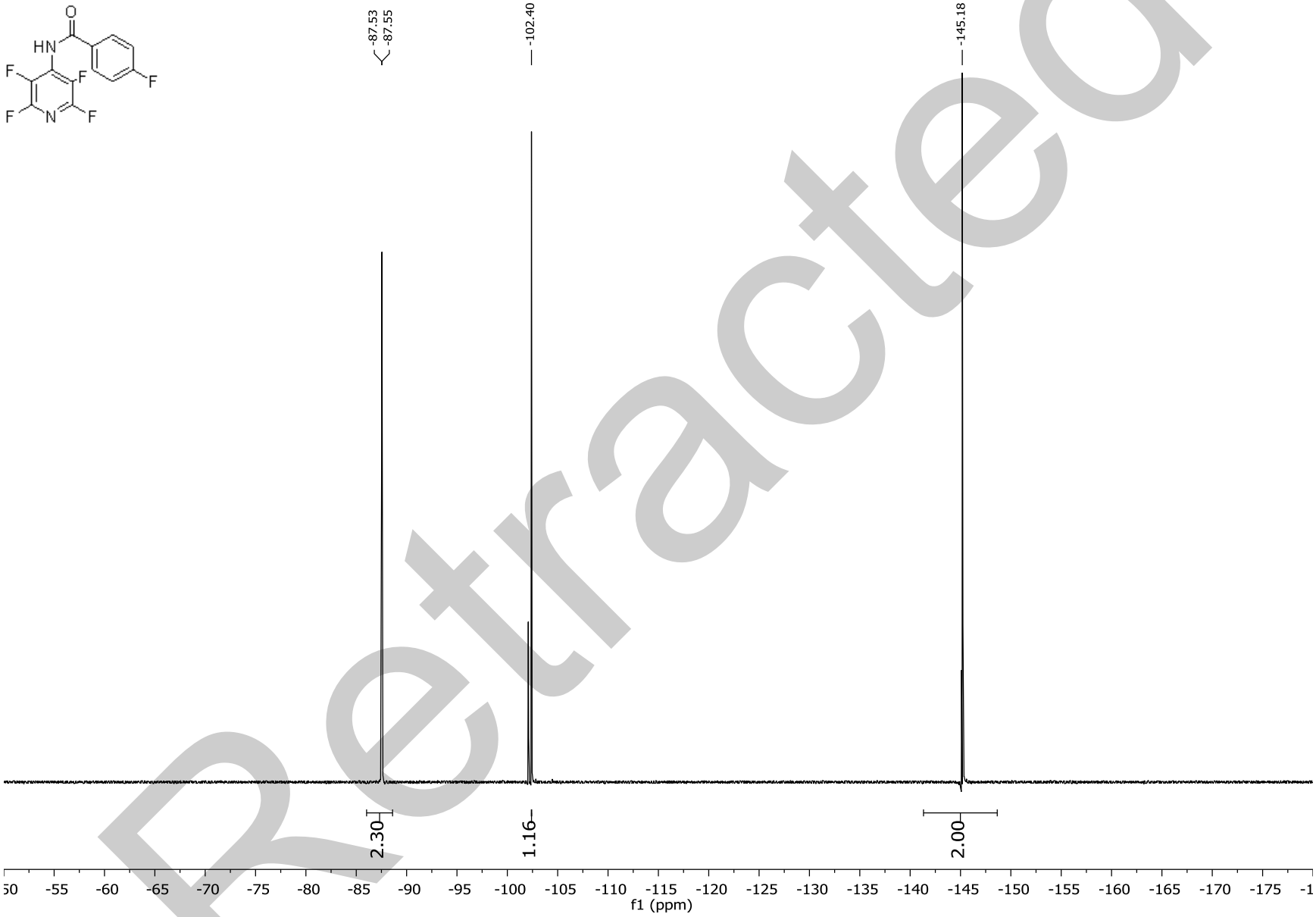
4g 4-methyl-*N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



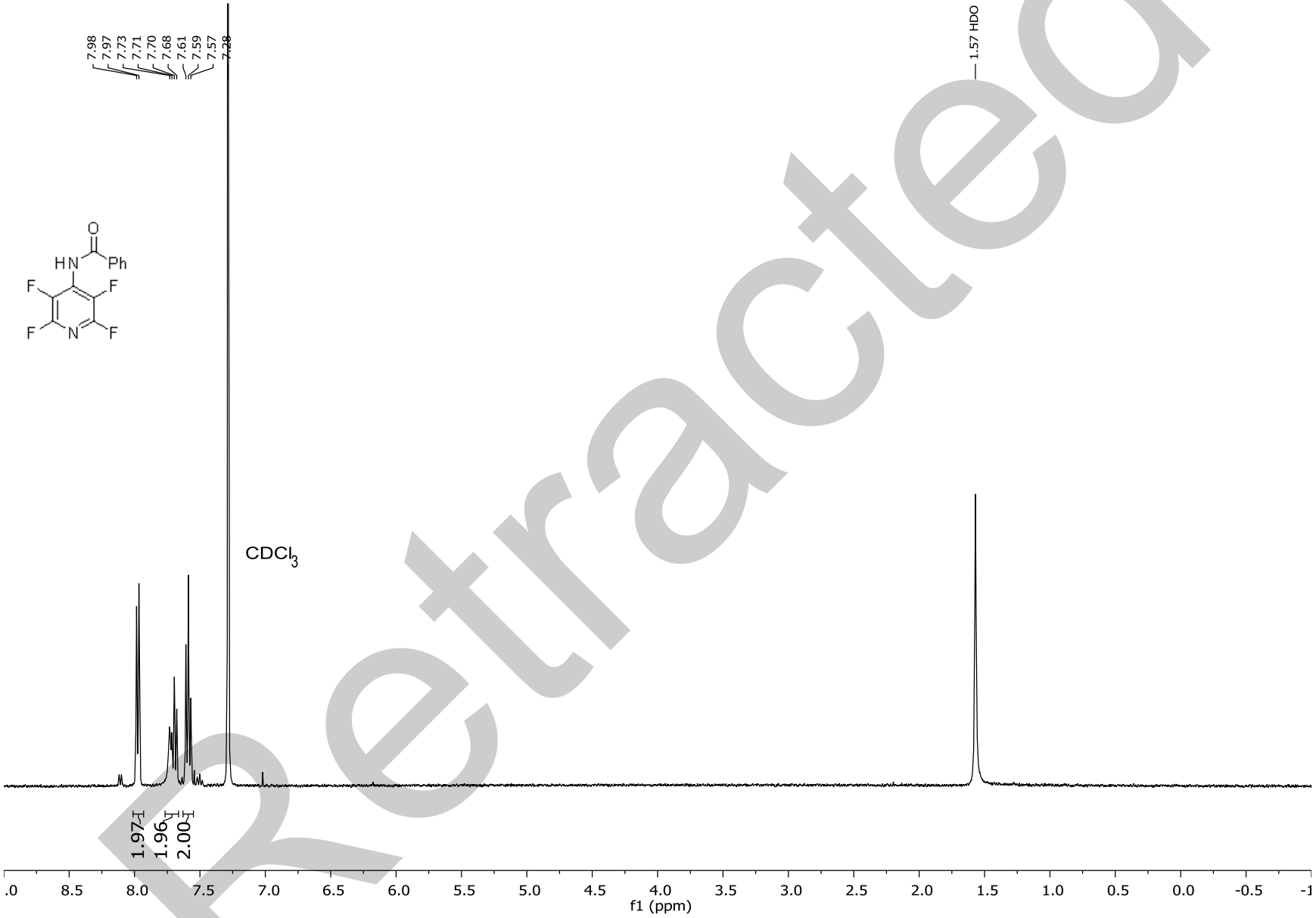
4h 4-fluoro-*N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



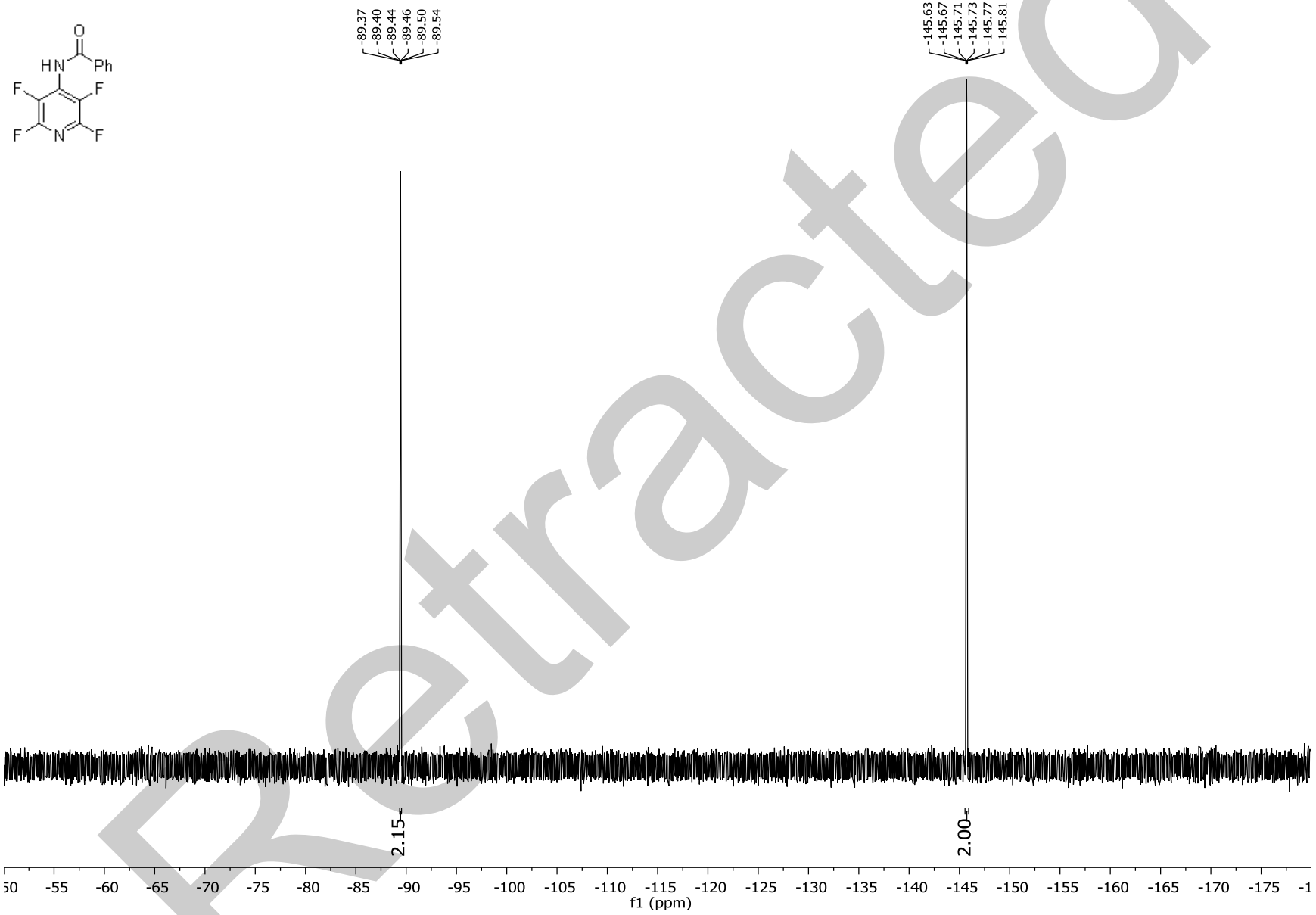
4h 4-fluoro-*N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



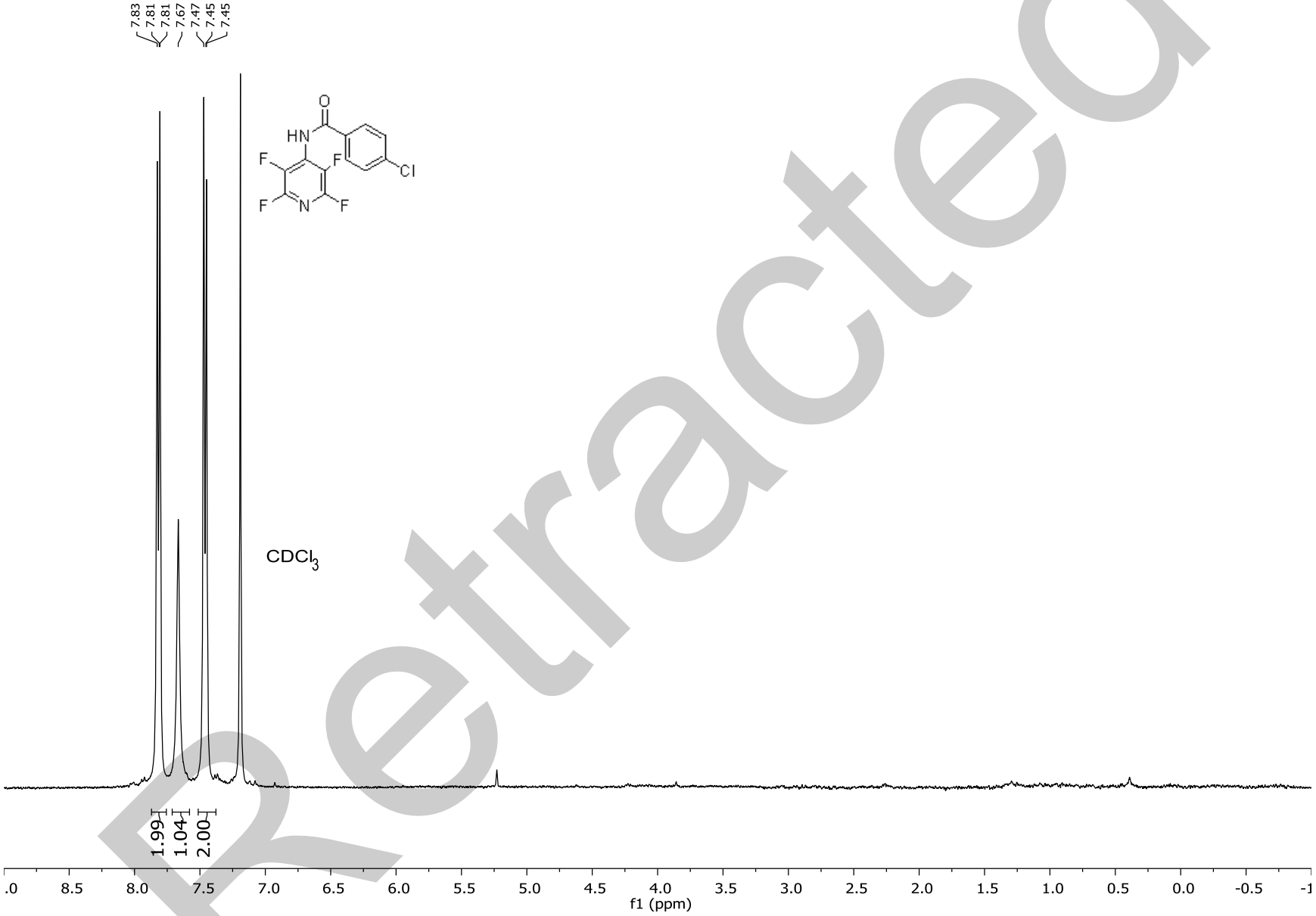
4i *N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



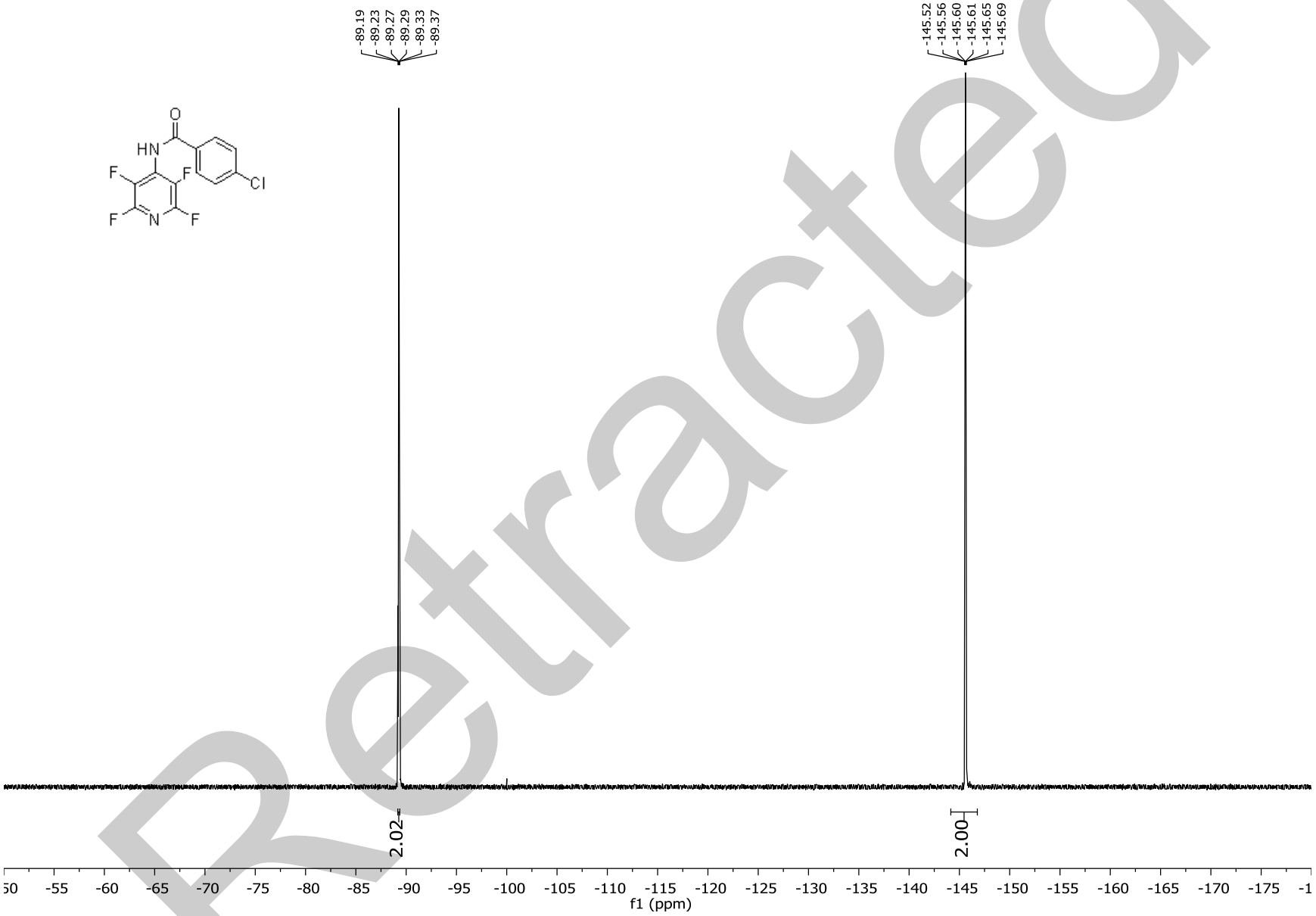
4i *N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



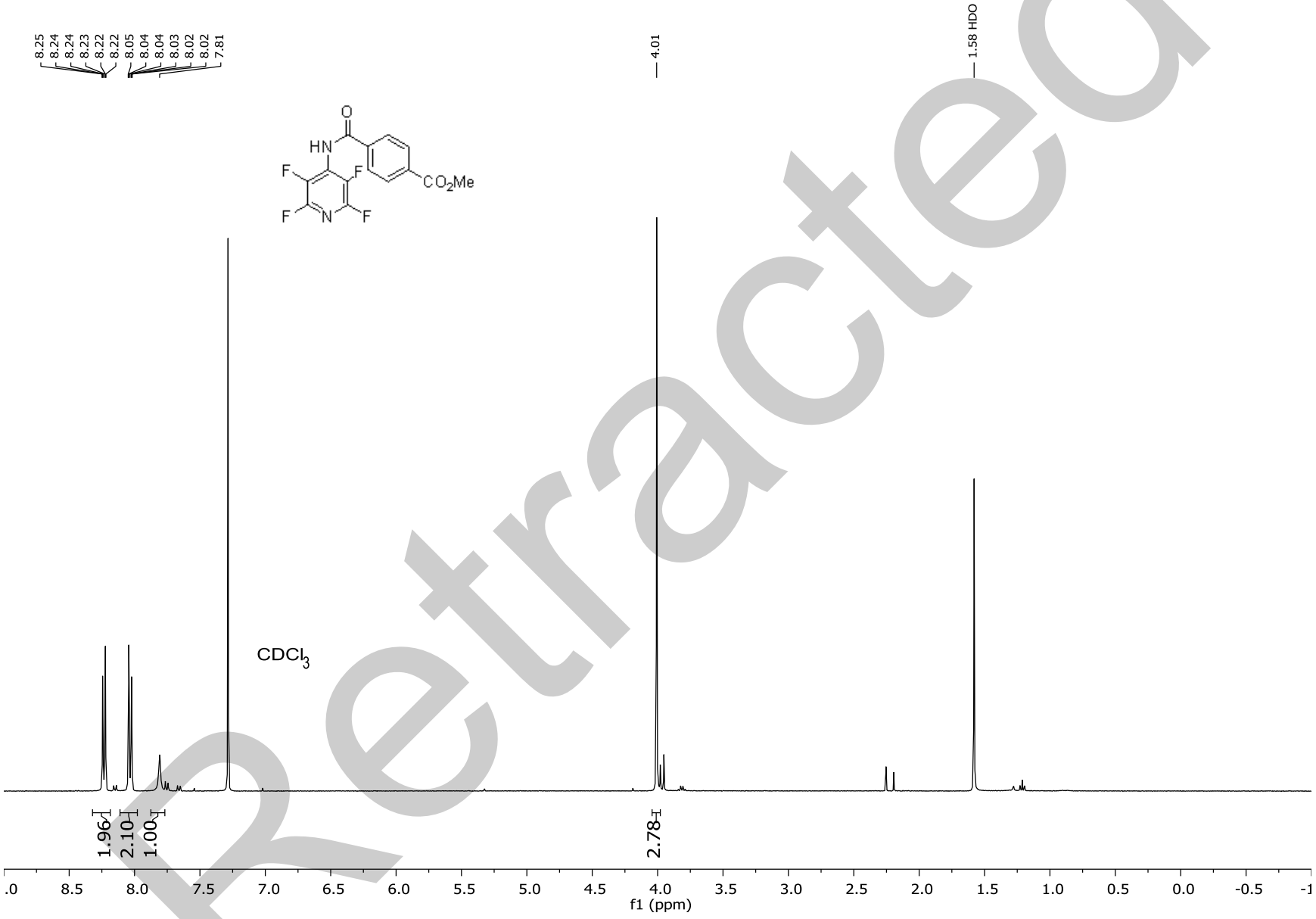
4j 4-chloro-*N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



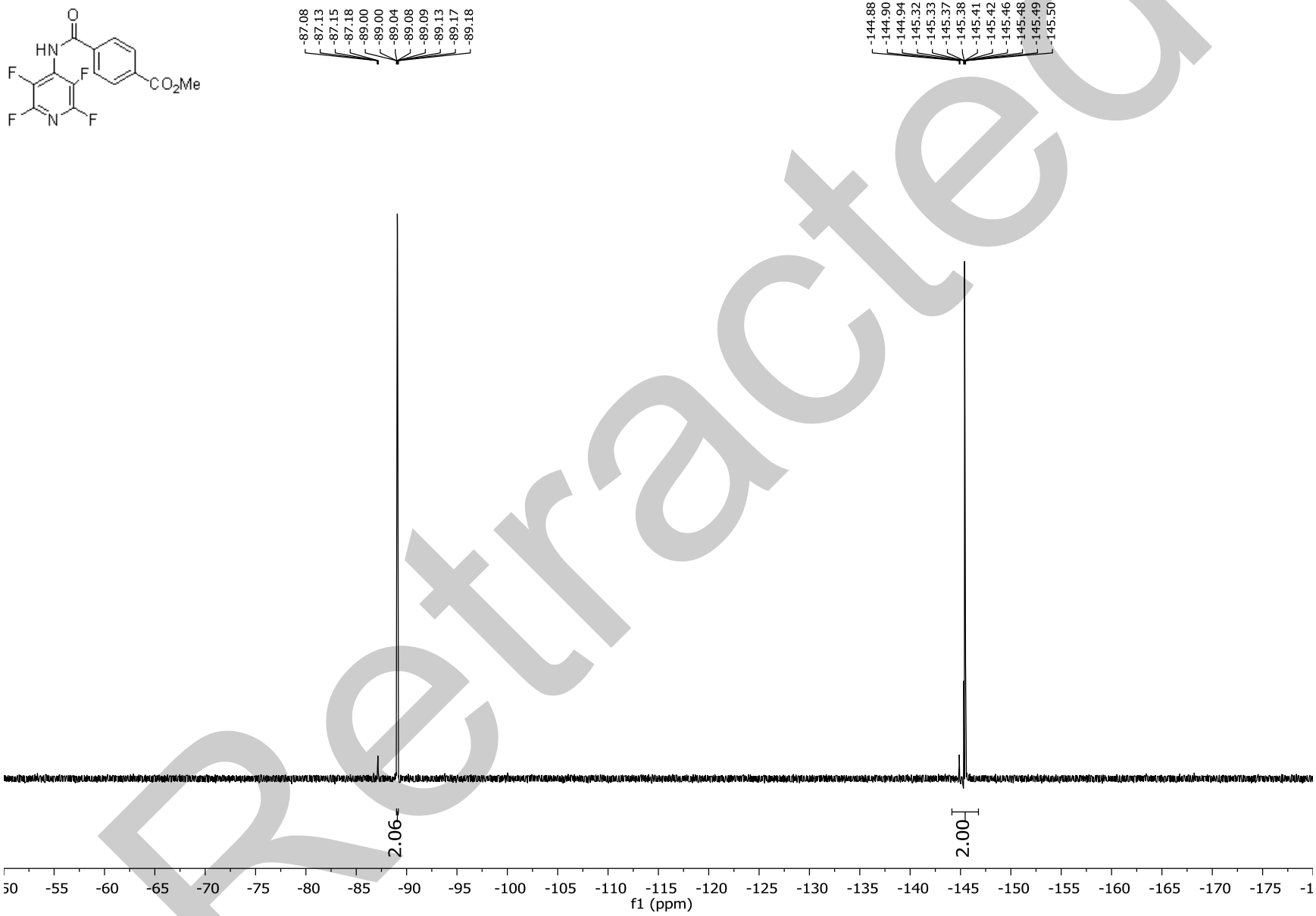
4j 4-chloro-*N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



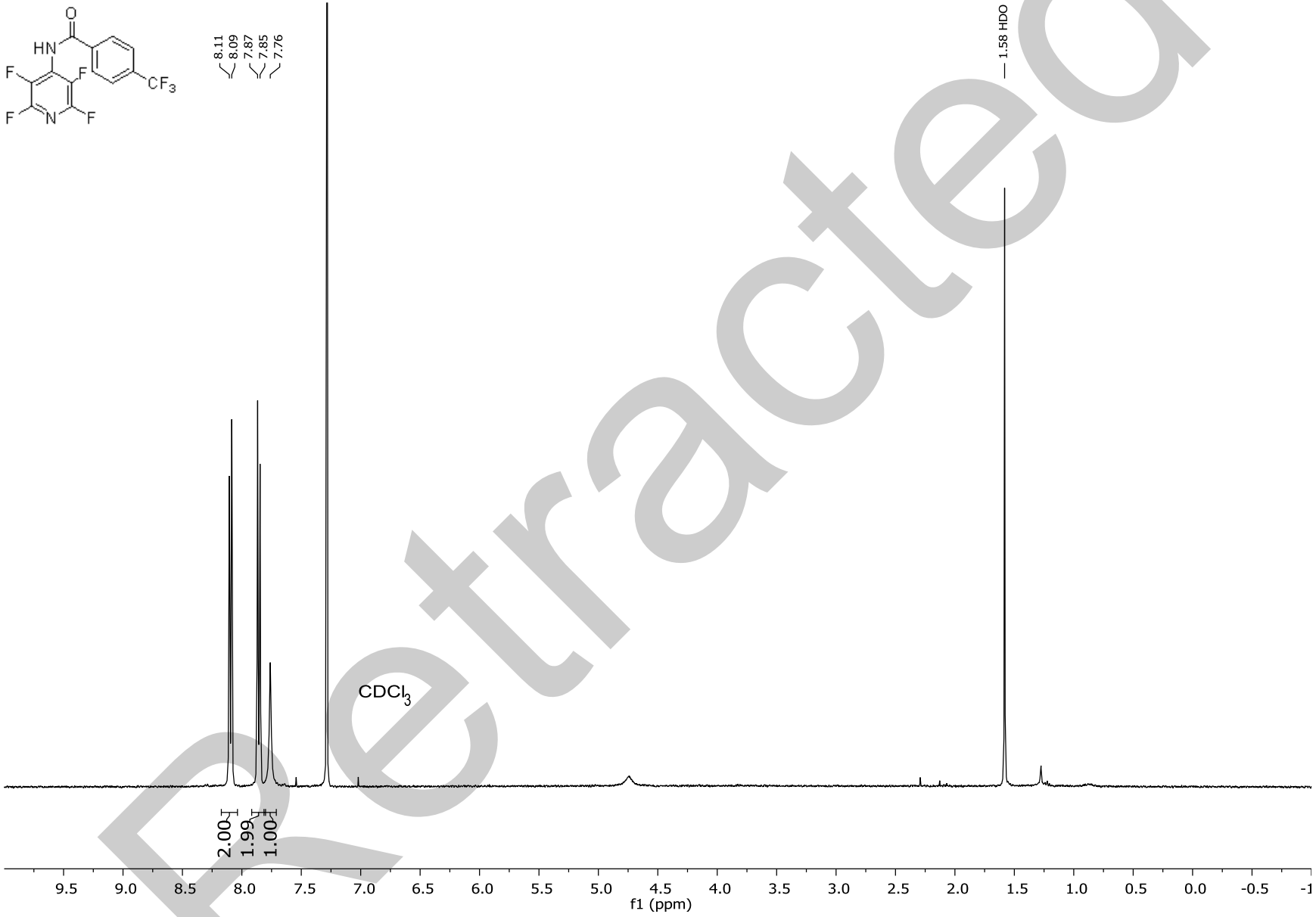
4k methyl 4-((perfluoropyridin-4-yl)carbamoyl)benzoate ^{1}H NMR (400 MHz, $CDCl_3$)



4k methyl 4-((perfluoropyridin-4-yl)carbamoyl)benzoate ^{19}F NMR (376 MHz, $CDCl_3$)

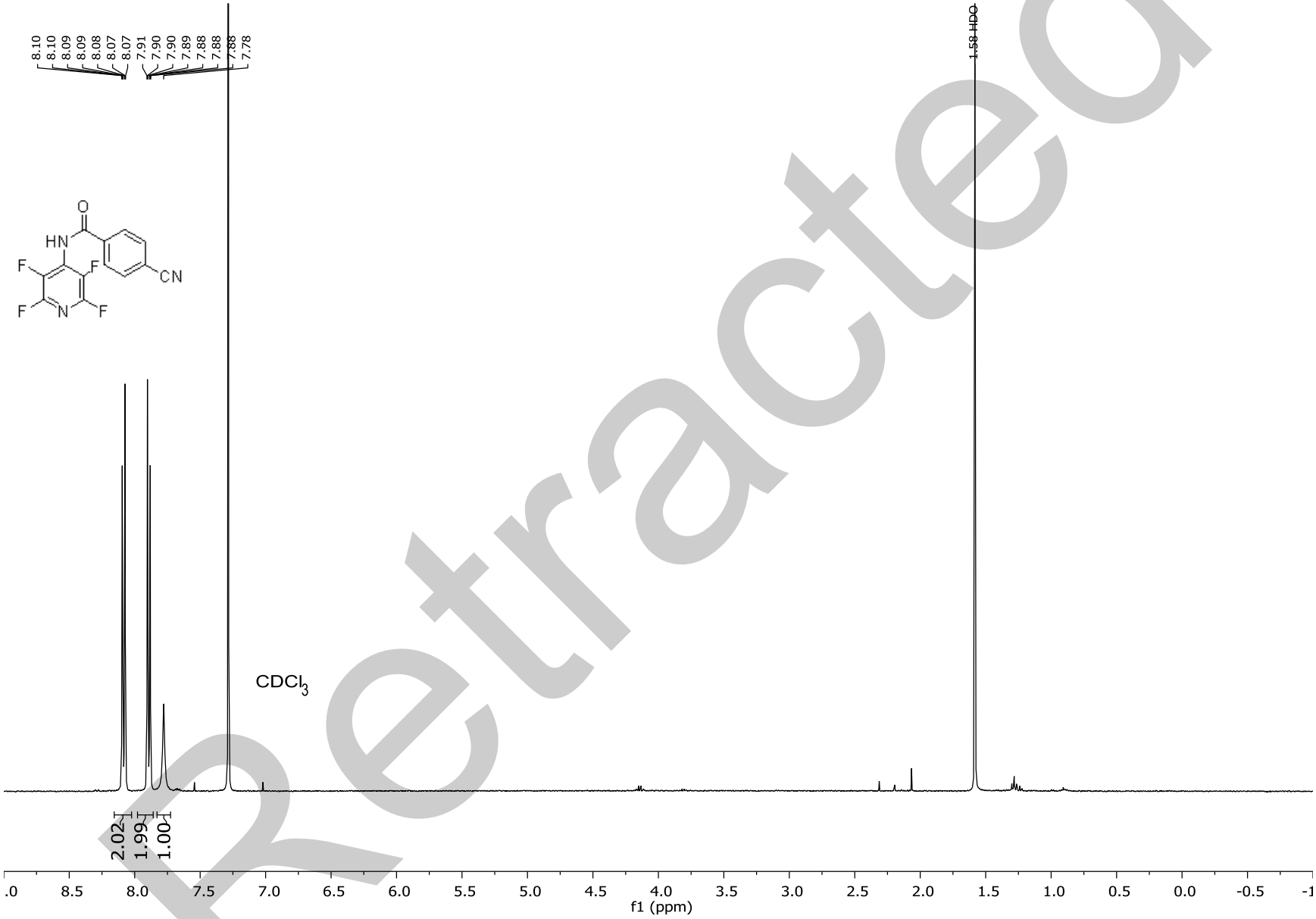


4l *N*-(perfluoropyridin-4-yl)-4-(trifluoromethyl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)

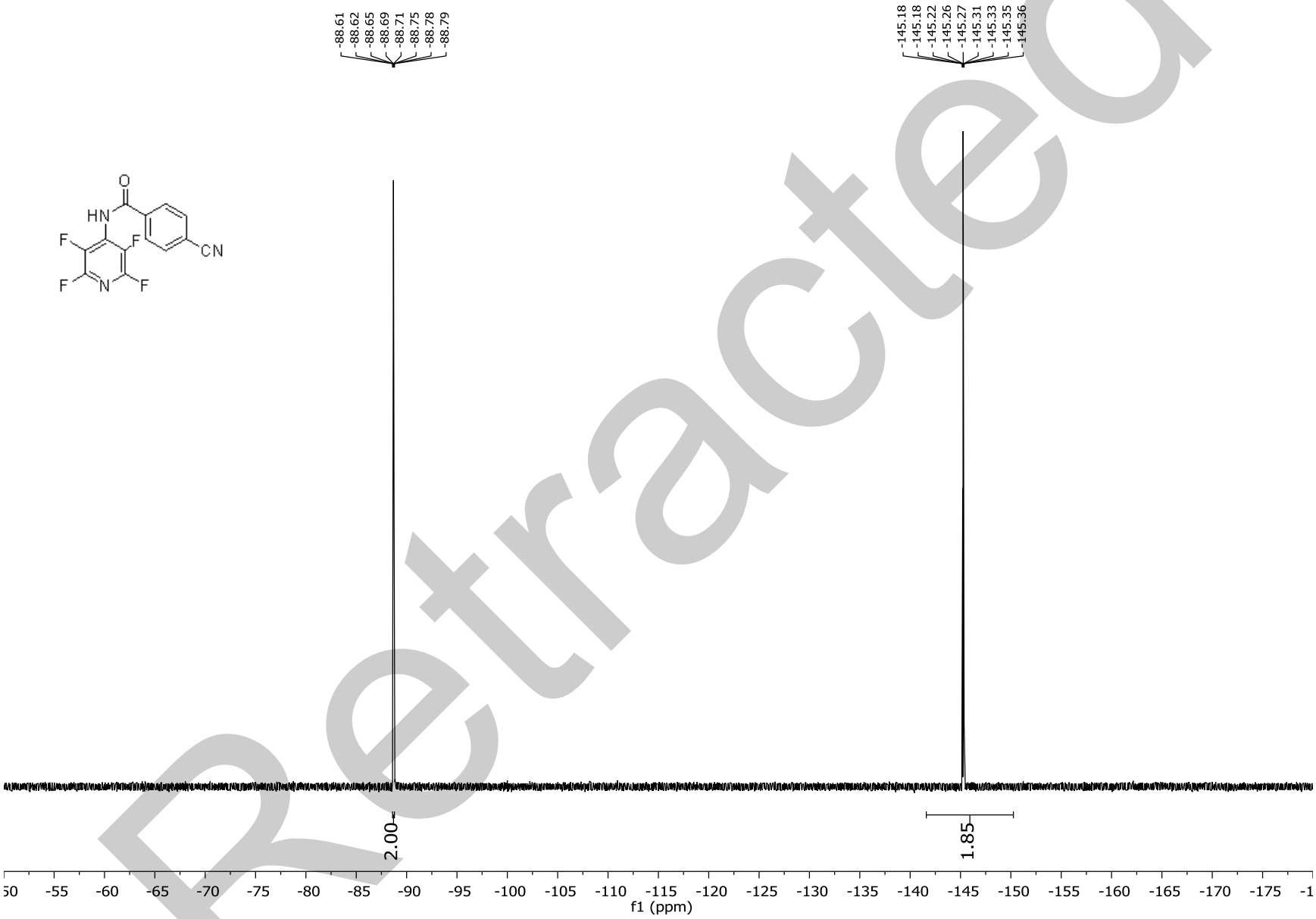


4l *N*-(perfluoropyridin-4-yl)-4-(trifluoromethyl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)

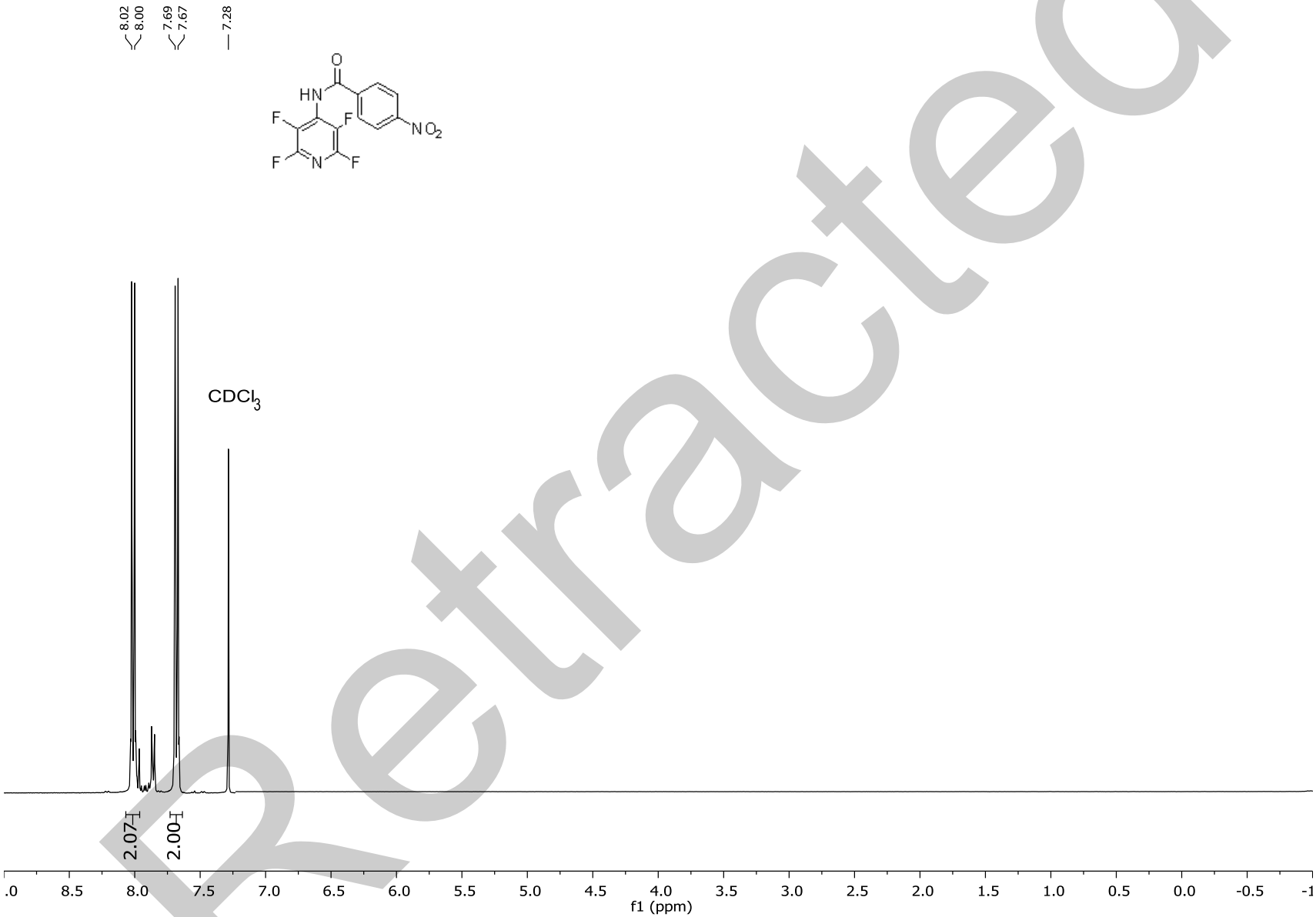
4m 4-cyano-*N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



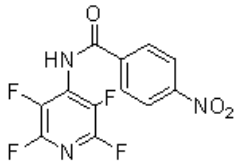
4m 4-cyano-*N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



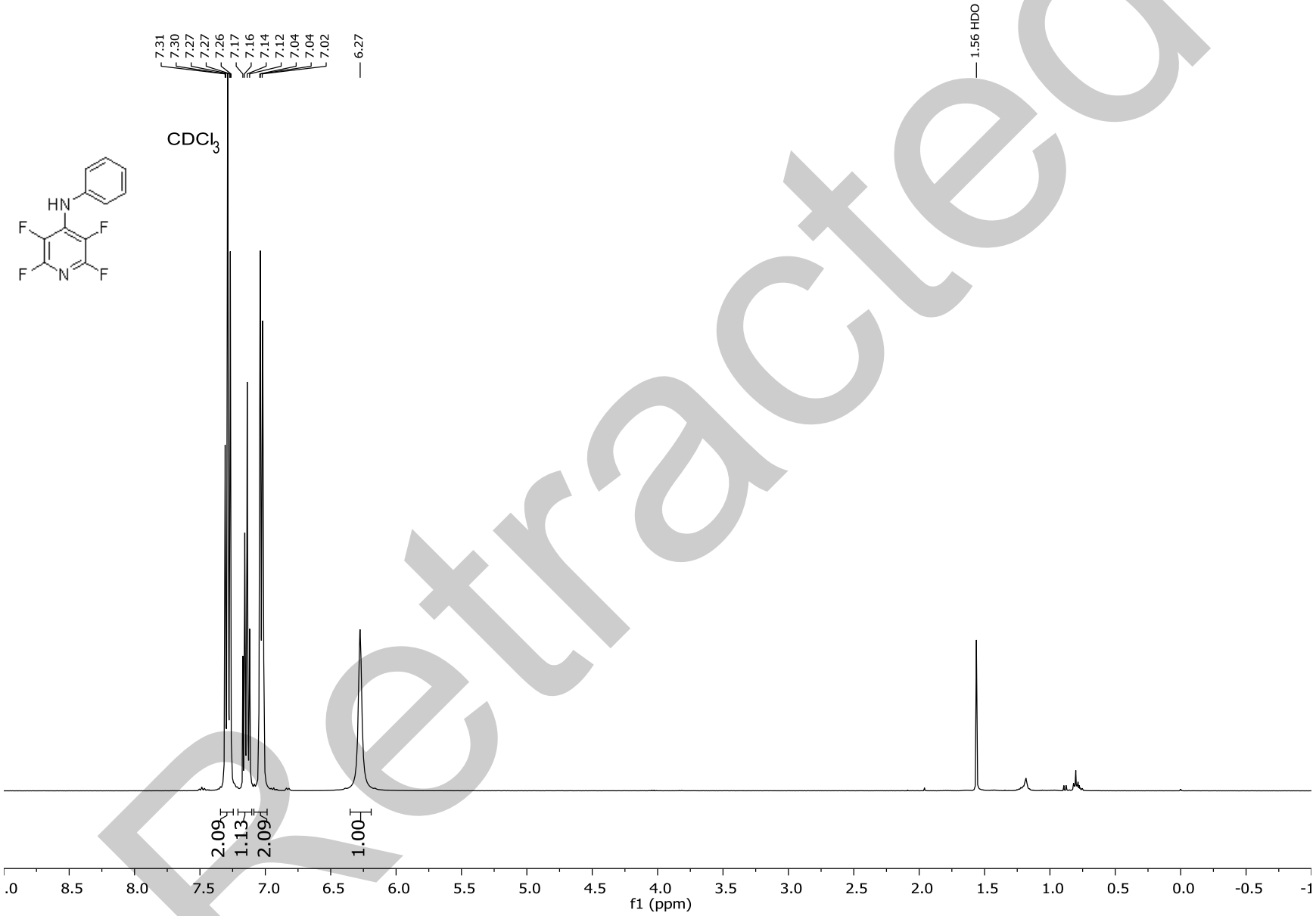
4n 4-4-nitro-*N*-(perfluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



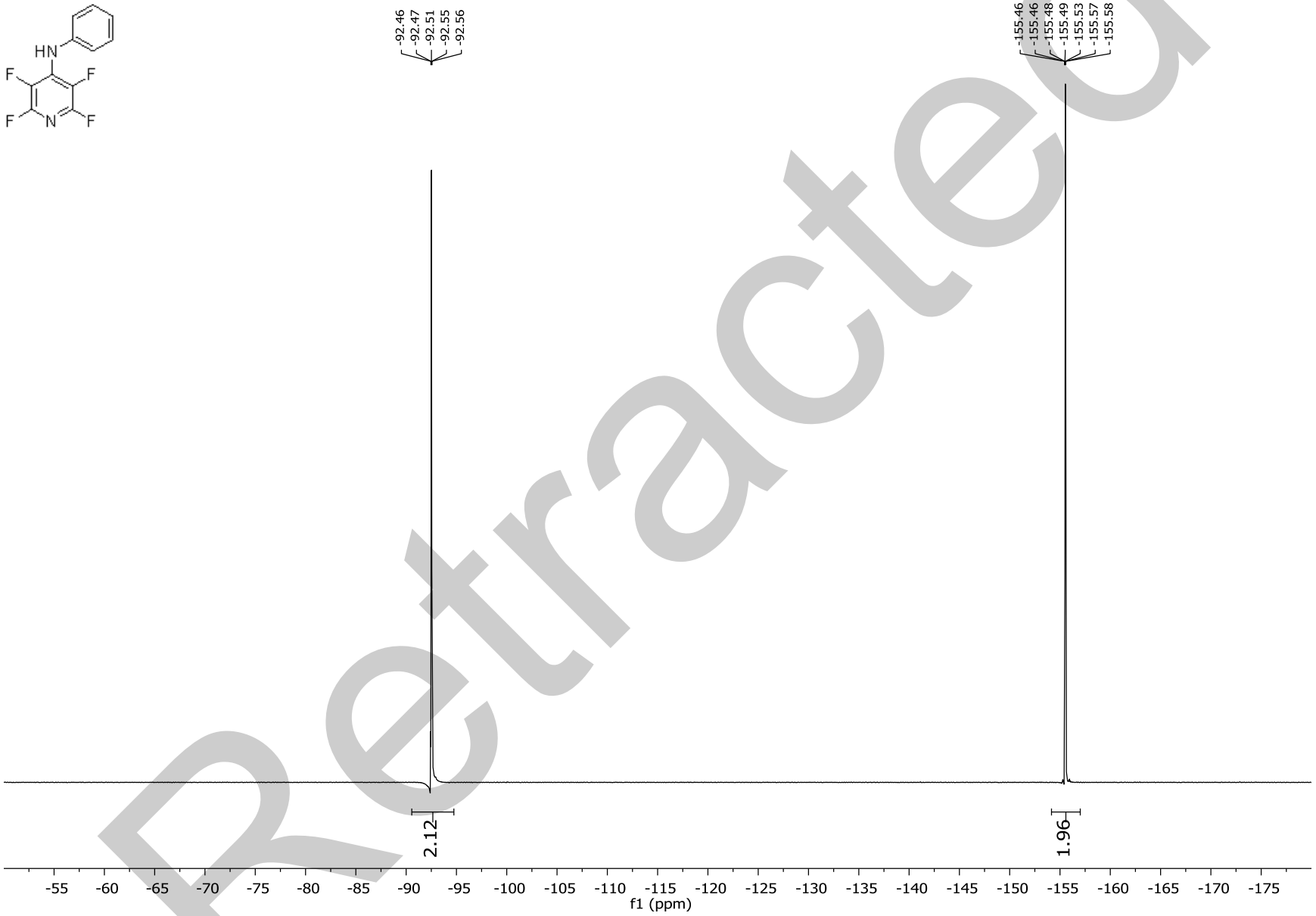
4n 4-4-nitro-*N*-(perfluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



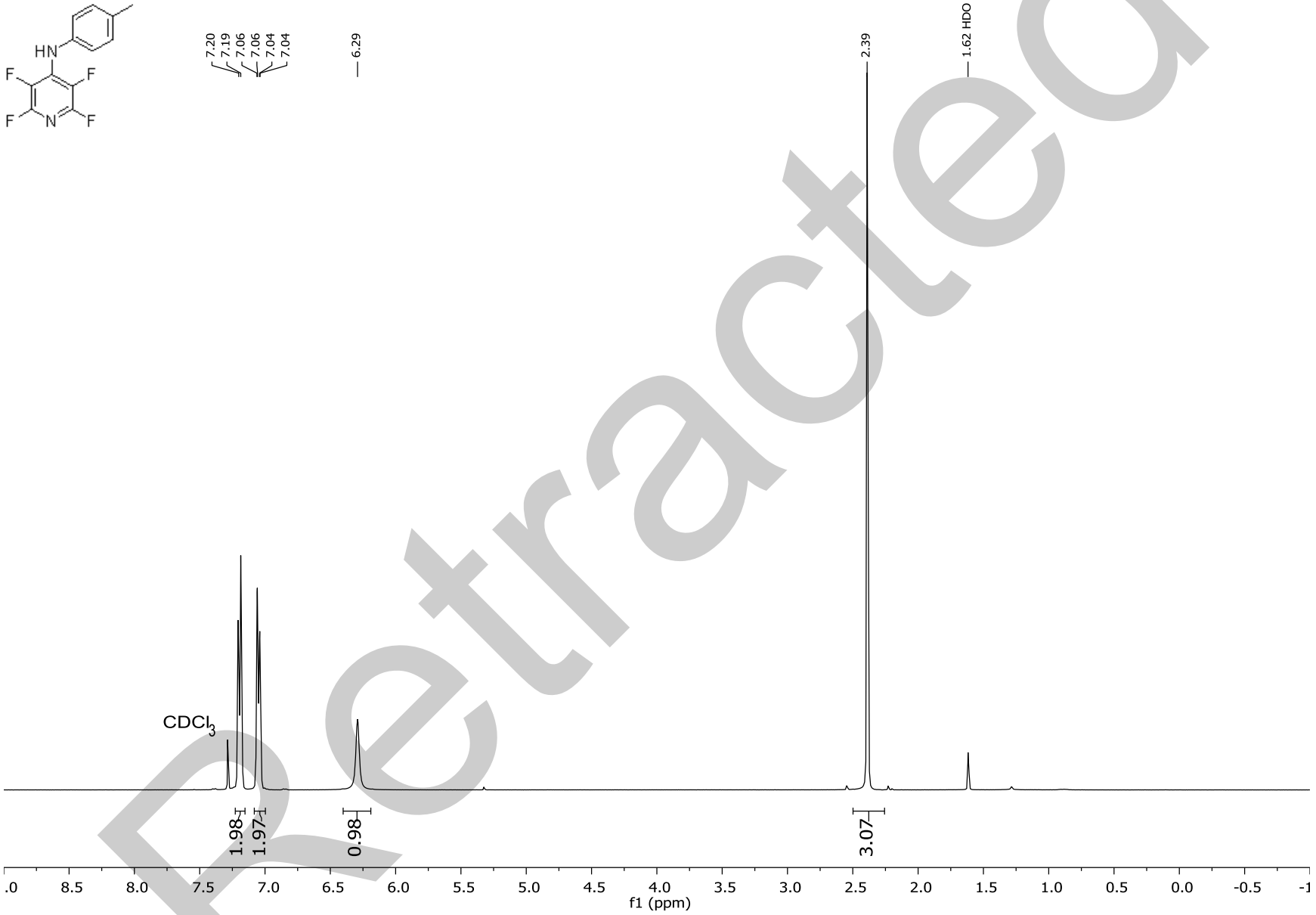
5a 2,3,5,6-tetrafluoro-*N*-phenylpyridin-4-amine ^{1}H NMR (400 MHz, $CDCl_3$)



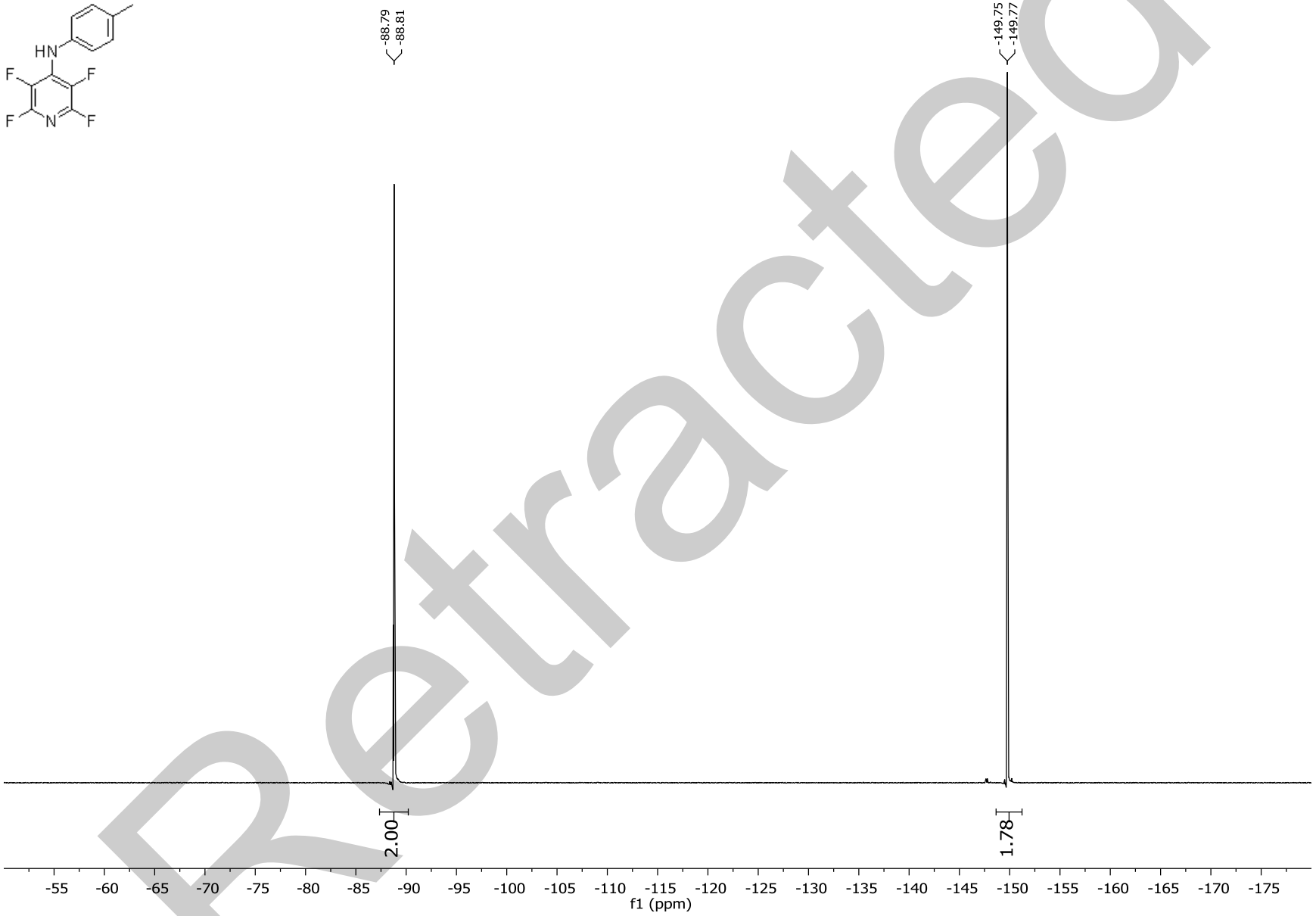
5a 2,3,5,6-tetrafluoro-*N*-phenylpyridin-4-amine ^{19}F NMR (376 MHz, $CDCl_3$)



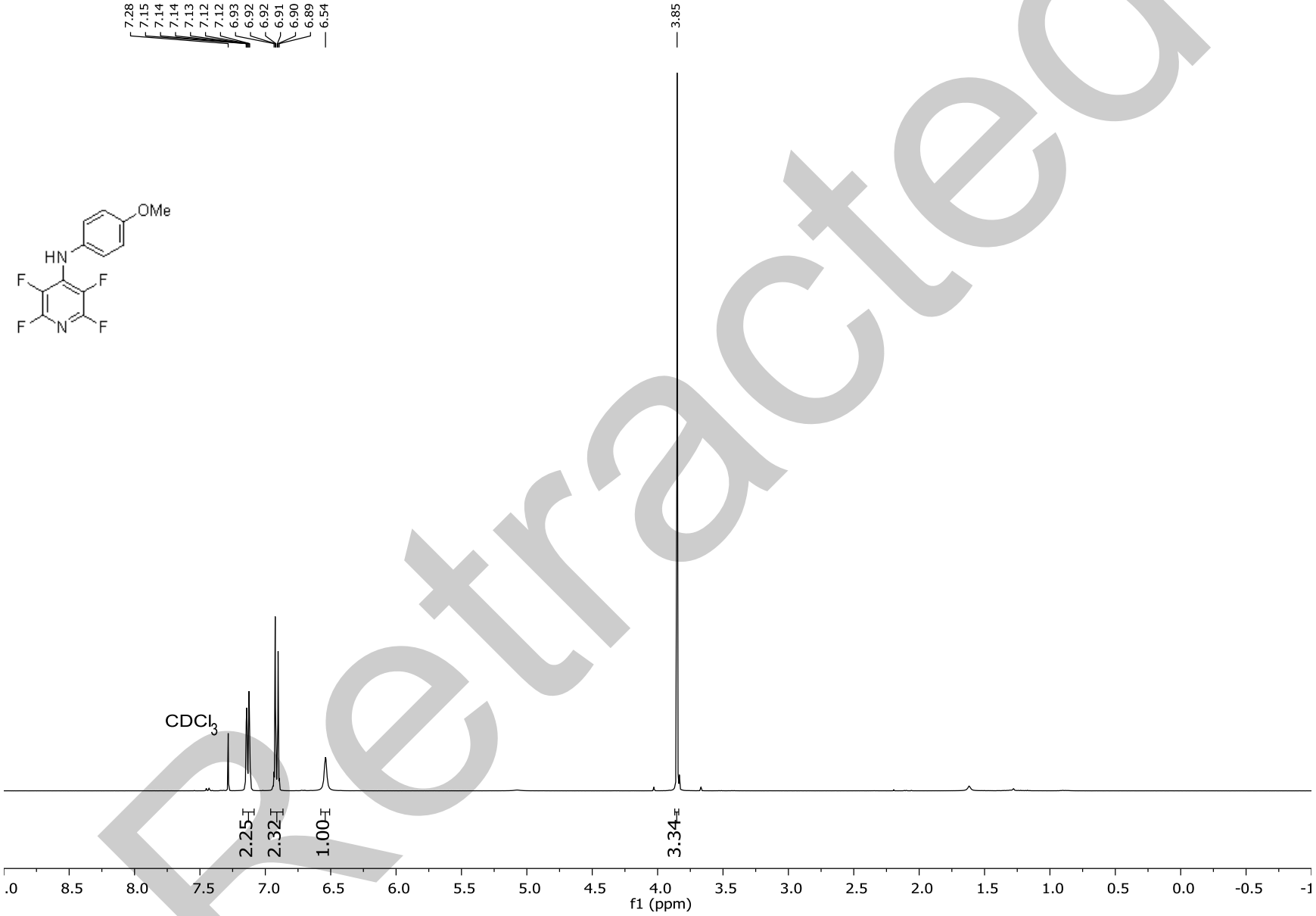
5b 2,3,5,6-tetrafluoro-*N*-(p-tolyl)pyridin-4-amine ^{1}H NMR (400 MHz, $CDCl_3$)



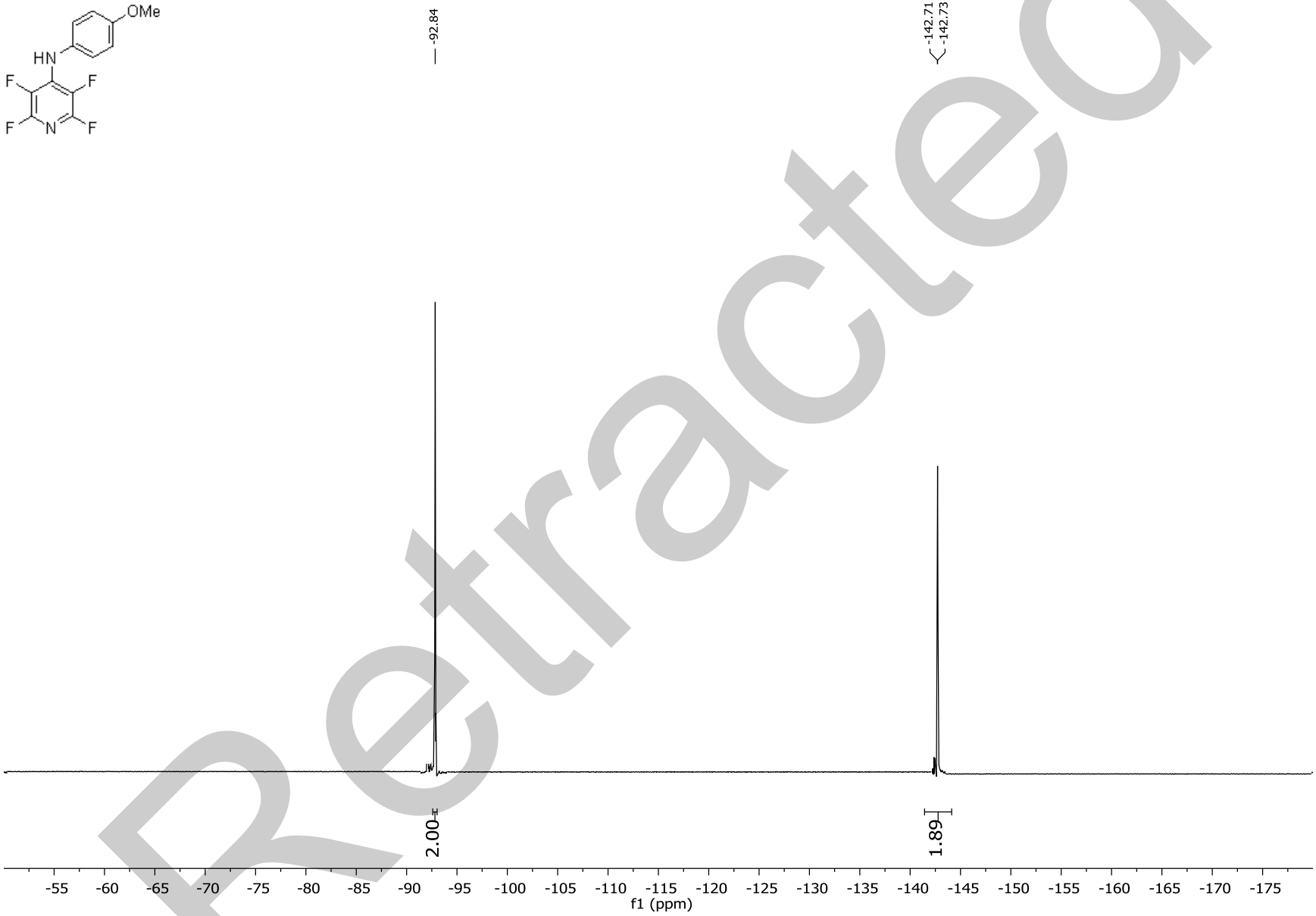
5b 2,3,5,6-tetrafluoro-*N*-(p-tolyl)pyridin-4-amine ^{19}F NMR (376 MHz, $CDCl_3$)



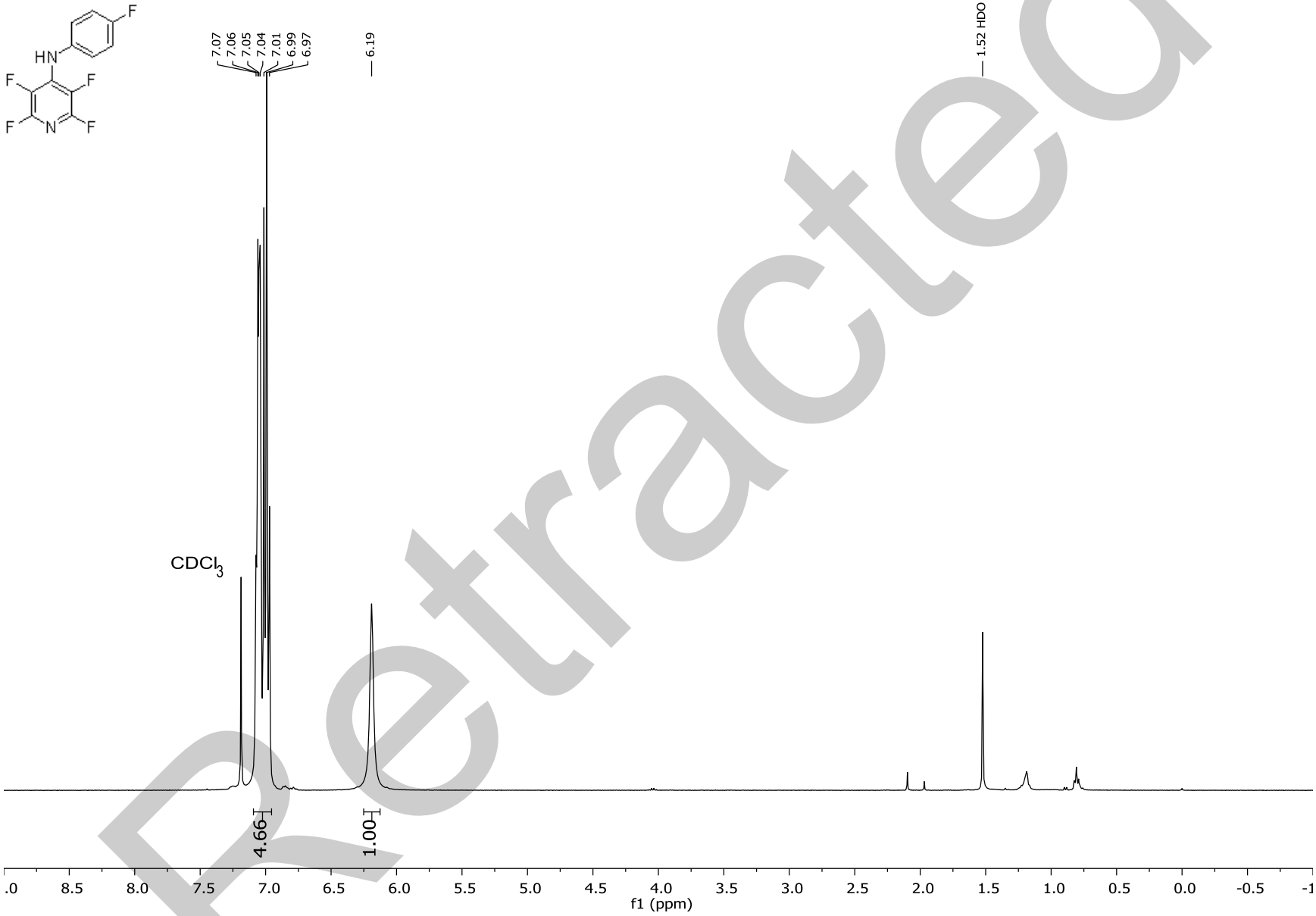
5c 2,3,5,6-tetrafluoro-*N*-(4-methoxyphenyl)pyridin-4-amine ^{1}H NMR (400 MHz, $CDCl_3$)



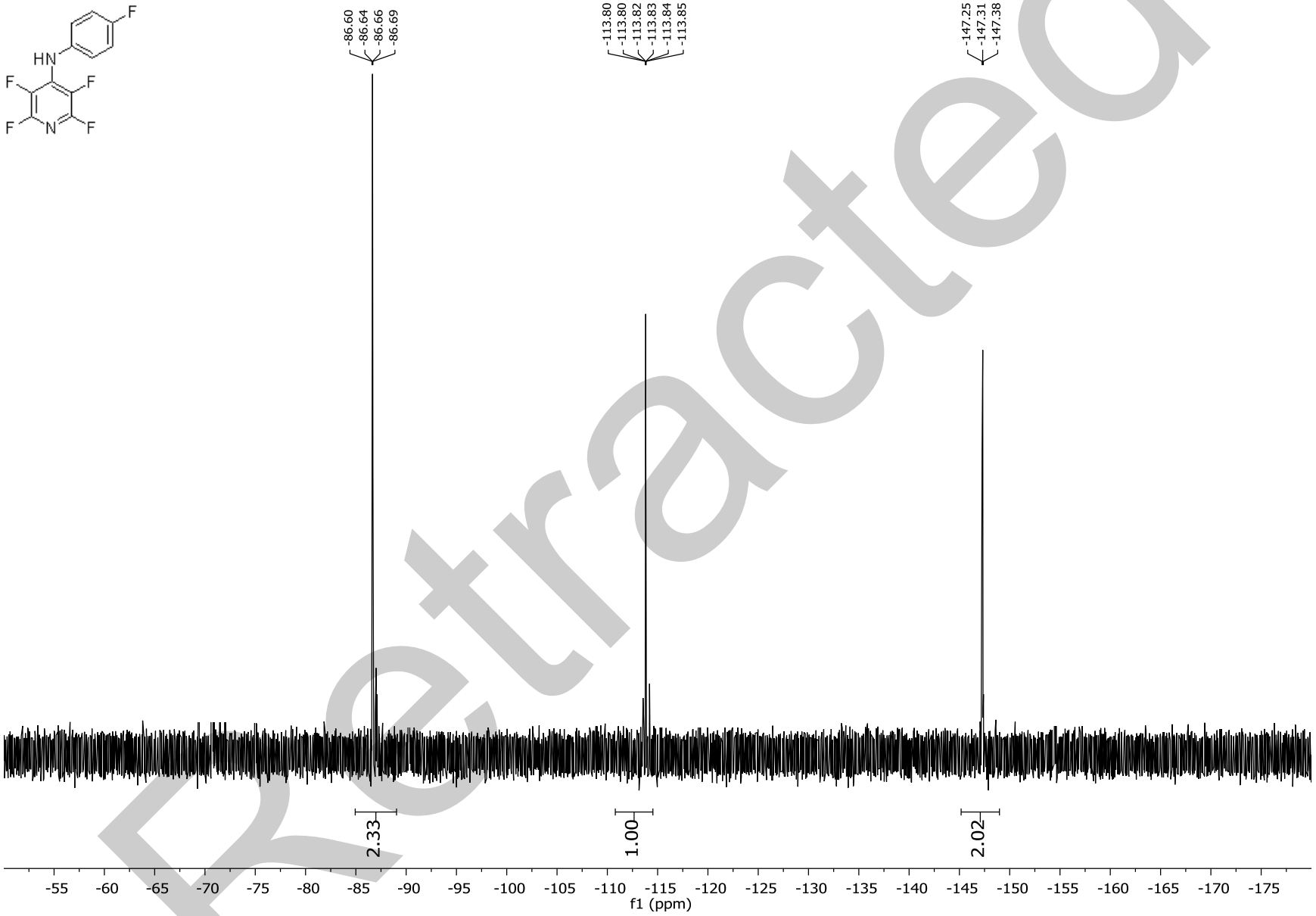
5c 2,3,5,6-tetrafluoro-*N*-(4-methoxyphenyl)pyridin--amine ^{19}F NMR (376 MHz, $CDCl_3$)



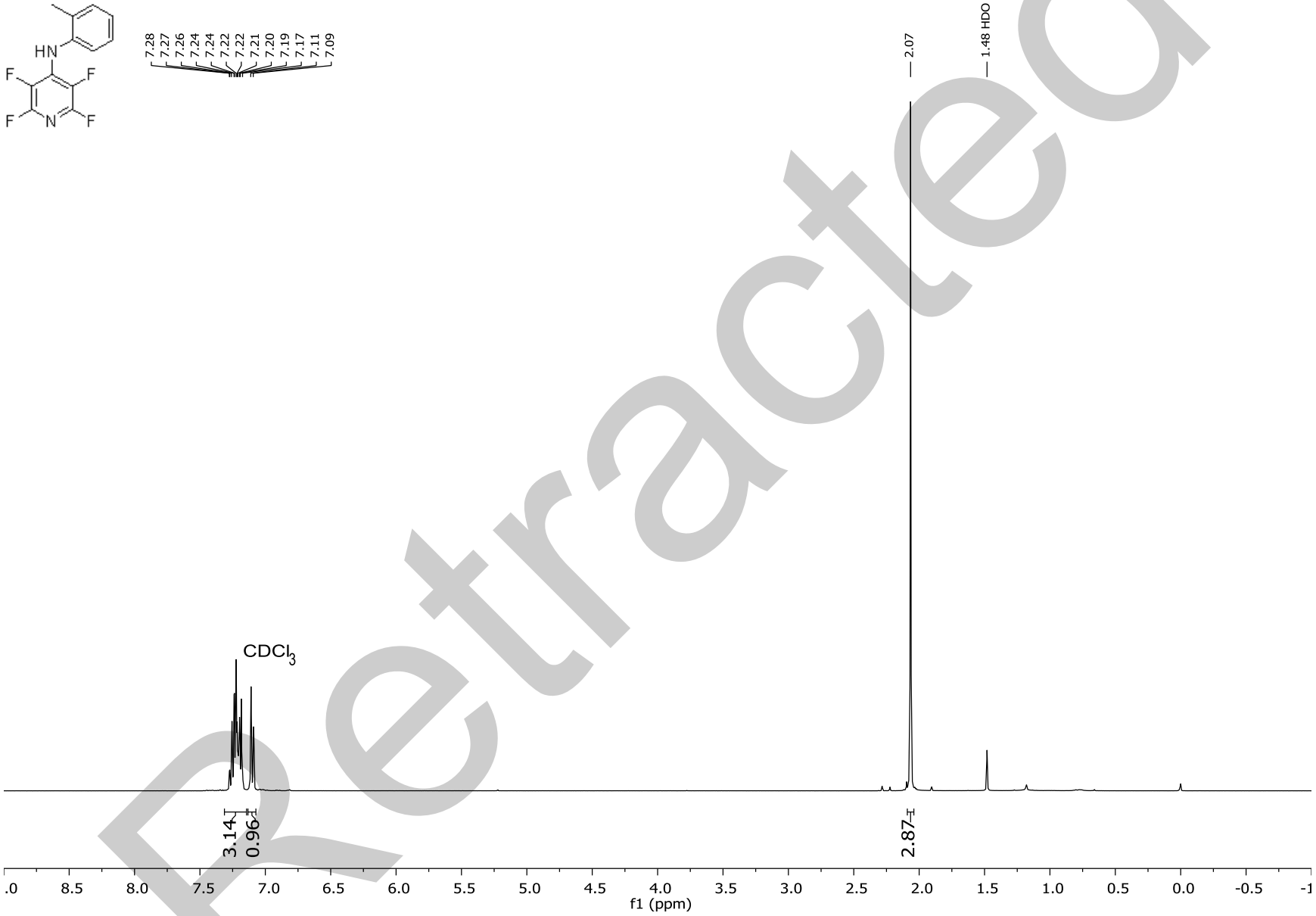
5d 2,3,5,6-tetrafluoro-*N*-(4-fluorophenyl)pyridin-4-amine ^{1}H NMR (400 MHz, $CDCl_3$)



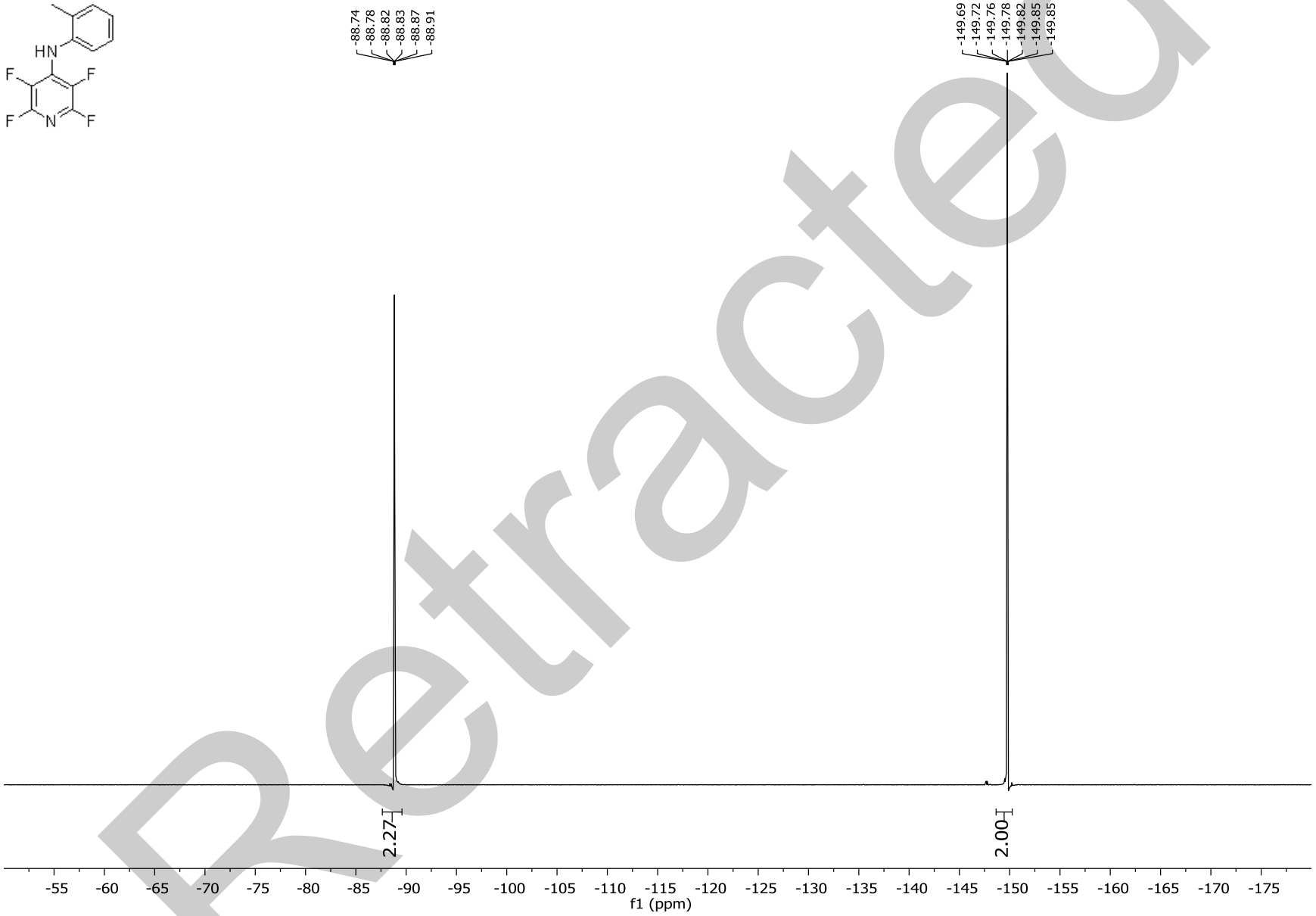
5d 2,3,5,6-tetrafluoro-*N*-(4-fluorophenyl)pyridin-4-amine ^{19}F NMR (376 MHz, $CDCl_3$)



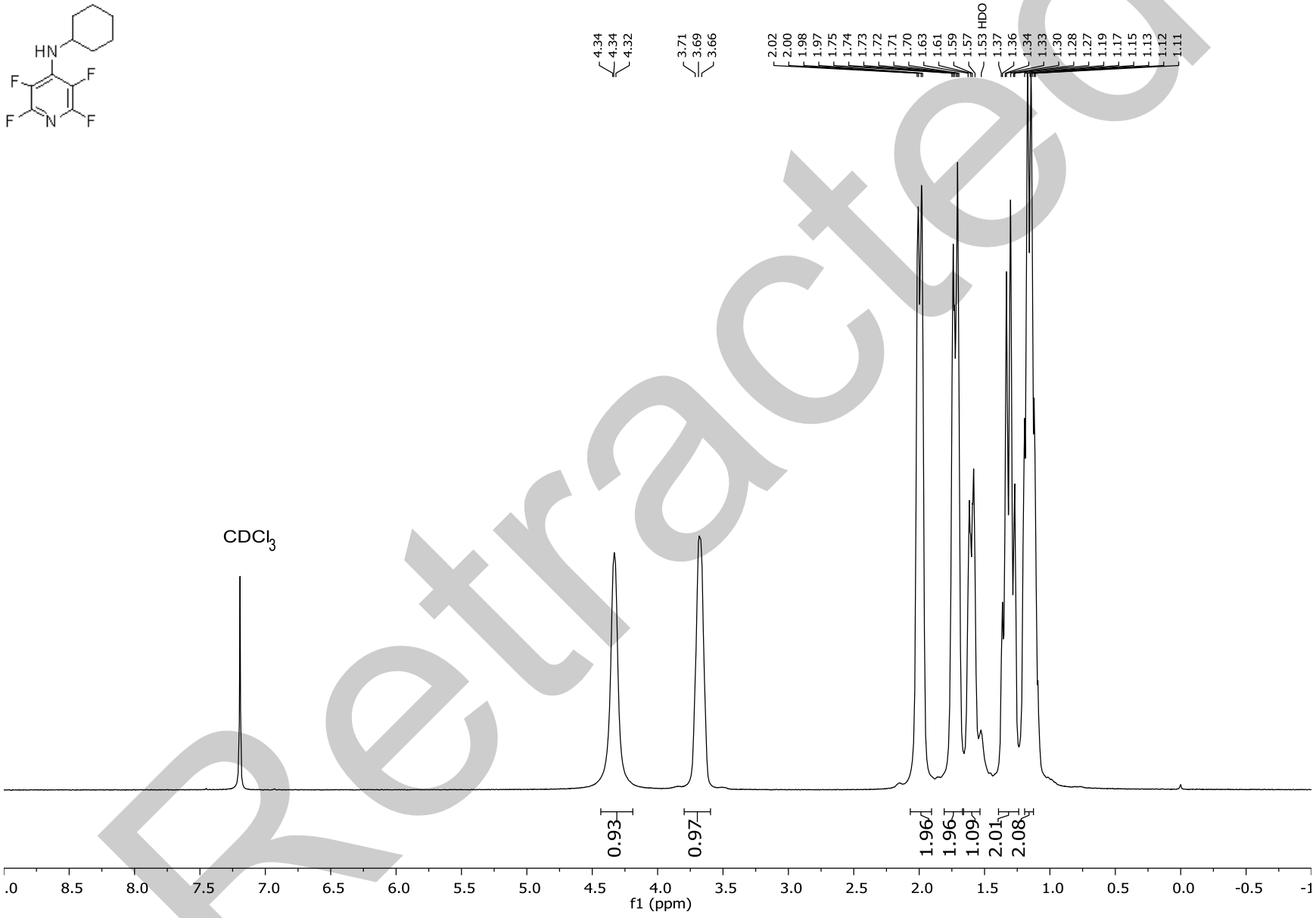
5e 2,3,5,6-tetrafluoro-*N*-(o-tolyl)pyridin-4-amine ^{1}H NMR (400 MHz, $CDCl_3$)



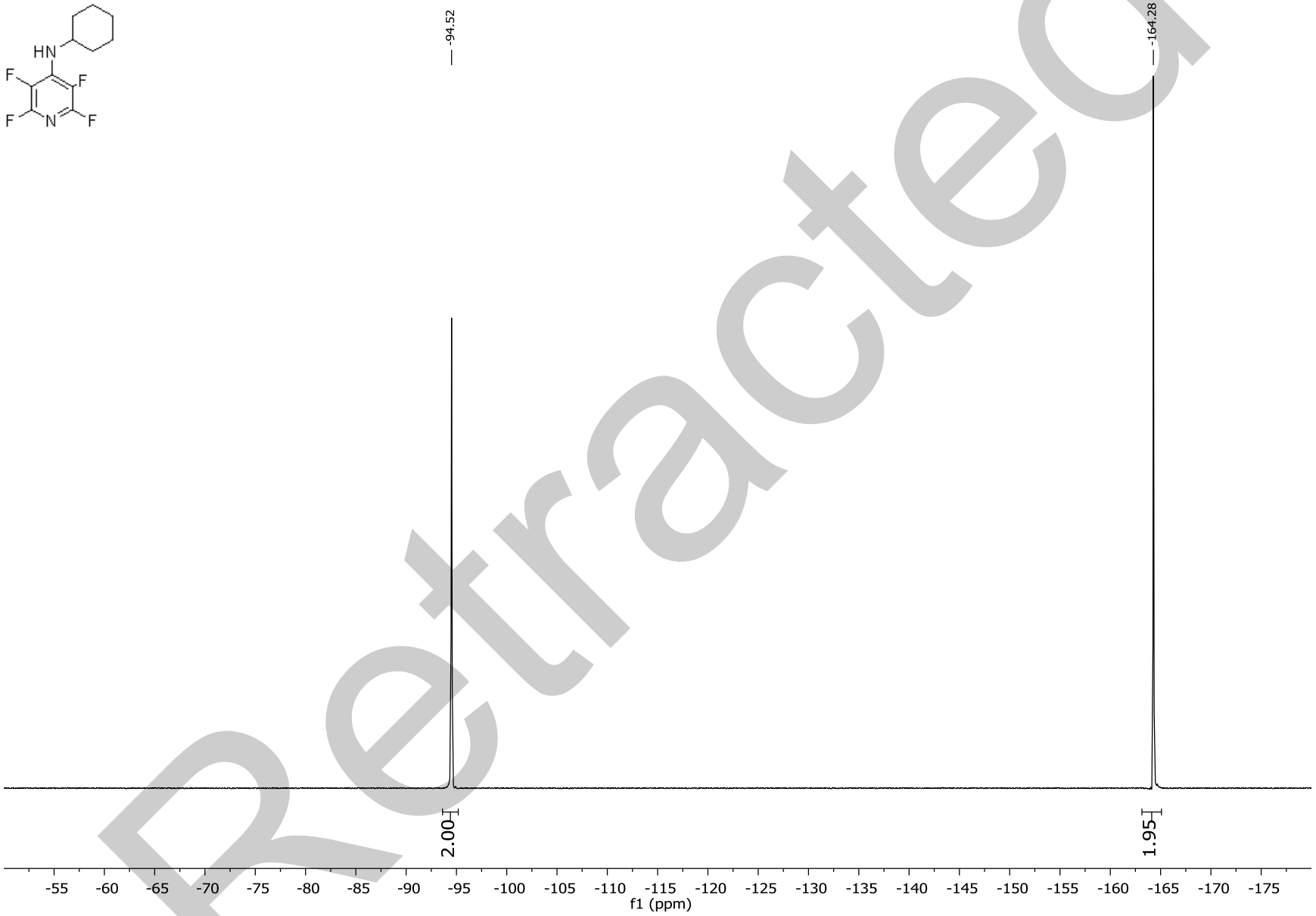
5e 2,3,5,6-tetrafluoro-*N*-(o-tolyl)pyridin-4-amine ^{19}F NMR (376 MHz, $CDCl_3$)



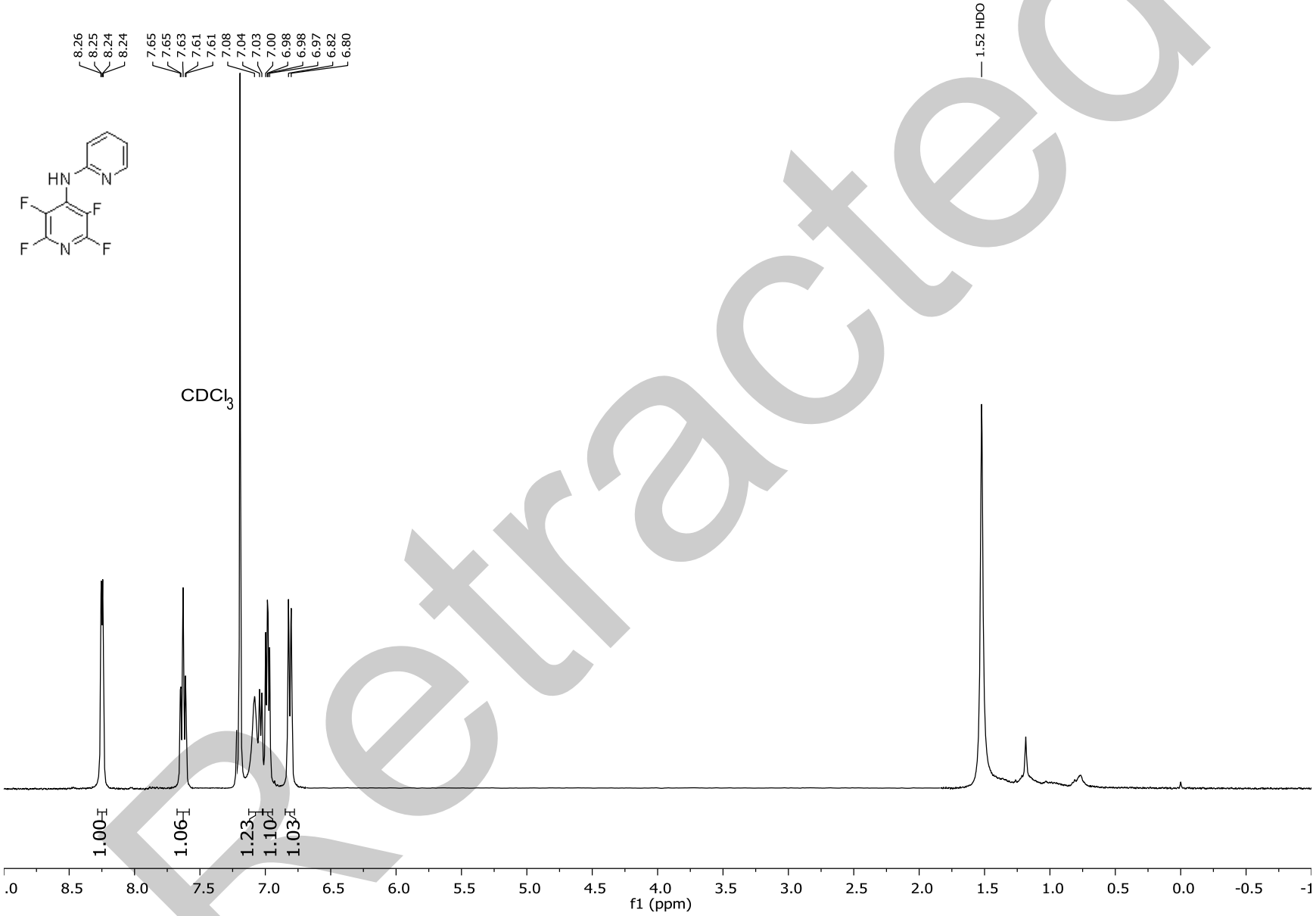
5f *N*-cyclohexyl-2,3,5,6-tetrafluoropyridin-4-amine *N*-cyclohexyl-2,3,5,6-tetrafluoropyridin-4-amine ^{1}H NMR (400 MHz, $CDCl_3$)



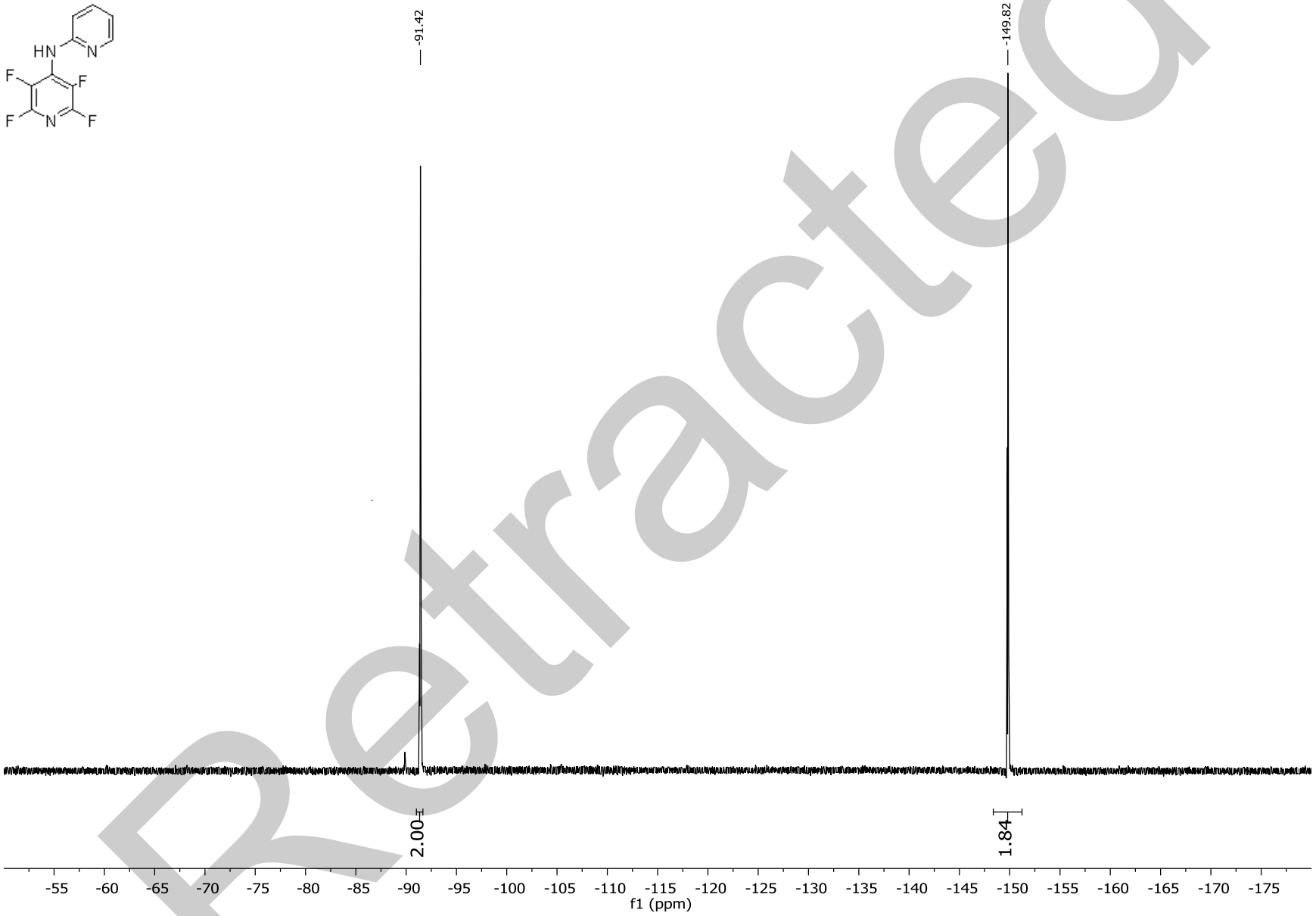
5f *N*-cyclohexyl-2,3,5,6-tetrafluoropyridin-4-amine *N*-cyclohexyl-2,3,5,6-tetrafluoropyridin-4-amine ^{19}F NMR (376 MHz, $CDCl_3$)



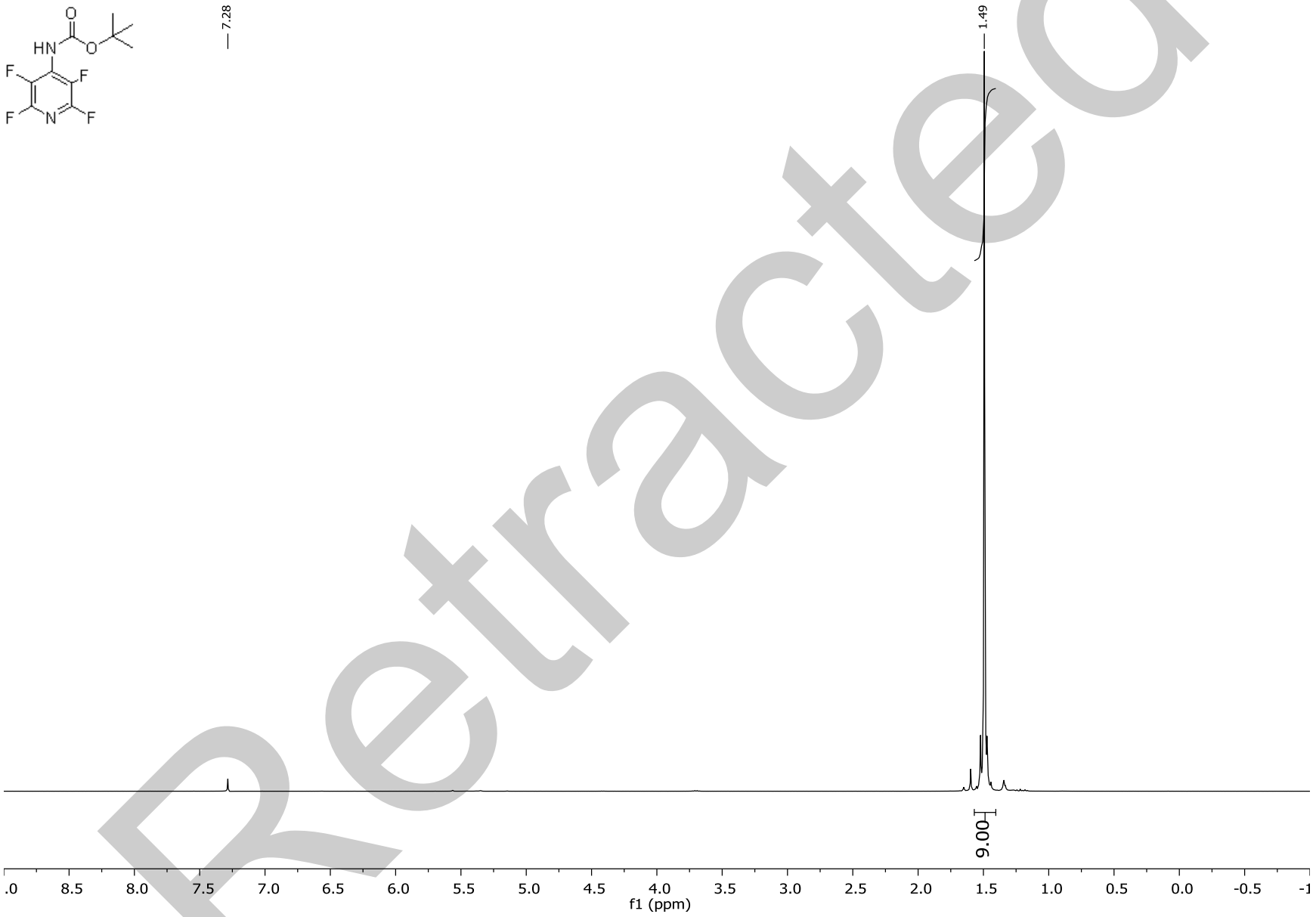
5g *N*-(perfluoropyridin-4-yl)pyridin-2-amine ^{1}H NMR (400 MHz, $CDCl_3$)



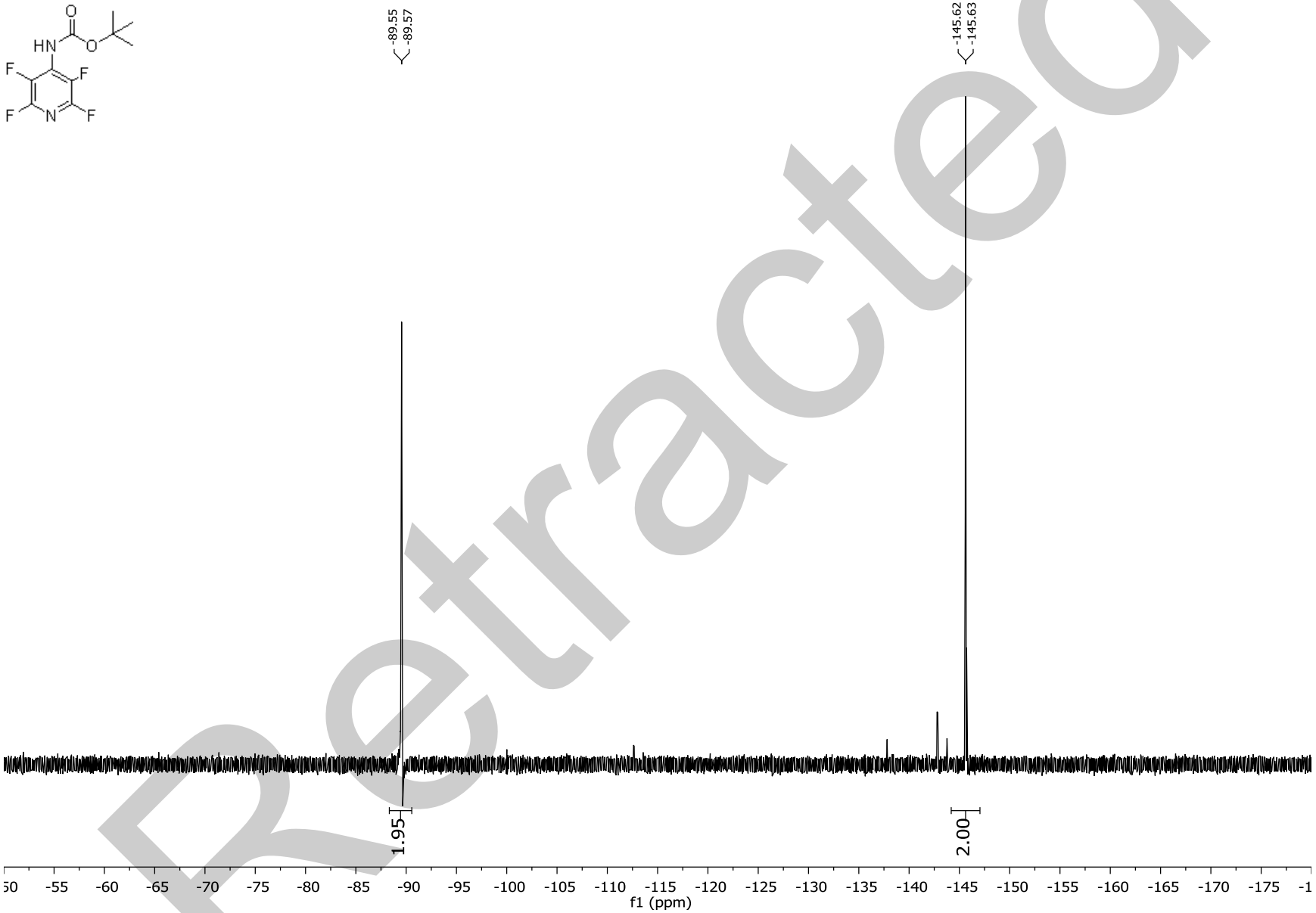
5g *N*-(perfluoropyridin-4-yl)pyridin-2-amine ^{19}F NMR (376 MHz, $CDCl_3$)



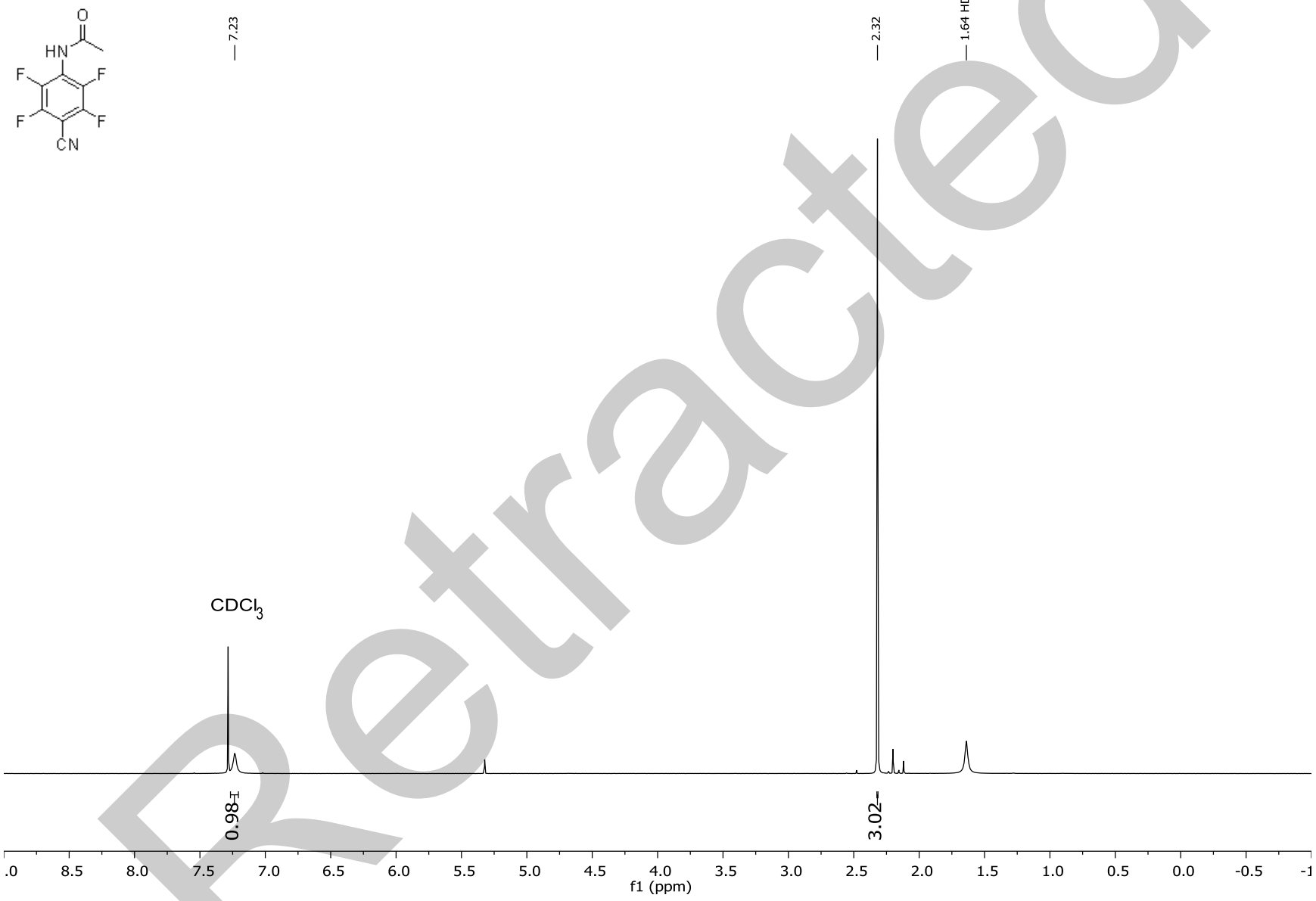
5h tert-butyl (perfluoropyridin-4-yl)carbamate ^{1}H NMR (400 MHz, $CDCl_3$)



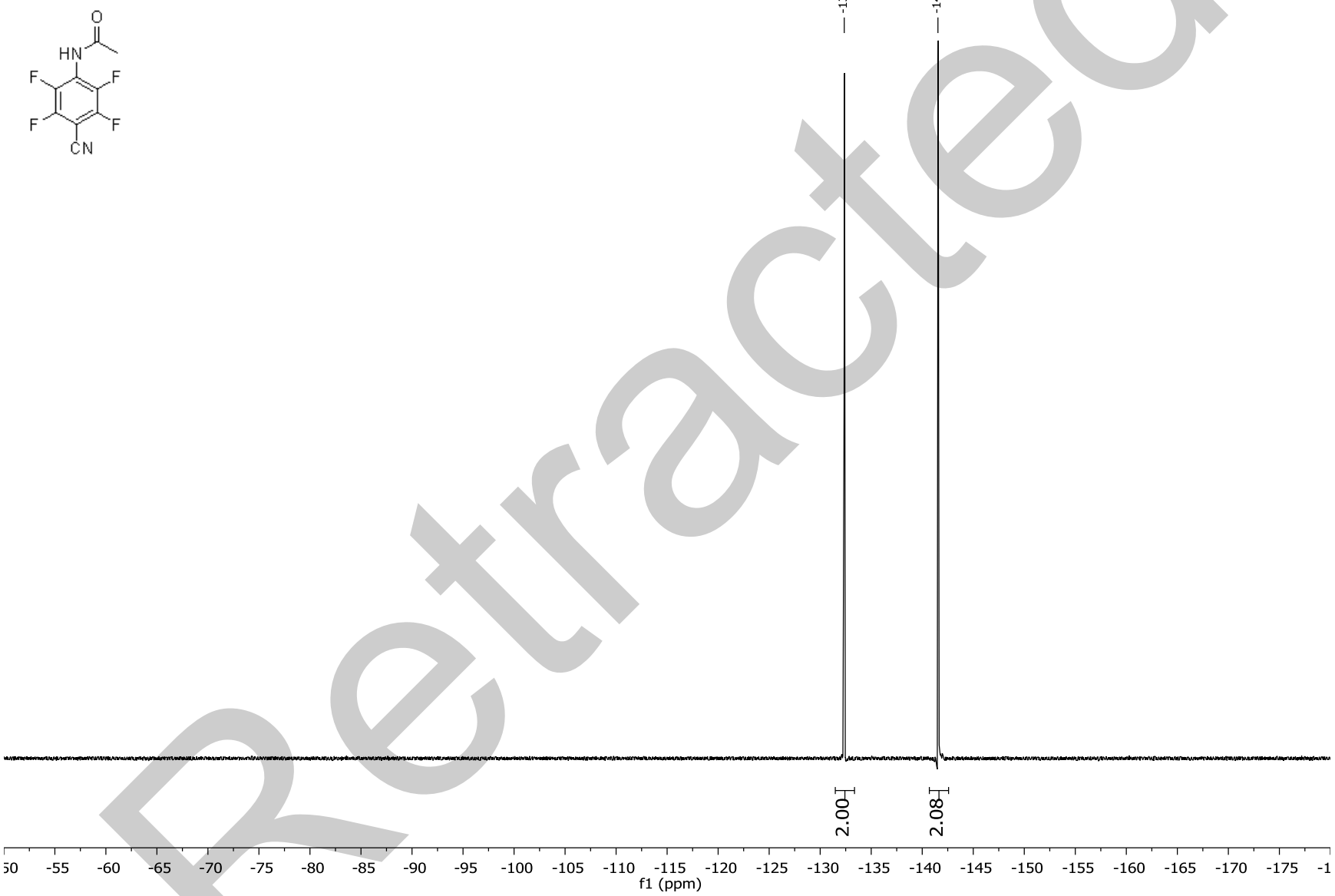
5h tert-butyl (perfluoropyridin-4-yl)carbamate ^{19}F NMR (376 MHz, $CDCl_3$)



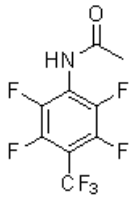
6a *N*-(4-cyano-2,3,5,6-tetrafluorophenyl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



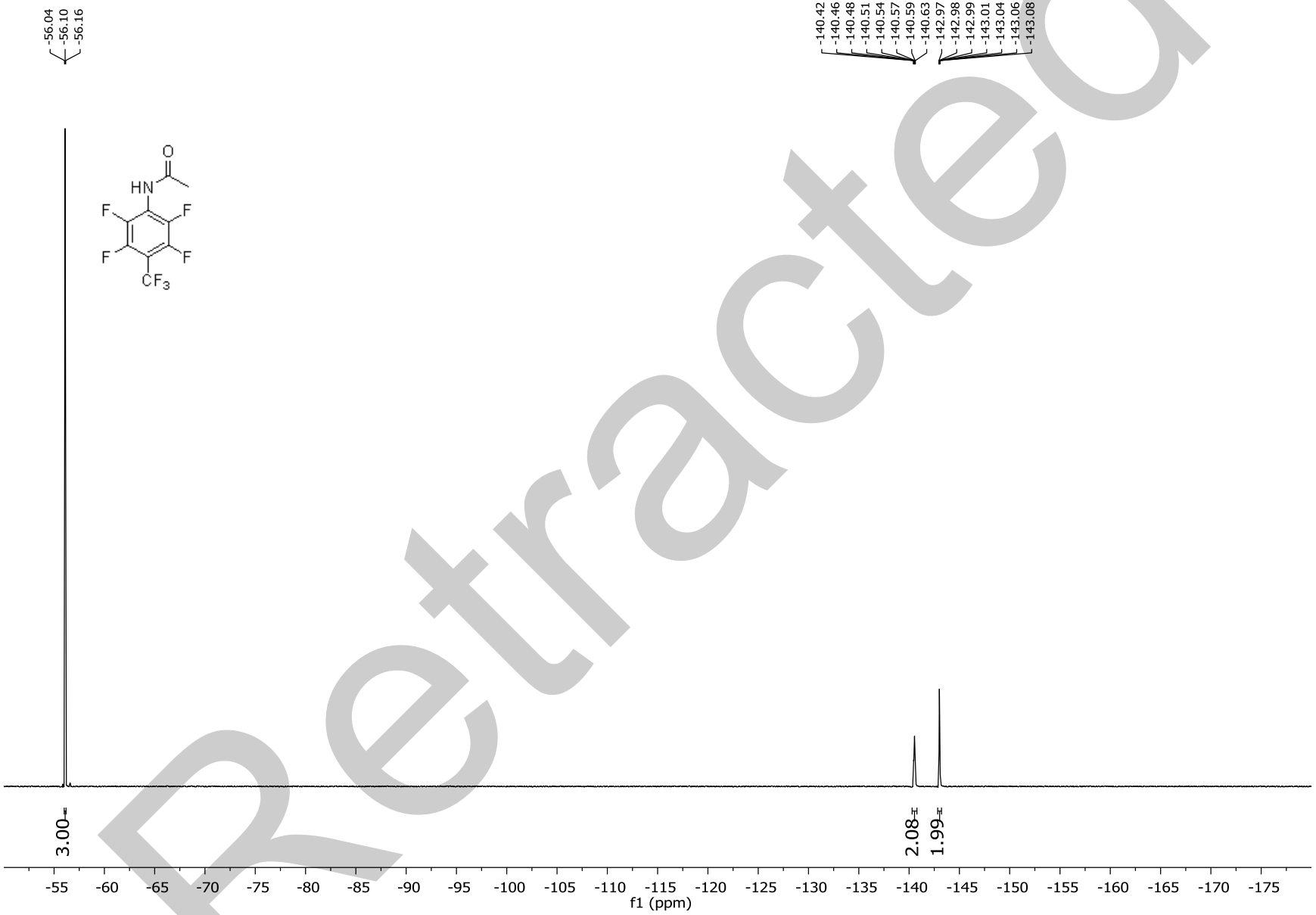
6a *N*-(4-cyano-2,3,5,6-tetrafluorophenyl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



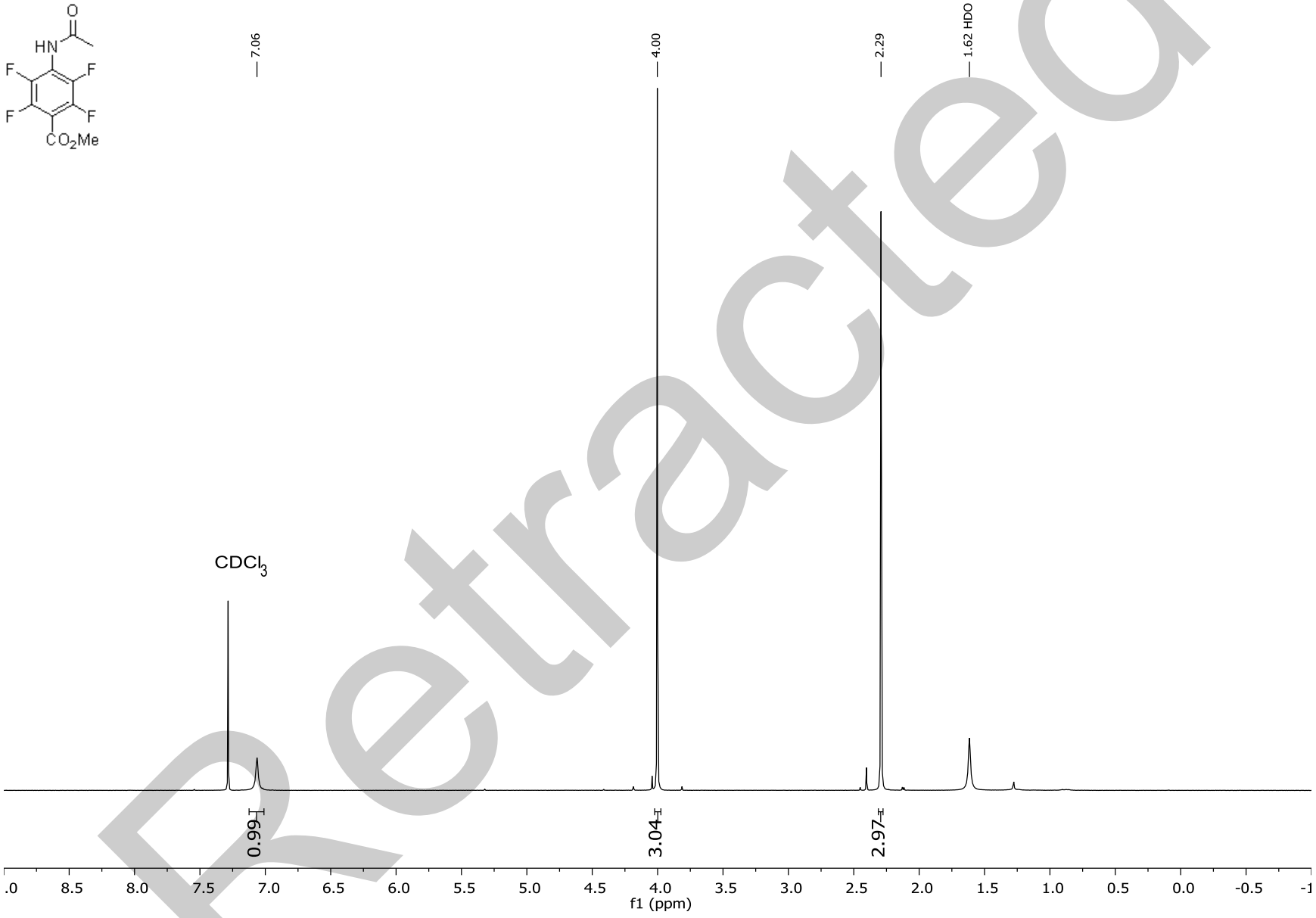
6b *N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



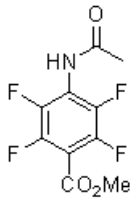
6b *N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



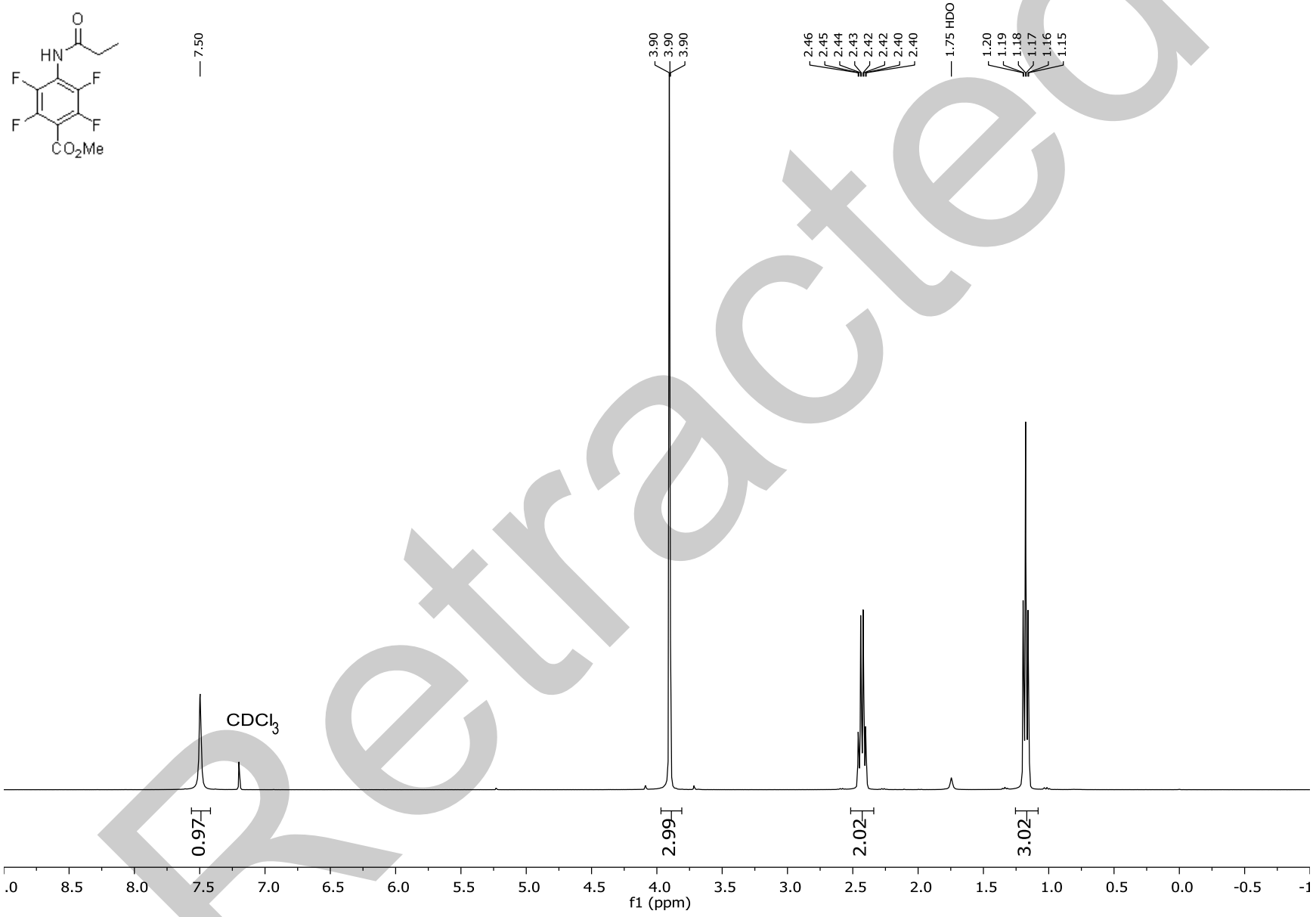
6c methyl 4-acetamido-2,3,5,6-tetrafluorobenzoate ^{1}H NMR (400 MHz, $CDCl_3$)



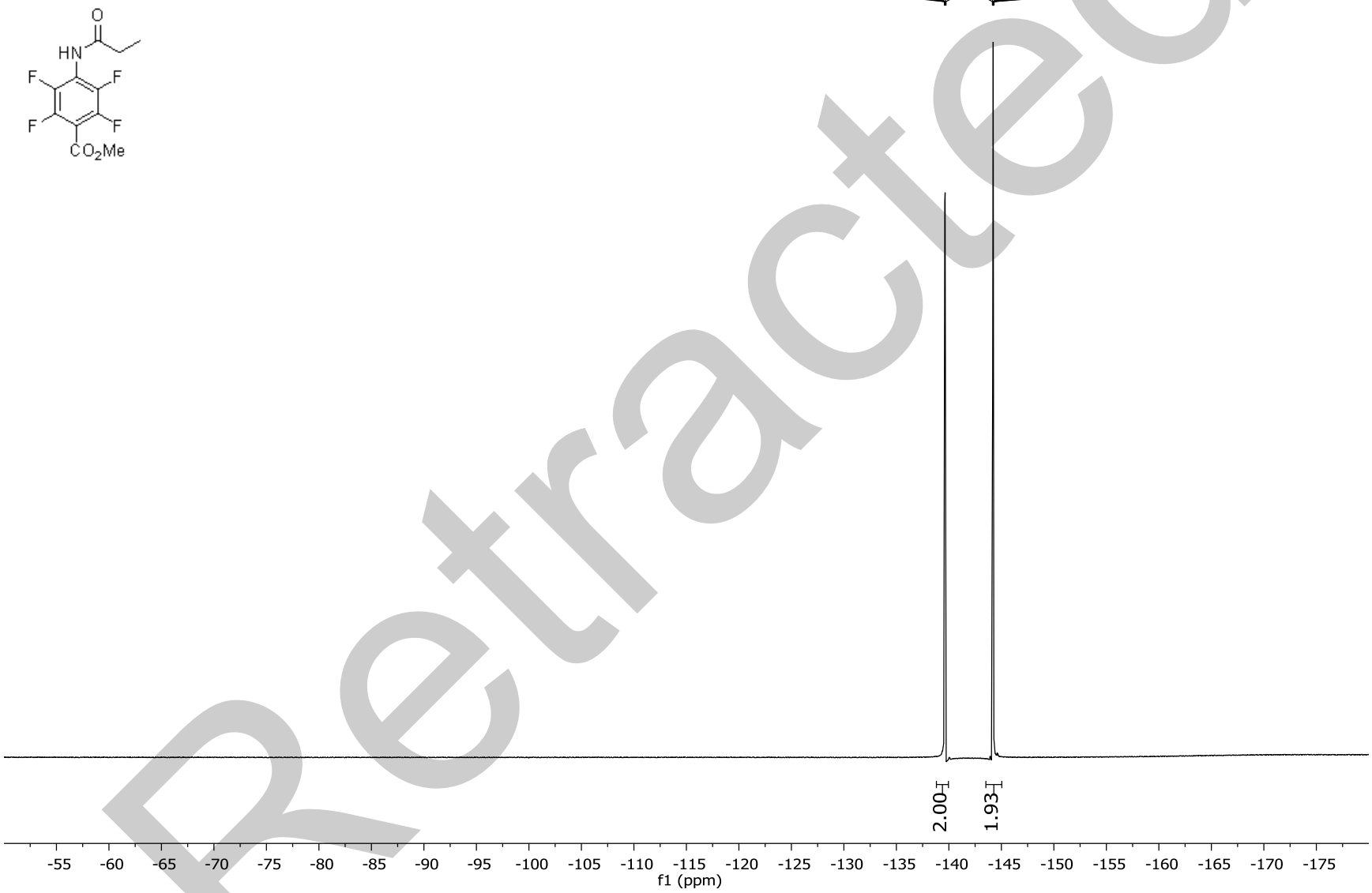
6c methyl 4-acetamido-2,3,5,6-tetrafluorobenzoate ^{19}F NMR (376 MHz, $CDCl_3$)



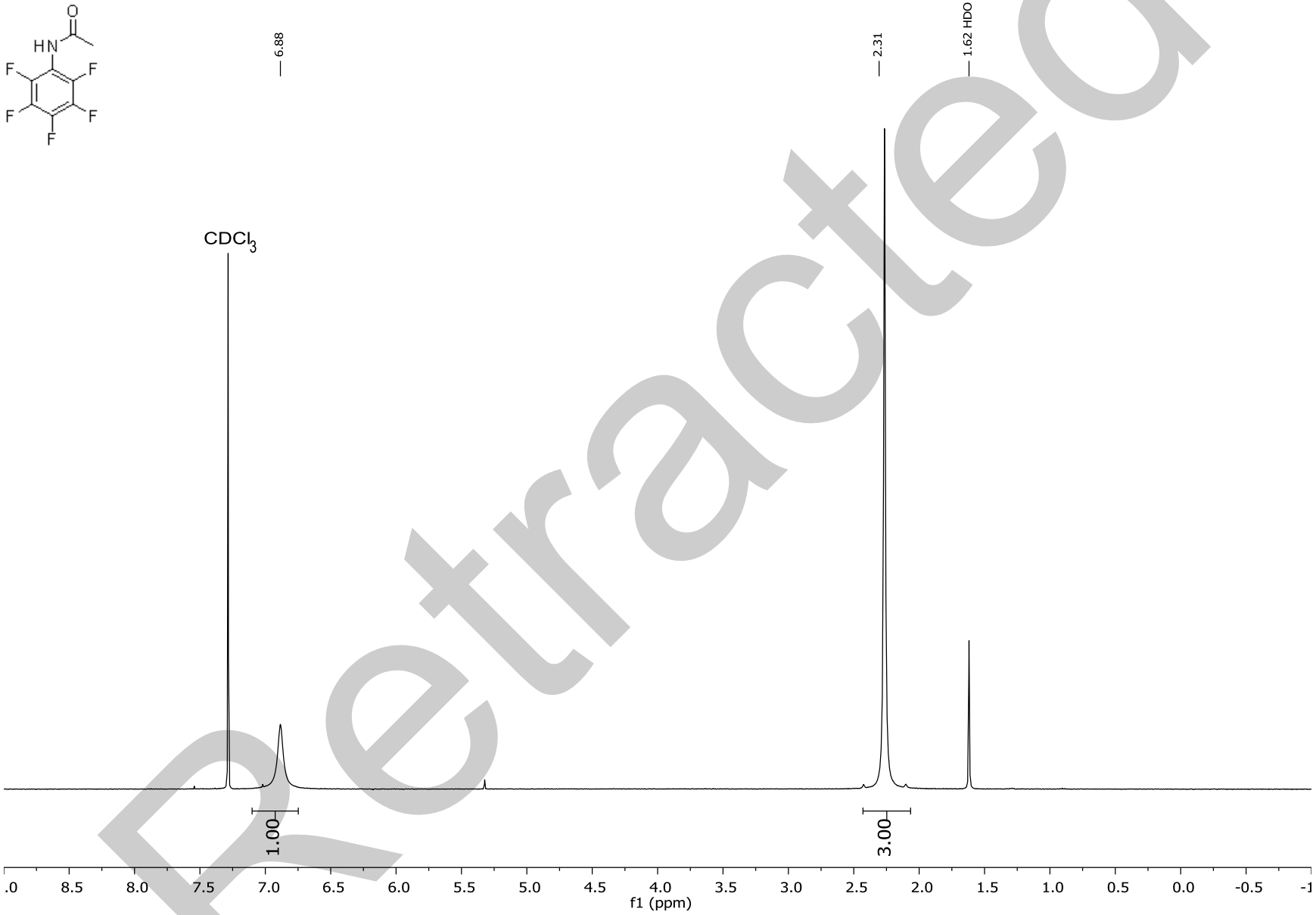
6d methyl 2,3,5,6-tetrafluoro-4-propionamidobenzoate ^{1}H NMR (400 MHz, $CDCl_3$)



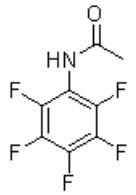
6d methyl 2,3,5,6-tetrafluoro-4-propionamidobenzoate ^{19}F NMR (376 MHz, $CDCl_3$)



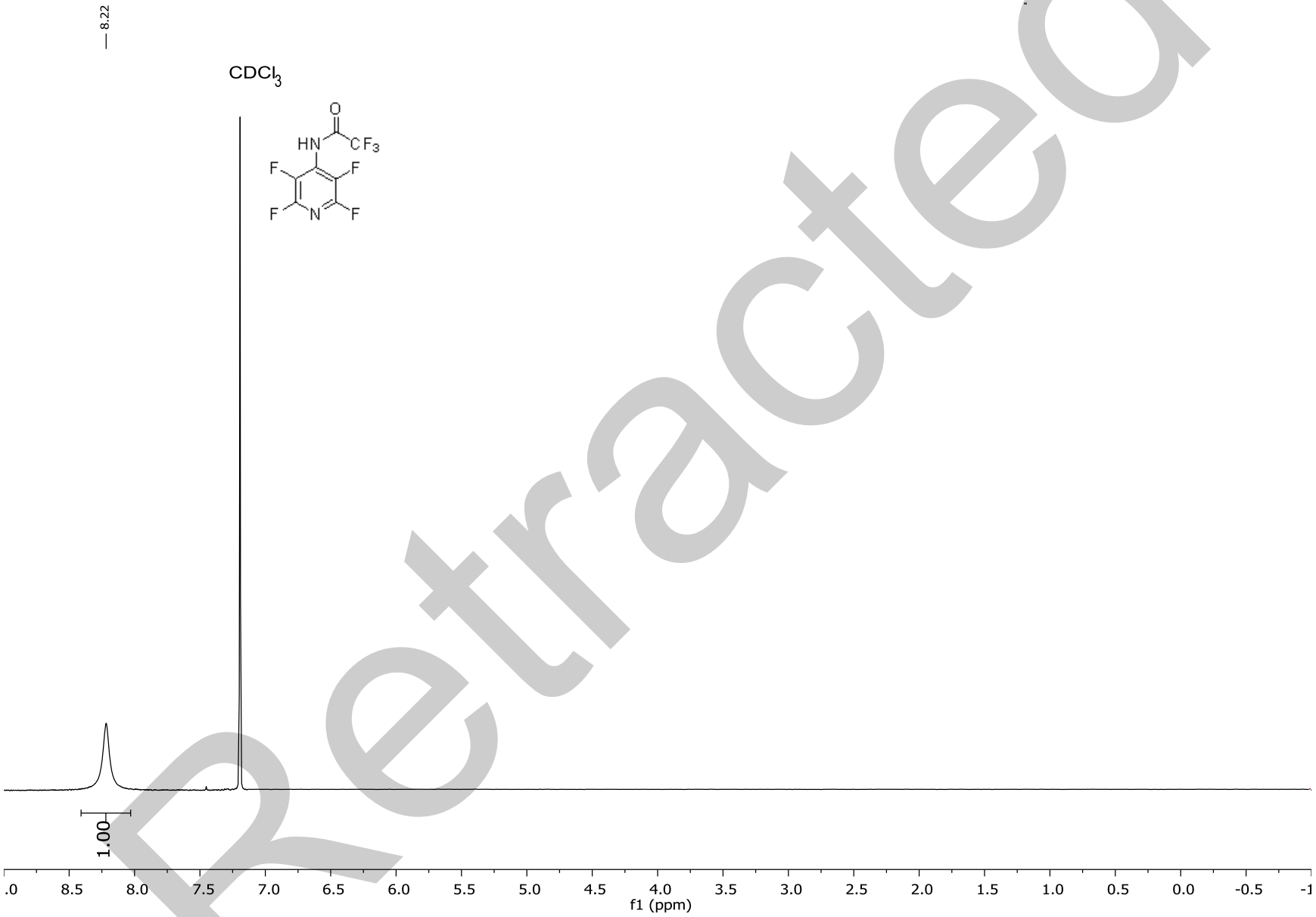
6e *N*-(perfluorophenyl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



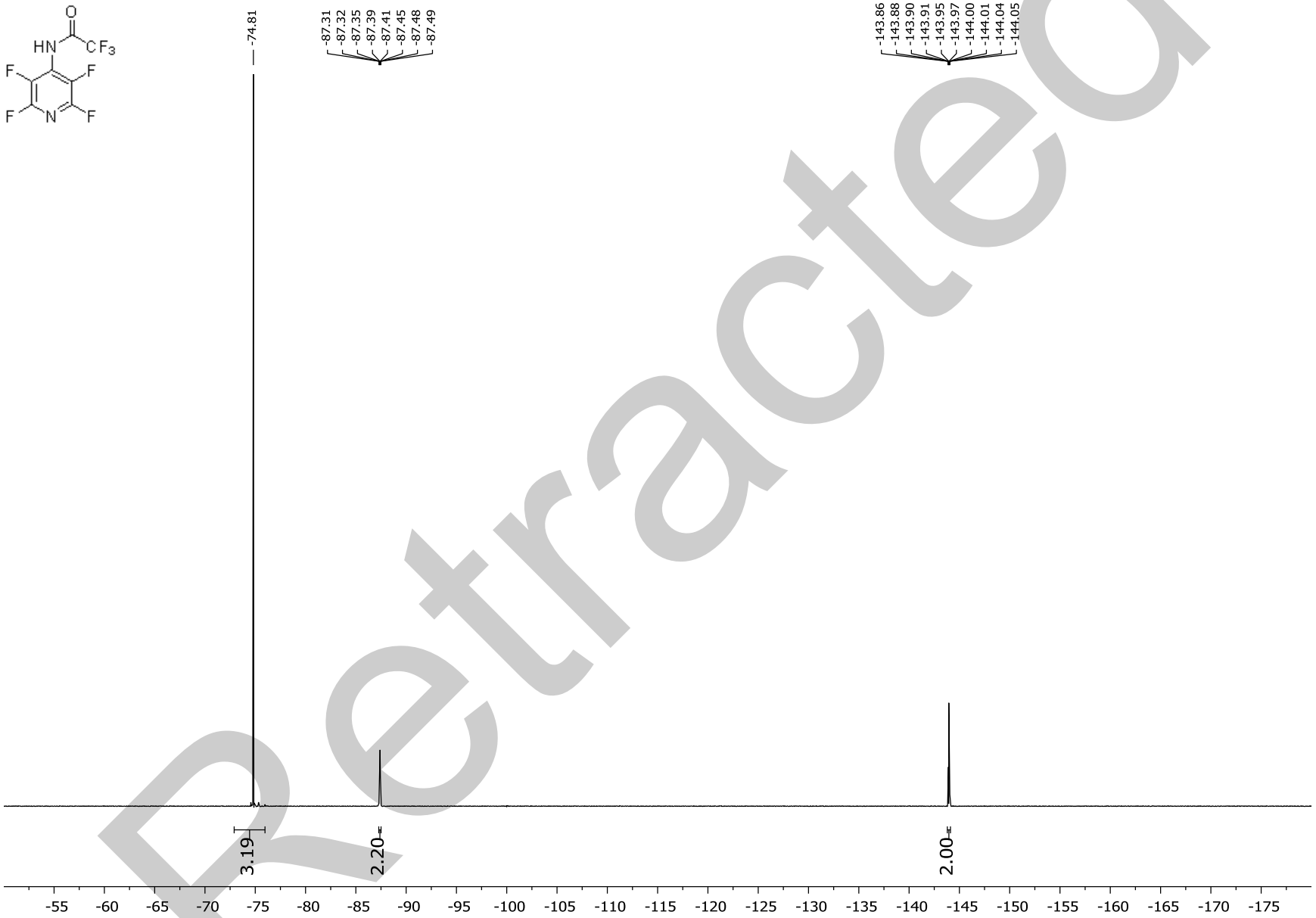
6e *N*-(perfluorophenyl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



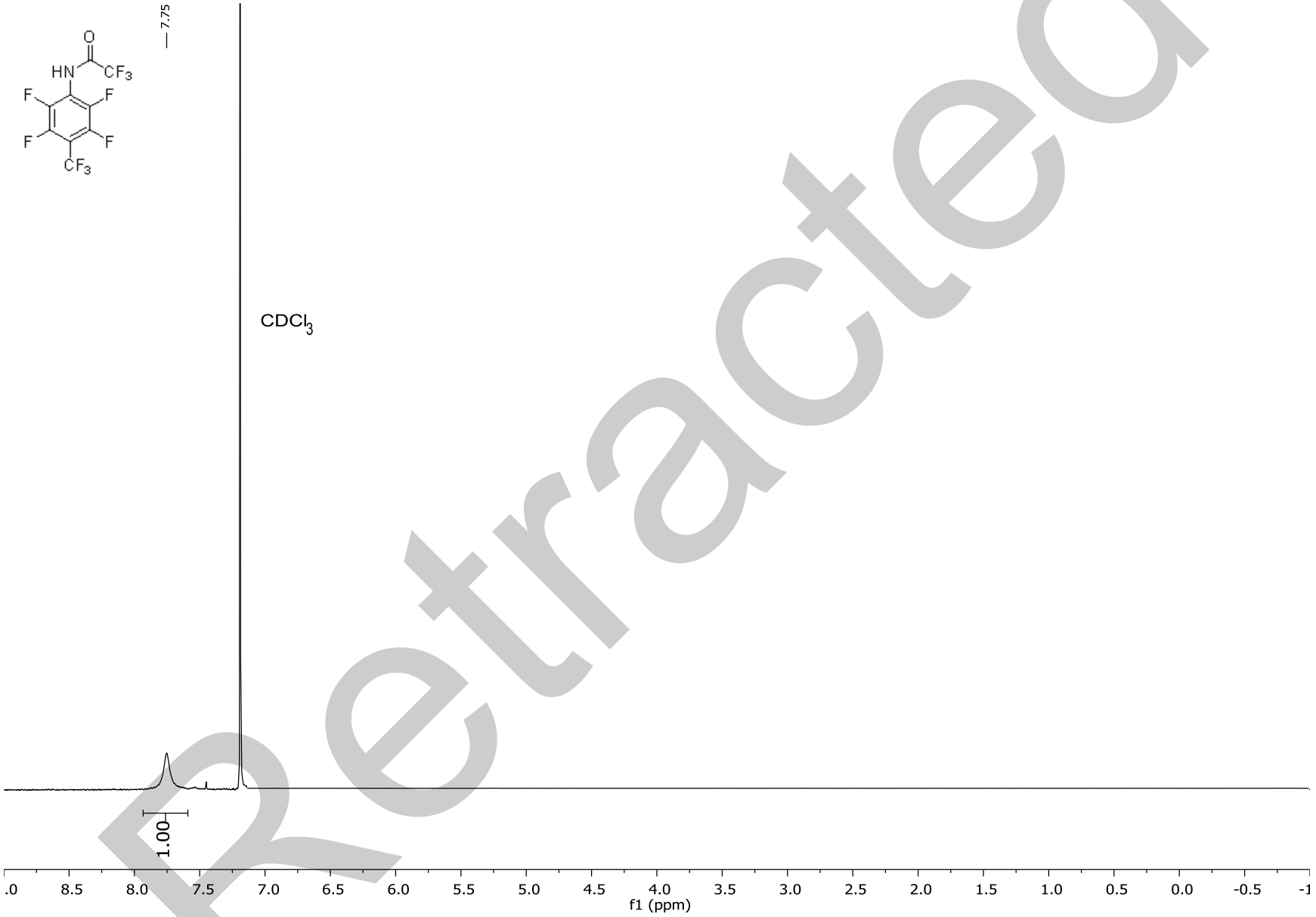
6f 2,2,2-trifluoro-*N*-(perfluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



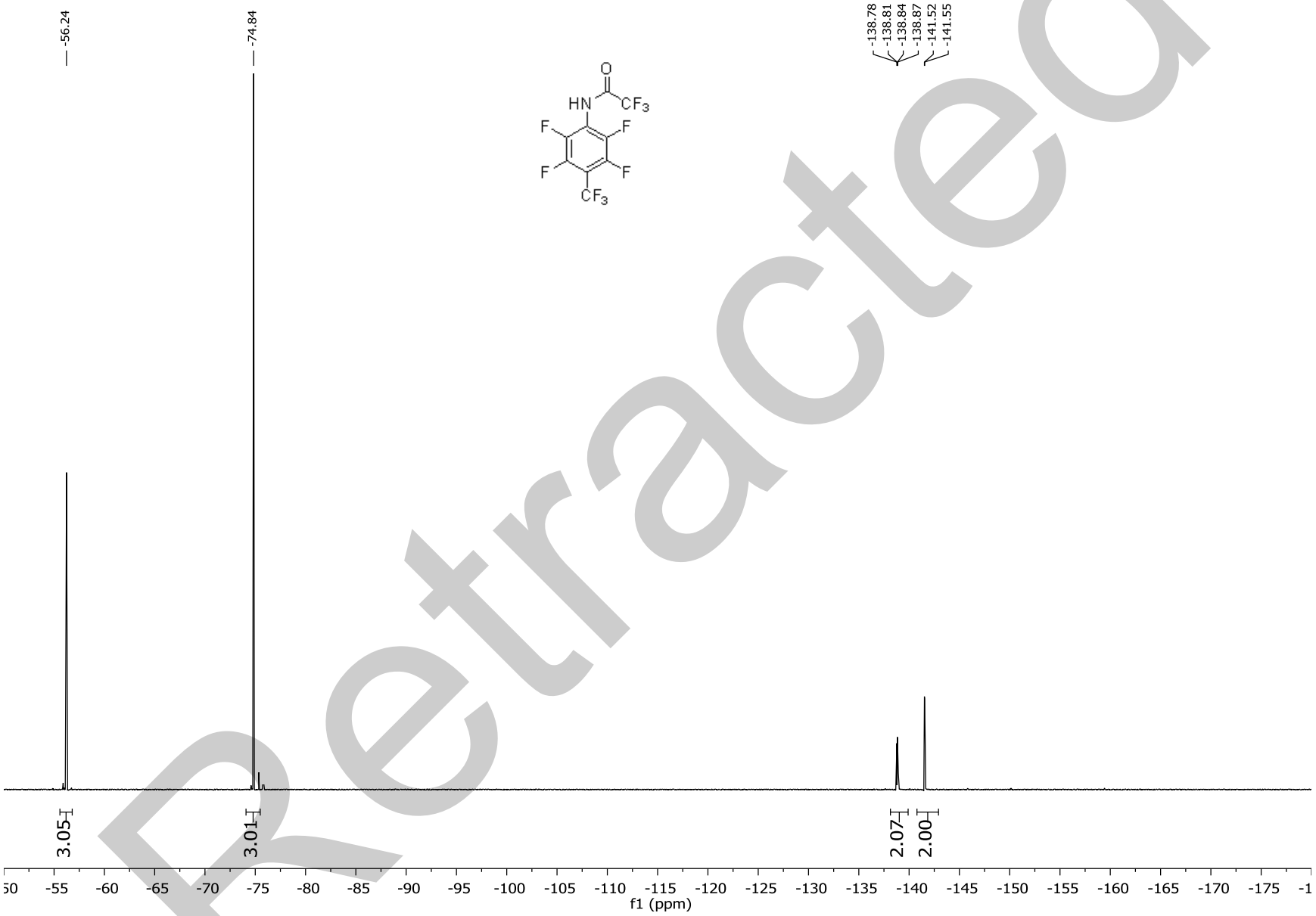
6f 2,2,2-trifluoro-*N*-(perfluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



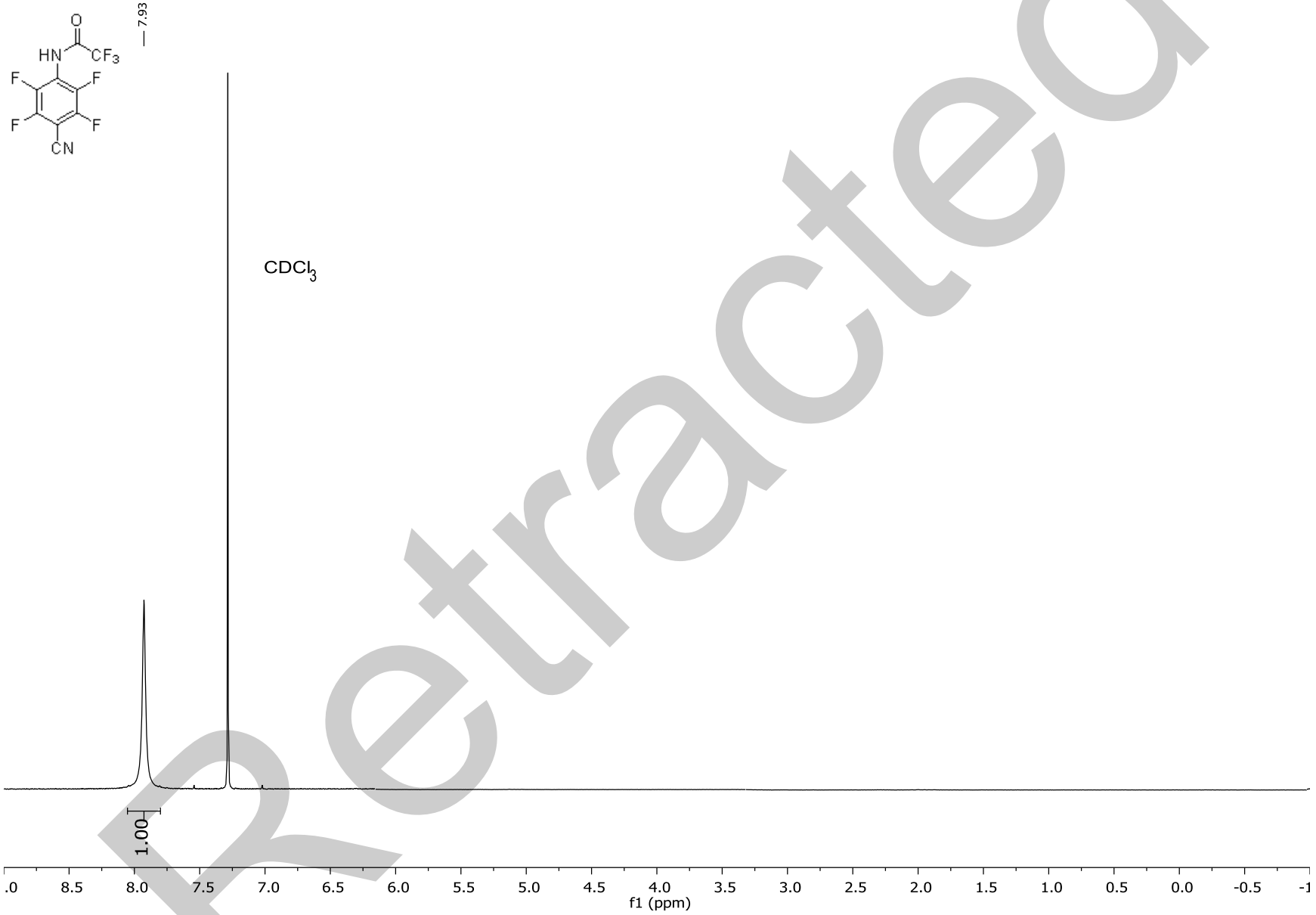
6g 2,2,2-trifluoro-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



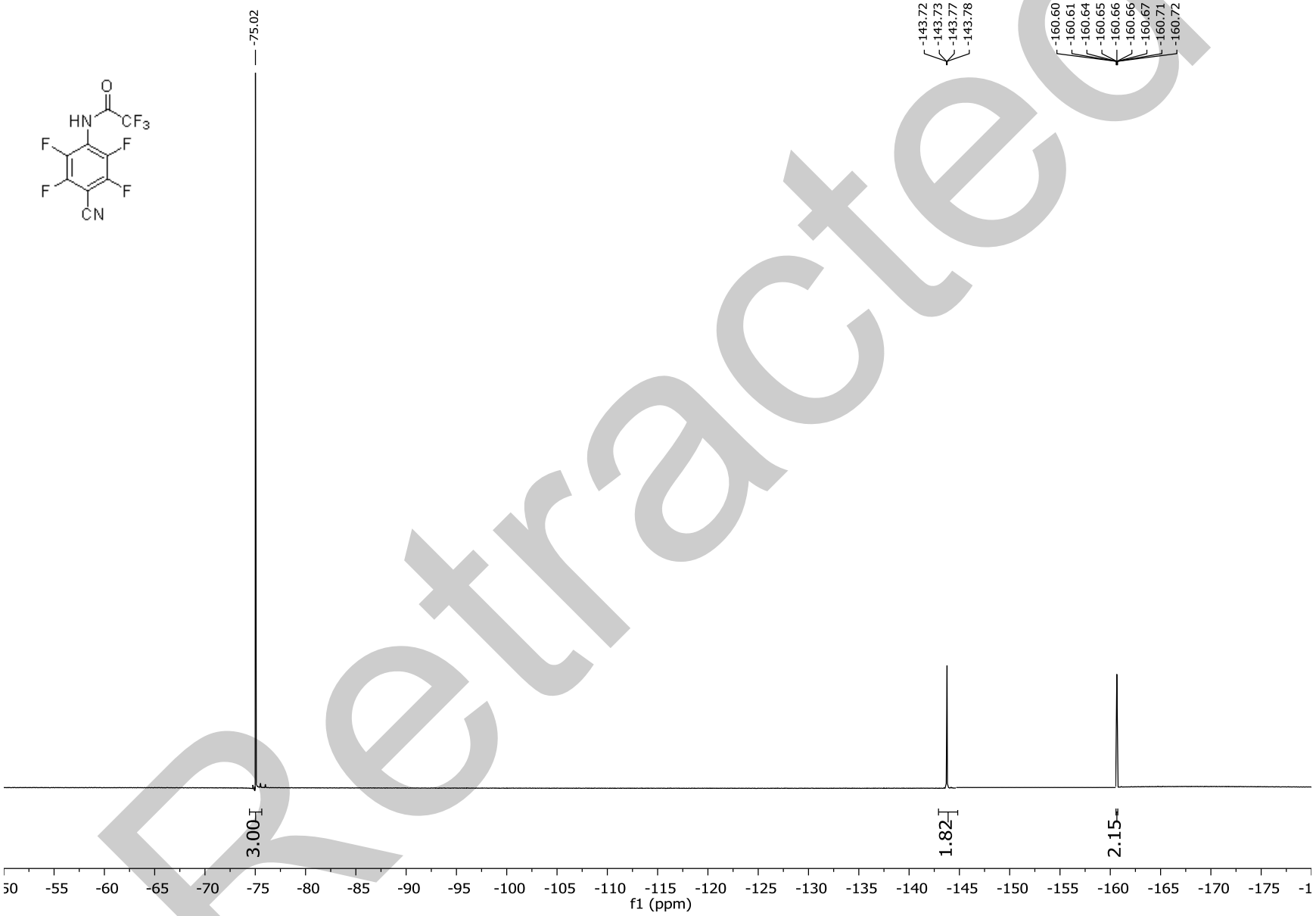
6g 2,2,2-trifluoro-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



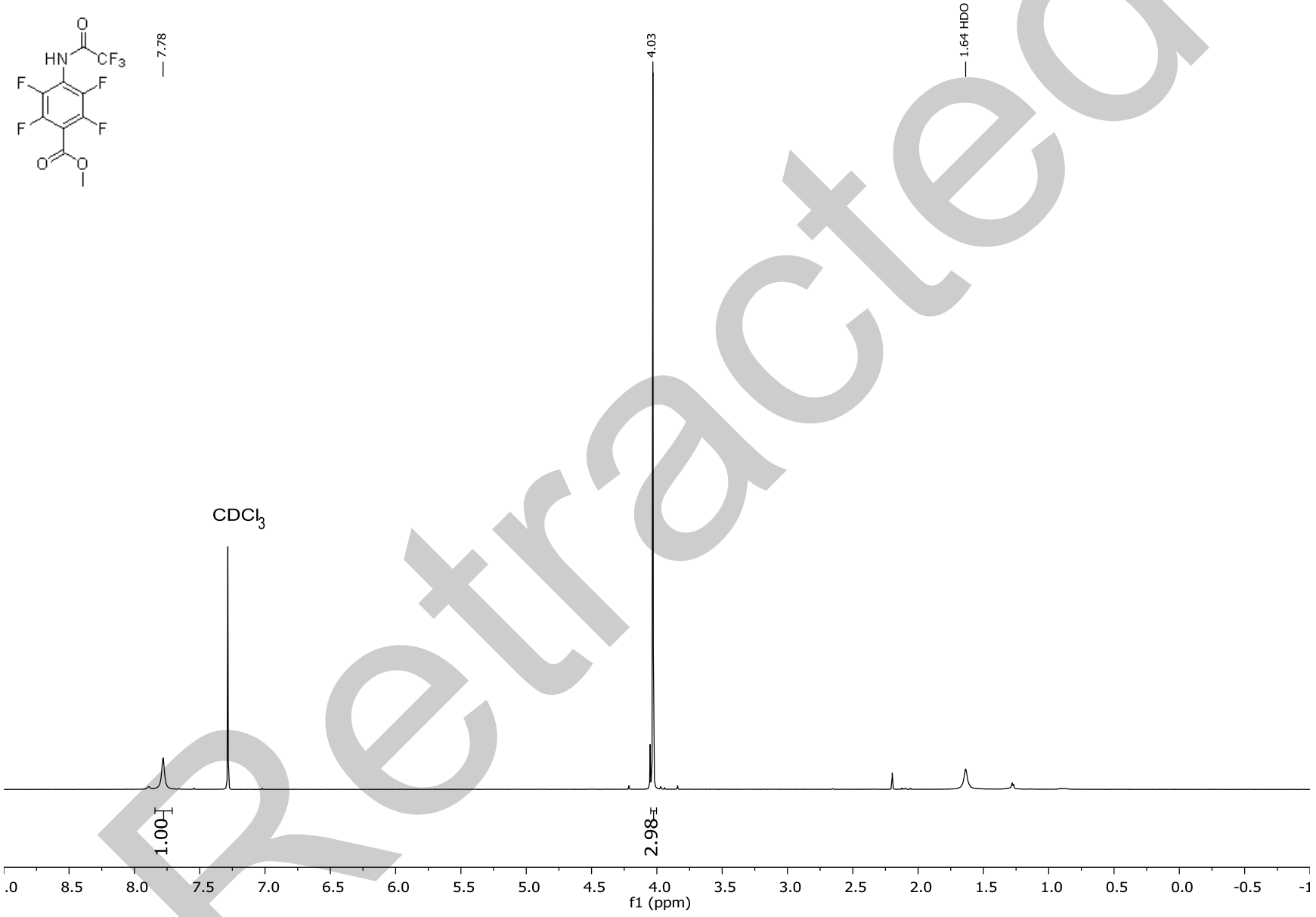
6h *N*-(4-cyano-2,3,5,6-tetrafluorophenyl)-2,2,2-trifluoroacetamide ^{1}H NMR (400 MHz, $CDCl_3$)



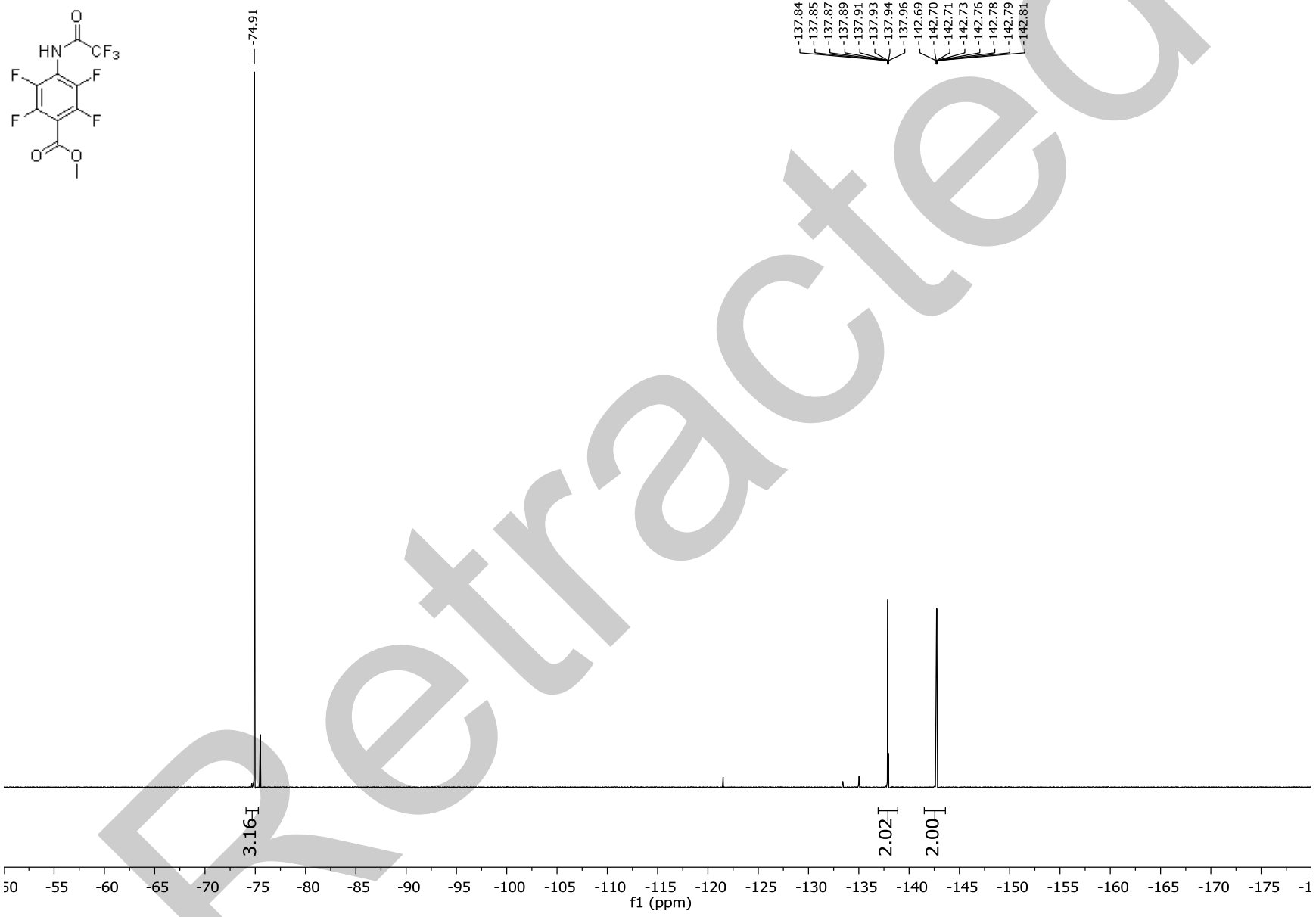
6h *N*-(4-cyano-2,3,5,6-tetrafluorophenyl)-2,2,2-trifluoroacetamide ^{19}F NMR (376 MHz, $CDCl_3$)



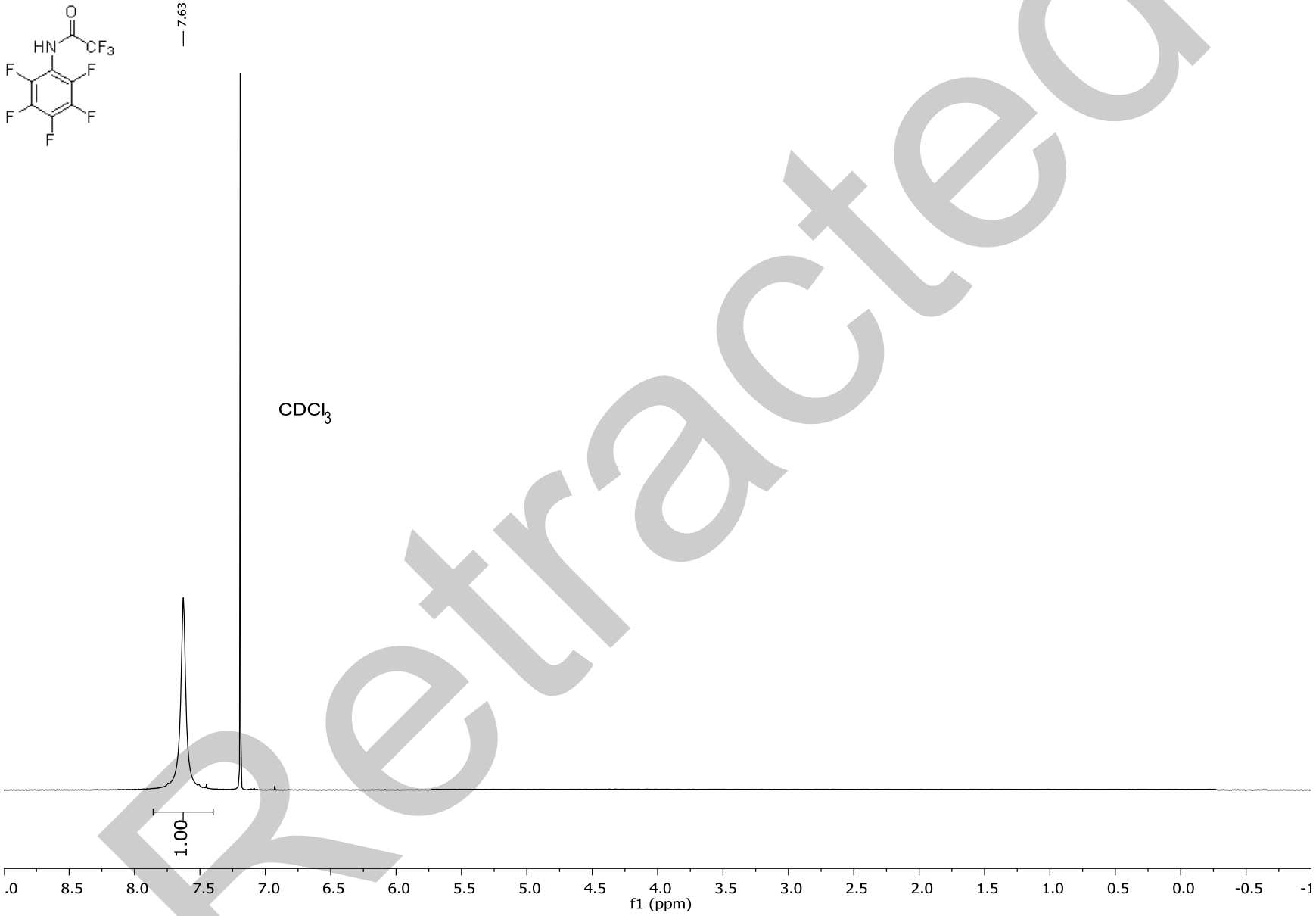
6i methyl 2,3,5,6-tetrafluoro-4-(2,2,2-trifluoroacetamido)benzoate ^{1}H NMR (400 MHz, $CDCl_3$)



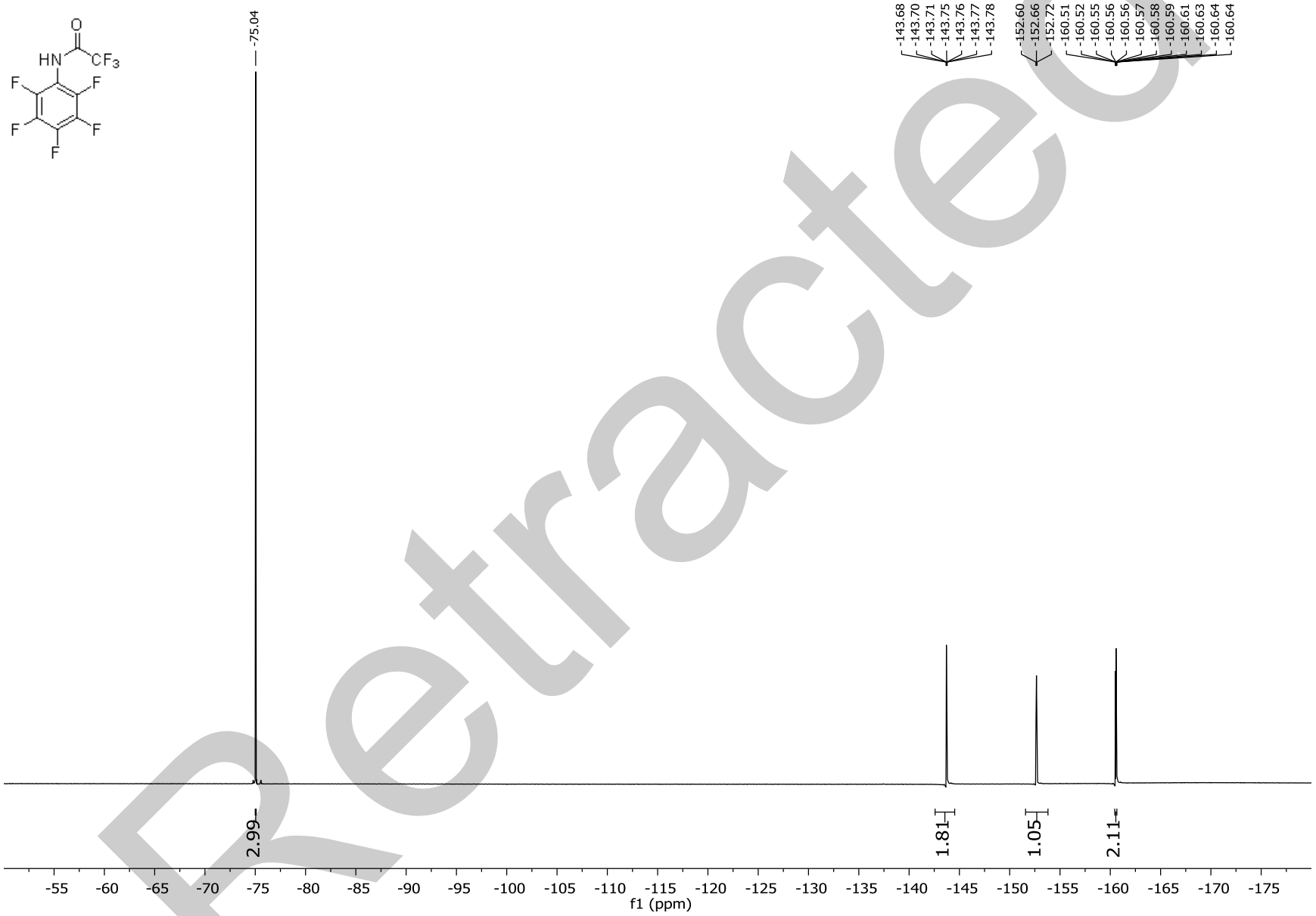
6i methyl 2,3,5,6-tetrafluoro-4-(2,2,2-trifluoroacetamido)benzoate ^{19}F NMR (376 MHz, $CDCl_3$)



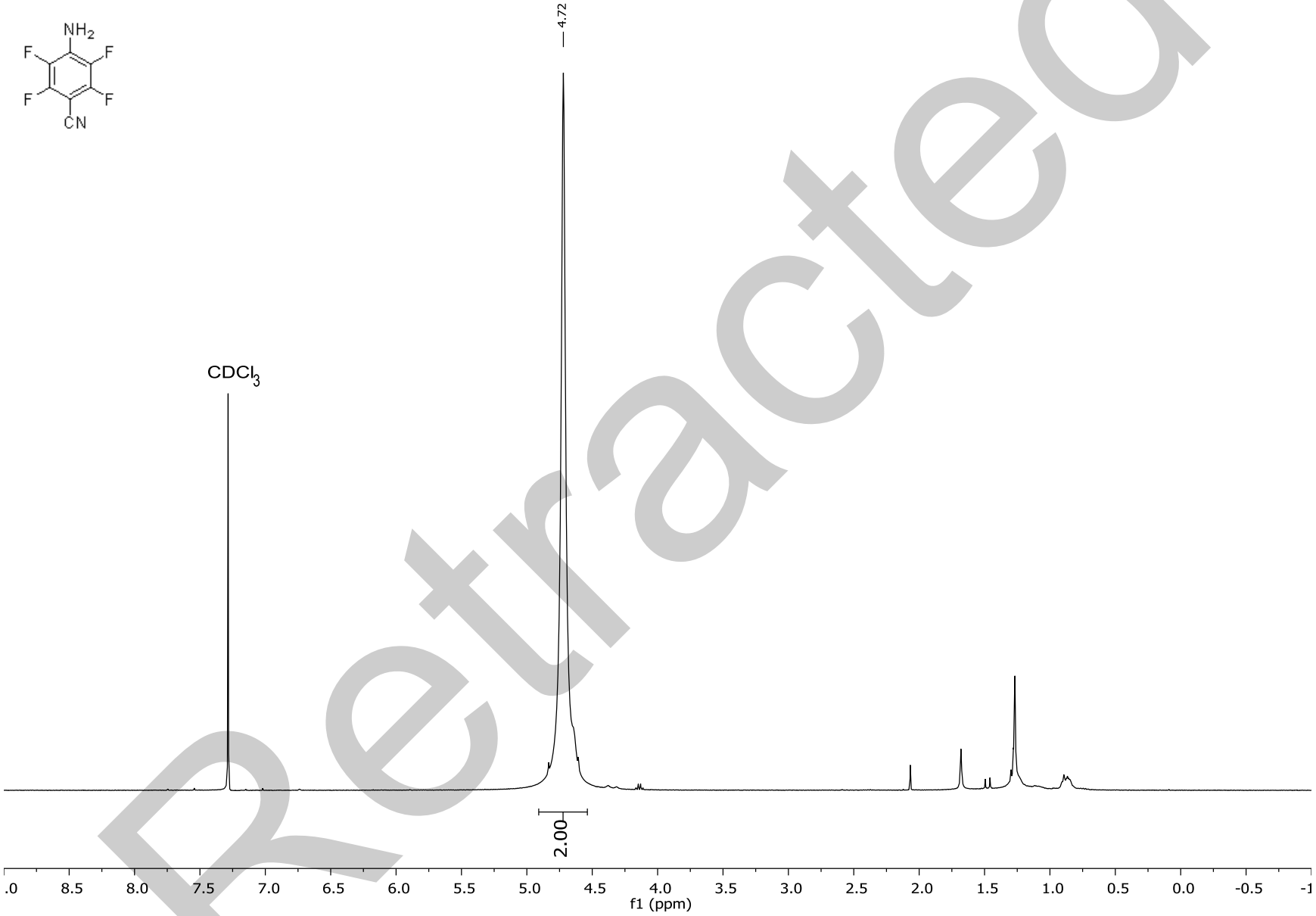
6j 2,2,2-trifluoro-*N*-(perfluorophenyl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



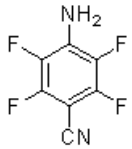
6j 2,2,2-trifluoro-*N*-(perfluorophenyl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



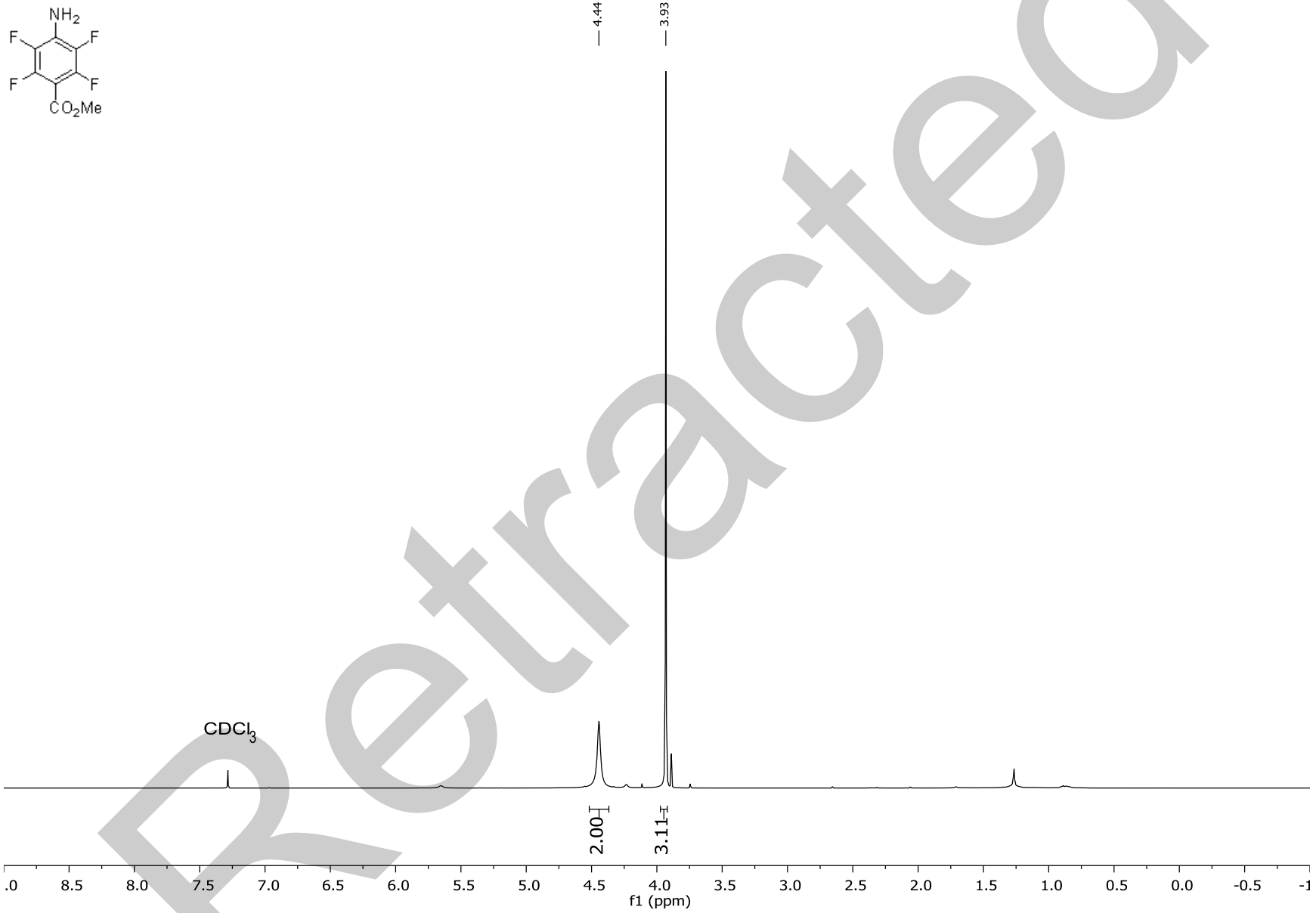
6m 4-amino-2,3,5,6-tetrafluorobenzonitrile ^{1}H NMR (400 MHz, $CDCl_3$)



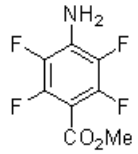
6m 4-amino-2,3,5,6-tetrafluorobenzonitrile ^{19}F NMR (376 MHz, $CDCl_3$)



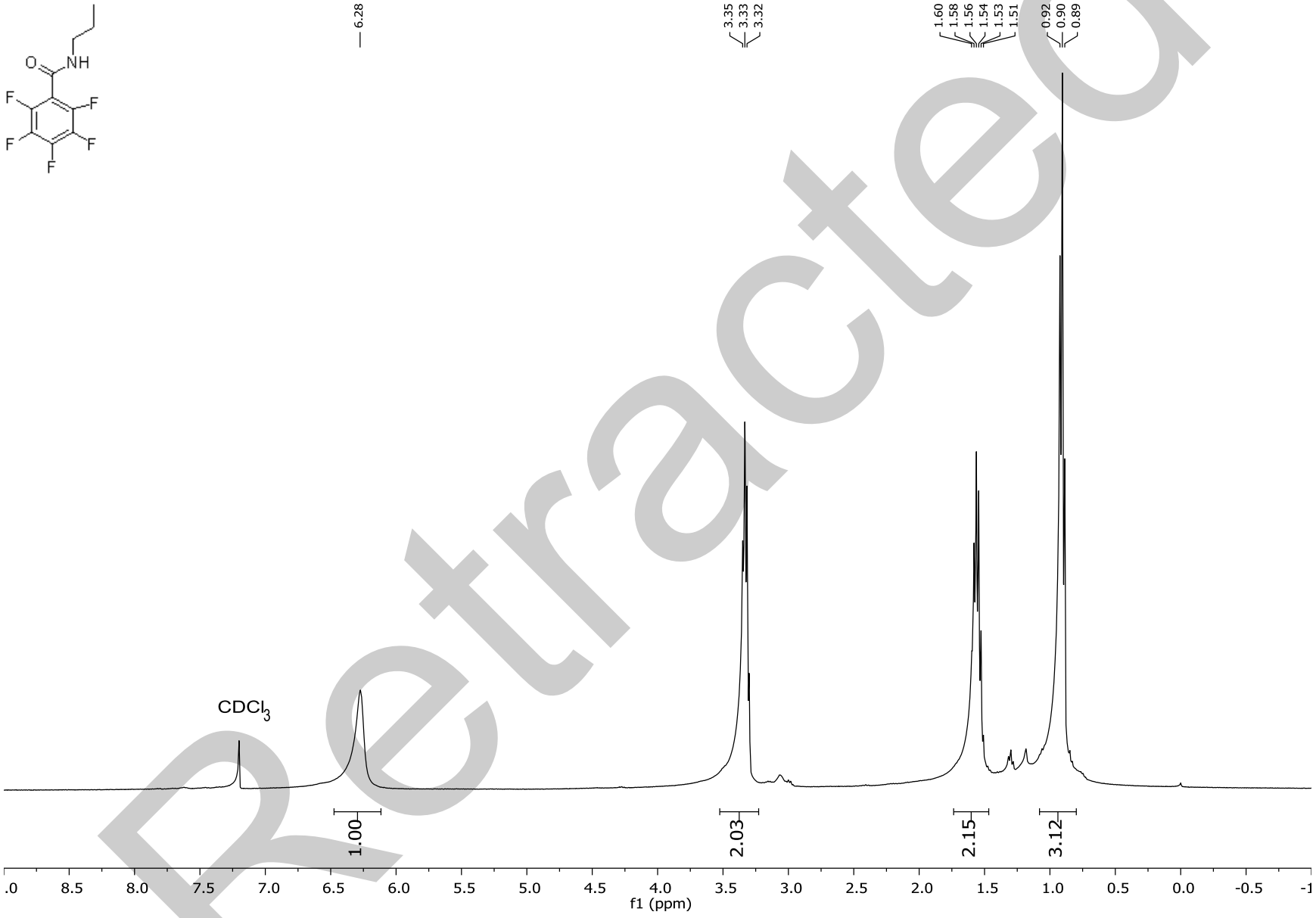
6n methyl 4-amino-2,3,5,6-tetrafluorobenzoate ^{1}H NMR (400 MHz, $CDCl_3$)



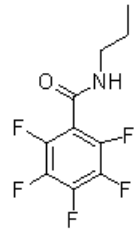
6n methyl 4-amino-2,3,5,6-tetrafluorobenzoate ^{19}F NMR (376 MHz, $CDCl_3$)



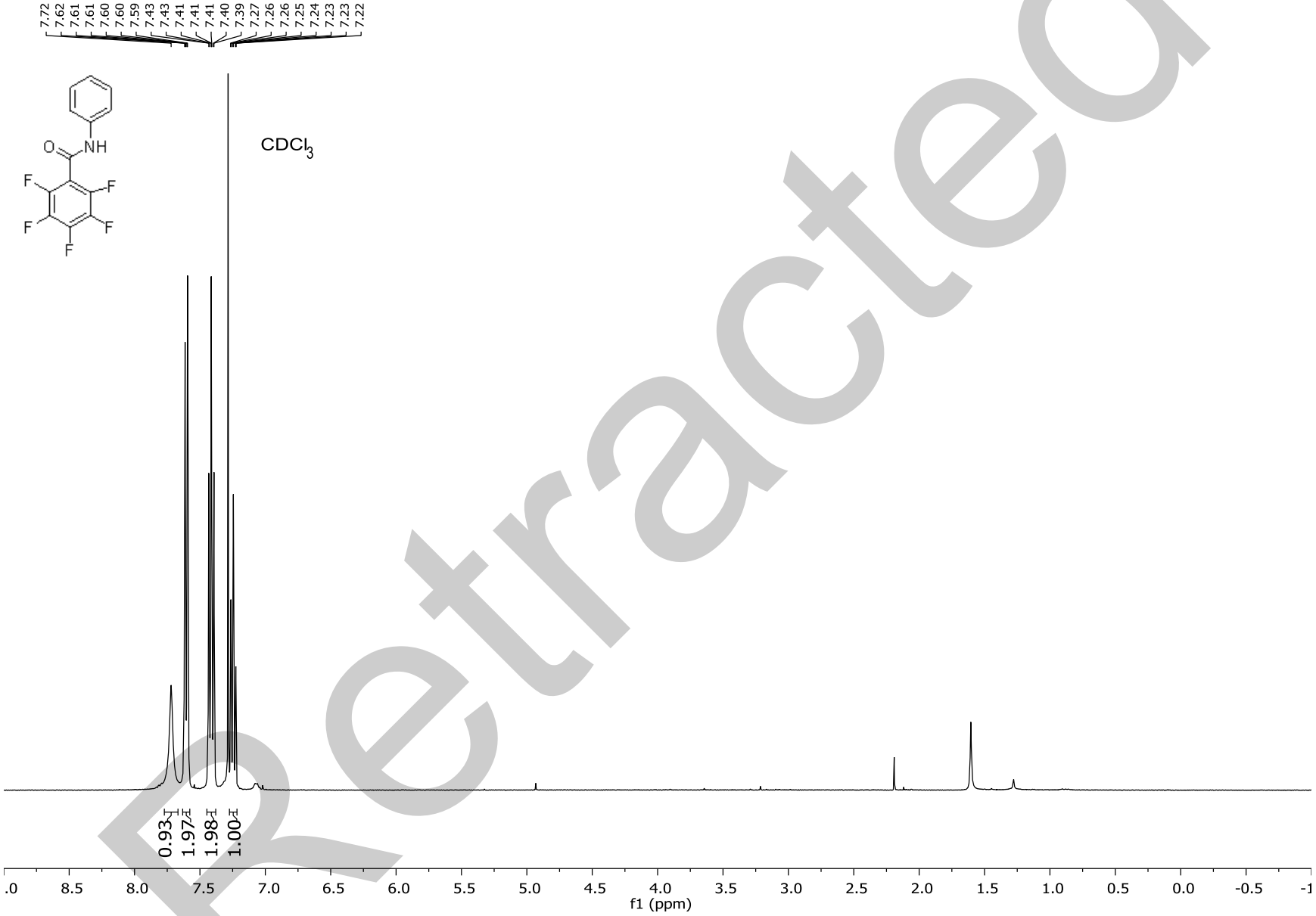
7a 2,3,4,5,6-pentafluoro-*N*-propylbenzamide ^{1}H NMR (400 MHz, $CDCl_3$)



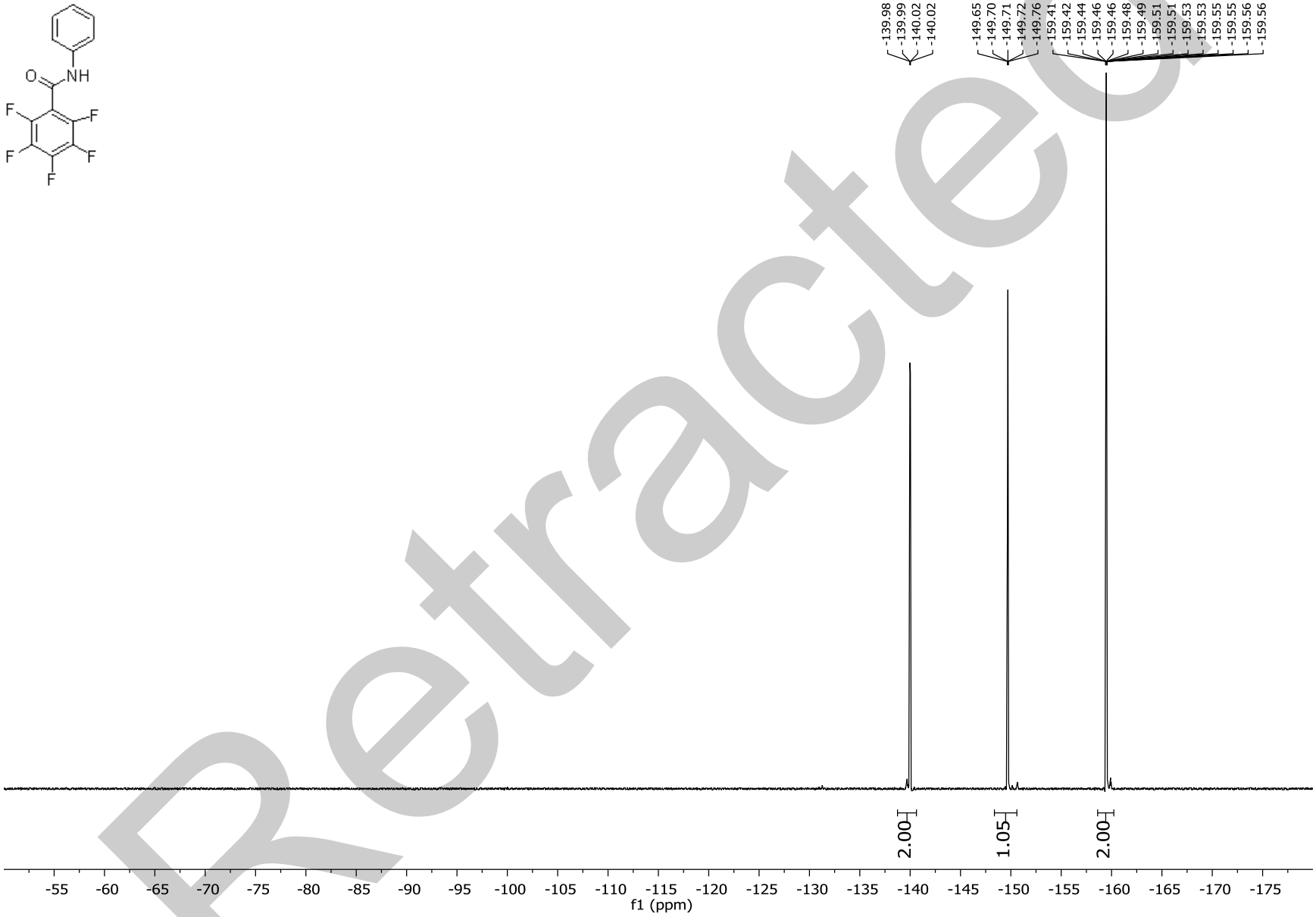
7a 2,3,4,5,6-pentafluoro-*N*-propylbenzamide ^{19}F NMR (376 MHz, $CDCl_3$)



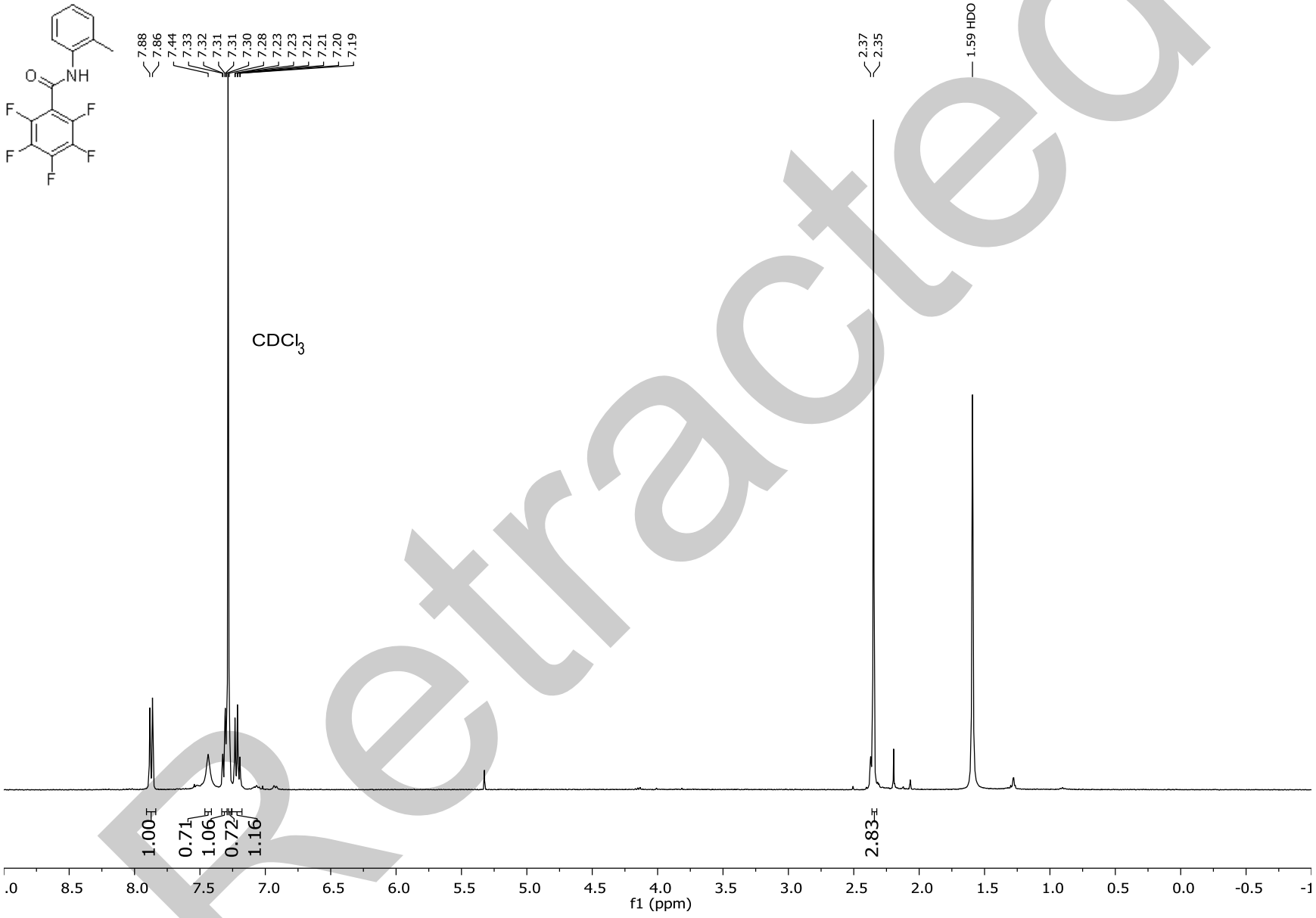
7b 2,3,4,5,6-pentafluoro-*N*-phenylbenzamide ^{1}H NMR (400 MHz, $CDCl_3$)



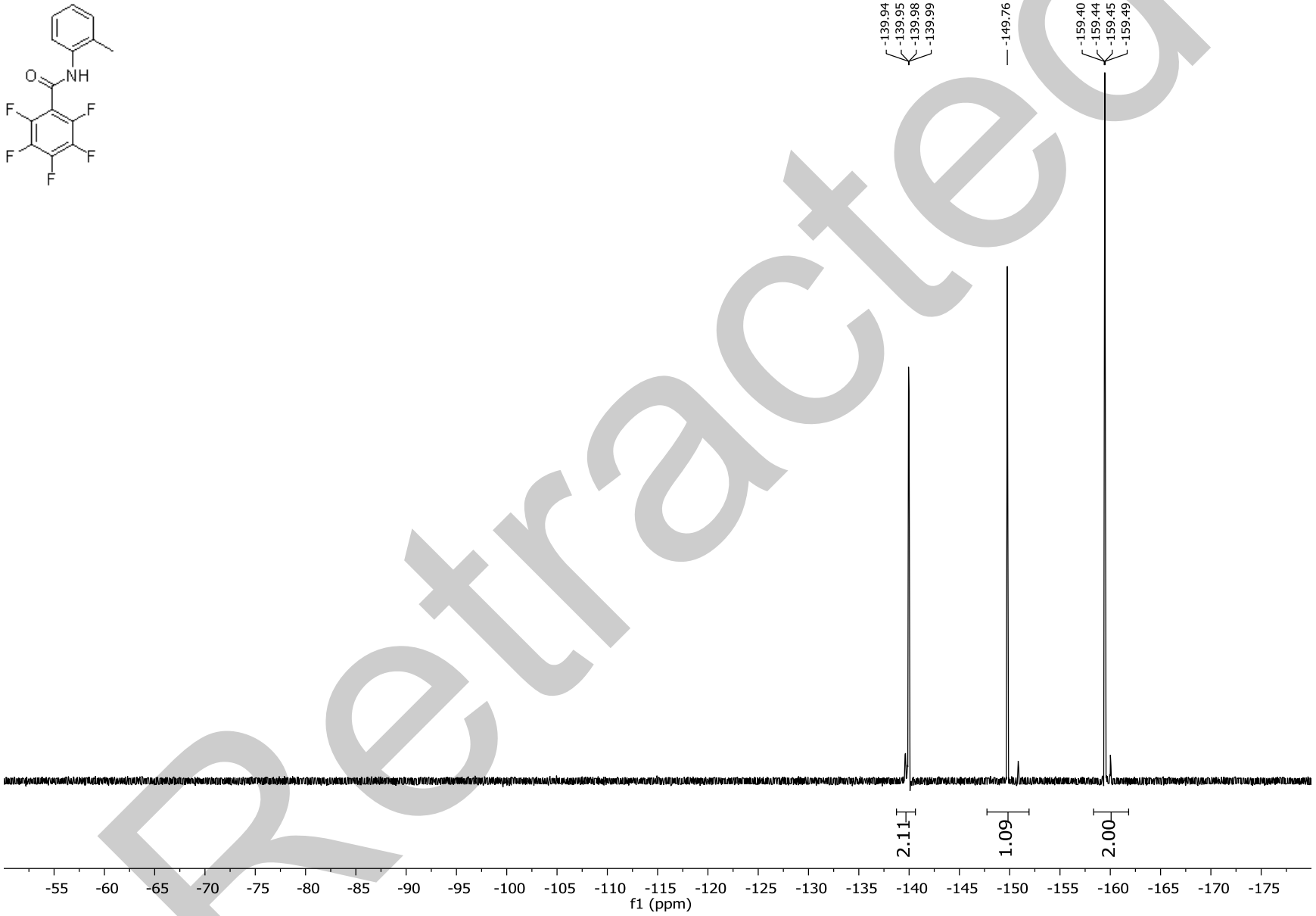
7b 2,3,4,5,6-pentafluoro-*N*-phenylbenzamide ^{19}F NMR (376 MHz, $CDCl_3$)



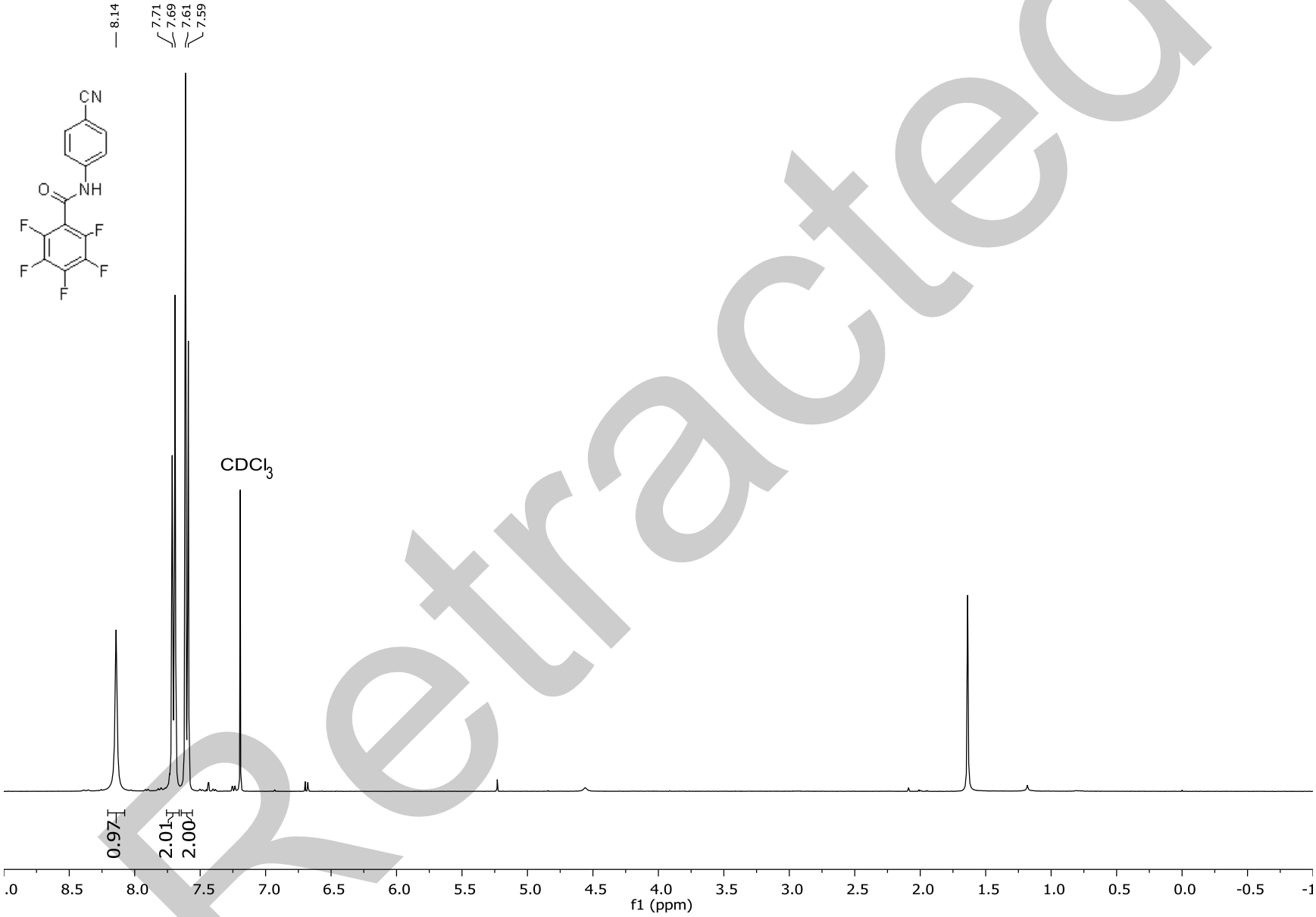
7c 2, 2,3,4,5,6-pentafluoro-*N*-(o-tolyl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



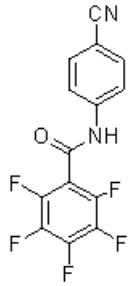
7c 2, 2,3,4,5,6-pentafluoro-*N*-(o-tolyl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



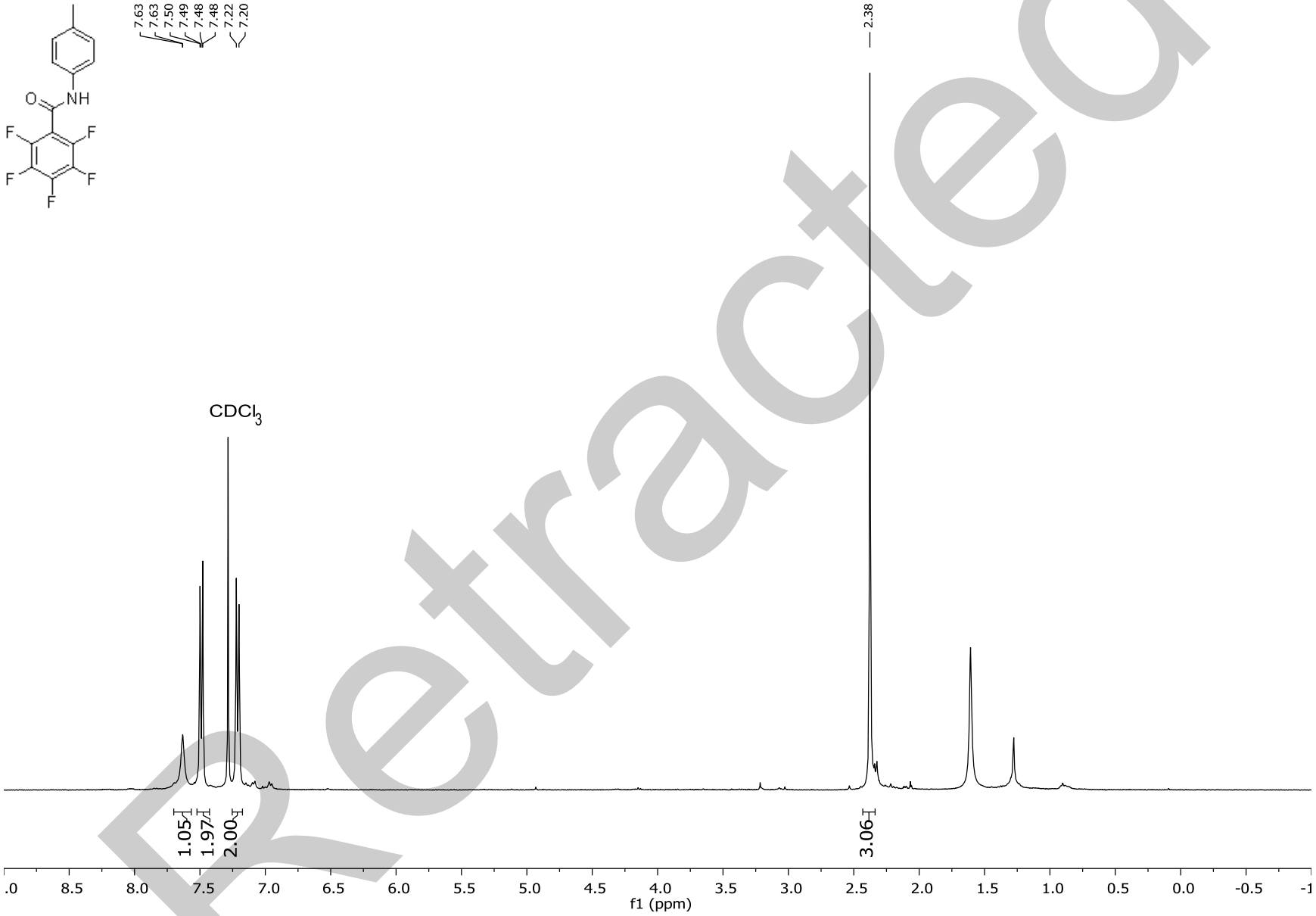
7d *N*-(4-cyanophenyl)-2,3,4,5,6-pentafluorobenzamide ^{1}H NMR (400 MHz, $CDCl_3$)



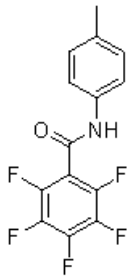
7d *N*-(4-cyanophenyl)-2,3,4,5,6-pentafluorobenzamide ^{19}F NMR (376 MHz, $CDCl_3$)



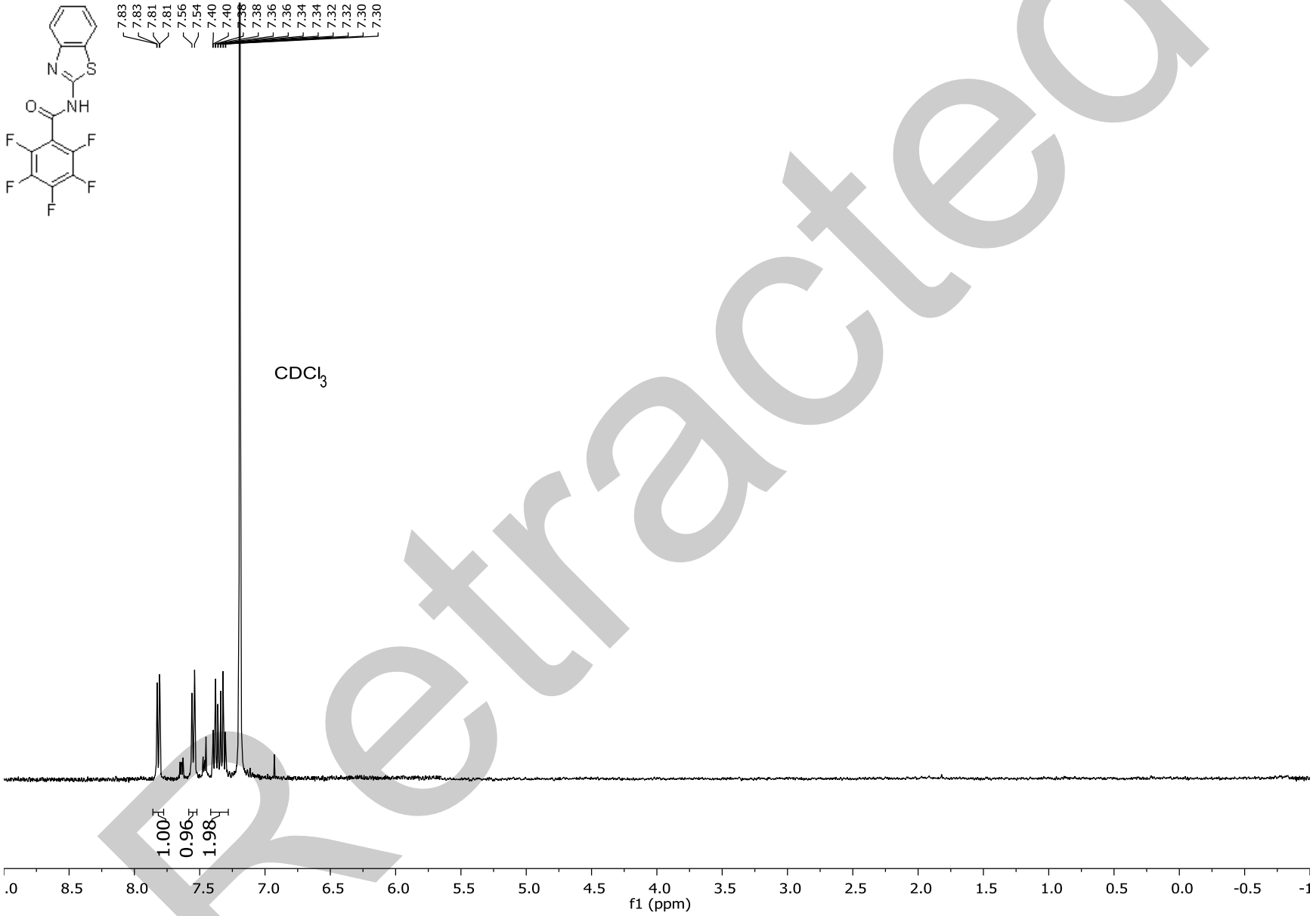
7e 2,3,4,5,6-pentafluoro-*N*-(p-tolyl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



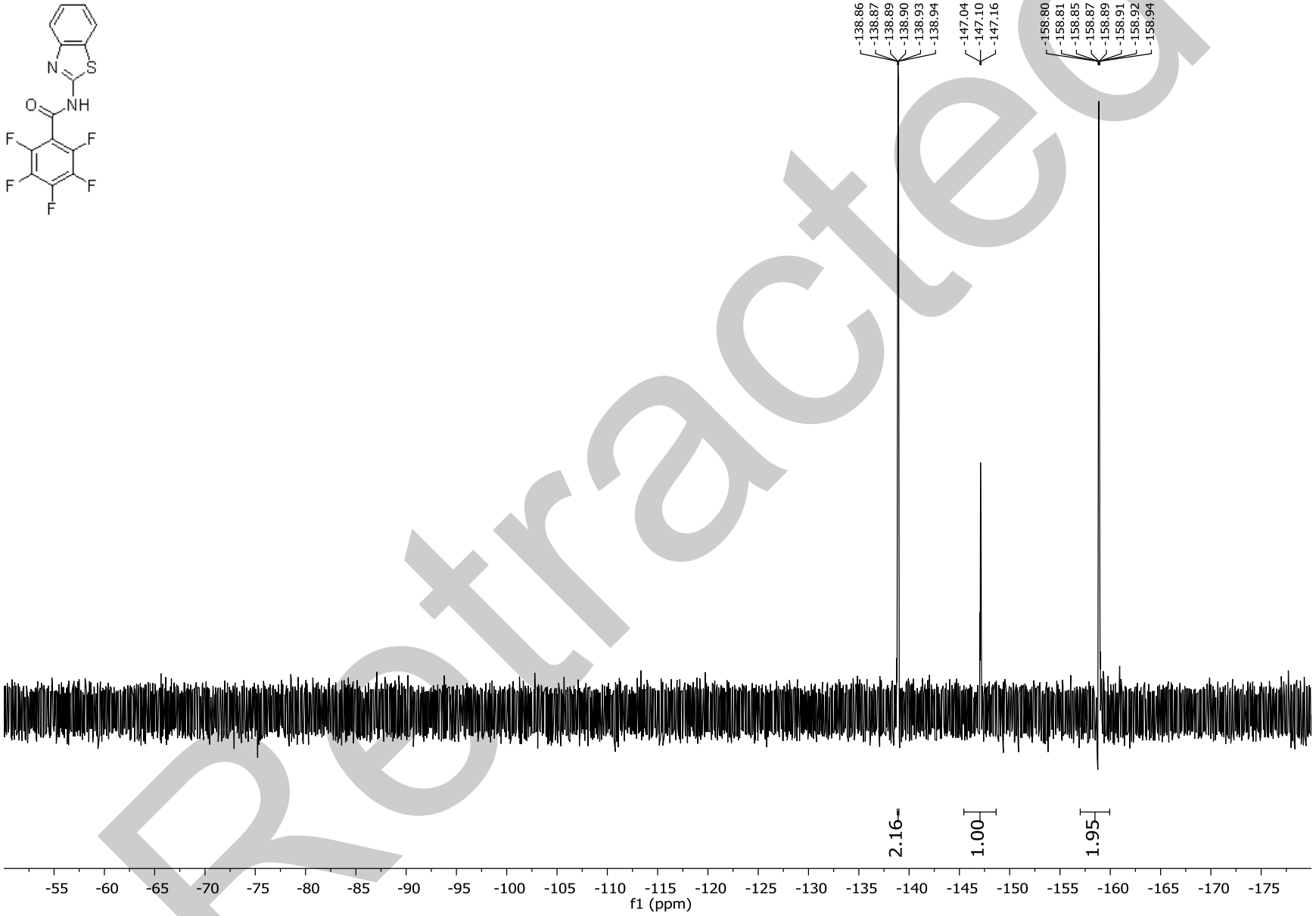
7e 2,3,4,5,6-pentafluoro-*N*-(p-tolyl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



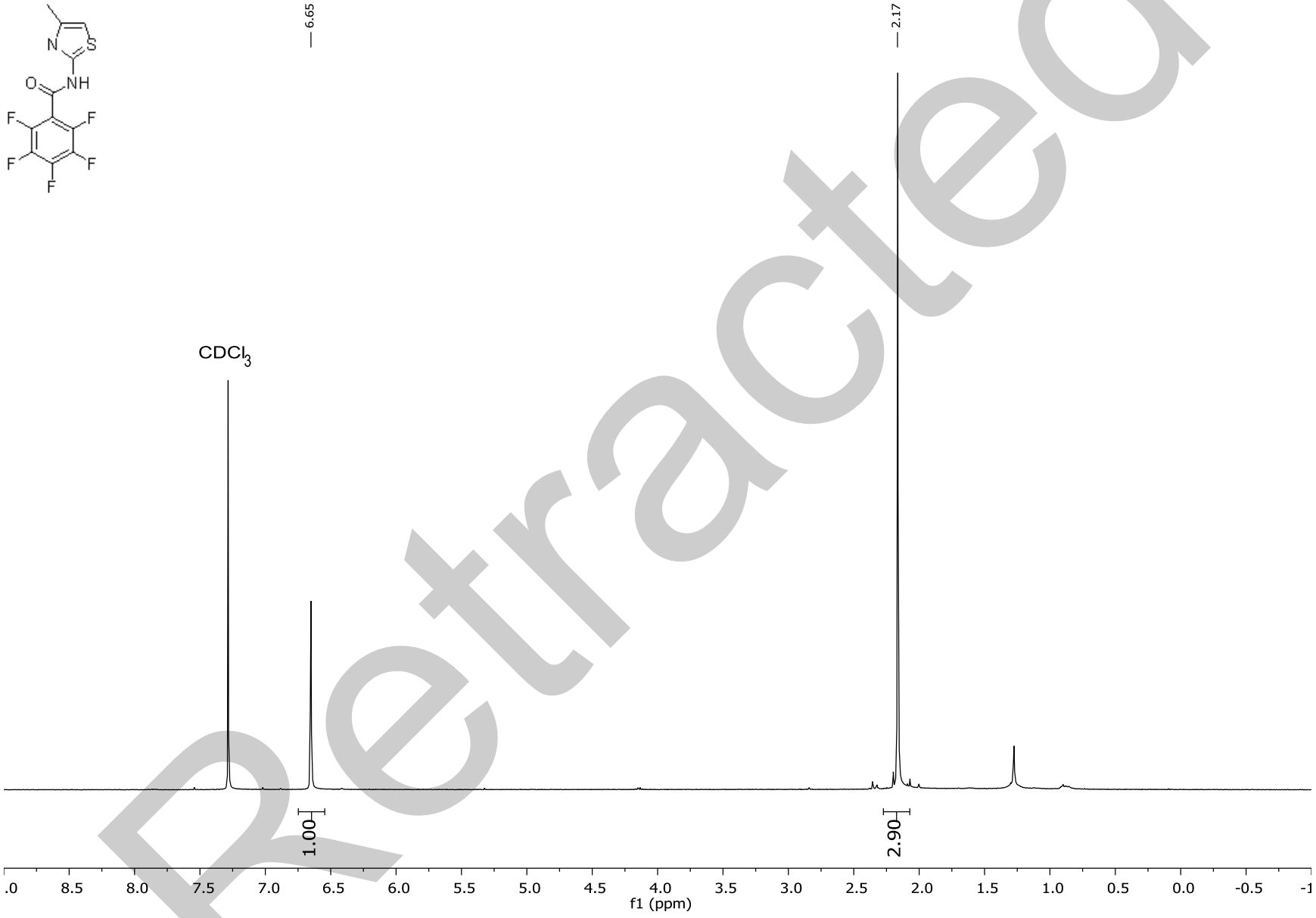
7f *N*-(benzo[d]thiazol-2-yl)-2,3,4,5,6-pentafluorobenzamide ^{1}H NMR (400 MHz, $CDCl_3$)



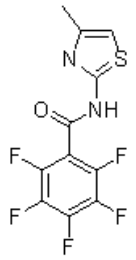
7f *N*-(benzo[d]thiazol-2-yl)-2,3,4,5,6-pentafluorobenzamide ^{19}F NMR (376 MHz, $CDCl_3$)



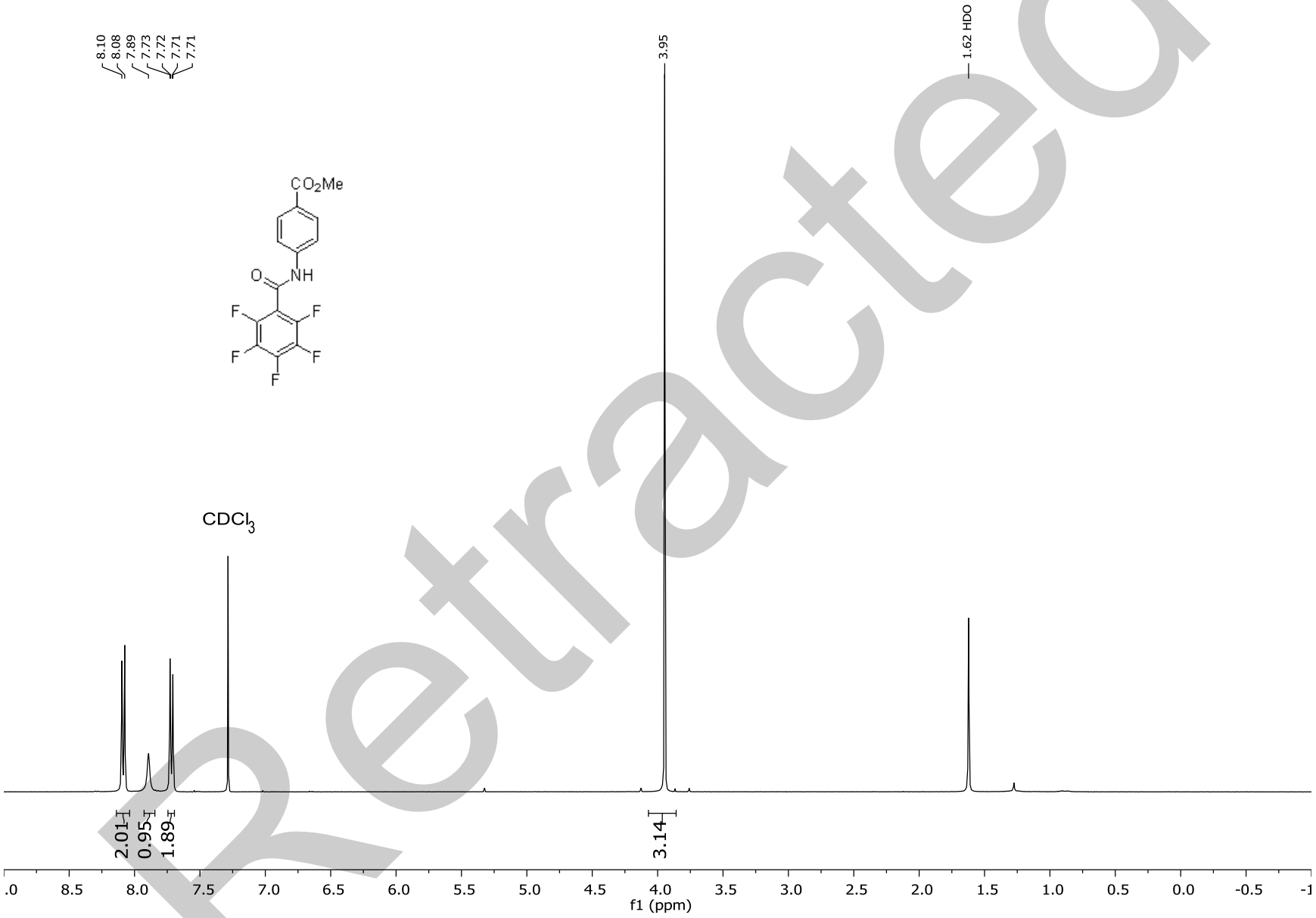
7g 2,3,4,5,6-pentafluoro-*N*-(4-methylthiazol-2-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



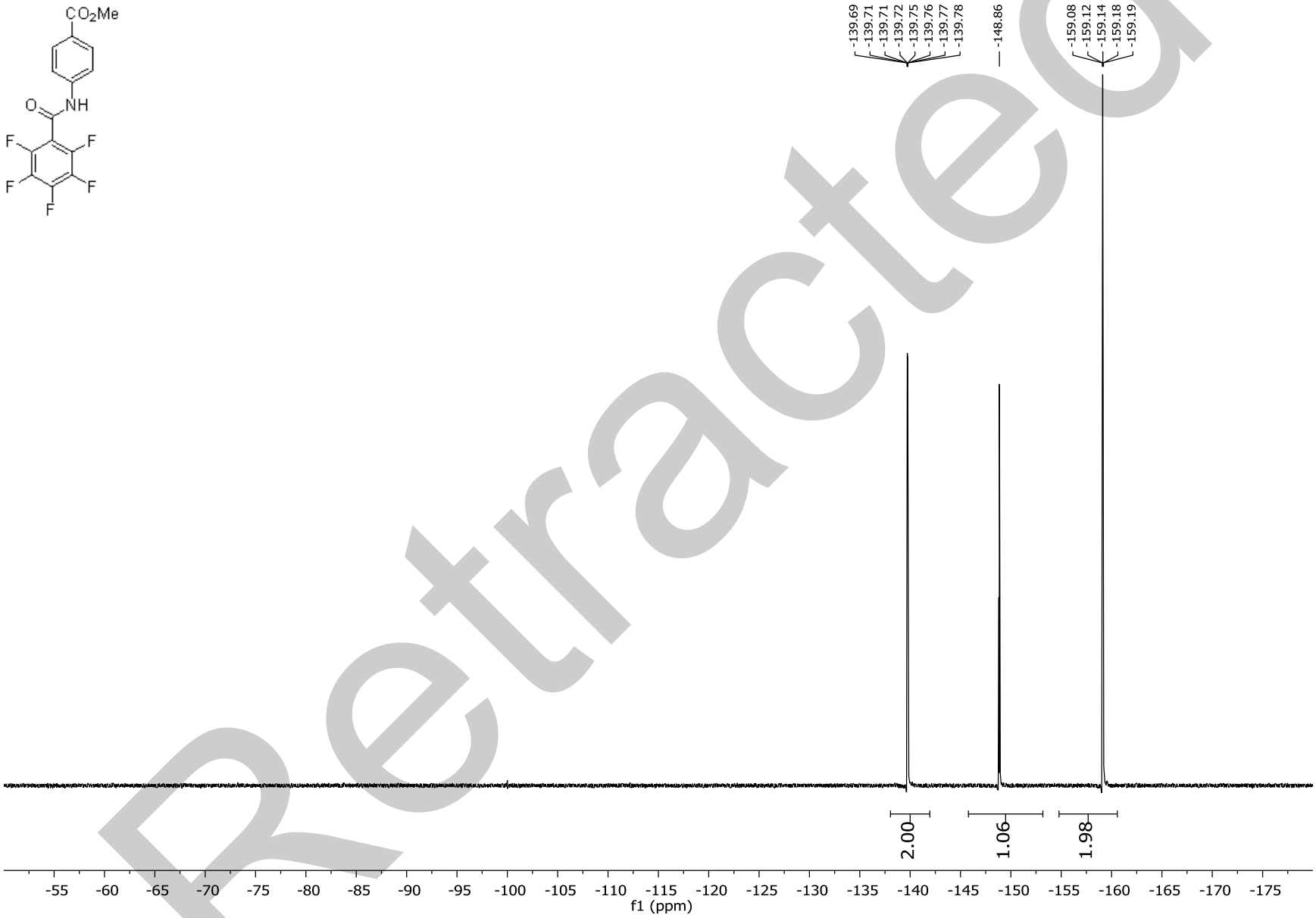
7g 2,3,4,5,6-pentafluoro-*N*-(4-methylthiazol-2-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



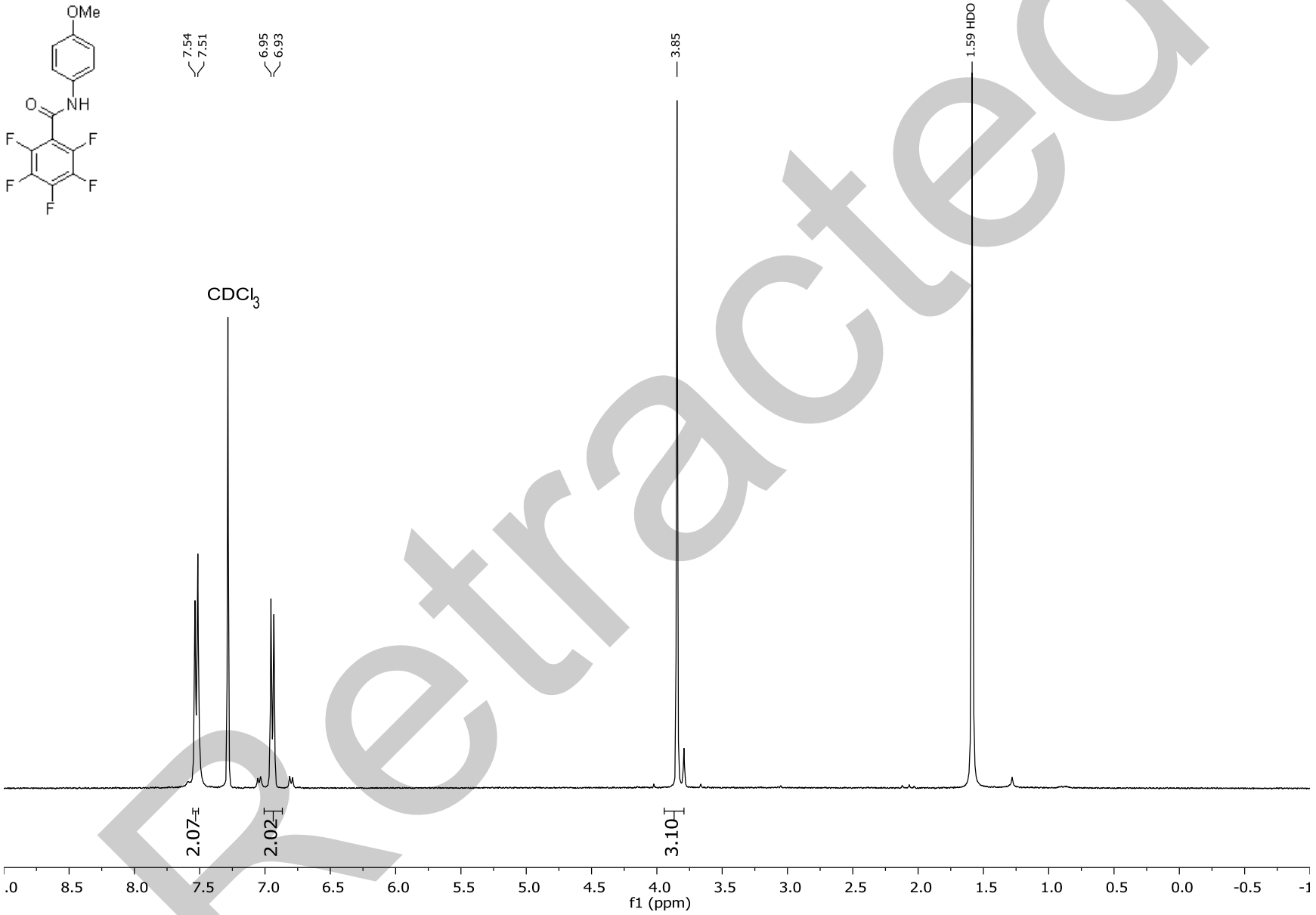
7h methyl 4-(perfluorobenzamido)benzoate ^{1}H NMR (400 MHz, $CDCl_3$)



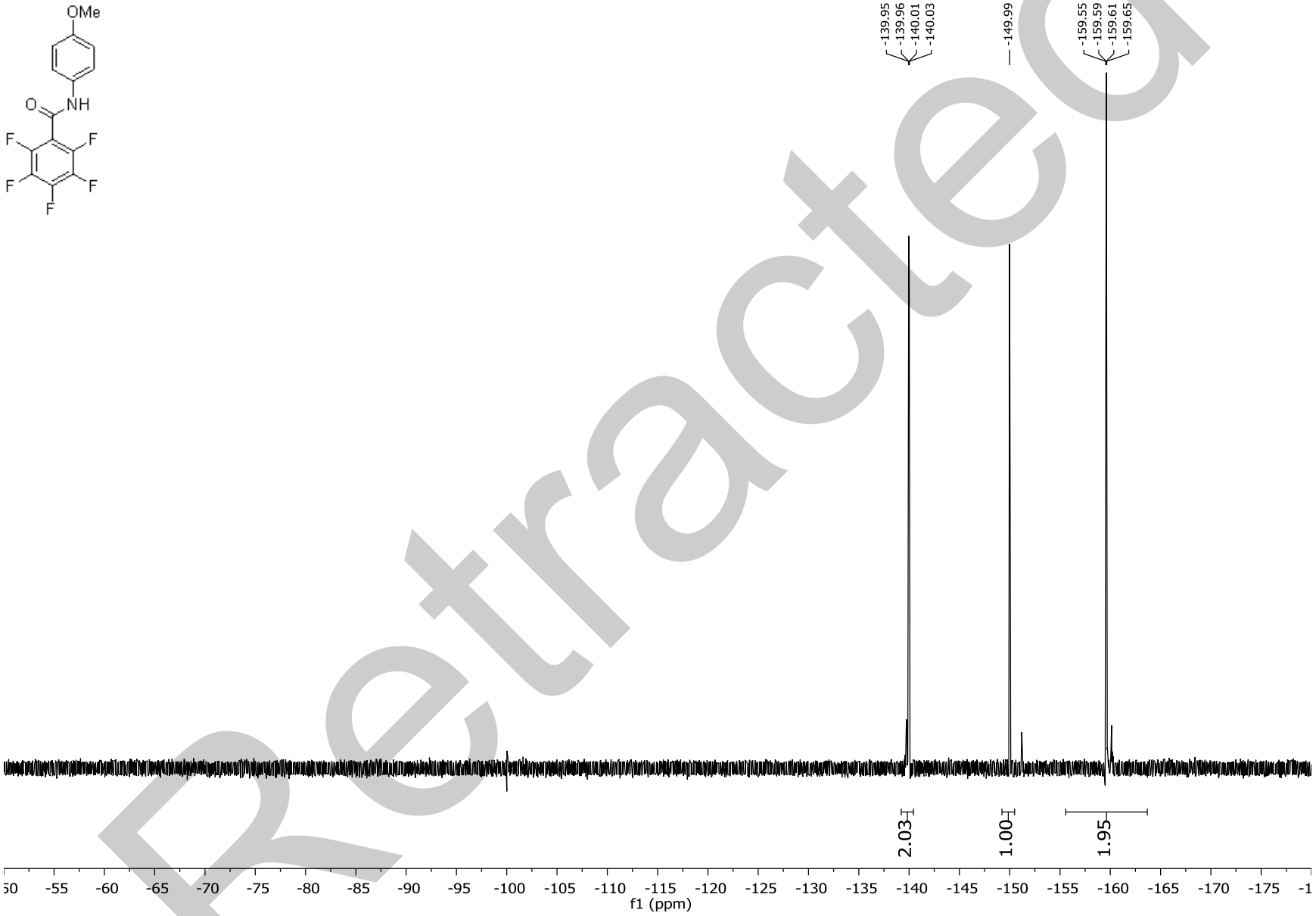
7h methyl 4-(perfluorobenzamido)benzoate ^{1}H NMR (400 MHz, $CDCl_3$) ^{19}F NMR (376 MHz, $CDCl_3$)



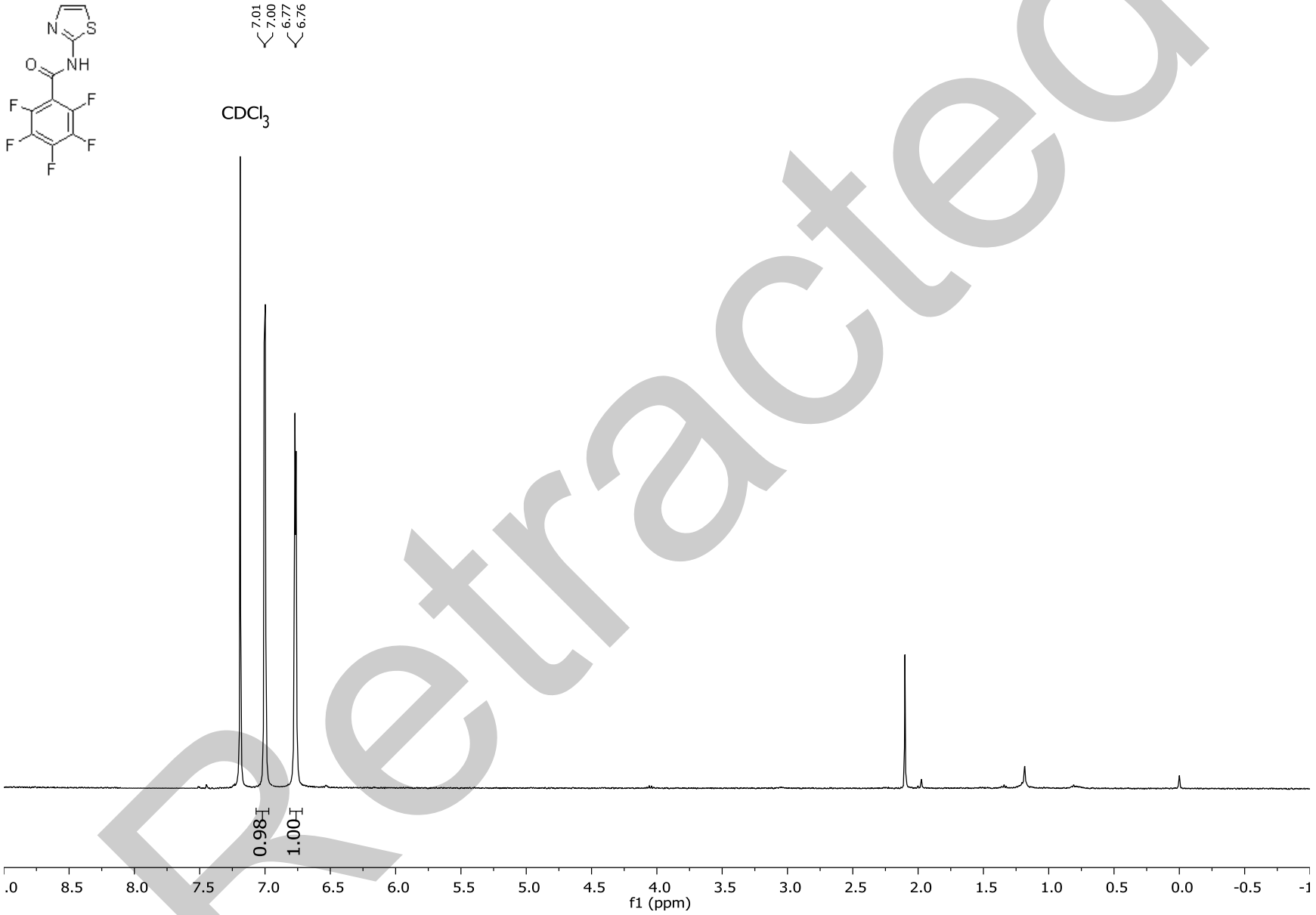
7i 2,3,4,5,6-pentafluoro-*N*-(4-methoxyphenyl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



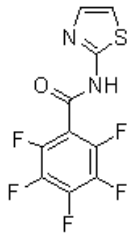
7i 2,3,4,5,6-pentafluoro-*N*-(4-methoxyphenyl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



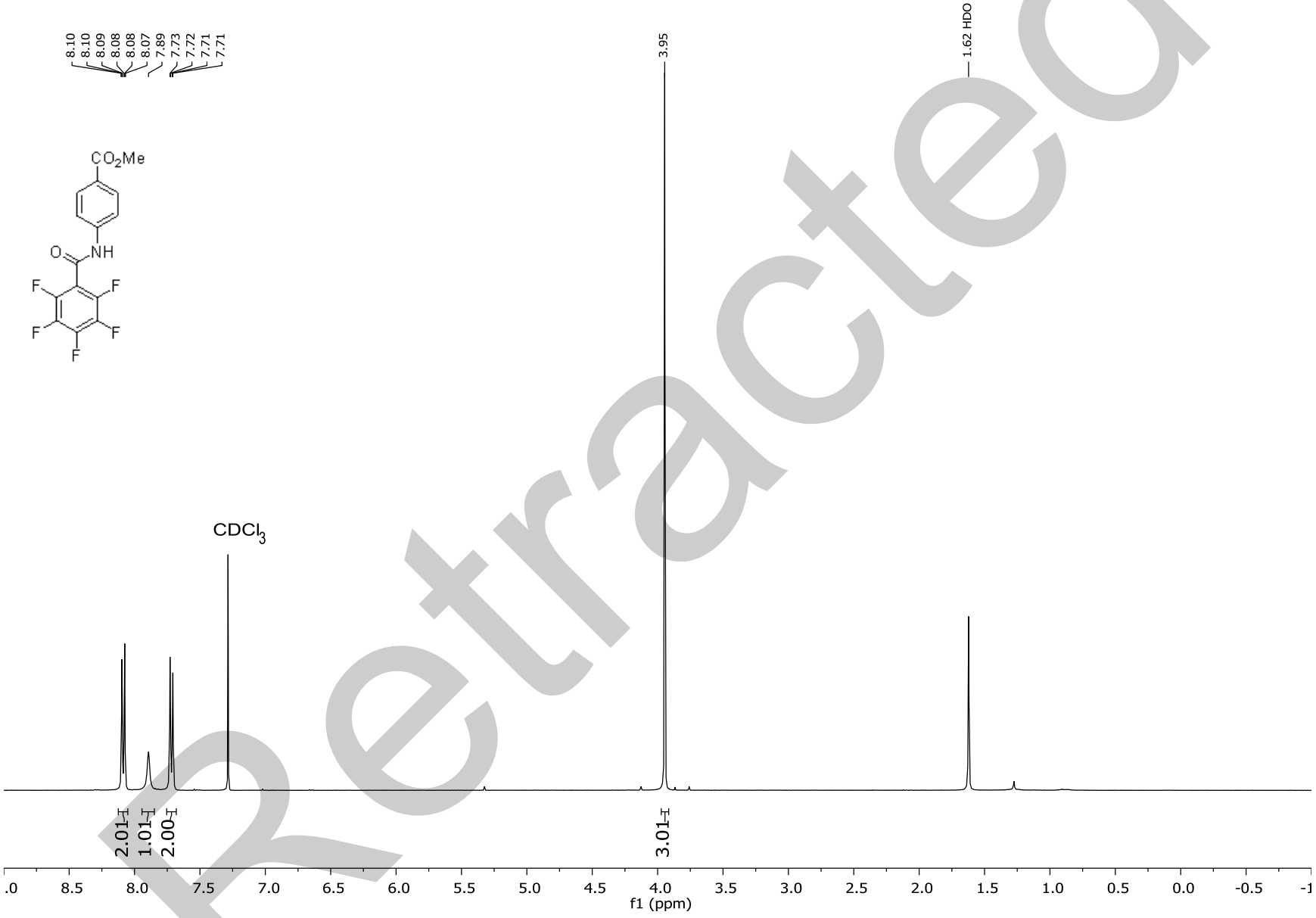
7j 2,3,4,5,6-pentafluoro-*N*-(thiazol-2-yl)benzamide ^{1}H NMR (400 MHz, $CDCl_3$)



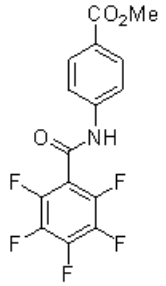
7j 2,3,4,5,6-pentafluoro-*N*-(thiazol-2-yl)benzamide ^{19}F NMR (376 MHz, $CDCl_3$)



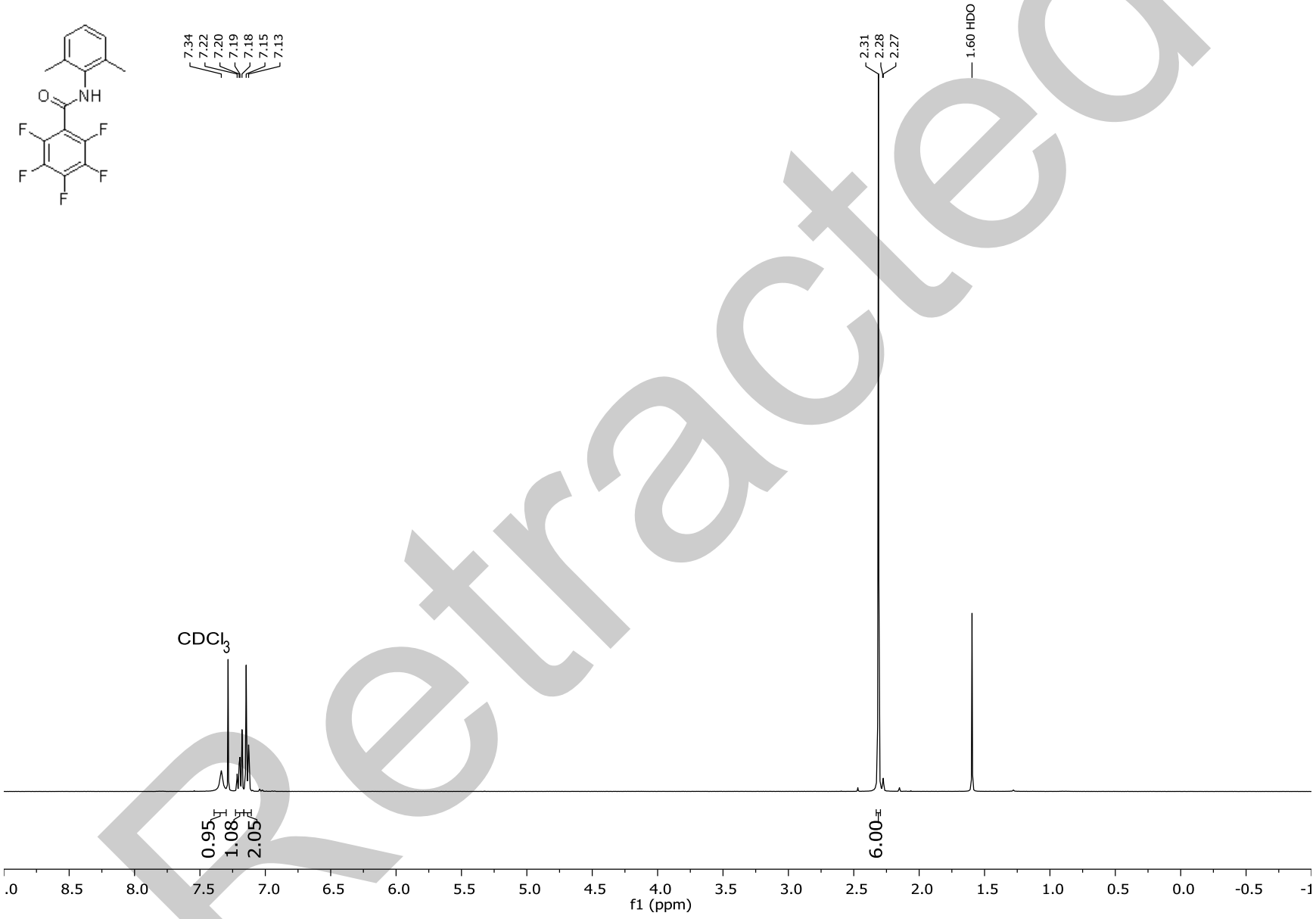
7h methyl 4-(perfluorobenzamido)benzoate ^{1}H NMR (400 MHz, $CDCl_3$)



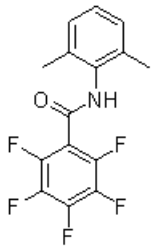
7h methyl 4-(perfluorobenzamido)benzoate ^{19}F NMR (376 MHz, $CDCl_3$)



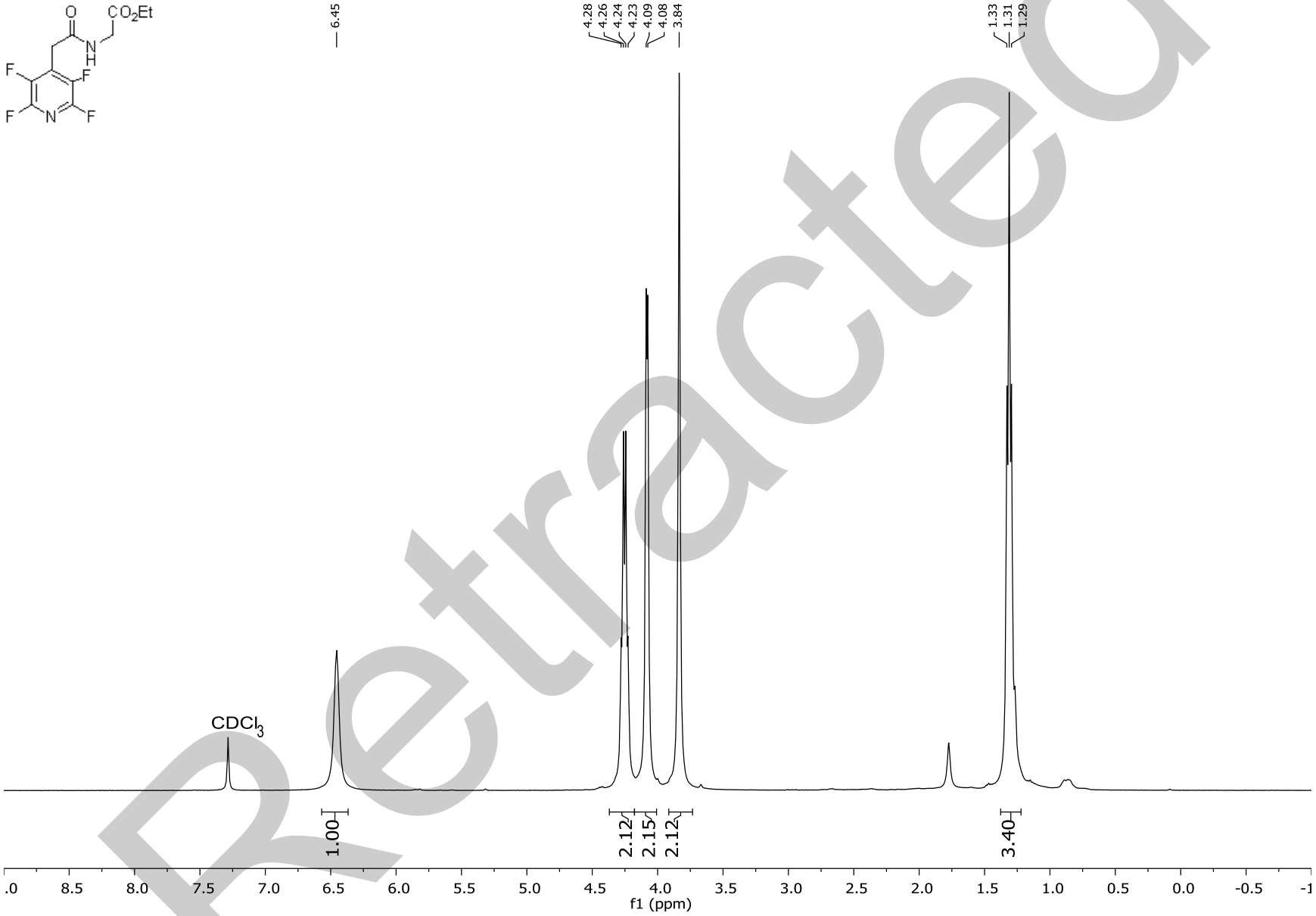
8a *N*-(2,6-dimethylphenyl)-2,3,4,5,6-pentafluorobenzamide ^{1}H NMR (400 MHz, $CDCl_3$)



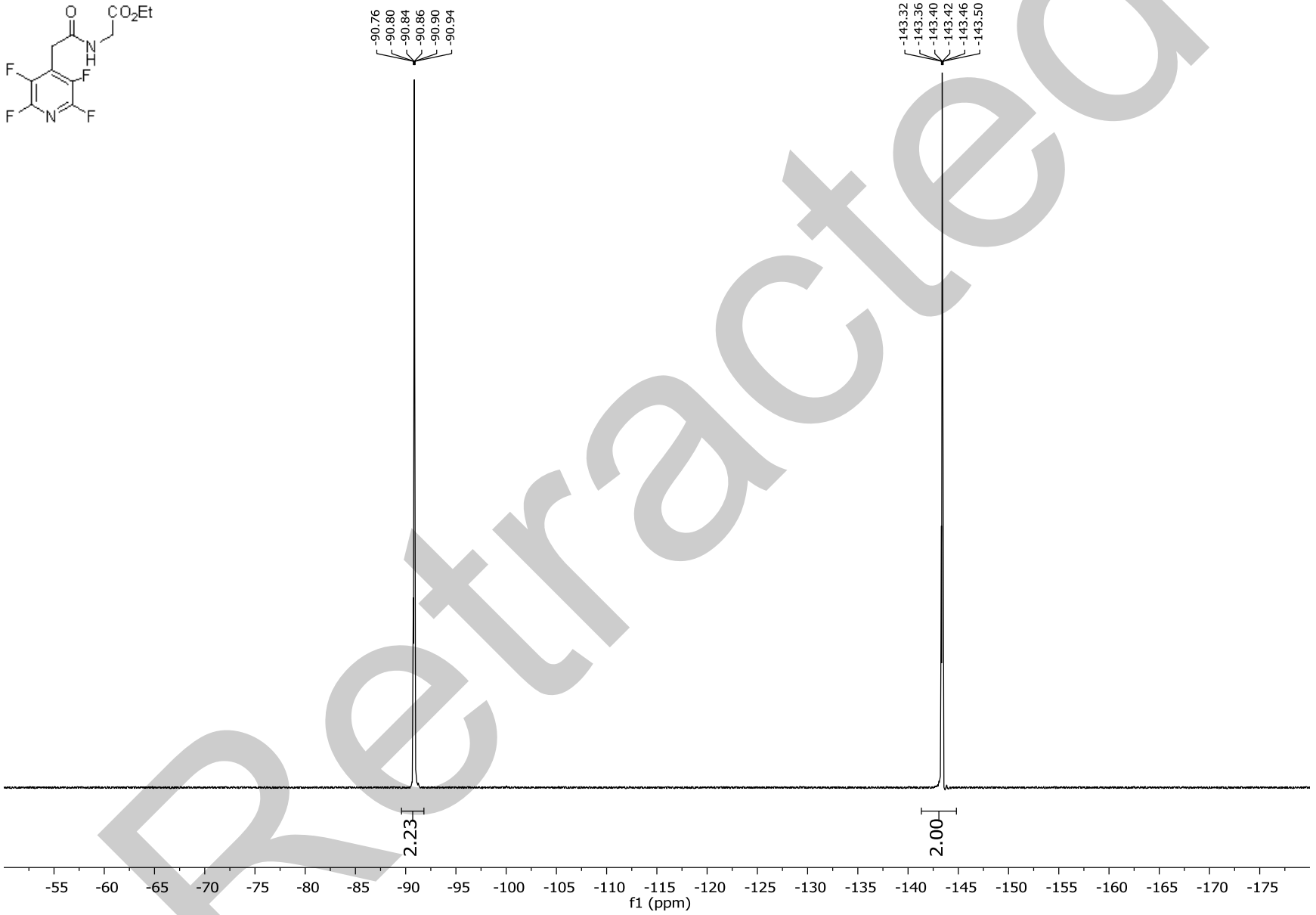
8a *N*-(2,6-dimethylphenyl)-2,3,4,5,6-pentafluorobenzamide ^{19}F NMR (376 MHz, $CDCl_3$)



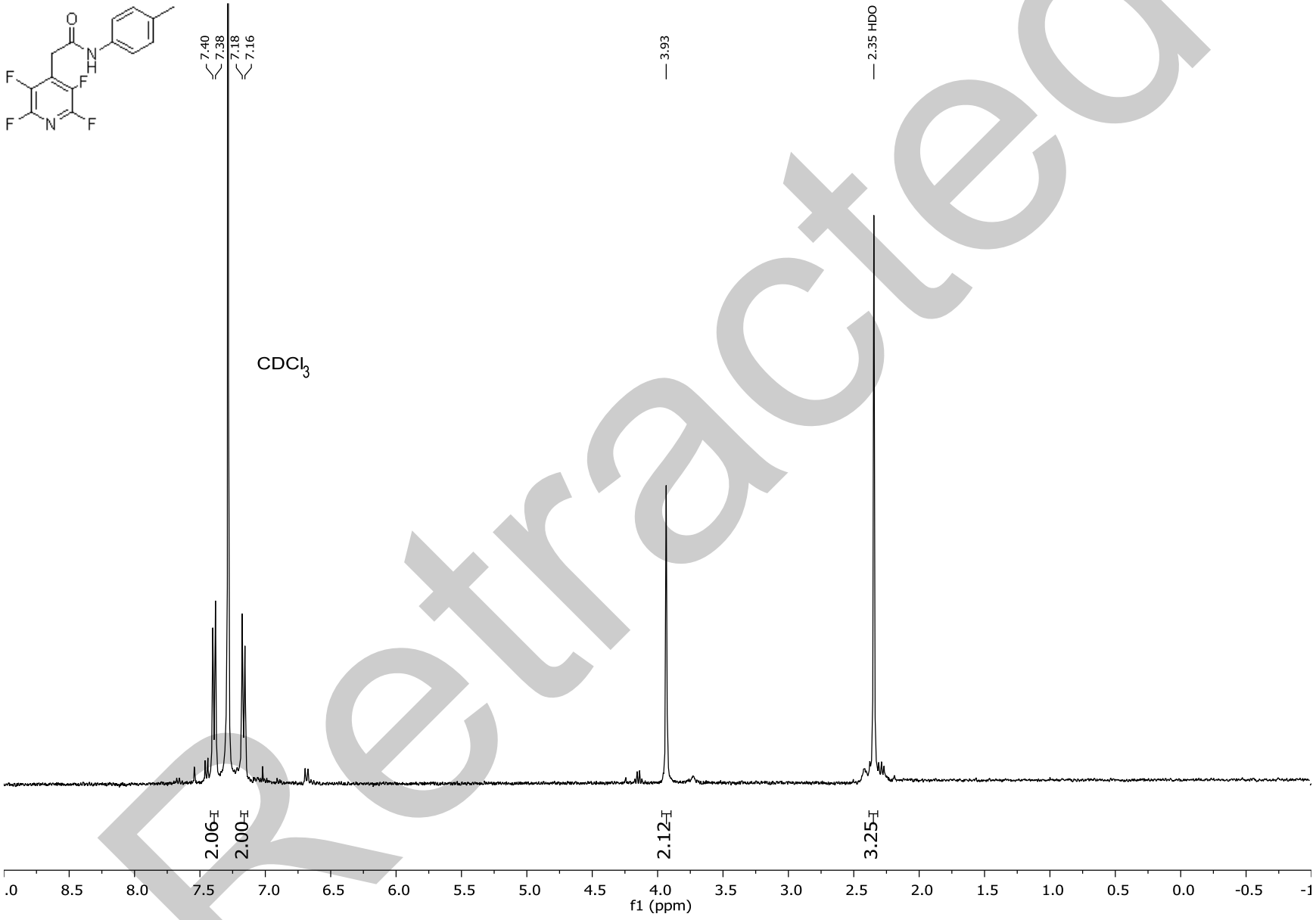
10a ethyl (2-(perfluoropyridin-4-yl)acetyl)glycinate ^{1}H NMR (400 MHz, $CDCl_3$)



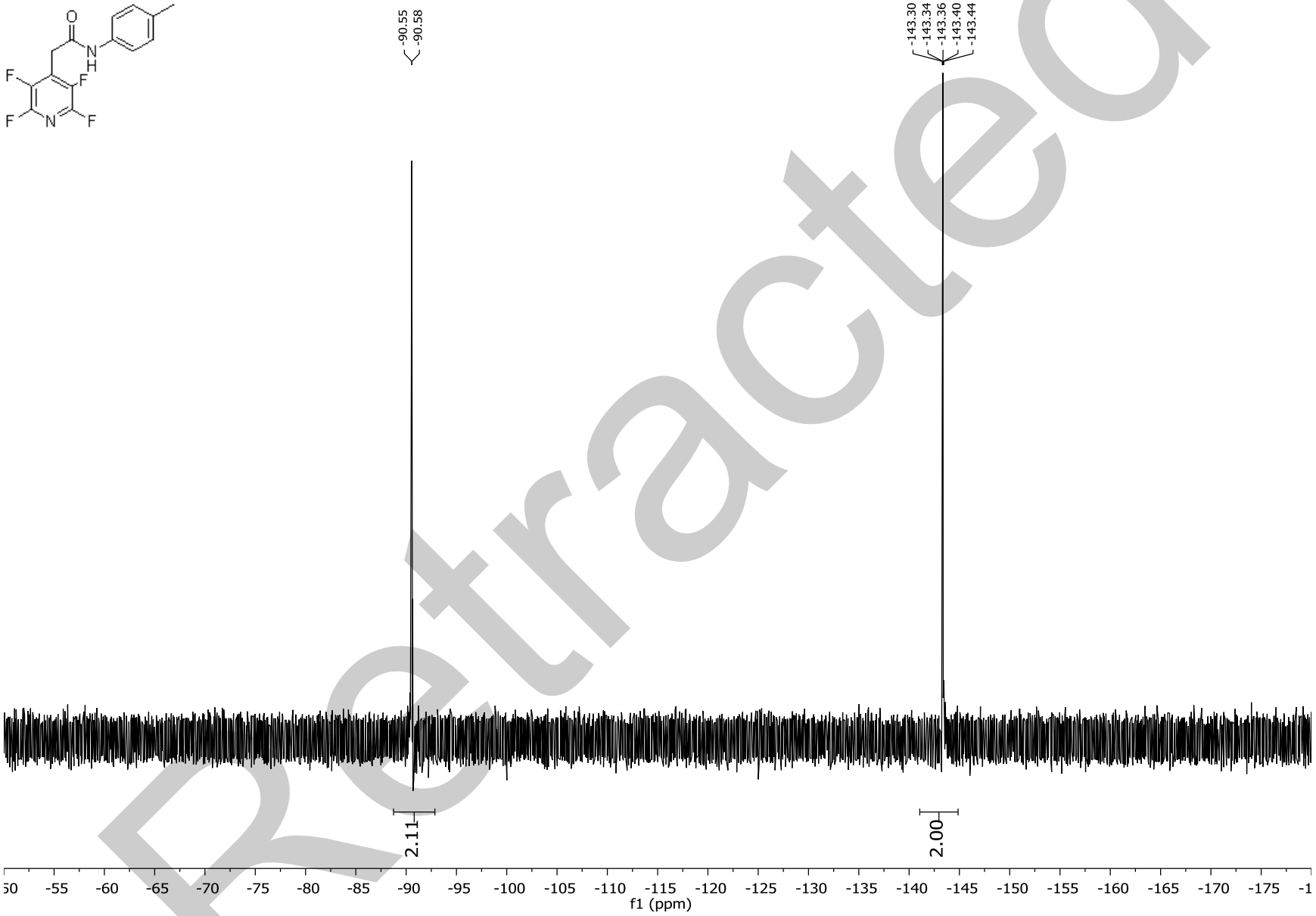
10a ethyl (2-(perfluoropyridin-4-yl)acetyl)glycinate ^{19}F NMR (376 MHz, $CDCl_3$)



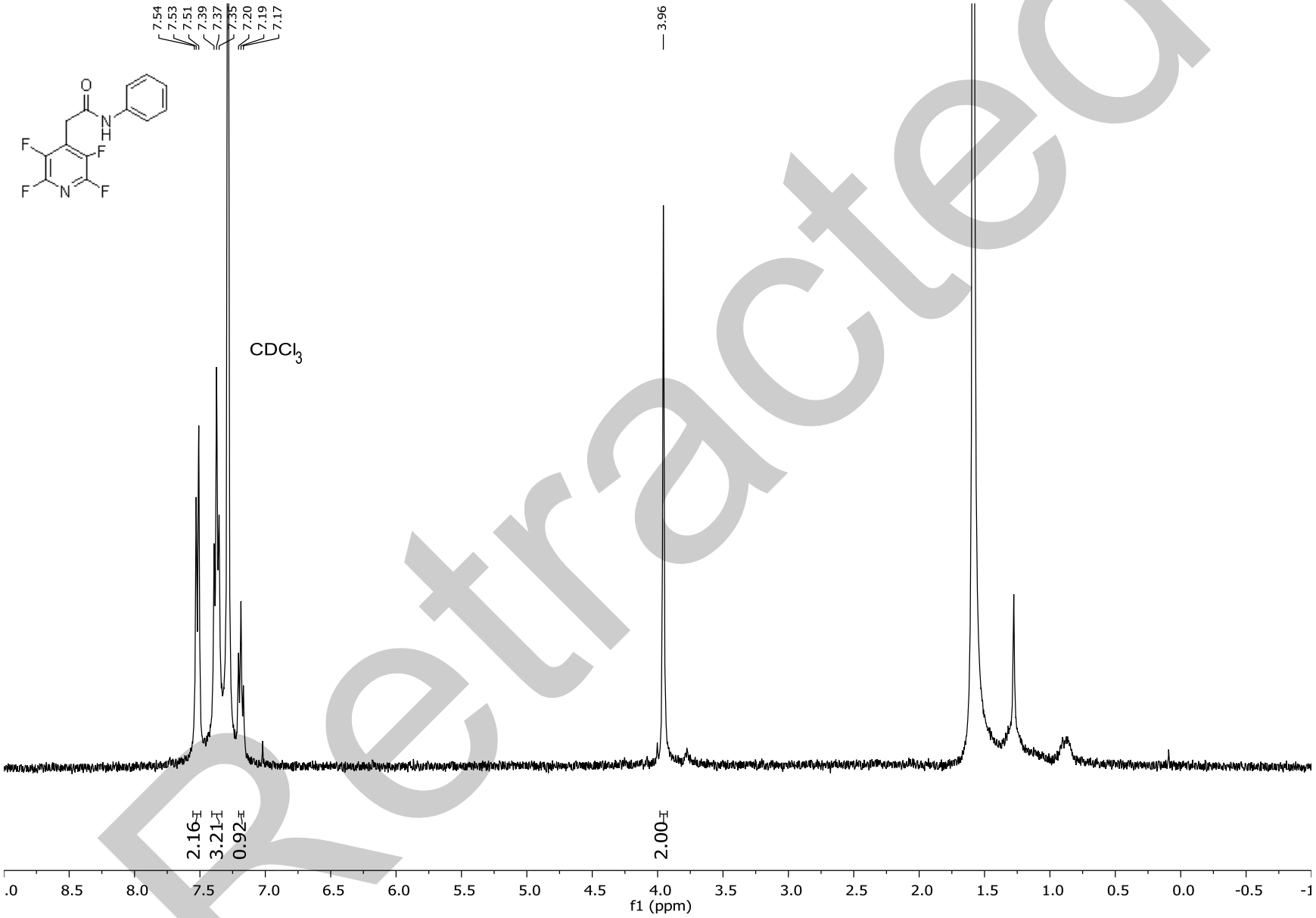
10b 2-(perfluoropyridin-4-yl)-*N*-(p-tolyl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



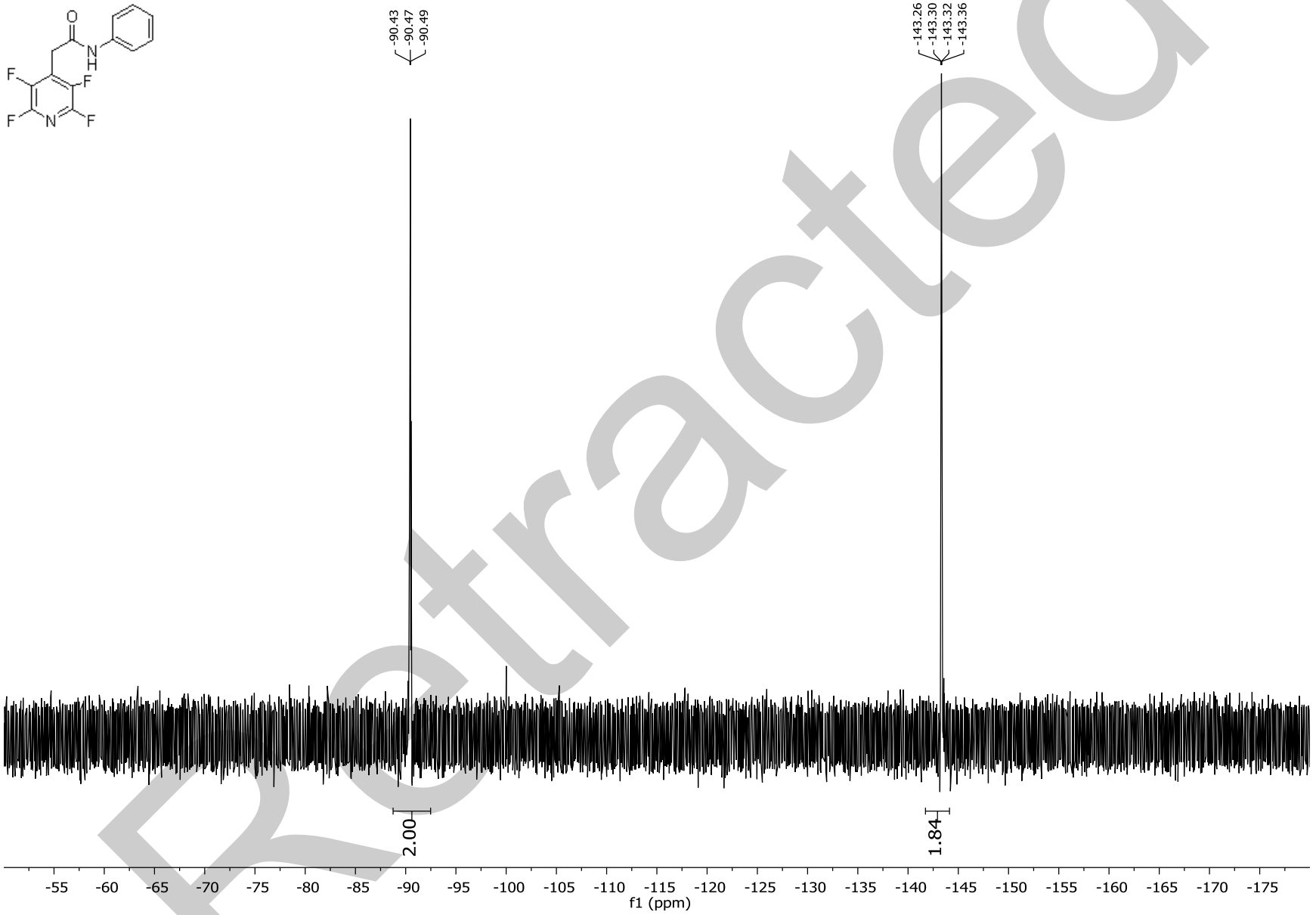
10b 2-(perfluoropyridin-4-yl)-*N*-(p-tolyl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



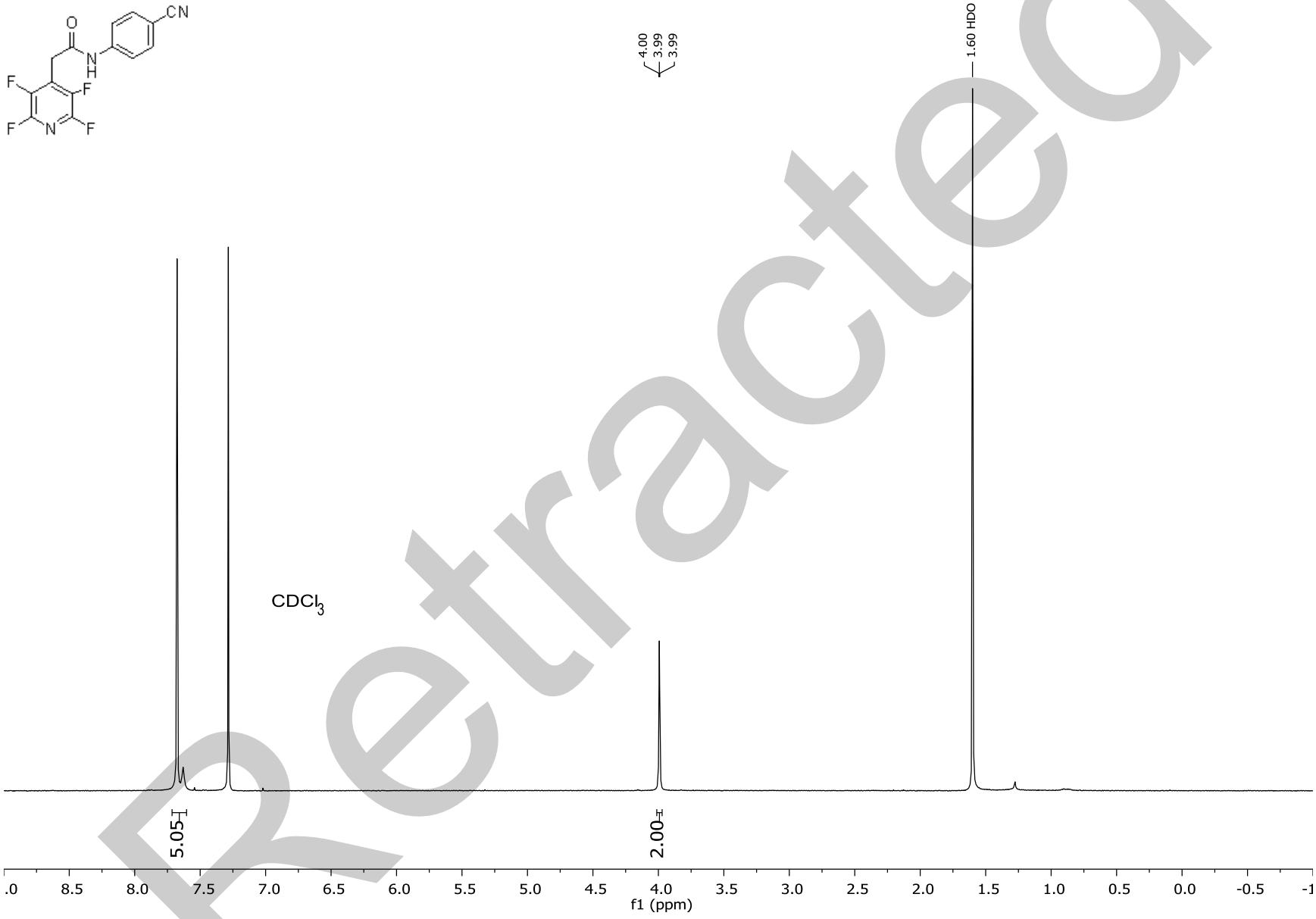
10c 2-(perfluoropyridin-4-yl)-*N*-phenylacetamide ^{1}H NMR (400 MHz, $CDCl_3$)



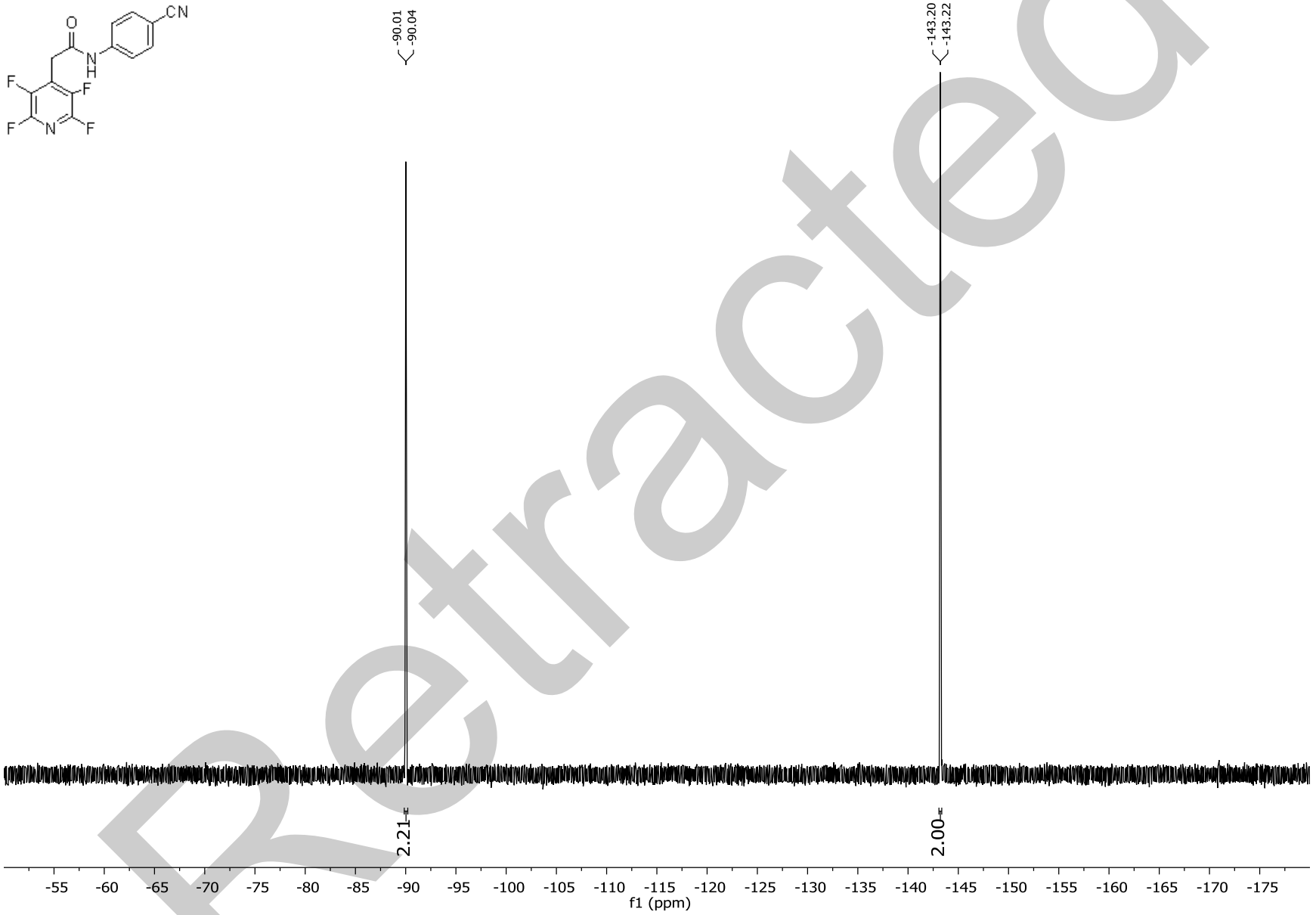
10c 2-(perfluoropyridin-4-yl)-*N*-phenylacetamide ^{19}F NMR (376 MHz, $CDCl_3$)



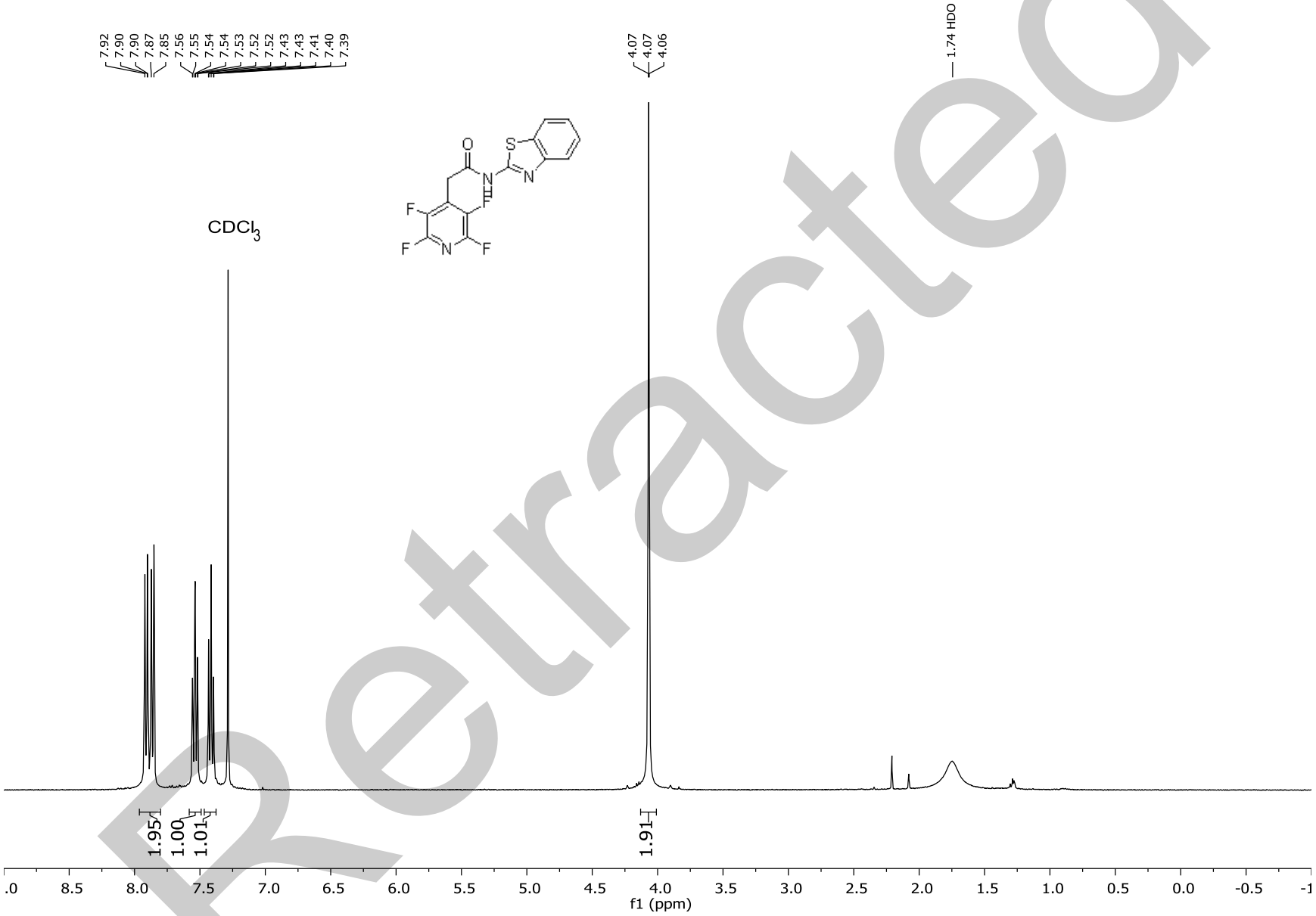
10d *N*-(4-cyanophenyl)-2-(perfluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



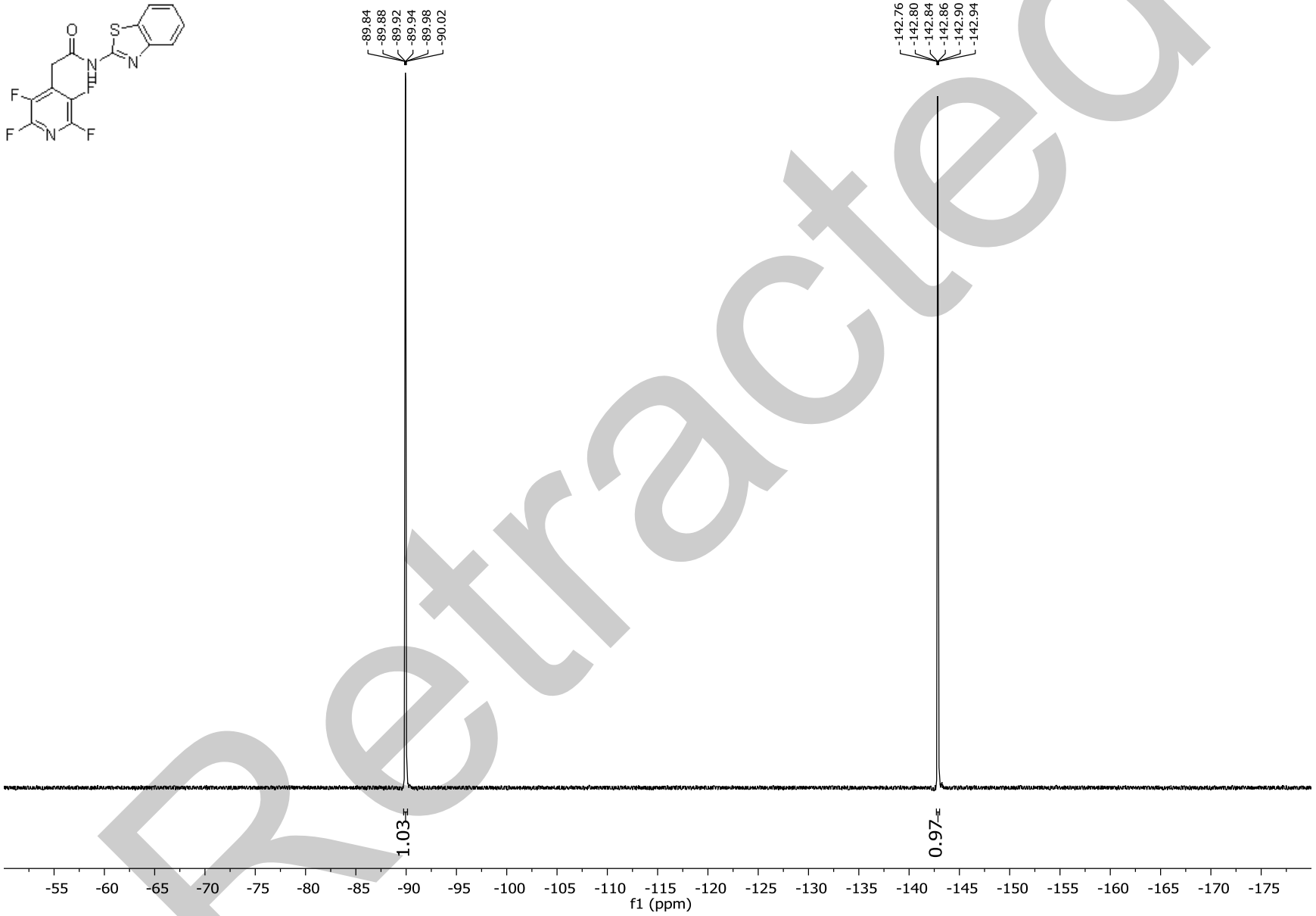
10e *N*-(4-cyanophenyl)-2-(perfluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



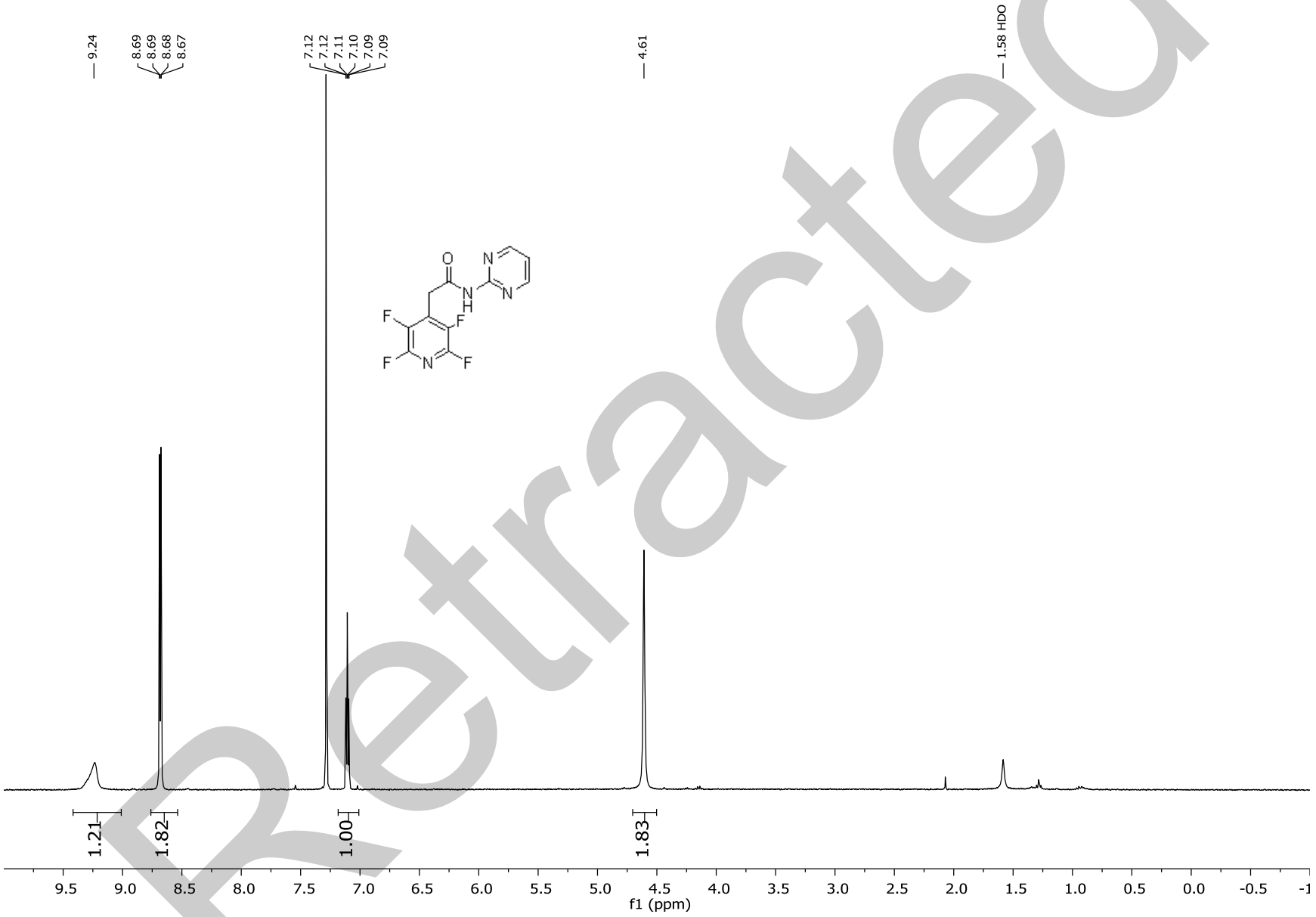
10e *N*-(benzo[d]thiazol-2-yl)-2-(perfluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



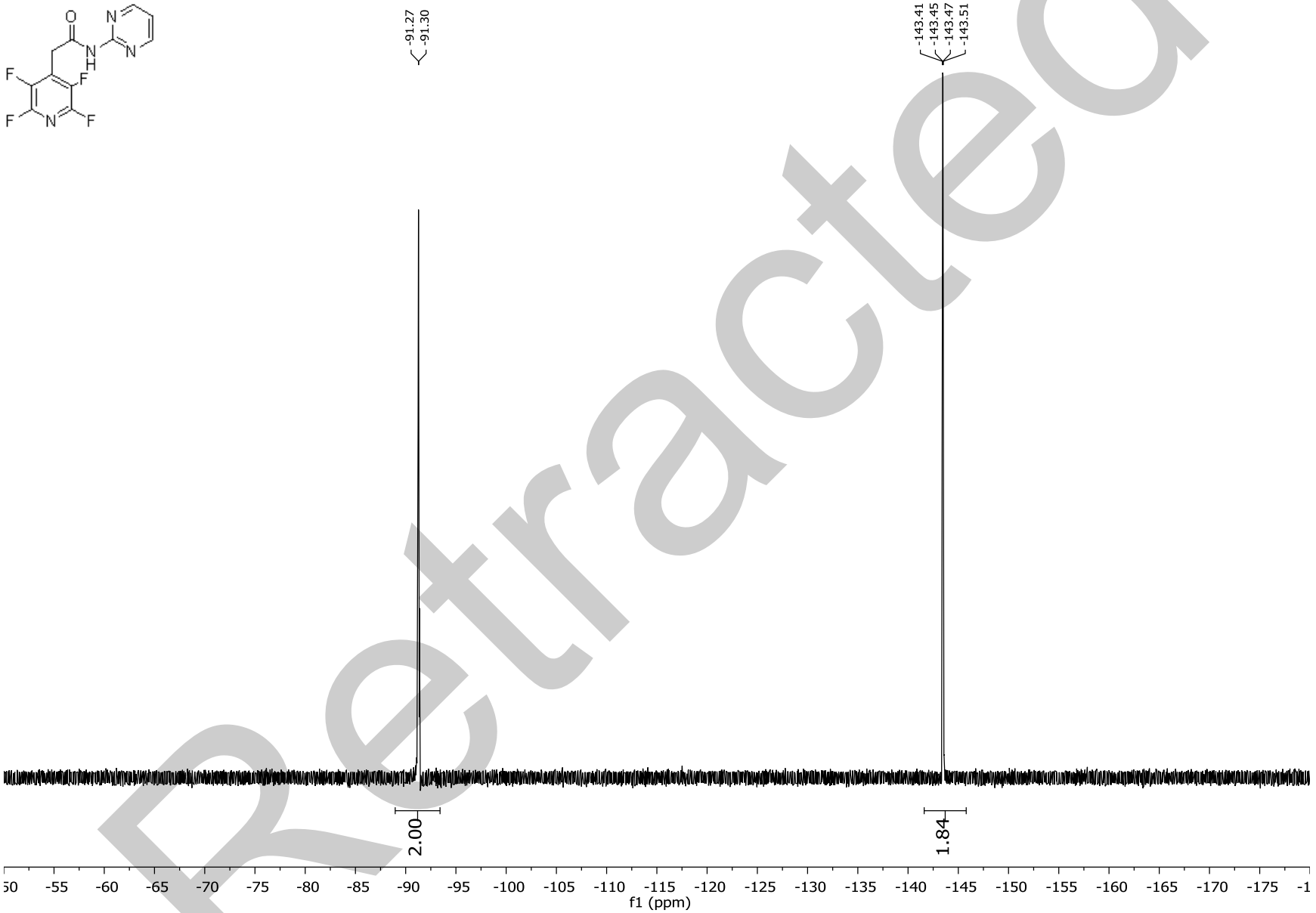
10e *N*-(benzo[d]thiazol-2-yl)-2-(perfluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



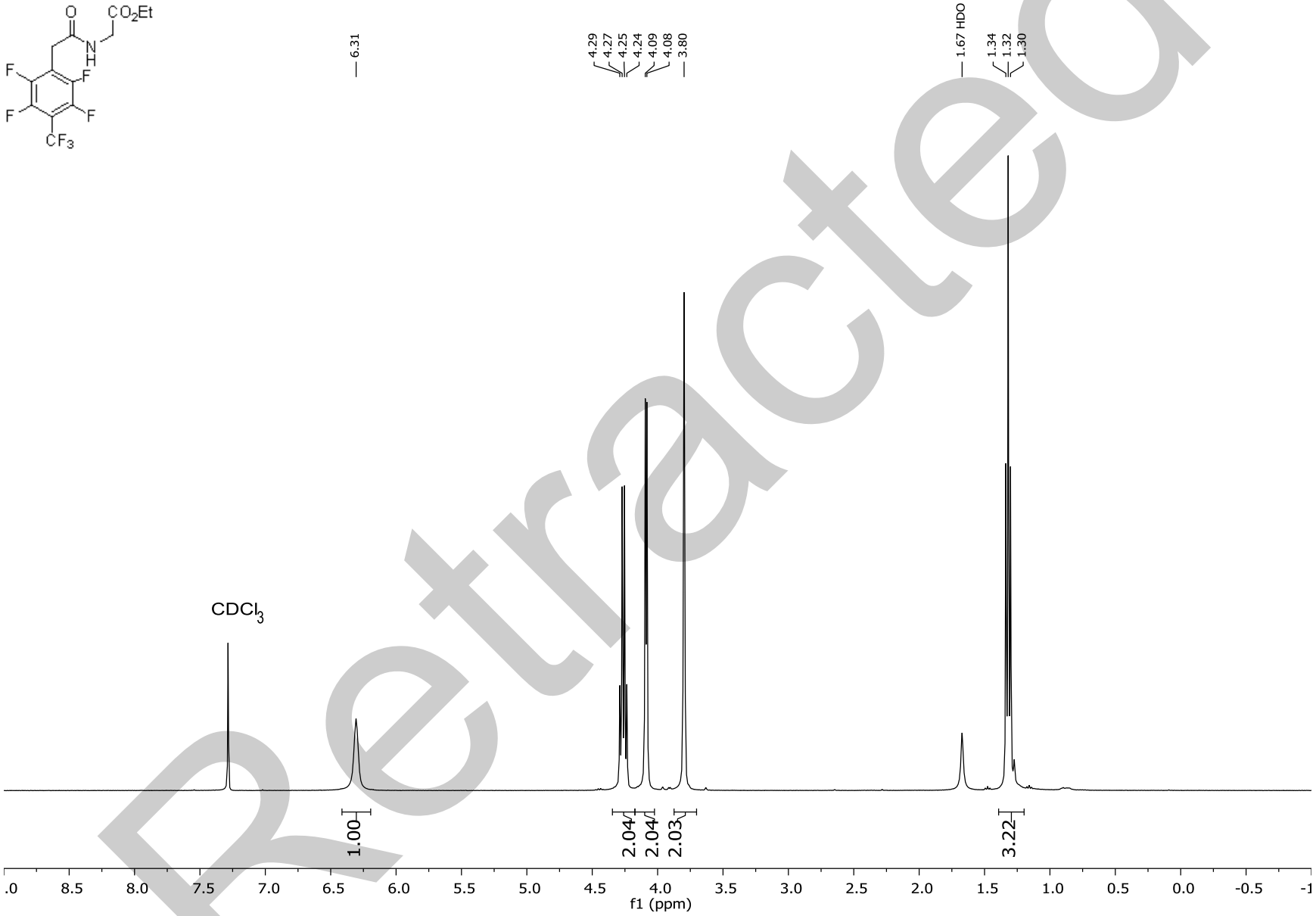
10f 2-(perfluoropyridin-4-yl)-*N*-(pyrimidin-2-yl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



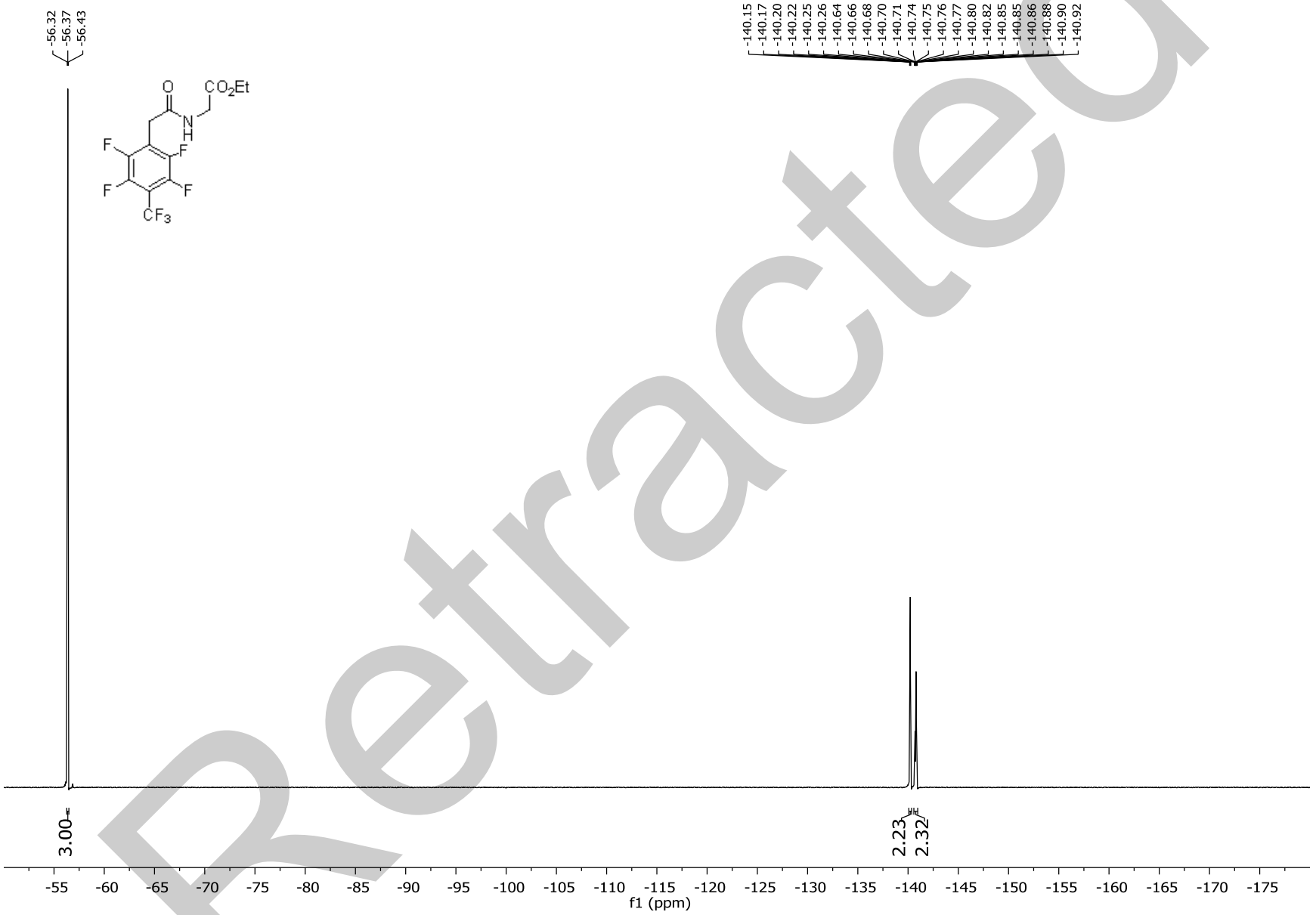
10f 2-(perfluoropyridin-4-yl)-*N*-(pyrimidin-2-yl)acetamide ^{1}H NMR (400 MHz, $CDCl_3$) ^{19}F NMR (376 MHz, $CDCl_3$)



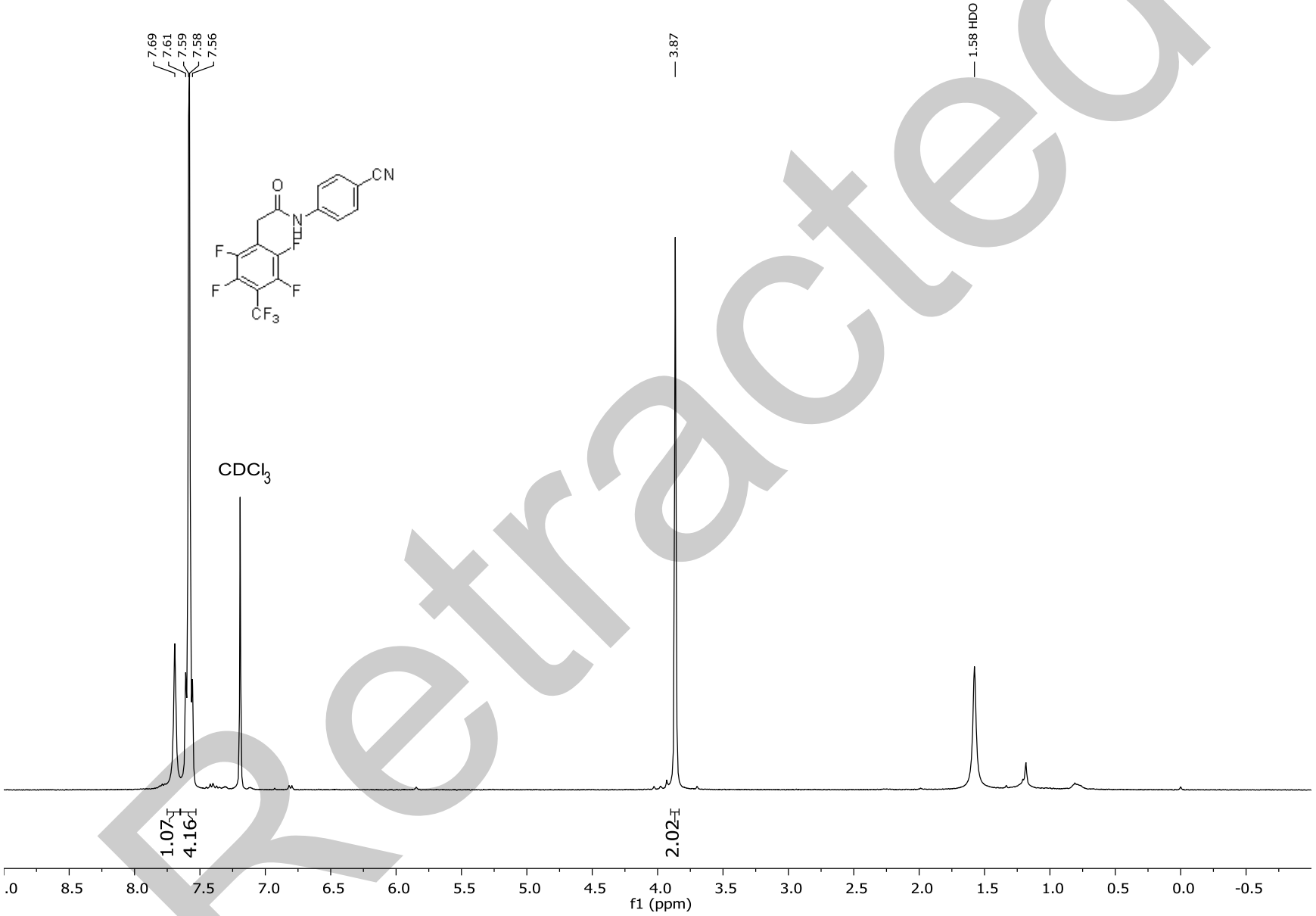
10g ethyl (2-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetyl)glycinate ^{1}H NMR (400 MHz, $CDCl_3$)



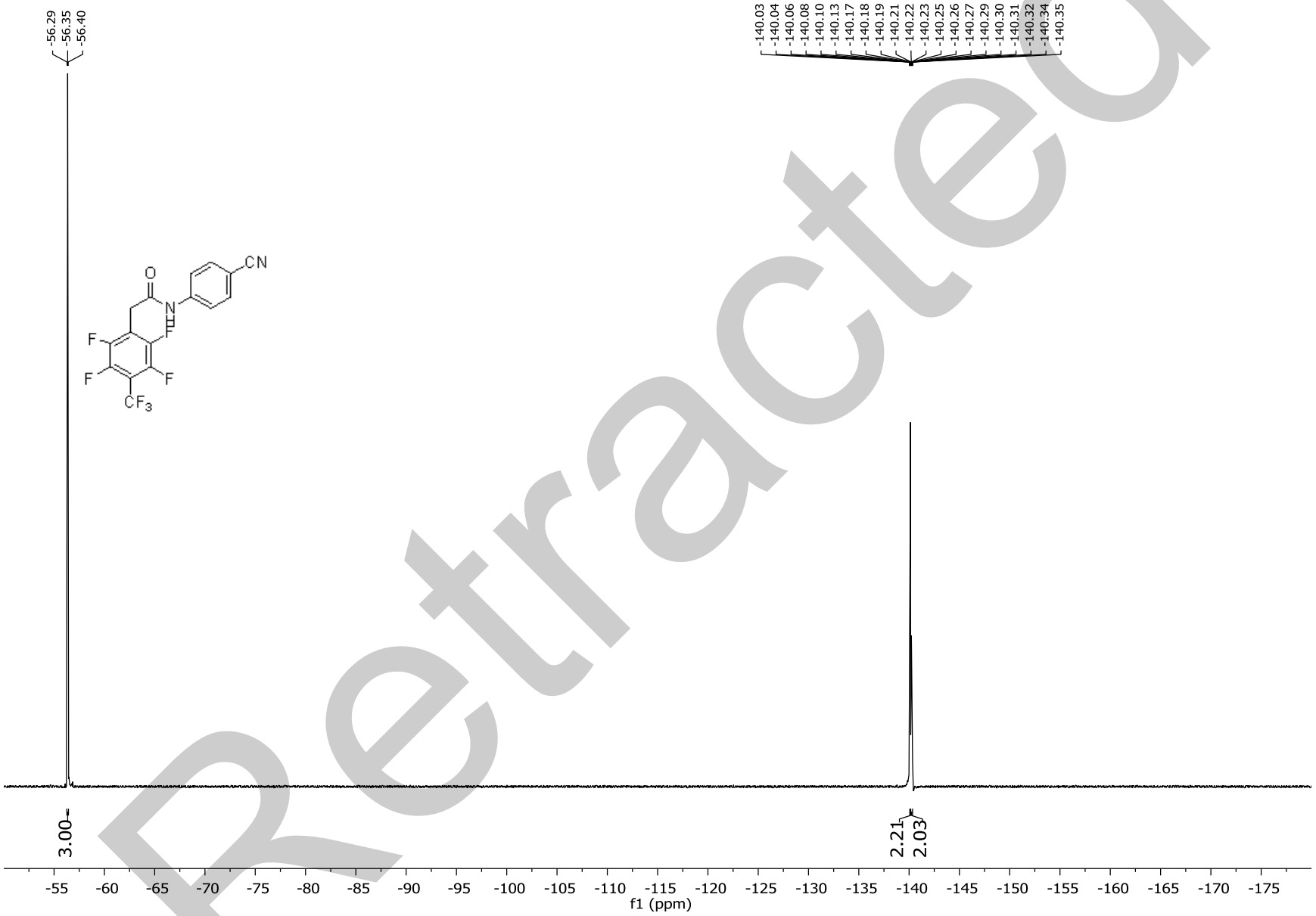
10g ethyl (2-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetyl)glycinate ^{19}F NMR (376 MHz, $CDCl_3$)



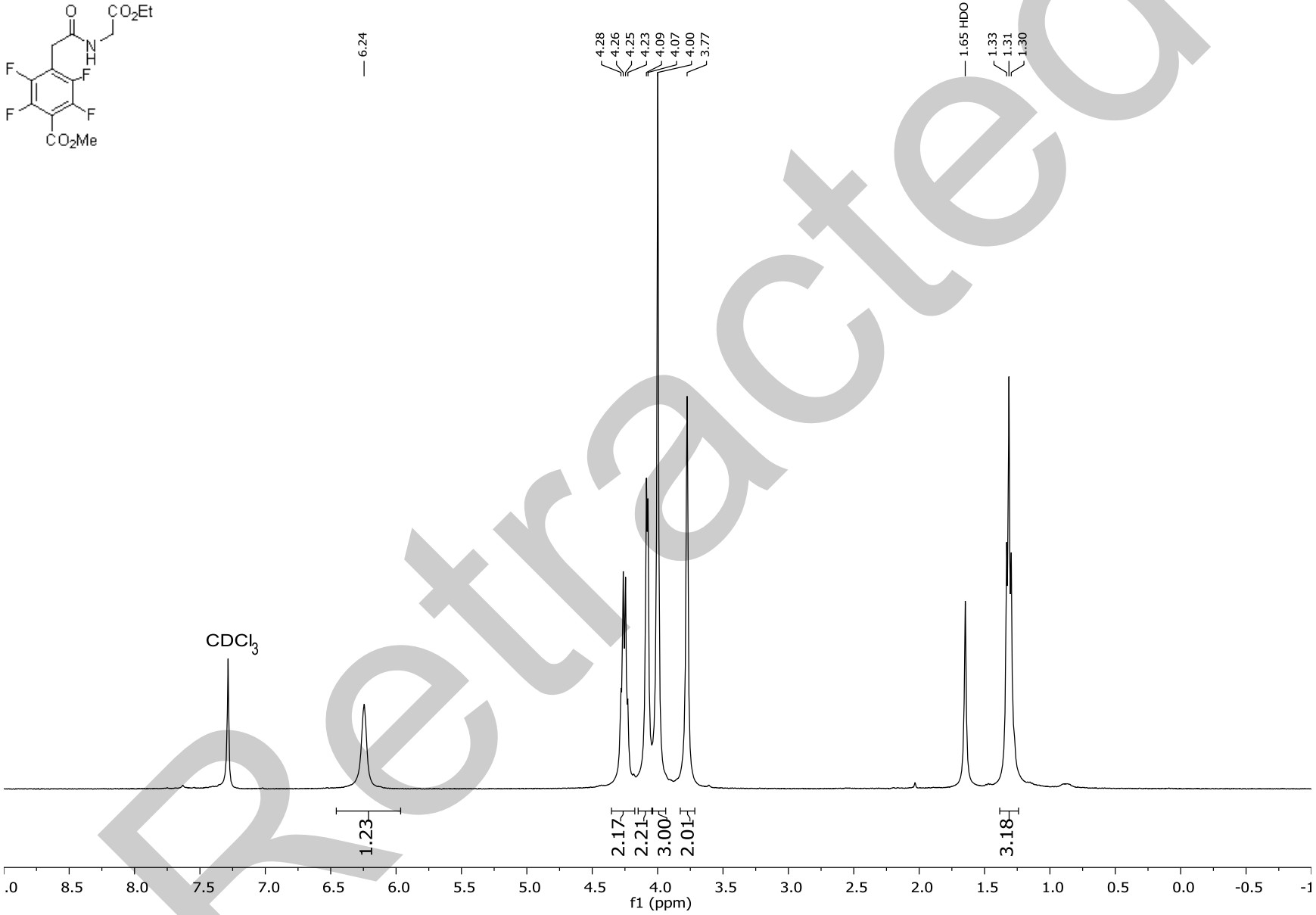
10h *N*-(4-cyanophenyl)-2-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl) acetamide ^{1}H NMR (400 MHz, $CDCl_3$)



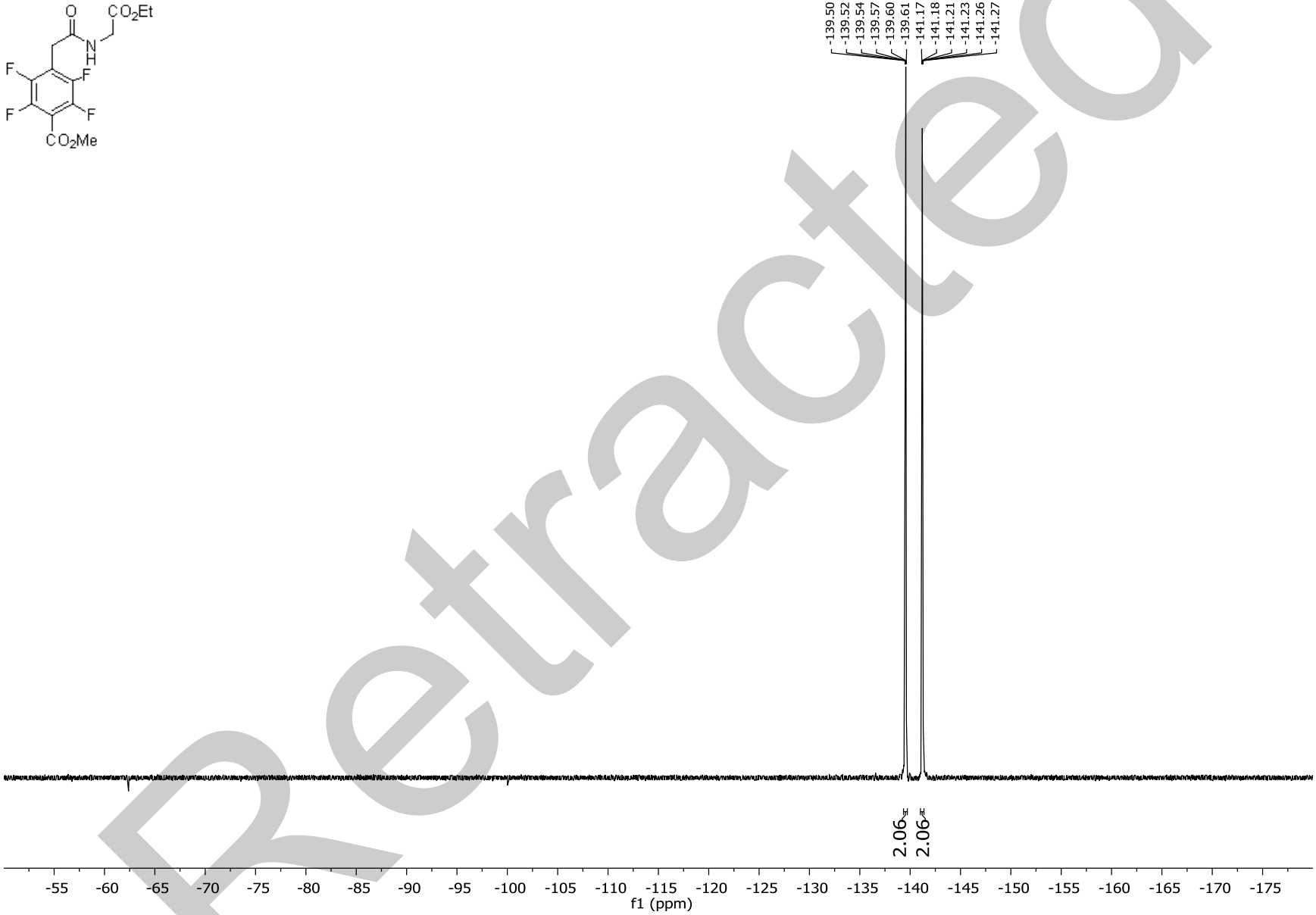
10h *N*-(4-cyanophenyl)-2-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl) acetamide ^{19}F NMR (376 MHz, $CDCl_3$)



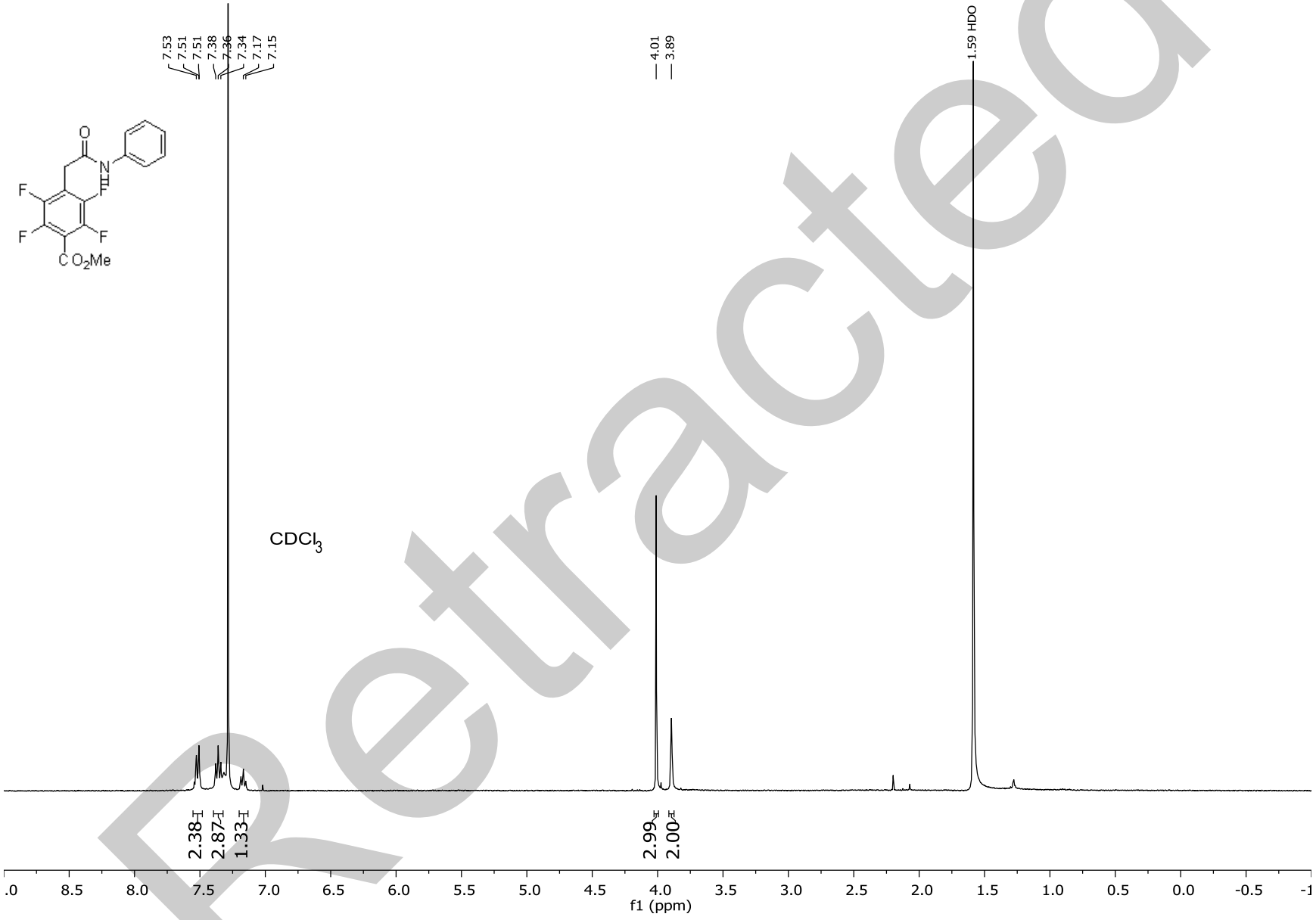
11a methyl 4-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate ^{1}H NMR (400 MHz, $CDCl_3$)



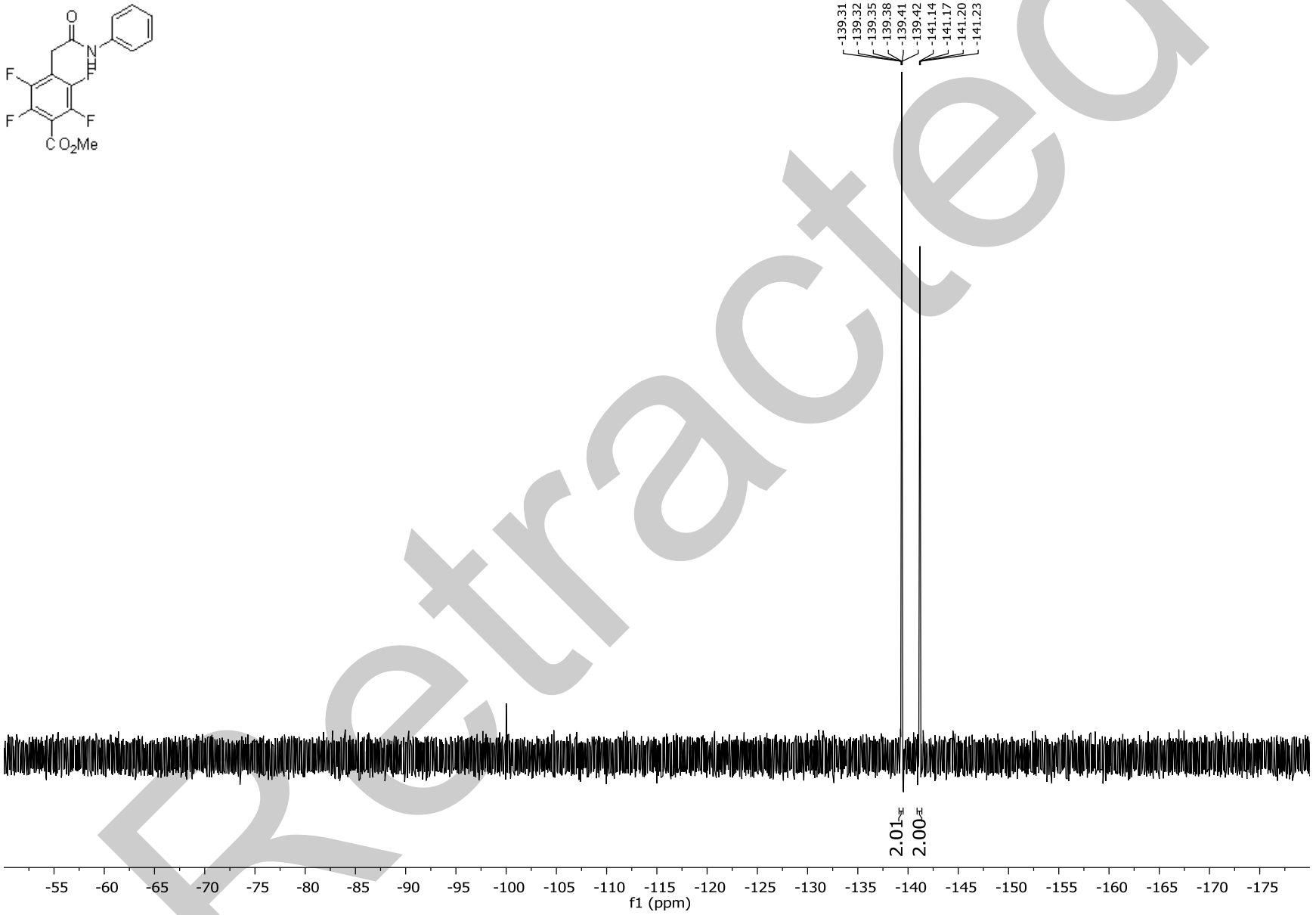
11a methyl 4-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate ^{19}F NMR (376 MHz, $CDCl_3$)



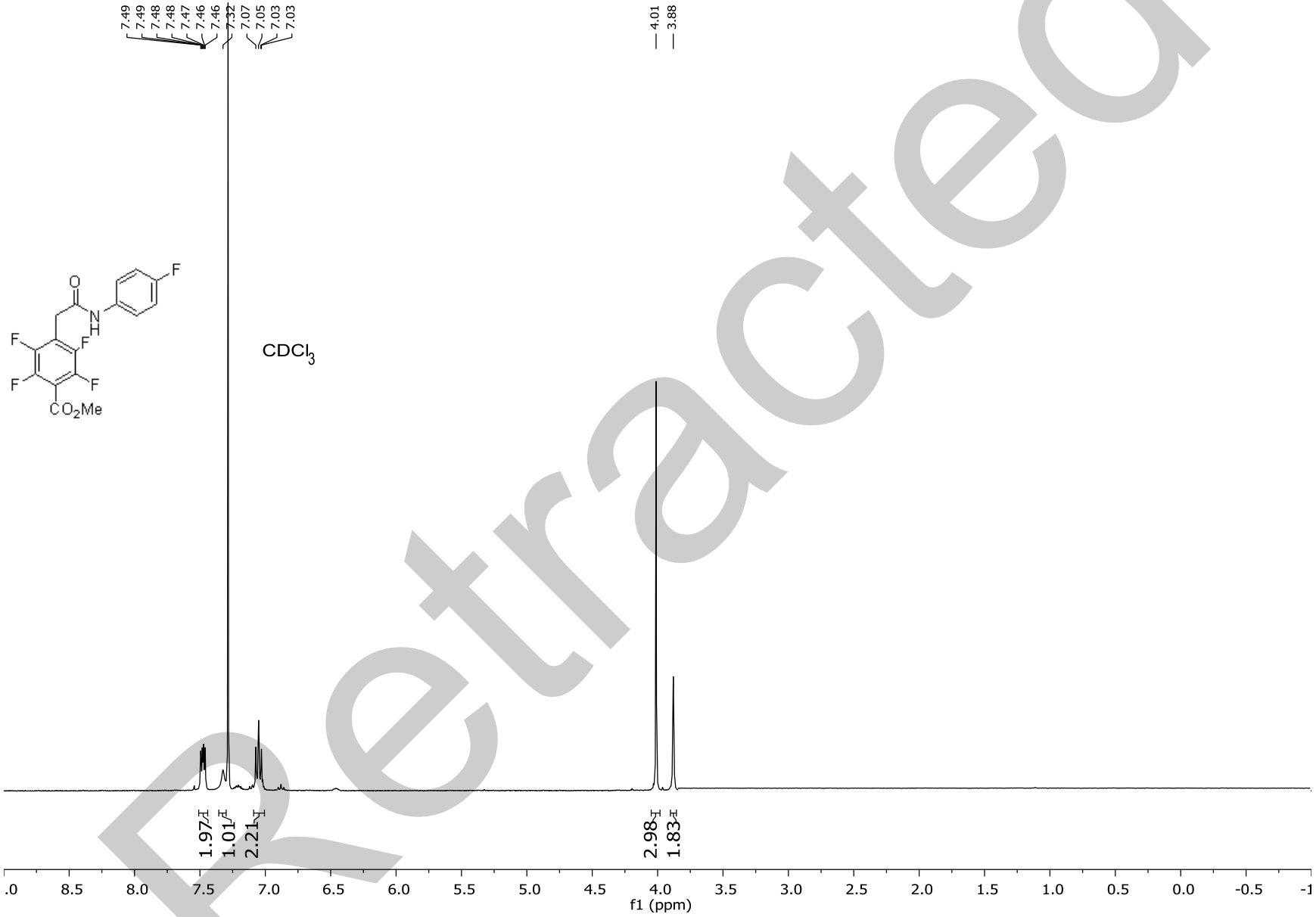
11b methyl 2,3,5,6-tetrafluoro-4-(2-oxo-2-(phenylamino)ethyl)benzoate ^{1}H NMR (400 MHz, $CDCl_3$)



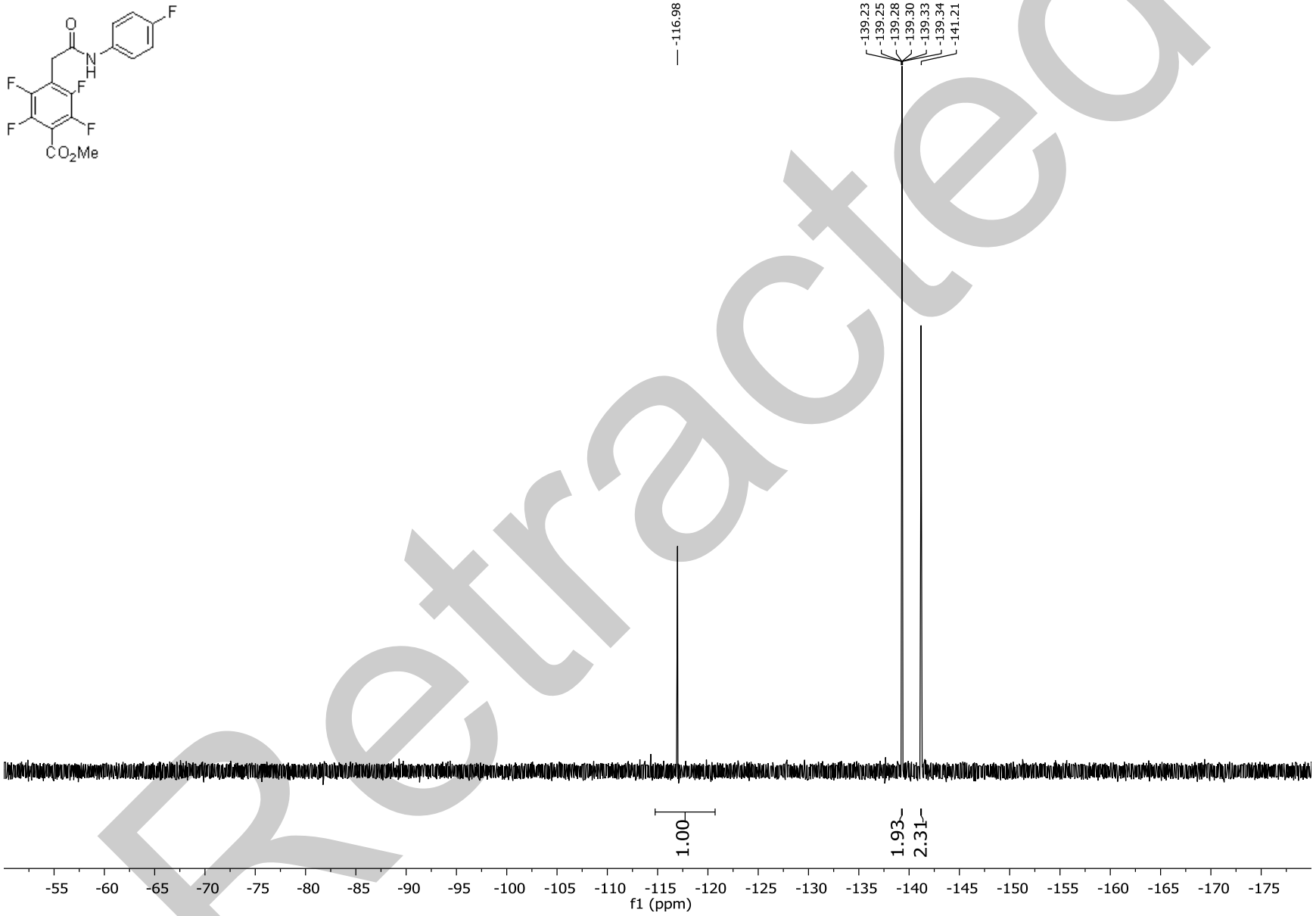
11b methyl 2,3,5,6-tetrafluoro-4-(2-oxo-2-(phenylamino)ethyl)benzoate ^{19}F NMR (376 MHz, $CDCl_3$)



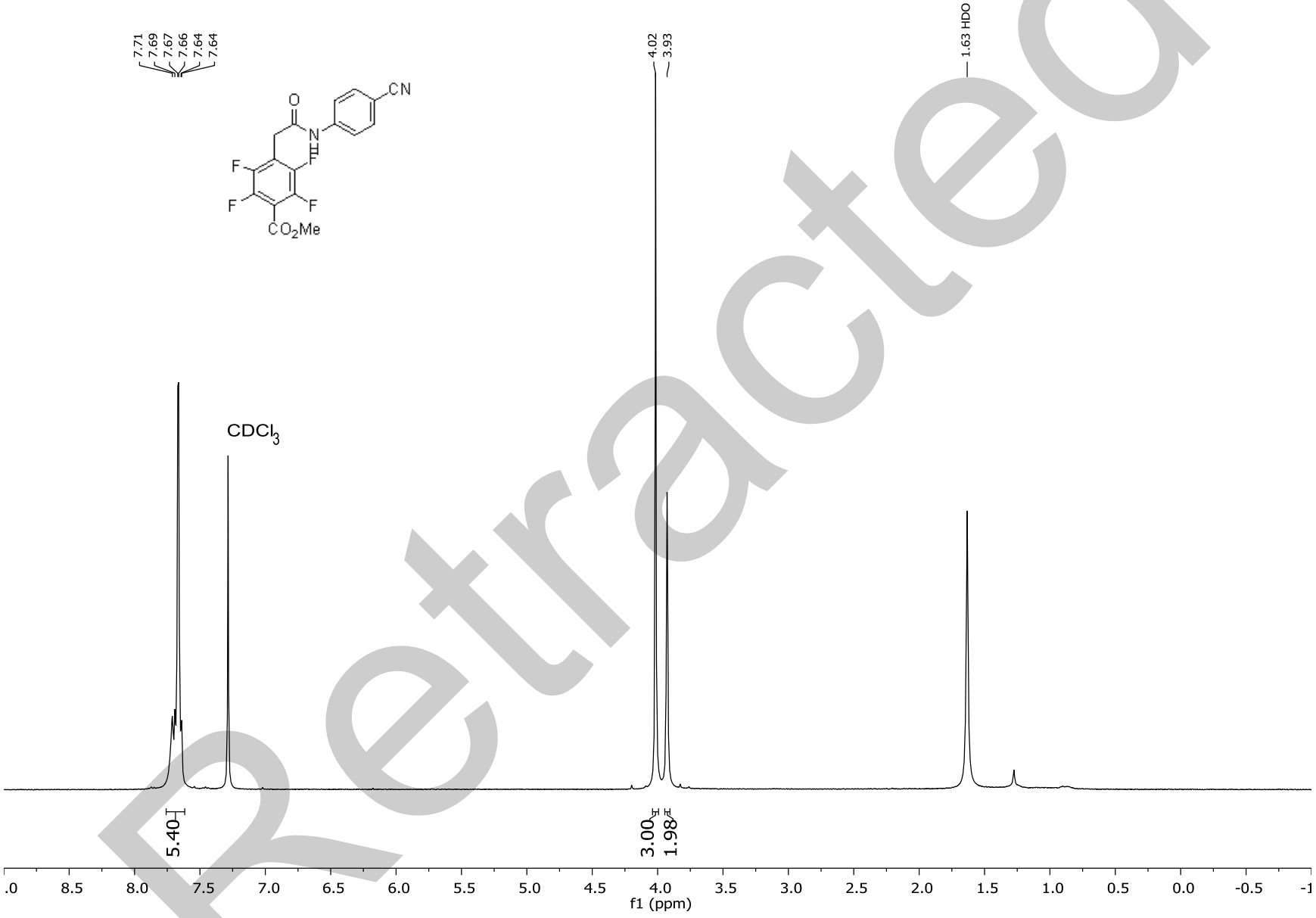
11c methyl 2,3,5,6-tetrafluoro-4-(2-((4-fluorophenyl)amino)-2-oxoethyl)benzoate ^{1}H NMR (400 MHz, $CDCl_3$)



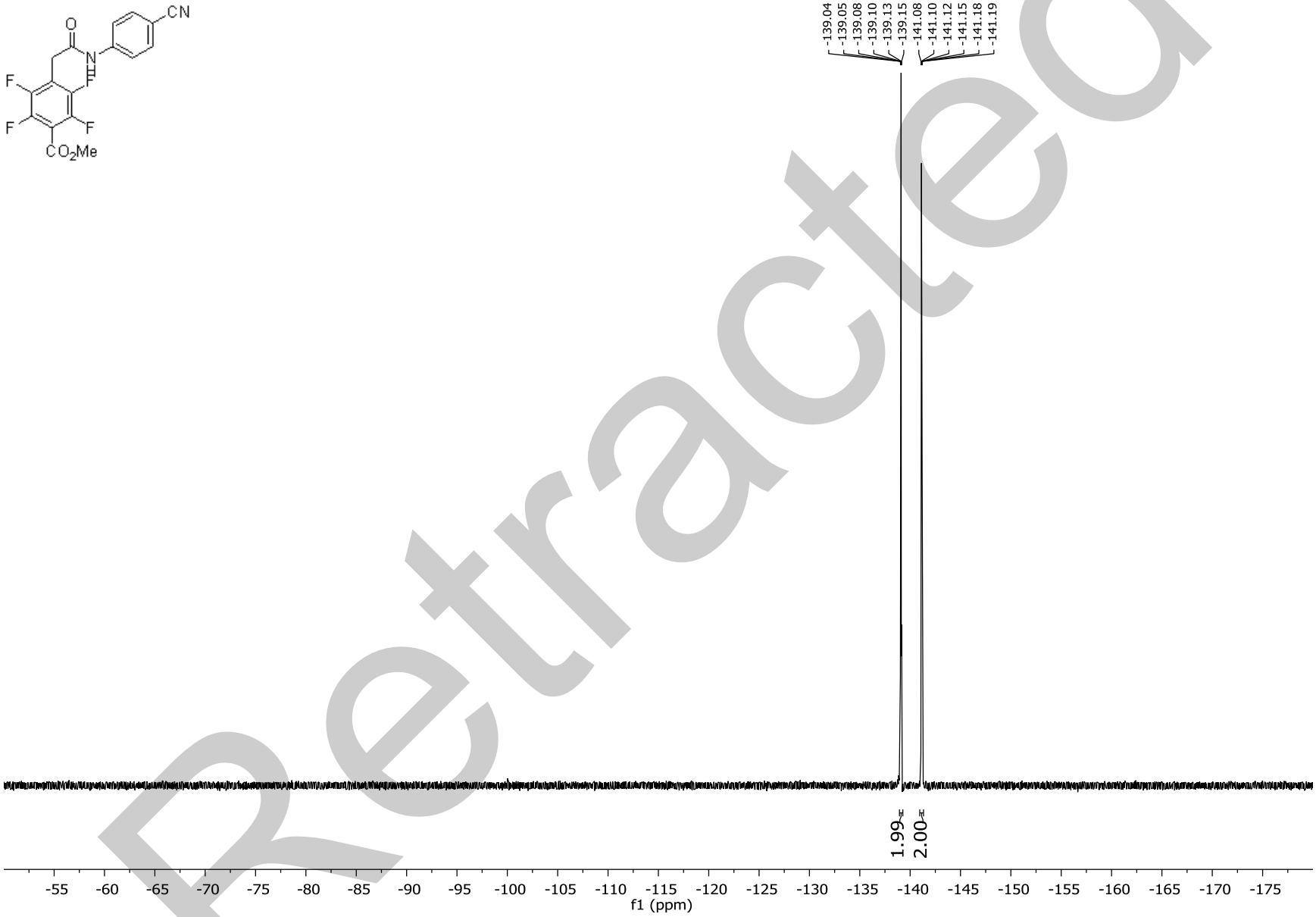
11c methyl 2,3,5,6-tetrafluoro-4-(2-((4-fluorophenyl)amino)-2-oxoethyl)benzoate ^{19}F NMR (376 MHz, $CDCl_3$)



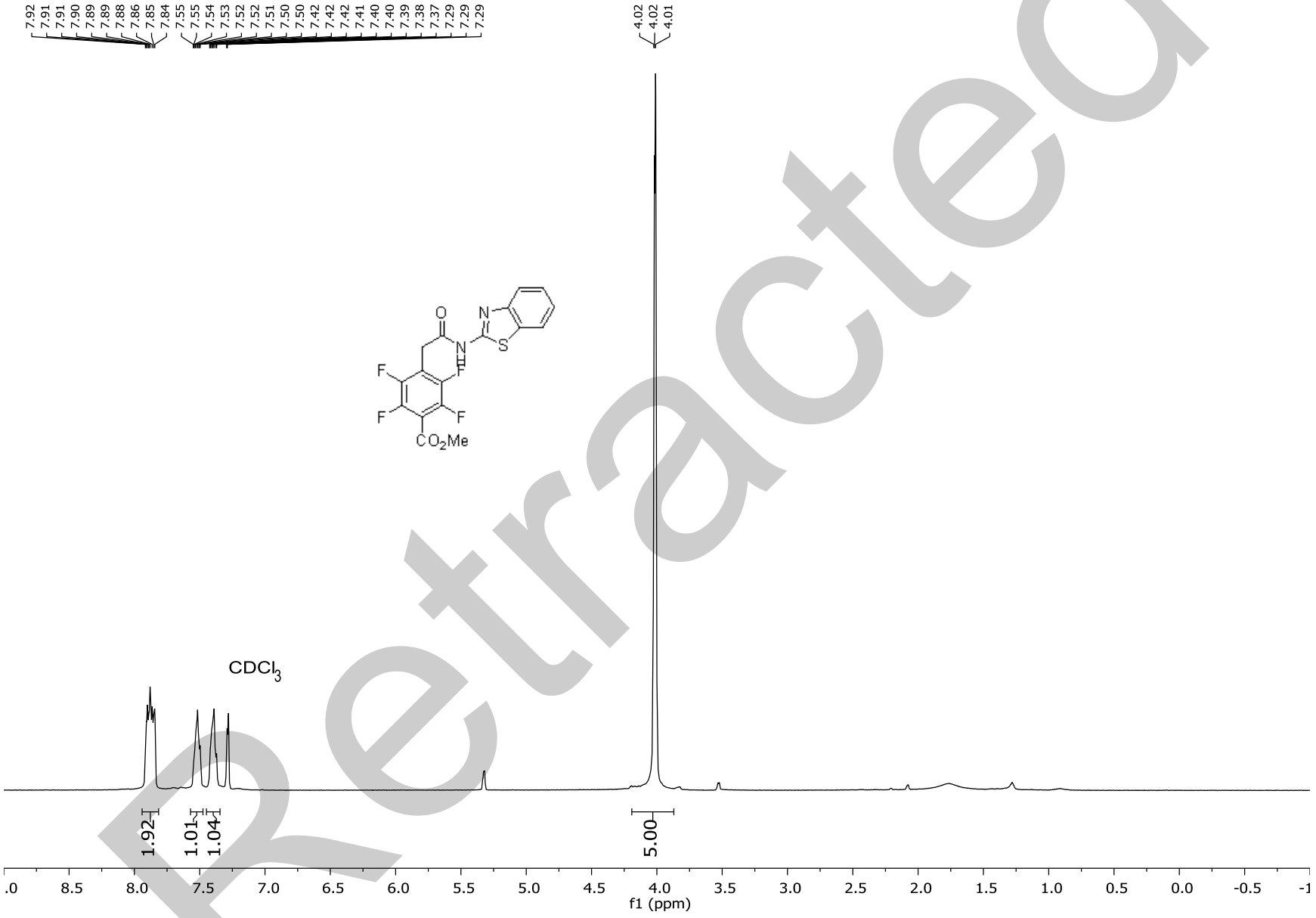
11d methyl 4-(2-((4-cyanophenyl)amino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate ^{1}H NMR (400 MHz, $CDCl_3$)



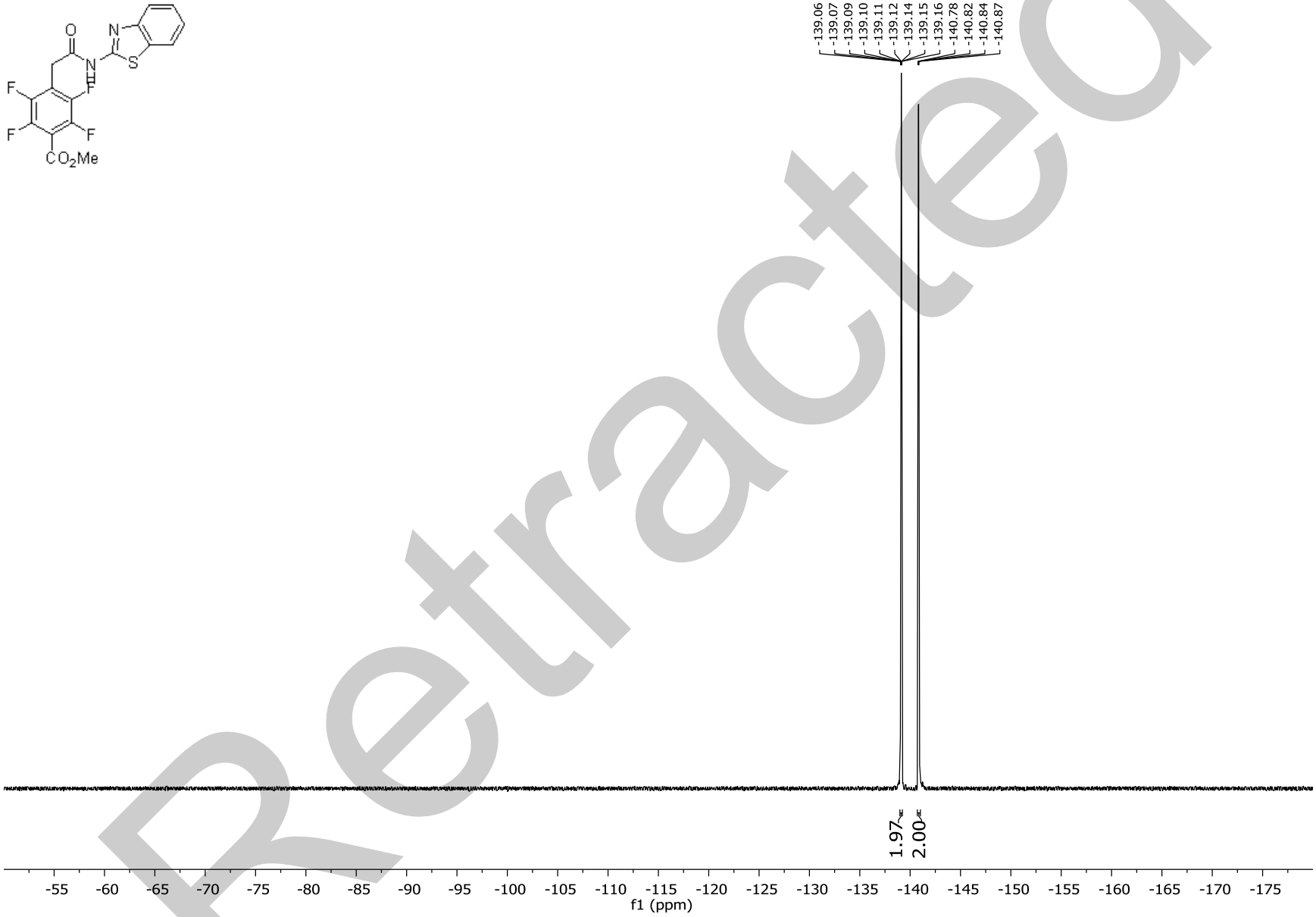
11d methyl 4-(2-((4-cyanophenyl)amino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate ^{19}F NMR (376 MHz, $CDCl_3$)



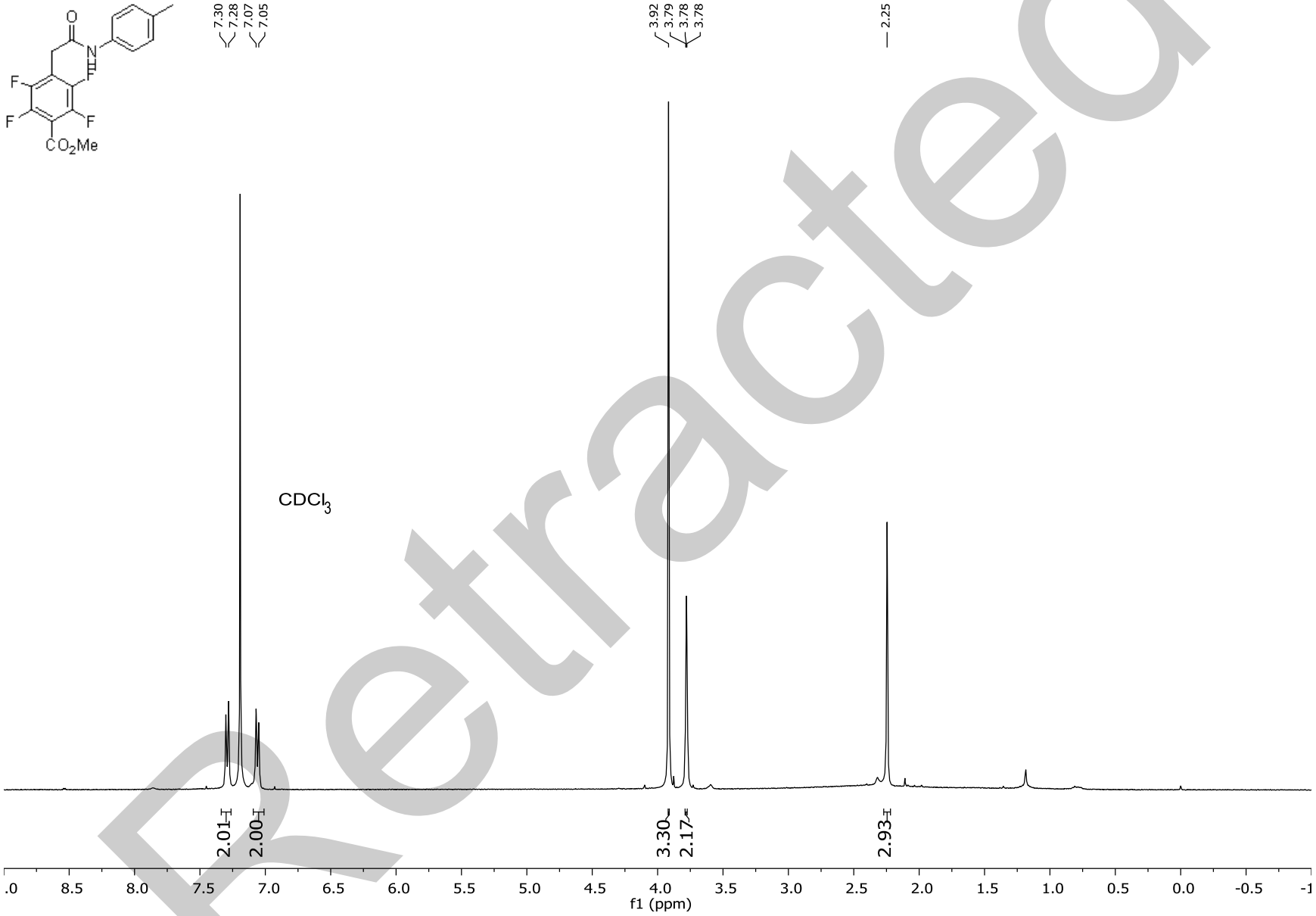
11e methyl 4-(2-(benzo[d]thiazol-2-ylamino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate ^{1}H NMR (400 MHz, $CDCl_3$)



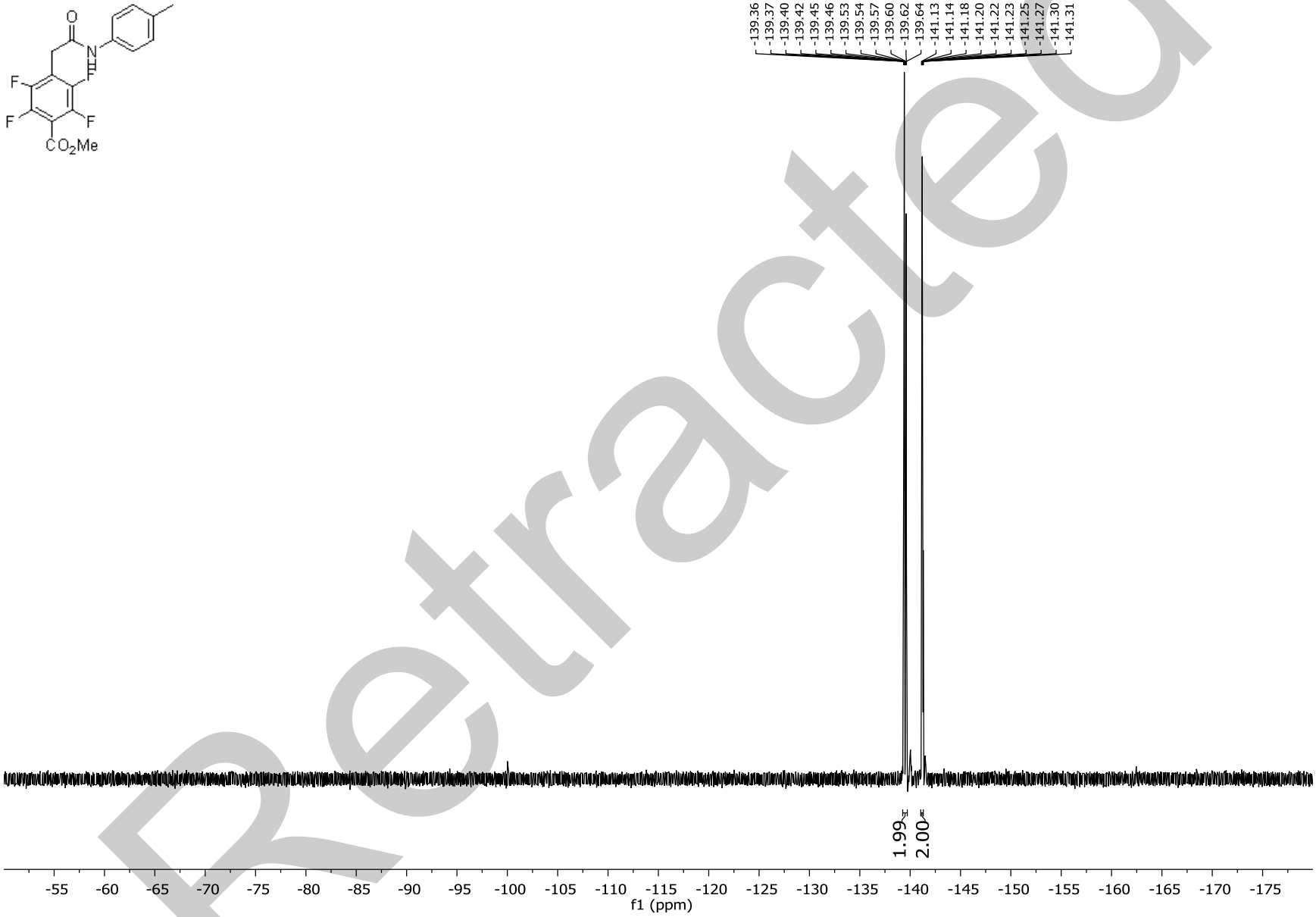
11e methyl 4-(2-(benzo[d]thiazol-2-ylamino)-2-oxoethyl)-2,3,5,6-tetrafluorobenzoate ^{19}F NMR (376 MHz, $CDCl_3$)



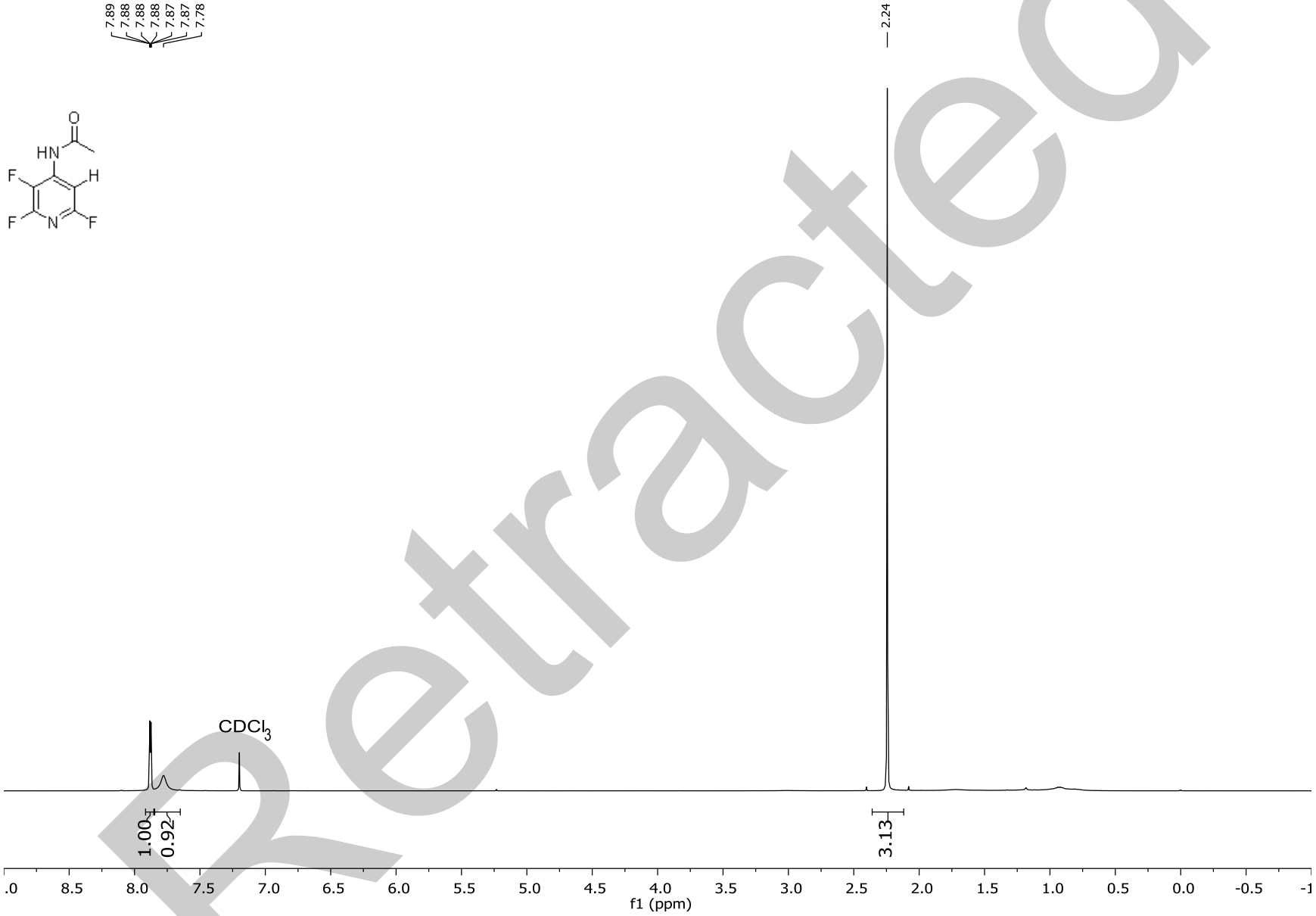
11f methyl 2,3,5,6-tetrafluoro-4-(2-oxo-2-(p-tolylamino)ethyl)benzoate ^{1}H NMR (400 MHz, $CDCl_3$)



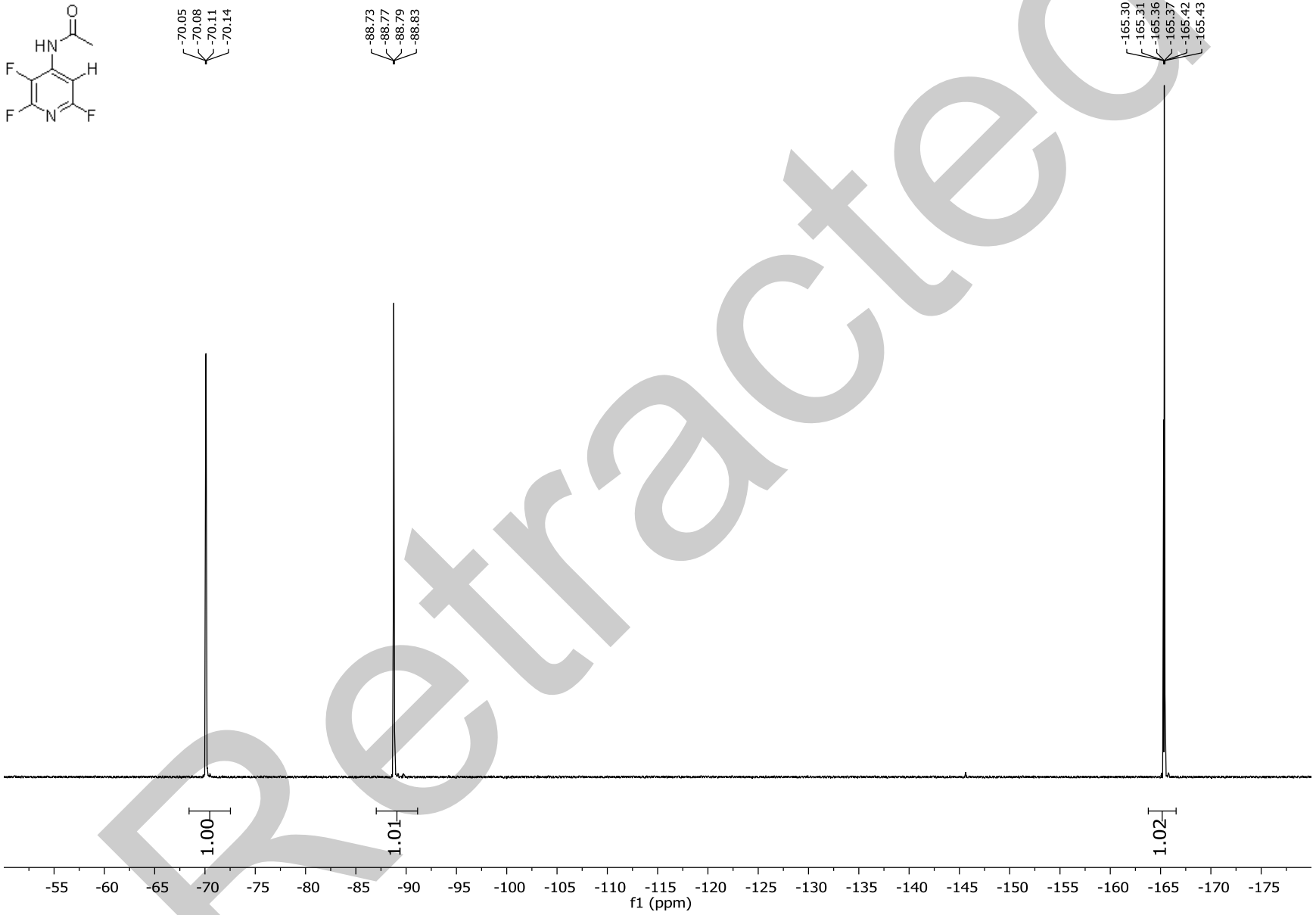
11f methyl 2,3,5,6-tetrafluoro-4-(2-oxo-2-(p-tolylamino)ethyl)benzoate ^{19}F NMR (376 MHz, $CDCl_3$)



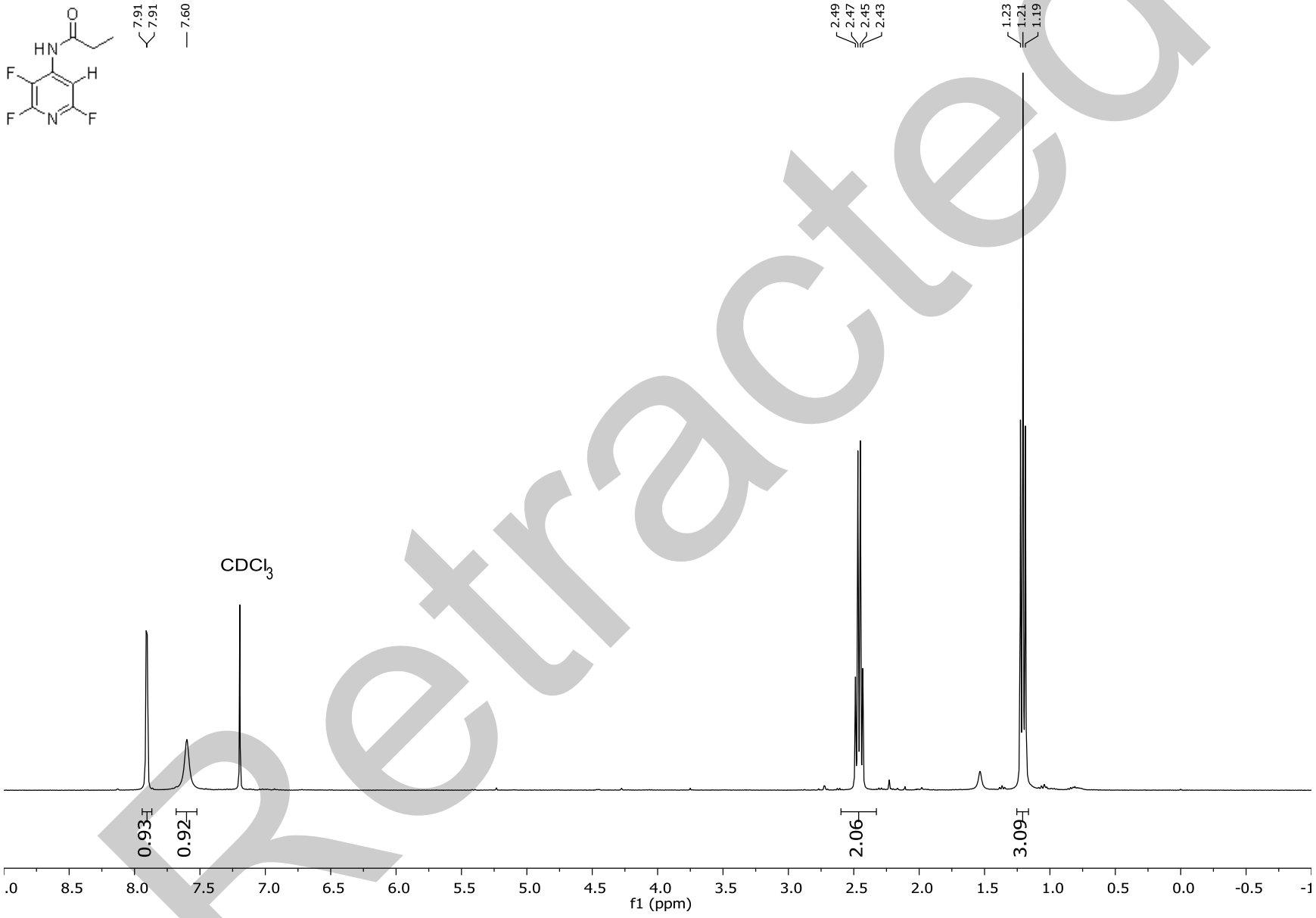
4a *N*-(2,3,6-trifluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



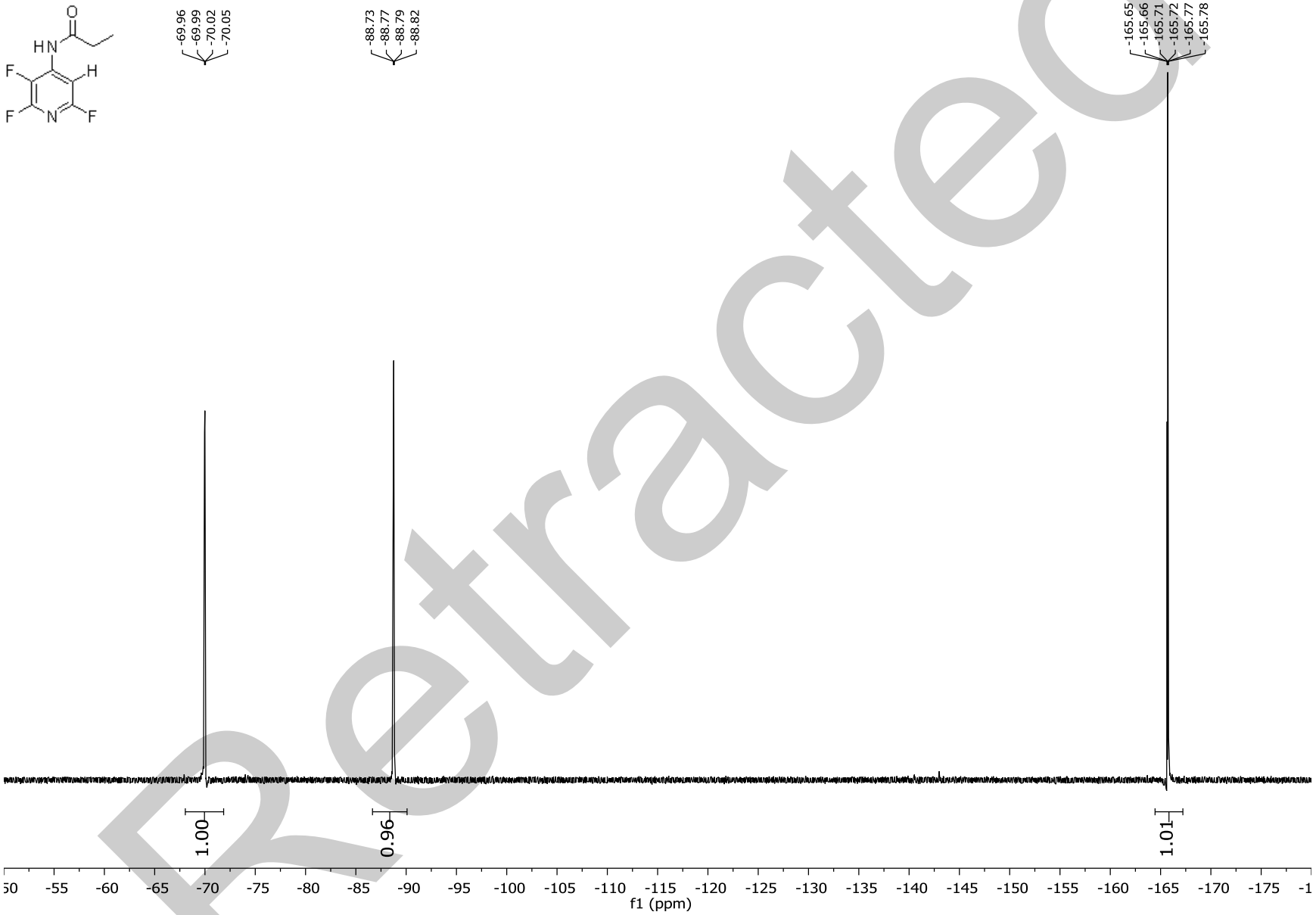
4a *N*-(2,3,6-trifluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



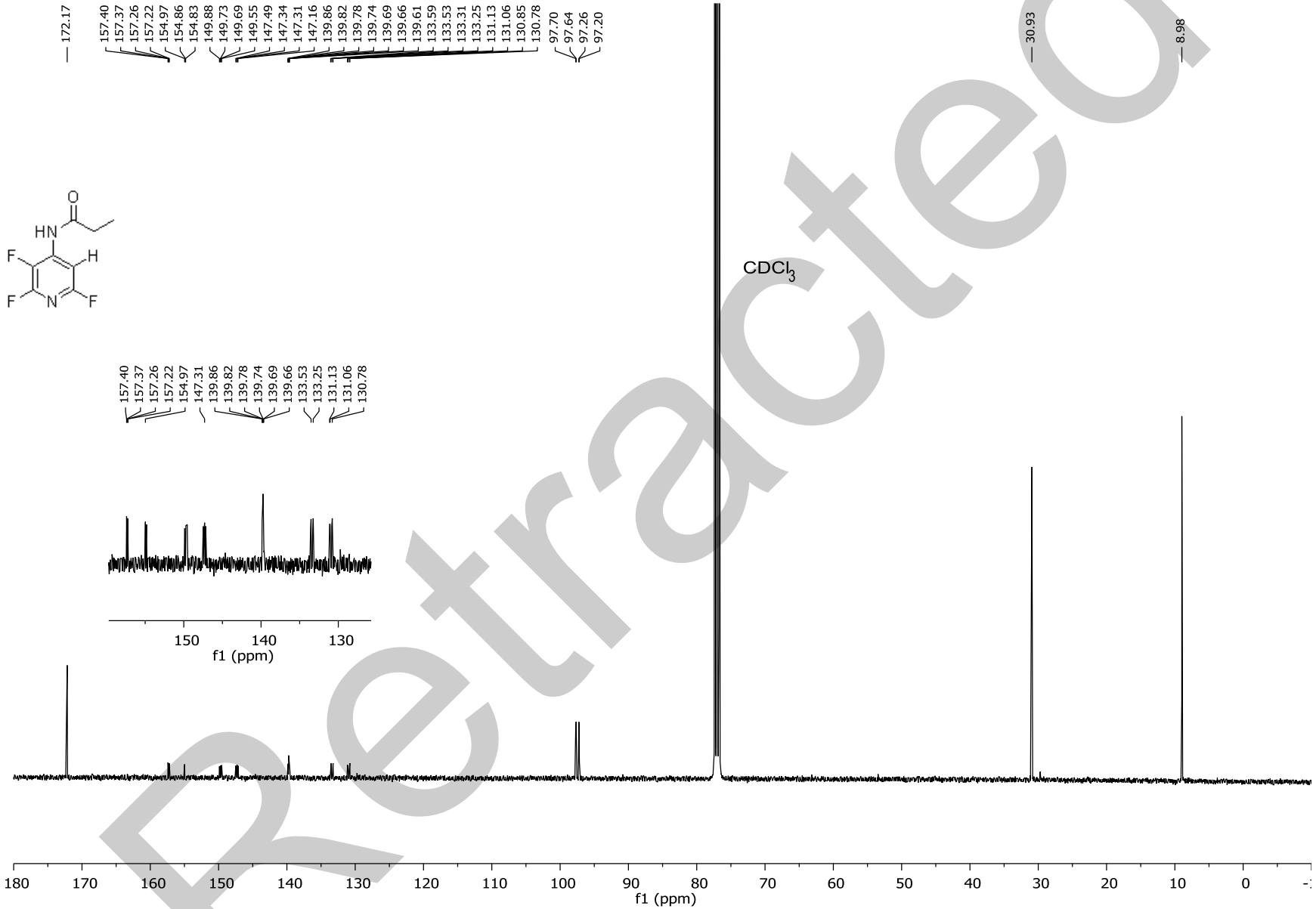
4b' *N*-(2,3,6-trifluoropyridin-4-yl)propionamide ^{1}H NMR (400 MHz, Chloroform-*d*)



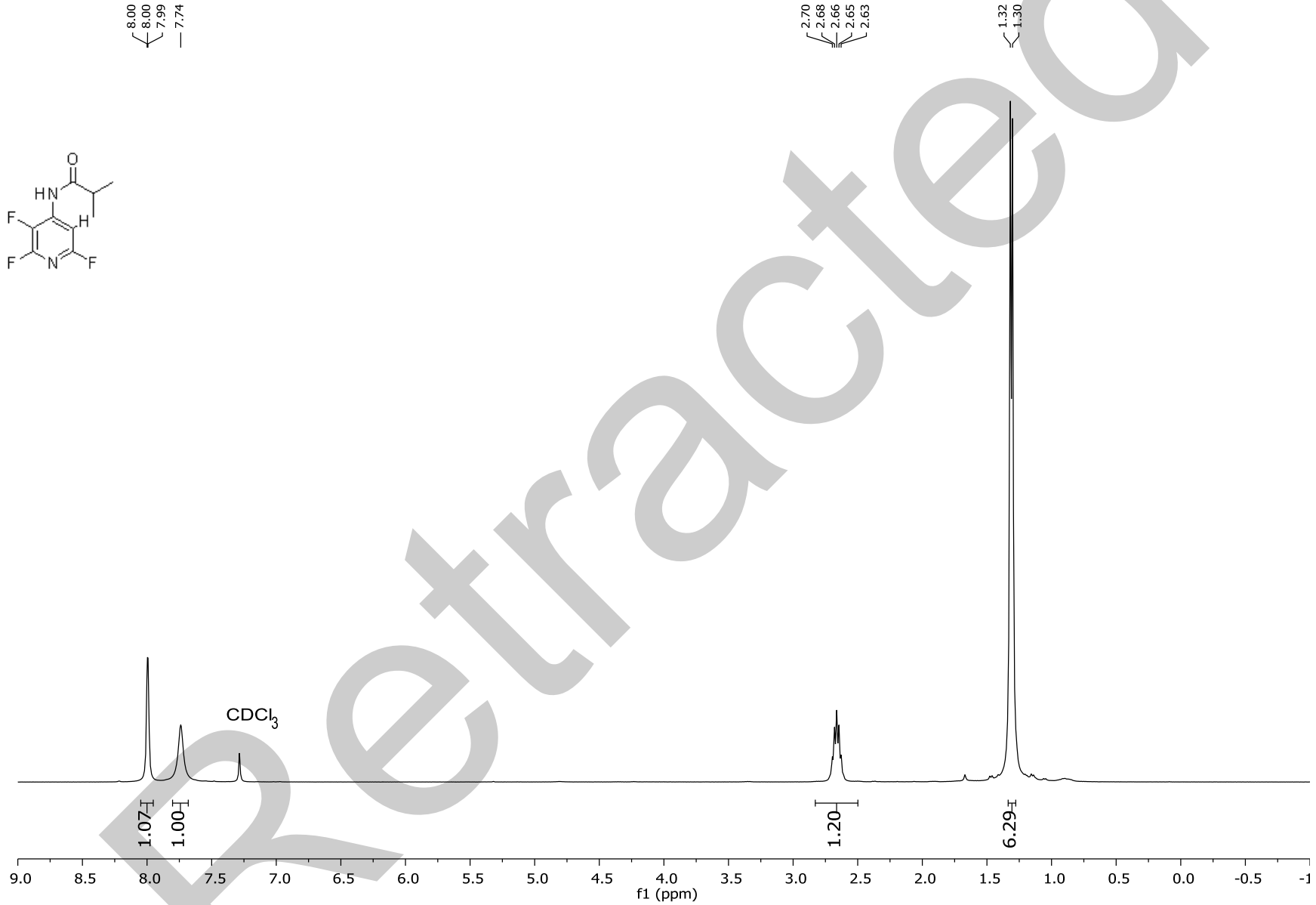
4b’ *N*-(2,3,6-trifluoropyridin-4-yl)propionamide ^{19}F NMR (376 MHz, Chloroform-*d*)



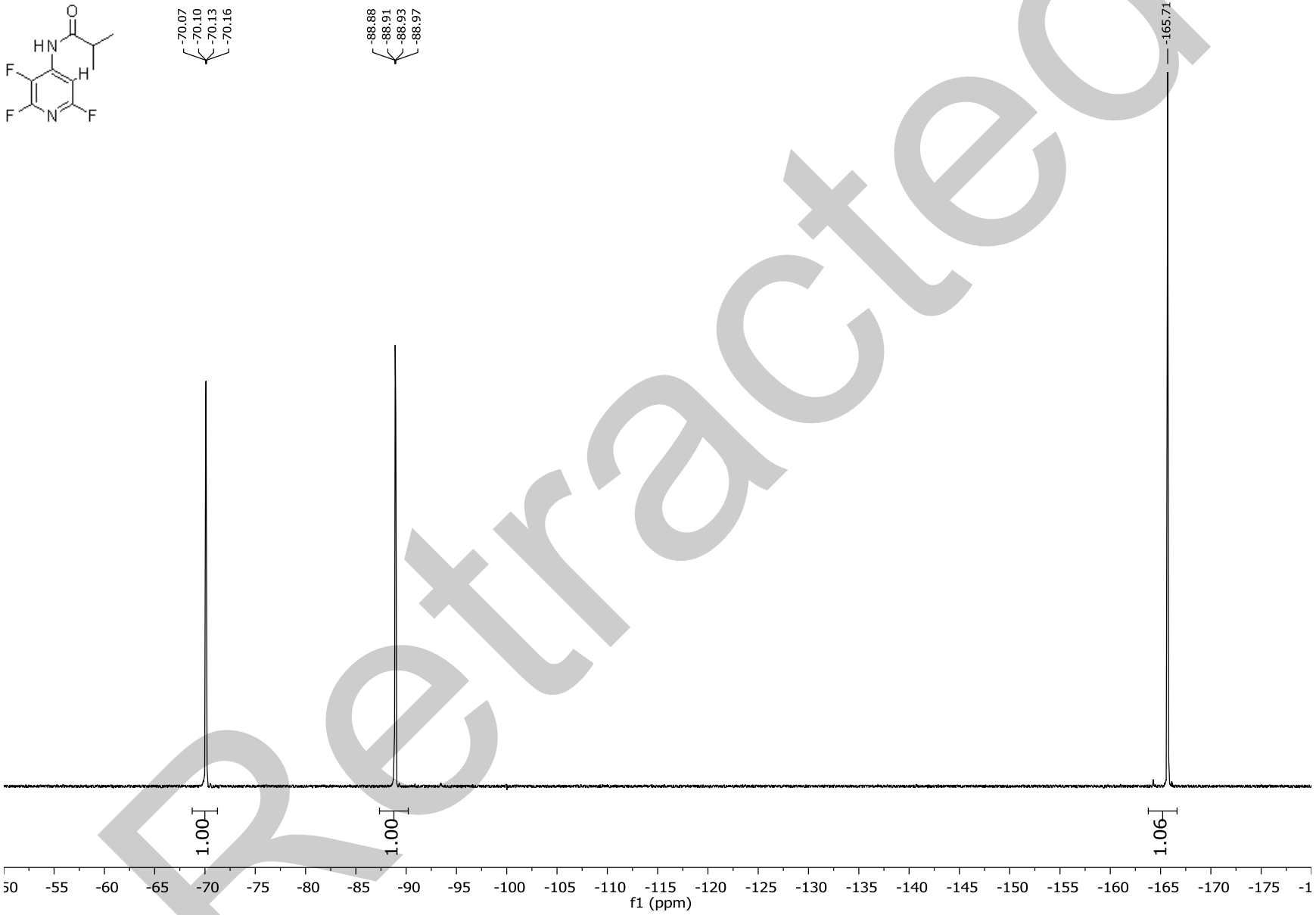
4b' *N*-(2,3,6-trifluoropyridin-4-yl)propionamide). ^{13}C NMR (101 MHz, Chloroform-*d*)



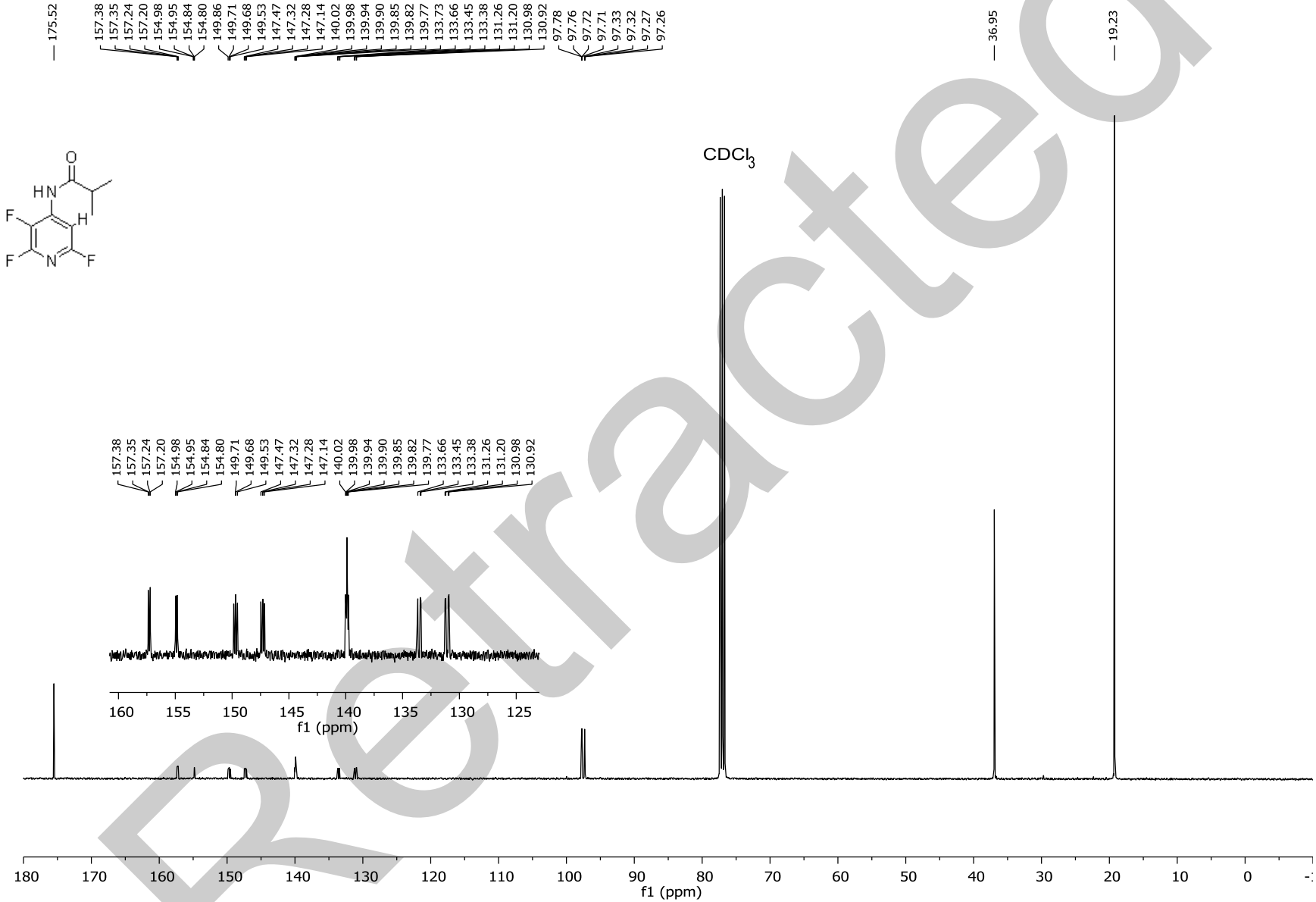
4c' *N*-(2,3,6-trifluoropyridin-4-yl)isobutyramide ^{1}H NMR (400 MHz, Chloroform-*d*)



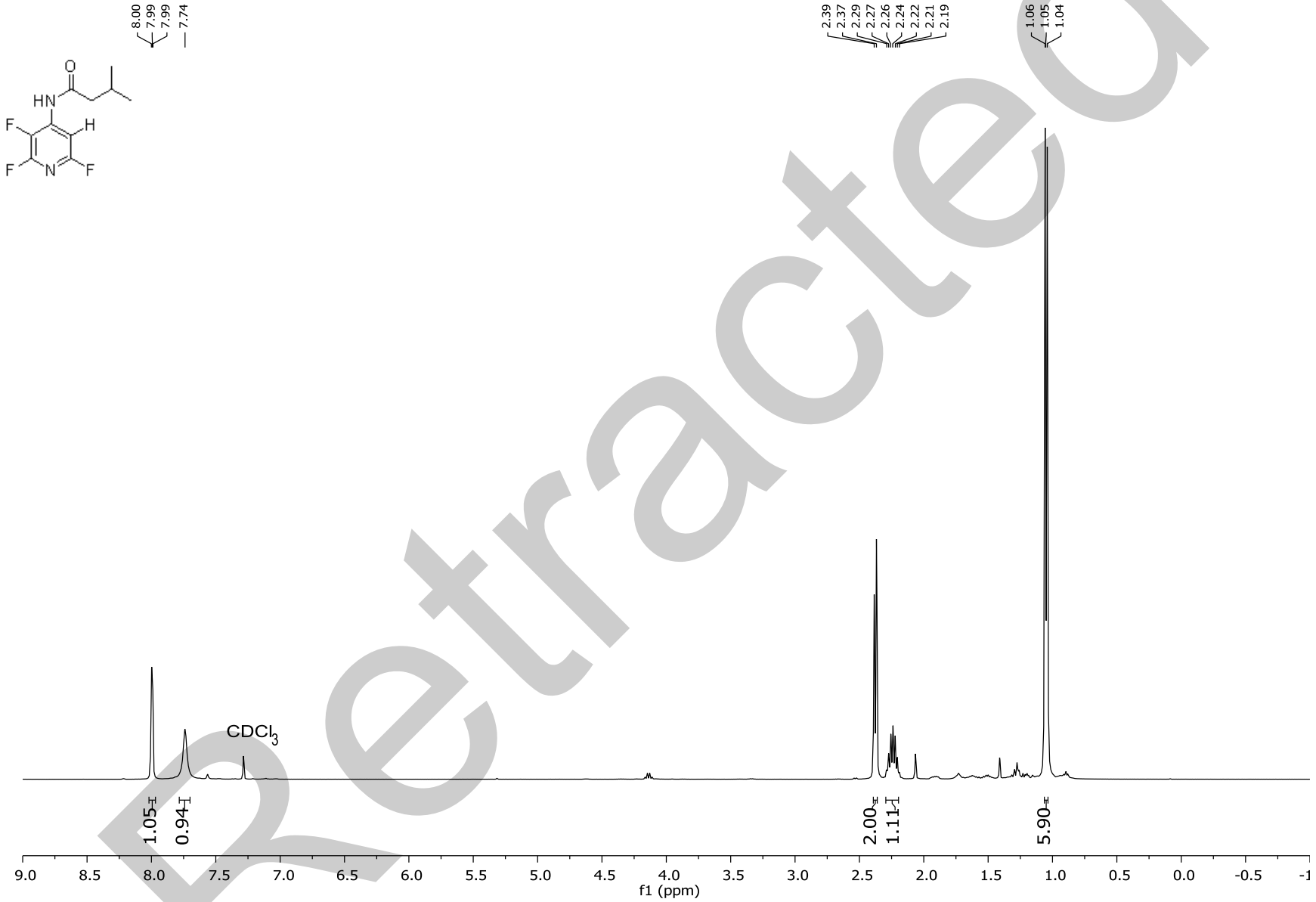
4c' *N*-(2,3,6-trifluoropyridin-4-yl)isobutyramide ^{19}F NMR (376 MHz, Chloroform-*d*)



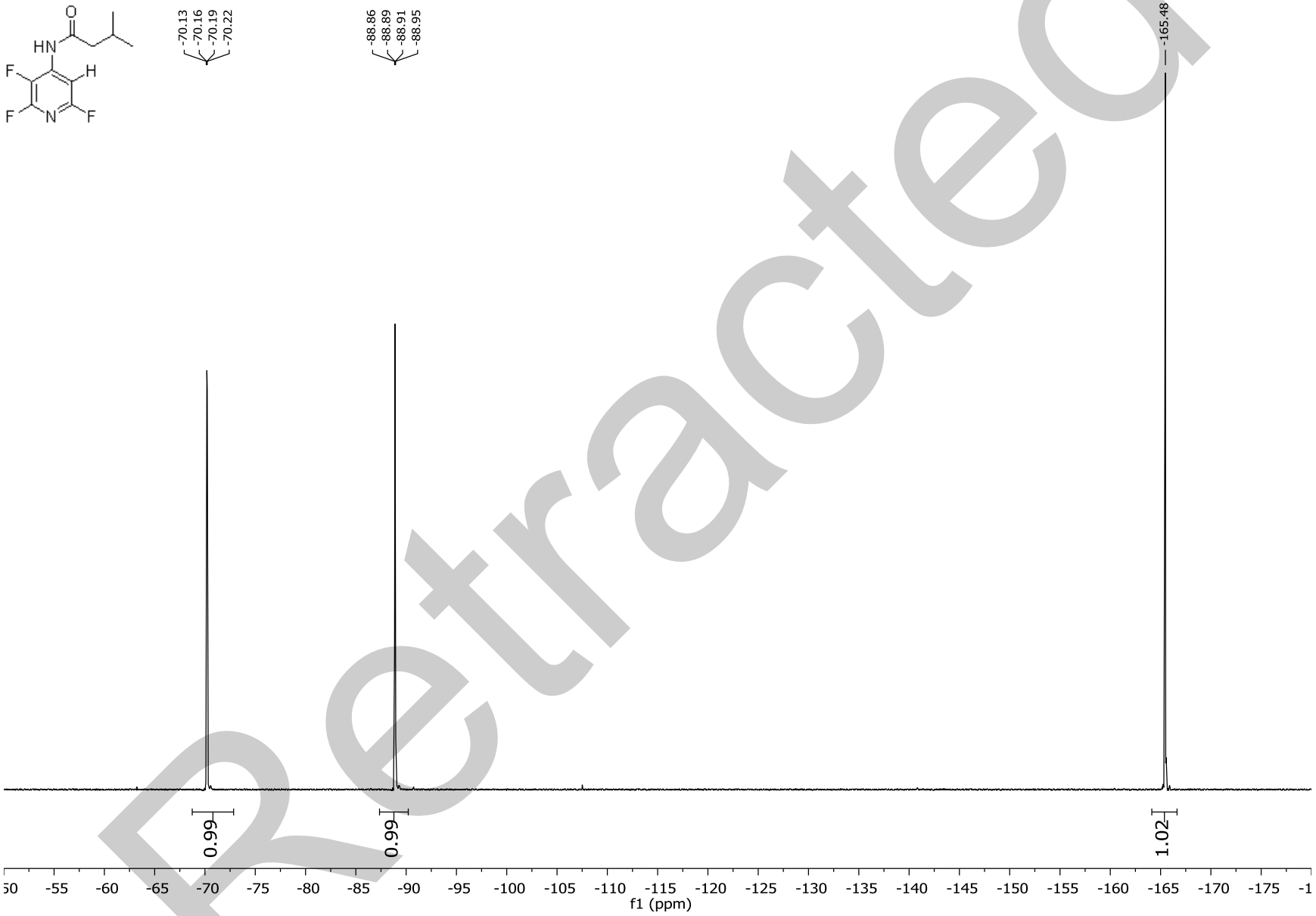
4c' *N*-(2,3,6-trifluoropyridin-4-yl)isobutyramide ^{13}C NMR (101 MHz, Chloroform-*d*)



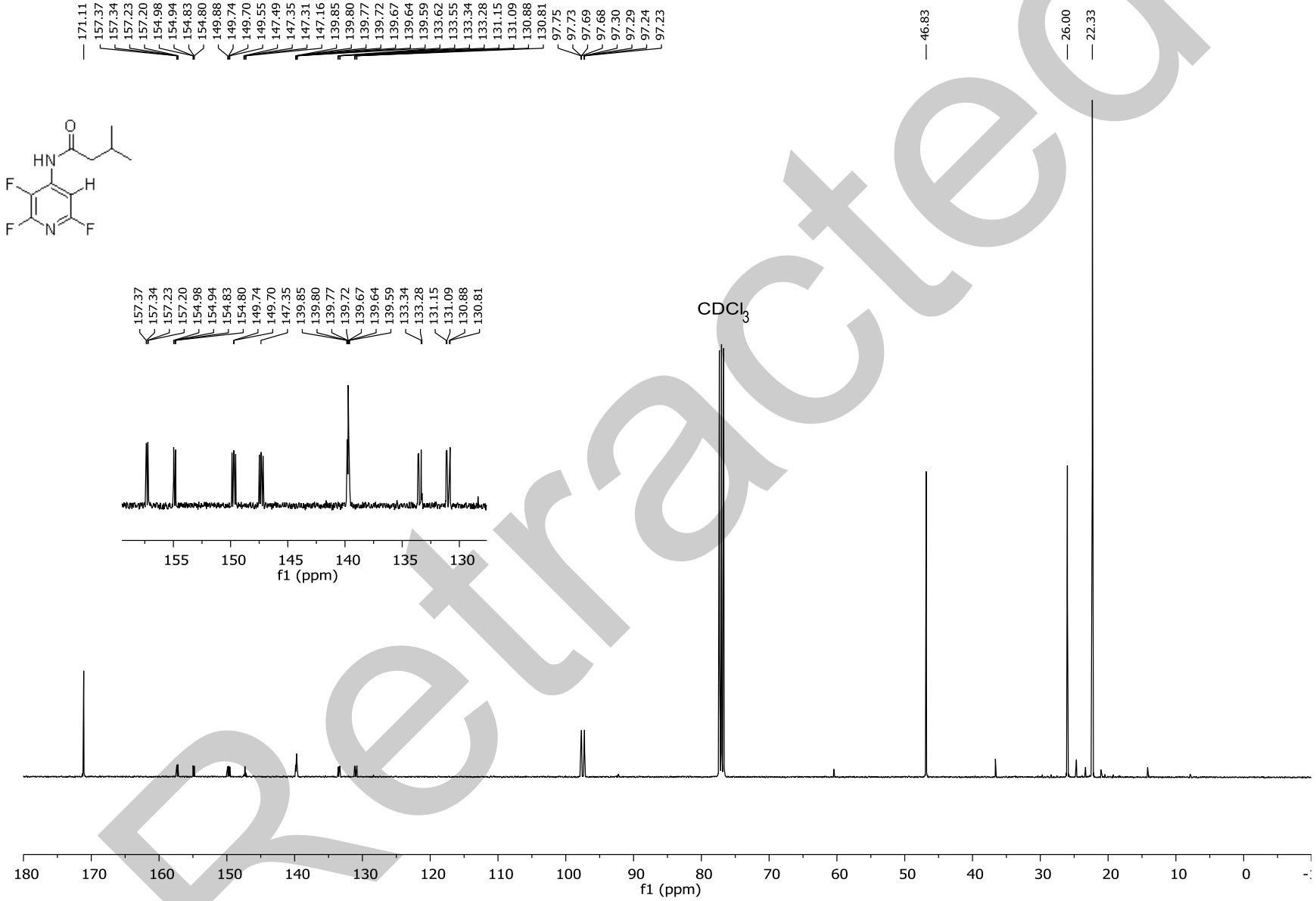
4d' 3-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)butanamide ^{1}H NMR (400 MHz, Chloroform-*d*)



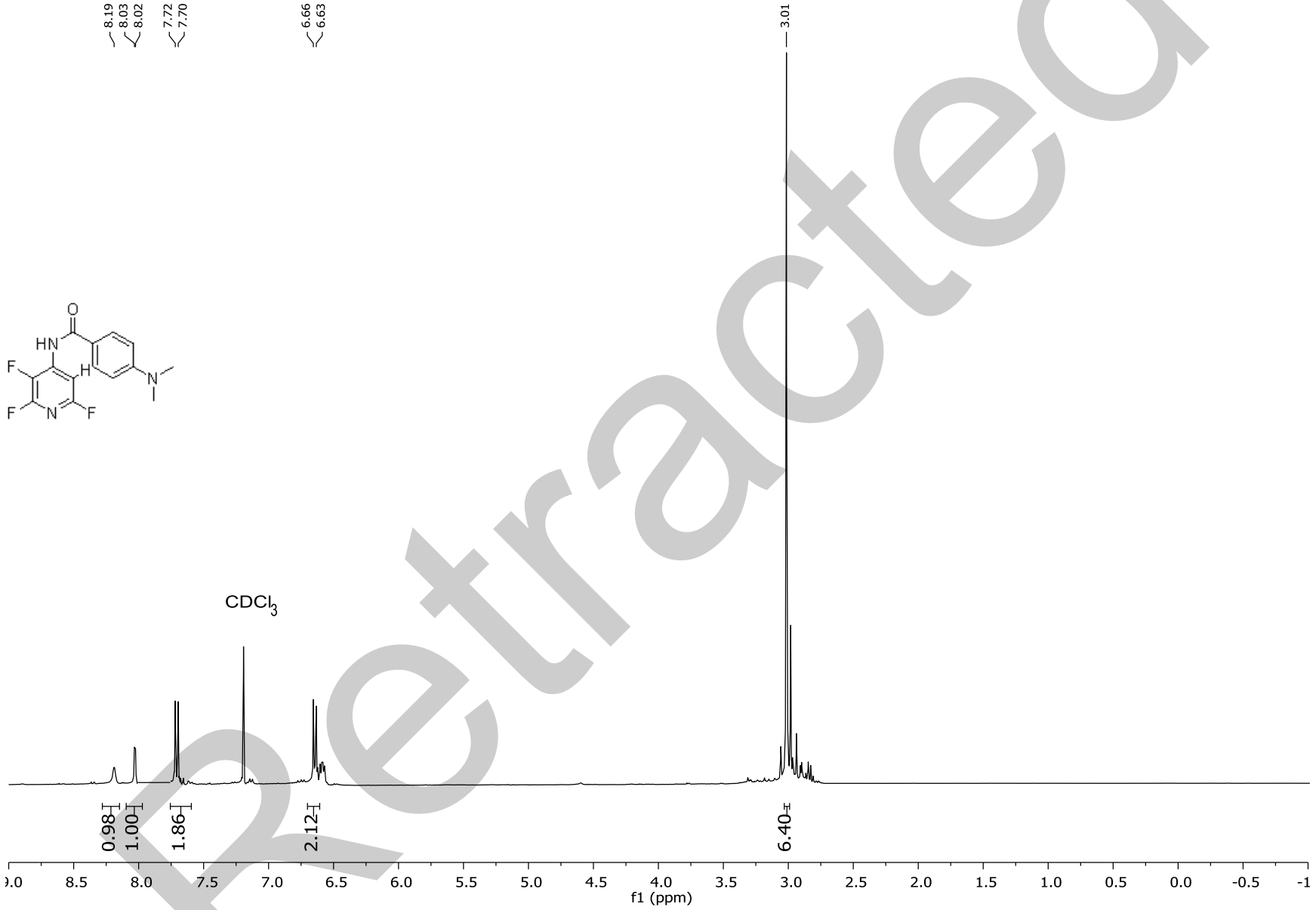
4d' 3-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)butanamide ^{19}F NMR (376 MHz, Chloroform-*d*)



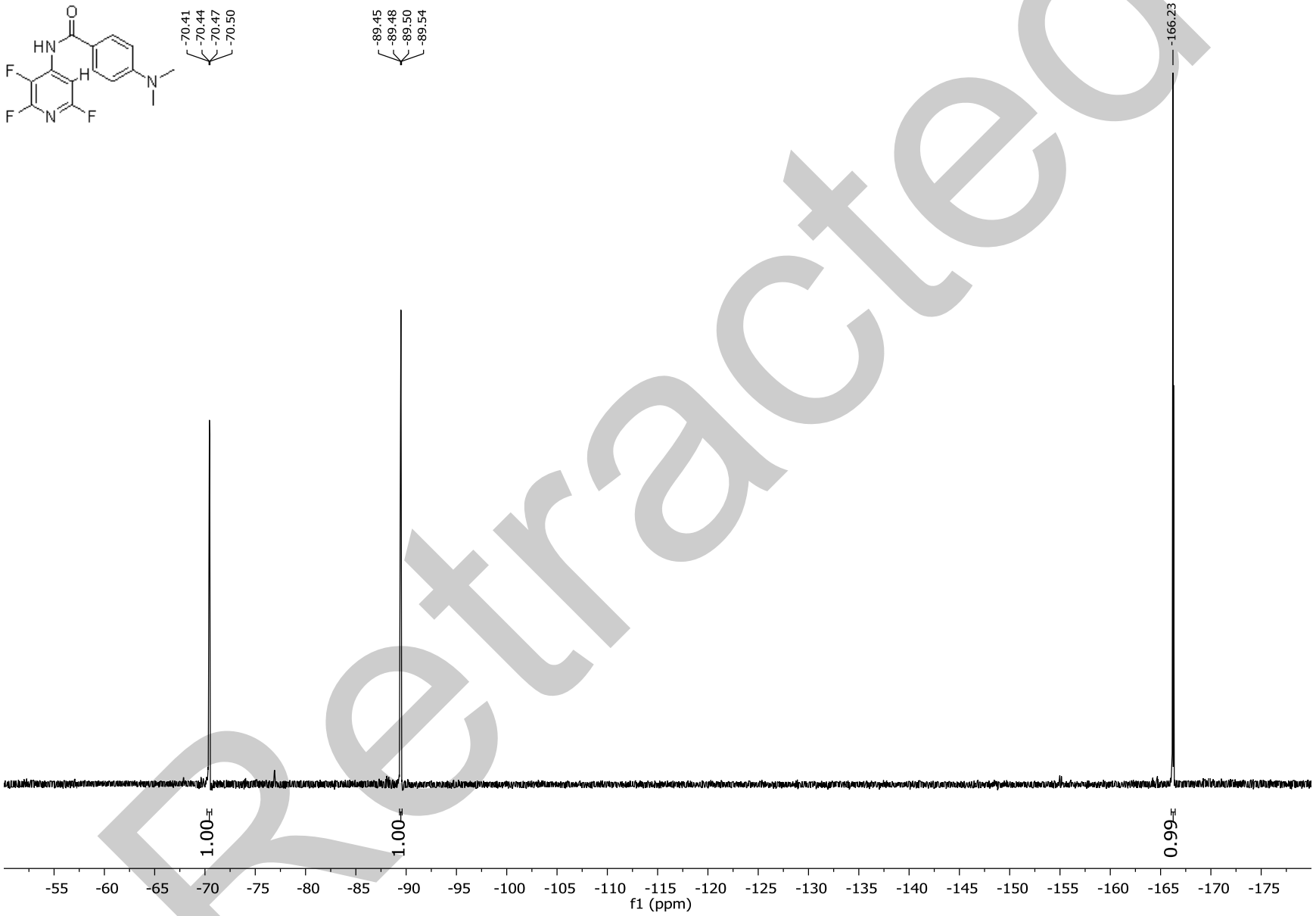
4d' 3-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)butanamide ^{13}C NMR (101 MHz, Chloroform-*d*)



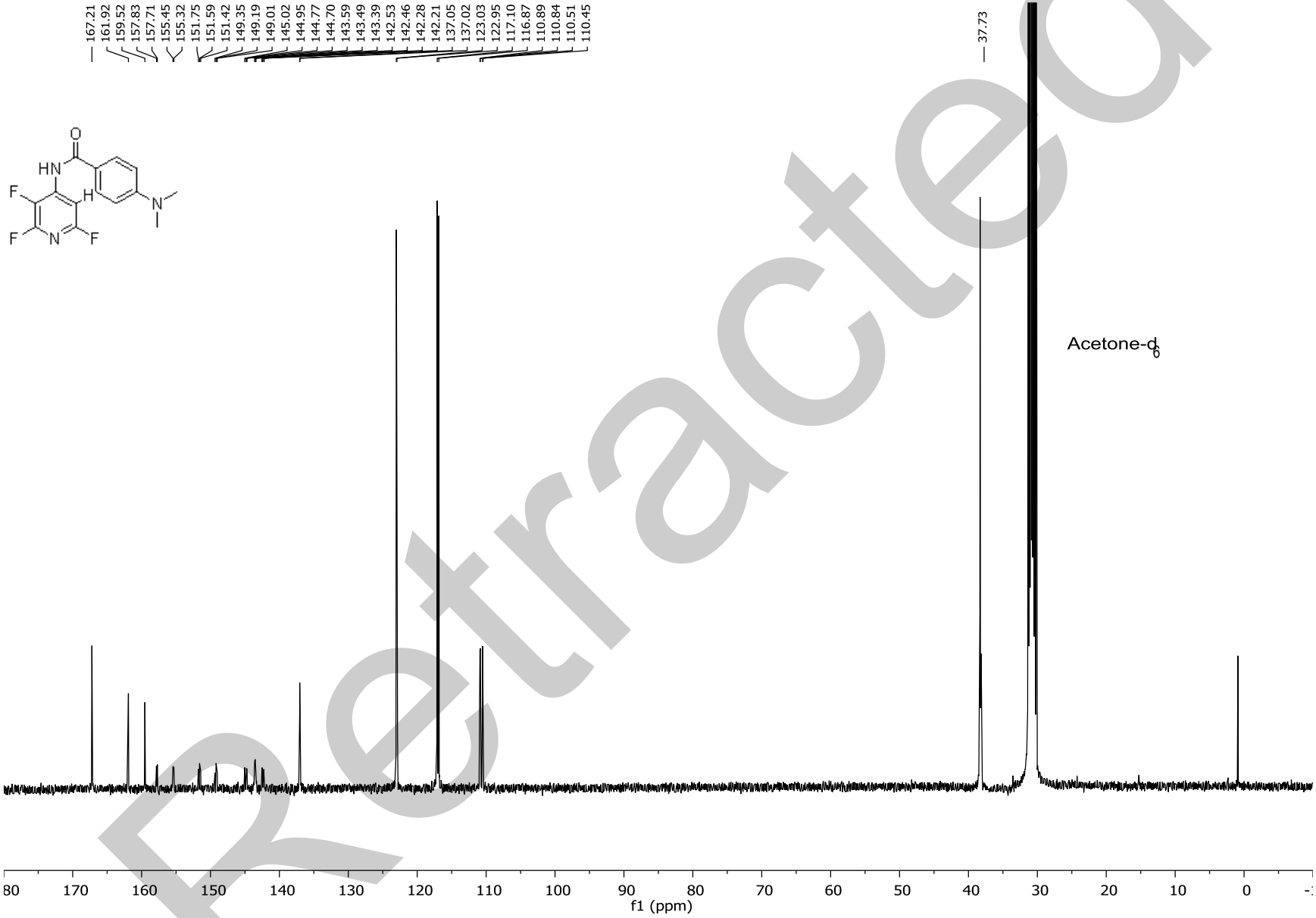
4e' 4-(dimethylamino)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



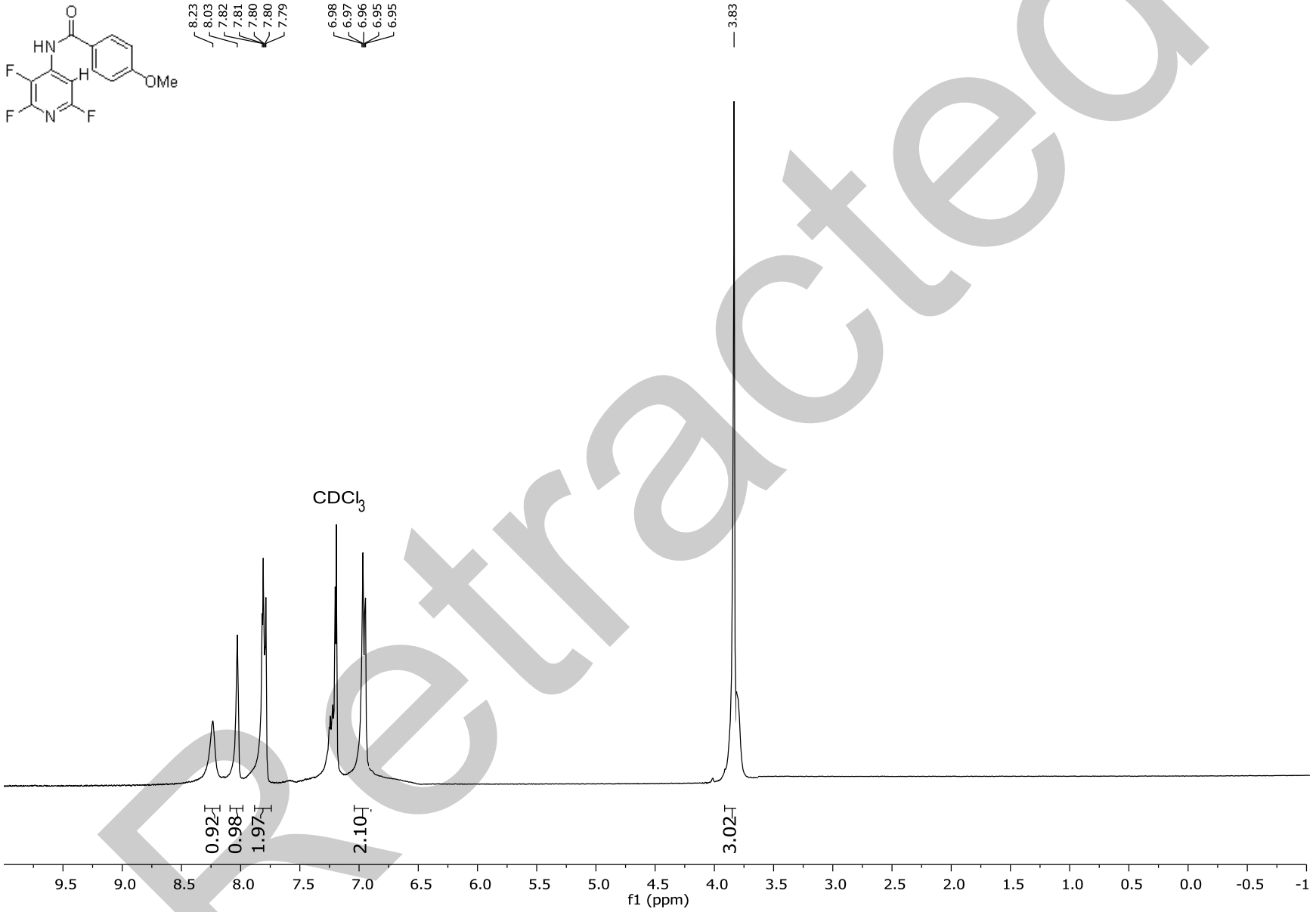
4e' 4-(dimethylamino)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



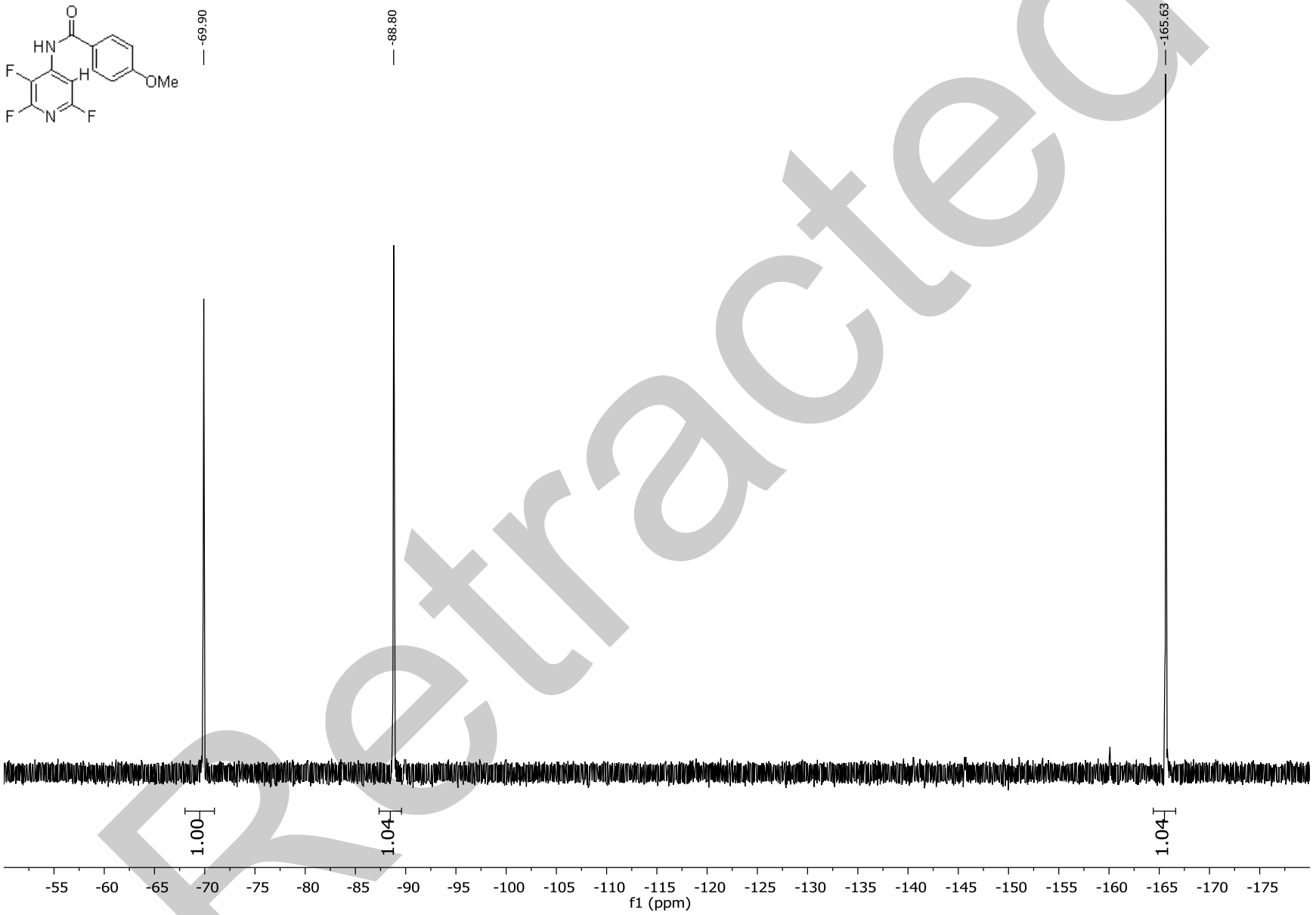
4 e' 4-(dimethylamino)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{13}C NMR (101 MHzAcetone-d$_6$)



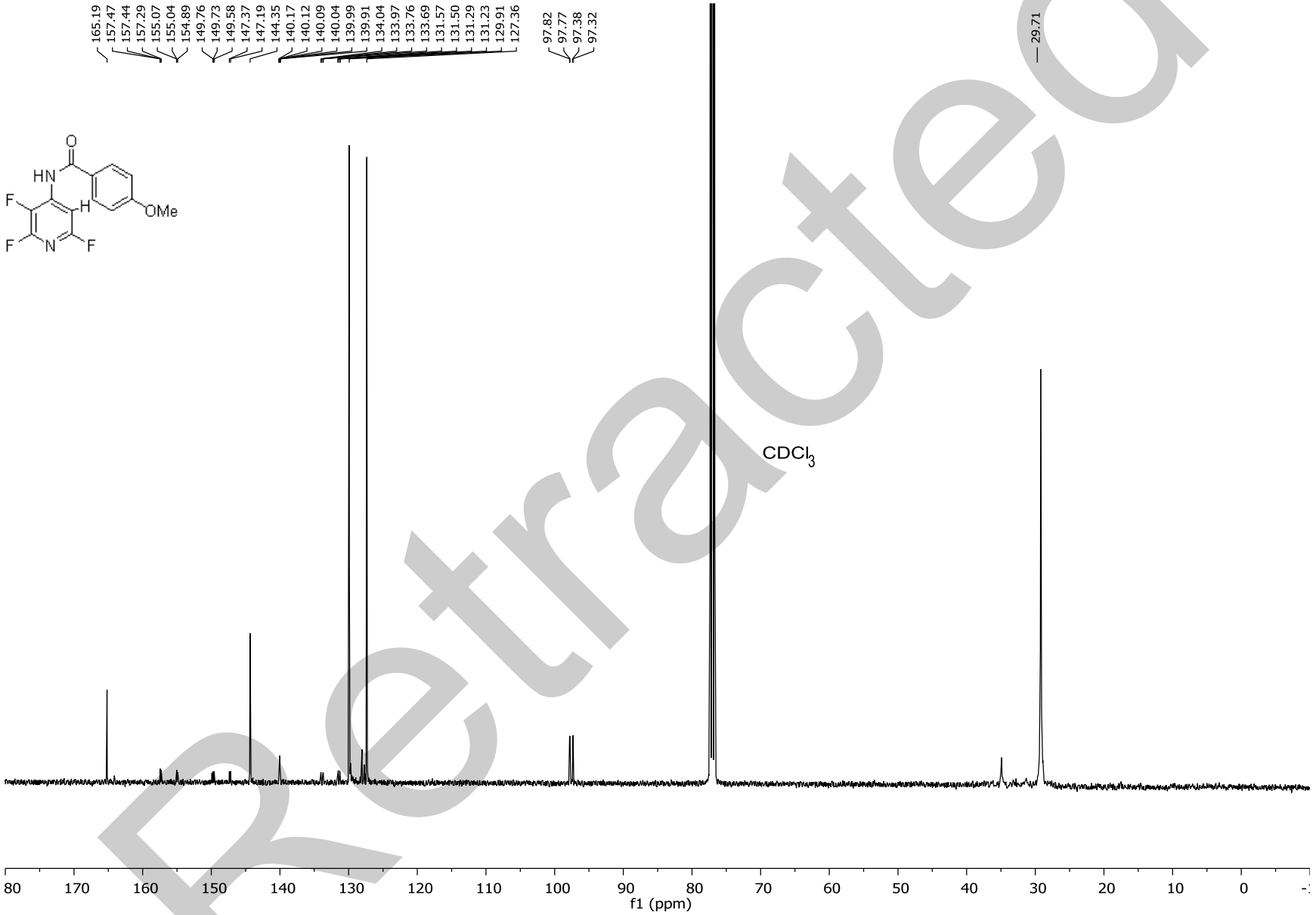
4f' 4-methoxy-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



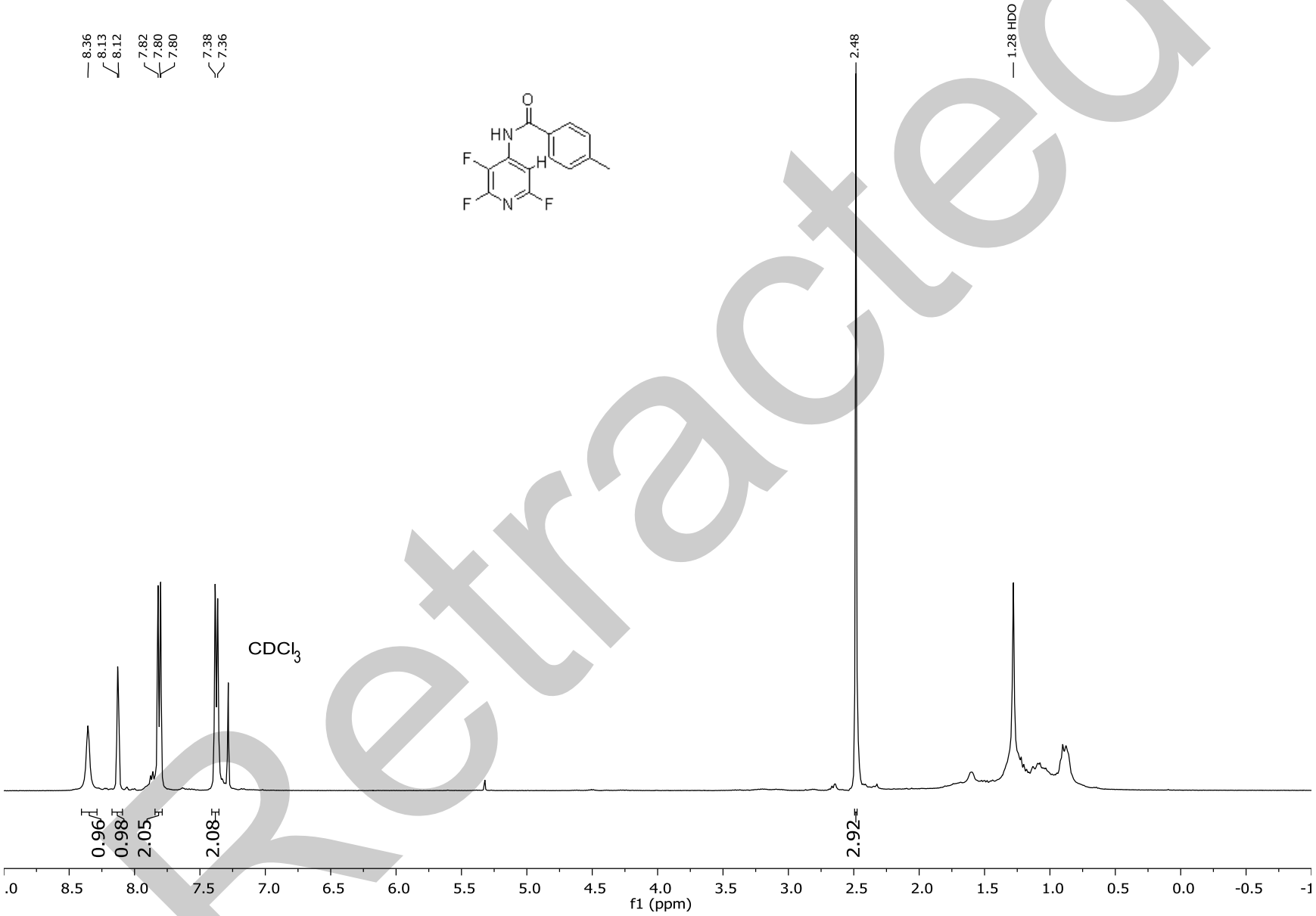
4f' 4-methoxy-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



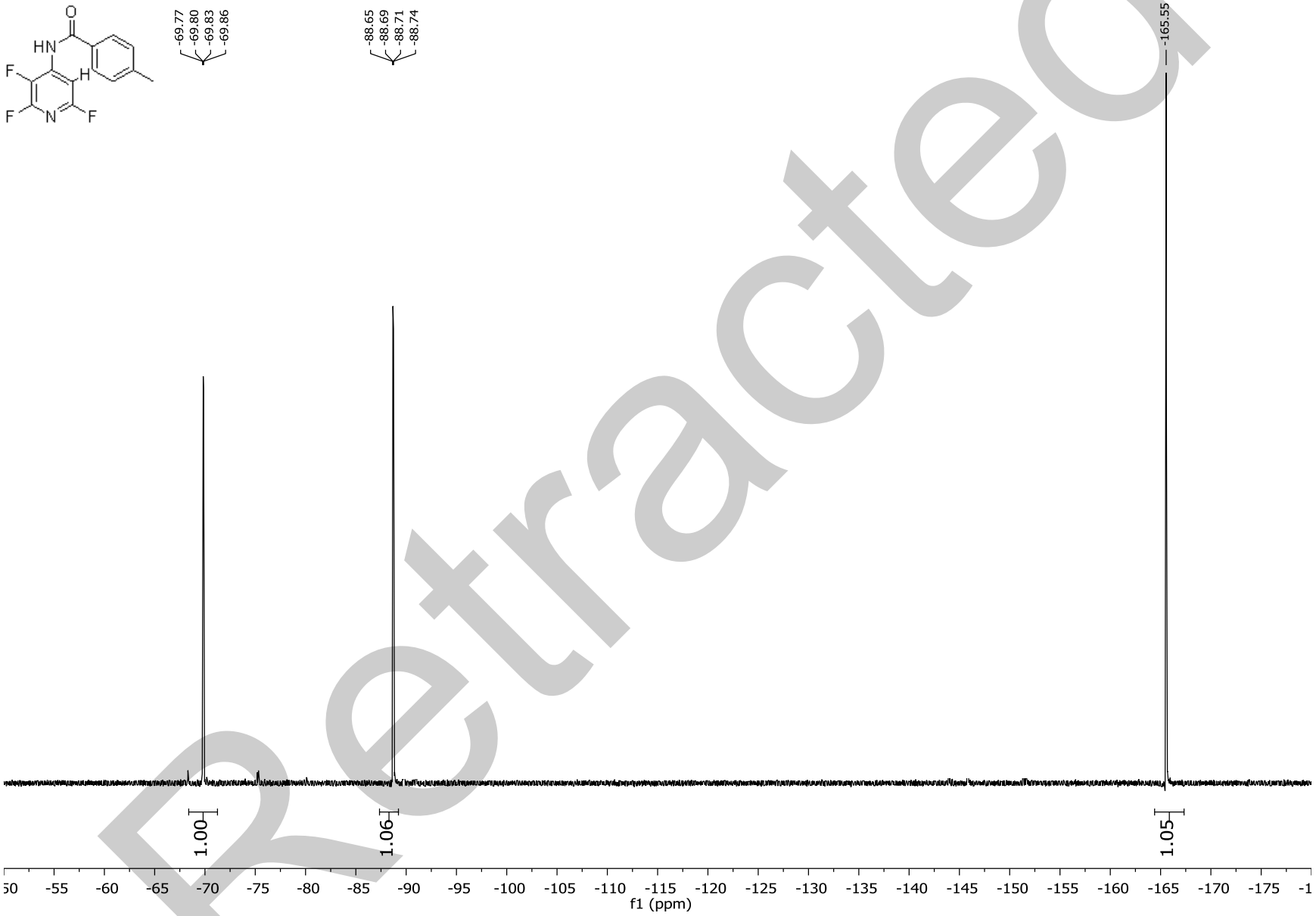
4f' 4-methoxy-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



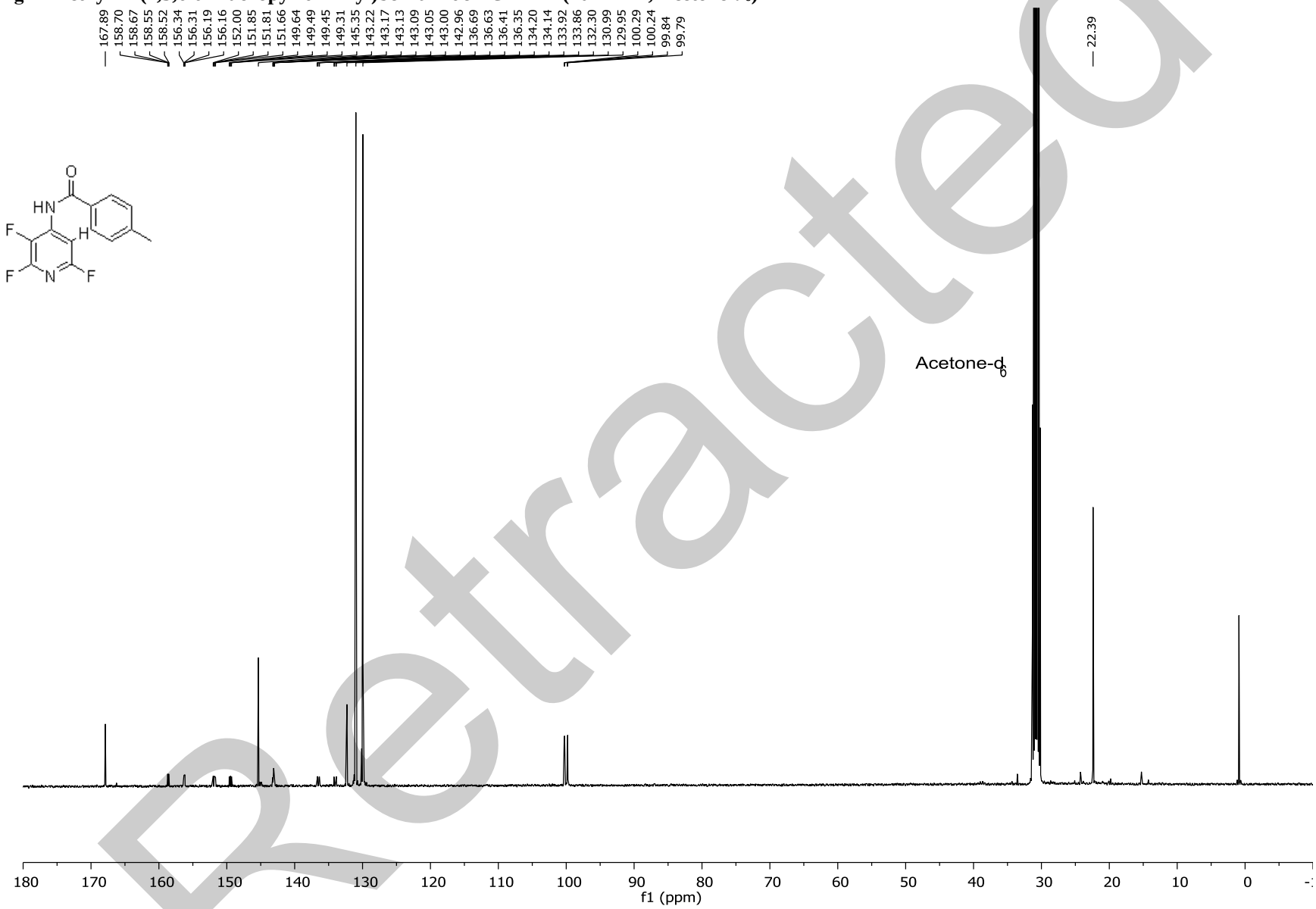
4g' 4-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



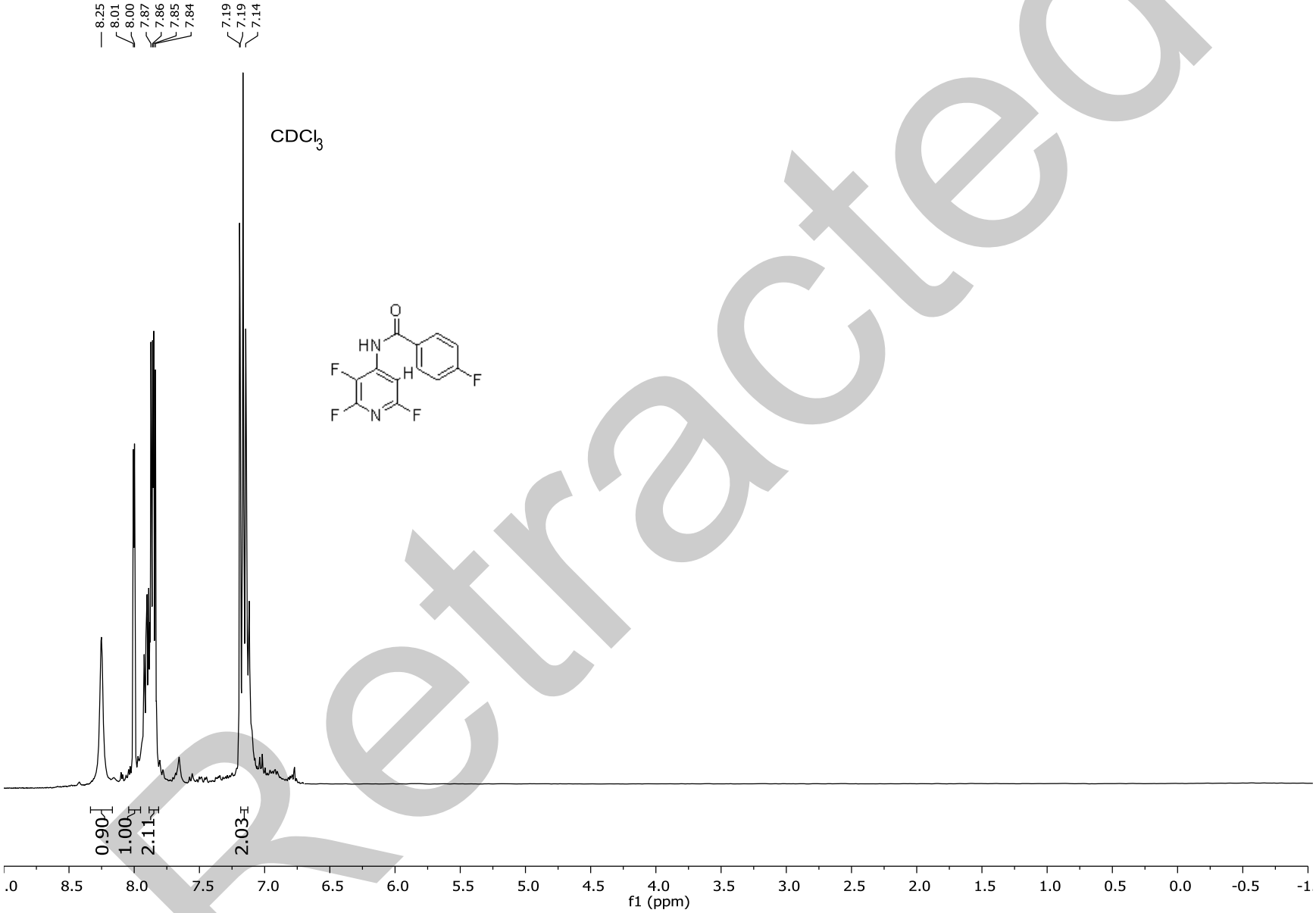
4g' 4-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



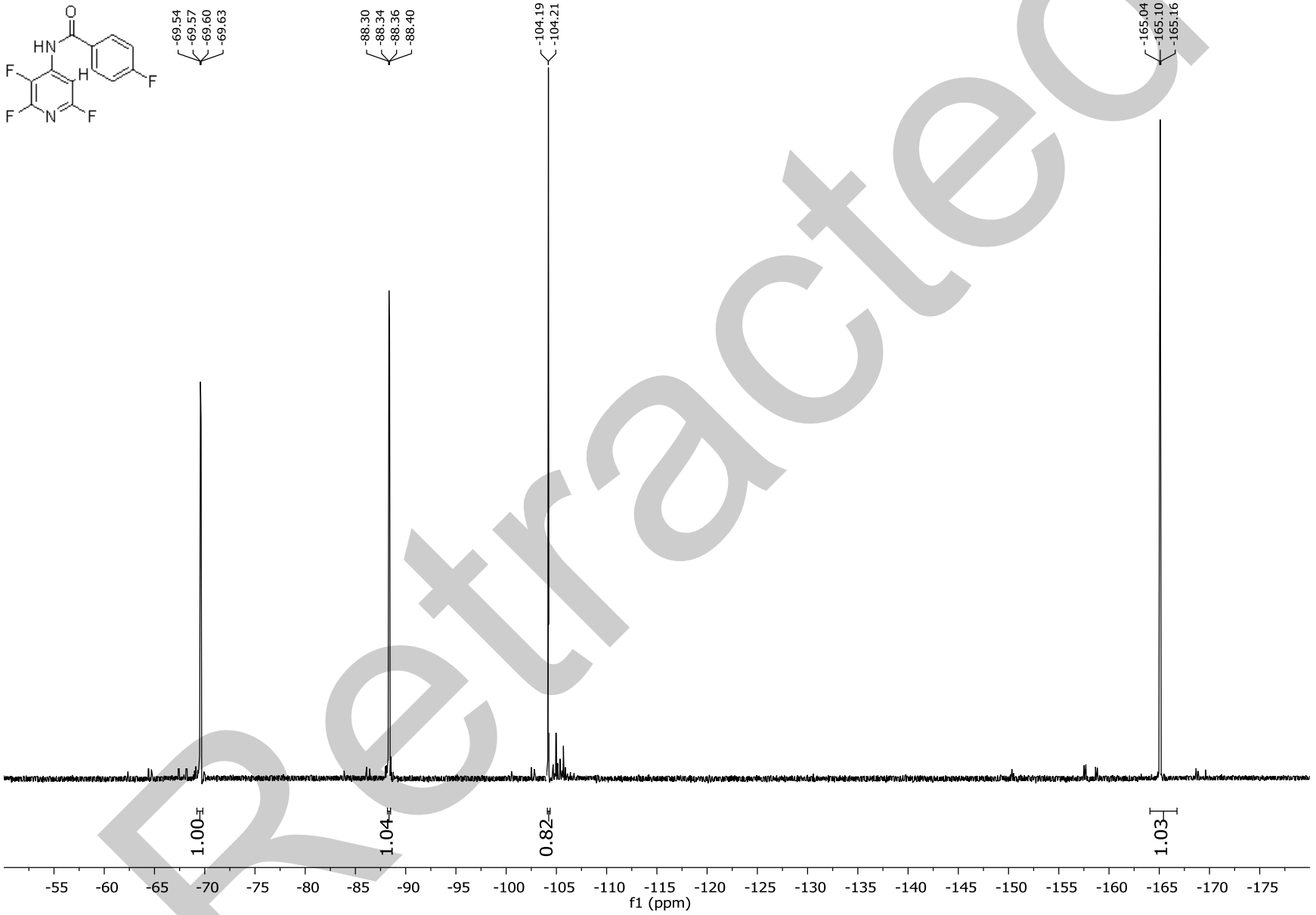
4g' 4-methyl-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{13}C NMR (101 MHz, Acetone-d_6)



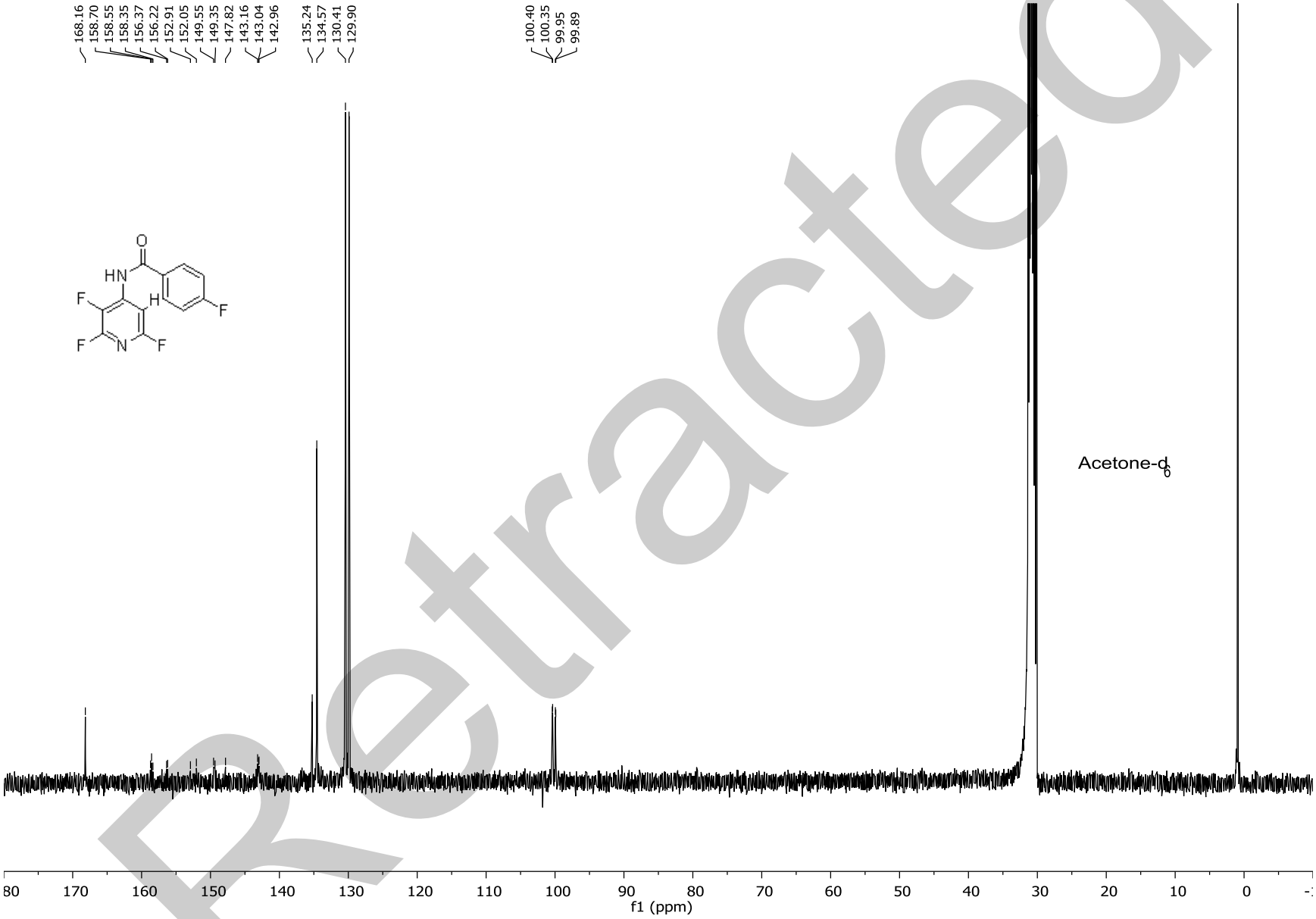
4h' 4-fluoro-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



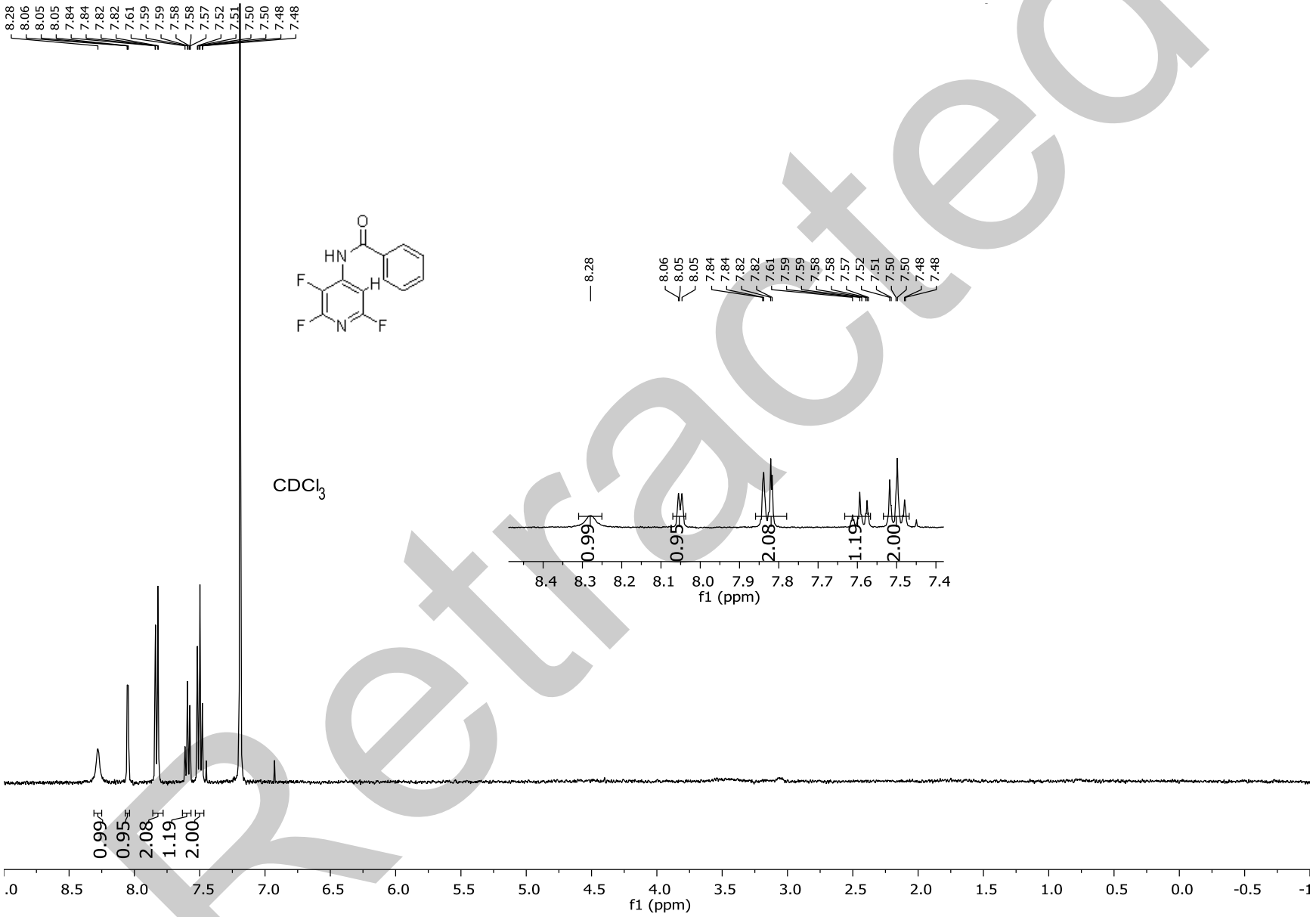
4 h' 4-fluoro-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



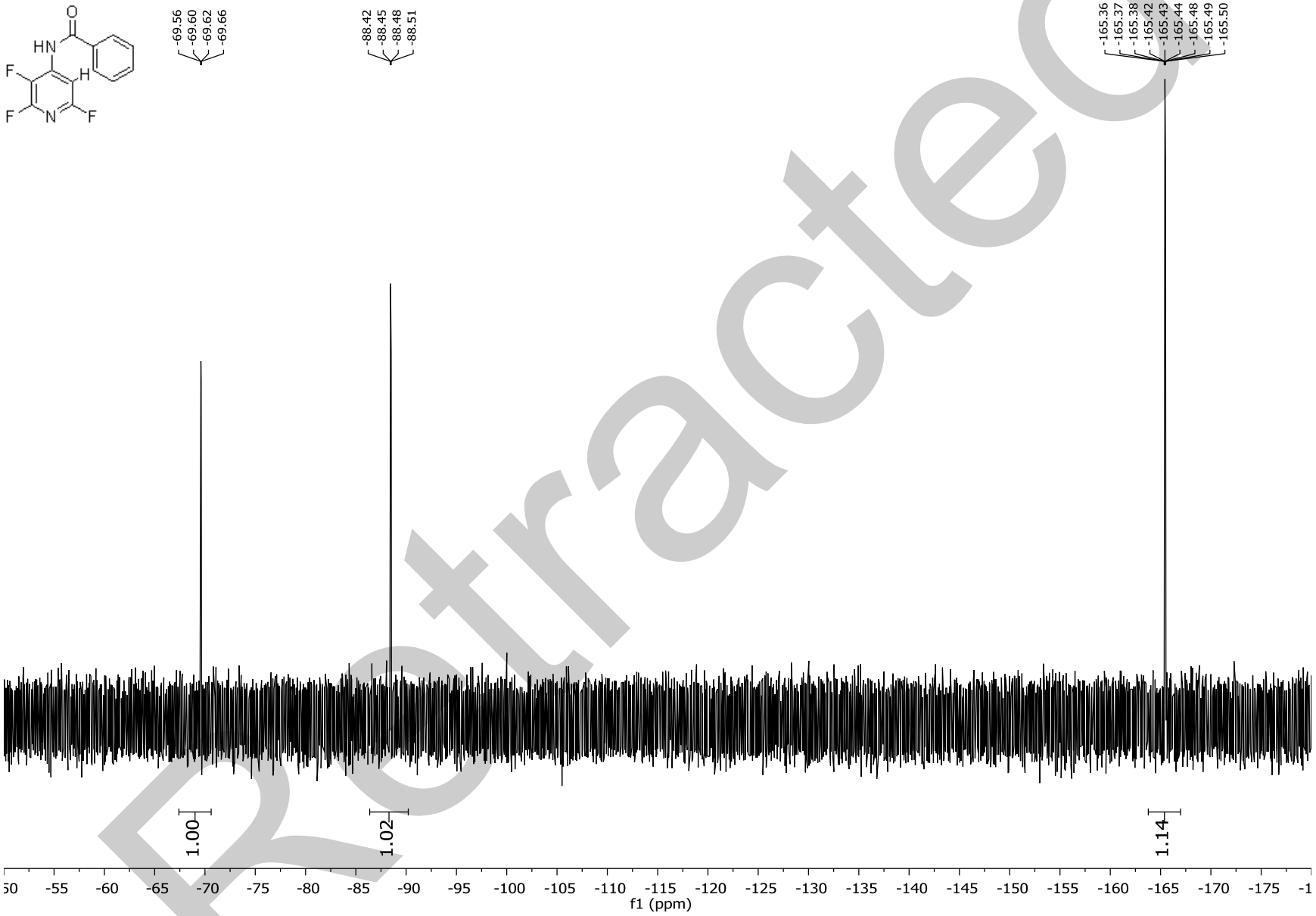
4h' 4-fluoro-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{13}C NMR (101 MHz, Acetone-d_6)



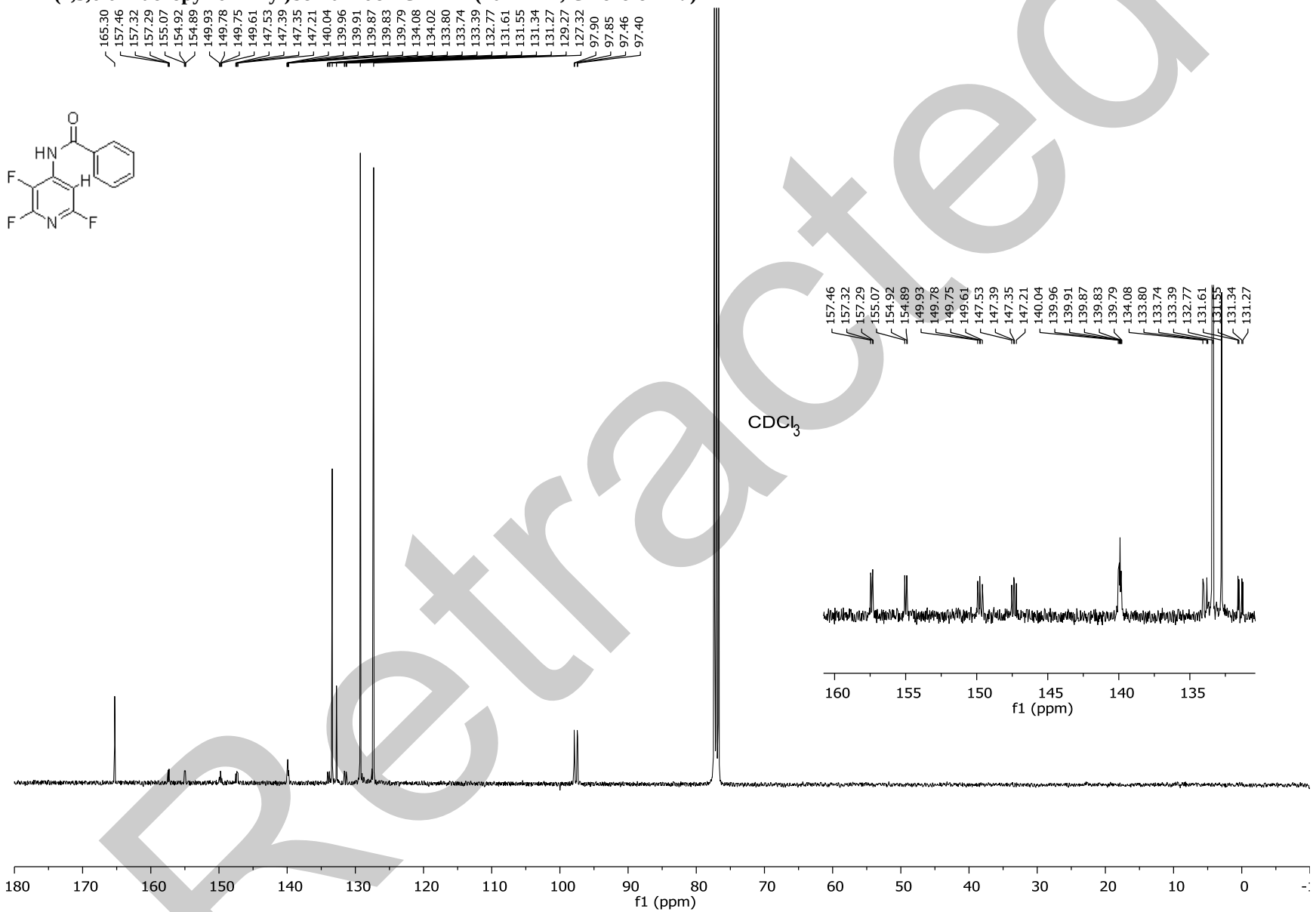
4i' *N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



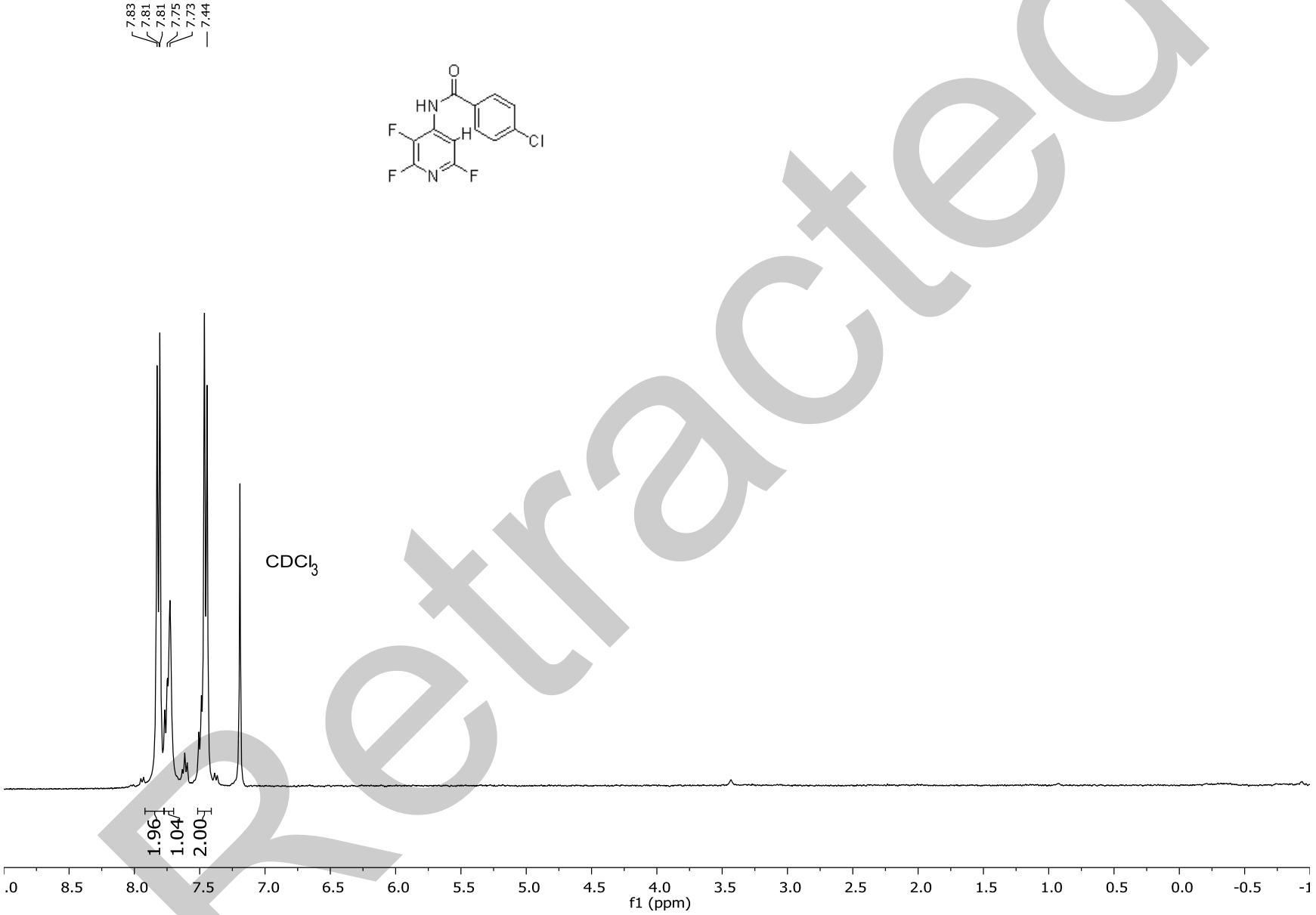
4i' *N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



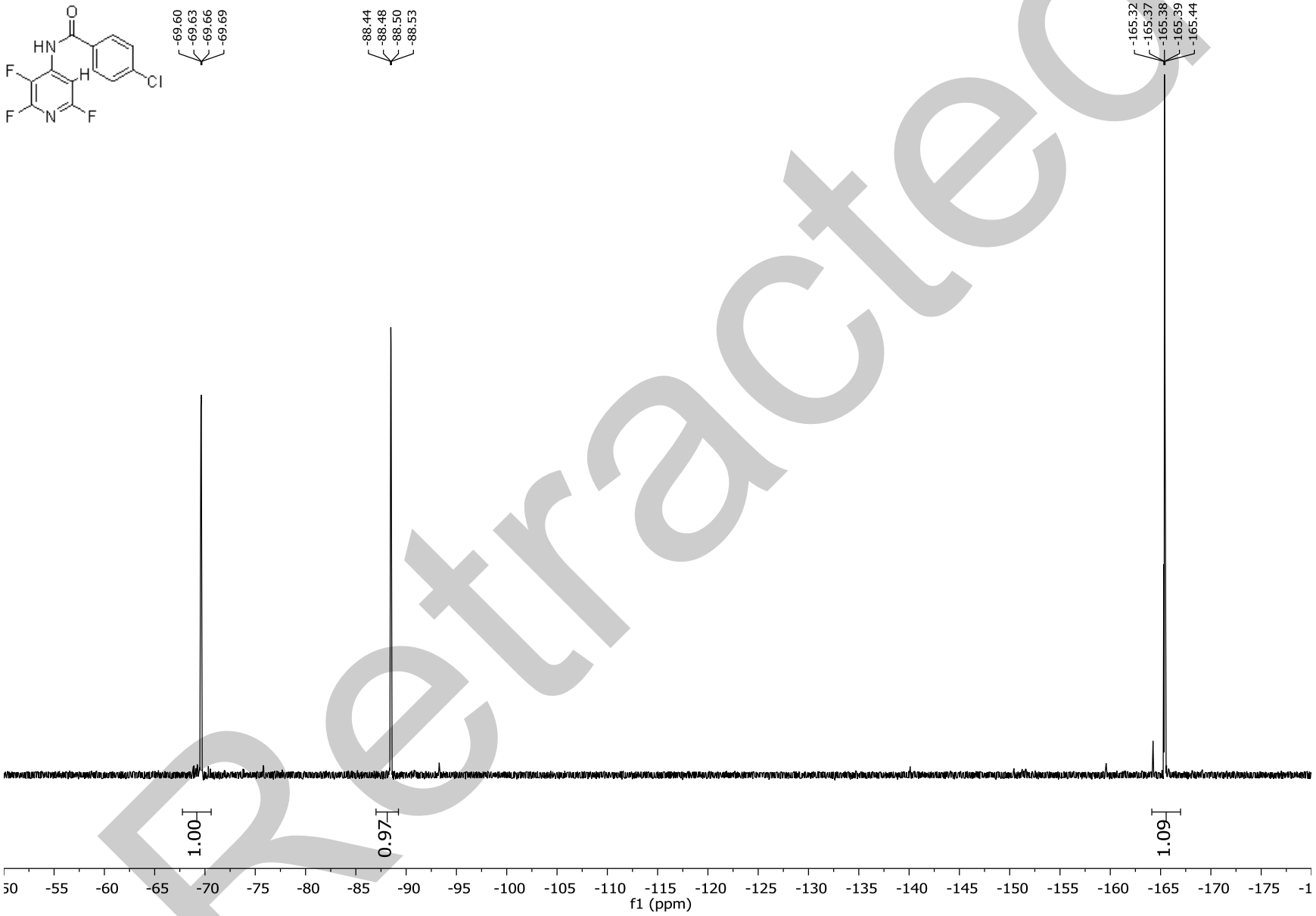
4i' *N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



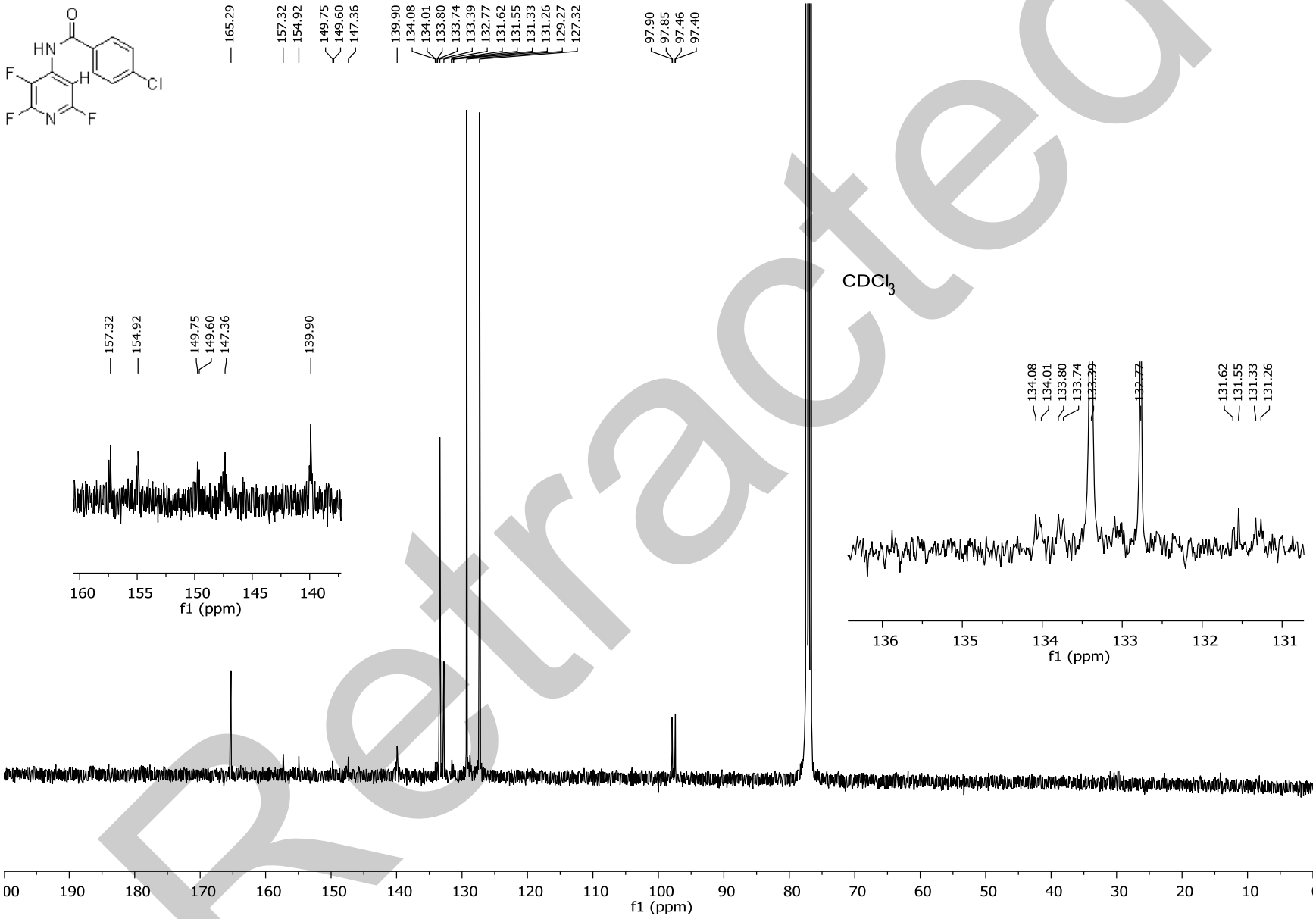
4j' 4-chloro-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



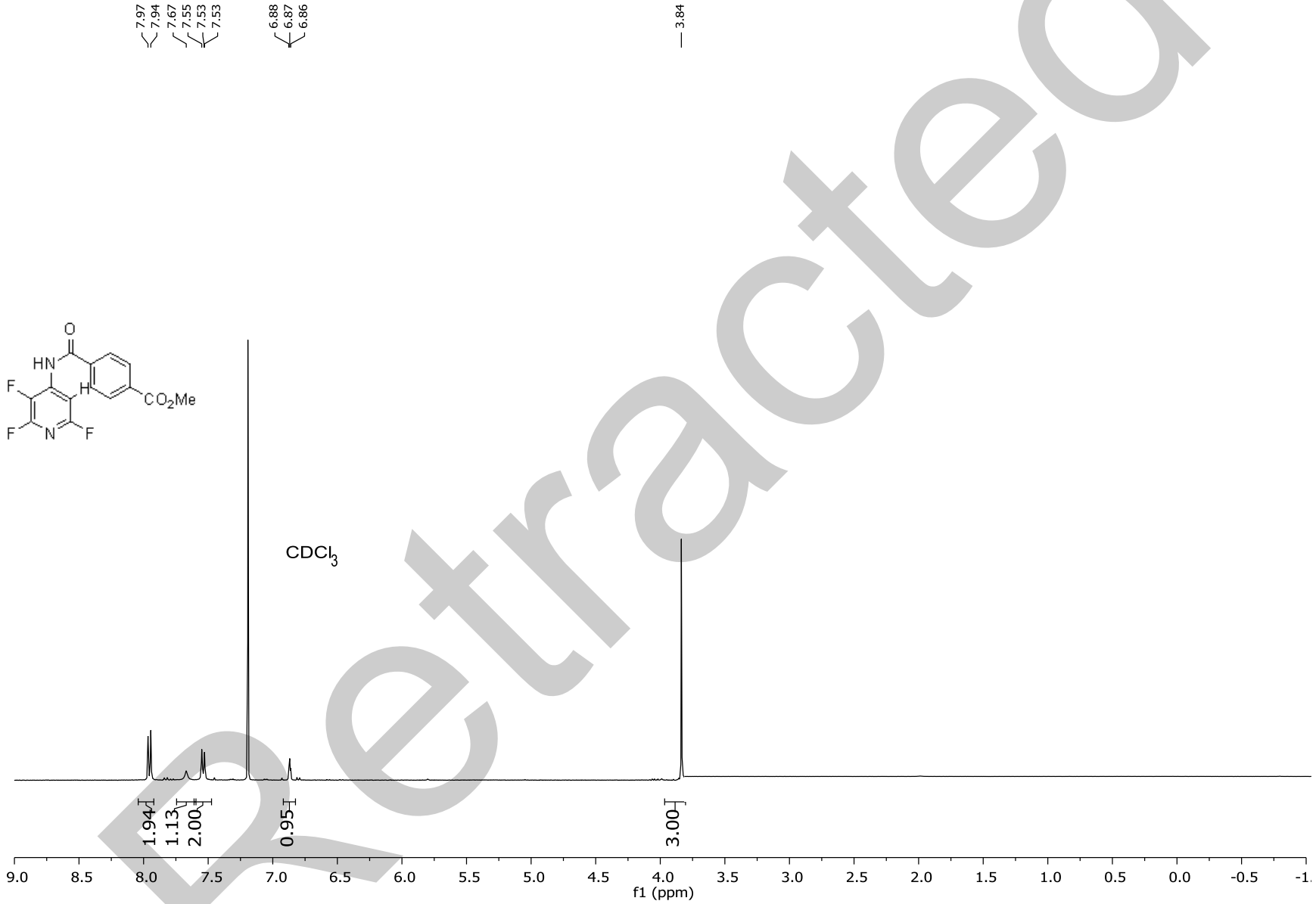
4j' 4-chloro-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



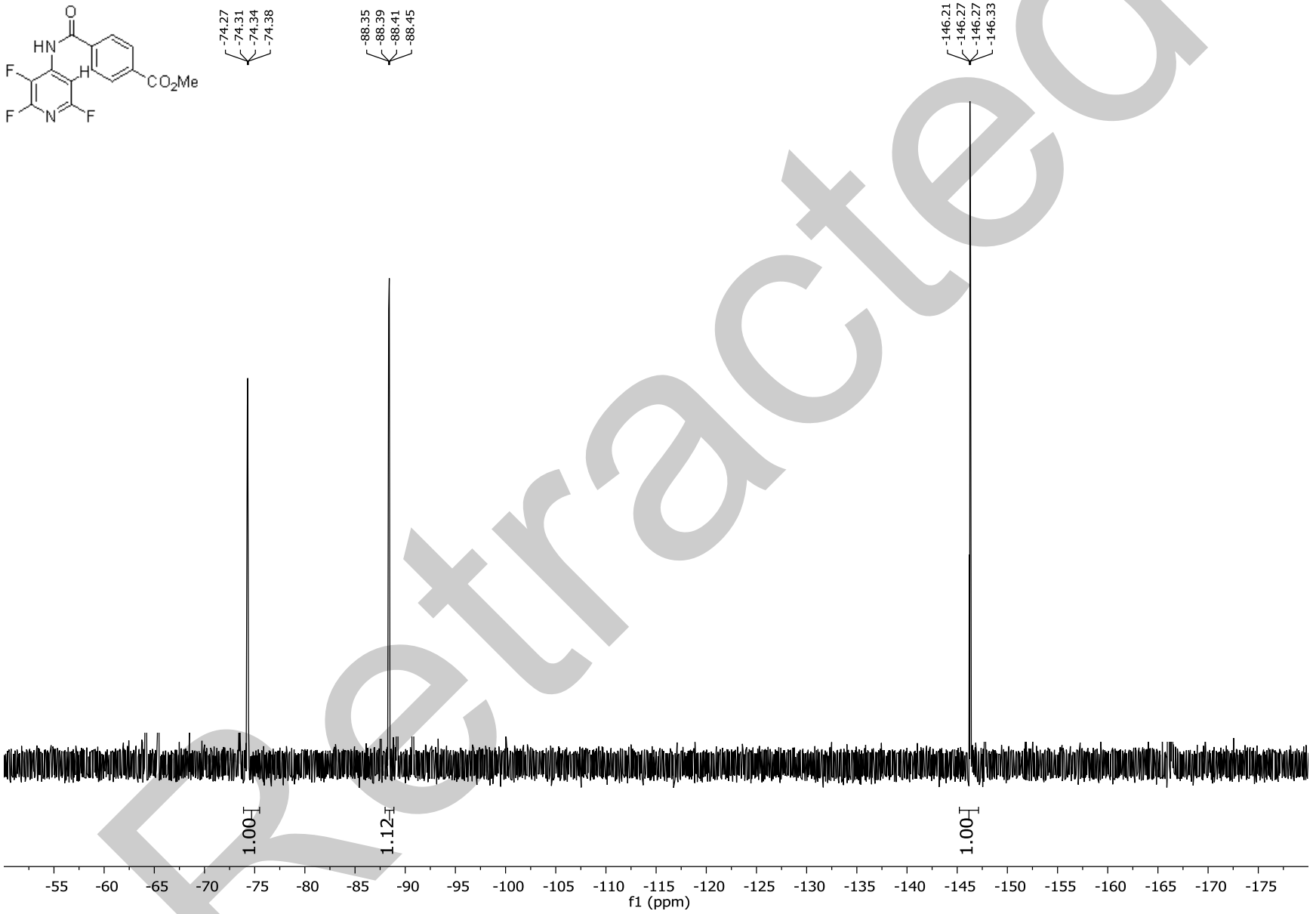
4j' 4-chloro-*N*-(2,3,6-trfluoropyridin-4-yl)benzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



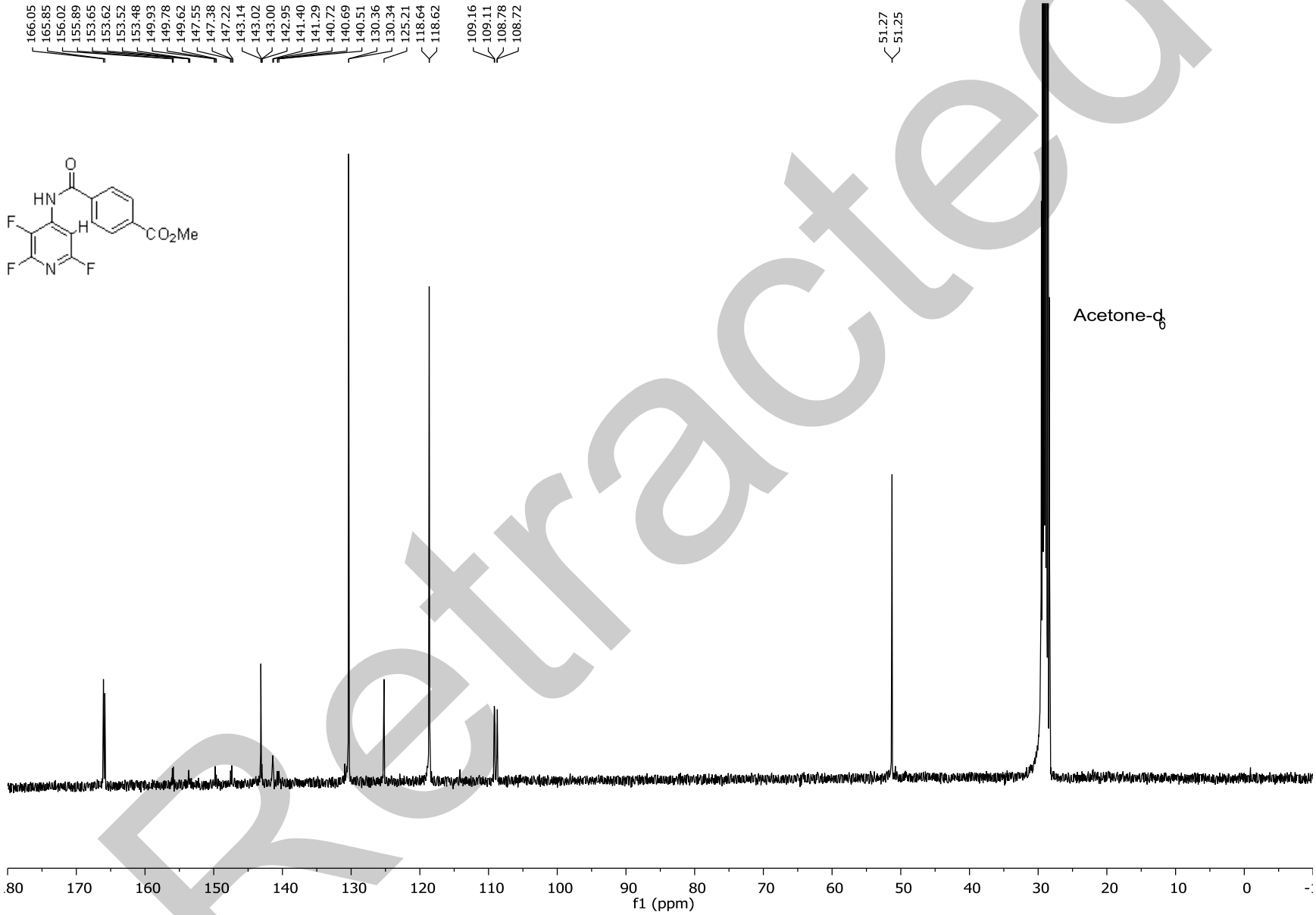
4k' methyl 4-((2,3,6-trifluoropyridin-4-yl)carbamoyl)benzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



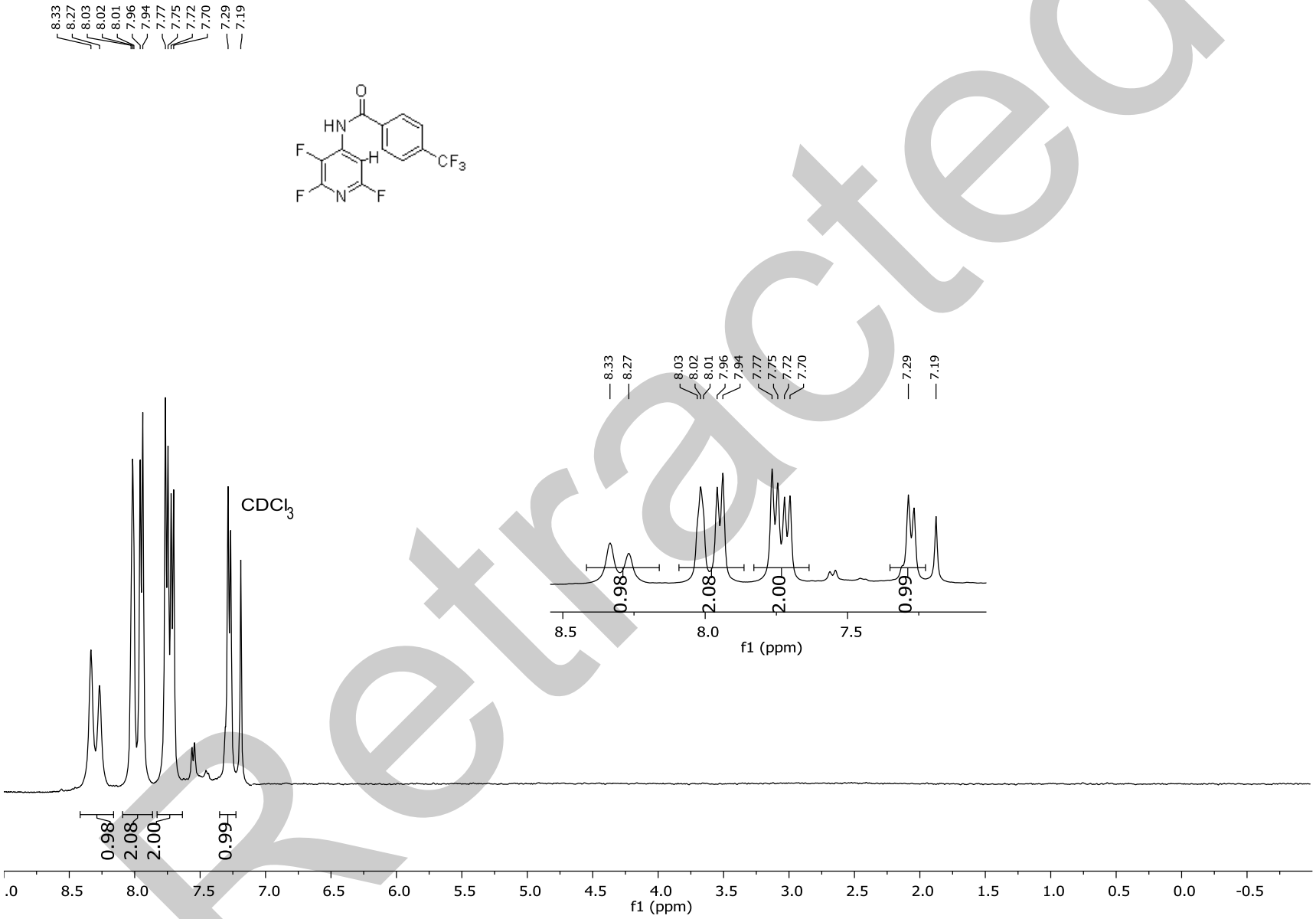
4k' methyl 4-((2,3,6-trifluoropyridin-4-yl)carbamoyl)benzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



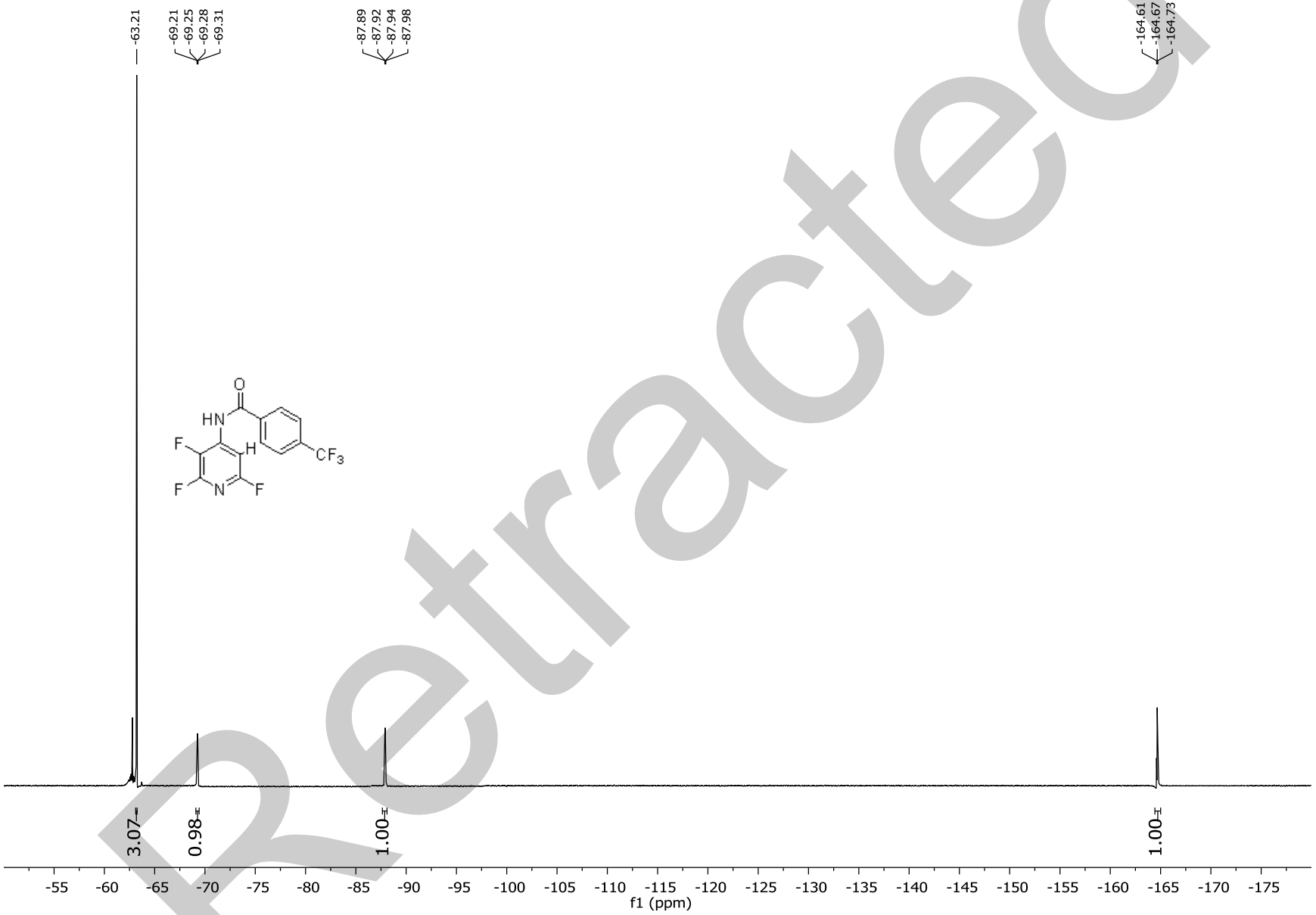
4k’ methyl 4-((2,3,6-trifluoropyridin-4-yl)carbamoyl)benzoate ^{13}C NMR (101 MHz, Acetone-d$_6$)



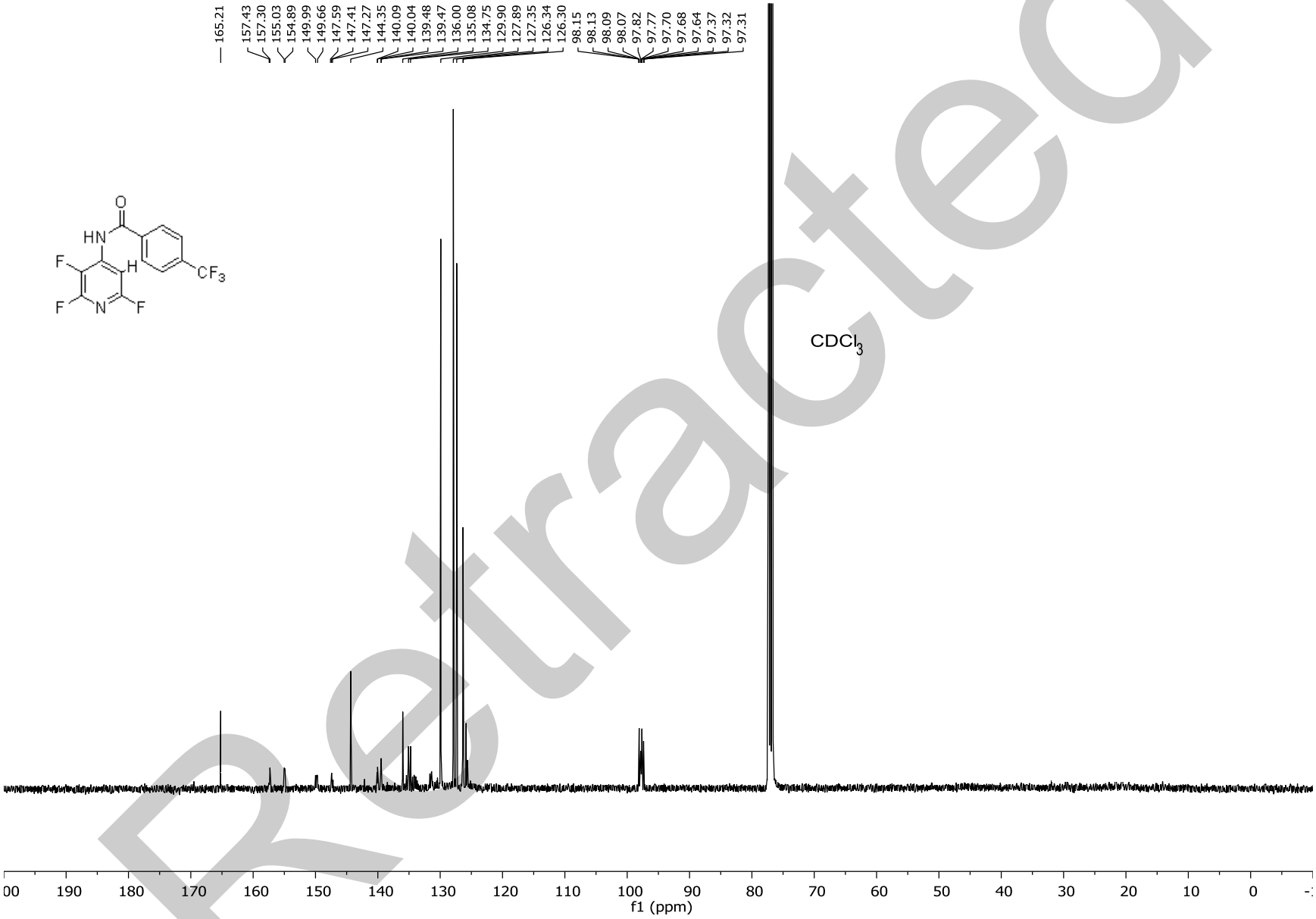
4l’ 4-(trifluoromethyl)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



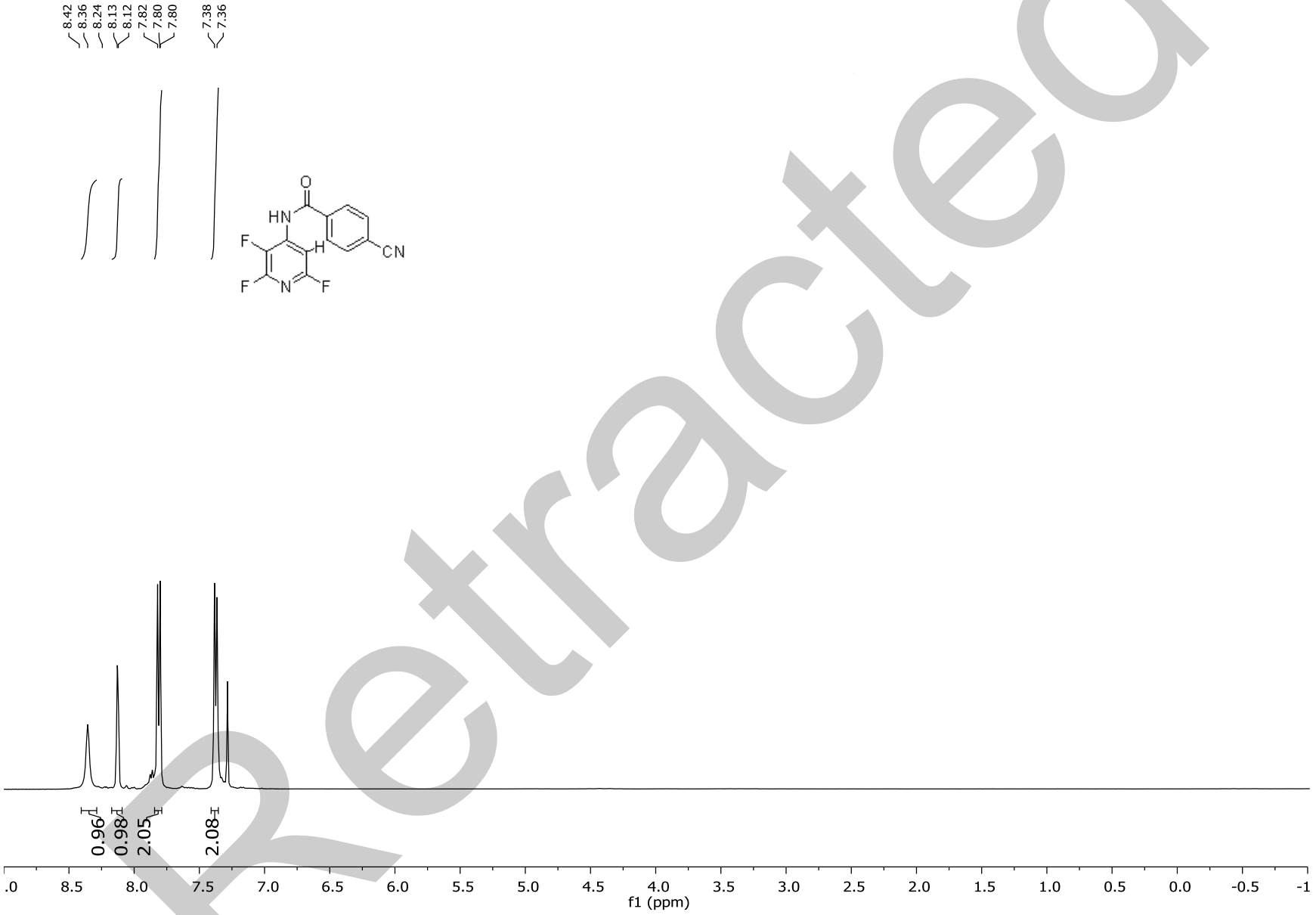
4l’ 4-(trifluoromethyl)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



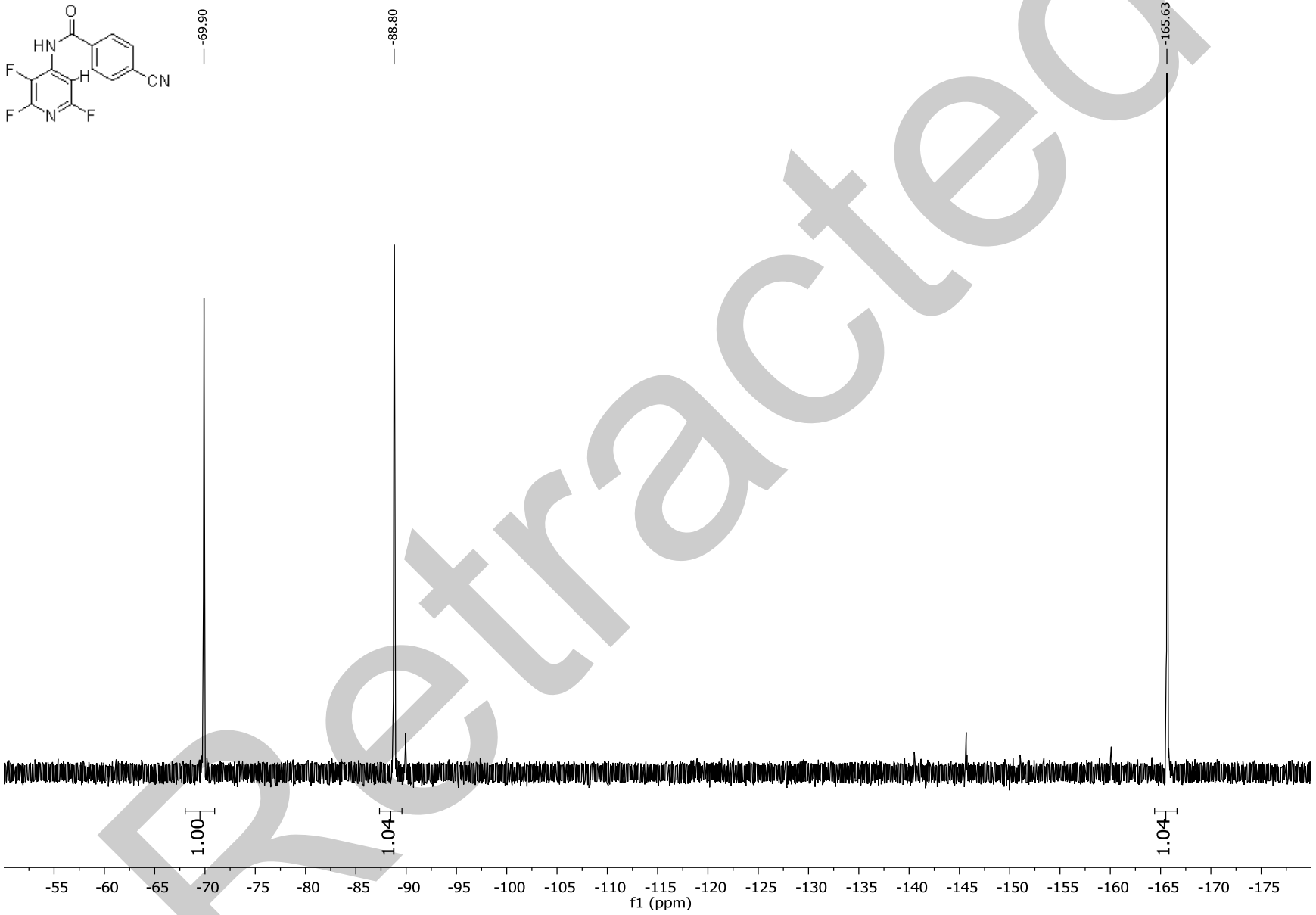
4l’ 4-(trifluoromethyl)-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{13}C NMR (101 MH, Chloroform-*d*)



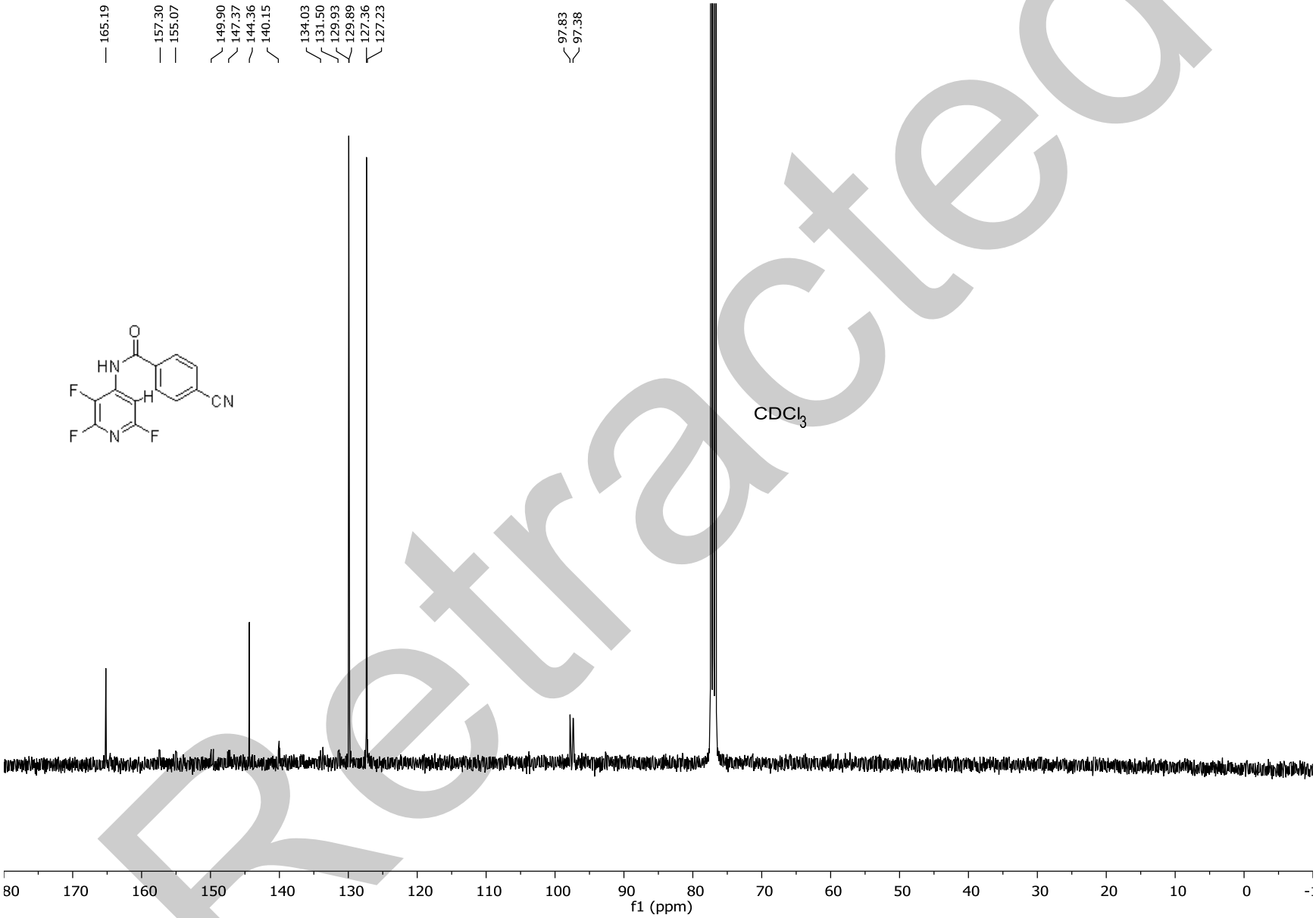
4m’ 4-cyano-N-(2,3,6-trifluoropyridin-4-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



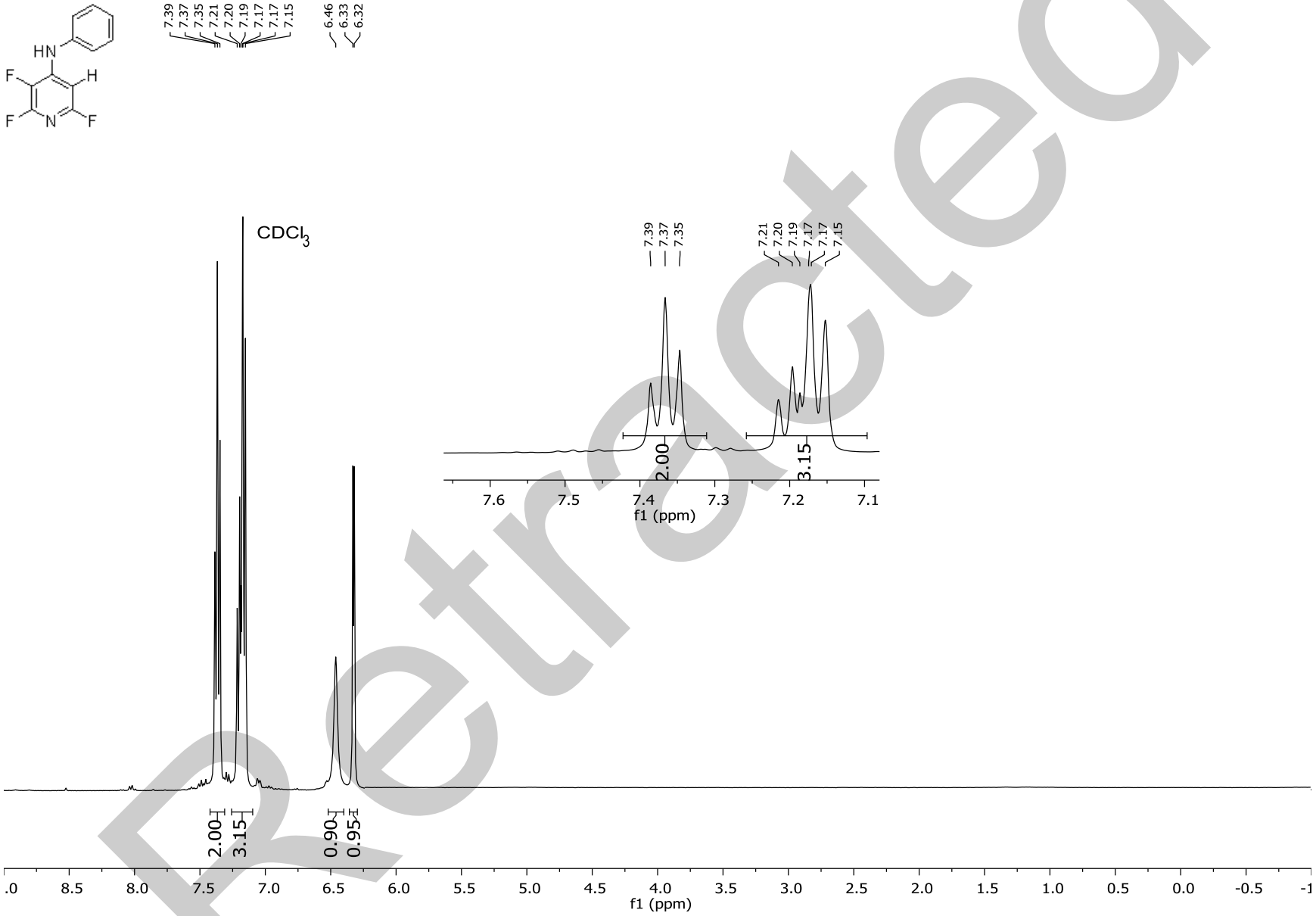
4m' 4-cyano-N-(2,3,6-trifluoropyridin-4-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



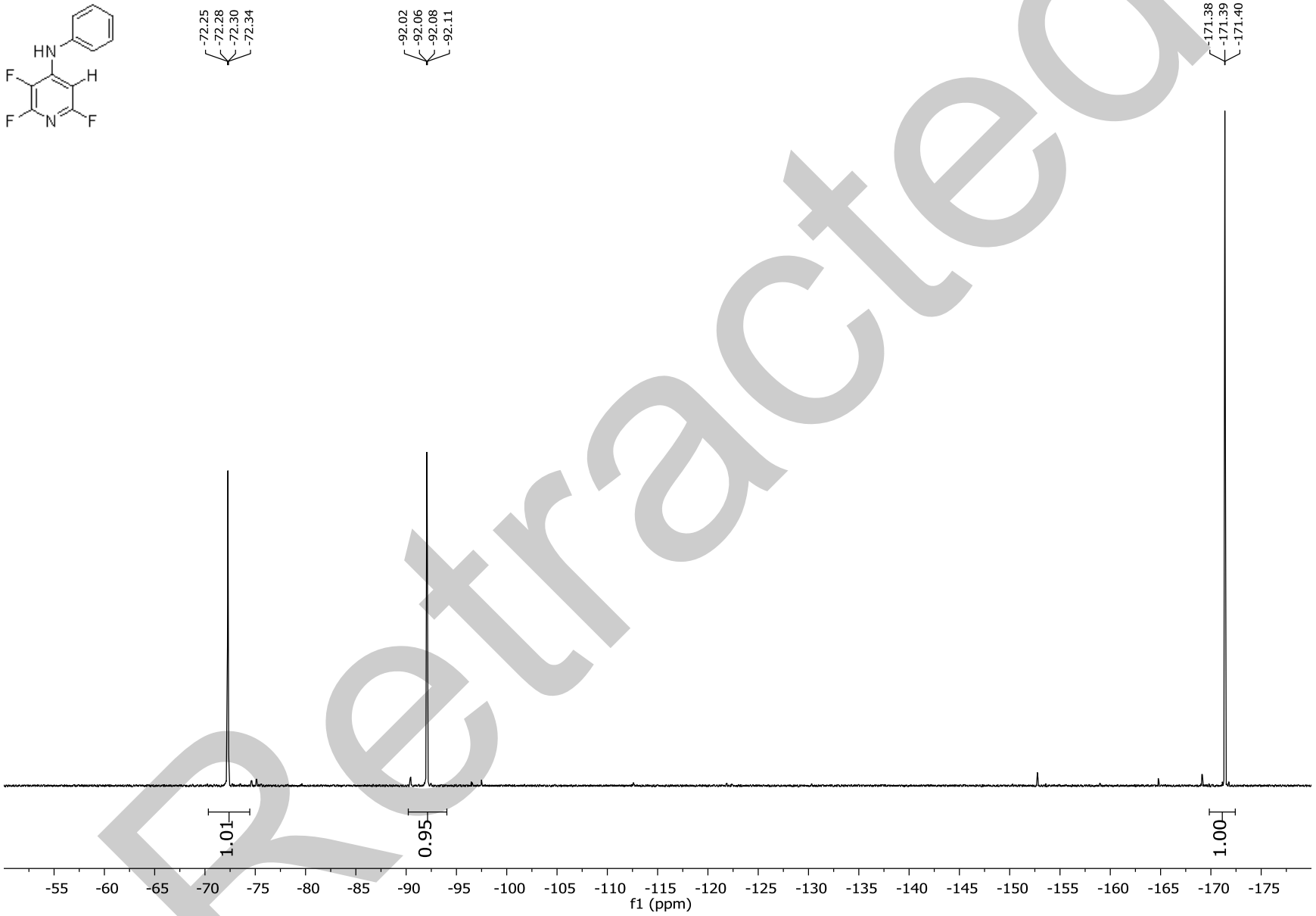
4m' 4-cyano-*N*-(2,3,6-trifluoropyridin-4-yl)benzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



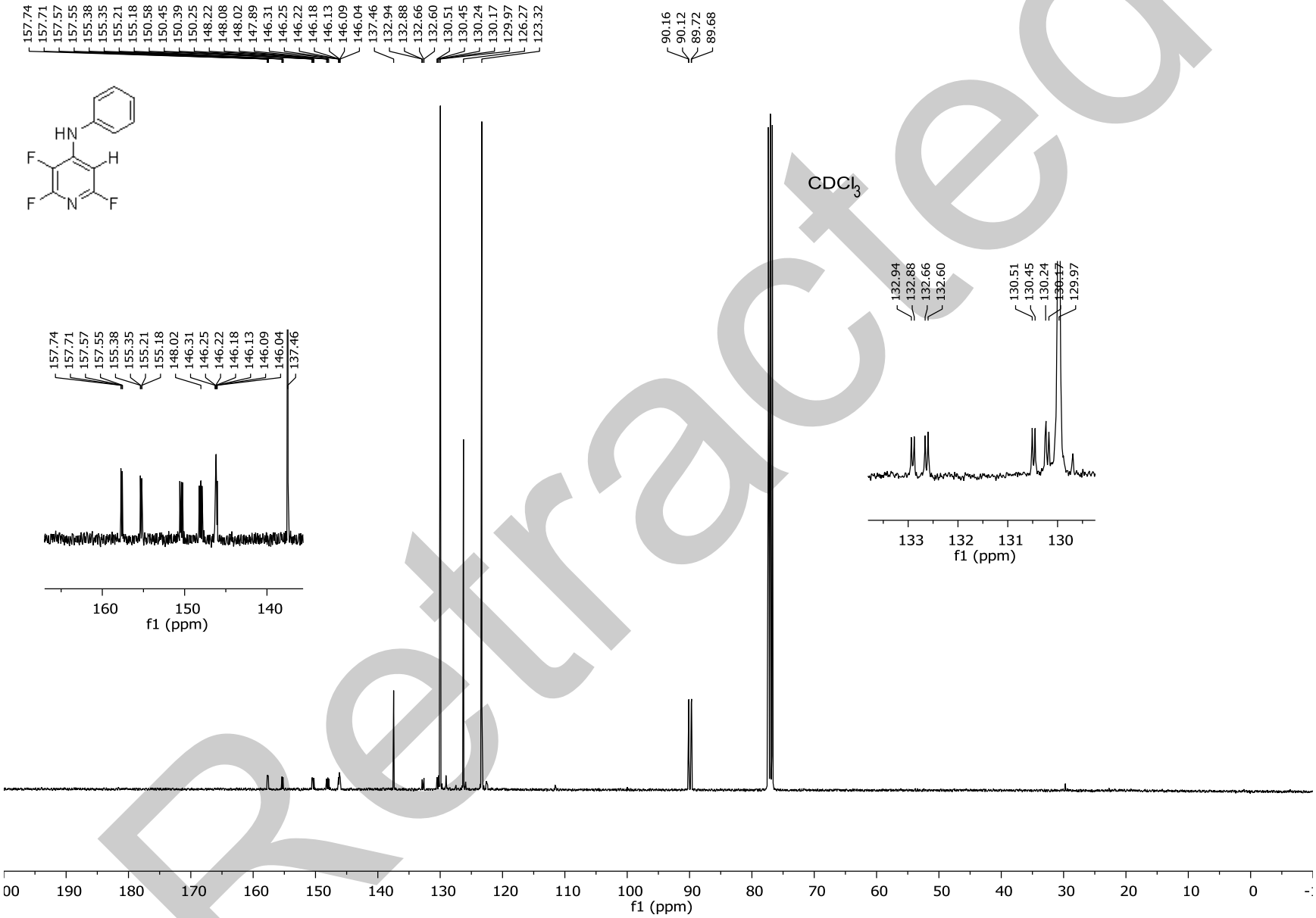
5a' 2,3,6-trifluoro-*N*-phenylpyridin-4-amine ^{1}H NMR (400 MHz, Chloroform-*d*)



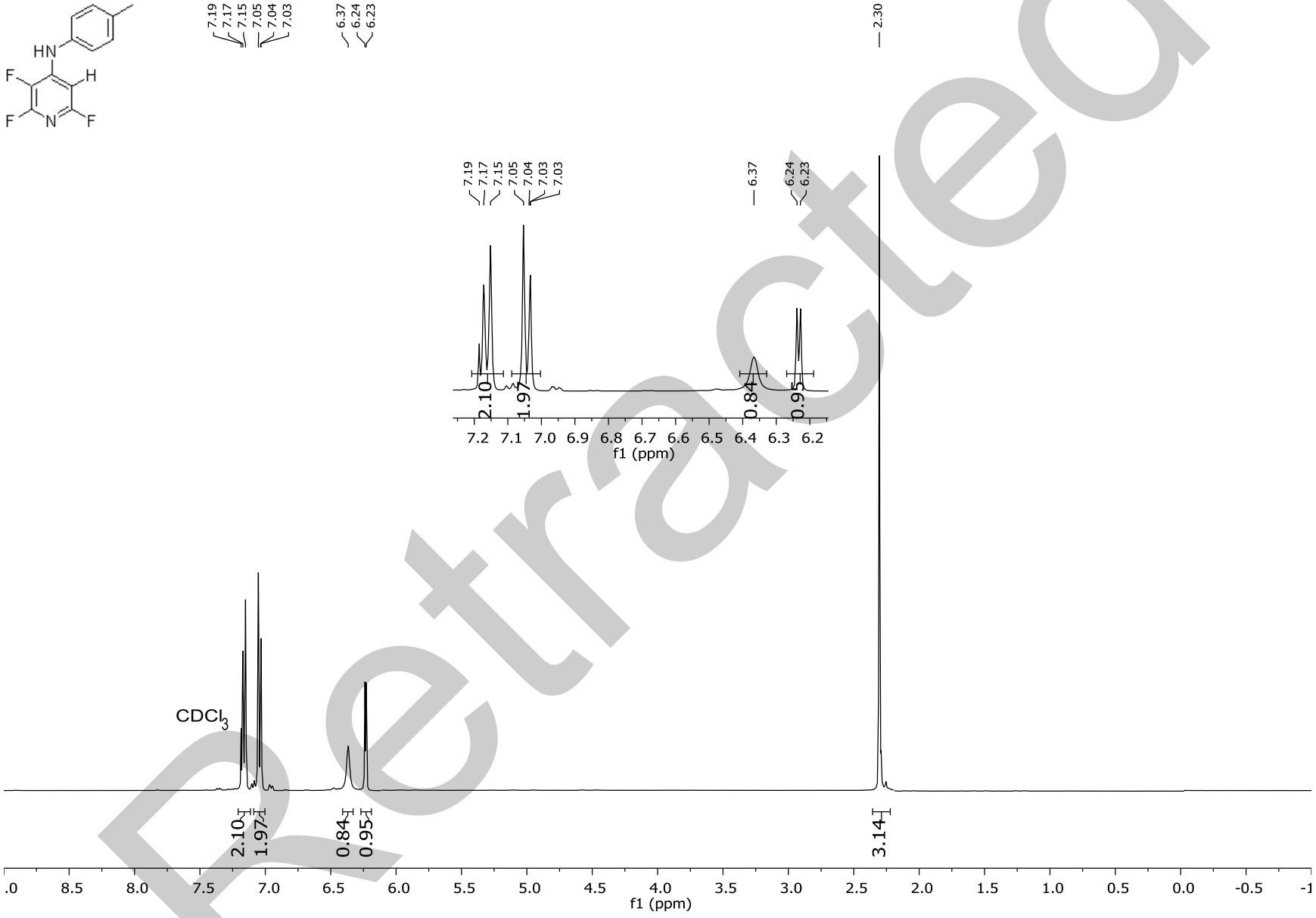
5a' 2,3,6-trifluoro-*N*-phenylpyridin-4-amine ^{19}F NMR (376 MHz, Chloroform-*d*)



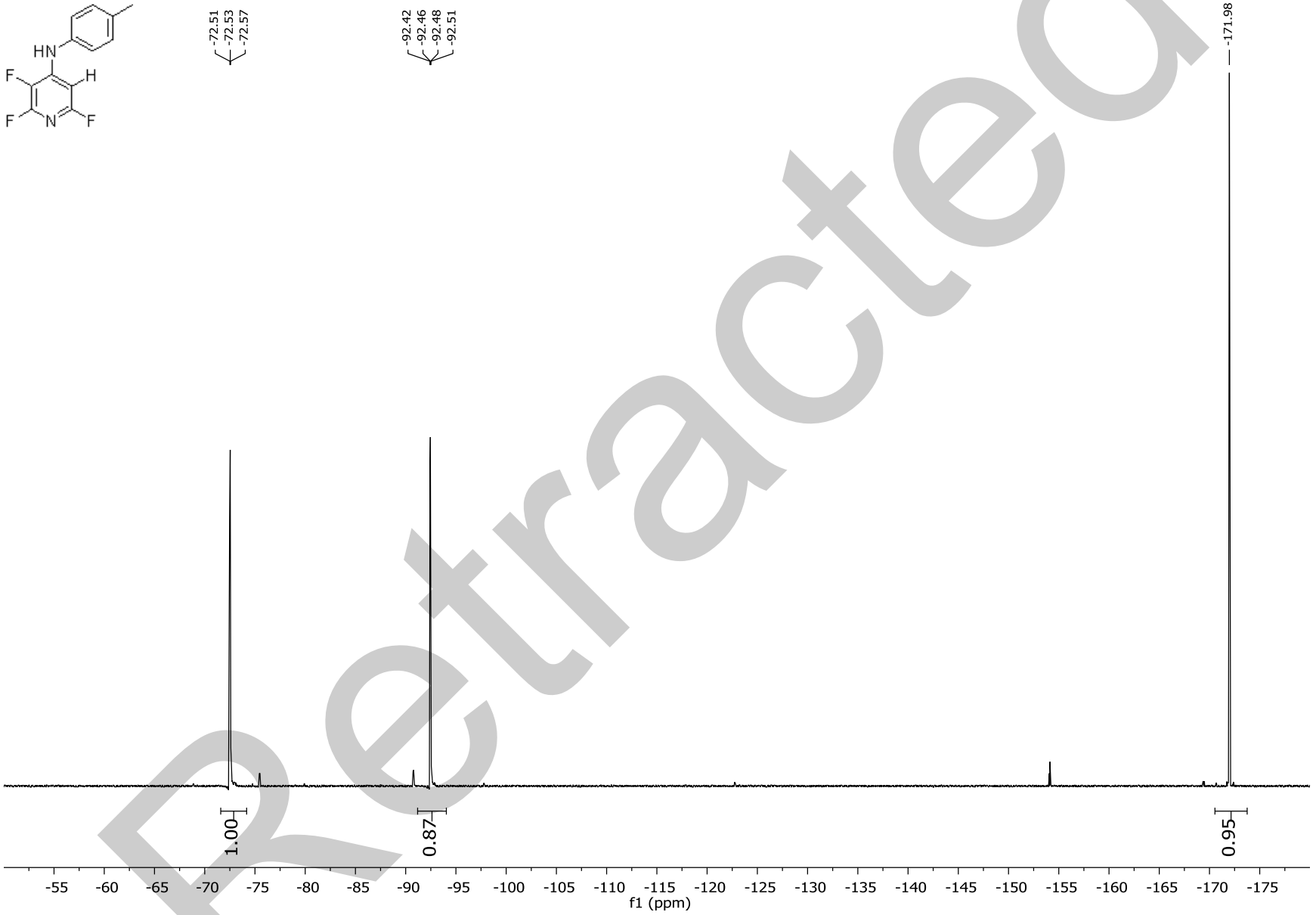
5a' 2,3,6-trifluoro-*N*-phenylpyridin-4-amine ^{13}C NMR (101 MHz, Chloroform-*d*)



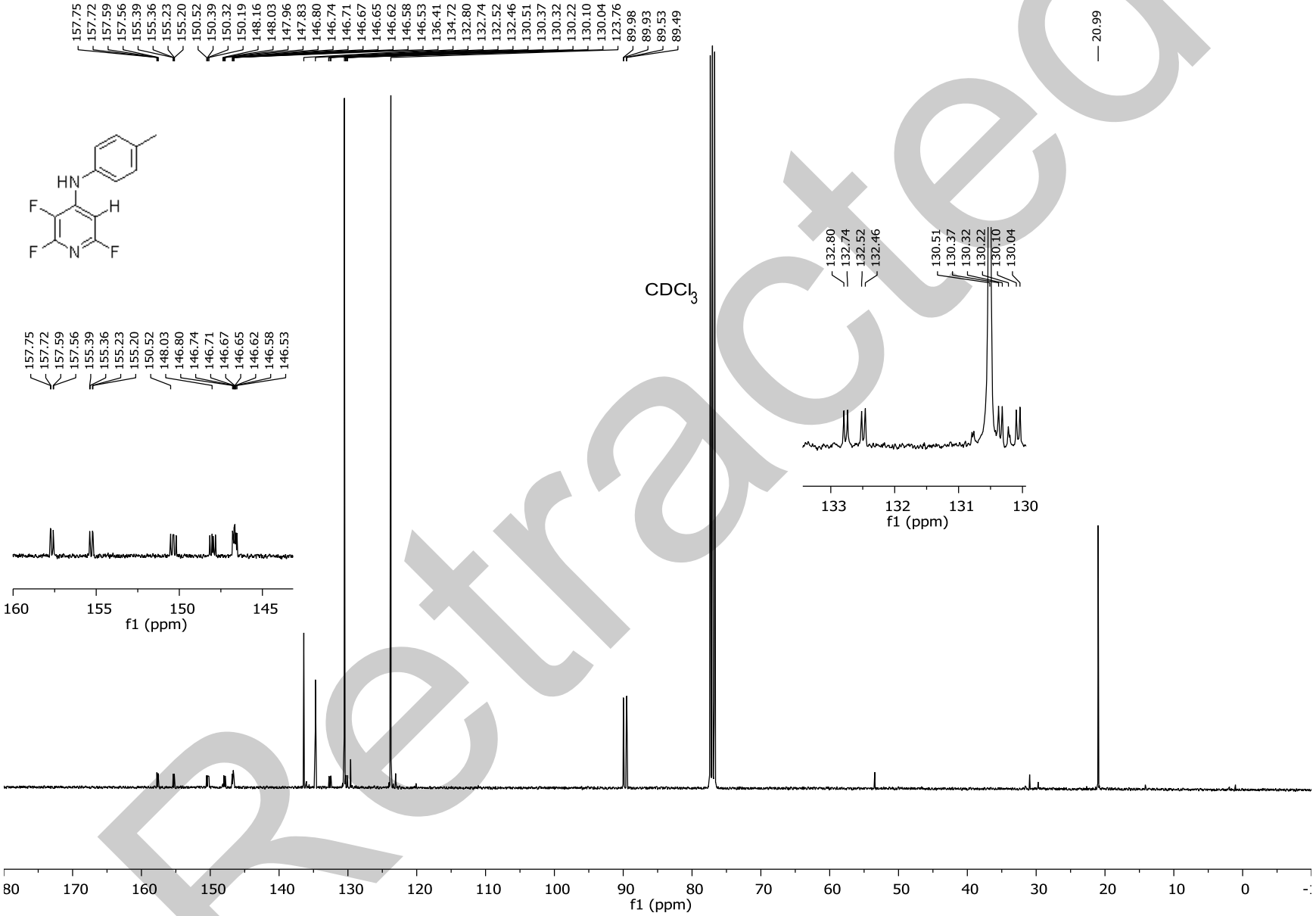
5b' 2,3,6-trifluoro-*N*-(p-tolyl)pyridin-4-amine ^{1}H NMR (400 MHz, Chloroform-*d*)



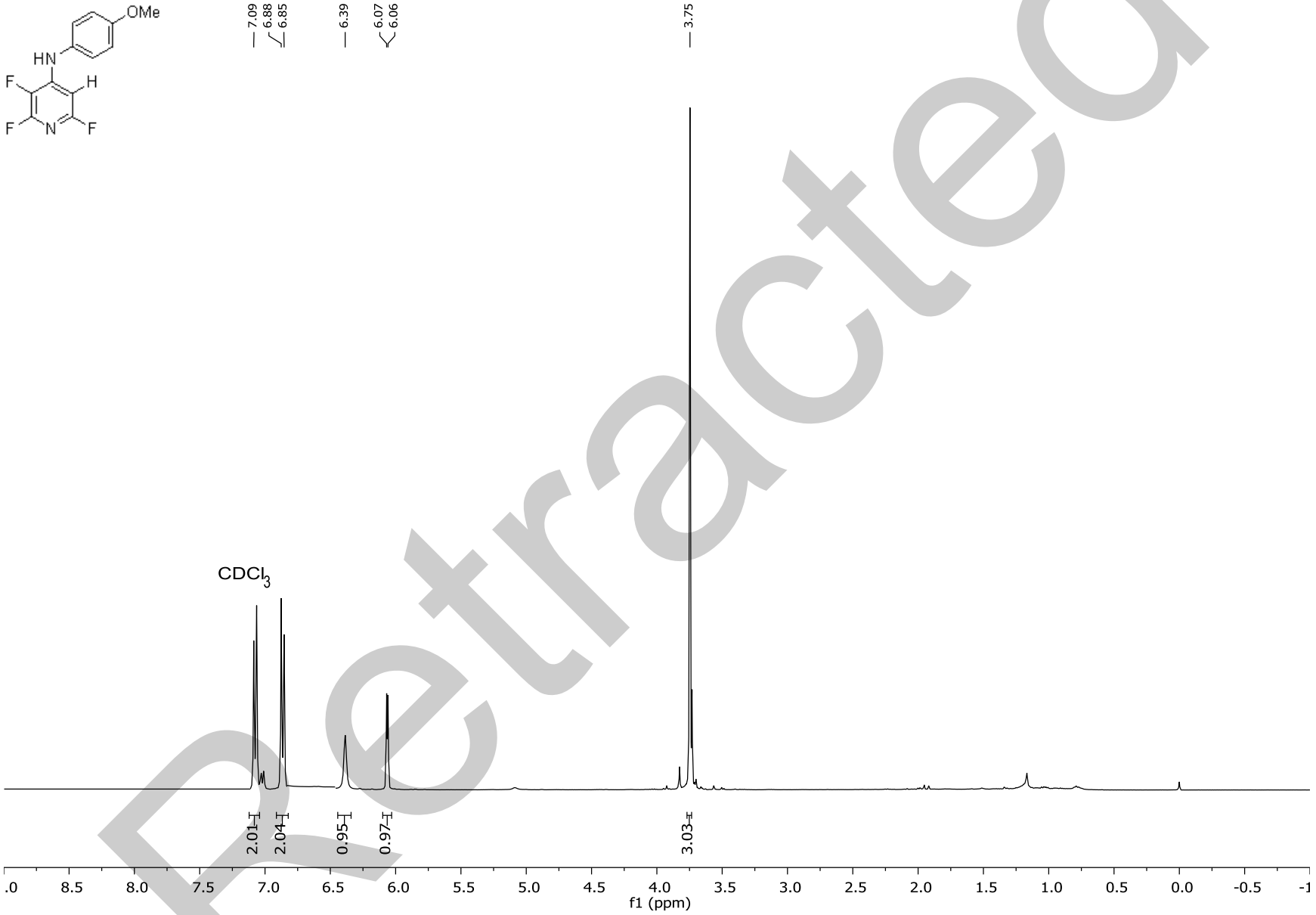
5b' 2,3,6-trifluoro-*N*-(*p*-tolyl)pyridin-4-amine ^{19}F NMR (376 MHz, Chloroform-*d*)



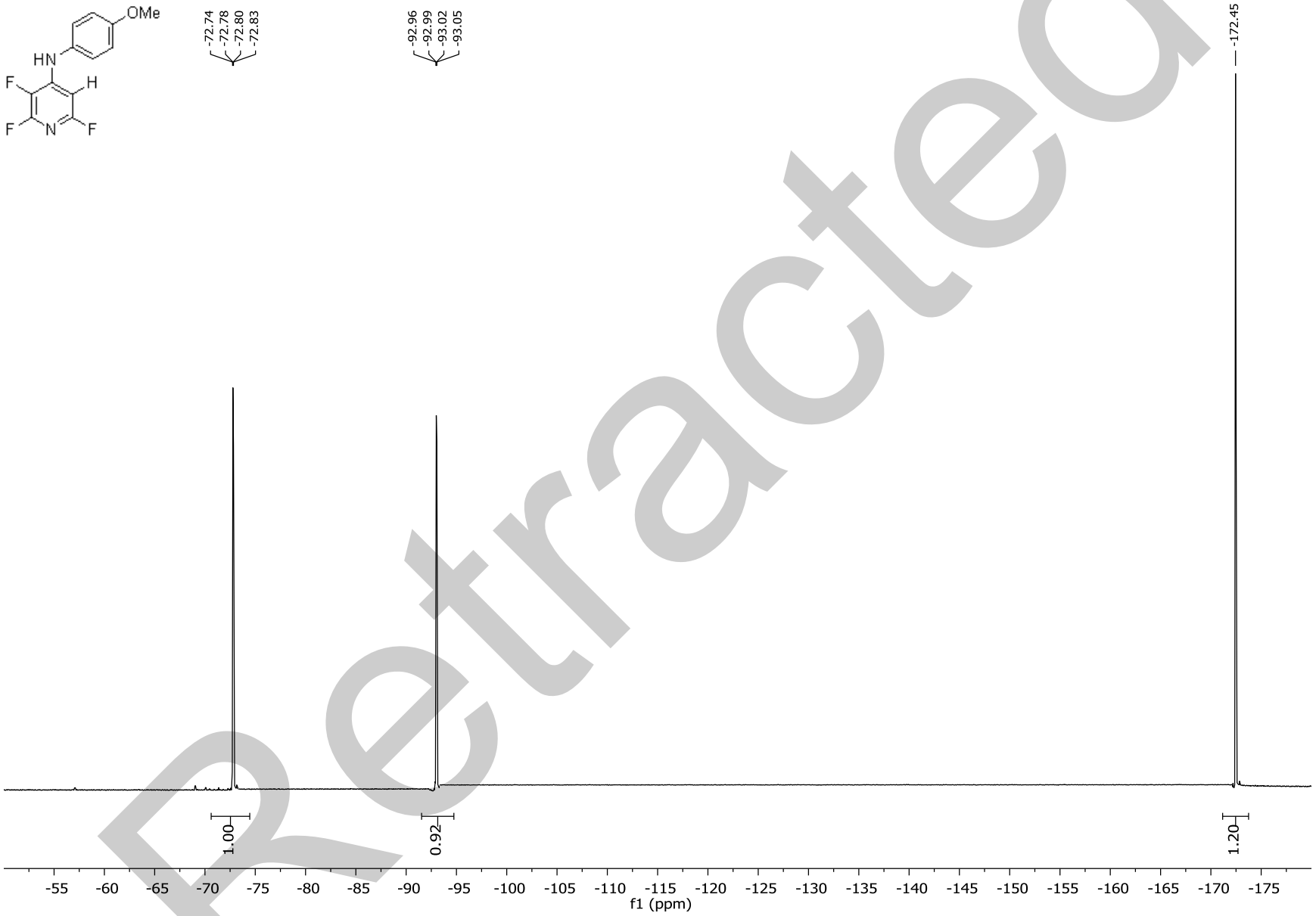
5b' 2,3,6-trifluoro-*N*-(*p*-tolyl)pyridin-4-amine ^{13}C NMR (101 MHz, Chloroform-*d*)



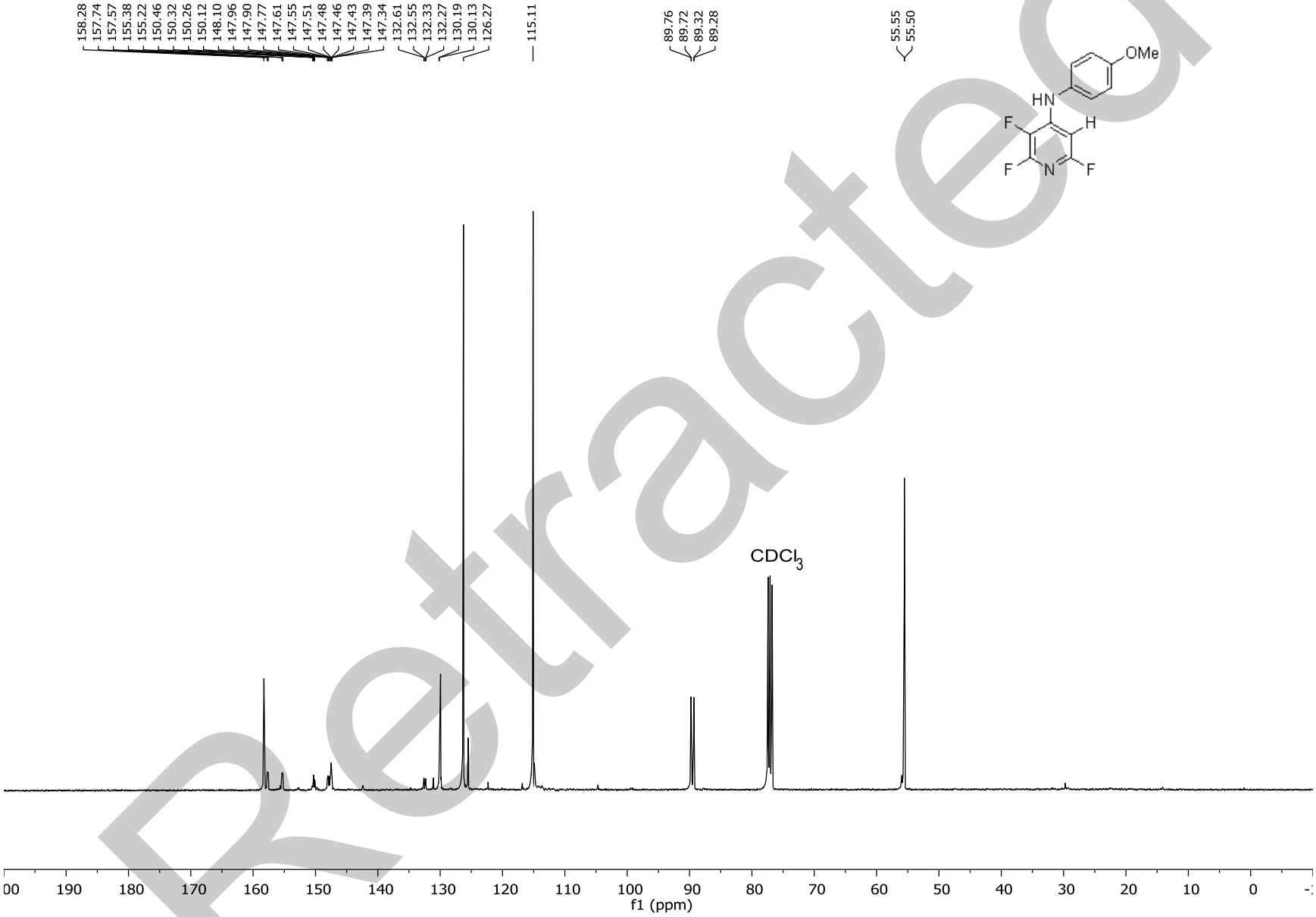
5c' 2,3,6-trifluoro-*N*-(4-methoxyphenyl)pyridin-4-amine ^{1}H NMR (400 MHz, Chloroform-*d*)



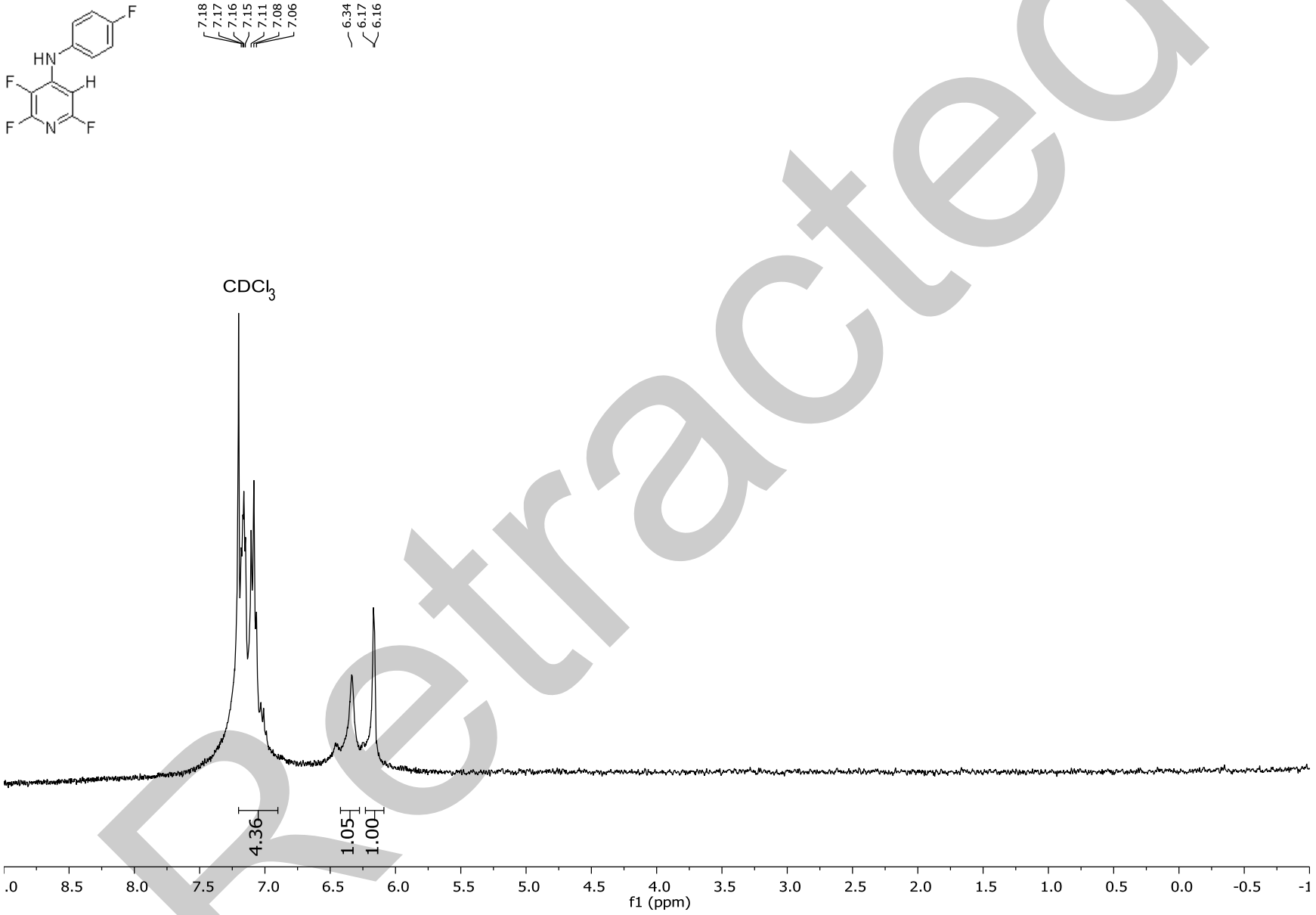
5c' 2,3,6-trifluoro-N-(4-methoxyphenyl)pyridin-4-amine ^{19}F NMR (376 MHz, Chloroform-*d*)



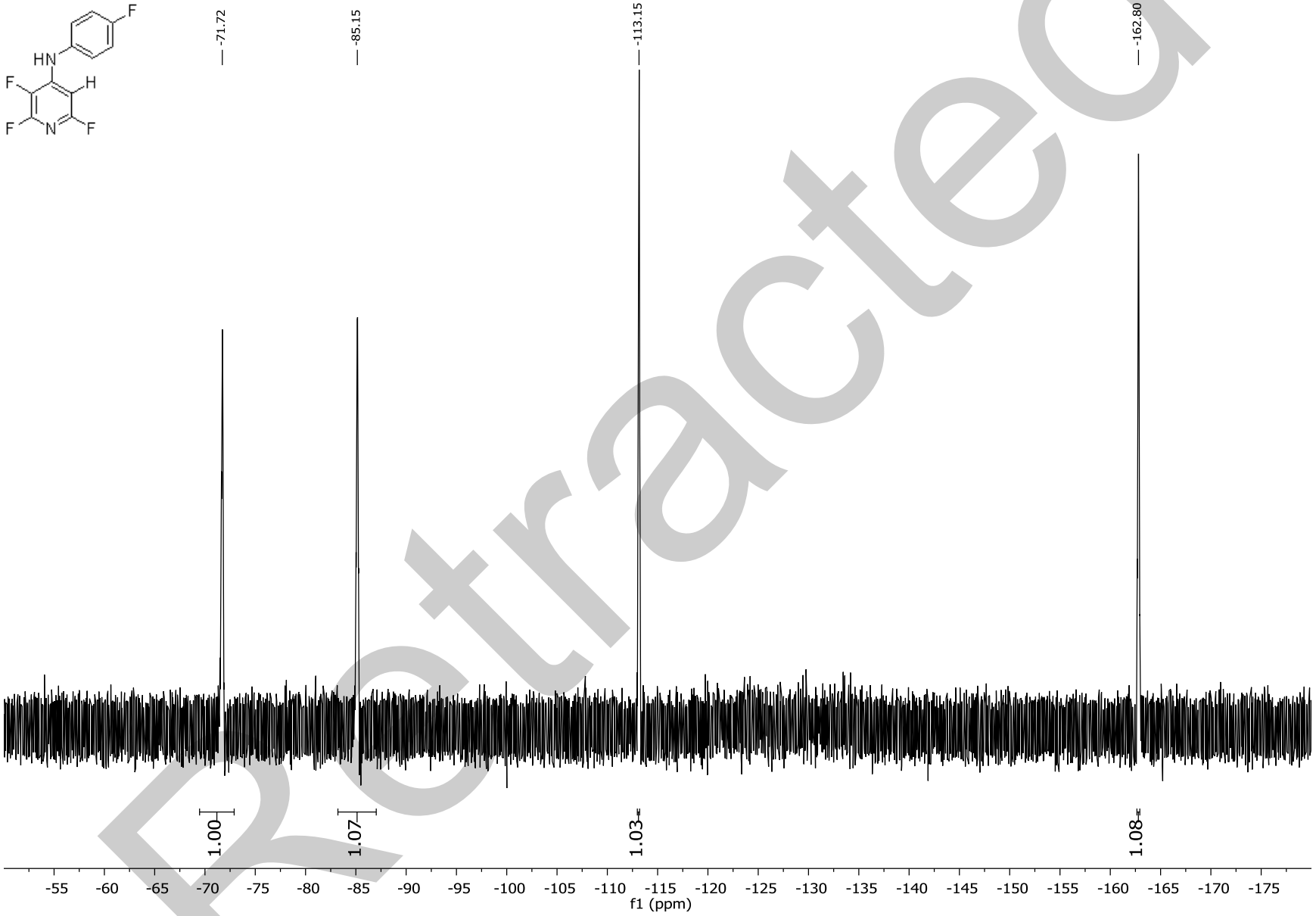
5c' 2,3,6-trifluoro-*N*-(4-methoxyphenyl)pyridin-4-amine ^{13}C NMR (101 MHz, Chloroform-*d*)



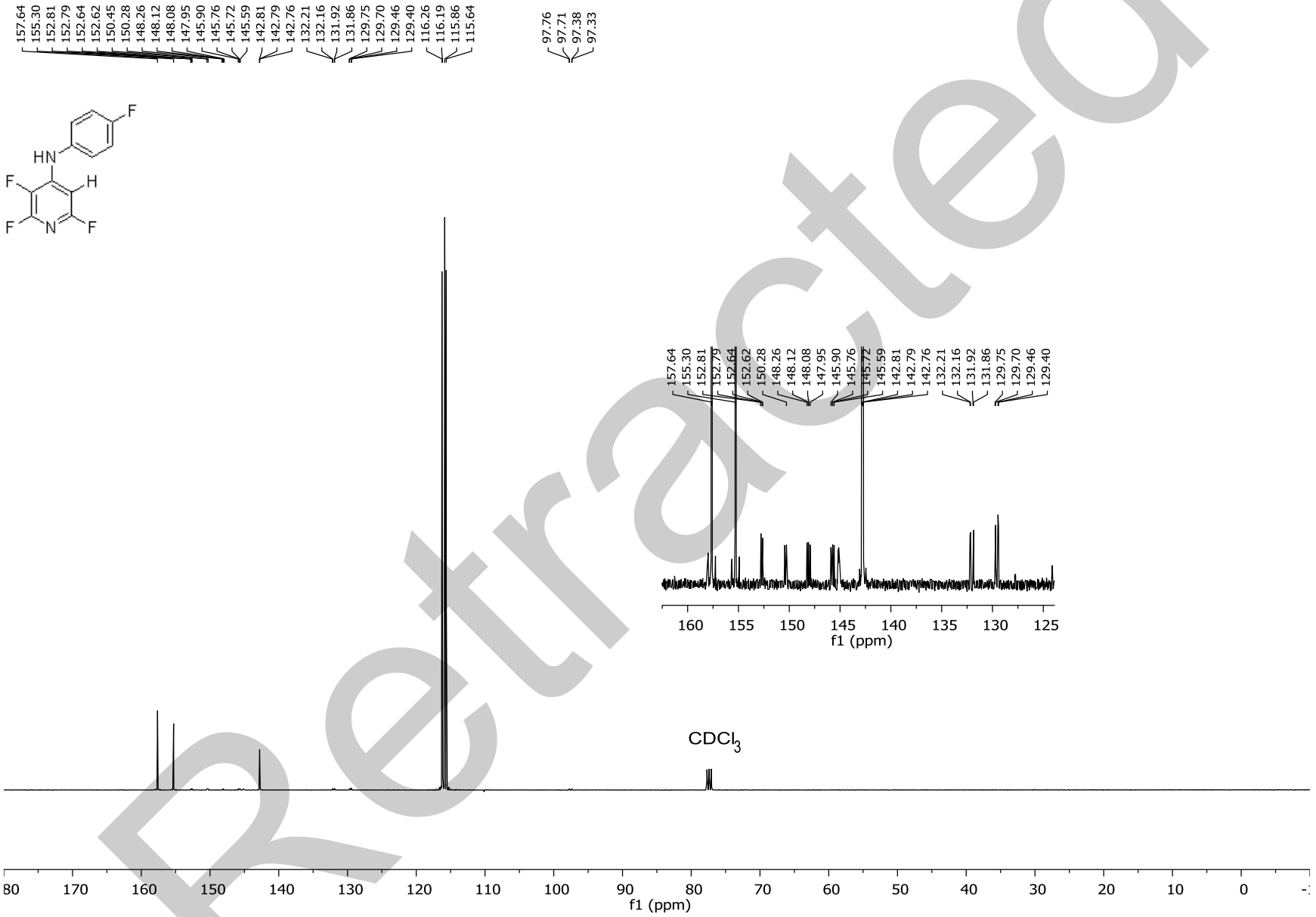
5d' 2,3,6-trifluoro-*N*-(4-fluorophenyl)pyridin-4-amine ^{1}H NMR (400 MHz, Chloroform-*d*)



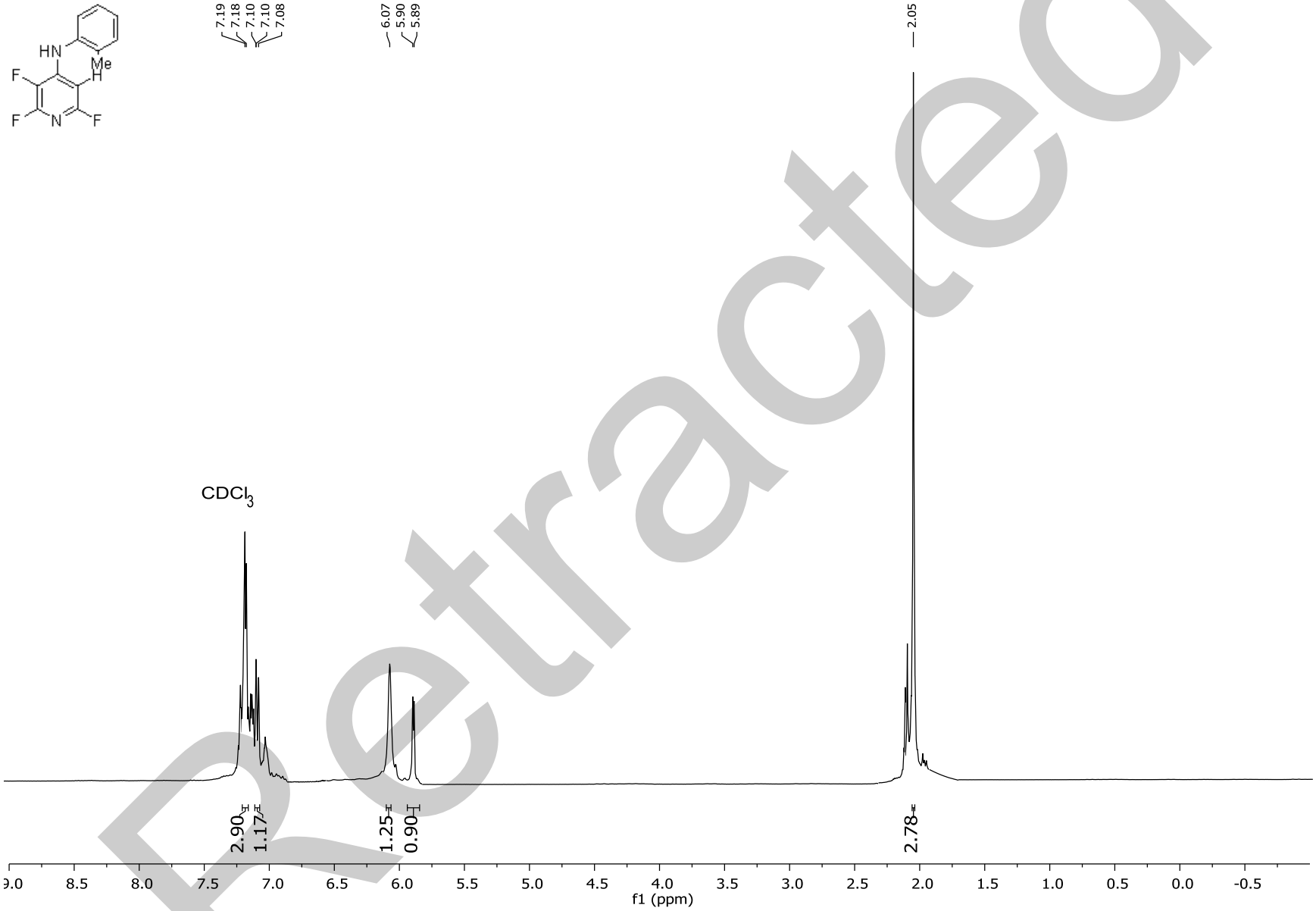
5d' 2,3,6-trifluoro-*N*-(4-fluorophenyl)pyridin-4-amine ^{19}F NMR (376 MHz, Chloroform-*d*)



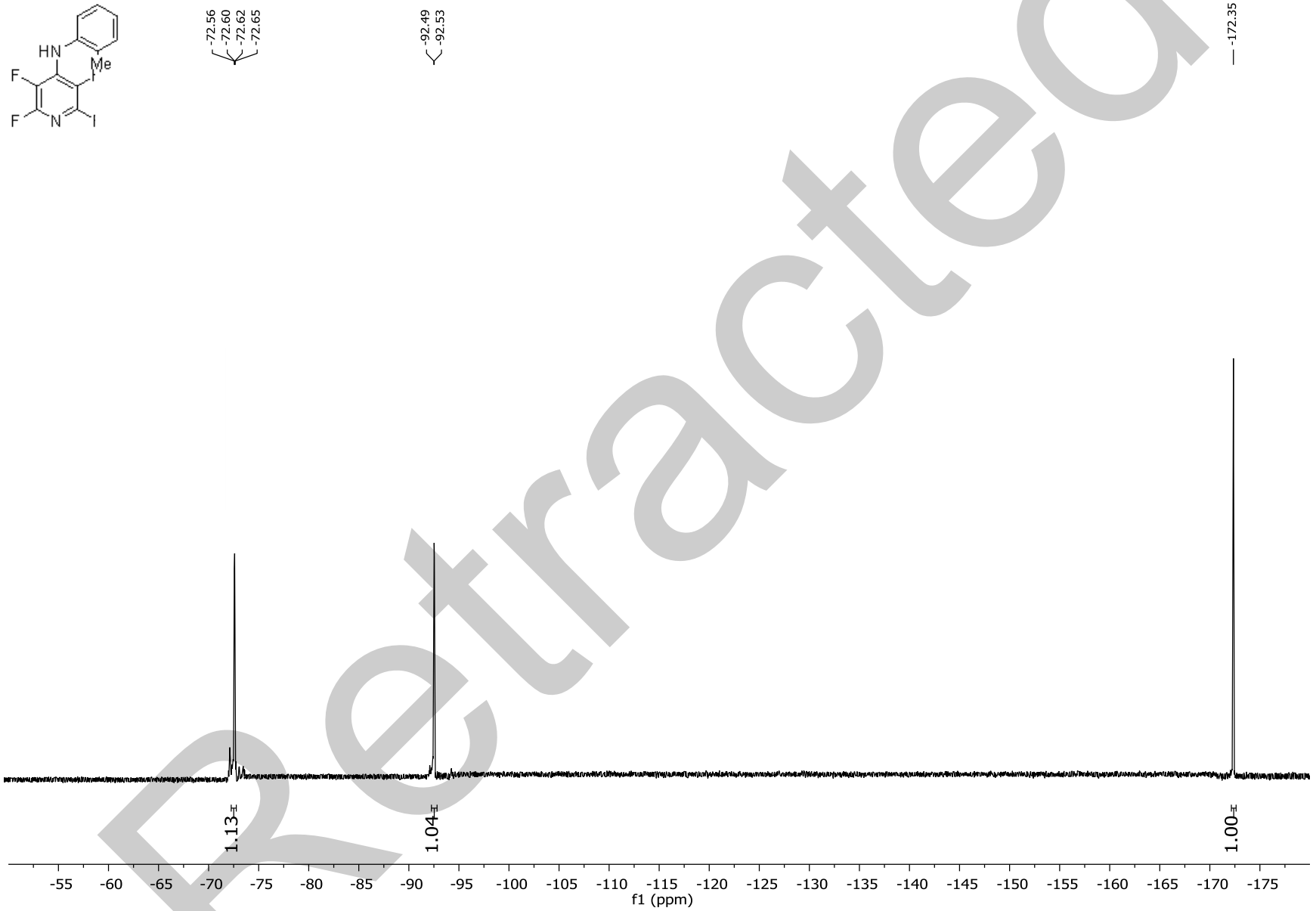
5d' 2,3,6-trifluoro-*N*-(4-fluorophenyl)pyridin-4-amine ^{13}C NMR (101 MHz, Chloroform-*d*)



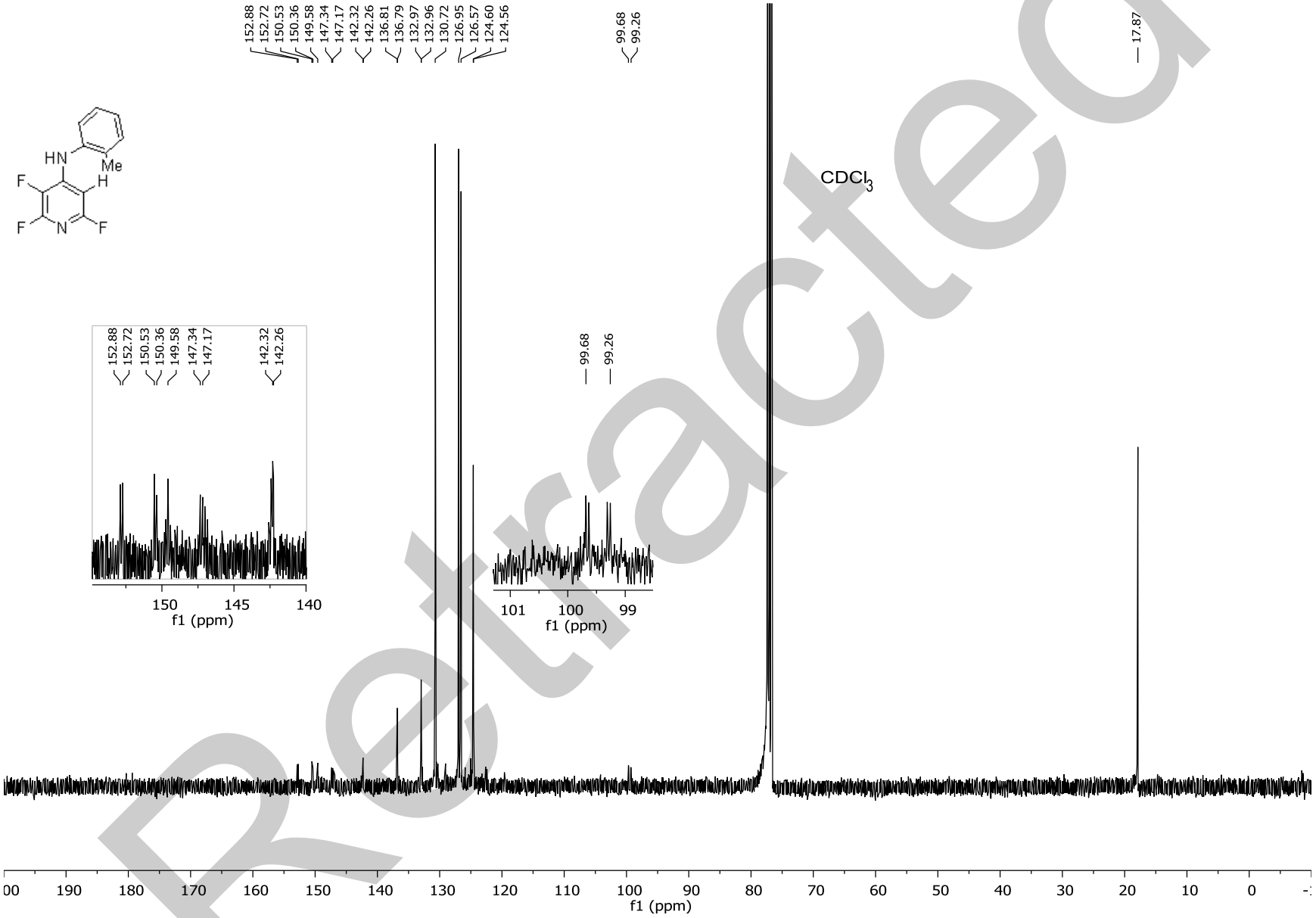
5e' 22,3,6-trifluoro-*N*-(*o*-tolyl)pyridin-4-amine ^{1}H NMR (400 MHz, Chloroform-*d*)



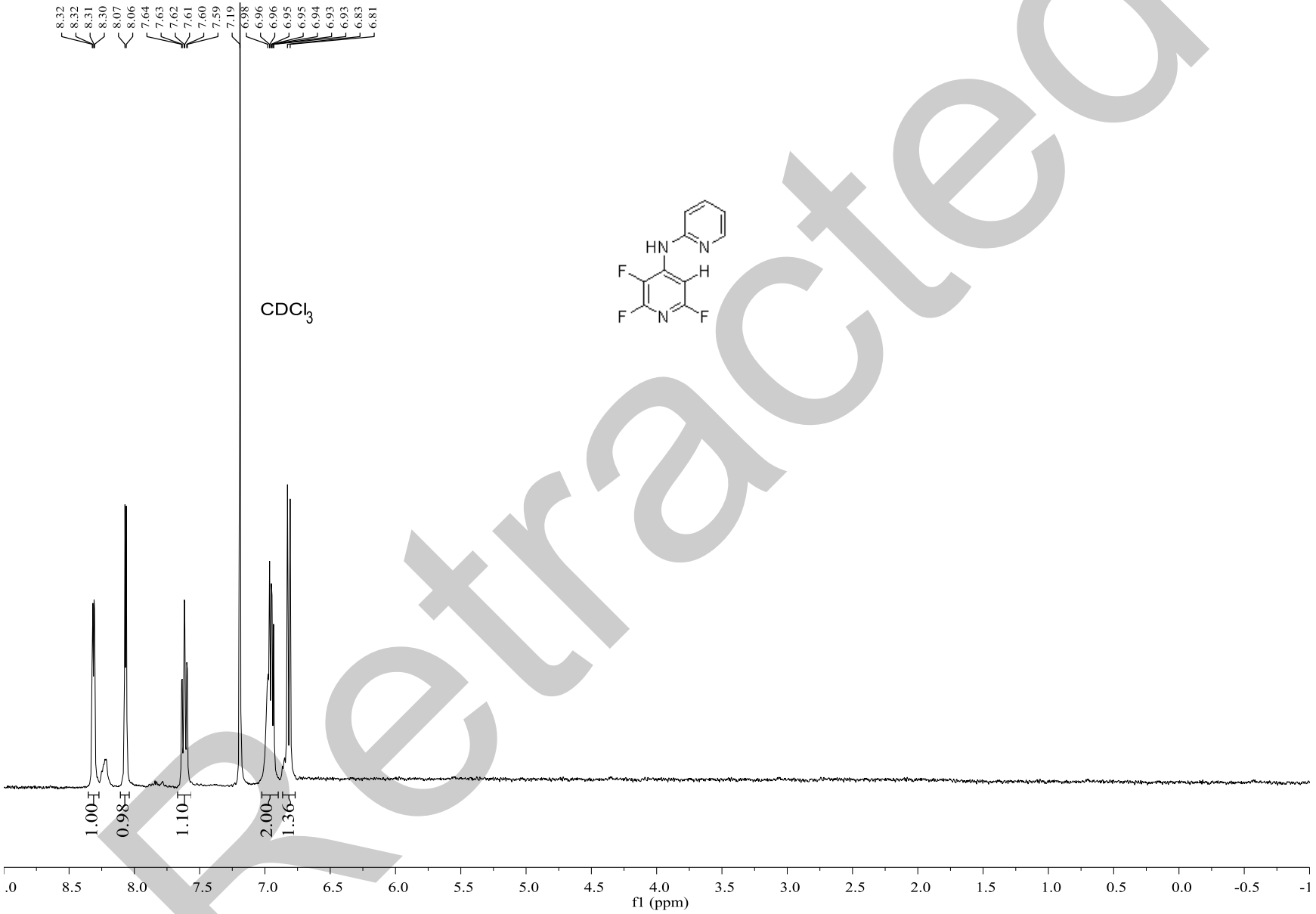
5e' 22,3,6-trifluoro-*N*-(*o*-tolyl)pyridin-4-amine ^{19}F NMR (376 MHz, Chloroform-*d*)



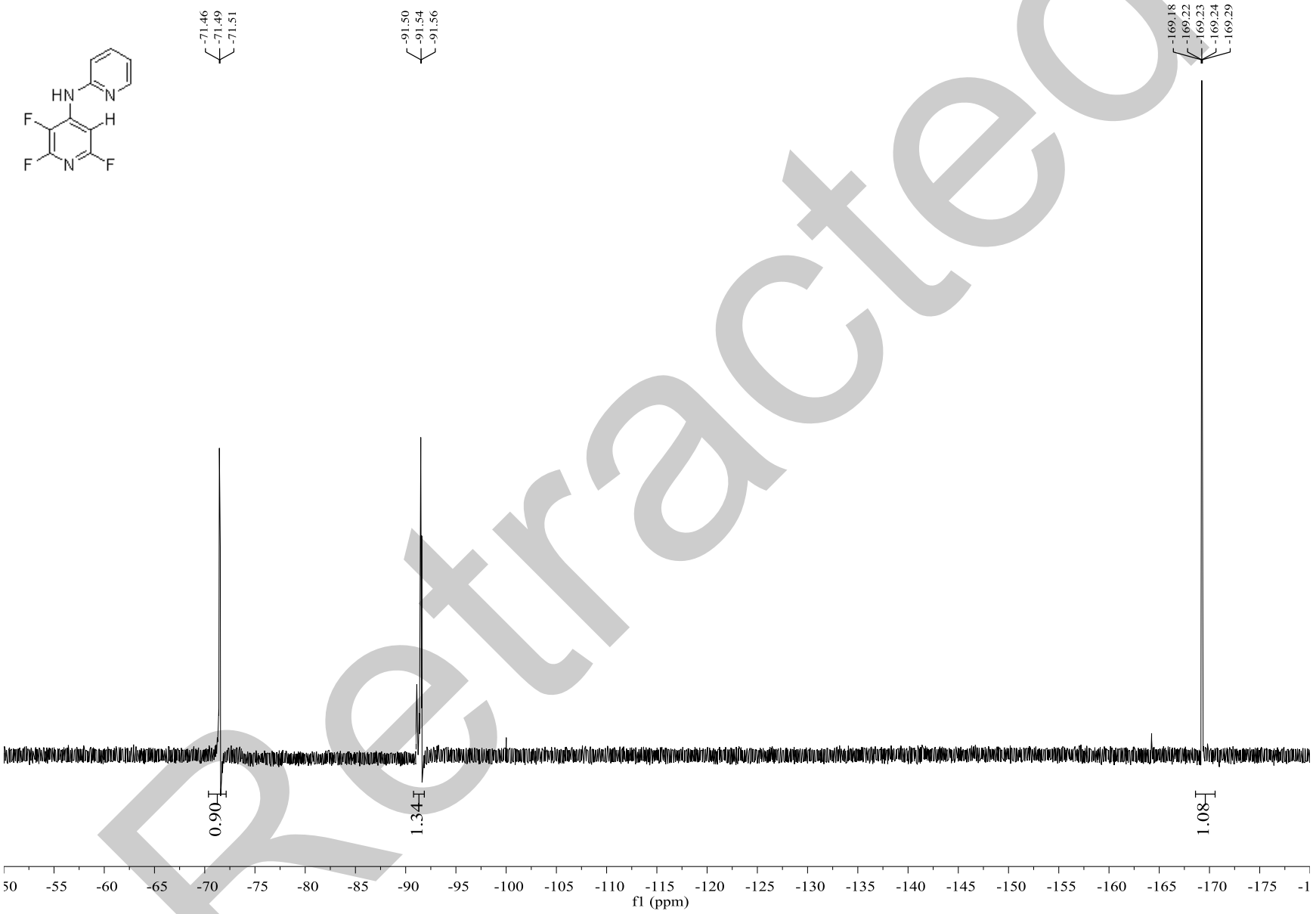
5e' 22,3,6-trifluoro-*N*-(*o*-tolyl)pyridin-4-amine ^{13}C NMR (101 MHz, Chloroform-*d*)



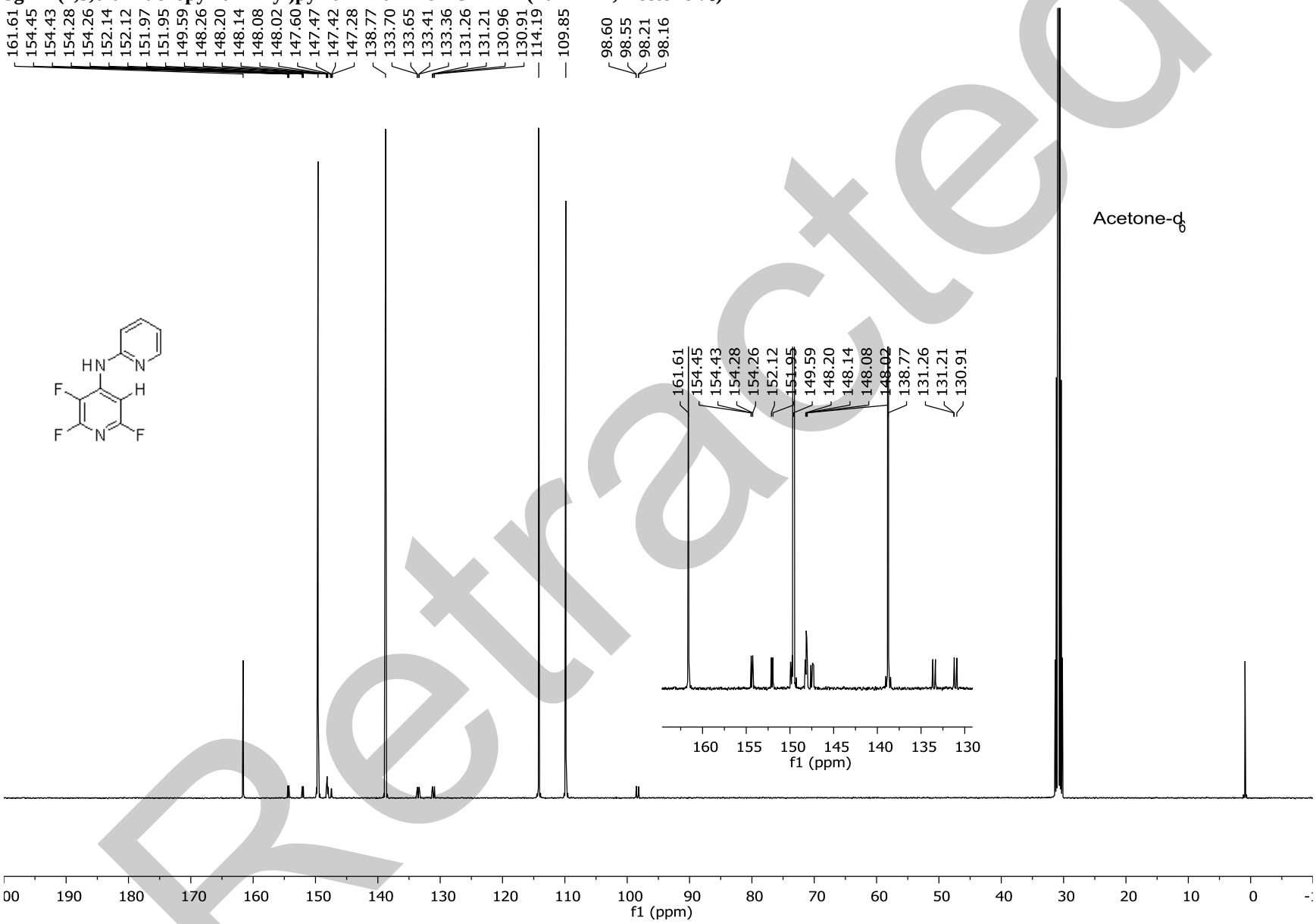
5g' *N*-(2,3,6-trifluoropyridin-4-yl)pyridin-2-amine ^{1}H NMR (400 MHz, Chloroform-*d*)



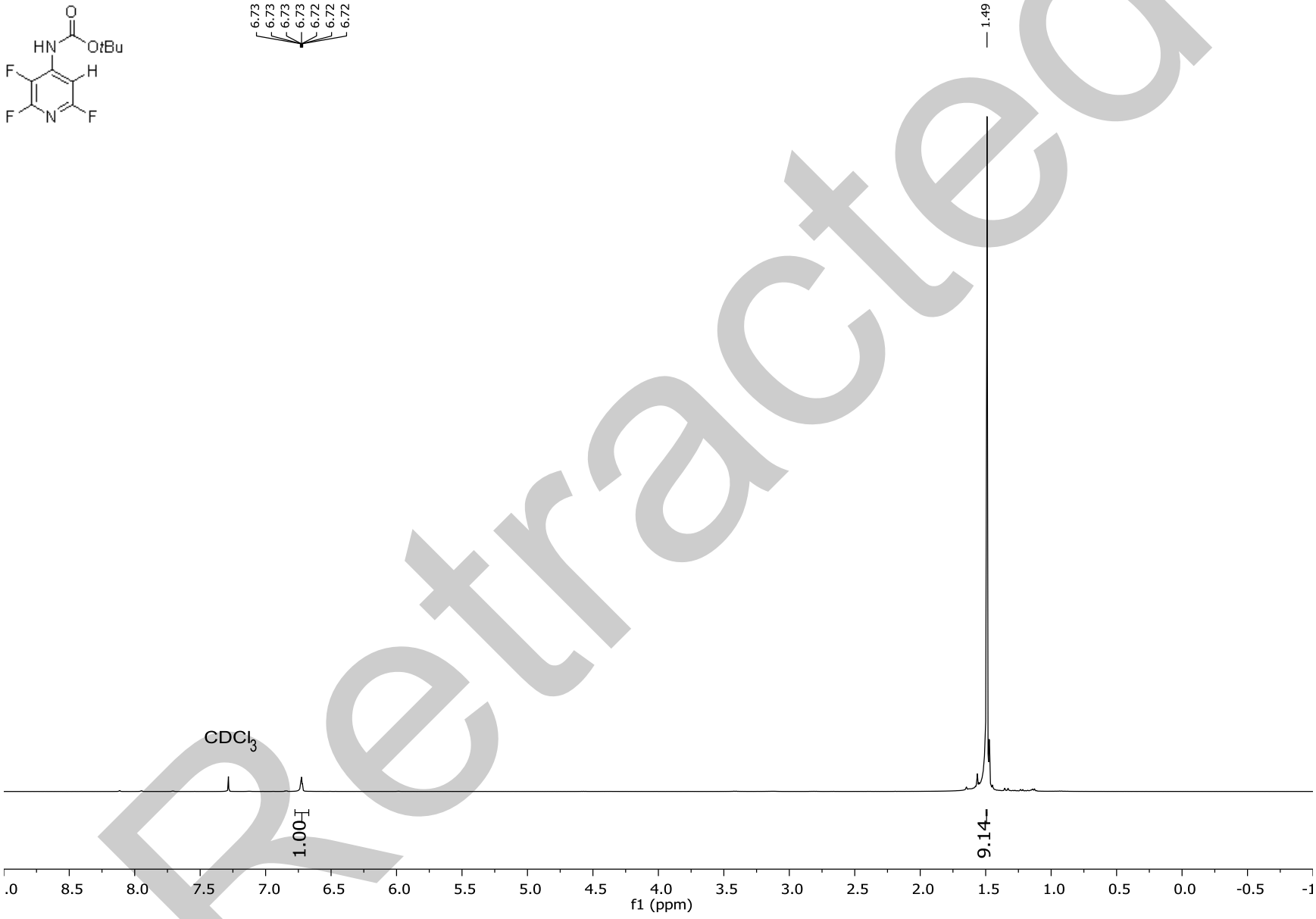
5g' *N*-(2,3,6-trifluoropyridin-4-yl)pyridin-2-amine ^{19}F NMR (376 MHz, Chloroform-*d*)



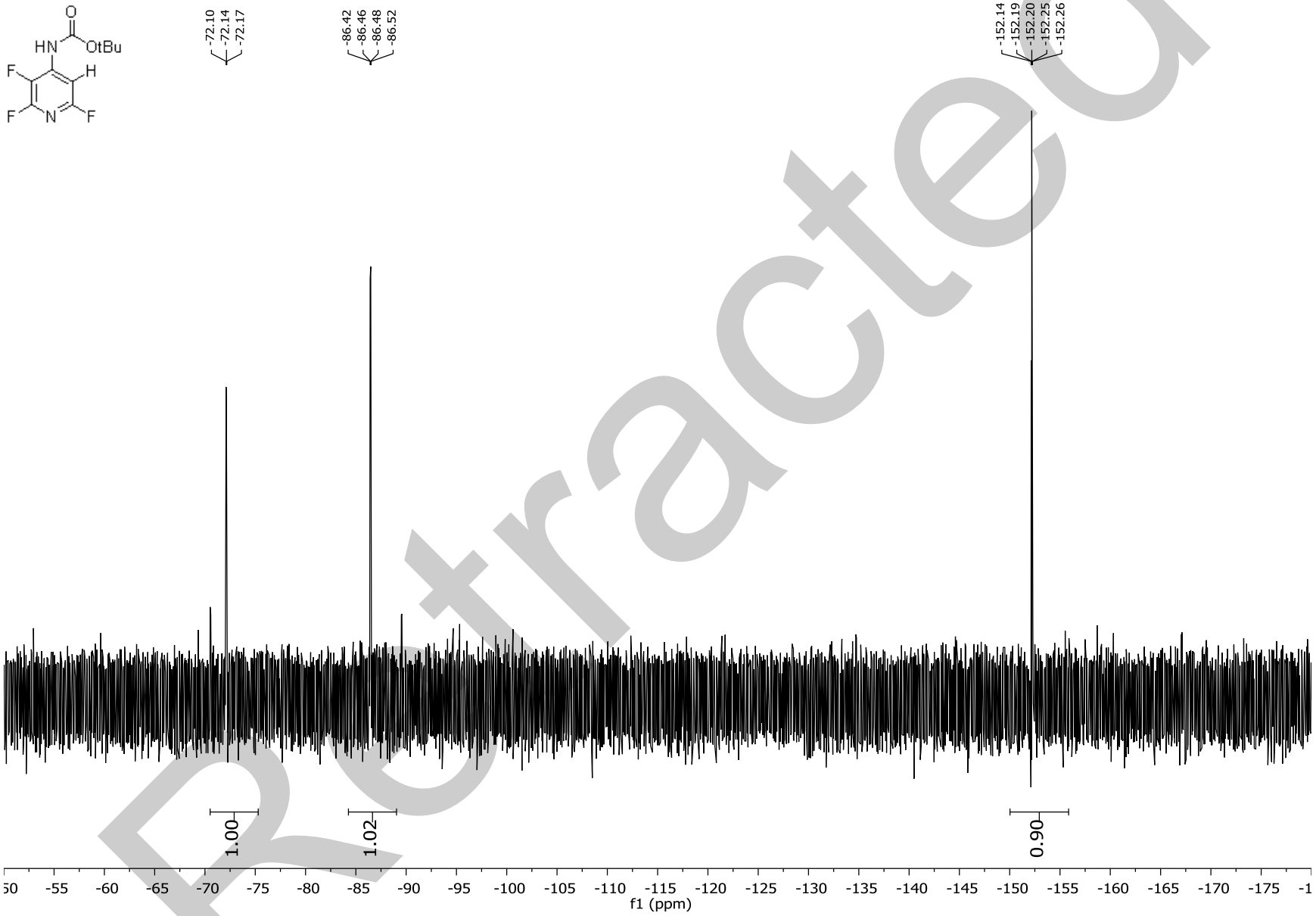
5g' *N*-(2,3,6-trifluoropyridin-4-yl)pyridin-2-amine ^{13}C NMR (101 MHz, Acetone-*d*$_6$)



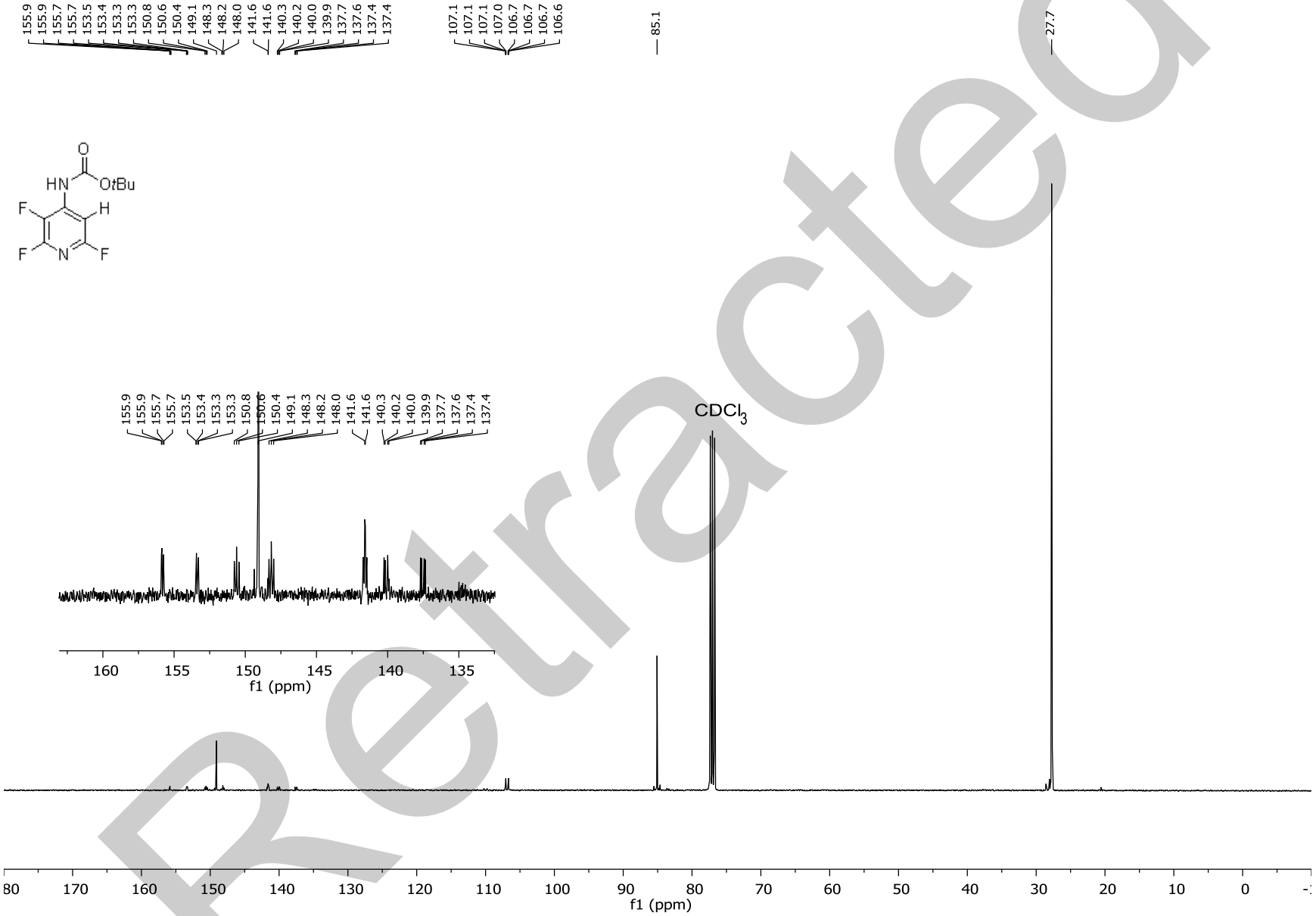
5h' *tert*-butyl (2,3,6-trifluoropyridin-4-yl)carbamate ^{1}H NMR (400 MHz, Chloroform-*d*)



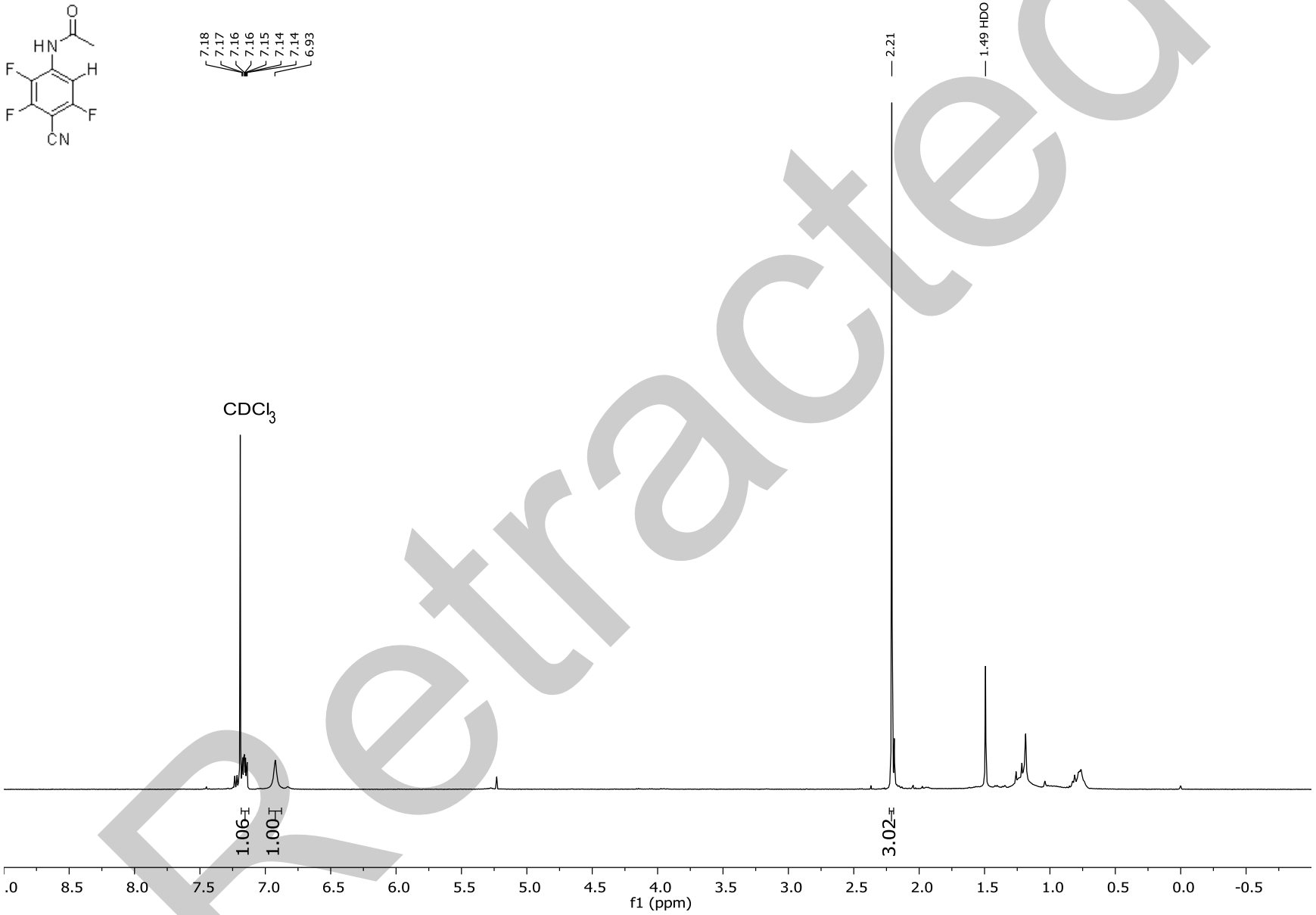
5h' *tert*-butyl (2,3,6-trifluoropyridin-4-yl)carbamate ^{19}F NMR (376 MHz, Chloroform-*d*)



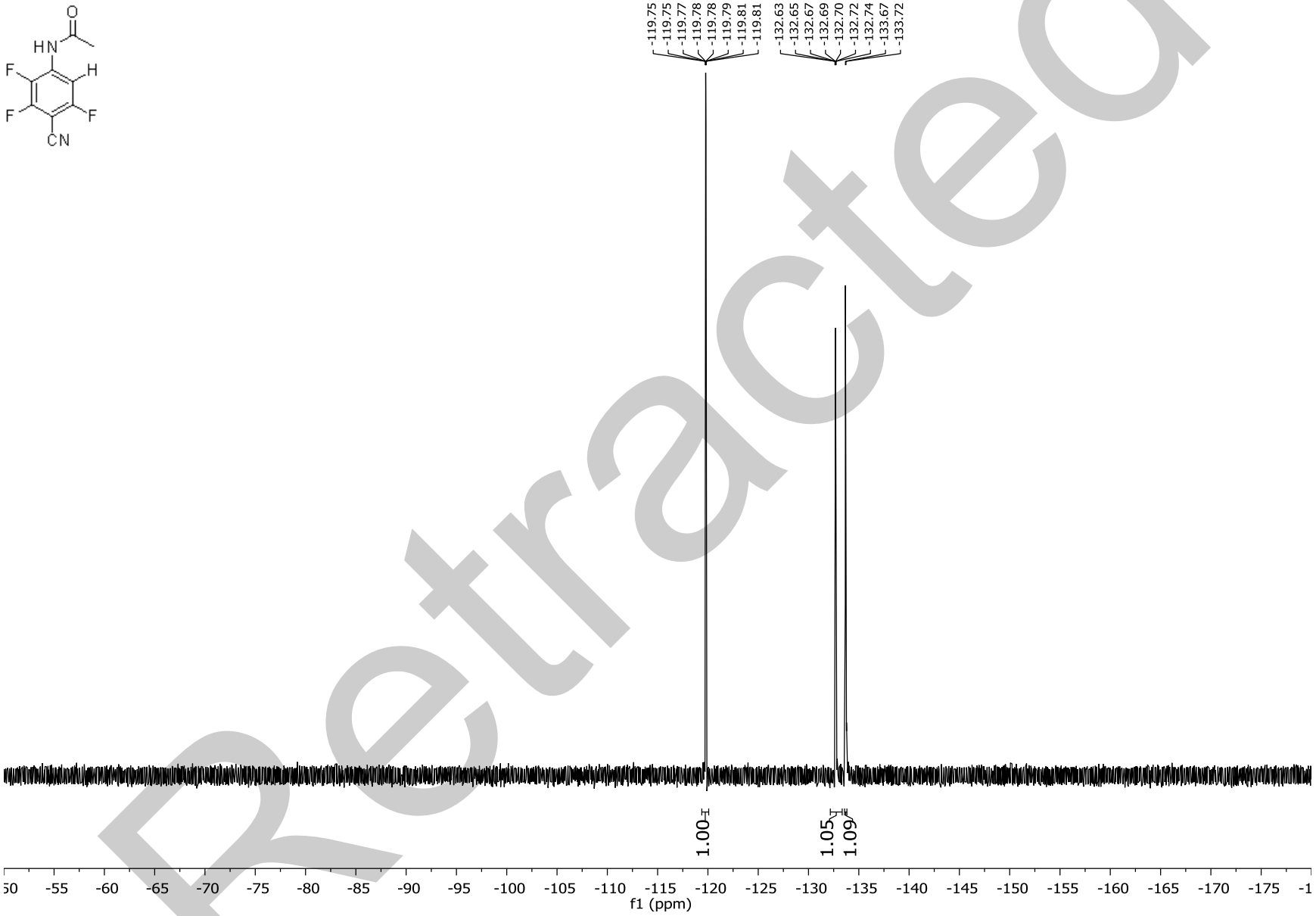
5h' *tert*-butyl (2,3,6-trifluoropyridin-4-yl)carbamate ^{13}C NMR (101 MHz, Chloroform-*d*)



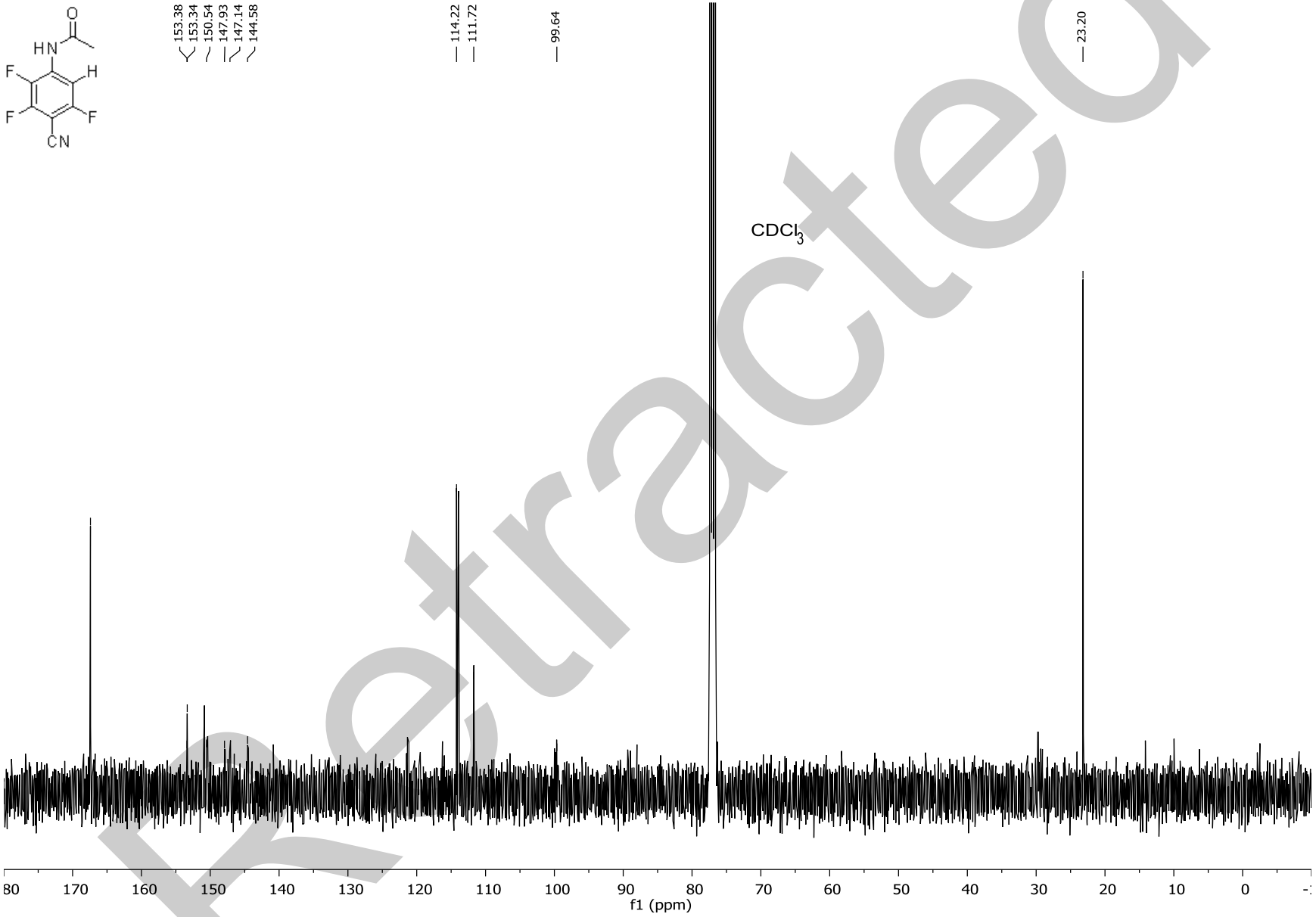
6a' *N*-(4-cyano-2,3,5-trifluorophenyl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



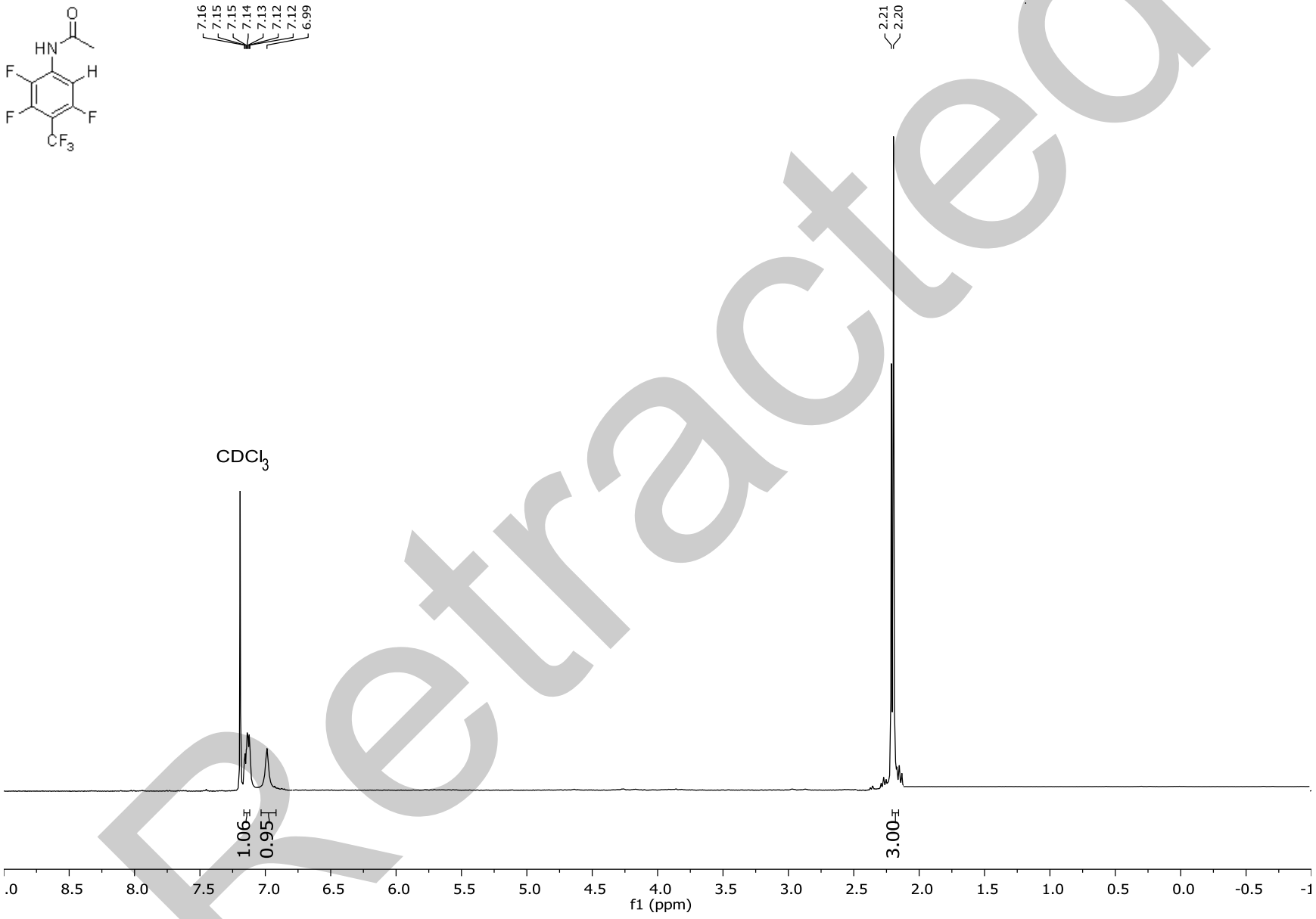
6a' *N*-(4-cyano-2,3,5-trifluorophenyl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



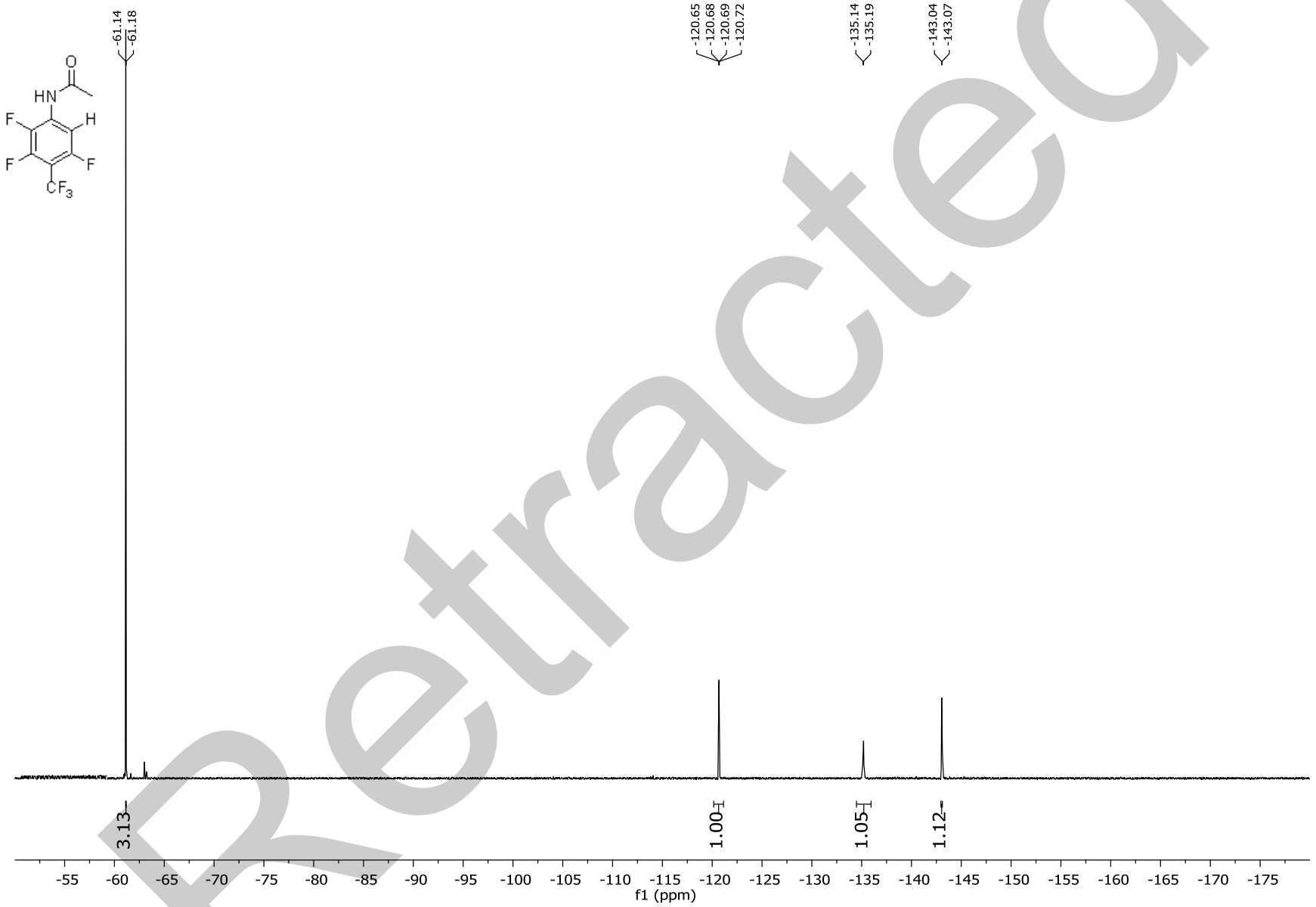
6a' *N*-(4-cyano-2,3,5-trifluorophenyl)acetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



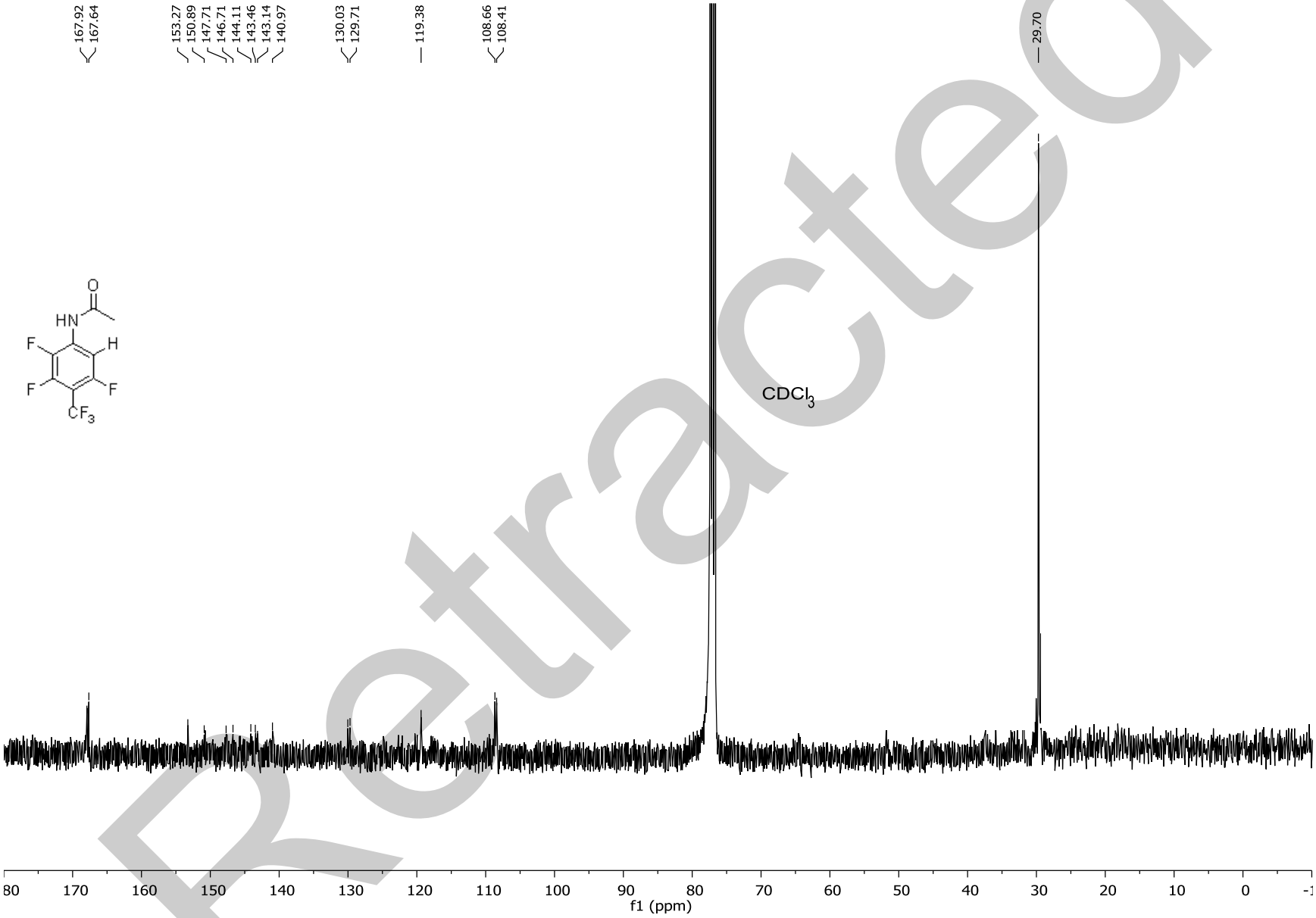
6b’ *N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



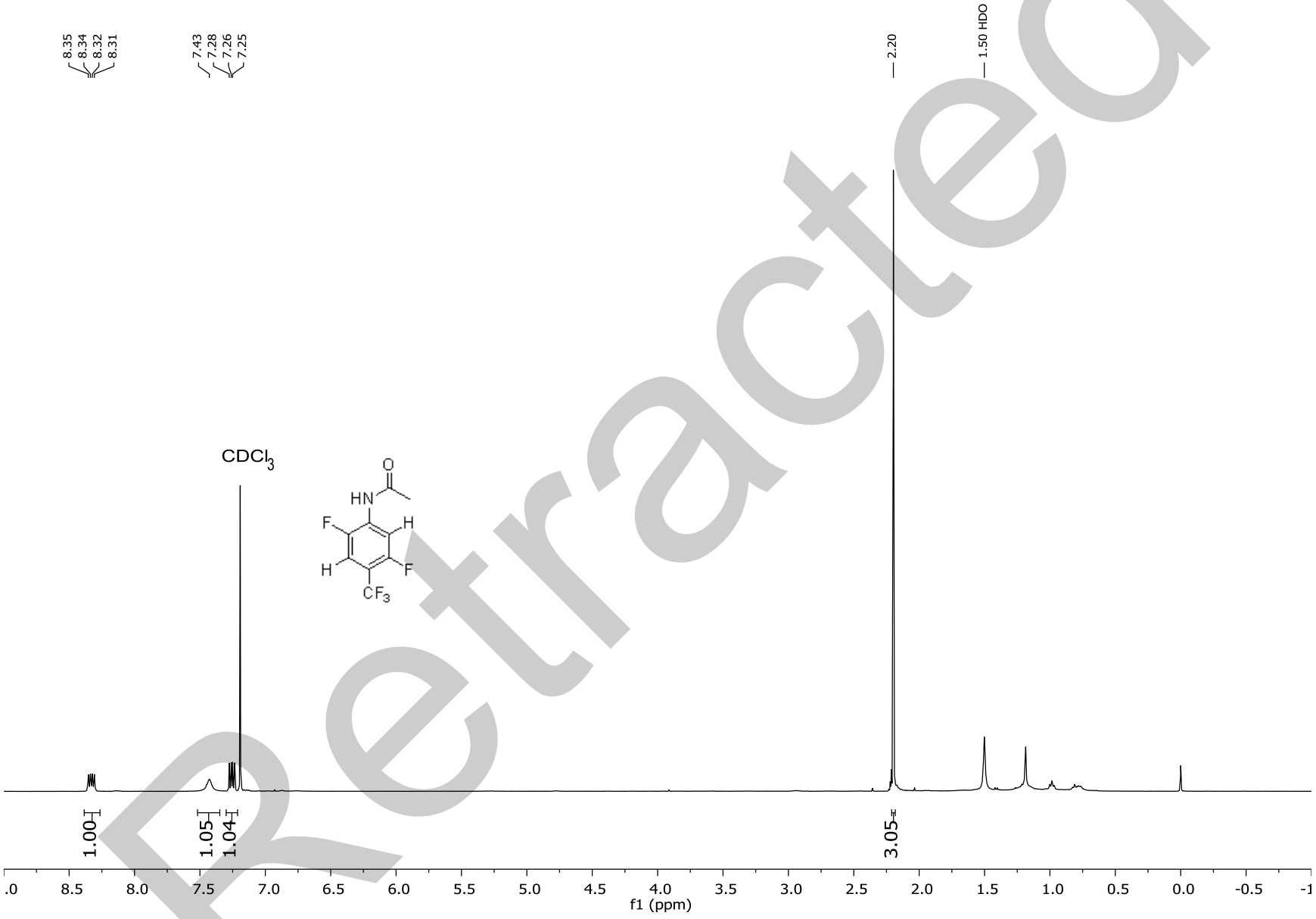
6b' *N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



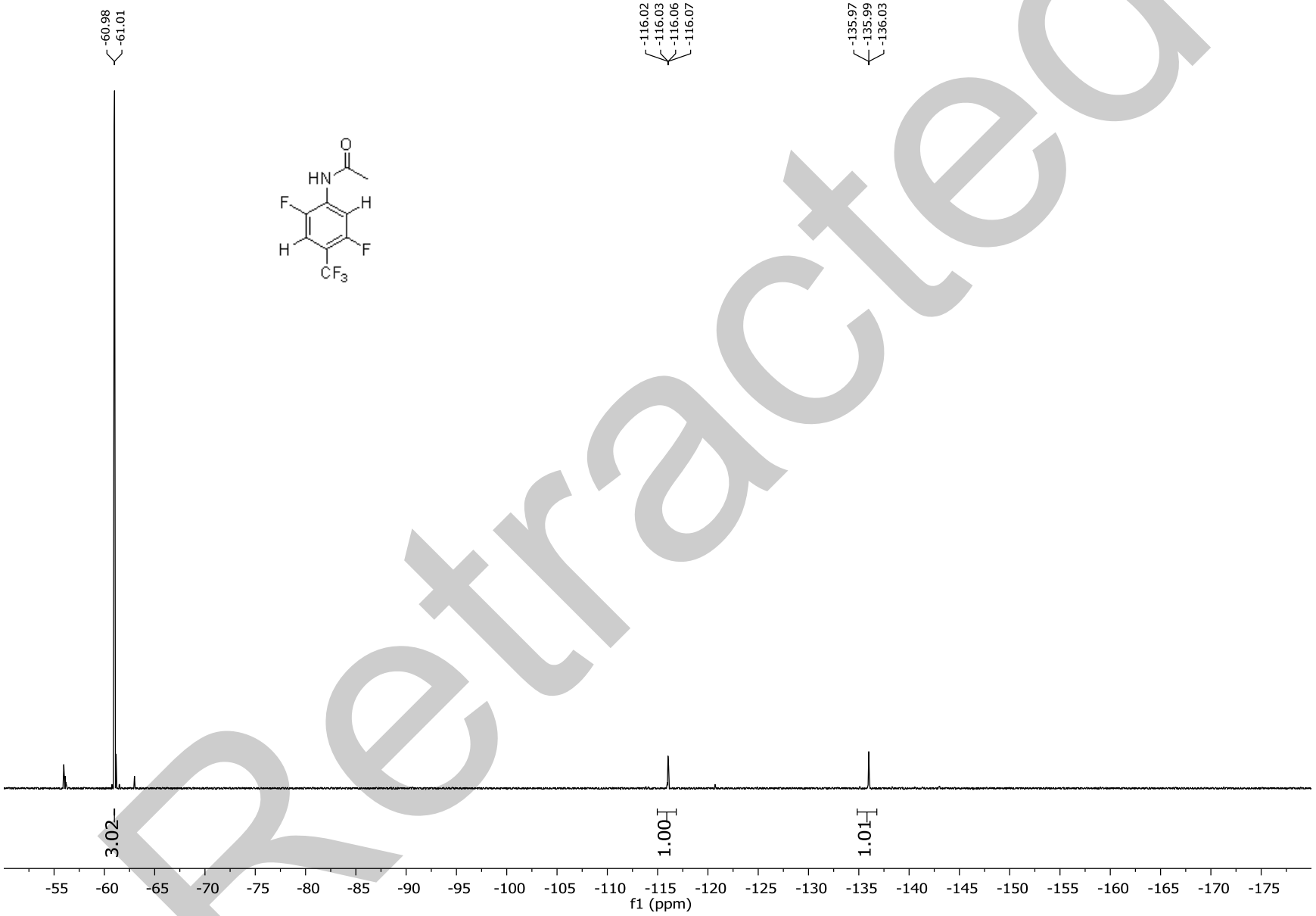
6b' *N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



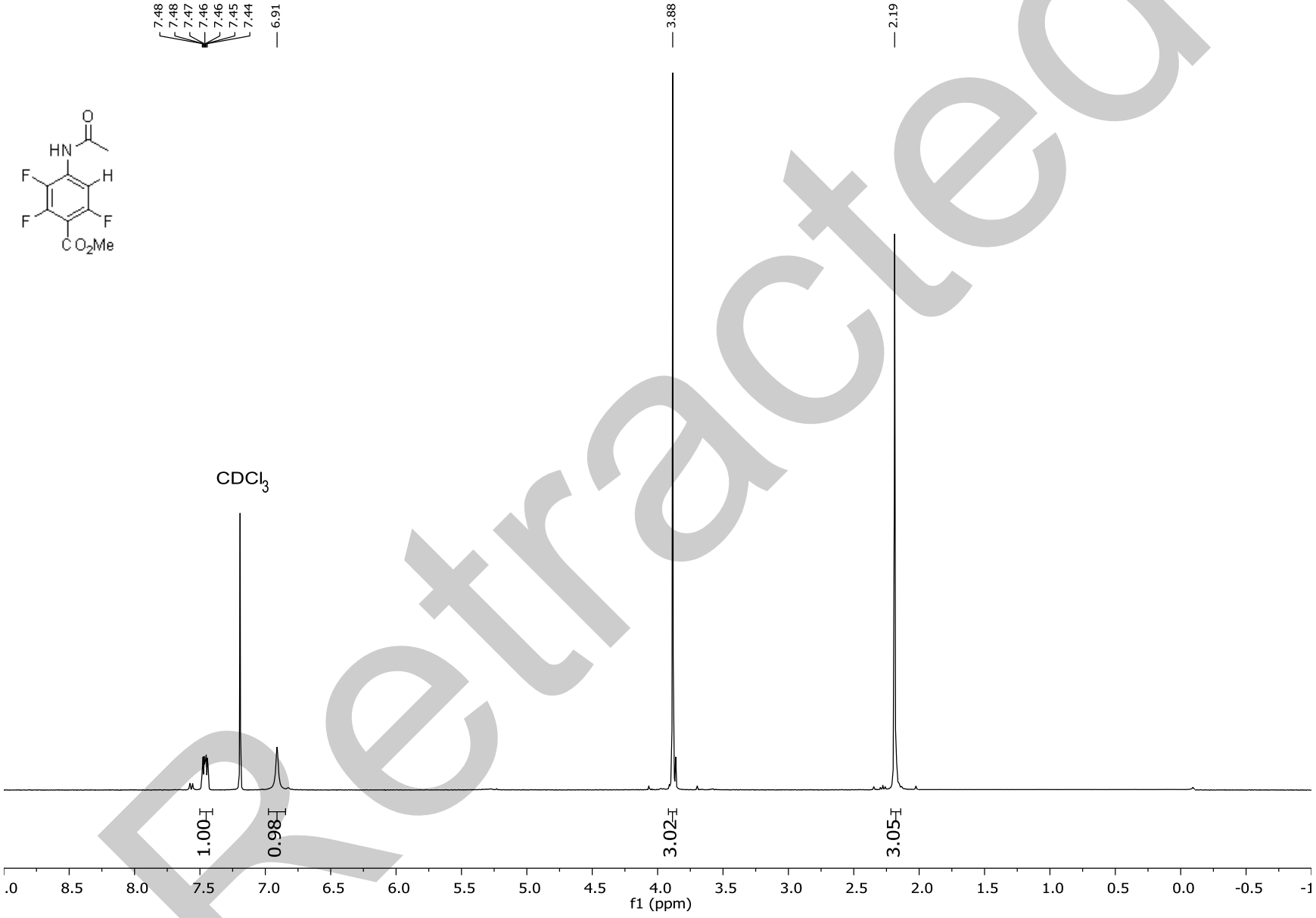
6b''' *N*-(2,5-difluoro-4-(trifluoromethyl)phenyl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



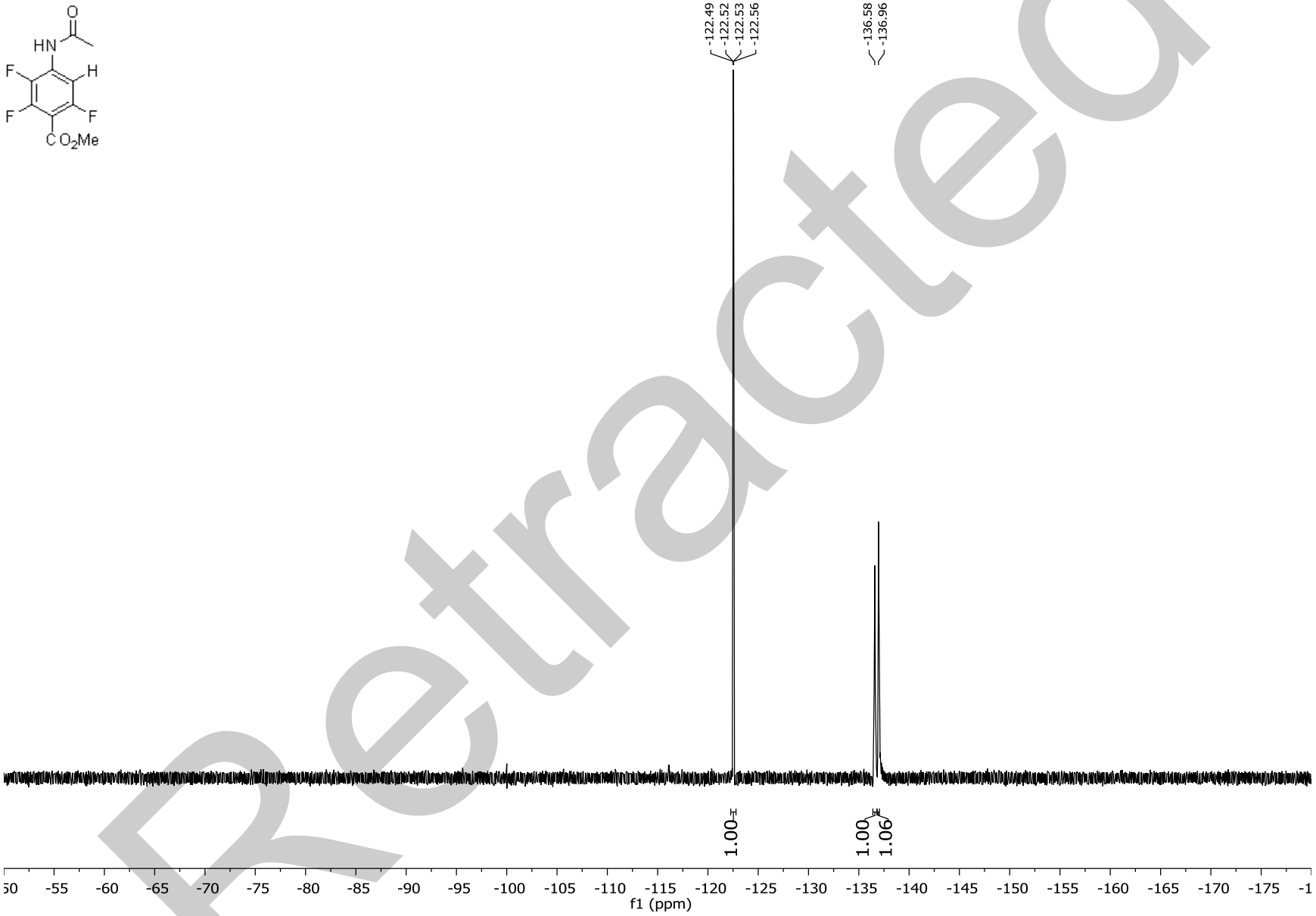
6b''' *N*-(2,5-difluoro-4-(trifluoromethyl)phenyl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



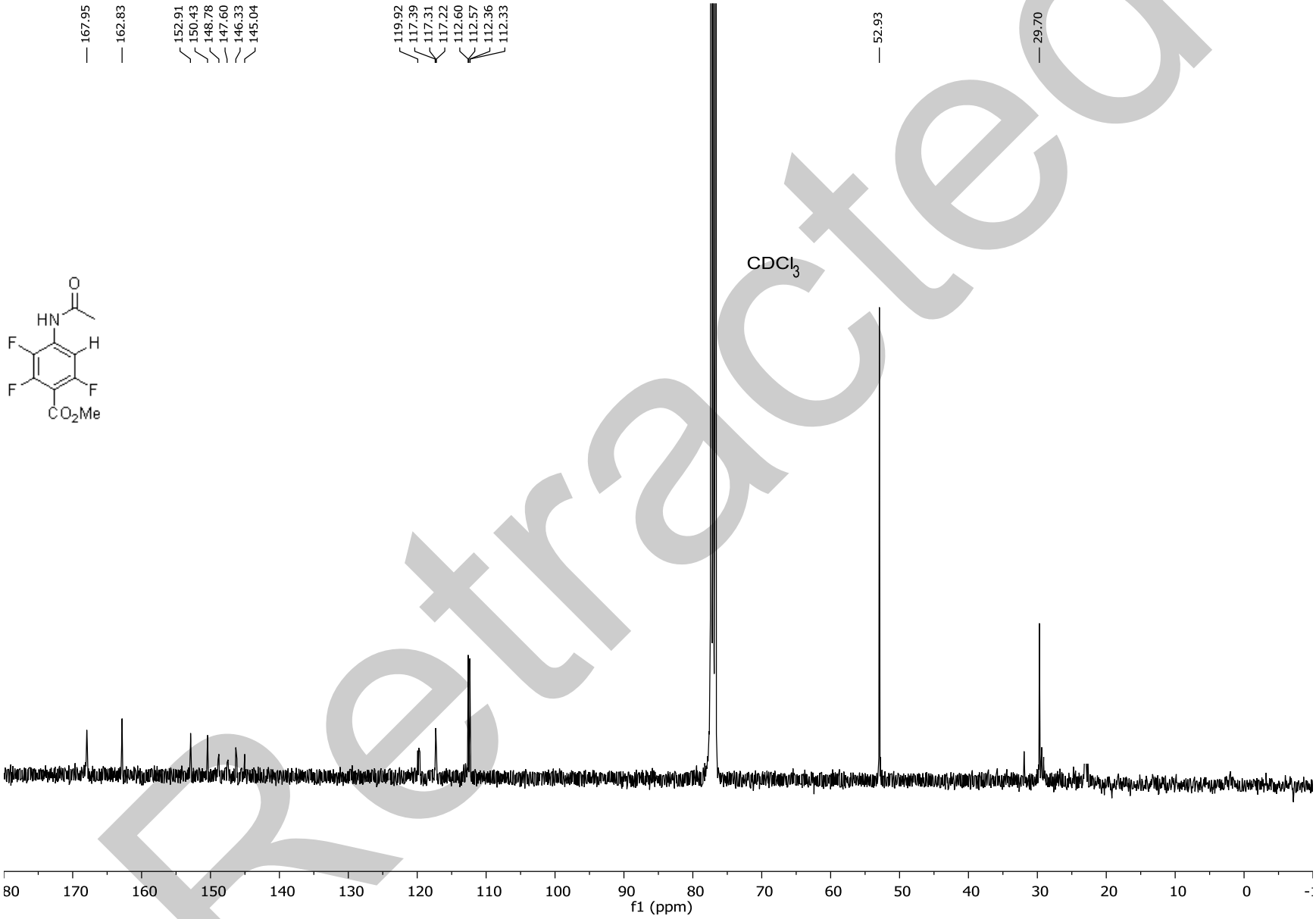
6c' methyl 4-acetamido-2,3,6-trifluorobenzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



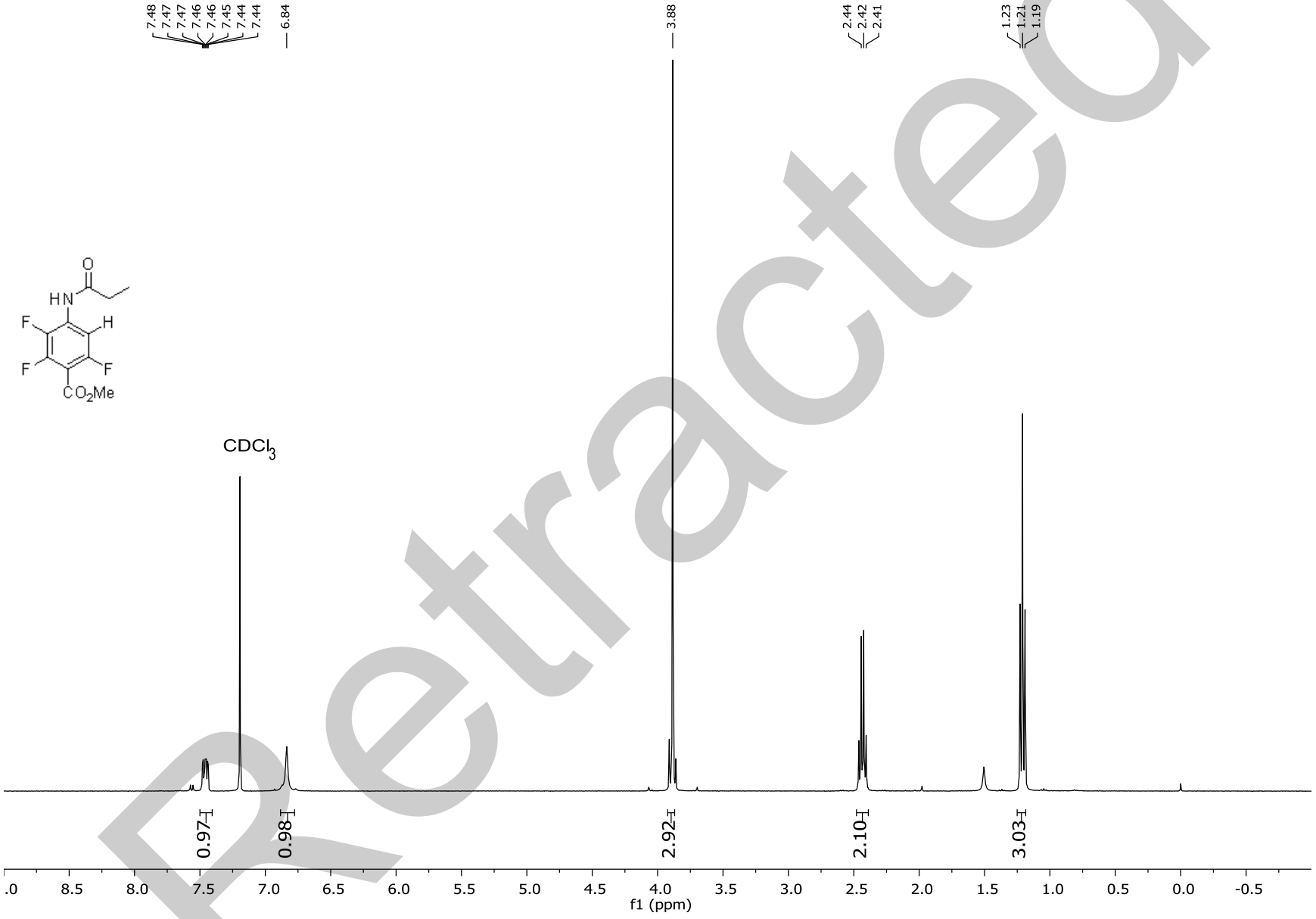
6c' methyl 4-acetamido-2,3,6-trifluorobenzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



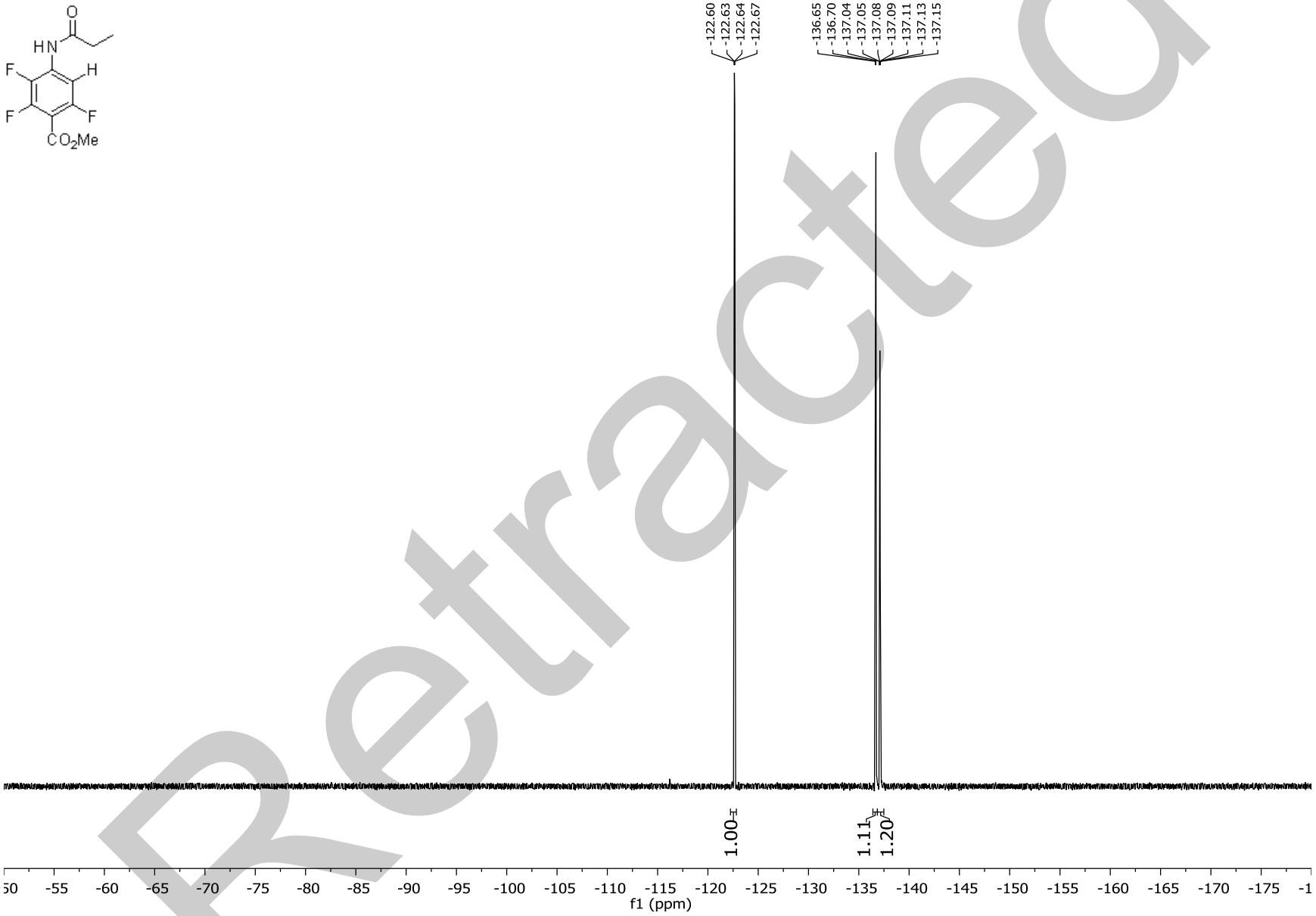
6c' methyl 4-acetamido-2,3,6-trifluorobenzoate ^{13}C NMR (101 MHz, Chloroform-*d*)



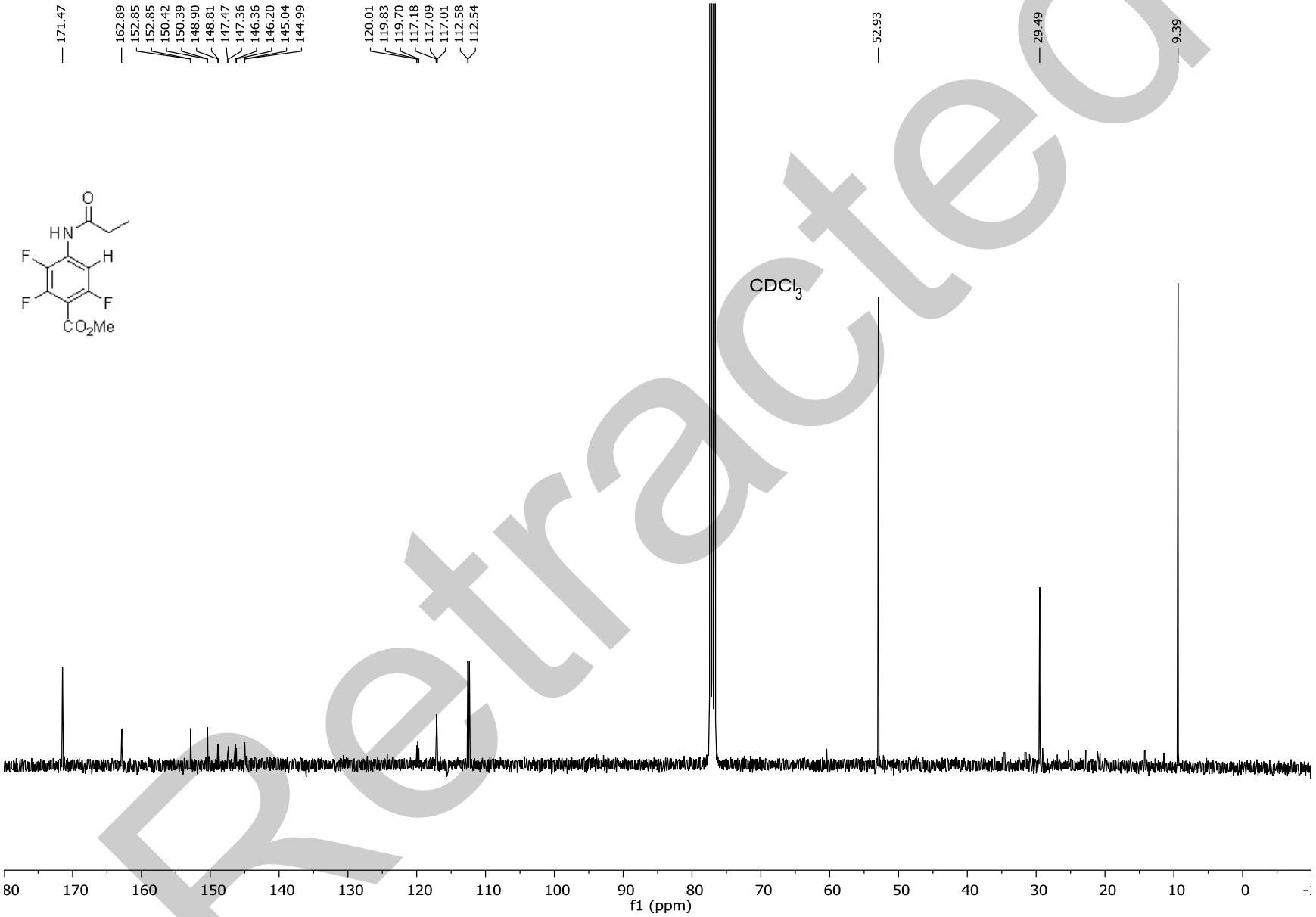
6d' methyl 2,3,6-trifluoro-4-propionamidobenzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



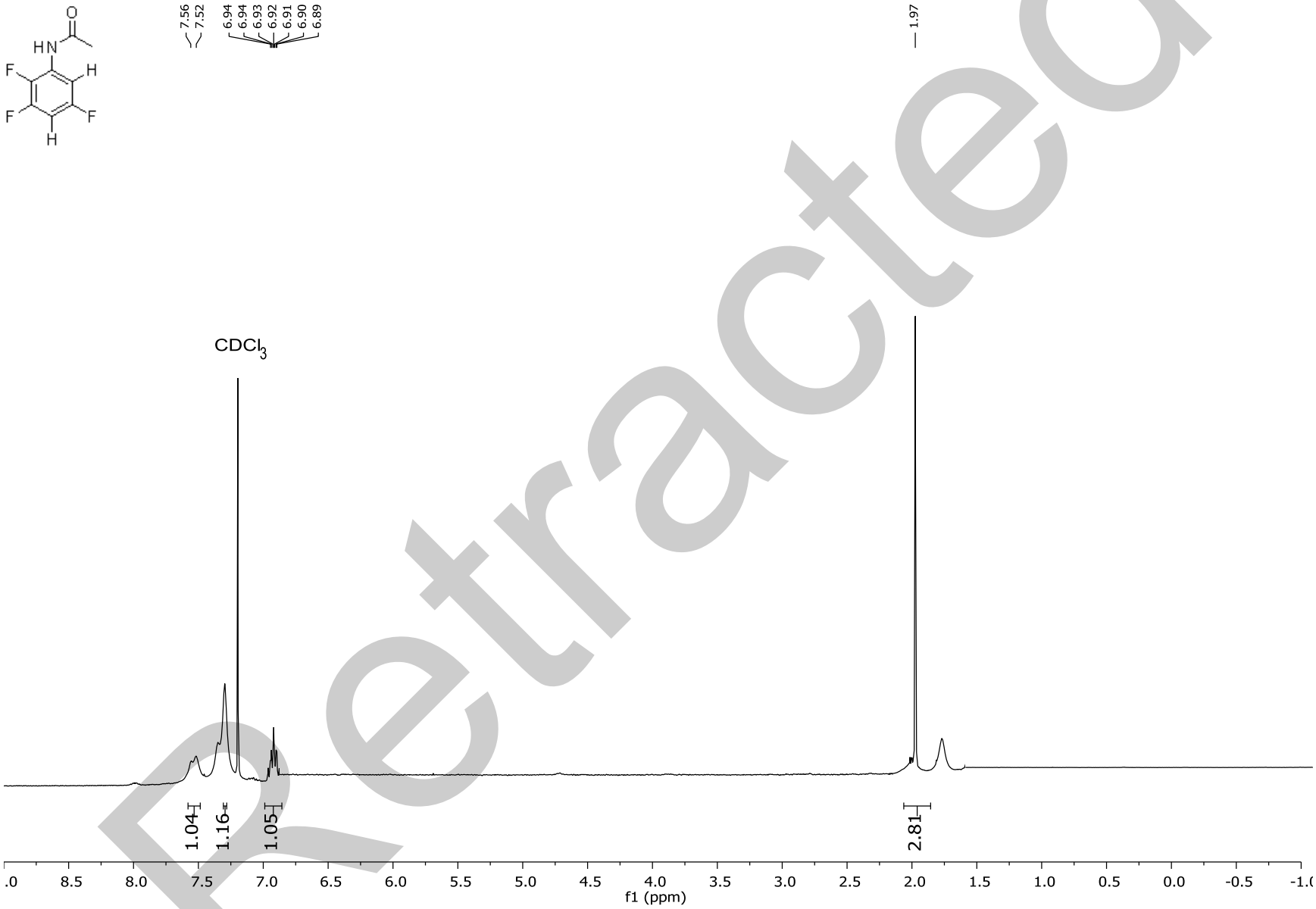
6d' methyl 2,3,6-trifluoro-4-propionamidobenzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



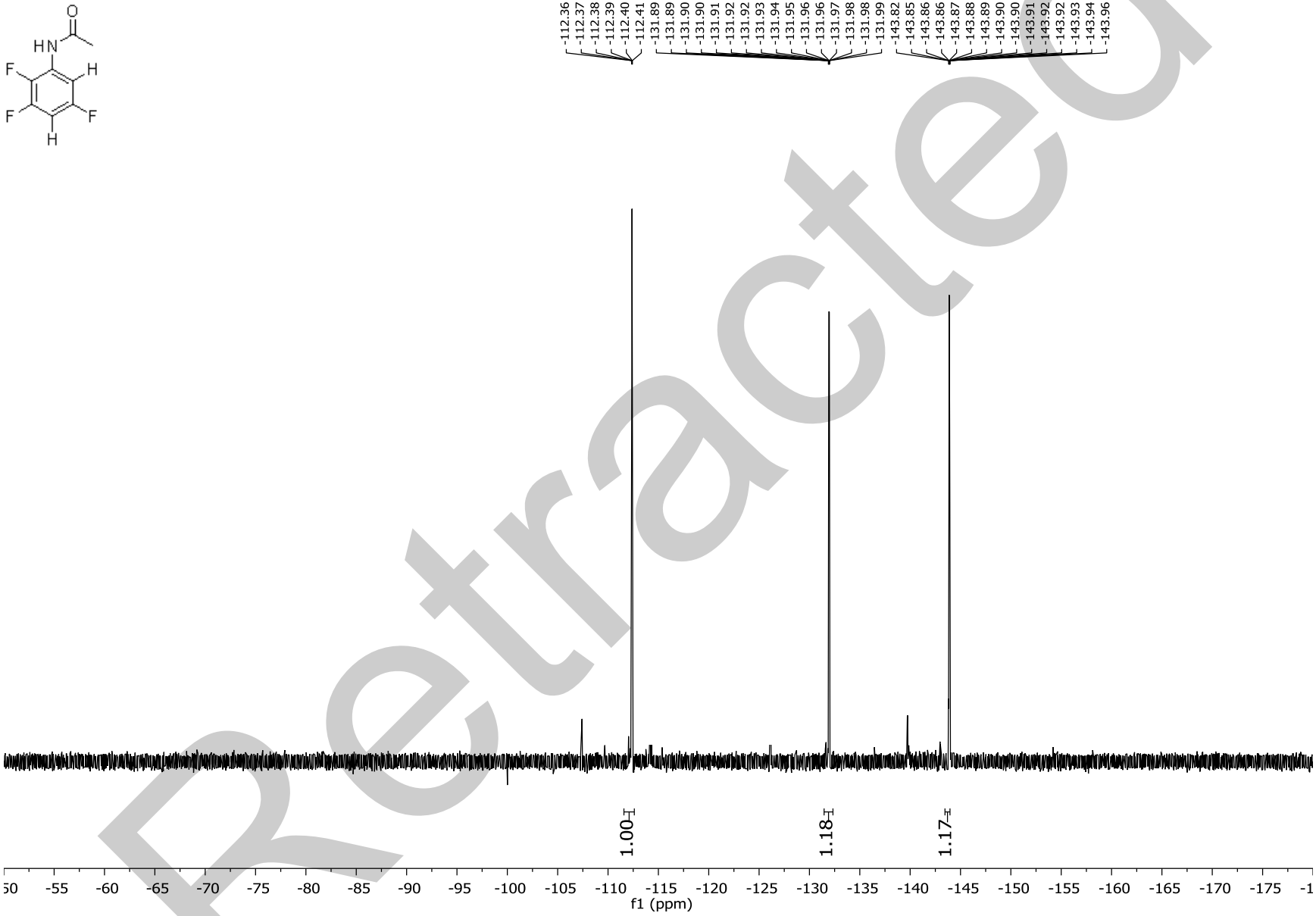
6d' methyl 2,3,6-trifluoro-4-propionamidobenzoate ^{13}C NMR (101 MHz, Chloroform-*d*)



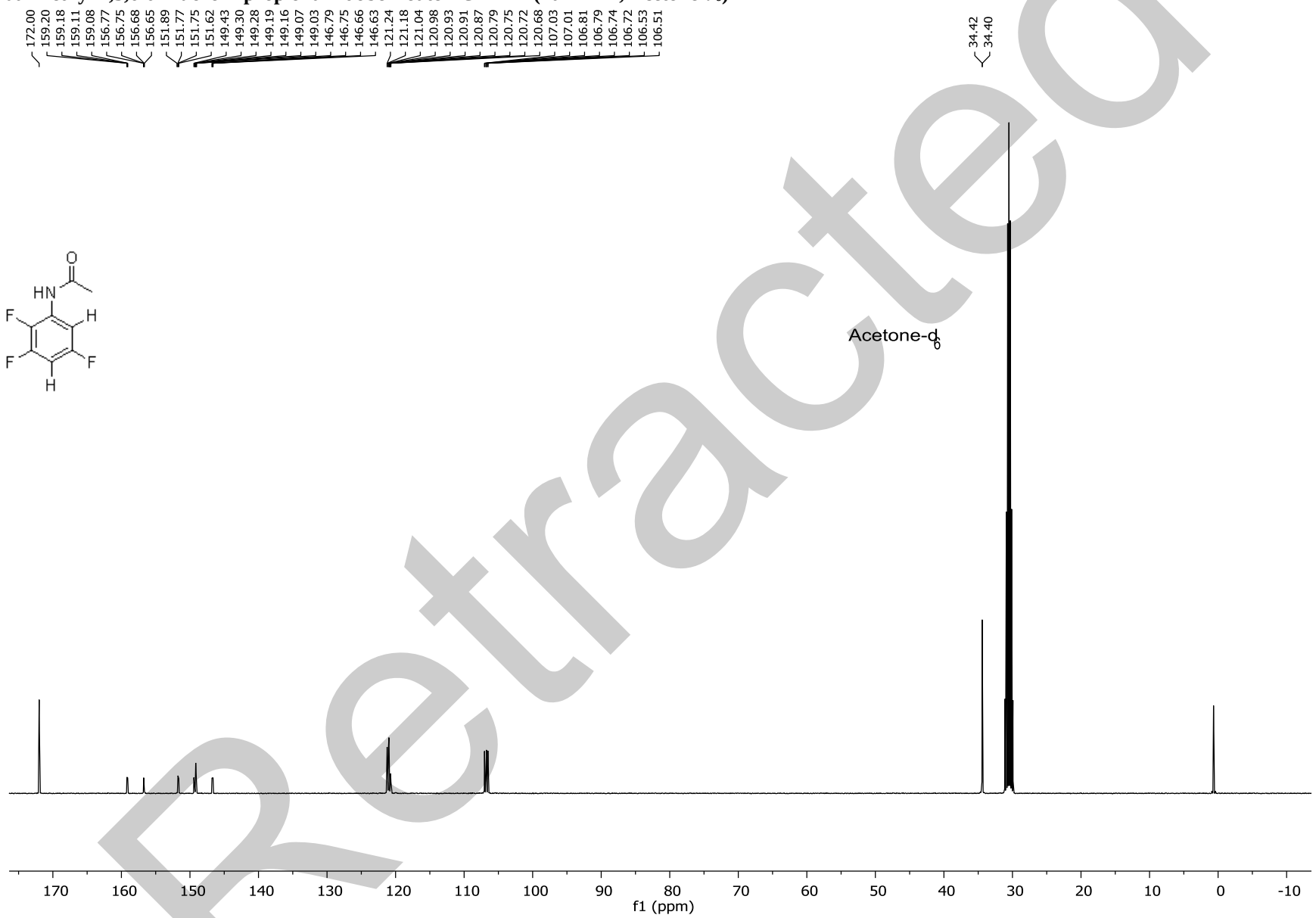
6e' methyl 2,3,6-trifluoro-4-propionamidobenzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



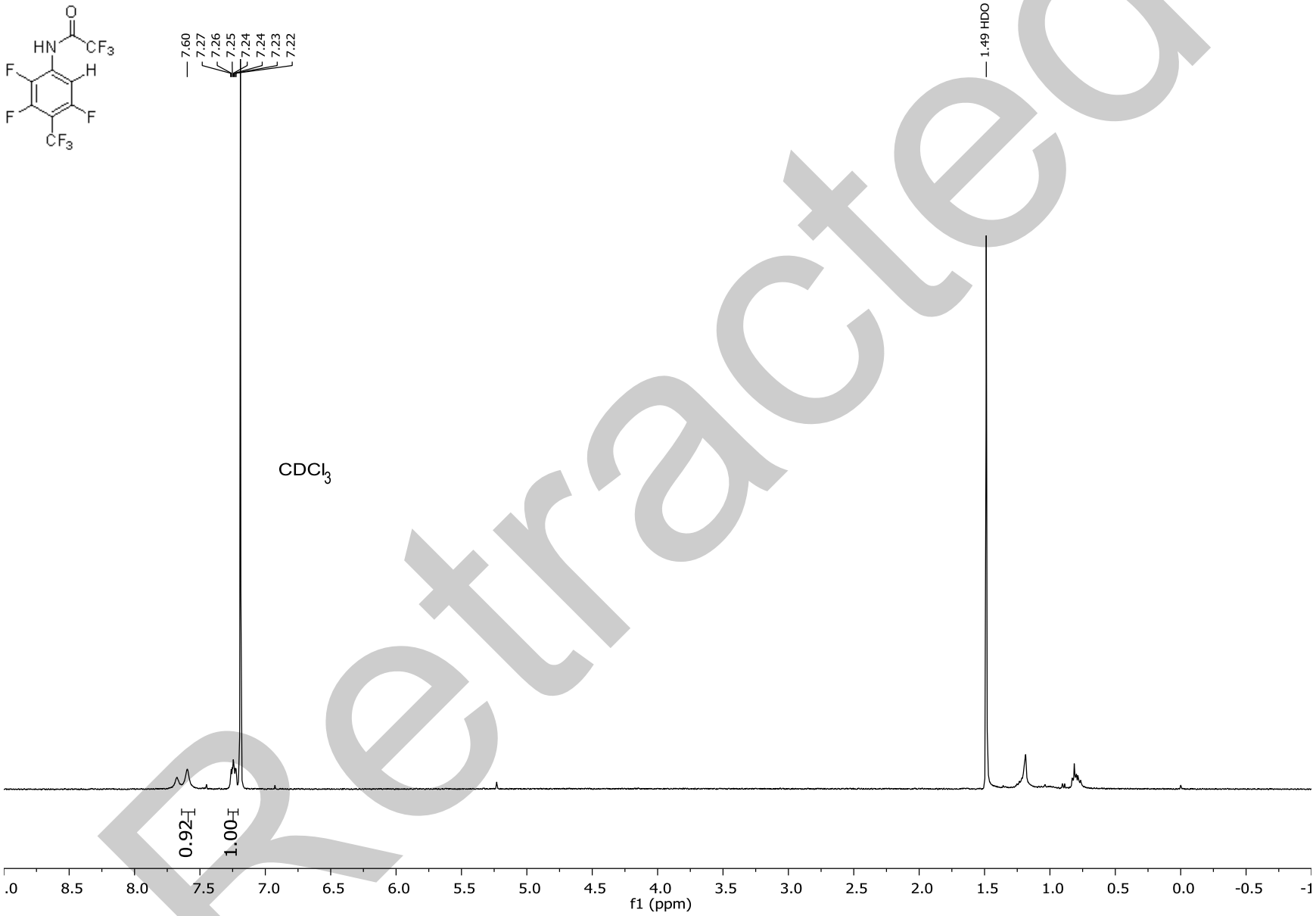
6e' methyl 2,3,6-trifluoro-4-propionamidobenzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



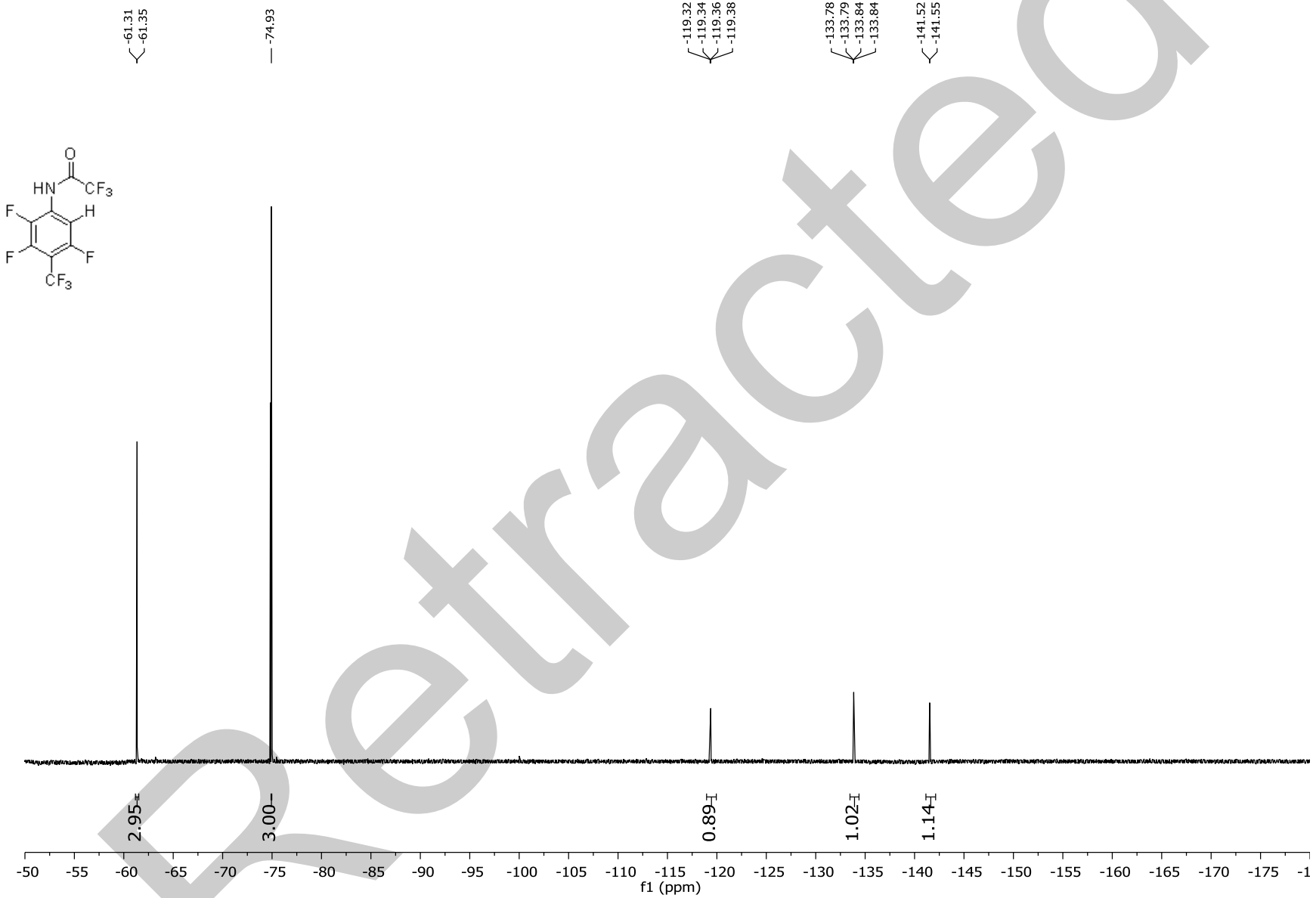
6e' methyl 2,3,6-trifluoro-4-propionamidobenzoate ^{13}C NMR (101 MHz, Acetone-d_6)



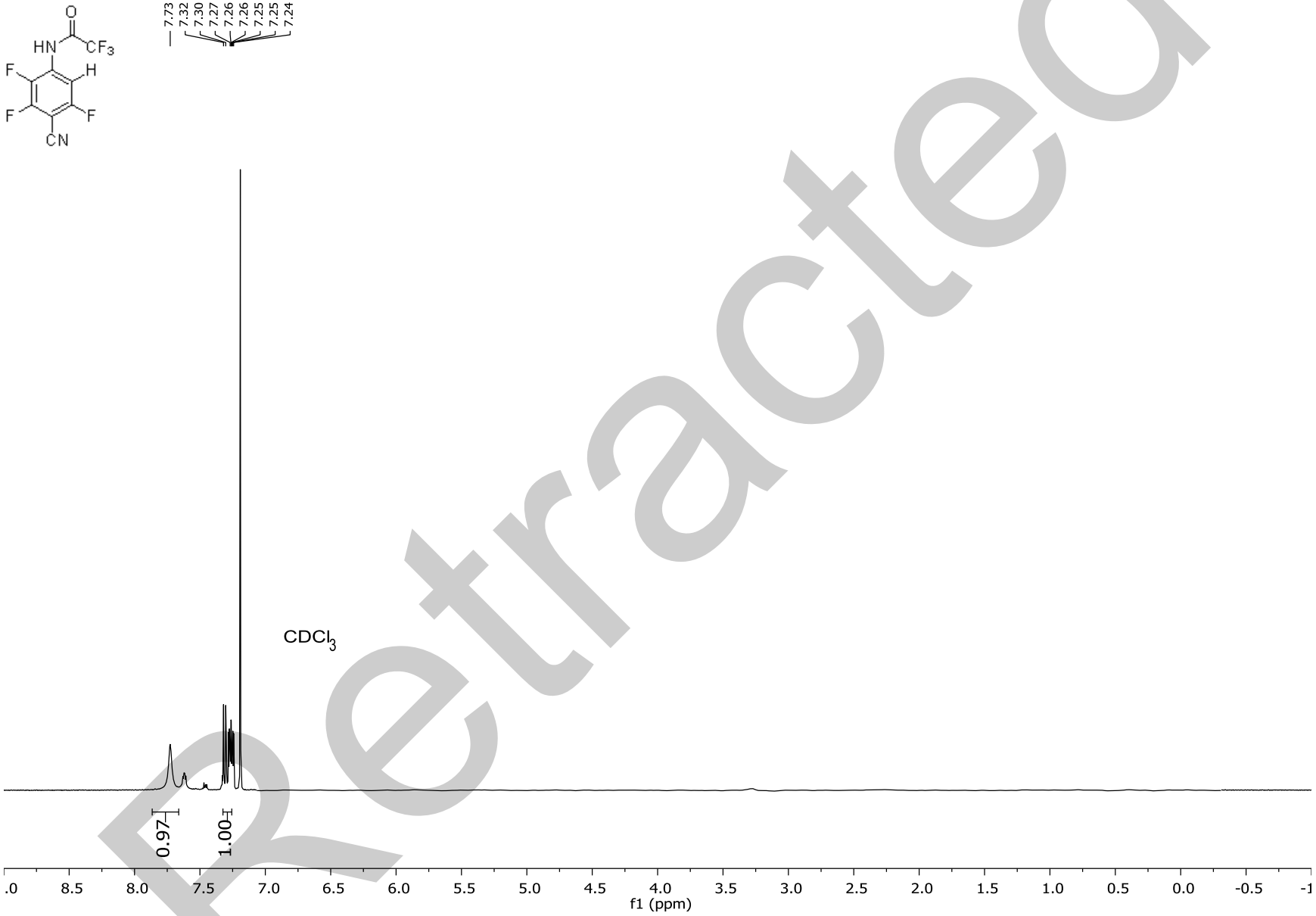
6g' 2,2,2-trifluoro-N-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



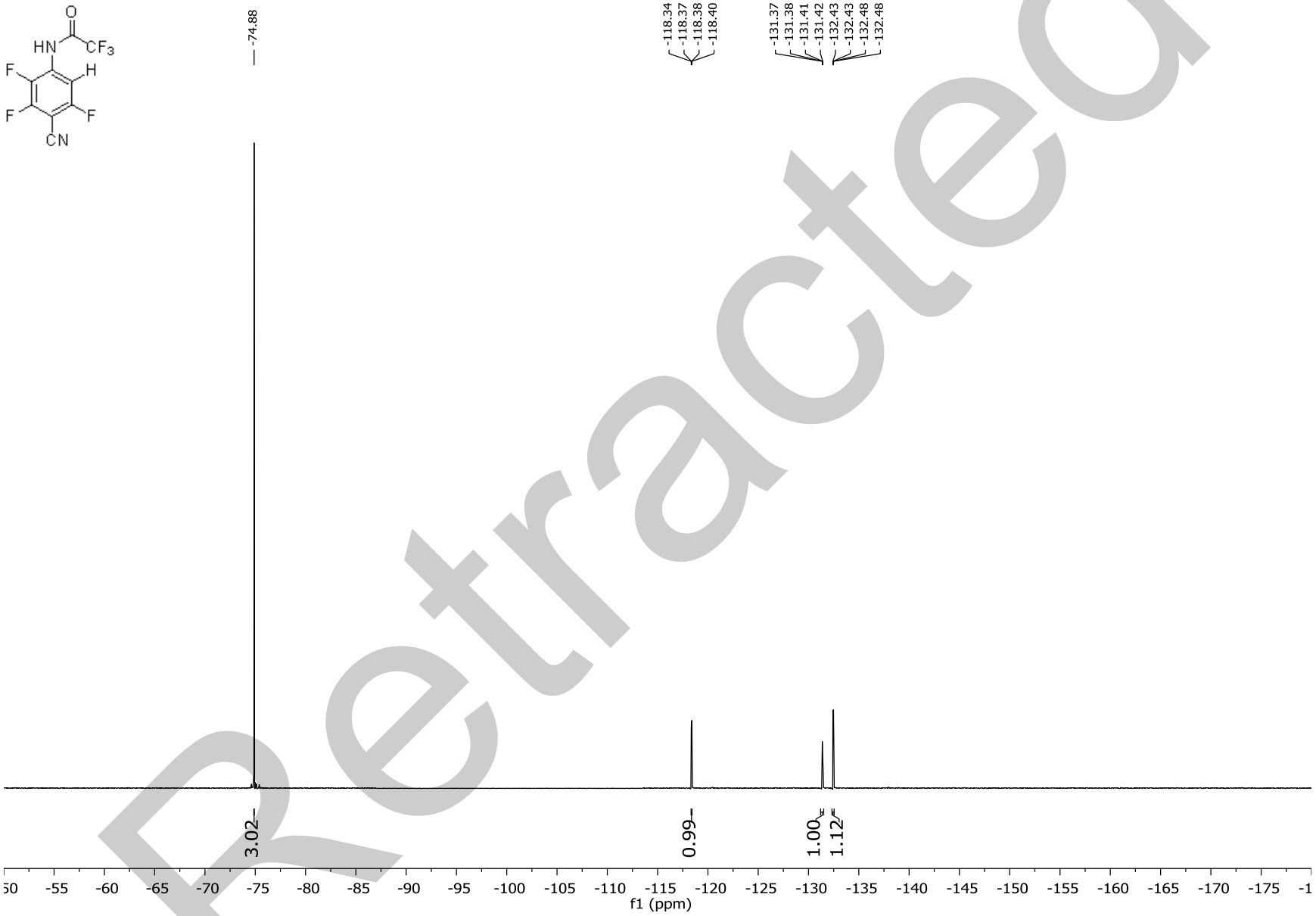
6g' 2,2,2-trifluoro-N-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



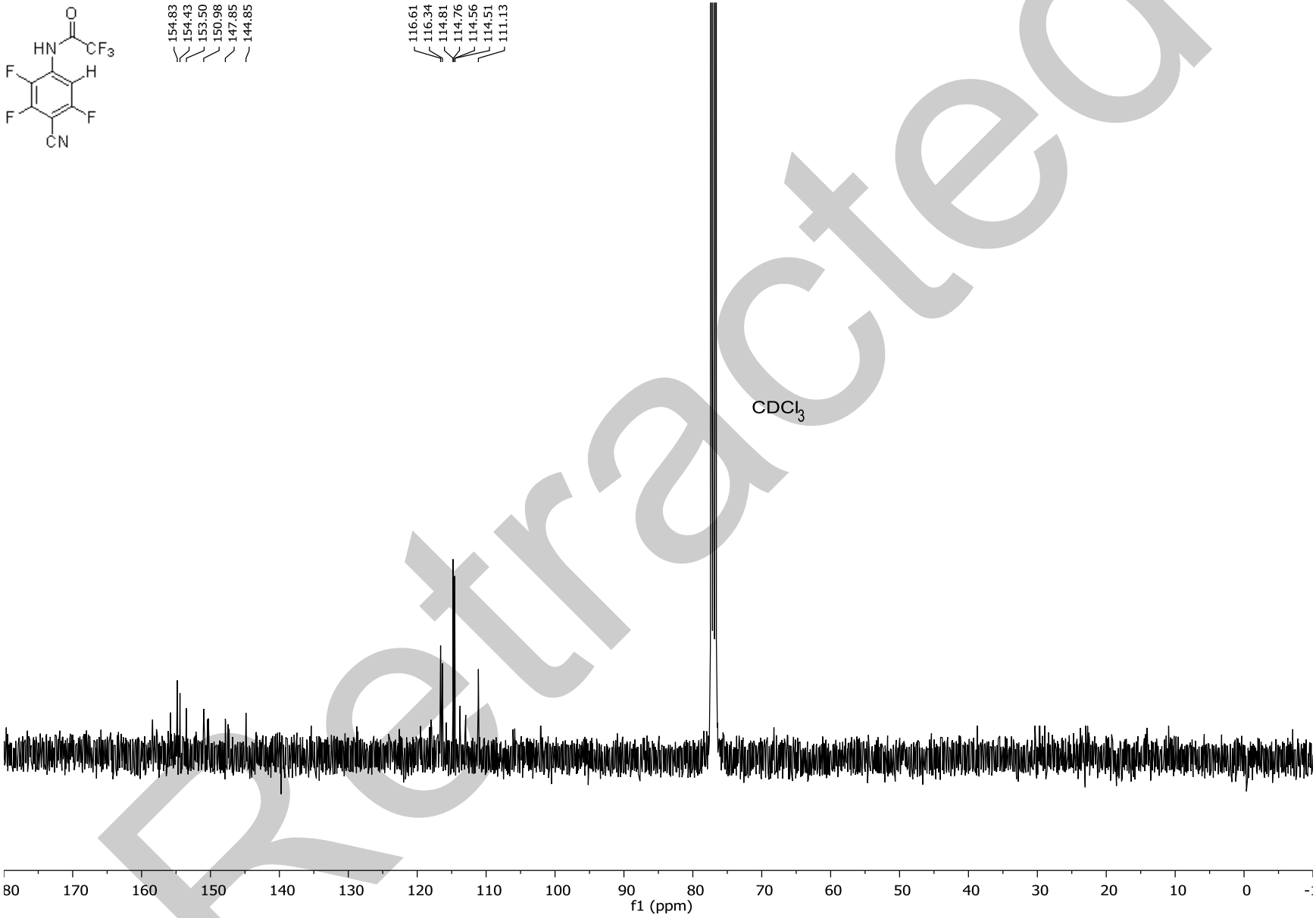
6h' *N*-(4-cyano-2,3,5-trifluorophenyl)-2,2,2-trifluoroacetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



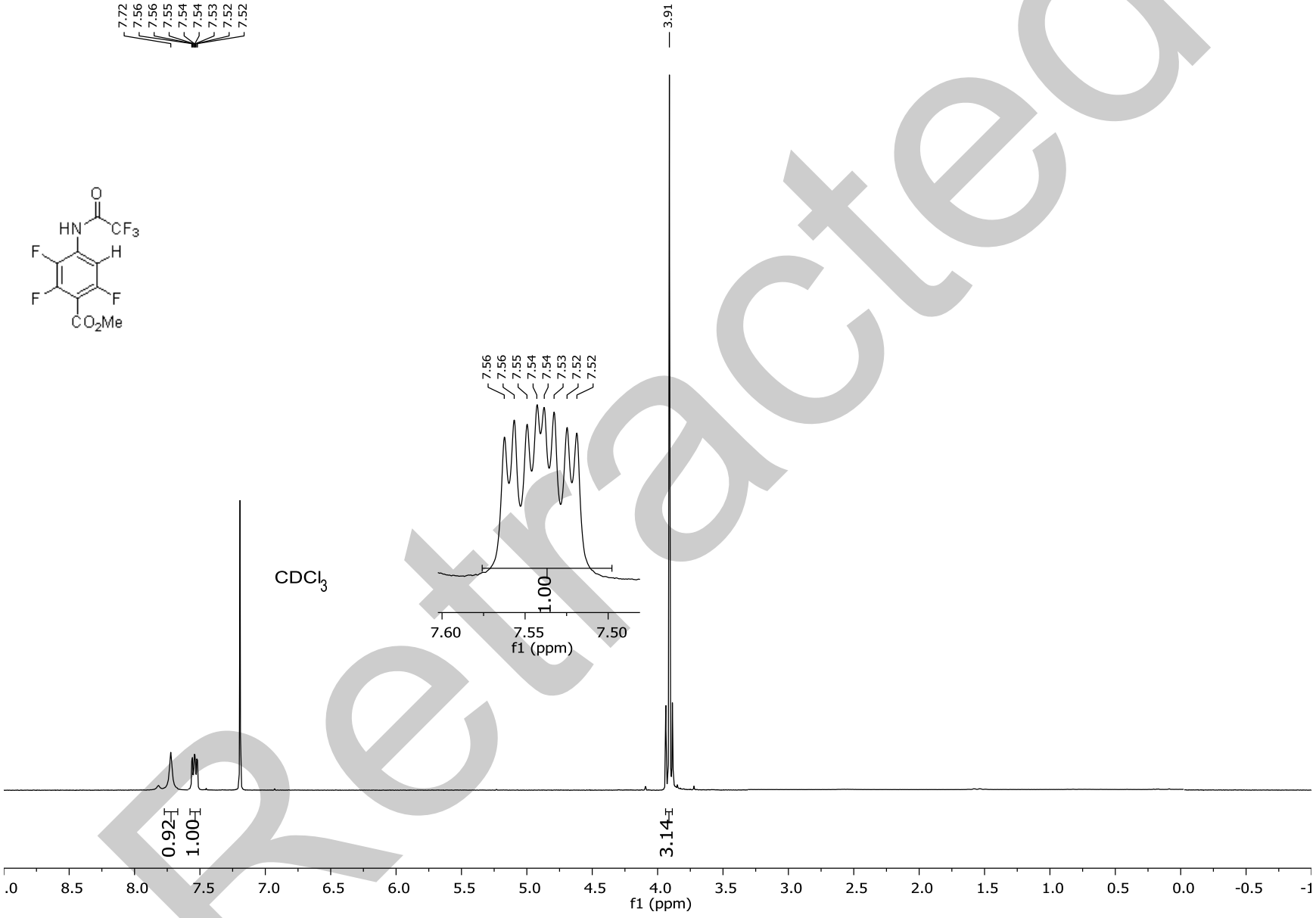
6h' *N*-(4-cyano-2,3,5-trifluorophenyl)-2,2,2-trifluoroacetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



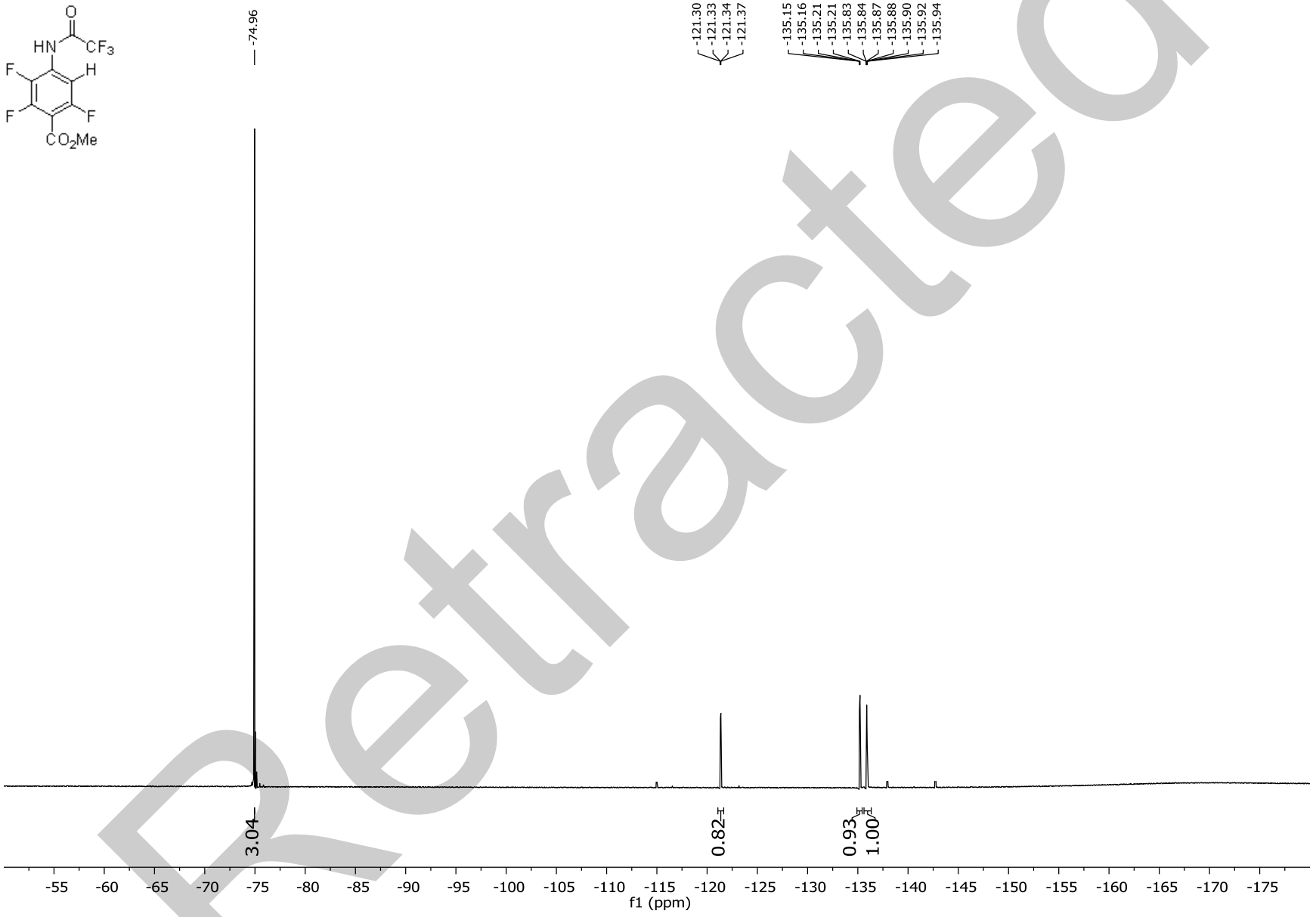
6h' *N*-(4-cyano-2,3,5-trifluorophenyl)-2,2,2-trifluoroacetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



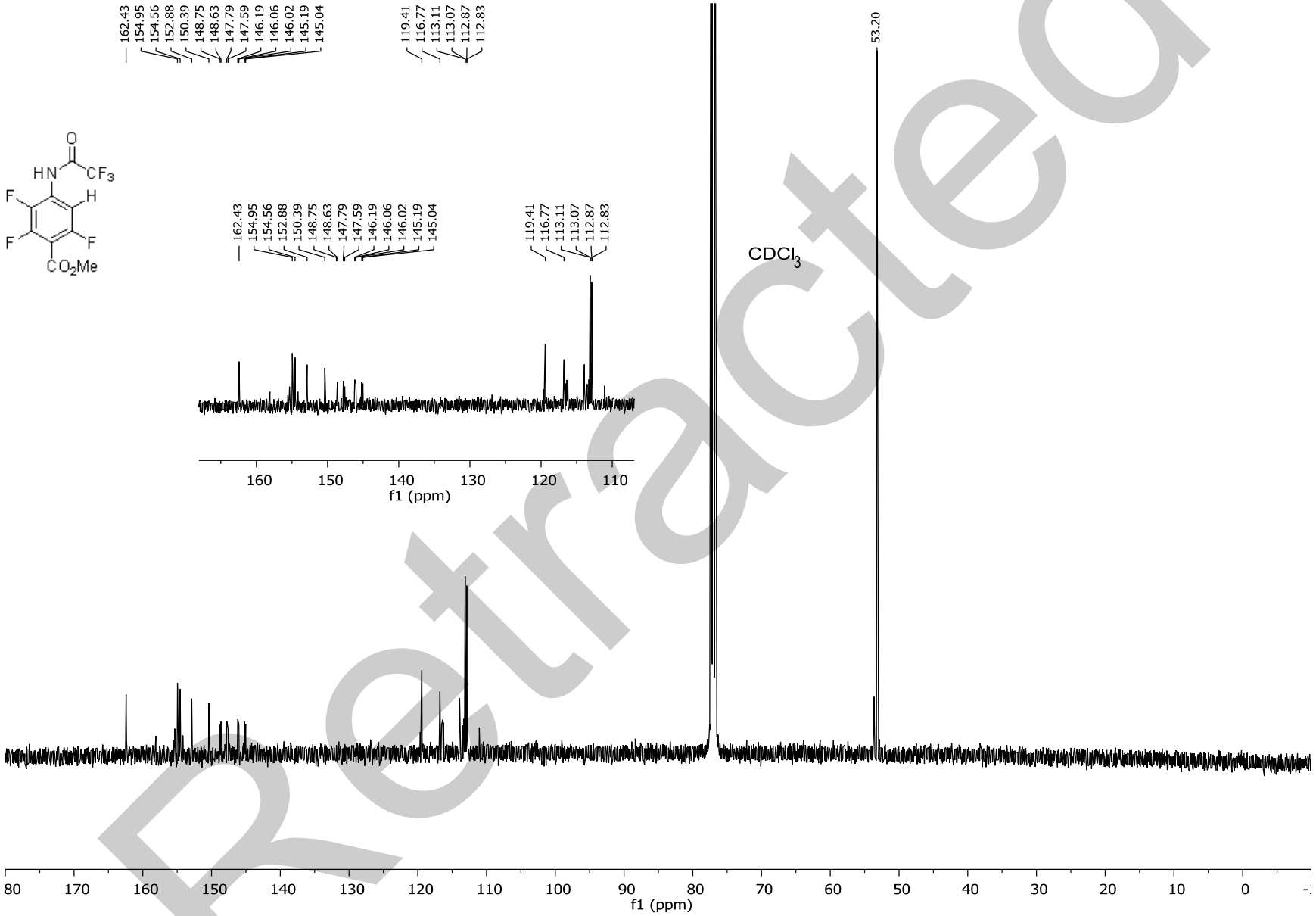
6i' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



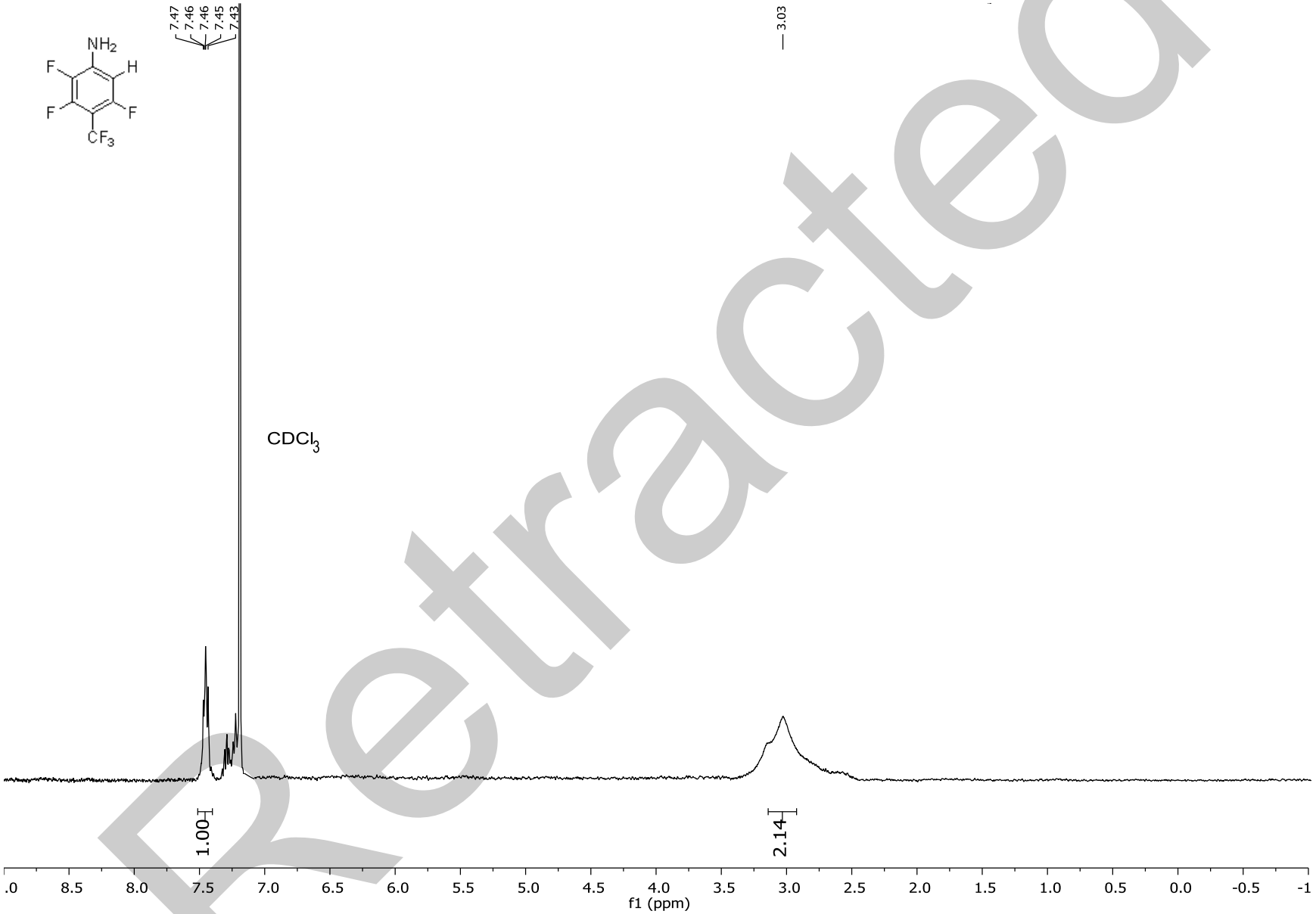
6i' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



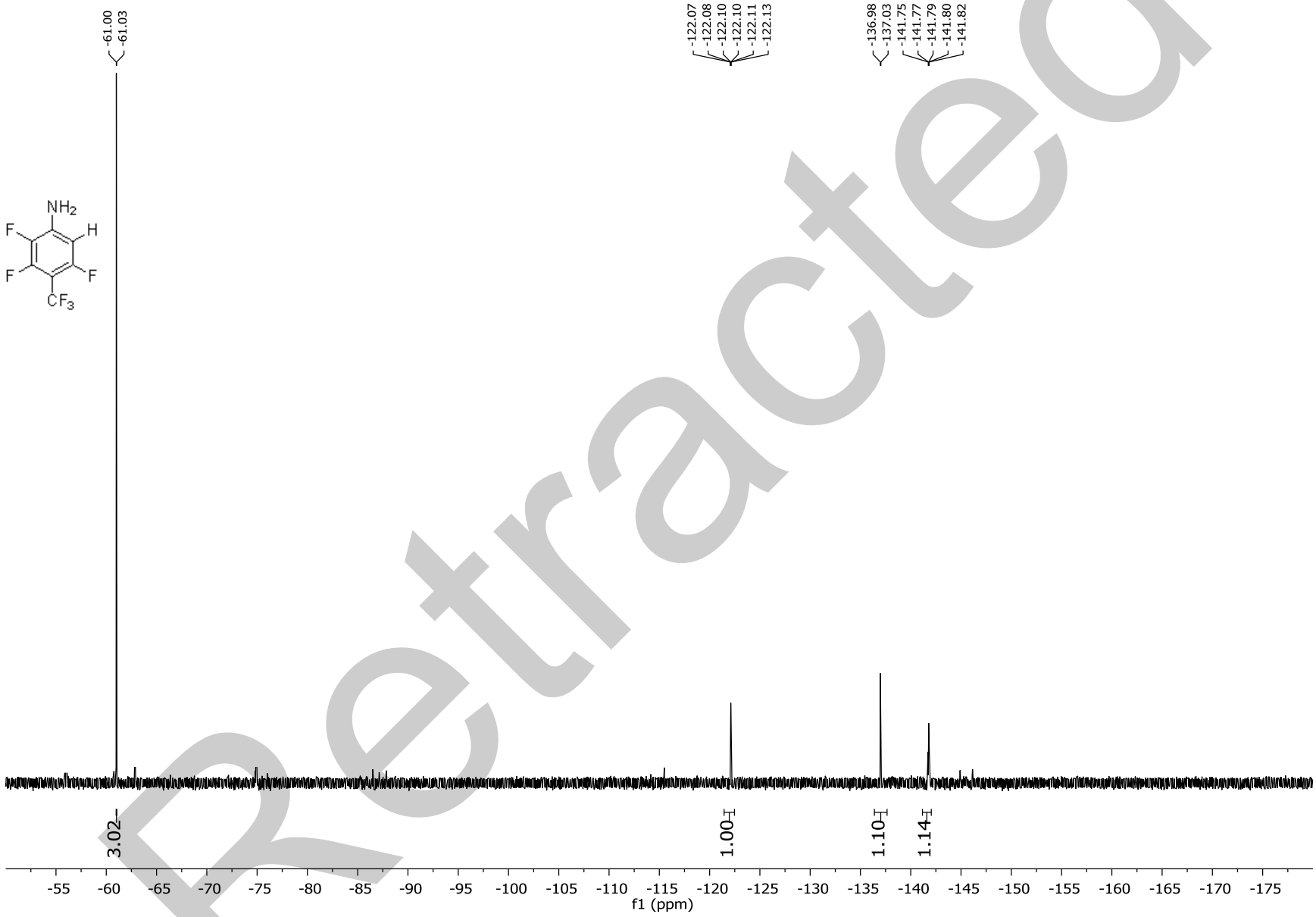
6i' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



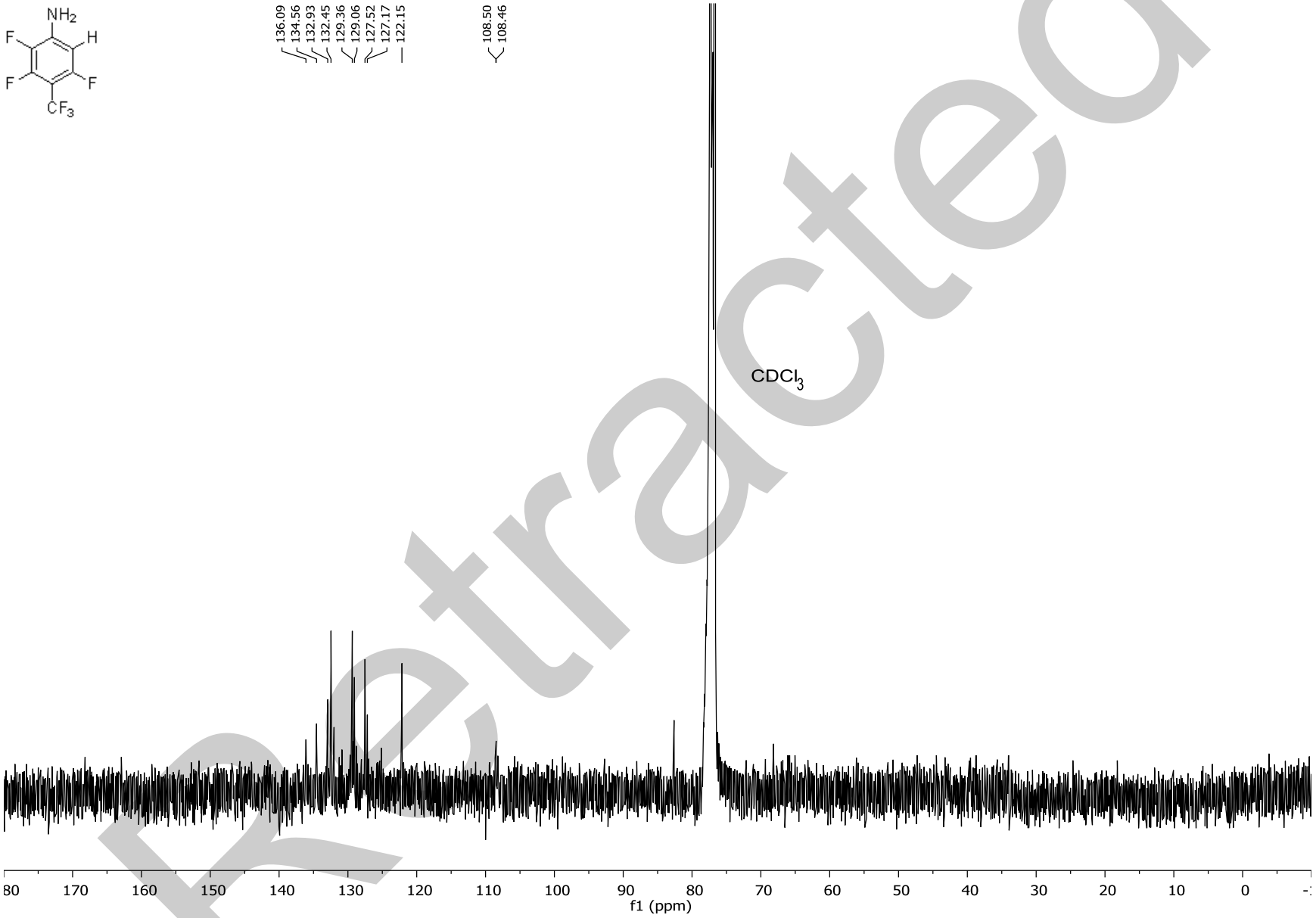
6l’ 2,3,5-trifluoro-4-(trifluoromethyl)aniline ^{1}H NMR (400 MHz, Chloroform-*d*)



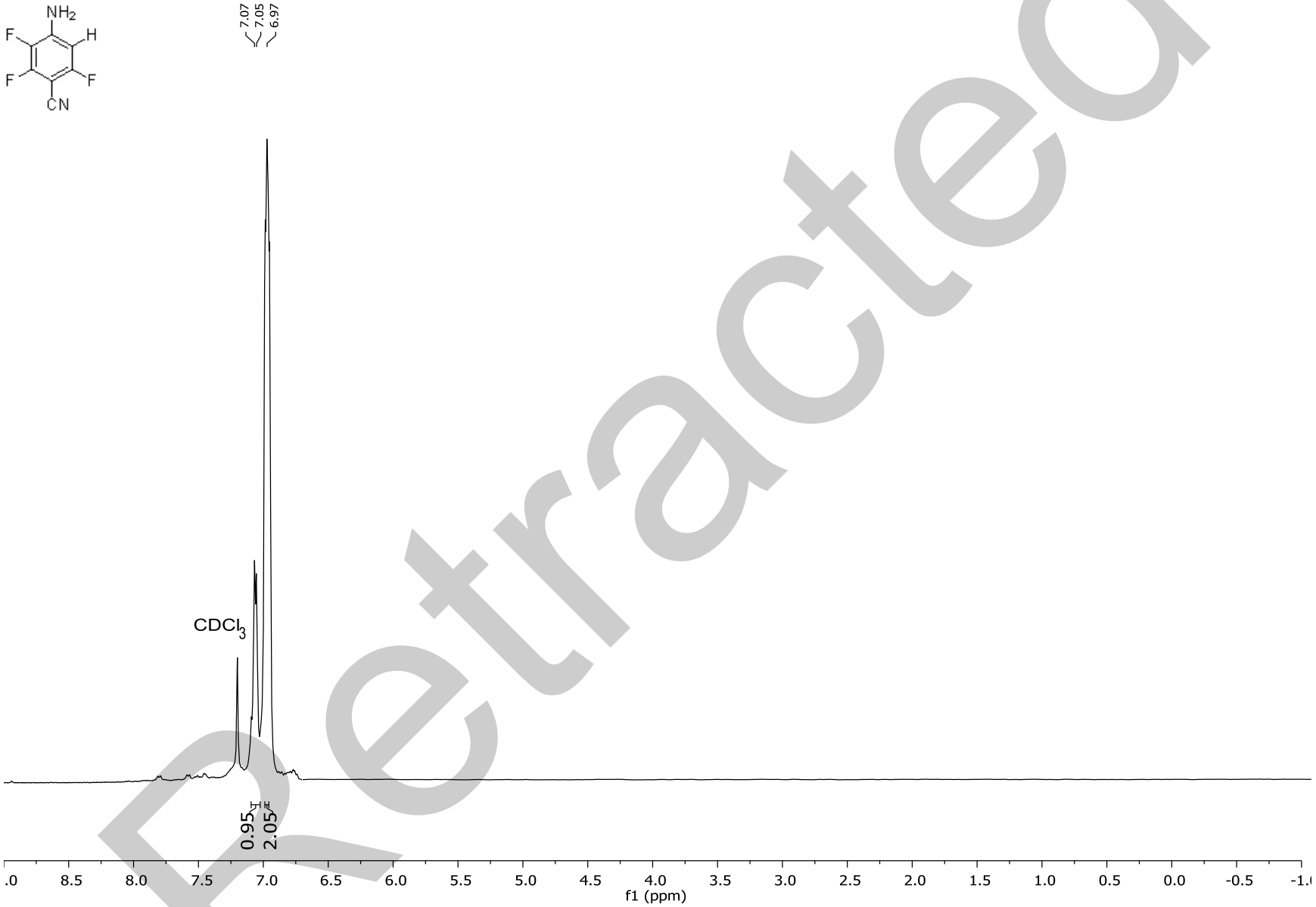
6l’ 2,3,5-trifluoro-4-(trifluoromethyl)aniline ^{19}F NMR (376 MHz, Chloroform-*d*)



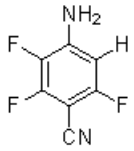
6l’ 2,3,5-trifluoro-4-(trifluoromethyl)aniline ^{13}C NMR (101 MHz, Chloroform-*d*)



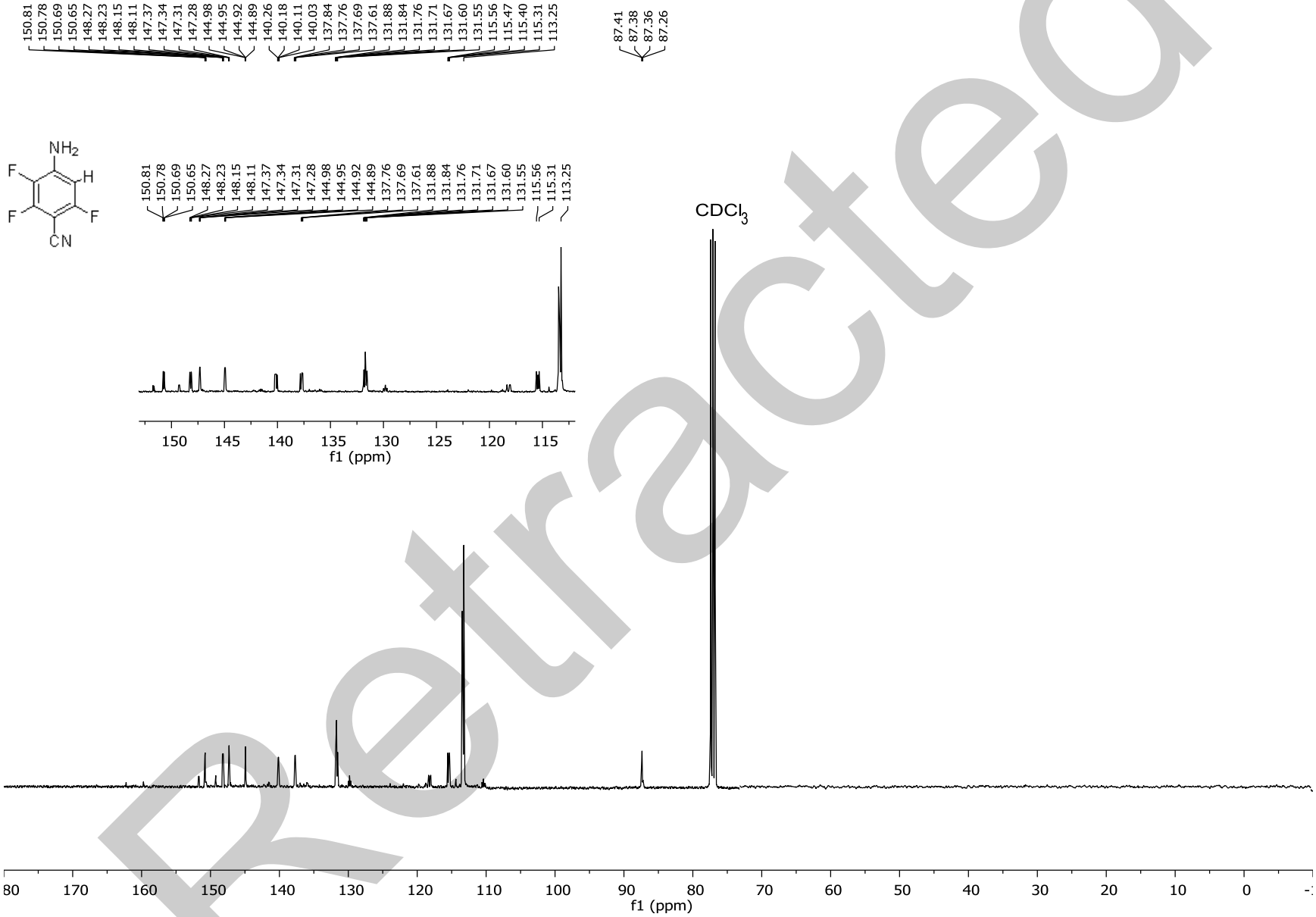
6m' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



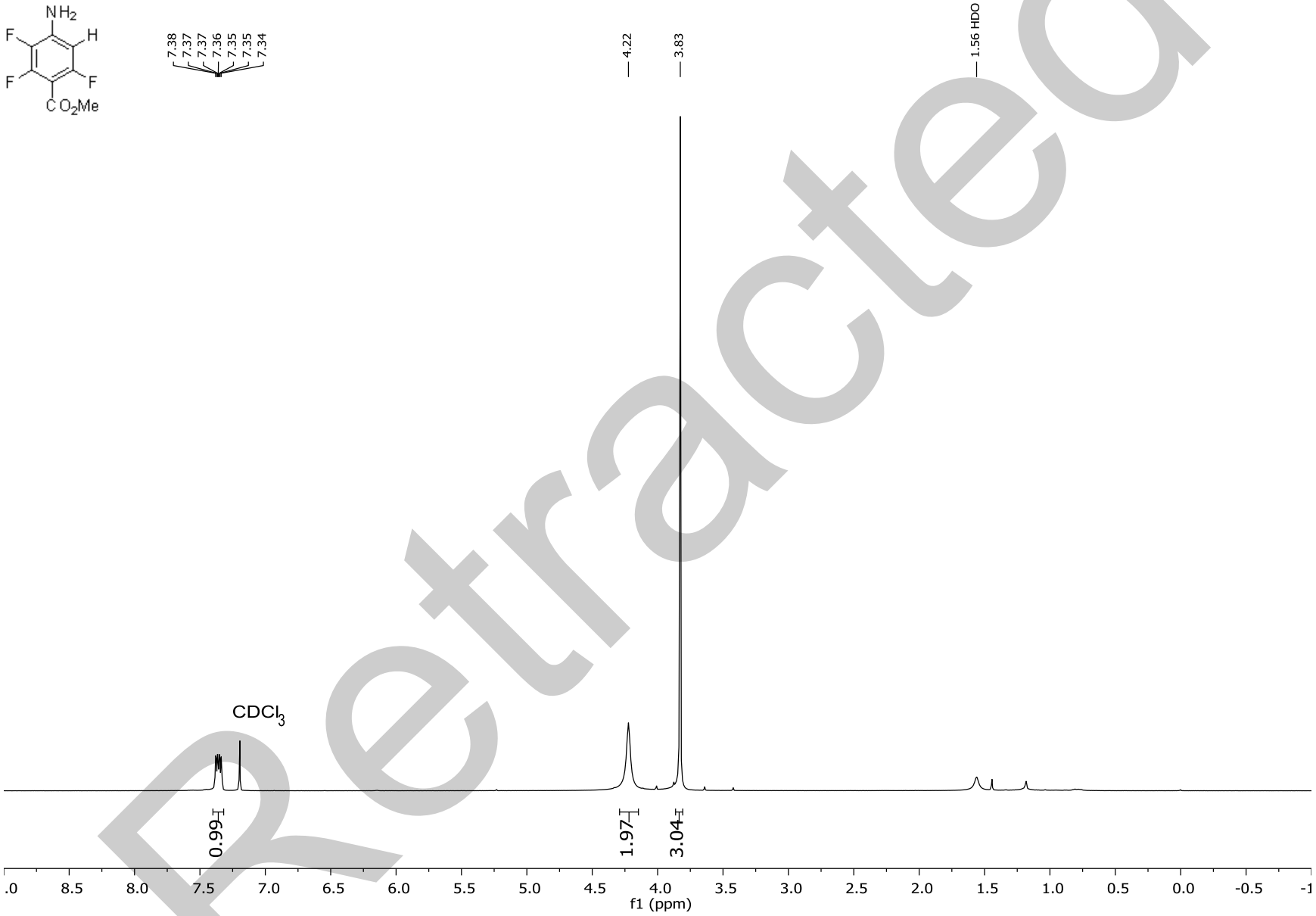
6m' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



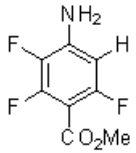
6m' 2,2,2-trifluoro-*N*-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



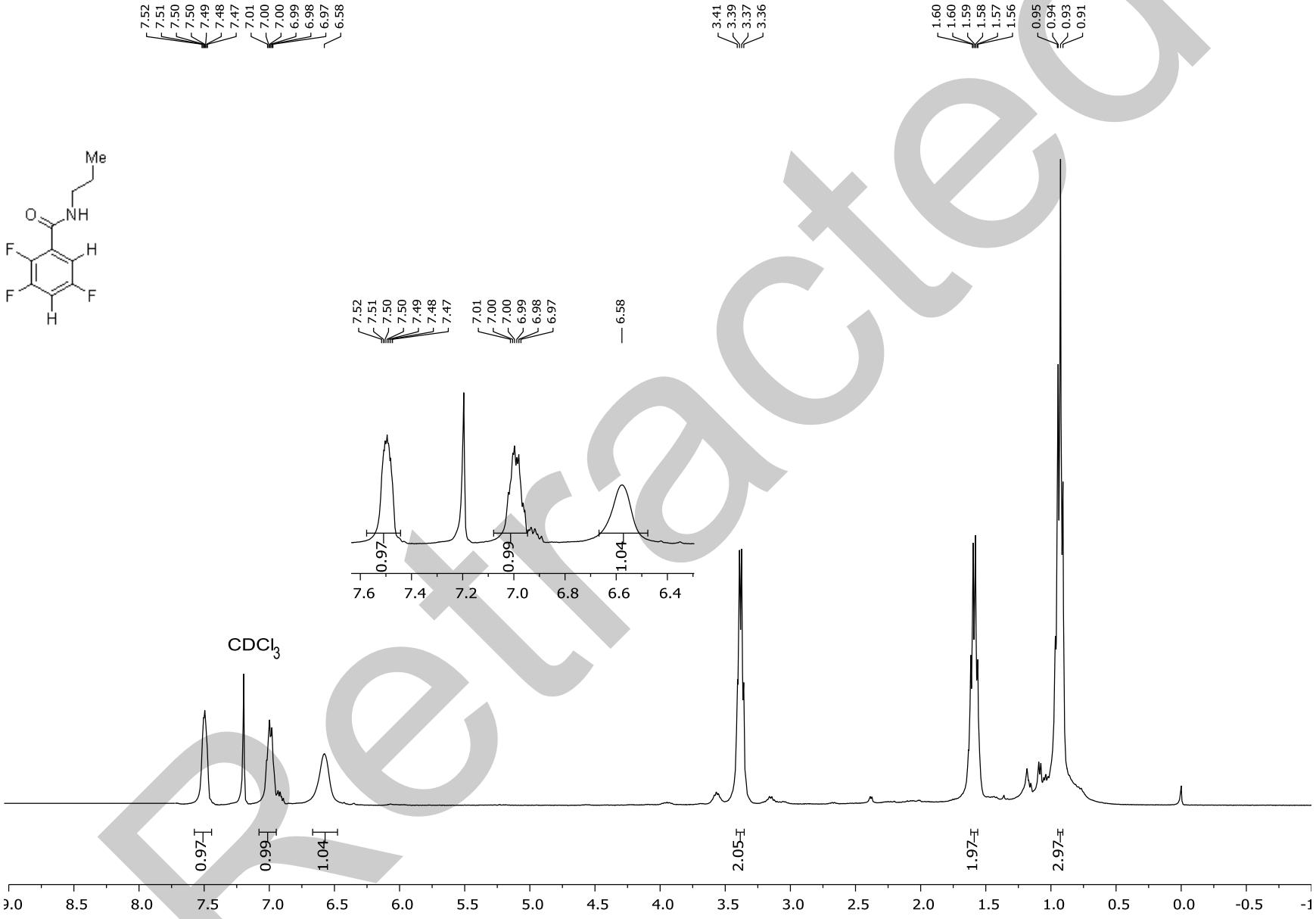
6n' methyl 4-amino-2,3,6-trifluorobenzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



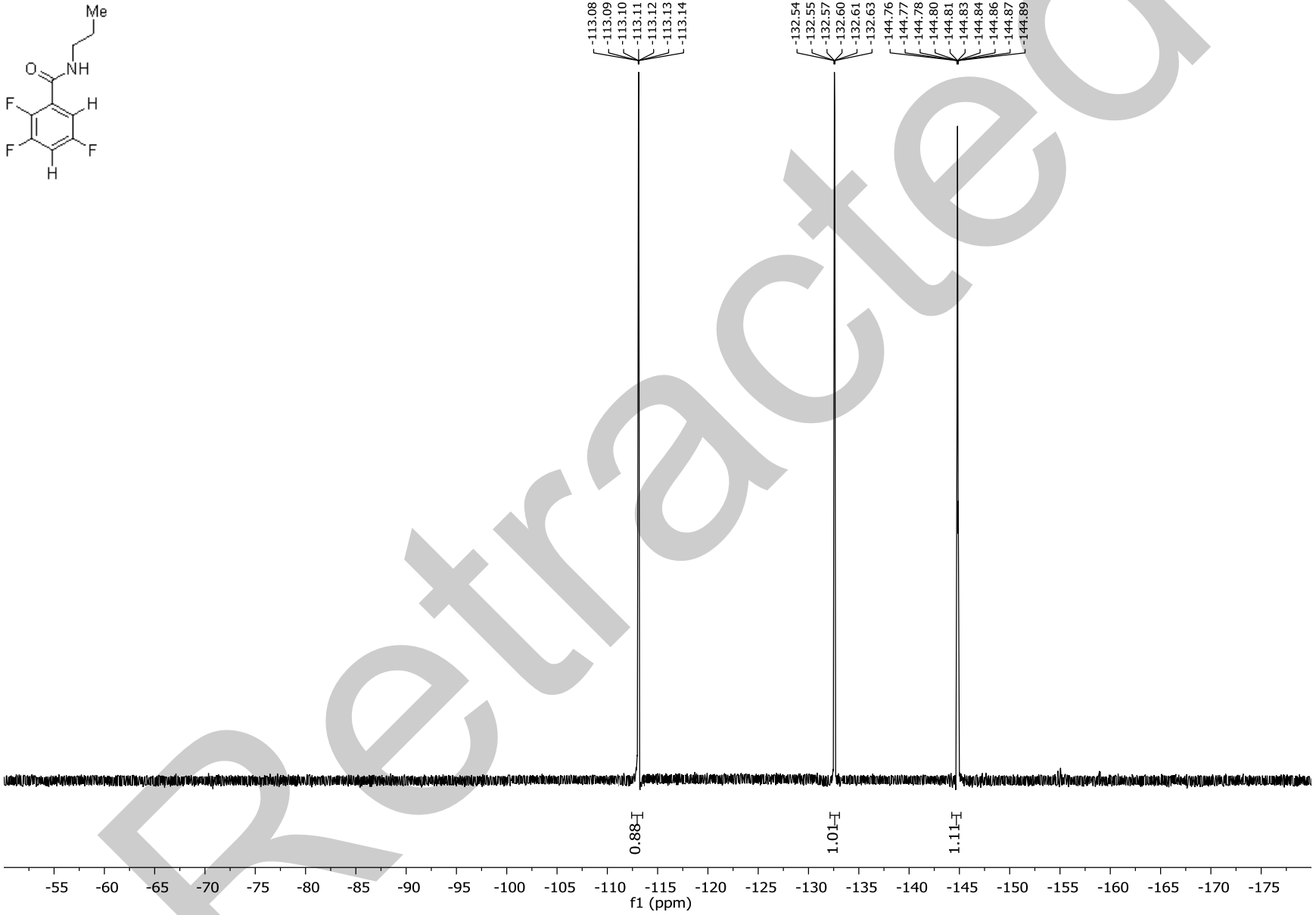
6n' methyl 4-amino-2,3,6-trifluorobenzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



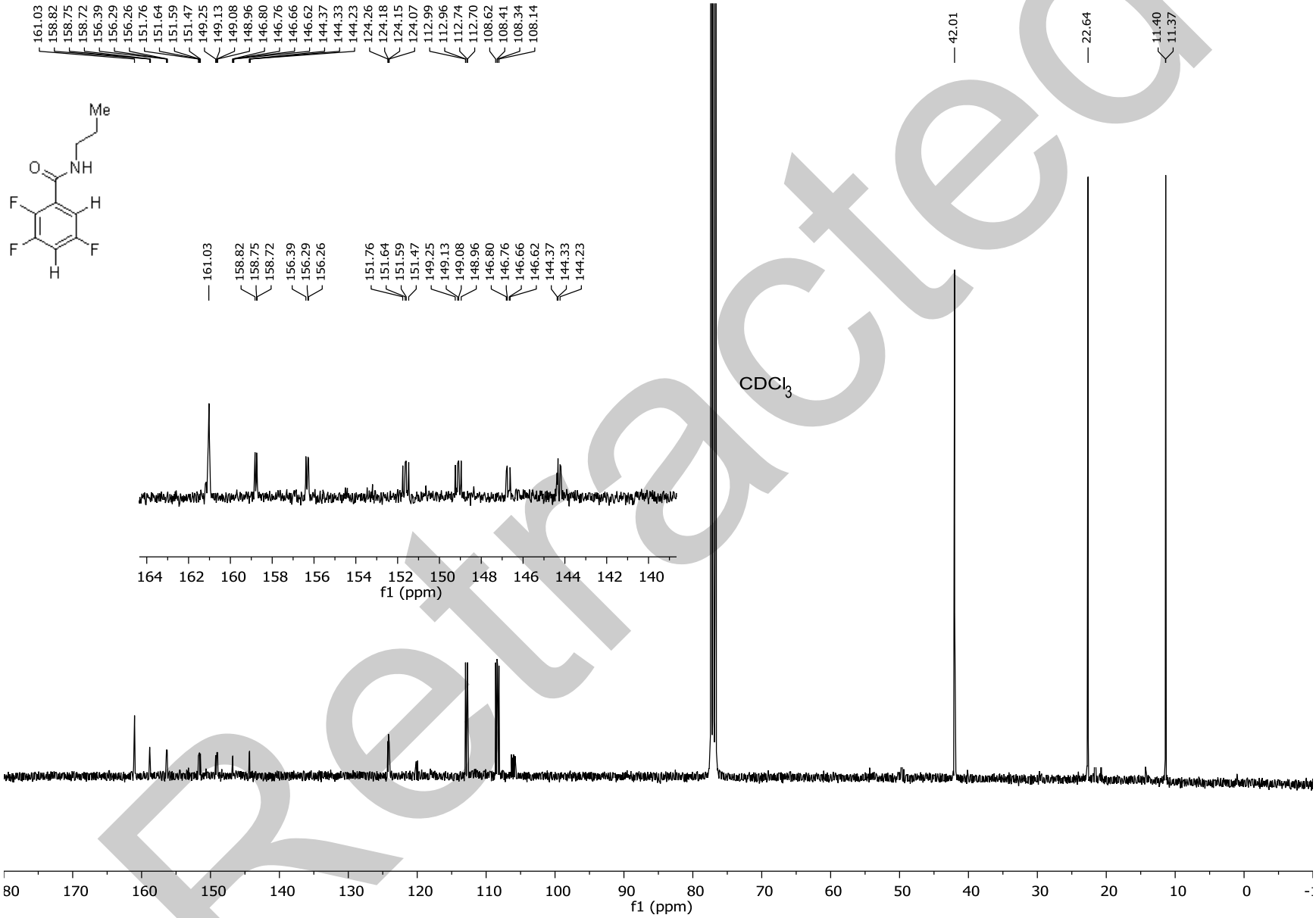
7a' 2,3,5-trifluoro-*N*-propylbenzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



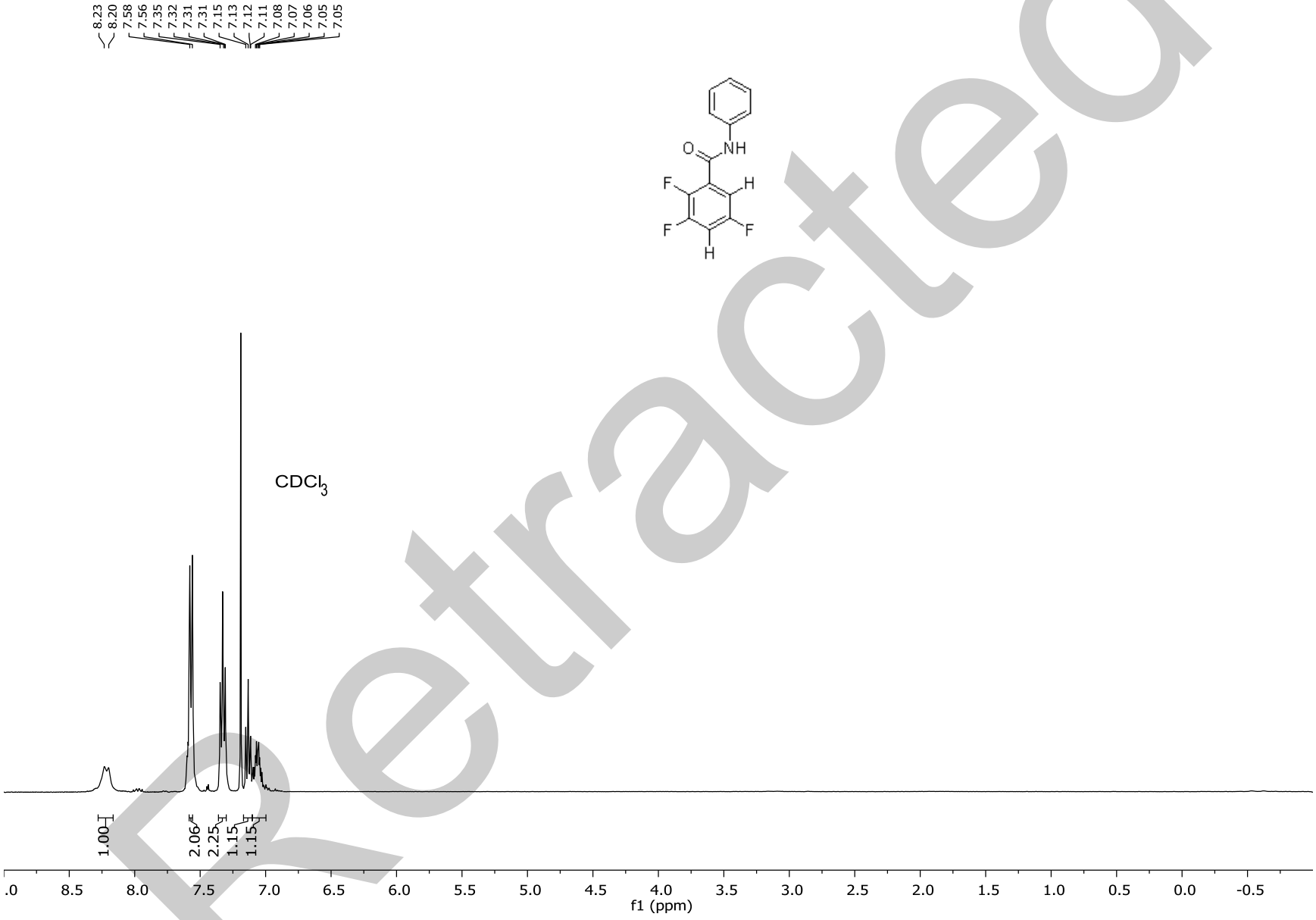
7a' 2,3,5-trifluoro-*N*-propylbenzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



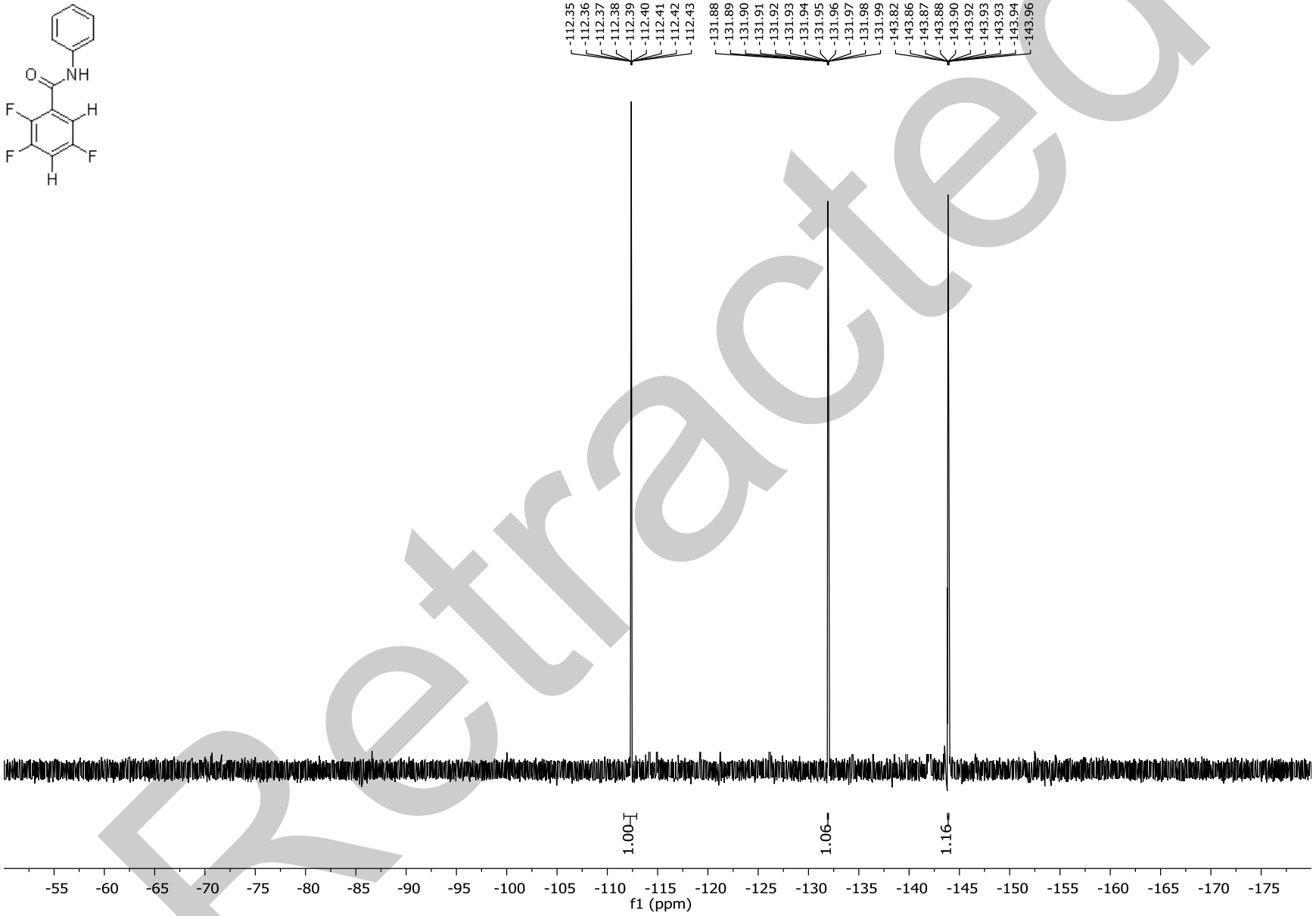
7a' 2,3,5-trifluoro-*N*-propylbenzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



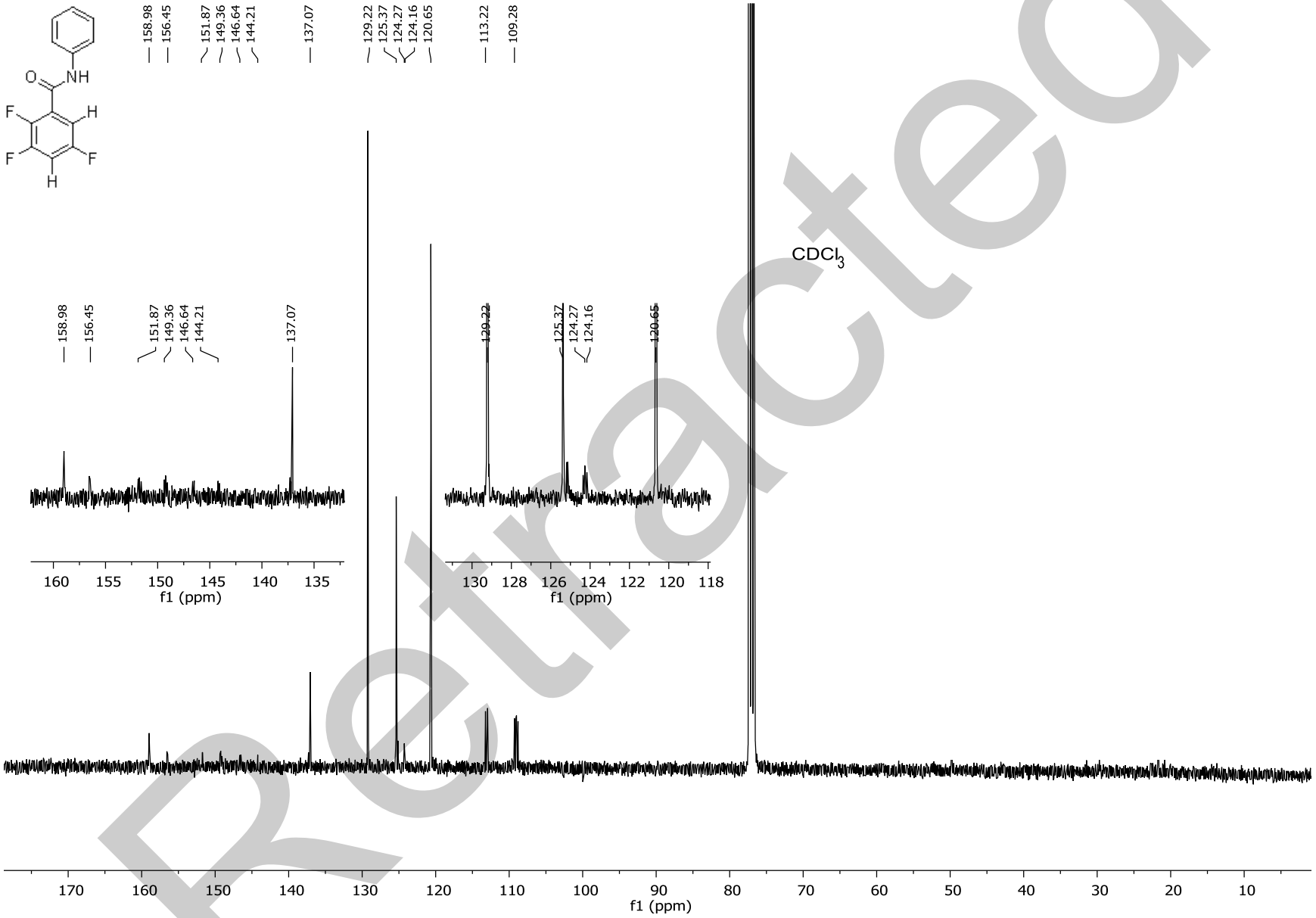
7b’ 2,3,5-trifluoro-*N*-phenylbenzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



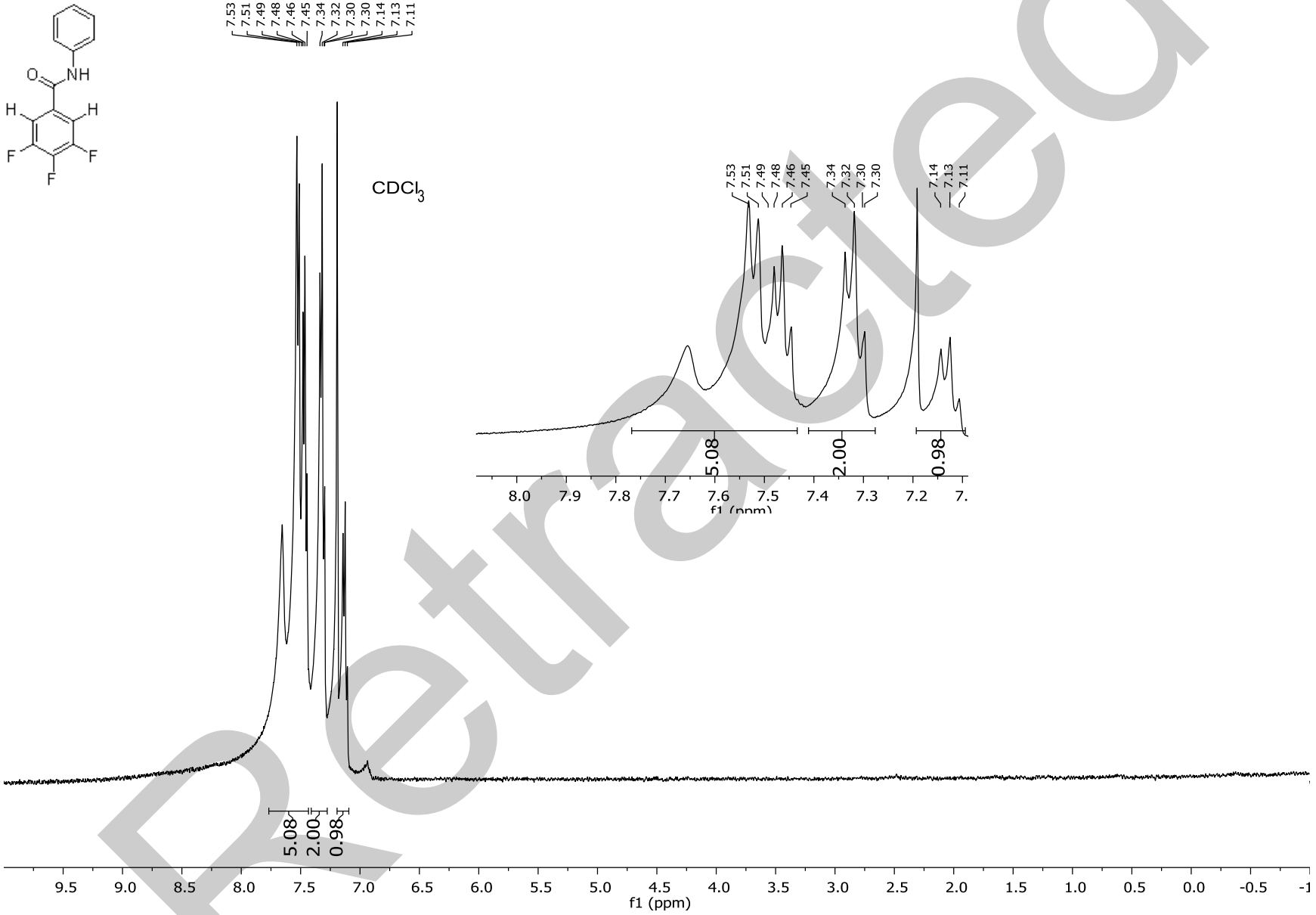
7b' 2,3,5-trifluoro-*N*-phenylbenzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



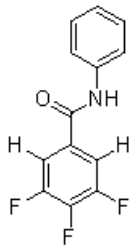
7b' 2,3,5-trifluoro-*N*-phenylbenzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



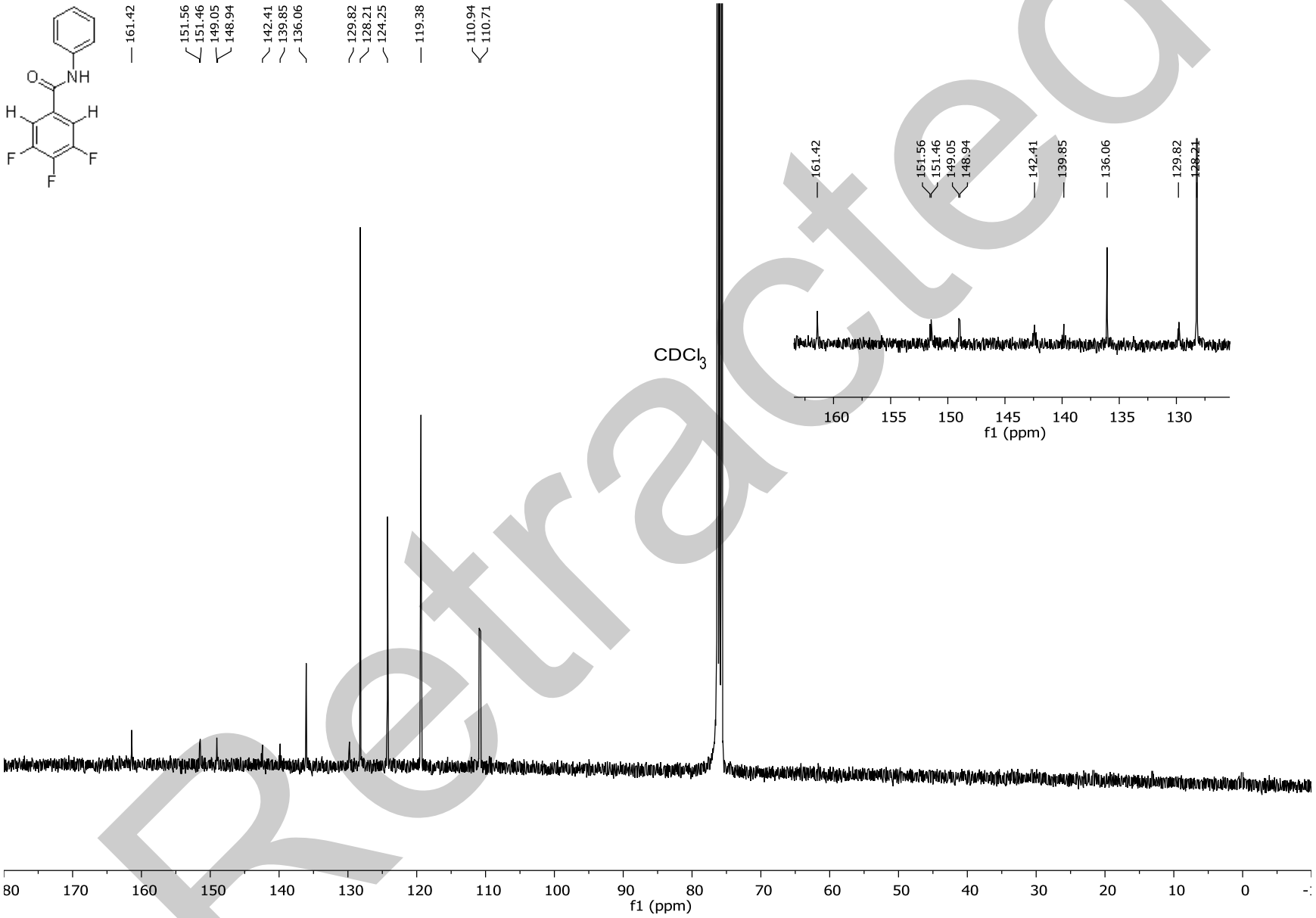
7b' 2,3,5-trifluoro-*N*-phenylbenzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



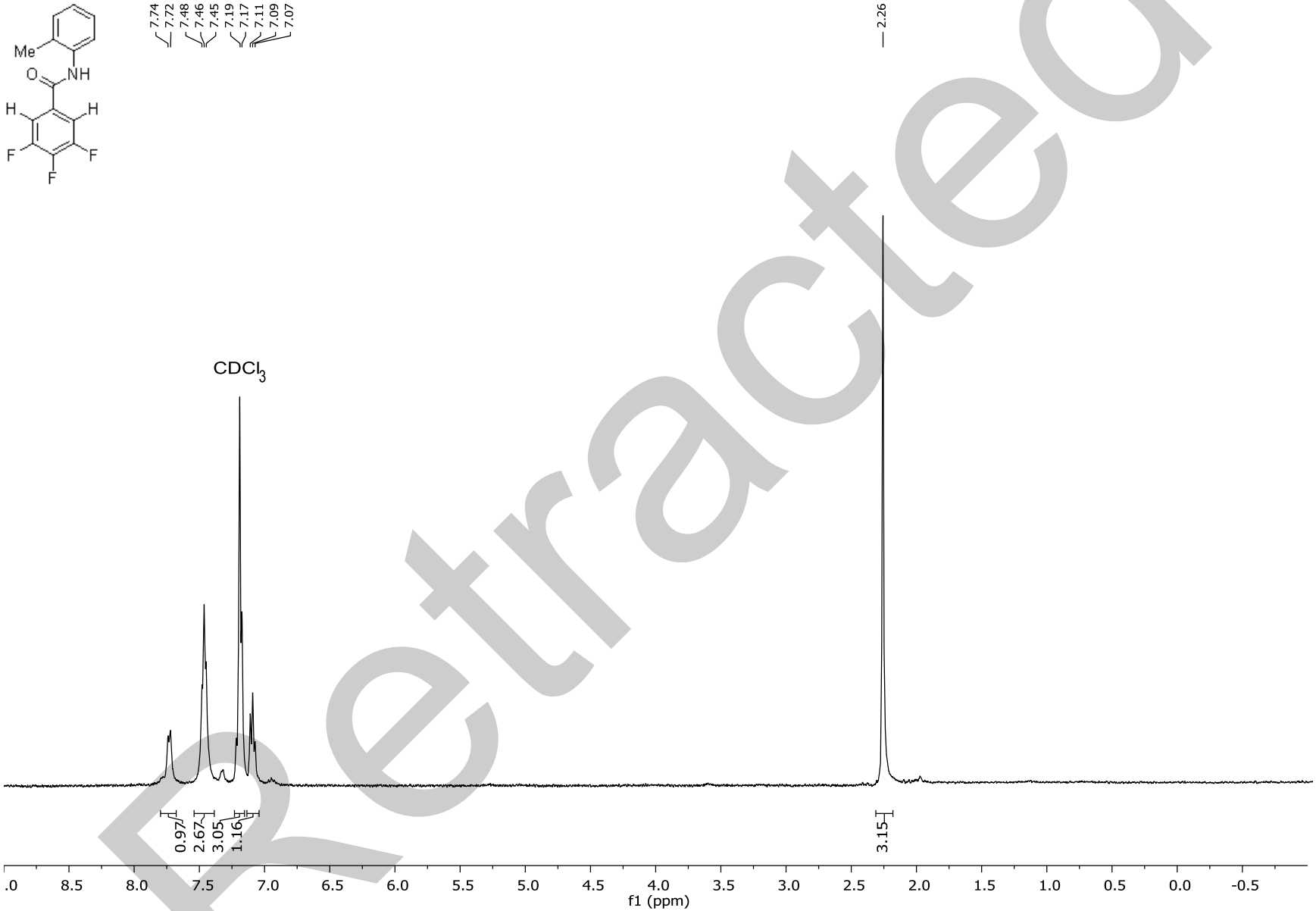
7b' 2,3,5-trifluoro-*N*-phenylbenzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



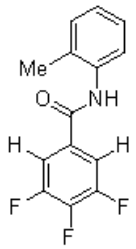
7b' 2,3,5-trifluoro-*N*-phenylbenzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



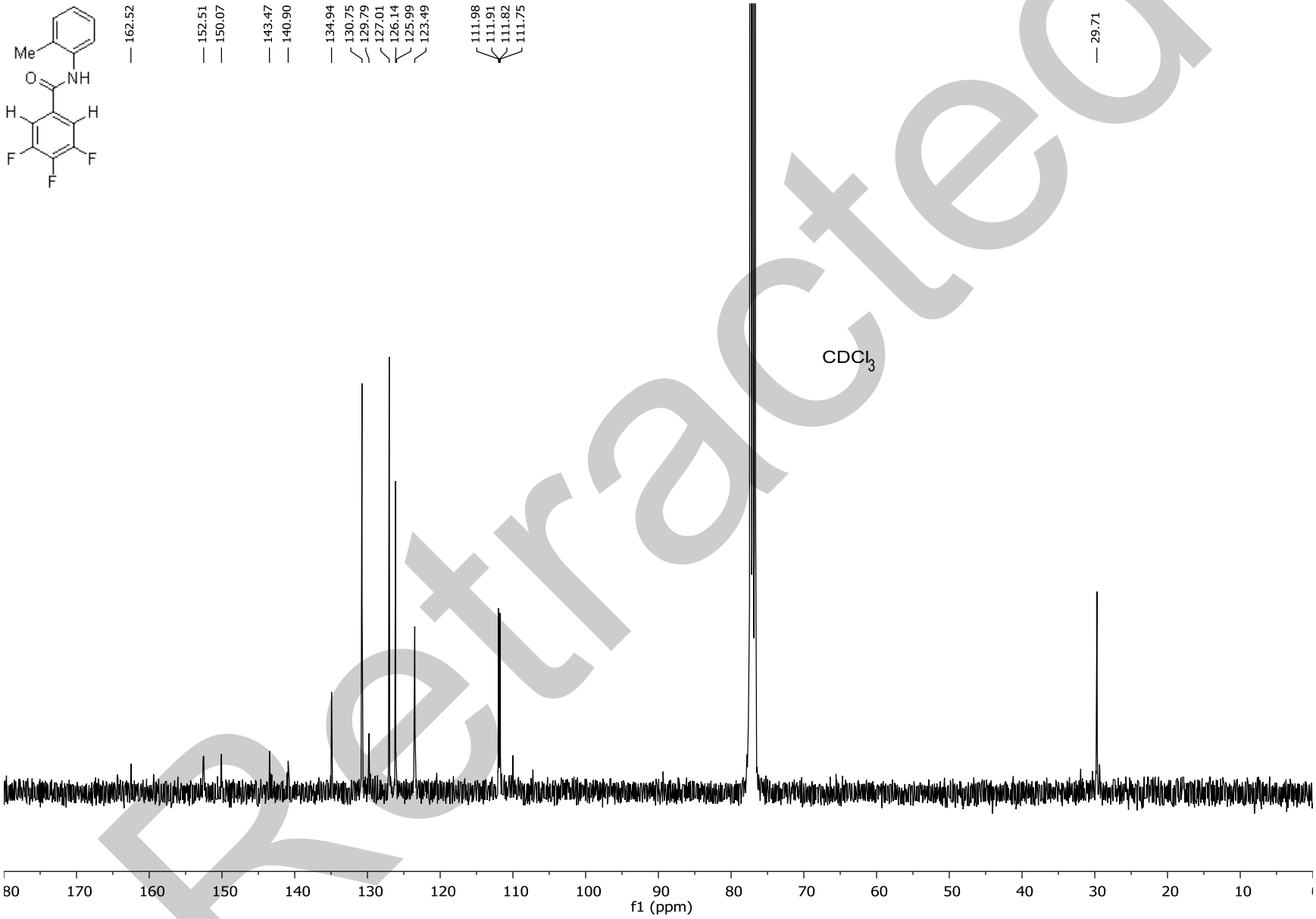
7c' 3,4,5-trifluoro-*N*-(*o*-tolyl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



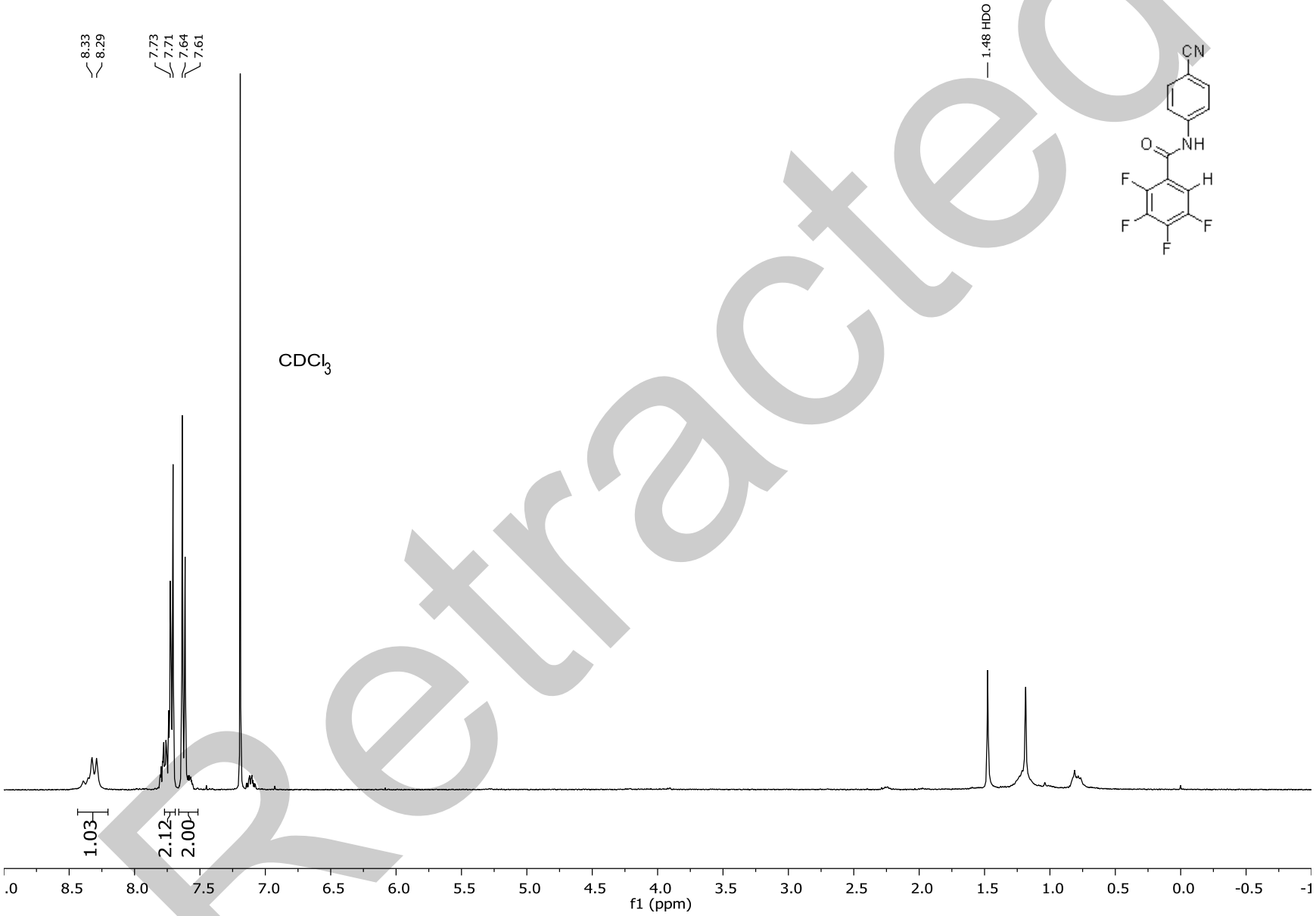
7c' 3,4,5-trifluoro-*N*-(*o*-tolyl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



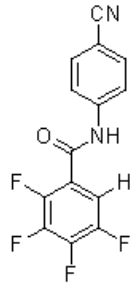
7c' 3,4,5-trifluoro-*N*-(o-tolyl)benzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



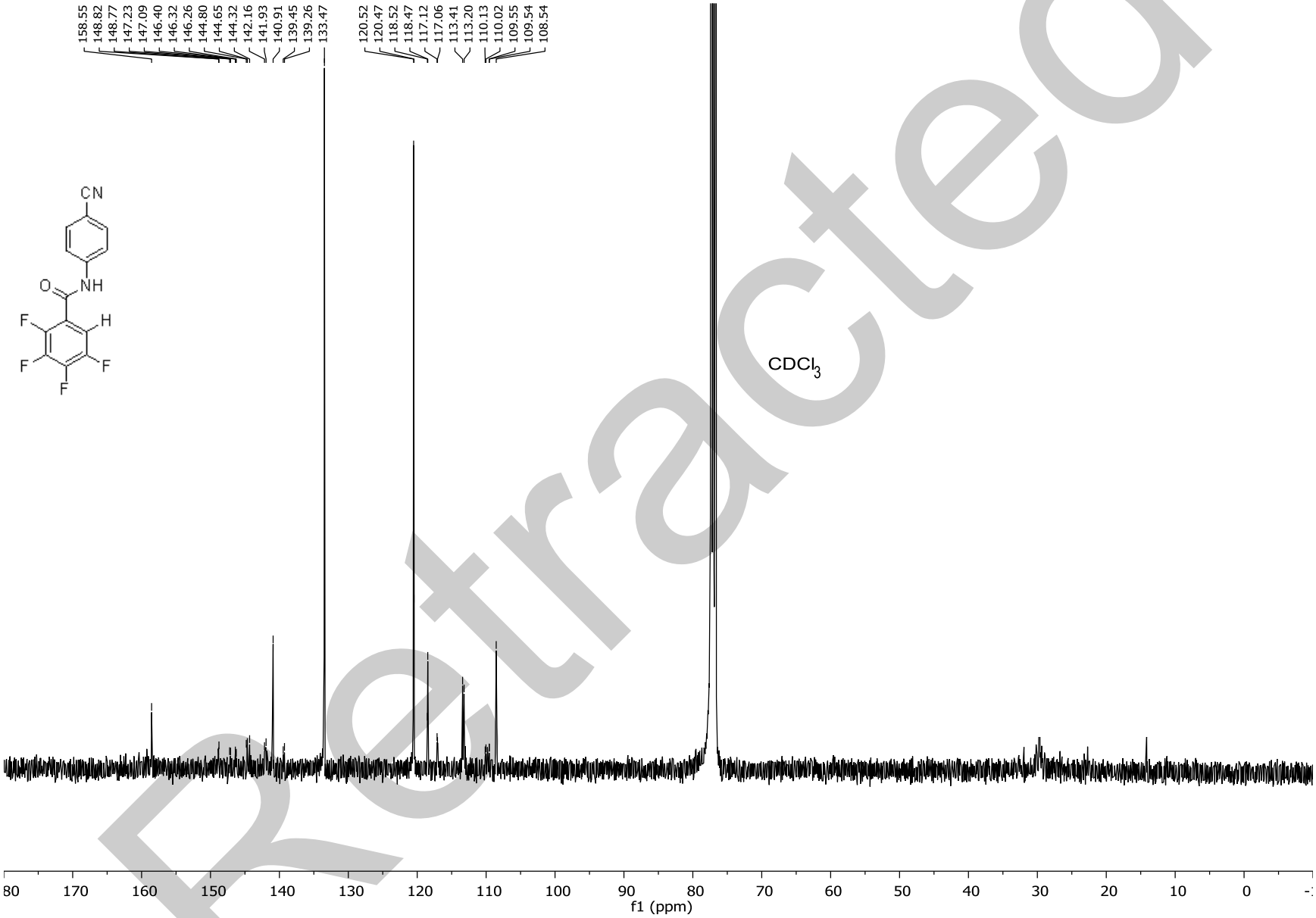
7d *N*-(4-cyanophenyl)-2,3,4,5-tetrafluorobenzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



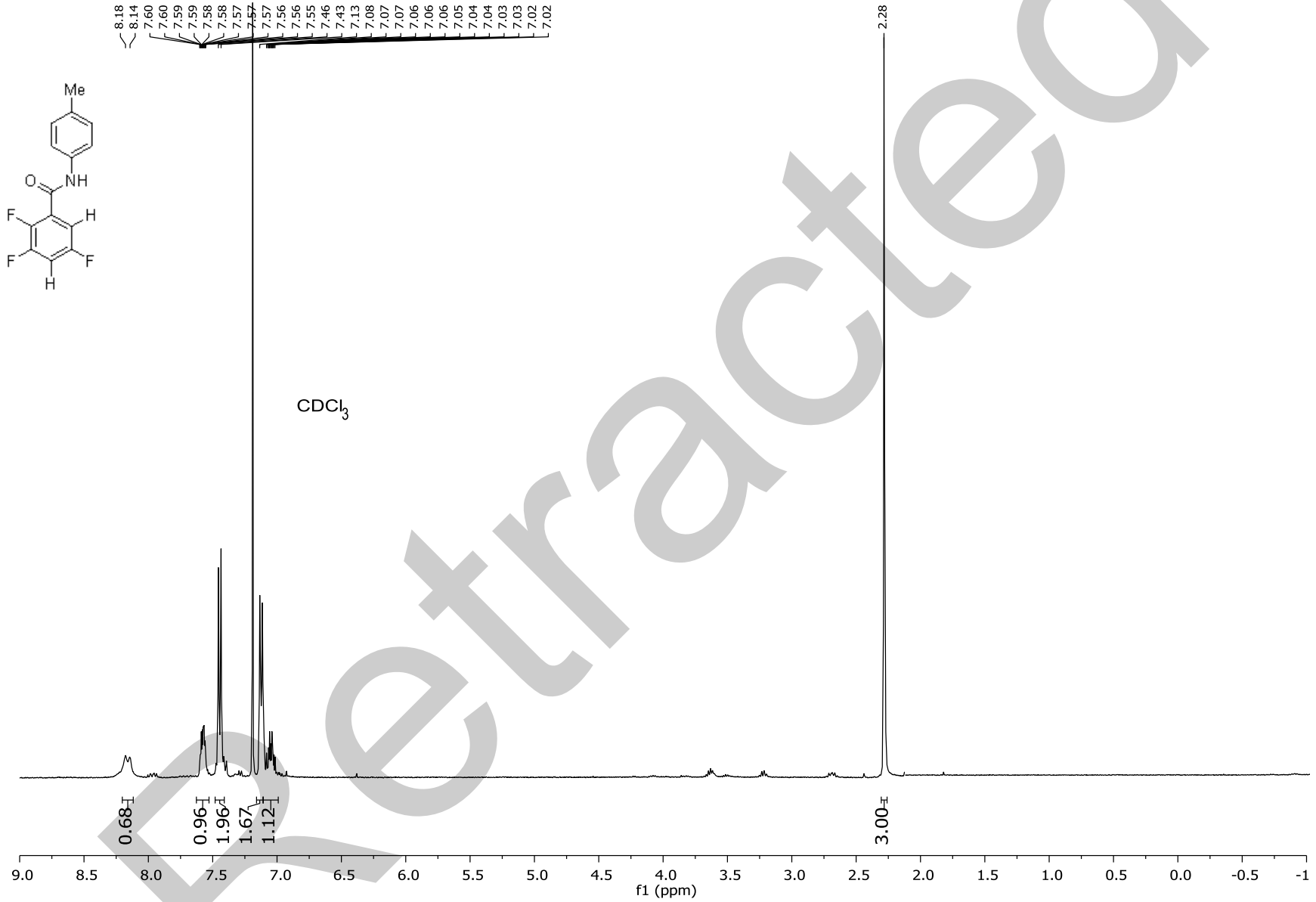
7d *N*-(4-cyanophenyl)-2,3,4,5-tetrafluorobenzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



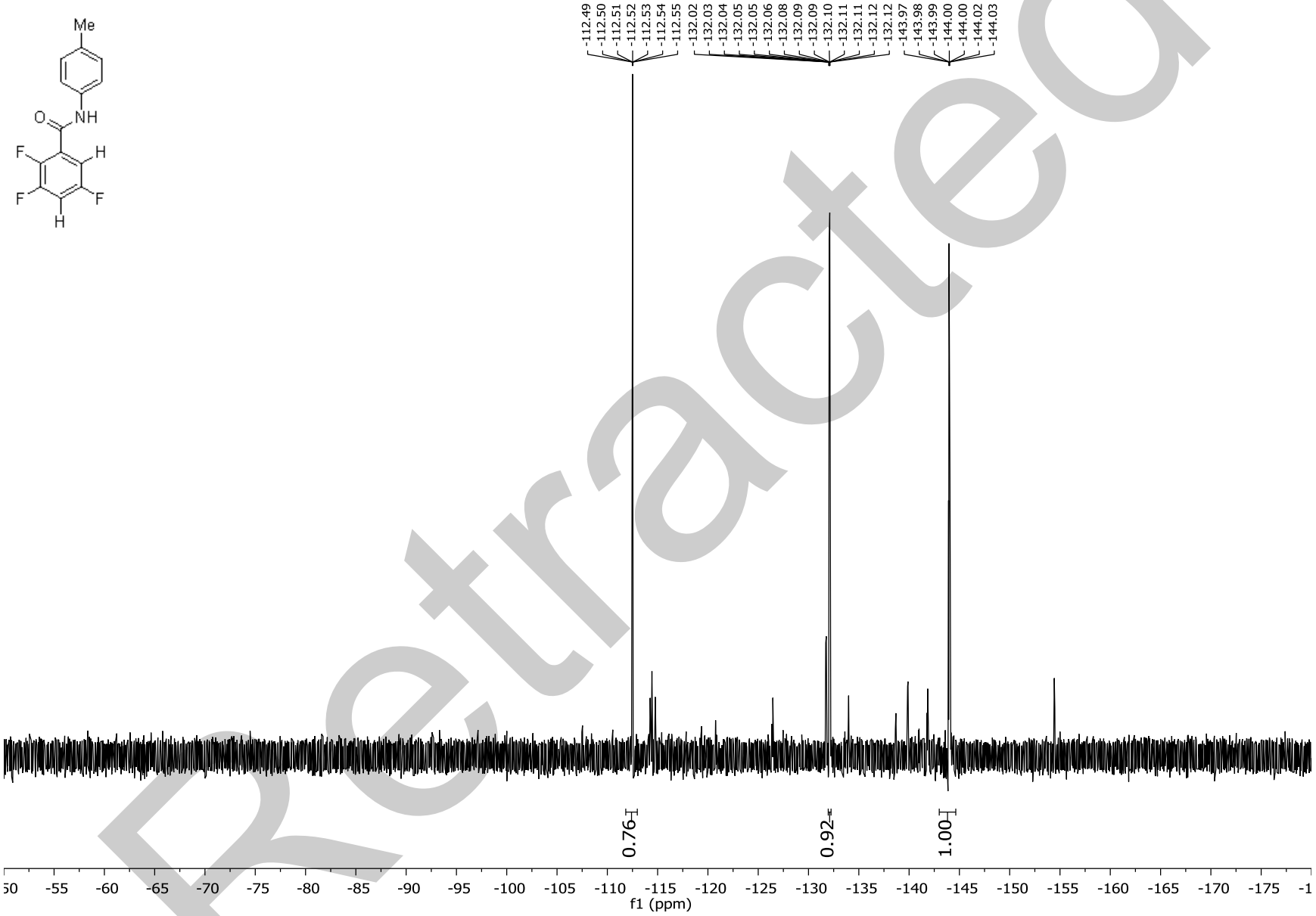
7d *N*-(4-cyanophenyl)-2,3,4,5-tetrafluorobenzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



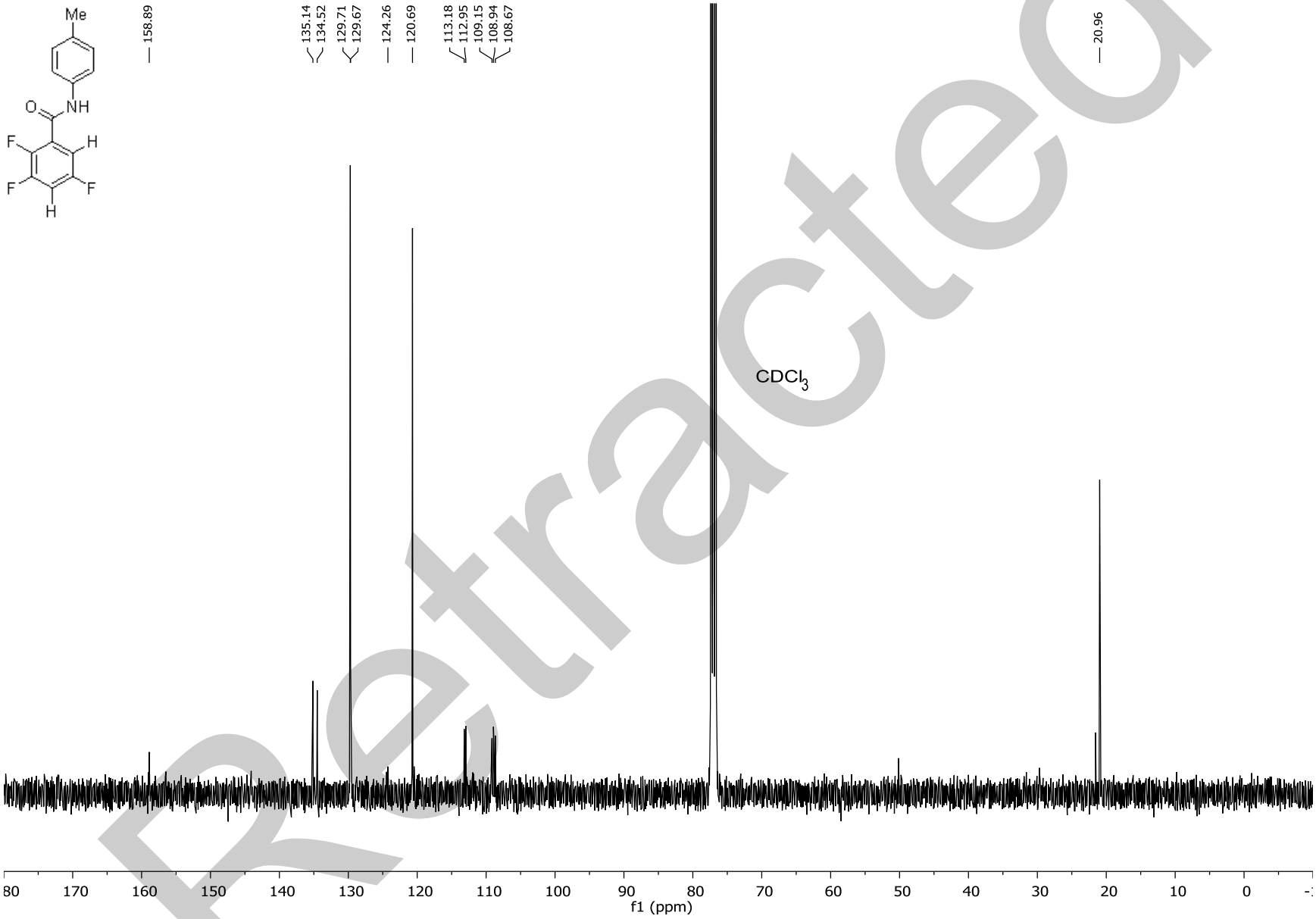
7e' 2,3,5-trifluoro-*N*-(*p*-tolyl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



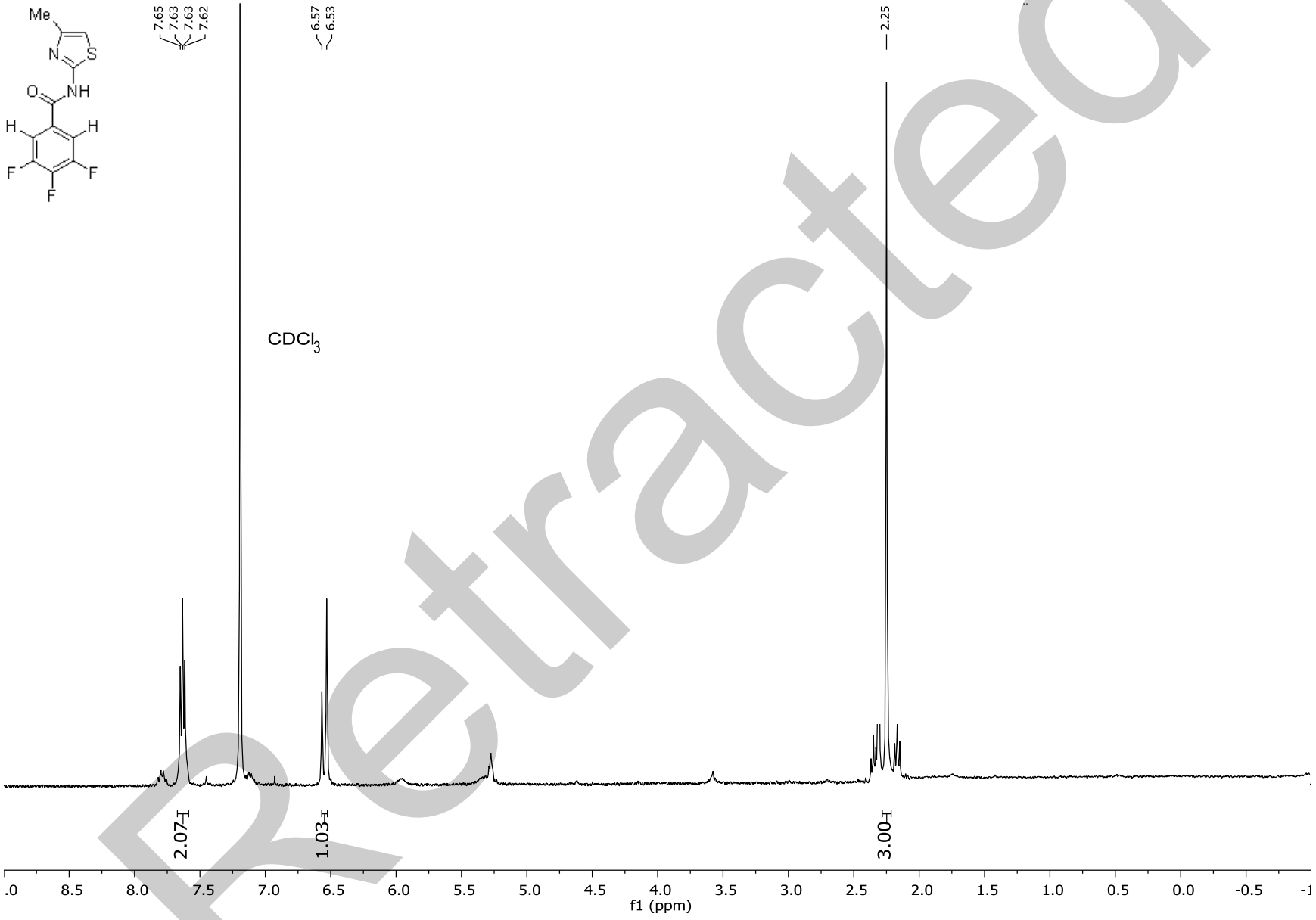
7e' 2,3,5-trifluoro-*N*-(p-tolyl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



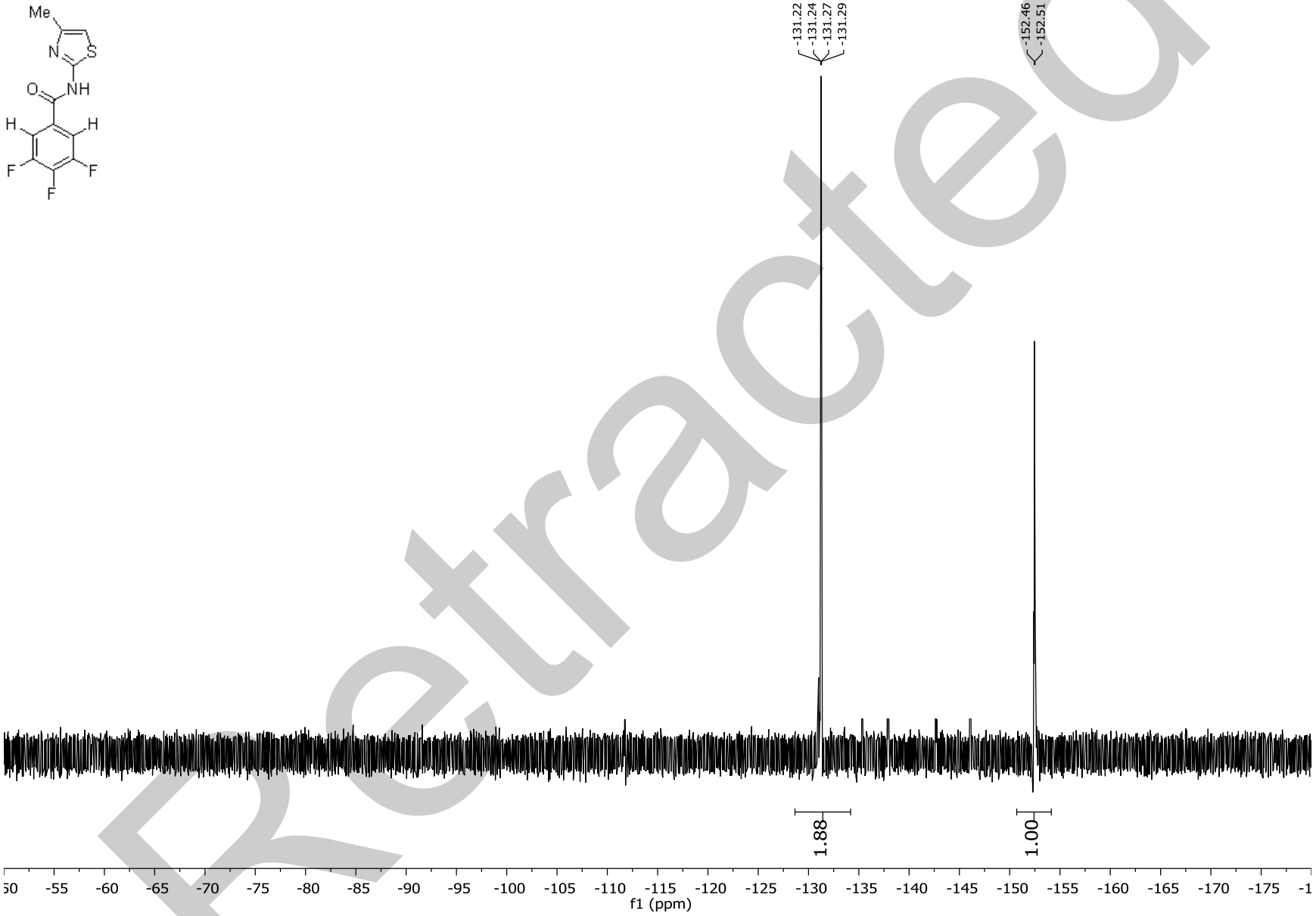
7e' 2,3,5-trifluoro-*N*-(*p*-tolyl)benzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



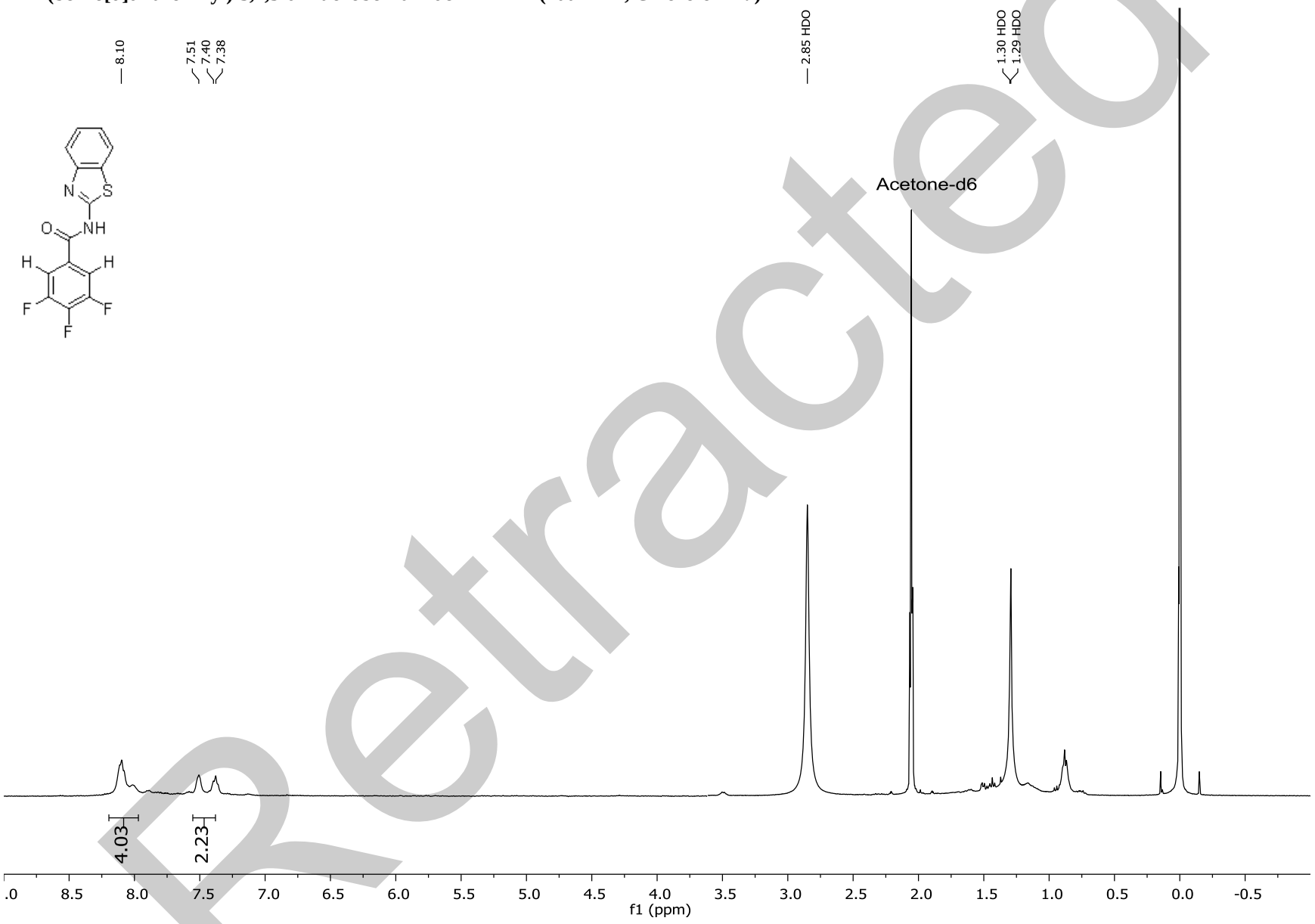
7f 3,4,5-trifluoro-*N*-(4-methylthiazol-2-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



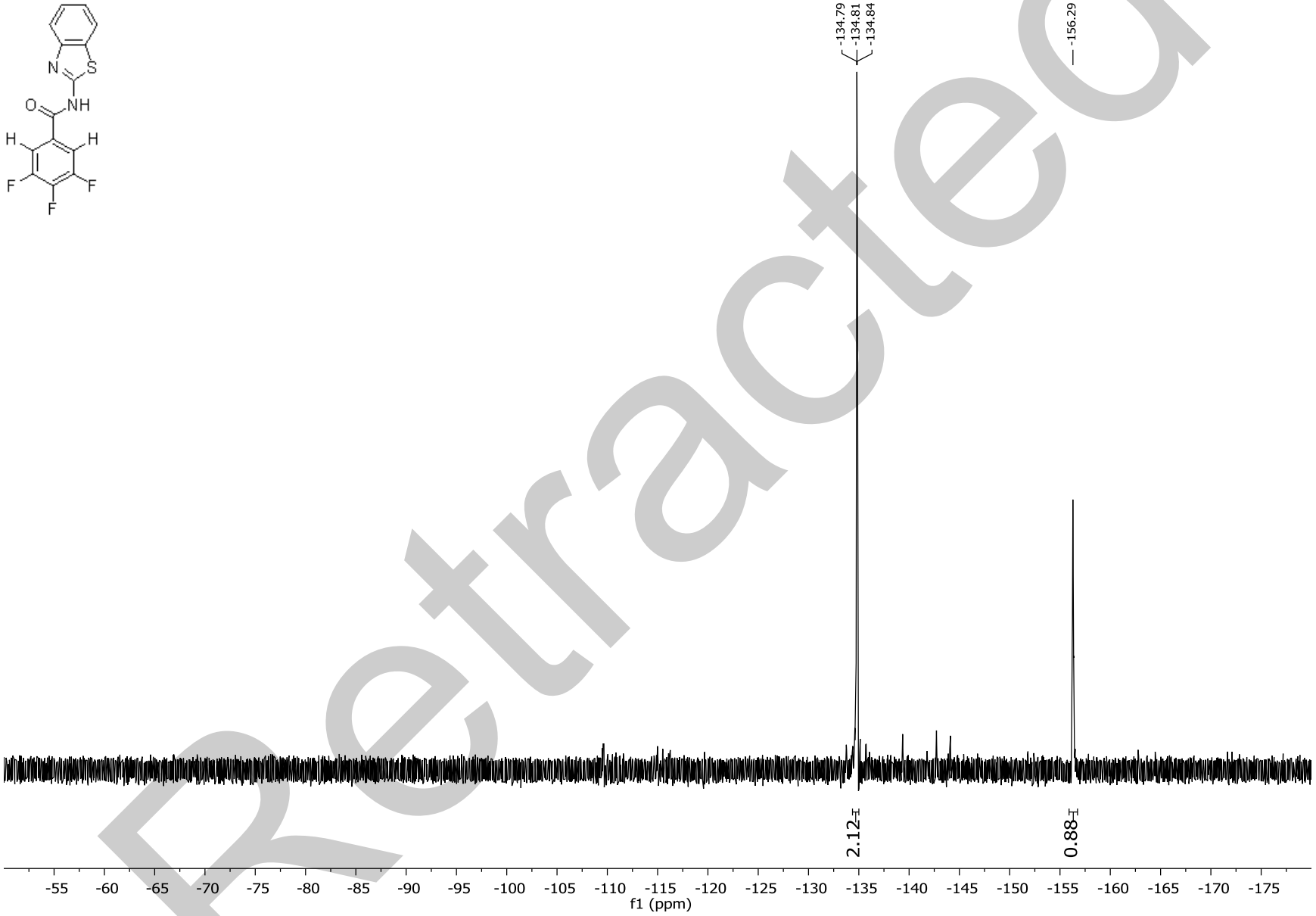
7f 3,4,5-trifluoro-*N*-(4-methylthiazol-2-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



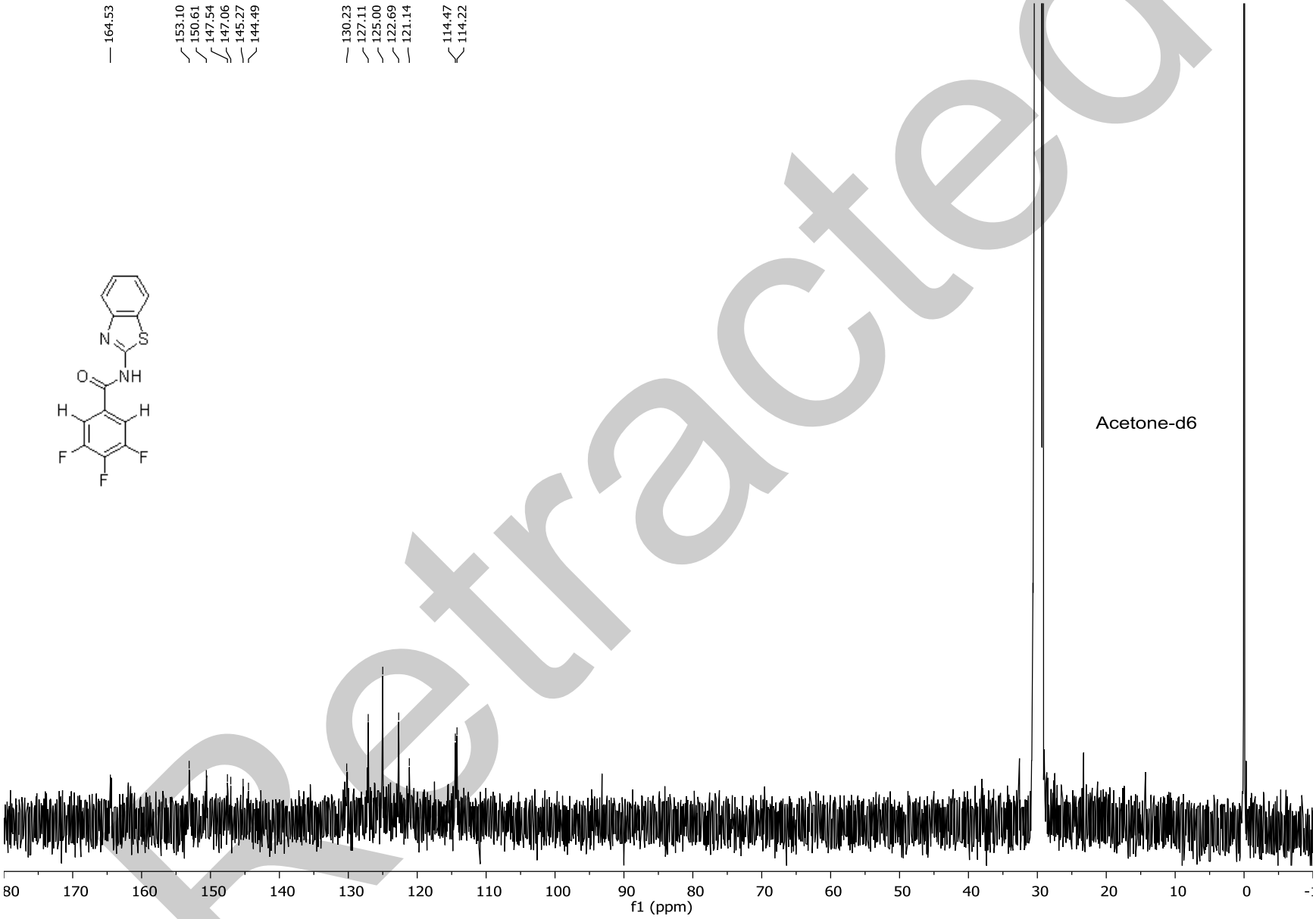
7f *N*-(benzo[d]thiazol-2-yl)-3,4,5-trifluorobenzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



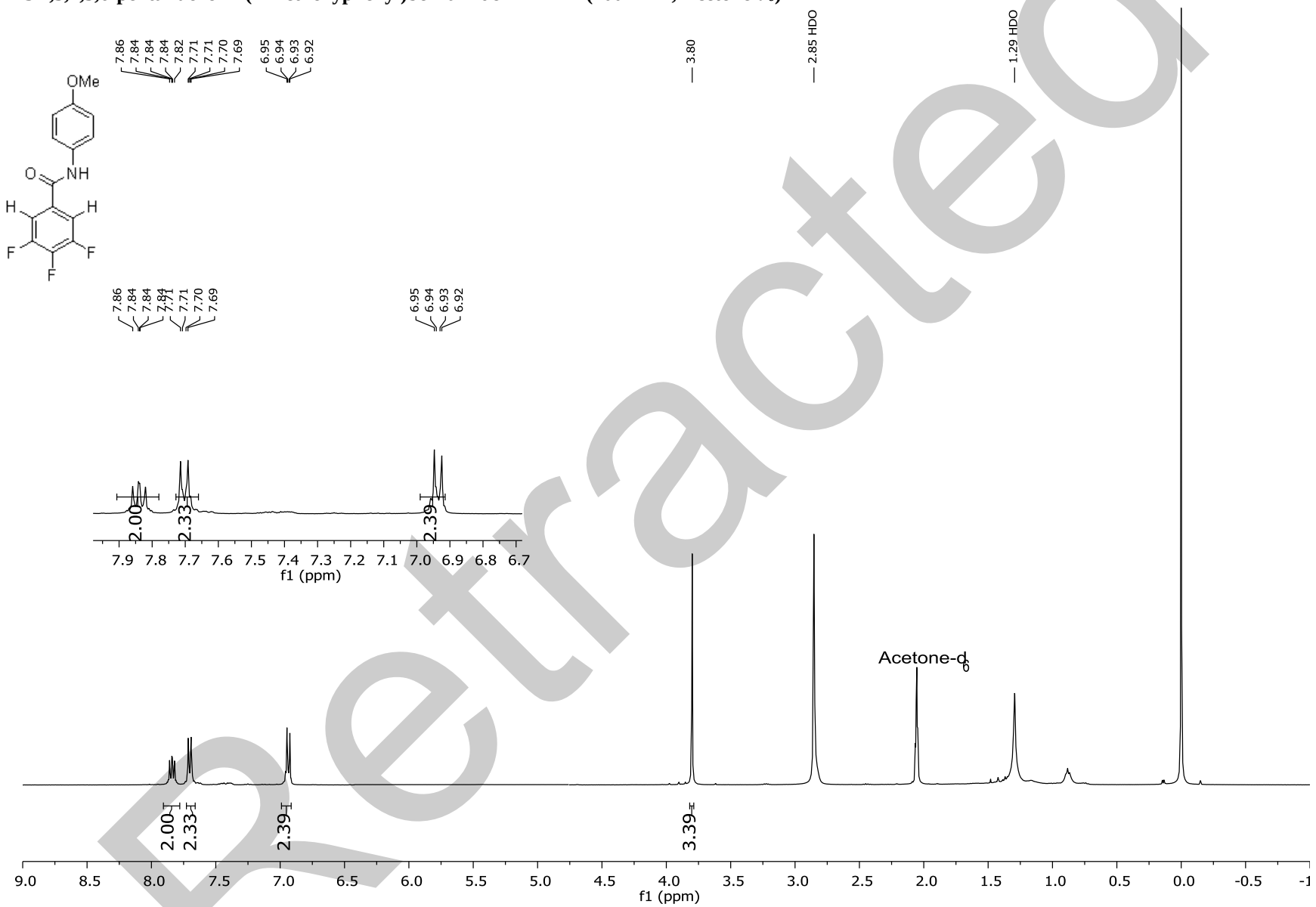
7f *N*-(benzo[d]thiazol-2-yl)-3,4,5-trifluorobenzamide ^{19}F NMR (376 MHz, Acetone-d_6)



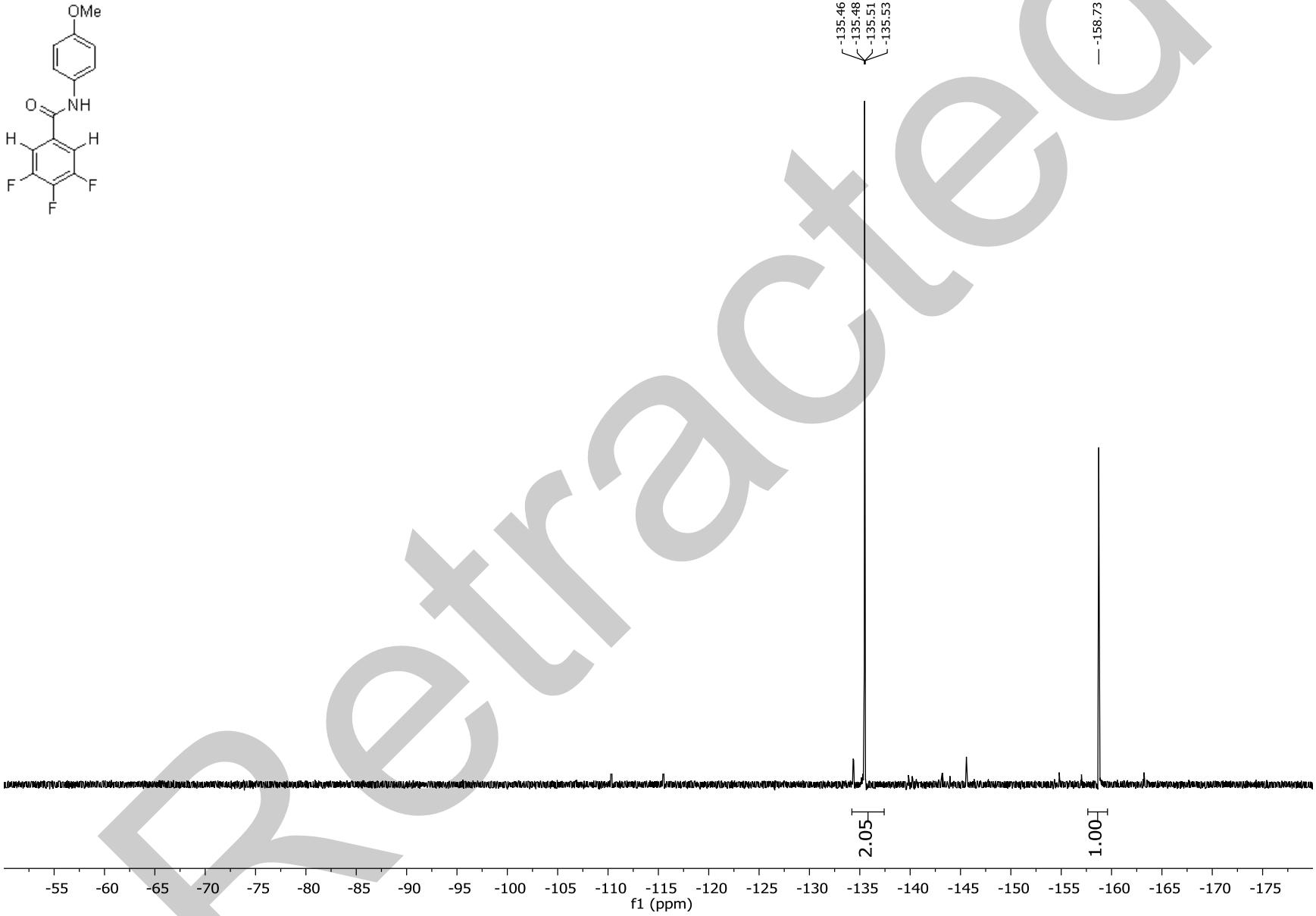
7i *N*-(benzo[d]thiazol-2-yl)-3,4,5-trifluorobenzamide ^{13}C NMR (101 MHz, Acetone-d$_6$)



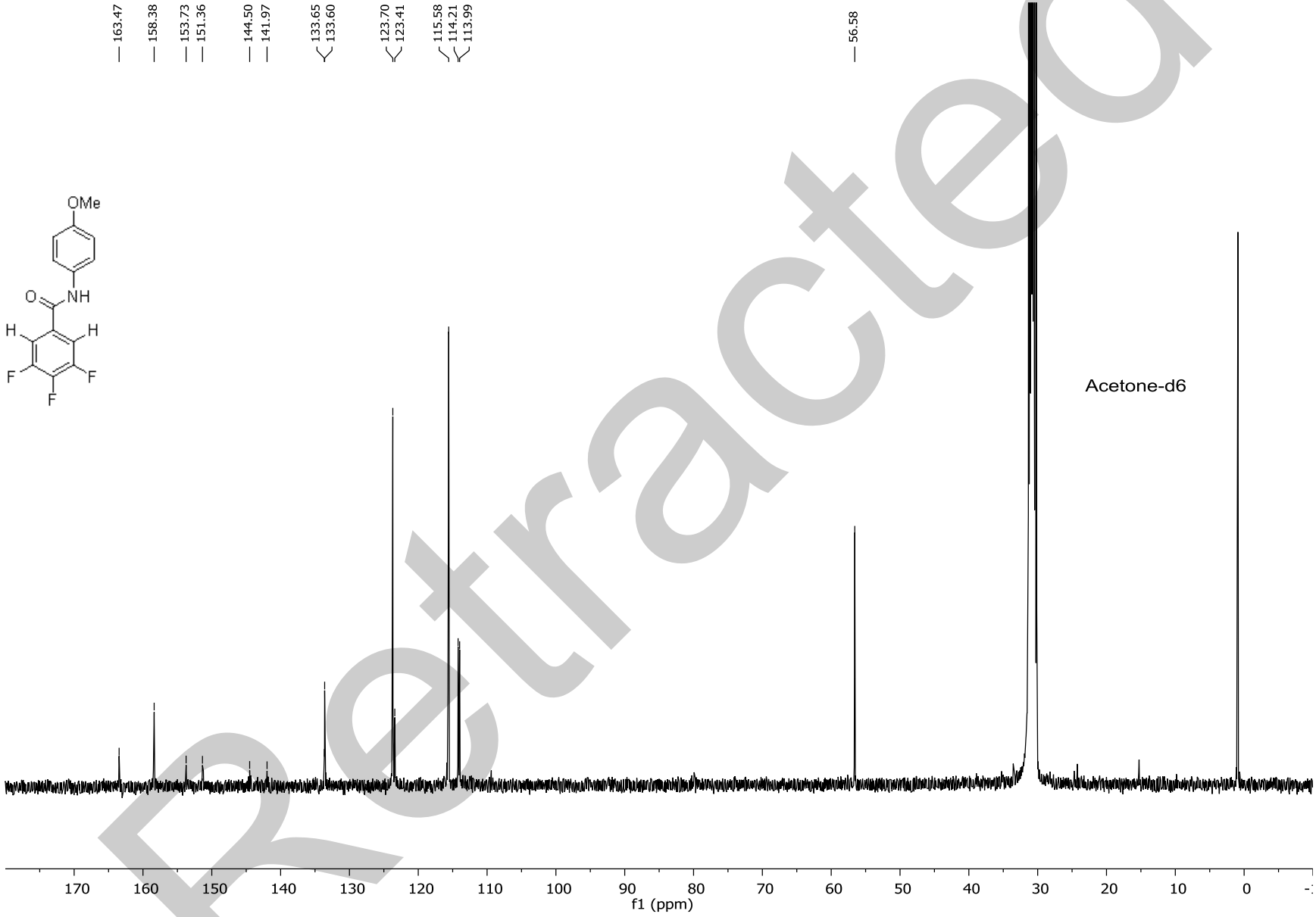
7i 3 2,3,4,5,6-pentafluoro-*N*-(4-methoxyphenyl)benzamide ^{1}H NMR (400 MHz, Acetone-d_6)



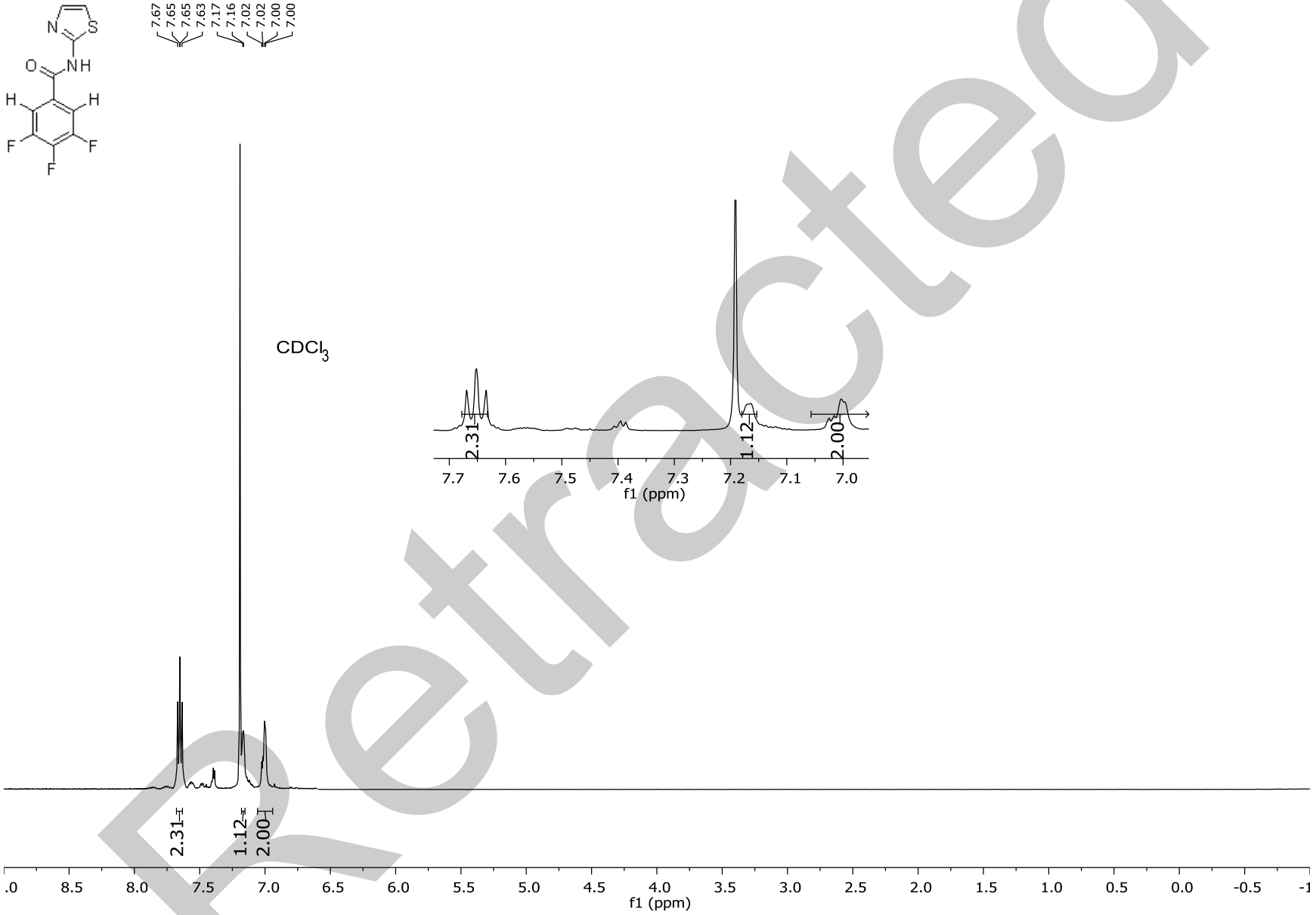
7i 3 2,3,4,5,6-pentafluoro-N-(4-methoxyphenyl)benzamide ^{19}F NMR (376 MHz, Acetone-d_6)



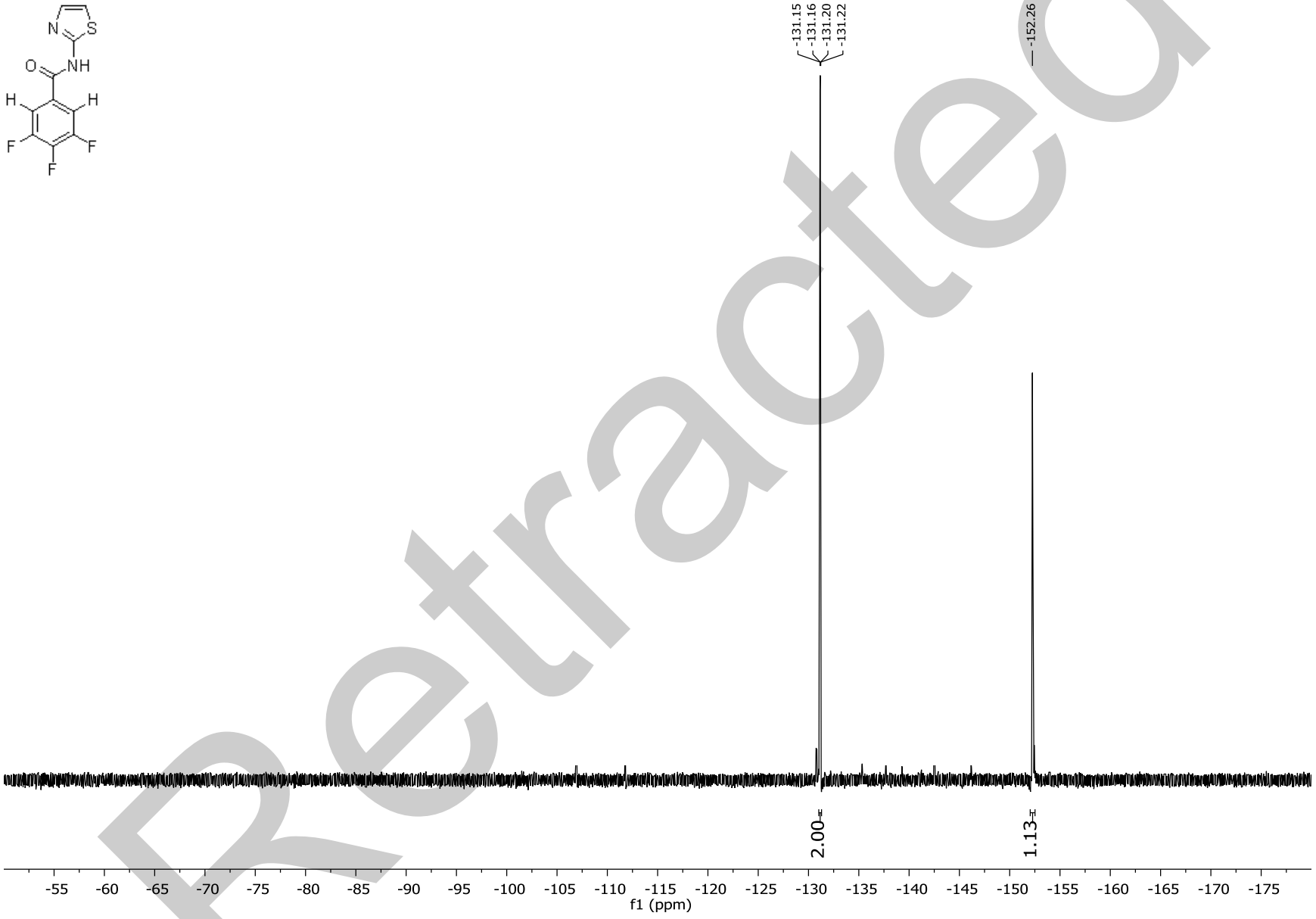
7i 3 2,3,4,5,6-pentafluoro-*N*-(4-methoxyphenyl)benzamide ^{13}C NMR (101 MHz, Acetone-d_6)



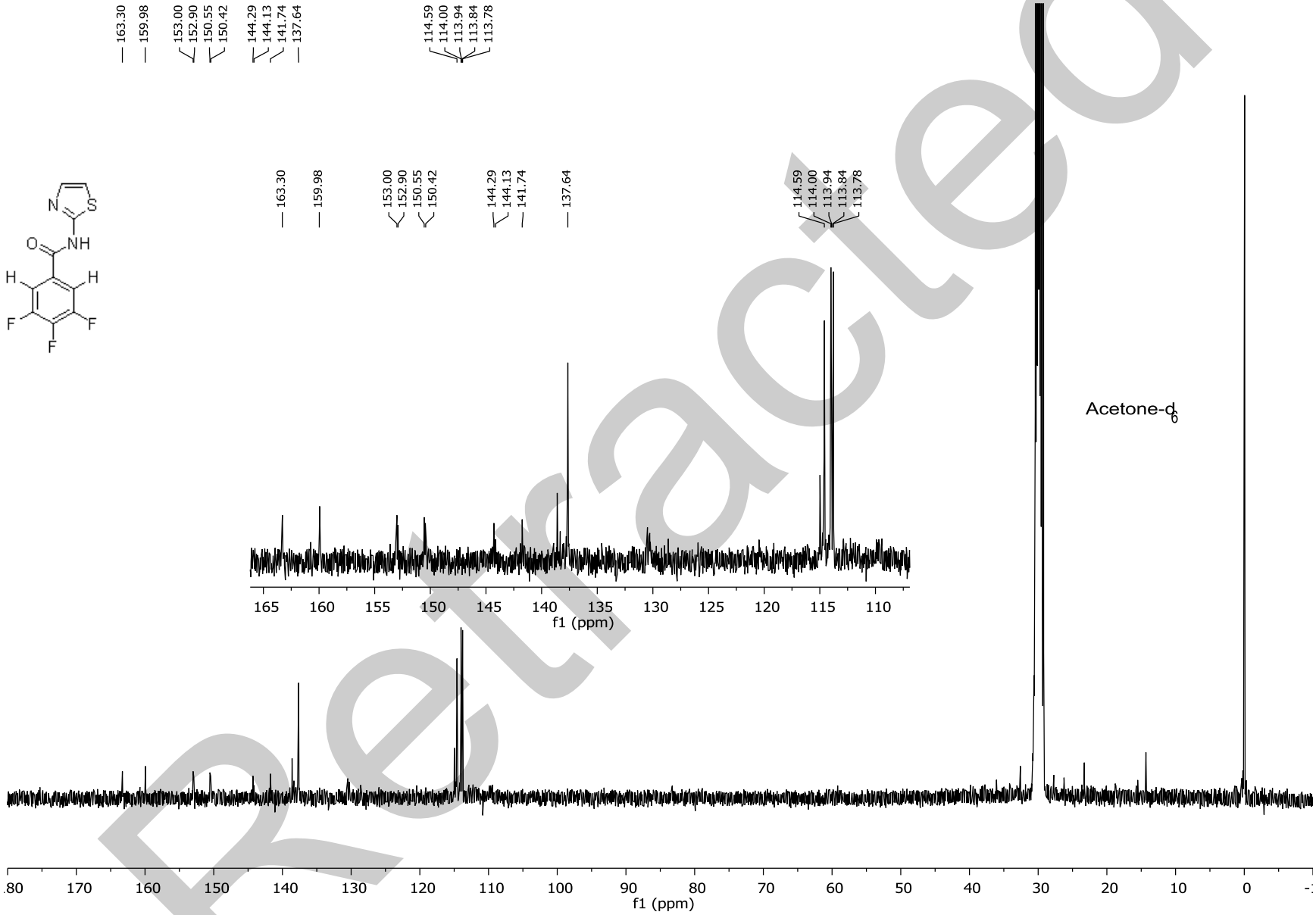
7j' 3,4,5-trifluoro-*N*-(thiazol-2-yl)benzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



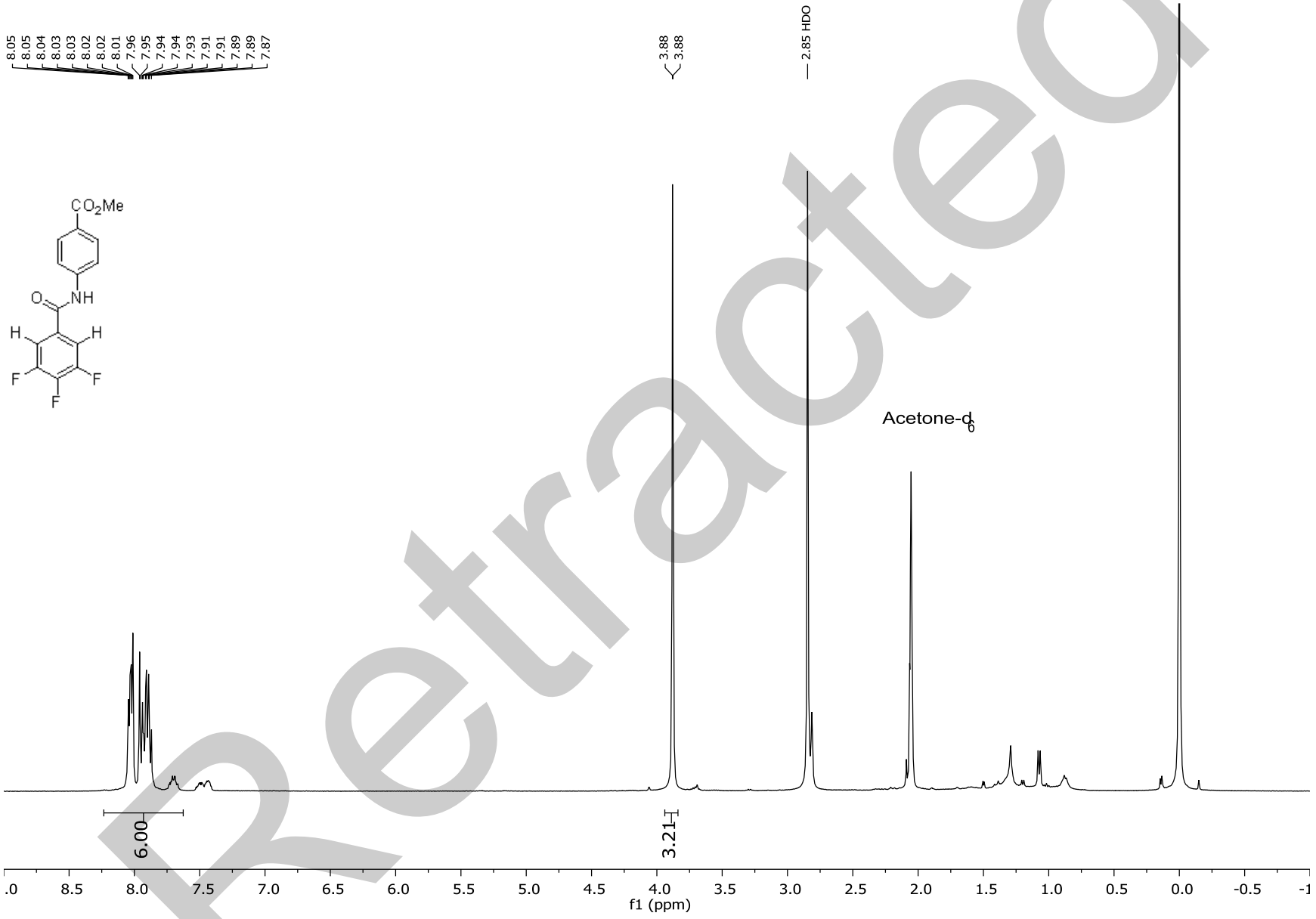
7j ’ 3,4,5-trifluoro-*N*-(thiazol-2-yl)benzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



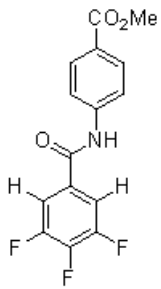
7i' 3,4,5-trifluoro-*N*-(thiazol-2-yl)benzamide ^{13}C NMR (101 MHz, Acetone-d_6)



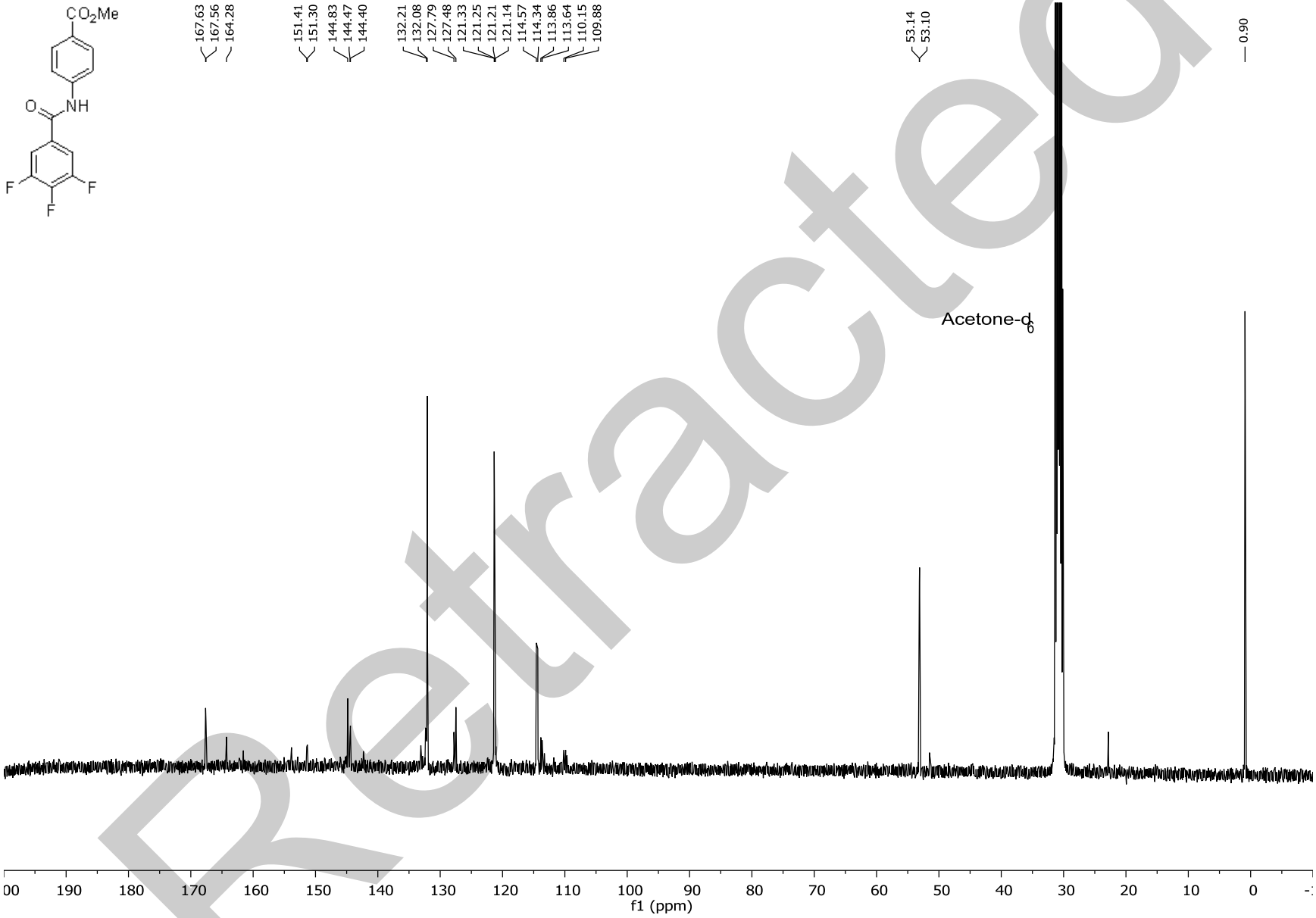
7h methyl 4-(3,4,5-trifluorobenzamido)benzoate ^{1}H NMR (400 MHz, Acetone-d_6)



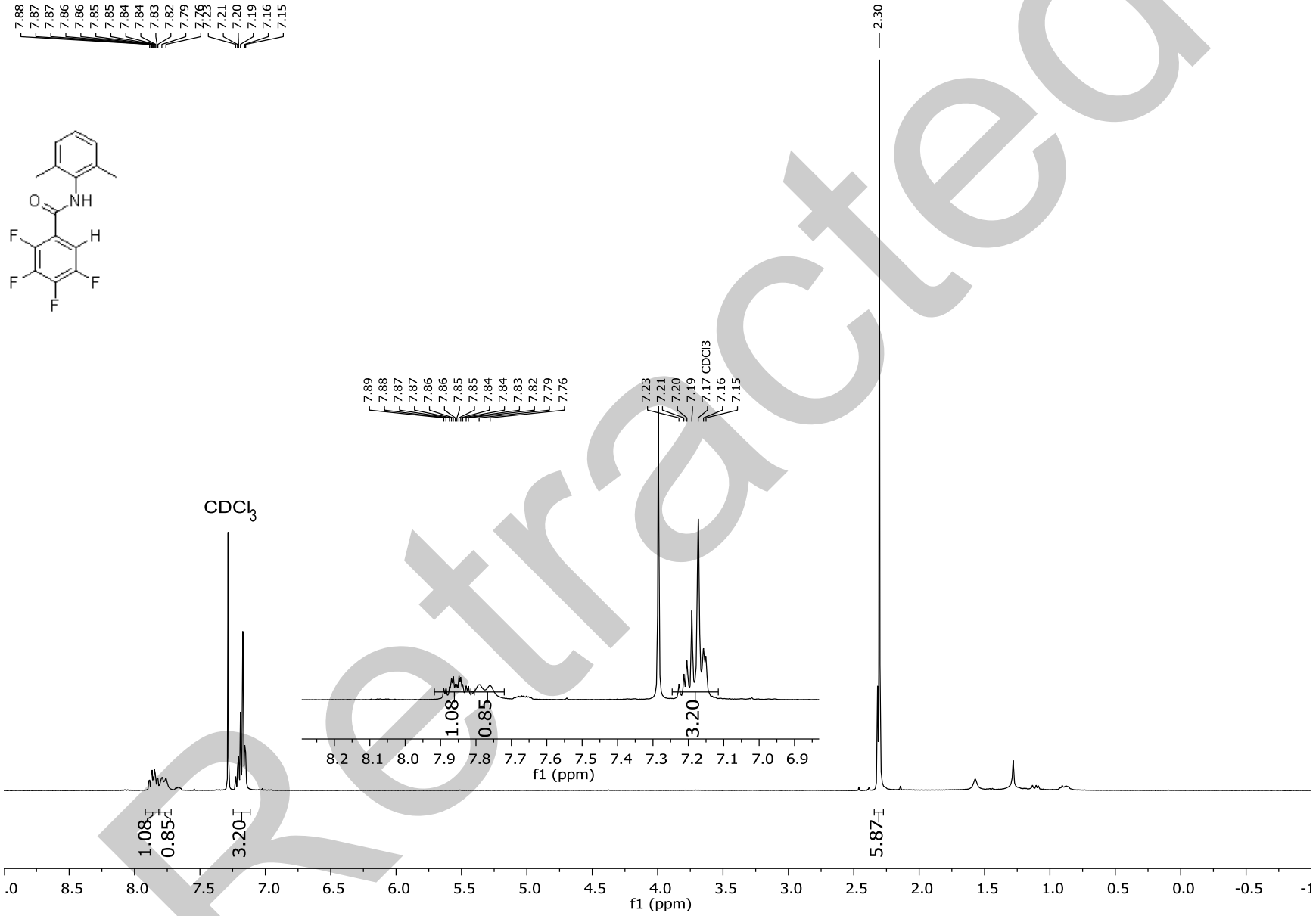
7h methyl 4-(3,4,5-trifluorobenzamido)benzoate ^{19}F NMR (376 MHz, Acetone-d_6)



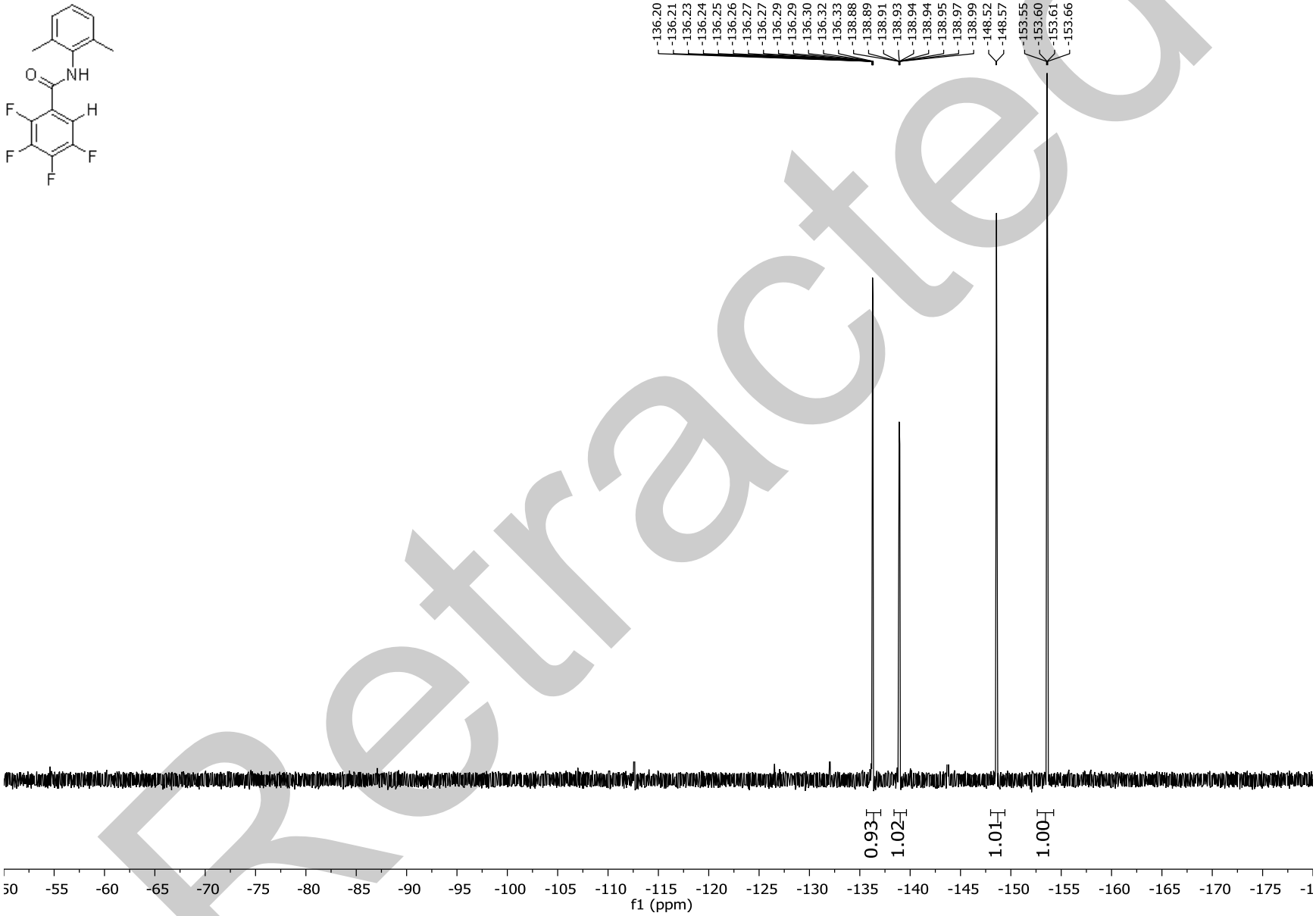
7h methyl 4-(3,4,5-trifluorobenzamido)benzoate ^{13}C NMR (101 MHz, Acetone-*d*$_6$)



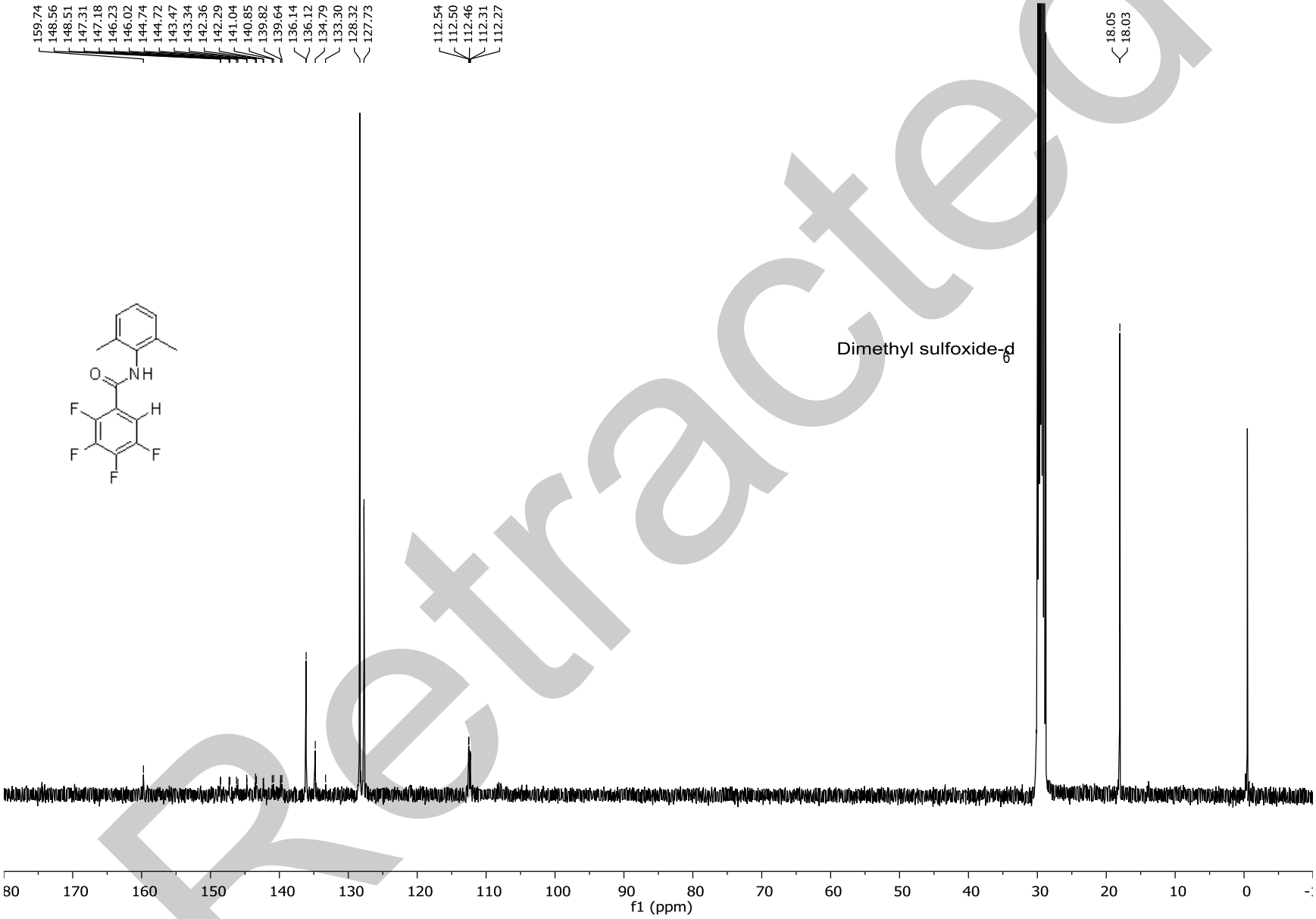
8a' N-(2,6-dimethylphenyl)-2,3,4,5-tetrafluorobenzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



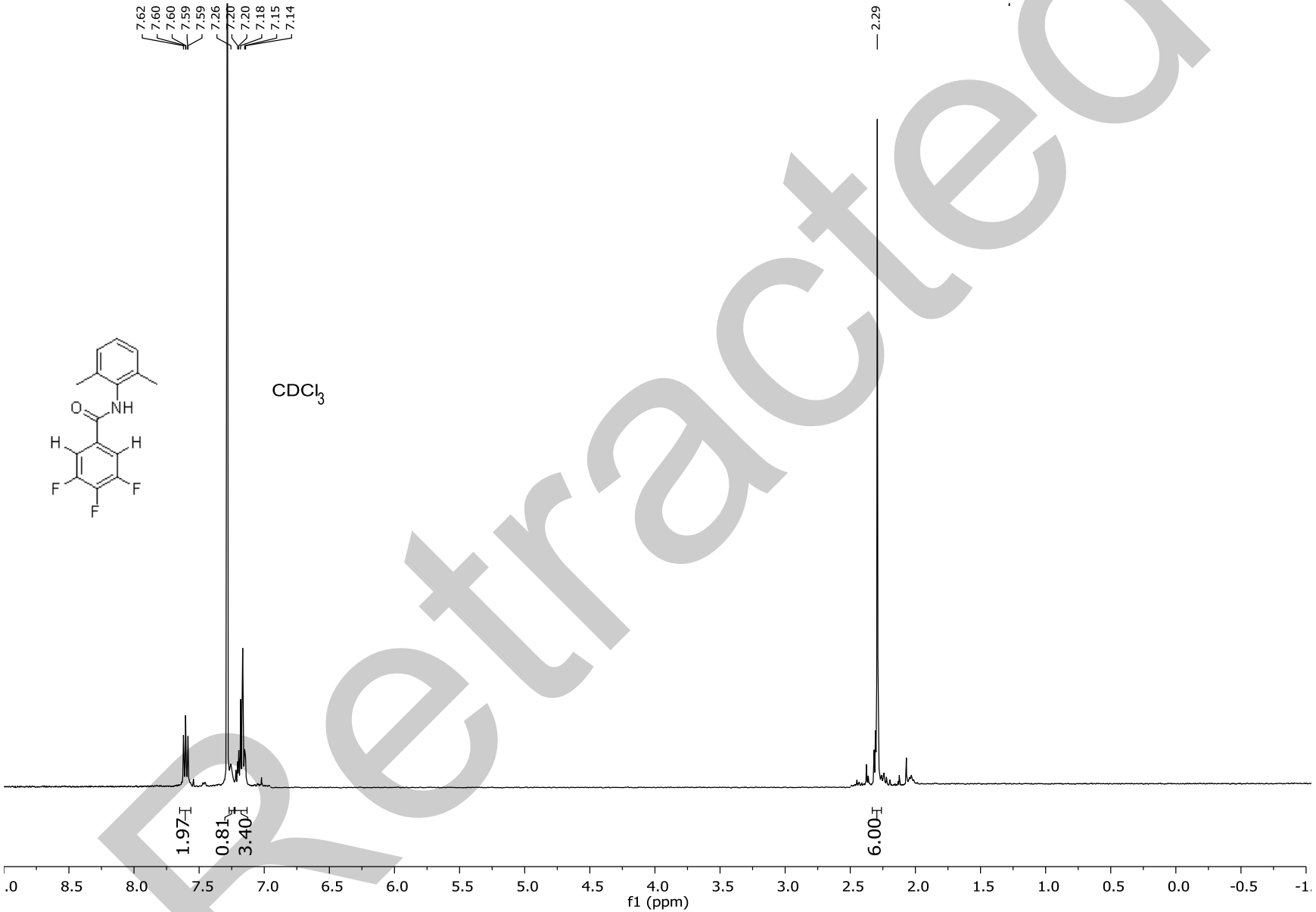
8a' *N*-(2,6-dimethylphenyl)-2,3,4,5-tetrafluorobenzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



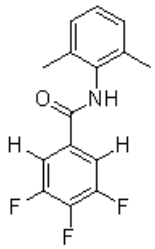
8a’ *N*-(2,6-dimethylphenyl)-2,3,4,5-tetrafluorobenzamide ^{13}C NMR (101 MHz, DMSO-d_6)



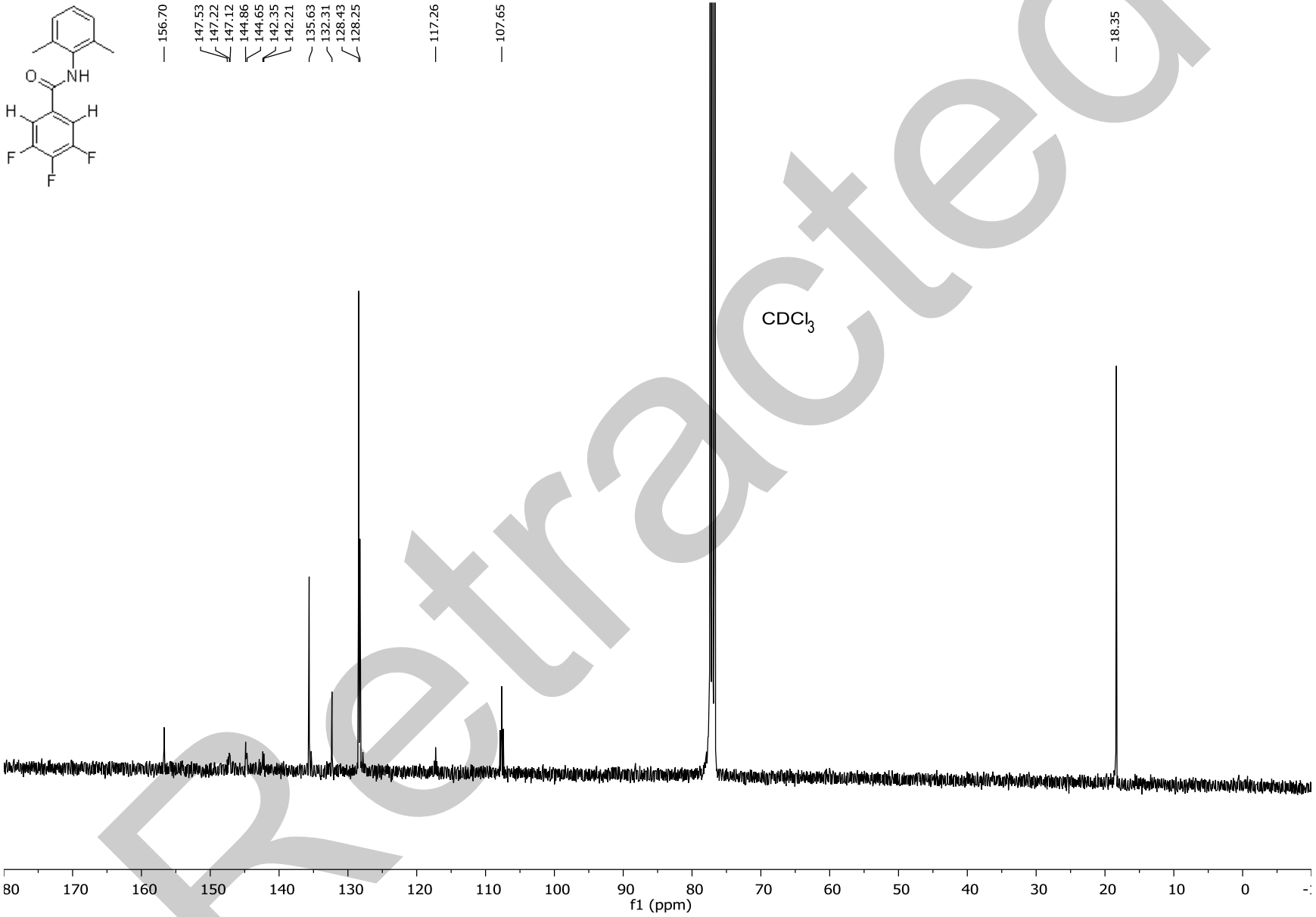
8a'' N-(2,6-dimethylphenyl)-3,4,5-trifluorobenzamid ^{1}H NMR (400 MHz, Chloroform-*d*)



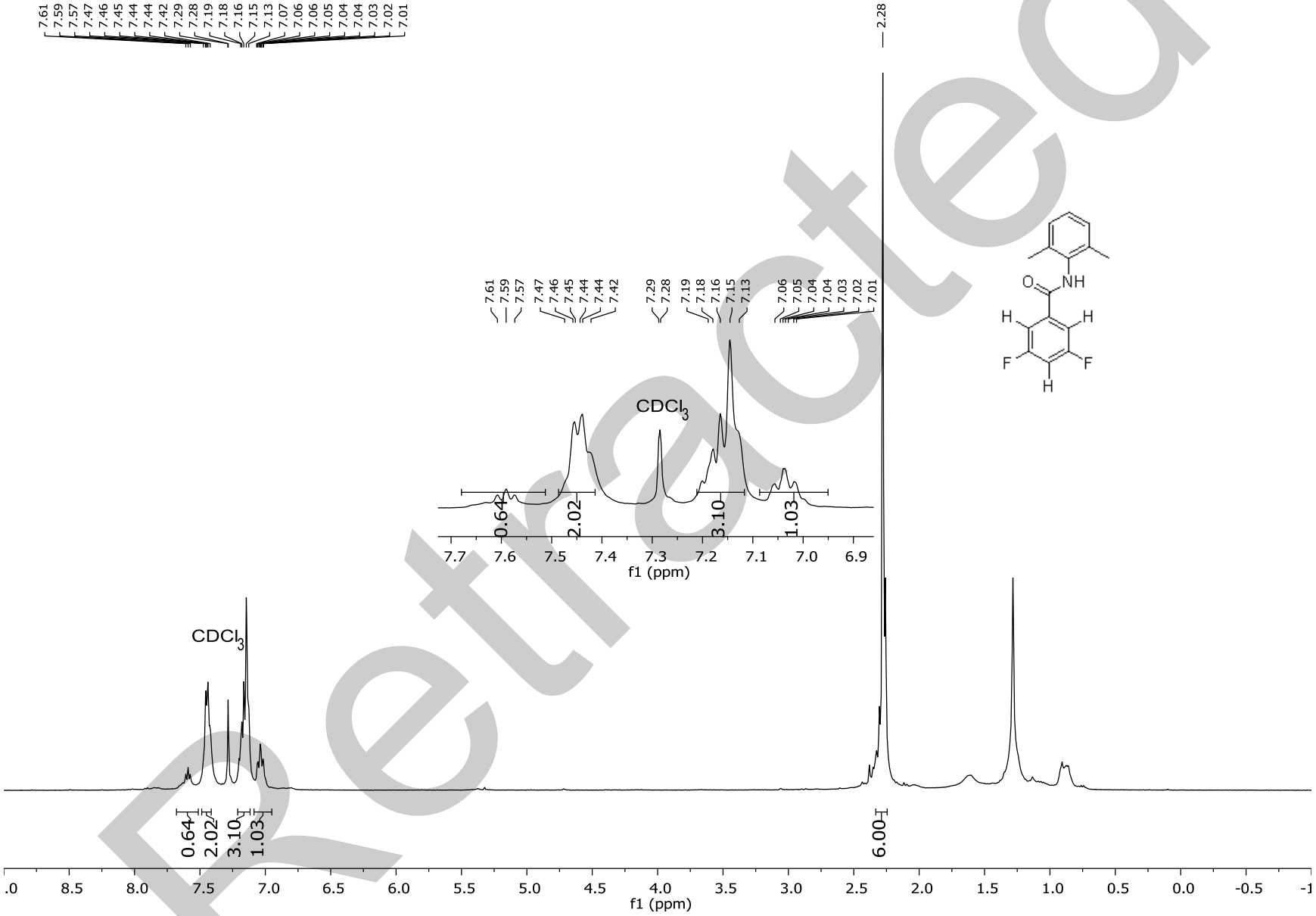
8a'' N-(2,6-dimethylphenyl)-3,4,5-trifluorobenzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



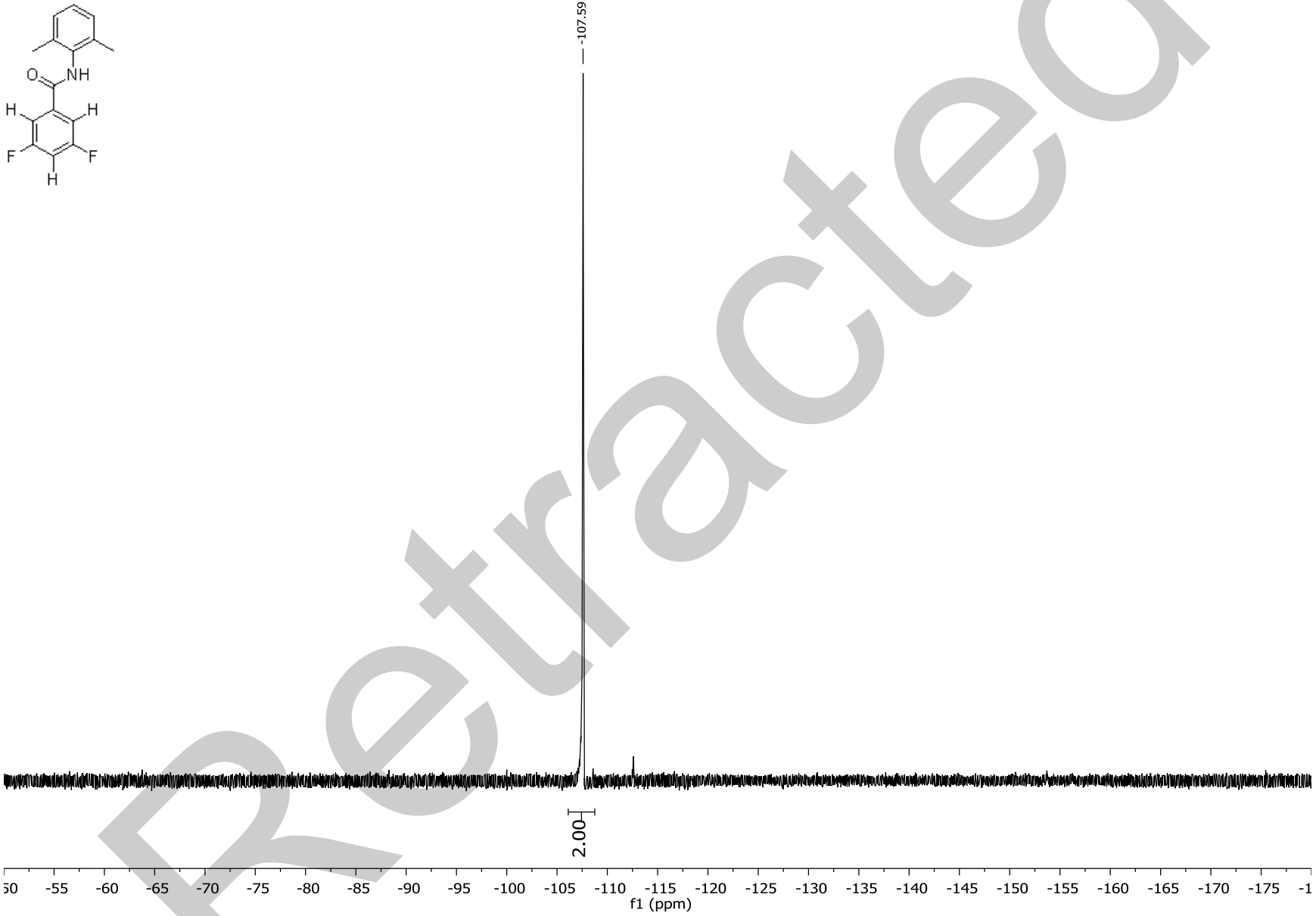
8a'' N-(2,6-dimethylphenyl)-3,4,5-trifluorobenzamide ^{19}F NMR (101 MHz, Chloroform-*d*)



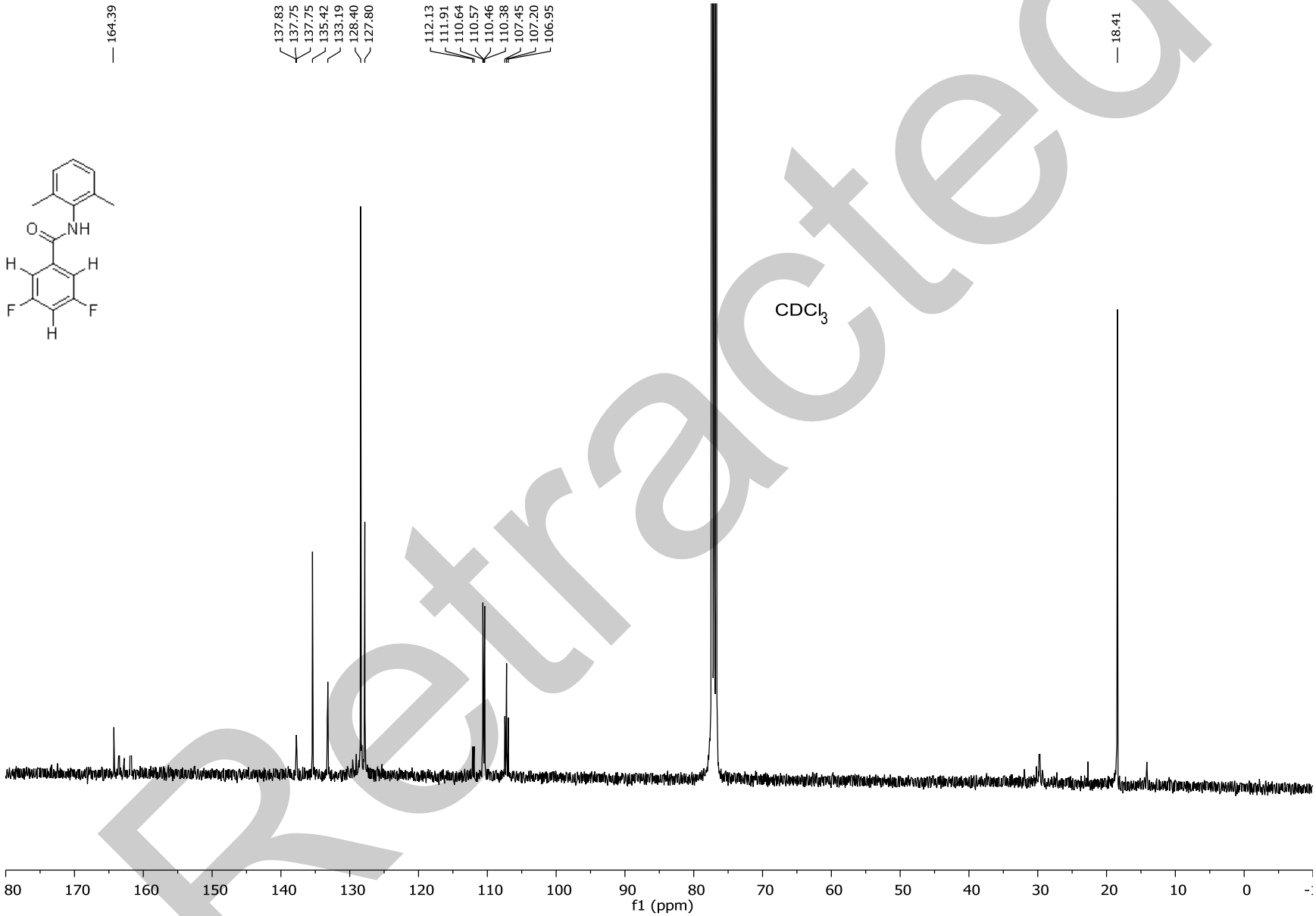
8a''' N-(2,6-dimethylphenyl)-3,5-difluorobenzamide ^{1}H NMR (400 MHz, Chloroform-*d*)



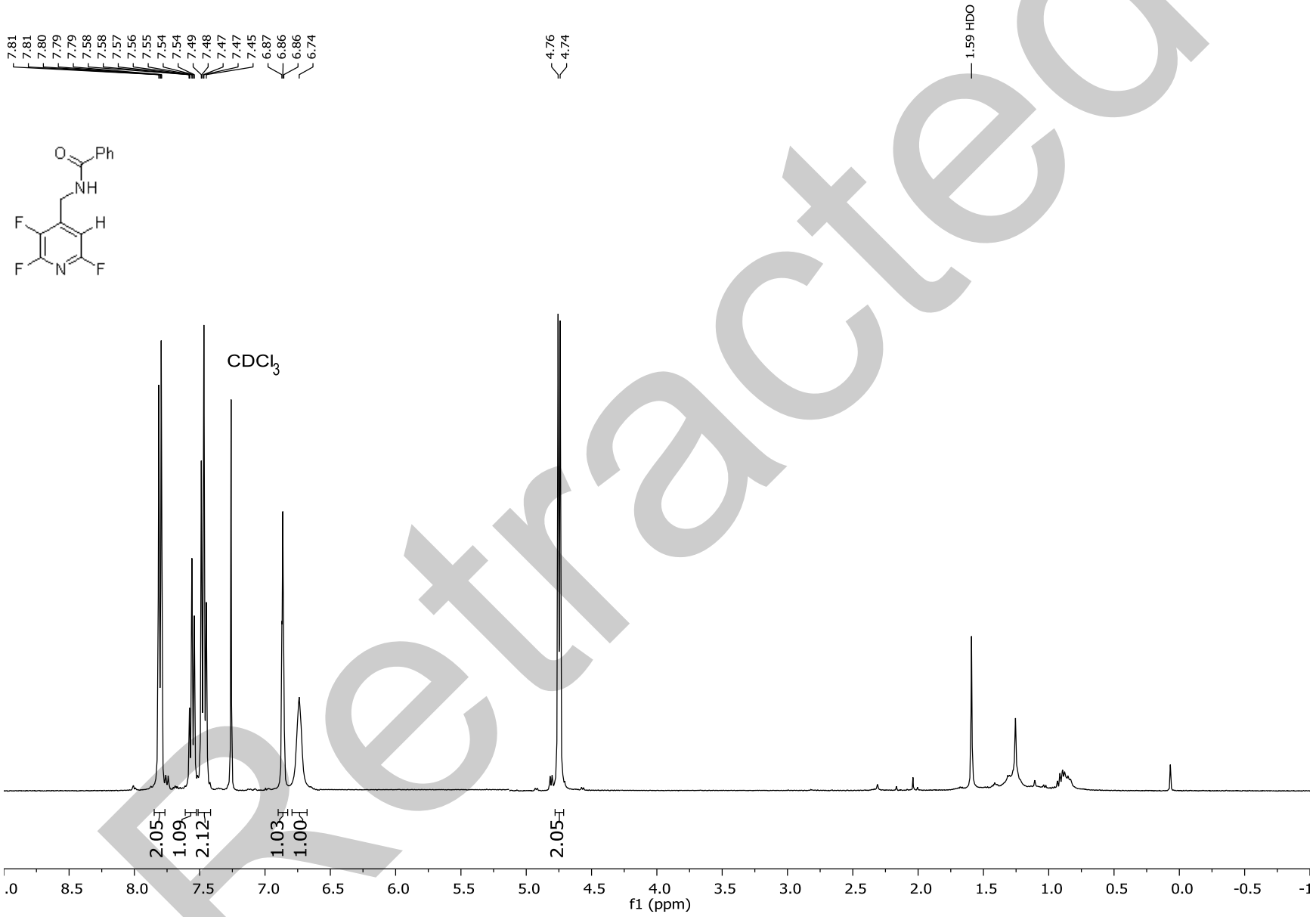
8a''' N-(2,6-dimethylphenyl)-3,5-difluorobenzamide ^{19}F NMR (376 MHz, Chloroform-*d*)



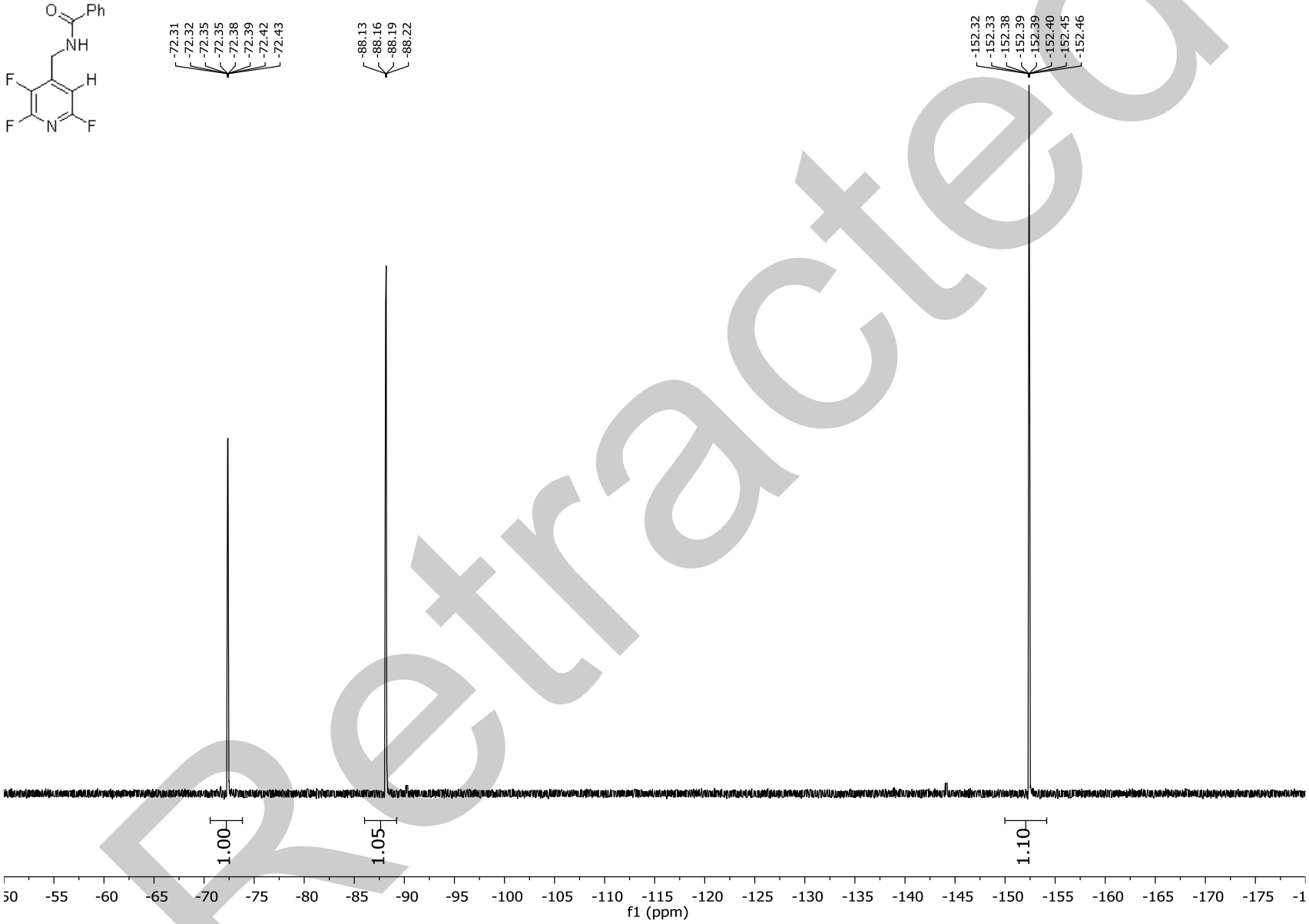
8a''' *N*-(2,6-dimethylphenyl)-3,5-difluorobenzamide ^{13}C NMR (101 MHz, Chloroform-*d*)



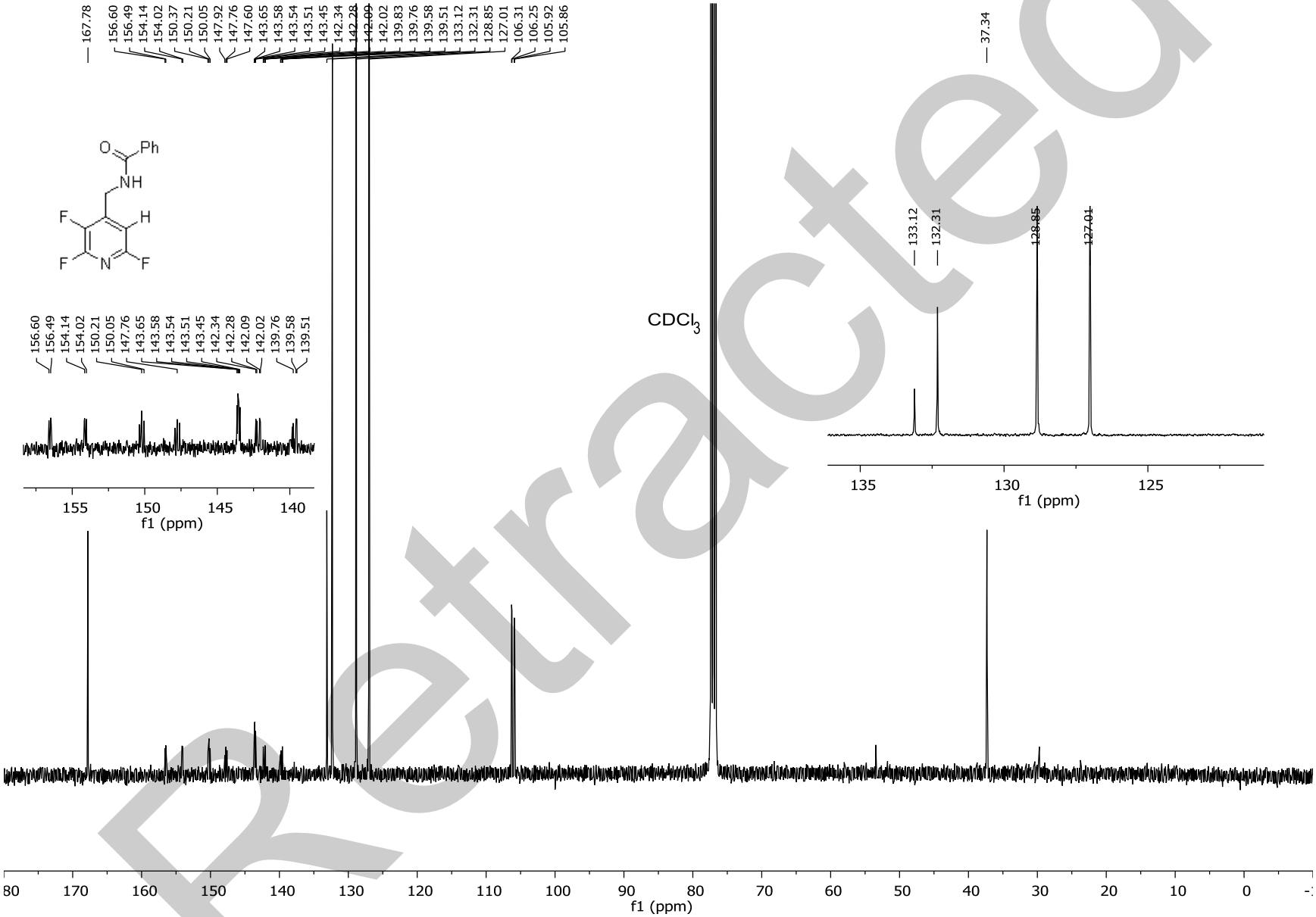
9a' 2-benzamido-2-(2,3,6-trifluoropyridin-4-yl)acetic acid ^{1}H NMR (400 MHz, Chloroform-*d*)



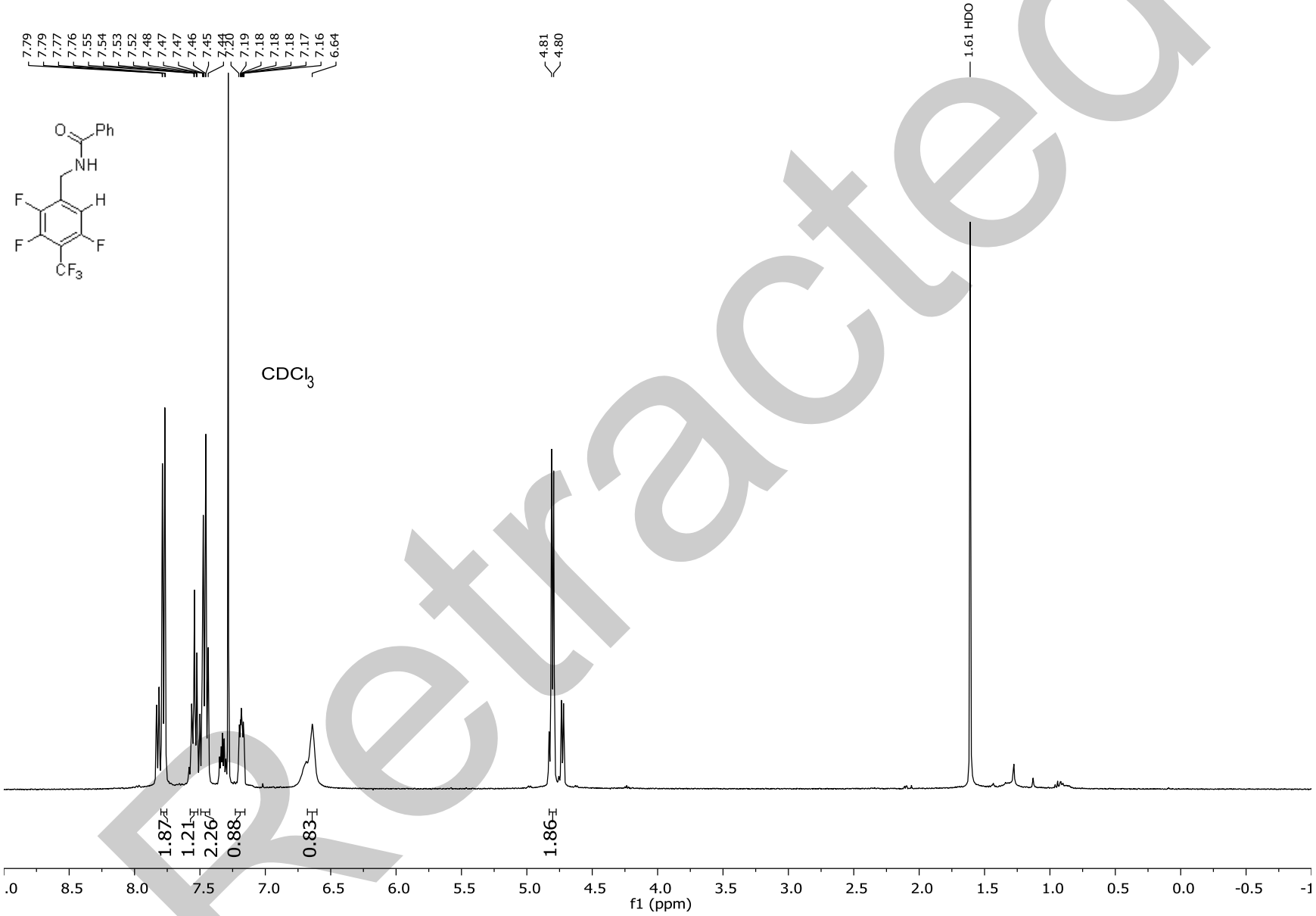
9a' 2-benzamido-2-(2,3,6-trifluoropyridin-4-yl)acetic acid ^{19}F NMR (376 MHz, Chloroform-*d*)



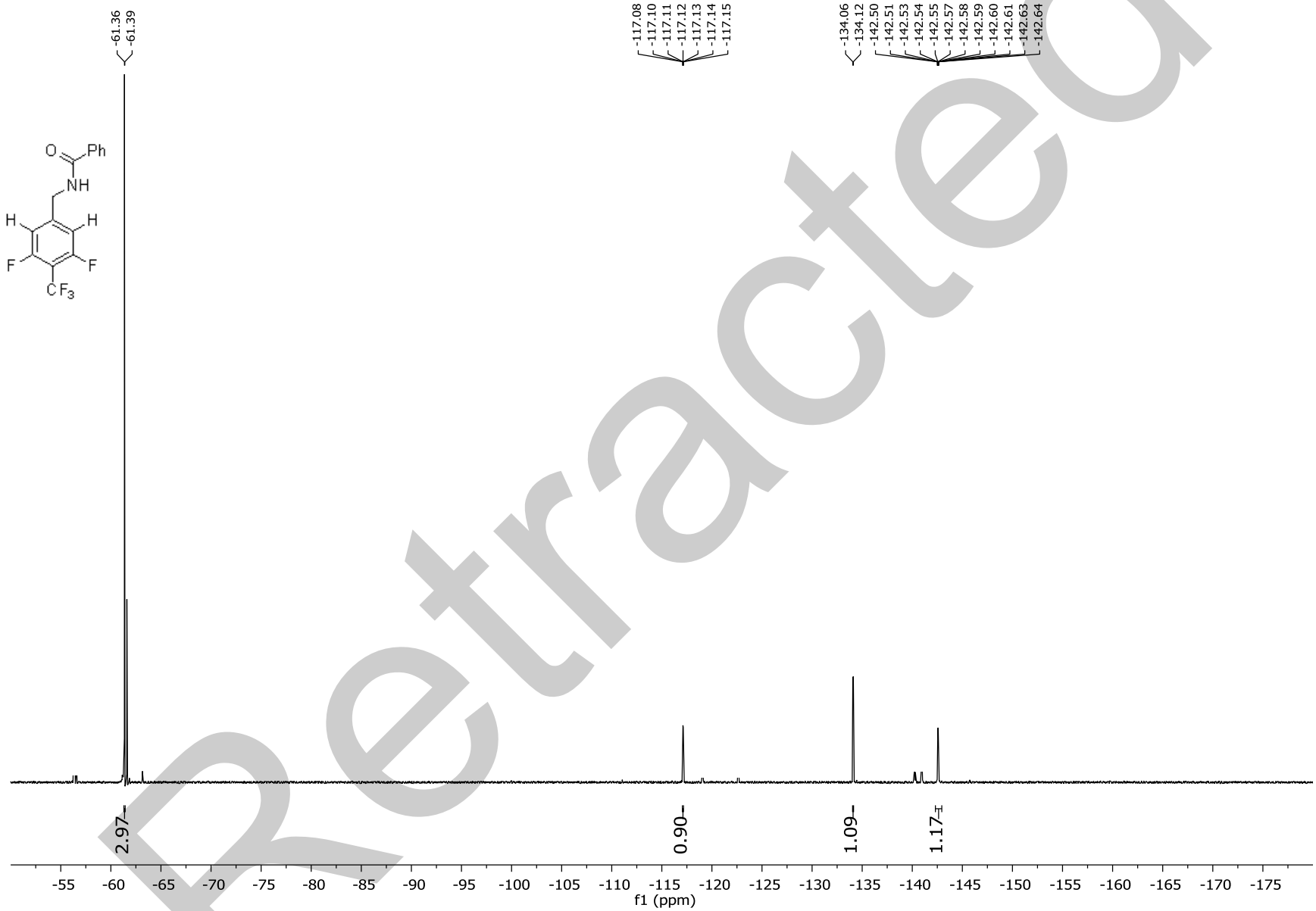
9a' 2-benzamido-2-(2,3,6-trifluoropyridin-4-yl)acetic acid ^{13}C NMR (101 MHz, Chloroform-*d*)



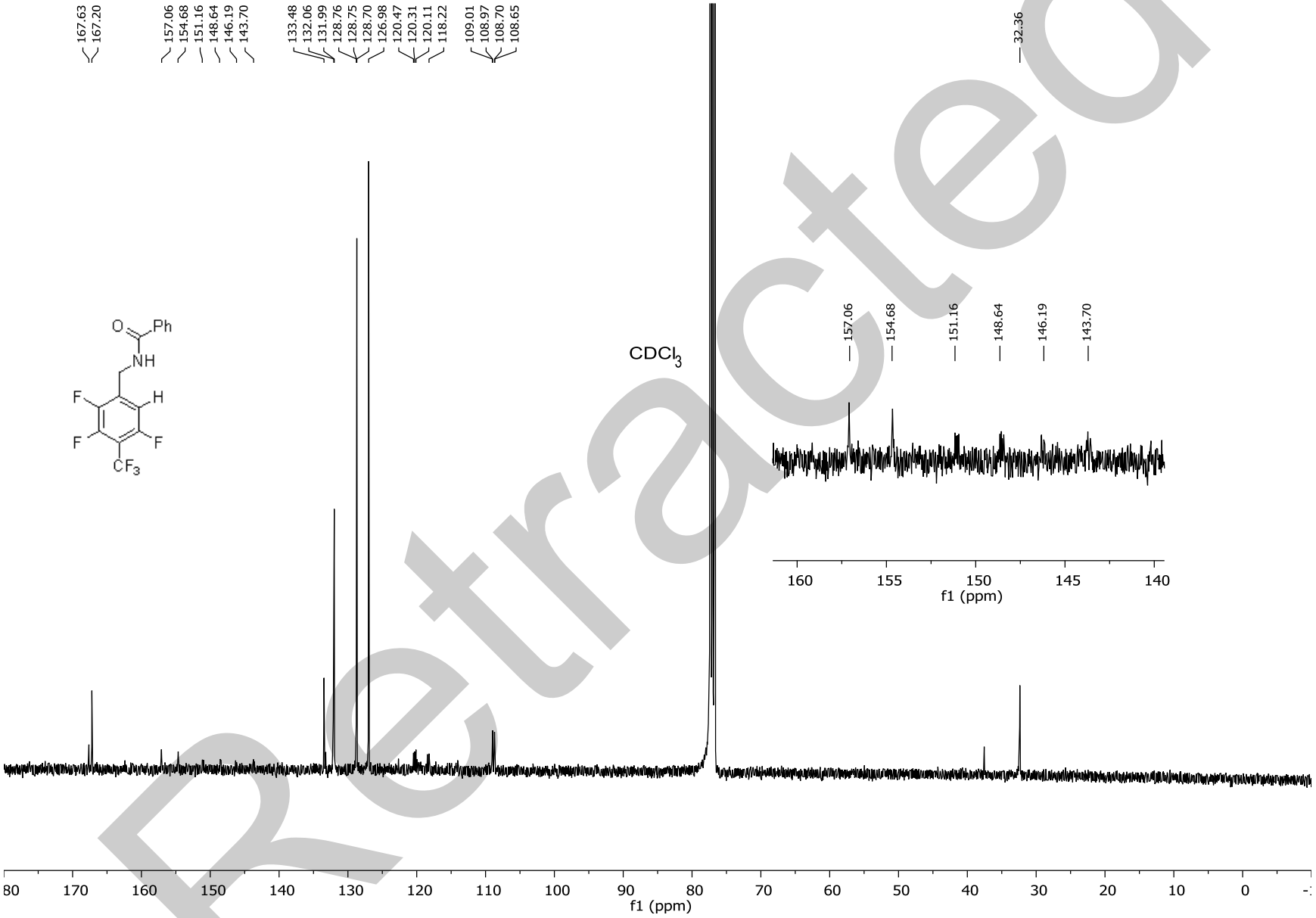
9b' 2-benzamido-2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetic acid ^{1}H NMR (400 MHz, Chloroform-*d*)



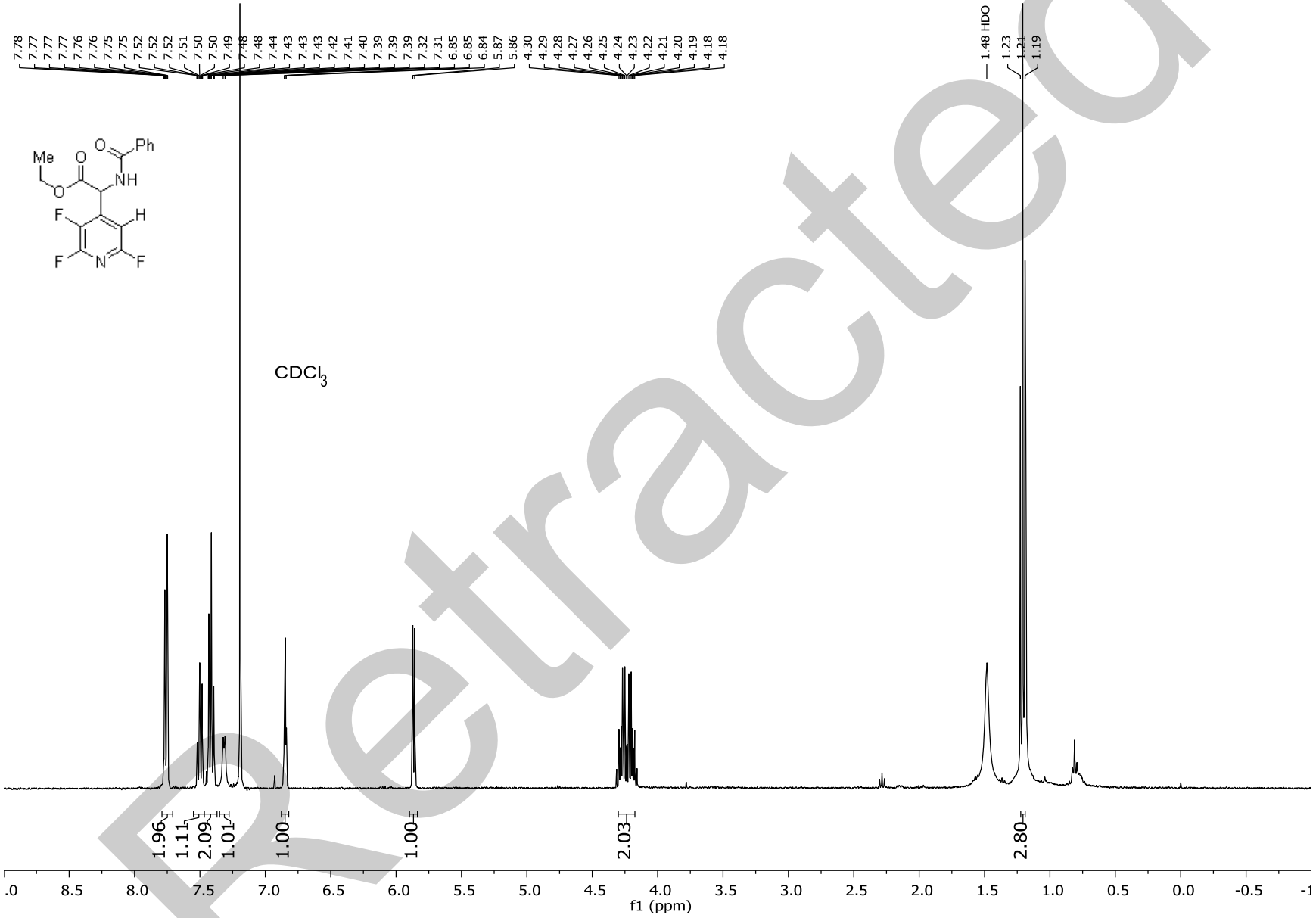
9b' 2-benzamido-2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetic acid ^{19}F NMR (376 MHz, Chloroform-*d*)



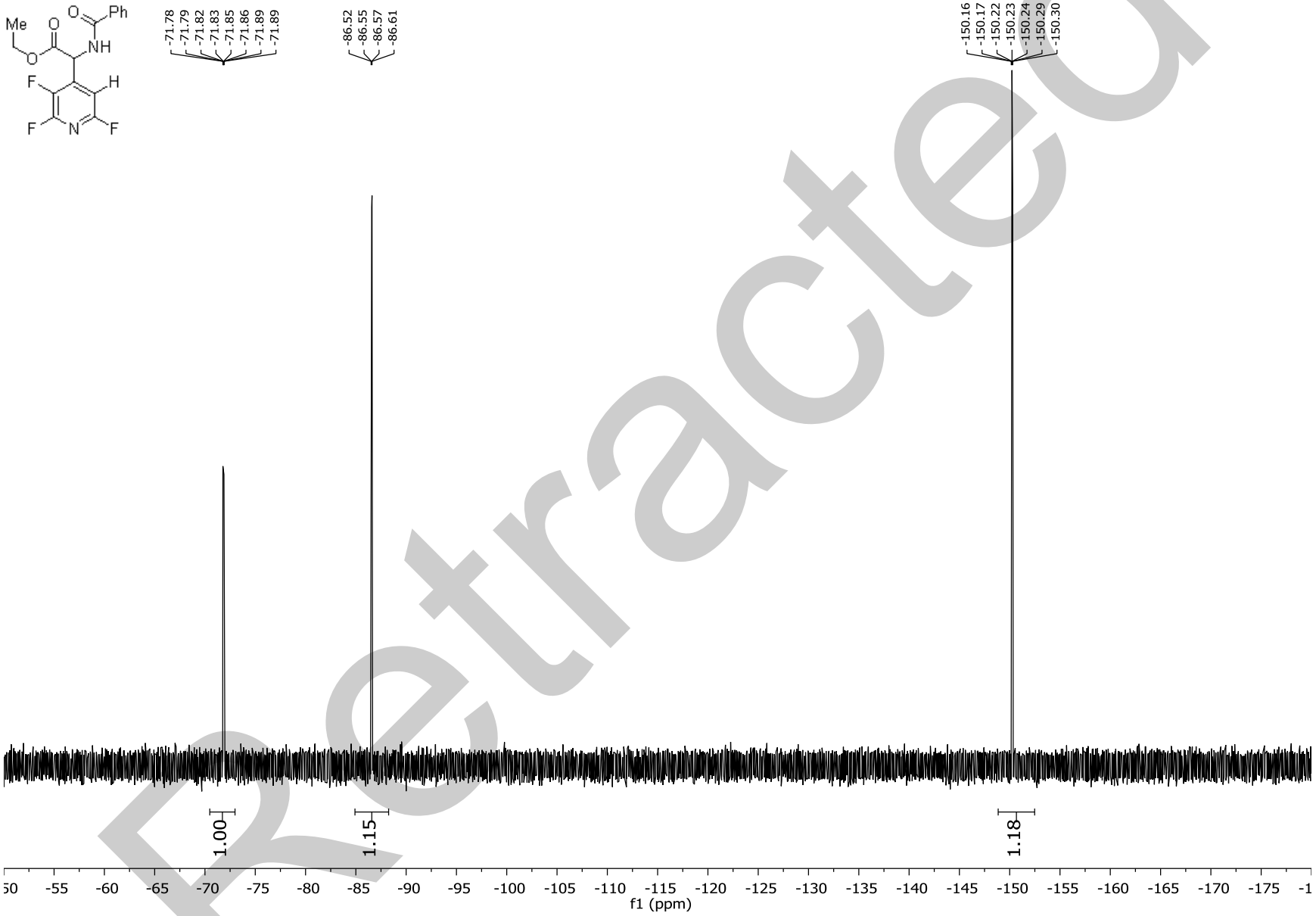
9b' 2-benzamido-2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetic acid ^{13}C NMR (101 MHz, Chloroform-*d*)



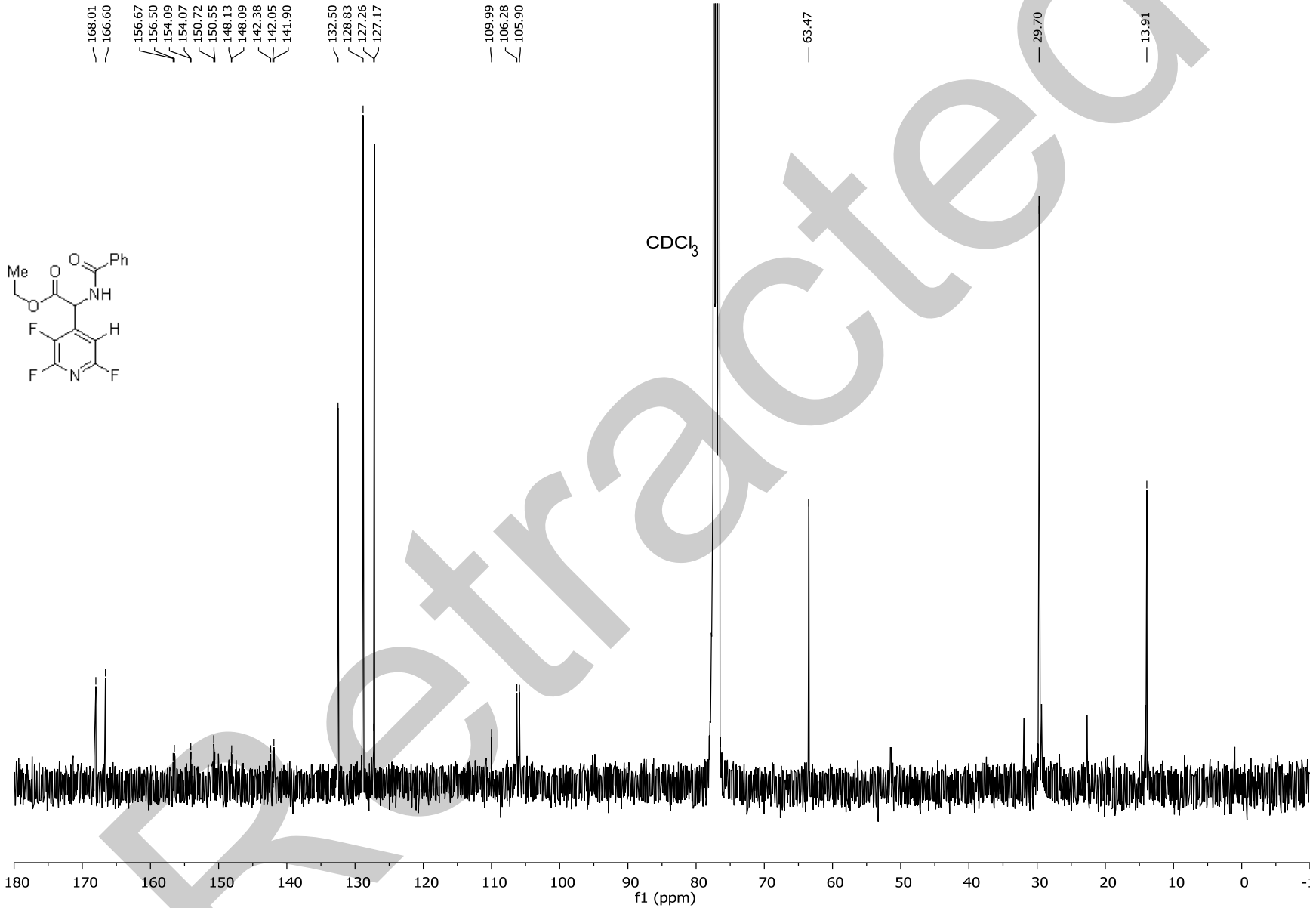
9c' ethyl 2-benzamido-2-(2,3,6-trifluoropyridin-4-yl)acetate ^{1}H NMR (400 MHz, Chloroform-*d*)



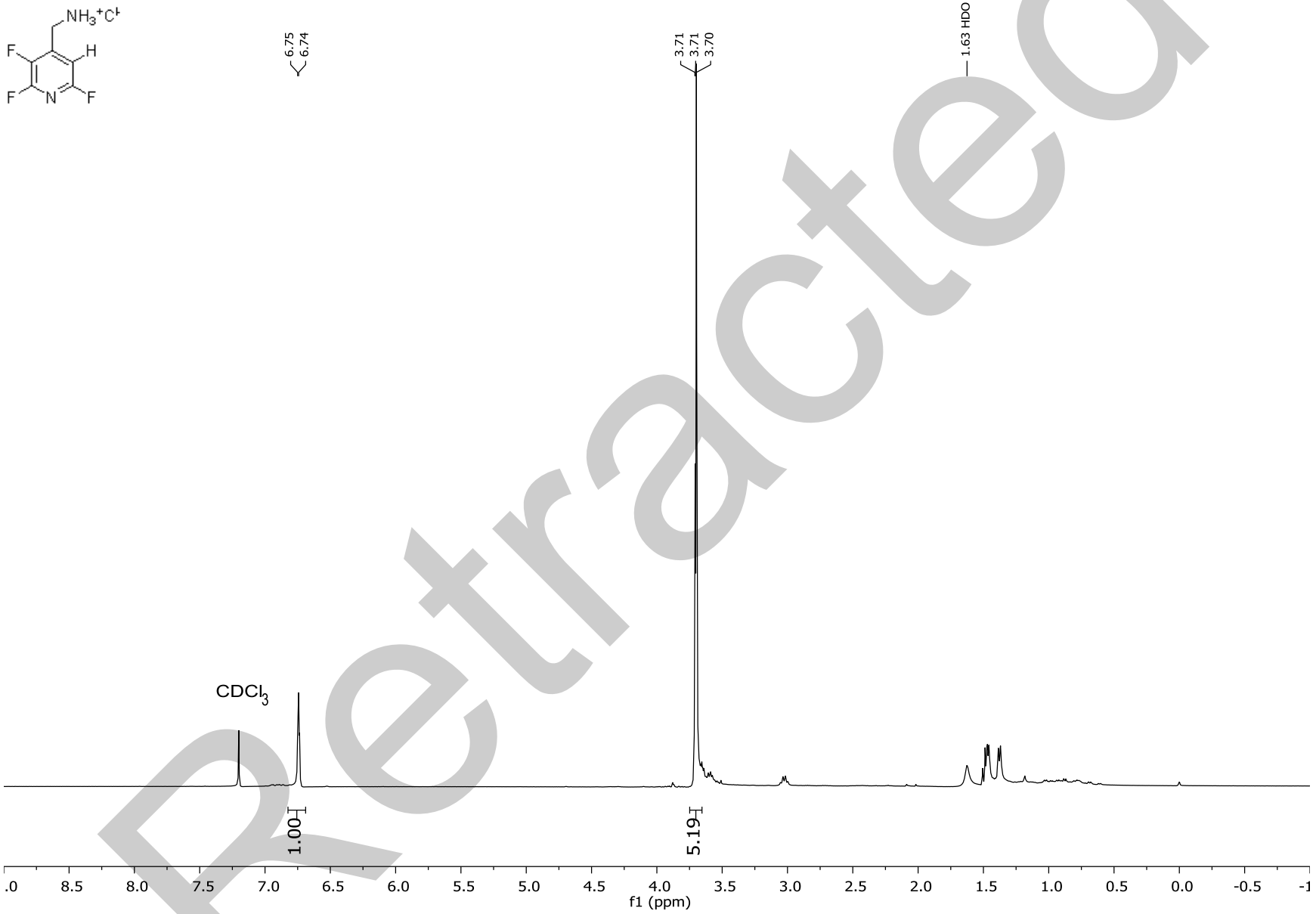
9c' ethyl 2-benzamido-2-(2,3,6-trifluoropyridin-4-yl)acetate ^{19}F NMR (376 MHz, Chloroform-*d*)



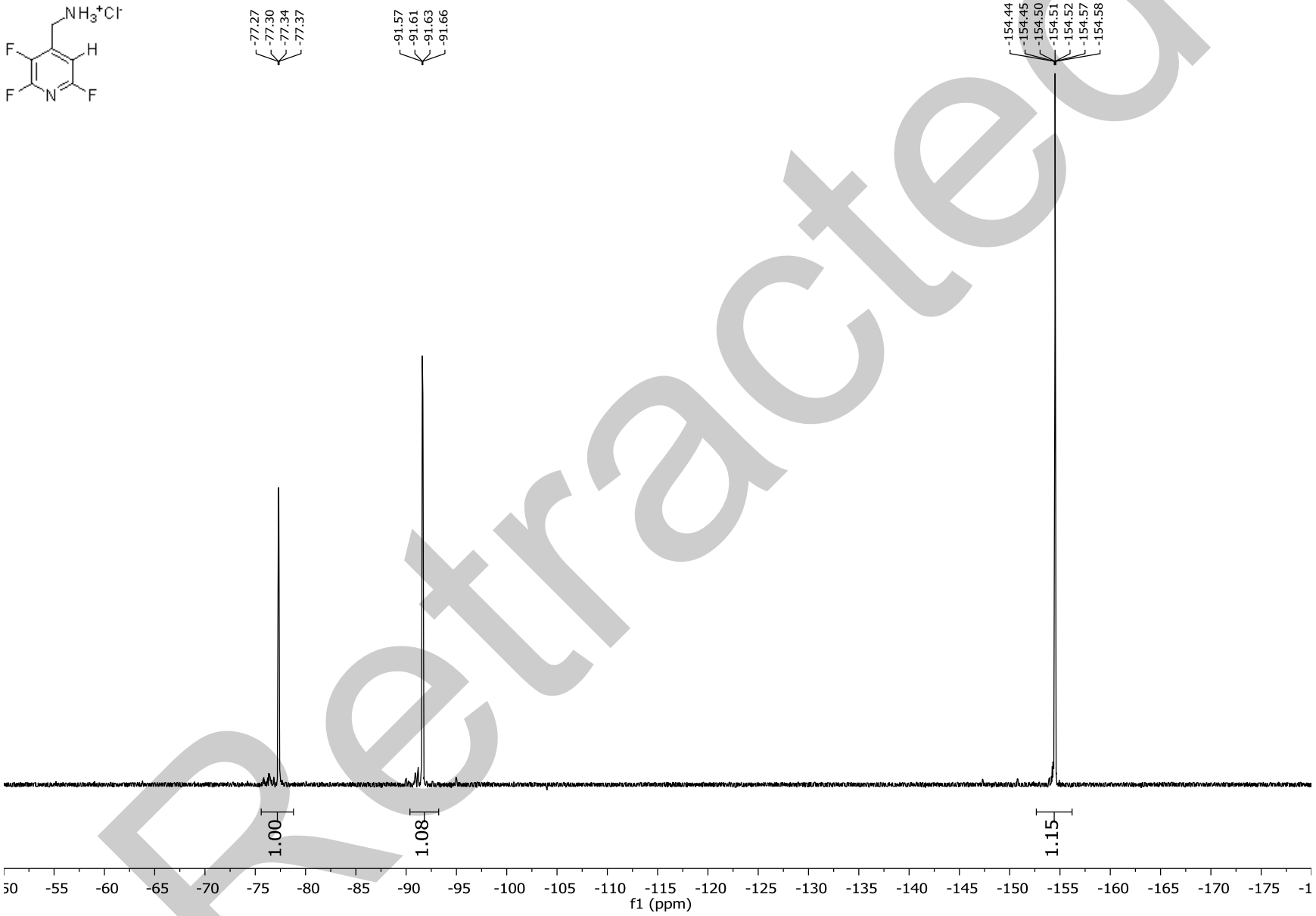
9c' ethyl 2-benzamido-2-(2,3,6-trifluoropyridin-4-yl)acetate ^{13}C NMR (101 MHz, Chloroform-*d*)



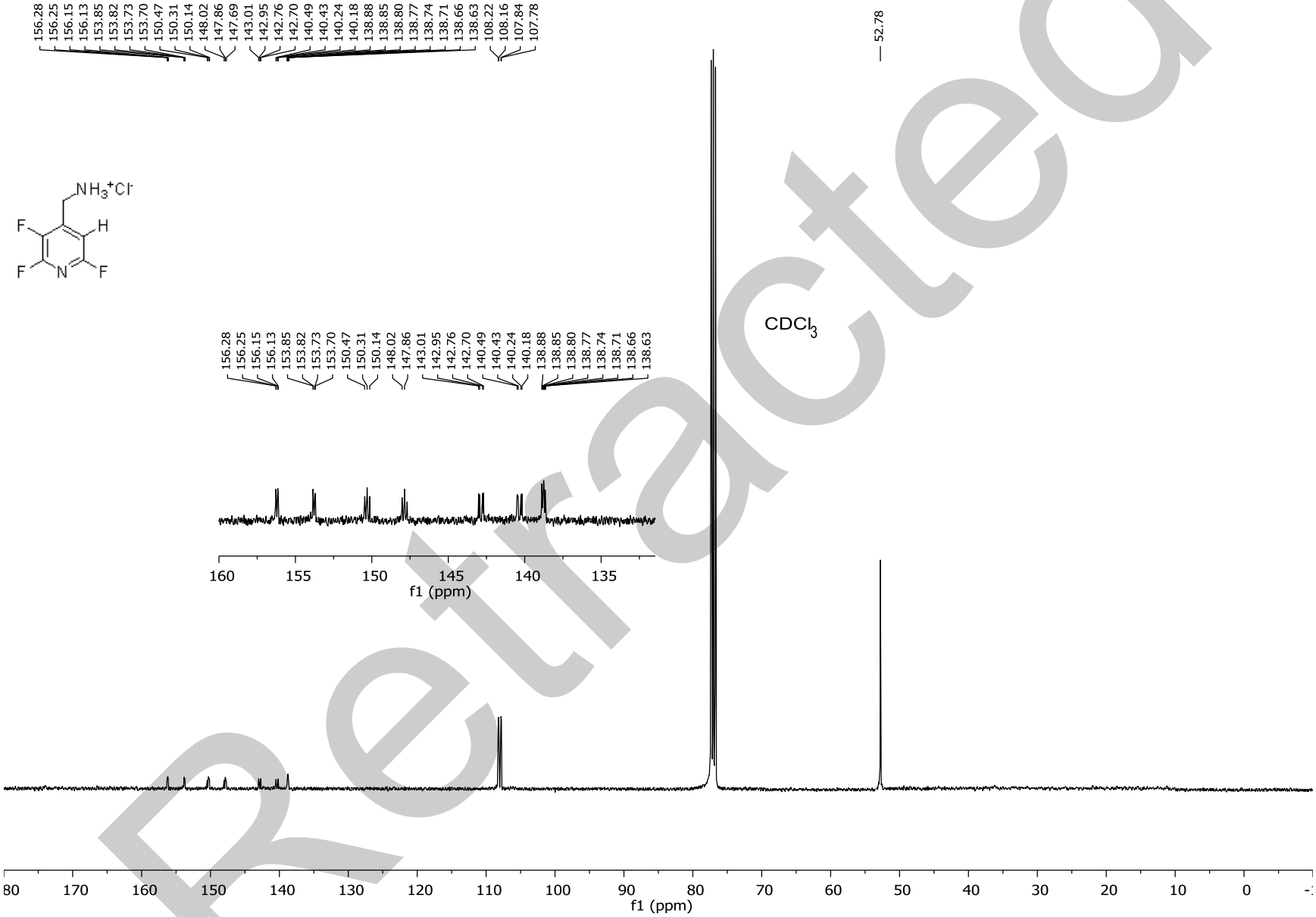
9d' (2,3,6-trifluoropyridin-4-yl))methanaminium chloride ^{1}H NMR (400 MHz, Chloroform-*d*)



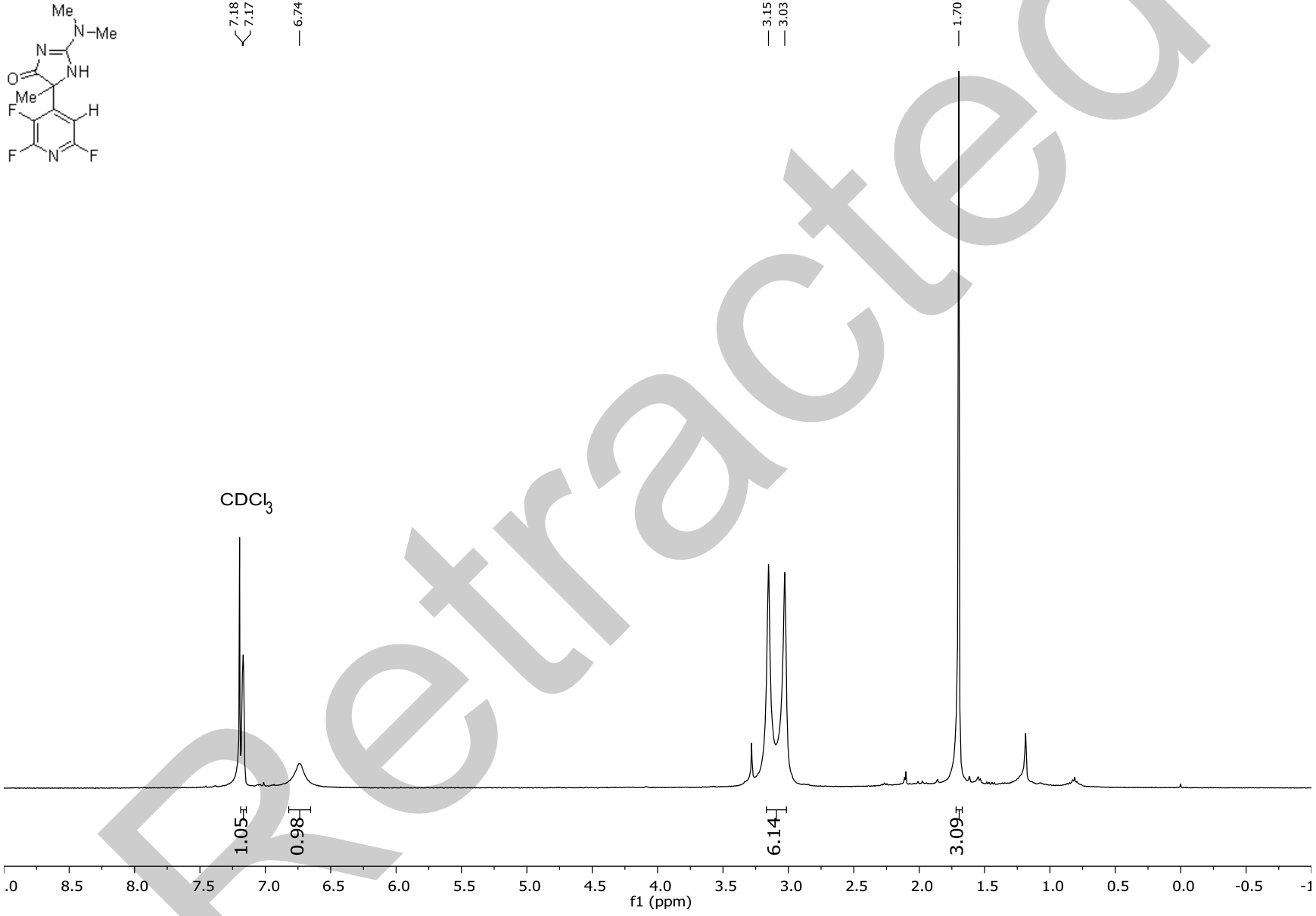
9d' (2,3,6-trifluoropyridin-4-yl))methanaminium chloride ^{19}F NMR (376 MHz, Chloroform-*d*)



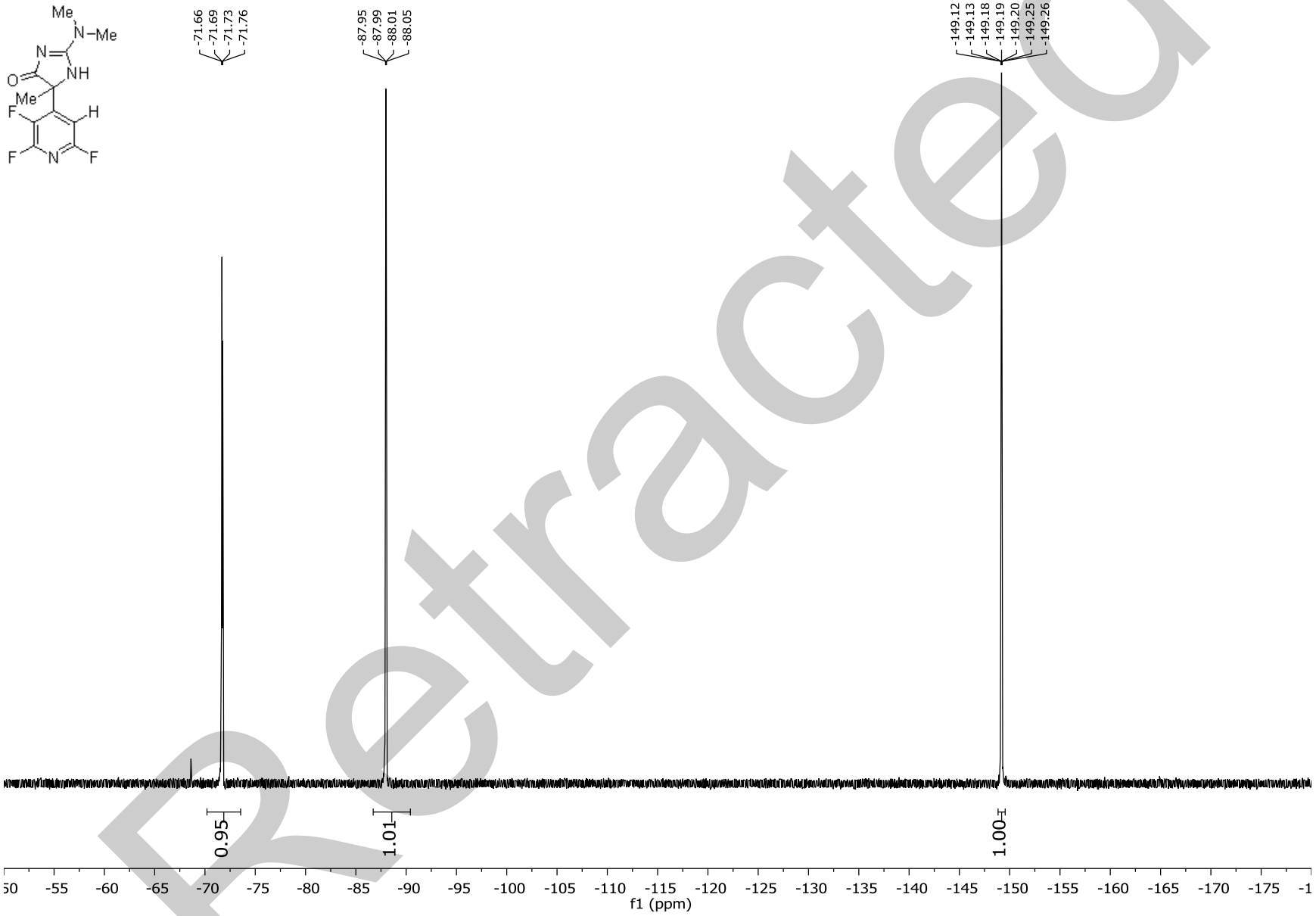
9d' (2,3,6-trifluoropyridin-4-yl))methanaminium chloride ^{13}C NMR (101 MHz, Chloroform-*d*)



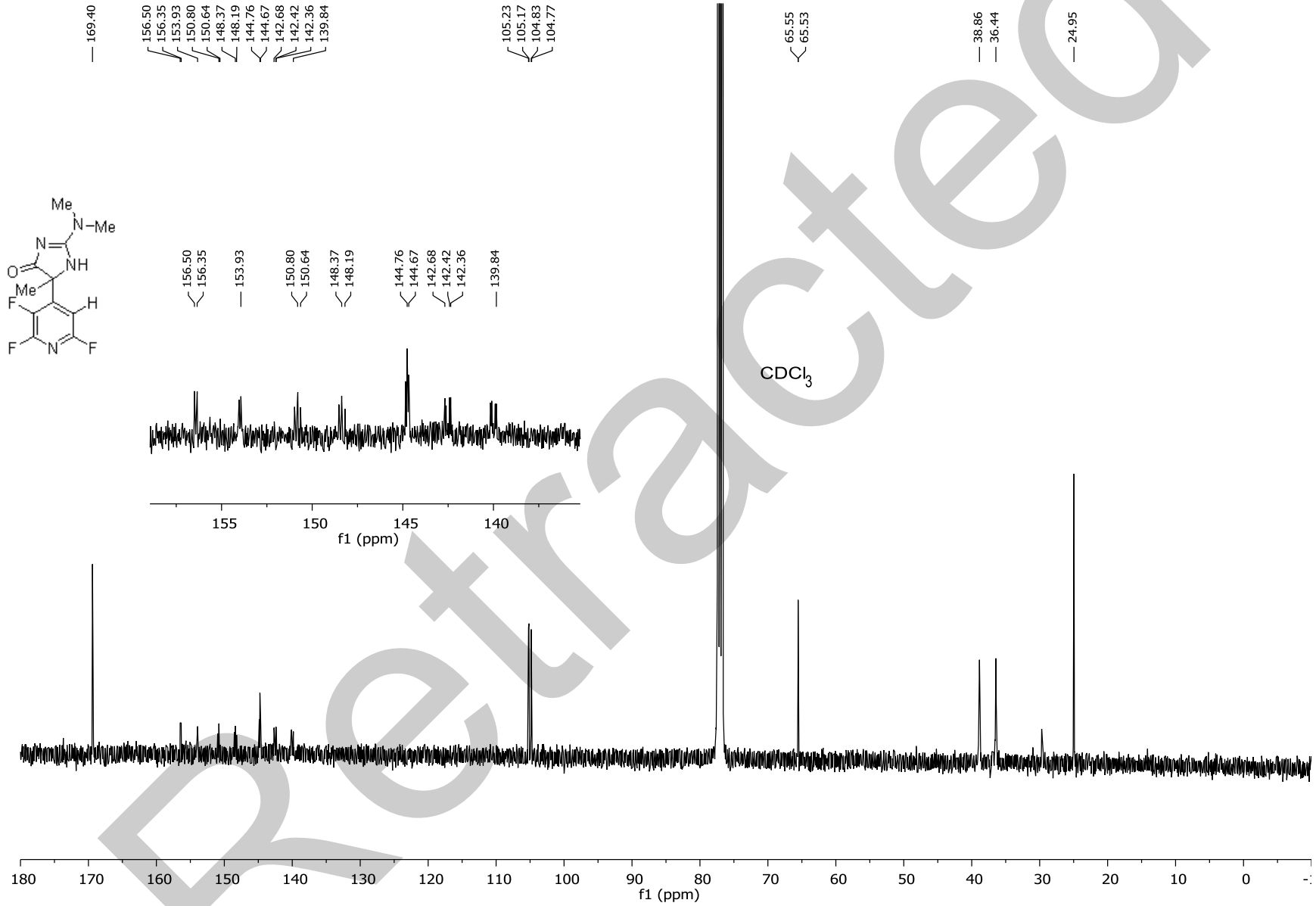
9e' 2-(dimethylamino)-5-methyl-5-(2,3,6-trifluoropyridin-4-yl)-1,5-dihydro-4*H*-imidazol-4-one ^{1}H NMR (400 MHz, Chloroform-*d*)



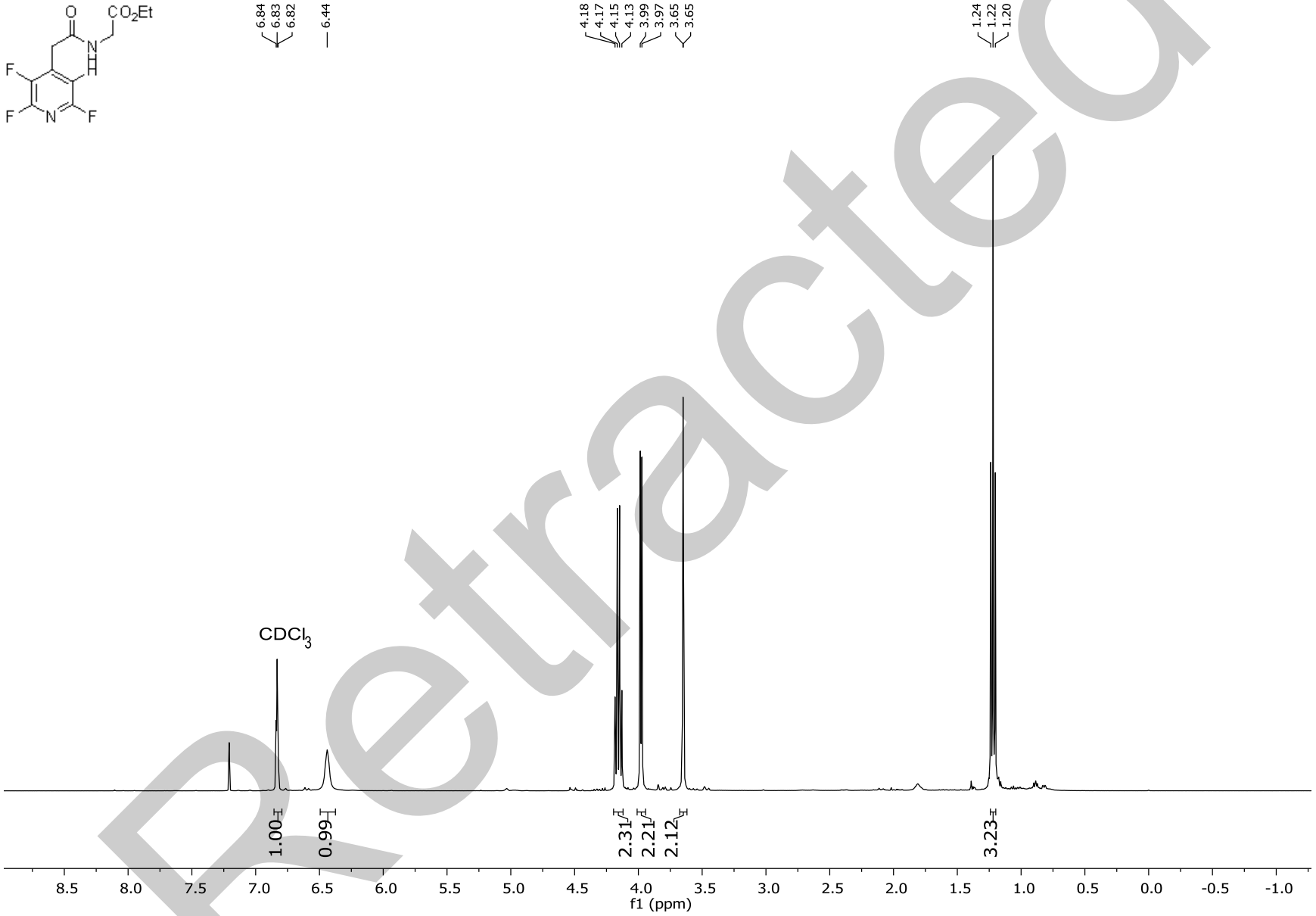
9d' 2-(dimethylamino)-5-methyl-5-(2,3,6-trifluoropyridin-4-yl)-1,5-dihydro-4*H*-imidazol-4-one ^{19}F NMR (376 MHz, Chloroform-*d*)



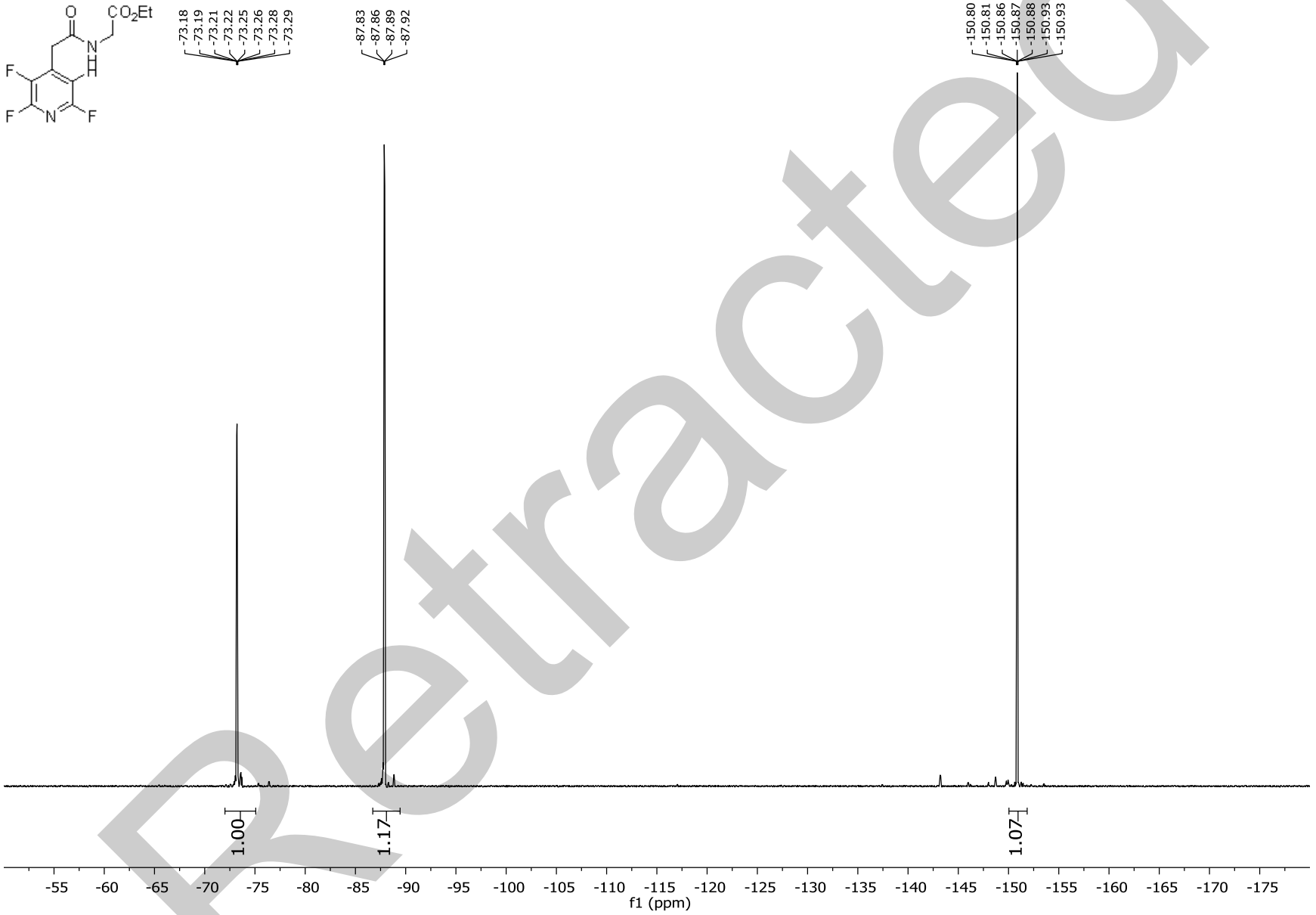
9d' 2-(dimethylamino)-5-methyl-5-(2,3,6-trifluoropyridin-4-yl)-1,5-dihydro-4*H*-imidazol-4-one ^{13}C NMR (101 MHz, Chloroform-*d*)



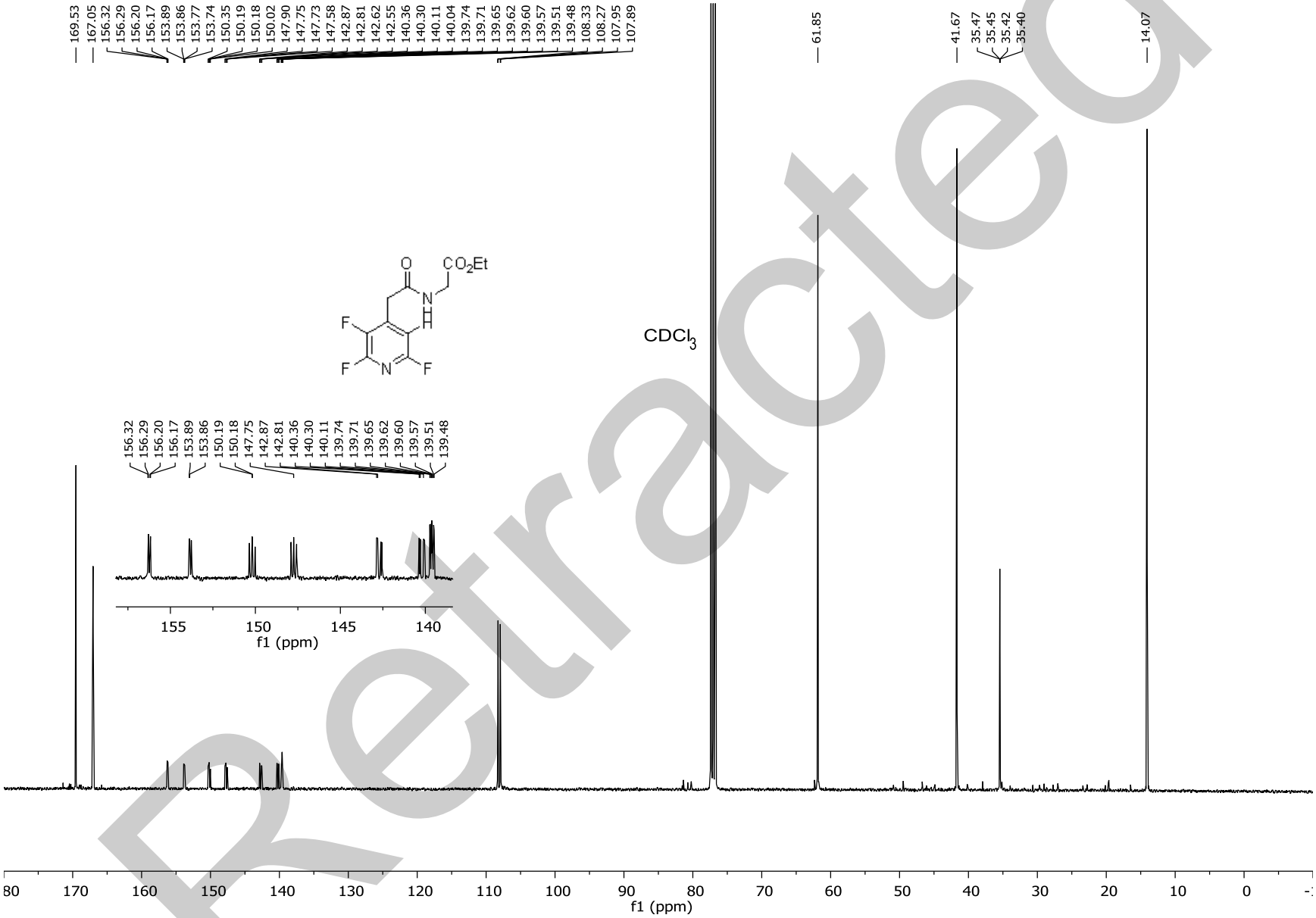
10a' methyl (2-(2,3,6-trifluoropyridin-4-yl)acetyl)glycinate^{1}H NMR (400 MHz, Chloroform-*d*)



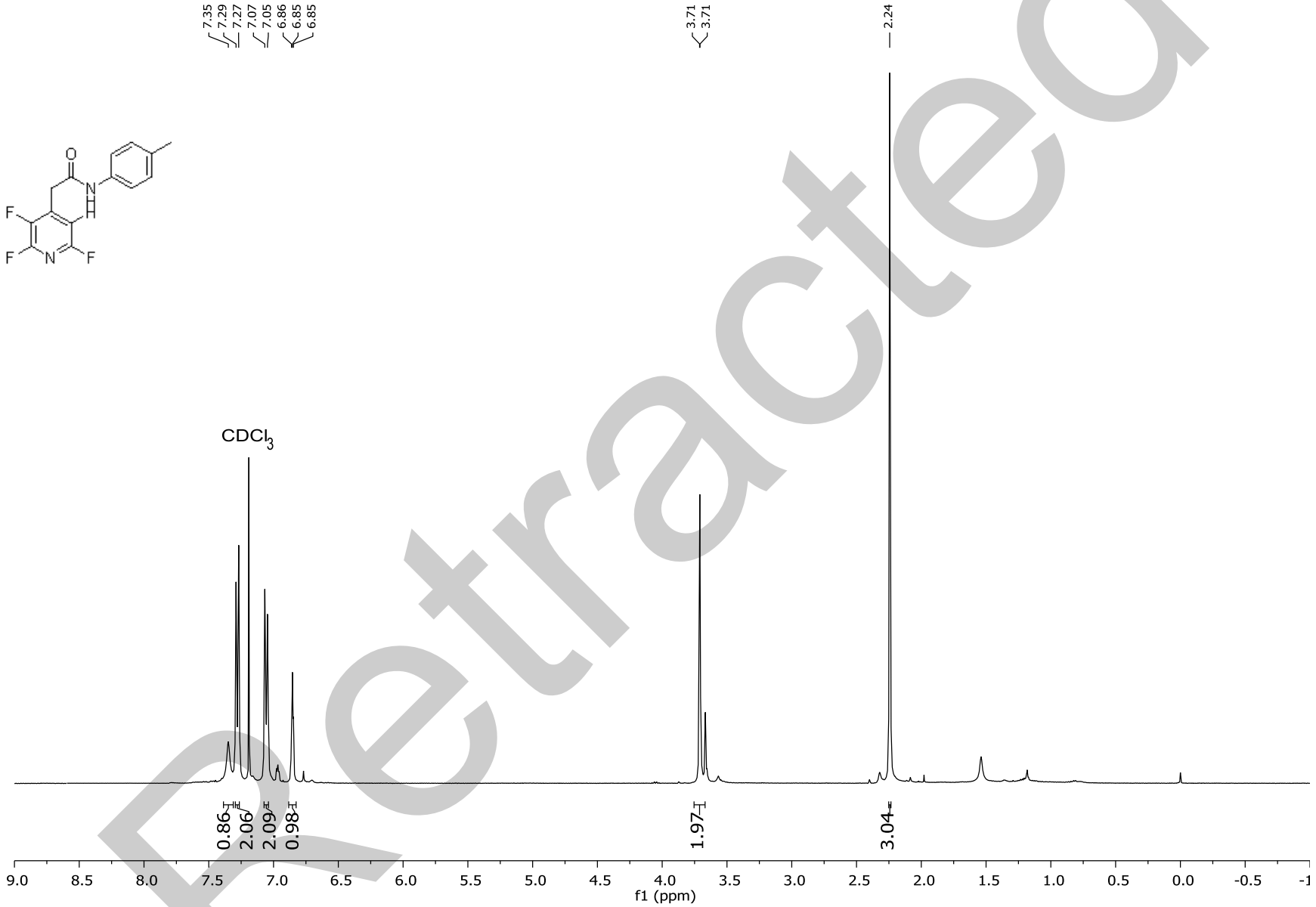
10a' methyl (2-(2,3,6-trifluoropyridin-4-yl)acetyl)glycinate ^{19}F NMR (376 MHz, Chloroform-*d*)



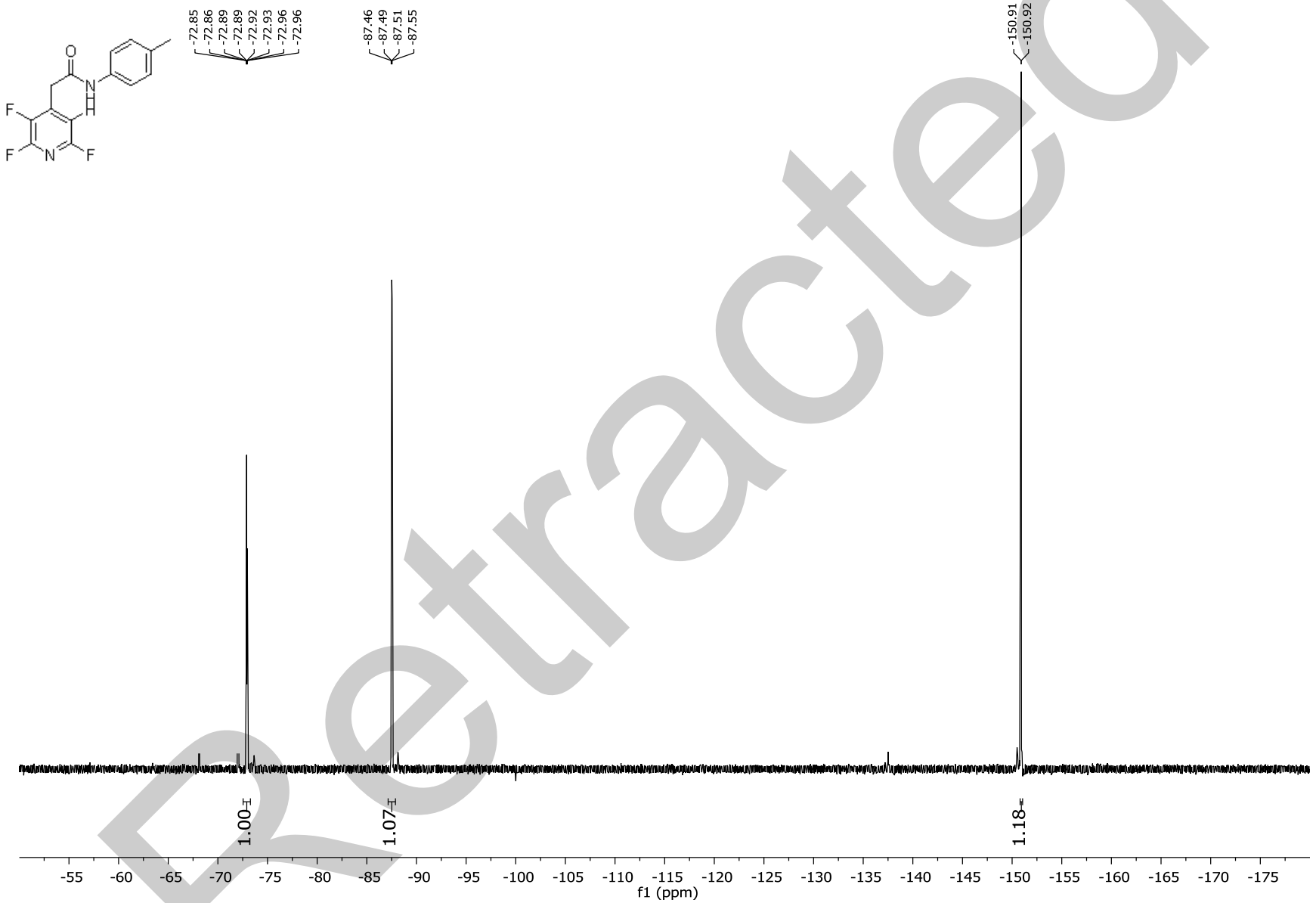
10a' methyl (2-(2,3,6-trifluoropyridin-4-yl)acetyl)glycinate ^{13}C NMR (101 MHz, Chloroform-*d*)



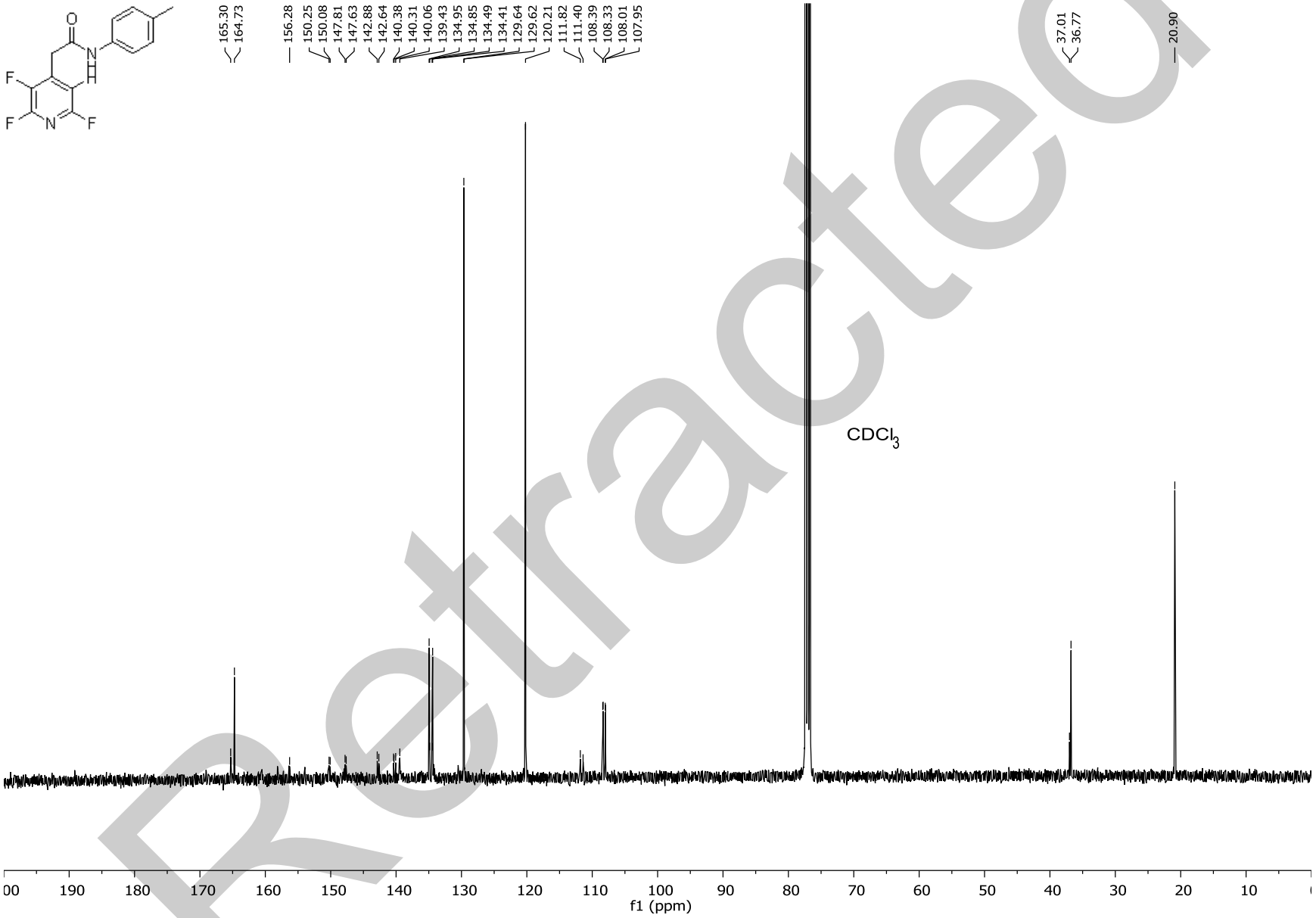
10b' *N*-(*p*-tolyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



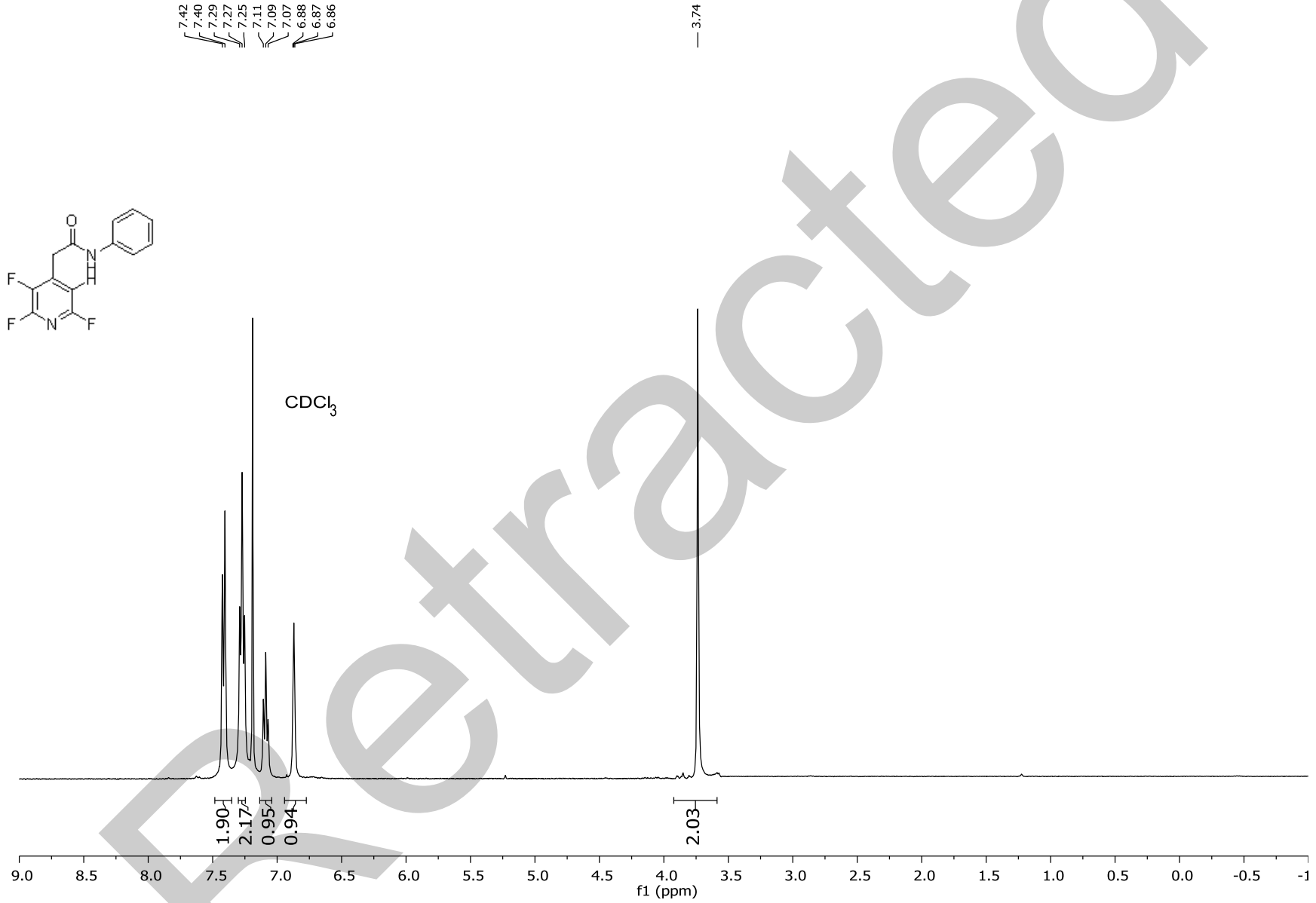
10b' *N*-(*p*-tolyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



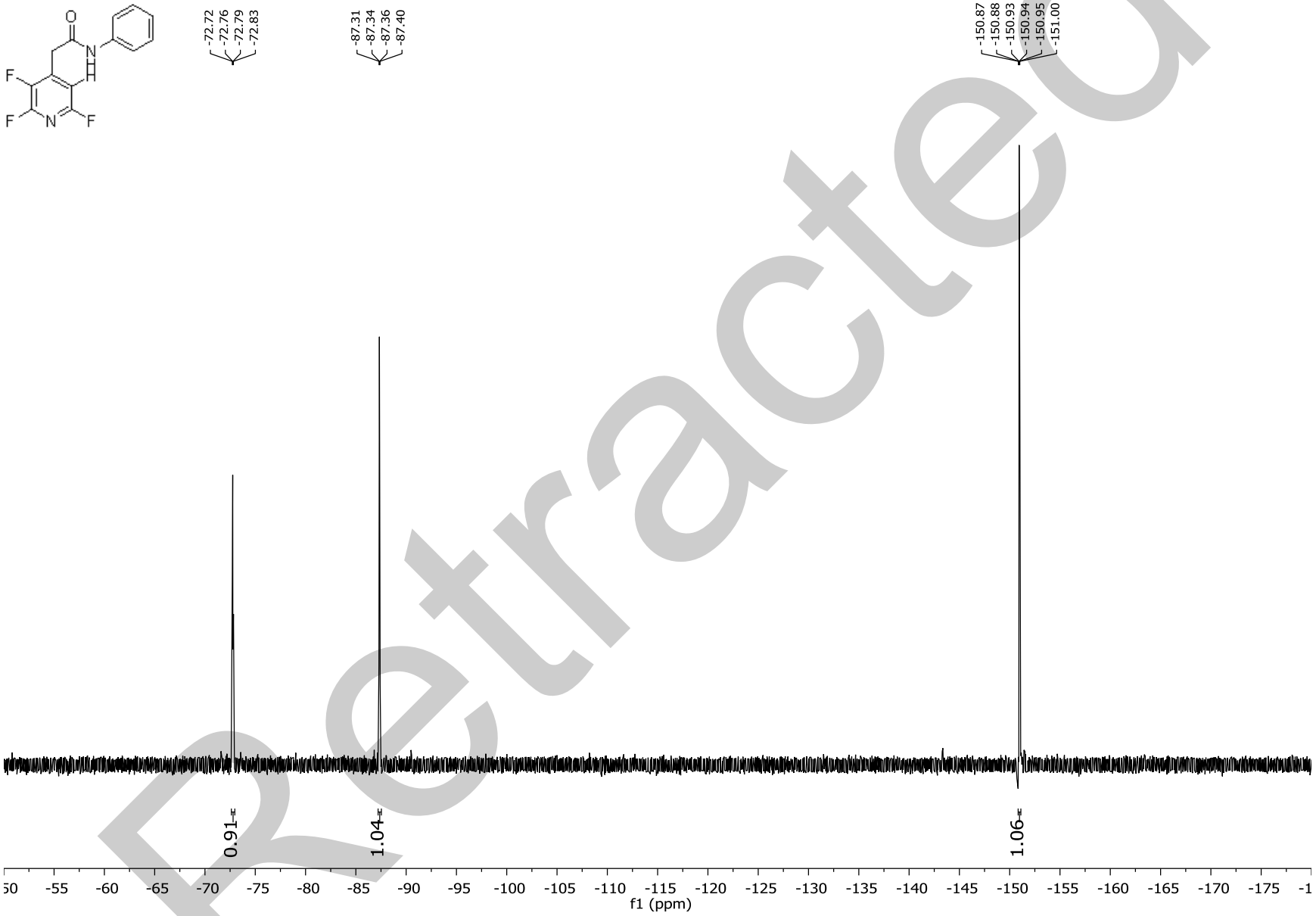
10b' *N*-(*p*-tolyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



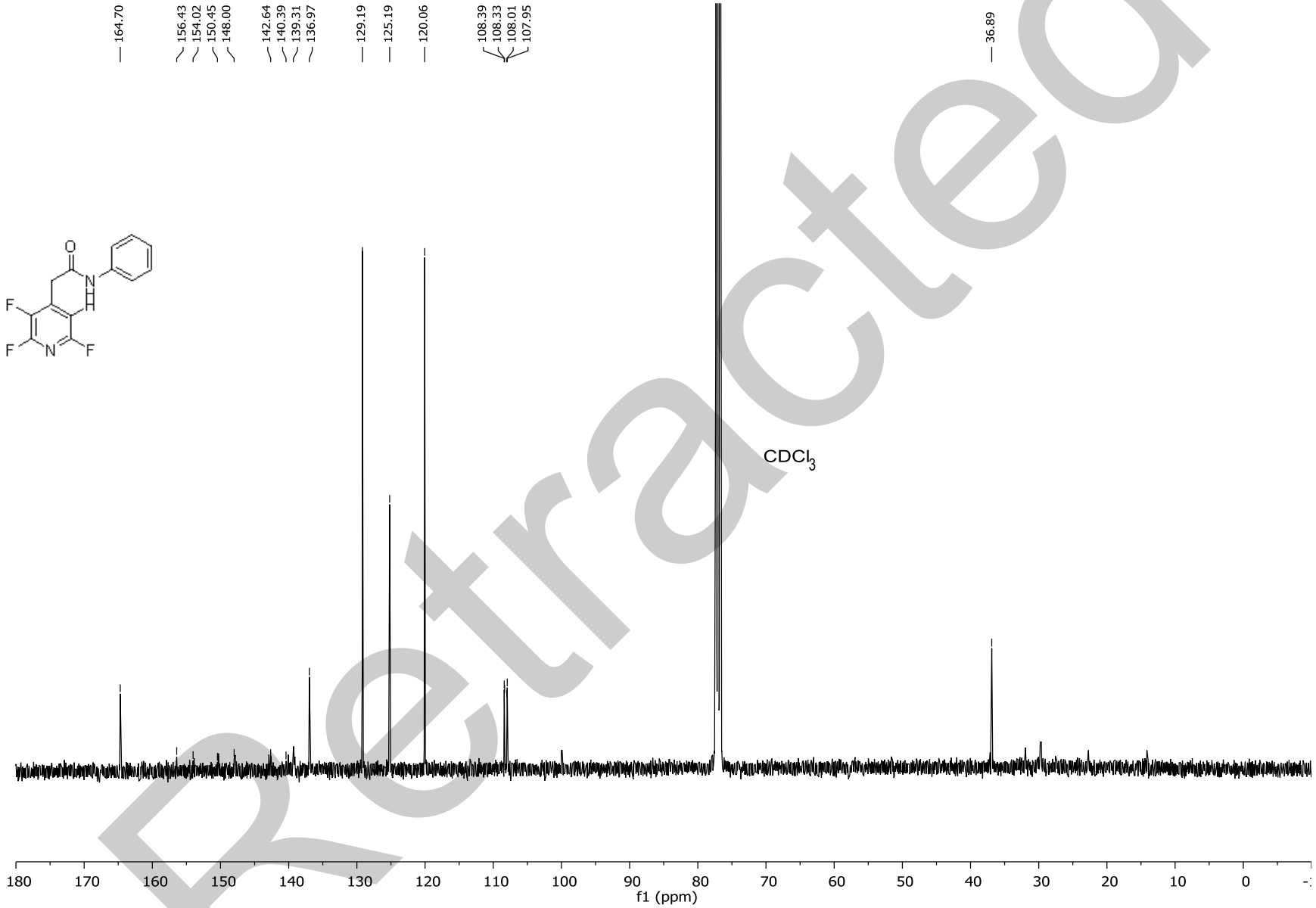
10c' *N*-phenyl-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



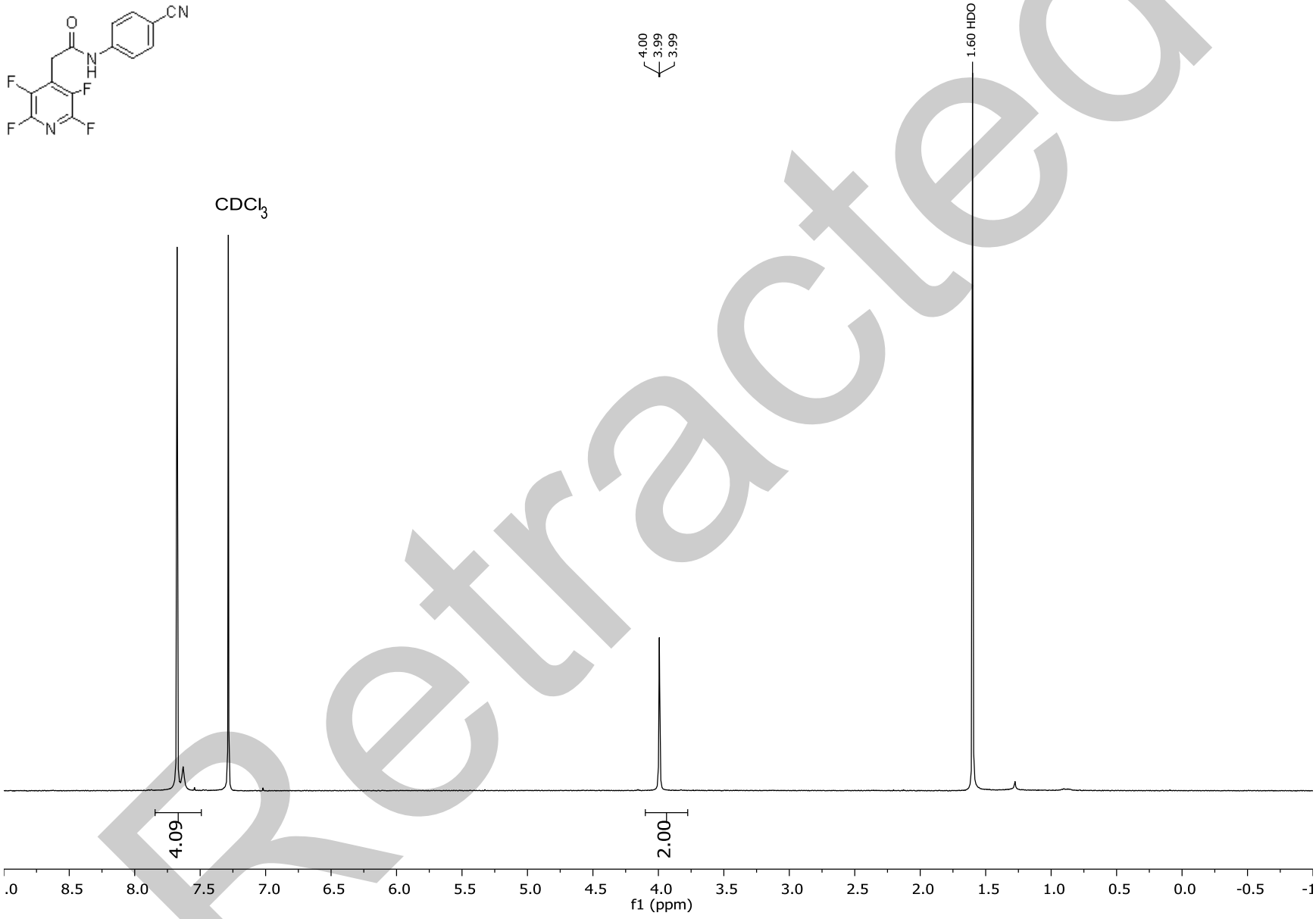
10c' *N*-phenyl-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



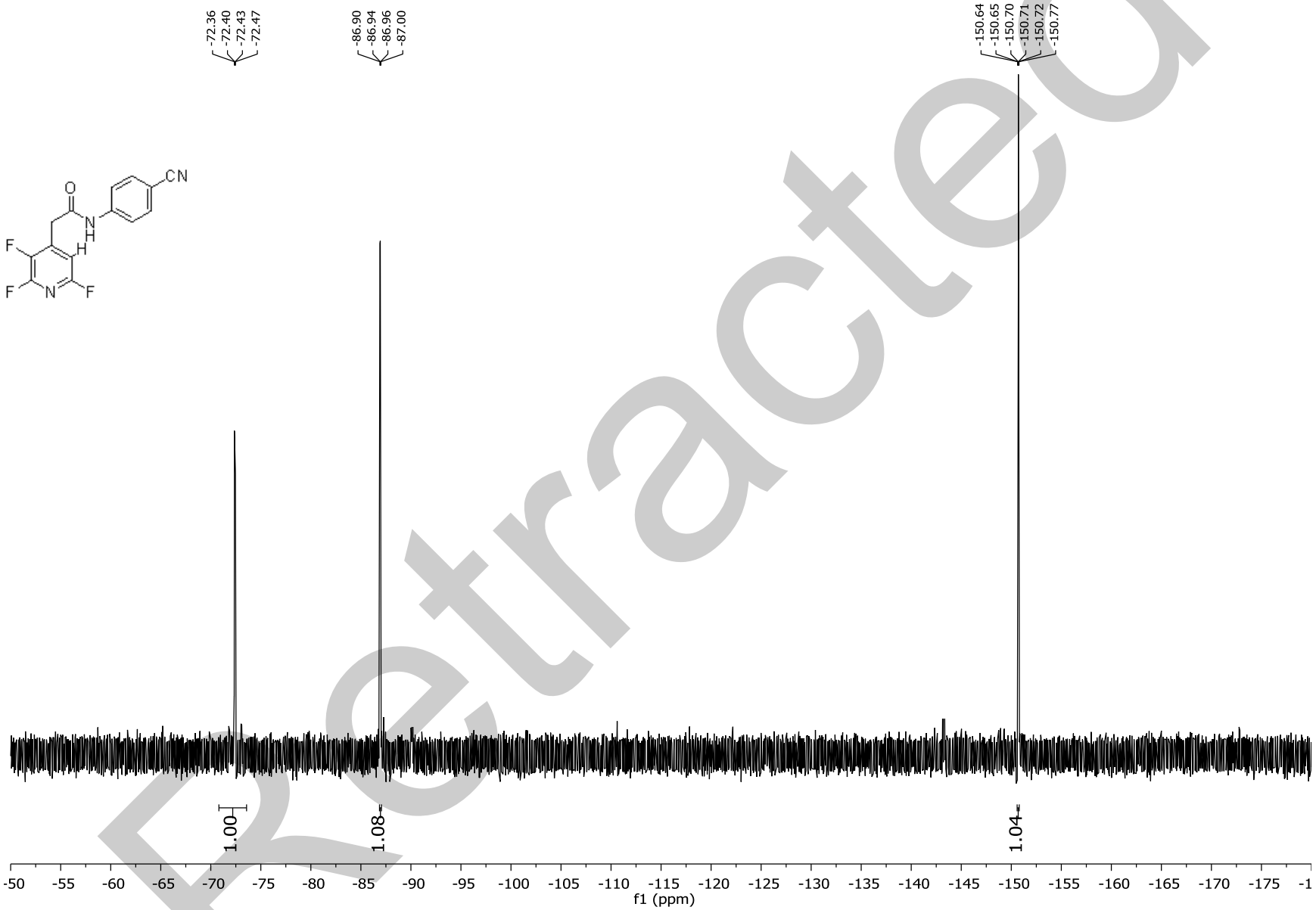
10c' *N*-phenyl-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



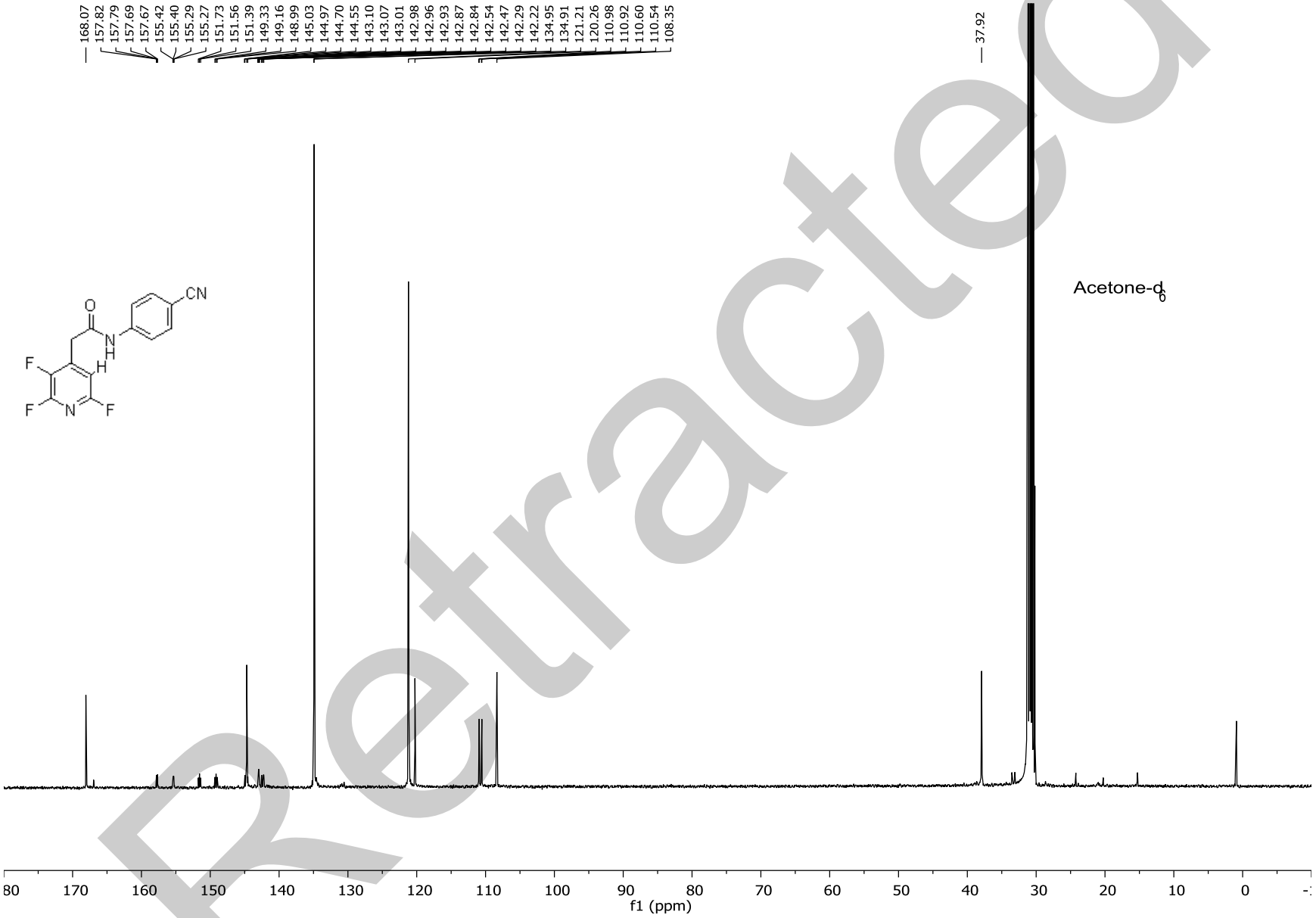
10d *N*-(4-cyanophenyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



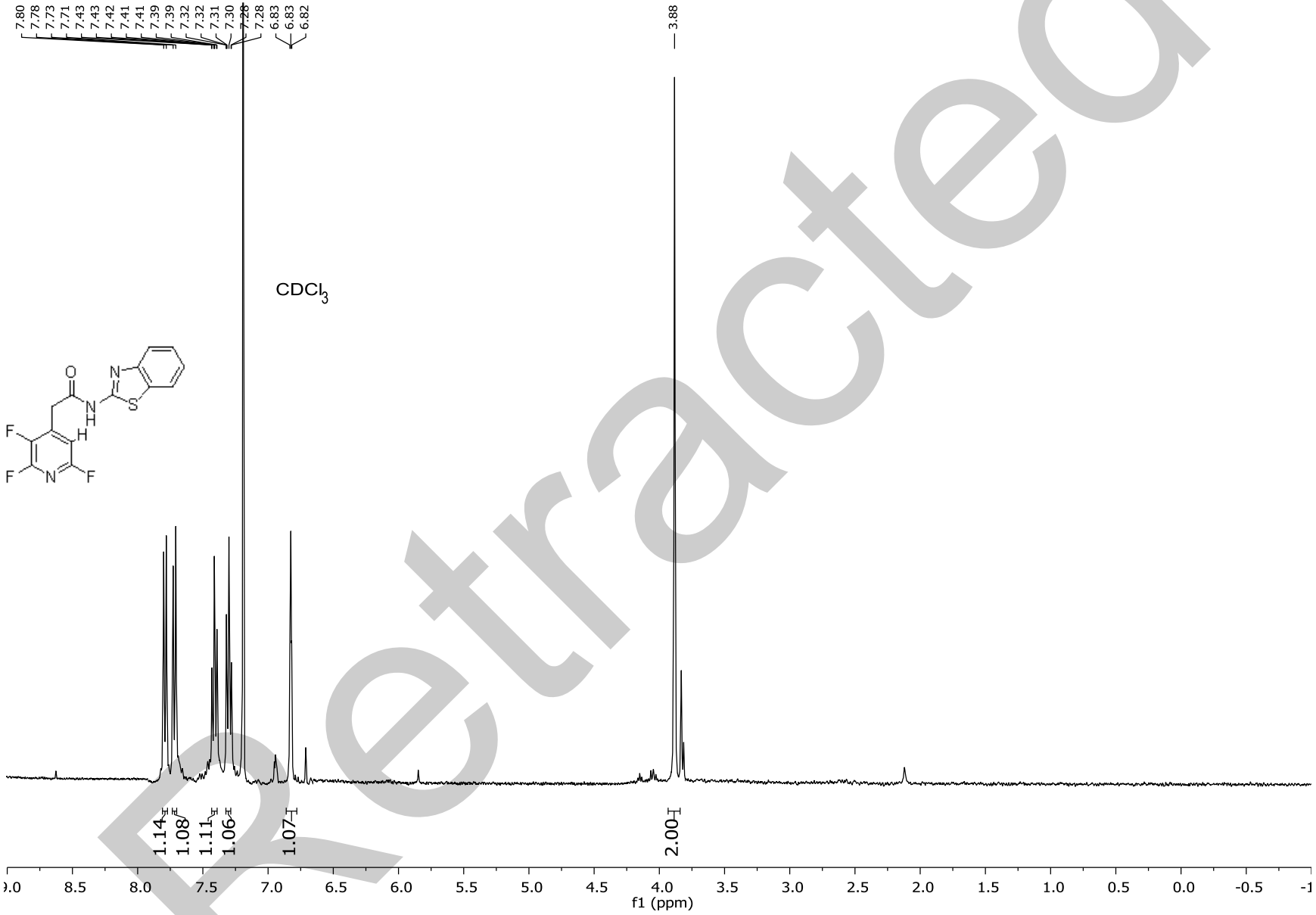
10d *N*-(4-cyanophenyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



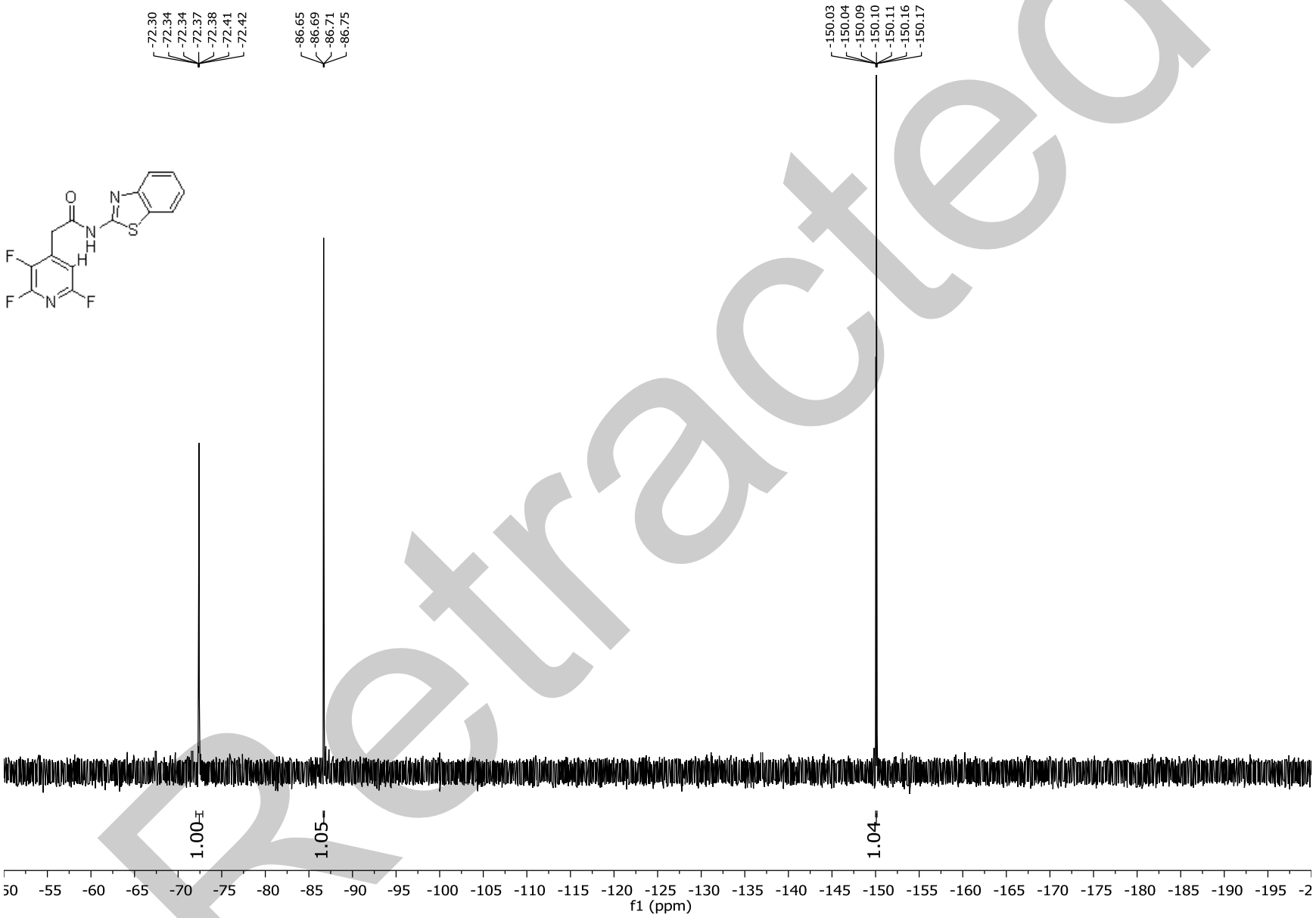
10d *N*-(4-cyanophenyl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



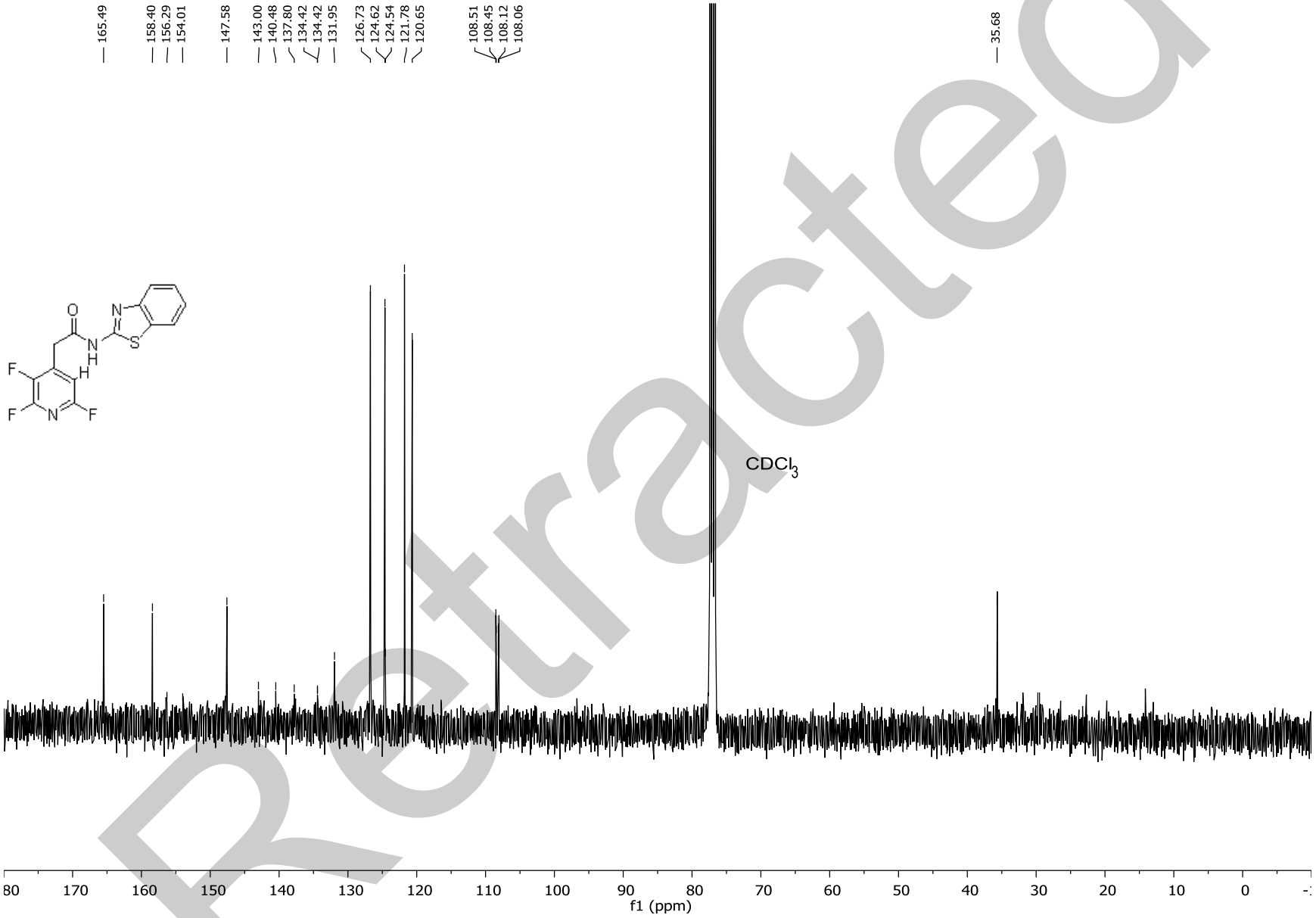
10e *N*-(benzo[d]thiazol-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



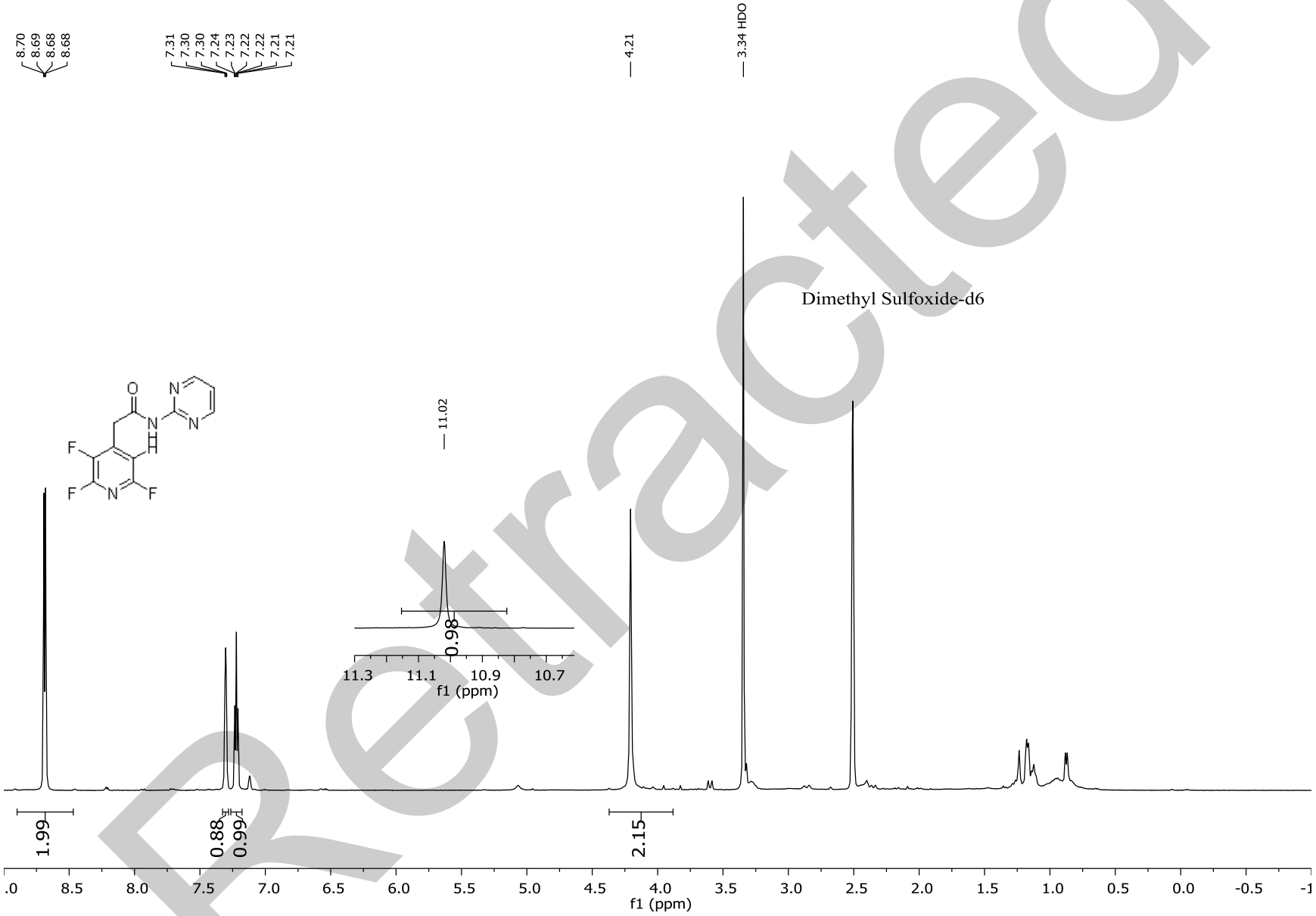
10e *N*-(benzo[d]thiazol-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



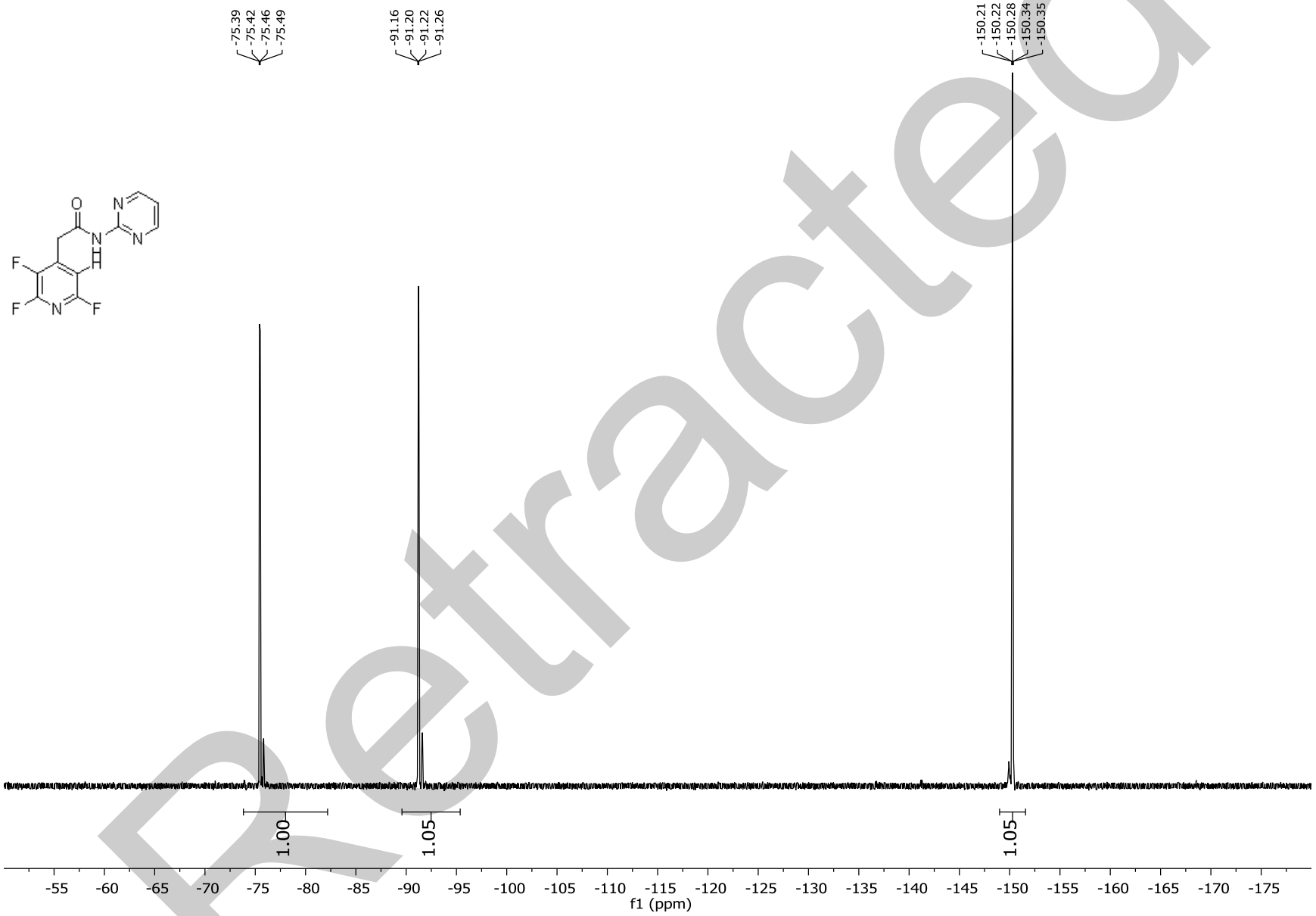
10e *N*-(benzo[d]thiazol-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide). ^{13}C NMR (101 MHz, Chloroform-*d*)



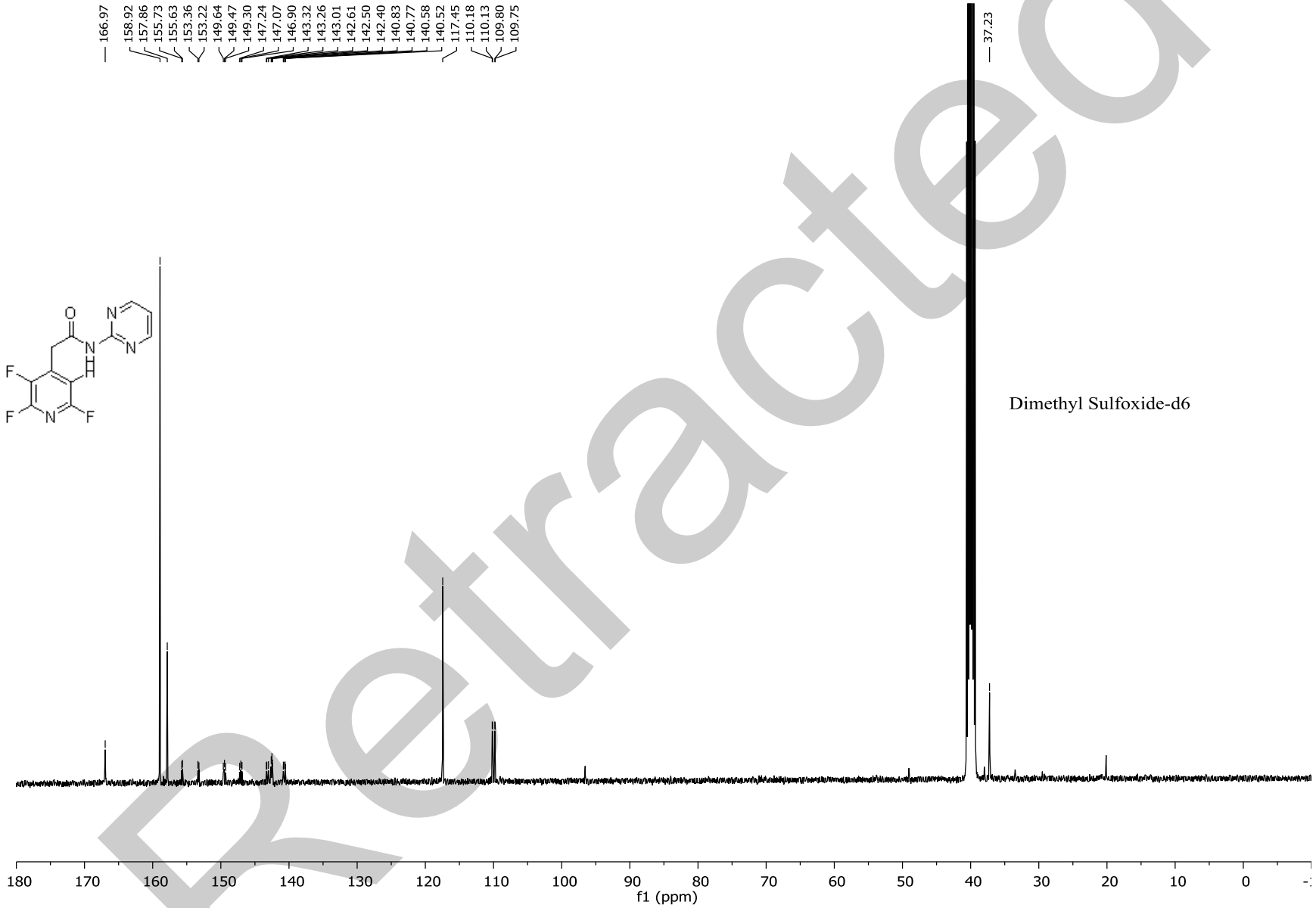
10f *N*-(pyrimidin-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{1}H NMR (400 MHz, Dimethyl Sulfoxide-d$_6$)



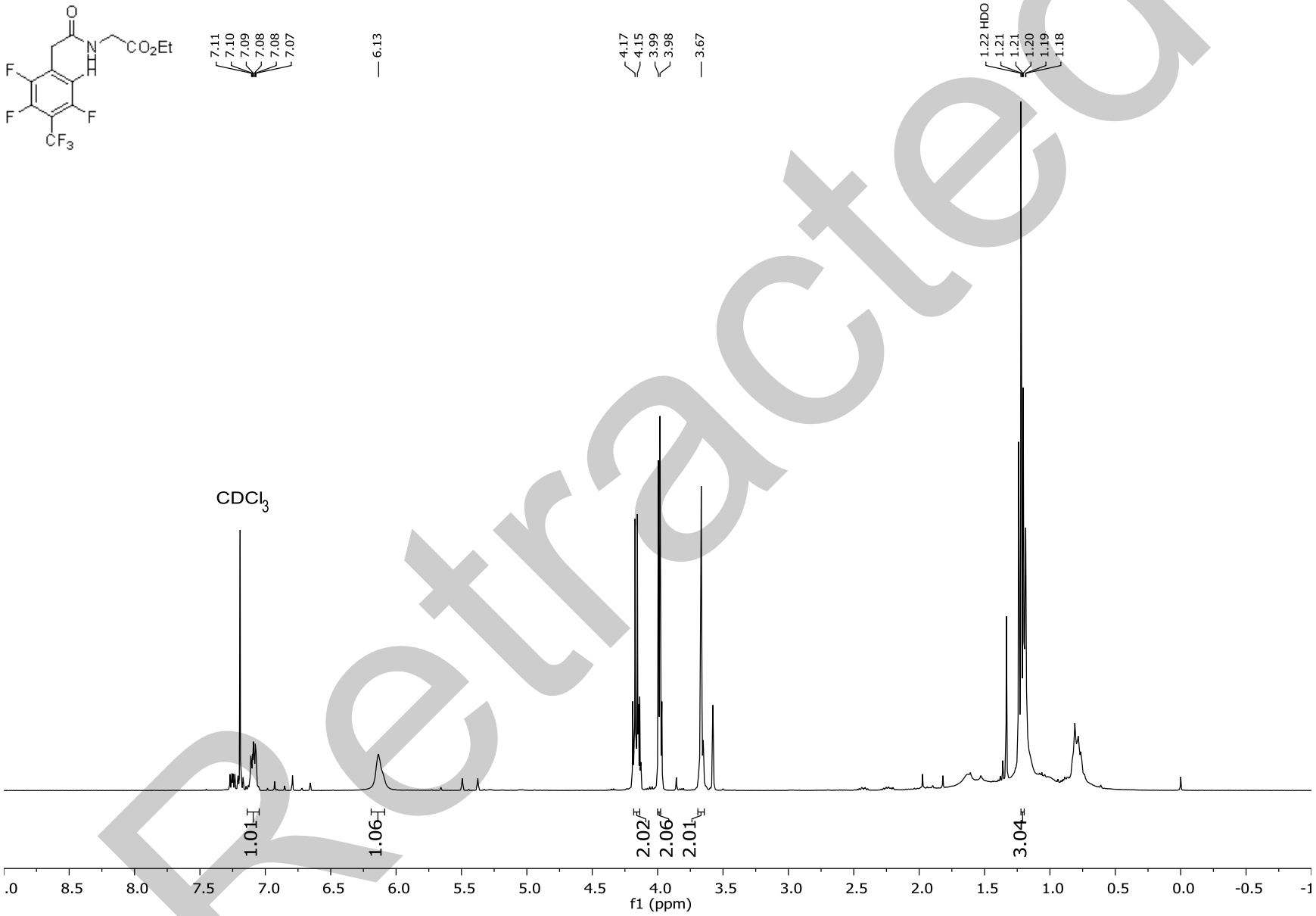
10f *N*-(pyrimidin-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{19}F NMR (376 MHz, Dimethyl Sulfoxide-d$_6$)



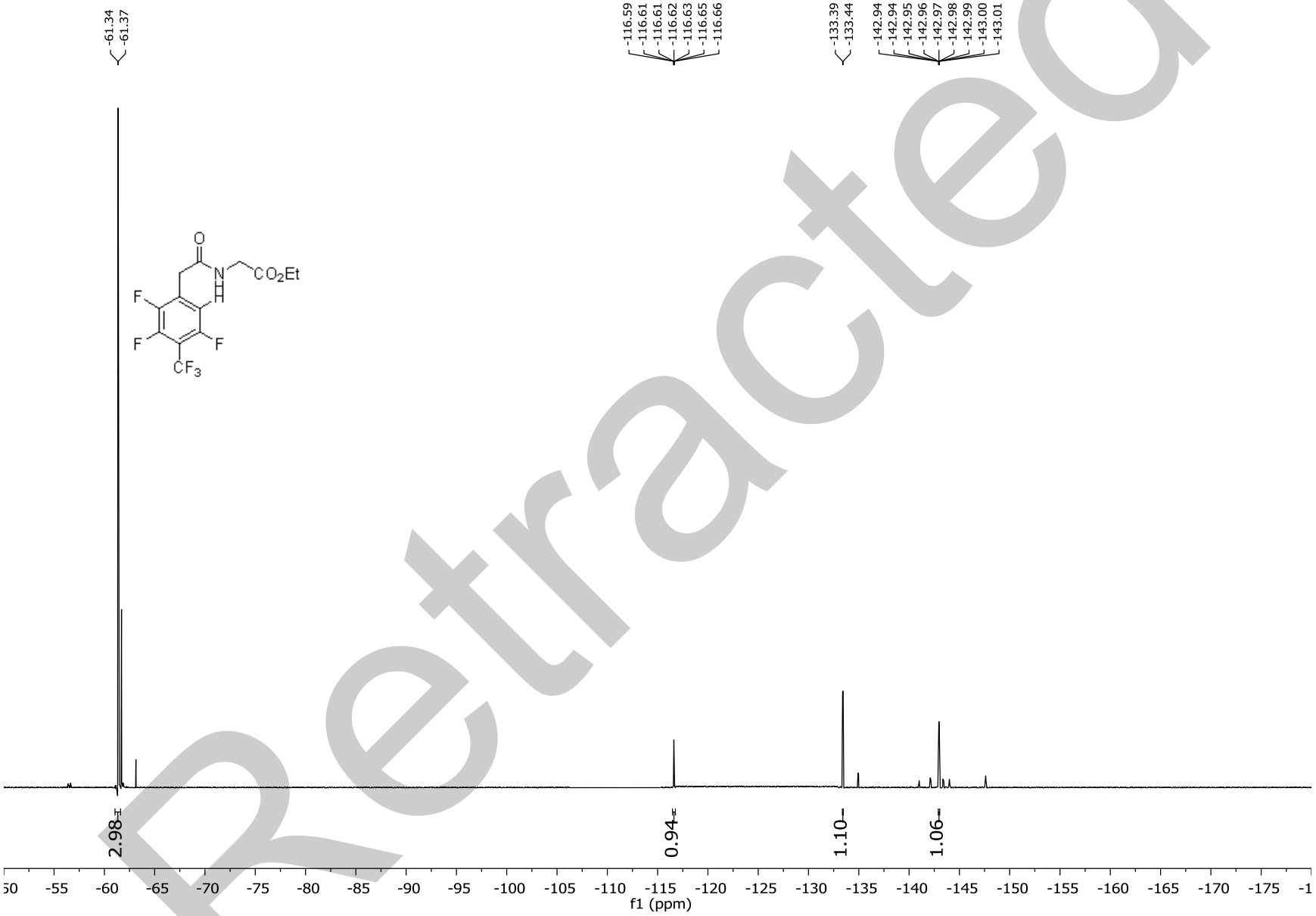
10f *N*-(pyrimidin-2-yl)-2-(2,3,6-trifluoropyridin-4-yl)acetamide ^{13}C NMR (101 MHz, Dimethyl Sulfoxide-d$_6$)



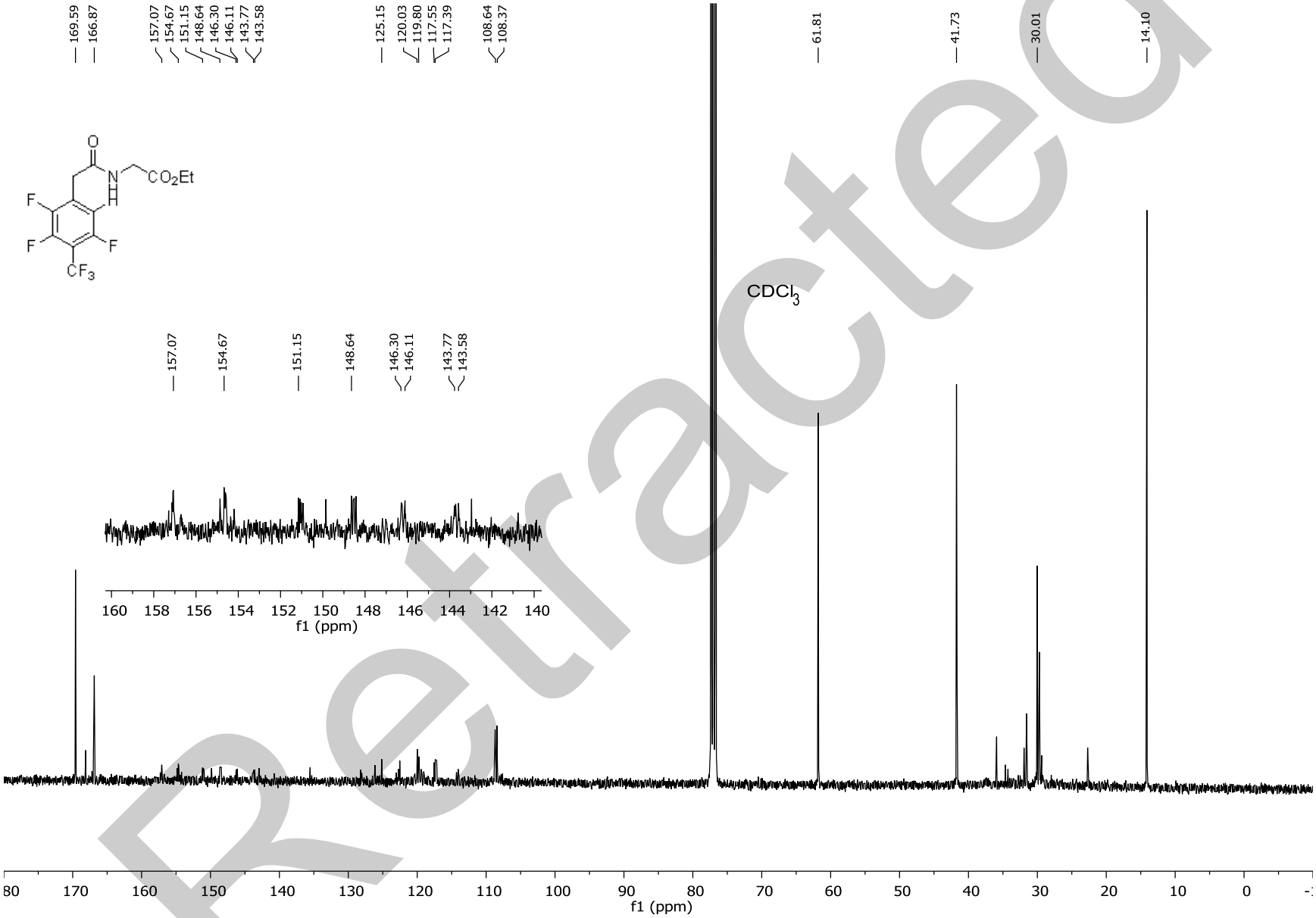
10g ethyl (2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetyl) glycinate . ^{1}H NMR (400 MHz, Chloroform-*d*)



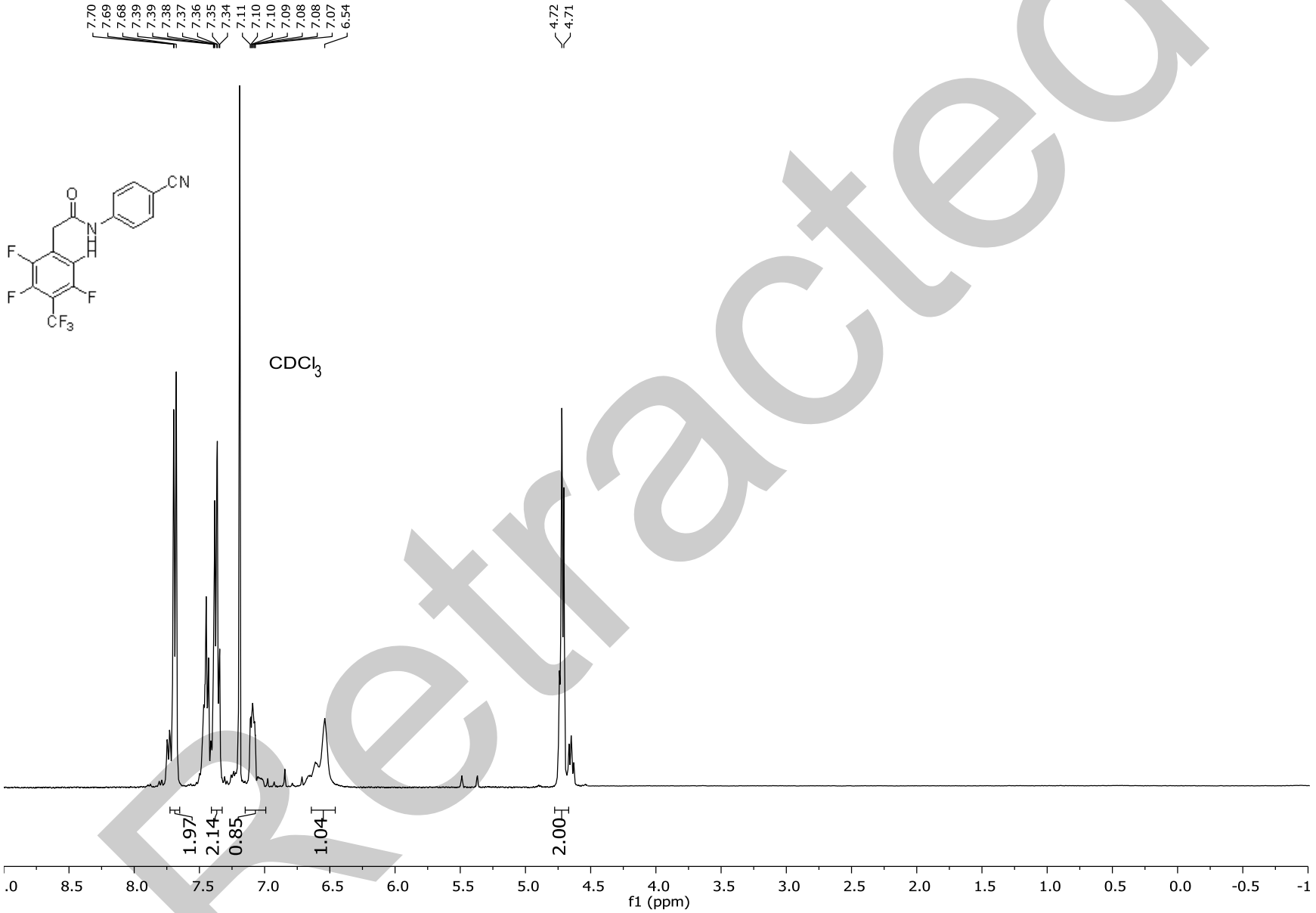
10g ethyl (2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetyl) glycinate ^{19}F NMR (376 MHz, Chloroform-*d*)



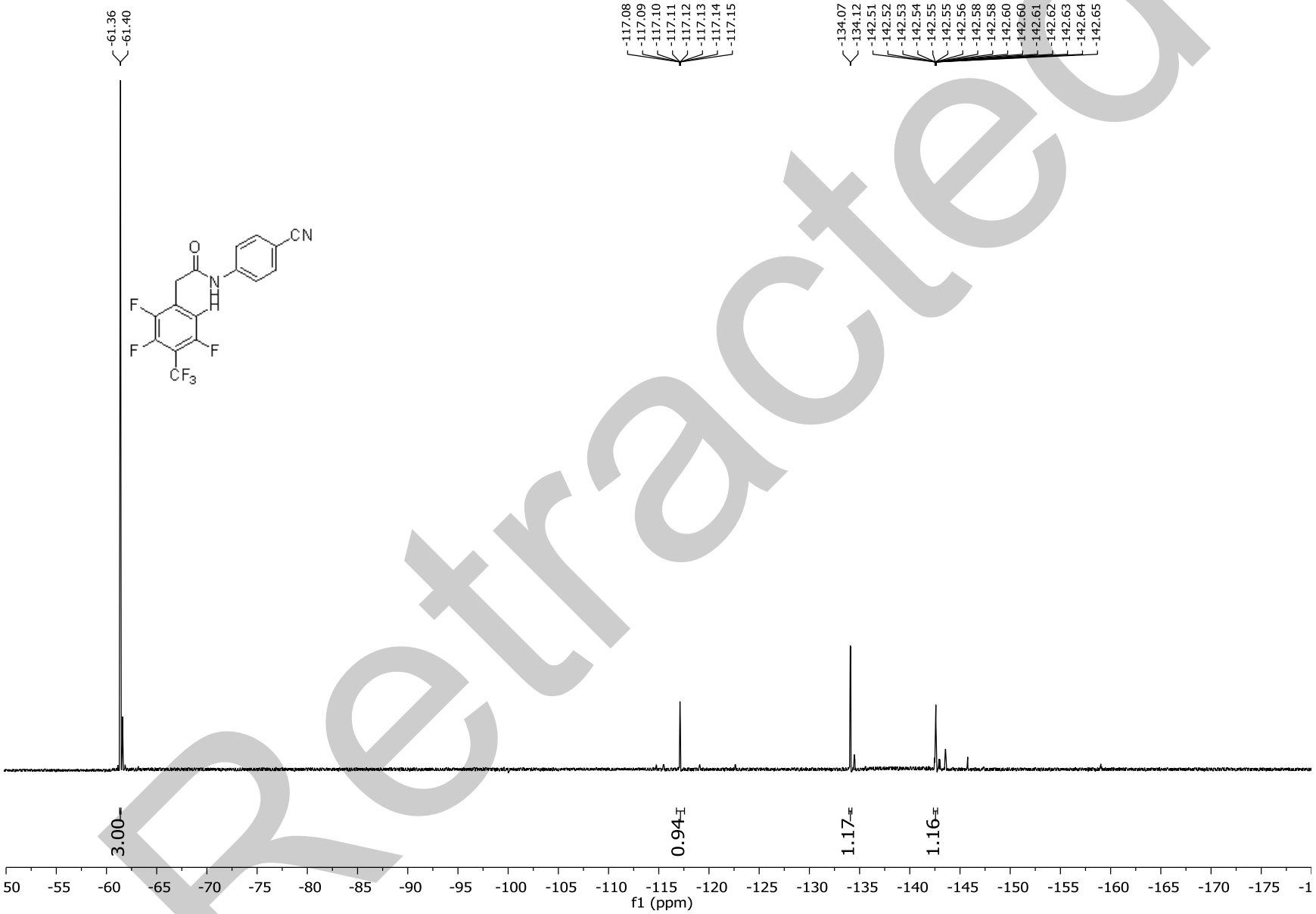
10g ethyl (2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl)acetyl) glycinate). ^{13}C NMR (101 MHz, Chloroform-*d*)



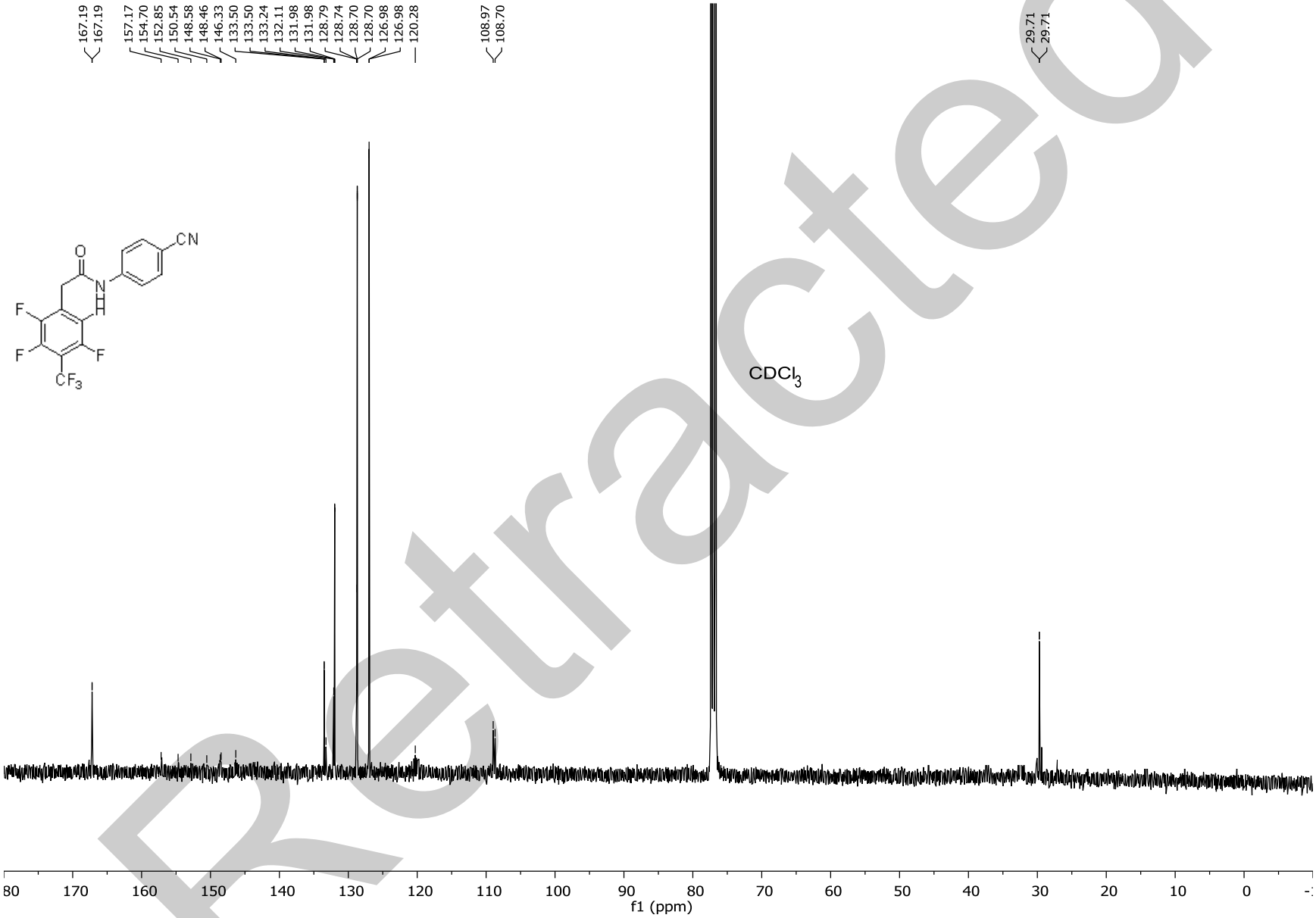
10h *N*-(4-cyanophenyl)-2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl) acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



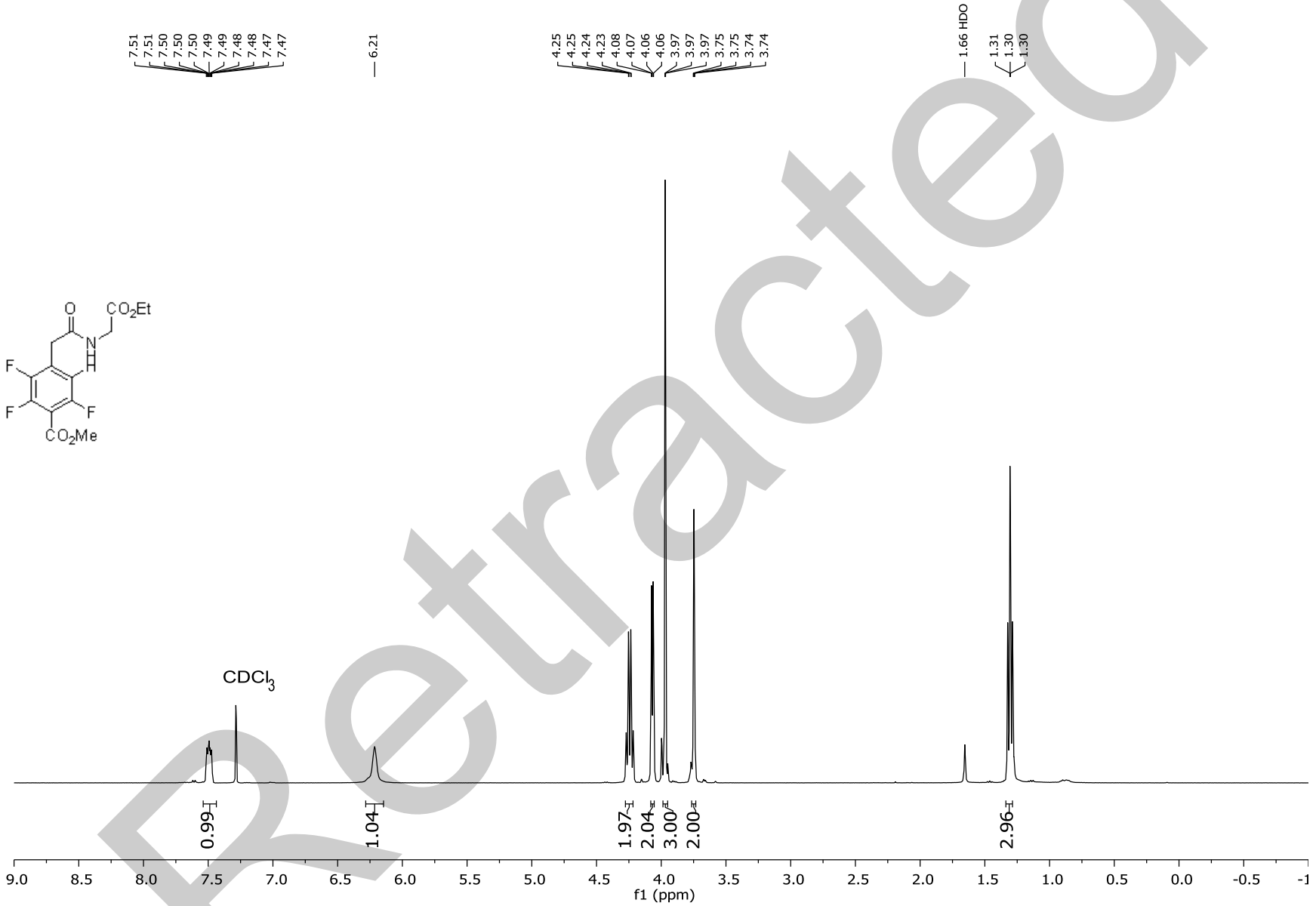
10g *N*-(4-cyanophenyl)-2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl) acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



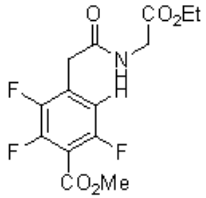
10g *N*-(4-cyanophenyl)-2-(2,3,5-trifluoro-4-(trifluoromethyl)phenyl) acetamide ^{13}C NMR (101 MHz, Chloroform-*d*)



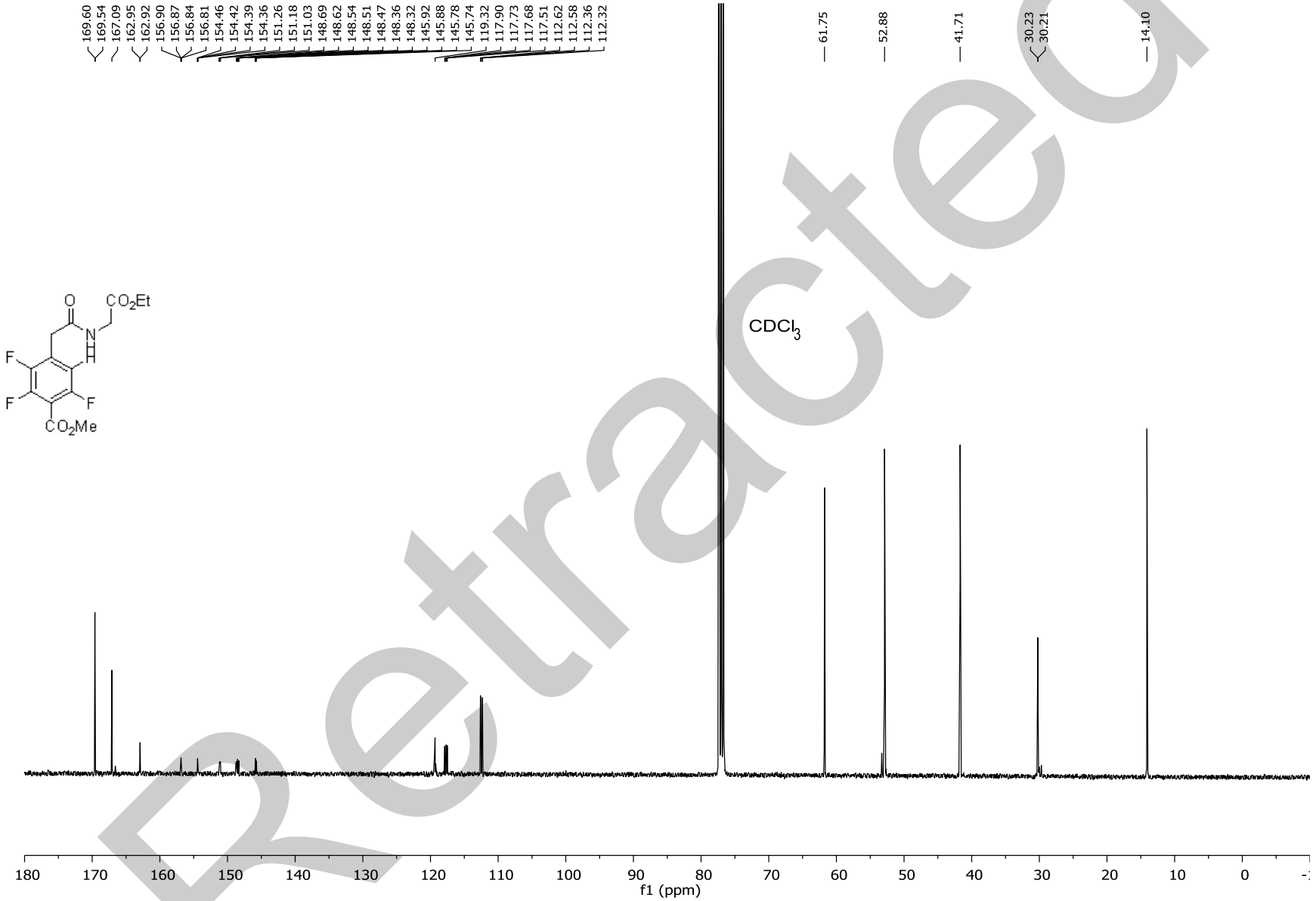
11a' methyl 4-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



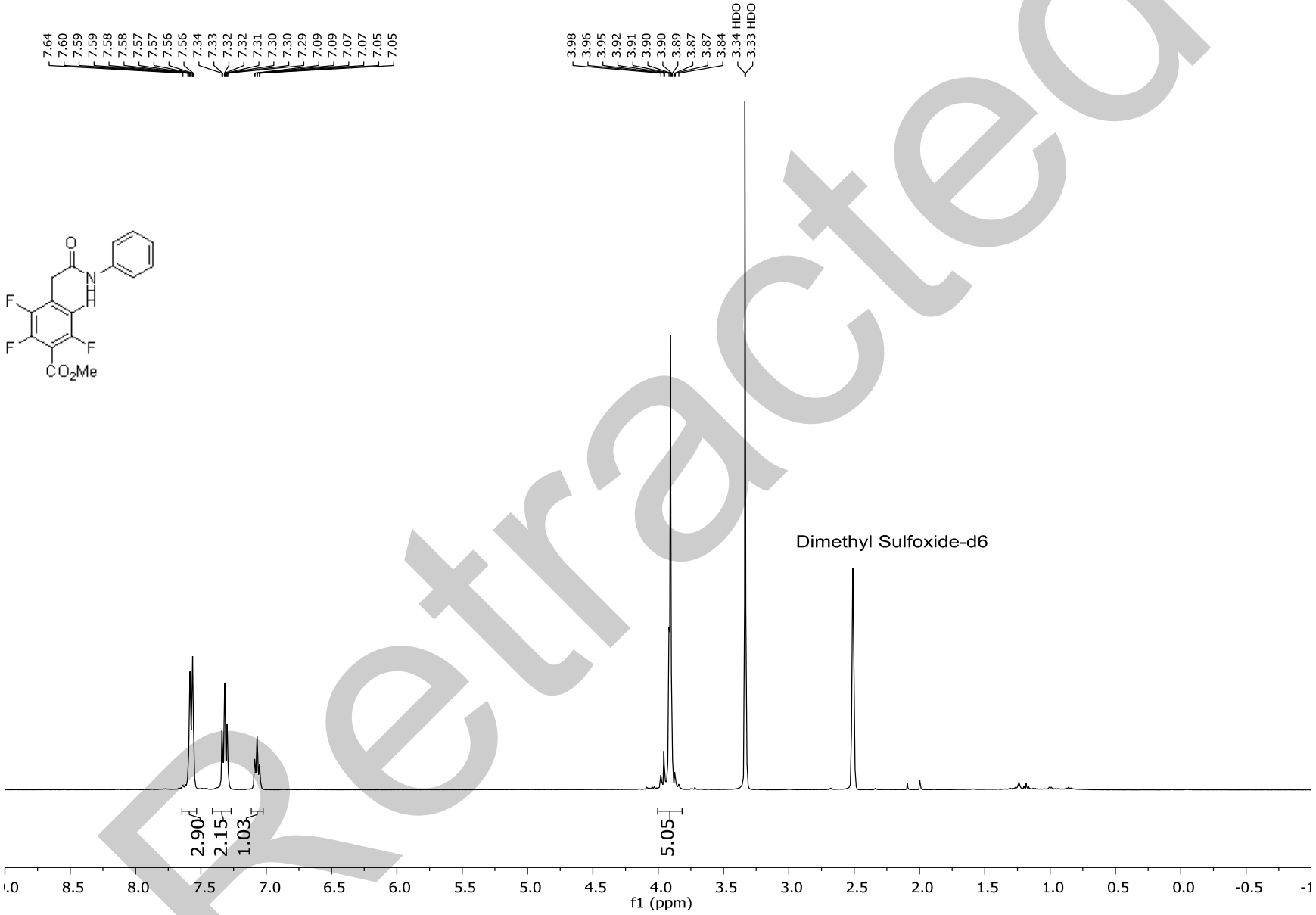
11a' methyl 4-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



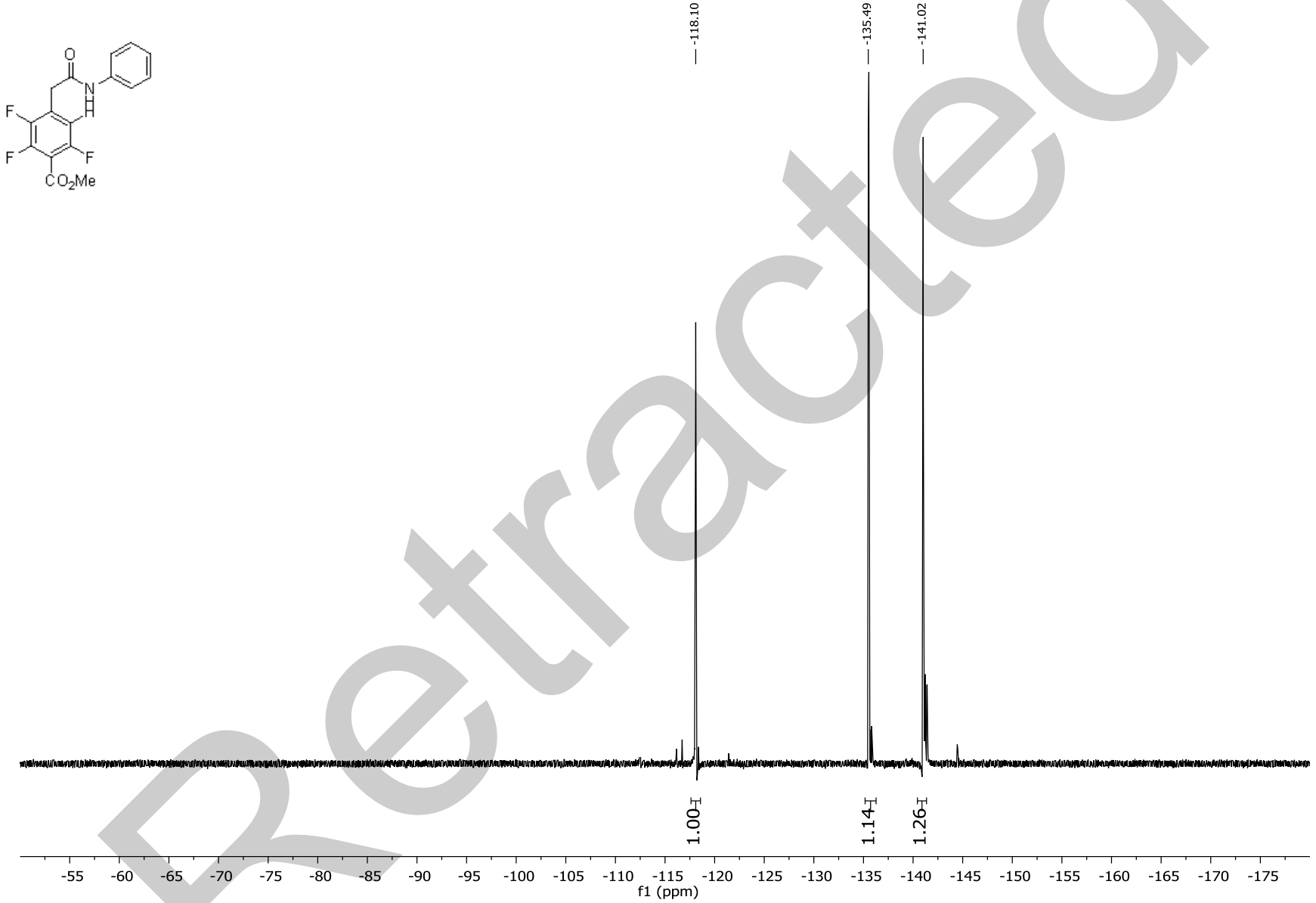
11a’ methyl 4-(2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{13}C NMR (101 MHz, Chloroform-*d*)



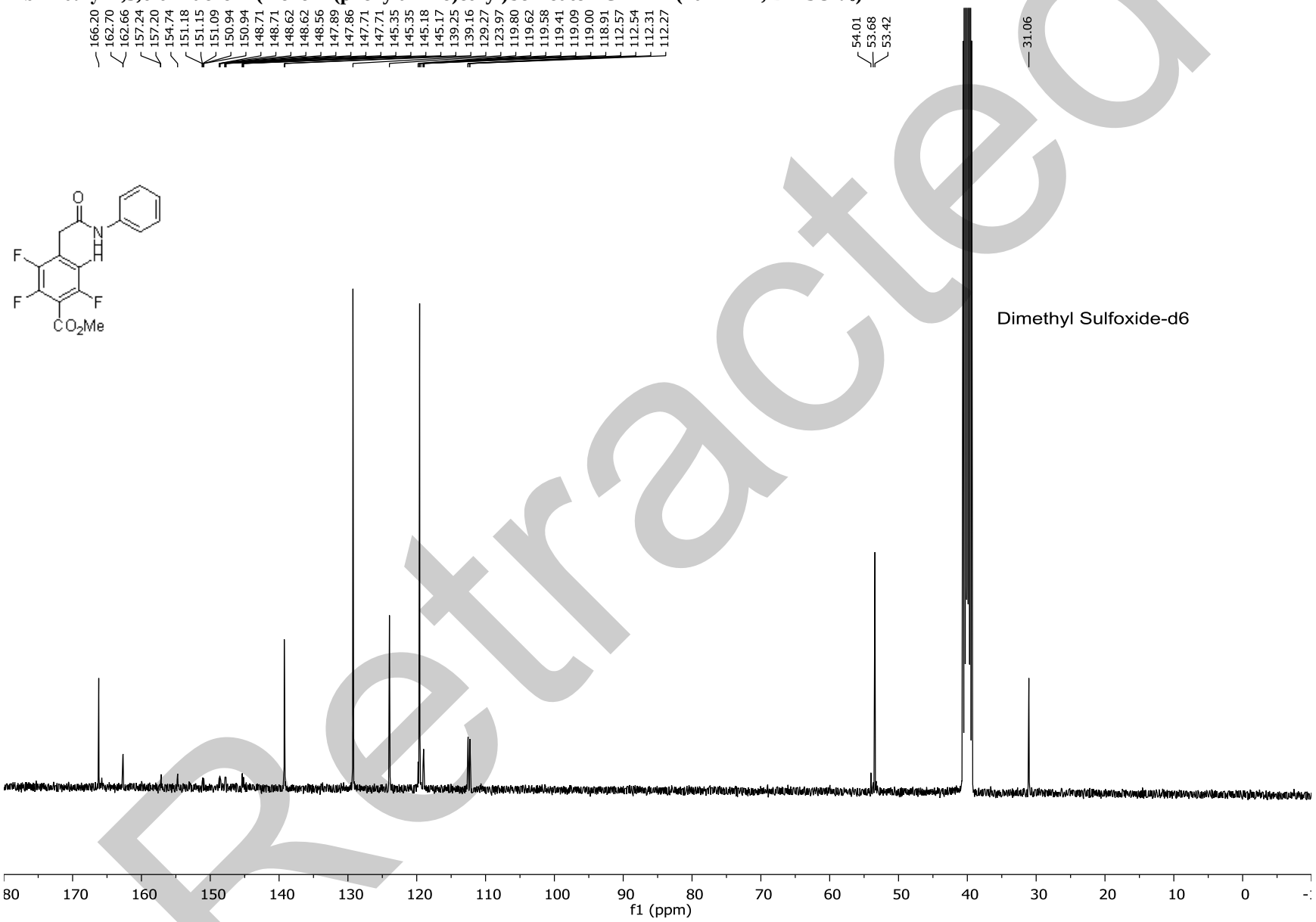
11b' methyl 2,3,6-trifluoro-4-(2-oxo-2-(phenylamino)ethyl)benzoate ^{1}H NMR (400 MHz, DMSO-d_6)



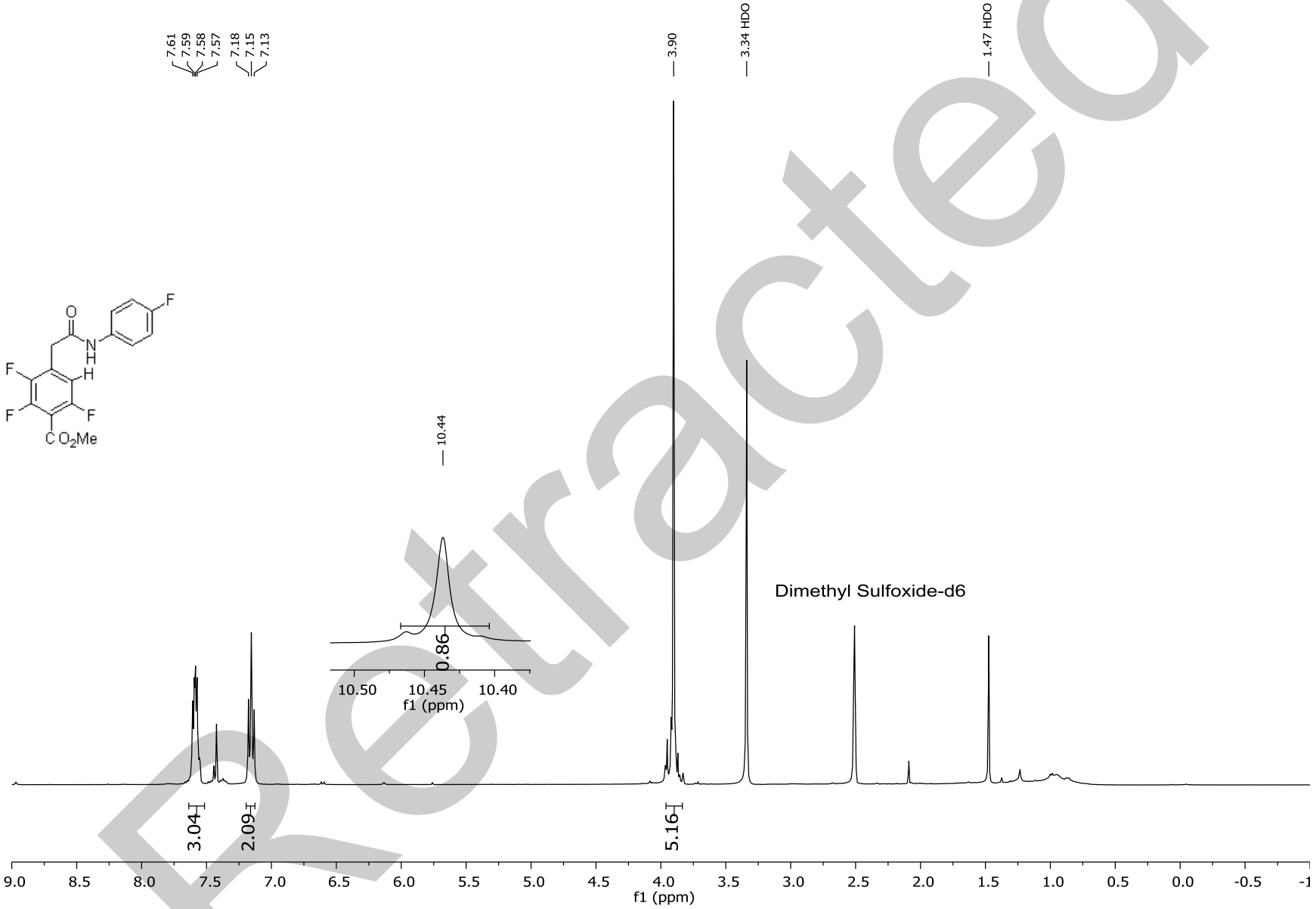
11b' methyl 2,3,6-trifluoro-4-(2-oxo-2-(phenylamino)ethyl)benzoate ^{19}F NMR (376 MHz, DMSO-d_6)



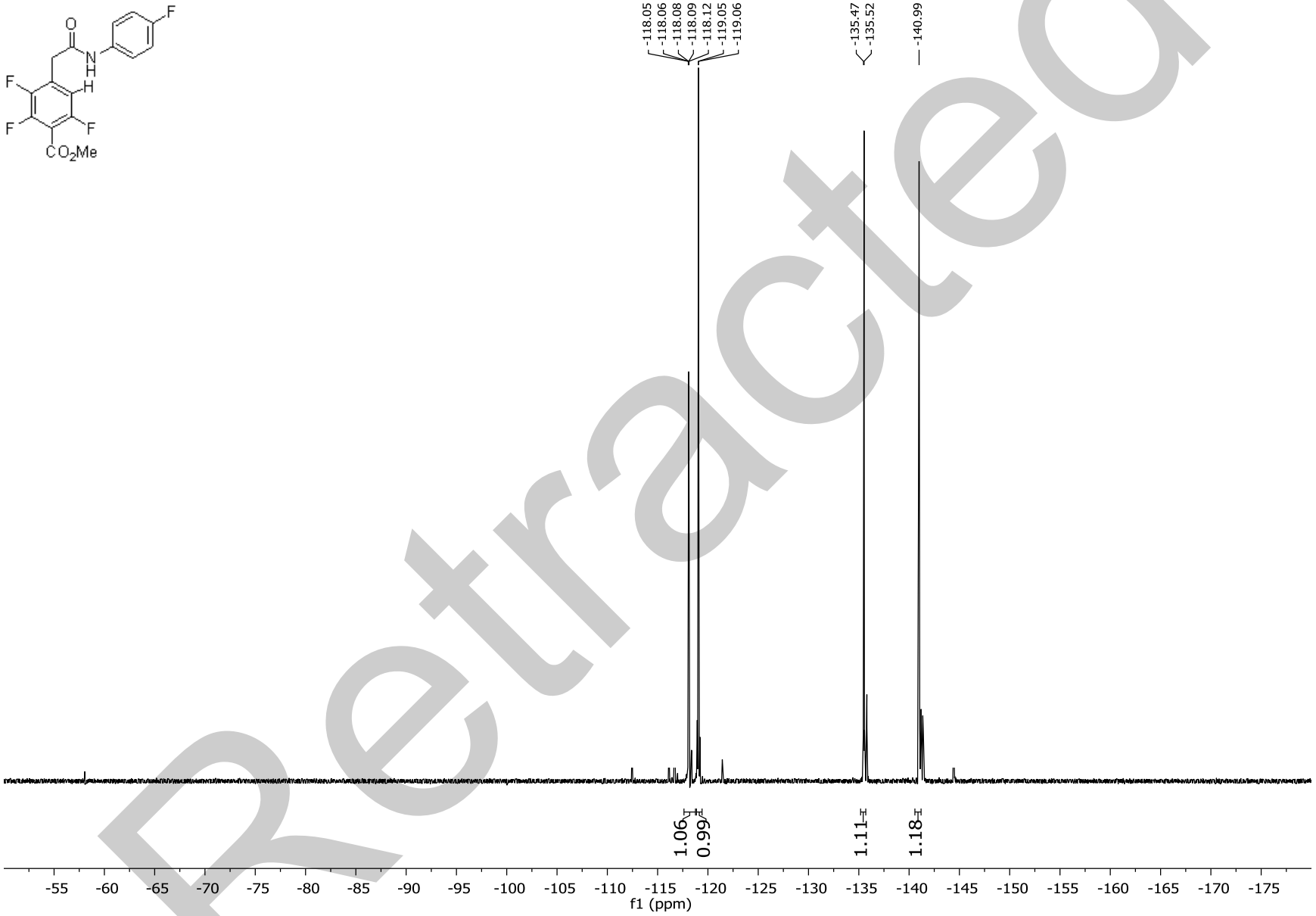
11b' methyl 2,3,6-trifluoro-4-(2-oxo-2-(phenylamino)ethyl)benzoate ^{13}C NMR (101 MHz, DMSO-d_6)



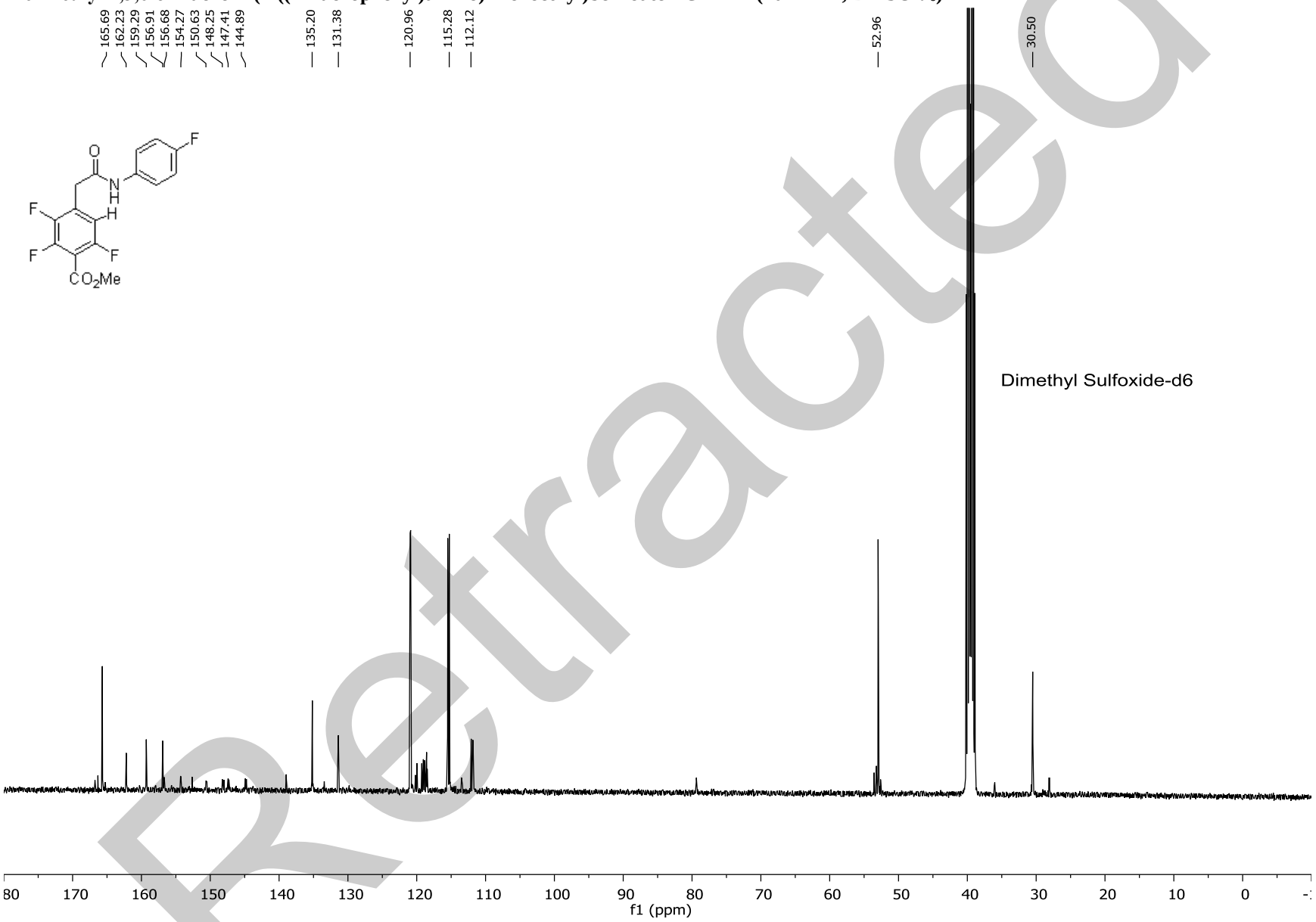
11c' methyl 2,3,6-trifluoro-4-(2-((4-fluorophenyl)amino)-2-oxoethyl)benzoate ^{1}H NMR (400 MHz, DMSO-d_6)



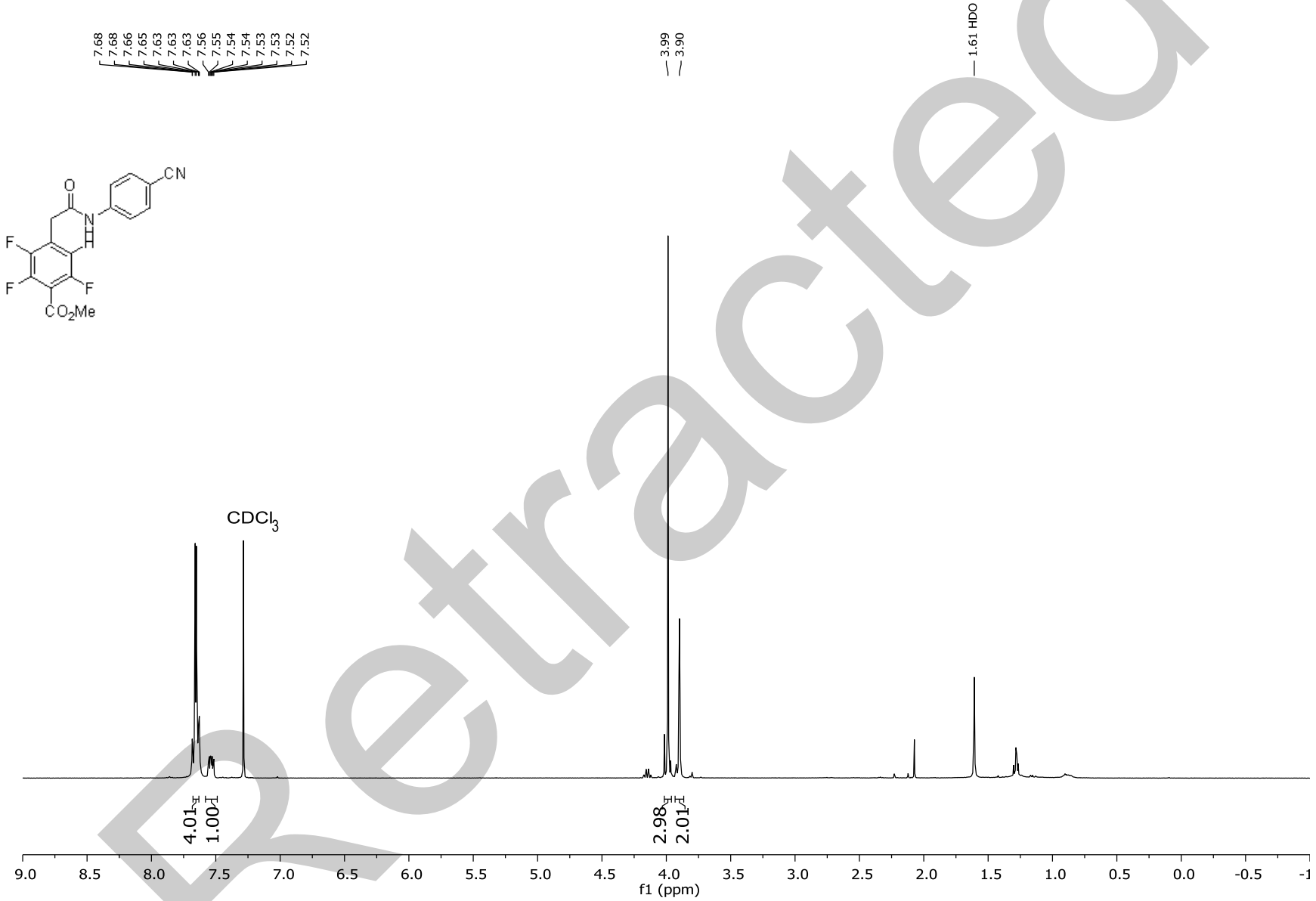
11c' methyl 2,3,6-trifluoro-4-(2-((4-fluorophenyl)amino)-2-oxoethyl)benzoate ^{19}F NMR (376 MHz, DMSO-d_6)



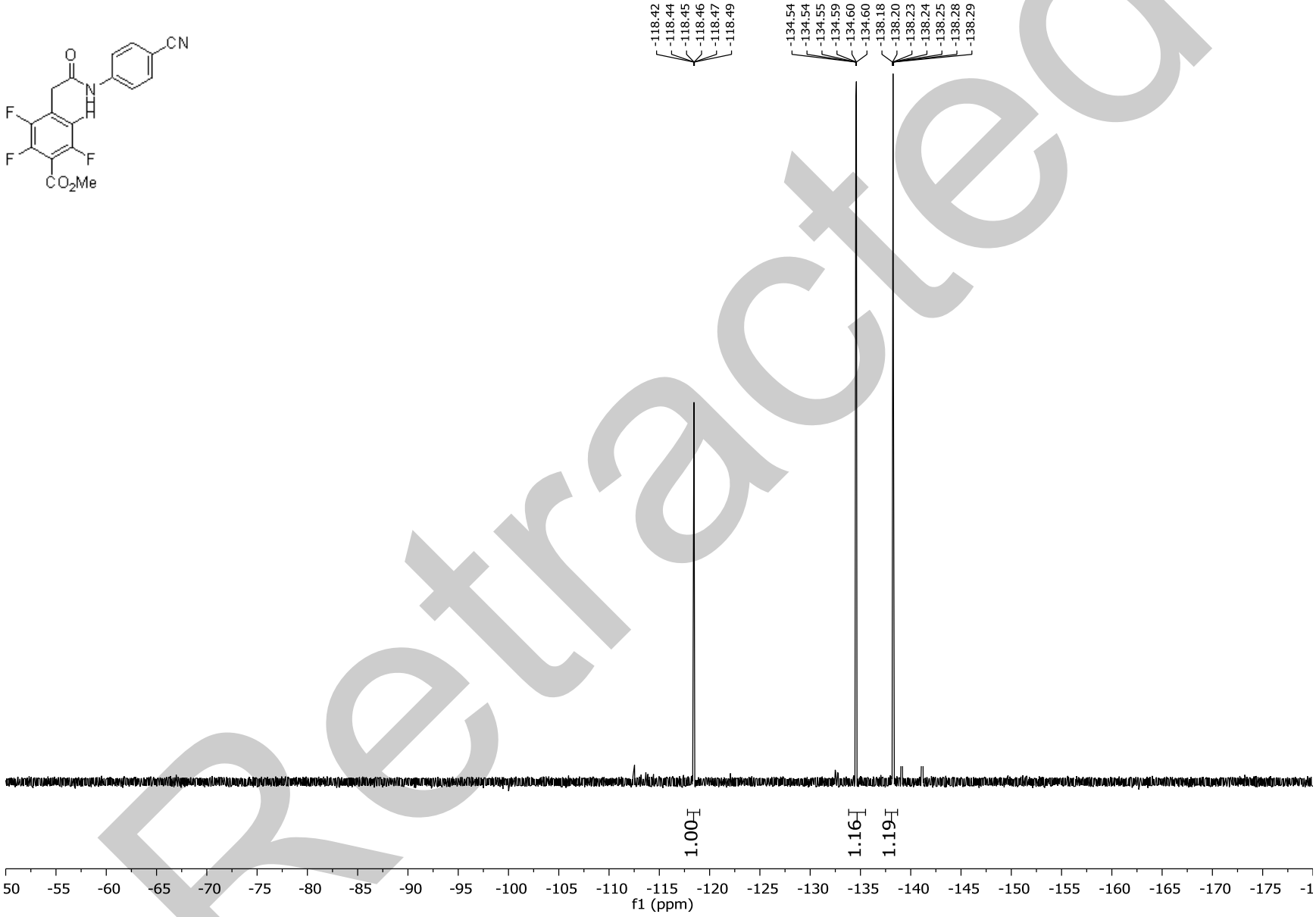
11c' methyl 2,3,6-trifluoro-4-(2-((4-fluorophenyl)amino)-2-oxoethyl)benzoate ^{13}C NMR (101 MHz, DMSO-d_6)



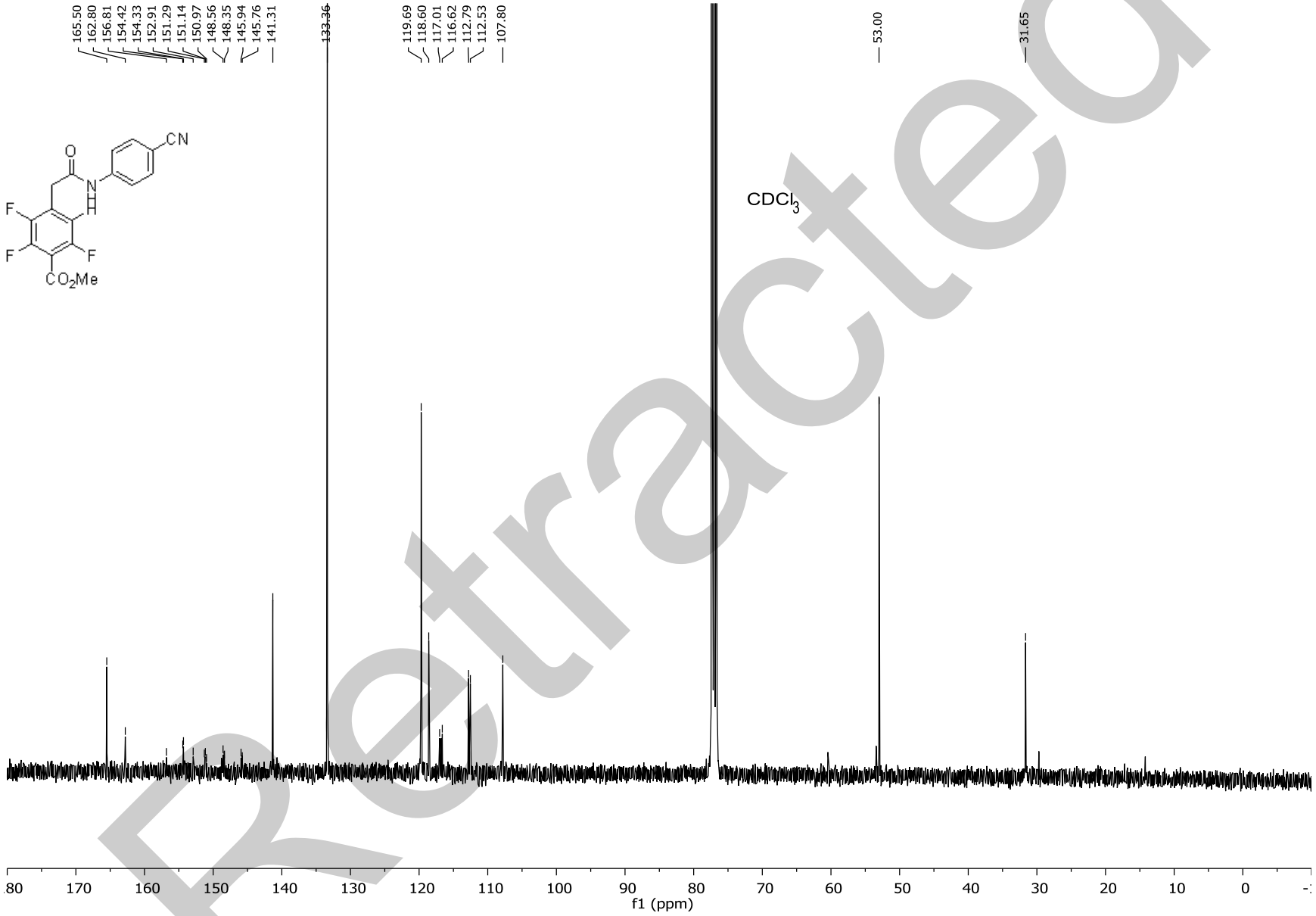
11d' methyl 4-(2-((4-cyanophenyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



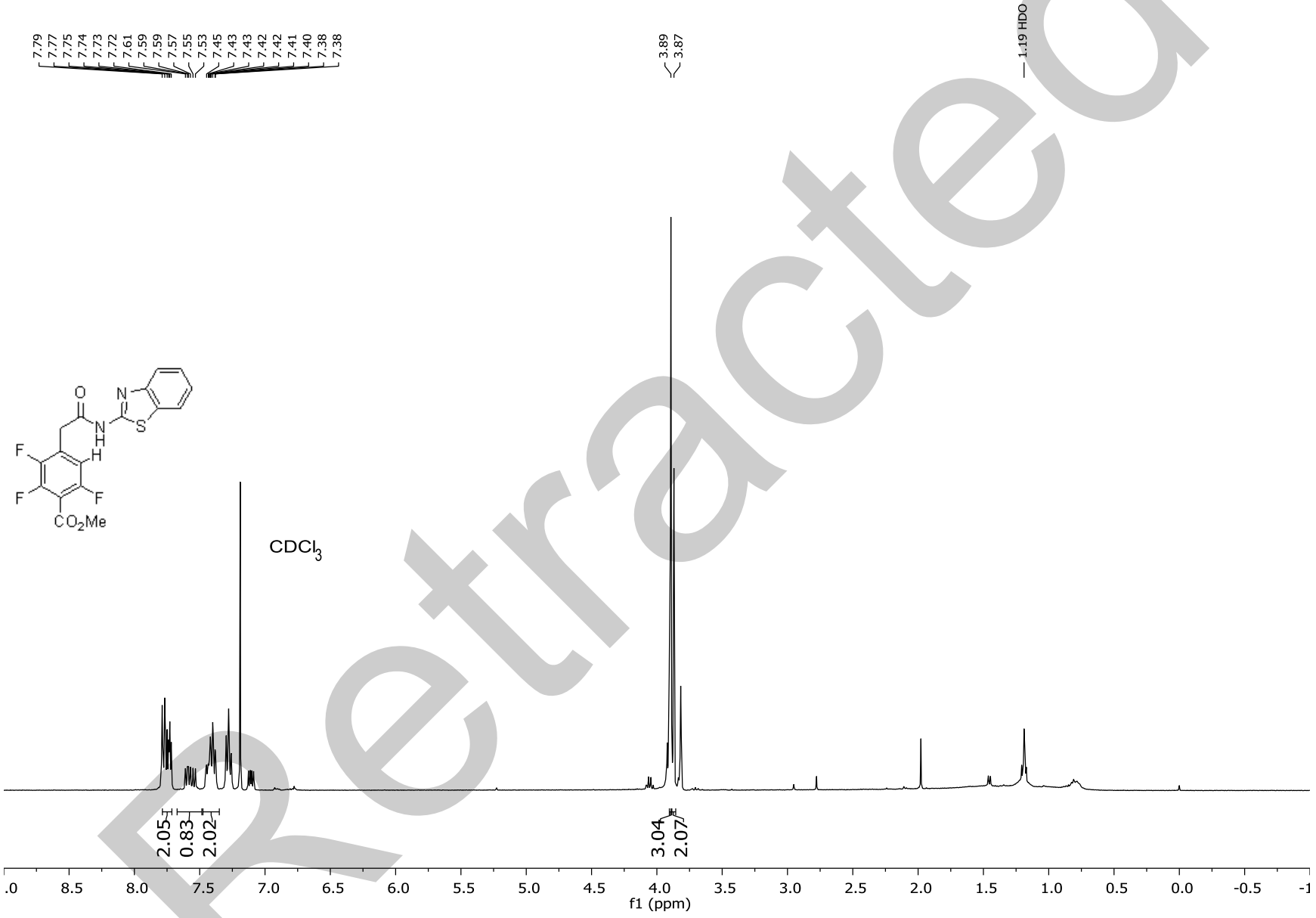
11d' methyl 4-(2-((4-cyanophenyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



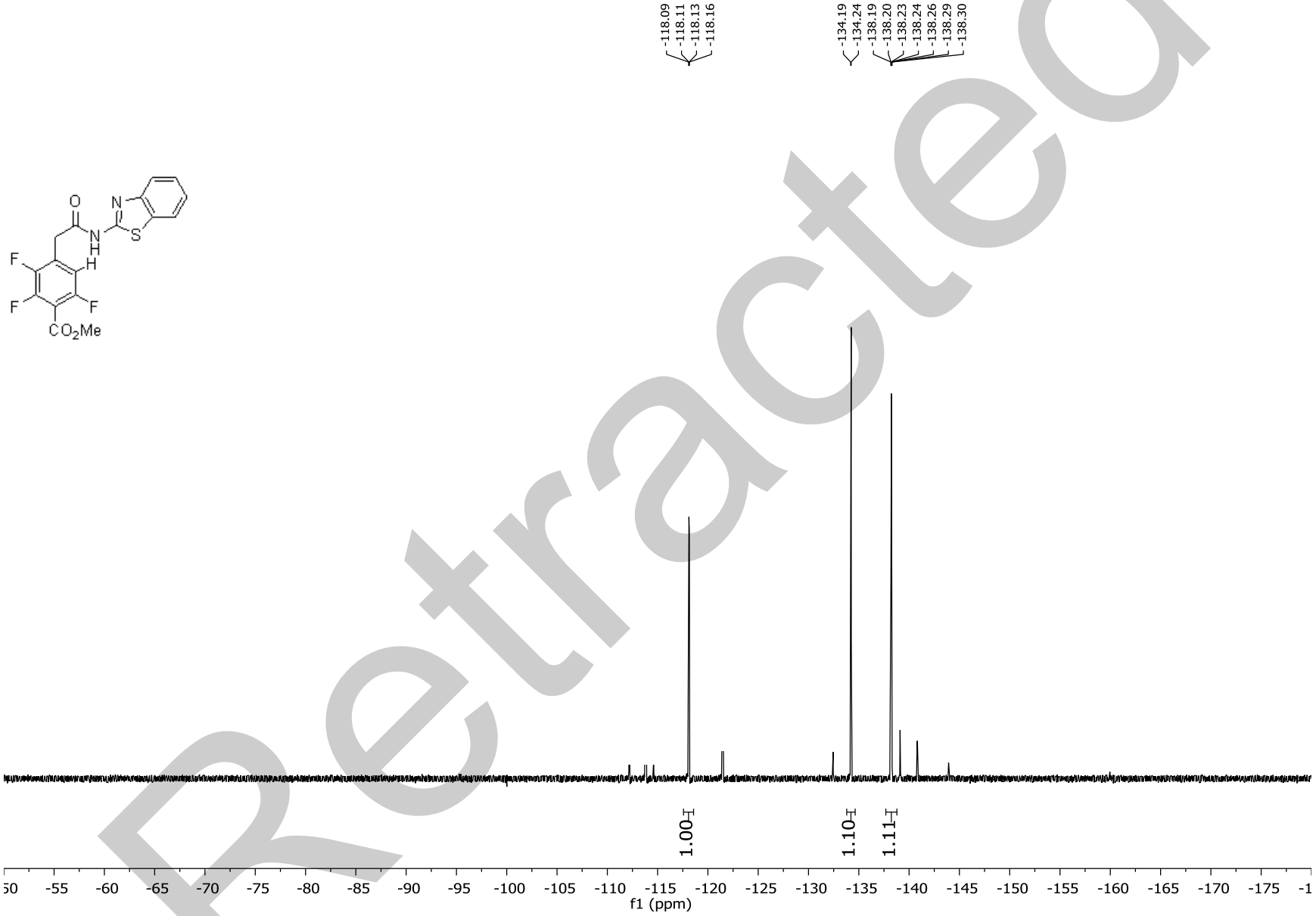
11d' methyl 4-(2-((4-cyanophenyl)amino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{13}C NMR (101 MHz, Chloroform-*d*)



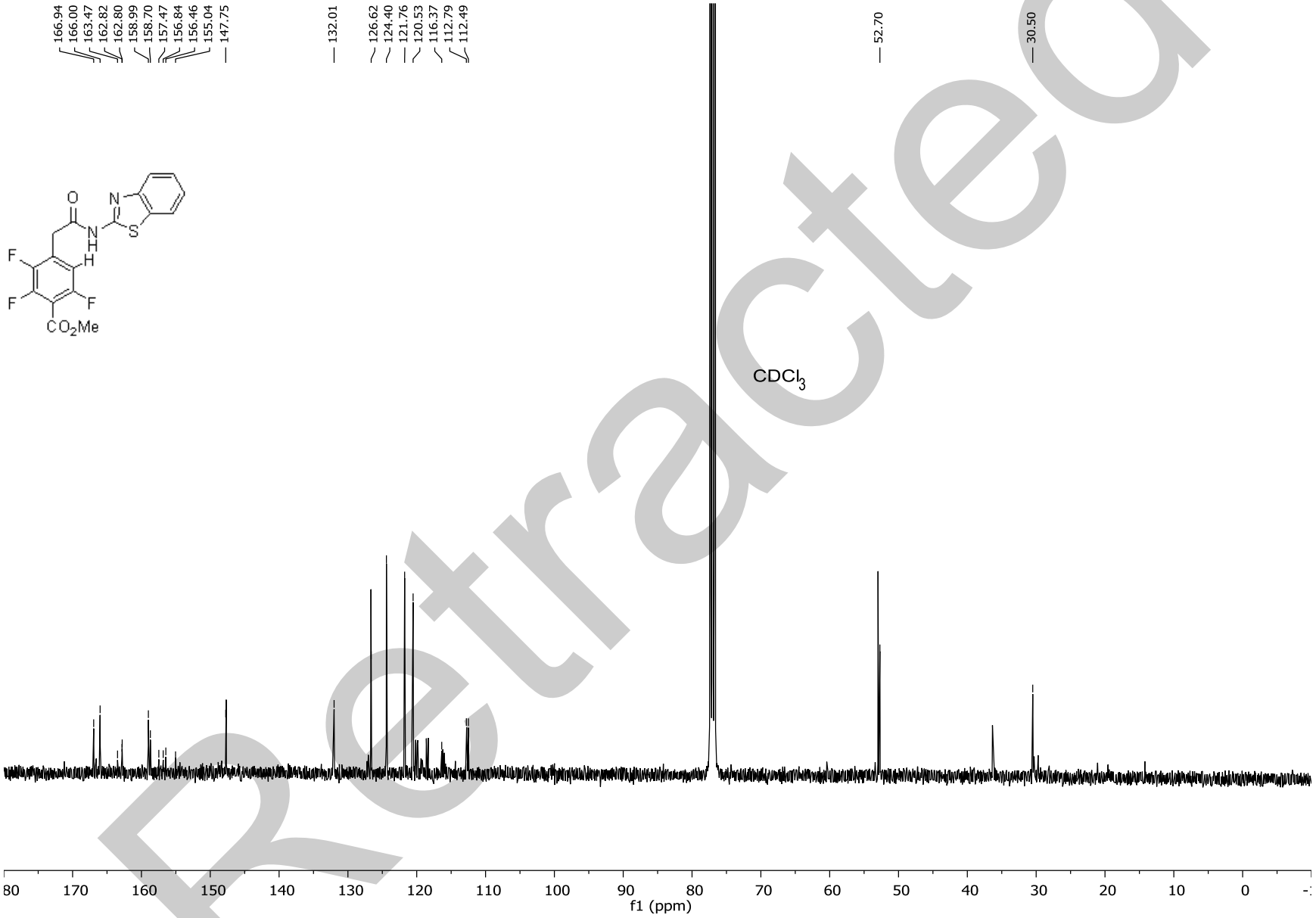
11e' methyl 4-(2-(benzo[d]thiazol-2-ylamino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



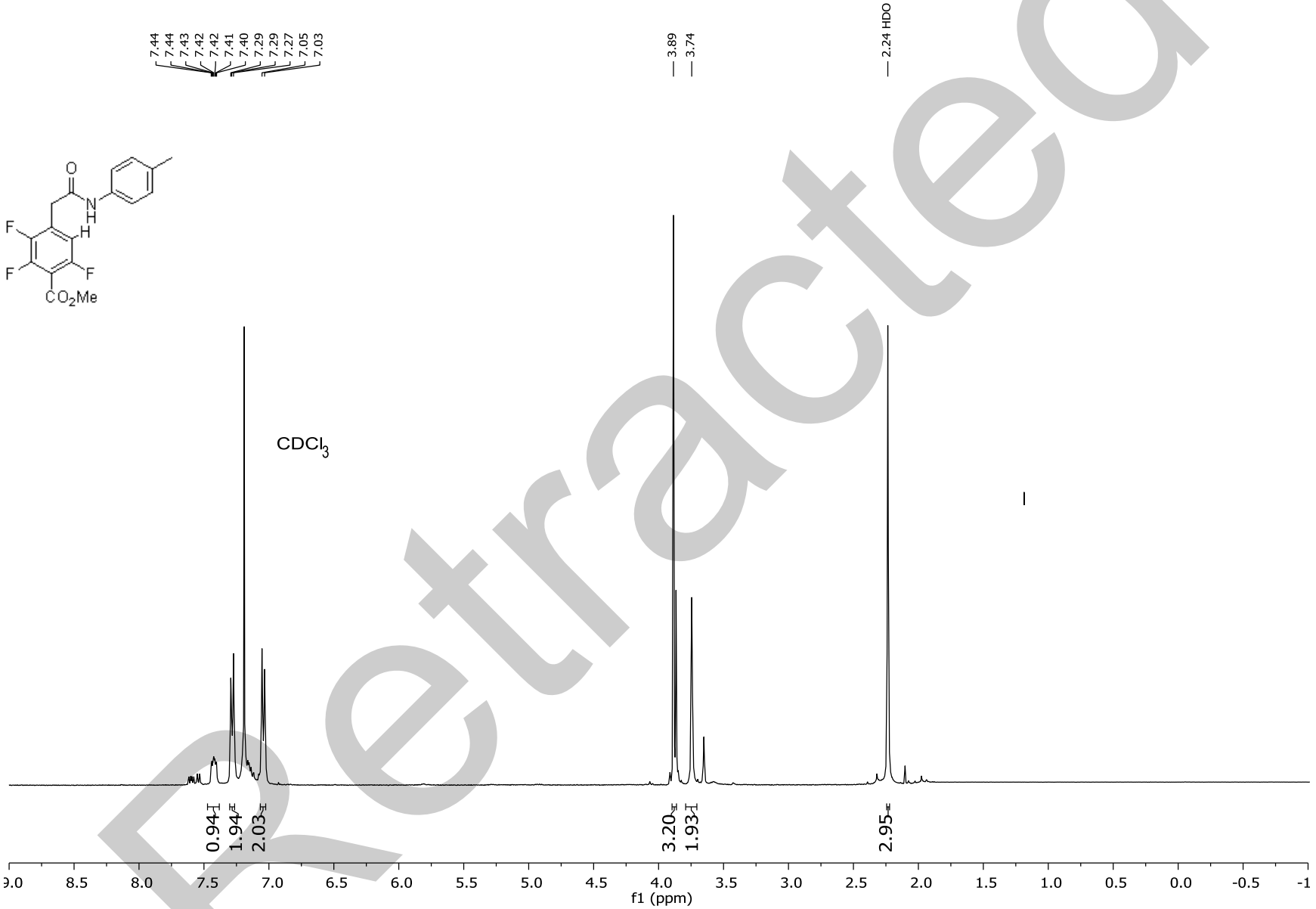
11e' methyl 4-(2-(benzo[d]thiazol-2-ylamino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



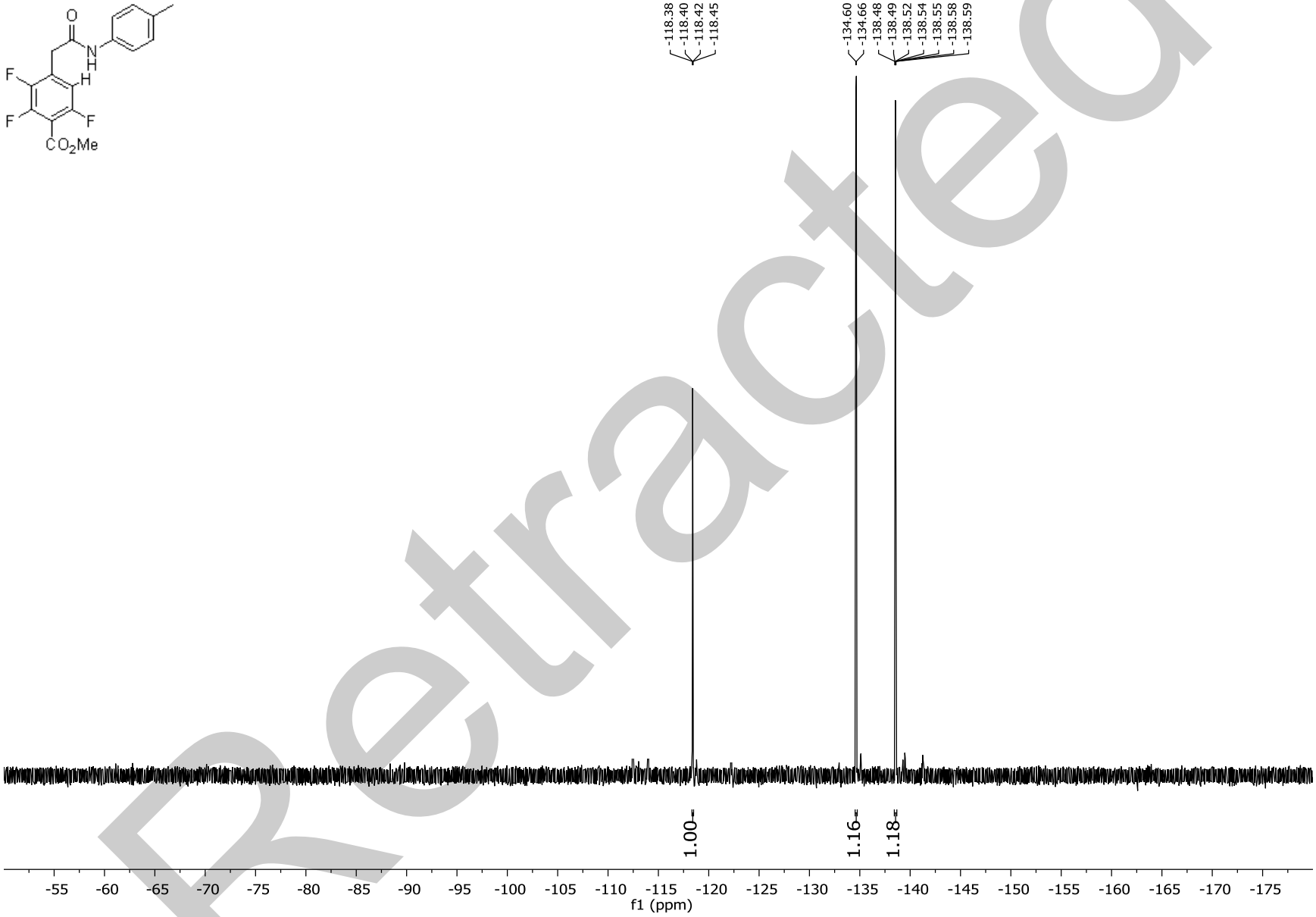
11e' methyl 4-(2-(benzo[d]thiazol-2-ylamino)-2-oxoethyl)-2,3,6-trifluorobenzoate ^{13}C NMR (101 MHz, Chloroform-*d*)



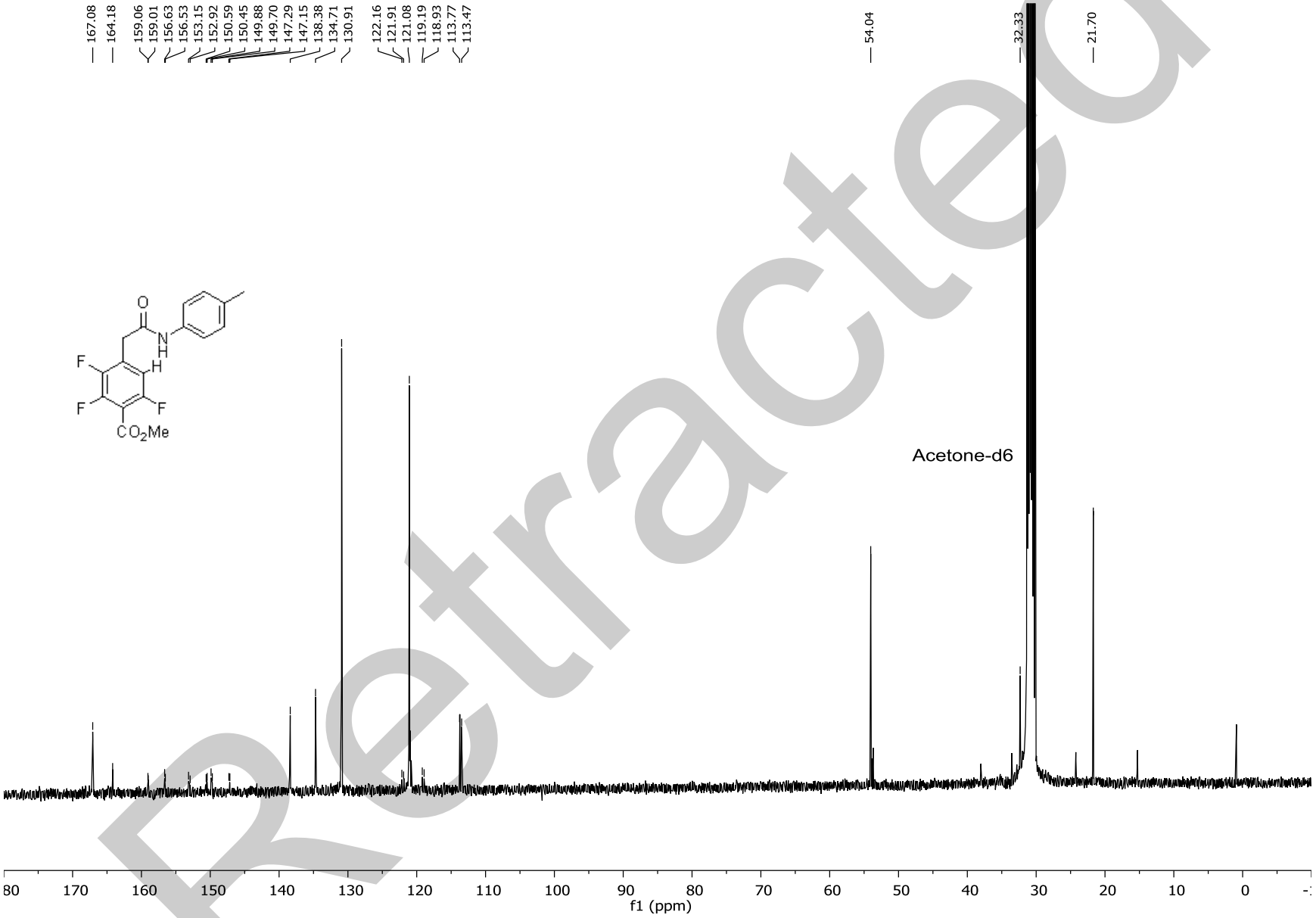
11f' methyl 2,3,6-trifluoro-4-(2-oxo-2-(p-tolylamino)ethyl)benzoate ^{1}H NMR (400 MHz, Chloroform-*d*)



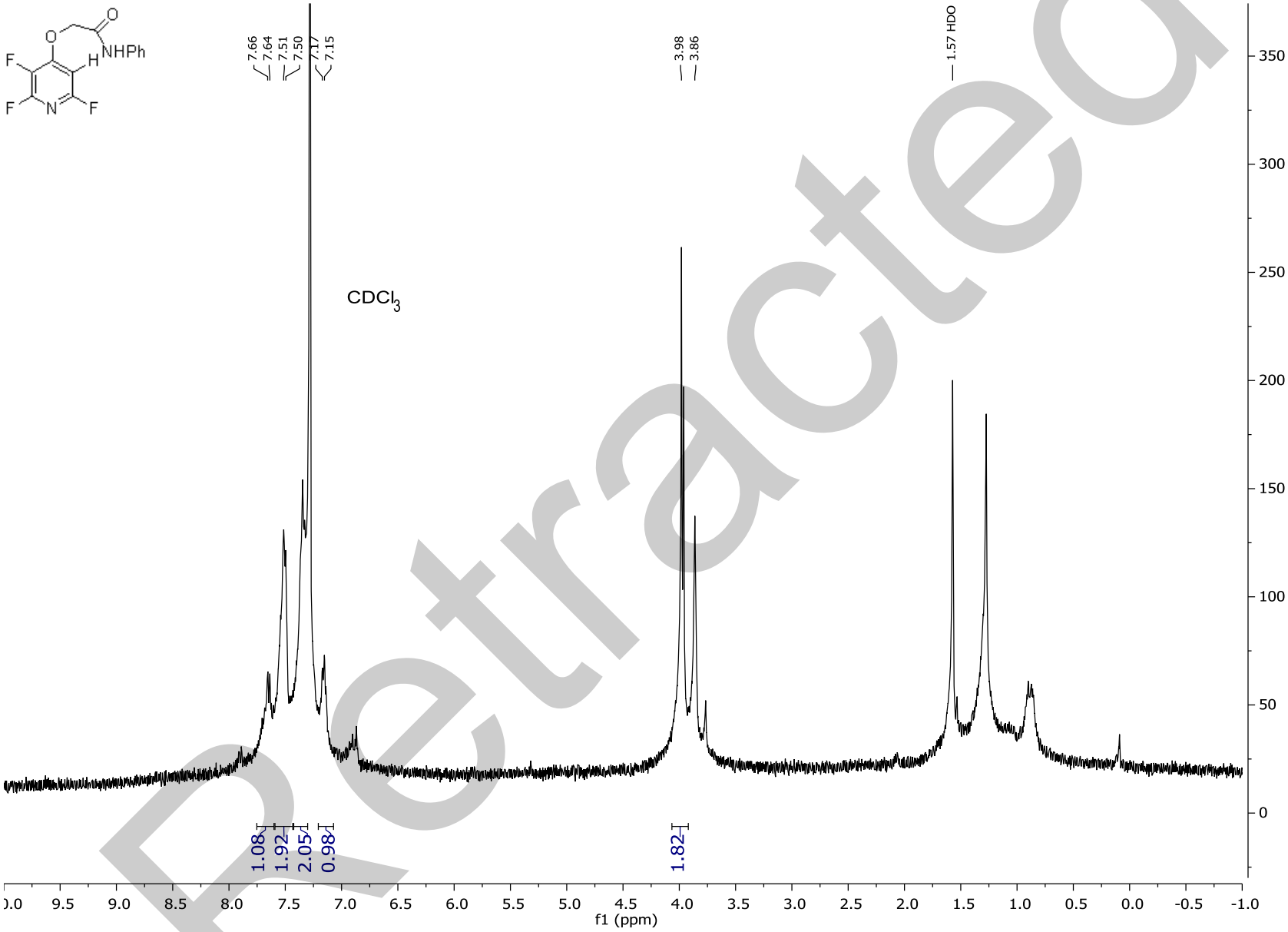
11f' methyl 2,3,6-trifluoro-4-(2-oxo-2-(p-tolylamino)ethyl)benzoate ^{19}F NMR (376 MHz, Chloroform-*d*)



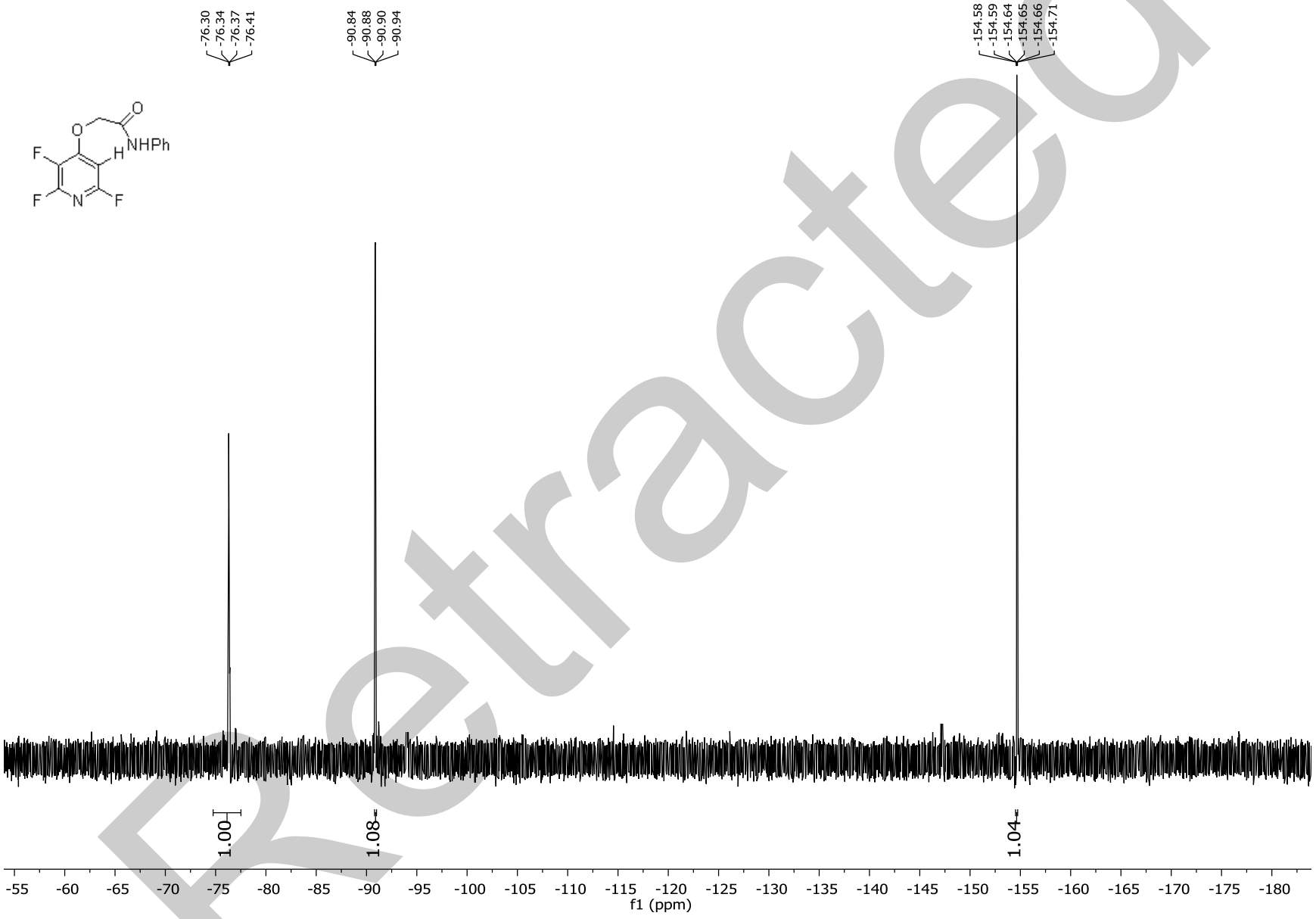
11f' methyl 2,3,6-trifluoro-4-(2-oxo-2-(p-tolylamino)ethyl)benzoate ^{13}C NMR (101 MHz, Acetone-d$_6$)



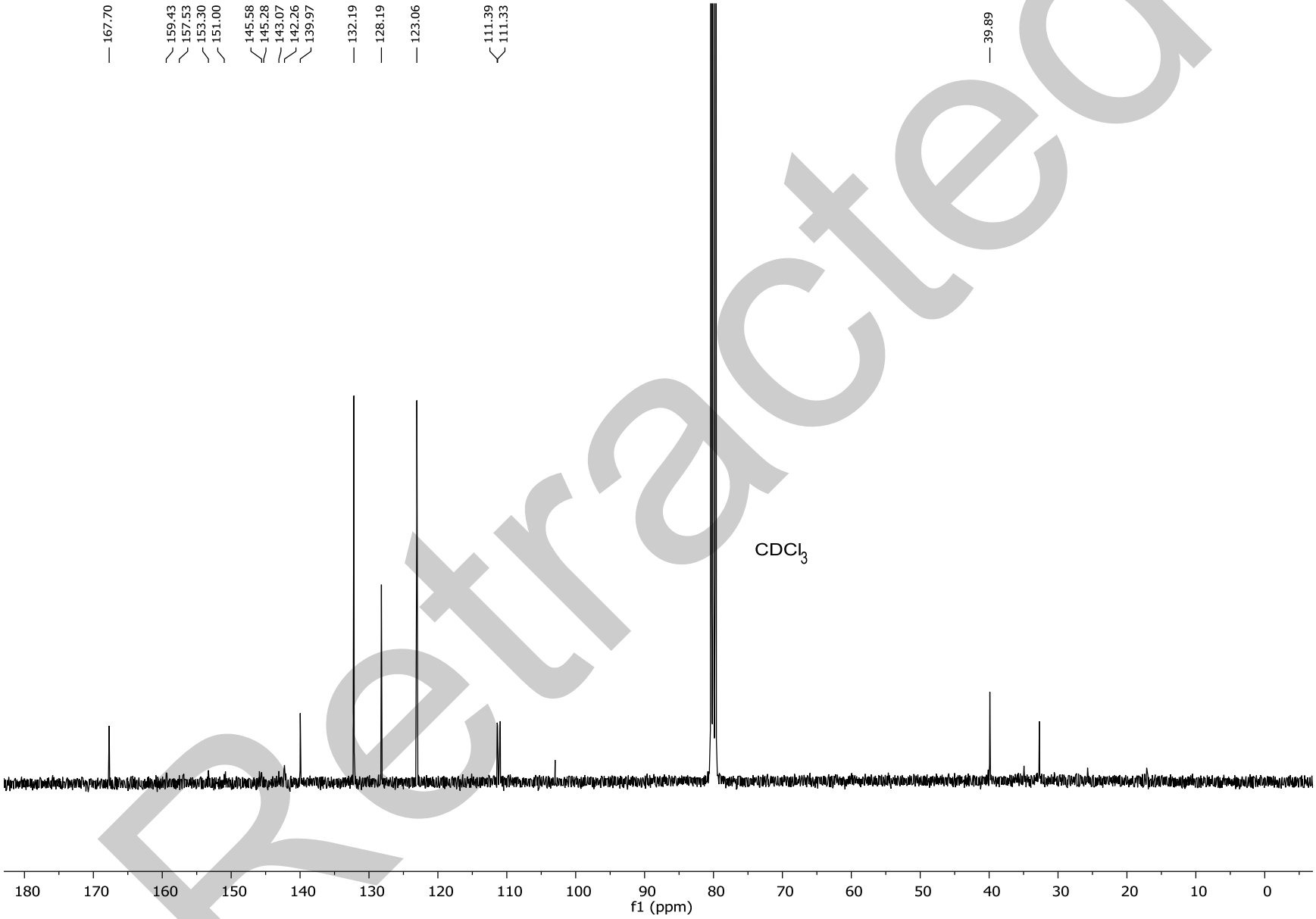
E11 *N*-phenyl-2-((2,3,6-trifluoropyridin-4-yl)oxy)acetamide^{1}H NMR (400 MHz, Chloroform-*d*)



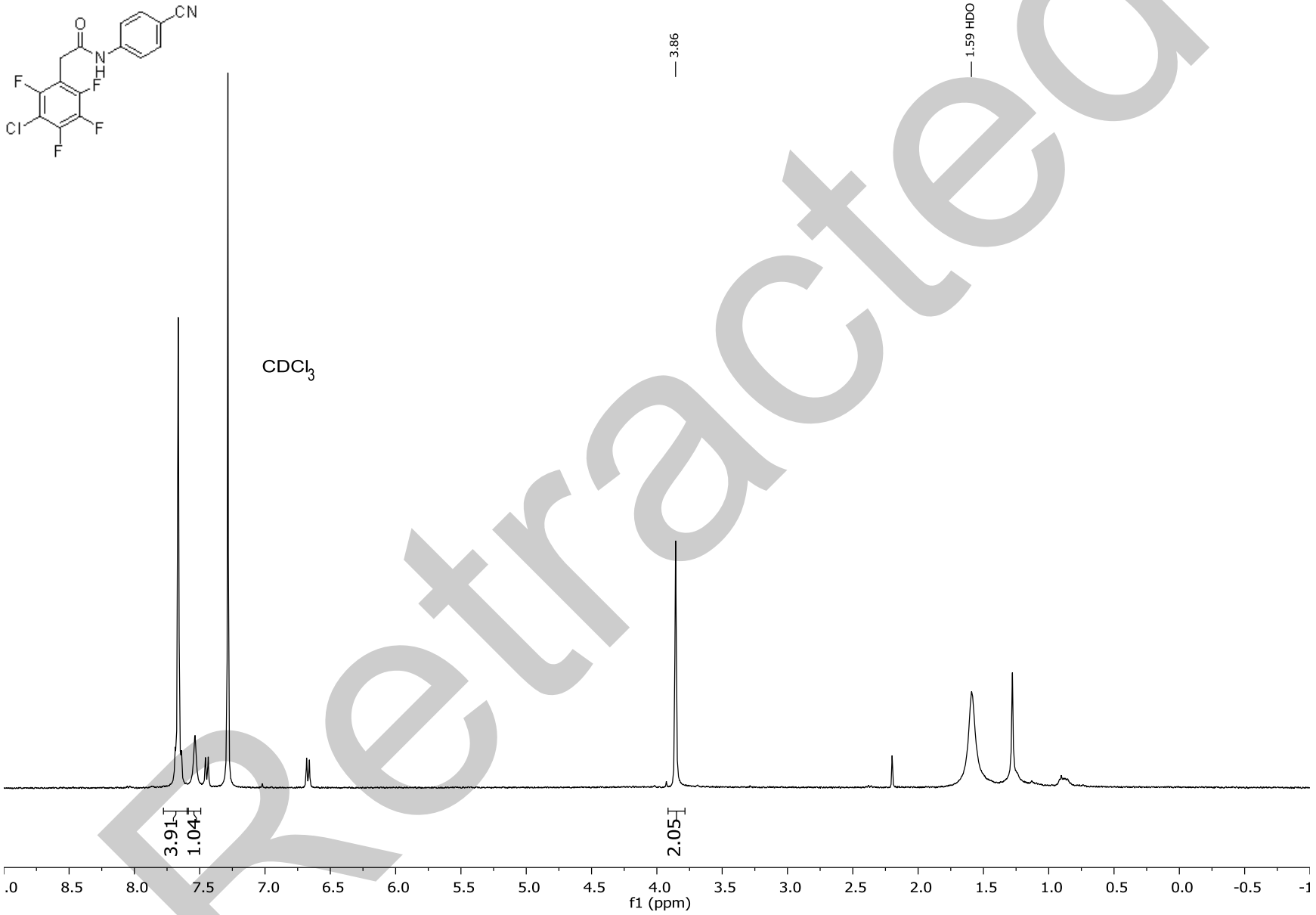
E11 *N*-phenyl-2-((2,3,6-trifluoropyridin-4-yl)oxy)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



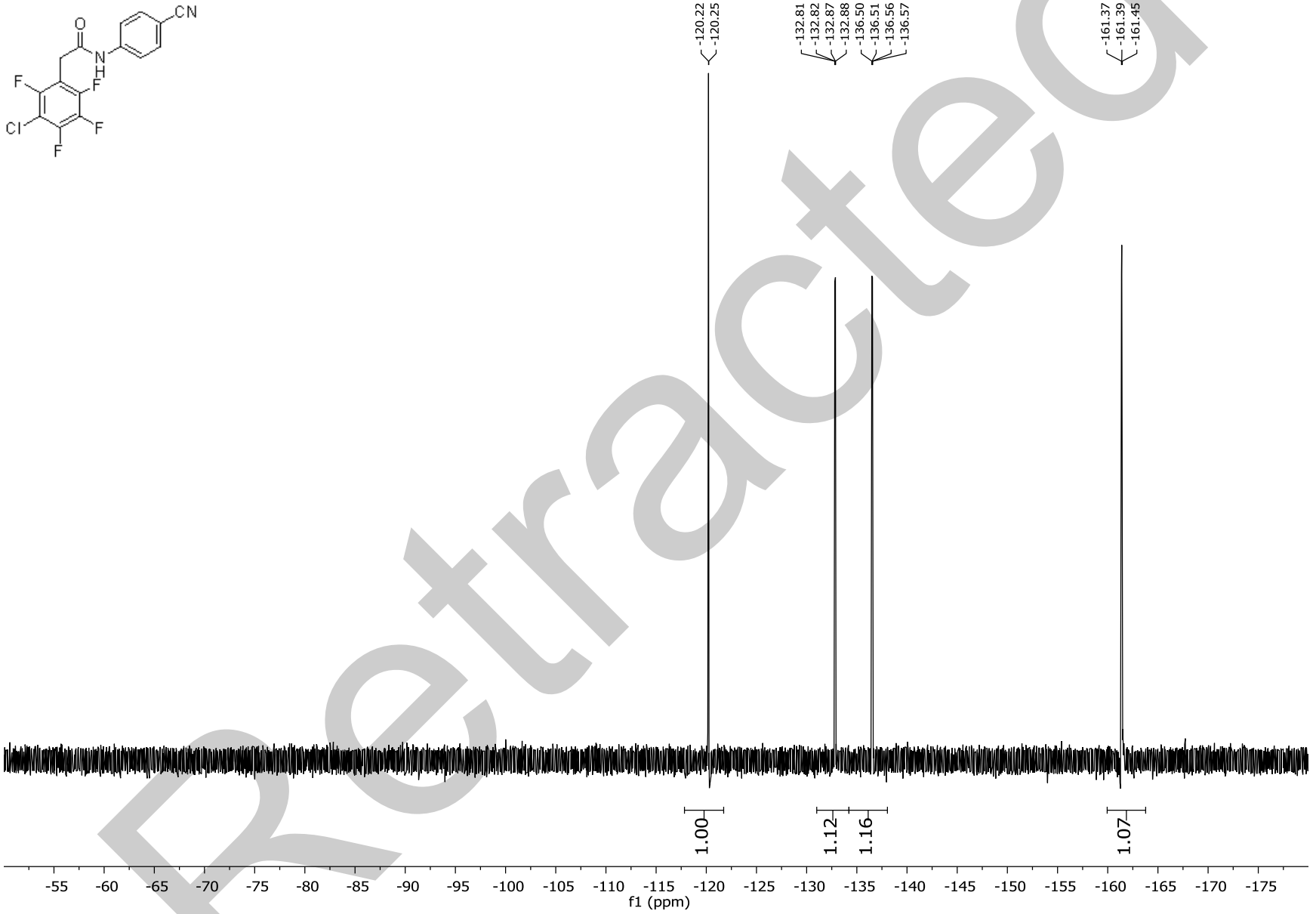
E11 *N*-phenyl-2-((2,3,6-trifluoropyridin-4-yl)oxy)acetamide ^{13}C NMR (101 MHz, Acetone-d$_6$)



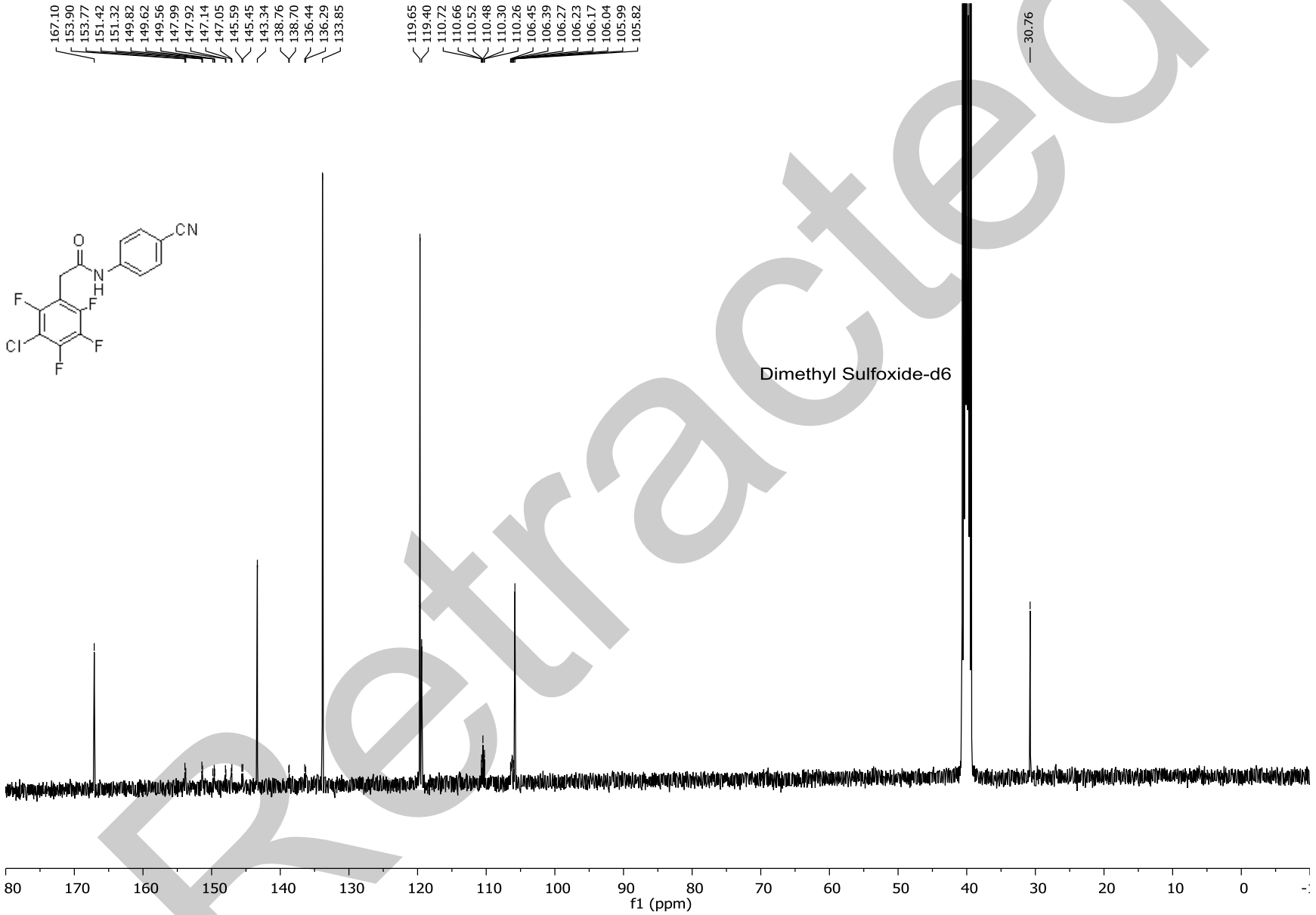
12b 2-(3-chloro-2,4,5,6-tetrafluorophenyl)-N-(4-cyanophenyl)acetamide ^{1}H NMR (400 MHz, Chloroform-*d*)



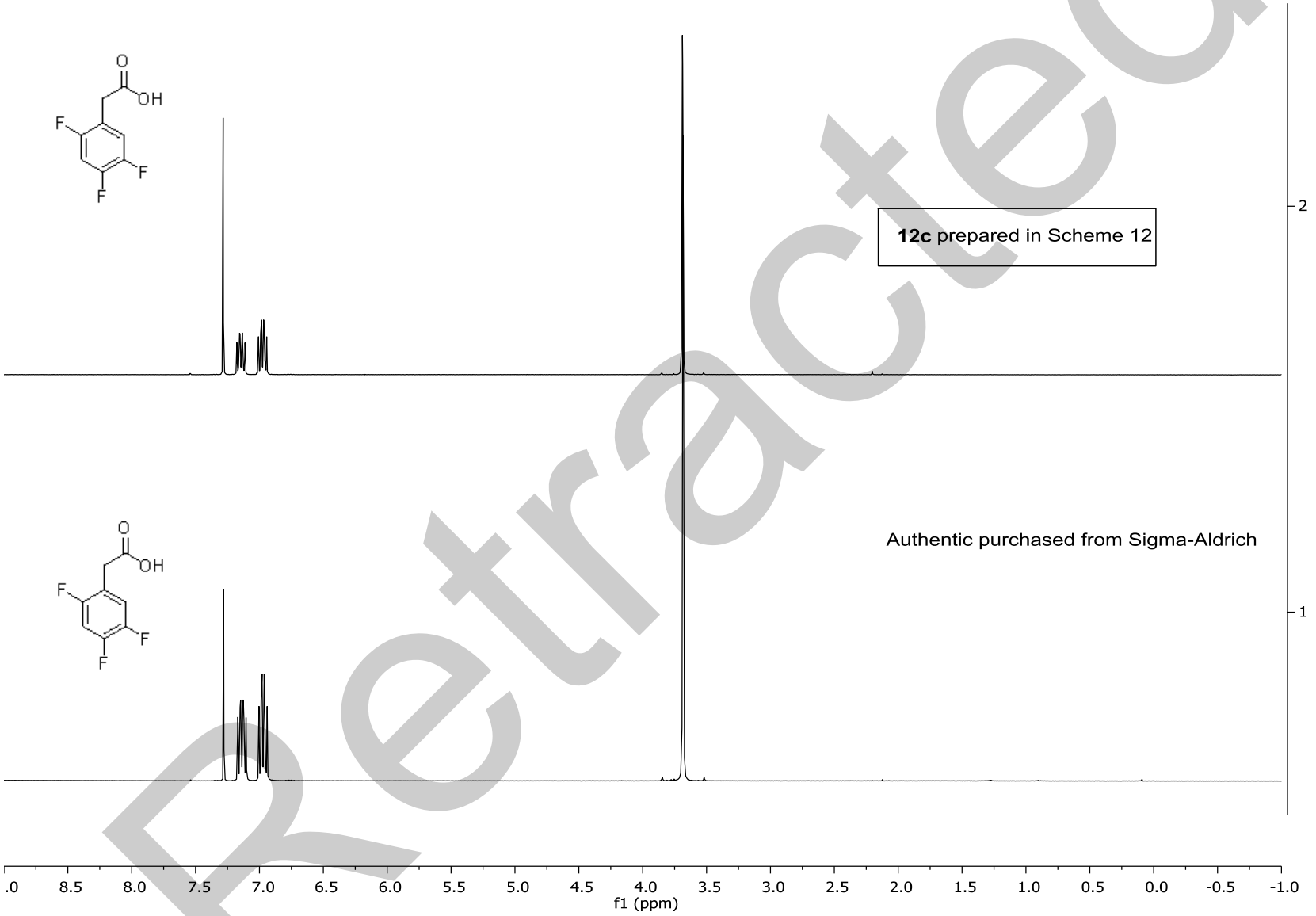
12b 2-(3-chloro-2,4,5,6-tetrafluorophenyl)-N-(4-cyanophenyl)acetamide ^{19}F NMR (376 MHz, Chloroform-*d*)



12b 2-(3-chloro-2,4,5,6-tetrafluorophenyl)-N-(4-cyanophenyl)acetamide ^{13}C NMR (101 MHz, Acetone-d$_6$)



12c 2-(2,4,5-trifluorophenyl)acetic acid ^{1}H NMR (400 MHz, Chloroform-*d*)



12c 2-(2,4,5-trifluorophenyl)acetic acid ^{19}F NMR (376 MHz, Chloroform-*d*)