Photocatalytic Hydrodefluorination; Facile Access to Partially Fluorinated Aromatics.

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Supporting Information

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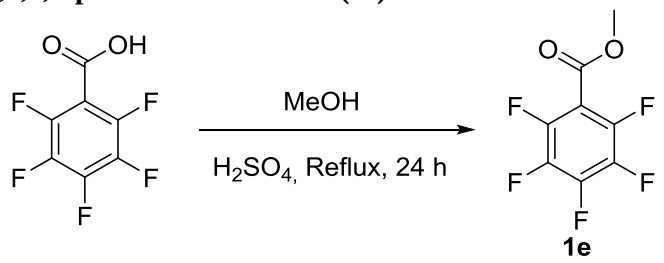
General Experimental

All reagents were obtained from commercial suppliers (Sigma-Aldrich, Oakwood chemicals, Alfa Aesar, Matrix Scientific) and used without further purification unless otherwise noted. Acetonitrile (CH_3CN) was dried over molecular sieves. *N*,*N*-diisopropylethylamine was purchased from Sigma-Aldrich. Photocatalyst *tris*(2-phenyl pyridinato-C^2, *N*)iridium(III)($Ir(ppy)_3$), 99%(purity), ($Ir(ppy)_3$) was obtained from Sigma-Aldrich. Methyl 2,3,4,5,6-pentafluorobenzoate (1e), tert-butyl 2,3,4,5,6-pentafluorobenzoate (1i), 2-(perfluorophenyl)benzo[*d*]oxazole (1j), 4,4'-((perfluoro-1,4-phenylene)bis(oxy))bis(bromobenzene) (1g), 4-amino-2,3,5,6-tetrafluorobenzonitrile (1m), 1,2,4,5-tetrafluoro-3-phenoxy-6-(trifluoromethyl)benzene (1n), O-ethyl S-(perfluorophenyl) carbonothioate (1o), *N*-(perfluoropyridin-4-yl)acetamide (1p), methyl 4-amino-2,3,5,6-tetrafluorobenzoate (1q), N-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide (1r), 1,2,3,4-tetrafluorodibenzo[b,e][1,4]dioxine (1t) and 4,5,6,7-tetrafluoro-2-phenylbenzofuran (1u) were synthesized according to literature procedures. Photocatalysts Ruthenium-tris(2,2′-bipyridyl) dichloride [$Ru(bpy)_3Cl_2$] and Tris(bipyrimidine)ruthenium(II) dichloride [$Ru(bpm)_3Cl_2$] were synthesized according to literature procedures.[16,17] Reactions were monitored by ^{19}F and GC-MS (QP 2010S, Shimadzu equipped with auto sampler). NMR spectra were obtained on 400 MHz Bruker Avance III spectrometer and 400 MHz Unity Inova spectrometer. ^1H and ^{13}C NMR chemical shifts are reported in ppm relative to the residual protio solvent peak (^1H, ^{13}C) and ^{19}F NMR shifts are reported using TFA as a standard. IR spectra were recorded on Perkin Elmer 2000 FT-IR. X-ray crystal structure was collected using a diffractometer with a Bruker APEX ccd area detector and graphite-monochromated Mo Kα radiation (λ = 0.71073 Å).Melting points were determined on Mel-Temp apparatus and reported uncorrected. GC analyses were carried out by Agilent 6850 Series GC system. Isolations were carried out using Teledyne Isco Combiflash Rf 200i flash chromatograph with Redisep Rf normal phase silica (4 g, 12 g, or 24 g) with product detection at 254 and 280 nm. Some isolations were performed using Sorbent Technology Silica Prep TLC Plates, w/UV254, glass backed, 1000 µm, 20 x 20 cm, and were visualized with ultraviolet light. Substrate synthesis reactions were monitored by thin layer chromatography (TLC) obtained from Sorbent Technology; Silica XHL TLC Plates, w/UV254, glass backed, 250 µm, and were visualized with ultraviolet light or potassium permanganate.

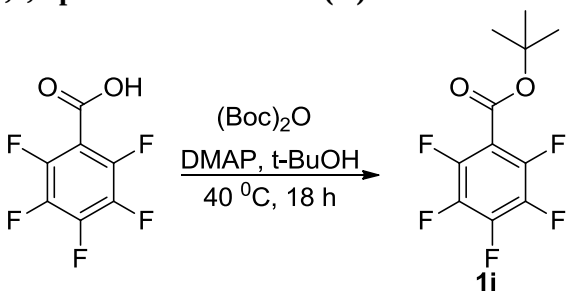
Photocatalytic reactions were set up in a light bath which is described below. Strips of blue LED's, (18 LED's/ft.) were purchased from Solid Apollo and were wrapped around on the walls of glass crystallization dish and secured with masking tape and then wrapped with aluminum foil. A lid which rest on the top was fashioned from cardboard and holes were made such that reaction tubes (12 × 75 mm cultural borosilicate tube) 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 45 ^oC with the aid of a sand bath connected to a thermostat.

Synthesis of Methyl 2,3,4,5,6-pentafluorobenzoate (1e)



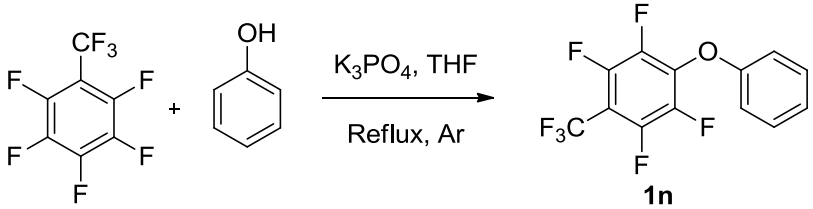
1e was prepared using an unoptimized procedure. In a 100 mL of round bottom flask, pentafluorobenzoic acid (Oakwood Chemicals) (2.0 g, 9.4 mmol), MeOH (32.0 g, 1000 mmol) were added followed by conc. H_2SO_4 (1.8 g, 18.8 mmol). The mixture was refluxed overnight and monitored by TLC (Hexane: EtOAc 90:10). After the completion of reaction it was concentrated *in vacuo*, dissolved in CH_2Cl_2 (25 mL) and added saturated Na_2CO_3 to neutralize the reaction mixture. CH_2Cl_2 layer was separated and aqueous layer was extracted with CH_2Cl_2 (5 × 20 mL) and combined organic layers were washed with brine (20 mL), water (20mL) and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to leave a colorless liquid methyl 2,3,4,5,6-pentafluorobenzoate in 75% yield (1.6 g, 7.2 mmol), that matches with NMR spectra of product reported in the literature.[1] The product was used without further purification.

Synthesis of tert-butyl 2,3,4,5,6-pentafluorobenzoate (1i)



1i was prepared by modified literature procedure.[2] In a 100 mL of round bottom flask, pentafluorobenzoic acid (Oakwood Chemicals) (2.0 g, 9.4 mmol) and dimethylaminopyridine (116 mg, 0.95 mmol) in tert-butanol (30 mL) was added di-tert-butyldicarbonate (4.1 g, 18.9 mmol), and the reaction heated to 40 °C for 18 hours. The reaction was quenched with 1M HCl (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organics were washed with saturated Na_2CO_3 (3 x 20 mL), followed by brine (1 x 15 mL) then concentrated *in vacuo* to yield tert-butyl 2,3,4,5,6-pentafluorobenzoate as a colorless liquid in 80% yield (2.0 g, 7.5 mmol), that matches with NMR spectra of product reported in the literature.[2] The product was used without further purification.

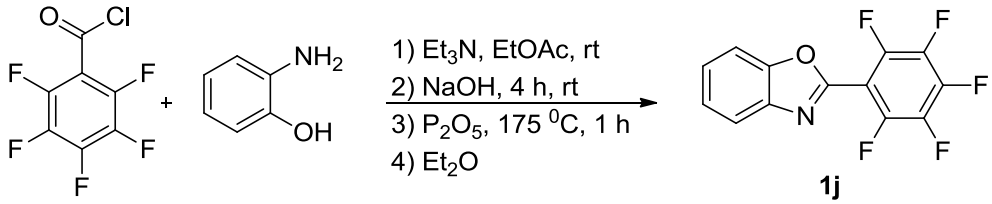
Synthesis of 1,2,4,5-tetrafluoro-3-phenoxy-6-(trifluoromethyl)benzene (1n)



1n was prepared by modified literature procedure.[3] In a 100 mL of round bottom flask octafluorotoluene (Oakwood Chemicals) (2.0 g, 8.47 mmol), phenol (956 mg, 10.2 mmol) in THF (50 mL) was added K_3PO_4 (3.6 g, 16.94 mmol), and the reaction mixture was refluxed for 8 hours under argon atmosphere

and monitored by TLC. The resulting suspension was filtered and the filtrate was diluted with CH_2Cl_2 (25 mL), washed successively with H_2O (10 mL) and brine (10 mL), dried over anhydrous $MgSO_4$, concentrated *in vacuo* to leave the crude product. The resultant crude residue was purified by automated flash chromatography using hexane to give the product 1,2,4,5-tetrafluoro-3-phenoxy-6-(trifluoromethyl)benzene as colorless crystals in 50% yield (1.3 g, 4.2 mmol), that match the NMR spectra of product reported in the literature.[3]

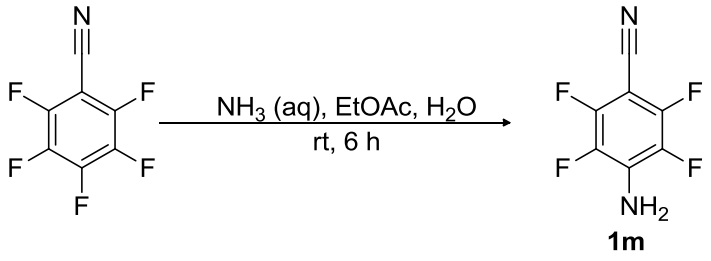
Synthesis of 2-(perfluorophenyl)benzo[*d*]oxazole (**1j**)



1j

1j was prepared by literature procedure.[4] Pentafluorbenzoic acid (3.0 g, 14.1 mmol) and DMF was slowly added to $SOCl_2$ (23.0 g, 200 mmol). The mixture was refluxed overnight under an Ar atmosphere. 2-(perfluorophenyl)benzo[*d*]oxazole was prepared by following literature procedure.[5] Triethylamine (1.7 g, 16.9 mmol) was added dropwise to a solution of 2-aminophenol (1.4 g, 12.7 mmol) and pentafluorobenzoyl chloride previously prepared (*vide supra*) in ethyl acetate (50 mL). Mixture was refluxed overnight and then aq NaOH (1M, 30 mL) was added and stirred for 3 hours at room temperature. The resulting mixture was extracted with EtOAc (5 × 20 mL) and washed with H_2O (25 mL) and brine (25 mL). Organic layer was dried over anhydrous $MgSO_4$ to yield 4 g of intermediate. P_2O_5 (4.0 g, 28 mmol) was added to the intermediate and then heated at 175 ^oC for 1 hour. After the mixture was cooled to room temperature ice water (50 mL) was added and mixture was extracted with EtOAc (5 × 20 mL). The combined organic layers were washed with aq NaOH (0.25 M, 50 mL), followed by water, brine and dried over anhydrous $MgSO_4$ and then concentrated *in vacuo* to leave the crude product. The resultant crude residue was purified by automated flash chromatography (hexane : EtOAc 90:10) to give the product 2-(perfluorophenyl)benzo[*d*]oxazole as white solid in 35% yield (1.2 g, 4.2 mmol), that matches with NMR spectra of product reported in the literature.[5]

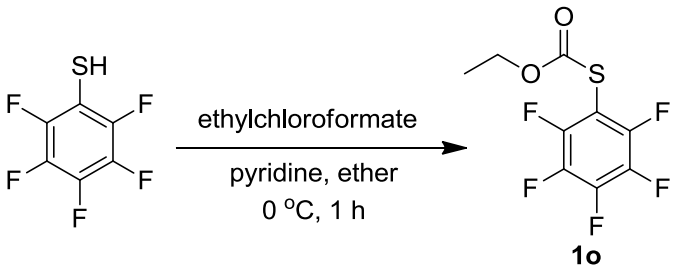
Synthesis of 4-amino-2,3,5,6-tetrafluorobenzonitrile (**1m**)



1m

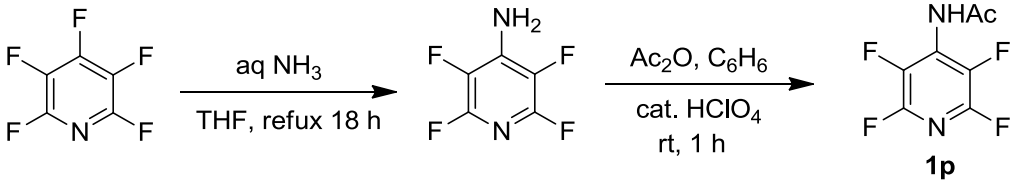
1m was prepared according to literature procedures.[6] To a solution of 2,3,4,5,6- pentafluorobenzonitrile (2 g, 10.4 mmol) in EtOAc (10 mL) was added a solution of aq. NH_3 (0.9 g,14.5 mmol, 28% w/w) and water (2 mL) dropwise and the reaction flask was stirred at room temperature for 6 hours. The reaction was monitored by TLC (hexane: EtOAc 90:10). Upon completion, water (4 mL) was added and stirred for 1 hour, and the resultant mixture was extracted with EtOAc (3 x 20 mL), dried over anhydrous sodium sulfate and then concentrated *in vacuo* to afford 2,3,5,6-tetrafluorobenzonitrile in 60 % yield (1.2 g, 6.3 mmol) as light yellow solid, which matches with NMR spectra of product reported in the literature.[6]

Synthesis of S-2o *O-ethyl S*-(2,3,5,6-tetrafluorophenyl) carbonothioate (**1o**)



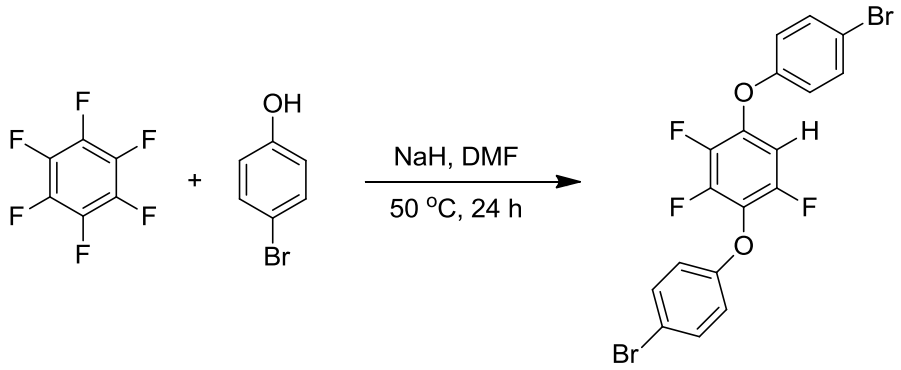
1o was synthesized according to a literature[7] procedure. In a 100 mL round bottom flask, pentafluorothiophenol (0.66 mL, 5 mmol), pyridine (0.6 mL, 7.5 mmol) and ether (17 mL) were added. The reaction mixture was stirred at 0 °C under Ar for 2 min and then ethylchloroformate (0.478 mL, 5mmol) was added to the reaction mixture dropwise and stirring was continued for 2 h. Reaction mixture was washed with cold HCl (1 x 20 mL 1M), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography using Hexane:DCM (0 % DCM for 10 cv and ramped slowly to 30 % DCM for 10-30 cv and then held at 35% DCM 30-35 cv) on 24 g silica column)) to afford *O*-ethyl *S*-perfluorophenyl carbonothioate in 29% yield (0.4 g, 1.47 mmol) as colorless liquid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.33 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -130.77 (dt, *J* = 21.7, 5.7 Hz, 2F), -149.18 (tt, *J* = 20.9, 3.9 Hz, 1F), -160.67 (tt, *J* = 21.1, 4.9 Hz, 2F).

Synthesis of N-(perfluoropyridin-4-yl)acetamide (**1p**)



1p was synthesized by following literature[8, 9] procedures. In a 50 mL reaction flask, pentafluoropyridine (0.3 mL , 2.96 mmol), conc. ammonia (1 mL), and THF (5 mL) were added. The reaction mixture was heated to reflux for 18 h. The flask was cooled to room temperature and THF was removed *in vacuo*. To the residue, water (10 mL) was added and aqueous portion was extracted with dichloromethane (3 x 10 mL). The combined DCM portion was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give 2,3,5,6-tetrafluoropyridin-4-amine as a yellow solid (0.544 g, 3.26 mmol) which was used without further purification in the acetylation step. In a 50 mL reaction flask, 2,3,5,6-tetrafluoropyridin-4-amine (0.544 g, 3.26 mmol), acetic anhydride (0.39 mL, 4.1 mmol), conc. $HClO_4$ (17µL, 0.28 mmol) and benzene (5 mL) were added and stirred at room temperature for 1h. The reaction mixture was extracted with ethyl acetate (3 x 10 mL). The combined ethyl acetate portion was washed with water (1 x 10 mL), 1 M HCl (1 x 10 mL) and brine (1 x 10 mL). The ethyl acetate portion was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography using hexane with 1% acetic acid:ethyl acetate (0 – 50% EtOAc for 30 cv and ramped to 100 % EtOAc for 30-40 cv) on 12 g silica column) to afford *N*-(perfluoropyridin-4-yl)acetamide in yield 33% (0.2 g, 1.47 mmol) as a white solid which was matched with literature.[9] 1H NMR (400 MHz, Chloroform-*d*) δ 7.12 (s, 0H), 2.30 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -89.87 (dq, *J* = 29.2, 14.0 Hz, 2F), -146.03 – -146.27 (m, 2F).

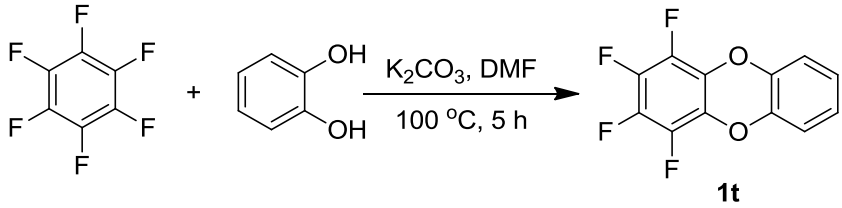
1,4-bis(4-bromophenoxy)benzene (**1g**)



1g

1g was synthesized by following literature[10] procedure. In a three necked 100 mL reaction flask, hexafluorobenzene (1.2 mL, 10.7 mmol), sodium hydride (428 mg, 10.7 mmol) and DMF (10 mL) were added. The suspension was stirred at 0 °C for 10 min and then 4- bromophenol (0.9 g, 5.35 mmol) was added dropwise to the suspension. The resulting mixture was stirred at 50 °C for 24 h. The reaction mixture was cooled to room temperature. The cooled mixture was diluted with water (50 mL) and extracted with ether (3 x 40 mL). The combined ether portion was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography using 100% hexanes to afford 1g in 16% yield (0.425 g, 0.86 mmol) as a colorless solid which was matched with literature.[10] ^{19}F NMR (376 MHz, Chloroform-*d*) δ -154.18 (s, 4F) .

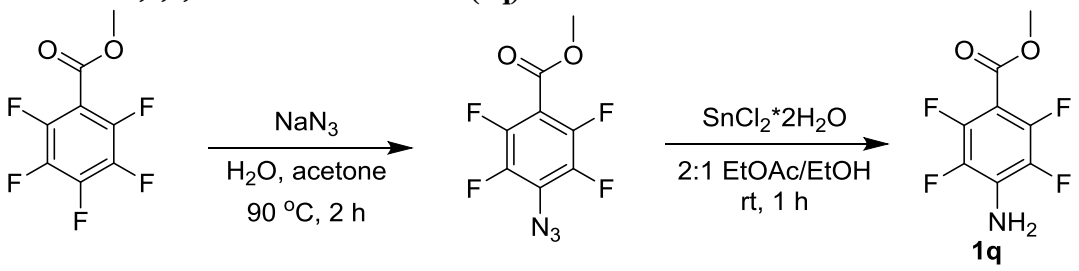
1,2,3,4-tetrafluorodibenzo[b,e][1,4]dioxine (**1t**)



1t

1t was synthesized by following literature[11] procedure. In a 100 mL reaction flask, hexafluorobenzene (1.15 mL, 10.0 mmol), potassium carbonate (1.38 g, 10.0 mmol), catechol (1.101 g, 10 mmol) and DMF (25 mL) were added. The reaction mixture was stirred at 100 °C for 5 h. The reaction mixture was cooled to room temperature. The cooled mixture was treated with 10 % HCl to obtain pH 4 and extracted with ethyl acetate (3 x 30 mL). The combined ethyl acetate was washed with water (3 x 30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford **1t** in 21% yield (0.528 g, 2.06 mmol) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.93 (m, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.99 (td, *J* = 16.7, 15.8, 10.0 Hz, 2F), -165.73 (td, *J* = 16.8, 15.8, 10.1 Hz, 2F).

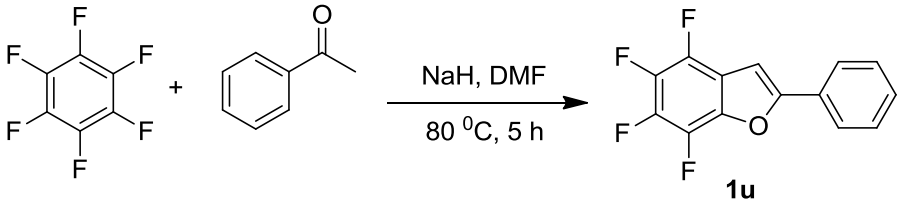
Methyl 4-amino-2,3,5,6-tetrafluorobenzoate (**1q**)



1q

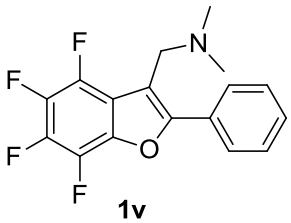
1q was synthesized by following literature procedures.[12,13] In a 50 mL reaction flask, methyl-2,3,4,5,6-pentafluorobenzoate (0.5 g, 2.2 mmol), sodium azide (186 mg, 2.86 mmol), acetone/ water (10 mL 2:1 v/v) were added. The reaction mixture was stirred at 90 ^{o}C for 2 h. The reaction mixture was cooled to room temperature and then diluted with water (60 mL). The reaction mixture was extracted with ether (3 x 20 mL). The combined ether portions were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford methyl 4-azido-2,3,5,6-tetrafluorobenzoate (0.451 g, 1.8 mmol) as a brown solid which matched with literature.[12] In a 50 mL round bottom flask, methyl 4-azido-2,3,5,6-tetrafluorobenzoate (0.426 g, 1.7 mmol), $SnCl_2$*$2H_2O$ (0.579 mg, 2.56 mmol), ethyl acetate / ethanol (15 mL 2:1 v/v) were added. The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated *in vacuo* and treated with sat. $NaHCO_3$ (20 mL). The aqueous mixture was extracted with dichloromethane (3 x 15 mL) and filtered through celite to obtain methyl-4-amino-2,3,5,6-tetrafluorobenzoate in crude yield 89% (0.438 g, 1.96 mmol) as a brownish yellow solid. The compound matched the literature.[13] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.89 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -141.03 – -141.22 (m, 2F), -162.62 – -162.76 (m, 2F).

4,5,6,7-tetrafluoro-2-phenylbenzofuran (**1u**)



1u

1u was synthesized by the following literature[14] procedure. To a suspension of hexafluorobenzene (1.15 mL, 10 mmol), NaH (0.24 g, 20 mmol) and DMF (10 mL), was added a solution of acetophenone (1.16 mL, 10 mmol) dropwise. The reaction mixture was stirred at 80 ^{o}C for 5 h. The reaction mixture was cooled to room temperature and poured into ether (100 mL). The reaction mixture was washed water (3 x 20 mL). The combined ether portions were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography using hexane:DCM (0 – 10% DCM for 15 cv and ramped to 100 % EtOAc for 15-25 cv) on 80 g silica column) to afford 4,5,6,7-tetrafluoro-2-phenylbenzofuran in yield 15% (0.4 g, 1.5 mmol) as a white solid which matched with the literature.[14] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (dt, *J* = 6.1, 1.3 Hz, 2H), 7.50 – 7.38 (m, 3H), 7.10 (d, *J* = 2.3 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -147.99 – -148.20 (m, 1F), -161.81 – -162.13 (m, 2F), -164.53 (ddd, *J* = 21.2, 15.1, 6.5 Hz, 1F).

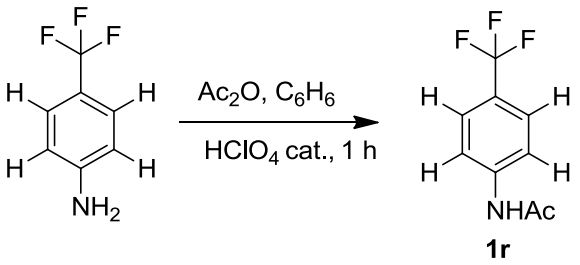


1v

(4,5,6,7-tetrafluoro-2-phenylbenzofuran-3-yl)-N,N-dimethylmethanamine (**1v**)

1v was obtained as a by-product in the synthesis of **1u** in 8% yield (0.28 g, 0.86 mmol) (*vide supra*) as a yellow waxy solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 8.00 (m, 2H), 7.49 (ddd, *J* = 17.5, 13.0, 11.6 Hz, 3H), 3.68 (s, 2H), 2.36 (s, 6H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -149.31 (dd, *J* = 20.8, 16.1 Hz, 1F), -162.22 (t, *J* = 19.7 Hz, 1F), -162.52 – -162.78 (m, 1F), -164.84 (t, *J* = 20.3 Hz, 1F). GC/MS (m/z, relative intensity) 323 (M+, 40), 308 (80), 279 (100), 251 (36), 201 (39).

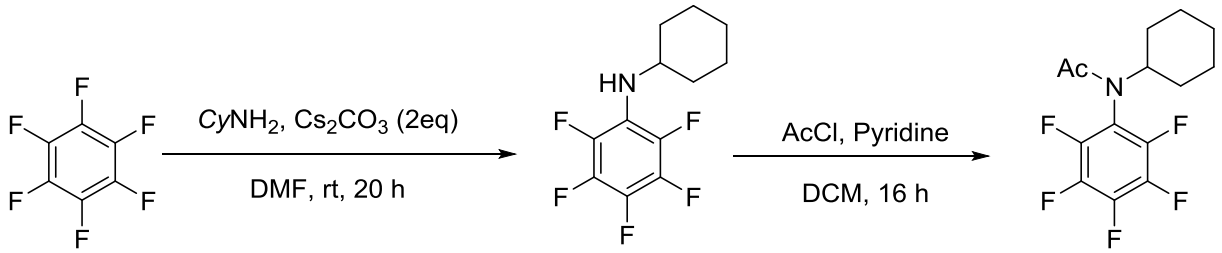
***N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide (1r)**



1r

1r was synthesized according to the literature [9] procedure. Starting amine was synthesized according to literature[8] procedure. In a 25 mL reaction flask, 2,3,5,6-tetrafluoro-4-(trifluoromethyl)benzenamine (0.5 g, 2.15 mmol), acetic anhydride (0.29 mL, 3.06 mmol), conc. $HClO_4$ (10µL) and benzene (5 mL) were added and stirred at room temperature for 1 h. The reaction mixture was extracted with ethyl acetate (3 x 10 mL). The combined ethyl acetate portion was washed with water (1 x 10 mL), 1 M HCl (1 x 10 mL) and brine (1 x 10 mL). The ethyl acetate portion was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. 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 24 g silica column) to afford *N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide in yield 76% (0.45 g, 1.63 mmol) as a white solid which matched with the literature.[9] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.86 (s, 1H), 2.27 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -56.53 (t, *J* = 21.7 Hz, 3F), -140.48 – -141.37 (m, 2F), -143.13 – -143.91 (m, 2F).

***N*-cyclohexyl-N-(perfluorophenyl)acetamide (1k)**

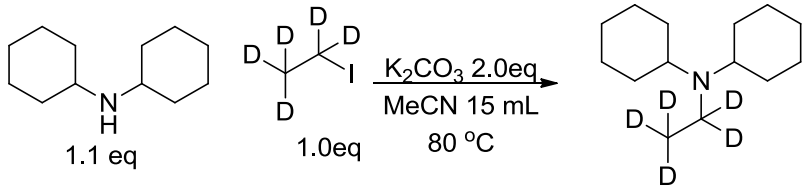


1k

N-cyclohexyl-2,3,4,5,6-pentafluoroaniline was synthesized following the literature[15] procedure. 1k was synthesized by the acylation of above amine. To an ice cold solution of *N*-cyclohexyl-2,3,4,5,6-pentafluoroaniline (1.9 g, 7.5 mmol), DCM (30 mL) and pyridine (1.2 mL, 15 mmol), acetyl chloride (1.0 mL, 15 mmol) was added dropwise. Reaction was stirred at room temperature for 16 hours. Reaction was quenched by adding sat. NH_4Cl (25 mL) and aq phase was extracted with DCM (20 x 5). The combined organics were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography using hexane:EtOAc (0 – 50% EtOAc for 15 cv and ramped to 100 % EtOAc for 15-18 cv and then hold for 18-21) on 80 g silica column to afford *N*-cyclohexyl-*N*-(perfluorophenyl)acetamide in yield 60% (86% purity) (1.35 g, 4.39 mmol) as a colorless solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.57 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.95 – 1.67 (m, 7H), 1.37 (tdd, *J* = 16.6, 8.3, 3.4 Hz, 2H), 0.91 – 0.78 (m, 4H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -141.86 (d, *J* = 18.3 Hz), -152.31 (t, *J* = 21.5 Hz), -160.90 – -161.13 (m). In ^{19}F NMR another set of 2:1:2 peaks with similar multiplicity was noticed which integrated to 14%. mp-58-60 ^{o}C.

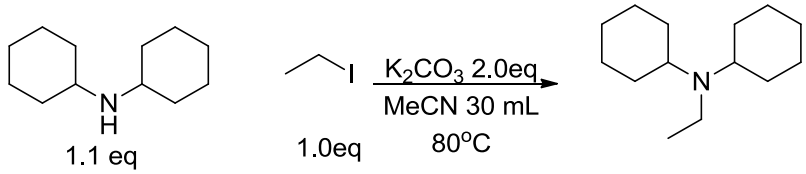
Synthesis of amines

Synthesis of *N, N* -dicyclohexyl-*N*-d_5-ethylamine

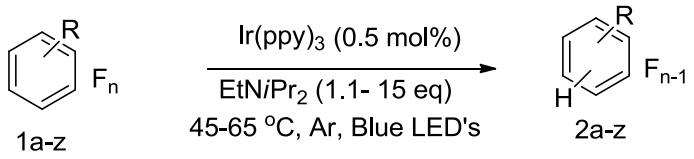


N, N -dicyclohexyl-*N*-d_5-ethylamine was prepared using an unoptimized procedure. In a pressure vial dicyclohexylamine (308 mg, 1.7 mmol), K_2CO_3 (428 mg, 3.1 mmol) and MeCN (15 mL) were added followed by) iodoethane-d_5 (250 mg, 1.55 mmol). The mixture was stirred 16 hours. Reaction was concentrated *in vacuo*, dissolved in CH_2Cl_2 (25 mL) and washed with 1M NaOH. CH_2Cl_2 layer was separated and aqueous layer was extracted with CH_2Cl_2 (5 × 20 mL) and combined organic layers were washed with brine (20 mL), water (20mL) and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo.* The resultant crude residue was purified by flash chromatography using DCM:MeOH (0% MeOH for 5 cv, 0-5% MeOH for 2-25 cv and ramped to 100 % MeOH for 25-35 cv) on 12 g silica column to afford a yellow liquid *N, N* -dicyclohexyl-*N*-d_5-ethylamine in 20% yield (65 mg, 0.3 mmol). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.72 – 2.42 (m, 2H), 1.73 (d, *J* = 8.4 Hz, 8H), 1.59 (d, *J* = 12.0 Hz, 2H), 1.31 – 1.01 (m, 10H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 58.00 , 39.37 (p, *J* = 19.8 Hz), 31.55 , 26.41 , 26.38 , 16.17 (ddd, *J* = 54.1, 37.0, 19.1 Hz).

Synthesis of *N, N* -dicyclohexyl-*N*-ethylamine



N, N -dicyclohexyl-*N*-ethylamine was prepared using an unoptimized procedure. In a pressure vial dicyclohexylamine (634 mg, 3.52 mmol), K_2CO_3 (883 mg, 6.4 mmol) and MeCN (30 mL) were added followed by) iodoethane (500 mg, 3.2 mmol). The mixture was stirred 16 hours. Reaction was concentrated *in vacuo*, dissolved in CH_2Cl_2 (25 mL) and washed with 1M NaOH. CH_2Cl_2 layer was separated and aqueous layer was extracted with CH_2Cl_2 (5 × 20 mL) and combined organic layers were washed with brine (20 mL), water (20mL) and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo.* The resultant crude residue was purified by flash chromatography using DCM:MeOH acetate (0% MeOH for 5 cv, 0-5% MeOH for 2-25 cv and ramped to 100 % EtOAc for 25-35 cv) on 12 g silica column) to afford a yellow liquid *N, N* -dicyclohexyl-*N*-ethylamine in 10% yield (67 mg, 0.32 mmol).



General procedure A for the photocatalytic hydrodefluorination reaction (reaction in culture tube)

A 12 x 75 mm borosilicate test tube fitted with rubber septum was charged *tris*(2- phenyl pyridinato-C^2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.5 mM, 1 mL in MeCN). Fluorinated starting material **1a-z** (1 eq) and *N, N*-diisopropylethylamine **(**1.1-15 eq) were added and the reaction was degassed at 0 °C to avoid evaporation of *N, N*-diisopropylethylamine and volatile starting materials via Ar bubbling for 5-10 min and then left under positive Ar pressure by removing the exit 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 45 °C (or 65 °C). The reaction was monitored by ^{19}F NMR and GC-MS. For ^{19}F NMR 0.3 mL of reaction mixture was diluted with 0.3 mL of $CDCl_3$ after the desired time period. 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.

General procedure B for the photocatalytic hydrodefluorination reaction (reaction NMR tube with C_6D_6 capillary)

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) ($Ir(ppy)_3$) (0.5 mM, 1 mL in MeCN). Fluorinated starting material **1a-z** (1 eq) and *N, N*-diisopropylethylamine (1.1-15 eq) were added and sealed glass capillary containing C_6D_6 was placed in NMR tube for locking purposes before degassing. Then the reaction was degassed at 0 °C to avoid evaporation of *N, N*-diisopropylethylamine and volatile starting materials via Ar bubbling for 5-10 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 (or 65 °C). The reaction was monitored by ^{19}F NMR. After the complete consumption of starting material, 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.

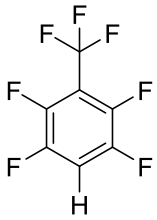
General procedure C for the photocatalytic hydrodefluorination reaction (reaction NMR tube)

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) ($Ir(ppy)_3$) (0.5 mM, 1 mL in MeCN). Fluorinated starting material **1a-z** (1 eq) and *N, N*-diisopropylethylamine **(**1.1-15 eq) were added and the reaction was degassed at 0 °C to avoid evaporation of *N, N*-diisopropylethylamine and volatile starting materials via Ar bubbling for 5-10 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 (or 65 °C). The reaction was monitored by ^{19}F NMR. After the complete consumption of starting material, 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 organic portions were combined and dried with anhydrous $MgSO_4$. The crude product was concentrated *in vacuo* and purified by normal phase chromatography. For ^{19}F NMR 0.3 mL of above reaction was diluted with 0.3 mL of $CDCl_3$.

Synthesis of 2a (2,3,5,6-tetrafluoropyridine)

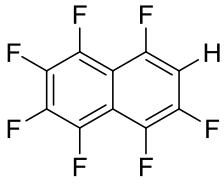
The general procedure A was followed using pentafluoropyridine (16.9 mg, 0.1 mmol, 1 eq), *N*,*N*-diisopropylethylamine (28.4 mg, 0.22 mmol, 2.2 eq) and 1.0 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2a** in 93% yield by ^{19}F NMR after adding trifluoroacetic acid (0.05 mmol, 3.8 µL). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -93.47, -141.41 – -141.66 (m). FT-IR cm^{-1}2983, 1696, 1472, 1396. GC/MS (m/z, relative intensity) 151 (M+, 100), 132 (10), 120 (17), 106 (23), 82 (50)

Synthesis of 2b (1,2,4,5-tetrafluoro-3-(trifluoromethyl)benzene)



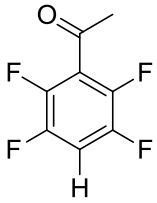
The general procedure B was followed using 1,2,3,4,5-pentafluoro-6-(trifluoromethyl)benzene (24.0 mg, 0.1 mmol, 1 eq), *N*,*N*-diisopropylethylamine (14.2 mg, 0.11 mmol, 1.1 eq) and 1.0 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2b** in 95% yield by ^{19}F NMR after adding trifluoroacetic acid (0.05 mmol, 3.8 µL). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -57.36 (t, *J* = 22.1 Hz), -137.75 – -137.93 (m), -142.02 – -142.35 (m). FT-IR cm^{-1} 3201, 1653. GC/MS (m/z, relative intensity) 218 (M+, 40), 200 (70),181 (69), 150 (60), 86 (100)

Synthesis of 2c (1,2,3,4,5,6,8-heptafluoronaphthalene)



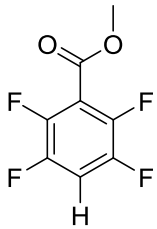
The general procedure B was followed at 65 °C in an NMR tube using perfluoronaphthalene (13.6 mg, 0.05 mmol, 1 eq), *N*,*N*-diisopropylethylamine (21.9 mg, 0.17 mmol, 3.3 eq) and 0.5 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2c** in 55% yield (at 57% conversion) by ^{19}F NMR after adding trifluoroacetic acid (0.025 mmol, 1.91 µL). ^{19}F NMR (376 MHz, Benzene-d_6) δ -118.78 – -119.11 (m), -136.47 – -136.61 (m), -147.16 (dt, *J* = 65.4, 16.3 Hz), -148.86 – -149.16 (m), -152.20 – -152.55 (m), -156.20 (t, *J* = 17.8 Hz), -158.84 – -159.03 (m) which matched with the literature.[18] FT-IR cm^{-1}3003, 2985, 1652, 1482.

Synthesis of 2d (1-(2,3,5,6-tetrafluorophenyl)ethan-1-one)



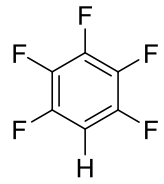
The general procedure A was followed using 1-(2,3,5,6-tetrafluorophenyl)ethanone (21.0 mg, 0.1 mmol, 1 eq), *N*,*N*-diisopropylethylamine (19.3 mg, 0.15 mmol, 1.5 eq) and 1.0 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2d** in 85% yield by ^{19}F NMR after adding trifluoroacetic acid (0.05 mmol, 3.8 µL). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.36 – -139.50 (m), -143.78 (tt, *J* = 12.9, 7.8 Hz). FT-IR cm^{-1} 2983, 1690, 1498. GC/MS (m/z, relative intensity) 192 (M+, 40), 177 (100), 149 (57), 99 (40),

Synthesis of 2e (methyl 2,3,5,6-tetrafluorobenzoate)



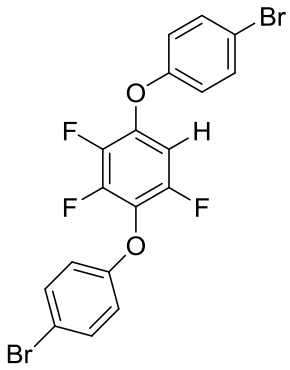
The general procedure B was using methyl 2,3,4,5,6-pentafluorobenzoate (**1e**) (22.6 mg, 0.1 mmol, 1 eq), *N*,*N*-diisopropylethylamine (14.2 mg, 0.11 mmol, 1.1 eq) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2e** in 75% yield by ^{19}F NMR after adding trifluoroacetic acid (0.025 mmol, 1.91 µL). ^{19}F NMR (376 MHz, Benzene-d_6) δ -139.83 – -140.47 (m), -142.19 – -142.36 (m). FT-IR cm^{-1}3018, 2966, 1733, 1495, 1268. GC/MS (m/z, relative intensity) 151 (M+, 100), 132 (10), 120 (17), 106 (23), 82 (50)

Synthesis of 2f (1,2,3,4,5-pentafluorobenzene)



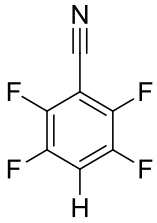
The general procedure A was followed using hexafluorobenzene (18.6 mg, 0.1 mmol, 1 eq), *N*,*N*-diisopropylethylamine (42.6 mg, 0.33 mmol, 3.3 eq) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2f** in 90% yield by ^{19}F NMR after adding trifluoroacetic acid (0.033 mmol, 2.54 µL). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -140.21 (dt, *J* = 20.1, 9.3 Hz), -155.76 (t, *J* = 19.6 Hz), -163.82 (ddt, *J* = 25.9, 12.7, 6.9 Hz) which matched with the literature.[19] FT-IR cm^{-1}3004, 2985, 1669, 1576.

Synthesis of 2g (4,4'-((2,3,5-trifluoro-1,4-phenylene)bis(oxy))bis(bromobenzene))



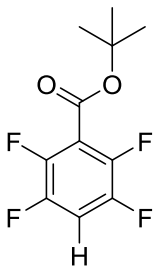
The general procedure B was followed at 65 °C in an NMR tube using 4,4'-((perfluoro-1,4-phenylene)bis(oxy))bis(bromobenzene) (**1g**) (49.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (42.6 mg, 0.33 mmol) and 1.0 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used. The crude material was purified by flash chromatography using hexane with 1% AcOH : ethyl acetate (0-5 % EtOAc for 40 cv and ramped to 100 % EtOAc for 40-70 cv and then held at 100% EtOAc 70-80 cv) on 24 g silica column) to afford **2g** in 50% isolated (23.7 mg, 0.05 mmol) as a white solid. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -129.96 (t, *J* = 10.5 Hz), -146.37 (dd, *J* = 19.9, 2.1 Hz), -156.28 (ddd, *J* = 19.8, 10.3, 7.0 Hz).^1H NMR (400 MHz, Chloroform-*d*) δ 7.40 (dd, *J* = 30.4, 9.0 Hz, 4H), 6.83 (dd, *J* = 33.6, 8.9 Hz, 4H), 6.60 (ddd, *J* = 10.6, 7.0, 2.5 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.59 , 154.94 , 152.58 – 149.85 (m), 147.97 – 144.29 (m), 142.28 – 138.72 (m), 133.13 , 132.75 (d, *J* = 56.9 Hz), 132.69 (d, *J* = 5.5 Hz), 128.69 – 128.06 (m), 120.01 , 117.35 , 117.14 , 115.90 , 103.30 (dd, *J* = 23.5, 3.3 Hz). FT-IR cm^{-1} 3047, 1593, 1551, 1267. GC/MS (m/z, relative intensity) 474 (M+, 100),365 (20), 222 (10), 155 (32), 76 (60). mp-84-86 °C.

Synthesis of 2h (2,3,5,6-tetrafluorobenzonitrile)



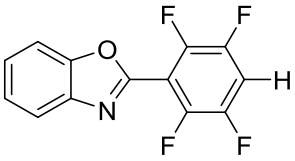
The general procedure A was followed using 2,3,4,5,6-pentafluorobenzonitrile (19.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (14.2 mg, 0.11 mmol) and 1.0 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2h** in 88% yield by ^{19}F NMR after adding trifluoroacetic acid (0.05 mmol, 3.8 µL). ^{19}F NMR (376 MHz, Acetonitrile-d_3) δ -135.38 – -135.56 (m), -138.43 (tdd, *J* = 15.6, 10.1, 6.0 Hz) which matched with the literature.[20] FT-IR cm^{-1} 2243, 1585, 1690, 1492. GC/MS (m/z, relative intensity) 175 (M+, 100), 144 (8), 124 (7), 106 (30).

Synthesis of 2i (tert-butyl 2,3,5,6-tetrafluorobenzoate)



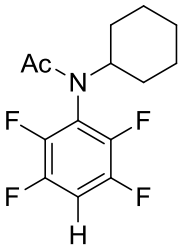
The general procedure B was followed at 45 °C using tert-butyl 2,3,4,5,6-pentafluorobenzoate (**1i**) (26.8 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (14.2 mg, 0.11 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2i** in 90% yield by ^{19}F NMR after adding trifluoroacetic acid (0.025 mmol, 1.9 µL). ^{19}F NMR (376 MHz, Benzene-d_6) δ -140.16 – -140.31 (m), -143.71 – -143.87 (m). FT-IR cm^{-}3045, 2986, 1730, 1600, 1551, 1437, 1267. Calculated HRMS(ESI) for $(C_{11}H_{10}F_4O_2$ $(M+NH_4)^+$ is 268.0961observed 268.1016.

Synthesis of 2j (2-(2,3,5,6-tetrafluorophenyl)benzo[d]oxazole)



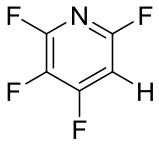
The general procedure A was followed using 2-(perfluorophenyl)benzo[d]oxazole (**1j**) (28.5 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (42.6 mg, 0.33 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN. After 24 hours, preperative TLC (hexane: EtOAc 90:10, 1% acetic acid) was done to isolate **2j** in 83% (22.2 mg, 0.083 mmol) as a light yellow solid. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -137.57 – -137.78 (m), -138.02 – -138.21 (m). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (dd, *J* = 85.7, 1.8 Hz, 1H), 7.96 – 7.63 (m, 1H), 7.46 (pd, *J* = 7.3, 1.2 Hz, 2H), 7.29 (tt, *J* = 9.2, 7.2 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.34 – 153.14 (m), 150.70 , 147.92 – 147.62 (m), 146.74 – 143.83 (m), 145.28 (dt, *J* = 243.4, 3.7 Hz), 141.31 , 126.75 , 125.36 , 121.17 , 111.25 , 108.87 (t, *J* = 22.4 Hz). FT-IR cm^{-1} 3001, 1653, 1551, 1653. GC/MS (m/z, relative intensity) 267 (M+, 100), 239 (25), 92 (20), 64 (60). mp-108-110 ^{o}C.

Synthesis of 2k (*N*-cyclohexyl-N-(2,3,5,6-tetrafluorophenyl)acetamide)



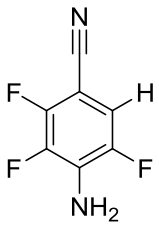
The general procedure C was followed using N-cyclohexyl-N-(perfluorophenyl)acetamide (**2k)** (25.0 mg, 0.08 mmol), *N*,*N*-diisopropylethylamine (42.6 mg, 0.33 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN. The crude material was purified by flash chromatography using hexane : diethyl ether (0 % for 1 cv, slowly ramped to 25 % ether for 1- 35 cv, to 100% ether for 35-54 cv, then held at 100% ether 54-57 cv), on 24 g silica column to afford **2k** in 61% (adjusted) yield (15.2 mg, 0.05 mmol) as a white solid. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -137.42 (dt, *J* = 21.9, 10.9 Hz), -142.00 – -142.18 (m). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.12 (tt, *J* = 9.6, 7.2 Hz, 1H), 4.52 (tt, *J* = 12.1, 3.6 Hz, 1H), 1.75 (s, 3H), 1.93 – 1.49 (m, 4H), 1.39 – 0.86 (m, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.59 , 147.94 – 145.79 (m), 145.52 – 143.25 (m), 121.14 – 120.53 (m), 106.87 (t, *J* = 22.7 Hz), 56.21 , 30.86 – 30.78 (m), 29.91 , 25.84 , 25.47 , 22.76 . FT-IR cm^{-1} 3043, 2924, 1678, 1505, 1306. GC/MS (m/z, relative intensity) 289 (M+, 3), 247 (15), 207 (53), 165 (42). mp-120-124 ^{o}C.

Synthesis of 2l (2,3,4,6-tetrafluoropyridine)



The general procedure B was followed at 45 ^{o}C using 3-chloro-2,4,5,6-tetrafluoropyridine (18.6 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (28.4 mg, 0.22 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2l** in 78% yield by ^{19}F NMR after adding trifluoroacetic acid (0.025 mmol, 1.9 µL). ^{19}F NMR (376 MHz, Benzene-d_6) δ -70.89 – -71.68 (m), -87.94 – -88.16 (m), -116.39 – -116.58 (m), -170.54 – -170.76 (m) which matches with the literature.[21] FT-IR cm^{-1}3013, 2985, 1634, 1463.

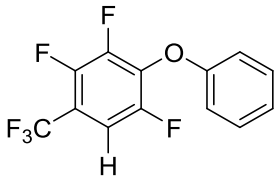
Synthesis of 2m (4-amino-2,3,5-trifluorobenzonitrile)



The general procedure A was followed using 4-amino-2,3,5,6-tetrafluorobenzonitrile (**1m**) (19.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (14.2 mg, 0.11 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used. 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 24 g silica column) to afford **2m** in 82% isolated yield (14.1 mg, 0.082 mmol) as a light brown solid. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -135.34 (ddd, *J* = 19.7, 11.3, 5.0 Hz), -135.56 – -135.68 (m), -154.14 (ddd, *J* = 19.3, 12.2, 1.9 Hz). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.37 (ddd, *J* = 10.6, 5.4, 2.2 Hz, 1H), 6.19 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.90 (ddd, *J* = 256.1, 12.4, 3.4 Hz), 146.59 (dd, *J* = 242.1,

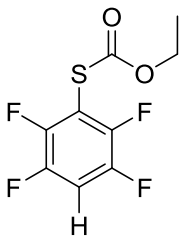
4.7 Hz), 146.53 (dd, *J* = 238.5, 0.7 Hz), 139.42 (ddd, *J* = 243.7, 14.9, 7.8 Hz), 131.91 (ddd, *J* = 17.3, 12.3, 3.6 Hz), 113.84 (ddd, *J* = 23.1, 3.1, 1.0 Hz), 88.20 (ddd, *J* = 14.5, 10.8, 2.1 Hz). FT-IR cm^{-1} 3414, 3357, 2924, 2234, 1642. GC/MS (m/z, relative intensity) 172 (M+, 100), 145(15), 125 (20), 75 (20). mp-82-86 ^{o}C.

Synthesis of 2n (1,3,4-trifluoro-2-phenoxy-5-(trifluoromethyl)benzene)



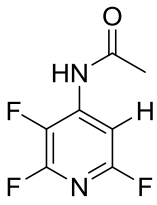
The general procedure B was followed using 4-amino-2,3,5,6-tetrafluorobenzonitrile (**1n**) (31.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (14.2 mg, 0.11 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2n** in 90% yield by ^{19}F NMR after adding trifluoroacetic acid (0.025 mmol, 1.9 µL). ^{19}F NMR (376 MHz, Benzene-d_6) δ -61.87 (d, *J* = 13.0 Hz), -130.93 (t, *J* = 11.4 Hz), -142.93 – -143.17 (m), -147.94 (d, *J* = 19.2 Hz). FT-IR cm^{-1}2980, 1653, 1591, 1511, 1385, 1491, 1233. GC/MS (m/z, relative intensity) 292 (M+, 100), 273 (8), 264 (7), 74 (100), 51 (48).

Synthesis of 2o (*O*-ethyl S-(2,3,5,6-tetrafluorophenyl) carbonothioate)



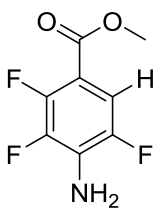
The general procedure A was followed using *O*-ethyl *S*-(perfluorophenyl) carbonothioate (**1o**) (54.0 mg, 0.2 mmol), *N*,*N*-diisopropylethylamine (28.4 mg, 0.22 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2o** in 72% ^{19}F NMR yield and 50% isolated yield (26.0 mg, 0.1 mmol). The crude material was purified by flash chromatography using hexane : DCM (0 % DCM for 10 cv and ramped slowly to 30 % DCM for 10-30 cv and then held at 35% DCM 30-35 cv) on 24 g silica column).[1] to obtain a mixture of para (90%) and ortho (10%) mono-HDF as a colorless liquid. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -131.69 – -131.83 (m), -137.71 – -137.86 (m). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (tt, *J* = 9.6, 6.4 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.80 , 148.14 – 145.26 (m), 147.20 – 144.23 (m), 109.76 – 107.46 (m), 66.90 – 64.40 (m), 14.06. FT-IR cm^{-1}3023, 2978, 1736, 1524, 1642. GC/MS (m/z, relative intensity) 255 (M+, 2), 209 (8), 182 (100), 137 (35).

Synthesis of 2p (*N*-(2,3,6-trifluoropyridin-4-yl)acetamide)



The general procedure A was followed using *N*-(perfluoropyridin-4-yl)acetamide (**1p**) (42 mg, 0.2 mmol), *N*,*N*-diisopropylethylamine (85.3 mg, 0.66 mmol) and 2 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2p** in 97% isolated yield (37.0 mg, 0.19 mmol) as a yellow solid. 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 24 g silica column). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -70.66 (dd, *J* = 22.8, 13.3 Hz), -89.31 (dd, *J* = 21.6, 13.3 Hz), -165.68 (t, *J* = 22.3 Hz). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 – 7.93 (m, 1H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.52 , 155.85 (ddd, *J* = 241.2, 14.5, 3.2 Hz), 148.34 (ddd, *J* = 240.6, 18.2, 14.5 Hz), 139.55 (ddd, *J* = 12.8, 8.1, 4.5 Hz), 132.03 (ddd, *J* = 248.5, 28.0, 6.6 Hz), 97.30 (ddd, *J* = 45.0, 5.7, 1.3 Hz), 24.62. FT-IR cm^{-1}3418, 3050, 2989, 1638,1550. GC/MS (m/z, relative intensity) 190 (M+, 9), 162 (30), 148 (100). mp-66-72 ^{o}C.

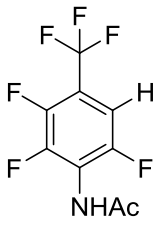
Synthesis of 2q (methyl 4-amino-2,3,5-trifluorobenzoate)



The general procedure A was followed using methyl 4-amino-2,3,5,6-tetrafluorobenzoate (**1q**) (44 mg, 0.2 mmol), *N*,*N*-diisopropylethylamine (85.3 mg, 0.66 mmol) and 2 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2q** in 99% isolated yield (40.6

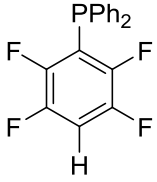
mg, 0.198 mmol) as a white solid. The crude material was purified by flash chromatography using hexane : ethyl acetate (0-10 % EtOAc for 25 cv and ramped to 100 % EtOAc for 10-52 cv and then held at 100% EtOAc 52-57 cv) on 12 g silica column). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.37 (q, *J* = 10.9 Hz), -139.21 (ddd, *J* = 19.2, 12.8, 5.8 Hz), -156.50 (ddd, *J* = 19.7, 10.1, 2.2 Hz). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (ddd, *J* = 11.2, 5.8, 2.3 Hz, 1H), 4.28 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.18 – 163.74 (m), 149.71 (dd, *J* = 11.7, 2.6 Hz), 144.90 (dd, *J* = 6.0, 2.4 Hz), 139.87 (ddd, *J* = 241.2, 16.9, 7.2 Hz), 147.70 – 129.62 (m), 112.27 (ddd, *J* = 21.8, 2.7, 1.2 Hz), 106.49 (dd, *J* = 8.6, 7.8 Hz), 52.49. FT-IR cm^{-1}3403, 3050, 2984, 1732, 1551. GC/MS (m/z, relative intensity) 205 (M+, 46), 174 (100), 146 (33). mp-107-108 ^{o}C.

Synthesis of 2r (*N*-(2,3,6-trifluoro-4-(trifluoromethyl)phenyl)acetamide)



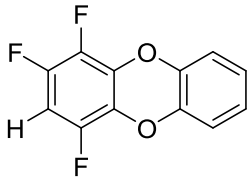
The general procedure A was followed using *N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide (**1r**) (27 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (14.2 mg, 0.11 mmol) and 1 mL of stock solution of Ir(ppy)$_3$ in CH_3CN was used to afford **2r** in 80% isolated yield (21.0mg, 0.08 mmol) as a yellow solid. 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 24 g silica column). ^{19}F NMR (376 MHz, Acetone-d_6) δ -61.95 (d, *J* = 13.0 Hz), -121.52 – -121.77 (m), -137.54 (d, *J* = 19.4 Hz), -145.46 – -145.73 (m). ^{1}H NMR (400 MHz, Acetone-d_6) δ 9.30 (s, 1H), 7.52 (ddd, *J* = 8.7, 5.8, 2.2 Hz, 1H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, Acetone-d_6) δ 167.62, 152.67 (dt, *J* = 248.1, 3.8 Hz), 147.95 – 145.04 (m), 146.56 – 143.64 (m), 121.80 (d, *J* = 277.8 Hz), 123.79 – 119.95 (m), 116.06 – 115.45 (m), 108.64 (dp, *J* = 27.2, 4.7 Hz), 21.80. FT-IR cm^{-1} 3441, 3022, 2978, 1644, 1521. GC/MS (m/z, relative intensity) 257 (M+, 2), 215 (60), 196 (20), 165 (11). mp-162-166 ^{o}C.

Synthesis of 2s (diphenyl(2,3,5,6-tetrafluorophenyl)phosphane)



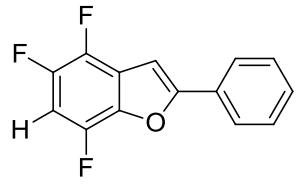
The general procedure B was followed at 45 ^{o}C using (perfluorophenyl)diphenylphosphane (35.2 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (42.6 mg, 0.33 mmol) and 1 mL of stock solution of Ir(ppy)$_3$ in CH_3CN was used to afford **2s** in 76% yield by ^{19}F NMR after adding trifluoroacetic acid (0.033 mmol, 2.52 µL). ^{19}F NMR (376 MHz, Benzene-d_6) δ -130.81 – -131.09 (m), -140.23 – -140.40 (m). FT-IR cm^{-1}3013, 2985, 1634, 1475. GC/MS (m/z, relative intensity) 334 (M+, 100), 183 (24), 154 (23).

Synthesis of 2t (1,2,4-trifluorodibenzo[b,e][1,4]dioxine)



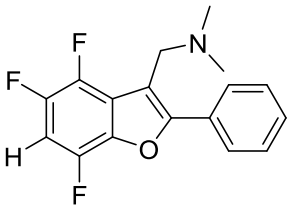
The general procedure A was followed using 1,2,3,4-tetrafluorodibenzo[b,e][1,4]dioxine (26.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (**1t**) (42.6 mg, 0.33 mmol) and 2 mL of stock solution of Ir(ppy)$_3$ in CH_3CN was used to afford **2t** in 45% (at 60% conv.) isolated yield (11.0 mg, 0.046 mmol) as a white solid. (Prep TLC with 100% hexanes). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.12 (t, *J* = 10.1 Hz), -141.97 (dd, *J* = 21.6, 10.2 Hz), -163.44 (ddd, *J* = 21.6, 10.0, 6.8 Hz). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.96 (m, 4H), 6.63 (td, *J* = 10.2, 6.7 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.16 – 144.21 (m), 143.80 (dd, *J* = 12.0, 3.8 Hz), 140.17 (d, *J* = 40.7 Hz), 136.19 (ddd, *J* = 247.5, 16.6, 4.7 Hz), 124.87 (d, *J* = 27.8 Hz), 116.69, 99.40 – 98.66 (m). FT-IR cm^{-1}3056, 1600, 1524, 1244. GC/MS (m/z, relative intensity) 238 (M+, 100), 209 (10), 182 (22), 50 (20). mp-108-112 ^{o}C.

Synthesis of 2u (4,5,7-trifluoro-2-phenylbenzofuran)



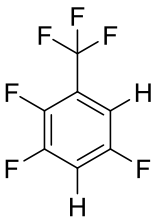
The general procedure B was followed at 65 °C using 4,5,6,7-tetrafluoro-2-phenylbenzofuran (**1u**) (27.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (42.6 mg, 0.33 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **2u** in 76%. ^{19}F NMR yield and 69% isolated yield (18.0 mg, 0.076 mmol). 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 24 g silica column) to obtain a mixture of mono HDF products (in 90%) and another isomer in 10% as a white solid. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.89 (ddd, *J* = 19.8, 9.7, 2.4 Hz), -143.61 (dd, *J* = 20.5, 10.7 Hz), -150.26 (td, *J* = 20.2, 6.0 Hz). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (dt, *J* = 6.1, 1.3 Hz, 2H), 7.52 – 7.40 (m, 3H), 7.15 (d, *J* = 2.6 Hz, 1H), 6.92 (ddd, *J* = 10.7, 9.7, 6.0 Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 158.38 , 145.04 (ddd, *J* = 241.9, 12.8, 9.3 Hz), 143.58 – 141.59 (m), 140.07 – 137.87 (m), 129.67 , 128.91 (d, *J* = 8.0 Hz), 125.30 , 121.68 (dt, *J* = 19.5, 3.4 Hz), 100.70 (dd, *J* = 24.8, 22.2 Hz). FT-IR cm^{-1} 3017, 2128, 1521, 1476, 1422, 1214. GC/MS (m/z, relative intensity) 248 (M+, 100), 219 (44), 201 (13), 124 (10). mp-59-64 °C.

Synthesis of 2v (*N*,*N*-dimethyl-1-(4,5,7-trifluoro-2-phenylbenzofuran-3-yl)methanamine)



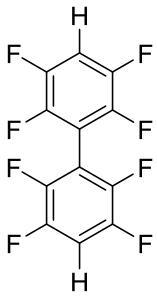
The general procedure B was followed at 65 °C using *N*,*N*-dimethyl-1-(4,5,6,7-tetrafluoro-2-phenylbenzofuran-3-yl)methanamine (**1v**) (24.0 mg, 0.75 mmol), *N*,*N*-diisopropylethylamine (32.0 mg, 0.33 mmol) and 0.75 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used. The crude material was purified 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 24 g silica column) to afford **2v** in 65% yield (20.0 mg ,0.065 mmol) as a colorless liquid. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -139.38 (dd, *J* = 19.7, 9.5 Hz), -143.85 (dd, *J* = 21.0, 10.7 Hz), -151.45 (td, *J* = 20.3, 5.7 Hz). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 7.6 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 3H), 6.92 (td, *J* = 10.1, 6.0 Hz, 1H), 3.68 (s, 2H), 2.35 (s, 6H). ^{13}C NMR (600 MHz, Chloroform-*d*) δ 156.63 , 146.61 – 144.62 (m), 144.04 – 141.83 (m), 140.31 (ddd, *J* = 248.4, 15.2, 3.8 Hz), 138.00 – 137.58 (m), 130.06 – 127.86 (m), 128.12 (d, *J* = 29.8 Hz), 123.06 (d, *J* = 14.5 Hz), 113.65 , 101.57 – 100.37 (m), 52.86 , 45.33 . FT-IR cm^{-1} 3063, 2987, 1601, 1245, 1421. GC/MS (m/z, relative intensity) 305 (M+, 305), 290 (80), 261 (100), 232 (30).

Synthesis of 3b (1,2,5-trifluoro-3-(trifluoromethyl)benzene)



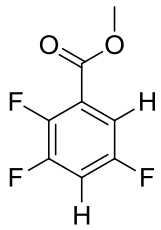
The general procedure A was followed using 1,2,3,4,5-pentafluoro-6-(trifluoromethyl)benzene (24.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (42.6 mg, 0.33 mmol) and 1.0 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **3b** in 86% yield by ^{19}F NMR after adding trifluoroacetic acid (0.05 mmol, 3.82 µL). ^{19}F NMR (376 MHz, Benzene-d_6) δ -61.64 (d, *J* = 13.2 Hz), -113.80 (ddd, *J* = 22.7, 8.0, 4.9 Hz), -132.17 – -132.28 (m), -146.12 (dddq, *J* = 26.0, 18.8, 13.2, 6.4, 5.1 Hz). FT-IR cm^{-1}3201, 1653. GC/MS (m/z, relative intensity) 200 (M+, 100), 181 (97), 150 (82), 81 (70).

Synthesis of 3w (2,2',3,3',5,5',6,6'-octafluoro-1,1'-biphenyl)



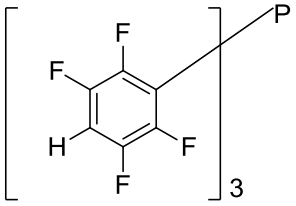
The general procedure A was followed using perfluoro-1,1'-biphenyl (66.8 mg, 0.2 mmol), *N*,*N*-diisopropylethylamine (85.2 mg, 0.66 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **3w** in 85% isolated yield (50.4 mg, 0.17 mmol) as a white solid. The crude material was 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- 40 cv), on 24 g silica column. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.08 – -138.25 (m), -138.58 – -138.82 (m). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.20 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.94 – 145.03 (m), 145.87 – 143.01 (m), 108.37 (t, *J* = 22.3 Hz). FT-IR cm^{-1} 3063,2988,1607. GC/MS (m/z, relative intensity) 298 (M+, 100), 280 (7), 260 (9), 229 (30). mp-66-74 °C.

Synthesis of 3e (methyl 2,3,5-trifluorobenzoate)



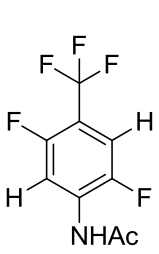
The general procedure A was followed using methyl 2,3,4,5,6-pentafluorobenzoate (**1e**) (22.6 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (77.45 mg, 0.60 mmol) and 1 mL of stock solution $Ir(ppy)_3$ in CH_3CN was used to afford **2e** in 73% yield by ^{19}F NMR after adding trifluoroacetic acid (0.025 mmol, 1.91 µL). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.85 (dtd, *J* = 15.7, 8.1, 3.5 Hz), -132.19 – -132.57 (m), -140.97 – -141.39 (m). FT-IR cm^{-1} 2963, 1738, 1691, 1468. GC/MS (m/z, relative intensity) 190 (M+, 29), 159 (100), 131 (56), 81 (49).

Synthesis of 3x (tris(2,3,5,6-tetrafluorophenyl)phosphine)



The general procedure A was followed using tris(pentafluorophenyl)phosphine (106.4 mg, 0.2 mmol), *N*,*N*-diisopropylethylamine (387.3 mg, 3.0 mmol) and 2 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **3x** in 78% isolated yield (75 mg, 0.16 mmol) as a white solid. The crude material was purified by flash chromatography using hexane : ethyl acetate (0 % EtOAc for 0-1 cv, 0 %-15% EtOAc for 1-10 cv, 15 % EtOAc for 10-18 cv, 15%-80% EtOAc for 18-23 cv, 80% EtOAc for 23- 30 cv, 80%- 100% EtOAc for 30-32 cv, then held at 100% EtOAc 32-35 cv), on 40 g silica column. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -130.86 – -131.12 (m), -137.66 (dd, *J* = 16.7, 8.5 Hz). ^{1}H NMR (400 MHz,Chloroform-*d*) δ 7.18 – 7.05 (m, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.40 (dtt, *J* = 244.8, 11.2, 11.2, 5.1, 5.1 Hz), 146.05 (ddd, *J* = 249.6, 9.6, 3.9 Hz), 111.78 – 108.62 (m), 109.07 (t, *J* = 22.5, 22.5 Hz). FT-IR cm^{-1}3050, 1603, 1550, 1490, 1368, 1245. GC/MS (m/z, relative intensity) 478 (M+, 100), 329 (40), 260 (36). mp-74-77 °C.

Synthesis of 3r (N-(2,5-difluoro-4-(trifluoromethyl)phenyl)acetamide)



The general procedure A was followed using N-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)acetamide (**1r**) (27.0 mg, 0.1 mmol), *N*,*N*-diisopropylethylamine (77.5 mg, 0.6 mmol) and 1 mL of stock solution of $Ir(ppy)_3$ in CH_3CN was used to afford **3r** in 74% isolated yield (17 mg, 0.07 mmol) as a yellow solid. 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 24 g silica column). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -61.43 (d, *J* = 12.6 Hz), -116.47 (ddt, *J* = 18.3, 12.6, 6.0 Hz), -136.36 – -136.51 (m). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 12.3, 6.5 Hz, 1H), 7.49 (s, 1H), 7.33 (dd, *J* = 10.6, 6.2 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (101

MHz, Chloroform-*d*) δ 168.39 , 155.99 (d, *J* = 251.2 Hz), 146.80 (d, *J* = 240.6 Hz), 131.13 – 130.75 (m), 121.87 (d, *J* = 271.5 Hz), 113.45 – 112.52 (m), 109.51 (dd, *J* = 28.5, 6.9 Hz). FT-IR cm^{-1}3442, 3025, 2977, 1653, 1521. GC/MS (m/z, relative intensity) 257 (M+, 6), 215 (40), 192 (17). mp-117-119 ^{o}C.

Catalyst turnover experiment and calculation

To assess the catalalyst robustness the following TON experiment was carried out using pentafluoropyridine as the substrate. An NMR tube was charged with *tris*(2- phenyl pyridinato-C^2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.00001 mmol in 0.5 mL of MeCN-d_3 made via serial dilution) and fitted with rubber septum (Ace glass, part no. 9096-25), pentafluoropyridine (0.05 mmol, 5.5 µL, 1 eq) and *N*,*N*-diisopropylethylamine (0.25 mmol,44.1µL,5 eq) were added. The reaction was degassed via Ar bubbling (at 0 ^{o}C) for 5-10 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 ^{o}C. The reaction progress was monitored periodically by ^{19}F NMR. Mixture of pentafluoropyridine and *N*,*N*-diisopropylethylamine (1:1 mol:mol) prepared and degassed in a 12 x 75 mm borosilicate test tube fitted with rubber septum. 7 portions of above substrate mixture were added over 96 hour period. A total of 0.275 mmol pentafluoropyridine (**1a**) and 0.475 mmol *N*,*N*-diisopropylethylamine were added. After the each addition, the NMR tube was degassed via Ar bubbling for 5-10 min in an ice bath and the septum was again parafilmed. After 96 hours detectable quantities of byproducts were observed in the ^{19}F NMR. The reaction was quenched by exposing it to air and ^{19}F NMR yield was obtained after adding trifluoroacetic acid (0.15 mmol, 11.5 µL) as internal standard.

The TON was calculated as follows. [0.275 mmol (**1a**)/0.00001 ($Ir(ppy)_3$)]*0.82(yield) =22,550 TON.

Effect of catalyst loading on HDF reaction

Five NMR reactions ranging from .05 mol% to 0.5 mol% catalyst were set up as below. 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) ($Ir(ppy)_3$) (1.0 mL, 0.5 mL, 0.2 mL, 0.1 mL from 0.5 mM catalyst solution in MeCN). Pentafluoropyridine (1 eq, 16.9 mg, 0.1 mmol) and *N*, *N*-diisopropylethylamine **(**3 eq, 19.4 mg, 0.15 mmol) were added and enough MeCN was added to give 1 mL total volume. Reactions were degassed under dark conditions (wrapped with foil) at 0 ^{o}C to avoid evaporation of *N, N*-diisopropylethylamine and volatile starting material via Ar bubbling for 5-10 min. NMR tubes were placed in a light bath and the lower portion of the tube was submerged under the water bath which was maintained at 45 ^{o}C. NMR tubes were taken out from light bath at 30 min, 1 h, 2 h, 3 h, 4 h and 5 h intervals and wrapped with aluminum foil to block the light while taking NMR. ^{19}F NMRs were recorded and conversions (Figure SI-1) and product formation (Figure SI-2) were calculated by integrating NMR signals of reactant and product. The initial rates of the reaction are shown in Figure SI-3 which indicates a positive correlation between catalyst loading and reaction rate.

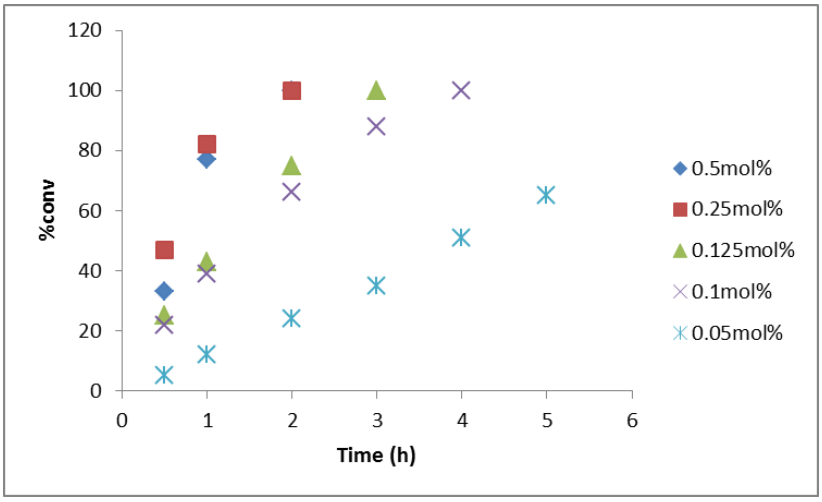


Figure SI-1. Effect of catalyst loading, conversion of pentafluoropyridine

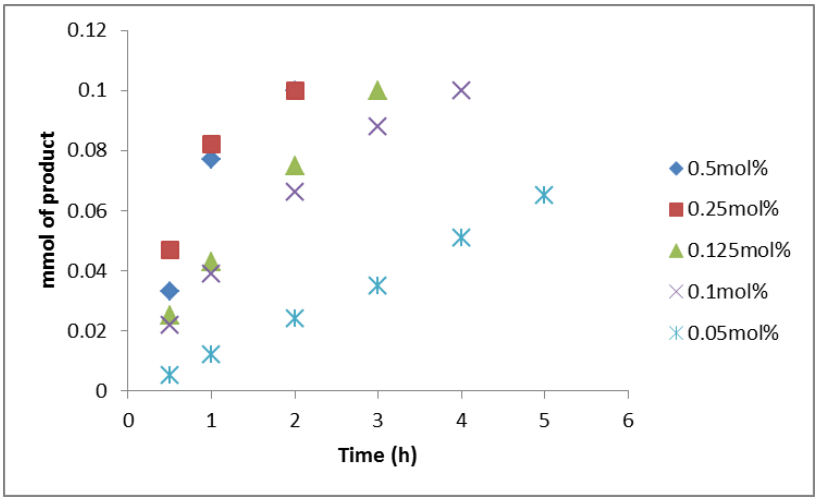


Figure SI-2. Effect of catalyst loading, mmols of tetrafluoropyridine produced

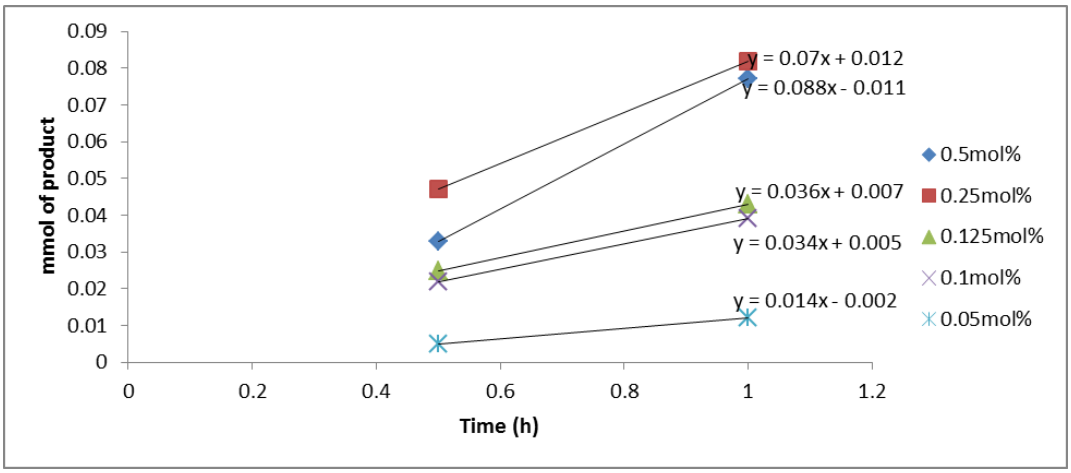


Figure SI-3. Effect of catalyst loading, initial rates of the reaction

Effect of substrate concentration HDF reaction

Five NMR reactions ranging from 0.075 to 0.35 M pentafluoropyridine were set up as below. 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) ($Ir(ppy)_3$) (0.2 mol% catalyst solution in MeCN). Pentafluoropyridine (1 eq, 0.05 mmol to 0.35 mmol) and *N*, *N*-diisopropylethylamine **(**2 eq) were added and enough MeCN was added to give 1 mL total volume. Reactions were degassed under dark conditions (wrapped in foil) at 0 ^{o}C to avoid evaporation of *N*, *N*-diisopropylethylamine and volatile starting material via Ar bubbling for 5-10 min. NMR tubes were placed in a light bath and the lower portion of the tube was submerged under the water bath which was maintained at 45 ^{o}C. NMR tubes were taken out from light bath at 30 min, 1 h, 2 h, 3 h, 4 h, 6 h and 17 h intervals and wrapped with aluminum foil to block the light while taking NMR. ^{19}F NMR spectra were recorded and conversions (Figure SI-4) and rate of product formation (Figure SI-5) were calculated by integrating NMR signals of reactant and product. The initial rates are shown in Figure SI-6. To the first approximation a 5X substrate leads to ~2X rate increase. However, given that the catalyst loading is held constant (~5X increase) and the demonstrated catalyst dependency, it appears that the reaction rate is pseudo-zero order in substrate.

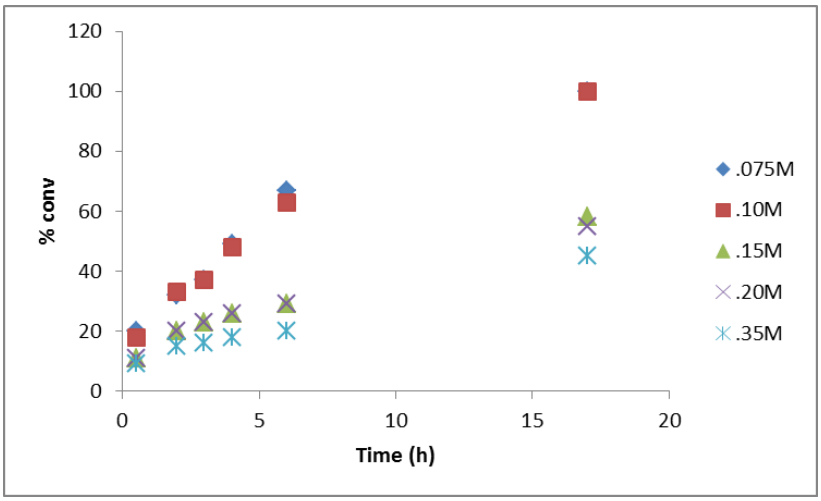


Figure SI-4. Effect of substrate concentration, conversion of pentafluoropyridine to tetrafluoropyridine

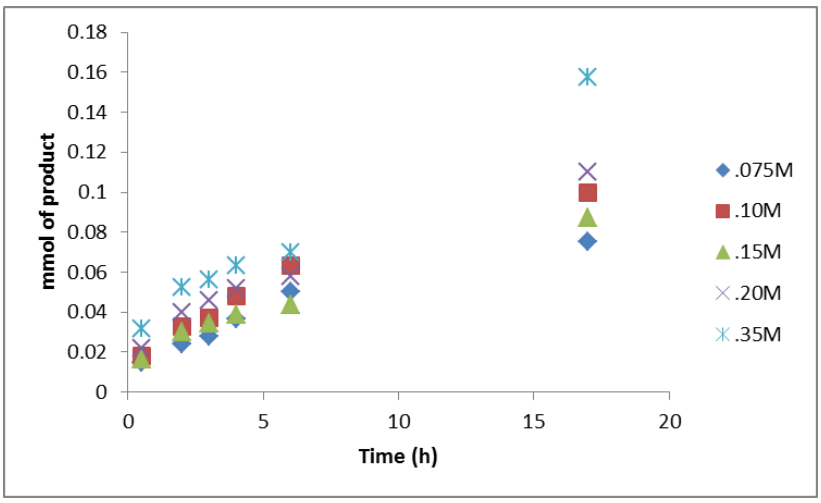


Figure SI-5. Effect of substrate concentration, mmols of tetrafluoropyridine

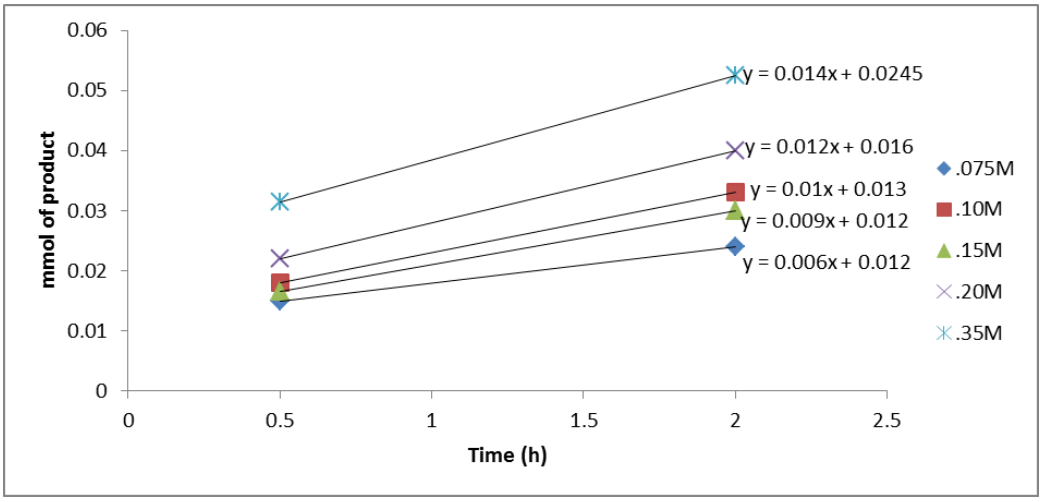


Figure SI-6. Effect of substrate concentration, initial rate of the reaction

Fate of fluoride in HDF 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) ($Ir(ppy)_3$) (0.5 mM, 0.5 mL in MeCN-d_3). Pentafluoropyridine (1 eq, 8.45 mg, 0.05 mmol) and *N*, *N*-diisopropylethylamine **(**3 eq, 19.4 mg, 0.15 mmol) were added and the reaction was degassed at 0 ^oC to avoid evaporation of *N*, *N*-diisopropylethylamine and volatile starting materials via Ar bubbling for 5-10 min. The NMR tube was placed in a light bath and the lower portion of the tube was submerged under the water bath which was maintained at 45 ^oC until complete consumption of pentafluoropyridine. ^{19}F NMR shows a single F^- signal at -123 ppm. Tetrabutylammonium fluoride was used as the external F^- source which gives F^- signal at -112 ppm in MeCN. When the HDF reaction was spiked with tetrabutylammonium fluoride (13.07 mg, 0.05 mmol) the ^{19}F NMR showed a single F^- signal at -125 ppm for the spiked sample (Figure SI-7).

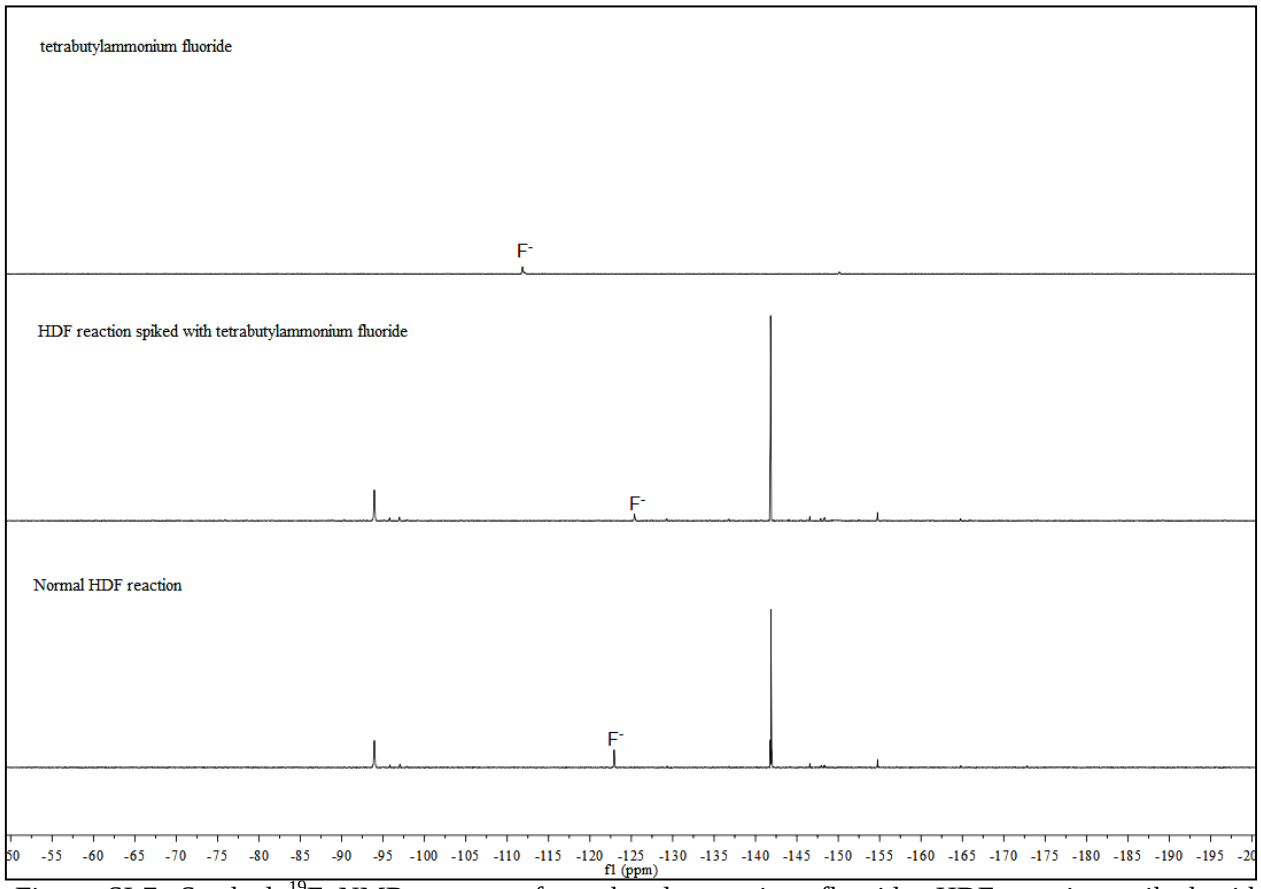
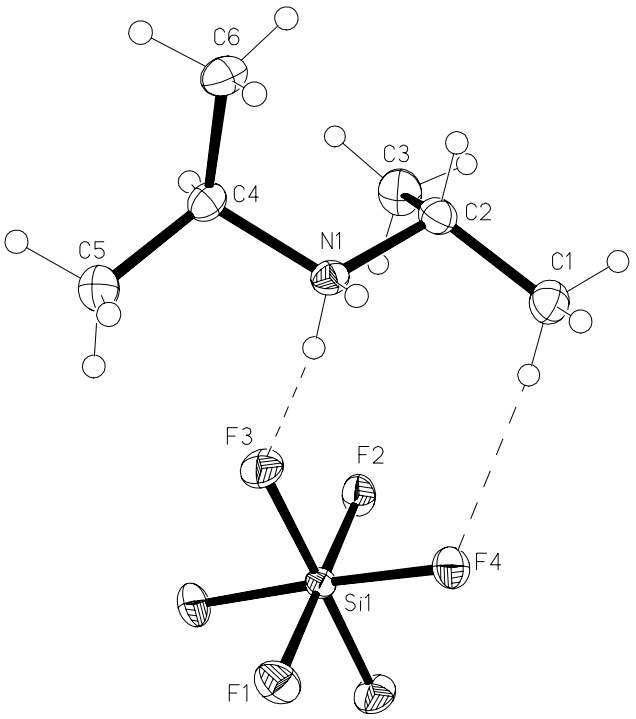


Figure SI-7. Stacked ^{19}F NMR spectra of tetrabutylammonium fluoride, HDF reaction spiked with tetrabutylammonium fluoride and normal HDF reaction in MeCN.

Isolation and characterization of the solid formed during HDF reaction

During the reaction progress a colorless crystalline solid formation was observed in the culture tube (12 x 75 mm borosilicate tube, Fisherbrand, catalog no. 14-961-26). The crystals were isolated by following method. After the completion of reaction with pentafluoropyridine solvent (MeCN) was removed using a degassed needle keeping the reaction under Ar conditions. Crystals were washed several times with dry MeCN to ensure complete removal of catalyst and other reaction components and crystals were dried under high vacuum conditions.

Crystal structure of isolated bis-diisopropyl ammonium hexafluorosilicate salt is shown below and cif file is available.



Empirical formula	$2(C_6 H_{16} N)^+(Si F_6)^-$	
	$C_{12} H_{32} F_6 N_2 Si$	
Formula weight	346.48	
Crystal system	monoclinic	
Space group	*C*2/*c*	
Color of crystal	colorless	
Unit cell dimensions	*a* = 12.3645(5) Å	α = 90°
	b = 11.5922(5) Å	β= 112.0309(7)°
	c = 12.7948(5) Å	γ= 90°
Volume	1699.99(12) $Å^3$	
Z, Z'	4, 0.5	
Density (calculated)	1.354 Mg/m3	
Wavelength	0.71073 Å	
Temperature	100(2) K	
F(000)	744	
Absorption coefficient	0.192 mm^{-1}	
Absorption correction	semi-empirical from equivalents	
Max. and min. transmission	0.974 and 0.912	
Theta range for data collection	2.499 to 28.305°	
Reflections collected	15531	
Independent reflections	2126 [R(int) = 0.0237]	
Data / restraints / parameters	2126 / 0 / 161	
wR(F^2 all data)	*wR*2 = 0.0879	
R(*F* obsd data)	*R*1 = 0.0304	
Goodness-of-fit on F^2	1.008	
Observed data [I > 2(I)]	1939	
Largest and mean shift / s.u.	0.001and 0.000	
Largest diff. peak and hole	0.378 and -0.183 e/$Å^3$	

Deuterium labelling experiment

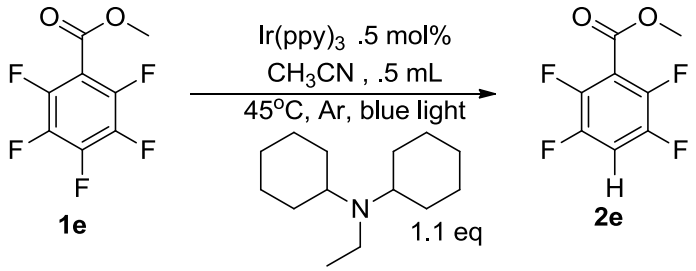
To determine the source of the H-atom 3 separate NMR tube reactions were performed. First, the HDF-reaction was performed with methyl-2,3,4,5,6-pentafluorobenzoate (**1e**) and Hünig's base in MeCN-d_3. Next, the HDF reaction was performed using *N, N* -dicyclohexyl-*N*-ethylamine and finally using *N, N* -dicyclohexyl-*N*-d_5-ethylamine.

No deuterium in corporation from the solvent occurred. The HDF-reaction proceeds as normal using the alternative and easily isolable amine *N, N* -dicyclohexyl-*N*-ethylamine giving HDF product **2e**. This result suggests that a deuterium labeling study should be informative. When the reaction is performed using an analogous deuterium labeled amine, deuterium was incorporated. This result confirms the amine as the source of the H/D-atom but also reveals that all α-C-H's can be transferred.

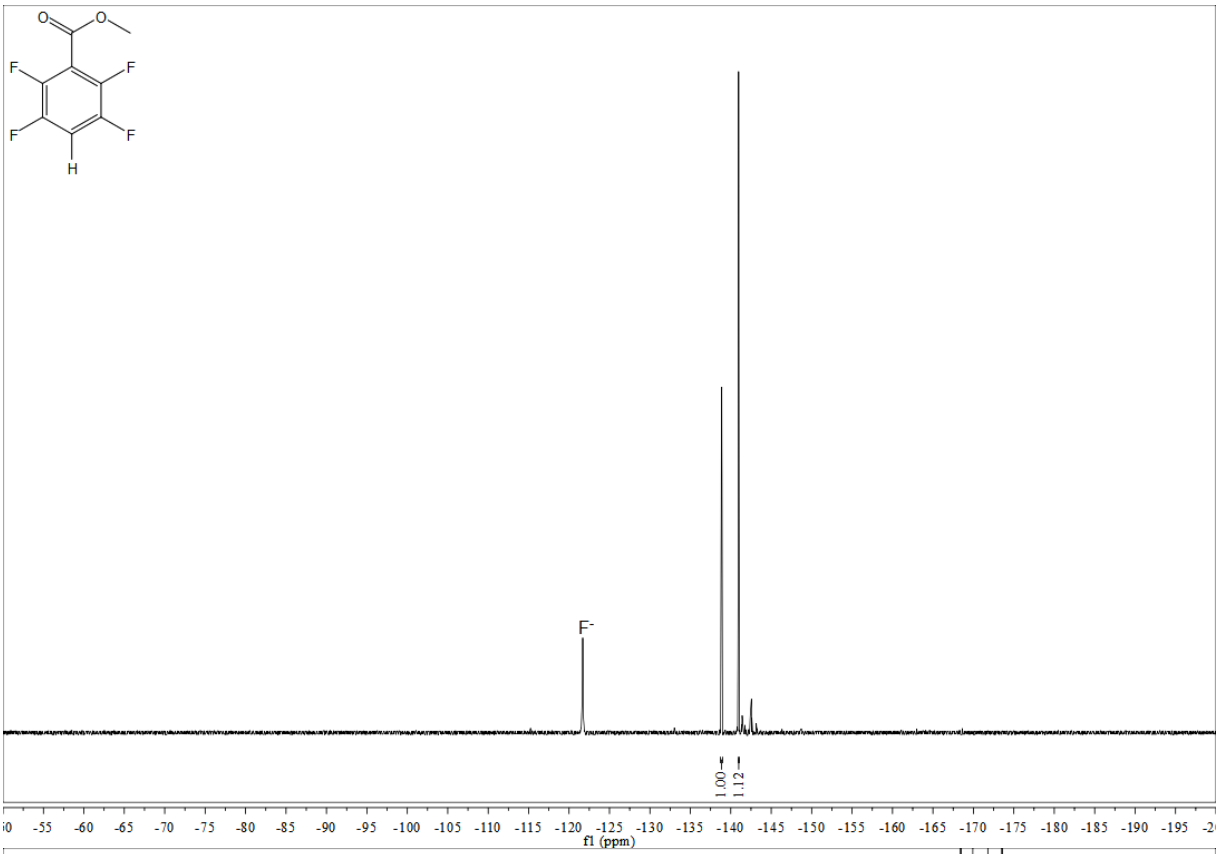
General procedure for deuterium labelling experiment

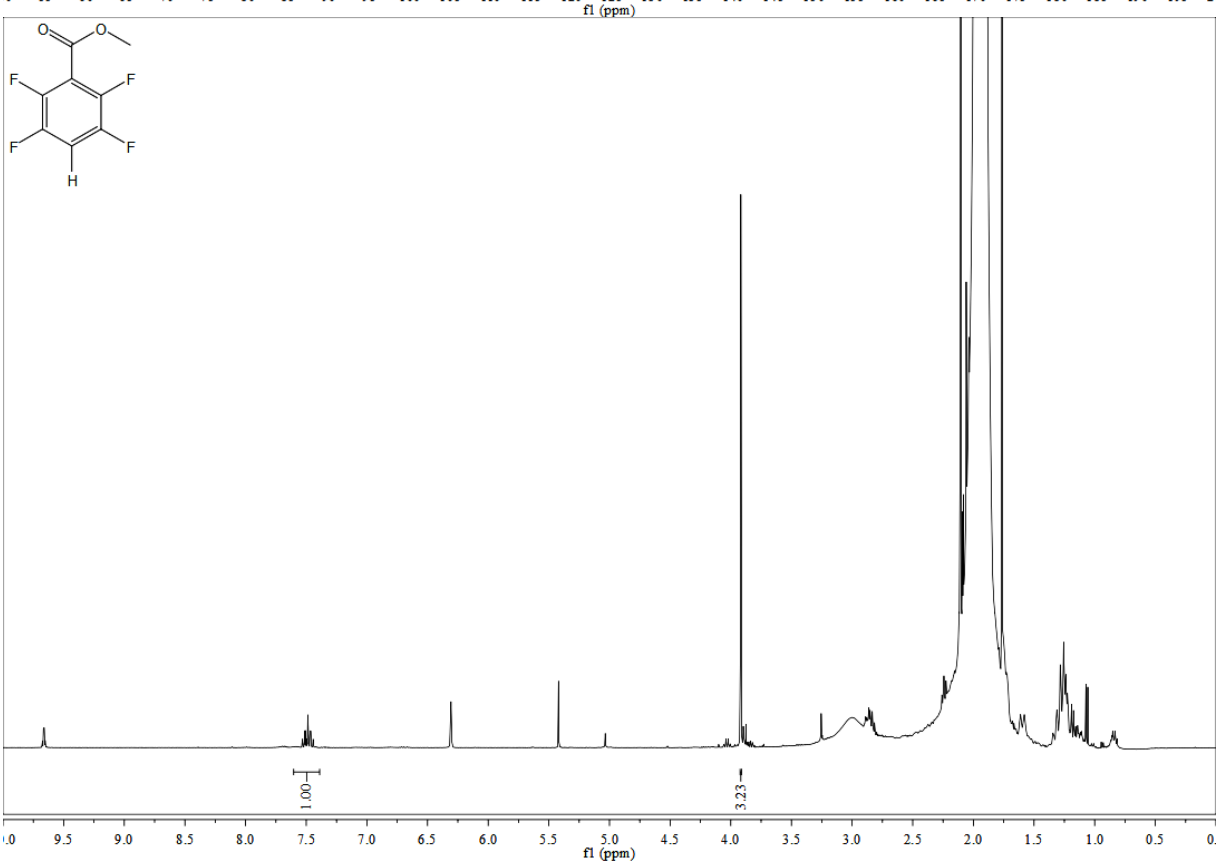
In an NMR tube capped with NMR septa (Ace glass, part no. 9096-25) was charged *tris*(2- phenyl pyridinato-C^2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.5 mM, 0.5 mL in MeCN). Methyl 2,3,4,5,6-pentafluorobenzoate (1 eq, 11.3 mg, 0.05 mmol) and amine (1.1 eq, 11.5 mg, 0.055 mmol) were added and sealed glass capillary containing C_6D_6 was placed in NMR tube for locking purposes before degassing. Then the reaction was degassed at 0 ^oC via 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 ^oC. ^{19}F NMR and GC-MS were recorded after 7 hours.

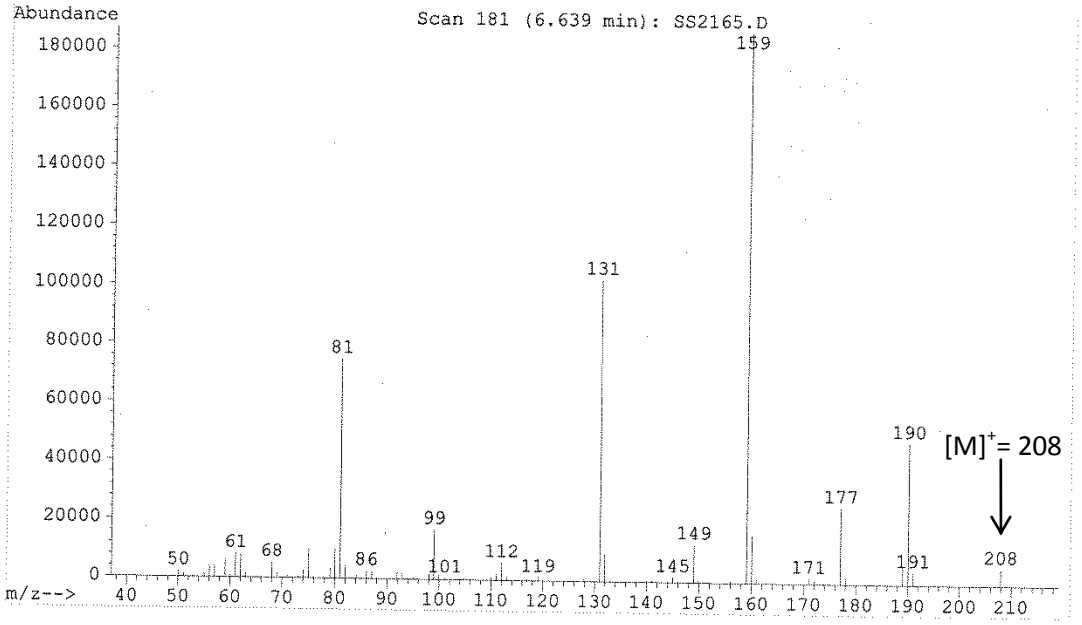
Reaction with *N, N* -dicyclohexyl-*N*-ethylamine



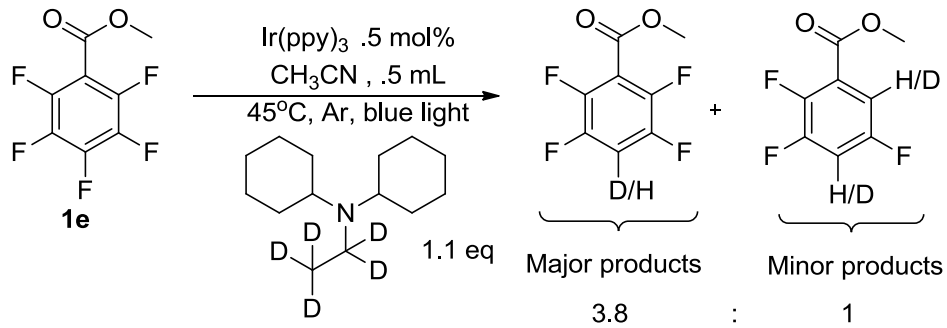
When *N, N* -dicyclohexyl-*N*-ethylamine was used as the amine and methyl-2,3,5,6-tetrafluorobenzoate (**2e**) was detected as the major product by ^{19}F NMR, ^1H NMR and GC-MS, consistent with the normal HDF reaction.


F
F
F
F
H
O
O
F-
1.00
1.12
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195
f1 (ppm)

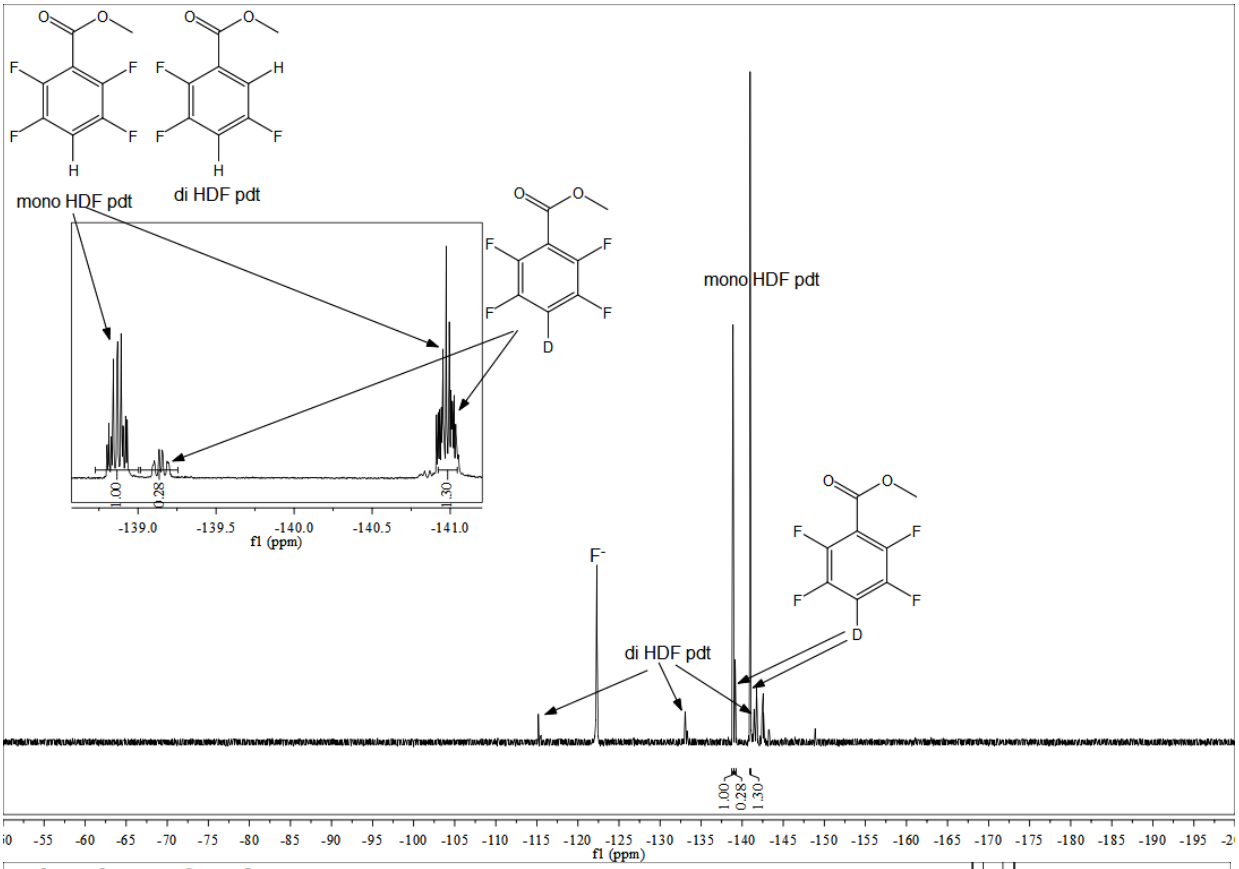

F
F
F
F
H
O
O
1.00
3.23
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



Reaction with *N, N* -dicyclohexyl-*N*-d_5-ethylamine



When *N, N* -dicyclohexyl-*N*-d_5-ethylamine and methyl-2,3,5,6-tetrafluorobenzoate (**1e**) were used, methyl-2,3,5,6-tetrafluorobenzoate (H/D-**2e**) in a 2.1/1 H/D ratio were detected as the major products along with di-HDF products (H/D-**3e**) by ^{19}F NMR, ^{1}H NMR and GC-MS.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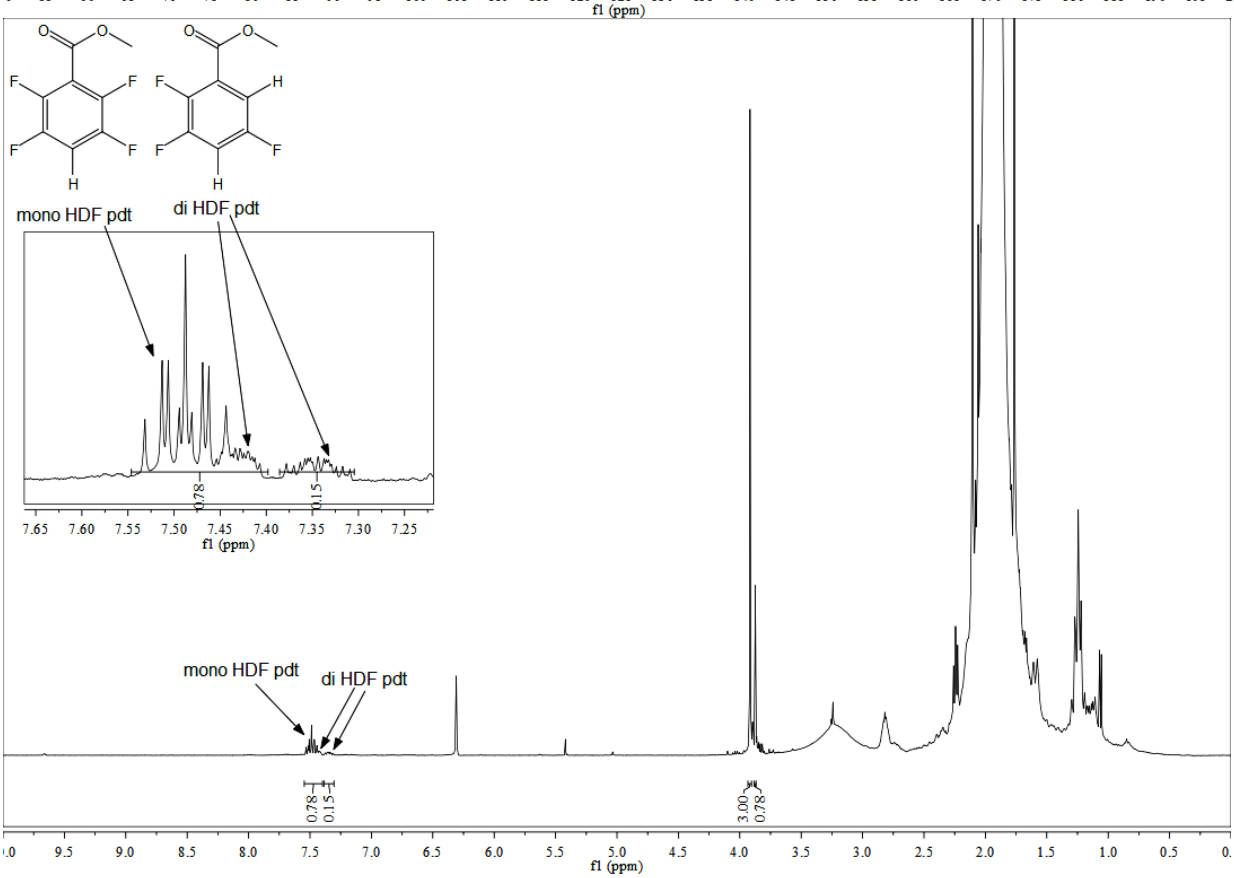
di HDF pdt
mono HDF pdt
F-
di HDF pdt
1.00
0.28
1.30
f1 (ppm)


mono HDF pdt
di HDF pdt
0.78
0.15
f1 (ppm)
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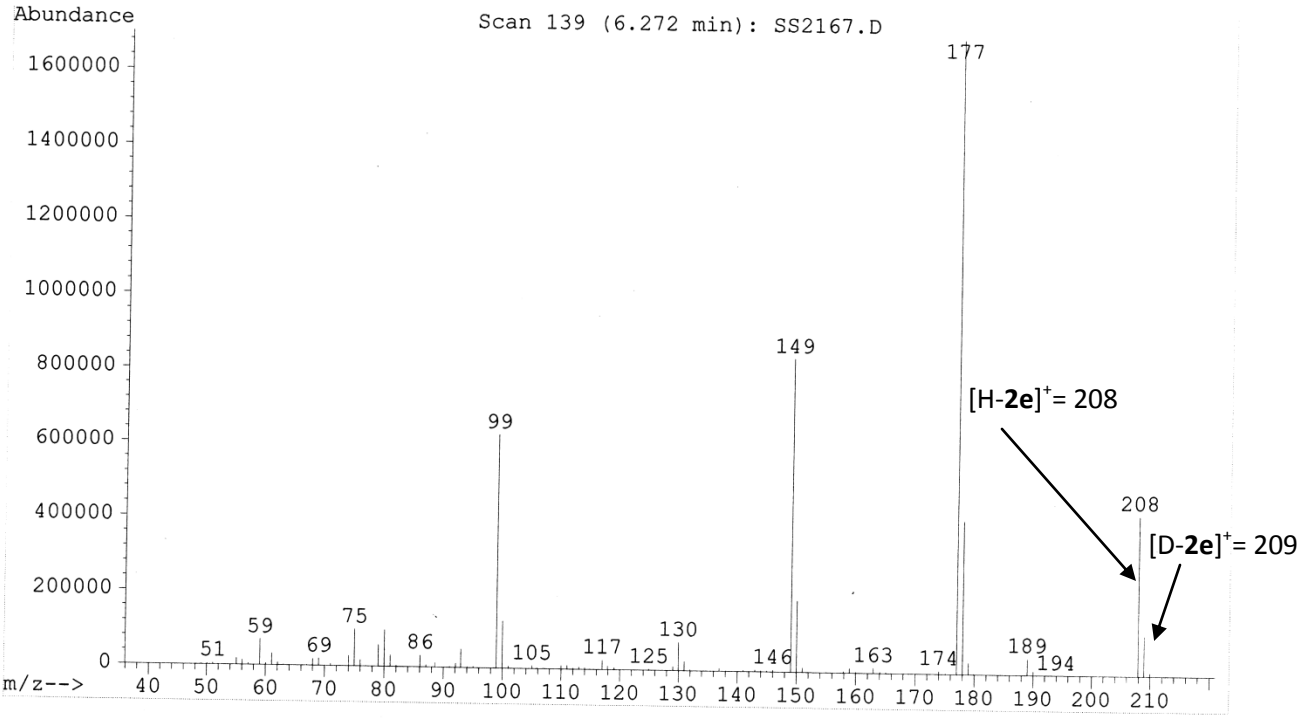
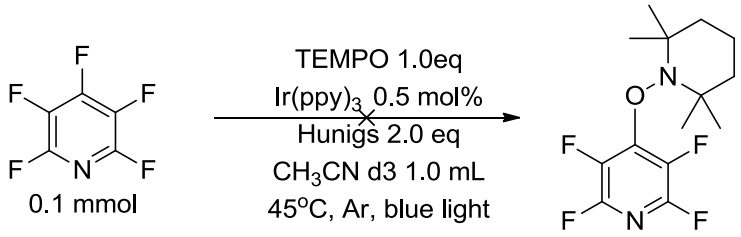
0.78
0.15
3.00
0.78
f1 (ppm)



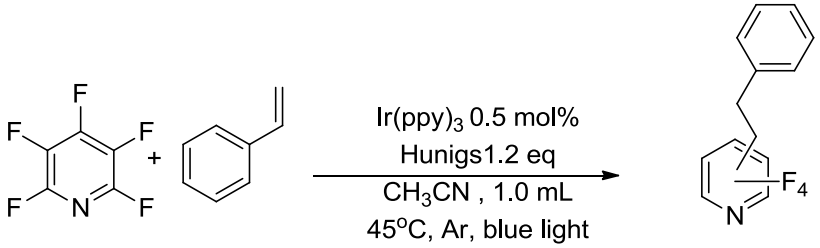
Radical trapping experiment

Reaction of pentafluoropyridine with TEMPO

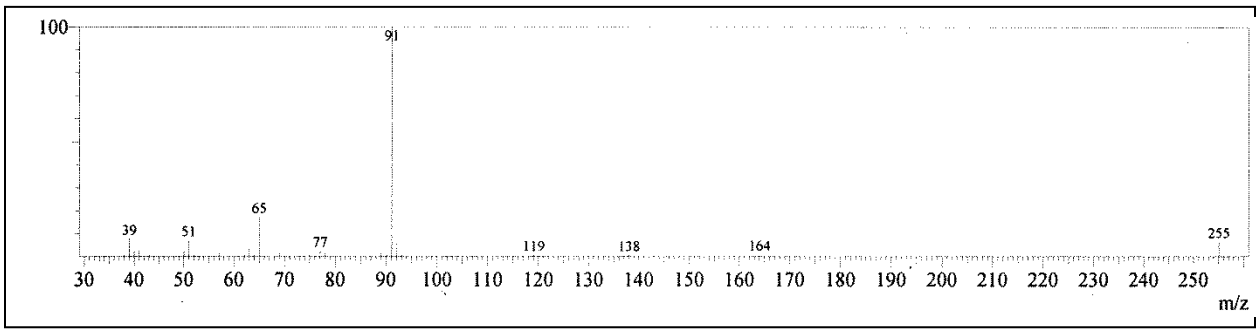


In an NMR tube capped with NMR septa (Ace glass, part no. 9096-25) was charged *tris*-(2- phenyl pyridinato-C^2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.5 mM, 1.0 mL in MeCN d_3). Pentafluoropyridine (1 eq, 16.9 mg, 0.1 mmol) and *N*, *N*-diisopropylethylamine (2.0 eq, 25.8 mg, 0.2 mmol) were added. Then the reaction was degassed at 0 ^oC to avoid evaporation of *N*, *N*-diisopropylethylamine and volatile starting materials via 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 ^oC. ^{19}F NMR was recorded after 6 hours. No reaction was observed. These results suggest that the TEMPO prevents electron transfer to the perfluoroarene which prevents fragmentation.

Reaction of pentafluoropyridine with styrene



A 12 x 75 mm borosilicate test tube fitted with rubber septum was charged *tris*(2- phenyl pyridinato-C^2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.5 mM, 1 mL in MeCN). Pentafluoropyridine (1 eq, 16.9 mg, 0.1 mmol), styrene (10.0 eq, 104.0 mg, 1.0 mmol) and *N, N*-diisopropylethylamine **(**1.2 eq, 16 mg, 0.12 mmol) were added and the reaction was degassed at 0 ^oC to avoid evaporation of *N, N*-diisopropylethylamine and volatile starting materials via Ar bubbling for 5-10 min and then left under positive Ar pressure by removing the exit 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 45 ^oC. After 20 hours reaction was quenched and GC-MS was recorded. Desired product (molecular ion at 255) was detected by GC-MS.



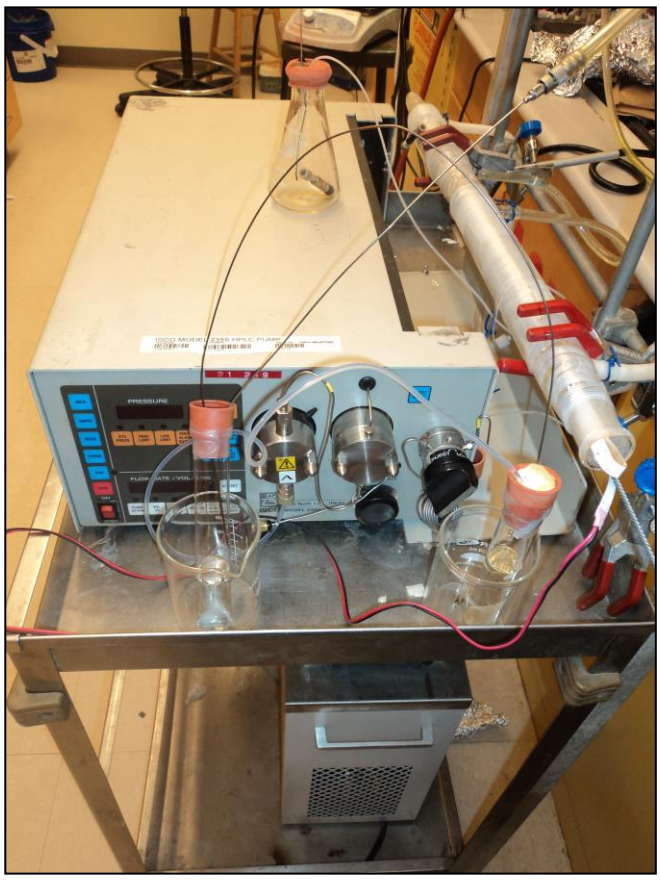
HDF in flow reactor

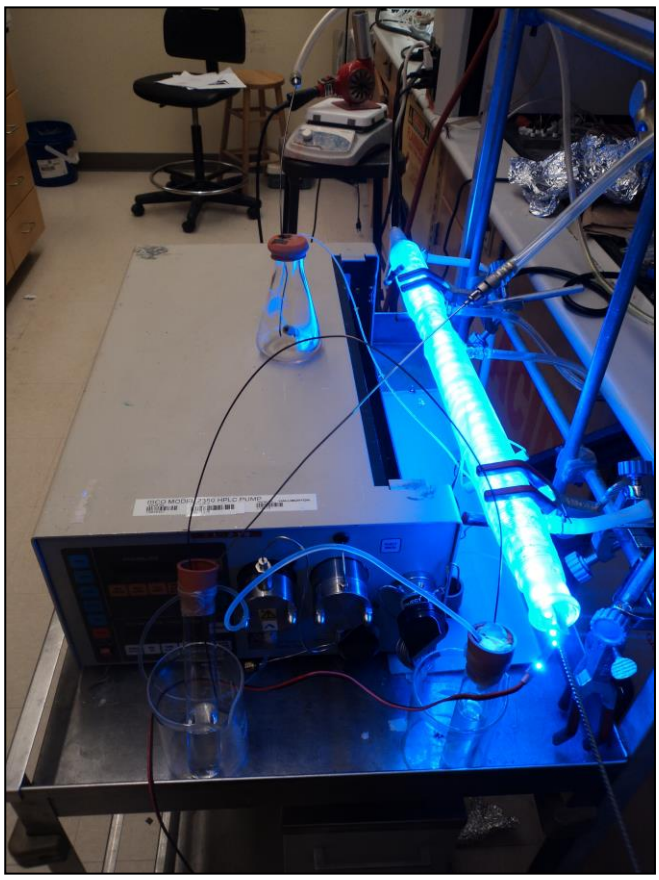
Pentafluoropyridine (1a) as the substrate

A flow reactor was fabricated in following way. A reflux condenser was wrapped with polyalkoxyteflon tubing (ID= 1.58 mm, 22.5 ft, 13.6 mL). Blue LED strips facing outwards were placed within the condenser. Heated mixture of water (45 ^oC) and ethylene glycol (colorless) was passed through the system to maintain a constant temperature. One end of polyalkoxyteflon tubing was connected to the HPLC pump and other end was directed to an empty collection flask. The reaction flask was joined to the inlet of HPLC pump. Before the reaction commencment the reaction tube and collection tube were flushed with Ar (15 min) and the tubing was flushed with degassed MeCN (50 mL). The reaction mixture of pentafluorpyridine (3 mmol, 0.33 mL, 1eq), *tris*(2- phenyl pyridinato-C^2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.0068 mmol, 5.4 mg) and *N,N*-diisopropylethylamine (12 mmol, 2.0 mL, 4 eq) in MeCN (30 mL) was degassed in a 25 x 150 borosilicate glass tube capped with rubber septum via Ar bubbling for 30 min in an ice bath. The reaction mixture was transferred to the reaction tube (25 x 150 borosilicate glass tube capped with rubber septum) stated above via a canula and reaction was again degassed for 15 min in an ice bath. Reaction mixture was pumped at 0.01 mL/min through 22.5 ft (total reactor volume= 13.6 mL, residence time 9 hours). Throughout the reaction, both reaction and collection tubes were kept under positive Ar pressure (bubbler). The residence time was 9 hours. After collecting the reaction mixture ^{19}F NMR showed 100% conversion and 82% yield after adding TFA (1.5 mmol, 114 µL).

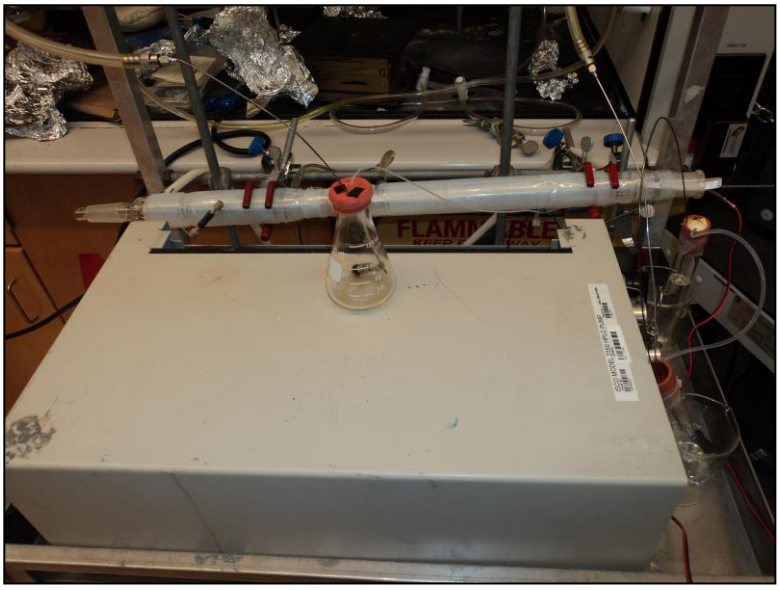
Octafluornapthelene (1c) as the substrate

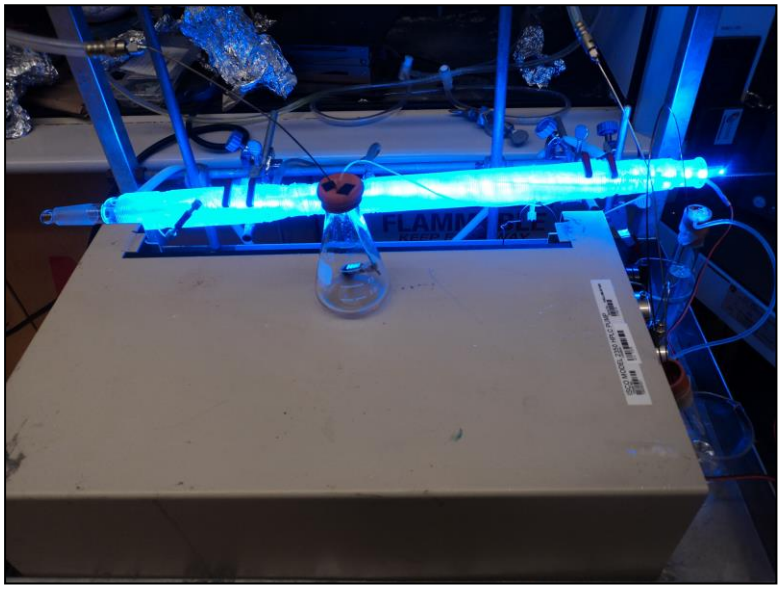
Reaction was carried out in the same way as above with some modifications. Two reflux condensers (in tandem) were wrapped with PFA perfluoroalkoxy tubing (IDEX Health and Science, ID= 0.76 mm, 200 ft, 28 mL) was wrapped tightly around connected condensers. Blue LED strips facing outwards were placed within the condenser. Heated mixture of water (65 ^{o}C) and ethylene glycol (colorless) was passed through the system along that flow to maintain a constant temperature. One end of polyalkoxyteflon tubing was connected to the HPLC pump and other end was directed to an empty collection flask. A standard union was placed on the collection end and a screw-plug was used to regulate the back pressure. This was found necessary to prevent the solvent from vaporizing within the tubing and causing irregularities in the retention time. The reaction flask was joined to the inlet of HPLC pump. Before reaction starts reaction tube and collection tube were flushed with Ar (15 min) and the tubing was flushed with degassed MeCN (50 mL). The reaction mixture of octafluoronapthalene (0.2 mmol, 54 mg, 1eq), *tris*(2- phenyl pyridinato-C^2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.001 mmol, 0.6 mg) and *N*,*N*-diisopropylethylamine (12 mmol, 2.0 mL, 4 eq) in MeCN (2.0 mL) was degassed in a 25 x 150 Borosilicate glass tube capped with rubber septum via Ar bubbling for 30 min in an ice bath. Reaction mixture was transferred to the reaction tube (25 x 150 borosilicate glass tube capped with rubber septum) as stated above via a canula and reaction was degassed again for 15 min in an ice bath. Reaction mixture was pumped at 0.01 mL/min. Throughout the reaction, both reaction and collection tubes were kept under positive Ar pressure (bubbler). The residence time was 20 hours. After collecting the reaction mixture ^{19}F NMR showed 53% conversion and 51% yield after adding TFA (0.1 mmol, 7.6 µL).





Front view of flow reactor





Lateral view of flow reactor

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2) Brown, Alan Daniel; Rawson, David James; Storer, Robert Ian; Swain, Nigel Alan Assignee: Pfizer Limited, UK.,Preparation of sulfonamide derivatives as Nav1.7 inhibitors , PCT Int. Appl., 2012007869
3) *Chem. Commun*., **2012**,48, 8553–8555
4) *Mag. Res . Chem*. **2004**, 42, 624-635
5) *J. Heterocycl. Chem*., **2001**, 38, 131-136,
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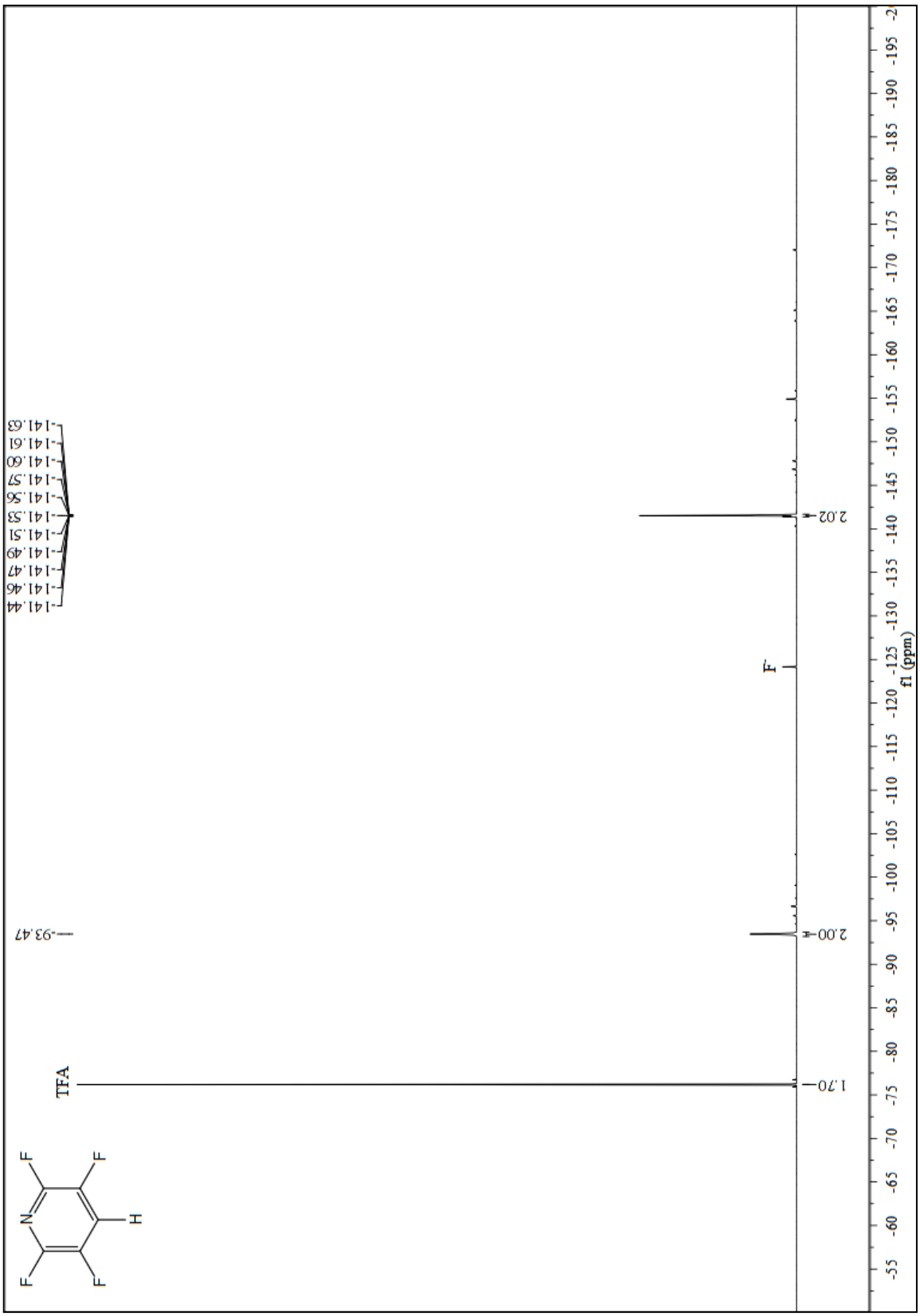
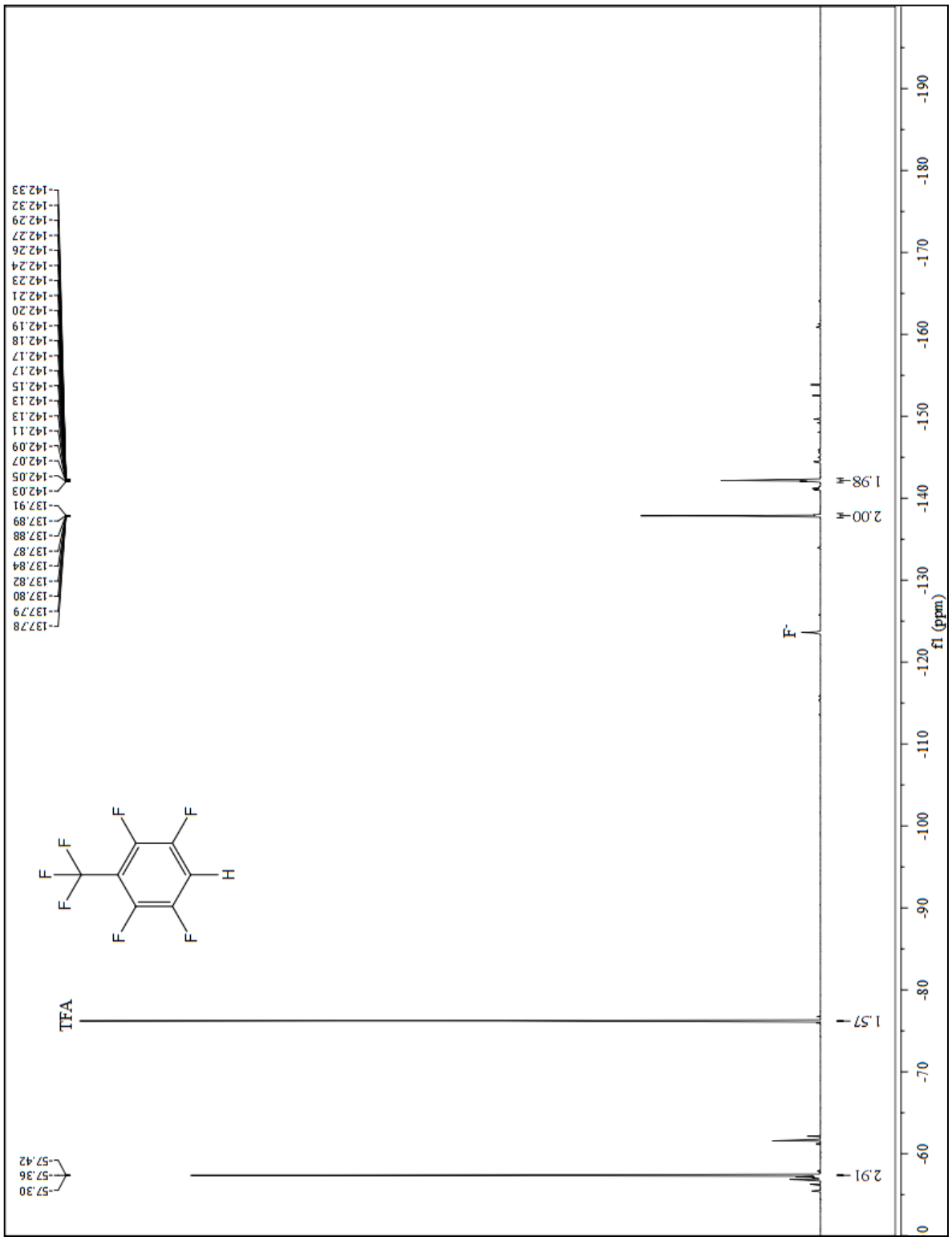
20) *Angew.Chem.Int.Ed*., **2013**, 52, 3203 –3207
21) *J. Fluorine Chem*., **1982**, 21 ,171-189

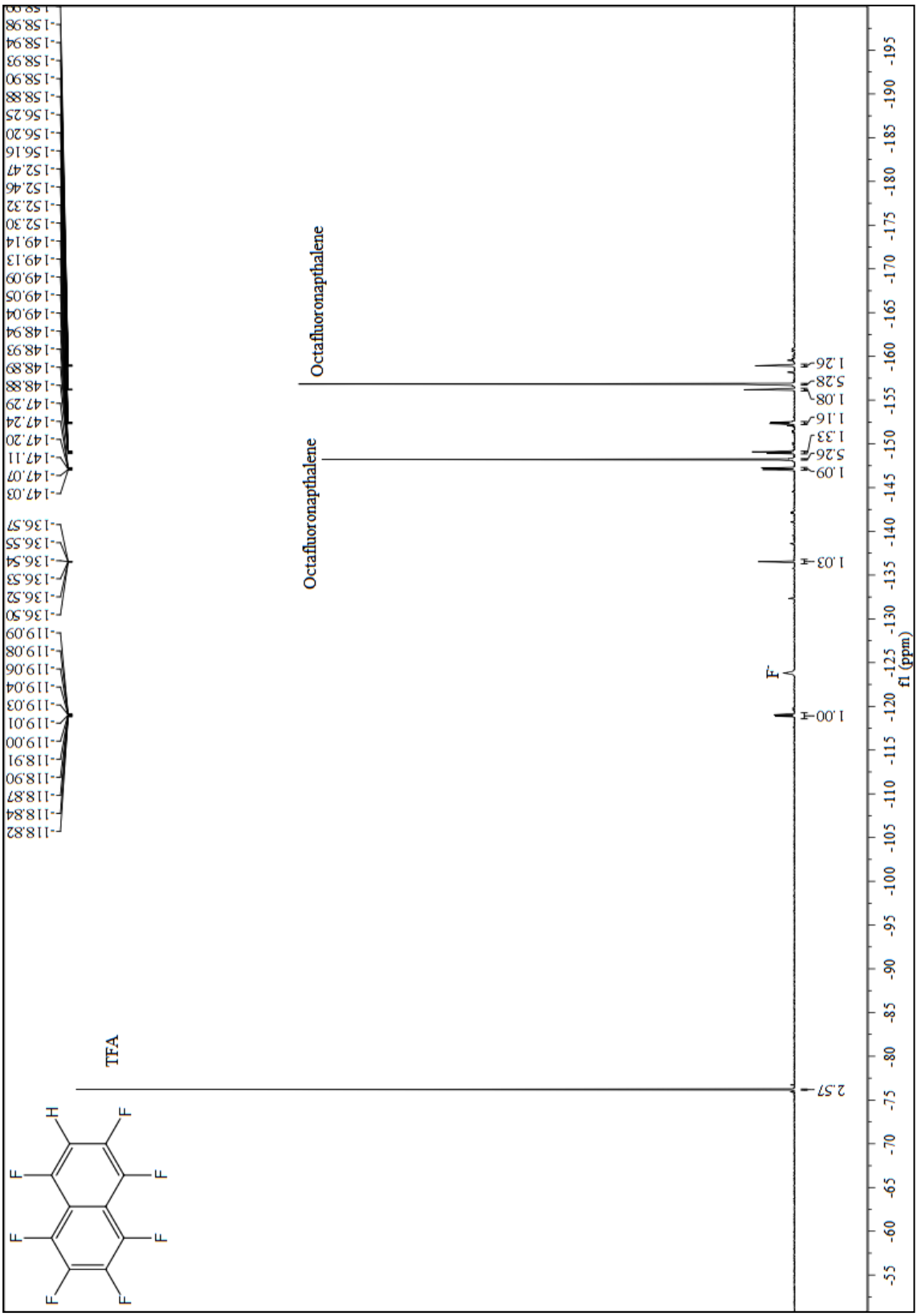
2a (2,3,5,6-tetrafluoropyridine)



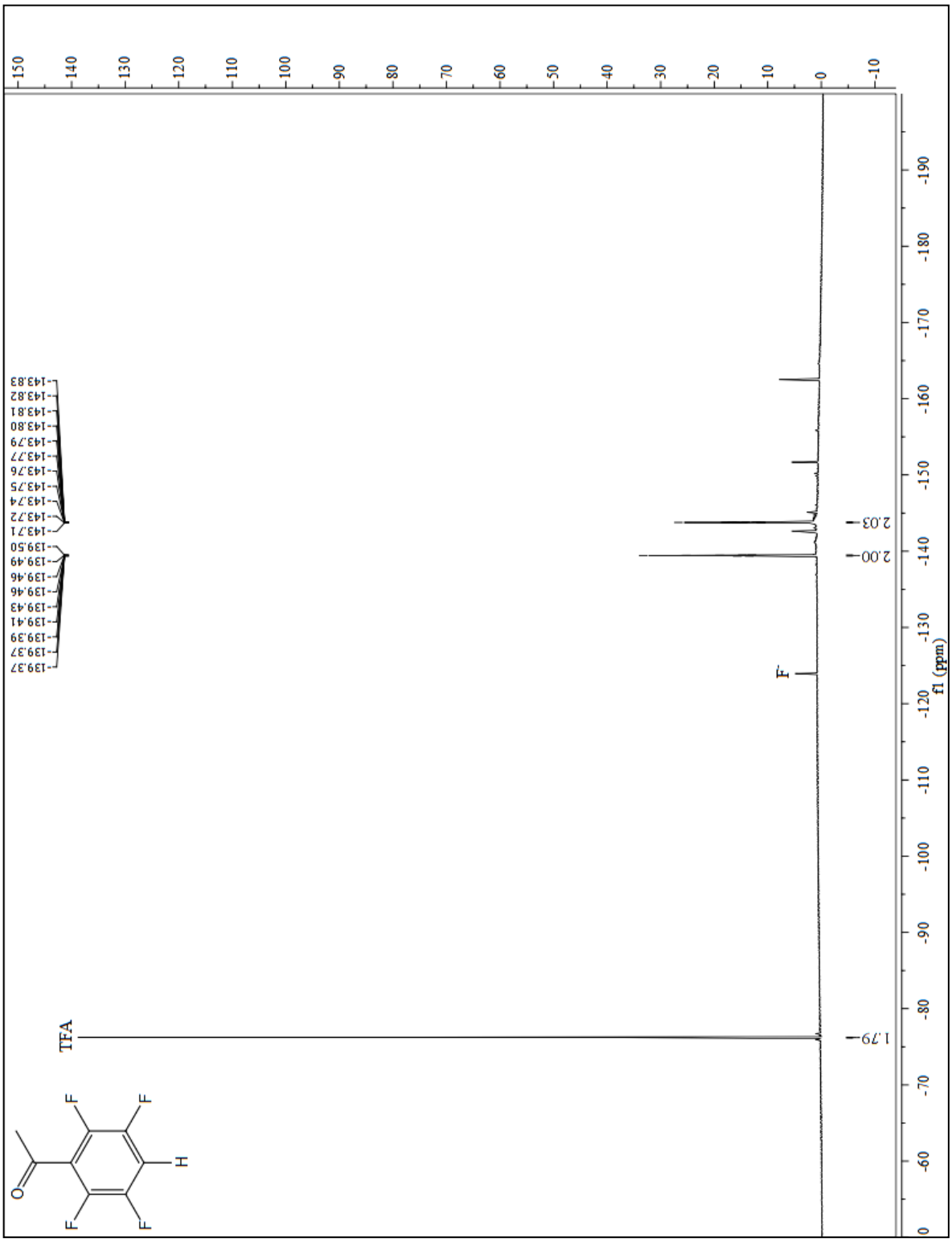
2b (1,2,4,5-tetrafluoro-3-(trifluoromethyl)benzene)



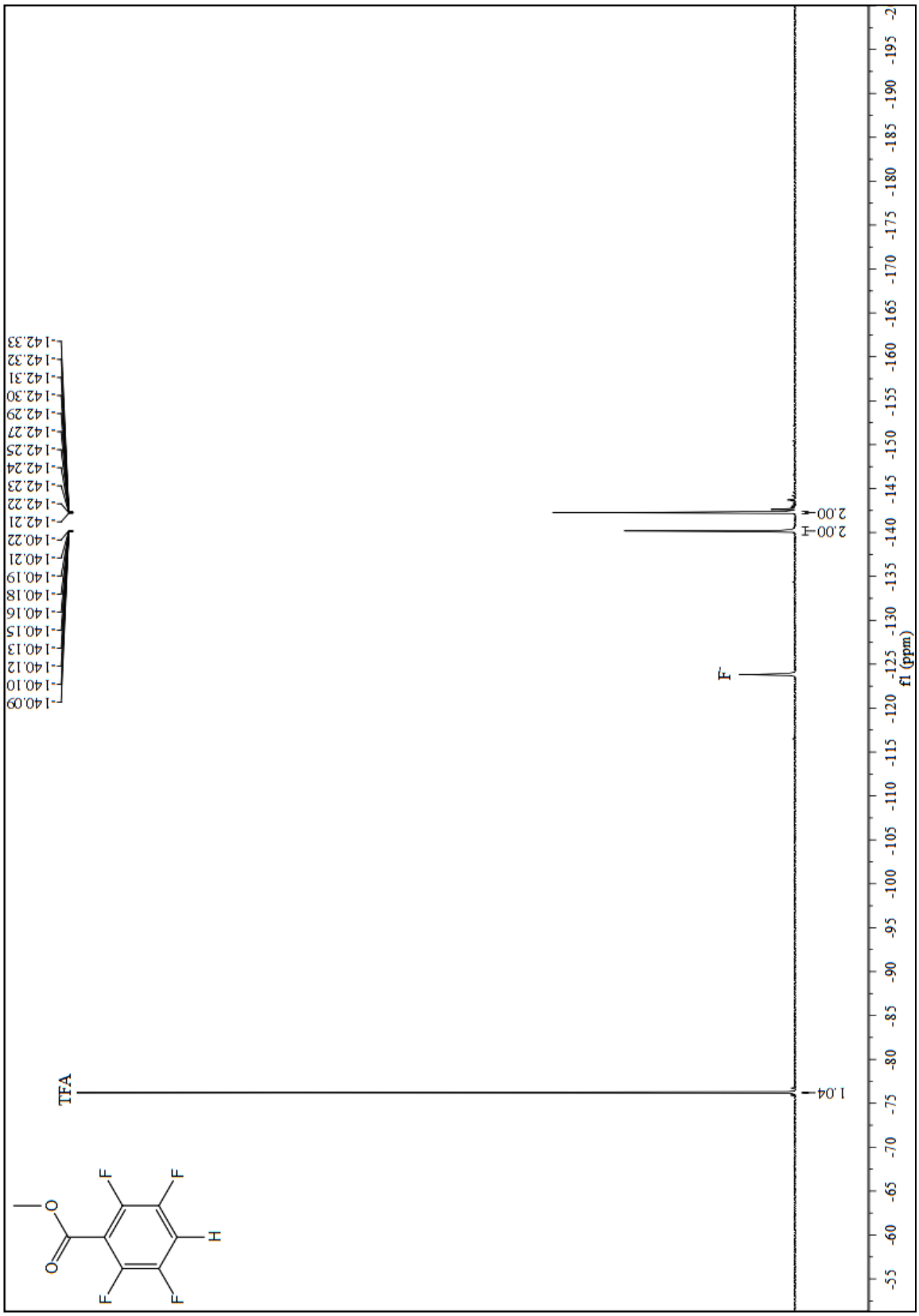
2c (1,2,3,4,5,6,8-heptafluoronaphthalene)



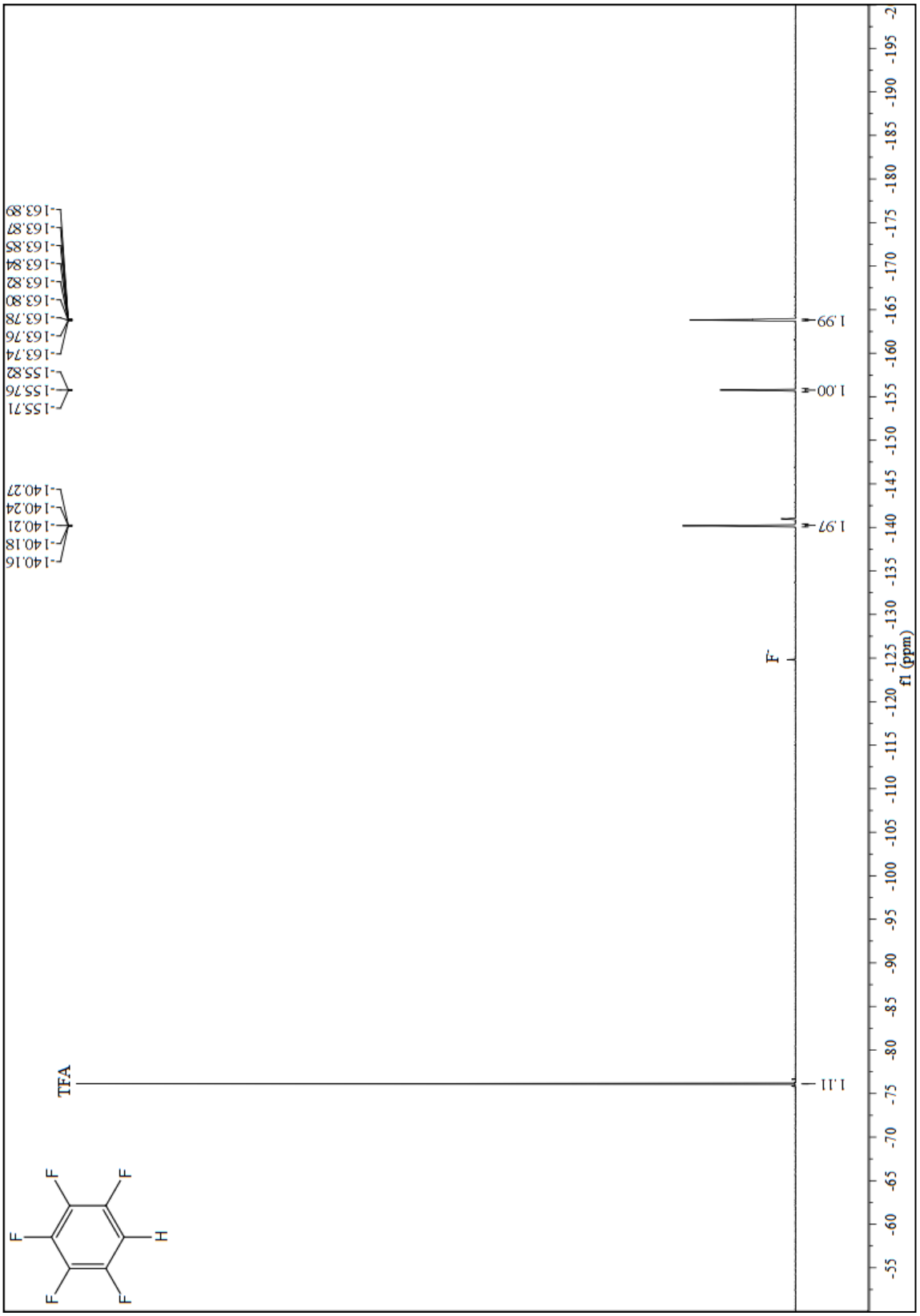
2d (1-(2,3,5,6-tetrafluorophenyl)ethan-1-one)



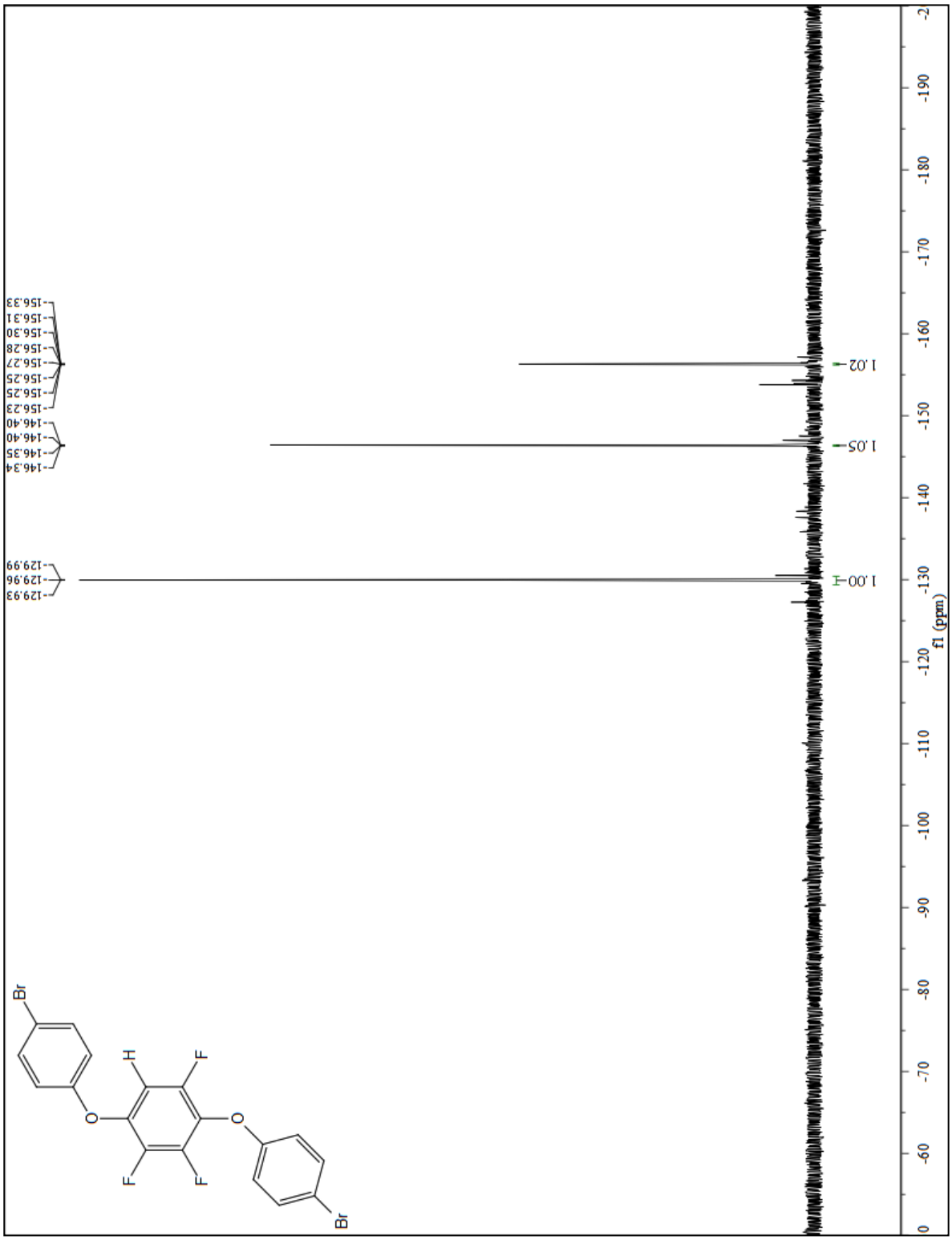
2e (methyl 2,3,5,6-tetrafluorobenzoate)



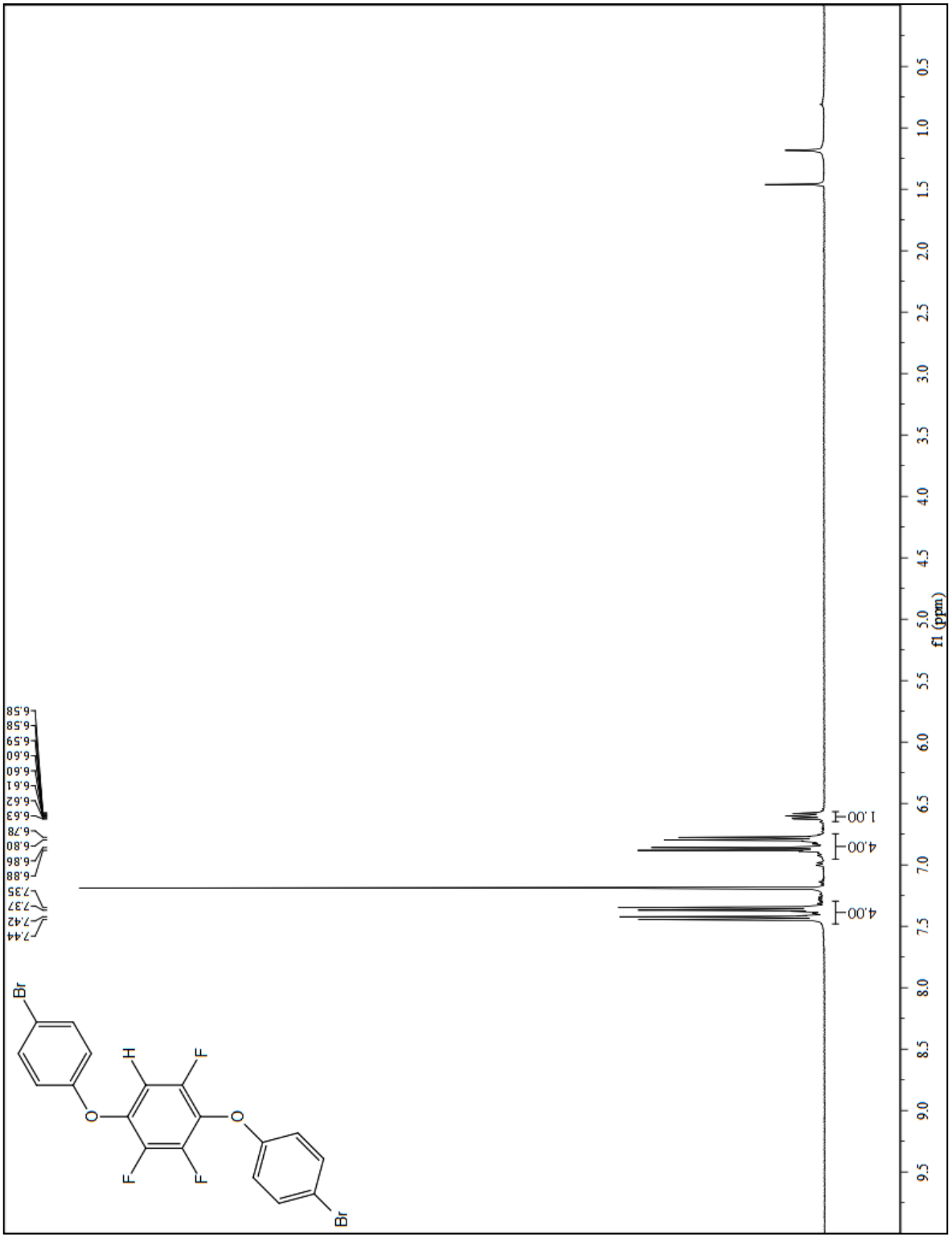
2f (1,2,3,4,5-pentafluorobenzene)



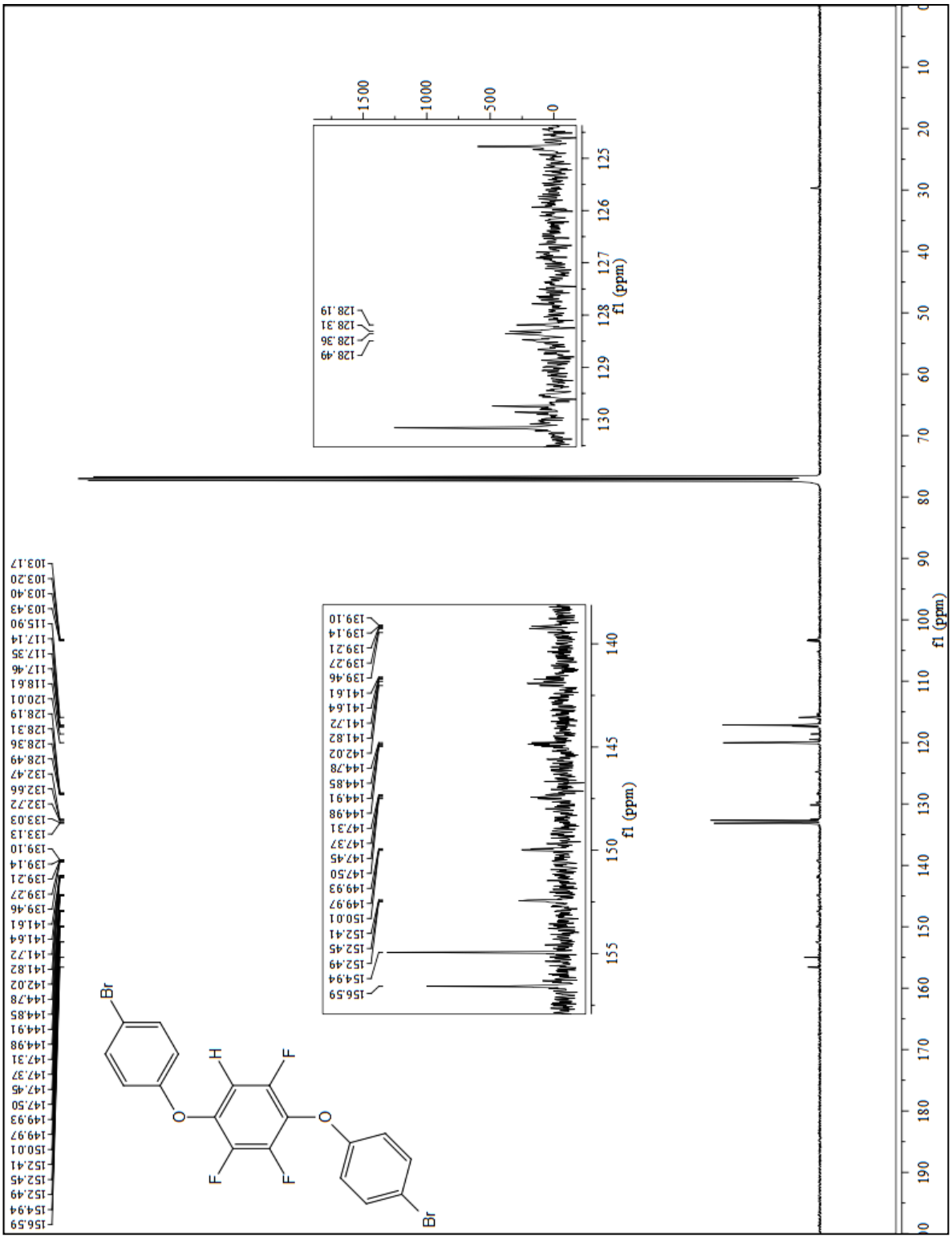
2g (4,4'-((2,3,5-trifluoro-1,4-phenylene)bis(oxy))bis(bromobenzene))



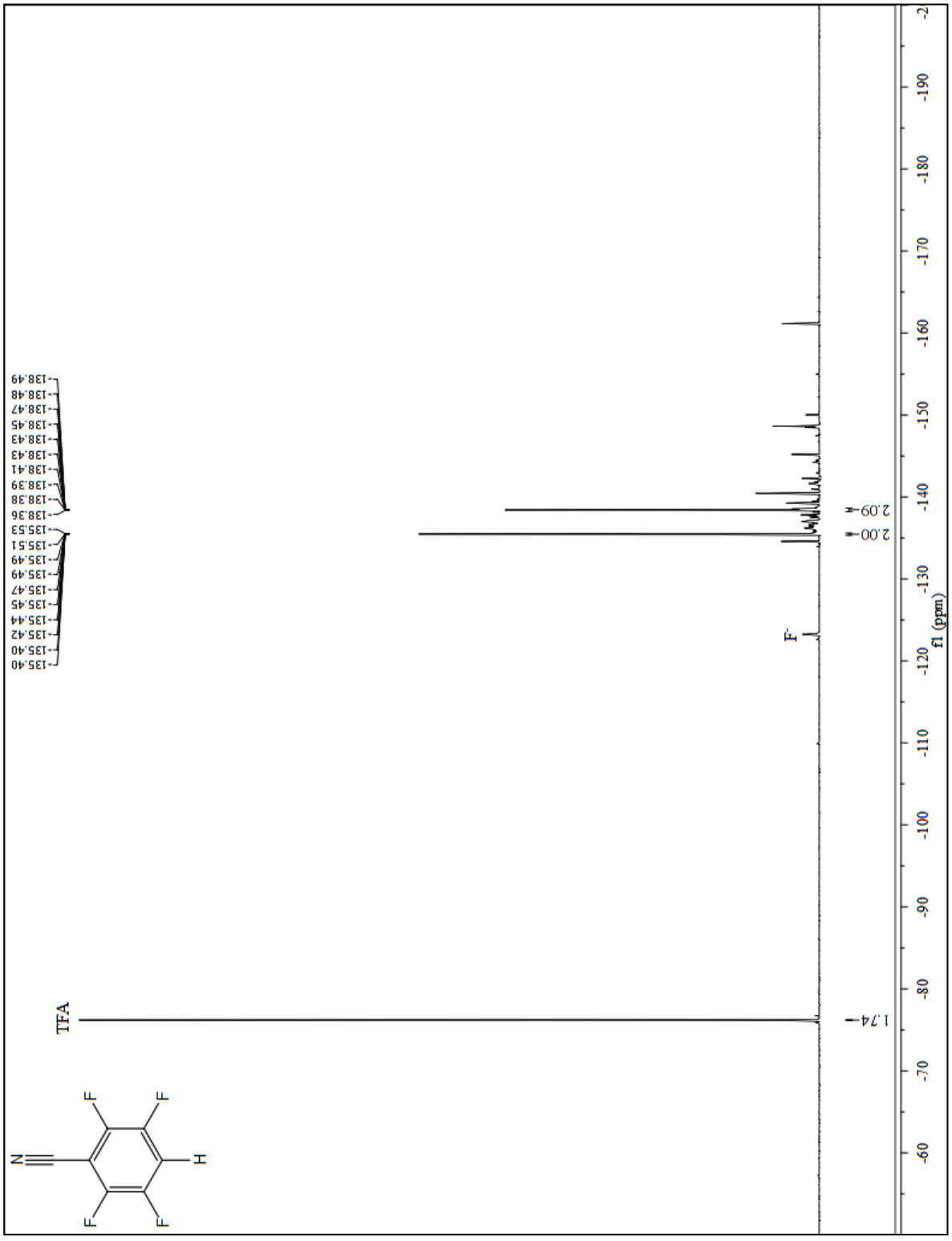
2g (4,4'-((2,3,5-trifluoro-1,4-phenylene)bis(oxy))bis(bromobenzene))



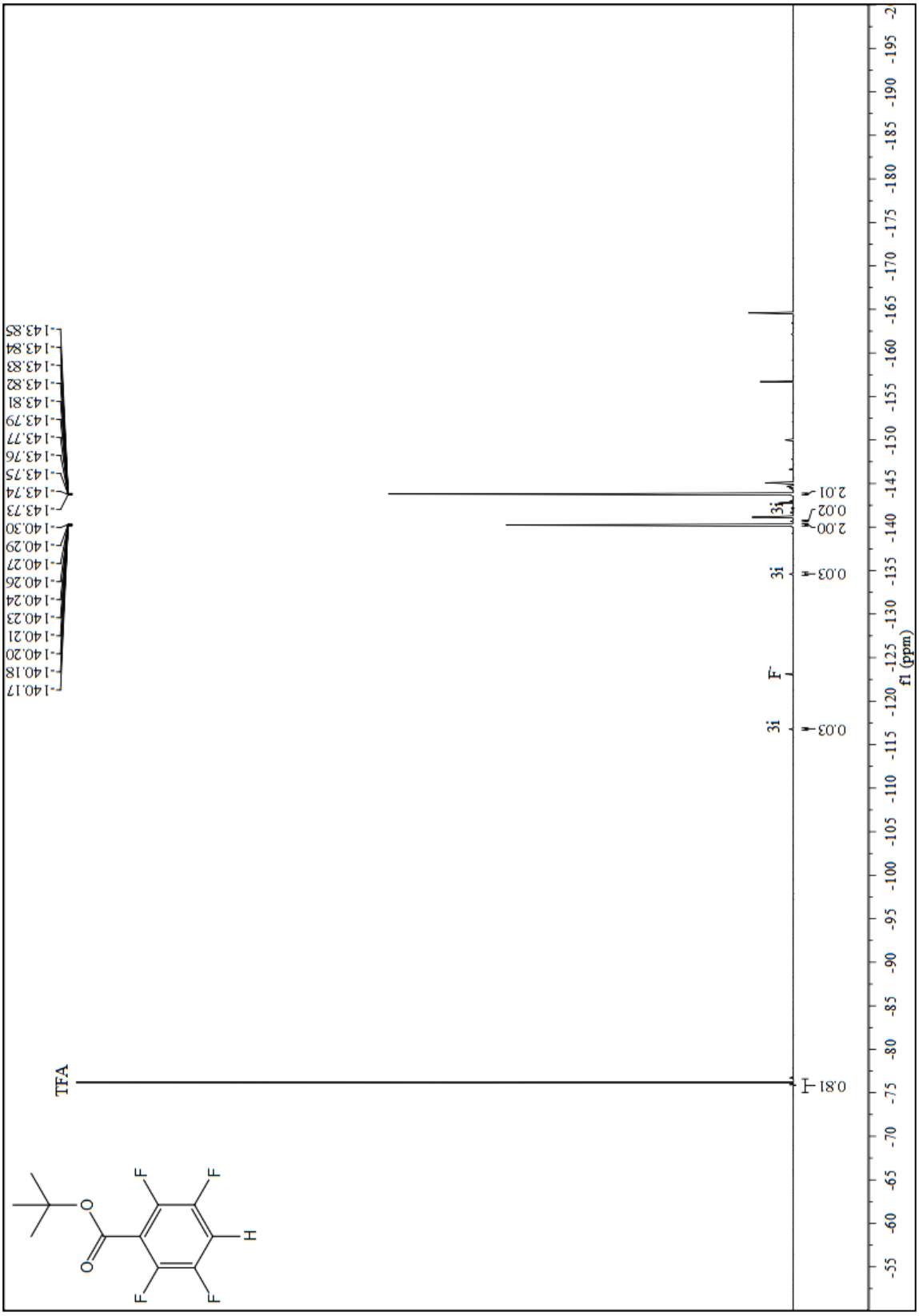
2g (4,4'-((2,3,5-trifluoro-1,4-phenylene)bis(oxy))bis(bromobenzene))



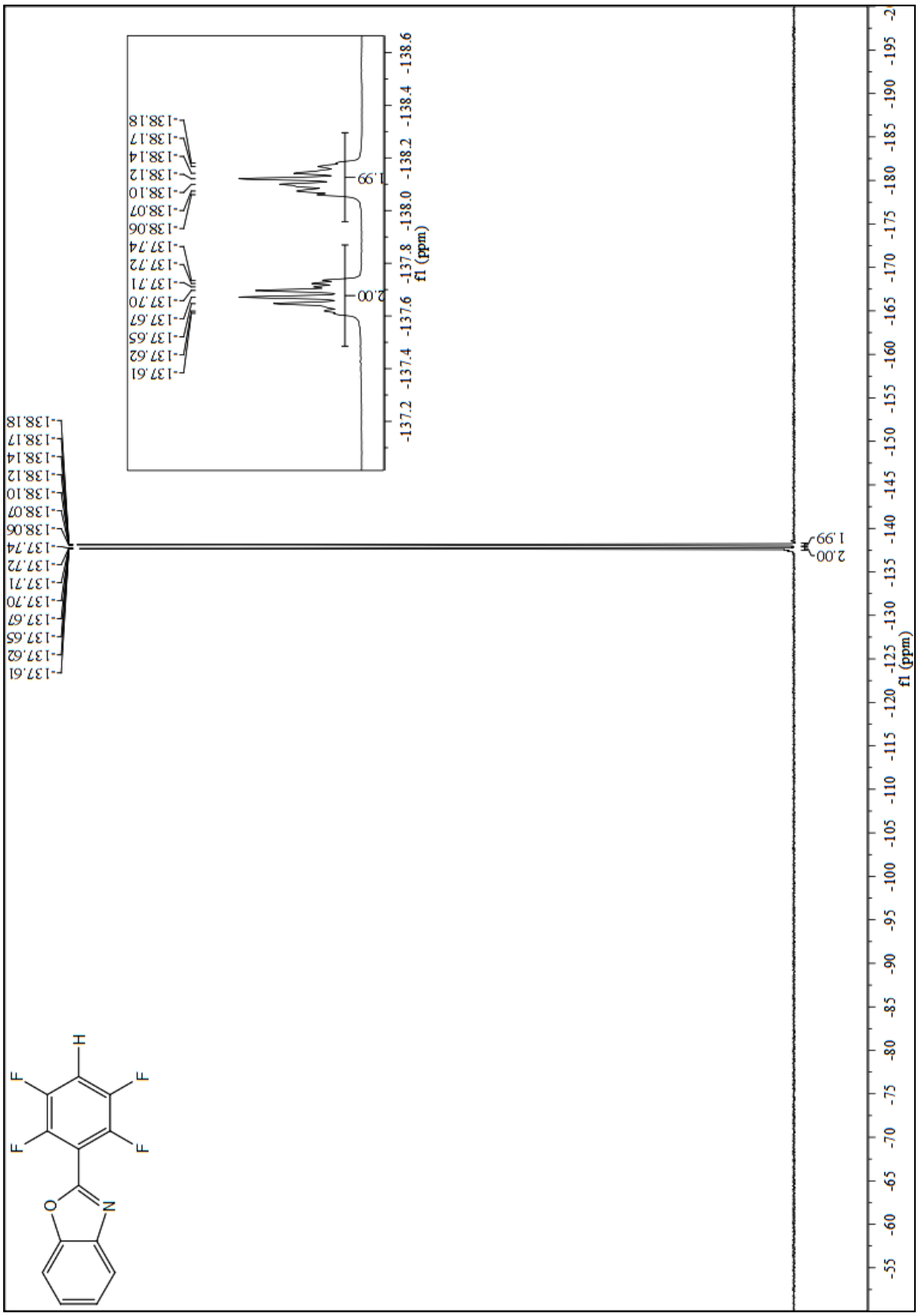
2h (2,3,5,6-tetrafluorobenzonitrile)



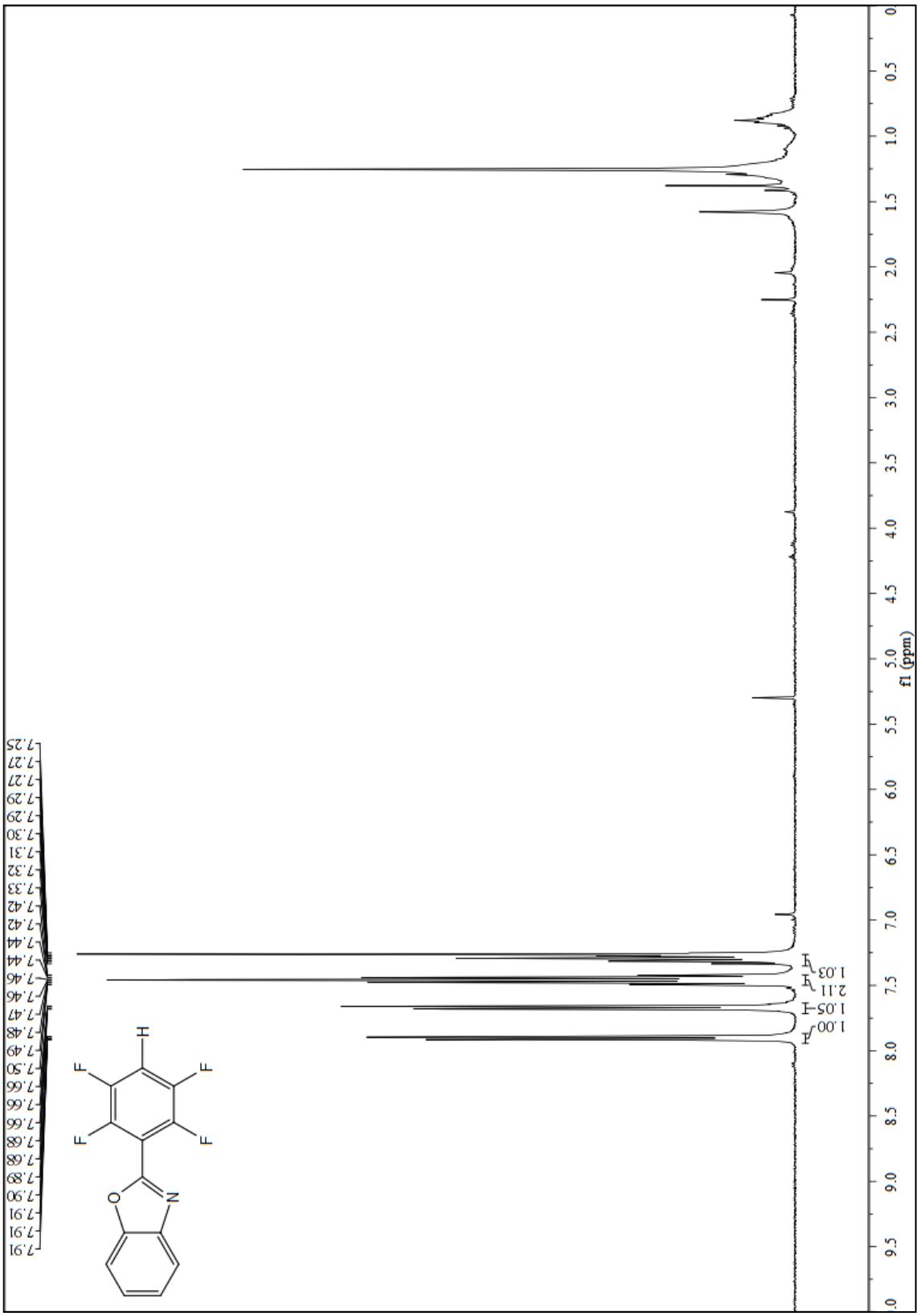
<u>2i</u> (tert-butyl 2,3,5,6-tetrafluorobenzoate)



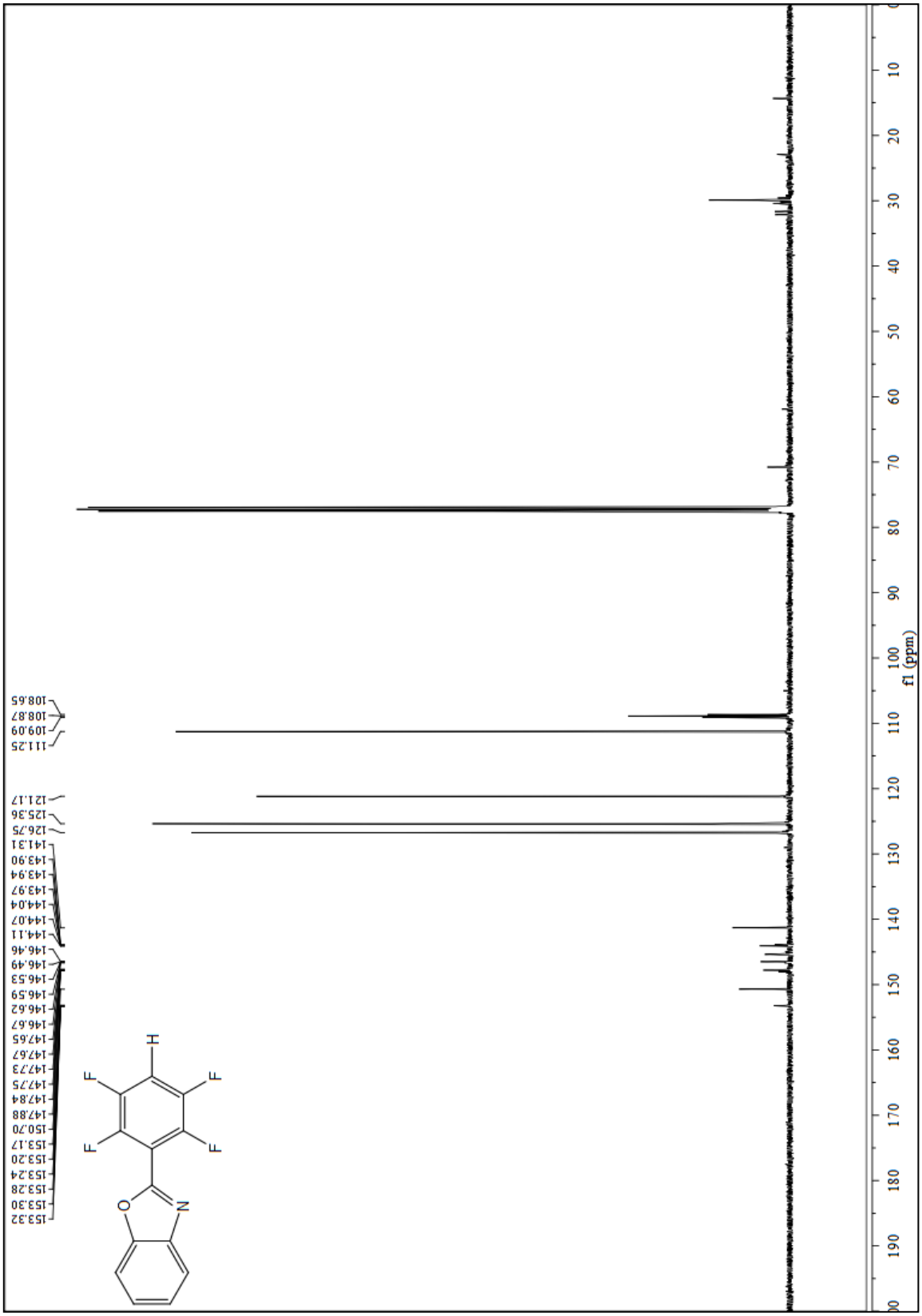
<u>2j</u> (2-(2,3,5,6-tetrafluorophenyl)benzo[d]oxazole)



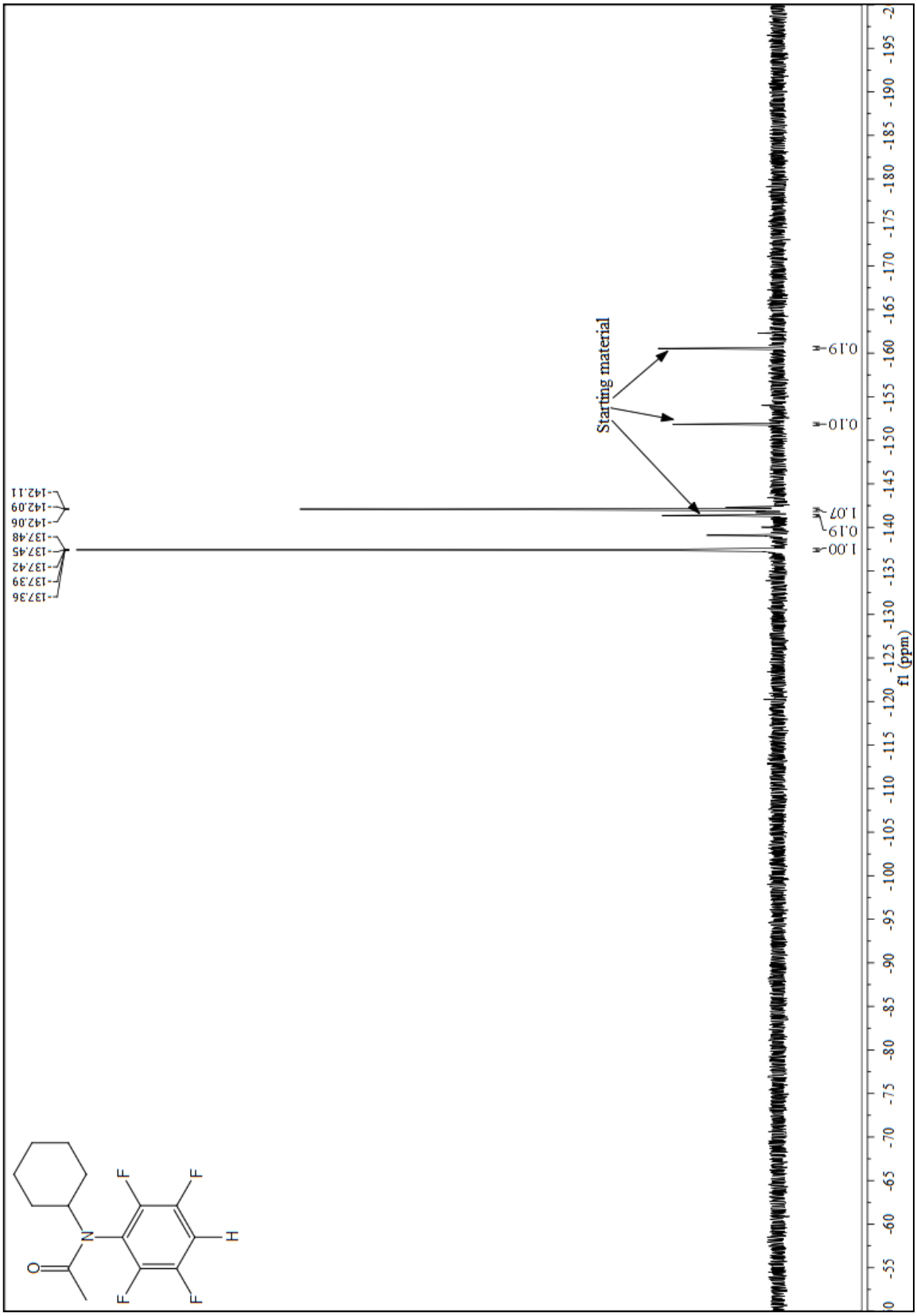
2i (2-(2,3,5,6-tetrafluorophenyl)benzo[d]oxazole)



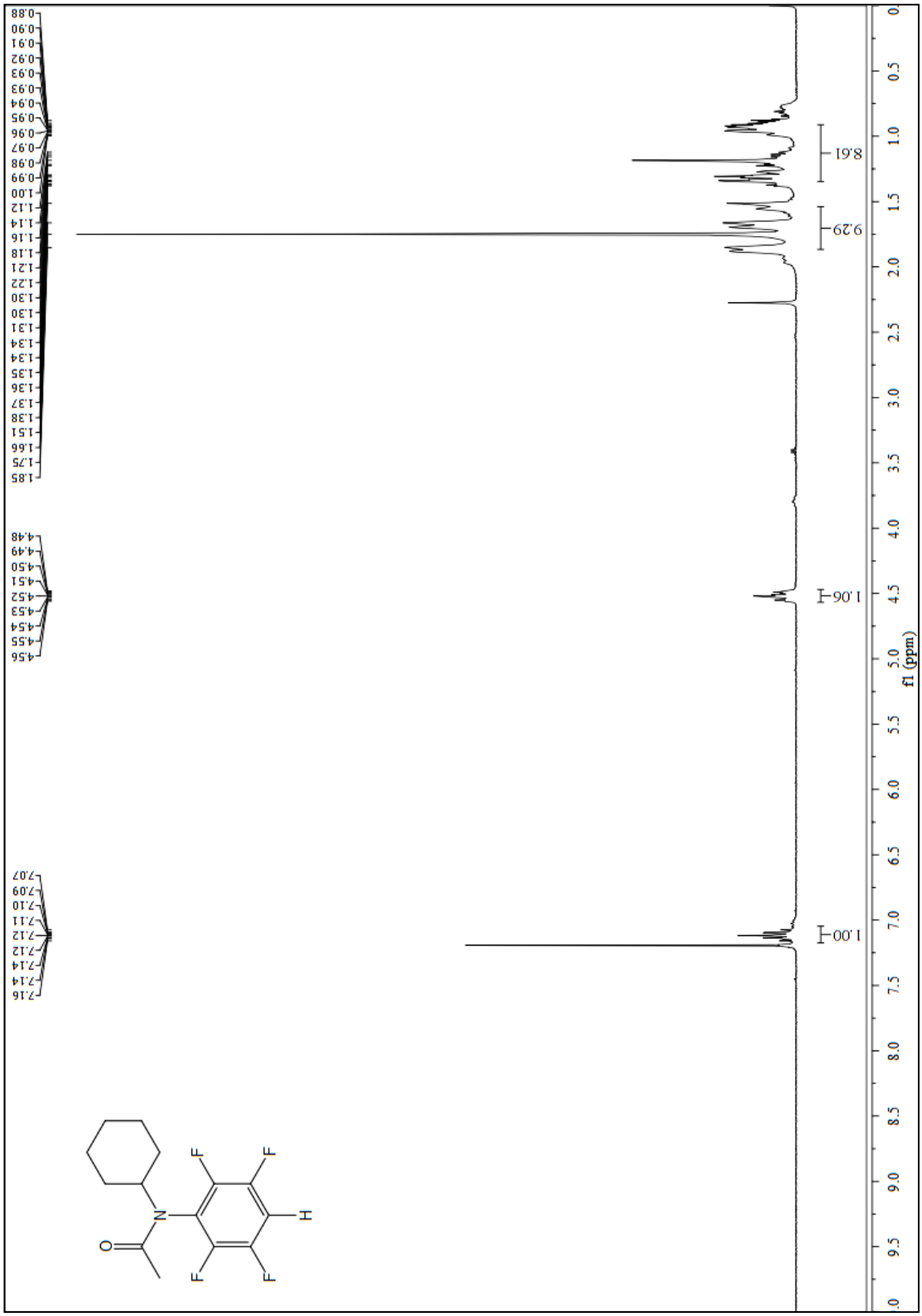
<u>2j</u> (2-(2,3,5,6-tetrafluorophenyl)benzo[d]oxazole



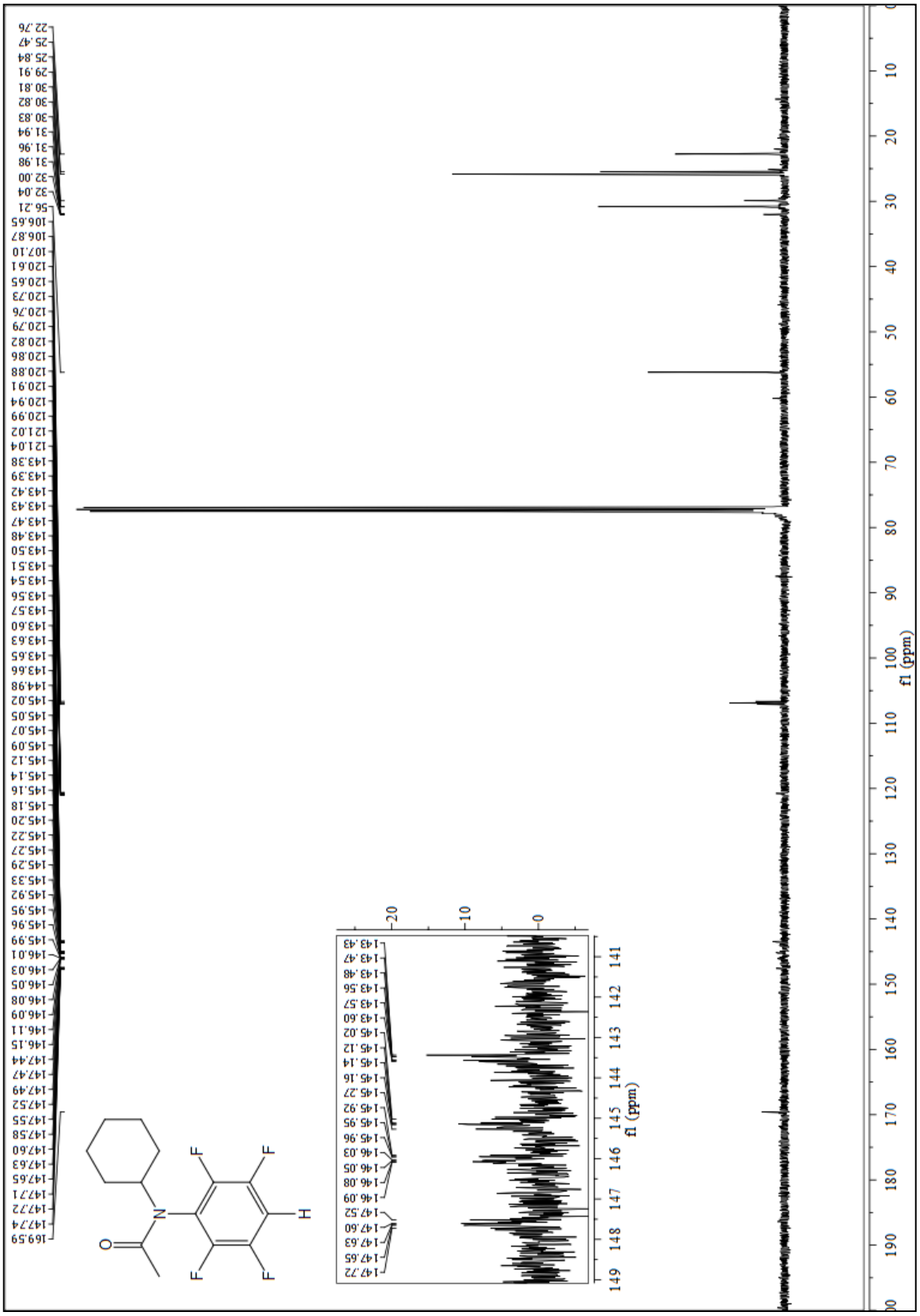
<u>2k</u> (*N*-cyclohexyl-N-(2,3,5,6-tetrafluorophenyl)acetamide)



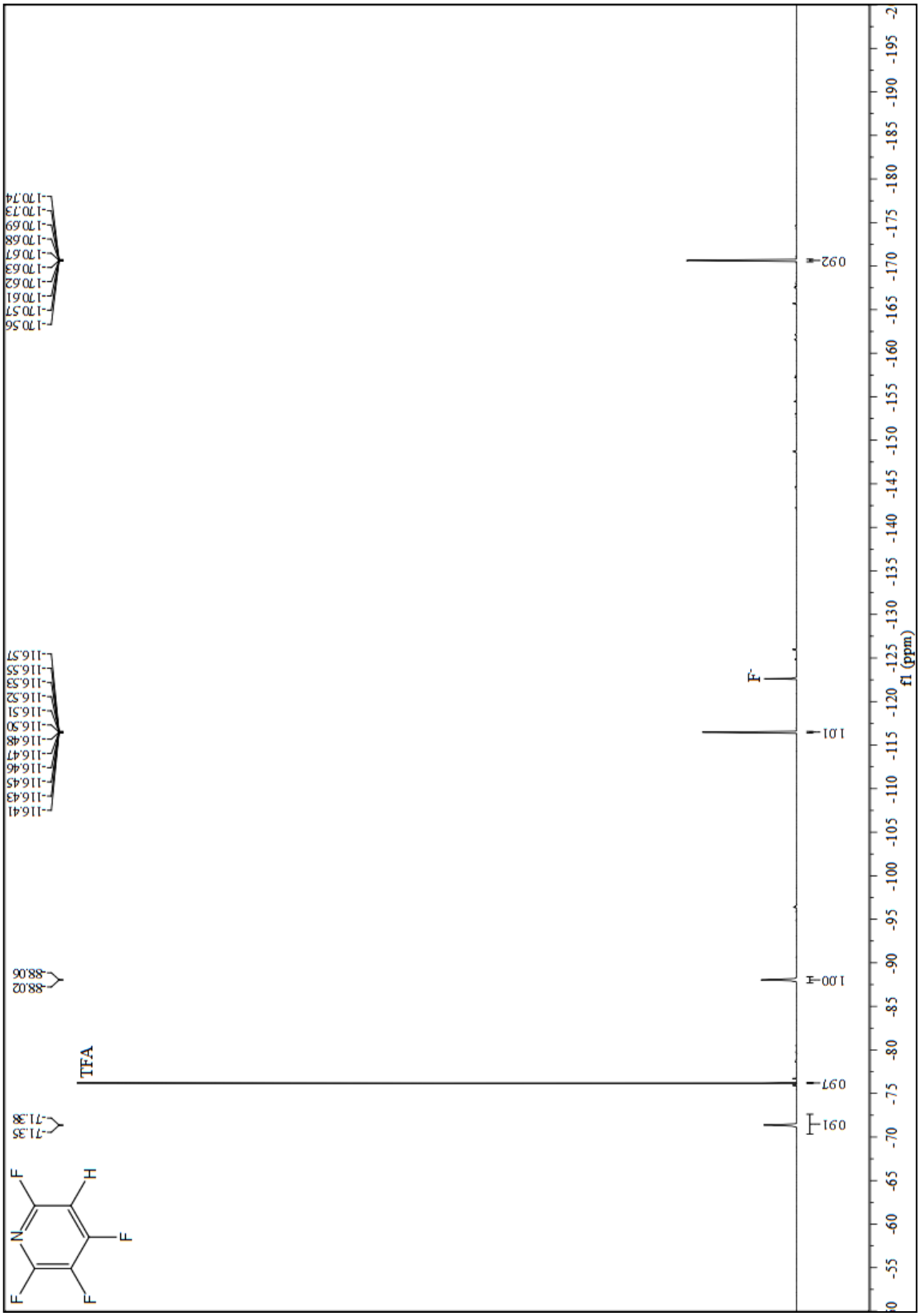
2k (***N*-cyclohexyl-N-(2,3,5,6-tetrafluorophenyl)acetamide)**



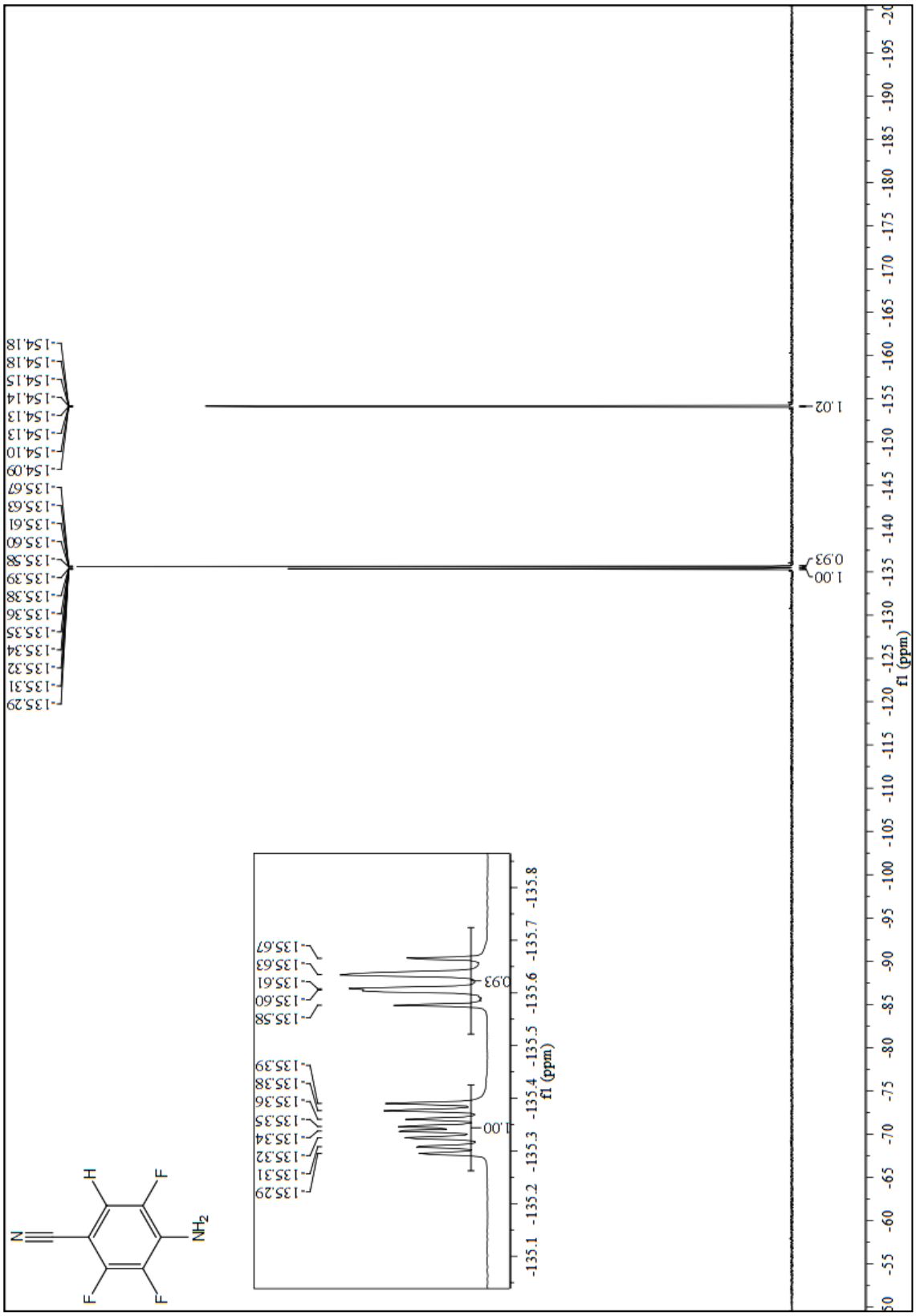
2k (***N*-cyclohexyl-*N*-(2,3,5,6-tetrafluorophenyl)acetamide)**



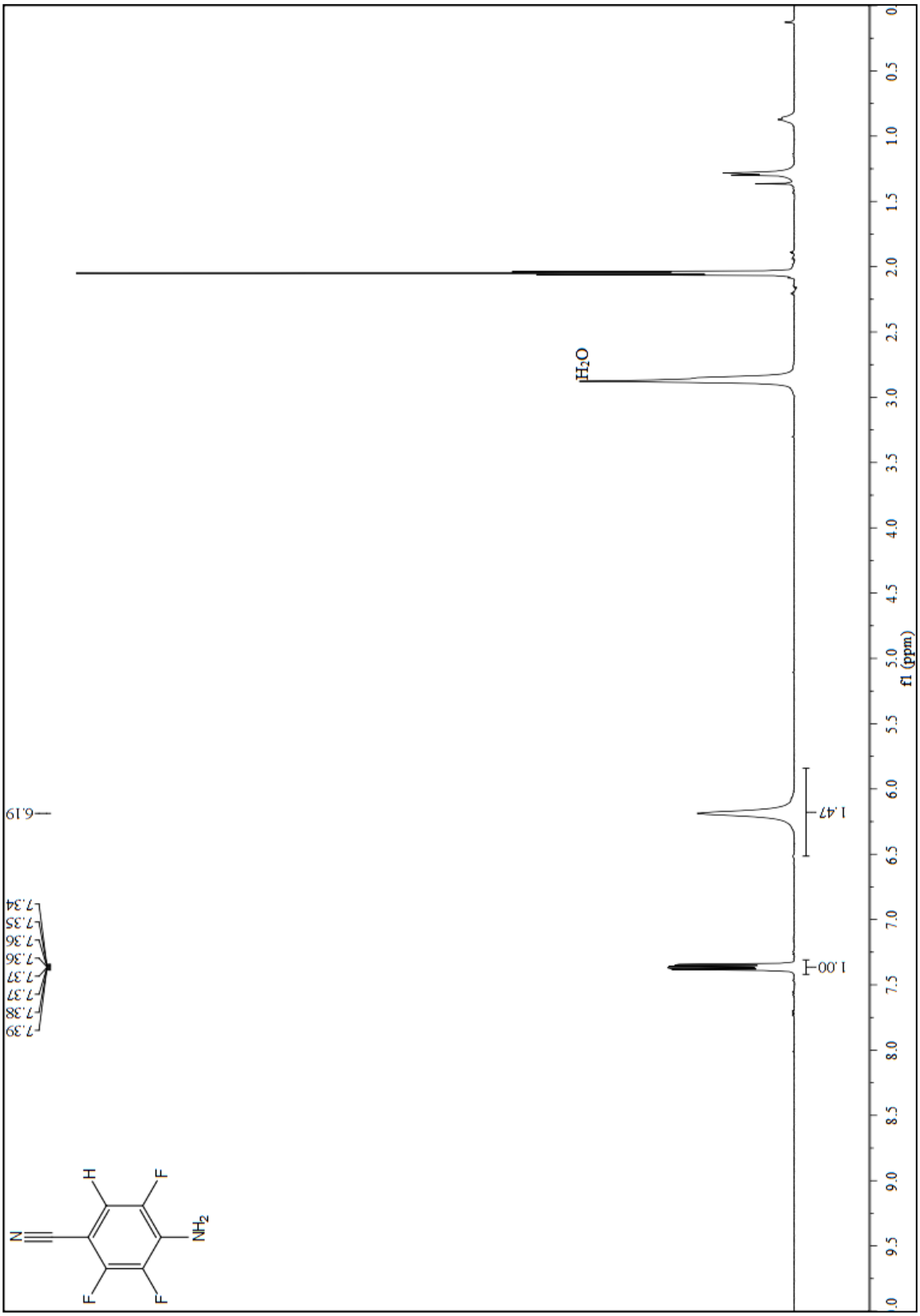
<u>2l</u> (2,3,4,6-tetrafluoropyridine)



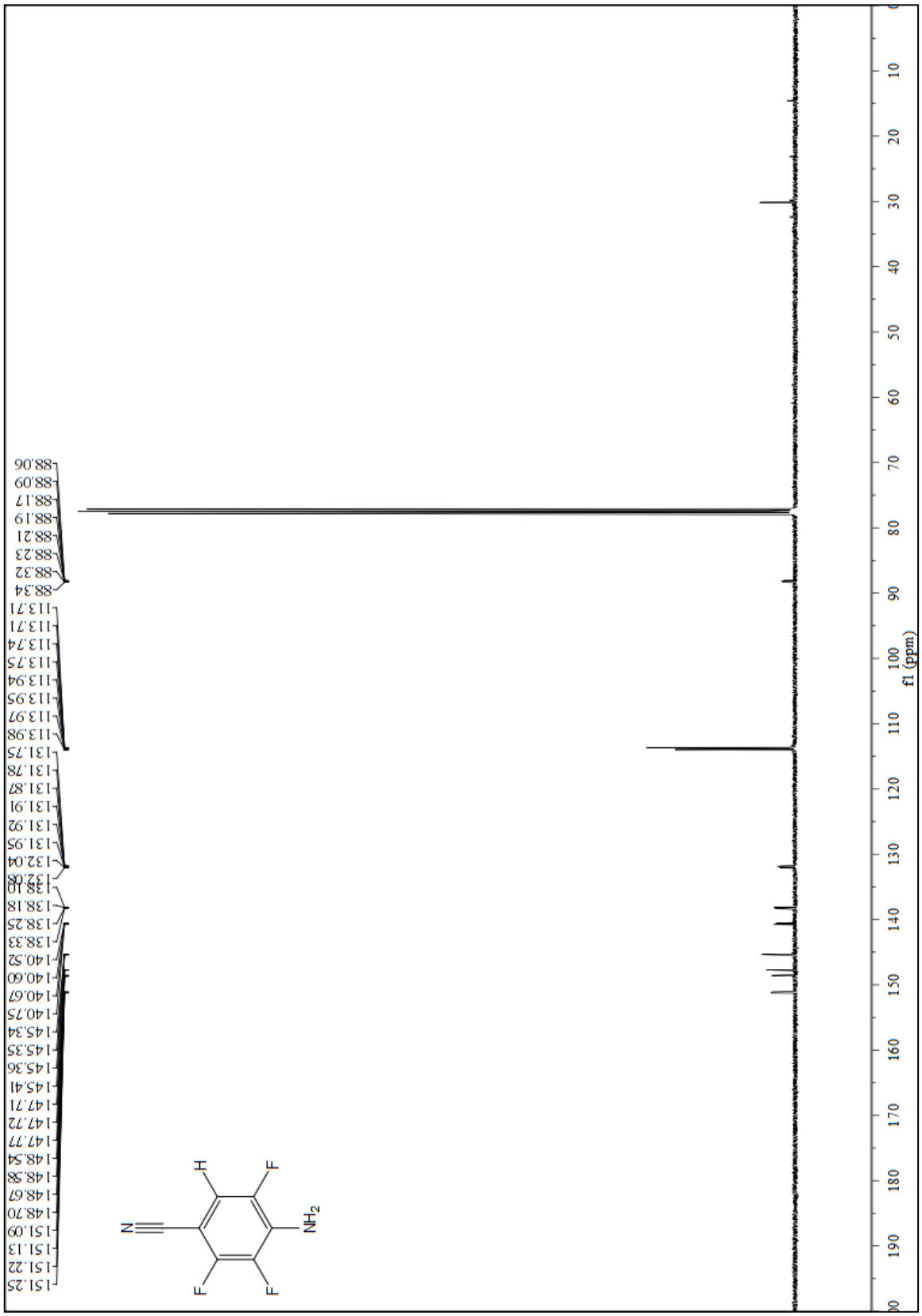
<u>2m</u> (4-amino-2,3,5-trifluorobenzonitrile)



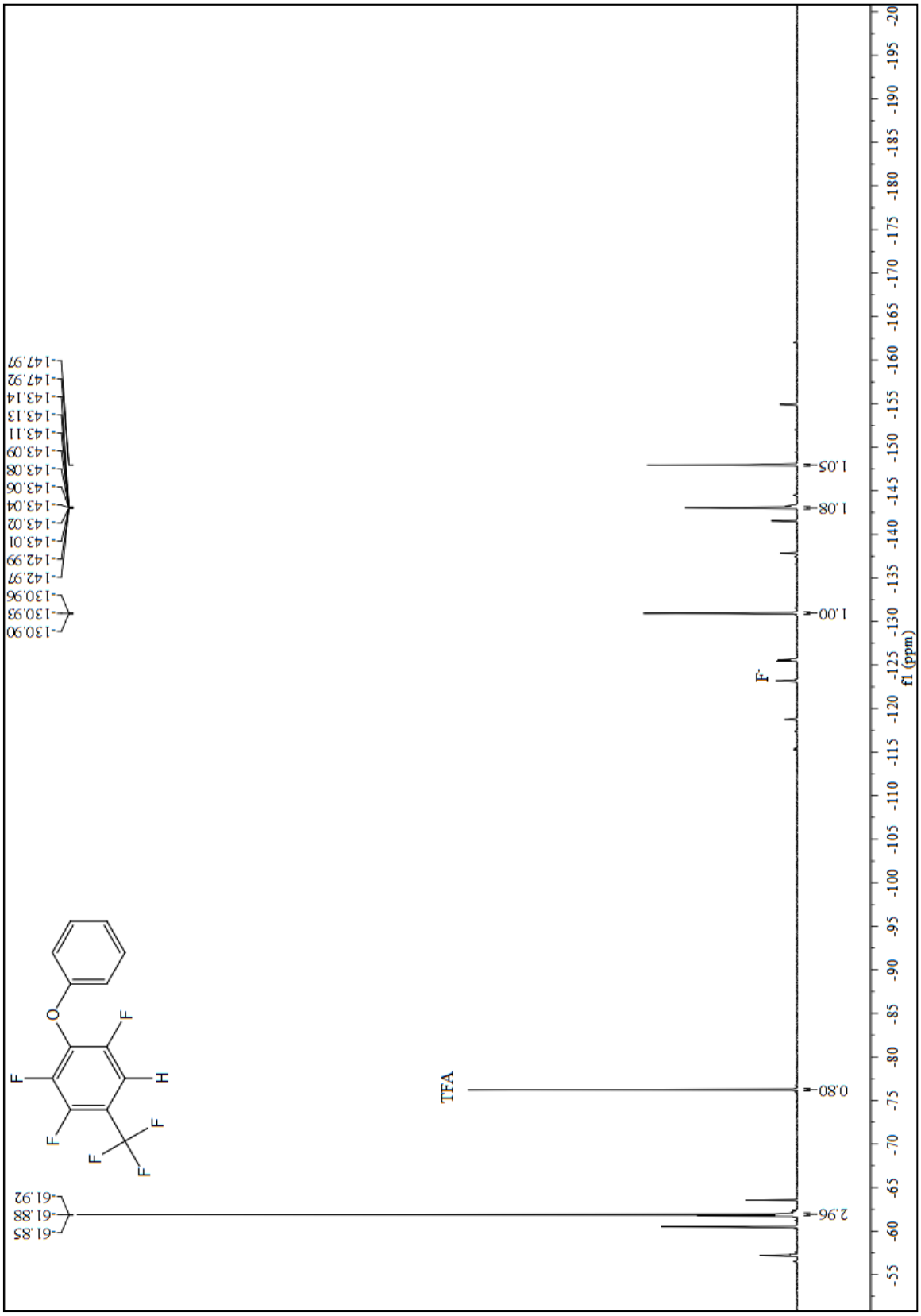
<u>2m</u> (4-amino-2,3,5-trifluorobenzonitrile)



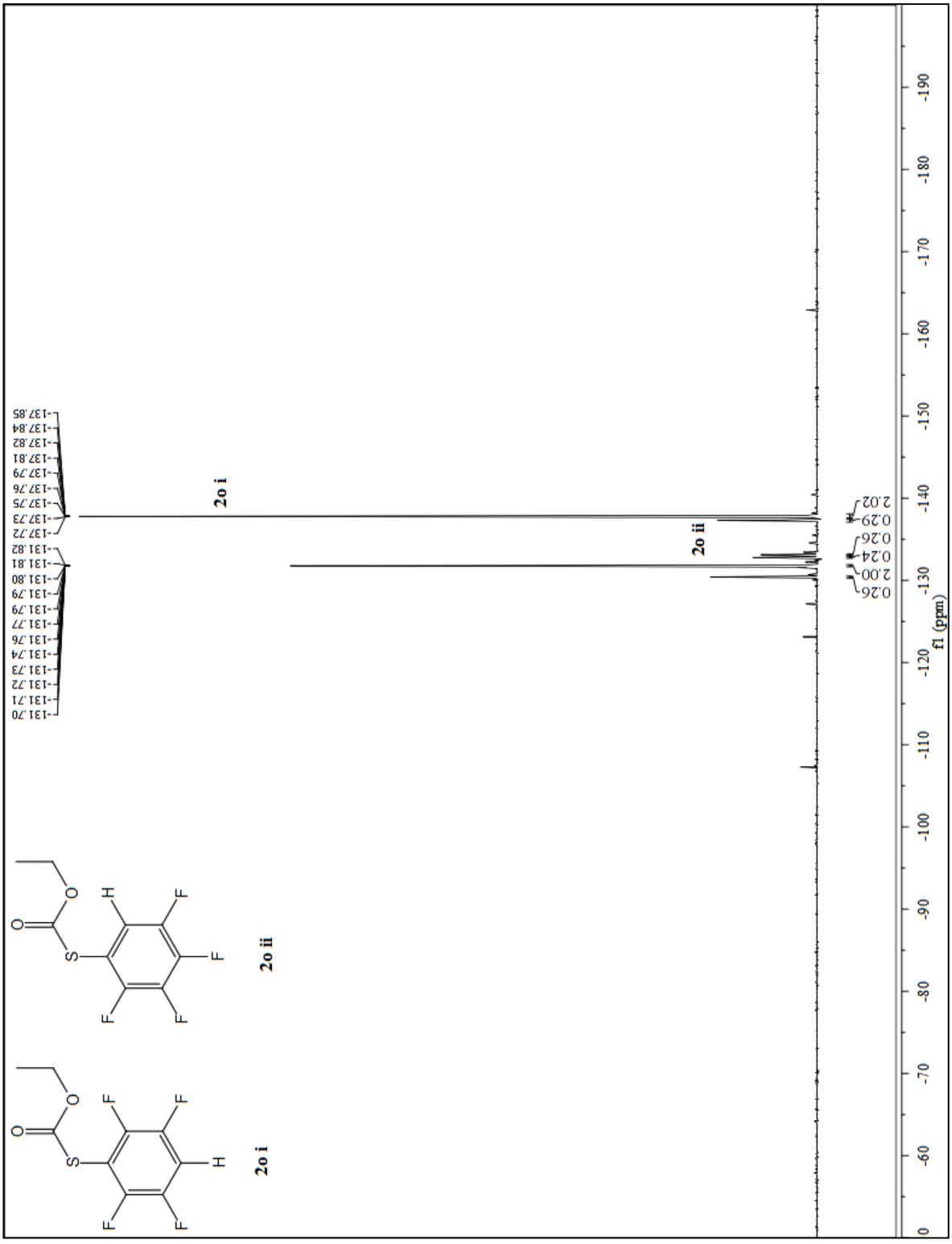
<u>2m</u> (4-amino-2,3,5-trifluorobenzonitrile)



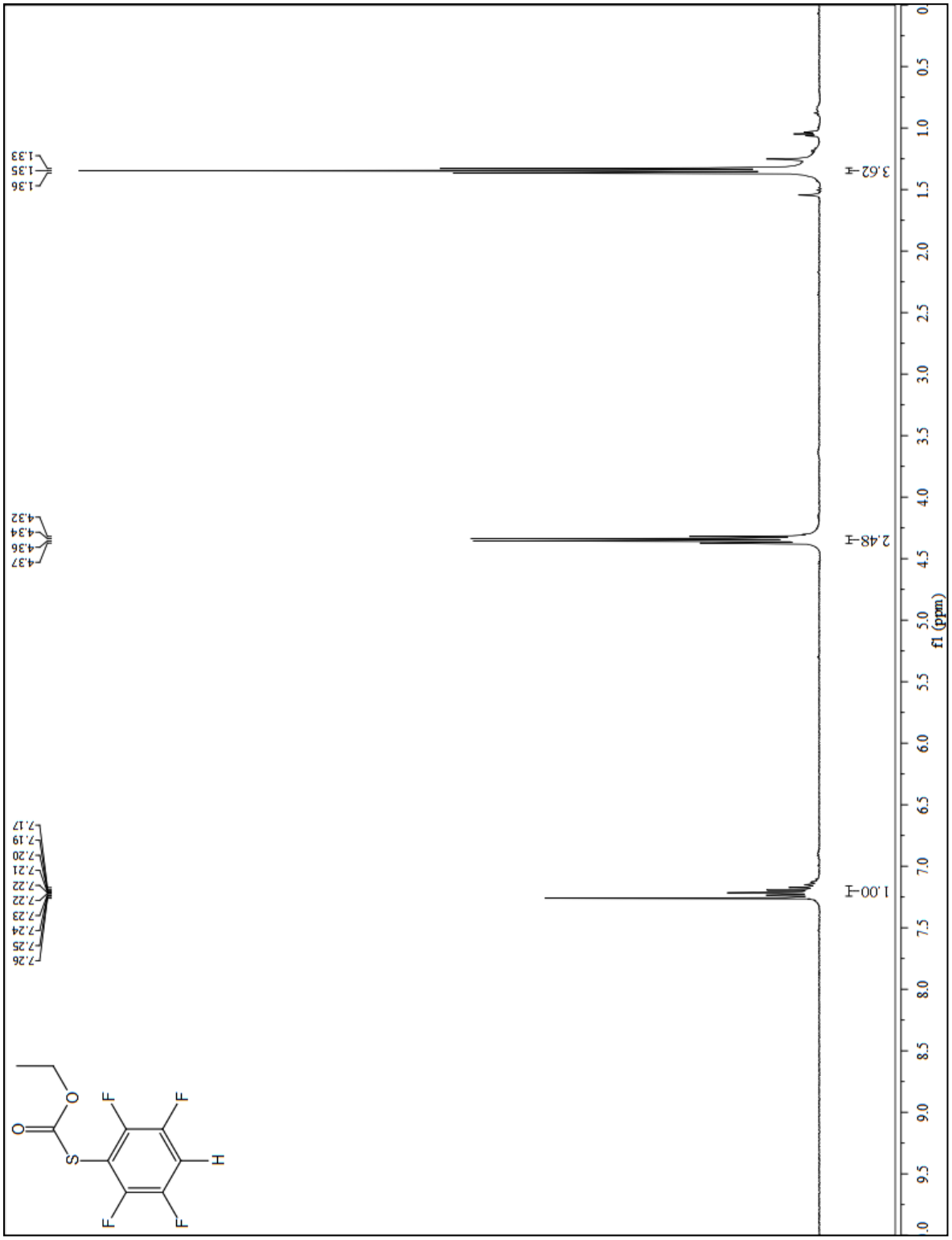
<u>2n</u> (1,3,4-trifluoro-2-phenoxy-5-(trifluoromethyl)benzene)



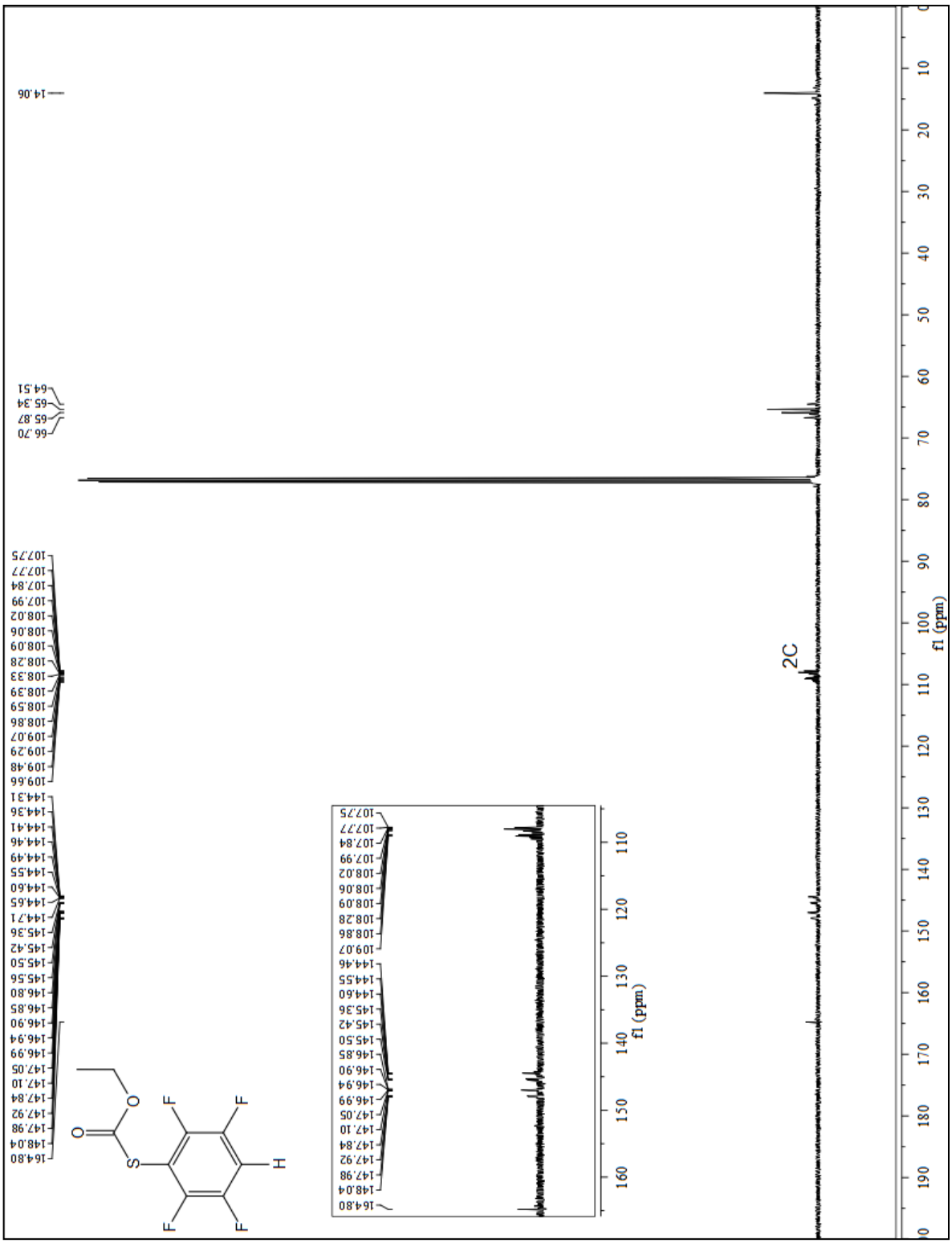
<u>2o</u> (*O*-ethyl *S*-(2,3,5,6-tetrafluorophenyl) carbonothioate)



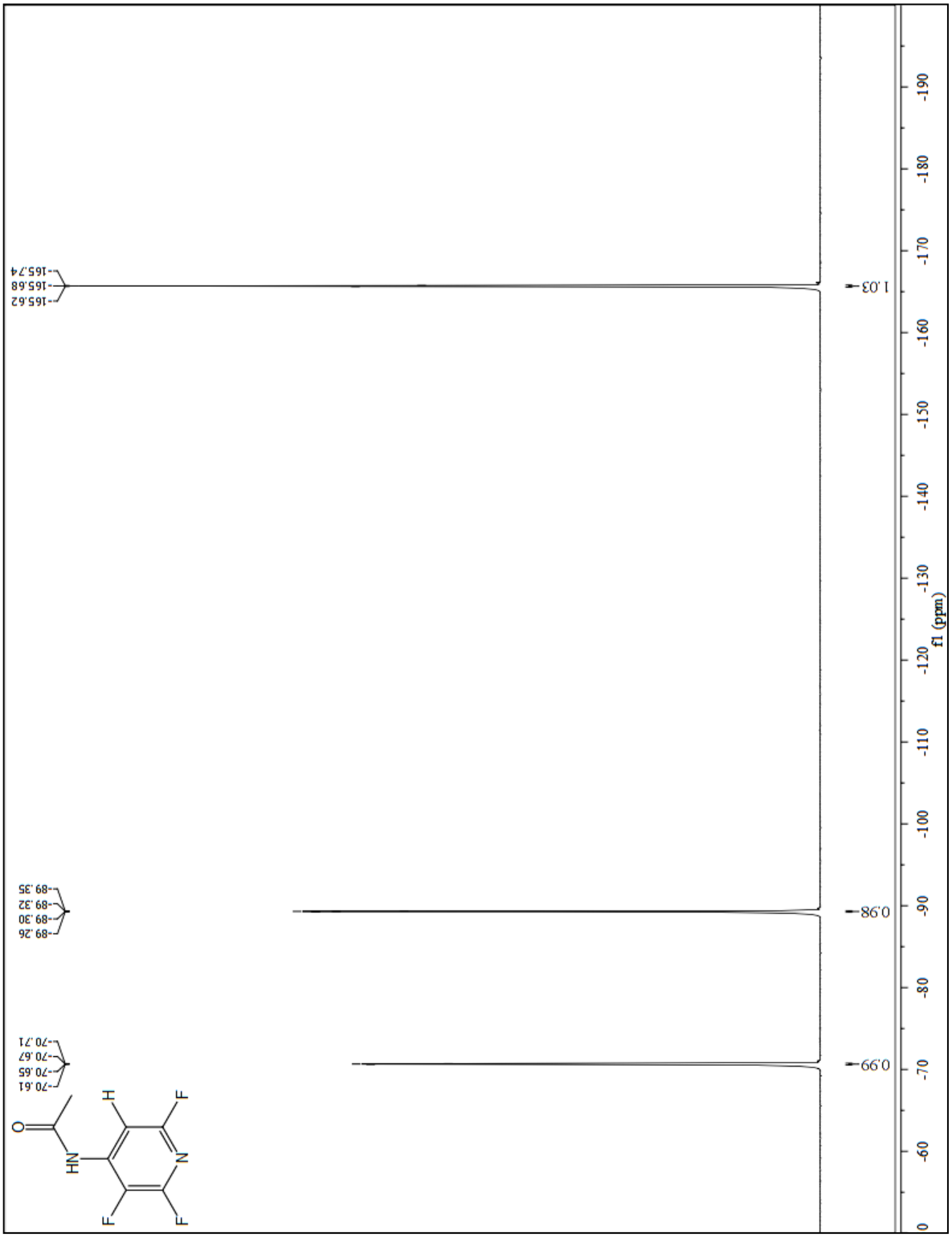
<u>2o</u> (*O*-ethyl *S*-(2,3,5,6-tetrafluorophenyl) carbonothioate)



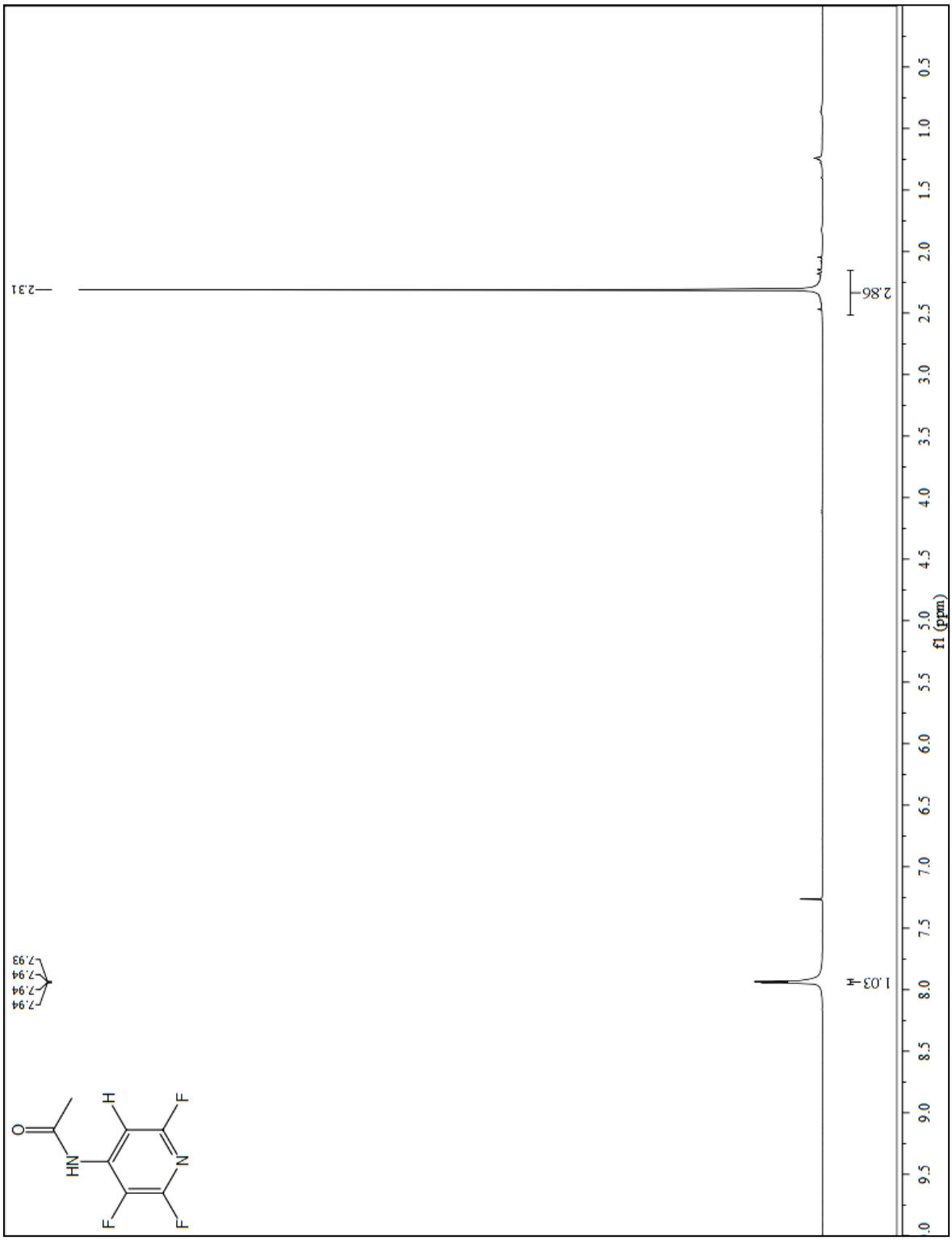
<u>2o</u> (*O*-ethyl *S*-(2,3,5,6-tetrafluorophenyl) carbonothioate)



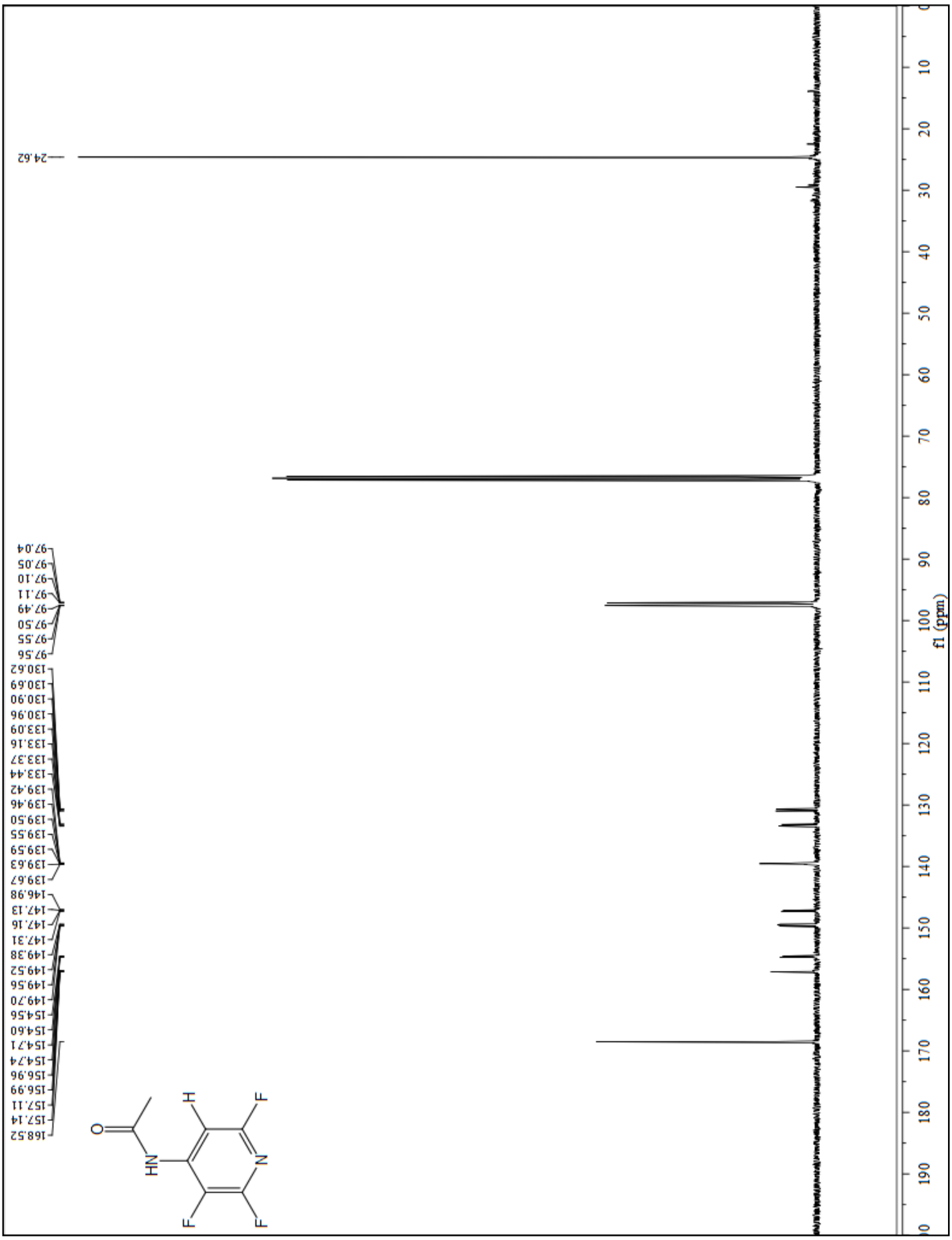
2p (*N*-(2,3,6-trifluoropyridin-4-yl)acetamide)



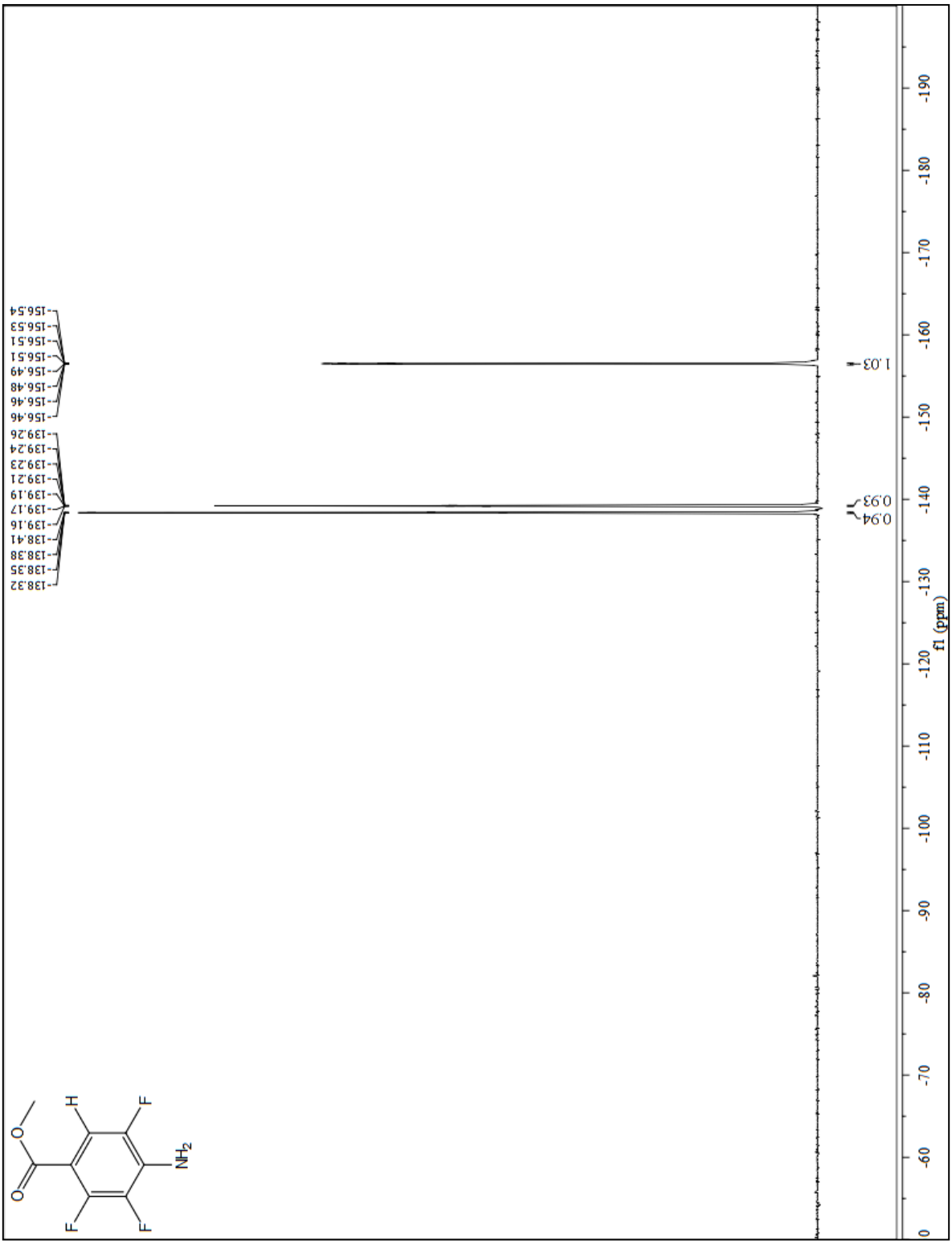
2p (*N*-(2,3,6-trifluoropyridin-4-yl)acetamide)



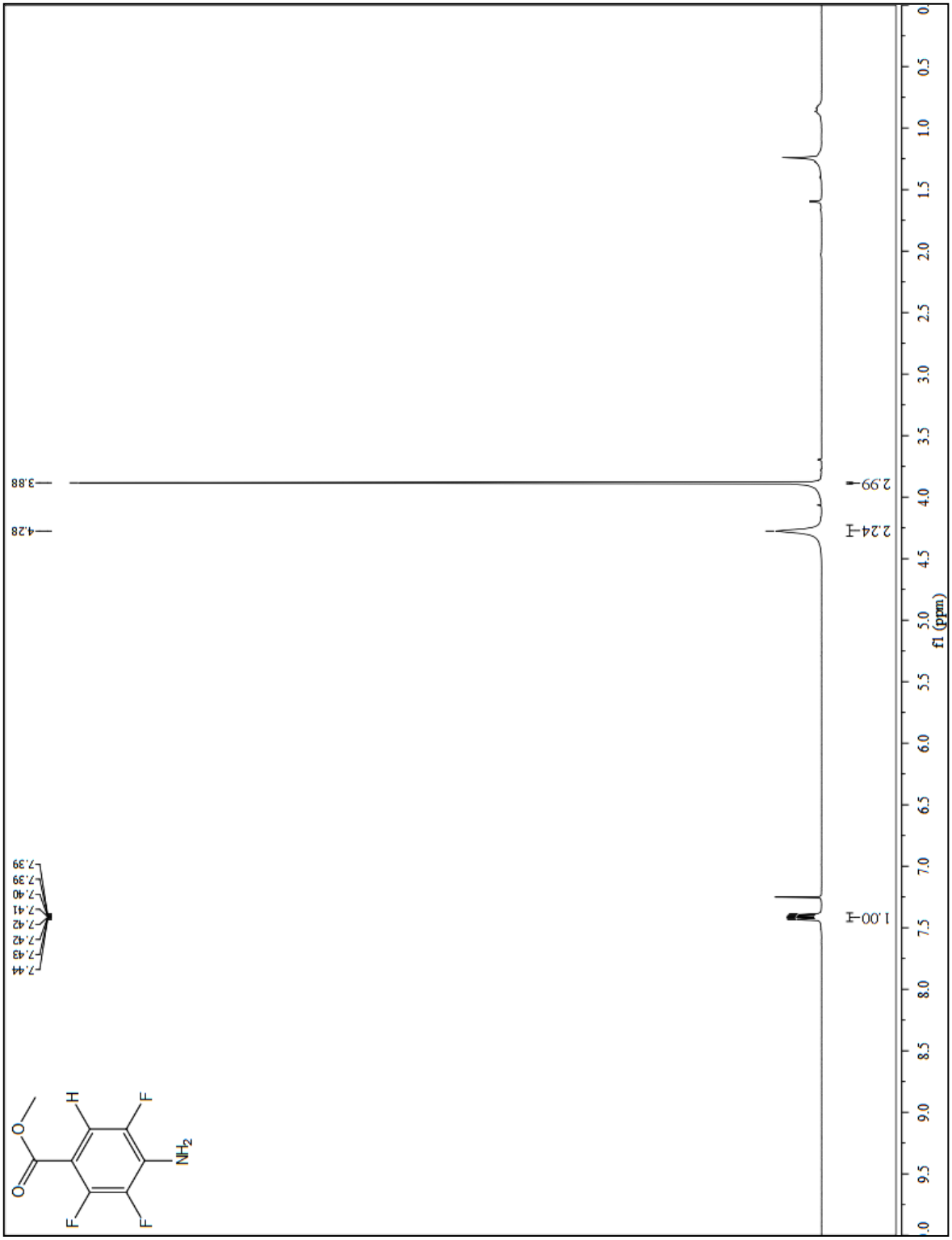
2p (*N*-(2,3,6-trifluoropyridin-4-yl)acetamide)



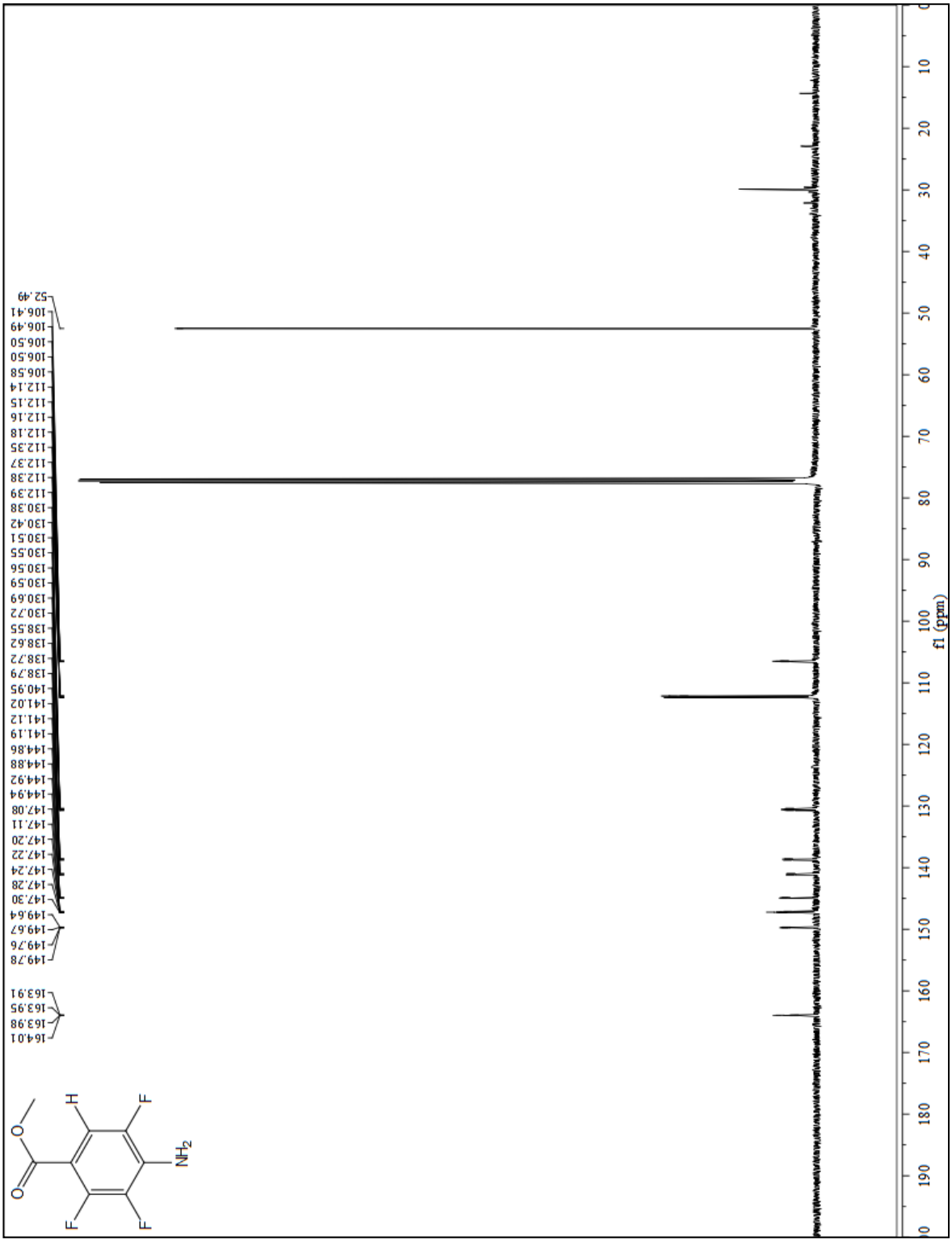
2q (methyl 4-amino-2,3,5-trifluorobenzoate)



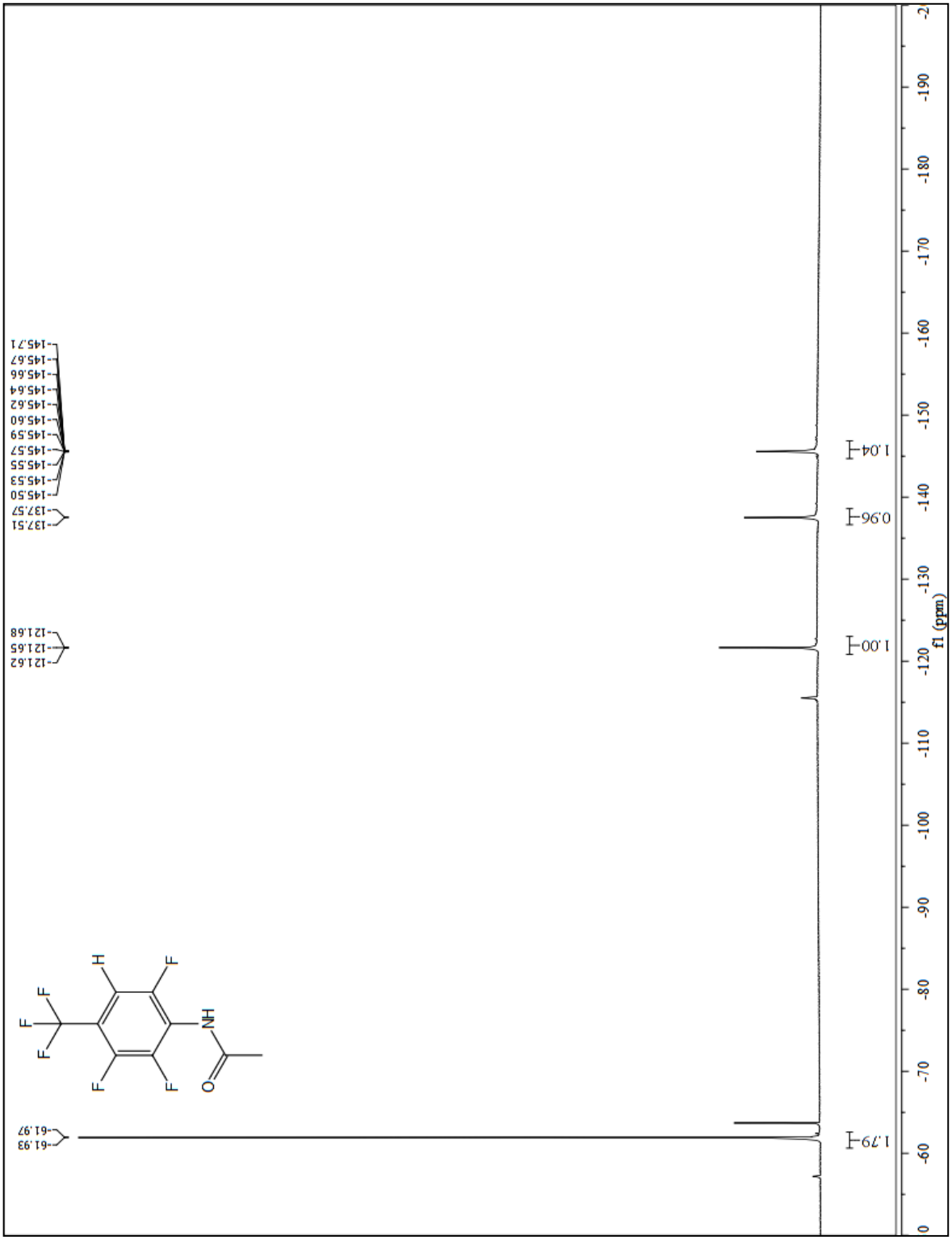
2q (methyl 4-amino-2,3,5-trifluorobenzoate)



2q (methyl 4-amino-2,3,5-trifluorobenzoate)



2r (*N*-(2,3,6-trifluoro-4-(trifluoromethyl)phenyl)acetamide)



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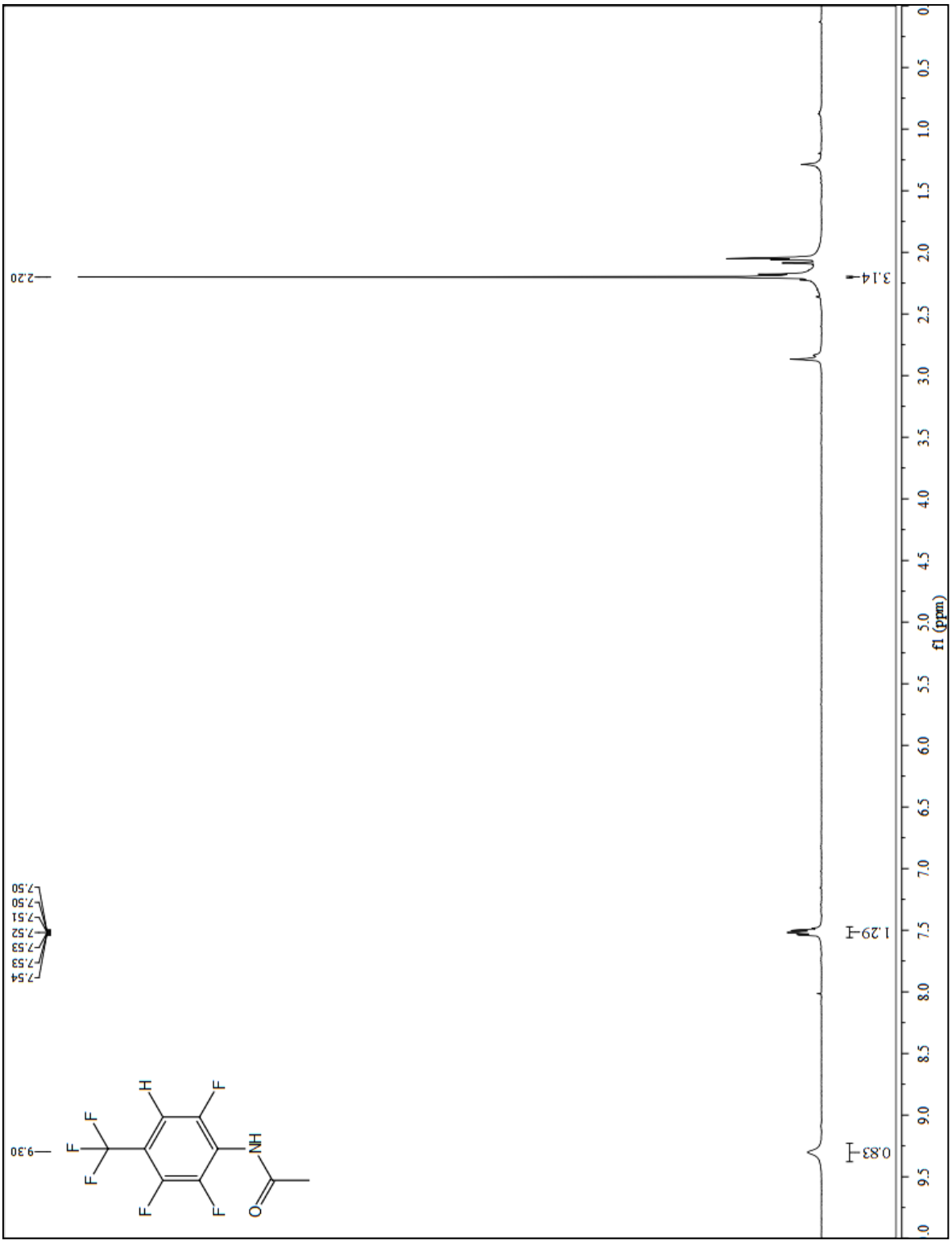
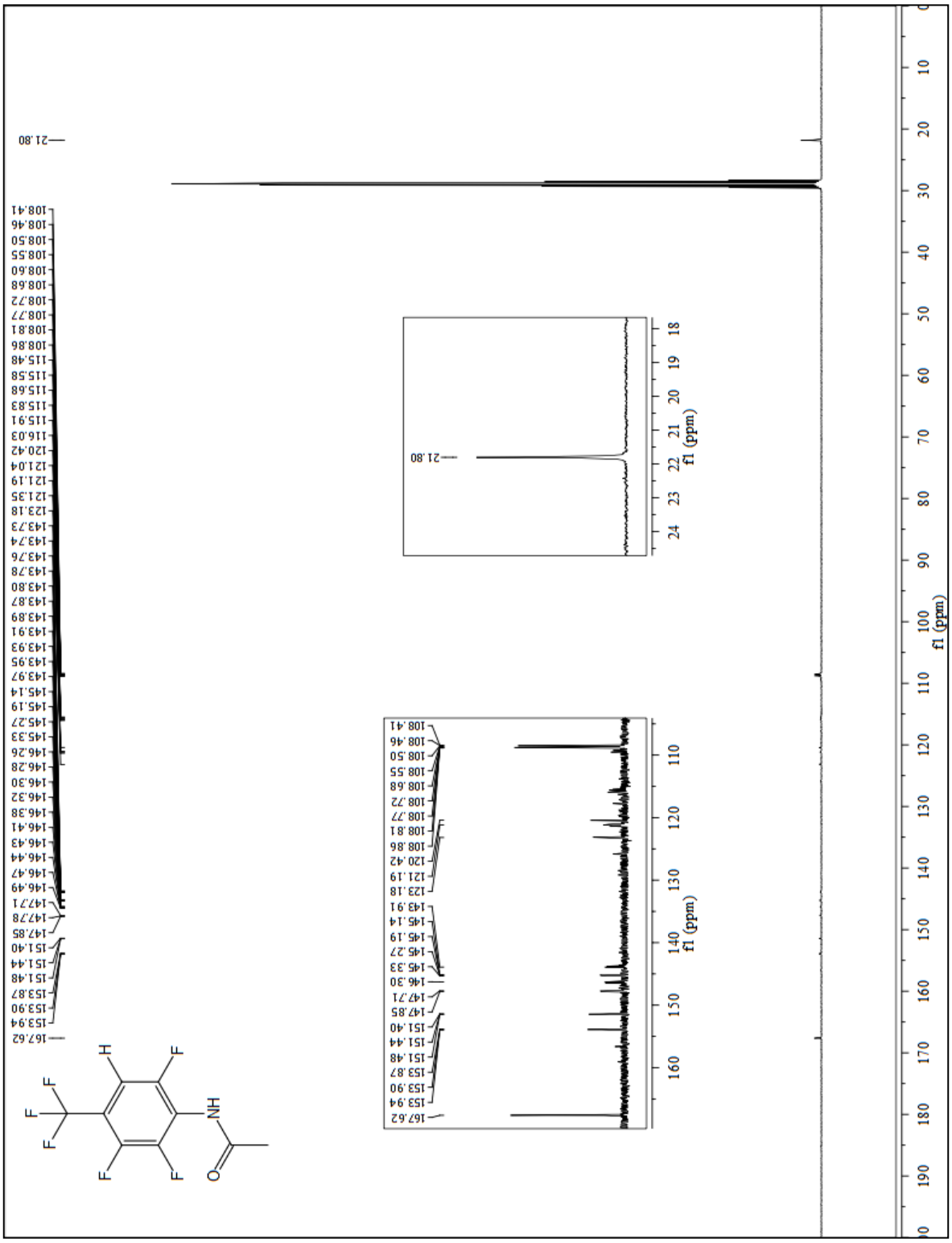
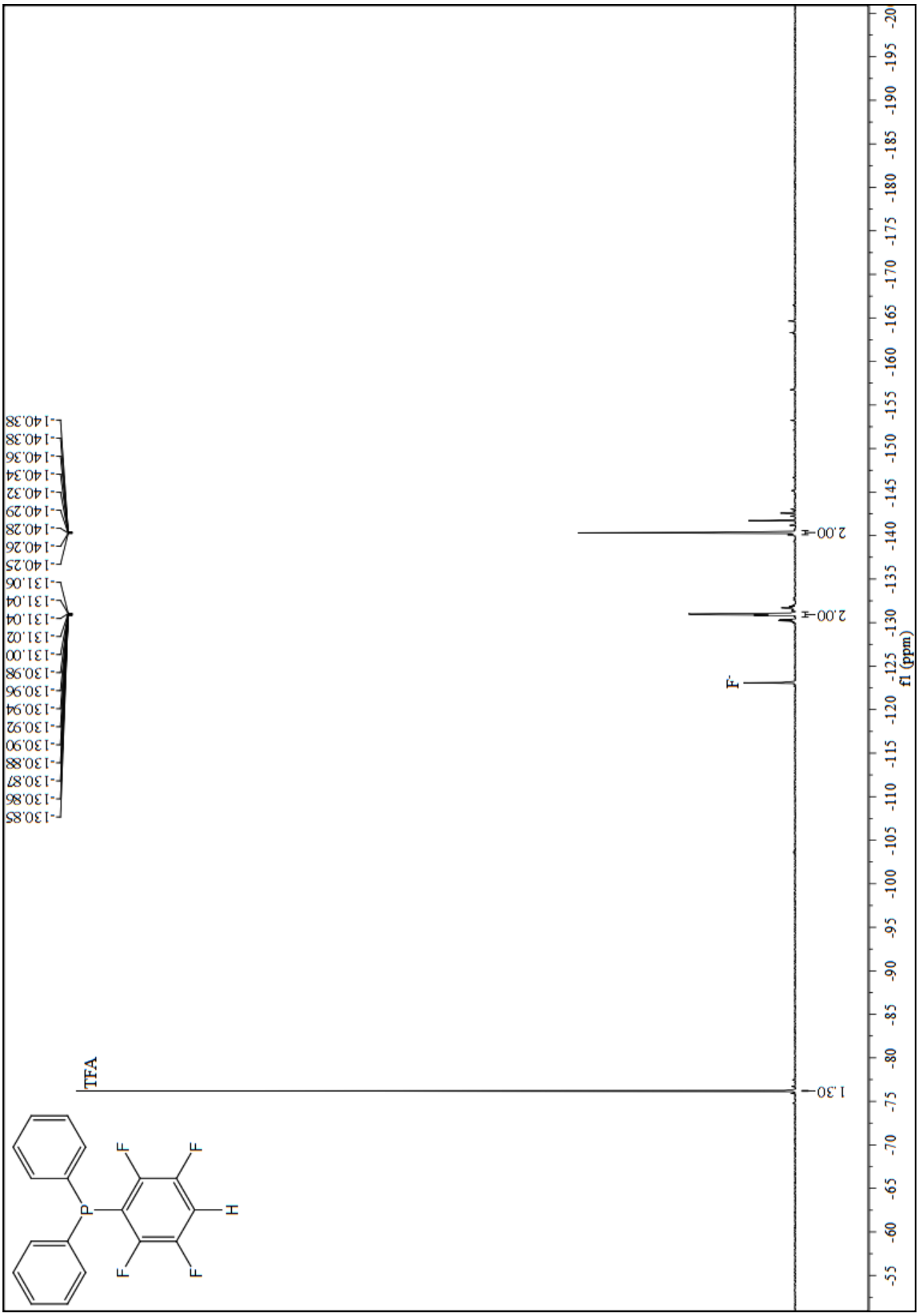


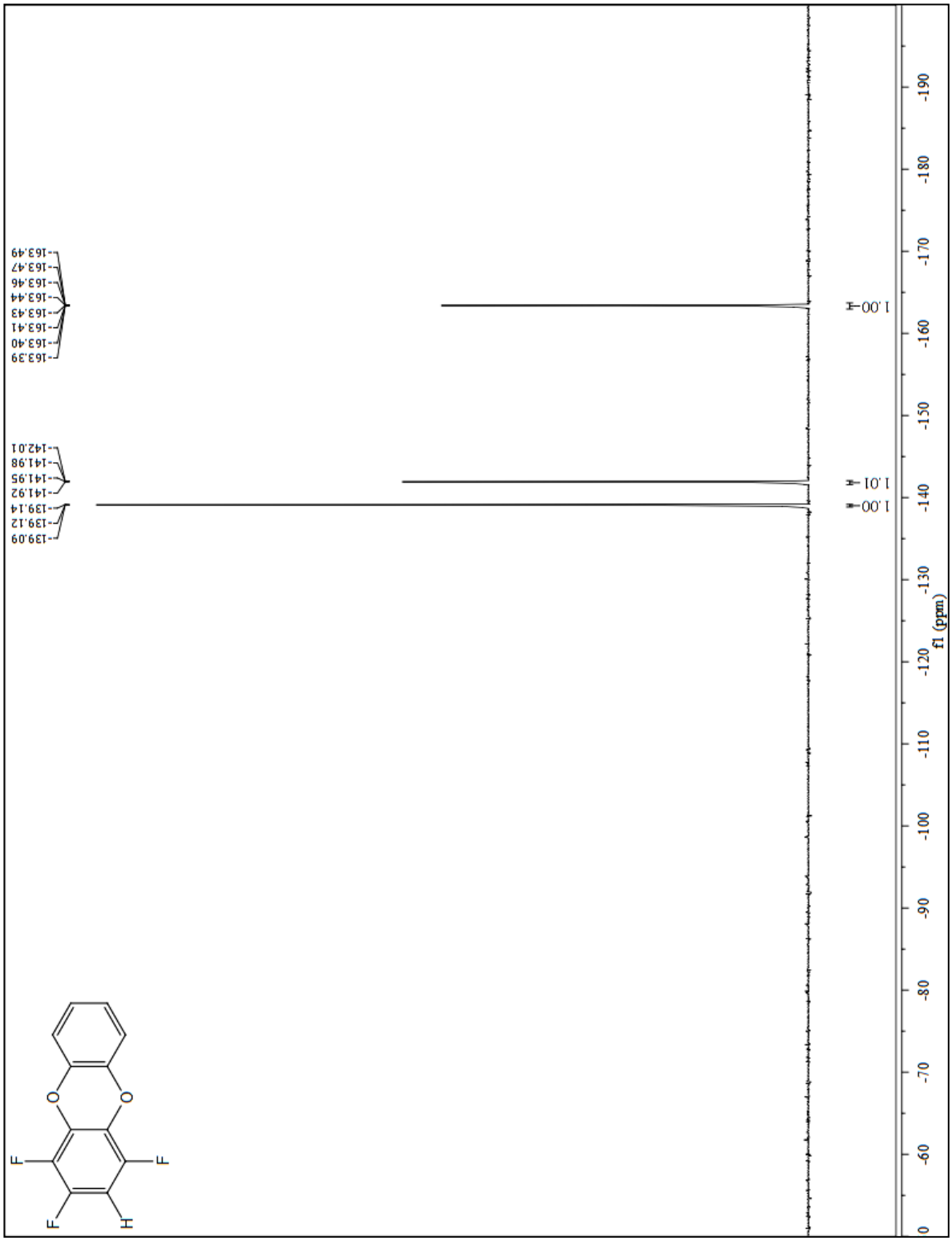
<u>2r</u> (*N*-(2,3,6-trifluoro-4-(trifluoromethyl)phenyl)acetamide)



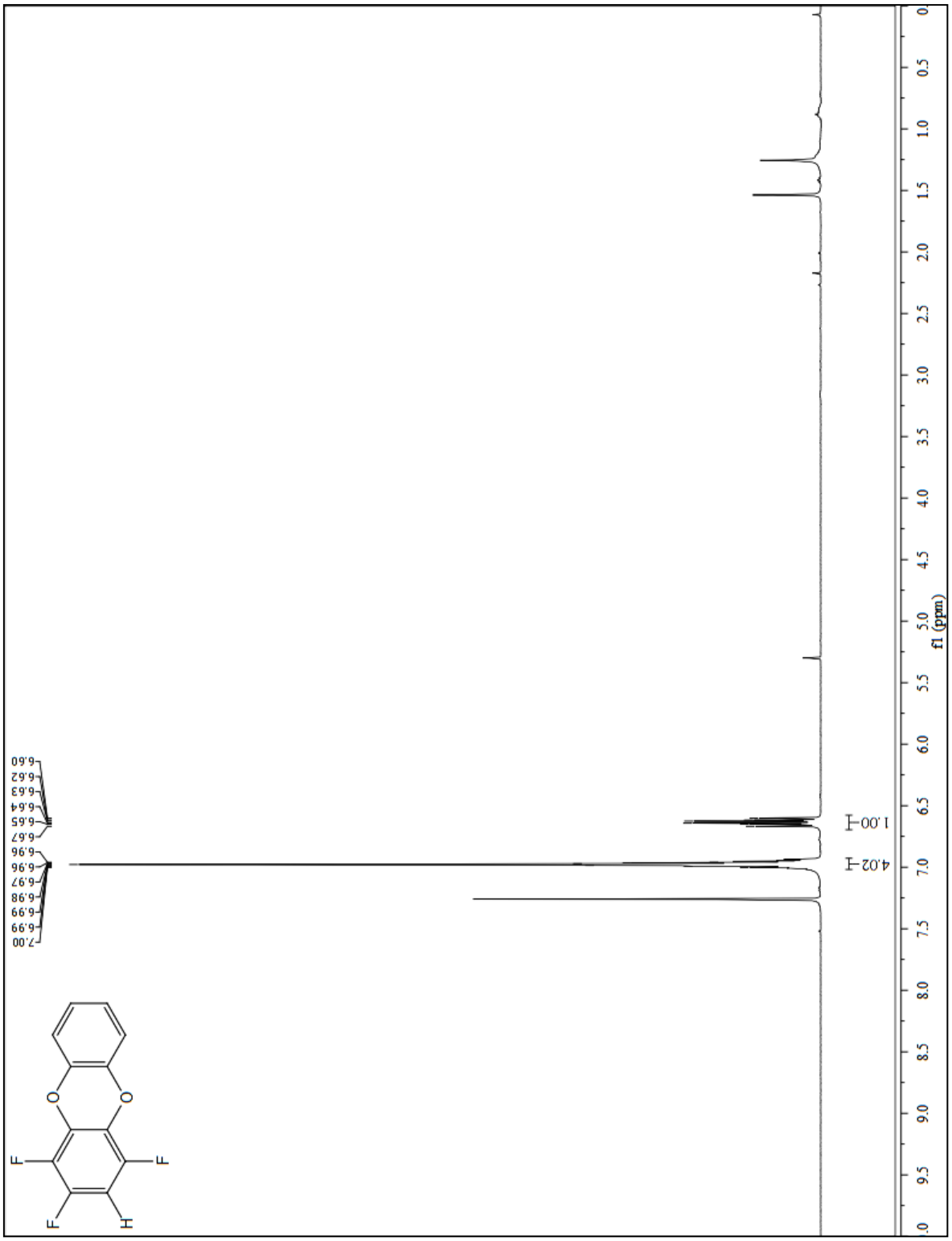
2s (diphenyl(2,3,5,6-tetrafluorophenyl)phosphane)



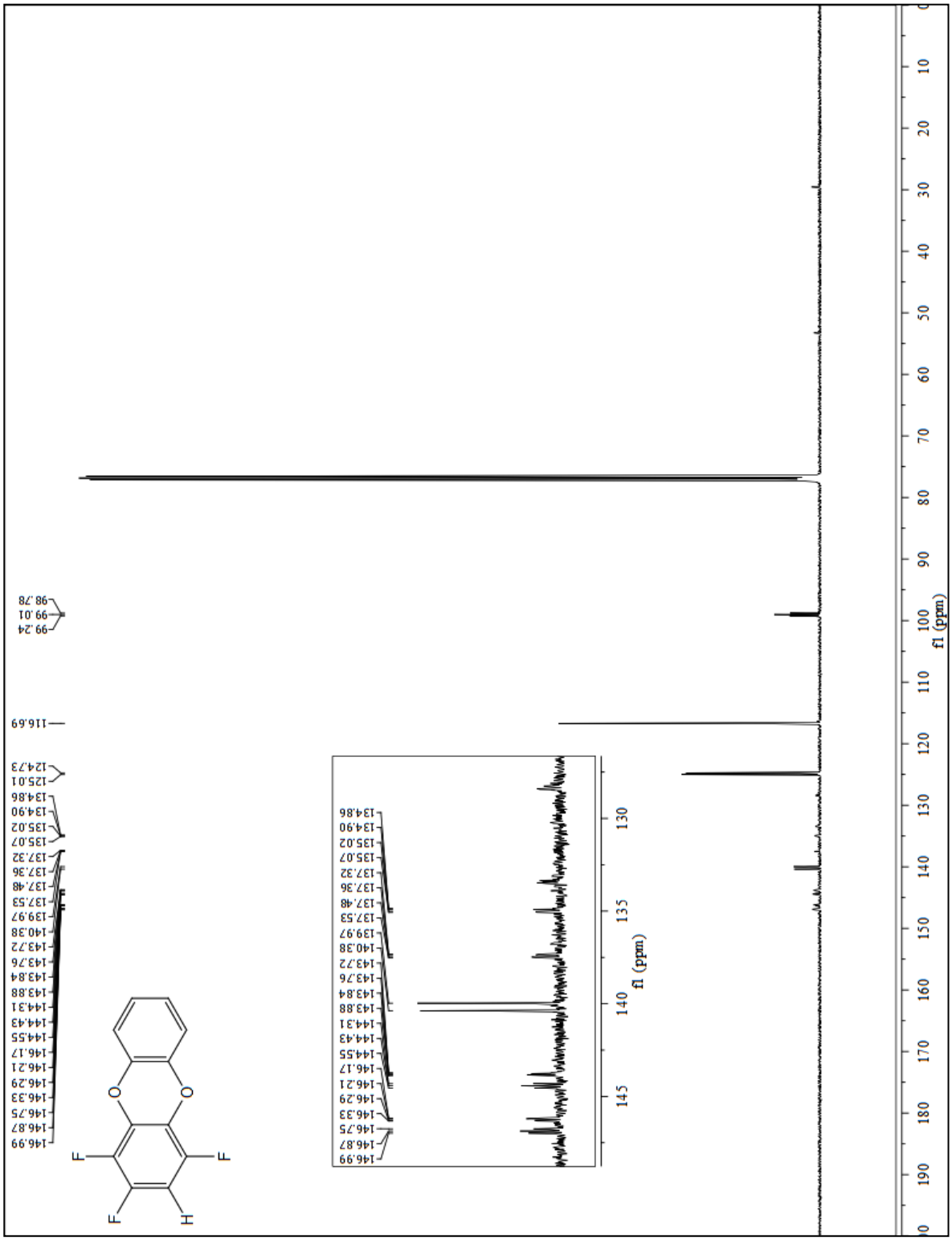
2t (1,2,4-trifluorodibenzo[b,e][1,4]dioxine)



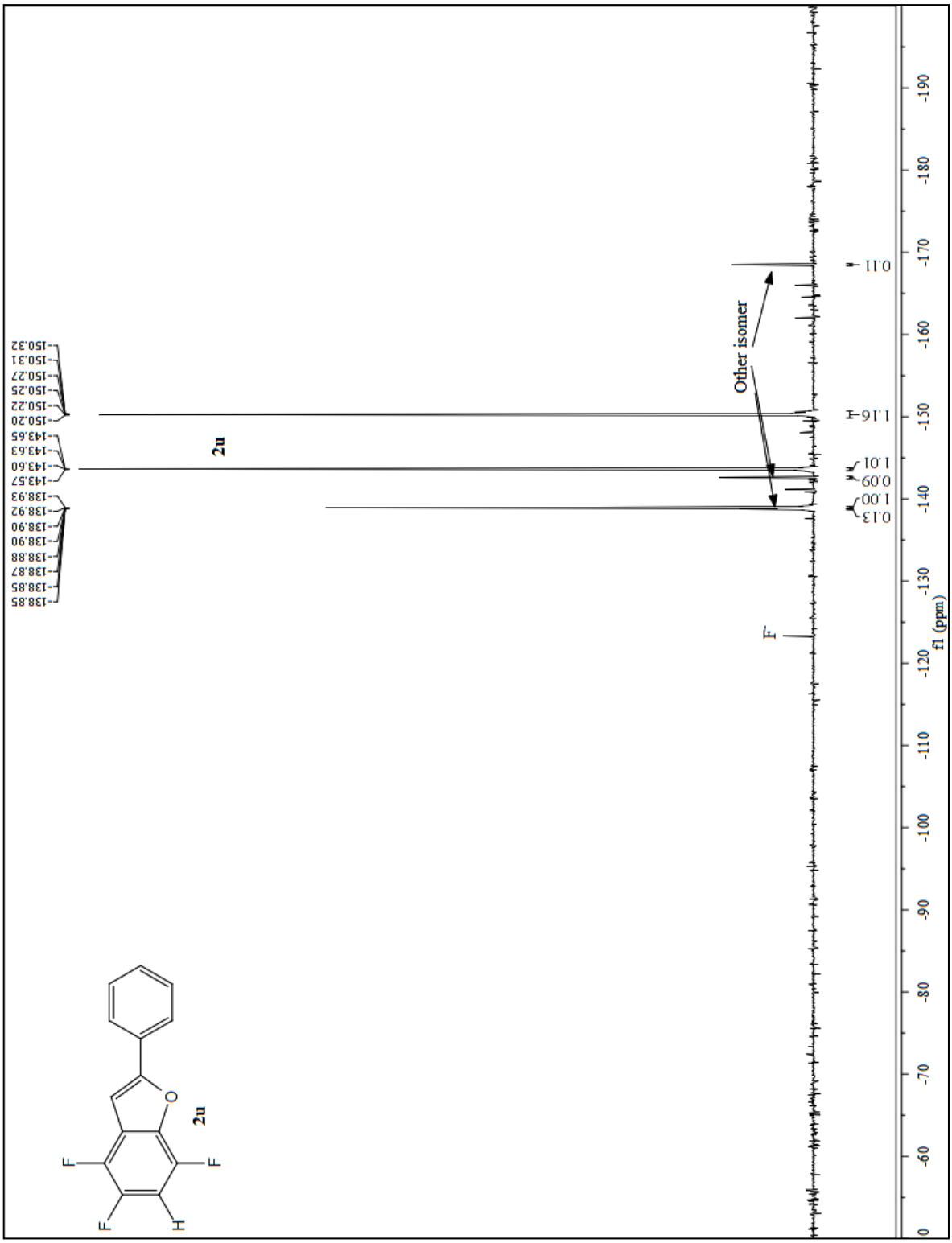
<u>2t</u> (1,2,4-trifluorodibenzo[b,e][1,4]dioxine)



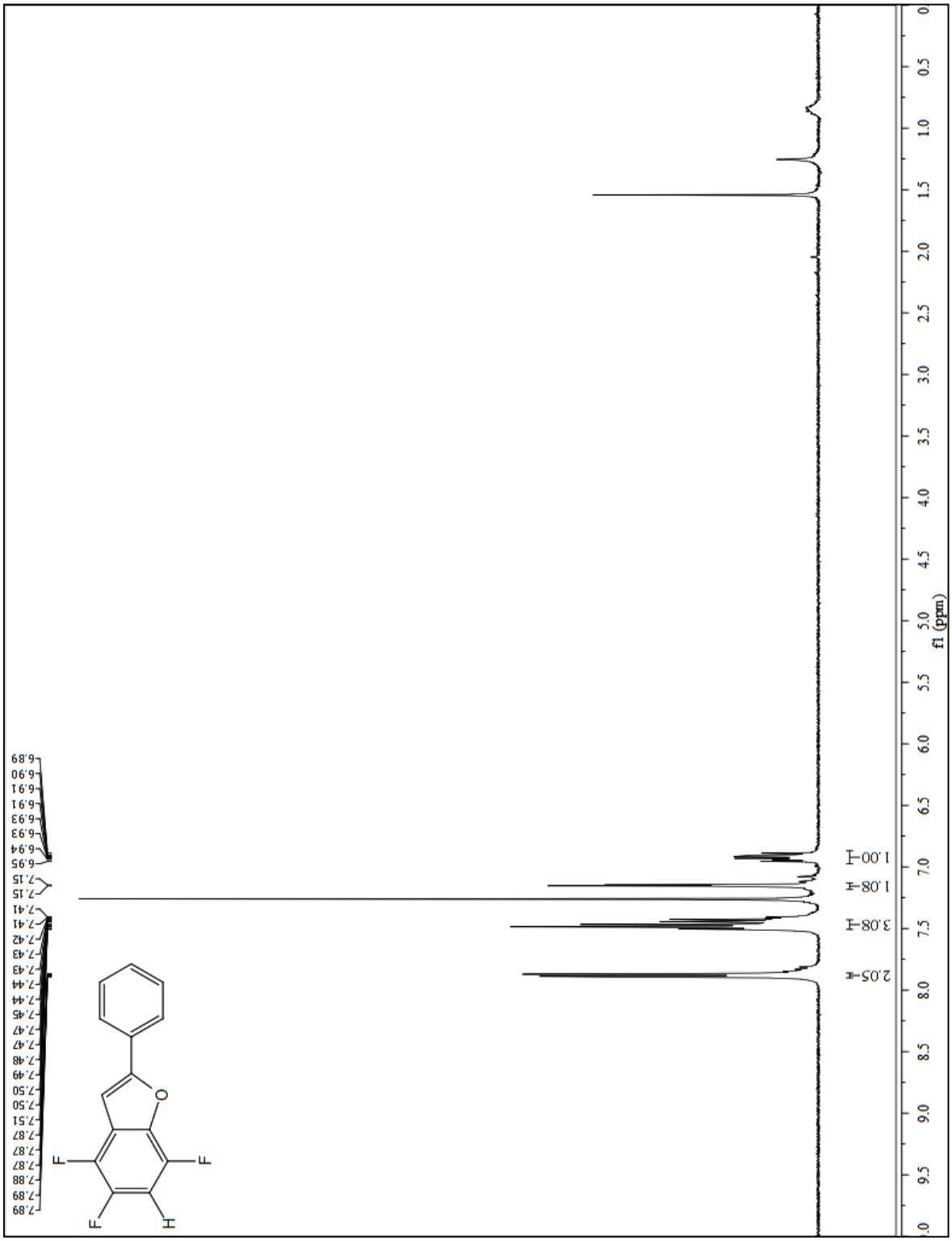
<u>2t</u> (1,2,4-trifluorodibenzo[b,e][1,4]dioxine)



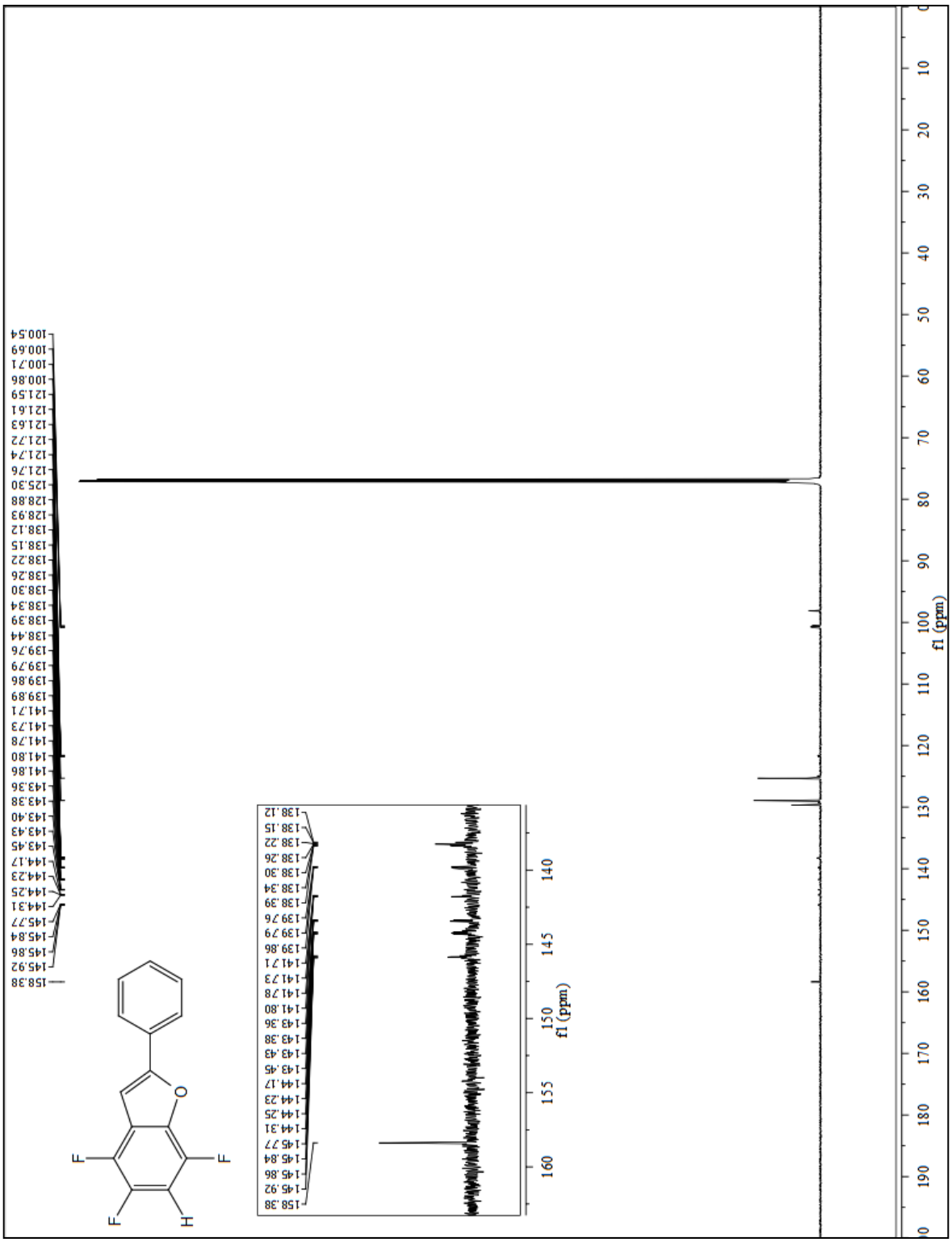
<u>2u</u> (4,5,7-trifluoro-2-phenylbenzofuran)



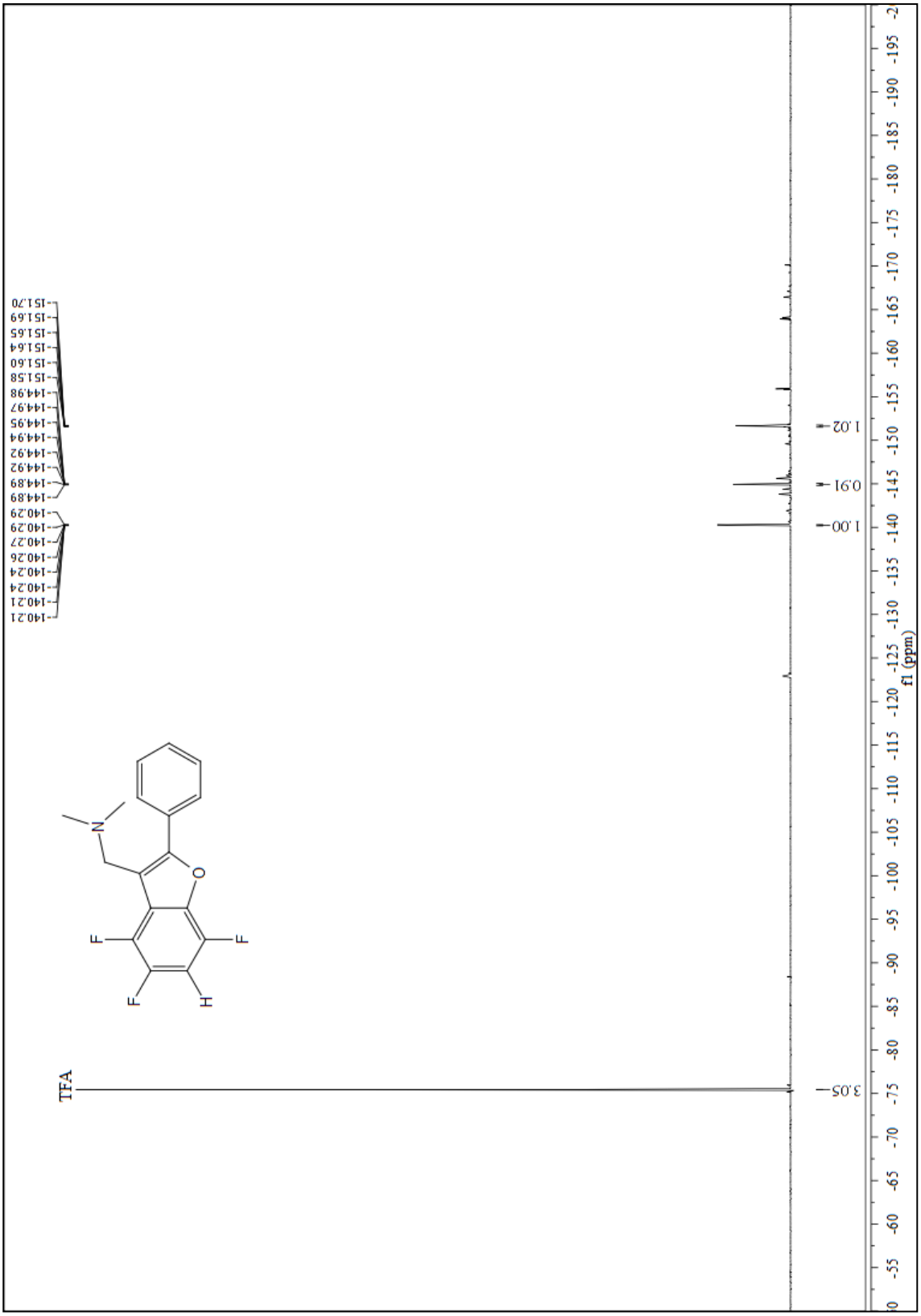
<u>2u</u> (4,5,7-trifluoro-2-phenylbenzofuran)



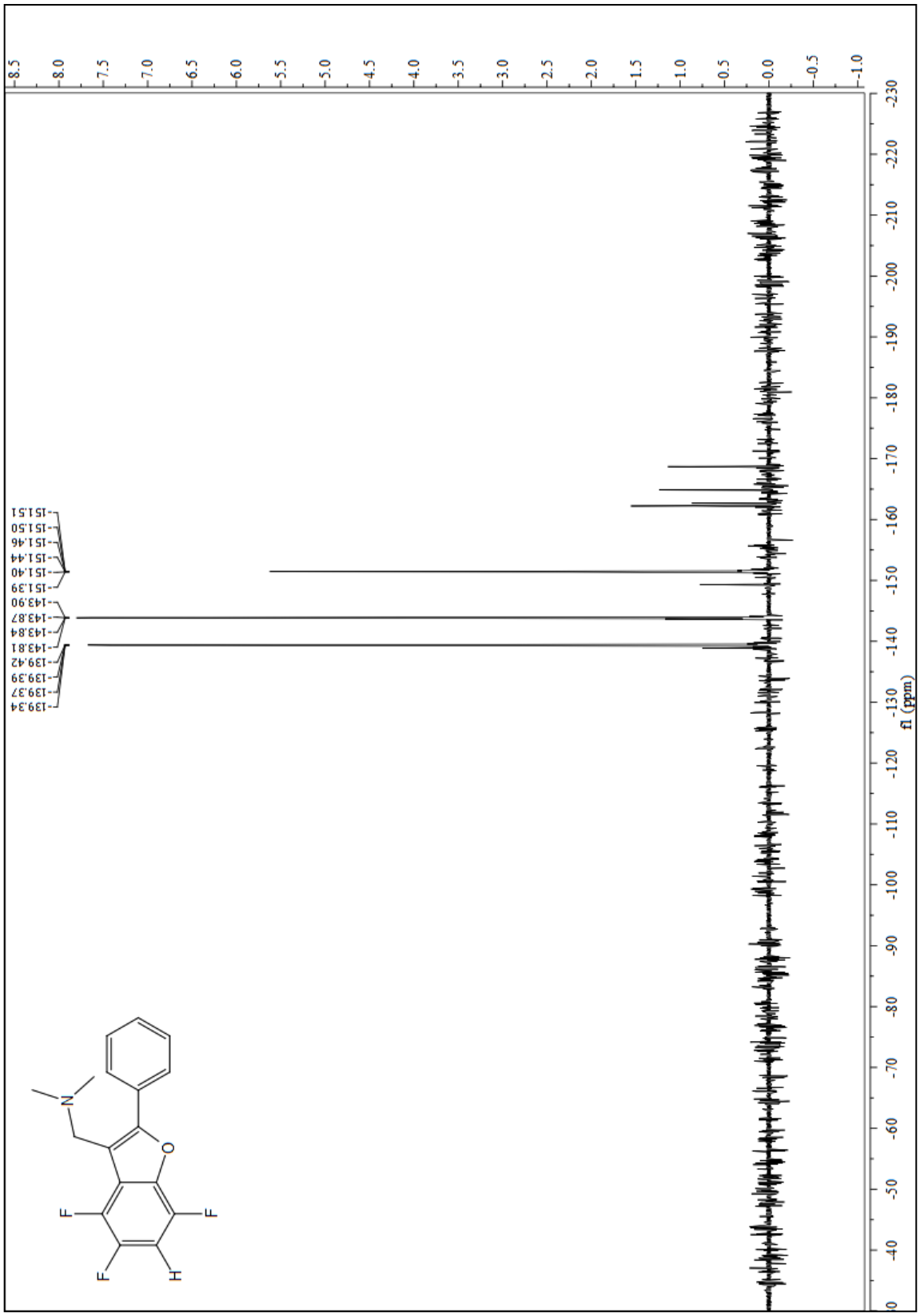
<u>2u</u> (4,5,7-trifluoro-2-phenylbenzofuran)



<u>2v</u> (*N*,*N*-dimethyl-1-(4,5,7-trifluoro-2-phenylbenzofuran-3-yl)methanamine) ^{19}F NMR yield

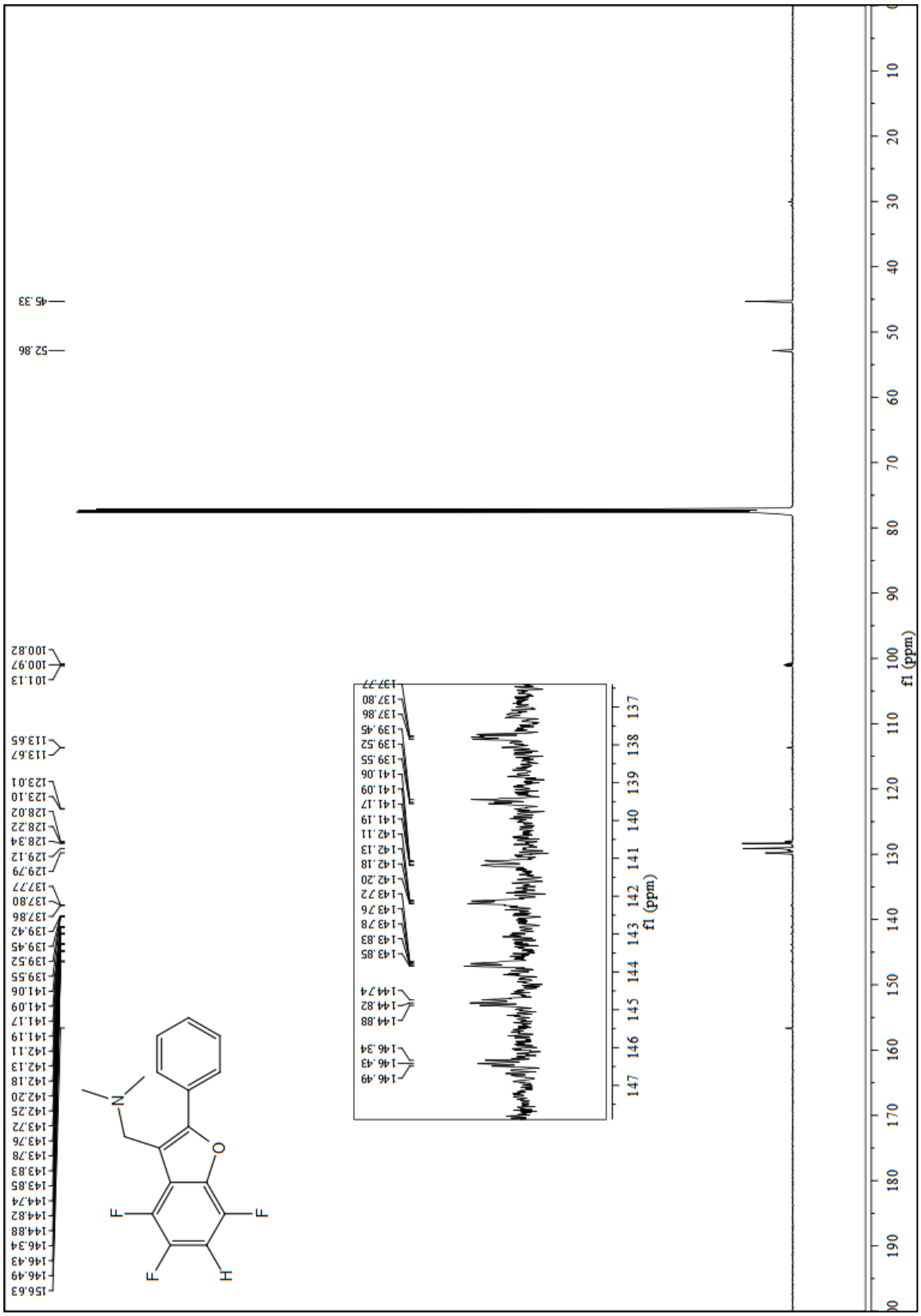


2v (***N,N*-dimethyl-1-(4,5,7-trifluoro-2-phenylbenzofuran-3-yl)methanamine)**

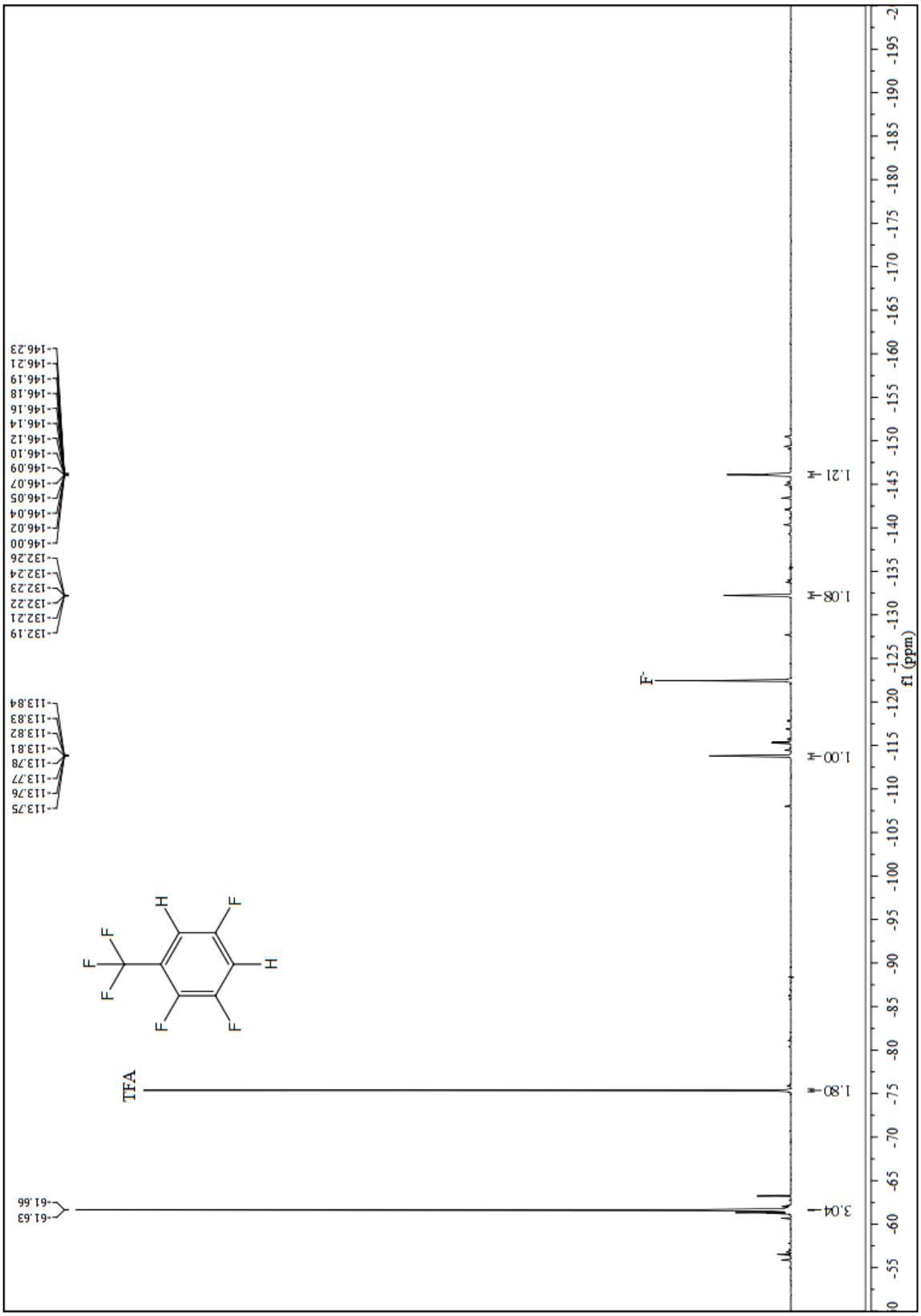


2v (***N,N*-dimethyl-1-(4,5,7-trifluoro-2-phenylbenzofuran-3-yl)methanamine)**

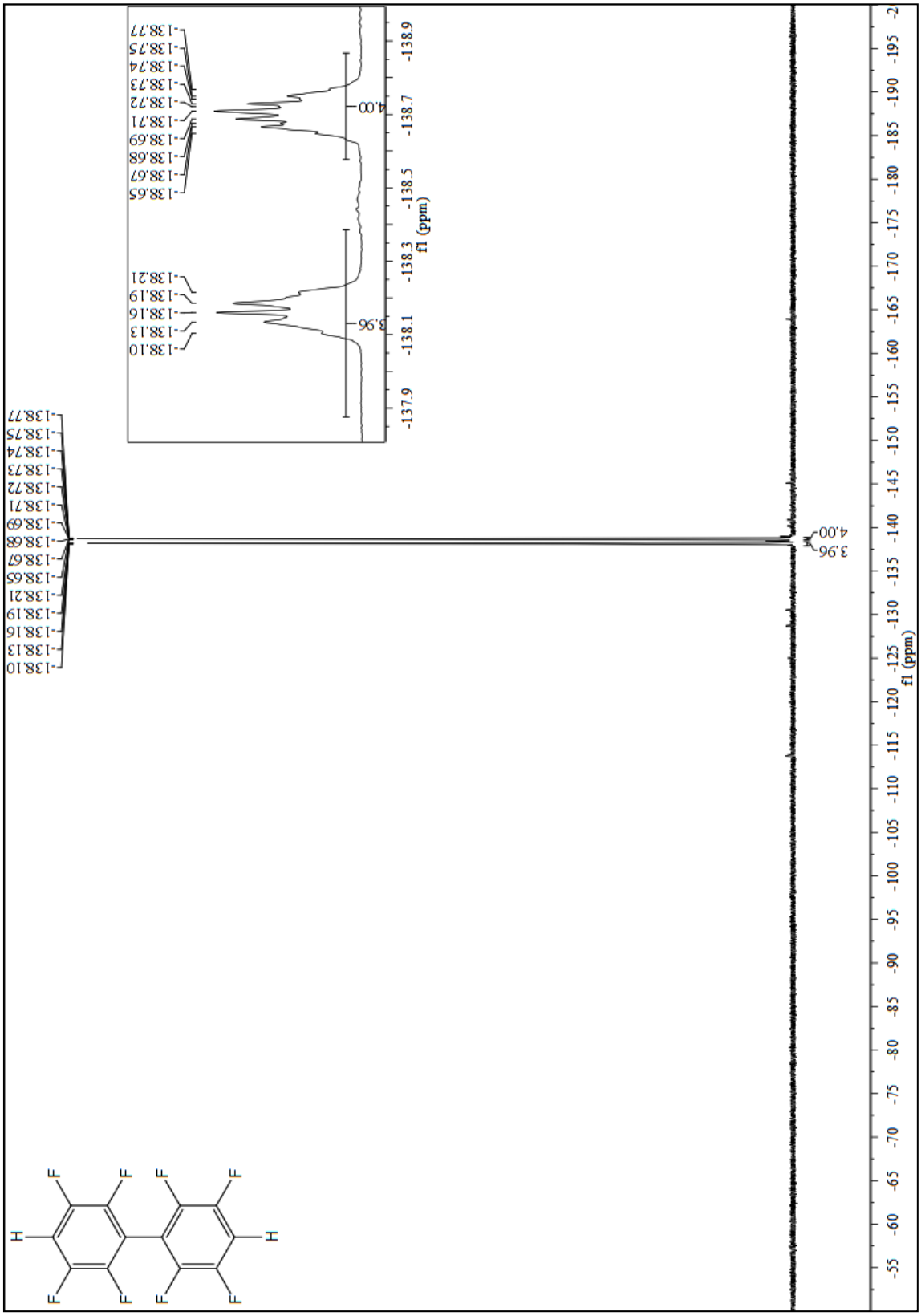
<u>2v</u> (*N*,*N*-dimethyl-1-(4,5,7-trifluoro-2-phenylbenzofuran-3-yl)methanamine)



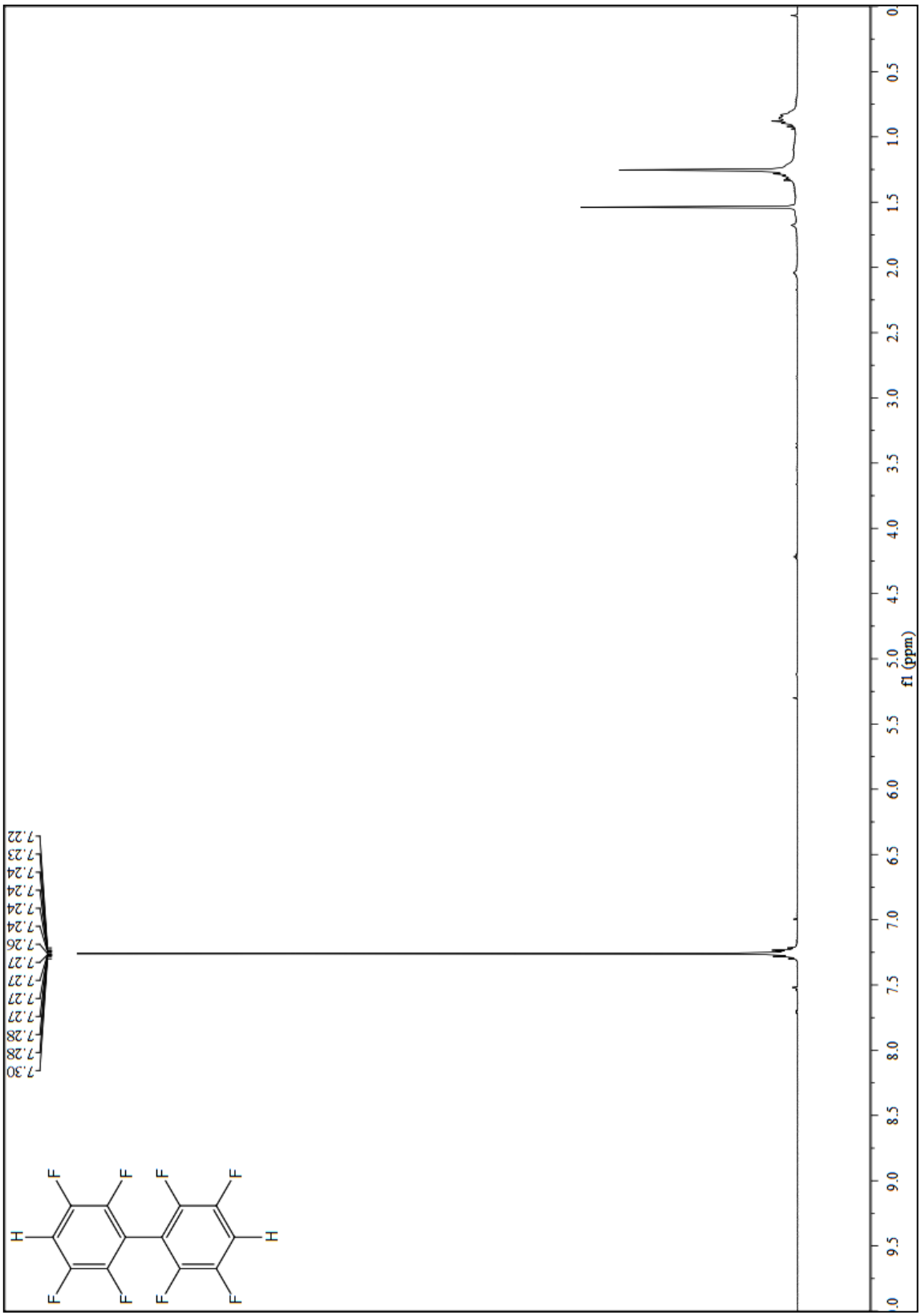
<u>3b</u> (1,2,5-trifluoro-3-(trifluoromethyl)benzene)



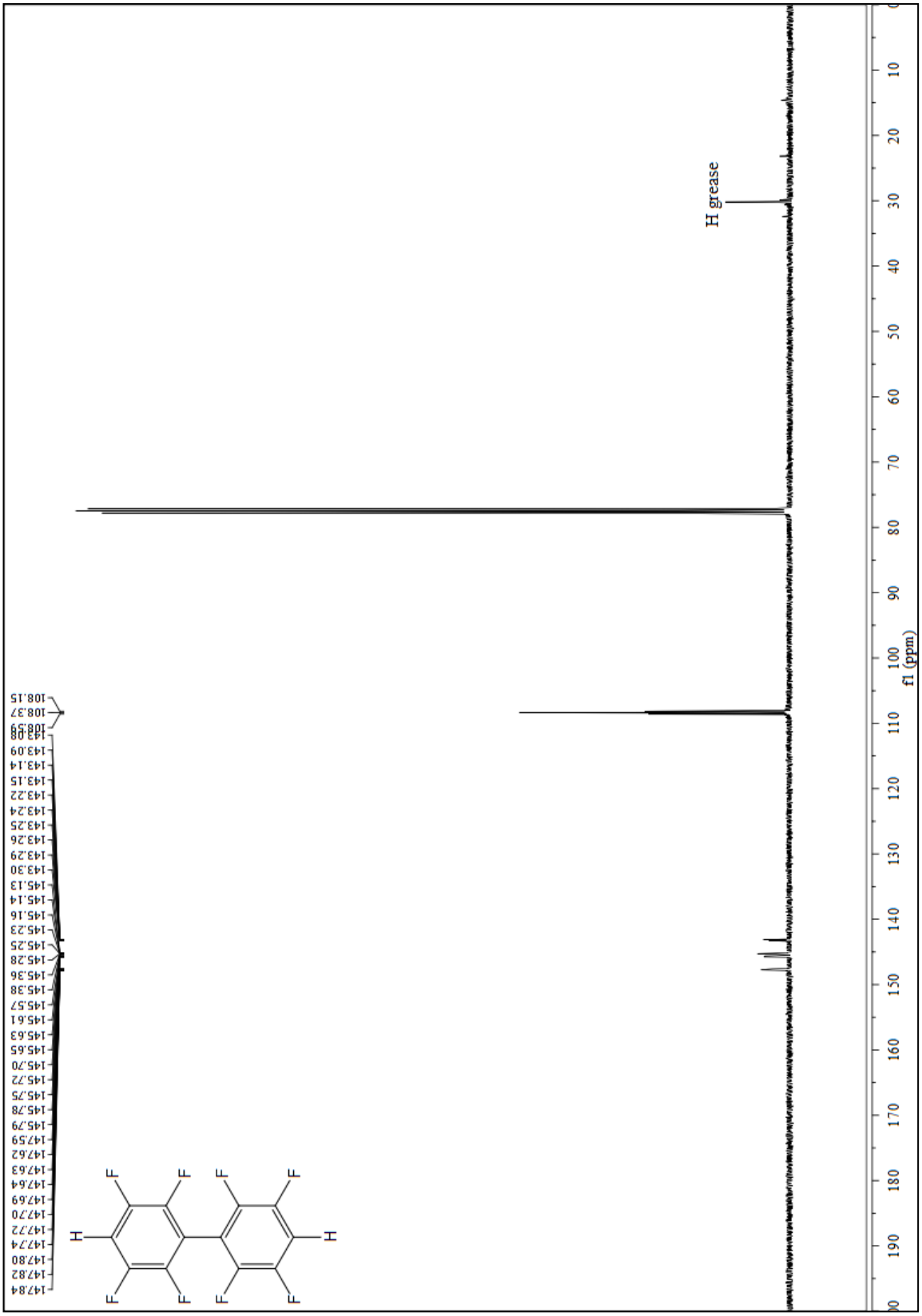
<u>3w</u> (2,2',3,3',5,5',6,6'-octafluoro-1,1'-biphenyl)



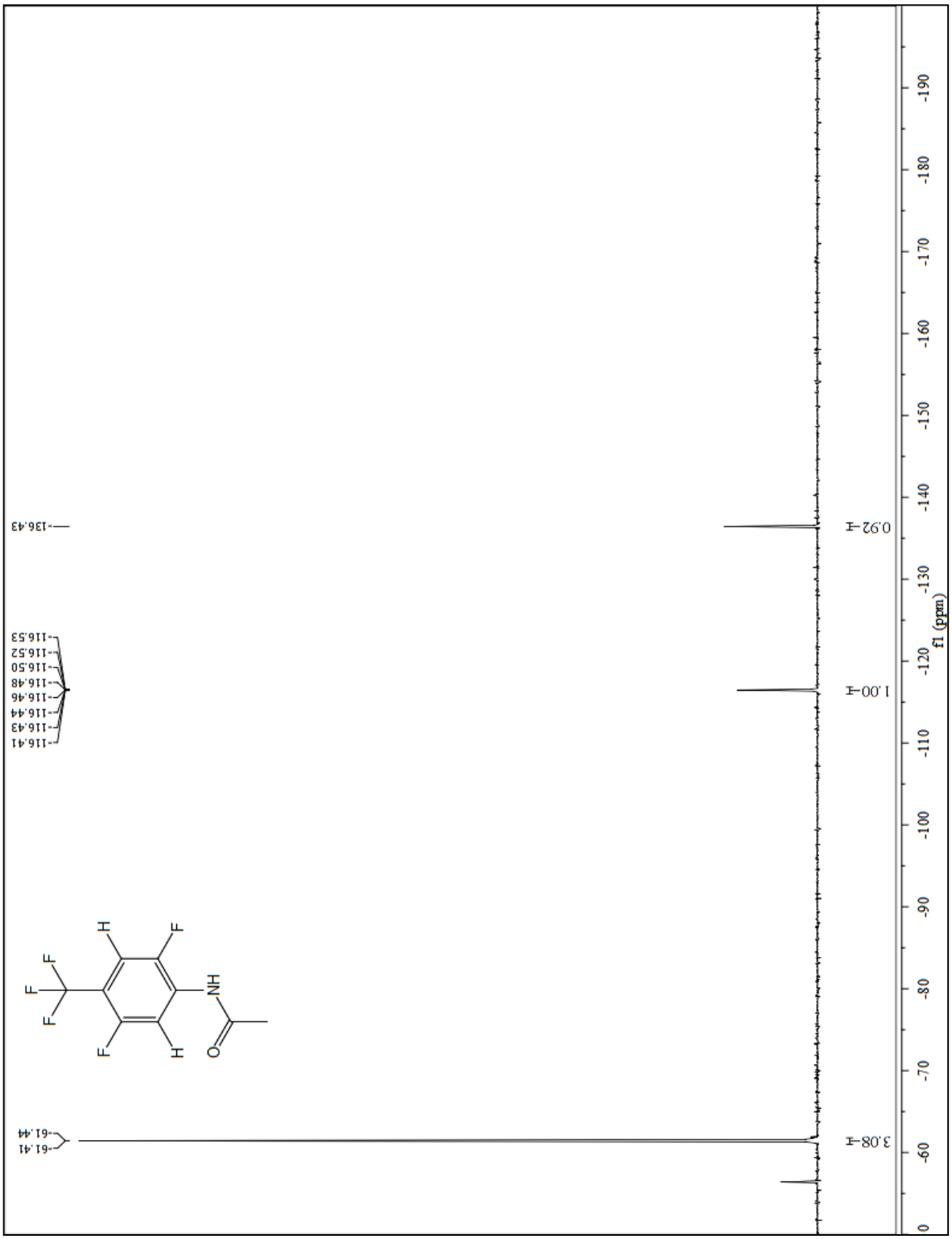
<u>3w</u> (2,2',3,3',5,5',6,6'-octafluoro-1,1'-biphenyl)



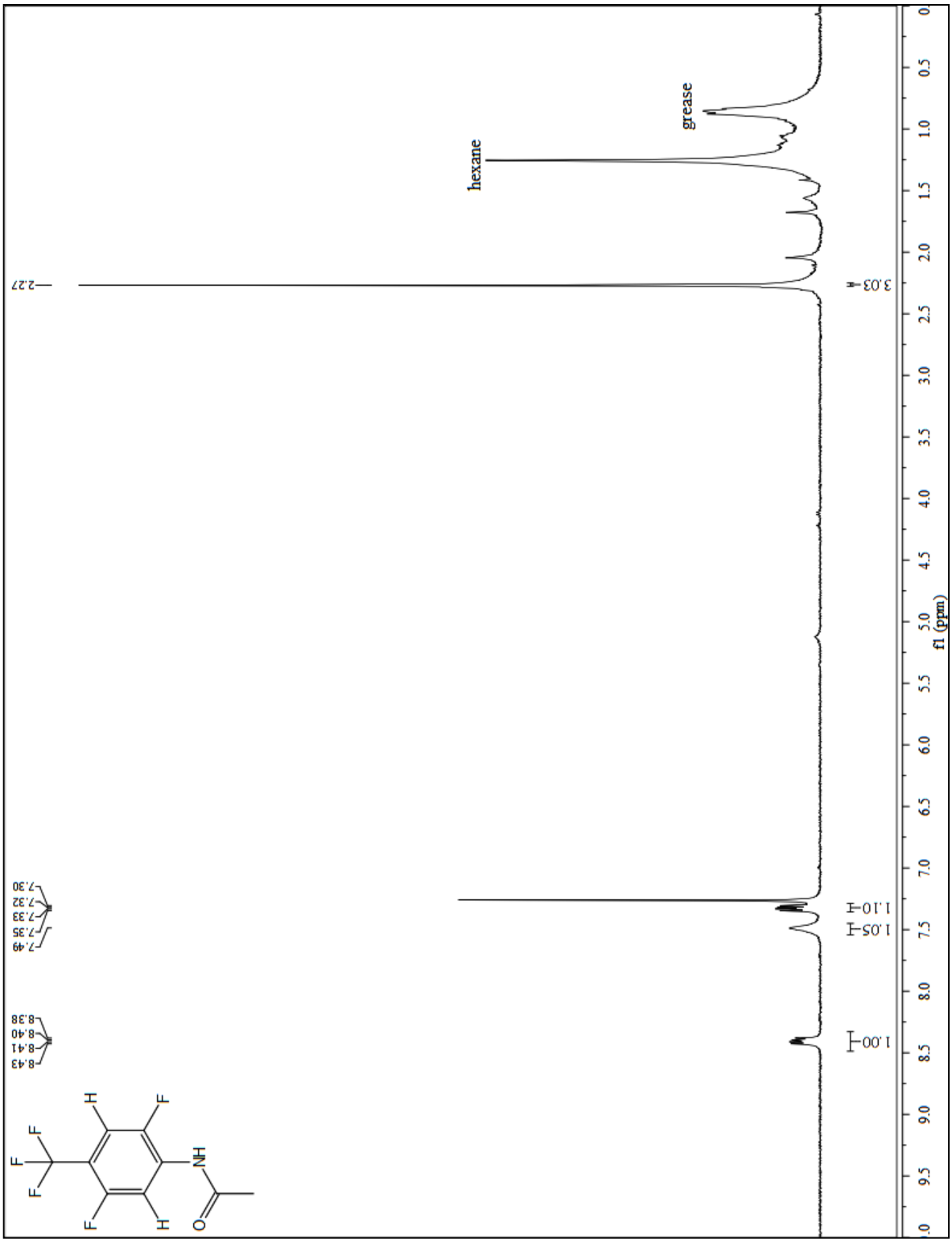
3w (2,2',3,3',5,5',6,6'-octafluoro-1,1'-biphenyl)



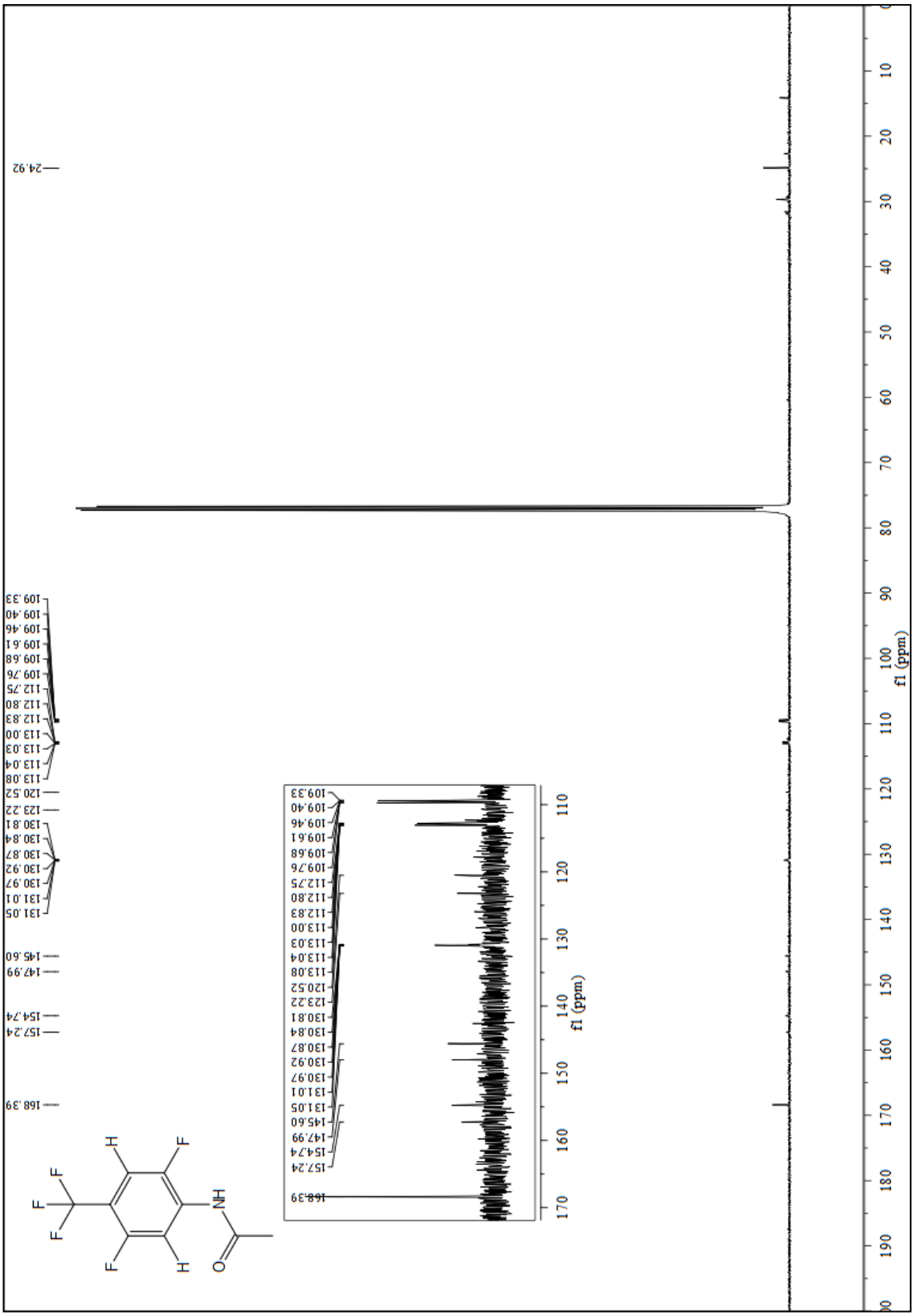
3r (N-(2,5-difluoro-4-(trifluoromethyl)phenyl)acetamide)



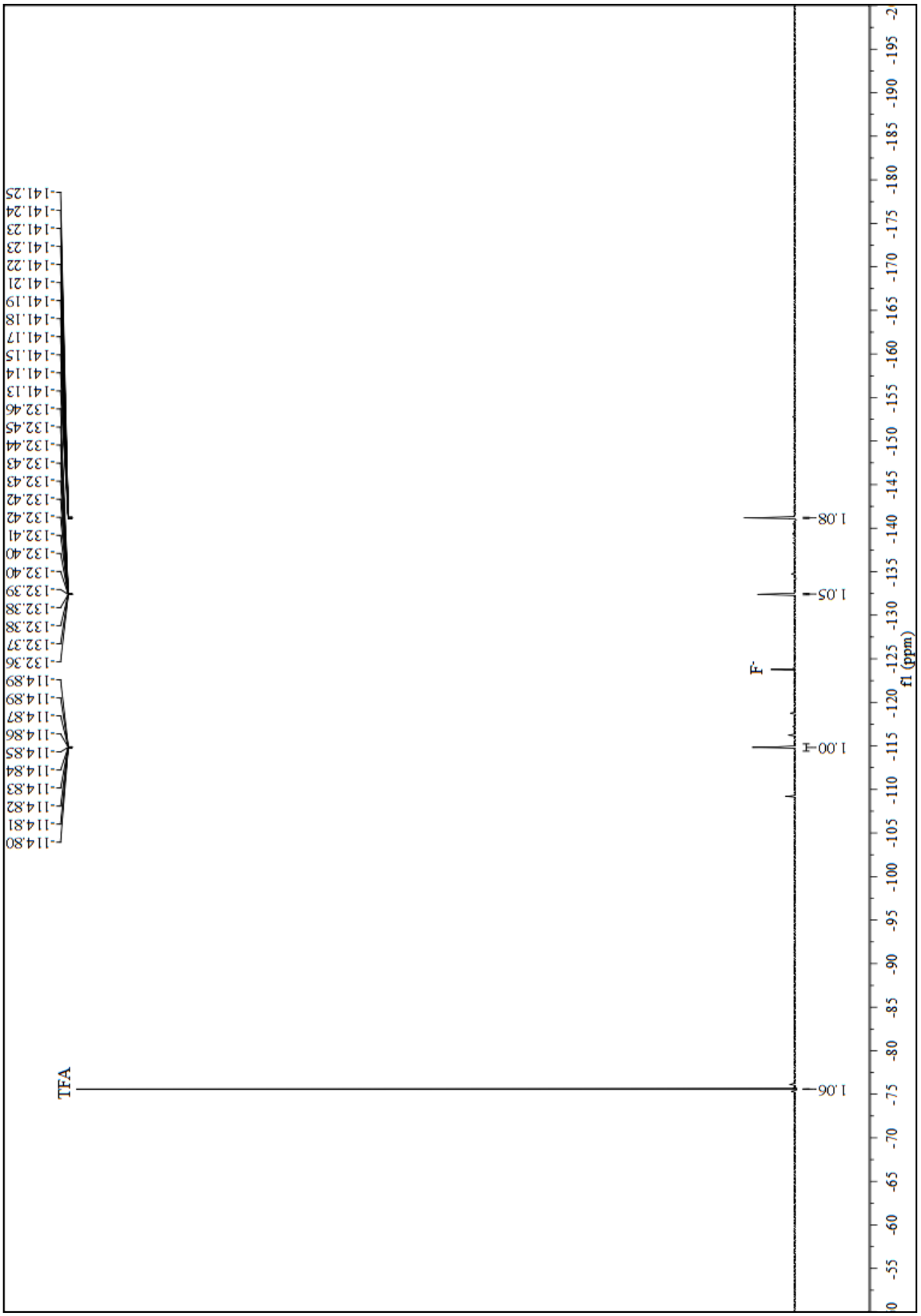
3r **(N-(2,5-difluoro-4-(trifluoromethyl)phenyl)acetamide)**



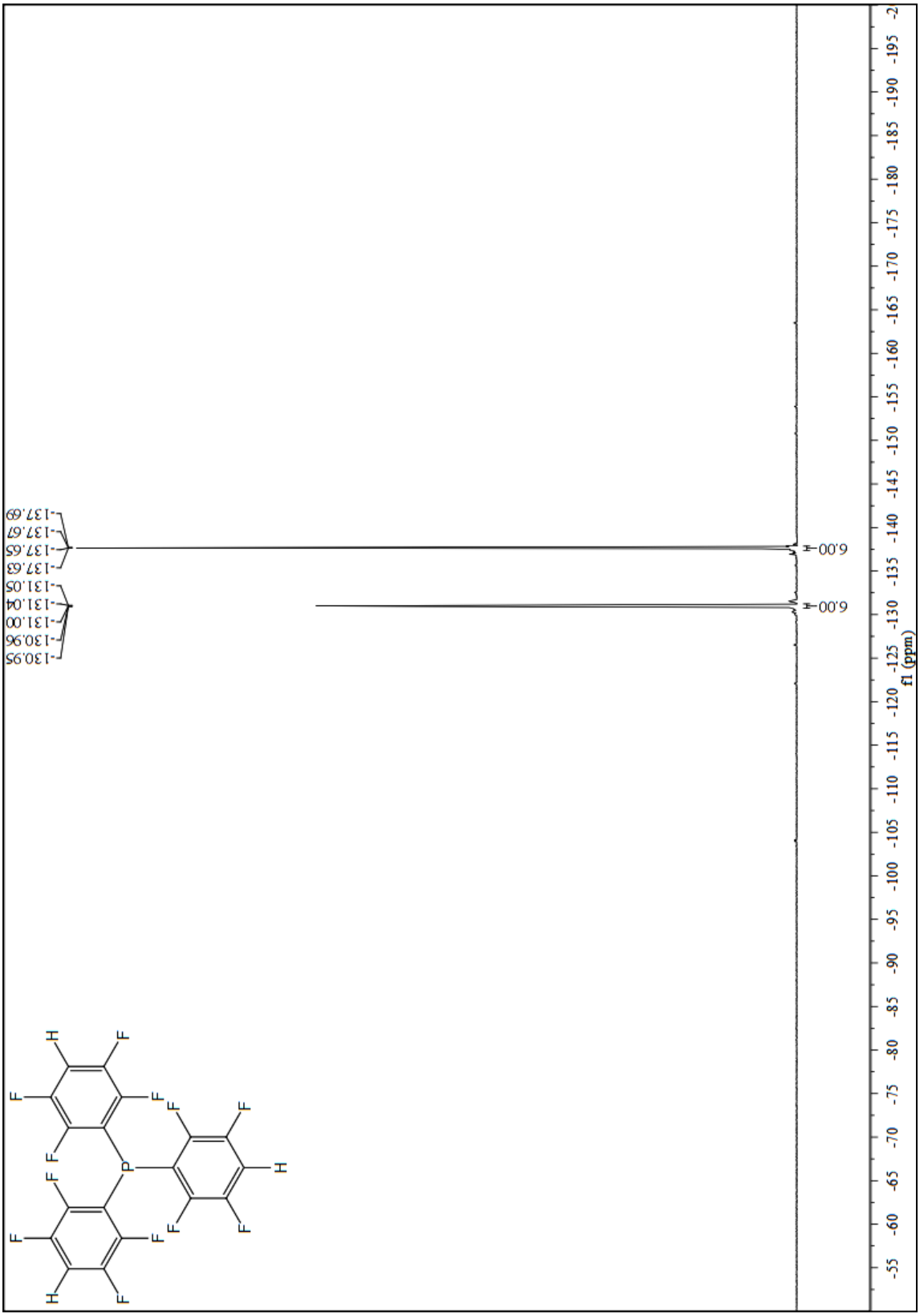
<u>3r</u> (N-(2,5-difluoro-4-(trifluoromethyl)phenyl)acetamide)



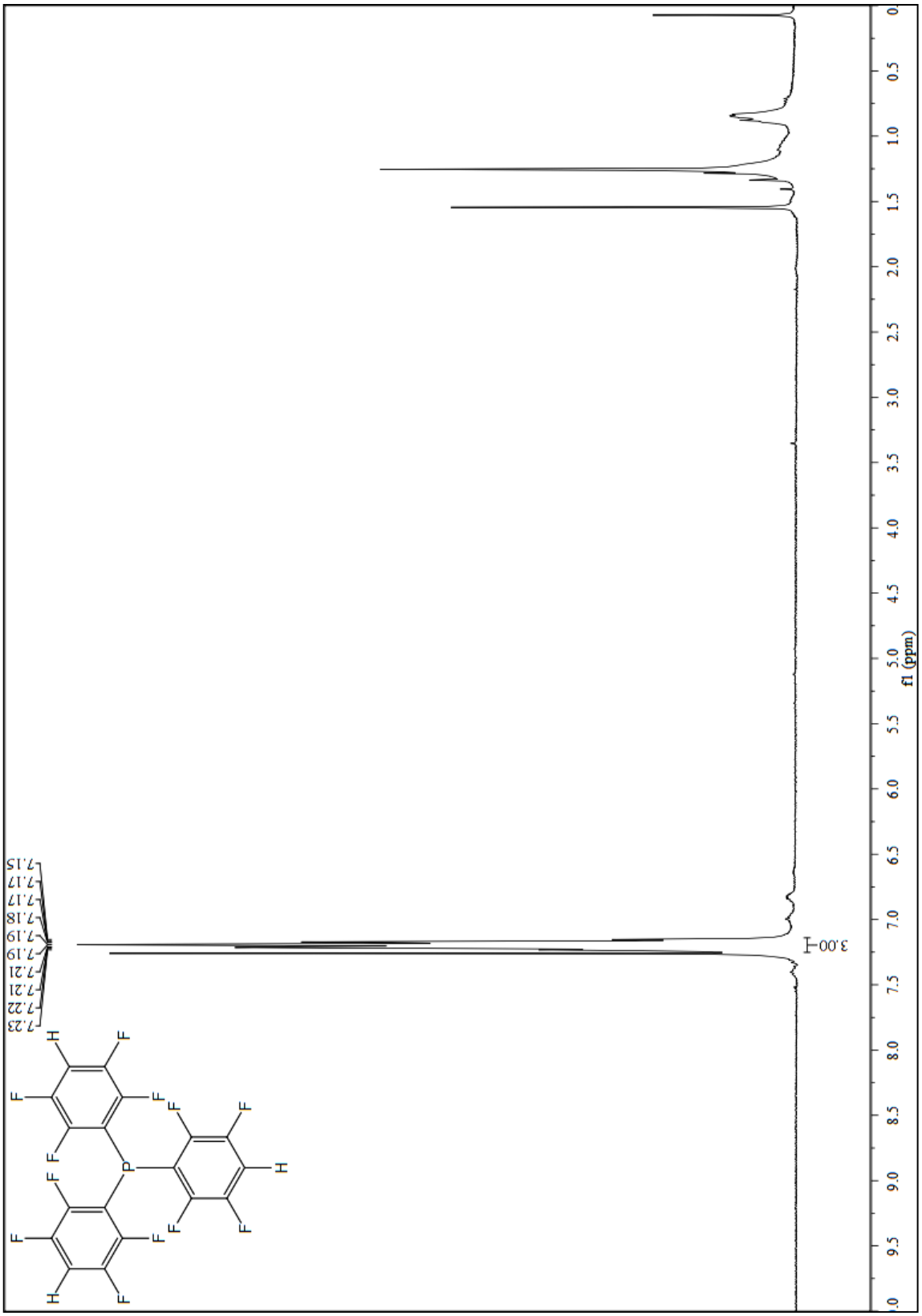
<u>3e</u> (methyl 2,3,5-trifluorobenzoate)



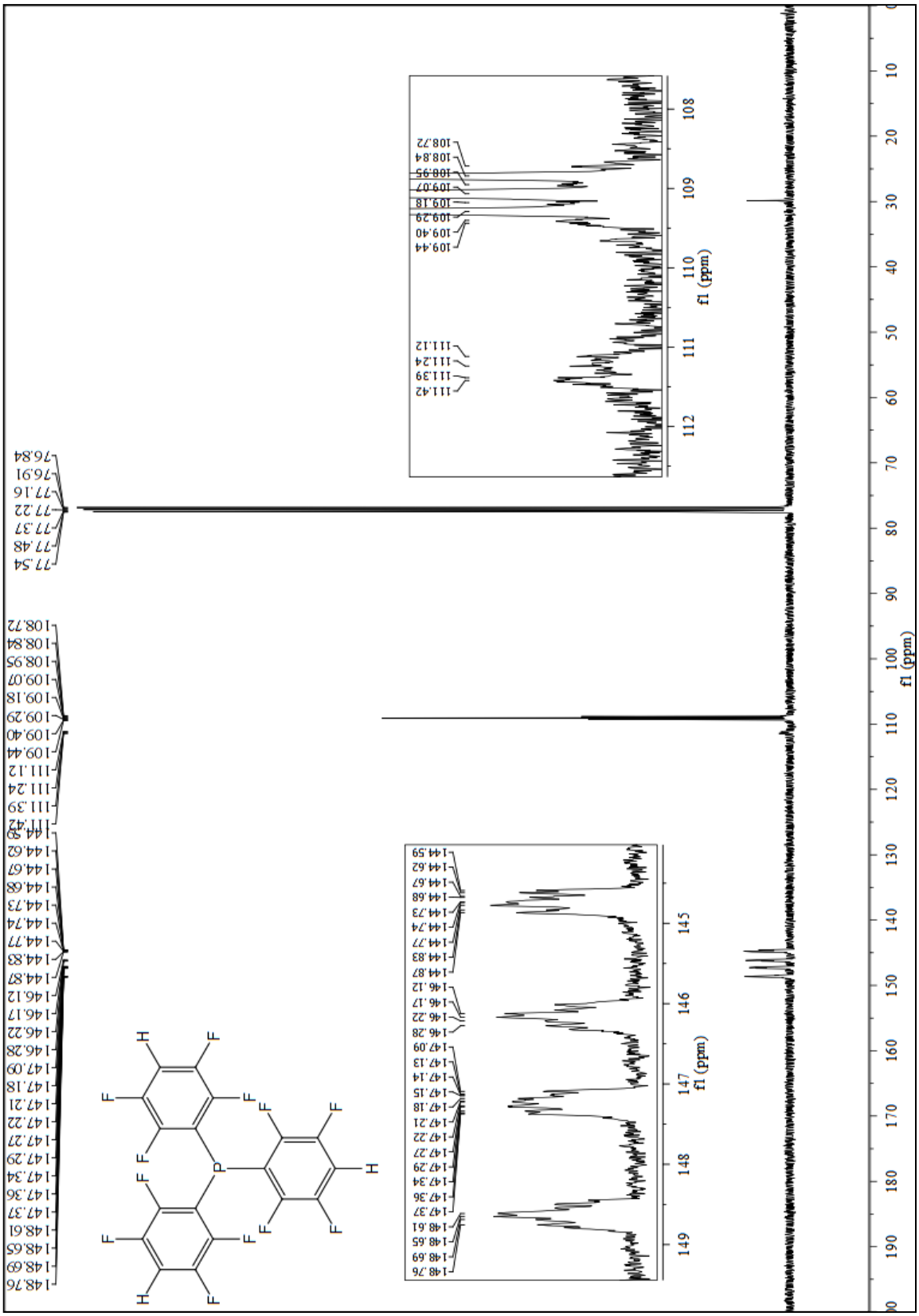
<u>3x</u> (tris(2,3,5,6-tetrafluorophenyl)phosphine)



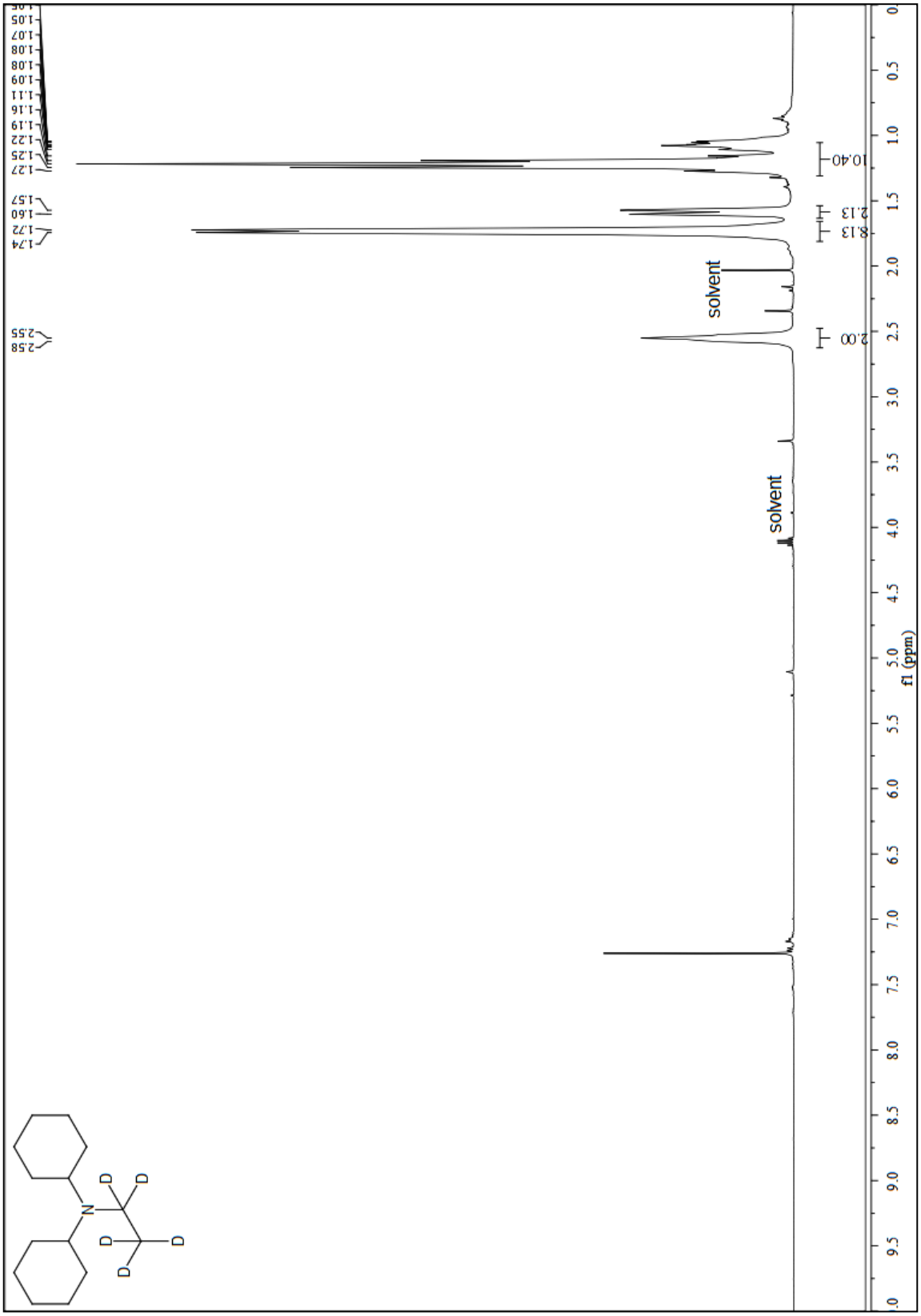
3x (tris(2,3,5,6-tetrafluorophenyl)phosphine)



3x (tris(2,3,5,6-tetrafluorophenyl)phosphine)



***N, N* -dicyclohexyl-*N*-d_5-ethylamine**



***N, N* -dicyclohexyl-*N*-d_5-ethylamine**