Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

for

Stereoselective metal-free catalytic synthesis of chiral trifluoromethyl aryl and alkyl amines.

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Table of Contents:

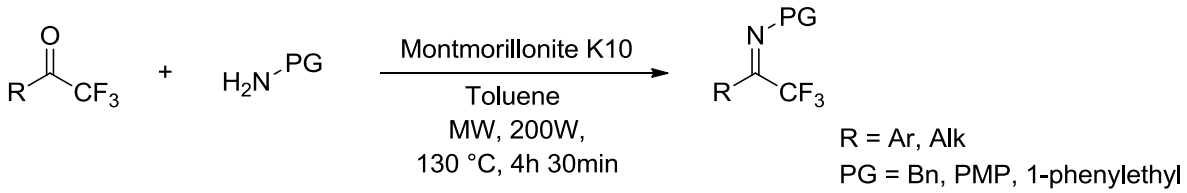
General Methods:

Dry solvents were purchased and stored under nitrogen over molecular sieves (bottles with crown caps). Reactions were monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F_{254} pre-coated glass plates (0.25 mm thickness) and visualized using UV light. Flash chromatography was carried out on silica gel (230-400 mesh). Proton NMR spectra were recorded on spectrometers operating at 300 MHz (Bruker Fourier 300 or AMX 300). Proton chemical shifts are reported in ppm (δ) with the solvent reference relative to tetramethylsilane (TMS) employed as the internal standard ($CDCl_3$ δ = 7.26 ppm). ^{13}C NMR spectra were recorded on 300 MHz spectrometers (Bruker Fourier 300 or AMX 300) operating at 75 MHz, with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ = 77.0 ppm). Reaction mixtures were centrifuged with MPW-260 laboratory centrifuge at 4500 rpm for 7 minutes. Enantiomeric excess determinations were performed under the conditions reported below with Agilent 1200 series HPLC. Mass spectra (MS) were performed at CIGA (Centro Interdipartimentale Grandi Apparecchiature), with mass spectrometer APEX II & Xmass software (Bruker Daltonics). Optical rotations were obtained on a polarimeter at 589 nm using a 5 mL cell with a length of 1 dm.

Starting materials: ethan-2,2,2-trifluoro-1-(4'-ethylphenoxyacetate)-1-ketone was prepared by literature method; all the other ketones (2,2,2-trifluoroacetophenone, 3'-methyl-2,2,2-trifluoroacetophenone, 4'-N,N-dimethylamino-2,2,2-trifluoroacetophenone, 4'-fluoro-2,2,2-trifluoroacetophenone, 4'-methyl -2,2,2-trifluoroacetophenone, 4'-methoxy -2,2,2-trifluoroacetophenone, 4'-chloro-2,2,2-trifluoroacetophenone, 4'-trifluoromethyl -2,2,2-trifluoroacetophenone, 1-cyclohexyl-2,2,2-trifluoro-ethanone, 1,1,1-trifluoro-2-butanone, 1,1,1-trifluoro-2-hexanone, 1,1,1-trifluoro-3-phenyl-2-propanone) and amines (4-methoxyaniline, benzylamine, 1-phenylethylamine) were obtained commercially. $HSiCl_3$ was freshly distilled before use.

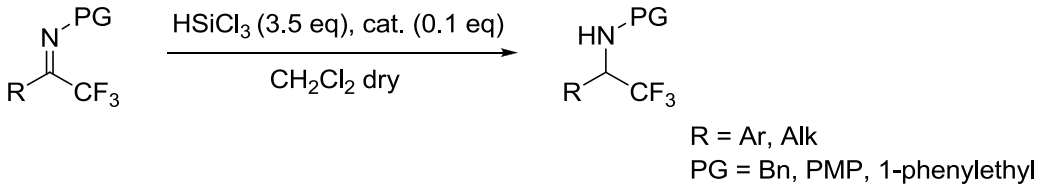
General procedures:

Imine synthesis:



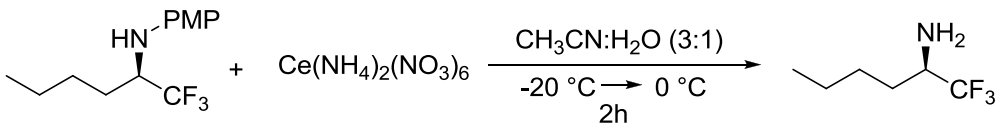
Toluene (6 mL), montmorillonite K10 (150 mg per 0.3 mmol), the amine (0.3 mmol, 1 eq.) and the ketone (0.3 mmol, 1 eq.) were introduced in a 25 mL vial. The stirred mixture was subjected to 200 W microwave irradiation and heated to 130 °C for 4 h 30 min. Constant microwave irradiation as well as simultaneous air-cooling (2 bar) were used during the entire reaction time. After cooling to room temperature, montmorillonite was removed by settling and subsequent centrifuge; finally the solvent was removed under reduced pressure. Purification methods for each product are reported below.

Imine reduction:



The catalyst (0.02 mmol, 0.1 eq.) and a solution 0.7 M of the imine in dry CH_2Cl_2 (0.2 mmol, 1 eq.) were introduced in a 10 mL vial under N_2 atmosphere and further diluted in 1 mL of dry CH_2Cl_2. The mixture was cooled to the desired temperature (see tables) and stirred for 15 min, after which a solution 1.6 M in CH_2Cl_2 of $HSiCl_3$ (0.7 mmol, 3.5 eq.) was added. The reaction mixture was stirred for the reported time (see tables). The reaction mixture was quenched with NaOH 10% aq. until a basic pH was reached. The mixture was stirred at room temperature for 30 min, filtered over celite pad and washed with CH_2Cl_2. The solvent was removed under reduced pressure and the desired amines were purified by flash column chromatography on silica gel.

Aliphatic amine deprotection[13]:

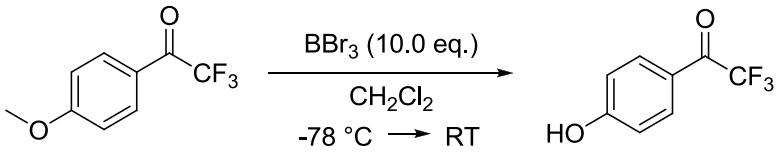


A solution of ammonium cerium (IV) nitrate (1.8 mmol, 5.0 eq.) in H_2O (2 mL) was added dropwise to a solution of the amine (0.36 mmol, 1.0 eq.) in CH_3CN (6 mL) at -20 °C. The temperature was allowed to rise till 0 °C and the reaction mixture was stirred at this temperature for 2 h. The solution was extracted with ethyl acetate, the collected organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The desired product was obtained in 80% yield on the crude product.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.04 (brs, 2H), 3.97-3.79 (m, 1H), 2.02-1.87 (m, 2H), 1.64-1.31 (m, 4H), 0.96-0.91 (m, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 124.60 (q, J = 281Hz), 53.82 (q, J = 31Hz), 27.19, 22.67, 13.95.
^{19}F NMR (300 MHz, $CDCl_3$) δ: -75.17.

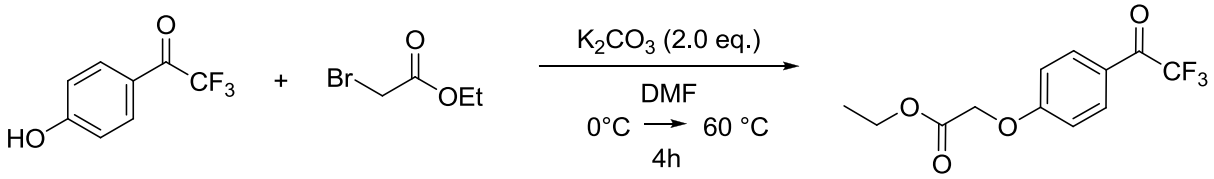
ethan-2,2,2-trifluoro-1-(4'-ethylphenoxyacetate)-1-ketone synthesis:

Demethylation[14] :



BBr_3 (14.7 mL, 1M solution in CH_2Cl_2, 14.7 mmol, 10.0 eq.) was slowly added at -78 °C to a solution of the substrate (1.47 mmol, 1.0 eq.) in dry CH_2Cl_2 (2.7 mL). The mixture was allowed to reach room temperature and stirred overnight. Then the reaction mixture was cooled to 0°C and quenched by addition of NaOH 10% aq. (20 mL). The aqueous phase was separated, extracted with CH_2Cl_2 and acidified with HCl 37% aq. up to pH = 2. Then NH_4OH was added to the solution until a basic pH was reached. The acqueous phase was extracted again with *n*-butanol. The collected organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The desired product was purified by flash column chromatography on silica gel with a 95:5 hexane/ethyl acetate mixture as eluent. The purification afforded the desired product in 88% yield.
R_f = 0.16 (9:1 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.00 (d, 2H, J = 9Hz), 6.96 (d, 2H, J = 9Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 179.35 (q, J = 34Hz), 162.44, 133.25, 122.77, 116.89 (q, J = 289 Hz), 116.14.
^{19}F NMR (300 MHz, $CDCl_3$) δ: -71.45.

Alkylation[15] :



K_2CO_3 (1.1 mmol, 2.0 eq.) and ethyl bromoacetate (0.63mmol, 1.1 eq.) were added to an ice-cold solution of the ketone (0.56 mmol, 1.0 eq.) in DMF (0.5 mL) under N_2 atmosphere. The reaction mixture was heated to 60 °C and stirred at this temperature for 4 h. The reaction mixture was washed with ice-cold water and extracted with ethyl acetate. The collected organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure.
The desired product was purified by flash column chromatography on silica gel with a 9:1 hexane/ethyl acetate mixture as eluent. The purification afforded the desired product in 33% yield.
R_f = 0.22 (9:1 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.04 (d, 2H, J = 9Hz), 7.00 (d, 2H, J = 9Hz), 4.7 (s, 2H), 4.27 (q, 2H, J = 7Hz), 1.29 (t, 3H, J = 7Hz).

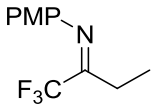
^{13}C NMR (75 MHz, $CDCl_3$) δ: 178.38 (q, J = 35Hz), 167.20, 162.92, 130.16, 123.17, 116.29 (q, J = 289 Hz), 114.46, 64.65, 61.19, 13.52.

^{19}F NMR (300 MHz, $CDCl_3$) δ: -72.21.

Products characterization:

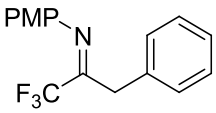
Imines:

N-(4'-Methoxyphenyl)-butan-1,1,1-trifluoro-2-imine (9)



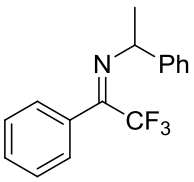
This product was purified by flash column chromatography on silica gel with a 9:1 hexane/ethyl acetate mixture as eluent. The purification afforded the desired product in 40% yield.
R_f = 0.37 (9:1 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.94 (d, 2H, J = 9Hz), 6.76 (d, 2H, J = 9Hz), 3.82 (s, 3H), 2.46 (q, 2H, J = 8Hz), 1.14 (t, 3H, J = 8Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.00 (q, J = 31Hz), 157.16, 154.59, 120.09, 120.05 (q, J = 278Hz), 114.38, 55.40, 21.80, 11.23.
^{19}F NMR (300 MHz, $CDCl_3$) δ: -76.11.

N-(4'-Methoxyphenyl)-3-phenylpropan-1,1,1-trifluoro-2-imine (13[5])



This product was purified by flash column chromatography on silica gel with a 9:1 hexane/ethyl acetate mixture as eluent. The purification afforded the desired product in 14% yield.
R_f = 0.44 (9:1 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.30-7.23 (m, 3H), 7.08-7.05 (m, 2H), 6.91 (d, 2H, J = 9Hz), 6.82 (d, 2H, J = 9Hz), 3.88 (s, 2H), 3.80 (s, 3H).
^{19}F NMR (300 MHz, $CDCl_3$) δ: -70.78.

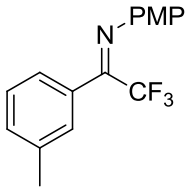
N-(1'-Phenylethyl)-ethan-2,2,2 -trifluoro-1-phenyl-1-imine (5-7)



This product was purified by distillation at P = 3 x 10^{-2} mbar and T = 130 °C. The purification afforded the desired product in 30% yield.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.54-7.52 (m, 3H), 7.39-7.29 (m, 5H), 7.24-7.22 (m, 2H), 4.58 (q, 1H, J = 7Hz), 1.46 (d, 3H, J = 7Hz).

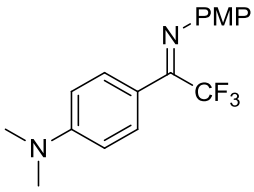
^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.65 (q, J = 33Hz), 143.84, 130.61, 130.08, 128.82, 128.67, 127.64, 127.30, 126.51, 119.87 (q, J = 278Hz), 61.44, 24.58.
^{19}F NMR (300 MHz, $CDCl_3$) δ: -71.46.

N-(4'-Methoxyphenyl)-ethan-2,2,2 -trifluoro-1-(3''-methylphenyl)-1-imine (Table 3, Entry 6)



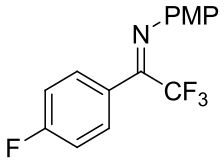
This product was purified by flash column chromatography on silica gel with a 95:5 hexane/ethyl acetate mixture as eluent. The purification afforded the desired product in 60% yield.
R_f = 0.23 (95:5 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.25-7.21 (m, 2H), 7.12-7.04 (m, 2H), 6.82-6.73 (m, 4H), 3.74 (s, 3H), 2.32 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.86, 155.49 (q, J = 34Hz), 139.77, 138.64, 130.74, 130.29, 128.85, 128.62, 125.71, 123.43, 120.19 (q, J = 276Hz), 113.96, 55.14, 21.24.
^{19}F NMR (300 MHz, $CDCl_3$) δ: -70.28.

N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-(N',N'-dimethylammino)-phenyl)-1-imine (Table 3, Entry 9)



This product was purified by flash column chromatography on silica gel with a 8:2 hexane/ethyl acetate mixture as eluent to remove the unreacted 4-methoxyaniline, followed by distillation at P = 3 x 10^{-2} mbar and T = 270 °C to remove the unreacted ketone. The purification afforded the desired product in 71% yield.
R_f = 0.15 (8:2 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.16 (d, 2H, J = 9Hz), 6.81-6.74 (m, 4H), 6.56 (d, 2H, J = 9Hz), 3.78 (s, 3H), 2.98 (s, 6H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.06, 155.40 (q, J = 33Hz), 151.04, 141.19, 130.41, 122.56, 116.73 (q, J = 278Hz), 116.63, 114.13, 111.14, 55.30, 39.88.
^{19}F NMR (300 MHz, $CDCl_3$) δ: -69.21.

N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-fluorophenyl)-1-imine (Table 3, Entry 4)



This product was purified by flash column chromatography on silica gel with a 95:5 hexane/ethyl acetate mixture as eluent. The purification afforded the desired product in 47% yield.

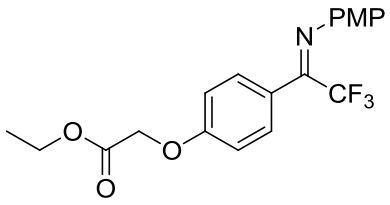
R_f = 0.29 (95:5 hexane/ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.16-7.12 (m, 2H), 6.96-6.90 (m, 2H), 6.64-6.62 (m, 4H), 3.65 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.39 (d, J = 250Hz), 157.90, 154.31 (q, J = 34Hz), 139.54, 130.96, 130.84, 126.61, 123.16, 119.94 (q, J = 277Hz), 116.21, 115.92, 114.12, 55.28.

^{19}F NMR (300 MHz, $CDCl_3$) δ: -70.37, -109.28.

N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-ethylphenoxyacetate)-1-imine (Table 3, Entry 10)



This product was purified by flash column chromatography on silica gel with a 85:15 hexane/ethyl acetate mixture as eluent. The purification afforded the desired product in 31% yield.

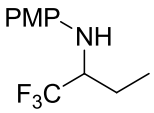
R_f = 0.25 (9:1 hexane/ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.18 (d, 2H, J = 9Hz), 6.83 (d, 2H, J = 9Hz), 6.74-6.72 (m, 4H), 4.59 (s, 2H), 4.25 (q, 2H, J = 7Hz), 3.75 (s, 3H), 1.28 (t, 3H, J = 7Hz).

^{19}F NMR (300 MHz, $CDCl_3$) δ: -70.11.

Amines:

N-(4'-Methoxyphenyl)-butan-1,1,1-trifluoro-2-amine (10)



This product was purified by flash column chromatography on silica gel with a 95:5 hexane/ethyl acetate mixture as eluent.

R_f = 0.45 (8:2 hexane/ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.78 (d, 2H, J = 9Hz), 6.64 (d, 2H, J = 9Hz), 3.75 (s, 3H), 3.71-3.59 (m, 1H), 3.27 (brs, 1H), 2.00-1.86 (m, 1H), 1.64-1.49 (m, 1H), 1.05 (t, 3H, J = 8Hz).

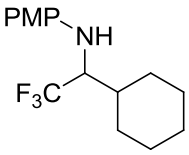
^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.56, 135.41, 128.69, 128.58, 128.18, 126.67, 126.04 (q, J = 281Hz), 61.66 (q, J = 28Hz), 56.03, 23.53, 14.07.

^{19}F NMR (300 MHz, CDCl3) δ: -76.30.

HRMS Mass (ESI+): m/z = calc. for $C_{11}H_{15}NOF_3^+$ = 234.11, found 234.11 [M + H].

The enantiomeric excess was determined by chiral HPLC with Daicel Chiralcel OD-H column, eluent: 99:1 Hex/IPA; 0.8 mL/min flow rate, detection: 242 nm, t_R 10.05 min (major), t_R 12.14 min (minor).

N-(4'-Methoxyphenyl)-ethan-1,1,1-trifluoro-2-cyclohexyl-2-amine (15)



This product was purified by flash column chromatography on silica gel with a 99:1 hexane/ethyl acetate mixture as eluent.

R_f = 0.42 (9:1 hexane/ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.83-6.79 (m, 2H), 6.68-6.64 (m, 2H), 3.78 (s, 3H), 3.71-3.58 (m, 1H), 3.57-3.42 (m, 1H), 1.99-1.64 (m, 6H), 1.45-1.08 (m, 5H).

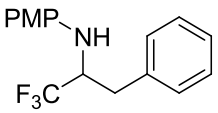
^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.79, 141.40, 126.47 (q, J = 284Hz), 114.92, 61.50 (q, J = 27Hz), 55.70, 38.62, 30.38, 27.34, 26.16, 25.96.

^{19}F NMR (300 MHz, CDCl3) δ: -72.74.

$[\alpha]_D^{22}$ = -3.6 (solvent: $CHCl_3$; *c* = 0.356 g/100 mL; λ = 589 nm).

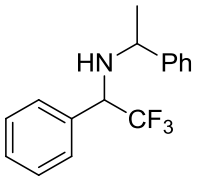
The enantiomeric excess was determined by chiral HPLC with Daicel Chiralcel OD-H column, eluent: 99:1 Hex/IPA; 0.8 mL/min flow rate, detection: 230 nm, t_R 7.79 min (major), t_R 9.35 min (minor).

N-(4'-Methoxyphenyl)-3-phenylpropan-1,1,1-trifluoro-2-amine (14[6])



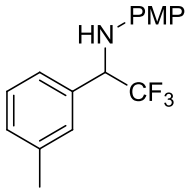
This product was purified by flash column chromatography on silica gel with a 99:1 hexane/ethyl acetate mixture as eluent.
R_f = 0.36 (9:1 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.32-7.26 (m, 5H), 6.74 (d, 2H, J = 9Hz), 6.53 (d, 2H, J = 9Hz), 4.08-4.04 (m, 1H), 3.74 (s, 3H), 3.41(m, 1H), 3.24 (m, 1H), 2.87 (m, 1H).
^{19}F NMR (300 MHz, CDCl3) δ: -75.69.

N-(1'-Phenylethyl)-ethan-2,2,2-trifluoro-1-phenyl-1-amine (6-8)



This product was purified by flash column chromatography on silica gel with a 9:1 hexane/ethyl acetate mixture as eluent.
R_f = 0.54 (8:2 hexane/ethyl acetate).
Data for *major*:
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45-7.27 (m, 10H), 4.11 (q, 1H, J = 7Hz), 4.04 (q, 1H, J = 7Hz), 1.97 (brs, 1H), 1.43 (d, 3H, J = 7Hz).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.08, 134.93, 128.23, 128.11, 127.71, 126.86, 126.21, 125.57 (q, J = 280Hz), 61.21 (q, J = 28Hz), 55.57, 23.02.
^{19}F NMR (300 MHz, CDCl3) δ: -73.42.
Data for *minor*:
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45-7.27 (m, 10H), 3.91 (q, 1H, J = 7Hz), 3.62 (q, 1H, J = 7 Hz), 1.97 (brs, 1H), 1.39 (d, 3H, J = 7Hz).
HRMS Mass (ESI+): m/z = calc for $C_{16}H_{17}NF_3^+$ = 280.13, found 280.13 [M + H].

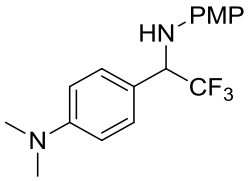
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(3''-methylphenyl)-1-amine (Table 3, Entry 6)



This product was purified by flash column chromatography on silica gel with a 95:5 hexane/ethyl acetate mixture as eluent.
R_f = 0.41 (8:2 hexane/ethyl acetate).

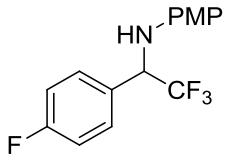
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.27-7.16 (m, 4H), 6.75 (d, 2H, J = 9Hz), 6.62 (d, 2H, 9Hz), 4.76 (q, 1H, J = 7Hz), 3.72 (s, 3H), 2.36 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.86, 139.20, 138.15, 133.84, 129.36, 128.27, 128.09, 124.74 (q, J = 280Hz), 124.49, 115.23, 114.40, 61.70 (q, J = 30Hz), 55.18, 20.94.
^{19} F NMR (300 MHz, $CDCl_3$) δ: -74.40.
HRMS Mass (ESI+): m/z = calc. for $C_{16}H_{17}NOF_3^+$ = 296.12, found 296.12 [M + H].
The enantiomeric excess was determined by chiral HPLC with Daicel Chiralcel OD-H column, eluent: 98:2 Hex/IPA; 0.8 mL/min flow rate, detection: 230 nm, t_R 14.89 min (minor), t_R 15.82 min (major).

N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-(N',N'-dimethylammino)-phenyl)-1-amine (Table 3, Entry 9)



This product was purified by flash column chromatography on silica gel with a 99:1 hexane/ethyl acetate mixture as eluent.
R_f = 0.33 (8:2 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.29 (d, 2H, J = 9Hz), 6.78-6.72 (m, 4H), 6.63 (d, 2H, J = 9Hz), 4.72 (q, 1H, 7Hz), 4.01 (brs, 1H), 3.74 (s, 3H), 2.97 (s, 6H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.70, 139.47, 128.18, 125 (q, J = 280Hz), 115.23, 114.36, 112.09, 60.80 (q, J = 29Hz), 55.26, 55.12, 39.98.
^{19} F NMR (300 MHz, $CDCl_3$) δ: -74.78.
HRMS Mass (ESI+): m/z = calc for $C_{17}H_{20}N_2OF_3^+$ = 325.15, found 325.15 [M + H].
The enantiomeric excess was determined by chiral HPLC with Daicel Chiralpack AD column, eluent: 9:1 Hex/IPA; 0.8 mL/min flow rate, detection: 230 nm, t_R 8.87 min (minor), t_R 22.79 min (major).

N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-fluorophenyl)-1-amine (Table 3, Entry 4)

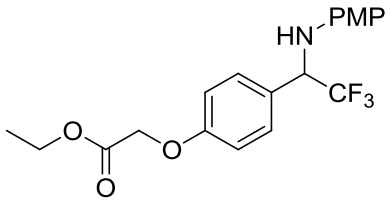


This product was purified by flash column chromatography on silica gel with a 9:1 hexane/ethyl acetate mixture as eluent.
R_f = 0.40 (8:2 hexane/ethyl acetate).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45-7.40 (m, 2H), 7.10-7.04 (m, 2H), 6.74 (d, 2H, 9Hz), 6.58 (d, 2H, 9Hz), 4.79 (q, 1H, J = 7Hz), 4.11 (brs, 1H), 3.71 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.07 (d, J = 246Hz), 153.43, 139.17, 130.03, 129.78, 129.67, 124.95 (q, J = 280Hz), 116.07, 115.76, 114.86, 61.07 (q, J = 29Hz), 55.63.
^{19} F NMR (300 MHz, $CDCl_3$) δ: -74.72, - 112.98.

HRMS Mass (ESI+): m/z = calc. for $C_{15}H_{14}NOF_4^+$ = 300.10, found 300.10 [M + H].

The enantiomeric excess was determined by chiral HPLC with Daicel Chiralpack AD column, eluent: 9:1 Hex/IPA; 0.8 mL/min flow rate, detection: 230 nm, t_R 12.01 min (minor), t_R 17.98 min (major).

N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-ethylphenoxyacetate)-1-amine (Table 3, Entry 10)



This product was purified by flash column chromatography on silica gel with a 9:1 hexane/ethyl acetate mixture as eluent.

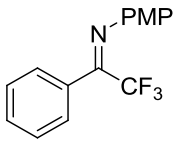
R_f = 0.22 (8:2 hexane/ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.36 (d, 2H, J = 9Hz), 6.90 (d, 2H, J = 9Hz), 6.72 (d, 2H, J = 9Hz), 6.58 (d, 2H, J = 9Hz), 4.74 (q, 1H, J = 7.5), 4.60 (s, 2H), 4.26 (q, 2H, J = 7Hz), 3.71 (s, 3H), 1.28 (t, 3H, J = 7Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.66, 158.36, 153.33, 139.48, 129.21, 127.42, 125.13 (q, J = 279Hz), 115.04, 115.03, 114.84, 65.43, 61.43, 61.12 (q, J = 37Hz), 55.64, 14.12.

^{19} F NMR (300 MHz, $CDCl_3$) δ: -74.72.

The enantiomeric excess was determined by chiral HPLC with Daicel Chiralcel OD-H column, eluent: 99:1Hex/IPA; 0.8 mL/min flow rate, detection: 280 nm, t_R 27.24 min (major), t_R 32.56 min (minor).



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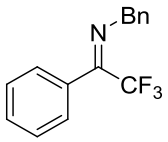

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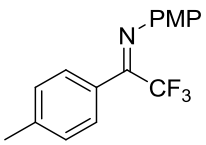

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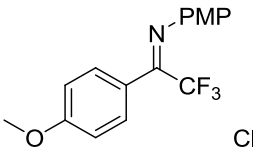

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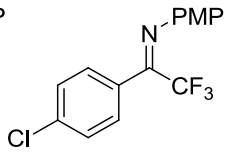

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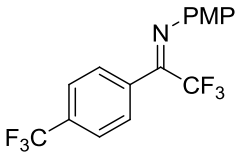

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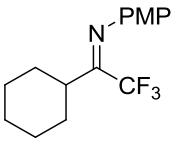

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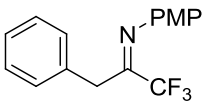

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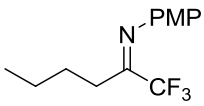

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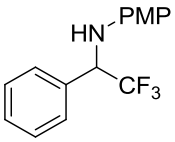

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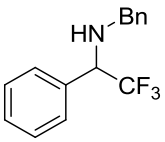

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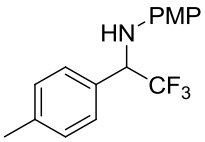

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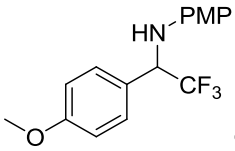

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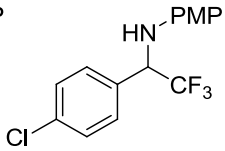

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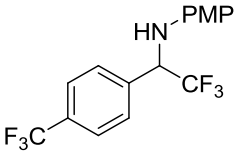

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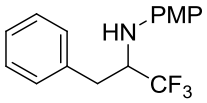

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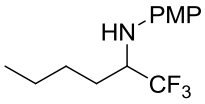
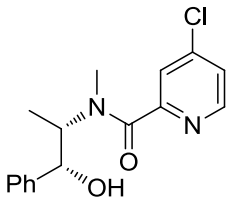


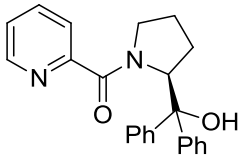
12

Imines **1**[1], **3**[2], **17**[1], **19**[1], **21**[1], **23**[1], **16**[4], **13**[5], **11**[7] and amines **2**[1], **4**[3], **18**[1], **20**[1], **22**[1], **24**[1], **14**[6], **12**[7] are already known in literature and analytical data agree with those reported.

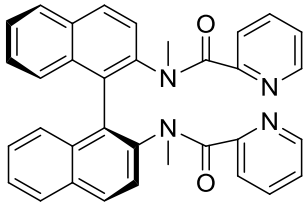
Catalysts:



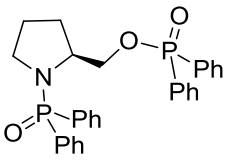
A



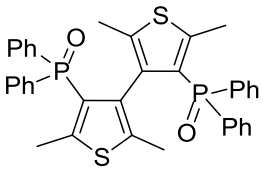
B



C



D



(*S*)

E

Catalysts **A**[8], **B**[9], **C**[10], **D**[11], **E**[12] are already known in literature and analytical data agree with those reported.

References:

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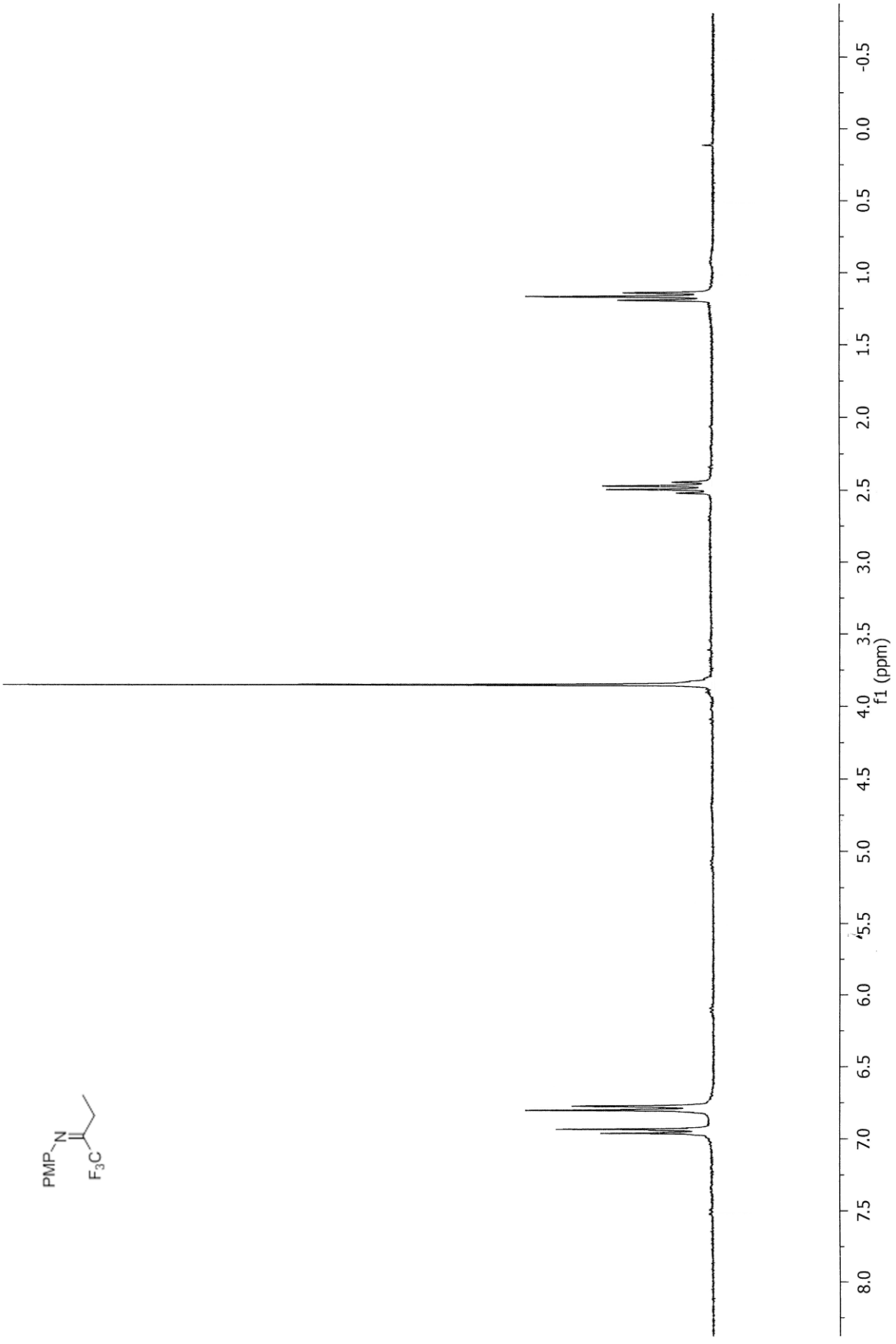
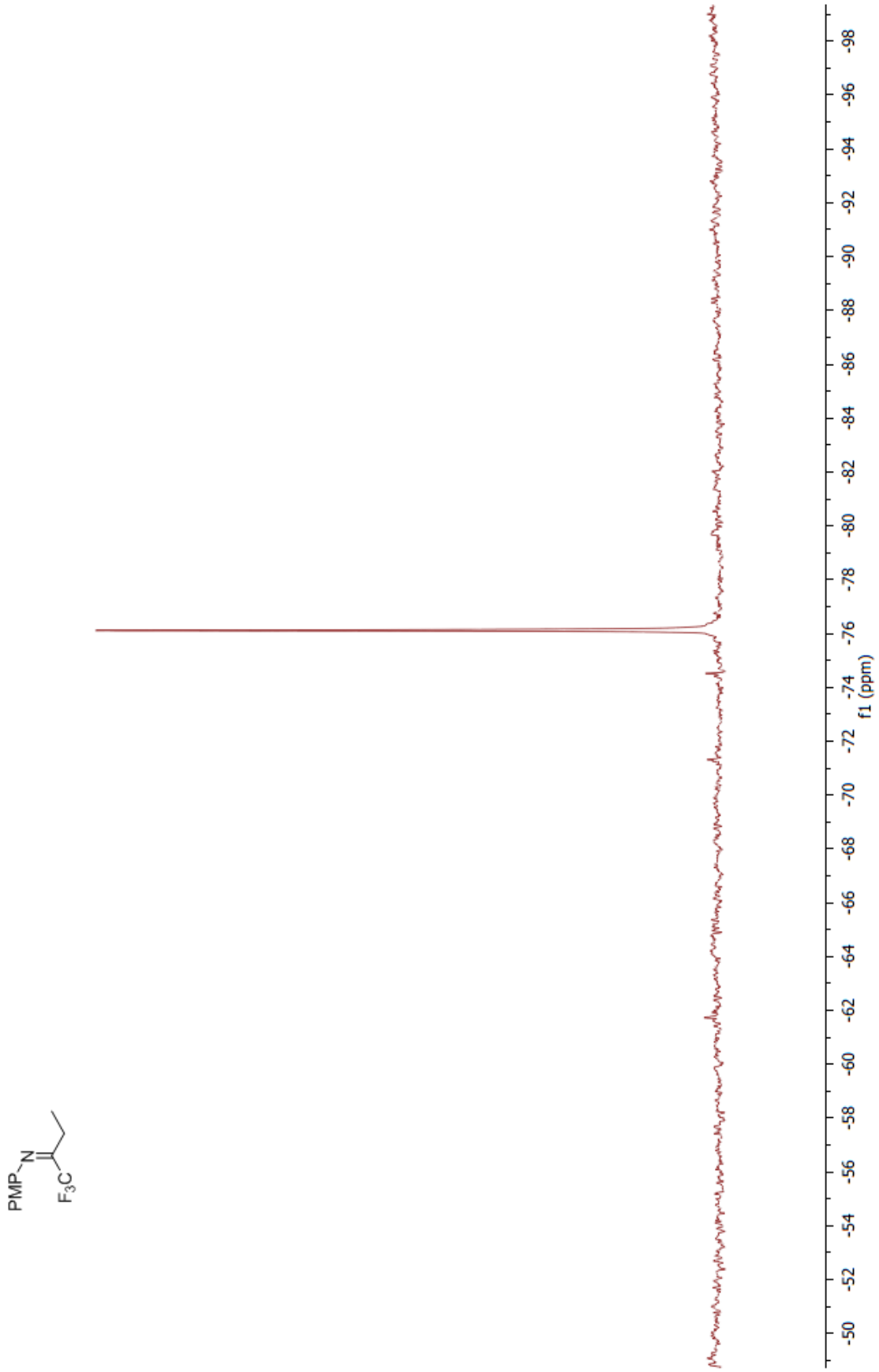
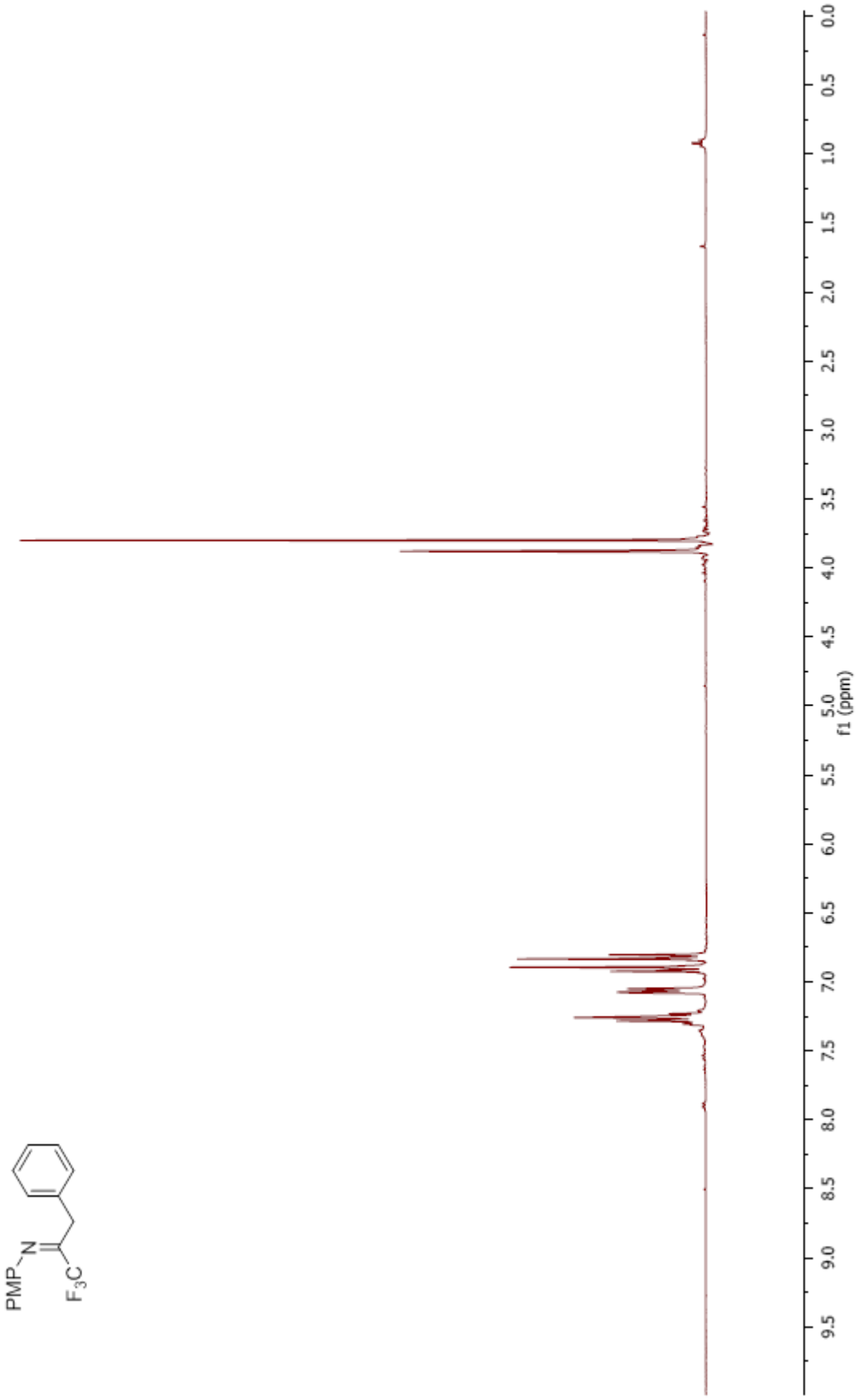
NMR Spectra:

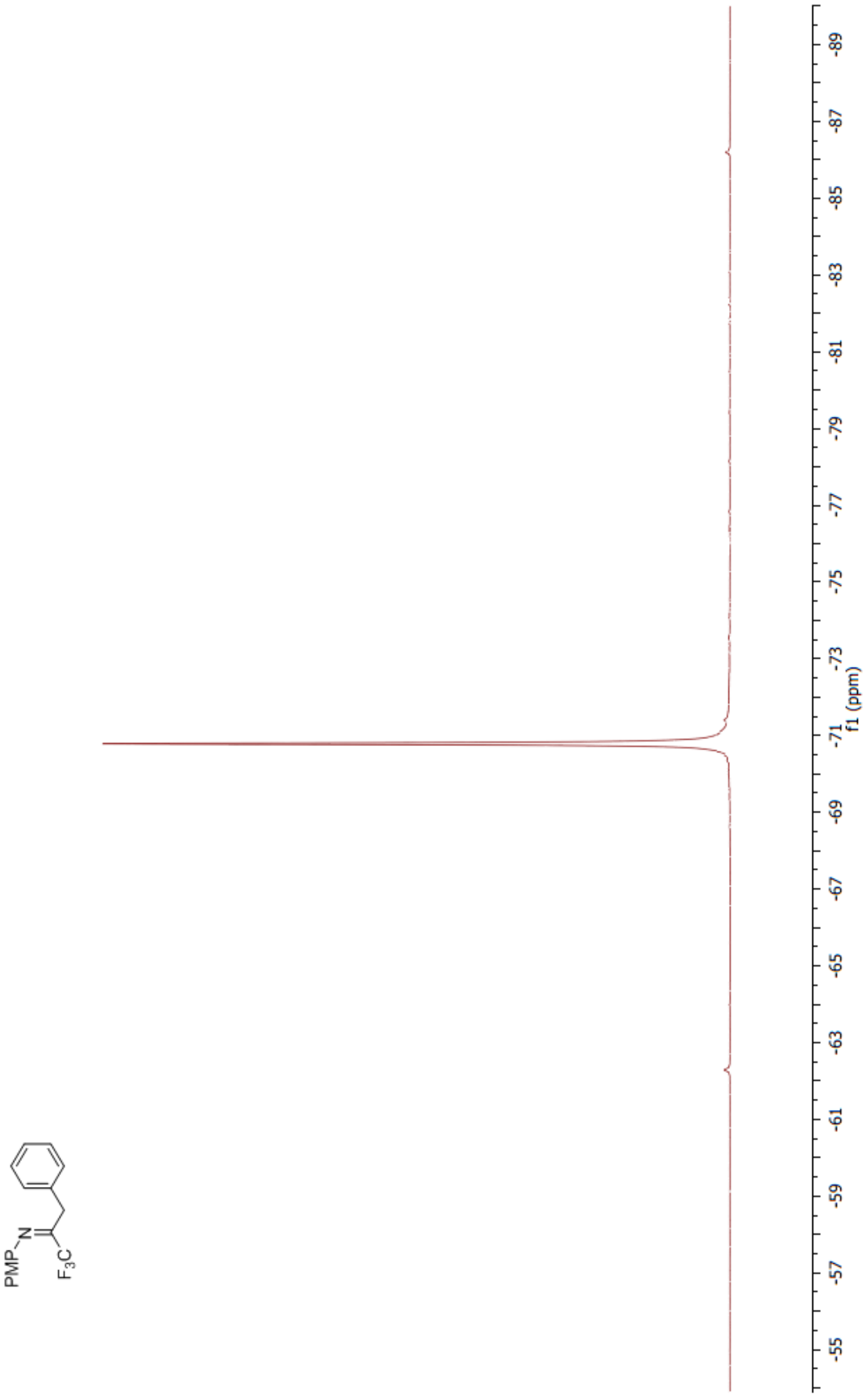
N-(4'-Methoxyphenyl)-butan-1,1,1-trifluoro-2-imine :




PMP
N
F3C
-50
-52
-54
-56
-58
-60
-62
-64
-66
-68
-70
-72
-74
-76
-78
-80
-82
-84
-86
-88
-90
-92
-94
-96
-98
f1 (ppm)

N-(4'-Methoxyphenyl)-3-phenylpropan-1,1,1-trifluoro-2-imine :




PMP
N
F3C
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-57
-59
-61
-63
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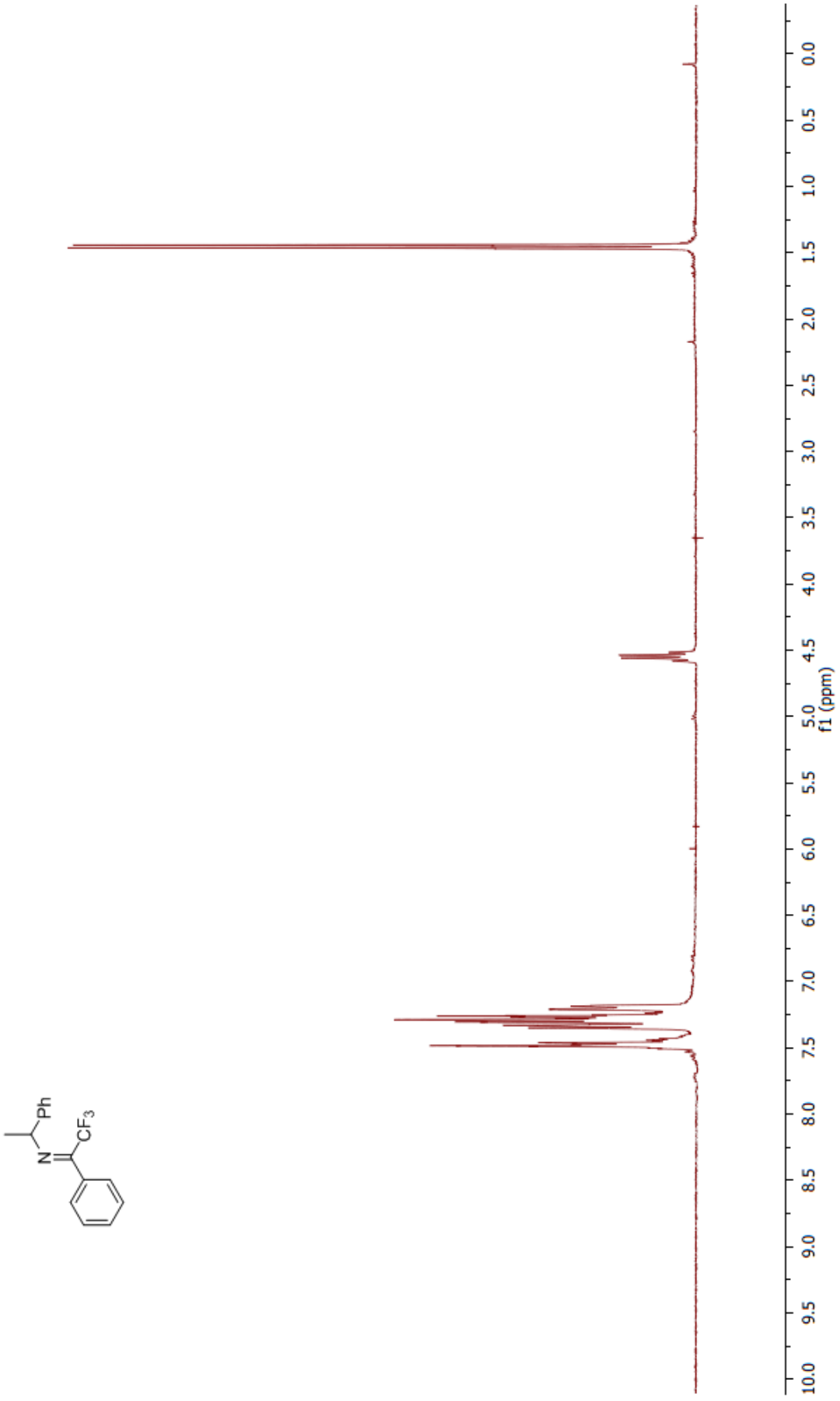
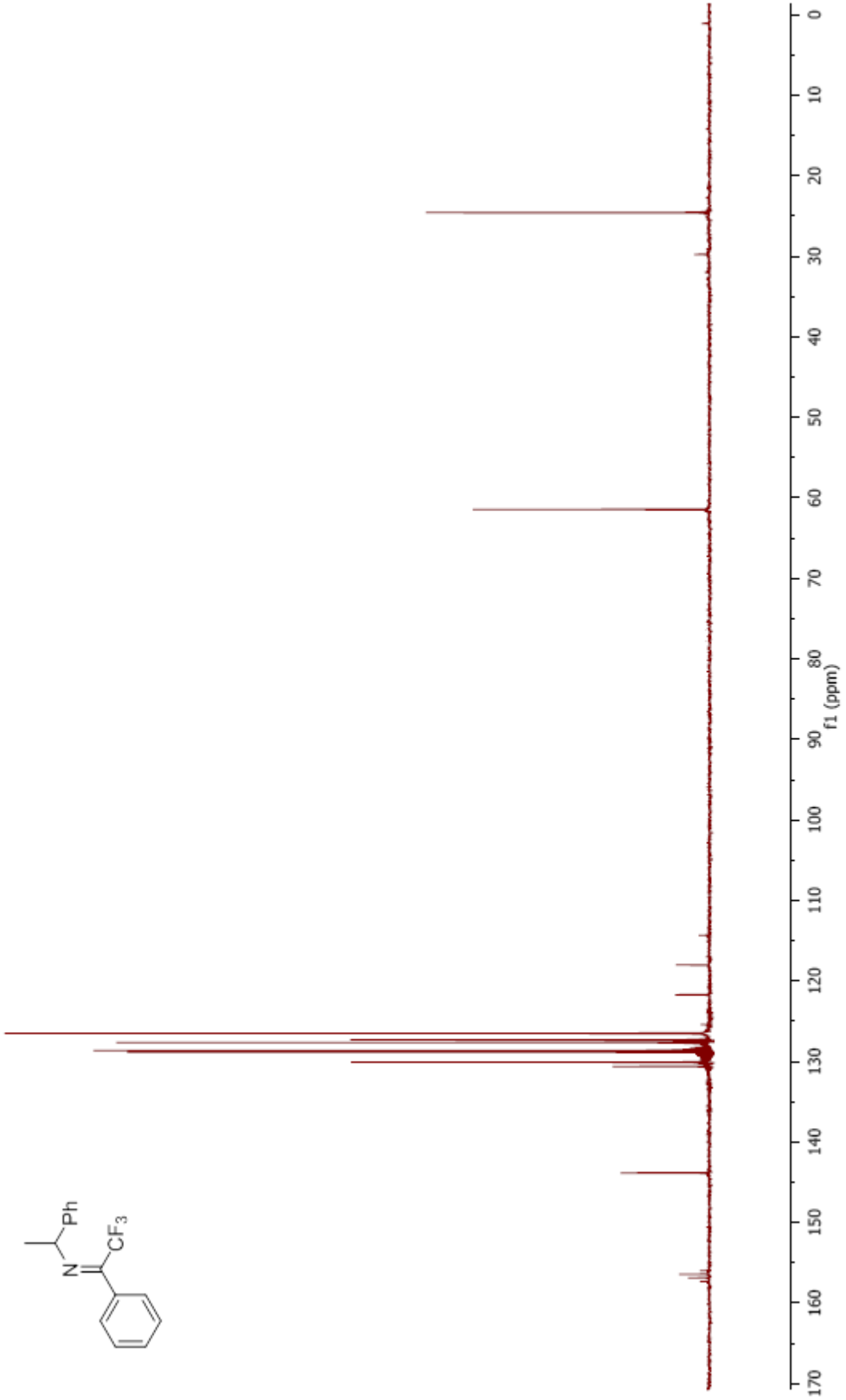
-67
-69
-71
-73
-75
-77
-79
-81
-83
-85
-87
-89
f1 (ppm)

N-(1'-Phenylethyl)-ethan-2,2,2 -trifluoro-1-phenyl-1-imine :




Ph
N
CF3
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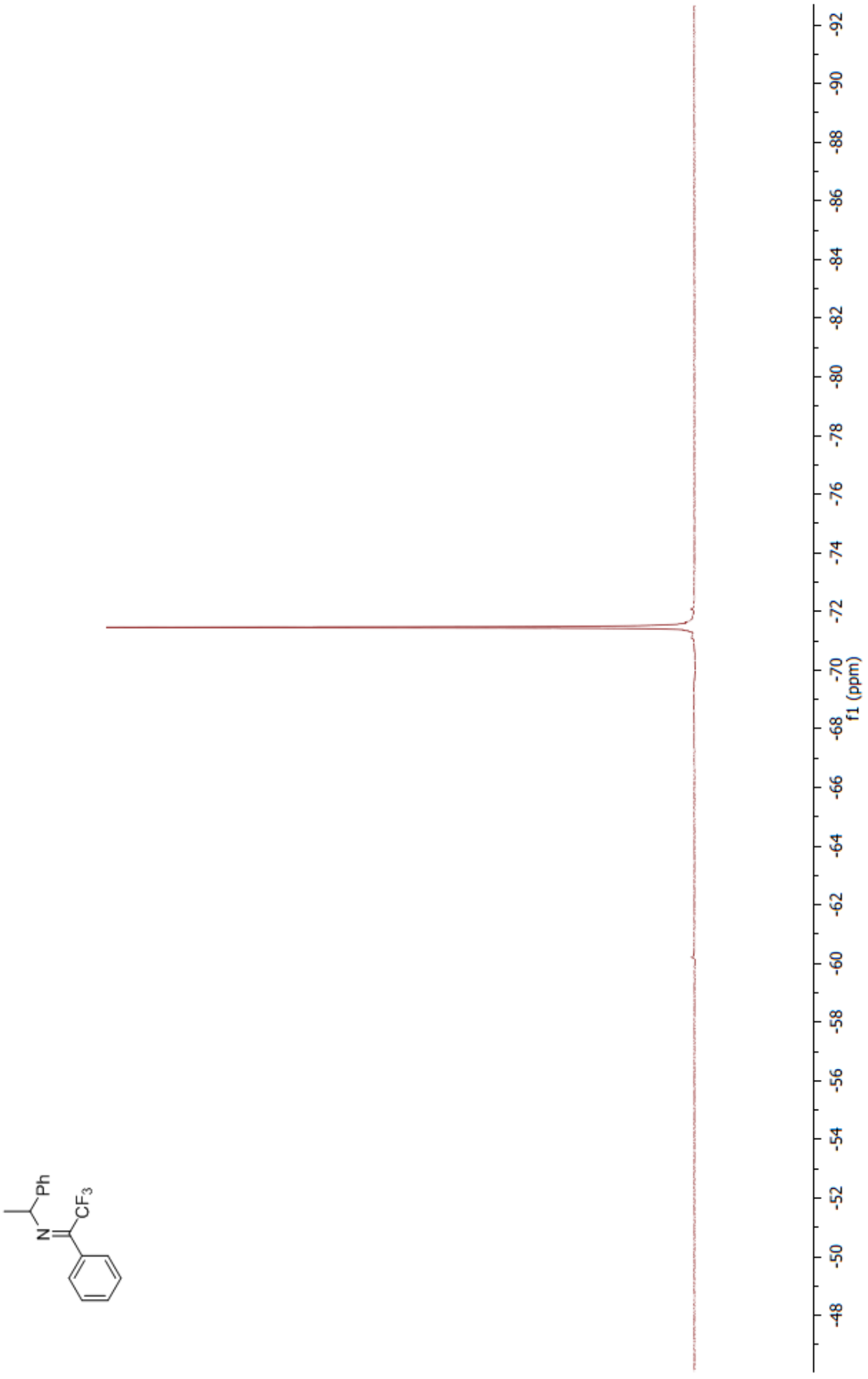
80
90
100
110
120
130
140
150
160
170
f1 (ppm)


Ph
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CF3
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-72
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-76
-78
-80
-82
-84
-86
-88
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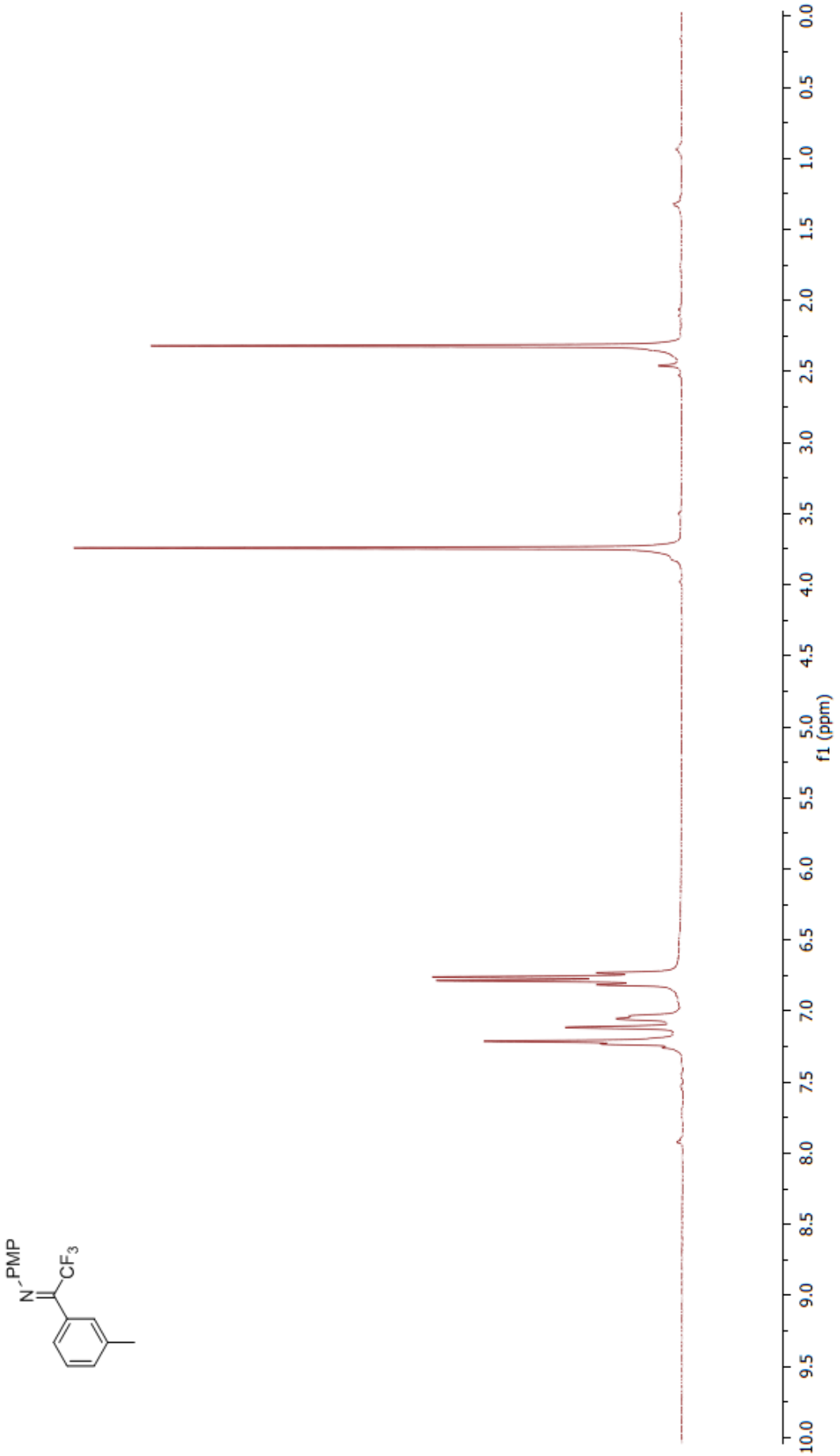
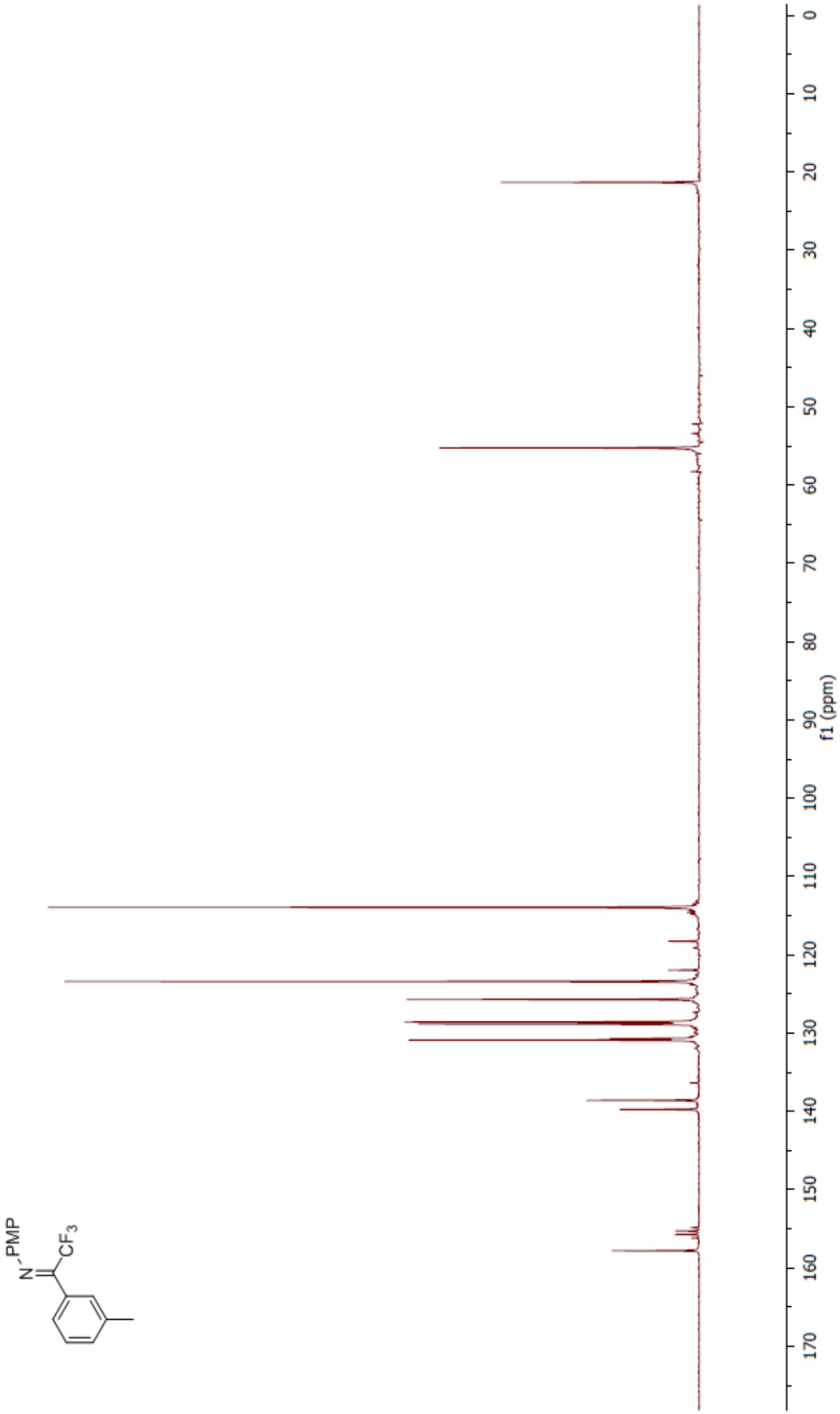
-92
f1 (ppm)

N-(4'-Methoxyphenyl)-ethan-2,2,2 -trifluoro-1-(3''-methylphenyl)-1-imine :




PMP
N
CF3
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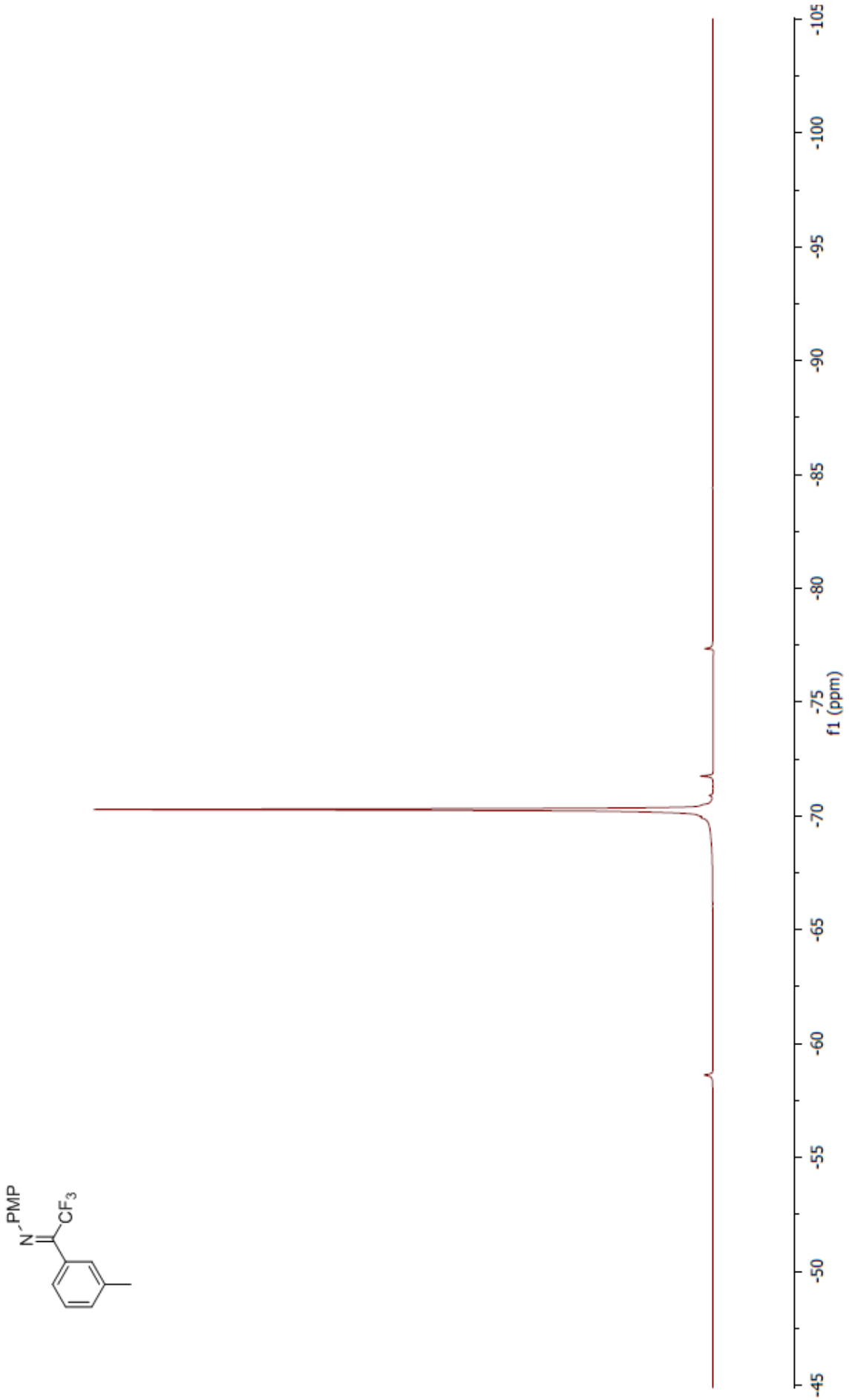
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
f1 (ppm)


PMP
N
CF3
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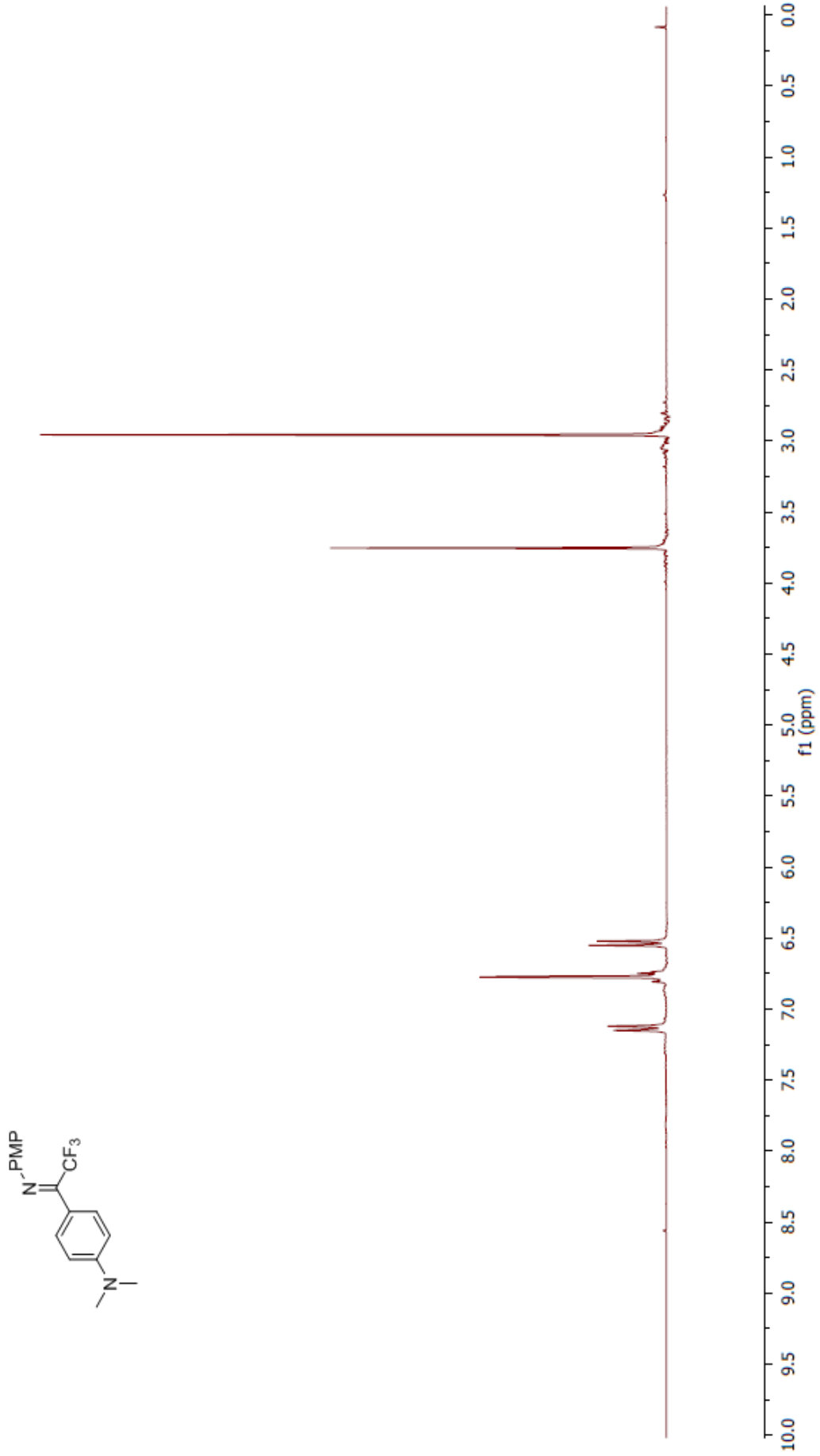
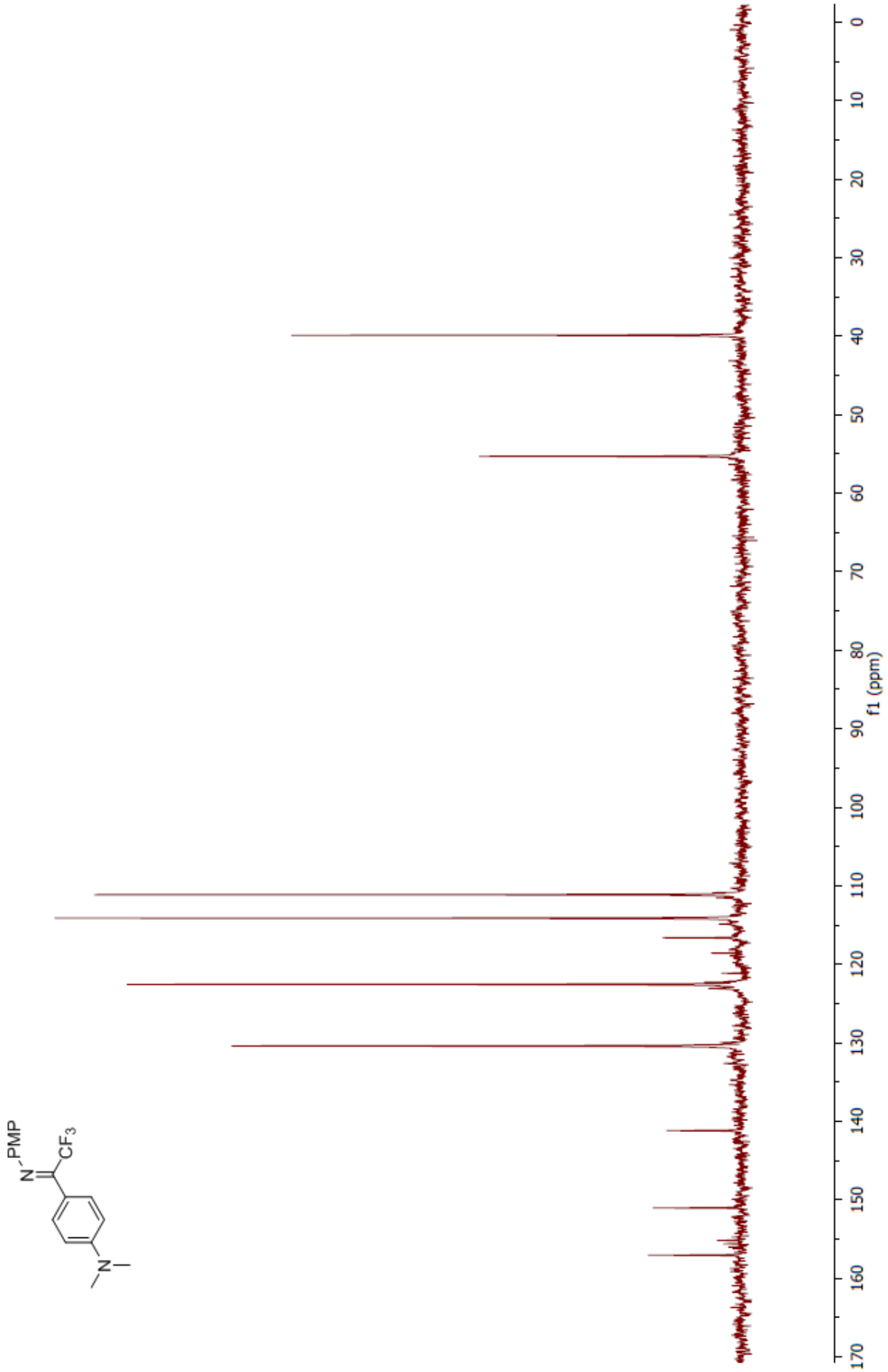
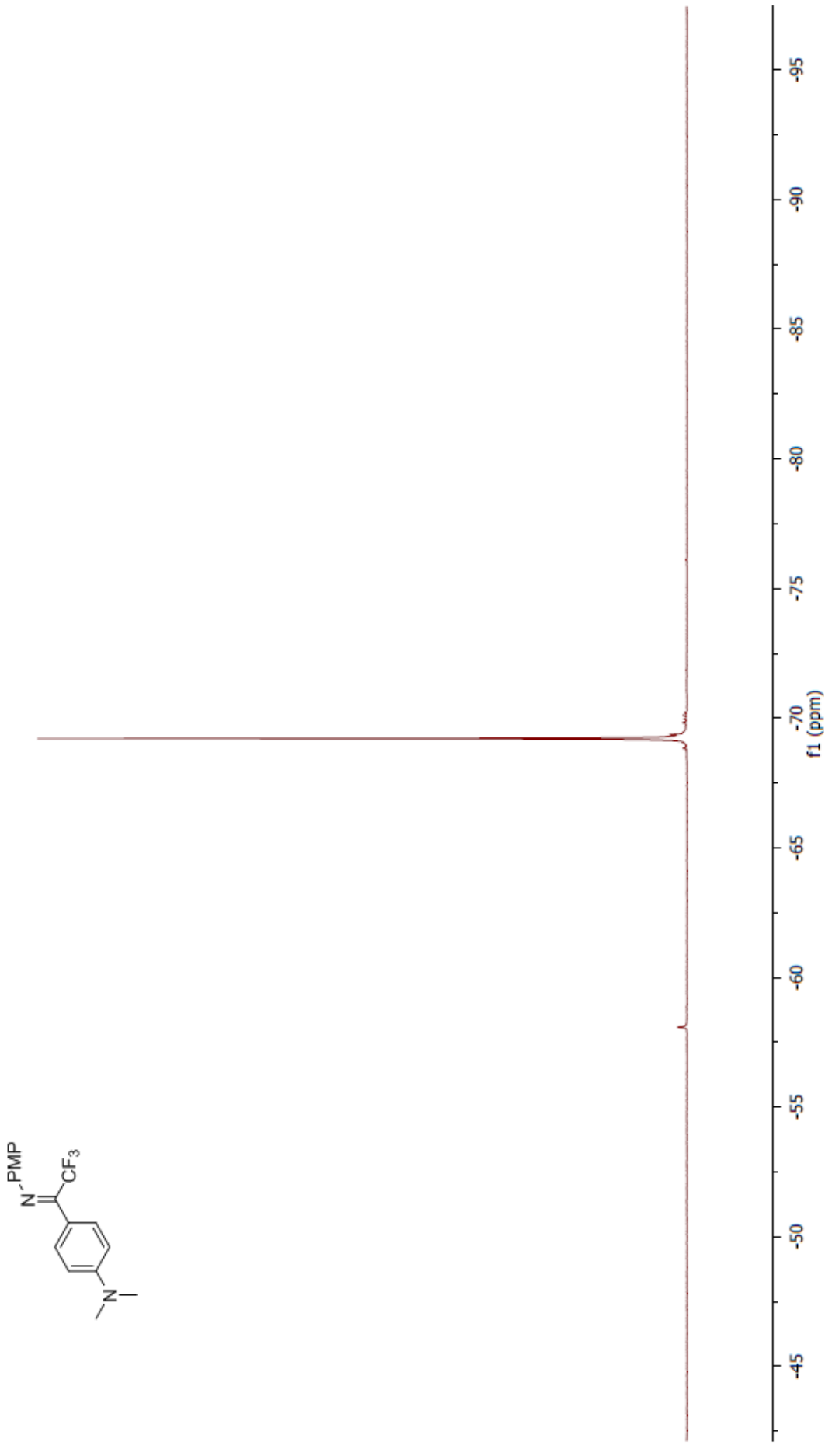
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
f1 (ppm)

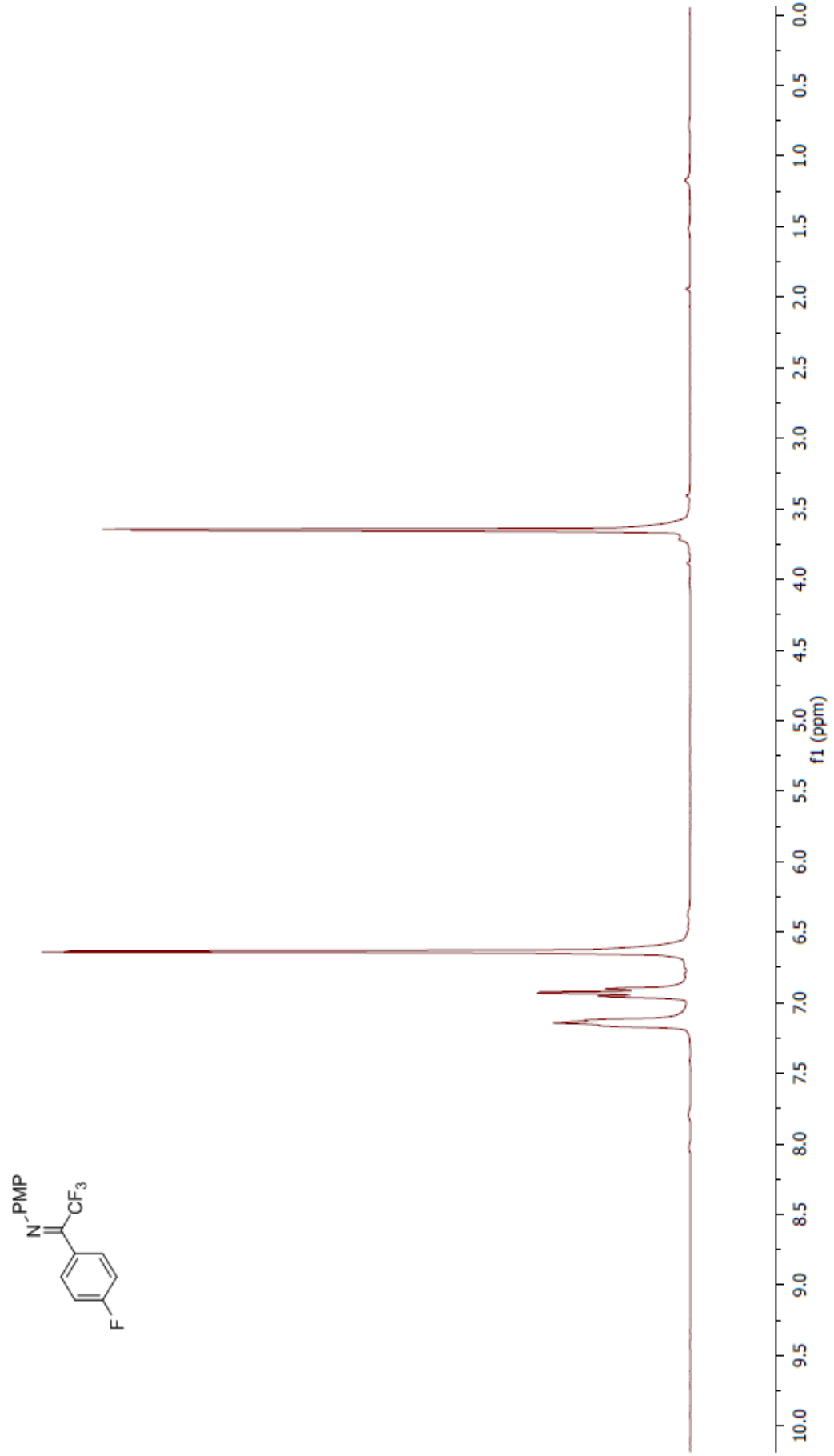
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-(N',N'-dimethylammino)-phenyl)-1-imine :

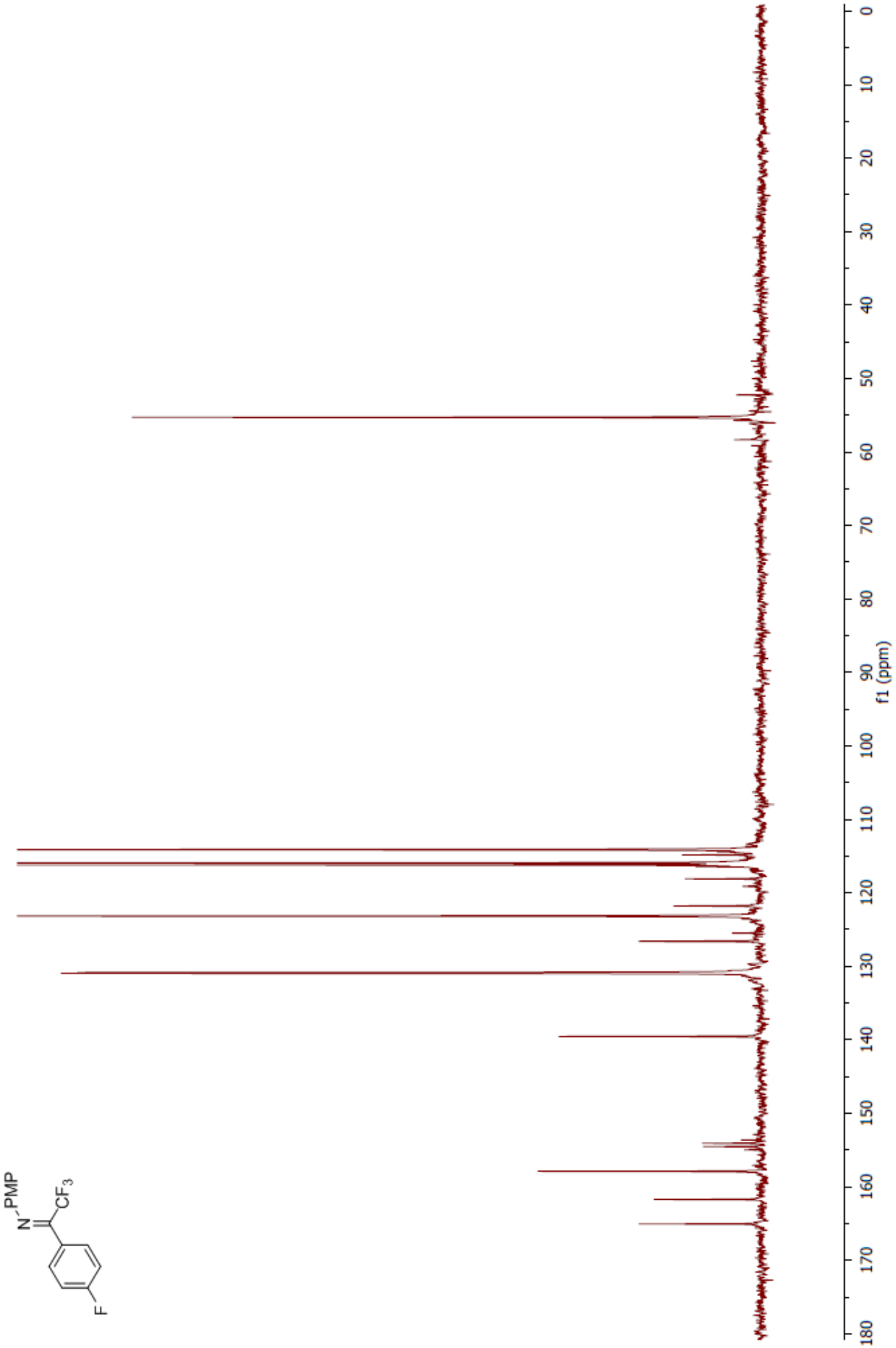


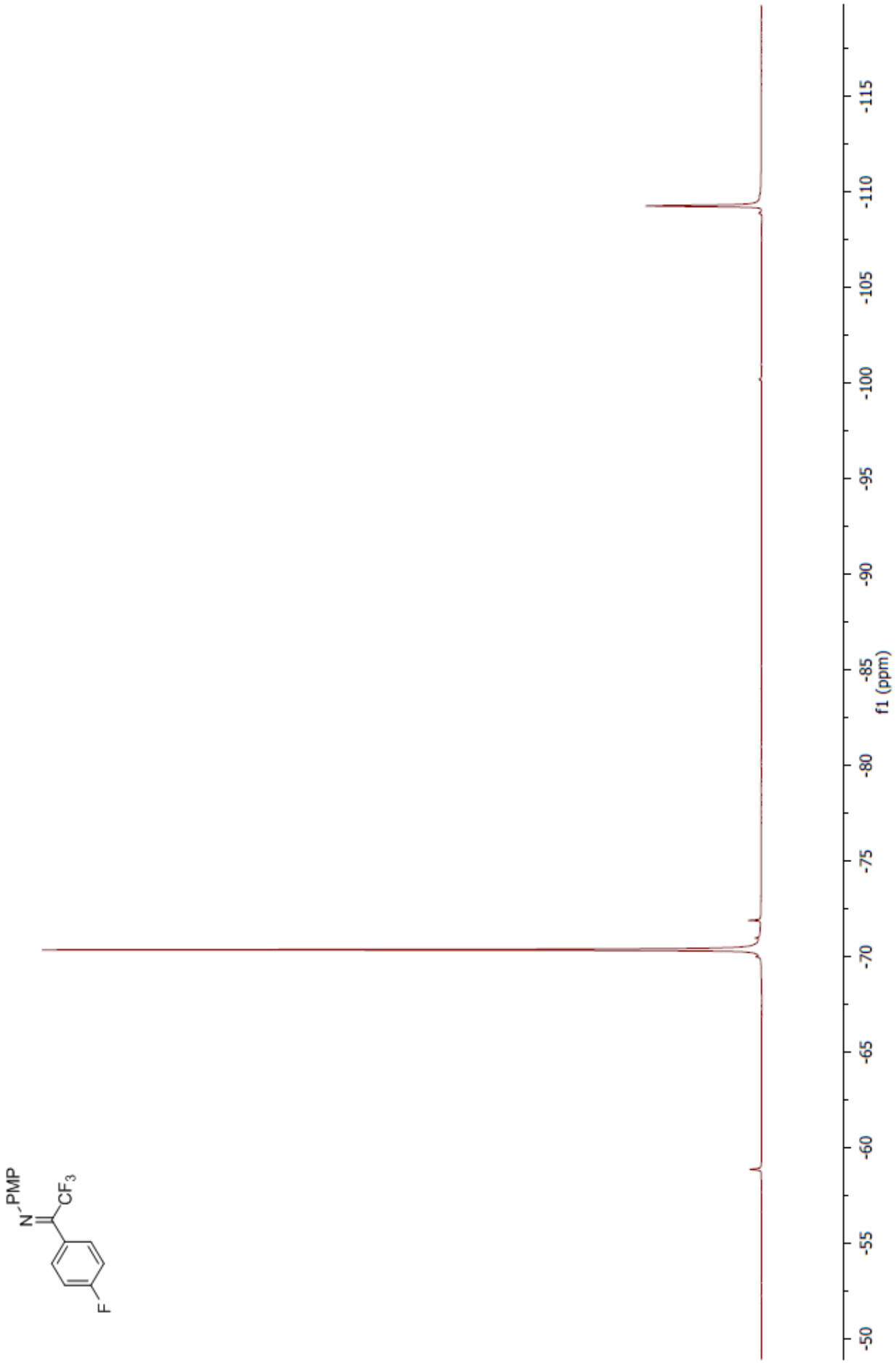

PMP
N
CF3
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
f1 (ppm)


PMP
N
CF3
N
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
f1 (ppm)

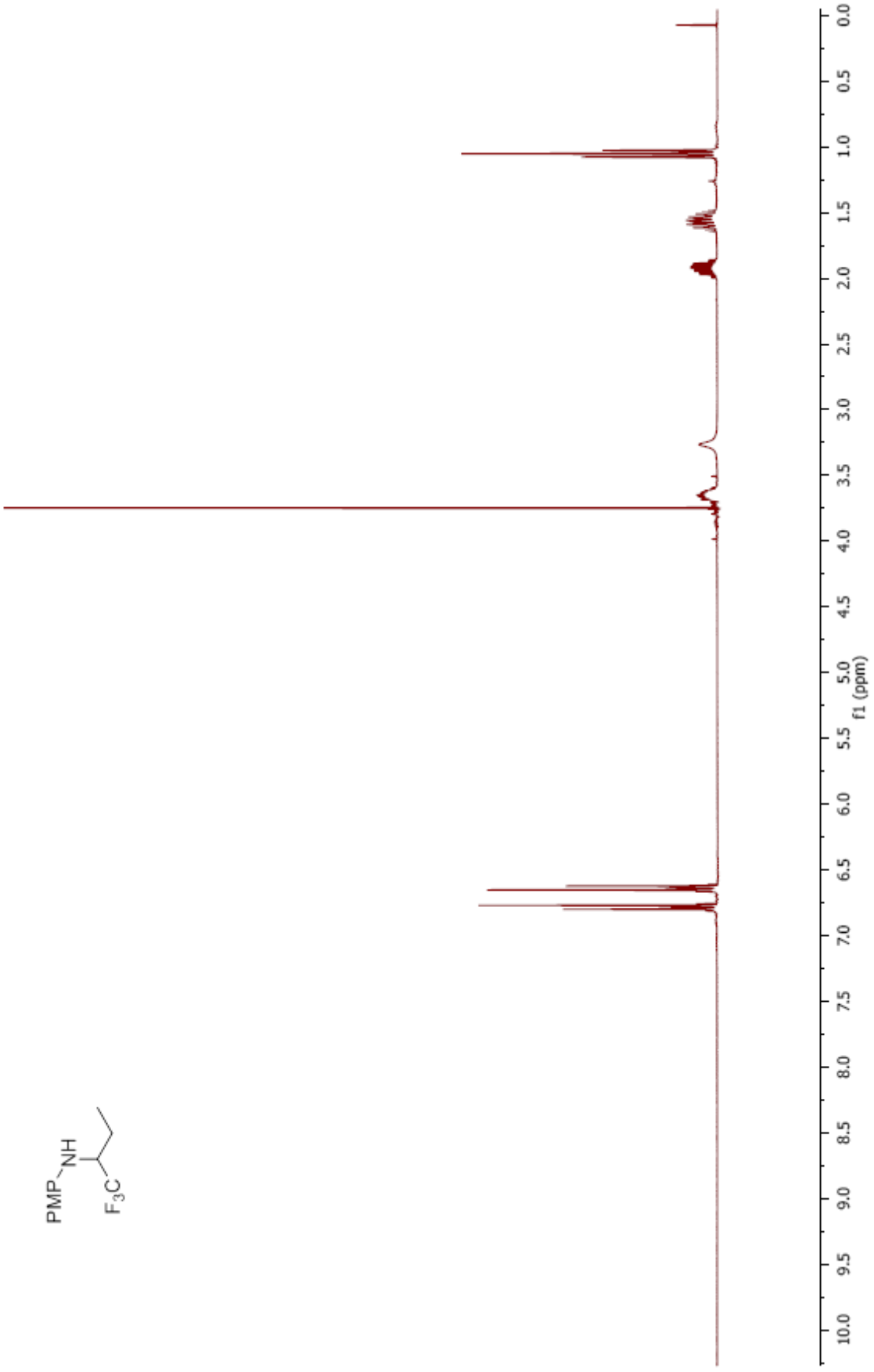
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-fluorophenyl)-1-imine :

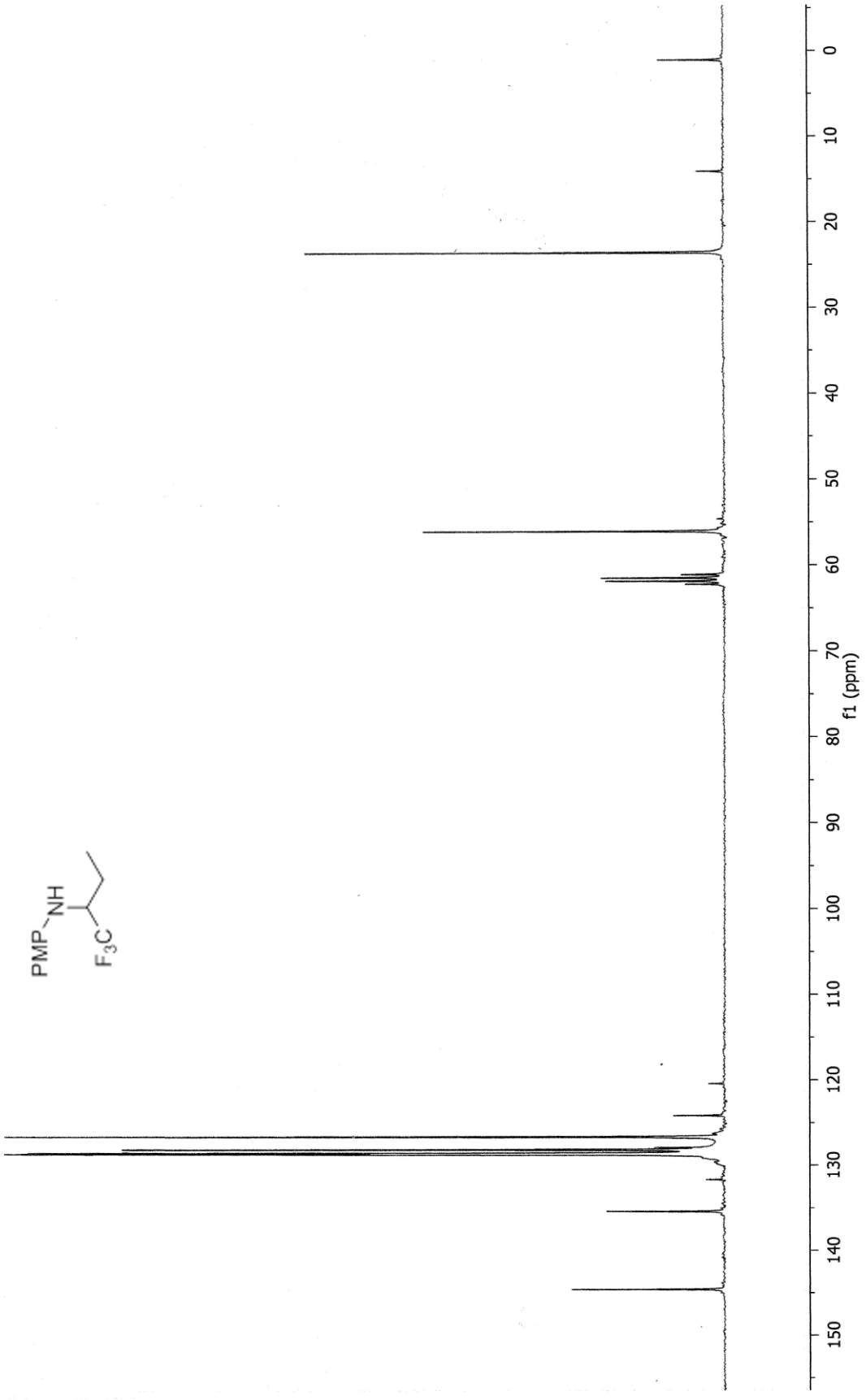


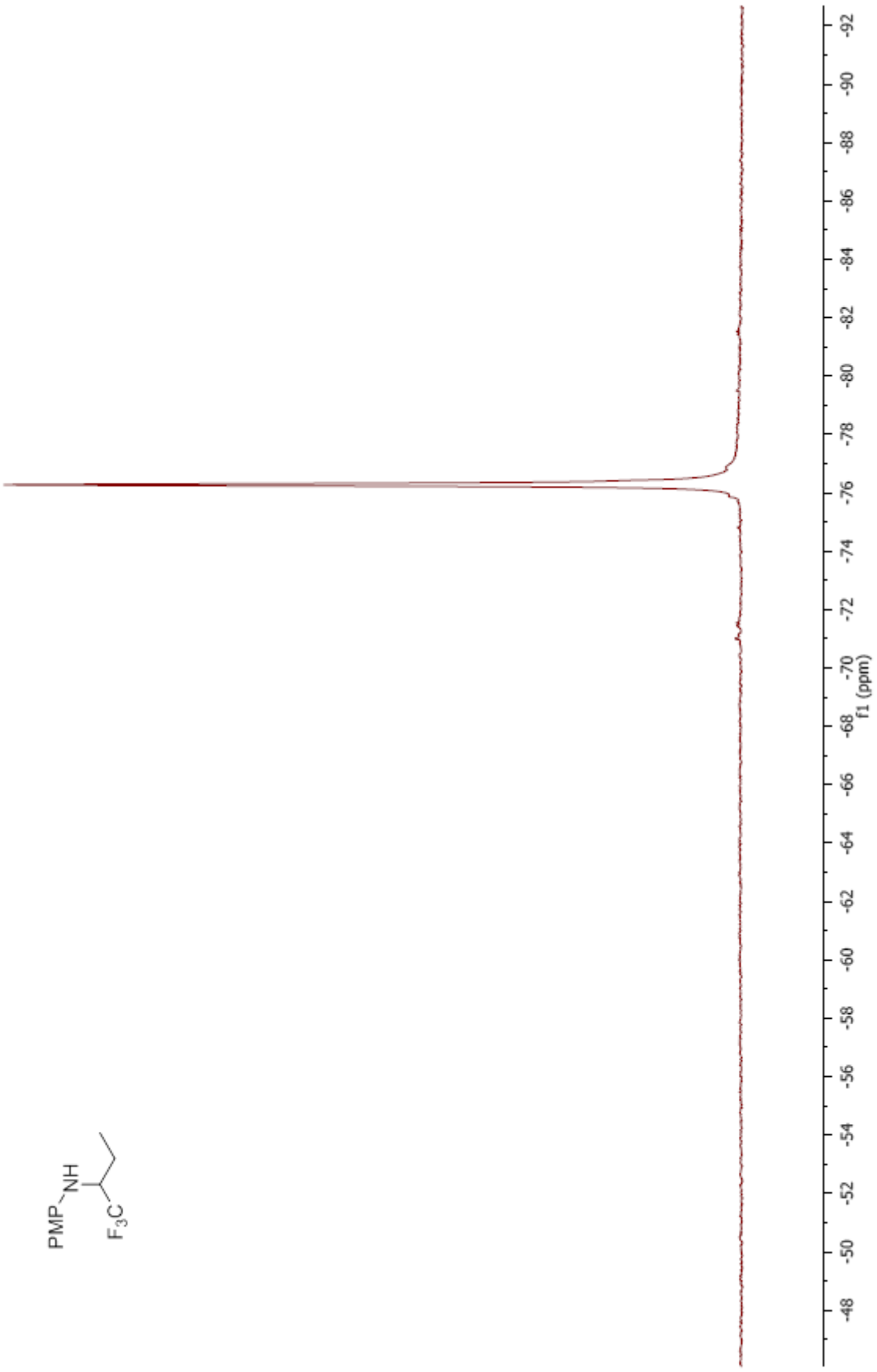

PMP
N
CF3
F
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)


PMP
N
CF3
F
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
f1 (ppm)

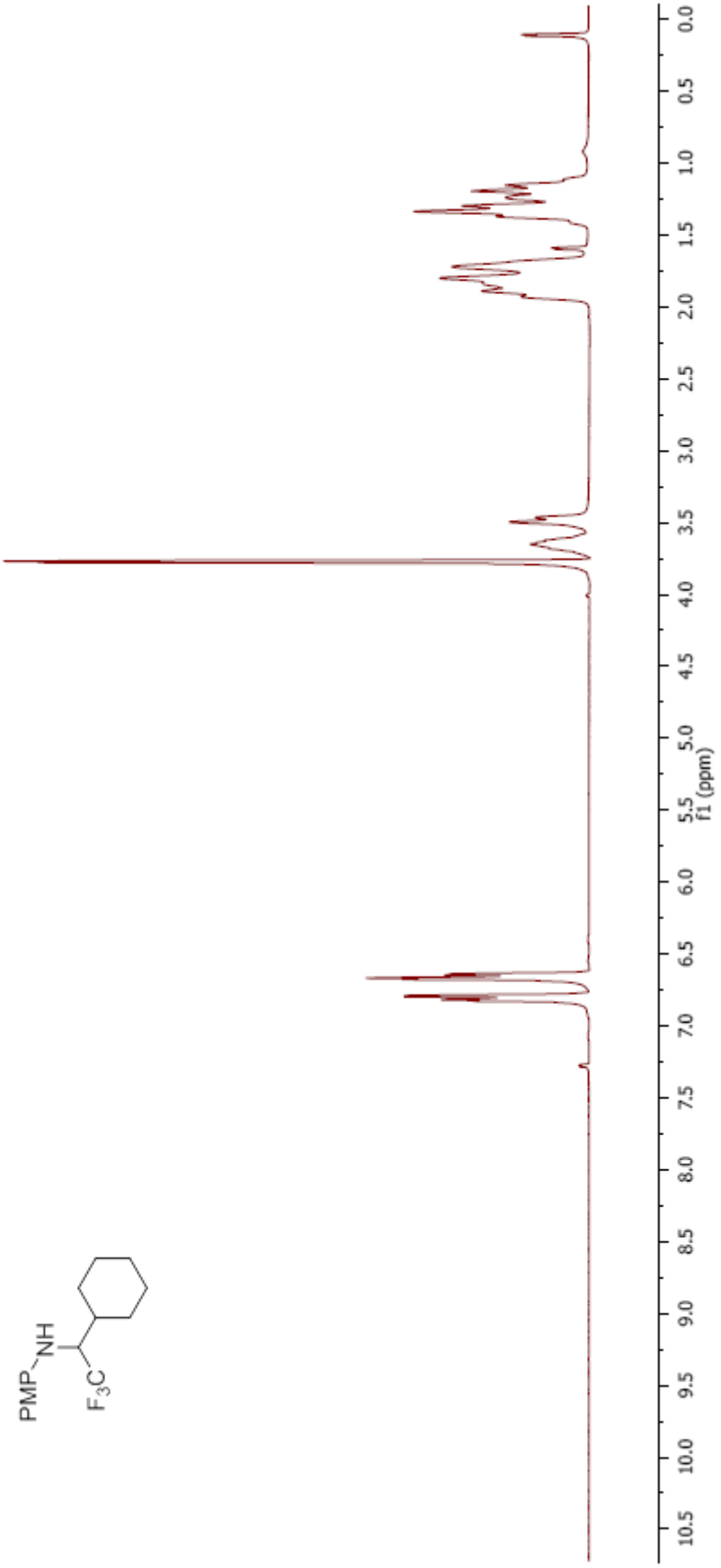
N-(4'-Methoxyphenyl)-butan-1,1,1-trifluoro-2-amine :

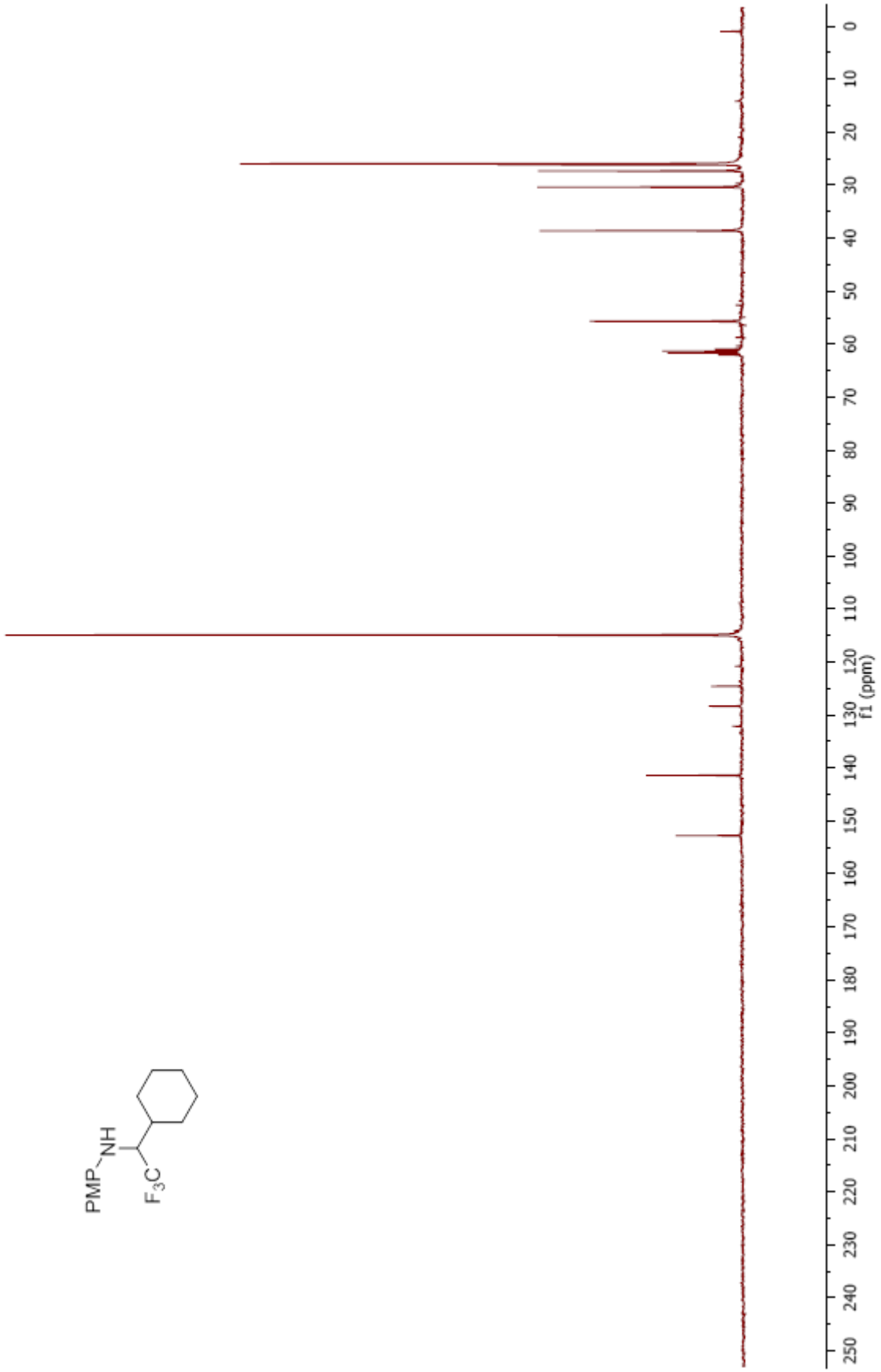


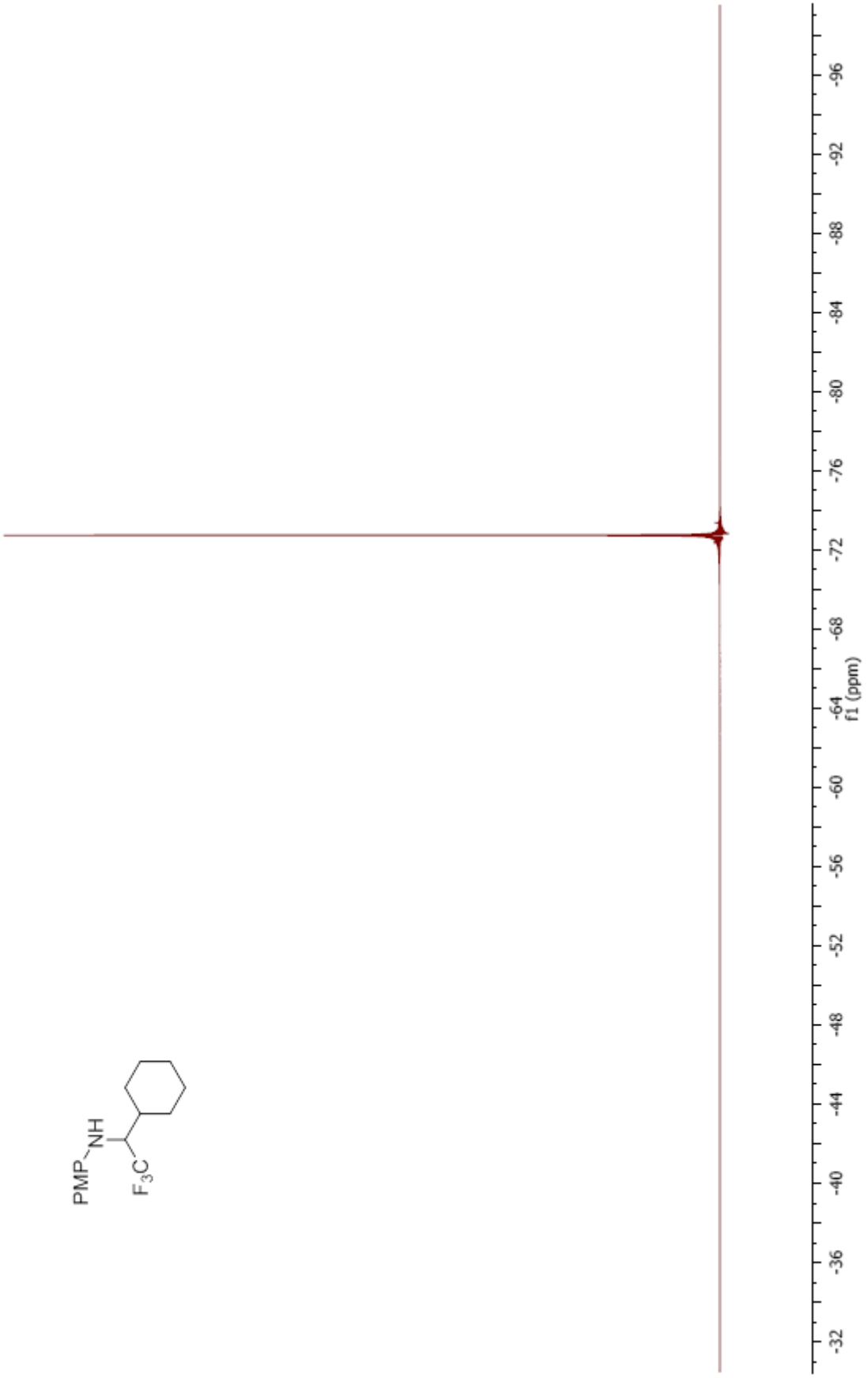

PMP
NH
F3C
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)


PMP
NH
F3C
-48
-50
-52
-54
-56
-58
-60
-62
-64
-66
-68
-70
-72
-74
-76
-78
-80
-82
-84
-86
-88
-90
-92
f1 (ppm)

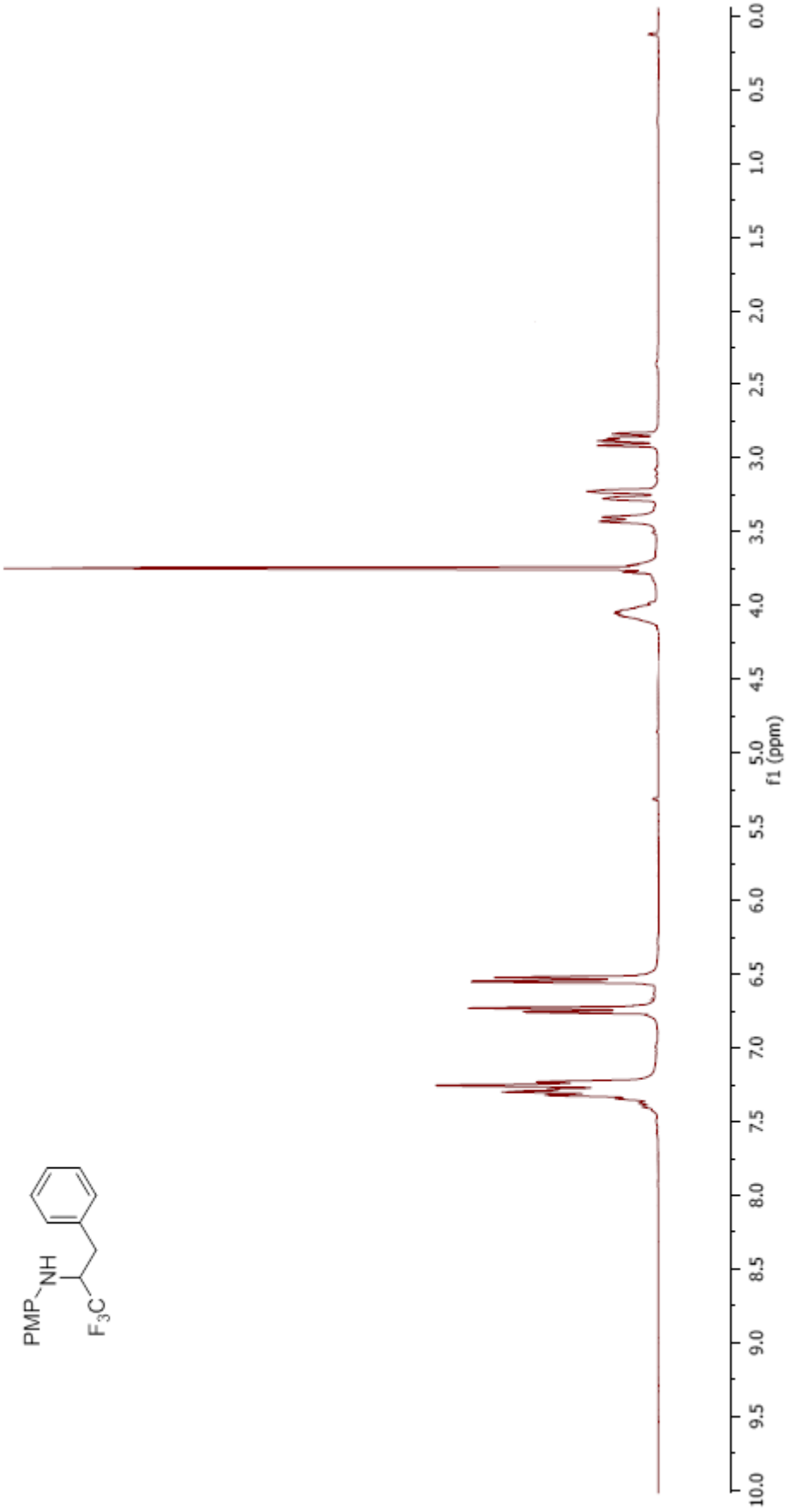
N-(4'-Methoxyphenyl)-ethan-1,1,1-trifluoro-2-cyclohexyl-2-amine :

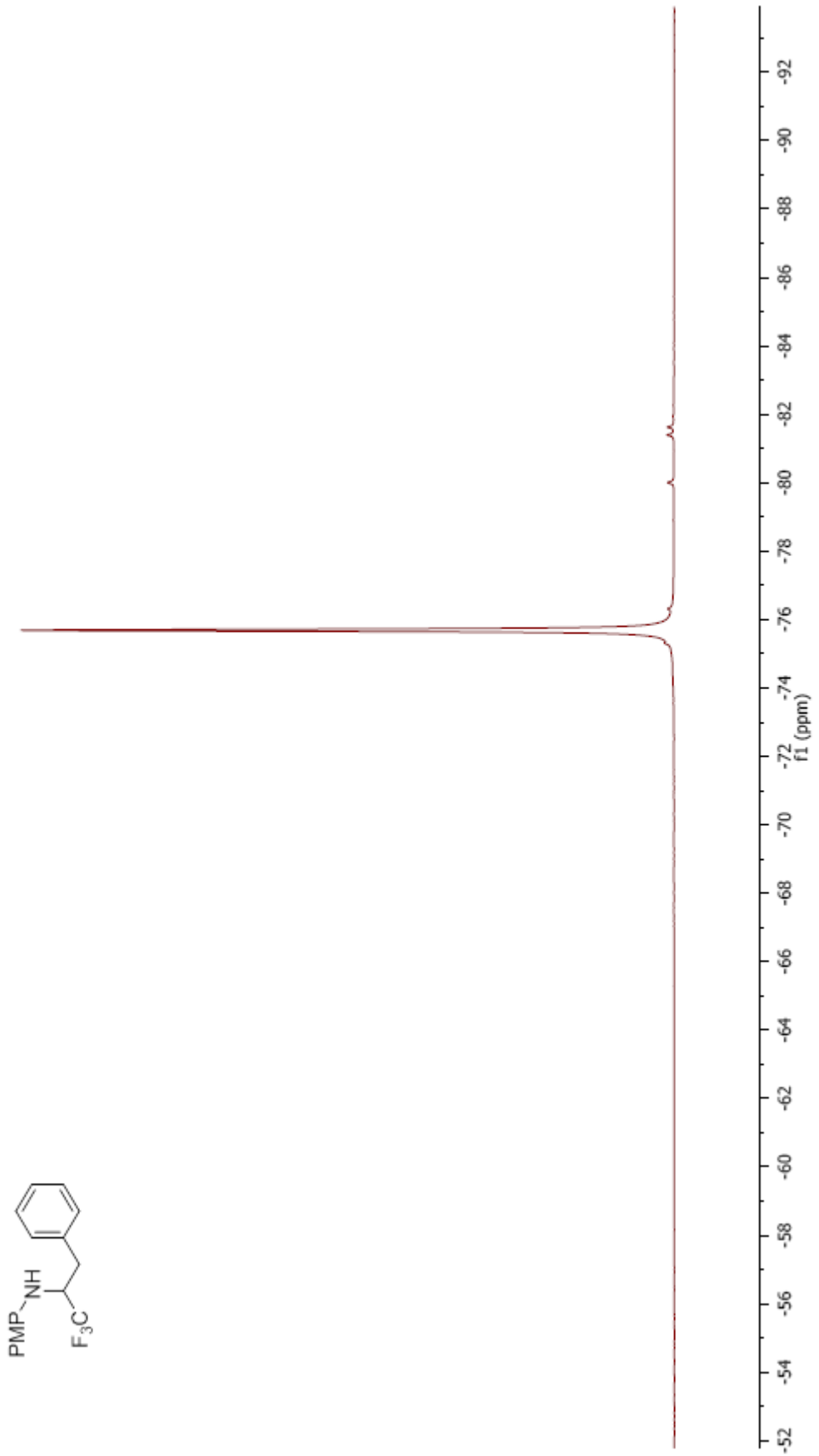



PMP
NH
F3C
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
240
250
f1 (ppm)

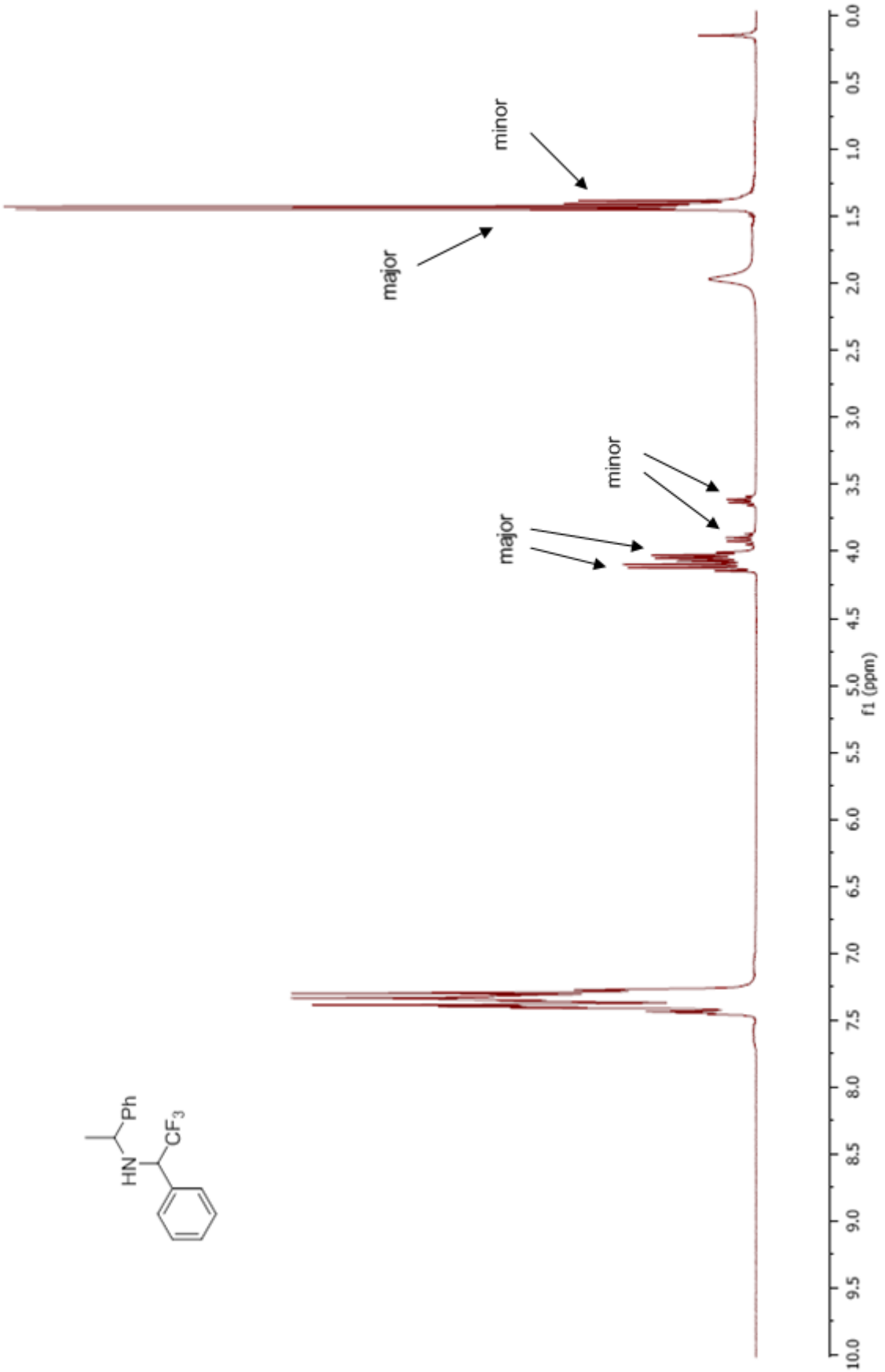

PMP
NH
F3C
-32
-36
-40
-44
-48
-52
-56
-60
-64
-68
-72
-76
-80
-84
-88
-92
-96
f1 (ppm)

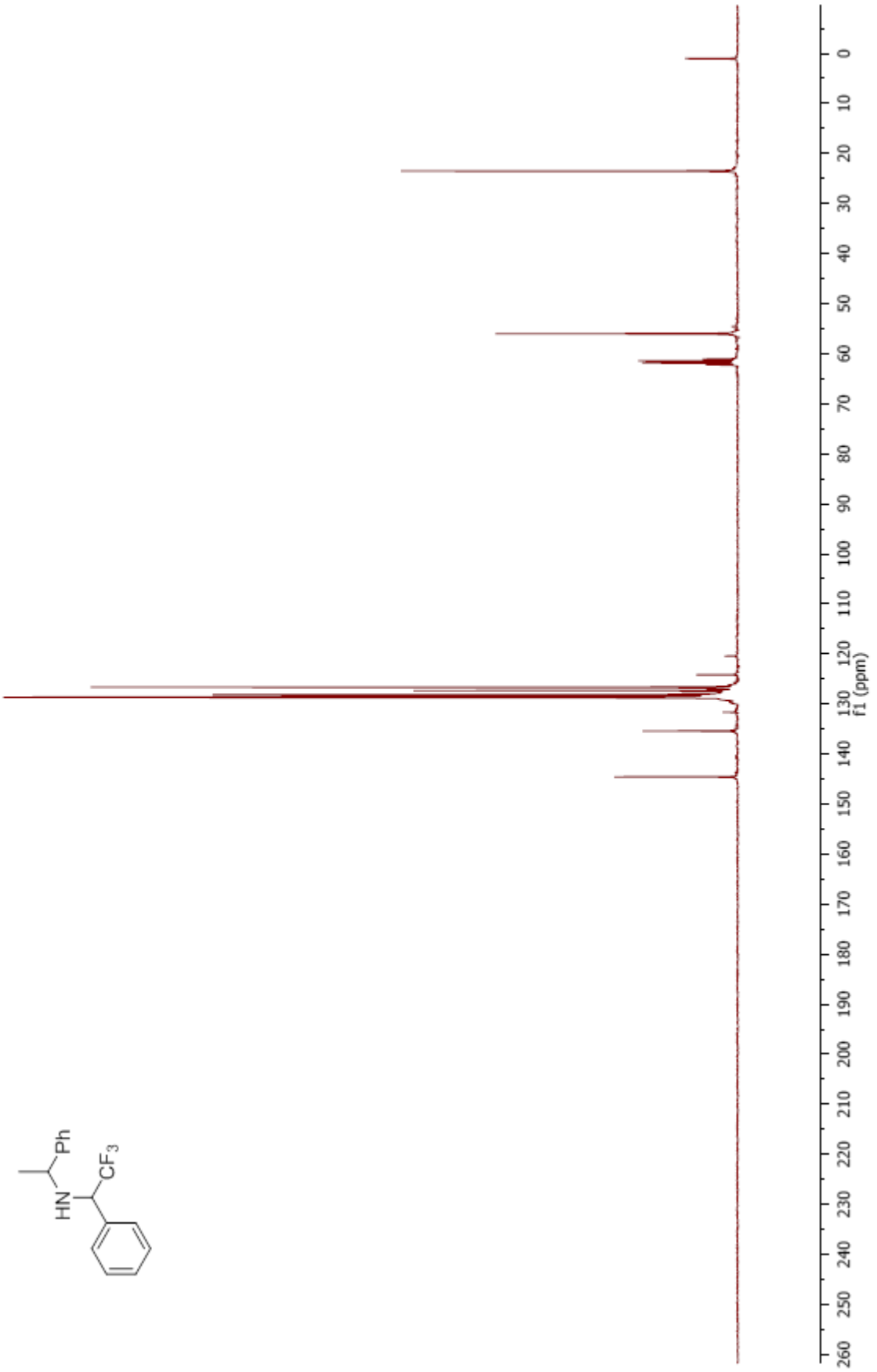
N-(4'-Methoxyphenyl)-3-phenylpropan-1,1,1-trifluoro-2-amine :

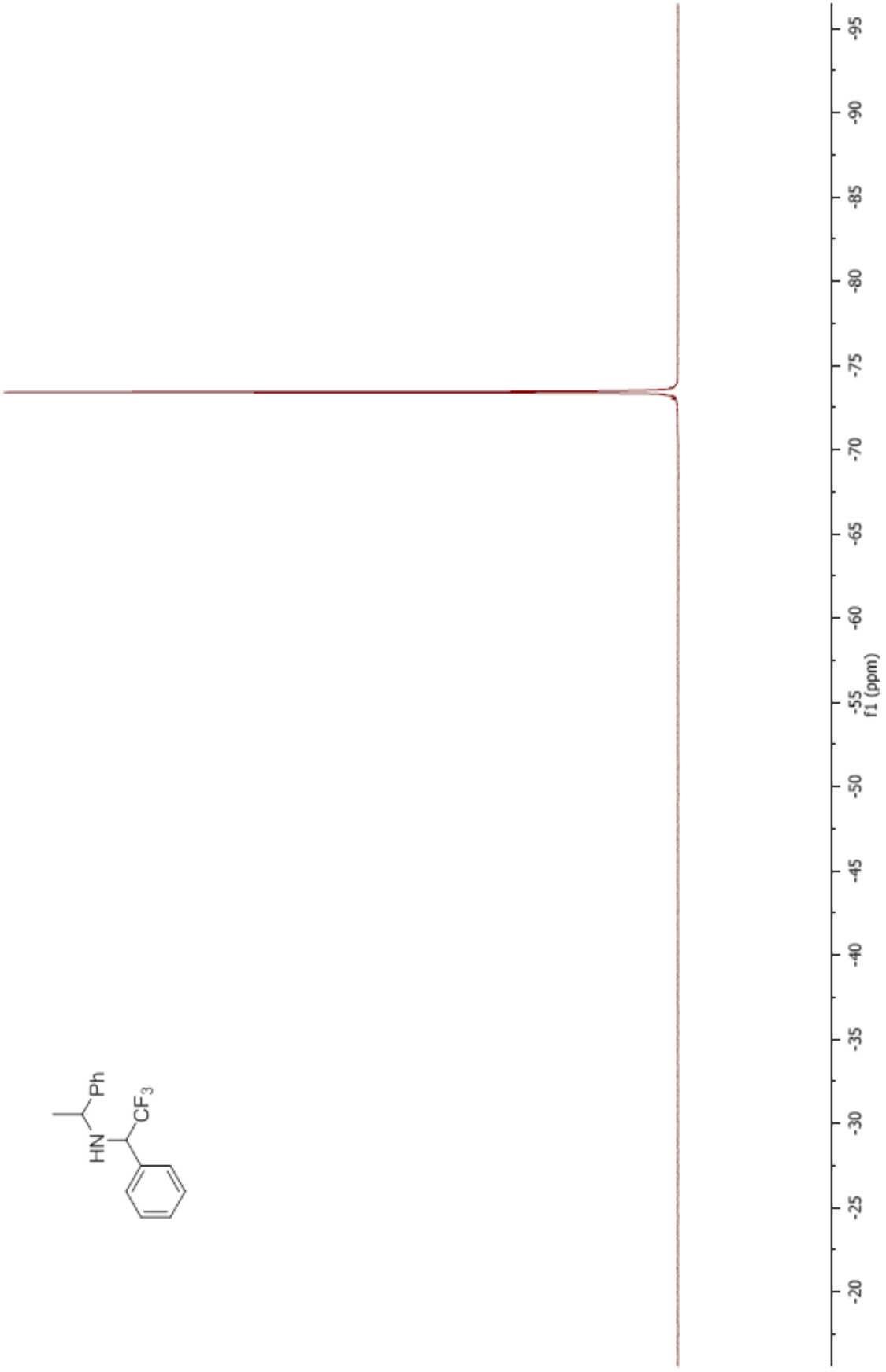



PMP
NH
F3C
-52
-54
-56
-58
-60
-62
-64
-66
-68
-70
-72
-74
-76
-78
-80
-82
-84
-86
-88
-90
-92
f1 (ppm)

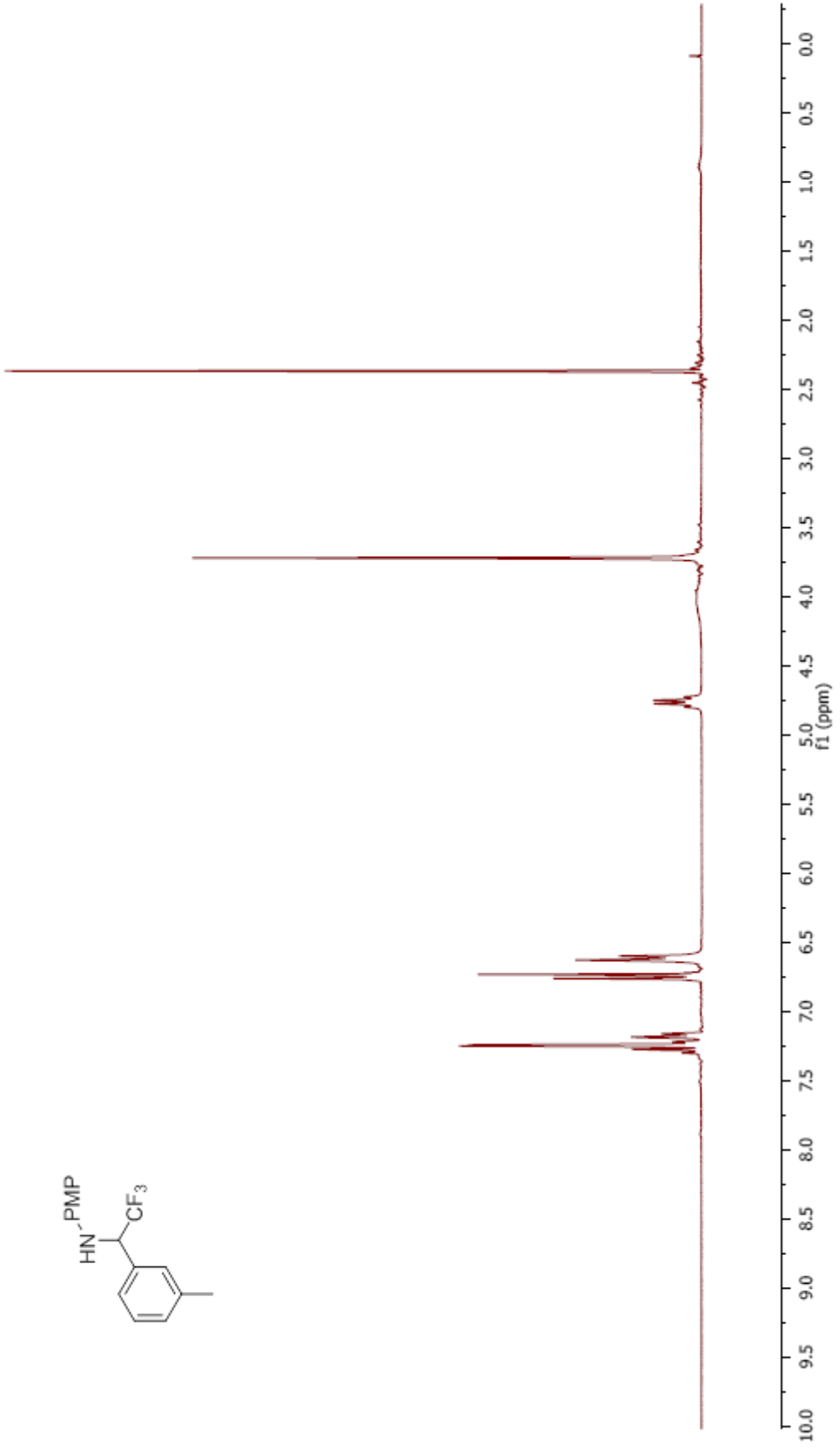
N-(1'-Phenylethyl)-ethan-2,2,2-trifluoro-1-phenyl-1-amine :

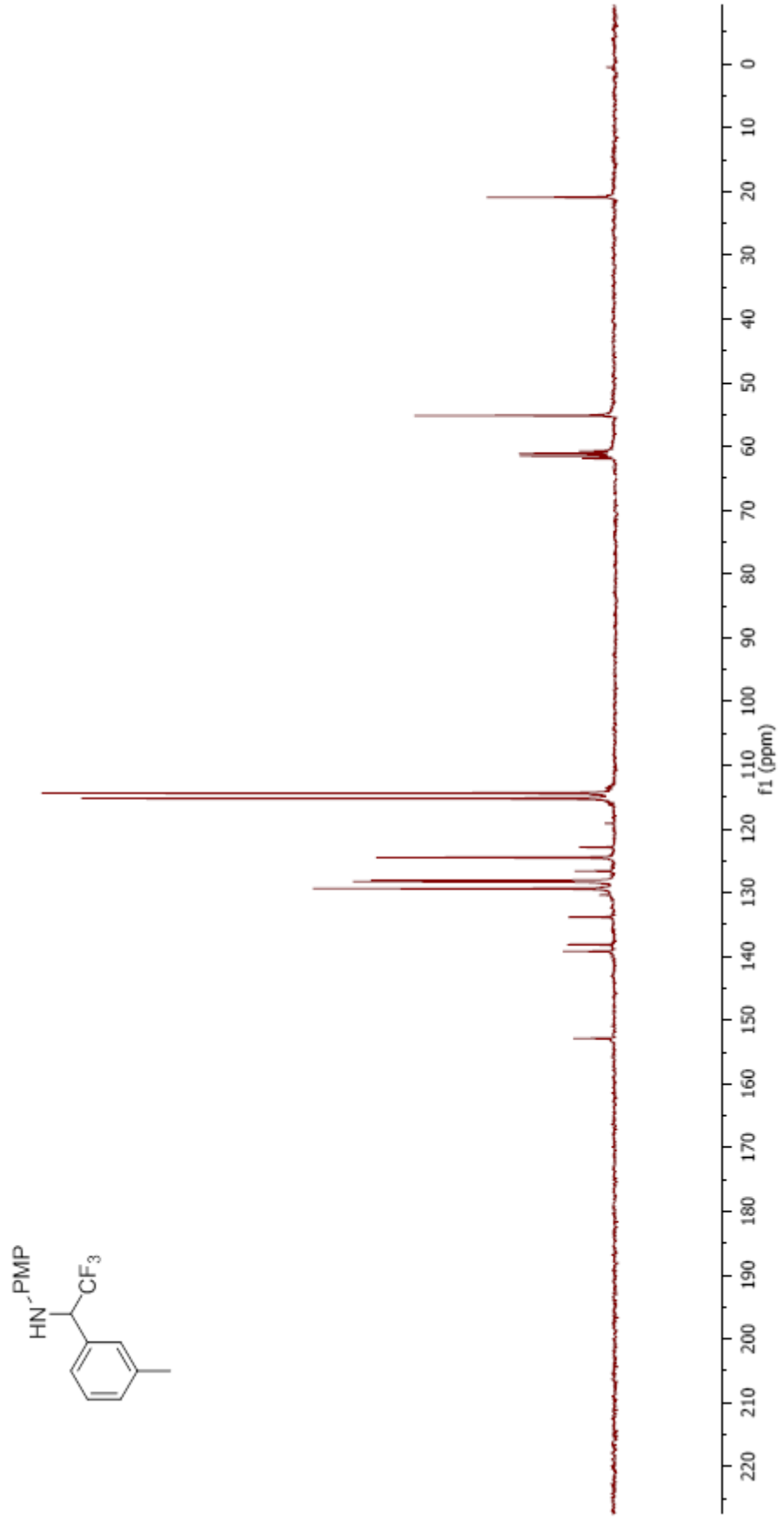


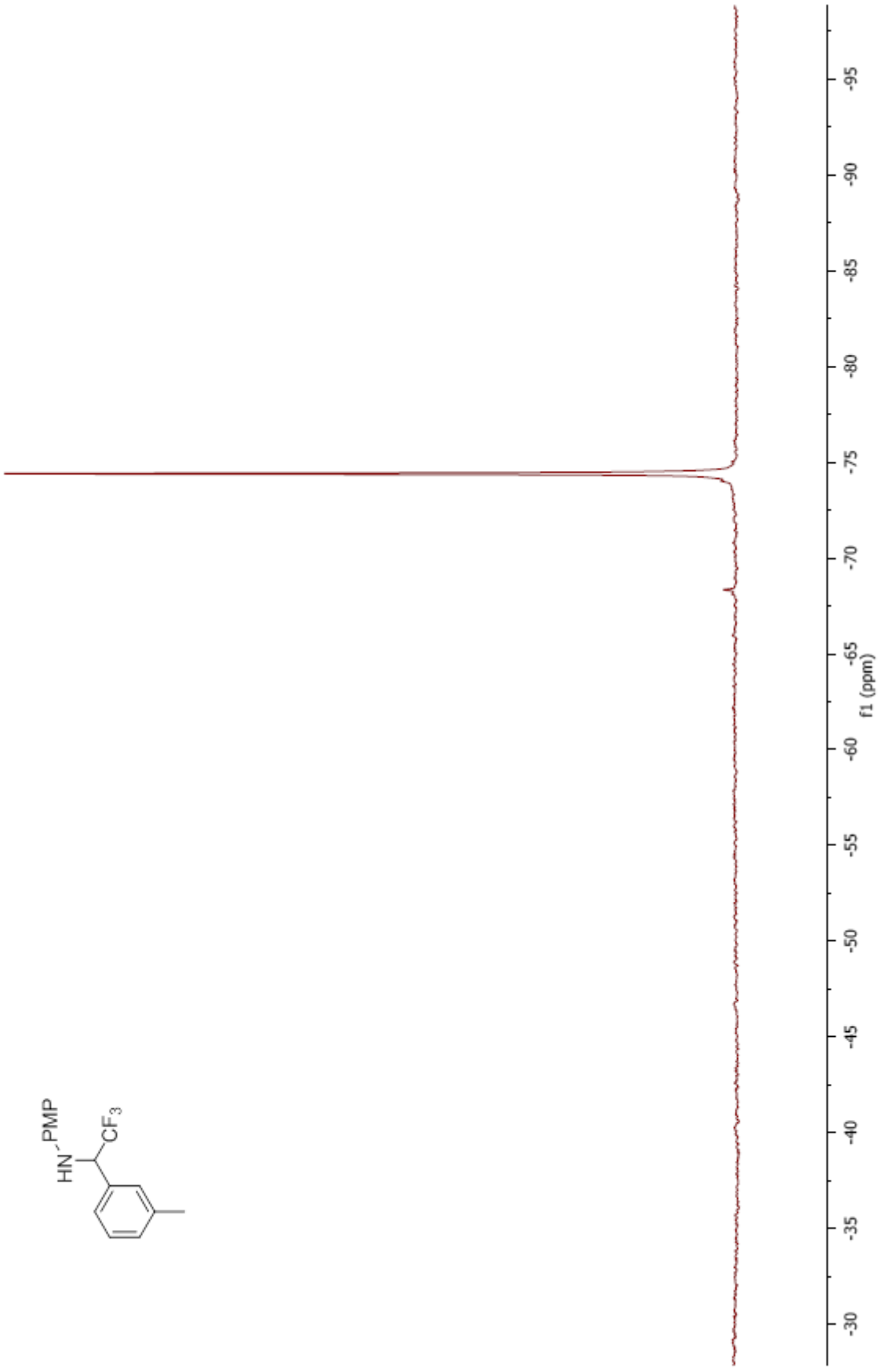



Ph
HN
CF3
-95
-90
-85
-80
-75
-70
-65
-60
-55
-50
-45
-40
-35
-30
-25
-20
f1 (ppm)

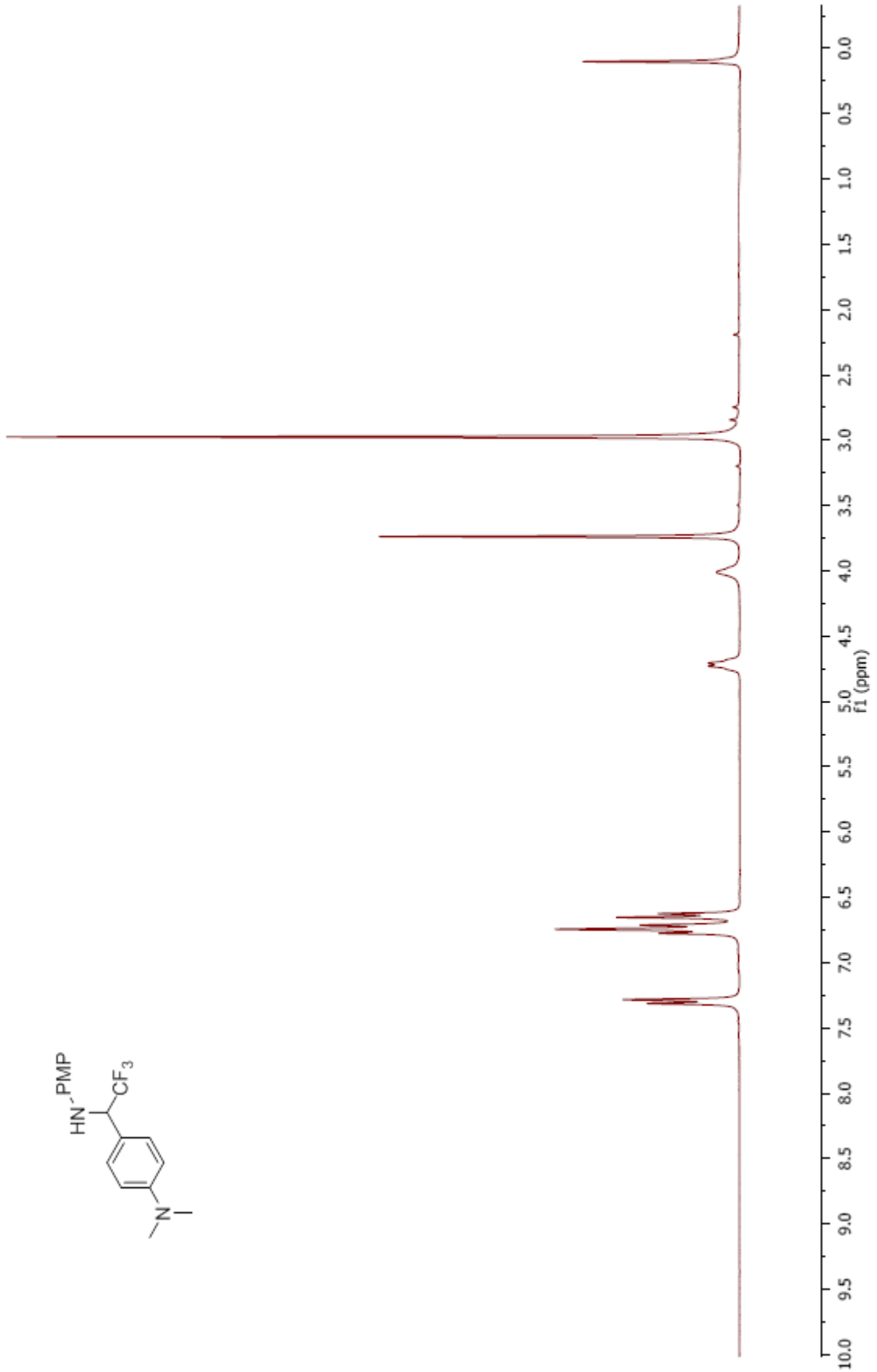
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(3''-methylphenyl)-1-amine :

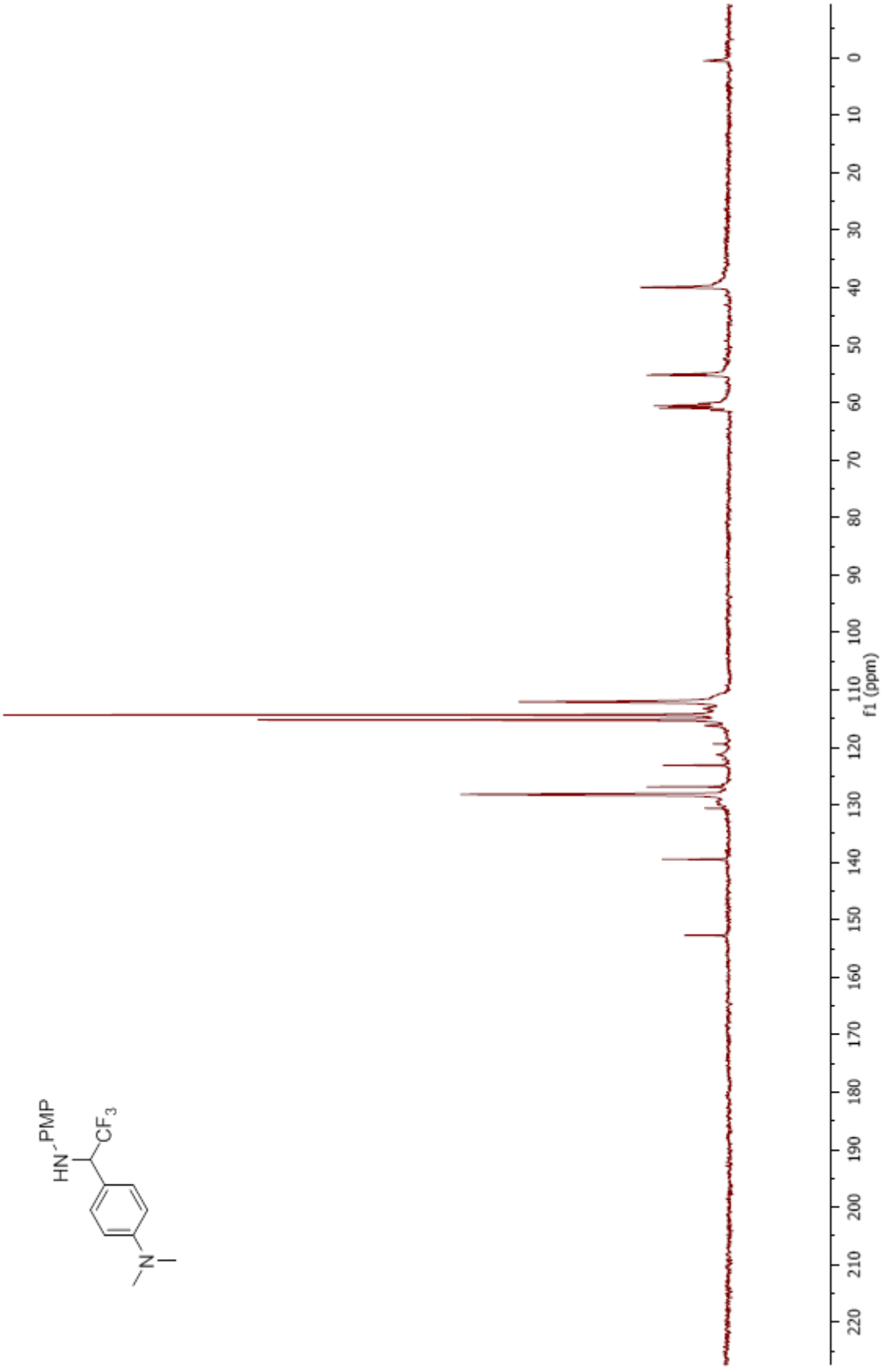


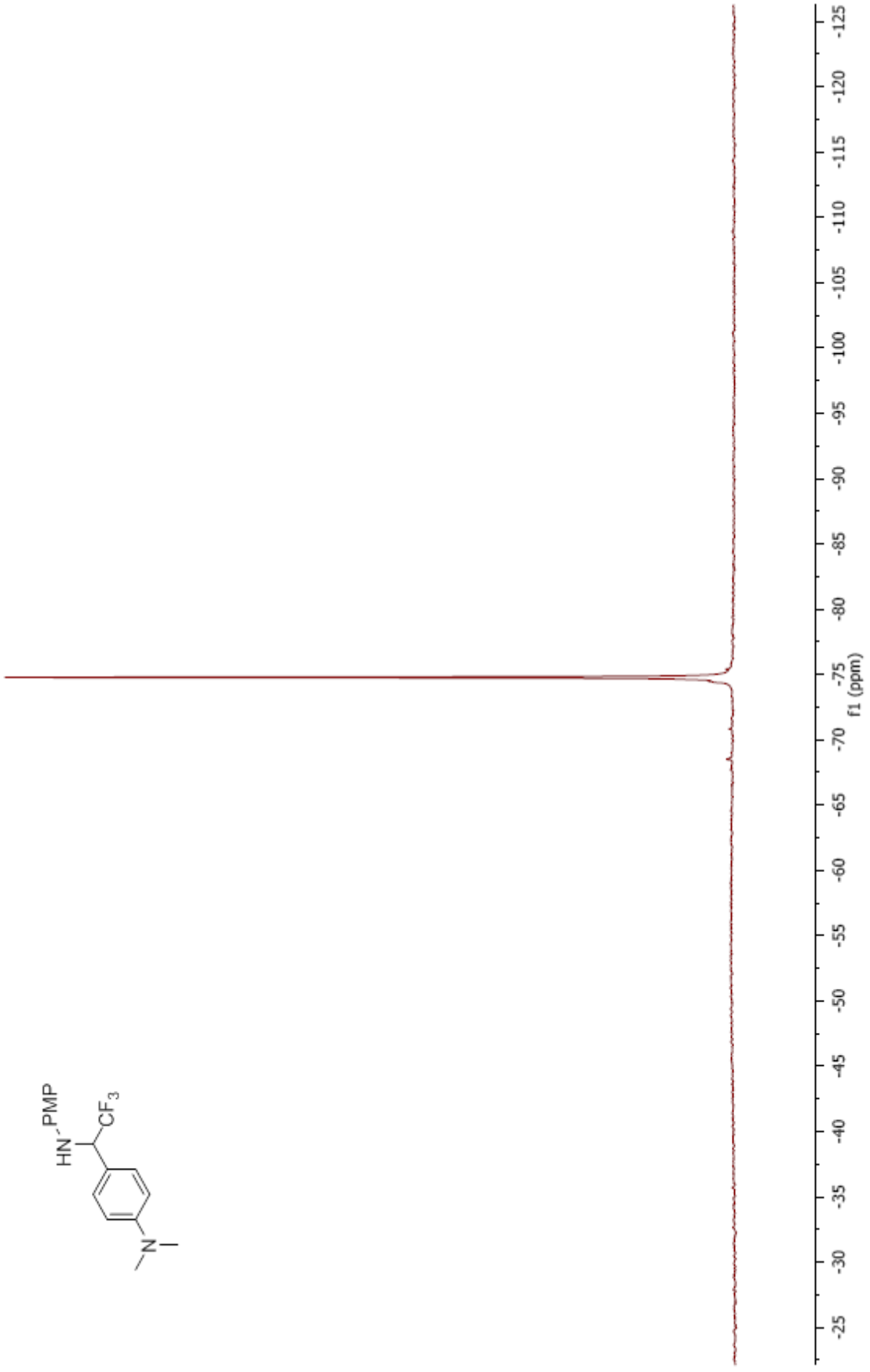

PMP
HN
CF3
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
f1 (ppm)


PMP
HN
CF3
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
f1 (ppm)

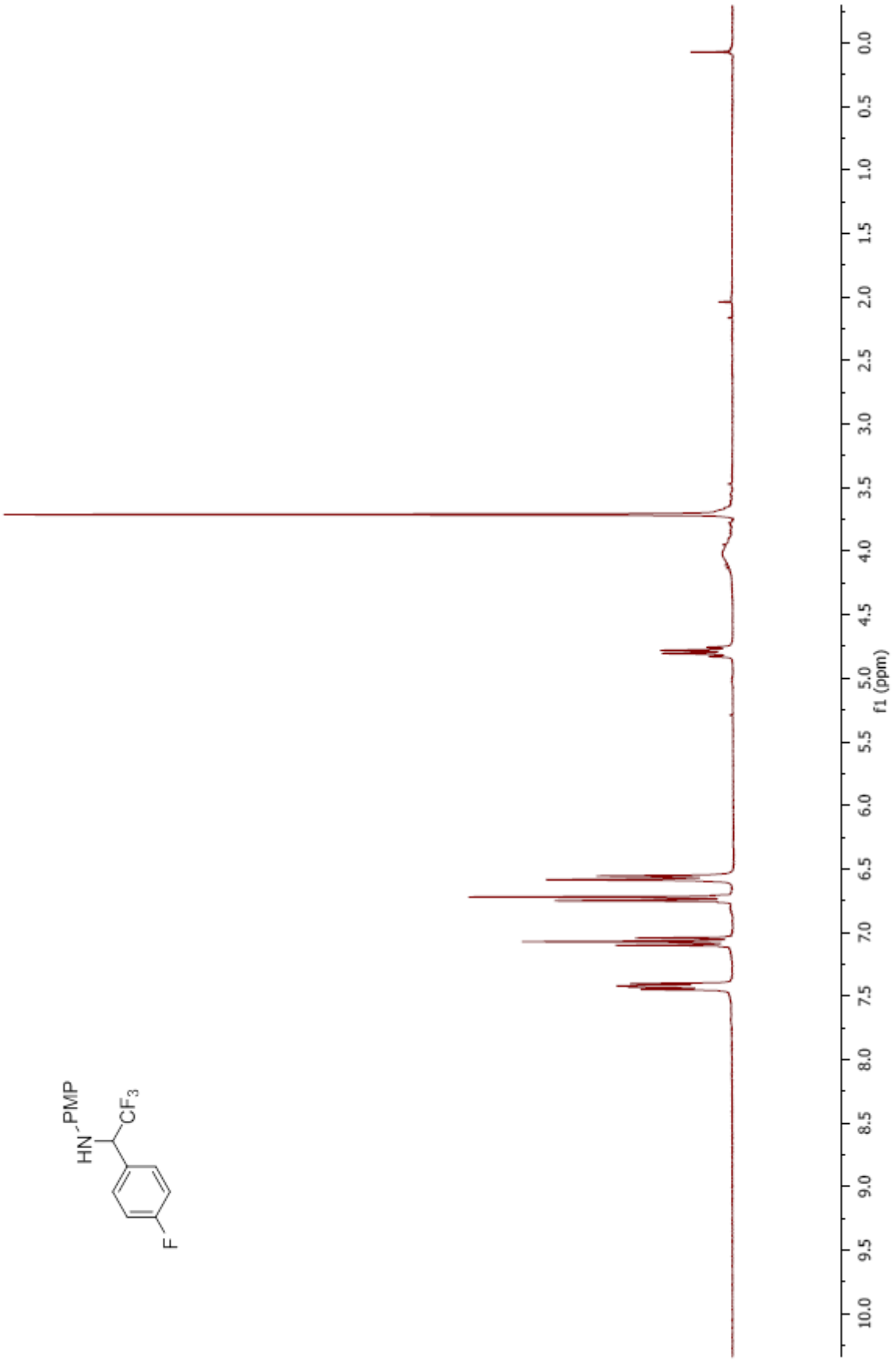
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-(N',N'-dimethylammino)-phenyl)-1-amine :

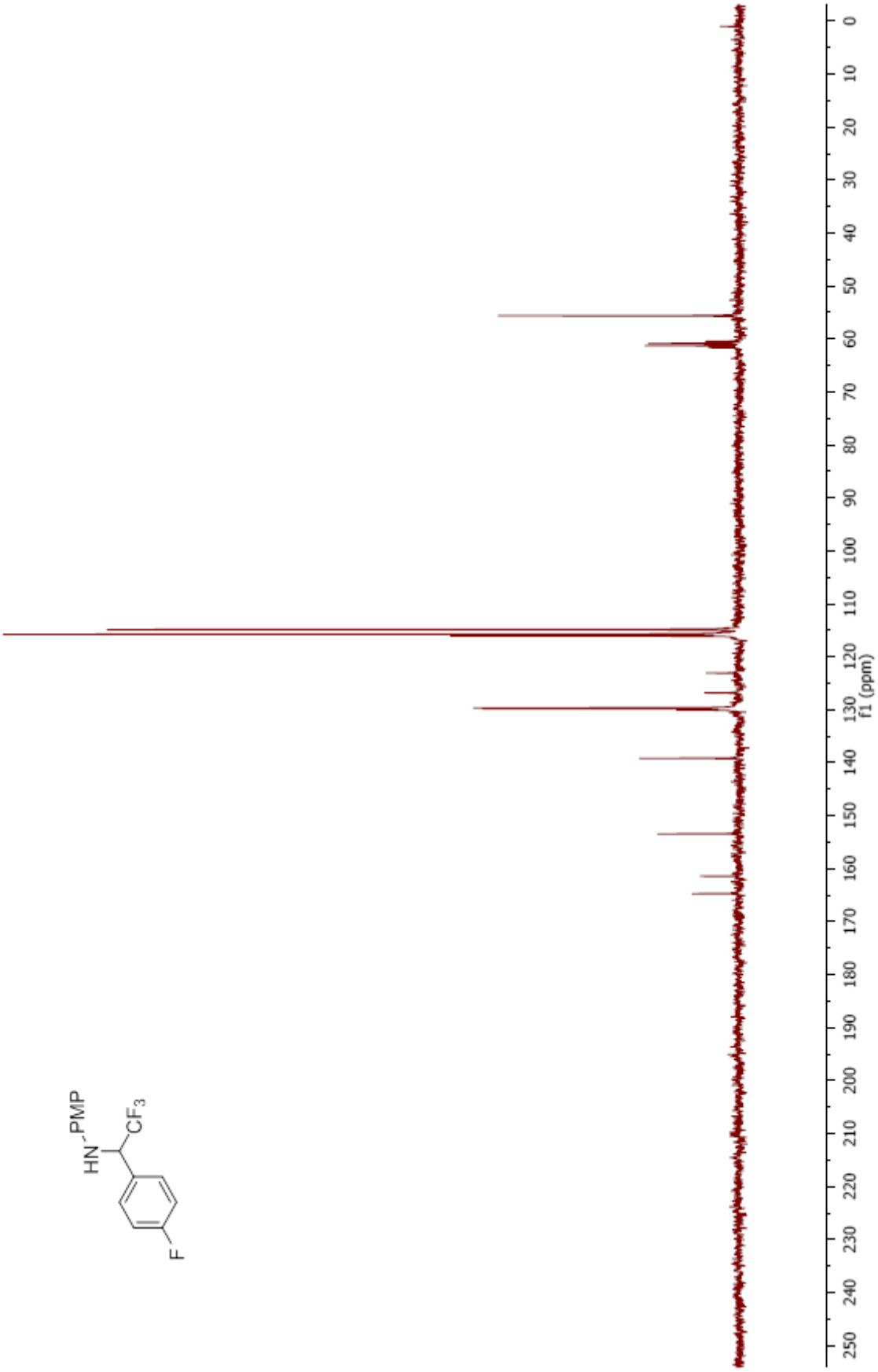


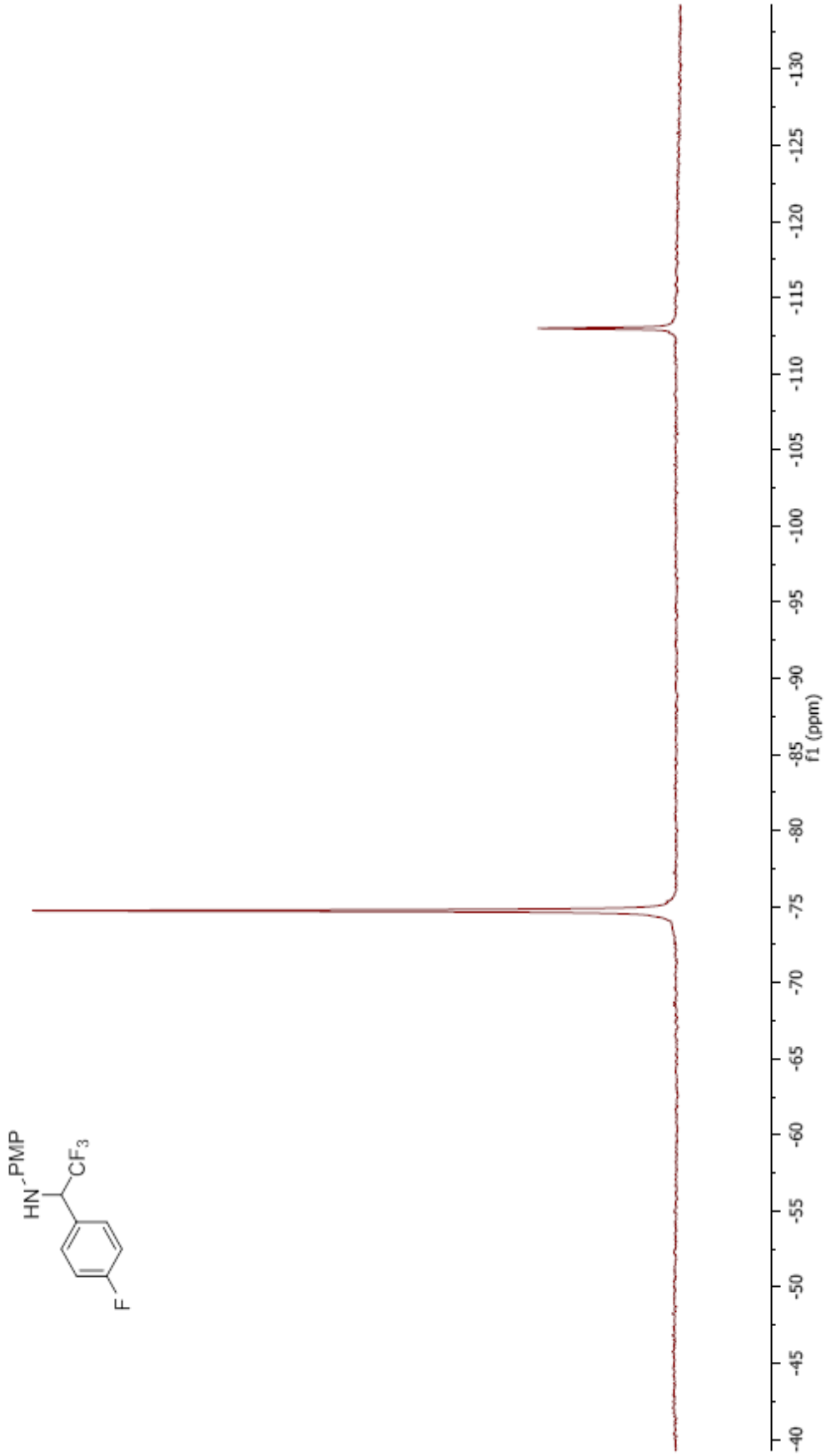

PMP
HN
CF3
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
f1 (ppm)


PMP
HN
CF3
N
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
f1 (ppm)

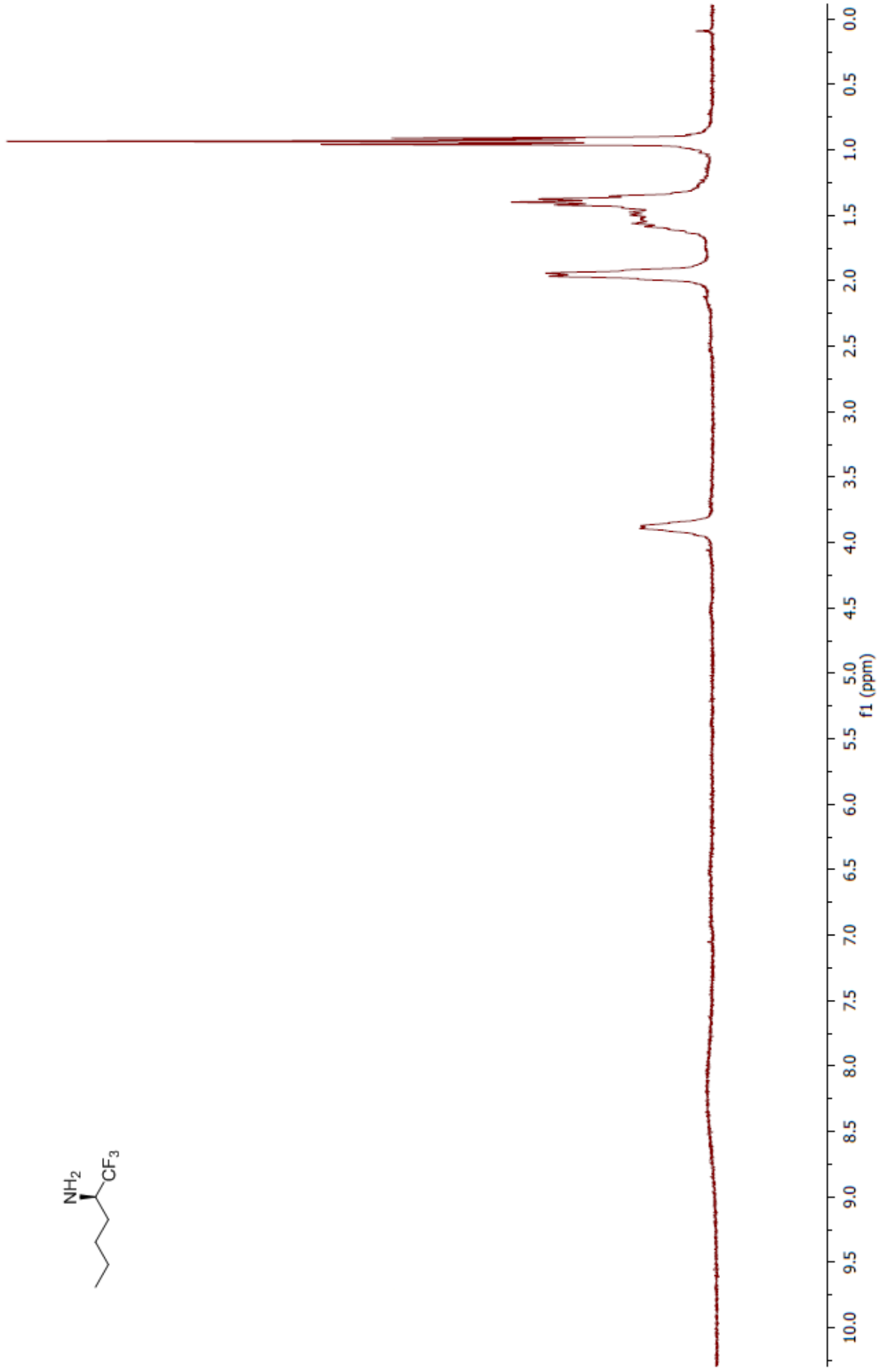
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-fluorophenyl)-1-amine :

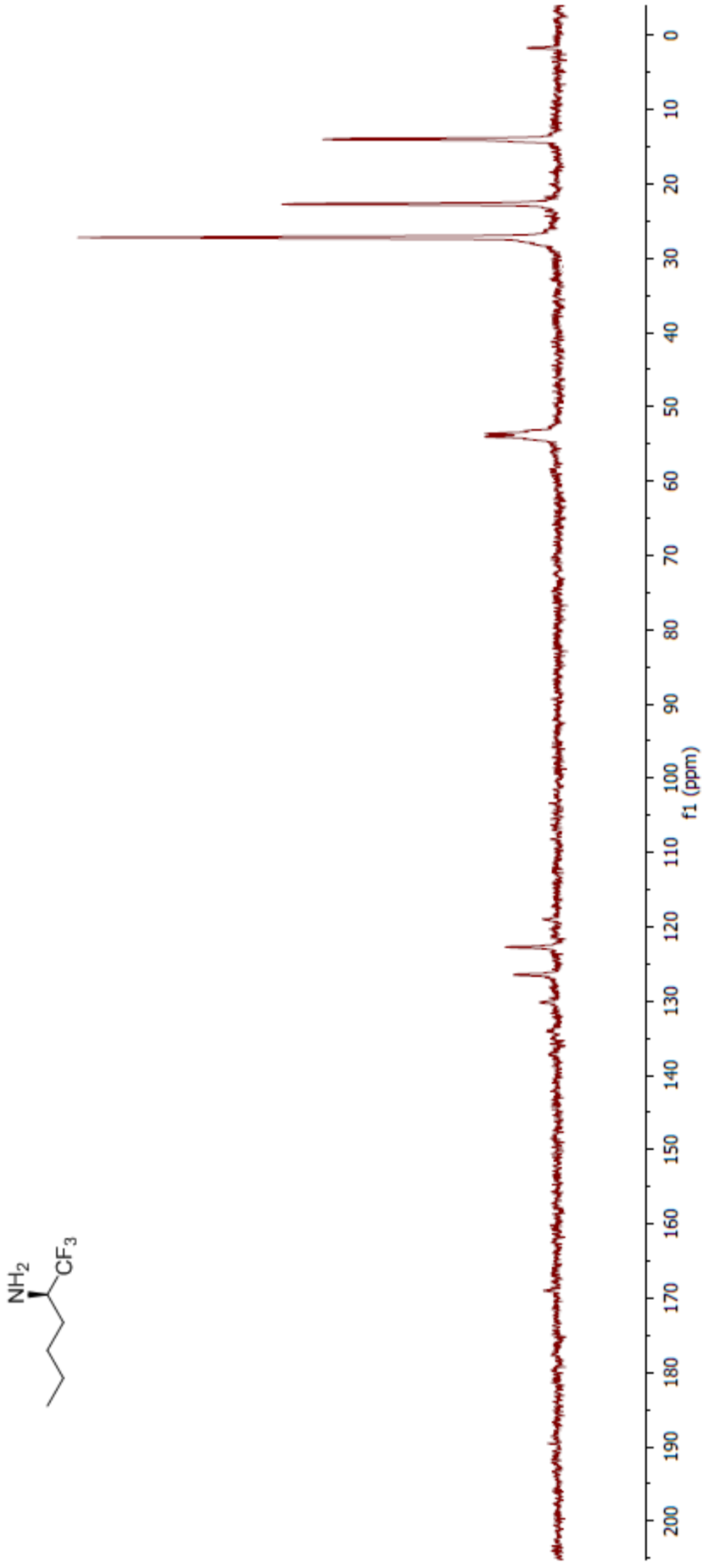


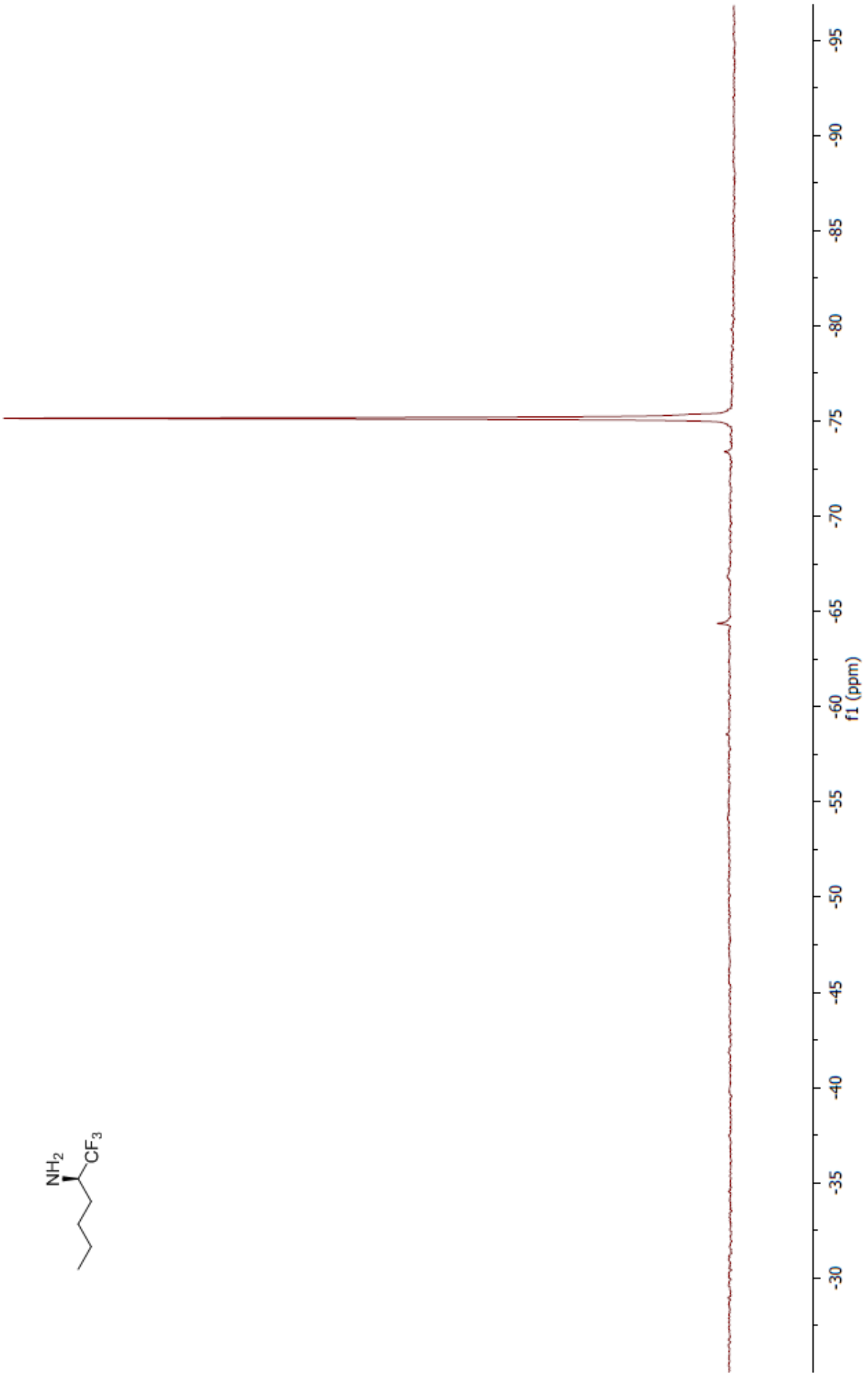

PMP
HN
CF3
F
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
240
250
f1 (ppm)


PMP
HN
CF3
F
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
f1 (ppm)

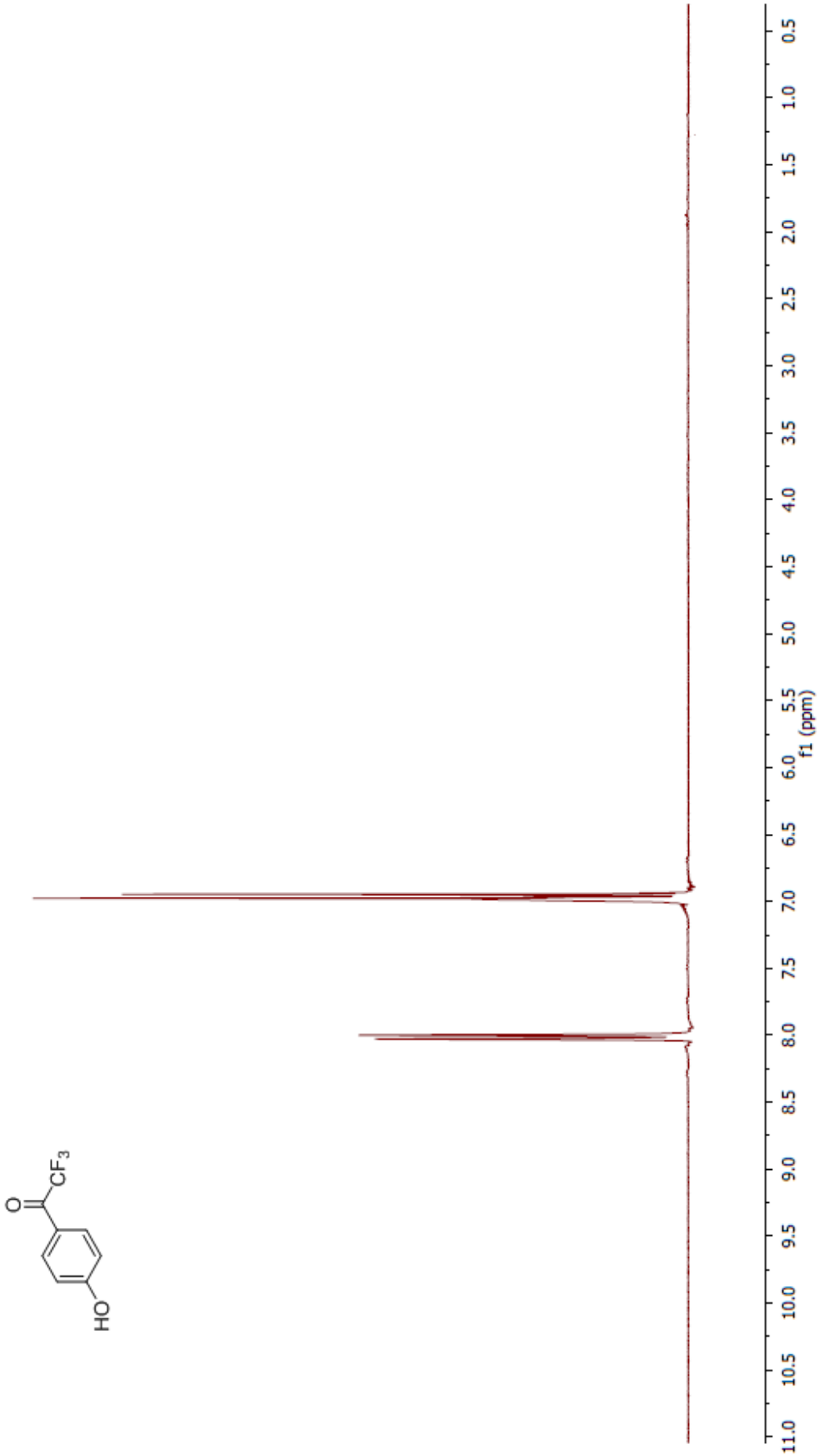
hexan-1,1,1-trifluoro-2-amine :

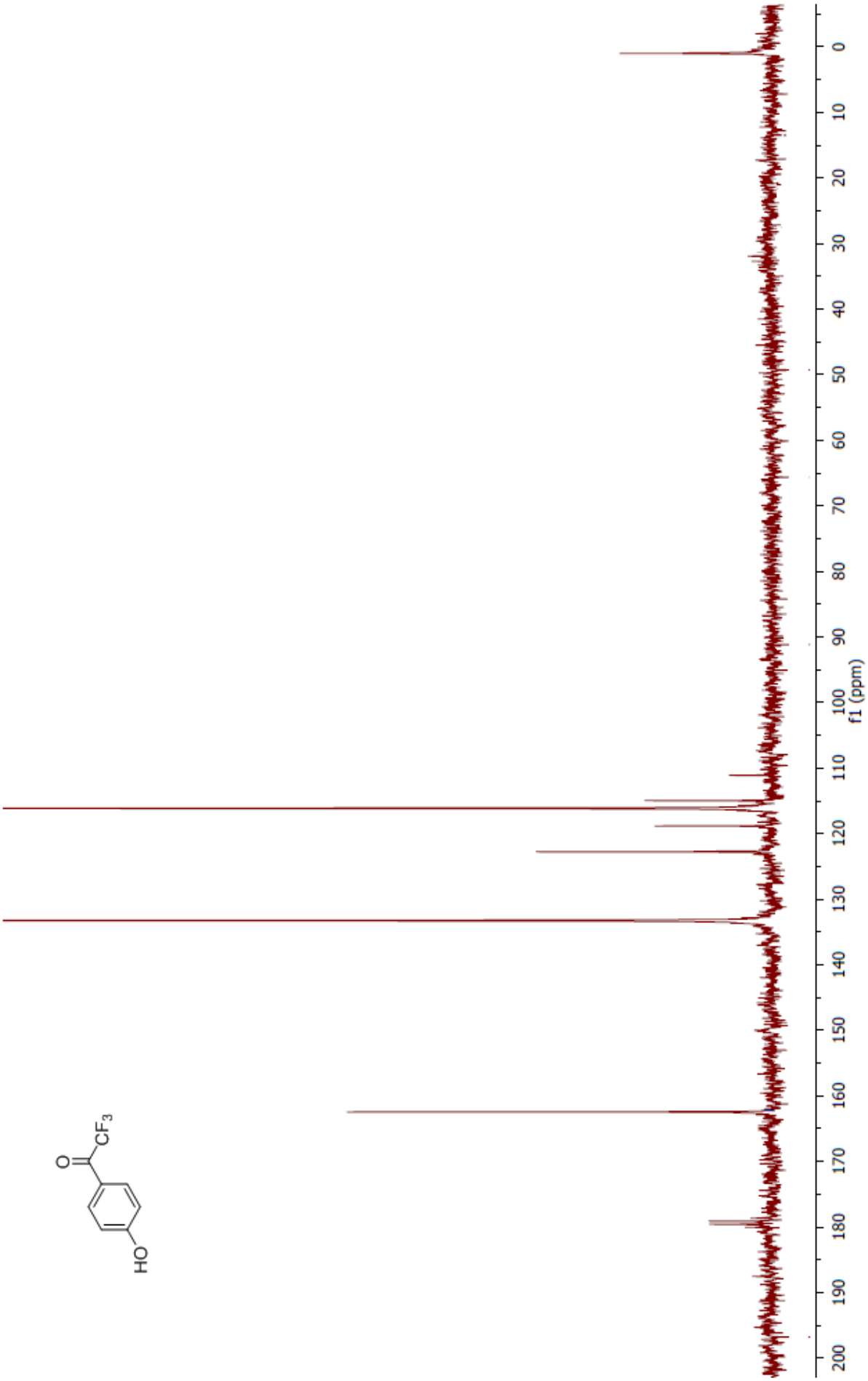

NH2
CF3
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

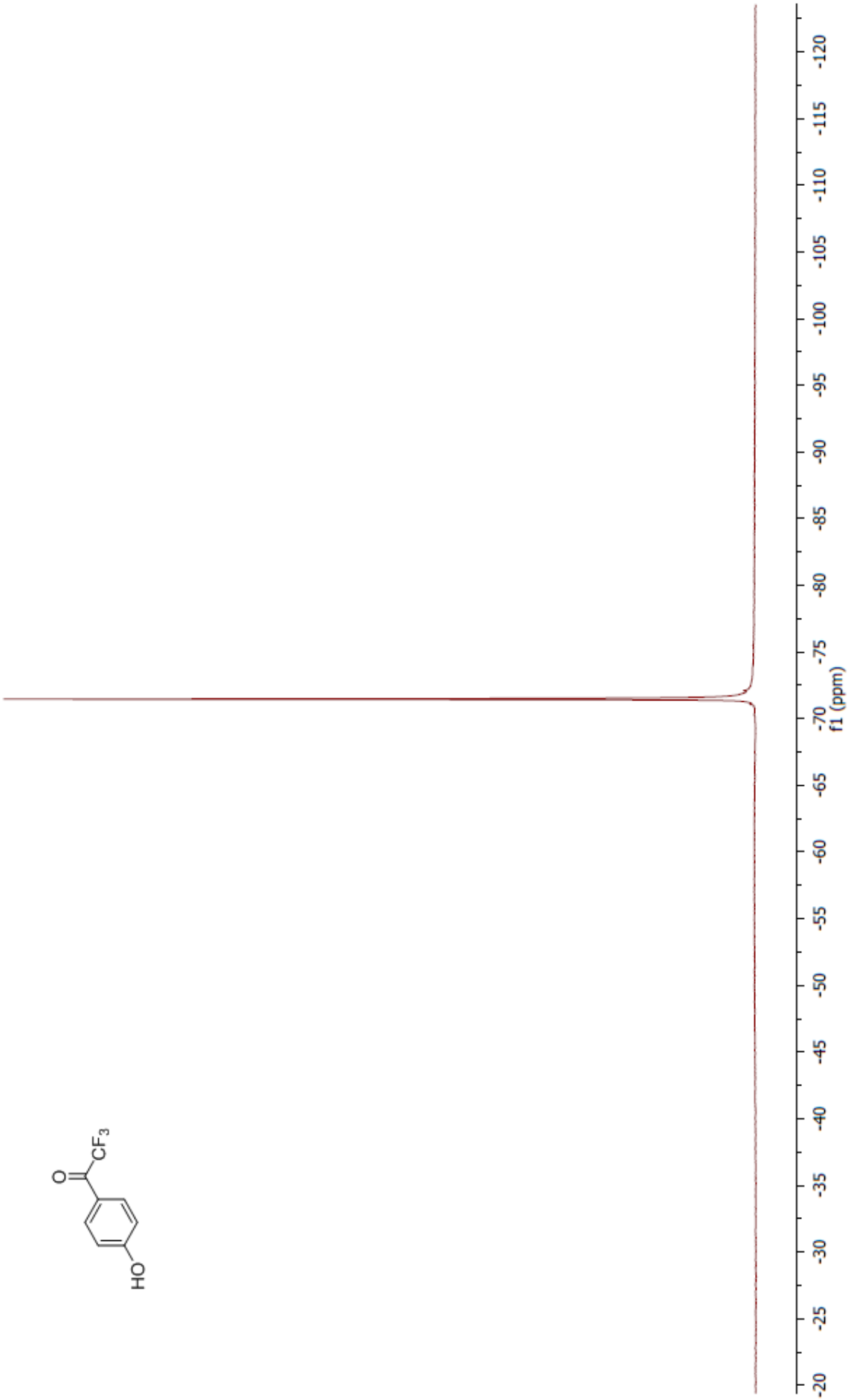

NH2
CF3
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
f1 (ppm)


NH2
CF3
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
f1 (ppm)

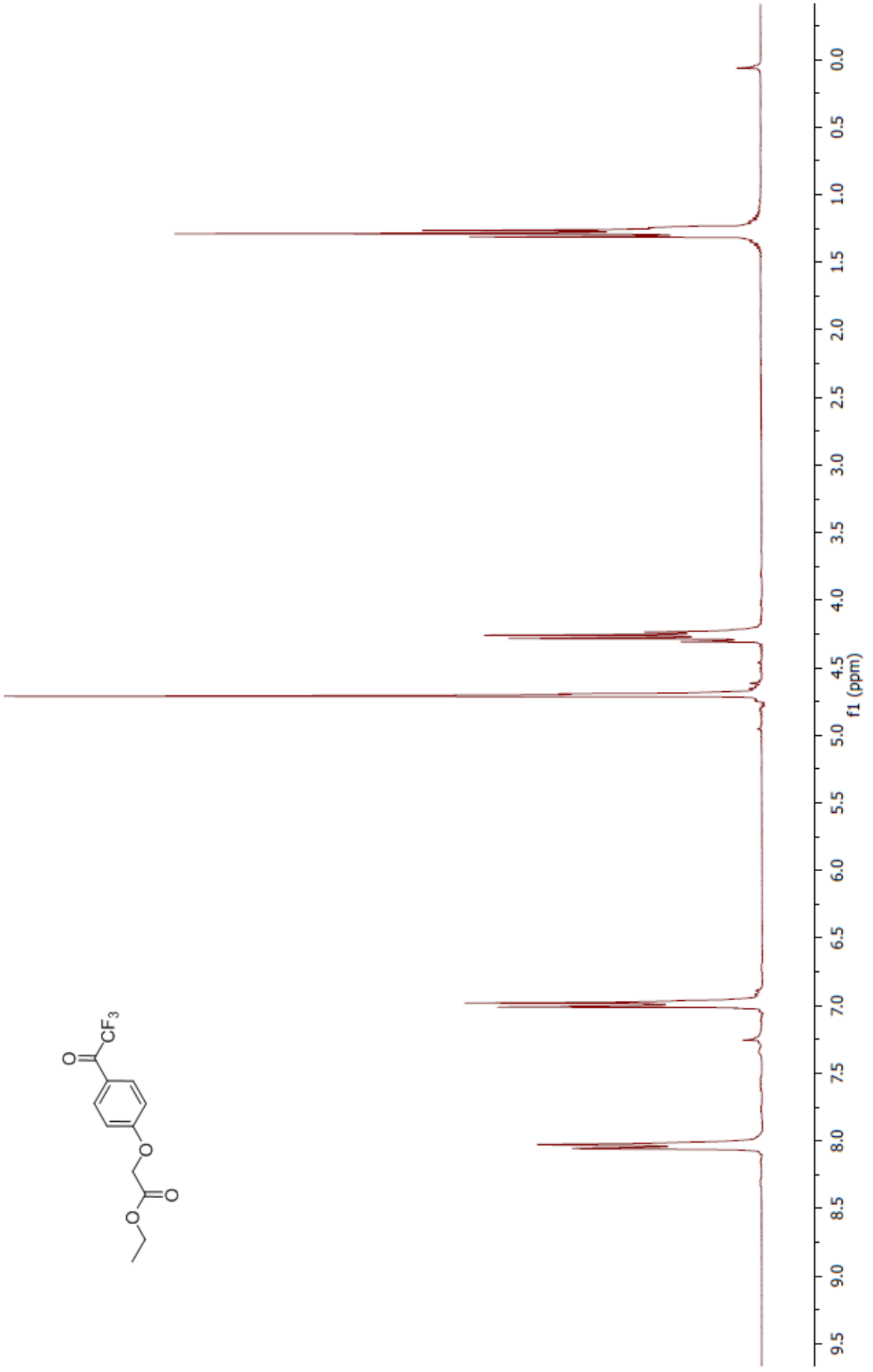
ethan-2,2,2-trifluoro-1-(4'-hydroxyphenyl)-1-ketone :

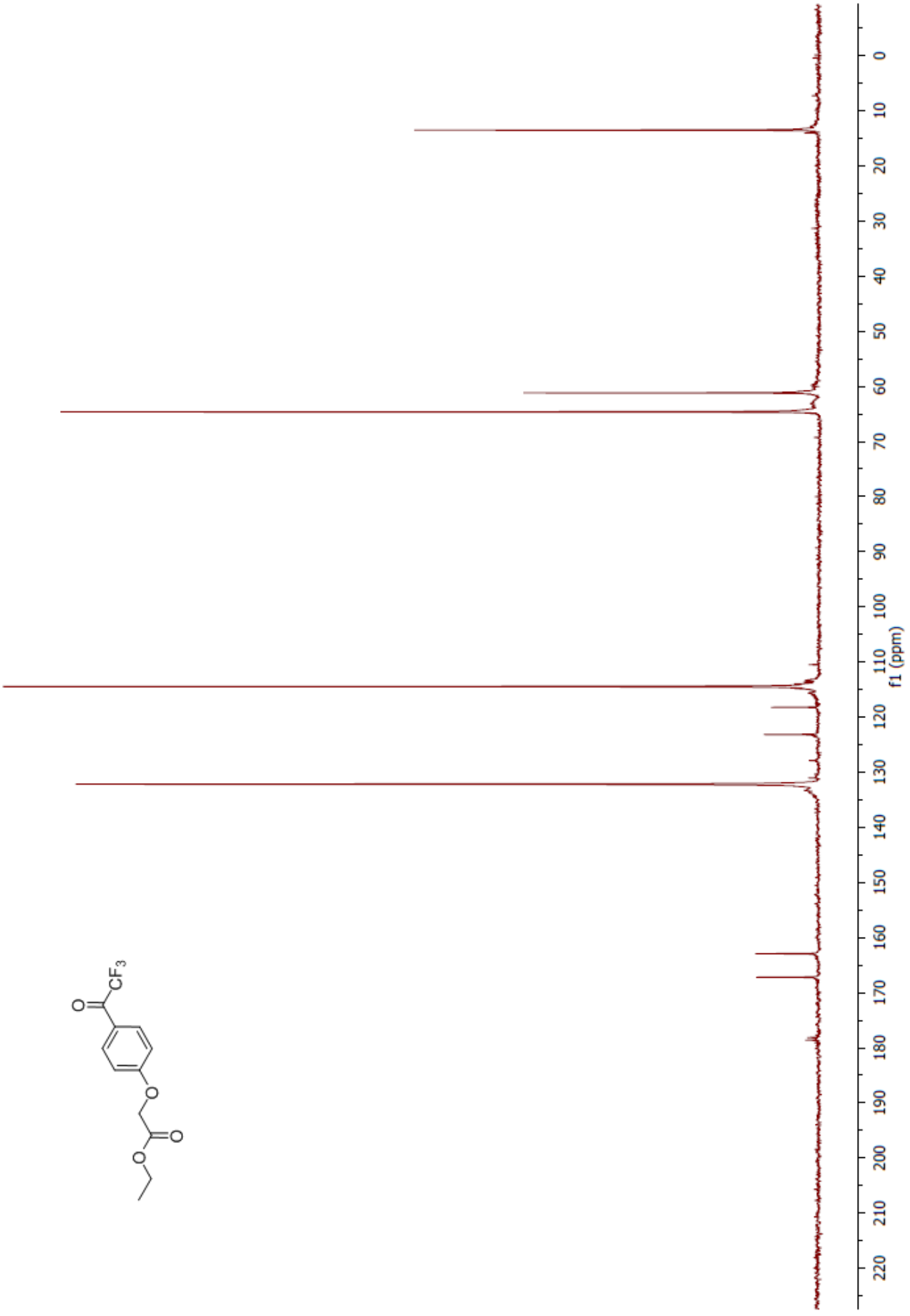


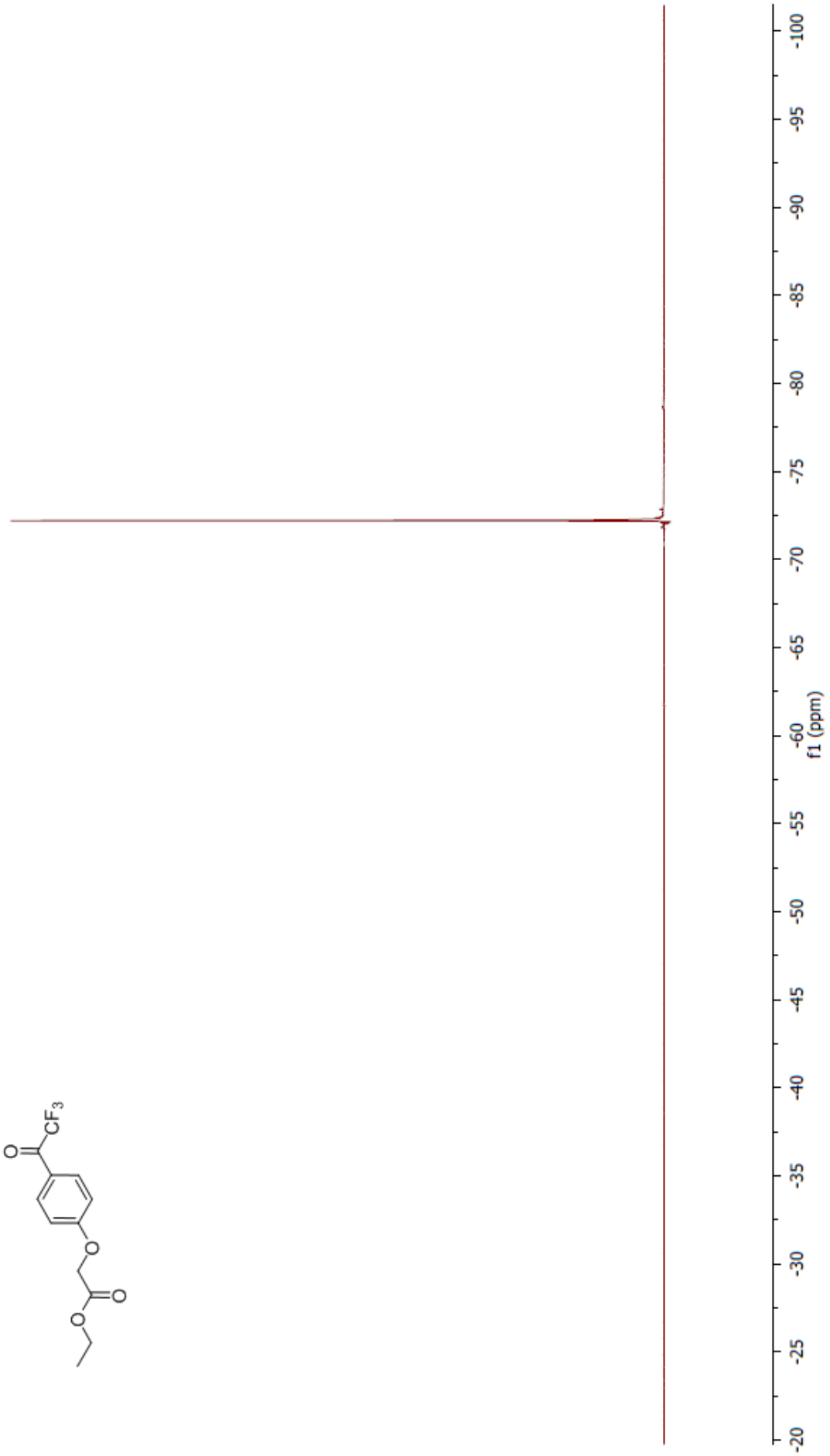



O
CF3
HO
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
f1 (ppm)

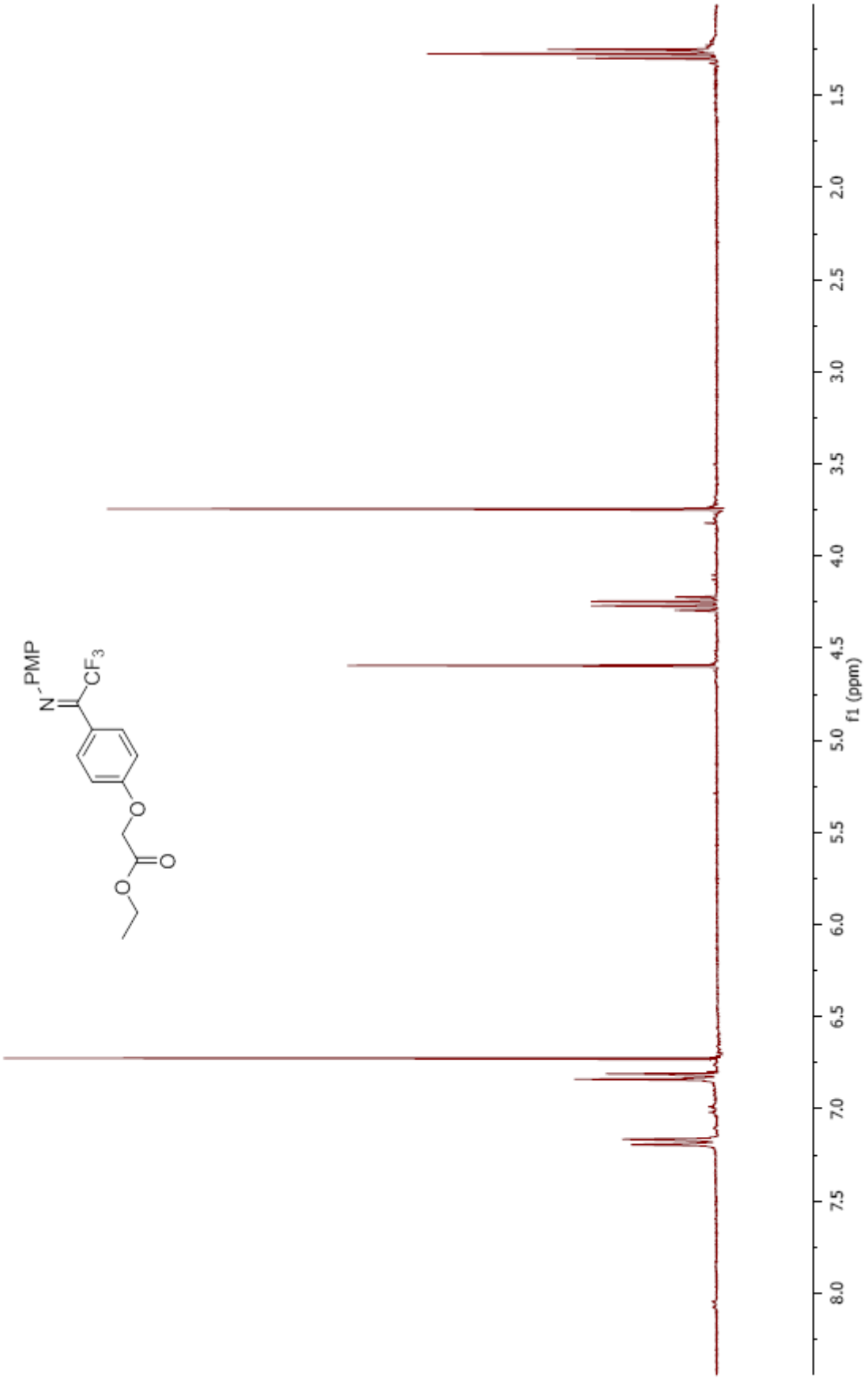
ethan-2,2,2-trifluoro-1-(4'-ethylphenoxyacetate)-1-ketone :

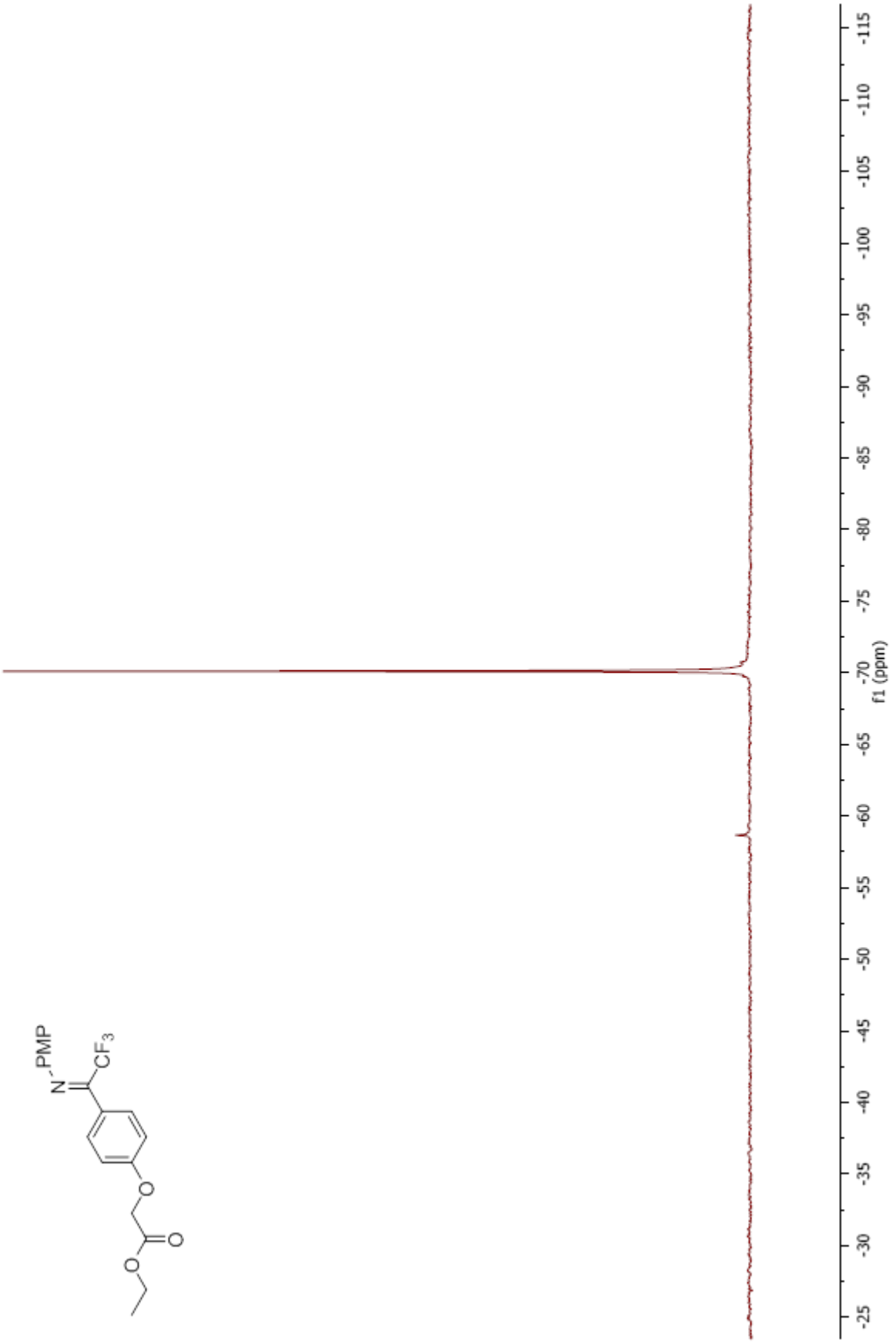




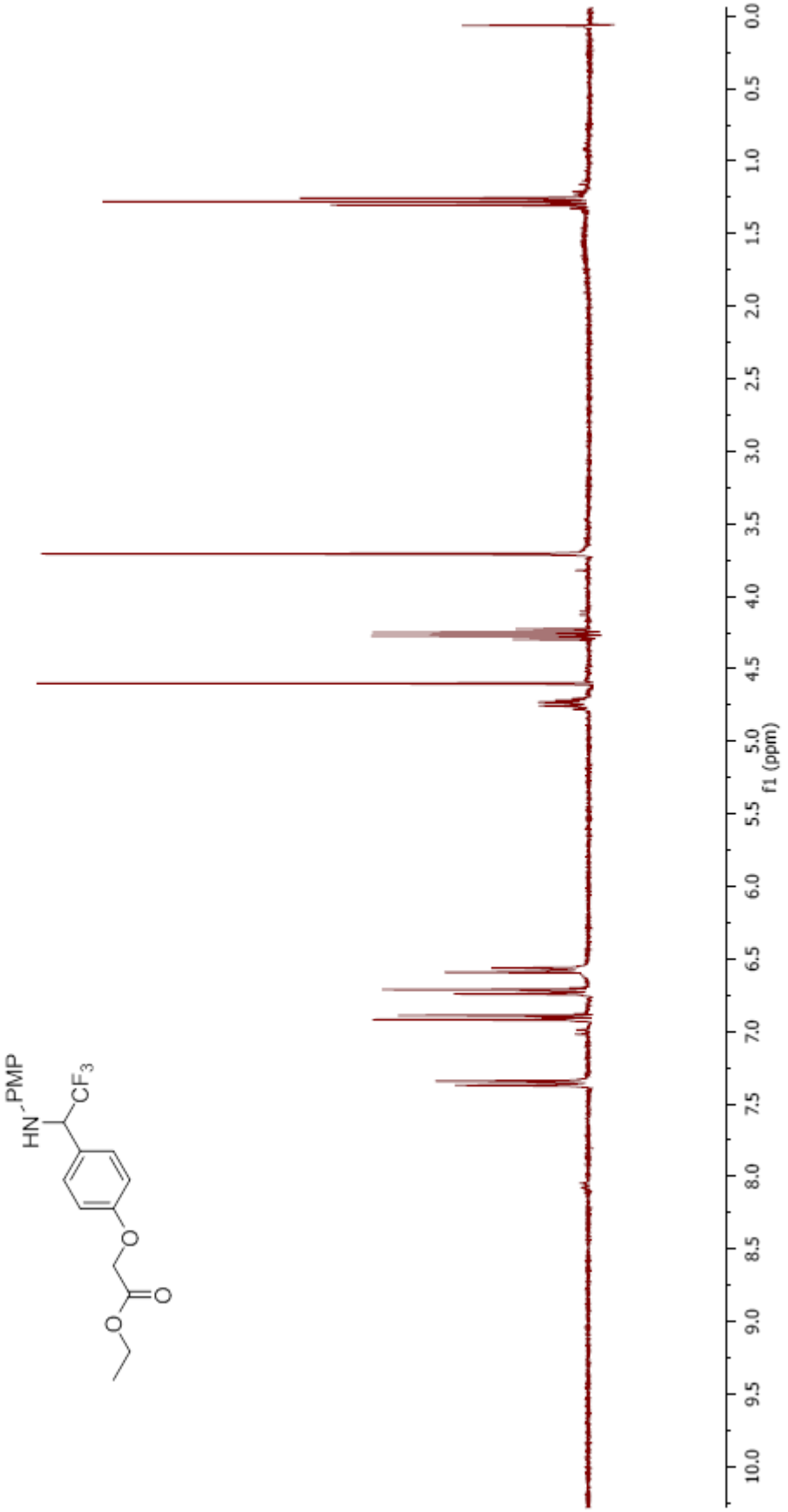

-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
f1 (ppm)
O
CF3
O
O
O

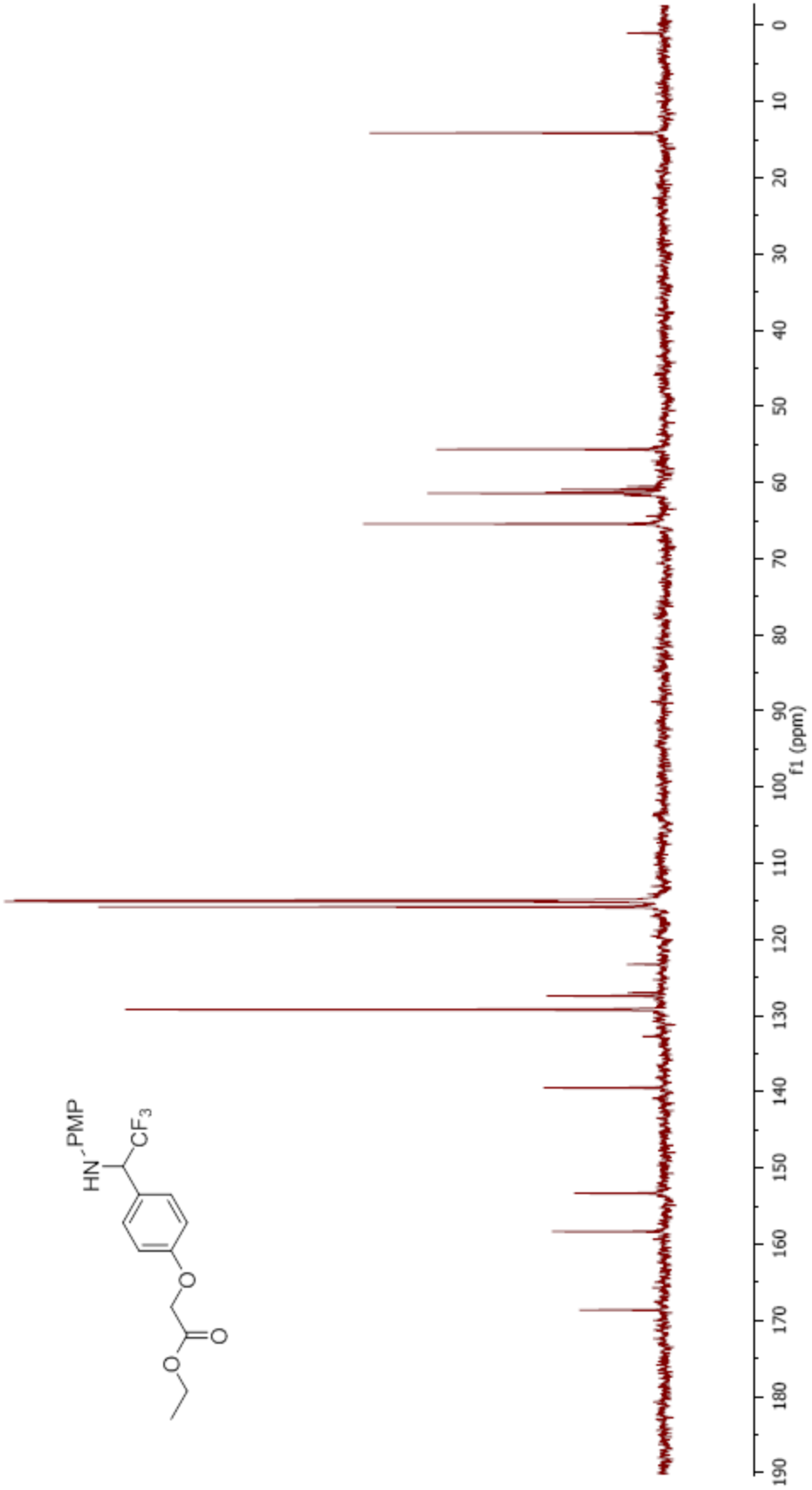
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-ethylphenoxyacetate)-1-imine :

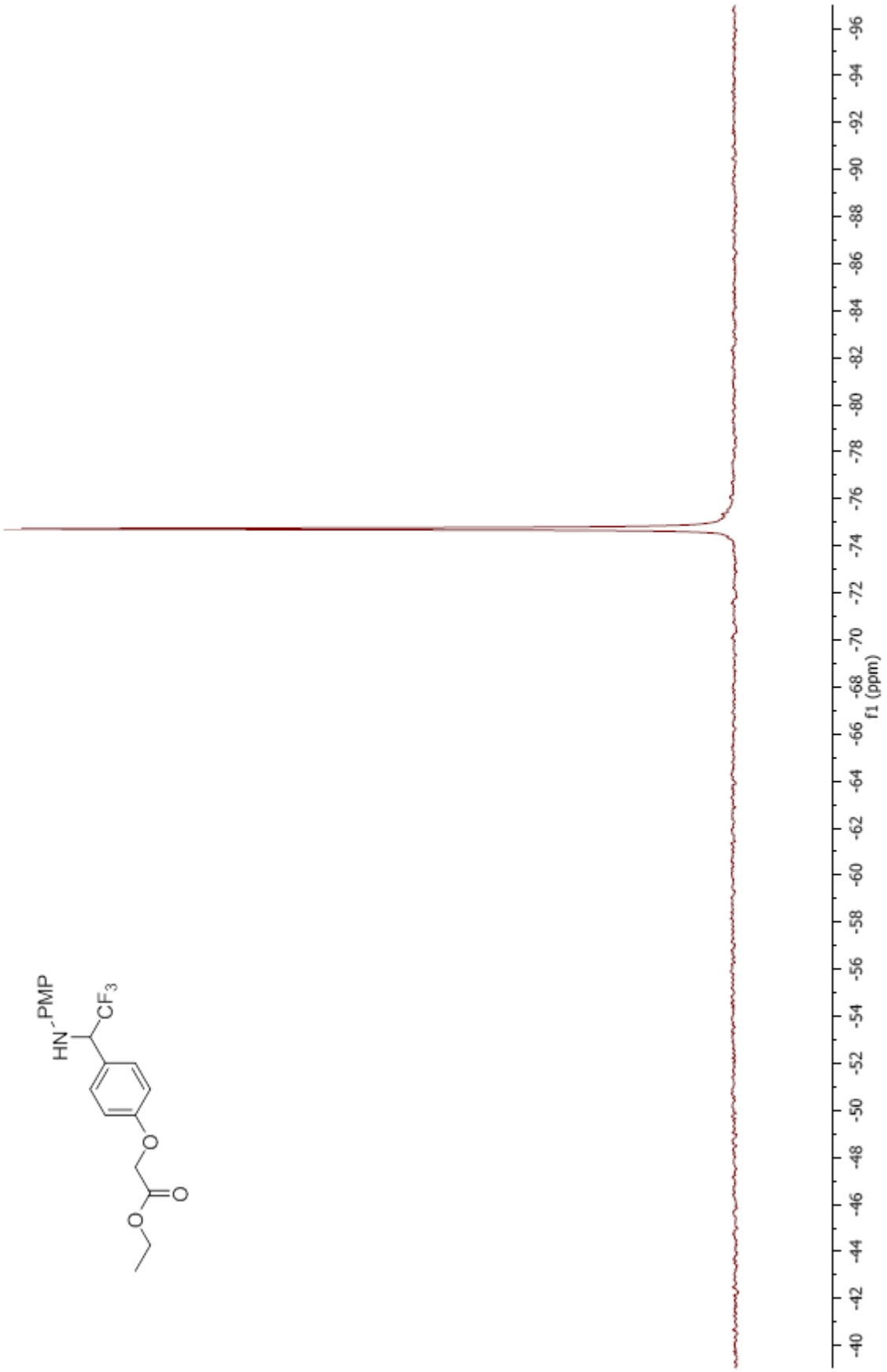



PMP
N
CF3
O
O
O
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
f1 (ppm)

N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-ethylphenoxyacetate)-1-amine :

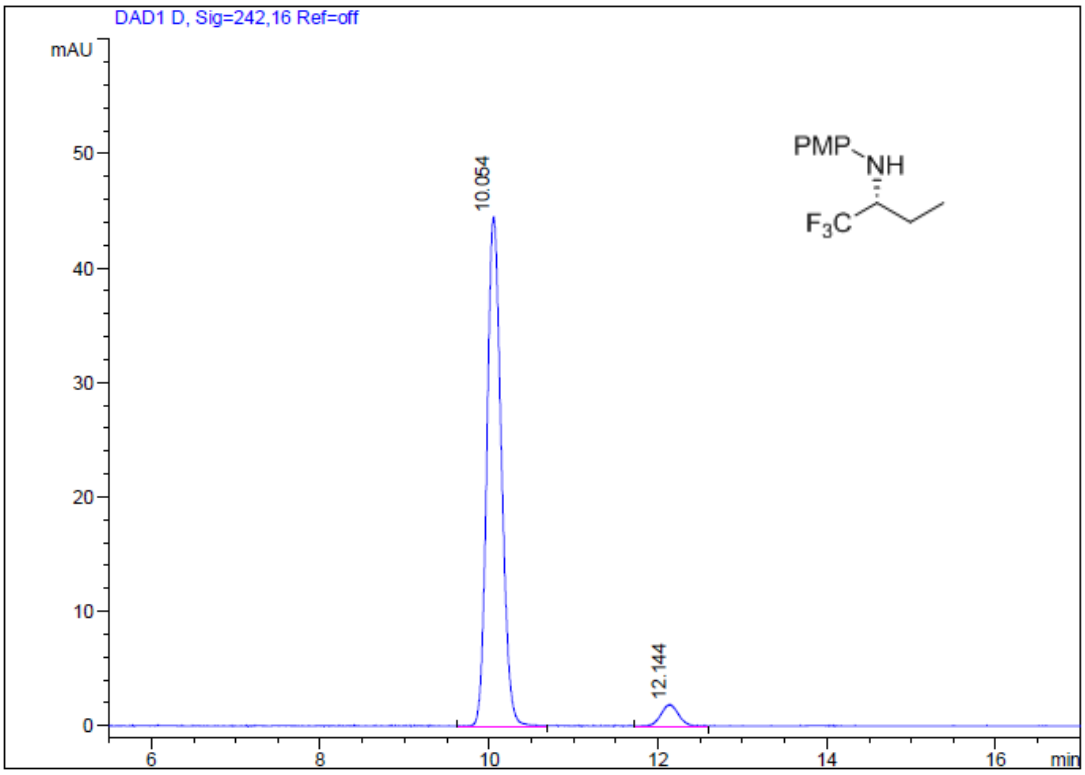




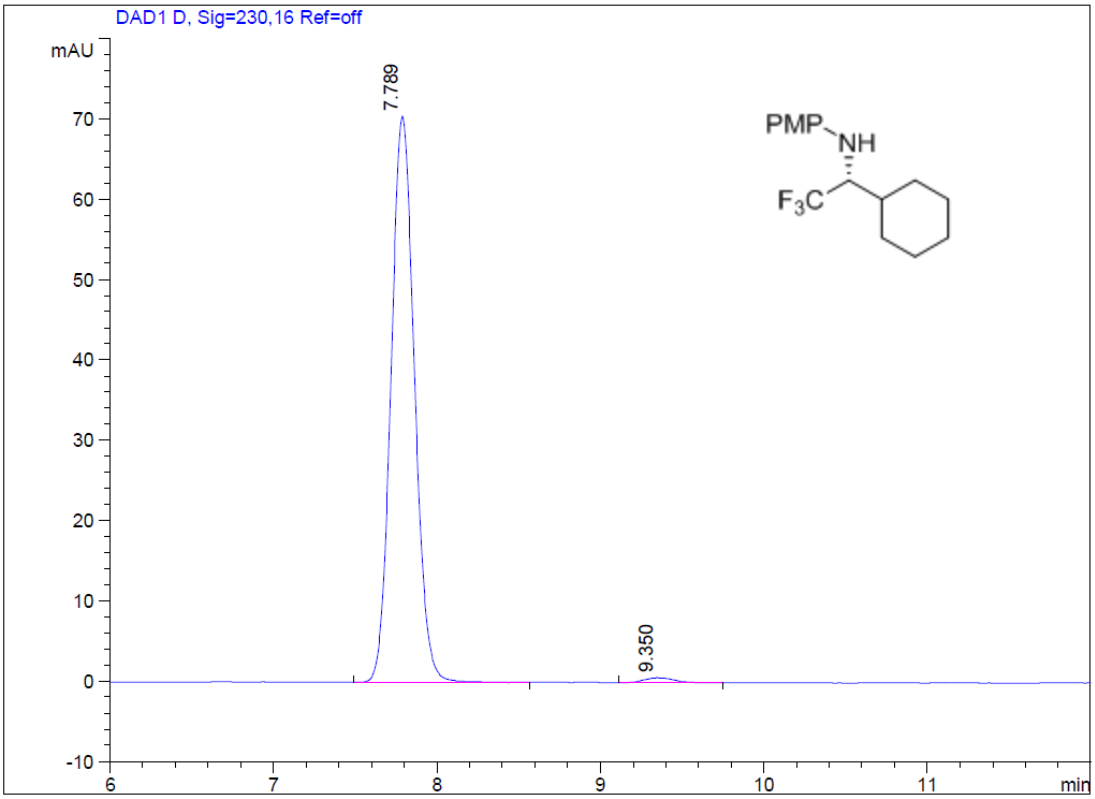

PMP
HN
CF3
O
O
O
O
-40
-42
-44
-46
-48
-50
-52
-54
-56
-58
-60
-62
-64
-66
-68
-70
-72
-74
-76
-78
-80
-82
-84
-86
-88
-90
-92
-94
-96
f1 (ppm)

HPLC Chromatograms:

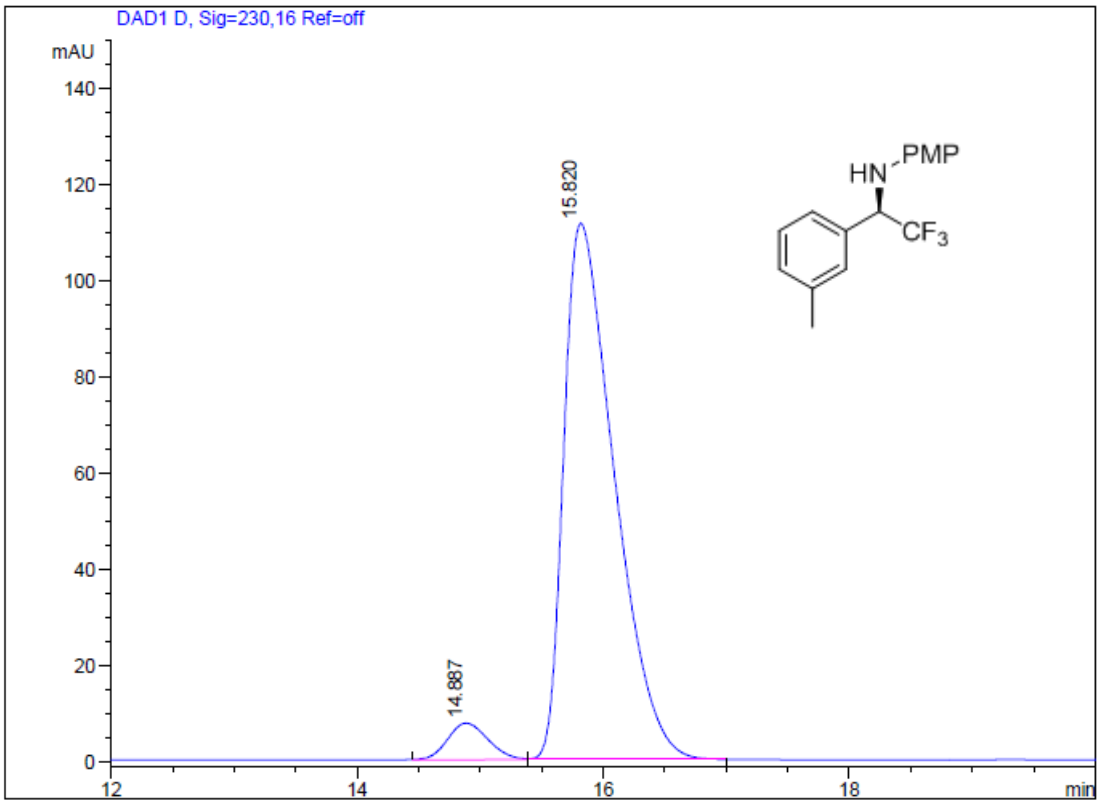
N-(4'-Methoxyphenyl)-butan-1,1,1-trifluoro-2-amine :



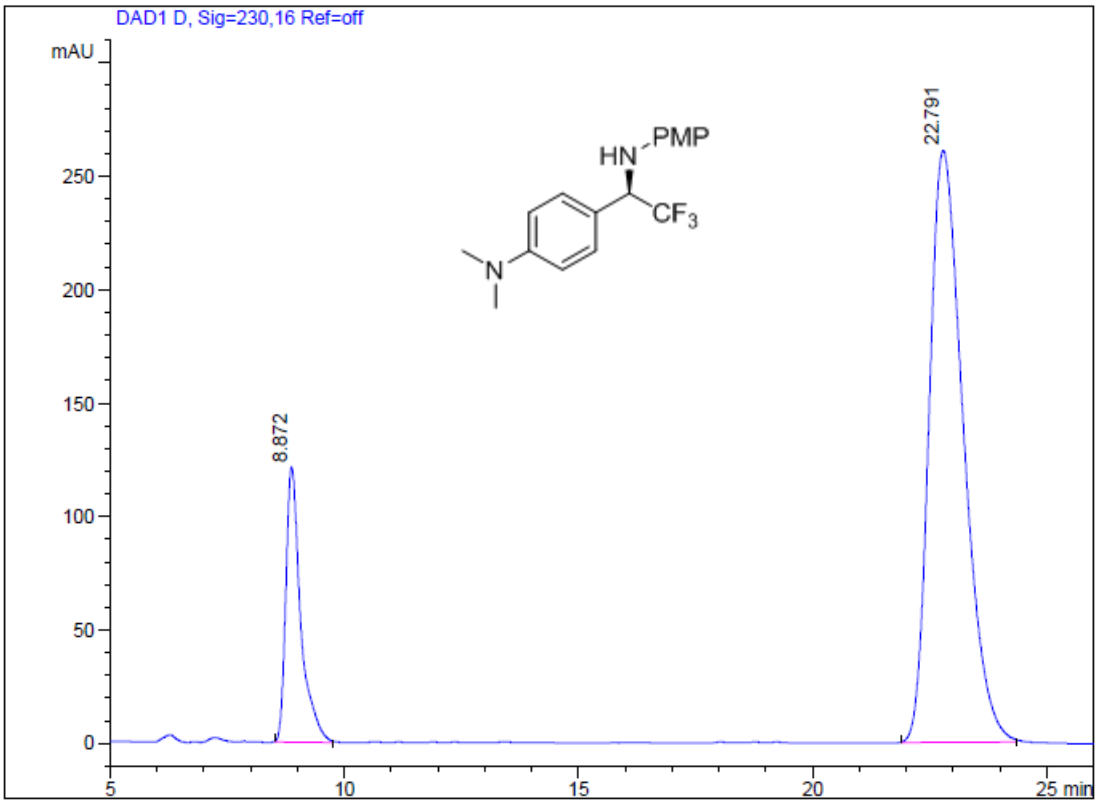
N-(4'-Methoxyphenyl)-ethan-1,1,1-trifluoro-2-cyclohexyl-2-amine :



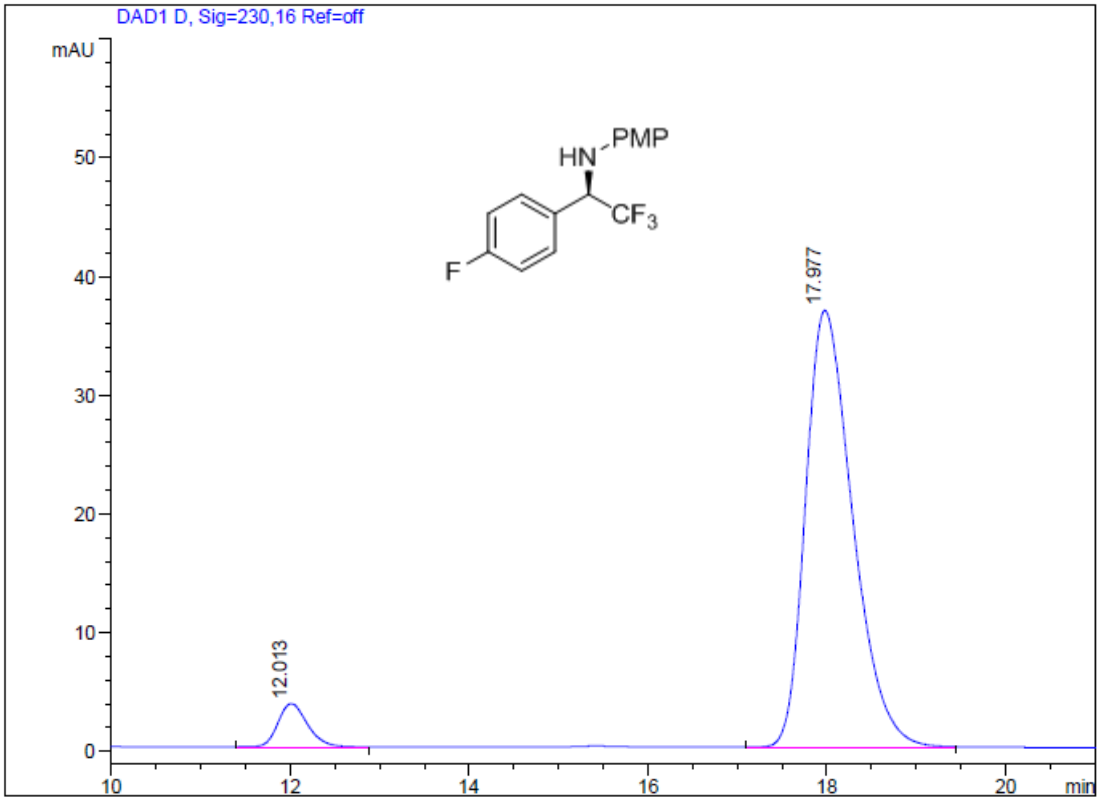
N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(3''-methylphenyl)-1-amine :



N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-(N',N'-dimethylammino)-phenyl)-1-amine :



N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-fluorophenyl)-1-amine :



N-(4'-Methoxyphenyl)-ethan-2,2,2-trifluoro-1-(4''-ethylphenoxyacetate)-1-amine :