Catalytic Enantioselective Synthesis of 2-Pyrazolines via One-Pot Condensation/6π-Electrocyclization: 3,5-Bis(Pentafluorosulfanyl)phenylthioureas as Powerful Hydrogen Bond Donors

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Supporting Information

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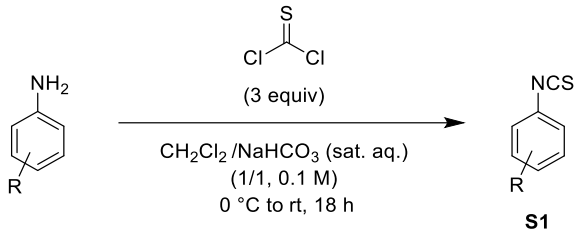
General Information: Reagents were purchased from commercial sources and were purified by distillation or recrystallization prior to use. Toluene was dried using a JC Meyer solvent purification system. Purification of reaction products was carried out by flash column chromatography using Sorbent Technologies Standard Grade silica gel (60 Å, 230–400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60 F254 plates. Visualization was accomplished with UV light and Dragendorff-Munier stains, followed by heating. Proton nuclear magnetic resonance spectra (^{1}H-NMR) were recorded on Bruker 400 MHz and 600 MHz instruments, and chemical shifts are reported in ppm using the solvent as an internal standard ($CDCl_3$ at 7.26 ppm, $(CD_3)_2SO$ at 2.50 ppm). Data are reported as app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = complex, br = broad; coupling constant(s) in Hz. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C-NMR) were recorded on Bruker 400 MHz and 600 MHz instruments and chemical shifts are reported in ppm using the solvent as an internal standard ($CDCl_3$ at 77.0 ppm, $(CD_3)_2SO$ at 39.52 ppm). High resolution mass spectra (HRMS) were obtained from an Agilent 6230 ESI-TOF instrument. Supercritical fluid chromatography (SFC) analysis was carried out on an Agilent 1260 Infinity II series instrument with auto sampler and multiple wavelength detectors. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Jasco P–2000 polarimeter at 589 nm and at 20 °C. α,β-Unsaturated ketones were prepared according to established procedures.[1] 3,5-Bis(pentafluoro-λ^6-sulfanyl)aniline was prepared according to a literature report.[2]

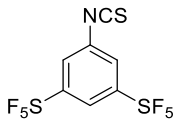
General Procedure A for the Preparation of Isothiocyanates



S1

To an ice cooled solution of the corresponding aniline (1 mmol, 1 equiv) in a mixture of saturated aqueous $NaHCO_3$ and CH_2Cl_2 (1:1, 5 mL/5 mL) was added thiophosgene (3 mmol, 3 equiv) under stirring. The resulting mixture was then allowed to warm to room temperature and stirred until the aniline was consumed as indicated by TLC (18 h). The layers were then separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were then dried over anhydrous Na_2SO_4, concentrated, and the residue purified by silica gel chromatography (using 2% EtOAc in hexanes as eluent).

(5-Isothiocyanato-1,3-phenylene)bis(pentafluoro-λ^6-sulfane)



S1b

To an ice cooled solution of 3,5-bis(pentafluoro-λ^6-sulfanyl)aniline (690 mg, 2 mmol) in a mixture of saturated aqueous $NaHCO_3$ and CH_2Cl_2 (1:1, 10 mL/10 mL) was added thiophosgene (0.46 mL, 6 mmol, 3 equiv) under stirring. The resulting mixture was then allowed to warm to room temperature and stirred for 18 h, then transferred to a separatory funnel. The layers were then separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were then dried over anhydrous Na_2SO_4, concentrated, and the residue purified by silica gel chromatography (using 2% EtOAc in hexanes as eluent) to provide **S1b** as a beige solid in 94% yield (728 mg).

Characterization data for S1b:

R_f = 0.70 in hexanes/EtOAc 95:5 v/v.

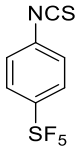
mp = 102–104 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03–7.99 (m, 1H), 7.74 (d, *J* = 1.86 Hz, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 154.2 (p, J_{C-F} = 20.6 Hz), 141.7, 133.7, 126.5–126.2 (m), 122.2.

^{19}F-NMR (377 MHz, $CDCl_3$): δ = 80.25 (p, J_{F-F} = 151.1 Hz, 2F), 63.01 (d, J_{F-F} = 151.3 Hz, 8F).

Pentafluoro(4-isothiocyanatophenyl)-λ^6-sulfane



S1c

Following general procedure A, compound **S1c** was obtained from 4-(pentafluoro-λ^6-sulfanyl)aniline (219 mg, 1 mmol, 1 equiv) and thiophosgene (0.23 mL, 3 mmol, 3 equiv) as a beige solid in 93% yield (243 mg).

Characterization data for S1c:

R_f = 0.75 in hexanes/EtOAc 95:5 v/v.

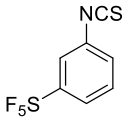
mp = 82–84 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.77–7.73 (m, 2H), 7.28 (d, *J* = 8.7 Hz, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 151.7 (p, J_{C-F} = 18.5 Hz), 139.1, 134.8, 127.6 (p, *J* = 4.5 Hz), 125.7.

^{19}F-NMR (565 MHz, $CDCl_3$): δ = 83.40 (p, J_{F-F} = 150.6 Hz, 1F), 63.07 (d, J_{F-F} = 150.4 Hz, 4F).

Pentafluoro(3-isothiocyanatophenyl)-λ^6-sulfane



S1d

Following general procedure A, compound **S1d** was obtained from 3-(pentafluoro-λ^6-sulfanyl)aniline (219 mg, 1 mmol, 1 equiv) and thiophosgene (0.23 mL, 3 mmol, 3 equiv) as a beige solid in 97% yield (253 mg).

Characterization data for S1d:

R_f = 0.72 in hexanes/EtOAc 95:5 v/v.

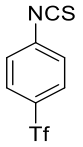
mp = 88–90 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.68–7.64 (m, 1H), 7.60 (app t, *J* = 1.9 Hz 1H), 7.47 (app t, *J* = 8.2 Hz, 1H), 7.37 (app d, *J* = 7.9 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 154.4 (p, J_{C-F} = 18.1 Hz), 138.7, 132.4, 129.8, 128.6, 124.5 (p, J_{C-F} = 4.7 Hz), 123.5 (p, J_{C-F} = 4.8 Hz).

^{19}F-NMR (565 MHz, $CDCl_3$): δ = 82.60 (p, J_{F-F} = 150.5 Hz, 1F), 62.68 (d, J_{F-F} = 150.6 Hz, 4F).

1-Isothiocyanato-4-((trifluoromethyl)sulfonyl)benzene



S1e

Following general procedure A, compound **S1e** was obtained from 4-((trifluoromethyl)sulfonyl)aniline (225 mg, 1 mmol, 1 equiv) and thiophosgene (0.23 mL, 3 mmol, 3 equiv) as a beige solid in 94% yield (251 mg).

Characterization data for S1e:

R_f = 0.70 in hexanes/EtOAc 95:5 v/v.

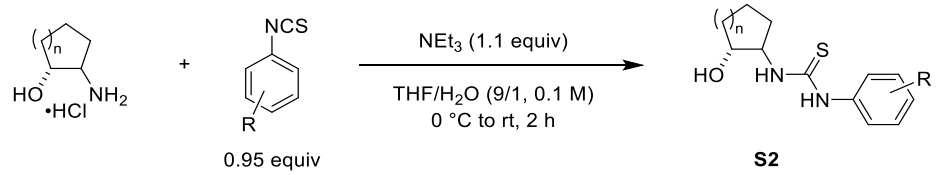
mp = 71–73 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.7 Hz, 2H), 7.50–7.43 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 141.5, 140.2, 132.5, 129.0, 126.9, 119.67 (q, J_{C-F} = 325.6 Hz).

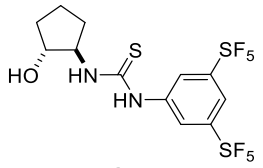
^{19}F-NMR (565 MHz, $CDCl_3$): δ = –78.20.

General Procedure B for the Preparation of Aminoalcohol-Derived Thioureas



To an ice cooled solution of the amino alcohol hydrochloride in THF/H_2O (9:1, 0.1 M) was added triethylamine (1.1 equiv), followed by isothiocyanate (0.95 equiv). The resulting mixture was then allowed to warm to room temperature and stirred for 2 h, then transferred to a separatory funnel. EtOAc (20 mL) was added, and the mixture washed with 1 M HCl (20 mL x 2). The combined aqueous layers were extracted with EtOAc (20 mL x 2), and the combined organic layers washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography (using 30% EtOAc in hexanes as eluent).

1-(3,5-Bis(pentafluoro-λ^6-sulfanyl)phenyl)-3-((1*R*,2*R*)-2-hydroxycyclopentyl)thiourea



S2b

To an ice cooled solution of (1*R*, 2*R*)-2-aminocyclopentan-1-ol hydrochloride (248 mg, 1.8 mmol) in THF/H_2O (9:1, 16.5 mL/1.5 mL) was added triethylamine (0.28 mL, 1.98 mmol, 1.1 equiv), followed by isothiocyanate **S1b** (662 mg, 1.71 mmol, 0.95 equiv). The resulting mixture was then allowed to warm to room temperature and stirred for 2 h, then transferred to a separatory funnel. EtOAc (50 mL) was added, and the mixture washed with 1 M HCl (50 mL x 2). The combined aqueous layers were extracted with EtOAc (50 mL x 2), and the combined organic layers washed with brine (50 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography (using 30% EtOAc in hexanes as eluent) to provide **S2b** as a white solid in 95% yield (793 mg).

Characterization data for S2b:

R_f = 0.20 in hexanes/EtOAc 50:50 v/v.

mp = 117–119 °C.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{20}}$ = +26.13 (c 0.5, $CHCl_3$).

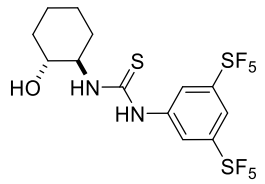
^{1}H NMR (500 MHz, $(CD_3)_2SO$): δ = 9.98 (s, 1H), 8.44 (s, 2H), 8.31 (s, 1H), 7.94 (s, 1H), 4.83 (br s, 1H), 4.40–4.20 (m, 1H), 4.04–3.92 (m, 1H), 2.20–1.98 (m, 1H), 1.95–1.76 (m, 1H), 1.75–1.55 (comp, 2H), 1.55–1.31 (comp, 2H).

^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ = 180.2, 152.3–151.4 (m), 142.0, 122.4, 116.8, 75.6, 62.3, 32.2, 29.1, 20.3.

^{19}F-NMR (565 MHz, $(CD_3)_2SO$): δ = 89.12 (p, $J_{F–F}$ = 151.9 Hz, 2F), 68.60 (d, $J_{F–F}$ = 151.9 Hz, 8F).

HRMS (ESI-TOF): Calculated for $C_{12}H_{15}F_{10}N_2OS_3$ $[M + H]^+$: 489.0181, found 489.0183.

1-(3,5-Bis(pentafluoro-λ^6-sulfanyl)phenyl)-3-((1*R*,2*R*)-2-hydroxycyclohexyl)thiourea



S2c

Following general procedure B, compound **S2c** was obtained from (1*R*, 2*R*)-2-aminocyclohexan-1-ol hydrochloride (76 mg, 0.5 mmol, 1 equiv) and isothiocyanate **S1b** (184 mg, 0.475 mmol, 0.95 equiv) as a white solid in 93% yield (222 mg).

Characterization data for S2c:

R_f = 0.24 in hexanes/EtOAc 50:50 v/v.

mp = 139–141 °C.

$[\alpha]_D^{20}$ = +86.67 (c 0.5, $CHCl_3$).

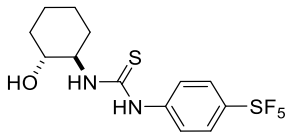
^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ = 10.03 (s, 1H), 8.45–8.40 (m, 2H), 8.29 (s, 1H), 7.93 (s, 1H), 4.70 (br s, 1H), 4.08–3.82 (m, 1H), 3.43–3.35 (m, 1H), 2.18–2.01 (m, 1H), 1.94–1.87 (m, 1H), 1.67–1.57 (comp, 2H), 1.34–1.09 (comp, 4H).

^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ = 179.7, 152.3–151.6 (m), 142.0, 122.2, 116.6, 70.8, 59.4, 34.3, 29.9, 24.0, 23.7.

^{19}F-NMR (377 MHz, $(CD_3)_2SO$): δ = 84.48 (p, J_{F-F} = 152.3 Hz, 2F), 63.92 (d, J_{F-F} = 152.2 Hz, 8F).

HRMS (ESI-TOF): Calculated for $C_{13}H_{17}F_{10}N_2OS_3$ $[M + H]^+$: 503.0338, found 503.0354.

1-((1*R*,2*R*)-2-Hydroxycyclohexyl)-3-(4-(pentafluoro-λ^6-sulfanyl)phenyl)thiourea



S2d

Following general procedure B, compound **S2d** was obtained from (1*R*, 2*R*)-2-aminocyclohexan-1-ol hydrochloride (121 mg, 0.8 mmol, 1 equiv) and isothiocyanate **S1c** (198 mg, 0.76 mmol, 0.95 equiv) as a white solid in 95% yield (272 mg).

Characterization data for S2d:

R_f = 0.31 in hexanes/EtOAc 50:50 v/v.

mp = 125–127 °C.

$[\alpha]_D^{20}$ = +59.76 (c 0.5, $CHCl_3$).

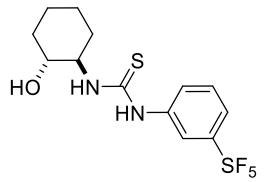
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 9.83 (s, 1H), 8.03 (s, 1H), 7.86–7.68 (comp, 4H), 4.75 (br s, 1H), 4.10–3.78 (m, 1H), 3.44–3.35 (m, 1H), 2.24–2.04 (m, 1H), 1.95–1.83 (m, 1H), 1.68–1.55 (comp, 2H), 1.35–1.00 (comp, 4H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 179.6, 147.2–146.5 (m), 143.3, 126.3, 120.7, 70.8, 59.3, 34.3, 30.0, 23.9, 23.7.

^{19}F-NMR (565 MHz, $(CD_3)_2SO$): δ = 88.90 (p, $J_{F–F}$ = 150.6 Hz, 1F), 65.03 (d, $J_{F–F}$ = 150.4 Hz, 4F).

HRMS (ESI-TOF): Calculated for $C_{13}H_{18}F_5N_2OS_2$ $[M + H]^+$: 377.0775, found 377.0789.

1-((1*R*,2*R*)-2-Hydroxycyclohexyl)-3-(3-(pentafluoro-λ^6-sulfanyl)phenyl)thiourea



S2e

Following general procedure B, compound **S2e** was obtained from (1*R*, 2*R*)-2-aminocyclohexan-1-ol hydrochloride (61 mg, 0.4 mmol, 1 equiv) and isothiocyanate **S1d** (99 mg, 0.38 mmol, 0.95 equiv) as a white solid in 92% yield (132 mg).

Characterization data for S2e:

R_f = 0.23 in hexanes/EtOAc 50:50 v/v.

mp = 149–151 °C.

$[\alpha]_D^{20}$ = +52.37 (c 0.5, $CHCl_3$).

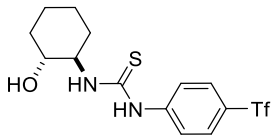
^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ = 9.73 (s, 1H), 8.28 (s, 1H), 7.95 (s, 1H), 7.70–7.60 (m, 1H), 7.59–7.46 (comp, 2H), 4.72 (br s, 1H), 4.06–3.81 (m, 1H), 3.44–3.34 (m, 1H), 2.17–2.04 (m, 1H), 1.94–1.83 (m, 1H), 1.70–1.52 (comp, 2H), 1.35–1.02 (comp, 4H).

^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ = 179.9, 152.7–152.2 (m), 140.8, 129.2, 125.5, 120.2, 118.9, 70.9, 59.1, 34.3, 30.1, 24.0, 23.7.

^{19}F-NMR (565 MHz, $(CD_3)_2SO$): δ = 87.53 (p, J_{F-F} = 150.6 Hz, 1F), 63.73 (d, J_{F-F} = 150.6 Hz, 4F).

HRMS (ESI-TOF): Calculated for $C_{13}H_{18}F_5N_2OS_2$ $[M + H]^+$: 377.0775, found 377.0791.

1-((1*R*,2*R*)-2-Hydroxycyclohexyl)-3-(4-((trifluoromethyl)sulfonyl)phenyl)thiourea



S2f

Following general procedure B, compound **S2f** was obtained from (1*R*, 2*R*)-2-aminocyclohexan-1-ol hydrochloride (121 mg, 0.8 mmol, 1 equiv) and isothiocyanate **S1e** (203 mg, 0.76 mmol, 0.95 equiv) as a white solid in 95% yield (276 mg).

Characterization data for S2f:

R_f = 0.34 in hexanes/EtOAc 50:50 v/v.

mp = 101–103 °C.

$[\alpha]_D^{20}$ = +98.87 (c 0.5, $CHCl_3$).

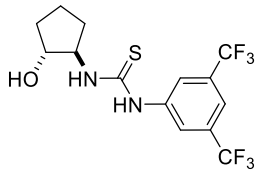
^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ = 10.19 (s, 1H), 8.43 (s, 1H), 8.10–7.85 (comp, 4H), 4.80 (s, 1H), 4.05–3.85 (m, 1H), 3.48–3.35 (m, 1H), 2.22–2.07 (m, 1H), 1.96–1.84 (m, 1H), 1.72–1.52 (comp, 2H), 1.38–1.00 (comp, 4H).

^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ = 179.3, 148.8, 131.9, 120.2, 119.6 (q, J_{C-F} = 326.1 Hz), 70.6, 59.5, 34.3, 29.7, 23.9, 23.7.

^{19}F-NMR (377 MHz, $(CD_3)_2SO$): δ = –78.82.

HRMS (ESI-TOF): Calculated for $C_{14}H_{18}F_3N_2O_3S_2$ $[M + H]^+$: 383.0705, found 383.0725.

1-(3,5-Bis(trifluoromethyl)phenyl)-3-((1*R*,2*R*)-2-hydroxycyclopentyl)thiourea



S2g

Following general procedure B, compound **S2g** was obtained from (1*R*, 2*S*)-2-aminocyclopentan-1-ol hydrochloride (110 mg, 0.8 mmol, 1 equiv) and 3,5-bis(trifluoromethyl)phenyl isothiocyanate (206 mg, 0.76 mmol, 0.95 equiv) as a white solid in 95% yield (269 mg).

Characterization data for S2g:

R_f = 0.34 in hexanes/EtOAc 50:50 v/v.

mp = 74–76 °C.

$[\alpha]_D^{20}$ = +32.44 (c 0.5, $CHCl_3$).

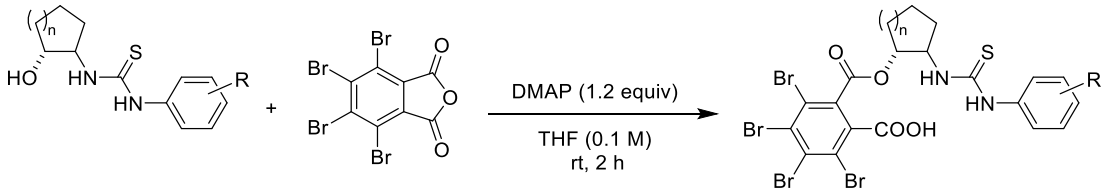
^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ = 9.88 (s, 1H), 8.50–8.00 (comp, 3H), 7.70 (s, 1H), 4.83 (br s, 1H), 4.43–4.16 (m, 1H), 4.04–3.93 (m, 1H), 2.20–2.02 (m, 1H), 1.96–1.77 (m, 1H), 1.75–1.25 (comp, 4H).

^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ = 180.3, 142.0, 130.1 (q, J_{C-F} = 32.2 Hz), 123.3 (q, J_{C-F} = 272.6 Hz), 121.6, 115.8, 75.6, 62.2, 32.2, 29.1, 20.3.

^{19}F-NMR (565 MHz, $(CD_3)_2SO$): δ = –61.60.

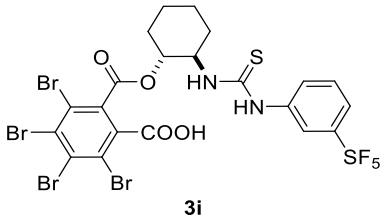
HRMS (ESI-TOF): Calculated for $C_{14}H_{15}F_6N_2OS$ $[M + H]^+$: 373.0804, found 373.0817.

General Procedure C for the Preparation of CBSCA Catalysts



To a solution of **S2** in THF (0.1 M) were added 4-*N,N*-dimethylaminopyridine (DMAP) (1.2 equiv) and tetrabromophthalic anhydride (1.2 equiv). The resulting mixture was stirred at room temperature for 2 h and then transferred to a separatory funnel. EtOAc (50 mL) was added and the solution washed with 1 M HCl (25 mL × 2), saturated aqueous $NaHCO_3$ (25 mL), and 1 M HCl (25 mL), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by neutral Al_2O_3 chromatography (using a gradient eluent from CH_2Cl_2 to MeOH/CH_2Cl_2 10:90 v/v to MeOH/CH_2Cl_2 20:80 v/v to MeOH/CH_2Cl_2/HCOOH 20:79:1 v/v/v). The combined fractions were concentrated and re-dissolved in CH_2Cl_2 (25 mL) and then washed with 1 M HCl (25 mL × 2). The combined aqueous layers were back-extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. Finally, the solvent was removed under reduced pressure and the resulting solid dried under high vacuum.

2,3,4,5-Tetrabromo-6-((((1*R*,2*R*)-2-(3-(3-(pentafluoro-λ^6-sulfanyl)phenyl)thioureido)cyclohexyl)oxy)carbonyl) benzoic acid



3i

Following general procedure C, compound **3i** was obtained from **S2e** (94 mg, 0.25 mmol, 1 equiv) and tetrabromophthalic anhydride (139 mg, 0.3 mmol, 1.2 equiv) as a light-yellow solid in 72% yield (151 mg).

Characterization data for 3i:

R_f = 0.29 in MeOH/CH_2Cl_2 10:90 v/v.

mp = 163–165 °C.

$[\alpha]_D^{20}$ = +32.53 (c 0.5, $CHCl_3$).

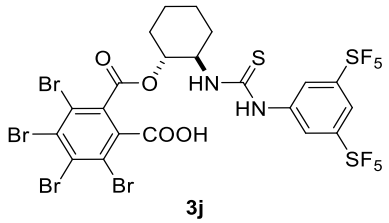
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 14.33 (br s, 1H), 9.78 (s, 1H), 8.22 (s, 1H), 7.98 (s, 1H), 7.70–7.46 (comp, 3H), 5.14–4.96 (m, 1H), 4.68–4.38 (m, 1H), 2.12–1.96 (comp, 2H), 1.77–1.62 (comp, 2H), 1.54–1.25 (comp, 4H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 180.1, 165.5, 163.9, 152.6–152.1 (m), 140.4, 136.5, 134.3, 131.7, 130.8, 129.1, 126.5, 122.0, 121.7, 120.8, 120.0, 76.3, 55.1, 30.3, 29.6, 23.4, 23.0.

^{19}F-NMR (377 MHz, $(CD_3)_2SO$): δ = 87.49 (p, J_{F-F} = 151.2 Hz, 1F), 63.81 (d, J_{F-F} = 151.1 Hz, 4F).

HRMS (ESI-TOF): Calculated for $C_{21}H_{16}{}^{79}Br^{79}Br^{81}Br^{81}BrF_5N_2O_4S_2$ $[M - H]^-$: 838.7170, found 838.7206.

2-((((1*R*,2*R*)-2-(3-(3,5-Bis(pentafluoro-λ^6-sulfanyl)phenyl)thioureido)cyclohexyl)oxy)carbonyl)-3,4,5,6-tetrabromobenzoic acid



3j

Following general procedure C, compound **3j** was obtained from **S2c** (126 mg, 0.25 mmol, 1 equiv) and tetrabromophthalic anhydride (139 mg, 0.3 mmol, 1.2 equiv) as a white solid in 81% yield (196 mg).

Characterization data for 3j:

R$_f$ = 0.24 in MeOH/CH_2Cl_2 10:90 v/v.

mp = 146–148 °C.

$[\alpha]_D^{20}$ = +16.18 (c 0.5, $CHCl_3$).

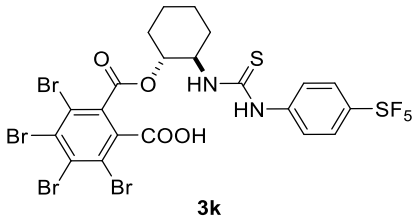
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 14.37 (br s, 1H), 10.12 (s, 1H), 8.47–8.23 (comp, 3H), 7.99 (s, 1H), 5.11–5.01 (m, 1H), 4.63–4.47 (m, 1H), 2.15–2.05 (m, 1H), 2.04–1.94 (m, 1H), 1.79–1.61 (comp, 2H), 1.52–1.18 (comp, 4H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 180.3, 165.5, 163.9, 152.1–151.0 (m), 141.8, 136.5, 134.3, 131.7, 130.7, 123.6, 122.0, 121.7, 117.3, 76.3, 55.3, 30.1, 29.5, 23.4, 22.9.

^{19}F-NMR (377 MHz, $(CD_3)_2SO$): δ = 84.49 (p, $J_{F–F}$ = 151.8 Hz, 2F), 64.05 (d, $J_{F–F}$ = 151.9 Hz, 8F).

HRMS (ESI-TOF): Calculated for $C_{21}H_{15}{}^{79}Br^{79}Br^{81}Br^{81}BrF_{10}N_2O_4S_3$ $[M – H]^-$: 964.6732, found 964.6724.

2,3,4,5-Tetrabromo-6-((((1*R*,2*R*)-2-(3-(4-(pentafluoro-λ^6-sulfanyl)phenyl)thioureido)cyclohexyl)oxy)carbonyl) benzoic acid



3k

Following general procedure C, compound **3k** was obtained from **S2d** (188 mg, 0.5 mmol, 1 equiv) and tetrabromophthalic anhydride (278 mg, 0.6 mmol, 1.2 equiv) as a white solid in 76% yield (319 mg).

Characterization data for 3k:

R$_f$ = 0.30 in MeOH/CH_2Cl_2 10:90 v/v.

mp = 137–139 °C.

$[\alpha]_D^{20}$ = +17.76 (c 0.5, $CHCl_3$).

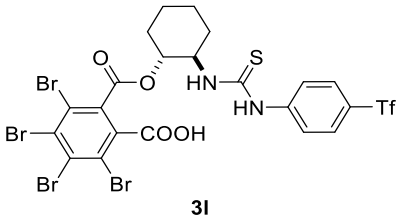
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 14.32 (br s, 1H), 9.95 (s, 1H), 8.15–7.60 (comp, 4H), 5.23–4.85 (s, 1H), 4.73–4.33 (s, 1H), 2.30–1.93 (comp, 2H), 1.90–1.00 (comp, 7H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 179.8, 165.6, 164.0, 147.9–147.0 (m), 143.0, 136.8, 134.3, 131.7, 130.8, 126.3, 122.1, 121.6, 76.3, 55.3, 30.2, 29.6, 23.4, 23.0.

^{19}F-NMR (565 MHz, $(CD_3)_2SO$): δ = 88.70 (p, $J_{F–F}$ = 150.6 Hz, 1F), 65.00 (d, $J_{F–F}$ = 150.6 Hz, 4F).

HRMS (ESI-TOF): Calculated for $C_{21}H_{16}{}^{79}Br^{79}Br^{81}Br^{81}BrF_5N_2O_4S_2$ $[M – H]^-$: 838.7170, found 838.7214.

2,3,4,5-Tetrabromo-6-((((1*R*,2*R*)-2-(3-(4-((trifluoromethyl)sulfonyl)phenyl)thioureido)cyclohexyl)oxy) carbonyl)benzoic acid



3l

Following general procedure C, compound **3l** was obtained from **S2f** (574 mg, 1.5 mmol, 1 equiv) and tetrabromophthalic anhydride (835 mg, 1.8 mmol, 1.2 equiv) as a white solid in 88% yield (1.12 g).

Characterization data for 3l:

R_f = 0.25 in MeOH/CH_2Cl_2 10:90 v/v.

mp = 124–126 °C.

$[\alpha]_D^{20}$ = +40.62 (c 0.5, $CHCl_3$).

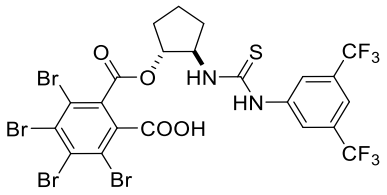
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 10.28 (s, 1H), 8.46–8.28 (m, 1H), 8.08–7.93 (comp, 4H), 5.11–4.99 (m, 1H), 4.64–4.45 (m, 1H), 2.13–2.00 (comp, 2H), 1.76–1.63 (comp, 2H), 1.53–1.27 (comp, 4H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 179.5, 165.5, 163.9, 148.2, 136.6, 136.0, 134.2, 131.8, 130.9, 130.6, 122.1, 121.6, 121.2, 119.5 (q, J_{C-F} = 326.1 Hz), 76.1, 55.2, 29.9, 29.5, 23.3, 22.9.

^{19}F-NMR (377 MHz, $(CD_3)_2SO$): δ = –78.77.

HRMS (ESI-TOF): Calculated for $C_{22}H_{16}{}^{79}Br^{79}Br^{81}Br^{81}BrF_3N_2O_6S_2$ $[M - H]^-$: 844.7101, found 844.7137.

2-((((1*R*,2*R*)-2-(3-(3,5-Bis(trifluoromethyl)phenyl)thioureido)cyclopentyl)oxy)carbonyl)-3,4,5,6-tetrabromobenzoic acid



3m

Following general procedure C, compound **3m** was obtained from **S2g** (558 mg, 1.5 mmol, 1 equiv) and tetrabromophthalic anhydride (835 mg, 1.8 mmol, 1.2 equiv) as a white solid in 65% yield (815 mg).

Characterization data for 3m:

R_f = 0.34 in MeOH/CH_2Cl_2 10:90 v/v.

mp = 105–107 °C.

$[\alpha]_D^{20}$ = +65.76 (c 0.5, $CHCl_3$).

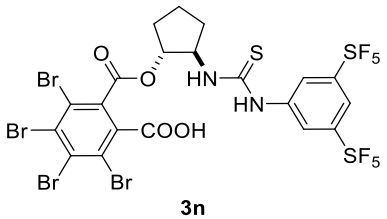
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 14.45 (br s, 1H), 10.01 (s, 1H), 8.45 (s, 1H), 8.22 (s, 2H), 7.75 (s, 1H), 5.35–5.28 (m, 1H), 4.82–4.62 (m, 1H), 2.20–2.02 (comp, 2H), 1.83–1.71 (comp, 3H), 1.64–1.53 (m, 1H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 180.5, 165.6, 163.8, 141.8, 136.5, 133.9, 131.9, 131.0, 130.1 (q, J_{C-F} = 32.2 Hz), 123.2 (q, J_{C-F} = 272.8 Hz), 122.2, 122.1, 116.3, 81.5, 59.6, 29.7, 29.3, 21.3.

^{19}F-NMR (565 MHz, $(CD_3)_2SO$): δ = –61.54.

HRMS (ESI-TOF): Calculated for $C_{22}H_{13}{}^{79}Br^{79}Br^{81}Br^{81}BrF_6N_2O_4S$ $[M - H]^-$: 834.7200, found 834.7239.

2-((((1*R*,2*R*)-2-(3-(3,5-Bis(pentafluoro-λ^6-sulfanyl)phenyl)thioureido)cyclopentyl)oxy)carbonyl)-3,4,5,6-tetrabromobenzoic acid



3n

To a solution of **S2b** (796 mg, 1.63 mmol) in THF (16 mL) were added 4-*N,N*-dimethylaminopyridine (DMAP) (239 mg, 1.96 mmol, 1.2 equiv) and tetrabromophthalic anhydride (909 mg, 1.96 mmol, 1.2 equiv). The resulting mixture was stirred at room temperature for 2 h and then transferred to a separatory funnel. EtOAc (150 mL) was added and the solution washed with 1 M HCl (60 mL × 2), saturated aqueous $NaHCO_3$ (60 mL), and 1 M HCl (60 mL), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue purified by neutral Al_2O_3 chromatography (using a gradient eluent from CH_2Cl_2 to MeOH/CH_2Cl_2 10:90 v/v to MeOH/CH_2Cl_2 20:80 v/v to MeOH/CH_2Cl_2/HCOOH 20:79:1 v/v/v). The combined fractions were concentrated and re-dissolved in CH_2Cl_2 (50 mL) and then washed with 1 M HCl (50 mL × 2). The combined aqueous layers were back-extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were dried over anhydrous Na_2SO_4. Finally, the solvent was removed under reduced pressure and the residue dried under high vacuum to provide **3n** as a white solid in 78% yield (1.21 g).

Characterization data for 3n:

R_f = 0.22 in MeOH/CH_2Cl_2 10:90 v/v.

mp = 129–131 °C.

$[\alpha]_D^{20}$ = +48.17 (c 0.5, $CHCl_3$).

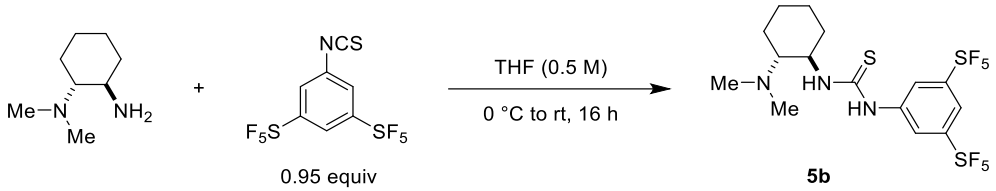
^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 14.37 (br s, 1H), 10.44 (s, 1H), 8.71 (s, 1H), 8.57–8.38 (m, 2H), 8.06–7.88 (m, 1H), 5.37–5.23 (m, 1H), 4.82–4.61 (m, 1H), 2.20–2.02 (comp, 2H), 1.84–1.54 (comp, 4H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 180.5, 165.7, 163.8, 152.3–151.5 (m), 141.9, 136.7, 133.9, 131.9, 130.9, 130.6, 122.7, 122.0, 117.1, 81.5, 59.6, 29.6, 29.3, 21.2.

^{19}F-NMR (377 MHz, $(CD_3)_2SO$): δ = 84.49 (p, J_{F-F} = 151.7, 2F), 64.01 (d, J_{F-F} = 151.7 Hz, 8F).

HRMS (ESI-TOF): Calculated for $C_{20}H_{13}{}^{79}Br^{79}Br^{81}Br^{81}BrF_{10}N_2O_4S_3$ $[M - H]^-$: 950.6576, found 950.6619.

Synthesis and Characterization of 1-(3,5-bis(pentafluoro-λ^6-sulfanyl)phenyl)-3-((1*R*,2*R*)-2-(dimethylamino)cyclohexyl)thiourea



To an ice cooled solution of (1*R*,2*R*)-*N*,*N*-dimethylcyclohexane-1,2-diamine (71 mg, 0.5 mmol, 1 equiv) in THF (1 mL, 0.5 M) isothiocyanate **S1b** (184 mg, 0.475 mmol, 0.95 equiv) was added dropwise. The resulting mixture was then allowed to warm to room temperature and stirred for 16 h and then the solvent was evaporated under reduced pressure. The residue was purified by silica gel chromatography (using a gradient eluent from MeOH/CH_2Cl_2 1:99 v/v to MeOH/CH_2Cl_2 3:97 v/v) to provide **5b** as a white solid in 74% yield (187 mg).

Characterization data for 5b:

R_f = 0.26 in CH_2Cl_2/MeOH 90:10 v/v.

mp = 165–167 °C.

$[\alpha]_D^{20}$ = –99. 22 (c 0.5, $CHCl_3$).

^{1}H NMR (600 MHz, $(CD_3)_2SO$): δ = 10.22 (s, 1H), 8.49–8.19 (comp, 3H), 7.91 (s, 1H), 4.30–3.95 (m, 1H), 2.62–2.52 (m, 1H), 2.32–2.10 (comp, 7H), 1.91–1.55 (comp, 3H), 1.31–1.05 (comp, 4H).

^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ = 178.7, 152.45–151.69 (m), 141.9, 121.6, 116.4, 65.1, 55.0, 54.9, 31.6, 24.6, 24.5, 21.2.

^{19}F-NMR (377 MHz, $(CD_3)_2SO$): δ = 84.42 (p, J_{F-F} = 152.2 Hz, 2F), 63.82 (d, J_{F-F} = 152.1 Hz, 8F).

HRMS (ESI-TOF): Calculated for $C_{15}H_{21}F_{10}N_3S_3$ $[M]^+$: 529.0738, found 529.0757.

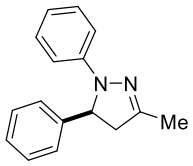
General procedure D for the Catalytic Enantioselective Synthesis of 2-pyrazolines

To a flame dried vial were successively added the α,β-unsaturated ketone (0.26 mmol, 1.05 equiv), acid catalyst **3n** (23.8 mg, 0.025 mmol, 10 mol%), 4 Å MS (100 mg), and dry toluene (2.5 mL, 0.1 M). Aryl hydrazine (0.25 mmol, 1 equiv) was then added, and the resulting mixture was stirred under nitrogen at room temperature for the indicated time before being quenched with triethylamine (50 μL). The resulting mixture was directly purified by flash chromatography on silica gel using EtOAc/hexanes/Et_3N (2/98/0.1) as the eluent.

Racemic products (for SFC assays) were prepared from the α,β-unsaturated ketone (0.1 mmol, 1 equiv), hydrazine (0.2 mmol, 2 equiv), and concentrated sulfuric acid (0.5 mmol, 5 equiv) in ethanol (1 mL, 0.1 M). The resulting mixture was stirred under reflux until α,β-unsaturated ketone was consumed as indicated by TLC and then directly purified by flash chromatography on silica gel using EtOAc/hexanes (2/98) as the eluent.

Characterization Data of Products

(*S*)-3-Methyl-1,5-diphenyl-4,5-dihydro-1*H*-pyrazole



2a

To a flame dried vial was added (*E*)-4-phenylbut-3-en-2-one (38 mg, 0.26 mmol, 1.05 equiv), acid catalyst **3n** (23.8 mg, 0.025 mmol, 10 mol%), 4 Å MS (100 mg), and dry toluene (2.5 mL, 0.1 M). To the resulting mixture phenylhydrazine (25 µL, 0.25 mmol, 1.0 equiv) was then added and the resulting mixture was stirred under nitrogen at room temperature for 28 h before being quenched with triethylamine (50 µL). The resulting mixture was directly purified by flash chromatography on silica gel using EtOAc/hexanes/Et_3N (2/98/0.1) as the eluent. Compound **2a** was obtained as a white solid in 96% yield (57 mg).

Characterization data for 2a:

R_f = 0.43 in hexanes/EtOAc 80:20 v/v.

mp = 129–131 °C.

$[\alpha]_D^{20}$ = –222.34 (c 0.5, $CHCl_3$, 92% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37–7.29 (comp, 4H), 7.29–7.23 (m, 1H), 7.18–7.11 (comp, 2H), 6.96–6.90 (comp, 2H), 6.78–6.71 (m, 1H), 5.02 (dd, *J* = 11.9, 8.1 Hz, 1H), 3.47–3.37 (m, 1H), 2.77–2.68 (m, 1H), 2.08 (s, 3H).

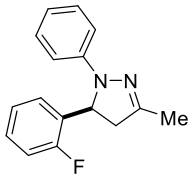
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.5, 146.0, 143.0, 129.0, 128.8, 127.3, 125.9, 118.6, 113.1, 64.7, 47.8, 15.9.

HRMS (ESI-TOF): Calculated for $C_{16}H_{17}N_2$ $[M + H]^+$: 237.1386, found 237.1387.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 254 nm, t_R = 3.9 min (major) and t_R = 5.2 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(2-Fluorophenyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazole



2b

Following general procedure D (reaction performed at room temperature for 32 h), compound **2b** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(2-fluorophenyl)but-3-en-2-one (43 mg, 0.26 mmol, 1.05 equiv) as a white solid in 91% yield (58 mg).

Characterization data for 2b:

R_f = 0.39 in hexanes/EtOAc 80:20 v/v.

mp = 76–78 °C.

$[\alpha]_D^{20}$ = –198.45 (c 0.5, $CHCl_3$, 93% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25–7.14 (comp, 2H), 7.14–7.07 (comp, 2H), 7.07–6.96 (m, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 5.24 (dd, *J* = 12.0, 7.6 Hz, 1H), 3.44 (dd, *J* = 17.6, 12.0 Hz, 1H), 2.64 (dd, *J* = 17.6, 7.6 Hz, 1H), 2.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.3 (d, J_{C-F} = 245.0 Hz), 149.0, 145.8, 129.5 (d, J_{C-F} = 13.3 Hz), 128.9, 128.8, 127.6 (d, J_{C-F} = 4.0 Hz), 124.66 (d, J_{C-F} = 3.5 Hz), 118.8, 115.5 (d, J_{C-F} = 20.9 Hz), 112.9, 58.0 (d, J_{C-F} = 2.9 Hz), 46.3, 15.9.

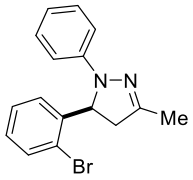
^{19}F-NMR (377 MHz, $CDCl_3$): δ = –118.84.

HRMS (ESI-TOF): Calculated for $C_{16}H_{15}FN_2$ $[M]^+$: 254.1219, found 254.1218.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 3.1 min (major) and t_R = 5.1 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(2-Bromophenyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazole



2c

Following general procedure D (reaction performed at room temperature for 32 h), compound **2c** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(2-bromophenyl)but-3-en-2-one (59 mg, 0.26 mmol, 1.05 equiv) as a white solid in 74% yield (58 mg).

Characterization data for 2c:

R_f = 0.34 in hexanes/EtOAc 80:20 v/v.

mp = 89–91 °C.

$[\alpha]_D^{20}$ = –216.5 (c 0.5, $CHCl_3$, 93% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 (d, *J* = 7.9 Hz, 1H), 7.39–7.17 (comp, 5H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.84 (t, *J* = 7.3 Hz, 1H), 5.42 (dd, *J* = 12.0, 7.6 Hz, 1H), 3.67 (dd, *J* = 17.7, 12.1 Hz, 1H), 2.69 (dd, *J* = 17.8, 7.5 Hz, 1H), 2.15 (s, 3H).

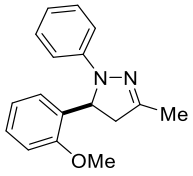
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.6, 145.5, 141.3, 133.0, 129.0, 128.9, 128.2, 127.6, 121.8, 118.7, 112.8, 63.9, 46.1, 15.9.

HRMS (ESI-TOF): Calculated for $C_{16}H_{16}BrN_2$ $[M + H]^+$: 315.0491, found 315.0503.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 9.4 min (major) and t_R = 7.1 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(2-Methoxyphenyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazole



2d

Following general procedure D (reaction performed at room temperature for 28 h), compound **2d** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(2-methoxyphenyl)but-3-en-2-one (46 mg, 0.26 mmol, 1.05 equiv) as a white solid in 97% yield (64 mg).

Characterization data for 2d:

R_f = 0.33 in hexanes/EtOAc 80:20 v/v.

mp = 66–68 °C.

$[\alpha]_D^{20}$ = –145.08 (c 0.5, $CHCl_3$, 83% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41–7.23 (comp, 4H), 7.07–6.95 (comp, 4H), 6.85 (t, *J* = 7.3 Hz, 1H), 5.43 (dd, *J* = 12.0, 7.6 Hz, 1H), 4.03 (s, 3H), 3.60 (dd, *J* = 17.7, 12.0 Hz, 1H), 2.71 (dd, *J* = 17.7, 7.6 Hz, 1H), 2.17 (s, 3H).

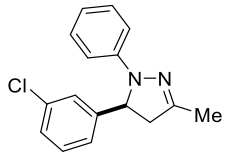
^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.0, 149.3, 146.0, 130.4, 128.8, 128.2, 126.6, 120.9, 118.2, 112.8, 110.4, 58.9, 55.4, 46.2, 16.0.

HRMS (ESI-TOF): Calculated for $C_{17}H_{18}N_2ONa$ $[M + Na]^+$: 289.1311, found 289.1329.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 7.8 min (major) and t_R = 8.5 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(3-Chlorophenyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazole



2e

Following general procedure D (reaction performed at room temperature for 28 h), compound **2e** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(3-chlorophenyl)but-3-en-2-one (47 mg, 0.26 mmol, 1.05 equiv) as a white solid in 82% yield (56 mg).

Characterization data for 2e:

R_f = 0.37 in hexanes/EtOAc 90:10 v/v.

mp = 75–77 °C.

$[\alpha]_D^{20}$ = –241.52 (c 0.5, $CHCl_3$, 94% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26 (s, 1H), 7.24–7.16 (comp, 2H), 7.15–7.06 (comp, 3H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.71 (t, *J* = 7.3 Hz, 1H), 4.91 (dd, *J* = 12.0, 8.1 Hz, 1H), 3.35 (dd, *J* = 17.6, 12.0 Hz, 1H), 2.64 (dd, *J* = 17.6, 8.1 Hz, 1H), 2.01 (s, 3H).

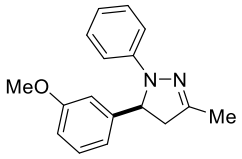
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4, 145.9, 145.2, 134.9, 130.4, 128.9, 127.7, 126.1, 124.1, 118.9, 113.1, 64.3, 47.7, 15.8.

HRMS (ESI-TOF): Calculated for $C_{16}H_{16}ClN_2$ $[M + H]^+$: 271.0997, found 271.1003.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.1 min (major) and t_R = 6.1 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(3-Methoxyphenyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazole



2f

Following general procedure D (reaction performed at room temperature for 28 h), compound **2f** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(3-methoxyphenyl)but-3-en-2-one (46 mg, 0.26 mmol, 1.05 equiv) as a white solid in 93% yield (62 mg).

Characterization data for 2f:

R_f = 0.31 in hexanes/EtOAc 90:10 v/v.

mp = 71–73 °C.

$[\alpha]_D^{20}$ = –332.11 (c 0.5, $CHCl_3$, 91% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34–7.27 (m, 1H), 7.20 (t, *J* = 7.8 Hz, 2H), 7.02–6.94 (comp, 3H), 6.91 (s, 1H), 6.88–6.76 (comp, 2H), 5.01 (dd, *J* = 11.9, 8.3 Hz, 1H), 3.82 (s, 3H), 3.45 (dd, *J* = 17.5, 11.9 Hz, 1H), 2.78 (dd, *J* = 17.6, 8.3 Hz, 1H), 2.12 (s, 3H).

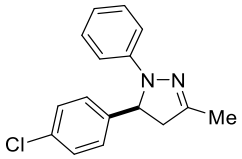
^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.2, 148.6, 146.2, 144.8, 130.1, 128.8, 118.7, 118.1, 113.1, 112.7, 111.3, 64.9, 55.2, 47.8, 15.9.

HRMS (ESI-TOF): Calculated for $C_{17}H_{19}N_2O$ $[M + H]^+$: 267.1492, found 267.1488.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.1 min (major) and t_R = 5.1 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(4-Chlorophenyl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazole



2g

Following general procedure D (reaction performed at room temperature for 28 h), compound **2g** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(4-chlorophenyl)but-3-en-2-one (47 mg, 0.26 mmol, 1.05 equiv) as a white solid in 85% yield (57 mg).

Characterization data for 2g:

R_f = 0.37 in hexanes/EtOAc 90:10 v/v.

mp = 94–96 °C.

$[\alpha]_D^{20}$ = –143.18 (c 0.5, $CHCl_3$, 92% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.28–7.21 (m, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.86 (t, *J* = 7.3 Hz, 1H), 5.07 (dd, *J* = 11.9, 8.0 Hz, 1H), 3.49 (dd, *J* = 17.5, 11.9 Hz, 1H), 2.76 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.16 (s, 3H).

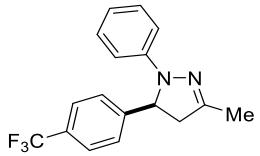
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4, 145.8, 141.5, 133.0, 129.2, 128.9, 127.3, 118.8, 113.1, 64.1, 47.7, 15.8.

HRMS (ESI-TOF): Calculated for $C_{16}H_{16}ClN_2$ $[M + H]^+$: 271.0997, found 271.1002.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.1 min (major) and t_R = 6.3 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-Methyl-1-phenyl-5-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazole



2h

Following general procedure D (reaction performed at room temperature for 40 h), compound **2h** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(4-(trifluoromethyl)phenyl)but-3-en-2-one (56 mg, 0.26 mmol, 1.05 equiv) as a white solid in 73% yield (55 mg).

Characterization data for 2h:

R_f = 0.31 in hexanes/EtOAc 90:10 v/v.

mp = 101–103 °C.

$[\alpha]_D^{20}$ = –241.24 (c 0.5, $CHCl_3$, 96% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.22–7.12 (m, 2H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 5.07 (dd, *J* = 12.0, 8.0 Hz, 1H), 3.45 (dd, *J* = 17.5, 12.1 Hz, 1H), 2.70 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.09 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4, 147.0, 145.7, 129.7 (q, J_{C-F} = 32.5 Hz), 128.9, 126.3, 126.1 (q, J_{C-F} = 3.9 Hz), 124.05 (q, J_{C-F} = 272.2 Hz), 119.0, 113.1, 64.3, 47.6, 15.8.

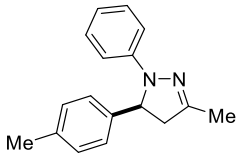
^{19}F-NMR (377 MHz, $CDCl_3$): δ = –62.44.

HRMS (ESI-TOF): Calculated for $C_{17}H_{16}F_3N_2$ $[M + H]^+$: 305.1260, found 305.1253.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 97/3, Flow rate = 2 mL/min, UV = 280 nm, t_R = 2.8 min (major) and t_R = 4.6 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-Methyl-1-phenyl-5-(p-tolyl)-4,5-dihydro-1*H*-pyrazole



2i

Following general procedure D (reaction performed at room temperature for 28 h), compound **2i** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(*p*-tolyl)but-3-en-2-one (42 mg, 0.26 mmol, 1.05 equiv) as a white solid in 90% yield (56 mg).

Characterization data for 2i:

R_f = 0.18 in hexanes/EtOAc 90:10 v/v.

mp = 81–83 °C.

$[\alpha]_D^{20}$ = –213.4 (c 0.5, $CHCl_3$, 88% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.24–7.11 (comp, 6H), 6.98–6.91 (m, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 4.99 (dd, *J* = 11.9, 8.1 Hz, 1H), 3.46–3.34 (m, 1H), 2.76–2.65 (m, 1H), 2.34 (s, 3H), 2.08 (s, 2H).

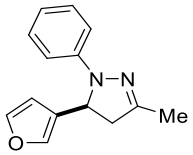
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.5, 146.1, 140.0, 137.0, 129.7, 128.8, 125.8, 118.5, 113.1, 64.5, 47.9, 21.1, 15.9.

HRMS (ESI-TOF): Calculated for $C_{17}H_{19}N_2$ $[M + H]^+$: 251.1543, found 251.1521.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 3.4 min (major) and t_R = 4.6 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(Furan-3-yl)-3-methyl-1-phenyl-4,5-dihydro-1*H*-pyrazole



2j

Following general procedure D (reaction performed at room temperature for 28 h), compound **2j** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(furan-3-yl)but-3-en-2-one (35 mg, 0.26 mmol, 1.05 equiv) as a white solid in 92% yield (52 mg).

Characterization data for 2j:

R_f = 0.41 in hexanes/EtOAc 90:10 v/v.

mp = 72–74 °C.

$[\alpha]_D^{20}$ = –236.12 (c 0.5, $CHCl_3$, 89% ee).

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.38–7.35 (m, 1H), 7.35–7.33 (m, 1H), 7.21–7.15 (m, 2H), 7.05–7.00 (m, 2H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.34–6.31 (m, 1H), 4.98 (dd, *J* = 11.5, 7.7 Hz, 1H), 3.34–3.25 (m, 1H), 2.79–2.71 (m, 1H), 2.08 (s, 3H).

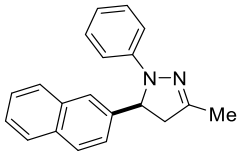
^{13}C NMR (150 MHz, $CDCl_3$) δ = 149.1, 146.3, 143.7, 139.2, 128.8, 127.1, 119.0, 113.5, 108.6, 57.0, 46.4, 16.0.

HRMS (ESI-TOF): Calculated for $C_{14}H_{15}N_2O$ $[M + H]^+$: 227.1179, found 227.1167.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.3 min (major) and t_R = 7.0 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-Methyl-5-(naphthalen-2-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazole



2k

Following general procedure D (reaction performed at room temperature for 24 h), compound **2k** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-(naphthalen-2-yl)but-3-en-2-one (52 mg, 0.26 mmol, 1.05 equiv) as a white solid in 97% yield (69 mg).

Characterization data for 2k:

R_f = 0.25 in hexanes/EtOAc 90:10 v/v.

mp = 111–113 °C.

$[\alpha]_D^{20}$ = –154.24 (c 0.5, $CHCl_3$, 90% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88–7.75 (comp, 4H), 7.53–7.41 (comp, 3H), 7.18–7.09 (m, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 5.18 (dd, *J* = 12.0, 8.2 Hz, 1H), 3.48 (dd, *J* = 17.6, 12.0 Hz, 1H), 2.79 (dd, *J* = 17.6, 8.2 Hz, 1H), 2.11 (s, 3H).

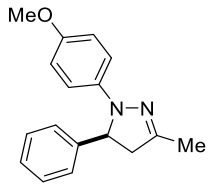
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.6, 146.2, 140.4, 133.5, 132.8, 129.1, 128.9, 127.9, 127.7, 126.3, 125.9, 124.6, 124.0, 118.7, 113.2, 65.1, 47.8, 15.9.

HRMS (ESI-TOF): Calculated for $C_{20}H_{19}N_2$ $[M + H]^+$: 287.1543, found 287.1534.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 95/5, Flow rate = 2 mL/min, UV = 230 nm, t_R = 11.9 min (major) and t_R = 13.3 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-1-(4-Methoxyphenyl)-3-methyl-5-phenyl-4,5-dihydro-1*H*-pyrazole



2l

Following general procedure D (reaction performed at room temperature for 28 h), compound **2l** was obtained from (4-methoxyphenyl)hydrazine (35 mg, 0.25 mmol, 1 equiv) and (*E*)-4-phenylbut-3-en-2-one (38 mg, 0.26 mmol, 1.05 equiv) as an off-white solid in 80% yield (53 mg).

Characterization data for 2l:

R_f = 0.37 in hexanes/EtOAc 85:15 v/v.

mp = 64–66 °C.

$[\alpha]_D^{20}$ = –386.28 (c 0.5, $CHCl_3$, 83% ee).

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.38–7.34 (comp, 4H), 7.31–7.26 (m, 1H), 6.92–6.88 (m, 2H), 6.77–6.73 (m, 2H), 4.90 (dd, *J* = 11.6, 9.5 Hz, 1H), 3.73 (s, 3H), 3.38 (dd, *J* = 17.3, 11.7 Hz, 1H), 2.74 (dd, *J* = 17.3, 9.5 Hz, 1H), 2.08 (s, 3H).

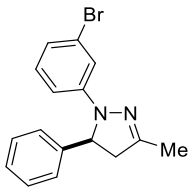
^{13}C NMR (150 MHz, $CDCl_3$) δ = 153.1, 148.4, 143.1, 141.1, 129.0, 127.4, 126.2, 114.9, 114.3, 66.4, 55.6, 48.0, 15.9.

HRMS (ESI-TOF): Calculated for $C_{17}H_{19}N_2O$ $[M + H]^+$: 267.1492, found 267.1504.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 5.0 min (major) and t_R = 8.5 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-1-(3-Bromophenyl)-3-methyl-5-phenyl-4,5-dihydro-1*H*-pyrazole



2m

Following general procedure D (reaction performed at room temperature for 28 h), compound **2m** was obtained from (3-bromophenyl)hydrazine (47 mg, 0.25 mmol, 1 equiv) and (*E*)-4-phenylbut-3-en-2-one (38 mg, 0.26 mmol, 1.05 equiv) as a white solid in 83% yield (65 mg).

Characterization data for 2m:

R_f = 0.41 in hexanes/EtOAc 90:10 v/v.

mp = 99–101 °C.

$[\alpha]_D^{20}$ = –221.08 (c 0.5, $CHCl_3$, 90% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38–7.31 (m, 2H), 7.31–7.22 (comp, 4H), 6.94 (t, *J* = 8.1 Hz, 1H), 6.87–6.81 (m, 1H), 6.71–6.64 (m, 1H), 5.00 (dd, *J* = 11.9, 7.4 Hz, 1H), 3.49–3.36 (m, 1H), 2.77–2.67 (m, 1H), 2.07 (s, 3H).

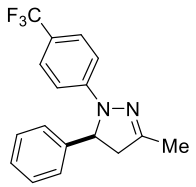
^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.3, 146.8, 142.3, 130.0, 129.1, 127.5, 125.7, 122.9, 121.1, 115.9, 111.1, 64.2, 47.8, 15.8.

HRMS (ESI-TOF): Calculated for $C_{16}H_{15}BrN_2$ $[M]^+$: 314.0419, found 314.0400.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.7 min (major) and t_R = 8.2 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-Methyl-5-phenyl-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazole



2n

Following general procedure D (reaction performed at room temperature for 28 h), compound **2n** was obtained from (4-(trifluoromethyl)phenyl)hydrazine (44 mg, 0.25 mmol, 1 equiv) and (*E*)-4-phenylbut-3-en-2-one (38 mg, 0.26 mmol, 1.05 equiv) as a white solid in 85% yield (65 mg).

Characterization data for 2n:

R_f = 0.35 in hexanes/EtOAc 90:10 v/v.

mp = 106–108 °C.

$[\alpha]_D^{20}$ = –356.06 (c 0.5, $CHCl_3$, 87% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38–7.32 (comp, 4H), 7.30–7.22 (comp, 3H), 6.93 (d, *J* = 8.7 Hz, 2H), 5.09 (dd, *J* = 12.0, 6.9 Hz, 1H), 3.52–3.43 (m, 1H), 2.80–2.72 (m, 1H), 2.09 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.0, 147.6, 142.0, 129.2, 127.7, 126.2 (q, $J_{C–F}$ = 3.6 Hz), 125.6, 124.9 (q, $J_{C–F}$ = 270.7 Hz), 119.6 (q, $J_{C–F}$ = 32.3 Hz), 112.0, 63.7, 47.8, 15.9.

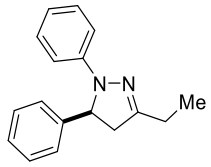
^{19}F-NMR (377 MHz, $CDCl_3$): δ = –62.44.

HRMS (ESI-TOF): Calculated for $C_{17}H_{16}F_3N_2$ $[M + H]^+$: 305.1260, found 305.1272.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 2.9 min (major) and t_R = 3.9 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-Ethyl-1,5-diphenyl-4,5-dihydro-1*H*-pyrazole



2o

Following general procedure D (reaction performed at room temperature for 28 h), compound **2o** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-1-phenylpent-1-en-3-one (42 mg, 0.26 mmol, 1.05 equiv) as a white solid in 91% yield (57 mg).

Characterization data for 2o:

R_f = 0.38 in hexanes/EtOAc 90:10 v/v.

mp = 66–68 °C.

$[\alpha]_D^{20}$ = –288.32 (c 0.5, $CHCl_3$, 88% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38–7.29 (comp, 4H), 7.29–7.23 (m, 1H), 7.19–7.10 (m, 2H), 6.95 (d, *J* = 8.1 Hz, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 5.00 (dd, *J* = 11.9, 8.1 Hz, 1H), 3.43 (dd, *J* = 17.4, 11.9 Hz, 1H), 2.73 (dd, *J* = 17.4, 8.1 Hz, 1H), 2.42 (q, *J* = 7.5 Hz, 2H), 1.21 (t, *J* = 7.5 Hz, 3H).

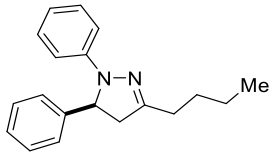
^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.1, 146.2, 143.1, 129.0, 128.8, 127.3, 125.9, 118.6, 113.1, 64.6, 46.0, 23.6, 11.2.

HRMS (ESI-TOF): Calculated for $C_{17}H_{19}N_2$ $[M + H]^+$: 251.1543, found 251.1554.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 5.4 min (major) and t_R = 6.7 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-Butyl-1,5-diphenyl-4,5-dihydro-1*H*-pyrazole



2p

Following general procedure D (reaction performed at room temperature for 28 h), compound **2p** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-1-phenylhept-1-en-3-one (49 mg, 0.26 mmol, 1.05 equiv) as a white solid in 91% yield (63 mg).

Characterization data for 2p:

R_f = 0.51 in hexanes/EtOAc 90:10 v/v.

mp = 68–70 °C.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{20}}$ = –298.57 (c 1.0, CH_2Cl_2, 90% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29–7.14 (comp, 5H), 7.10–7.01 (m, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.65 (t, *J* = 7.3 Hz, 1H), 4.91 (dd, *J* = 11.9, 8.0 Hz, 1H), 3.33 (dd, *J* = 17.4, 11.9 Hz, 1H), 2.63 (dd, *J* = 17.4, 8.0 Hz, 1H), 2.32 (t, *J* = 7.7 Hz, 2H), 1.55–1.45 (m, 2H), 1.38–1.26 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H).

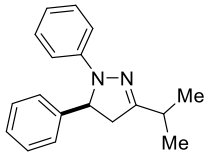
^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 146.2, 143.1, 129.0, 128.8, 127.3, 125.9, 118.5, 113.1, 64.5, 46.2, 29.9, 28.9, 22.5, 13.8.

HRMS (ESI-TOF): Calculated for $C_{19}H_{22}N_2$ $[M]^+$: 278.1783, found 278.1772.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 8.7 min (major) and t_R = 9.8 min (minor).

The absolute configuration of (*S*)-**2p** ($[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{20}}$ = –298.57 (c 1.0, CH_2Cl_2, 90% ee)) was assigned by comparison with the (*R*)-enantiomer reported in the literature ($[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{23}}$ = +336.02 (c 1.0, CH_2Cl_2, 94% ee)).[3]

(*S*)-3-Isopropyl-1,5-diphenyl-4,5-dihydro-1*H*-pyrazole



2q

Following general procedure D (reaction performed at room temperature for 28 h), compound **2q** was obtained from phenylhydrazine (25 μL, 0.25 mmol, 1 equiv) and (*E*)-4-methyl-1-phenylpent-1-en-3-one (46 mg, 0.26 mmol, 1.05 equiv) as a white solid in 89% yield (59 mg).

Characterization data for 2q:

R_f = 0.37 in hexanes/EtOAc 90:10 v/v.

mp = 90–92 °C.

$[\alpha]_D^{20}$ = –196.5 (c 0.5, $CHCl_3$, 82% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31–7.17 (comp, 6H), 7.11–7.05 (m, 2H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.68 (t, *J* = 7.3 Hz, 1H), 4.93 (dd, *J* = 11.9, 8.1 Hz, 1H), 3.37 (dd, *J* = 17.4, 11.9 Hz, 1H), 2.74–2.61 (comp, 2H), 1.15 (d, *J* = 1.4 Hz, 3H), 1.13 (d, *J* = 1.4 Hz, 3H).

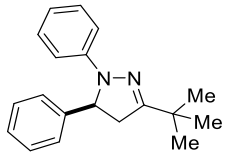
^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.5, 146.3, 143.2, 129.0, 128.8, 127.3, 125.9, 118.5, 113.2, 64.7, 44.0, 29.7, 20.3.

HRMS (ESI-TOF): Calculated for $C_{18}H_{21}N_2$ $[M + H]^+$: 265.1699, found 265.1727.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 98/2, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.0 min (major) and t_R = 4.3 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-(*Tert*-butyl)-1,5-diphenyl-4,5-dihydro-1*H*-pyrazole



2r

Following general procedure D (reaction performed at room temperature for 28 h), compound **2r** was obtained from phenylhydrazine (25 µL, 0.25 mmol, 1 equiv) and (*E*)-4,4-dimethyl-1-phenylpent-1-en-3-one (49 mg, 0.26 mmol, 1.05 equiv) as a colorless oil in 86% yield (60 mg).

Characterization data for 2r:

R_f = 0.51 in hexanes/EtOAc 90:10 v/v.

$[\alpha]_D^{20}$ = –171.18 (c 0.5, $CHCl_3$, 69% ee).

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.39–7.31 (comp, 4H), 7.30–7.26 (m, 1H), 7.19–7.14 (m, 2H), 7.01–6.96 (m, 2H), 6.79–6.73 (m, 1H), 5.01 (dd, *J* = 11.8, 8.1 Hz, 1H), 3.49 (dd, *J* = 17.2, 11.8 Hz, 1H), 2.78 (dd, *J* = 17.2, 8.1 Hz, 1H), 1.26 (s, 9H).

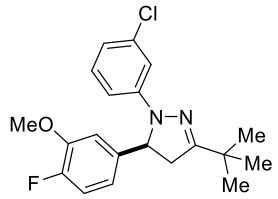
^{13}C NMR (150 MHz, $CDCl_3$) δ = 158.7, 146.4, 143.2, 129.0, 128.8, 127.3, 125.9, 118.5, 113.2, 65.1, 43.2, 33.8, 28.3.

HRMS (ESI-TOF): Calculated for $C_{19}H_{22}N_2$ $[M]^+$: 278.1783 found 278.1788.

SFC: Daicel Chiralcel OD-H, column temperature = 40 °C, CO_2/MeOH = 95/5, Flow rate = 2 mL/min, UV = 280 nm, t_R = 8.8 min (major) and t_R = 9.7 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-3-(*Tert*-butyl)-1-(3-chlorophenyl)-5-(4-fluoro-3-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole



2s

Following general procedure D (reaction performed at room temperature for 28 h), compound **2s** was obtained from (3-chlorophenyl)hydrazine (36 mg, 0.25 mmol, 1 equiv) and (*E*)-1-(4-fluoro-3-methoxyphenyl)-4,4-dimethylpent-1-en-3-one (62 mg, 0.26 mmol, 1.05 equiv) as a white solid in 88% yield (79 mg).

Characterization data for 2s:

R_f = 0.34 in hexanes/EtOAc 80:20 v/v.

mp = 125–127 °C

$[\alpha]_D^{20}$ = –314.22 (c 0.5, $CHCl_3$, 72% ee).

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.07–6.99 (comp, 3H), 6.85–6.76 (comp, 2H), 6.73–6.64 (comp, 2H), 4.93 (dd, *J* = 11.7, 7.4 Hz, 1H), 3.83 (s, 3H), 3.46 (dd, *J* = 17.3, 11.7 Hz, 1H), 2.73 (dd, *J* = 17.3, 7.4 Hz, 1H), 1.23 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$) δ = 159.8, 151.7 (d, $J_{C–F}$ = 246.0 Hz), 148.3 (d, $J_{C–F}$ = 10.5 Hz), 147.1, 138.87 (d, $J_{C–F}$ = 3.9 Hz), 134.6, 129.8, 118.5, 117.9 (d, $J_{C–F}$ = 7.2 Hz), 116.5 (d, $J_{C–F}$ = 18.2 Hz), 113.3, 111.0, 110.5 (d, $J_{C–F}$ = 2.2 Hz), 64.4, 56.3, 43.2, 33.9, 28.2.

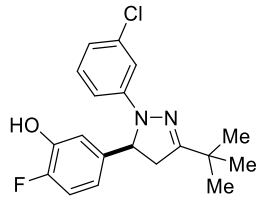
^{19}F-NMR (377 MHz, $CDCl_3$): δ = –136.70.

HRMS (ESI-TOF): Calculated for $C_{20}H_{23}ClFN_2O$ $[M + H]^+$: 361.1477, found 361.1458.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 98/2, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.8 min (major) and t_R = 5.2 min (minor).

The absolute configuration was assigned by analogy.

(*S*)-5-(3-(*Tert*-butyl)-1-(3-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-2-fluorophenol



2t

Following general procedure D (reaction performed at room temperature for 28 h), compound **2t** was obtained from (3-chlorophenyl)hydrazine (36 mg, 0.25 mmol, 1 equiv) and (*E*)-1-(4-fluoro-3-hydroxyphenyl)-4,4-dimethylpent-1-en-3-one (58 mg, 0.26 mmol, 1.05 equiv) as a white solid in 92% yield (80 mg).

Characterization data for 2t:

R_f = 0.22 in hexanes/EtOAc 60:40 v/v.

mp = 109–111 °C

$[\alpha]_D^{20}$ = –155.18 (c 0.5, $CHCl_3$, 61% ee).

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.07–6.98 (comp, 3H), 6.93–6.87 (m, 1H), 6.78–6.72 (m, 1H), 6.71–6.63 (comp, 2H), 5.26 (s, 1H), 4.91 (dd, *J* = 11.8, 7.2 Hz, 1H), 3.44 (dd, *J* = 17.4, 11.8 Hz, 1H), 2.71 (dd, *J* = 17.4, 7.2 Hz, 1H), 1.22 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$) δ = 159.6, 150.3 (d, $J_{C–F}$ = 237.2 Hz), 146.9, 144.0 (d, $J_{C–F}$ = 14.4 Hz), 139.5 (d, $J_{C–F}$ = 3.3 Hz), 134.6, 129.8, 118.3, 117.9 (d, $J_{C–F}$ = 6.6 Hz), 116.1 (d, $J_{C–F}$ = 18.2 Hz), 114.5 (d, $J_{C–F}$ = 1.6 Hz), 113.2, 110.9, 63.8, 43.1, 33.8, 28.2.

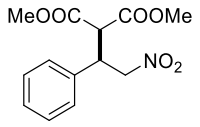
^{19}F-NMR (377 MHz, $CDCl_3$): δ = –142.14.

HRMS (ESI-TOF): Calculated for $C_{19}H_{21}ClFN_2O$ $[M + H]^+$: 347.1321, found 347.1311.

SFC: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 9.6 min (major) and t_R = 11.0 min (minor).

The absolute configuration was assigned by analogy.

Dimethyl (*R*)-2-(2-nitro-1-phenylethyl)malonate



4

To a flame dried vial were successively added dimethyl malonate (0.5 mmol, 2 equiv), catalyst **5b** (10.3 mg, 0.025 mmol, 10 mol%), and dry toluene (2.5 mL, 0.1 M). Trans-β-nitrostyrene (0.25 mmol, 1 equiv) was then added, and the resulting mixture was stirred under nitrogen at room temperature for 6 h. The resulting mixture was directly purified by flash chromatography on silica gel using EtOAc/hexanes (20/80) as the eluent to afford **4** as a colorless oil in 95% yield (67 mg).

Characterization data for 4:

$\mathbf{R_f}$ = 0.2 in hexanes/EtOAc 80:20 v/v.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{20}}$ = –5.03 (c 1.0, $CHCl_3$, 94% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28–7.13 (comp, 5H), 4.89–4.76 (comp, 2H), 4.17 (td, *J* = 9.0, 5.2 Hz, 1H), 3.79 (d, *J* = 9.0 Hz, 1H), 3.68 (s, 3H), 3.48 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.8, 167.2, 136.1, 129.0, 128.4, 127.8, 77.3, 54.7, 53.0, 52.8, 42.9.

HRMS (ESI-TOF): Calculated for $C_{13}H_{15}NO_6Na$ $[M + Na]^+$: 304.0792, found 304.0796.

SFC: Daicel Chiralcel AD-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 230 nm, t_R = 3.3 min (major) and t_R = 2.9 min (minor).

The absolute configuration of **8a** ($[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{20}}$ = –5.03 (c 1.0, $CHCl_3$, 94% ee)) was assigned by comparison with the compound reported in the literature ($[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{23}}$ = –6.02 (c 1.0, $CHCl_3$, 97% ee)).[4]

References

1 X. Liu, X. Xu, L. Pan, Q. Zhang and Q. Liu, *Org. Biomol. Chem.*, 2013, **11**, 6703-6706.

2 Y.-D. Yang, E. Tokunaga, H. Akiyama, N. Saito and N. Shibata, *ChemMedChem*, 2014, **9**, 913-917.

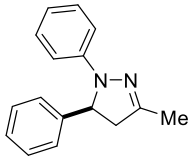
3 D.-Y. Zhang, L. Shao, J. Xu and X.-P. Hu, *ACS Catal.*, 2015, **5**, 5026-5030.

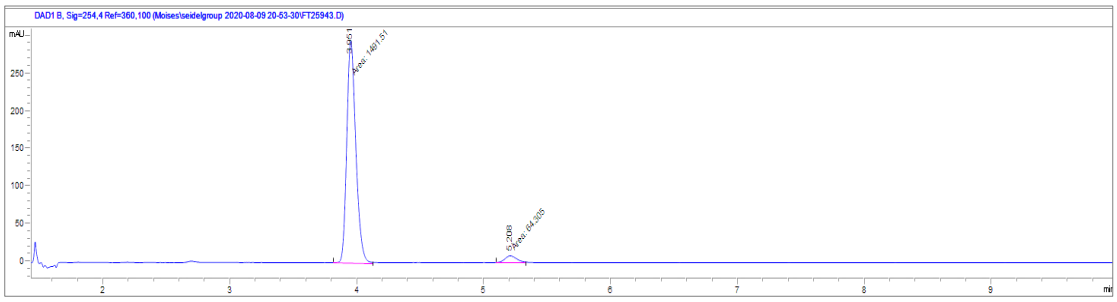
4 L. Zhang, M.-M. Lee, S.-M. Lee, J. Lee, M. Cheng, B.-S. Jeong, H.-g. Park and S.-s. Jew, *Adv. Synth. Catal.*, 2009, **351**, 3063-3066.

SFC Profiles

SFC Profile of **2a**

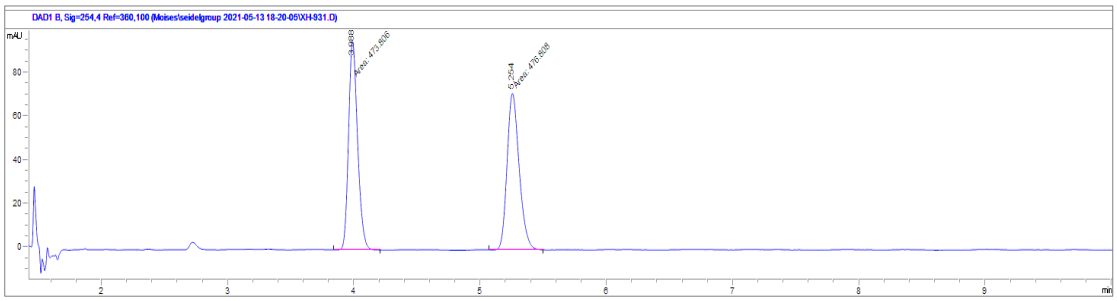
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 254 nm, t_R = 3.9 min (major) and t_R = 5.2 min (minor).





Peak	Retention time (min)	Area %
1	3.951	95.867
2	5.208	4.133

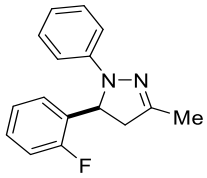
Racemic sample

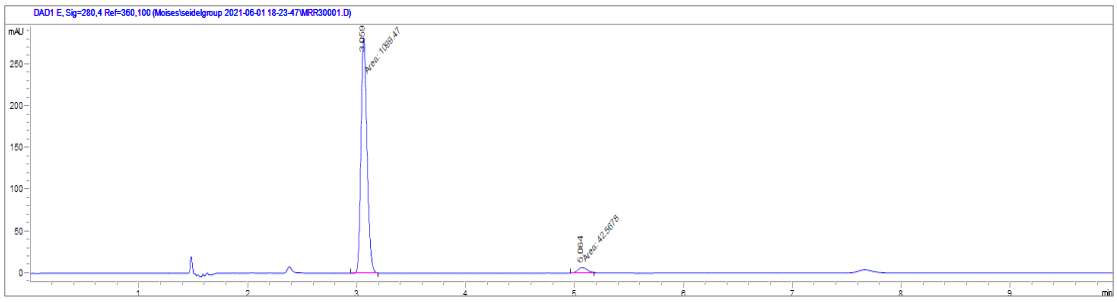


Peak	Retention time (min)	Area %
1	3.988	50.085
2	5.254	49.915

SFC Profile of **2b**

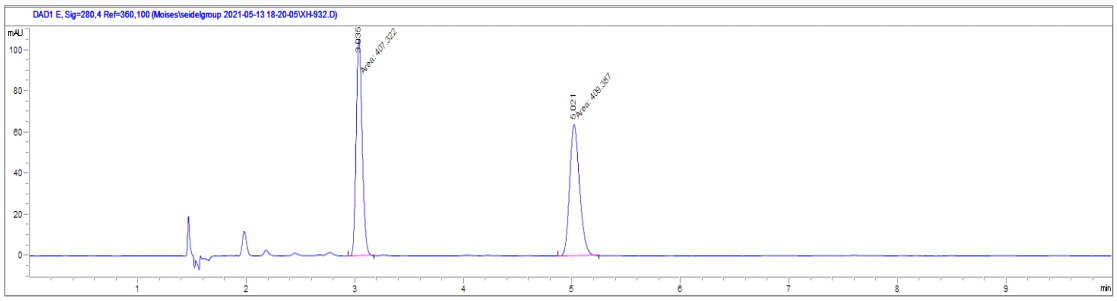
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 3.1 min (major) and t_R = 5.1 min (minor).





Peak	Retention time (min)	Area %
1	3.059	96.273
2	5.064	3.727

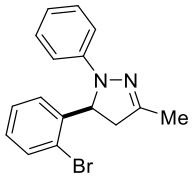
Racemic sample

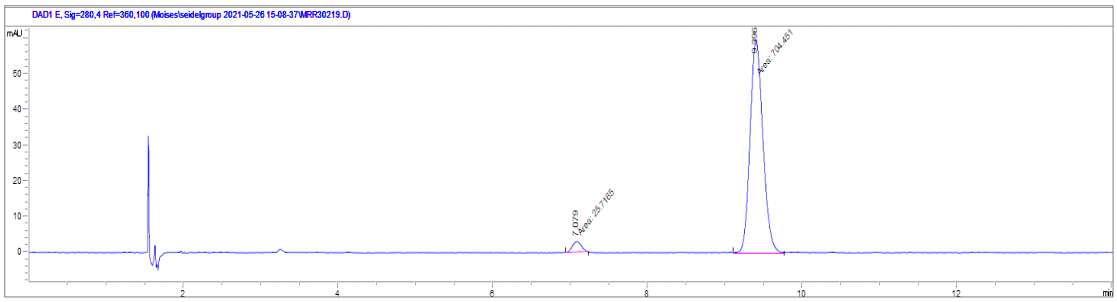


Peak	Retention time (min)	Area %
1	3.035	49.874
2	5.021	50.126

SFC Profile of **2c**

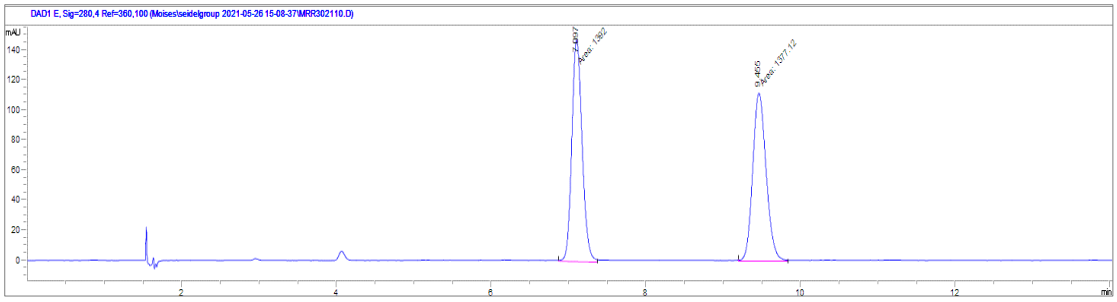
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 9.4 min (major) and t_R = 7.1 min (minor).





Peak	Retention time (min)	Area %
1	7.079	3.522
2	9.396	96.478

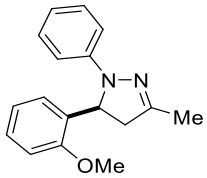
Racemic sample

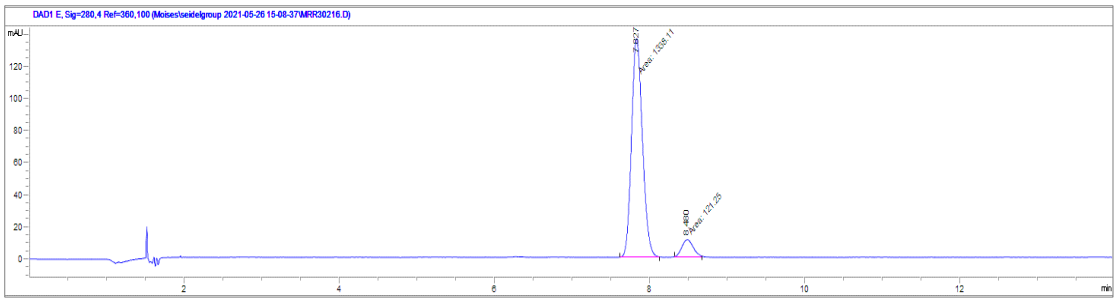


Peak	Retention time (min)	Area %
1	7.097	50.169
2	9.455	49.831

SFC Profile of **2d**

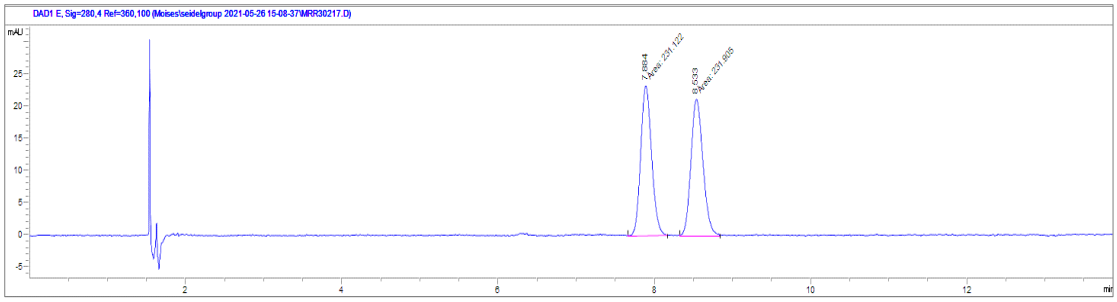
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 7.8 min (major) and t_R = 8.5 min (minor).





Peak	Retention time (min)	Area %
1	7.827	91.692
2	8.480	8.308

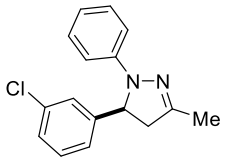
Racemic sample

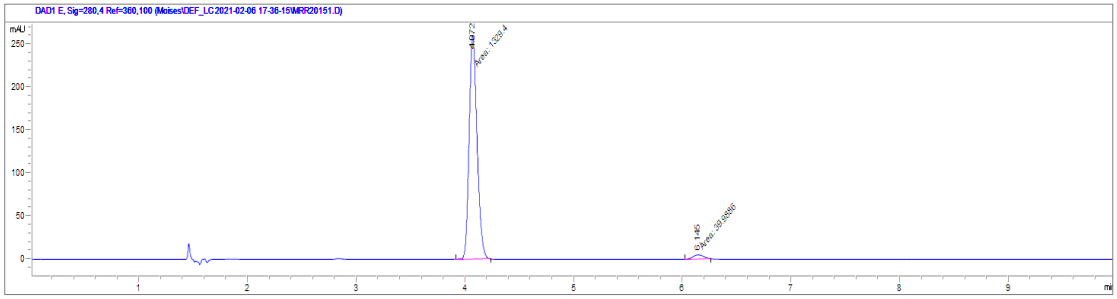


Peak	Retention time (min)	Area %
1	7.884	49.915
2	8.533	50.085

SFC Profile of **2e**

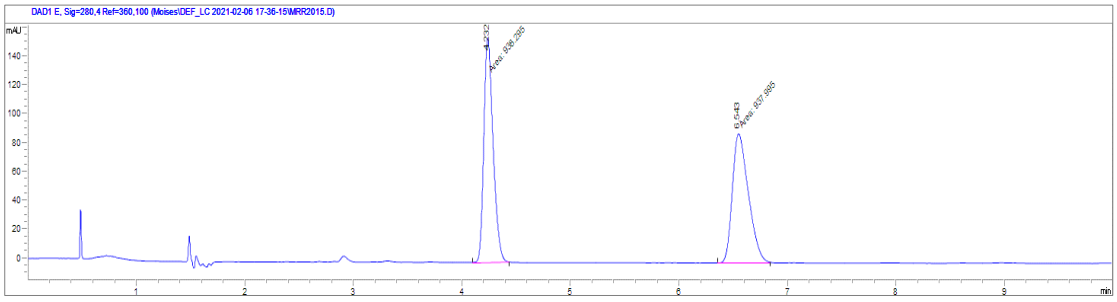
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.1 min (major) and t_R = 6.1 min (minor).





Peak	Retention time (min)	Area %
1	4.072	97.080
2	6.145	2.9200

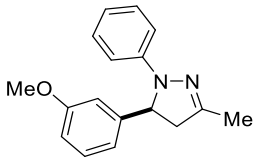
Racemic sample

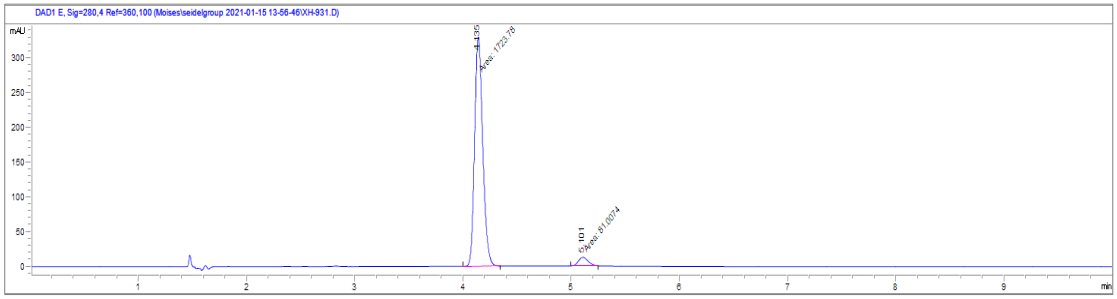


Peak	Retention time (min)	Area %
1	4.232	50.008
2	6.543	49.992

SFC Profile of **2f**

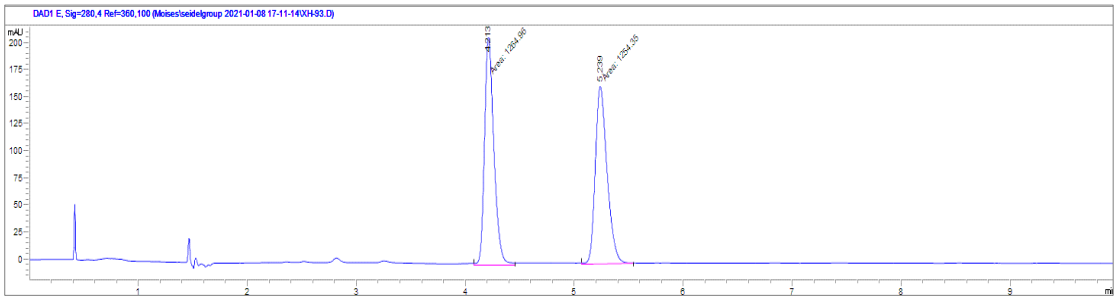
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.1 min (major) and t_R = 5.1 min (minor).





Peak	Retention time (min)	Area %
1	4.135	95.512
2	5.101	4.488

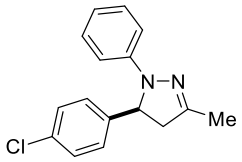
Racemic sample

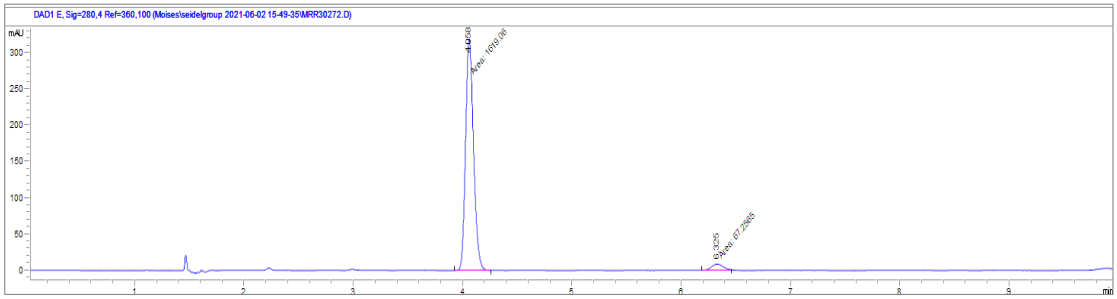


Peak	Retention time (min)	Area %
1	4.213	50.211
2	5.230	49.789

SFC Profile of **2g**

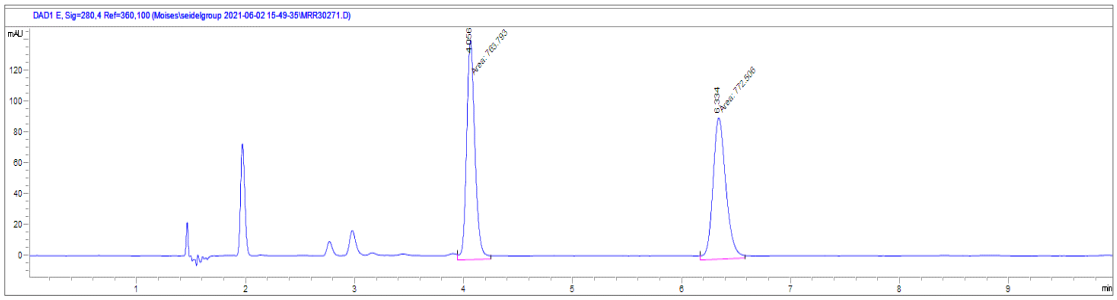
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.1 min (major) and t_R = 6.3 min (minor).





Peak	Retention time (min)	Area %
1	4.058	96.012
2	6.325	3.988

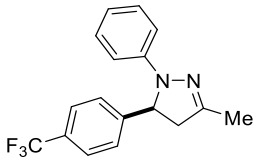
Racemic sample

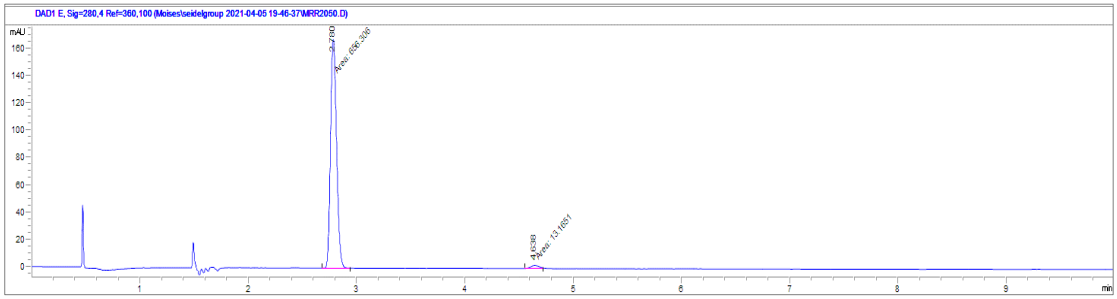


Peak	Retention time (min)	Area %
1	4.056	49.716
2	6.334	50.284

SFC Profile of **2h**

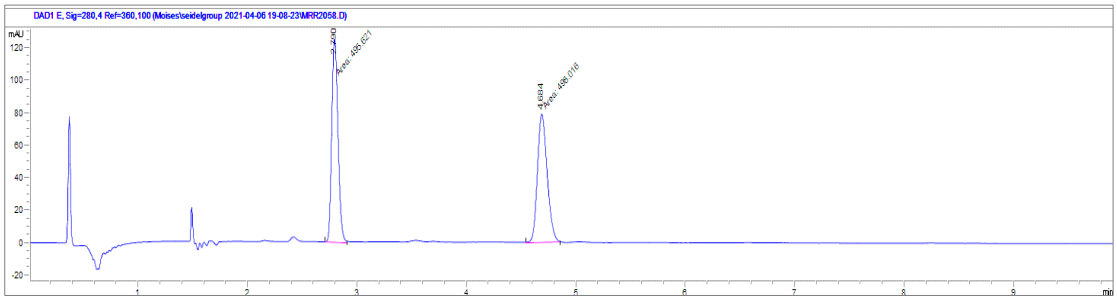
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 97/3, Flow rate = 2 mL/min, UV = 280 nm, t_R = 2.8 min (major) and t_R = 4.6 min (minor).





Peak	Retention time (min)	Area %
1	2.78	98.034
2	4.638	1.966

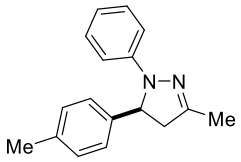
Racemic sample

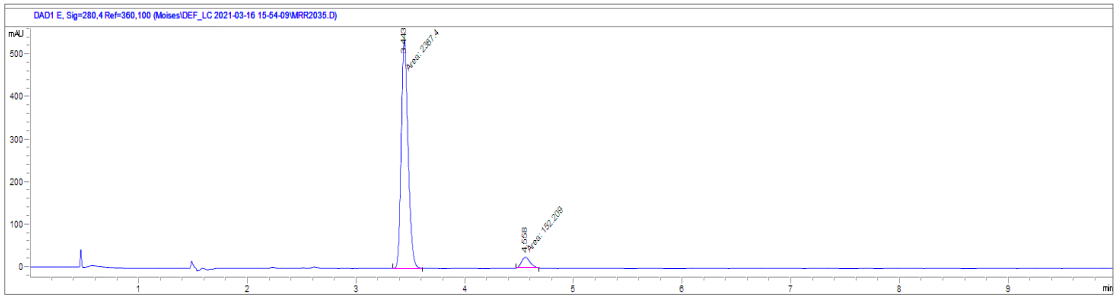


Peak	Retention time (min)	Area %
1	2.79	49.879
2	4.684	50.121

SFC Profile of **2i**

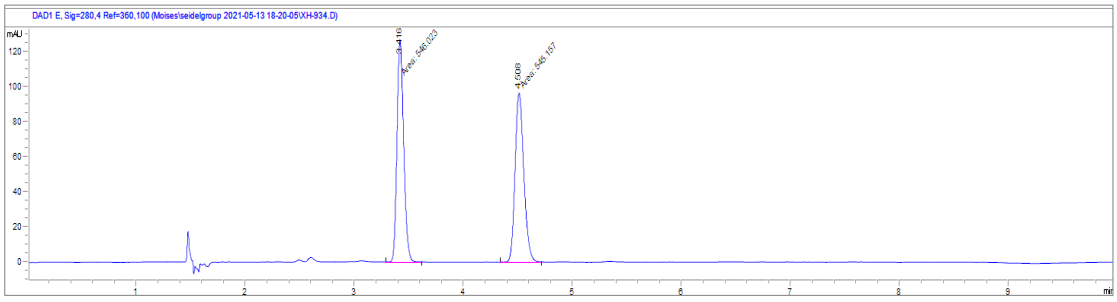
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 3.4 min (major) and t_R = 4.6 min (minor).





Peak	Retention time (min)	Area %
1	3.443	94.007
2	4.558	5.993

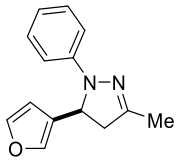
Racemic sample

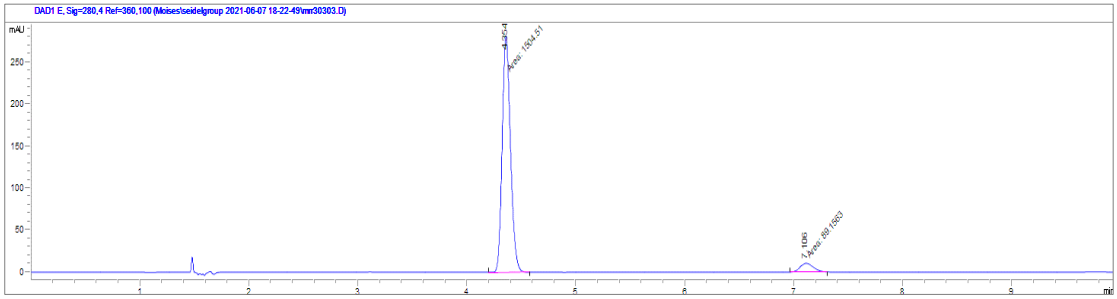


Peak	Retention time (min)	Area %
1	3.416	50.040
2	4.508	49.960

SFC Profile of **2j**

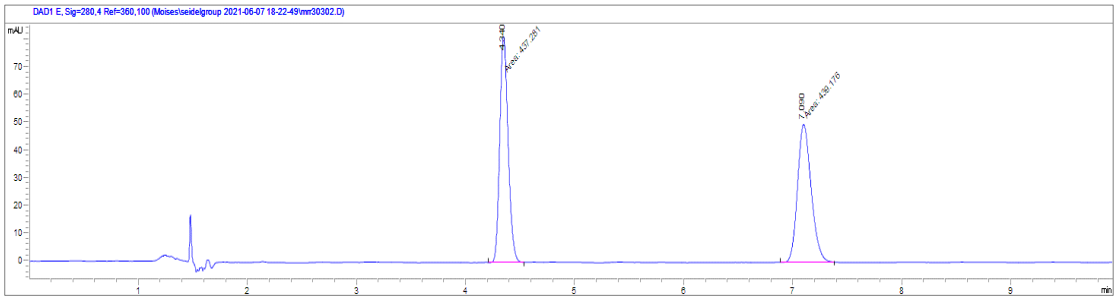
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.3 min (major) and t_R = 7.0 min (minor).





Peak	Retention time (min)	Area %
1	4.354	94.406
2	7.016	5.594

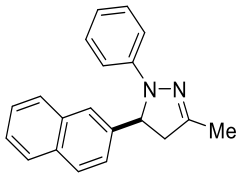
Racemic sample

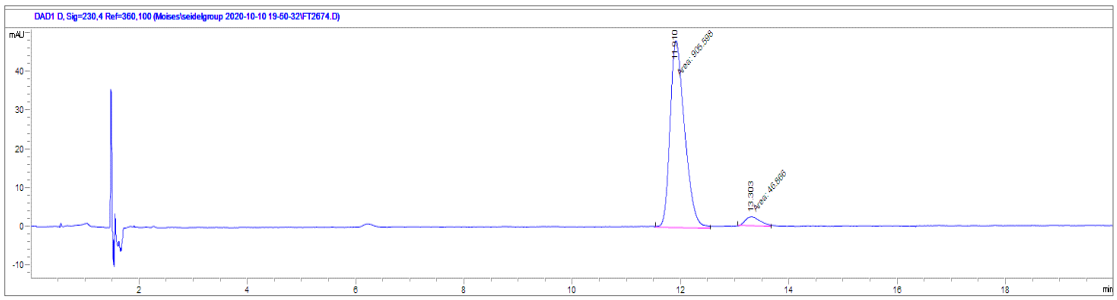


Peak	Retention time (min)	Area %
1	4.34	49.892
2	7.09	50.108

SFC Profile of **2k**

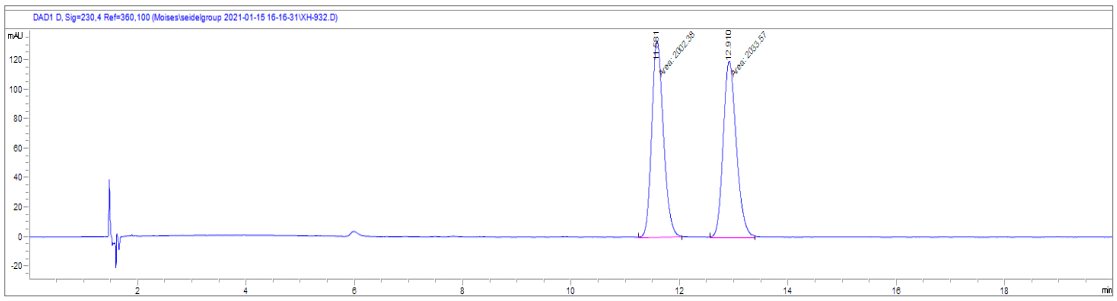
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 95/5, Flow rate = 2 mL/min, UV = 230 nm, t_R = 11.9 min (major) and t_R = 13.3 min (minor).





Peak	Retention time (min)	Area %
1	11.91	95.080
2	13.303	4.920

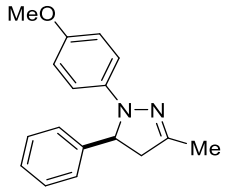
Racemic sample

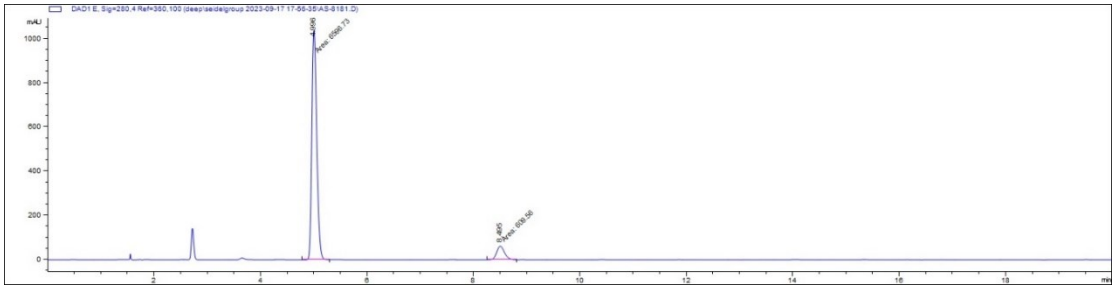


Peak	Retention time (min)	Area %
1	11.581	49.613
2	12.91	50.387

SFC Profile of **2l**

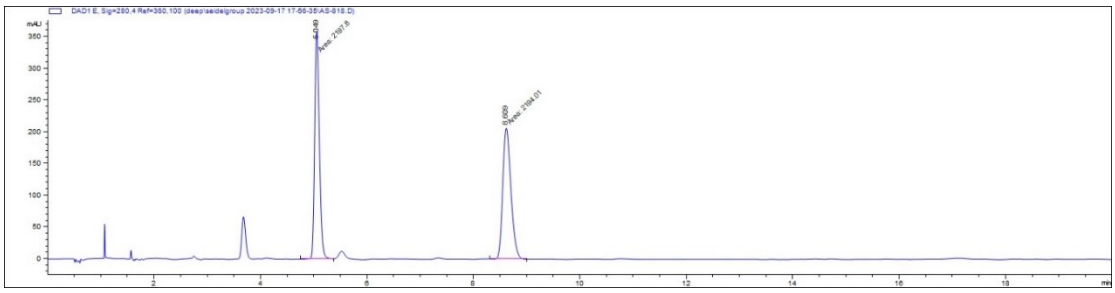
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 5.0 min (minor) and t_R = 8.5 min (major).





Peak	Retention time (min)	Area %
1	4.996	91.541
2	8.495	8.459

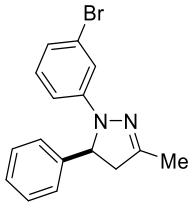
Racemic sample

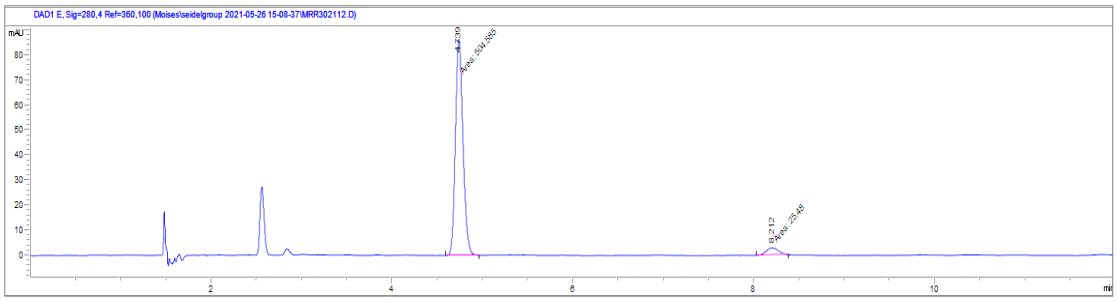


Peak	Retention time (min)	Area %
1	5.049	50.043
2	8.609	49.957

SFC Profile of **2m**

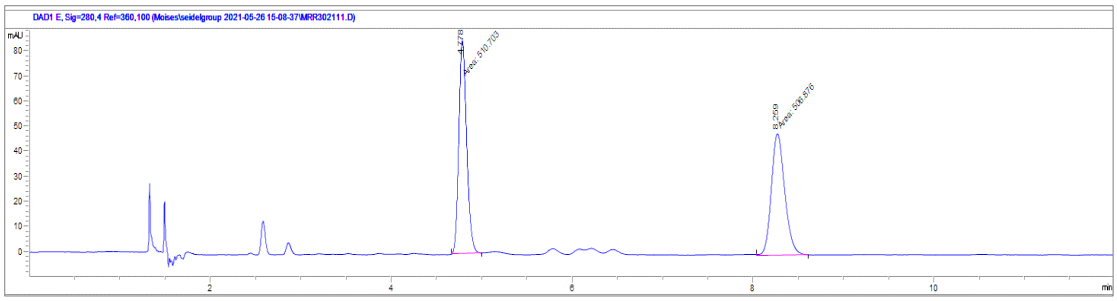
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.7 min (minor) and t_R = 8.2 min (major).





Peak	Retention time (min)	Area %
1	4.739	95.193
2	8.212	4.807

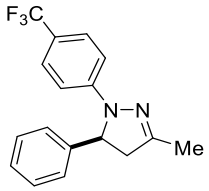
Racemic sample

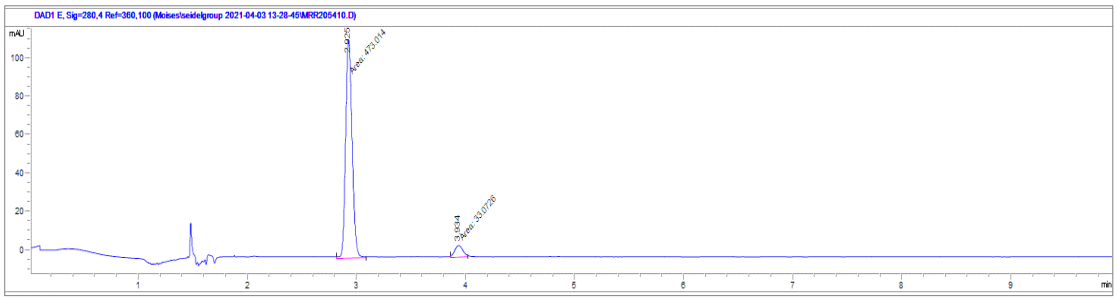


Peak	Retention time (min)	Area %
1	4.778	50.188
2	8.259	49.812

SFC Profile of **2n**

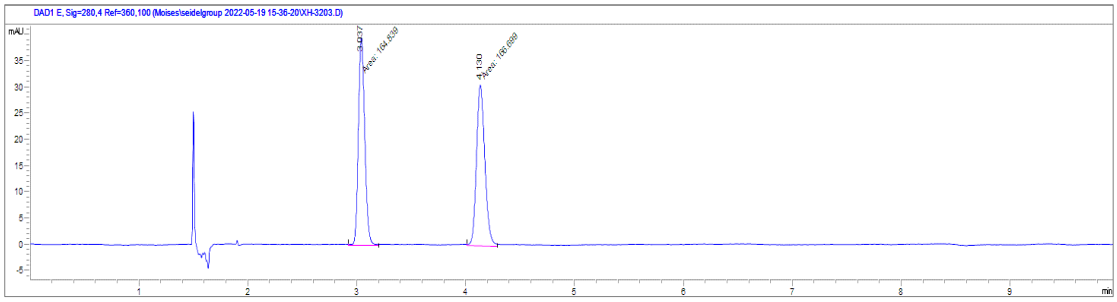
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 2.9 min (major) and t_R = 3.9 min (minor).





Peak	Retention time (min)	Area %
1	2.925	93.465
2	3.934	6.536

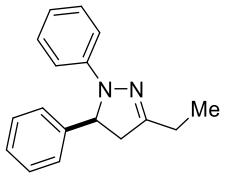
Racemic sample

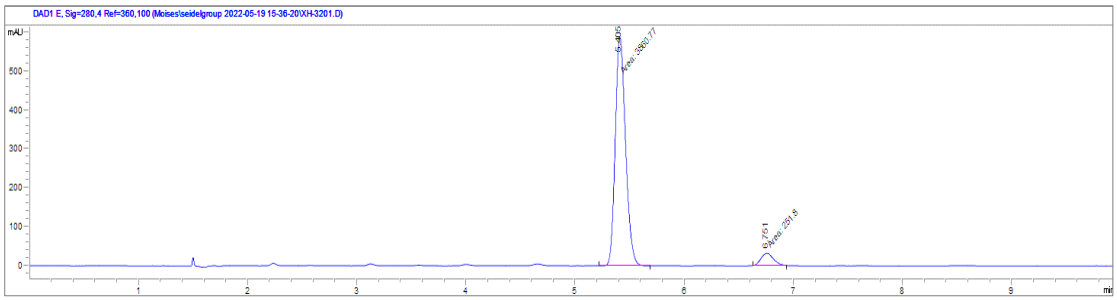


Peak	Retention time (min)	Area %
1	3.037	49.719
2	4.131	50.281

SFC Profile of **2o**

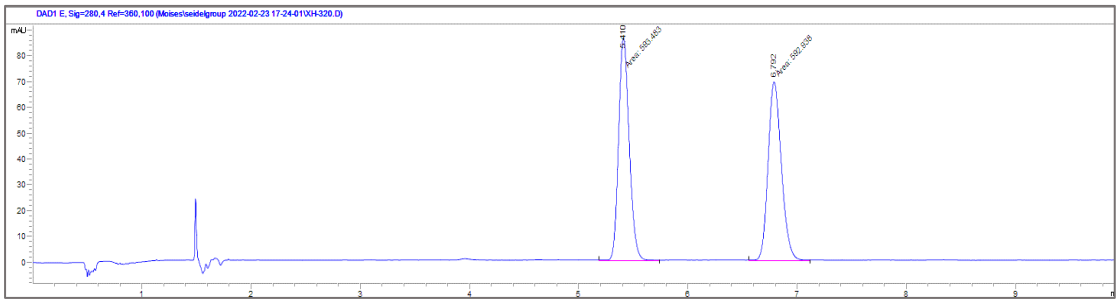
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 80/20, Flow rate = 2 mL/min, UV = 280 nm, t_R = 5.4 min (major) and t_R = 6.7 min (minor).





Peak	Retention time (min)	Area %
1	5.405	93.877
2	6.751	6.123

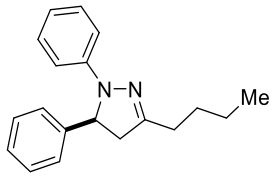
Racemic sample

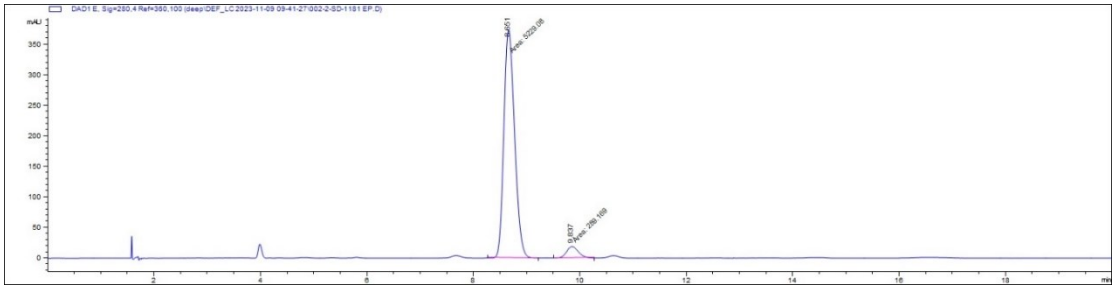


Peak	Retention time (min)	Area %
1	5.41	49.922
2	6.792	50.078

SFC Profile of **2p**:

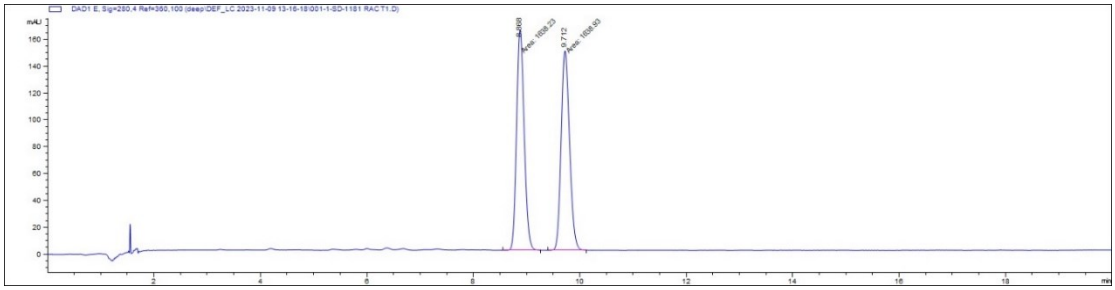
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 8.7 min (major) and t_R = 9.8 min (minor).





Peak	Retention time (min)	Area %
1	8.651	94.760
2	9.837	5.240

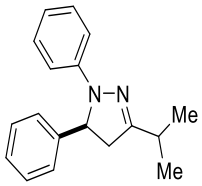
Racemic sample

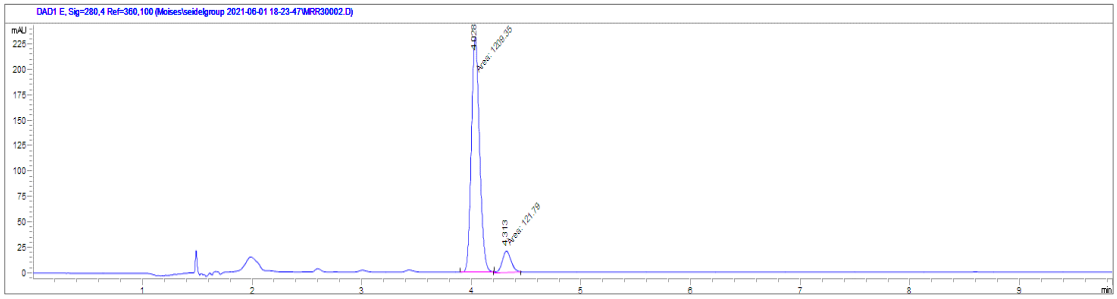


Peak	Retention time (min)	Area %
1	8.868	49.989
2	9.712	50.011

SFC Profile of **2q**:

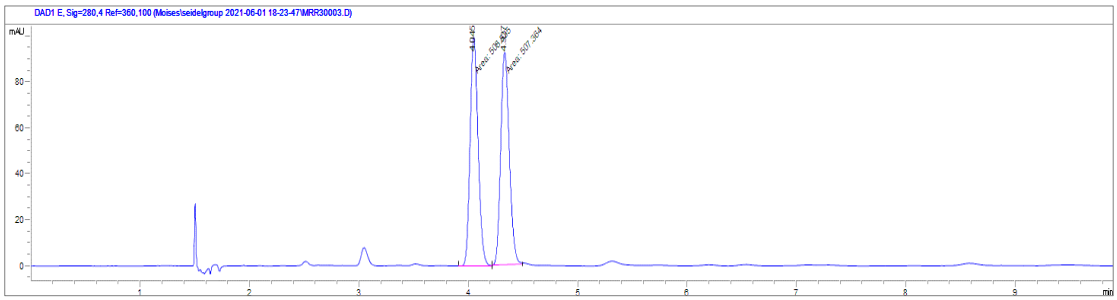
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 98/2, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.0 min (major) and t_R = 4.3 min (minor).





Peak	Retention time (min)	Area %
1	4.028	90.851
2	4.313	9.149

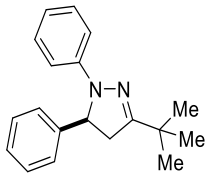
Racemic sample

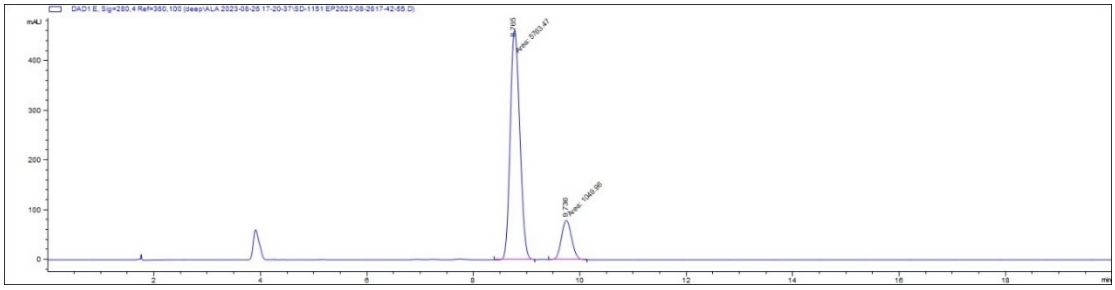


Peak	Retention time (min)	Area %
1	4.045	50.058
2	4.327	49.942

SFC Profile of **2r**:

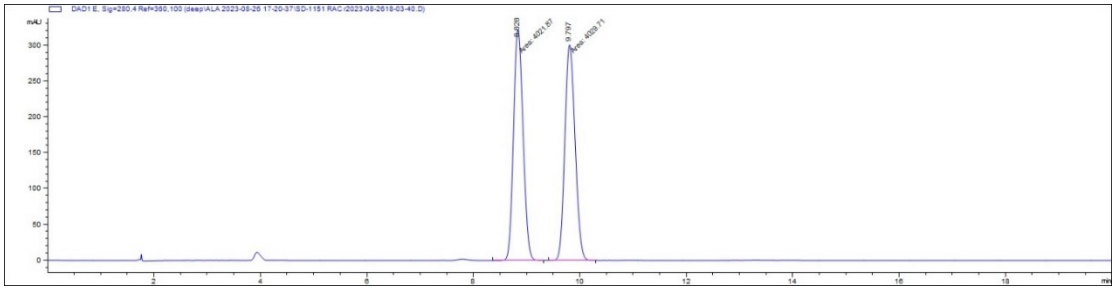
Conditions: Daicel Chiralcel OD-H, column temperature = 40 °C, CO_2/MeOH = 95/5, Flow rate = 2 mL/min, UV = 280 nm, t_R = 8.8 min (major) and t_R = 9.7 min (minor).





Peak	Retention time (min)	Area %
1	8.765	84.590
2	9.736	15.410

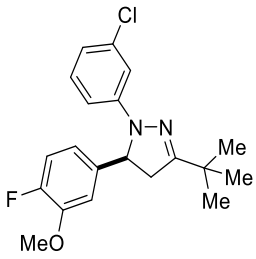
Racemic sample

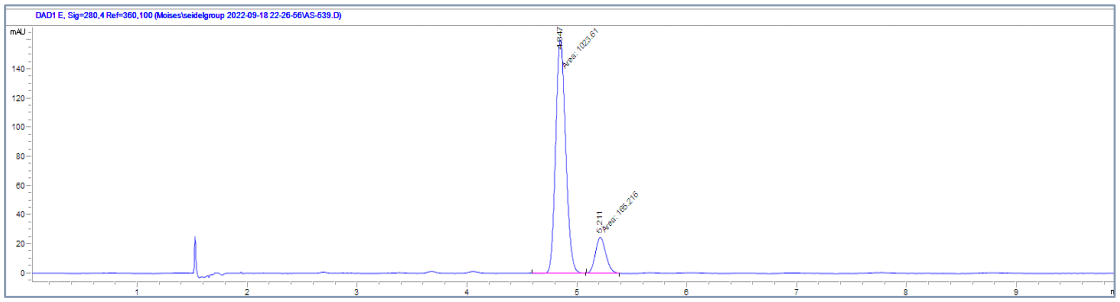


Peak	Retention time (min)	Area %
1	8.828	49.951
2	9.797	50.049

SFC Profile of **2s**

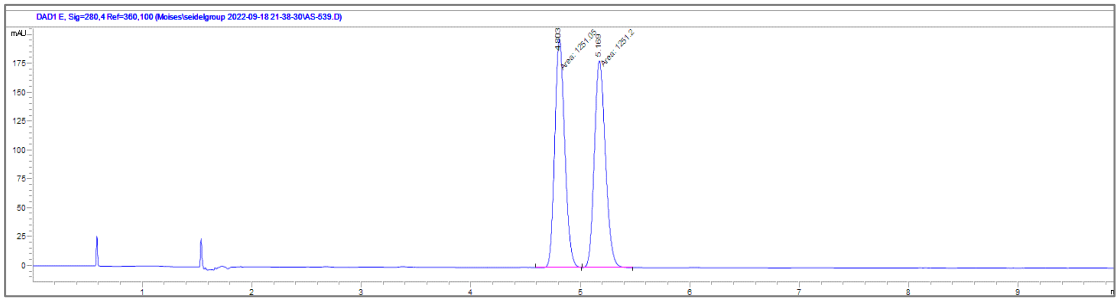
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 98/2, Flow rate = 2 mL/min, UV = 280 nm, t_R = 4.8 min (major) and t_R = 5.2 min (minor).





Peak	Retention time (min)	Area %
1	4.847	86.103
2	5.211	13.897

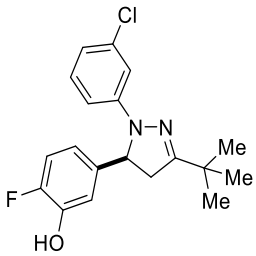
Racemic sample

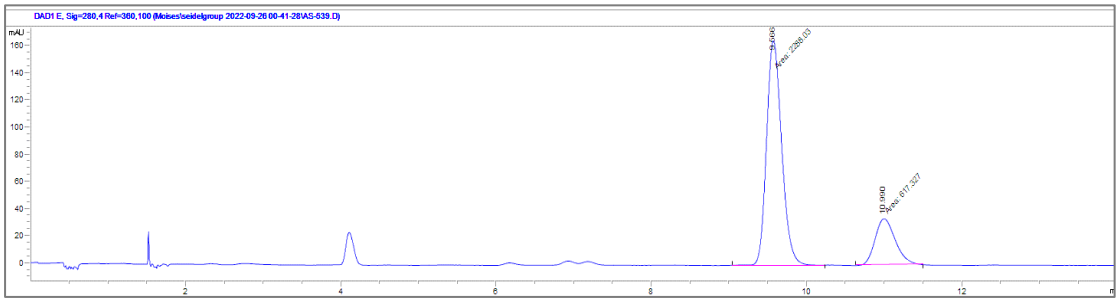


Peak	Retention time (min)	Area %
1	4.803	49.997
2	5.169	50.003

SFC Profile of **2t**

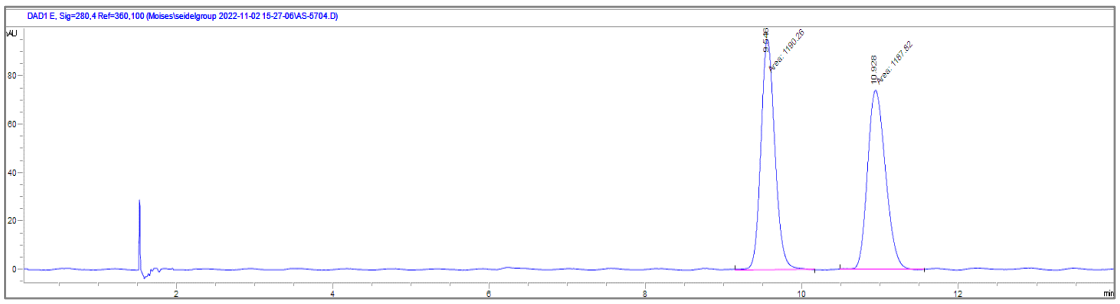
Conditions: Daicel Chiralcel OJ-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 280 nm, t_R = 9.6 min (major) and t_R = 11.0 min (minor).





Peak	Retention time (min)	Area %
1	9.566	80.621
2	10.99	19.379

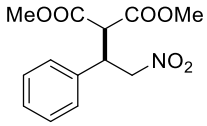
Racemic sample

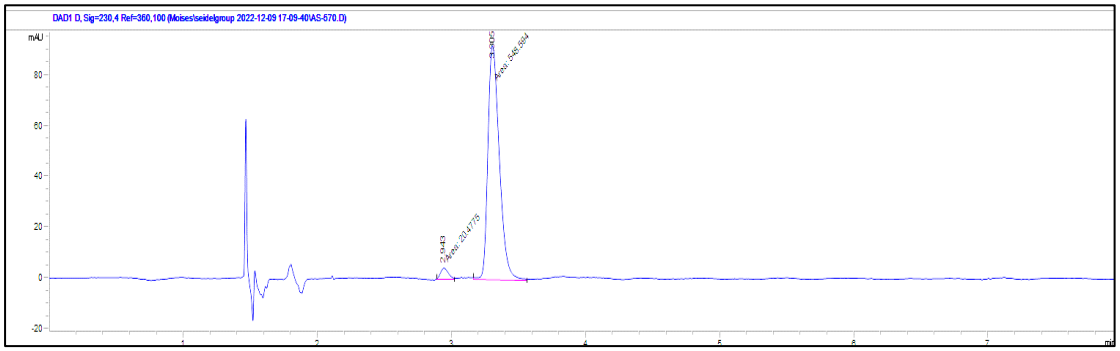


Peak	Retention time (min)	Area %
1	9.546	50.051
2	10.928	49.949

SFC Profile of **4**

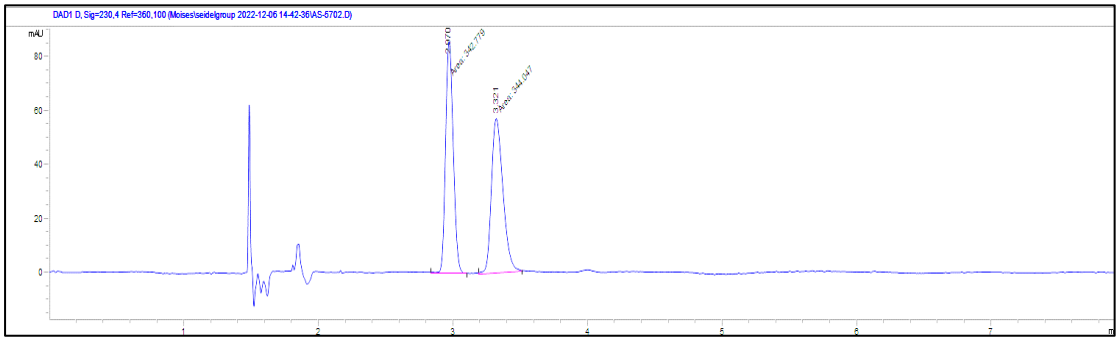
Conditions: Daicel Chiralcel AD-H, column temperature = 40 °C, CO_2/MeOH = 90/10, Flow rate = 2 mL/min, UV = 230 nm, t_R = 3.3 min (major) and t_R = 2.9 min (minor).





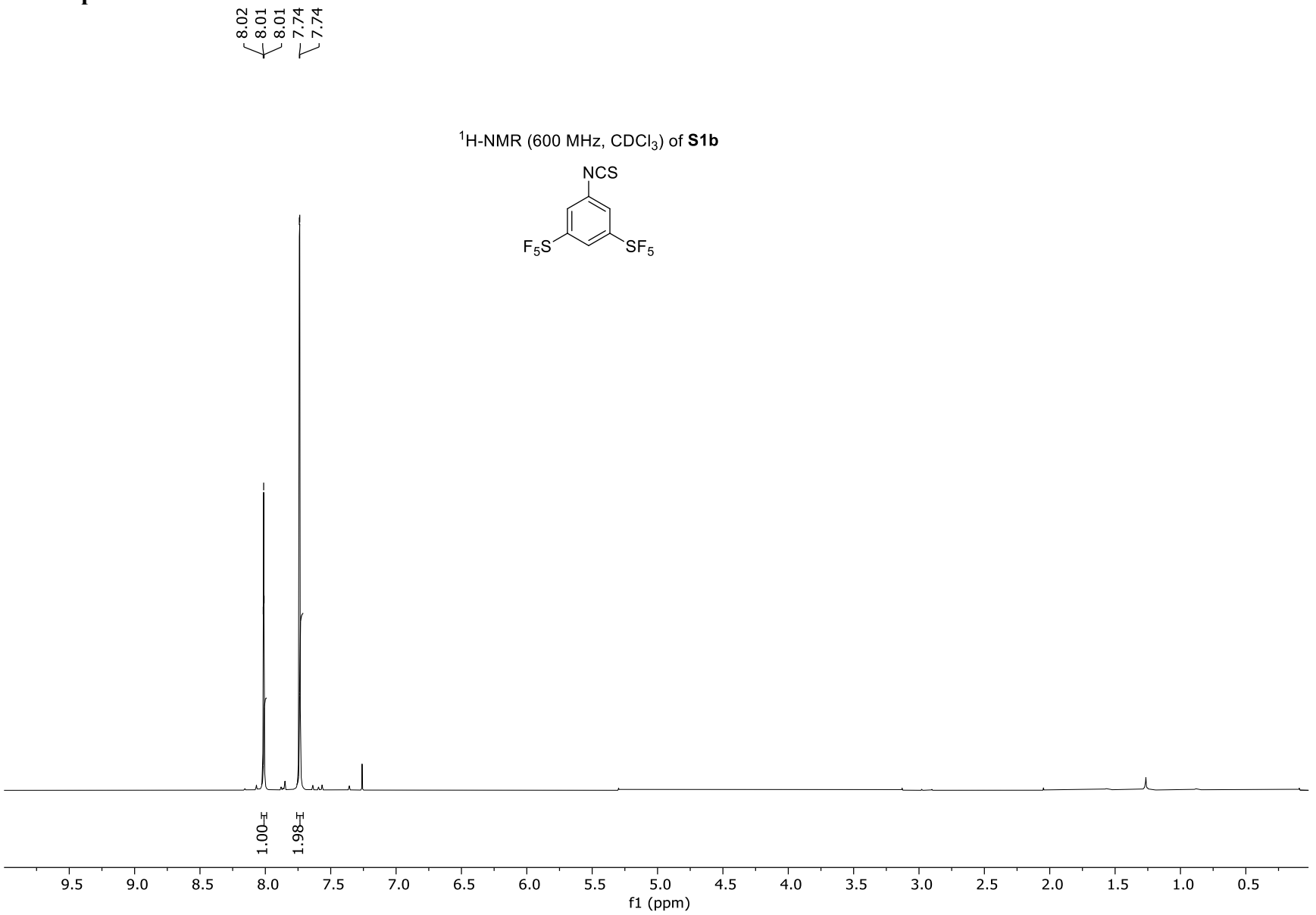
Peak	Retention time (min)	Area %
1	2.943	2.924
2	3.305	97.076

Racemic sample



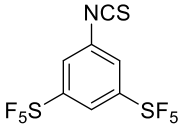
Peak	Retention time (min)	Area %
1	2.97	49.908
2	3.321	50.092

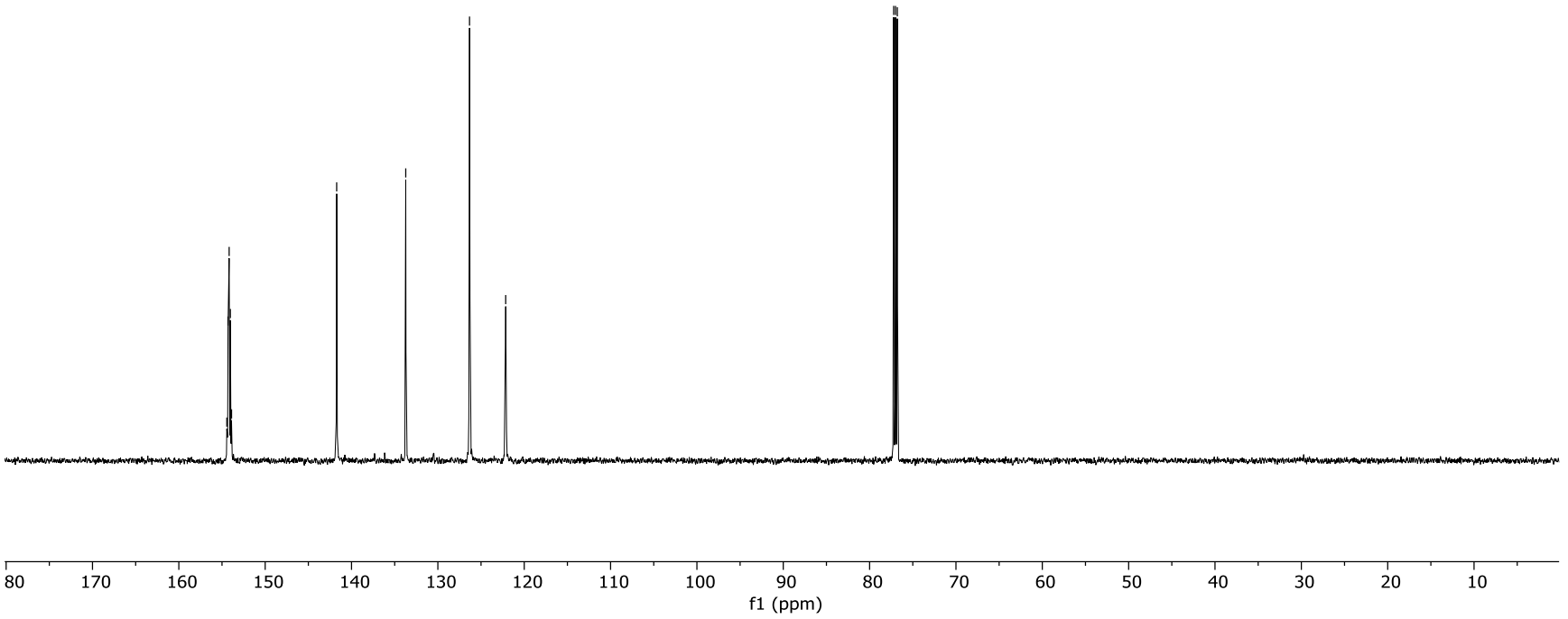
NMR Spectra


8.02
8.01
8.01
7.74
7.74
^{1}H-NMR (600 MHz, $CDCl_3$) of **S1b**
NCS
F_5S
SF_5
1.00
1.98
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)

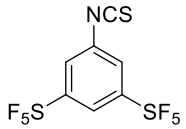
154.44
154.31
154.17
154.03
153.90
141.72
133.72
126.33
122.15
77.21
77.00
76.79

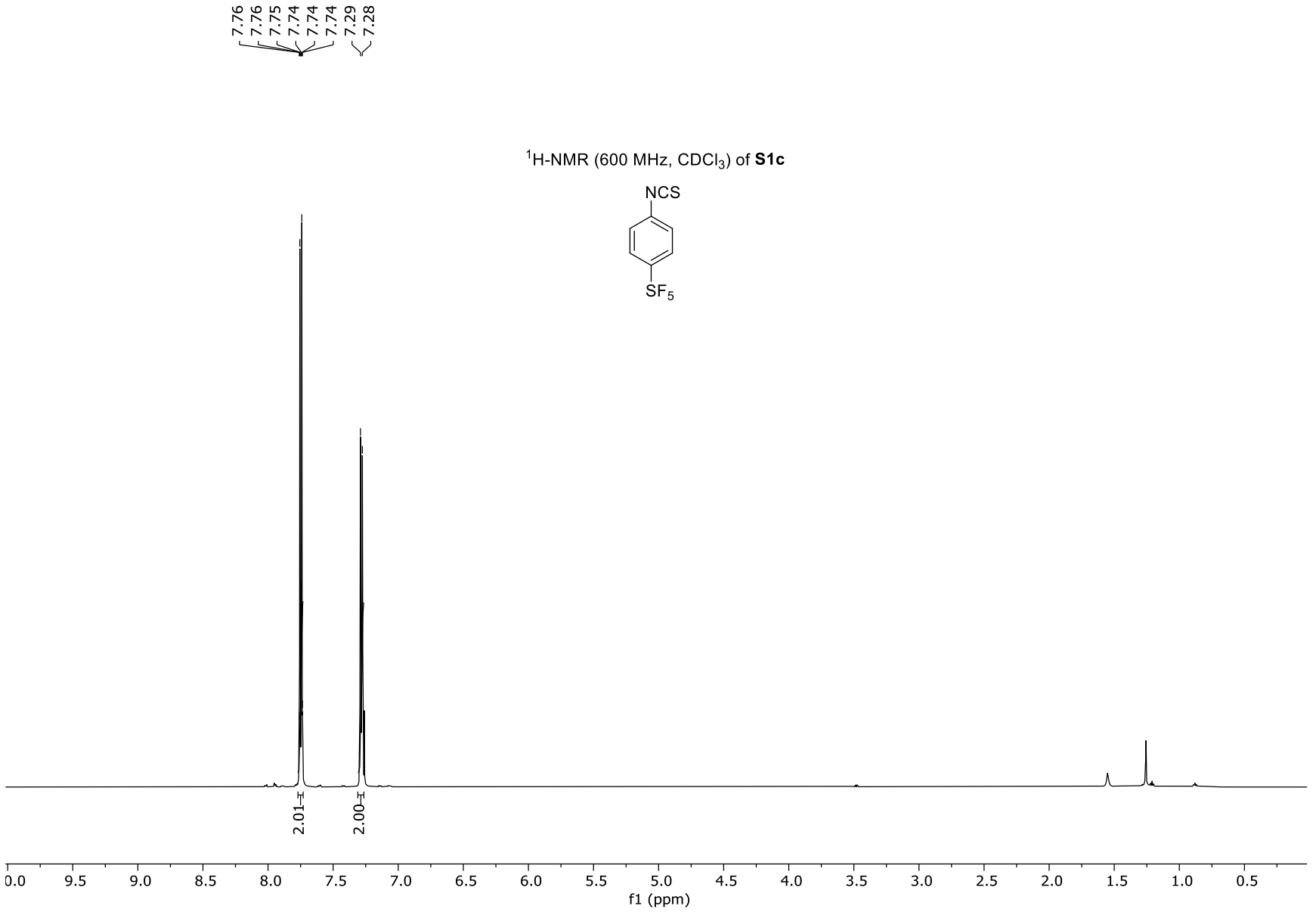
^{13}C-NMR (150 MHz, $CDCl_3$) of **S1b**

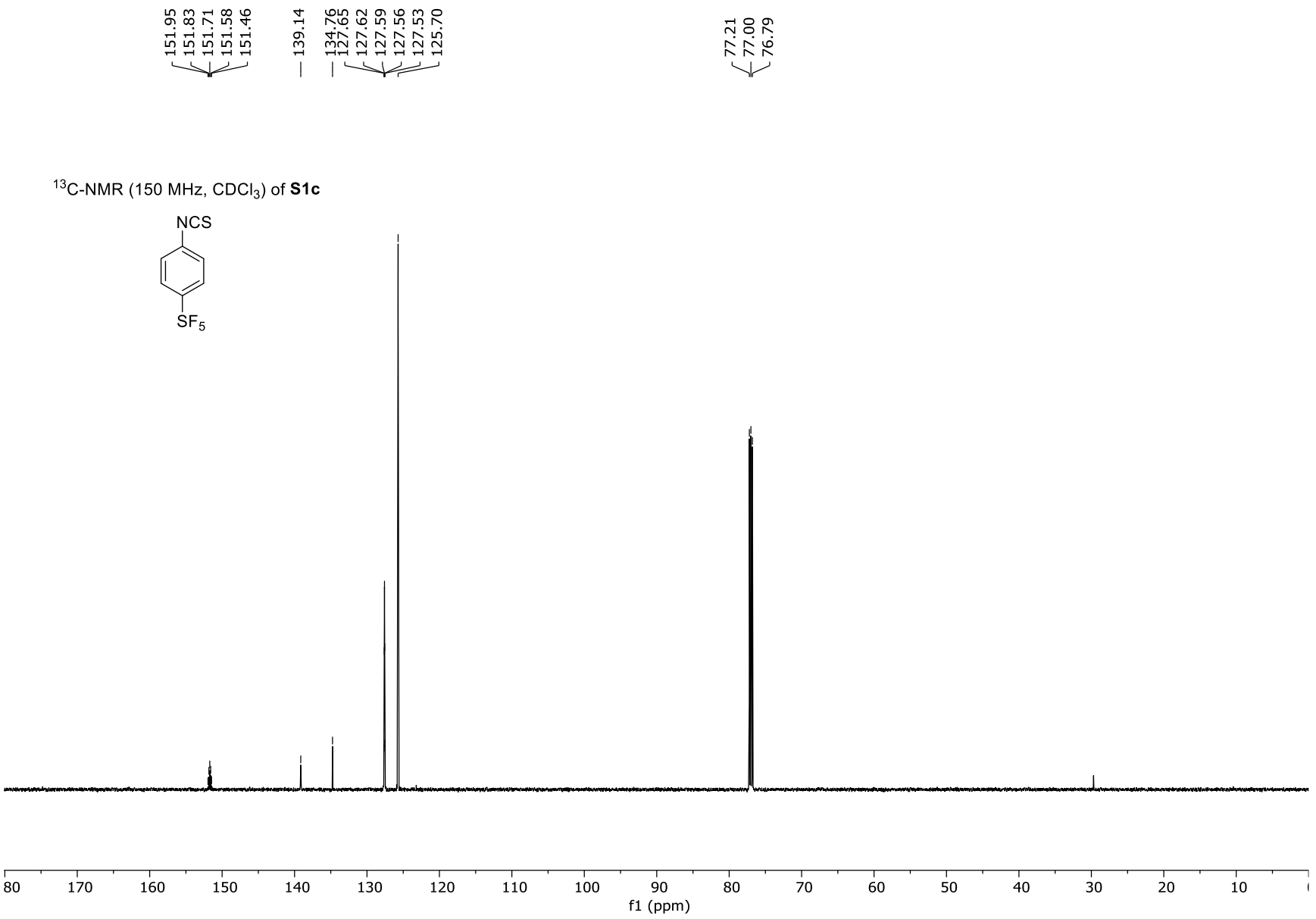




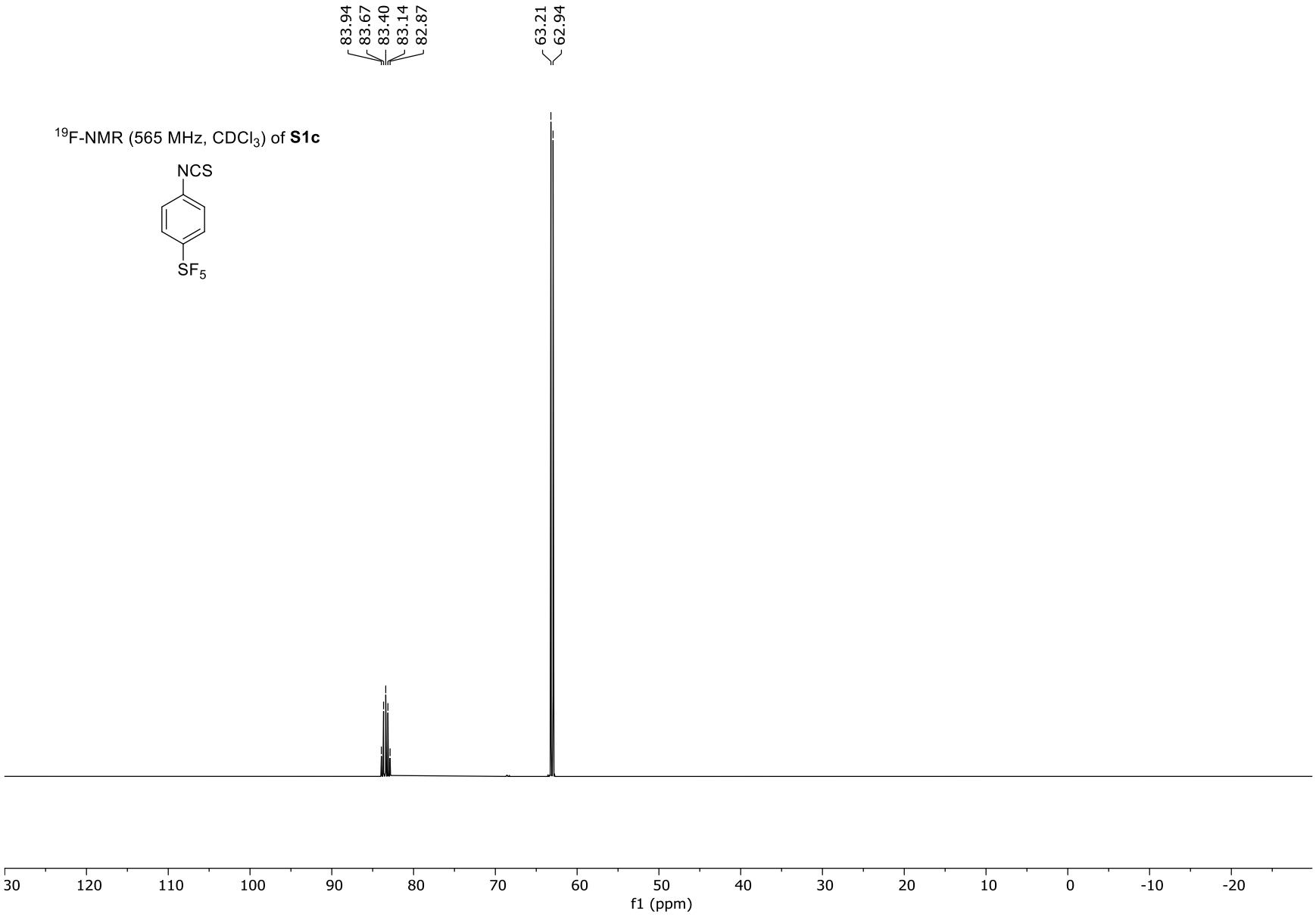
^{19}F-NMR (377 MHz, $CDCl_3$) of **S1b**

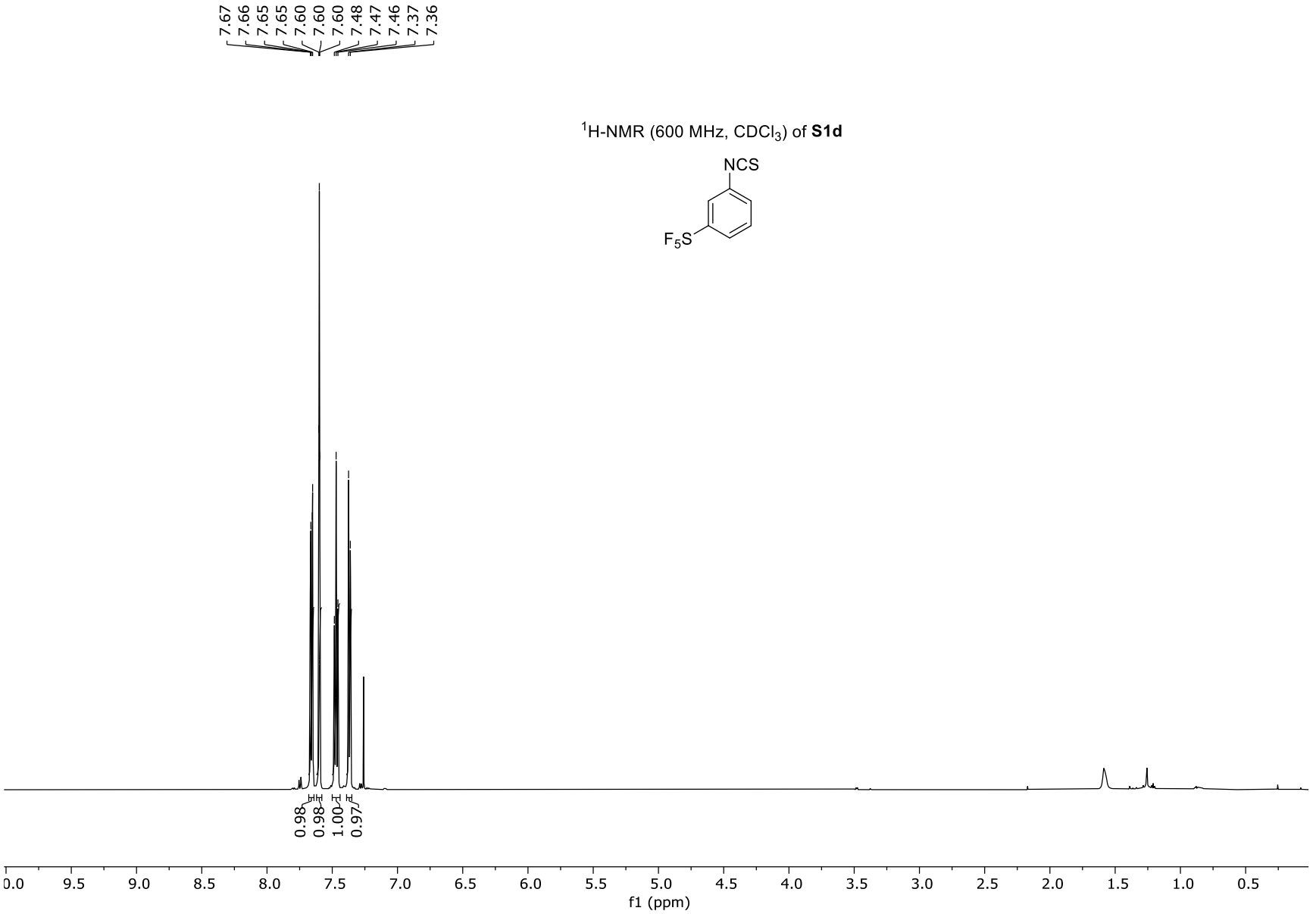


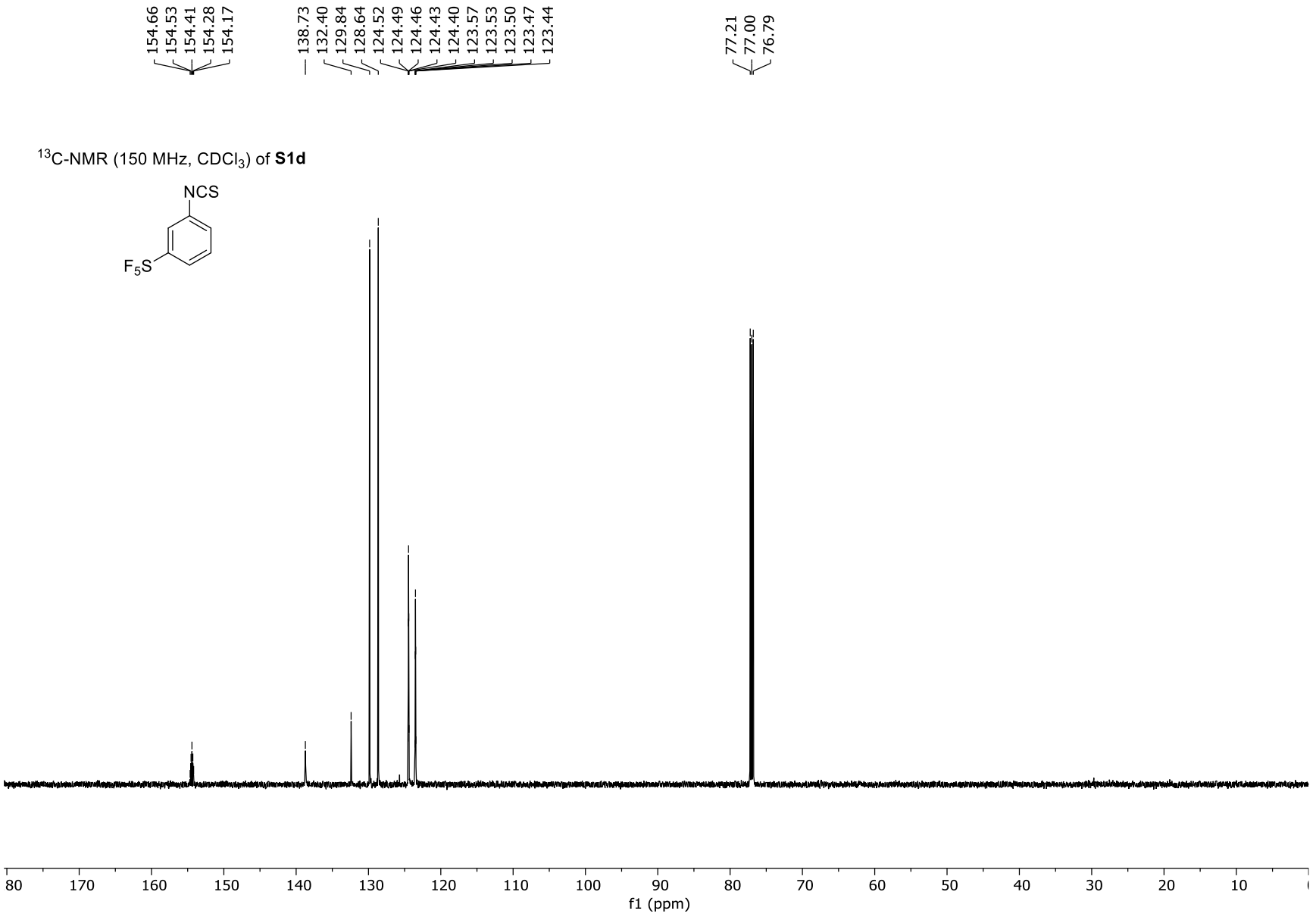

7.76
7.76
7.75
7.74
7.74
7.74
7.29
7.28
^{1}H-NMR (600 MHz, $CDCl_3$) of **S1c**
NCS
SF_5
2.01
2.00
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



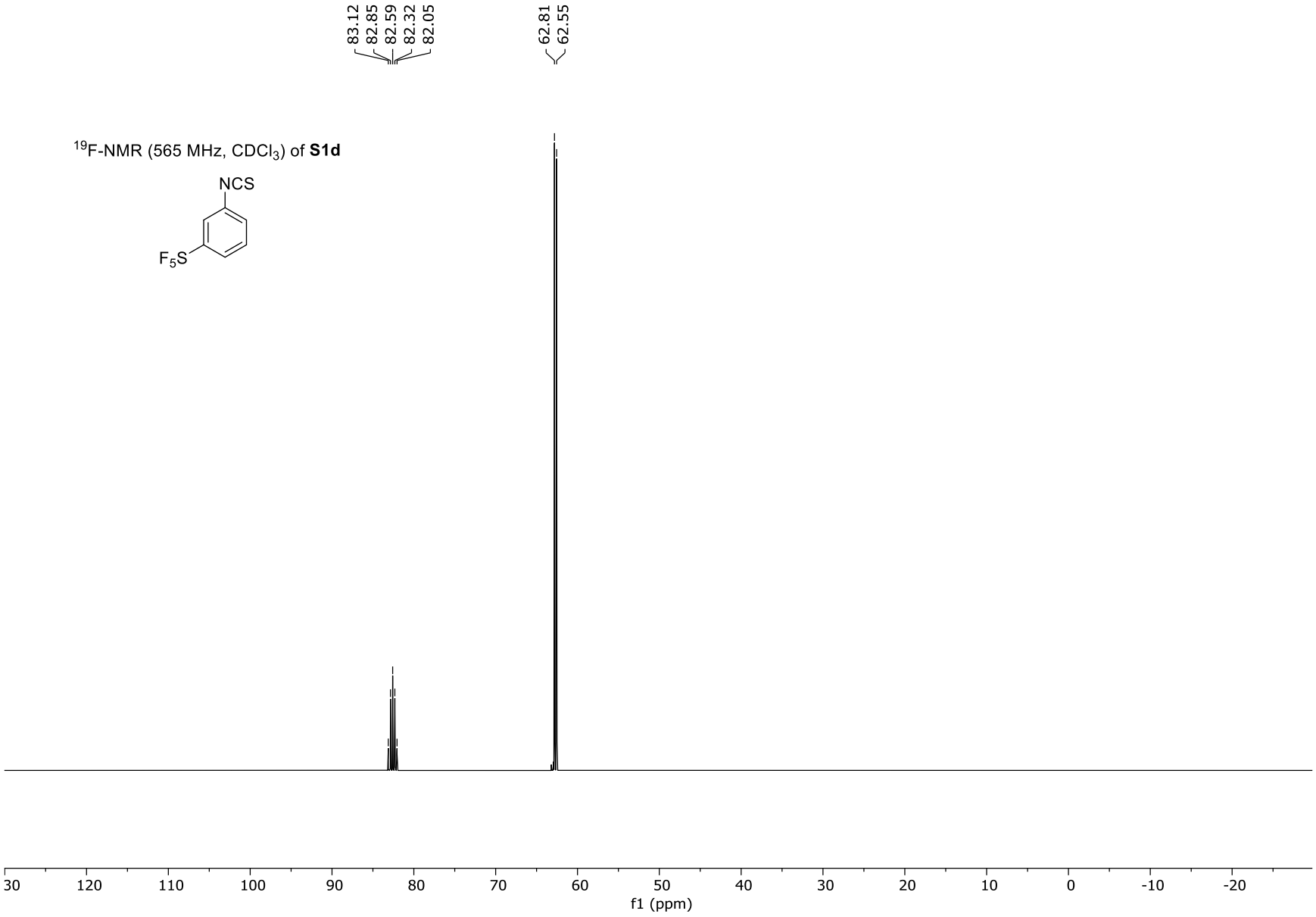
^{13}C-NMR (150 MHz, $CDCl_3$) of **S1c**

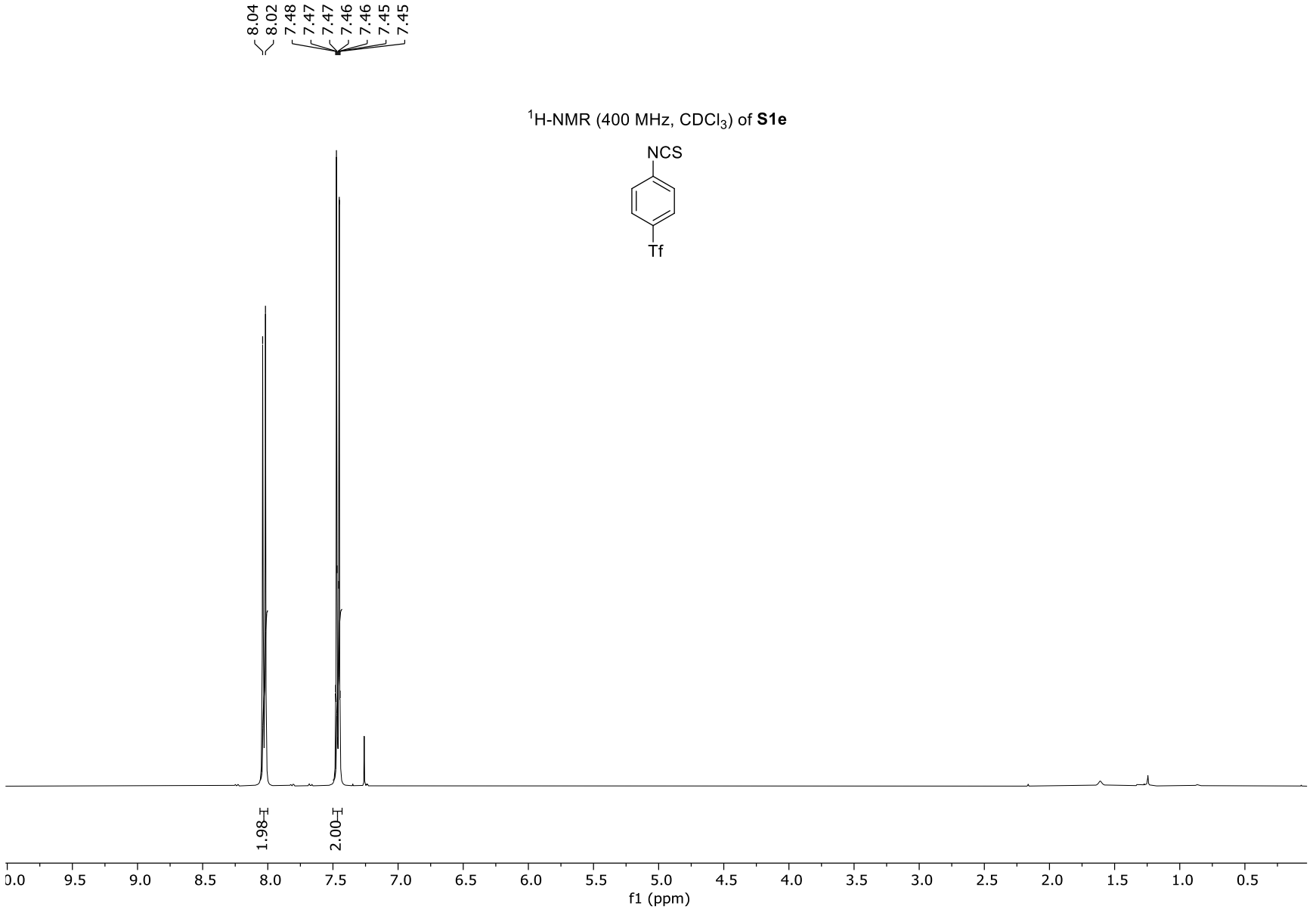

83.94
83.67
83.40
83.14
82.87
63.21
62.94
^{19}F-NMR (565 MHz, $CDCl_3$) of **S1c**
NCS
SF_5
30
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


7.67
7.66
7.65
7.65
7.60
7.60
7.60
7.48
7.47
7.46
7.37
7.36
^{1}H-NMR (600 MHz, $CDCl_3$) of **S1d**
NCS
F_5S
0.98
0.98
1.00
0.97
0.0
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
f1 (ppm)

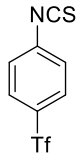


^{13}C-NMR (150 MHz, $CDCl_3$) of **S1d**

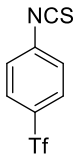

83.12
82.85
82.59
82.32
82.05
62.81
62.55
19F-NMR (565 MHz, CDCl3) of S1d
NCS
F5S
30
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

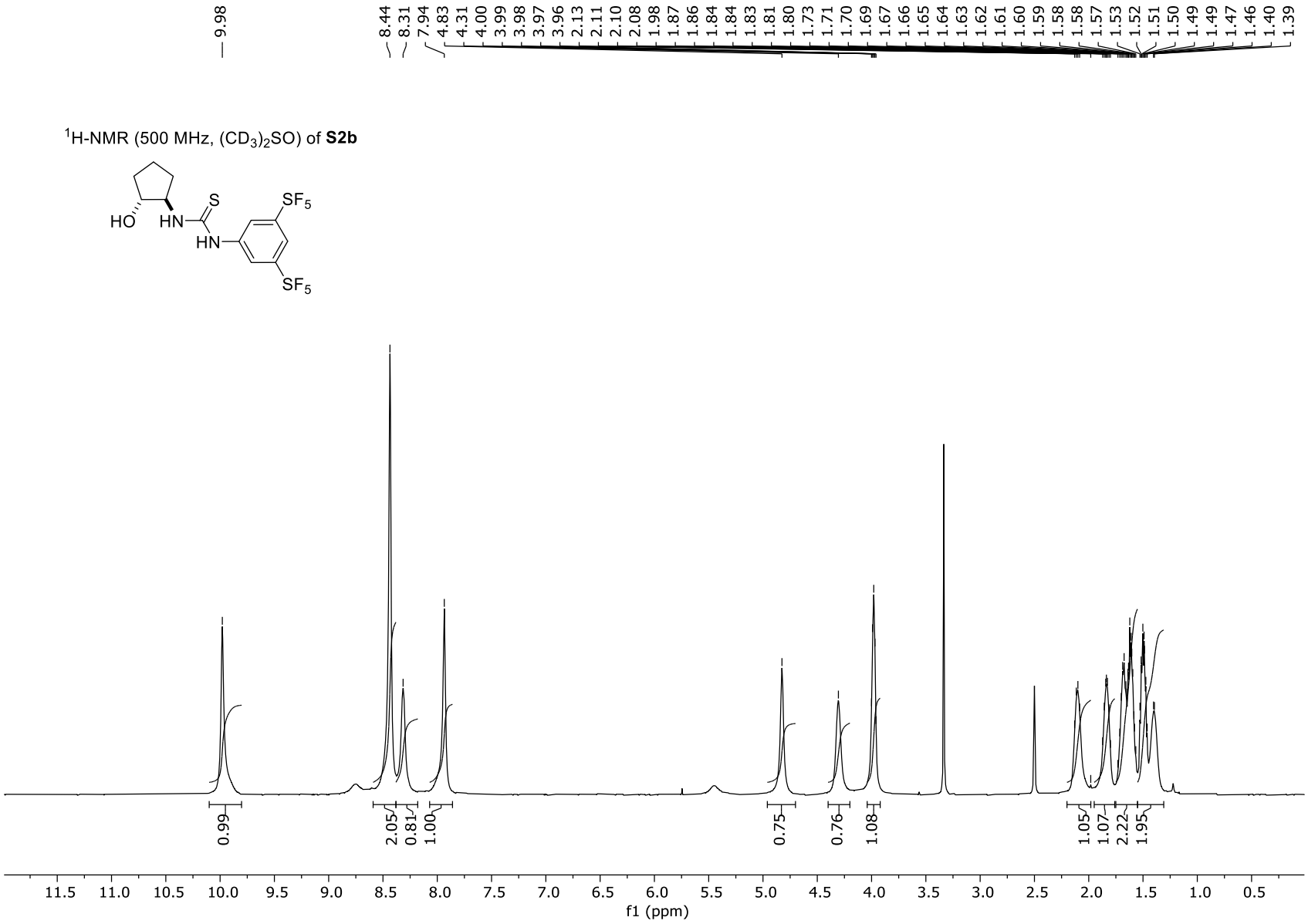

8.04
8.02
7.48
7.47
7.47
7.46
7.46
7.45
7.45
^{1}H-NMR (400 MHz, $CDCl_3$) of **S1e**
NCS
Tf
1.98
2.00
f1 (ppm)

^{13}C-NMR (150 MHz, $CDCl_3$) of **S1e**

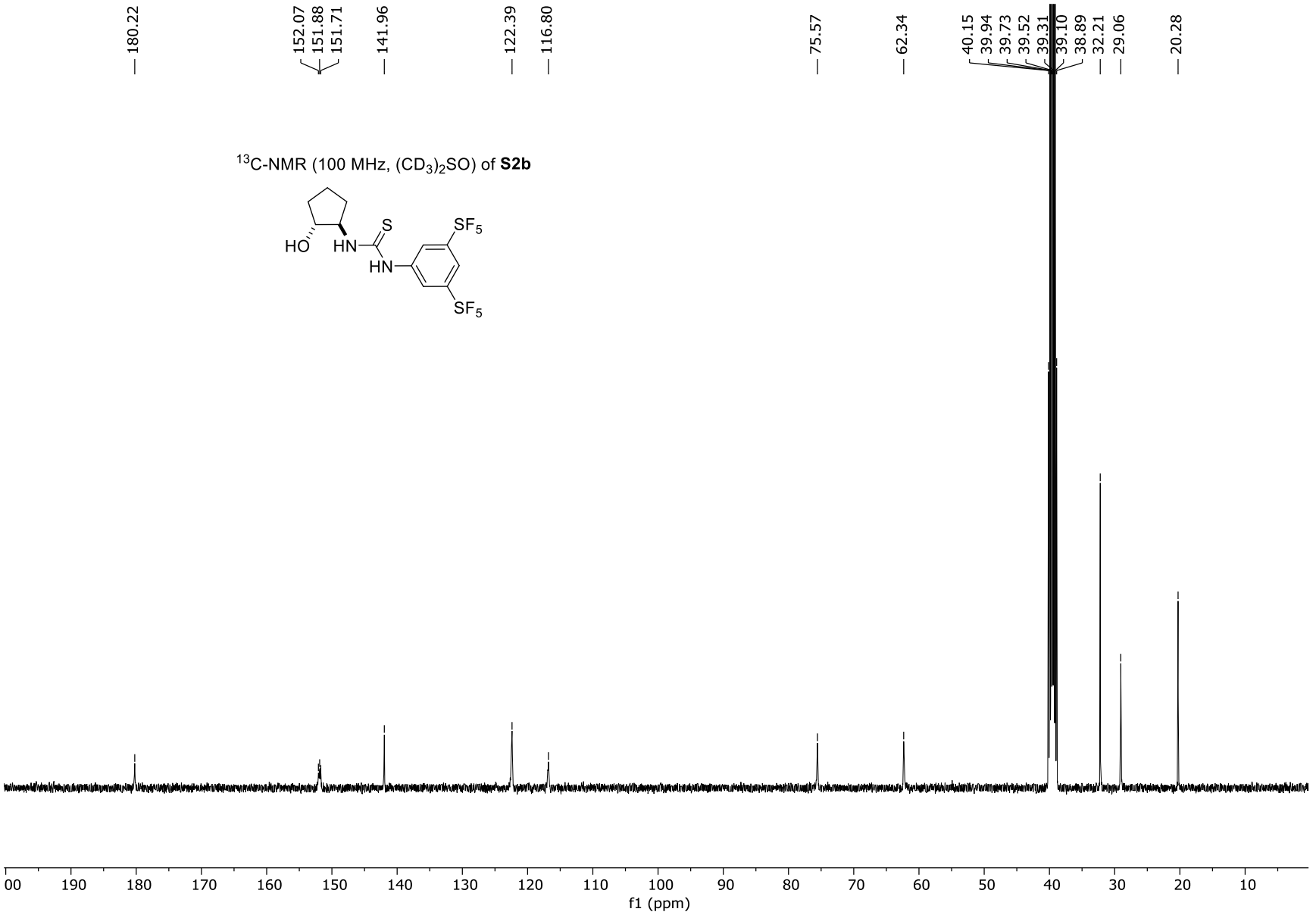


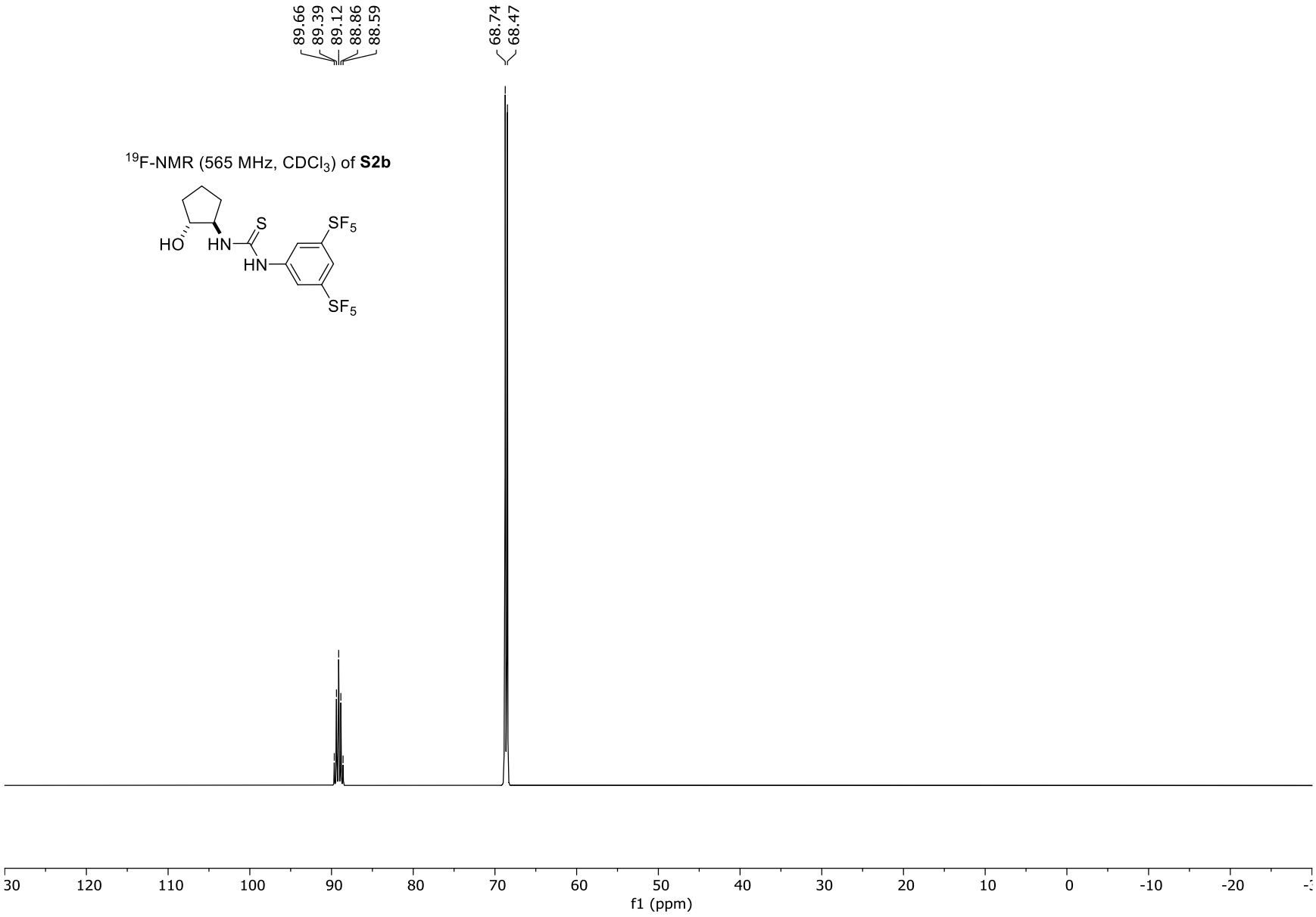
^{19}F-NMR (565 MHz, $CDCl_3$) of **S1e**

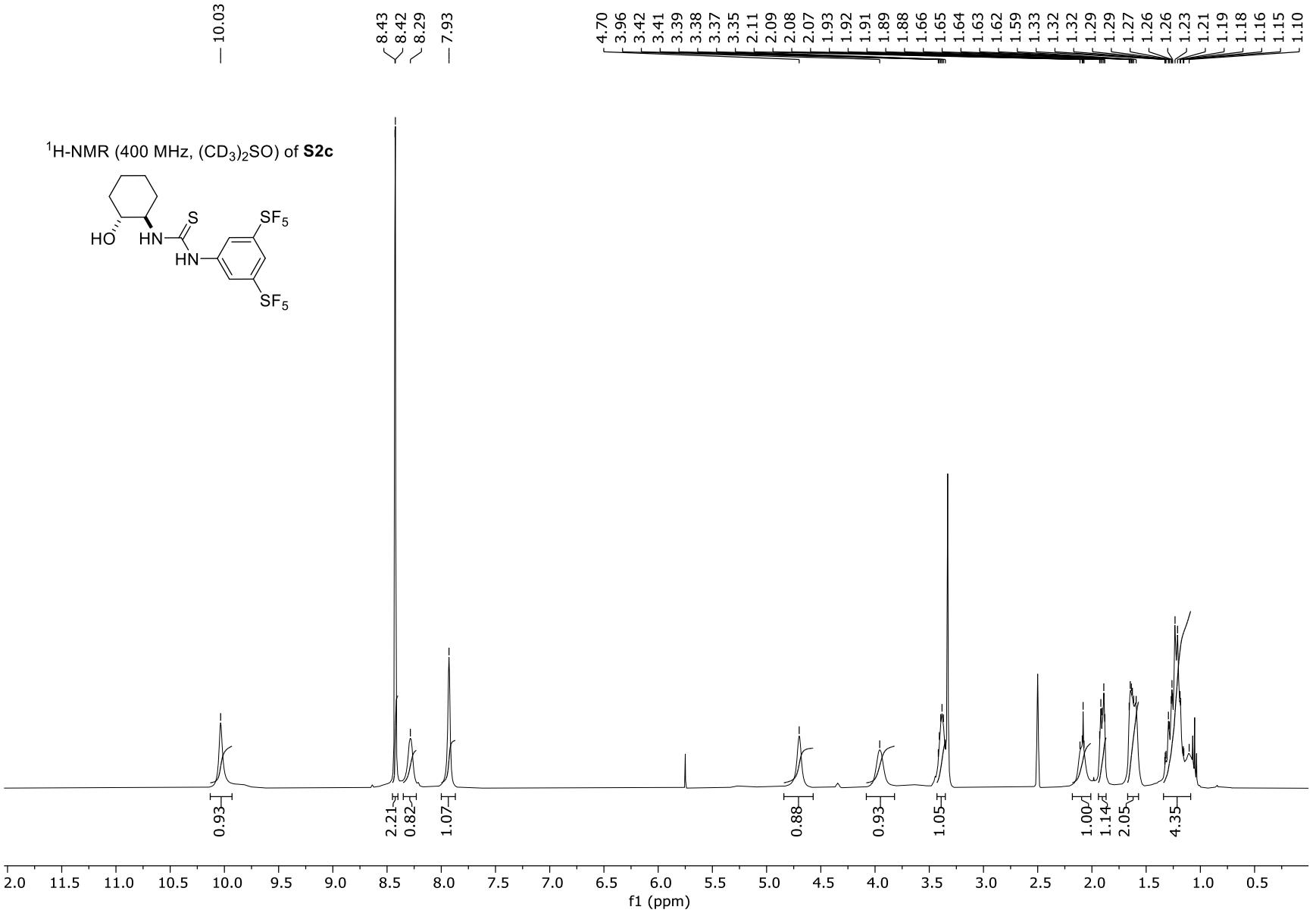


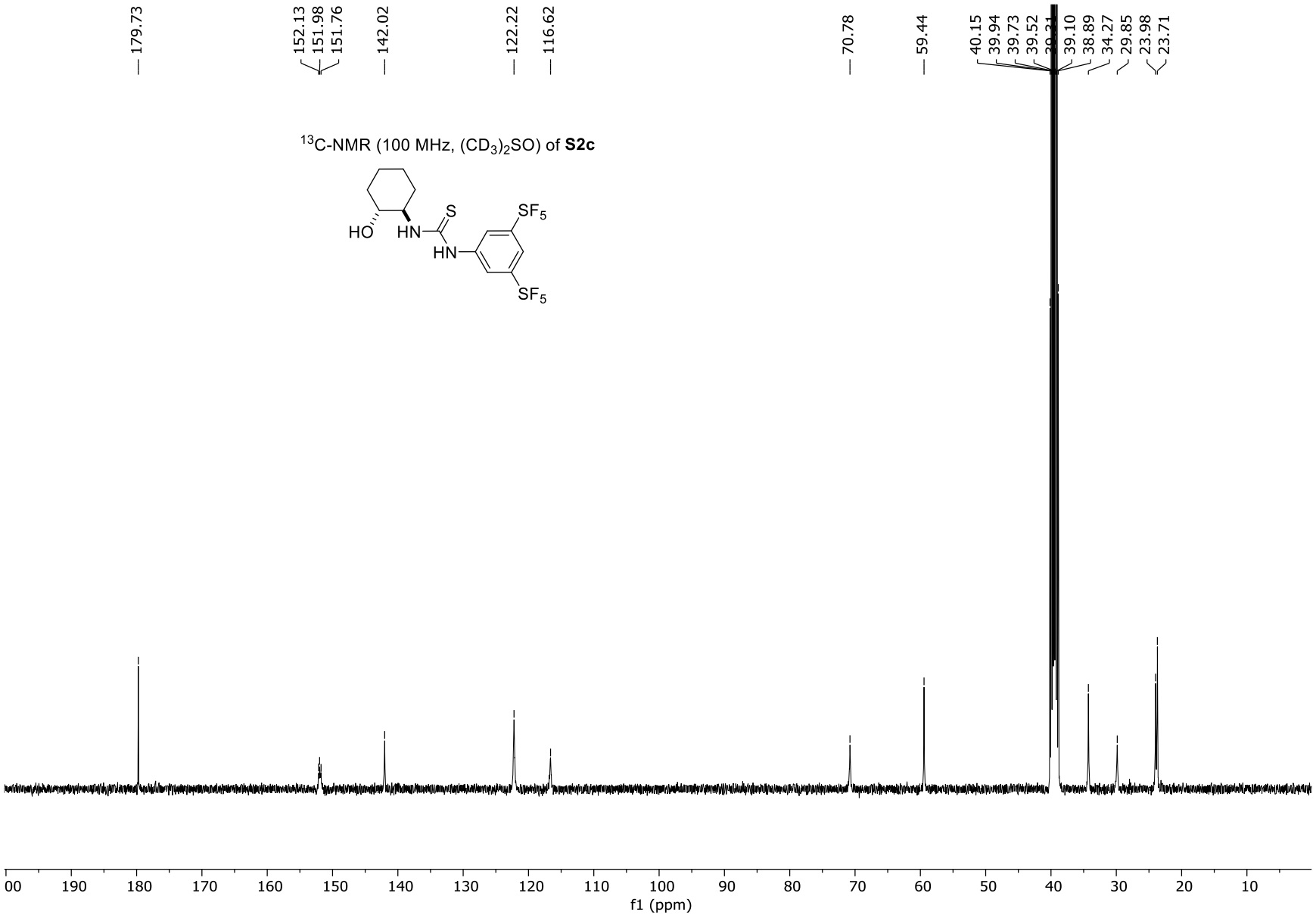


^{1}H-NMR (500 MHz, $(CD_3)_2SO$) of **S2b**

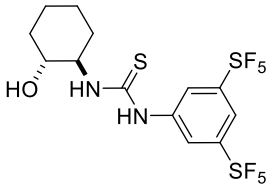

180.22
152.07
151.88
151.71
141.96
122.39
116.80
75.57
62.34
40.15
39.94
39.73
39.52
39.31
39.10
38.89
32.21
29.06
20.28
13C-NMR (100 MHz, (CD3)2SO) of S2b
HO
HN
S
HN
SF5
SF5
f1 (ppm)

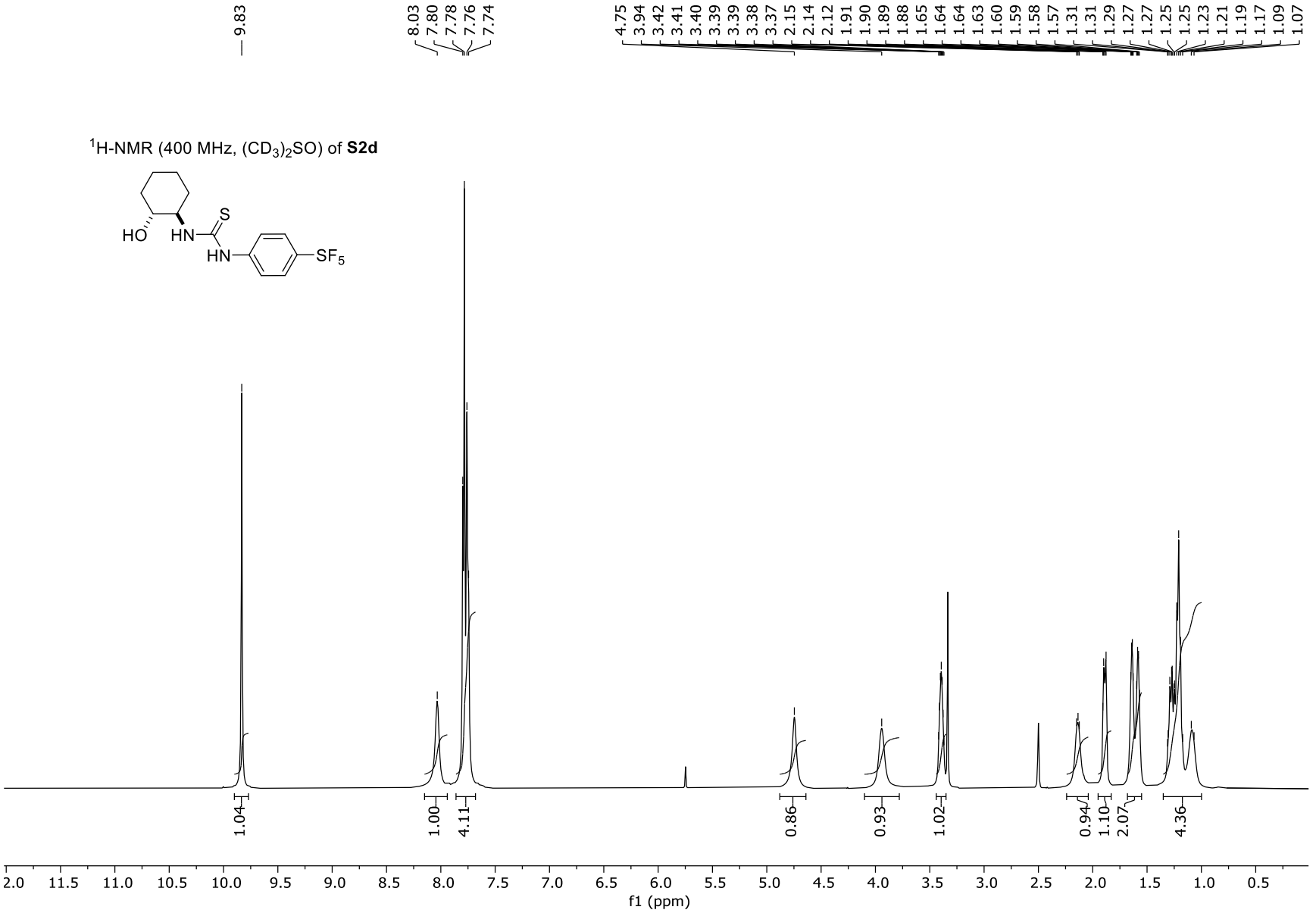

89.66
89.39
89.12
88.86
88.59
68.74
68.47
^{19}F-NMR (565 MHz, $CDCl_3$) of **S2b**
HO
HN
S
HN
SF_5
SF_5
30
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

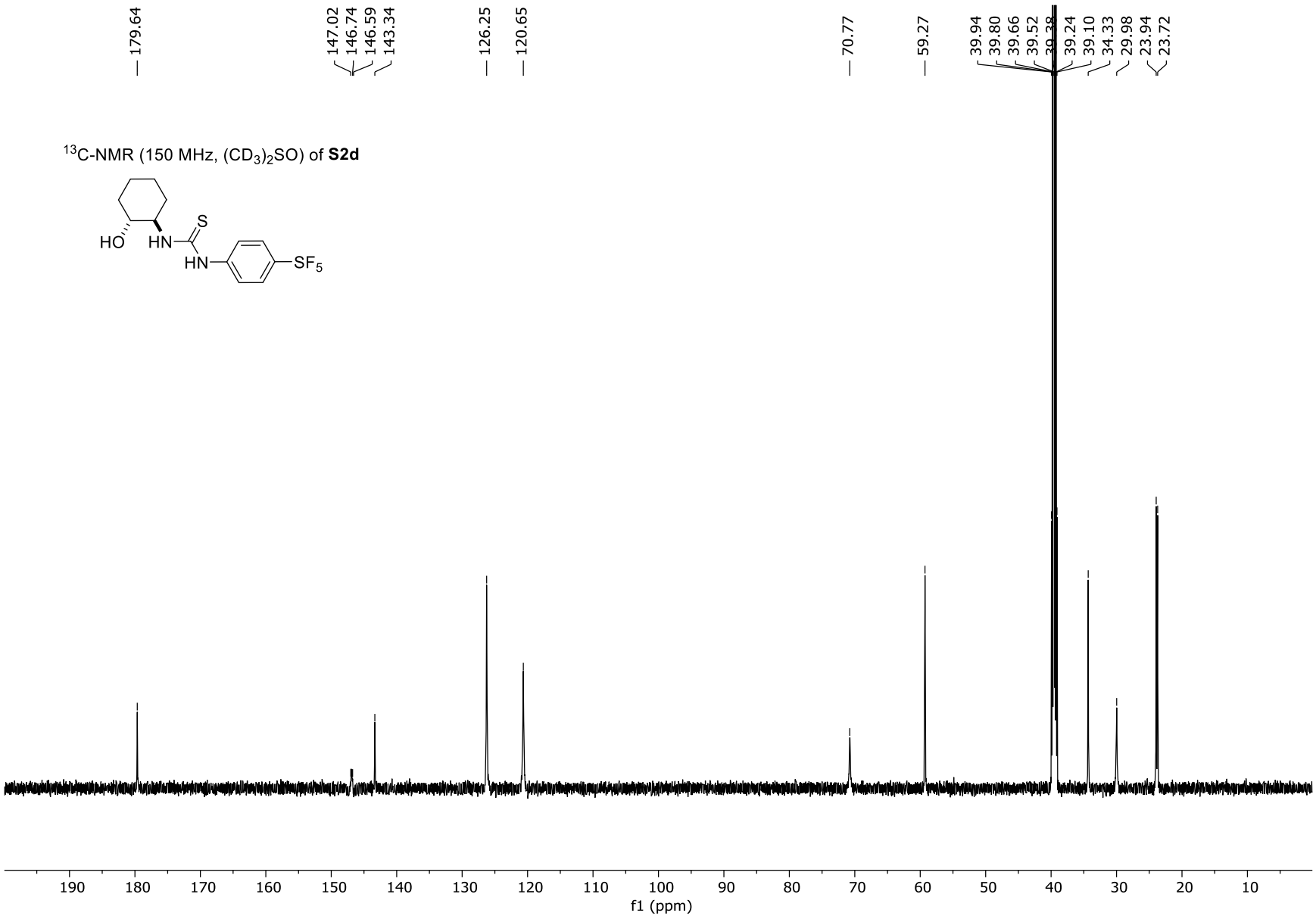

10.03
8.43
8.42
8.29
7.93
4.70
3.96
3.42
3.41
3.39
3.38
3.37
3.35
2.11
2.09
2.08
2.07
1.93
1.92
1.91
1.89
1.88
1.66
1.65
1.64
1.63
1.62
1.59
1.33
1.32
1.32
1.29
1.29
1.27
1.26
1.26
1.23
1.21
1.19
1.18
1.16
1.15
1.10
^{1}H-NMR (400 MHz, $(CD_3)_2SO$) of **S2c**
HO
HN
S
HN
SF_5
SF_5
0.93
2.21
0.82
1.07
0.88
0.93
1.05
1.00
1.14
2.05
4.35
2.0
11.5
11.0
10.5
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
f1 (ppm)


179.73
152.13
151.98
151.76
142.02
122.22
116.62
70.78
59.44
40.15
39.94
39.73
39.52
39.31
39.10
38.89
34.27
29.85
23.98
23.71
13C-NMR (100 MHz, (CD3)2SO) of S2c
HO
HN
S
HN
SF5
SF5
f1 (ppm)

^{19}F-NMR (377 MHz, $(CD_3)_2SO$) of **S2c**

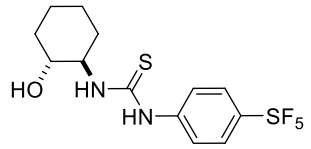



9.83
8.03
7.80
7.78
7.76
7.74
4.75
3.94
3.42
3.41
3.40
3.39
3.39
3.38
3.37
2.15
2.14
2.12
1.91
1.90
1.89
1.88
1.65
1.64
1.64
1.63
1.60
1.59
1.58
1.57
1.31
1.31
1.29
1.27
1.27
1.25
1.25
1.23
1.21
1.19
1.17
1.09
1.07
1H-NMR (400 MHz, (CD3)2SO) of S2d
HO
HN
S
HN
SF5
1.04
1.00
4.11
0.86
0.93
1.02
0.94
1.10
2.07
4.36
2.0
11.5
11.0
10.5
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
f1 (ppm)

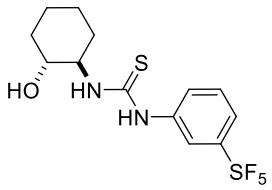


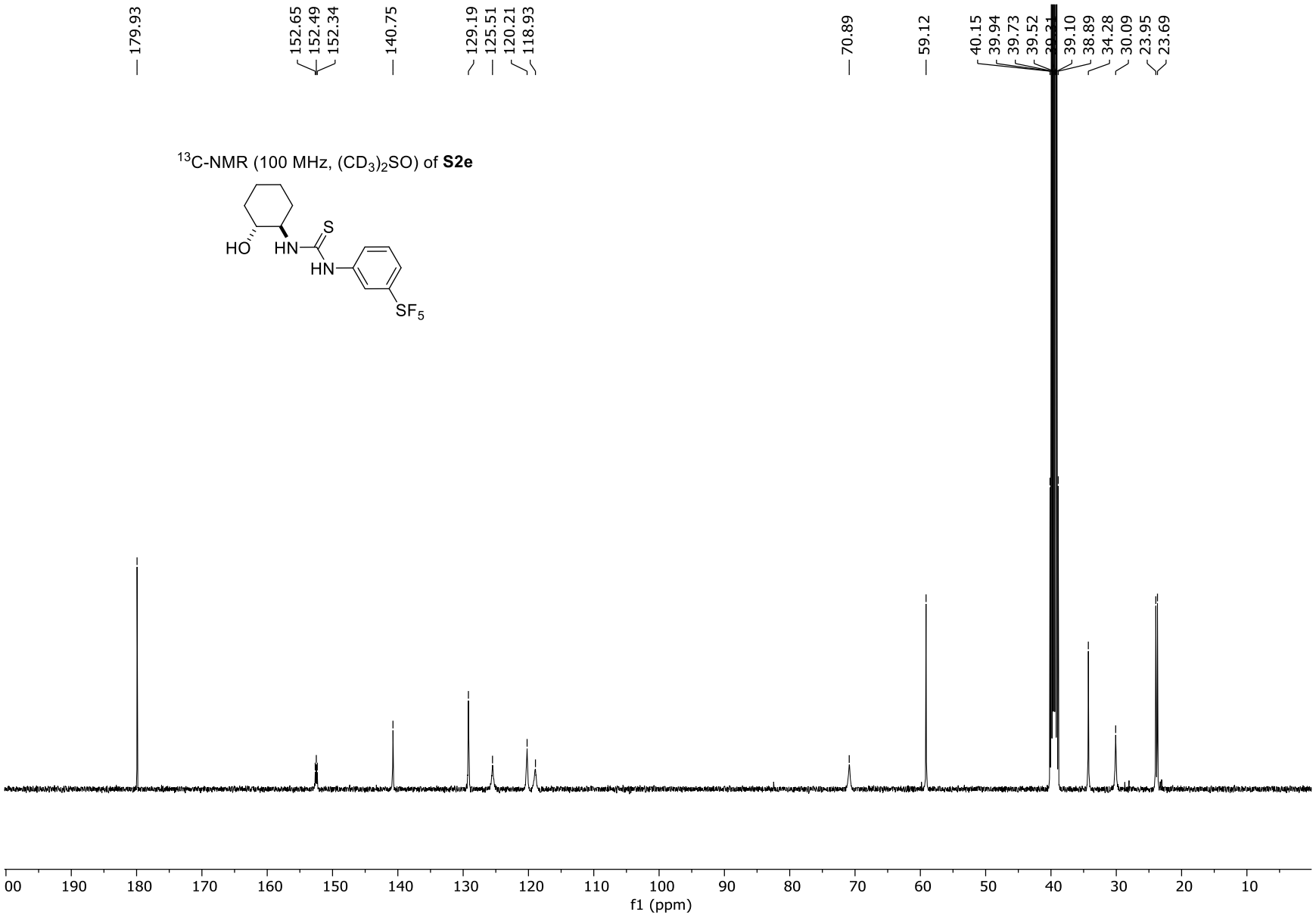
^{13}C-NMR (150 MHz, $(CD_3)_2SO$) of **S2d**

^{19}F-NMR (565 MHz, $(CD_3)_2SO$) of **S2d**

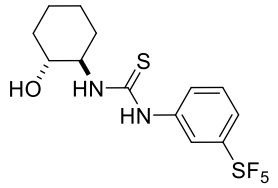


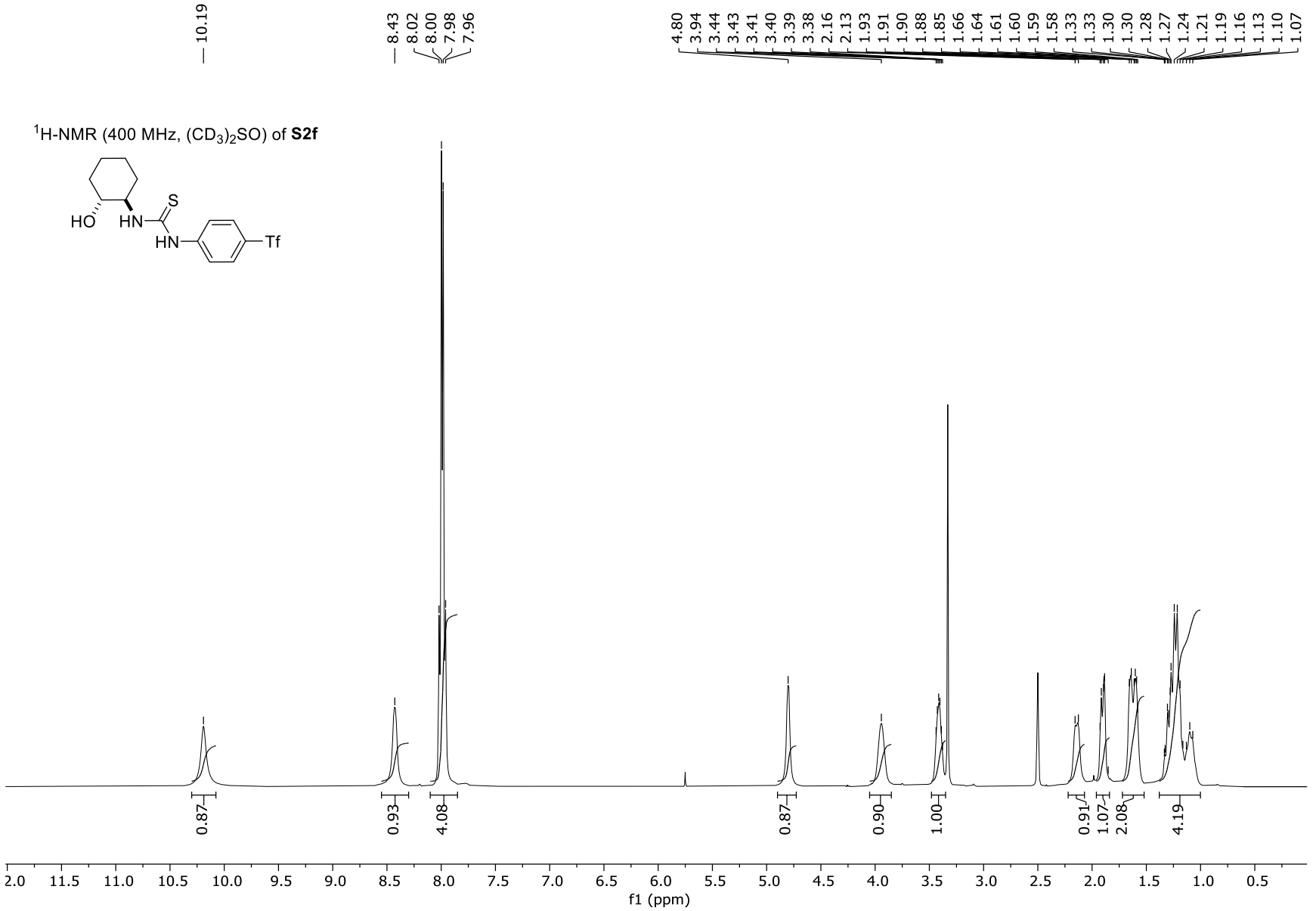
^{1}H-NMR (400 MHz, $(CD_3)_2SO$) of **S2e**

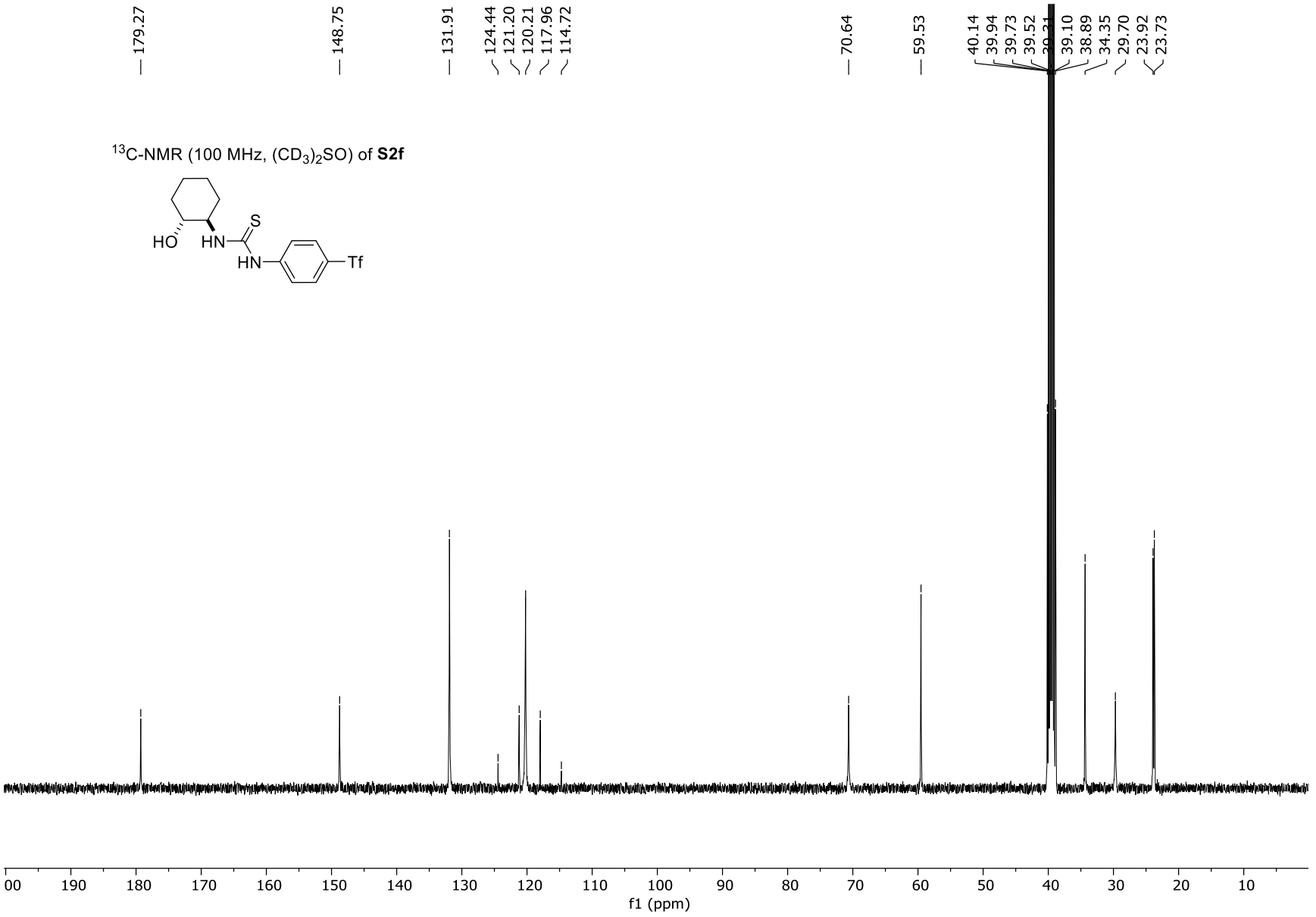



179.93
152.65
152.49
152.34
140.75
129.19
125.51
120.21
118.93
70.89
59.12
40.15
39.94
39.73
39.52
39.31
39.10
38.89
34.28
30.09
23.95
23.69
^{13}C-NMR (100 MHz, $(CD_3)_2SO$) of **S2e**
HO
HN
S
HN
SF_5
f1 (ppm)

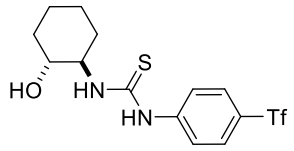
^{19}F-NMR (565 MHz, $(CD_3)_2SO$) of **S2e**

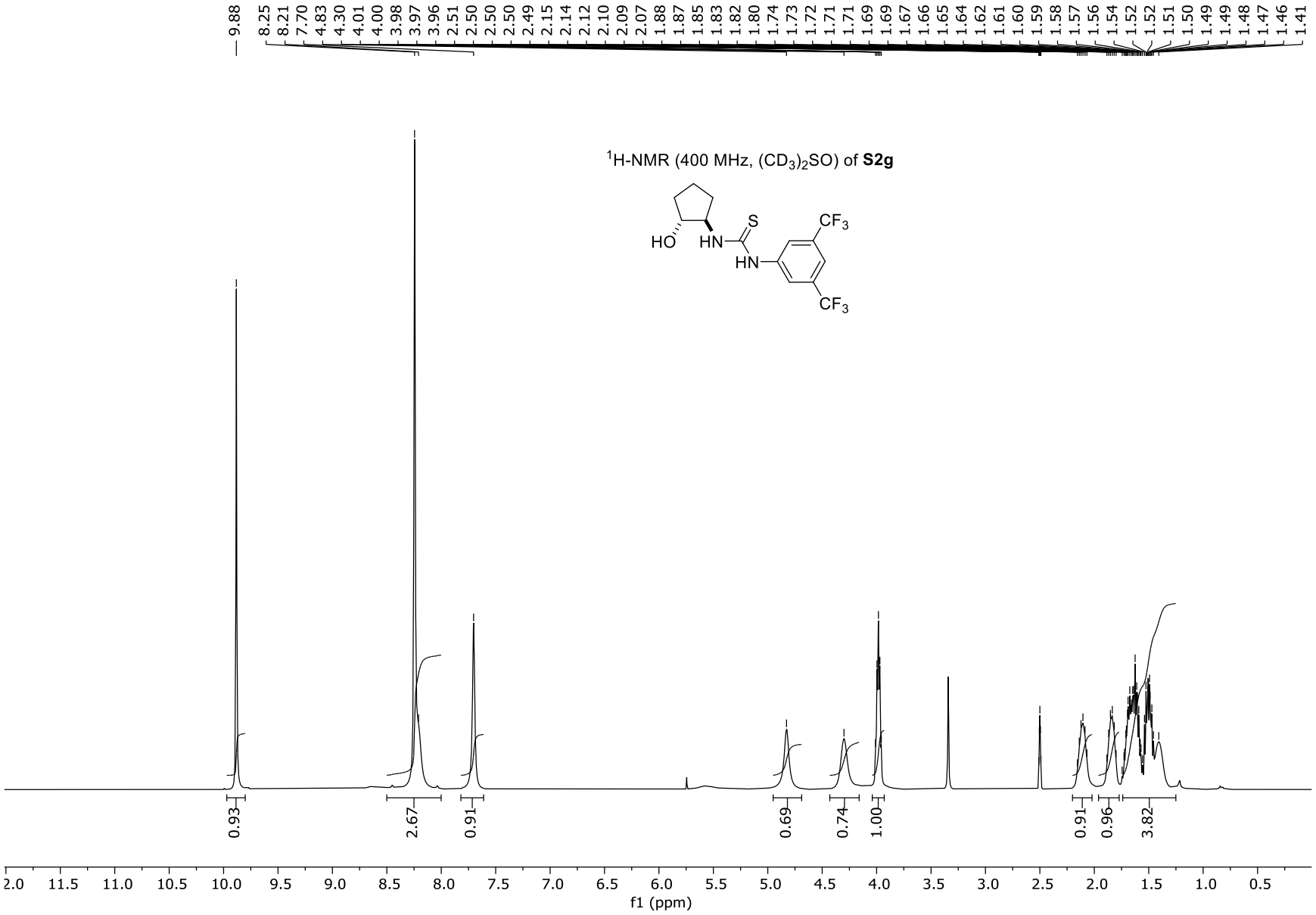


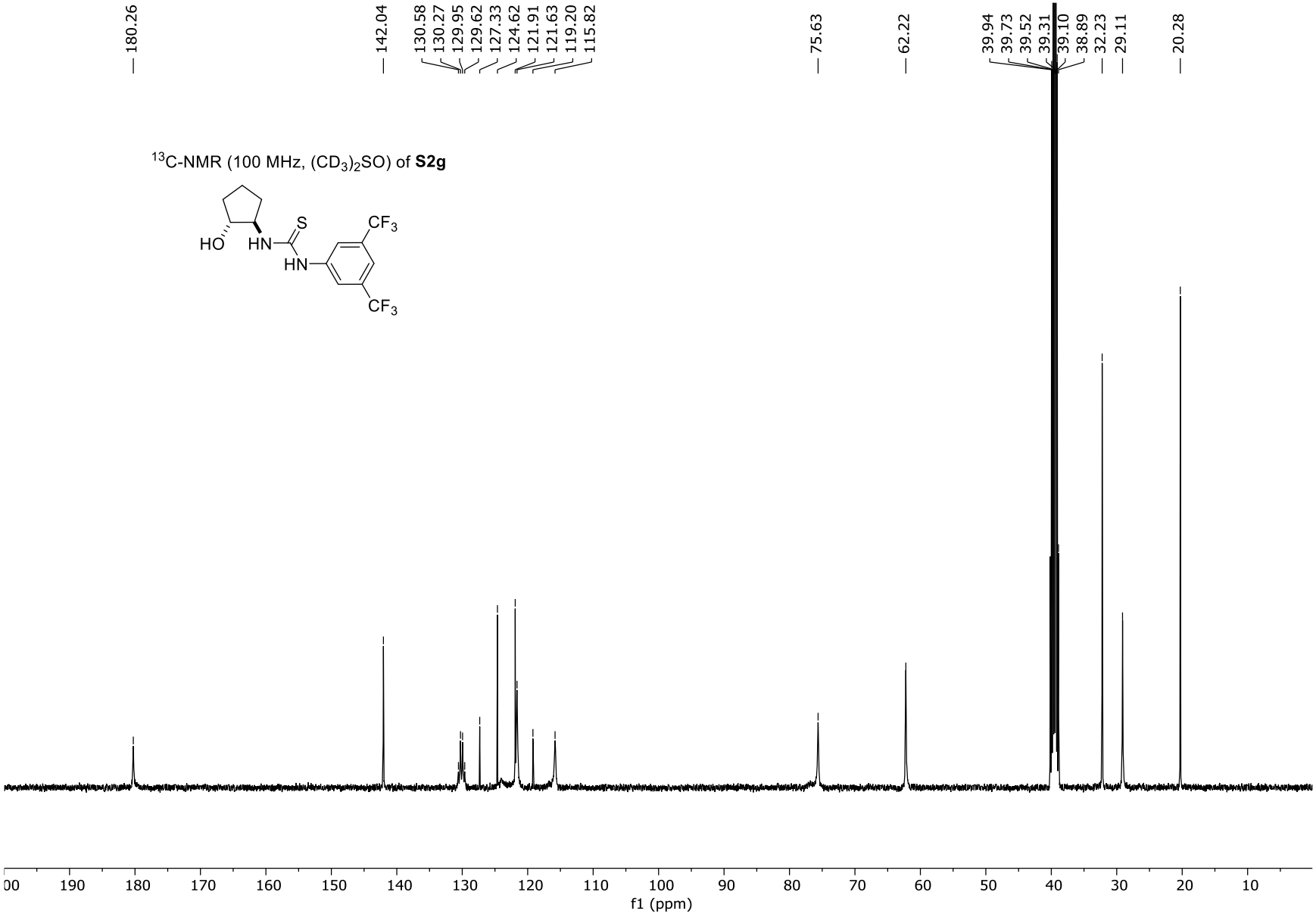

10.19
8.43
8.02
8.00
7.98
7.96
4.80
3.94
3.44
3.43
3.41
3.40
3.39
3.38
2.16
2.13
1.93
1.91
1.90
1.88
1.85
1.66
1.64
1.61
1.60
1.59
1.58
1.33
1.30
1.30
1.28
1.27
1.24
1.21
1.19
1.16
1.13
1.10
1.07
^{1}H-NMR (400 MHz, $(CD_3)_2SO$) of **S2f**
HO
HN
S
HN
Tf
0.87
0.93
4.08
0.87
0.90
1.00
0.91
1.07
2.08
4.19
f1 (ppm)


179.27
148.75
131.91
124.44
121.20
120.21
117.96
114.72
70.64
59.53
40.14
39.94
39.73
39.52
39.31
39.10
38.89
34.35
29.70
23.92
23.73
^{13}C-NMR (100 MHz, $(CD_3)_2SO$) of **S2f**
HO
HN
S
HN
Tf
f1 (ppm)

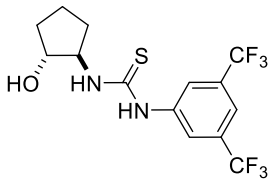
^{19}F-NMR (377 MHz, $(CD_3)_2SO$) of **S2f**



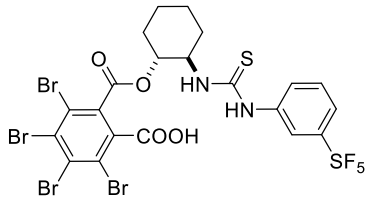

9.88
8.25
8.21
7.70
4.83
4.30
4.01
4.00
3.98
3.97
3.96
2.51
2.50
2.50
2.50
2.49
2.15
2.14
2.12
2.10
2.09
2.07
1.88
1.87
1.85
1.83
1.82
1.80
1.74
1.73
1.72
1.71
1.71
1.69
1.69
1.67
1.66
1.65
1.64
1.62
1.61
1.60
1.59
1.58
1.57
1.56
1.54
1.52
1.52
1.51
1.50
1.49
1.49
1.48
1.47
1.46
1.41
^{1}H-NMR (400 MHz, $(CD_3)_2SO$) of **S2g**
HO
HN
S
HN
CF_3
CF_3
0.93
2.67
0.91
0.69
0.74
1.00
0.91
0.96
3.82
f1 (ppm)

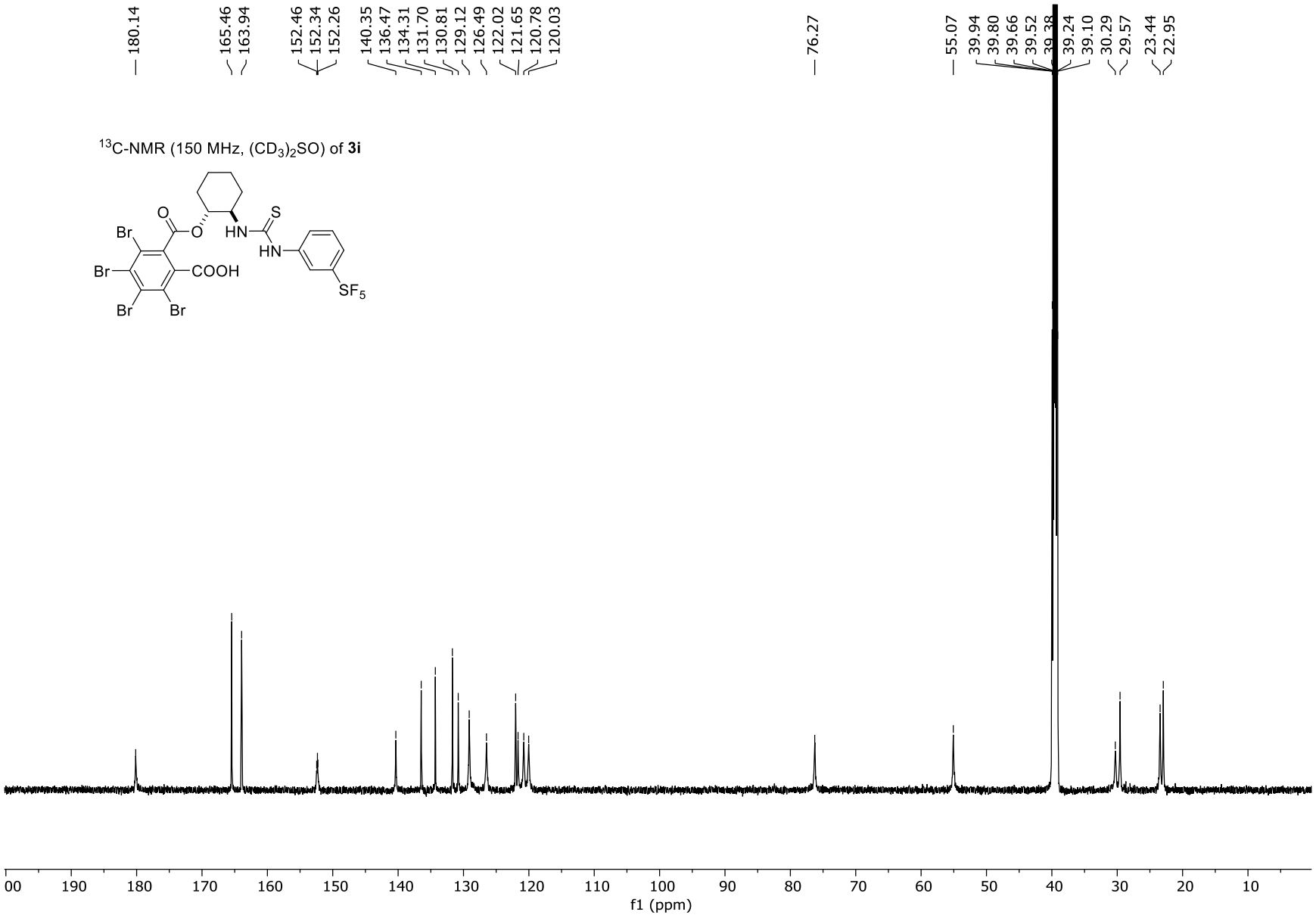

180.26
142.04
130.58
130.27
129.95
129.62
127.33
124.62
121.91
121.63
119.20
115.82
75.63
62.22
39.94
39.73
39.52
39.31
39.10
38.89
32.23
29.11
20.28
13C-NMR (100 MHz, (CD3)2SO) of S2g
HO
HN
S
HN
CF3
CF3
f1 (ppm)

^{19}F-NMR (565 MHz, $(CD_3)_2SO$) of **S2g**

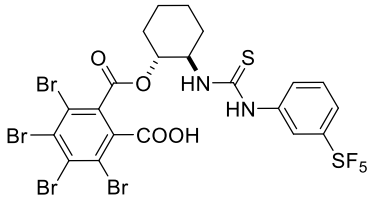


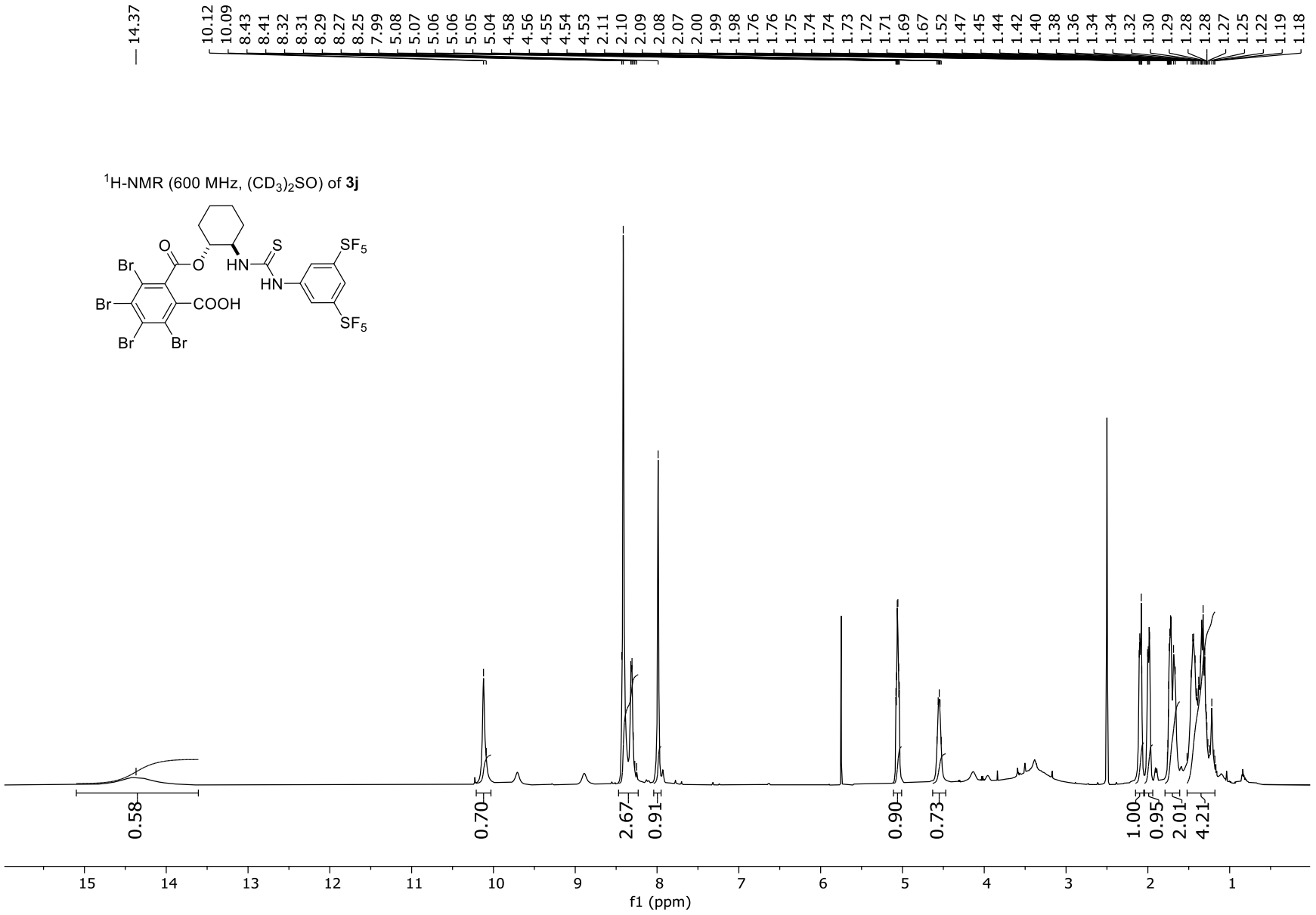
^{1}H-NMR (600 MHz, $(CD_3)_2SO$) of **3i**

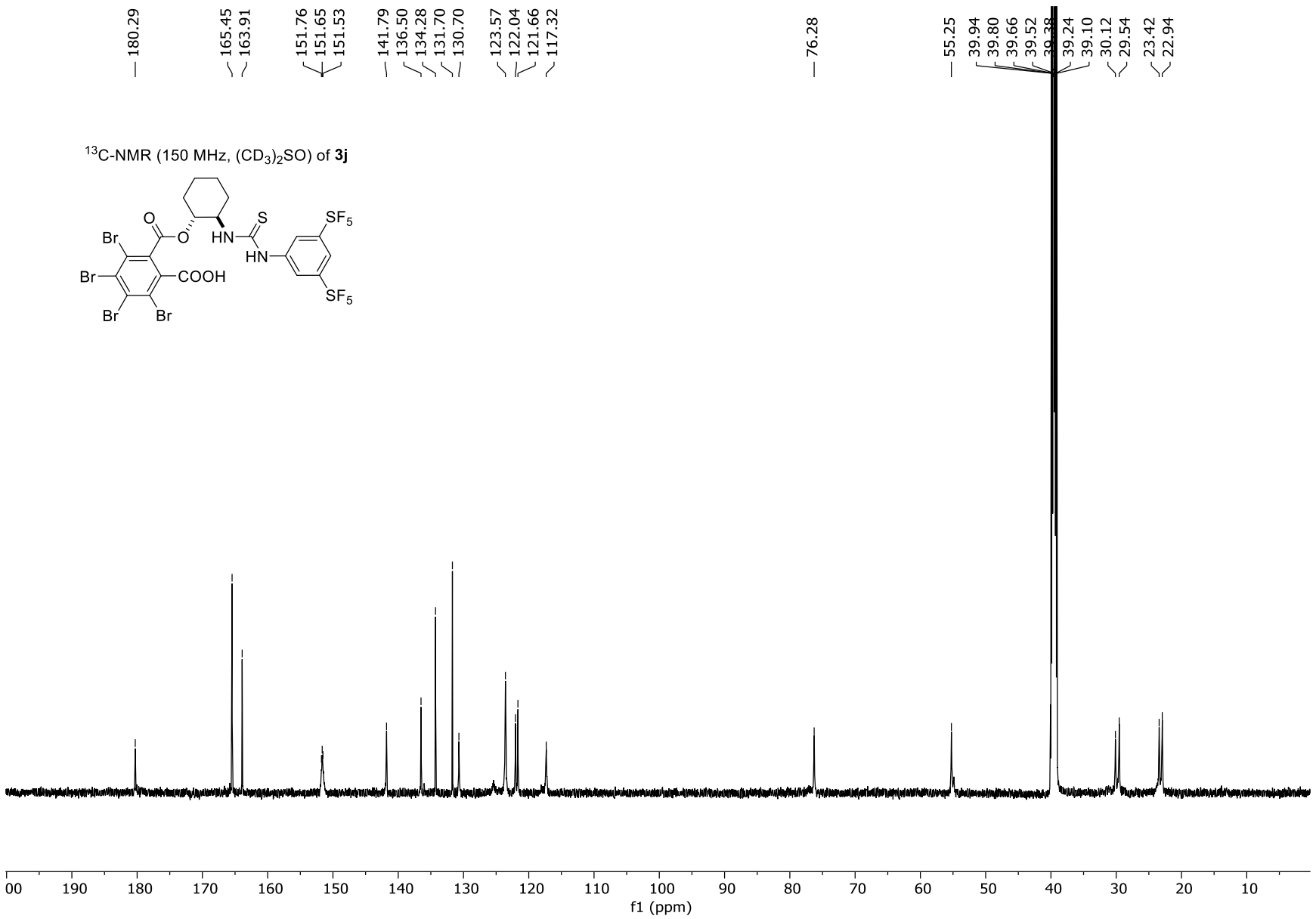


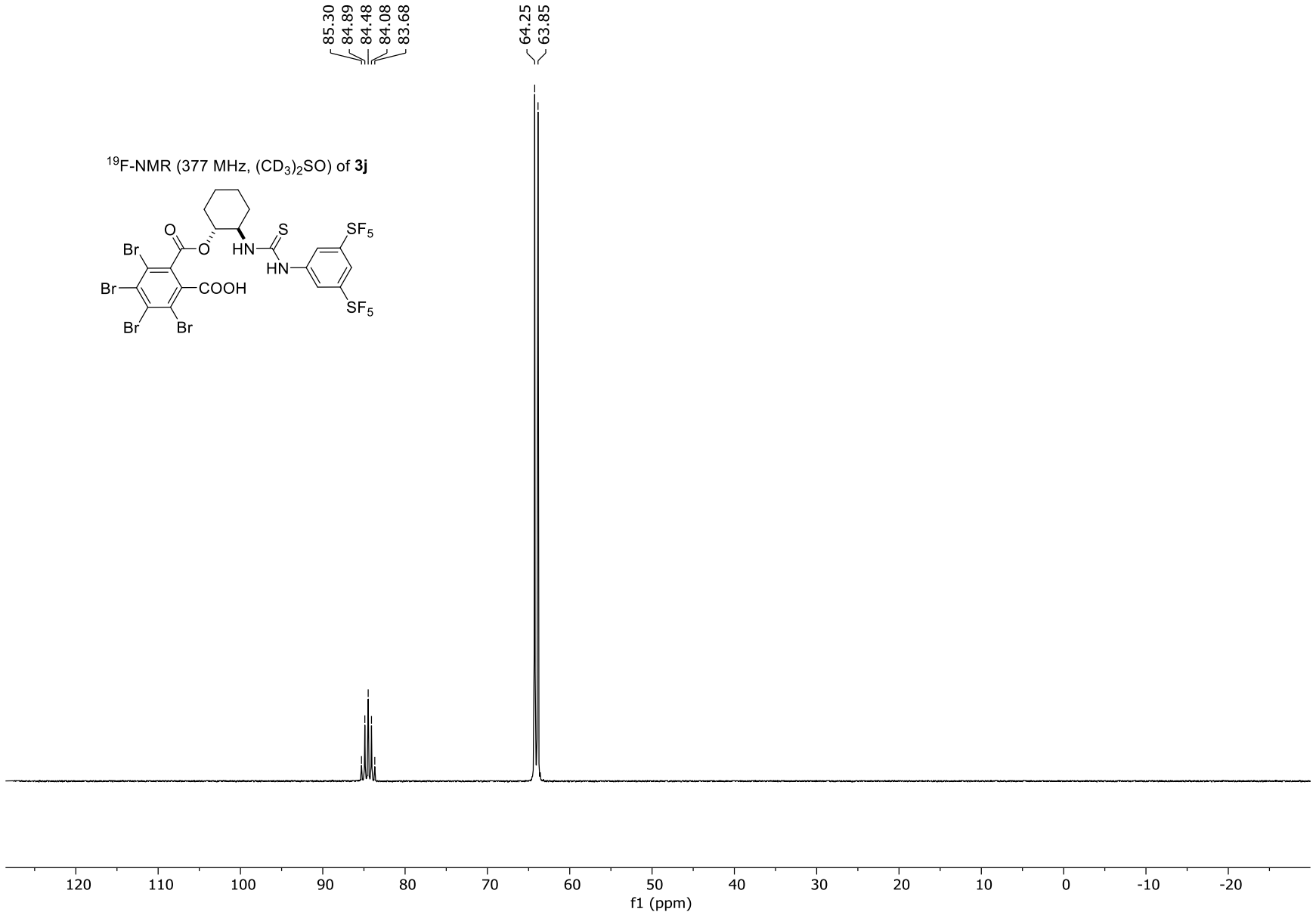

180.14
165.46
163.94
152.46
152.34
152.26
140.35
136.47
134.31
131.70
130.81
129.12
126.49
122.02
121.65
120.78
120.03
76.27
55.07
39.94
39.80
39.66
39.52
39.38
39.24
39.10
30.29
29.57
23.44
22.95
^{13}C-NMR (150 MHz, $(CD_3)_2SO$) of **3i**
O
O
HN
S
HN
Br
Br
Br
Br
COOH
SF_5
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

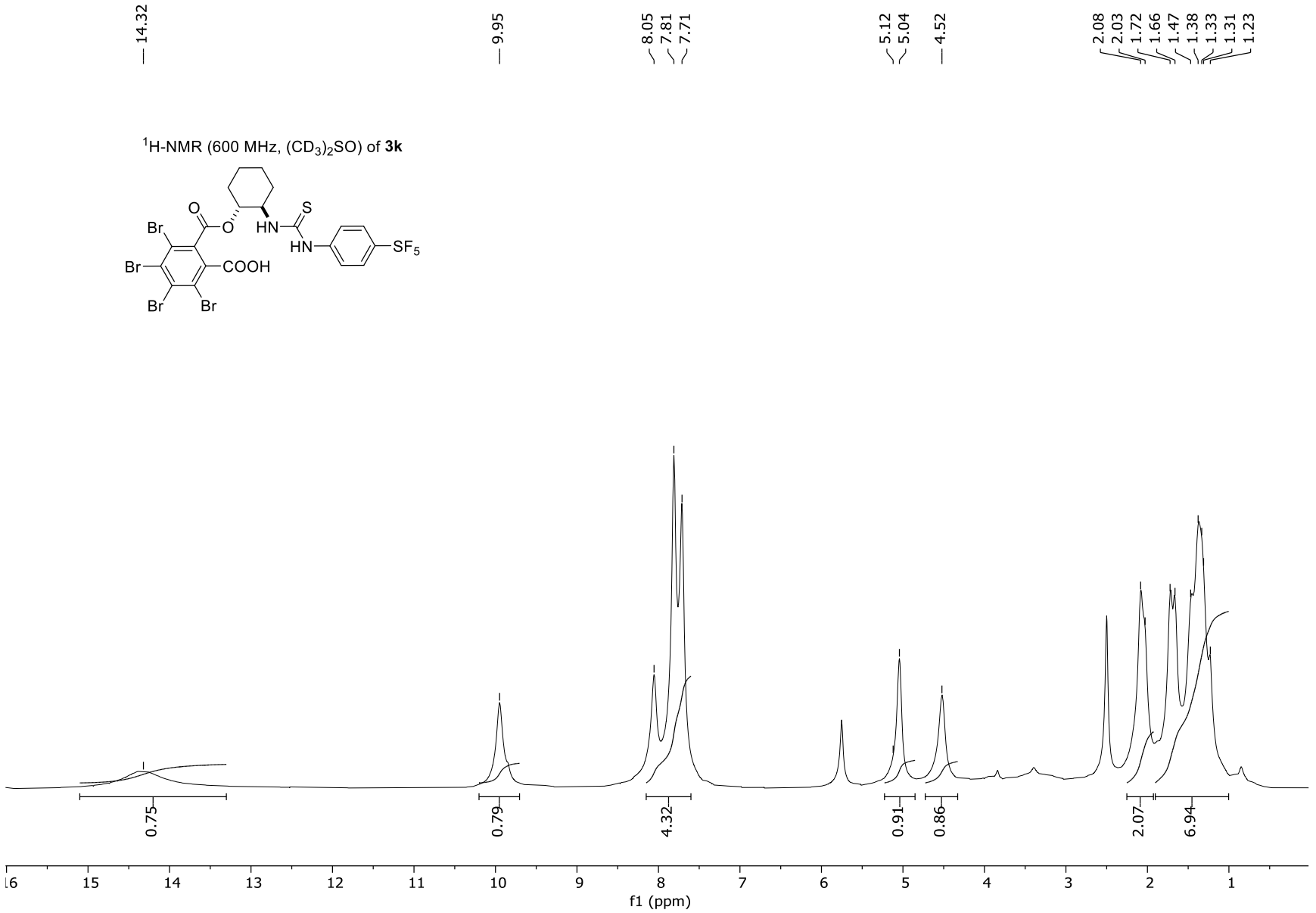
^{19}F-NMR (377 MHz, $(CD_3)_2SO$) of **3i**

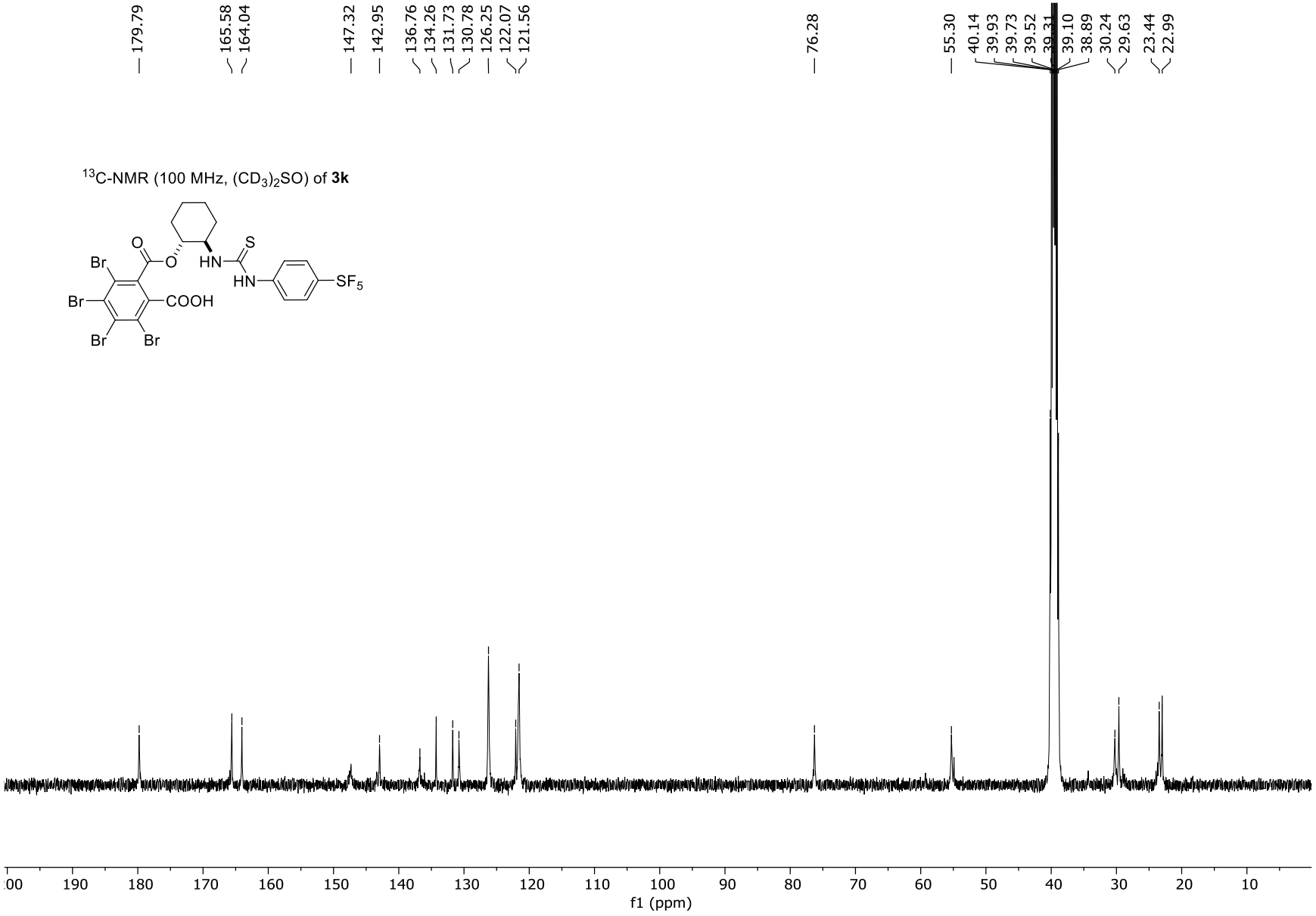


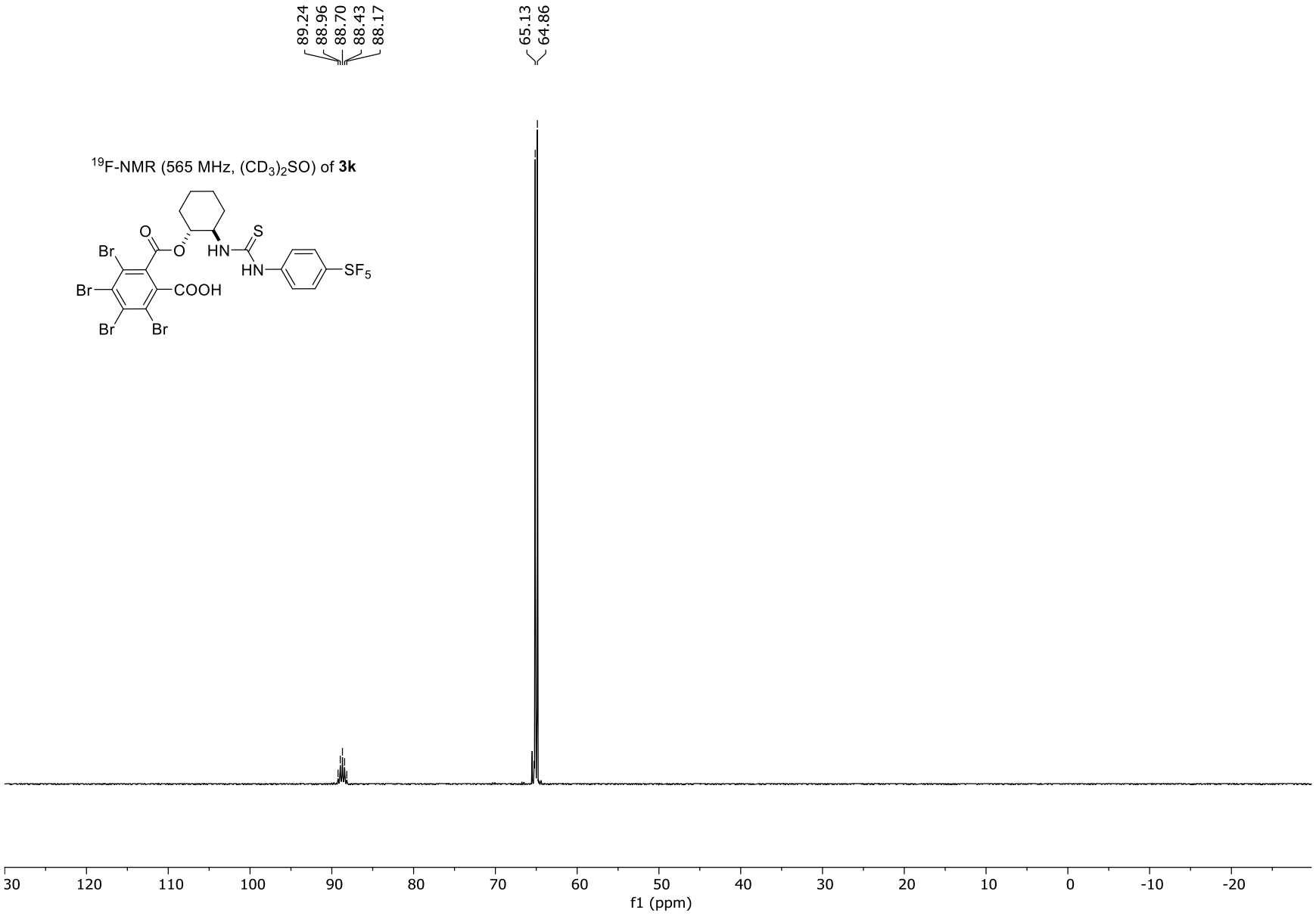

14.37
10.12
10.09
8.43
8.41
8.32
8.31
8.29
8.27
8.25
7.99
5.08
5.07
5.06
5.06
5.05
5.04
4.58
4.56
4.55
4.54
4.53
2.11
2.10
2.09
2.08
2.07
2.00
1.99
1.98
1.76
1.76
1.75
1.74
1.74
1.73
1.72
1.71
1.69
1.67
1.52
1.47
1.45
1.44
1.42
1.40
1.38
1.36
1.34
1.34
1.32
1.30
1.29
1.28
1.28
1.27
1.25
1.22
1.19
1.18
1H-NMR (600 MHz, (CD3)2SO) of 3j
Br
Br
Br
Br
O
O
COOH
HN
S
HN
SF5
SF5
0.58
0.70
2.67
0.91
0.90
0.73
1.00
0.95
2.01
4.21
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
f1 (ppm)

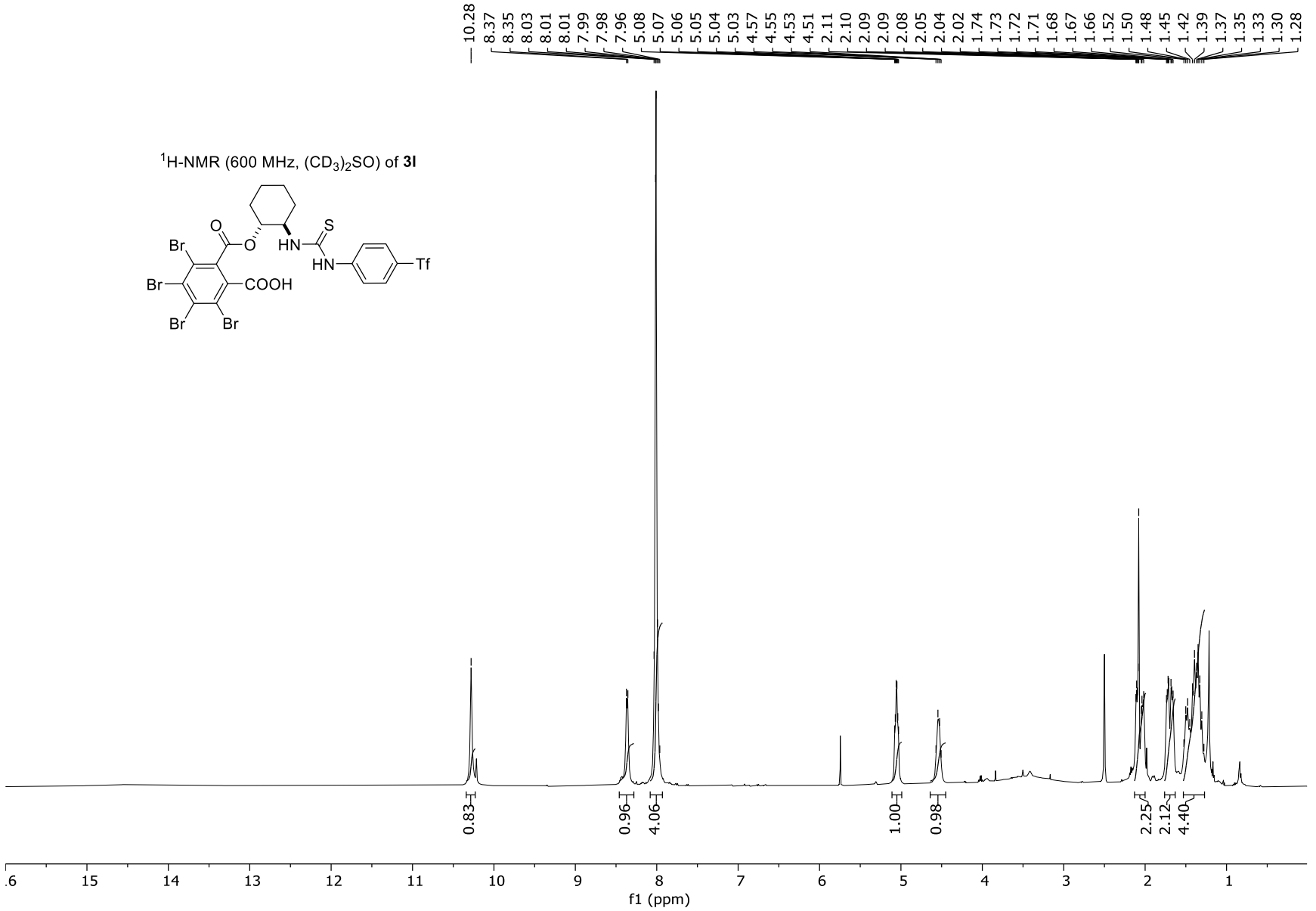

180.29
165.45
163.91
151.76
151.65
151.53
141.79
136.50
134.28
131.70
130.70
123.57
122.04
121.66
117.32
76.28
55.25
39.94
39.80
39.66
39.52
39.38
39.24
39.10
30.12
29.54
23.42
22.94
13C-NMR (150 MHz, (CD3)2SO) of 3j
O
O
HN
S
HN
SF5
SF5
Br
Br
Br
Br
COOH
f1 (ppm)

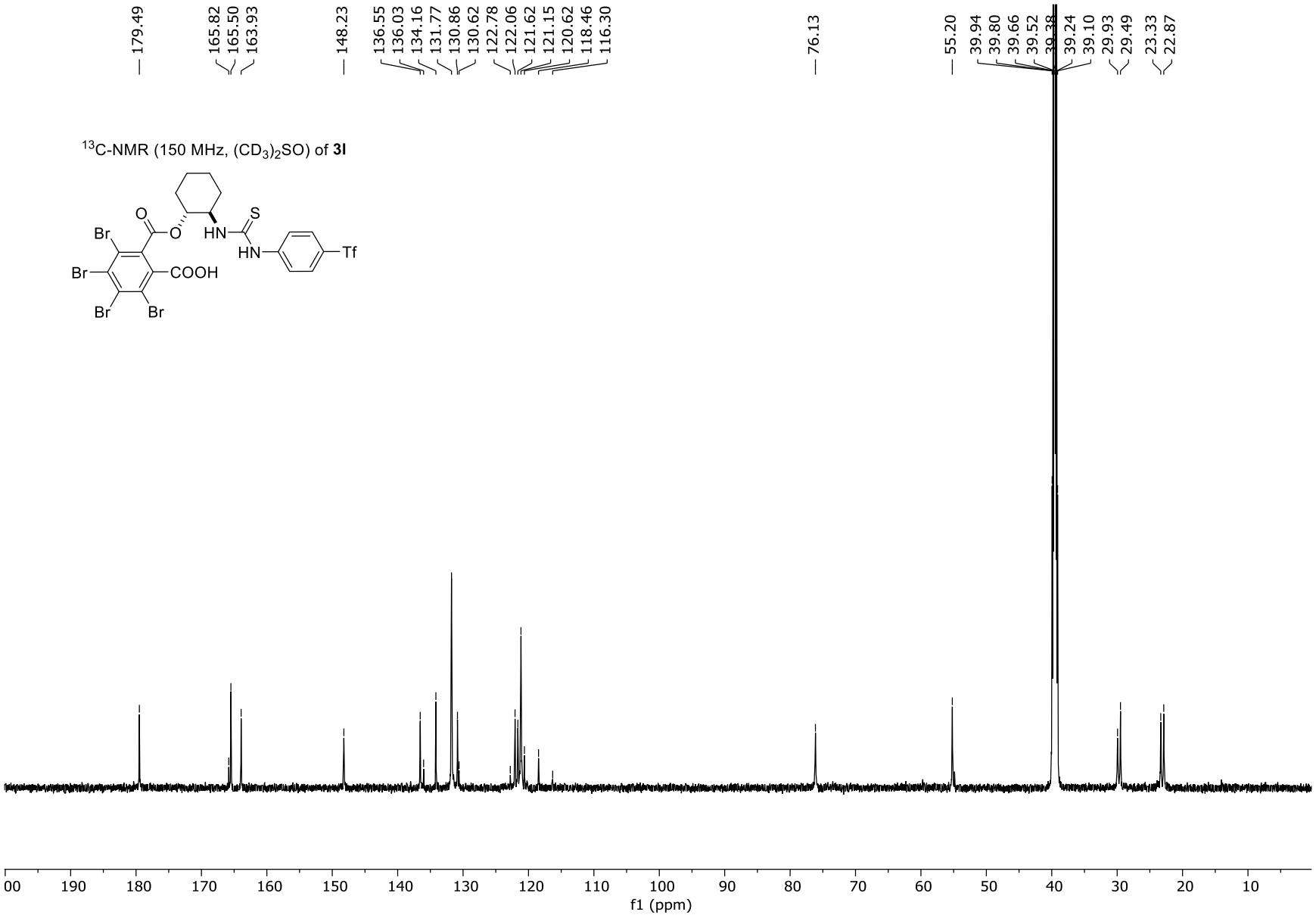

85.30
84.89
84.48
84.08
83.68
64.25
63.85
19F-NMR (377 MHz, (CD3)2SO) of 3j
O
O
HN
S
HN
SF5
SF5
Br
Br
Br
Br
COOH
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


14.32
9.95
8.05
7.81
7.71
5.12
5.04
4.52
2.08
2.03
1.72
1.66
1.47
1.38
1.33
1.31
1.23
^{1}H-NMR (600 MHz, $(CD_3)_2SO$) of **3k**
O
O
HN
S
HN
SF_5
Br
Br
Br
Br
COOH
0.75
0.79
4.32
0.91
0.86
2.07
6.94
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
f1 (ppm)

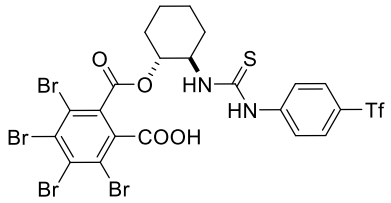

179.79
165.58
164.04
147.32
142.95
136.76
134.26
131.73
130.78
126.25
122.07
121.56
76.28
55.30
40.14
39.93
39.73
39.52
39.31
39.10
38.89
30.24
29.63
23.44
22.99
13C-NMR (100 MHz, (CD3)2SO) of 3k
O
O
HN
S
HN
SF5
Br
Br
Br
Br
COOH
f1 (ppm)

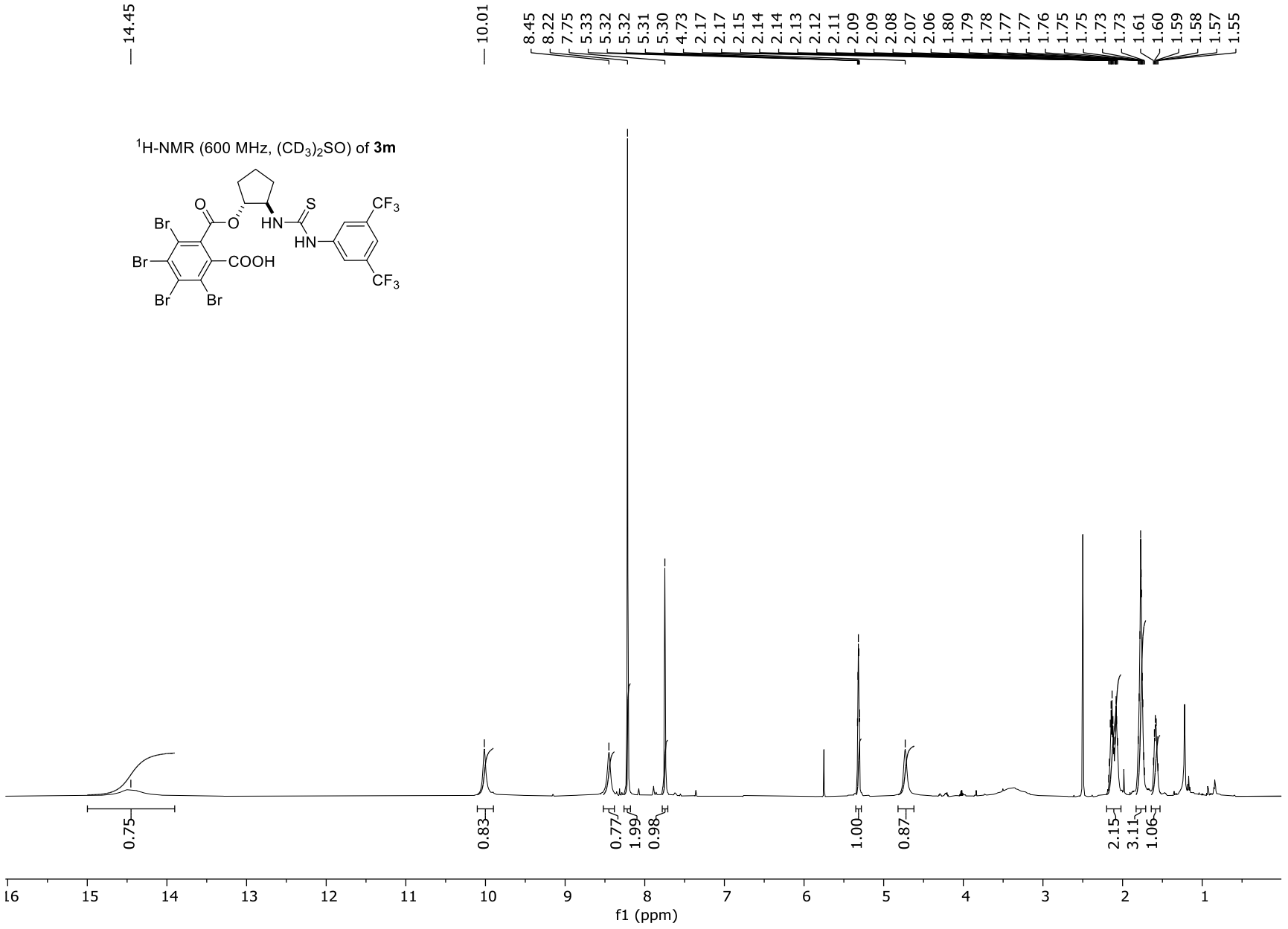

89.24
88.96
88.70
88.43
88.17
65.13
64.86
^{19}F-NMR (565 MHz, $(CD_3)_2SO$) of **3k**
Br
Br
Br
Br
COOH
O
O
HN
S
HN
SF_5
30
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

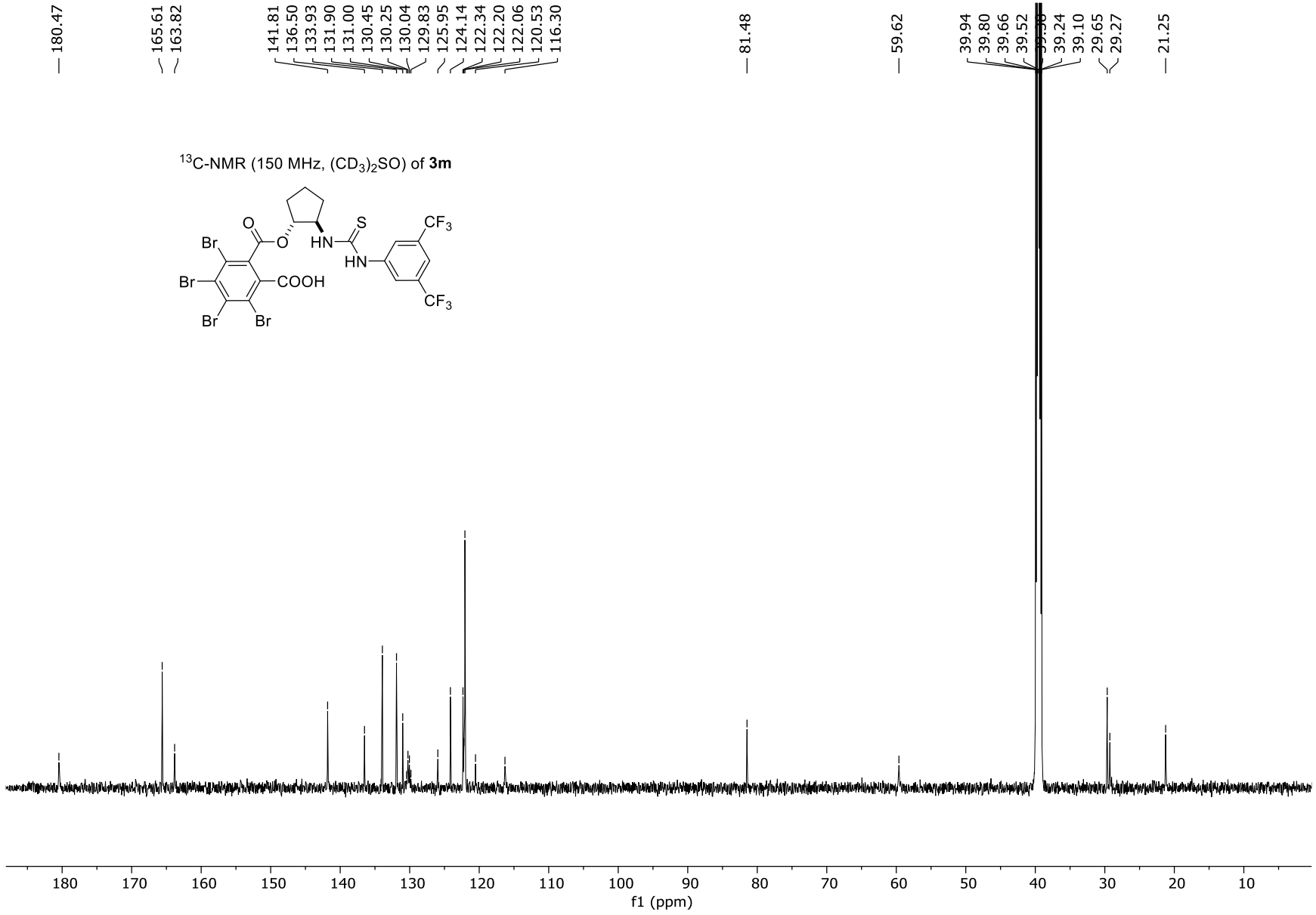

10.28
8.37
8.35
8.03
8.01
8.01
7.99
7.98
7.96
5.08
5.07
5.06
5.05
5.04
5.03
4.57
4.55
4.53
4.51
2.11
2.10
2.09
2.09
2.08
2.05
2.04
2.02
1.74
1.73
1.72
1.71
1.68
1.67
1.66
1.52
1.50
1.48
1.45
1.42
1.39
1.37
1.35
1.33
1.30
1.28
^{1}H-NMR (600 MHz, $(CD_3)_2SO$) of **3l**
Br
Br
Br
Br
COOH
O
O
HN
S
HN
Tf
0.83
0.96
4.06
1.00
0.98
2.25
2.12
4.40
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
f1 (ppm)


179.49
165.82
165.50
163.93
148.23
136.55
136.03
134.16
131.77
130.86
130.62
122.78
122.06
121.62
121.15
120.62
118.46
116.30
76.13
55.20
39.94
39.80
39.66
39.52
39.38
39.24
39.10
29.93
29.49
23.33
22.87
13C-NMR (150 MHz, (CD3)2SO) of 3l
O
O
HN
S
HN
Tf
Br
Br
COOH
Br
Br
f1 (ppm)

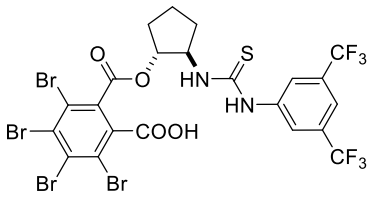
^{19}F-NMR (377 MHz, $(CD_3)_2SO$) of **3l**

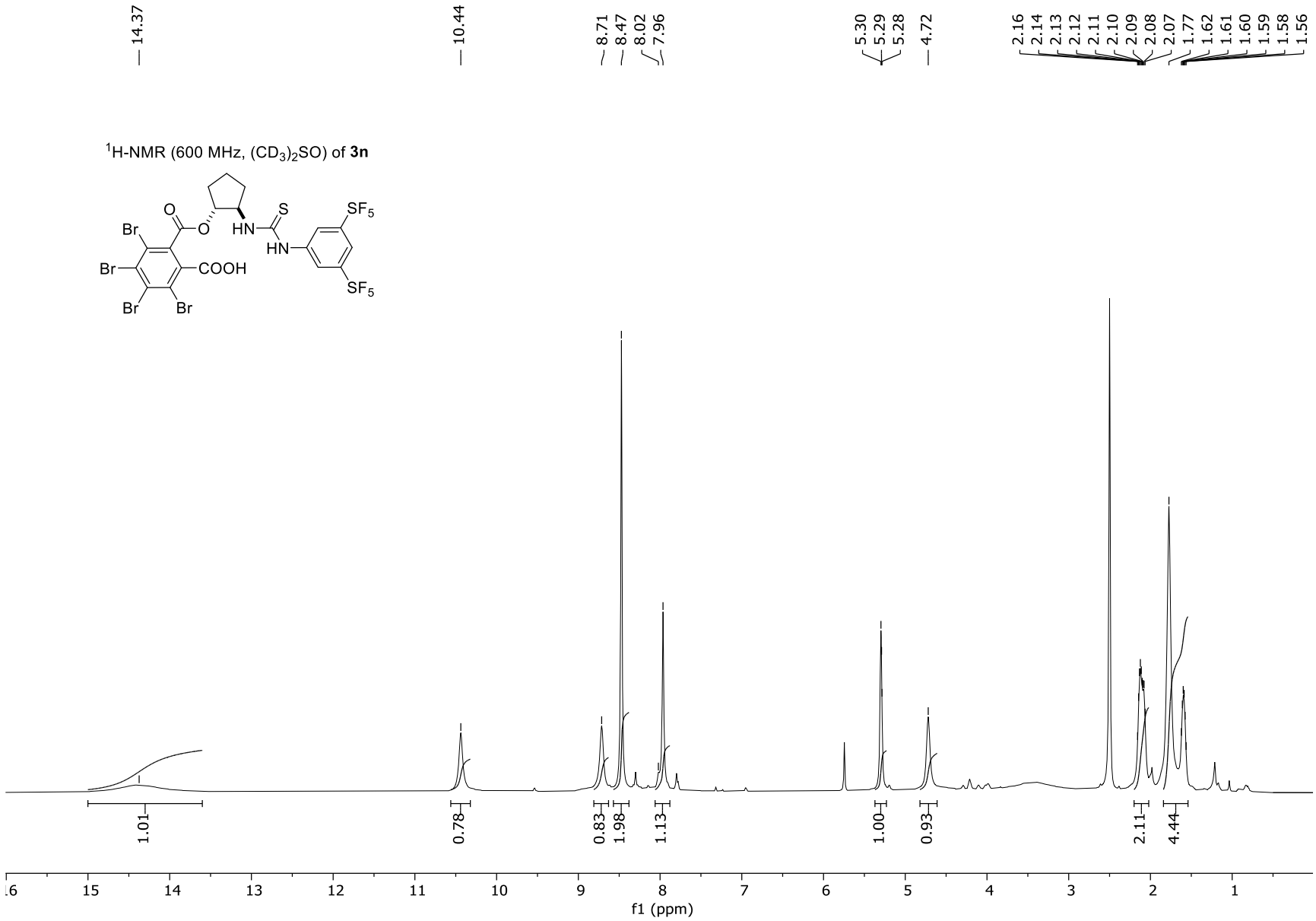


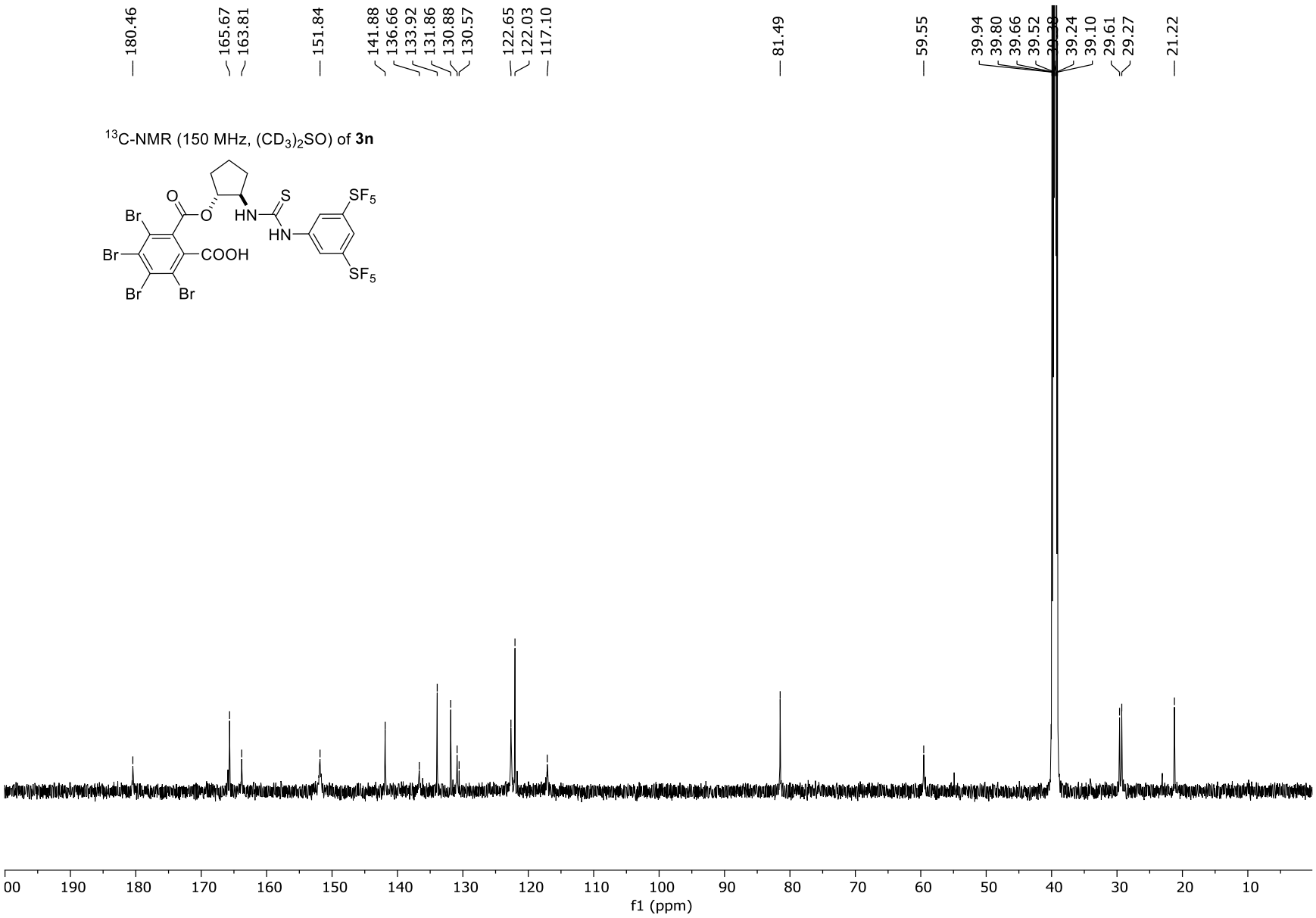

14.45
10.01
8.45
8.22
7.75
5.33
5.32
5.32
5.31
5.30
4.73
2.17
2.17
2.15
2.14
2.14
2.13
2.12
2.11
2.09
2.09
2.08
2.07
2.06
1.80
1.79
1.78
1.77
1.77
1.76
1.75
1.75
1.73
1.73
1.61
1.60
1.59
1.58
1.57
1.55
^{1}H-NMR (600 MHz, $(CD_3)_2SO$) of **3m**
O
O
HN
S
HN
CF$_3$
CF$_3$
Br
Br
Br
Br
COOH
0.75
0.83
0.77
1.99
0.98
1.00
0.87
2.15
3.11
1.06
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
f1 (ppm)


180.47
165.61
163.82
141.81
136.50
133.93
131.90
131.00
130.45
130.25
130.04
129.83
125.95
124.14
122.34
122.20
122.06
120.53
116.30
81.48
59.62
39.94
39.80
39.66
39.52
39.38
39.24
39.10
29.65
29.27
21.25
13C-NMR (150 MHz, (CD3)2SO) of 3m
O
O
HN
S
HN
CF3
CF3
Br
Br
Br
Br
COOH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

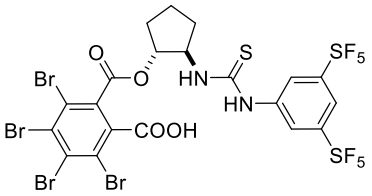
^{19}F-NMR (377 MHz, $(CD_3)_2SO$) of **3m**

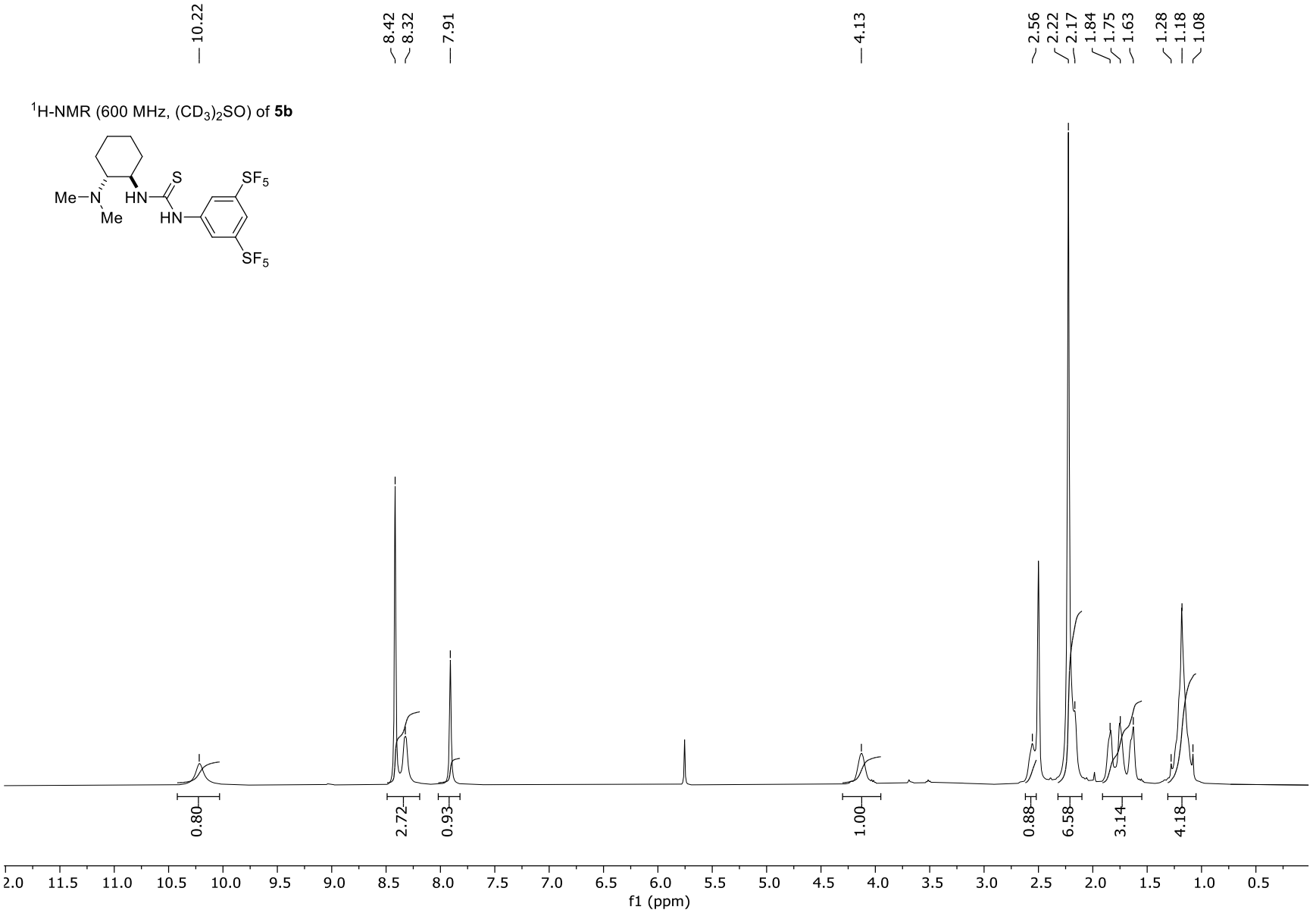



14.37
10.44
8.71
8.47
8.02
7.96
5.30
5.29
5.28
4.72
2.16
2.14
2.13
2.12
2.11
2.10
2.09
2.08
2.07
1.77
1.62
1.61
1.60
1.59
1.58
1.56
1H-NMR (600 MHz, (CD3)2SO) of 3n
Br
Br
Br
Br
O
O
HN
S
HN
SF5
SF5
COOH
1.01
0.78
0.83
1.98
1.13
1.00
0.93
2.11
4.44
f1 (ppm)

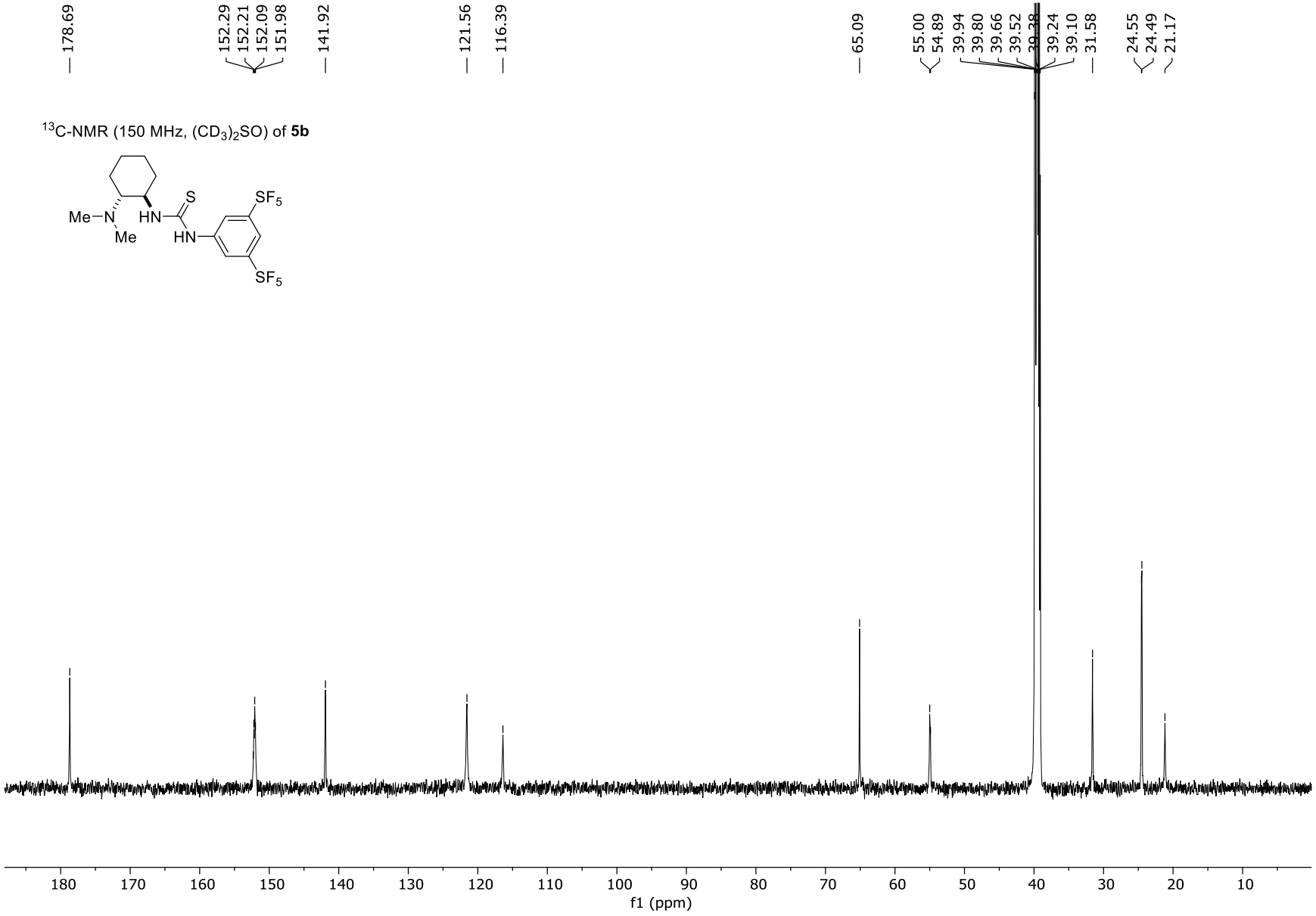

180.46
165.67
163.81
151.84
141.88
136.66
133.92
131.86
130.88
130.57
122.65
122.03
117.10
81.49
59.55
39.94
39.80
39.66
39.52
39.38
39.24
39.10
29.61
29.27
21.22
13C-NMR (150 MHz, (CD3)2SO) of 3n
O
O
HN
S
HN
SF5
SF5
Br
Br
Br
Br
COOH
f1 (ppm)

^{19}F-NMR (377 MHz, $(CD_3)_2SO$) of **3n**

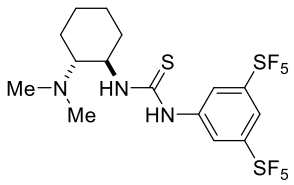


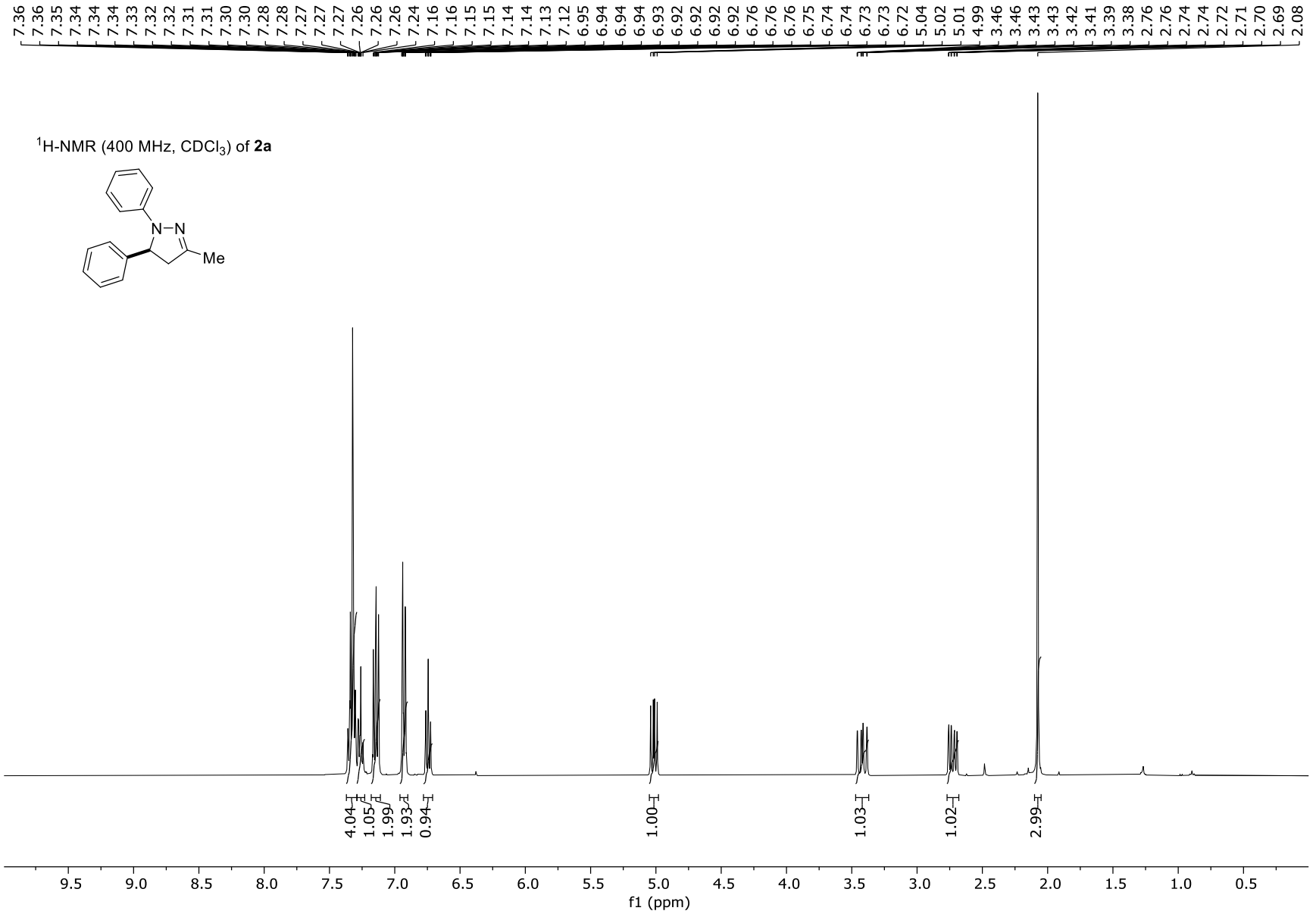


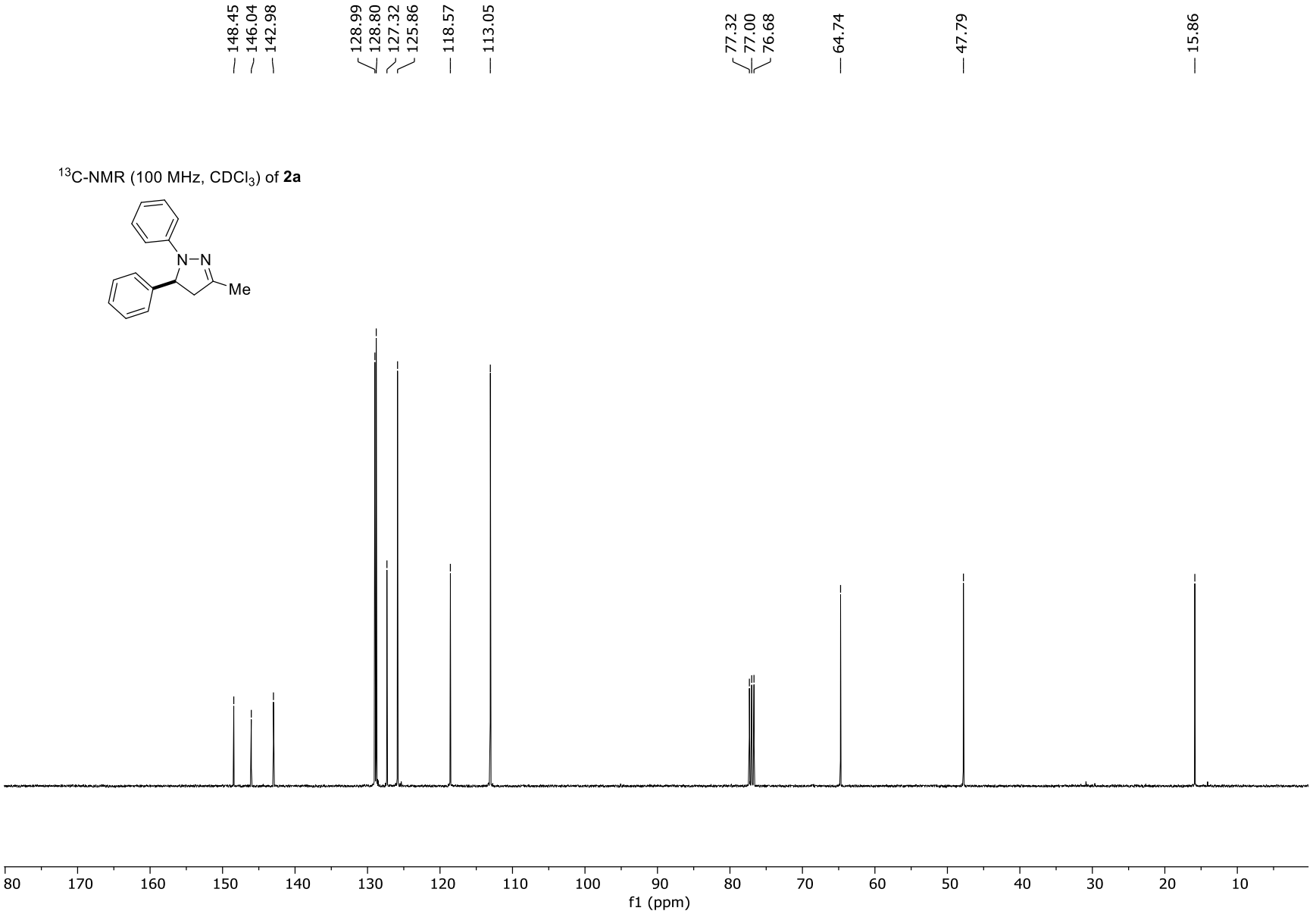
^{1}H-NMR (600 MHz, $(CD_3)_2SO$) of **5b**


178.69
152.29
152.21
152.09
151.98
141.92
121.56
116.39
65.09
55.00
54.89
39.94
39.80
39.66
39.52
39.38
39.24
39.10
31.58
24.55
24.49
21.17
13C-NMR (150 MHz, (CD3)2SO) of 5b
Me
N
Me
HN
S
HN
SF5
SF5
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

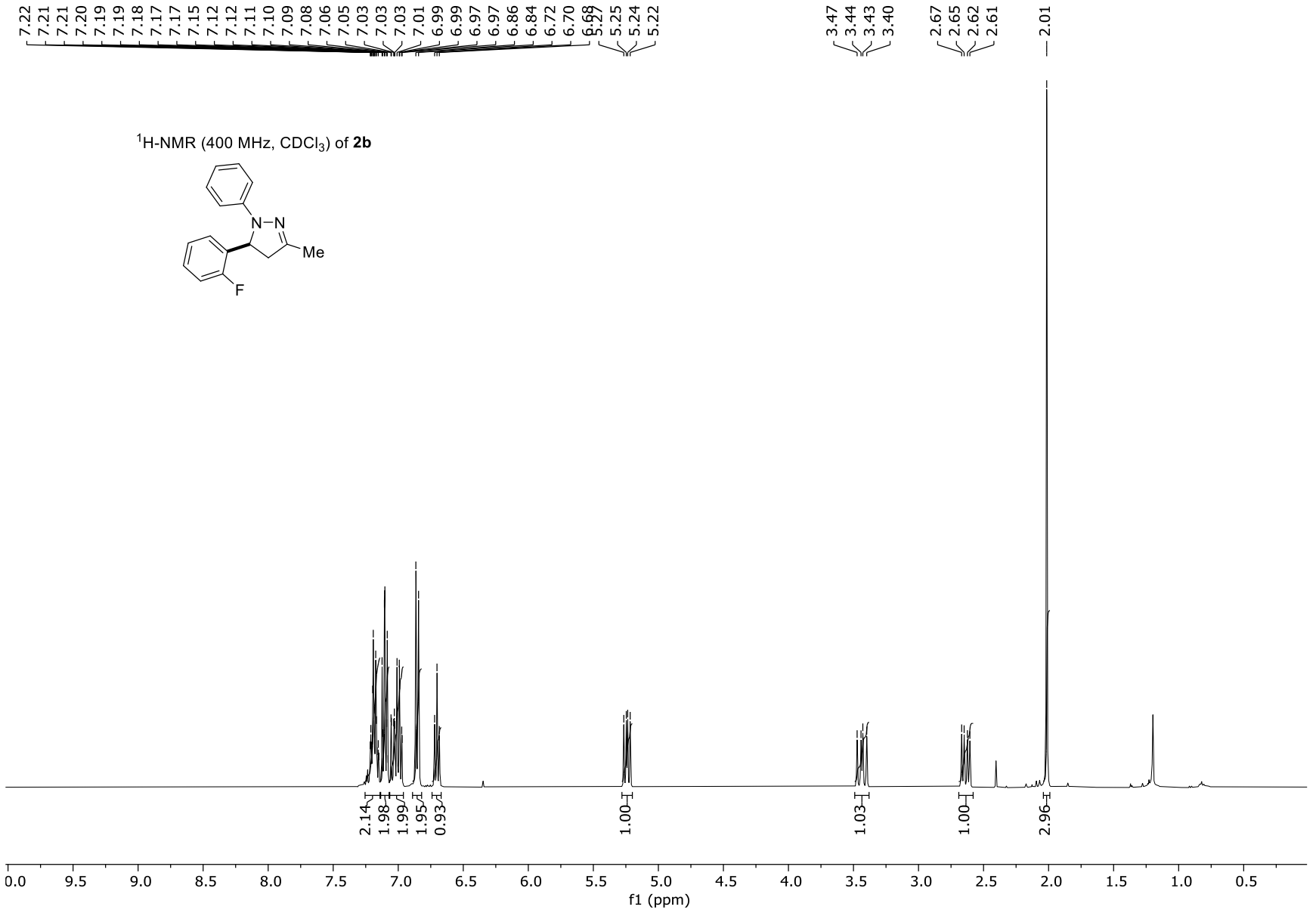
^{19}F-NMR (377 MHz, $(CD_3)_2SO$) of **5b**

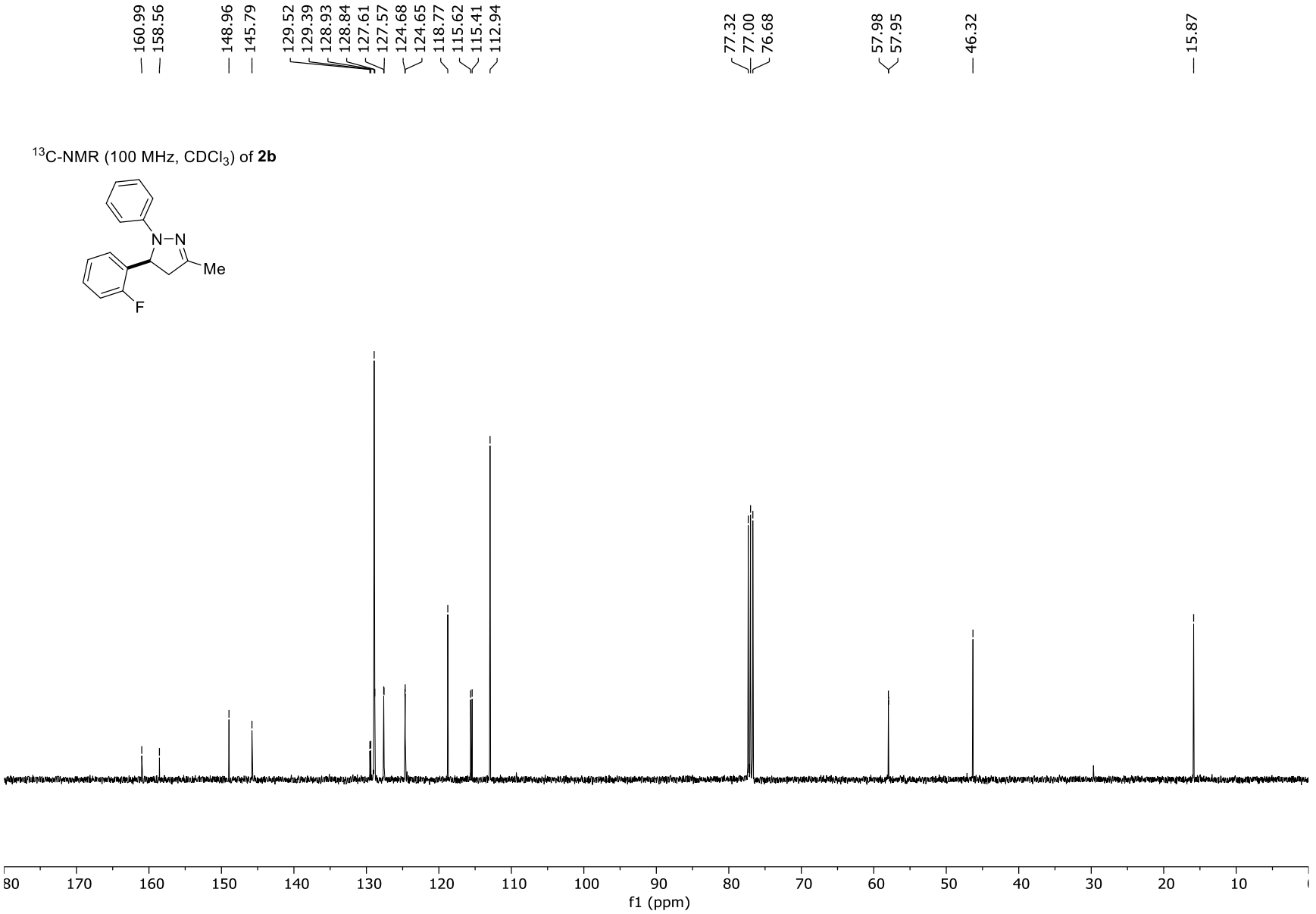



7.36 7.36 7.35 7.34 7.34 7.34 7.33 7.32 7.32 7.31 7.31 7.30 7.30 7.28 7.28 7.27 7.27 7.27 7.26 7.26 7.24 7.16 7.16 7.15 7.15 7.14 7.14 7.13 7.12 6.95 6.94 6.94 6.94 6.93 6.92 6.92 6.92 6.92 6.76 6.76 6.76 6.75 6.74 6.74 6.73 6.73 6.72 5.04 5.02 5.01 4.99 3.46 3.46 3.43 3.43 3.42 3.41 3.39 3.38 2.76 2.76 2.74 2.74 2.72 2.71 2.70 2.69 2.08
^{1}H-NMR (400 MHz, $CDCl_3$) of **2a**
N–N
Me
4.04 1.05 1.99 1.93 0.94 1.00 1.03 1.02 2.99
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)



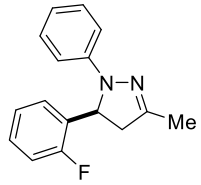
^{13}C-NMR (100 MHz, $CDCl_3$) of **2a**

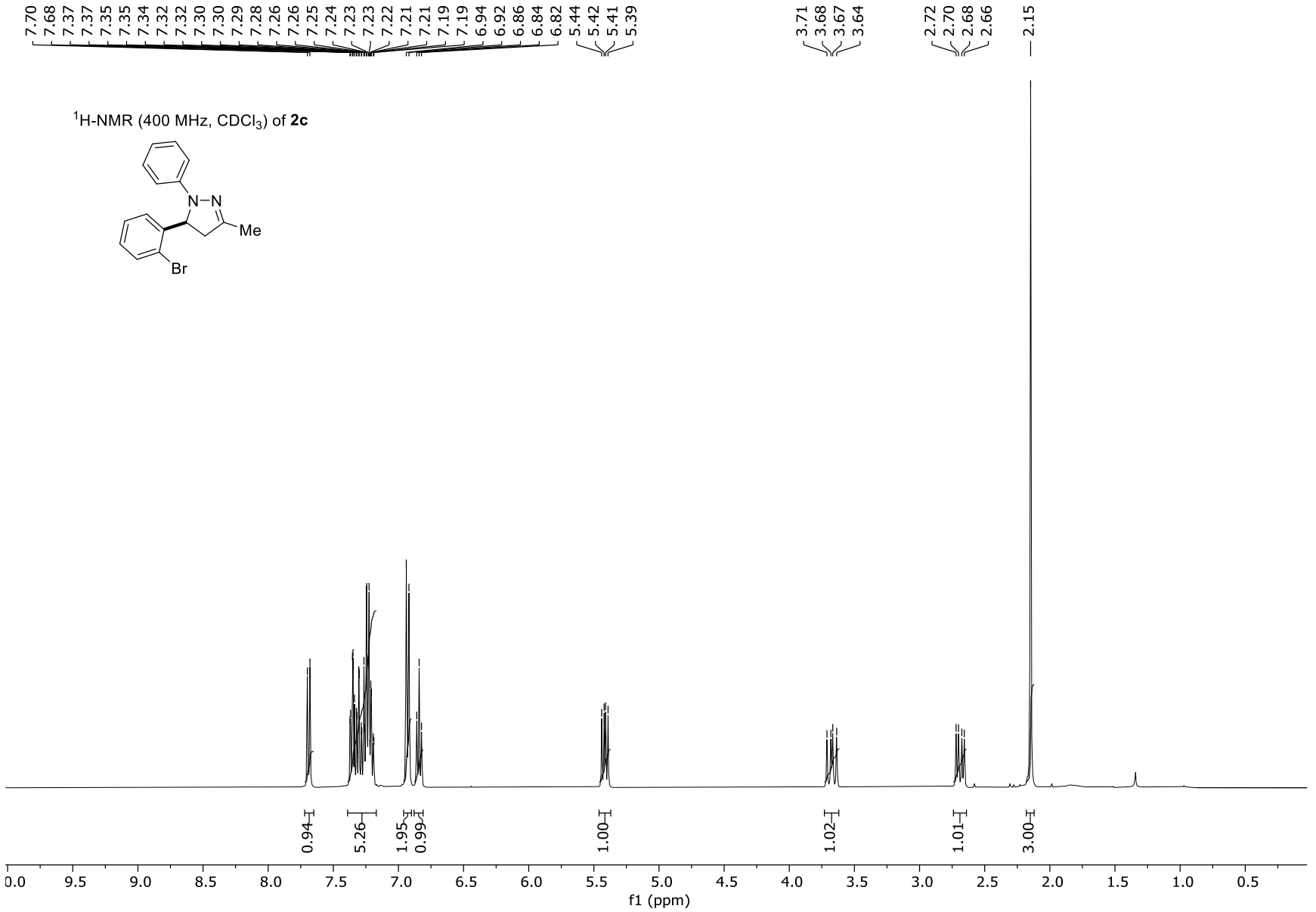

7.22
7.21
7.21
7.20
7.19
7.19
7.18
7.17
7.17
7.15
7.12
7.12
7.11
7.10
7.09
7.08
7.06
7.05
7.03
7.03
7.03
7.01
6.99
6.99
6.97
6.97
6.86
6.84
6.72
6.70
6.68
5.27
5.25
5.24
5.22
3.47
3.44
3.43
3.40
2.67
2.65
2.62
2.61
2.01
1H-NMR (400 MHz, CDCl3) of 2b
N–N
Me
F
2.14
1.98
1.99
1.95
0.93
1.00
1.03
1.00
2.96
0.0
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
f1 (ppm)

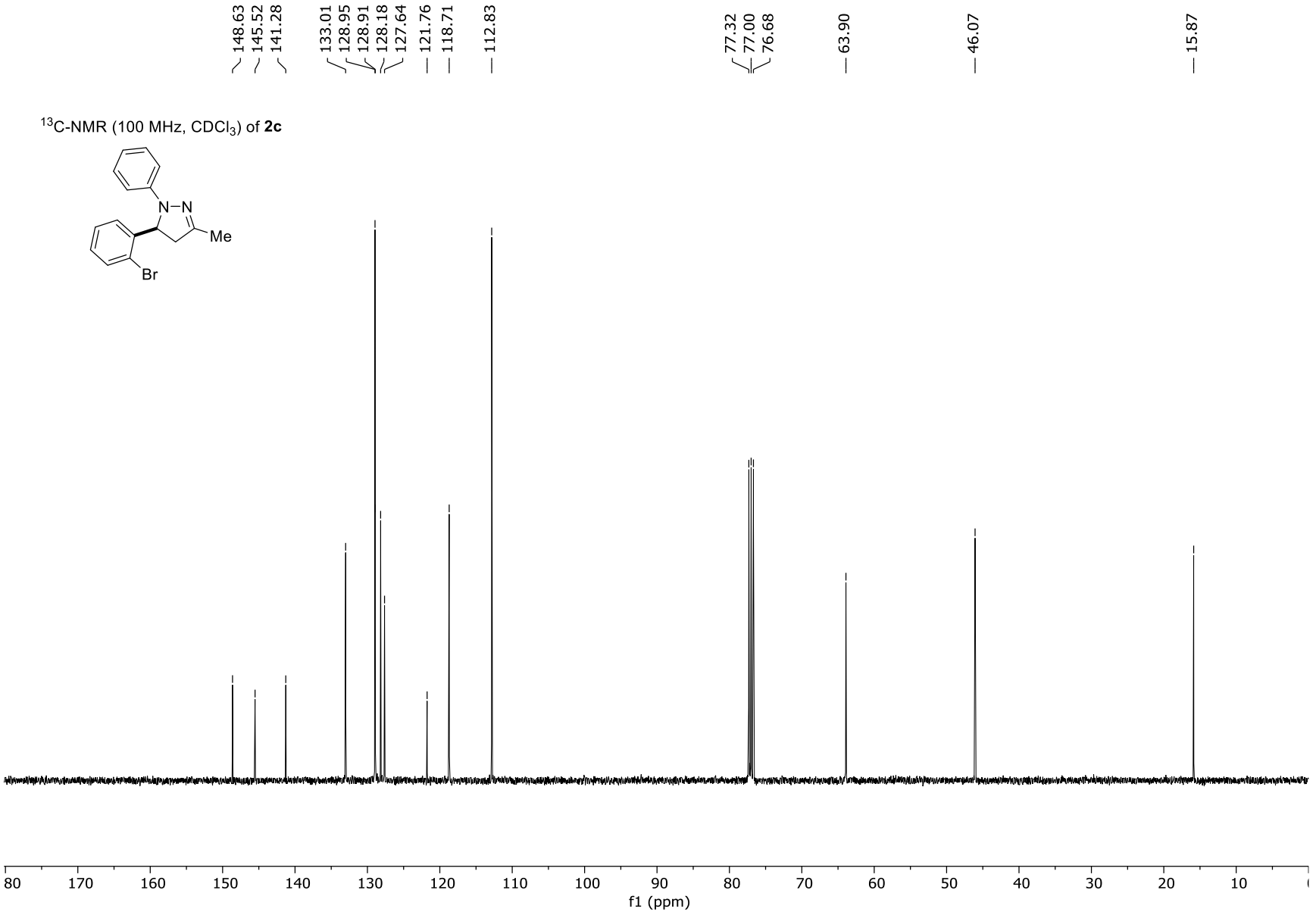


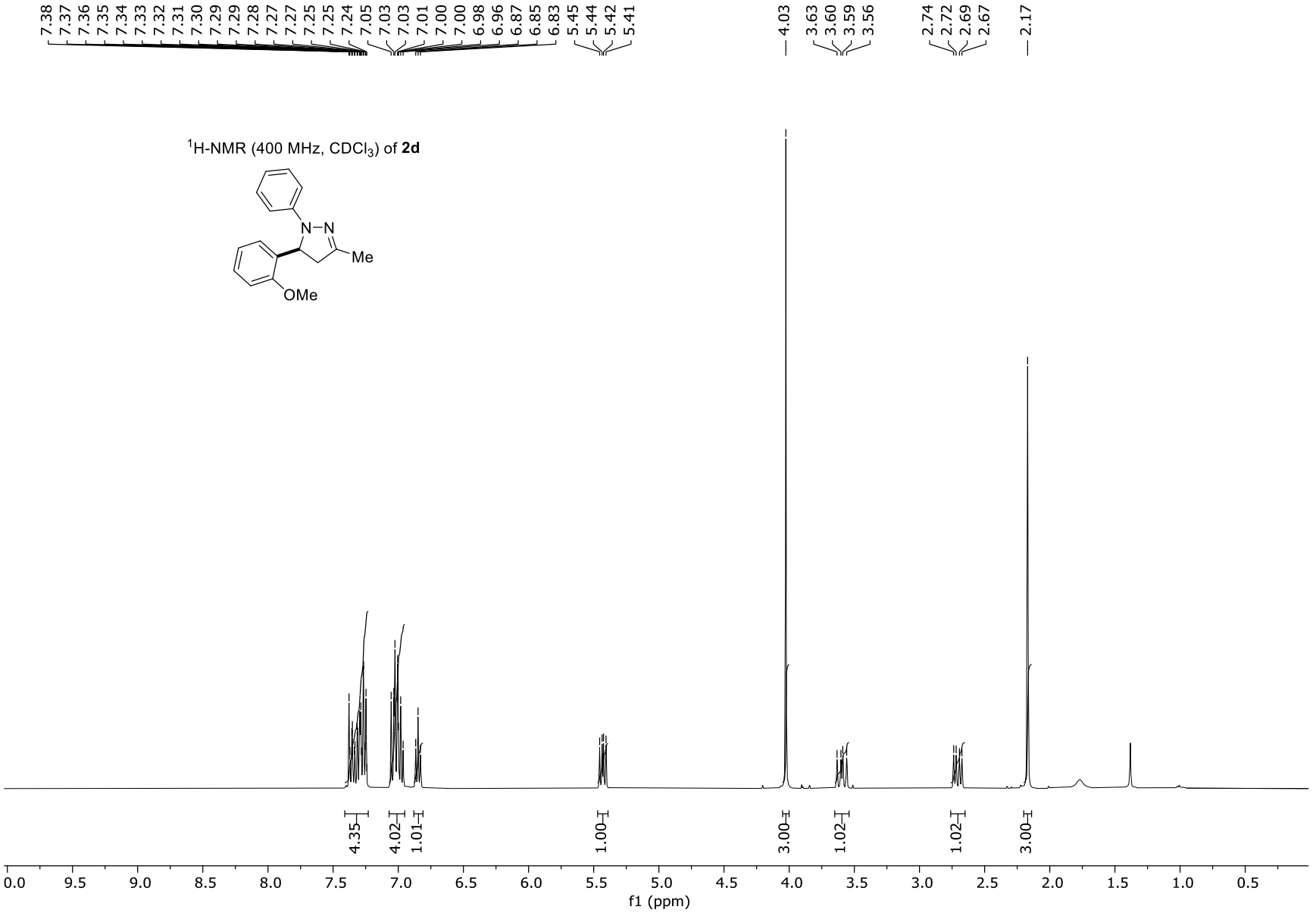
^{13}C-NMR (100 MHz, $CDCl_3$) of **2b**

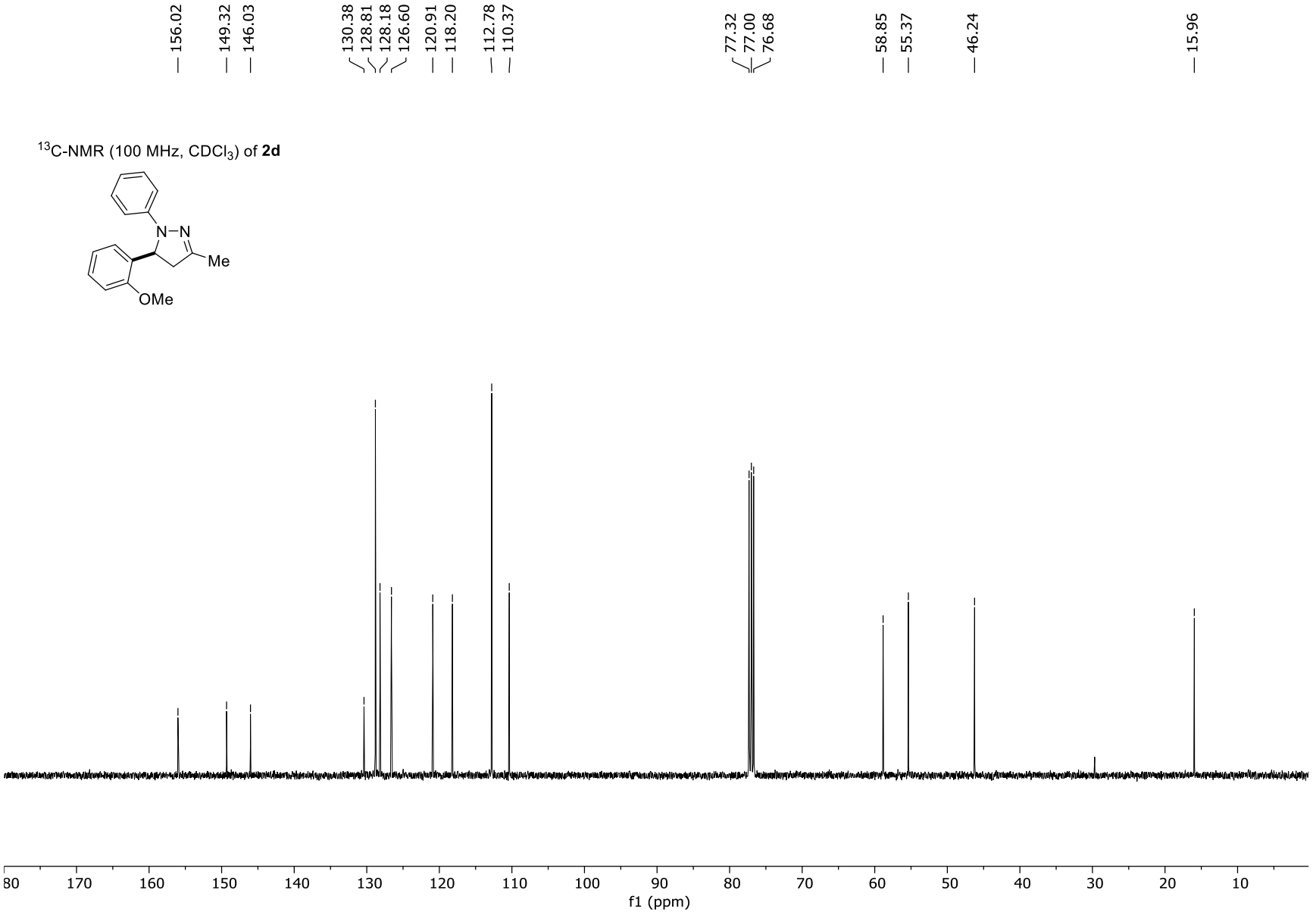
^{19}F-NMR (377 MHz, $CDCl_3$) of **2b**



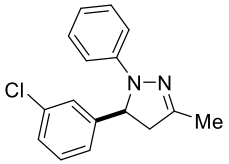

7.70
7.68
7.37
7.37
7.35
7.35
7.34
7.32
7.32
7.30
7.30
7.29
7.28
7.26
7.26
7.25
7.24
7.23
7.23
7.22
7.21
7.21
7.19
7.19
6.94
6.92
6.86
6.84
6.82
5.44
5.42
5.41
5.39
3.71
3.68
3.67
3.64
2.72
2.70
2.68
2.66
2.15
1H-NMR (400 MHz, CDCl3) of 2c
N–N
Me
Br
0.94
5.26
1.95
0.99
1.00
1.02
1.01
3.00
0.0
9.5
9.0
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
f1 (ppm)


148.63
145.52
141.28
133.01
128.95
128.91
128.18
127.64
121.76
118.71
112.83
77.32
77.00
76.68
63.90
46.07
15.87
13C-NMR (100 MHz, CDCl3) of 2c
N–N
Me
Br
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.38
7.37
7.36
7.35
7.34
7.33
7.32
7.31
7.30
7.29
7.29
7.28
7.27
7.27
7.25
7.25
7.24
7.05
7.03
7.03
7.01
7.00
7.00
6.98
6.96
6.87
6.85
6.83
5.45
5.44
5.42
5.41
4.03
3.63
3.60
3.59
3.56
2.74
2.72
2.69
2.67
2.17
1H-NMR (400 MHz, CDCl3) of 2d
N–N
Me
OMe
4.35
4.02
1.01
1.00
3.00
1.02
1.02
3.00
0.0
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
f1 (ppm)

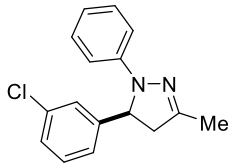

156.02
149.32
146.03
130.38
128.81
128.18
126.60
120.91
118.20
112.78
110.37
77.32
77.00
76.68
58.85
55.37
46.24
15.96
13C-NMR (100 MHz, CDCl3) of 2d
N–N
Me
OMe
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

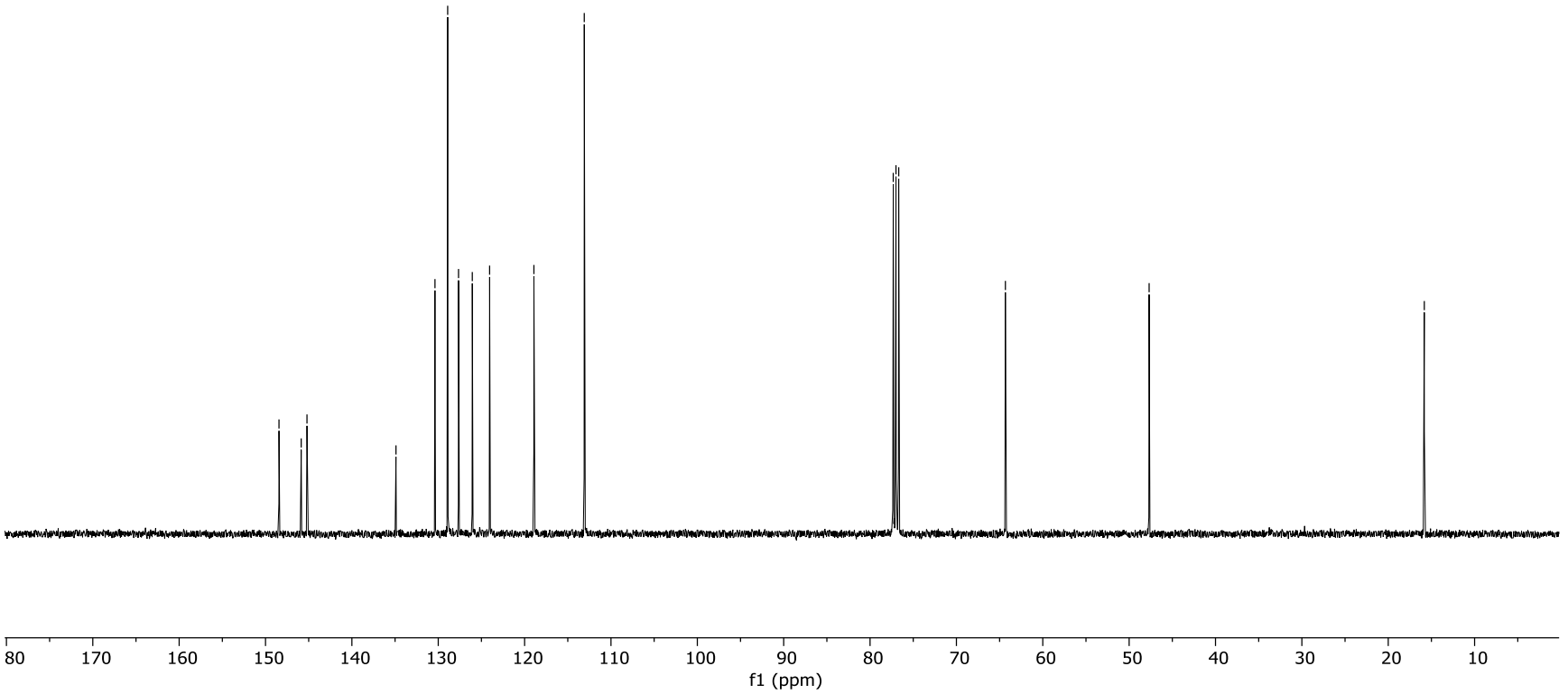
^{1}H-NMR (400 MHz, $CDCl_3$) of **2e**

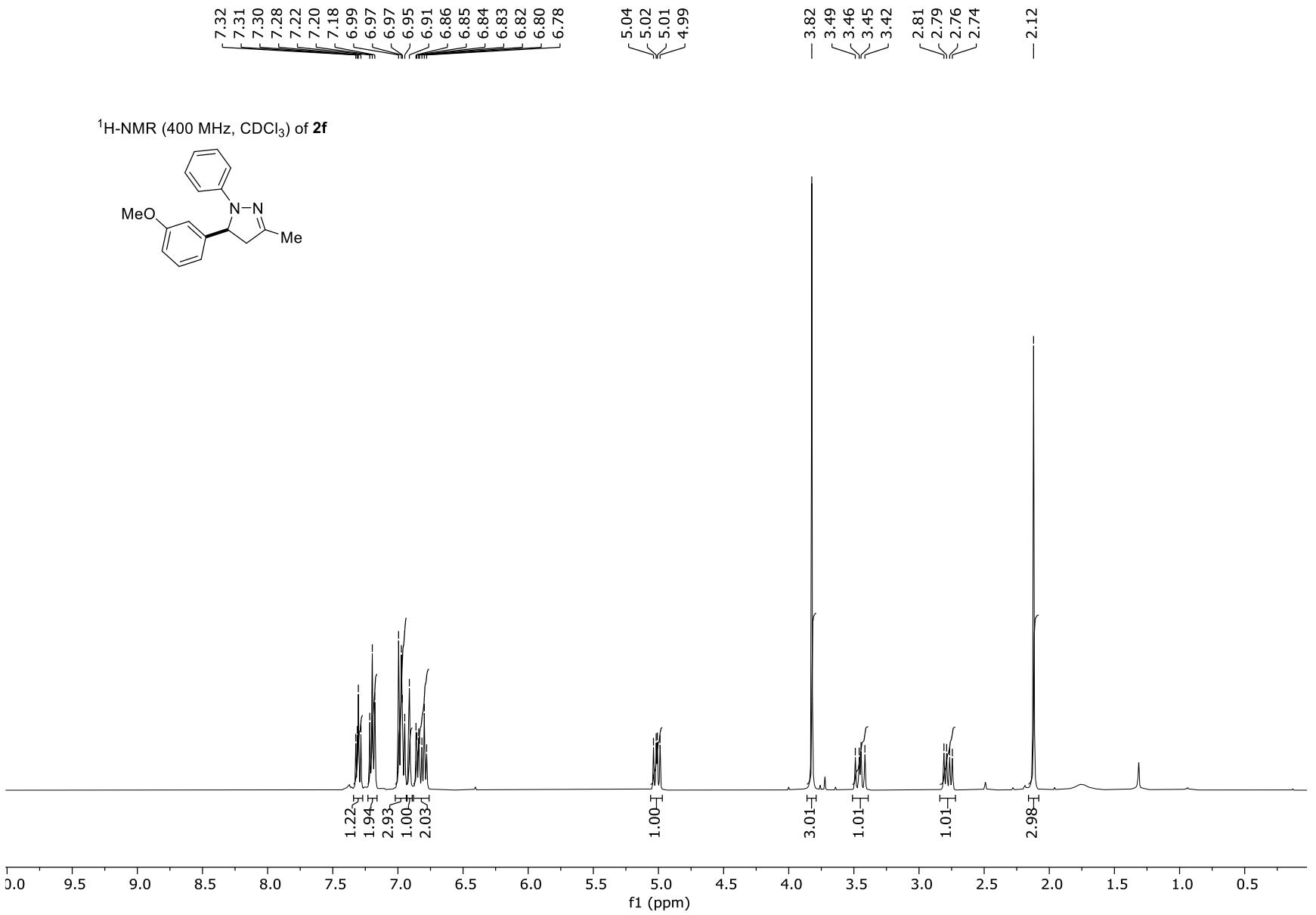


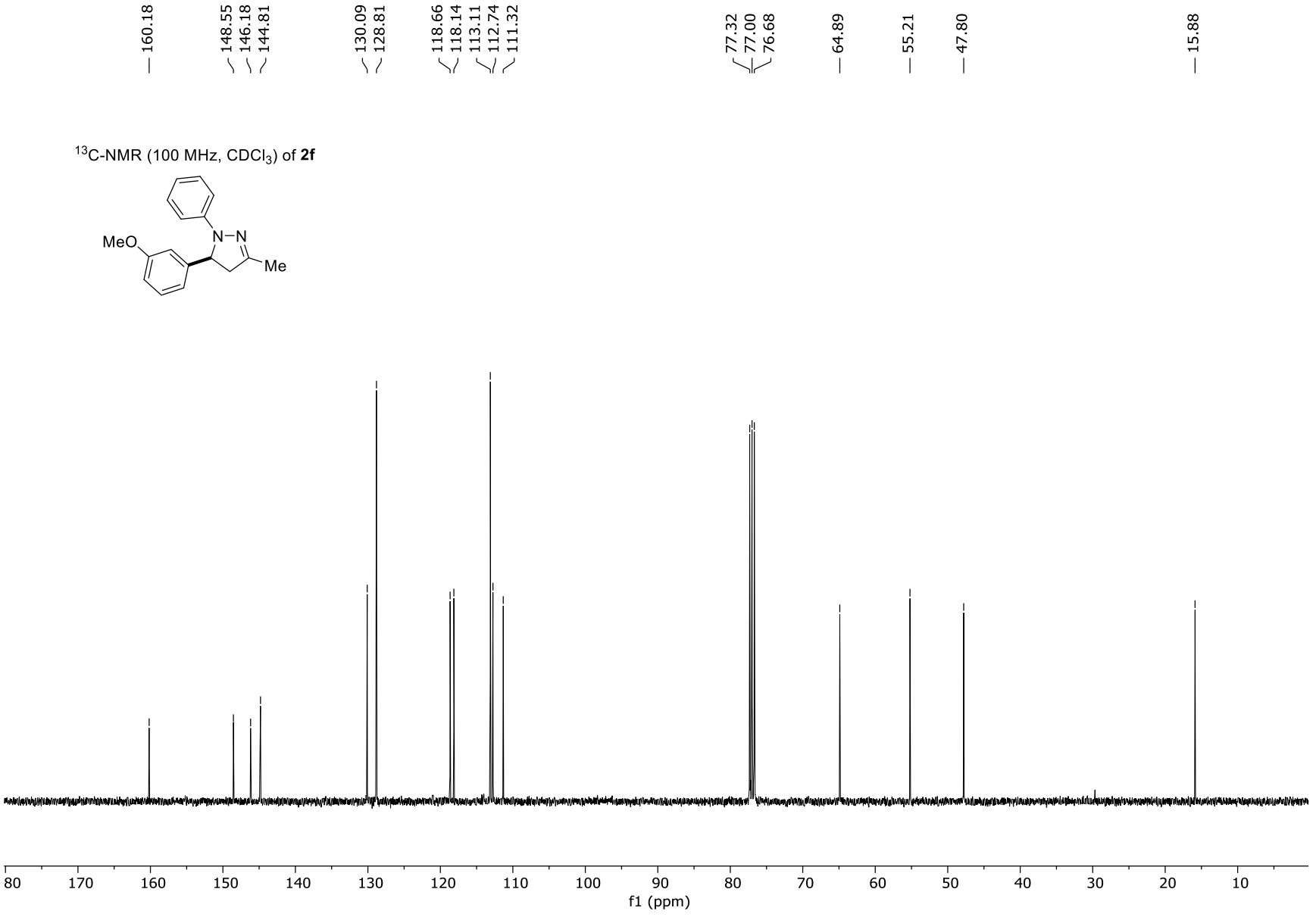
148.44
145.87
145.20
134.90
130.38
128.91
127.65
126.06
124.05
118.92
113.09
77.32
77.00
76.68
64.33
47.69
15.82

^{13}C-NMR (100 MHz, $CDCl_3$) of **2e**

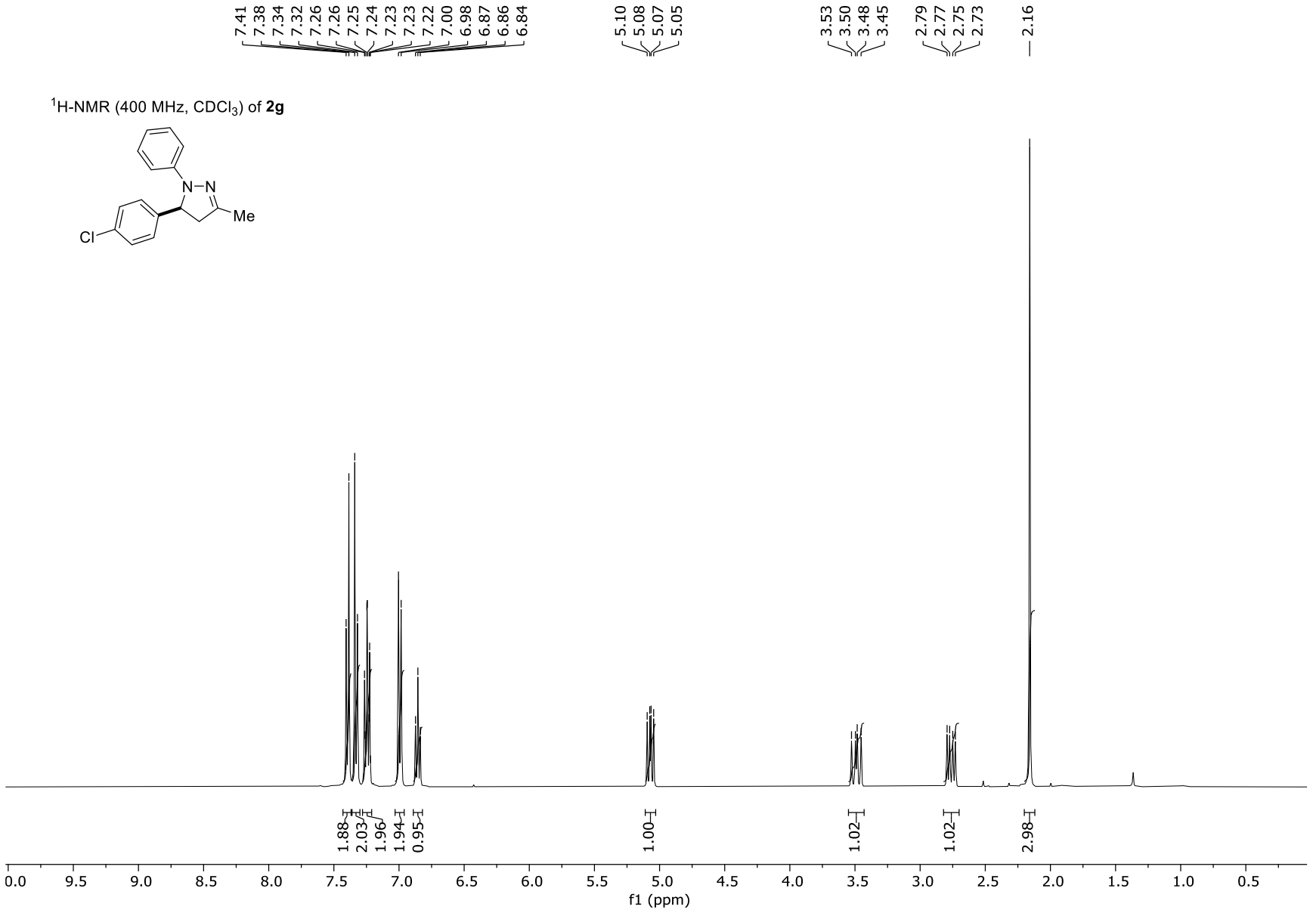




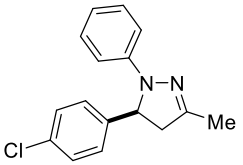

7.32
7.31
7.30
7.28
7.22
7.20
7.18
6.99
6.97
6.97
6.95
6.91
6.86
6.85
6.84
6.83
6.82
6.80
6.78
5.04
5.02
5.01
4.99
3.82
3.49
3.46
3.45
3.42
2.81
2.79
2.76
2.74
2.12
1H-NMR (400 MHz, CDCl3) of 2f
MeO
N–N
Me
1.22
1.94
2.93
1.00
2.03
1.00
3.01
1.01
1.01
2.98
f1 (ppm)



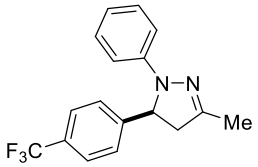
^{13}C-NMR (100 MHz, $CDCl_3$) of **2f**


7.41
7.38
7.34
7.32
7.26
7.26
7.25
7.24
7.23
7.23
7.22
7.00
6.98
6.87
6.86
6.84
5.10
5.08
5.07
5.05
3.53
3.50
3.48
3.45
2.79
2.77
2.75
2.73
2.16
1H-NMR (400 MHz, CDCl3) of 2g
N–N
Me
Cl
1.88
2.03
1.96
1.94
0.95
1.00
1.02
1.02
2.98
0.0
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
f1 (ppm)

^{13}C-NMR (100 MHz, $CDCl_3$) of **2g**

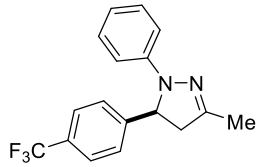


^{1}H-NMR (400 MHz, $CDCl_3$) of **2h**

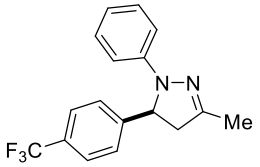


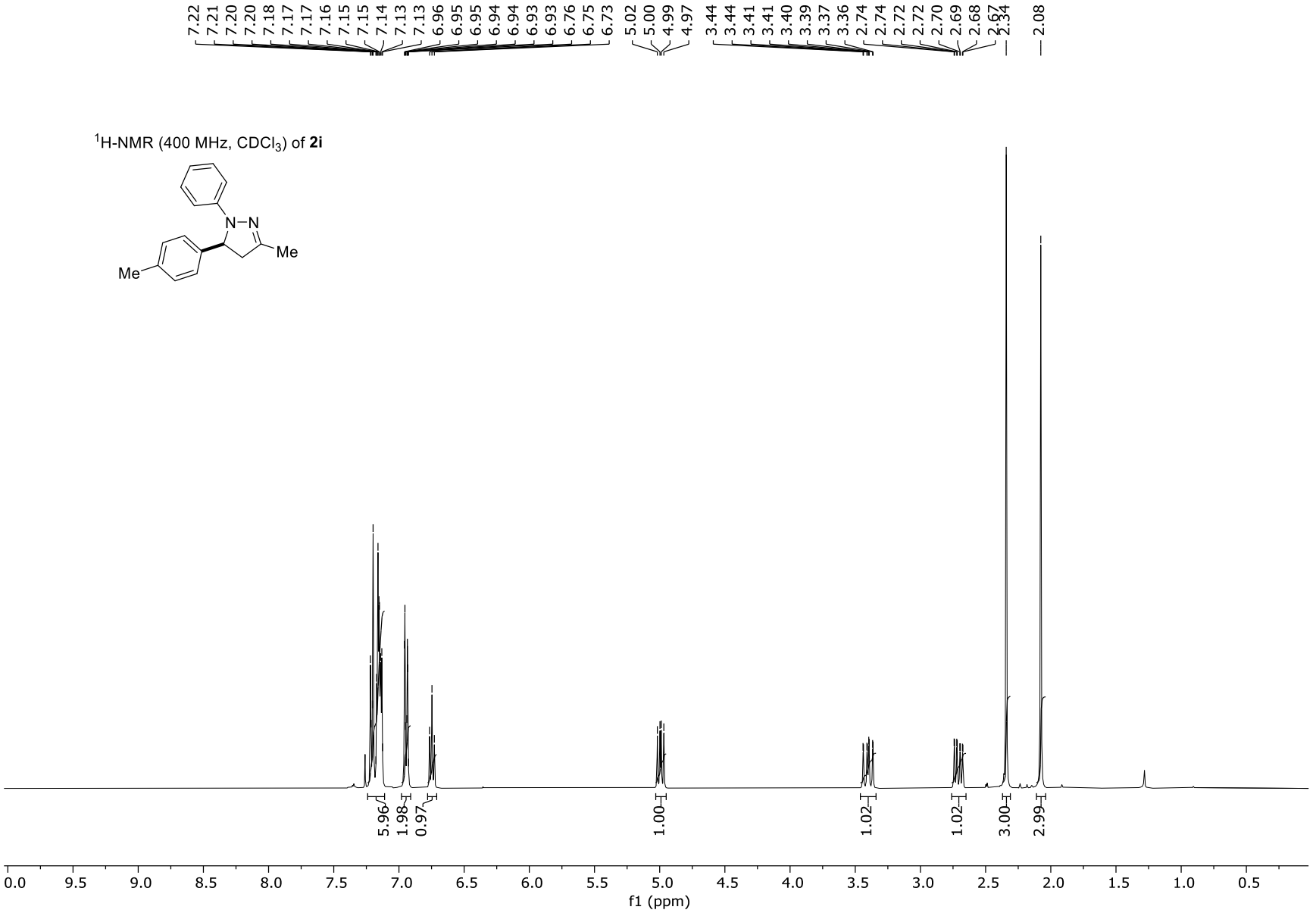
148.41
147.00
145.72
130.17
129.85
129.53
129.21
128.94
128.10
126.29
126.12
126.08
126.04
126.00
125.40
122.69
119.99
119.00
113.08
77.32
77.00
76.68
64.28
47.55
15.78

^{13}C-NMR (100 MHz, $CDCl_3$) of **2h**



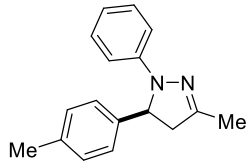
^{19}F-NMR (377 MHz, $CDCl_3$) of **2h**



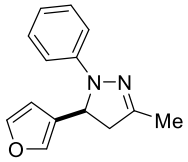

7.22
7.21
7.20
7.20
7.18
7.17
7.17
7.16
7.15
7.15
7.14
7.13
7.13
6.96
6.95
6.95
6.94
6.94
6.93
6.93
6.76
6.75
6.73
5.02
5.00
4.99
4.97
3.44
3.44
3.41
3.41
3.40
3.39
3.37
3.36
2.74
2.74
2.72
2.72
2.70
2.69
2.68
2.67
2.34
2.08
1H-NMR (400 MHz, CDCl3) of 2i
N–N
Me
Me
5.96
1.98
0.97
1.00
1.02
1.02
3.00
2.99
0.0
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
f1 (ppm)

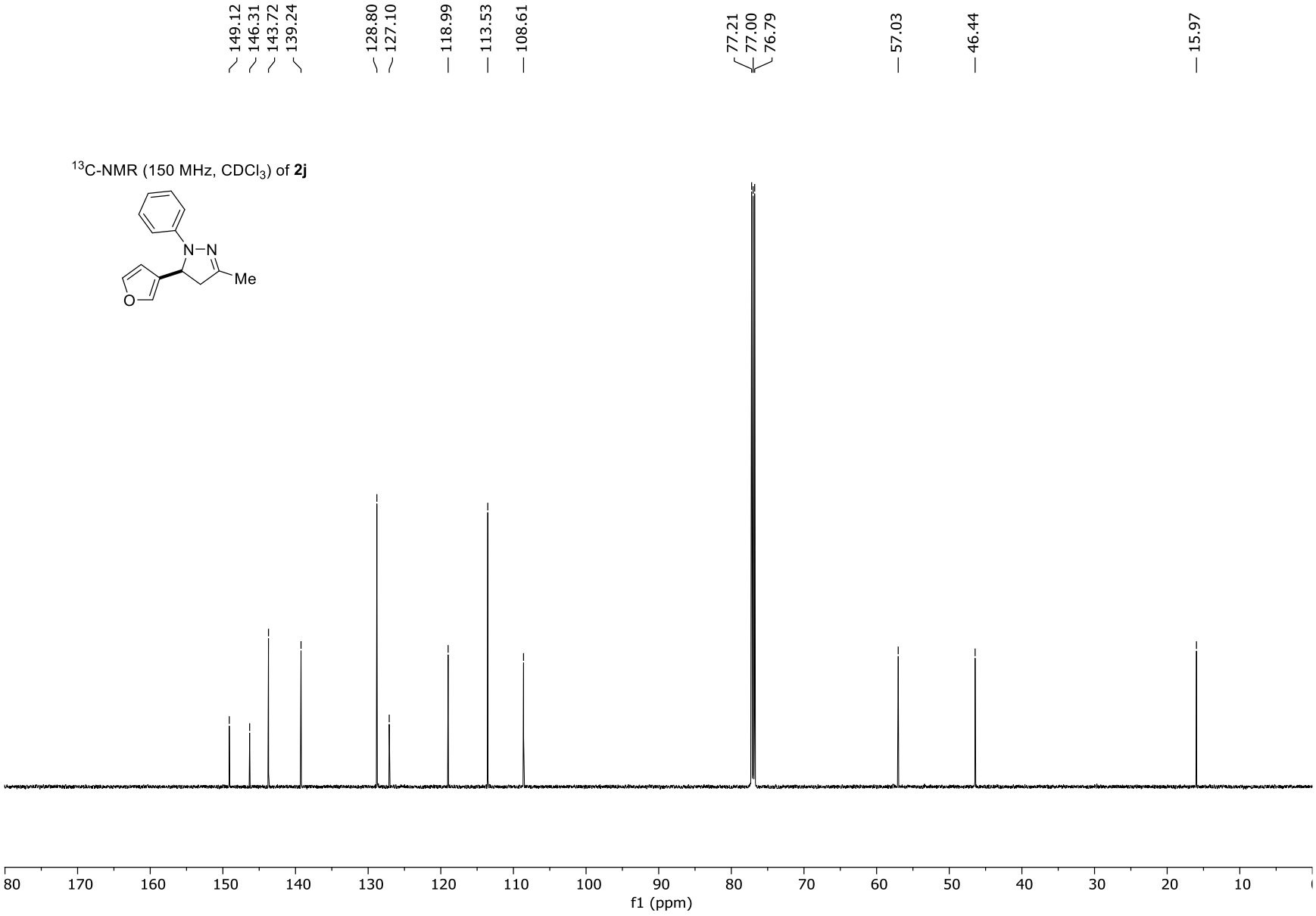
148.49
146.09
140.02
136.96
129.66
128.79
125.78
118.50
113.05
77.32
77.00
76.68
64.52
47.87
21.06
15.90

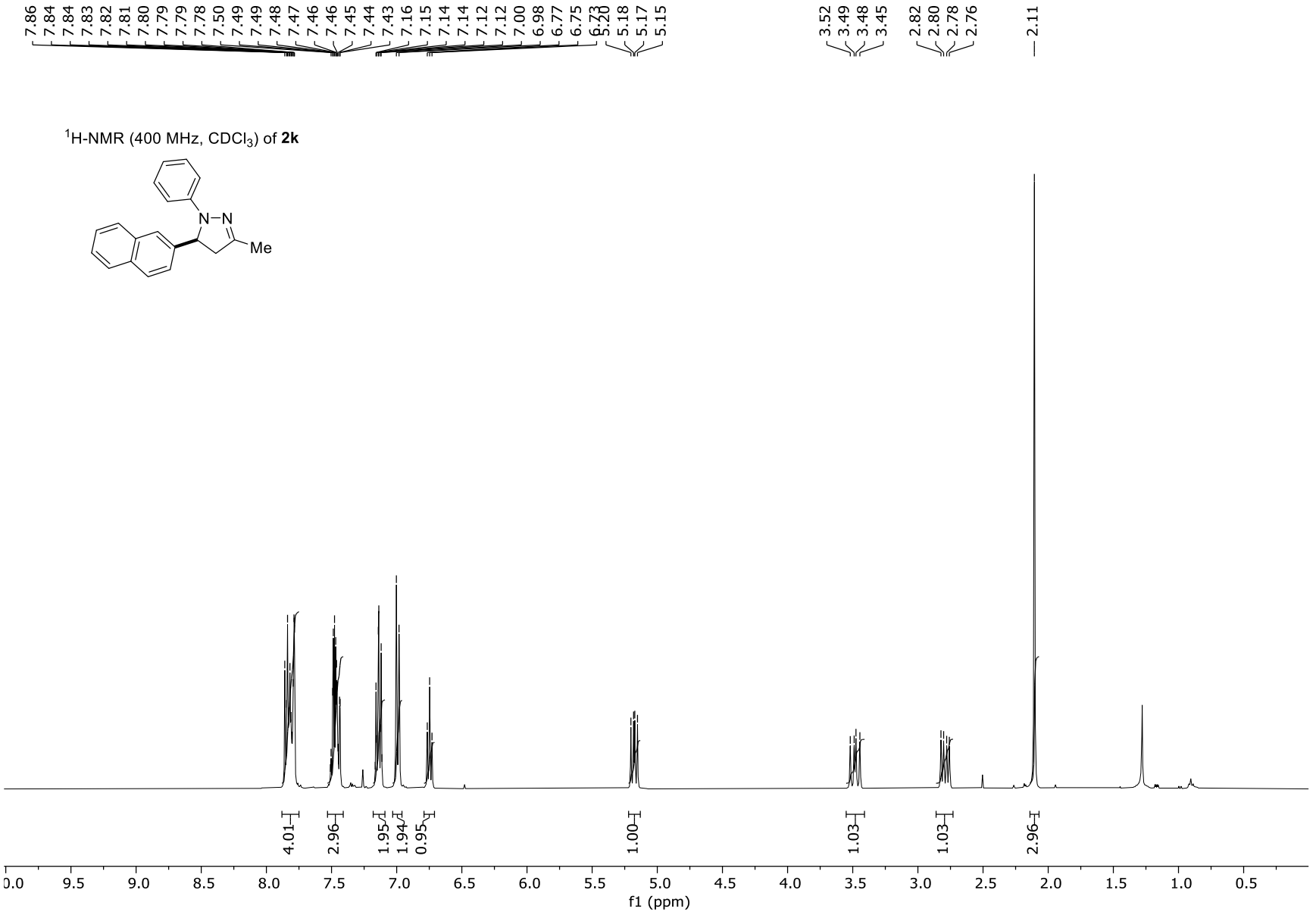
^{13}C-NMR (100 MHz, $CDCl_3$) of **2i**



^{1}H-NMR (600 MHz, $CDCl_3$) of **2j**

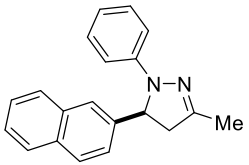


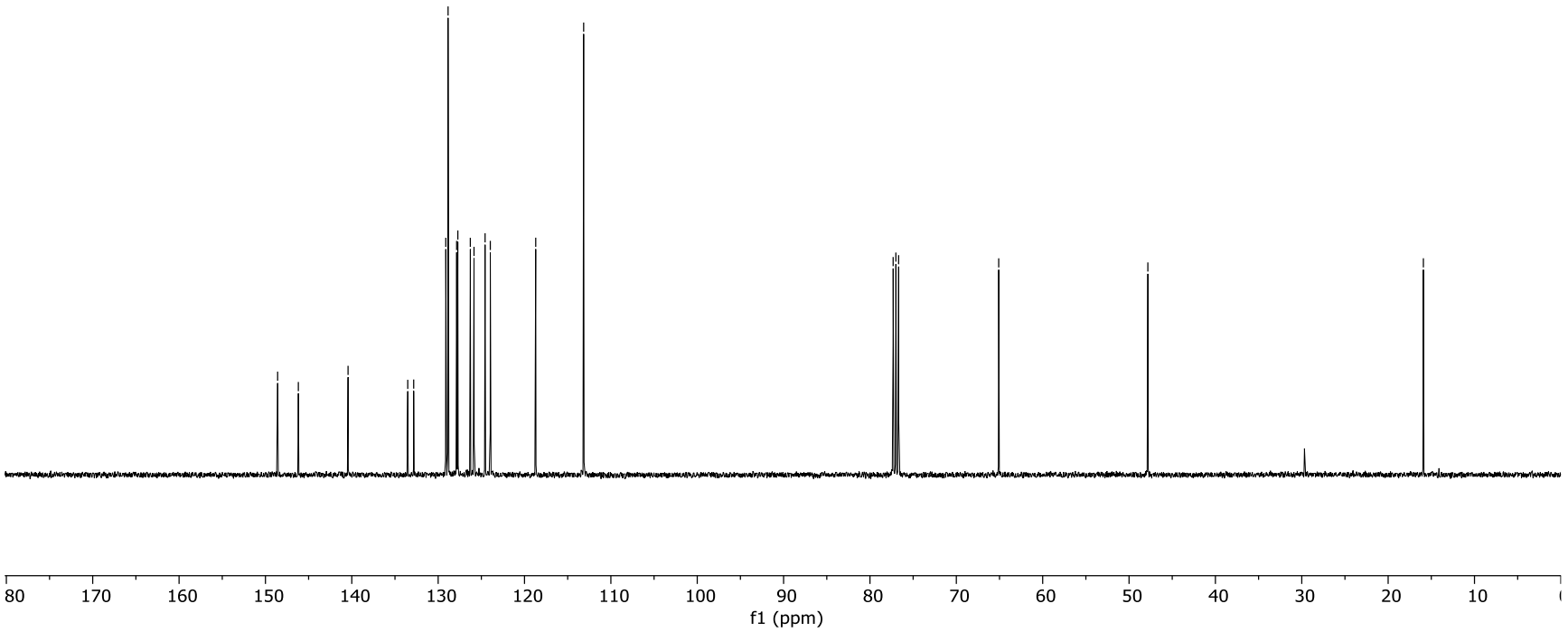

149.12
146.31
143.72
139.24
128.80
127.10
118.99
113.53
108.61
77.21
77.00
76.79
57.03
46.44
15.97
13C-NMR (150 MHz, CDCl3) of 2j
N–N
Me
O
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

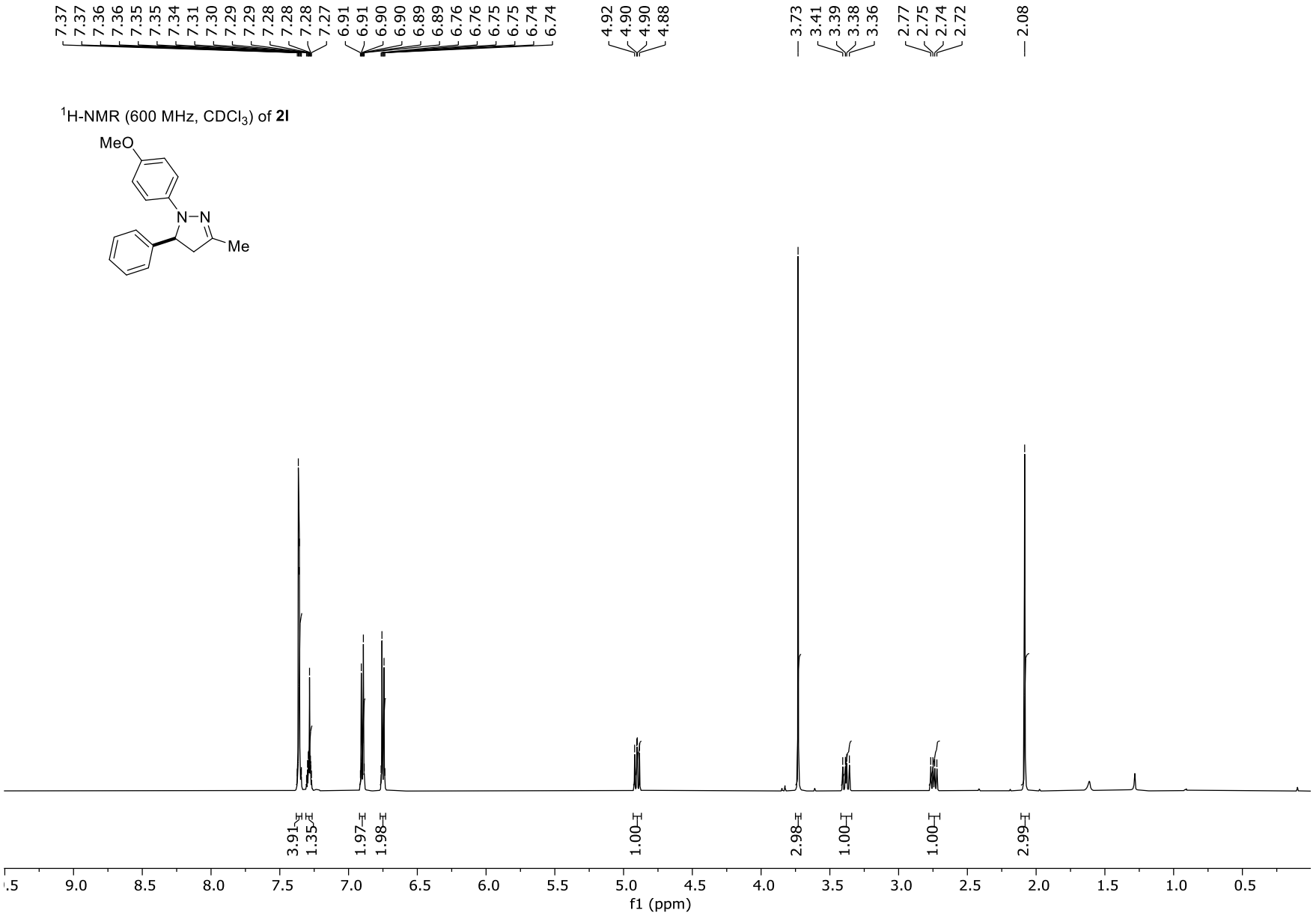

7.86
7.84
7.84
7.83
7.82
7.81
7.80
7.79
7.79
7.78
7.50
7.49
7.49
7.48
7.47
7.46
7.46
7.45
7.44
7.43
7.16
7.15
7.14
7.14
7.12
7.12
7.00
6.98
6.77
6.75
5.18
5.17
5.15
3.52
3.49
3.48
3.45
2.82
2.80
2.78
2.76
2.11
1H-NMR (400 MHz, CDCl3) of 2k
N–N
Me
4.01
2.96
1.95
1.94
0.95
1.00
1.03
1.03
2.96
f1 (ppm)

148.59
146.19
140.43
133.52
132.83
129.12
128.85
127.86
127.72
126.28
125.85
124.57
123.96
118.70
113.15
77.32
77.00
76.68
65.09
47.82
15.92

^{13}C-NMR (100 MHz, $CDCl_3$) of **2k**

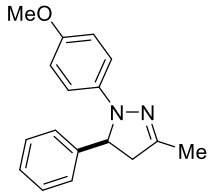


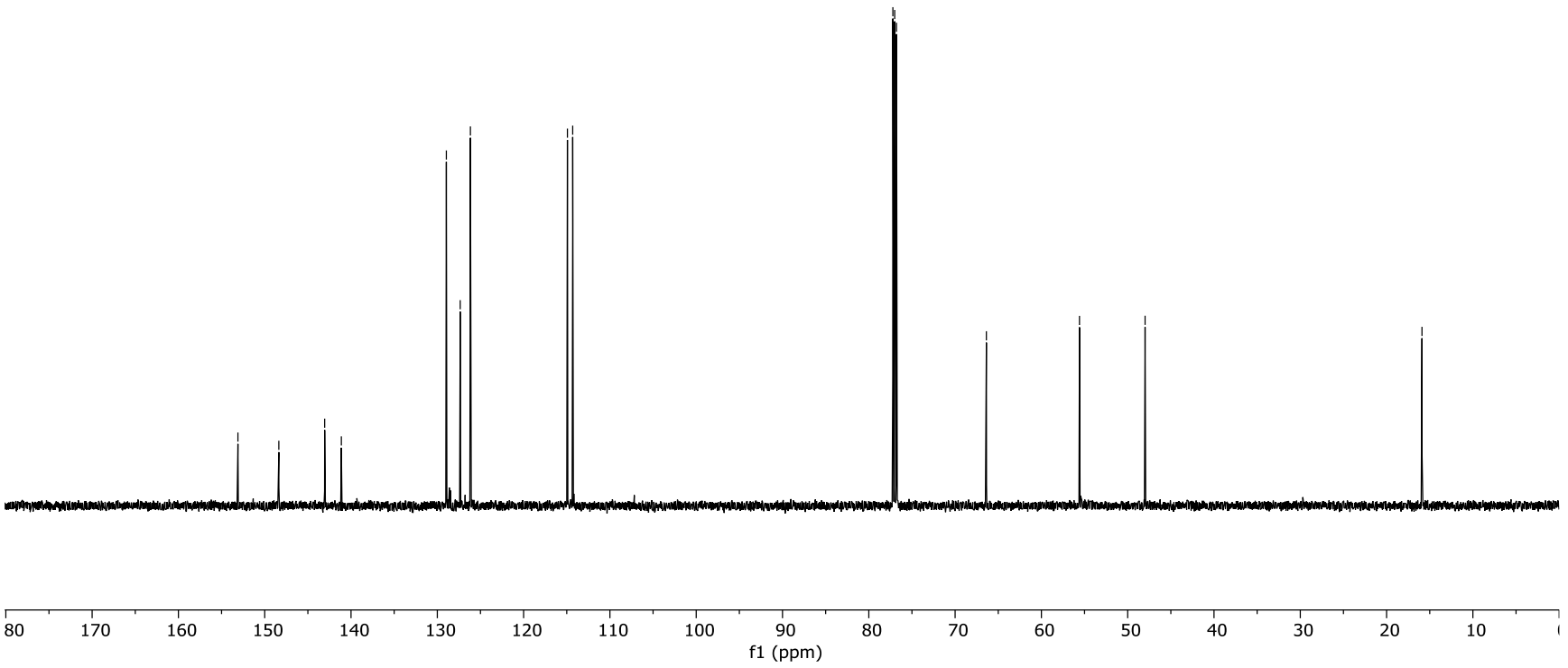


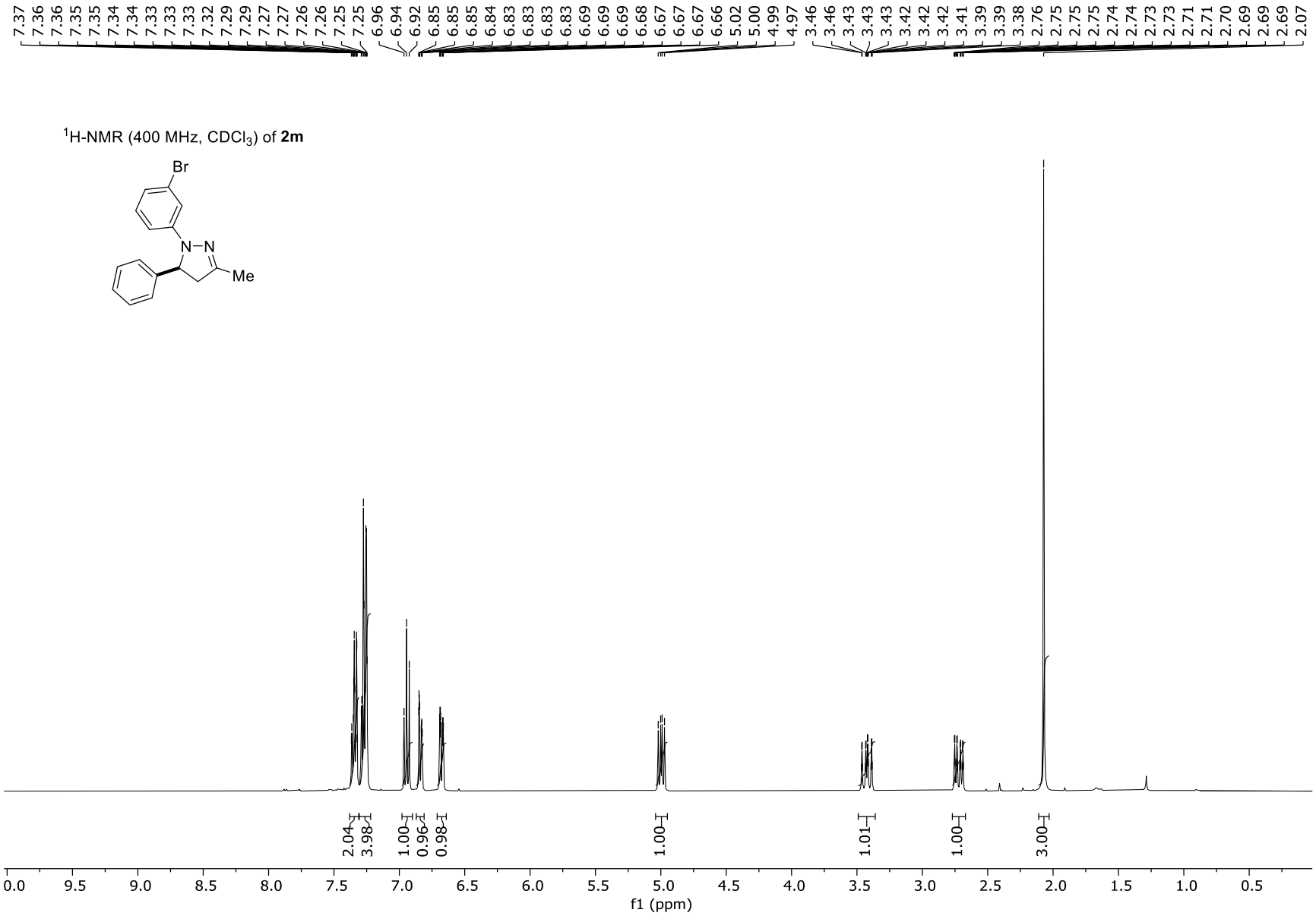

7.37
7.37
7.36
7.36
7.35
7.35
7.34
7.31
7.30
7.29
7.29
7.28
7.28
7.28
7.27
6.91
6.91
6.90
6.90
6.89
6.89
6.76
6.76
6.75
6.75
6.74
6.74
4.92
4.90
4.90
4.88
3.73
3.41
3.39
3.38
3.36
2.77
2.75
2.74
2.72
2.08
1H-NMR (600 MHz, CDCl3) of 2l
MeO
N–N
Me
3.91
1.35
1.97
1.98
1.00
2.98
1.00
1.00
2.99
f1 (ppm)

153.10
148.36
143.05
141.12
128.95
127.35
126.17
114.92
114.31
77.21
77.00
76.79
66.37
55.59
47.98
15.90

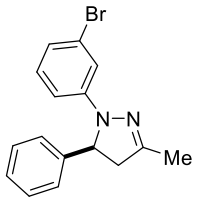
^{1}H-NMR (150 MHz, $CDCl_3$) of **2l**

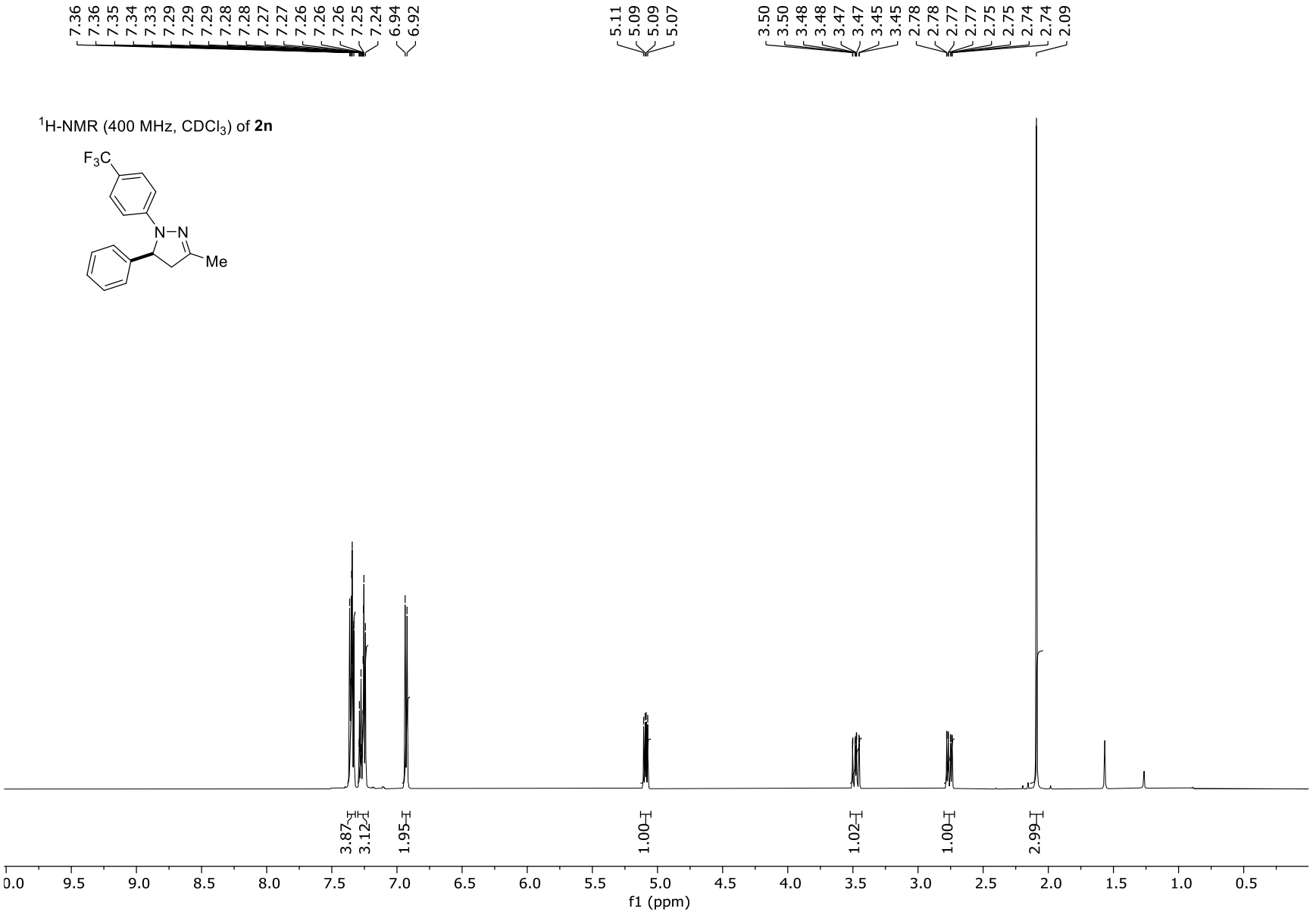


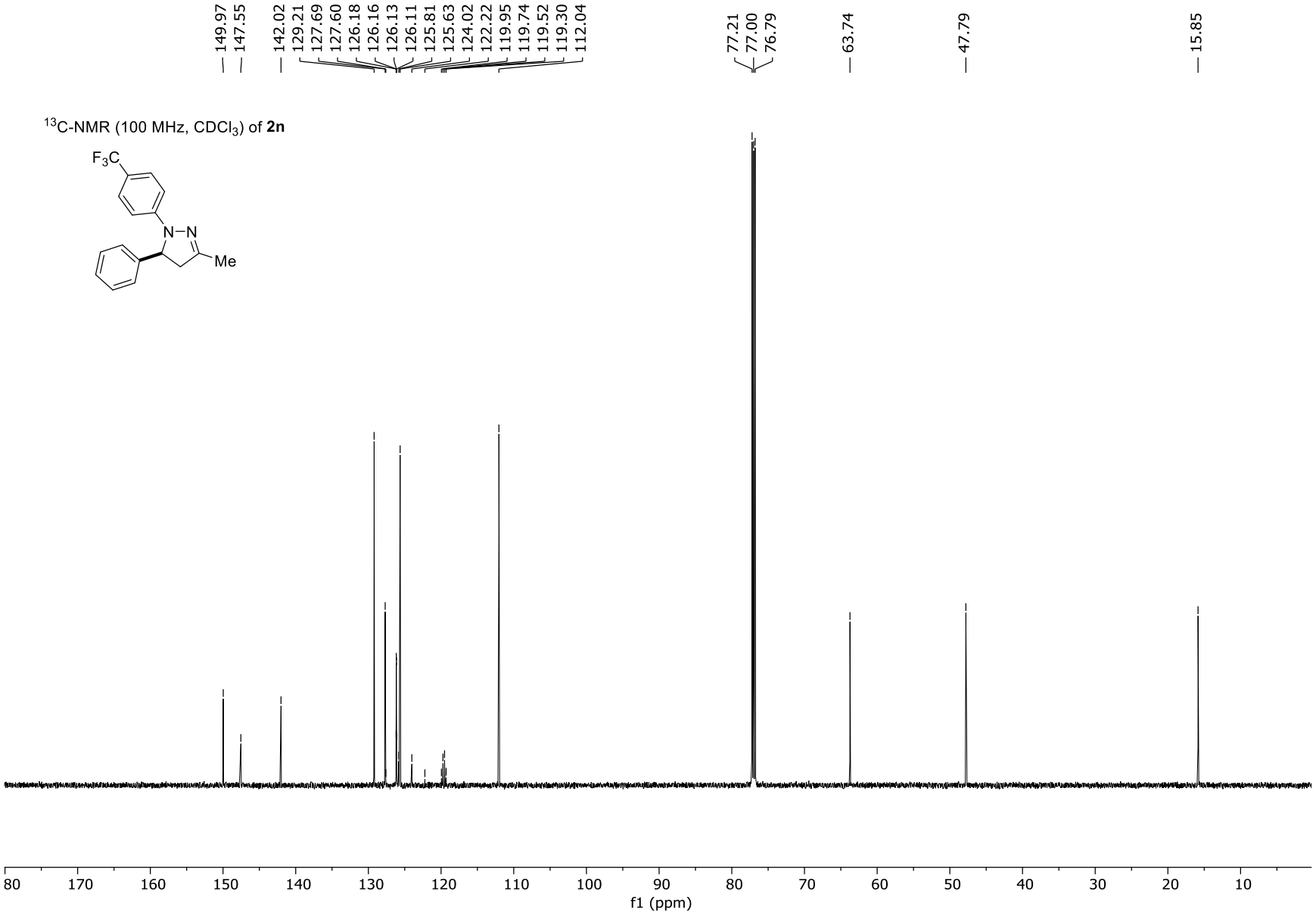



7.37 7.36 7.36 7.35 7.35 7.34 7.34 7.33 7.33 7.33 7.32 7.29 7.29 7.27 7.27 7.26 7.26 7.25 7.25 6.96 6.94 6.92 6.85 6.85 6.85 6.84 6.83 6.83 6.83 6.83 6.69 6.69 6.69 6.68 6.67 6.67 6.67 6.66 5.02 5.00 4.99 4.97 3.46 3.46 3.43 3.43 3.43 3.42 3.42 3.42 3.41 3.39 3.39 3.38 2.76 2.75 2.75 2.75 2.74 2.74 2.73 2.73 2.71 2.71 2.70 2.69 2.69 2.69 2.07
^{1}H-NMR (400 MHz, $CDCl_3$) of **2m**
Br
N–N
Me
2.04
3.98
1.00
0.96
0.98
1.00
1.01
1.00
3.00
0.0 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
f1 (ppm)

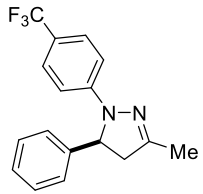
^{13}C-NMR (100 MHz, $CDCl_3$) of **2m**

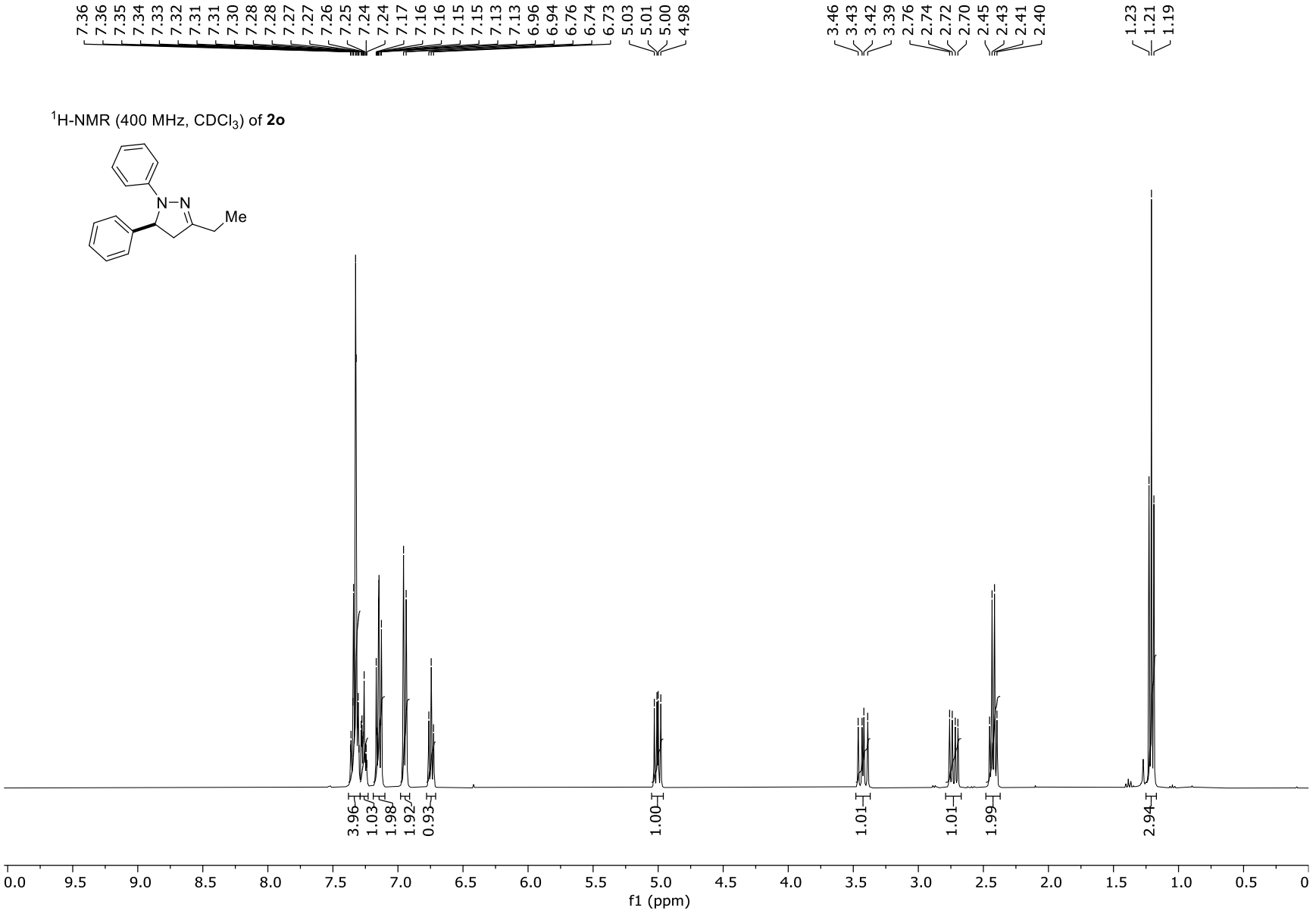



7.36
7.36
7.35
7.34
7.33
7.29
7.29
7.29
7.28
7.28
7.27
7.27
7.26
7.26
7.26
7.25
7.24
6.94
6.92
5.11
5.09
5.09
5.07
3.50
3.50
3.48
3.48
3.47
3.47
3.45
3.45
2.78
2.78
2.77
2.77
2.75
2.75
2.74
2.74
2.09
1H-NMR (400 MHz, CDCl3) of 2n
F3C
N–N
Me
3.87
3.12
1.95
1.00
1.02
1.00
2.99
f1 (ppm)

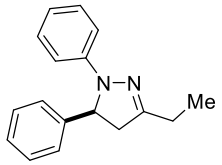

149.97
147.55
142.02
129.21
127.69
127.60
126.18
126.16
126.13
126.11
125.81
125.63
124.02
122.22
119.95
119.74
119.52
119.30
112.04
77.21
77.00
76.79
63.74
47.79
15.85
13C-NMR (100 MHz, CDCl3) of 2n
F3C
N–N
Me
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

^{19}F-NMR (377 MHz, $CDCl_3$) of **2n**

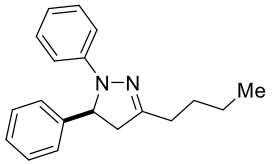



7.36
7.36
7.35
7.34
7.33
7.32
7.31
7.31
7.30
7.28
7.28
7.27
7.27
7.26
7.25
7.24
7.24
7.17
7.16
7.16
7.15
7.15
7.13
7.13
6.96
6.94
6.76
6.74
6.73
5.03
5.01
5.00
4.98
3.46
3.43
3.42
3.39
2.76
2.74
2.72
2.70
2.45
2.43
2.41
2.40
1.23
1.21
1.19
1H-NMR (400 MHz, CDCl3) of 2o
N–N
Me
3.96
1.03
1.98
1.92
0.93
1.00
1.01
1.01
1.99
2.94
0.0
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
f1 (ppm)

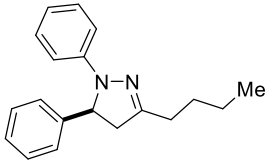
^{13}C-NMR (100 MHz, $CDCl_3$) of **2o**



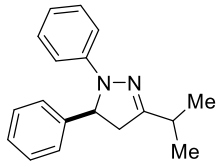
^{1}H-NMR (400 MHz, $CDCl_3$) of **2p**

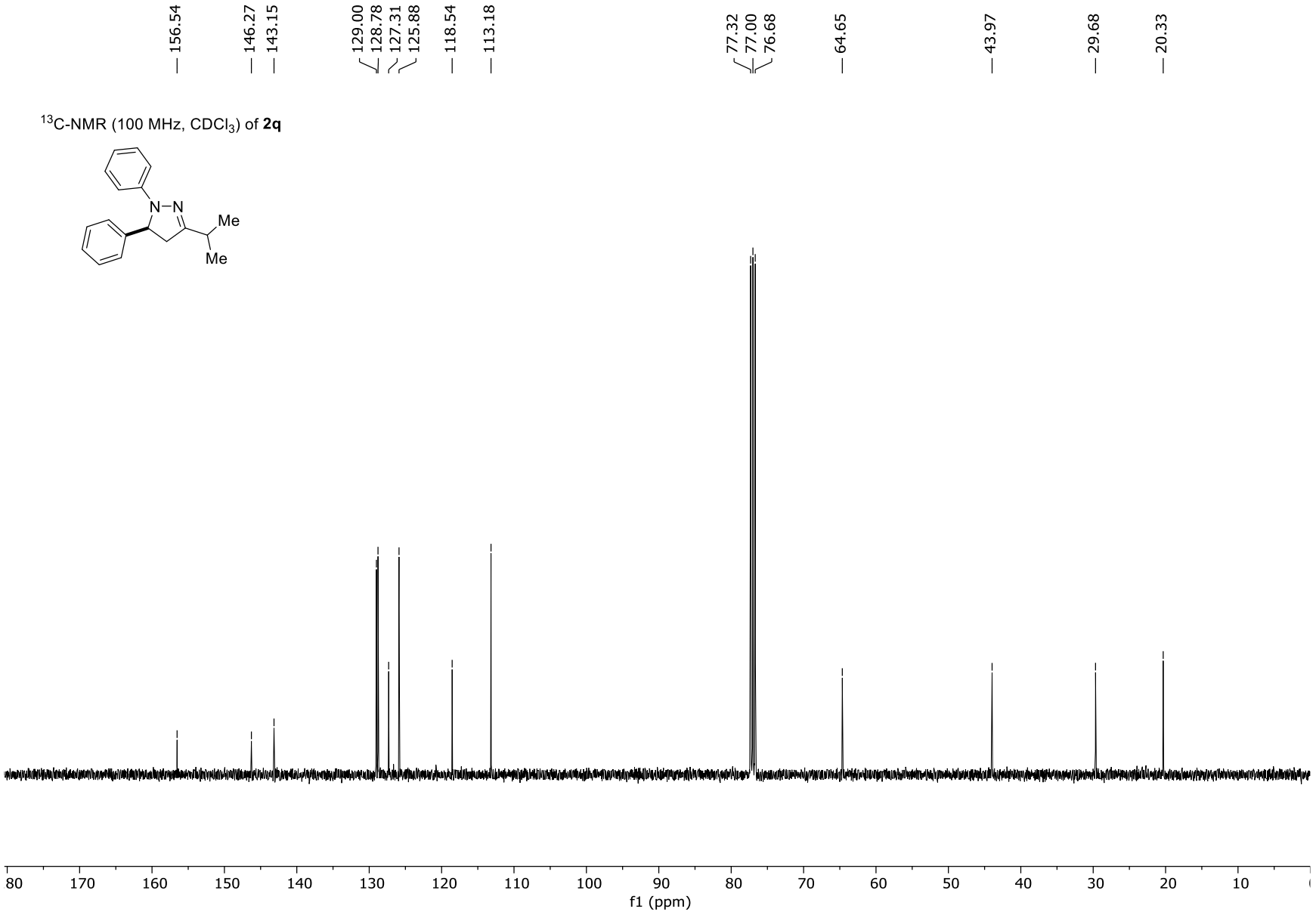


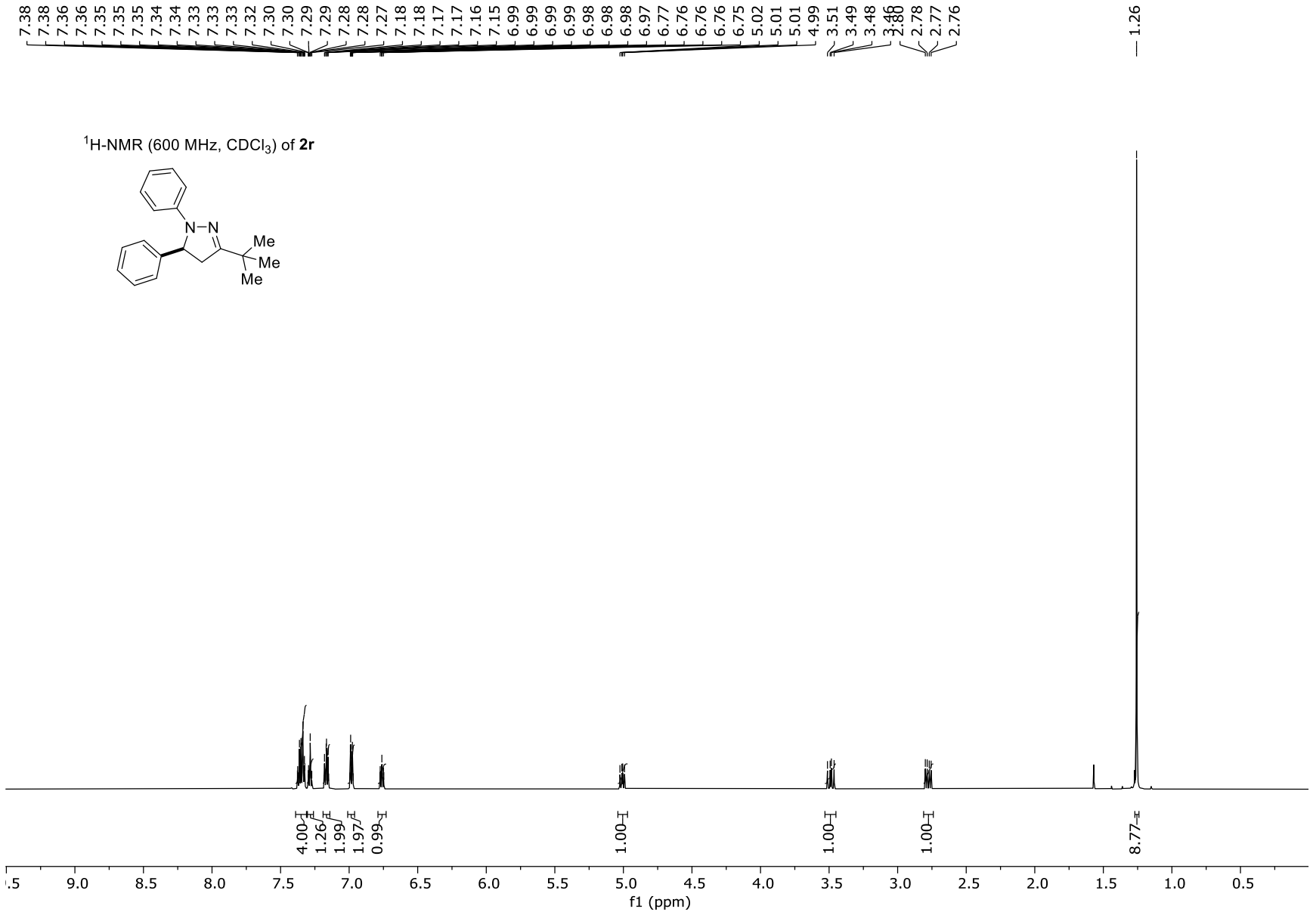
^{13}C-NMR (100 MHz, $CDCl_3$) of **2p**

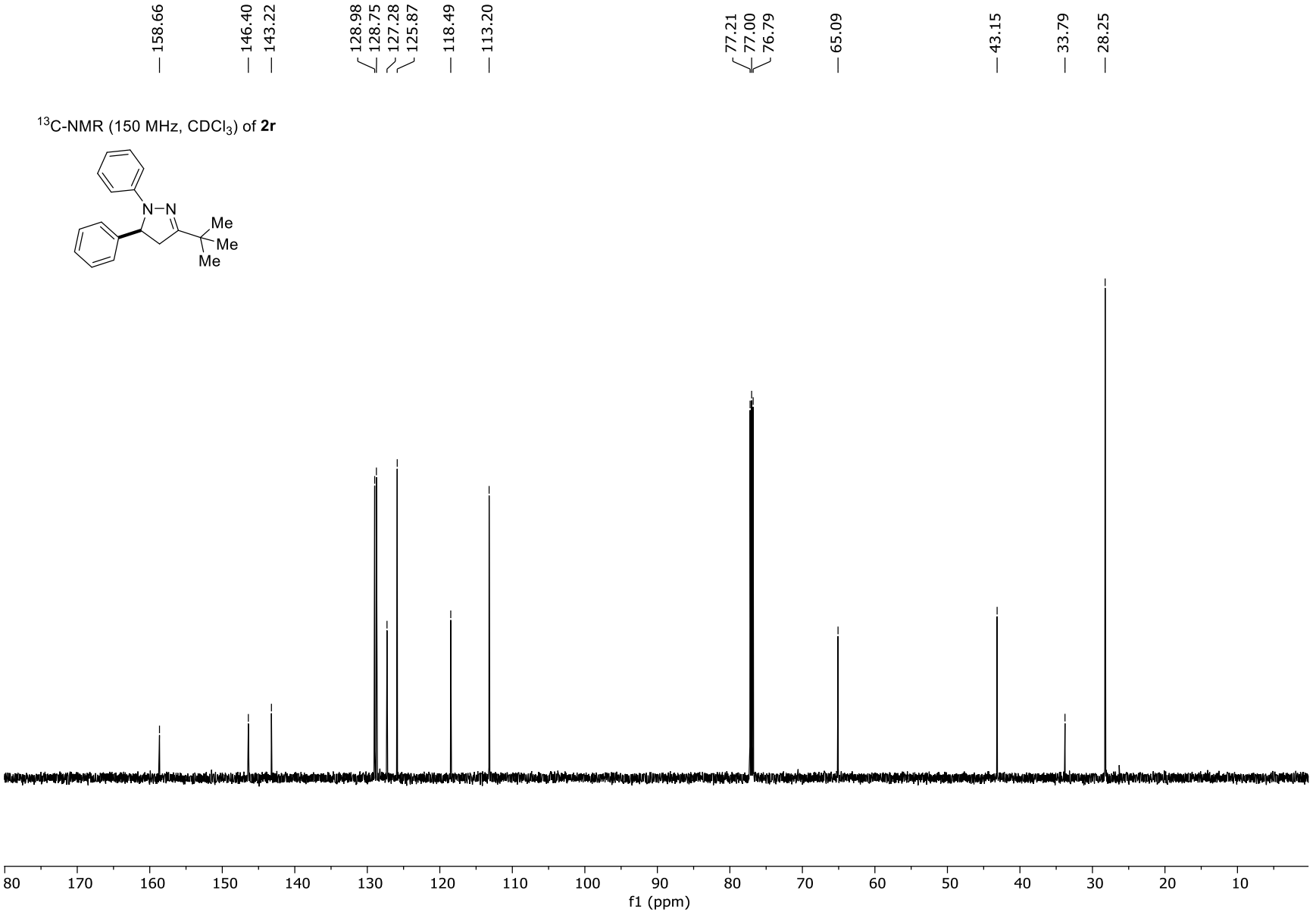


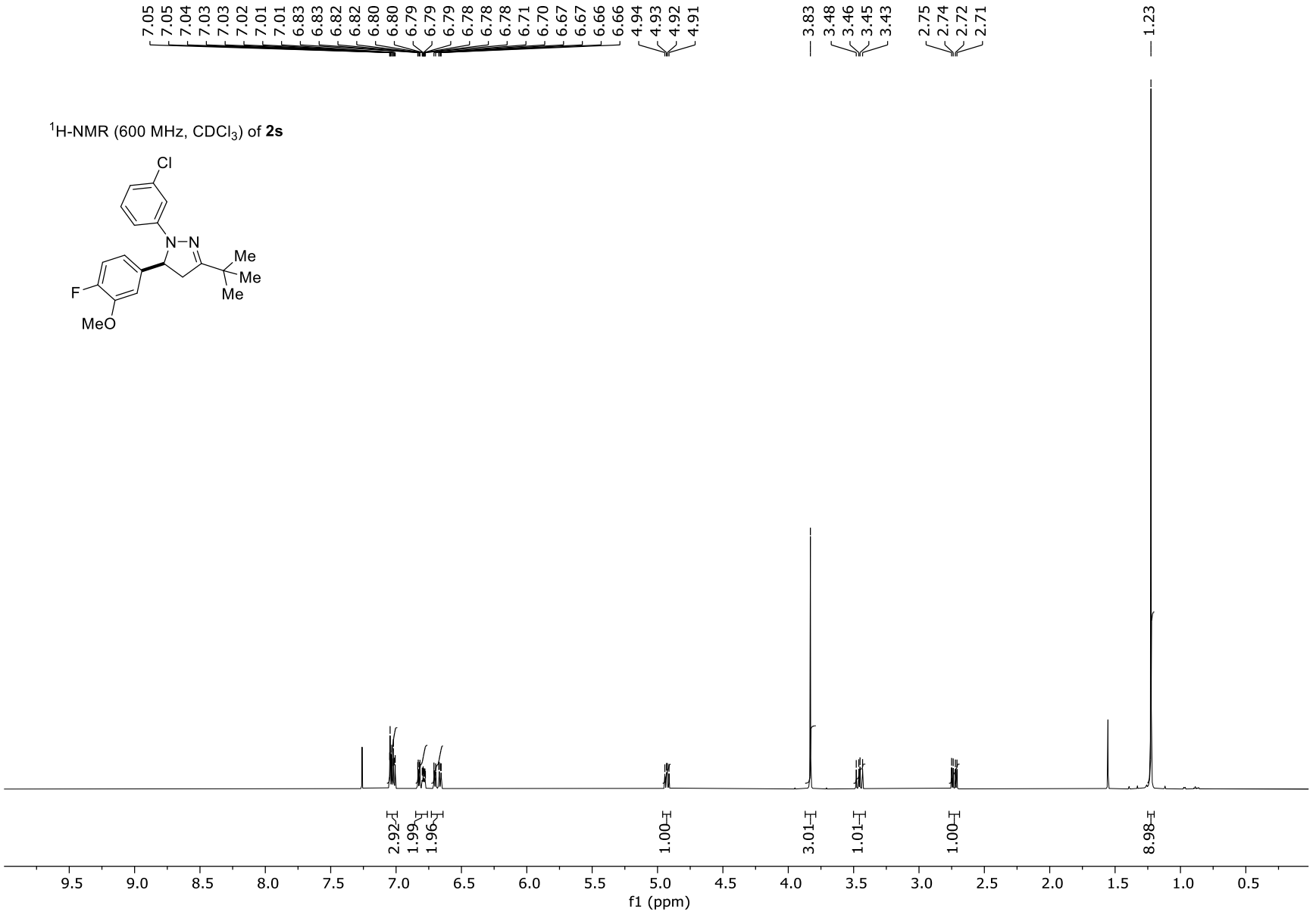
^{1}H-NMR (400 MHz, $CDCl_3$) of **2q**




156.54
146.27
143.15
129.00
128.78
127.31
125.88
118.54
113.18
77.32
77.00
76.68
64.65
43.97
29.68
20.33
^{13}C-NMR (100 MHz, $CDCl_3$) of **2q**
N–N
Me
Me
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

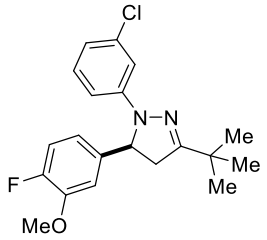

7.38
7.38
7.36
7.36
7.35
7.35
7.35
7.34
7.34
7.33
7.33
7.33
7.32
7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.18
7.18
7.17
7.17
7.16
7.15
6.99
6.99
6.99
6.99
6.98
6.98
6.98
6.97
6.77
6.76
6.76
6.76
6.75
5.02
5.01
5.01
4.99
3.51
3.49
3.48
3.46
3.46
2.80
2.78
2.77
2.76
1.26
1H-NMR (600 MHz, CDCl3) of 2r
N–N
Me
Me
Me
4.00
1.26
1.99
1.97
0.99
1.00
1.00
1.00
8.77
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)


158.66
146.40
143.22
128.98
128.75
127.28
125.87
118.49
113.20
77.21
77.00
76.79
65.09
43.15
33.79
28.25
13C-NMR (150 MHz, CDCl3) of 2r
N–N
Me
Me
Me
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

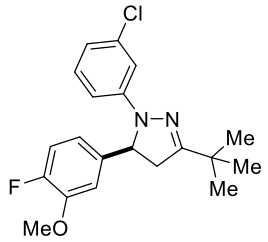

7.05
7.05
7.04
7.03
7.03
7.02
7.01
7.01
6.83
6.83
6.82
6.82
6.80
6.80
6.79
6.79
6.79
6.78
6.78
6.78
6.71
6.70
6.67
6.67
6.66
6.66
4.94
4.93
4.92
4.91
3.83
3.48
3.46
3.45
3.43
2.75
2.74
2.72
2.71
1.23
1H-NMR (600 MHz, CDCl3) of 2s
Cl
N–N
Me
Me
Me
F
MeO
2.92
1.99
1.96
1.00
3.01
1.01
1.00
8.98
9.5
9.0
8.5
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)

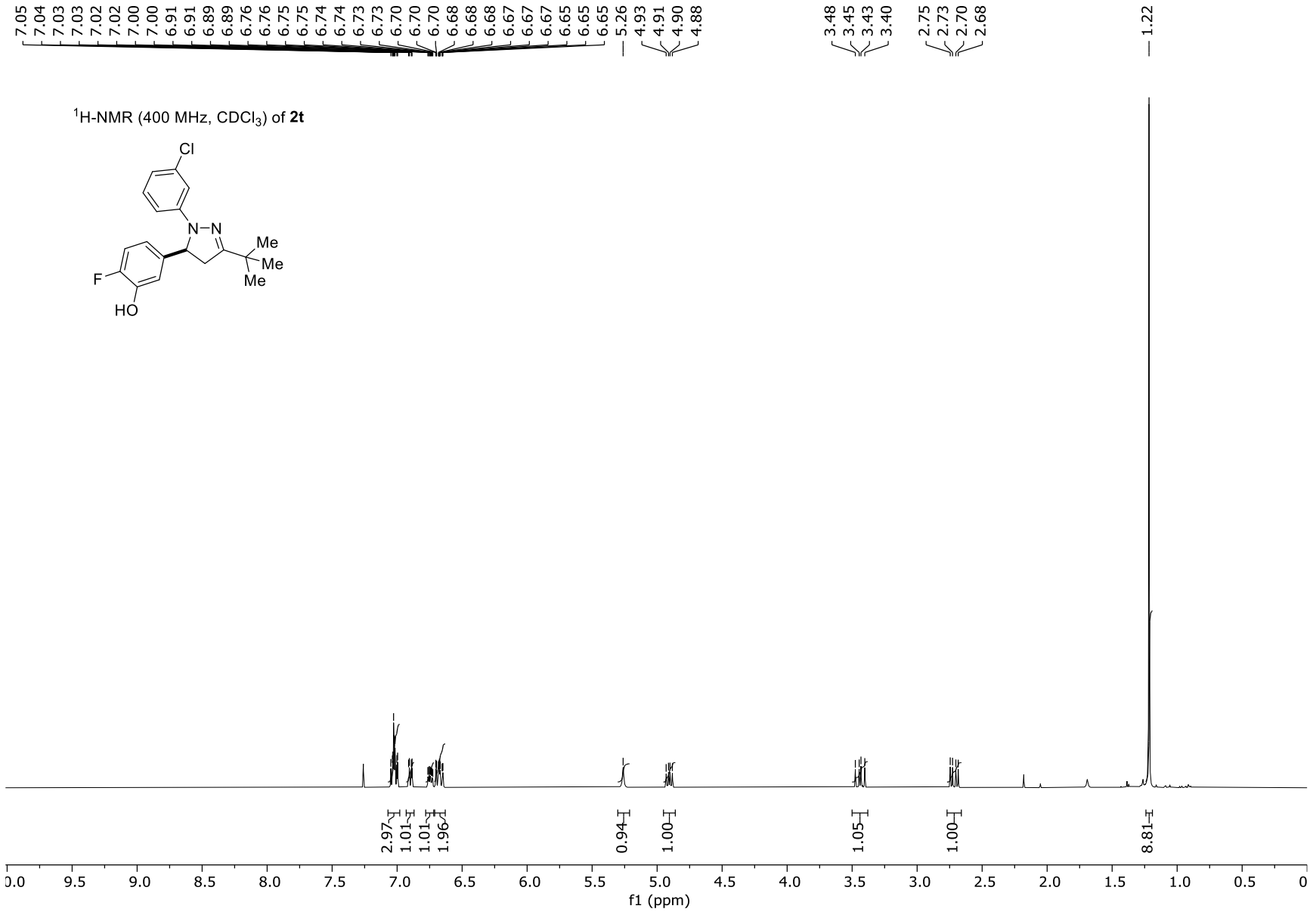
159.75
152.50
150.87
148.29
148.22
147.07
138.88
138.85
134.62
129.77
118.48
117.96
117.91
116.52
116.40
113.30
110.97
110.47
110.45
77.21
77.00
76.79
64.39
56.26
43.22
33.86
28.21

^{13}C-NMR (150 MHz, $CDCl_3$) of **2s**



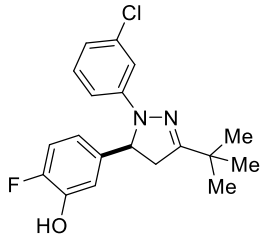
^{19}F-NMR (377 MHz, $CDCl_3$) of **2s**



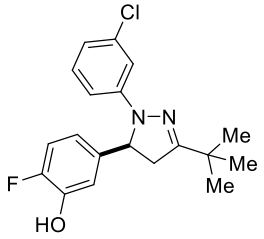

7.05
7.04
7.03
7.03
7.02
7.02
7.00
7.00
6.91
6.91
6.89
6.89
6.76
6.76
6.75
6.75
6.74
6.74
6.73
6.73
6.70
6.70
6.70
6.68
6.68
6.68
6.67
6.67
6.67
6.65
6.65
5.26
4.93
4.91
4.90
4.88
3.48
3.45
3.43
3.40
2.75
2.73
2.70
2.68
1.22
1H-NMR (400 MHz, CDCl3) of 2t
Cl
N–N
Me
Me
Me
F
HO
2.97
1.01
1.01
1.96
0.94
1.00
1.05
1.00
8.81
f1 (ppm)

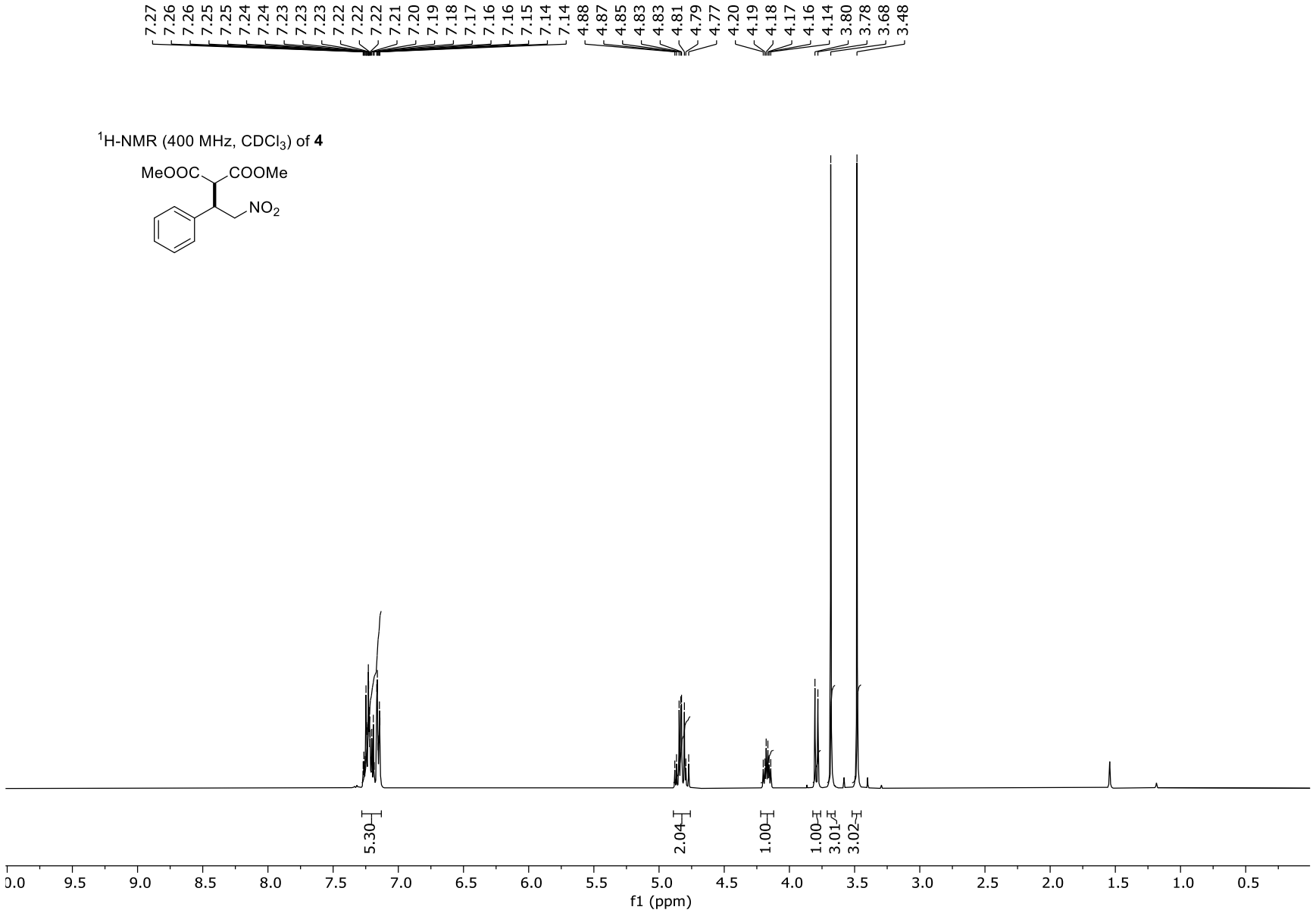
159.57
151.05
149.48
146.85
144.05
143.96
139.54
139.51
134.60
129.75
118.32
117.89
117.85
116.14
116.02
114.50
114.49
113.18
110.88
77.21
77.00
76.79
63.84
43.10
33.82
28.19

^{13}C-NMR (150 MHz, $CDCl_3$) of **2t**



^{19}F-NMR (377 MHz, $CDCl_3$) of **2t**




7.27
7.26
7.26
7.25
7.25
7.24
7.24
7.23
7.23
7.23
7.22
7.22
7.22
7.21
7.20
7.19
7.18
7.17
7.16
7.16
7.15
7.14
7.14
4.88
4.87
4.85
4.83
4.83
4.81
4.79
4.77
4.20
4.19
4.18
4.17
4.16
4.14
3.80
3.78
3.68
3.48
^{1}H-NMR (400 MHz, $CDCl_3$) of **4**
MeOOC
COOMe
NO_2
5.30
2.04
1.00
1.00
3.01
3.02
f1 (ppm)

^{13}C-NMR (100 MHz, $CDCl_3$) of **4**