Catalytic asymmetric conjugate addition of terminal alkynes to β-trifluoromethyl α,β-enones†

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SUPPORTING INFORMATION

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General Experimental Methods

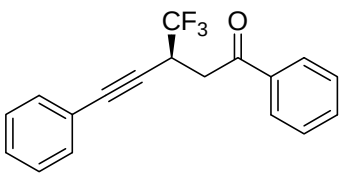
Reactions were carried out under nitrogen in round bottom flasks oven-dried overnight at 120 ºC. Commercial reagents were used as purchased. β-Trifluoromethyl-α,β-enones **1** were prepared from the corresponding substituted acetophenones and trifluoroacetaldehyde hemiacetal as described in the literature.[1] Toluene was distilled from CaH_2. Tetrahydrofuran (THF) was distilled from Na. Triethylamine was dried and stored on 4 Å molecular sieves. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm. Melting points were determined in capillary tubes. NMR spectra were run at 300 MHz for ^{1}H and at 75 MHz for ^{13}C NMR using residual nondeuterated solvent ($CHCl_3$) as internal standard (δ 7.26 and 77.0 ppm, respectively), and at 282 MHz for ^{19}F NMR using $CFCl_3$ as internal standard. Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments. High resolution mass spectra (ESI) were recorded on a Q-TOF spectrometer equipped with an electrospray source with a capillary voltage of 3.3 kV (ESI). Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC analyses were performed in a chromatograph equipped with a UV diode-array detector using chiral stationary columns from Daicel.

Typical procedures and characterization data for compounds 3

General procedure for the enantioselective alkynylation reaction

$[Cu(CH_3CN)_4]BF_4$ (5.7 mg, 0.018 mmol) and **L4** (12.4 mg, 0.018 mmol) were placed in a dry round bottom flask which was purged with nitrogen. THF (0.2 mL) was added and the mixture was stirred for 1.5 h at room temperature. Then, a solution of β-trifluoromethyl-α,β-enone **2** (0.090 mmol) in dry THF (1.0 mL) was added via syringe, followed of triethylamine (12.5 μL, 0.090 mmol). The solution was placed in a bath at 40 °C. After 10 min, the alkyne **1** (0.675mmol) was added and the solution was stirred at 40 °C under nitrogen until the reaction was complete (TLC). The reaction mixture was quenched with 20% aqueous NH_4Cl (1.0 mL), extracted with CH_2Cl_2 (2 × 15 mL), washed with brine (15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:diethyl ether mixtures afforded compound **3**.

(*S*)-(–)-3-(Trifluoromethyl)-1,5-diphenylpent-4-yn-1-one (3aa)

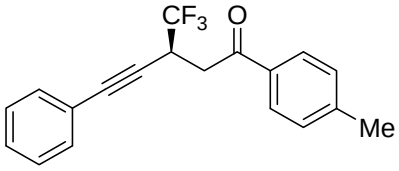


Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (85%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 8.1 min, minor enantiomer t_r = 10.1 min.

$[\alpha]_D^{20}$ –34.7 (*c* 0.81, $CHCl_3$, 85% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03-7.99 (m, 2H), 7.62 (ddd, *J* = 6.6, 1.3 Hz, 2H), 7.40-7.37 (m, 2H), 7.31-7.24 (m, 3H), 4.29-4.16 (m,

1H), 3.60 (dd, *J* = 17.3, 8.9 Hz, 1H), 3.42 (dd, *J* = 17.3, 4.2 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.5 (C), 136.1 (C), 133.8 (CH), 131.9 (2CH), 128.8 (2CH), 128.6 (CH), 128.2 (2CH), 128.2 (2CH), 125.3 (q, $J_{C\text{-}F}$ = 263.0 Hz, CF_3), 122.0 (C), 84.3 (C), 81.4 (q, $J_{C\text{-}F}$ = 6.5 Hz, C), 38.3 (CH_2), 33.7 (q, $J_{C\text{-}F}$ = 41.2 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.6 (s, 3F); HRMS (ESI) *m/z*: 303.0893 $(M + H)^+$, $C_{18}H_{14}F_3O$ requires 303.0991.

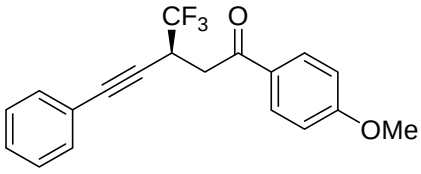
(*S*)-(–)-3-(Trifluoromethyl)-5-phenyl-1-*p*-tolylpent-4-yn-1-one (3ab)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 8.1 min, minor enantiomer t_r = 9.1 min.

$[\alpha]_D^{20}$ –28.5 (*c* 0.89, $CHCl_3$, 80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.88 (m, 2H), 7.40-7.36 (m, 2H), 7.31-7.26 (m, 5H), 4.26-4.19 (m, 1H), 3.56 (dd, *J* = 17.2, 8.9 Hz, 1H), 3.39 (dd, *J* = 17.2, 4.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.1 (C), 144.7 (C), 133.6 (C), 131.9 (2CH), 129.5 (2CH), 128.6 (CH), 128.2 (2CH), 127.2 (2CH), 125.4 (q, $J_{C\text{-}F}$ = 279.3 Hz, CF_3), 122.0 (C), 84.7 (C), 84.2 (C), 38.1 (CH_2), 33.7 (q, $J_{C\text{-}F}$ = 31.7 Hz, CH), 21.7 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.6 (s, 3F); HRMS (ESI) *m/z*: 317.1148 $(M + H)^+$, $C_{19}H_{16}F_3O$ requires 317.1141.

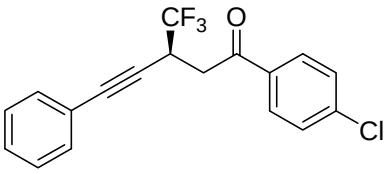
(*S*)-(–)-3-(Trifluoromethyl)-1-(4-methoxyphenyl)-5-phenylpent-4-yn-1-one (3ac)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralpak IC), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 9.0 min, minor enantiomer t_r = 8.0 min.

$[\alpha]_D^{20}$ –40.9 (*c* 0.91, $CHCl_3$, 80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (dt, *J* = 9, 3 Hz, 2H), 7.29-7.26 (m, 2H), 7.19-7.16 (m, 3H), 6.89-6.84 (dt, *J* = 9, 3 Hz, 2H), 4.16-4.09 (m, 1H), 3.70 (s, 3H), 3.43 (dd, *J* = 18, 9 Hz, 1H), 3.25 (dd, , *J* = 18, 3 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 193.0 (C), 164.0 (C), 131.9 (2CH), 130.6 (2CH), 129.2 (C), 128.6 (CH), 128.2 (2CH), 125.4 (q, $J_{C\text{-}F}$ = 279.4 Hz, CF_3), 122.1 (C), 114.0 (2CH), 84.3 (C), 82.0 (q, $J_{C\text{-}F}$ = 3.8 Hz, C), 55.5 (CH_3), 37.9 (CH_2), 33.8 (q, $J_{C\text{-}F}$ = 31.6 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.6 (s, 3F); HRMS (ESI) *m/z*: 333.1088 $(M + H)^+$, $C_{19}H_{16}F_3O_2$ requires 333.1097.

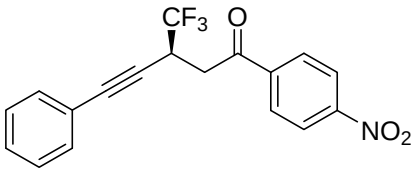
(*S*)-(−)-1-(4-Chlorophenyl)-3-(trifluoromethyl)-5-phenylpent-4-yn-1-one (3ad)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 7.5 min, minor enantiomer t_r = 10.9 min.

$[\alpha]_D^{20}$ −32.7 (*c* 0.81, $CHCl_3$, 80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (dt, *J* = 9.0, 3.0 Hz, 2H), 7.48 (dt, *J* = 9.0, 2.4 Hz, 2H), 7.40-7.36 (m, 2H), 7.31-7.24 (m, 3H), 4.27-4.14 (m, 1H), 3.55 (dd, *J* = 17.3, 8.9 Hz, 1H), 3.38 (dd, *J* = 17.3, 4.2 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 193.4 (C), 140.4 (C), 134.4 (C), 131.9 (2CH), 129.6 (2CH), 129.2 (2CH), 128.7 (CH), 128.2 (CH), 125.4 (q, $J_{C\text{-}F}$ = 279.3 Hz, CF_3), 121.9 (C), 84.5 (C), 81.6 (q, $J_{C\text{-}F}$ = 3.9 Hz, C), 38.3 (CH_2), 33.7 (q, $J_{C\text{-}F}$ = 31.5 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.7 (s, 3F); HRMS (ESI) *m/z*: 337.0592/339.0564 $(M + H)^+$ 100/32.0, $C_{18}H_{13}F_3O_3Cl$ requires 337.0607/339.0578.

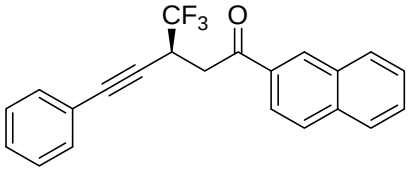
(*S*)- (−)-3-(Trifluoromethyl)-1-(4-nitrophenyl)-5-phenylpent-4-yn-1-one (3ae)



Purified by flash chromatography eluting with hexane-diethyl ether (95:05). Enantiomeric excess (70%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 95:05, 1 mL/min, major enantiomer t_r = 20.1 min, minor enantiomer t_r = 31.2 min.

$[\alpha]_D^{20}$ −25.2 (*c* 0.60, $CHCl_3$, 70% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (dt, *J* = 9.0, 3.0 Hz, 2H), 8.16 (dt, *J* = 9.0, 3.0 Hz, 2H), 7.40-7.25 (m, 5H), 4.27-4.15 (m, 1H), 3.63 (dd, *J* = 17.5, 8.9 Hz, 1H), 3.47 (dd, *J* = 17.5, 4.2 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 193.2 (C), 150.7 (C), 140.4 (C), 131.9 (2CH), 129.3 (2CH), 128.9 (CH), 128.3 (2CH), 125.1 (q, $J_{C\text{-}F}$ = 281.3 Hz, CF_3), 124.1 (2CH), 121.7 (C), 84.8 (C), 81.1 (C), 38.9 (CH_2), 33.7 (q, $J_{C\text{-}F}$ = 31.9 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.6 (s, 3F); HRMS (ESI) *m/z*: 348.0851 $(M + H)^+$, $C_{18}H_{13}F_3NO_3$ requires 348.0848.

(*S*)-(−)-3-(Trifluoromethyl)-1-(naphthalene-3-yl)-5-phenylpent-4-yn-1-one (3af)

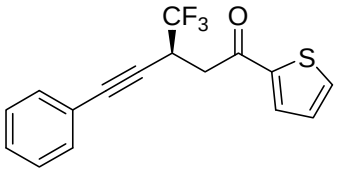


Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 16.3 min, minor enantiomer t_r = 19.1 min.

$[\alpha]_D^{20}$ −118.6 (*c* 1.30, $CHCl_3$, 84% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.05 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.90 (dd, *J* = 10.2, 8.6 Hz, 2H), 7.65-7.54 (m, 2H), 7.38-7.35 (m, 2H), 7.28-7.20 (m, 3H), 4.35-4.22 (m, 1H), 3.73 (dd, *J* =

17.2, 8.9 Hz, 1H), 3.54 (dd, J = 17.2, 4.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.4 (CH), 135.9 (C), 133.5 (C), 132.4 (C),131.8 (2CH), 130.12 (CH), 129.64 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.2 (2CH), 127.8 (CH), 127.0 (CH), 125.4 (q, $J_{C\text{-}F}$ = 279.4 Hz, CF_3), 123.7 (CH), 122.0 (C), 84.4 (C), 81.9 (q, $J_{C\text{-}F}$ = 3.5 Hz, C), 38.3 (CH_2), 33.8 (q, $J_{C\text{-}F}$ = 31.8 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.5 (s, 3F); HRMS (ESI) *m/z*: 353.1148 $(M + H)^+$, $C_{22}H_{16}F_3O$ requires 353.1148.

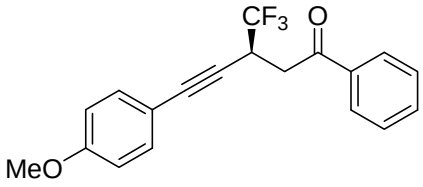
(*S*)-(−)-3-(Trifluoromethyl)-5-phenyl-1-(thiophen-2-yl)pent-4-yn-1-one (3ag)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (90%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 10.5 min, minor enantiomer t_r = 15.2 min.

$[\alpha]_D^{20}$ −6.1 (*c* 1.09, $CHCl_3$, 90% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (dd, J = 3.8, 1.1 Hz, 1H), 7.68 (dd, J = 5, 1.1 Hz, 1H), 7.36-7.33 (m, 2H), 7.28-7.22 (m, 3H), 7.14 (dd, J = 5, 3.8 Hz, 1H), 4.23-4.10 (m, 1H), 3.47 (dd, J = 16.6, 8.9 Hz, 1H), 3.32 (dd, , J = 16.6, 4.5 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.4 (C), 143.2 (C), 134.7 (CH), 132.7 (CH), 131.9 (2CH), 128.7 (CH), 128.3 (CH), 128.2 (2CH), 125.2 (q, $J_{C\text{-}F}$ = 278.7 Hz, CF_3), 121.9 (C), 84.7 (C), 81.5 (C), 38.7 (CH_2), 33.8 (q, $J_{C\text{-}F}$ = 31.7 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.7 (s, 3F); HRMS (ESI) *m/z*: 309.0550 $(M + H)^+$, $C_{16}H_{12}F_3OS$ requires 309.0555.

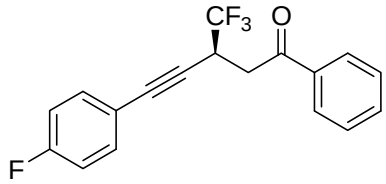
(*S*)-(−)-3-(Trifluoromethyl)-5-(4-methoxyphenyl)-1-phenylpent-4-yn-1-one (3ba)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (83%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 15.9 min, minor enantiomer t_r = 14.4 min.

$[\alpha]_D^{20}$ −20.3 (*c* 0.93, $CHCl_3$, 83% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02-7.99 (m, 2H), 7.64-7.59 (m, 1H), 7.53-7.47 (m, 2H), 7.31 (dt, J = 9, 3 Hz, 2H), 6.79 (dt, J = 9, 3 Hz, 2H), 4.27- 4.14 (m, 1H), 3.79 (s, 3H), 3.58 (dd, J = 17.2, 8.9 Hz, 1H), 3.41 (dd, J = 17.2, 4.2 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.7 (C), 159.8 (C), 136.1 (C), 133.7 (CH), 133.3 (2CH), 128.8 (2CH), 128.2 (2CH), 125.4 (q, $J_{C\text{-}F}$ = 279.1 Hz, CF_3), 114.1 (C), 113.8 (2CH), 84.2 (C), 80.4 (q, $J_{C\text{-}F}$ = 3.5 Hz, C), 55.3 (CH_3), 38.3 (CH_2), 33.7 (q, $J_{C\text{-}F}$ = 31.7 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.7 (s, 3F); HRMS (ESI) *m/z*: 333.1088 $(M + H)^+$ $C_{19}H_{16}F_3O_2$ requires 333.1097.

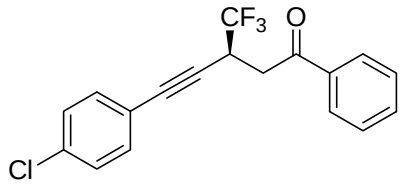
(*S*)-(−)-3-(Trifluoromethyl)-5-(4-fluorophenyl)-1-phenylpent-4-yn-1-one (3ca)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 8.8 min, minor enantiomer t_r = 10.8 min.

$[\alpha]_D^{20}$ −15.7 (*c* 1.15, $CHCl_3$, 80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02-7.99 (m, 2H), 7.65-7.60 (m, 1H), 7.53-7.48 (m, 2H), 7.39-7.34 (m, 2H), 7.00-6.93 (m, 2H), 4.24-4.17 (m, 1H), 3.59 (dd, *J* = 17.3, 9 Hz, 1H), 3.42 (dd, *J* = 17.3, 4.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.5 (C), 162.7 (d, *J* = 249.9 Hz, C), 136.0 (C), 133.9 (CH), 133.8 (d, *J* = 8.5 Hz, 2CH), 128.8 (2CH), 128.2 (2CH), 125.3 (q, *J* = 279.2 Hz, CF_3), 118.1 (d, *J* = 3.5 Hz, C), 115.5 (d, $J_{C\text{-}F}$ = 22.1 Hz, 2CH), 83.3 (C), 81.6 (q, $J_{C\text{-}F}$ = 5.1 Hz, C), 38.2 (CH_2), 33.6 (q, $J_{C\text{-}F}$ = 31.6 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.6 (s, 3F), −110.7 (s, 1F); HRMS (ESI) *m/z*: 321.0892 $(M + H)^+$, $C_{18}H_{13}F_4O$ requires 321.0897.

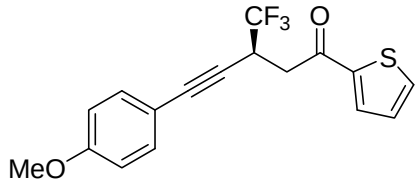
(*S*)-(−)-5-(4-Chlorophenyl)-3-(trifluoromethyl)-1-phenylpent-4-yn-1-one (3da)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (77%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 10.5 min, minor enantiomer t_r = 11.5 min.

$[\alpha]_D^{20}$ −20.4 (*c* 0.90, $CHCl_3$, 77% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02-7.99 (m, 2H), 7.62 (ddd, *J* = 6.6, 3.9, 1.3 Hz, 1H), 7.54-7.48 (m, 2H), 7.33-7.22 (m, 4H), 4.26-4.15 (m, 1H), 3.59 (dd, *J* = 17.3, 9 Hz, 1H), 3.42 (dd, *J* = 17.3, 4.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 194.4 (C), 136.0 (C), 134.7 (C), 133.8 (CH), 133.1 (2CH), 128.8 (2CH), 128.6 (2CH), 128.2 (2CH), 125.3 (q, $J_{C\text{-}F}$ = 279.4 Hz, CF_3), 120.5 (C), 83.2 (C), 80.9 (C), 38.2 (CH_2), 33.7 (q, $J_{C\text{-}F}$ = 31.7 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.5 (s, 3F); HRMS (ESI) *m/z*: 337.0594 / 339.0553 $(M + H)^+$ 100 / 28.9 $C_{18}H_{13}ClF_3O$ requires 337.0607 / 339.0578.

(*S*)-(−)-3-(Trifluoromethyl)-5-(4-methoxyphenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3bg)

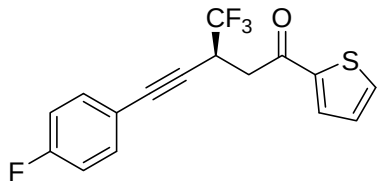


Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AY-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 25.3 min, minor enantiomer t_r = 16.8 min.

$[\alpha]_D^{20}$ −7.3 (*c* 0.98, $CHCl_3$, 93% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.72-7.70 (m, 1H), 7.32-7.28 (m, 2H), 7.17 (dd, *J* = 5, 3.8 Hz, 1H), 6.81-

6.77 (m, 2H), 4.23-4.11 (m, 1H), 3.79 (s, 3H), 3.48 (dd, J = 16.6, 8.9 Hz, 1H), 3.33 (dd, J = 16.6, 4.5 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.5 (C), 159.8 (C), 143.3 (C), 134.7 (CH), 133.3 (2CH), 132.6 (CH), 128.3 (CH), 125.2 (q, J_{C-F} = 279.3 Hz, CF_3), 114.0 (C), 113.8 (2CH), 84.6 (C), 80.0 (q, J_{C-F} = 3.3 Hz, C), 55.3 (CH_3), 38.8 (CH_2), 33.8 (q, J_{C-F} = 31.7 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.8 (s, 3F); HRMS (ESI) *m/z*: 338.0592 $(M + H)^+$ $C_{17}H_{14}F_3O_2S$ requires 338.0588.

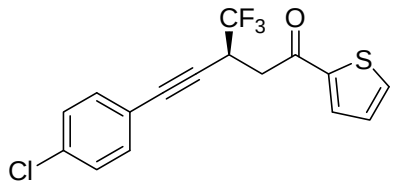
(*S*)-(−)-3-(Trifluoromethyl)-5-(4-fluorophenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3cg)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (90%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 12.6 min, minor enantiomer t_r = 14.9 min.

$[\alpha]_D^{20}$ −6.4 (*c* 1.03, $CHCl_3$, 90% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, J = 3.9, 1.1 Hz, 1H), 7.72 (dd, J = 5, 1.1 Hz, 1H), 7.38-7-32 (m, 2H), 7.18 (dd, J = 5, 3.9 Hz, 1H), 7.00-6.93 (m, 2H), 4.23-4.08 (m, 1H), 3.49 (dd, J = 16.7, 9 Hz, 1H), 3.35 (dd, J = 16.7, 4.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.3 (C), 162.7 (d, J = 250 Hz, C), 143.2 (C), 134.8 (CH), 133.8 (d, J = 8.5 Hz, 2CH), 132.7 (CH), 128.3 (CH), 125.0 (q, J_{C-F} = 279.5 Hz, CF_3), 118.0 (C), 115.5 (d, J = 22.1 Hz, 2CH), 83.6 (C), 81.2 (q, J_{C-F} = 3.6 Hz, C), 38.7 (CH_2), 33.8 (q, J_{C-F} = 31.9 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.6 (s, 3F), −110.7 (s, 1F); HRMS (ESI) *m/z*: 327.0455 $(M + H)^+$ $C_{16}H_{11}F_4OS$ requires 327.0461.

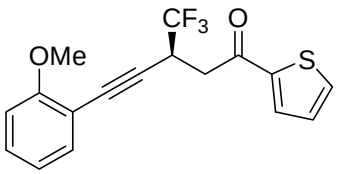
(*S*)-(−)- 5-(4-Chlorophenyl)-3-(trifluoromethyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3dg)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralpak IC), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 6.5 min, minor enantiomer t_r = 7.0 min.

$[\alpha]_D^{20}$ −6.9 (*c* 1.06, $CHCl_3$, 84% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, J = 3.9, 1.0 Hz, 1H), 7.22 (dd, J = 4.9, 1.0 Hz, 1H), 7.31-7.23 (m, 4H), 7.18 (dd, J = 4.9, 3.9 Hz, 1H), 4.21-4.14 (m, 1H), 3.49 (dd, J = 16.7, 9.0 Hz, 1H), 3.35 (dd, J = 16.7, 4.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.3 (C), 143.1 (C), 134.8 (C), 134.8 (CH), 133.1 (2CH), 132.6 (CH), 128.6 (2CH), 128.4 (CH), 125.1 (q, J_{C-F} = 279.6 Hz, CF_3), 120.4 (C), 83.6 (C), 82.5 (C), 38.6 (CH_2), 33.9 (q, J_{C-F} = 31.9 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.5 (s, 3F); HRMS (ESI) *m/z*: 343.0158 / 345.0128 $(M + H)^+$ 100 / 36.7 $C_{16}H_{11}ClF_3OS$ requires 343.0171 / 345.0142.

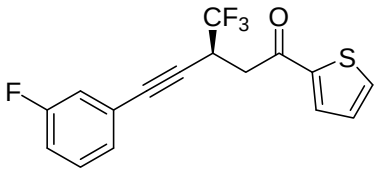
(*S*)-(−)-3-(Trifluoromethyl)-5-(2-methoxyphenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3eg)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (98%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 95:05, 1 mL/min, major enantiomer t_r = 10.7 min, minor enantiomer t_r = 13.2 min.

$[\alpha]_D^{20}$ −7.8 (*c* 0.90, $CHCl_3$, 98% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.70 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.34-7.24 (m, 2H), 7.17 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.91-6.77 (m, 2H), 4.29-4.21 (m, 1H), 3.78 (s, 3H), 3.52 (dd, *J* = 16.6, 8.5 Hz, 1H), 3.36 (dd, *J* = 16.6, 4.8 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.5 (C), 160.4 (C), 143.4 (C), 134.5 (CH), 133.7 (CH), 132.6 (CH), 130.1 (CH), 128.3 (CH), 125.2 (q, $J_{C\text{-}F}$ = 279.5 Hz, CF_3), 120.3 (CH), 111.3 (C), 110.8 (CH), 85.5 (C), 81.1 (C), 55.7 (CH_3), 38.9 (CH_2), 34.1 (q, $J_{C\text{-}F}$ = 31.8 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.6 (s, 3F); HRMS (ESI) *m/z*: 338.0590 $(M + H)^+$ $C_{17}H_{14}F_3O_2S$ requires 338.0588.

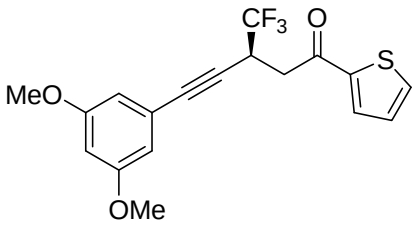
(*S*)-(−)-3-(Trifluoromethyl)-5-(3-fluorophenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3fg)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (99%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 13.7 min, minor enantiomer t_r = 10.9 min.

$[\alpha]_D^{20}$ −8.3 (*c* 0.87, $CHCl_3$, 99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 2.7, 1.3 Hz, 1H), 7.74 (ddd, *J* = 9.7, 4.9, 1.1 Hz, 1H), 7.28-7.14 (m, 3H), 7.08-6.98 (m, 2H), 4.25-4.13 (m, 1H), 3.50 (dd, *J* = 16.7, 9.0 Hz, 1H), 3.36 (dd, *J* = 16.7, 4.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.2 (C), 162.2 (d, $J_{C\text{-}F}$ = 246.7 Hz, C), 143.1 (C), 134.8 (CH), 132.7 (CH), 129.8 (d, $J_{C\text{-}F}$ = 8.6 Hz, CH), 128.4 (CH), 127.8 (d, $J_{C\text{-}F}$ = 3.1 Hz, CH), 125.1 (q, $J_{C\text{-}F}$ = 279.4 Hz, CF_3), 123.7 (d, $J_{C\text{-}F}$ = 9.4 Hz, C), 118.7 (d, $J_{C\text{-}F}$ = 23.0 Hz, CH), 116.1 (d, *J* = 21.2 Hz, CH), 83.4 (q, $J_{C\text{-}F}$ = 3.4 Hz, C), 82.5 (d, $J_{C\text{-}F}$ = 3.5 Hz, C), 38.6 (CH_2), 33.8 (q, $J_{C\text{-}F}$ = 31.9 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.6 (s, 3F), −113.4 (s, 1F); HRMS (ESI) *m/z*: 327.0457 $(M + H)^+$ $C_{16}H_{11}F_4OS$ requires 327.0461.

(*S*)-(−)-3-(trifluoromethyl)-5-(3,5-dimethoxyphenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3gg)

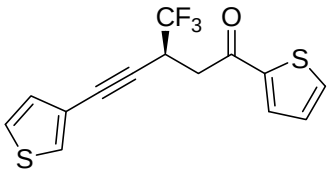


Purified by flash chromatography eluting with hexane-diethyl ether (95:05). Enantiomeric excess (86%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 95:05, 1 mL/min, major

enantiomer t_r = 11.2 min, minor enantiomer t_r = 12.5 min.

$[\alpha]_D^{20}$ –7.0 (*c* 0.93, $CHCl_3$, 86% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.71 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.17 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.51 (d, *J* = 2.3 Hz, 2H), 6.42 (t, *J* = 2.3 Hz, 1H), 4.22-4.15 (m, 1H), 3.75 (s, 6H), 3.49 (dd, *J* = 16.6, 8.9 Hz, 1H), 3.35 (dd, *J* = 16.6, 4.5 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.4 (C), 160.4 (2C), 143.2 (C), 134.7 (CH), 132.7 (CH), 130.7 (CH), 125.2 (q, $J_{C\text{-}F}$ = 279.3 Hz, CF_3), 123.2 (C), 109.6 (2CH), 102.3 (CH), 84.7 (C), 80.0 (q, $J_{C\text{-}F}$ = 3.4 Hz, C), 55.4 ($2CH_3$), 38.7 (CH_2), 33.8 (q, $_{C\text{-}F}J$ = 31.8 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.6 (s, 3F); HRMS (ESI) *m/z*: 368.0690 $(M + H)^+$ $C_{18}H_{15}F_3O_3S$ requires 368.0694.

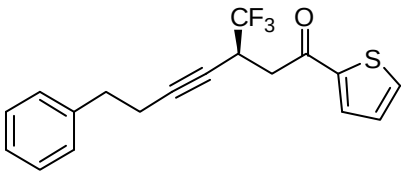
(*S*)-(–)-3-(Trifluoromethyl)-1-(thiophen-2-yl)-5-(thiophen-3-yl)pent-4-yn-1-one (3hg)



Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (88%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 11.1 min, minor enantiomer t_r = 15.5 min.

$[\alpha]_D^{20}$ –5.4 (*c* 0.86, $CHCl_3$, 88% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.71 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.40 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.22 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.17 (dd, *J* = 5.0, 3.9 Hz, 1H), 7.04 (dd, *J* = 5.0, 1.2 Hz, 1H), 4.22-4.11 (m, 1H), 3.49 (dd, *J* = 16.7, 8.9 Hz, 1H), 3.34 (dd, *J* = 16.7, 4.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.3 (C), 143.2 (C), 134.7 (CH), 132.6 (CH), 129.9 (CH), 129.7 (CH), 128.3 (CH), 125.3 (CH), 125.1 (q, $J_{C\text{-}F}$ = 279.5 Hz, CF_3), 120.9 (C), 81.1 (q, $J_{C\text{-}F}$ = 3.5 Hz, C), 79.9 (C), 38.7 (CH_2), 33.8 (q, $J_{C\text{-}F}$ = 31.7 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.6 (s, 3F); HRMS (ESI) *m/z*: 314.0043 $(M + H)^+$ $C_{14}H_9F_3OS_2$ requires 314.0047.

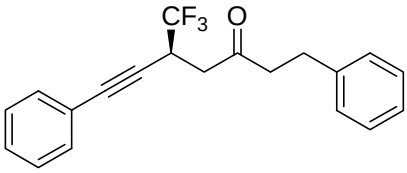
(*S*)-(+)-7-phenyl-1-(thiophen-2-yl)-3-(trifluoromethyl)hept-4-yn-1-one (3ig)



Purification by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralcel AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 9.7 min, minor enantiomer t_r = 10.8 min.

$[\alpha]_D^{20}$ +1.2 (*c* 0.73, $CHCl_3$, 92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (td, *J* = 4.7, 1.2 Hz, 2H), 7.26-7.12 (m, 6H), 4.05 (m, 1H), 3.31 (dd, *J* = 16.6, 9.0 Hz, 1H), 3.19 (dd, *J* = 16.6, 4.5 Hz, 1H), 2.74 (t, *J* = 7.2 Hz, 2H), 2.42 (td, *J* = 7.5, 2.4 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.6 (C), 143.4 (C), 140.3 (C), 134.5 (CH), 132.5 (CH), 128.5 (2CH), 128.3 (3CH), 126.2 (CH), 125.5 (q, $J_{C\text{-}F}$ = 277.5 Hz, CF_3), 84.6 (C), 73.3 (C), 38.9 (CH_2), 34.6 (CH_2), 33.3 (q, $J_{C\text{-}F}$ = 30.8 Hz, CH), 20.8 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ –72.1 (s, 3F); HRMS (ESI) *m/z*: 337.0854 $(M + H)^+$ $C_{18}H_{16}F_3OS$ requires 337.0868.

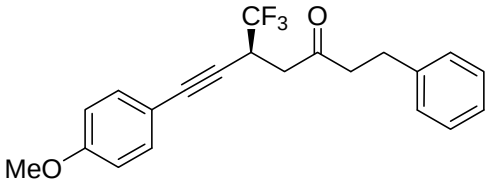
(*S*)-(+)-5-(Trifluoromethyl)-1,7-diphenylhept-6-yn-3-one (3ah)



Purification by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (79%) was determined by chiral HPLC (Chiralcel AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 6.6 min, minor enantiomer t_r = 9.6 min.

$[\alpha]_D^{20}$ +6.1 (*c* 0.8, $CHCl_3$, 79% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.36 (m, 2H), 7.35-7.22 (m, 5H), 7.24-7.14 (m, 2H), 3.99 (m, 1H), 3.01-2.78 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 204.3 (C), 140.4 (C), 131.9 (CH), 128.7 (CH), 128.6 (CH), 128.3 (CH), 126.3 (CH), 125.1 (q, $J_{C\text{-}F}$ = 277.1 Hz, CF_3), 121.9 (C), 84.4 (C), 81.5 (q, $J_{C\text{-}F}$ = 3.6 Hz, C), 44.7 (CH_2), 42.1 (CH_2), 33.4 (q, $J_{C\text{-}F}$ = 31.7 Hz, CH), 29.5 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.8 (s, 3F); HRMS (ESI) *m/z*: 331.1306 $(M + H)^+$ $C_{20}H_{18}F_3O$ requires 331.1304.

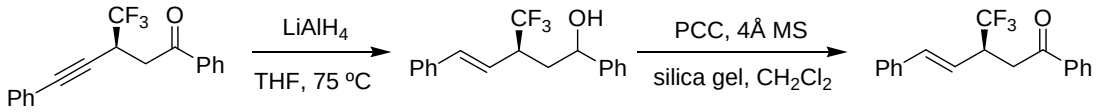
(*S*)-(+)-5-(Trifluoromethyl)-7-(4-methoxyphenyl)-1-phenylhept-6-yn-3-one (3bh)



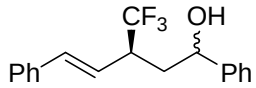
Purification by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (82%) was determined by chiral HPLC (Chiralcel AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 11.3 min, minor enantiomer t_r = 17.4 min.

$[\alpha]_D^{20}$ +3.0 (*c* 0.5, $CHCl_3$, 82% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 9.0 Hz, 2H), 7.31-7.12 (m, 6H), 6.82 (d, *J* = 9.0 Hz, 2H), 3.98 (m, 1H), 3.81 (s, 3H), 3.00-2.78 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 204.4 (C), 159.9 (C), 140.5 (C), 140.5 (CH), 133.4 (CH), 128.6 (CH), 128.3 (CH), 126.3 (CH), 125.2 (q, $J_{C\text{-}F}$ = 278.3 Hz, CF_3), 114.0 (C), 113.9 (CH), 84.3 (C), 80.1 (q, $J_{C\text{-}F}$ = 1.6 Hz, C), 55.3 (CH_3), 44.8 (CH_2), 42.1 (CH_2), 33.4 (q, $J_{C\text{-}F}$ = 31.5 Hz, CH), 29.5 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.9 (s, 3F); HRMS (ESI) *m/z*: 361.1415 $(M + H)^+$ $C_{21}H_{20}F_3O_2$ requires 361.1410.

Determination of the absolute configuration of (*S*)-(–)-3aa

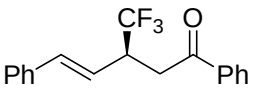


(*E*,*S*)-3-(Trifluoromethyl)-1,5-diphenylpent-4-en-1-ol (4)



Lithium aluminium hydride (12.1 mg, 0.320 mmol) was added to a solution of **3aa** (16.1 mg, 0.053 mmol, 80% *ee*) in dry THF (1.5 mL) at room temperature, and the solution was stirred overnight at 75 ºC. The reaction mixture was quenched with 20 % aqueous NH_4Cl (1.0 mL), extracted with CH_2Cl_2 (2 x 15 mL), washed with brine (15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:EtOAc (98:02) afforded compound **4** (16.2 mg, 99%) as a mixture of diastereomers.

(*E*,*S*)-3-(Trifluoromethyl)-1,5-diphenylpent-4-en-1-one (5)[2,3]

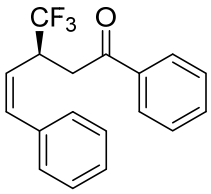


To a 25 mL round-bottom flask equipped with a magnetic stirring bar was added PCC (137 mg, 0.64 mmol), 4Å MS (300 mg), silica gel (300 mg) and CH_2Cl_2 (10 mL). The mixture was cooled to 0 ºC and the mixture of alcohols **4** (16.2 mg, 0.05 mmol) in CH_2Cl_2 (1 mL) was added dropwise. The reaction was warmed up to room temperature and was stirred for 3 h. The mixture was filtered through a pad of silica gel eluting with CH_2Cl_2. The solvent was removed under reduced pressure. The residual crude product was purified by flash column chromatography eluting with hexane:Et_2O (99:01) to afford the ketone **5** (10.5 mg, 66%).

Enantiomeric excess (78%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 9.6 min, minor enantiomer t_r = 10.8 min. (lit[2,3], Chiralpak AD-H, hexane-^{i}PrOH 99.6:0.4, flow = 0.7 mL/min, *R*-enantiomer t_r = 19.3 min, *S*-enantiomer t_r = 16.3 min); $[\alpha]_D^{20}$ +4.9 (*c* 0.57, CCl_4, 78% *ee*) {lit[2,3] $[\alpha]_D^{20}$ –16.5 (0.95, CCl_4, 40% *ee*) for the *R*-isomer]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98-7.95 (m, 2H), 7.62-7.57 (m, 1H), 7.51-7.46 (m, 2H), 7.37-7.24 (m, 5H), 6.70 (d, *J* = 15.9 Hz, 1H), 6.04 (dd, *J* = 15.9, 8.6 Hz, 1H), 3.93-3.83 (m, 1H), 3.40-3.38 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 195.4 (C), 136.4 (C), 136.3 (CH), 136.1 (C), 133.6 (CH), 128.8 (2CH), 128.5 (2CH), 128.1 (CH), 128.1 (2CH), 126.9 (q, *J* = 274.7 Hz, CF_3), 121.5 (q, *J* = 2.4 Hz, CH), 42.6 (q, *J* = 27.7 Hz, CH), 37.4 (s, CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ –71.2 (s, 3F); HRMS (ESI) *m/z*: 305.1158 $(M + H)^+$ $C_{18}H_{16}F_3O$ requires 305.1153.

Synthetic transformations of compound 3aa. Synthesis of compounds 6 and 7

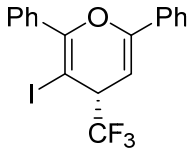
(*Z*,*S*)-(−)-1,5-Diphenyl-3-(trifluoromethyl)pent-4-en-1-one (6)



A solution of (*S*)-**3aa** (10.6 mg, 0.035 mmol, 80% *ee*) in benzene (0.5 mL) was stirred in the presence of Lindlar's catalyst (2.5 mg) under hydrogen atmosphere (balloon) for 1 h. Then, the reaction mixture was filtered through a pad of Celite® eluting with EtOAc. The solvent was removed under reduced pressure to give **5** (9.4 mg, 88%). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 7.7 min, minor enantiomer t_r = 7.3 min.

$[\alpha]_D^{20}$ −70.2 (*c* 0.45, $CHCl_3$, 80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.71 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.40 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.22 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.17 (dd, *J* = 5.0, 3.9 Hz, 1H), 7.04 (dd, *J* = 5.0, 1.2 Hz, 1H), 4.22-4.11 (m, 1H), 3.49 (dd, *J* = 16.7, 8.9 Hz, 1H), 3.34 (dd, *J* = 16.7, 4.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 195.5 (C), 136.3 (C), 135.9 (C), 135.7 (CH), 133.4 (CH), 128.7 (2CH), 128.4 (2CH), 128.3 (2CH), 128.1 (2CH), 127.5 (CH), 125.1 (q, *J* = 279.5 Hz, CF_3), 123.8 (q, *J* = 2.3 Hz, CH), 38.3 (q, *J* = 27.4 Hz, CH), 38.0 (q, *J* = 1.8 Hz, CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.0 (s, 3F); HRMS (ESI) *m/z*: 305.1159 $(M + H)^+$ $C_{18}H_{16}F_3O$ requires 305.1153.

(*R*)-(−)-3-Iodo-2,6-diphenyl-4-(trifluoromethyl)-4*H*-pyran (7).

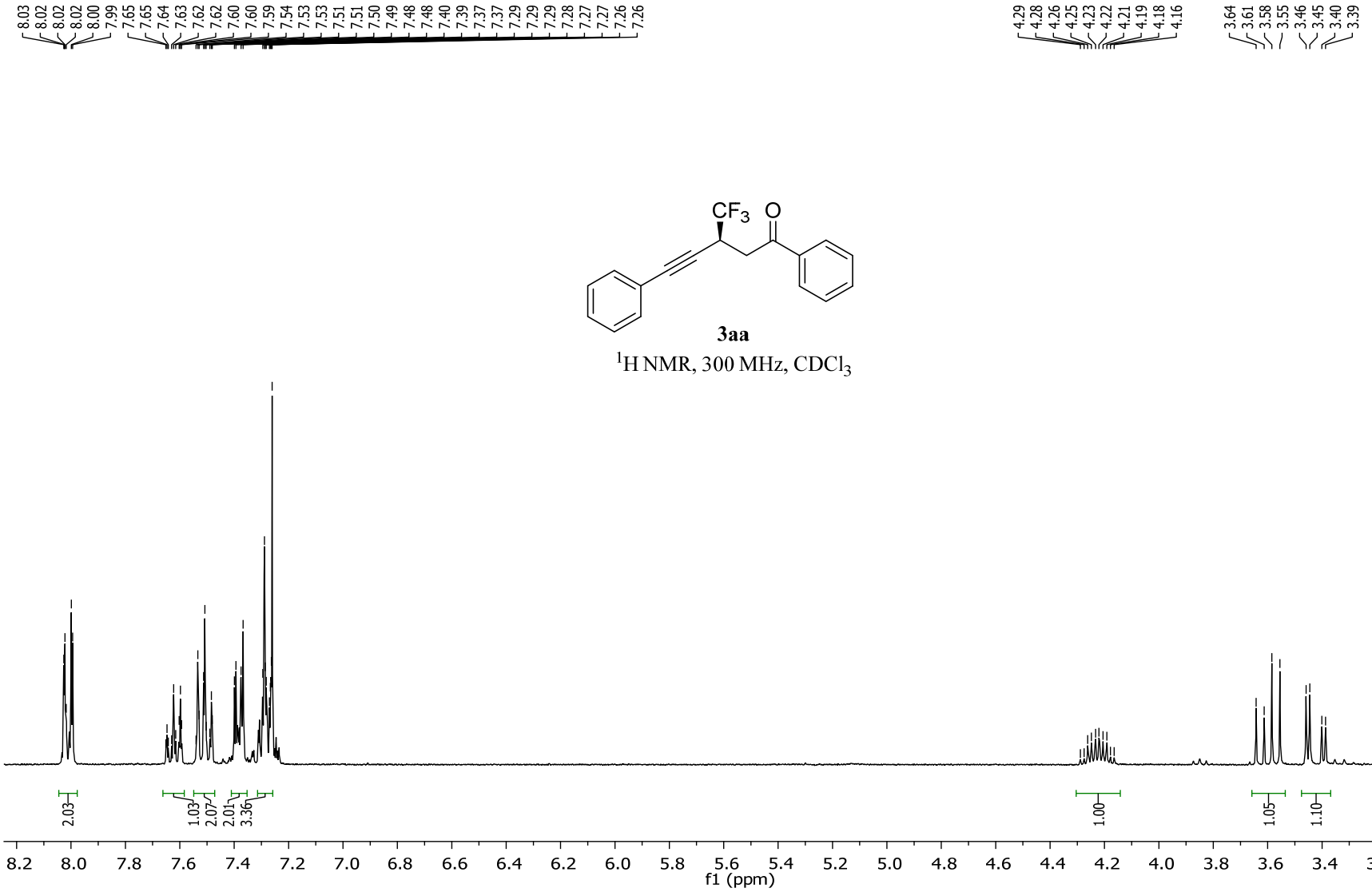


A solution of I_2 (30.1 mg, 0.119 mmol) in CH_2Cl_2 (2 mL) was added to a mixture of (*S*)-**3aa** (18 mg, 0.060 mmol 85% *ee*) and $NaHCO_3$ (10 mg, 0.119 mmol) under nitrogen atmosphere. The solution was stirred overnight at 40 ºC (reflux). The reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ (1.0 mL), extracted with CH_2Cl_2 (2 × 15 mL), washed with brine (15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:Et_2O (98:02) gave compound **7** (19.9 mg, 77%). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 6.5 min, minor enantiomer t_r = 4.7 min.

$[\alpha]_D^{20}$ −7.0 (*c* 0.45, $CHCl_3$, 84% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69-7.58 (m, 4H), 7.54-7.42 (m, 3H), 7.42-7.34 (m, 3H), 5.29 (d, *J* = 5.8 Hz, 1H), 4.16-4.02 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 155.1 (C), 153.1 (C), 135.9 (C), 132.3 (C), 129.9 (CH), 129.7 (2CH), 129.6 (CH), 128.7 (C), 128.5 (2CH), 128.2 (2CH), 125.4 (q, *J* = 223.7 Hz, CF_3), 125.0 (2CH), 90.4 (q, *J* = 1.8 Hz, CH), 49.5 (q, *J* = 22.7 Hz, CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −74.4 (s, 3F); HRMS (ESI) *m/z*: 428.9961 $(M + H)^+$ $C_{18}H_{13}F_3IO$ requires 428.9958.

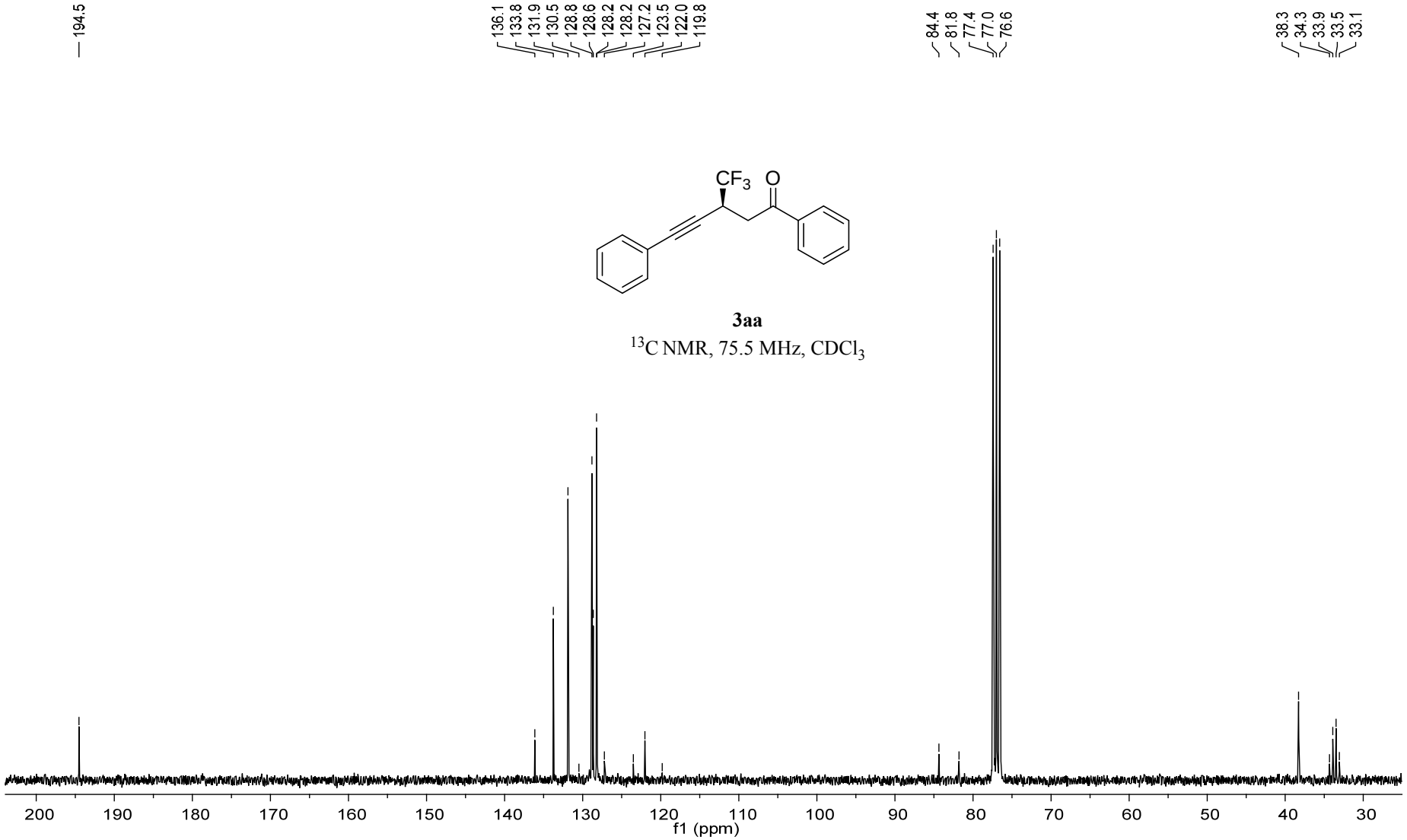
1. G. Blay, I. Fernández, M. C. Muñoz, J. R. Pedro, C. Vila *Chem. Eur. J.*, **2010**, *16*, 9117-9122.
2. (a) A. Morigaki, T. Tanaka, T. Miyabe, T. Ishihara, T. Konno, *Org. Biomol. Chem.*, 2013, **11**, 586; (b) T. Konno, T. Tanaka, A. Morigaki, T. Ishihara, *Tetrahedron Lett.*, 2008, **49**, 2106

3. We thank Professor Tsutomu Konno, Kyoto Institute of Technology, for sending us complete characterization data of compound (*E*,*R*)-**5**.



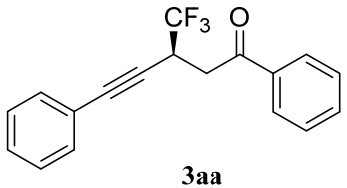
3aa

^{1}H NMR, 300 MHz, $CDCl_3$



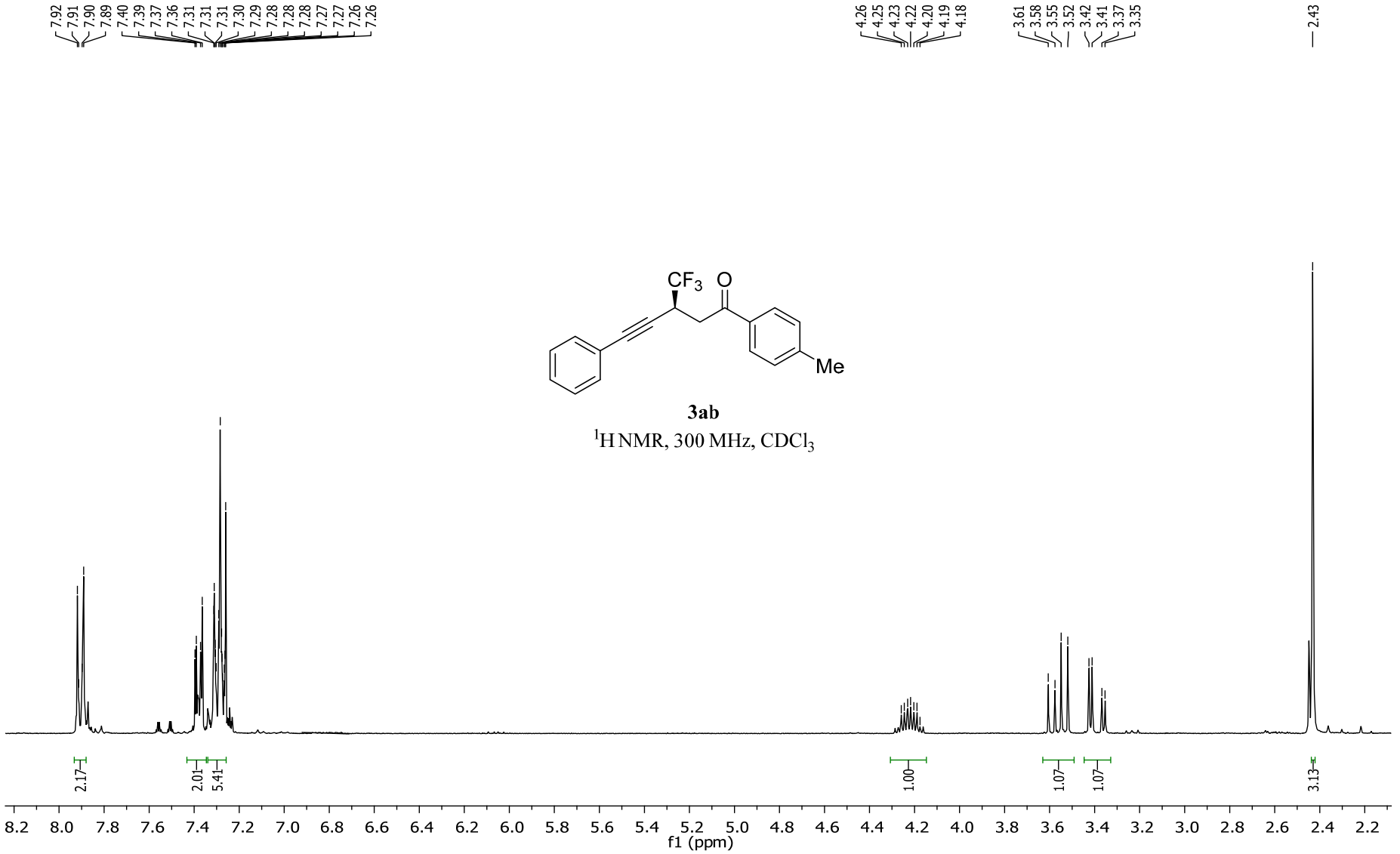
3aa

^{13}C NMR, 75.5 MHz, $CDCl_3$



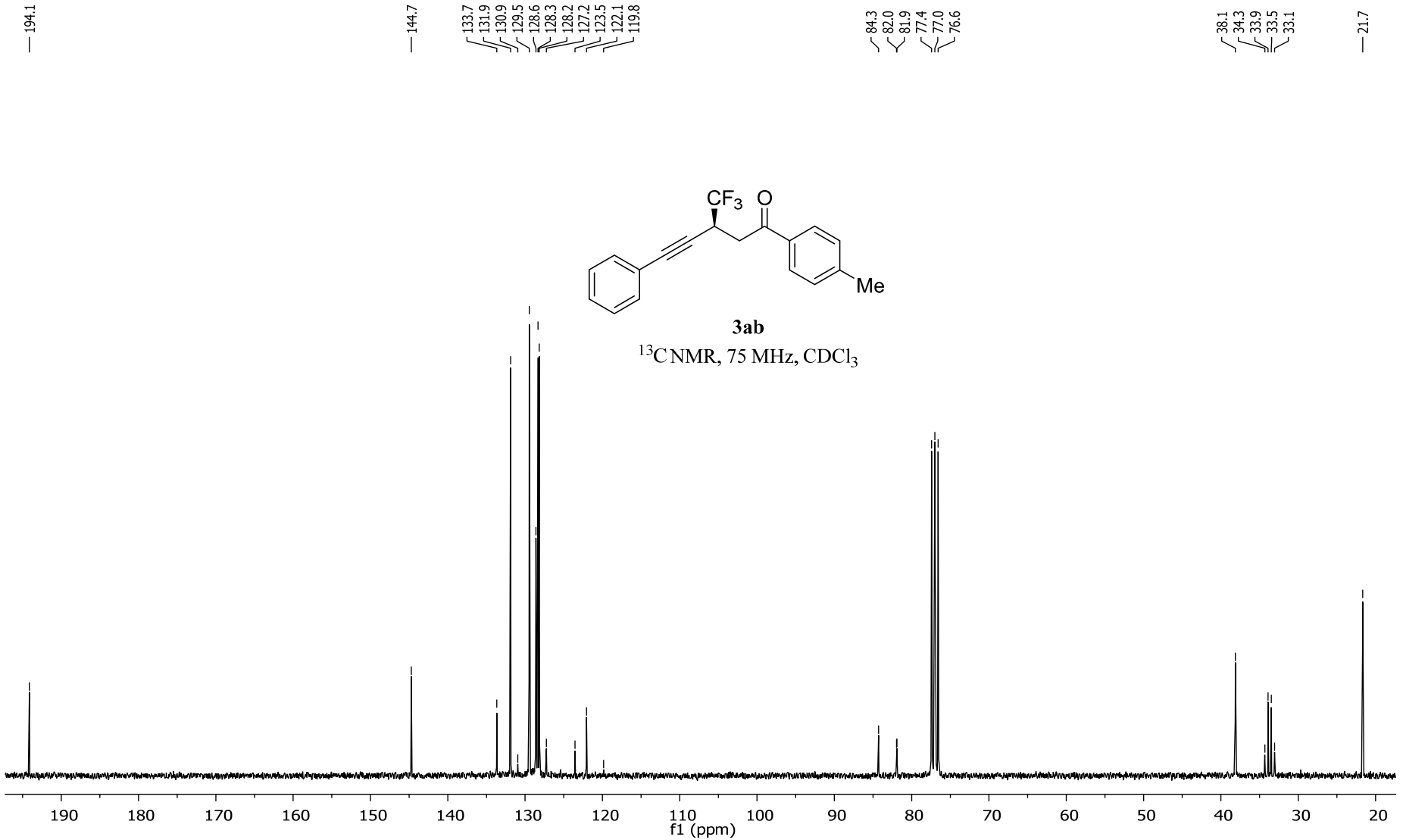
3aa

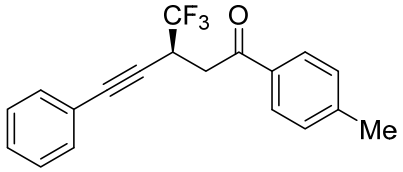
^{19}F NMR, 282 MHz, $CDCl_3$



3ab

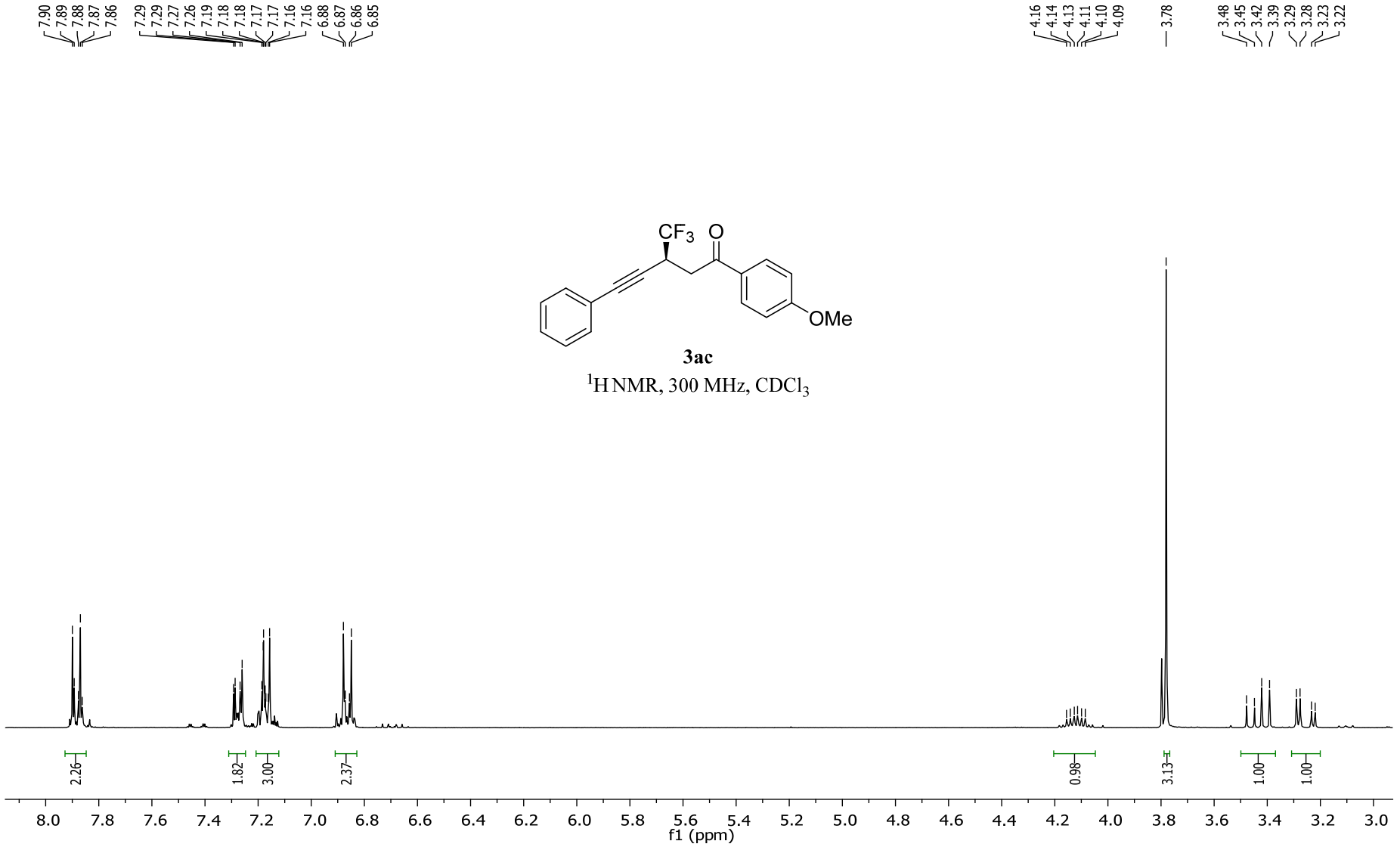
^{1}H NMR, 300 MHz, $CDCl_3$





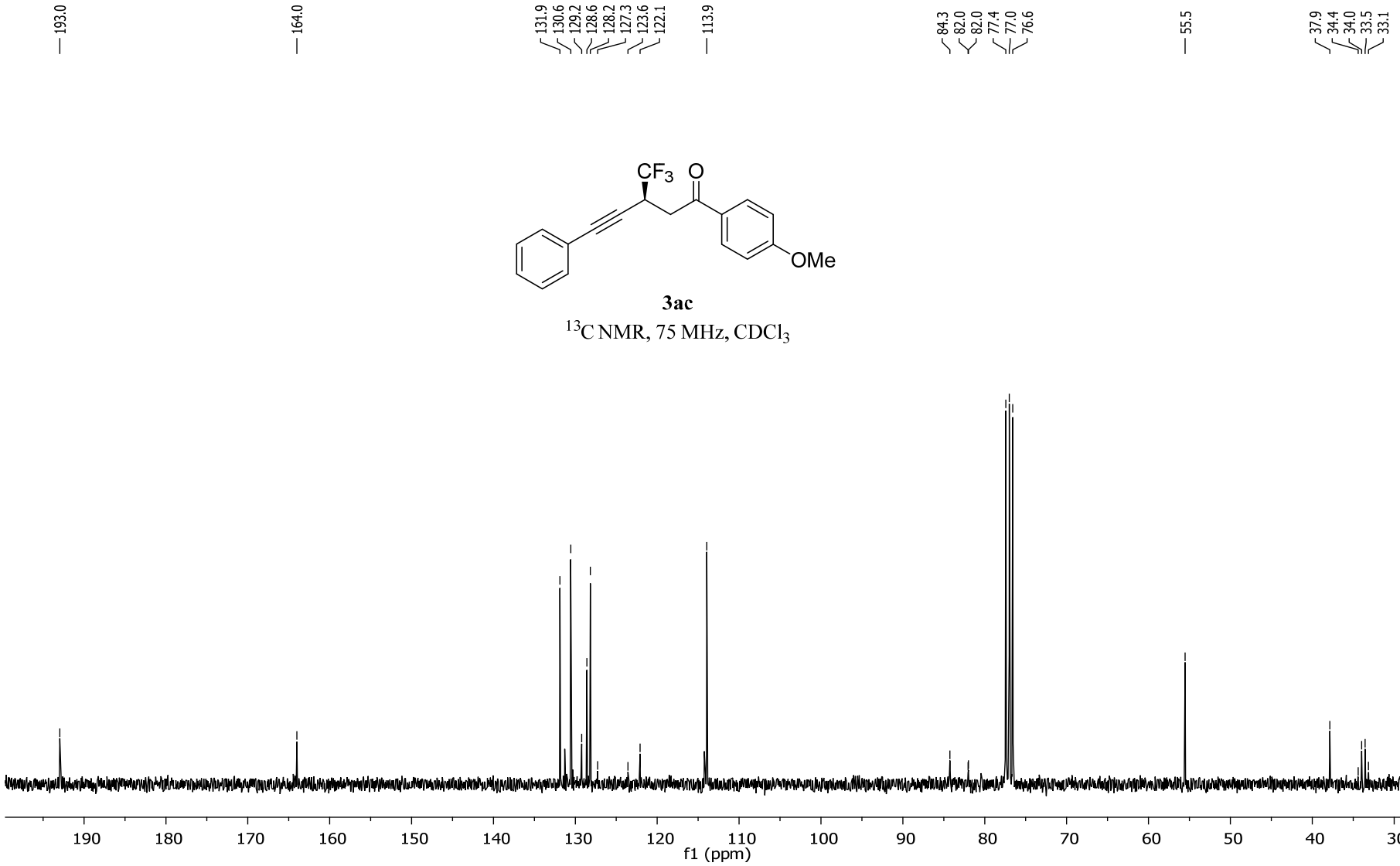
3ab

^{19}F NMR, 282 MHz, $CDCl_3$



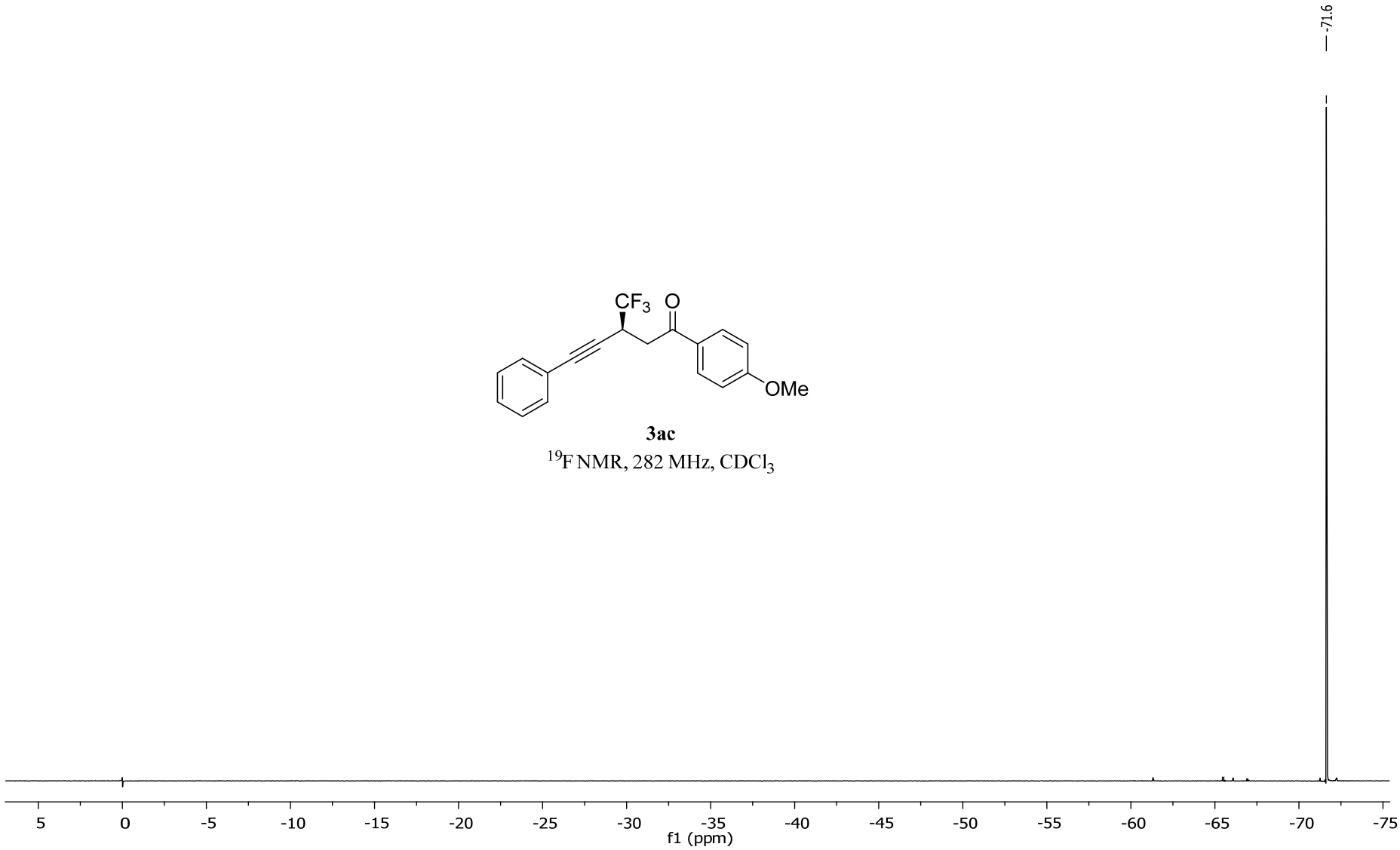
3ac

^{1}H NMR, 300 MHz, $CDCl_3$



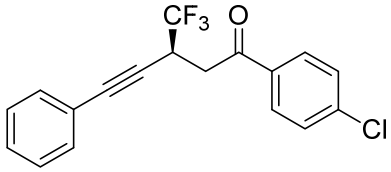
3ac

^{13}C NMR, 75 MHz, $CDCl_3$



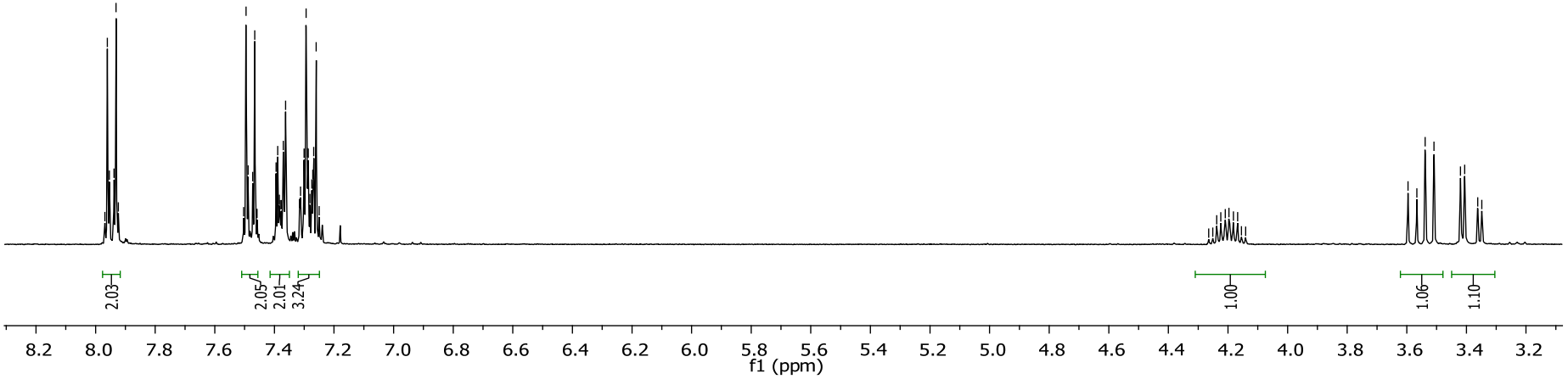
3ac

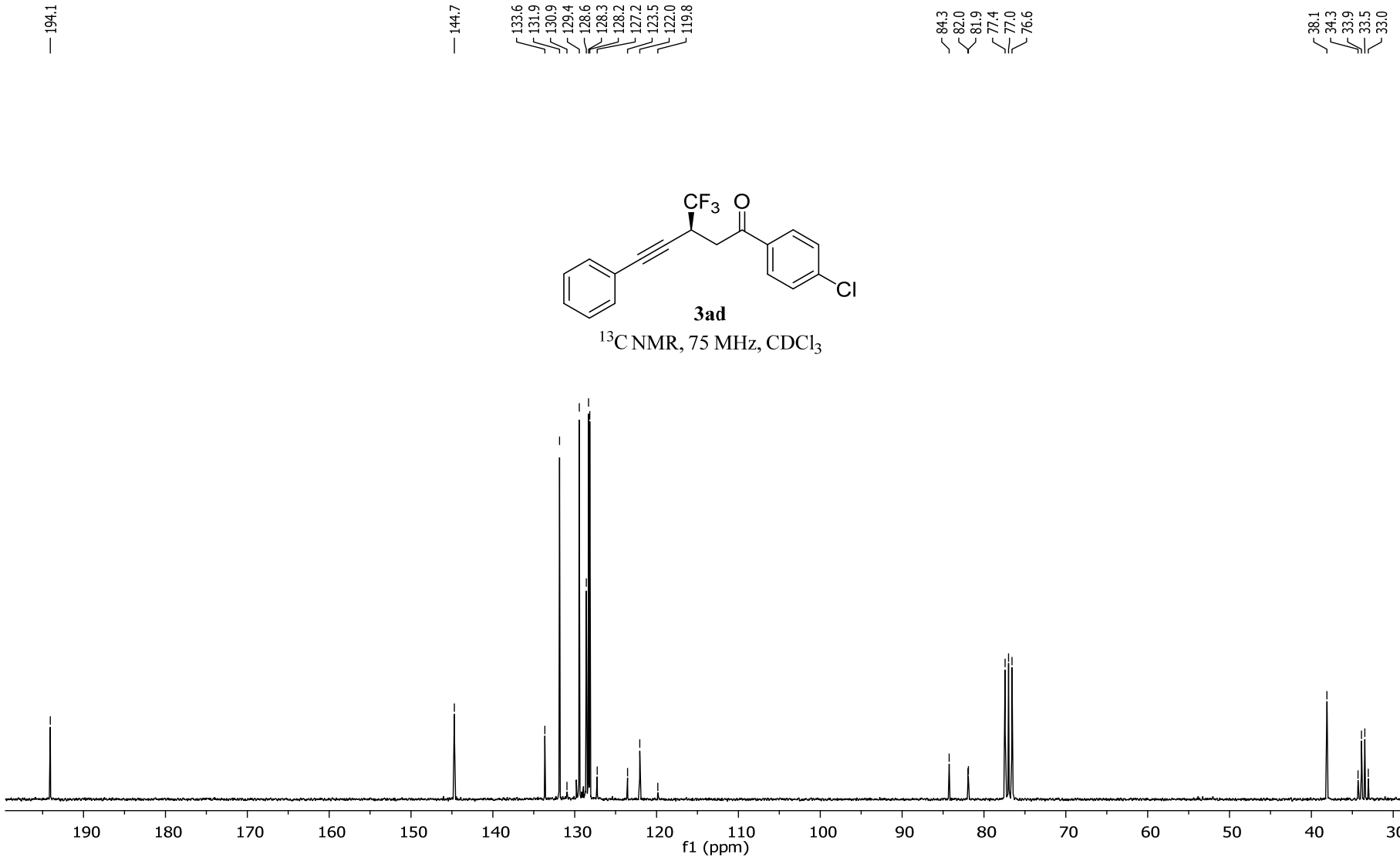
^{19}F NMR, 282 MHz, $CDCl_3$

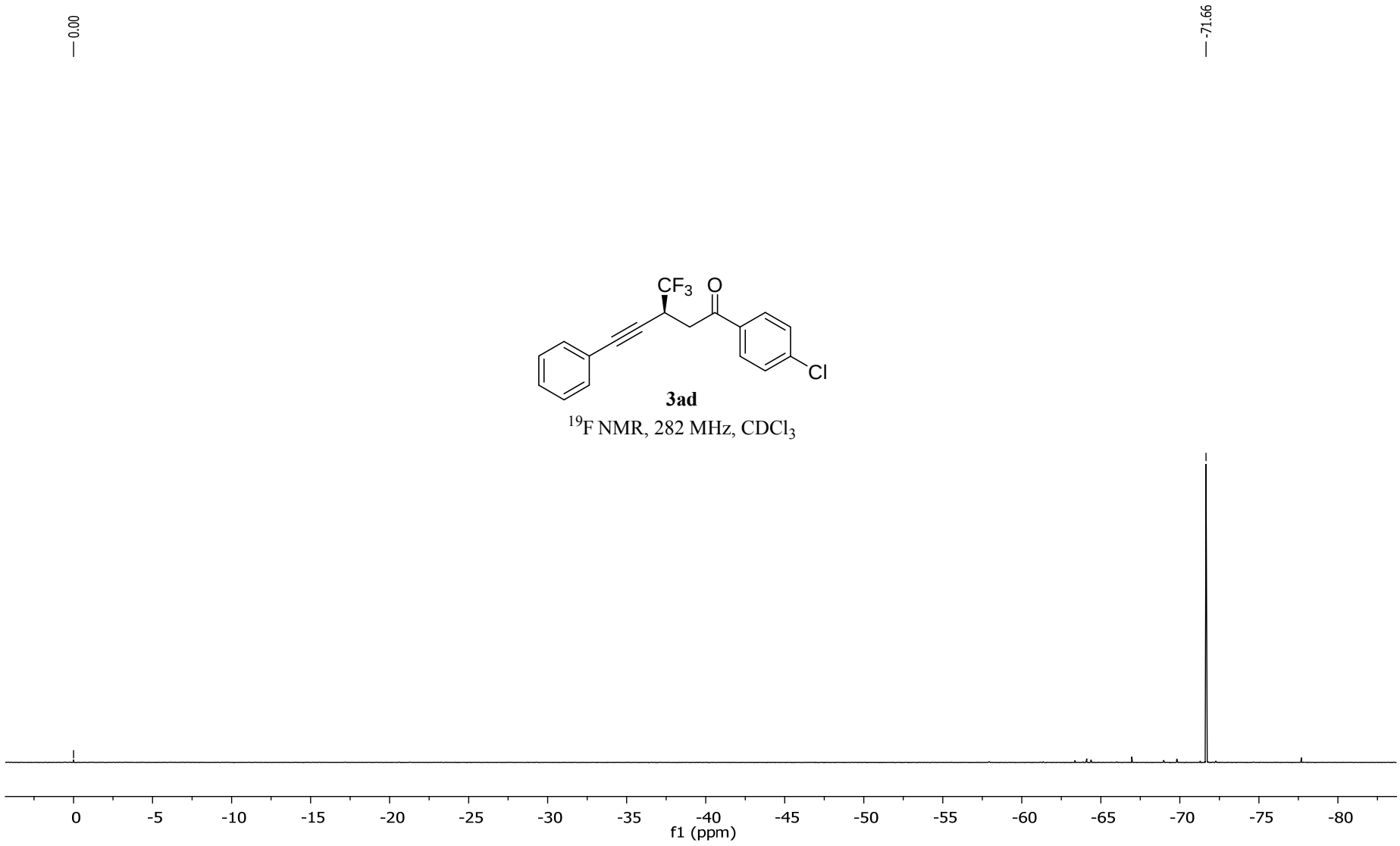


3ad

^{1}H NMR, 300 MHz, $CDCl_3$

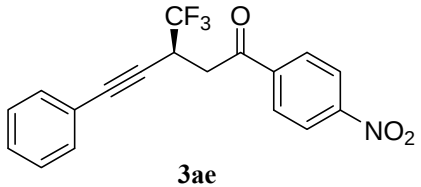






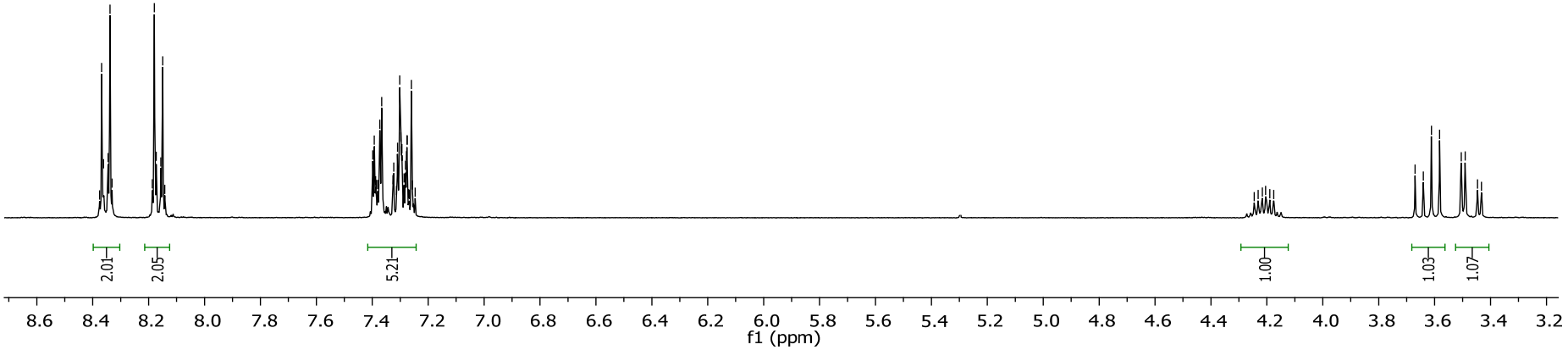
3ad

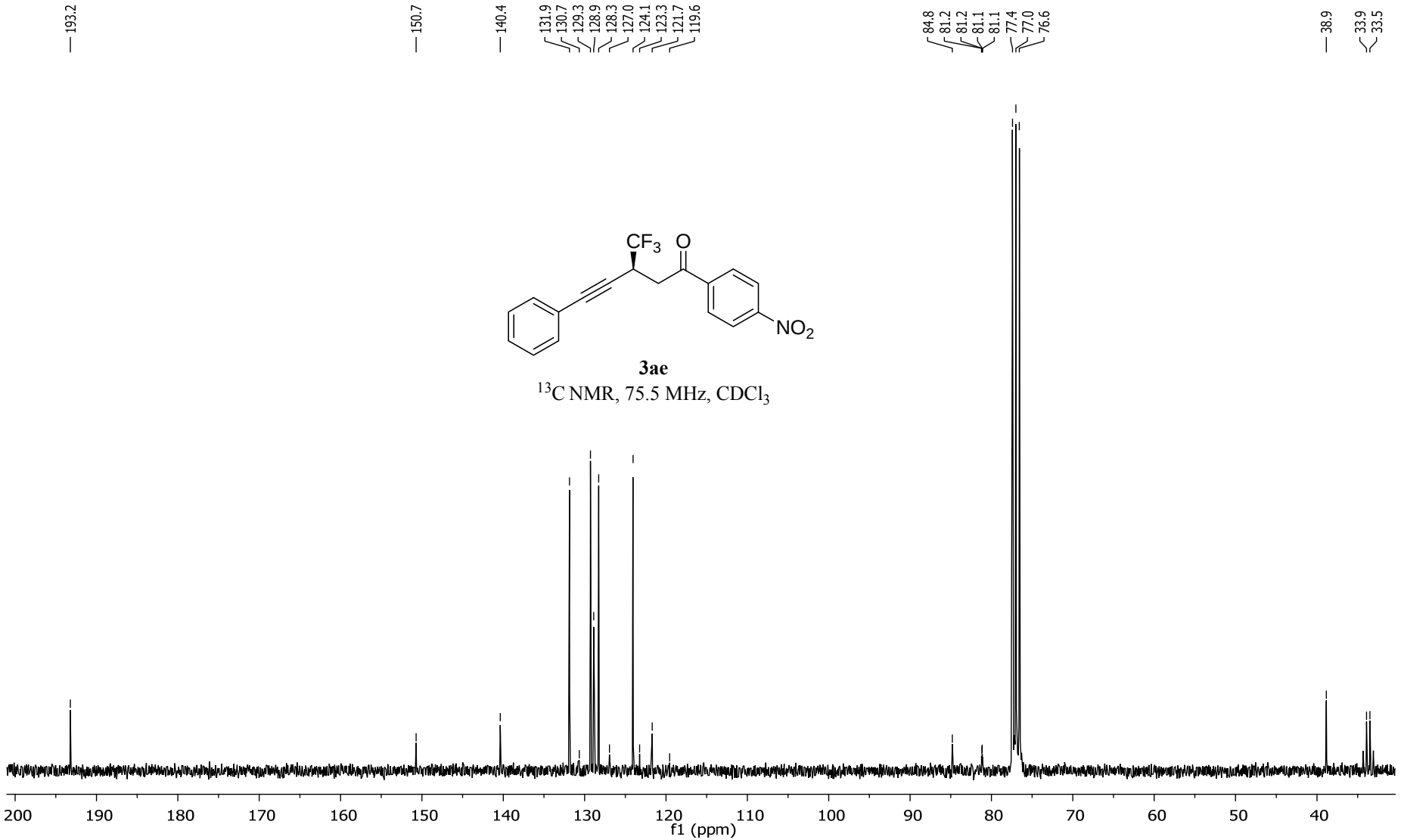
^{19}F NMR, 282 MHz, $CDCl_3$



3ae

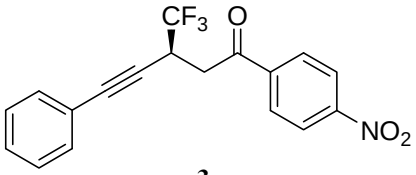
^{1}H NMR, 300 MHz, $CDCl_3$





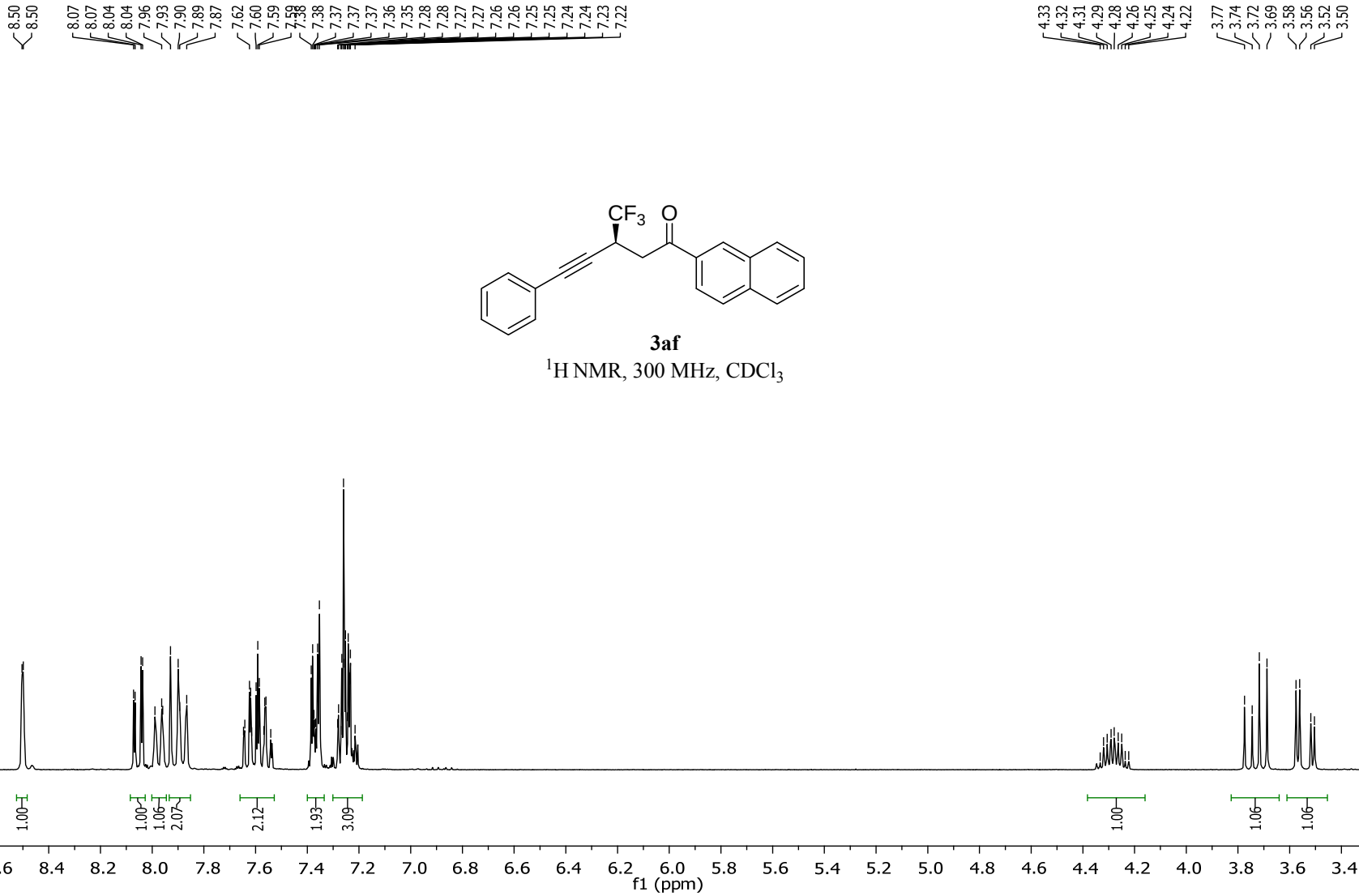
3ae

^{13}C NMR, 75.5 MHz, $CDCl_3$



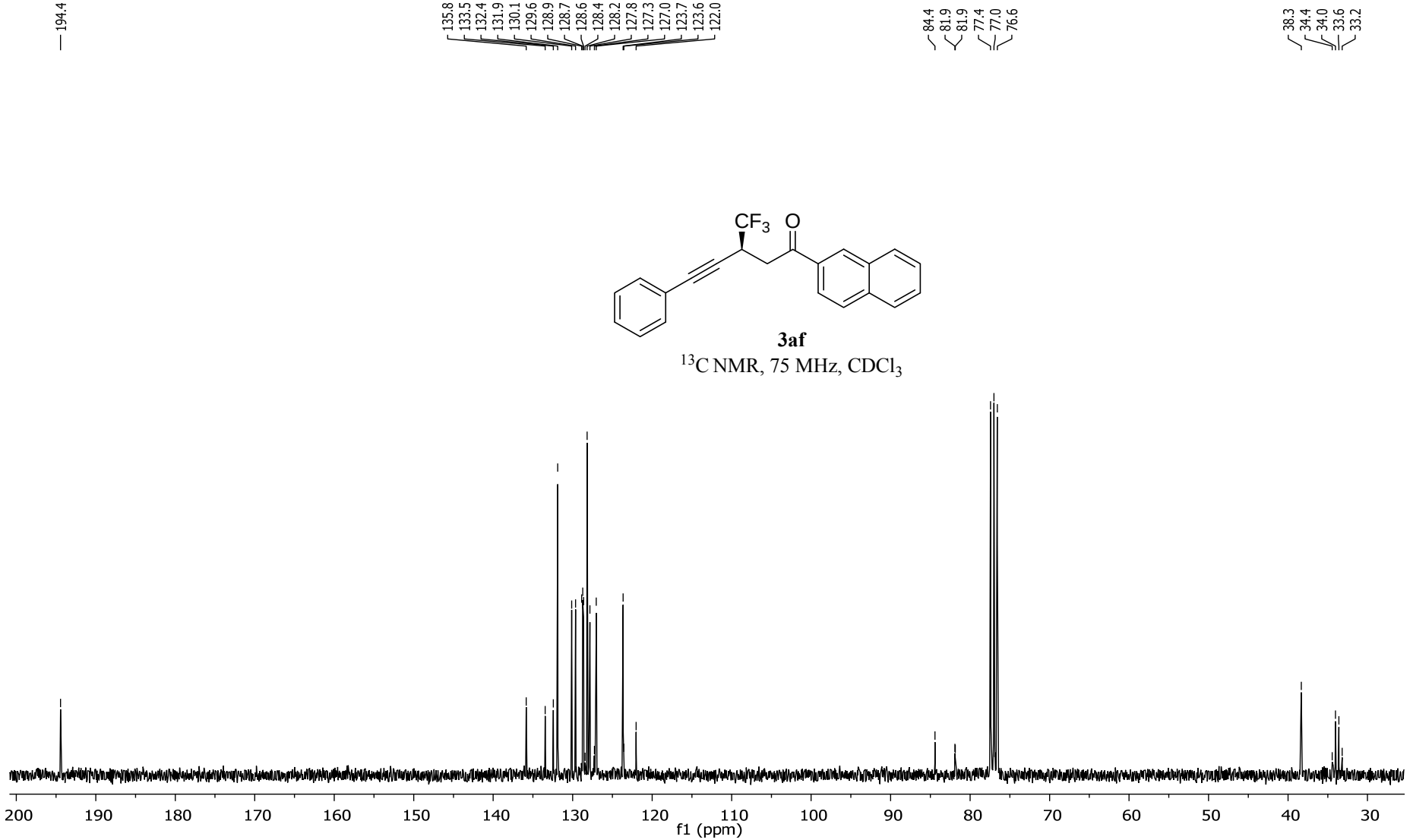
3ae

^{19}F NMR, 282 MHz, $CDCl_3$



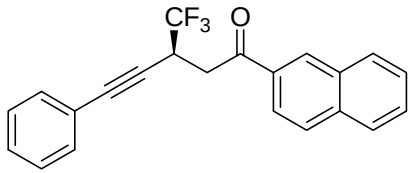
3af

^{1}H NMR, 300 MHz, $CDCl_3$



3af

^{13}C NMR, 75 MHz, $CDCl_3$



3af

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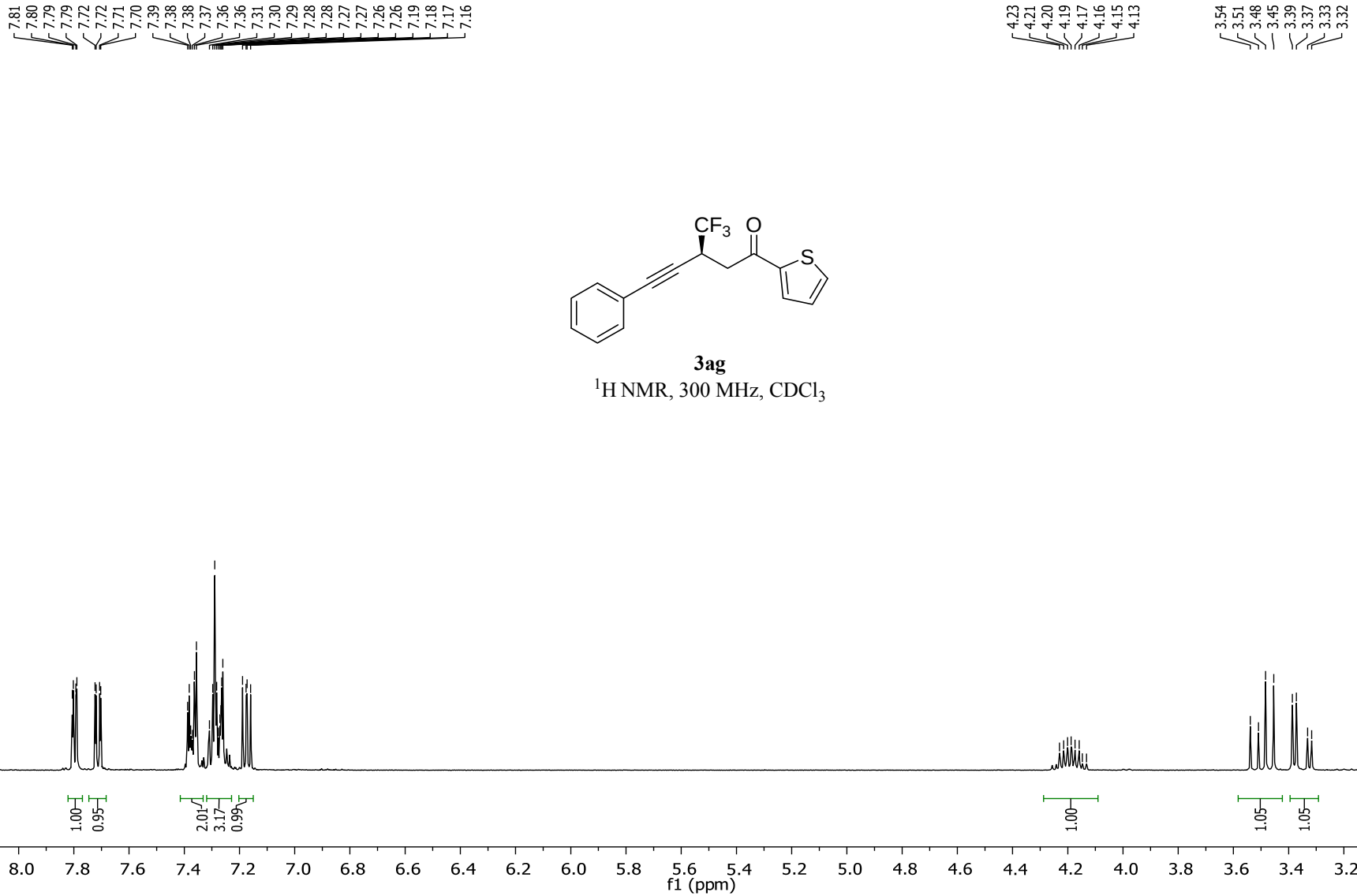

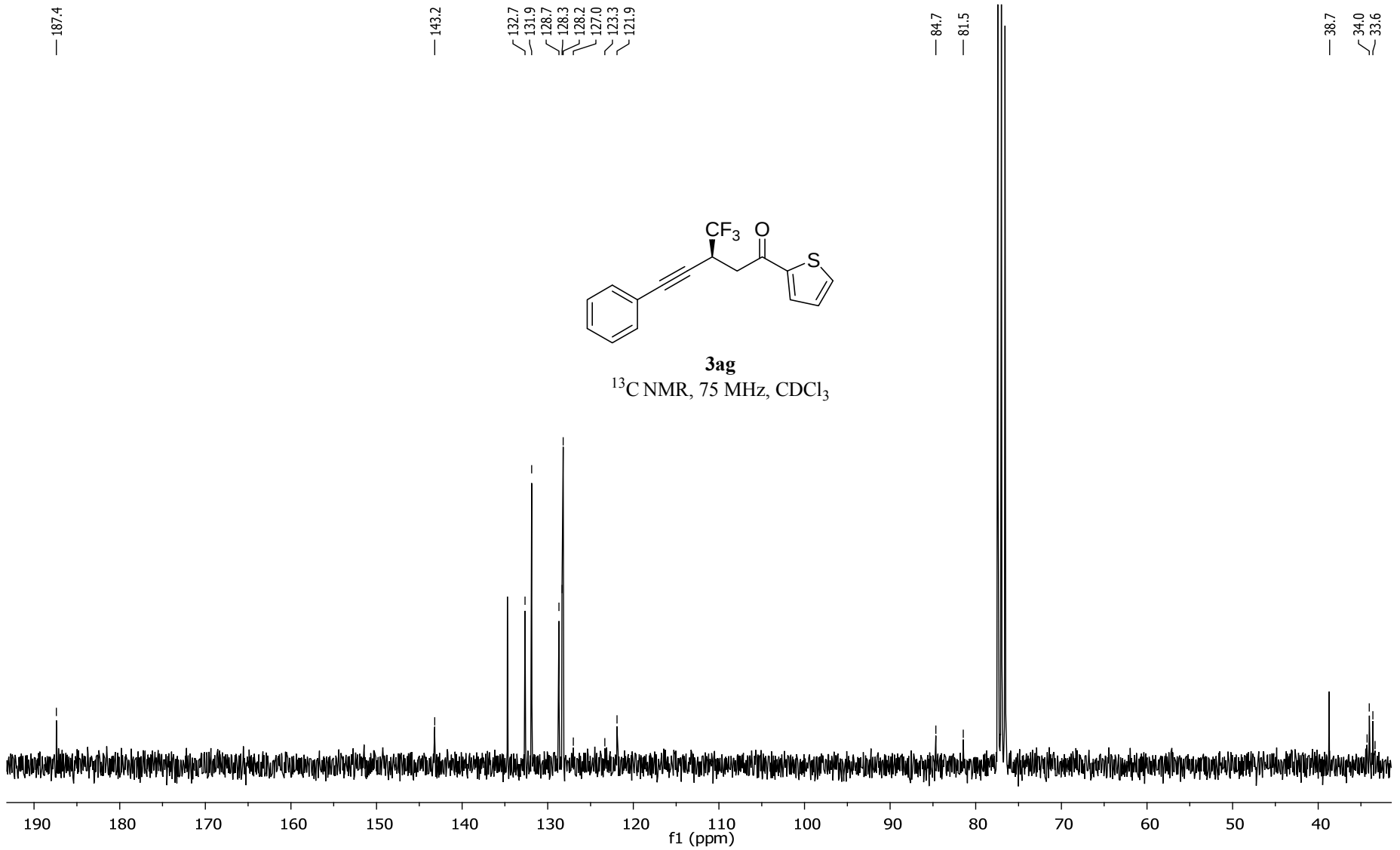

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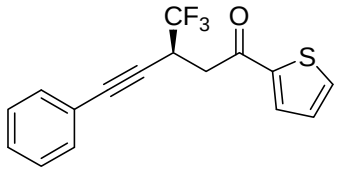

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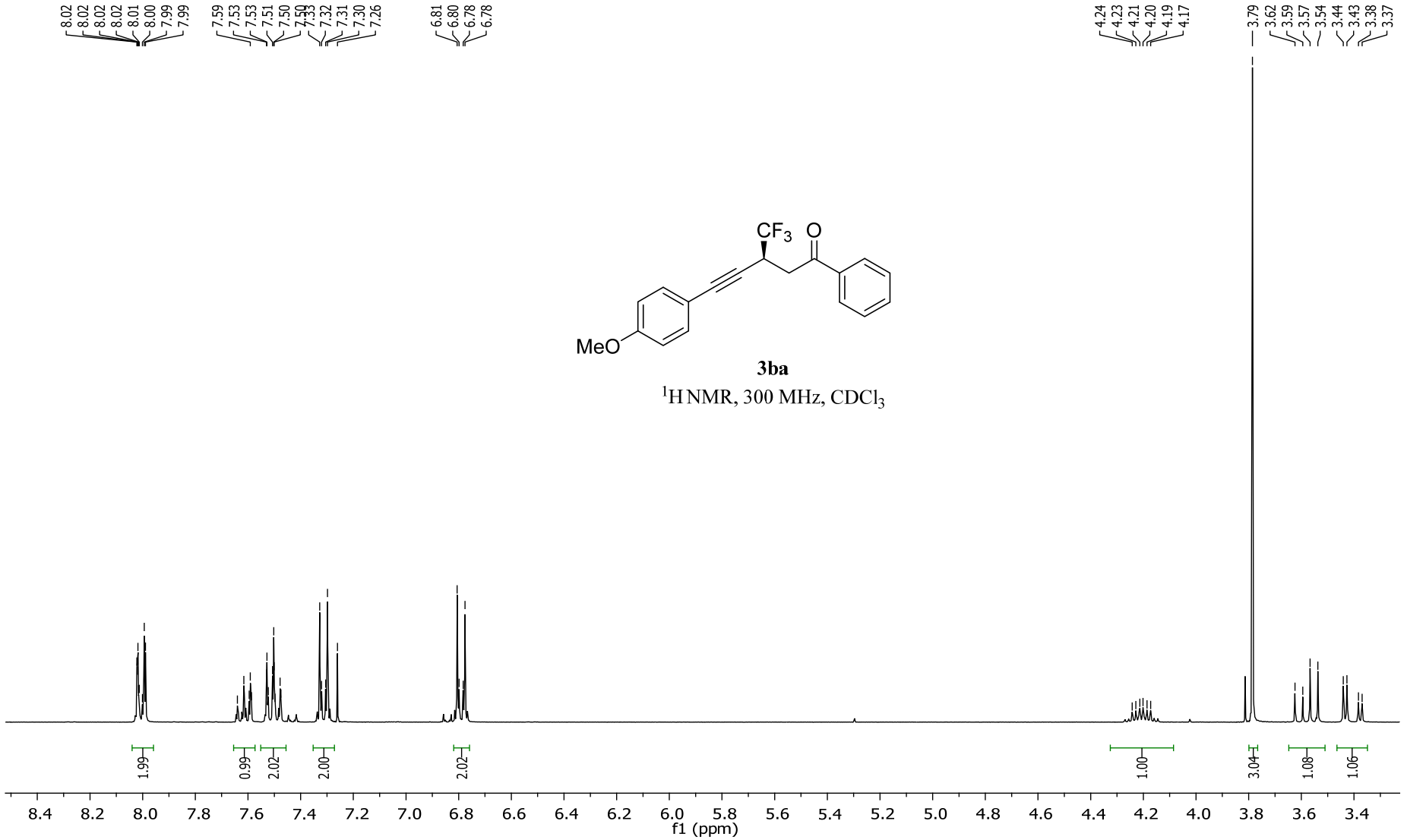

3ba

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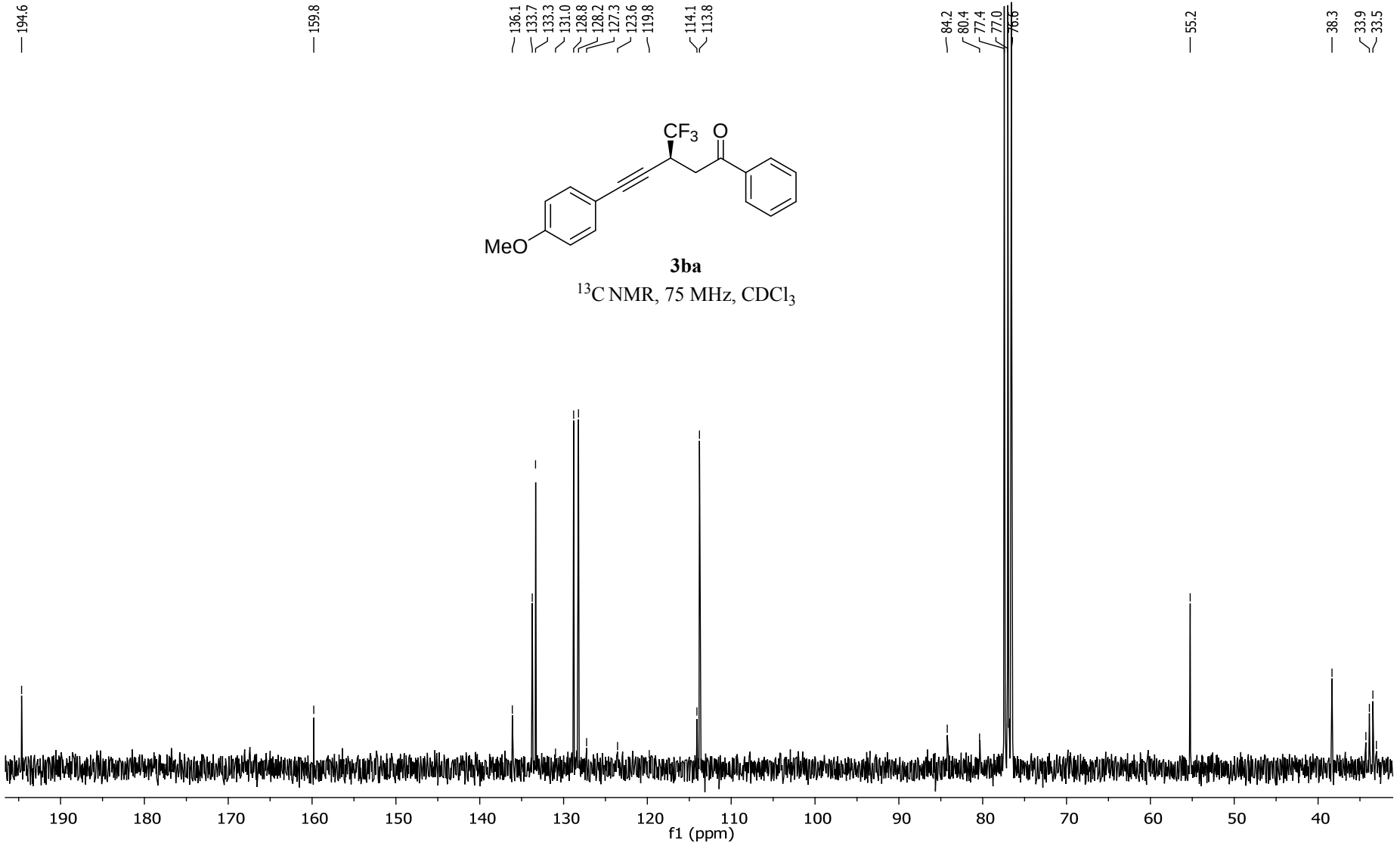

3ba

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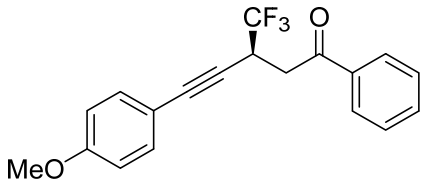

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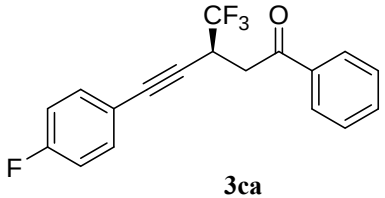

3ca

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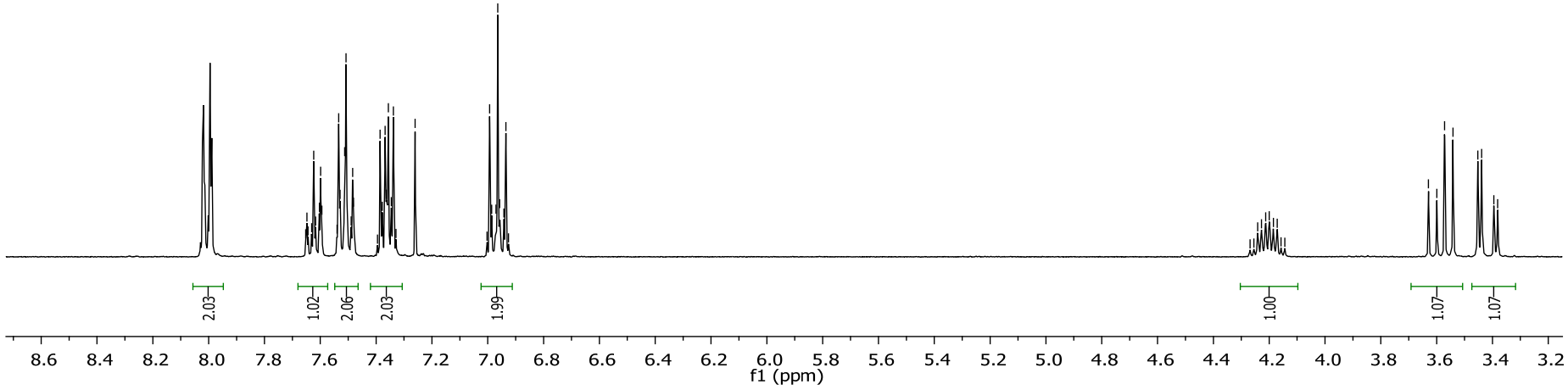

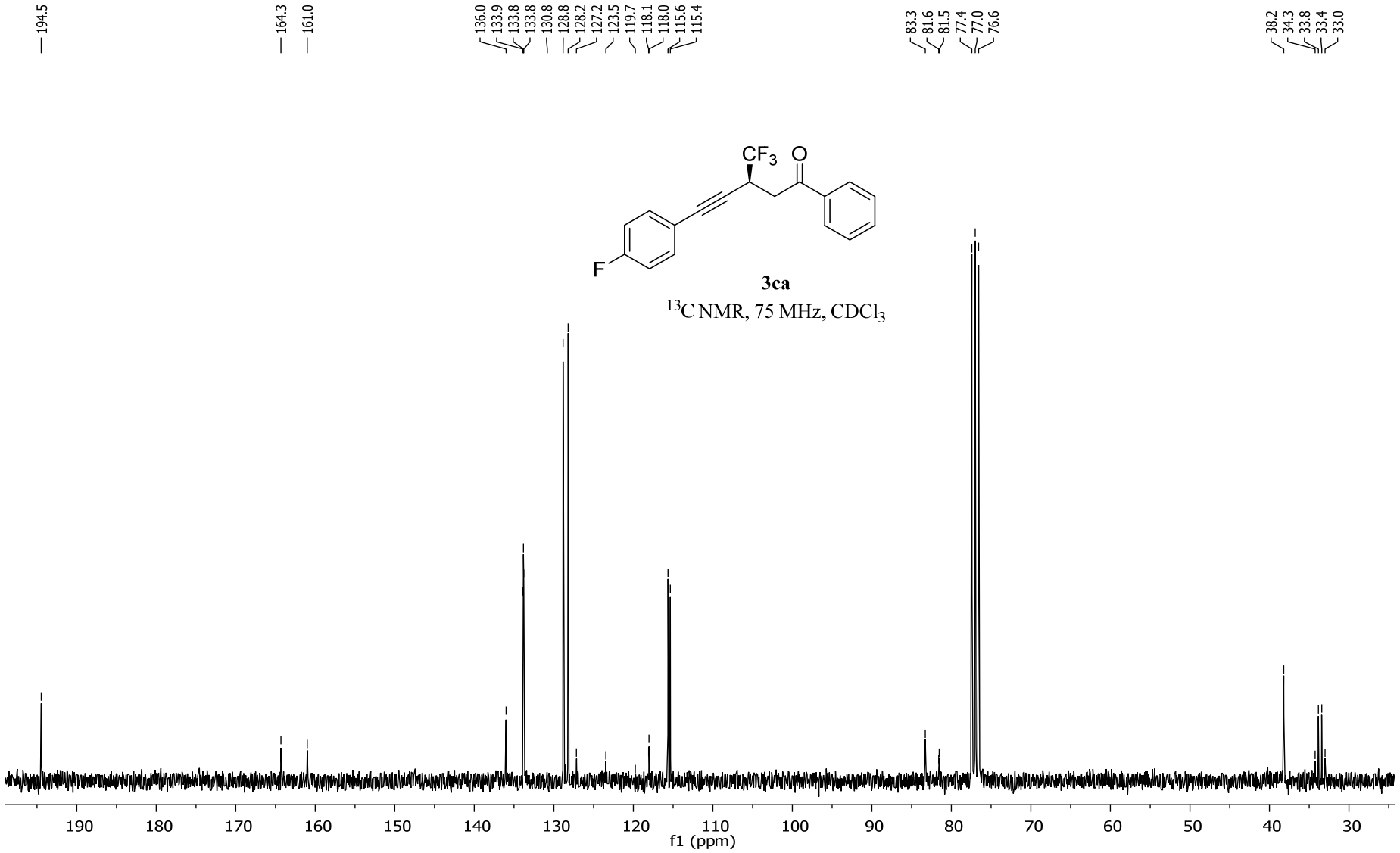

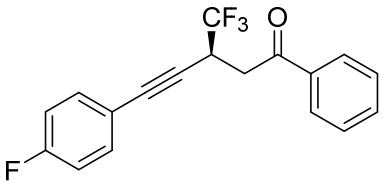

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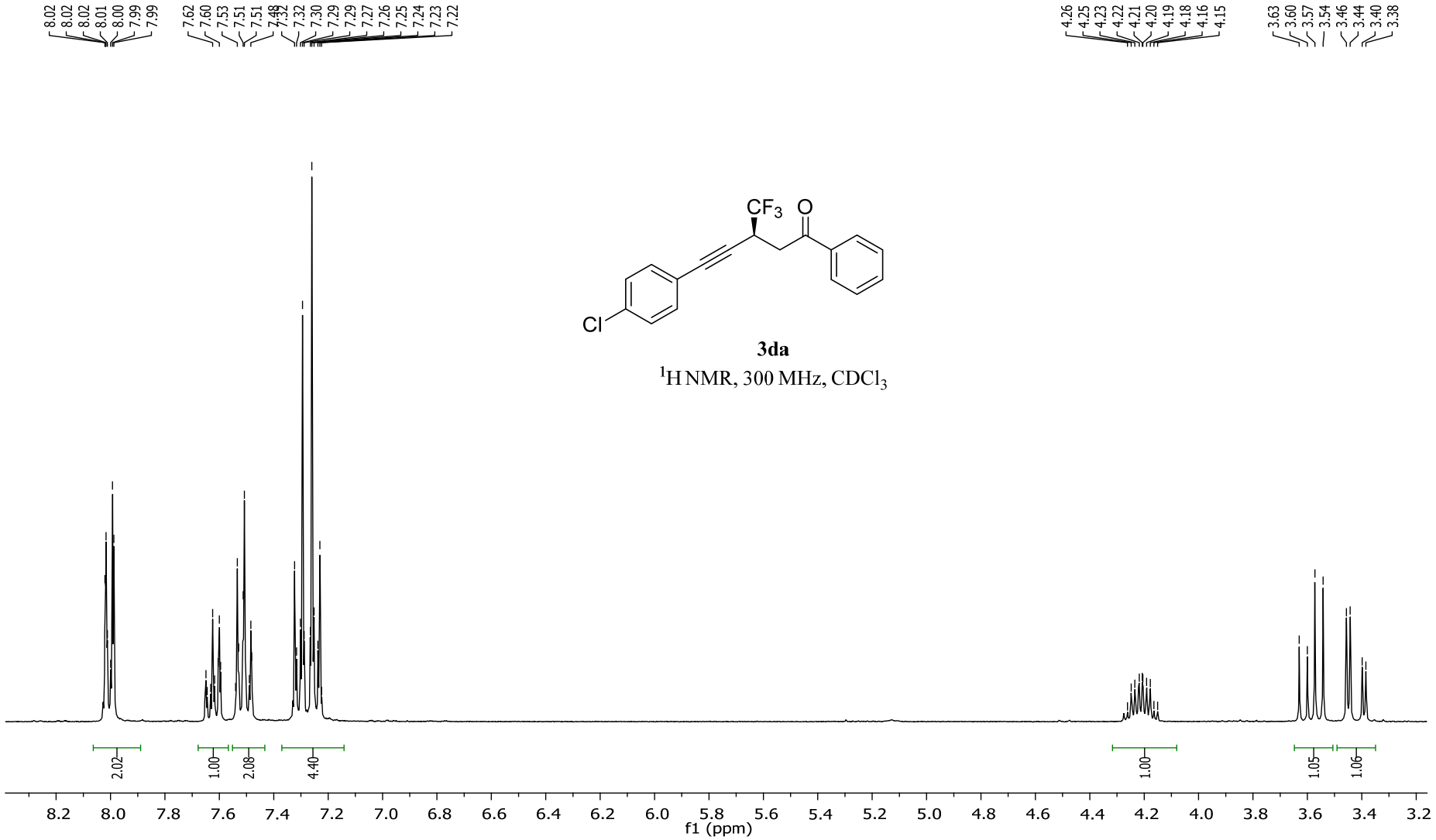

3da

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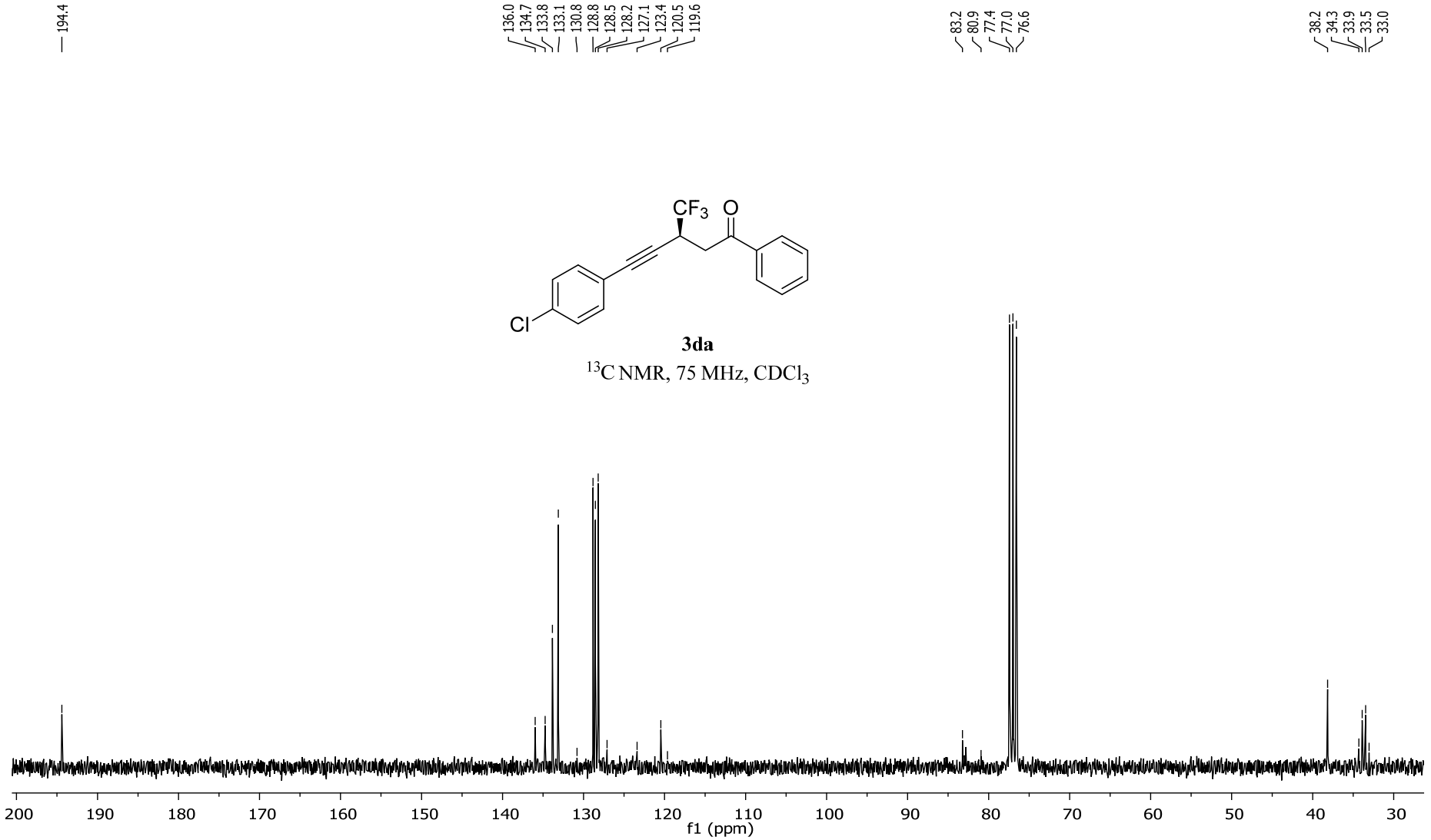

3da

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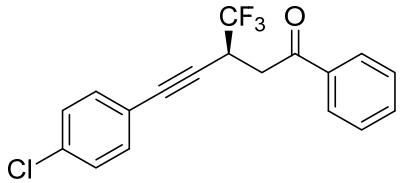

3da

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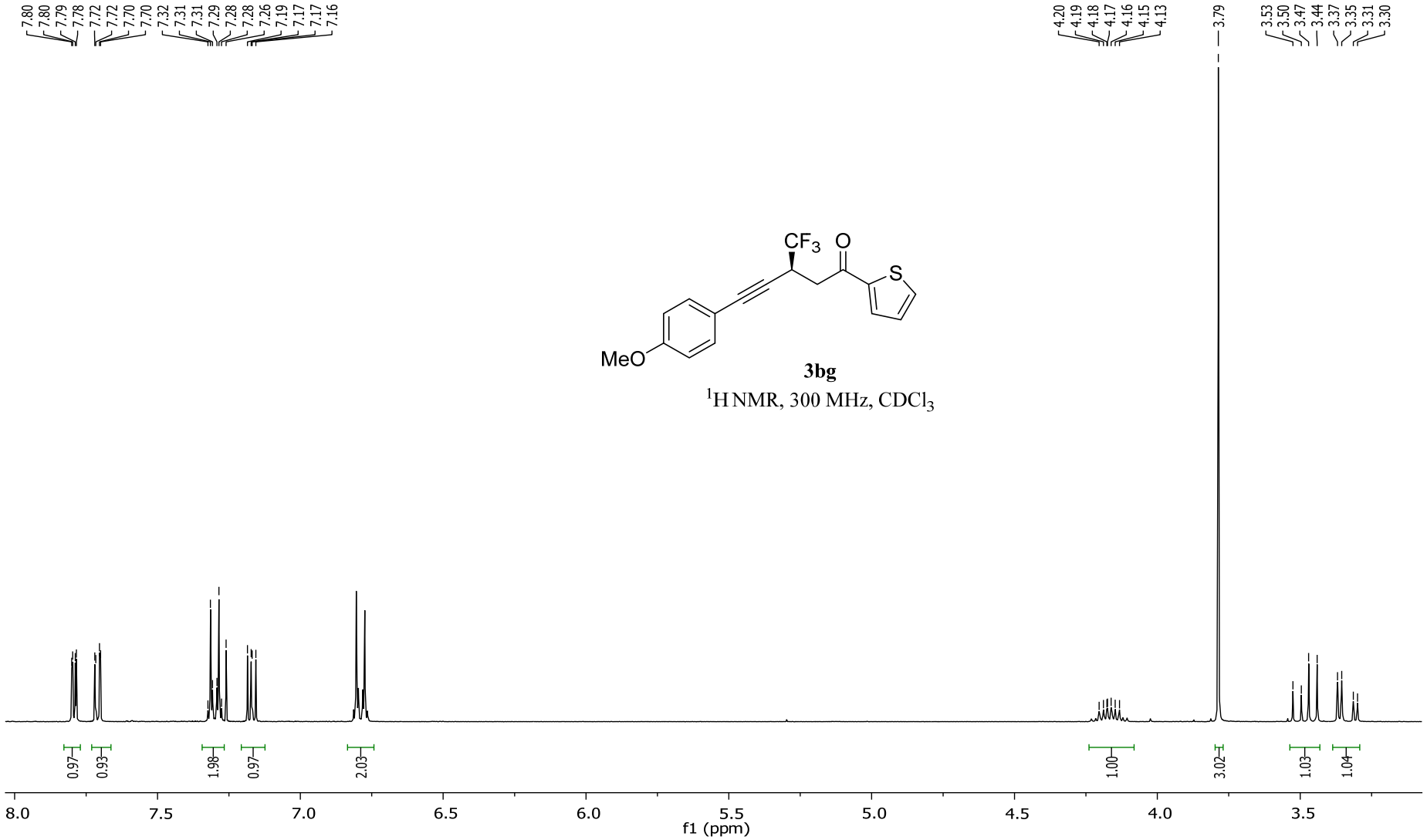

3bg

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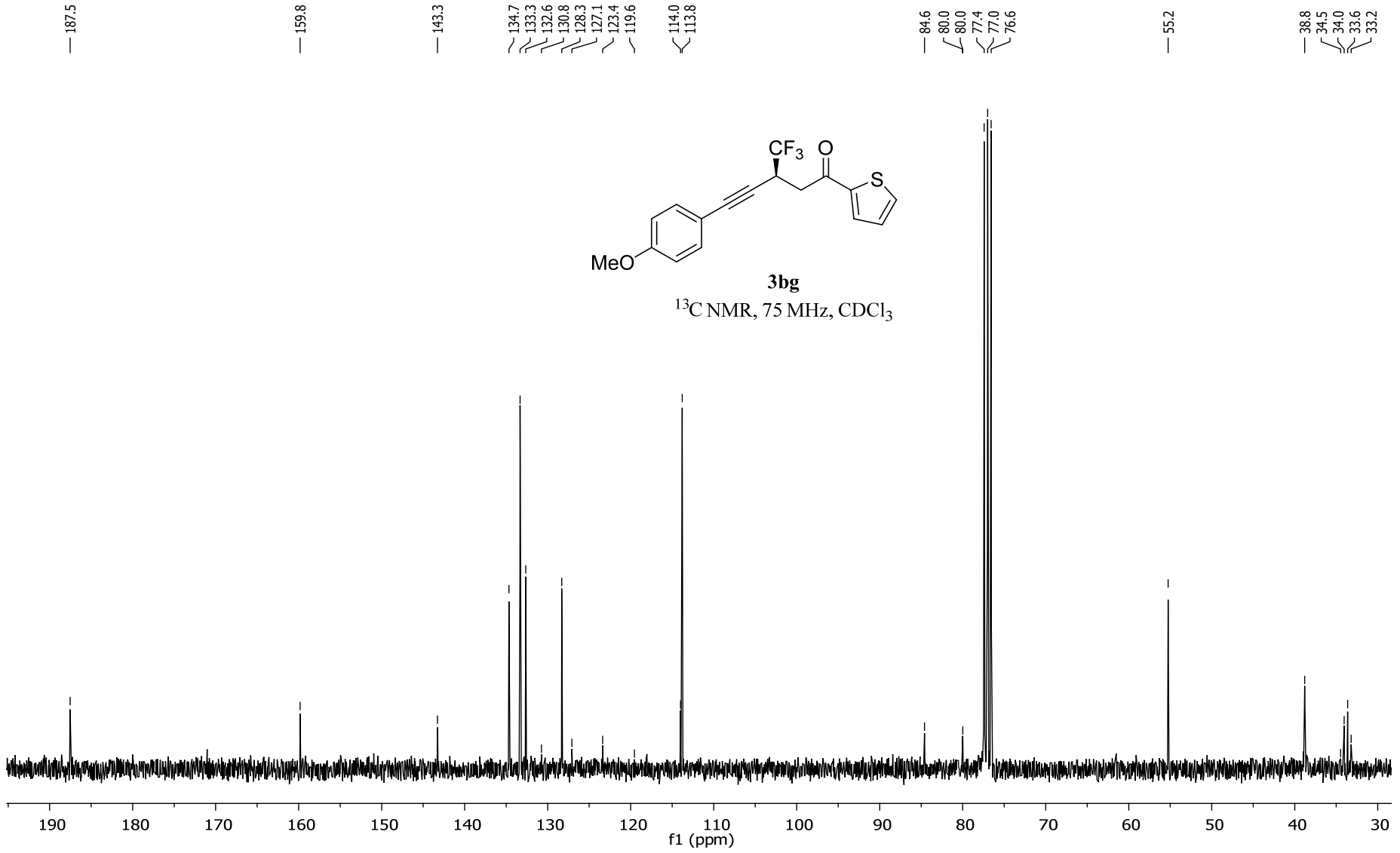

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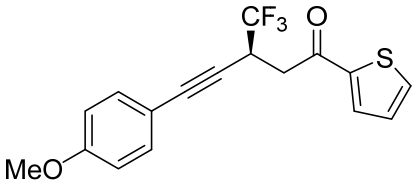

3bg

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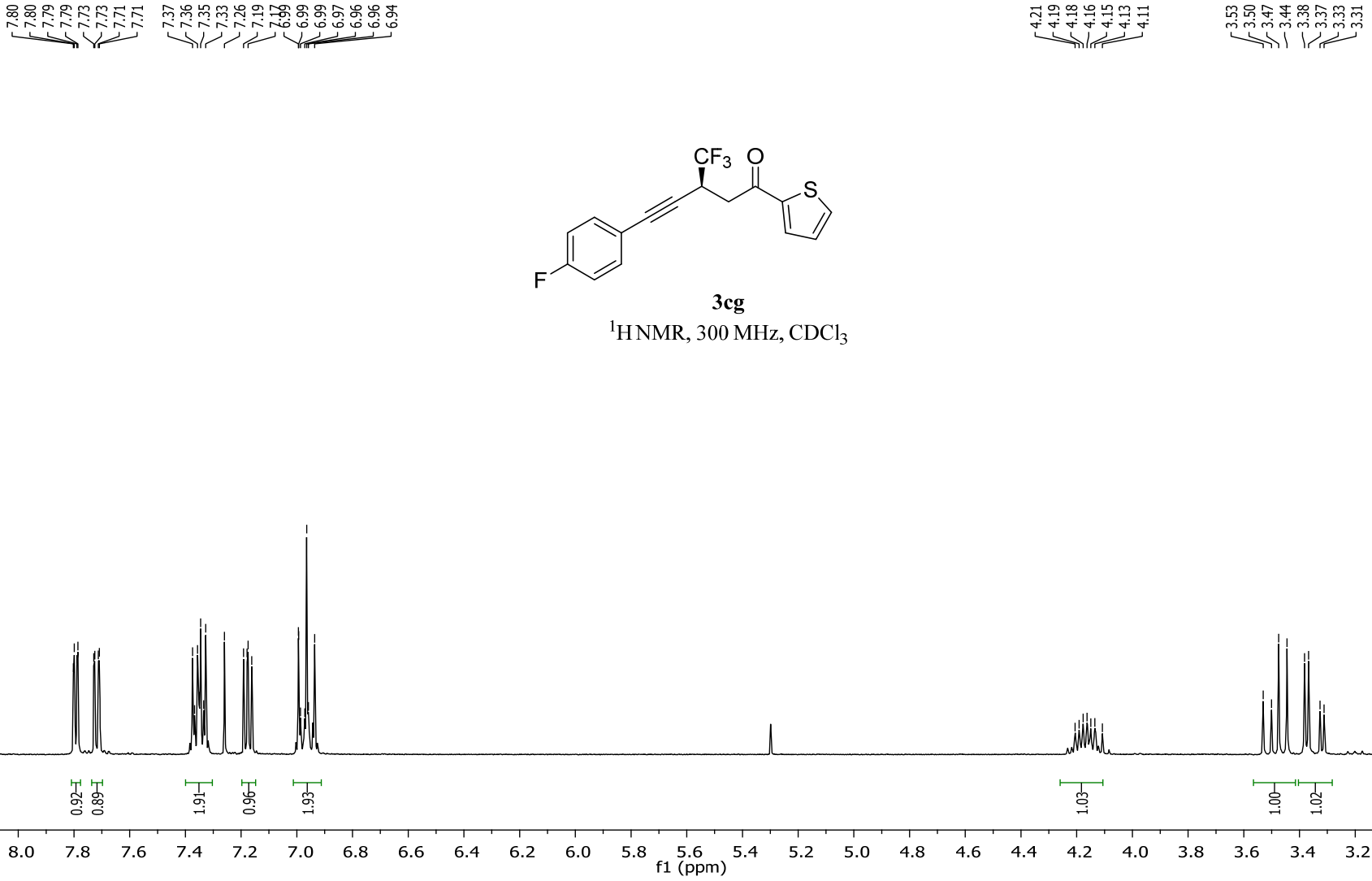

3cg

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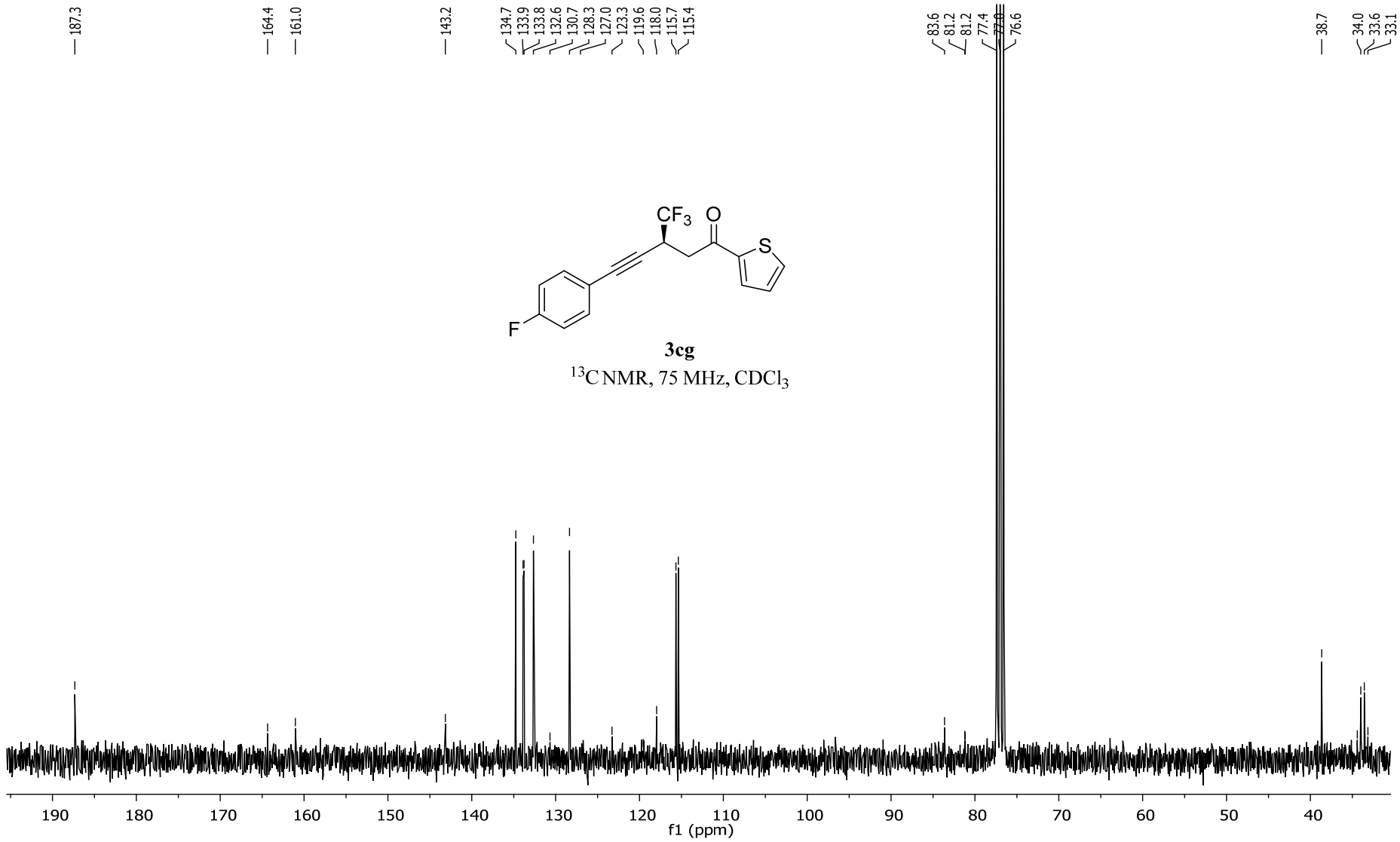

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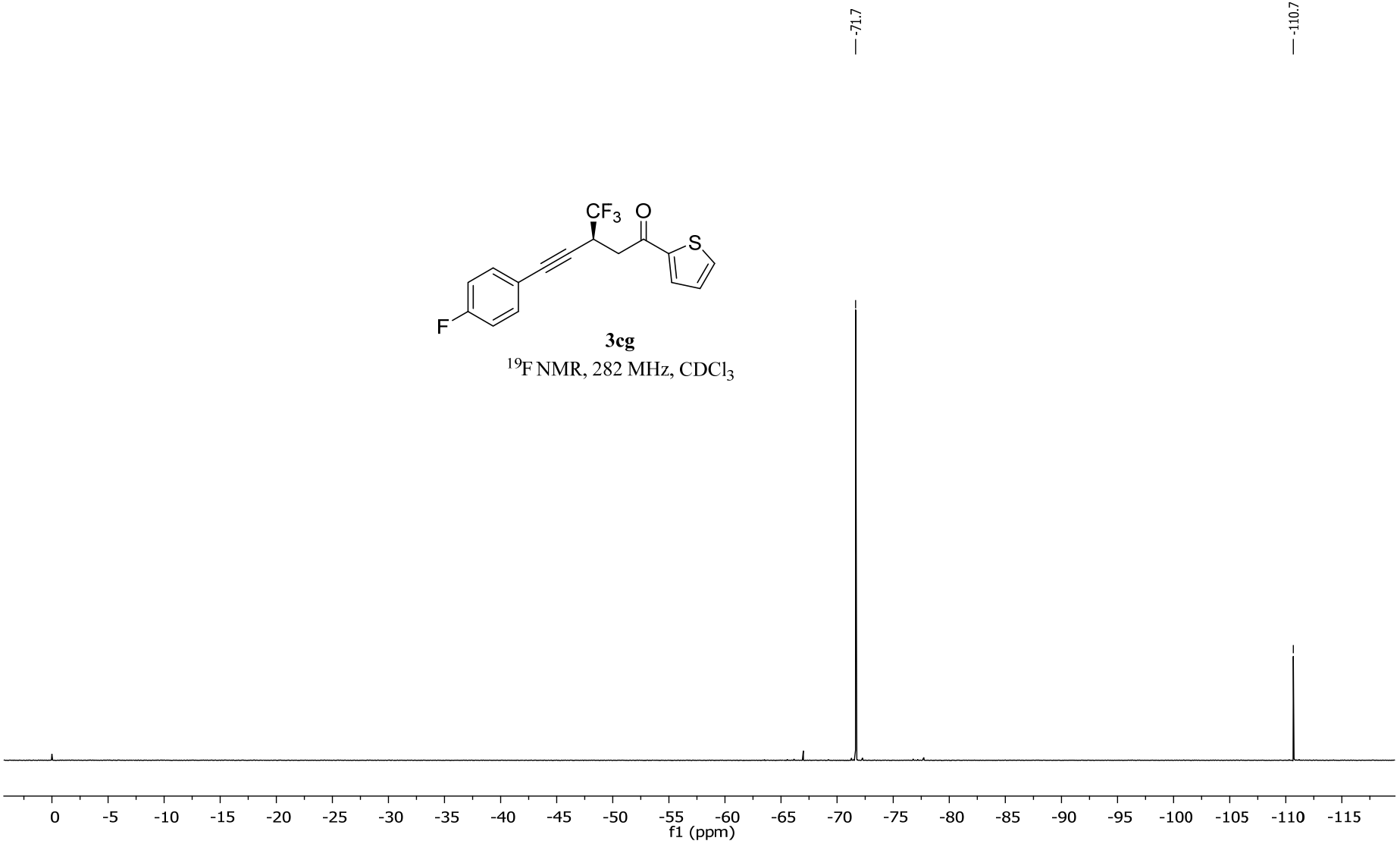

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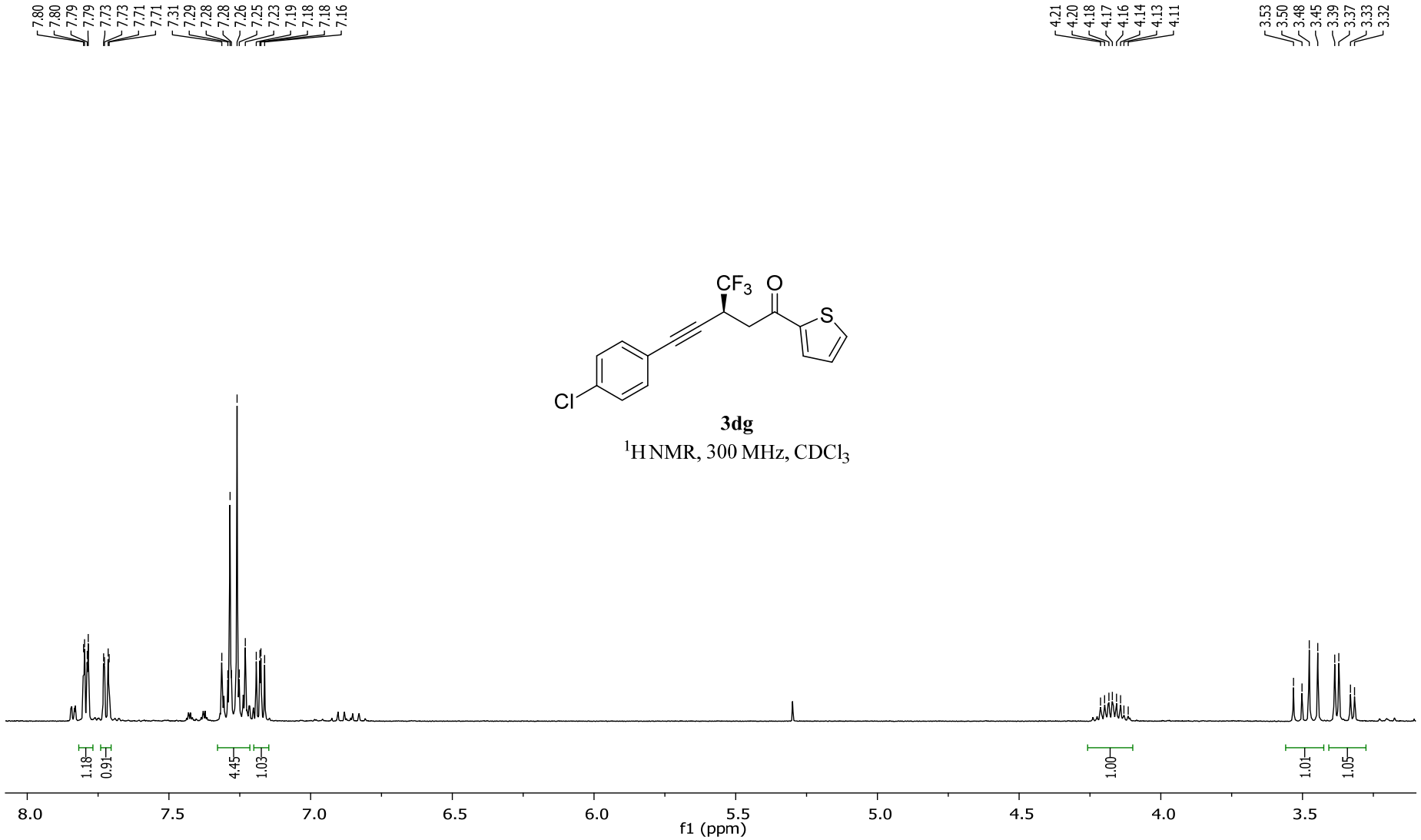

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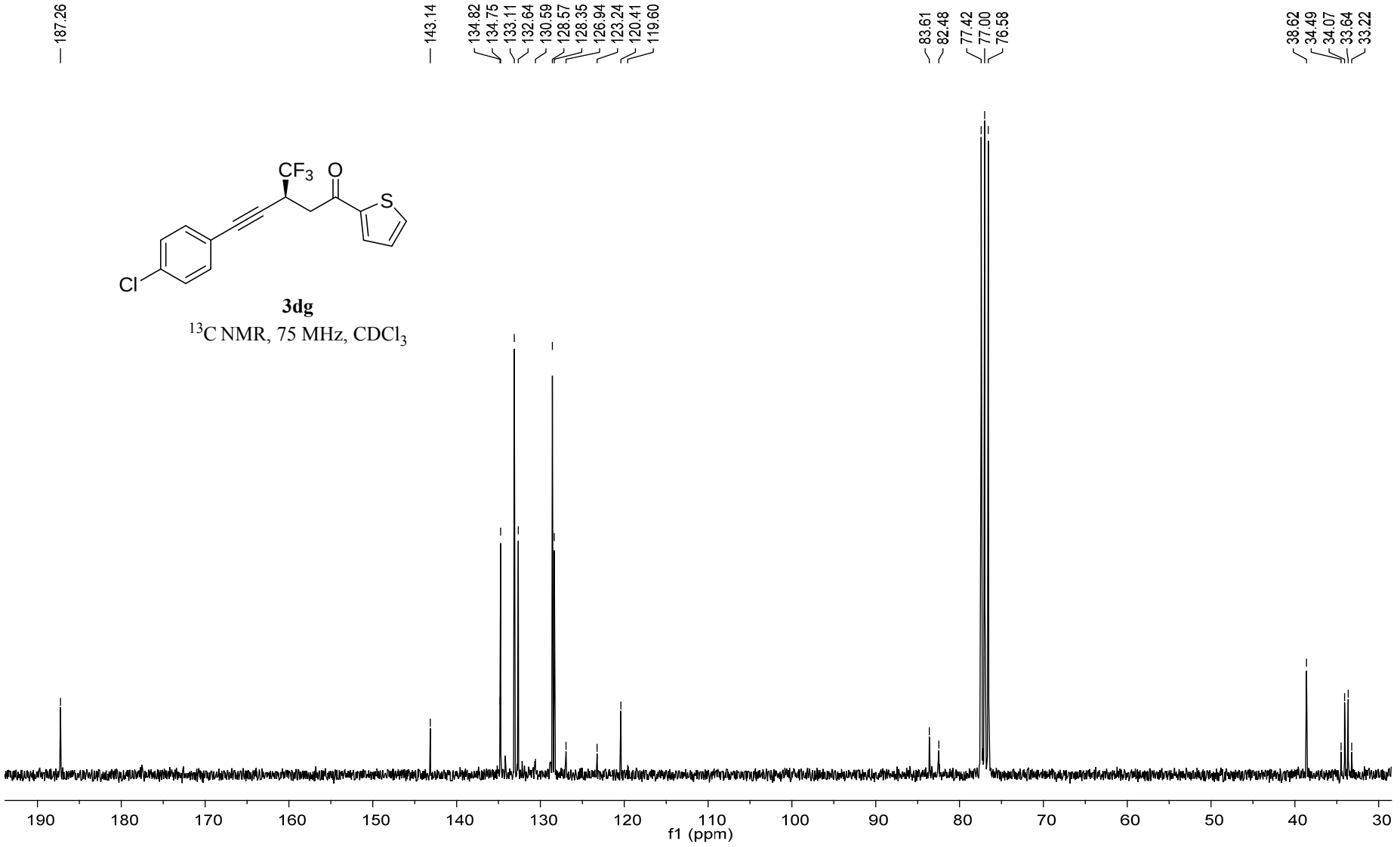
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83.61
82.48
77.42
77.00
76.58
38.62
34.49
34.07
33.64
33.22
CF3
O
S
Cl
3dg
13C NMR, 75 MHz, CDCl3
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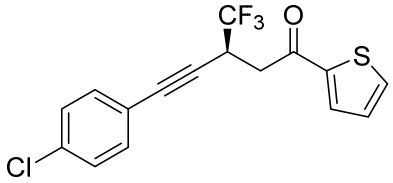
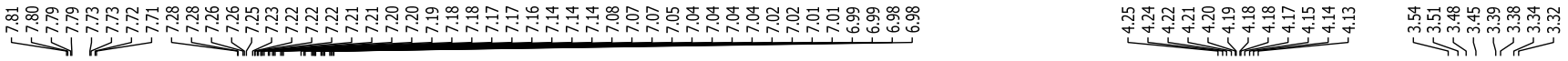
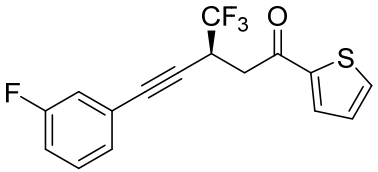
f1 (ppm)



3dg

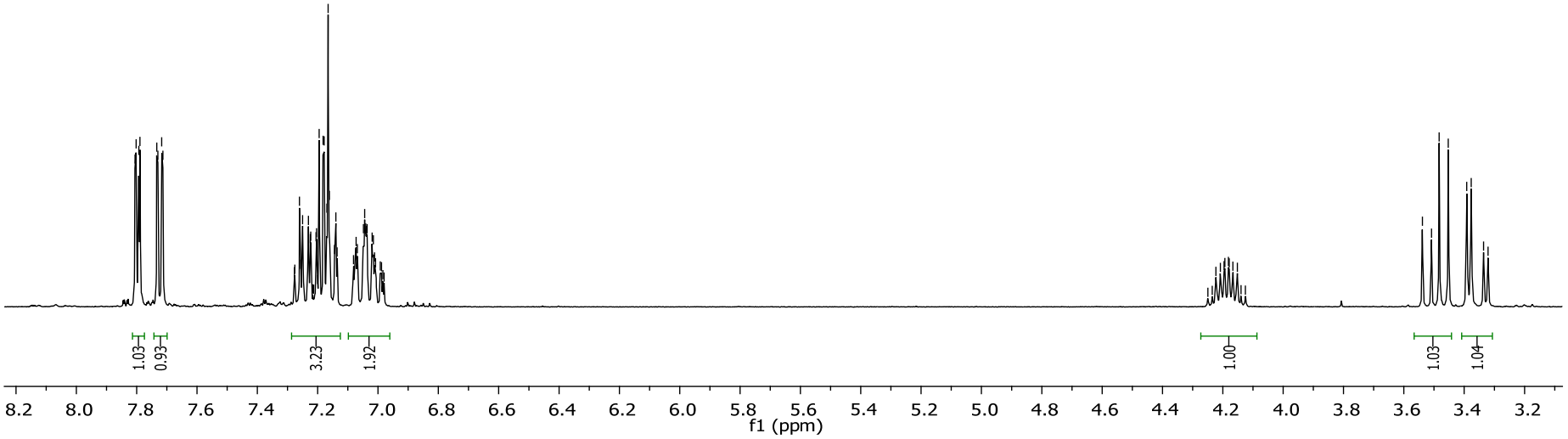
^{19}F NMR, 282 MHz, $CDCl_3$

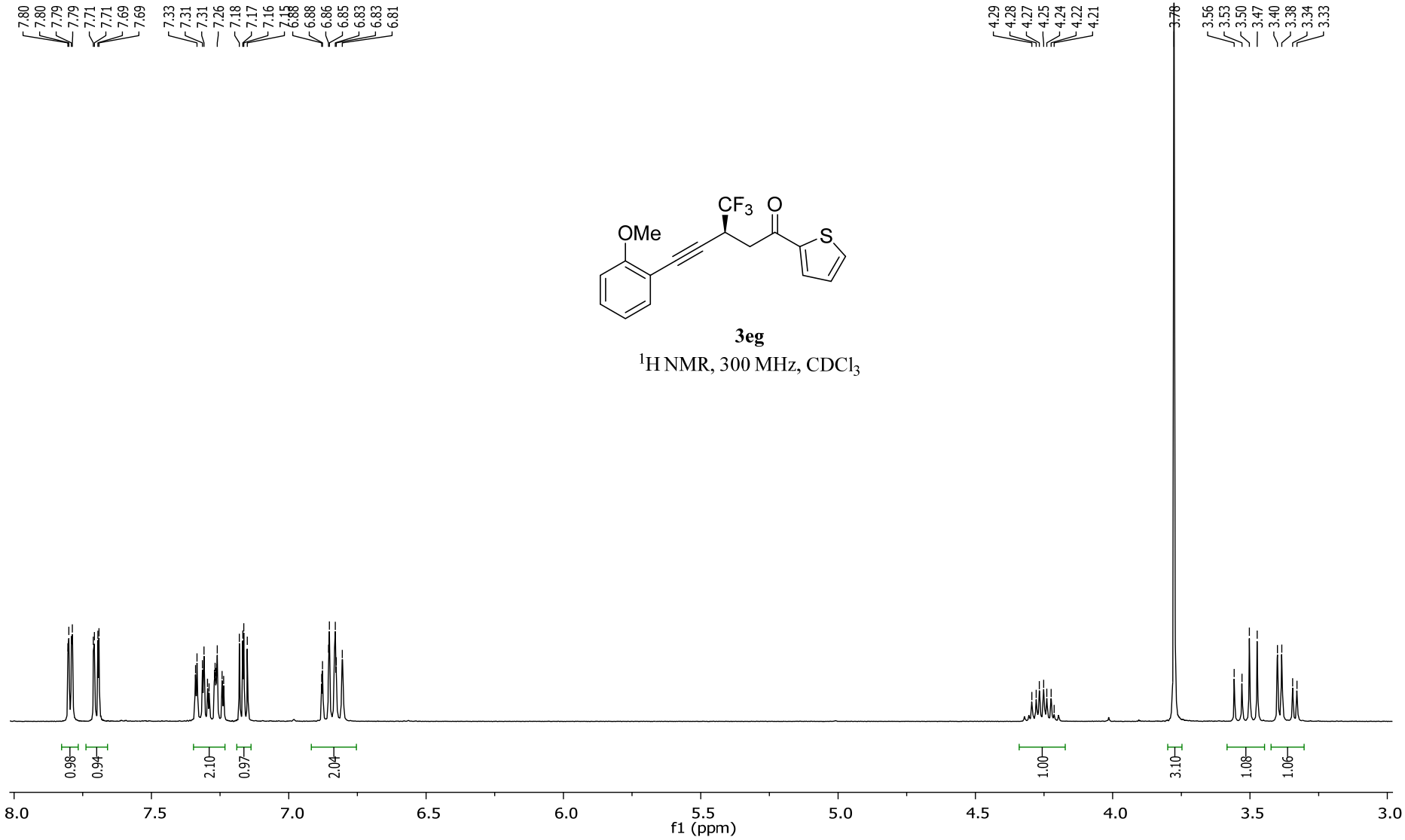




3fg

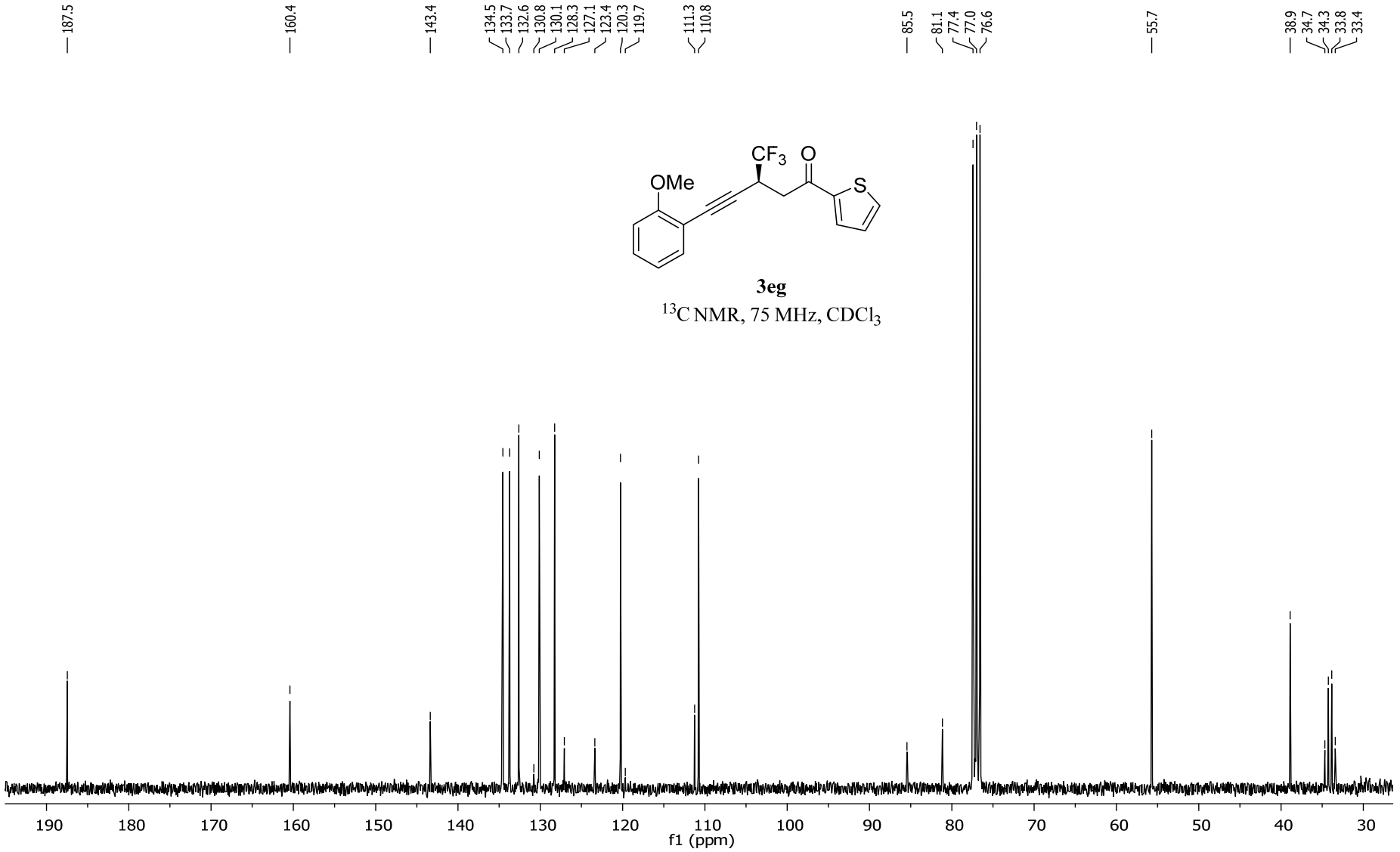
^{1}H NMR, 300 MHz, $CDCl_3$

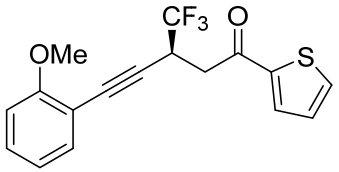




3eg

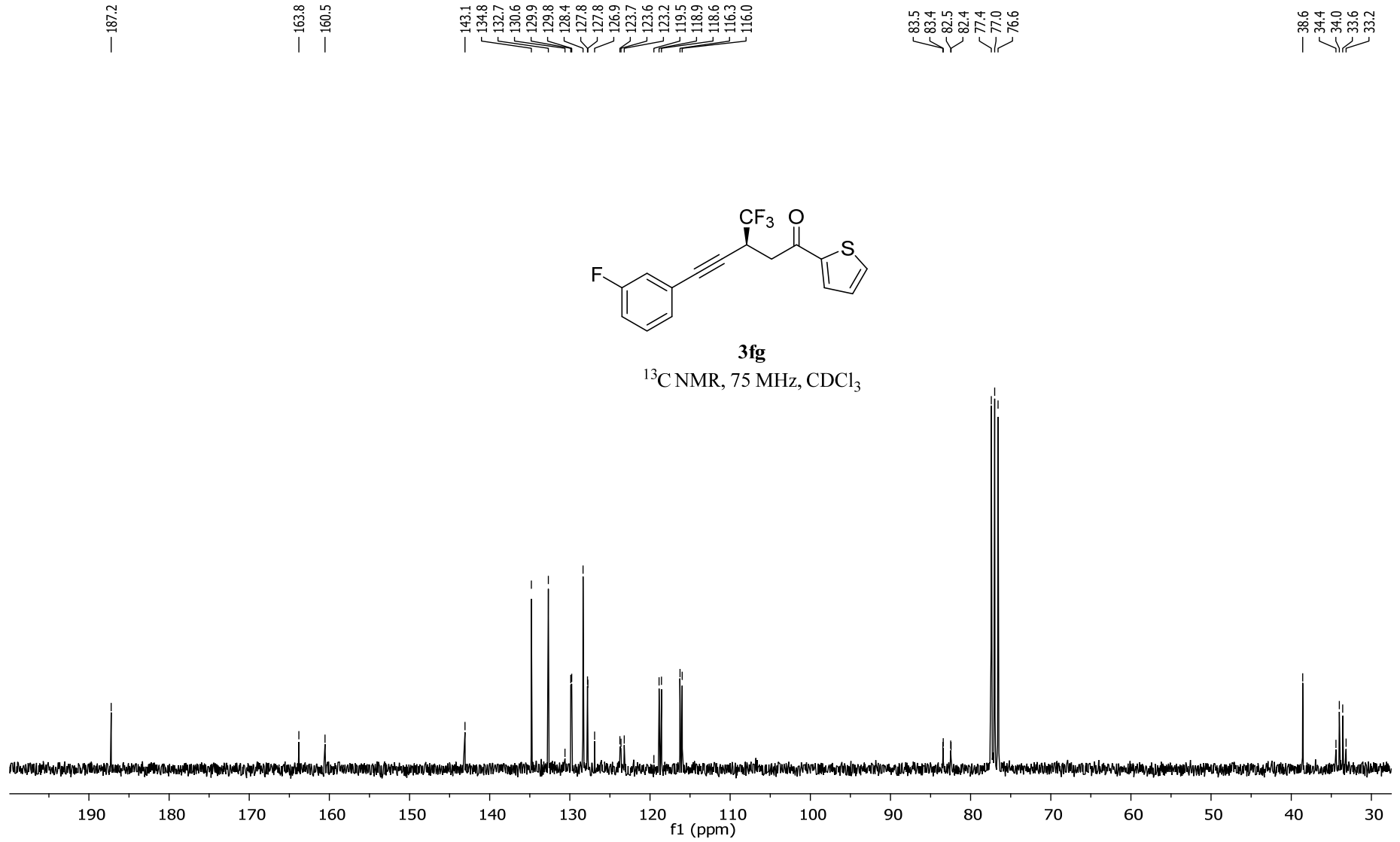
^{1}H NMR, 300 MHz, $CDCl_3$





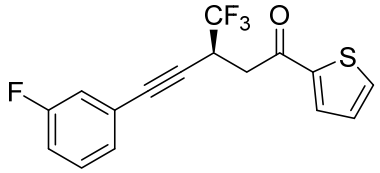
3eg

^{19}F NMR, 282 MHz, $CDCl_3$



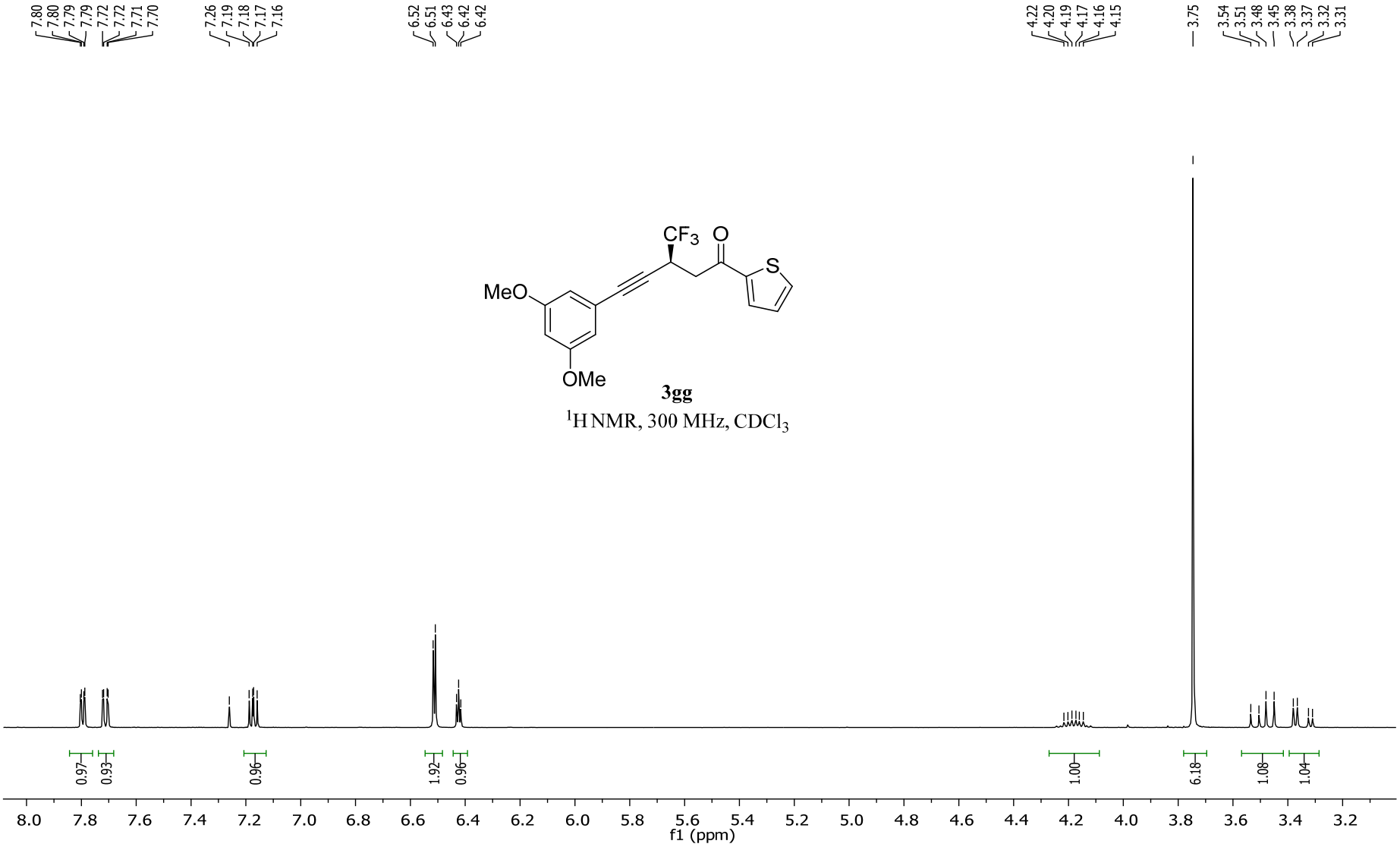
3fg

^{13}C NMR, 75 MHz, $CDCl_3$



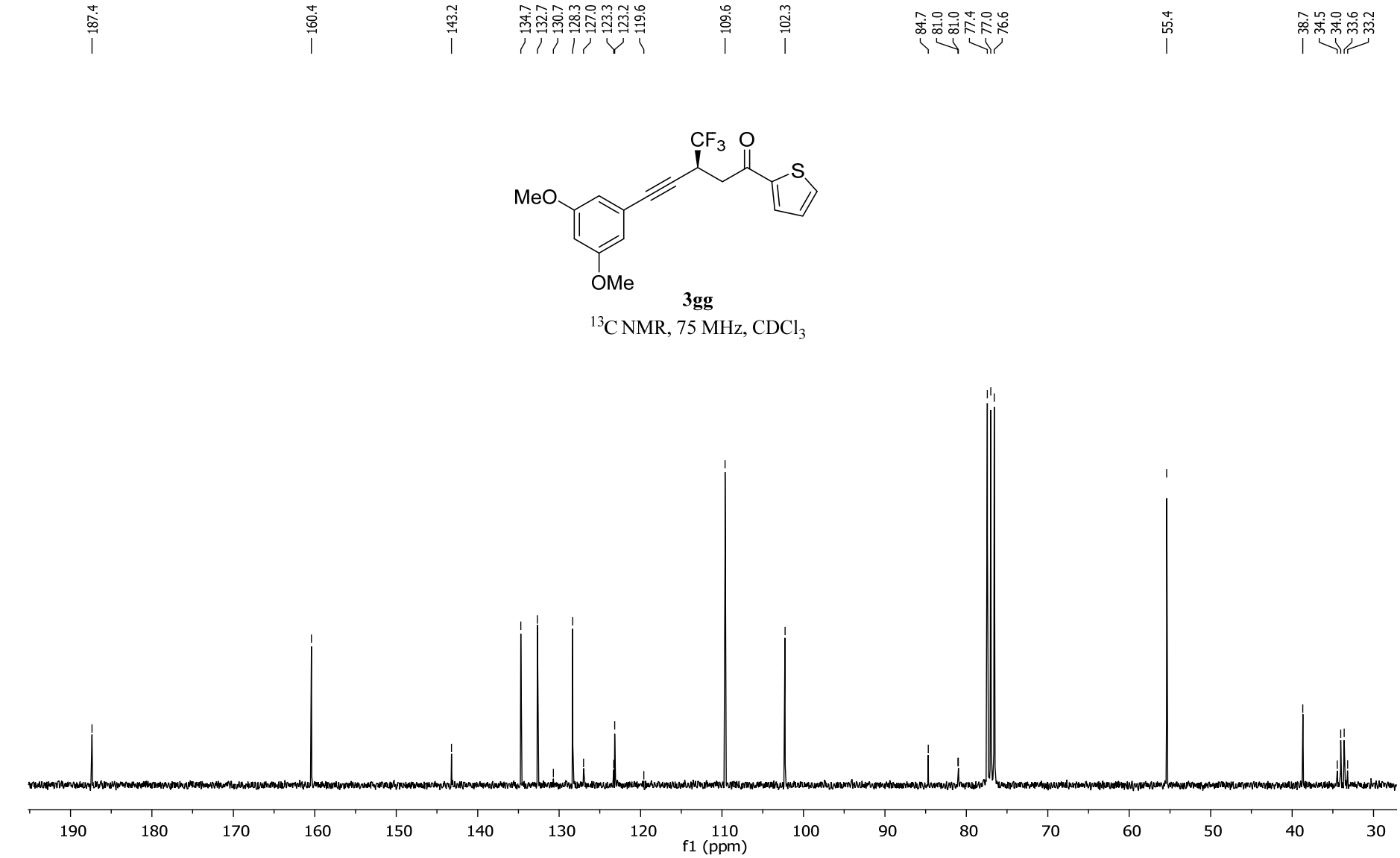
3fg

^{19}F NMR, 282 MHz, $CDCl_3$



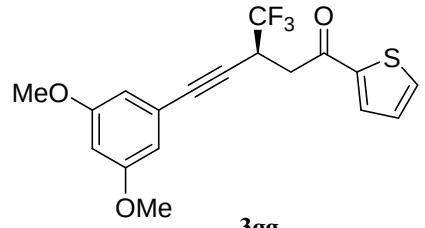
3gg

^{1}H NMR, 300 MHz, $CDCl_3$



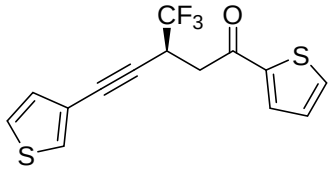
3gg

^{13}C NMR, 75 MHz, $CDCl_3$



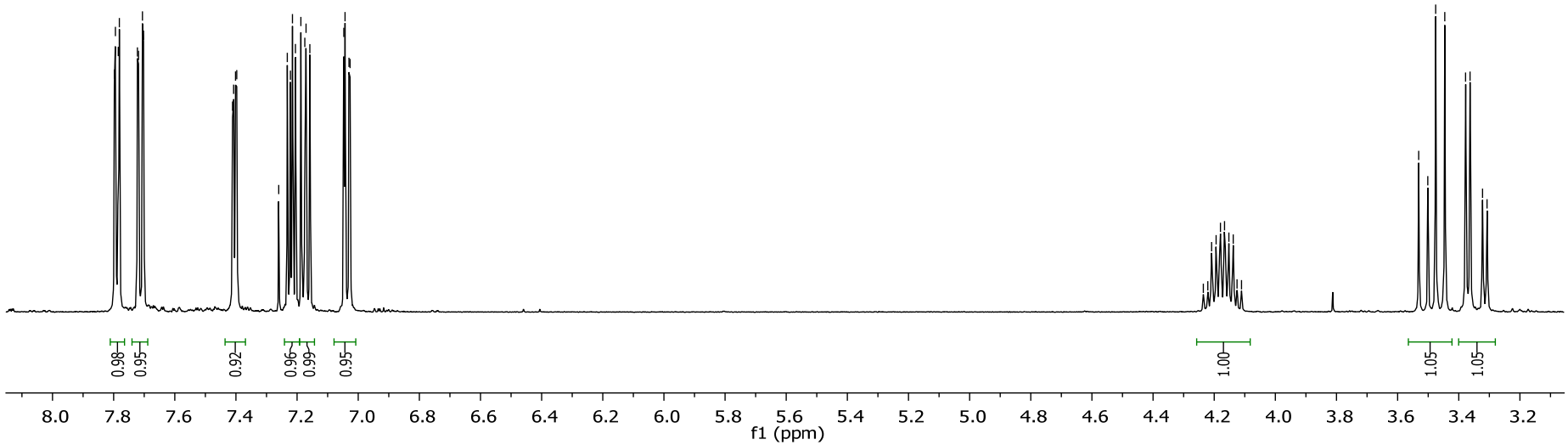
3gg

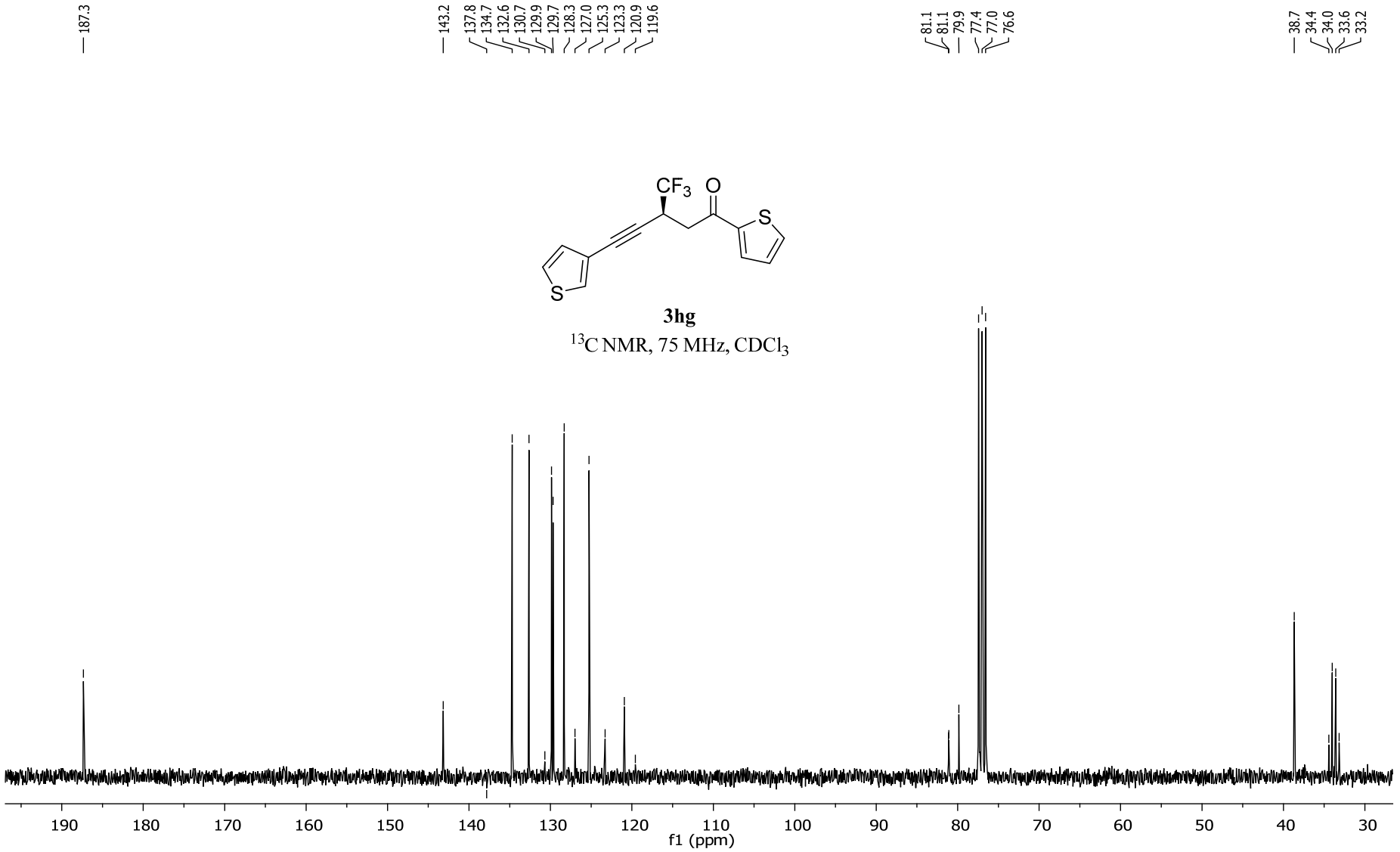
^{19}F NMR, 282 MHz, $CDCl_3$

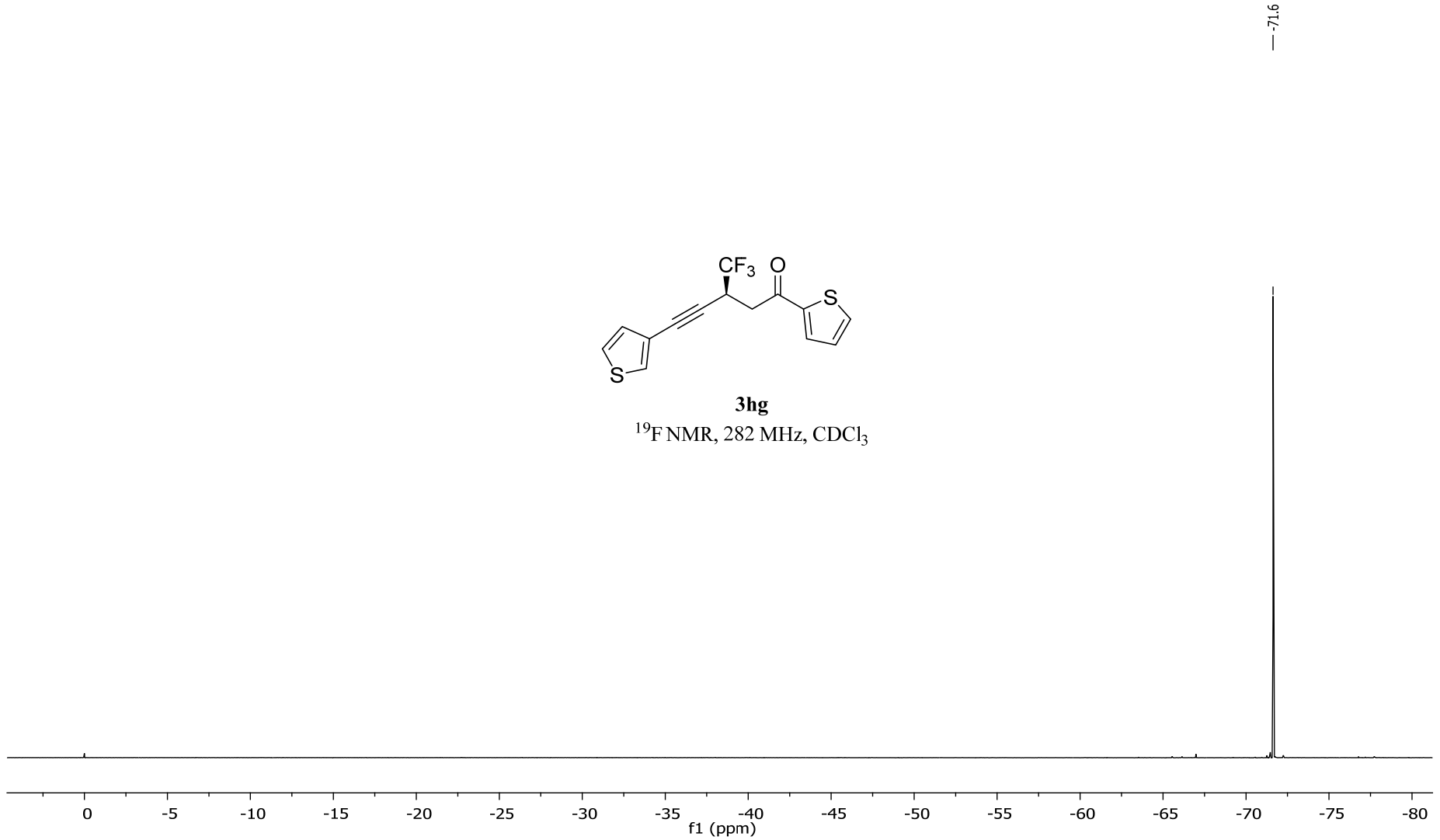


3hg

^{1}H NMR, 300 MHz, $CDCl_3$

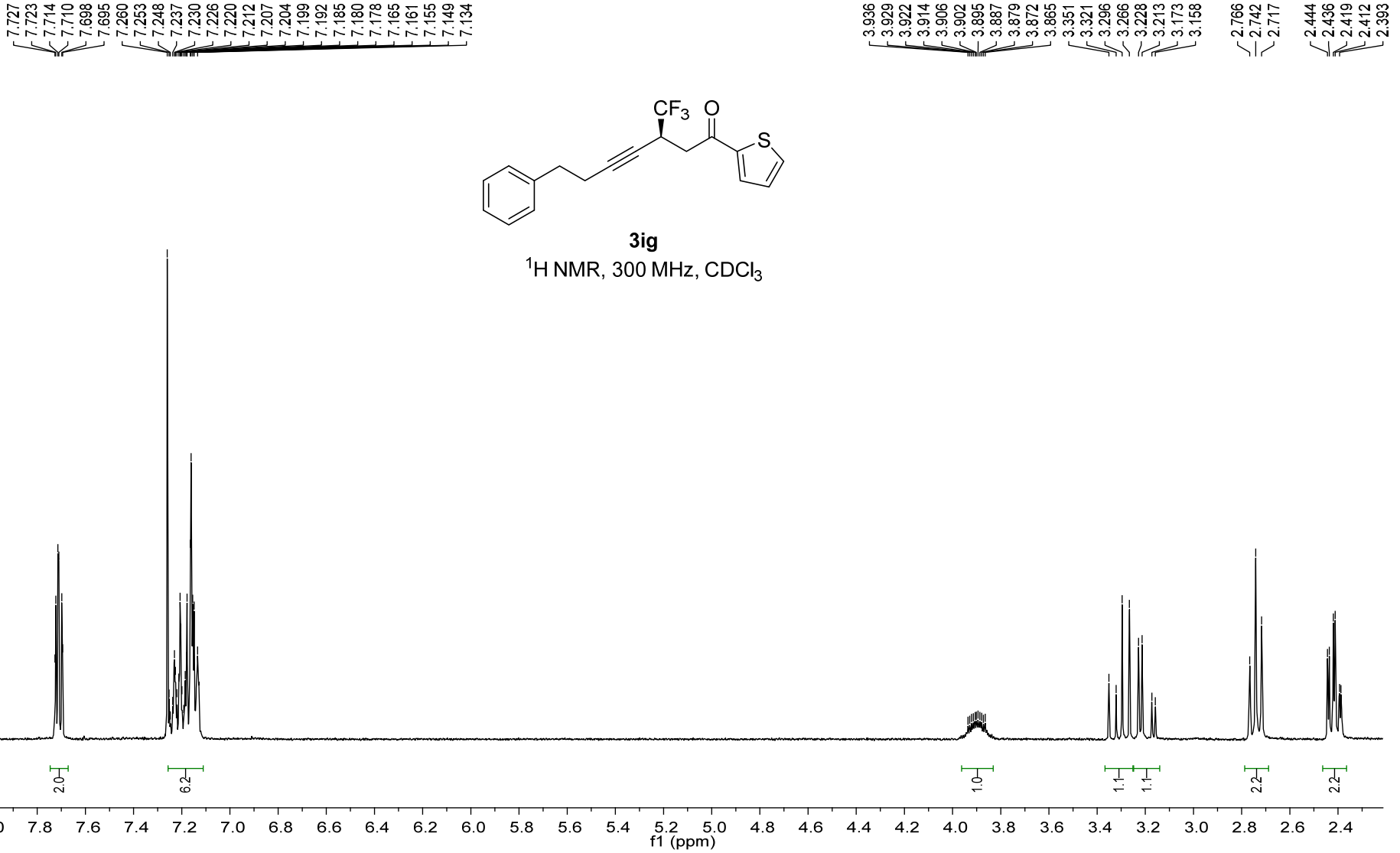






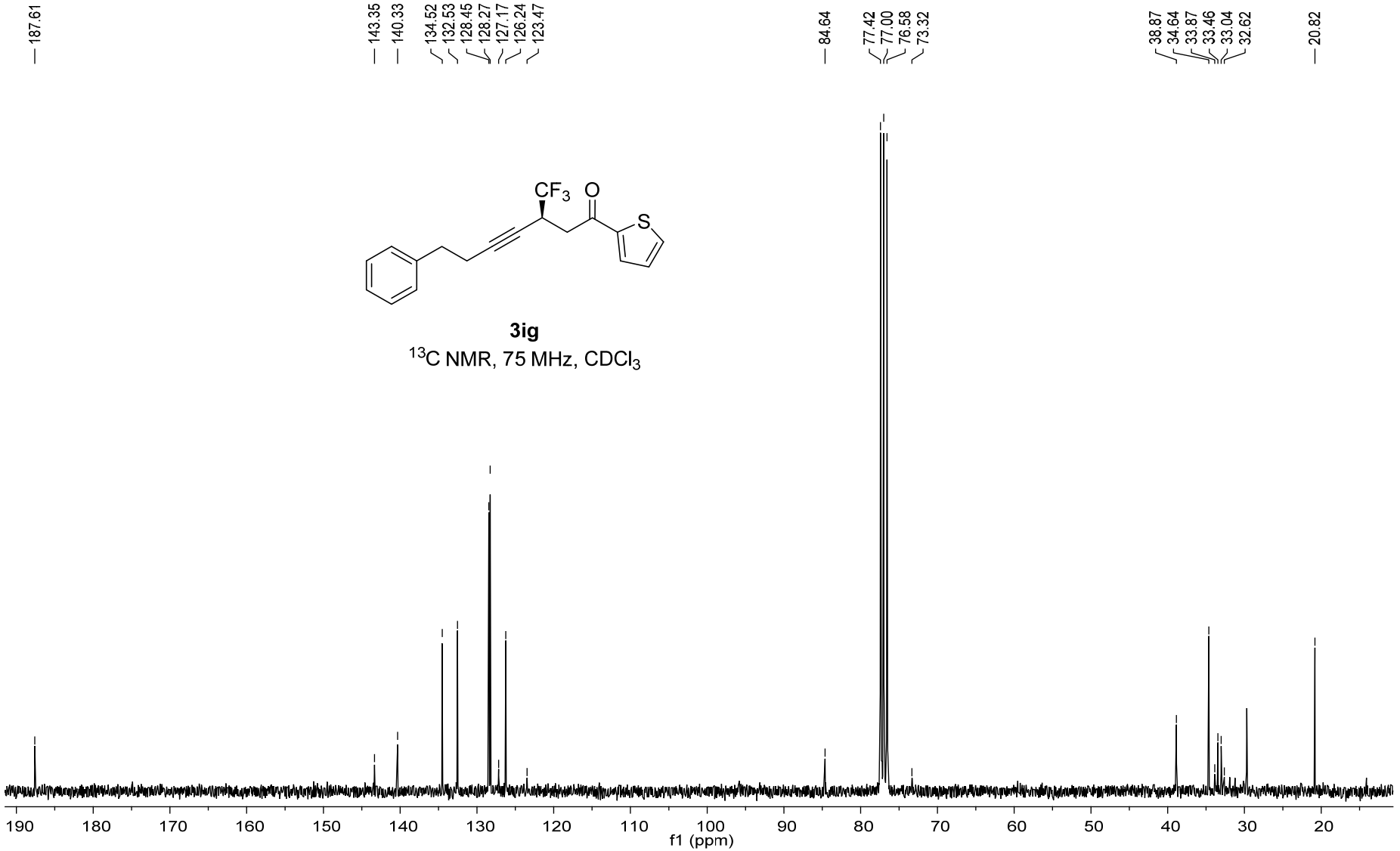
3hg

^{19}F NMR, 282 MHz, $CDCl_3$



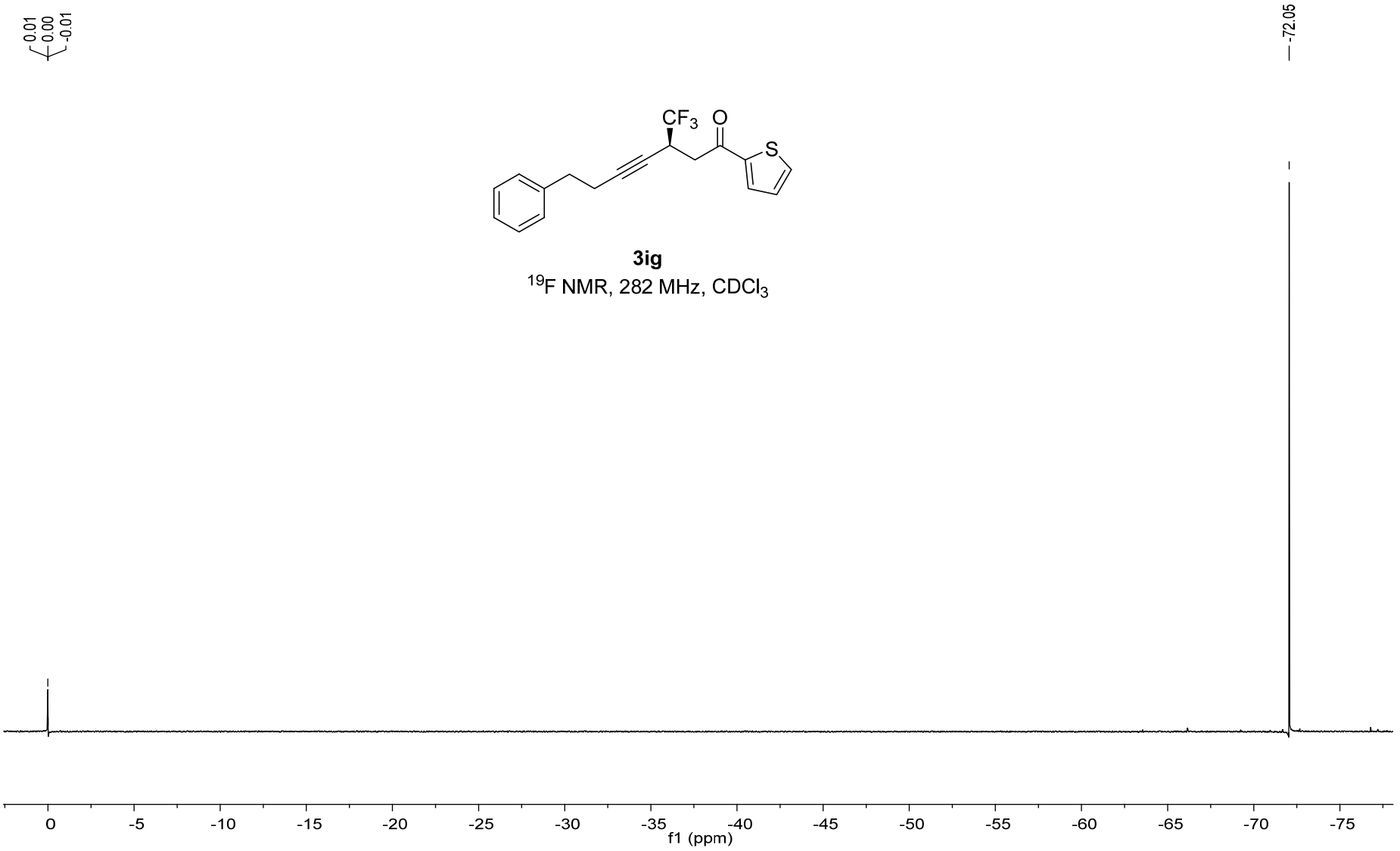
3ig

^{1}H NMR, 300 MHz, $CDCl_3$



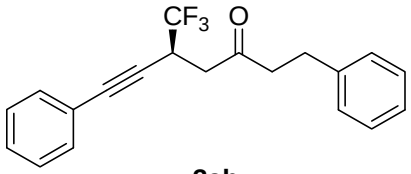
3ig

^{13}C NMR, 75 MHz, $CDCl_3$



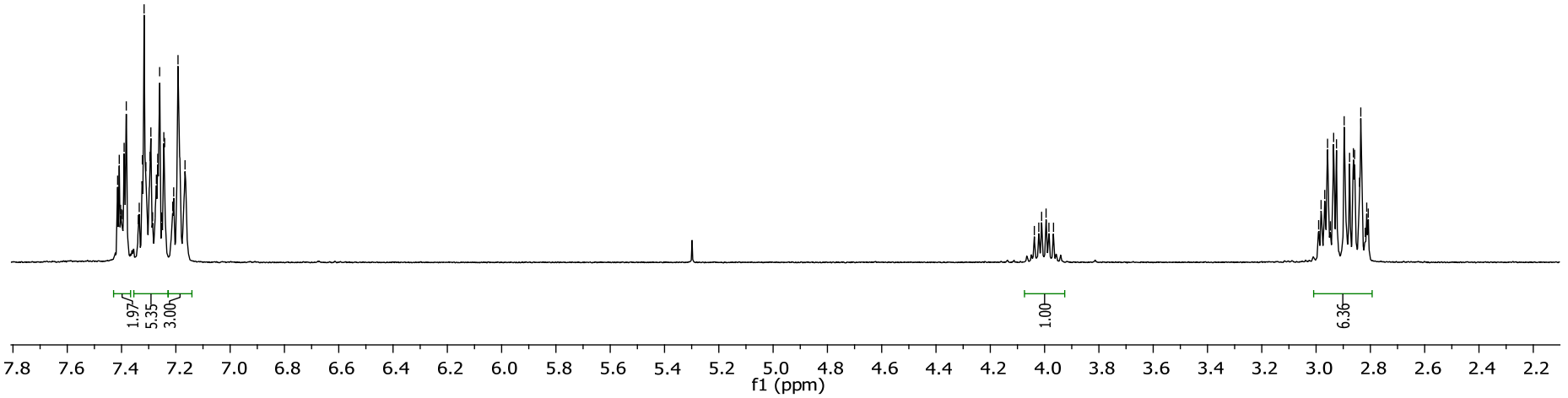
3ig

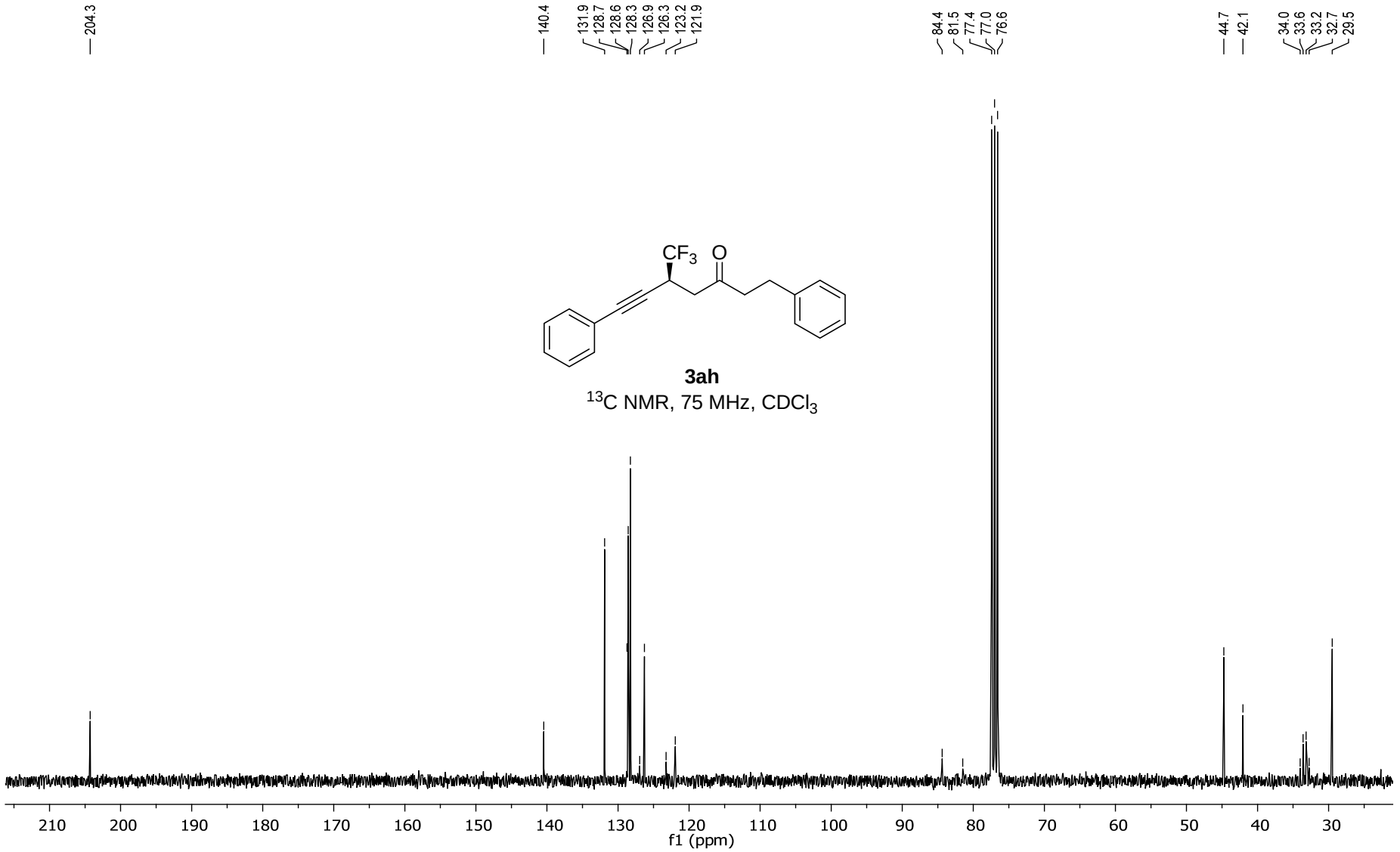
^{19}F NMR, 282 MHz, $CDCl_3$



3ah

^{1}H NMR, 300 MHz, $CDCl_3$





3ah

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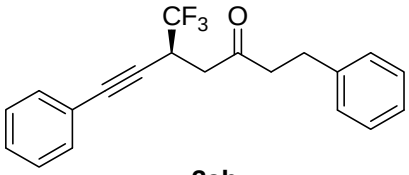

3ah

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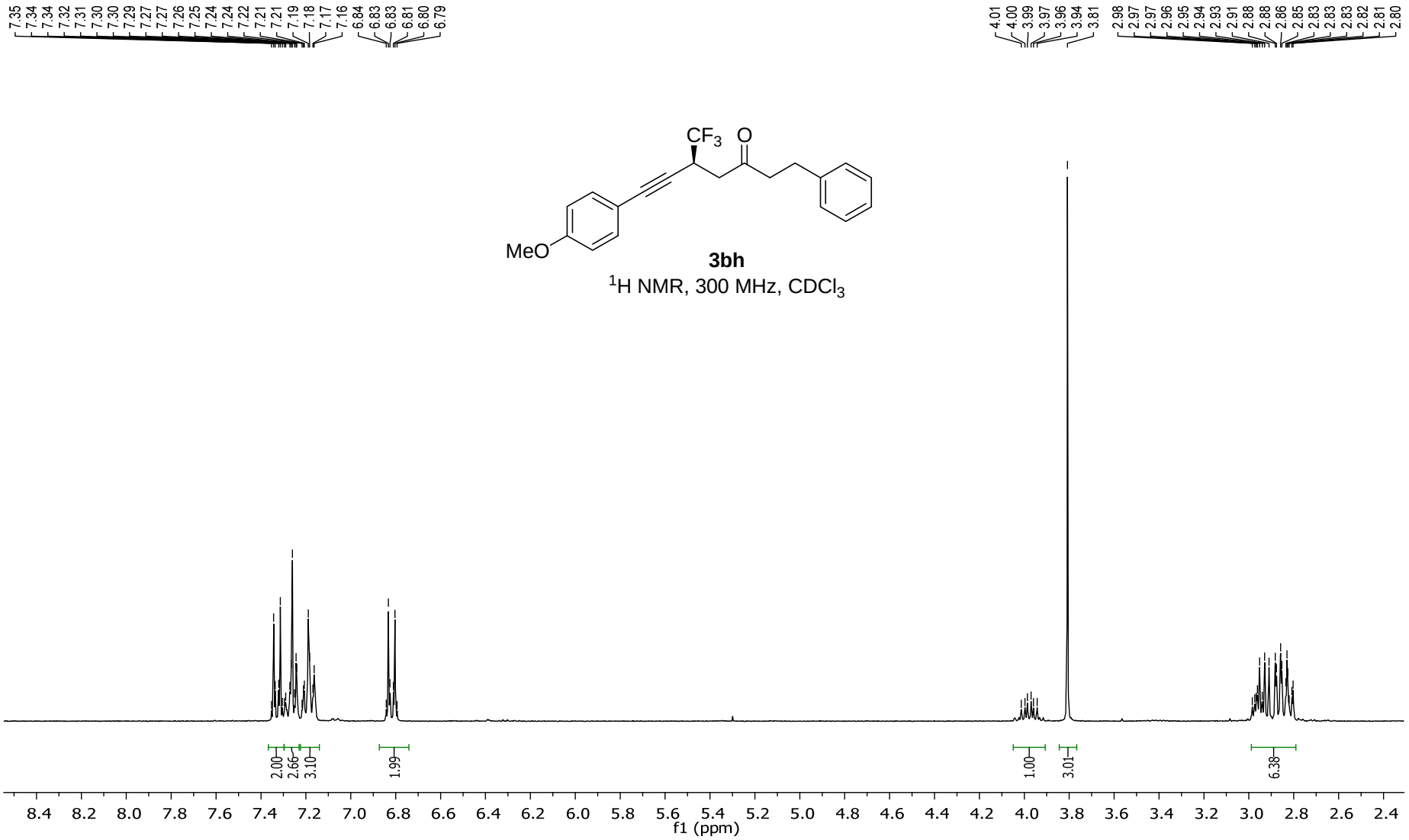
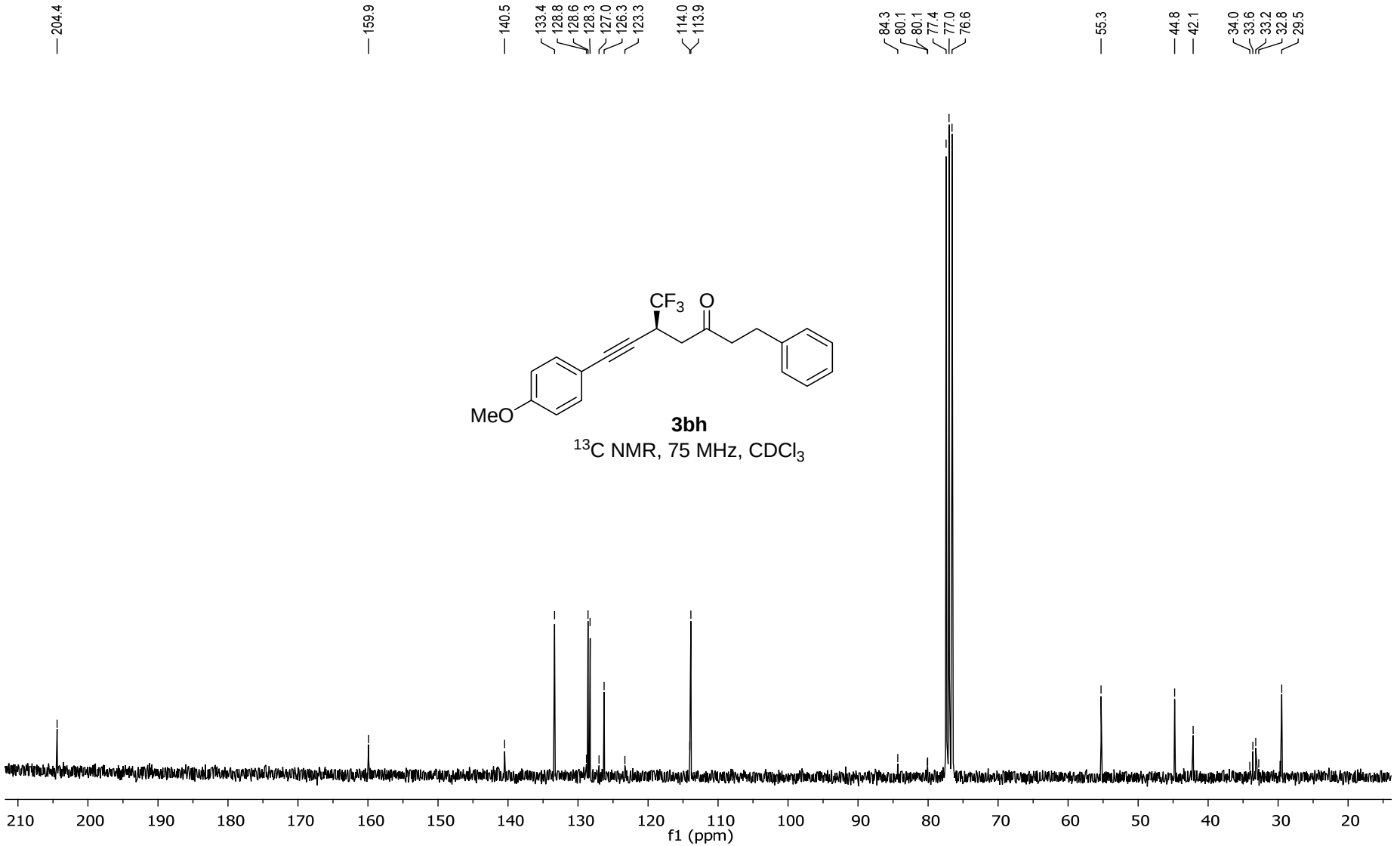
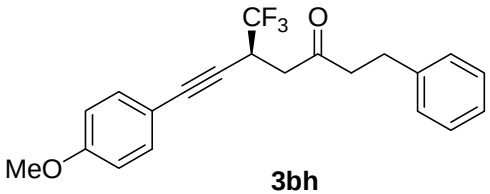
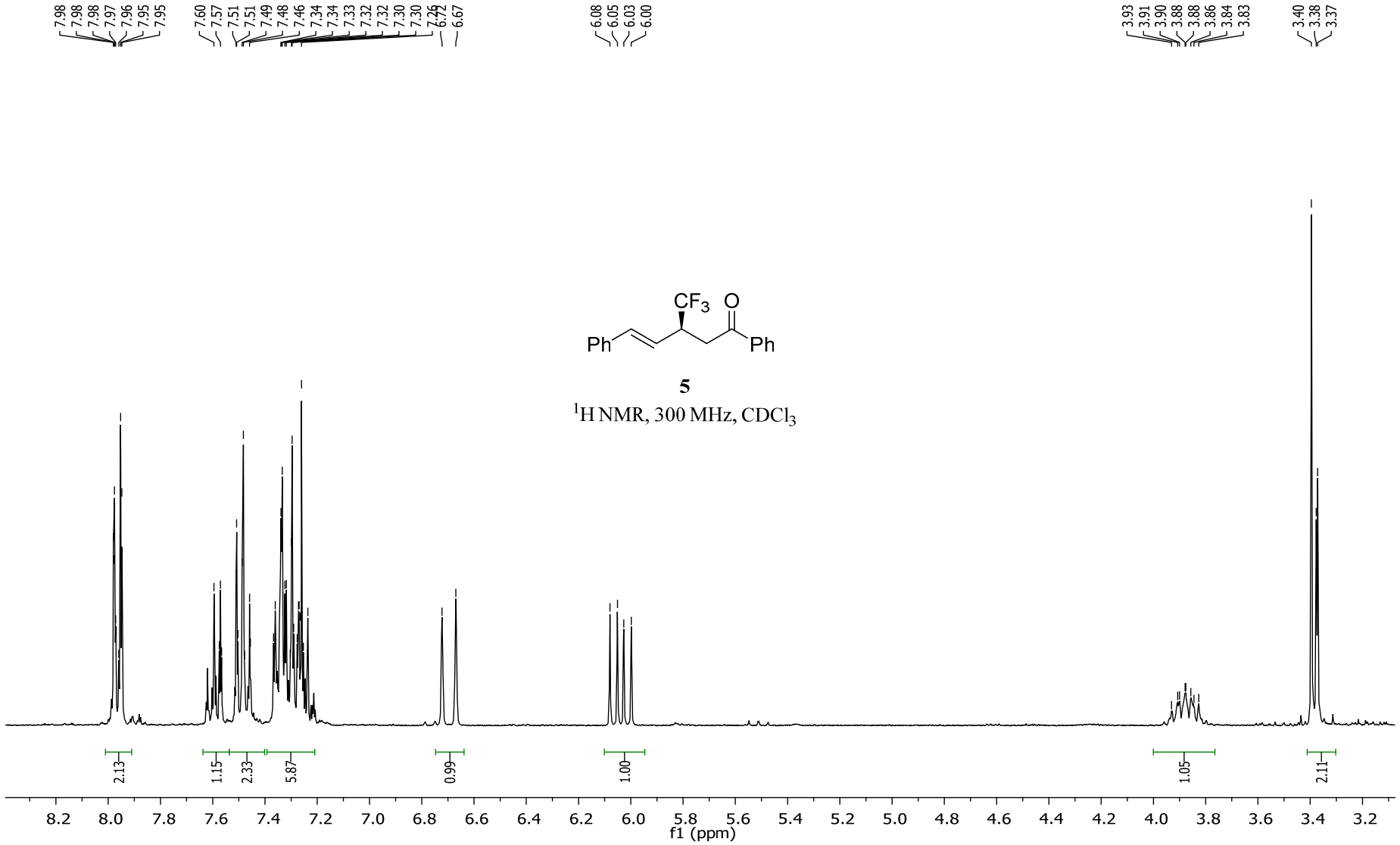






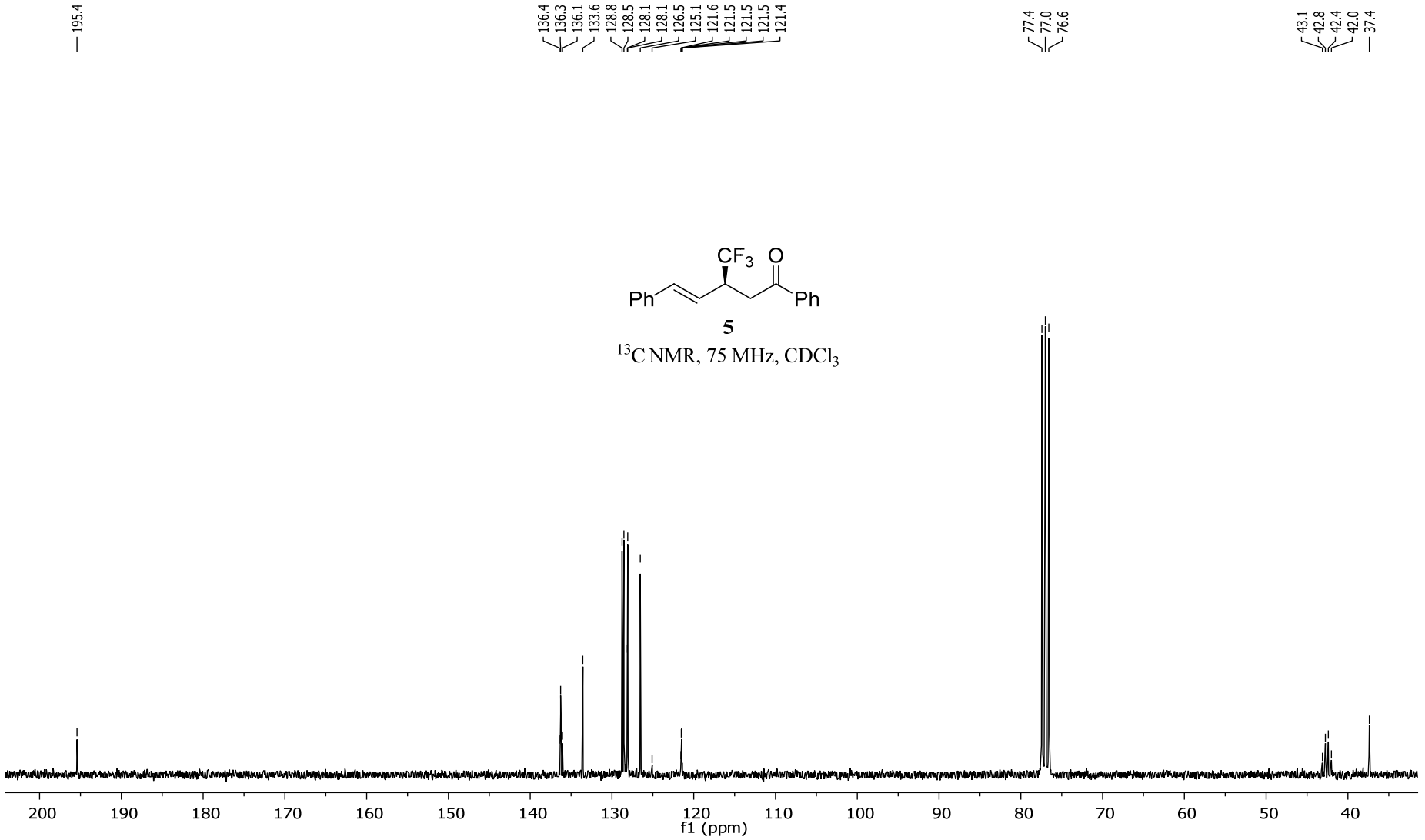
3bh

^{19}F NMR, 282 MHz, $CDCl_3$



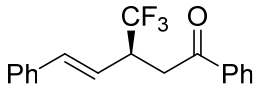
5

^{1}H NMR, 300 MHz, $CDCl_3$



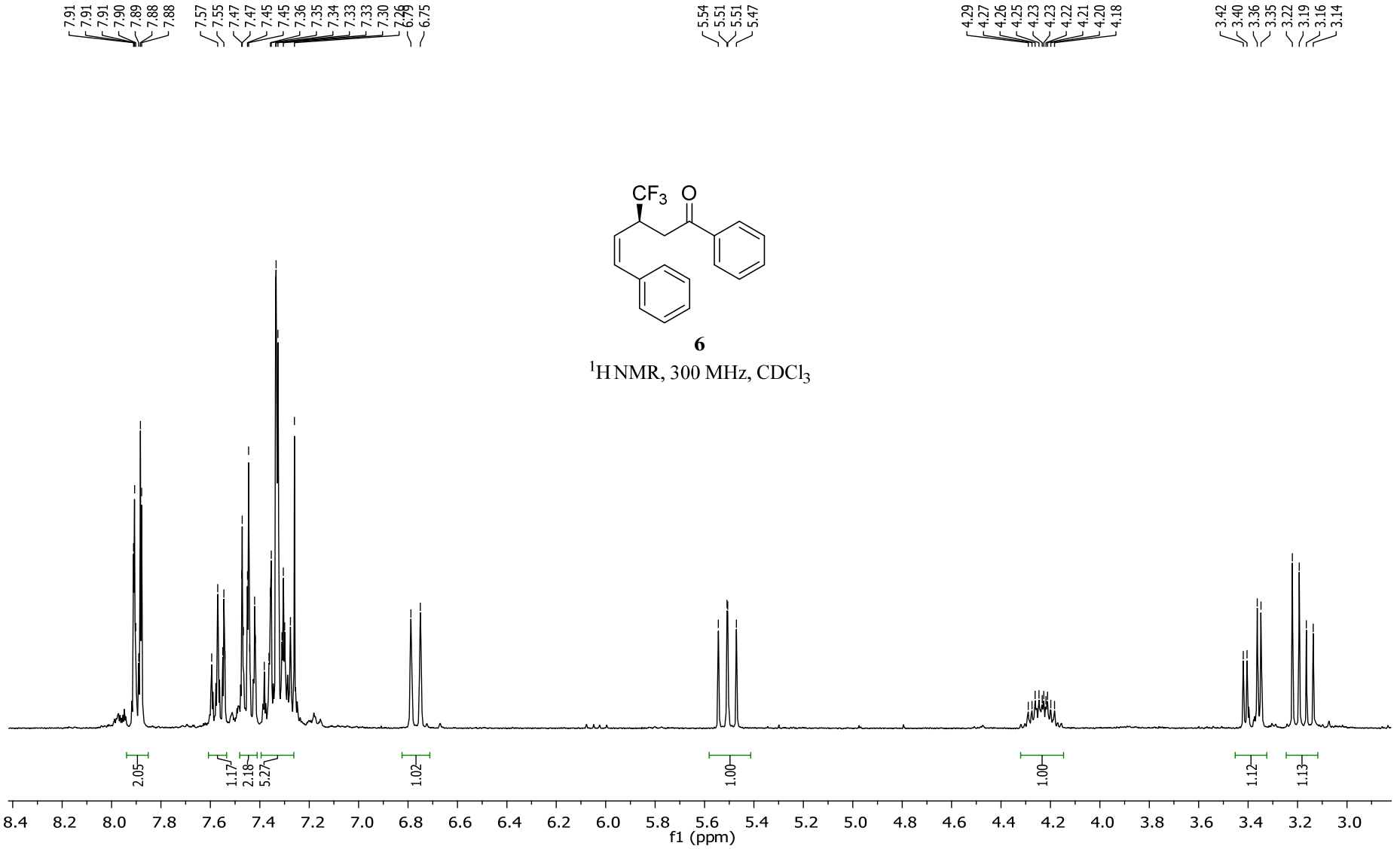
5

^{13}C NMR, 75 MHz, $CDCl_3$



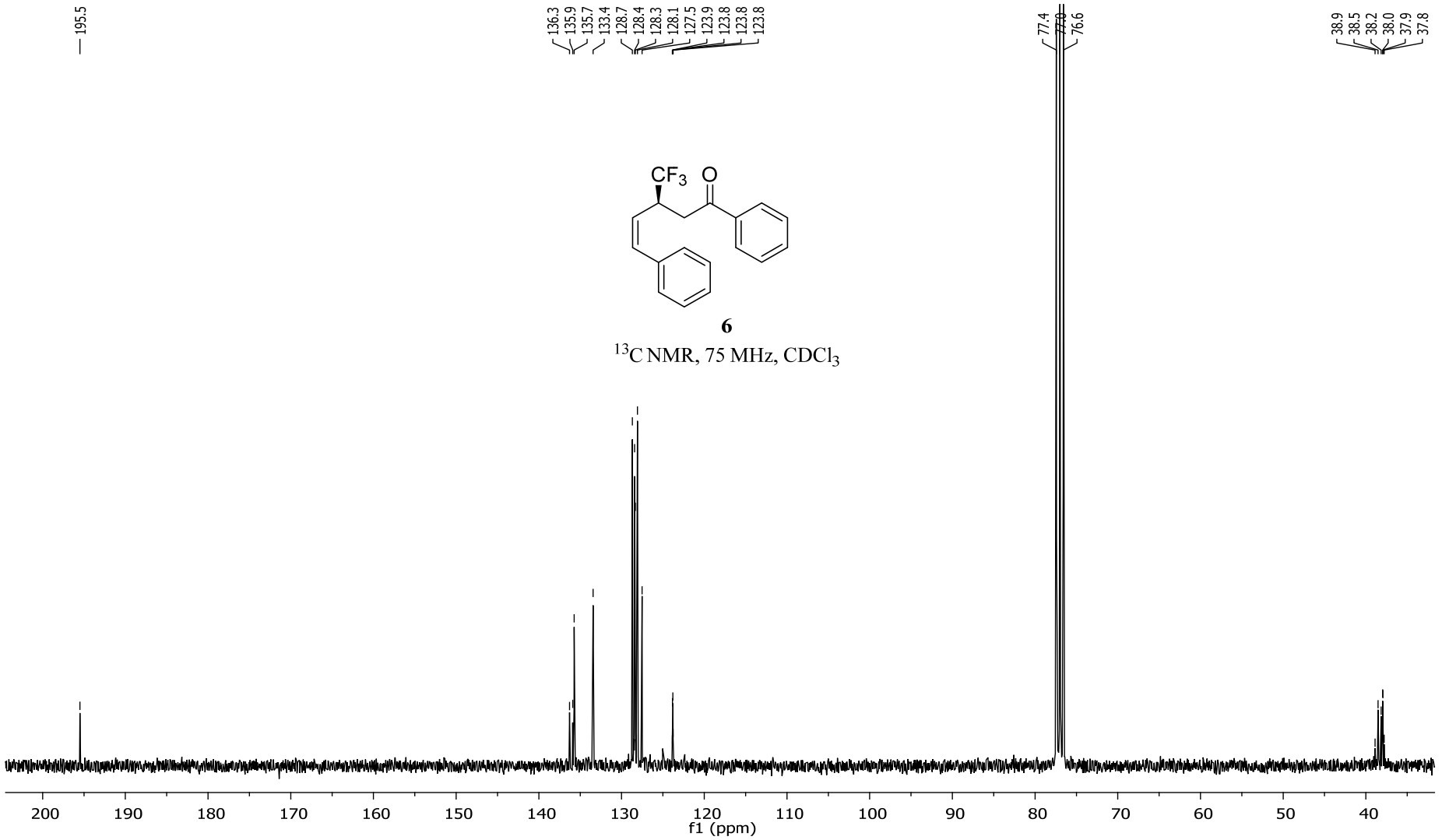
5

^{19}F NMR, 282 MHz, $CDCl_3$



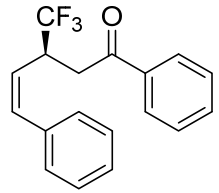
6

^{1}H NMR, 300 MHz, $CDCl_3$



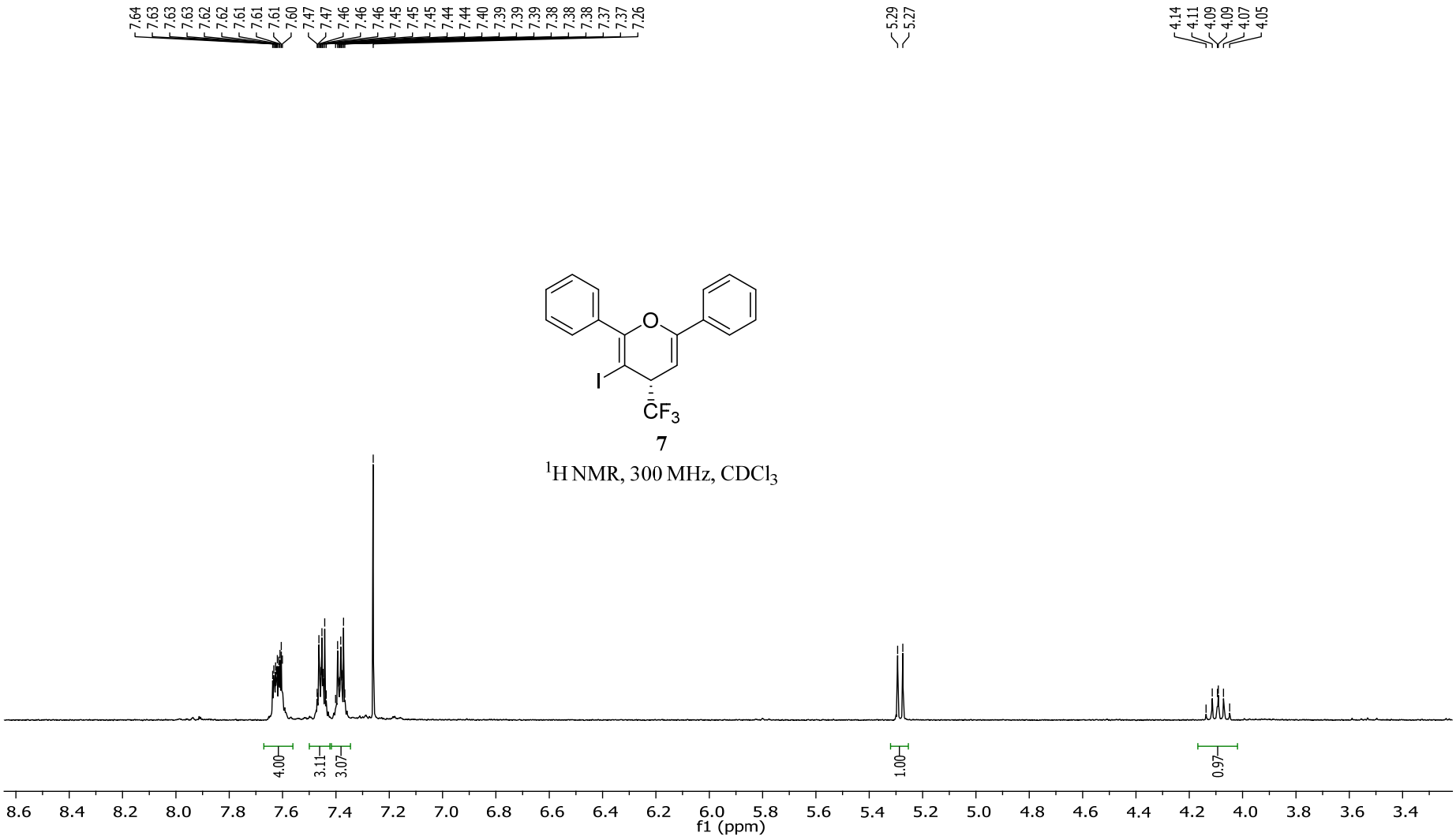
6

^{13}C NMR, 75 MHz, $CDCl_3$



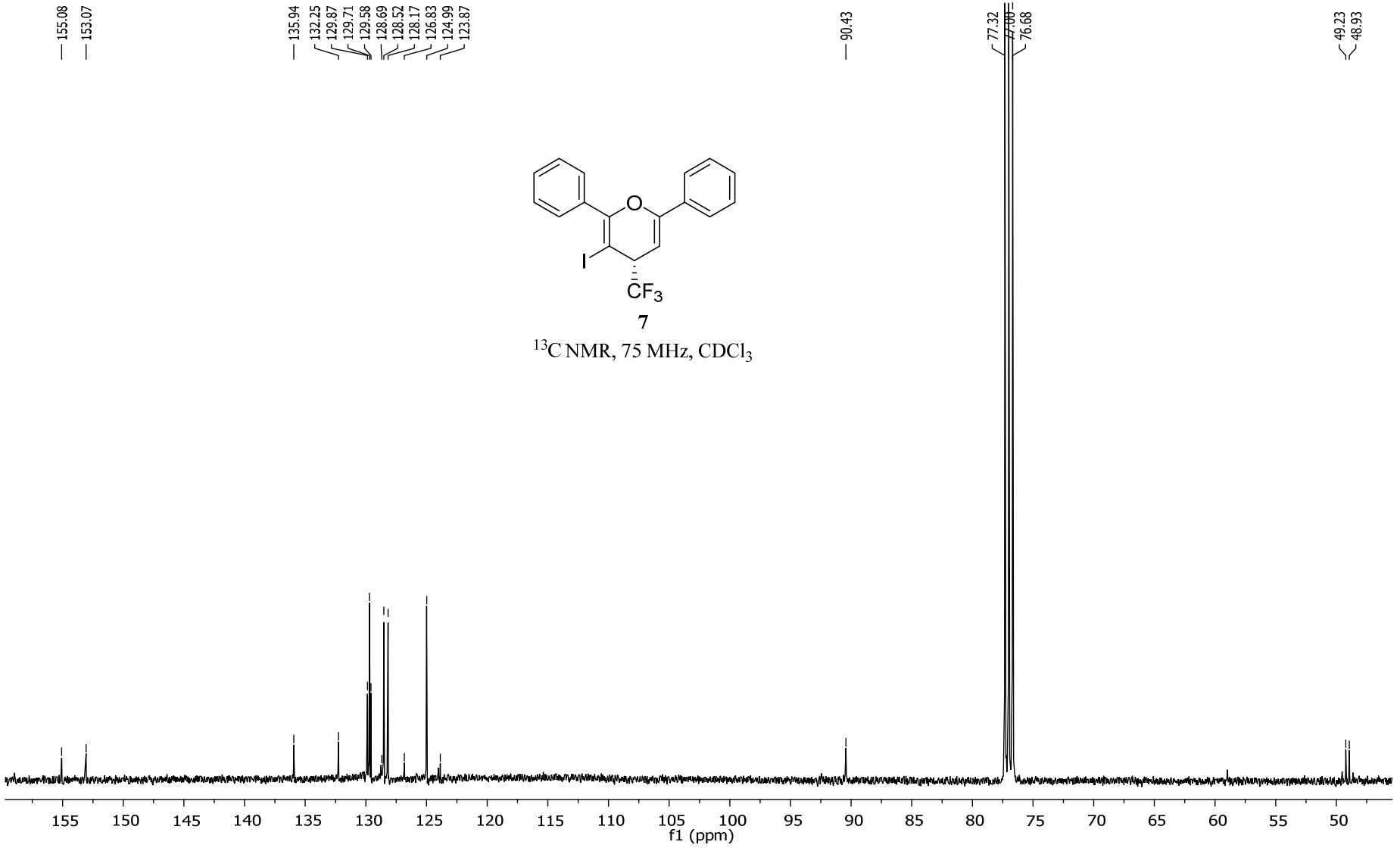
6

^{19}F NMR, 282 MHz, $CDCl_3$



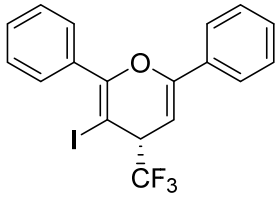
7

^{1}H NMR, 300 MHz, $CDCl_3$



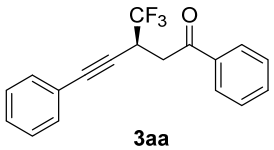
7

^{13}C NMR, 75 MHz, $CDCl_3$



7

^{19}F NMR, 282 MHz, $CDCl_3$



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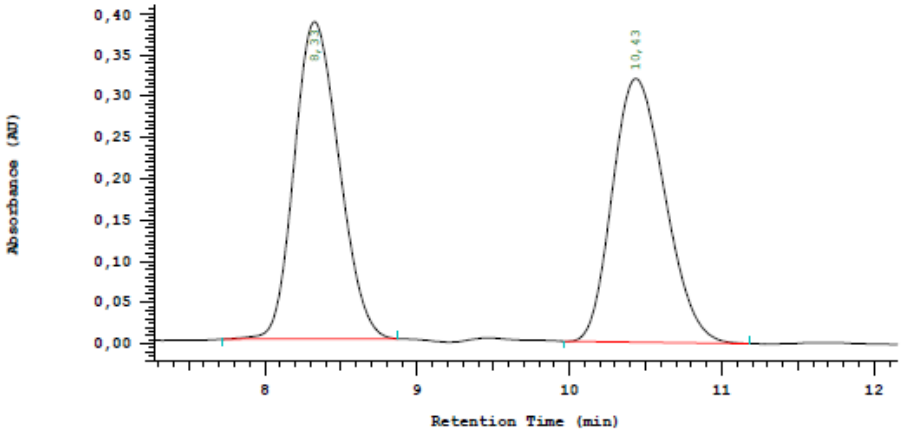

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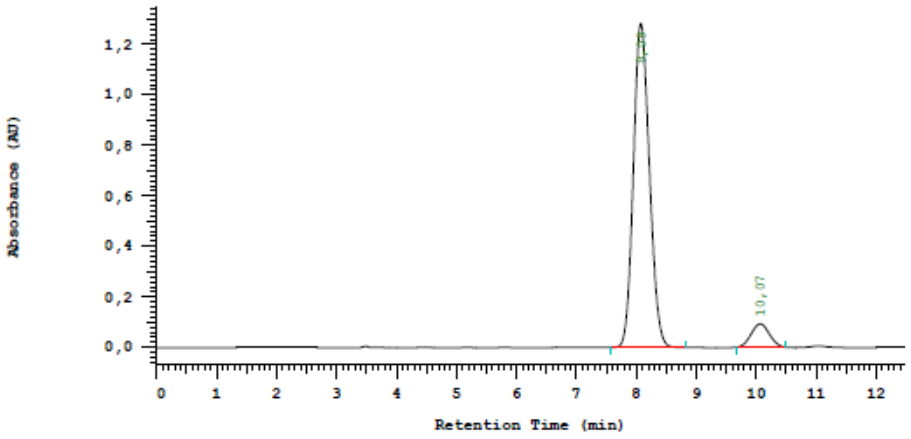
		7759956	100,000



No.	RT	Area	Area %	Name
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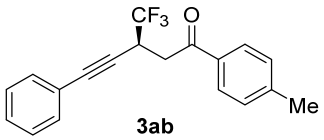
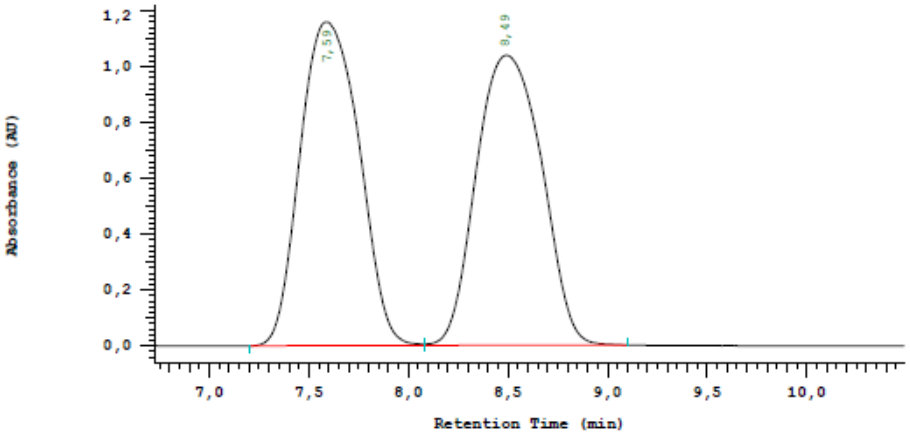


3ab



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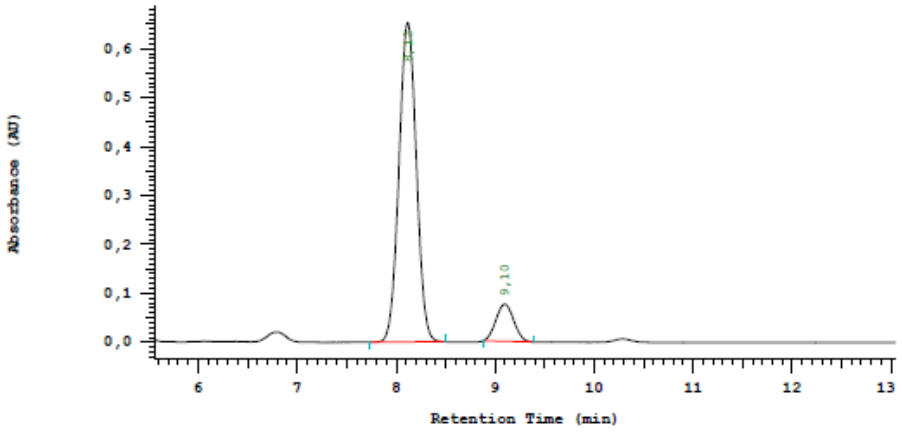

No.	RT	Area	Area %	Name
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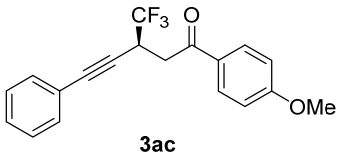

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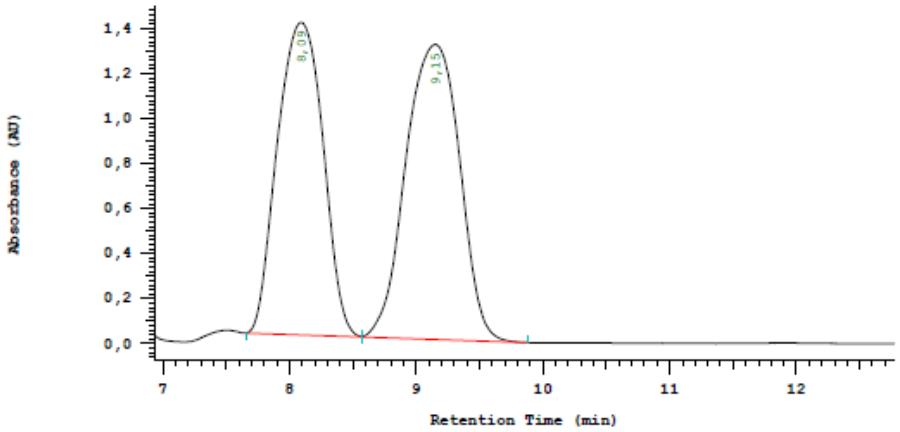

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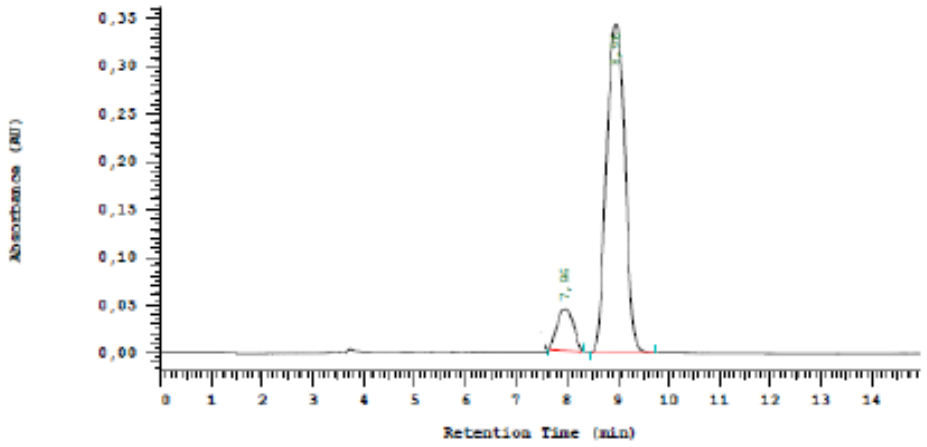

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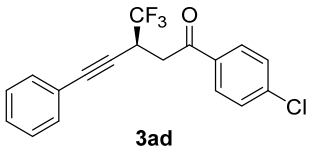

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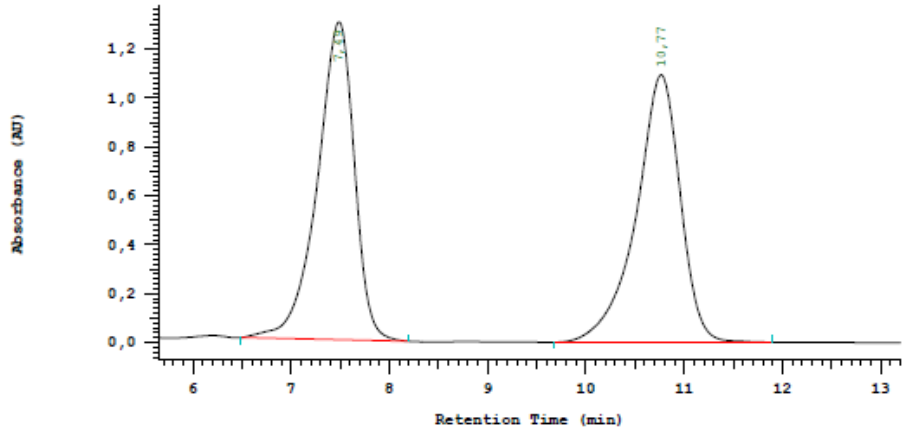

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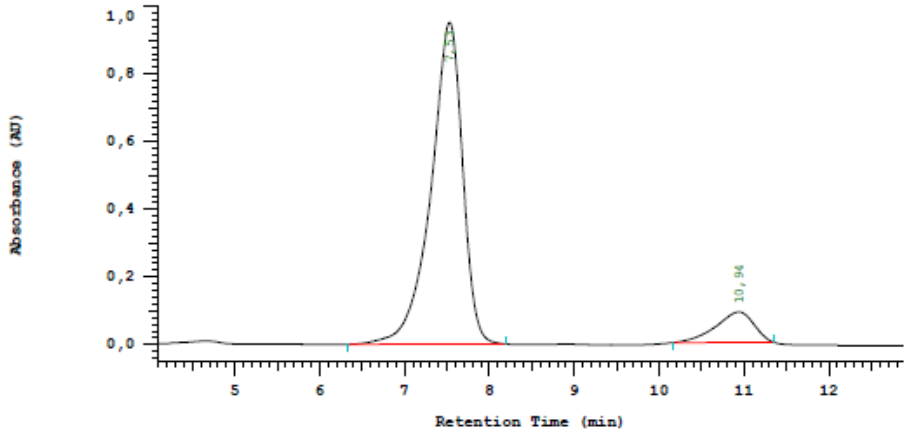

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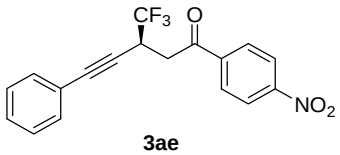
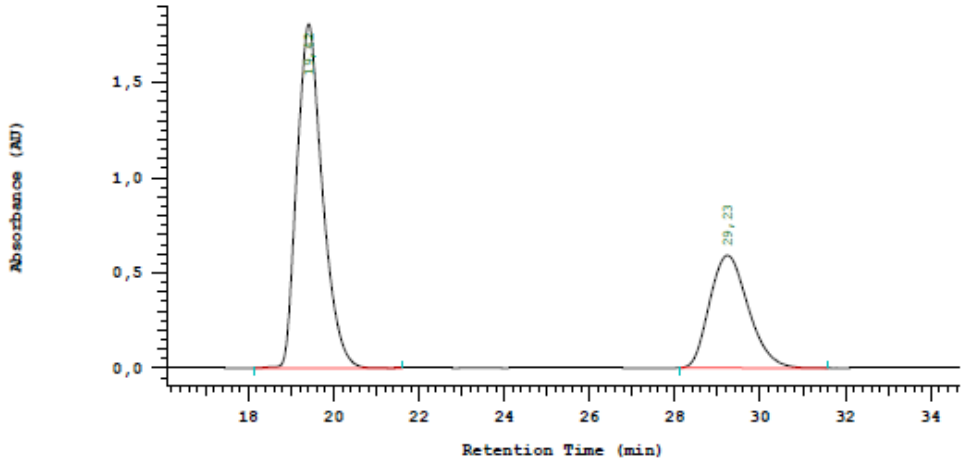


3ae



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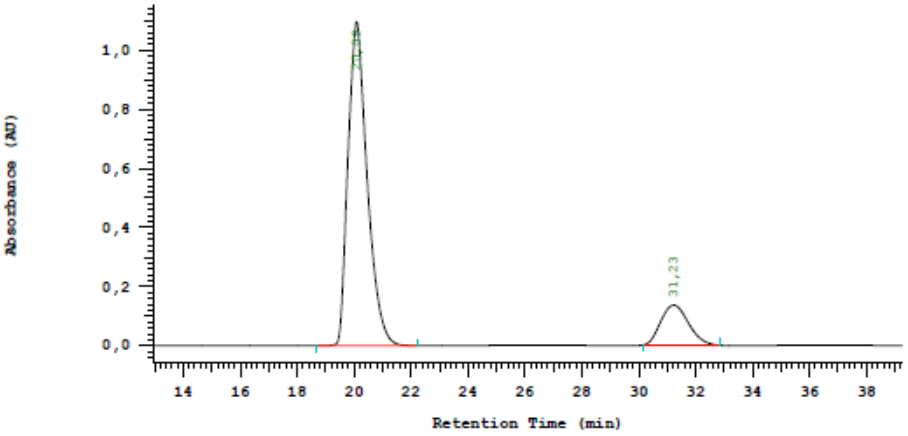

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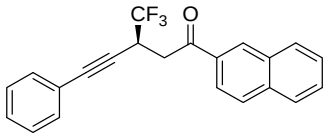
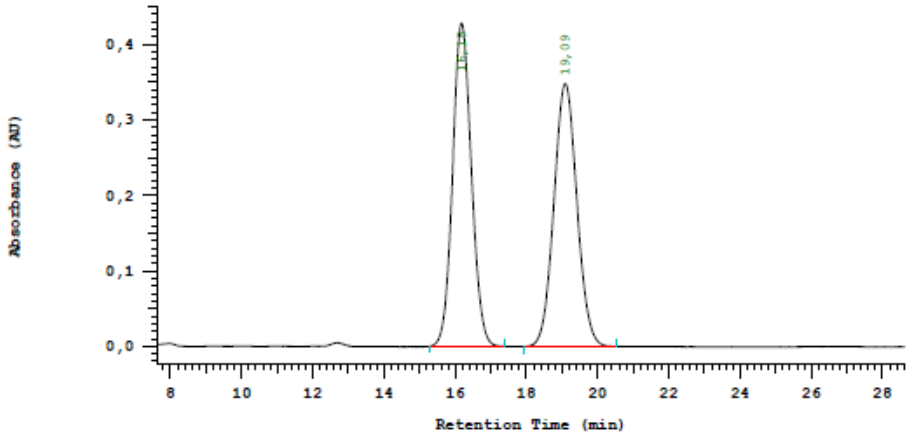


3af



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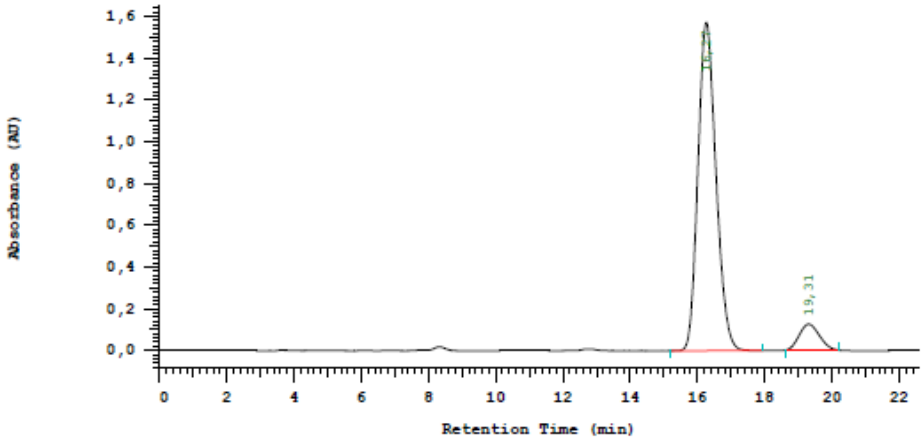

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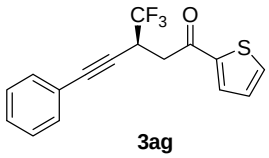
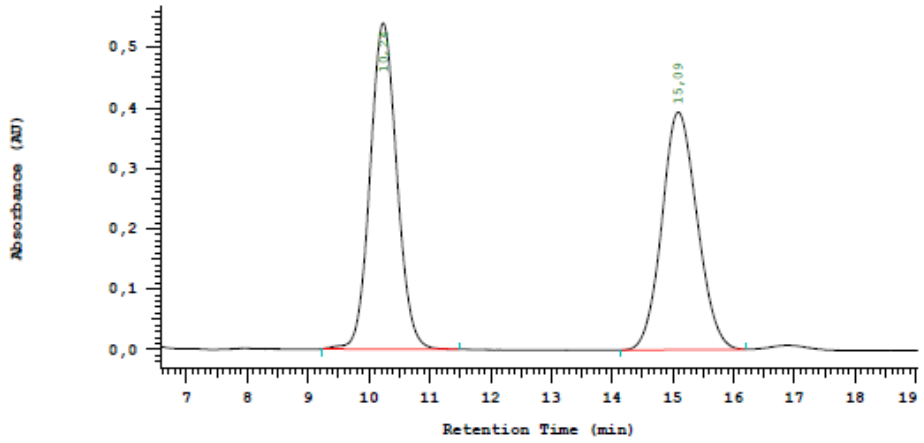
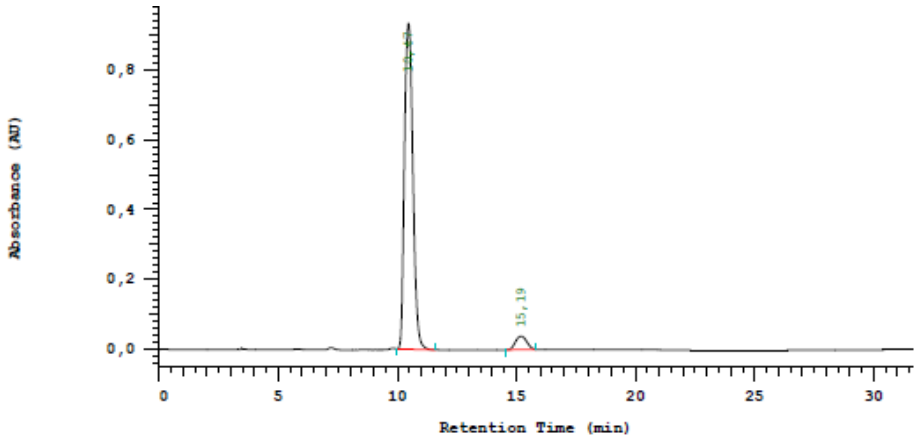


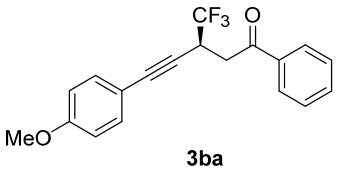
3ag



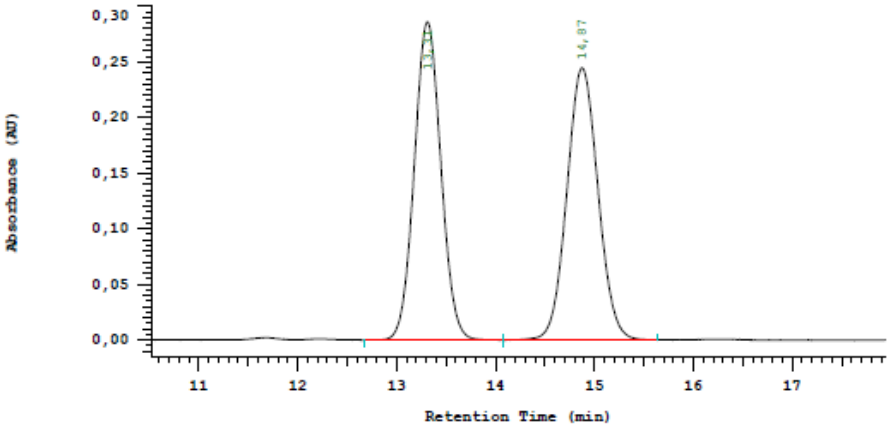
No.	RT	Area	Area %	Name
1	10,24	8252040	51,023	
2	15,09	7921200	48,977	
		16173240	100,000	



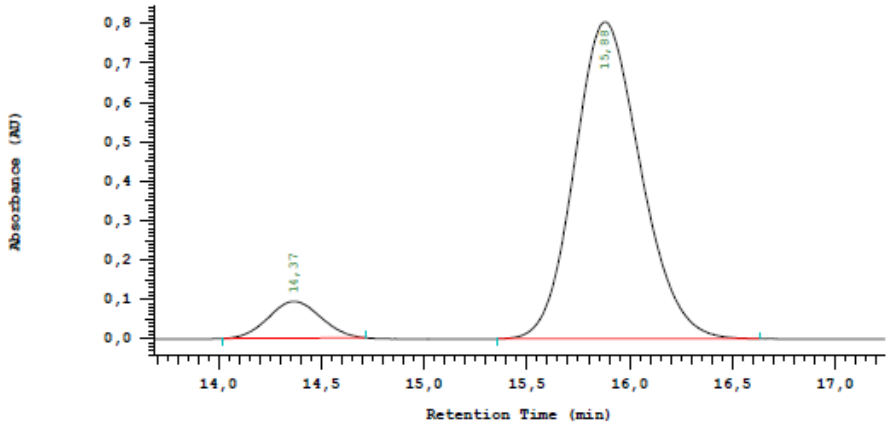
No.	RT	Area	Area %	Name
1	10,47	11482160	94,873	
2	15,19	620500	5,127	
		12102660	100,000	



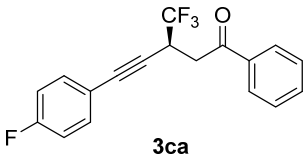
3ba



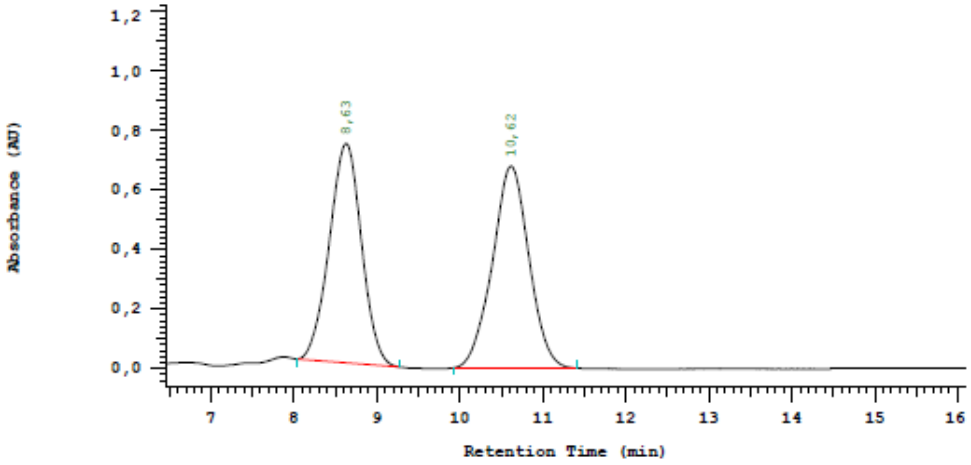
No.	RT	Area	Area %	Name
1	13,31	2676360	49,920	
2	14,87	2684990	50,080	
		5361350	100,000	



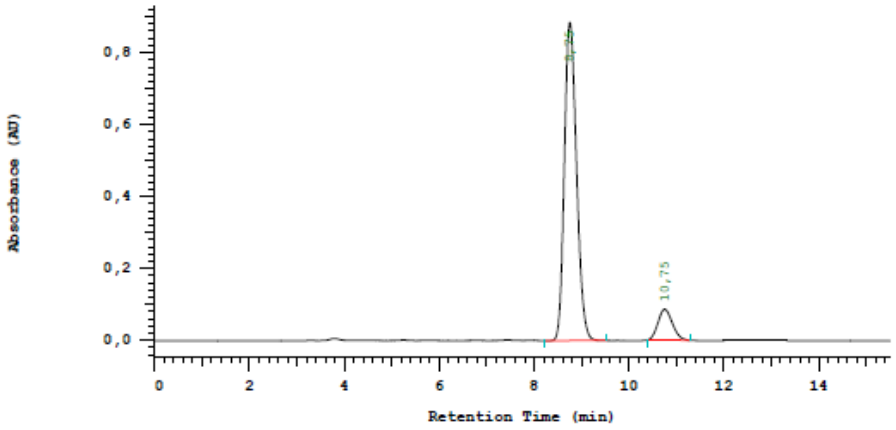
No.	RT	Area	Area %	Name
1	14,37	828280	8,426	
2	15,88	9001520	91,574	
		9829800	100,000	



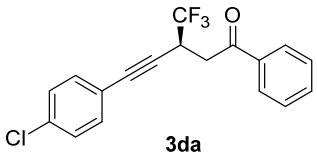
3ca



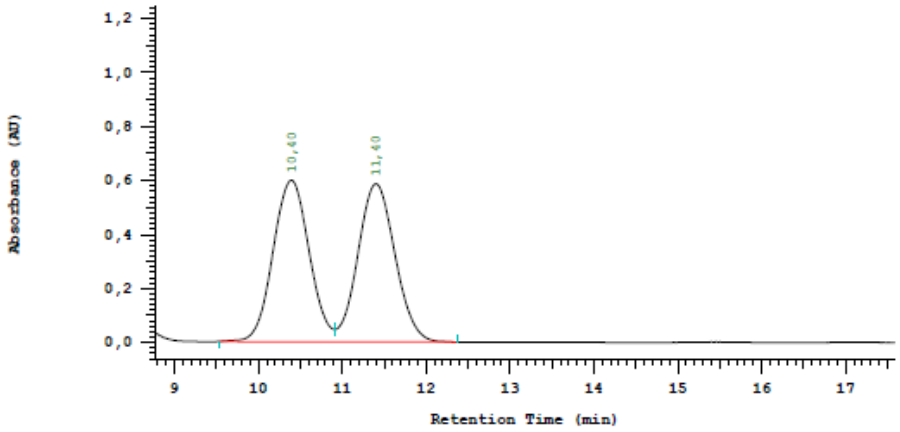
No.	RT	Area	Area %	Name
1	8,63	9960184	48,927	
2	10,62	10396870	51,073	
		20357054	100,000	



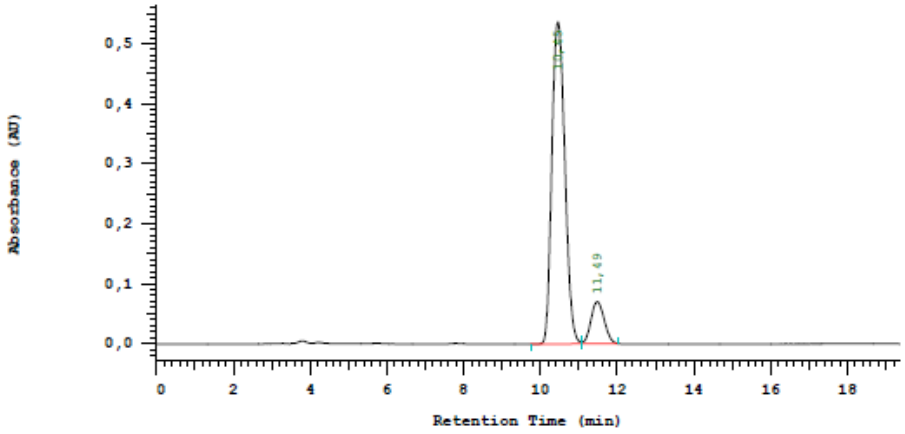
No.	RT	Area	Area %	Name
1	8,75	7870600	89,774	
2	10,75	896555	10,226	
		8767155	100,000	



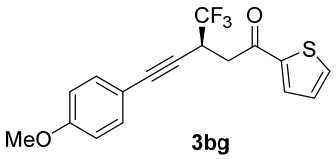
3da



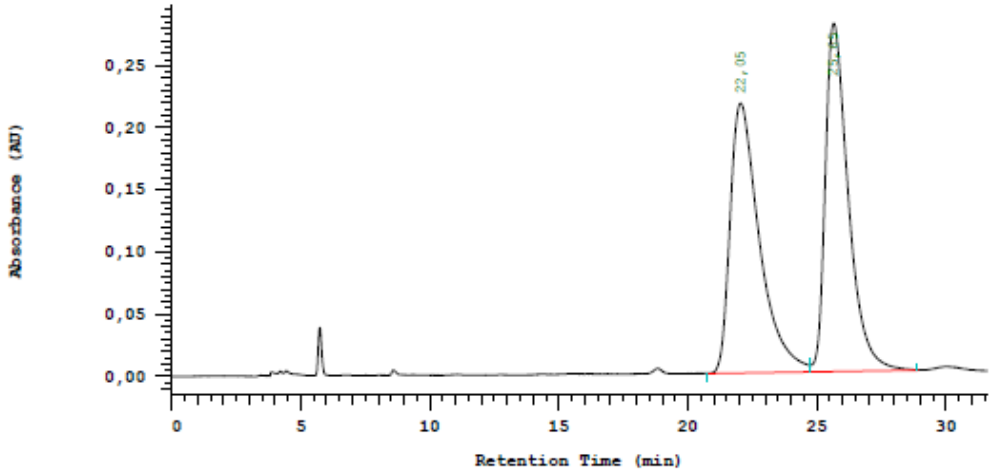
No.	RT	Area	Area %	Name
1	10,40	8928930	49,846	
2	11,40	8984144	50,154	
		17913074	100,000	



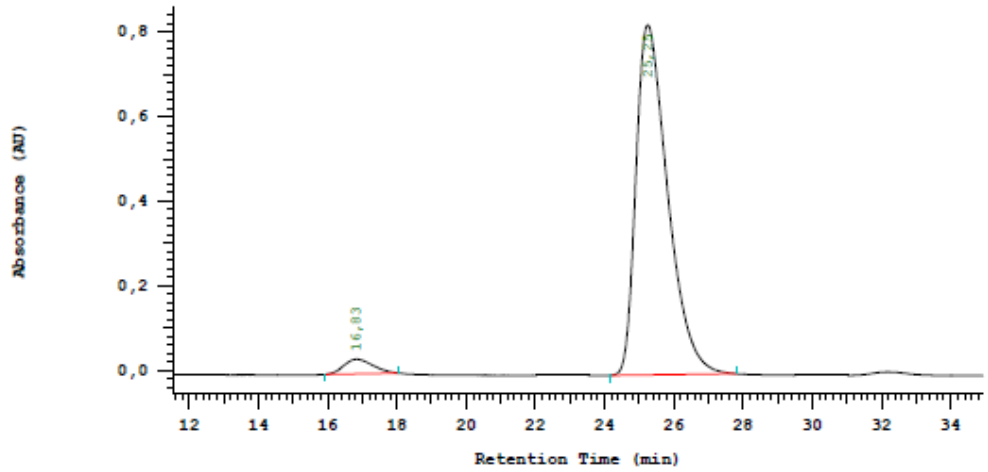
No.	RT	Area	Area %	Name
1	10,45	6311811	88,204	
2	11,49	844093	11,796	
		7155904	100,000	



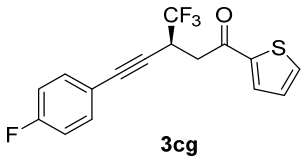
3bg



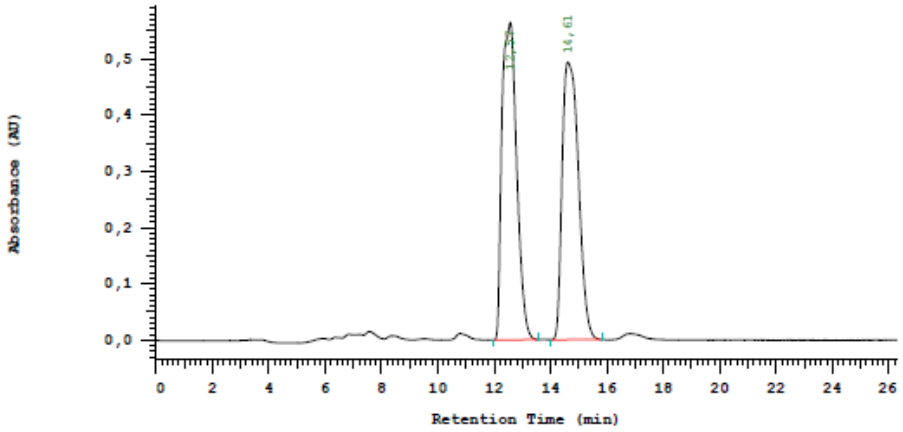
No.	RT	Area	Area %	Name
1	22,05	8539349	49,710	
2	25,65	8638890	50,290	
		17178239	100,000	



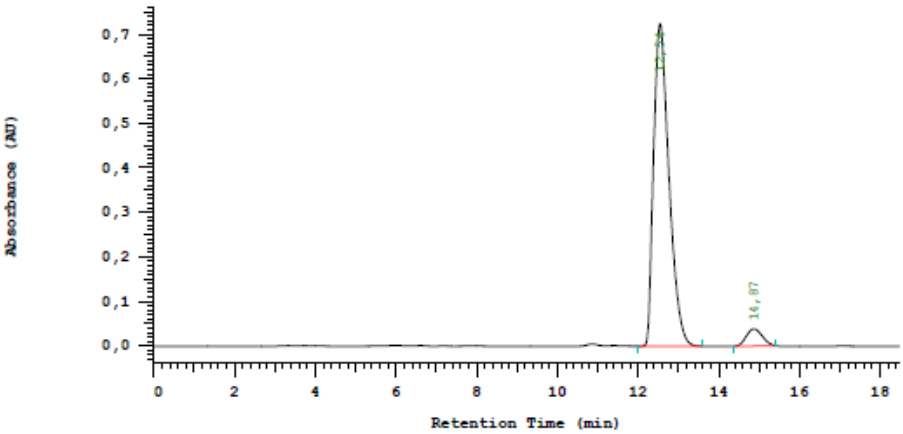
No.	RT	Area	Area %	Name
1	16,83	1004280	3,679	
2	25,25	26295569	96,321	
		27299849	100,000	



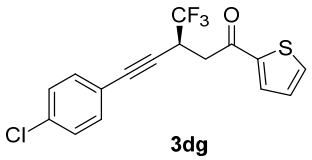
3cg



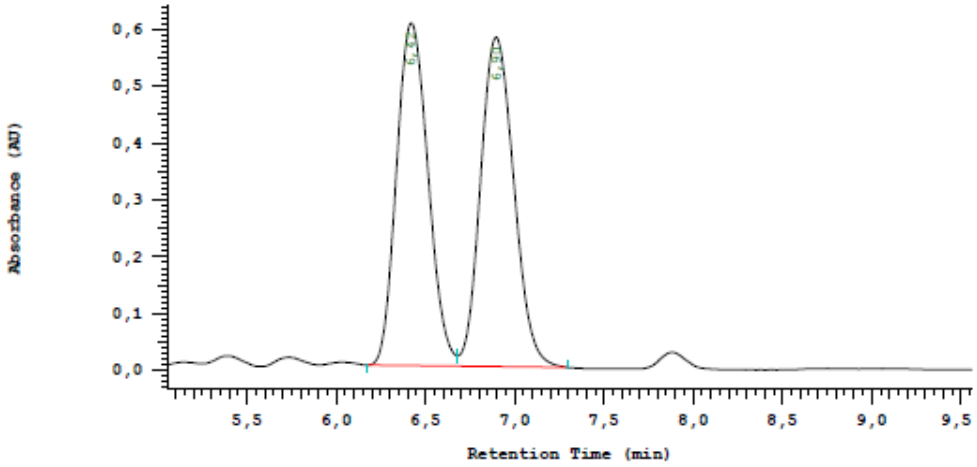
No.	RT	Area	Area %	Name
1	12,57	10194740	50,636	
2	14,61	9938569	49,364	
		20133309	100,000	



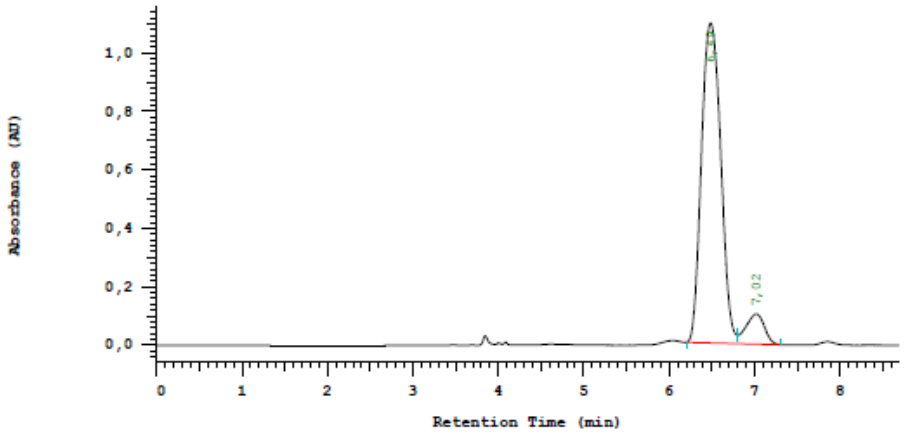
No.	RT	Area	Area %	Name
1	12,54	9551030	94,769	
2	14,87	527170	5,231	
		10078200	100,000	



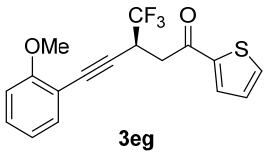
3dg



No.	RT	Area	Area %	Name
1	6,42	3692928	49,562	
2	6,90	3758161	50,438	
		7451089	100,000	



No.	RT	Area	Area %	Name
1	6,49	8573328	91,762	
2	7,02	769626	8,238	
		9342954	100,000	



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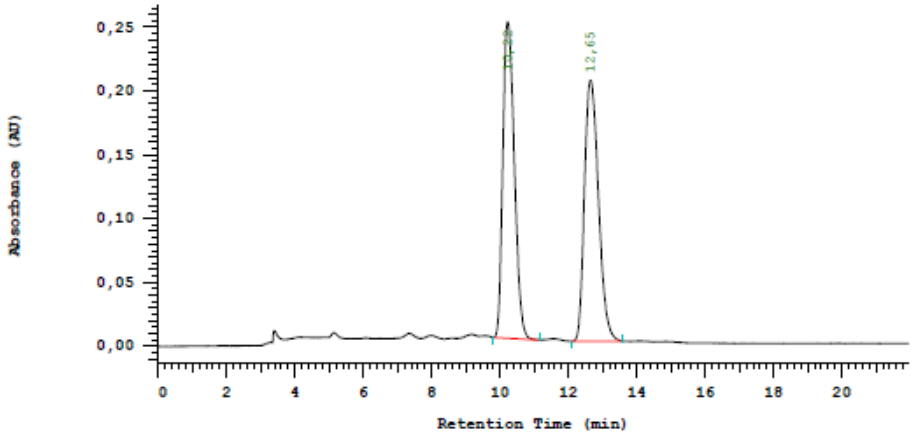
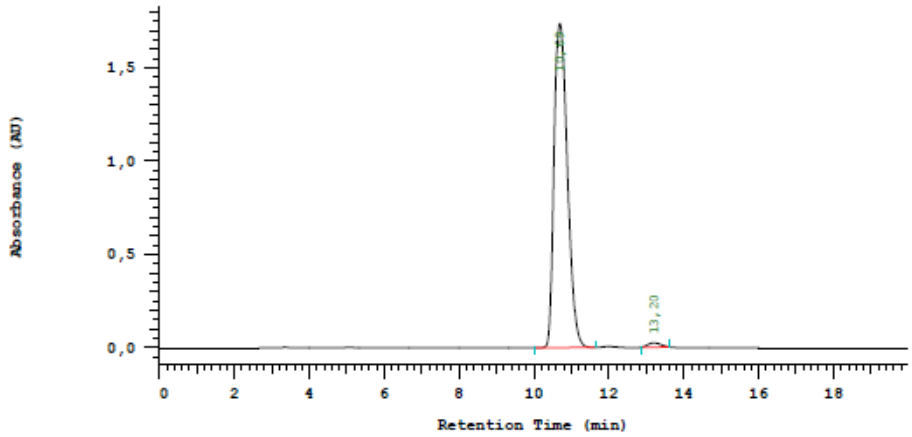
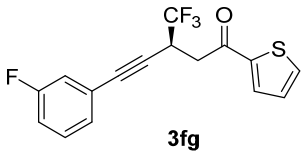


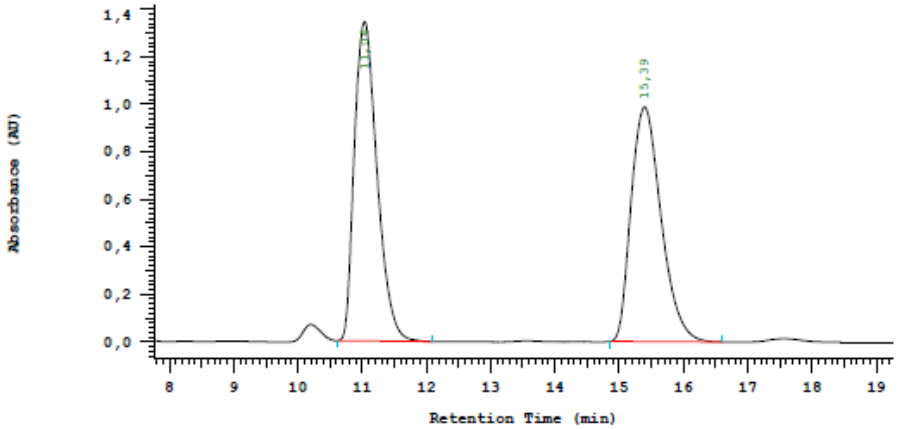
No.	RT	Area	Area %	Name
1	10,22	2889530	49,821	
2	12,65	2910330	50,179	
		5799860	100,000	



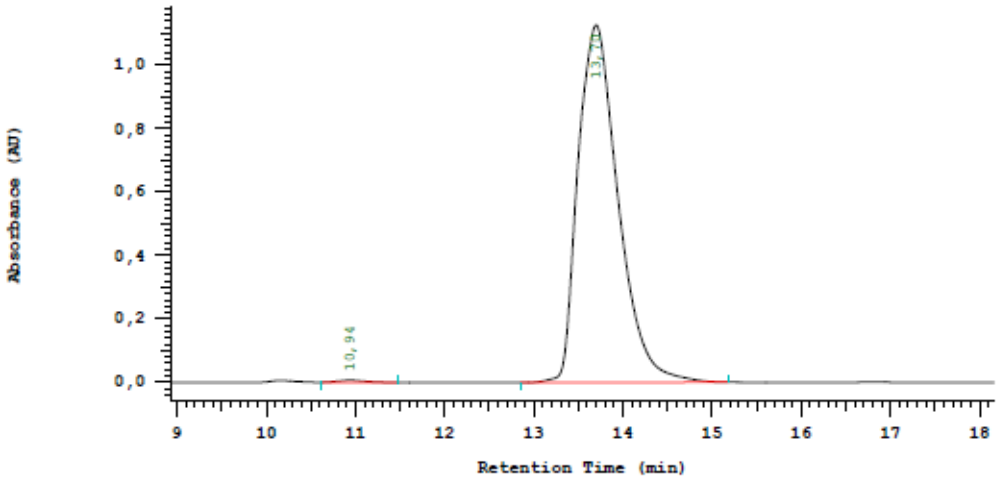
No.	RT	Area	Area %	Name
1	10,69	21493235	98,728	
2	13,20	276845	1,272	
		21770080	100,000	



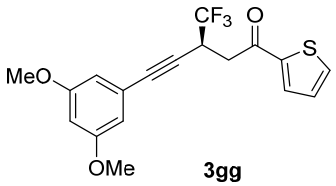
3fg



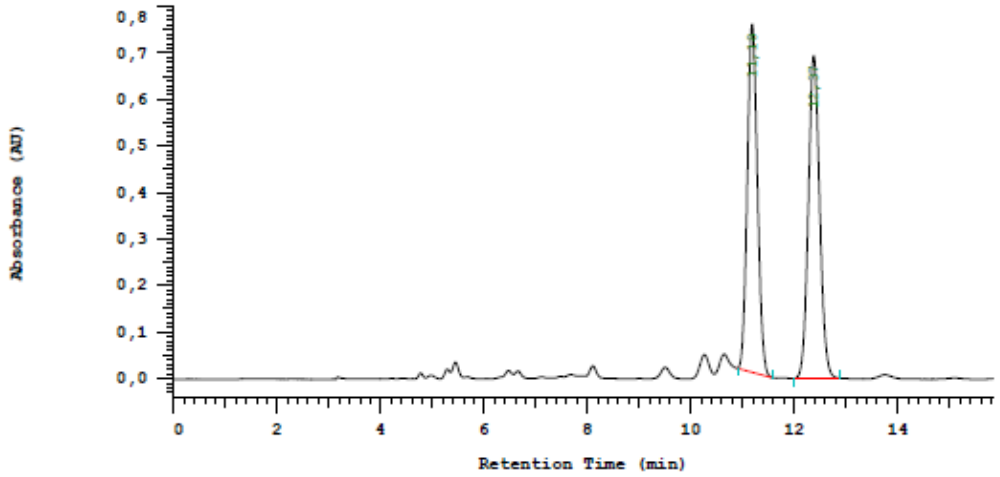
No.	RT	Area	Area %	Name
1	11,04	16499859	50,751	
2	15,39	16011619	49,249	
		32511478	100,000	



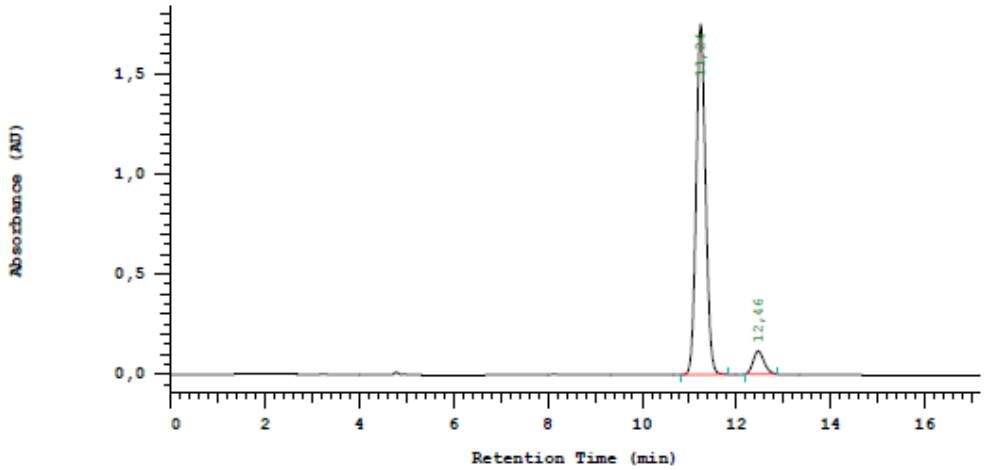
No.	RT	Area	Area %	Name
1	10,94	75945	0,429	
2	13,70	17638089	99,571	
		17714034	100,000	



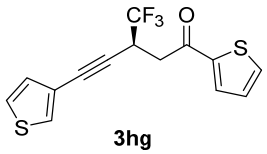
3gg



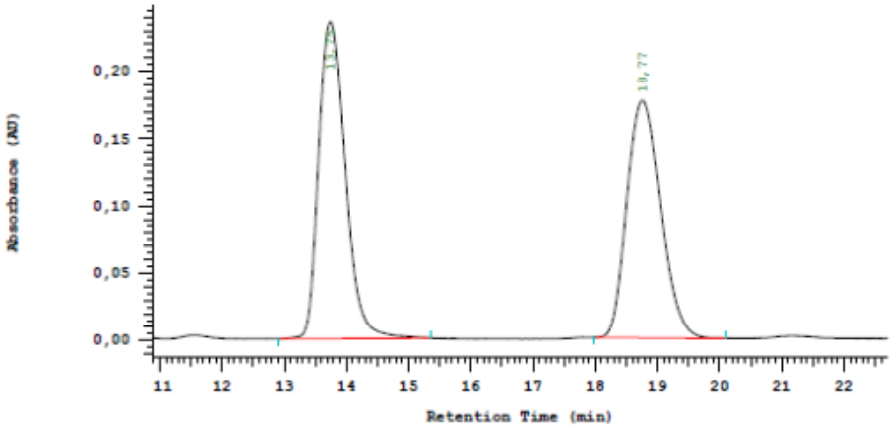
No.	RT	Area	Area %	Name
1	11,18	5055040	48,820	
2	12,37	5299460	51,180	
		10354500	100,000	



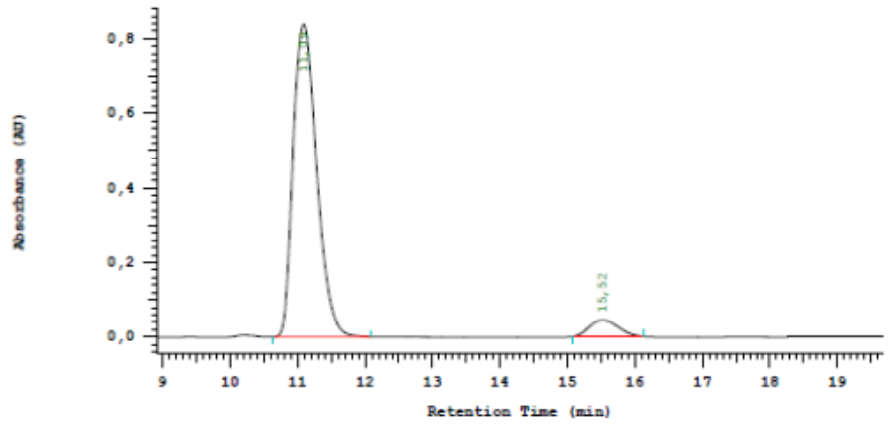
No.	RT	Area	Area %	Name
1	11,24	12062089	92,800	
2	12,46	935910	7,200	
		12997999	100,000	



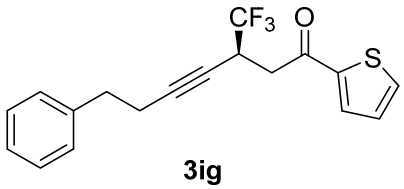
3hg



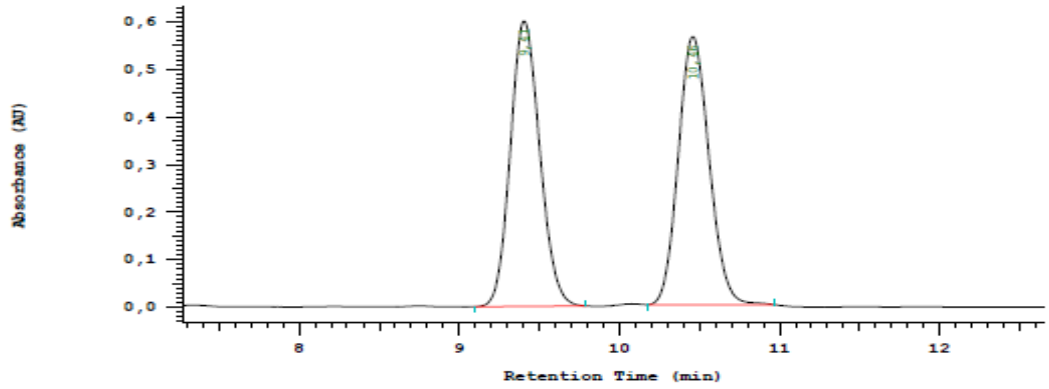
No.	RT	Area	Area %	Name
1	13,75	3495870	51,248	
2	18,77	3325550	48,752	
		6821420	100,000	



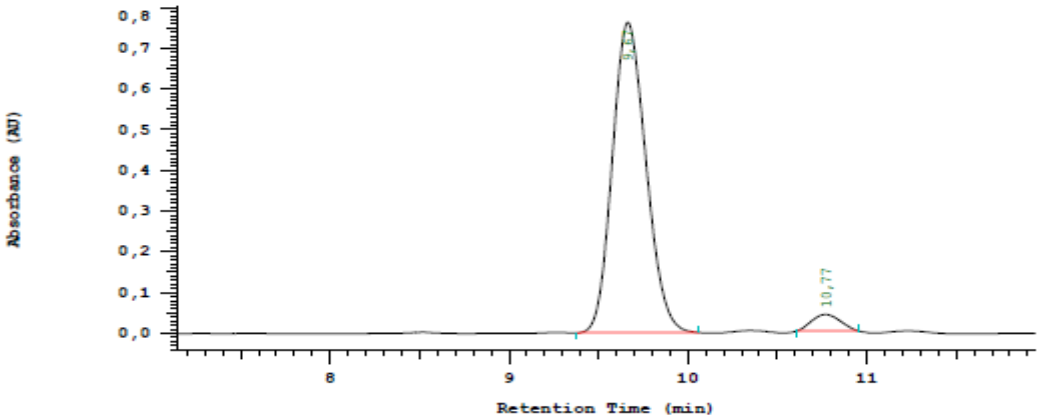
No.	RT	Area	Area %	Name
1	11,09	10169350	93,933	
2	15,52	656800	6,067	
		10826150	100,000	



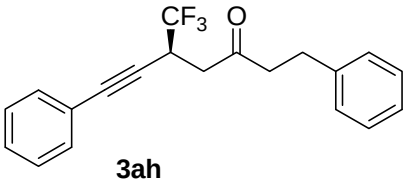
3ig



No.	RT	Area	Area %
1	9,41	3829870	50,388
2	10,46	3770840	49,612
		7600710	100,000



No.	RT	Area	Area %
1	9,67	4974620	95,792
2	10,77	218520	4,208
		5193140	100,000



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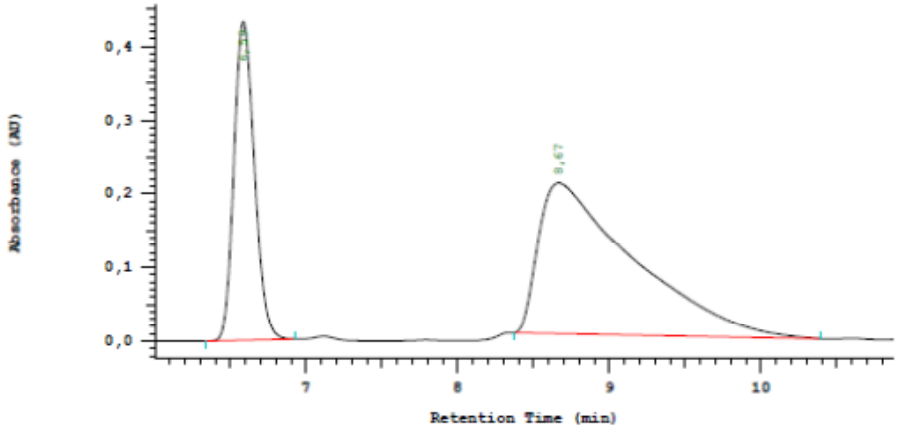
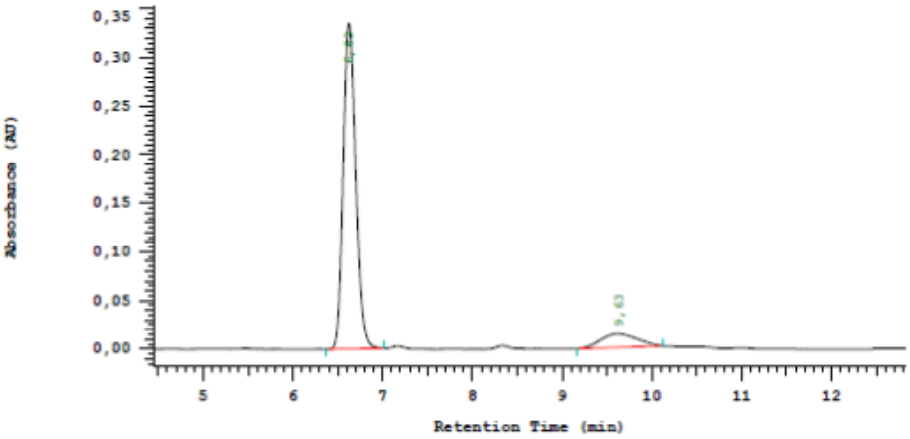
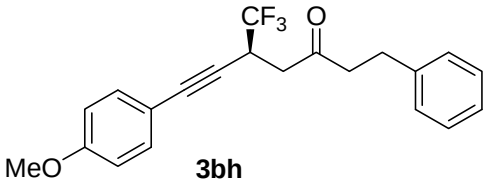


No.	RT	Area	Area %	Name
1	6,59	2026100	31,286	
2	8,67	4449964	68,714	
		6476064	100,000	



No.	RT	Area	Area %	Name
1	6,63	1625410	89,295	
2	9,63	194860	10,705	
		1820270	100,000	



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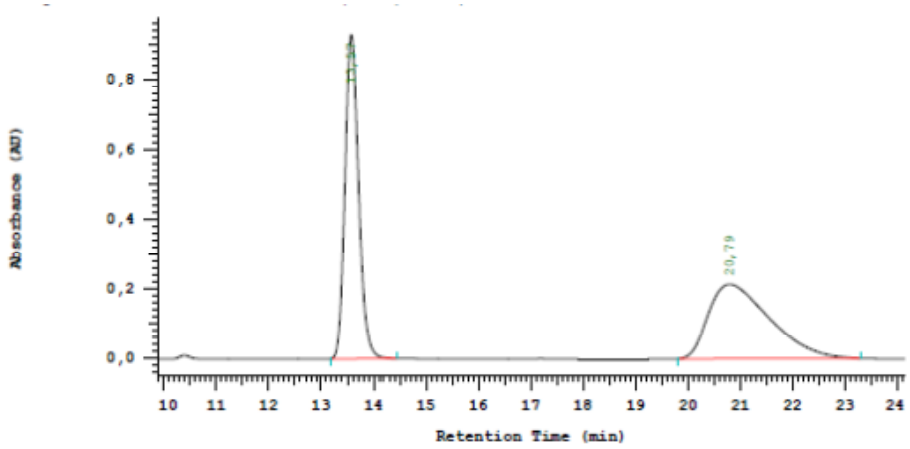
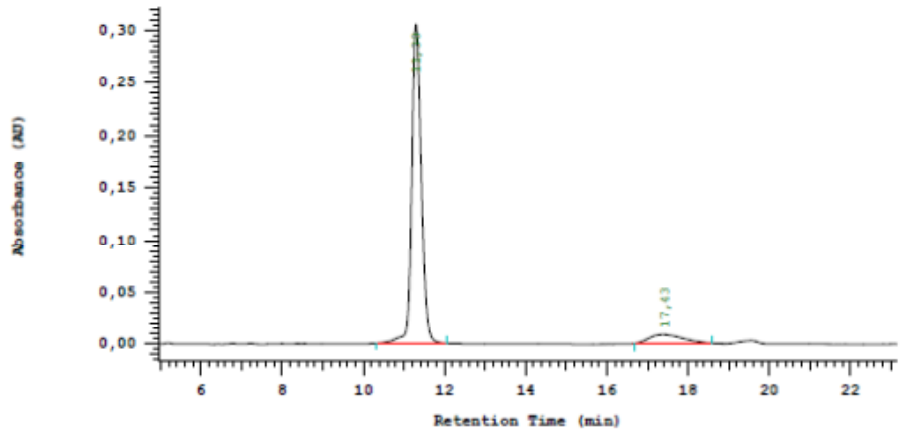
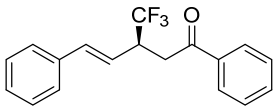


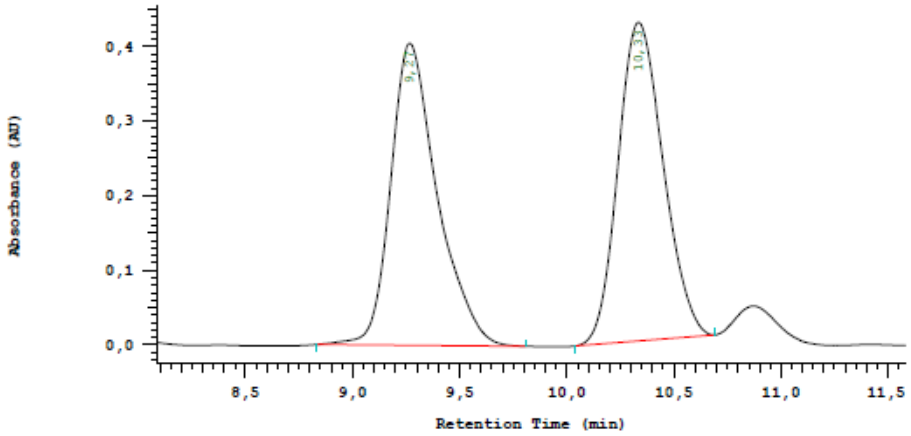
No.	RT	Area	Area %	Name
1	13,57	8411390	49,176	
2	20,79	8693320	50,824	
		17104710	100,000	



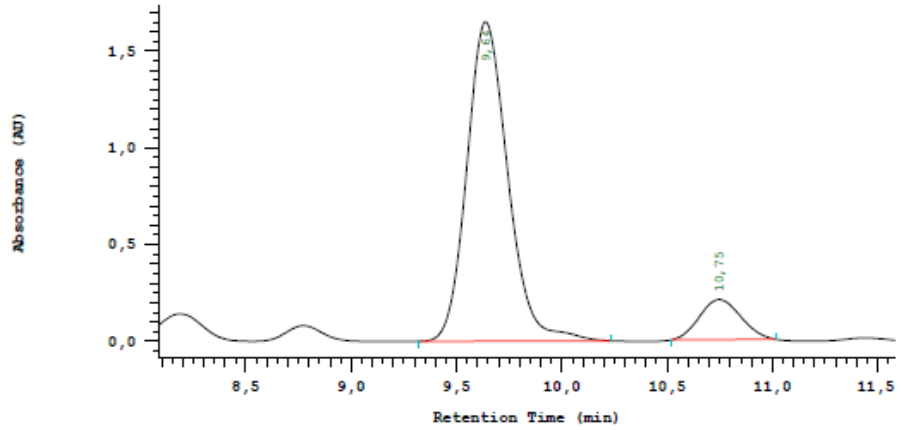
No.	RT	Area	Area %	Name
1	11,30	2495555	90,986	
2	17,43	247250	9,014	
		2742805	100,000	



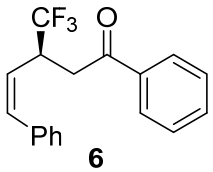
5



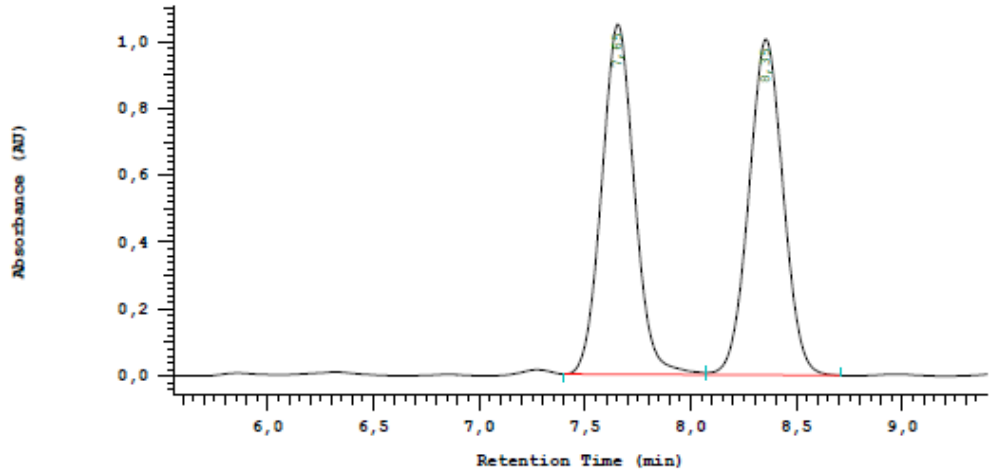
No.	RT	Area	Area %	Name
1	9,27	3064390	49,523	
2	10,33	3123390	50,477	
		6187780	100,000	



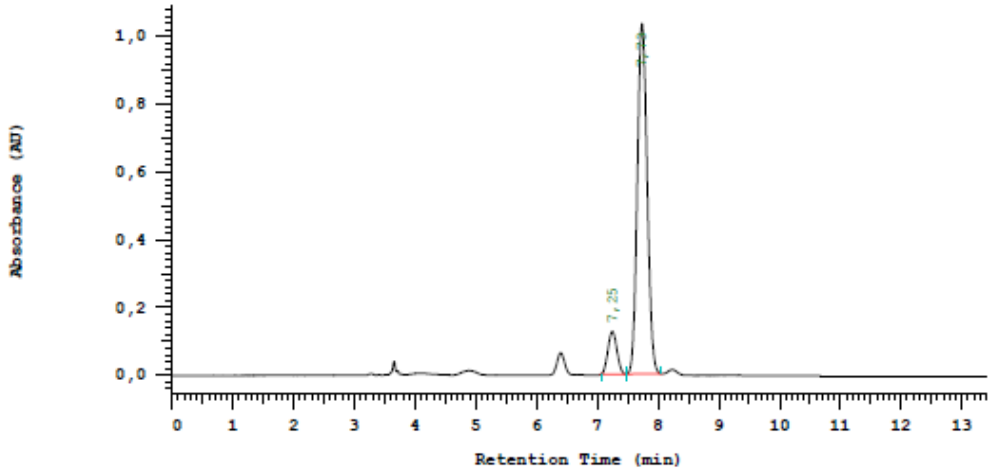
No.	RT	Area	Area %	Name
1	9,64	11183110	88,822	
2	10,75	1407330	11,178	
		12590440	100,000	



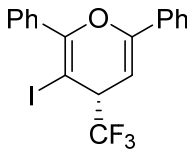
6



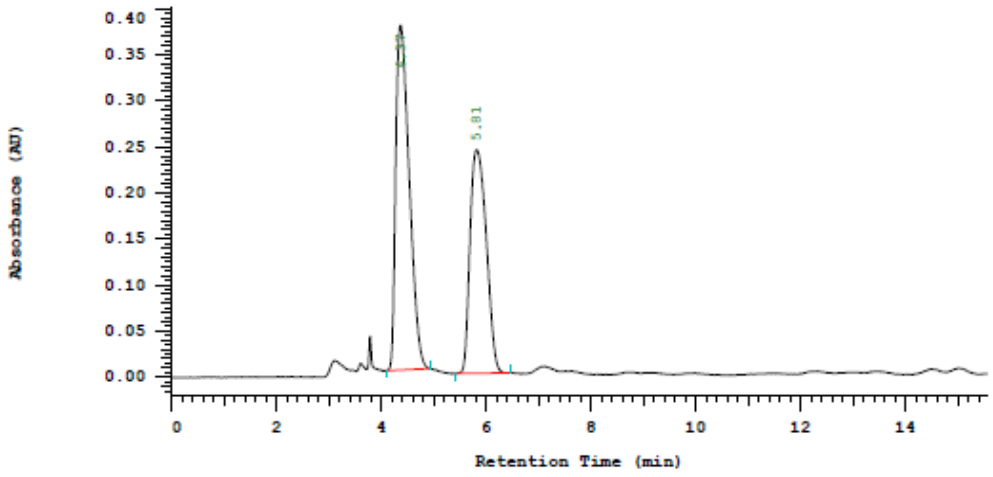
No.	RT	Area	Area %	Name
1	7,65	5623247	49,805	
2	8,35	5667342	50,195	
		11290589	100,000	



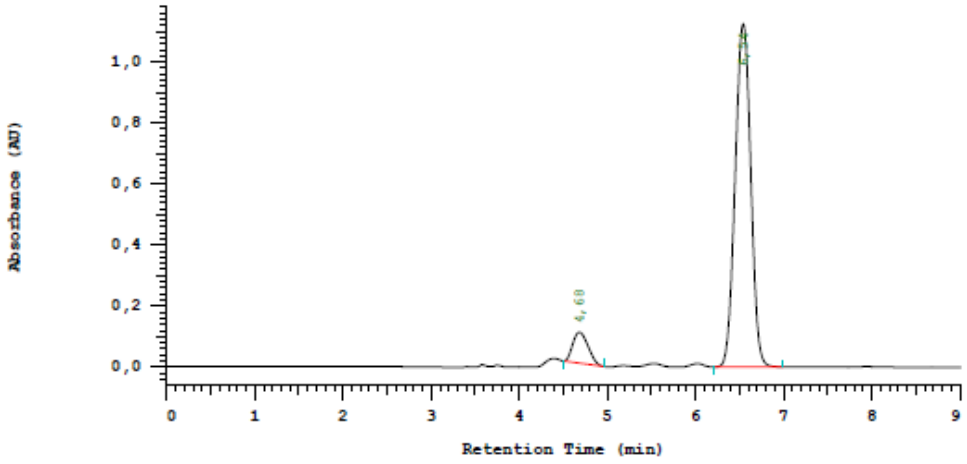
No.	RT	Area	Area %	Name
1	7,25	648834	10,065	
2	7,73	5797605	89,935	
		6446439	100,000	



7



No.	RT	Area	Area %	Name
1	4.37	3358774	56.245	
2	5.81	2612945	43.755	
		5971719	100.000	



No.	RT	Area	Area %	Name
1	4,68	610950	8,102	
2	6,54	6930169	91,898	
		7541119	100,000	