Highly Enantioselective Copper(I)-Catalyzed Conjugate Addition of 1,3-Diynes to α,β-Unsaturated Trifluoromethyl Ketones

Amparo Sanz-Marco,[a] Gonzalo Blay,*[a] M. Carmen Muñoz,[b] and José R. Pedro*[a]

[a] *Departament de Química Orgànica, Facultat de Química, Universitat de València, C/Dr. Moliner, 50, E-46100 Burjassot (València), Spain*

[b] Departament de Física Aplicada, Universitat Politècnica de València, Camí de Vera s/n, E-46022-València, Spain

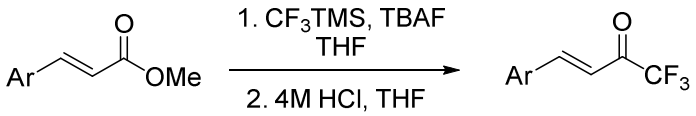
SUPPORTING INFORMATION

Table of Contents:

General Experimental Methods

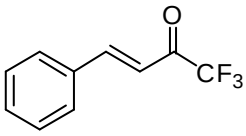
Reactions were carried out under nitrogen in round bottom flasks oven-dried overnight at 120 ºC. Commercial reagents were used as purchased. Stock solutions of 1,3-diynes **2**in diethyl ether were prepared as described in the literature, stored in the freezer and a required aliquot concentrated under reduced pressure prior to use.[1]Toluene was distilled from CaH_2. 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 non deuterated 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. Chiral GLC analyses were carried out in an chromatograph equipped with a flame ionization detector using nitrogen (1 mL/min) as carrier gas, $T_{injector}$ = 220 ◦C, $T_{detector}$ = 220 ◦C.

Typical procedure for the synthesis of α,β-unsaturated trifluoromethyl ketones 1.[2]



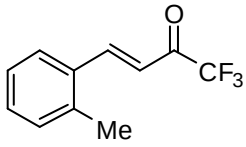
Trifluoromethyltrimethylsilane (0.34 mL, 2.31 mmol) was added to a solution of the corresponding α,β-unsaturated methyl ester (1.85 mmol) in pentane (1 mL) at room temperature under nitrogen atmosphere. A 1 M solution of tetrabutylammonium fluoride (TBAF) in THF (5 μL, 0.046 mmol) was added at 0 ºC and the reaction mixture was allowed to warm to room temperature and stirred for 18 h. Then, the solvent was removed under reduced pressure. The residue was dissolved in THF (1 mL) and treated with 4 M aqueous HCl (1 mL). After 10 h, the reaction mixture was diluted with diethyl ether (20 mL), washed with brine (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:EtOAc (99:01) gave the corresponding enones **1**.

(*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one (1a)[3]



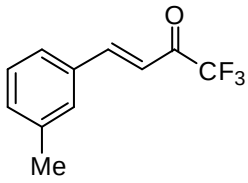
Yellow oil, 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 16.0 Hz, 1H), 7.68-7.70 (m, 2H), 7.51-7.42 (m, 3H), 7.03 (dd, *J* = 16.0, 0.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.5 (q, $J_{C\text{-}F}$ = 35.1 Hz, C), 146.9 (CH), 139.3 (C), 131.8 (CH), 130.9 (CH), 126.5 (CH), 126.3 (CH), 116.7 (CH), 116.4 (q, $J_{C\text{-}F}$ = 290.9 Hz, CF_3), 18.9 (CH_3); ^{19}F NMR(282 MHz, $CDCl_3$) δ −78.3 (s, 3F). Data consistent with the literature.[3]

(*E*)-1,1,1-trifluoro-4-(*o*-tolyl)but-3-en-2-one (1b)[4]



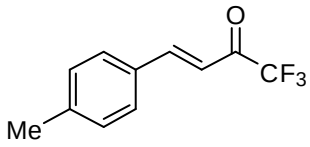
Yellow oil, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 15.8 Hz, 1H), 7.70-7.68 (m, 1H), 7.39 (dt, *J* = 3.9, 1.4 Hz, 1H), 7.29-7.25 (m, 1H), 6.96 (dd, *J* = 15.8, 0.8 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5 (q, $J_{C\text{-}F}$ = 35.1 Hz, C), 146.9 (CH), 139.3 (C), 131.8 (CH), 130.9 (CH), 126.5 (CH), 126.3 (CH), 116.7 (CH), 116.4 (q, $J_{C\text{-}F}$ = 290.9 Hz, CF_3), 18.9 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ −78.3 (s, 3F). Data consistent with the literature.[4]

(*E*)-1,1,1-trifluoro-4-(*m*-tolyl)but-3-en-2-one (1c)[5]



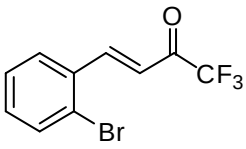
Yellow oil, 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 16.0 Hz, 1H), 7.39-7.37 (m, 2H), 7.31-7.26 (m, 2H), 6.95 (dd, *J* = 16.0, 0.8 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0 (q, $J_{C\text{-}F}$ = 35.3 Hz, C), 150.4 (CH), 139.0 (C), 133.2 (CH), 129.8 (CH), 129.1 (CH), 126.5 (CH), 116.4 (q, $J_{C\text{-}F}$ = 290.8 Hz, CF_3), 116.3 (CH), 21.2 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.1 (s, 3F). Data consistent with literature.[5]

(*E*)-1,1,1-trifluoro-4-(*m*-tolyl)but-3-en-2-one (1d)[6]



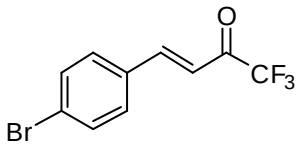
Yellow oil, 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 15.9 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 6.97 (dd, *J* = 15.9, 0.7 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0 (q, $J_{C\text{-}F}$ = 35.3 Hz, C), 150.2 (CH), 143.4 (C), 130.7 (C), 130.0 (2CH), 129.3 (2CH), 116.5 (q, $J_{C\text{-}F}$ = 291.0 Hz, CF_3), 115.6 (CH), 21.7 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.2 (s, 3F). Data consistent with the literature.[6]

(*E*)-4-(2-bromophenyl)-1,1,1-trifluorobut-3-en-2-one (1e)[3]



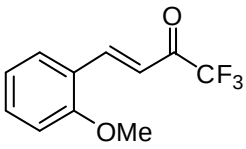
Yellow oil, 54% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 (d, *J* = 16.0 Hz, 1H), 7.72 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.67 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.39-7.30 (m, 2H), 6.99-6.94 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.8 (q, $J_{C\text{-}F}$ = 35.7 Hz, C), 148.3 (CH), 136.7 (C), 133.9 (CH), 133.0 (CH), 128.1 (CH), 128.0 (CH), 119.1 (CH), 116.3 (q, $J_{C\text{-}F}$ = 290.9 Hz, CF_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.0 (s, 3F). Data consistent with the literature.[3]

(*E*)-4-(4-bromophenyl)-1,1,1-trifluorobut-3-en-2-one (1f)[3]



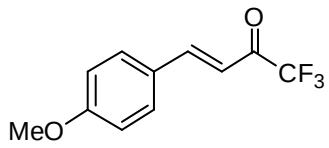
Yellow oil, 75% yield.^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 16.0 Hz, 1H), 7.65-7.55 (m, 2H), 7.55-7.45 (m, 2H), 7.00 (dd, *J* = 16.0, 0.8 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 179.9 (q, *J* = 35.3 Hz, C), 148.6 (CH), 132.6 (2CH), 132.2 (C), 130.4 (2CH), 127.0 (C), 117.1 (CH), 116.3 (q, *J* = 290.7 Hz, CF_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.1 (s, 3F). Data consistent with literature.[3]

(*E*)-1,1,1-trifluoro-4-(2-methoxyphenyl)but-3-en-2-one (1g)[4]



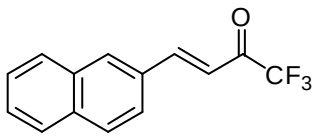
Yellow oil, 63% yield.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, *J* = 16.0 Hz, 1H), 7.60 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.46 (ddd, *J* = 8.5, 7.4, 1.7 Hz, 1H), 7.14 (dd, *J* = 16.1, 0.9 Hz, 1H), 7.01 (td, *J* = 7.5, 0.7 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 180.5 (q, *J* = 34.6 Hz, C), 159.6 (C), 145.8 (CH), 133.7 (CH), 130.3 (CH), 122.4 (C), 120.9 (CH), 117.1 (CH), 116.5 (q, *J* = 290.9 Hz, CF_3), 111.4 (CH), 55.6 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.0 (s, 3F). Data consistent with literature.[4]

(*E*)-1,1,1-trifluoro-4-(4-methoxyphenyl)but-3-en-2-one (1h)[3]



Yellow oil, 73% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 15.8 Hz, 1H), 7.63-7.60 (m, 2H), 6.97-6.94 (m, 2H), 6.89 (dd, *J* = 15.8, 0.8 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 179.9 (q, $J_{C\text{-}F}$ = 35.3 Hz, C), 163.2 (C), 149.9 (CH), 131.4 (2CH), 126.2 (C), 116.4 (q, $J_{C\text{-}F}$= 290.9 Hz, CF_3), 114.8 (2CH), 114.1 (CH), 55.5 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.0 (s, 3F). Data consistent with literature.[3]

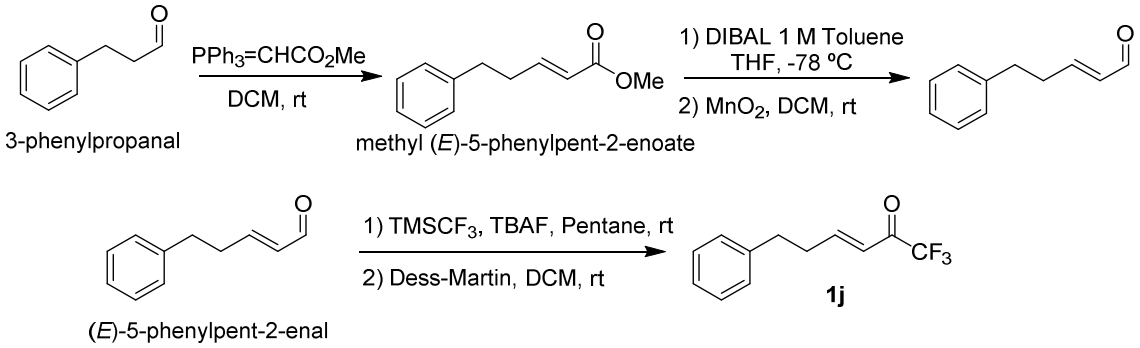
(*E*)-1,1,1-trifluoro-4-(naphthalen-2-yl)but-3-en-2-one (1i)[3]



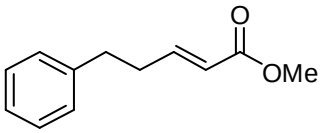
Yellow solid, mp 63-65 ºC, 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, *J* = 15.9 Hz, 1H), 8.06 (s, 1H), 7.92-7.85 (m, 3H), 7.73 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.62-7.53 (m, 2H), 7.12 (dd, *J* = 15.9, 0.8 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 180.0 (q, $J_{C\text{-}F}$ = 35.2 Hz, C), 150.2 (CH), 135.1 (C), 133.1 (C), 132.7 (CH), 130.8 (C),

129.1 (CH), 129.0 (CH), 128.4 (CH), 127.9 (CH), 127.1 (CH), 123.3 (CH), 116.6 (CH), 116.4 (q, $J_{C\text{-}F}$= 290.8 Hz, CF_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.0 (s, 3F). Data consistent with literature.[3]

Synthesis of (*E*)-1,1,1-trifluoro-6-phenylhex-3-en-2-one (1j) and aliphatic enones 1k and 1l.

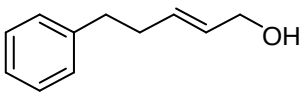


Methyl (*E*)-5-phenylpent-2-enoate[7]



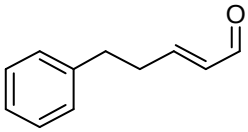
To a stirred solution of 3-phenylpropanal (0.33 mL, 2.49 mmol) in dichloromethane (10 mL), Wittig ylide Ph_3PCHCO_2Me (1.0 g, 2.99 mmol) was added at room temperature under nitrogen atmosphere. After 24 h, the solvent was evaporated under reduced pressure and the resulting crude was purified by column chromatography to give methyl (*E*)-5-phenylpent-2-enoate as a liquid (425 mg, 90%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.38-7.23 (m, 5H), 7.07 (dt, *J* = 15.7, 6.8 Hz, 1H), 5.91 (dt, *J* = 15.7, 1.6 Hz, 1H), 3.78 (s, 3H), 2.86-2.81 (m, 2H), 2.62-2.54 (m, 2H). Data consistent with literature.[7]

(*E*)-5-phenylpent-2-en-1-ol[8]



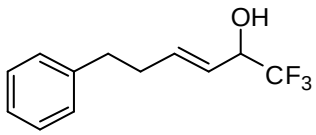
DIBAL–H (4.2 mL, 4.20 mmol, 1 M in toluene) was added to a solution of (*E*)-5-phenylpent-2-enoate (400 mg, 2.10 mmol) in tetrahydrofuran (5 mL) at −78 ºC under nitrogen atmosphere. After 4 h, saturated aqueous Roche's salt solution (8 mL) and ethyl acetate (6 mL) were added and stirred for 1h. The organic layer was separated and dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The residue was purified by column chromatography to give (*E*)-5-phenylpent-2-en-1-ol (320 mg, 94%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.32-7.27 (m, 2H), 7.22-7.18 (m, 3H), 5.78-5.63 (m, 2H), 4.09 (d, *J* = 5.0 Hz, 2H), 2.75-2.68 (m, 2H), 2.43-2.37 (m, 2H), 1.46 (brs, 1H). Data consistent with literature.[8]

(*E*)-5-phenylpent-2-enal[9]



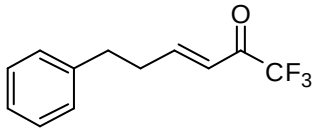
To a stirred solution of (*E*)-5-phenylpent-2-en-1-ol (300 mg, 1.86 mmol) in dichloromethane (16 mL), MnO_2 (2.97 g, 34.2 mmol) was added at room temperature under nitrogen atmosphere. After 72 h, dichloromethane was evaporated and the resulting crude was purified by column chromatography to give methyl (*E*)-5-phenylpent-2-enal as a liquid (278 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (d, *J* = 7.8 Hz, 1H), 7.34-7.29 (m, 2H), 7.24-7.18 (m, 3H), 6.87 (dt, *J* = 15.6, 6.6 Hz, 1H), 6.14 (ddt, *J* = 15.7, 7.9, 1.5 Hz, 1H), 2.87-2.82 (m, 2H), 2.71-2.63 (m, 2H). Data consistent with literature.[9]

(*E*)-1,1,1-trifluoro-6-phenylhex-3-en-2-ol[10]



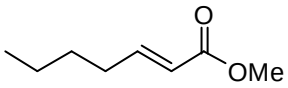
A 1M solution of TBAF in THF (0.16 mL, 0.156 mmol) was added to a solution of (*E*)-5-phenylpent-2-enal (250 mg, 1.56 mmol) and $TMSCF_3$ (0.3 mL, 2.06 mmol) in pentane (1 mL) at 0 ºC under nitrogen atmosphere and the resulting mixture was allowed to reach room temperature. After 24 h, pentane was evaporated under reduced pressure. THF (1 mL) and 4M aqueous HCl (1 mL) were added, and the mixture was stirred 24 h. Then, the organic layer was separated, dried over anhydrous $MgSO_4$ and evaporated. Purification by column chromatography gave (*E*)-1,1,1-trifluoro-6-phenylhex-3-en-2-ol (340 mg, 94%).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.18 (m, 5H), 6.07-5.98 (m, 1H), 5.55 (dd, *J* = 15.5, 6.8 Hz, 1H), 4.44-4.34 (m, 1H), 2.78-2.73 (m, 2H), 2.49-2.42 (m, 2H), 2.24 (d, *J* = 5.6 Hz, 1H). Data consistent with literature.[10]

(*E*)-1,1,1-trifluoro-6-phenylhex-3-en-2-one (1j)



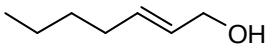
Dess-Martin periodinane (720 mg, 1.70 mmol) was added in one portion to a solution of (*E*)-1,1,1-trifluoro-6-phenylhex-3-en-2-ol(300 mg, 1.30 mmol) in dichloromethane (2.6 mL) at room temperature under nitrogen atmosphere. After 48 h, the resulting suspension was poured into 3 mL of a 5:1 mixture of saturated aqueous $Na_2S_2O_3$ solution and saturated aqueous $NaHCO_3$ solution. The organic layer washed with water, dried over $MgSO_4$ and evaporated. The residue was purified by column chromatography to give **1j** (200 mg, 67%).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.11 (m, 6H), 6.36 (dd, *J* = 15.8, 1.1 Hz, 1H), 2.81-2.76 (m, 2H), 2.64-2.56 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 179.7 (q, J_{C-F} = 35.3 Hz, C), 155.2 (CH), 139.9 (C), 128.6 (2CH), 128.3 (2CH), 126.5 (CH), 121.9 (CH), 116.4 (q, J_{C-F}= 290.8 Hz, CF_3), 34.8 (CH_2), 33.8 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.0 (s, 3F). HRMS (ESI) *m/z*: 228.0754 $(M+H)^+$, $C_{12}H_{11}F_3O$ requires 228.0762.

Methyl (*E*)-hept-2-enoate[11]



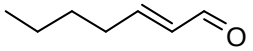
Prepared from valeraldehyde following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (dt, *J* = 15.6, 7.0 Hz, 1H), 5.74 (dt, *J* = 15.6, 1.6 Hz, 1H), 3.64 (s, 3H), 2.13 (qd, *J* = 7.2, 1.5 Hz, 2H), 1.39-1.23 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 3H). Data consistent with literature.[11]

(*E*)-Hept-2-en-1-ol



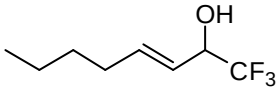
Prepared following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72-5.55 (m, 2H), 4.06-4.04 (m, 2H), 2.02 (dd, *J* = 13.1, 6.5 Hz, 2H), 1.83 (br s, OH), 1.39-1.26 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H).

(*E*)-Hept-2-enal[12]



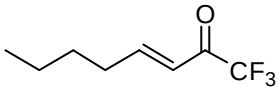
Prepared following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.49 (d, *J* = 7.9 Hz, 1H), 6.84 (dt, *J* = 15.6, 6.8 Hz, 1H), 6.11 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H), 2.37-2.29 (m, 2H), 1.54-1.30 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H). Data consistent with literature.[12]

(*E*)-1,1,1-Trifluorooct-3-en-2-ol[13]



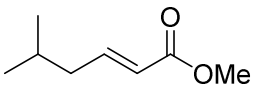
Prepared following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.03-5.93 (m, 1H), 5.55-5.48 (m, 1H), 4.41-4.37 (m, 1H), 2.21 (br s, OH), 2.15-2.08 (m, 2H), 1.45-1.28 (m, 4H), 0.93-0.86 (m, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ −80.0 (s, 3F). Data consistent with literature.[13]

(*E*)-1,1,1-Trifluorooct-3-en-2-one (1k)[13]



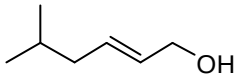
Prepared following the above procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dt, *J* = 15.3, 7.0 Hz, 1H), 6.40 (ddd, *J* = 15.8, 2.6, 1.5 Hz, 1H), 2.34 (ddd,*J* = 14.8, 7.2, 1.6 Hz, 2H), 1.52-1.46 (m, 2H), 1.41-1.33 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.8 (q, $J_{C\text{-}F}$ = 35.1 Hz, C), 157.0 (CH), 121.3 (CH), 116.2 (q, $J_{C\text{-}F}$= 290.9 Hz, CF_3), 32.9 (CH_2), 29.6 (CH_2),22.2 (CH_2),15.2 (CH_3). Data consistent with literature.[13]

Methyl (*E*)-5-methylhex-2-enoate[14]



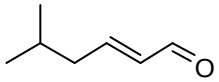
Prepared following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95 (dt, *J* = 15.6, 7.0 Hz, 1H), 5.80 (dt, *J* = 15.6, 1.7 Hz, 1H), 3.70 (s, 3H), 2.17-2.04 (m, 3H), 0.92 (d, *J* = 6.6 Hz, 6H). Data consistent with literature.[14]

(*E*)-5-Methylhex-2-en-1-ol[15]



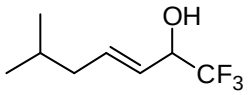
Prepared following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68-5.63 (m, 2H), 4.69 (d, *J* = 4.6 Hz, 2H), 1.97-1.91 (m, 2H), 1.70-1.56 (m, 1H), 1.42 (br s, OH), 0.89 (d, *J* = 6.6 Hz, 6H). Data consistent with literature.[15]

(*E*)-5-Methylhex-2-enal[16]



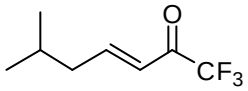
Prepared following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (d, *J* = 7.9 Hz, 1H), 7.11-7.01 (m, 1H), 5.82 (dt, *J* = 15.6, 1.5 Hz, 1H), 2.26-2.10 (m, 2H), 1.87-1.74 (m, 1H), 0.96 (d, *J* = 6.9 Hz, 6H). Data consistent with literature.[16]

(*E*)-1,1,1-Trifluoro-6-methylhept-3-en-2-ol



Prepared following the above procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.00-5.90 (m, 1H), 5.50 (dd, *J* = 15.4, 6.9 Hz, 1H), 4.44-4.36 (m, 1H), 2.02-1.97 (m, 2H), 1.72-1.63 (m, 1H), 0.90 (dd, *J* = 6.6, 2.2 Hz, 6H); ^{19}F NMR (282 MHz, $CDCl_3$) δ –80.0 (s, 3F).

(*E*)-1,1,1-Trifluoro-6-methylhept-3-en-2-one (1l)

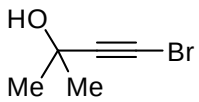


Prepared following the above procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.24 (m, 1H), 6.38 (dd, *J* = 15.7, 1.1 Hz, 1H), 2.22-2.18 (m, 2H), 1.87-1.79 (m, 1H), 0.93 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6 (q, $J_{C\text{-}F}$ = 35.1 Hz, C), 155.7 (CH), 122.4 (CH), 116.2 (q, $J_{C\text{-}F}$= 291.0 Hz, CF_3), 42.3 (CH_2), 27.8 (CH), 22.2 ($2CH_3$); ^{19}F NMR (282 MHz, $CDCl_3$) δ –78.0 (s, 3F); HRMS (ESI) *m/z*: 181.0844 $(M+H)^+$, $C_8H_{12}F_3O$ requires 181.0840.

Synthesis and characterization of 1,3-diynes 2

1,3-Diynes **2** were synthesized according to the procedure described in the literature.[1]

4-Bromo-2-methylbut-3-yn-2-ol

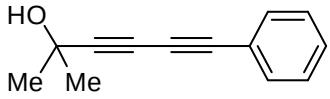


Br_2 (3.9 mL, 0.077 mol) was added dropwise via syringe to a stirred solution of KOH (30.1 g, 0.536 mol) in H_2O (200 mL) at 0 ºC. After 15 min, 2-methyl-3-butyn-2-ol (10 mL, 0.103 mol) was added dropwise via an addition funnel. After 1 h, the mixture was warmed to rt and extracted with Et_2O (3 x 50 mL). The organic phase was dried with $MgSO_4$, filtered, concentrated, and purified by column chromatography on silica gel to afford 4-bromo-2-methyl-3-but-3-yn-2-ol in 75% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.51 (br s, 1H), 1.49 (s, 6H). Data consistent with literature.[17]

Representative procedure: 2-Methyl-6-phenylhexa-3,5-diyn-2-ol

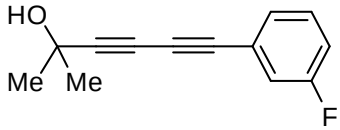
CuCl (23.3 mg, 0.24 mmol) was added to a solution of 30% $BuNH_2/H_2O$ (30 mL). The blue color was quenched by the addition of a spatula of $H_2NOH \cdot HCl$. Phenylacetylene (**2a**, 1.29 mL, 11.76 mmol) was added and the reaction mixture was cooled to 0 ºC, becoming a yellow cloudy solution. A solution of 4-bromo-2-methyl-3-but-3-yn-2-ol (2.0 g, 12.35 mmol) in Et_2O (5 mL) was added. Then, a spatula of $NH_2(OH) \cdot HCl$ was added to the reaction mixture. After 5 min, the mixture was warmed to rt and extracted with Et_2O (2 x 25 mL). The organic layer was dried with $MgSO_4$, filtered, concentrated, and purified by column chromatography on silica gel to afford 2-methyl-6-phenylhexa-3,5-diyn-2-ol (1.93 g, 89%).

2-Methyl-6-phenylhexa-3,5-diyn-2-ol



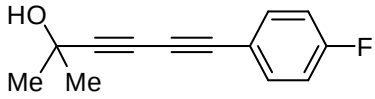
89% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.37-7.32 (m, 3H), 2.12 (br s, 1H), 1.59 (s, 6H). Data consistent with the literature.[18]

6-(3-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol



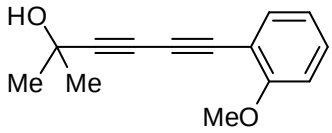
71% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 7.18-7.14 (m, 1H), 7.10-7.03 (m, 1H), 1.58 (s, 6H). Data consistent with the literature.[18]

6-(4-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol



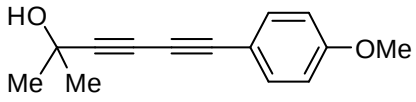
80% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.44 (m, 2H), 7.04-6.98 (m, 2H), 2.06 (br s, 1H), 1.58 (s, 6H). Data consistent with the literature.[19]

6-(2-Methoxyphenyl)-2-methylhexa-3, 5-diyn-2-ol



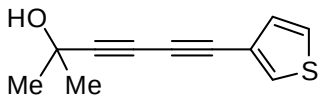
83% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.32 (ddd, *J* = 8.3, 7.6, 1.7 Hz, 1H), 6.92-6.85 (m, 2H), 3.87 (s, 3H), 2.14 (br s, 1H), 1.57 (s, 6H). Data consistent with the literature.[20]

6-(4-Methoxyphenyl)-2-methylhexa-3, 5-diyn-2-ol



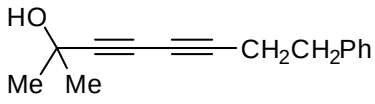
78% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.38 (m, 2H), 6.84-6.79 (m, 2H), 3.79 (s, 3H), 2.60 (br s, 1H), 1.57 (s, 6H). Data consistent with the literature.[19]

2-Methyl-6-(thiophen-3-yl)hexa-3,5-diyn-2-ol



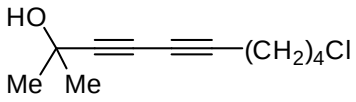
80% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.27 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.13 (dd, *J* = 5.0, 1.2 Hz, 1H), 2.01 (br s, 1H), 1.57 (s, 6H). Data consistent with the literature.[19]

2-Methyl-8-phenylocta-3,5-diyn-2-ol



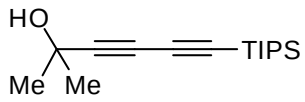
84% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.29 (m, 2H), 7.27-7.20 (m, 3H), 2.86 (t, *J* = 7.5 Hz, 2H), 2.59 (t, *J* = 7.5 Hz, 2H), 2.22 (br s, 1H), 1.54 (s, 6H). Data consistent with the literature.[17]

11-Chloro-2-methylundeca-3,5-diyn-2-ol



85% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.56 (t, *J* = 6.5 Hz, 2H), 2.34 (t, *J* = 6.9 Hz, 2H), 1.93-1.85 (m, 2H), 1.75-1.65 (m, 2H), 1.53 (s, 6H).

2-Methyl-6-(triisopropylsilyl)hexa-3,5-diyn-2-ol

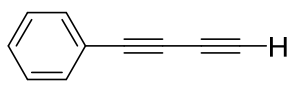


61% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.95 (br s, 1H), 1.54 (s, 6H), 1.08 (s, 21H). Data consistent with the literature.[17]

Synthesis of 1,3-diynes 2

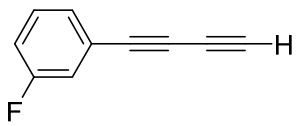
A solution of the required diynol (7.71 mmol) in toluene (10 mL) was added to a mixture of K_2CO_3 (1.07 g, 7.71 mmol) and 18-crown-6 (0.61 g, 2.31 mmol) in toluene (13 mL) under nitrogen atmosphere at room temperature. The reaction mixture was heated at reflux until the reaction was determined to be complete by TLC (1-2 h). Then, the reaction was cooled to room temperature, extracted with EtOAc (2 × 50 mL), dried over $MgSO_4$ and concentrated. The crude oil was purified by column chromatography on silica gel to give the terminal 1,3-diynes **2**. The 1,3-diynes were passed through a short plug of alumina and then stored in Et_2O solution (200 mL) in the freezer. Prior to use they were concentrated via rotary evaporation.

Buta-1,3-diyn-1-ylbenzene (2a)



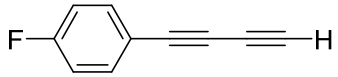
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.49 (m, 2H), 7.40-7.28 (m, 3H), 2.46 (s, 1H). Data consistent with the literature.[17]

1-(Buta-1,3-diyn-1-yl)-3-fluorobenzene (2b)



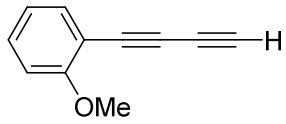
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H), 7.23-7.16(m, 1H), 7.13-7.06 (m, 1H), 2.51 (s, 1H).

1-(Buta-1,3-diyn-1-yl)-4-fluorobenzene (2c)



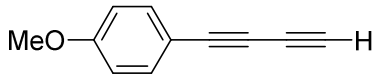
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.46 (m, 2H), 7.06-6.98 (m, 2H), 2.47 (s, 1H).

1-(Buta-1,3-diyn-1-yl)-2-methoxybenzene (2d)



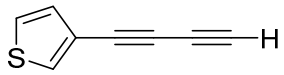
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.33 (ddd, *J* = 8.4, 7.5, 1.7 Hz, 1H), 6.89 (td, *J* = 7.5, 1.0 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 2.52 (s, 1H). Data consistent with the literature.[20]

1-(Buta-1,3-diyn-1-yl)-4-methoxybenzene (2e)



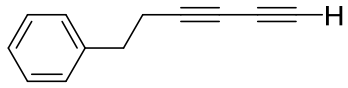
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.42 (m, 2H), 6.85-6.81 (m, 2H), 3.81 (s, 3H), 2.45 (s, 1H). Data consistent with the literature.[20]

3-(Buta-1,3-diyn-1-yl)thiophene (2f)



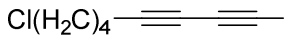
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.27 (dd, J = 5.0, 3.0 Hz, 1H), 7.15 (dd, *J* = 5.0, 1.2 Hz, 1H), 2.46 (s, 1H).

Hexa-3,5-diyn-1-ylbenzene (2g)



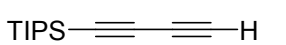
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.19 (m, 5H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.55 (d, J = 7.5 Hz, 2H), 1.97 (t, *J* = 1.2 Hz, 1H). Data consistent with the literature.[17]

9-Chlorononа-1,3-diyne (2h)



^{1}H NMR (300 MHz, $CDCl_3$) δ 3.54 (t, *J* = 6.4 Hz, 2H), 2.31 (td, *J* = 7.0, 1.2 Hz, 2H), 1.97 (t, *J* = 1.2 Hz, 1H), 1.93-1.84 (m, 2H), 1.77-1.64 (m, 2H).

Buta-1,3-diyn-1-yltriisopropylsilane (2i)



^{1}H NMR (300 MHz, $CDCl_3$) δ 2.07 (s, 1H), 1.09 (s, 21H).

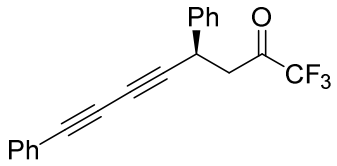
Typical procedures and characterization data for compounds 3

General procedure for the enantioselective conjugate diynylation reaction

$[Cu(CH_3CN)_4]BF_4$ (1.1 mg, 0.0034 mmol) and (*R*)-**L1** (4.1 mg, 0.0034 mmol) were added to a dried round bottom flask which was purged with nitrogen. Toluene (0.2 mL) was added via syringe and the mixture was stirred for 1.5 h at room temperature under nitrogen atmosphere. Then, a solution of α,β-unsaturated trifluoromethyl ketone **1**(0.144 mmol) in toluene (1.0 mL)was added via syringe, followed of triethylamine (2 µL, 0.0144 mmol). The solution was stirred for 10 min at room temperature. Then a solution of 1,3-diyne **2** (0.188 mmol) in toluene (1.0 mL) was added via syringe and the solution

was stirred at room temperature 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 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:ethyl acetate mixtures afforded compound **3**.

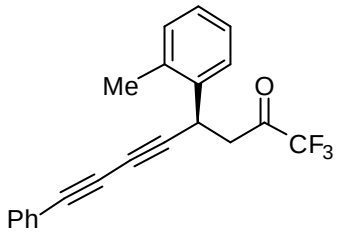
(*R*)-1,1,1-trifluoro-4,8-diphenylocta-5,7-diyn-2-one (3aa)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 95:05, 1 mL/min, major enantiomer t_r = 4.96 min, minor enantiomer t_r = 4.61 min.

$[\alpha]_D^{20}$ –29.3 (*c* 1.05, $CHCl_3$) (93% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.48 (m, 2H), 7.42-7.29 (m, 8H), 4.41 (dd, *J* = 7.9, 6.2 Hz, 1H), 3.37 (ddd, *J* = 18.7, 7.9, 0.5 Hz, 1H), 3.19 (ddd, *J* = 18.7, 6.2, 0.5 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1 (q, $J_{C\text{-}F}$ = 36.2 Hz, C), 138.3 (C), 132.6 (2CH), 129.2 (CH), 129.1 (2CH), 128.4 (2CH), 127.9 (CH), 127.4 (2CH), 121.5 (C), 115.3 (q, $J_{C\text{-}F}$ = 291.8 Hz, CF_3), 82.2 (C), 77.3 (C), 73.5 (C), 68.4 (C), 44.4 (CH_2), 32.6 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.7 (s, 3F); HRMS (ESI) *m/z*: 327.0982 $(M+H)^+$, $C_{20}H_{14}F_3O$ requires 327.0997.

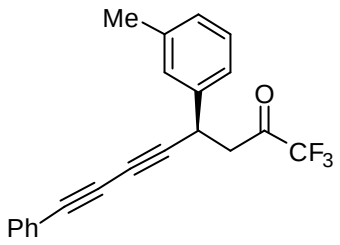
(*S*)-1,1,1-trifluoro-8-phenyl-4-(*o*-tolyl)octa-5,7-diyn-2-one (3ba)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 95:05, 1 mL/min, major enantiomer t_r = 16.0 min, minor enantiomer t_r = 11.8 min.

$[\alpha]_D^{20}$ –35.2 (*c* 1.02, $CHCl_3$) (94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.45 (m, 3H), 7.36-7.31 (m, 3H), 7.25-7.19 (m, 3H), 4.59 (dd, *J* = 8.7, 5.4 Hz, 1H), 3.37 (ddd, *J* = 18.7, 8.7, 0.5 Hz, 1H), 3.16 (ddd, *J* = 18.7, 5.4, 0.5 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.7 (q, $J_{C\text{-}F}$ = 36.2 Hz, C), 136.8 (C), 135.5 (C), 133.0 (2CH), 131.5 (CH), 129.6 (CH), 128.8 (2CH), 128.3 (CH), 127.5 (CH), 127.3 (CH), 121.9 (C), 115.7 (q, $J_{C\text{-}F}$ = 291.6 Hz, CF_3), 82.8 (C), 77.9 (C), 74.0 (C), 68.3 (C), 43.4 (CH_2), 29.4 (CH), 19.7 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.6 (s, 3F); HRMS (ESI) *m/z*: 341.1160 $(M+H)^+$, $C_{21}H_{16}F_3O$ requires 341.1153.

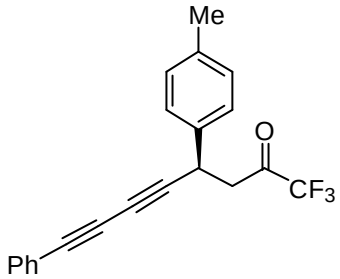
(*S*)-1,1,1-trifluoro-8-phenyl-4-(*m*-tolyl)octa-5,7-diyn-2-one (3ca)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.1 min, minor enantiomer t_r = 4.6 min.

$[\alpha]_D^{20}$ −18.9 (*c* 1.00, $CHCl_3$) (93% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.36-7.31 (m, 3H), 7.23-7.11 (m, 4H), 4.37 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.36 (ddd, *J* = 18.7, 8.1, 0.5 Hz, 1H), 3.17 (ddd, *J* = 18.7, 6.1, 0.5 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1 (q, $J_{C\text{-}F}$ = 36.4 Hz, C), 138.9 (C), 138.2 (C), 132.6 (2CH), 129.2 (CH), 128.9 (CH), 128.7 (CH), 128.4 (2CH), 128.0 (CH), 124.4 (CH), 121.5 (C), 115.3 (q, $J_{C\text{-}F}$ = 291.9 Hz, CF_3), 82.3 (C), 77.2 (C), 73.6 (C), 68.3 (C), 44.4 (CH_2), 32.5 (CH), 21.4 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.7 (s, 3F); HRMS (ESI) *m/z*: 341.1164 (M+ H)$^+$, $C_{21}H_{16}F_3O$ requires 341.1153.

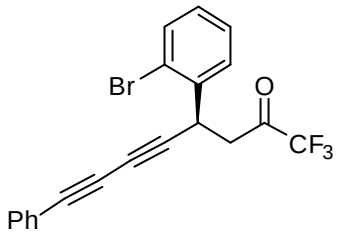
(*R*)-1,1,1-trifluoro-8-phenyl-4-(*p*-tolyl)octa-5,7-diyn-2-one (3da)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.4 min, minor enantiomer t_r = 4.9 min.

$[\alpha]_D^{20}$ −25.8 (*c* 0.84, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.36-7.26 (m, 5H), 7.19-7.16 (m, 2H), 4.37 (dd, *J* = 7.7, 6.4 Hz, 1H), 3.35 (ddd, *J* = 18.7, 7.7, 0.5 Hz, 1H), 3.17 (ddd, *J* = 18.7, 6.4, 0.5 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1 (q, $J_{C\text{-}F}$ = 36.2 Hz, C), 137.7 (C), 135.3 (C), 132.6 (2CH), 129.7 (2CH), 129.2 (CH), 128.4 (2CH), 127.2 (2CH), 121.5 (C), 115.3 (q, $J_{C\text{-}F}$ = 291.8 Hz, CF_3), 82.5 (C), 77.2 (C), 73.6 (C), 68.3 (C), 44.4 (CH_2), 32.2 (CH), 21.0 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.7 (s, 3F); HRMS (ESI) *m/z*: 341.1150 (M+ H)$^+$, $C_{21}H_{16}F_3O$ requires 341.1153.

(*S*)-4-(2-bromophenyl)-1,1,1-trifluoro-8-phenylocta-5,7-diyn-2-one (3ea)

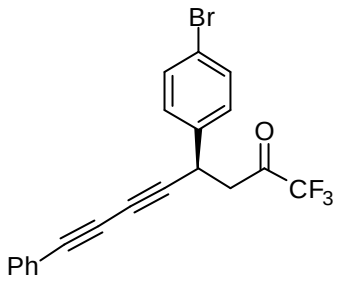


Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.2 min, minor enantiomer t_r = 4.8 min.

$[\alpha]_D^{20}$ −95.3 (*c*0.55, $CHCl_3$) (94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.58 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.52-7.48 (m, 2H), 7.39-7.32 (m, 4H), 7.22-7.16 (m, 1H), 4.85 (dd, *J* = 7.8, 5.8 Hz, 1H), 3.25 (m, 1H), 3.23 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.2 (q, $J_{C\text{-}F}$ = 36.4 Hz, C), 137.7 (C), 133.7 (CH), 133.0 (2CH),

130.0(CH), 129.9 (CH), 129.7 (CH), 128.8 (2CH), 128.6 (CH), 123.3 (C), 121.8 (C), 115.7 (q, J_{C-F} = 291.7 Hz, CF_3), 81.4 (C), 77.8 (C), 73.9 (C), 69.5 (C), 43.2 (CH_2), 33.1 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.5 (s, 3F); HRMS (ESI) *m/z*: 405.0096/407.0075 $(M+H)^+$98.8/100.0, $C_{20}H_{13}BrF_3O$ requires 405.0102/407.0081.

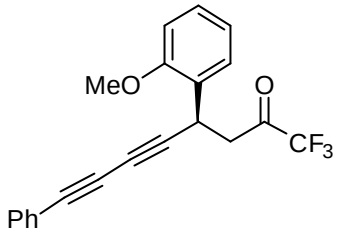
(*R*)-4-(4-bromophenyl)-1,1,1-trifluoro-8-phenylocta-5,7-diyn-2-one (3fa)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 7.5 min, minor enantiomer t_r = 6.9 min.

$[\alpha]_D^{20}$ −19.9 (*c* 0.78, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.47 (m, 4H), 7.37-7.27 (m, 5H), 4.37 (t, *J* = 7.0 Hz, 1H), 3.35 (ddd, *J* = 18.8, 7.5, 0.4 Hz, 1H), 3.16 (ddd, *J* = 18.8, 6.5, 0.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.8 (q, J_{C-F} = 36.6 Hz, C), 137.3 (C), 132.6 (2CH), 132.2 (2CH), 129.3 (CH), 129.1 (2CH), 128.4 (2CH), 121.9 (C), 121.3 (C), 115.2 (q, J_{C-F} = 291.6 Hz, CF_3), 81.4 (C), 77.6 (C), 73.3 (C), 68.8 (C), 44.2 (CH_2), 32.1 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.7 (s, 3F); HRMS (ESI) *m/z*: 405.0099/407.0078 $(M+H)^+$98.8/100.0, $C_{20}H_{13}BrF_3O$ requires 405.0102/407.0081.

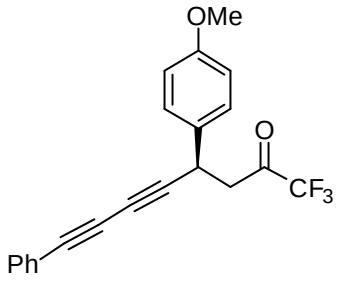
(*S*)-1,1,1-trifluoro-4-(2-methoxyphenyl)-8-phenylocta-5,7-diyn-2-one (3ga)



Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 95:05, 1 mL/min, major enantiomer t_r = 4.8 min, minor enantiomer t_r = 4.6 min.

$[\alpha]_D^{20}$ −23.5 (*c*1.01, $CHCl_3$) (94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.51-7.48 (m, 2H), 7.36-7.27 (m, 4H), 7.01 (td, J = 7.5, 1.1 Hz, 1H), 6.89 (dd, *J* = 8.3, 0.9 Hz, 1H), 4.75 (dd, *J* = 7.8, 5.7 Hz, 1H), 3.85 (s, 3H), 3.21 (dd, *J* = 6.6, 2.5 Hz,2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.5 (q, J_{C-F} = 35.6 Hz, C), 156.9 (C), 132.6 (2CH), 129.1 (CH), 129.1 (CH), 128.7 (CH), 128.4 (2CH), 126.1 (C), 121.7 (C), 121.0 (CH), 115.4 (q, J_{C-F} = 292.1 Hz, CF_3), 110.6 (CH), 82.4 (C), 76.6 (C), 73.8 (C), 68.1 (C), 55.4 (CH_3), 42.6 (CH_2), 27.4 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.7 (s, 3F); HRMS (ESI) *m/z*: 357.1107 $(M+H)^+$, $C_{21}H_{16}F_3O_2$ requires 357.1102.

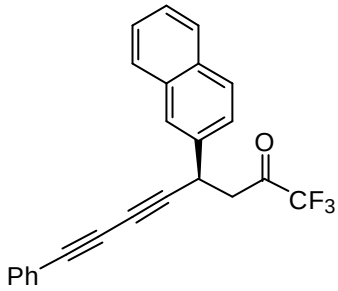
(*R*)-1,1,1-trifluoro-4-(4-methoxyphenyl)-8-phenylocta-5,7-diyn-2-one (3ha)



Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 9.6 min, minor enantiomer t_r = 8.3 min.

$[\alpha]_D^{20}$ –31.6 (*c* 0.70, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.36-7.26 (m, 5H), 6.92-6.87 (m, 2H), 4.38-4.31 (m, 1H), 3.80 (s, 3H), 3.33 (ddd, *J* = 18.6, 7.6, 0.5 Hz, 1H), 3.20-3.12 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.2 (q, $J_{C\text{-}F}$ = 36.4 Hz, C), 159.2 (C), 132.5 (2CH), 130.3 (C), 129.2 (CH), 128.5 (2CH), 128.4 (2CH), 121.5 (C), 115.2 (q, $J_{C\text{-}F}$ = 297.6 Hz, CF_3), 114.4 (2CH), 82.5 (C), 77.2 (C), 73.5 (C), 68.2 (C), 55.3 (CH_3), 44.5 (CH_2), 31.8 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.8 (s, 3F); HRMS (ESI) *m/z*: 357.1112 $(M+H)^+$, $C_{21}H_{16}F_3O_2$ requires 357.1102.

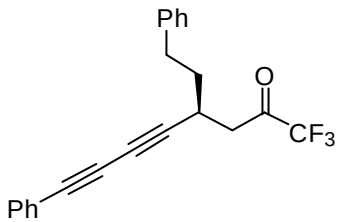
(*R*)-1,1,1-trifluoro-4-(naphthalene-2-yl)-8-phenylocta-5,7-diyn-2-one (3ia)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 8.3 min, minor enantiomer t_r = 7.3 min.

$[\alpha]_D^{20}$ –38.8 (*c* 1.00, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.83 (m, 4H), 7.54-7.48 (m, 5H), 7.37-7.29 (m, 3H), 4.59 (dd, *J* = 7.8, 6.2 Hz, 1H), 3.45 (dd, *J* = 18.4, 7.8 Hz, 1H), 3.29 (dd, *J* = 18.4, 6.2 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1 (q, $J_{C\text{-}F}$ = 36.4 Hz, C), 135.5 (C), 133.4 (C), 132.8 (C), 132.6 (2CH), 129.3 (CH), 129.1 (CH), 128.4 (2CH), 127.9 (CH), 127.7 (CH), 126.6 (CH), 126.4 (CH), 126.3 (CH), 125.0 (CH), 121.5 (C), 115.3 (q, $J_{C\text{-}F}$ = 291.9 Hz, CF_3), 82.1 (C), 77.4 (C), 73.5 (C), 68.7 (C), 44.3 (CH_2), 32.7 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.7 (s, 3F); HRMS (ESI) *m/z*: 377.1158 $(M+H)^+$, $C_{24}H_{16}F_3O$ requires 377.1153.

(*S*)-1,1,1-trifluoro-4-phenethyl-8-phenylocta-5,7-diyn-2-one (3ja)

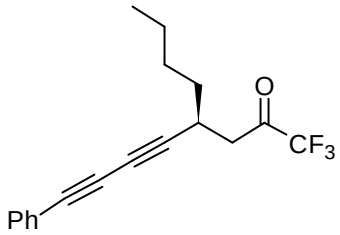


Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.1 min, minor enantiomer t_r = 4.8 min.

$[\alpha]_D^{20}$ –44.5 (*c* 0.44, $CHCl_3$) (84% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2H), 7.37-7.29 (m, 5H), 7.24-7.21 (m, 3H), 3.15-3.02 (m, 2H), 2.95-2.73 (m, 3H), 1.91-1.83 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.6 (q, $J_{C\text{-}F}$ = 36.1 Hz, C), 140.6 (C),

132.6 (2CH), 129.2 (CH), 128.6 (2CH), 128.5 (2CH), 128.4 (2CH), 126.3 (CH), 121.6 (C), 115.3 (q, J_{C-F} = 292.0 Hz, CF_3), 83.5 (C), 77.2 (C), 73.6 (C), 67.7 (C), 41.4 (CH_2), 35.8 (CH_2), 33.3 (CH), 26.5 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.8 (s, 3F); HRMS (ESI) *m/z*: 355.1329 $(M+H)^+$, $C_{22}H_{18}F_3O$ requires 355.1310.

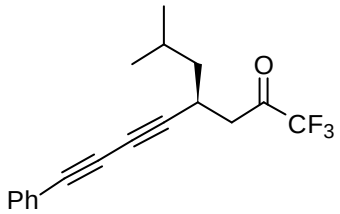
(*S*)-4-Butyl-1,1,1-trifluoro-8-phenylocta-5,7-diyn-2-one (3ka)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (87%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 14.0 min, minor enantiomer t_r = 9.5 min.

$[\alpha]_D^{20}$ −3.8 (*c* 0.63, $CHCl_3$) (87% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.46 (m, 2H), 7.36-7.28 (m, 3H), 3.15-3.00 (m, 2H), 2.88 (dd, *J* = 18.3, 6.0 Hz, 1H), 1.55-1.49 (m, 2H), 1.43-1.34 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (q, J_{C-F} = 35.8 Hz, C), 132.5 (2CH), 129.1 (CH), 128.4 (2CH), 121.7 (C), 115.4 (q, J_{C-F} = 291.9 Hz, CF_3), 84.2 (C), 76.3 (C), 73.7 (C), 67.0 (C), 41.5 (CH_2), 33.9 (CH_2), 29.2 (CH), 26.9 (CH_2), 22.3 (CH_2)13.9 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.8 (s, 3F); HRMS (ESI) *m/z*: 307.1312 $(M+H)^+$, $C_{18}H_{18}F_3O$ requires 307.1310.

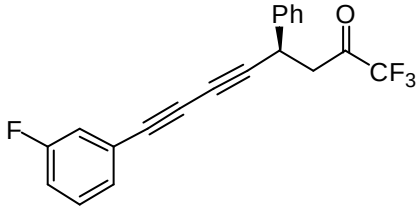
(*S*)-1,1,1-Trifluoro-4-isobutyl-8-phenylocta-5,7-diyn-2-one (3la)



Purified by flash chromatography eluting with hexane-ethyl acetate (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 = 10.9 min, minor enantiomer t_r = 9.1 min.

$[\alpha]_D^{20}$ −5.6 (*c* 0.51, $CHCl_3$) (88% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.46 (m, 2H), 7.36-7.28 (m, 3H), 3.15-3.00 (m, 2H), 2.88 (dd, *J* = 18.3, 6.0 Hz, 1H), 1.55-1.49 (m, 2H), 1.43-1.34 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.8 (q, J_{C-F} = 35.9 Hz, C), 132.5 (2CH), 129.1 (CH), 128.4 (2CH), 121.7 (C), 115.3 (q, J_{C-F} = 291.9 Hz, CF_3), 84.0 (C), 76.3 (C), 73.7 (C), 67.0 (C), 43.3 (CH_2), 41.9 (CH_2), 26.1 (CH), 25.2 (CH),23.2 (CH_3),21.2 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.8 (s, 3F); HRMS (ESI) *m/z*: 307.1317 $(M+H)^+$,$C_{18}H_{18}F_3O$ requires 307.1310.

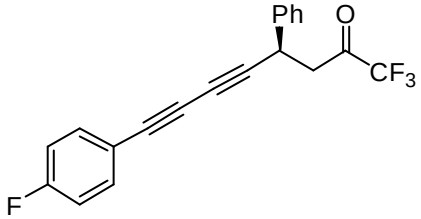
(*R*)-1,1,1-trifluoro-8-(3-fluorophenyl)-4-phenylocta-5,7-diyn-2-one (3ab)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (90%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.9 min, minor enantiomer t_r = 5.3 min.

$[\alpha]_D^{20}$ –15.7 (*c* 0.60, $CHCl_3$) (90% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.26 (m, 7H), 7.19-7.15 (m, 1H), 7.10-7.06 (m, 1H), 4.41 (dd, *J* = 7.9, 6.1 Hz, 1H), 3.37 (ddd, *J* = 18.7, 8.0, 0.5 Hz, 1H), 3.18 (dd, *J* = 18.7, 6.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.0 (q, *J* = 36.3 Hz, C), 162.2 (d, *J* = 247.3 Hz, C), 138.1 (C), 130.1 (d, *J* = 8.5 Hz, CH), 129.1 (2CH), 128.5 (d, *J* = 3.2 Hz, CH), 128.0 (CH), 127.4 (2CH), 123.4 (d, *J* = 9.5 Hz, C), 119.3 (d, *J* = 22.9 Hz, CH), 116.8 (d, $J_{C\text{-}F}$ = 21.3 Hz, CH), 115.3 (q, *J* = 291.7 Hz, CF_3), 82.9 (C), 77.5 (C), 75.8 (q, $J_{C\text{-}F}$ = 3.4 Hz, C), 68.1 (C), 44.4 (CH_2), 32.6 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.7 (s, 3F), –112.8 (s, 1F); HRMS (ESI) *m/z*: 345.0910 $(M+H)^+$, $C_{20}H_{13}F_4O$ requires 345.0903.

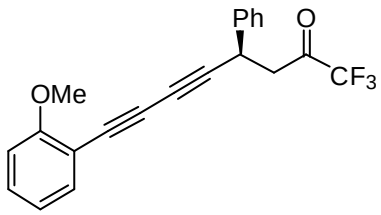
(*R*)-1,1,1-trifluoro-8-(4-fluorophenyl)-4-phenylocta-5,7-diyn-2-one (3ac)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 8.9 min, minor enantiomer t_r = 6.5 min.

$[\alpha]_D^{20}$ –14.5 (*c* 0.67, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.45 (m, 2H), 7.41-7.29 (m, 5H), 7.04-6.98 (m, 2H), 4.40 (dd, *J* = 8.0, 6.1 Hz, 1H), 3.36 (dd, *J* = 18.7, 8.0 Hz, 1H), 3.18 (dd, *J* = 18.7, 6.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.0 (q, $J_{C\text{-}F}$ = 36.4 Hz, C), 163.0 (d, $J_{C\text{-}F}$ = 251.6 Hz, C), 138.2 (C), 134.6 (d, $J_{C\text{-}F}$ = 8.5 Hz, 2CH), 129.1 (2CH), 128.0 (CH), 127.4 (2CH), 117.6 (d, *J* = 3.7 Hz, C), 115.9 (d, $J_{C\text{-}F}$ = 22.3 Hz, 2CH), 115.3 (q, $J_{C\text{-}F}$ = 291.8 Hz, CF_3), 82.2 (C), 76.2 (C), 73.3 (C), 68.3 (C), 44.4 (CH_2), 32.6 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.8 (s, 3F), –109.0 (s, 1F); HRMS (ESI) *m/z*: 345.0913 $(M+H)^+$, $C_{20}H_{13}F_4O$ requires 345.0903.

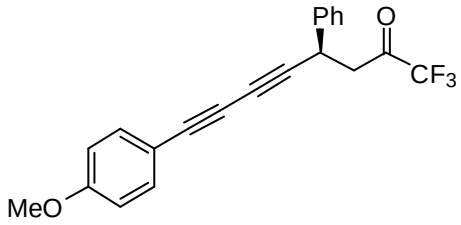
(*R*)-1,1,1-trifluoro-8-(2-methoxyphenyl)-4-phenylocta-5,7-diyn-2-one (3ad)



Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 95:05, 1 mL/min, major enantiomer t_r = 6.6 min, minor enantiomer t_r = 6.3 min.

$[\alpha]_D^{20}$ –17.0 (*c* 0.91, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.29 (m, 7H), 6.90 (td, *J* = 7.5, 1.0 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 4.41 (dd, *J* = 7.7, 6.3 Hz, 1H), 3.88 (s, 3H), 3.41-3.32 (m, 1H), 3.23-3.14 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.0 (q, $J_{C\text{-}F}$ = 36.3 Hz, C), 161.5 (C), 138.4 (C), 134.5 (CH), 130.7 (CH), 129.0 (2CH), 127.9 (CH), 127.4 (2CH), 120.5 (CH), 115.3 (q, $J_{C\text{-}F}$ = 291.8 Hz, CF_3), 110.7 (CH), 110.6 (CH), 82.7 (C), 77.3 (C), 73.8 (C), 68.7 (C), 55.8 (CH_3), 44.4 (CH_2), 32.6 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.7 (s, 3F); HRMS (ESI) *m/z*: 357.1109 $(M+H)^+$, $C_{21}H_{16}F_3O_2$ requires 357.1102.

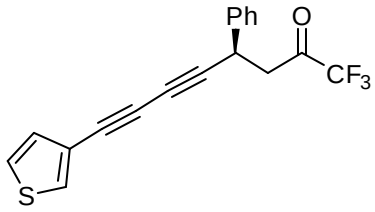
(*R*)-1,1,1-trifluoro-8-(4-methoxyphenyl)-4-phenylocta-5,7-diyn-2-one (3ae)



Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (91%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 80.20, 1 mL/min, major enantiomer t_r = 11.7 min, minor enantiomer t_r = 8.0 min.

$[\alpha]_D^{20}$ –32.7 (*c* 0.75, $CHCl_3$) (91% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.30 (m, 7H), 6.86-6.81 (m, 2H), 4.40 (dd, *J* = 7.9, 6.2 Hz, 1H), 3.81 (s, 3H), 3.36 (ddd, *J* = 18.6, 7.9, 0.5 Hz, 1H), 3.18 (ddd, *J* = 18.6, 6.2, 0.5 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1 (q, J_{C-F} = 36.7 Hz, C), 160.4 (C), 138.5 (C), 134.2 (2CH), 129.0 (2CH), 127.9 (CH), 127.4 (2CH), 115.3 (q, J_{C-F} = 291.6 Hz, CF_3), 114.1 (2CH), 113.4(C), 81.6 (C), 77.5 (C), 72.4 (C), 68.7 (C), 55.3 (CH_3), 44.5 (CH_2), 32.6 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.8 (s, 3F); HRMS (ESI) *m/z*: 357.1115 $(M+H)^+$, $C_{21}H_{16}F_3O_2$ requires 357.1102.

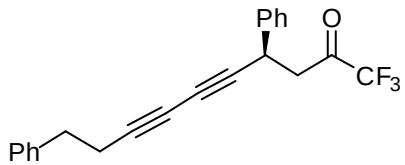
(*R*)-1,1,1-trifluoro-4-phenyl-8-(thiophen-3-yl)octa-5,7-diyn-2-one (3af)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 8.4 min, minor enantiomer t_r = 7.1 min.

$[\alpha]_D^{20}$ –26.6 (*c* 0.86, $CHCl_3$) (94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.41-7.25 (m, 5H), 7.26 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.13 (dd, J = 5.0, 1.2 Hz, 1H), 4.40 (dd, *J* = 7.9, 1.6 Hz, 1H), 3.36 (ddd, *J* = 18.6, 7.9, 0.5 Hz, 1H), 3.18 (ddd, *J* = 18.7, 6.1, 0.5 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.0 (q, *J* = 36.3 Hz, C), 138.3 (C), 131.4 (CH), 130.2 (CH), 129.1 (2CH), 127.9 (CH), 127.4 (2CH), 125.6 (CH), 120.6 (C), 115.3 (q, *J* = 291.7 Hz, CF_3), 82.0 (C), 73.2 (C), 72.5 (C), 68.4 (C), 44.4 (CH_2), 32.6 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.8 (s, 3F); HRMS (ESI) *m/z*: 333.0569 $(M+H)^+$, $C_{18}H_{12}F_3OS$ requires 333.0561.

(*R*)-1,1,1-trifluoro-4,10-diphenyldeca-5,7-diyn-2-one (3ag)

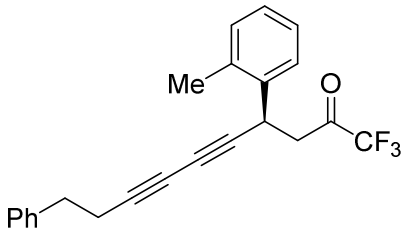


Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 6.4 min, minor enantiomer t_r = 5.7 min.

$[\alpha]_D^{20}$ –14.2 (*c* 0.90, $CHCl_3$) (93% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.19 (m, 10H), 4.31 (dd, *J* = 7.6, 6.5 Hz, 1H), 3.31 (ddd, *J* = 18.6, 7.9, 0.5 Hz, 1H), 3.13 (ddd, *J* = 18.6, 6.2, 0.4 Hz, 1H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.57 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR

(75.5 MHz, $CDCl_3$) δ 188.1 (q, $J_{C\text{-}F}$ = 36.3 Hz, C), 140.0 (C), 138.5 (C), 129.0 (2CH), 128.5 (2CH), 128.3 (2CH), 127.8 (CH), 127.3 (2CH), 126.5 (CH), 115.2 (q, $J_{C\text{-}F}$ = 291.6 Hz, CF_3), 79.3 (C), 75.6 (C), 68.7 (C), 65.3 (C), 44.5 (CH_2), 34.5 (CH_2), 32.3 (CH), 21.4 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.8 (s, 3F); HRMS (ESI) *m/z*: 355.1317 $(M+H)^+$, $C_{22}H_{18}F_3O$ requires 355.1310.

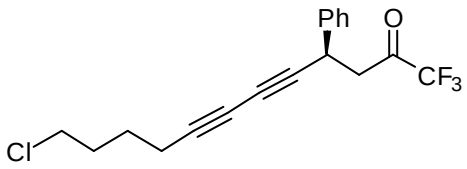
(*S*)-1,1,1-trifluoro-10-phenyl-4-(*o*-tolyl)deca-5,7-diyn-2-one (3bg)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (95%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.4 min, minor enantiomer t_r = 5.1 min.

$[\alpha]_D^{20}$ –6.1 (*c* 1.15, $CHCl_3$) (95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.41 (m, 1H), 7.33-7.17 (m, 8H), 4.49 (dd, *J* = 8.7, 5.4 Hz, 1H), 3.30 (dd, *J* = 18.5, 8.7 Hz, 1H), 3.09 (dd, *J* = 18.5, 5.4 Hz, 1H), 2.84 (t, *J* = 7.5 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.3 (q, $J_{C\text{-}F}$ = 36.5 Hz, C), 140.0 (C), 136.6 (C), 135.0 (C),131.0 (CH), 128.5 (2CH), 128.3 (2CH), 127.8 (CH), 127.1 (CH), 126.8 (CH), 126.5 (CH), 115.3 (q, $J_{C\text{-}F}$ = 291.9 Hz, CF_3), 79.0 (C), 75.8 (C), 68.1 (C), 65.4 (C), 43.0 (CH_2), 34.5 (CH_2), 28.7 (CH), 21.4 (CH_2), 19.2 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ –79.7 (s, 3F); HRMS (ESI) *m/z*: 369.1470 $(M+H)^+$, $C_{23}H_{20}F_3O$ requires 369.1466.

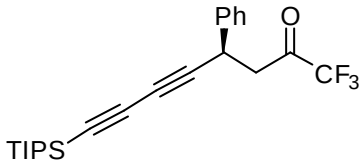
(*R*)-12-chloro-1,1,1-trifluoro-4-phenyldodeca-5,7-diyn-2-one (3ah)



Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 7.5 min, minor enantiomer t_r = 6.6 min.

$[\alpha]_D^{20}$ −11.7 (*c* 0.89, $CHCl_3$) (93% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.26 (m, 5H), 4.30 (dd, *J* = 7.5, 6.5 Hz, 1H), 3.55 (t, *J* = 6.4 Hz, 2H), 3.30 (ddd, *J* = 18.6, 7.9, 0.5 Hz, 1H), 3.12 (ddd, *J* = 18.6, 6.9, 0.5 Hz, 1H), 2.33 (td, *J* = 6.9, 1.0 Hz, 1H), 1.94-1.84 (m, 2H), 1.74-1.64 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1 (q, $J_{C\text{-}F}$ = 36.2 Hz, C), 138.5 (C), 129.0 (2CH), 127.8 (CH), 127.3 (2CH), 115.2 (q, $J_{C\text{-}F}$ = 291.8 Hz, CF_3), 79.2 (C), 75.5 (C), 68.6 (C), 65.3 (C), 44.5 (CH_2), 44.3 (CH_2), 32.2 (CH), 31.4 (CH_2), 25.3 (CH_2), 18.5 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.8 (s, 3F); HRMS (ESI) *m/z*: 341.0930/343.0899 $(M+H)^+$ 100.0/31.7, $C_{18}H_{17}ClF_3O$ requires 341.0920/343.0891.

(*R*)-1,1,1-trifluoro-4-phenyl-8-(triisopropylsilyl)octa-5,7-diyn-2-one (3ai)

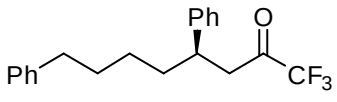


Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (85%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 8.6 min, minor enantiomer t_r = 6.1 min.

$[\alpha]_D^{20}$ −14.5 (*c* 0.77, $CHCl_3$) (85% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.29 (m, 5H), 4.33 (t, *J* = 6.0 Hz, 1H), 3.34 (ddd, *J* = 18.8, 7.5, 0.5 Hz, 1H), 3.16 (ddd, *J* = 18.8, 6.5, 0.5 Hz, 1H), 1.08 (s, 21H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.0 (q, $J_{C\text{-}F}$ = 36.3 Hz, C), 138.2 (C), 129.0 (2CH), 127.9 (CH), 127.4 (2CH), 115.2 (q, $J_{C\text{-}F}$ = 291.9 Hz, CF_3), 89.1 (C), 83.3 (C), 76.3 (C), 69.0 (C), 44.3 (CH_2), 32.2 (CH), 18.5 ($6CH_3$), 11.2 (3CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ −79.8 (s, 3F); HRMS (ESI) *m/z*: 407.2024 $(M+H)^+$, $C_{23}H_{30}F_3OSi$ requires 407.2018.

Synthetic transformations of compounds 3

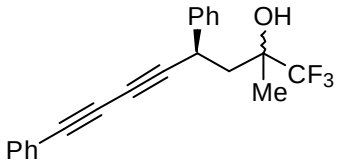
(*R*)-1,1,1-trifluoro-4,8-diphenyloctan-2-one (4)



A solution of compound **3aa** (10 mg, 0.031 mmol, 93% ee) in EtOAc (0.4 mL) was stirred under hydrogen atmosphere in the presence of 10% Pd/C (3 mg) for 30 min at room temperature. Then, the reaction mixture was filtered through a short pad of silica gel, which was washed with EtOAc, and the solvent was removed under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:EtOAc (99:01) gave compound **4** (9.2 mg, 89%). Enantiomeric excess (92%) was determined by chiral HPLC, Chiralcel OD-H, hexane-*i*PrOH 99:01, 1mL/min, major enantiomer t_r = 10.8 min, minor enantiomer t_r = 7.6 min.

$[\alpha]_D^{20}$ –2.3 (*c* 0.78, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.21 (m, 5H), 7.20-7.09 (m, 5H), 3.26-3.16 (m, 1H), 3.02-2.99 (m, 2H), 2.56-2.50 (m, 2H), 1.70-1.48 (m, 4H), 1.28-1.17 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 190.2 (q, J_{C-F} = 35.1 Hz, C), 143.0 (C), 142.4 (C), 128.7 (2CH), 128.3 (2CH), 128.3 (2CH), 127.3 (2CH), 126.8 (CH), 125.7 (CH), 115.4 (q, J_{C-F} = 292.2 Hz, CF_3), 43.5 (CH_2), 39.7 (CH), 35.9 (CH_2), 35.6 (CH_2), 31.2 (CH_2), 26.8 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ –80.0 (s, 3F); HRMS (ESI) *m/z*: 335.1631 $(M+H)^+$, $C_{20}H_{22}F_3O$ requires 335.1623.

(4*R*)-1,1,1-trifluoro-2-methyl-4,8-diphenylocta-5,7-diyn-2-ol (5)

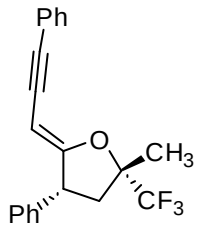


A commercial 3 M solution of MeMgCl in THF (77 μL, 0.230 mmol) was diluted with diethyl ether (0.3 mL) and cooled to 0 ºC under nitrogen. A solution of compound **3aa** (50 mg, 0.153 mmol) in dry diethyl ether (0.5 mL) was added dropwise via syringe and the reaction mixture was allowed to reach room temperature. After 2 h, the reaction was quenched with a solution of citric acid (1 mL). The aqueous layer was extracted with diethyl ether (3 x 15 mL) and the organic layer was dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash chromatography eluting with hexane:EtOAc (99:01) gave **5** (40.8 mg, 78%) as a ca. 4.5:1 mixture of two diastereomeric alcohols. Enantiomeric excess (91%) was determined by chiral HPLC, Chiralpak AY-H, hexane-*i*PrOH 99:01, 1 mL/min, *major diastereomer*: major enantiomer t_r = 23.2 min, minor enantiomer t_r = 16.1 min.

Major (1*S*,4*R*)-diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.45 (m, 2H), 7.39-7.31 (m, 8H), 4.04 (dd, *J* = 9.8, 4.9 Hz, 1H), 2.53 (s, OH), 2.38 (dd, *J* = 14.5, 9.8 Hz, 1H), 2.10 (dd, *J* = 14.5, 4.9 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 140.2 (C), 132.5 (2CH), 129.2 (CH), 129.1 (2CH), 128.4 (2CH), 127.6 (CH), 127.4 (2CH), 121.5 (C), 84.1 (C), 77.2 (C), 73.7 (q, J_{C-F} = 28.5 Hz, C), 73.5 (C), 69.1 (C), 42.6 (CH_2), 33.3 (CH), 20.3 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ –84.0 (s, 3F).

Minor (1*R*,4*R*)-diastereomer (representative peaks taken from the diastereomeric mixture): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (dd, *J* = 9.8, 4.3 Hz, 1H), 2.54 (s, 1H), 2.23-2-17 (m, 2H), 1.58 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ –83.1 (s, 3F).

(2*S*,4*R*,*Z*)-2-methyl-4-phenyl-5-(3-phenylpro-2-yn-1-ylidene)-2-(trifluoromethyl)tetrahydrofuran (6)



AgOTf (10.0 mg, 0.038 mmol) was added to a solution of the diastereomeric mixture of **5** (26 mg, 0.076 mmol) in THF (0.5 mL) at rt under nitrogen atmosphere and the mixtures was stirred overnight. Then, removal of the solvent under reduced pressure followed by flash chromatography eluting with hexane:EtOAc (99:01) allowed to obtain furan **6** as the major product (15.6 mg, 60%).Enantiomeric excess (92%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 99:01, 1 mL/min, major enantiomer t_r = 13.3 min, minor enantiomer t_r = 27.4 min. The cyclization product resulting from the minor diastereomer of **5** could not be obtained pure in sufficient amount.

$[\alpha]_D^{20}$ –5.9 (*c*1.00, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.25 (m, 10H), 4.30 (d, *J* = 2.2 Hz, 1H), 4.18 (ddd, *J* = 11.5, 9.3, 2.2 Hz, 1H), 2.50 (dd, *J* = 12.9, 11.5 Hz, 1H), 2.40 (dd, *J* = 12.9, 9.3 Hz, 1H), 1.63 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 168.5 (C), 138.5 (C), 131.3 (2CH), 129.0 (2CH), 128.5 (2CH), 128.1 (2CH), 127.8 (CH), 127.5 (CH), 125.2 (q, $J_{C\text{-}F}$ = 254.4 Hz, CF_3), 124.1 (C), 93.1 (C), 84.8 (C), 84.2 (C), 81.0 (CH), 47.3 (CH), 40.0 (CH_2), 20.3 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ –82.2 (s, 3F); HRMS (ESI) *m/z*: 343.1300 $(M+H)^+$, $C_{21}H_{18}F_3O$ requires 343.1310.

The stereochemistry of compound **6** was determined by NOESY experiments (See figure S1 and NOESY experiment in the NMR spectra section). A relevant interaction was observed between the CH_3 group at C2 (δ 1.63) and H4 (δ 4.18) which indicated the *trans* disposition between the Me group at C2 and the phenyl group at C4. NOE was also observed between one of the hydrogens of the phenyl group at C4 (δ7.30) and the olefinic hydrogen H1' (δ 4.30) which indicated the Z geometry of the exocyclic double bond. Other spatial interactions detected in the NOESY experiment are shown in figure S1.

The cyclization product resulting from the minor diastereomer of **5** could not be obtained pure in sufficient amount.

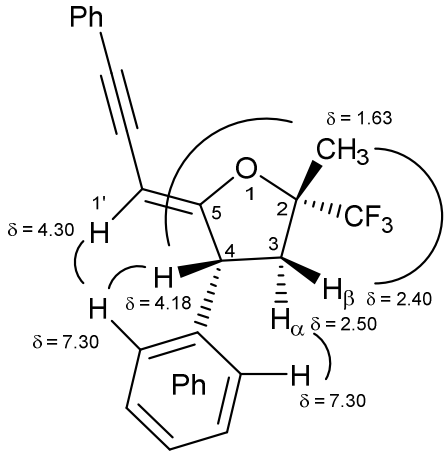
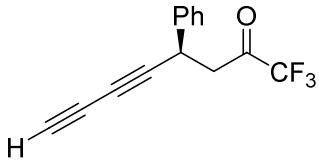


Figure S1. Interactions observed in NOESY experiment with compound **6**.

(*R*)-1,1,1-trifluoro-4-phenylocta-5,7-diyn-2-one (7)



AcOH (4 μL, 0.096 mmol) and 1M TBAF in THF (68 μL, 0.068 mmol) were added to a solution of **3aa** (35.4 mg, 0.087 mmol) in THF (1 mL) at 0 °C under N_2 atmosphere. After 4 h, the reaction was quenched with H_2O (1 mL). The aqueous layer was extracted with diethyl ether (3 x 15 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash chromatography eluting with hexane:EtOAc (99:01) gave **7** (15 mg, 70%). Enantiomeric excess (85%) was determined by GLC (Supelco β-dex-225, T_{column}= 100 °C (5 min) to 150 °C at 5 °C/min), major enantiomer t_r = 20.2 min, minor enantiomer t_r = 19.9 min.

$[\alpha]_D^{20}$ –6.0 (*c* 0.80, $CHCl_3$) (85%); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.30 (m, 5H), 4.31 (t, *J* = 7.0 Hz, 1H), 3.33 (dd, *J* = 18.7, 7.9 Hz, 1H), 3.15 (dd, *J* = 18.7, 6.2 Hz, 1H), 2.10 (d, *J* = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 187.9 (q, *J* = 36.1 Hz, C), 137.9 (C), 129.1 (2CH), 128.0 (CH), 127.3 (2CH), 115.2 (q, *J* = 291.6 Hz, CF_3), 76.1 (C), 68.0 (C), 67.6 (C), 67.1 (CH), 44.2 (CH_2), 32.1 (CH); ^{19}F NMR ($CDCl_3$, 282 MHz) δ –79.8 (s, 3F). HRMS (ESI) *m/z*: 250.0601 $(M+ H)^+$, $C_{14}H_9F_3O$ requires 250.0605.

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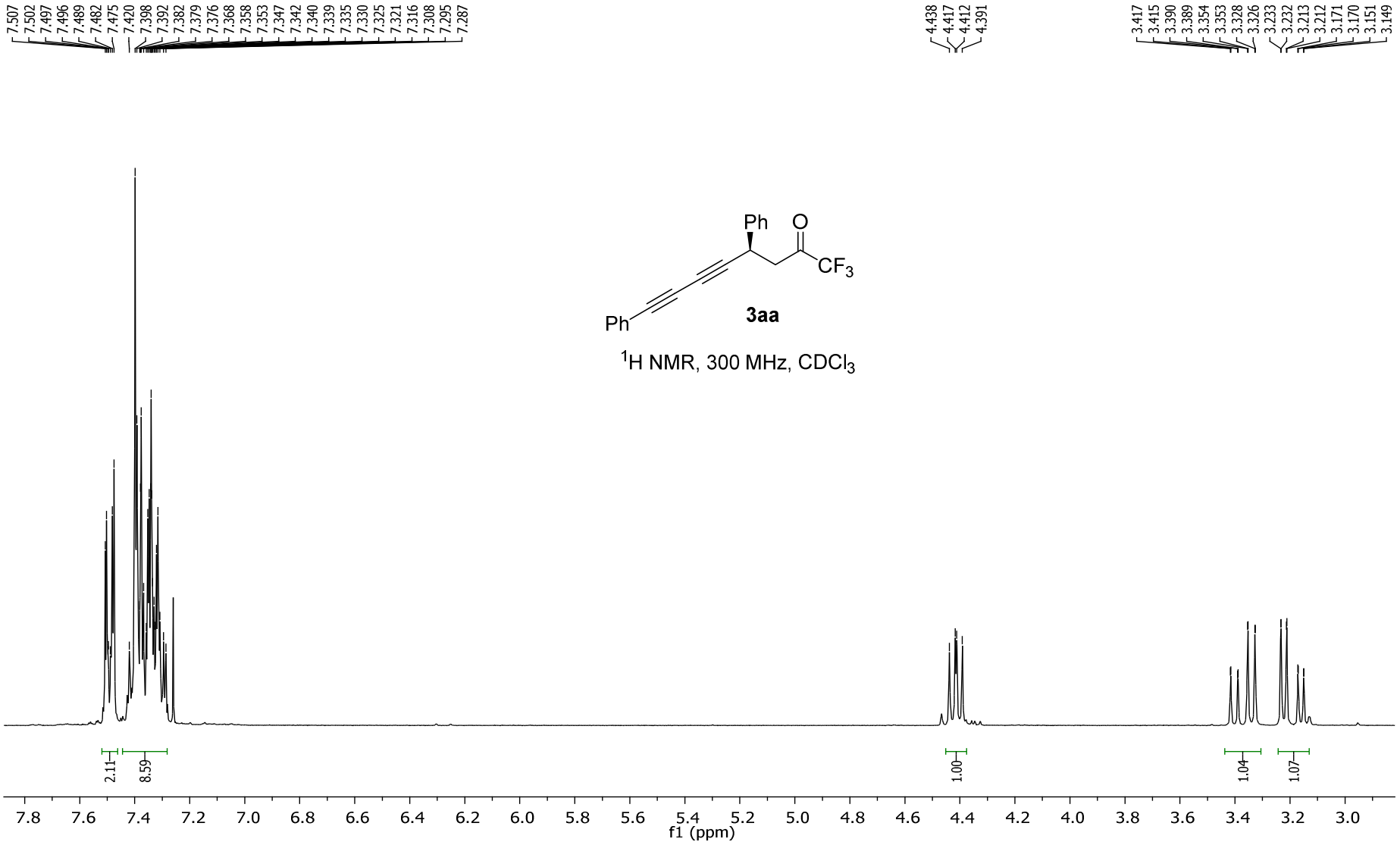
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3.170
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Ph
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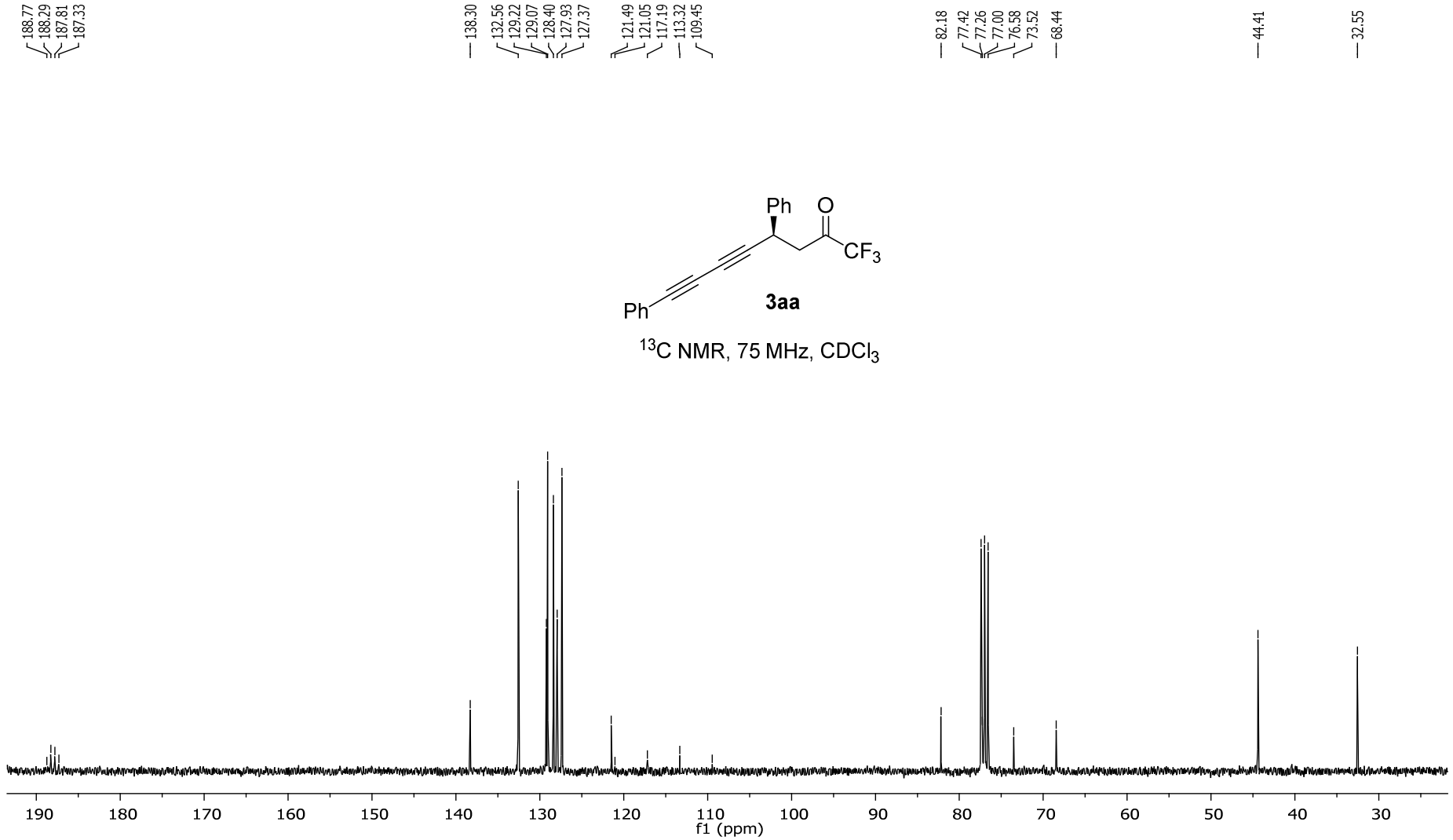
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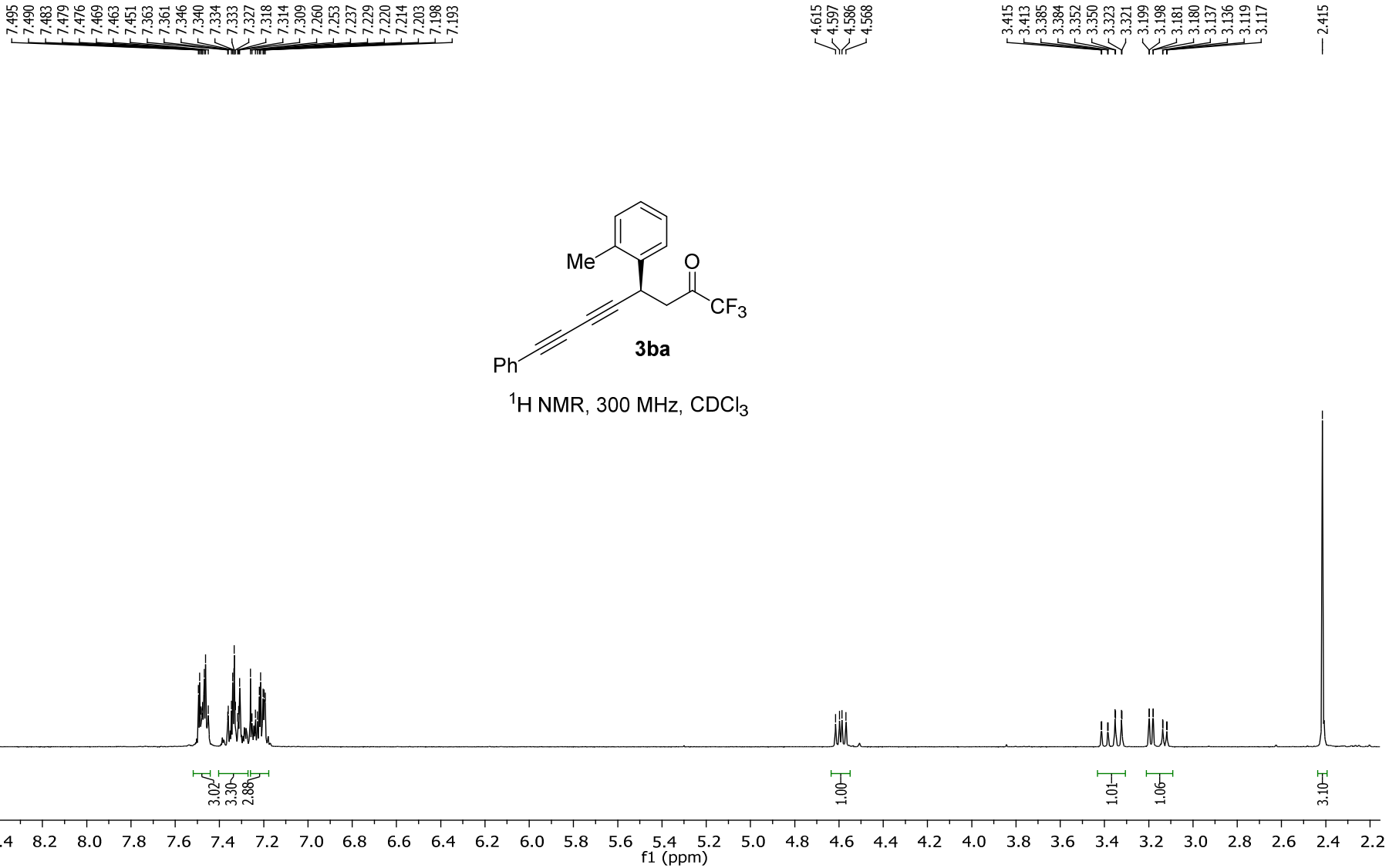
f1 (ppm)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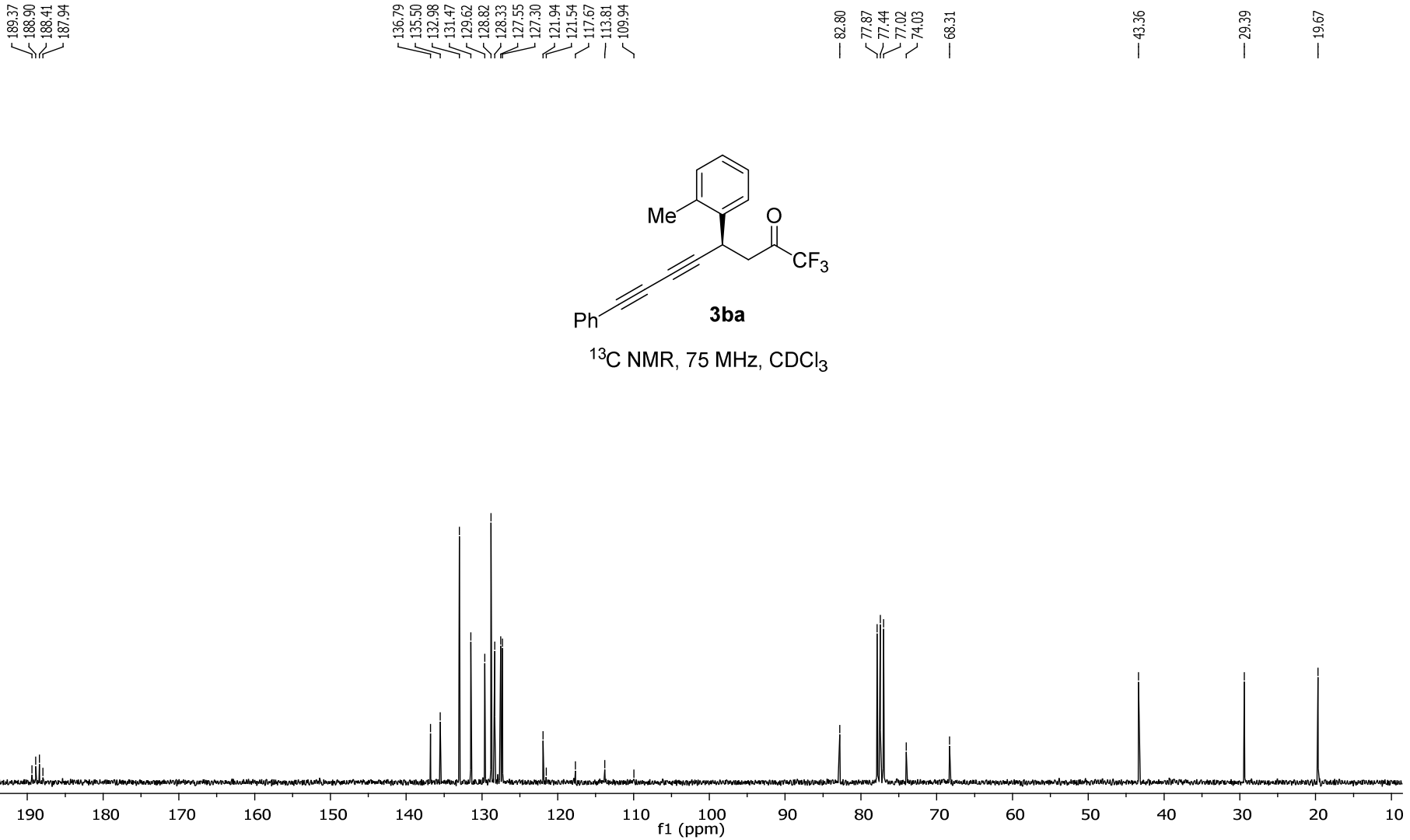
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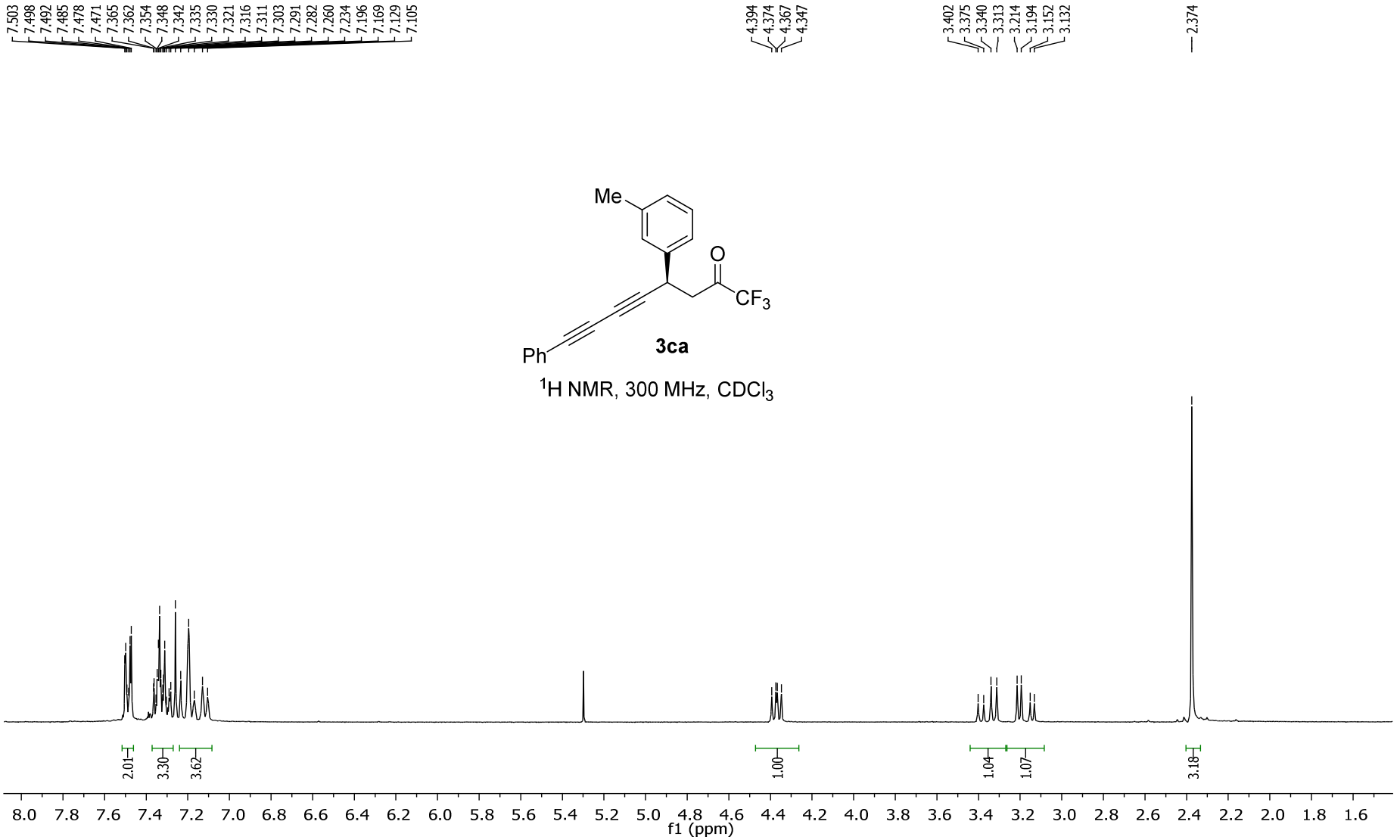
f1 (ppm)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1.07
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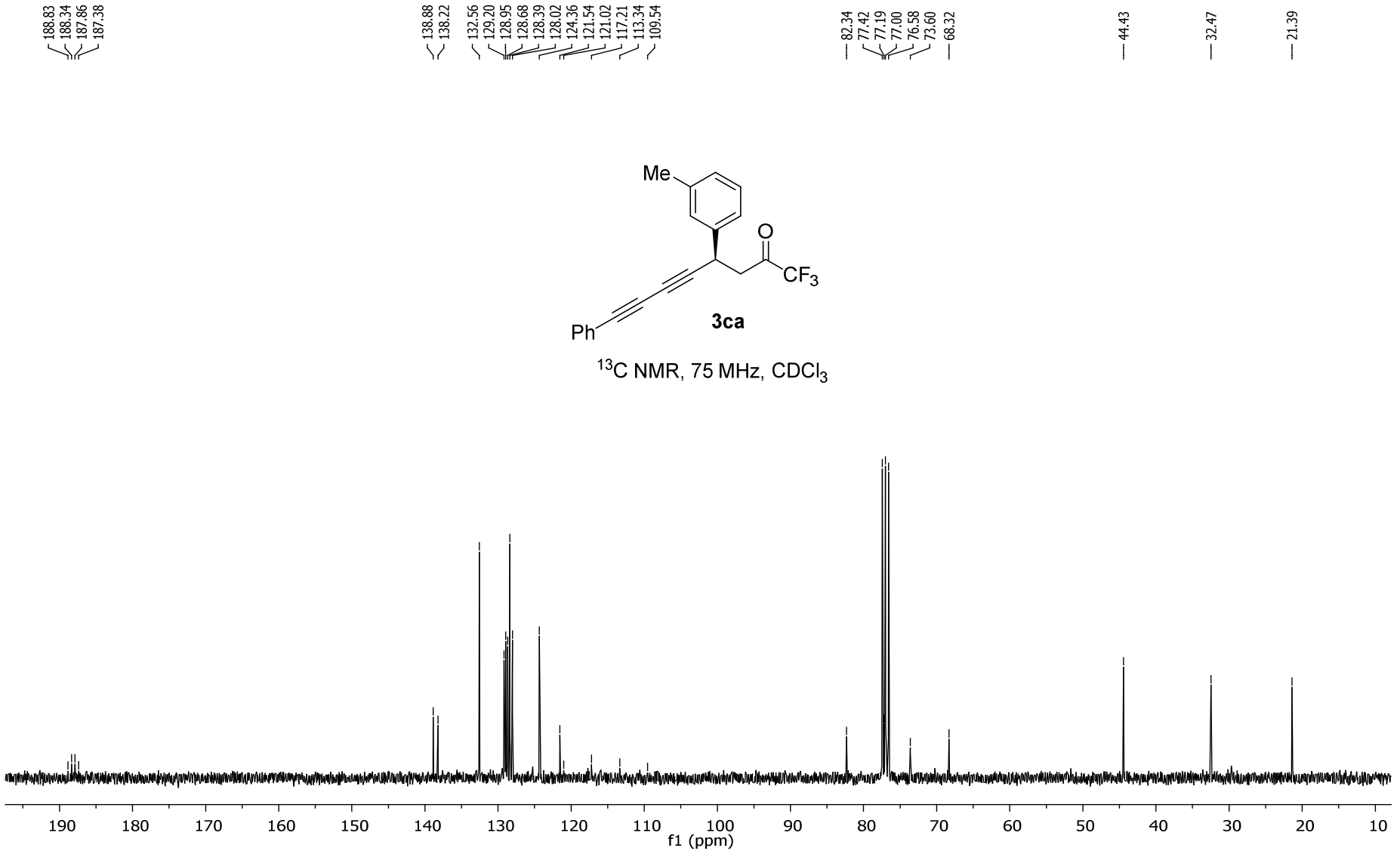
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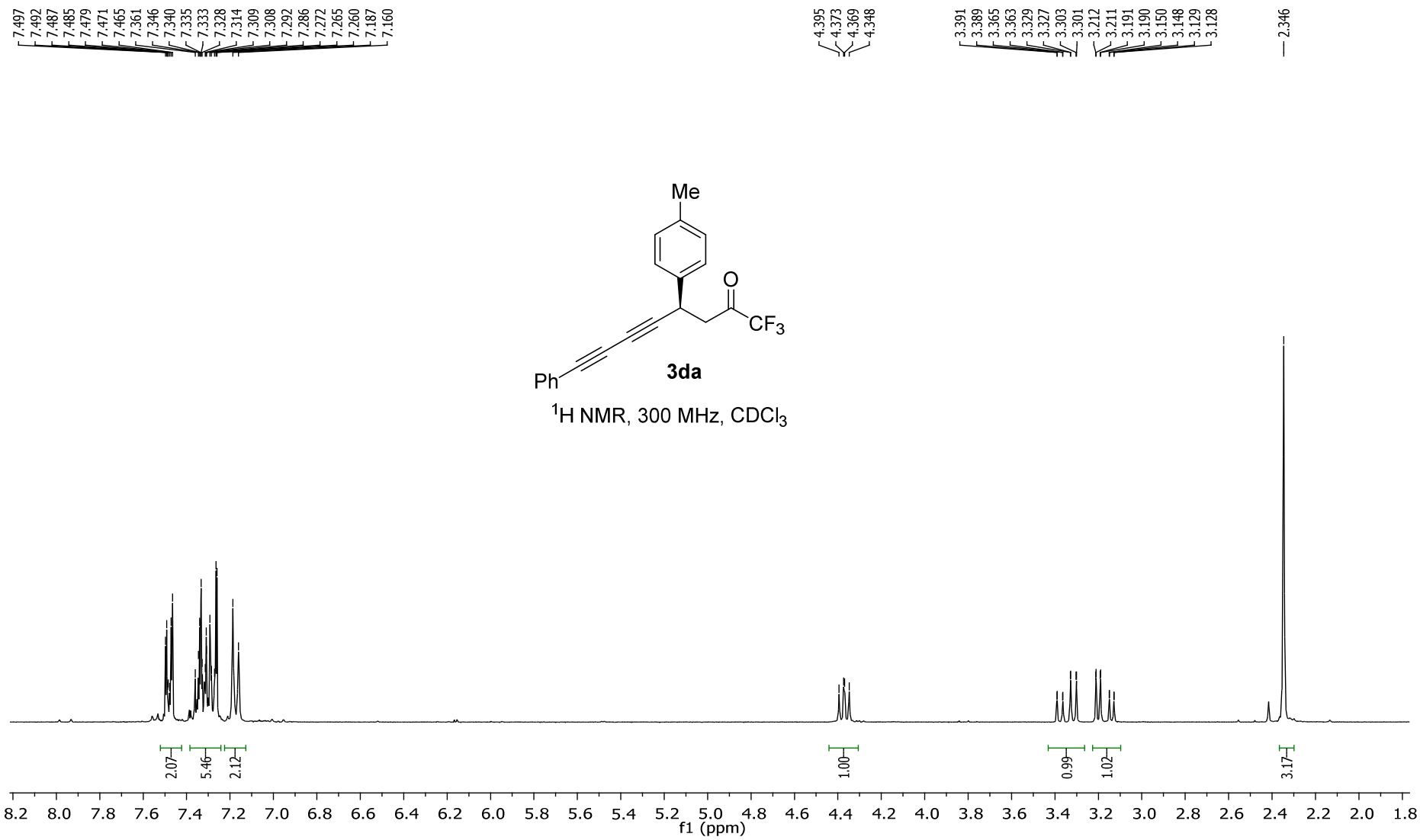
f1 (ppm)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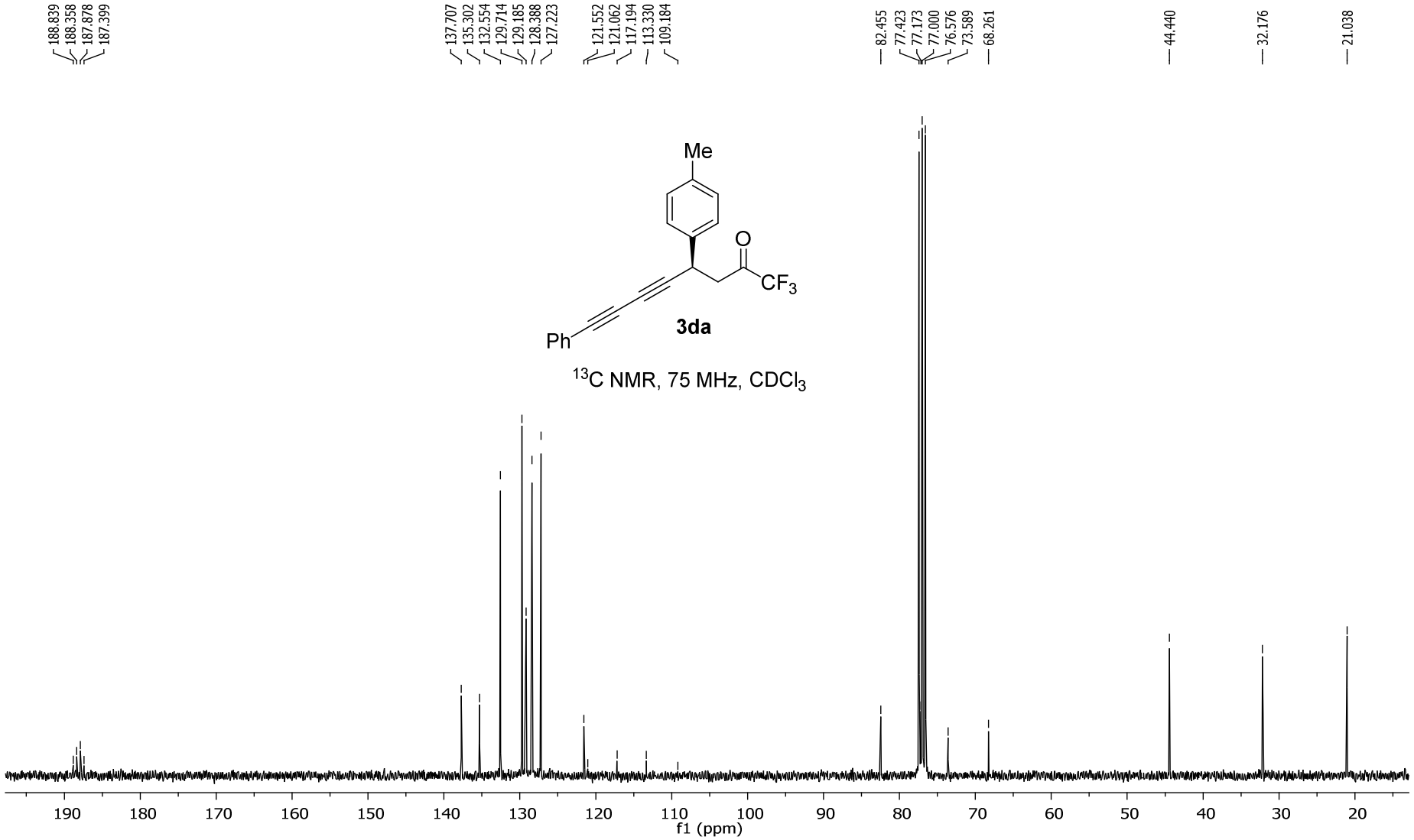
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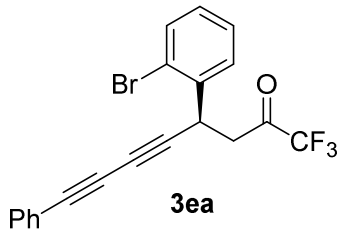
f1 (ppm)



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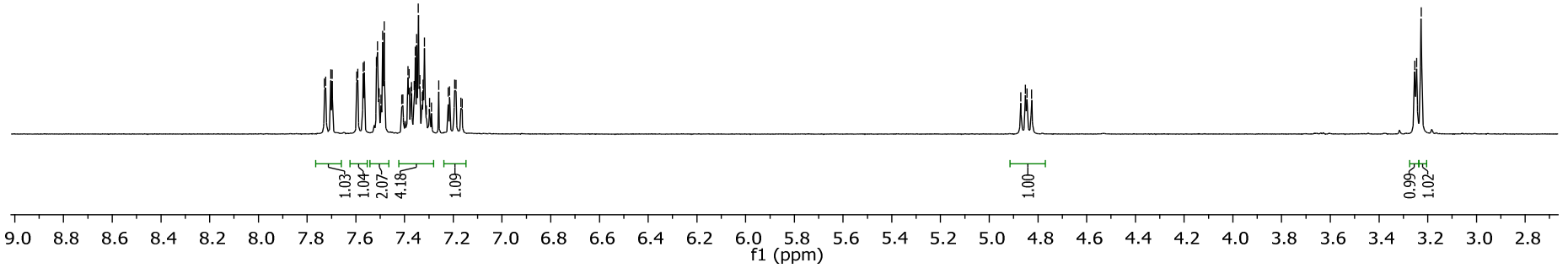

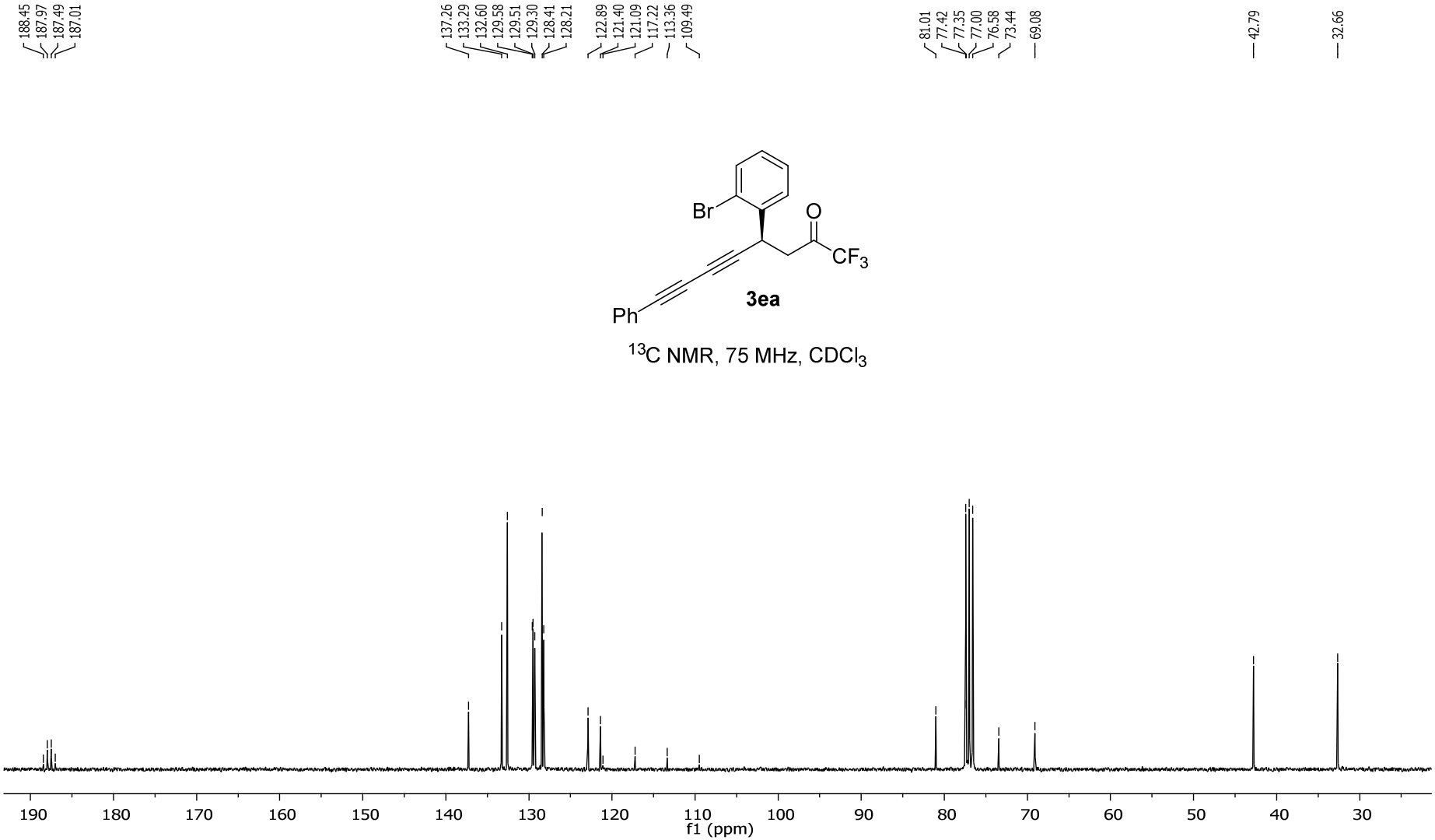
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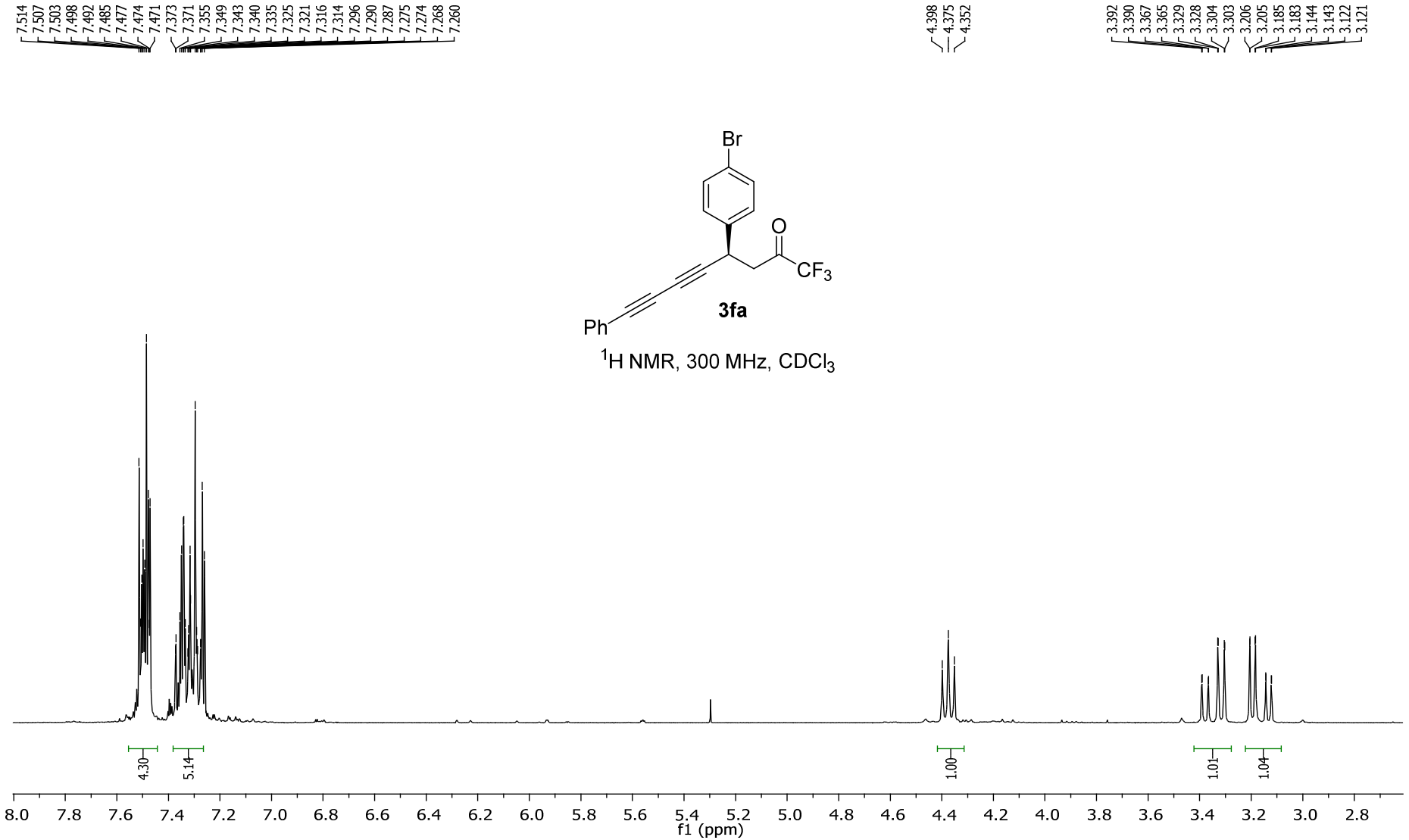
f1 (ppm)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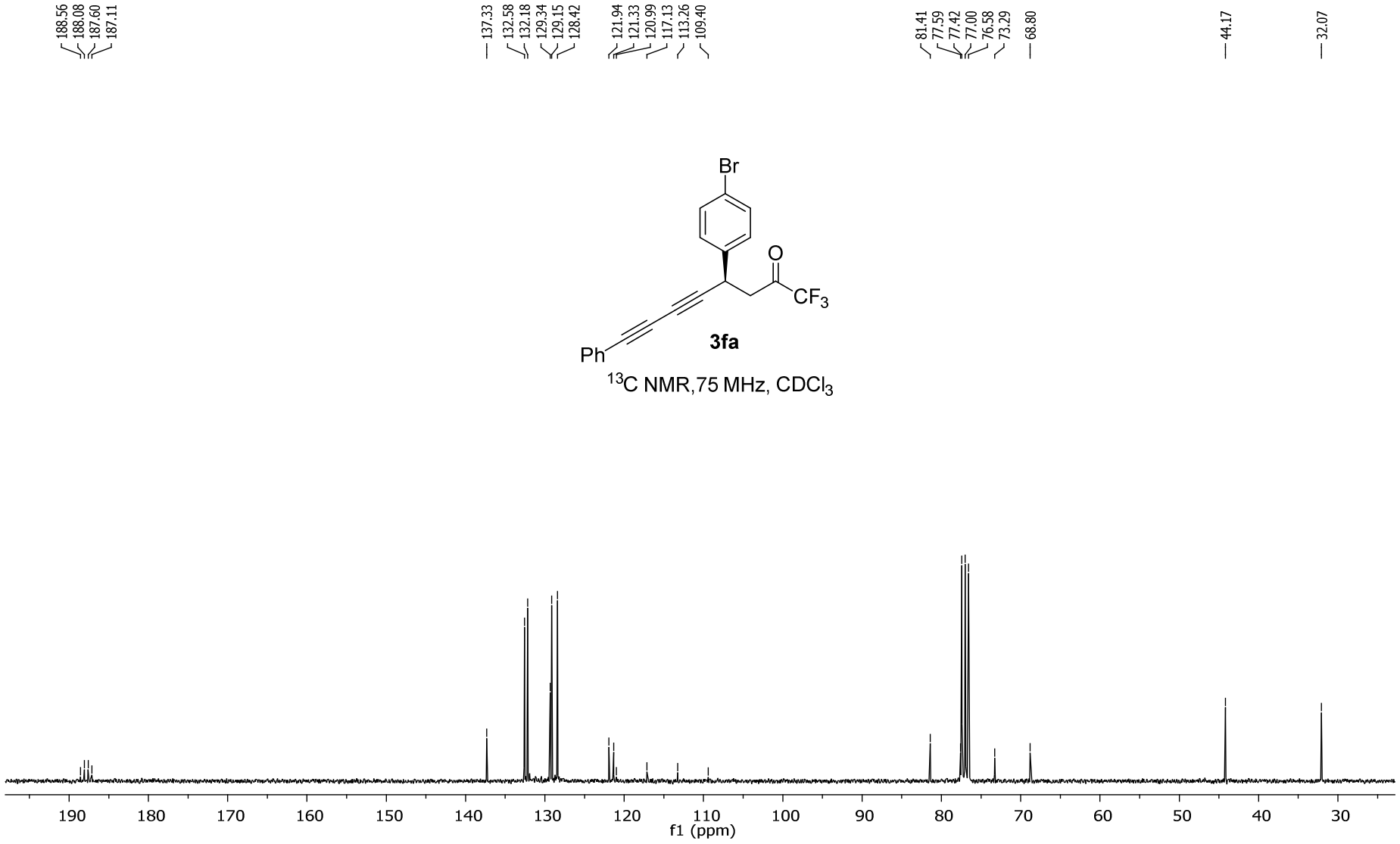
f1 (ppm)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32.07
Br
O
CF3
Ph
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13C NMR,75 MHz, CDCl3
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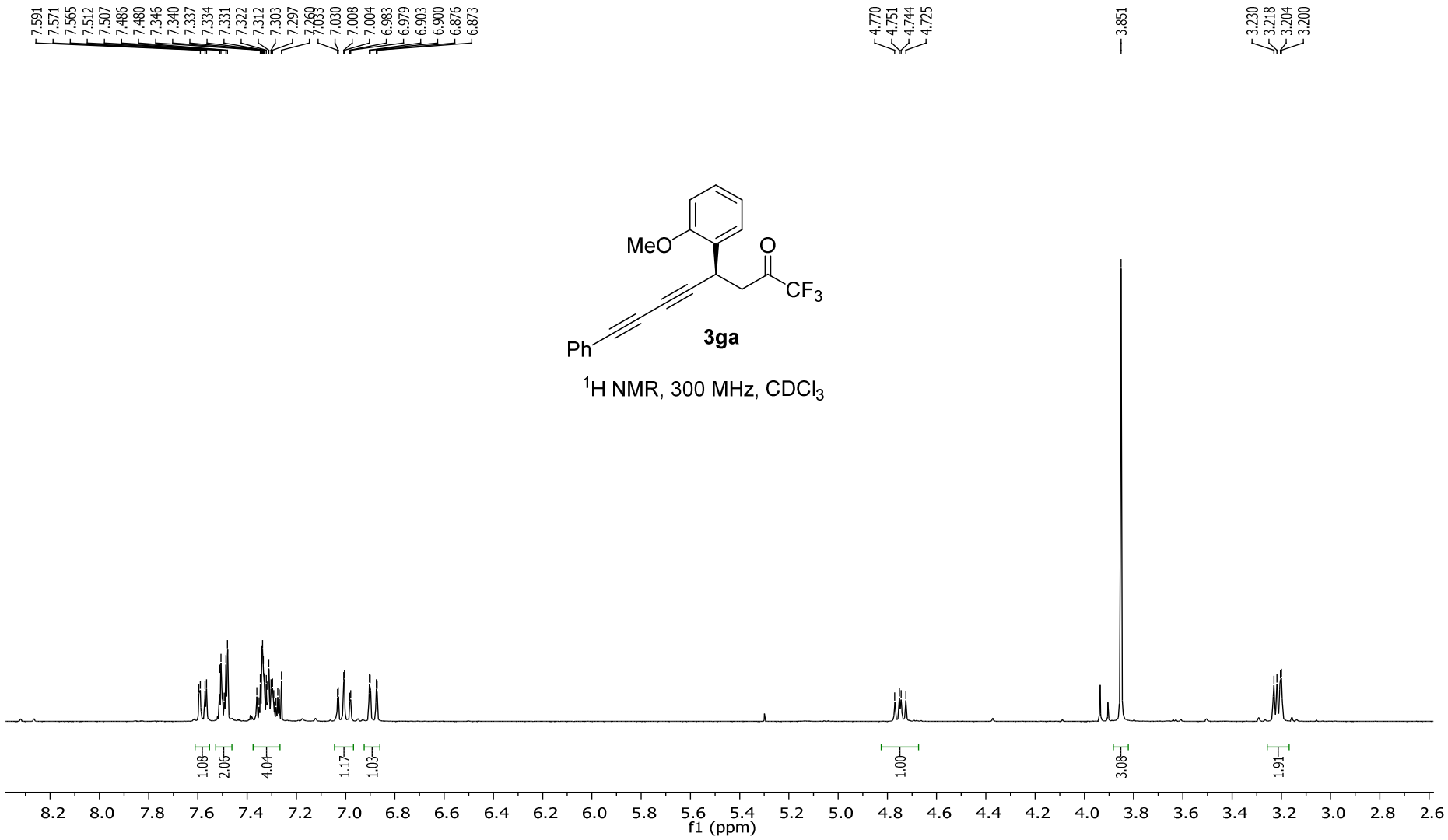
f1 (ppm)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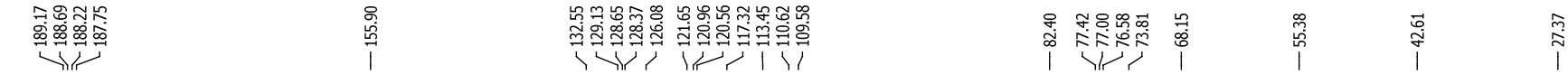
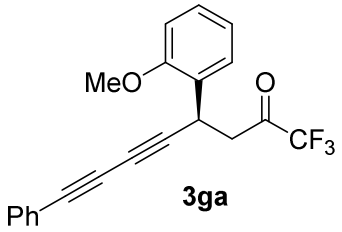
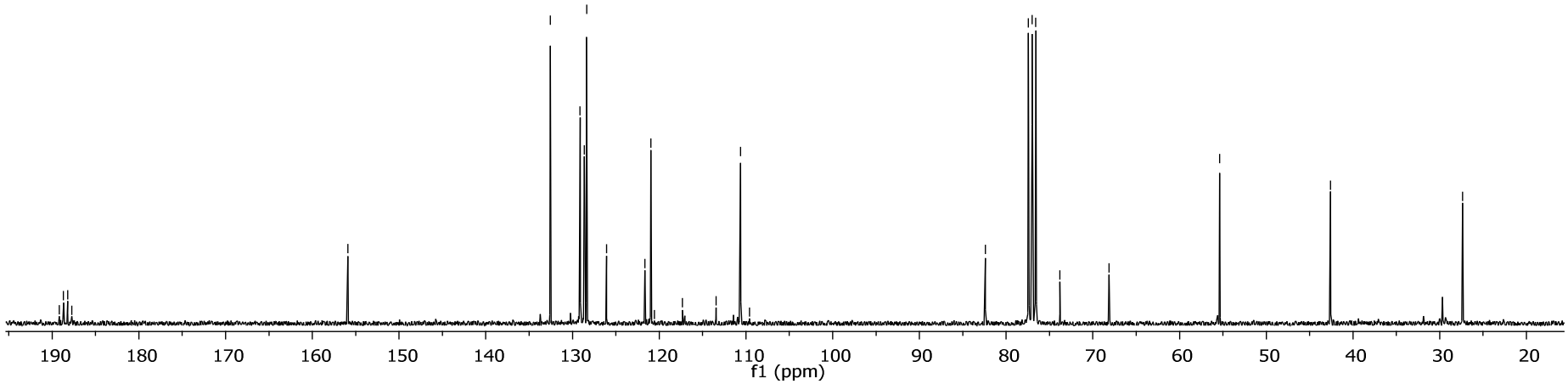
1.91
f1 (ppm)

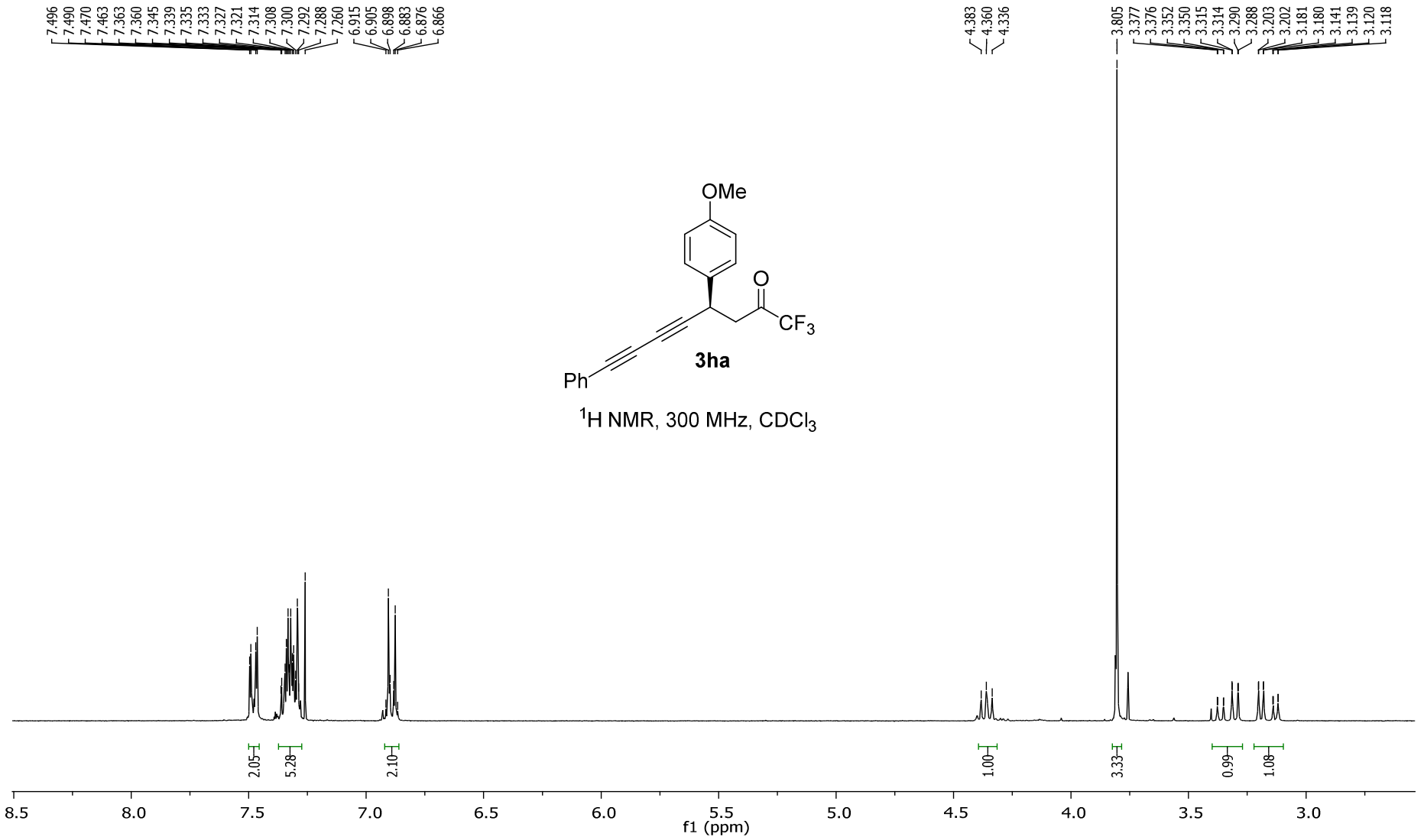




3ga

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

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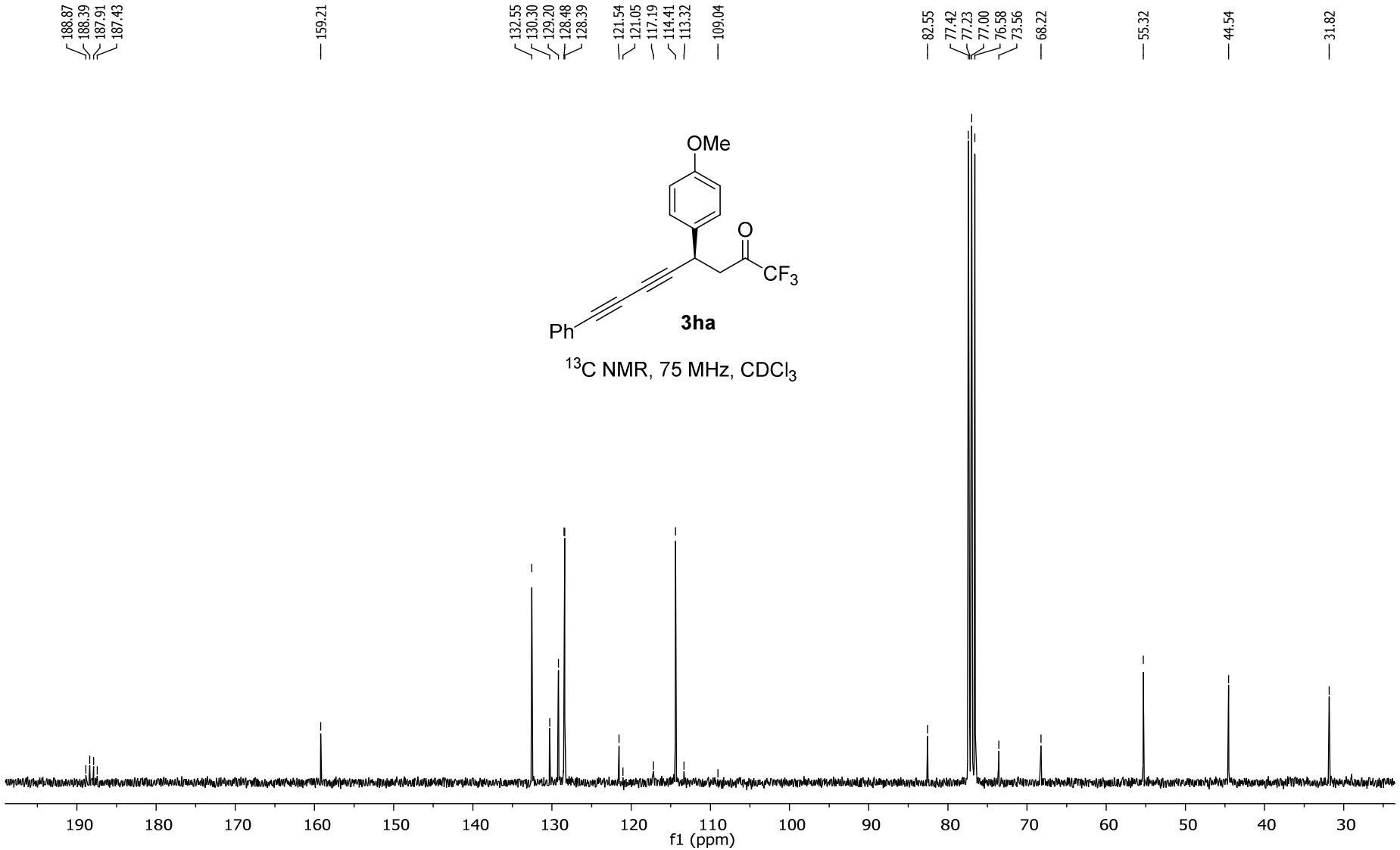
7.490
7.470
7.463
7.363
7.360
7.345
7.339
7.335
7.333
7.327
7.321
7.314
7.308
7.300
7.292
7.288
7.260
6.915
6.905
6.898
6.883
6.876
6.866
4.383
4.360
4.336
3.805
3.377
3.376
3.352
3.350
3.315
3.314
3.290
3.288
3.203
3.202
3.181
3.180
3.141
3.139
3.120
3.118
OMe
O
CF3
Ph
3ha
1H NMR, 300 MHz, CDCl3
2.05
5.28
2.10
1.00
3.33
0.99
1.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f1 (ppm)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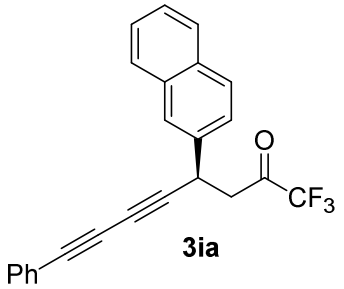
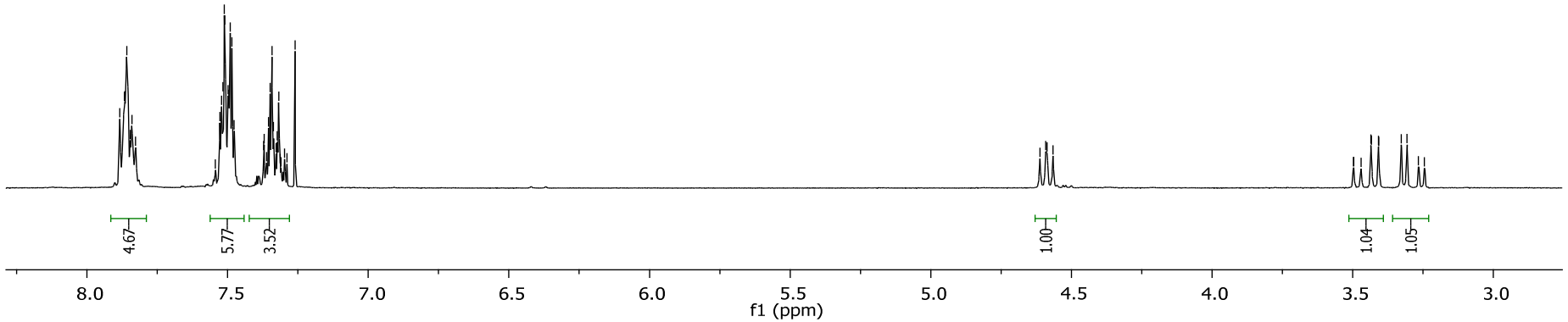
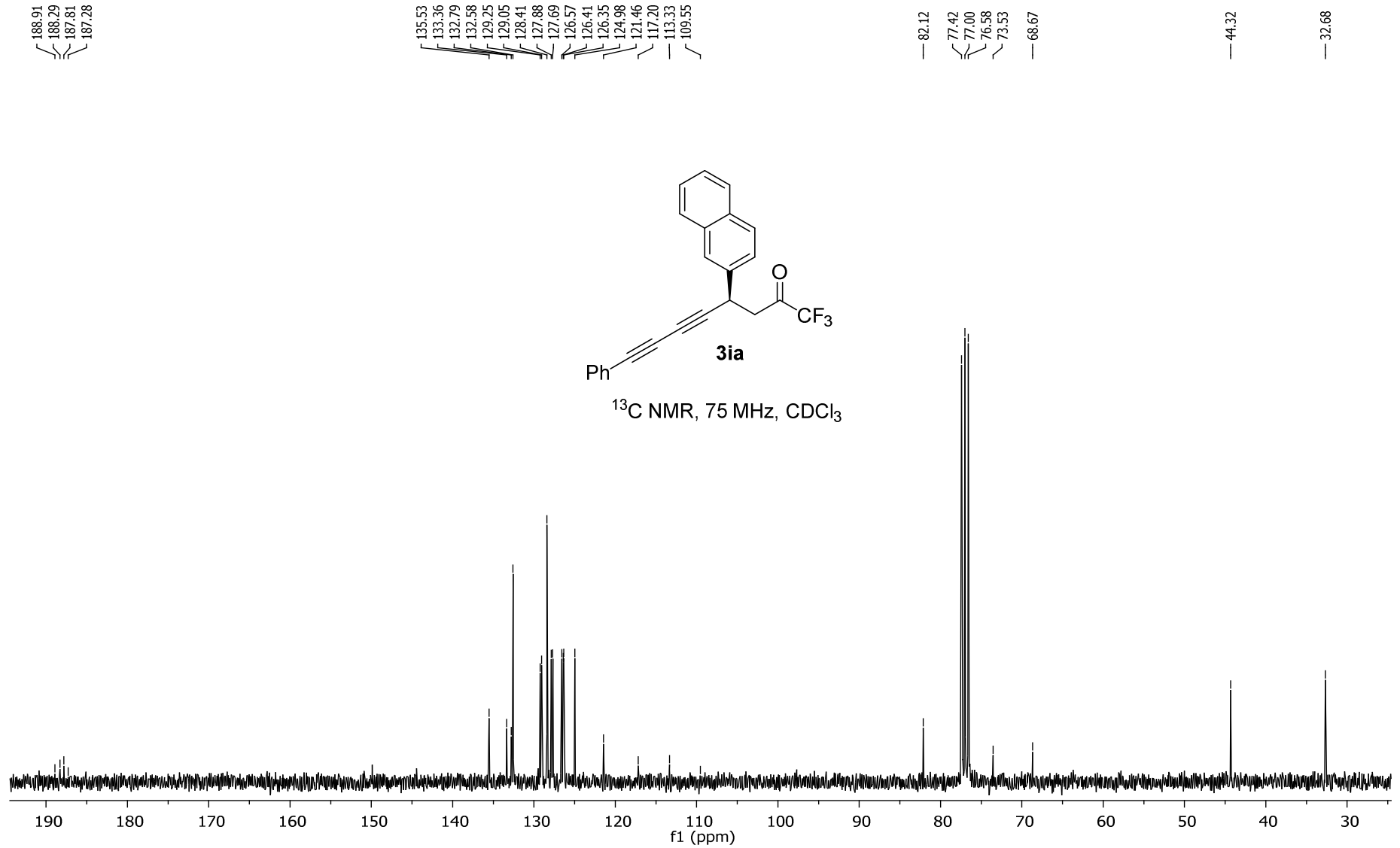
188.39
187.91
187.43
159.21
132.55
130.30
129.20
128.48
128.39
121.54
121.05
117.19
114.41
113.32
109.04
82.55
77.42
77.23
77.00
76.58
73.56
68.22
55.32
44.54
31.82
OMe
O
CF3
Ph
3ha
13C NMR, 75 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)



3ia

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

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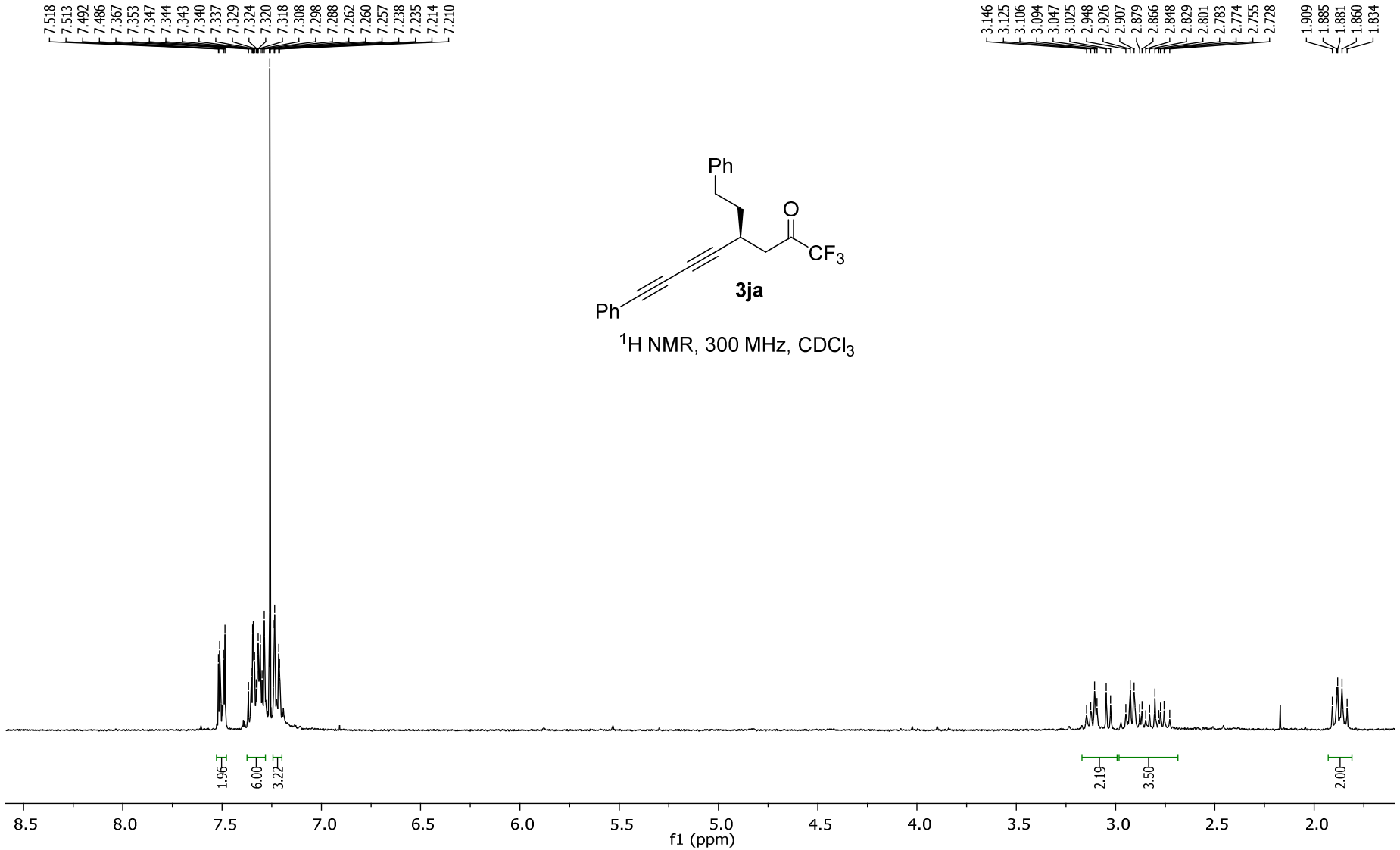
188.29
187.81
187.28
135.53
133.36
132.79
132.58
129.25
129.05
128.41
127.88
127.69
126.57
126.41
126.35
124.98
121.46
117.20
113.33
109.55
82.12
77.42
77.00
76.58
73.53
68.67
44.32
32.68
O
CF3
Ph
3ia
13C NMR, 75 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)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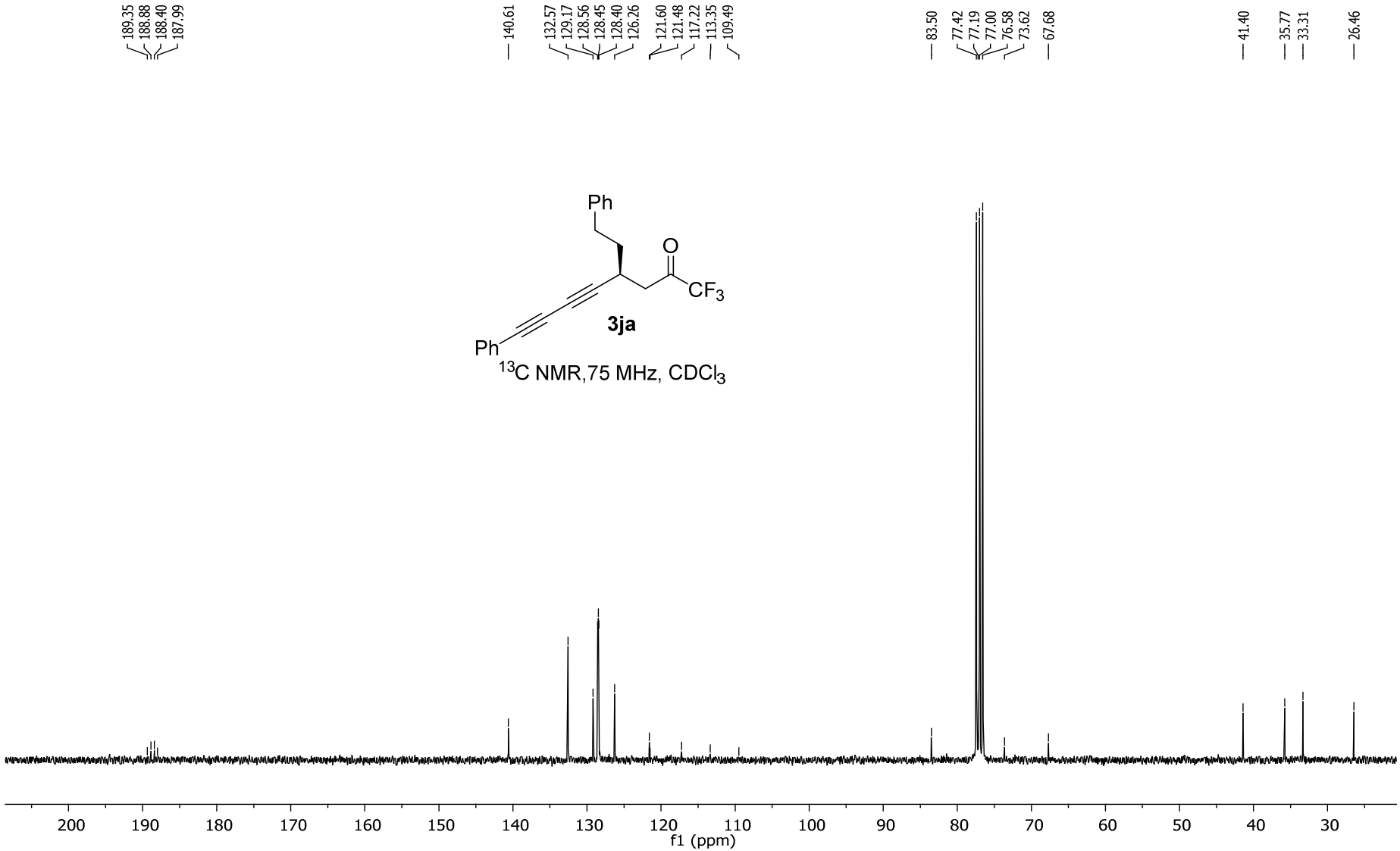
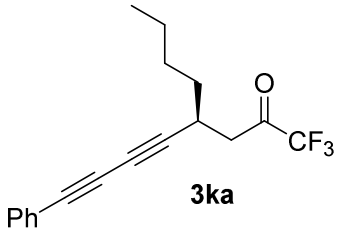
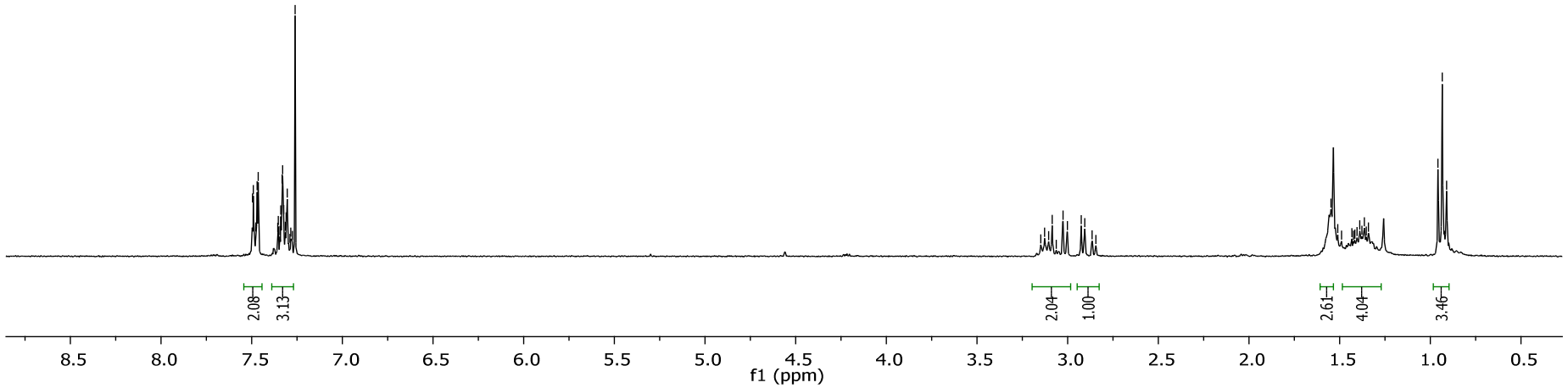
7.513
7.492
7.486
7.367
7.353
7.347
7.344
7.343
7.340
7.337
7.329
7.324
7.320
7.318
7.308
7.298
7.288
7.262
7.260
7.257
7.238
7.235
7.214
7.210
3.146
3.125
3.106
3.094
3.047
3.025
2.948
2.926
2.907
2.879
2.866
2.848
2.829
2.801
2.783
2.774
2.755
2.728
1.909
1.885
1.881
1.860
1.834
Ph
O
CF3
Ph
3ja
1H NMR, 300 MHz, CDCl3
1.96
6.00
3.22
2.19
3.50
2.00
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
f1 (ppm)

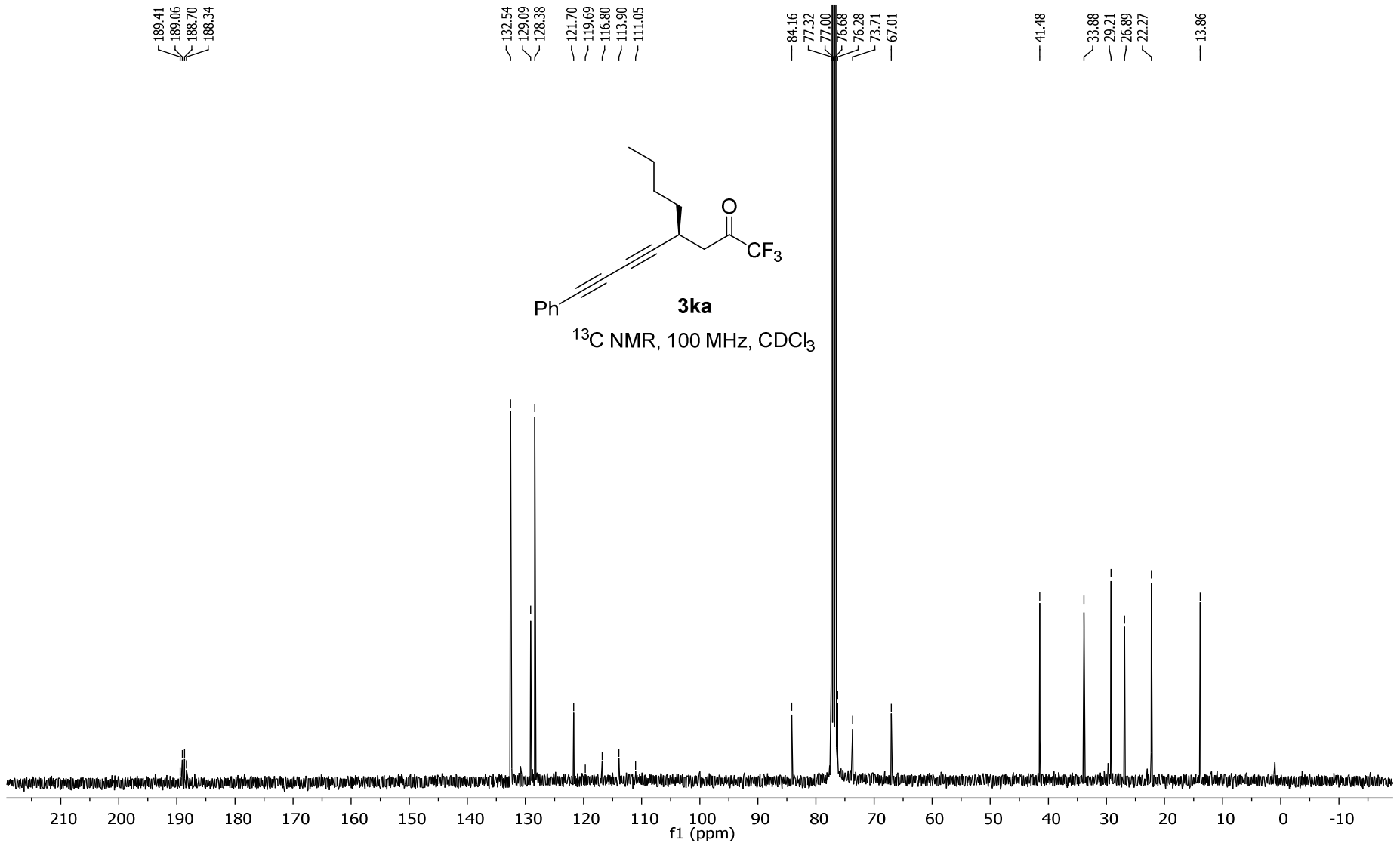

189.35
188.88
188.40
187.99
140.61
132.57
129.17
128.56
128.45
128.40
126.26
121.60
121.48
117.22
113.35
109.49
83.50
77.42
77.19
77.00
76.58
73.62
67.68
41.40
35.77
33.31
26.46
Ph
O
CF3
3ja
Ph
13C NMR,75 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)



3ka

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

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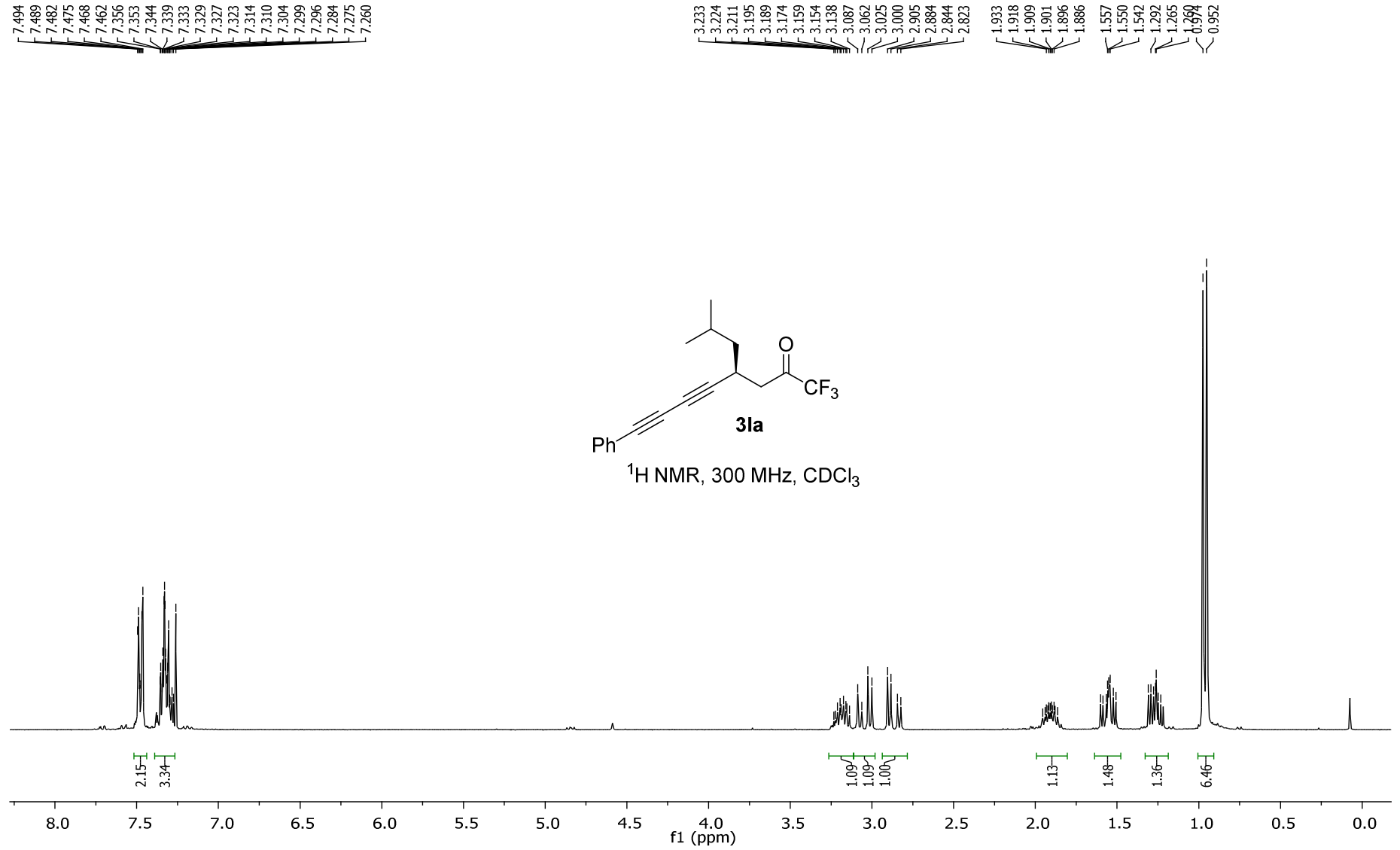
189.06
188.70
188.34
132.54
129.09
128.38
121.70
119.69
116.80
113.90
111.05
84.16
77.32
77.00
76.68
76.28
73.71
67.01
41.48
33.88
29.21
26.89
22.27
13.86
O
CF3
Ph
3ka
13C NMR, 100 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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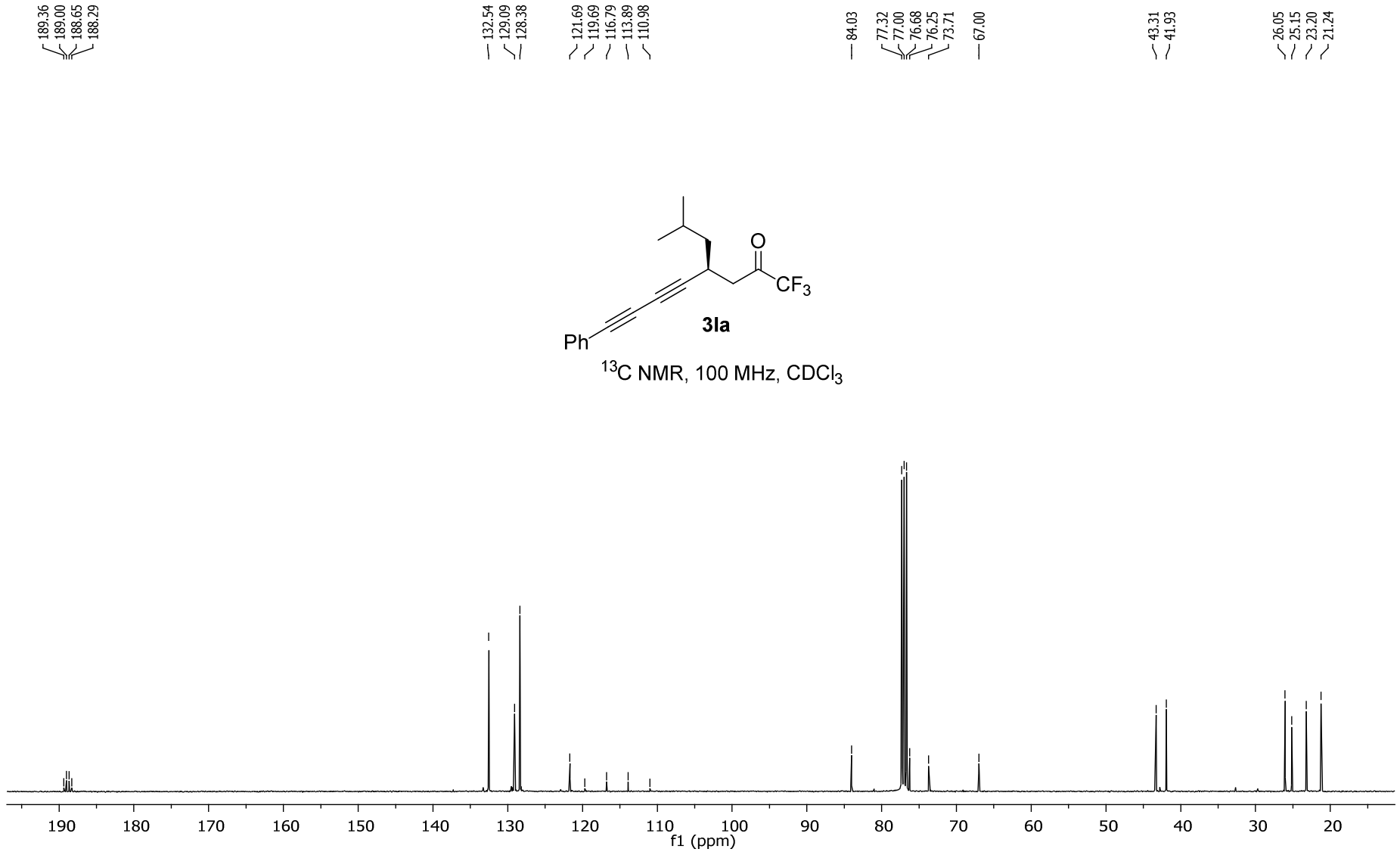
7.489
7.482
7.475
7.468
7.462
7.356
7.353
7.344
7.339
7.333
7.329
7.327
7.323
7.314
7.310
7.304
7.299
7.296
7.284
7.275
7.260
3.233
3.224
3.211
3.195
3.189
3.174
3.159
3.154
3.138
3.087
3.062
3.025
3.000
2.905
2.884
2.844
2.823
1.933
1.918
1.909
1.901
1.896
1.886
1.557
1.550
1.542
1.292
1.265
1.260
0.974
0.952
O
CF3
Ph
3la
1H NMR, 300 MHz, CDCl3
2.15
3.34
1.09
1.09
1.00
1.13
1.48
1.36
6.46
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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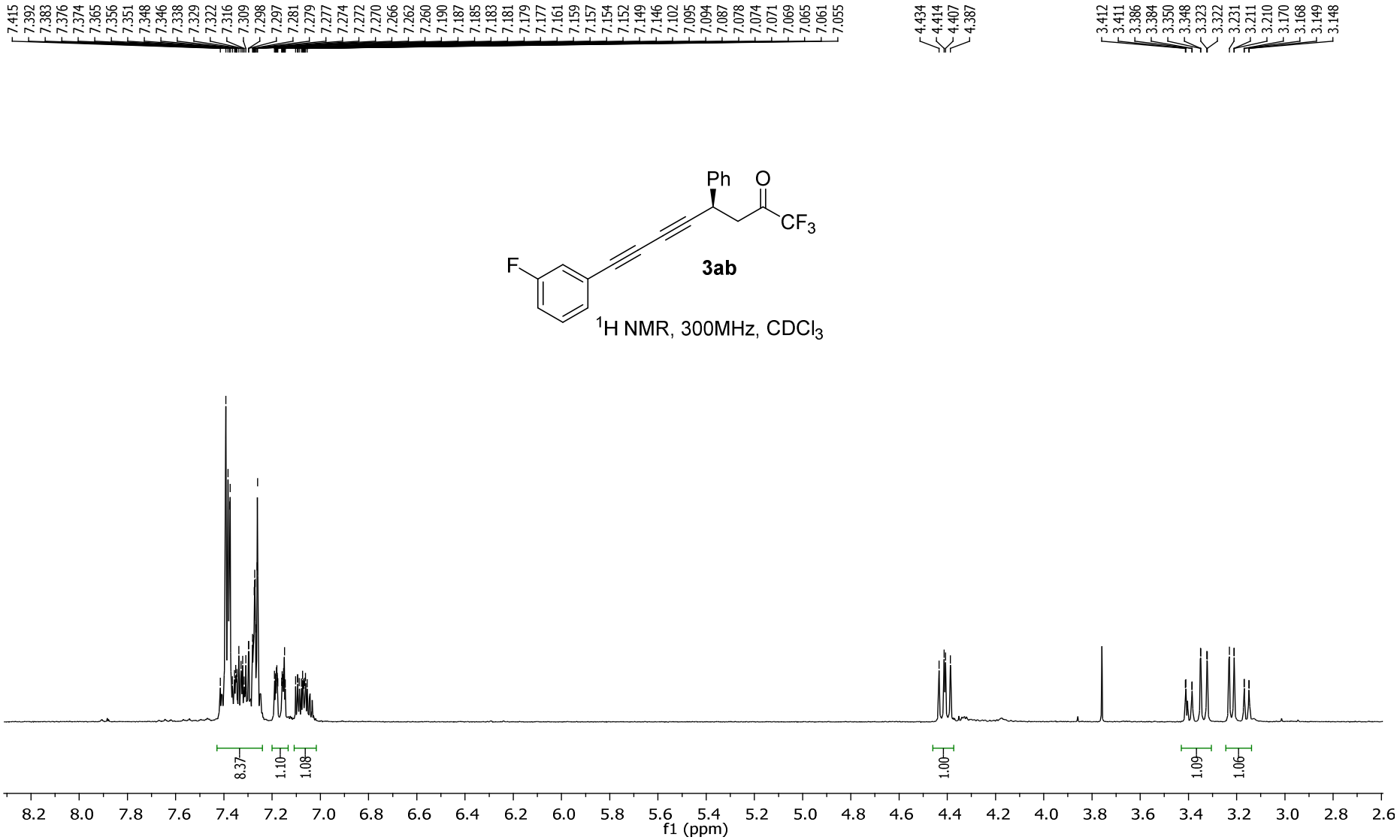
188.65
188.29
132.54
129.09
128.38
121.69
119.69
116.79
113.89
110.98
84.03
77.32
77.00
76.68
76.25
73.71
67.00
43.31
41.93
26.05
25.15
23.20
21.24
O
CF3
Ph
3la
13C NMR, 100 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)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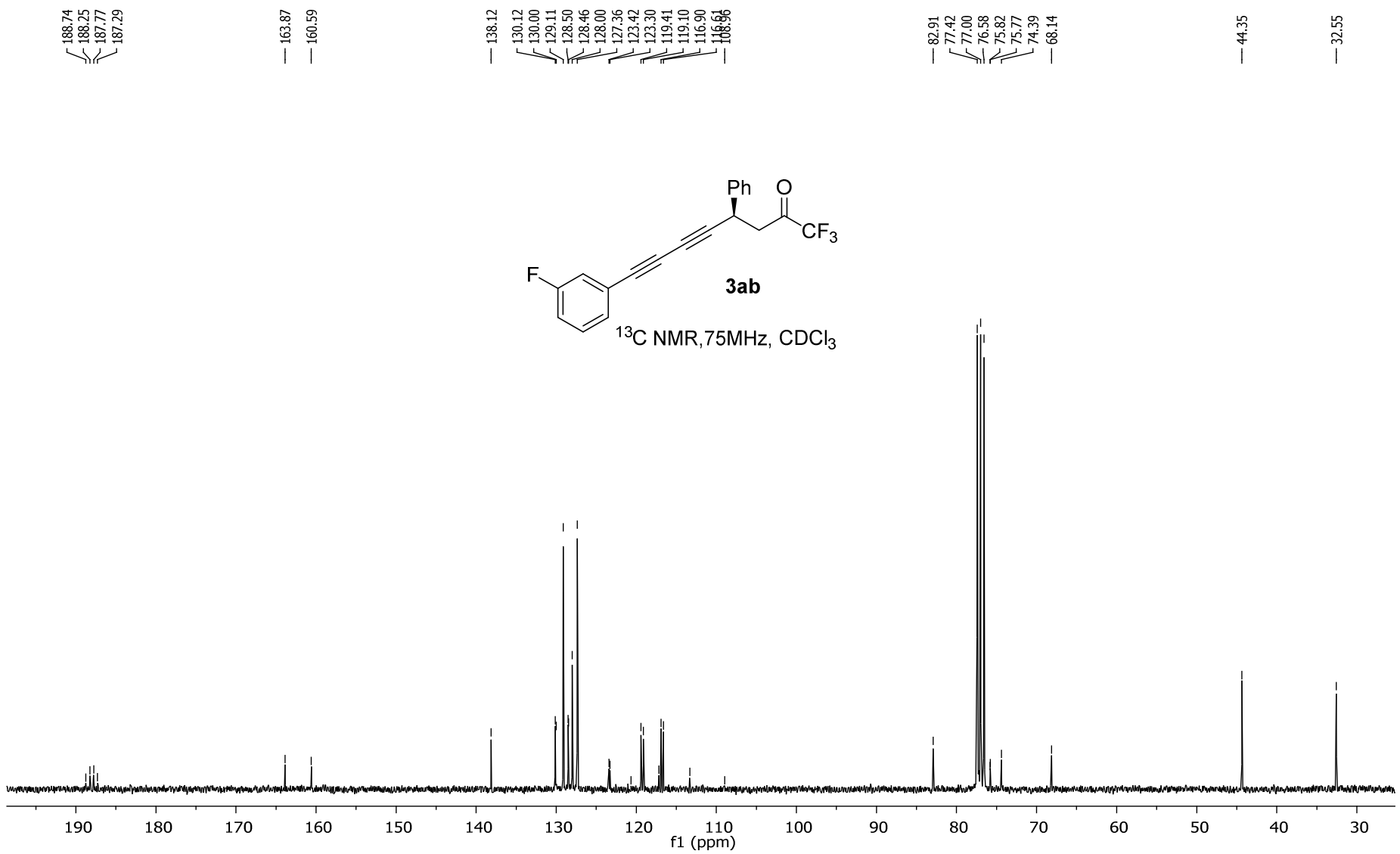
7.392
7.383
7.376
7.374
7.365
7.356
7.351
7.348
7.346
7.338
7.329
7.322
7.316
7.309
7.298
7.297
7.281
7.279
7.277
7.274
7.272
7.270
7.266
7.262
7.260
7.190
7.187
7.185
7.183
7.181
7.179
7.177
7.161
7.159
7.157
7.154
7.152
7.149
7.146
7.102
7.095
7.094
7.087
7.078
7.074
7.071
7.069
7.065
7.061
7.055
4.434
4.414
4.407
4.387
3.412
3.411
3.386
3.384
3.350
3.348
3.323
3.322
3.231
3.211
3.210
3.170
3.168
3.149
3.148
Ph
O
CF3
F
3ab
1H NMR, 300MHz, CDCl3
8.37
1.10
1.08
1.00
1.09
1.06
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
f1 (ppm)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187.77
187.29
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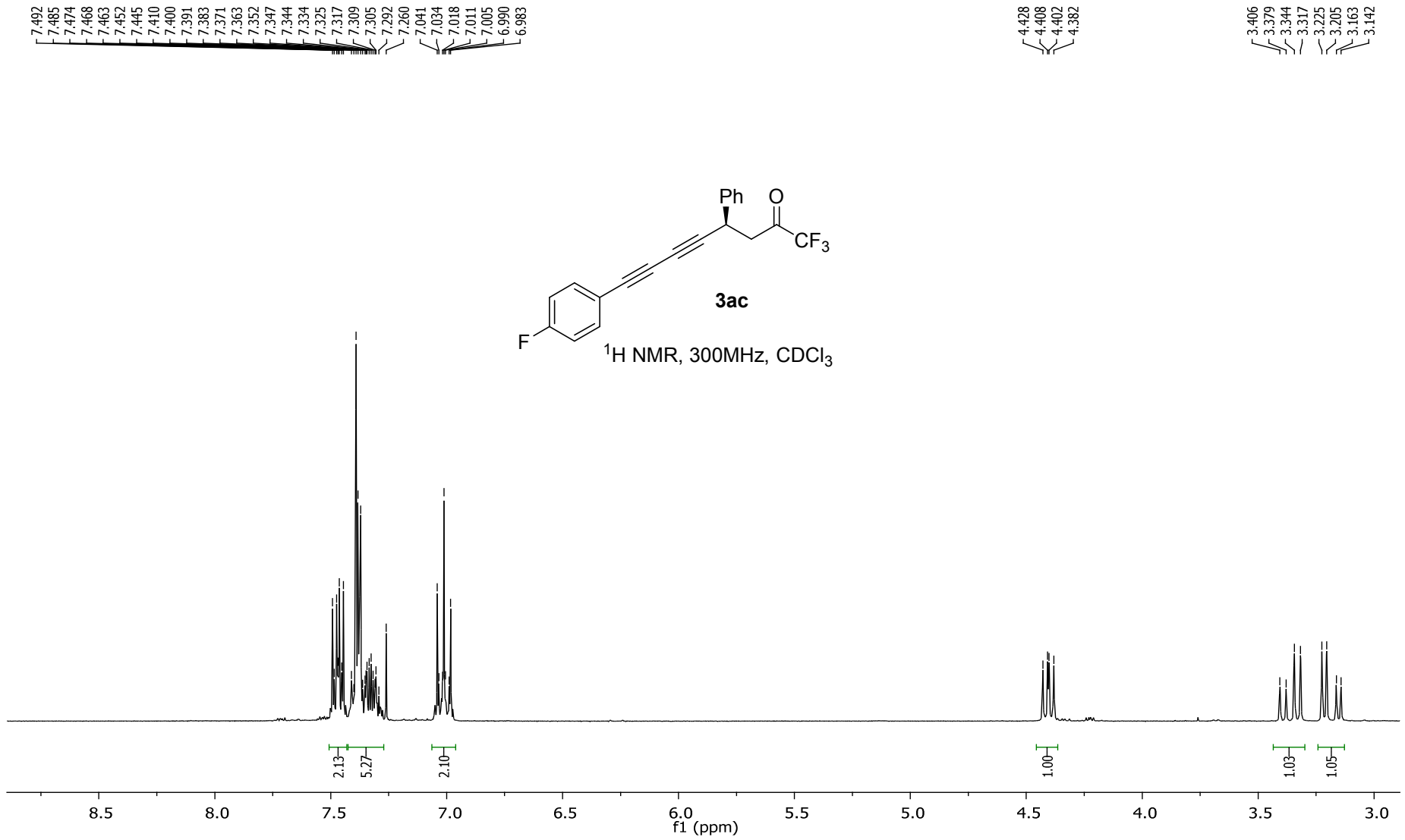
160.59
138.12
130.12
130.00
129.11
128.50
128.46
128.00
127.36
123.42
123.30
119.41
119.10
116.90
82.91
77.42
77.00
76.58
75.82
75.77
74.39
68.14
44.35
32.55
Ph
O
CF3
F
3ab
13C NMR,75MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)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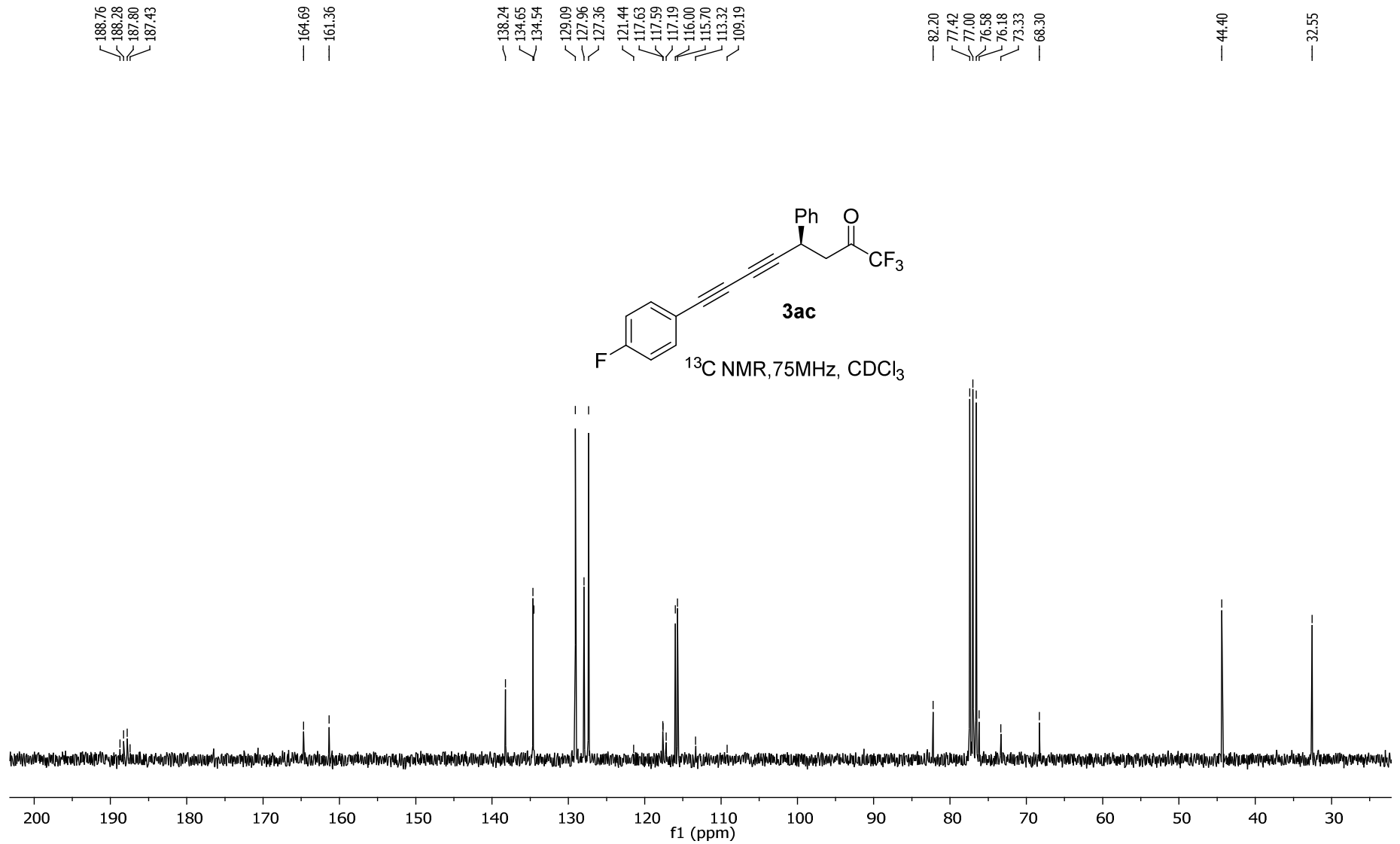
7.468
7.463
7.452
7.445
7.410
7.400
7.391
7.383
7.371
7.363
7.352
7.347
7.344
7.334
7.325
7.317
7.309
7.305
7.292
7.260
7.041
7.034
7.018
7.011
7.005
6.990
6.983
4.428
4.408
4.402
4.382
3.406
3.379
3.344
3.317
3.225
3.205
3.163
3.142
Ph
O
CF3
F
3ac
1H NMR, 300MHz, CDCl3
2.13
5.27
2.10
1.00
1.03
1.05
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f1 (ppm)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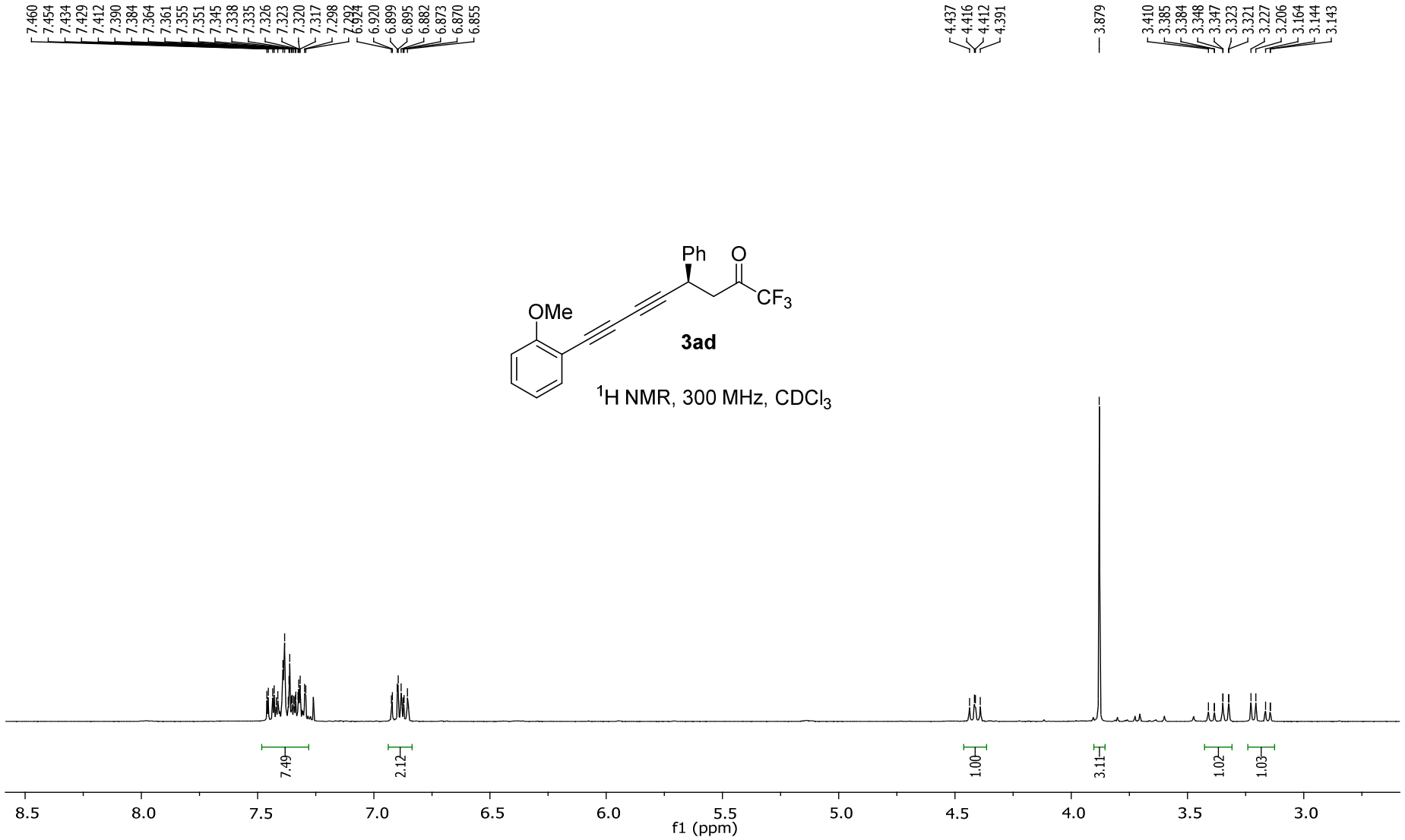
187.43
164.69
161.36
138.24
134.65
134.54
129.09
127.96
127.36
121.44
117.63
117.59
117.19
116.00
115.70
113.32
109.19
82.20
77.42
77.00
76.58
76.18
73.33
68.30
44.40
32.55
Ph
O
CF3
F
3ac
13C NMR,75MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)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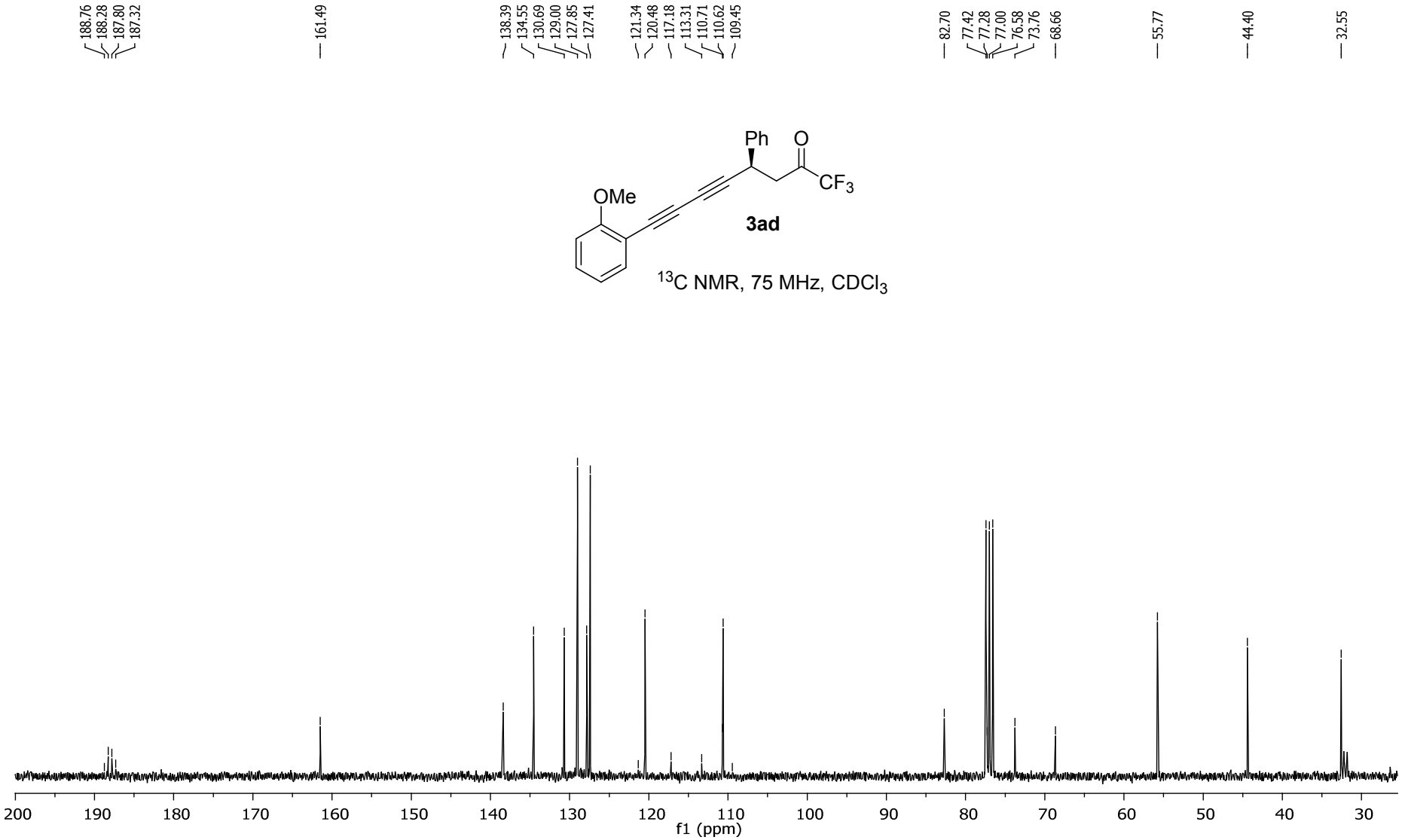
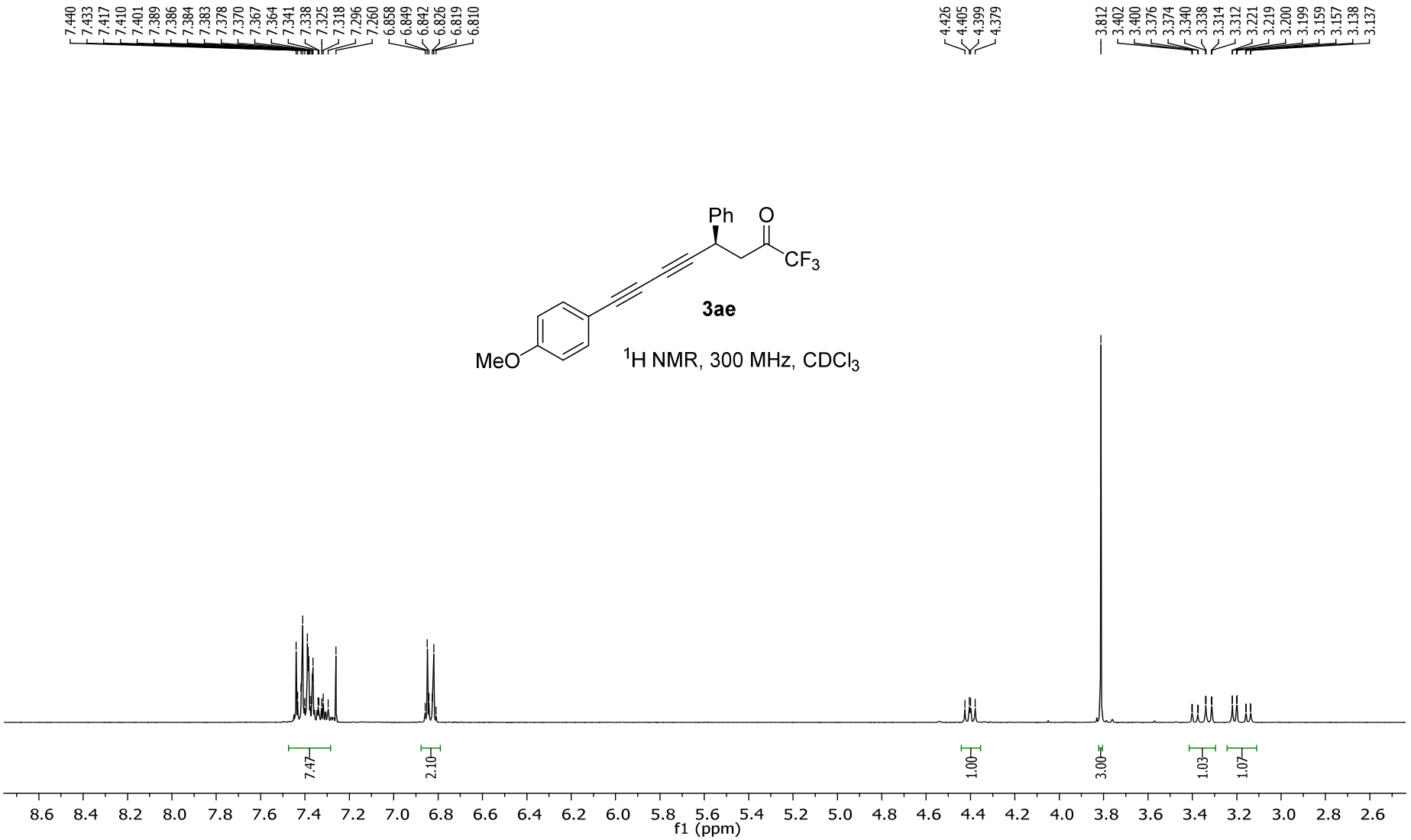
7.390
7.384
7.364
7.361
7.355
7.351
7.345
7.338
7.335
7.326
7.323
7.320
7.317
7.298
6.920
6.899
6.895
6.882
6.873
6.870
6.855
4.437
4.416
4.412
4.391
3.879
3.410
3.385
3.384
3.348
3.347
3.323
3.321
3.227
3.206
3.164
3.144
3.143
Ph
O
CF3
OMe
3ad
1H NMR, 300 MHz, CDCl3
7.49
2.12
1.00
3.11
1.02
1.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f1 (ppm)


188.76
188.28
187.80
187.32
161.49
138.39
134.55
130.69
129.00
127.85
127.41
121.34
120.48
117.18
113.31
110.71
110.62
109.45
82.70
77.42
77.28
77.00
76.58
73.76
68.66
55.77
44.40
32.55
Ph
O
CF3
OMe
3ad
13C NMR, 75 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)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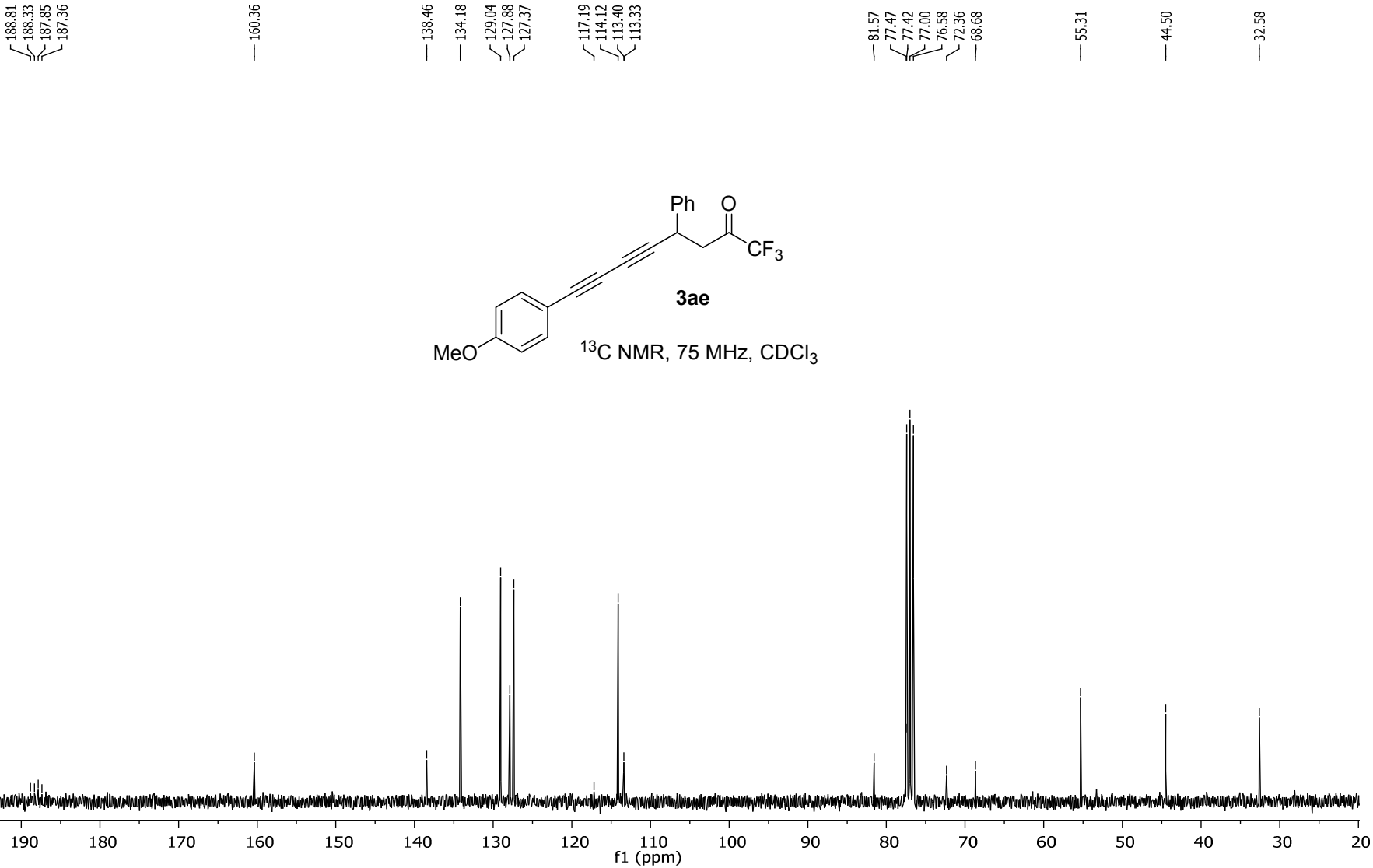
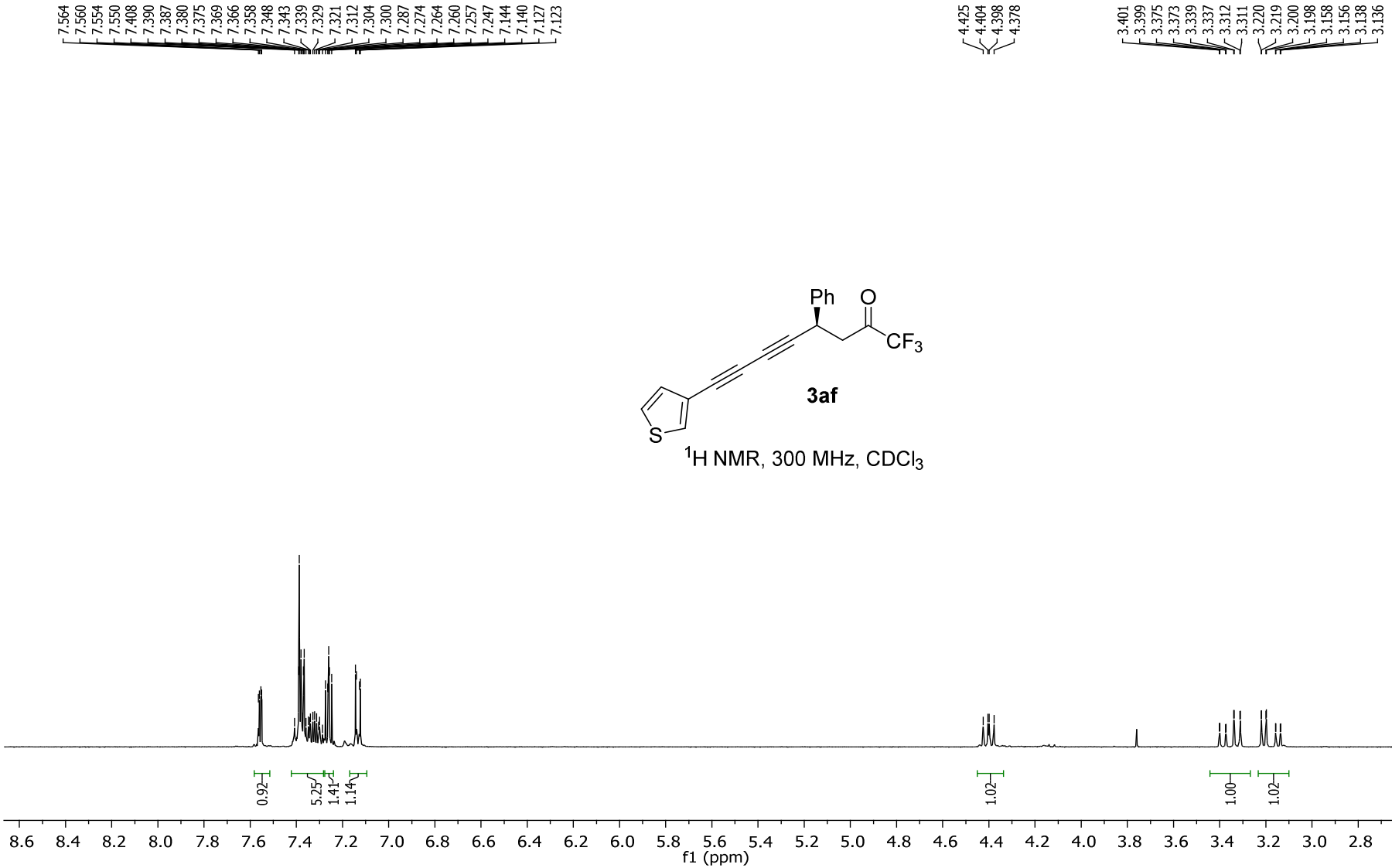
7.417
7.410
7.401
7.389
7.386
7.384
7.383
7.378
7.370
7.367
7.364
7.341
7.338
7.325
7.318
7.296
7.260
6.858
6.849
6.842
6.826
6.819
6.810
4.426
4.405
4.399
4.379
3.812
3.402
3.400
3.376
3.374
3.340
3.338
3.314
3.312
3.221
3.219
3.200
3.199
3.159
3.157
3.138
3.137
Ph
O
CF3
MeO
3ae
1H NMR, 300 MHz, CDCl3
7.47
2.10
1.00
3.00
1.03
1.07
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6
f1 (ppm)


188.81
188.33
187.85
187.36
160.36
138.46
134.18
129.04
127.88
127.37
117.19
114.12
113.40
113.33
81.57
77.47
77.42
77.00
76.58
72.36
68.68
55.31
44.50
32.58
Ph
O
CF3
3ae
MeO
13C NMR, 75 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)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7.560
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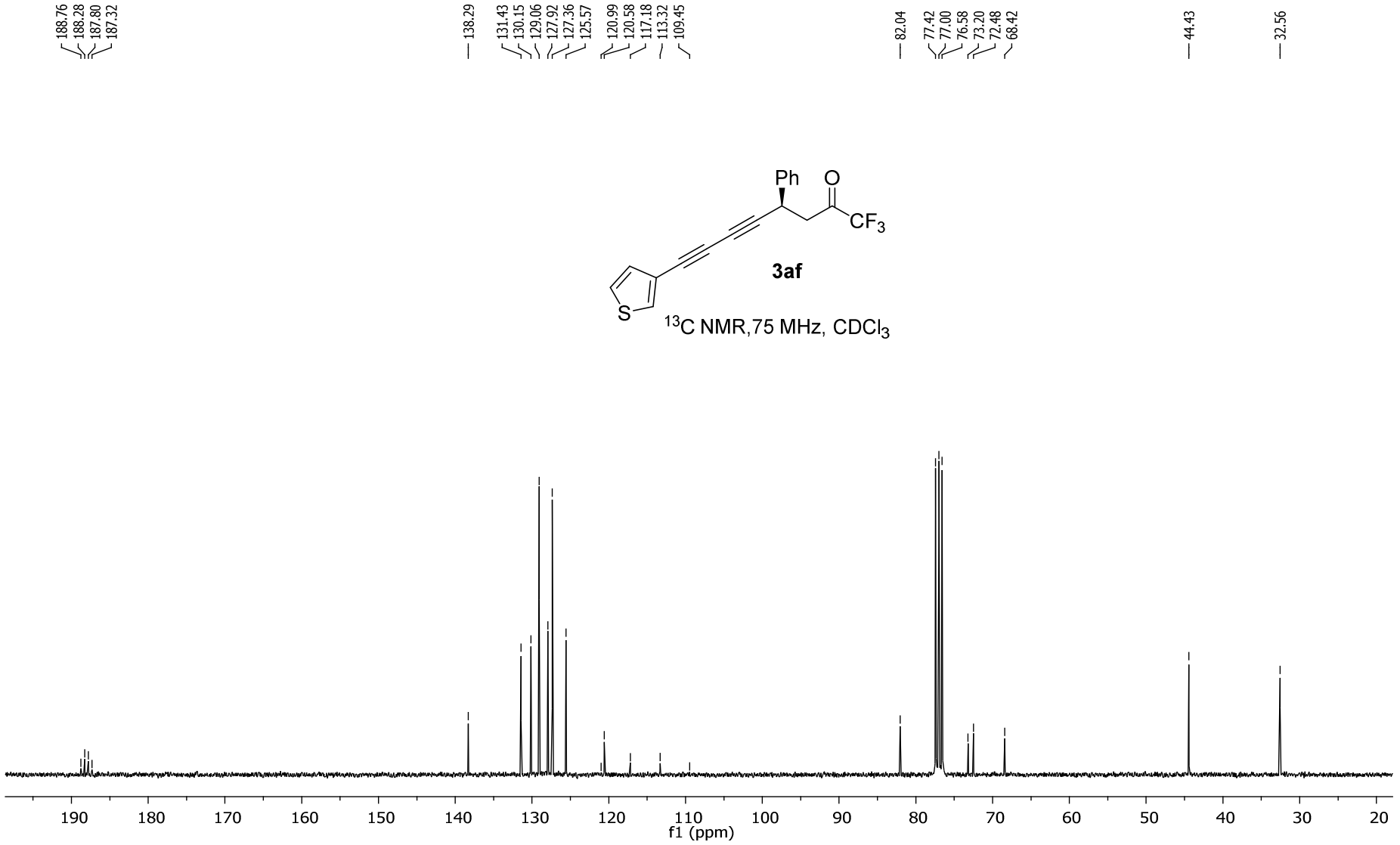
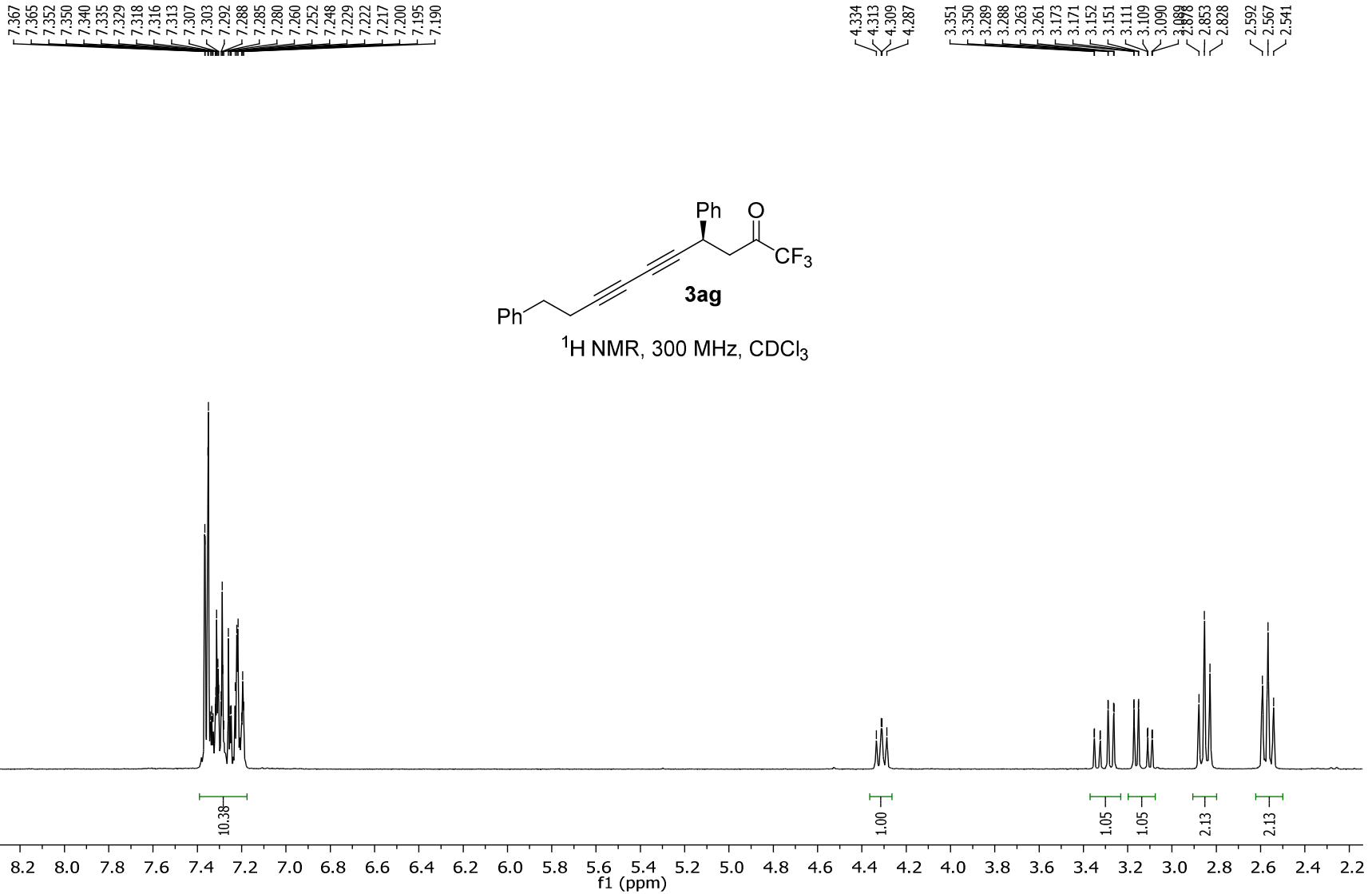
7.550
7.408
7.390
7.387
7.380
7.375
7.369
7.366
7.358
7.348
7.343
7.339
7.329
7.321
7.312
7.304
7.300
7.287
7.274
7.264
7.260
7.257
7.247
7.144
7.140
7.127
7.123
4.425
4.404
4.398
4.378
3.401
3.399
3.375
3.373
3.339
3.337
3.312
3.311
3.220
3.219
3.200
3.198
3.158
3.156
3.138
3.136
Ph
O
CF3
S
3af
1H NMR, 300 MHz, CDCl3
0.92
5.25
1.41
1.14
1.02
1.00
1.02
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
f1 (ppm)


188.76
188.28
187.80
187.32
138.29
131.43
130.15
129.06
127.92
127.36
125.57
120.99
120.58
117.18
113.32
109.45
82.04
77.42
77.00
76.58
73.20
72.48
68.42
44.43
32.56
Ph
O
CF3
S
3af
13C NMR,75 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)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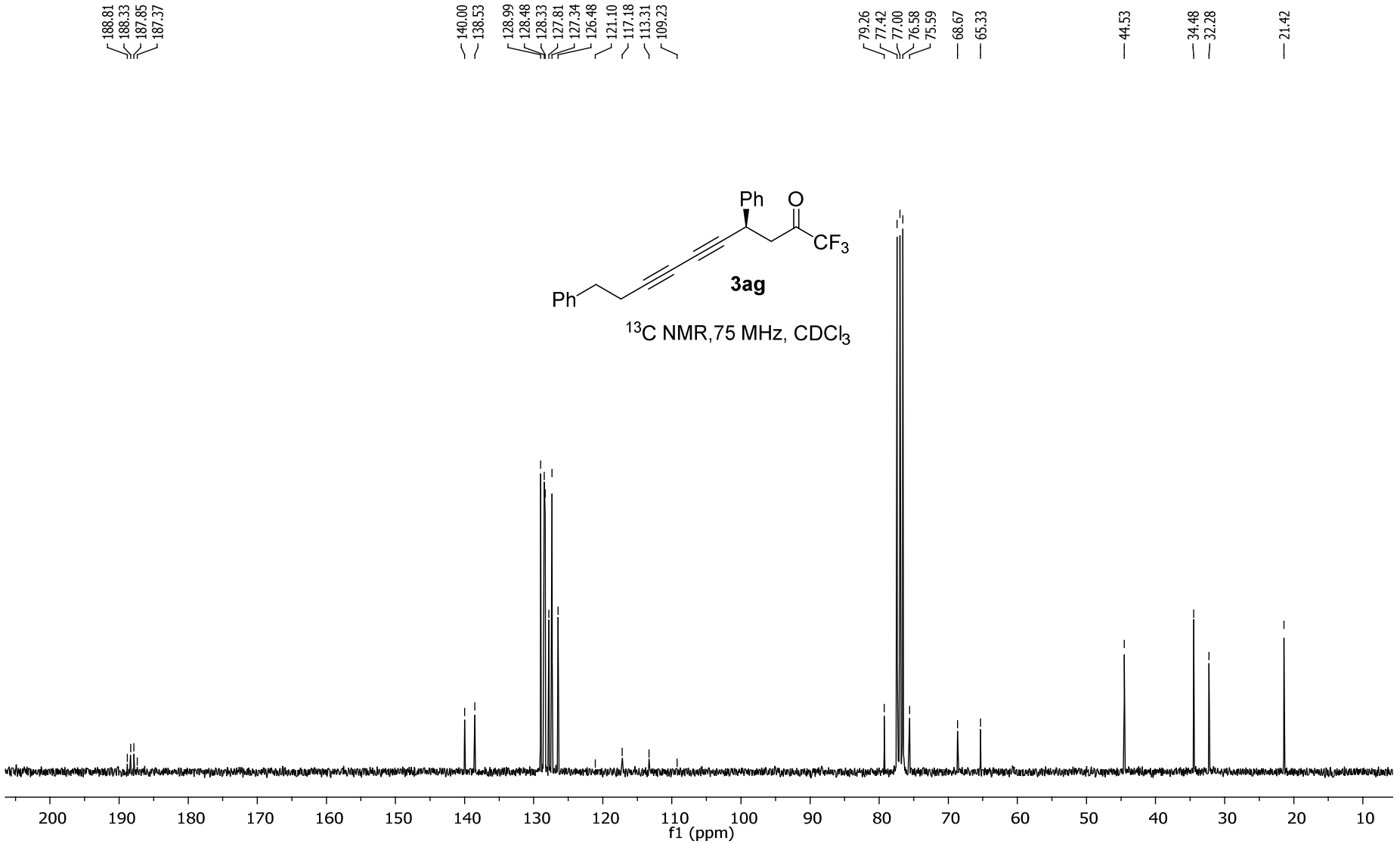
7.365
7.352
7.350
7.340
7.335
7.329
7.318
7.316
7.313
7.307
7.303
7.292
7.288
7.285
7.280
7.260
7.252
7.248
7.229
7.222
7.217
7.200
7.195
7.190
4.334
4.313
4.309
4.287
3.351
3.350
3.289
3.288
3.263
3.261
3.173
3.171
3.152
3.151
3.111
3.109
3.090
2.878
2.853
2.828
2.592
2.567
2.541
Ph
O
CF3
Ph
3ag
1H NMR, 300 MHz, CDCl3
10.38
1.00
1.05
1.05
2.13
2.13
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2
f1 (ppm)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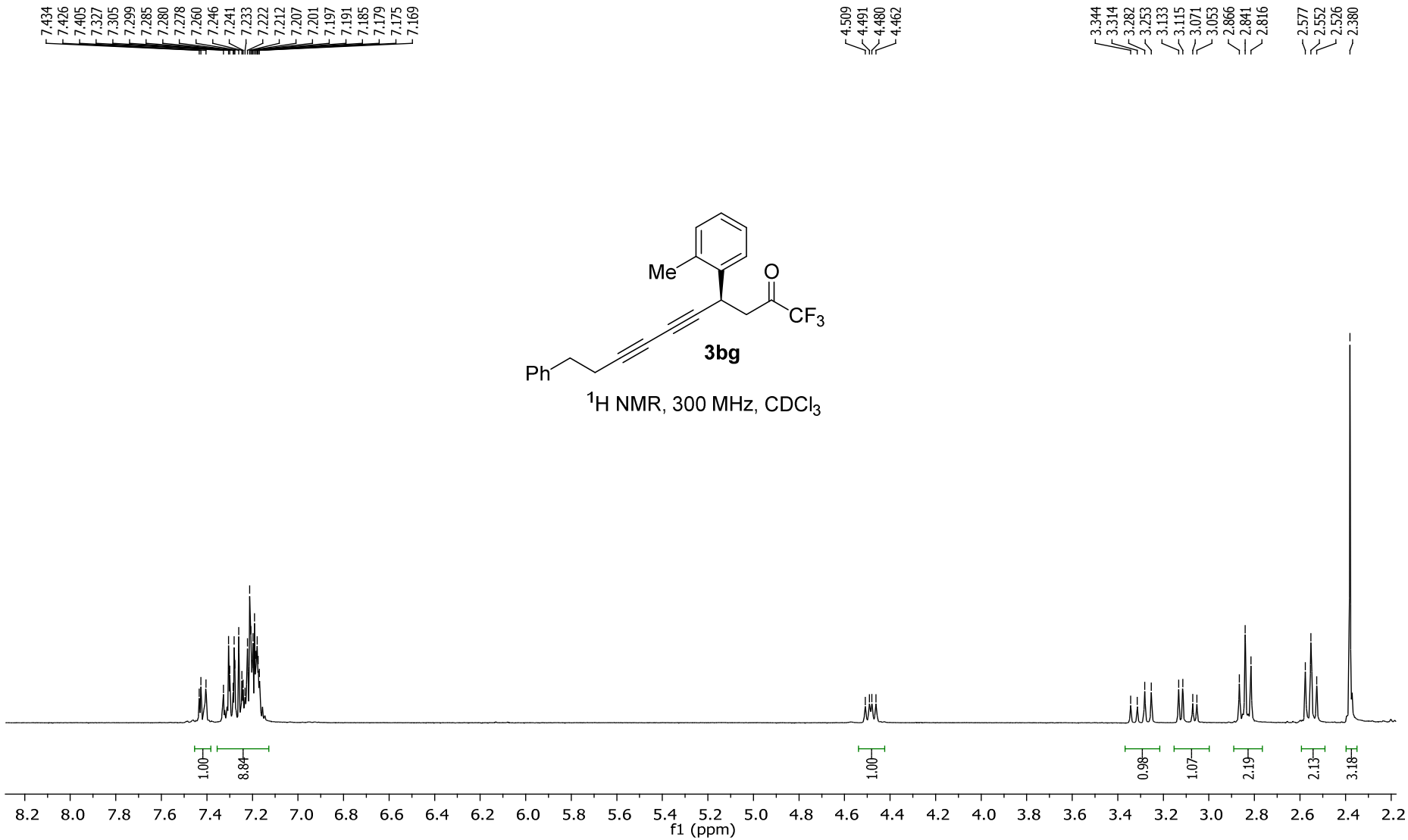
187.85
187.37
140.00
138.53
128.99
128.48
128.33
127.81
127.34
126.48
121.10
117.18
113.31
109.23
79.26
77.42
77.00
76.58
75.59
68.67
65.33
44.53
34.48
32.28
21.42
Ph
O
CF3
Ph
3ag
13C NMR,75 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.426
7.405
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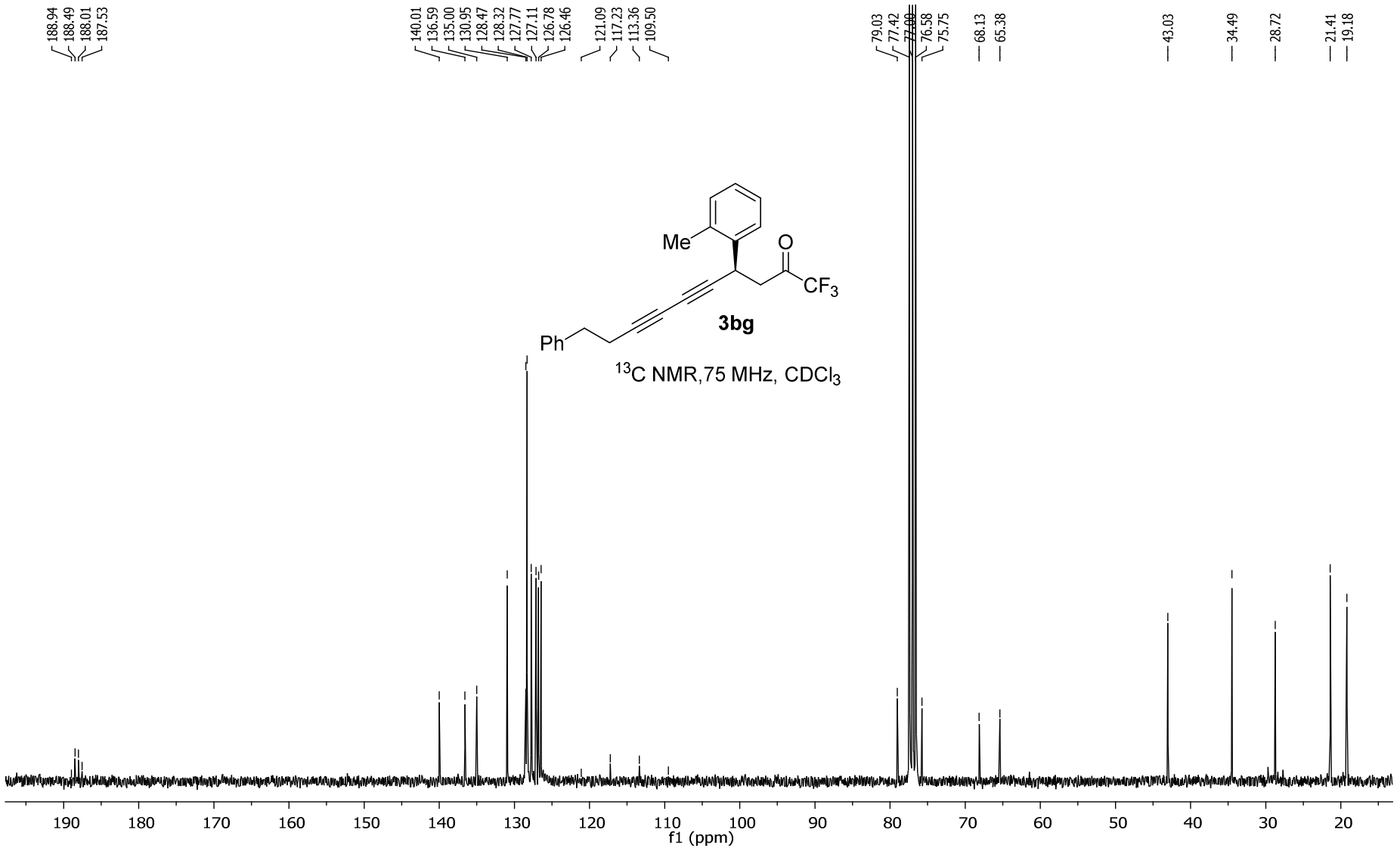
7.305
7.299
7.285
7.280
7.278
7.260
7.246
7.241
7.233
7.222
7.212
7.207
7.201
7.197
7.191
7.185
7.179
7.175
7.169
4.509
4.491
4.480
4.462
3.344
3.314
3.282
3.253
3.133
3.115
3.071
3.053
2.866
2.841
2.816
2.577
2.552
2.526
2.380
Me
O
CF3
Ph
3bg
1H NMR, 300 MHz, CDCl3
1.00
8.84
1.00
0.98
1.07
2.19
2.13
3.18
8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2
f1 (ppm)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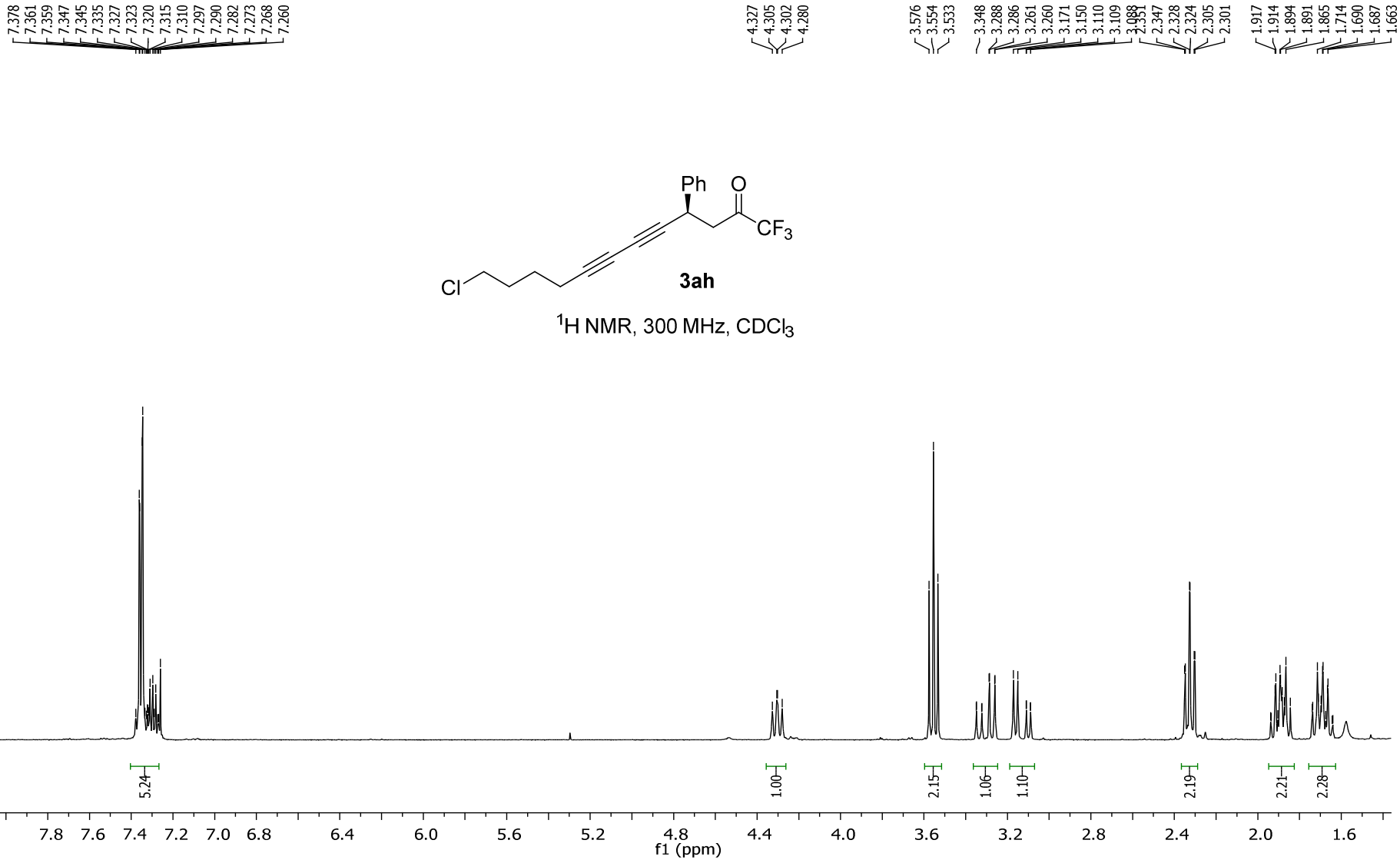
188.01
187.53
140.01
136.59
135.00
130.95
128.47
128.32
127.77
127.11
126.78
126.46
121.09
117.23
113.36
109.50
79.03
77.42
77.00
76.58
75.75
68.13
65.38
43.03
34.49
28.72
21.41
19.18
Me
O
CF3
Ph
3bg
13C NMR,75 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)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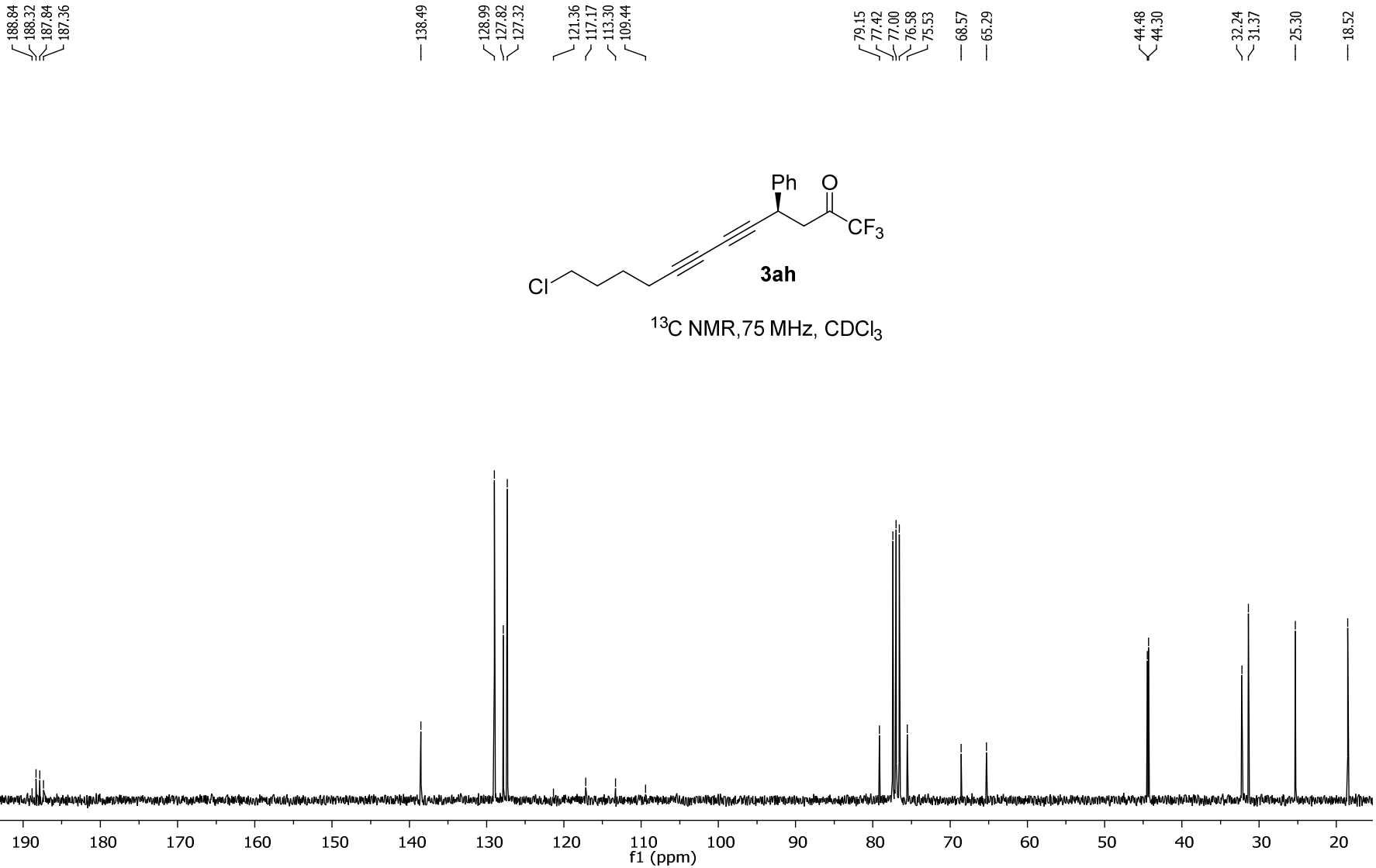
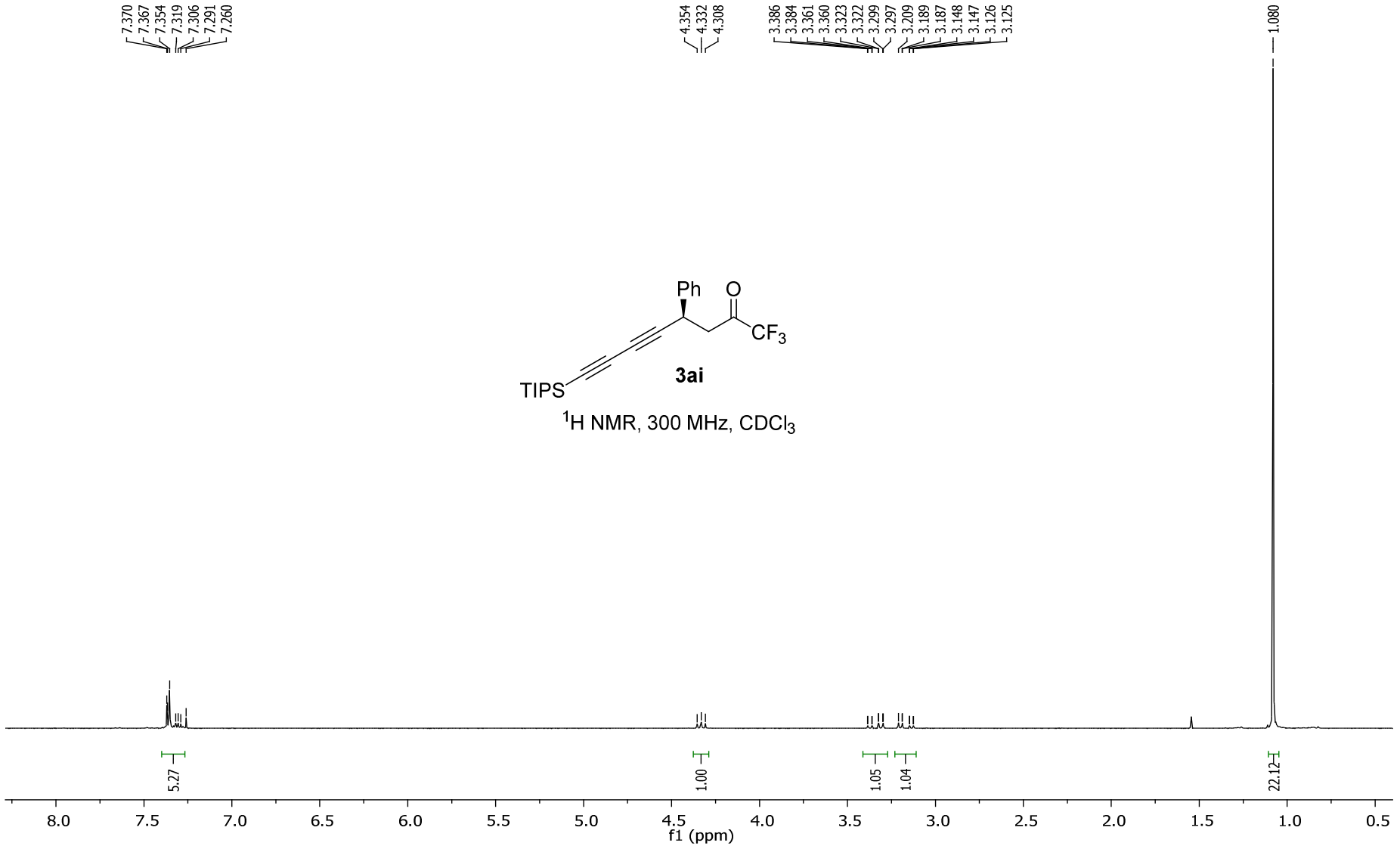
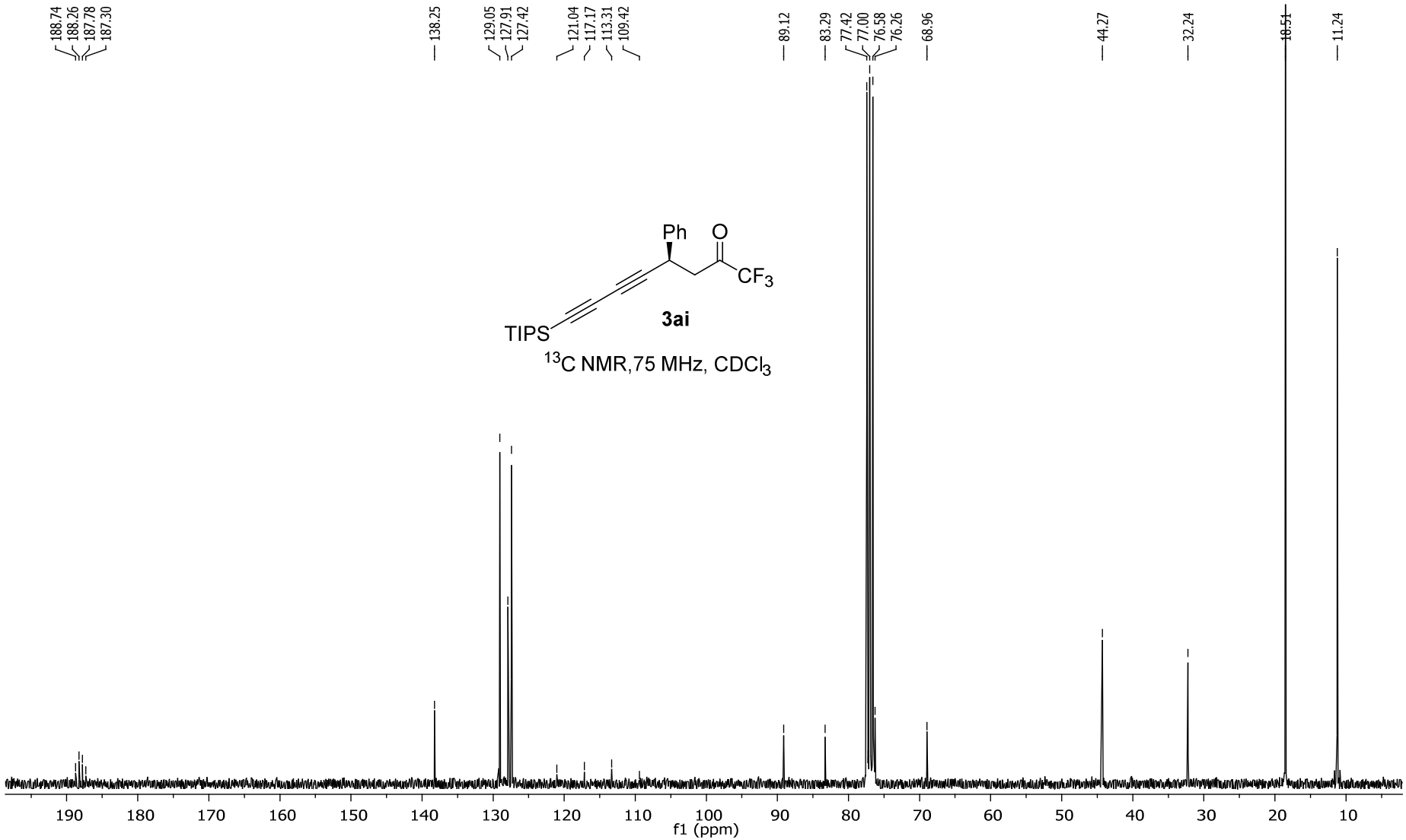
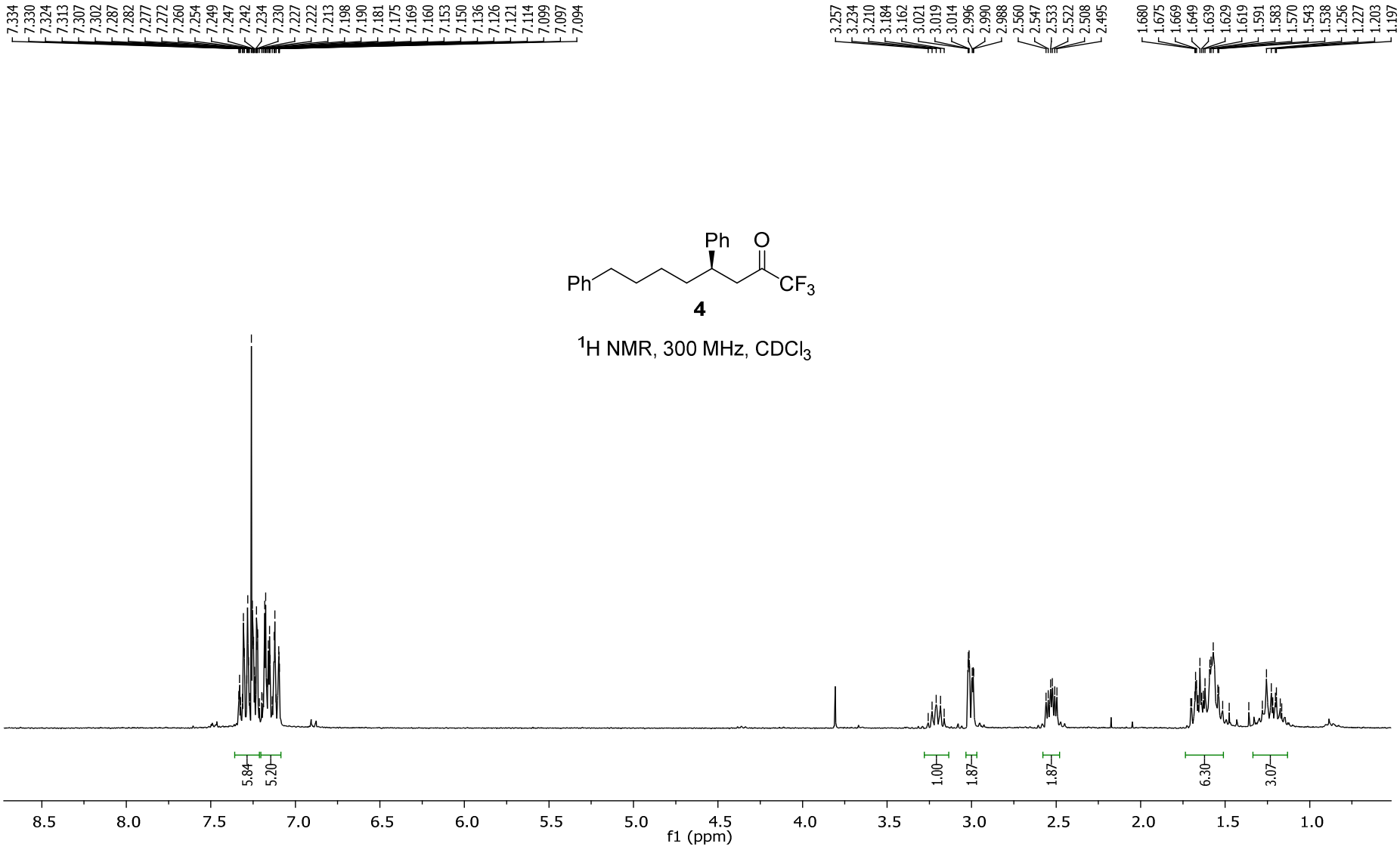
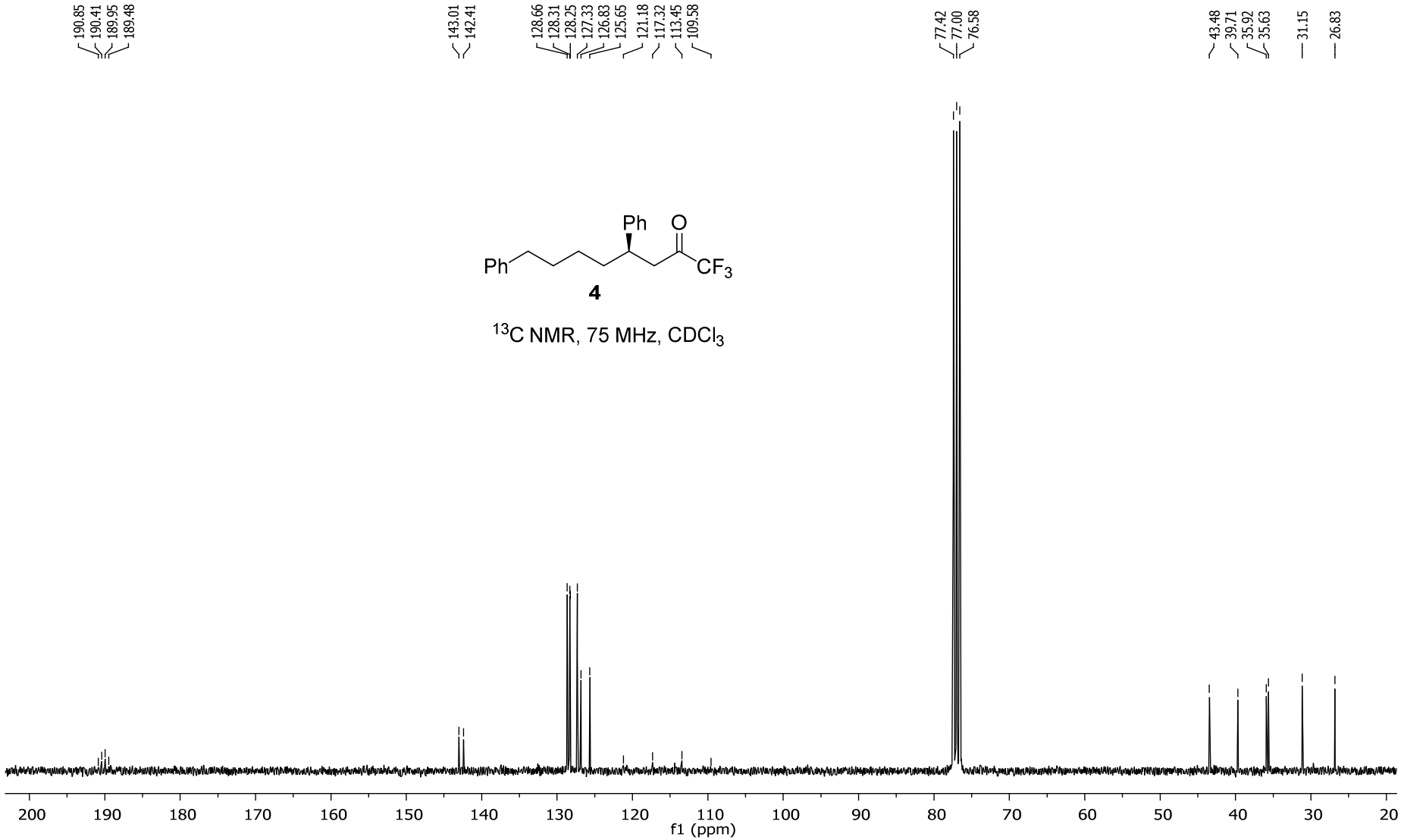
7.361
7.359
7.347
7.345
7.335
7.327
7.323
7.320
7.315
7.310
7.297
7.290
7.282
7.273
7.268
7.260
4.327
4.305
4.302
4.280
3.576
3.554
3.533
3.348
3.288
3.286
3.261
3.260
3.171
3.150
3.110
3.109
2.347
2.328
2.324
2.305
2.301
1.917
1.914
1.894
1.891
1.865
1.714
1.690
1.687
1.663
Ph
O
CF3
Cl
3ah
1H NMR, 300 MHz, CDCl3
5.24
1.00
2.15
1.06
1.10
2.19
2.21
2.28
7.8
7.6
7.4
7.2
7.0
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
f1 (ppm)

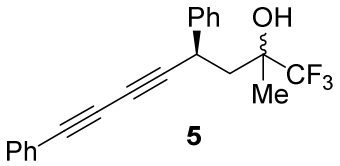

188.84
188.32
187.84
187.36
138.49
128.99
127.82
127.32
121.36
117.17
113.30
109.44
79.15
77.42
77.00
76.58
75.53
68.57
65.29
44.48
44.30
32.24
31.37
25.30
18.52
Ph
O
CF3
Cl
3ah
13C NMR,75 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


7.370
7.367
7.354
7.319
7.306
7.291
7.260
4.354
4.332
4.308
3.386
3.384
3.361
3.360
3.323
3.322
3.299
3.297
3.209
3.189
3.187
3.148
3.147
3.126
3.125
1.080
Ph
O
CF3
TIPS
3ai
1H NMR, 300 MHz, CDCl3
5.27
1.00
1.05
1.04
22.12
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)


188.74
188.26
187.78
187.30
138.25
129.05
127.91
127.42
121.04
117.17
113.31
109.42
89.12
83.29
77.42
77.00
76.58
76.26
68.96
44.27
32.24
18.51
11.24
Ph
O
CF3
TIPS
3ai
13C NMR,75 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

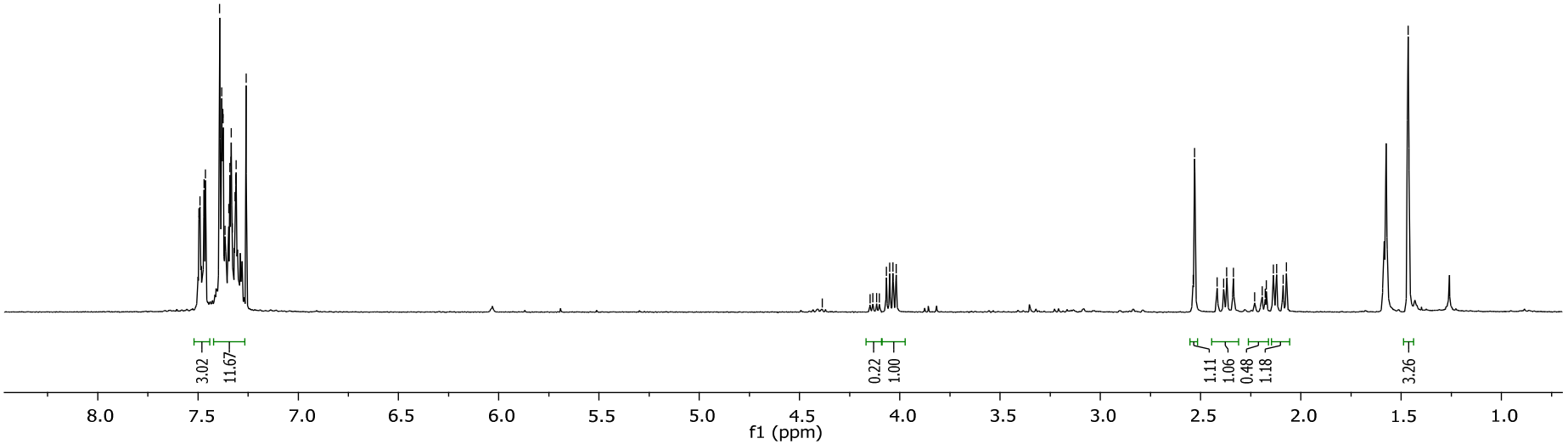

7.334
7.330
7.324
7.313
7.307
7.302
7.287
7.282
7.277
7.272
7.260
7.254
7.249
7.247
7.242
7.234
7.230
7.227
7.222
7.213
7.198
7.190
7.181
7.175
7.169
7.160
7.153
7.150
7.136
7.126
7.121
7.114
7.099
7.097
7.094
3.257
3.234
3.210
3.184
3.162
3.021
3.019
3.014
2.996
2.990
2.988
2.560
2.547
2.533
2.522
2.508
2.495
1.680
1.675
1.669
1.649
1.639
1.629
1.619
1.591
1.583
1.570
1.543
1.538
1.256
1.227
1.203
1.197
Ph
O
Ph
CF3
4
1H NMR, 300 MHz, CDCl3
5.84
5.20
1.00
1.87
1.87
6.30
3.07
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
f1 (ppm)

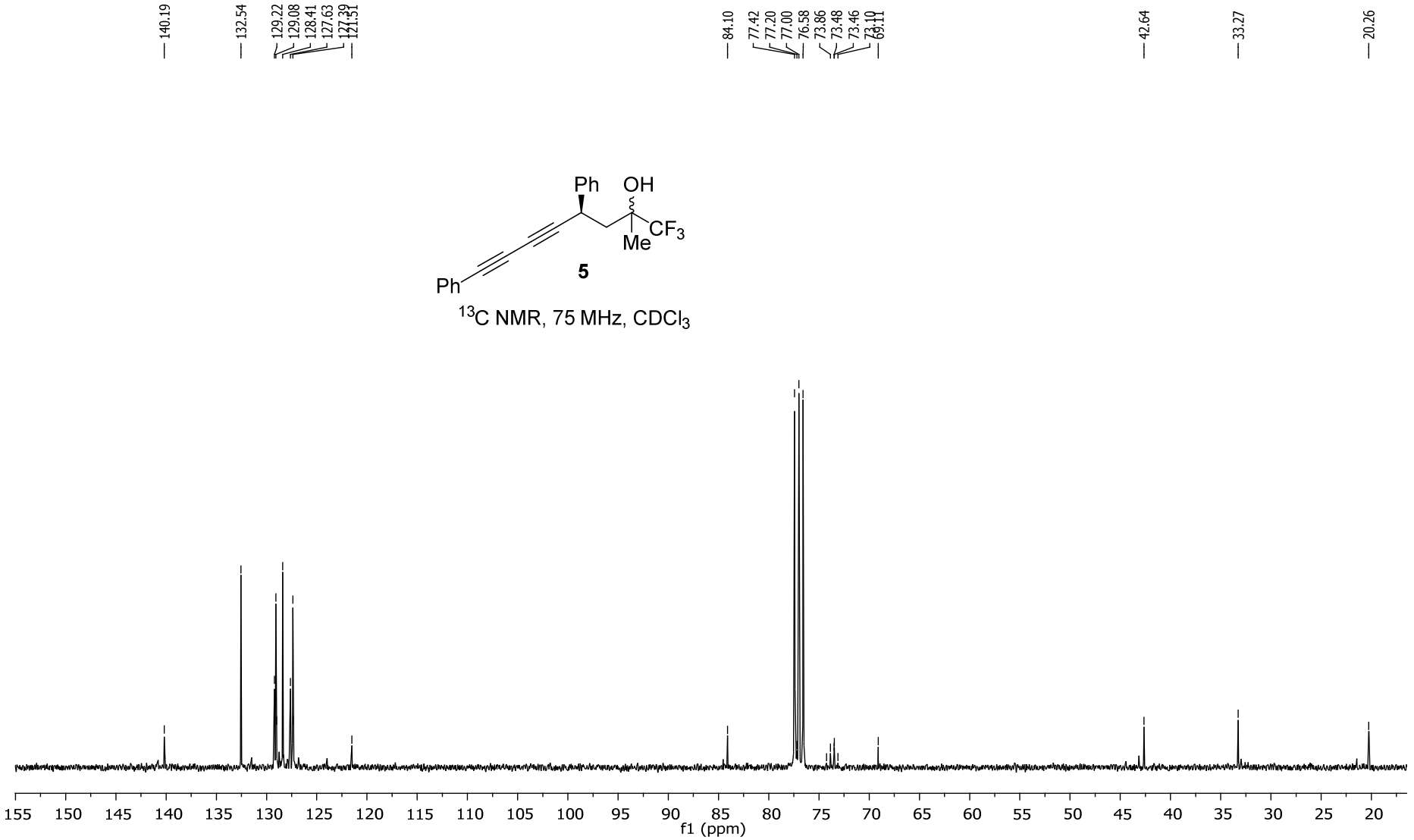

190.85
190.41
189.95
189.48
143.01
142.41
128.66
128.31
128.25
127.33
126.83
125.65
121.18
117.32
113.45
109.58
77.42
77.00
76.58
43.48
39.71
35.92
35.63
31.15
26.83
Ph
O
Ph
CF3
4
13C NMR, 75 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

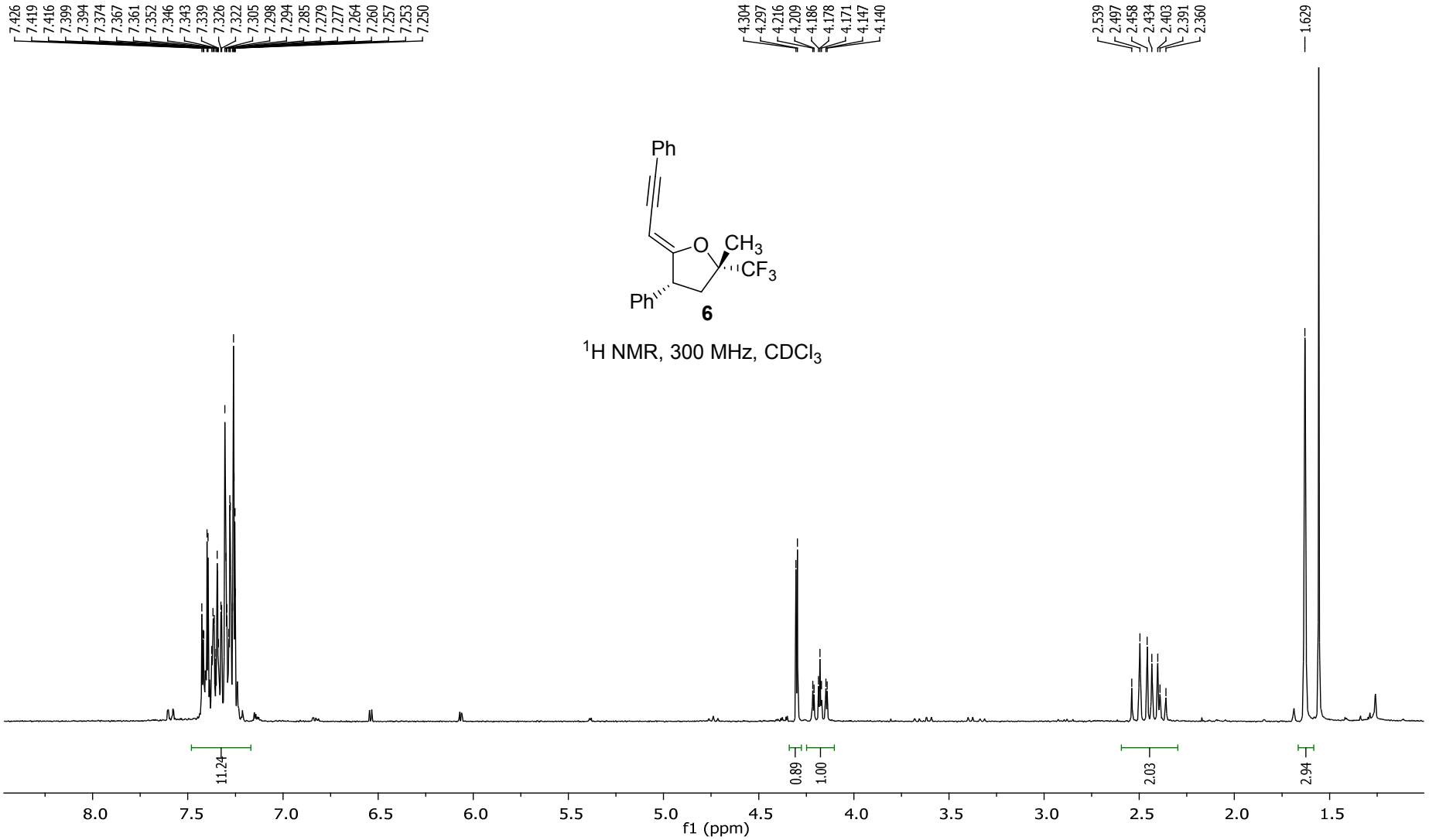


5

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




140.19
132.54
129.22
129.08
128.41
127.63
84.10
77.42
77.20
77.00
76.58
73.86
73.48
73.46
69.11
42.64
33.27
20.26
Ph
OH
CF3
Me
Ph
5
13C NMR, 75 MHz, CDCl3
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)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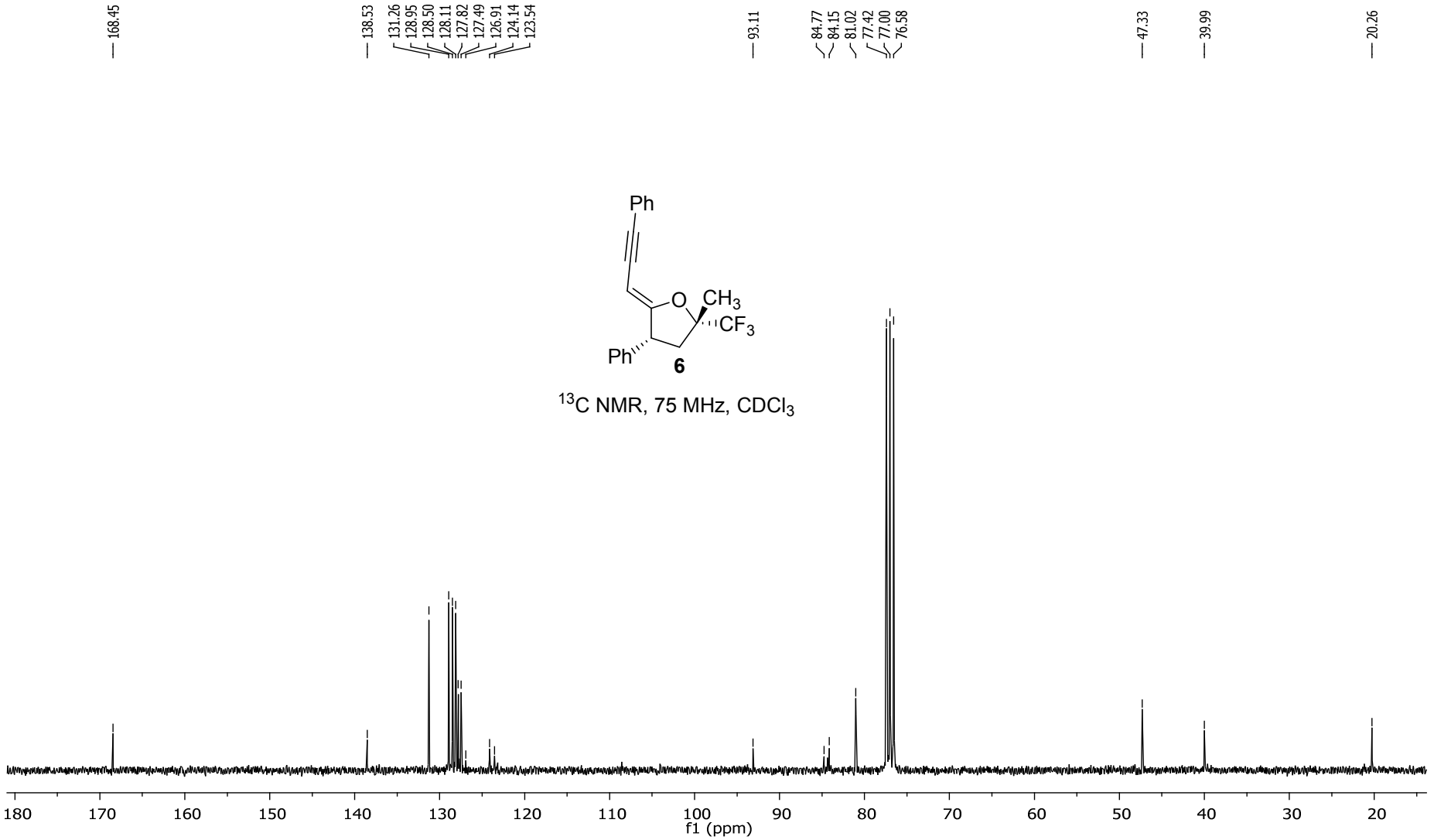
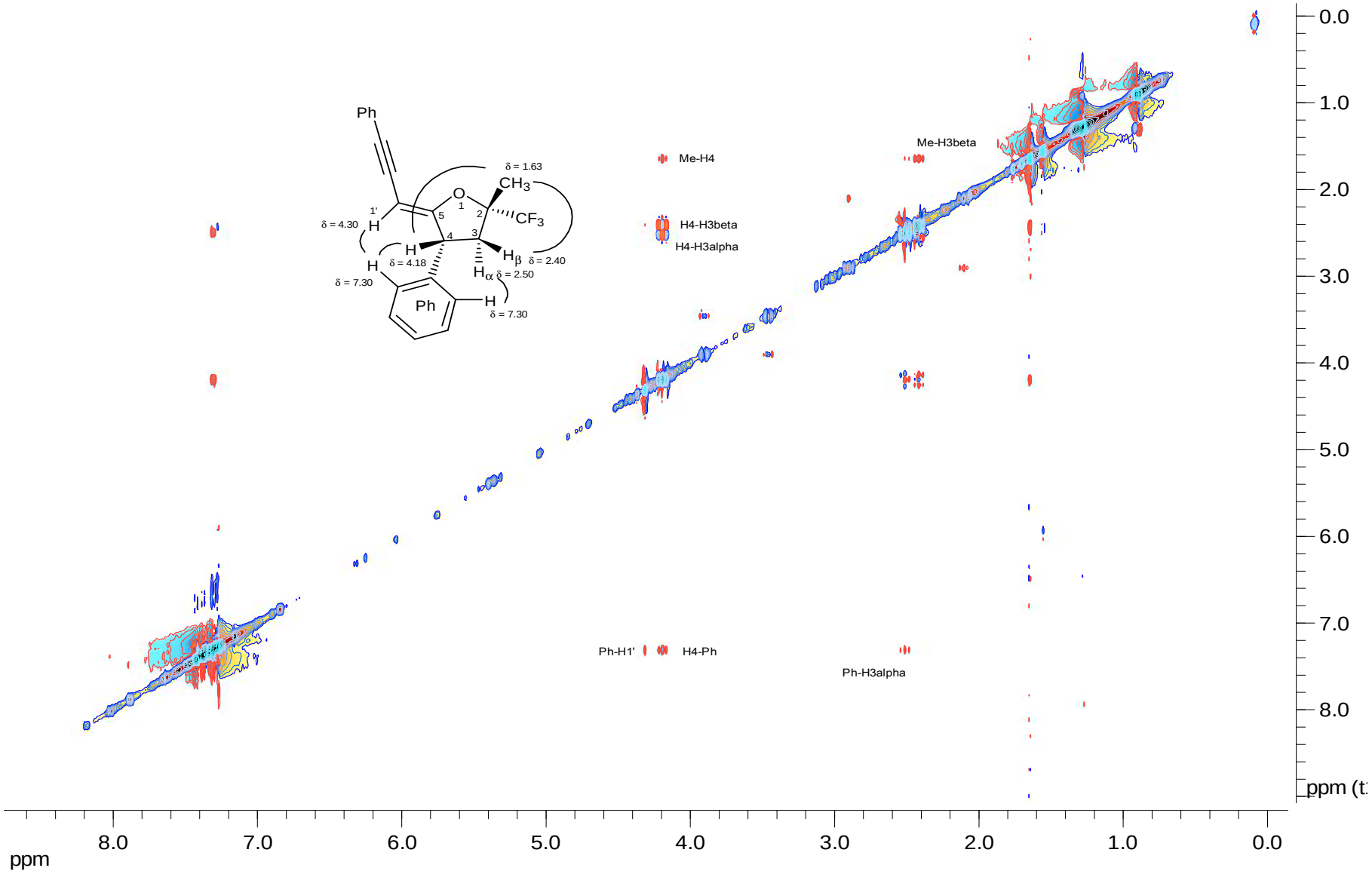
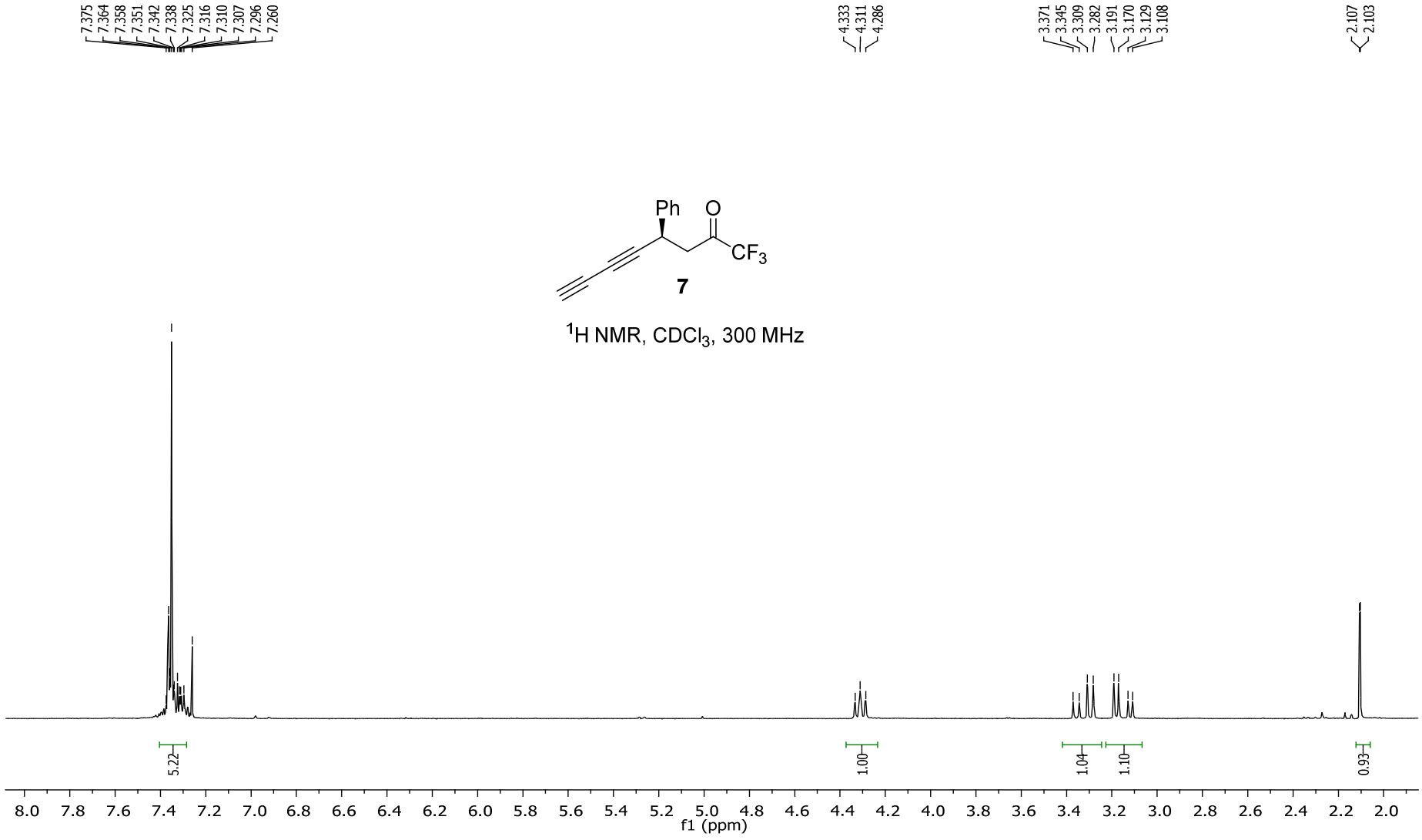
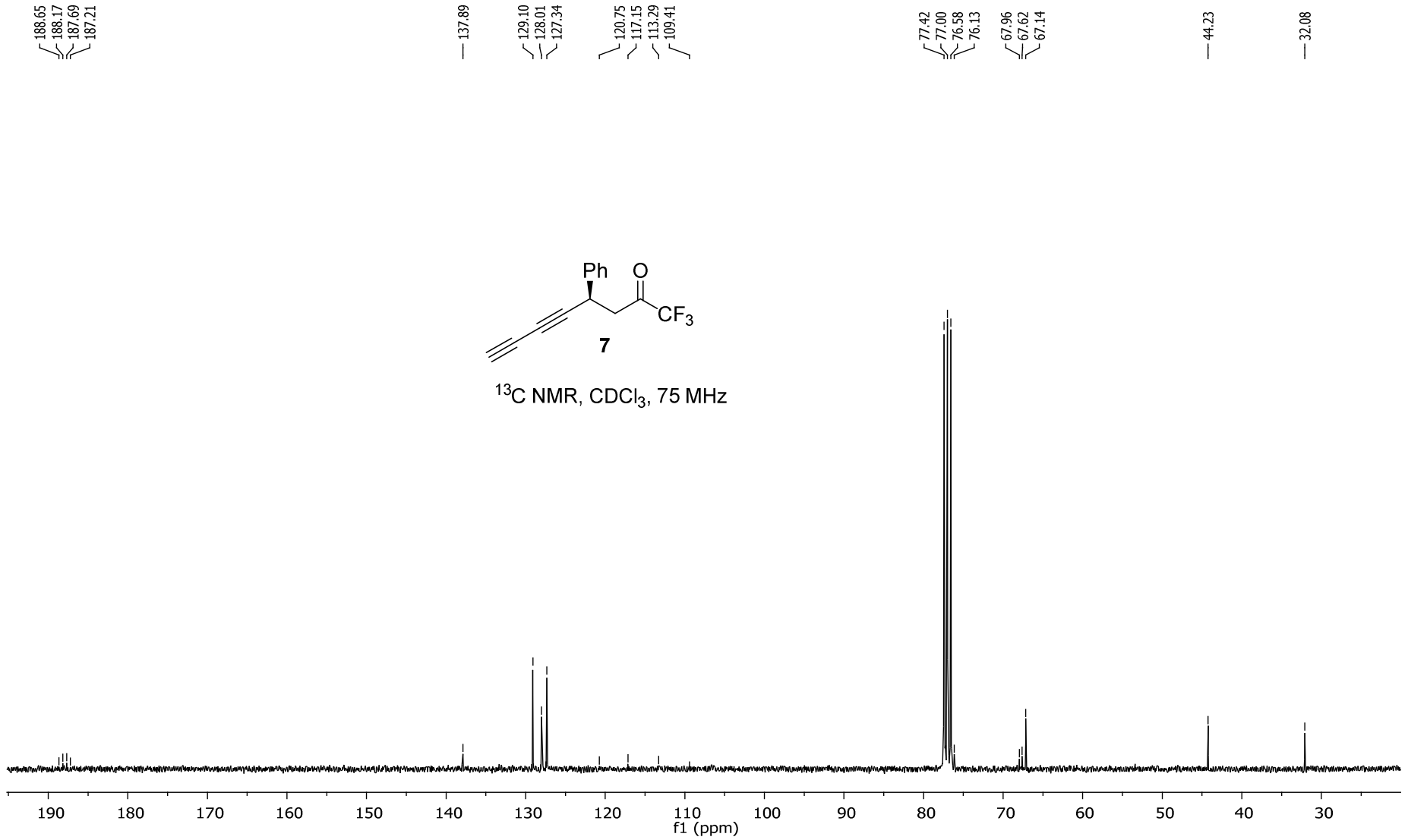
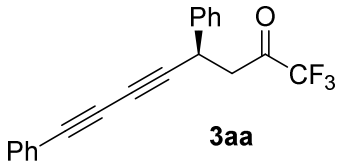
7.419
7.416
7.399
7.394
7.374
7.367
7.361
7.352
7.346
7.343
7.339
7.326
7.322
7.305
7.298
7.294
7.285
7.279
7.277
7.264
7.260
7.257
7.253
7.250
4.304
4.297
4.216
4.209
4.186
4.178
4.171
4.147
4.140
2.539
2.497
2.458
2.434
2.403
2.391
2.360
1.629
Ph
O
CH3
CF3
Ph
6
1H NMR, 300 MHz, CDCl3
11.24
0.89
1.00
2.03
2.94
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
f1 (ppm)


168.45
138.53
131.26
128.95
128.50
128.11
127.82
127.49
126.91
124.14
123.54
93.11
84.77
84.15
81.02
77.42
77.00
76.58
47.33
39.99
20.26
Ph
O
CH3
CF3
Ph
6
13C NMR, 75 MHz, CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

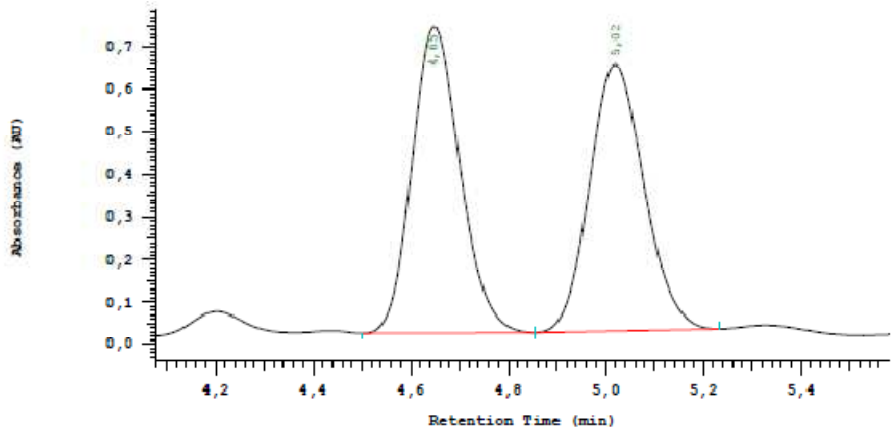

Ph
δ = 1.63
CH3
O
1
2
CF3
1'
H
δ = 4.30
5
4
3
H
δ = 4.18
Hβ δ = 2.40
H
δ = 7.30
Hα δ = 2.50
Ph
H
δ = 7.30
Me-H4
Me-H3beta
H4-H3beta
H4-H3alpha
Ph-H1'
H4-Ph
Ph-H3alpha
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (t
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm


7.375
7.364
7.358
7.351
7.342
7.338
7.325
7.316
7.310
7.307
7.296
7.260
4.333
4.311
4.286
3.371
3.345
3.309
3.282
3.191
3.170
3.129
3.108
2.107
2.103
Ph
O
CF3
7
1H NMR, CDCl3, 300 MHz
5.22
1.00
1.04
1.10
0.93
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
f1 (ppm)


188.65
188.17
187.69
187.21
137.89
129.10
128.01
127.34
120.75
117.15
113.29
109.41
77.42
77.00
76.58
76.13
67.96
67.62
67.14
44.23
32.08
Ph
O
CF3
7
13C NMR, CDCl3, 75 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)



3aa



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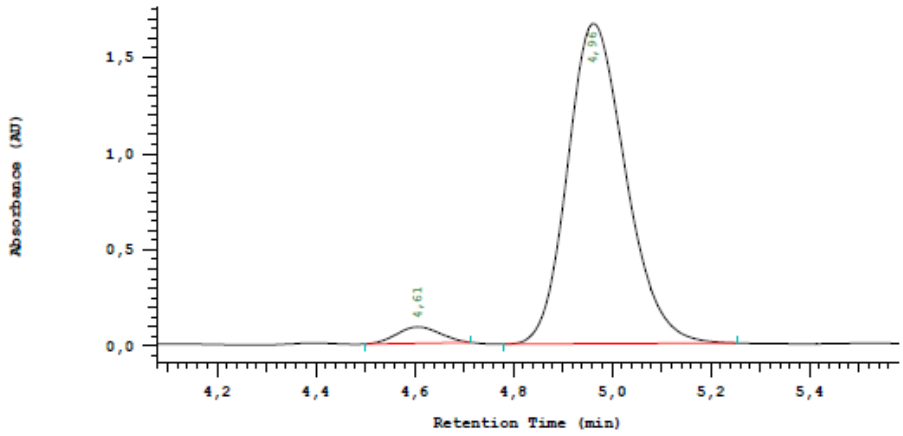
2	5,02	2428560	49,620	
		4894320	100,000	



No.	RT	Area	Area %	Name
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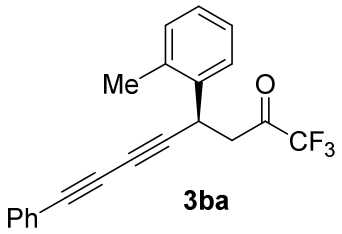
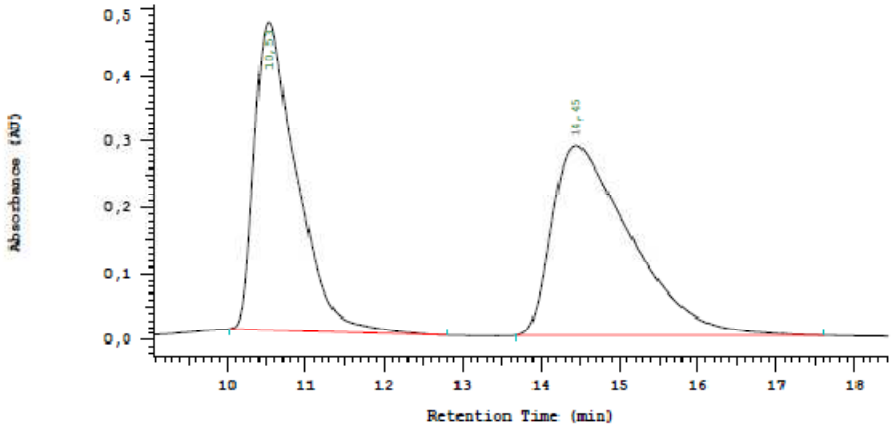
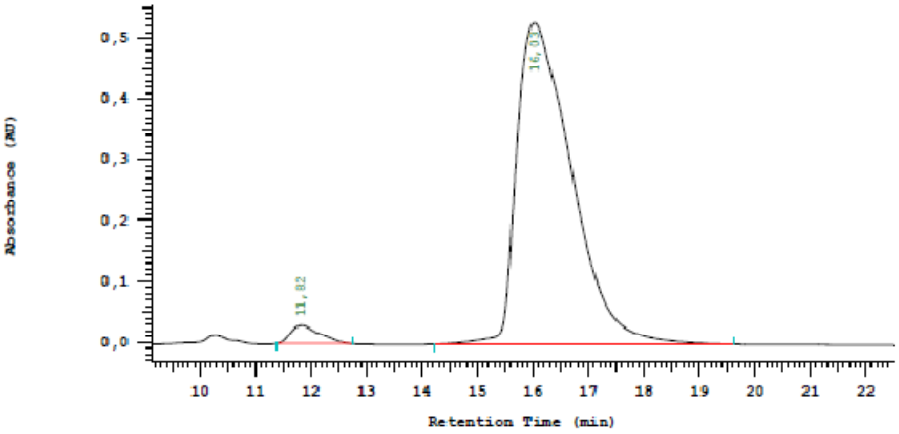
2	4,96	6815740	96,366	
		7072760	100,000	



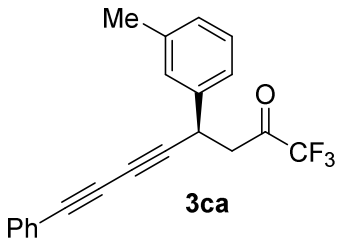
3ba



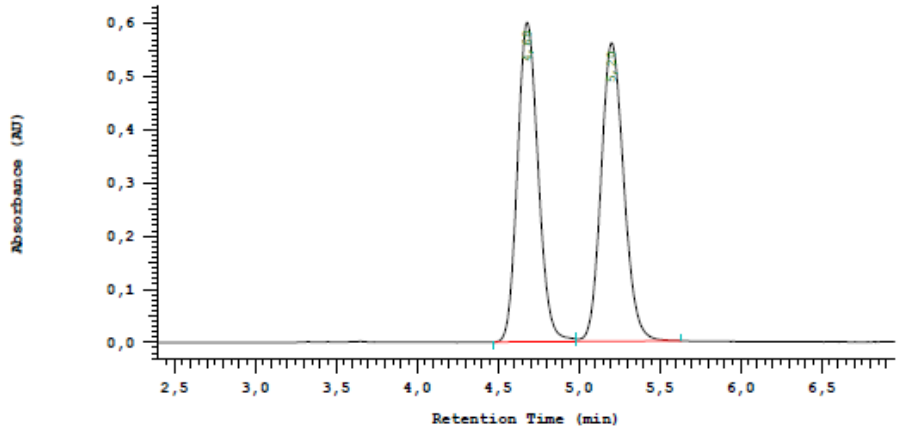
No.	RT	Area	Area %	Name
1	10,53	8678849	46,540	
2	14,45	9969369	53,460	
		18648218	100,000	



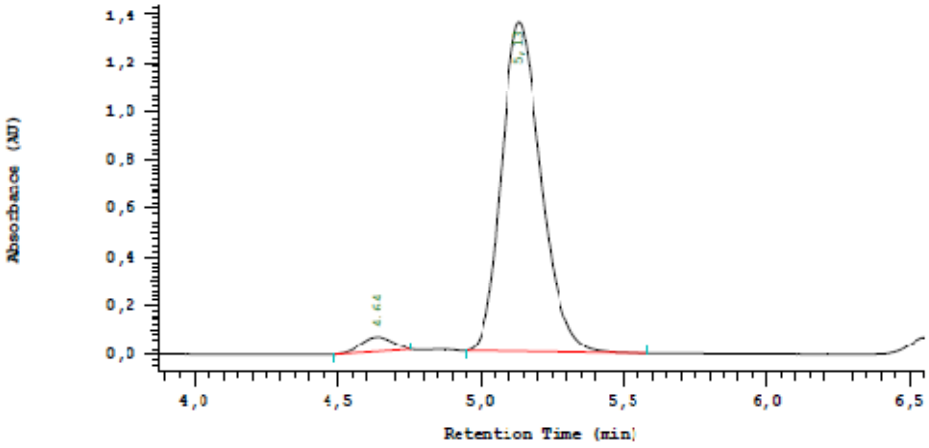
No.	RT	Area	Area %	Name
1	11,82	571890	3,041	
2	16,03	18232734	96,959	
		18804624	100,000	



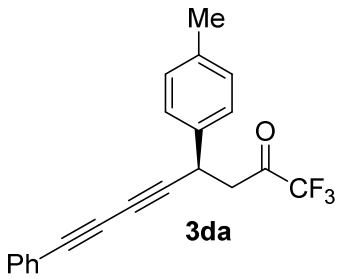
3ca



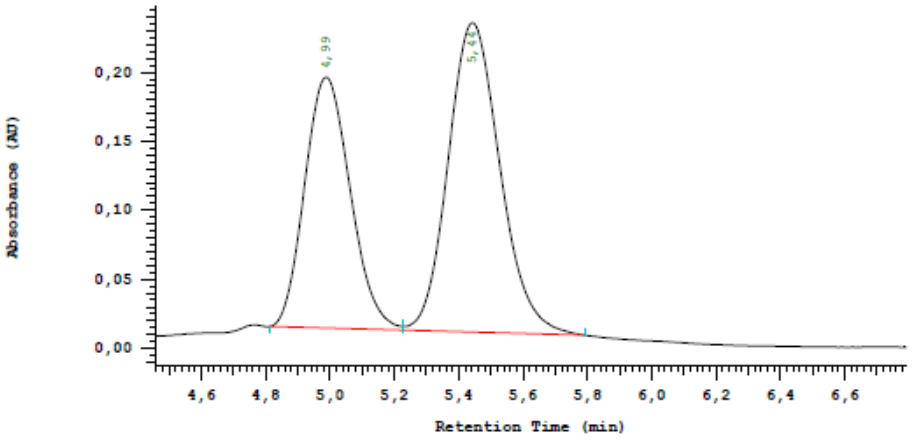
No.	RT	Area	Area %	Name
1	4,68	2681421	49,375	
2	5,20	2749298	50,625	
		5430719	100,000	



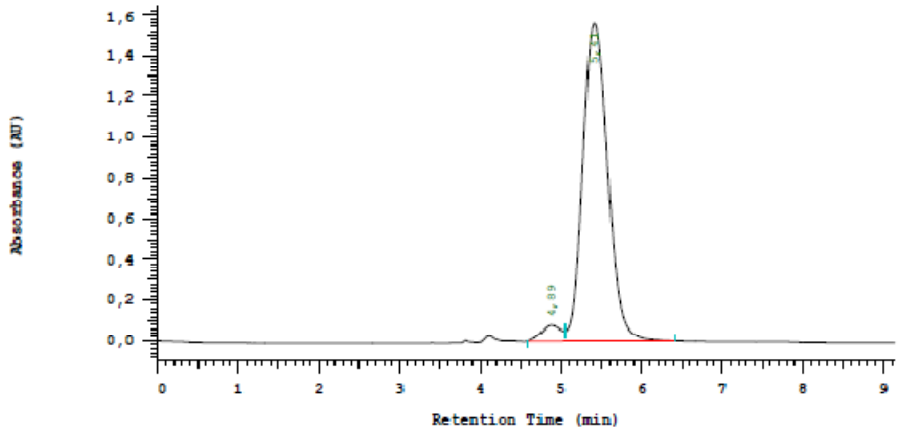
No.	RT	Area	Area %	Name
1	4,64	224090	3,346	
2	5,13	6473650	96,654	
		6697740	100,000	



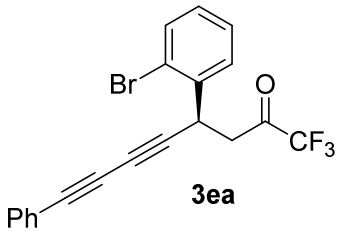
3da



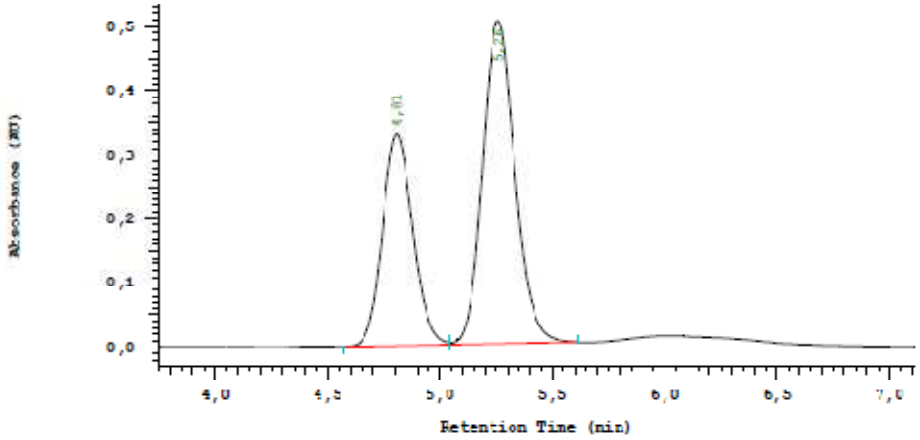
No.	RT	Area	Area %	Name
1	4,99	892965	41,562	
2	5,44	1255550	58,438	
		2148515	100,000	



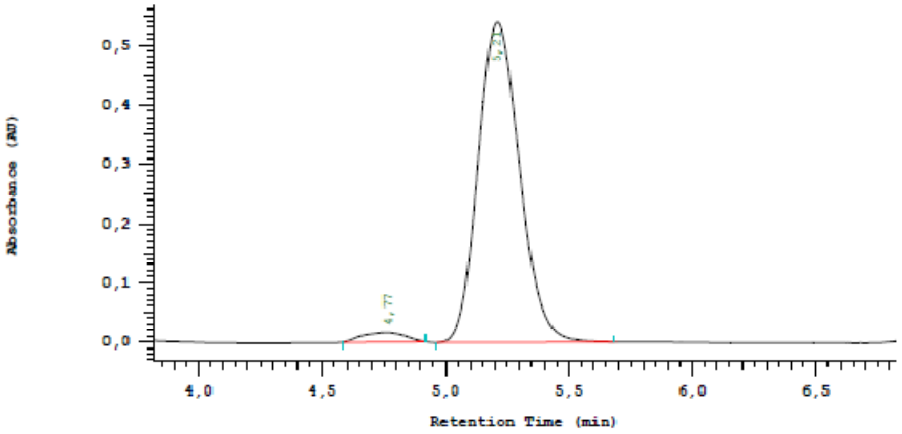
No.	RT	Area	Area %	Name
1	4,89	684287	3,904	
2	5,41	16843182	96,096	
		17527469	100,000	



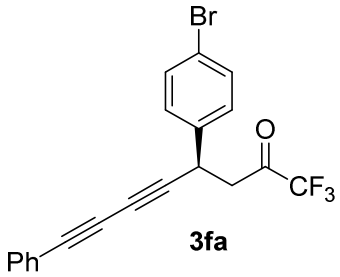
3ea



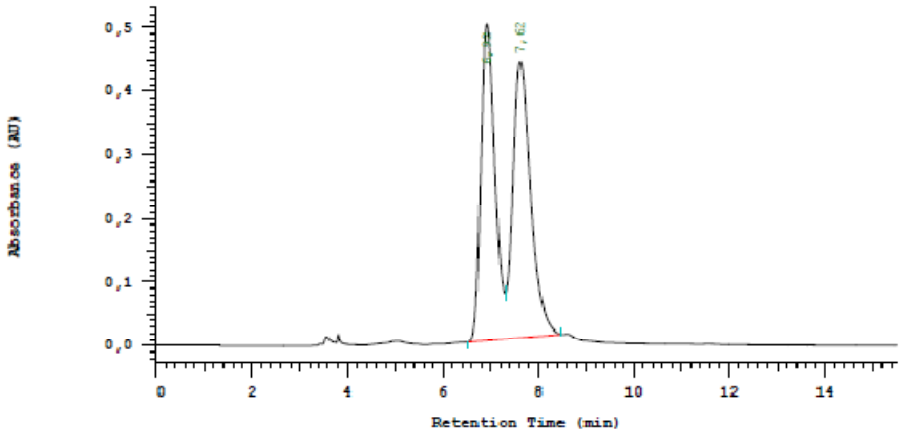
No.	RT	Area	Area %	Name
1	4,81	1555938	38,221	
2	5,26	2514991	61,779	
		4070929	100,000	



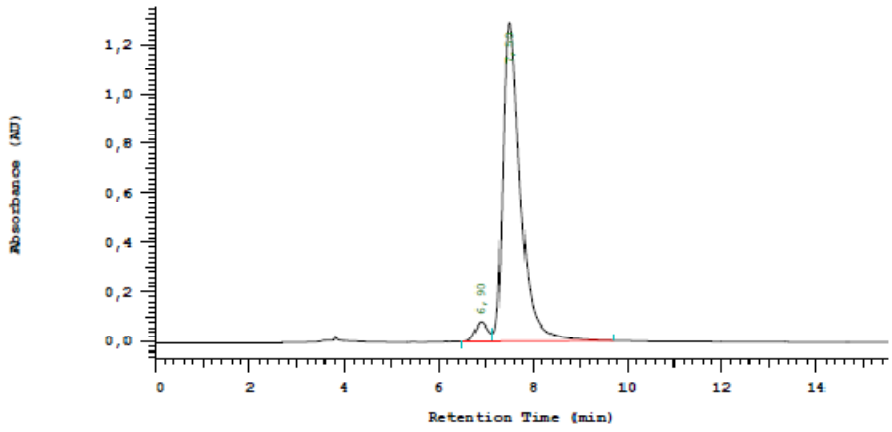
No.	RT	Area	Area %	Name
1	4,77	95880	2,942	
2	5,21	3162605	97,058	
		3258485	100,000	



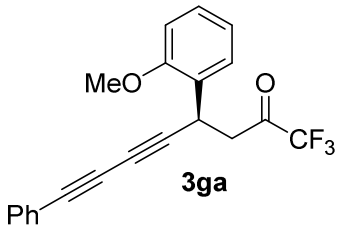
3fa



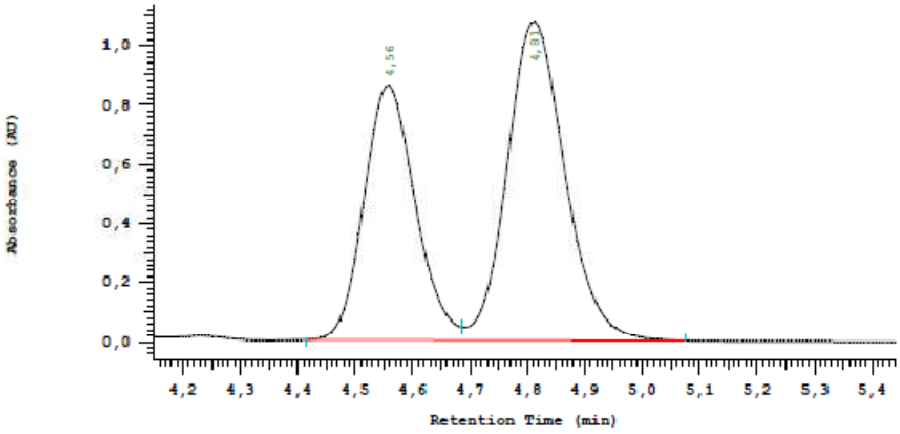
No.	RT	Area	Area %	Name
1	6,92	5136516	47,433	
2	7,62	5692533	52,567	
		10829049	100,000	



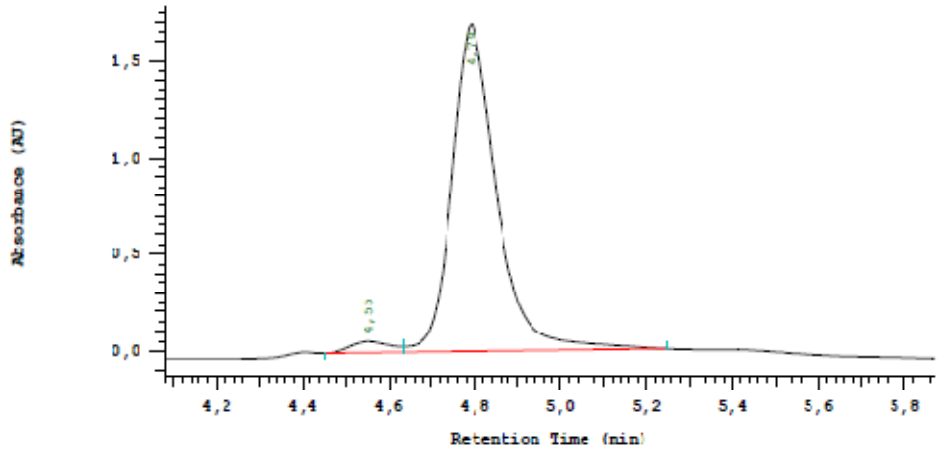
No.	RT	Area	Area %	Name
1	6,90	723662	4,134	
2	7,50	16780606	95,866	
		17504268	100,000	



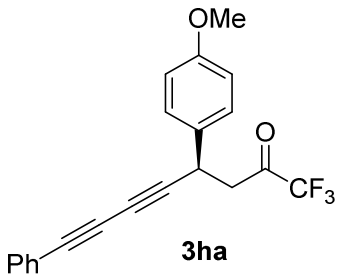
3ga



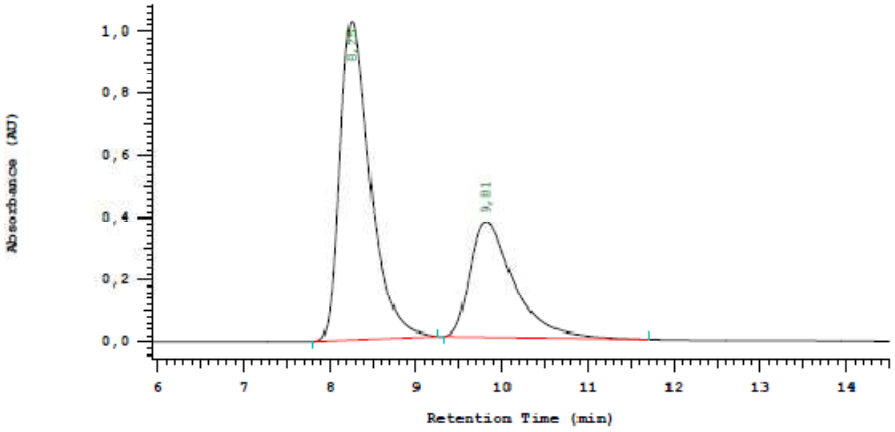
No.	RT	Area	Area %	Name
1	4,56	2669087	41,420	
2	4,81	3774937	58,580	
		6444024	100,000	



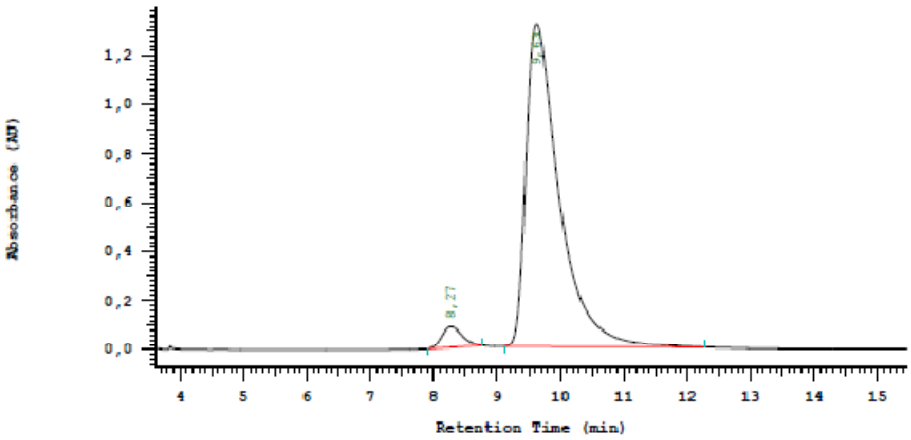
No.	RT	Area	Area %	Name
1	4,55	173215	2,769	
2	4,79	6082759	97,231	
		6255974	100,000	



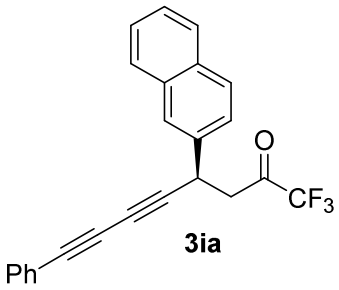
3ha



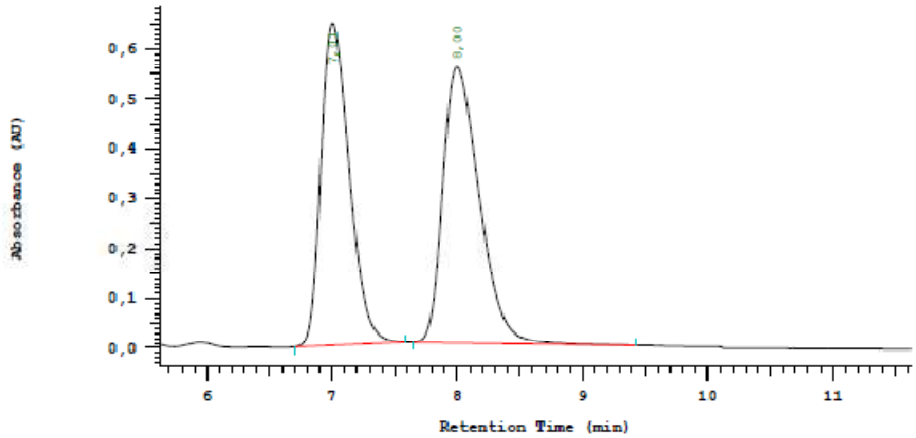
No.	RT	Area	Area %	Name
1	8,25	12612009	65,706	
2	9,81	6582744	34,294	
		19194753	100,000	



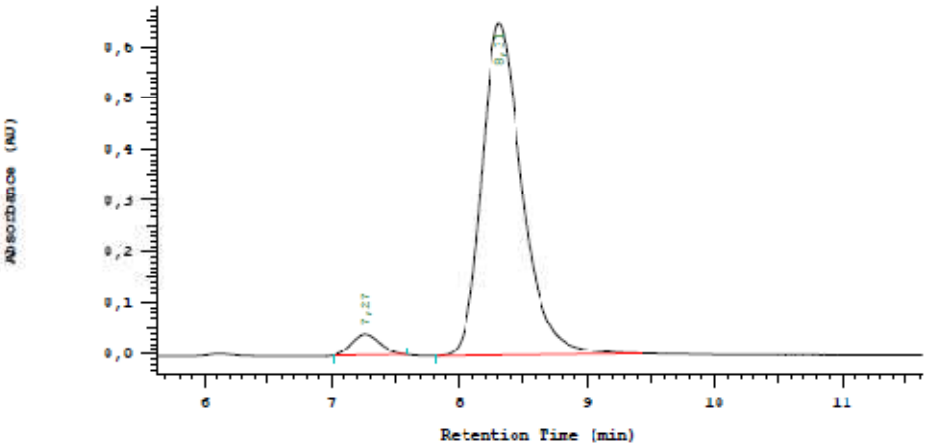
No.	RT	Area	Area %	Name
1	8,27	959560	3,830	
2	9,63	24093489	96,170	
		25053049	100,000	



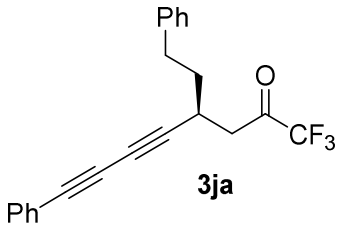
3ia



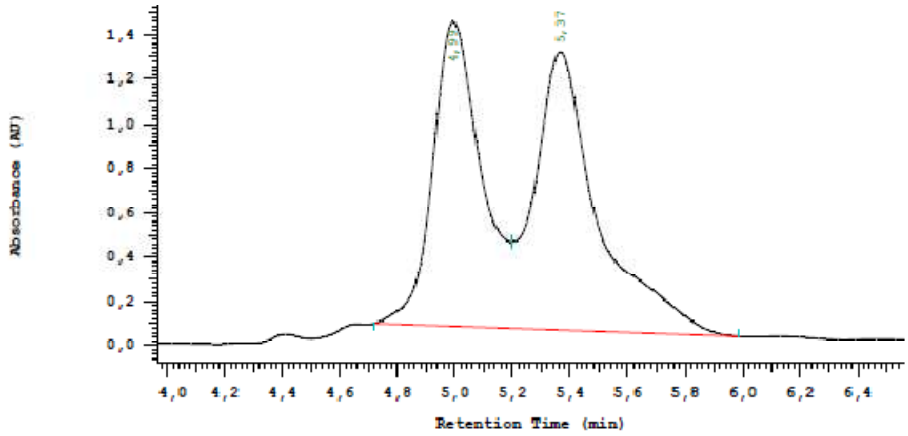
No.	RT	Area	Area %	Name
1	7,01	5097430	47,640	
2	8,00	5602400	52,360	
		10699830	100,000	



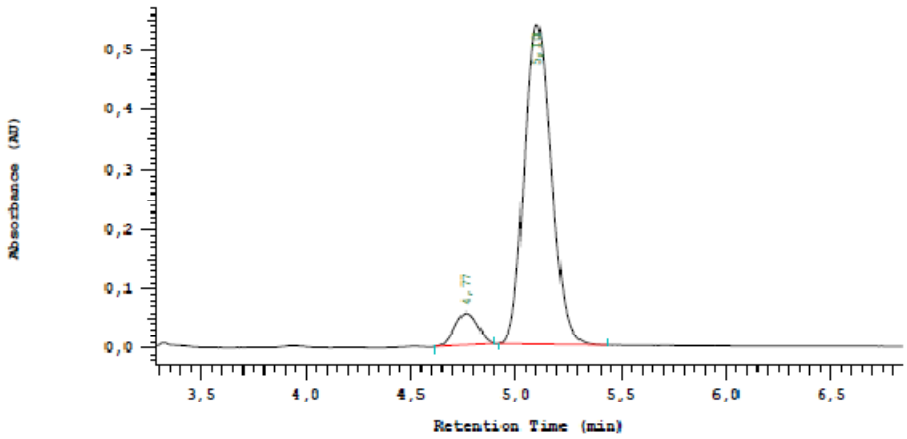
No.	RT	Area	Area %	Name
1	7,27	313310	4,220	
2	8,31	7111649	95,780	
		7424959	100,000	



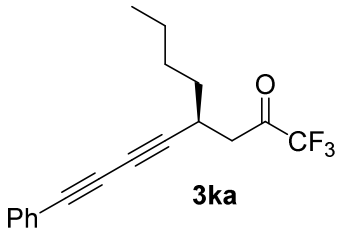
3ja



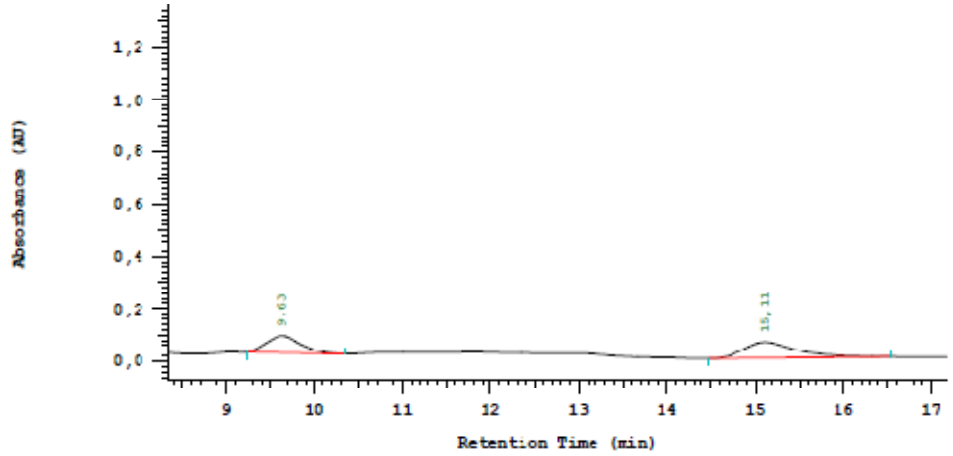
No.	RT	Area	Area %	Name
1	4,99	8081701	45,712	
2	5,37	9597828	54,288	
		17679529	100,000	



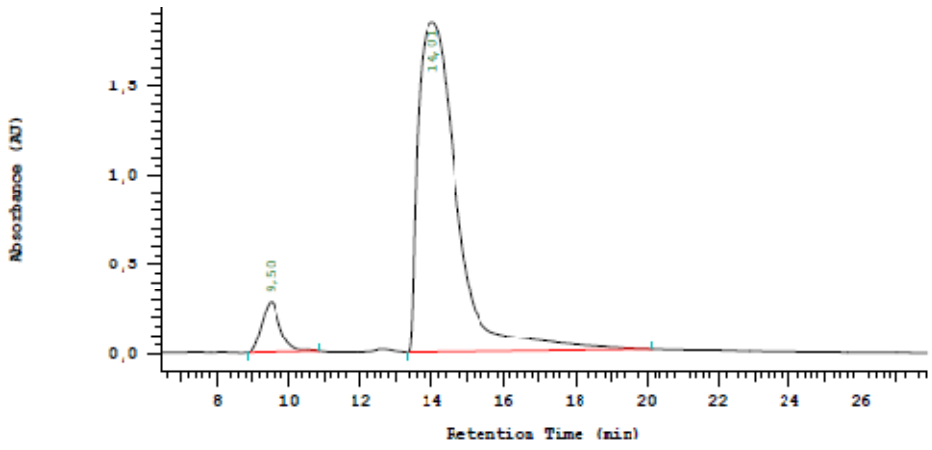
No.	RT	Area	Area %	Name
1	4,77	209190	7,909	
2	5,10	2435920	92,091	
		2645110	100,000	



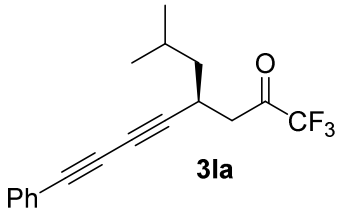
3ka



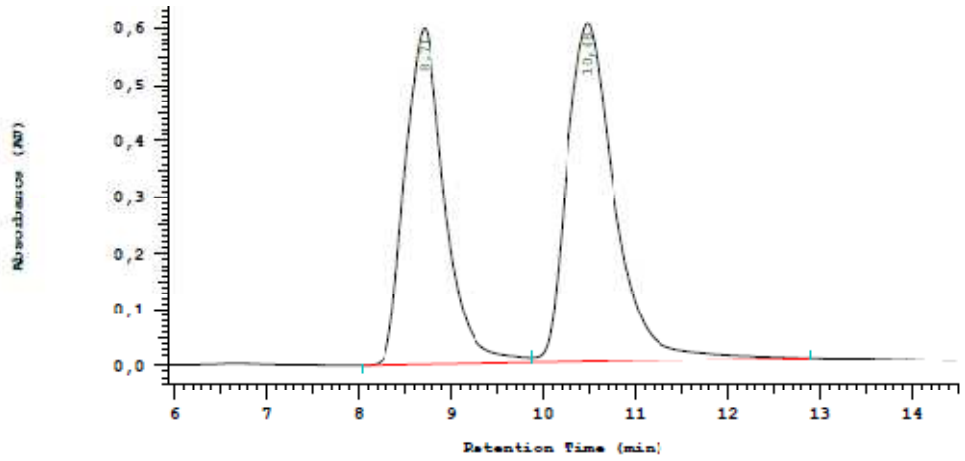
No.	RT	Area	Area %	Name
1	9,63	871793	40,807	
2	15,11	1264565	59,193	
		2136358	100,000	



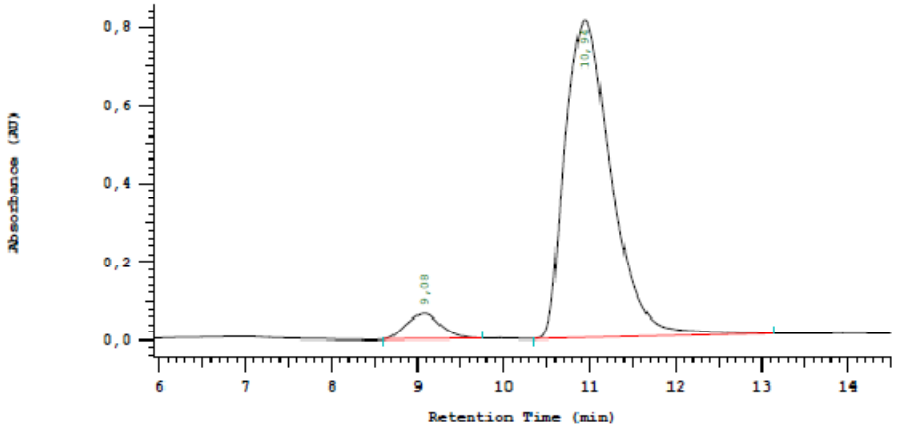
No.	RT	Area	Area %	Name
1	9,50	4845669	6,584	
2	14,01	68755020	93,416	
		73600689	100,000	



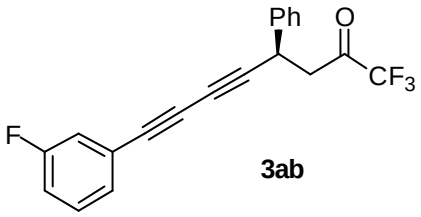
3la



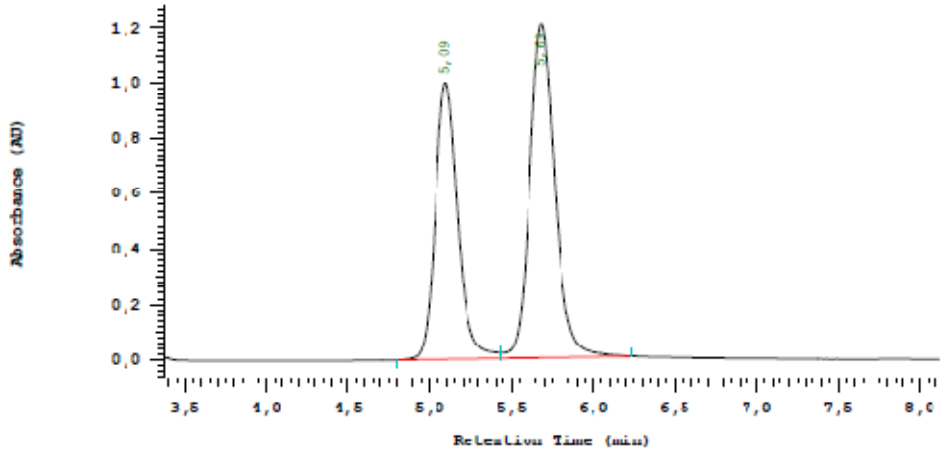
No.	RT	Area	Area %	Name
1	8,71	8989552	45,278	
2	10,48	10864597	54,722	
		19854149	100,000	



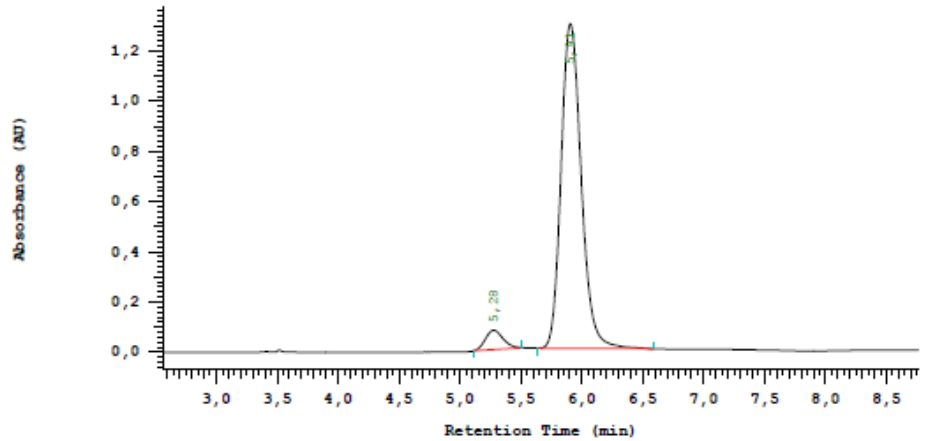
No.	RT	Area	Area %	Name
1	9,08	933955	5,787	
2	10,94	15204374	94,213	
		16138329	100,000	



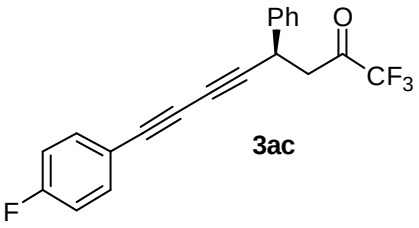
3ab



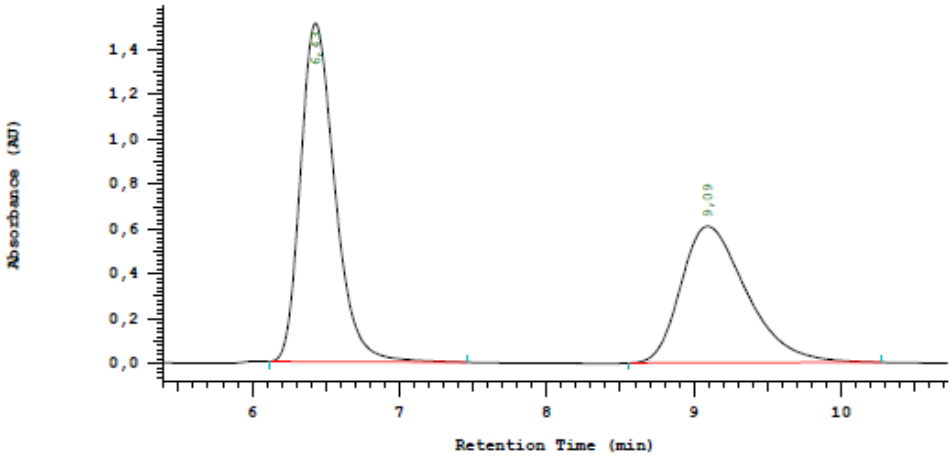
No.	RT	Area	Area %	Name
1	5,09	4728612	42,648	
2	5,68	6358912	57,352	
		11087524	100,000	



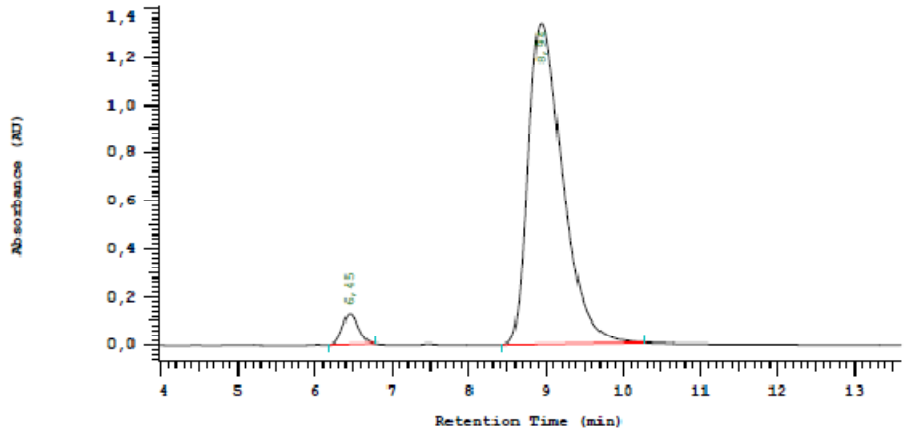
No.	RT	Area	Area %	Name
1	5,28	382970	4,891	
2	5,91	7447430	95,109	
		7830400	100,000	



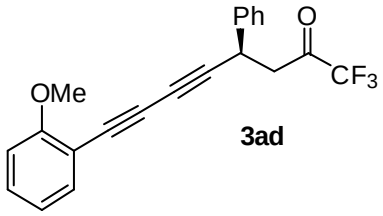
3ac



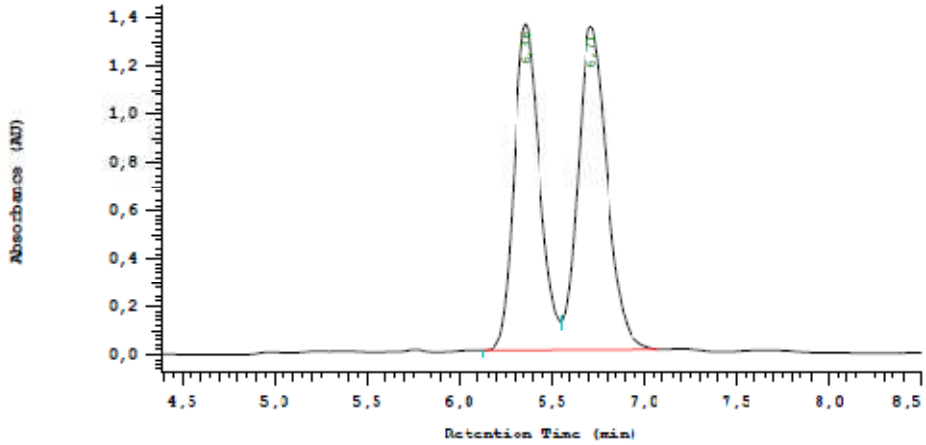
No.	RT	Area	Area %	Name
1	6,43	12217009	56,425	
2	9,09	9434744	43,575	
		21651753	100,000	



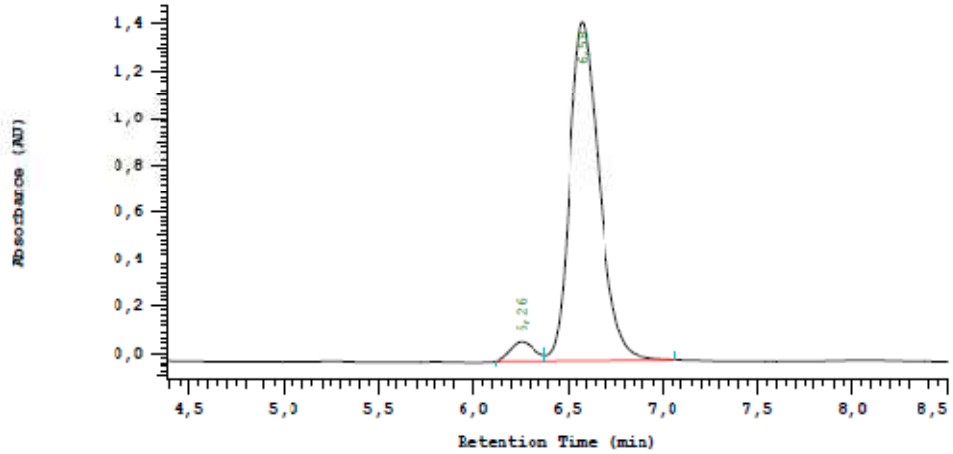
No.	RT	Area	Area %	Name
1	6,45	914700	4,241	
2	8,94	20654849	95,759	
		21569549	100,000	



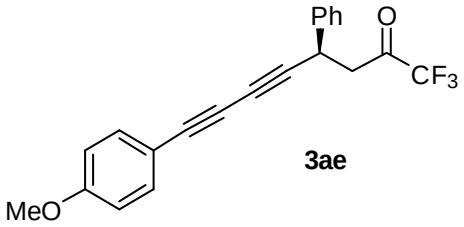
3ad



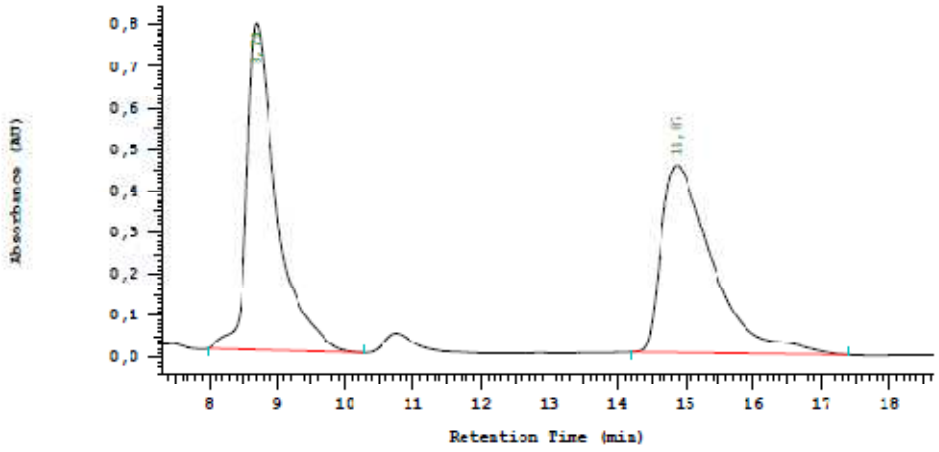
No.	RT	Area	Area %	Name
1	6,36	6495509	46,866	
2	6,71	7364260	53,134	
		13859769	100,000	



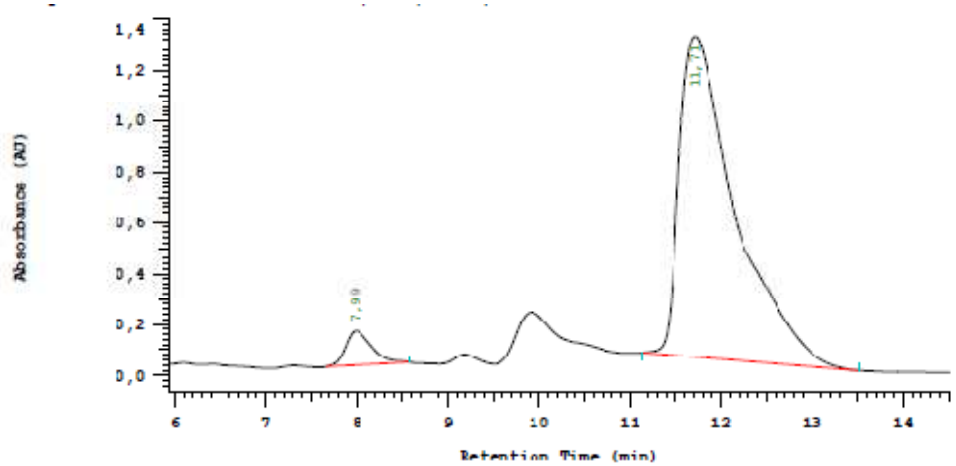
No.	RT	Area	Area %	Name
1	6,26	342438	4,235	
2	6,58	7743531	95,765	
		8085969	100,000	



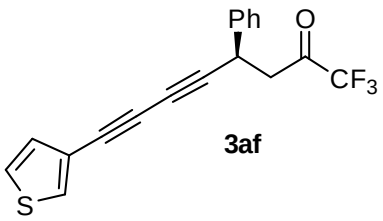
3ae



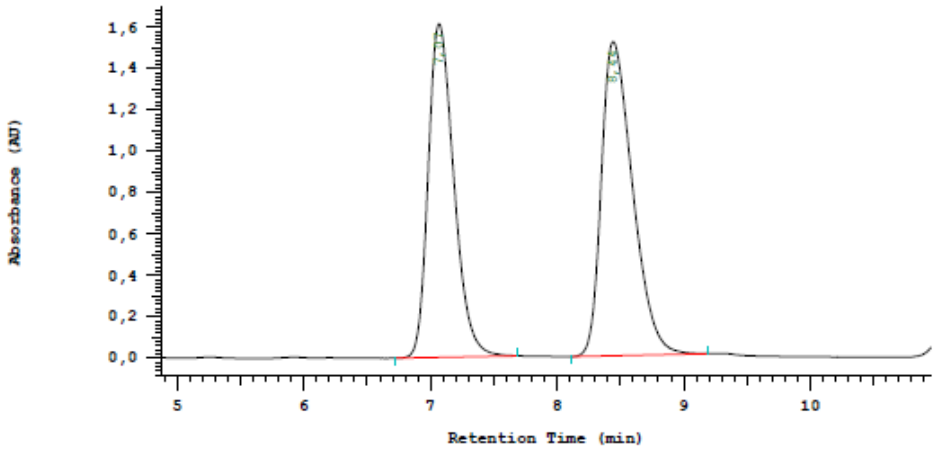
No.	RT	Area	Area %	Name
1	8,70	11899390	50,292	
2	14,87	11761444	49,708	
		23660834	100,000	



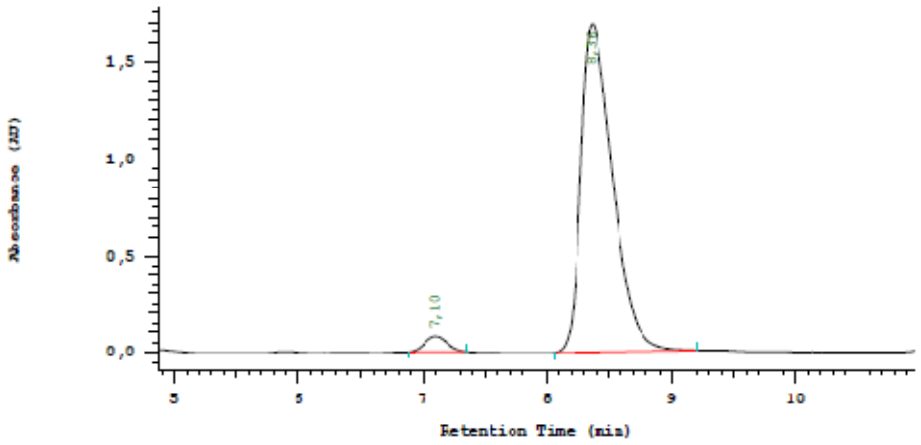
No.	RT	Area	Area %	Name
1	7,99	1317470	4,692	
2	11,71	26760145	95,308	
		28077615	100,000	



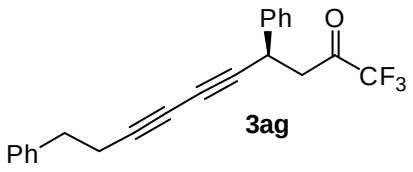
3af



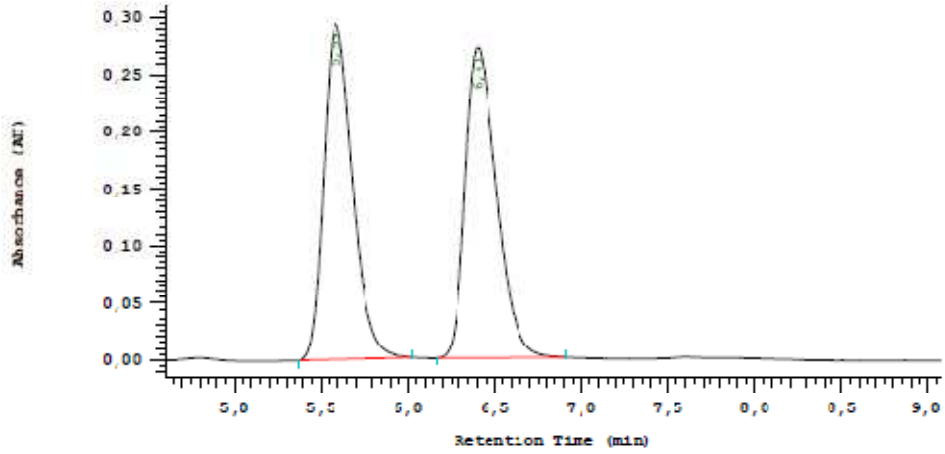
No.	RT	Area	Area %	Name
1	7,07	11345104	46,558	
2	8,44	13022510	53,442	
		24367614	100,000	



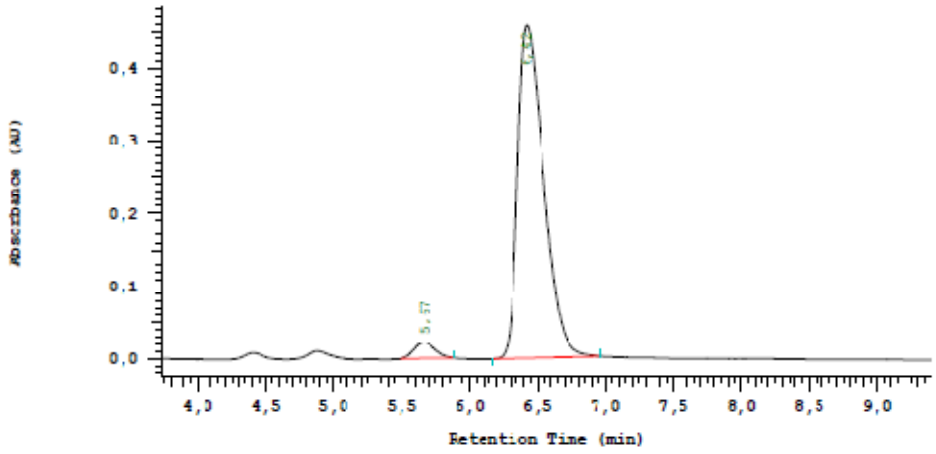
No.	RT	Area	Area %	Name
1	7,10	453060	2,958	
2	8,36	14863920	97,042	
		15317000	100,000	



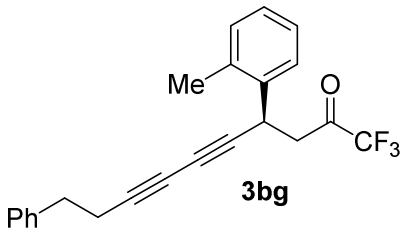
3ag



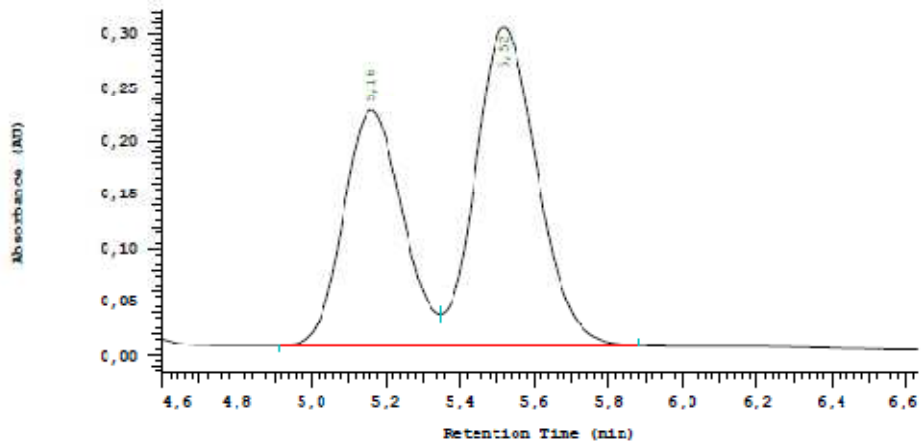
No.	RT	Area	Area %	Name
1	5,59	1666740	49,487	
2	6,41	1701300	50,513	
		3368040	100,000	



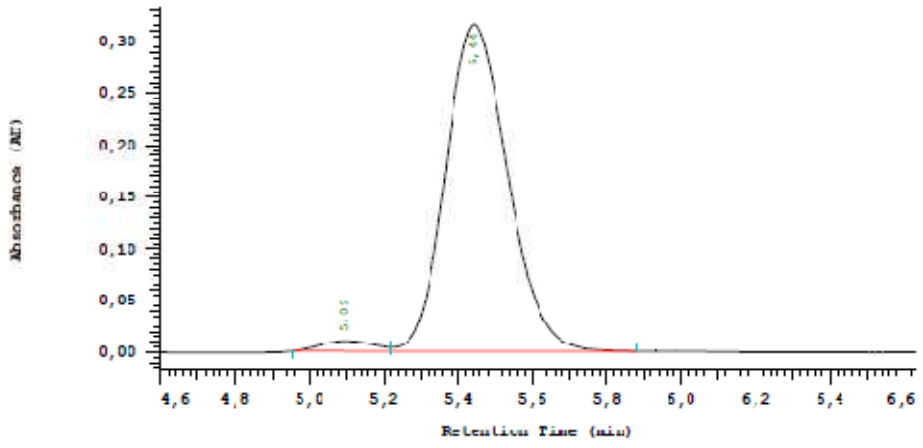
No.	RT	Area	Area %	Name
1	5,67	111960	3,582	
2	6,42	3013840	96,418	
		3125800	100,000	



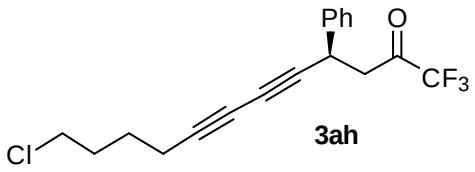
3bg



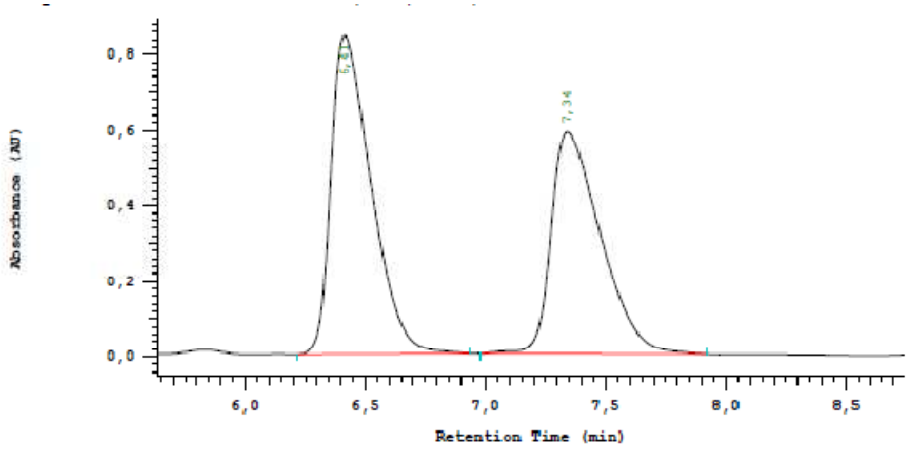
No.	RT	Area	Area %	Name
1	5,16	1203620	41,271	
2	5,52	1712730	58,729	
		2916350	100,000	



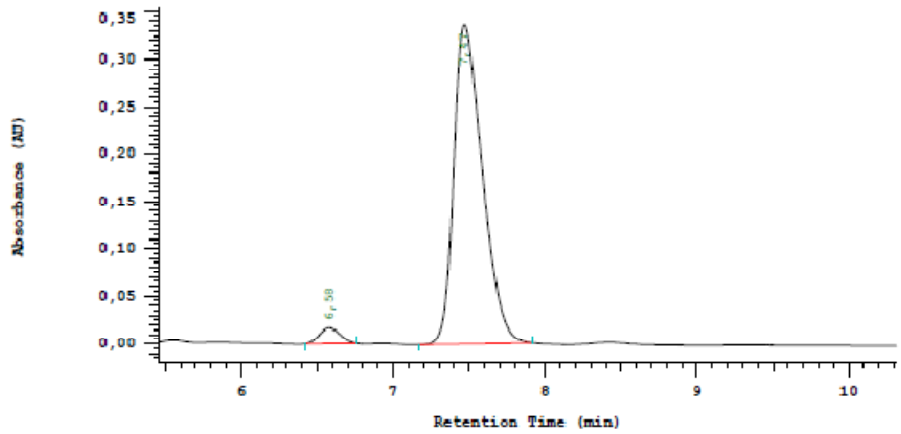
No.	RT	Area	Area %	Name
1	5,09	46615	2,495	
2	5,44	1821564	97,505	
		1868179	100,000	



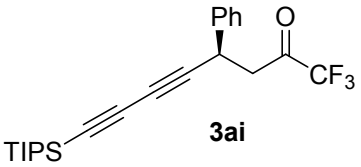
3ah



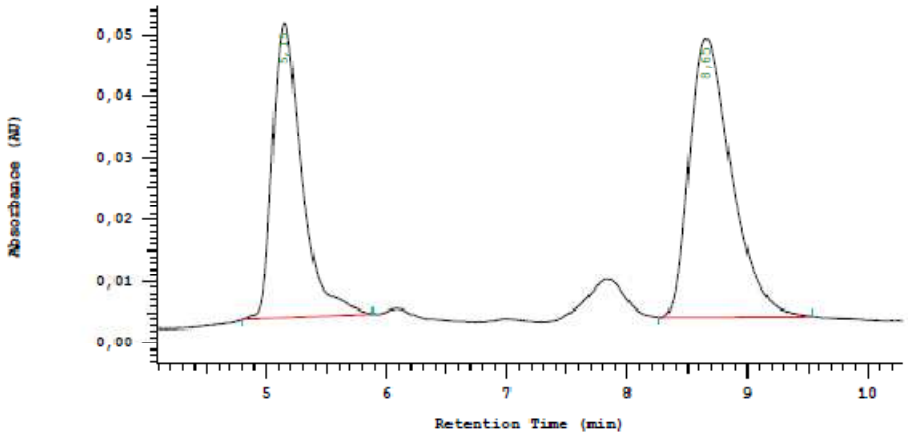
No.	RT	Area	Area %	Name
1	6,41	4885935	53,752	
2	7,34	4203895	46,248	
		9089830	100,000	



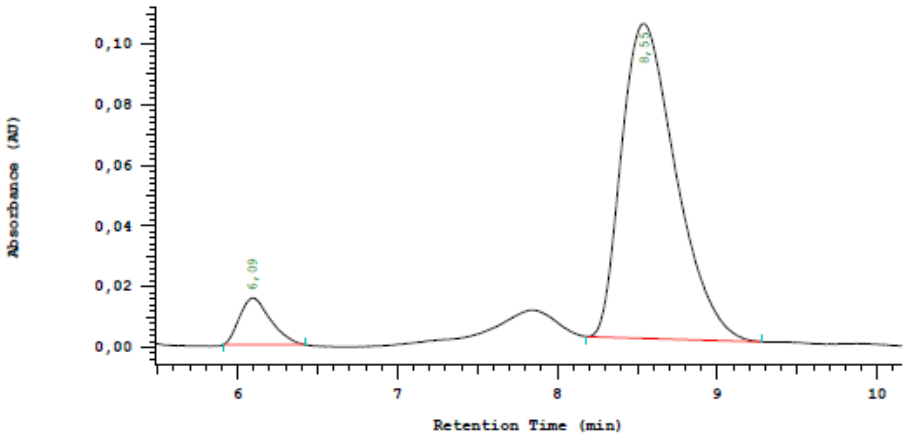
No.	RT	Area	Area %	Name
1	6,58	79900	3,499	
2	7,47	2203660	96,501	
		2283560	100,000	



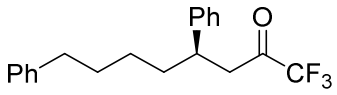
3ai



No.	RT	Area	Area %	Name
1	5,15	402000	42,335	
2	8,65	547580	57,665	
		949580	100,000	



No.	RT	Area	Area %	Name
1	6,09	103290	7,765	
2	8,55	1226890	92,235	
		1330180	100,000	



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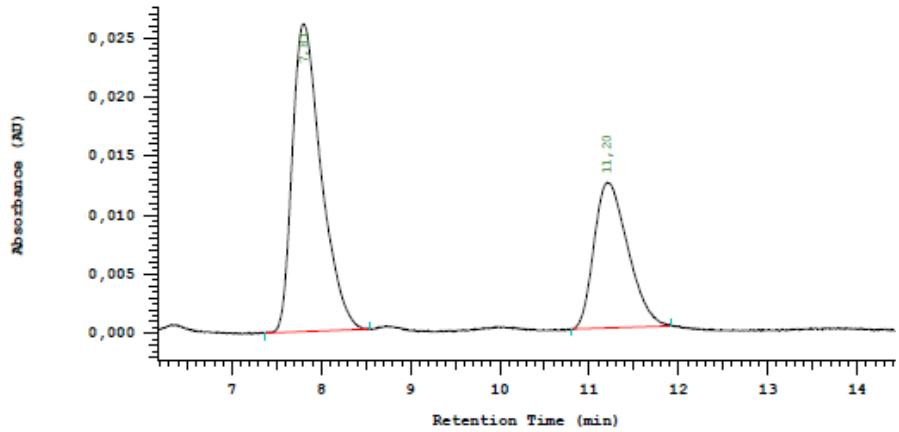
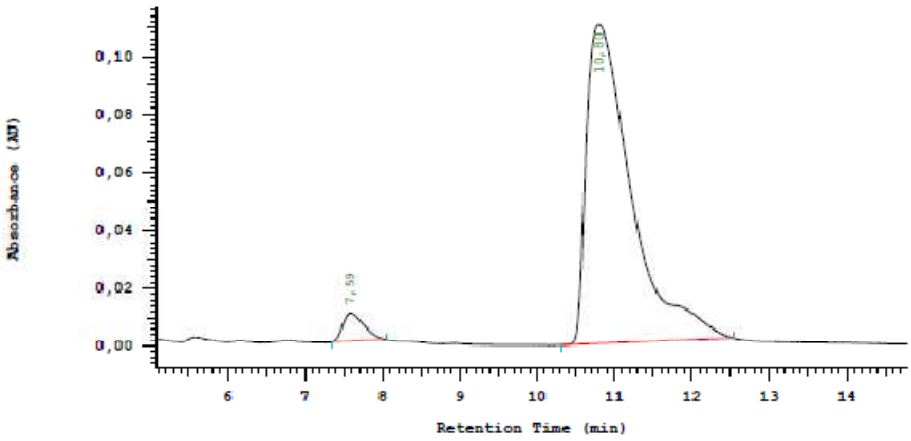
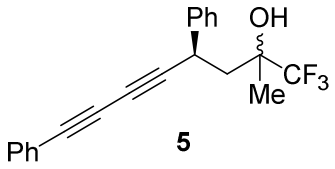


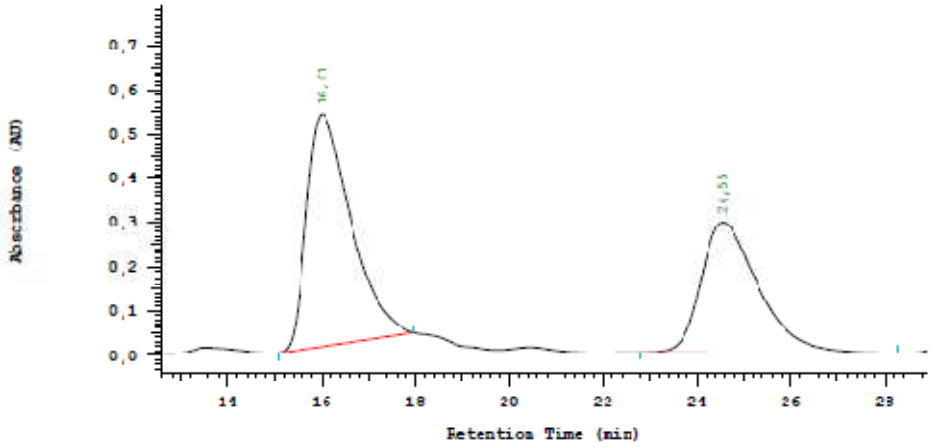
No.	RT	Area	Area %	Name
1	7,81	292440	64,377	
2	11,20	161825	35,623	
		454265	100,000	



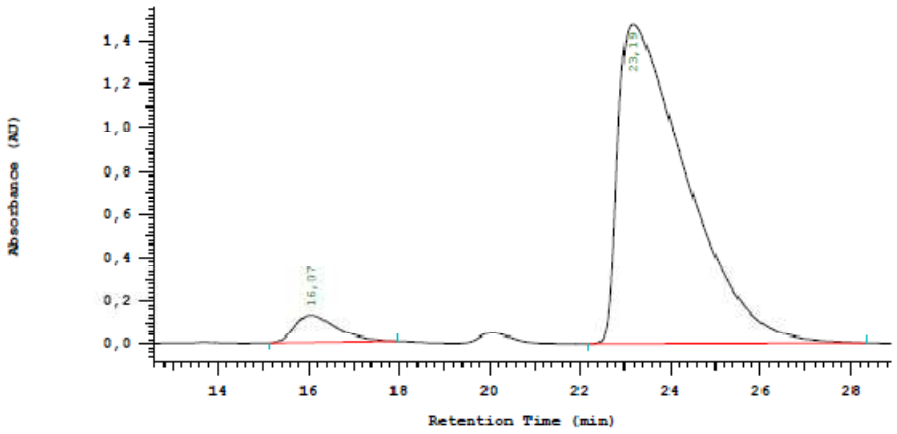
No.	RT	Area	Area %	Name
1	7,59	92900	4,029	
2	10,80	2212770	95,971	
		2305670	100,000	



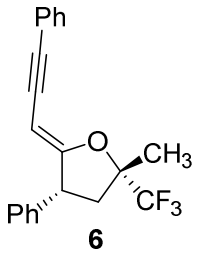
5



No.	RT	Area	Area %	Name
1	16,01	17112915	57,875	
2	24,55	12455609	42,125	
		29568524	100,000	



No.	RT	Area	Area %	Name
1	16,07	4191960	5,111	
2	23,19	77826252	94,889	
		82018212	100,000	



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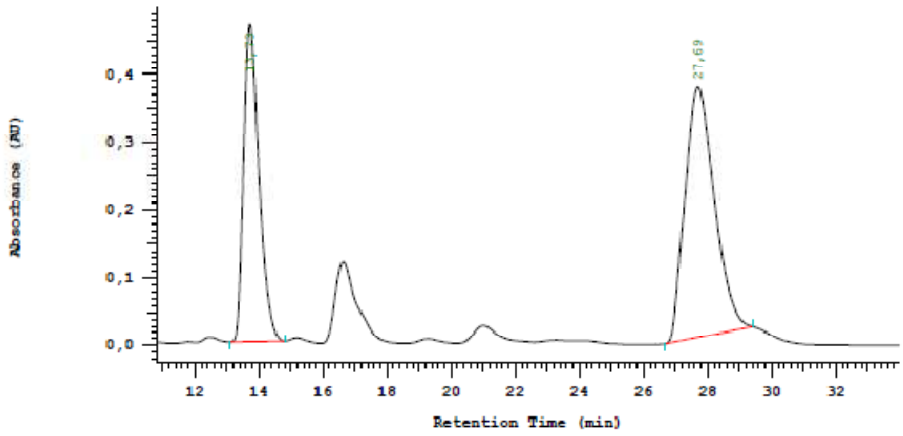
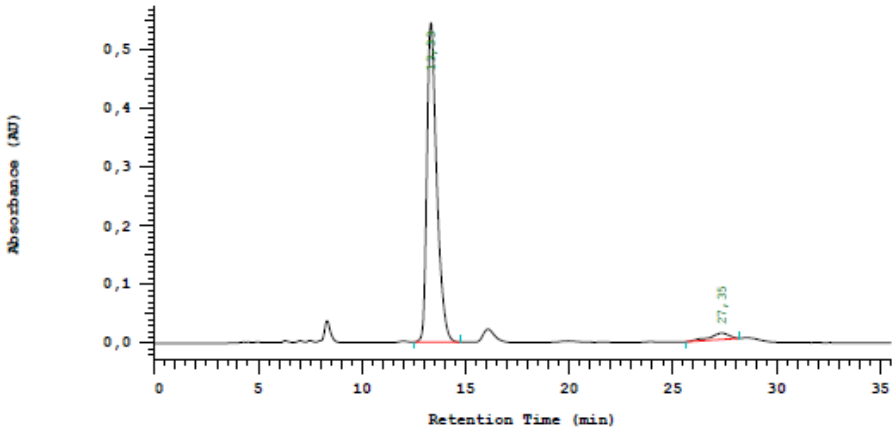
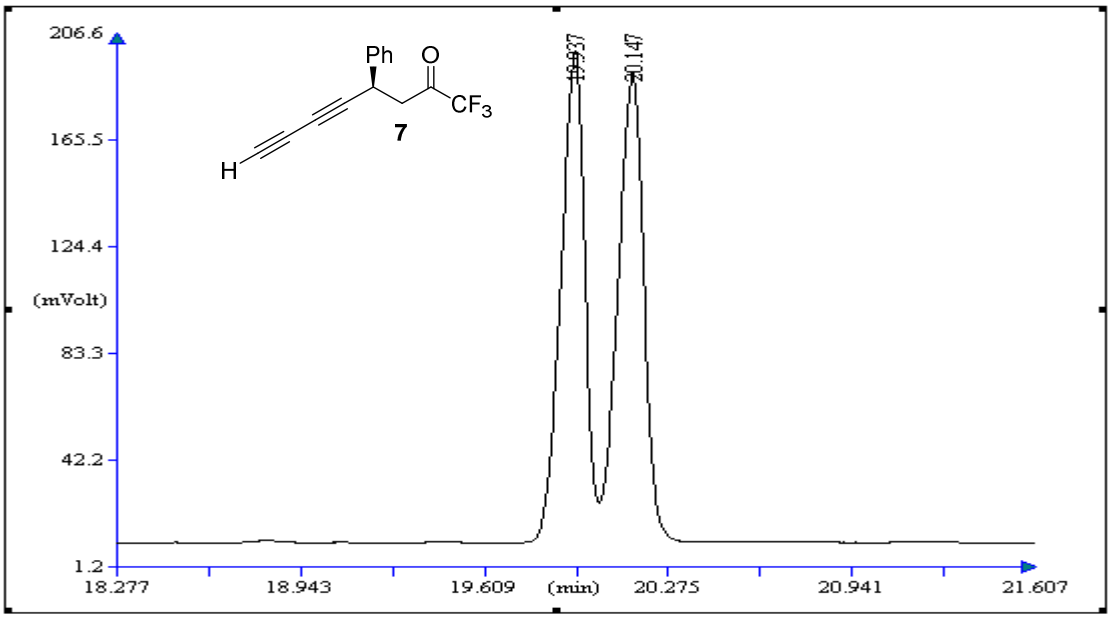


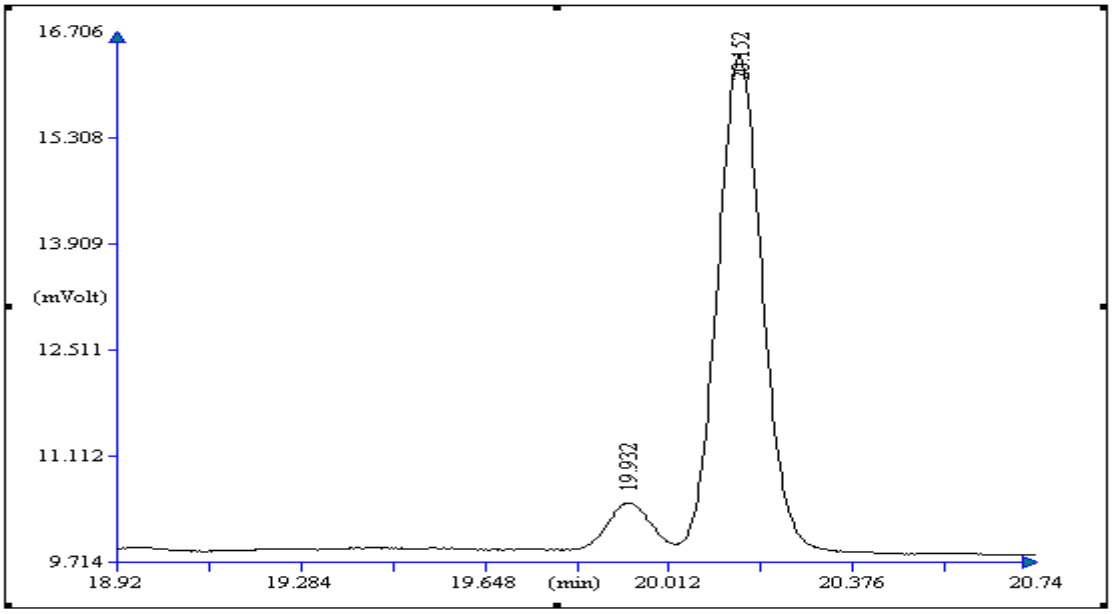
No.	RT	Area	Area %	Name
1	13,73	7843499	39,970	
2	27,69	11780098	60,030	
		19623597	100,000	



No.	RT	Area	Area %	Name
1	13,33	8947060	96,240	
2	27,35	349510	3,760	
		9296570	100,000	



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)
1	19.937	11373440	49.242
2	20.147	11723590	50.758
		23097020	



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)
1	19.932	29844	7.160
2	20.152	386946	92.840
		416790	

X-ray data for compound **3af**: crystallized from dichloromethane/*n*-hexane at -20 °C; $C_{18}H_{11}F_3O_1S_1$; M_r=332.33; monoclinic; space group = $P2_1$; a = 5.5930(1), b = 8.1070(3); c = 17.5700(5) Å; α = 90.00, β = 95.029(2), γ= 90.00°; V = 793.60(4) Å^3; Z = 2; ρ_{calcd} = 1.391 Mg m^{-3} ; μ= 0.235 mm^{-1}; F(000) = 240. A colourless crystal of 0.04x0.08x0.10 mm^3 was used; 2709 [R(int) = 0.0399] independent reflections were collected on a Enraf Nonius CCD diffractomer by using graphite-monochromated MoKα radiation (λ = 0.71073 Å) operating at 50 kV and 30 mA. The cell parameters were determined and refined by a least-squares fit of all reflections. The structure was solved by direct methods and Fourier synthesis. It was refined by full-matrix least-squares procedures on F^2 (SHELXL-97). All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included in calculated positions and refined riding on the respective carbon atoms. Final R(ωR) values were R = 0.0689 and ωR = 0.1968. CCDC-1046444 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

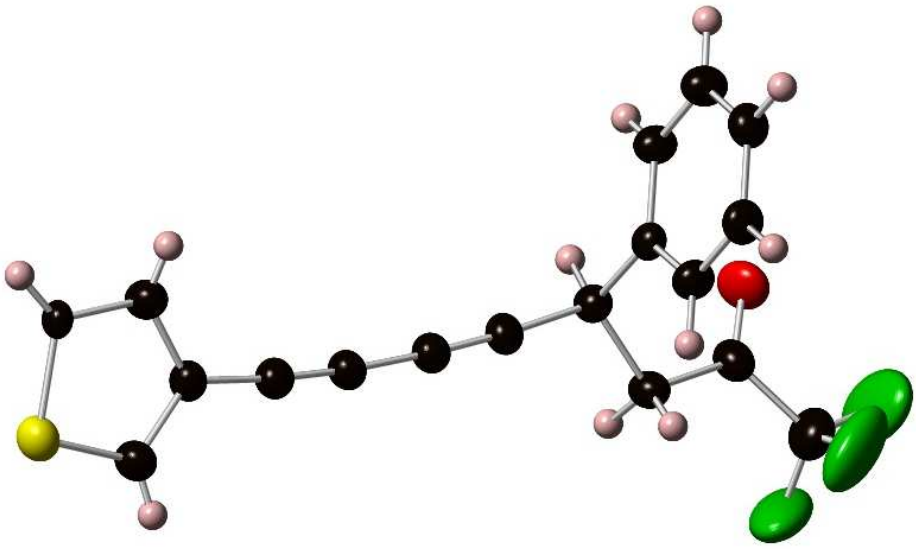


Figure S2. ORTEP plot for the X-ray structure of compound **3af**. The thermal ellipsoids are drawn at the 50% probability level.